Anchoring and Reacting On-Surface to Achieve Programmability

Xuechao Li, Haitao Ge, Renjie Xue, Minghui Wu, and Lifeng Chi*

ABSTRACT: On-surface synthesis has developed into a modern method to fabricate low-dimensional molecular nanostructures with atomic precision. It impresses the chemistry community mostly via its simplicity, selectivity, and programmability during the synthesis. However, an insufficient mechanistic understanding of on-surface reactions and the discriminations in methodologies block it out from the conventional cognition of reaction and catalysis, which inhibits the extensive implication of on-surface synthesis. In this Perspective, we summarize the empirical paradigms of conceptually appealing programmability in on-surface synthesis. We endeavor to deliver the message that the impressive programmability is related to chemical heterogeneity which can also be coded at the molecular level and deciphered by the catalytic surfaces in varying chemical environments as specific chemical selectivity. With the assistance of structure-sensitive techniques, it is possible to recognize the chemical heterogeneity on surfaces to provide insight into the programmable on-surface construction of molecular nanoarchitectures and to reshape the correlation between the mechanistic understanding in on-surface synthesis and conventional chemistry.

KEYWORDS: on-surface chemistry, on-surface synthesis, molecular nanostructures, STM, nc-AFM

With the development of ultraresolved scientific tools and a growing understanding of structure-function relations, it is demanding to fabricate macroscopic systems with atomic precision in the nanoscale.1 One of the promising prospects in nanotechnology is the bottom-up construction of macroscopic systems autonomously with self-recognized molecular units. This bottom-up method has greatly facilitated multidiscipline research interest2 and has become burgeoning in the field of surface science to produce supramolecular architectures through noncovalent synthesis that are capable of specific functions.3 Though comprehensive enough to conceive and engineer those well-structured molecular architectures, the noncovalent feature usually introduces structural volatility and poor electron correlation compared with synthesized organic polymers or natural two-dimensional materials. The soaring appeal for new carbon-based materials on-demand for modern society has triggered investigations to prepare artificial nanoarchitectures that are composed of covalently linked molecular units with structural rigidity and flexible electronic modulation. It has taken years for the idea to grow, and it has finally attracted extensive interest for on-surface chemistry (OSC) after the pioneering work from Grill et al. in 2007,4 which is also termed as on-surface synthesis (OSS). For the first time, they demonstrated that on-surface covalent architectures can be artificially programmed into one-dimensional nanowires or two-dimensional networks by changing the position of the reactive groups and controlling the reaction hierarchy by varying the type of reactive groups.

Utilizing diverse on-surface reactions, OSS is now capable of the production of solution-inaccessible molecular nanostructures and compounds on catalytic metal surfaces through thermal activation or on nonmetal surfaces with an alternative stimulus. It is now a proven powerful tool to realize hypothesized (or predicted) model structures with atomic precision, such as edge determined graphene nanoribbons (GNRs),5,6 nanographenes,7,8 individual polyyacylenes,9,10 and various new carbon allotropes in topology11–13 (see Figure 1). Combined with in situ, versatile microscopic and spectroscopic characterizations, intensively explored OSS has provided solid verification for the synthesized molecular structures as well as comprehensive insight into the structure-related novel properties and emergent physics such as π-magnetism8,14 and topological band engineering.15

The fast development of OSS has mostly impressed the chemistry community in terms of its simplicity, selectivity, and determinism16 to prepare on-surface nanoarchitectures.
through elementary on-surface reactions in a programmable manner. There have been many review articles presenting the diversity of OSS through a systematic description of the reaction categories, structures, and empirical reaction strategies. However, few of them have emphasized the mechanism behind the demonstrated order within OSS. The reaction mechanism of OSS is a big topic and can actually vary a lot from system to system depending on the chemical functionalities and the catalytic environment. In this Perspective, we reflect on recent advances in OSS and encompass the conceptually appealing paradigm of programmability in OSS. Inspired by the environment-specific chemical selectivity, we endeavor to deliver the message that the programmability in OSS is related to chemical heterogeneity which is coded at the molecular level and interpreted by the catalytic surfaces with a specific chemical environment. With the help of emergent structure-sensitive techniques like bond-resolved noncontact atomic force microscopy (BR-AFM), it is now becoming possible to recognize such chemical heterogeneities to provide insight into how to program the on-surface construction of novel nanoarchitectures and chemicals with predictability on the molecular level.

