p-MePhSO$_3$H: Triterpene alcohol (50 mg), dissolved in 40 mL of *i*-PrOH or AcOH containing 25 mg of *p*-toluenesulfonic acid monohydrate, was stirred at 80 °C. The isomerization product, extracted with diethyl ether, was neutralized by washing it with a sodium bicarbonate solution and then with water and dried over anhydrous sodium sulfate.

Separation of the Isomerization Products. The reaction product obtained by means of a preparative-scale isomerization of **1a** was separated into three bands, which were cochromatographed with authentic 5α-cholestane (R_c 5.6; the R_c value of cholesterol was taken as 1.0), **5a** (R_c 2.7), and **1a**/**3a** (R_c 2.1), respectively, on silica gel TLC. The oily material from the least polar band exhibited a number of peaks with short retention times (RRT <0.5) in GLC. This was regarded as a mixture of dehydrated triterpenes, since it had strong IR absorptions (capillary; ν_{max} 2950, 2850, 1460, 1380, 1370, 1363 cm^{-1}) correlated with steroidal hydrocarbons devoid of hydroxy groups and since the spectrum was quite similar to that of 5α-cholestane (KBr; ν_{max} 2950, 2850, 1460, 1380, 1370 cm^{-1}). The fraction from the medium-polar band was a mixture of two cucurbitane-type isomers (**5a** and **6a**). When subjected to argentic TLC after acetylation, this yielded the acetates of pure **5a** and **6a** separated. The fraction from the most polar band was a mixture of three lanostane-type isomers and the starting material. After acetylation, this was submitted to repetitive argentic TLC, which eventually led to the isolation of **2a**, **3a**, and **4a** as the acetate derivatives. The isolation of each reaction product from a preparative-scale isomerization of **1b** was performed in the same way as has been described above for the reaction product of **1a**.

Physical Data. For the melting points, the R_c values in argentic TLC, and the RRT in the GLC of the acetate derivatives of the triterpene alcohols described here, see Table II, and for the ^{1}H NMR data of the acetates of new and uncommon triterpene alcohols, see Table III. The mass spectral data (m/z > 200) for those triterpene acetates listed in Table III are given below. As for **6a** acetate, the ^{13}C NMR data also are described below.

5α-Lanosta-7,24-dien-3β-ol (2b) acetate: MS, m/z 468 (M$^+$, relative intensity, 39), 453 (92), 408 (6), 393 (100), 355 (31), 315 (13), 311 (11), 295 (13), 270 (24), 257 (18), 255 (31), 243 (15), 241 (13), 229 (18), 215 (11), 201 (11).

5α-Lanosta-7,25-dien-3β-ol (2c) acetate: MS, m/z 468 (M$^+$, relative intensity 33), 453 (86), 408 (5), 393 (100), 337 (16), 289 (10), 283 (24), 270 (23), 257 (16), 255 (33), 229 (19), 227 (12), 215 (12).

5α-Lanosta-8,25-dien-3β-ol (3c) acetate: MS, m/z 468 (M$^+$, relative intensity 37), 453 (80), 393 (100), 283 (16), 241 (12), 229 (13), 215 (13).

5α-Lanosta-9(11),25-dien-3β-ol (4c) acetate: MS, m/z 468 (M$^+$, relative intensity 24), 453 (67), 393 (100), 355 (71), 283 (12), 255 (12), 241 (12), 229 (14), 215 (12), 201 (12).

10α-Cucurbit-5-en-3β-ol (5a) acetate: MS, m/z 470 (M$^+$, relative intensity 5), 455 (14), 410 (18), 395 (22), 276 (100), 261 (77).

Anhydrolitsomentol (5b) acetate: MS, m/z 468 (M$^+$, relative intensity 4), 453 (4), 408 (28), 393 (14), 274 (100), 259 (69), 231 (16), 205 (16).

10α-Cucurbita-5,25-dien-3β-ol (5c) acetate: MS, m/z 468 (M$^+$, relative intensity 3), 453 (7), 408 (26), 393 (17), 274 (100), 259 (46), 218 (10), 205 (12).

