CHEMISTRY
A European Journal

Accepted Article

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Reaction Selectivity in On-Surface Chemistry by Surface Coverage Control - Alkyne Dimerization versus Alkyne Trimerization

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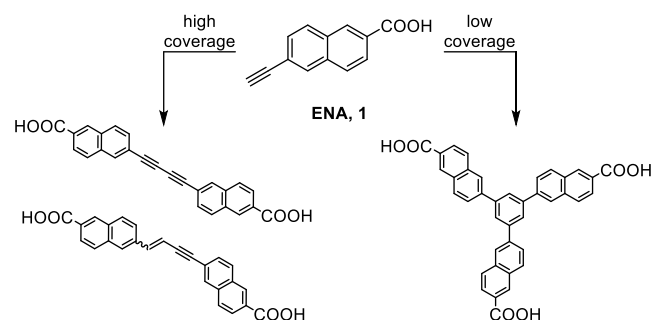
Abstract: This work reports the influence of molecular coverage in on-surface C–C-bond formation on reaction outcome. 6-Ethynyl-2-naphthoic acid (ENA) was chosen as organic component and Ag(111) as substrate. The alkyne moiety in ENA can either react via dimerization to ENA-dimers (Glaser coupling or hydroalkynylation) or cyclotrimerization to generate a benzene core as connecting moiety. Dimer formation is preferred at high surface coverage whereas trimerization is the major reaction pathway at low coverage. Mechanistic studies are provided.

Introduction

On-surface synthesis, by which well-defined covalent nanostructures can be constructed at noble metal surfaces, is an important and steadily growing research area in molecular nanotechnology.[1-7] Recently, various two dimensional reactions such as the Ullman coupling,[8-12] imine coupling,[13-15] dehydration of boronic acids,[16] carbene dimerization,[17,18] acylation,[19,20] cycloaddition,[21-24] decarboxylation[25] and dehydrogenation[10,26-29] have been disclosed. Whereas ligands can steer reaction outcome (selectivity) in solution phase transition metal-based catalysis, ligands are missing in on-surface chemistry and hence

such a tool is not available in this field. Therefore, the general question of how to steer/control reactivity in on-surface chemistry arises. An obvious route is to test different substrates with different reconstruction such as Au(111), Au(100), Ag(111), Cu(111), etc. This is indeed a general approach currently followed in this area. Also protective group strategies that are well established in solution phase chemistry have been developed.[30-32] In addition, additives have been used to supress a certain reaction[33,34] and preorganization by different self-assembled structures has been shown to influence the reactivity.[35,36] Alternatively, one can run the process at different coverages[37-39] or temperatures[40] and use these readily varied reaction parameters for product control. However, to date only few examples on reaction control based on surface coverage in two dimensional chemistry have been reported.[41]

Herein, we show that the surface coverage of 6-ethynyl-2-naphthoic acid (ENA **1**, its synthesis is described in the Supporting Information) steers reaction outcome on the Ag(111) substrate. Whereas at high coverage the alkyne dimerization is the preferred reaction path, at low coverage trimerization is the major reaction pathway (Scheme 1). Alkyne dimerizations (Glaser coupling[27,28] and hydroalkynylation[28]) and also the alkyne trimerization[24,28,42,43] leading to a benzene core (or rarely *cis*-enediyne) are known processes in on-surface chemistry. However, investigation of the dimerization/trimerization-selectivity as a function of surface coverage has not been reported to date. In addition, we try to shed light on the reaction mechanism by the investigation of model compounds that could represent intermediates in a stepwise hydroalkynylation/formal cycloaddition pathway.

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Scheme 1. Surface coverage as a reaction parameter to steer selectivity – alkyne dimerization versus alkyne trimerization.

