

Oriented Electric Field-Driven Cis-Azobenzene Selective Diborylation Reaction at the Single-Molecule Level

PA Sreelakshmi, Reetu Rani Mondal, Laust Rask, Susanne Leitherer,* Oscar Berlin Obel, Umar Rashid, Joseph M. Hamill, Kurt V. Mikkelsen, K. Geetharani,* and Veerabhadrrao Kaliginedi*



Cite This: <https://doi.org/10.1021/jacs.6c05830>



Read Online

ACCESS |



Metrics & More

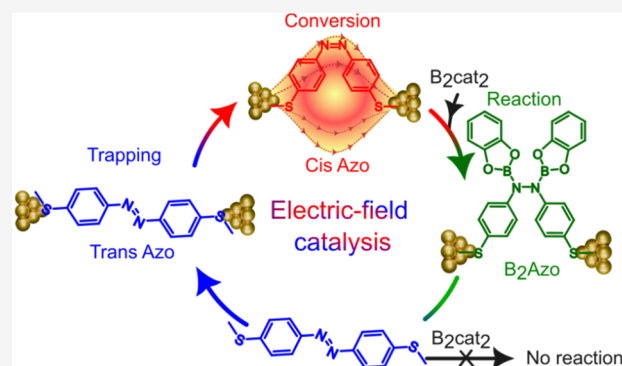


Article Recommendations



Supporting Information

ABSTRACT: The development of catalysts with a built-in electric field to catalyze and control complex chemical reactions under mild conditions with exceptional stereo and regioselectivity remains a key objective in synthetic chemistry. In this work, we demonstrate a novel approach in which the intrinsic electric field within a break junction nanocavity triggers and probes a substrate-selective, multistep cis-azobenzene diborylation reaction in the dark at the single-molecule level under ambient conditions. Our results combine the key aspects of electric field catalysis and substrate recognition to drive reactions in a nanoscale confined environment. The study further demonstrates how the reactivity landscape for the “N=N” bond functionalization and borylation reactions can be tuned by an oriented external electrical field present within a nanometallic junction, opening a new avenue in borylation chemistry. Furthermore, theoretical studies corroborate the experimental finding by revealing how the trans–cis-azobenzene isomerization energy landscape can be reshaped in the presence of an electric field to facilitate a cis-azobenzene selective diborylation reaction without the aid of a metal catalyst or external light irradiation.



INTRODUCTION

Molecular recognition is a cornerstone of biological function, governed by the complementary paradigms of induced fit and conformational selection, which together enable highly specific stereochemical interactions between biomolecules.¹ These principles have profoundly influenced synthetic chemistry as well, inspiring the design of stereoselective reactions and catalytic pathways capable of achieving high yield and purity.² Reaction strategies that emulate the organizational and dynamic features of biological machinery often prove to be the most efficient, echoing nature's ability to direct chemical transformations with remarkable precision. Chemists have long appreciated the importance of nanoconfinement effects^{3,4} and electrostatic field effects^{5–7} in enzymatic catalysis, where structurally restricted active sites create unique microenvironments that stabilize transition states and modulate reactivity.⁸ Developing synthetic analogues that replicate such substrate specificity and catalytic efficiency of enzymes remains an ongoing challenge.

In this direction, nanometallic cavities with a built-in electric field created by the break junction techniques have emerged as an analogue of enzymatic active sites, offering confined geometries capable of selective substrate recognition and catalysis.^{9–12} Although the break junction technique was initially discovered for single-molecular charge-transport studies, it is now a frontrunner in the field of electrostatic

catalysis.^{13,14} It allows a unique way of probing chemical reactions in real time with single-molecular sensitivity and high temporal resolution, outperforming any existing analytical techniques.^{9,14–16} Moreover, the oriented electric field present in the nanojunction is known as a smart, vectorial reagent capable of driving complex, multistep transformations that are otherwise inaccessible.^{17–22} Additionally, biological multi-enzyme assemblies, such as cytochrome P450, which selectively processes nitrogen- and sulfur-containing substrates,²³ and different transpeptidases with orthogonal substrate specificities,²⁴ highlight the power of sequential, substrate-tailored transformations. Mimicking such complexity at the nanoscale could greatly expand the synthetic capabilities of nanoconfined environments created by the break junction technique. However, the potential of the break junction technique in triggering and detecting an electric field-catalyzed multistep selective reaction has not been unveiled yet.

In this regard, borylation reactions are one of the important classes of reactions and are vital for producing a variety of key

Received: March 19, 2026

Revised: May 8, 2026

Accepted: May 11, 2026

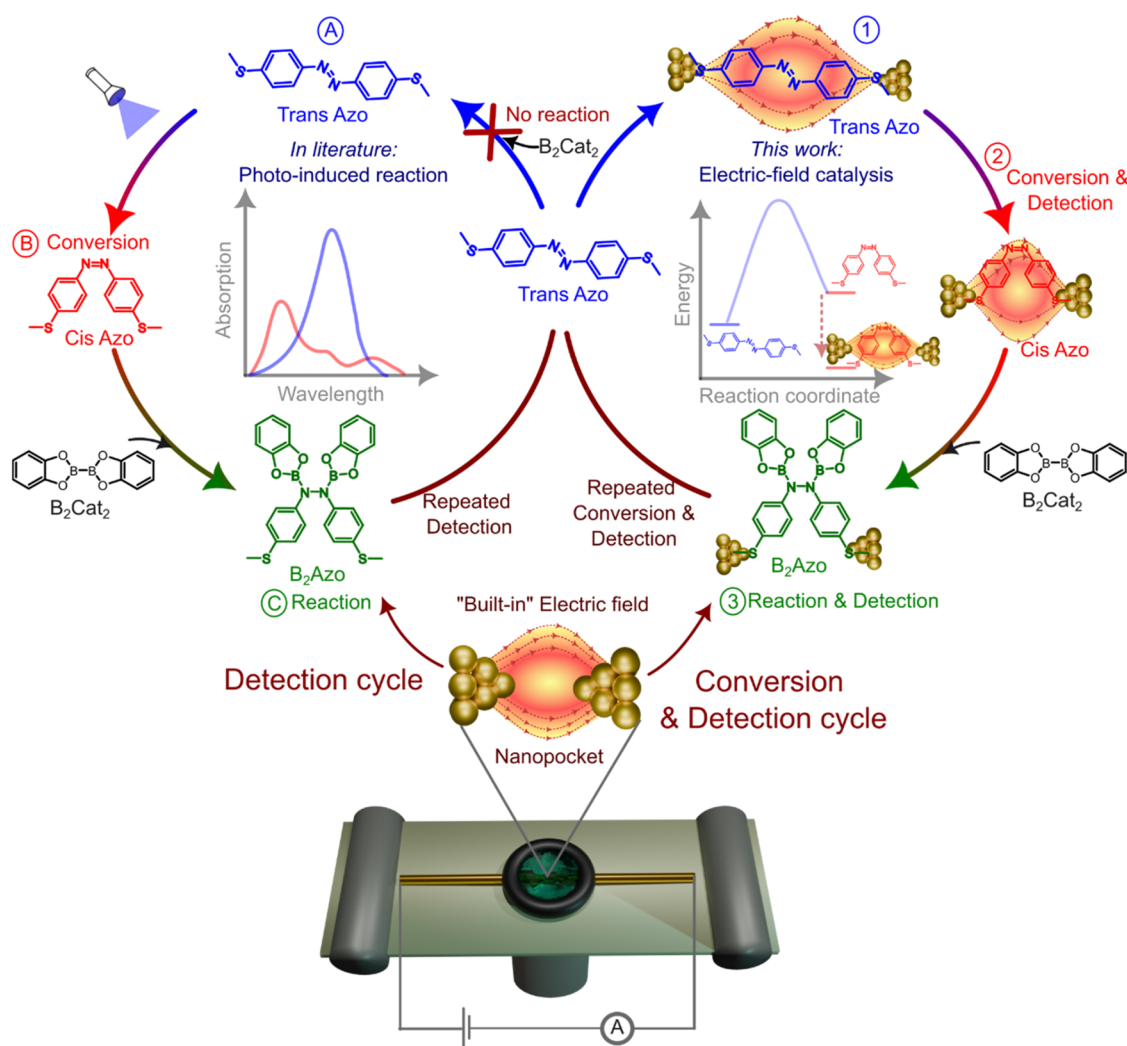


Figure 1. Detection cycle represents the light-induced cis-azobenzene selective diborylation probed by a mechanically controlled break junction setup (detection cycle, left side). Borylation reaction does not occur with the trans isomer of azobenzene (step A), while converting trans-azobenzene derivative to the cis isomer via photoirradiation (step B) leads to the formation of diborylated product (step C). The conversion and detection cycle demonstrates the triggering of cis-selective azobenzene diborylation with the oriented electric field present within the nanopocket of the break junction. The built-in electric field of the break junction nanocavity catalyzes the trans–cis-azobenzene isomerism (steps 1 and 2), followed by triggering the selective diborylation reaction (step 3), which can be monitored in real time.

