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[2] It is, for example, well known that electron-rich, disklike aromatic compounds such as radial multialkynylbenzene derivatives and triphenylene ethers form charge-transfer complexes with flat, nitrofluorenone-based electron acceptors. The CT interactions may cause the stabilization as well as the induction of columnar mesophases. The columnar phases formed by the binary mixtures are usually hexagonal (Col_h) or nematic columnar (N_{col}): H. Bengs, M. Ebert, O. Karthaus, B. Kohne, K. Praefcke, H. Ringsdorf, J. H. Wendorff, R. Wüstefeld, *Adv. Mater.* **1990**, *2*, 141; M. Ebert, G. Frick, C. Baehr, J. H. Wendorff, R. Wüstefeld, H. Ringsdorf, *Liq. Cryst.* **1992**, *11*, 293; K. Praefcke, J. D. Holbrey, *J. Inclusion Phenom. Mol. Recognit. Chem.* **1996**, *24*, 19.
[3] The association of 2,6-diacylaminopyridines with complementary uracil derivatives, for example, leads to the induction of columnar phases on either a hexagonal[4, 5] or a rectangular[6] two-dimensional array. Here, however, the two components are not mesomorphic by themselves.
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[11] The mixtures were prepared by combining solutions of the triazines **1** with either acceptor **2** or **3** in dichloromethane. Similar to triphenylene ethers, the dark brownish color that appears indicates complex formation through charge-transfer interactions. All thermal investigations were performed after evaporating the solvent, drying the residues in a vacuum, and annealing the samples in the isotropic state.
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[14] Suggestion by one of the referees.

Combinatorial Surface Chemistry—Is it Possible?**

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Combinatorial chemistry and biological-based approaches have emerged as powerful aids for the discovery of novel pharmaceutical agents and biomaterials.[1] Since its introduction in the early 1990s, combinatorial chemistry has revolutionized the medicinal chemistry area. The combinatorial technique, applied to discover novel materials and catalysts, is making significant progress in another research area.[2–4]

However, the basic essence of combinatorial chemistry has yet to be completely employed. Nature is the best combinatorial chemist, showing four deoxyribonucleotides and twenty amino acids underly the whole biological world through the combination of these small molecular species. Indeed, one may think a long polypeptide chain is a combination of different amino acids connected through amide bonds. The long polypeptide chains then fold into a three-dimensional protein structure through noncovalent bonds between the amino acid residues. As a result, the active site of a protein can be envisaged merely as a combination of amino acids in a three-dimensional space.

This fundamental feature of proteins suggests a very interesting clue for the creation of their mimics. Amphiphilic lipid molecules are a class of molecules well studied by surface chemists. At the two-dimensional air–water interface, the hydrophilic polar moiety embeds into the water phase and the hydrophobic alkyl chain orients towards the air phase. When compressed at the interface, the amphiphilic molecules will move and assemble into organized supramolecular structures, known as Langmuir monolayers. If the polar moieties are functionalized with different peptides, such as a peptide library, the self assembly of these functional lipids may form proteinlike supramolecular structures, as illustrated in Figure 1.

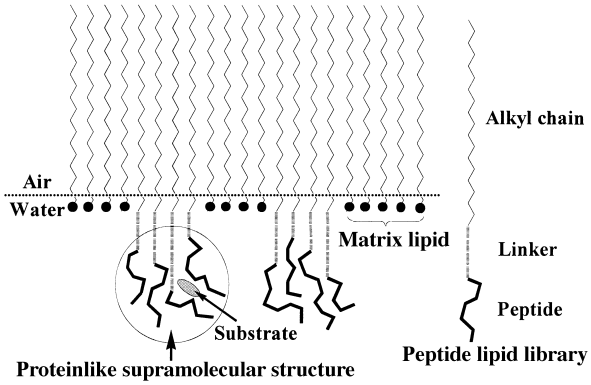

Figure 1. An illustration of the self assembly of peptide–lipid library components at the air–water interface to form proteinlike supramolecular structures.

Yu et al. recently reported that the self assembly of a peptide lipid led to the formation of a collagenlike structure at the air–water interface.[5] Kunitake has shown that two peptide lipids could combine together at the air–water interface to form a unique binding site for a specific peptide guest.[6] Furthermore, it was found that nonpeptide lipids could also combine together at the air–water interface to form receptors for different, small organic guest molecules.[7] These previous works strongly support the feasibility of the proposed two-dimensional combinatorial approach.

