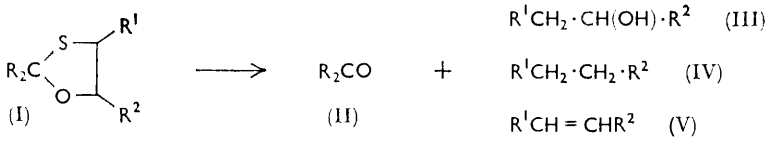
1164. *Studies in Organic Sulphur Compounds. Part XVII.*[1] *The Synthesis of Previously Inaccessible Acylated Enamines by Desulphurisation of Thiazolidines*

By N. S. Crossley, Carl Djerassi, and M. A. Kielczewski

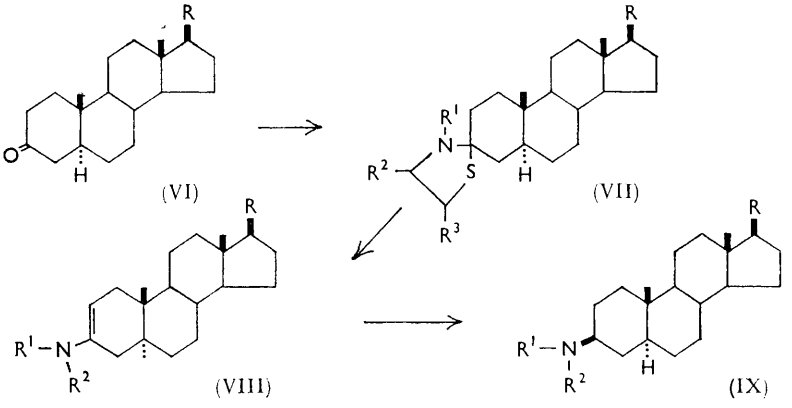
The Raney nickel desulphurisation of a variety of thiazolidines, thiazolidones, and tetrahydro-1,3-thiazines has been shown to take an unusual course in many cases, and under selected conditions, good yields of acylated enamines were obtained. Other aspects of the desulphurisation of these compounds are discussed.

In a previous Paper [2] in this Series it was shown that the Raney nickel desulphurisation of cyclic hemithioketals (I) can lead to ketones (II), accompanied either by the alcohol (III) or the hydrocarbons (IV) and (V) depending upon the solvent used. Of particular interest was the " oxygen introduction " mechanism which was proposed to account for the formation of both the alcohol (III) and the ketone (II) in more than 50% yield.



We report here [3] the extension of these studies to include the analogous compounds in which the heterocyclic ring contains sulphur and nitrogen. Previous work [4] in this field has been confined chiefly to the desulphurisation of thiazolid-4-ones and rhodanines.

Most of the experiments with hemithioketals were done with spiro-compounds derived from 5α-cholestan-3α-one (VI; R = C_8H_{17}) and, anticipating a close parallel, we chose for initial study the analogous spirothiazolidines. Condensation of 5α-cholestan-3-one (VI; R = C_8H_{17}) with 2-mercaptoethylamine in the presence of toluene-*p*-sulphonic acid gave



the thiazolidine (VII; R = C_8H_{17}, $R^1 = R^2 = R^3 = H$). The thiazolidine was acetylated and Table 1 shows the results of the Raney nickel desulphurisation of this acetyl compound (VII; R = C_8H_{17}, R^1 = Ac, $R^2 = R^3 = H$) in three solvents. In benzene (Expts. 1 and 2) and in ethanol (Expt. 5) the major product was the unsaturated amide (VIII;

[1] Part XVI, D. A. Lightner and C. Djerassi, *Tetrahedron*, 1965, **21**, 583.
[2] C. Djerassi, M. Shamma, and T. Y. Kan, *J. Amer. Chem. Soc.*, 1958, **80**, 4823.
[3] For preliminary account see C. Djerassi, N. S. Crossley, and M. A. Kielczewski, *J. Org. Chem.*, 1962, **27**, 1112.
[4] F. C. Brown, *Chem. Rev.*, 1961, **61**, 463.

R = C_8H_{17}, R^1 = Ac, R^2 = Et). The structure of this unexpected product is based on the following evidence: (*a*) infrared absorption at 1610 cm.$^{-1}$, (*b*) ultraviolet absorption at 202 (ε 10,380) and 220 mμ (ε 4720), (*c*) n.m.r. absorption for one proton at 4·45 τ, (*d*) acid hydrolysis to 5α-cholestan-3-one (VI; R = C_8H_{17}), (*e*) lithium aluminium hydride reduction to an unstable enamine, which rapidly decomposed to 5α-cholestan-3-one, and which was shown to be compound (VIII; R = C_8H_{17}, R^1 = R^2 = Et) by infrared and mass spectrometry. This evidence does not exclude termination of the double bond at C-4.

TABLE 1

Desulphurisation of *N*-acetyl-5α-cholestane-3-spiro-2′-thiazolidine

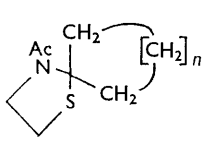
Expt.	Solvent	Age of catalyst (days)	pH	Reflux time (hr.)	Yield of (VIII; R = C_8H_{17}, R^1 = Ac, R^2 = Et) (%)	Yield of 5α-cholestan-3-one (%)
1	C_6H_6	7	7·65	5	89	—
2	C_6H_6	31	7·65	20	90	—
3	Me_2CO	61	7·35	24	19	63
4	Me_2CO	18	8·50	24	34	57
5	EtOH	52	8·20	16	63	—

The unsaturated amide was the minor product when the desulphurisation was carried out in acetone (Expts. 3 and 4). In this solvent the *N*-acetylthiazolidine appeared to behave like its hemithioketal analogue and the major product was 5α-cholestan-3-one (VI; R = C_8H_{17}). Both the *N*-acetylthioazolidine (VII; R = C_8H_{17}, R^1 = Ac, R^2 = R^3 = H) and the unsaturated amide (VIII; R = C_8H_{17}, R^1 = Ac, R^2 = Et) were shown to be unchanged after prolonged heating in acetone in the presence of base.

In other experiments in which benzene was the solvent, the unsaturated amide (VIII; R = C_8H_{17}, R^1 = Ac, R^2 = Et) was contaminated with small amounts of two closely related compounds. These were identified as 3β-acetamido-5α-cholestane [5] (IX; R = C_8H_{17}, R^1 = Ac, R^2 = H) and 3β-ethylacetamido-5α-cholestane (IX; R = C_8H_{17}, R^1 = Ac, R^2 = Et) by thin-layer-chromatographic comparison with authentic samples. They are apparently produced by a pathway which does not involve the unsaturated amide (VIII; R = C_8H_{17}, R^1 = Ac, R^2 = Et) since this compound was unchanged after further treatment with Raney nickel in benzene.

Similar results were encountered in the 5α-androstane series. The unsaturated amide (VIII; R = H, R^1 = Ac, R^2 = Et) was the major product (51%) of desulphurisation with 15-day-old Raney nickel in benzene of the *N*-acetylthiazolidine (VII; R = H, R^1 = Ac, R^2 = R^3 = H) made from 5α-androstan-3-one (VI; R = H). In addition two other products were isolated and identified as 3β-acetamido-5α-androstane (IX; R = R^2 = H, R^1 = Ac) (11%), and 5α-androstane-3-one (VI; R = H) (8%).

