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Synthesis of (14*R*)- and (14*S*)-14-De(hydroxymethyl)-14-hydroxymycaminosyl Tylonolides

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The title compounds **29** and **19** have been prepared from mycaminosyl tylonolide 9,20-bis(ethylene acetal) via 9 (for **19**) and 13 steps (for **29**). The key step in the synthesis of **19** is Baeyer-Villiger reaction applied to 2′,4′-di-*O*-acetyl-3-*O*-*t*-butyldimethylsilyl-23-deoxy-23-oxomycaminosyl tylonolide 9,20-bis(ethylene acetal), and the desired 14-*O*-formyl derivative is obtained with other products including 12,13-epoxy and 14-*C*-carboxylic acid. The key step in the synthesis of **29** is Mitsunobu reaction applied to (14*S*)-2′,4′-di-*O*-acetyl-3-*O*-*t*-butyldimethylsilyl-14-de(hydroxymethyl)-14-hydroxymycaminosyl tylonolide 9,20-bis(ethylene acetal), and the desired (14*R*)-acyloxy product is obtained by inversion at C-14, with other compounds including 10(11), 12(22),13(14)-triene and 12-acyloxy-10(11),13(14)-diene.

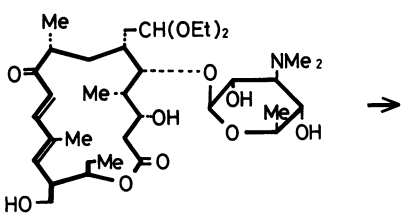
Several derivatives substituted at C-23 of mycaminosyl tylonolide (MT), a macrolide antibiotic, had been prepared in our laboratory; these include 23-*O*-acyl,[1] 23-deoxy-23-halo,[1] 23-dialkylamino-23-deoxy,[2,3] and 23-acylamido-23-deoxy[4] derivatives. Recently we also prepared 23-C-alkyl[3] and 23-C-alkylidene-23-deoxy derivatives[6] from a 14-C-aldehyde,[5] a key synthetic intermediate, by the reaction using Grignard and Wittig reagents. Some of these synthesized compounds showed marked antibacterial activities against Gram-negative bacteria, to which usual macrolide antibiotics have almost no activity.

Since the above derivatives were all concerned with the substitutions at C-23, we changed our attention to attach functional groups directly at C-14 with cleavage of the C(14)–C(23) bond. One reason for this transformation is that the replacement of the projecting hydroxymethyl group at C-14 with a small functional group will result in a fundamental change in antibacterial activity. In this paper we describe the syntheses of two 14-de(hydroxymethyl)-14-hydroxy derivatives (**19**, **29**) of mycaminosyl tylonolide.

Results and Discussion

Treatment of mycaminosyl tylonolide diethyl acetal[7] (**1**) with ethylene glycol in the conditions described in the Experimental section gave the 9,20-bis(ethylene acetal) **2**. Presence of a ethylene acetal fragment at C-9 was confirmed indirectly by the shift values of H-10 (δ 5.75) and H-11 (δ 6.36), which differ, respectively, from those of usual 9-keto derivatives (δ ≈6.3 and ≈7.3). Acetylation of **2** with acetic anhydride in acetonitrile[8] gave the 2′,4′-di-*O*-acetyl derivative (**3**). Treatment of **3** with *t*-butylchlorodimethylsilane in the conditions reported[5,9] gave the 3,23-bis(*O*-*t*-butyldimethylsilyl) derivative (**4**). The 23-*O*-silyl group was then selectively removed with use of limited amount of tetrabutylammonium fluoride in oxolane to afford the 3-*O*-silyl derivative (**5**). Oxidation of **5** with dimethyl sulfoxide in the presence of pyridinium trifluoroacetate and dicyclohexylcarbodiimide in a manner as reported[5,9] gave the 14-C-aldehyde (**6**).

In order to introduce an oxygen atom at C-14 with splitting of the 14-C-aldehyde group, Baeyer-Villiger reaction was examined for **6** after several kinds of unsuccessful reactions were tested. In **6**, the two carbonyl groups at C-9 and C-20 are protected and the carbonyl at C-23 remains free. For such a C-aldehyde fragment, however, successful application of Baeyer-Villiger reaction has not been described yet to our knowledge. When **6** was treated with 3 molar equivalents of *m*-chloroperbenzoic acid in chloroform, an unstable compound supposed the *N*-oxide (**7**) of **6** was first produced, then four products [**8**, **9**(trace), **10**(trace), and **11**; in the order of mobility] followed. Presence of the 3′-dimethylamino *N*-oxide group in **7** (for the isolation: see the Experimental section for **12**)



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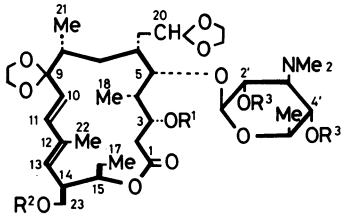
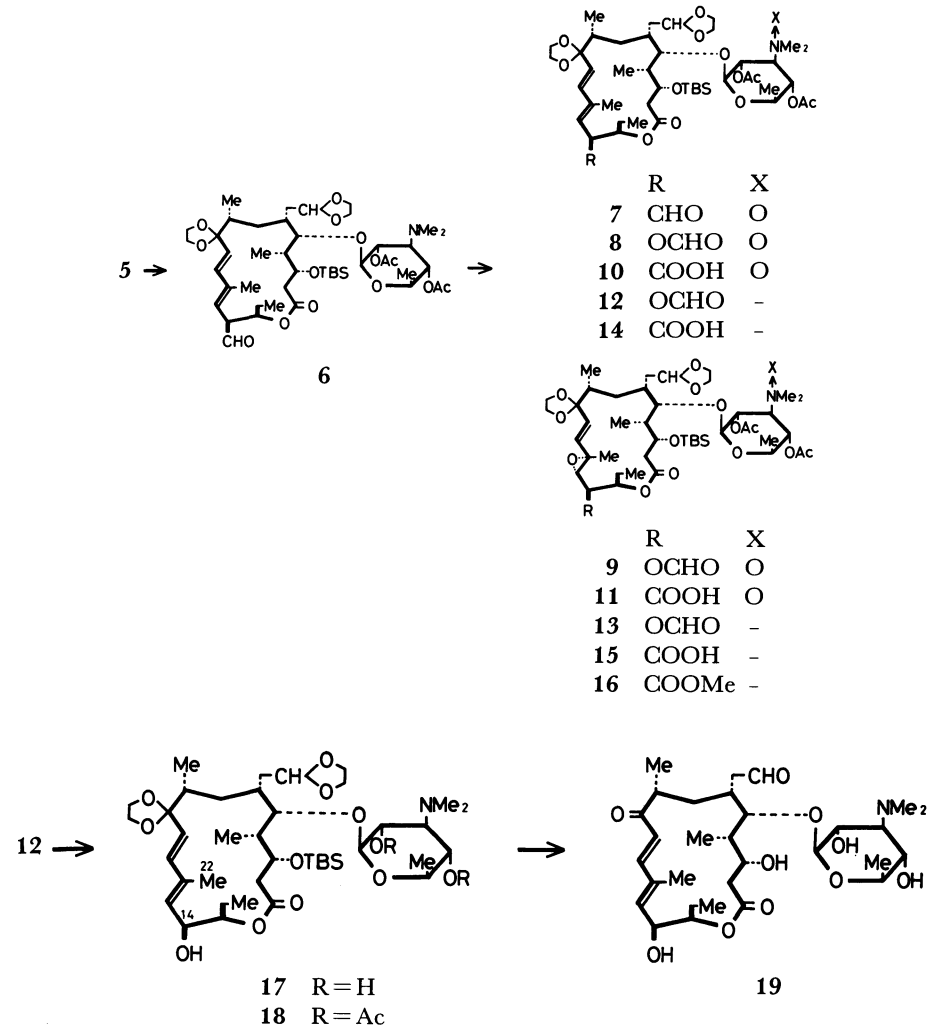


