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## The Structures of the Exfoliamycins

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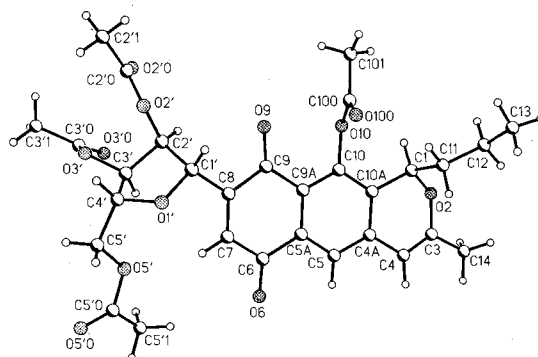
Recently, we have reported the isolation and characterization of the exfoliamycins (**1**~**3**), new antibacterial naphthoquinone C-glycosides from *Streptomyces exfoliatus*<sup>2</sup>). The connectivity within the unusual pentosyl moiety could not be proved unambiguously, because of signal overlapping in the <sup>1</sup>H NMR spectra. The situation took a turn to the better by using tetra-*O*-acetyl-anhydroexfoliamycin (**4**) but no stereochemical details could be given for the tetrahydrofuran residue. In this paper we wish to report the X-ray structure analysis of **4** and detailed NOE experiments in case of **2**. Both investigations lead to the structures of **1**~**3** including their relative stereochemistry<sup>3</sup>).

Crystals of **4** (orange needles, C<sub>30</sub>H<sub>32</sub>O<sub>12</sub>, MW 584.6) were obtained by liquid-liquid diffusion from a dichloromethane-hexane solvent system at 8°C. The size of the X-ray specimen was about 0.5 × 0.4 × 0.3 mm. Data were collected on a Siemens-Stoe-AED-diffractometer with graphite monochromated MoK<sub>α</sub> radiation (λ = 71.073 pm). The crystal data are as follows: Orthorhombic, space group P2<sub>1</sub>2<sub>1</sub>2<sub>1</sub>. Cell dimensions, a = 531.9 (1), b = 1861.6 (2), c = 2876.8 (3) pm, V = 2.8486 (7) nm<sup>3</sup>, Z = 4, D<sub>calc</sub> = 1.363 Mg/m<sup>3</sup>, μ = 0.106 mm<sup>-1</sup>, data collec-

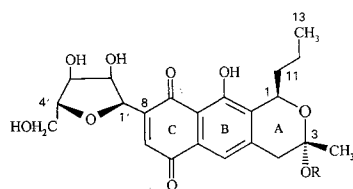
tion with profile fitting method<sup>4</sup>) at -120°C, 2θ range = 8 to 45°, 5451 reflections measured, all 3750 unique reflections used for refinement. The crystal structure was solved by direct methods (SHELXS-90<sup>5</sup>) and the 385 parameters were refined by full matrix least squares method on F<sup>2</sup> (SHELXL-93<sup>6</sup>). Non hydrogen atoms were refined anisotropically. A riding model starting from calculated positions was employed for the hydrogen atoms. The absolute structure could not be determined reliably. R1 = 0.0451 for I > 2σ(I) and wR2 = 0.1014 for all data, w<sup>-1</sup> = σ<sup>2</sup>(F<sub>o</sub><sup>2</sup>) + (0.048P)<sup>2</sup> + 0.1449P with P = (F<sub>o</sub><sup>2</sup> + 2F<sub>c</sub><sup>2</sup>)/3, max. residual density 158 e<sup>-</sup> nm<sup>-3</sup> (R1 = Σ(|F<sub>o</sub> - |F<sub>c</sub>||)/Σ|F<sub>o</sub>|, wR2 = (Σw(F<sub>o</sub><sup>2</sup> - F<sub>c</sub><sup>2</sup>)<sup>2</sup>/ΣwF<sub>o</sub><sup>4</sup>)<sup>1/2</sup>). Further details of the crystal structure investigation are available on request from the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich technische Information mbH, D-76344 Eggenstein-Leopoldshafen (Germany), on quoting the depository number CSD-401386, the names of the authors and the journal citation.

