CHEMISTRY

Direct flipping dynamics and guantized enrichment of chirality at single-molecule resolution

Weilin Hu¹⁺, Zhiyun Zhang²⁺, Wan Xiong³⁺, Mingyao Li¹⁺, Yong Yan^{1,4}, Caiyao Yang¹, Qi Zou²*, Jing-Tao Lü³*, He Tian², Xuefeng Guo^{1,5}*

Chirality is an important aspect of nature, and numerous macroscopic methods have been developed to understand and control chirality. For the chiral tertiary amines, their flexible flipping process makes it possible to achieve high chiral controllability without bond formation and breaking. Here, we present a type of stable chiral singlemolecule devices formed by tertiary amines, using graphene-molecule-graphene single-molecule junctions. These single-molecule devices allow real-time, in situ, and long-time measurements of the flipping process of an individual chiral nitrogen center with high temporal resolution. Temperature- and bias voltage-dependent experiments, along with theoretical investigations, revealed diverse chiral intermediates, indicating the regulation of the flipping dynamics by energy-related factors. Angle-dependent measurements further demonstrated efficient enrichment of chiral states using linearly polarized light by a symmetry-related factor. This approach offers a reliable means for understanding the chirality's origin, elucidating microscopic chirality regulation mechanisms, and aiding in the design of effective drugs.

INTRODUCTION

Chirality, one of the most important properties in the natural world (1-6), plays a notable role in many biofunctions (7) and other unconventional phenomena, such as chirality-induced spin selectivity (8, 9) and the Casimir effect (10, 11). Asymmetric chiral catalysis (12, 13) was honored with the Nobel Prize in Chemistry in 2001 and 2021. Subtle differences in chirality can lead to enormous changes in properties. For instance, the dextrorotatory isomer of thalidomide has sedative effects, whereas the levorotatory isomer causes teratogenicity (14). Accordingly, it is of critical importance to develop methods for modulating chirality and elucidating chiral mechanisms to enable the construction of functional systems (15). Polarized light is frequently used to enrich chirality in macroscopic synthesis experiments, such as chiral enrichment of axial chiral alkenes by circularly polarized light (16) and stereostructural regulation of azobenzene polymerization by linearly polarized light (LPL) via the Weigert effect (17). However, there remains a formidable challenge in understanding the detailed processes of chiral transitions and the microscopic mechanisms of chiral enrichment.

Single-molecule platforms represent a potential target for finding a solution to this challenge. Several techniques are available for

†These authors contributed equally to this work.



Copyright © 2024 Authors, some rights reserved; exclusive licensee American Association for the Advancement of Science. No claim to original U.S. Government Works. Distributed under a Creative Commons Attribution NonCommercial License 4.0 (CC BY-NC).

single-molecule detection including electrical methods (18), optical methods (19), mechanical methods (20), and nanopore methods (21). Electrical methods (22) are particularly attractive because of their compatibility, reliability, and flexibility. The high temporal resolution and label-free features of single-molecule electrical detection allow observations of a specific chiral state during configuration flipping. Two key characteristics of chirality provide the opportunity to ping. Two key characteristics of chirality provide the opportunity to regulate chirality in the single-molecule platform. First, the interaction distinction between molecules with different chiralities and the silicon substrate enlarges the differences in their relative energies (23). In addition to this dominant effect, parity violation arising from a weak Z force induces a minute intrinsic energy difference between enantiomers (about 10^{-11} J/mol) (24). Both characters imply that chirality can be modulated by changing the molecule's energy [by modificing the temperature (25) entired field (26) electrical field (26). modifying the temperature (25), optical field (26), electrical field (27), and so on]. Second, the distinct electrical dipole moments of chiral states can be coupled with the electrical vector of polarized light, which is parallel to the plane of polarization. Thus, chiral enrichment could be achieved by symmetry (28), such as by changing the plane of polarization in the LPL (29). The current work combines energy and symmetry regulations at graphene-molecule-graphene single-molecule junctions (GMG-SMJs) (Fig. 1A) (30) to show that (i) different chiral intermediates of tertiary amine are detected at GMG-SMJs with fast temporal resolution (~17 µs) at low temperature (~160 K), which is impossible at the macroscopic scale; (ii) molecular chirality can be regulated by changing the energy of the system (i.e., by modifying the temperature and voltage) to increase the pro-

RESULTS

Device fabrication and electrical characterization

direction of LPL) to enrich chirality.

GMG-SMJs were fabricated according to a previously reported procedure (22). Briefly, single-layer graphene was prepared on copper foils via chemical vapor deposition and transferred to silicon wafers

portion of energy-favored species; and (iii) molecular chirality can

be further regulated by manipulating the symmetry (i.e., polarization

¹Beijing National Laboratory for Molecular Sciences, National Biomedical Imaging Center, College of Chemistry and Molecular Engineering, Peking University, 292 Chengfu Road, Haidian District, Beijing 100871, P. R. China. ²Key Laboratory for Advanced Materials and Feringa Nobel Prize Scientist Joint Research Center, Frontiers Science Center for Materiobiology and Dynamic Chemistry, School of Chemistry and Molecular Engineering, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, P. R. China. ³School of Physics, Institute for Quantum Science and Engineering and Wuhan National High Magnetic Field Center, Huazhong University of Science and Technology, 1037 Luoyu Road, Wuhan 430074, P. R. China. ⁴Center for Molecular Systems and Organic Devices, Key Laboratory for Organic Electronics and Information Displays and Institute of Advanced Materials, Nanjing University of Posts and Telecommunications, Nanjing 210023, P. R. China. ⁵Center of Single-Molecule Sciences, Institute of Modern Optics, Frontiers Science Center for New Organic Matter, College of Electronic Information and Optical Engineering, Nankai University, 38 Tongyan Road, Jinnan District, Tianjin 300350, P. R. China.