	R^1	R^2	R^3
2	H	H	H
3	H	H	Ac
4	TBS	TBS	Ac
5	TBS	H	Ac

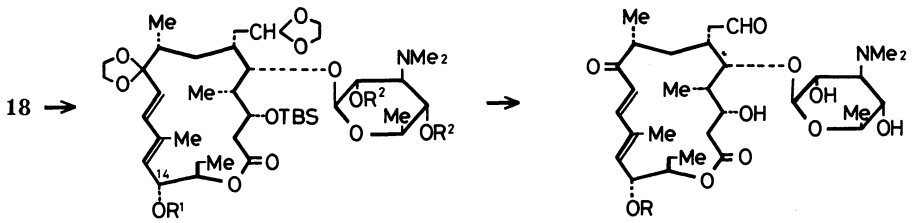
TBS: $SiMe_2Bu^t$



was supported by the shift value of the methyl protons of dimethylamino group (δ 3.23[10]) in the ^{1}H NMR spectrum. The minor product **8**, was presumed, according to its ^{1}H NMR spectrum, the desired product having a formyl ester at C-14 and 3′-dimethylamino *N*-oxide group. As these products were all unstable and considered to have the *N*-oxide structure, de(*N*-oxid)ation was immediately carried out. When, however, triphenylphosphine was used in the presence of acetic acid, a typical procedure for de(*N*-oxid)ation, 9-acetal group was simultaneously hydrolyzed. Thus triphenyl phosphite [$(PhO)_3P$] was attempted as the reducing agent in an inert solvent to successfully give a reaction mixture. Column chromatography of the mixture gave the desired protected 14-formyloxy derivative (**12**) in 24% yield from **5** through **6** and **8**, together with **13** (from **9**), **14** (from **10**), and **15** (from **11**). The structure of **14** is thought to be, from the nature of the reagent, the 14-C-carboxylic acid derivative formed by oxidation of **7**, but the structure remains to be studied.

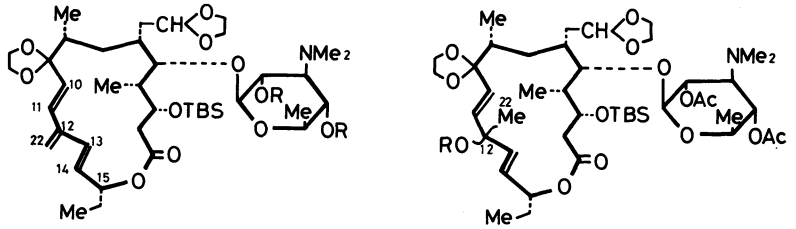
The structure of **12** was determined by the ^{1}H NMR spectrum; signals for a *t*-butyldimethylsilyl, two acetyls, and two ethylene acetal groups (estimated by the signal integration between δ 3.8—4.0) were observed. The low shift value of H-14 (δ 5.49), and the accordance of $J_{13,14}$(=10 Hz) and $J_{14,15}$(=10 Hz) values with those of other MT derivatives[9,11] including **6** indicate that the aldehyde group at C-14 of **6** was replaced by a formyloxy group with retention of the configuration at C-14. Presence of the formyl group was also supported by appearance of a singlet at low field (δ 8.03).

The structure of **13** was concluded to be the 12,13-epoxy analog of **12**. In its ^{1}H NMR spectrum, H-11, H-14, Me-22, and especially H-13 (δ 3.15) showed marked upfield shifts, in comparison with those of **12**, indicating the disappearance of the double bond between C(12)-C(13). Other proton resonances showed approximate accordance with those of **12** in shift and *J* value. Considering from the reaction reagent, it is clear that the double bond was oxidized to the epoxide, with the C(10)-C(11) double bond remained intact. The structure of **13** was also supported by the UV spectrum[12] and TLC detection [**13** was inert under UV lamp (2536 Å)]. The absolute configurations around the epoxide ring could not be decided, but if the reagent approaches from the less-hindered side, 12*S*,13*S* structure is expected. This assumption was sustained by similarity of the ^{1}H NMR spectra (δ and *J* values,



	R^1	R^2
20	CHO	Ac
23	H	H
25	H	Ac
26	Ac	Ac

28 R=Ac
29 R=H



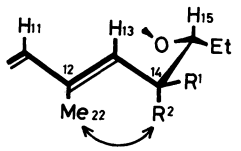
21 R=Ac
24 R=H

22 R=CHO
27 R=Ac

especially $J_{13,14}$) between **13** and rosaramicin, a 16-membered macrolide antibiotic, which contains (12*S*, 13*S*)-12,13-epoxy structure.[13,14]

The structure of another product **15** was determined to be 12,13-epoxy-14-C-carboxylic acid by methylation with diazomethane to give the corresponding methyl ester (**16**), and the similarity of the ^{1}H NMR spectrum with that of **13** with only lacking the formyl proton signal ($\delta \approx 8$). In conclusion, on oxidation with *m*-chloroperbenzoic acid, the 14-C-aldehyde (**6**) was majorly converted to the 12,13-epoxy-14-C-carboxylic acid (**15**), but Baeyer-Villiger reaction also did occur to give the desired 14-*O*-formyl product **12**.

Treatment of **12** in hot methanol removed the acetyl and formyl groups to give **17**, which, on acetylation with acetic anhydride in acetonitrile, gave the 2′,4′-di-*O*-acetyl derivative (**18**). The configuration at C-14 of **18** was determined by the NOE experiment, in that 10% enhancement of H-14 was observed[11] on irradiation of Me-22. This result also supported the structure of **12**.



	R^1	R^2
12	OCHO	H
18	OH	H
20	H	OCHO
25	H	OH

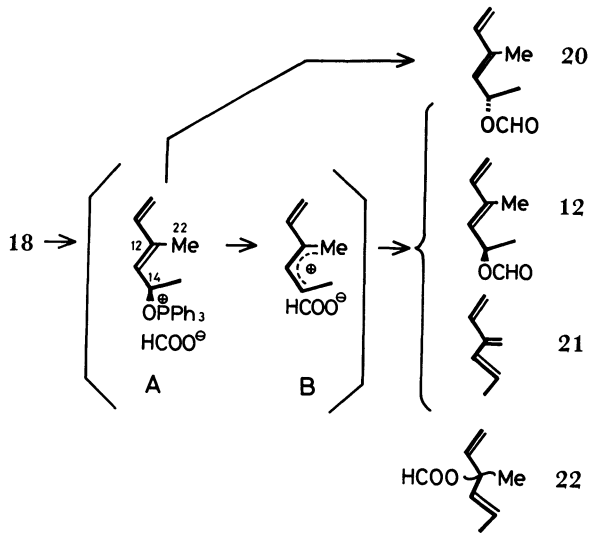
Removal of the silyl and acetal groups of **17** with tetrabutylammonium fluoride in oxolane, and acidic treatment followed gave the desired (14*S*)-14-hydroxy compound (**19**). It is noteworthy that **19** was stably obtained under acidic conditions but the corresponding (14*R*)-14-hydroxy compound (**29**) later mentioned was unstable and converted into several products by the same treatment.

