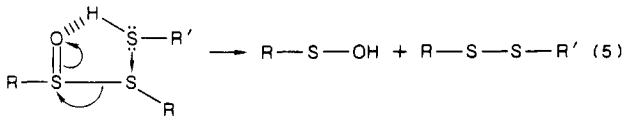
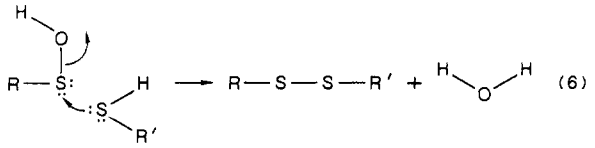
been evoked in reactions believed to involve sulfenic acids. On the basis of the greater than 50% isolated yield of disulfide and the absence of any thiosulfonate or thiolsulfonate-derived products, we do not believe that a thermal disproportionation mechanism can account for the formation of disulfide. Therefore, we favor a nucleophilic displacement at sulfur of thiosulfinate by thiol aided by a "push-pull" weakening of the S-S bond (eq 5).[14] Of



course, one cannot rule out the formation of disulfides by direct nucleophilic attack of thiol on the sulfur of sulfenic acid (eq 6).[11]



Experimental Section

General Procedure for the Preparation of Starting Materials. The specific example given for the preparation of 2-[(2-pyridinylmethyl)sulfinyl]-1*H*-benzimidazole (entry 1, Table I) is representative of a general procedure used for the synthesis of the starting materials.

a. To a solution of sodium hydroxide (8.0 g, 0.2 mol) in water (20 mL) was added ethanol (200 mL) followed by 2-mercaptobenzimidazole (16.4 g, 0.1 mol). The yellow solution was treated with 2-picolyl chloride hydrochloride (16.4 g, 0.1 mol) and heated under reflux with stirring for 2.5 h. The chilled reaction mixture was filtered, the solid was washed with absolute ethanol (50 mL), and the filtrate was concentrated under reduced pressure, azeotroped with toluene (150 mL), treated with acetone (250 mL), and filtered. The filtrate was removed under reduced pressure to give a beige solid. Recrystallization from ethanol–water (1:1) afforded 22.3 g of 2-[(2-pyridinylmethyl)thio]-1*H*-benzimidazole: mp 100–102 °C; NMR ($CDCl_3$) δ 4.4 (s, 2, CH_2), 6.98–7.72 (m, 7, Ar H), 8.53 (d, 1, Ar H), 9.3–11.3 (br s, 1, NH). Anal. Calcd for $C_{13}H_{11}N_3S$: C, 64.70; H, 4.59; N, 17.41; S, 13.28. Found: C, 64.41; H, 4.63; N, 18.35; S, 13.23.

b. A vigorously stirred solution of 2-[(2-pyridinylmethyl)-thio]-1*H*-benzimidazole (7.24 g, 0.03 mol) in chloroform (40 mL) was cooled to 0–5 °C (internal temperature) and treated during 10 min with solid *m*-chloroperbenzoic acid (6.1 g, 0.0353 mol) in small portions. The reaction mixture was further stirred for 10 min, the precipitated benzoic acid was filtered off, methylene chloride (30 mL) was added, and the organic layer was washed with a saturated solution of sodium bicarbonate (3 × 25 mL), water (2 × 25 mL) and saturated brine, and the organic solvent was dried through anhydrous Na_2SO_4. Removal of the solvent in vacuo gave the crude product, which was recrystallized from acetonitrile to yield 5.94 g of 2-[(2-pyridinylmethyl)sulfinyl]-1*H*-benzimidazole: mp 154–156 °C; IR ($CHCl_3$, cm^{-1}) 3063, 2970, 2890, 2810, 1600, 1500, 1480, 1471, 1438, 1270, 1136, 1110, 1091, 1009; NMR ($CDCl_3$) δ 4.37 (s, 2, SCH_2), 6.98–7.72 (m, 7, Ar H), 8.53 (dd, 1 Ar H). Anal. Calcd for $C_{13}H_{11}N_3OS$: C, 60.68; H, 4.31; N, 16.33; S, 12.46. Found: C, 60.28; H, 4.32; N, 16.46; S, 12.49.

