

SAM.^[9] This kinetic inhibition towards spontaneous adsorption was not observed when Bu₄NPF₆ was used instead of Bu₄NBF₄. The rate of spontaneous adsorption in the presence of tetrafluoroborate is sufficiently slow to allow the selective electrochemisorption described herein.

We have developed an electrochemical method for the selective formation of self-assembled monolayers on a particular gold electrode in the presence of another nearby electrode. The monolayers produced are very similar in thickness, wettability, blocking of heterogeneous electron transfer, and elemental composition to analogous SAMs formed by the chemisorption of alkanethiols. The selectivity of this synthetic method should allow the preparation of microelectrode arrays with differentiated surface chemistry, a goal of great importance in the fabrication of sophisticated sensor arrays.^[5-7, 21, 22] Other attractive features of this electro-synthesis of SAMs are: a) the control it provides over the degree of coverage; b) the short time (less than a minute) needed to form a SAM; c) the ability to form SAMs easily on gold that is not freshly evaporated; and d) the use of precursors without an unpleasant odor (for precursor alkyl groups containing more than about ten carbon atoms). The formation of SAMs by the electrochemical oxidation of alkyl thiosulfates may be extendable to other metals, as long as anodic dissolution of the metal does not interfere at the potential necessary to oxidize the Bunte salts. In preliminary experiments, we found that SAMs can also be formed from aqueous solutions by the reduction of an alkyl thiosulfate, a process known to produce thiols.^[10]

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Building Supramolecular Nanostructures at Surfaces by Hydrogen Bonding**

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Supramolecular structures formed by the self-assembly of functional molecular building blocks are a promising class of materials for future technologies.^[1-3] Particularly useful for their fabrication is hydrogen bonding,^[4] which provides both high selectivity and directionality.^[5] Hydrogen-bonded archi-

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structures are abundant in biological systems, which has motivated their exploitation in supramolecular chemistry.^[6] This has been demonstrated particularly for systems in solution, molecular crystals, and for two-dimensional layers.^[1, 3, 4, 7–10] Herein we demonstrate that novel supramolecular nanostructures can be generated at surfaces on the basis of this concept. Scanning tunneling microscopy experiments were performed on 4-[*trans*-2-(pyrid-4-yl-vinyl)]benzoic acid adsorbed onto a metal surface.^[11, 12] A one-dimensional supramolecular nanograting was fabricated at a Ag(111) surface by cooperative self-assembly.

Molecular self-assembly at surfaces is governed by the subtle balance between intermolecular and molecule–surface interactions, which can be tuned by the appropriate choice of substrate material and symmetry. Promising achievements have been reported in this field.^[13–16] For the present study we employed 4-[*trans*-2-(pyrid-4-yl-vinyl)]benzoic acid (PVBA, Figure 1a), which has been specifically designed to form

onto different well-defined single-crystal metal surfaces by organic molecular beam epitaxy.^[17, 18] The resulting molecular arrangements were subsequently characterized in situ by temperature-controlled scanning tunneling microscopy (STM).