The production of acylated enamines such as (VIII) by the desulphurisation of *N*-acetylthiazolidines appears to be a reaction of general application providing the conditions are



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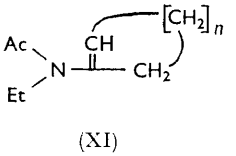

(XI)

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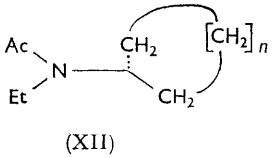


(XII)

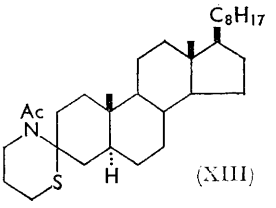
chosen carefully. For example, the age of the catalyst is a critical factor in the course of desulphurisation of compounds in which a simple ring system replaces the steroid nucleus. The *N*-acetylthiazolidine (X; *n* = 3) was made from cyclohexanone and was desulphurised in benzene. With catalyst which was 39 days old the unsaturated compound (XI; *n* = 3) was obtained in high yield. With catalyst which was 5 and 6 days old a mixture of at

[5] D. P. Dodgson and R. D. Haworth, *J.*, 1952, 67.

least four compounds was obtained, one of which was identified as the saturated amide [6] (XII; $n = 3$). Traces of biphenyl and *N*-acetyl-*N*-ethylaniline were also detected. All these products were purified by preparative gas chromatography and identified by their mass and n.m.r. spectra. The corresponding cyclopentane compound (X; $n = 2$) gave similar results and the formation of the acetylated enamine was again favoured by using an old catalyst. The most volatile product was identified as *N*-ethylacetamide and the relative proportions of this, the acetylated enamine (XI; $n = 2$), and the acetylated amine (XII; $n = 2$) were 1 : 12 : 45 in the case of catalyst which was 3 days old and 1 : 8 : 1 when the catalyst was 30 days old.

The straight-chain analogues of (XI) and (XII) were obtained by the desulphurisation of *N*-acetyl-2-hexylthiazolidine and, in agreement with the above results, the proportion of unsaturated amide increased when older and especially degassed Raney nickel was used.

Returning to thiazolidines of the spiro-type, the generality of the reaction leading to the otherwise inaccessible enamines was demonstrated with three other types of compound. Condensation [7] of 5α-cholestan-3-one (VI; R = C_8H_{17}) with 3-mercaptopropylamine,



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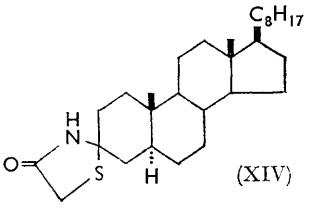


(XIV)

followed by acetylation, gave the *N*-acetyltetrahydro-1,3-thiazine (XIII) which, on desulphurisation with Raney nickel (42 days old) in benzene, gave the acetylated enamine (VIII; R = C_8H_{17}, R^1 = Ac, R^2 = Pr^n) in 66% yield. The n.m.r. spectrum of this product showed a signal for one vinylic proton at τ 4·45, and it was hydrolysed by acid to 5α-cholestan-3-one (VI; R = C_8H_{17}).

Condensation of 5α-cholestan-3-one (VI; R = C_8H_{17}) and 5α-androstan-3-one (VI; R = H) with (+)-cysteine [8] followed by acetylation and diazomethane methylation gave the *N*-acetylthiazolidine (VII; R = C_8H_{17}, R^1 = Ac, R^2 = CO_2Me, R^3 = H) and (VII; R = R^3 = H, R^1 = Ac, R^2 = CO_2Me). The cholestane derivative was desulphurised in benzene with Raney nickel (15 days old) and the major product (64%) was the unsaturated amido-ester (VIII; R = C_8H_{17}, R^1 = Ac, R^2 = CHMe·CO_2Me) which was unchanged after further treatment with Raney nickel in benzene or ethanol. Therefore, the minor product, 3β-acetamido-5α-cholestane (IX; R = C_8H_{17}, R^1 = Ac, R^2 = H), isolated in 10% yield, was the product of a separate desulphurisation. The unsaturated amido-ester (VIII; R = H, R^1 = Ac, R^2 = CHMe·CO_2Me) was obtained in 69% yield accompanied by 5% of 3β-acetamido-5α-androstane (IX; R = R^2 = H, R^1 = Ac) after desulphurisation of the androstane derivative (VII; R = R^3 = H, R^1 = Ac, R^2 = CO_2Me) with Raney nickel (17 days old) in benzene.

The desulphurisation of some 2-spirothiazolid-4-ones has also been investigated and found to constitute another route to acylated enamines (see Table 2). The starting materials were made by reaction of a ketone with thioglycolic acid and ammonium carbonate.[9] Thus, 5α-cholestan-3-one gave both diastereoisomers of the thiazolidone (XIV) which were separated by chromatography on a column of alumina, isomer (A) having m. p. 264—265° and isomer (B), m. p. 312—314°. Except in one experiment, in which a trace of acetamide was isolated, desulphurisation of both isomers in acetone gave only 5α-cholestan-3-one. Neither thiazolidone isomer was affected by prolonged heating

[6] A. Skita and H. Rolfes, *Ber.*, 1920, **53**, 1242.
[7] E. D. Bergmann and A. Kaluszyner, *Rec. Trav. chim.*, 1959, **78**, 327.
[8] S. Lieberman, P. Brazeau, and L. B. Hariton, *J. Amer. Chem. Soc.*, 1948, **70**, 3094.
[9] A. R. Surrey and R. A. Cutler, *J. Amer. Chem. Soc.*, 1954, **76**, 578.

in acetone containing a trace of sodium hydroxide, thus demonstrating that Raney nickel was required for production of the ketone (VI; R = C_8H_{17}).

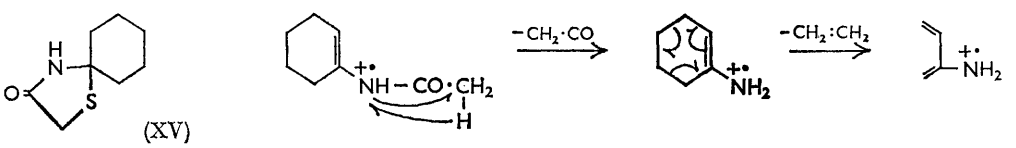
On desulphurisation in benzene, both isomers gave a poor recovery of three products which could be separated almost completely by chromatography on a silica column. They were shown to be 5α-cholestan-3-one (VI; R = C_8H_{17}), 3-acetamido-5α-cholest-2-ene (VIII; R = C_8H_{17}, R^1 = Ac, R^2 = H), and 3β-acetamido-5α-cholestane (IX; R = C_8H_{17}, R^1 = Ac, R^2 = H). The structure of the second product was established by mass spectrometry which showed the anticipated molecular-ion peak at *m/e* 427. In addition, this product could be hydrolysed by acid to 5α-cholestan-3-one and reduced by Raney nickel in ethanol to 3β-acetamido-5α-cholestane (IX; R = C_8H_{19}, R^1 = Ac, R^2 = H). When the desulphurisation of compound (XIV) was carried out in ethanol, 3β-acetamido-5α-cholestane was obtained directly (see Table 2).

