The *S*-Alkylation of Sulphides by an Activated Carbohydrate Epimine under Acidic Catalysis: The Formation of α-Acetamido-sulphides. Part 2.[1] Reactions with Cyclic Sulphides and with Sulphides bearing an Additional Nucleophilic Sulphur Substituent

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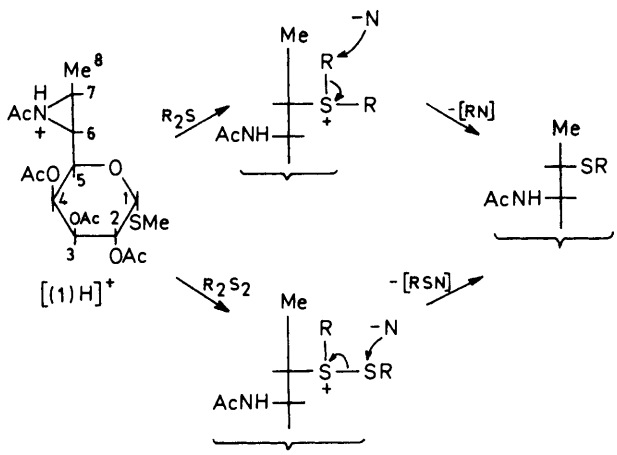
Methyl 2,3,4-tri-*O*-acetyl-6,7-acetylepimino-6,7,8-trideoxy-1-thio-D-*erythro*-α-D-*galacto*-octopyranoside (1) reacts with cyclic sulphides in the presence of acetic acid to give 7(*S*)-(ω-acetoxyalkyl)thioamides *via* attack by acetate ion on the intermediate cyclic sulphonium salts. The co-formation of the 7(*S*)-{[3-(3-acetoxypropyl)-thio]propyl}thio-derivative (8) from the reaction with thietan demonstrated that collapse of the cyclic sulphonium salt could be occasioned by nucleophilic attack by a sulphide sulphur atom also.

αω-Bis(methylthio)alkanes yield monosulphonium salts which collapse to the 7(*S*)-methylthio-derivative (11) by neighbouring group participation of the sulphide sulphur atom; this participation is inefficient with a 1,3-di-substituted alkane. With ω-(alkylthio)alkanethiols, the efficiency of participation of the thiol sulphur atom again controls the manner of collapse of the intermediate sulphonium salt. With these sulphide–thiol reagents, the co-formation of [(ω-alkylthio)alkyl]thio-derivatives is unexpected.

METHYL 2,3,4-TRI-*O*-ACETYL-6,7-ACETYLEPIMINO-6,7,8-TRIDEOXY-1-THIO-D-*erythro*-α-D-*galacto*-OCTOPYRANOSIDE (1) derived from the carbohydrate portion of the antibiotic lincomycin,† reacts readily with alcohols in the presence of acetic acid to give α-alkoxy-amides,[2] but thiols do not participate in this ring-opening of the epimine.[1] Dialkyl sulphides are alkylated under these conditions, however, giving α-acetamido-sulphonium salts, which collapse by nucleophilic attack on carbon to give α-acetamidosulphides.[1] The usefulness of the method is limited to sulphides of high nucleophilic reactivity, the formation of the α-acetoxy-amide by competitive ring-opening by acetate ion predominating with sulphides containing bulky alkyl groups. The method can be extended to the introduction of higher alkylthio-substituents by using dialkyl disulphides: the initially formed dialkyl(alkylthio)sulphonium salts collapse by nucleophilic attack on the sulphenyl sulphur atom to give the α-acetamidosulphides (Scheme 1), although limitations to this approach, too, were discussed.[1]

Neither of these approaches afforded a good route for the introduction of a (substituted alkyl)thio-substituent. For example, 2-hydroxyethyl methyl sulphide gave the 7-(2-hydroxyethyl)thio-derivative (2) in 51% yield, but it was accompanied by the 7-acetate (15%) and the 7-methylthio-derivative (11) (26%), formed by nucleophilic attack at the α-methylene carbon atom of the unsymmetrical trialkylsulphonium salt.[1] Only the 7-acetate could be isolated from the attempted reaction with the symmetrical reagent thiodiglycol [bis-(2-hydroxyethyl)-sulphide].



SCHEME 1

The collapse of these intermediate sulphonium salts to sulphides was assumed to be occasioned by the nucleophilic attack of acetate ion on a carbon atom adjacent to the sulphonium sulphur atom; the presence of ethyl acetate in the crude reaction mixture from the reagent diethyl sulphide had been demonstrated.[1] On this assumption, ω-acetoxyalkylthio-derivatives should be available by the use of symmetrical cyclic sulphides, in which greater nucleophilic reactivity of the sulphide

† Lincocin is the trademark of The Upjohn Company for lincomycin hydrochloride.

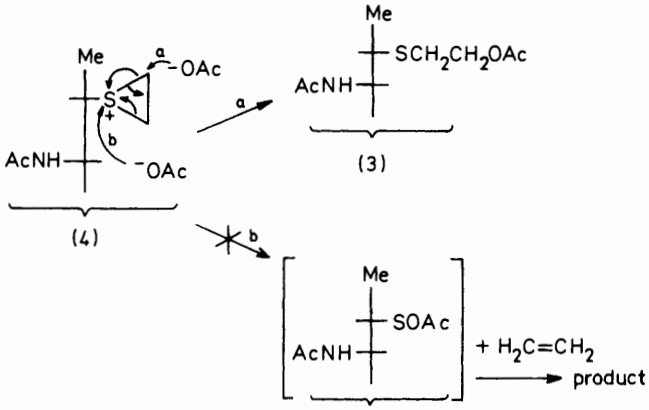
[1] Part 1, B. Bannister, *J.C.S. Perkin I*, 1977, 1057.
[2] B. Bannister, *J.C.S. Perkin I*, 1974, 360.

sulphur atom might be expected than in the acyclic analogues, and from which the intermediate sulphonium salt can give rise to only one sulphide product.

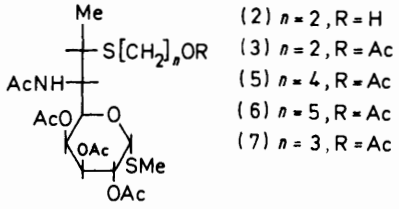
However, in the case of thiiranium salts, there are conflicting reports concerning the extent of nucleophilic attack by acetate ion on a carbon atom adjacent to the sulphonium sulphur atom *versus* attack on the sulphonium sulphur atom itself. Thus, Helmkamp and his co-workers [3] have reported that reaction between *S*-methyl-8-thiabicyclo[6.1.0]nonanium 2,4,6-trinitrobenzenesulphonate and sodium acetate yields little of the 2-acetoxycyclo-octyl methyl sulphide, the main product being cyclo-octene resulting from attack on the sulphonium sulphur atom. Jones and his co-workers [4] similarly have explained the formation of cholest-4-ene as major product from both *trans*-4-methylthiocholestan-5-ols, on attempted dehydration with thionyl chloride, as involving methylthiiranium salt formation followed by nucleophilic attack of chloride ion on the sulphur atom. Further evidence in support of nucleophilic attack on the sulphur atom in thiiranium salts has been adduced from a study of the solvolysis of 2-chlorocyclo-octyl 4-chlorophenyl sulphide by Schmidt and Fitzgerald,[5] but their results do not confirm the generality of preferential nucleophilic attack on the sulphur atom in such systems.

