The surface derivatization method described here is not limited to porous silicon, but is also applicable to hydride-terminated crystalline silicon. Reduction of butyl iodide on n-type crystalline silicon leads to an organic layer that is stable in boiling chloroform, aqueous ethanolic HF and 0.1M KOH as demonstrated by the difference between contact angles measured on derivatized and nonderivatized surfaces, respectively.

Experimental Section

All reagents were obtained from commercial sources and used as received. *tert*-butyl 6-bromo-hexanoate was prepared from 6-bromohexanoic acid and *tert*-butanol according to the literature.[18] Acetonitrile and THF were dried and distilled prior to use. Solutions of organo halides containing electrolyte were freeze-pump-thaw degassed three times to remove traces of oxygen and stored under nitrogen.

Porous silicon samples were prepared from n-type (P-doped) and p-type (B-doped) silicon wafers with a (100) orientation and with a resistivity of approximately 1 Ωcm. Porous silicon samples with areas of 0.25 cm^2 were etched in 48 % aqueous HF/EtOH (1/1) for 2 min at a current density of 40 mA cm^{-2}. Both n- and p-type wafers were illuminated during the etching procedure[19] with a 300-W tungsten lamp adjusted to an intensity of approximately 100 mW cm^{-2} to produce luminescent samples. The porous layers were approximately 3–5 μm thick (determined by scanning electron microscopy). After the etching process the samples were rinsed with ethanol and dichloromethane, dried under a stream of nitrogen, and evacuated in a one- or two-compartment electrochemical cell equipped with a platinum auxiliary electrode and in some cases a Ag/AgBr pseudo-reference electrode. Crystalline silicon samples (n-type) were degreased in boiling chloroform. The native silicon oxide layer was removed immediately before the derivatization step by soaking in 2 % aqueous HF.

Derivatization was performed by passing a cathodic current (usually 10 mA cm^{-2}) through 1–2 mL of the organo halide solution that was previously added to the porous silicon sample. The p-type porous silicon samples were illuminated with 200 mW cm^{-2} white light to supply sufficient photocurrent. After derivatization the solution was removed and the sample rinsed sequentially with glacial acetic acid, ethanol, and dichloromethane.

Derivatization of single-crystal silicon samples was monitored indirectly by comparing contact angles (water droplets) measured on derivatized and nonderivatized areas, respectively. Prior to the measurement the entire sample was immersed in boiling chloroform (15 min) and in 48 % aqueous 1/1 HF/EtOH (2 min) to remove any adsorbed or Si–O bonded species, and then dipped in 0.1M aqueous KOH to render the nonderivatized, silicon hydride terminated areas hydrophilic.

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Keywords: electrochemistry · organo halides · reductions · silicon · surface chemistry

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S-Cylindrophanes: From Metal Tweezers to Metal Sandwiches[**]

Mark Mascal,* Jean-Luc Kerdelhué,
Alexander J. Blake, and Paul A. Cooke

Over the years effort has been directed at attempts to produce cyclophane-based macrobicycles **1** for the purpose of metal ion encapsulation.[1] In cases where the metal–arene core structure is intrinsically stable, such as in the ferrocenophanes, this has been a straightforward matter of building the cage around the metal. Where weaker interactions would be involved, however, the receptor must be put together first and the metal introduced later. This is the case when the aromatic system is benzene. Although the basic proposition is a simple one—that is, to create a cavity between two benzene rings and involve the π systems in the binding of a metal—its realization

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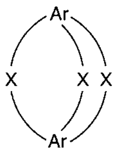

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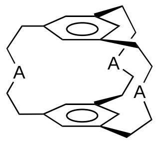


2a, A = NH
2b, A = NMe
2c, A = O
2d, A = S

demands some respect for the conformational preferences of chains which link aromatic rings together.[2] If the chains are to incorporate heteroatoms for the purpose of coordination to the guest, the first cyclophane which comes into consideration is the *sym*-[5.5.5] system **2**. This is because with anything less than five atoms in the bridges, no reasonable conformation exists in which both the rings and the chains can participate in metal ion complexation.[3] Cyclophanes with even numbers of atoms in the bridges are known to be conformationally mobile,[4] making the [6.6.6] homologue unattractive, and in the [7.7.7] the rings are too far from the midpoint of the cavity for significant interaction with a metal. In [*n*.*n*.*n*] systems where *n* is odd, it is a further condition that ligating functionalities be located at odd-numbered positions in the chains (except for the 1- or *n*-position), which converge towards the center of the cavity, unlike those in the even-numbered positions, which are divergent.