We now for the first time report our study of Langmuir monolayers made of peptide lipid libraries. Library **LIB** and three sublibraries **SUB1**, **SUB2**, and **SUB3** (Table 1) were synthesized through the solid-phase peptide synthesis techni-

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Supporting information for this article is available on the WWW under http://www.wiley-vch.de/home/angewandte/ or from the author.

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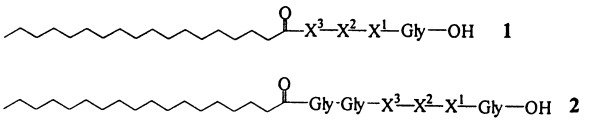
Table 1. The structures and the building blocks for the synthesis of the peptide lipid library and sublibraries.



Library	X^1, X^2, X^3	Components
LIB	Gly, Glu, Ser, His, Tyr	250
SUB1	Gly, Ser, Tyr	54
SUB2	Gly, Glu, Tyr	54
SUB3	Glu, Ser, His	54

que[8] with a mixing–splitting method.[9] Five amino acids—Gly, Glu, Ser, His, and Tyr—were used as building blocks. After the coupling of the last variable amino acid residue to the beads (Wang Resin), half of the resin was then taken out to couple with two more glycine units. The two extra Gly amino acids serve as a linker to extend the length of the remaining peptide lipids. The two portions of the resins were then combined and coupled with the succinimidyl ester of stearic acid (SA) to produce **1** and **2**, without and with the two extra Gly spacer units, respectively. Through the spacer extension, there are peptide lipids of different lengths, which, on combination, form a pseudo three-dimensional structure at the interface (Figure 1). As a result, the library **LIB** contains 250 components and each of the three sublibraries contains 54 components. The three sublibraries are part of the original library **LIB**.

The surface chemistry of the lipid libraries was studied. In contrast to traditional Langmuir monolayer studies, the present study used a lipid library instead of only one or a few lipids at the air–water interface. Surface pressure–area isotherm measurements show that, as a whole, these library and sublibrary samples formed monolayers at the air–water interface (Figure 2). A technical point was raised during the isotherm measurements of these lipid library and sublibrary samples. Since the library components are mixed together through the mixing–splitting synthesis, the library components are not addressed individually. An exact molecular weight of the library sample cannot be calculated. Therefore, when preparing the spreading solution, all the library and sublibrary samples were presumed to have an mean molecular weight of 600 g mol^{-1}, corresponding to a molecule with a C_{18} hydrocarbon alkyl chain and a peptide chain with three to five amino acid residues. The molecular areas in the isotherm may not reflect the actual average molecular area of the library components. Therefore, it is not appropriate to compare the molecular areas of monolayers from one library to another. However, this will not affect the molecular recognition and binding studies of the peptide lipid library, as discussed later, because only the molecular area changes upon binding of substrate are important.

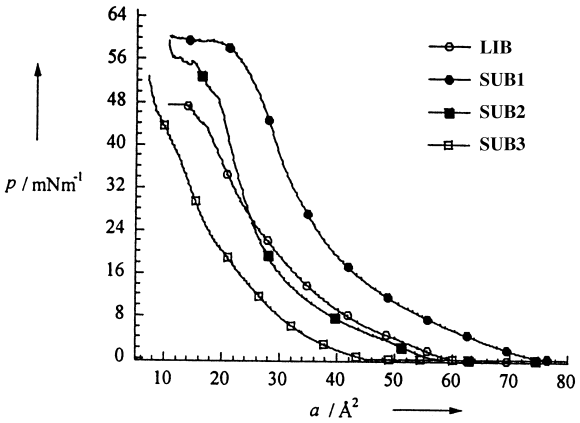


Figure 2. The surface pressure–area per molecule (p–a) isotherms of monolayers of the peptide lipid libraries **LIB**, **SUB1**, **SUB2**, and **SUB3** on a pure water subphase (pH 5.8, 20 °C).

We then have attempted to use these library and sublibrary monolayers for molecular recognition of maltose as well as other sugar molecules. It is known that the binding site of the maltose binding protein (MBP) is exceptionally rich in polar and aromatic amino acid residues.[10] The polar, charged side chains hydrogen bond with the maltose hydroxyl group and the stacking of the aromatic residues provides the majority of the van der Waals contacts with maltose. Among the amino acid building blocks chosen for the lipid library and sublibrary synthesis, two are charged amino acids (His and Glu) and one is aromatic (Tyr). Since these amino acid residues exist in the different positions of the peptide–lipid library components, the spatial combination of these amino acid residues in the lipid library monolayers may lead to the formation of specific binding sites for maltose, similar to the binding site of MBP.