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Results and Discussion

Based on the knowledge that thermal annealing of ENA at the Au(111) surface exclusively forms dimers by Glaser coupling,[41] and that the reactivity of ENA towards C–C-bond formation at Cu(111) is very low due to strong molecule-substrate interaction (SI-Figure 1), we decided to focus on the Ag(111) surface. The STM image recorded after depositing close to 1 monolayer (ML) of ENA onto the Ag(111) substrate revealed that a highly ordered self-assembly structure, controlled by hydrogen bonding between carboxyl groups and Van-der-Waals interactions among ENA molecules, is formed (Figure 1.a). Interestingly, we identified that the ENA appears in two different 2D-enantiomers[44] in the self-assembly structure, as indicated by the black and red chemical structures in the Figure°1.b zoom-in image.
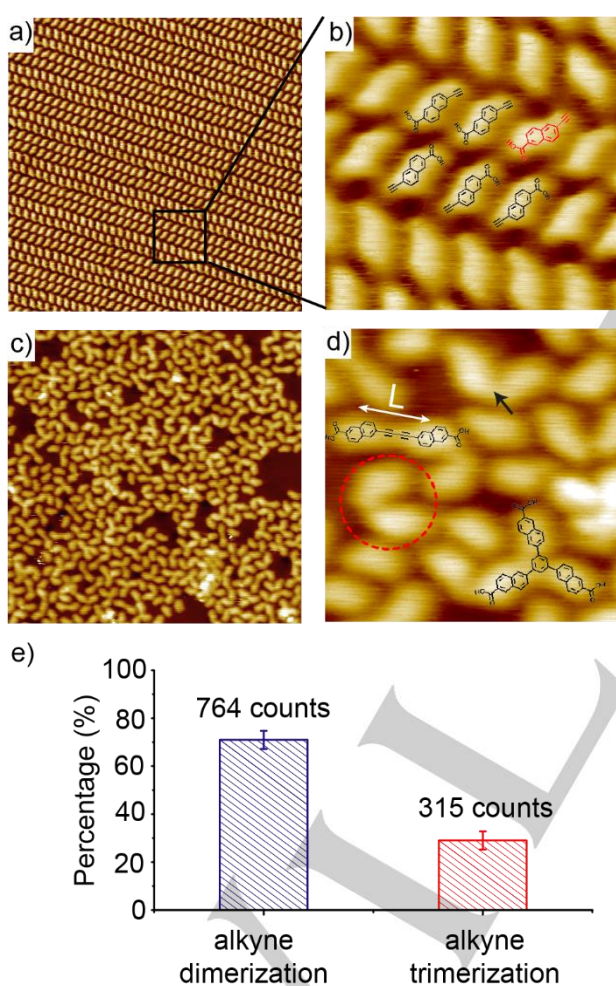

Figure 1. High coverage case. a) STM image of unreacted monomers in self-assembly structure (–0.1 V, 500 pA, 25 nm × 25 nm), and b) its high resolution image (3,6 nm × 3,6 nm). c) Overview STM image of the reaction products after annealing to 117 °C (–0.5 V, 10 pA, 21 nm × 21 nm). d) A high resolution image after annealing to 117 °C (4 nm × 4 nm). e) Products ratio between the dimers formed by Glaser coupling/hydroalkynylation and trimers formed by alkyne trimerization.

