Note

TOTAL SYNTHESIS AND BIOLOGICAL EVALUATION OF UNNATURAL (−)-MEDERMYCIN [(−)-LACTOQUINOMYCIN]

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Kalafungin[1,2] (**1**), nanaomycin D[1,2] (**2**) and medermycin[3~5] (**3**: lactoquinomycin[6]) are members of a family of pyranonaphthoquinone antibiotics. Kalafungin (**1**) and nanaomycin D (**2**) are enantiomers and, interestingly, are endowed with almost the same antibacterial activities. Structurally, kalafungin (**1**) is a major segment of medermycin (**3**).

Consequently, in order to provide additional insight into their mode of action, we have synthesized the unnatural (−)-enantiomer (**3'**) of medermycin having a *C*-glycoside and have examined its antibacterial activity.

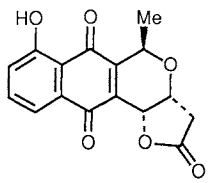
Since we have already accomplished the first total synthesis of natural (+)-medermycin[7] (**3**), we applied the same protocol to the present synthesis by using L-rhamnose as the enantiomeric starting material.

The physico-chemical and spectral data of (−)-medermycin (**3'**) (mp ~155°C (dec)[6,7]; $[\alpha]_D^{23}$ −264° (*c* 0.12, MeOH)[6,7]) and its hydrochloride

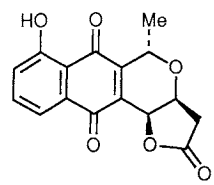
Table 1. Antibacterial activities of hydrochlorides of **3** and **3'**.

	MIC (μg/ml)	
	3·HCl	**3'**·HCl
Staphylococcus aureus FDA 209P	<0.47	<0.47
S. aureus Smith	<0.47	<0.47
S. aureus MS 9610	<0.47	<0.47
Micrococcus luteus FDA 16	3.75	1.87
M. luteus PCI 1001	3.75	1.87
Bacillus anthracis	0.94	0.94
B. subtilis NRRL B-558	<0.47	<0.47
B. subtilis PCI 219	<0.47	0.94
Corynebacterium bovis 1810	3.75	1.87
Escherichia coli NIHJ	30	15
Shigella dysenteriae JS 11910	30	15
Salmonella typhi T-63	>30	>15
Proteus vulgaris OX 19	30	15
Pseudomonas aeruginosa A3	>30	>15
Klebsiella pneumoniae PCI 602	>30	>15
Mycobacterium smegmatis ATCC 607	>30	>15
Candida albicans 3147	>30	>15

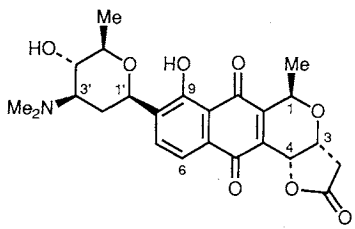
Medium: Mueller-Hinton agar (Difco).



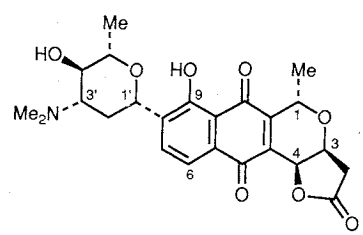
Kalafungin (**1**)



Nanaomycin D (**2**)



(+)-Medermycin (**3**: lactoquinomycin)



(−)-Medermycin (**3'**)

(mp ~190°C (dec)[3,7]; $[\alpha]_D^{23}$ −183° (*c* 0.08, MeOH)[3,7]) were completely identical with those of authentic samples† of natural (+)-medermycin (**3**) and its hydrochloride except for the signs of optical rotations.

Remarkably, the antibacterial activities (Table 1) of unnatural (−)-medermycin (**3'**) were almost the same as those of natural (+)-medermycin (**3**), indicating that the stereochemistry of the *C*-glycoside and lactone moieties was not significantly responsible for the nature of their biological activities.

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