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Syntheses of 23-C-Substituted Derivatives of Mycaminosyl Tylonolide and 4′-Deoxymycaminosyl Tylonolide[1)]

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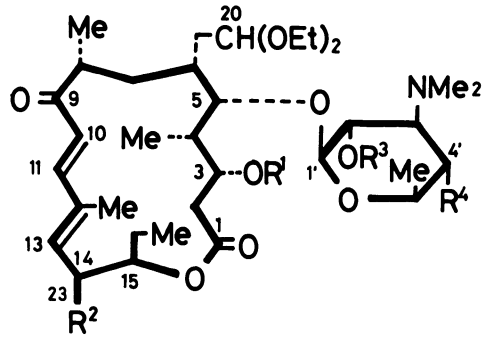
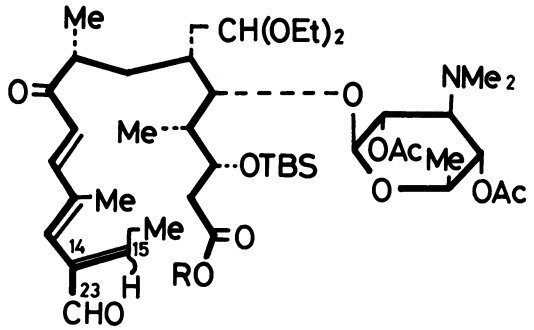
23-C-Substituted derivatives of mycaminosyl tylonolide (MT) and 4′-deoxymycaminosyl tylonolide (DT) have been prepared by the reaction of protected 23-aldehyde derivatives, 2′,4′-di-*O*-acetyl-3-*O*-*t*-butyldimethylsilyl-23-deoxy-23-oxomycaminosyl tylonolide diethyl acetal (**5**) and 2′-*O*-acetyl-3-*O*-*t*-butyldimethylsilyl-23,4′-dideoxy-23-oxomycaminosyl tylonolide diethyl acetal (**26**), with several Grignard reagents and methyllithium. The final products were (23*S*)- and (23*R*)-23-C-methyl (**13a**, **13b**), -ethyl (**14a**, **14b**), -butyl (**15a**, **15b**), -phenyl (**16b**, **16a**), -allyl (**17a**, **17b**), -vinyl (**18a**, **18b**), -ethynyl (**19b**, **19a**) derivatives of MT, and (23*S*)- and (23*R*)-23-C-methyl (**28a**, **28b**), -vinyl (**29a**, **29b**), and -ethynyl (**30b**, **30a**) derivatives of DT. Their configurations at 23-position were determined by the NOE difference spectroscopy on **13a** and **13b**.

As previously reported,[2)] 23-dialkylamino-23-deoxymycaminosyl tylonolides and their 4′-deoxy analogs had considerable antibacterial activities against both Gram-positive and -negative bacteria. Since, generally, macrolide antibiotics are active only against Gram-positive bacteria, the species of the substituents at C-23 of mycaminosyl tylonolides seem important in terms of antibacterial spectrum. This prompted us to modify the substituents at C-23 with new ones. This paper describes[1)] the syntheses of 23-C-alkyl and 23-C-aryl derivatives of mycaminosyl tylonolide (MT) and 4′-deoxymycaminosyl tylonolide[3)] (DT) by way of the C-23- aldehyde intermediates.



	R^1	R^2	R^3	R^4
1	H	CH_2OH	Ac	OAc
2	$SiMe_2tBu$	CH_2OSiMe_2tBu	Ac	OAc
3	H	CH_2OSiMe_2tBu	Ac	OAc
4	$SiMe_2tBu$	CH_2OH	Ac	OAc
5	$SiMe_2tBu$	CHO	Ac	OAc
8	$SiMe_2tBu$	CH_2OH	H	OH
9	$SiMe_2tBu$	CHO	H	OH
11a	$SiMe_2tBu$	(*S*)CH(OH)Me	Ac	OAc
11b	$SiMe_2tBu$	(*R*)CH(OH)Me	Ac	OAc
12a	$SiMe_2tBu$	(*S*)CH(OH)Me	H	OH
12b	$SiMe_2tBu$	(*R*)CH(OH)Me	H	OH
20	$SiMe_2tBu$	CH_2OSiMe_2tBu	H	OH
21	$SiMe_2tBu$	CH_2OSiMe_2tBu	H	$OSO_2CH_2C_6H_5$
22	$SiMe_2tBu$	CH_2OSiMe_2tBu	H	I
23	$SiMe_2tBu$	CH_2OSiMe_2tBu	H	H
24	$SiMe_2tBu$	CH_2OSiMe_2tBu	Ac	H
25	$SiMe_2tBu$	CH_2OH	Ac	H
26	$SiMe_2tBu$	CHO	Ac	H
27a	$SiMe_2tBu$	(*S*)CH(OH)Me	Ac	H
27b	$SiMe_2tBu$	(*R*)CH(OH)Me	Ac	H

2′,4′-Di-*O*-acetylmycaminosyl tylonolide diethyl acetal[3)] (**1**) was treated with *t*-butylchlorodimethylsilane in the presence of imidazole in *N*,*N*-dimethylformamide (DMF), whereupon the 3,23-di-*O*-silyl derivative (**2**) was obtained almost quantitatively with slight amount of 23-*O*-silyl derivative **3**. Selective removal of the 23-*O*-silyl group of **2** was carried out by treatment with tetrabutylammonium fluoride in oxolane. The *O*-silyl protection proved to be superior to *O*-tetrahydrofuranylation, -tetrahydropyranylation, or -methoxymethylation, because the 3,23-di(acetal) derivatives prepared were difficult to remove selectively their 23-*O*-protecting groups. Oxidation of the resulting 23-hydroxy compound **4** was examined with several reagents; pyridinium chlorochromate (PCC) oxidized the dimethylamino group in addition to the 23-hydroxyl group, dimethyl sulfoxide (DMSO)–acetic anhydride gave a large amount of 23-*O*-(methylthiomethyl) by-product, DMSO-$(COCl)_2$ in the presence of triethylamine (Swern oxidation) gave a large amount of open-macrolactone compound **6**, and only DMSO–dicyclohexylcarbodiimide (DCC) in



6 R: H
7a, b R: Me

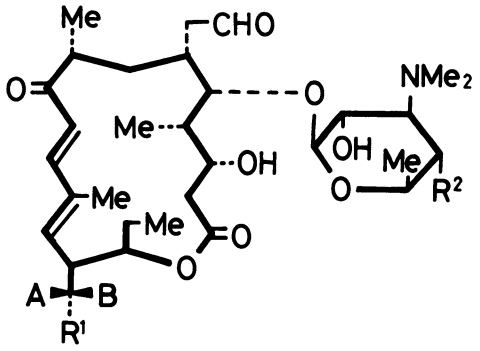
TBS: *t*-butyldimethylsilyl

the presence of pyridinium trifluoroacetate gave the desired product **5** in high yield with slight **6**. The isolated **5** was unstable and readily converted to **6** by β-elimination in the presence of base such as triethylamine or its own basicity caused by 3′-dimethylamino group. The ^{1}H-NMR spectrum of **6** showed, by the decoupling method, that **6** had a new double bond between C-14 and C-15, and was a mixture of two geometrical isomers (the ratio being changed between 2:3—2:1 depending upon the slight change in experimental conditions; but the cause was not pursued). Methylation of **6** with diazomethane gave the corresponding esters **7a** and **7b** proving the presence of a carboxylic acid in **6**.

We next tried to prepare the unprotected 23-oxo derivative (**10**) of MT from **5**. De-*O*-acetylation of **5** in an usual manner[3] (in methanol, 50 °C, 24 h), however, gave the desired de-*O*-acetyl derivative (**9**) in only low yield, possibly by the presence of the unstable 23-aldehyde group. We therefore converted **4** to the 3-*O*-silyl-2′,4′-diol (**8**) which was oxidized by the DMSO–DCC method as described above to afford the 23-oxo derivative (**9**) in a moderate yield (50%). Removal of the acetal and 3-*O*-silyl protecting groups with 5% hydrofluoric acid in acetonitrile gave the 23-oxo compound **10** in a low yield. Efforts to improve the yield were unsuccessful. The presence of two aldehyde groups in **10** was proved by the ^{1}H-NMR spectrum, the signal of the new 23-CHO proton being appeared at δ 9.69.