^{*}Corresponding author. Email: guoxf@pku.edu.cn (X.G.); jtlu@hust.edu.cn (J.-T.L.); zougi@ecust.edu.cn (Q.Z.)



Fig. 1. Structure and characterization of single-molecule devices. (A) Schematic diagram of a WON-based single-molecule device, showing the planar and two bent structures. (B) Molecular structures of WON and HON. (C) Electrical properties at 300 K of the rejoined single-molecule devices by WON and HON, respectively, showing the current-voltage (*I-V*) curves before (black) and after connection of the molecules (purple for WON and orange for HON). (D) Optical demonstration of the connection in a WON-rejoined single-molecule device (inset shows enlarged image without background).

with the aid of poly(methylmethacrylate). Then, graphene strips were obtained by photolithography and covered with gold electrodes to produce graphene transistor arrays. Graphene point contacts were functionalized with carboxyl groups using dashed line lithography with the poly(methylmethacrylate) template and oxygen plasma etching (*31*). We designed and synthesized two dihydrodibenzo[*a,c*] phenazine-based molecules with amino end groups (WON and HON) (Fig. 1B), which were inserted into nanogapped graphene point electrodes with covalent amide bonds to construct stable GMG-SMJs. Notably, three methylene groups were introduced into each side of the molecular backbone to reduce the effects of molecule-electrode coupling (*32*). Further details about the molecular synthesis (figs. S1, S2, and S104 to S122) and device fabrication (figs. S3 and S4) are provided in the Supplementary Materials.

As a family of prototypical vibration-induced emission (VIE) compounds, various studies have been conducted on the transformation between the planar and bent states of WON and HON (the flipping of the nitrogen configuration) under illumination (33–39). The lone pair electrons of nitrogen can be regarded as a substituent, which constitutes the chiral tertiary amine and undergoes chiral flipping with the other three different groups on the nitrogen atom. Typically, vibration-induced flipping of nitrogen brings about the chirality difference; however, this process is too rapid to detect at the macroscopic scale. Therefore, WON and HON were integrated into the single-molecule platform to capture chiral states with high temporal resolution. The successful fabrication of GMG-SMJ was confirmed by testing whether a closed loop was formed after connecting the molecules between source and drain electrodes (Fig. 1C and figs. S5 and S6). Electrical signals of graphene and graphene oxide (fig. S7) were tested for comparison in the Supplementary Materials. In addition, we designed the control molecule without the nitrogen

centers, WON-control (fig. S8), and conducted corresponding control experiments (figs. S9 and S10). In addition, the inelastic electron tunneling spectroscopies of 20 WON-based GMG-SMJs showed the consistent characteristic vibration mode of the phenazine ring and the amide mode, which further demonstrated the successful connection (fig. S11). The effective connection of WON was also demonstrated using a self-built photoelectrical integrated characterization system (40). Single-molecule connection analysis in section S4 and high-resolution microscopic imaging of the device confirmed the single-molecule connection because only one bright spot was imaged between the graphene electrode arrays (Fig. 1D). Other optical demonstrations are shown in the Supplementary Materials (figs. S12 to S14).

Real-time electrical measurement and species attribution

Distinct stereostructures of a molecule lead to diverse electron distributions, which could contribute to differences in conductance according to the theory of molecular electronics (41). Therefore, to monitor the molecular structure in real time, we recorded changes in the conductance (current) using high-speed sampling by applying a constant source-drain bias voltage. Three conductive states (highest, middle, and lowest) were observed on WON-based GMG-SMJs while applying a constant bias voltage of 500 mV at 160 K (Fig. 2A). Control experiments using graphene and graphene oxide showed only a single conductance state (fig. S7), suggesting that the conductance changes on WON-based GMG-SMJs originate from molecules, rather than graphene or graphene oxide. Furthermore, we conducted similar experiments (figs. S9 and S10) using WON-control, which showed only one conductance state. These phenomena prove that the conductivity changes mainly result from changes in the phenazine ring. Two types of switching clearly occurred during the measurement: from the highest to middle and from middle to the lowest



Fig. 2. Electrical characterization and signal attribution of WON-based GMG-SMJs. (A) *I-t* curve of a WON-based GMG-SMJ at 160 K by applying a voltage of 500 mV. (B) Enlarged *I-t* curve and current distribution histograms of three conductance states after Gaussian fitting of *I-t* measurements. (C) Schematic structures attributed to the three conductance states identified in *I-t* curves (dihedral angles between benzene and phenanthrene are labeled). (D) Transmission spectra of three states. Downward arrows denote the dominate *p*-HOMOs of these states.

Fig. 2B). Given the possible changes in configuration of the tertiary amine molecules at 160 K, we attributed these three conduction states to ground-state configuration reversals caused by tertiary amine chiral flipping (Fig. 2C), with a vibration energy of $\sim 10^{-2}$ eV (on a scale of ~100 K) and a dwell time of about milliseconds, similar to the stereoelectronic effect reported before (41). Moreover, excited states from the electronic transitions of WON were not considered because of their ultrashort picosecond lifetime (34). The difference in the steric hindrances of the groups around the nitrogen atoms and the reduction in potential along the molecule under the transverse electric field diminish the molecular symmetry (42), which results in distinct conductance and energy between configurations. The resulting broken symmetries lead to three possible flipping states predicted by the theory: upward (W0), planar (W1), and downward (W2) (fig. S15). Here, W0 and W2 could be considered as two chiral states of WON. To accurately ascribe the conductance states to the corresponding flipping states, we performed transmission calculations. As shown in Fig. 2D, the perturbed highest occupied molecular orbital (p-HOMO) of W1 is more proximate to the graphene Fermi level than that of W2, and, thus, the W1 conductance is higher than the W2 conductance. Although the *p*-HOMO of W0 is the farthest to the Fermi level of graphene, it has the largest peak value, thus leading to the highest state. Consequently, these theoretical results show that the conductance sequence is W0 > W1 > W2. We also conducted the analogous

species analysis of HON and corresponding transmission spectra (fig. S16), which shows similar chiral configuration flipping (fig. S17).

