On-Surface Synthesis of Five-Membered Carbon Ring from a Terminal Alkynyl Bromide: a [4+1] Annulation

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ABSTRACT: We report an on-surface synthesis of five-membered carbon ring *via* a [4+1] annulation reaction, starting from a simple terminal alkynyl bromide, 4-bromoethynyl-biphenyl, on Ag(110). The combination of scanning tunneling microscopy (STM), synchrotron radiation photoemission spectroscopy (SRPES), and density functional theory (DFT) calculations unravel the reaction pathway and mechanism. Three basic reaction steps are involved, successively including the formation of alkynyl–Ag–alkynyl bridged organometallic dimer, the generation of alkylidene carbene intermediate, and the final [4+1] annulation involving a hydrogen transfer step.

TOC GRAPHICS

KEYWORDS on-surface synthesis; cyclization; scanning tunneling microscopy; density functional theory calculation; synchrotron radiation photoemission spectroscopy

As the central core in many natural products and pharmaceuticals, such as furans, oxazoles, pyrroles, *etc.* the synthesis of five-membered carbocyclic and heterocyclic organic compounds *via* annulation reactions has attracted intensive attention from synthetic chemists over 130 years.^{1,2} The classical synthetic method is based on [3+2] cycloaddition reactions.^{3,4} In contrast, because of the immediate availability of the preliminary materials and more concise synthetic pathways, formal [4+1] annulation reactions have been developed in recent decades.^{1,5-7} Dipolar CO and CN based synthons have often served as the C1 sources in the [4+1] annulations in solution phase chemistry.

On-surface organic synthesis occurring under ultra-high vacuum (UHV) conditions has received rapid development over the last decade.⁸ Numerous low-dimensional nanostructures have been synthesized and characterized with the aid of atomic-resolution scanning probe microscopy (SPM).⁹ The most outstanding examples are graphene-based nanosheets and nanoribbons.^{10,11} The local electronic properties of these can be drastically modulated by controlled embedding of non-benzenoid ring topologies.^{10,12} A pentagon is the most popular and accessible nonbenzenoid ring, which can be constructed *via* intramolecular dehydrocyclization reaction on metal surfaces.^{10,12-14} The two-dimensional template effect of a surface promotes the intramolecular dehydrocyclization reactions often involved in the fabrication of planar nanographene-based structures.^{15,16}

Compared to intramolecular dehydrocyclization reactions,^{17,18} intermolecular annulation reactions for the synthesis of five-membered rings on surfaces are much more difficult, although they are desirable approaches to produce a versatile range of pentagons. In addition to not having the usual extrinsic catalyst typical in solution-based reactions, other challenges include limited molecular diffusivity on the surface and homocoupling side reactions.⁸ To date, the only

reported example for the construction of five-membered ring *via* on-surface intermolecular annulation approach is azide-alkyne [3+2] cycloaddition.¹⁹⁻²¹ However, to our knowledge, [4+1] annulation reaction has not been achieved at surfaces.

Scheme 1. Reaction pathway for the formation of five-membered carbon ring *via* [4+1] annulation on Ag(110), starting from BEBP 1. The intermediates and final products are denoted as 2, 3, 3', and 4.

Herein, we report the high-yield synthesis of a five-membered carbon ring from a simple terminal alkynyl bromide, *i.e.*, 4-bromoethynyl-biphenyl (BEBP; **1**; Scheme 1) on Ag(110) *via* a [4+1] annulation mechanism. The complete reaction pathway is shown in Scheme 1. The alkylidene carbene (in product **3**) generated after the dissociation of C–Ag–C linked organometallic dimer **2**, acts as the C1 source for the [4+1] annulation. On the other hand, a reversible hydrogen transfer from the *ortho* H atom in the phenyl group to the alkylidene carbene of **3** could easily take place (forming isomer **3'**; C4 source). Consequently, thermodynamically-stable five-membered carbocyclic product **4** is obtained after C–C coupling between **3** and **3'**. The whole reaction process and mechanism are investigated by the combination of STM, SRPES, and DFT calculations.