Cucurbit-5(10)-en-3β-ol (6a) acetate: high-resolution MS, m/z 470.4128 (M$^+$, $C_{32}H_{54}O_2$, calcd 470.4121, relative intensity 5), 455,3843 ($C_{31}H_{51}O_2$, 28), 410.3932 ($C_{30}H_{50}$, 84), 395.3647 ($C_{29}H_{47}$, 100), 367.3346 ($C_{27}H_{33}$, 10), 297.2543 ($C_{22}H_{33}$, 10), 288.2772 ($C_{21}H_{36}$, 5), 273.2539 ($C_{20}H_{33}$, 7), 219.2085 ($C_{16}H_{27}$, 7), 207.2088 ($C_{15}H_{27}$, 26); ^{13}C NMR δ 15.2 (C_{31}), 19.2 (C_{32}), 21.3 (CH_3OCO), 22.5 (C_{26}), 22.8 (C_{27}), 24.1 (C_{23}), 28.0 (C_{25}), 36.2 (C_{20}), 36.5 (C_{22}), 39.5 (C_{24}), 78.3 (C_3), 132.1 and 133.6 (C_5 and C_{10}), 171.0 (MeOCO), 18.4, 18.6, 21.5, 22.1, 24.3, 27.9, 31.5, 32.0, 33.2, 34.1, 36.8, 42.7, 45.7, 50.0, 50.8. The partial assignment of the ^{13}C NMR given above was based on the comparison with the literature data.[14]

Cucurbita-5(10),24-dien-3β-ol (6b) acetate: MS, m/z 468 (M$^+$, relative intensity 9), 453 (18), 408 (100), 393 (98), 286 (9), 217 (24), 205 (65), 203 (24), 201 (15).

Cucurbita-5(10),25-dien-3β-ol (6c) acetate: MS, m/z 468 (M$^+$, relative intensity 10), 453 (30), 408 (100), 393 (95), 297 (13), 217 (11), 205 (33).

Acknowledgment. We thank Drs. T. Takido and M. Aimi for NMR and mass spectra. Our thanks are also due to Prof. Y. Ichinohe for valuable comments.

Registry No. **1a**, 4657-58-3; **1a** acetate, 4575-74-0; **1b**, 469-38-5; **1b** acetate, 1259-10-5; **1c** acetate, 70587-99-4; **2a** acetate, 4488-99-7; **2b** acetate, 6562-09-0; **2c** acetate, 88392-47-6; **3a** acetate, 1724-19-2; **3b** acetate, 2671-68-3; **3c** acetate, 88392-48-7; **4a** acetate, 1180-88-7; **4b** acetate, 55570-91-7; **4c** acetate, 88392-49-8; **5a**, 35030-61-6; **5a** acetate, 33593-25-8; **5b**, 35012-08-9; **5b** acetate, 35030-57-0; **5c** acetate, 88392-50-1; **6a**, 88392-51-2; **6a** acetate, 88392-52-3; **6b** acetate, 88392-53-4; **6c** acetate, 88392-54-5.

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Regiospecific Synthesis of 9-Desoxoerythromycin A

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Recently, we described the synthesis of cyclic thionocarbonate **1**[1] in conjunction with an investigation into erythromycin aglycon modifications. In the course of the investigation we recognized **1** as a potential entry into aglycon deoxygenated erythromycins. This note details the synthesis of 9-desoxoerythromycin A (**3**).

We anticipated that exposure of **1** to tri-*n*-butyltin hydride in the presence of a radical initiator[2] would lead to a mixture of C-9-desoxo (**3**) as well as C-11-desoxy (**5**) materials, and we fully expected the regioisomers to be amenable to separation via chromatography. Thus, we believed the sequence would permit rapid preparation of reasonable quantities of **3** and **5**, although it would most certainly not be regiospecific. When the tin radical reaction was attempted, it did result in the preparation of **3** and **5**, as well as a number of other products. Unfortunately, the yield of the desired materials was extremely low (<10%) and separation of these materials proved tedious. Thus, we sought an alternative synthetic route.

