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LETTERS

## A tower-shaped prototypic molecule designed as an atomically sharp tip for AFM applications

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### Abstract

The synthesis of macrocycle **1** using a series of Sonogashira coupling reactions is described. This tower-shaped prototypic molecule tapers to a single hydrogen atom and is designed to serve as an atomically sharp molecular tip for atomic force microscopy imaging studies. © 1999 Elsevier Science Ltd. All rights reserved.

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Atomic force microscopy (AFM) is a relatively recent<sup>1</sup> and rapidly expanding<sup>2</sup> atomic level analytical technique that directly images three-dimensional surfaces of non-conducting (e.g. biological) substrates.<sup>3</sup> The AFM images are formed by reconstructing the contour of force interactions exerted between the scanning tip and the surface. Although not precisely defined, the resolution of AFM is limited by the large tip size relative to the dimensional parameters of individual substrate molecules. Mechanically produced tips composed of silicon nitride with a radius of curvature of about 200 Å are available commercially.<sup>4</sup> Even with this limitation, remarkable images have been obtained for objects ranging from biomolecules to miniature devices.

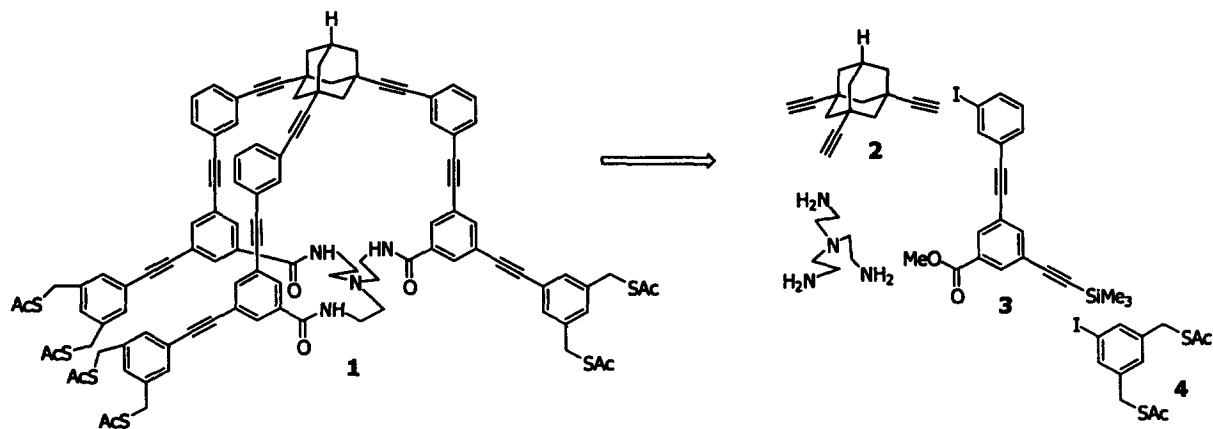
Obviously, finer tips will be required to achieve resolution on an atomic scale, particularly when imaging is performed in liquid media. A molecular tip composed of a protein-like molecule designed to bind to the crystal corner of an AFM tip has been proposed by Drexler.<sup>5</sup> A multiwalled carbon nanotube attached to a conventional silicon tip has been used for AFM imaging work.<sup>6</sup> More recently, interesting caltrop shaped molecules based on a differentially substituted tetrahedral silicon atom have been developed as potential AFM tips.<sup>7</sup> Herein, we report the synthesis of tip **1**<sup>8</sup> by adaptation of elegant chemistry leading to dendrimers and linear oligomeric phenylacetylenes.<sup>9</sup> Adamantane was chosen for the tip of the tower for several reasons: (a) the adamantane ring system is rigid; (b) adamantane can be selectively functionalized at three of the bridgehead carbons, thus allowing attachment of the legs; and (c) the adamantane unit tapers the tower to a single hydrogen atom or other moiety attached to the fourth