After subsequent annealing to 117 °C (all annealing treatments in our experiments were performed for 30 minutes and monitored by an IR detector), dimerization at the alkyne position (Glaser coupling and hydroalkynylation) forming 2D-diastereomers of the linear (32.8 ± 3%, Glaser coupling and *trans*-enyne) and bent (67.2 ± 3%, *cis*- and *gem*-enyne) dimers (Figure 1.c) were observed. The dimers are not forming an ordered structure, because they are mixed together with unreacted monomers and other not identified products. For example, we noted in addition to the alkyne activation also an activation of the carboxylic acid, which is reflected by the addition reaction of the acid to the triple bond. However, due to the difficulty in distinguishing carboxylic-addition linkages with the bent hydroalkynylation structures (Figure 1.d, red circle), this minor side reaction was included in the statistical analysis as counts for the bent dimers, since our focus lies on the alkyne dimerization and alkyne trimerization reactions. The majority of the dimeric structures were generated by an alkyne dimerization via hydroalkynylation (see Scheme 1), which is a known side reaction in on-surface Glaser coupling.[28] Along with these alkynyl dimerization reactions, also regioselective trimerization of alkyne moieties forming an arene core with 3 naphthyl substituents at positions 1, 3 and 5 occurred, together with rare *cis*-enediyne formation (corresponding to the Y-shape trimers).[24,28,43] In order to determine selectivity of the alkyne dimerization (major products) versus alkyne trimerization, we performed a statistical analysis on the product ratio between alkyne dimers and trimers of ENA and found ENA-dimers in (71 ± 3.8)%, while the trimer products were formed with a frequency of (29 ± 3.8)%, as shown in Figure 1.e. This statistic is based on 1079 product forming events.

To confirm successful covalent C–C bond formation in the dimeric Glaser coupling product we measured the center-to-center distance between the conjugated naphthyl groups in these structures, which led to a value of 1.01 ± 0.03 nm. This distance is much shorter than the theoretical value of 1.16 nm calculated for the gas phase ENA-dimer (SI-Figure 2). The shorter distance measured in the experiment is likely caused by a thermal deprotonation of the terminal carboxyl groups,[45] which should lead upon stronger interaction of the carboxyl functionalities with the Ag substrate to a bending of the ENA-dimer. This effect should shorten the measured distance between the two naphthyl moieties in the Glaser conjugated dimer, because the molecules are not lying flat at the surface. In order to further study this bending effect we performed DFT calculations of ENA-dimers at an Ag surface (Figure 2). The computational results agreed well with the experimental data. Whereas for the ENA-dimer with protonated acid functions a flat structure with a naphthyl center-to-center distance of 1.17 nm was calculated (Figure 2.a,b), the corresponding deprotonated ENA-dimer showed strong interaction between the carboxyl moieties and the surface. This in turn leads to a bending of the π-system (Figure 2.d,e). The images of such bended ENA-dimers will appear with narrower distances (images are recorded from the top). Therefore, we also calculated STM-images for both systems (Figure 2.c,f) and found for the protonated dimer a distance of 1.20 nm. For its doubly

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deprotonated congener the definition of the anchor points is ambiguous, and hence the experimental value of 1.01 nm has been included in the figure.
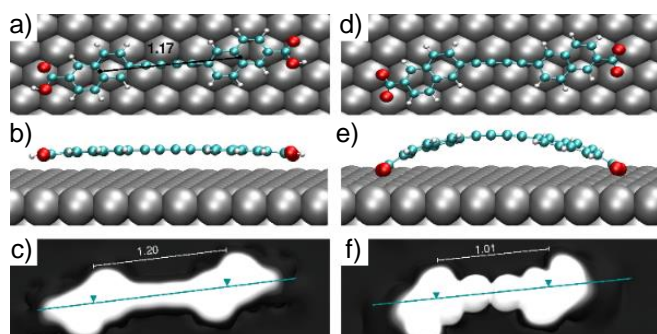

Figure 2. Optimized geometries of ethynyl-2-naphtoic acid (a,b) and activated ethynyl-2-naphthoate (d,e). Both are shown from the top (a,d) and from the side (b,e). In c) and f) the corresponding STM simulations are shown. Distances are given in nanometers.

It can clearly be seen that this distance is compatible with our simulation (for details on the calculation see SI). Furthermore, to support our assumption that deprotonation of the carboxylic acid groups occurred during thermal annealing, we ex situ synthesized the Glaser coupled ENA-dimer 6,6'-(1,4-buta-1,3-diynyl)-bis(2-naphthoic acid) and tested its self-assembly and annealing at Ag (111). After annealing to 113 °C we again found shortening of the naphthyl center-to-center distance in the ENA-dimers as noted after the on-surface dimerization of the ENA monomer. This further supports that activation of the carboxylic acid function at the annealing temperature is occurring (SI-Figure 4).