chemical substrates.^{25–30} Moreover, borylation of azobenzene provides a precursor for many organic molecules, including different hydrazine derivatives.³¹ In general, the addition of a boron reagent to an N=N double bond needs the aid of a transition metal catalyst.^{31–33} Only highly reactive boron compounds are known to undergo reaction without an external agent. Recent works have achieved a metal-free borylation reaction for azobenzene compounds using external light irradiation.³⁴ The reaction is highly specific to the cis-azobenzene form, and the borylation is achieved under light irradiation with a Lewis acidic diboron reagent. However, an electric field-induced reaction pathway has not been identified yet in the borylation reaction of N=N double bonds.^{35–37}

With this aim, in this study, we discuss a novel method of utilizing the break junction technique to trigger and probe the same multistep cis-azobenzene selective diborylation in the dark at the single-molecule level, thereby broadening the scope of boron chemistry. Additionally, our study sheds light on how an oriented electric field can reshape the relative energy profiles of trans–cis-azobenzene derivatives and thereby

promote selective reaction pathways, demonstrating the transition from electric field as “catalytic accelerator” to “selective reagent”. In spite of extensive use as photoswitches in molecular junctions,³⁸ the identification of an electric field-induced trans–cis isomerism of azobenzene in the dynamic break junction technique under normal environmental conditions remains unknown, yet achieving such control could introduce new dimensions to azobenzene-based functional materials as well. In this work, we have utilized the built-in electrical field in the metallic nanopocket of the break junction to induce geometrical isomerization of the azobenzene derivative, followed by inducing a catalyst-free cis-azobenzene selective diborylation reaction in the dark (Figure 1).

RESULT AND DISCUSSION

In this work, to probe the cis-azobenzene substrate-selective diborylation reaction, we synthesized a simple azobenzene unit, terminated with the –SMe groups to provide stable and improved interactions with the gold electrodes used in single-

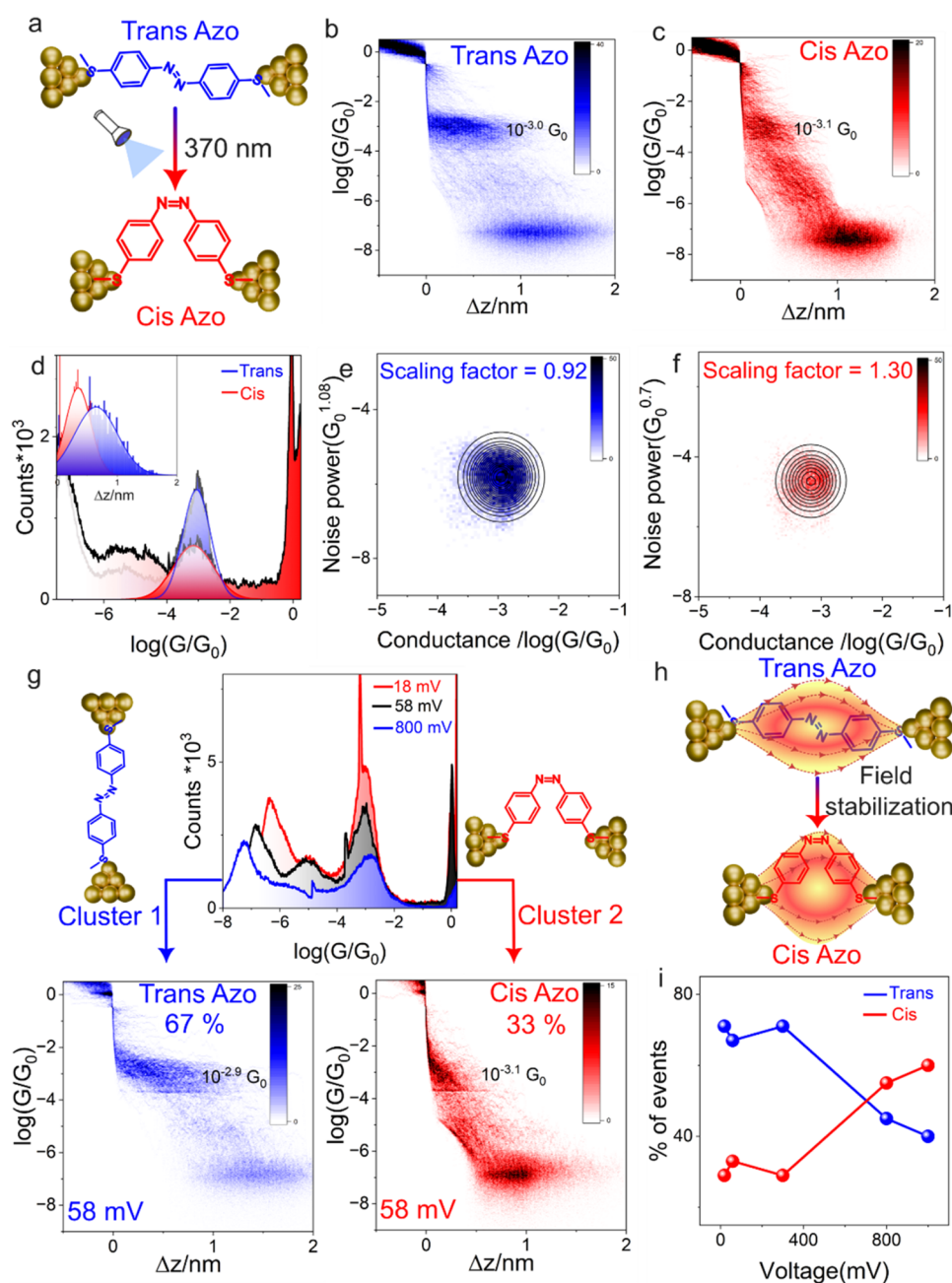


Figure 2. (a) Schematic representation of trans-to-cis isomerization under external light irradiation (b) 2D conductance–distance histogram corresponding to trans-azobenzene and (c) cis-azobenzene. (d) Combined 1D conductance histogram corresponding to trans- and cis-azobenzene. The corresponding plateau length histogram is shown as the inset. (e) 2D histogram of normalized noise power against the average conductance corresponding to the trans-azobenzene and (f) cis-azobenzene. (g) Combined 1D conductance histogram for the trans-azobenzene measurement at different applied bias (1D histogram, upper panel) and representative cluster data showing the trans- and cis-like features at a 58 mV applied bias (2D histograms, lower panel). (h) Schematic representation of the electric field-induced trans-to-cis isomerization of azobenzene. (i) Trend in the percentage of trans- and cis-like features within the overall data obtained at different applied potentials.

molecular conductance measurements (see [Supporting Information Section 1](#) for the synthesis details). Subsequently, the isomerization of trans-azobenzene to cis-azobenzene under 370 nm light irradiation is confirmed by UV–vis spectroscopy³⁹ (Figure 2a and [Supporting Information Section 2](#)).