General Procedure for the Preparation of Unsymmetrical Sulfides (Table I). To a magnetically stirred solution of Bim-$S^+(\rightarrow O)$-R (1.0 mmol) in 20 mL of 95% ethanol was added 3.0 mmol of R′-SH. Stirring was then continued at 25 °C or at elevated temperatures. (See Table I for reaction times and reaction temperatures.) The ethanol solvent was then removed in vacuo, pentane or pentane–ether solvent mixture was added to precipitate the insoluble thioether side product, and the resulting solid was removed by suction filtration. Concentration of the filtrate in vacuo afforded the crude disulfide product. The crude product was then purified by LPLC or flash chromatography with 0–50% ethyl acetate in hexane as the eluent.

The homogeneity of the purified disulfides was established by ^1H and ^{13}C NMR, TLC analyses, and high-resolution mass spectroscopy. The latter technique was especially diagnostic for detecting the absence of any symmetrical disulfides in the final unsymmetrical disulfide products. In the reactions studied, the symmetrical disulfides were readily distinguishable by TLC from the desired unsymmetrical products. The absence of any undesired symmetrical disulfides in the final product was further ruled out by HRMS exact mass measurement.

(13) Davis, F. A.; Isenberg, N.; Koch, P.; Ciuffarin, E.; Fava, A. *J. Am. Chem. Soc.* **1970**, *92*, 5971. Kice, J. L.; Large, G. B. *Tetrahedron Lett.* **1965**, 3537.

(14) Shreeve, J. M. *Acc. Chem. Res.* **1973**, *6*, 387. Tsukamoto, G.; Watanabe, T.; Utsumi, I. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 2566.

(15) Taniguchi, T.; Uebayashi, Y.; Sakimoto, R.; Ishii, K. Jpn Patent 15646, 1962.

(16) Böhme, H.; van Ham, G. *Justus Liebigs Ann. Chem.* **1958**, *617*, 62.

Aglycon Modifications of Erythromycin A: Regiospecific and Stereospecific Elaboration of the C-12 Position

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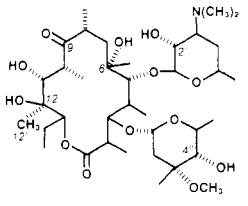
Received March 9, 1987

We have previously reported the incorporation of carbon nucleophiles at the C-9 position of erythromycin A (1) via the intermediacy of the readily available thionocarbonate **2**.[1] As a consequence of this research, we sought to prepare a synthetic intermediate that would allow incorporation of moieties at the relatively inaccessible C-12 position of **1**. The central consideration of the synthetic plan was the preparation of an intermediate that would ultimately permit the regiospecific and stereospecific functionalization of the C-12 position of erythromycin A (1). We now detail not only the synthesis of an intermediate (**5**), which fulfills these requirements, but also the stereospecific conversion of olefin **5** into the corresponding C-12, C-12′ modified diol **6**.



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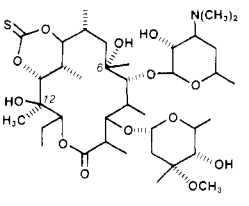

2

Regiospecific Olefin Formation. The blocked olefin **4** was selected as the synthetic target, since, in principle, it presents the opportunity to stereoselectively manipulate the C-12 through C-9 positions; however, the preparation of **4** presents the obvious difficulty of regioselectively dehydrating the C-12 position in such a fashion as to prepare the corresponding exocyclic double bond isomer. A suitable substrate to test the selectivity of olefin formation between the C-6 and C-12 positions is bisacetylated

(1) Hauske, J. R.; Guadliana, M.; Kostek, G. *J. Org. Chem.* **1983**, *48*, 5138.

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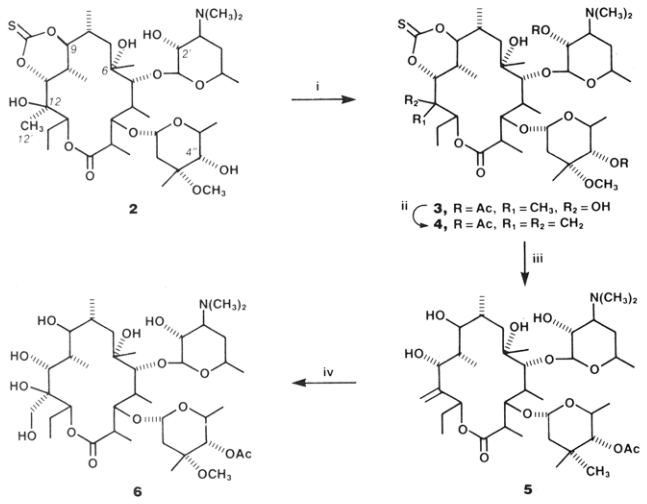
Scheme I[a]



[a] (i) Ac_2O/Pyr/cat. DMAP; (ii) $SOCl_2$/Pyr −1 °C → +7 °C; (iii) $NaBH_4$/isopropyl alcohol, methanol; (iv) OsO_4/*tert*-butyl alcohol-/$NaIO_4$.