Since the alkyne trimerization product is also of interest for future applications towards synthesis of two dimensional polymers, we wondered whether it is possible to reverse selectivity, dimerization versus trimerization, towards trimer formation. Both reactions occur in the same temperature range and we believed that alkyne trimers are not formed from the dimeric products (bisalkynes or enynes). Therefore, we assumed that the coverage might determine selectivity. Likely, alkyne trimerization where three units are involved in the overall reaction needs more space to reach the reactive relative orientation of the alkynes as compared to the alkyne dimerization. At high coverage (~ 1 ML), ENA molecules will not have enough free space for trimerization, thus the ENA-dimers will be the dominant products (we ignore molecular desorption from the surface during the reaction). On the other hand, at low coverage (less than 0.5 ML), there will be much more free space for molecules to diffuse to eventually reach a reactive orientation for ENA-trimer formation.

To examine the assumed effect of coverage on product selectivity, we deposited ENA-molecules onto the Ag(111) surface at a coverage of around 0.3 ML (Figure 3.a). In the obtained self-assembly structure, we found that ENAs always appear as pairs via hydrogen bonding between –COOH groups. These pairs further aggregate via Van-der-Waals interactions to larger assembly structures (Figure 3.b). It is obvious that much more free space for molecules to adjust and react is present at

low coverage as compared to the high coverage assembly structures (compare with Figure 1.a,b). Indeed, after thermal annealing at 123 °C we found ENA-trimers as major reaction products (Figure 3.c). The ENA-trimers were formed as regioisomerically pure compounds (1,3,5-trisubstituted benzene
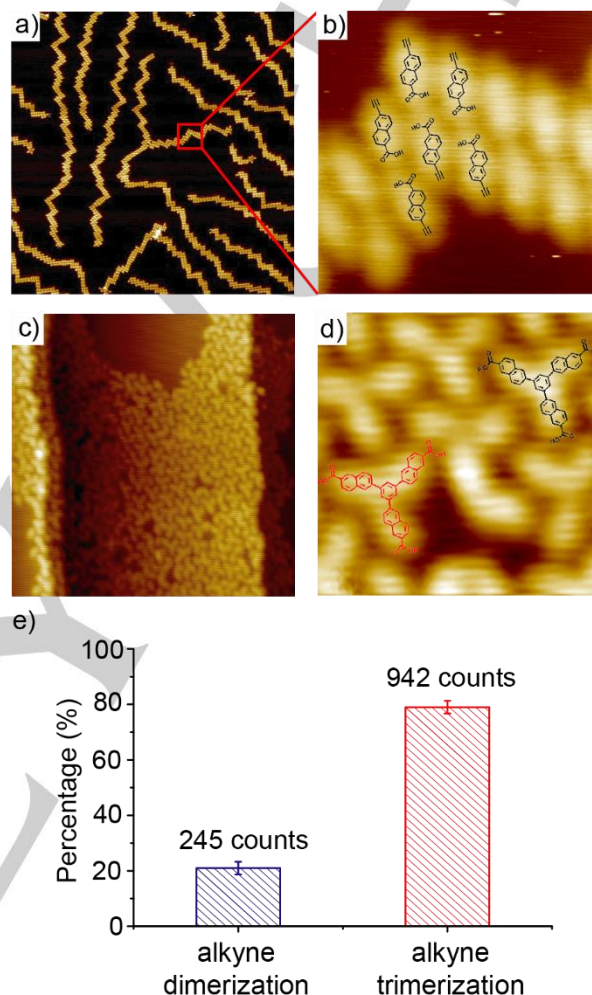