To benchmark the single-molecular charge-transport characteristics of trans- and cis-azobenzene, we probed the photoisomerization reaction using a custom-developed mechanically controlled break junction (MCBJ) setup.⁴⁰ In the break junction technique, to create single-molecular junctions, two atomically sharp electrodes are created by breaking a single

gold wire mounted on a flexible steel plate.⁴⁰ A nanometer-scale gap is created between these electrodes to trap the desired molecule and form a metal–molecule–metal junction in solution under ambient conditions. The molecular junction is characterized by measuring the current as a function of electrode separation (Δz) under a constant applied bias, where the voltage across the electrodes serves as the source of the electric field, effectively transforming the nanojunction into a nanoreactor with a built-in electric field.¹³ Figure 2b shows the two-dimensional conductance–distance histogram created by overlaying more than 1000 such current–distance traces

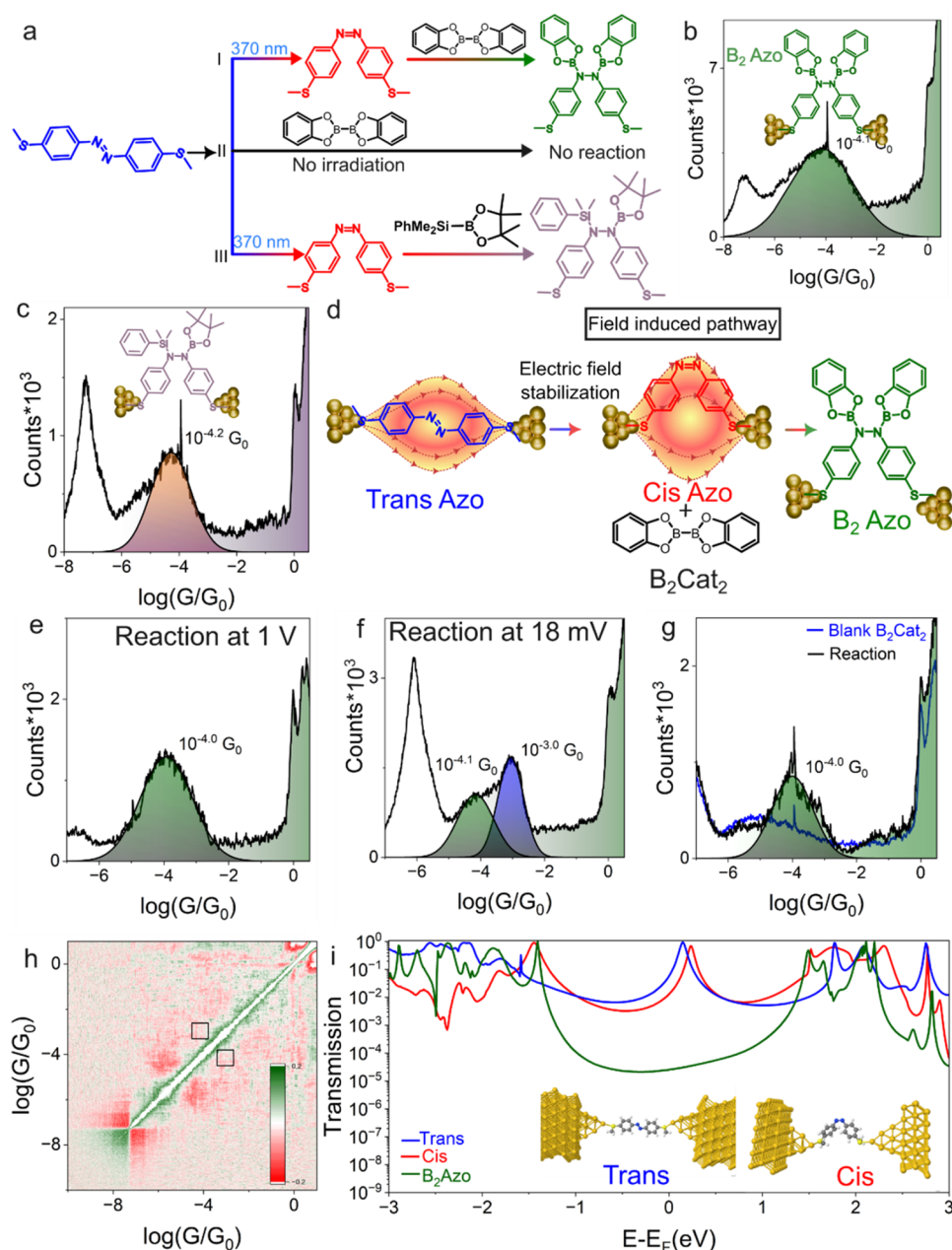


Figure 3. (a) Schematic representation of cis-selective diborylation and silaborylation achieved via external light irradiation. (b) 1D conductance histogram corresponding to the measurement of B₂Azo and (c) silaborylated product. (d) Schematic representation of electric field-induced cis-selective diborylation. (e) 1D conductance histogram corresponding to the cluster showing the product signature at an applied bias of 1 V. (f) 1D conductance histogram for the reaction at 18 mV. (g) Combined 1D conductance histogram corresponding to the measurement for blank B₂Cat₂ and the addition of azobenzene to the same setup. (h) Conductance correlation diagram for the measurement of *in-situ* diborylation reaction. (i) Calculated transmission spectra corresponding to the trans-, cis-azobenzene, and B₂Azo.

obtained from the trans-azobenzene measurement. The higher conductance region above 1 G₀ (G₀ = 77.5 μS) corresponds to the metal–metal contact, followed by a sharp drop corresponding to the gold snap back (Δz_{corr} = 0.5 nm).⁴¹ Subsequently, the formation of a metal–molecule–metal junction appears as a plateau in the current–distance histogram (10⁻³ G₀). Upon further pulling, the electrodes separate, breaking the single-molecule junction, and the current drops to the noise floor of the instrument (<10⁻⁶ G₀) (see Supporting Information Section 3 for more details).⁴¹ Corresponding to the single-molecular measurements of trans-azobenzene, a clear single-molecular plateau is observed

around ~10⁻³ G₀ with a plateau length (z_{trans} = Δz_{trans} + Δz_{corr}) around 1.2 nm after correcting for the snap back distance,⁴¹ confirming the single-molecular junction formation with the trans-azobenzene derivative.

Further, to characterize the cis-azobenzene, we *in-situ* irradiated the trans-azobenzene solution with a 370 nm light source and carried out the single-molecular conductance measurement. Figure 2c shows the conductance–distance histogram corresponding to the cis-azobenzene where a single plateau around 10^{-3.1} G₀ with a smaller plateau length of 0.7 nm (z_{cis} = Δz_{cis} + Δz_{corr}) is observed. Although both cis and trans showed similar conductance values, a clear difference

observed in the plateau lengths of cis and trans confirms the photoisomerization reaction in the MCBJ measurements (Figure 2d), as trans form is longer than cis isomer.³⁸ In order to get deeper insight into the molecular junction configuration and the nature of electrode–molecule interaction, we performed flicker ($1/f$) noise analysis for both the isomeric forms. The scaling exponent extracted from the noise power–conductance relationship, a metric reflecting the balance between through-bond and through-space transport pathways^{42,43} was found to be 1.3 for the cis isomer and 0.9 for the trans isomer (Figure 2e,f and Supporting Information Section 4). The observed flicker noise power value suggests that in both isomers, the charge transport is dominated by a through-bond pathway.

To rationalize the observed conductance trend, we performed I–V spectroscopy measurements by holding the molecular junction for 150 ms and sweeping the bias from -1.5 to 1.5 V. By fitting the I–V using a single level model^{14,44} (Supporting Information Figure S5), the coupling parameter Γ and the molecular orbital offset energy ΔE (energy difference between the Fermi level and the nearest molecular orbital) were determined to be 40 meV and 1.0 eV, respectively, for the trans isomer. For the cis isomer, Γ decreased to 35 meV and ΔE shifted slightly to 0.97 eV. Such a reduction in coupling is sufficient to offset the expected increase in tunnelling efficiency, thus rationalizing the similar conductance values observed for cis form with a smaller plateau length than trans form.⁴⁵ Together, these findings explain the similar conductance values for the two isomers despite their structural differences.