Next, inversion of configuration of the hydroxyl group at C-14 of **19** was attempted to obtain the 14*R* isomer **29**. At first, several substitution reactions were tried for the 14-*O*-sulfonyl derivatives of **18**, but only fruitless results were obtained. Attempt to oxidize **18** to the 14-carbonyl derivative, followed by reduction with sodium borohydride to obtain the 14*R* alcohol, also failed only giving **21** (see later). When, however, Mitsunobu reaction[15] was appled to **18** in benzene in the presence of formic acid, the (14*R*)-formyloxy derivative (**20**) was obtained in a moderate yield (≈50%) with other products (**21** and **22**). Comparison of the ^{1}H NMR spectra of **20** and **12** (14*S* isomer of **20**) showed that there were marked differences in the shift and *J* values between them in relation to H-14 (**20**: δ 5.82, $J_{13,14}$=6, $J_{14,15}$=2.5 Hz; **12**: δ 5.49, $J_{13,14}$=$J_{14,15}$=10 Hz). The lower shift of H-14 of **20** indicates that the H-14 is pseudoequatorial for the average macrolactone plane, and this is in accord with the small *J* values showing the gauche relationships between H-14 and H-13, and H-14 and H-15.

In the ^{1}H NMR spectrum of the by-product **21**, the signal of Me-22 (δ 1.73) of **18** disappeared, and, instead, a pair of small doublet (H-22a,b), typical for a terminal methylene, appeared at low field (δ 5.00 and 5.07). The proton of H-14 also resonated at low field (δ 5.57) and coupled with H-13 (δ 6.34, $J_{13,14}$=15.5 Hz) and H-15 ($J_{14,15}$=7.5 Hz). These results indicate that **21** has a *trans, trans*-10,11 : 13,14-dieno-12-C-methylene struc-

ture. The structure of **21** was also confirmed by the ^{1}H NMR spectrum (and the ^{1}H shift-correlated 2D spectrum) of the deacetyl derivative (**24**).

The second by-product **22** in Mitsunobu reaction seems to have a similar structure with that of **21**, because both compounds had almost the same J values relating to $J_{10,11}$, $J_{13,14}$, and $J_{14,15}$. However, in **22**, Me-22 appeared as a singlet at δ 1.62 (**21** has a 22-methylene), the shift being different from the usual value ($\delta \approx$1.8), and a formyl proton (δ 8.05) was observed. These results indicate that compound **22** is 12-formyloxy-10,11 : 13,14-diene. The reaction mechanism will be that the 14-*O*-phosphonic intermediate[15] (A) of **18** born during Mitsunobu reaction detaches the phosphoniooxy portion to give the intermediate (B) and it



was converted to **20** (and **12**), **21**, and **22** by the action of the formate anion attacked at C-14, H-22, and C-12, respectively. Direct pathway from A to **20** is also considered. The absolute configuration at C-12 of **22**, however, remained undetermined. Disappointingly treatment of **22** and **24** with methanol or 0.1 mol dm^{-3} hydrochloric acid in water-acetonitrile (10 : 1) gave, respectively, a complex mixture indicating there is no hope to obtain the corresponding deblocked derivatives. Deacylation of **20** with methanol (to give **23**) followed by 2′,4′-di-*O*-acetylation gave **25**. In the ^{1}H NMR experiment, no NOE between H-14 and Me-22 was observed supporting indirectly the strucure of **25** and therefore **20**. Unexpectedly deblocking of **23** in an acidic medium to obtain **29** gave a complex mixture. This suggests that the presence of the (14*R*)-hydroxyl group of **23**, unlike the (14*S*)-hydroxyl, make the compound labile against acid. Therefore we intended to change the unstable 14-*O*-formyl group of **20** into an acid-stable *O*-acetyl group. Thus Mitsunobu reaction was carried out on **18** in the presence of acetic acid, whereupon the (14*R*)-acetoxy derivative (**26**) was obtained with **21** and the acetyl congener (**27**) of **22**. Successive treatment of **26** with methanol (to give the 2′,4′-diol derivative), tetrabutylammonium fluoride in oxolane (to remove the silyl group), and hydrochloric acid in aqueous acetonitrile (to remove acetal groups) gave the 14-*O*-acetyl derivative (**28**), all other protecting groups being removed. Finally, basic treatment (NH_3 in aq acetonitrile) of **28** gave the desired product (**29**).

The compound **19** exhibited almost the same or slightly better antibacterial activity in comparison with that of MT, whereas **29** had much weaker activity (see Experimental). Although these two compounds showed no characteristic antibacterial activity, some of the derivatives prepared from them showed remarkable antibacterial activity, which will be reported in another paper.[16] Therefore **19** and **29** will serve as useful compounds, instead of MT, for preparation of new types of macrolides.

Experimental

General. Optical rotations were measured with a Perkin-Elmer 241 polarimeter. Thin-layer chromatography (TLC) was carried out on Kieselgel 60 F-254 (E. Merck) silica gel with detection by spraying with sulfuric acid, followed by slight heating. Column chromatography was performed on Wakogel C-200 or Kieselgel 60, 230—400 mesh (E. Merck). ^{1}H NMR spectra were recorded at 250 MHz with a Bruker WM 250 spectometer.

Mycaminosyl Tylonolide 9,20-Bis(ethylene acetal) (2). A flask containing **1**[11] (38.5 g), ethylene glycol (37 ml), pyridinium *p*-toluenesulfonate (18 g), *p*-toluenesulfonic acid (5.7 g of monohydrate was dried at 100 °C in vacuo for 1 h), sulfolane (200 ml), and benzene (800 ml) was connected to a Soxhlet-type extractor[17] filled with molecular sieves 4A (250 ml, activated at 220 °C under a stream of nitrogen) with a reflux condenser, and the mixture was refluxed for 48 h. On TLC with chloroform-methanol-28% aqueous ammonia (10 : 1 : 0.1), the solution showed spots at R_f 0.3 (**2**, major) and R_f 0.25 (trace; cf. **1**: R_f 0.3). The mixture was poured into an ice-cold, half-saturated aqueous sodium hydrogencarbonate solution (1 L), and extracted with chloroform (1 L×3). The organic solution was washed with aqueous sodium sulfate (saturated, 1 L), dried (Na_2SO_4), and concentrated. The residue was again extracted with benzene (2 L) and the organic solution was washed with aqueous sodium sulfate (saturated, 0.7 L×3), dried (Na_2SO_4), and concentrated. The residue was chromatographed on a silica-gel column with chloroform-methanol-28% aqueous ammonia (25 : 1 : 0.1) to give a solid of **2**, 24.4 g (62%), $[\alpha]_D^{20}$ +13° (*c* 1, chloroform); ^{1}H NMR ($CDCl_3$) δ=2.50 (6H, s, NMe_2), 4.31 (1H, d, $J_{1',2'}$=7.5 Hz, H-1′), 5.30 (1H, d, H-13), 5.75 (1H, d, H-10), 6.36 (1H, d, H-11).