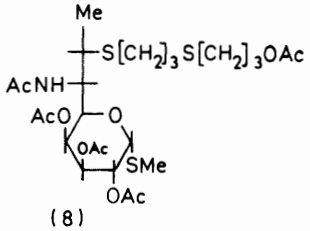
In the event, reaction of (1) with thiiran in the presence of acetic acid gave the 7-(2-acetoxyethyl)thio-derivative (3) in 69% yield, identified by comparison with the product of *O*-acetylation of (2), the only other product being the 7-acetate, thus demonstrating both that nucleophilic attack on the thiiranium ion (4) by acetate ion was indeed responsible for the collapse to sulphide, and that such attack occurred on the carbon atom (Scheme 2, route a), there being no evidence for attack on the sulphur atom (route b). Extensive polymerisation of the reagent made the reaction impratical on anything other than a small scale, however. Schmidt and Fitzgerald [5] found that nucleophilic attack occurred to a greater extent at the sulphonium sulphur atom than at the adjacent carbon atom in fused bicyclic thiiranium salts containing nine-, eight-, and seven-membered rings than in those containing five- and six-membered rings, and related this to the greater steric hindrance to the approach of a nucleophile to the carbon atom of the thiiranium salt in the larger bicyclic systems. Evidence concerning steric hindrance to the approach of both nucleophilic and electrophilic reagents to the sulphur atom of 7(*S*)-thio-substituents in this present series, occasioned by the carbohydrate side-chain, has been discussed,[1] and this hindrance appears to account for the exclusive attack on the carbon atom of the intermediate thiiranium salt in this instance.

Reaction of the epimine with thiolan gave the 7-(4-acetoxybutyl)thio-derivative (5) and, with thian, the 7-(5-acetoxypentyl)thio-derivative (6), again accompanied by only the 7-acetate. However, whereas (5)



SCHEME 2





(8)

was formed in 71% yield, the yield of (6) was only 11%. The reasons for this drastic reduction in the yield of desired product in the case of the six-membered ring are not clear; no hindrance about the sulphur atom is evident in either the 'half-chair' conformation of thiolan [6] or the slightly puckered chair conformation of thian.[7] Hindrance to the approach of acetate ion to the α-methylene group of the thianium salt, exerted by the equatorial hydrogen atom of the adjacent methylene group, would be expected [8] to make the ring-opening much slower than that of the thiolanium salt, in which the corresponding methylene hydrogen atoms are eclipsed; however, there is no evidence in the present work for the displacement of the original sulphide from the

[3] D. J. Pettitt and G. K. Helmkamp, *J. Org. Chem.*, 1964, **29**, 2702; D. C. Owsley, G. K. Helmkamp, and S. N. Spurlock, *J. Amer. Chem. Soc.*, 1969, **91**, 3606.

[4] D. N. Jones, J. Blenkinsopp, A. C. F. Edwards, E. Helmy, and R. J. K. Taylor, *J.C.S. Perkin I*, 1973, 2602.

[5] G. H. Schmidt and P. H. Fitzgerald, *J. Amer. Chem. Soc.*, 1971, **93**, 2547.

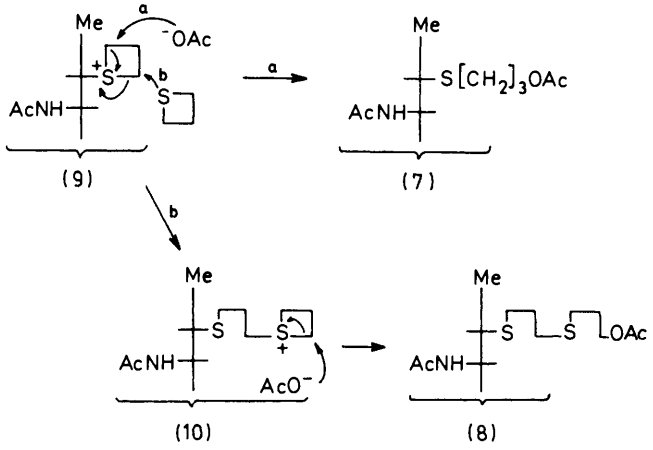
[6] Z. Nahlovska, B. Nahlovsky, and H. M. Seip, *Acta. Chem. Scand.*, 1969, **23**, 3534; A. Garbesi, G. Barbarella, and A. Zava, *J.C.S. Chem. Comm.*, 1973, 155.

[7] H. R. Buys, *Rec. Trav. chim.*, 1969, **88**, 1003.

[8] A. C. Knipe and C. J. M. Stirling, *J. Chem. Soc.* (*B*), 1968, 1218; Y. Yano, M. Ishihara, W. Tagaki, and S. Oae, *Internat. J. Sulfur Chem.*, 1972, **2A**, 169; see also E. L. Allred and S. Winstein, *J. Amer. Chem. Soc.*, 1967, **89**, 4012, for similar differences between five- and six-membered cyclic oxonium salts.

sulphonium salt by nucleophilic attack at C-7,[1] and the yield must be the consequence of the unexpectedly lower nucleophilic reactivity of thian.

From the reaction with thietan, however, two products were obtained in addition to some 7-acetate, separation being achieved by countercurrent distribution. The more polar product was the expected 7-(3-acetoxypropyl)thio-derivative (7) (37%); the ^{1}H n.m.r. spectrum of the less polar material was generally similar to that of (7), but it showed additional methylene and SCH_2 signals (total six protons), indicating the presence of a second $SCH_2CH_2CH_2$ grouping, and the structure was confirmed by the mass spectrum (M^+ 611). This 7-[3-(3-acetoxypropylthio)propyl]thio-derivative (8) was formed in 33% yield. The initial sulphonium salt (9) from thietan is thus subject to equally effective nucleophilic attack by acetate ion (route a) to give (7) or by excess of reagent (route b) to give a second sulphonium salt (10), which then collapses to (8) by attack of acetate ion (Scheme 3).



SCHEME 3

Neither the factors which limit the nucleophilic attack of excess of reagent to the initial sulphonium salt, nor those which restrict this alternative mode of attack in the cyclic series to thietan, are understood. The earlier assumption that the collapse of sulphonium salts derived from acyclic sulphides was occasioned by attack of acetate ion as nucleophile is thus shown to be unwarranted, though plausible, since there is no evidence permitting a distinction to be drawn between initial attack by acetate ion to give alkyl acetate, and initial attack by excess of reagent to give a trialkylsulphonium salt which eventually is cleaved by acetate ion to regenerate sulphide and form alkyl acetate.

The literature is not especially informative about the relative reactivities of nucleophiles in displacements at α-carbon atoms of sulphonium salts. The reaction of sulphonium salts with certain nucleophiles has been studied extensively by Ingold and Hughes and their collaborators,[9a] mainly with reference to olefin formation in the presence of strong bases; their concern with variation of nucleophile was with the changing molecularity of the reaction as the basicity of the nucleophile was altered.[9b] In an examination of the transference of methyl groups from substituted phenyldimethylsulphonium salts to various nucleophiles, Coward and Sweet [10] found the relative reactivities to be in the order $NCS^- > R_2NH > HO^-$ and, indeed, consider sulphonium salts to be extremely resistant to attack by oxygen nucleophiles; the same order of reactivity has been reported [11] in enzyme-catalysed reactions of methyl-group transference from analogues of the biological *trans*-methylating agent *S*-adenosyl-L-methionine involving acetylserotonin *O*-methyltransferase, histamine *N*-methyltransferase, and homocysteine *S*-methyltransferase. On the other hand, Kice and Favstritsky,[12] using ^{1}H n.m.r. techniques, found an equilibrium to be established very rapidly between dimethyl sulphide and the dimethyl(methylthio)sulphonium ion, owing to nucleophilic attack of the dimethyl sulphide on the sulphenyl sulphur atom, whereas Caserio and her collaborators found that, although no reaction was discernible on the n.m.r. time scale between dimethyl sulphide and the trimethylsulphonium ion,[13] an irreversible reaction occurred on prolonged contact between dimethyl sulphide and the dimethyl(methylthio)sulphonium ion with the generation of dimethyl disulphide and the trimethylsulphonium ion, resulting from nucleophilic attack of the dimethyl sulphide on the methyl carbon atom.[14] Although the solvolysis of *S*-alkylthiiranium salts in aqueous solution was found to be favoured greatly over reaction with chloride ion,[15] water was found to compete inefficiently with chloride or bromide ion in the ring-opening of *S*-arylthiiranium salts.[16] An interesting case of competition between nucleophiles in the collapse of a sulphonium salt has been reported by Ramirez and his collaborators.[17] In aqueous solution, the main pathway of decomposition of *S*-methylmethionine sulphonium salts gives homoserine *via* intramolecular attack on the adjacent methylene group by carboxylate anion (Scheme 4, route a) in neutral and basic media, but degradation to methionine becomes important when the carboxylate anion concentration is suppressed by lowering the pH, intermolecular attack by liberated dimethyl sulphide now occurring on one of the sulphonium methyl groups (route b).