TABLE 2

Desulphurisation of 5α-cholestane-3-spiro-2′-thiazolid-4′-one

Isomer	Age of catalyst (days)	pH	Solvent	Reflux time (hr.)	Yield of 5α-cholestan-3-one (VI; R = C_8H_{17}) (%)	Yield of unsaturated amide (VIII; R = C_8H_{17}, R^1 = Ac, R^2 = H) (%)	Yield of saturated amide (IX; R = C_8H_{17}, R^1 = Ac, R^2 = H) (%)
(A)	9	7·5	EtOH	21	—	—	60
(B)	1	7·3	EtOH	17	—	—	66
(A)	10	8·2	Me_2CO	22	90	—	—
(B)	2	8·3	Me_2CO	19	90	—	—
(A)	20	7·6	C_6H_6	22	9	27	4
(B)	14	8·2	C_6H_6	18	11	14	22

The spirothiazolidone (XV) was made by condensing cyclohexanone with thioglycolic acid and ammonium carbonate. It was desulphurised in benzene with Raney nickel (5 days old) and gave a homogeneous product which was identical with an authentic sample of acetamidocyclohexane.[10] However, the behaviour of this thiazolidone (XV) was similar to that of the *N*-acetylthiazolidine (X; *n* = 3) since, on desulphurisation in benzene with an older catalyst (23 days), three products were detected and separated by gas chromatography. These were acetamidocyclohexane, acetamide and 1-acetamidocyclohex-1-ene and they were present in the approximate ratio of 2 : 3 : 4. The structure of the



(XV)

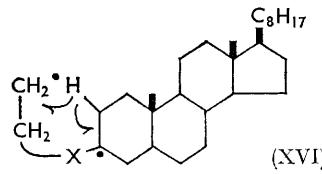
acetylated enamine was proved by mass spectrometry which showed a molecular-ion peak at *m/e* 139 and three prominant peaks at *M* −42 (loss of CH_2:C:O), *M* −43 (loss of CH_3·CO) and *M* −70 (loss of CH_2:C:O and CH_2:CH_2 as shown above), as well as by its n.m.r. spectrum (olefinic proton signal at 4·45 τ).

In all the examples so far the substrates have been amides. Disappointing results were obtained in the desulphurisation of non-acetylated thiazolidines. For example, in benzene, the thiazolidine (VII; R = C_8H_{17}, R^1 = R^2 = R^3 = H) gave only 5α-cholestan-3-one and, although in one experiment a 77% yield was obtained, in four other experiments the highest yield was 25% and the lowest 4%. This represented the organic material which was recovered by washing the catalyst with methylene chloride. Nothing more was obtained on further washing with methanol, tetrahydrofuran, or dilute hydrochloric acid. It had been hoped to include arylated thiazolidines in this work but in one experiment with one diastereoisomer of the 5′-phenylthiazolidine (VII; R = C_8H_{17}, R^1 = R^2 =

[10] A. Baeyer, *Annalen*, 1893, **278**, 88.

H, R^3 = Ph), made by condensing 5α-cholestan-3-one with 2-mercapto-2-phenylethylamine, no organic material could be recovered from the catalyst. In acetone, however, the thiazolidine (VII; R = C_8H_{17}, R^1 = R^2 = R^3 = H) could be desulphurised reproducibly to give 5α-cholestan-3-one (59—68%) and 5α-cholestan-3β-ol (7—15%). Of incidental interest was the observation that the thiazolidine (VII; R = C_8H_{17}, R^1 = R^2 = R^3 = H) could be desulphurised by lithium in ethylamine [11] to give 3β-ethylamino-5α-cholestane in 87% yield.

It is apparent from these results that Raney nickel desulphurisation can proceed by several different pathways, even in the same solvent. However, under certain circumstances the mechanism leading to the acylated enamines can become dominant. As was suggested in the Paper [2] describing the desulphurisation of hemithioketals, radicals are the most likely intermediates in hydrocarbon solvents. Therefore, in all the experiments in which benzene was the solvent, homolytic fission of both C–S bonds is probably the first step, and it is the further reactions of the diradical, for example (XVI; X = NAc), produced which determines the nature of the product. An attractive explanation for



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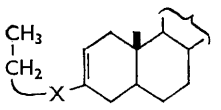

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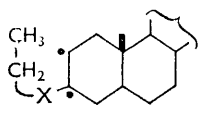

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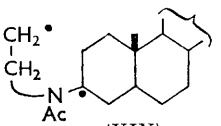

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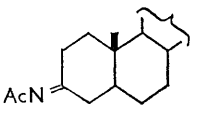

(XX)

the formation of the unsaturated products would involve intramolecular abstraction of hydrogen from C-2. This type of mechanism was proposed Part XIV [12] to account for the formation of 5α-cholest-2-ene in the Raney-nickel desulphurisation of the ethylene dithioketal of 5α-cholestan-3-one. In that case the thioenol ether (XVII; X = S) would be formed from the diradical and subsequently desulphurised. This mechanism could not be disproved by experiments with Raney nickel containing active deuterium, but an alternative explanation, namely that the homolysis of the C–H bond was effected by an external radical source leading to the diradical (XVIII; X = S), was thought to be equally probable. In the case of the *N*-acetylthiazolidines the latter appears to be the only acceptable mechanism because, on desulphurisation of the *N*-acetylthiazolidine made from 2,2,4,4[$^2H_4$]5α-androstan-3-one, one deuterium atom was lost from ring A and mass spectrometry showed that it did not appear on the β-C-atom of the side-chain. This mechanism would be expected to operate also when X = O, *i.e.*, on desulphurisation of hemithioketals in benzene. Therefore, it could be argued that the ethyl enol ether (XVII; X = O) was an intermediate in these reactions but it did not survive either the reaction or the isolation procedure. In a recent article,[13] Eliel and Krishnamurthy have shown that after Raney-nickel desulphurisation under mild conditions of the hemithioketal made from 5α-cholestan-3-one and an isolation procedure which avoids acid-washed alumina the enol ether (XVII; X = O) can be isolated. In the present instance, we suggest that the saturated *N*-ethylacetamide products (IX; R^1 = Et, R^2 = Ac) are derived by a normal desulphurisation mechanism in which the intermediate diradical (XIX) takes up

[11] N. S. Crossley and H. B. Henbest, *J.*, 1960, 4413.
[12] C. Djerassi and D. H. Williams, *J.*, 1963, 4046.
[13] E. L. Eliel and S. Krishnamurthy, *J. Org. Chem.*, 1965, **30**, 848.

two hydrogen radicals from the catalyst. Collapse of the 1,4-diradical (XIX) with loss of ethylene followed by hydrogenation of the acylimine (XX) would account for the formation of the saturated acetamido-compounds (IX; $R^1 = H$, $R^2 = Ac$). The increased amount of saturated products (IX) with fresher catalyst is thus rationalised. Both these products were obtained from the desulphurisation of the tetradeuterated *N*-acetylthiazolidine and mass spectrometry showed that the *N*-ethylacetamide (IX; $R = H$, $R^1 = Et$, $R^2 = Ac$) contained four deuterium atoms, thus demonstrating unambiguously that this saturated amide could not have arisen by further hydrogenation of the acylated enamine (VIII). The mass spectrum of the acetamido-compound (IX; $R = R^1 = H$, $R^2 = Ac$) showed the presence of a non-deuterated product and mono-, di-, tri, and tetra-deuterated species, the mono-deuterated being the most abundant. This can be explained readily, since, if the acylimine (XX) is an intermediate here, exchange of allylic deuterium for hydrogen on the surface of the catalyst is likely.