Figure 1. (a) High-resolution STM image of the sample pre-pared by deposition of BEBP **1** on Ag(110) held at 313 K. The two high-symmetry directions of the Ag(110) surface are indicated. The observed dark and bright dots are pointed by yellow and white arrows respectively. (b) DFT simulated STM image of the alkynyl–Ag–alkynyl organometallic dimer **2**. $U_{\text{bias}} = -2.0$ V. (c) Constant height STM image of **2** with a CO-functionalized tip recorded at 4.3 K. Tunneling parameters: (a) $U = -2.0$ V, $I = -0.2$ nA; (c) $U = 10$ mV.

Figure 1a displays the STM image recorded after depositing 0.7 ML BEBP **1** onto the Ag(110) surface held at 313 K (overview STM image is seen in Figure S1, Supporting Information). Dimeric species with a dot in their centers are formed on the sample, as observed in Figure 1a. These dimers orient along the high symmetric direction [001] of the Ag(110) surface, implying a strong molecule-surface interaction. According to many previous works,²²⁻²⁵ the dimers should be assigned to alkynyl–Ag–alkynyl linked organometallic structures formed after the C–Br dissociation of **1**. The interstitial Ag adatoms exhibit relatively dark features in the STM image, agreeing well with the DFT result (Figure 1b). The organometallic structure is further confirmed by STM images recorded at 4.3 K with CO-functionalized probes in the repulsive interaction regime (Figure 1c).²⁶ Under these conditions, the phenyl groups and interstitial Ag atom are

clearly recognized, whereas the triple bonds appear as minima in the recorded signal. C 1s SRPES shown in Figure 2a provides another evidence for the formation of **2**. In addition to the massive signal of the π -system of the molecular backbone with a binding energy of 285.1 eV, a small shoulder peak is observed at 283.9 eV, which is a fingerprint of the C–Ag bonds.^{27–30} The C–Ag peak amounts to 5% of the total C 1s intensity, in fair agreement with the ideal value of 7% (1/14) derived from the molecular structure of **2**.

Figure 2. (a) C 1s and (b) Br 3d SRPES of BEBP on the Ag(110) surface at 313 K and after annealing to 473 K.

On the other hand, the complete dissociation of C–Br bonds at 313 K is confirmed by Br 3d SRPES (Figure 2b) where the binding energy of Br 3d_{5/2} is located at 68.2 eV.^{30,31} The chemisorbed Br adatoms on Ag(110) can be identified as either bright or dark dots (with an approximate ratio of 1:1) in the STM image (white and yellow arrows, respectively, Figure 1a). The different brightness may be caused by the different adsorption sites (*e.g.*, short bridge site and hollow site).³²

Figure 3. (a) Overview STM image recorded after annealing the sample prepared at 313 K to 473 K. (b) High-resolution STM of the well-ordered island composed of asymmetric tetramer **4**, overlaid with the DFT optimized molecular models. (c) STM image of an area where intermediates **2**, **3**, and byproduct cumulene **5** can be observed at the edge of a large island of the main product **4**. (d) CO-tip STM image of **5** recorded at 4.3 K. (e) DFT-simulated STM image of the product **4** containing a five-membered carbon ring in its structure (red arrow). (f) CO-tip constant height STM image of **4** recorded at 4.3 K. Tunneling parameters: (a) $U = -1.8$ V, $I = -0.3$ nA; (b) $U = -1.7$ V, $I = -0.3$ nA; (c) $U = -1.4$ V, $I = -0.3$ nA; (d) $U = -0.8$ V, $I = -0.1$ nA; (f) $U = -10$ mV.

Interestingly, annealing the sample to 473 K leads to the formation of large-area well-ordered close-packed islands composed of tetramers, as shown in STM images in Figure 3a.