The kinetics and thermodynamics of the chiral transition process were analyzed to confirm the species attributions based on the assumptions described above. Meanwhile, we tested the energy-based regulations (temperature and electric field) and symmetry-based regulation (polarization plane of LPL) of chiral states.

Energy regulation

To understand the energy-based regulations of chiral flipping, we investigated the dynamic transitions between enantiomers while changing the temperature and voltage. Five representative temperaturedependent I-t curves at 600 mV and voltage-dependent I-t curves at 160 K of a WON-based SMJ are presented in Fig. 3 [A (figs. S18 to S20) and B (figs. S21 and S22)] respectively. Specifically, Fig. 3A presents the real-time I-t curves, corresponding enlargements, and current distribution histograms from 100 to 160 K at 600 mV. To investigate the effect of different bias voltages, that is, the electric field strengths, on regulating the enantiomers, we performed realtime current measurements at different voltages from 10 to 600 mV at 160 K to produce the I-t curves, corresponding enlargements, and conductance-based histograms, as shown in Fig. 3B. Three distinct conductance states were clearly and reproducibly observed in the *I-t* curves, which are shown in red, orange, and blue, from high to low, respectively. At low voltages and temperatures, switching between the highest conductance state (W0) and the middle state (W1) was the dominant process, whereas the transformation from W1 to the lowest state (W2) gradually became clearer at higher temperatures and voltages. As shown in the column plot of the three states (Fig. 3C), as the temperature increased, W0 decreased, and the other states increased. The trend in the chiral states as a function of bias voltage shows similar rules, as shown in fig. S23. In addition, increasing energy, such as temperature and bias voltage, leads to faster switching between two enantiomers. In most cases, W1 is an inevitable intermediate along the transition pathway between W0 and W2. However, when the temperature and bias voltage were sufficiently high (such as 160 K and 600 mV, respectively), we occasionally observed direct transitions between W0 and W2. With the increase in temperature, the transition between these two chiral states gradually accelerates, and the planar intermediate disappears (fig. S20). Furthermore, we also conducted the room-temperature solution viscosity-dependent experiments at 300 K (figs. S24 and S25). The results showed that the viscosity obviously affected the transition between the two chiral states, similarly to the results of macroscopic experiments (43). With the increase in solution viscosity, the transition between the two chiral states gradually decreased.

We propose the concept of single-molecule enantiomeric ratio (SM-*er*) to measure the degree of chiral regulation on the single-molecule platform. The macroscopic enantiomeric ratio *er* refers to the ratio of one enantiomer relative to another (often regarded as the ensemble average among a large number of molecules). In the single-molecule device, only one molecule can be probed, and, therefore, it does not appropriately fit the concept of the macroscopic *er*. However, according to statistical thermodynamics, ensemble average is equal to time average. Therefore, the time-averaged statistics of a single molecule with different chiral configurations can be measured to estimate the single-molecule chirality changes. The relative proportions of different chiral states during the transition process can be defined as SM-*er*.



Downloaded from https://www.science.org at Peking University on September 17, 2024

Fig. 3. Effects of temperature and voltage on the nitrogen flipping dynamics in WON-based GMG-SMJs. (A) *I*-*t* curves, corresponding enlarged curves, and histograms at 100, 110, 120, 140, and 160 K with an applied voltage of 600 mV, respectively. **(B)** *I*-*t* curves, corresponding enlarged curves, and current distribution histograms at 10, 100, 150, 500, and 600 mV under 160 K. **(C)** Proportions of three conductance states at different temperatures. **(D)** Plots of the thermodynamic parameters with electricity-justified Van't Hoff equation fitting (error bars were calculated from data obtained from three devices). **(E)** Theoretical potential energy surface calculations of the flipping states of WON-based GMG-SMJs with the electrical field strength of 0.5 V/nm.

In the current case, the proportion (ratio) of W2 [P(W2)] relative to that of W0 [P(W0)] is considered as the SM-*er* according to the following formula:

SM - er = P(W2) / P(W0)

Only the ratio of W2 to W0 is considered to be meaningful to chirality here. Exceptionally, the whole structure is supposed to be

achiral when the planar W1 is completely occupied (the component proportions of W2 and W0 are zero), which shows that the concept of SM-*er* is no longer valid. We found that the SM-*er* increased with the rising temperature (fig. S26) and voltage (fig. S27). These results indicated that increasing the system energy (by increasing the temperature or voltage) tends to enrich the higher-energy chiral state. The equilibrium constant K (from W0 to W2) is determined at four

