136.0, 158.9; $[\alpha]_D^{25} = +41.1$ ($c = 1.0$, benzene); elemental analysis calcd for $C_{11}H_{14}O_2$: C 74.13, H 7.92; found: C 74.13, H 8.07. Other physical and spectroscopic data (TLC, IR, and ^{1}H NMR) were identical with those in the literature.[3k, 4, 14b] The enantioselectivity was determined to be 93% *ee* by HPLC analysis on a chiral column (Chiralcel OD-H, Daicel Chemical Industries, Ltd., hexane/*i*PrOH 20/1, flow rate 1.0 mL min^{-1}): $t_{major} =$ 10.1 min (*R*), $t_{minor} = 11.8$ min (*S*).

1-(*p*-Bromophenyl)-3-buten-1-ol (Table 2, entry 6): ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 43.6$, 72.5, 118.6, 121.1, 127.5 (2C), 131.3 (2C), 133.9, 142.7; $[\alpha]_D^{29} = +47.0$ ($c = 1.0$, benzene); elemental analysis calcd for $C_{10}H_{11}OBr$: C 52.89, H 4.88; found: C 52.90, H 5.12. Other physical and spectroscopic data (TLC, IR, and ^{1}H NMR) were identical with those in the literature.[4, 15] The enantioselectivity was determined to be 93% *ee* by HPLC analysis on a chiral column (Chiralcel OJ, Daicel Chemical Industries, Ltd., hexane/*i*PrOH 9/1, flow rate 0.5 mL min^{-1}): $t_{minor} = 16.0$ min, $t_{major} = 17.3$ min. The absolute configuration is unknown.

Received: July 1, 1999 [Z 13663 IE]
German version: *Angew. Chem.* **1999**, *111*, 3916 – 3919

Keywords: aldehydes · allylsilanes · asymmetric catalysis · nucleophilic additions · silver

[1] a) K. Sato, M. Kira, H. Sakurai, *J. Am. Chem. Soc.* **1989**, *111*, 6429; see also b) G. Cerveau, C. Chuit, R. J. P. Corriu, C. Reye, *J. Organomet. Chem.* **1987**, *328*, C17; c) A. Hosomi, S. Kohra, Y. Tominaga, *J. Chem. Soc. Chem. Commun.* **1987**, 1517.

[2] Review: C. Chuit, R. J. P. Corriu, C. Reye, J. C. Young, *Chem. Rev.* **1993**, *93*, 1371.

[3] Reviews on catalytic asymmetric allylations: a) W. R. Roush in *Comprehensive Organic Synthesis*, *Vol. 2* (Eds.: B. M. Trost, I. Fleming, C. H. Heathcock), Pergamon, Oxford, **1991**, p. 1; b) Y. Yamamoto, N. Asao, *Chem. Rev.* **1993**, *93*, 2207; c) T. Bach, *Angew. Chem.* **1994**, *106*, 433; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 417; d) D. Hoppe in *Houben-Weyl: Methods of Organic Chemistry*, *Vol. E21* (Eds.: G. Helmchen, R. W. Hoffmann, J. Mulzer, E. Schaumann), Thieme, Stuttgart, **1995**, p. 1357; e) A. H. Hoveyda, J. P. Morken, *Angew. Chem.* **1996**, *108*, 1378; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1262; notable examples of chiral Lewis acid-catalyzed asymmetric allylations using allylic trimethylsilanes: f) K. Furuta, M. Mouri, H. Yamamoto, *Synlett* **1991**, 561; g) K. Ishihara, M. Mouri, Q. Gao, T. Maruyama, K. Furuta, H. Yamamoto, *J. Am. Chem. Soc.* **1993**, *115*, 11490; h) S. Aoki, K. Mikami, M. Terada, T. Nakai, *Tetrahedron* **1993**, *49*, 1783; i) D. R. Gauthier, Jr., E. M. Carreira, *Angew. Chem.* **1996**, *108*, 2521; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2363; see also j) R. O. Duthaler, A. Hafner, *Angew. Chem.* **1997**, *109*, 43; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 43; notable examples of chiral Lewis base-catalyzed asymmetric allylations with allylic trichlorosilanes: k) S. E. Denmark, D. M. Coe, N. E. Pratt, B. D. Griedel, *J. Org. Chem.* **1994**, *59*, 6161; l) K. Iseki, Y. Kuroki, M. Takahashi, Y. Kobayashi, *Tetrahedron Lett.* **1996**, *37*, 5149; m) K. Iseki, Y. Kuroki, M. Takahashi, S. Kishimoto, Y. Kobayashi, *Tetrahedron* **1997**, *53*, 3513; n) K. Iseki, S. Mizuno, Y. Kuroki, Y. Kobayashi, *Tetrahedron Lett.* **1998**, *39*, 2767; o) M. Nakajima, M. Saito, M. Shiro, S. Hashimoto, *J. Am. Chem. Soc.* **1998**, *120*, 6419; p) K. Iseki, S. Mizuno, Y. Kuroki, Y. Kobayashi, *Tetrahedron* **1999**, *55*, 977.