It was found that with 10 mM D-maltose as a subphase, the molecular areas of the library and sublibrary monolayers were all expanded. However, the molecular area expansions caused by the existence of maltose in the subphase are different from one library monolayer to the other (Figure 3). While the **LIB** monolayer only exhibits slight expansion on the maltose subphase at the surface pressure lifting point ($\approx$4 Å^2 molecule^{-1}) compared to pure water subphase, **SUB2** with Gly, Glu, and Tyr building blocks exhibits the largest expansion of molecular area ($\approx$12 Å^2 molecule^{-1}).

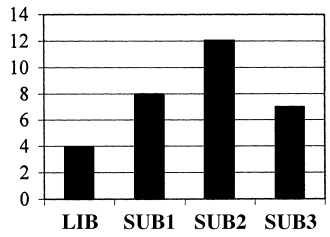


Figure 3. The increases of the molecular area (Å^2 molecule^{-1}) of the library and sublibrary monolayers on maltose subphase (10 mM in water, pH 5.8) compared to the pure water subphase. The area increases were calculated based on the molecular area increases at the surface pressure lifting point of the isotherms.

In any combinatorial chemistry study, one key issue is to identify the active components from a library. Our study suggests that the peptide lipids in **SUB2** are more active towards maltose than the components from other sublibraries. This result can be explained by the following fact: For **SUB1** there is a lack of polar amino acid residues, while in **SUB3** there is a lack of aromatic amino acid residues. Only **SUB2** contains both polar charged (Glu) and aromatic (Tyr) amino

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acid residues, the structural elements in the binding site of MBP.[10] The spatial combination of these charged and aromatic amino acid residues in different positions of peptide lipids at the air–water interface lead to the formation of appropriate binding sites for maltose. The sublibrary **SUB2** monolayer can mimic the structural feature and function of MBP more efficiently than the other sublibrary monolayers. As for **LIB**, since it contains both active and inactive peptide lipids, the actual concentration of active peptide lipids in the monolayer is lower and the observed binding activity is therefore smaller, compared to the sublibraries.

It has been reported[11] that the binding of maltose or its higher homologs to MBP induces major changes in both the fluorescence and UV absorption spectra of MBP, due to the van der Waals interactions between maltose and the aromatic residues of MBP in the binding site. Depending on the structures of the substrates, blue or red shifts of the absorption bands are observed. To verify the binding of maltose to the library monolayers, we have examined the UV/Vis absorption spectra of the **SUB2** monolayer on water and a 10 mM maltose subphase (Figure 4). Interestingly, like the MBP–maltose

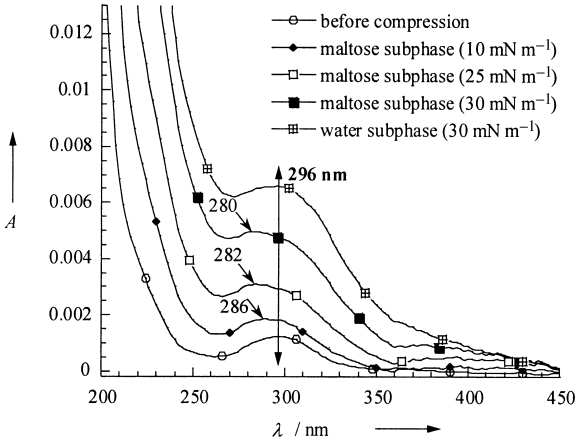

Figure 4. The UV/Vis absorption spectra (absorbance A, wavelength λ) of **SUB2** monolayer on 10 mM maltose subphase compared to the pure water subphase. Spectra of the monolayer on water at surface pressures lower than 30 mN m^{-1} are not shown. The maximum UV absorption of the monolayer on the water subphase remains at 296 nm from the beginning of the compression until its collapse.

complex, the absorption band of the **SUB2** monolayer at around 296 nm (arising from Tyr residues) significantly blue shifted in the presence of maltose. Before compression, the maximum absorption of the **SUB2** monolayer appeared at 296 nm on both subphases and under continuous compression this absorption band remained at 296 nm on pure water subphase at all stages of compression. However, on a 10 mM maltose subphase, this absorption band shifted to 286, 282, and 280 nm at monolayer surface pressures of 10, 25, and 30 mN m^{-1}, respectively, a gradual and significant blue shift upon compression. Combined with the surface pressure–area isotherm measurements, these results confirm that maltose molecules bind to the **SUB2** monolayer with strong intermolecular interactions. The aromatic Tyr residue in the sublibrary should play a significant role for the binding activity. Although there is only one polar and one aromatic amino acid in the library, the three-dimensional combination of the same amino acids in different positions can still lead to the formation of an efficient binding site.