Figure 3. Low coverage case. a) STM image of the molecular monomers with sub-monolayer (< 0.5 ML) coverage (–1 V, 10 pA, 82 nm × 82 nm). b) High resolution image (4 nm × 4 nm). c) Overview STM images of the reaction products after annealing to 123 °C (–1 V, 50 pA, 25 nm × 25 nm). d) High-resolution image (4 nm × 4 nm) of the reaction product after annealing at 123 °C. e) The product ratio between dimers and trimers after reaction.

core, together with rarely *cis*-enediyne Y-shape trimers) as different 2D-diastereomers as indicated by the black and red chemical structures in Figure 3.d. In analogy to the above statistical analysis, the product ratio under low coverage conditions was estimated. We found that the ENA-trimers occurred at a frequency of $(79 \pm 2.3)\%$, while formation of ENA-dimers was largely suppressed $(21 \pm 2.3)\%$ (Figure 3.e). These results clearly show that trimerization is preferred over the Glaser coupling and hydroalkynylation if thermal annealing is conducted

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under low coverage conditions. Notably, previous studies showed that the trimerization of ENA did not occur on Au(111) at low and also at high coverage.[41]

To investigate if alkyne trimers are formed from the dimeric products (mainly enynes) or via trimerization of three individual monomers, three potential model dimers **2-4** (Figure 4) were synthesized *ex situ* (*via* hydroalkynylation for *trans*- and *gem*-enyne **2**, **4** or formal semihydrogenation for *cis*-enyne **3**; see SI for details on the synthesis of these dimers) and further analysed on Ag(111) in codeposition with ENA.
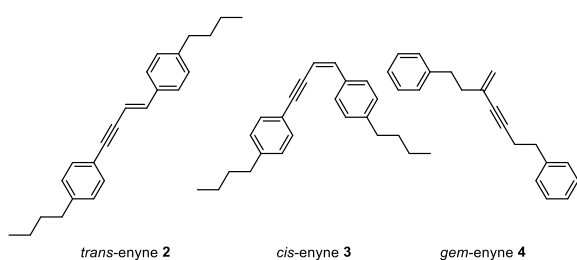
Figure 4. Model dimers **2-4** prepared.

Note that these model compounds must differ in structure from the "real" ENA-dimers in order to distinguish whether trimers derive from the reaction of these dimers with ENA. The ENA-trimers resulting from the corresponding ENA-dimers and via trimerization of ENA are not distinguishable. Of course the acid moieties after deprotonation lead to stronger interaction of the organic compounds with the substrates (see Figure 2). To increase Van-der-Waals interactions, the model compounds were therefore charged with alkyl or phenylalkyl groups.

The *ex situ* synthesized linear *trans*-enyne **2** was found to form purely separated self-assembly structures, coexisting with ENA self-assembly structures (as shown in Figure 5.a and its inset). After annealing up to 117 °C, no obvious dimerization or trimerization products were observed (only few were identified, as shown Figure 5.b). This indicates that the *trans*-enyne compounds **2** suppress the dimerization and also the trimerization of ENA. Further annealing up to 132 °C led to the formation of significant amounts of ENA dimers and trimers (Figure 5.c). However, trimers resulting from ENA addition to the *trans*-enyne **2**, that were unambiguously identified as Y-shape trimers (Figure 5.d), were rarely observed and most of the trimers derive from three ENA molecules.
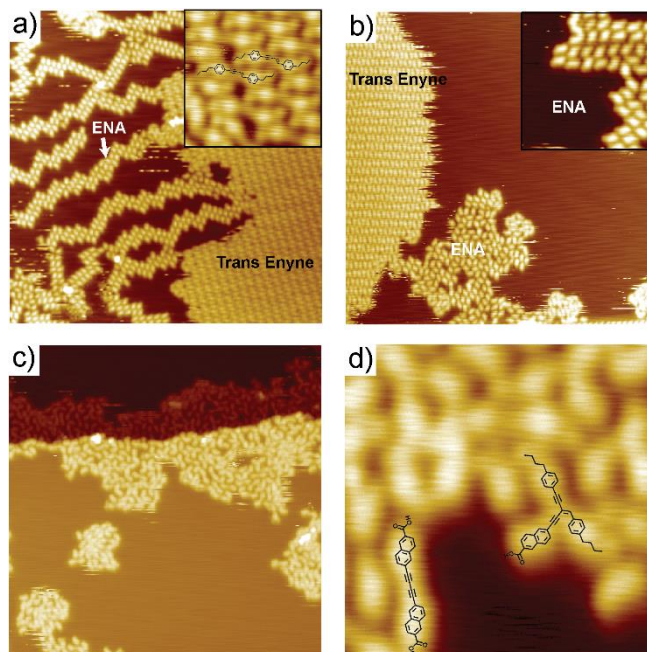