[4] The BINAP · AgOTf complex was shown to be a good chiral catalyst for asymmetric allylation of aldehydes with allylic trialkyltin compounds: A. Yanagisawa, H. Nakashima, A. Ishiba, H. Yamamoto, *J. Am. Chem. Soc.* **1996**, *118*, 4723.

[5] For an example of fluoride-ion-catalyzed reaction of allylsilanes with aldehydes, see a) A. Hosomi, A. Shirahata, H. Sakurai, *Tetrahedron Lett.* **1978**, 3043; see also b) E. Nakamura, M. Shimizu, I. Kuwajima, J. Sakata, K. Yokoyama, R. Noyori, *J. Org. Chem.* **1983**, *48*, 932.

[6] A significant amount of the inert 2:1 complex of (*R*)-BINAP and AgF was formed in addition to the reactive 1:1 complex when an equimolar amount of (*R*)-BINAP was added to AgF in CH_3OH. Various ratios of the mixture in CD_3OD were investigated by ^{1}H NMR spectroscopy, and a 0.6/1 mixture was found to give the desired 1:1 complex without significant formation of the 2:1 complex.

[7] H. Takaya, K. Mashima, K. Koyano, M. Yagi, H. Kumobayashi, T. Taketomi, S. Akutagawa, R. Noyori, *J. Org. Chem.* **1986**, *51*, 629. (*R*)- and (*S*)-*p*-Tol-BINAP are commercially available (AZmax).

[8] Aliphatic aldehydes were unreactive under the standard reaction conditions. For example, the reaction with hydrocinnamaldehyde at $-20\,^\circ$C for 30 min and then at room temperature for 8 h gave the allylated product in only 3% yield and with 85% *ee*.

[9] a) G. Courtois, L. Miginiac, *J. Organomet. Chem.* **1974**, *69*, 1; b) R. W. Hoffmann, *Angew. Chem.* **1982**, *94*, 569; *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 555.

[10] A. Yanagisawa, A. Ishiba, H. Nakashima, H. Yamamoto, *Synlett* **1997**, 88.

[11] The ^{13}C NMR spectrum (75 MHz, CH_3OD, 25 °C, CH_3OD; $\delta = 49.0$) showed a new peak at $\delta = 50.7$, which was ascribable to $(CH_3O)_3SiF$. The formation of this compound is an indication for a crotylsilver species. Signals assignable to the crotylsilver or hydrolyzed butenes were not observed.

[12] R. W. Hoffmann, T. Herold, *Chem. Ber.* **1981**, *114*, 375.

[13] a) M. Kusakabe, Y. Kitano, Y. Kobayashi, F. Sato, *J. Org. Chem.* **1989**, *54*, 2085; b) U. S. Racherla, Y. Liao, H. C. Brown, *J. Org. Chem.* **1992**, *57*, 6614.

[14] a) M. Riediker, R. O. Duthaler, *Angew. Chem.* **1989**, *101*, 488; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 494; b) K. Sugimoto, S. Aoyagi, C. Kibayashi, *J. Org. Chem.* **1997**, *62*, 2322.

[15] For another method of preparation of the racemic compound, see a) C. Chen, Y. Shen, Y.-Z. Huang, *Tetrahedron Lett.* **1988**, *29*, 1395; for a method of analytical resolution of the racemic compound, see b) R. L. Halterman, W. R. Roush, L. K. Hoong, *J. Org. Chem.* **1987**, *52*, 1152.

Membrane Anchoring and Intervesicle Transfer of a Derivative of the Antibiotic Moenomycin A**

Alexej Anikin, Andrij Buchynskyy, Uwe Kempin, Katka Stembera, Peter Welzel,* and Gabriela Lantzsch*

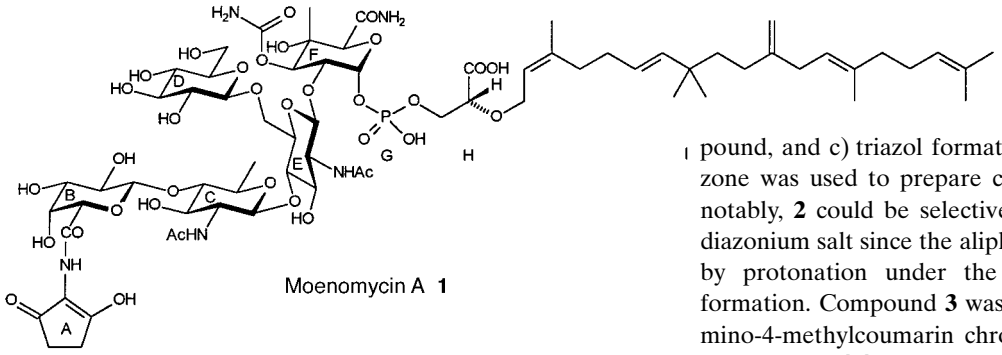
The glycopeptide antibiotics, which have vancomycin as a prominent example, are of increasing importance in the treatment of bacterial infections because of the problem of resistance.[1] They function by binding (as dimers or using a