Methylation of **5** with methylmagnesium bromide in oxolane gave the two 23-C-methyl derivatives (*S* and *R*) in low yields with several by-products including the reduction product **4**; formation of this kind of reduction product **4** sometimes occurs in the reaction with the Grignard reagent. The low yields of the methyl products **11a**, **11b** may be resulted from the partial reaction of the carbonyl group at C-9 of **5** with the Grignard reagent as well as opening of the macrolactone ring during the reaction. In the ^{1}H-NMR spectra, the major product **11a** showed new methyl signals (doublet) at δ 1.12, and the minor (**11b**), at δ 1.22. Since **4** was produced from **5** with limited amount of sodium cyanotrihydroborate, the same R-configuration[4,5] at C-14 of **11a,b** with that of MT was concluded. This was supported by the ^{1}H-NMR spectra of **11a** and **11b**, in that both $J_{13,14}$ and $J_{14,15}$ showed, respectively, almost identical values with those of MT.[5] When **5** was methylated with methyllithium in ether, **11a** was obtained in a better yield. Methanolysis of **11a** and **11b** gave the deacetyl derivatives (**12a** and **12b**), which were led, by deblocking with hydrochloric acid in acetonitrile, to the final 23-C-methyl products **13a**, **13b**.

In the ^{1}H-NMR spectra of **13a** and **13b**, the signals of Me-24 appeared at δ 1.15 and 1.24 (each doublet), respectively, and the methyl configurations were determined by the NOE difference spectroscopy[6] (Fig. 1). Irradiation at δ 1.15 (Me-24) of **13a** caused pronounced positive signal enhancements of H-13, -14, and -23 (the signals of H-5′ were also slightly enhanced possibly by the simultaneous irradiation of Me-6′), whereas irradiation at δ 1.24 (Me-24; Me-21 and Me-6′ were also irradiated simultaneously inevitably) of **13b** caused similar enhancements of H-13, -15, and -23, as well as those of H-10 and 5′. The sharp difference between **13a** and **13b** was that **13a** gave enhancement of H-14, and **13b**, H-15. To satisfy the above result on **13a**, the Me-24 should come stereochemically to the position to bisect the projection angle formed by the C(13)–C(14) and C(14)–H(14) sides (Fig. 1). On the other hand, the small value of $J_{14,23}$(=2 Hz) indicates that H-23 should take gauche (not antiperiplanar) position with respect



	ac*	A	B	R^1	R^2
MT		H	H	OH	OH
DT		H	H	OH	H
10		=O		H	OH
13a	*S*	OH	H	Me	OH
13b	*R*	H	OH	Me	OH
14a	*S*	OH	H	Et	OH
14b	*R*	H	OH	Et	OH
15a	*S*	OH	H	Bu	OH
15b	*R*	H	OH	Bu	OH
16a	*R*	OH	H	C_6H_5	OH
16b	*S*	H	OH	C_6H_5	OH
17a	*S*	OH	H	$CH_2CH=CH_2$	OH
17b	*R*	H	OH	$CH_2CH=CH_2$	OH
18a	*S*	OH	H	$CH=CH_2$	OH
18b	*R*	H	OH	$CH=CH_2$	OH
19a	*R*	OH	H	C≡CH	OH
19b	*S*	H	OH	C≡CH	OH
28a	*S*	OH	H	Me	H
28b	*R*	H	OH	Me	H
29a	*S*	OH	H	$CH=CH_2$	H
29b	*R*	H	OH	$CH=CH_2$	H
30a	*R*	OH	H	C≡CH	H
30b	*S*	H	OH	C≡CH	H

* Absolute configuration at C-23 by Cahn-Ingold-Prelog specifications.

to H-14 (the projection angle of H(14)–C(14)–C(23)–H(23) should be 68° according to a literature[7]). This conclusion was also supported by another NOE experiment: irradiation of H-23 of **13a** caused positive signal enhancement only of H-14 (12.6%). These results indicate that the absolute configuration at C-23 of **13a** is *S*. In the case of **13b**, the Me-24 was concluded to take the position to bisect the projection angle formed by the C(13)–C(14) and C(14)–C(15) sides. Again from the $J_{14,23}$ value (=6 HZ), the gauche relationship between H-14 and H-23 is concluded (the projection angle of H(14)–C(14)–C(23)–H(23) should be 50°[7]). This conclusion was also supported by another NOE experiment: irradiation of H-23 of **13b** caused positive signal enhancements of H-14 (5%) and H-15 (8%). The absolute configuration at C-23 of **13b** is, therefore, determined to be *R*. Another aspect worthy to mention was that, in **13b**, NOE was observed (not clear in **13a**) between Me-21 and H-10, suggesting close spatial relationship between them.

Other 23-C-substituted derivatives of MT were prepared by treatment of **5** with several other Grignard reagents, that is, ethyl-, butyl-, phenyl-, allyl-, vinyl-, and ethynylmagnesium bromides. In all cases two

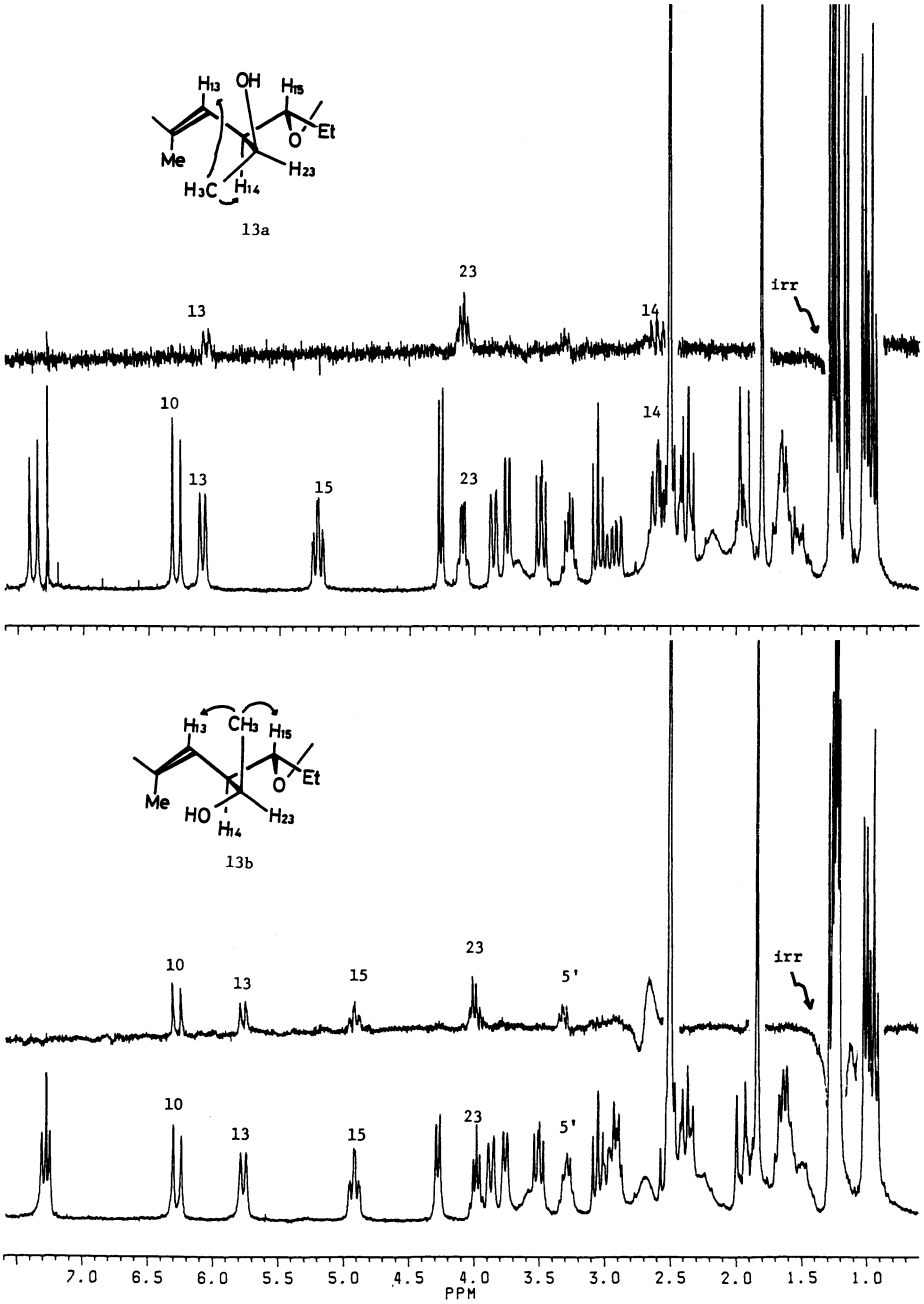


Fig. 1.