[9] (*a*) C. K. Ingold, 'Structure and Mechanism in Organic Chemistry,' Bell, London, 1953, ch. 8. p. 420; (*b*) J. L. Gleave, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 1935, 236; M. H. R. Hoffmann and E. D. Hughes, *ibid.*, 1964, 1259; H. M. R. Hoffmann, *ibid.*, 1965, 823.

[10] J. K. Coward and W. D. Sweet, *J. Org. Chem.*, 1971, **36**, 2337.

[11] V. Zappia, C. R. Zydek-Cwick, and F. Schlenk, *J. Biol. Chem.*, 1969, **244**, 4499.

[12] J. L. Kice and N. A. Favstritsky, *J. Amer. Chem. Soc.*, 1969, **91**, 1751.

[13] S. H. Smallcombe and M. C. Caserio, *J. Amer. Chem. Soc.*, 1971, **93**, 5826.

[14] J. K. Kim and M. C. Caserio, *J. Amer. Chem. Soc.*, 1974, **96**, 1930.

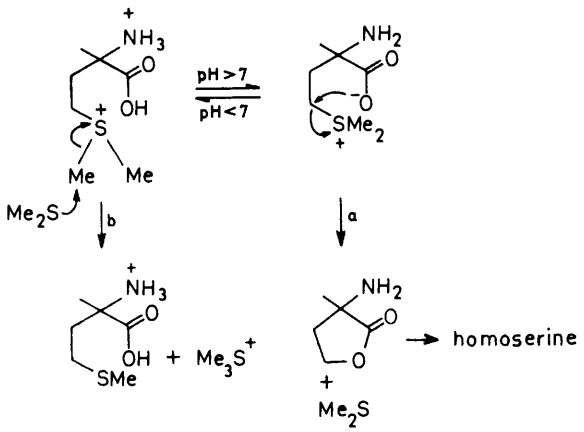
[15] P. D. Bartlett and C. G. Swain, *J. Amer. Chem. Soc.*, 1949, **71**, 1406.

[16] R. Bird and C. J. M. Stirling, *J.C.S. Perkin II*, 1973, 1221.

[17] F. Ramirez, J. L. Finnan, and M. Carlson, *J. Org. Chem.*, 1973, **38**, 2597.

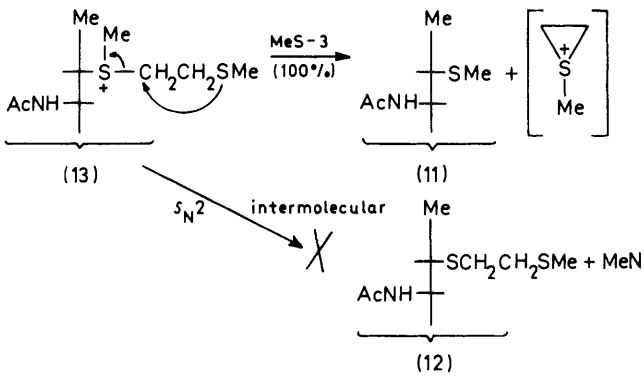
Since, under appropriate conditions, nucleophilic attack at a carbon atom of the intermediate sulphonium salt by a sulphide is possible, it was of interest to examine the reaction between the epimine and a sulphide containing a second nucleophilic thio-substituent which could become involved in the collapse of the sulphonium salt by neighbouring group participation. Chosen first was a second methylthio-substituent in a series of αω-bis(methylthio)alkanes.

With 1,2-bis(methylthio)ethane, reaction occurred to give a trace only of the 7-acetate, and the major product (93%) was identified as the known [1] 7-methylthio-derivative (11). There was no indication of the formation of the 7-[(2-methylthio)ethyl]thio-derivative (12).



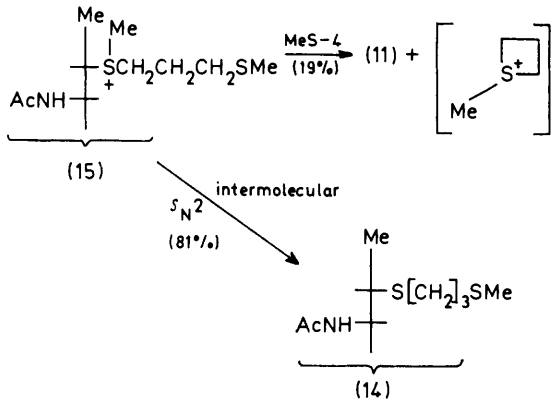
SCHEME 4

Neighbouring group participation by the methylthio-group in the β-position in the intermediate sulphonium salt (13) (MeS-3 participation in the Winstein notation [18]) thus outweighs completely intermolecular attack by any nucleophile on the methyl group (Scheme 5).



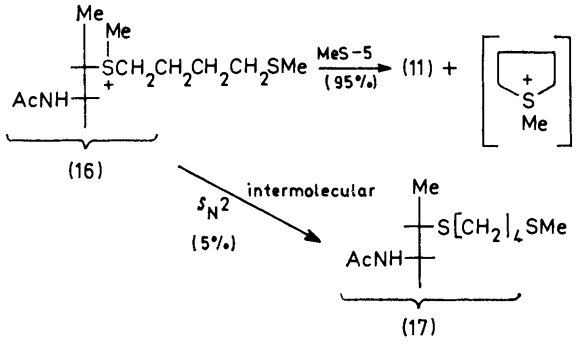
SCHEME 5

With 1,3-bis(methylthio)propane, the 7-methylthio-derivative (11) was again formed (14%) but the major product was the 7-[(3-methylthio)propyl]thio-derivative (14) (61%). As expected, MeS-4 participation is much less effective than MeS-3, thus permitting the initial sulphonium salt (15) to exist long enough to suffer major collapse by intermolecular nucleophilic attack on the methyl group to give (14) (Scheme 6).



SCHEME 6

With 1,4-bis(methylthio)butane, the 7-methylthio-derivative (11) again became the major product (78%), owing to efficient MeS-5 participation in the cleavage of the sulphonium salt (16); however, unlike the MeS-3 participation, which circumvented intermolecular attack on the ion (13), a small yield (5%) of the 7-[(4-methylthio)butyl]thio-derivative (17) was obtained (Scheme 7).