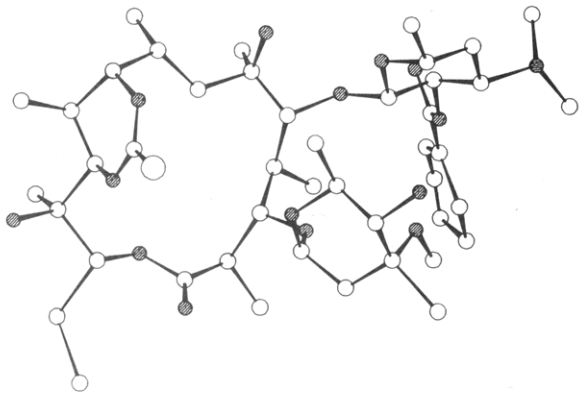


Figure 1. X-ray structure of thionocarbonate **7**.

thionocarbonate **3**. Intermediate **2** was bisacetylated under standard conditions[2] (see Scheme I) affording carbohydrate-blocked thionocarbonate **3** (90% yield), which, upon prolonged exposure to acetic anhydride in the presence of a large excess of 4-(dimethylamino)pyridine, primarily resulted in the acetylation of the *C-12 carbinolic center*.[3] Since the C-12 center of **3** was acetylated in preference to the C-6 position of **3**, we anticipated that dehydration with thionyl chloride in the presence of pyridine would also be selective for the C-12 carbinol. As expected, when thionyl chloride was allowed to react with a pyridine/ethyl acetate solution of the blocked thionocarbonate **3**, a smooth conversion to olefin **4** (the yield was 50%) was observed. Presumably, steric effects control the formation of the exocyclic double bond isomer. Specifically, the C-12, C-13 endocyclic double bond would be prohibited by the unfavorable syn arrangement of the C-13 ethyl with the C-12 methyl. Additionally, it is not possible to maintain the C-9, C-11 cyclic thionocarbonate in a system containing a C-11 sp^2-hybridized center, which would be required by a C-11, C-12 double bond isomer. Although the formation of the exocyclic double bond isomer may be most easily rationalized on the basis of steric considerations, it is difficult to rationalize a priori the selectivity observed between the C-12 and C-6 sites. Thus, we determined the solid state

(2) Hauske, J. R.; Guadliana, M. *J. Org. Chem.* **1982**, *47*, 5019.
(3) The regioselectivity was established by the deuterium isotope shift effect on the carbon spectrum of the resulting C-12 acetate. For a representative example of such an analysis, see ref 1.

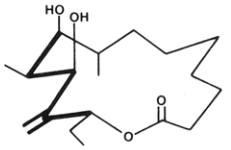
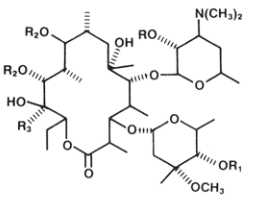


Figure 2. Proposed solution conformation of olefin **5**.

Table I. Bond Distances for the Environments Localized at C-6 and C-12 in Thionocarbonate 7 As Calculated via FRODO

atoms	distance, Å	torsional angle	atoms	distance, Å	torsional angle
C_6OH–C_6CH_3	2.34		$C_{12}OH$–$C_{12}CH_3$	2.45	
C_6OH–C_5	2.26		$C_{12}OH$–C_{11}	2.52	
C_6OH–C_5O	2.74	−70°	$C_{12}OH$–$C_{11}OH$	2.81	+56°
C_6OH–C_7	2.23		$C_{12}OH$–C_{13}	2.56	
			$C_{12}OH$–$C_{13}CH_2$	3.10	
Sum of Effective van der Waals Radius					
C_6	15.1		C_{12}	18.1	

structure of a closely related analogue, namely the 2′-benzoate **7**, in the hope that the solid state conformation



7, R = *CO*Ø; R_1 = H; R_2 = CS; R_3 = CH_3
8, R = *CO*Ø; R_1 = Ac; R_2 = H; R_3 = CH_2OH

might reveal the underlying reason for the observed regioselectivity. The X-ray structure of **7** appears in Figure 1.