Interestingly, we observed that even though the trans-to-cis conversion is around 60% in the UV–vis studies (Supporting Information Figure S3), the conductance measurements of the cis isomer showed no significant current–distance traces corresponding to the trans isomer. Initially, we hypothesized that the trans–cis equilibrium is reshaped within the electric field present in our nanojunction; in fact, the field stabilizes the cis form of azobenzene more than the trans form due to the dipole moment.¹¹ To test our hypothesis, we subjected the trans-azobenzene derivative to different electric field strengths and monitored the corresponding changes by the single-molecular conductance measurements. As shown in Figure 2g, we observed almost no change in the conductance value after driving the applied bias from 18 mV to 800 mV. Interestingly, after clustering the data using principal component analysis combined with k-means++ clustering,^{46,47} we observed that within the measurement, there are conductance traces with both higher and lower plateau lengths, indicating the presence of a cis–trans mixture in the measurement medium, as shown in the lower panel of Figure 2g. However, the NMR spectrum of synthesized trans-azobenzene (Supporting Information Figure S1) shows no signature corresponding to the cis form, suggesting that the formation of cis-azobenzene is within the measurement unit itself, indicative of a field-induced transformation (Figure 2h). Further, we quantified the number of trans- and cis-like features present in the data after clustering the overall data set obtained at each applied bias (see Supporting Information for the complete data, Figures S6–S10). The resulting trend, shown in Figure 2i, clearly suggests that with increasing bias, the presence of cis-like features increases, confirming that the isomerization is driven by the oriented electric field, as previously demonstrated under ultrahigh-vacuum conditions.^{48–50}

Our experimental results reveal that azobenzene isomerization in solution can be triggered by a low applied bias under ambient conditions. The observation and its interpretation become plausible when considering the dipole moments of the two isomers: the cis isomer, possessing a finite dipole moment, can be stabilized more effectively under an external electric field than the trans isomer, which has a near-zero dipole moment.^{11,51} At this point, we realized and envisaged that carrying out a cis-azobenzene selective diborylation reaction under dark conditions and tracking the product signature can be turned into a perfect probe for identifying the field-induced trans-to-cis isomerization, if the single-molecular conductance signature for the diborylated product is distinctly different from the reactant azobenzene.

Further, we set out to probe the intended cis-azobenzene selective diborylation reaction by using the break junction technique (Figure 3a). We have previously reported the photoinduced cis-azobenzene selective diborylation reaction,³⁴ and the same reaction is carried out to obtain the pure diborylated product (B_2Azo) for single-molecular characterization (see Supporting Information Section 7 for the synthesis details). When trans-azobenzene was reacted with bis-(catecholato)diboron (B_2Cat_2) in toluene for 12 h under 370 nm light irradiation in a nitrogen atmosphere, the diborylated product (B_2Azo) was obtained. The same reaction with trans-azobenzene in the absence of light failed to produce the diborylated product, suggesting the selective reactivity of the cis form. Similarly, as a control, a silaborylated azobenzene, which is more stable than the diborylated form, was obtained on reacting trans-azobenzene with silaborane, (dimethylphenyl)silylboronic acid pinacol ester ($PhMe_2Si-Bpin$), under 370 nm light irradiation (Figure 3a) (see Supporting Information Section 8 for the synthesis details).³⁴ Figure 3b shows the one-dimensional (1D) conductance histogram corresponding to the B_2Azo measurement with a clear conductance peak at $10^{-4} G_0$.

Figure 3c shows the 1D conductance histogram corresponding to the silaborylated product. The conductance value is similar to that of the diborylated product, which further confirms the trapping of the borylated product between the electrodes.

As our previous experiments suggested an *in-situ* trans-to-cis isomerization in the absence of light, we carried out the diborylation reaction within MCBJ to trigger the same cis-azobenzene selective diborylation reaction using the oriented electric field (Figure 3d). Envisaging a higher chance of conversion (trans–cis isomerism) at higher applied voltages, we carried out the reaction in our MCBJ setup at an applied potential of 1 V. To our delight, after classifying the overall data into clusters, we could observe the $10^{-4} G_0$ feature, similar to the conductance plateau obtained for the diborylated product (Figures 3e and S15). It further implies that the cis form of the azobenzene is getting formed in the nanojunction, and in the presence of B_2Cat_2 , it is getting converted into the diborylated product, similar to the photoirradiated reaction.³⁴ To verify that this is, in fact, the scenario, the reaction is done in the dark at a lower applied bias inside the break junction setup. Figure 3f shows the 1D conductance histogram corresponding to the reaction at 18 mV, and we clearly observe a peak at $10^{-4.1} G_0$ (Figure S16). This result fits well with our observation of the occurrence of trans-to-cis conversion at both lower and higher applied bias (Figure 2i).

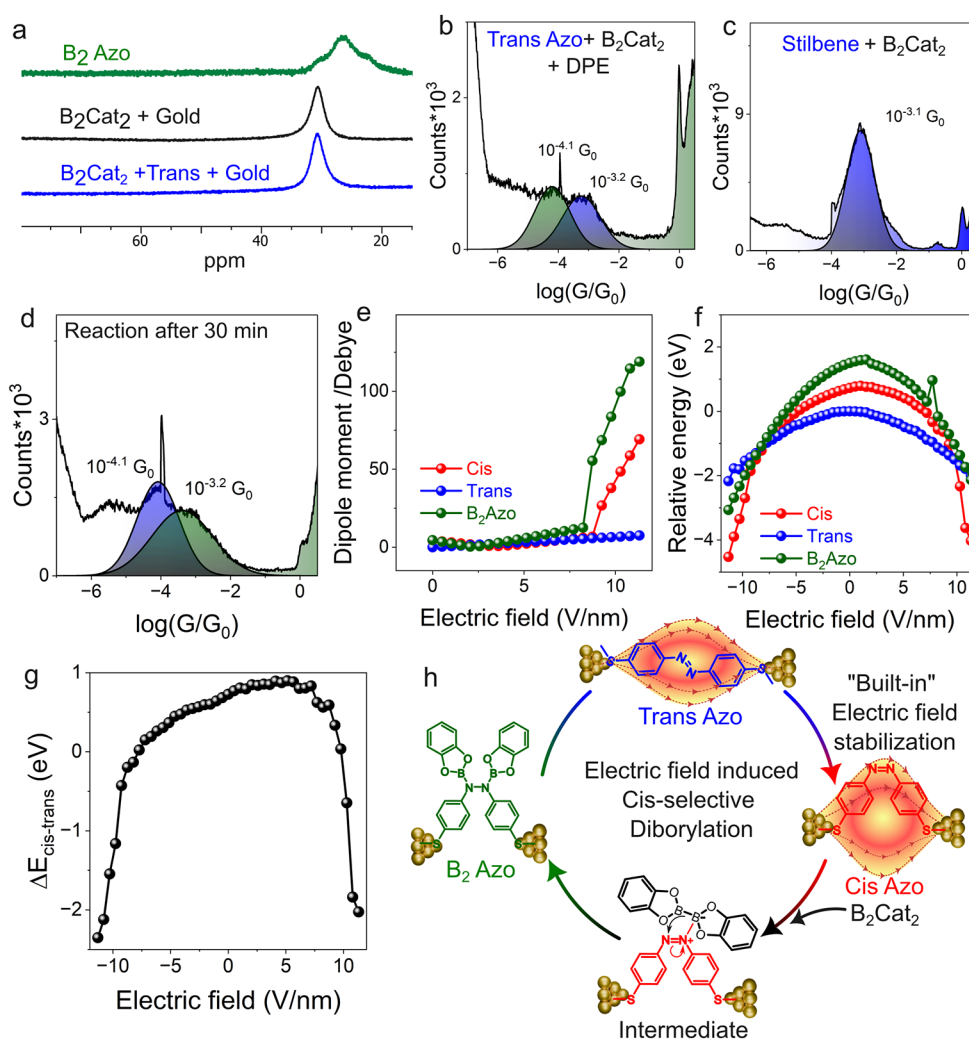


Figure 4. (a) Stacked boron NMR spectra corresponding to B_2Azo (green spectra), B_2Cat_2 solution in the presence of gold (black spectra) and *ex-situ* reaction in the presence of gold (blue spectra) under the dark. (b) 1D conductance histogram corresponding to the *in-situ* diborylation reaction in the presence of the radical scavenger DPE. (c) 1D conductance histogram for the *in-situ* diborylation reaction of stilbene in the dark. (d) 1D conductance histogram for the light-induced reaction mixture after 30 min. (e) Single-point calculations of dipole moment and (f) relative energies of geometry optimization calculations of cis-, trans-, and B_2Azo structures. The energies are shown relative to the energy of the trans structure at zero electric field. (g) Energy difference ΔE between cis and trans azobenzene in electric field, calculated from geometry optimization calculations. (h) Schematic illustration of the cis-azobenzene-specific diborylation reaction triggered by electric field.