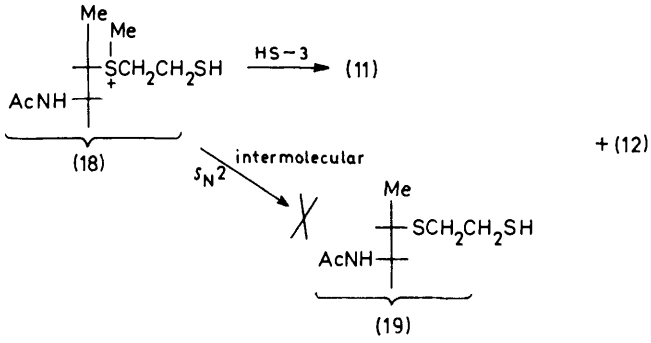
SCHEME 7

Since thiols had been found to be unreactive as nucleophiles in the ring-opening of the activated epimine, it was of interest to determine the course of reactions of sulphides containing, as a second nucleophilic sulphur substituent, the thiol group.

Reaction of the epimine with 2-(methylthio)ethanethiol gave two products in addition to a trace of the 7-acetate. The major product (69% yield) was the 7-methylthio-derivative (11), indicating that HS-3 participation is an efficient method of collapse of the initial sulphonium salt (18). The second product showed ^{1}H n.m.r. signals at δ($CDCl_3$) 1.91—2.15 (18 H, 6s), indicative of six OAc, NAc, and SMe groups, and δ 2.75 (4 H, m), corresponding to SCH_2CH_2S. In accordance with this, the mass spectrum showed a molecular ion at *m/e* 511 and a significant ion at *m/e* 404 ($M^+ - SCH_2CH_2SMe$), giving the structure of the minor product as (12) (13% yield), the material which did *not* result from

[18] S. Winstein, E. Alfred, L. Heck, and R. Glick, *Tetrahedron*, 1958, **3**, 1.

the reaction with 1,2-bis(methylthio)ethane (above). There was no indication of the formation of the terminal thiol (19) (Scheme 8). That neighbouring group



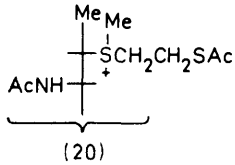
SCHEME 8

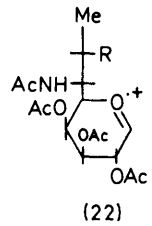
participation was responsible for the collapse of the ion (18) to the major product (11) was demonstrated by examining the reaction with *S*-acetyl 2-(methylthio)-ethanethiol, in which the nucleophilicity of the original thiol sulphur atom is reduced drastically. The 7-methylthio-derivative was formed in only 9% yield, the major product now being the 7-[(2-acetylthio)ethyl]thio-derivative (20) (65%), showing $\lambda_{max.}$ 231 nm, characteristic of a *S*-thioacetate.[19]

From the reaction product with 3-(methylthio)-propanethiol, countercurrent distribution gave three symmetrical peaks; the least polar material (*K* 0.32) was the 7-acetate (35%), and a minor component (*K* 0.82) was the 7-methylthio-derivative (11) (7%), consistent with the inefficiency of HS-4 participation in the collapse of the sulphonium salt (21) (Scheme 9). The third, major, component (*K* 2.33) appeared in the region expected for the known 7-[(3-methylthio)propyl]thio-derivative (14), from which it was not distinguished by t.l.c. in several solvent systems, but it did not behave as a pure compound on crystallisation. G.l.c. showed this material to be a mixture of two compounds, separated incompletely (retention times 28 and 30 min) in an area ratio of 1 : 4, respectively, the area of the 30 min peak being increased by the co-injection of the known (14). G.l.c.–mass spectrometric examination of the mixture showed a molecular ion at *m/e* 525 for the more polar component, as expected for (14); in the spectrum of the less polar component, the ion of highest mass occurred at *m/e* 464, which could not be M^+. However, a common fragment ion in the fully acetylated methyl thiolincosaminide series results from the loss of the aglycone group with the formation of the oxonium ion (22),[2] suggesting that the molecular weight of the material was 511, 14 m.u. less than that of the other component, and that the substituent at C-7 was $SCH_2CH_2CH_2SH$.

Acetylation of this mixture in pyridine–acetic anhydride gave a product which showed the original t.l.c. zone of the *K* 2.33 material, plus a poorly separated zone, of slightly lower R_F value, which quenched the fluorescence under u.v. light of a phosphor-containing silica plate, consonant with the formation of an *S*-thioacetate.[19] G.l.c.–mass spectrometric examination of the acetylated material showed the presence of the same peak of retention time 30 min, the disappearance of the 28 min peak, and a new peak of retention time 45 min, with a molecular ion at *m/e* 553, in agreement with the formation of the $SCH_2CH_2CH_2SAc$ substituent; the relative areas were now 1 : 1.7, respectively. Extended countercurrent distribution effected the separation, and direct comparison of the *K* 1.0 material identified it as the 7-[(3-methylthio)propyl]thio-derivative (14) (20% yield). The structure of the *K* 0.67 material, the major component, was established on the basis of ^1H n.m.r. signals at $\delta(CDCl_3)$ (2 H, t, $SCH_2CH_2CH_2S$), 2.35 (3 H, s, SAc), 2.67 (2 H, t, SCH_2CH_2), and 2.98 (2 H, t, CH_2-CH_2SAc), u.v. absorption at $\lambda_{max.}$ 231 nm, and by the isolation of the same material, the 7-[(3-acetylthio)-propyl]thio-derivative (23), as the major product from the reaction between the epimine and *S*-acetyl 3-(methylthio)propanethiol.

The relative areas of the g.l.c. peaks of the components of the mixtures differed markedly before and after acetylation. Since the cleavage of sulphides to *S*-alkyl thioacetates by reaction with acetyl halides at room temperature has been reported[20] it was necessary to see if any cleavage of (14) to (23) occurred in pyridine–





acetic anhydride. No u.v.-absorbing product was formed, and (14) was recovered quantitatively; the discrepancies between the recorded areas of the g.l.c. peaks simply reflect differing responses of the detector to the various components.

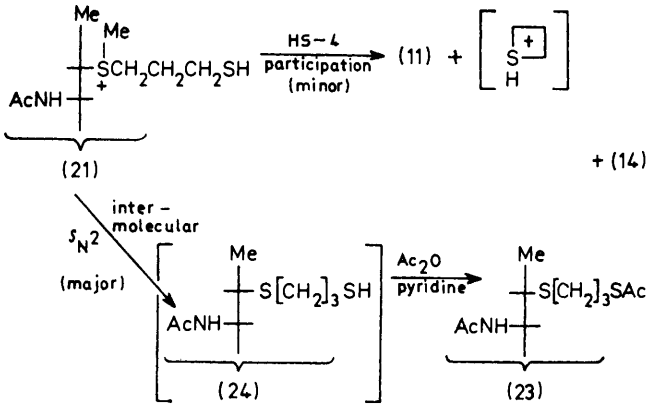
Thus, the inefficiency of the HS-4 participation in the collapse of the ion (21) is equivalent to that of MeS-4 participation in the collapse of the ion (15), and permits the existence of the ion (21) for a time sufficient for significant intermolecular nucleophilic attack at the methyl group to occur, leading to the thiol (24), isolated as the *S*-acetyl-derivative (23) (Scheme 9).

With the reagent 4-(methylthio)butanethiol, the epimine (1) gave the 7-methylthio-derivative (11) as major product (71% yield) and again a terminal methylthio-derivative (17) was formed, though in low yield. Therefore, as with HS-3 participation in the collapse of the ion (18), HS-5 participation in the collapse of the ion (25) is seen to be an efficient process, there being no discernible formation of the terminal thiol (26) (Scheme 10). The absence of (26) would indicate

[19] M. J. Janssen, in ' The Chemistry of Carboxylic Acids and Esters,' ed. S. Patai, Interscience, New York, 1969, ch. 15, p. 713.