The molecules experience the potential energy surface of the metal substrate upon adsorption, which makes specific geometries energetically favorable. The ease with which these sites can be changed by either translational or rotational processes, that is, the surface mobility, is a key parameter for the arrangement of molecules at surfaces. Similarly important is the strength and nature of the intermolecular interactions that compete with the molecule–substrate interactions. As a third parameter, the magnitude of the thermal energy governs the level of ordering that can be achieved. The balance of these factors controls molecular self-assembly at surfaces. The STM data reproduced in Figure 1b–d demonstrate how self-assembly can be tuned for a given molecule by the choice of substrate material and symmetry. The interaction of PVBA with the transition metal surface Pd(110) is visualized in Figure 1b. The two-lobe shape of the individual molecules resolved in the image is associated with the pyridyl and phenylene rings. Strong π bonding to Pd surface atoms enforces a flat adsorption geometry. Two distinct molecular orientations exist exclusively which allow for the accommodation of the molecular units at sites on the anisotropic substrate with high symmetry.^[19, 20] At small coverages a random distribution of isolated molecules is found even well above room temperature where thermal mobility becomes appreciable, which demonstrates the dominance of the adsorbate–substrate interactions with this system.^[19, 20] Low-temperature aggregation and growth of dendritic molecular islands is observed on switching to the more inert Cu(111) surface (Figure 1c), which is indicative of a higher surface mobility and greater lateral interactions. However, the PVBA adsorption geometry is not unique as is deduced from the irregularities in the dendritic arms and the coexistence of the flat adsorbed molecules with single ones in upright orientations,^[21] which are imaged as spherically symmetrical protrusions. Annealing the sample results in only flat lying species, however, a regular molecular ordering is obstructed by strong lateral interactions with Cu adatoms evaporated from the substrate steps. These complications are absent at the Ag(111) surface. The STM topograph in Figure 1d reveals that flat adsorption of PVBA prevails on Ag(111). Again, island formation is already found at low temperatures, and inspection of the island shapes reveals that their formation must be a result of attractive interactions between the molecular endgroups. This observation is in line with the directional interactions expected from the formation of hydrogen bonds. Molecular strings thus evolve at the surface, and their curved shape signals that the substrate corrugation experienced by the molecules must be rather weak. This effect is attributed to the smoothness of the close-packed geometry of the substrate and the weak bonding between the adsorbate and the noble metal surface. The observed growth scenario can be considered as a diffusion-limited aggregation of rodlike particles, which is subject to anisotropic interactions. Accordingly, the irregularity of the formed agglomerates suggests that their

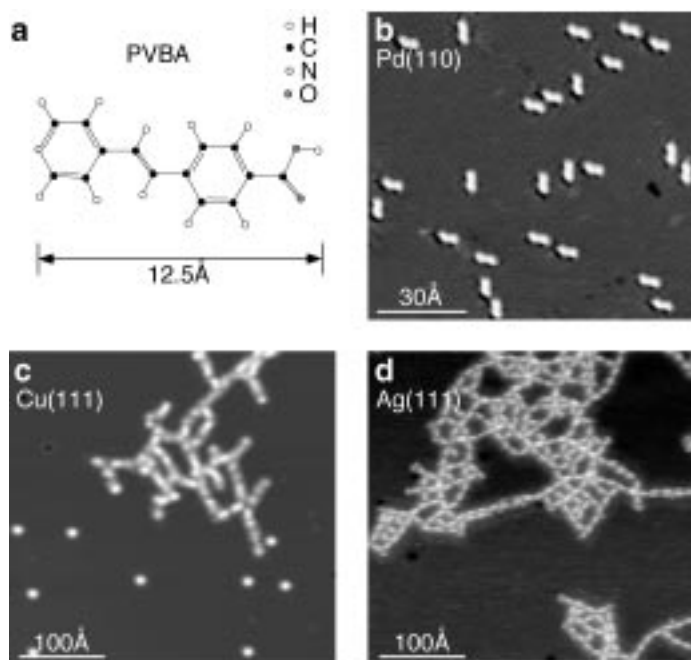


Figure 1. a) Molecular structure of 4-[*trans*-2-(pyrid-4-yl-vinyl)]benzoic acid (PVBA) with a pyridyl group at the head and a benzoic acid moiety at the tail. Pictures b–d show STM topographs of PVBA on different single-crystal metal substrates: b) Strong adsorbate–substrate interaction on a Pd(110) surface: isolated, immobile PVBA molecules lie flat in two distinct orientations (measured at 325 K) and remain randomly distributed upon annealing at 450 K. c) On a Cu(111) surface flat molecules in dendritic islands coexist with isolated molecules in an upright bonding configuration (single protrusions) after adsorption at 160 K. d) The complex aggregation of PVBA lying flat on Ag(111) reflects the surface mobility and attractive interactions between molecular endgroups at 125 K.