With these principles in mind, we recently synthesized a series of aza- and oxacyclophanes **2a**–**c**.[5, 6] Structural predictions based on the above conformational arguments could be substantiated by X-ray crystal structure determinations, which revealed the cylindrical nature of these molecules. These "cylindrophanes" functioned as metal tweezers, clasping copper(I) and silver(I) ions between the two aromatic rings as shown in Figure 1 a. However, no inclusion in the cavity was possible in these cases due to the prohibitive distance from the heteroatoms to the center of the trigonal plane which they define ($\geq$2.5 Å). We now describe the mixed π/n-donor macrobicycle **2d**, which is capable of trapping Cu^I and Ag^I guests in a trigonal-planar ligand field in the heart of the receptor, sandwiched by the two aromatic rings.

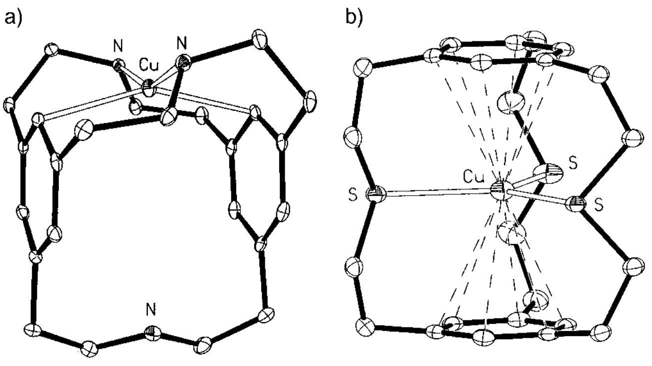
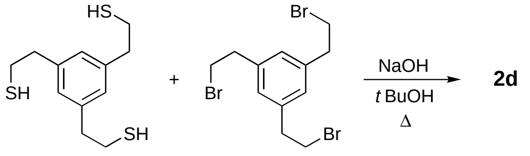


Figure 1. a) A view of the complex cation in the crystal structure of $[Cu(\mathbf{2a})]BF_4$. b) A view of the complex cation in the crystal structure of $[Cu(\mathbf{2d})]BF_4 \cdot 0.5\,CH_3OH$.

The synthetic approach taken to **2d** was simpler than that required for the preparation of **2a**–**c**, in which the cage was assembled by a [2+2+2] cyclotrimerization strategy. A hexaoxo analogue of **2d** had been made previously by reaction of 1,3,5-tris(bromoacetyl)benzene and sodium sulfide in 0.2 % yield.[7] A modified approach employing the known trithiol **3**[8] and tribromide **4**,[9] however, gave the target compound **2d** in 66 % yield [Eq. (1)].



(1)

3 **4**

Simple combination of **2d** with $AgBF_4$ in CH_2Cl_2 or $[Cu(MeCN)_4]BF_4$ in CH_2Cl_2/MeCN (3/1) gave the stable 1:1 complexes $[Ag(\mathbf{2d})]BF_4$ and $[Cu(\mathbf{2d})]BF_4$. Their ^1H NMR spectra ($CDCl_3$) showed a substantial interaction between the metals and **2d**, as indicated by the shifts of the SCH_2 signals ($\Delta\delta = +0.6-0.7$) relative to those of the free ligand. Most interesting, however, was the marked downfield shift of the aromatic protons ($\Delta\delta = 0.20$ in $[Ag(\mathbf{2d})]BF_4$, 0.12 in $[Cu(\mathbf{2d})]BF_4$), comparable to the deshielding experienced by the aromatic proton in the bis(η^1) complex $[Ag(\mathbf{2a})]OTf$ ($\Delta\delta = 0.13$ versus **2a**; $Tf = F_3CSO_2$).[6]