The solid-state structure of **7** does reveal some interesting conformational features. An analysis of the steric environments proximal to the C-6 and C-12 centers of thionocarbonate **7** was achieved by calculating the distances to the neighboring centers by utilizing FRODO software on an Evans and Sutherland PS300 instrument. Table I lists the data demonstrating that the C-12 position is *somewhat less sterically encumbered* than the C-6 position. For example, the distance between the C-6 hydroxyl oxygen and the C-6 methyl substituent is 2.34 Å vs. 2.45 Å for the corresponding C-12 substituents and, furthermore, this trend is maintained throughout the comparison of the neighboring sites (see the table). Although this data is supportive of a somewhat less sterically demanding C-12 position, a more meaningful indicator of the molecular environment would be a measure of the local molecular volume for the C-6 and C-12 centers. This may be most easily accomplished by a consideration of the volume described by the effective van der Waals radii, and the resulting comparison (C_6 = 15.1 vs. C_{12} = 18.1) supports the notion that the C-12 position has a reduced steric demand.

Stereospecific Diol Formation. With the exocyclic olefin **4** in hand, the synthetic problem was reduced to the stereospecific preparation of diol **6**. This aspect of the synthetic design was addressed by a consideration of the presumed conformation of olefin **5**, which is illustrated in Figure 2. The oxidizing agent was selected on the basis of this model, since any oxidant that is directed by steric control will deliver oxygen selectively from the β-face; thus, the resulting stereochemistry of the C-12 position will be identical with that of the natural product. Therefore, we

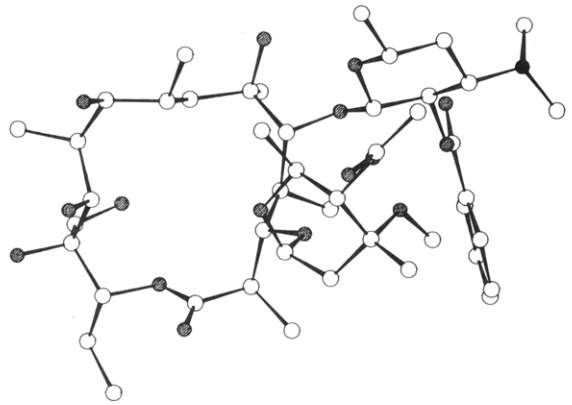


Figure 3. X-ray structure of 12,12′-diol **8**.

selected OsO_4 as the oxidant.[4] Prior to oxidizing the double bond, the thionocarbonyl moiety was removed via treatment with $NaBH_4$, affording olefin **5**. OsO_4 was subsequently added to a THF/H_2O solution of **5**, producing diol **6** (the yield was 55%). The stereochemistry of the resulting product (**6**) was established by the solid-state analysis of the 2′-benzoate analogue **8**. The X-ray structure of **8** appears in Figure 3, and as expected, it clearly defines the stereochemistry at the C-12 position to be identical with that of the natural product **1**.

In summary, therefore, we have prepared diol **6** via the stereospecific oxidation of the exocyclic olefin **5**. Intermediate **5** was readily prepared by the regioselective dehydration of the C-12 carbinol of the blocked intermediate **3**.

Experimental Section

Nuclear magnetic resonance spectra were recorded on a Bruker (^1H NMR, 250 MHz; ^{13}C NMR, 62.8 MHz) or a Varian (^1H NMR, 300 MHz; ^{13}C NMR, 75 MHz) spectrometer. The carbon type (methine, methylene, methyl, or quaternary) was determined by DEPT experiments. Mass spectra were recorded on an AEI MS-30 spectrometer equipped with a D5-50 data system. X-ray data processing was done at Yale University on a departmental NMRVAX 11/750 (Digital Equipment Corp.) using the Enraf-Nonius SDP-PLUS programs and MULTAN 80, a system of computer programs for the automatic solution of crystal structures from X-ray diffraction data: P. Main, S. E. Hull, L. Lessinger, G. Germain J. P. Declercq, and M. M. Woolfson. The programs URANUS and SKK-PUB, programs to generate plot and tables, respectively, were written by Simon Kay Kearsley, Yale University, 1985.