It is possible that the mechanism of desulphurisation of the thiazolidines and the hemithioketals in acetone is also very similar. The major product in all cases was the ketone and, conceivably, nucleophilic attack by hydroxide ion on C-3 facilitated by co-ordination of an electron-deficient metal with sulphur is the critical step, as was suggested earlier.[2]

In a recent article, Drefahl and Huebner [14] have shown that Raney-nickel desulphurisation of *N*-acetyl-5α-cholestane-3-spiro-2′-thiazolidine (VII; $R = C_8H_{17}$, $R^1 = Ac$, $R^2 = R^3 = H$) in methanol gives 3-(*N*-ethylacetamido)-5α-cholest-2-ene (VIII; $R = C_8H_{17}$, $R^1 = Ac$, $R^2 = Et$) together with 5α-cholestan-3-one (VI; $R = C_8H_{17}$); the mechanism of the reaction was not discussed further.

Experimental

Optical rotations refer to chloroform solutions. M. p.s were determined on a Kofler hot-stage apparatus. We are indebted to Mr. E. Meier for microanalyses and Dr. H. Budzikiewitz for mass spectra.

General Procedure for Desulphurisation.—The W2 Raney nickel catalyst was prepared according to Mozingo [15] and the amount of catalyst used was approximately ten times the weight of subtrate. The volume of solvent, excluding that used for washing, was usually 100—200 c.c./g. of substrate. When acetone was the solvent the catalyst was washed ten times with acetone and then heated under reflux for 30 min. before addition of the substrate. In the benzene experiments, the catalyst was washed five times with ethanol, ten times with benzene, and a little benzene was distilled out in a stream of nitrogen before addition of a benzene solution of the substrate from which a little benzene had been distilled. In all cases the pH measured was that of the water under which the catalyst had been stored. At the end of the reaction the solvent was decanted and the catalyst washed with methylene chloride and, in some cases, with methanol. The combined washings were filtered and evaporated before purification, examples of which are given below.

N-*Acetyl-5α-cholestane-3-spiro-2′-thiazolidine* (VII; $R = C_8H_{17}$, $R^1 = Ac$, $R^2 = R^3 = H$). A mixture of 5α-cholestan-3-one (7·73 g.), 2-mercaptoethylamine (3·30 g.), and benzene (200 c.c.) was heated under a water-trap in an atmosphere of nitrogen for 47 hr. The crude product (8·72 g.), m. p. 134—137°, was isolated with benzene, and a small sample crystallised from ethyl acetate to give *5α-cholestane-3-spiro-2′-thiazolidine* (VII; $R = C_8H_{17}$, $R^1 = R^2 = R^3 = H$), m. p. 136—137°, $[\alpha]_D^{26}$ +25·9° (*c* 1·16) (Found: C, 77·85; H, 11·15; N, 3·3; S, 7·0. $C_{29}H_{51}NS$ requires C, 78·1; H, 11·5; N, 3·1; S, 7·2%). A mixture of the crude thiazolidine (1·1 g.), acetic anhydride (2 c.c.) and pyridine (20 c.c.) was kept at room temperature for 14 hr. The product, isolated with chloroform, crystallised from ethyl acetate to give the N-*acetylthiazolidine* (0·79 g.), m. p. 171—172°, $[\alpha]_D^{26}$ +46·8° (*c* 1·12) (Found: C, 76·1; H, 10·9; N, 3·0; S, 6·5. $C_{31}H_{53}NOS$ requires C, 76·3; H, 10·95; N, 2·9; S, 6·6%) (lit.,[14] m. p. 172—173°, $[\alpha]_D$ +47°).

[14] G. Drefahl and M. Huebner, *J. prakt. Chem.*, 1964, **23**, 149.
[15] Z. Pelah, M. A. Kielczewski, J. M. Wilson, M. Onashi, H. Budzikiewicz, and C. Djerassi, *J. Amer. Chem. Soc.*, 1963, **85**, 2470.

N-Acetyl-5α-androstane-3-spiro-2′-thiazolidine (VII; R = R^2 = R^3 = H, R^1 = Ac). A mixture of 5α-androstan-3-one (1·2 g.), 2-mercaptoethylamine (2·0 g.), toluene-*p*-sulphonic acid monohydrate (30 mg.), and benzene (50 c.c.) was heated under a water-trap for 36 hr. The crude product (1·4 g.), m. p. 100—105°, was isolated with benzene, and a small sample crystallised from ethyl acetate to give *5α-androstane-3-spiro-2′-thiazolidine* (VII; R = R^1 = R^2 = R^3 = H), m. p. 110—111° (Found: C, 75·5; H, 10·7; N, 4·0; S, 9·7. $C_{21}H_{33}NOS$ requires C, 75·6; H, 10·6; N, 4·2; S, 9·6%), $\nu_{max.}$ (KBr) 3260 cm.$^{-1}$. A mixture of the crude thiazolidine (1·2 g.), acetic anhydride (2 c.c.), potassium carbonate (1·0 g.), and ether (50 c.c.) was kept at room temperature for 15 hr. The product, isolated with ether, crystallised from ethyl acetate to give the *N-acetylthiazolidine* (0·8 g., 62%), m. p. 184—185°, $[\alpha]_D^{31}$ +36·1° (*c* 1·08) (Found: C, 73·7; H, 10·1; N, 3·6; S, 8·7%; *M*, 375. $C_{23}H_{37}NOS$ requires C, 73·6; H, 9·9; N, 3·7; S, 8·5; *M*, 375%) $\nu_{max.}$ (KBr) 1632 cm.$^{-1}$.

Desulphurisation of N-Acetyl-5α-cholestane-3-spiro-2′-thiazolidine (VII; R = C_8H_{17}, R^1 = Ac, R^2 = R^3 = H).—(*a*) *In benzene* (*Table* 1, *Exp.* 1). At the end of the desulphurisation of the *N*-acetylthiazolidine (500 mg.), the benzene was decanted and the catalyst washed with boiling methylene chloride (5 × 50 c.c.). The benzene and combined washings were filtered and the solvent distilled to give a solid (332 mg.), m. p. 105—135° which was crystallised from ethyl acetate to give *3-(N-ethylacetamido)-5α-cholest-2-ene* (VIII; R = C_8H_{17}, R^1 = Ac, R^2 = Et) (75 mg.), m. p. 145—146°, $[\alpha]_D^{27.5}$ +61·5° (*c* 1·22) (Found: C, 81·1; H, 11·7; N, 3·3; O, 3·8. $C_{31}H_{53}NO$ requires C, 81·6; H, 11·7; N, 3·0; O, 3·5%), $\nu_{max.}$ ($CHCl_3$) 1610 cm.$^{-1}$, $\lambda_{max.}$ (MeOH) 202 (ε 10,380) and 220 mμ (ε 4720) (lit.,[15] m. p. 145—146°, $[\alpha]_D$ +58·8°). The catalyst was washed with boiling methanol (5 × 50 c.c.) and the washings were filtered and evaporated to give a solid (160 mg.), m. p. 125—135°. This product and the combined mother liquors were dissolved in methylene chloride and chromatographed on acid-washed alumina (50 g.). Methylene chloride–methanol (20 : 1) eluted a solid (335 mg.), m. p. and mixed m. p. 142—144°. The yield was therefore 410 mg. (89%).

(*b*) *In acetone* (*Table* 1, *Expt.* 3). At the end of the desulphurisation of the *N*-acetylthiazolidine (500 mg.) the acetone was decanted and the catalyst was washed with boiling methylene chloride (5 × 50 c.c.). After evaporation of the solvent from the combined washings, the residue was dissolved in methylene chloride and chromatographed on neutral alumina. Methylene chloride eluted 5α-cholestan-3-one (249 mg., 63%), m. p. and mixed m. p. 128—130°. Methylene chloride–methanol (50 : 1) eluted 3-(*N*-ethylacetamido)-5α-cholest-2-ene (VIII; R = C_8H_{17}, R^1 = Ac, R^2 = Et) (82 mg., 19%), m. p. and mixed m. p. 139—140°.