Found: C, 60.48; H, 8.46; N, 1.88%. Calcd for $C_{35}H_{59}NO_{12}\cdot 1/2H_2O$: C, 60.52; H, 8.65; N, 2.02%.

2′,4′-Di-*O*-acetylmycaminosyl Tylonolide 9,20-Bis(ethylene acetal) (3). A solution of **2** (17.2 g) and acetic anhydride (5.6 g) in acetonitrile (172 ml) was kept at room temperature overnight. Evaporation with several additions of toluene gave a residue, that was extracted with benzene, and the organic solution was washed with aqueous sodium hydrogencarbonate (saturated), dried (Na_2SO_4), and concentrated to give a solid of **3**, 17.4 g (90%), $[\alpha]_D^{20}$ -17° (*c* 1, chloroform);

^{1}H NMR ($CDCl_3$) δ=2.01 and 2.05 (each 3H, s, Ac ×2), 2.34 (6H, s, NMe_2), 2.77 (1H, t, $J_{2',3'}=J_{3',4'}$=10 Hz, H-3'), 4.65 (1H, d, $J_{1',2'}$=7.5 Hz, H-1'), 4.76 (1H, t, H-4'), 4.95 (1H, dd, H-2'), 5.34 (1H, d, $J_{13,14}$=10 Hz, H-13), 5.70 (1H, d, $J_{10,11}$=16 Hz, H-10), 6.39 (1H, d, H-11).

Found: C, 60.69; H, 8.02; N, 1.94%. Calcd for $C_{39}H_{63}NO_{14}$: C, 60.86; H, 8.19; N, 1.82%.

2',4'-Di-*O*-acetyl-3,23-bis(*O*-*t*-butyldimethylsilyl)mycaminosyl Tylonolide 9,20-Bis(ethylene acetal) (4). A mixture of **3** (17.4 g), imidazole (9.2 g), and *t*-butylchlorodimethylsilane (17 g) in *N*,*N*-dimethylformamide (140 ml) was heated at 80 °C for 9 h. Evaporation with several additions of xylene gave a residue, that was extracted with benzene. The solution was washed with aqueous sodium hydrogencarbonate (saturated), aqueous sodium sulfate (saturated), dried (Na_2SO_4), and concentrated to give a solid of **4**, 22 g (97%). An analytical sample was obtained by column chromatography with toluene-ethyl acetate (4:1), $[\alpha]_D^{20}$ −58° (*c* 1, chloroform); ^{1}H NMR ($CDCl_3$) δ=0.01, 0.02, 0.03, and 0.13 (each 3H, s, $SiMe_2$×2), 0.87 and 0.89 (each 9H, s, Si-Bu^t ×2), 1.71 (3H, s, Me-22), 2.05 and 2.06 (each 3H, s, Ac ×2), 2.35 (6H, s, NMe_2), 2.72 (1H, t, H-3'), 4.45 (1H, d, H-1'), 4.76 (1H, t, H-4'), 4.90 (2H, H-2',15), 5.37 (1H, d, H-13), 5.55 (1H, d, H-10), 6.34 (1H, d, H-11).

Found: C, 61.55; H, 8.88; N, 1.66%. Calcd for $C_{51}H_{91}NO_{14}Si_2$: C, 61.38; H, 9.13; N, 1.40%.

2',4'-Di-*O*-acetyl-3-*O*-(*t*-butyldimethylsilyl)mycaminosyl Tylonolide 9,20-Bis(ethylene acetal) (5). To an ice-cold solution of **4** (22 g) in oxolane (220 ml) was added a 1 mol dm^{-3} solution (20 ml) of tetrabutylammonium fluoride (1 molar equivalent for **4**) in oxolane, and the solution was kept at room temperature for 2 h. On checking by TLC with toluene-ethyl acetate (2:1), the solution showed a major spot at R_f 0.27. Evaporation gave a residue, that was extracted with benzene. The organic solution was then treated in a manner as described for **4**, to give, after column chromatography with toluene-ethyl acetate (1:1 → 1:2, gradually changed), a solid of **5**, 16 g (82%), $[\alpha]_D^{20}$ −54° (*c* 1, chloroform); ^{1}H NMR ($CDCl_3$): δ=0.02 and 0.15 (each 3H, s, $SiMe_2$), 0.89 (9H, s, Si-Bu^t), 0.94 (3H, t, Me-17), 1.75 (3H, s, Me-22), 2.05 and 2.06 (each 3H, s, Ac ×2), 2.34 (6H, s, NMe_2), 2.74 (1H, t, H-3'), 2.79 (1H, m, H-14), 4.44 (1H, d, H-1'), 4.76 (1H, t, H-4'), 4.87 (1H, dt, $J_{14,15}=J_{15,16a}$=10, $J_{15,16b}$=3 Hz, H-15), 4.90 (1H, dd, H-2'), 5.36 (1H, d, $J_{13,14}$=10 Hz, H-13), 5.60 (1H, d, H-10), 6.39 (1H, d, H-11).

Found: C, 60.76; H, 8.58; N, 1.57%. Calcd for $C_{45}H_{77}NO_{14}Si$: C, 61.15; H, 8.72; N, 1.58%.

(14*S*)-2',4'-Di-*O*-acetyl-3-*O*-(*t*-butyldimethylsilyl)-14-de(hydroxymethyl)-14-(formyloxy)mycaminosyl Tylonolide 9,20-Bis(ethylene acetal) (12). A solution of **5** (5.02 g), pyridinium trifluoroacetate (1.67 g), and dicyclohexylcarbodiimide (2.37 g) in dry DMSO-benzene (1:1, 50 ml) was stirred at room temperature overnight, then poured into 1,4-dioxane (20 ml) containing oxalic acid dihydrate (1 g). Precipitates occured were filtered off with aid of benzene. The filtered solutions were concentrated, and the residue was extracted with benzene. The extracts were washed as described for **4**, and concentrated. The residual syrup, that showed on TLC with toluene-ethyl acetate (2:1) a single spot at R_f 0.42, was passed through a short column with toluene-ethyl acetate (3:1) to give an unstable solid of **6**, 4.7g. ^{1}H NMR ($CDCl_3$ at 90 MHz) δ=0.90 (9H, s, Si-Bu^t), 1.80 (3H, s, Me-22), 2.07 (6H, s, Ac ×2), 2.38 (6H, s, NMe_2), 3.65 (1H, dt, $J_{13,14}=J_{14,15}$=10 Hz, H-14), 4.47 (1H, d, H-1'), 5.40 (1H, d, H-13), 5.72 (1H, d, H-10), 6.43 (1H, d, H-11), 9.67 (1H, d, $J_{14,23}$=2.8 Hz, H-23).