products, namely, (*S*)- and (*R*)-23-C-ethyl (**14a**, **14b**), (*S*)- and (*R*)-23-C-butyl (**15a**, **15b**), (*R*)- and (*S*)-23-C-phenyl (**16a**, **16b**), (*S*)- and (*R*)-23-C-allyl (**17a**, **17b**), (*S*)- and (*R*)-23-C-vinyl (**18a**, **18b**), and (*R*)- and (*S*)-23-C-ethynyl derivatives (**19a**, **19b**) of mycaminosyl tylonolide (MT) were produced with by-products accompanied. These products were purified by column chromatography, but with difficulty owing to their close mobilities between products and by-products. The faster-moving products (compounds attached "**a**" to the numbers) had, in all cases, small $J_{14,23}$ values (2—3 Hz) in their ^{1}H-NMR spectra, being the same with the value of **13a**, and the slower-moving (compounds attached "**b**" to the numbers), larger $J_{14,23}$ values (5.5—6.8 Hz), being the same with the value of **13b**. These data are shown in Table 1 with some chemical shifts. The absolute configurations at C-23 of the faster- and slower-moving products were, therefore, specified L and D, respectively, independent of the RS specifications by Cahn-Ingold-Prelog. The fact that L-isomers were always predominating except for the ethynyl derivatives (**19a,b**) will be reasonable from the Felkins model[8] describing the approach of the Grignard reagent to a carbonyl carbon (Fig. 2).

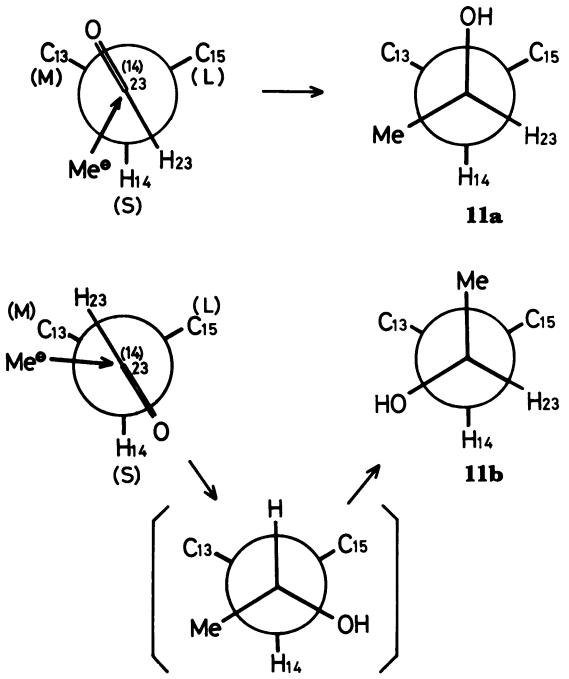


Fig. 2.

The 4′-deoxy analogs (DT-series) of the above MT-series having 23-C-methyl (**28a,b**), -vinyl (**29a,b**), and -ethynyl (**30a,b**) groups were next prepared. In order to remove the C-4′ hydroxyl group before 23-C-alkylation, **2** was solvolyzed with hot methanol, and the 2′,4′-diol (**20**) was treated with phenylmethanesulfonyl chloride. The 4′-*O*-benzylsulfonyl derivative (**21**) was then treated with sodium iodide in 2-butanone, and the 4′-iodo derivative (**22**) was reduced

Table 1. Proton Chemical Shift Data[a] of the Products Prepared [the structure at C-23 is -CHR(OH)]

Compound	R[b]	H-10	H-11	H-13	H-14	H-15	Me-17	Me-18	Me-21	Me-22	H-23	3′-NMe_2	$J_{14,23}$[c]
MT	H	6.27	7.30	5.88	2.88	4.98	0.95	1.01	1.22	1.83	3.73	2.55	5.5
13a	Me	6.28	7.38	6.08	2.60	5.20	0.95	1.02	1.22	1.80	4.09	2.50	2
13b	Me	6.27	7.27	5.76	2.91	4.91	0.94	1.01	1.22	1.84	3.98	2.51	6
14a	Et	6.28	7.36	6.07	2.68	5.24	0.95	1.02	1.22	1.81	3.75	2.51	2
14b	Et	6.25	7.24	5.72	2.90	4.96	0.94	1.01	1.22	1.84	3.69	2.51	6.3
15a	Bu	6.27	7.34	6.05	2.66	5.23	0.96	1.01	1.21	1.80	3.82	2.50	2
15b	Bu	6.25	7.25	5.72	2.88	4.97	0.94	1.00	1.21	1.83	3.73	2.51	6.3
16a	Ph	6.14	7.29	6.15	2.88	5.32	1.01	1.00	1.17	1.46	5.03	2.50	2.5
16b	Ph	6.14	7.08	5.55	3.15	4.97	0.95	0.99	1.18	1.72	4.84	2.49	6.8
17a	all	6.30	7.39	6.11	2.69	5.25	0.95	1.02	1.22	1.79	3.90	2.50	2
17b	all	6.26	7.26	5.70	2.86	4.98	0.93	1.00	1.22	1.83	3.8	2.50	6.8
18a	vin	6.27	7.35	6.05	2.75	5.22	0.97	1.01	1.22	1.78	4.37	2.51	2.5
18b	vin	6.26	7.27	5.76	3.03	4.92	0.95	1.01	1.22	1.84	4.31	2 50	5.5
19a	eth	6.32	7.39	6.10	2.91	5.22	0.96	1.02	1.22	1.84	4.62	2.51	2.5
19b	eth	6.30	7.42	6.11	3.11	5.08	0.96	1.02	1.22	1.84	4.56	2.50	5
28a	Me	6.32	7.42	6.12	2.58	5.20	0.95	1.09	1.21	1.79	4.11	2.28	2
28b	Me	6.33	7.31	5.80	2.94	4.89	0.94	1.08	1.20	1.83	3.99	2.27	6.3
29a	vin	6.30	7.39	6.08	2.73	5.22	0.96	1.09	1.21	1.70	4.39	2.27	2.5
29b	vin	6.30	7.32	5.78	3.0	4.89	0.95	1.08	1.21	1.82	4.32	2.27	5.8
30a	eth	6.34	7.41	6.12	2.90	5.23	0.95	1.09	1.21	1.83	4.63	2.27	3.0
30b	eth	6.34	7.42	6.10	3.10	5.07	0.96	1.10	1.27	1.84	4.55	2.27	5.5
Multipl.		d	d	d	ddd	dt	t	d	d	s or d		s	

a) Measured at room temperature; 50 °C for compounds MT, **15a** and **15b**. b) Abbreviations: all=allyl, vin=vinyl, and eth=ethynyl. c) Multiplicities of H-23 were dq (for 23-L products) and quintet (23-D products).

with tributylstannane to give the 4′-deoxy derivative (**23**). The above reaction sequence is fundamentally the same with the procedure previously reported.[3] Acetylation of **23** gave the 2′-*O*-acetyl-4′-deoxy derivative (**24**). The all-protected derivative was then subjected to the procedure described in the MT-series, that is, 23-de-*O*-silylation (to give **25**), oxidation (to give the 23-oxo derivative, **26**), alkylation with methylmagnesium bromide or the other Grignard reagents (to give **27a**, **27b**, and other 23-C-alkyl derivatives), and deblocking to give the final products (**28a,b**, **29a,b**, and **30a,b**). Elemental analyses of the products are shown in Table 2 with some other data.