The results of the X-ray analysis of **4** are given in Fig. 1<sup>7</sup>). The six-membered ring A is puckered at C-1 and O-2. The plane of the tetrahydrofuran residue in the envelope conformation (C-2' ~ C-1' ~ O-1' ~ C-4') shows an angle of 66.0° with the plane of the essentially flat naphthoquinone portion (ring B and C). The absolute stereochemistry could not be determined but the relative stereochemistry of the stereocenters at C-1 and in the

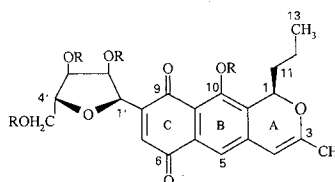
Fig. 1. Crystal structure of tetra-*O*-acetyl-anhydroexfoliamycin (**4**).



The absolute configuration has not been proved.



- 1 R = H (exfoliamycin)  
2 R = CH<sub>3</sub> (3-*O*-methylexfoliamycin)

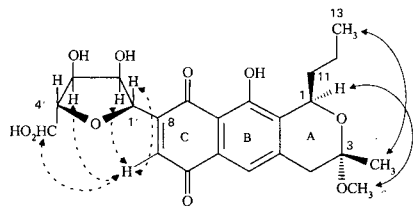


- 3 R = H (anhydroexfoliamycin)  
4 R = Ac

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Fig. 2. NOESY analysis (300 MHz, acetone- $d_6$ ) of 3-*O*-methylexfoliamycin (**2**).



tetrahydrofuran residue were obtained. The latter is in accordance with a C-glycosidically bound ribose. Assuming that the producing strain has accepted D-ribose as precursor, the absolute configuration could be derived as given in the formulae 1~4.

The relative stereochemistry of ring A of **2** could be determined by a NOESY experiment<sup>8)</sup>. A significant NOE (nuclear Overhauser enhancement) effect between 13- $H_3$  in the propyl chain and 3- $CH_3$  as well as between 3- $OCH_3$  and 1- $H$  caused us to assume that the paired groups are located on the same side of the ring plane (Fig. 2). Far off four striking NOE effects between 7- $H$  and 1'- $H$ , 2'- $H$ , 3'- $H$  and 5'- $H_2$  confirmed the sugar ribose, which was likewise analyzed by X-ray methods.

## References

- 1) POTTERAT, O.; H. ZÄHNER, J. W. METZLER & S. FREUND: Metabolic products of microorganisms. 269. 5-Phenylpentadienoic-acid derivatives from *Streptomyces* sp., *Helv. Chim. Acta* 77: 569~574, 1994
- 2) POTTERAT, O.; H. ZÄHNER, C. VOLKMANN & A. ZEECK: Exfoliamycin and related metabolites, new naphthoquinone antibiotics from *Streptomyces exfoliatus*. *J. Antibiotics* 46: 346~349, 1993
- 3) VOLKMANN, C.: Strukturauflklärung neuer Naphthochinon-Antibiotika aus Streptomyceten und Synthese neuer Pyron-Derivate in Anlehnung an biologisch aktive Naturstoffe. Ph.D. Thesis, University of Göttingen, Cuvillier Verlag Göttingen, 1994
- 4) CLEGG, W.: Faster data collection without loss of precision. An extension of the learnt profile method. *Acta Crystallogr. (A)* 37: 22~28, 1981
- 5) SHELDRIK, G. M.: Phase annealing in SHELX-90. Direct methods for larger structures. *Acta Crystallogr. (A)* 46: 467~473, 1990
- 6) SHELDRIK, G. M.: SHELXL-93, Universität Göttingen 1993
- 7) SHELDRIK, G. M.: XP Molecular Graphics, Siemens A. X. I., Madison 1988
- 8) KESSLER, H.; M. GEHRKE & C. GRIESINGER: Two-dimensional NMR spectroscopy, principles and survey of the experiments. *Angew. Chemie, Int. Ed. Engl.* 27: 460~507, 1988