[20] E. L. Gustus and P. G. Stevens, *J. Amer. Chem. Soc.*, 1933, **55**, 378; H, Bohme and J. Roehr, *Annalen*, 1961, 648, 21.

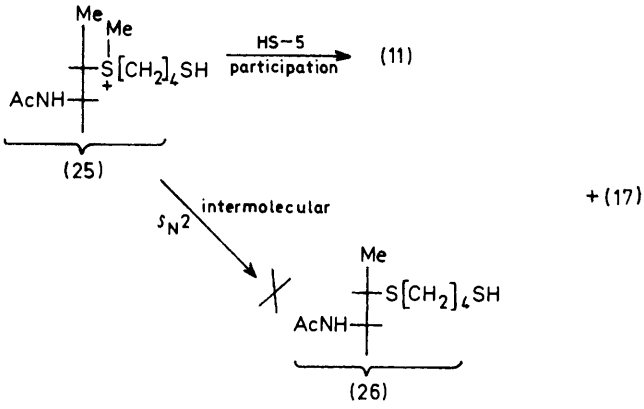
that, under these circumstances, HS-5 participation is somewhat more effective than MeS-5 participation, since in the reaction with 1,5-bis(methylthio)butane, a



SCHEME 9

small yield of the product (17) *not* resulting from participation was formed.

Anchimeric assistance by the sulphide sulphur atom has been well established in the hydrolysis of alkyl halogenoalkyl sulphides, with those involving three-, five-,



SCHEME 10

or six-membered-ring transition states showing marked enhancement of reaction rates relative to four-membered-ring transition states.[21] Similarly, neighbouring group participation accounts for migrations of alkylthio-groups of carbohydrate dithioacetals *via* cyclic sulphonium salts to positions 2,[22] 4,[23] and 5.[23,24] Migrations from position 1 to position 3 appear to be unknown, apparently again because of the inefficiency of RS-4 participation.

These reactions in the present work, involving neighbouring group participation of the methylthio-group in the sulphonium salts (13), (15), and (16), and of the thiol group in the sulphonium salts (18), (21), and (25), fall into the category of favoured *exo-tetrahedral* cyclic reactions in the recent nomenclature of Baldwin.[25] Since thiols themselves are not alkylated under these general conditions by the acetylated epimine (1),[1] the formation from the ω-(methylthio)alkanethiols of the products (12), (14), and (17), is unexpected. That they might arise by intramolecular *trans*-methylation involving HS-5, -6, and -7 participation, respectively, is questionable in the light of Eschenmoser's investigations, which indicate that the ring sizes involved in such transition states are unfavourable in endocyclic intramolecular S_N reaction pathways,[26] and such reactions fall into the class of disfavoured 5- to 7-*endo-tetrahedral* cyclic reactions.[25] However, it is possible that sulphur, as a second row element, may have less stringent requirements for the geometry of the transition state than carbon or oxygen as first row elements.[27] An examination of the nature of the reactions involved in the formation of these unexpected products will be the subject of a forthcoming paper in this series.

The conversion of these acetylated carbohydrate derivatives into the (7*S*)-7-(substituted thio)-7-deoxylincomycins, and the biological properties of these analogues of lincomycin, will be reported elsewhere.

EXPERIMENTAL

General experimental procedures have been described previously,[2] together with details of spectral determinations, the method of analysis of countercurrent distribution results, and the definition of the distribution coefficient K.[1] Countercurrent distribution analyses were conducted after 500 transfers. If separations were incomplete, the higher number of transfers utilised for separation is indicated. Solvent systems used were 95% ethanol–water–ethyl acetate–cyclohexane in the proportions (v/v) 1 : 1 : 1 : 3 (System A), 1 : 1 : 1 : 2 (System B), or 1 : 1 : 0.5 : 3 (System C). The sulphides used were obtained commercially, except where noted otherwise, and were redistilled before use. With compounds of structure ascertained earlier, products were identified by comparison (m.p., mixed m.p., t.l.c., spectrometric examination) with authentic samples.

Reactions of the Tetra-acetylepimine (1) *with Cyclic Sulphides*

Methyl (7S)-N-*Acetyl*-2,3,4-*tri*-O-*acetyl*-7-*deoxy*-7-[(2-*acetoxyethyl*)*thio*]-1-*thio*-α-*lincosaminide* (3).—Acetic acid (5.25 g, 86.8 mmol) was added to a suspension of the tetra-acetylepimine [2] (5.0 g, 12.4 mmol) in thiiran (50 g, 833 mmol) in a sealed tube, and the mixture was heated in a steam-bath for 20 h; the solid dissolved rapidly. After cooling, the contents of the tube were rinsed out with dichloromethane, and filtered from much gelatinous polymer; the filtrate was washed with saturated aqueous sodium hydrogen carbonate, and dried (Na_2SO_4). Removal of the solvent gave a yellow

[21] A. Streitwieser, jun., *Chem. Rev.*, 1956, **56**, 680; B. Capon, *Quart. Rev.*, 1964, **18**, 45.
[22] L. Goodman, *Adv. Carbohydrate Chem.*, 1967, **22**, 109, and references cited therein.
[23] N. A. Hughes, R. Robson, and S. A. Saeed, *Chem. Comm.*, 1968 1381.
[24] J. S. Brimacombe, *Fortschr. Chem. Forsch.*, 1970, **14**, 367, and references cited therein.
[25] J. E. Baldwin, *J.C.S. Chem. Comm.*, 1976, 734.
[26] L. Tenud, S. Faroog, J. Seible, and A. Eschenmoser, *Helv. Chim. Acta*, 1970, **53**, 2059.
[27] E. Ciuffarin and G. Guaraldi, *J. Amer. Chem. Soc.*, 1969, **91**, 1745; J. E. Baldwin, J. Cutting, W. Dupont, L. Kruse, L. Silberman, and R. C. Thomas, *J.C.S. Chem. Comm.*, 1976, 736.

syrup, from which more polymeric material (R_F 0.66) was removed by chromatography on silica in ethyl acetate–Skellysolve B * (2 : 1); the column was then eluted with ethyl acetate to give a colourless solid (6.20 g). Counter-current distribution (c.c.d.) (System A) gave two peaks, K 0.25 (1.55 g, 27%), the known [2] tetra-acetate, and K 0.53, the 7-(2-*acetoxyethyl*)*thiotetra-acetate* (3) (4.47 g, 69%), which separated from ethyl acetate as needles, m.p. 206—207°, $[\alpha]_D$ +180° (*c* 0.829 in $CHCl_3$), δ 1.33 (3 H, d, *J* 8 Hz, 8-H_3), 1.95—2.17 (18 H, 5s, 4 OAc + NAc + SMe), 2.85 (2 H, t, *J* 7 Hz, SCH_2CH_2O), 3.27 (1 H, q, H-7), 4.30 (2 H, t, *J* 7 Hz, OCH_2CH_2S), and 5.63 (1 H, d, *J* 5 Hz, NH), *m/e* 524 (M^+ +1), 476 (M^+ −SMe), 463 (M^+ −HOAc), 416 (M^+ −SMe −OAc), and 404 (M^+ −SCH_2CH_2OAc) (Found: C, 48.1; H, 6.4; N, 2.6; S, 11.95. $C_{21}H_{33}NO_{10}S_2$ requires C, 48.2; H, 6.35; N, 2.7; S, 12.25%).

On acetylation of the 7-(2-hydroxyethyl)thio-derivative (2) [1] in pyridine–acetic anhydride overnight at room temperature, an essentially quantitative yield of the 7-(2-acetoxyethyl)thio-derivative, m.p. 206—207°, was obtained by removal of volatile materials and direct crystallisation from ethyl acetate.