Antibacterial spectra[1] of these products showed diverse activity results, but D-series products always had stronger activities than those of the corresponding L-isomers. Compound **10** showed markedly decreased antibacterial activity.

Experimental

General. Grignard reagents (MeMgBr, EtMgBr, *n*-BuMgBr, PhMgBr, AllylMgBr) were purchased from Tokyo Kasei Kogyo Co., Ltd., and methyllithium (1.5 M solution in diethyl ether 1 M=1 mol dm^{-3}), from Aldrich Chem. Co. Thin-layer chromatography (TLC) was carried out on kieselgel 60 F-254 silica gel (E. Merck) 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). Optical rotations were measured with a Perkin-Elmer 241 polarimeter. ^{1}H-NMR spectra were recorded at 250 MHz at room temperature, unless otherwise stated, in the FT mode with a Bruker WM 250 spectrometer, or at 90 MHz with a Varian EM-390 spectrometer.

2′,4′-Di-*O*-acetyl-3,23-bis(*O*-*t*-butyldimethylsilyl)mycaminosyl Tylonolide Diethyl Acetal (2). To a mixture of **1**[3] (22.5 g) and imidazole (12.1 g) in dry *N*,*N*-dimethylformamide (23 ml) was added *t*-butylchlorodimethylsilane (22.4 g) and the solution was heated at 75 °C overnight. Evaporation with several additions of xylene gave a residue, that was extracted with benzene (2 L). The solution was washed with saturated aqueous sodium hydrogencarbonate, saturated aqueous sodium sulfate, dried (Na_2SO_4), and evaporated to give a solid (29 g). The solid showed, on TLC with toluene–ethyl acetate (2:1), spots at R_f 0.7 (**2**), 0.65 (trace, **3**), and 0 (cf **1**: R_f=0.15). An analytical sample of **2** was prepared by silica-gel column chromatography with toluene–ethyl acetate (3:1), $[\alpha]_D^{22}$ −11° (*c* 1, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ=−0.04, 0.03, 0.04, and 0.17 (each 3H s, $SiMe_2$×2), 0.87 (18H s, Si-*t*Bu×2), 1.78 (3H s with slight splittings, Me-22), 2.06 and 2.07 (each 3H s Ac×2), 2.34 (6H s, NMe_2), 3.67 (2H, H-23a,b), 3.98 (1H sl. br d, $J_{2b,3}$[7] ≈6.5 Hz, H-3), 4.35 (1H br d, *J*≈7.5 Hz, H-1′), 4.75 (1H t, J=10 Hz, H-4′), 4.89 (1H dd, *J*=7.5 and 10 Hz, H-2′), 5.78 (1H d, $J_{13,14}$=10.5 Hz, H-13), 6.25 (1H d, $J_{10,11}$=15 Hz, H-10), 7.18 (1H d, H-11).

Found: C, 62.47; H, 9.32; N, 1.56%. Calcd for $C_{51}H_{93}NO_{13}Si_2$: C, 62.26; H, 9.46; N, 1.42%.

3: $[\alpha]_D^{22}$ −12° (*c* 1, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ=0.05 and 0.06 (each 3H s, $SiMe_2$), 0.89 (9H s, Si-*t*-Bu), 1.79 (3H s with slight splittings, Me-22), 2.06 and 2.07 (each 3H s,

Table 2.

Compound	Yield[a]	$[\alpha]_D^{22}$ (*c* 1, $CHCl_3$)	Formula	C (%)		H (%)		N (%)	
				Found	Calcd	Found	Calcd	Found	Calcd
13a	26	−10°	$C_{32}H_{53}NO_{10}$	62.50	62.85	8.54	8.67	2.21	2.29
13b	7.8	+16°	$C_{32}H_{53}NO_{10}$	62.54	62.85	8.66	8.67	2.25	2.29
14a	21	−6°	$C_{33}H_{55}NO_{10}\cdot H_2O$	61.89	61.58	8.61	8.86	1.94	2.17
14b	4	+9°	$C_{33}H_{55}NO_{10}$	63.31	63.36	8.84	8.80	2.28	2.24
15a	8	+7°	$C_{35}H_{59}NO_{10}$	64.34	64.32	9.03	9.04	2.32	2.14
15b	2.3	+30°	$C_{35}H_{59}NO_{10}$	64.07	64.32	9.01	9.04	2.16	2.14
16a	21	+81°	$C_{37}H_{55}NO_{10}$	66.01	65.97	8.36	8.17	1.95	2.08
16b	9.2	+30°	$C_{37}H_{55}NO_{10}\cdot 2/3H_2O$	64.73	64.82	8.24	8.13	2.09	2.04
17a	7	+40°	$C_{34}H_{55}NO_{10}$	63.89	64.05	8.60	8.63	2.23	2.20
17b	3.8	−10°	$C_{34}H_{55}NO_{10}\cdot H_2O$	62.55	62.29	8.41	8.70	2.07	2.14
18a	29	−3°	$C_{33}H_{53}NO_{10}\cdot H_2O$	61.69	61.78	8.23	8.58	2.27	2.18
18b	7	0°	$C_{33}H_{53}NO_{10}$	63.32	63.56	8.56	8.51	2.05	2.25
19a	13	+65°	$C_{33}H_{51}NO_{10}$	63.61	63.77	8.47	8.21	2.02	2.25
19b	14	−39°	$C_{33}H_{51}NO_{10}\cdot H_2O$	61.42	61.97	7.96	8.29	2.21	2.19
28a	20	−16°	$C_{32}H_{53}NO_9$	64.25	64.54	8.80	8.91	2.41	2.35
28b	7	+12°	$C_{32}H_{53}NO_9\cdot 1/2H_2O$	63.81	63.58	8.87	8.94	2.44	2.32
29a	18	0°	$C_{33}H_{53}NO_9$	64.97	65.24	8.76	8.73	2.50	2.31
29b	8	0°	$C_{33}H_{53}NO_9$	65.46	65.24	8.81	8.73	2.27	2.31
30a	6.2	+7°	$C_{33}H_{51}NO_9$	65.71	65.45	8.54	8.43	2.29	2.31
30b	6.3	−36°	$C_{33}H_{51}NO_9$	65.10	65.45	8.30	8.43	2.23	2.31

a) Based on **4** or **25** and after purification; the 23-L and 23-D products were, respectively, purified in the same manner; in **13b** and **14b**, however, the yields were estimated from the mixture of the product and MT owing to difficulty of separation.

AcX2), 2.34 (6H s, NMe_2), ≈3.68 (H-23a,b), 3.78 (1H dd, $J_{3,OH}$≈4.5, $J_{2b,3}$=10 Hz, H-3), 4.40 (1H d, J=7.5 Hz, H-1'), 4.77 (1H t, H-4'), 4.91 (1H dd, H-2'), 5.87 (1H d, H-13), 6.31 (1H d, H-10), 7.25 (1H d, H-11); Irradiation at δ 2.46 (dd, H-2b)[7] collapsed the double doublets of H-3 to a doublet.

Found: C, 62.22; H, 8.99; N, 1.42%. Calcd for $C_{45}H_{79}NO_{13}Si$: C, 62.14; H, 9.09; N, 1.61%.