Preparation of 9,11-Cyclic Thionocarbonate 12,12′-Exocyclic Olefin 4. To a methylene chloride solution (2.7 L) of **2** (290.0 g, 0.37 mol) containing triethylamine (171 mL, 1.2 mol) and (dimethylamino)pyridine (10.7 g, 0.09 mol) was added, in a dropwise fashion, acetic anhydride (99 mL, 1.0 mol), such that the reaction temperature never exceeded 30 °C. After the resulting solution was stirred overnight, TLC [silica gel, $CHCl_3/MeOH/NH_3$ (9:1:0.1)] indicated no remaining starting **2** and one, less polar UV-positive material. Water (1 L) was then added, and the pH was adjusted to 9.6 (6 N NaOH). The organic layer was separated, washed with water (3 × 500 mL) and aqueous saturated sodium chloride (1 × 500 mL), dried over anhydrous sodium sulfate, and concentrated in vacuo. The resulting yellowish solid was crystallized from hot diethyl ether (1.5 L), affording colorless, crystalline **3** (260 g). High-resolution mass spectral analysis supported bisacetate formation, *m/e* 200.1280 (2′-acetyldesosamine, $C_{10}H_{18}NO_3$), 201.1110 (4″-acetylcladinose, $C_{10}H_{17}O_4$).

To a mechanically stirred ethyl acetate solution (1.5 L) of **3** (122 g, 0.14 mol) and triethylamine (537 mL, 3.9 mol), which was maintained at −1 °C, was rapidly added thionyl chloride (10 mL, 0.13 mol), such that the reaction temperatures did not exceed 7 °C. After the thionyl chloride addition was complete, the reaction mixture was stirred for 10 min, and TLC [silica gel (impregnated with formamide), $CHCl_3$ and silica gel, $CHCl_3/MeOH/NH_3$ (9:1:0.1)] indicated starting material and one major new material (ca. 1:1 ratio). Additional thionyl chloride (5 mL, 0.065 mol) was added, again the reaction temperature was never allowed to surpass 7 °C, and after stirring for 15 min, TLC [silica gel (impregnated with formamide), $CHCl_3$] indicated starting material and one major new material (ca. 1:2 ratio). A final addition of thionyl chloride (2 mL, 0.026 mol) was made, and after stirring at 7 °C for 15 min, TLC [silica gel (impregnated with formamide), $CHCl_3$] indicated a starting material to product ratio of about 1:9. After being stirred an additional 30 min at 7 °C, the reaction mixture was poured into a stirring mixture of ethyl acetate/water (250 mL/1 L) and the pH was adjusted to 9.6. The organic layer was separated, washed with water (3 × 500 mL), treated with Darco, dried over anhydrous sodium sulfate, and concentrated in vacuo, affording a yellow solid (130 g). The solid was crystallized from isopropyl alcohol/water to afford colorless crystalline **4** (62 g, mp 249–252 °C): ^1H NMR ($CDCl_3$) δ 0.85–1.30 (m), 1.50–1.80 (m), 1.95 (s), 2.00 (s), 2.25 (s), 2.27–2.80 (m), 3.29 (s), 3.55 (br d), 3.71 (s), 3.80 (m), 3.95 (br d), 4.10 (br s), 4.15 (m), 4.35 (d), 4.60 (d), 4.80 (m), 4.95 (br s), 5.25 (s), 5.51 (s), 5.55 (d); ^{13}C NMR ($CDCl_3$) δ 190.4 (CS), 174.8 (lactone), 169.9 (acetyl), 169.6 (acetyl), 138.5 (Q), 116.4 (CH_2), 99.4 (CH), 94.7 (CH), 91.6 (CH), 82.8 (CH), 77.9 (CH), 77.7 (CH), 76.8 (CH), 75.8 (CH), 73.5 (Q), 72.8 (Q), 71.2 (CH), 68.1 (CH), 63.5 (CH), 62.8 (CH), 48.8 (CH_3), 43.9 (CH), 42.5 (CH), 40.5 [2 (CH_3)], 38.4 (CH_2), 34.5 (CH_2), 32.5 (CH), 31.0 (CH_2), 30.5 (CH), 29.0 (CH_2), 21.8 (CH_3), 21.31 (CH_3), 21.2 (CH_3), 21.0 (CH_3), 20.6 (CH_3), 17.3 (CH_3), 16.8 (CH_3), 14.2 (CH_3), 11.3 (CH_3), 10.6 (CH_3), 9.2 (CH_3). Anal. Calcd for $C_{42}H_{69}O_{14}NS$: C, 59.76; H, 8.24; N, 1.66; S, 3.80. Found: C, 59.55; H, 8.09; N, 1.63; S, 3.69.