To confirm that the $10^{-4} G_0$ feature originates as a consequence of diborylation reaction and not from any sort of B_2Cat_2 interaction with the gold, we conducted the conductance measurement for only the B_2Cat_2 solution and found no conductance feature, as shown in Figure 3g.⁵²

Further adding azobenzene to the same setup resulted in the appearance of the peak corresponding to the expected product, which reinforces the occurrence of the reaction in our setup in the dark (Figure 3g). Additionally, the correlation diagram shown in Figure 3h confirms that the features present at $10^{-3} G_0$ and $10^{-4} G_0$ are negatively correlated, i.e., they originate from different species present inside the solution. All of the above experiments solidify the catalyst-free electric field-driven cis-azobenzene selective borylation reaction in the break junction setup, which is otherwise driven by external light irradiation.³⁴

To rationalize our experimental findings, we performed theoretical calculations and obtained transmission spectra corresponding to the trans and cis isomers of azobenzene and the diborylated product (Figure 3i). The spectra show a

similar conductance trend, corroborating our experimental results. The transport calculations were performed using density functional theory (DFT) with the generalized gradient approximation (GGA) and the Perdew–Burke–Ernzerhof (PBE) functional in combination with nonequilibrium Green's functions (NEGFs) as implemented in TranSIESTA.⁵³ The Au(111) electrodes with pyramidal Au tips were attached to the molecules' termini to build molecular junctions. Details of the simulations are given in the Supporting Information Section 13. As shown in the transmission in Figure 3i, we find that low-bias transport through the trans and cis configurations is dominated by a LUMO-related resonance (for the molecular orbitals of the three species, see Supporting Information Figure S28). We have extracted the zero-bias conductance from the transmission at the Fermi energy, $E_F = 0$, via $G = T(E_F)G_0$. Consistent with experiment, the trans configuration exhibits a slightly higher conductance of $5.7 \times 10^{-2} G_0$ than the cis configuration ($1.3 \times 10^{-2} G_0$), while the product state shows a markedly reduced conductance of $2.7 \times 10^{-5} G_0$ arising

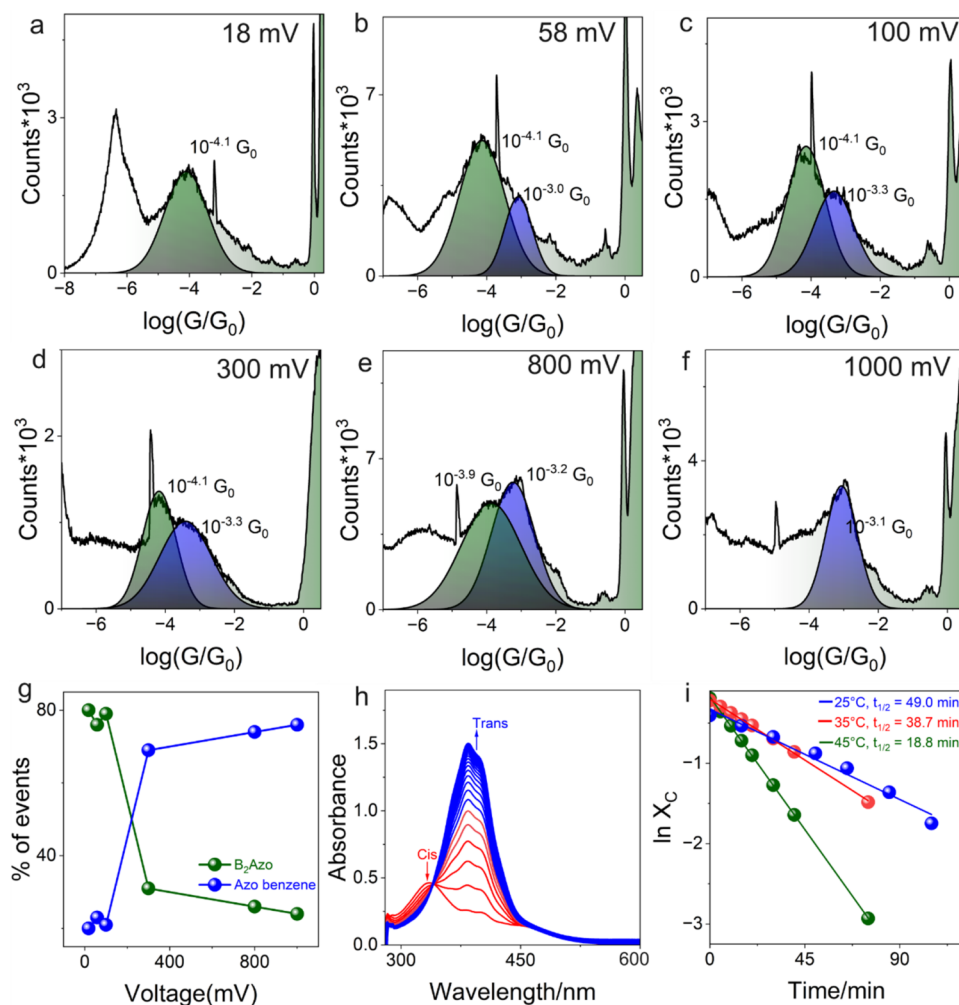


Figure 5. 1D conductance histogram for the *in-situ* reaction in dark at an applied bias of (a) 18 mV, (b) 58 mV, (c) 100 mV, (d) 300 mV, (e) 800 mV, and (f) 1 V. (g) Trend in percentage of product formed at different applied biases. (h) UV-vis spectra corresponding to the back-conversion of cis-azobenzene to trans-azobenzene at 45 °C. (i) Plot for the mole fraction of cis form versus time at different temperatures.

primarily from the weak coupling of its molecular resonances to the electrodes.

To rigorously establish that an interfacial electric field drives the reaction, we investigated the mechanistic aspects. Apart from the involvement of the electric field, the reaction could proceed via two alternative pathways. (1) gold catalysis and (2) a radical species-mediated pathway. First, to eliminate the possibility of gold catalysis, we carried out the diborylation reaction *ex-situ* in the presence of gold. Figure 4a shows the boron NMR signature corresponding to the expected diborylated product (green spectrum). We examined the B_2Cat_2 ^{11}B NMR spectra in the presence of gold, as shown in the black line, the characteristic peak corresponding to the B_2Cat_2 species without any shift was observed. The blue spectrum corresponds to the diborylation reaction performed in the presence of gold, which also shows an unreacted B_2Cat_2 species (see the Supporting Information, Section 10 for the details of the reaction). Additionally, previous reports show that the adsorption of azobenzene on a gold surface induces no structural changes in the molecule, thereby eliminating the possibility of gold catalysis.^{48–50,54–56}

To check the possibility of a radical-mediated pathway in the presence of an interfacial electric field, we performed the *in-situ* reaction in the presence of a radical scavenger, 1,1-diphenyl-

ethylene (DPE), where we again observed the product formation (Figure 4b). Furthermore, if it is a radical pathway, the stilbene derivatives are also expected to react with B_2Cat_2 to form the diborylated product. However, no new peak was observed in the case of an *in-situ* reaction carried out with the stilbene instead of azobenzene (Figure 4c). These experimental results suggest that the reaction is solely induced by the electric field present in the molecular junction. To see whether we can capture any possible intermediate formed during the reaction, we measured the reaction mixture after 30 min of external reaction; however, we observed no new conductance feature (Figure 4d). It is also possible that even if an intermediate is formed, the associated conductance difference is too small to be resolved within our experimental resolution, as the intermediate formed can be electronically very similar to the product.