[*] Prof. Dr. P. Welzel, Dr. A. Anikin, Dipl.-Chem. A. Buchynskyy, Dr. U. Kempin, Dipl.-Biochem. K. Stembera
Institut für Organische Chemie der Universität
Talstrasse 25, D-04103 Leipzig (Germany)
Fax: (+49) 341-973-6599
E-mail: welzel@organik.orgchem.uni-leipzig.de

Dr. G. Lantzsch
Institut für Experimentelle Physik I der Universität
Vor dem Hospitltore 1, D-04103 Leipzig (Germany)
Fax: (+49) 341-973-2599
E-mail: lantzsch@rz.uni-leipzig.de

[**] This work was supported by the Deutsche Forschungsgemeinschaft (Innovationskolleg "Chemisches Signal und biologische Antwort"), the Fonds der Chemischen Industrie, and by Hoechst Marion Roussel. We wish to thank Prof. Dr. A. Blume (Institut für Physikalische Chemie, Halle) for the opportunity to perform the stopped flow experiments in his institute, Prof. A. C. Rodloff and Mrs. B. Pless (Institut für Medizinische Mikrobiologie and Infektionsepidemiologie, Leipzig) for their assistance in determining the MIC values, and Dr. D. Müller (Ruhr-Universität Bochum) and Dr. T. Staroske (University of Cambridge) for the mass spectra.

membrane anchor) to the membrane-anchored peptidoglycan precursors terminating in D-Ala–D-Ala and thus prevent transglycosylation (and/or transpeptidation[2]) in the final phase of peptidoglycan biosynthesis of the bacterial cell wall. There is another class of compounds that interfere with the transglycosylation reaction, namely the moenomycins (for example, moenomycin A (**1**)). However, their mode of action



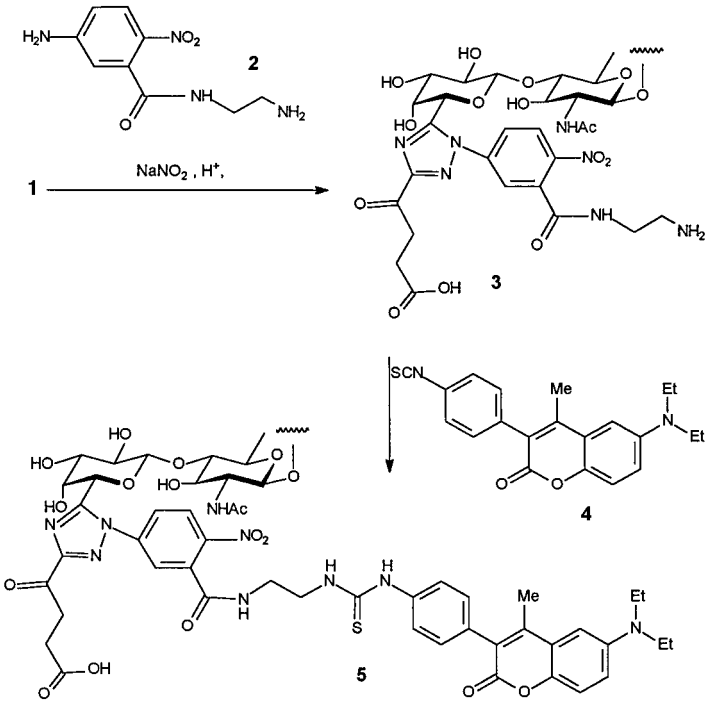
is completely different. They have been shown to bind reversibly to the enzyme and thus inhibit growing of the peptidoglycan polysaccharide strands.[3] The moenomycins are, therefore, unique tools for elucidating the structure of the enzyme and the detailed mechanism of the transglycosylation reaction.

The structure–activity relationships of the moenomycins have been studied extensively[4] and a mechanism of their mode of action has been proposed.[5] It is assumed that they compete with the subtrate(s) of the transglycosylation reaction for a binding site at the enzyme, most probably for the binding site of the growing peptidoglycan chain (the glycosyl donor).[5] The oligosaccharide part of the moenomycin-type transglycosylase inhibitors is recognized with high selectivity by the enzyme.[4] However, there is another prerequisite for antibiotic activity: membrane anchoring of the antibiotic through its lipid part. Thus, removal of the C_{25} lipid from moenomycin[6] or introduction of one or several OH groups into the lipid chain[7] causes complete loss of antibiotic activity.