In our previous report on erythromycin aglycon modifications,[1] we described the regiospecific and stereospecific incorporation of nucleophiles at the C-9 position of erythromycin A via nucleophilic displacements on thionocarbonate **1**. Since it is known[3] that thionocarbonates are susceptible to rearrangement to thiocarbonates, we considered the possibility of regiospecifically incorporating sulfur into the C-9 position of **1** via its conversion to thiocarbonate **2**. In principle, this sequence would permit the preparation of only *one* desoxo material, after desulfurization with Raney Ni. Thus, exposure of **1** to KI in DMF solvent afforded thiocarbonate **2**. The structural assignment of the thiocarbonate as a C-9-thia β-stereoisomer was established by ^{13}C NMR deuterium isotope experiments in analogy to those previously reported.[1,4] When **2** was treated with Raney Ni in ethanol solvent, the corresponding 9-desoxoerythromycin A (**3**) was smoothly produced. Alternatively, thiocarbonate **2** may first be

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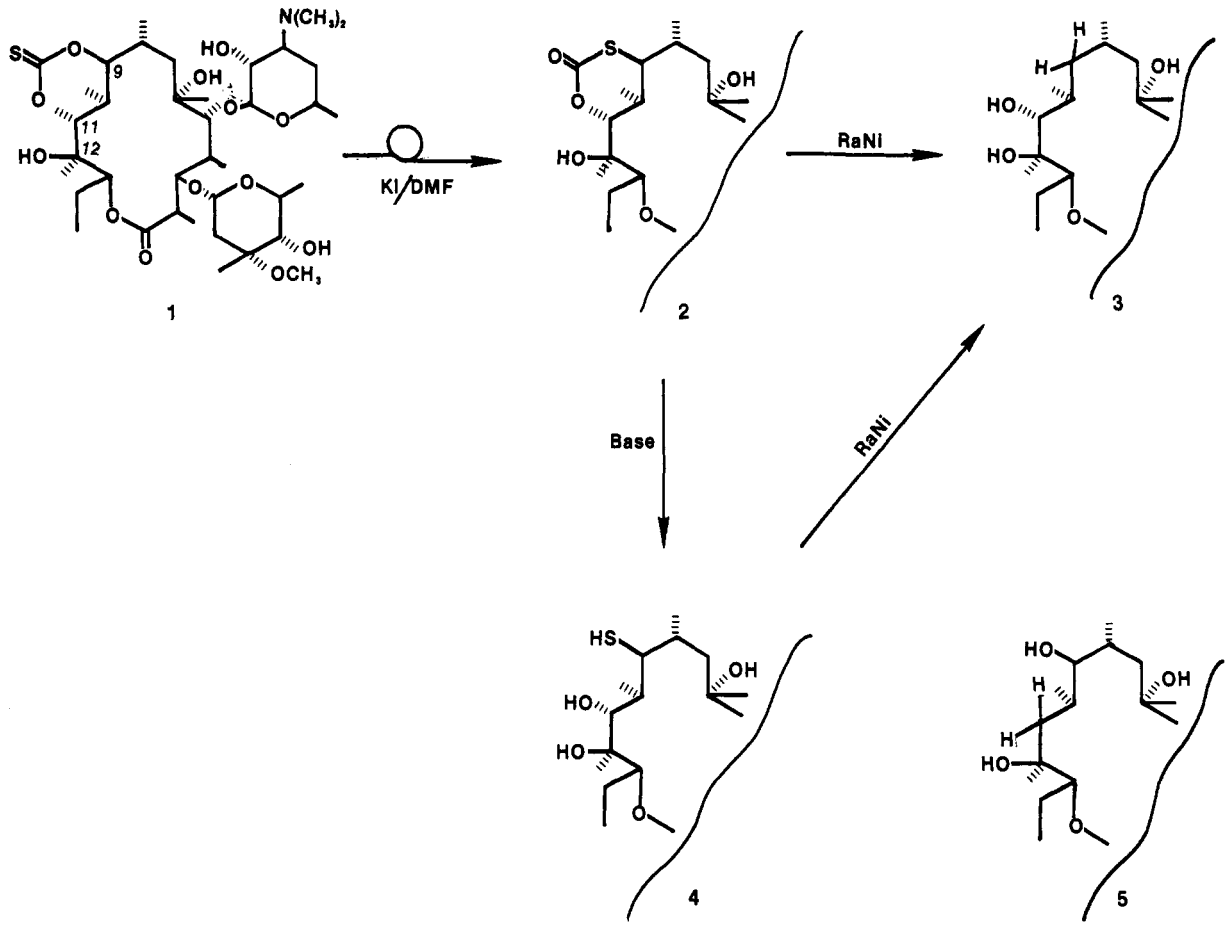
0022-3263/84/1949-0712$01.50/0