**PARADIGM OF PROGRAMMABLE OSS**

As a subdiscipline of surface chemistry, OSS inherits typical topics on adsorption, diffusion, and reactions on surfaces, while more emphasis is laid on the structure identification and physicochemical analysis of the products remaining on the surface. It is apparently different from the conventional realm of heterogeneous catalysis in which the products are released to the gaseous phase normally after the reaction. A variety of classical organic reactions, such as the Ullmann reaction, Glaser reaction, and Sonogashira reaction, have been examined on single crystal surfaces and present distinct differences in reaction mechanisms compared with the solution chemistry. The mechanistic difference still provides an intense topic of research which is out of the focus of this Perspective. The core issue of OSS is to construct new chemicals with desired structures and functions utilizing these elementary on-surface reactions. Constructive OSS can be divided into on-surface polymerization and on-surface intramolecular transformation, covering not only the creation of covalent connectivity among homogeneous or heterogeneous functional molecular units for nanoscale integration and fabrication but also chemical transformation within the molecule with incredible stereoselectivity. As the target structures are tuned to be more and more complex, the synergy and competition of multiple reactive sites or of different elementary reactions become essential and are actually achievable as programmability in OSS. It is therefore of interest to explore the origin of reaction order or reaction sequence in a microscopic prospect. Before touching that point, we have to first make clarifications on typical paradigms of programmable OSS: hierarchical on-surface reactions and templating growth.

**Hierarchical On-Surface Reactions**

Programmability is naturally related to hierarchy, and different on-surface reactions can be programmed in sequence to facilitate OSS as demonstrated in Figure 2a. The reaction sequence is usually defined by the threshold temperature of different on-surface reactions which is usually interpreted with the chemoselectivity of given chemical functionalities. The vast amount of successful syntheses of GNRs represents very good examples of how predictability can be achieved via hierarchical OSS. The rough profile is constructed by dehalogenative aryl–aryl coupling while the formation of GNRs is dominated by intramolecular cyclodehydrogenation afterward. The scenario of hierarchical OSS is simple in conception but quite difficult to harness. The competition and synergy of different reaction pathways in the real case are still insufficiently understood so far. Accordingly, the categories of on-surface reactions have to be sustainably enriched for constructing covalent interconnectivity with an enhanced flexibility in decision-making. It is worth noting that the hierarchy would also be established with merely one reaction type or chemical functionality which presents high regioselectivity and stereoselectivity in the molecular units, such as multistep on-surface cyclodehydrogenation. In this homogeneous situation, a discussion on the origin of hierarchy is well-deserved.

** Templating Growth**

Aside from reactions, the arrangement of molecular units would decide the order in another aspect. With the lowering of the translational degree of freedom (diffusivity) in a confined condition, the reaction barrier would decline, and the regioselectivity would steer according to the preorganized configurations. By a rational selection of monomer structure and tuning the subtle balance between molecule–molecule interactions and molecule–substrate interactions in the system, an organized molecular arrangement and selective intermolecular reactions can be achieved in a programmable manner. A wide applicable idea to achieve this, for example, is to put the molecules under natural surface constrictions like surface corrugations or terrace edges to introduce confined migration and steric preorganization for selective one-dimensional polymerization (see Figure 2b). Noncovalent interactions (including van der Waals interactions, hydrogen bonding, metal–organic coordination, metal–organic hybrid-
ization, or any combination of the aforementioned), which are the driving forces for molecular self-assembly, can also mimic such a confinement known as the template effect to lower the activation barrier and enhance chemical selectivity of recognized guest molecules. Moreover, it is also feasible to introduce extra directing groups in the precursor to prefunctionalize particular “templating” structures (see Figure 2c,d) and later transform them into target structures by activating the reacting groups in a hierarchical manner. For templates that are not involved in the products, they are, however, sometimes easily consumed during the reaction or hardly desorb from the surface which would limit the polymerization degree as a consequence. Nevertheless, the role of the on-surface residue could be much more complicated as demonstrated in some recent works which present enhanced chemical selectivity with the assistance of leaving groups such as halogens.

