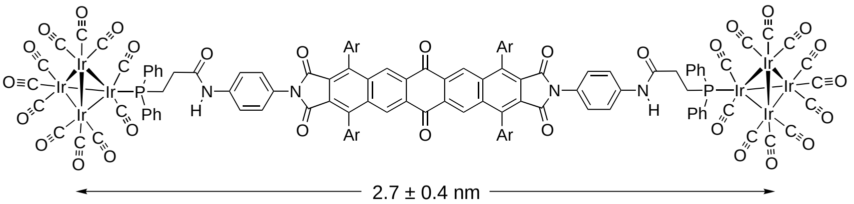
Building Photogenic Molecules—Molecules Made for Direct Individual Observation**

Harry L. Anderson*

How far away can you see a man with the naked eye? This school physics question used to irritate me. The "correct" answer is 10 km. You are meant to work it out by estimating the diffraction limit of your eye; it is the distance at which you should just be able to resolve his head from his feet (if he stands 2 m tall, your pupils are 3 mm wide, and it is a clear day). But resolving his head from his feet is not enough to distinguish him from a gatepost. On the other hand, if he is standing under a spotlight you could see him as an unresolved point of light from almost any distance (limited by the brightness of the light, the whiteness of his coat, the darkness of the background, and his ability to tolerate bright light); you might be able to tell that he is not a gatepost by watching him wander around and by the color of his coat. Looking at individual molecules raises similar issues. This article highlights the synthesis of molecules which are "big enough to see", and briefly outlines the techniques used to see them individually (in contrast to techniques such as X-ray crystallography which average over large populations).

Until about ten years ago, nobody thought it would be possible to see individual molecules with visible light but single-molecule fluorescence spectroscopy is now thriving.[1] A confocal microscope can be used to observe individual fluorescent molecules in solution, in real time, as they diffuse in and out of a focused laser beam (probe volume ≈ 0.5 μm^3).[2] Near-field scanning optical microscopy (NSOM) enables individual fluorescent molecules to be located with a resolution of about 50 nm, an order of magnitude better than the $\lambda/2$ diffraction limit of a conventional optical microscope.[3] This is still not enough to resolve molecular detail, except in gigantic molecules such as DNA (which can be several millimeters long). Beautiful pictures of fluorescent-labeled DNA molecules uncoiling in a shear field have enabled theories of polymer conformational dynamics to be tested with single molecules.[4]

Techniques for imaging matter with atomic resolution have advanced rapidly over the last 30 years. The first was field ion microscopy (FIM).[5] Here, the sample consists of a very sharp anode in a low pressure helium atmosphere; protruding atoms on the anode tip ionize the helium to generate cations, which are accelerated towards a fluorescent screen and create an image of the atomic arrangement on the tip. Unfortunately, organic molecules do not survive this treatment. In the late 1970s, transmission electron microscopy (TEM) became the second technique to achieve atomic resolution.[6] This method relies on the scattering of high energy electrons as they pass through a thin sample. TEM can reveal individual heavy atoms but organic molecules do not normally show up because they produce too little scattering and are damaged by electrons. Miller and co-workers evaded this problem by attaching tetrairidium clusters to each end of their molecule to give **1**; TEM images of this compound show pairs of dots at 2.7 ± 0.4 nm separation, which is the expected length (the length range is due to the flexibility of the amide linker).[7] Recently, the same Ir_4 clusters have been used to visualize viral capsid proteins.[8] The third and most important technique for seeing atoms is scanning tunneling microscopy (STM).[5, 9] Binnig and Rohrer invented STM in 1982 and were awarded the Nobel Prize in Physics for it only four years later (together with Ruska for electron microscopy). In the simplest form of this technique, a sharp tungsten electrode is scanned over the surface of a conducting sample; feedback from the tunneling current between the electrode tip and the



1 (Ar = *p-tert*-butylphenyl)

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[*] Dr. H. L. Anderson
University of Oxford
Department of Chemistry
Dyson Perrins Laboratory
South Parks Road, Oxford OX1 3QY (UK)
Fax: (+44) 1865-275674
E-mail: harry.anderson@chem.ox.ac.uk