Whereas the structure–activity relationships in the oligosaccharide part of the moenomycins are fairly well understood the role of the lipid moiety has remained elusive. Attempts to study the interaction of the lipid part of moenomycin with artificial membranes (1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC) vesicles) by isothermal titration calorimetry at concentrations in the range of the minimal inhibitory concentration (MIC, see below) failed since the method was not sensitive enough.[8]

We describe herein successful experiments that allowed the quantitation of the interaction of moenomycin with artificial membranes by means of fluorescence methods. These experiments give information for the first time on the extent of the anchoring of moenomycin to membranes, as expressed by a partition coefficient, and of the transfer of moenomycin from one vesicle to another, as expressed by a rate constant. The former information is important for developing an understanding of the contribution of moenomycin membrane anchoring for the interaction with the enzyme (and to its antibiotic activity). The latter is important in the context of pharmacokinetics, since unfavorable transport properties of the moenomycins have until now precluded their use in human medicine.

Units C and E–I of **1** are indispensible for antibiotic activity.[4] We wanted, therefore, to attach the fluorescent label to unit A. A sequence of a) reaction of the enolized β-diketone unit of moenomycin A with the diazonium salt obtained from **2**, b) Japp–Klingemann ring cleavage of the thus formed azo compound, and c) triazol formation of the intermediate amidrazone was used to prepare compound **3** (Scheme 1).[9] Most notably, **2** could be selectively converted into the aromatic diazonium salt since the aliphatic amino group was protected by protonation under the conditions of diazonium salt formation. Compound **3** was then coupled to the 7-diethylamino-4-methylcoumarin chromophore by reaction with isothiocyanate **4**[10] to provide thiourea **5**. The compound was purified by careful chromatographic separations and was characterized by electrospray ion cyclotron resonance mass spectrometry (ESI-ICR-MS) and by its fluorescence spectra (λ_{ex}: 396 nm, λ_{em}: 477 nm,[11] in methanol). The MIC values against seven different *Staphylococcus aureus* strains were determined by a microdilution method on microtiter plates. Under these conditions moenomycin A turned out to be more active by a factor of 10 (MIC in the range of 6.9×10^{-9} mol L^{-1}) than previously assumed.[4] A MIC of 1.7×10^{-7} mol L^{-1} was determined for **3** and 1.2×10^{-6} mol L^{-1} for **5**. The reason for the difference in antibiotic activity is not understood at present, but both **3** and **5** appear to be well suited for future binding studies with the enzyme (work is in progress).



Scheme 1. Synthesis of **5**.

 © WILEY-VCH Verlag GmbH, D-69451 Weinheim, 1999 1433-7851/99/3824-3704 $ 17.50+.50/0 *Angew. Chem. Int. Ed.* **1999**, *38*, No. 24

Moenomycin A is known to form micelles in aqueous solution above a definite concentration (the critical micelle concentration, cmc). The cmc has been shown to depend on the pH and the ion strength (about 5×10^{-4} mol L^{-1} at pH 6.8).[12] At concentrations of $50-200 \times 10^{-9}$ mol L^{-1} the coumarin-labeled moenomycin derivative **5** gave clear dispersions in water, which indicates the existence of monomers and/or micelles. The fluorescence intensity increased to a new stable value upon addition of unilamellar POPC vesicles to the aqueous dispersion of **5** (Figure 1). This effect reflects the

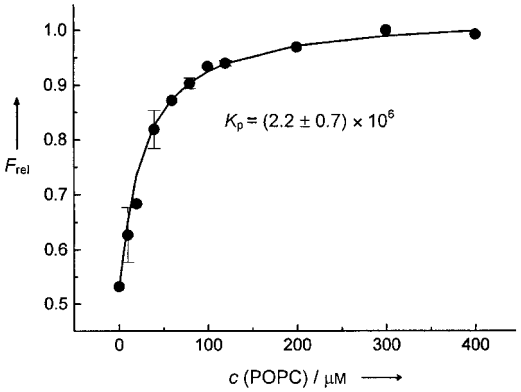


Figure 1. Fluorescence intensity of **5** as a function of the lipid concentration. The experimental data represent the average of three measurements with different concentrations of **5** (50, 100, and 200 nM).

insertion of **5** into the vesicles. The partition coefficient K_p was obtained from the dependence of the fluorescence intensity on the POPC concentration and K_p is defined as X^m/X^w, where X^m and X^w are the molar fractions of **5** incorporated into the membranes and in the water phase, respectively. The current fluorescence intensity is then described by Equation (1). The

$$F = (K_p F_\infty + W F_0/C_L)/(W/C_L + K_p) \quad (1)$$

fluorescence intensities F_0 and F_∞ are the fluorescence intensities if all molecules of **5** are dissolved in water and incorporated into the membrane, respectively. W is the concentration of water (55 mol L^{-1}) and C_L is the lipid concentration in the sample. Using this formalism K_p was determined to be $(2.2 \pm 0.7) \times 10^6$ (see Figure 1).