In spite of the two aforementioned typical paradigms of programmable OSS, another growing thought is to directly transform noncovalent self-assembly into stereospecific nanoarchitectures which has quite the potential to prepare largescale two-dimensional polymers. The challenge for this stereospecific transformation is that the morphology might collapse when covalent bonds form owing to the increase of bonding strength and decline of bonding length, which limited the idea mainly in solid/liquid implications allowing for defect healing. However, for most thermally activated on-surface reactions, the thermal and chemical stability of noncovalent structures cannot afford the temperature threshold of a reaction which often leads to limited selectivity and relatively small domain sizes after the reaction. Therefore, a feasible approach is to introduce order with an assembly strategy and then trigger the reaction with an alternative stimulus like light irradiation (as shown in Figure 2e) and electric field control.

Figure 2. Typical examples to fabricate molecular nanostructures in a programmable manner. (a) Hierarchical on-surface reactions for the sequential fabrication of nanostructures. Reproduced with permission from ref 27. Copyright 2012 Springer Nature. (b) Selective alkane polymerization under surface confinement for templating growth of one-dimensional structures. Reproduced with permission from ref 29. Copyright 2011 AAAS. (c) Noncovalent chiral templates for the preparation of chiral structures. Reproduced with permission from ref 32. Copyright 2016 American Chemical Society. (d) Metal–organic coordination template for the hierarchical construction of conjugated nanostructures. Reproduced with permission from ref 33. Copyright 2019 The Author(s) by CC-BY 4.0 https://creativecommons.org/licenses/by/4.0/. (e) Stereospecific transformation from noncovalent assembly into covalent frameworks through on-surface photopolymerization. Reproduced with permission from ref 38. Copyright 2021 Springer Nature.
by scanning probe microscopy. For certain kinds of reactions, such processes appear to be more efficient in introducing chemical selectivity than thermal activation. Since the reaction mechanism of alternative stimuli is different, herein, we will not discuss it any further.

Effect of Heterogeneity on Chemical Selectivity

Looking at the achieved on-surface programmability, the hierarchy is seriously related to chemical heterogeneity regarding the hierarchical chemical environment and various chemical functionalities. Despite the particularly successful story of artificially programming OSS, the conceptually appealing programmability is still limited in efficiency. On one hand, it would be time-consuming to pre-edit the precursors with distinguishable reactive groups. On the other hand, it is challenging to react the precursors with a controllable chemical selectivity of the functionalized chemical groups because the choice of precursors and the substrate makes a profound difference for the selectivity of a target reaction. An illustrative case is that of the archetypical bianthracene derivative 10,10′-dibromo-9,9′-bianthracene (DBBA), which undergoes the conventional route of on-surface dehalogenation and cyclodehydrogenation to yield armchair-GNRs. On Cu(111), (3,1)-chiral-GNRs are preferred through selective dehydrogenative coupling at 2,2′-sites DBBA in contrast to the conversant dehalogenative coupling at 10,10′-positions. Even with the same catalytic surface and reactive group, specific bonding behavior would also be unexpectedly differentiated according to various molecular lengths. Though inspired by specific chemical selectivity achieved in OSS, it is unfortunate that the influence of molecule–molecule interactions and molecule–substrate interactions in OSS is often vaguely described. The inadequate description makes it challenging to analyze the variables during the reactions and to draw general rules for the mentality of designing OSS based on the collective knowledge of chemistry.

In solution chemistry, chemical selectivity is often interpreted by the catalysts’ structure and adapted generally on particular chemical functionalities. However, except for flexible choices of catalysts (the underpinning substrates), it would become extraordinarily difficult to modify intermediate structures sterically and electronically and choose among competing reaction pathways. For example, Glaser-type acetylenic homocoupling is favored on silver surfaces while miscellaneous side reactions occur on gold and copper surfaces for uniaxial terminal alkynes which has still not been handled so far. The question therefore is in what way can the surface decide the reaction pathways for different surfaces and identical functionalities? Perhaps the molecules themselves can also help to make the decision. This raises the major consideration in this Perspective that chemical heterogeneity, regardless of different chemical functionalities and different surfaces, could be introduced among reactive functionalities through varying the molecular configurations and conformations upon adsorption. For 9,11-dibromonaphtho[1,2,3,4-ghi]perylene, the bromine atom (Br) bound to the C9 position is more easily detached under electron injection compared with Br bound to the C11 position because the Br atom at C9 is closer to the salt surface. Apart from the reactive functionalities, the remaining part of the molecule (backbones) would contribute to adsorption, diffusion, and intermolecular interactions.