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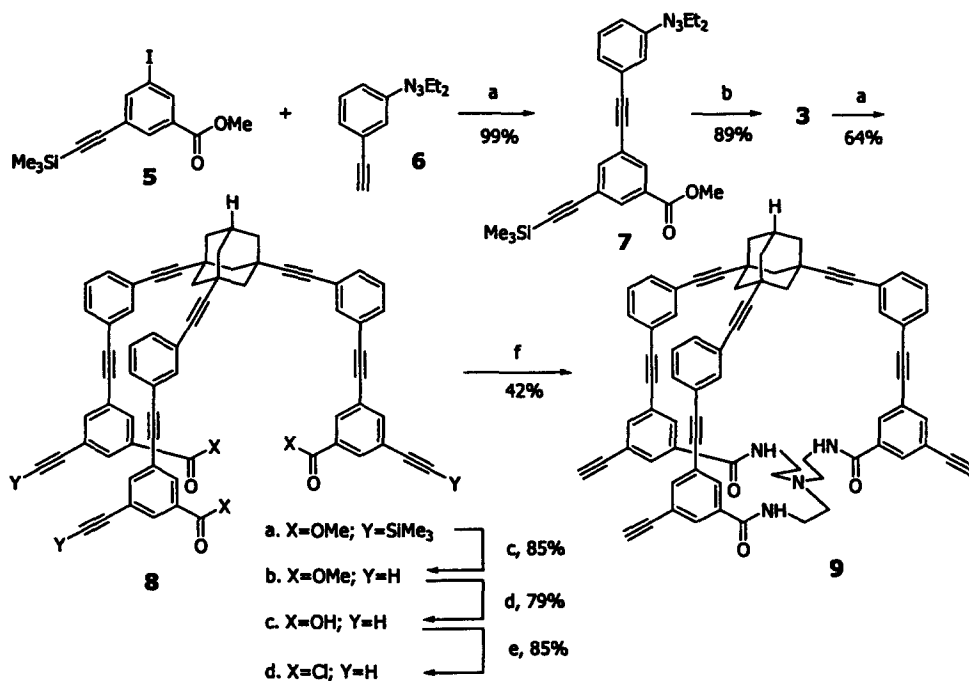
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bridgehead carbon atom. The S atoms in the feet are designed to anchor the tip to a thin film of gold placed on a conventional AFM tip. The base of tip 1 is deliberately wide so that adjacent tip molecules bound to the convex gold coated surface do not interfere with imaging by the uppermost single tip.

A retrosynthetic disconnection of tip 1 into four building blocks is shown in Scheme 1. Leg 3 was synthesized as follows. A palladium catalyzed Sonogashira coupling reaction between iodide 5<sup>10</sup> and phenylacetylene 6 gave ester triazene 7<sup>11,12</sup> in 99% yield (Scheme 2).



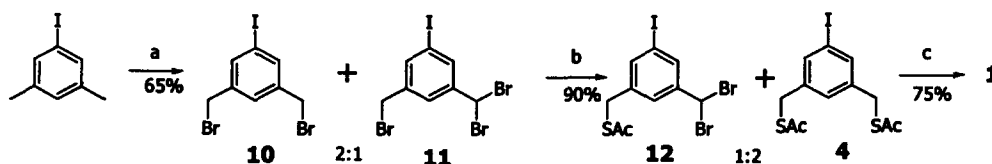
Scheme 1.



Scheme 2. Reagents and conditions: (a) 0.05 equiv. Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>, 0.20 equiv. CuI, 1 equiv. of 5, 1 equiv. of 6 (for 7) or 1 equiv. of 3, 1/3 equiv. of 2 (for 8a), Et<sub>3</sub>N, reflux, 20 h; (b) MeI, 120°C in sealed tube, 30 h; (c) K<sub>2</sub>CO<sub>3</sub>, CHCl<sub>3</sub>/MeOH, rt, 2.5 h; (d) 20% NaOH, CHCl<sub>3</sub>/EtOH, rt, 4 h; (e) (COCl)<sub>2</sub>, DMF (catalytic), benzene, rt, 20 h; (f) solution 1: 0.2008 mmol of 8d and 508 μL of DMA in 10 mL of C<sub>6</sub>H<sub>5</sub>Cl; solution 2: 0.410 mmol of tris(2-aminoethyl)amine in 10 mL of C<sub>6</sub>H<sub>5</sub>Cl. Both solutions were added to 150 mL of C<sub>6</sub>H<sub>5</sub>Cl using a two lines syringe pump at 1 mL/h, and then stirred for 20 h at rt