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surface is used to keep the tip at a fixed distance (about 0.5 nm) from the surface; this tunneling current is extremely dependent on the distance—nearly all the current flows from the most prominent atom of the tip, so atom-sized variations in the height, or the work function, of the surface can be imaged. This opened the way to direct observation of simple molecules such as benzene,[10] naphthalene,[11] phthalocyanines,[12] and porphyrins.[13, 14] The spectacular resolution which can be achieved by STM is illustrated by the image of a single-walled carbon nanotube in Figure 1 a, which reveals the hexagonal-ring structure and helicity of the nanotube; simultaneous current–voltage measurements showed that this particular nanotube has a metallic character.[15] STM also led to the invention of many other scanning probe microscopies, such as NSOM (above) and atomic force microscopy (AFM), which images surfaces by measuring the force they exert on a scanning tip.[16] AFM gives lower resolution than STM but does not require electrically conductive samples. Figure 1 b shows an AFM image of dendron-jacketed polymer **2**; comparison of the weight-averaged contour length of these wormlike objects (142 nm) with the calculated average length for an all-*trans* conformation (101 nm) shows that the backbone is almost fully extended by the dendron jacket.[17]

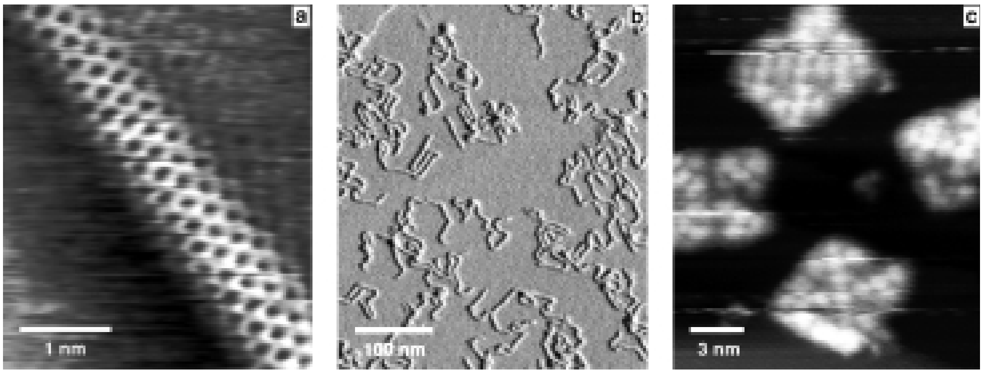
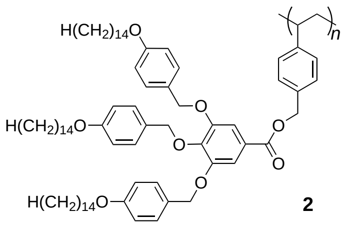


Figure 1. A triptych of molecular images: a) A single-walled carbon nanotube imaged by STM at 77 K (reproduced from ref. [15] with permission); b) AFM micrograph of dendron jacketed polymer **2** on pyrolytic graphite (reproduced from ref. [17]); c) STM image of porphyrin henicosamer **5** on a Cu(111) surface (reproduced from ref. [19] with permission).



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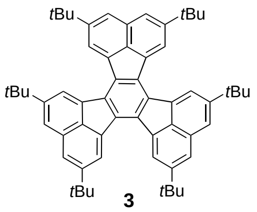
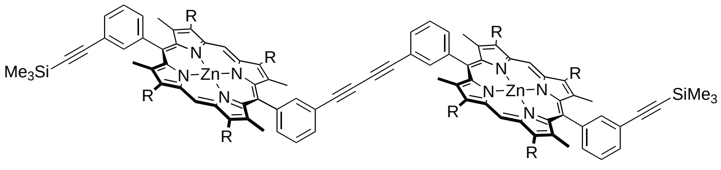
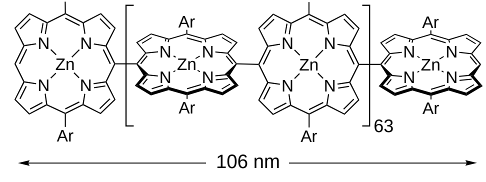