To a solution of the solid in chloroform (90 ml) were added powdered sodium hydrogencarbonate (1.4 g) and *m*-chloroperbenzoic acid (3.01 g), and the mixture was stirred at room temperature for 3 h. On checking by TLC with chloroform-methanol (5:1), the solution just after the reaction started showed a single spot at R_f 0.46 (**7**; cf. **6**: R_f 0.91; **7** could be isolated by stopping the reaction within 5 min and succeeding prompt purification), and after 3 h, four spots at R_f 0.2 (major, non-sensitive to UV light, **11**), 0.35 (trace, **10**), 0.45 (trace, non-sensitive to UV light, **9**), and 0.53 (minor, **8**). After addition of chloroform (500 ml), the organic solution was washed with aqueous sodium sulfate (saturated), dried (Na_2SO_4), and concentrated to give an unstable mixture of products (≈4.6 g). In a run, **8** was isolated, though in a poor yield, by column chromatography with chloroform-methanol (9:1); ^{1}H NMR ($CDCl_3$) δ=0.04 and 0.12 (each 3H, s, $SiMe_2$), 0.86 (9H, s, Si-Bu^t), 1.87 (3H, s, Me-22), 2.09 and 2.12 (each 3H, s, Ac ×2), 3.23 (6H, s, N(O)Me_2), ≈5.02 (H-15), 5.37 (1H, d, $J_{13,14}$=10 Hz, H-13), ≈5.48 (1H, t, $J_{14,15}$=10 Hz, H-14), ≈5.69 (1H, d, $J_{10,11}$=16 Hz, H-10), 6.27 (1H, d, H-11), 8.04 (1H, s, OCHO).

To an ice-cold solution of the product mixture in toluene (46 ml) was added triphenyl phosphite (4.2 ml) and the solution kept at room temperature overnight. On checking by TLC with previous developing system, all the spots of the starting products disappeared with appearance of spots with larger R_f values, respectively, and with toluene-ethyl acetate (1:1), well-separated four spots of R_f 0.05 (major, **15**), 0.13 (trace, **14**), 0.55 (trace, **13**), and 0.68 (minor, **12**) appeared. Concentration of the reaction mixture gave a product mixture, that was separated by column chromatography with toluene-ethyl acetate (3:1 → 2:1) to give solids of **12**, 1.22 g (24%) and **13**, 0.28 g (5%). On subsequent change of the developing systems to chloroform-acetone (3:1) and then chloroform-methanol (5:1), solids of **14**, 0.28 g (5.5%) and **15**, 2.15 g (41%) were obtained, respectively.

12: $[\alpha]_D^{20}$ −35° (*c* 2, chloroform); UV_{max} (CH_3OH) 233 nm (ε 21,000); ^{1}H NMR ($CDCl_3$) δ=0.04 and 0.15 (each 3H, s, $SiMe_2$), 0.84 (3H, d, Me-21), 0.90 (9H, s, Si-Bu^t), 0.94 (3H, t, Me-17), 1.04 (3H, d, Me-18), 1.15 (3H, d, Me-6'), 1.86 (3H, s, Me-22), 2.04 and 2.05 (each 3H, s, Ac ×2), 2.34 (6H, s, NMe_2), 2.72 (1H, t, H-3'), 4.42 (1H, d, H-1'), 4.76 (1H, t, H-4'), 4.90 (1H, dd, H-2'), 5.03 (1H, dt, H-15), 5.34 (1H, d, H-13), 5.49 (1H, t, $J_{13,14}=J_{14,15}$=10 Hz, H-14), 5.70 (1H, d, $J_{10,11}$=16 Hz, H-10), 6.30 (1H, d, H-11), 8.03 (1H, s, OCHO).

Found: C, 60.03; H, 8.08; N, 1.66%. Calcd for $C_{45}H_{75}NO_{15}Si$: C, 60.20; H, 8.36; N, 1.56%.

(12*S*,13*S*)-2',4'-Di-*O*-acetyl-3-*O*-(*t*-butyldimethylsilyl)-12,13-epoxy-12,13-dihydro-14-de(hydroxymethyl)-14-(formyloxy)-mycaminosyl Tylonolide 9,20-Bis(ethylene acetal) (13): $[\alpha]_D^{20}$ −18° (*c* 1, chloroform); UV_{max} (CH_3OH) 213 nm (ε 3,000); ^{1}H NMR ($CDCl_3$) δ=0.04 and 0.13 (each 3H, s, $SiMe_2$), 0.89 (9H, s, Si-Bu^t), 0.92 (3H, t, Me-17), 1.01 (3H, d, Me-18), 1.16 (3H, d, Me-6'), 1.47 (3H, s, Me-22), 2.06 and 2.07 (each 3H, s, Ac ×2), 2.34 (6H, s, NMe_2), 2.74 (1H, t, H-3'), 3.15 (1H, d, $J_{13,14}$=9.3 Hz, H-13), 4.41 (1H, d, H-1'), 4.77 (1H, t, H-4'), 4.91 (1H, dd, H-2'), ≈4.97 (2H, H-14,20), 5.13 (1H, dt, H-15), 5.67 (1H, d, $J_{10,11}$=16 Hz, H-10), 5.77 (1H, d, H-11), 8.14 (1H, s, OCHO).

Found: C, 59.30; H, 8.01; N, 1.76%. Calcd for $C_{45}H_{75}NO_{16}Si$: C, 59.15; H, 8.21; N, 1.53%.

(12*S*,13*S*)-2′,4′-Di-*O*-acetyl-3-*O*-(*t*-butyldimethylsilyl)-14-de(hydroxymethyl)-14-carboxy-12,13-epoxy-12,13-dihydromycaminosyl Tylonolide 9,20-Bis(ethylene acetal) (15): $[\alpha]_D^{20}$ −31° (*c* 1, chloroform); UV_{max} (CH_3OH) 213 nm (ε 4,300); ^1H NMR ($CDCl_3$) δ=0.02 and 0.13 (each 3H, s, $SiMe_2$), 0.89 (9H, s, Si-Bu^t), 0.93 (3H, t, Me-17), 1.00 (3H, d, Me-18), 1.17 (3H, d, Me-6′), 1.41 (3H, s, Me-22), 2.07 and 2.09 (each 3H, s, Ac ×2), 2.38 (6H, s, NMe_2), 2.84 (1H, t, H-3′), 3.28 (1H, d, $J_{13,14}$=9.3 Hz, H-13), 4.43 (1H, d, H-1′), 4.80 (1H, t, H-4′), ≈4.95 (2H, H-2′, 20), 5.31 (1H, m, H-15), 5.65 (1H, d, $J_{10,11}$=16 Hz, H-10), 5.79 (1H, d, H-11).

Found: C, 58.82; H, 7.96; N, 1.66%. Calcd for $C_{45}H_{75}NO_{16}Si$: C, 59.15; H, 8.21; N, 1.53%.