Heating **7** in methyl iodide at 120°C gave aryl iodide **3**, (89%) which was then coupled to triethynyladamantane **2**<sup>13</sup> by the same cross-coupling reaction giving protected triester **8a**. Desilylation of **8a** with potassium carbonate in CHCl<sub>3</sub>/MeOH gave the triester **8b**, (85%) which was hydrolyzed with aqueous sodium hydroxide to give **8c**, (79%). Yields were lower when the hydrolysis and desilylation steps were combined. Triacid **8c** was converted into tris acid chloride **8d** (85%) using excess oxalyl chloride. Careful reaction of **8d** with tris(aminoethyl)amine under high dilution conditions<sup>14</sup> gave the macrocyclic amide **9**,<sup>15</sup> in 42% yield.

The foot fragment **4** was synthesized as shown in Scheme 3. 5-Iodo-*m*-xylene was treated with NBS to give a mixture of mono-, di- and tribromides from which a mixture of dibromide **10** and tribromide **11** could be easily obtained (65%) by column chromatography. Treatment of the mixture of **10** and **11** with triethylammonium thiolacetate (prepared in situ by mixing 1 equiv. of Et<sub>3</sub>N and 1 equiv. of thioacetic acid in THF) yielded **4**, (90%) which was easily separated from the accompanying dibromide **12**. Foot **4** was coupled with triethynyltriamide **9** to give tip **1**. Although the thiolacetate groups could be converted into free thiol groups for chemical bonding to the gold coated tip surfaces if necessary, it may be possible to attach the tip molecule directly through thiolacetates.<sup>16</sup> Tip **1** serves as a prototype for a series of tips with different apex atoms, legs and feet which are under development in our laboratory.



Scheme 3. Reagents and conditions: (a) 2 equiv. NBS, CCl<sub>4</sub>, 250 watt incandescent lamp, rt, 6 h; (b) 1 equiv. of Et<sub>3</sub>NH<sup>+</sup>AcS<sup>-</sup> for each CH<sub>2</sub>Br group, THF, rt, 10 min; (c) 0.05 equiv. Pd(PPh<sub>3</sub>)Cl<sub>2</sub>, 0.20 equiv. CuI, 1 equiv. of **4**, 1/3 equiv. of **9**, Et<sub>3</sub>N/benzene, reflux, 20 h