Acid Hydrolysis of 3-(N-Ethylacetamido)-5α-cholest-2-ene (VIII; R = C_8H_{17}, R^1 = Ac, R^2 = Et).—A solution of the amide (460 mg.) in ethanol (500 c.c.) and concentrated hydrochloric acid (250 c.c.) was heated under reflux for 24 hr. On cooling, a solid precipitated and was collected. A solution in methylene chloride was washed with aqueous potassium carbonate and the solvent distilled. Crystallisation of the residue from ether gave 5α-cholestan-3-one (187 mg.), m. p. and mixed m. p. 128—129°.

Lithium Aluminium Hydride Reduction of 3-(N-Ethylacetamido)-5α-Cholest-2-ene (VIII; R = C_8H_{17}, R^1 = Ac, R^2 = Et).—The amide (200 mg.) was added in small portions to a stirred suspension of lithium aluminium hydride (1·0 g.) in ether (100 c.c.). The mixture was heated under reflux for 6 hr. and stirred at room temperature overnight. After decomposition of the excess of hydride with sufficient ethyl acetate, the mixture was filtered and the filtrate evaporated. The product, a gum (167 mg.), showed no carbonyl absorption in the infrared region and gave a mass-spectrometric molecular weight of 441. ($C_{31}H_{35}N$ requires 441.) During attempted crystallisation of this gum from ethyl acetate decomposition occurred to give material having an infrared spectrum identical with that of 5α-cholestan-3-one.

Desulphurisation of N-Acetyl-5α-androstane-3-spiro-2′-thiazolidine (VII; R = R^2 = R^3 = H, R^1 = Ac) *in Benzene*.—The *N*-acetylthiazolidine (400 mg.) was desulphurised with Raney nickel (15 days old, pH 7·4). A residue of 338 mg. was obtained, m. p. 160—200°, and was shown to contain four compounds. These were partially separated by chromatography on a column of silica (7 g.), eluting with ethyl acetate. The first 230 mg. which was eluted was crystallised twice from ethyl acetate to give *3-(N-ethylacetamido)-5α-androst-2-ene* (VIII; R = H, R^1 = Ac, R^2 = Et) (100 mg.), m. p. 175°, $[\alpha]_D^{29}$ +68·4 (*c* 1·0) (Found: C, 80·2; H, 10·8; N, 4·0%; *M*, 343. $C_{23}H_{37}NO$ requires C, 80·4; H, 10·9; N, 4·1%; *M*, 343), $\nu_{max.}$ (KBr) 1650 cm.$^{-1}$. Further elution gave 75 mg. which was crystallised from ethyl acetate to give *3β-acetamido-5α-androstane* [15] (IX; R = R^2 = H, R^1 = Ac) (12 mg.), m. p. 247—248° (Found: C, 79·7;

H, 11·1; N, 4·4%; *M*, 317. $C_{21}H_{35}NO$ requires C, 79·4; H, 11·1; N, 4·4%; *M*, 317), $\nu_{max.}$ (KBr) 3280, 1630 cm.$^{-1}$. The combined mother-liquors were separated in two portions by preparative thin-layer chromatography on two glass plates (20 × 20 cm.) covered with silica, and eluted with ethyl acetate. In this way 3-(*N*-ethylacetamido)-5α-androst-2-ene (72 mg., total yield, 51%) and 3β-acetamido-5α-androstane (26 mg., total yield, 11%) were obtained. In addition, 5α-androstan-3-one (VI; R = H) (27 mg.), identified by its infrared spectrum, was isolated.

N-*Acetylcyclohexanespiro-2′-thiazolidine* (X; *n* = 3).—A mixture of cyclohexanone (980 mg.), 2-mercaptoethylamine (1·5 g.), toluene-*p*-sulphonic acid monohydrate (10 mg.), and benzene (50 c.c.) was heated under a water separator in a stream of nitrogen for 6 hr. The solution was cooled, washed with water (3 × 15 c.c.), and the solvent evaporated. The residue (1·69 g.) was heated under reflux with acetic anhydride (4 c.c.) and ether (100 c.c.) for 6 hr. After being left at room temperature overnight the solution was washed with water (4 × 20 c.c.) and with aqueous potassium carbonate. Evaporation of the ether gave a crude product (1·8 g., 94%), m. p. 93—95°. The pure N-*acetylthiazolidine* had m. p. 95—96° (from hexane) (Found: C, 60·55; H, 8·7; N, 6·9; S, 16·0. $C_{10}H_{17}NOS$ requires C, 60·3; H, 8·6; N, 7·0; S, 16·0%), $\nu_{max.}$ (KBr) 1630 cm.$^{-1}$.

N-*Acetylthiazolidine-2-spirocyclopentane* (X; *n* = 2).—Cyclopentanone was condensed with 2-mercaptoethylamine and the product acetylated to give the N-*acetylthiazolidine*, m. p. 48—51° (Found: C, 59·1; H, 8·3; N, 7·3; S, 16·9. $C_9H_{15}NOS$ requires C, 58·4; H, 8·1; N, 7·6; S, 17·3%).

N-*Acetyl-2-hexylthiazolidine*.—Heptanal was condensed with 2-mercaptoethylamine and the product acetylated to give the N-*acetylthiazolidine*, b. p. 120°/0·2 mm., n_D^{25} 1·4985 (Found: C, 61·7; H, 9·9; N, 6·45; S, 14·55. $C_{11}H_{24}NOS$ requires C, 61·4; H, 9·8; N, 6·5; S, 14·9%).

Desulphurisation of N-*Acetylcyclohexanespiro-2′-thiazolidine* (X; *n* = 3) *in Benzene*.—(*a*) The *N*-acetylthiazolidine (1·2 g.) was desulphurised with Raney nickel (39 days old, pH 7·5). The oil which was obtained was distilled (b. p. 125°/0·5 mm.) and the distillate (957 mg.) was shown to contain six compounds by gas chromatography. One of these accounted for 90% of the product and was identified as 1-(N-*ethylacetamido*)*cyclohex*-1-*ene* (XI; *n* = 3) by mass spectrometry (*M*$^+$, 167) and n.m.r. spectrometry (olefinic proton signal at τ 5·6).

(*b*) The *N*-acetylthiazolidine (500 mg.) was desulphurised with Raney nickel (5 days old, pH 8·9). The residue, an oil (375 mg.), was separated into three fractions by preparative gas chromatography on a column of phenyldiethanolamine succinate (PDEAS) at 195°. The fraction having a retention time of 15 min. was collected (10 mg.) and shown to be mainly biphenyl (*M*$^+$, 154; aromatic proton n.m.r. absorption between τ 7·0 and 7·57). The fraction having a retention time of 17 min. was collected (22 mg.). Mass spectrometry indicated that it was mainly *N*-acetyl-*N*-ethylaniline (*M*$^+$, 163). The fraction having a retention time of 20 min. was collected and distilled. The distillate (30 mg.) was shown to be homogenous by reinjection but a satisfactory analysis could not be obtained. The mass-spectrometric molecular weight of 169 indicated that the product was *N*-ethylacetamidocyclohexane (XII; *n* = 3).

