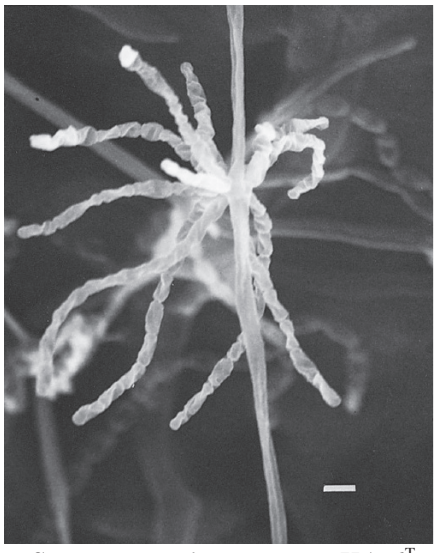
Leucomycin©

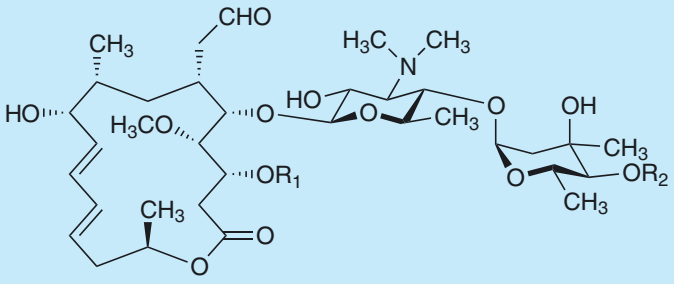
See also "Macrolide Antibiotics" (p. 368)

1. Discovery, producing organism and structures[1-10)]

Leucomycin was originally isolated from the culture broth of *Streptomyces kitasatoensis* strain KA-6^T by T. Hata and his co-workers in 1953[1)]. Since then, ten components of the antibiotic complex were isolated by means of silica gel and alumina column chromatographies[2)].

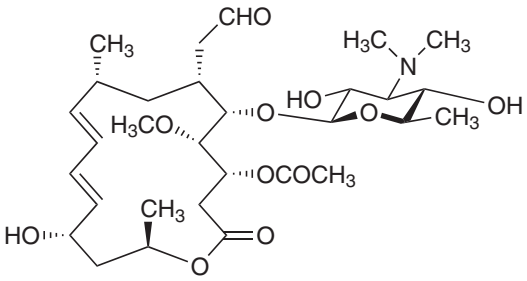


Streptomyces kitasatoensis KA-6^T

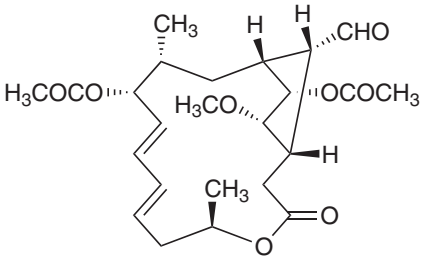


	R_1	R_2
Leucomycin A_1	H	$COCH_2CH(CH_3)_2$
Leucomycin A_3	$COCH_3$	$COCH_2CH(CH_3)_2$
Leucomycin A_4	$COCH_3$	$COCH_2CH_2CH_3$
Leucomycin A_5	H	$COCH_2CH_2CH_3$
Leucomycin A_6	$COCH_3$	$COCH_2CH_3$
Leucomycin A_7	H	$COCH_2CH_3$
Leucomycin A_8	$COCH_3$	$COCH_3$
Leucomycin A_9	H	$COCH_3$
Leucomycin U	$COCH_3$	H
Leucomycin V	H	H

The molecular structure of demycarosylleucomycin A_3(later corrected to be demycarosyl-*iso*-leucomycin A_3), a hydrolytic product of leucomycin A_3, was determined by means of X-ray crystallographic analysis[6)]. The absolute configuration of the lactone ring of leucomycin A_3, except for the chirality of C-9, was established by X-ray analysis. The chirality of C-9 was determined by allylic rearrangement of the hydroxyl group at C-9 to C-13 during acid hydrolysis[6,7)]. The absolute configuration at C-9 was assigned as (*S*) on the basis of the benzoate or Mill's rule for leucomycin A_3 and its derivatives[8)]. After extensive IR and NMR spectroscopic analysis of leucomycin A_3 and 9-epi-leucomycin A_3[9)], the absolute configuration at C-9 was reassigned as (*R*). In order to resolve these differences and determine the configuration at C-3 as well as those at C-9 and C-17 of 3, 6-bicycloleucomycin A_3, a derivative obtained by treatment of leucomycin A_3 with lithium hydroxide in ethanol, analysis of diacetyl-3,6-bicycloleucomycinolide A_3 by X-ray crystallography was performed, and the configuration at C-9 was further confirmed to be (*R*)[10)]. The total synthesis of leucomycin A_3 has been reported by two groups. The first total synthesis was reported by Tatsuta *et al*.[11)] (See Appendix-I).



Demycarosylleucomycin A_3
(Demycarosyl-*iso*-leucomycin A_3)



Diacetyl-3,6-bicycloleucomycin A_3

2. Physical data (Leucomycin A_3)[2)]
White powder. $C_{42}H_{69}NO_{15}$; mol wt 785.46. Sol. in $CHCl_3$, EtOH, dioxane, EtOAc, acetone. Easily crystallized from benzene.

3. Biological activity[12,13)]
1) Antimicrobial activity[12)]

	Test organism	MIC (μg/ml)	
	Staphylococcus aureus	*Bacillus subtilis*	*Klebsiella pneumoniae*
Leucomycin A_1	0.04	0.60	10
Leucomycin A_3	0.04	0.60	10
Leucomycin A_4	0.15	1.25	10
Leucomycin A_5	0.80	0.30	5
Leucomycin A_6	0.04	0.60	10
Leucomycin A_7	0.15	0.30	10
Leucomycin A_8	0.60	2.50	10
Leucomycin A_9	0.30	1.25	10
Leucomycin U	3.12	6.25	25
Leucomycin V	3.12	—	25

2) Leucomycin A_3 showed effective action against influenza A virus infection *in vivo*.[13)]

3. Leucomycin is commercially available as antibacterial medicine.

4. References

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