Further, dipole moments were computationally calculated in the presence of an electric field ranging from 0 V/nm to 11.31 V/nm with steps of 0.514 V/nm on three structures of cis-, trans-, and diboryl azobenzenes as seen in Figure 4e. We note that, owing to limitations of the model, the applied electric fields and induced dipole moments are higher than those typically achievable under experimental conditions. Additionally, we have computationally optimized the cis-, trans-, and

B₂Azo structures in the presence of an electric field in the *z*-direction ranging from −11.31 V/nm to 11.31 V/nm with steps of 0.541 V/nm, as shown in Figure 4f. As the dipole moments of the *cis*- and B₂Azo structures are more strongly affected by the electric field than that of the *trans* structure, the energies of the *cis*- and B₂Azo structures are lowered more than that of the *trans* structure, in the low-field limit consistent with $E = -\vec{\mu} \cdot \vec{E}$, where $\vec{\mu}$ is the dipole moment. From these calculations, the energy difference between the *cis*- and *trans*-azobenzene structures indicates that, at sufficiently high electric fields, the *cis* configuration becomes more stable than the *trans* configuration ($\Delta E = E_{\text{cis}} - E_{\text{trans}} < 0$), as shown in Figure 4g. The B₂Azo structure follows the same trends as the *cis* structure. All calculations were done in Orca 6;^{57,58} for the single-point dipole moments, a PBE0^{59,60}/aug-cc-pVDZ⁶¹ level of theory was used, and for geometry optimizations, a CAM-B3LYP⁶²/6-311G**⁶³ level of theory with the Tight-Opt criterion was used.

These results clearly indicate that the *trans*-azobenzene is getting converted to the *cis* isomer within the biased nanojunction. Further, the boron reagent attacks the *cis* isomer of the azobenzene and forms a charge-separated species, leading to the product formation as reported in the literature³⁴ (Figure 4h). We believe that the charge-separated intermediate is getting stabilized in the presence of the electric field, and the reaction is driven forward. These results confirm the electric field-driven *trans*–*cis* isomerization of azobenzene, followed by the triggering of *cis*-azobenzene selective diborylation reaction (Figure 4h).

To further extend the study, we looked at the efficiency of the reaction at different applied biases. Figure 5a–f (Supporting Information Figures S21–26) clearly shows that the amount of product is decreasing with increasing the applied bias (Figure 5g). This trend is opposite to what we expected, as we observed an increase in the *cis*-like feature with an increase in bias during the conductance measurement of *trans*-azobenzene, as shown in Figure 2i. To understand the effect of joule heating at a higher applied bias^{14,64} on the *cis*–*trans* isomerization reaction, we first probed the temperature-dependent back-conversion of *cis* to *trans* isomerization using UV–vis spectroscopy and observed a decrease in the half-life of the *cis* isomer at higher temperatures (Figure 5h,i). However, we realized that the continuous electric field across the junction can prevent this back-conversion effect, portraying the efficiency of the nanojunction in driving the reaction efficiently and probing them simultaneously. These observations led us to conclude that the decrease in the diborylated product may be due to the low stability of the product at higher applied voltages.

CONCLUSION

To summarize, our study combines the effect of substrate recognition and electric field catalysis at the single-molecule level to drive a *cis*-azobenzene selective diborylation reaction. Although the break junction technique has already been shown to probe a wide range of chemical reactions, our study extends the scope of its capability in detecting and inducing multistep substrate-selective reaction pathways. Beyond molecular switching, this work opens new directions for borylation and silaborylation chemistry. To our knowledge, no previous study has demonstrated diborylation reactions mediated by an external electric field. Our findings, therefore, reveal an unexplored reactivity landscape for N=N bond functionaliza-

tion and expand the range of electric field-driven synthetic transformations. Considering the broad utility of the borylation reaction, this study paves the way for designing catalyst-free, energy-effective synthetic protocols for diborylation.

Additionally, given the broad utility of azobenzene, our findings further show that photoexcitation can be functionally substituted with an external electric field. In azobenzene-based functional materials, the electric field represents an additional stimulus for molecular switching under normal environmental conditions. Notably, in devices incorporating two or more photochromic units, an applied field may act as an orthogonal trigger that operates without perturbing neighboring components, an opportunity that could be exploited in molecular logic architectures. Additionally, azobenzene motifs are widely integrated into nanoscale molecular machines, where reversible switching is typically achieved through light or thermal input. Our results indicate that these units also respond directly to electric fields, introducing a third independent mode of actuation for future device designs.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/jacs.6c05830>.

Synthesis procedure and characterization; all conductance measurement data; and theoretical calculations (PDF)

AUTHOR INFORMATION

Corresponding Authors

Susanne Leitherer – Department of Chemistry and Nano-Science Center, University of Copenhagen, 2100 Copenhagen Ø, Denmark; orcid.org/0000-0002-5437-2729; Email: sls@chem.ku.dk

K. Geetharani – Department of Inorganic and Physical Chemistry, Indian Institute of Science, Bangalore 560012, India; orcid.org/0000-0003-2064-1297; Email: geetharani@iisc.ac.in

Veerabhadrarao Kaliginedi – Department of Inorganic and Physical Chemistry, Indian Institute of Science, Bangalore 560012, India; orcid.org/0000-0002-4361-741X; Email: vkaliginedi@iisc.ac.in

Authors

PA Sreelakshmi – Department of Inorganic and Physical Chemistry, Indian Institute of Science, Bangalore 560012, India; orcid.org/0009-0001-8009-5825

Reetu Rani Mondal – Department of Inorganic and Physical Chemistry, Indian Institute of Science, Bangalore 560012, India

Laust Rask – Department of Chemistry, University of Copenhagen, 2100 Copenhagen Ø, Denmark

Oscar Berlin Obel – Department of Chemistry, University of Copenhagen, 2100 Copenhagen Ø, Denmark

Umar Rashid – Department of Inorganic and Physical Chemistry, Indian Institute of Science, Bangalore 560012, India; orcid.org/0000-0001-6583-061X

Joseph M. Hamill – Department of Chemistry and Nano-Science Center, University of Copenhagen, 2100 Copenhagen Ø, Denmark; orcid.org/0000-0002-9024-4636

Kurt V. Mikkelsen – Department of Chemistry, University of Copenhagen, 2100 Copenhagen Ø, Denmark; orcid.org/0000-0003-4090-7697

Complete contact information is available at:
<https://pubs.acs.org/10.1021/jacs.6c05830>

Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

V.K., P.A.S., and U.R. acknowledge the funding support from the Indian Institute of Science, DST grant (DST/IC/Austria/call2024/P-27) and ANRF-ARG grant (ANRF/ARG/2025/004891/CS). K.G. and R.R.M. acknowledge the funding support from the Science and Engineering Research Board (SERB) (CRG/2023/004627). P.A.S., R.R.M., and U.R. acknowledge the financial support from the Prime Minister Research Fellowship (PMRF), Government of India. S.L. acknowledges funding from the Novo Nordisk Foundation (grant reference number NNF210C0071282).