Methyl (7S)-N-*Acetyl*-2,3,4-*tri*-O-*acetyl*-7-*deoxy*-7-[(4-*acetoxybutyl*)*thio*]-1-*thio*-α-*lincosaminide* (5).—Reaction between the tetra-acetylepimine (5.0 g) and thiolan (50 g) in the presence of acetic acid, using the standard work-up procedure followed by c.c.d. (System B), gave the 7-acetate, K 0.4 (1.21 g), and the 7-[(4-*acetoxybutyl*)*thio*]*tetra-acetate* (5), K 1.32 (4.86 g, 71%), rosettes of needles from ethyl acetate, m.p. 149—150°, $[\alpha]_D$ +171° (*c* 0.881 in $CHCl_3$), δ 1.31 (3 H, d, *J* 7 Hz, 8-H_3), 1.70 (4 H, t, *J* 4 Hz, $SCH_2CH_2CH_2CH_2S$), 1.92—2.15 (18 H, 6s, 4 OAc + NAc + SMe), 2.65 (2 H, t, *J* 7 Hz, SCH_2CH_2), and 4.12 (2 H, t, *J* 7 Hz, OCH_2CH_2), *m/e* 551 (M^+), 504 (M^+ −SMe), 492 (M^+ −OAc), and 444 (M^+ −SMe −HOAc) (Found: C, 50.0; H, 6.9; N, 2.5; S, 11.35. $C_{23}H_{37}NO_{10}S_2$ requires C, 50.1; H, 6.8; N, 2.5; S, 11.6%).

Methyl (7S)-N-*Acetyl*-2,3,4-*tri*-O-*acetyl*-7-[(5-*acetoxypentyl*)*thio*]-1-*thio*-α-*lincosaminide* (6).—From the tetra-acetylepimine (10.0 g) in thian (100 g) under the usual conditions, c.c.d. (System B) gave a major peak, K 0.40 [the 7-acetate (9.5 g)], and the desired product (6), K 2.12 (1.61 g), contaminated with a trace of more polar material (t.l.c.), from which it was purified by chromatography on silica in ethyl acetate–Skellysolve B (1 : 1). The product (6), R_F 0.13 (1.49 g, 11%), separated from ethyl acetate–Skellysolve B in needles, m.p. 158—159°, $[\alpha]_D$ +169° (*c* 0.602 in $CHCl_3$), δ 1.57br (6 H, $CH_2[CH_2]_3CH_2$), 1.93—2.17 (18 H, 6s, 4 OAc + NAc + SMe), 2.63 (2 H, t, *J* 7 Hz, SCH_2CH_2), and 4.10 (2 H, t, *J* 7 Hz, OCH_2CH_2), *m/e* 565 (M^+), 518 (M^+ −SMe), 506 (M^+ −OAc), and 446 (M^+ −OAc −HOAc) (Found: C, 50.9; H, 6.9; N, 2.4; S, 11.2. $C_{24}H_{39}NO_{10}S_2$ requires C, 50.95; H, 6.95; N, 2.5; S, 11.3%).

Methyl (7S)-N-*Acetyl*-2,3,4-*tri*-O-*acetyl*-7-*deoxy*-7-[(3-*acetoxypropyl*)*thio*]-1-*thio*-α-*lincosaminide* (7) *and Methyl* (7S)-N-*Acetyl*-2,3,4-*tri*-O-*acetyl*-7-*deoxy*-7-{3-[(3-*acetoxypropyl*)*thio*]*propylthio*}-1-*thio*-α-*lincosaminide* (8).—The crude product from the tetra-acetylepimine (10.0 g) in thietan (50 g) and acetic acid (5.25 g) showed only one zone on t.l.c., R_F 0.28 [ethyl acetate–Skellysolve B (2 : 1)]. C.c.d. (System B) gave the 7-acetate, K 0.40 (2.30 g), and two major peaks, K 1.00 and 2.33, showing single zones on t.l.c. of R_F 0.50 and 0.53, respectively [acetone–Skellysolve B (1 : 1)]. The more polar material was the 7-[(3-*acetoxypropyl*)*thio*]*tetra-acetate* (7) (4.96 g, 37%), needles from ethyl acetate–Skellysolve B, m.p. 172.5—174°, $[\alpha]_D$ +178° (*c* 0.936 in $CHCl_3$), δ 1.85 (2 H, t, *J* 7 Hz, $OCH_2CH_2CH_2S$), 1.94—2.16 (18 H, 6s, 4 OAc + NAc + SMe), 2.68 (2 H, t, *J* 7 Hz, SCH_2CH_2), and 4.17 (2 H, t, *J* 7 Hz, OCH_2CH_2), *m/e* 538 (M^+ +1), 537 (M^+), 522 (M^+ −Me), 490 (M^+ −SMe), 478 (M^+ −OAc), 430 (M^+ −SMe −HOAc), and 404 (M^+ −$SCH_2CH_2CH_2OAc$) (Found: C, 49.3; H, 6.6; N, 2.7; S, 11.8. $C_{22}H_{35}NO_{10}S_2$ requires C, 49.15; H, 6.6; N, 2.6; S, 11.8%). The material, K 2.33, was shown to be the 7-{[3-(*acetoxypropyl*)*thio*]*propylthio*}*tetra-acetate* (8) (5.03 g, 33%), needles from ethyl acetate–Skellysolve B, m.p. 117—118°, $[\alpha]_D$ +149° (*c* 0.997 in $CHCl_3$), δ 1.87, 1.93 overlapping (4 H, 2t, *J* 7 Hz, $SCH_2CH_2CH_2SCH_2CH_2CH_2O$), 1.94—2.17 (18 H, 5s, 4 OAc + NAc + SMe), 2.61 (2 H, t, *J* 7.5 Hz, $SCH_2CH_2CH_2SCH_2CH_2CH_2$), 2.66, 2.72 overlapping (4 H, 2t, *J* 7.5 Hz, $SCH_2CH_2CH_2SCH_2$), and 4.19 (2 H, t, *J* 6 Hz, OCH_2CH_2), *m/e* 611 (M^+), 564 (M^+ −SMe), and 552 (M^+ −OAc) (Found: C, 49.4; H, 6.7; N, 2.35; S, 15.9. $C_{25}H_{41}NO_{10}S_3$ requires C, 49.1; H, 6.8; N, 2.3; S, 15.7%).

Reactions of the Tetra-acetylepimine (1) *with* αω-*Bis*(*methylthio*)*alkenes*

1,2-*Bis*(*methylthio*)*ethane*; *the* (7S)-7-*Deoxy*-7-*methylthio-tetra-acetate* (11).—From the tetra-acetylepimine (10.0 g) in 1,2-bis(methylthio)ethane [28] (100 g) were obtained, following c.c.d. (System A), the 7-acetate (trace; K 0.25) and the 7-methylthio-tetra-acetate [1] (11) (10.40 g, 93%; K 0.82), m.p. 225—226° (rods from ethyl acetate–Skellysolve B).