Figure 5. *Trans*-enyne **2** with ENA on Ag(111) surface. a) STM overview image (-1.1 V, 10 pA, 40 nm × 40 nm) of ENA and *trans*-enyne **2** co-adsorbed on Ag(111) surface and its high resolution image on trans-enyne (inset, -1.1 V, 10 pA, 4 nm × 4 nm). b) STM overview image (-1.1 V, 10 pA, 40 nm × 40 nm), and the high resolution image on ENAs (inset, -1.1 V, 10 pA, 4 nm × 4 nm), after annealing to 117 °C. c) and d) STM overview (c, -1.7 V, 10 pA, 40 nm × 40 nm) and high resolution (d, -1.7 V, 10 pA, 5 nm × 5 nm) images of the products after annealing to 132 °C.

In contrast, the *cis*-enyne **3** shows a clearly bent structure (Figure 6.a-inset) and forms a disordered self-assembly structure that separately coexists with the ENA self-assembly structures (Figure 6.a and b). After thermal annealing to 130 °C and 150 °C, it was found that similar to the *trans*-enyne case, the ENA reactions were suppressed by the *cis*-enynes **3** (Figure 6.c,d and e,f). Moreover, trimers resulting from the on-surface reaction of ENA with a *cis*-enyne moiety were not identified. Considering the structures of the ENA-trimers that are formed with excellent regiochemistry as 1,3,5-trisubstituted benzene derivatives, reaction of **2** or **3** with ENA would need additional rearrangement steps, since formal cycloaddtion would lead to the 1,2,4-trisubstituted arenes in both cases.