temperatures (in the range of 100 to 160 K) based on the ratio of the Gaussian fit-integrated peak areas in the *I*-t statistical histograms. The lifetime (τ) of each species is determined by single-exponential fitting of the time intervals in idealized I-t curves (fig. S28) and is used to compute the conversion rate constant $(k = 1/\tau)$ together with the activation energy (fig. S34). According to the justified Van't Hoff equation (detailed explanations are provided in section \$13.1; figs. \$29 to S32), it is possible to obtain the thermodynamic parameters [$\Delta H =$ 1.62 \pm 0.09 kcal/mol, ΔS = 5.36 \pm 0.33 cal/(mol·K), and ΔG = 0.76 ± 0.10 kcal/mol for W0 to W2] (Fig. 3D), whose orders of magnitude are consistent with the potential energy surface (Fig. 3E). Here, the flipping of the tertiary amine transforms the whole structure, including a dihydrodibenzo[*a*,*c*]phenazine system, which is not consistent with a simple flipping, such as NH₃ (44). The detected planar state is supposed to be the relaxation state of the whole structure after planarization, which is a relatively stable intermediate. Note that the relatively high barrier can be crossed with thermal energy under the assistance of the electrical field, and it is proposed that the electrical field plays an important role by decreasing the flipping barrier to a large extent in most cases (detailed explanations are presented in section S13.2; figs. S33 and S34). Analogous results are obtained from other repeated experiments on WON-based GMG-SMJs (figs. S18 to S22) and HON-based GMG-SMJs (figs. S71 and S72) under identical conditions, thus confirming the reproducibility of this analytical method. Overall, the energy-based methods relying on temperature and voltage are suitable for regulating molecular chirality according to the potential energy differences.

Symmetry regulation

Chirality regulation by symmetry manipulations represents another potential approach to achieving chirality enrichment even if the target enantiomer is not energy-favored. Here, "symmetry" refers to the matching relationships between the electric dipole moment of the molecule and the electric displacement vector of LPL at different angles. Both LPL and circularly polarized light have been used to achieve chiral control (45–48), which the latter is favored because of its simplicity and less depolarization. In general, randomly oriented particles tend to have some depolarization properties under LPL at the macroscopical scale (49). However, the depolarization caused by random orientation can be easily resolved on SMJs. In the devices used in this study, the orientation of the single molecule is constrained between two amide linkages, which promises the effective regulation by LPL.

A linear polarizer was placed on the light path between the light source (368 \pm 5 nm) and the sample chamber. LPL with a particular alignment of the polarization vector was generated by rotating the polarization direction (fig. S38). Symmetry-regulation (angle-dependent) experiments were conducted at 160 K and 500 mV. Note that the angle-dependent experiment is focused on the relative difference in how the LPL at different angles regulates chirality, which largely excludes the influence of external thermal effects. The ratio of the SM-*er* [*P*(W2)/*P*(W0)] under LPL to that in dark is defined as the enrichment factor ($\rho[\theta]$) according to the following formula:

$$\rho[\theta] = \frac{\mathrm{SM} - er_{\mathrm{LPL}}}{\mathrm{SM} - er_{\mathrm{Dark}}} = \frac{\left[P(\mathrm{W2})/P(\mathrm{W0})\right]_{\mathrm{LPL}}}{\left[P(\mathrm{W2})/P(\mathrm{W0})\right]_{\mathrm{Dark}}}$$

where θ denotes the polarization direction of LPL. Similarly, the whole structure is supposed to be achiral when the planar W1 is completely occupied (the component proportions of W2 and W0 are zero), which indicates that the concept of $\rho[\theta]$ is no longer valid. Here, $\rho[\theta]$ symbolizes the capacity of enriching the chirality by LPL as a function of the polarization plane angle. Specifically, we measured the changes of p as the polarization direction rotated from 0° to 180° (Fig. 4A shows the angles of 0°, 45°, and 90°, while the statistical conclusions and other angles are listed in figs. S39 to S46 and table S1). Here, θ reflects the relative angle between the light polarization plane and the direction of the linkage in the GMG-SMJ. As shown in Fig. 4B, W2 was more enriched under LPL with the polarization direction of 90° than at 0°. As the polarization direction changes from 0° to 90°, ρ increases, which is consistent with the circular results (LPL direction ranging from 0° to 360°). The highest change in the enrichment factors $\rho[\theta]$ at different polarization directions was ~16 times (3.65 at 90°/0.23 at 0°) for WON. We conducted repeated experiments and statistical analysis of the data spanning the entire duration using WON-based GMG-SMJs (figs. S47 to S70) and analogous experiments using HON (Fig. 4C, figs. S73 to S103, and table S2). The highest change in the enrichment factors $\rho[\theta]$ at different polarization directions was ~4 times (1.43 at 0°/0.33 at 90°) for HON. Similar results were obtained for these two molecules although the enrichment directions and enrichment degrees are different, which can be explained by two reasons: the chiral state attributions of both molecules and the different dipole moments under the electrical field (fig. S35). Here, ultraviolet light can excite WON to different vibrational excited states [VIE mechanisms (33) in fig. S37], and further relaxation results in different vibrational ground states in our electrical tests. The order of interaction between the dipole moments of different chiral states in WON and HON and polarized light is different. The ratio of the interactions between different chiral states of the molecule and LPL at different angles (Fig. 4, B and C) is defined as ρ_{ML} , which is thoroughly discussed in section S13.3 (figs. S35 to S37). There exists a good agreement between theoretical prediction and experimental results. Chiral enrichment with arbitrary directions by LPL suggests effective and quantized LPL regulations of enantiomers at the chiral SMJ.

DISCUSSION

This work demonstrates unprecedented regulations of molecular chirality through in situ flipping dynamics measurements at singlemolecule resolution. The flipping preference of the molecule in the special solid-state single-molecule device, which was fabricated through covalently integrating individual tertiary-amine molecules into graphene point contacts, contributes to the chirality of the junction. Two reliable methods have been developed to regulate the chiral enrichment at chiral SMJs: energy-based (relying on changes in temperature or voltage) and symmetry-based (using polarized light). In particular, LPL treatment leads to arbitrary and quantitative control of chiral enrichment, as confirmed by systematic angledependent experiments. The demonstrated success in controlling SM-er at the tertiary amine single-molecule platform provides a possibility to understand the origins of chirality formation and regulating chirality at the single-molecule level. Furthermore, this may expand the scope and potential applicability of chirality research to facilitate asymmetric synthesis, chiral biofunctionalization, and drug discovery.