■ REFERENCES

- (1) Koshland, D. E. Application of a Theory of Enzyme Specificity to Protein Synthesis. *Proc. Natl. Acad. Sci. U.S.A.* **1958**, *44* (2), 98–104.
- (2) Breslow, R. Biomimetic Chemistry and Artificial Enzymes: Catalysis by Design. *Acc. Chem. Res.* **1995**, *28* (3), 146–153.
- (3) Ye, R.; Mao, X.; Sun, X.; Chen, P. Analogy between Enzyme and Nanoparticle Catalysis: A Single-Molecule Perspective. *ACS Catal.* **2019**, *9* (3), 1985–1992.
- (4) Bunjes, O.; Hedman, D.; Rittmeier, A.; Paul, L. A.; Siewert, I.; Ding, F.; Wenderoth, M. Making and Breaking of Chemical Bonds in Single Nanoconfined Molecules. *Sci. Adv.* **2022**, *8* (36), No. eabq7776.
- (5) Warshel, A.; Sharma, P. K.; Kato, M.; Xiang, Y.; Liu, H.; Olsson, M. H. M. Electrostatic Basis for Enzyme Catalysis. *Chem. Rev.* **2006**, *106* (8), 3210–3235.
- (6) Fafarman, A. T.; Sigala, P. A.; Schwans, J. P.; Fenn, T. D.; Herschlag, D.; Boxer, S. G. Quantitative, Directional Measurement of Electric Field Heterogeneity in the Active Site of Ketosteroid Isomerase. *Proc. Natl. Acad. Sci. U.S.A.* **2012**, *109* (6), E299–E308.
- (7) Fried, S. D.; Bagchi, S.; Boxer, S. G. Extreme Electric Fields Power Catalysis in the Active Site of Ketosteroid Isomerase. *Science* **2014**, *346* (6216), 1510–1514.
- (8) Tokuriki, N.; Tawfik, D. S. Protein Dynamism and Evolvability. *Science* **2009**, *324* (5924), 203–207.
- (9) Ciampi, S.; Darwish, N.; Aitken, H. M.; Díez-Pérez, I.; Coote, M. L. Harnessing Electrostatic Catalysis in Single Molecule, Electrochemical and Chemical Systems: A Rapidly Growing Experimental Tool Box. *Chem. Soc. Rev.* **2018**, *47* (14), 5146–5164.
- (10) Zang, Y.; Zou, Q.; Fu, T.; Ng, F.; Fowler, B.; Yang, J.; Li, H.; Steigerwald, M. L.; Nuckolls, C.; Venkataraman, L. Directing Isomerization Reactions of Cumulenes with Electric Fields. *Nat. Commun.* **2019**, *10*, No. 4482.
- (11) Aragonès, A. C.; Haworth, N. L.; Darwish, N.; Ciampi, S.; Bloomfield, N. J.; Wallace, G. G.; Díez-Pérez, I.; Coote, M. L. Electrostatic Catalysis of a Diels–Alder Reaction. *Nature* **2016**, *531* (7592), 88–91.
- (12) Shaik, S. My Vision of Electric-Field-Aided Chemistry in 2050. *ACS Phys. Chem. Au* **2024**, *4* (3), 191–201.
- (13) Sreelakshmi, P.; Mahashaya, R.; Leitherer, S.; Rashid, U.; Hamill, J. M.; Nair, M.; Rajamalli, P.; Kaliginedi, V. Electric Field-Induced Sequential Prototropic Tautomerism in Enzyme-like Nano-pocket Created by Single Molecular Break Junction. *J. Am. Chem. Soc.* **2024**, *146* (51), 35242–35251.
- (14) Rashid, U.; Medrano Sandonas, L.; Chatir, E.; Ziani, Z.; Sreelakshmi, P.; Cobo, S.; Gutierrez, R.; Cuniberti, G.; Kaliginedi, V. Mapping the Extended Ground State Reactivity Landscape of a Photoswitchable Molecule at a Single Molecular Level. *J. Am. Chem. Soc.* **2025**, *147* (1), 830–840.
- (15) Stone, I.; Starr, R. L.; Zang, Y.; Nuckolls, C.; Steigerwald, M. L.; Lambert, T. H.; Roy, X.; Venkataraman, L. A Single-Molecule Blueprint for Synthesis. *Nat. Rev. Chem.* **2021**, *5* (10), 695–710.
- (16) Chen, H.; Jia, C.; Zhu, X.; Yang, C.; Guo, X.; Stoddart, J. F. Reactions in Single-Molecule Junctions. *Nat. Rev. Mater.* **2023**, *8* (3), 165–185.
- (17) Shaik, S.; Ramanan, R.; Danovich, D.; Mandal, D. Structure and Reactivity/Selectivity Control by Oriented-External Electric Fields. *Chem. Soc. Rev.* **2018**, *47* (14), 5125–5145.
- (18) Yang, C.; Guo, Y.; Zhang, H.; Guo, X. Utilization of Electric Fields to Modulate Molecular Activities on the Nanoscale: From Physical Properties to Chemical Reactions. *Chem. Rev.* **2025**, *125* (1), 223–293.
- (19) Shaik, S.; Danovich, D.; Kalita, S.; Dubey, K. D. Oriented Electric Fields—Universal Catalysts. *Acc. Chem. Res.* **2025**, *58* (19), 3071–3080.
- (20) Long, Z.; Meng, J.; Weddle, L. R.; Videla, P. E.; Menzel, J. P.; Cabral, D. G. A.; Liu, J.; Qiu, T.; Palasz, J. M.; Bhattacharyya, D.; Kubiak, C. P.; Batista, V. S.; Lian, T. The Impact of Electric Fields on Processes at Electrode Interfaces. *Chem. Rev.* **2025**, *125* (3), 1604–1628.
- (21) Léonard, N. G.; Dhaoui, R.; Chantarojsiri, T.; Yang, J. Y. Electric Fields in Catalysis: From Enzymes to Molecular Catalysts. *ACS Catal.* **2021**, *11* (17), 10923–10932.
- (22) Shaik, S.; Mandal, D.; Ramanan, R. Oriented Electric Fields as Future Smart Reagents in Chemistry. *Nat. Chem.* **2016**, *8* (12), 1091–1098.
- (23) Yan, C.; Wei, G.; Jin, Z.; Li, X.; Yang, L.; Zou, L.; Yang, L. Elucidating the Substrate Specificity of Cytochrome P450 Enzymes: Insights into N- And S-Containing Small-Molecule Metabolism. *Engineering* **2025**, *54*, No. S2095809925004400.
- (24) Zhou, Y.; De Veer, S. J.; Tyler, T. J.; Chen, Y.; Durek, T.; Craik, D. J.; Rehm, F. B. H. Asparaginyl Ligases with Engineered Substrate Specificity for Controlled, Sequential Transpeptidation Reactions. *J. Am. Chem. Soc.* **2025**, *147* (25), 21824–21831.
- (25) Neeve, E. C.; Geier, S. J.; Mkhalid, I. A. I.; Westcott, S. A.; Marder, T. B. Diboron(4) Compounds: From Structural Curiosity to Synthetic Workhorse. *Chem. Rev.* **2016**, *116* (16), 9091–9161.
- (26) Ishiyama, T.; Matsuda, N.; Murata, M.; Ozawa, F.; Suzuki, A.; Miyaura, N. Platinum(0)-Catalyzed Diboration of Alkynes with Tetrakis(Alkoxy)diboranes: An Efficient and Convenient Approach to *Cis*-Bis(Boryl)Alkenes. *Organometallics* **1996**, *15* (2), 713–720.
- (27) Bonet, A.; Pubill-Ulldemolins, C.; Bo, C.; Gulyás, H.; Fernández, E. Transition-Metal-Free Diboration Reaction by Activation of Diboron Compounds with Simple Lewis Bases. *Angew. Chem. Int. Ed.* **2011**, *50* (31), 7158–7161.
- (28) Dewhurst, R. D.; Neeve, E. C.; Braunschweig, H.; Marder, T. B. Sp^2 – Sp^3 Diboranes: Astounding Structural Variability and Mild Sources of Nucleophilic Boron for Organic Synthesis. *Chem. Commun.* **2015**, *51* (47), 9594–9607.
- (29) Nagashima, Y.; Hirano, K.; Takita, R.; Uchiyama, M. *Trans*-Diborylation of Alkynes: *Pseudo*-Intramolecular Strategy Utilizing a Propargylic Alcohol Unit. *J. Am. Chem. Soc.* **2014**, *136* (24), 8532–8535.
- (30) Cuenca, A. B.; Shishido, R.; Ito, H.; Fernández, E. Transition-Metal-Free B–B and B–Interelement Reactions with Organic Molecules. *Chem. Soc. Rev.* **2017**, *46* (2), 415–430.
- (31) Hommer, H.; Nöth, H.; Sachdev, H.; Schmidt, M.; Schwenk, H. Contributions to the Chemistry of Boron, 231. Synthesis and Structures of Borylated Hydrazines. *Chem. Ber.* **1995**, *128* (12), 1187–1194.