Scheme I



converted to the corresponding C-9-β-mercaptan 4 upon exposure to aqueous base and subsequently desulfurized to 3 (Scheme I summarizes the overall sequence). The overall yield of crystalline 3 was 60%.

In summary, therefore, we have been able to synthesize 9-desoxoerythromycin A (3) directly, without recourse to a blocking–deblocking sequence, via the regiospecific rearrangement of thionocarbonate 1 to thiocarbonate 2 and subsequent desulfurization.

Experimental Section

General Methods. NMR spectra were obtained on a Varian XL-100 or a Bruker 250-MHZ spectrometer. The preparation of thionocarbonate 1 has been reported.[1]

Preparation of 9,11-Cyclic-Thiocarbonate Erythromycin A (2). To a DMF solution (50 mL) of 9,11-cyclic-thionocarbonate erythromycin A (1; 5.0 g, 6.4 mmol) was added in one portion KI (10 g, 60.2 mmol), and the resulting solution was allowed to stir under nitrogen at 130 °C for 3 h. After this period, TLC [silica/$CHCl_3$/MeOH/NH_3 (9:1:0.1)] showed no remaining starting material on the basis of the disappearance of UV activity. The reaction mixture was added to a mixture of methylene chloride/water (200 mL:150 mL), and the pH was adjusted to 11 with aqueous sodium hydroxide (6 N). The organic layer was separated, washed with water (4 × 100 mL) and saturated aqueous sodium chloride (1 × 100 mL), and dried over anhydrous sodium sulfate. The solution was concentrated in vacuo, affording the crude thiocarbonate 2 as a pale yellow solid (5.2 g). The crude thiocarbonate was crystallized from diethyl ether to afford colorless, crystalline 2 (4.1 g, mp 241–246 °C): ^1H NMR ($CDCl_3$) δ 0.91 (t), 1.10 (d), 1.15–1.40 (m), 1.45–2.00 (m), 2.15 (br d), 2.30 (s), 2.35–2.55 (m), 2.65 (dq), 3.09 (br dd), 3.35 (s), 3.60 (br d), 3.95 (dd), 4.05 (s), 4.10 (br s), 4.65 (d), 4.90–5.00 (m); ^{13}C NMR ($CDCl_3$) δ 176.1 (off-resonance, s), 167.0 (s), 101.4 (d), 94.6 (d), 83.9 (d), 79.7 (d), 77.3, 75.8, 74.1, 72.9, 72.8, 72.7, 70.5 (d), 69.1 (d), 65.7 (d), 64.5 (d), 58.0 (d), 48.9 (q), 43.9, 43.6, 40.0 (q), 38.1, 34.3, 28.8, 26.8, 22.5, 21.8, 21.2, 20.8, 19.5, 17.5, 16.8, 14.9, 12.5, 11.0, 8.8.

Anal. Calcd for $C_{38}H_{67}O_{13}NS$: C, 58.67; H, 8.68; N, 1.80; S, 4.12. Found: C, 58.73; H, 8.71; N, 1.79; S, 4.23.