3

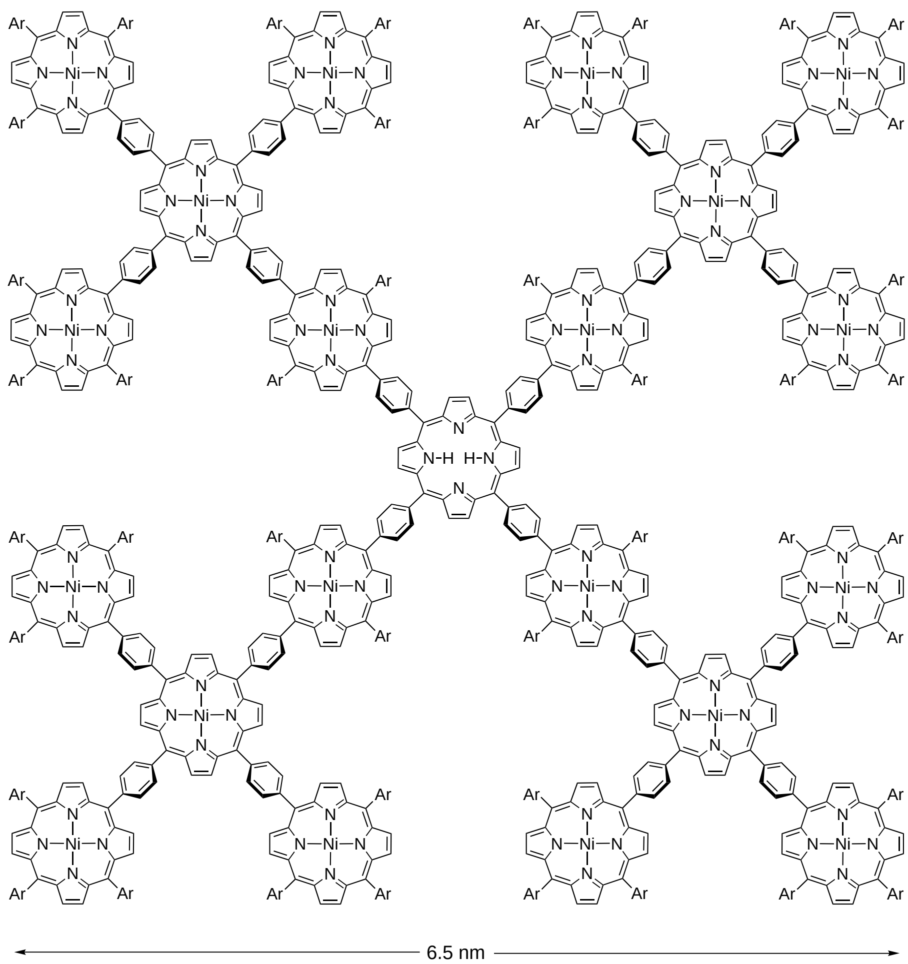
In order to view individual molecules by STM, it is essential to limit their motion. They need to be securely adsorbed onto a solid surface and it helps to use rigid molecules and low temperatures. Images of large symmetric molecules are easiest to interpret. Gimzewski and coworkers have reported amazing STM images of hexa-*tert*-butyl decacylene **3** on a Cu(100) surface at room temperature.[14] Steric interactions in a close-packed monolayer keep these molecules stationary and a lobe is seen for each of the six *t*Bu groups of each molecule but, at gaps in the monolayer, the molecules have space to spin, which blurs their STM images and forms "supramolecular bearings". Gimzewski's team has also used a STM tip to reposition porphyrin molecules on a surface, building supramolecular noncovalent porphyrin arrays on an individual basis.[14] Porphyrins and porphyrin oligomers are particularly suitable for STM because of their large, rigid structures. Welland, Sanders, and co-workers have used STM to observe molecules of the porphyrin dimer **4** in *cisoid* and *transoid* conformations, in which the planes of the porphyrin moieties lie perpendicular to the underlying copper surface.[18] Sakata's group have reported images of a porphyrin henicosamer **5** consisting of 20 nickel porphyrins linked by a central free-base unit (Figure 1 c).[19] Steric interactions force the *para*-phenylene linkers perpendicular to the porphyrins, so the whole molecule tends to adopt a square-planar geometry. The square pattern of 21 porphyrins is clearly visible and its size (6.5 nm × 6.5 nm) matches the expected dimensions. Even this giant porphyrin 21-mer is dwarfed by the linear porphyrin 128-mer **6** reported recently by Osuka and co-workers;[20] with a calculated length of 106 nm, this molecule should be long enough to be resolved by NSOM. Neighbouring porphyrin units in **6** are approximately orthogonal, which must contribute to its surprisingly high solubility. This twisted conformation prevents conjugation but energy transfer may still be efficient, so the structure may behave as a long distance "photonic molecular wire". As synthetic mol-



4 ($R = CH_2CH_2CO_2Me$)



6 (Ar = 3,5-dioctyloxyphenyl)



5 (Ar = 3,5-diisoamyloxyphenyl)

ecules grow to nanoscopic and even microscopic sizes, direct observation will become an increasingly important characterization technique because it gives information on shape without the need for crystallization and without statistical averaging.