strong hydrogen bonds and has been used to form thin films for application in nonlinear optics.^[11, 12] This planar and rigid molecule comprises a pyridyl group as the head and a carboxylic acid group as the tail and is ideal for self-assembly by head-to-tail hydrogen bonding.^[11, 12] Small amounts of PVBA were evaporated under ultra-high vacuum conditions

onto different well-defined single-crystal metal surfaces by organic molecular beam epitaxy.^[17, 18] The resulting molecular arrangements were subsequently characterized in situ by temperature-controlled scanning tunneling microscopy (STM).

shape results from kinetic limitations, whereby thermal equilibrium is not attained.

The data reproduced in Figure 2 show that well-ordered supramolecular structures evolve on Ag(111) when the thermal energy is augmented by adsorption or annealing at

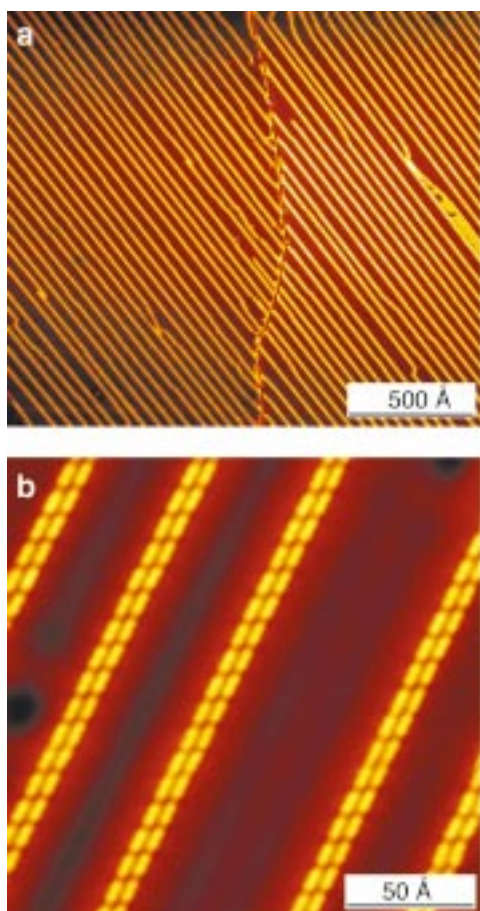


Figure 2. Formation of a one-dimensional supramolecular PVBA superstructure by self-assembly mediated by H-bond formation on an Ag(111) surface at 300 K (measured at 77 K). a) An STM topograph of a single domain extending over two terraces demonstrates ordering at the μm scale. b) A close-up image of the self-assembled twin chains reveals that they consist of coupled rows of PVBA molecules.

300 K. The overview picture (Figure 2a) reveals the formation of highly regular, one-dimensional supramolecular arrangements in a domain that extends over two neighboring terraces that are separated by an atomic step. The molecular stripes run straight along a $\langle 11\bar{2} \rangle$ direction of the Ag lattice. In agreement with the threefold symmetry of Ag(111) three rotational domains of this structure exist, which usually extend in the μm -range on the surface. A close-up view of some molecular stripes (Figure 2b) reveals that the one-dimensional superstructure actually consists of two chains of PVBA.^[22] The molecular axis is oriented along the chain direction, in agreement with the expected formation of hydrogen bonds between the PVBA end groups. The chain periodicity amounts to 15.0 \AA , that is $p = 3\sqrt{3}a$, where a is the Ag(111) surface lattice constant (2.89 \AA). The rows of PVBA within the twin chains are shifted by $\Delta p \approx 3.7 \text{ \AA}$ with respect

to each other. This observation suggests an intricate coupling mechanism between adjacent rows separated by $d \approx 2.4a$. The extreme stability of the low-temperature scanning tunneling micrograph^[23, 24] employed for this study allows for the elucidation of fine chain details, as demonstrated by the high-resolution data shown in Figure 3. Firstly, a slight