1,3-*Bis*(*methylthio*)*propane*; *Methyl* (7S)-N-*Acetyl*-2,3,4-*tri*-O-*acetyl*-7-*deoxy*-7-{[(3-*methylthio*)*propyl*]*thio*}-1-*thio*-α-*lincosaminide* (14).—The crude product from the tetra-acetylepimine (10.0 g) and 1,3-bis(methylthio)propane (100 g), showed three zones on t.l.c. [acetone–Skellysolve B (1 : 1)], R_F 0.45, 0.52, and 0.60, the former two not being distinguished from zones due to the 7-acetate and 7-methylthio-derivatives, respectively. C.c.d. (System A) gave peaks of K 0.25 (1.66 g) (the 7-acetate), K 0.92 (1.60 g, 14%) [the 7-methylthio-derivative (11)], and K 2.24, shown to be the 7-{[(3-*methylthio*)propyl]*thiotetra-acetate* (14) (7.97 g, 61%), needles from ethyl acetate, m.p. 211—212°, $[\alpha]_D$ +181° (*c* 1.092 in $CHCl_3$), δ 1.88 (2 H, t, *J* 6.5 Hz, $SCH_2CH_2CH_2S$), 1.93—2.17 (18 H, 5s, 3 OAc + NAc + 2 SMe), and 2.65, 2.77 overlapping (4 H, 2t, *J* 6.5 Hz, $SCH_2CH_2CH_2S$), *m/e* 525 (M^+), 478 (M^+ −SMe), 466 (M^+ −OAc), 436 (M^+ −$[CH_2]_3SMe$), and 404 (M^+ −$S[CH_2]_3SMe$) (Found: C, 48.0; H, 6.8: N, 2.6; S, 18.1. $C_{21}H_{35}NO_8S_3$ requires C, 48.0; H, 6.7; N, 2.7; S, 18.3%).

1,4-*Bis*(*methylthio*)*butane*; *Methyl* (7S)-N-*Acetyl*-2,3,4-*tri*-O-*acetyl*-7-*deoxy*-7-{[(4-*methylthio*)*butyl*]*thio*}-1-*thio*-α-*lincosaminide* (17).—From reaction of the tetra-acetylepimine (10.0 g) and 1,4-bis(methylthio)butane (100 g), followed by c.c.d. (System A), were obtained three components, K 0.28 (7-acetate), K 0.95 [the 7-methylthio-derivative (11); 8.76 g, 78%], and K 3.54, shown to be the 7-{[(4-*methylthio*)*butyl*]*thio*}*tetra-acetate* (17) (610 mg, 5%), needles from ethyl acetate, m.p. 184.5—185°, $[\alpha]_D$ +174° (*c* 0.926 in $CHCl_3$), δ 1.73 (4 H, m, *J* 7 Hz, $SCH_2CH_2CH_2CH_2S$), 1.92—2.15 (18 H, 5s, 3 OAc + NAc + 2 SMe), and

* A saturated hydrocarbon fraction, b.p. 60—71°, Skelly Oil Co., Kansas City, Missouri, U.S.A.

[28] G. T. Morgan and W. Ledbury, *J. Chem. Soc.*, 1922, **121**, 2882.

2.63, 2.52 overlapping (4 H, 2t, J 7 Hz, $SCH_2[CH_2]_2CH_2S$), *m/e* 539 (M^+), 492 (M^+ —SMe), 480 (M^+ —OAc), and 404 (M^+ —$S[CH_2]_4SMe$) (Found: C, 48.8; H, 6.8; N, 2.6; S, 17.5. $C_{22}H_{37}NO_8S_3$ requires C, 48.95; H, 6.9; N, 2.6; S, 17.8%).

Reactions of the Tetra-acetylepimine (1) *with ω-(Methylthio)alkanethiols*

2-(*Methylthio*)*ethanethiol; Methyl* (7S)-N-*Acetyl*-2,3,4-*tri*-O-*acetyl*-7-*deoxy*-7-{[(2-*methylthio*)*ethyl*]*thio*}-1-*thio*-α-*lincosaminide* (12).—The crude product from the tetra-acetylepimine (10.0 g) and 2-(methylthio)ethanethiol [29] (100 g) showed a major (R_F 0.45) and a minor (R_F 0.38) zone on t.l.c. [acetone–Skellysolve B (1 : 1)], not differentiated from zones due to the 7-methylthio-compound (11) and the 7-acetate, respectively. C.c.d. (System A) gave three peaks, K 0.25 (7-acetate, small), K 0.88 (7-methylthio-derivative; 7.74 g, 69%), and K 1.84, shown to be the 7-{[(2-*methylthio*)*ethyl*]*thio*}*tetra-acetate* (12) (1.76 g, 13%), needles from ethyl acetate–Skellysolve B, m.p. 236—237°, $[\alpha]_D$ +183° (*c* 0.928 in $CHCl_3$), δ 1.91—2.15 (18 H, 6s, 3 OAc + NAc + 2 SMe), and 2.75 (4 H, m, SCH_2CH_2S), *m/e* 511 (M^+), 451 (M^+ —HOAc), and 404 (M^+ —SCH_2CH_2SMe) (Found: C, 47.0; H, 6.9; N, 2.5; S, 18.5. $C_{20}H_{33}NO_8S_3$ requires C, 46.9; H, 6.5; N, 2.7; S, 18.8%).

S-2-(*Methylthio*)*ethyl Thioacetate*.—The 2-(methylthio)-ethanethiol (61.4 g) was acetylated overnight in pyridine–acetic anhydride at room temperature. Volatile material was removed by distillation at atmospheric pressure, and the residue was dissolved in chloroform, the solution was washed with saturated aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated at 40 °C under reduced pressure. Distillation through a micro-Vigreux column gave S-2-(*methylthio*)*ethyl acetate* as a liquid, b.p. 100—101° at 16 mmHg (111.5 g, 90%), $\nu_{max.}$ (neat) 1 685 cm^{-1} (thiolacetate), $\lambda_{max.}$ 208 (ε 2 650) and 231 nm (4 250), δ 2.17 (3 H, s, SCH_3), 2.33 (3 H, s, $SCOCH_3$), and 2.82 (4 H, m, SCH_2CH_2S), *m/e* 150 (M^+), 107 (M^+ —Ac), 103 (M^+ —SMe), and 74 (M^+ —HSAc) (Found: C, 39.9; H, 6.6; S, 43.1. $C_5H_{10}OS_2$ requires C, 40.0; H, 6.7; S, 42.7%).

Methyl (7S)-N-*Acetyl*-2,3,4-*tri*-O-*acetyl*-7-*deoxy*-7-{[(2-*acetylthio*)*ethyl*]*thio*}-1-*thio*-α-*lincosaminide* (20).—The tetra-acetylepimine (10.0 g) and the *S*-acetyl thiol (76 g) gave a crude product showing on t.l.c. [acetone–Skellysolve B (1 : 1)] two minor zones, R_F 0.45 and 0.61, coincident with those from the 7-acetate and the 7-methylthio-derivatives, respectively, and a major zone, R_F 0.50. C.c.d. (System A) gave materials of K 0.30 (7-acetate; 2.16 g), K 0.92 (the 7-methylthio-derivative; 1.01 g, 9%), and K 1.55, the 7-{[(2-*acetylthio*)*ethyl*]*thio*}*tetra-acetate* (20) (8.68 g, 65%), needles from ethyl acetate, m.p. 198—199°, $[\alpha]_D$ +168° (*c* 1.034 in $CHCl_3$), $\nu_{max.}$ (Nujol) 1 700 and 1 680 cm^{-1} (MeCOS), $\lambda_{max.}$ 231 nm (ε 4 150), δ 1.94—2.18 (15 H, 5s, 3 OAc + NAc + SMe), 2.37 (3 H, s, $SCOCH_3$), 2.80 (2 H, t, J 4 Hz, SCH_2CH_2), and 3.04 (2 H, t, J 4 Hz, CH_2CH_2SAc), *m/e* 492 (M^+ —SMe), 479 (M^+ —HOAc), and 463 (M^+ —SAc) (Found: C, 46.8; H, 6.05; N, 2.6; S, 17.5. $C_{21}H_{33}NO_9S_3$ requires C, 46.7; H, 6.2; N, 2.6; S, 17.6%).