Preparation of 12,12′-Exocyclic Olefin 5. To a mechanically stirred isopropyl alcohol (500 mL) suspension of thionocarbonate **4** (50.0 g, 59 mmol) was added in a portionwise fashion sodium borohydride (5.0 g, 132 mmol), and the resulting mixture was allowed to stir at room temperature overnight. After this period, TLC [silica gel, $CHCl_3/MeOH/NH_3$ (9:1:0.1)] indicated no remaining starting **4** and one, more polar material. The reaction mixture was then poured into a stirring mixture of methylene chloride/water (2.0 L/2.5 L), and the organic layer was separated, washed with aqueous saturated sodium chloride (3 × 400 mL), dried over anhydrous sodium sulfate, and concentrated in vacuo affording a colorless solid (25 g). The aqueous fractions were combined and continuously extracted with chloroform, affording, after concentration, a pale yellow solid (13 g). These materials were combined (38 g) and refluxed in methanol (250 mL) for 4 h. After this period, TLC [silica gel, $CHCl_3/MeOH/NH_3$ (9:1:0.1)] indicated essentially no starting material and mostly (ca. 90%) one, more polar material. The reaction mixture was allowed to cool to room temperature and concentrated in vacuo, affording a pale yellow solid (40 g). The solid was allowed to dissolve in a stirring mixture of tetrahydrofuran/bleach (50 mL/50 mL) and allowed to stir at 0 °C for 5 min, at which time the tetrahydrofuran was removed in vacuo. The resulting solution was added to a stirring mixture of methylene chloride/water (250 mL/200 mL) and phase separated, and the aqueous layer was reextracted with fresh methylene chloride (250 mL). The combined organic layers were washed with aqueous saturated sodium chloride (2 × 75 mL), dried over anhydrous sodium sulfate, and concentrated in vacuo, affording a colorless solid (33 g). The solid was added to a stirring mixture of methylene chloride/water (170 mL/170 mL), and the pH was adjusted to 5.1 (6 N HCl). After phase separation, fresh methylene chloride (150 mL) was added, and the pH was adjusted to 6.1 (6 N HCl). The methylene chloride extracts were combined, added to water (500 ml), pH adjusted to 9.5 (6 N NaOH), phase separated, dried over anhydrous sodium sulfate, and concentrated in vacuo, affording **5** as a colorless solid (27 g): ^{13}C NMR ($CDCl_3$) δ 175.0 (lactone), 165.8 (acetyl), 146.3 (Q), 115.2 (CH_2), 102.0 (CH), 95.1 (CH), 84.5 (CH), 81.1 (CH), 79.2 (CH), 78.0 (CH), 76.8 (CH), 74.4 (Q), 72.6 (Q), 70.5 (CH), 69.4 (CH), 68.6 (CH), 64.9 (CH), 63.3 (CH), 49.0 (CH_3), 43.5 (CH), 43.3 (CH), 40.1 [2 (CH_3)], 39.4 (CH_2), 34.8 (CH_2), 34.8 (CH), 34.0 (CH), 29.0 (CH_2), 27.7 (CH_2), 21.8 (CH_3), 21.2 (CH_3), 21.1 (CH_3), 20.5 (CH_3), 19.3 (CH_3), 17.0 (CH_3), 13.2 (CH_3), 11.8 (CH_3), 10.4 (CH_3), 9.6 (CH_3).

(4) Vedejs, E.; McClure, C. K. *J. Am. Chem. Soc.* **1986**, *108*, 1094.