2',4'-Di-*O*-acetyl-3-*O*-*t*-butyldimethylsilylmycaminosyl Tylonolide Diethyl Acetal (4). To an ice-cold solution of crude **2** (29 g) in oxolane (290 ml) was added a M solution (29.5 ml) of tetrabutylammonium fluoride (1 moler equivalent for **2**) in oxolane (the solution contained <5% of water, Aldrich Chem. Co., Wisconsin, U.S.A.), and the solution was kept at room temperature for 1 h. On cheking by TLC with toluene–ethyl acetate (1:1), the solution showed a major spot at R_f 0.45. Evaporation gave a residue, that was extracted with benzene (1 L). The organic solution was washed with saturated aqueous sodium hydrogencarbonate, saturated aqueous sodium sulfate, dried (Na_2SO_4), and evaporated. The residue was chromatographed on a silica-gel column with toluene–ethyl acetate (3:2) to give a solid of **4**, 19.7 g (72% from **1**); $[\alpha]_D^{22}$ −10° (*c* 1, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ=−0.04 and 0.175 (each 3H s, $SiMe_2$), 0.87 (9H s, Si-*t*-Bu), 1.82 (3H, Me-22), 2.06 and 2.07 (each 3H s, AcX2), 2.34 (6H s, NMe_2), 3.98 (1H d, $J_{2b,3}$=7 Hz, H-3), 4.35 (1H br d, H-1'), 4.74 (1H t, H-4'), 4.89 (1H dd, H-2'), 5.74 (1H d, H-13), 6.28 (1H d, H-10), 7.18 (1H d, H-11).

Found: C, 62.35; H, 8.98; N, 1.53%. Calcd for $C_{45}H_{79}NO_{13}Si$: C, 62.14; H, 9.09; N, 1.61%.

2',4'-Di-*O*-acetyl-3-*O*-*t*-butyldimethylsilyl-23-deoxy-23-oxomycaminosyl Tylonolide Diethyl Acetal (5). A mixture of **4** (2.24 g), pyridinium trifluoroacetate (747 mg) and dicyclohexylcarbodiimide (2.13 g) in benzene–dimethyl sulfoxide (1:1, 45 ml) was stirred at room temperature overnight. Oxalic acid dihydrate (1.95 g) in 1,4-dioxane (22.5 ml) was added and the mixture was stirred for 30 min. The resulting precipitates were filtered off with aid of benzene, and the organic solution was concentrated. The residue was extracted with benzene and the solution was thoroughly washed with saturated aqueous sodium hydrogencarbonate (to remove dimethyl sulfoxide), saturated aqueous sodium sulfate, dried (Na_2SO_4), and evaporated. The residue showed, on TLC with toluene–ethyl acetate (1:1), two spots at R_f 0.55 (**5**) and R_f 0.3 (minor, **6**). Column chromatography of the residue with toluene–ethyl acetate (2:1→1:1) gave solids of **5**, 1.93 g (86%) and **6**, 0.32 g (14%).

5: $[\alpha]_D^{22}$ −40° (*c* 1, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ=−0.04 and 0.17 (each 3H s, $SiMe_2$), 0.88 (9H s, Si-*t*-Bu), 1.85 (3H, Me-22), 2.07 and 2.08 (each 3H s, AcX2), 2.36 (6H s, NMe_2), 3.57 (1H dt, H-14), 3.99 (1H d, H-3), 4.37 (1H d, H-1'), 4.75 (1H t, H-4'), 4.89 (1H dd, H-2'), 5.25 (1H dt, H-15), 5.77 (1H d, H-13), 6.33 (1H d, H-10), 7.18 (1H d, H-11), 9.67 (1H d, H-23); $J_{2b,3}$=7,5, $J_{10,11}$=16, $J_{13,14}$=10, $J_{14,15}$=9, $J_{14,23}$=3.8, $J_{15,16a}$=9.5, $J_{15,16b}$=2.5, $J_{1',2'}$=7.5 Hz. Irradiation of H-14 collapsed the double triplets of H-15 to a broadened doublet, and the doublets of H-13 and H-23 to a singlet, respectively. Irradiation of H-23 collapsed the double triplets of H-14 to a triplet.

Found: C, 62.24; H, 8.77; N, 1.49%. Calcd for $C_{45}H_{77}NO_{13}Si$: C, 62.28; H, 8.88; N, 1.61%.

6: $[\alpha]_D^{25}$ −32° (*c* 1, $CHCl_3$); ^{1}H-NMR ($CDCl_3$; the ratio of the components of **6** changed (A/B=2/1—2/3) depending on the experimental conditions, on which no study was carried out): δ=0.06 (for A/2) and 0.09 (A/2 +B) (6H in total, each s, $SiMe_2$), 0.90 (9H d, Si-*t*-Bu), 1.25(B) and 1.69(A) (3H in total, each s with small splittings, Me-22), 2.06 (6H s, AcX2), 2.34 (6H s, NMe_2), ≈2.3 (H-16), ≈2.5 (H-2), 3.96 (1H m, H-3), 4.38 (1H d, H-1'), 4.59 (1H m, H-20), 4.74 (1H t, H-4'), 4.90 (1H dd, H-2'), 6.26(B) and 6.28(A) (1H in total, each d, H-10), 6.36 (1H sl. br s, H-13), 6.69(A) and 6.72(B) (1H in total, each t, H-15), 7.11(B) and 7.33(A) (1H in total, each d, H-11), 9.44(A) and 9.46(B) (1H in total, each s, H-23); $J_{10,11}$=15.5, $J_{13,16}$≦1, $J_{15,16a}$=$J_{15,16a}$=7.5 Hz. Irradiation of H-16 collapsed the triplet of H-15 to a singlet and sharpened the broad singlet of H-13. Irradiation of H-13 sharpened the signals of both H-16 and H-23.

Esterification of 6 (obtained by a run) with Diazomethane (to give 7a and 7b). To a solution of **6** (65.4 mg) in chloroform (0.65 ml) was added 0.3 M diazomethane in ether (1.8 ml) and the solution was kept at room temperature for 1 h. The solution showed, on TLC with toluene–ethyl acetate (2:1), two spots at R_f 0.35 and R_f 0.25. Evaporation gave a residue, that was subjected to column chromatography with hexane–ethyl acetate (4:1→2:1) to give solids of **7a** (R_f=0.35), 25.4 mg (38%) and **7b** (R_f=0.25), 19.5 mg (29%).

7a: ^{1}H-NMR ($CDCl_3$) δ=0.04 and 0.08 (each 3H s, $SiMe_2$), 0.89 (9H s, Si-*t*-Bu), 2.04 and 2.06 (each 3H s, AcX 2), 2.25 (2H quintet, H-16), 2.34 (6H s, NMe_2), a set of eight signals typical for the AB part of an ABX system centered at 2.50 (2H, J=6.75 and 15 Hz, H-2a,b), 3.67 (3H s, CO_2Me), 4.03 (1H m, H-3), 4.40 (1H d, J=7.5 Hz, H-1'), 4.55 (1H m, H-20), 4.72 (1H t, H-4'), 4.89 (1H dd, H-2'), 6.25 (1H sl. br s, H-13), 6.35 (1H d, H-10), 6.67 (1H sl, br t, H-15), 7.11 (1H d, H-11), 9.46 (1H s, H-23); $J_{10,11}$=15.5, $J_{15,16a}$=$J_{15,16b}$=7.5 Hz.

7b: ^{1}H-NMR ($CDCl_3$) δ=0.04 and 0.08 (each 3H s, $SiMe_2$), 0.89 (9H s, Si-*t*-Bu), 2.05 (6H s, AcX2), 2.27 (2H quintet, H-16), 2.34 (6H s, NMe_2), 2.52 (2H, H-2a,b), 3.69 (3H s, CO_2Me), 4.05 (1H, br, H-3), 4.41 (1H d, H-1'), 4.58 (1H t, H-20), 4.72 (1H t, H-4'), 4.89 (1H dd, H-2'), 6.27 1H d, H-10), 6.35 (1H sl. br s, H-13), 6.63 (1H t, $J_{15,16a}$ =$J_{15,16b}$=7.5 Hz, H-15), 7.32 (1H d, H-11), 9.46 (1H s, H-23).

In the 250 MHz ^{1}H shift-correlated 2D NMR spectrum, Me-17 could be correlated to H-16, and the latter, to H-15.