3-(*Methylthio*)*propanethiol*.—Propane-1,3-dithiol (200 g, 1.85 mol) was added to a solution of sodium ethoxide [from sodium (42.6 g, 1.85 g atom)] in ethanol (1 200 ml) at 0 °C, followed by methyl iodide (263 g, 1.85 mol) over 40 min, and the mixture was stirred overnight and allowed to warm to room temperature. Most of the ethanol was removed by distillation at 100 °C and 40 mmHg, and sodium iodide was filtered off and washed with ether. The solvent was removed by distillation at atmospheric pressure, and the residue was fractionated through a spinning-band column. Redistillation of the appropriate fraction [chosen on the basis of g.l.c. retention time, using propane-1,3-dithiol and 1,3-bis(methylthio)propane as reference standards] gave 3-(*methylthio*)*propanethiol* as a liquid (52 g, 23%), b.p. 76—77° at 24 mmHg, δ 1.40 (1 H, t, J 7 Hz, CH_2SH), 1.88 (2 H, t, $SCH_2CH_2CH_2S$), 2.13 (3 H, s, SCH_3), and 2.62 (4 H, t, $SCH_2CH_2CH_2S$), *m/e* 122 (M^+), 107 (M^+ —Me), 88 (M^+ —H_2S), and 74 (M^+ —MeSH) (Found: C, 39.5; H, 8.1; S; 52.5. $C_4H_{10}S_2$ requires C, 39.3; H, 8.25; S, 52.5%).

Methyl (7S)-N-*Acetyl*-2,3,4-*tri*-O-*acetyl*-7-*deoxy*-7-{[(3-*methylthio*)*propyl*]*thio*}-1-*thio*-α-*lincosaminide* (14) *and Methyl* (7S)-N-*Acetyl*-2,3,4-*tri*-O-*acetyl*-7-*deoxy*-7-{[(3-*acetylthio*)-*propyl*]*thio*}-1-α-*lincosamide* (23).—C.c.d. (System A) of the crude product from the tetra-acetylepimine (10.0 g) and 3-(methylthio)propanethiol (50 g) gave well separated components of K 0.32, 0.82, and 2.33 in the expected regions for the 7-acetate, the 7-methylthio-compound (11), and the 7-[(3-methylthio)propyl]thio-compound (14), respectively. The most polar material was identified as the 7-acetate (3.96 g, 35%), and the minor component as the 7-methylthio-derivative (10) (757 mg, 7%), shown to be homogeneous by g.l.c. (1% OV-17 on 60—80 mesh GasChrom Q in a ¼ in × 3 ft stainless steel column; 275 °C isothermal). The K 2.33 material crystallised poorly from ethyl acetate in needles, sintering at 200°, m.p. 205—215° [m.p. of (13), 211—212°], and was shown by g.l.c. to be a mixture (see Discussion section).

This mixture was acetylated overnight at room temperature in acetic anhydride–pyridine to give a solid (6.27 g); c.c.d. (System C) after 1 000 transfers gave components of K 0.67 and 1.00, the latter being identified as the 7-[(3-methylthio)propyl]thio-derivative (14), m.p. 211—212° (2.58 g, 20%). The more polar component, shown to be the 7-{[(3-*acetylthio*)*propyl*]*thio*}*tetra-acetate* (23) (4.17 g, 30%), separated from ethyl acetate–Skellysolve B in needles, m.p. 170—170.5°, $[\alpha]_D$ +170° (*c* 1.049 in $CHCl_3$), $\nu_{max.}$ (Nujol) 1 745 (ester), 1 685 (thiolacetate), 1 650 (amide I), and 1 550 (amide II) cm^{-1}, $\lambda_{max.}$ 231 nm (ε 4 450), δ 1.73 (2 H, t, J 7 Hz, $SCH_2CH_2CH_2S$), 1.93—2.17 (15 H, 5s, 3 OAc + NAc + SMe), 2.35 (3 H, s, $SCOCH_3$), 2.67 (2 H, t, J 7 Hz, SCH_2CH_2), and 2.98 (2 H, t, J 7 Hz, CH_2CH_2SAc), *m/e* 553 (M^+), 506 (M^+ —SMe), 494 (M^+ —OAc), 464 (M^+ —SMe —$H_2C{=}C{=}O$), 446 (M^+ —MeSH —OAc), and 404 (M^+ —$S[CH_2]_3SAc$) (Found: C, 47.6; H, 6.4; N, 2.6; S, 17.7. $C_{22}H_{35}NO_9S_3$ requires C, 47.7; H, 6.4; N, 2.5; S, 17.4%).

S-3-(*Methylthio*)*propyl Thioacetate*.—The thiol was acetylated overnight at room temperature in acetic anhydride–pyridine, and the product isolated in the usual way. Fractionation through a micro-Vigreux column gave the *thioacetate* as a liquid, b.p. 116—118° at 16 mmHg, showing one peak on g.l.c. at 172 °C (10% UCW-98, programmed from 120 to 200 °C), $\nu_{max.}$ 1 690 cm^{-1} (thiolacetate), $\lambda_{max.}$ 232 nm (ε 4 250), δ 1.85 (2 H, t, J 6 Hz, $SCH_2CH_2CH_2S$), 2.08 (3 H, s, SCH_3), 2.33 (3 H, s, $SCOCH_3$), 2.57 (2 H, t, J 6 Hz, CH_2CH_2SMe), and 3.00 (2 H, t, J 6 Hz, CH_2CH_2SAc) (Found: C, 44.0; H, 7.3; S, 39.1. $C_6H_{12}OS_2$ requires C, 43.9; H, 7.4; S, 39.0%).

Under the standard conditions, the tetra-acetylepimine (10.0 g) and the thioacetate (130 g) gave, after c.c.d.

[29] E. M. Meade and F. N. Woodward, *J. Chem. Soc.*, 1948, 1894.

(System A) three components: *K* 0.28 (the 7-acetate; 3.10 g. 27%), *K* 0.96 [the 7-methylthio-compound (11); 1.16 g, 10%], and *K* 1.87 {the 7-[(3-acetylthio-propyl]thio-derivative (23) (7.45 g, 54%)}, m.p. 170—170.5°, identical with the material obtained from the reaction with the thiol itself, followed by *S*-acetylation.

4-(*Methylthio*)*butanethiol*.—This was prepared by mono-*S*-methylation of butane-1,4-dithiol as described above for 3-(methylthio)propanethiol. Following fractionation through a spinning-band column, 4-(*methylthio*)*butanethiol* was obtained as a liquid (74%), b.p. 98—99° at 15 mmHg, homogeneous on g.l.c., δ 1.47 (1 H, t, *J* 6 Hz, CH_2SH), 1.78 (4 H, m, $SCH_2CH_2CH_2CH_2S$), 2.18 (3 H, s, SCH_3), and 2.60 (4 H, t, *J* 6 Hz, $SCH_2CH_2CH_2CH_2S$) (Found: C, 44.2; H, 9.0; S, 47.0. $C_5H_{12}S_2$ requires C, 44.0; H, 8.9; S, 47.1%).

Methyl (7S)-N-*Acetyl*-2,3,4-*tri*-O-*acetyl*-7-*deoxy*-7-{[(4-*methylthio*)*butyl*]*thio*}-1-*thio*-α-*lincosaminide* (17).—Under the standard conditions, the product from the tetra-acetylepimine (9.56 g) in 4-(methylthio)butanethiol (82 g) gave three peaks on c.c.d. (System A): *K* 0.25 (the 7-acetate; 1.97 g, 18%), *K* 0.88 (the 7-methylthio-compound; 7.60 g, 71%), and *K* 2.70 {the 7-[(4-methylthio)butyl]thio-derivative (17); 610 mg, 5%}, m.p. 184—185°, identical with the minor product from the reaction with 1,4-bis-(methylthio)butane.

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