As an important comparison, we have also examined the binding activity of the **SUB2** monolayer towards two other sugar molecules, D-glucose and sucrose. The surface pressure–area isotherms show the existence of glucose or sucrose in the aqueous subphase introduced almost no area expansion of the monolayer (Figure 5), in stark contrast to the maltose

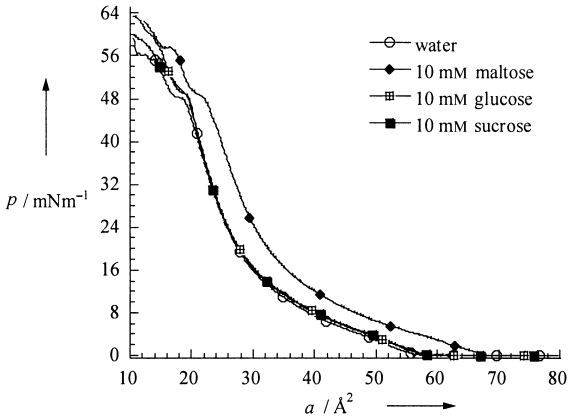

Figure 5. The surface pressure–area per molecule (p–a) isotherms of the **SUB2** monolayer on water (pH 5.8) and 10 mM sugar (maltose, glucose, and sucrose) subphases.

subphase. Furthermore, the UV/Vis absorption spectra of the **SUB2** monolayer with a 10 mM sucrose subphase show that the absorption band arising from Tyr residues appeared at 278 nm on this subphase and remained unchanged at this wavelength over the whole compression range. The dynamic property of the **SUB2** monolayer is not affected by the sucrose from the subphase. Both the surface pressure–area isotherms and UV/Vis absorption spectra indicate that the **SUB2** monolayer does not bind with sucrose as efficiently as with maltose. Even as a simple and small library, the **SUB2** monolayer already exhibits receptor specificity.

In summary, the present study has shown that a novel approach, that of combinatorial surface chemistry, is possible and can become a very facile and powerful technique in the design and creation of artificial proteins and enzymes. While peptide–lipid libraries can be conveniently synthesized using solid phase peptide synthesis techniques, a lipid library can be treated as a single lipid for monolayer studies by Langmuir techniques. With the presence of a large amount of molecular diversity, the chances of finding a good combination of peptide moieties to form a desired proteinlike supramolecular structures should increase.

The synthesis of peptide lipid libraries and experimental conditions for the surface chemistry studies are available in the Supporting Information. Surface pressure–area isotherms of peptide lipid library samples on maltose subphase and the UV/Vis absorption spectra of the **SUB2** monolayer on the sucrose subphase are also included.

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Selenium-Bridged Gold(I) Complex Cations $[Au_{10}Se_4(dppm)_4]^{2+}$ and $[Au_{18}Se_8(dppe)_6]^{2+}$**

Dieter Fenske,* Timo Langetepe, Manfred M. Kappes, Oliver Hampe, and Patrick Weis

The syntheses and possible applications of polynuclear complexes are presently being investigated by several research groups.[1] For instance, transition metal complexes have been reported in which the metal centers are bridged by main group element atoms.[2, 3] Sulfur-bridged cluster complexes of Groups 9 and 10 are among the known examples. Selenium- or tellurium-bridged compounds have been more rare up till now. However, chalcogen-bridged complexes of the coinage metals are predicted to feature physical properties of special interest. In contrast to the great number of known copper and silver compounds, only a few homologous gold species have been synthesized. This can certainly be attributed in part to the more restricted coordination chemistry of monovalent gold.[4, 5] The complexes are often stabilized by protecting phosphane ligands, which suppress further reaction to binary chalcogenides. According to quantum-chemical investigations of PR_3-substituted Cu_2E cluster complexes (R = organic group; E = S, Se), the compounds that have been characterized up to now appear to be metastable in most cases.[6] Nevertheless, the formation of various interesting molecules containing gold atoms has been described recently.[7] Examples are $[\{(Ph_3P)Au\}_4S]$ (Laguna et al.),[7h] $[\{CSAu(PPh_3)\}_6]$ (Schmidbaur et al.),[7i] and $[Au_{12}S_8]^{4-}$ (Strähle et al.).[7c] However, only a few reports concern chalcogen-bridged gold complexes which are clad by bidentate phosphane ligands.[8]