SCIENCE ADVANCES | RESEARCH ARTICLE



Fig. 4. Angle dependence of LPL on the flipping dynamics of WON/HON-based GMG-SMJs (368 \pm 5 nm, 160 K). (A) *I*-*t* curves, corresponding enlarged curves, and current distribution histograms of a WON-based GMG-SMJ at polarization directions of 0°, 45°, and 90° (the results of the rest degrees are provided in figs. S39 to S46) when applying a voltage of 500 mV without and with polarized light. (B) Experimental: The three-dimensional (3D) distribution color map of enrichment factor $\rho[\theta]$ as a function of LPL angle (θ) in a WON-based GMG-SMJ, demonstrating the effect of chiral enrichment by LPL in the case of WON. Theoretical: The 3D distribution color map of enrichment factor $\rho[\theta]$ as a function of LPL angle (θ) in a WON-based GMG-SMJ, demonstrating the effect of chiral enrichment by LPL in the case of WON. Theoretical: The 3D distribution color map of enrichment factor $\rho[\theta]$ as a function of the LPL angle (θ) in an HON-based GMG-SMJ, demonstrating the effect of chiral enrichment by LPL in the case of HON. Theoretical: The 3D distribution color map of enrichment factor $\rho[\theta]$ as a function of the LPL angle (θ) in an HON-based GMG-SMJ, demonstrating the effect of chiral enrichment by LPL in the case of HON. Theoretical: The 3D distribution color map of enrichment factor $\rho[\theta]$ as a function of the LPL angle (θ) in an HON-based GMG-SMJ, demonstrating the effect of chiral enrichment by LPL in the case of HON. Theoretical: The 3D distribution color map of interaction ratio between light and different chiral states ρ_{ML} as a function of LPL angle (θ) in an HON-based GMG-SMJ.

MATERIALS AND METHODS

Molecular synthesis

The details of molecular synthesis are provided in the Supplementary Materials.

Device fabrication and molecular connection

Single-layer graphene was prepared on a 25-µm-thick copper film by chemical vapor deposition and transferred to the surface of a silicon wafer with a 300-nm-thick silicon oxide layer. To locate the graphene, gold marks (8-nm Cr/60-nm Au) were thermally deposited on the wafer. Then, reactive ion etching was applied to prepare graphene strips using a photolithographic mask. After patterning via photolithography, the electrode arrays (8-nm Cr/60-nm Au) were deposited by thermal evaporation. Last, the graphene transistor was etched using a dashed line lithographic technique of electron-beam lithography and reactive ion etching to obtain nanogapped graphene point contacts with carboxylic acid terminations.

WON/HON molecules were connected to the graphene gap following a dehydration reaction, where 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride and the prepared transistors were immersed in anhydrous pyridine ($\sim 10^{-4}$ M) for 48 hours in the dark under an argon atmosphere. The transistors were then removed and washed with distilled water and acetone at least three times.

Electrical characterization

The *I-V* curves were obtained using an Agilent 4155C semiconductor parameter system and a Karl Suss (PM5) manual probe station. The *I-t* curves were obtained using a vacuum cryogenic probe station (Lakeshore TTPX) featuring the Model 336 controller with the liquid nitrogen cooling system in a vacuum environment. The constant voltage was determined by the DC auxiliary output of the UHFLI lock-in amplifier, and a DL1211 amplifier was used to amplify the current signal. A high-speed acquisition card (NI-DAQ) was used to record the data at a rate of 57,600 Sa/s.

Optical characterization

The transistor was positioned in close contact with a Nikon Ni-E microscope equipped with a $\times 100$ objective lens, and the device was

excited via a stochastic optical reconstruction microscopy process with an electron-multiplying charge-coupled device with 50-ms exposure. The Advanced Research software was used to reconstruct and analyze images. A total of 3000 photos were taken by superhighresolution fluorescence microscopy with a 50-ms exposure and were reconstructed to obtain the single-molecule resolution photograph.

Theoretical calculations

First-principles calculations of the isolated molecules were performed using density functional theory as implemented in the Vienna ab initio simulation package (50, 51). The ion-electron interactions were described with the projector augmented wave method. A cutoff energy of 400 eV was used for the plane-wave basis set. The electron exchange-correlation effect was described using the generalized gradient approximation with the Perdew-Burke-Ernzerhof functional. All atoms were relaxed until the force was less than 0.02 eV/Å. The criterion for the total energy was set as 1×10^{-5} eV. The climbing image nudged elastic band method (52) was used to perform calculations and determine the minimum energy transformation pathways and energy barriers associated with various structures.

The transport device model comprised three parts, i.e., left electrode, central region, and right electrode. Both electrodes were semiinfinite graphene, and the central region consisted of H0, H1, H2, W0, W1, and W2. The transmission function was obtained via an ab initio nonequilibrium Green's function approach based on density functional theory using the TranSIESTA program (53, 54). The transmission spectra were obtained using a 10 by 10 by 1 *k*-point sampling.