Figure 3. Chemical heterogeneity-induced selectivity of identical chemical groups on surfaces. (a) Abnormal hopping behavior of DATP molecules on Cu(111) caused by the different sublattice binding affinities of two identical amino groups in a single DATP molecule and the consequential enhanced hydrogen-bonding affinity. (b) Programmable synthesis of nanographene on the rutile titania surface through multistep dehydrodimerizations (HF-zipping). Reproduced with permission from ref 47. Copyright 2019 AAAS. (c) Cascade dehydrogenation of n-alkanes on Cu(110) which causes the stereospecific formation of length-determined polyacetylene structures (polyene) epitaxially anchored on the copper ridges.
recognition and would even participate in the reaction as a competitor or in a hierarchical manner. We have demonstrated the unusual symmetry-breakdown behavior of 4,4″-diamino-p-terphenyl (DATP) molecules on the Cu(111) surface by lattice mismatch which contributes to asymmetric intermolecular recognition. The binding affinities of identical amino groups in a single DATP molecule vary with each other due to the epitaxial adsorption of the p-terphenyl backbone along the [112] direction which forces one of the amino groups above either the fcc site or hcp site as presented in Figure 3a. The site-induced variations in precursor adsorption may be minor under thermal fluctuation, but they inspire us to inspect molecular behavior with regard to their chemical nature. Considering the relative homogeneity of the surface, the chemical selectivity and the reaction hierarchy could also be coded at the molecular level and interpreted by the catalytic surface. This steric heterogeneity may also account for multistep elimination reactions as frequently observed in selective cyclodehydrogenation and defluorination “zipping” reactions that proceed in a cascade manner (Figure 3b).

### EXPERIMENTAL IDENTIFICATION OF CHEMICAL HETEROGENEITY

As stated, the chemical heterogeneity of anchoring molecules can be realized by their configurational and conformational details on surfaces. Conventional STM imaging, though useful for the identification of adsorption sites and packing periodicity, is only sensitive to frontier molecular orbitals near the Fermi level. It is not straightforward for STM alone to provide this detailed information for analyzing on-surface reactions. A typical solution applied in OSS is characteristic of capturing thermodynamically stable states to complete the complicated reaction puzzles with the assistance of theoretical calculations. Nevertheless, the experimental accuracy of our description on the chemicals and intermediates together with the capability to capture these states remarkably defines the...
confidence of the interpreted reaction mechanism. Recent advances in noncontact AFM with high-sensitivity Q-plus sensors and CO-tip functionalization bring a brand-new solution which can directly characterize the geometric details of a single molecule with bond-resolved resolution. This new technique allows the identification of the exact chemical structure and configurations of not only products and byproducts but also transient and metastable intermediate states dissipated on surfaces, revealing the steric information between the molecule and the catalysts which is more understandable by the chemistry community.

With the help of structure-sensitive characterizations, steric information including molecular conformations and adsorption configurations can support a more accurate model analysis in which the chemical selectivity on surfaces is converged into a determined reaction sequence and occurrence of particular intermediate structures severely. This is well-illustrated by our recent work which directly transform a single n-alkane molecule into the corresponding all-trans conjugated polyene molecule with extremely high stereospecificity as shown in Figure 3c. By scrutinizing the adsorption configuration before and after the transformation with BR-AFM, we found that the stereospecific transformation is actually derived from epitaxial adsorption between the alkenyl group and the underpinning Cu(110) ridges. The elimination of each hydrogen atom in the methyl and methylene group opens the reaction route of the next elimination step of the neighboring methylene, acting in a domino-like manner. Moreover, n-alkane molecules would adopt different adsorption configurations (tilt-on or flat-on geometry) according to their assembly restricted adsorption on a ridge site or groove site. Compared with the groove sites, the ridge sites even present an enhanced catalytic performance ascribed to the declined distance between the carbon atoms and the catalytic copper row atoms. This is consistent with the morphological investigation that one-third of the alkane molecules transform in priority. The reliance between reactivity and the distance from the catalytic substrate implies the feasibility to steer the reaction sequence by introducing anchoring groups. For example, by introducing conjugated phenyl and naphthyl groups which chemisorbed on Cu(110), the anchoring effect of substituents remarkably pulls the alkyl chains downward to the surface and initiates alkane dehydrogenation from the substituent site rather than the terminal methylene groups. It is worth noting that molecular proximity to the surface is actually related to the variation in electronic interaction between the molecule and the catalytic substrate for steered chemical selectivity, which has not been quantitatively described so far.