The transfer of **5** between POPC vesicles has been investigated by fluorescence resonance energy transfer (FRET), a powerful tool for studying interbilayer transfer of membrane-anchored molecules. An especially useful donor/acceptor pair has been described by Silvius et al. who reported that the fluorescence of 7-diethylamino-4-methylcoumarin (see above) is efficiently quenched by the (4-dimethylamino)azobenzene chromophore (DABS, λ_{abs}: 447 nm).[11] For this investigation we used **5** and the DABS-labeled phospholipid **6**, which was prepared essentially as published by Silvius et al.[11] Figure 2 illustrates the results of quenching experiments. POPC vesicles containing different amounts of the quencher lipid **6** were asymmetrically loaded with appropriate amounts of donor **5**. The fluorescence intensity of **5** decreases as increasing molar percentages of **6** are incorporated in the vesicles. When compared with the results reported by Silvius et al. it is clear that a somewhat higher percentage of **6**

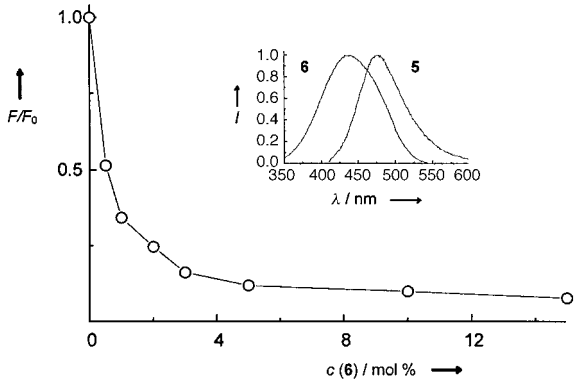
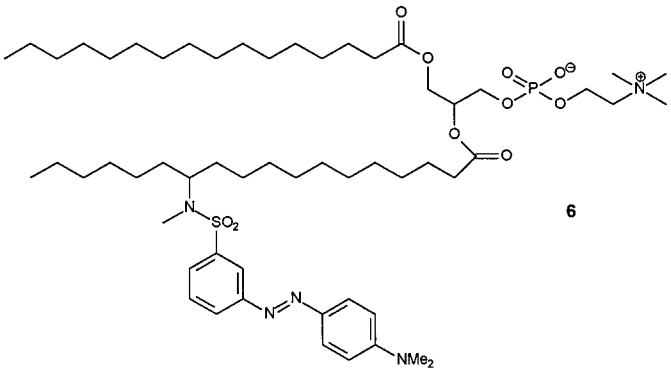


Figure 2. Quenching of the coumarin fluorescence of **5** incorporated into POPC vesicles for increasing concentrations of **6**. The inset shows the overlap of the absorption spectrum of **6** with the fluorescence spectrum of **5**.

(0.57 mol %) is needed to achieve the half-maximal energy transfer. This is most probably a consequence of differences in the location of the donor group in the two systems. The interbilayer transfer experiments were performed as indicated in Figure 3. Addition of POPC vesicles to vesicles containing donor **5** and acceptor lipid **6** resulted in an increase of



fluorescence intensity (see Figure 4), whereas the mixing of vesicles loaded with the donor with vesicles containing only the acceptor led to a decrease in the fluorescence intensity. The opposite effects observed in the two approaches demonstrates the intervesicle transfer of **5**. In the first case the number of quenched donor molecules diminishes on transfer

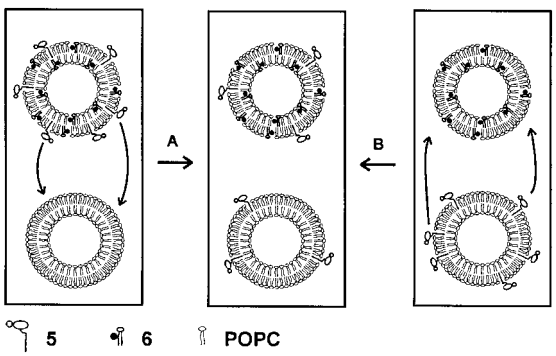


Figure 3. Principle of the interbilayer transfer experiments. A) "Empty" vesicles are added to donor- and acceptor-labeled vesicles, and B) donor-labeled vesicles are added to acceptor-labeled vesicles.