(12*S*,13*S*)-2′,4′-Di-*O*-acetyl-3-*O*-(*t*-butyldimethylsilyl)-12,13-epoxy-12,13-dihydro-14-de(hydroxymethyl)-14-(methoxycarbonyl)mycaminosyl Tylonolide 9,20-Bis(ethylene acetal) (16). To a solution of **15** (62 mg) in chloroform (0.6 ml) was added diazomethane in ether and the solution was kept at room temperature for 1 h. The solution showed, on TLC with toluene-ethyl acetate (2:1), a single spot at R_f 0.37 (cf. **15**: R_f 0). Evaporation gave a residue, that was subjected to column chromatography with toluene-ethyl acetate (2:1) to give a solid of **16**, 55 mg (87%). $[\alpha]_D^{20}$ −38° (*c* 1, chloroform); *m/z* 927 (M^+); ^1H NMR ($CDCl_3$) δ=0.90 (9H, s, Si-Bu^t), 1.41 (3H, s, Me-22), 2.05 and 2.07 (each 3H, s, Ac ×2), 2.37 (6H, s, NMe_2), 3.78 (3H, s, COOMe), 4.41 (1H, d, H-1′), 5.30 (1H, m, H-15), 5.62 (1H, d, H-10), 5.80 (1H, d, H-11).

Found: C, 59.37; H, 8.34; N, 1.47%. Calcd for $C_{46}H_{77}NO_{16}Si$: C, 59.52; H, 8.36; N, 1.51%.

(14*S*)-2′,4′-Di-*O*-acetyl-3-*O*-*t*-butyldimethylsilyl-14-de(hydroxymethyl)-14-hydroxymycaminosyl Tylonolide 9,20-Bis(ethylene acetal) (18). A solution of **12** (1.2 g) in methanol (24 ml) was heated at 50 °C overnight. Evaporation gave a solid, that was purified by column chromatography with chloroform-methanol-28% aqueous ammonia (30:1:0.1 → 10:1:0.1) to give a solid of **17**. A solution of the solid and acetic anhydride (0.3 ml) in acetonitrile (11 ml) was treated similarly as described for **3** to give a solid of **18**, 1.04 g (89% based on **12**), TLC: R_f 0.46 with toluene-ethyl acetate=1:1 (cf. **12**: R_f 0.68), $[\alpha]_D^{20}$ −61° (*c* 2, chloroform); ^1H NMR ($CDCl_3$) δ=0.04 and 0.15 (each 3H, s, $SiMe_2$), 0.83 (3H, d, Me-21), 0.90 (9H, s, Si-Bu^t), 0.96 (3H, t, Me-17), 1.04 (3H, d, Me-18), 1.14 (3H, d, Me-6′), 1.73 (3H, s, Me-22), 2.04 and 2.06 (each 3H, s, Ac ×2), 2.34 (6H, s, NMe_2), 2.72 (1H, t, H-3′), 4.30 (1H, dt, $J_{13,14}$=$J_{14,15}$=10 Hz, $J_{14,OH}$=4 Hz, H-14), 4.43 (1H, d, H-1′), 4.76 (1H, t, H-4′), 4.80 (1H, m, H-15), 4.90 (1H, dd, H-2′), 5.43 (1H, d, H-13), 5.68 (1H, d, H-10), 6.33 (1H, d, H-11).

Found: C, 61.05; H, 8.61; N, 1.51%. Calcd for $C_{44}H_{75}NO_{14}Si$: C, 60.76; H, 8.63; N, 1.61%.

(14*S*)-14-De(hydroxymethyl)-14-hydroxymycaminosyl Tylonolide (19). To a solution of **17** (57.8 mg) in oxolane (1 ml) was added a 1 mol dm^{-3} oxolane solution (0.22 ml) of tetrabutylammonium fluoride, and the solution was kept at room temperature overnight. Concentration gave a residue, that was extracted with chloroform. The organic solution was washed with aqueous sodium sulfate (saturated), dried (Na_2SO_4), and concentrated. To the residual syrup in acetonitrile (0.3 ml) was added 0.1 mol dm^{-3} aqueous hydrochloric acid (2.9 ml) and the solution was kept at room temperature overnight. TLC of the solution with chloroform-methanol-28% aqueous ammonia (10:1:0.1) showed a single spot at R_f 0.25 (**19**). After neutralization with excess sodium hydrogencarbonate, the reaction mixture was extracted with chloroform. The obtained product was purified by a short column with chloroform-methanol-28% aqueous ammonia (15:1:0.1) to give a solid of **19**, 35.7 mg (83%), $[\alpha]_D^{20}$ −24° (*c* 1, chloroform); ^1H NMR ($CDCl_3$) δ=0.97 (3H, t, Me-17), 1.02 (3H, d, Me-18), 1.22 (3H, d, Me-21), 1.27 (3H, d, Me-6′), 1.83 (3H, s, Me-22), 2.36 (1H, t, $J_{2',3'}$=$J_{3',4'}$=10 Hz, H-3′), 2.50 (6H, s, NMe_2), 3.06 (1H, t, H-4′), 3.48 (1H, dd, H-2′), 4.25 (1H, d, H-1′), 4.45 (1H, t, $J_{13,14}$=$J_{14,15}$=9 Hz, H-14), 4.84 (1H, dt, $J_{15,16a}$=9, $J_{15,16b}$=3 Hz, H-15), 5.83 (1H, d, H-13), 6.34 (1H, d, H-10), 7.30 (1H, d, H-11), 9.70 (1l, s, H-20).

Found: C, 60.81; H, 8.15; N, 2.62%. Calcd for $C_{30}H_{49}NO_{10}\cdot 1/2H_2O$: C, 60.81; H, 8.44; N, 2.36%.

(14*R*)-2′,4′-Di-*O*-acetyl-3-*O*-*t*-butyldimethylsilyl-14-de(hydroxymethyl)-14-(formyloxy)mycaminosyl Tylonolide 9,20-Bis(ethylene acetal) (20). To a cold (5—6 °C) solution of **18** (436 mg) and triphenylphosphine (300 mg) in benzene (4.4 ml) were added diethyl azodicarboxylate (0.17 ml) and formic acid (42 μl, distilled from 99% commercial formic acid) and the solution was stirred at room temperature for 1 h. TLC of the resulting solution with toluene-ethyl acetate (2:1) showed three spots (except for those of the reagents) at R_f 0.5 (**21**), 0.45 (major, **20**), and 0.36 (**22**). Benzene (30 ml) was added, and the solution was washed with aqueous sodium hydrogencarbonate (saturated), aqueous sodium sulfate (saturated), dried (Na_2SO_4), and concentrated. The residue was chromatographed on a column with hexane-ethyl acetate (3:1, 80 ml), and then toluene-ethyl acetate (3:1) to give solids of **21**, 57 mg (13%), **20**, 240 mg (54%; contaminated by 10% of **12**), and **22**, 87 mg (19%).

20: ^1H NMR ($CDCl_3$; the signals for **12** were not recorded) δ=0.08 and 0.11 (each 3H, s, $SiMe_2$), 0.85 (3H, d, Me-21), 0.91 (3H, t, Me-17), 0.92 (3H, d, Me-18), 0.94 (9H, s, Si-Bu^t), 1.14 (3H, d, Me-6′), 1.82 (3H, s, Me-22), 2.03 and 2.06 (each 3H, s, Ac ×2), 2.34 (6H, s, NMe_2), 2.69 (1H, t, H-3′), 4.46 (1H, d, H-1′), 4.76 (1H, t, H-4′), 4.90 (1H, dd, H-2′), 5.20 (1H, d, $J_{13,14}$=6 Hz, H-13), 5.25 (1H, ddd, H-15), 5.46 (1H, d, $J_{10,11}$=15 Hz, H-10), 5.82 (1H, dd, $J_{14,15}$=2.5 Hz, H-14), 6.15 (1H, d, H-11), 8.15 (1H, s, OCHO).