CONCLUSIONS AND OUTLOOK

Though powerful enough, BR-AFM-based characterization lacks chemical specificity which is the advantage of conventional ensemble-averaging characterizations such as infrared spectroscopy (IR), Raman spectroscopy, electron energy loss spectroscopy (EELS), X-ray photoelectron spectroscopy (XPS), and X-ray standing wave analysis (XSW). The complementary chemical interpretation by these ensemble-averaging techniques is meant to become a thriving technique in on-surface synthesis to deepen the understanding of reaction mechanisms and eventually promote the precise fabrication as preliminarily demonstrated in Figure 4a. Before that, one has to consider the matching of different systems and the establishment of unaffected sample transfer routes. An even emphasis should be laid on the in situ integration of complementary characterizations overwhelming the resolution limit. Thanks to the fast development of near-field optics, tip-enhanced Raman spectroscopy (TERS) is now possible to be integrated into conventional scanning probe systems to extract valuable chemical information on surface adsorbed molecules and structural change with even submolecular resolution. Recently, chemical heterogeneity identification at the single-bond limit has also been reported beyond the AFM resolution (Figure 4bc). We believe that the instrumental development would inevitably benefit the on-surface investigation and provide additional chemical information to build a comprehensive reaction model.

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Notes

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**REFERENCES**

(1) Barth, J. V.; Costantini, G.; Kern, K. Engineering atomic and molecular nanostructures at surfaces. *Nature* 2005, 437 (7059), 671–679.

(2) Palma, C. A.; Cecchini, M.; Samori, P. Predicting self-assembly: from empirism to determinism. *Chem. Soc. Rev.* 2012, 41 (10), 3713–3730.

(3) Barth, J. V. Molecular architectonics on metal surfaces. *Annu. Rev. Phys. Chem.* 2007, 58, 375–407.

(4) Grill, L.; Dyer, M.; Lafferentz, L.; Person, M.; Peters, M. V.; Hecht, S. Nano-architectonics by covalent assembly of molecular building blocks. *Nat. Nanotechnol.* 2007, 2 (11), 687–691.

(5) Cai, J.; Ruffieux, P.; Jafar, R.; Bieri, M.; Braun, T.; Blankenburg, S.; Mooth, M.; Seitzsonen, A. P.; Saleh, M.; Feng, X.; Müllen, K.; Fasel, R. Atomically precise bottom-up fabrication of graphene nanoribbons. *Nature* 2010, 466 (7305), 470–473.

(6) Ruffieux, P.; Wang, S.; Yang, B.; Sánchez-Sánchez, C.; Liu, J.; Dienel, T.; Talirz, L.; Shinde, P.; Pignedoli, C.; Passerone, D.; Dumslafl, T.; Feng, X.; Müllen, K.; Fasel, R. On-surface synthesis of graphene nanoribbons with zigzag edge topology. *Nature* 2016, 531 (7595), 489–492.

(7) Zhong, Q.; Hu, Y.; Niu, K.; Zhang, H.; Yang, B.; Ebeling, D.; Tschakert, J.; Cheng, T.; Schirmeisen, A.; Natori, A.; Müllen, K.; Chi, L. Benzofused perylenes or double helicenes? Different cyclo-[18]carbon. *Nano-architectonics by covalent assembly of molecular carbon allotropes.* *JACS Au* pubs.acs.org/jacsau https://doi.org/10.1021/jacsau.1c00397

(8) Mishra, S.; Beyer, D.; Eime, K.; Kuzelieke, S.; Berger, R.; Groning, O.; Pignedoli, C. A.; Mullen, K.; Lijjeroth, P.; Ruffieux, P.; Feng, X.; Fasel, R. Topological frustration induces unconventional magnetism in a nanographene. *Nat. Nanotechnol.* 2020, 15 (1), 22–28.