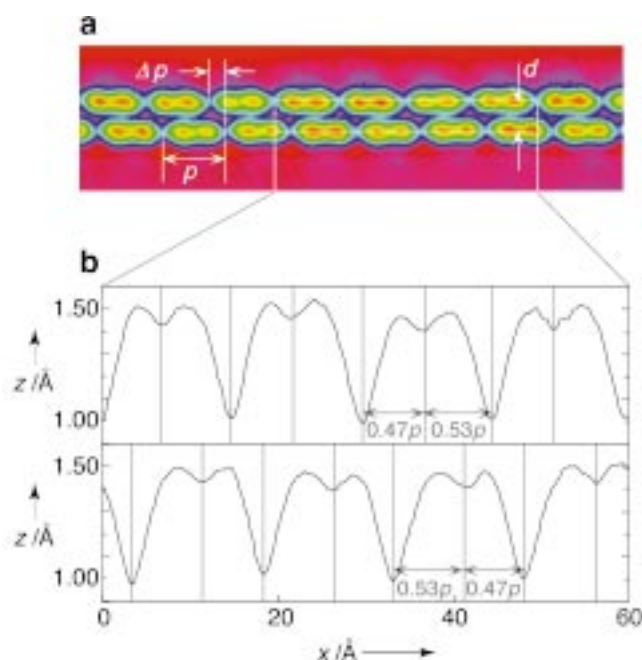


Figure 3. High-resolution STM data of a PVBA twin chain. a) The chain periodicity p in the $[11\bar{2}]$ direction is $3a\sqrt{3} = 15 \text{ \AA}$, the PVBA inter-row distance d is $\approx 2.4a$. b) The STM contours along the lines indicated in (a) demonstrate the head-to-tail coupling of the PVBA molecules along the rows and the antiparallel molecular alignment in adjacent rows.

asymmetry of the molecules becomes apparent in the topograph (Figure 3a), namely, in the upper row the right lobes of all the molecules appear oval, while the left lobes have a round shape. This inequality is elucidated by the STM contour lines shown in Figure 3b. The longer, oval lobe is associated with the benzoic acid moiety of PVBA. Hence, there is indeed a head-to-tail coupling of PVBA in the chains. Secondly, the data reveal that in the lower row the left lobe of all the PVBA molecules is more extended, opposite to the configuration in the upper row. Hence, the molecules in adjacent rows exhibit antiparallel alignment.

The observed features of the supramolecular structure are rationalized by the model proposed in Figure 4a, where a montage of an Ag(111) atomic resolution image with a self-assembled twin chain drawn to scale is shown. The orientation of the molecular chains reflects a good match between the PVBA subunits and the high-symmetry lattice positions. This result also accounts for the chain periodicity being a multiple of Ag lattice units. When an unrelaxed molecular configuration is assumed,^[25] the length of the $\text{OH} \cdots \text{N}$ hydrogen bond is 2.5 \AA . This distance is larger than those of similar types of H-bonds in crystals of nucleic acid components and isonicotinic acid (a lower analogue of PVBA), where values in the range of $1.5\text{--}2.1 \text{ \AA}$ exist.^[26, 27] Nevertheless, the proximity of the coupled groups can be associated with the formation of