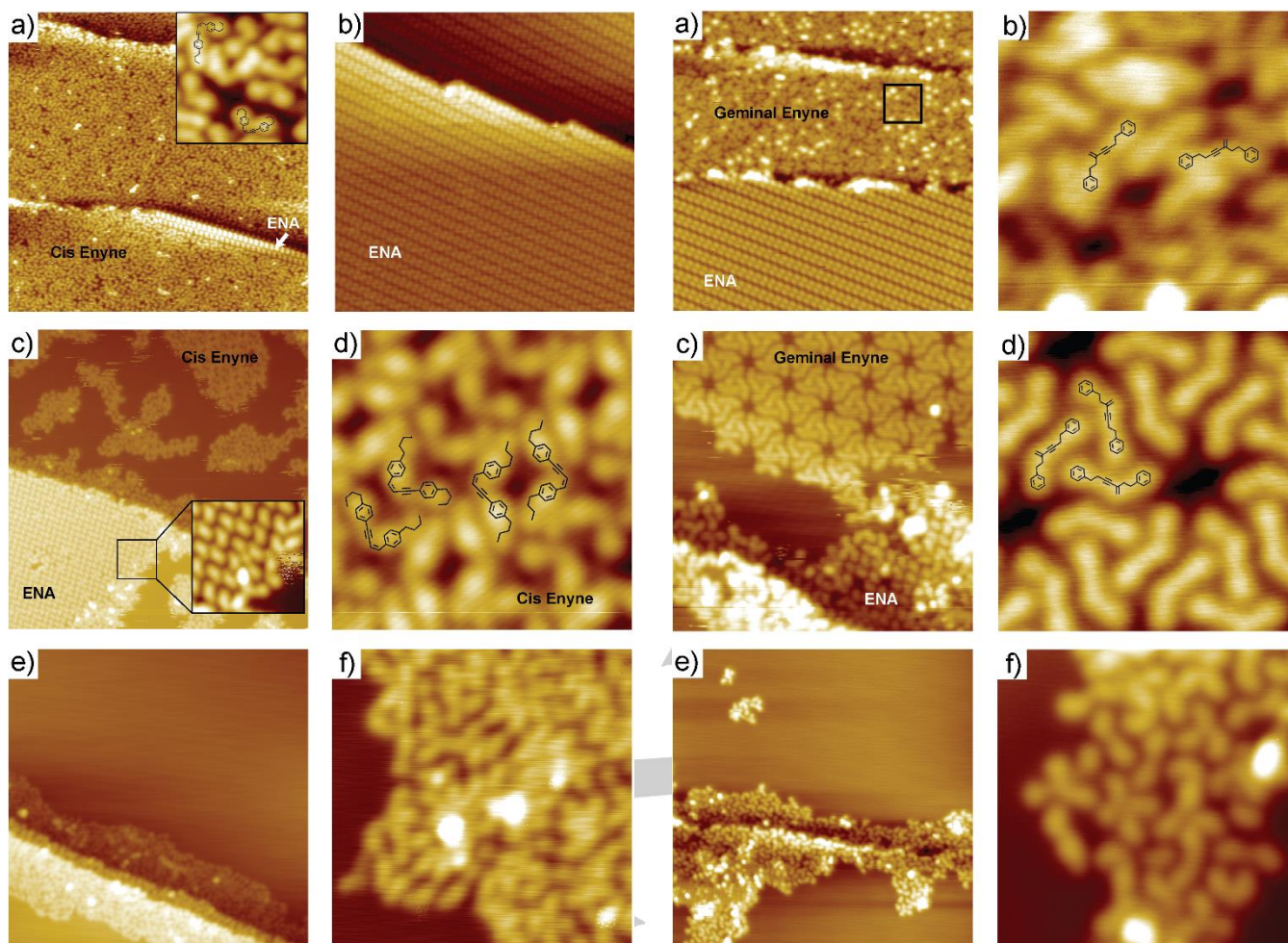
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Figure 6. *Cis*-enyne **3** with ENA on Ag(111) surface. a) and b), STM images of *cis*-enyne (a, -2 V, 10 pA, 40 nm × 40 nm, and its inset -0.5 V, 30 pA, 4 nm × 4 nm) and ENA (b, -1 V, 10 pA, 40 nm × 40 nm) in separated phases as co-adsorbed on Ag(111). c) and d), STM overview image (c, -2 V, 10 pA, 40 nm × 40 nm and c-inset image of ENA phase, -2 V, 10 pA, 5 nm × 5 nm) and zoom-in image of cis-enyne **3** (d, -2 V, 30 pA, 5 nm × 5 nm) after annealing to 130 °C. e) and f), STM images after annealing to 150 °C, an overview image (e, -1 V, 10 pA, 40 nm × 40 nm) and zoom-in image of products (f, -0.5 V, 30 pA, 10 nm × 10 nm).

Figure 7. *Gem*-enyne **4** with ENA on Ag(111) surface. a) STM image of *gem*-enyne and ENA co-adsorbed on Ag(111) (-1.5 V, 10 pA, 40 nm × 40 nm) and b) zoomed-in image of *gem*-enyne area (black square in a, -1.5 V, 20 pA, 5 nm × 5 nm). c) and d) STM images after annealing to 122 °C (c, -1.5 V, 10 pA, 20 nm × 20 nm) and zoomed-in image of *gem*-enyne area (d, -1 V, 30 pA, 5 nm × 5 nm). e) and f), STM images recorded after annealing to 145 °C (e, overview -1.7 V, 10 pA, 40 nm × 40 nm and f, Zoom-in on the products, -1.5 V, 10 pA, 8 nm × 8 nm).