Supplementary Materials

This PDF file includes: Sections S1 to S23 Figs. S1 to S122 Tables S1 and S2 References

REFERENCES AND NOTES

- P. Peluso, B. Chankvetadze, Recognition in the domain of molecular chirality: From noncovalent interactions to separation of enantiomers. *Chem. Rev.* **122**, 13235–13400 (2022).
- 2. J. R. Brandt, F. Salerno, M. J. Fuchter, The added value of small-molecule chirality in technological applications. *Nat. Rev. Chem.* **1**, 0045 (2017).
- 3. S. F. Mason, Origins of biomolecular handedness. Nature 311, 19–23 (1984).
- O. Stetsovych, M. Švec, J. Vacek, J. V. Chocholoušová, A. Jančařík, J. Rybáček, K. Kosmider, I. G. Stará, P. Jelínek, I. Starý, From helical to planar chirality by on-surface chemistry. *Nat. Chem.* 9, 213–218 (2017).
- D. Ayuso, O. Neufeld, A. F. Ordonez, P. Decleva, G. Lerner, O. Cohen, M. Ivanov, O. Smirnova, Synthetic chiral light for efficient control of chiral light–matter interaction. *Nat. Photonics* 13, 866–871 (2019).
- X. Duan, S. Kamin, F. Sterl, H. Giessen, N. Liu, Hydrogen-regulated chiral nanoplasmonics. Nano Lett. 16, 1462–1466 (2016).
- G. Lebreton, C. Géminard, F. Lapraz, S. Pyrpassopoulos, D. Cerezo, P. Spéder, E. M. Ostap, S. Noselli, Molecular to organismal chirality is induced by the conserved myosin 1d. *Science* 362, 949–952 (2018).
- Q. Qian, H. Ren, J. Zhou, Z. Wan, J. Zhou, X. Yan, J. Cai, P. Wang, B. Li, Z. Sofer, B. Li, X. Duan, X. Pan, Y. Huang, X. Duan, Chiral molecular intercalation superlattices. *Nature* 606, 902–908 (2022).
- Y.-H. Kim, Y. Zhai, H. Lu, X. Pan, C. Xiao, E. A. Gaulding, S. P. Harvey, J. J. Berry, Z. V. Vardeny, J. M. Luther, M. C. Beard, Chiral-induced spin selectivity enables a room-temperature spin light-emitting diode. *Science* **371**, 1129–1133 (2021).
- C. M. Wilson, G. Johansson, A. Pourkabirian, M. Simoen, J. R. Johansson, T. Duty, F. Nori, P. Delsing, Observation of the dynamical Casimir effect in a superconducting circuit. *Nature* **479**, 376–379 (2011).