2′,4′-Di-*O*-acetyl-3-*O*-*t*-butyldimethylsilyl-14-de(hydroxymethyl)-12(22),13-dieno-12,13-dihydromycaminosyl Tylonolide 9,20-Bis(ethylene acetal) (21): $[\alpha]_D^{20}$ −59° (*c* 1, chloroform); ^1H NMR ($CDCl_3$) δ=0.14 and 0.17 (each 3H, s, $SiMe_2$), 0.84 (3H, d, Me-21), 0.94 (3H, d, Me-18), 0.95 (9H, s, Si-Bu^t). 0.96 (3H, t, Me-17), 1.14 (3H, d, Me-6′), 2.00 and 2.05 (each 3H, s, Ac ×2), 2.34 (6H, s, NMe_2), 2.69 (1H, t, H-3′), 4.45 (1H, d, H-1′), 4.75 (1H, t, H-4′), 4.91 (1H, dd, H-2′), 5.00 and 5.07 (each 1H, d, *J*≈2 Hz, H-22a, b), ≈5.05 (1H, H-15), 5.50 (1H, d, $J_{10,11}$=16 Hz, H-10), 5.57 (1H, dd, $J_{13,14}$=15.5, $J_{14,15}$=7.5 Hz, H-14), 6.30 (1H, d, H-11), 6.34 (1H, d, H-13).

Found: C, 61.99; H, 8.29; N, 1.64%. Calcd for $C_{44}H_{73}NO_{13}Si$: C, 62.04; H, 8.58; N, 1.65%.

2′,4′-Di-*O*-acetyl-3-*O*-*t*-butyldimethylsilyl-14-de(hydroxymethyl)-12-formyloxy-13-eno-12,13-dihydromycaminosyl Tylonolide 9,20-Bis(ethylene acetal) (22): $[\alpha]_D^{20}$ −50° (*c* 1, chloroform); *m/z* 897 (M^+): ^1H NMR ($CDCl_3$) δ=0.12 and 0.13 (each 3H, s, $SiMe_2$), 0.89 (3H, d, Me-21), 0.92 (3H, d, Me-18), 0.93 (9H, s, Si-Bu^t), 0.94 (3H, t, Me-17), 1.13 (3H, d, Me-6′), 1.62 (3H, s, Me-22), 2.03 and 2.04 (each 3H, s, Ac ×2), 2.33 (6H, s, NMe_2), 2.70 (1H, t, $J_{2',3'}$=$J_{3',4'}$=10 Hz, H-3′), 4.40 (1H, d, H-1′), 4.74 (1H, t, H-4′), 4.89 (1H, dd, H-2′), 4.96 (1H, t, $J_{15,16a}$=6.5, $J_{15,16b}$=0 Hz, H-15), 5.00 (1H, dd, H-20), 5.52 (1H, dd, $J_{13,14}$=16, $J_{14,15}$=6.5 Hz, H-14), 5.53 (1H, d, $J_{10,11}$=16

Hz, H-10), 5.72 (1H, d, H-13), 6.02 (1H, d, H-11), 8.05 (1H, s, OCHO).

Found: C, 60.29; H, 8.57; N, 1.32%. Calcd for $C_{45}H_{75}NO_{15}Si$: C, 60.20; H, 8.36; N, 1.56%.

(14*R*)-3-*O*-*t*-Butyldimethylsilyl-14-de(hydroxymethyl)-14-hydroxymycaminosyl Tylonolide 9,20-Bis(ethylene acetal) (23). A solution of **20** (200 mg) in methanol (2 ml) was heated at 50 °C overnight. Evaporation gave a residue, that was chromatographed on a column with chloroform-methanol-28% aqueous ammonia (30 : 1 : 0.1 → 20 : 1 : 0.1) to give a solid of **23**, 163 mg (92%), $[\alpha]_D^{20}$ −76° (*c* 1, chloroform); ^{1}H NMR ($CDCl_3$) δ=0.09 and 0.11 (each 3H, s, $SiMe_2$), 0.91 (9H, s, Si-Bu^t), 1.78 (3H, s, Me-22), 2.50 (6H, s, NMe_2), 3.55 (1H, dd, $J_{1',2'}$=7.5, $J_{2',3'}$=10 Hz, H-2'), 4.34 (1H, d, H-1'), 5.12 (1H, ddd, $J_{14,15}$=2, $J_{15,16a}$=6, $J_{15,16b}$=8.5 Hz, H-15), 5.31 (1H, d, $J_{13,14}$=6 Hz, H-13), 5.41 (1H, d, $J_{10,11}$=16 Hz, H-10), 6.18 (1H, d, H-11).

Found: C, 61.30; H, 9.17; N, 1.82%. Calcd for $C_{40}H_{71}NO_{12}Si$: C, 61.15; H, 9.04; N, 1.78%.

3-*O*-*t*-Butyldimethylsilyl-14-de(hydroxymethyl)-12(22),13-dieno-12,13-dihydromycaminosyl Tylonolide 9,20-Bis(ethylene acetal) (24). Compound **21** (58 mg) was treated similarly as described for **23** to give a solid of **24**, 40 mg (76%), $[\alpha]_D^{20}$ −64° (*c* 1, chloroform); *m/z*767 (M^+); ^{1}H NMR (C_6D_6) δ=0.10 and 0.24 (each 3H, s, $SiMe_2$), 0.80 (3H, t, Me-17), 1.03 (9H, s, Si-Bu^t), 2.32 (6H, s, NMe_2), 4.53 (1H, d, H-1'), 4.91 (1H, d, $J_{22a,22b}$=2 Hz, H-22a), 5.02 (1H, t, $J_{14,15}$=$J_{15,16a}$=7.5, $J_{15,16b}$=0 Hz, H-15), 5.04 (1H, d, H-22b), 5.30 (1H, dd, H-20), 5.58 (1H, dd, $J_{13,14}$=15 Hz, H-14), 5.99 (1H, d, $J_{10,11}$=16 Hz, H-10), 6.52 (1H, d, H-13), 6.56 (1H, d, H-11).

Found: C, 62.57; H, 8.80; N, 1.95%. Calcd for $C_{40}H_{69}NO_{11}Si$: C, 62.58; H, 9.00; N, 1.83%.

(14*R*)-2',4'-Di-*O*-acetyl-3-*O*-*t*-butyldimethylsilyl-14-de(hydroxymethyl)-14-hydroxymycaminosyl Tylonolide 9,20-Bis(ethylene acetal) (25). Compound **23** (190 mg) was treated with acetic anhydride (54 μl) in acetonitrile (2 ml) in a manner as described for **3** to give a solid of **25**, 193 mg (92%), $[\alpha]_D^{20}$ −63° (*c* 1, chloroform); ^{1}H NMR ($CDCl_3$) δ=0.09 and 0.11 (each 3H, s, $SiMe_2$), 0.94 (9H, s, Si-Bu^t), 1.76 (3H, s, Me-22), 2.04 and 2.06 (each 3H, s, Ac ×2), 2.35 (6H, s, NMe_2), 2.68 (1H, t, H-3'), 4.46 (1H, d, H-1'), 4.54 (1H, dt, $J_{13,14}$=6, $J_{14,15}$=2, $J_{14,OH}$=6 Hz, H-14), 4.75 (1H, t, H-4'), 4.90 (1H, dd, H-2'), 5.12 (1H, dq, $J_{15,16a}$=6, $J_{15,16b}$=6 Hz, H-15), 5.30 (1H, d, H-13), 5.42 (1H, d, H-10), 6.17 (1H, d, H-11).