Preparation of 9-Desoxoerythromycin A (3). To a stirring ethanol solution (80 mL) of 2 (2.0 g, 2.5 mmol) maintained under a nitrogen atmosphere was added in one portion Raney Ni (12.0 g) and the resulting slurry heated to reflux. After 2 h, TLC [silica/$CHCl_3$/MeOH/NH_3 (6:1:0.1)] indicated no remaining starting material and one, major more polar material. The mixture was allowed to cool to room temperature and filtered through Celite and the Celite was washed with ethanol (3 × 100 mL). The filtrate and washes were concentrated in vacuo, affording crude 3 (1.96 g). The crude material was crystallized from isopropyl ether (25 mL), affording crystalline, colorless 3 (1.3 g, mp 197–200 °C): ^1H NMR (Me_2SO-d_6) δ 0.85 (t), 0.95 (d), 1.10–1.40 (m), 1.50–2.00 (m), 2.30 (s), 2.35–2.60 (m), 2.65 (br s), 2.80 (br dd), 2.90 (d), 3.10 (t), 3.20–3.30 (m), 3.35 (s), 3.50–3.70 (m), 3.81 (d), 4.05 (m), 4.10 (m), 4.70 (d), 4.80 (dd), 5.15 (br d); ^{13}C NMR ($CDCl_3$) δ 174.9 (off-resonance, s), 101.6 (d), 95.6 (d), 81.6 (d), 78.9 (d), 77.6, 76.6, 74.4, 73.7, 72.5, 70.8, 69.2 (d), 67.3 (d), 65.0 (d), 64.1 (d), 48.7 (q), 40.3 (q), 38.7, 37.9, 29.2, 27.6, 25.1, 25.0, 23.2, 22.8, 21.3, 21.1, 18.6, 17.1, 15.5, 14.8, 10.9, 9.4.

Anal. Calcd for $C_{37}H_{69}O_{12}N$: C, 61.72; H, 9.66; N, 1.95. Found: C, 61.20; H, 9.46; N, 1.93.

Preparation of 9-Mercaptoerythromycin A (4). To an isopropyl alcohol/water solution (5 mL:10 mL) of 2 (2.5 g, 3.2 mmol) was added in one portion LiOH (1.25 g, 52.2 mmol) and the resulting mixture was stirred at room temperature. After 4.5 h, TLC [silica/formamide inpregnated/$CHCl_3$/isopropyl alcohol (95:5) and silica/$CHCl_3$/MeOH/NH_3 (9:1:0.1)] showed no remaining starting material. The reaction mixture was filtered, concentrated in vacuo to one-half its volume, and added to a stirring mixture of methylene chloride/water (100 mL:50 mL). The pH was adjusted to 8.3 and the organic layer was separated, dried over anhydrous sodium sulfate, and concentrated in vacuo, affording a colorless solid (2.4 g). The solid was dissolved in a methanol/chloroform solution (95:5) and filtered through a bed

of silica eluted with methanol/chloroform/ammonia solvents (93:7:0.04). The solute was concentrated in vacuo, affording colorless, crude 4 (1.8 g), which was crystallized from isopropyl ether to afford colorless, crystalline 4 (1.65 g): ^{1}H NMR ($CDCl_3$) δ 0.91 (t), 1.10–1.50 (m), 1.60–2.00 (m), 2.30 (s), 2.40–2.70 (m), 2.85 (dd), 3.08 (t), 3.35 (s), 3.50–3.60 (m), 3.70 (br s), 3.95 (br t), 4.00 (m), 4.65 (d), 4.95–5.05 (m); ^{13}C NMR ($CDCl_3$) δ 176.5 (off-resonance, s), 101.8 (d), 94.8 (d), 84.1 (d), 77.5, 77.3, 76.6, 73.3, 72.7, 70.4, 70.3, 69.3, 65.8 (d), 65.1 (d), 54.8 (d), 49.1 (q), 44.0, 43.7, 40.2 (q), 39.9, 36.0, 34.4, 32.0, 28.6, 22.7, 22.1, 21.4, 21.0, 17.9, 16.7, 15.3, 12.5, 11.3, 9.1.

Anal. Calcd for $C_{37}H_{69}O_{12}NS$: C, 59.90; H, 9.25; N, 1.86. Found: C, 59.51; H, 9.27; N, 2.01.

Acknowledgment. We thank R. Ware and Dr. E. Whipple for assistance in obtaining spectral data and invaluable discussions with regard to the interpretations.