 © WILEY-VCH Verlag GmbH, D-69451 Weinheim, 1999 1433-7851/99/3824-3705 $ 17.50+.50/0

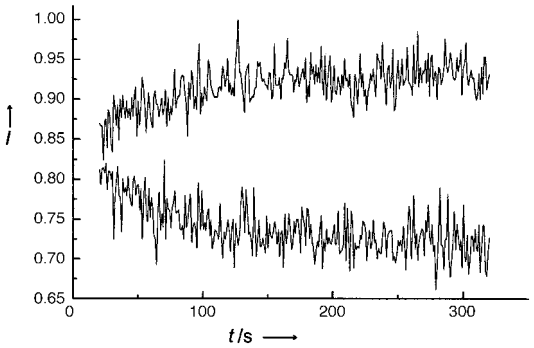


Figure 4. Plot of the fluorescence intensity for the two interbilayer transfer experiments A and B (see Figure 3).

into the acceptor-free vesicles, while in the second case it increases as they transfer into the acceptor-filled vesicle. The fraction of transferred molecules of **5**, $X = n_D/(n_D + n_{DQ})$, can be estimated from Equation (2), where n_D, n_{DQ}, and F_{TX} denote the number of donor molecules not quenched and

$$X = (F_\infty - F_0)/(F_{TX} - F_0) \quad (2)$$

quenched and the fluorescence intensity after addition of Triton X-100 (1%), respectively. Three experiments using different amounts of acceptor lipid **6** (0.5, 1, and 2%) yielded $X = 0.4 - 0.5$, which is reasonable for mixing equal amounts of lipid.

The transfer of **5** is a fast process and $t_{1/2}$ can be roughly estimated to be in the range of seconds (see Figure 4). Subsequent stopped-flow experiments (Figure 5) yielded

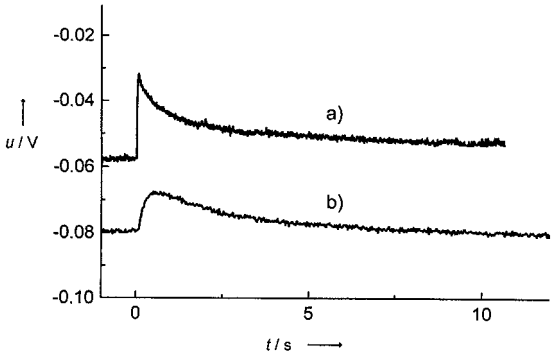


Figure 5. Plot of the voltage in the stopped-flow experiments a) upon addition of POPC vesicles to an aqueous solution of **5** (insertion) and b) on mixing of vesicles labeled with **5** and **6** with "empty" vesicles (transfer). A decrease in the voltage indicates an increase in the fluorescence.

$k_t = 0.25 \pm 0.05\ s^{-1}$ from Equation (3), which is obtained by integration of Equation (4). V_0 and V_∞ are the read voltages

$$V(t) = -k_t\,|\,V_0 - V_\infty\,|\,t \quad (3)$$

$$k_t = [(dV(t)/dt)_{t\to 0}]/(V_\infty - V_0) \quad (4)$$

(inversely proportional to the fluorescence intensity) immediately after combining the POPC vecicles and the aqueous solutions of **5** in the cell and after equilibration, respectively. The initial rate constant $k_t = 0.25\ s^{-1} = 15\ min^{-1}$ is comparable to values found for short chain phospholipid conjugates (C_{11} or C_{12} unbranched alkyl chains).[13]

The insertion of **5** into the lipid vesicles was also observed by stopped flow experiments. The initial rate of this process, $k_i = 0.8\ s^{-1}$, was found to be comparable to the intervesicle transfer rate.

In conclusion, we have set up an experimental system that has allowed the investigation of the interaction of moenomycin-type compounds with artificial membranes for the first time. These results can be used in competition experiments to study new moenomycin analogues and, thus, are expected to form the basis for the rational design of transglycosylase inhibitors with improved transport properties. Work along these lines is in progress.

Experimental Section

3 was prepared essentially as described for a thiol analogue.[9] It was purified by ultrafiltration (Amicon INC, YM3) and the subsequent chromatographic purifications: a) flash chromatography (FC; silica gel, 1-propanol/2 mol L^{-1} ammonia 7/3), b) medium pressure chromatography (MPLC; RP_{18}, methanol/water 1/1). The yield was 38%. The ^{13}C NMR spectrum was fully in accord with the structure. $C_{78}H_{117}N_{10}O_{37}P$ (1817.80, 1817.73), FAB-MS (matrix: nitrobenzyl alcohol): m/z 1817.3 ($[M+H]^+$), 1839.6 ($[M+Na]^+$).

5 was prepared by reaction of **3** with **4** in a pyridine/DMF (1/10) solution at 20 °C. After 48 h the solvents were evaporated and the residue purified by chromatography a) FC (silica gel, chloroform/methanol 20/12 → chloroform/methanol/water 20/12/2, 2×), b) MPLC (RP_{18}, acetonitrile/water 1/1, 3×). The yield was 25%. $C_{99}H_{137}N_{12}O_{39}PS$ (2182.26, 2180.86), ESI-ICR-MS: m/z: 2181.8685 ($[M+H]^+$, calcd: 2181.8642), 2203.7990 ($[M+Na]^+$, calcd: 2203.8462).

MIC values were determined by a serial twofold microdilution method (Iso-Sensitest medium, Oxoid). A series of decreasing concentrations of the compound under investigation was prepared in the medium. For inoculations 1×10^5 cfu mL^{-1} were used. The MICs were determined (absence of visible turbidity) after 24 h at 37 °C.