Corresponding C 1s SRPES data (Figure 2a) shows that the C–Ag signal disappears indicating

that the tetramer product should be a covalent species. Figure 3b displays a high-resolution STM image of an area of the well-ordered island of tetramer. The tetramer shows an unexpected asymmetric structure, including two relatively long arms and two short arms (white and blue arrows, respectively). To explore the detailed structure of the tetramer, we investigated the species located at the edge of the well-ordered island (Figure 3c). There are three observations to note. (1) A few organometallic dimers **2** still exist. (2) “Hockey stick” like dimers are observed, which are extremely similar to **3** (Scheme 1). In fact, **3** is the only reasonable structure generated from EBP featuring “hockey stick” morphology. (3) The symmetric byproduct tetramer **5** should be assigned to cumulene species *via* the coupling of two dimers **3** (Figure S2).³³ The high-resolution STM image of **5** recorded at 4.3 K (Figure 3d) further confirms the structure. Two-bright-dots feature in the center is the fingerprint for the formation of cumulene **5**. DFT simulated STM images of **3** and **5** and more discussion are shown in Figure S2.

However, **5** only appears as a minor byproduct. Thus, a different reaction mechanism from **3** to **4** may be expected for the formation of the main product (asymmetric tetramer **4** in Figure 3b). Upon H transfer from *ortho* C–H in phenyl to alkylidene carbene of **3** (forming **3'**, Scheme 1), another **3** can act as the C1 source and couple with **3'** *via* [4+1] annulation (forming asymmetric tetramer product **4**; Scheme 1). Hydrogen migrations over similar distances as those proposed here have been observed previously in other organic adsorbates at even lower temperatures,^{34,35} supporting the proposed scenario. The reaction scheme is corroborated by the fact that both the DFT optimized molecular model (overlay in Figure 3b) and the DFT-simulated STM image (Figure 3e) of product **4** match well with the experimental STM image of **4** (Figure 3b). The five-membered carbon ring is indicated by a red arrow in the simulated STM image in Figure 3e. Another defining feature is a segment of **4** with relatively bright contrast, indicated by yellow

arrows in both experimental and simulated STM images, thus a good agreement is achieved. Note that the simulated STM image has a higher resolution than that of experimental ones, thus the assignments of the abundant electronic states in the bright region is nicely resolved. In contrast, in the case of experiment, the lower resolution causes the bright region to extend over a wider range.

A constant height STM image of **4** recorded at 4.3 K with CO-functionalized probes in the repulsive regime was also obtained to further confirm the structure, as shown in Figure 3f. The slightly different appearance of experimental and calculated STM images relates to the fact that the calculations simulate a conventional STM mapping of the local density of states (LDOS), while the contrast in the bond-resolving experimental images with CO-functionalized probes is largely determined by the CO tilting imposed by the tip-sample interaction. The adsorption configuration of product **4** on Ag(110) is not flat due to steric repulsions, which is indeed the reason for the enhanced contrast marked with the yellow arrow in the constant current image (Figure 3b). Bond-resolving images of organic molecules with CO-functionalized probes, whether by STM or also in non-contact atomic force microscopy (nc-AFM) mode, never render such clear images with non-planar structures as they do with flat molecules.^{36,37} That is the reason why the bonding structure of some regions of **4** cannot be identified well in Figure 3f. However, the phenyl and alkynyl groups as well as the central bond (white arrow) of indene unit in the right part of **4** (on the basis of the yellow dashed line) can be recognized. Another high-resolution STM image of **4** obtained with an unknown molecule-tip is shown in Figure S3, where a perfect agreement between experiment and theoretical results are achieved.

Figure 4. (a) DFT calculated reaction pathways for the formation of main product **4** and byproduct cumulene **5**. (b) Reaction pathways for the formation of intermediate **3**. (c) Reaction pathways for alkynyl-alkynyl coupling.

These experimental observations demonstrate the selective synthesis of product **4** *via* [4+1] annulation on Ag(110) in >80% yield. Next, we explore the underlying reaction mechanism with DFT calculations. First, the competition between the formation of **4** and **5** is studied (Figure 4a).