3-*O*-*t*-Butyldimethylsilylmycaminosyl Tylonolide Diethyl Acetal (8). A solution of **4** (100 mg) in methanol (2 ml) was heated at 50 °C for 24 h. Evaporation was followed by extraction of the residue with chloroform. The organic solution was washed with saturated aqueosu sodium hydrogencarbonate, saturated aqueous sodium sulfate, dried (Na_2SO_4), and evaporated to give a solid of **8**, 89 mg (98%); $[\alpha]_D^{22}$ −2° (*c* 1, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ=−0.04 and 0.18 (each 3H s, $SiMe_2$), 0.85 (9H s, Si-*t*-Bu), 0.93 (3H t, Me-17), 0.99 (3H d, Me-18), 1,83 (3H, Me-22), 2.50 (6H s, NMe_2), 3.03 (1H t, H-4'), 3,53 (1H dd, H-2'), 4.02 (1H sl. br d, H-3), 4.27 (1H sl. br d, H-1'), 4.73 (1H br dd, H-20), 4.90 (1H dt, H-15), 5.77 (1H d, H-13), 6.27 (1H d, H-10), 7.21 (1H d, H-11); $J_{2b,3}$=6, $J_{4,18}$=7, $J_{10,11}$=16, $J_{13,14}$=10, $J_{14,15}$=$J_{15,16a}$=9, $J_{15,16b}$=2.5, $J_{1',2'}$=6.5, $J_{2'3'}$=$J_{3'4'}$=$J_{4'5'}$=10Hz.

Found: C, 62.77; H, 9.41; N, 1.71%. Calcd for $C_{41}H_{75}NO_{11}Si$: C, 62.68; H, 9.55; N, 1.78%.

3'-*O*-*t*-Butyldimethylsilyl-23-deoxy-23-oxomycaminosyl

Tylonolide Diethyl Acetal (9). From 5. A solution of **5** (22.2 mg) in methanol (0.1 ml) was heated at 50 °C for 24 h. TLC (chloroform–methanol–28% aqueous ammonia= 10:1:0.1) of the reaction mixture showed two spots at R_f 0.3 (**9**) and R_f 0.01 (major). Evaporation was followed by extraction of the residue with chloroform. The solution was washed with saturated aqueous sodium sulfate, dried (Na_2SO_4), and evaporated. The residue was chromatographed on a silica-gel column with chloroform–methanol–28% aqueous ammonia (20:1:0.1) to give a solid of **9**, 6.9 mg (34%).

From 8. A mixture of **8** (300 mg), pyridinium trifluoroacetate (74 mg) and dicyclohexylcarbodiimide (315 mg) in benzene–dimethyl sulfoxide (1:1, 6 ml) was stirred at room temperature overnight. The solution showed, on TLC with chloroform–methanol–28% aqueous ammonia (10:1:0.1), a spot at R_f 0.3 (major, **9**) with several minors. The solution was then treated as usual to give, after chromatography (chloroform–methanol–28% aqueous ammonia=10:1:0.1), a solid of **9**, 150 mg (50%); $[\alpha]_D^{23}$ −40° (*c* 1, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ=−0.04 and 0.16 (each 3H s, $SiMe_2$), 0.89 (9H s, Si-*t*-Bu), 1.85 (3H d, $J\approx1$ Hz, Me-22), 2.56 (6H s, NMe_2), 4.02 (1H d, H-3), 4.35 (1H d, H-1′), 5.25 (1H dt, H-15), 5.78 (1H d, H-13), 6.32 (1H d, H-10), 7.19 (1H d, H-11), 9.66 (1H d, H-23); $J_{14,15}\approx9$, $J_{14,23}$=3.8 Hz.

Found: C, 62.53; H, 9.13; N, 1.90%. Calcd for $C_{41}H_{73}NO_{11}Si$: C, 62.83; H, 9.32; N, 1.42%.

23-Deoxy-23-oxomycaminosyl Tylonolide (10). To a solution of **9** (20 mg) in acetonitrile (0.1 ml) in a silicone vessel was added 10% aqueous hydrofluoric acid (0.1 ml) and the solution was kept at 27 °C overnight. The solution showed, on TLC with chloroform–methanol–28% aqueous ammonia (5:1:0.1), spots at R_f 0.38 (**10**) and R_f 0. Afrer addition of saturated aqueous sodium hydrogencarbonate (0.5 ml), the reaction mixture was extracted with chloroform. The organic solutioon was washed with saturated aqueous sodium sulfate, dried (Na_2SO_4), and evaporated. The residue was chromatographed over silica gel with chloroform–methanol (7:1) to give an unstable solid of **10**, 3.9 mg (26%); $[\alpha]_D^{22}$ −60° (*c* 1, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ=0.96 (3H t, Me-17), 1.02 (3H d, Me-18), 1.22 (3H d, Me-21), 1.27 (3H d, Me-6′), 1.87 (3H d, $J\approx1$ Hz, Me-22), 1.96 (1H d, H-2a), 2.40 (1H t, H-3′), 2.52 (6H s, NMe_2), 2.56 (1H dd, H-2b), 2.96 (1H ddd, H-19b), 3.07 (1H t, H-4′), 3.27 (1H m, H-5′), 3.49 (1H dd, H-2′), 3.65 (1H dt, H-14), 3.74 (1H dd, H-5), 3.87 (1H d, H-3), 4.27 (1H d, H-1′), 5.30 (1H dt, H-15), 5.83 (1H d, H-13), 6.36 (1H d, H-10), 7.31 (1H d, H-11), 9.69 (1H d, H-23), 9.71 (1H s, H-20); $J_{13,14}$= $J_{14,15}$=10, $J_{14,23}$=3.8 Hz; other *J* values were almost the same with those of the related compounds reported.[7] Irradiation of H-14 collapsed the double triplets of H-15 to double doublets, and the doublets of H-13 and H-23 to a singlet, respectively.

Found: C, 61.47; H, 8.41; N, 2.44%. Calcd for $C_{31}H_{49}NO_{10}\cdot1/2\ H_2O$: C, 61.59; H, 8.28; N, 2.32%.

(23*S*)- and (23*R*)-2′4′-Di-*O*-acetyl-3-*O*-*t*-butyldimethylsilyl-23-C-methylmycaminosyl Tylonolide Diethyl Acetal (11a, 11b). Procedure A. To a cold (−78 °C) solution of **5** (570 mg) in oxolane (7 ml) was added methylmagnesium bromide (1 ml of M solution in oxolane) and the mixture was stirred at the temperature for 1.5 h, then kept at room temperature for 1 h. The reaction mixture was poured into an ice-cold half-saturated aqueous ammonium chloride (30 ml) and extracted with chloroform. The organic solution combined was washed with saturated aqueous sodium sulfate, dried (Na_2SO_4), and evaporated to give a residue. Silica-gel column chromatography of the residue with toluene–ethyl acetate (2:1) gave, from the earlier fractions, a solid of **11a**, 236 mg (36%), and from the later, a mixture of **11b** and **4**, 114 mg, the both compounds had the same mobility on chromatogram.

11a: $[\alpha]_D^{21}$ −10° (*c* 1, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ=−0.04 and 0.18 (each 3H s, $SiMe_2$), 0.87 (9H s, Si-*t*Bu), 1.12 (3H d, Me-24), 1.78 (3H short-spaced d, Me-22), 2.06 and 2.08 (each 3H s, AcX2), 2.35 (6H s, NMe_2), 2.45 (1H dd, $J_{2,3}$=7, $J_{2a,b}$=19 Hz, H-2b), 2.49 (1H dt, H-14), 2.73 (1H t, H-3′), 3.98 (1H br d, H-3), 4.10 (H-23), 4.36 (1H br d, H-1′), 4.68 (1H, br, H-20), 4.75 (1H t, H-4′), 4.89 (1H dd, H-2′), 5.13 (1H dt, H-15), 5.96 (1H d, H-13), 6.27 (1H d, H-10), 7.23 (1H d, H-11); $J_{13,14}$=10, $J_{14,15}$=9, $J_{14,23}$=2.5, $J_{23,Me\text{-}24}$=7 Hz. Irradiation of H-23 collapsed the doublet of Me-24 and the double triplets of H-14 to a singlet and a triplet, respectively.