Registry No. 1, 87902-84-9; 2, 88377-46-2; 3, 88377-47-3; 4, 88377-48-4.

Secondary Enamide and Thioenamide Photochemistry. A New Spiroannelation Method

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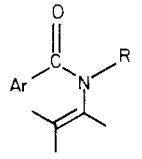
Owing to mesomerism, which confers to the amide group a partial double bond character, aromatic enamides, a class of compounds in which this chromophore connects two unsaturated systems, possess a marked degree of hexatrienic character. This property induces most of their photochemical reactions and thus irradiation of a great number of these compounds, particularly type a (R ≠ H),

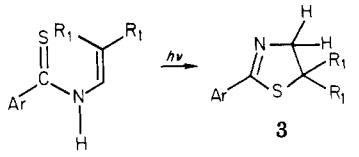


type a, R ≠ H
type b, R = H

results in stilbene–phenanthrene-like photoconversion, providing a general approach toward a wide variety of six-membered lactams.[1] To our knowledge the only exceptions concern some of these models in which the double bond is acyclic. Their irradiation leads mainly to aromatic enamino ketones,[2,3] products of photo-Fries rearrangement.

Surprisingly, few reports have dealt with the photochemical properties of type b (R = H) secondary enamides. Ninomiya[4] only reported recently an elegant synthesis of haemanthidine that proceeds via photocyclization of a secondary enamide in which the double bond α to the nitrogen atom is further conjugated with a carbonyl group. Within the framework of our systematic studies of the photochemistry of conjugated hexatrienic systems[3,5] we have therefore investigated the photochemical behavior of a number of these heteroatomic systems. The results obtained led us to undertake a comparative study of their sulfur analogues.

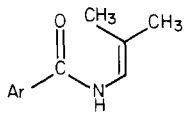
Scheme I



2

a, Ar = Ph; R_1 = CH_3
b, Ar = α-naphthyl; R_1 = CH_3
c, Ar = *o*-biphenylyl; R_1 = CH_3
d, Ar = Ph; R_1,R_1 = $(CH_2)_5$
e, Ar = α-naphthyl; R_1,R_1 = $(CH_2)_5$
f, Ar = β-naphthyl; R_1,R_1 = $(CH_2)_5$
g, Ar = *o*-biphenylyl; R_1,R_1 = $(CH_2)_5$
h, Ar = CH_2Ph; R_1,R_1 = $(CH_2)_5$

Enamides **1a–c** are readily accessible by direct condensation of the appropriate aromatic amide (phenyl-, α-naphthyl-, and *o*-biphenylylcarboxamide) with isobutyraldehyde. Although many problems may apparently arise from the use of aliphatic aldehydes,[6] the desired enamides were obtained exclusively when the α,β-disubstituted aldehyde was used.



1a, Ar = phenyl
b, Ar = α-naphthyl
c, Ar = *o*-biphenylyl

Irradiation of secondary enamides **1a–c** in neutral solvent and under various conditions left the starting compounds unchanged. Long-time irradiation (3 days) resulted mainly in degradation products and polymeric material. This absence of photoreactivity has been recently observed for rather similar systems,[7] and it was then thought that it might be of interest to investigate the photochemical behavior of the sulfur analogues of **1a–c**. There are indeed many examples of dramatic differences in the photochemical reactions of carbonyl and thiocarbonyl compounds. For example, while benzanilide is photoconverted into phenanthridinone,[8] irradiation of thiobenzanilide has been reported to yield 2-phenylbenzo[*b*]thiazole.[9] We have also recently observed that some acyclic aromatic enamides give rise photochemically to Fries rearrangement products whereas their thio analogues photocyclize normally to yield isoquinolinethione derivatives.[3] On the other hand the thioenamide group has been reported to add easily carbon–carbon double bonds inter-[10,11] and intramolecularly[12] and this aptitude could be interesting for our models.

The synthesis of thioenamides **2a–c** could be accomplished by treating the amide with P_2S_5 under a variety of conditions,[13,14] but the best sulfurating agent with re-

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