Preparation of 12,12′-Diol 6. A mechanically stirred solution of olefin **5** (20.0 g, 26.2 mmol) in tetrahydrofuran/water (360 mL/40 mL) was adjusted to pH 6.1 (3 N HCl), and osmium tetraoxide/*tert*-butyl alcohol (2.5% solution, 40 mL, 3.9 mmol) was added at room temperature. After the dark amber solution was stirred at room temperature for 1 h, sodium metaperiodate (11.2 g, 52.4 mmol) was added, and the resulting mixture was stirred at room temperature for 22 h. After this period, TLC [silica gel, CH_2Cl_2/MeOH/NH_3 (9:1:0.1)] indicated little starting **5** (ca. 10%) and essentially one, more polar material. Tetrahydrofuran (100 mL) and aqueous sodium sulfite (1 M, 220 mL) were added, and the mixture was stirred at room temperature for 15 min. The reaction mixture was then poured into a stirring mixture of methylene chloride/water (800 mL/1400 mL) and phase separated, and the aqueous phase was reextracted with methyl chloride (3 × 400 mL), dried over anhydrous sodium sulfate, and concentrated in vacuo, affording an amber solid (19.1 g). The solid was added to a stirring mixture of methylene chloride/water (100 mL/100 mL) and the pH was adjusted to 2.6. The phases were separated, the pH of the aqueous phase was readjusted to 4.8, and the aqueous phase was extracted with methylene chloride (2 × 150 mL). The phases were separated, the pH of the aqueous phase was finally adjusted to 9.5, and the aqueous phase was extracted with methylene chloride (3 × 200 mL). The methylene chloride extracts at pH 9.5 contained no starting material [TLC; silica gel, CH_2Cl_2/MeOH/NH_3 (9:1:0.1)] and upon drying over anhydrous sodium sulfate and concentration in vacuo afforded a colorless solid (14 g). The solid was dissolved in chloroform (60 mL) and allowed to stand at room temperature for 15 min, affording a thick crystalline mass. At this point, hexane (180 mL) was added with vigorous stirring, and the resulting slurry was stirred at room temperature overnight, which afforded, after filtration, colorless crystalline **6** (11 g, mp 148–151 °C): ^{1}H NMR ($CDCl_3$) δ 0.79 (t), 0.95–1.20 (m), 1.45–1.90 (m), 1.99 (s), 2.25 (s), 2.35–2.70 (m), 3.22 (s), 3.40 (br m), 3.55 (dd), 3.65 (s), 3.70 (m), 3.85 (s), 3.95 (d), 4.25 (m), 4.59 (dd), 4.91 (d), 5.05 (dd); ^{13}C NMR ($CDCl_3$) δ 176.2 (lactone), 170.4 (acetyl), 101.5 (CH), 95.4 (CH), 83.0 (CH), 82.7 (CH), 78.3 (CH), 78.1 (CH), 77.5 (CH), 75.5 (Q), 74.6 (Q), 72.5 (Q), 70.9 (CH), 69.2 (CH), 68.1 (CH), 64.1 (CH), 63.2 (CH), 61.9 (CH_2), 49.0 (CH_3), 44.3 (CH), 41.9 (CH), 40.1 [2 (CH_3)], 36.4 (CH_2), 34.7 (CH_2), 34.3 (CH), 32.0 (CH), 29.5 (CH_2), 23.7 (CH_3), 22.1 (CH_2), 21.1 (CH_3), 21.0 (CH_3), 20.5 (CH_3), 19.4 (CH_3), 17.3 (CH_3), 15.1 (CH_3), 13.7 (CH_3), 11.0 (CH_3), 9.1 (CH_3); high-resolution mass spectrum, *m/e* 635.3554 (P – desosamine, $C_{31}H_{55}O_{13}$), 592.3720 (P – 4″-acetylcladinose β-cleavage, $C_{29}H_{54}NO_{11}$), 576.3687 (P – 4″-acetylcladinose, $C_{29}H_{54}NO_{10}$), 434.2814 (aglycon, $C_{21}H_{38}O_9$), 201.1104 (4″-acetylcladinose, $C_{10}H_{17}O_4$), 158.1158 (desosamine, $C_8H_{16}NO_2$). Anal. Calcd for $C_{39}H_{71}O_{15}N$: C, 58.99; H, 8.95; N, 1.76. Found: C, 58.77; H, 8.83; N, 1.72.

X-ray Analysis. Thionocarbonate **2** and diol **6** were converted to their corresponding 2′-benzoates, compounds **7** and **8**, respectively, since these derivatives gave crystals suitable for X-ray analysis. They were prepared via exposure to an equivalent amount of either benzoic anhydride or benzoyl chloride in methylene chloride solvent.