Found: C, 62.59; H, 9.17; N, 1.67%. Calcd for $C_{46}H_{80}NO_{13}Si$: C, 62.59; H, 9.07; N, 1.59%.

11b: $[\alpha]_D^{21}$ +11° (*c* 1, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ=−0.04 and 0.18 (each 3H s, $SiMe_2$), 0.87 (9H s, Si-*t*Bu), 1.22 (3H d, Me-24), 1.83 (3H short-spaced d, Me-22), 2.06 and 2.07 (each 3H s, AcX2), 2.34 (6H s, NMe_2), 2.47 (1H dd, H-2b), 2.73 (1H t, H-3′), 2.88 (1H dt, H-14), 3.98 (1H br d, H-3), 3.98 (1H br d, H-23), 4.35 (1H d, H-1′), 4.68 (1H, br, H-20), 4.75 (1H t, H-4′), 4.85 (1H, H-15), 4.89 (1H dd, H-2′), 5.73 (1H d, H-13), 6.27 (1H d, H-10), 7.18 (1H d, H-11); $J_{13,14}$=$J_{14,15}$=10, $J_{14,23}$=6, $J_{23,Me\text{-}24}$=6.5 Hz. Irradiation at δ=3.98 collapsed the doublet of Me-24 and double triplets of H-14 to a singlet and a triplet, respectively.

Procedure B. To a cold (−78 °C) solution of **5** (310 mg) in dry diethyl ether (3.1 ml) was added methyllithium (0.25 ml of 1.5 M solution in diethyl ether) and the mixture was stirred in the cold for 1.5 h, then the resulting yellow suspension was kept at room temperature for 1 h. Work-up as described for Procedure A gave a crude mixture. Silica-gel column chromatography of the mixture with toluene–ethyl acetate (2:1→1:1) gave solids of **11a**, 140 mg (44%) and **11b**, 36 mg (≈11%, slightly contaminated with **4**).

(23*S*)-23-C-Methylmycaminosyl Tylonolide (13a). A solution of **11a** (236 mg) in methanol (2.4 ml) was heated at 50 °C overnight. Evaporation gave a solid of **12a**. To a solution of the solid in acetonitrile (1.2 ml) was added M aqueous hydrochloric acid (1.2 ml) and the solution was kept at 37 °C overnight. On TLC with chloroform–methanol–28% aqueous ammonia (9:1:0.1), the solution showed a spot (R_f=0.23). Addition of saturated aqueous sodium hydrogencarbonate (10 ml) was followed by extraction of the mixture with chloroform. The organic solution isolated was washed with saturated aqueous sodium sulfate, dried (Na_2SO_4), and evaporated to give a solid (178 mg). Silica-gel column chromatography with chloroform–methanol–28% aqueous ammonia (20:1:0.1→10:1:0.1) gave a solid of **13a**, 121 mg (74%).

13a: ^{1}H-NMR ($CDCl_3$) δ=1.15 (3H d, Me-24), 1.27 (3H d, Me-6′), 2.36 (1H t, *J*=10 Hz, H-3′), 2.93 (1H ddd, *J*=1.5, 10, and 17.5 Hz, H-19b), 3.05 (1H t, *J*=10 Hz, H-4′), 3.27 (1H m, H-5′), 3.49 (1H dd, H-2′), 3.75 (1H d, H-5), 3.86 (1H sl. br d, H-3), 4.26 (1H d, *J*=7.5 Hz, H-1′), 9.69 (1H

s, H-20); $J_{13,14}$=10.8, $J_{14,15}$=$J_{15,16a}$=9.5, $J_{15,16b}$=3, $J_{23,Me\text{-}24}$= 7.5 Hz. Irradiation of H-14 collapsed the signals of H-13, H-15, and H-23 to a singlet, a broad doublet, and a quartet, respectively. Irradiation of H-23 collapsed the doublet of Me-24 to a singlet.

(23*R*)-23-C-Methylmycaminosyl Tylonolide (13b). A solution of crude **11b** (114 mg obtained by Procedure A) was treated as described for **13a** and the products were twice chromatographed (to remove MT accompanied) as described, to give solids of **13b**, 39 mg (7.8% from **4**) and mycaminosyl tylonolide (19 mg).

13b: ^{1}H-NMR ($CDCl_3$) δ=1.24 (3H d, Me-24), 1.27 (3H d, Me-6'), 2.37 (1H t, H-3'), 3.05 (1H t, H-4'), 3.28 (1H m, H-5'), 3.50 (1H dd, H-2'), 3.76 (1H d, H-5), 3.87 (1H d, H-3), 4.28 (1H d, H-1'), 9.70 (1H s, H-20); $J_{13,14}$=10.5, $J_{14,15}$=$J_{15,16a}$=9.0, $J_{15,16b}$=3, $J_{23,Me\text{-}24}$≈6 Hz. Irradiation of H-23 collapsed the signals of H-14 and Me-24 to a triplet and a singlet, respectively.

General Procedure for the Syntheses of 14a,b—19a,b. A mixture of **4** (900 mg), pyridinium trifluoroacetate (300 mg) and dicyclohexylcarbodiimide (850 mg) in benzene–dimethyl sulfoxide (1:1 18 ml) was stirred at room temperature for 6 h and the mixture was treated as described for **5** to give, without chromatography, a crude product (900 mg). To a cold (−78 °C) solution of the product in dry oxolane (9 ml) was added ethylmagnesium bromide (0.8 ml of 3 M solution in ether; for the preparation of **14a,b**), butylmagnesium bromide (1.2 ml of 2 M solution in oxolane, for **15a,b**), phenylmagnesium bromide (1.2 ml of 2 M solution in oxolane, for **16a,b**), allylmagnesium bromide (2.4 ml of M solution in ether, for **17a,b**), vinylmagnesium bromide [prepared from magnesium turnings (960 mg) and vinyl bromide (3.5 ml) in oxolane (20 ml) and used 2 ml of this solution; for **18a,b**] or ethynylmagnesium bromide [prepared by dropwise addition of EtMgBr (5 ml of 3 M solution in ether) to acetylene saturated in oxolane (10 ml) at 0—5 °C and used 4 ml of this red solution; for **19a,b**], and the mixture was kept at −78 °C for 1 h (at 0—5 °C for **19**), then kept at room temperature for 1 h. Work-up as described for **11a,b** gave, after column chromatography with toluene–ethyl acetate (2:1), a mixture of reaction products. Each product mixture was then methanolized and hydrolyzed as described for **13a** to give, after column chromatography with chloroform–methanol–28% aqueous ammonia (20:1:0.1→10:1:0.1), a final set of products as the solids of **14a,b—19a,b** (see Table 2).

3,23-Bis(*O*-*t*-butyldimethylsilyl)-4'-deoxymycaminosyl Tylonolide Diethyl Acetal (23). A solution of **2** (14.4 g) in methanol (144 ml) was heated at 50 °C overnight. Evaporation gave a residue, that was extracted with chloroform. The organic solution was washed with saturated aqueous sodium hydrogencarbonate, saturated aqueous sodium sulfate, dried (Na_2SO_4), and evaporated to give a solid of **20** (12.7 g, 96%). To a cold (−40 °C) solution of the solid (12.7 g) in pyridine (127 ml) was added phenylmethanesulfonyl chloride (2.7 g initially, and 1.38 g after 1 hour) and the solution was kept at −40 °C for 5.5 h in total. After addition of water (0.5 ml), the solution was concentrated to give a residue, that was extracted with chloroform. The organic solution was washed with saturated aqueous sodium hydrogencarbonate, saturated aqueous sodium sulfate, dried (Na_2SO_4), and evaporated. The residue showed, on TLC with toluene–ethyl acetate (2:1), a spot at R_f 0.65 (major, **21**) with trace spots of R_f 0.8 and R_f 0. A mixture of the residue and sodium iodide (4.2 g) in 2-butanone (127 ml) was heated at 80 °C for 1 h. TLC (toluene–ethyl acetate 2:1) of the solution showed a spot (**22**) of the same R_f value with that of **21**. Filtration followed by evaporation gave a solid, that was extracted with benzene. The organic solution was washed with 0.1 M aqueous sodium thiosulfate, saturated aqueous sodium sulfate, dried (Na_2SO_4), and evaporated to give a solid. To a solution of the solid in benzene (127 ml) was added tributylstannane (12.3 g) and the solution was refluxed for 9 h. TLC (cyclohexane–acetone 7:4) of the solution showed a major spot at R_f 0.25 (**23**). Evaporation gave a syrup, that was twice chromatographed over silica gel with chloroform–methanol (20:1) to give solids of **23**, 10.3 g (82%) and **20**, 0.31 g. **23**: $[\alpha]_D^{20}$ −7° (*c* 1, $CHCl_3$).