Desulphurisation of N-*Acetylthiazolidine-2-spirocyclopentane* (10, *n* = 2) *in Benzene*..—(*a*) The *N*-acetylthiazolidine (215 mg.) was desulphurised with Raney nickel (30 days old, pH 7·5). The residue, an oil (158 mg.) was separated into three fractions by preparative gas chromatography on a PDEAS column at 160° using helium as the carrier gas. Fraction 1 (retention time 4 min.) was identified as *N*-ethylacetamide, (*M*$^+$, 86). Fraction 2 (retention time 8 min.) was identified as 1-(N-*ethylacetamido*)*cyclopent*-1-*ene* (XI; *n* = 2) (*M*$^+$, 153). Fraction 3 (retention time 12 min.) was identified as N-*ethylacetamidocyclopentane* (XII; *n* = 2) by gas-chromatographic comparison with an authentic sample synthesised from cyclopentylamine. The ratio of the peak areas of these three fractions was 1 : 8 : 1.

(*b*) The *N*-acetylthiazolidine (1·0 g.) was desulphurised with Raney nickel (3 days old, pH 7·6). The residue, an oil (725 mg.) contained the three compounds described in the previous experiment in the ratio 1 : 12 : 45.

Desulphurisation of N-*Acetyl-2-hexylthiazolidine in Benzene*.—(*a*) The *N*-acetylthiazolidine (500 mg.) was desulphurised with Raney nickel (13 days old, pH 7·3). An oil (326 mg.) was obtained which was homogeneous by gas chromatography and, on distillation, gave N-*acetyl*-N-*ethylheptylamine* (303 mg., 70%), b. p. 110°/0·2 mm. (Found: C, 71·2; H, 12·2; N, 7·6%; *M*, 185. $C_{11}H_{23}NO$ requires C, 71·3; H, 12·5; N, 7·6%; *M*, 185).

(*b*) The *N*-acetylthiazolidine (1·08 g.) was desulphurised with Raney nickel (45 days old, pH 7·5). Gas-chromatographic analysis of the crude product (780 mg.) showed that it was a mixture of six compounds. Four of these, having retention times between 1 and 10 min. (PDEAS column at 165° with nitrogen as the carrier gas) were not identified and accounted for 25% of the recovered material. A compound having a retention time of 11 min. was collected (10 mg.) and distilled. The mass-spectrometric molecular weight of 183 and the fact that the 2,4-dinitrophenylhydrazone of heptanal (m. p. and mixed m. p. 104°) was obtained from it on heating with 2,4-dinitrophenylhydrazine sulphate showed that it was 1-(*N-ethylacetamido*)*hept-1-ene*, wich accounted for 16% of the recovered material. The other product (59%), retention time 14 min., was *N*-acetyl-*N*-ethylheptylamine, gas-chromatographically identical with the product from the previous experiment. Degassing of the nickel catalyst by heating for 2 hr. at 200°/0·15 mm. prior to desulphurisation increased the yield of enamine at the expense of the saturated analogue.

N-Acetyl-5α-Cholestane-3-spiro-2′-tetrahydro-1′,3′-thiazine (XIII).—A mixture of 5α-cholestan-3-one (300 mg.), 3-mercaptopropylamine (250 mg.), toluene-*p*-sulphonic acid monohydrate (10 mg.), and benzene (50 c.c.) was heated under a water-separator in a stream of nitrogen for 48 hr. The cooled solution was washed with water (3 × 10 c.c.) and the benzene distilled. The crude product (390 mg.) was crystallised from ethyl acetate and gave material of m. p. 128—129° (285 mg., 80%). The pure *5α-cholestane-3-spiro-2′-tetrahydro-1′,3′-thiazine* had m. p. 132—133°, $[\alpha]_D^{27}$ +30·4° (*c* 0·96) (Found: C, 78·2; H, 11·6; N, 3·0; S, 7·0. $C_{30}H_{53}NS$ requires C, 78·4; H, 11·6; N, 3·05; S, 7·0%). A solution of the tetrahydro-1,3-thiazine (187 mg.) in pyridine (4 c.c.) and acetic anhydride (0·4 c.c.) was kept at room temperature for 24 hr. Water (50 c.c.) was added and the mixture was extracted with methylene chloride (5 × 15 c.c.). The extracts were washed with water (3 × 10 c.c.) and the solvent distilled. Crystallisation of the residue from ethyl acetate gave the *N-acetyltetrahydro-1,3-thiazine* (185 mg., 96%), m. p. 182—183°, $[\alpha]_D^{25}$ +44·5° (*c* 0·63) (Found: C, 76·4; H, 11·2; N, 3·1; S, 6·6. $C_{32}H_{55}NOS$ requires C, 76·6; H, 11·05; N, 2·8; S, 6·4%) $\nu_{max.}$ (KBr) 1630 cm.$^{-1}$.

Desulphurisation of N-Acetyl-5α-cholestane-3-spiro-2′-tetrahydro-1′,3′-thiazine (XIII) *in Benzene*.—The *N*-acetyltetrahydro-1,3-thiazine (500 mg.) was desulphurised with Raney nickel (42 days old, pH 7·25). The solvent was evaporated from the washings to give a solid residue (352 mg.), m. p. 90—100°. A solution in methylene chloride was filtered through neutral alumina and the product (308 mg., 66%), m. p. 123—127°, crystallised from ethyl acetate to give the pure 3-(*N-propylacetamido*)-*5α-cholest-2-ene* (VIII; R = C_8H_{17}, R^1 = Ac, R^2 = Pr^n), m. p. 128—129°, $[\alpha]_D^{27}$ +58·5° (*c* 0·1) (Found: C, 81·7; H, 11·8; N, 2·9. $C_{32}H_{55}NO$ requires C, 81·8; H, 11·8; N, 2·9%).

The unsaturated amide (175 mg.), dissolved in a mixture of ethanol (150 c.c.) and hydrochloric acid (50 c.c.), was refluxed for 3 hr. The product was isolated with methylene chloride, the extracts being filtered through neutral alumina to give 5α-cholestan-3-one (87 mg.), m. p. and mixed m. p. 128—129°.

N-Acetyl-5α-androstane-3-spiro-2′-(4′-methoxycarbonyl)thiazolidine (VII; R = R^3 = H, R^1 = Ac, R^2 = CO_2Me).—To a solution of 5α-androstan-3-one (1·20 g.) in ethanol (30 c.c.) was added a solution of (+)-cysteine hydrochloride (710 mg.) and potassium acetate (760 mg.) in 50% aqueous ethanol (17 c.c.). After 24 hr. at room temperature the product was collected by filtration, washed with aqueous ethanol, and dried to give crude *5α-androstane-3-spiro-2′-thiazolidine-4′-carboxylic acid* (VII; R = R^1 = R^3 = H, R^2 = CO_2H) (1·52 g.), m. p. 230°. The crude thiazolidine (1·20 g.) was dissolved in pyridine (24 c.c.), acetic anhydride (2·4 c.c.) was added and the mixture was kept at room temperature for 3 hr. After acidification with dilute hydrochloric acid the crude *N-acetyl compound* (VII; R = R^3 = H, R^1 = Ac, R^2 = CO_2H) (1·26 g.), m. p. 260°, was filtered off. This product (1·00 g.), suspended in ether (50 c.c.) was treated with an excess of diazomethane in ether. After 30 min. the ether was evaporated and the residue crystallised from ethyl acetate to give the *N-acetyl methyl ester* (788 mg.), m. p. 224—226° $[\alpha]_D^{27}$ −33·0° (*c* 1·0) (Found: C, 69·4; H, 8·9; N, 3·15; S, 7·5. $C_{25}H_{37}NO_3S$ requires C, 69·3; H, 9·0; N, 3·2; S, 7·4%), $\nu_{max.}$ (KBr) 1740, 1650 cm.$^{-1}$.