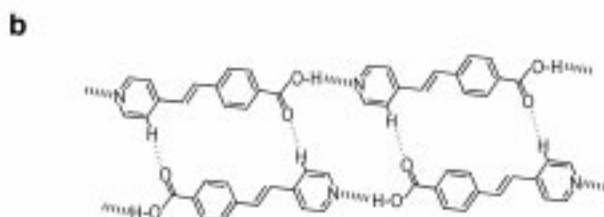
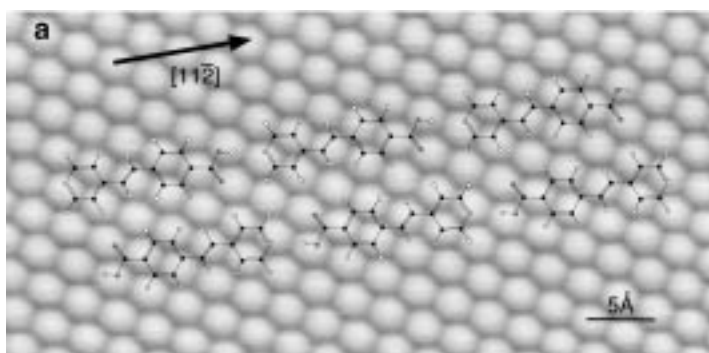


Figure 4. a) Montage of an atomic-resolution image of Ag(111) with a proposed model of the self-assembled twin chain of PVBA drawn to scale illustrating the match of the molecular geometry and substrate lattice. b) Repeat motif of the PVBA supramolecular twin chains with weak OH...N and possible weak CH...OC hydrogen bonds indicated.

weak H-bonds (Figure 4b).^[5] It is possible that the presence of the metal surface electrons might influence the hydrogen bonding. Solid-state ¹⁵N NMR spectroscopy has demonstrated that proton transfer does not occur with PVBA in crystallites.^[11] The coupling of the PVBA in adjacent rows is associated with weak intermolecular attractions. The antiparallel alignment and the relative displacement allow for a complementary assembly of two equivalent PVBA molecules, which are accommodated in similar adsorption geometries. In addition to the expected electrostatic interactions between the polar molecules, a weak CH...OC hydrogen bonding is feasible. The corresponding CH...OC distance is approximately 2.9 Å, close enough for a weak interaction.^[28] The geometrical arrangement is a compromise between the lateral intermolecular interaction and the bonding to the substrate.^[29] There is a slight outward relaxation of the rows away from the centers of the hollow-site positions as a result of the inter-row distance of 2.4a. This relaxation and the suggested inward orientation of the C=O group prevent two-dimensional growth and thus account for the directional self-assembly of the twin chain. The rather regular mesoscopic ordering of the supramolecular chains into a grating, reminiscent of mesoscopic superstructures induced by relaxation of surface strain,^[30, 31] can be rationalized by the operation of weak, long-range repulsive dipole–dipole interactions between the twin chains.^[32]

It is interesting to note that chiral species of PVBA exist at the surface which undergo spontaneous enantioresolution in the self-assembly process. Only one enantiomer is present in the model shown in Figure 4 (while arrangements are feasible with a combination of different enantiomers, they lead to energetically less-favorable structures^[33]). This observation is related to the distinct directional shift in the twin chains: it is

always the right PVBA row that appears to be displaced by the distance Δp in the chain direction. Accordingly the opposite shift is encountered, and was indeed observed, with the other enantiomer.

Our findings and suggestions that the self-assembly of properly designed molecules by noncovalent bonding opens up novel avenues for the positioning of functional units in supramolecular architectures at surfaces by organic molecular beam epitaxy. It is believed that this approach will be valuable for the future fabrication of nanoscale devices and supramolecular engineering.

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Ring-Closing Alkyne Metathesis: Application to the Stereoselective Total Synthesis of Prostaglandin E₂-1,15-Lactone**