^{1}H-NMR ($CDCl_3$) δ=−0.05, 0.02, 0.03, and 0.18 (each 3H s, $SiMe_2$×2), 1.78 (3H d, Me-22), 2.28 (6H s, NMe_2), 4.00 (1H d, H-3), 4.24 (1H d, H-1'), 4.75 (1H m, H-20), 4.93 (1H dt, H-15), 5.79 (1H d, H-13), 6.26 (1H d, H-10), 7.20 (1H d, H-11).

Found: C, 63.68; H, 9.81; N, 1.79%. Calcd for $C_{47}H_{88}NO_{10}Si_2$: C, 63.95, H, 9.98; N, 1.59%.

2'-*O*-Acetyl-3,23-bis(*O*-*t*-butyldimethylsilyl)-4'-deoxymycaminosyl Tylonolide Diethyl Acetal (24). A mixture of **23** (8.56 g) and acetic anhydride (1.17 ml) in acetonitrile (86 ml) was kept at room temperature for 6 h. Evaporation with several additions of toluene gave a residue, that was extracted with chloroform. The organic solution was washed with saturated aqueous sodium hydrogencarbonate, saturated aqueous sodium sulfate, dried (Na_2SO_4), and evaporated to give a residue. Silica-gel column chromatography with toluene–ethyl acetate (1:1→1:2) gave a solid of **24**, 7.42 g. (82%); $[\alpha]_D^{22}$ +1° (*c* 1, $CHCl_3$).

^{1}H-NMR ($CDCl_3$) δ=−0.05, 0.03, 0.05, and 0.18 (each 3H s, SiM_2×2), 1.78 (3H d, Me-22), 2.08 (3H s, Ac), 2.27 (6H s, NMe_2), 4.28 (1H d, H-1'), ≈4.7 (2H, H-2', 20), 4.93 (1H dt, H-15), 5.78 (1H d, H-13), 6.25 (1H d, H-10), 7.19 (1H d, H-11).

Found: C, 63.49; H, 9.68; N, 1.48%. Calcd for $C_{49}H_{90}NO_{11}Si_2$: C, 63.63; H, 9.74; N, 1.52%.

2'-*O*-Acetyl-3-*O*-*t*-butyldimethylsilyl-4'-deoxymycaminosyl Tylonolide Diethyl Acetal (25). To an ice-cold solution of **24** (7.3 g) in oxolane (73 ml) was added a M solution of tetrabutylammonium fluoride in oxolane (8.7 ml) and the mixture was kept at room temperature for 2 h. Work-up as described for **24** gave a crude product, having, on TLC (chloroform–acetone 1:1), a single spot (R_f 0.5). It was purified by column chromatography with chloroform–acetone (6:5) to give a solid of **25**, 6 g (93%); $[\alpha]_D^{20}$ +4° (*c* 1, $CHCl_3$).

^{1}H-NMR ($CDCl_3$) δ=−0.05 and 0.18 (each 3H s, $SiMe_2$), 1.82 (3H s, Me-22), 2.08 (3H s, Ac), 2.27 (6H s, NMe_2), 4.29 (1H d, H-1'), ≈4.75 (2H, H-2', 20), 4.89 (1H dt, H-15), 5.75 (1H d, H-13), 6.30 (1H d, H-10), 7.18 (1H d, H-11).

Found: C, 62.80; H, 9.21; N, 1.80%. Calcd for $C_{43}H_{77}NO_{11}Si \cdot 1/2\ H_2O$: C, 62.93; H, 9.51; N, 1.71%.

(23*S*)- and (23*R*)-2'-*O*-Acetyl-3-*O*-*t*-butyldimethylsilyl-4'-deoxy-23-C-methylmycaminosyl Tylonolide Diethyl Acetal (27a, 27b). To a solution of **25** (900 mg) in benzene–dimethyl sulfoxide (1:1, 18 ml) were added pyridinium tri-

fluoroacetate (230 mg) and dicyclohexylcarbodiimide (914 mg) and the mixture was stirred at room temperature for 4 h. After addition of oxalic acid dihydrate (372 mg) in 1,4-dioxane (9 ml), the mixture was stirred for 1 h. Filtration followed by concentration of the solution gave a syrup. A benzene solution of the syrup was washed with saturated aqueous sodium hydrogencarbonate, saturated aqueous sodium sulfate, dried (Na_2SO_4), and evaporated to give a solid, 900 mg; TLC: R_f 0.5 with toluene–acetone (3:2). The ^{1}H-NMR spectrum (90 MHz, in $CDCl_3$) of this solid showed a doublet ($J_{14,23}$=3 Hz) at δ 9.75 (CHO at C-23).

To a cold (−78 °C) solution of the solid (900 mg) in dry oxolane (9 ml) was added methylmagnesium bromide in oxolane (1.6 ml of M solution) and the solution was kept at −78 °C for 1 h. The reaction mixture was poured into an ice-cold half-saturated aqueous ammonium chloride (30 ml) and extracted with chloroform. The organic solution was washed with saturated aqueous sodium sulfate, dried (Na_2SO_4), and evaporated to give a solid, that showed several spots including R_f 0.47 (major, **27a**) and 0.41 (minor, **27b** and **25**) on TLC with toluene–acetone (3:2). Column chromatography with toluene–acetone (4:1→1:1) gave solids of crude **27a**, 384 mg (≈42%) and **27b**, 131 mg (contaminated with **25**).

27a: ^{1}H-NMR ($CDCl_3$) δ=−0.04 and 0.18 (each 3H s, $SiMe_2$), 1.12 (3H d, $J_{23,Me\text{-}24}$=7.5 Hz, Me-24), 1.78 (3H d, Me-22), 2.09 (3H s, Ac), 2.26 (6H s, NMe_2), 2.47 (1H m, H-14), 4.09 (1H dq, $J_{14,23}$=2.5 Hz, H-23), 5.14 (1H dt, H-15).

27b: ^{1}H-NMR ($CDCl_3$; the signals for **25** were not recorded) δ=1.20 (3H d, $J_{23,Me\text{-}24}$=6 Hz, Me-24), 2.09 (3H s, Ac), 2.89 (1H m, H-14), 4.30 (1H d, H-1′).

(23*S*)- and (23*R*)-4′-Deoxy-23-C-methylmycaminosyl Tylonolide (28a, 28b). A solution of **27a** (384 mg) in methanol (7 ml) was heated at 50 °C overnight. Evaporation gave a residue of the deacetylated product. To a solution of the residue in acetonitrile (1.5 ml) was added M aqueous hydrochloric acid (1.5 ml) and the solution was kept at 37 °C overnight. After addition of saturated aqueous sodium hydrogencarbonate (10 ml), the mixture was extracted with chloroform. The organic solution was washed with saturated aqueous sodium sulfate, dried (Na_2SO_4), and evaporated. Column chromatography of the residue with chloroform–methanol–28% aqueous ammonia (15:1:0.1) gave a solid of **28a**, 130 mg (50% from **27a**). Compound **27b** (131 mg) was likewise treated as described above to give, after column chromatography, solids of **28b**, 47 mg (7% from **25**) and DT, 20 mg.

General Procedure for the Syntheses of 29a,b and 30a,b. A mixture of **25** (900 mg), dicyclohexylcarbodiimide (914 mg), and pyridinium trifluoroacetate (230 mg) in benzene–dimethyl sulfoxide (1;1, 18 ml) was stirred at room temperature overnight. Work-up as described for **27a,b** gave the final products.

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