(9) Wang, S.; Sun, Q.; Groning, O.; Widmer, R.; Pignedoli, C. A.; Cai, L.; Yu, X.; Yuan, B.; Li, C.; Ju, H.; Zhu, J.; Ruffieux, P.; Fasel, R.; Xu, W. On-surface synthesis and characterization of individual polycatenane chains. *Nat. Chem.* 2019, 11 (10), 924–930.

(10) Li, X.; Niu, K.; Zhang, J.; Yu, X.; Zhang, H.; Wang, Y.; Guo, Q.; Wang, P.; Li, F.; Hao, Z.; Xu, C.; Tang, Y.; Xu, Z.; Lu, S.; Liu, P.; Xue, G.; Wei, Y.; Chi, L. Direct transformation of n-alkane into all-trans conjugated polyethylene via cascade dehydrogenation. *Nat. Sci. Rev.* 2021, 8 (9), 20893.

(11) Kaiser, K.; Scriven, L. M.; Schulz, F.; Gavel, P.; Gross, L.; Anderson, H. L. An sp-hybridized molecular carbon allotrope, cyclo[18]carbon. *Science* 2019, 365 (6459), 1299–1301.

(12) Fan, Q.; Martin-Jimenez, D.; Ebeling, D.; Krug, C. K.; Brechmann, L.; Kohlmeier, C.; Hilt, G.; Hieringer, W.; Schirmeisen, A.; Gottfried, J. M. Nanoribbons with nonalternant topology from fusion of polypylene: carbon allotropes beyond graphene. *J. Am. Chem. Soc.* 2019, 141 (44), 17713–17720.

(13) Fan, Q.; Yan, L.; Tripp, M. W.; Krejci, O.; Dimosthenous, S.; Kachel, S. R.; Chen, M.; Foster, A. S.; Koert, U.; Lijjeroth, P.; Gottfried, J. M. Biphenylene network: A nonbenzenoid carbon allotrope. *Science* 2021, 372 (6544), 852–856.

(14) Cai, J.; Ruffieux, P.; Eime, K.; Ortiz, R.; Fernandez-Rossier, J.; Berger, R.; Groning, O.; Pignedoli, C. A.; Fasel, R.; Feng, X.; Ruffieux, P. Collective all-carbon magnetism in triangular dimers. *Angew. Chem., Int. Ed.* 2020, 59 (29), 12041–12047.

(15) Rizzo, D. J.; Veber, G.; Jiang, J.; McCurdy, R.; Cao, T.; Bronner, C.; Chen, T.; Louis, S. G.; Fischer, F. R.; Crommie, M. F. Inducing metallicity in graphene nanoribbons via zero-mode superlattices. *Science* 2020, 369 (6511), 1597–1603.