Unilamellar POPC vesicles containing **6** and loaded with **5** (1.5 mL of 300 μM) were mixed with an equal volume of an equal amount of empty POPC vesicles by stirring. In an analogous series of experiments vesicles with only **6** were mixed with vesicles loaded with **5**. The probe content of the samples was determined by the fluorescence intensity in the presence of 1% Triton X-100, which eliminates the energy transfer. All fluorescence values were corrected for the background using the appropriate blank values as well as for inner filter effects using fluorescence values determined in the presence of Triton X-100. The influence of Triton X-100 on the quantum yield of **5** was also accounted for. All measurements were carried out at room temperature on a CD900 spectrofluorometer (Edinburgh Instruments) using 1 nm slits for excitation and 1.5 nm for emission monochromators. The stopped-flow-instrument Hi-Tech Scientific SF51 was used for fast kinetic measurements.

Received: June 29, 1999 [Z13647IE]
German version: *Angew. Chem.* **1999**, *111*, 3931 – 3935

Keywords: antibiotics · fluorescence spectroscopy · glycolipids · liposomes · phospholipids

[1] Reviews: D. H. R. Williams, B. Bardsley, *Angew. Chem.* **1999**, *111*, 1264 – 1286; *Angew. Chem. Int. Ed.* **1999**, *38*, 1172 – 1193; K. C. Nicolaou, C. N. C. Boddy, S. Bräse, N. Winssinger, *Angew. Chem.* **1999**, *111*, 2230 – 2287; *Angew. Chem. Int. Ed.* **1999**, *38*, 2096 – 2152.

[2] For a recent discussion of the mechanism, see M. Ge, Z. Chen, H. R. Onishi, J. Kohler, L. L. Silver, R. Kerns, S. Fukuzawa, C. Thompson, D. Kahne, *Science* **1999**, *284*, 507 – 511.

 © WILEY-VCH Verlag GmbH, D-69451 Weinheim, 1999 1433-7851/99/3824-3706 $ 17.50+.50/0

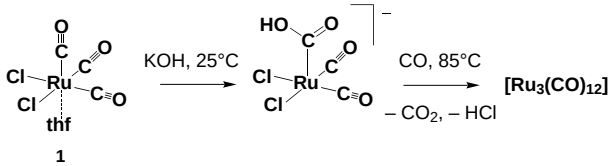
[3] P. Welzel in *Antibiotics and Antiviral Compounds—Chemical Synthesis and Modifications* (Eds.: K. Krohn, H. Kirst, H. Maas), VCH, Weinheim, **1993**, pp. 373 – 378, and references therein.
[4] N. El-Abadla, M. Lampilas, L. Hennig, M. Findeisen, P. Welzel, D. Müller, A. Markus, J. van Heijenoort, *Tetrahedron* **1999**, *55*, 699 – 722.
[5] O. Ritzeler, L. Hennig, M. Findeisen, P. Welzel, D. Müller, A. Markus, G. Lemoine, M. Lampilas, J. van Heijenoort, *Tetrahedron* **1997**, *53*, 1675 – 1694.
[6] S. Marzian, M. Happel, U. Wagner, D. Müller, P. Welzel, H.-W. Fehlhaber, A. Stärk, H.-J. Schütz, A. Markus, M. Limbert, Y. van Heijenoort, J. van Heijenoort, *Tetrahedron* **1994**, *50*, 5299 – 5308.
[7] U. Kempin, L. Hennig, P. Welzel, S. Marzian, D. Müller, H.-W. Fehlhaber, A. Markus, Y. van Heijenoort, J. van Heijenoort, *Tetrahedron* **1995**, *51*, 8471 – 8482, and references therein.
[8] H. Heerklotz, A. Donnerstag, G. Klose, P. Welzel, A. Markus, A. Giel, unpublished results.
[9] U. Kempin, L. Hennig, D. Müller, A. Markus, P. Welzel, *Tetrahedron Lett.* **1996**, *37*, 5087 – 5090; U. Kempin, L. Hennig, D. Knoll, P. Welzel, D. Müller, A. Markus, J. van Heijenoort, *Tetrahedron* **1997**, *53*, 17669 – 17690.
[10] **8** was prepared by the following route: a) reaction of 7-diethylamino-4-methyl-coumarin with the diazonium salt obtained from *N*-(4-aminophenyl)-acetamide, b) hydrolysis of the amide, c) reaction with thiophosgene.
[11] See: J. R. Silvius, R. Leventis, P. M. Brown, M. Zuckermann, *Biochemistry* **1987**, *26*, 4279 – 4287.
[12] G. Lantzsch, H. Binder, H. Heerklotz, P. Welzel, G. Klose, *Langmuir* **1998**, *14*, 4095 – 4104.
[13] J. Silvius, R. Leventis, *Biochemistry* **1993**, *32*, 13318 – 13326.