- (32) Braunschweig, H.; Kupfer, T. Stoichiometric and Homogeneous-Catalytic Diboration of the NN Double Bond of Azobenzene. *J. Am. Chem. Soc.* **2008**, *130* (13), 4242–4243.
- (33) Ansell, M. B.; Kostakis, G. E.; Braunschweig, H.; Navarro, O.; Spencer, J. Synthesis of Functionalized Hydrazines: Facile Homogeneous (N-Heterocyclic Carbene)-Palladium(0)-Catalyzed Diboration and Silaboration of Azobenzenes. *Adv. Synth. Catal.* **2016**, *358* (23), 3765–3769.
- (34) Mondal, R. R.; Pal, A. K.; Geetharani, K. Catalyst-Free Diborylation and Silaboration of Azoarenes: A Simple Photoinduced Approach. *Angew. Chem. Int. Ed.* **2025**, *64* (3), No. e202415913.
- (35) Shaik, S.; Danovich, D.; Joy, J.; Wang, Z.; Stuyver, T. Electric-Field Mediated Chemistry: Uncovering and Exploiting the Potential of (Oriented) Electric Fields to Exert Chemical Catalysis and Reaction Control. *J. Am. Chem. Soc.* **2020**, *142* (29), 12551–12562.
- (36) Weberg, A. B.; Murphy, R. P.; Tomson, N. C. Oriented Internal Electrostatic Fields: An Emerging Design Element in Coordination Chemistry and Catalysis. *Chem. Sci.* **2022**, *13* (19), 5432–5446.
- (37) Kareem, S.; Vali, S. R.; Reddy, B. V. S. Electric-Field-Induced Organic Transformations. *Eur. J. Org. Chem.* **2023**, *26* (20), No. e202300103.
- (38) Ferri, V.; Elbing, M.; Pace, G.; Dickey, M. D.; Zharnikov, M.; Samori, P.; Mayor, M.; Rampi, M. A. Light-Powered Electrical Switch Based on Cargo-Lifting Azobenzene Monolayers. *Angew. Chem. Int. Ed.* **2008**, *47* (18), 3407–3409.
- (39) Bandara, H. M. D.; Burdette, S. C. Photoisomerization in Different Classes of Azobenzene. *Chem. Soc. Rev.* **2012**, *41* (5), 1809–1825.
- (40) Rashid, U.; Chatir, E.; Sandonas, L. M.; Sreelakshmi, P.; Dianat, A.; Gutierrez, R.; Cuniberti, G.; Cobo, S.; Kaliginedi, V. Dithienylethene-Based Single Molecular Photothermal Linear Actuator. *Angew. Chem. Int. Ed.* **2023**, No. e202218767.
- (41) Kaliginedi, V.; Moreno-García, P.; Valkenier, H.; Hong, W.; García-Suárez, V. M.; Buitier, P.; Otten, J. L. H.; Hummelen, J. C.; Lambert, C. J.; Wandlowski, T. Correlations between Molecular Structure and Single-Junction Conductance: A Case Study with Oligo(Phenylene-Ethynylene)-Type Wires. *J. Am. Chem. Soc.* **2012**, *134* (11), 5262–5275.
- (42) Adak, O.; Rosenthal, E.; Meisner, J.; Andrade, E. F.; Pasupathy, A. N.; Nuckolls, C.; Hybertsen, M. S.; Venkataraman, L. Flicker Noise as a Probe of Electronic Interaction at Metal–Single Molecule Interfaces. *Nano Lett.* **2015**, *15* (6), 4143–4149.
- (43) Rashid, U.; Bro-Jørgensen, W.; Harilal, K.; Sreelakshmi, P.; Mondal, R. R.; Pisharam, V. C.; Parida, K. N.; Geetharani, K.; Hamill, J. M.; Kaliginedi, V. Chemistry of the Au–Thiol Interface through the Lens of Single-Molecule Flicker Noise Measurements. *J. Am. Chem. Soc.* **2024**, *146* (13), 9063–9073.
- (44) Opodi, E. M.; Song, X.; Yu, X.; Hu, W. A Single Level Tunneling Model for Molecular Junctions: Evaluating the Simulation Methods. *Phys. Chem. Chem. Phys.* **2022**, *24* (19), 11958–11966.
- (45) Nitzan, A.; Ratner, M. A. Electron Transport in Molecular Wire Junctions. *Science* **2003**, *300* (5624), 1384–1389.
- (46) Hamill, J. M.; Zhao, X. T.; Mészáros, G.; Bryce, M. R.; Arenz, M. Fast Data Sorting with Modified Principal Component Analysis to Distinguish Unique Single Molecular Break Junction Trajectories. *Phys. Rev. Lett.* **2018**, *120* (1), No. 016601.
- (47) Cabosart, D.; El Abbassi, M.; Stefani, D.; Frisenda, R.; Calame, M.; Van Der Zant, H. S. J.; Perrin, M. L. A Reference-Free Clustering Method for the Analysis of Molecular Break-Junction Measurements. *Appl. Phys. Lett.* **2019**, *114* (14), No. 143102.
- (48) Choi, B.-Y.; Kahng, S.-J.; Kim, S.; Kim, H.; Kim, H. W.; Song, Y. J.; Ihm, J.; Kuk, Y. Conformational Molecular Switch of the Azobenzene Molecule: A Scanning Tunneling Microscopy Study. *Phys. Rev. Lett.* **2006**, *96* (15), No. 156106.
- (49) Alemani, M.; Peters, M. V.; Hecht, S.; Rieder, K.-H.; Moresco, F.; Grill, L. Electric Field-Induced Isomerization of Azobenzene by STM. *J. Am. Chem. Soc.* **2006**, *128* (45), 14446–14447.
- (50) Henzl, J.; Mehlhorn, M.; Gawronski, H.; Rieder, K.; Morgenstern, K. Reversible Cis – Trans Isomerization of a Single Azobenzene Molecule. *Angew. Chem. Int. Ed.* **2006**, *45* (4), 603–606.
- (51) Hartley, G. S.; Le Fèvre, R. J. W. 119. The Dipole Moments of Cis- and Trans-Azobenzenes and of Some Related Compounds. *J. Chem. Soc.* **1939**, *0* (0), 531–535.
- (52) Li, Y.; Zhao, C.; Wang, R.; Tang, A.; Hong, W.; Qu, D.; Tian, H.; Li, H. In Situ Monitoring of Transmetalation in Electric Potential-Promoted Oxidative Coupling in a Single-Molecule Junction. *CCS Chem.* **2023**, *5* (1), 191–199.
- (53) Papior, N.; Lorente, N.; Frederiksen, T.; García, A.; Brandbyge, M. Improvements on Non-Equilibrium and Transport Green Function Techniques: The next-Generation Transiesta. *Comput. Phys. Commun.* **2017**, *212*, 8–24.
- (54) Godey, S.; Therssen, H.; Guérin, D.; Mélin, T.; Lenfant, S. Electroisomerization Blinking of an Azobenzene Derivative Molecule. *Nanotechnology* **2025**, *36* (10), No. 105702.
- (55) Yadav, K.; Mahapatra, S.; Halbritter, T.; Heckel, A.; Gopakumar, T. G. Low-Threshold Reversible Electron-Induced and Selective Photoinduced Switching of Azobenzene Derivatives under Ambient Conditions. *J. Phys. Chem. Lett.* **2018**, *9* (21), 6326–6333.
- (56) Scheil, K.; Gopakumar, T. G.; Bahrenburg, J.; Temps, F.; Maurer, R. J.; Reuter, K.; Berndt, R. Switching of an Azobenzene-Tripod Molecule on Ag(111). *J. Phys. Chem. Lett.* **2016**, *7* (11), 2080–2084.
- (57) Neese, F. The ORCA Program System. *WIREs Comput. Mol. Sci.* **2012**, *2* (1), 73–78.
- (58) Neese, F. Software Update: The ORCA Program System—Version 5.0. *WIREs Comput. Mol. Sci.* **2022**, *12* (5), No. e1606.
- (59) Perdew, J. P.; Burke, K.; Ernzerhof, M. Generalized Gradient Approximation Made Simple. *Phys. Rev. Lett.* **1996**, *77* (18), 3865–3868.
- (60) Perdew, J. P.; Burke, K.; Ernzerhof, M. Generalized Gradient Approximation Made Simple [Phys. Rev. Lett. 77, 3865 (1996)]. *Phys. Rev. Lett.* **1997**, *78* (7), 1396.
- (61) Dunning, T. H. Gaussian Basis Sets for Use in Correlated Molecular Calculations. I. The Atoms Boron through Neon and Hydrogen. *J. Chem. Phys.* **1989**, *90* (2), 1007–1023.
- (62) Yanai, T.; Tew, D. P.; Handy, N. C. A New Hybrid Exchange–Correlation Functional Using the Coulomb-Attenuating Method (CAM-B3LYP). *Chem. Phys. Lett.* **2004**, *393* (1–3), 51–57.
- (63) Krishnan, R.; Binkley, J. S.; Seeger, R.; Pople, J. A. Self-Consistent Molecular Orbital Methods. XX. A Basis Set for Correlated Wave Functions. *J. Chem. Phys.* **1980**, *72* (1), 650–654.
- (64) Cirera, B.; Wolf, M.; Kumagai, T. Joule Heating in Single-Molecule Point Contacts Studied by Tip-Enhanced Raman Spectroscopy. *ACS Nano* **2022**, *16* (10), 16443–16451.