Found: C, 60.50; H, 8.46; N, 1.77%. Calcd for $C_{44}H_{75}NO_{14}Si$: C, 60.76; H, 8.63; N, 1.61%.

(14*R*)-14-Acetoxy-2',4'-di-*O*-acetyl-3-*O*-*t*-butyldimethylsilyl-14-de(hydroxymethyl)mycaminosyl Tylonolide 9,20-Bis(ethylene acetal) (26). To a cold (5 °C) solution of **18** (100 mg) and triphenylphosphine (70 mg) in benzene (1 ml) were added diethyl azodicarboxylate (41 μl) and acetic acid (16 μl) and the solution was stirred at room temperature for 1 h. TLC of the resulting solution with toluene-ethyl acetate (2 : 1) showed three spots at R_f 0.52 (**21**), 0.44 (**26**), and 0.34 (**27**). Work-up as described for **20** gave **26**, 72 mg (65%), $[\alpha]_D^{23}$ −38° (*c* 1, chloroform); ^{1}H NMR ($CDCl_3$) δ=0.96 (9H, s, Si-Bu^t), 1.83 (3H, s, Me-22), 2.05 and 2.06 (each 3H, s, Ac ×2), 2.15 (3H, s, AcO-14), 2.35 (6H, s, NMe_2), 4.50 (1H, d, H-1'), 4.80 (1H, t, H-4'), 4.93 (1H, dd, H-2'), 5.23 (1H, d, $J_{13,14}$=6 Hz, H-13), 5.26 (1H, dq, $J_{14,15}$=2.5, $J_{15,16a}$=6, $J_{15,16b}$=9 Hz, H-15), 5.48 (1H, d, H-10), 5.75 (1H, dd, H-14), 6.26 (1H, d, H-11).

Found: C, 60.84; H, 8.36; N, 1.33%. Calcd for $C_{46}H_{77}NO_{15}Si$: C, 60.59; H, 8.45; N, 1.54%.

(14*R*)-14-Acetoxy-14-de(hydroxymethyl)mycaminosyl Tylonolide (28). A solution of **26** (61 mg) in methanol (1 ml) was heated at 37 °C overnight. Evaporation gave a residue, that was chromatographed on a column with chloroform-methanol-28% aqueous ammonia (30 : 1 : 0.1) to give a solid. A solution of the solid and a 1 mol dm^{-3} oxolane solution (0.2 ml) of tetrabutylammonium fluoride in oxolane (1 ml) was kept at room temperature for 3 h. Usual work-up gave a syrup, that was dissolved in acetonitrile (0.25 ml). After addition of 0.1 mol dm^{-3} hydrochloric acid (1 ml), the solution was kept at room temperature for 6 h. After usual work-up, the syrup obtained was chromatographed on a column with chloroform-methanol-28% aqueous ammonia (25 : 1 : 0.1) to give a solid of **28**, 23 mg (41%). $[\alpha]_D^{20}$ −64° (*c* 1, chloroform); ^{1}H NMR ($CDCl_3$) δ=0.92 (3H, t, Me-17), 1.05 (3H, d, Me-18), 1.21 (3H, d, Me-21), 1.26 (3H, d, Me-6'), 1.93 (3H, s, Me-22), 2.16 (3H, s, AcO-14), 2.35 (1H, t, H-3'), 2.50 (6H, s, NMe_2), 3.06 (1H, t, H-4'), 3.51 (1H, dd, H-2'), 4.26 (1H, d, H-1'), 5.21 (1H, dq, $J_{14,15}$=2.5, $J_{15,16a}$=6, $J_{15,16b}$=9 Hz, H-15), 5.67 (1H, dd, $J_{13,14}$=6.5 Hz, H-14), 5.75 (1H, d, H-13), 6.34 (1H, d, $J_{10,11}$=16 Hz, H-10), 7.16 (1H, d, H-11), 9.71 (1H, s, H-20).

Found: C, 61.19; H, 8.11; N, 2.36%. Calcd for $C_{32}H_{51}NO_{11}$: C, 61.44; H, 8.16; N, 2.24%.

(14*R*)-14-De(hydroxymethyl)-14-hydroxymycaminosyl Tylonolide (29). A solution of **28** (167 mg) in 28% aqueous ammonia-methanol (1 : 10, 3 ml) was kept at room temperature for 4 h. TLC (chloroform-methanol-28% aqueous ammonia 10 : 1 : 0.1) of the solution showed spots at R_f 0.28 (**28**), R_f 0.25 (**29**) and R_f 0. Evaporation gave a residue, that was chromatographed on a column with chloroform-methanol-28% aqueous ammonia (15 : 1 : 0.1) to give solids of **29**, 49 mg (38%) and **28** recovered (30 mg). $[\alpha]_D^{20}$ −21° (*c* 1, chloroform); ^{1}H NMR ($CDCl_3$) δ=0.99 (3H, t, Me-17), 1.04 (3H, d, Me-18), 1.21 (3H, d, Me-21), 1.28 (3H, d, Me-6'), 1.98 (3H, s, Me-22), 2.36 (1H, t, H-3'), 2.52 (6H, s, NMe_2), 3.06 (1H, t, H-4'), 3.50 (1H, dd, H-2'), 4.28 (1H, d, H-1'), 4.63 (1H, dt, $J_{13,14}$=6, $J_{14,15}$=$J_{14,OH}$=2.5 Hz, H-14), 5.10 (1H, ddd, $J_{15,16a}$=6, $J_{15,16b}$=8.5 Hz, H-15), 5.80 (1H, d, H-13), 6.35 (1H, d, $J_{10,11}$=16 Hz, H-10), 7.18 (1H, d, H-11), 9.72 (1H, s, H-20).

Found: C, 60.52; H, 8.23; N, 2.17%. Calcd for $C_{30}H_{49}NO_{10}\cdot 1/2H_2O$: C, 60.81; H, 8.44; N, 2.36%.

Antibacterial Activity of 19, 29, and MT (MIC, μg/ml). *Staphylococcus aureus* 209 P: 0.78 (**19**), 6.25 (**29**), 0.78 (MT); *Staphylococcus aureus* Smith: 0.78, 6.25, 0.78; *Bacillus subtilis* NRRL B-558: 3.12, 25, 3.12; *Escherichia coli* NIHJ: 3.12, 25, 6.25; *Klebsiella pneumoniae* PCI 602: 1.56, 6.25, 3.12; *Shigella dysenteriae* JS 11910: 0.39, 1.56, 0.78; *Serratia marcescens*: 12.5, 100, 25; *Pseudomonas aeruginosa* A3: 6.25, 50, 12.5.

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