that the "better" measures won't improve power to find genetic effects. However, cigarette consumption can be measured very reliably (i.e., precisely and accurately), but it still is not necessarily a reliable measure of actual tobacco exposure. Years of education can certainly be measured precisely, but it is still a noisy phenotype given the wide range of attainment and experiences that may result from the same number of years of education. Ultimately, in the case of the study by Rietveld *et al.*, the question remains: What, exactly, is being measured? It seems that a genetic association has been observed for "something," but exactly what will require considerably more work. The nebulous nature of the phenotype makes this task considerably more difficult than in the case of heaviness of smoking.

A reasonable assumption is that educational attainment, and the years spent in schooling, partly reflects intellectual ability; those with a higher intelligence quotient (IQ) generally do better at school. So is this, by the backdoor, the first successful study of the genetics of IQ? That will certainly reignite some old disputes.

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CHEMISTRY

Seeing the Reaction

A molecule is imaged at atomic resolution as it undergoes a chemical reaction.

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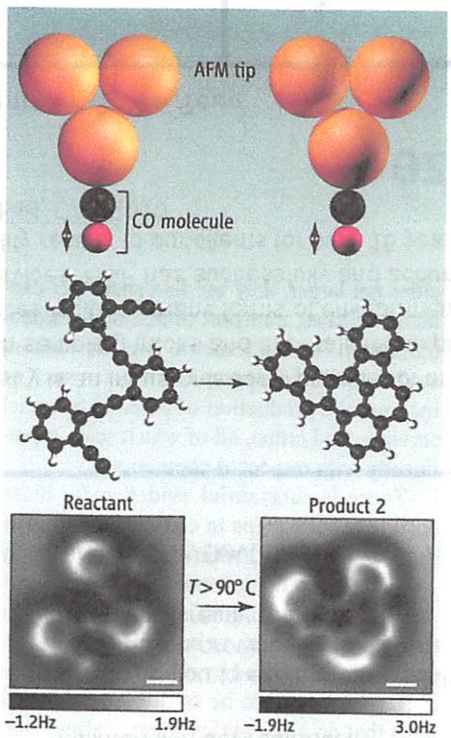
What happens as a molecule goes through a chemical reaction? Model studies have provided important insights into these processes, but it remains extremely difficult to follow all the atomic rearrangements of a chemical reaction experimentally. In many cases, a reaction cannot be observed directly in real space, for example, because the reactants are in the gas state, zooming around at the speed of sound. On page 1434 of this issue, de Oteyza *et al.* (*1*) report atomically resolved imaging of a complex molecule as it undergoes a chemical reaction on a metal surface.

The authors investigated the molecule phenylene-1,2-ethynylene ($C_{26}H_{14}$) adsorbed on a silver surface. Upon heating above 90°C, the molecule split into several different chemical products (see the figure). The authors imaged several different products with scanning tunneling microscopy and identified them with the help of noncontact atomic force microscopy (*2*). They calculated the reaction pathway by density functional theory.

Three challenges had to be met to successfully perform this experiment. First, the authors had to find and synthesize a molecule that undergoes a reaction within the experimentally accessible temperature range, with both reactants and products remaining attached to the metal substrate surface within a viewing field accessible by the microscope.



Before and after. Schematic view of the reactant phenylene-1,2-ethynylene molecule (left) and product 2, one of three different products imaged by de Oteyza *et al.* with atomic force microscopy (AFM). Previous AFM studies focused on imaging individual molecules. Several challenges had to be overcome to extend the method to imaging both the reactant and the reaction products.

Second, they had to overcome the "fat and sticky finger problem" (*3*), which arises because the metal atoms of the probe are large relative to the hydrogen and carbon atoms in organic molecules and exert relatively large attractive forces (*4*). Meyer and co-workers have found a fine solution to this problem by attaching a carbon monoxide molecule to the end of the metal tip, which enabled unprecedented spatial resolution of pentacene, an organic molecule (*5*). This is the imaging method used by de Oteyza *et al.*

Third, the force sensor that holds the metal tip had to be sufficiently sensitive to probe the tiny forces between the carbon monoxide molecule and the organic molecule to be probed. To obtain their results, de Oteyza *et al.* had to operate their atomic force microscope in the small-amplitude mode and perform highly precise frequency measurements (*6*). Further challenges were associated with the complex sample and tip preparation and with heating the sample to initiate the reaction and then cooling it to image acquisition temperature. Overall, the work is a masterful experimental achievement.

The interpretation of image data is comparatively simple for flat hydrocarbons [such as pentacene (*5*) and phenylene-1,2-ethynylene studied by de Oteyza *et al.*], where the submolecular contrast is due to Pauli repulsion between the oxygen atom that terminates the tip and the carbon and hydrogen atoms that constitute the molecule (*7*). The flat orientation of the molecule results in a

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