## Acknowledgements

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11. 300 MHz  $^1\text{H}$  NMR: **7** ( $\text{CDCl}_3$ )  $\delta$  0.27 (s, 9H), 1.28 (brt,  $J=6.9$ , 6H), 3.78 (q,  $J=7.2$ , 4H), 3.94 (s, 3H), 7.30 (m, 2H), 7.42 (m, 1H), 7.60 (s, 1H), 7.80 (t,  $J=0.9$ , 1H), 8.07 (t,  $J=1.5$ , 1H), 8.13 (dd,  $J=0.9$ , 1.5, 1H); **3** ( $\text{CDCl}_3$ )  $\delta$  0.27 (s, 9H), 3.94 (s, 3H), 7.10 (t,  $J=8.0$ , 1H), 7.48 (d,  $J=7.5$ , 1H), 7.69 (d,  $J=8.1$ , 1H), 7.78 (s, 1H), 7.89 (s, 1H), 8.09 (s, 1H), 8.11 (s, 1H); **8a** ( $\text{CDCl}_3$ )  $\delta$  0.26 (s, 27H), 1.93 (brs, 6H), 2.06 (m, 1H), 2.16 (brs, 6H), 3.98 (s, 9H), 7.29 (t,  $J=7.5$ , 2H), 7.38 (d,  $J=7.5$ , 3H), 7.42 (d,  $J=7.5$ , 3H), 7.59 (s, 3H), 7.78 (s, 2H), 8.07 (s, 3H), 8.11 (s, 3H); **8b** ( $\text{CDCl}_3$ )  $\delta$  1.93 (brs, 6H), 2.16 (brs, 6H), 2.26 (brs, 1H), 3.15 (s, 3H), 3.94 (s, 9H), 7.29 (t,  $J=7.5$ , 3H), 7.38 (d,  $J=7.8$ , 3H), 7.43 (d,  $J=7.5$ , 3H), 7.59 (s, 3H), 7.79 (s, 3H), 8.10 (s, 3H), 8.15 (s, 3H); **8c** (50%  $\text{CD}_3\text{OD}/\text{CDCl}_3$ )  $\delta$  2.57 (brs, 6H), 2.13 (brs, 6H), 2.22 (brs, 1H), 3.40 (s, 3H), 7.28 (t,  $J=7.5$ , 3H), 7.36 (d,  $J=8.1$ , 3H), 7.41 (d,  $J=7.5$ , 3H), 7.55 (s, 3H), 7.74 (s, 3H), 8.04 (s, 3H), 8.10 (s, 3H); **8d** ( $\text{CDCl}_3$ )  $\delta$  1.93 (brs, 6H), 2.16 (brs, 6H), 2.27 (m, 1H), 3.21 (s, 3H), 8.20 (t,  $J=1.5$ , 3H), 7.31 (t,  $J=7.8$ , 3H), 7.40 (dt,  $J=1.5$ , 8.1, 3H), 7.45 (dt,  $J=1.5$ , 7.8, 3H), 7.60 (t,  $J=1.5$ , 3H), 7.89 (t,  $J=1.5$ , 3H), 8.16 (t,  $J=1.5$ , 3H); **9** ( $\text{CDCl}_3$ )  $\delta$  1.91 (brs, 6H), 2.17 (AB,  $J=12.6$ , 6H), 2.26 (brs, 1H), 2.95 (t,  $J=7.5$ , 6H), 3.14 (s, 3H), 3.59 (q,  $J=6.3$ , 6H), 6.54 (t,  $J=5.1$ , 3H), 7.25–7.32 (m, 3H), 7.34 (td,  $J=1.5$ , 7.5, 3H), 7.39 (td,  $J=1.5$ , 7.5, 3H), 7.64 (brs, 3H), 7.69 (t,  $J=1.5$ , 3H), 7.73 (t,  $J=1.5$ , 3H), 7.92 (t,  $J=1.5$ , 3H); **9** ( $\text{CDCl}_3$ , two drops  $\text{CD}_3\text{OD}$ )  $\delta$  1.88 (brs, 6H), 2.16 (AB,  $J=12.9$ , 6H), 2.22 (brs, 1H), 2.85 (t,  $J=6.9$ , 6H), 3.13 (s, 3H), 3.47 (m, 6H), 7.24 (t,  $J=7.5$ , 3H), 7.31 (brd,  $J=7.5$ , 3H), 7.36 (brd,  $J=7.5$ , 3H), 7.60 (brs, 3H), 7.67 (brs, 3H), 7.83 (t,  $J=1.5$ , 3H), 7.85 (brs, 3H); **4** ( $\text{CDCl}_3$ )  $\delta$  2.36 (s, 6H), 4.00 (s, 4H), 7.15 (brs, 1H), 7.51 (brs, 2H); **1** ( $\text{CDCl}_3$ )  $\delta$  1.93 (brs, 6H), 2.20 (AB,  $J=13.4$ , 6H), 2.29 (m, 1H), 2.37 (s, 18H), 3.02 (t,  $J=7.3$ , 6H), 3.62–3.71 (m, 6H), 4.08 (s, 12H), 6.49 (t,  $J=5.3$ , 3H), 7.18 (s, 3H), 7.25–7.30 (m, 3H), 7.31–7.39 (m, 12H), 7.42 (d,  $J=7.6$ , 3H), 7.47–7.54 (m, 18H), 7.69 (d,  $J=8.5$ , 6H), 7.76 (d,  $J=8.5$ , 6H), 8.01 (s, 3H).
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