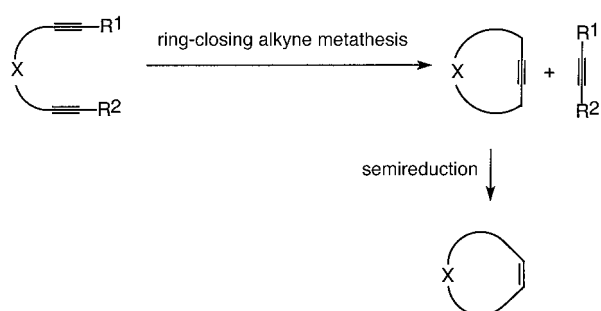
Alois Fürstner* and Karol Grela

Dedicated to Professor Günther Wilke on the occasion of his 75th birthday

Among the few limitations that infringe upon the superb overall application profile of ring-closing olefin metathesis (RCM), the lack of control over the configuration of the newly formed double bond constitutes a significant handicap when applied to the macrocyclic series.^[1] The cycloalkenes formed are usually obtained as mixtures of the *E* and *Z* isomers, with the *E* isomers dominating in most of the recorded examples.^[1, 2] This constitutes a significant drawback in many natural product syntheses as can be clearly seen, for example, from the epothilone case.^[3]

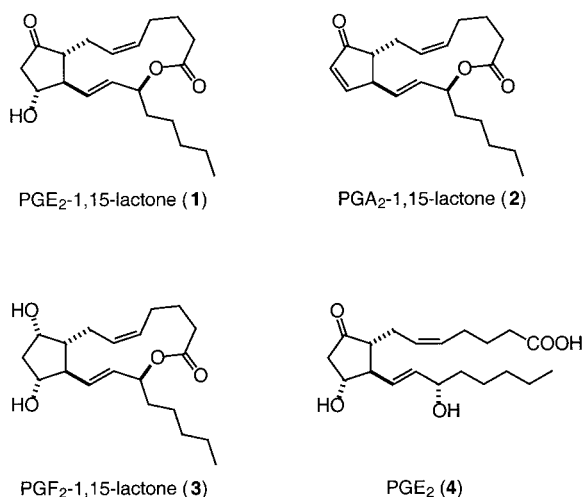
To circumvent this inherent problem, we have recently proposed an indirect but stereoselective approach to macrocyclic *Z* alkenes which comprises a ring-closing metathesis reaction of diyne substrates followed by semireduction of the resulting cycloalkyne products (Scheme 1).^[4] Schrock-type tungsten alkylidyne complexes such as [W(≡CCMe₃)(*O*tBu)₃]^[5] as well as a newly discovered molybdenum chloride species formed in situ from [Mo{N(*t*Bu)(Ar)}₃] and CH₂Cl₂^[6, 7] were found to be efficient precatalysts for this unprecedented type of ring-forming reaction.^[8] In terms of functional group compatibility, these initiator systems exhibit complementary behavior.

To gain a better understanding of the relevance and scope of this conceptually new approach, we were prompted to



Scheme 1. Stereoselective synthesis of macrocyclic *Z* alkenes by ring-closing alkyne metathesis and subsequent semireduction.

extend our studies beyond model compounds and to venture into the total synthesis of biologically significant and structurally more demanding targets. We felt that prostaglandin lactones such as **1–3**, a rather unique class of natural products isolated from the nudibranch *Tethys fimbria*,^[9, 10] would provide an ideal testing ground in this respect.



PGE₂-1,15-lactone **1** as a prototype member of this family exerts strong biological effects in vitro and in vivo, including a significant decrease of gastric secretion when administered intravenously in dogs (90% at a dose of 100 μg kg⁻¹)^[10c] as well as ichthyotoxic properties at 1–10 μg mL⁻¹ concentrations.^[9] Furthermore, **1** is readily hydrolyzed into parent prostaglandin E₂ **4** by various esterases and therefore constitutes an attractive prodrug for this physiologically highly active metabolite.^[10c, 11] In view of differing enzyme activity distribution in tissue, one may even envisage its sustained and localized release. From the chemical point of view, the intrinsically labile β -hydroxy ketone substructure of all members of the PGE series towards acid as well as base renders lactone **1** a formidable probe for the applicability of the alkyne metathesis/Lindlar reduction strategy to sensitive compounds in general.

The results of our investigations are summarized in Scheme 2. Three-component coupling^[12] as the most elegant method for the construction of prostaglandin skeletons accounts for a straightforward formation of the required cyclization precursor **13**. Thus, commercially available prop-

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