Crystals of $[Cu(\mathbf{2d})]BF_4$ could be grown by slow evaporation of a solution in dichloromethane. The X-ray crystal structure[10a] shows copper occupying the center of the cavity (Figure 1 b), in contrast to the dynamic mode of peripheral complexation it experiences in **2a**. The S–Cu distances are 2.370(2), 2.380(3), and 2.412(3) Å, with S-Cu-S angles of 119.00(9), 119.91(9), and 121.08(9)°. A mirror plane passes through the metal and three sulfur atoms, and the distance from the metal to the centroids of the benzene rings is 2.97 Å with a centroid-Cu-centroid angle of 178.4°.[11]

$[Ag(\mathbf{2d})]BF_4$ was crystallized by slow diffusion of methanol into a solution of the complex in acetonitrile. Crystallographically, it is isostructural with $[Cu(\mathbf{2d})]BF_4$,[10b] with respective angles and distances as follows: S–Ag, 2.577(2), 2.578(2), and 2.631(2) Å; S-Ag-S, 117.72(5), 119.98(6) and 122.31(5)°; Ag–centroid 2.92 Å; centroid-Ag-centroid, 177.5°.[12]

The NMR data had indicated that the phenyl rings in $[M(\mathbf{2d})]^+$ (M = Cu, Ag) do not simply block the apical positions but actually coordinate the metal. A statistical study of the nature of η^6-type bonding in the solid state using the Cambridge Structural Database[13, 14] provides some valuable insights into this mode of complexation. The sampling in the Database of a cylindrical volume 1 Å in diameter and 5 Å in height extending from the centroid of any benzene ring produces 2523 examples of metal atoms occupying this space.[15] The results are represented graphically by the aryl centroid–metal distance histogram in Figure 2. The plot is clearly bimodal, with the massive peak centered around 1.75 Å, corresponding to classic η^6 complexes of the central transition metals. A conspicuous discontinuity precedes a second maximum around 3.1 Å, thereby establishing a firm statistical grounding for the general description of these longer contacts as real, although certainly weak, interactions. Inspection of the hitset in this region uncovers four examples

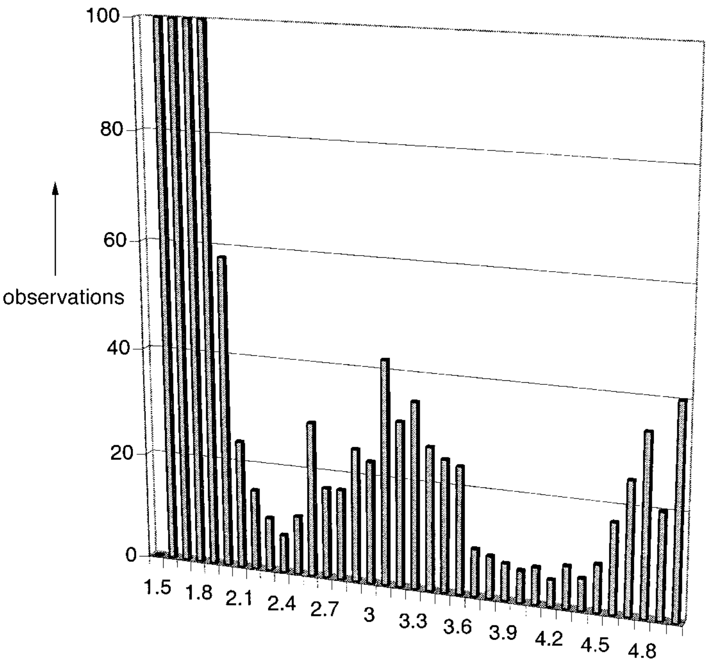


Figure 2. Aryl centroid–metal distance histogram. The bars between 1.4 and 1.9 Å (a total of 1832 observations) are off the scale.

of η^6 bonding for Ag^I (aryl centroid–metal 2.89–3.37 Å),[16] but none for Cu^I. Several univalent gallium- and thallium–arene complexes as described by Schmidbaur are also present.[17] Eight observations of "sandwiched" metals can be found,[18] for example $[Cs(p\text{-xylene})_2]^+$, with an aryl centroid–metal distance of 3.4 Å.[19] Finally, the upward trend in the plot towards 5 Å arises not as a result of direct aryl–metal contact, but of the fixed relationships between arenes and metals in the preponderance of [2.2]paracyclophane complexes with an η^6-bound metal and μ-bridged bis(η^6) metal species in the Database.

