Measurement of a linear free energy relationship one molecule at a time

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A systematic study of the dehydrogenation of substituted thiophenols by controlled charge injection from the tip of a scanning tunneling microscope (STM) reveals a pronounced dependence of the reaction yield on the position and the chemical nature of the substituent. We evaluate the dehydrogenation rate of *para*-halo-substituted species within a linear free energy relationship, namely the Hammett equation. The resultant ρ value of 1.4 can faithfully predict the reaction rates of molecules that are *meta*-halo-substituted or *para*-methyl-substituted. The positive sign of ρ suggests a negatively charged transition state at the core of the STM-induced process, and the magnitude of the ρ value indicates that the presence of the substrate does not preclude substantial substituent effects. The applicability of the Hammett equation to single-molecule chemistry offers facile prediction of the rate of STM-based single-molecule chemistry in a field, which so far has been addressed by focusing on involved quantum-mechanical modeling of its underlying processes.

Hammett equation | scanning tunneling microscopy | single-molecule chemistry

The groundbreaking work of the groups of Eigler (1), Avouris (2), Gimzewski (3), Weiss (4), Rieder (5), and, most recently, Ho (6), has converted the scanning tunneling microscope (STM) from an imaging instrument (7) to a versatile tool capable (i) of control of chemical reactions (8) and (ii) of spectroscopic identification of their reactants and products (9). With the availability of commercial instrumentation for these procedures (10), the need for facile prediction of STM-based single-molecule chemistry becomes imminent. In conventional organic chemistry, linear free energy relationships such as the Hammett equation[†] have proven to be powerful tools for the prediction of the reactivity of a broad range of compounds (13–17). Here, we present the transfer of the Hammett equation to the realm where individual molecules are excited one at a time to form specific chemical bonds.

The Hammett equation (Eq. 1) predicts the impact of the substituent X on the rate (or equilibrium) constant, k , of the reaction $Z \rightarrow Z'$, where Z is a reactive group attached to the same aromatic ring as X.

The σ value describes how a specific substituent affects the acidity of benzoic acid in water (i.e., $Z = \text{COOH}$, $Z' = \text{COO}^-$). These values can be found tabulated in the literature; for the purpose of this manuscript, they are assumed to be universal constants. The ρ value indicates how susceptible a reaction $Z \rightarrow Z'$ is to substitution at the aromatic ring. It compares Z's susceptibility to the susceptibility of benzoic acid in water, which has by definition a ρ value of 1. Because of its simplicity and strong predictive power, the Hammett equation found applications all over organic chemistry, and their number is still growing.

We explore the validity of a linear free energy relationship similar to the Hammett equation at the realm of single-molecule chemistry by a systematic study of thiophenols (TP) rather than benzoic acids, i.e., $Z = \text{SH}$. TPs are relatively simple molecules that, nevertheless, exhibit a wide range of physical and chemical properties. As an important building block of most molectronic concepts proposed to date, their STM-induced reactivity has potential for future STM-based fine-tuning of molectronic circuitry. In a previous study (18), we showed that the thiol group of 2,5-dichlorothiophenol does not dehydrogenate upon deposition onto Cu(111) at 16 K. Attachment of electrons at a bias of several hundred millivolts of either polarity can cause hydrogen abstraction, and the resultant thiolate is locked rigidly into the surface. We ascertained these findings by STM-based vibrational spectroscopy (18). Before dehydrogenation, TPs rotate around their S substrate anchor even at 16 K, suggesting that the interaction of the aryl moiety with the substrate is very weak. We attribute the high rotational mobility of the aryl moiety to the length of the on-top S–Cu bond (19), which suspends the aryl moiety substantially above the substrate. Their weak substrate interactions render TPs highly suitable for the search for a substrate-independent phenomenon.

We prepare our Cu(111) single-crystal sample by several cycles of sputtering (Ar^+ , 2 kV) and annealing (700 K) at a base pressure $<3 \times 10^{-11}$ torr (1 torr = 133 Pa). Low coverages ($<0.1\%$ of a monolayer) of TPs are deposited after cooling to 16 K. Fig. 1*a* shows an STM image of TP molecules on Cu(111) at 16 K. The flower shape of the adsorbates originates from the benzene ring rotating around the thiol bond through six sets of orientations where it is in registry with the top substrate layer (20). Substituted TPs behave in a similar fashion (Fig. 1*b–d*). The increase of the feature diameter from *para*-F-TP (Fig. 1*b*) to *para*-Br-TP (Fig. 1*d*) reflects the increased size of the halo-substituent (Supporting Text and Figs. 5–7, which are published as supporting information on the PNAS web site).