Novel Polymeric Carbonylhaloruthenium(I) Polyanions: Rational Design and Self-Reorganization in the Presence of CO_2 and H_2O**

Luc Maurette, Bruno Donnadieu, and Guy Lavigne*

Dedicated to Professor René Poilblanc on the occasion of his 65th birthday

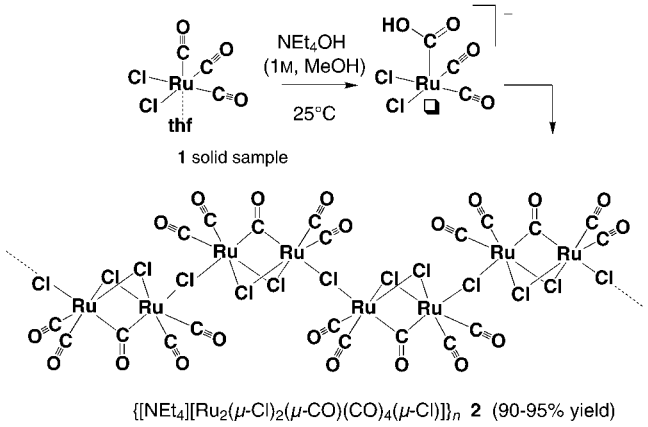
We recently reported that Ru^{II} is readily reduced to Ru^0 by simple treatment of $[Ru(CO)_3Cl_2(thf)]$ (**1**) with KOH followed by thermally induced decarboxylation of the incipient hydroxy-carbonyl adduct at 85 °C under CO (1 atm) to produce $[Ru_3(CO)_{12}]$ (Scheme 1).[1] The reaction is understood in terms of a reductive elimination of HCl[2, 3] from an unstable "acid"[4] hydrido intermediate. Though elusive, the latter is prone to insertion reactions in the presence of olefins or alkynes.[1, 5, 6] Upon simply replacing KOH by $[NEt_4][OH]$ with the aim to obtain highly concentrated solutions of the hydroxy-carbonyl adduct for a ^{13}C NMR investigation, we were surprised to observe that CO_2 evolution was becoming significant at room temperature, and occurred at rates apparently depending both on the nature of the counterion and the concentration.



1

Scheme 1. Reaction of **1** with KOH.

Typically, when one equivalent of a concentrated methanolic solution of $[NEt_4][OH]$ (1 mL, 1.5 M) was added to a solid sample of **1** (500 mg, 1.5 mmol) at 25 °C, rapid dissolution of the complex was observed within seconds along with gas evolution (strong $\nu(CO_2)$ IR absorption at 2338 cm^{-1}) and development of an intense red color. This was rapidly followed by nearly quantitative precipitation of a red-orange microcrystalline product. High-quality homogeneous single crystals of this product were obtained from slightly modified experiments where **1** was dissolved in a minimum amount of ethanol or methanol (1 – 2 mL) prior to the addition of the hydroxide. This complex, recovered in 90 – 95 % yield, was formulated as **2** (Scheme 2) on the basis of an X-ray structure analysis revealing its polymeric nature (Figure 1).[7]



Scheme 2. Synthesis of the polymeric polyanion **2**. The square represents a vacant coordiation site.

The structure of **2** is based on the discrete association of identical monoanionic dimeric units. The basic motive is a face-sharing bioctahedron in which two ruthenium centers are connected through two bridging halides and one bridging carbonyl group. Each ruthenium atom bears two terminal carbonyl groups in a *fac* arrangement with the bridging one. The third halide (*trans* to the bridging CO) serves as a symmetric bridge between neighboring units of the polymeric chain. Though the metal – metal separation within the dimer is 2.964(1) Å, an electron count reveals that, formally, there is no metal – metal bond.

Complex **2** appears to be the first representative of the family of binary halo-carbonyl Ru^I species. Indeed, the relevant edge double-bridged Ru^I prototype $[Ru_2X_2(CO)_6]$ recently identified by Fachinetti, Funaioli et al.[8] for X = trifluoroacetate, is still unknown for X = halide,[9] though a number of phosphane-substituted derivatives have been prepared from other precursors.[10, 11]

[*] Dr. G. Lavigne, Dipl.-Chem. L. Maurette, Dr. B. Donnadieu
Laboratoire de Chimie de Coordination du CNRS
205 route de Narbonne, F-31077 Toulouse, Cedex 4 (France)
Fax: (+33) 5-61-55-30-03
E-mail: lavigne@lcc-toulouse.fr

[**] We thank Dr Noël Lugan, Prof. Giuseppe Fachinetti, and Dr Tiziana Funaioli for helpful discussions. This work was supported by the CNRS.

 © WILEY-VCH Verlag GmbH, D-69451 Weinheim, 1999 1433-7851/99/3824-3707 $ 17.50+.50/0