To address that critical point, we also included the geminal substituted enyne **4** into this study that could lead in a cycloaddition-type on-surface reaction with ENA to the targeted 1,3,5-trisubstituted system. It was found that **4** also shows a bent structure, which forms a disordered self-assembly structure (separated from the ENA structures, as shown in Figure 7.a and b). After thermal annealing to 122 °C, it was surprisingly found that the molecules of the *gem*-enyne **4** form a chiral supramolecular assembly structure (Figure 7.c and d), while self-reactions ENA monomers can occasionally be observed (Figure 7.c). After further annealing up to 145 °C, no clear trimers derived from the reaction of ENA with a *gem*-enyne **4** could be identified (Figure 7.e and f).

Overall the experiments with the *cis*/*trans*/*gem*-enynes **2-4** with ENA reveal that alkyne trimers are likely not formed from the dimeric products (enynes) that are generated as intermediates in a sequential process. In the case of the *trans*-enyne, a reaction takes place after mixing of the different adsorbates, but the product cannot further react to form a benzene core. For *cis*- and *gem*-enyne, the formation of the ENA low coverage self-assembled structure is suppressed and thus the homotrimerization. This indicates that bent hydroalkynylation products interfere the benzene core formation. Accordingly, low coverages of the ENA suppress hydroalkynylation and enhance trimerization. However, since we did not observe other intermediates on surface we can currently not exclude formation of Ag-cyclopentadienes derived from two ENAs and an Ag-adatom as intermediates that further react with ENA to the observed trimers. Direct trimerization with three appropriately preoriented ENAs on surface is a likely process. This

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preorientation requires (a) more space for the molecules and (b) a less polluted surface which is supported by the improved results obtained at low surface coverage. Preorientation of three alkynes with C3-symmetry where substituents point away from each other might explain the observed 1,3,5-regioselectivity.

Conclusions

In summary, we have investigated on-surface reactivity of ENA at the Ag(111) surface upon varying the surface coverage of the organic molecule. We have found that at high coverage, ENA molecules mainly react via Glaser homocoupling or hydroalkynylation to ENA-dimers (71%), whereas at low surface coverage alkyne trimerization is the major reaction pathway (79%). These results show that surface coverage can be used as a readily variable reaction parameter to control/steer on-surface selectivity. This kind of reaction control has rarely been used in on-surface chemistry and it is recommended in future studies to vary along the metal substrate also the surface coverage. Mechanistic studies reveal that the trimers are likely not formed sequentially from enyne dimers with subsequent reaction with an ENA monomer.

Acknowledgements

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FULL PAPER

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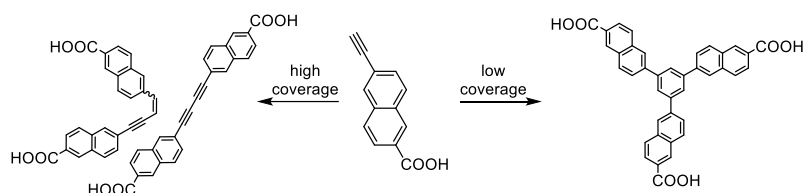
Coverage matters! This communication reports reaction control in on-surface chemistry as a function of surface coverage. 6-Ethynyl-2-naphthoic acid (ENA) reacts either via alkyne dimerization (hydrovinylation/alkyne homocoupling) or alkyne trimerization on Ag(111). It is shown that at high surface coverage dimers are formed in 71% selectivity whereas at low coverage trimerization is the favoured reaction pathway (79%).

Reaction Selectivity in On-Surface Chemistry by Surface Coverage Control - Alkyne Dimerization versus Alkyne Trimerization