Desulphurisation of N-Acetyl-5α-androstane-3-spiro-3′-(4′-methoxycarbonyl)thiazolidine (VII; R = R^3 = H, R^1 = Ac, R^2 = CO_2Me) *in Benzene*.—The *N*-acetylthiazolidine (400 mg.) was desulphurised with Raney nickel (17 days old, pH 7·4). The residue (295 mg.) was chromatographed in two portions on preparative silica gel chromatoplates developed with ethyl acetate. Extraction of one band gave 3-[N-(*methoxycarbonylethyl*)*acetamido*]-*5α-androst-2-ene* (VIII;

R = H, R^1 = Ac, R^2 = CHMe·CO_2Me) (205 mg., 55%), m. p. 125—128° (from ether), $[\alpha]_D^{27}$ +47° (*c* 1·0) (Found: C, 74·55; H, 10·1; N, 3·4. $C_{25}H_{39}NO_3$ requires C, 74·8; H, 9·8; N, 3·6%)], $\nu_{max.}$ (KBr) 1740, 1655 cm.$^{-1}$, while from the more polar band there was isolated 17 mg. of 3β-acetamido-5α-androstane (IX; R = R^2 = H, R^1 = Ac), which was identified by mixed m. p. and infrared comparison with an authentic specimen.[16]

N-*Acetyl-5α-cholestane-3-spiro-2′-(4′-methoxycarbonyl)thiazolidine* (VII; R = C_8H_{17}, R^1 = Ac, R^2 = CO_2Me, R^3 = H).—5α-Cholestan-3-one was condensed with (+)-cysteine hydrochloride and the product acetylated and then methylated to give the N-*acetyl methyl ester*, m. p. 209—211° (from ethanol), $[\alpha]_D^{25}$ −9·7° (*c* 1·0) (Found: C, 72·6; H, 10·0; N, 2·8. $C_{33}H_{55}NO_3S$ requires C, 72·6; H, 10·0; N, 2·6%), $\nu_{max.}$ (KBr) 1722, 1655 cm.$^{-1}$.

Desulphurisation of N-*Acetyl-5α-cholestane-3-spiro-2′-(4′-methoxycarbonyl)thizolidine* (VII; R = C_8H_{17}, R^1 = Ac, R^2 = CO_2Me, R^3 = H) *in Benzene*.—The *N*-acetylthiazolidine (1·12 g.) was desulphurised with Raney nickel (15 days old, pH 8·2). The crude product (886 mg.) was dissolved in methylene chloride and chromatographed on a silica column (20 g.) Ethyl acetate eluted 3-[N-(1-*methoxycarbonylethyl)acetamido*]-5α-*cholest-2-ene* (VIII; R = C_8H_{17}, R^1 = Ac, R^2 = CHMe·CO_2Me) (670 mg., 64%), m. p. 133°, $[\alpha]_D^{27}$ +53° (*c* 1·0) (Found: C, 76·5; H, 10·5; N, 3·0. $C_{33}H_{55}NO_3$ requires C, 77·1; H, 10·8; N, 2·7%), $\nu_{max.}$ (KBr) 1735, 1645 cm.$^{-1}$. Ethyl acetate then eluted 3β-acetamido-5α-cholestane (IX; R = C_8H_{17}, R^1 = Ac, R^2 = H) (85 mg.) m. p. and mixed m. p. 249—250°.

5α-*Cholestane-3-spiro-2′-thiazolid-4′-one* (XIV).—A mixture of 5α-cholest-3-one (10 g.), thioglycolic acid (20 g.), ammonium carbonate (22 g.), and benzene (150 c.c.) was heated under a water-separator for 20 hr. Most of the benzene was evaporated and a methylene chloride solution of the residue, after being washed with water (4 × 200 c.c.), was filtered through a column of neutral alumina (110 g.). Methylene chloride eluted material of m. p. 260—264° (3·1 g., 25%). The pure *thiazolidone* (XIV, isomer A) had m. p. 264—265° (from ethyl acetate), $[\alpha]_D^{35}$ +20·6° (*c* 1·07) (Found: C, 75·8; H, 10·7; N, 3·2; S, 7·0. $C_{29}H_{49}NOS$ requires C, 75·8; H, 10·4; N, 3·05; S, 7·2%), $\nu_{max.}$ (KBr) 3110, 3020, 1670 cm.$^{-1}$. Methylene chloride–methanol (50 : 1) eluted material of m. p. 310° (6·5 g., 55%). The pure *thiazolidone* (XIV, isomer B) had m. p. 312—314° (from ethyl acetate), $[\alpha]_D^{36}$ +26·6° (*c* 1·02) (Found: C, 76·0; H, 10·6; N, 3·2; S, 7·2%), $\nu_{max.}$ (KBr) 3100, 3020, 1690 cm.$^{-1}$.

Desulphurisation of 5α-*Cholestane-3-spiro-2′-thiazolid-4′-one* (XIV, isomer A) *in Benzene*.—The thiazolidone (1·0 g.) was desulphurised with Raney nickel (20 days old, pH 7·6). The residue (525 mg.) was dissolved in methylene chloride and chromatographed on a column of silica (10 g.). Methylene chloride eluted 5α-cholestan-3-one (80 mg., 9%), identified by its infrared spectrum. Methylene chloride then eluted 3-*acetamido-5α-cholest-2-ene* (VIII; R = C_8H_{17}, R^1 = Ac, R^2 = H) (254 mg., 27%), m. p. 215° (from ethyl acetate), $[\alpha]_D^{25}$ +68·1° (*c* 1·0) (Found: C, 80·9; H, 11·6; N, 3·2%; *M*, 427. $C_{29}H_{49}NO$ requires C, 80·4; H, 11·55; N, 3·2%; *M*, 427], $\nu_{max.}$ (KBr) 1650 cm.$^{-1}$, $\nu_{max.}$ ($CHCl_3$) 1675 cm.$^{-1}$. Finally, methylene chloride eluted 3β-acetamido-5α-cholestane (IX; R = C_8H_{17}, R^1 = Ac, R^2 = H) (34 mg., 4%), m. p. and mixed m. p. 245—247°.

Desulphurisation of 5α-*Cholestane-3-spiro-2′-thiazolid-4-one* (XIV, isomer B) *in Benzene*.—The thiazolidone (1·5 g.) was desulphurised with Raney nickel (14 days old, pH 8·2). By a procedure similar to that described in the previous experiment there was isolated 5α-cholestan-3-one (141 mg., 11%), 3-acetamido-5α-cholest-2-ene (200 mg., 14%), and 3β-acetamido-5α-cholestane (305 mg., 22%).

Cyclohexanespiro-2′-thiazolid-4′-one (XV).—Ammonium carbonate (12 g.) and thioglycolic acid (12 c.c.) were added to cyclohexanone (5 g.) in benzene (300 c.c.) and the mixture was heated under a water-trap for 24 hr. Most of the benzene was evaporated and replaced by methylene chloride. After washing with water the solution was filtered through neutral alumina and the solvent evaporated to give the *thiazolidone* (8·3 g., 95%), m. p. 180—181°. An analytical sample (3·9 g.), m. p. 181—182°, was obtained after four crystallisations from ethyl acetate (Found: C, 55·9; H, 7·8; N, 8·5; S, 18·5. $C_8H_{13}NOS$ requires C, 56·1; H, 7·65; N, 8·2; S, 18·7%), $\nu_{max.}$ (CS_2) 3120, 3020, 1680 cm.$^{-1}$.