Whilst trigonal-planar coordination of Ag^I and Cu^I is uncommon,[20] bis(η^6) complexation of these metals is unprecedented.[21] This report of the cryptation of metal ions in thiacylindrophane **2d**, with its nearly ideal Ar⋯Ar separation for longer range metal–arene bonding, provides the first example of Ag^I and Cu^I sandwiches and indeed the only structurally characterized Cu^I–aryl centroid interaction. We look forward to investigating the interaction of **2d** with other metals, and the effects of adding an electron to $[M(\mathbf{2d})]^+$, which should delocalize between the two rings and metal center.

Experimental Section

2d: A solution of trithiol **3**[8] (0.463 g, 1.79 mmol) and sodium hydroxide (0.22 g, 5.5 mmol) in ethanol (40 mL) and a solution of tribromide **4**[9] (0.715 g, 1.79 mmol) in toluene (40 mL) were introduced simultaneously over 12 h into refluxing *tert*-butyl alcohol (200 mL) under nitrogen with stirring. The mixture was heated at reflux for a further 15 h and filtered, and the solvent evaporated. The solid residue was purified by chromatography (10% ethyl acetate in hexane) to give **2d** (0.493 g, 66%) as a white solid. M.p. 184–186 °C; ^1H NMR (250 MHz, $CDCl_3$): $\delta = 2.52$ (12H, t, $J = 6.8$ Hz), 2.72 (12H, t, $J = 6.8$ Hz), 6.73 (6H, s); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 35.6$, 36.0, 126.9, 140.8; MS (FAB): m/z: 415 $[M^+ + H]$; elemental analysis calcd for $C_{24}H_{30}S_3$: C 69.51, H 7.29; found: C 69.38, H 7.35.

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Keywords: coordination modes · cyclophanes · macrocycles · sandwich complexes

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[1] The term "macrobicycle" as applied here is used as an analogy to cryptand macrobicycles with aromatic rings counted as bridgeheads, and is not intended to be a formal description of the ring system.

[2] For a detailed treatment on conformational aspects of larger rings, see J. Dale, *Angew. Chem.* **1966**, *78*, 1070–1093; *Angew. Chem. Int. Ed. Engl.* **1966**, *5*, 1000–1021.

[3] Metals which participate in strong η^6 bonding to benzene rings could of course be encapsulated without recourse to "cryptation". No *sym*-[*n.n.n*]cyclophane has yet been used for this purpose, even though the well known [3.3]paracyclophane–chromium bis(η^6) complexes demonstrate the potential for this type of inclusion: R. Benn, N. E. Blank, M. W. Haenel, J. Klein, A. R. Koray, K. Weidenhammer, M. L. Ziegler, *Angew. Chem.* **1980**, *92*, 45–46; *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 44–45. Silver(I), which has a high affinity for π systems, also forms a stable complex with an all-hydrocarbon "deltaphane" $[(\eta^1)_3$-silver-1,2,4,5-[2.2.2.2.2.2]cyclophane]: H. C. Kang, A. W. Hanson, B. Eaton, V. Boekelheide, *J. Am. Chem. Soc.* **1985**, *107*, 1979–1985.

[4] The analogous [*n.n*]paracyclophanes and *sym*-[*n.n.n*]cyclophanes where *n* is an odd number reside however in deep potential energy wells with benzene rings parallel: reference [2] and M. Mascal, J.-L. Kerdelhué, A. S. Batsanov, M. J. Begley, *J. Chem. Soc. Perkin Trans. 1* **1996**, 1141–1151.