X-ray Analysis of Benzoate 7. The structure of **7** was determined by X-ray crystallography with a crystal that measured 1.00 × 0.50 × 0.50 mm. Diffraction measurements were made on an Enraf-Nonius CAD-4 fully automated diffractometer with graphite monochromated Cu K_α radiation. Preliminary indications of the unit cell based on 25 randomly selected reflections revealed orthorhombic symmetry with the following lattice parameters: a = 14.445 (2) Å, b = 17.857 (7) Å, and c = 27.242 (3) Å with $\alpha = \beta = \gamma = 90.0°$. The space group, on the basis of the observed systematic extinctions, was determined to be $P2_12_12_1$ (No. 19), Z = 4 with one molecule of composition $C_{45}H_{71}O_{14}NS$ forming the asymmetric unit. The calculated density was 1.67 g/cm^3. There were 4896 reflections collected with $2\theta \leq 114°$, of those reflections 3254 (66%) with $1 \geq 3\sigma(I)$ were adjudged observed.

The structure was solved by using MULTAN 80. After numerous runs of varying the number of Es used in Normal, MULTAN 80 was tried with six special and three general reflections. There were 421 E values ≥ 1.626 used. This run produced 576 sets of which set 512 was distinct from the rest and had a combined figure of merit of 2.7913. The electron-density map of that set revealed 56 of the 61 atoms comprising the molecule. Those 56 atoms were used as a phasing model in Karle recycling, which yielded 59 atoms. Two successive iterations of the WFO option in Normal produced the entire 61 non-hydrogen atom structure. The following full-matrix refinements of the non-hydrogen atoms resulted in convergence to a crystallographic unweighted residual of 0.184 and a weighted residual of 0.286.

X-ray Analysis of Benzoate 8. The structure of **8** was determined by X-ray crystallography with a crystal that measured 0.37 × 0.35 × 0.27 mm. Diffraction measurements were made on an Enraf-Nonius CAD-4 fully automated diffractometer with graphite monochromated Cu K_α radiation. Preliminary indications of the unit cell based on 25 randomly selected reflections revealed orthorhombic symmetry with the following lattice parameters: a = 12.083 (3) Å, b = 19.763 (8) Å, and c = 20.508 (4) Å, with $\alpha = \beta = \gamma = 90.0°$. The space group was $P2_12_12_1$ (No. 19), Z = 4 with one molecule of composition $C_{46}H_{75}O_{16}N$ and one molecule of water forming the asymmetric unit. The calculated density was 1.22 g/cm^3. There were 3708 reflections collected with $2\theta \leq 114°$, of those reflections 2989 (81%) with $1 \geq 3\sigma(I)$ were adjudged observed.

The structure was solved by using MULTAN 80. The phasing of 386 E values ≥ 1.538 resulted in an electron density map that revealed 59 out of the 63 non-hydrogen atoms. The complete structure was revealed with the WFPO option in Normal. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were calculated using SDP program HYDRO, and added to the structure calculations. The following full-matrix refinement of the non-hydrogen atoms and addition of the hydrogen atoms to the structure factor calculations, without refinement of their positions, resulted in convergence to a standard crystallographic unweighted residual of 0.046 and a weighted residual of 0.048.

Acknowledgment. We thank R. Ware and D. Sweet for assistance in obtaining spectra and A. Grodski and D. Watrous for synthesizing preparative quantities of all intermediates.

Supplementary Material Available: Tables containing fractional coordinates, temperature factors, bond distances, torsional angles, and anisotropic temperature factors for Figures 1 and 3 (21 pages). Ordering information is given on any current masthead page.

Synthesis of Symmetrical Bis(aryl)sulfur Diimides

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Received February 24, 1987

The Peterson reaction involves the addition of an α-silyl carbanion to the carbonyl group of a ketone or aldehyde to yield a β-silyl alkoxide, which decomposes to an alkene and a silanoate.[1] Similarly, the reaction of the sodium salt of hexamethyldisilazane with nonenolizable ketones yields *N*-(trimethylsilyl)imines.[2]

$$Ph_2C{=}O + Na^+{}^-N[Si(CH_3)_3]_2 \rightarrow Ph_2C{=}NSi(CH_3)_3 + (CH_3)_3SiO^-$$

Bis(trimethylsilyl)carbodiimide has been prepared by the reaction of sodium bis(trimethylsilyl)amide with phosgene,[3] while reaction of lithium (trimethylsilyl)amides

(1) For a recent review, see: Weber, W. P. *Silicon Reagents for Organic Synthesis*: Springer-Verlag: Berlin, 1983; pp 58–76.
(2) Kruger, C.; Rochow, E. G.; Wannagat, U. *Chem. Ber.* **1963**, *96*, 2132.

0022-3263/87/1952-4625$01.50/0 © 1987 American Chemical Society