We investigate the reactivity of the surface thiols by exposing their rotation center to a constant tunneling current at +700 mV sample bias while arresting the feedback loop. After ≈ 1 ms to 1 s, an abrupt step in the tunneling current appears (Fig. 2*a*) that corresponds to the formation of the thiolate. The thiolate is locked rigidly into the surface and appears as a single oval protrusion similar to that in ref. 18. We repeated this experiment on hundreds of molecules at identical bias and tunneling current. The resultant distribution of durations follows a decaying exponential (Fig. 2*a* Inset), from which a decay rate can be calculated at typically $\leq 15\%$ fit uncertainty. By repeating the experiment at different currents [but identical voltage, as realized by slight ($<10\%$) variation of the tip

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Abbreviations: STM, scanning tunneling microscope; TP, thiophenol.

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[†]The Hammett equation (11) is part of any introductory course in organic chemistry (12).

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Fig. 3. Comparison of our data with Hammett σ values. (a) Comparison between measured (open bars) and literature (filled bars) Hammett σ values assuming a ρ value of ≈ 1.4 , derived from the best fit for the three *para*-X-TP molecules (unshaded area). The satisfactory correlation between measured and literature σ values in the shaded areas shows that a ρ value of 1.4 is capable of predicting reaction rates of substituted TPs. (b) Conventional representation of the correlation between the rate constants. The x axis indicates the ratio of the acid dissociation constants of benzoic acids in water (i.e., the σ value), and the y axis shows the ratio measured for TPs on Cu(111). A linear fit yields a ρ of 1.4 at a fit uncertainty of ± 0.1 .

findings suggest that in the STM-based reaction, a negatively charged transition state plays an important role (which does not conflict with the electron attachment process used here). The ρ values of phenol in water and TP in 1:1 water/ethanol solution are 2.5 and 2.2, respectively (14) [values were derived for 1:1 water-ethanol solutions (21)]. A value larger than 1 indicates that the reaction is more susceptible to substitution than benzoic acid in water ($\rho = 1$). For TP (and phenol) this can be rationalized by the closer proximity of the abstracted hydrogen to the aryl ring and the substituent than in the case of benzoic acid. Thermal desorption experiments by Meyers and Gellman (17) showed that the rate of Ullmann coupling between substituted iodobenzenes may also be understood in the framework of the Hammett equation even if the reaction proceeds under vacuum on a Cu(111) surface. Their ρ value of 6.0 ± 3.3 has a positive sign as reported here, which the authors interpret similarly as an electron-rich transition state. Although comparison of quantities obtained under very different conditions is problematic, we regard it as remarkable that in both experiments a ρ value larger than 1 was found. This finding indicates that potential screening by the substrate electron density does not preclude or supersede strong interactions between substituents and reactive groups on aromatic rings. Consequently, linear free energy relationships resembling the Hammett equation may be applicable quite generally to surface (single-molecule) chemistry.

Previously, STM-based molecular excitations had been analyzed by using either semiquantum mechanical models (5, 6) or sophisticated simulation of the electronic setup of the molecule–substrate system (22) and/or the tunneling process (10, 23, 24). These approaches yield quantitative results for the

Fig. 4. STM images and STM-based excitation of further thiophenols. (a–c) STM images of *para*-methyl-TP (–288 mV, 72 pA), *meta*-F-TP (–292 mV, 51 pA), and *meta*-Cl-TP (–273 mV, 58 pA) obtained at 16 K. The petals in *b* and *c* appear bent because of the asymmetric halo-substitution. (d) The linear dependence of the reaction rate on the tunneling current indicates a one-electron process similar to Fig. 2.

excitation of simple species such as CO or ammonia. Systematic investigations of the STM-based reactivity of a class of substances (such as TPs in this study) have not been conducted so far. The former set of models do not lend themselves to the evaluation of data on polyatomic organic molecules because they lack the detail to permit predictions that depend on individual substituents. The latter class of models are computationally very involved, and modeling of the dynamics of substituted aromatic systems on metal surfaces tests the limits of the computer power currently available. At this stage, such modeling is not readily applicable for experimentalists. Consequently, simple semiempirical models and linear free energy relationships (such as the one presented here) may be the only available avenue toward the prediction of variations in STM-based reactivity between closely related organic substances.

In the solution phase, effects of mobility and solvation often overshadow the intrinsic molecular properties that were at the center of Hammett's original interest. The single-molecule measurements presented here offer a conceptually direct way to the original theoretical underpinning presented by Hammett.[§] Historically, the Hammett equation paved the way for a systematic understanding of reaction rates and mechanisms in organic chemistry. This, in turn, led to the synthesis of a far wider range of reaction products. We hope that the development of simple guiding principles for single-molecule chemistry may similarly spark developments toward a better understanding of its mechanisms and rate dependencies and, ultimately, to its application in the construction of involved surface structures.

[§]Our experiments are complementary to gas phase measurements in as much as the substrate provides for nonradiative deexcitation of reactants, facile momentum conservation, and stabilization of the abstracted hydrogen.

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