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[10] a) X-ray structure analysis of $[Cu(\mathbf{2d})]BF_4 \cdot 0.5\,CH_3OH$: $C_{24}H_{30}CuS_3{}^+BF_4{}^- \cdot 0.5\,CH_3OH$, $M_r = 581.03$, colorless rectangular plate $0.60 \times 0.54 \times 0.13$ mm, monoclinic, space group $P2_1/m$, $a = 8.391(4)$, $b = 17.971(7)$, $c = 16.329(8)$ Å, $\beta = 97.09(3)°$, $V = 2443(2)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.579\,g\,cm^{-3}$, $\mu(Mo_{K\alpha}) = 1.196\,mm^{-1}$. Stoe Stadi-4 four-circle diffractometer, $Mo_{K\alpha}$ radiation, $\lambda = 0.71073$ Å, $T = 150(2)$ K, ω/θ scans. Of 3890 reflections measured ($2\theta_{max} = 45°$), 3322 were unique (merging at $R = 0.060$), giving 2641 with $F \geq 4\sigma(F)$; all 3322 were retained in all calculations. Crystal decay (10.8%) was corrected for, and absorption corrections ($T_{min} = 0.529$, $T_{max} = 0.860$) were applied numerically during data processing. Structure solution utilized direct methods[22] and difference Fourier syntheses. One of the independent half-cations exhibited disorder affecting the copper and the surrounding ligand framework, which was modeled by allowing three alternative sites for the metal. Refinement was by full-matrix least squares[23] on F^2, non-solvent H atoms were introduced at geometrically calculated positions and thereafter allowed to ride on their parent C atoms with $U_{iso}(H) = 1.2\,U_{eq}(C)$. Final R_1 $[F \geq 4\sigma(F)] = 0.0576$, wR_2 [all data] $= 0.154$, $S\,[F^2] = 1.17$ for 341 refined parameters. The final ΔF synthesis showed no residual feature above 1.35 e Å^{-3}.[10c] b) X-ray structure analysis of $[Ag(\mathbf{2d})]BF_4$: $C_{24}H_{30}AgS_3{}^+BF_4{}^-$, $M_r = 609.34$, colorless rod $0.51 \times 0.16 \times 0.09$ mm, monoclinic, space group $P2_1/m$, $a = 8.440(2)$, $b = 17.966(4)$, $c = 16.247(4)$ Å, $\beta = 96.06(3)°$, $V = 2449.8(10)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.652\,g\,cm^{-3}$, $\mu(Mo_{K\alpha}) = 1.121\,mm^{-1}$. Of 6933 reflections measured as described for $[Cu(\mathbf{2d})]BF_4$ ($2\theta_{max} = 50°$), 4448 were unique (merging at $R = 0.064$), giving 3655 with $F \geq 4\sigma(F)$; all 4448 were retained in all calculations. Crystal decay (7.2%) was corrected for, and absorption corrections ($T_{min} = 0.821$, $T_{max} = 0.898$) were applied numerically during data processing. Structure solution

utilized heavy-atom methods[22] and difference Fourier syntheses. Refinement was carried out as described for [Cu(**2d**)]BF_4. Final R_1 [$F \geq 4\sigma(F)$] = 0.0416, wR_2 [all data] = 0.100, S [F^2] = 1.06 for 310 refined parameters. The final ΔF synthesis showed no residual feature above 1.47 e $Å^{-3}$.[10c] c) Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-111910 ([Cu(**2d**)]BF_4) and 111911 ([Ag(**2d**)]BF_4). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[11] Data represent the ordered half-molecule in the asymmetric unit.

[12] Data represent one of two very similar half-molecules in the asymmetric unit.

[13] Cambridge Structural Database Version 5.16 (190307 structures, October 1998 release): F. H. Allen, O. Kennard, *Chem. Des. Automat. News* **1993**, *8*, 31–37.

[14] The United Kingdom Chemical Database Service: D. A. Fletcher, R. F. McMeeking, D. Parkin, *J. Chem. Inf. Comput. Sci.* **1996**, *36*, 746–749.