Herein $[Au_{10}Se_4(dppm)_4]Br_2$ (**1**) and $[Au_{18}Se_8(dppe)_6]X_2$ (**2**; X = Cl: **2a**, X = (PF_6): **2b**, X = BPh_4: **2c**; dppm = bis(diphenylphosphanyl)methane, dppe = bis(diphenylphosphanyl)ethane), two ionic compounds possessing such ligands and displaying remarkable stability, are introduced. Yellow crystals of **1** result from the reaction of $[(AuBr)_2(dppm)]$ with $Se(SiMe_3)_2$ [Eq. (1)].

$$5[(AuBr)_2(dppm)] + 4Se(SiMe_3)_2 \longrightarrow \underset{\mathbf{1}}{[Au_{10}Se_4(dppm)_4]Br_2} + 8Me_3SiBr + dppm \quad (1)$$

The molecular structure of **1** was determined by single-crystal X-ray structure analysis.[9] In the cation of **1**, eight gold atoms (Au3–Au10) form an irregular, corrugated octagon which is centered by two further gold atoms (Au1, Au2; Figure 1). Thus, six Au_3 triangles and four Au_4 rectangles are

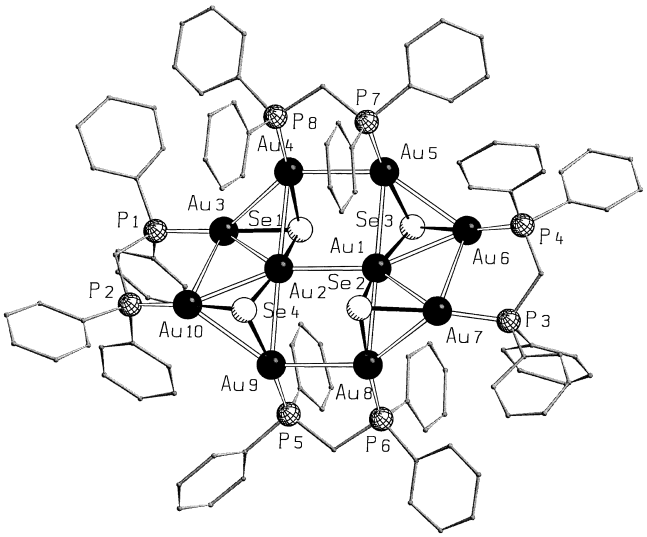

Figure 1. Structure of the cation of **1** in the crystal. Selected bond lengths [pm] and angles [°]: Au1–Au2 312.7(1), Au1–Au5 306.1(1), Au1–Se2 246.1(2), Au2–Au3 314.4(1), Au3–Au4 336.3(1), Au3–Au10, Au3–P1 227.8(6), Au3–Se1 242.9(2), Au4–Au5 309.6(1), Au4–Se1 242.3(2), Au4–P8 226.6(5), Se1–Se3 362.1(4); Au2-Se1-Au3 80.20(7), Au3-Au4-Au5 136.28(4), Au3-Au2-Au4 65.16(3), Au4-Au2-Au9 175.93(4), Se1-Au3-P1 168.5(2), Se1-Au4-P8 177.2(2), Se1-Au2-Se4 168.60(9).

generated. Four of the triangles (Au2, Au3, Au4; Au1, Au5, Au6; Au1, Au7, Au8; Au2, Au9, Au10) are μ_3-bridged by selenium atoms in such a way that the two neighboring Au_3 faces bind one selenium atom above and one below the average plane of the gold atoms. Selenium atoms which are positioned on the same side of the Au_{10} "plane" (Se1, Se3 and Se2, Se4) slightly approach each other through the Au_4 rectangle (Se1–Se3 362.1(4), Se2–Se 4372.4(4) pm). The peripheral gold atoms (Au3–Au10) additionally bind to one phosphorus atom of the dppm ligands. Each of these eight metal centers is therefore nearly linearly coordinated by one phosphorus and one selenium atom. In contrast, the inner gold atoms (Au1, Au2) bind almost linearly to two selenium

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