- 11. D. A. R. Dalvit, Shaking photons out of the vacuum. Nature 479, 303–304 (2011).
- 12. D. W. C. MacMillan, The advent and development of organocatalysis. *Nature* **455**, 304–308 (2008).
- Y. Huang, A. M. Walji, C. H. Larsen, D. W. C. MacMillan, Enantioselective organo-cascade catalysis. J. Am. Chem. Soc. 127, 15051–15053 (2005).
- 14. M. E. Franks, G. R. Macpherson, W. D. Figg, Thalidomide. Lancet 363, 1802–1811 (2004).
- K. T. Barrett, A. J. Metrano, P. R. Rablen, S. J. Miller, Spontaneous transfer of chirality in an atropisomerically enriched two-axis system. *Nature* 509, 71–75 (2014).
- P. M. Huck Nina, F. Jager Wolter, B. de Lange, L. Feringa Ben, Dynamic control and amplification of molecular chirality by circular polarized light. *Science* 273, 1686–1688 (1996).
- J. S. Kang, N. Kim, T. Kim, M. Seo, B.-S. Kim, Circularly polarized light-driven supramolecular chirality. *Macromol. Rapid Commun.* 43, e2100649 (2022).
- M. Li, H. Fu, B. Wang, J. Cheng, W. Hu, B. Yin, P. Peng, S. Zhou, X. Gao, C. Jia, X. Guo, Dipole-modulated charge transport through pnp-type single-molecule junctions. J. Am. Chem. Soc. 144, 20797–20803 (2022).
- S. Subramanian, H.-Y. Wu, T. Constant, J. Xavier, F. Vollmer, Label-free optical singlemolecule micro- and nanosensors. *Adv. Mater.* 30, e1801246 (2018).
- A. Doerr, Single-molecule force analysis, unplugged. Nat. Methods 13, 970–971 (2016).
 Y.-L. Ying, Z.-Y. Li, Z.-L. Hu, J. Zhang, F.-N. Meng, C. Cao, Y.-T. Long, H. Tian, A time-resolved
- Y.-L. Ying, Z.-Y. Li, Z.-L. Hu, J. Zhang, F.-N. Meng, C. Cao, Y.-I. Long, H. Han, A time-resolved single-molecular train based on aerolysin nanopore. *Chem* 4, 1893–1901 (2018).
 Y. Li, C. Yang, X. Guo, Single-molecule electrical detection: A promising route toward the
- Y. Li, C. Yang, X. Guo, Single-molecule electrical detection: A promising route toward the fundamental limits of chemistry and life science. Acc. Chem. Res. 53, 159–169 (2020).
- L. Rodrigo, P. Pou, R. Martínez-Casado, A. J. Martínez-Galera, J. M. Gómez-Rodríguez, R. Pérez, Characterizing self-assembled molecular layers on weakly interacting substrates: The role of van der Waals and the chemical interactions. *Nano Futures* 2, 045002 (2018).
- P. Schwerdtfeger, T. Saue, J. N. P. van Stralen, L. Visscher, Relativistic second-order many-body and density-functional theory for the parity-violation contribution to the C-F stretching mode in CHFCIBr. *Phys. Rev. A* 71, 012103 (2005).
- N. Xin, J. Wang, C. Jia, Z. Liu, X. Zhang, C. Yu, M. Li, S. Wang, Y. Gong, H. Sun, G. Zhang, Z. Liu, G. Zhang, J. Liao, D. Zhang, X. Guo, Stereoelectronic effect-induced conductance switching in aromatic chain single-molecule junctions. *Nano Lett.* **17**, 856–861 (2017).
- B. J. Sussman, D. Townsend, M. Y. Ivanov, A. Stolow, Dynamic stark control of photochemical processes. *Science* **314**, 278–281 (2006).
- C. Li, Z. P. Wang, Y. Lu, X. Q. Liu, L. Wang, Conformation-based signal transfer and processing at the single-molecule level. *Nat. Nanotechnol.* 12, 1071–1076 (2017).
- A. F. Ordonez, O. Smirnova, Propensity rules in photoelectron circular dichroism in chiral molecules. II. General picture. *Phys. Rev. A* 99, 043417 (2019).
- V. M. Botnaryuk, L. V. Gorchak, V. N. Pleshka, V. Y. Rud, Y. V. Rud, Photosensitivity of InP/CdS heterostructures in linearly polarized light. *Sem. Ther.* **31**, 194–196 (1997).
- C. Jia, B. Ma, N. Xin, X. Guo, Carbon electrode-molecule junctions: A reliable platform for molecular electronics. Acc. Chem. Res. 48, 2565–2575 (2015).
- Y. Cao, S. Dong, S. Liu, L. He, L. Gan, X. Yu, M. L. Steigerwald, X. Wu, Z. Liu, X. Guo, Building high-throughput molecular junctions using indented graphene point contacts. *Angew. Chem. Int. Ed. Engl.* 51, 12228–12232 (2012).
- C. C. Jia, A. Migliore, N. Xin, S. Y. Huang, J. Y. Wang, Q. Yang, S. P. Wang, H. L. Chen, D. M. Wang, B. Y. Feng, Z. R. Liu, G. Y. Zhang, D. H. Qu, H. Tian, M. A. Ratner, H. Q. Xu, A. Nitzan, X. F. Guo, Covalently bonded single-molecule junctions with stable and reversible photoswitched conductivity. *Science* **352**, 1443–1445 (2016).
- Z. Zhang, W. Song, J. Su, H. Tian, Vibration-induced emission (VIE) of *N*,*N*⁻disubstituteddihydribenzo[*a*,*c*]phenazines: Fundamental understanding and emerging applications. *Adv. Funct. Mater.* **30**, 1902803 (2020).
- Q. Zou, X. Chen, Y. Zhou, X. Jin, Z. Zhang, J. Qiu, R. Wang, W. Hong, J. Su, D.-H. Qu, H. Tian, Photoconductance from the bent-to-planar photocycle between ground and excited states in single-molecule junctions. *J. Am. Chem. Soc.* **144**, 10042–10052 (2022).
- X. Jin, S. Li, L. Guo, J. Hua, D.-H. Qu, J. Su, Z. Zhang, H. Tian, Interplay of steric effects and aromaticity reversals to expand the structural/electronic responses of dihydrophenazines. J. Am. Chem. Soc. 144, 4883–4896 (2022).
- Z. Zhang, C.-L. Chen, Y.-A. Chen, Y.-C. Wei, J. Su, H. Tian, P.-T. Chou, Tuning the conformation and color of conjugated polyheterocyclic skeletons by installing ortho-methyl groups. *Angew. Chem. Int. Ed. Engl.* 57, 9880–9884 (2018).
- X. Li, C. Zhang, C. Wang, W. Ye, Q. Zhang, Z. Zhang, J. Su, Y. Chen, H. Tian, Modular synthesis of (C-10 to C-13)-substituted-9,14-diaryl-9,14-dihydrodibenzo[*a,c*]phenazines via a subsequent Buchwald–Bartwig amination and C–H amination strategy. *Chem. Commun.* 56, 2260–2263 (2020).
- W. Chen, C.-L. Chen, Z. Zhang, Y.-A. Chen, W.-C. Chao, J. Su, H. Tian, P.-T. Chou, Snapshotting the excited-state planarization of chemically locked *N*,*N*'-disubstituted dihydrodibenzo[*a*,*c*]phenazines. *J. Am. Chem. Soc.* **139**, 1636–1644 (2017).
- W. Song, W. Ye, L. Shi, J. Huang, Z. Zhang, J. Mei, J. Su, H. Tian, Smart molecular butterfly: An ultra-sensitive and range-tunable ratiometric thermometer based on dihydrophenazines. *Mater. Horiz.* 7, 615–623 (2020).