[15] The query was constructed by defining three points on an aromatic ring: x, one C atom of the ring; o, the centroid of the ring; and y, the centroid of one of the C–C bonds parallel to xo. A metal atom at point m would have x,y coordinates $x_m = om\cos(x\hat{o}m)$ and $y_m = om\cos(y\hat{o}m)$. The radius of the cylinder (r) was defined by the relationship $x_m^2 + y_m^2 \leq r^2$, and the 5 Å height of the cylinder was limited by constraining om.

[16] CSD refcodes: DOCPAM, TEXZUR, YUHDEK, ZODZAT.

[17] H. Schmidbaur, *Angew. Chem.*, **1985**, *97*, 893–904; *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 893–904.

[18] In all cases the benzene rings are associated independently to the metal. CSD refcodes: BEDBER, DEKMAH, FICXEU, HALVEV, JIVTEN, JIVTIR, SEJKAT, SIRROA.

[19] J. L. Atwood, W. E. Hunter, R. D. Rogers, J. A. Weeks, *J. Inclusion Phenom.* **1985**, *3*, 113–123.

[20] A total of 9141 crystal structures in the Cambridge Structural Database contain Cu and 1605 contain Ag, of which 104 (1.1%) and 32 (2.0%), respectively, exhibit the metal in a trigonal-planar ligand field (i.e., trivalent with bond angles between 115° and 125°). It must be noted that it is not possible using the CSD's QUEST-3D software to specify metal oxidation states, so the above figures for Cu include both Cu^I and Cu^{II}.

[21] Two examples are found in the literature where a crown ether incorporates a single benzene ring whose centroid is involved in bonding to Tl^I (metal–centroid, 2.96 Å) and Ag^I (metal–centroid, 2.89 Å): F. Fages, J.-P. Desvergne, H. Bouas-Laurent, J. Hinschberger, P. Marsau, M. Petraud, *Nouv. J. Chim.*, **1988**, *12*, 95–106; H. Andrianatoadndro, Y. Barrans, P. Marsau, J. P. Desvergne, F. Fages, H. Bouas-Laurent, *Acta Crystallogr. Sect. B* **1995**, *51*, 293–300, respectively.

[22] SHELXS-97: G. M. Sheldrick, *Acta Crystallogr. Sect. A* **1990**, *46*, 467–473.

[23] G. M. Sheldrick, *SHELXL-97*, University of Göttingen, **1997**.

N-Oxidation of Epothilone A–C and *O*-Acyl Rearrangement to C-19- and C-21-Substituted Epothilones[**]

Gerhard Höfle,[*] Nicole Glaser, Michael Kiffe, Hans-Jürgen Hecht, Florenz Sasse, and Hans Reichenbach

Dedicated to Professor Wolfgang Steglich
on the occasion of his 65th birthday

Epothilone A (**1a**) and B (**1b**) form the parent compounds of a new family of cytotoxic and antifungal macrolides from the mycobacterium *Sorangium cellulosum*.[1] According to Bollag et al.,[2] their effect upon eucaryontic cells is based on the induction of tubulin polymerization and stabilization of microtubules, causing a massive disruption in mitosis and ultimately programmed cell death (apoptosis). This mechanism, which had been extremely rare for a long time, was first observed for taxol (paclitaxel),[3] and has recently been reported for discodermolide,[4] a polyketide from marine sponges, and eleutherobin,[5] a diterpene from soft coral. The high in vitro activity against multiresistant tumor cell lines[2, 6, 7] as well as other beneficial properties[1, 8] quickly made the epothilones interesting candidates for cancer chemotherapy and for total synthesis.[9]

First results of in vivo studies on mouse models were reported by Danishefsky et al. In these studies, not epothilone B (**1b**), which demonstrated the highest in vitro activity, but the significantly less active deoxyepothilone B (= epothilone D, **1d**) showed a promising therapeutic range with good activity against sensitive and multiresistant tumors up to the point of complete remission.[10]

In the search for possible clinically suitable derivatives, we have concentrated our efforts on the isolation of natural structural variations[11] and the chemical modification of the epothilones obtained by fermentation.[12] We report herein the unexpectedly simple functionalization of the thiazol moiety.

During the preparation of epothilones by fermentation from *Sorangium cellulosum*, numerous structural variants from biosynthesis and biotransformation were obtained in addition to the main components A and B. Particularly

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