(16) Grill, L.; Hecht, S. Covalent on-surface polymerization. *Nat. Chem.* 2020, 12 (2), 115–130.
dimensional covalent organic frameworks via solid–vapor interface reactions. J. Am. Chem. Soc. 2013, 135 (28), 10470–10474.
(38) Grossmann, L.; King, B. T.; Reichlmaier, S.; Hartmann, N.; Rosen, J.; Heckl, W. M.; Björk, J.; Lackinger, M. On-surface photopolymerization of two-dimensional polymers ordered on the mesoscale. Nat. Chem. 2021, 13 (8), 730–736.
(39) Zhan, G.; Cai, Z. F.; Martinez-Abadia, M.; Mateo-Alonso, A.; De Feyter, S. Real-time molecular-scale imaging of dynamic network switching between covalent organic frameworks. J. Am. Chem. Soc. 2020, 142 (13), 5964–5968.
(40) Li, L.; Mahaptra, S.; Liu, D.; Lu, Z.; Jiang, N. On-surface synthesis and molecular engineering of carbon-based nanoarchitectures. ACS Nano 2021, 15 (3), 3578–3585.
(41) Cai, J.; Ruffieux, P.; Jaafar, R.; Bieri, M.; Braun, T.; Blankenburg, S.; Muoth, M.; Seislonen, A. P.; Saleh, M.; Feng, X.; Mullen, K.; Fasel, R. Atomically precise bottom-up fabrication of graphene nanoribbons. Nature 2010, 466 (7305), 470–473.
(42) Han, P.; Akagi, K.; Federici Canova, F.; Mutoh, H.; Shiraki, S.; Iwaya, K.; Weiss, P. S.; Asao, N.; Hitsugui, T. Bottom-up graphene-nanoribbon fabrication reveals chiral edges and enantioselectivity. ACS Nano 2014, 8 (9), 9181–9187.
(43) Han, Y.; Wang, J.; Song, L.; Zheng, Y.; Li, Y.; Lin, H.; Li, Q.; Chi, L. A fundamental role of the molecular length in forming metal–organic hybrids of phenol derivatives on silver surfaces. J. Phys. Chem. Lett. 2021, 12 (7), 1869–1875.
(44) Li, X.; Zhang, H.; Chi, L. On-surface synthesis of graphyne-based nanostructures. Adv. Mater. 2019, 31 (42), e1804087.
(45) Pavlicek, N.; Majzik, Z.; Collazos, S.; Meyer, G.; Perez, D.; Guittain, E.; Pena, D.; Gross, L. Generation and characterization of a meta-aryne on Cu and NaCl surfaces. ACS Nano 2017, 11 (11), 10768–10773.
(46) Zhong, Q.; Ebeling, D.; Tschakert, J.; Gao, Y.; Bao, D.; Du, S.; Li, C.; Chi, L.; Schirmeisen, A. Symmetry breakdown of 4,4'-terphenyl on a Cu(111) surface by lattice mismatch. Nat. Commun. 2018, 9 (1), 3277.
(47) Kolmer, M.; Zuzak, R.; Steiner, A. K.; Zajac, L.; Engelund, M.; Godlewski, S.; Szymonski, M.; Amsharov, K. Fluorine-programmed nanozipping to tailored nanographenes on rutile TiO(2) surfaces. Science 2019, 363 (6422), 57–60.
(48) Giessibl, F. J.; Hembacher, S.; Bielefeldt, H.; Mannhart, J. Subatomic Features on the Silicon (111)−(7 × 7) Surface Observed by Atomic Force Microscopy. Science 2000, 289 (5478), 422–426.
(49) Riss, A.; Paz, A. P.; Wickenburg, S.; Tsai, H. Z.; De Oteyza, D. G.; Bradley, A. J.; Ugeda, M. M.; Gorman, P.; Jung, H. S.; Crommie, M. F.; Rubio, A.; Fischer, F. R. Imaging single-molecule reaction intermediates stabilized by surface dissipation and entropy. Nat. Chem. 2016, 8 (7), 678–83.
(50) Judd, C. J.; Junqueira, F. L. Q.; Haddow, S. L.; Champness, N. R.; Duncan, D. A.; Jones, R. G.; Saywell, A. Structural characterisation of molecular conformation and the incorporation of adatoms in an on-surface Ullmann-type reaction. Commun. Chem. 2020, 3 (1), 166.
(51) Mahaptra, S.; Li, L.; Schütz, J. F.; Jiang, N. Tip-enhanced Raman spectroscopy: Chemical analysis with nanoscale to angstrom scale resolution. J. Chem. Phys. 2020, 153 (1), 010902.
(52) Zhang, R.; Zhang, Y.; Dong, Z. C.; Jiang, S.; Zhang, C.; Chen, L. G.; Zhang, L.; Liao, Y.; Aizpurua, J.; Luo, Y.; Yang, J. L.; Hou, J. G. Chemical mapping of a single molecule by plasmon-enhanced Raman scattering. Nature 2013, 498 (7452), 82–86.
(53) Zhang, Y.; Yang, B.; Ghafoor, A.; Zhang, Y.; Zhang, Y.-F.; Wang, R.-P.; Yang, J.-L.; Luo, Y.; Dong, Z.-C.; Hou, J. G. Visually constructing the chemical structure of a single molecule by scanning Raman picroscopy. Natl. Sci. Rev. 2019, 6 (6), 1169–1175.
(54) Lee, J.; Crampton, K. T.; Tallarida, N.; Apkarian, V. A. Visualizing vibrational normal modes of a single molecule with atomically confined light. Nature 2019, 568 (7750), 78–82.
(55) Xu, J.; Zhu, X.; Tan, S.; Zhang, Y.; Li, B.; Tian, Y.; Shan, H.; Cui, X.; Zhao, A.; Dong, Z.; Yang, J.; Luo, Y.; Wang, B.; Hou, J. G. Determining structural and chemical heterogeneities of surface species at the single-bond limit. Science 2021, 371 (6531), 818–822.