Desulphurisation of Cyclohexanespiro-2′-thiazolid-4′-one (XV) *in Benzene*.—(*a*) The thiazolidone (1·0 g.) was desulphurised with Raney nickel (5 days old, pH 8·9). The combined washings were filtered and evaporated to give the product (517 mg. 63%), m. p. 99—101°. On crystallisation from hexane pure *N*-acetylcyclohexylamine m. p. 103—104° (lit.,[10] 104°) was obtained.

(*b*) The thiazolidone (150 mg.) was desulphurised with Raney nickel (23 days old, pH 7·8). The product was an oil (92 mg.) which was separated into three components by preparative gas chromatography on a 15% PDEAS column (4·5 mm. × 1 m.) at 193° using nitrogen as the carrier gas. The fraction having a retention time of 2·2 min. was a solid, m. p. 69°, and had an infrared spectrum identical with that of acetamide. The fraction having a retention time of 6·8 min. was also a solid, m. p. 103—104°, and the infrared spectrum was identical with that of *N*-acetylcyclohexylamine. The fraction having a retention time of 12 min. was an oil and was identified by its mass spectrum (M^+ 139) as 1-*acetamidocyclohex*-1-*ene*. These three products were present in the ratio 3 : 2 : 4, respectively.

5α-*Cholestane*-3-*spiro*-2′-(5′-*phenyl*)*thiazolidine* (VII; R = C_8H_{17}, $R^1 = R^2 = H$, R^3 = Ph). A mixture of 5α-cholestan-3-one (4 g.), 2-mercapto-2-phenylethylamine (2 g.), toluene-*p*-sulphonic acid (100 mg.), and methanol (400 c.c.) was heated under reflux for 1 hr. A quarter of the methanol was distilled off and a crystalline product (2·8 g.), m. p. 185—189°, was collected from the cooled solution. After saturation with hot ethyl acetate, material of m. p. 193—195° (1·4 g., 23%) was obtained. The pure *thiazolidine* (isomer A) had m. p. 195—196° (from ethyl acetate–chloroform), $[\alpha]_D^{26}$ −6·0° (*c* 1·0) (Found: C, 80·6; H, 10·8; N, 2·5; S, 6·1. $C_{35}H_{55}NS$ requires C, 80·6; H, 10·6; N, 2·7; S, 6·15%), $\nu_{max.}$ ($CHCl_3$) 2940, 1600 cm.$^{-1}$.

The methanol mother-liquors were evaporated to small volume and cooled, and the crude product was collected and crystallised from ethyl acetate to give the *thiazolidine* (isomer B) (320 mg., 5%), m. p. 134—136°, $[\alpha]_D^{28}$ +44·0° (*c* 1·0) (Found: C, 80·5; H, 10·5; N, 2·6; S, 6·2%), $\nu_{max.}$ ($CHCl_3$) 2940, 1590 cm.$^{-1}$. After chromatography of the mother-liquors on neutral alumina a further 350 mg. of isomer (B), m. p. 134—136°, were obtained, in addition to 5α-cholestan-3-one (250 mg.).

Lithium in Ethylamine Desulphurisation of 5α-*Cholestane*-3-*spiro*-2′-*thiazolidine* (VII; R = C_8H_{17}, $R^1 = R^2 = R^3 = H$).—A solution of the thiazolidine (500 mg.) in anhydrous ethylamine (100 c.c.) was cooled to −10° and small pieces of lithium (1·0 g.) were added. The mixture was stirred vigorously, a persistent blue colour appearing after 15 min. After 90 min. the colour was dispersed with water (3 c.c.) and the ethylamine was allowed to evaporate Water (250 c.c.) was added and the mixture was extracted with methylene chloride (3 × 75 c.c.) to give a crude product (462 mg.), m. p. 73—80°, which was filtered through neutral alumina in methylene chloride containing 1% of methanol and crystallised from methanol to give 3β-(*N*-ethylamino)-5α-cholestane (IX; R = C_8H_{17}, R^1 = Et, R^2 = H) (406 mg., 87%), m. p. 81—83°, mixed m. p. 82—84°, $[\alpha]_D^{28}$ +19·2° (*c* 1·0).

Preparation and Desulphurisation of N-*Acetyl*-2,2,4,4-[$^2H_4$]-5α-*androstane*-3-*spiro*-2′-*thiazolidine*.—5α-Androstan-3-one (308 mg.), m. p. 102°, was added to a solution of sodium (53 mg.) in CH_3OD (6 c.c.). The mixture was refluxed and deuterium oxide (1 c.c.) added. After 20 min. the solvents were evaporated *in vacuo*. The residue was dissolved in CH_3OD (6 c.c.) and deuterium oxide (1 c.c.) and, after refluxing for 20 min., the solvents were evaporated. This procedure was repeated twice more before washing in ethereal solution (20 c.c.) of the residue with deuterium oxide (3 × 4 c.c.). The ether was evaporated to give 2,2,4,4-[$^2H_4$]-5α-androstan-3-one (30 mg.). The mass spectrum showed [$^2H_4$], 90% and [$^2H_3$], 10%.

Deuterium oxide (2 × 10 c.c.) was evaporated *in vacuo* from 2-mercaptoethylamine hydrochloride (300 mg.) and deuterium oxide (2 × 6 c.c.) was evaporated *in vacuo* from toluene-*p*-sulphonic acid (191 mg.). The residues were combined and dissolved in benzene (130 c.c.), 2,2,4,4-[$^2H_4$]-5α-androstan-3-one (185 mg.) was added and the mixture was refluxed for 17 hr. After washing the cooled solution with water (3 × 100 c.c.) the benzene was evaporated and potassium carbonate (750 mg.) and acetic anhydride (0·5 c.c.) were added to a solution of the residue in ether (20 c.c.). The mixture was kept at room temperature for 10 hr. and was then filtered and the solvent evaporated to give the *N*-acetylthiazolidine (157 mg.), m. p. 183°, identified by its mass spectrum (d_1, 4%; d_2, 18%; d_3, 37%; d_4, 39%). This product was desulphurised with Raney nickel (2 g., 26 days old, pH 7·4) in benzene (30 c.c.), the mixture being refluxed for 23 hr. The product (136 mg.) was separated into three compounds on a preparative silica thin-layer chromatoplate. From one band 3-(*N*-ethylacetamido)-2,4,4-[$^2H_3$]-5α-androst-2-one (12 mg.), m. p. 173° (from ethyl acetate), identified by its mass spectrum (d_0, 3%; d_1, 12%; d_2, 34%; d_3, 48%) was obtained. From a second band 3β-acetamido-2,2,4,4-[$^2H_4$]-5α-androstane (6 mg.), identified by its mass spectrum (d_0, 20%; d_1, 27%; d_2, 16%; d_3, 20%; d_4, 17%) was obtained after crystallisation from ethyl acetate. From the

mother liquors 3β-(*N*-ethylacetamido)-2,2,4,4-[$^2H_4$]-5α-androstane was obtained. Its mass spectrum showed (d_0, 9%; d_1, 11%; d_2, 12%; d_3, 29%; d_4, 35%).

The authors are indebted to the National Institute of Health of the U.S. Public Health Service for a research grant and to the Rockefeller Foundation for a fellowship to M. A. K. while on leave from the University of Poznan, Poland.

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