- C. Yang, Z. Liu, Y. Li, S. Zhou, C. Lu, Y. Guo, M. Ramirez, Q. Zhang, Y. Li, Z. Liu, K. N. Houk, D. Zhang, X. Guo, Electric field–catalyzed single-molecule Diels-Alder reaction dynamics. *Sci. Adv.* 7, eabf0689 (2021).
- L. Meng, N. Xin, J. Wang, J. Xu, S. Ren, Z. Yan, M. Zhang, C. Shen, G. Zhang, X. Guo, S. Meng, Atomically precise engineering of single-molecule stereoelectronic effect. *Angew. Chem. Int. Ed. Engl.* 60, 12274–12278 (2021).
- N. D. Lang, P. Avouris, Understanding the variation of the electrostatic potential along a biased molecular wire. *Nano Lett.* 3, 737–740 (2003).
- H. Wang, Y. Li, Y. Zhang, J. Mei, J. Su, A new strategy for achieving single-molecular white-light emission: Using vibration-induced emission (VIE) plus aggregation-induced emission (AIE) mechanisms as a two-pronged approach. *Chem. Commun.* 55, 1879–1882 (2019).
- O. Egorov, M. Rey, A. V. Nikitin, D. Viglaska, New ab initio potential energy surfaces for NH₃ constructed from explicitly correlated coupled-cluster methods. J. Phys. Chem. A **125**, 10568–10579 (2021).
- M. Neugebauer, P. Banzer, S. Nechayev, Emission of circularly polarized light by a linear dipole. Sci. Adv. 5, eaav7588 (2019).
- D. Zhu, W. Jiang, Z. Ma, J. Feng, X. Zhan, C. Lu, J. Liu, J. Liu, Y. Hu, D. Wang, Y. S. Zhao, J. Wang, Z. Wang, L. Jiang, Organic donor-acceptor heterojunctions for high performance circularly polarized light detection. *Nat. Commun.* 13, 3454 (2022).
- J. Xiong, Q. Yang, Y. Li, S.-T. Wu, Holo-imprinting polarization optics with a reflective liquid crystal hologram template. *Light Sci. Appl.* 11, 54 (2022).
- F. Mortaheb, K. Oberhofer, J. Riemensberger, F. Ristow, R. Kienberger, U. Heiz, H. Iglev, A. Kartouzian, Enantiospecific desorption triggered by circularly polarized light. *Angew. Chem. Int. Ed. Engl.* 58, 15685–15689 (2019).
- W. Sun, Z. Liu, G. Videen, Q. Fu, K. Muinonen, D. M. Winker, C. Lukashin, Z. Jin, B. Lin, J. Huang, For the depolarization of linearly polarized light by smoke particles. J. Quant. Spectrosc. Radiat. Transf. 122, 233–237 (2013).
- G. Kresse, J. Furthmüller, Efficiency of ab-initio total energy calculations for metals and semiconductors using a plane-wave basis set. *Comput. Mater. Sci.* 6, 15–50 (1996).
- G. Kresse, J. Furthmüller, Efficient iterative schemes for ab initio total-energy calculations using a plane-wave basis set. *Phys. Rev. B* 54, 11169–11186 (1996).
- G. Henkelman, B. P. Uberuaga, H. Jónsson, A climbing image nudged elastic band method for finding saddle points and minimum energy paths. J. Chem. Phys. 113, 9901–9904 (2000).
- J. M. Soler, E. Artacho, J. D. Gale, A. García, J. Junquera, P. Ordejón, D. Sánchez-Portal, The SIESTA method for ab initio order-N materials simulation. J. Phys.: Condens. Matter. 14, 2745–2779 (2002).

- M. Brandbyge, J.-L. Mozos, P. Ordejón, J. Taylor, K. Stokbro, Density-functional method for nonequilibrium electron transport. *Phys. Rev. B* 65, 165401 (2002).
- M. D. Bartholomä, A. R. Vortherms, S. Hillier, B. Ploier, J. Joyal, J. Babich, R. P. Doyle, J. Zubieta, Synthesis, cytotoxicity, and insight into the mode of action of Re(CO)₃ thymidine complexes. *ChemMedChem* 5, 1513–1529 (2010).
- C. Jia, J. Wang, C. Yao, Y. Cao, Y. Zhong, Z. Liu, Z. Liu, X. Guo, Conductance switching and mechanisms in single-molecule junctions. *Angew. Chem. Int. Ed.* 52, 8666–8670 (2013).
- T. Bohamud, M. Reutzel, A. Adamkiewicz, U. Höfer, M. Dürr, Electric-field-induced depolarization of Si–C bond leads to a strongly reduced barrier for alkyl-hopping on Si(001). J. Phys. Chem. C 124, 5270–5274 (2020).
- T. Shao, X. Wang, H. Dong, S. Liu, D. Duan, Y. Li, P. Song, H. Jiang, Z. Hou, C. Gao, Y. Xiong, A stacked plasmonic metamaterial with strong localized electric field enables highly efficient broadband light-driven CO₂ hydrogenation. *Adv. Mater.* **34**, 2202367 (2022).
- X.-Y. Xu, H. Guo, C. Zhao, Probing the electric field effect on the catalytic performance of Mn-doped graphene to CO oxidation. J. Phys. Chem. C 121, 27983–27991 (2017).

Acknowledgments

Funding: We acknowledge primary financial supports from the National Key R&D Program of China (2021YFA1200101 and 2022YFE0128700 to X.G.), the National Natural Science Foundation of China (21933001, 21227806, and 22150013 to X.G.; 21790361, 22335004, and 22175064 to Q.Z.; and 22273029 to J.-T.L.), Shanghai Municipal Sci. & Tech. Major Project (2018SHZDZX03 to Q.Z.), the Tencent Foundation through the XPLORER PRIZE (to X.G.), and the Natural Science Foundation of Beijing (2222009 to X.G.). Author contributions: X.G., H.T., and Q.Z. conceived and designed the experiments. W.H. and M.L. fabricated the devices and performed the device measurements. Z.Z. carried out the molecular synthesis. W.X. built and analyzed the theoretical model and performed the quantum transport calculations. X.G., H.T., J.-T.L., Q.Z., W.H., M.L., Z.Z., Y.Y., C.Y., and W.X. analyzed the data and wrote the paper. All the authors discussed the results and commented on the manuscript. **Competing interests:** The authors declare that they have no competing interests. **Data and materials availability:** All data needed to evaluate the conclusions in the paper are present in the paper and/or the Supplementary Materials.

Submitted 17 January 2024 Accepted 6 June 2024 Published 12 July 2024 10.1126/sciadv.ado1125