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[1] W. E. Moerner, M. Orrit, *Science* **1999**, *283*, 1670–1676; S. Weiss, *Science* **1999**, *283*, 1676–1683; Y. Ishii, T. Yanagida, *Single Mol.* **2000**, *1*, 5–13.

[2] S. Nie, D. T. Chiu, R. N. Zare, *Science* **1994**, *266*, 1018–1021.

[3] E. Betzig, R. J. Chichester, *Science* **1993**, *262*, 1422–1425; T. Basché, *Angew. Chem.* **1994**, *106*, 1805–1807; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1723–1725; R. Zenobi, V. Deckert, *Angew. Chem.* **2000**, *112*, 1814–1825; *Angew. Chem. Int. Ed.* **2000**, *39*, 1746–1756.

[4] D. E. Smith, H. P. Babcock, S. Chu, *Science* **1999**, *283*, 1724–1727.

[5] J. C. Rivière, *Surface Analytical Techniques*, Oxford University Press, Oxford, **1990**.

[6] E. Ruska, *Angew. Chem.* **1987**, *99*, 611–621; *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 595–605.

[7] F. R. Furuya, L. L. Miller, J. F. Hainfeld, W. C. Christopfel, P. W. Kenny, *J. Am. Chem. Soc.* **1988**, *110*, 641–643.

[8] N. Cheng, J. F. Conway, N. R. Watts, J. F. Hainfeld, V. Joshi, R. D. Powell, S. J. Stahl, P. E. Wingfield, A. C. Steven, *J. Struct. Biol.* **1999**, *127*, 169–167.

[9] G. Binnig, H. Rohrer, *Angew. Chem.* **1987**, *99*, 622–631; *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 606–614.

[10] H. Ohtani, R. J. Wilson, S. Chiang, C. M. Mate, *Phys. Rev. Lett.* **1988**, *60*, 2398–2401; P. S. Weiss, D. M. Eigler, *Phys. Rev. Lett.* **1993**, *71*, 3139–3142.

[11] V. M. Hallmark, S. Chiang, J. K. Brown, C. Wöll, *Phys. Rev. Lett.* **1991**, *66*, 48–51.

[12] P. H. Lippel, R. J. Wilson, M. D. Miller, C. Wöll, S. Chiang, *Phys. Rev. Lett.* **1989**, *62*, 171–174.

[13] M. Kunitake, U. Akiba, N. Batina, K. Itaya, *Langmuir* **1997**, *13*, 1607–1615.

[14] J. K. Gimzewski, C. Joachim, *Science* **1999**, *283*, 1683–1688.

[15] T. W. Odom, J.-L. Huang, P. Kim, C. M. Lieber, *Nature* **1998**, *391*, 62–64.

[16] C. F. Quate, *Surf. Sci.* **1994**, *299/300*, 980–995.

[17] S. A. Prokhorova, S. S. Sheiko, M. Möller, C.-H. Ahn, V. Percec, *Macromol. Rapid Commun.* **1998**, *19*, 359–366.

[18] N. Bampos, C. N. Woodburn, M. E. Welland, J. K. M. Sanders, *Angew. Chem.* **1999**, *111*, 2949–2953; *Angew. Chem. Int. Ed.* **1999**, *38*, 2780–2783.

[19] K. Sugiura, H. Tanaka, T. Matsumoto, T. Kawai, Y. Sakata, *Chem. Lett.* **1999**, 1193–1194.

[20] N. Aratani, A. Osuka, Y. H. Kim, D. H. Jeong, D. Kim, *Angew. Chem.* **2000**, *112*, 1517–1521; *Angew. Chem. Int. Ed.* **2000**, *39*, 1458–1462.