As stated above, **5** is produced from the coupling between two dimers **3**, while **4** is the product of the coupling between **3** and **3'**. The energy change for H transfer from *ortho* C–H in phenyl to alkylidene carbene is +0.51 eV. This reaction step can thus be considered a reversible and spontaneous process at 473 K. Note that the reaction barrier for H transfer is not a critical limitation, because the adjacent biradical induced C–H activation typically has a low energy barrier (~1.1 eV) as reported previously.³⁸ Further, the formation of **4** *via* [4+1] annulation implies an energy gain of 5.35 eV (I), more than the 3.21 eV gained in the formation of cumulene **5** (II). A [4+1] annulation is thus the thermodynamically favored reaction pathway. Besides, although energy barriers for both pathways are negligible,^{33,36} the geometry factor of [4+1] annulation is less rigid than the formation of cumulene, where two alkylidene carbenes should align “head-to-head” to couple. Therefore, [4+1] annulation should also dominate kinetically.

The formation of intermediate **3** containing a alkylidene carbene (from **2**) with high regioselectivity on Ag(110) is also an interesting reaction step. We denote the terminal ethynylene C atom of EBP as C1 and the other ethynylene C atom as C2 (Figure 4b). When a radical ethynylene in another EBP attacks this EBP, it might couple with either the C1 or C2 atom, labelled as the C1 and C2 path in Figures 4c and 4b, respectively. Previous studies show that after the injection of Ag/Au adatom of **2** on Ag(111)/Au(111), Glaser couplings (alkynyl-alkynyl coupling, C1 path) take place.^{25,39} However, in the experiments on Ag(110), no Glaser coupling product has been observed. The mechanism is unraveled in Figures 4b and 4c. On Ag(110), the energy barrier for the dissociation of one C–Ag bond in **2** is calculated to be 1.28 eV. Then, after molecular diffusion on the surface, the radical-alkynyl addition reaction (C2 path) could take place^{40,41} after overcoming an energy barrier of 1.24 eV, forming intermediate **3**

with an alkylidene carbene (Figure 4b). In contrast, the energy barrier of direct Glaser coupling reaction (C1 path) is calculated to be 2.36 eV (Figure 4c), which is much higher than that of radical-alkynyl addition reaction C2 (additional calculations are shown in Figure S4).

It should be noted that the possibility of product **4** formed by intramolecular cyclization of product **5** can be excluded. In this reaction, the C–H bond activation of a phenyl moiety is necessary for the cyclization reaction. However, because all the radicals are neutralized after the C–C coupling between two intermediates **3** forming cumulene **5**, it is difficult for the C–H bond activation to occur at 473 K without an adjacent radical in the phenyl.^{38,42} To our knowledge, the reaction of cumulene forming a pentagon occurs only at a very high temperature of 650 K on metal surfaces, after the dehydrogenation of phenyl moieties (arXiv:2004.04918; unpublished results). In fact, as widely reported by previous studies, the cumulene structures are kinetically stable molecules on metal surfaces and tend to maintain the linear and planar structure at moderate temperatures.^{33,35,43} Any other more complicated mechanisms are not considered because they are neither supported by our experiments nor reported previously.

In conclusion, we synthesized five-membered carbon rings *via* a formal [4+1] annulation approach on a surface, starting from a simple terminal alkynyl bromide molecule, BEBP, on Ag(110). The reaction includes three basic steps. First, an alkynyl–Ag–alkynyl bridged organometallic dimer is generated after debromination of BEBP. Second, the radical-alkynyl addition reaction takes place, as the kinetically favorable pathway after the dissociation of the C–Ag bond. Finally, after a reversible H transfer step, the [4+1] annulation reaction thermodynamically dominates, forming a five-membered carbon ring. The Ag(110) surface plays two indispensable roles for the synthesis of **4**. First, the surface stabilizes active radical species, which often have a short lifetime in solution. Second, the appropriate interaction between

alkynyl and the Ag(110) surface inhibits the Glaser coupling but favors the radical-alkynyl addition. This finding provides a promising new approach to construct pentagon-embedded low-dimensional functional nanostructures on surfaces.

ASSOCIATED CONTENT

Supporting Information. Detailed descriptions of experimental and theoretical procedures, additional experimental and DFT simulated STM images. The following files are available free of charge (PDF).

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Notes

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