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Nanoscale 1,3,5,7-Tetrasubstituted Adamantanes and *p*-Substituted Tetraphenyl-methanes for AFM Applications

Quan Li, Aleksey V. Rukavishnikov, Pavel A. Petukhov, Tatiana O. Zaikova, and John F. W. Keana*

Department of Chemistry, University of Oregon, Eugene, Oregon 97403-1253

jkeana@oregon.uoregon.edu

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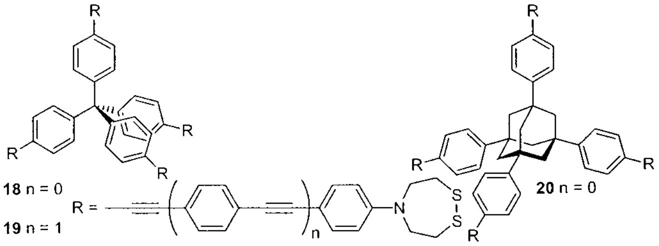
ABSTRACT



Tetrahedrally shaped nanoscale molecules 18–20 were synthesized from the corresponding tetraiodide by a series of Sonogashira coupling reactions. Three of the sulfur-containing termini are intended for eventual binding to a gold-coated conventional AFM tip, while the fourth terminus scans the sample. AFM images of 19 demonstrate that the molecule is sufficiently large and rigid to be imaged by a conventional AFM tip.

Atomic force microscopy (AFM) is a powerful, relatively recent,[1] and rapidly expanding[2−4] molecular imaging technique of broad applicability. Among the several capabilities of the technique is the ability to observe individual biomolecules such as DNA as they lay on an atomically flat surface either in air or in a buffer solution. A major factor limiting resolution in AFM is the sharpness of the AFM tip that scans the sample. The sharpest commercially available tips for tapping mode AFM are conically or pyramidally shaped etched silicon or silicon nitride tips with a nominal radius of curvature as low as ∼4−50 nm (uncoated). The aspect ratio (tip height/base)[5] is another important tip feature. Tips with the best combination of aspect ratio and sharpness reported to date have a multiwalled (MWNT)[6,7] (∼9 nm radius) or single-walled (SWNT) carbon nanotube (∼3 nm, ultimate limit, ∼0.5−0.7 nm radius[7]) as the functioning tip.[8] Methods of attachment of the nanotubes to conventional tips require specialized equipment. Yao and Tour[9] recently published some interesting caltrop-shaped tetrasubstituted silanes with potential as tips for AFM imaging. At about the same time, we described the synthesis of a prototypic

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[2] For an introduction to AFM and an overview, see: Colton, R. J.; Baselt, D. R.; Dufrene, Y. F.; Green, J. B. D.; Lee, G. U. *Curr. Opin. Chem. Biol.* **1997**, *1*, 370.

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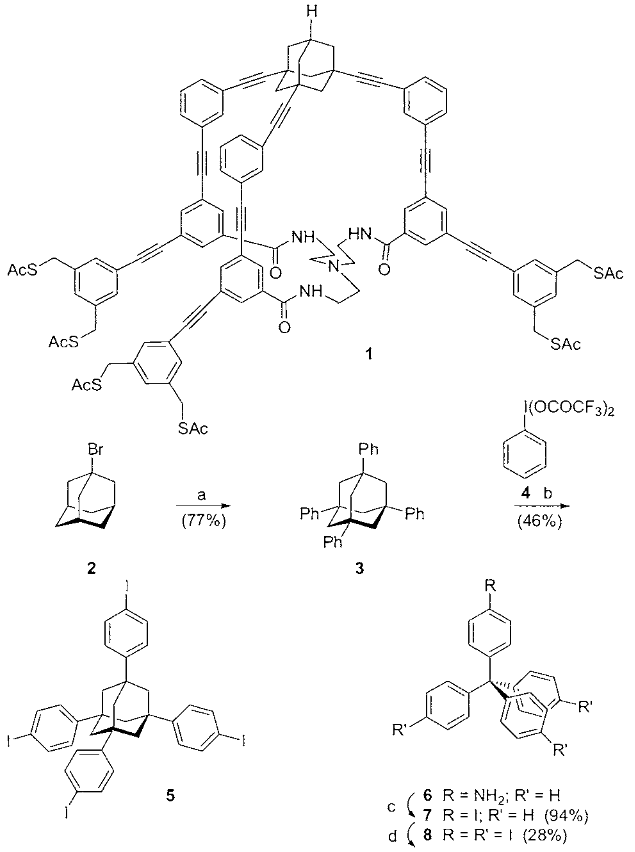
10.1021/ol026495+ CCC: $22.00

Scheme 1[a]



[a] Reaction conditions: (a) *t*-BuBr, $AlCl_3$, PhH, Δ 2 h; (b) **4**, I_2, (c) $NaNO_2$, HCl, then KI; (d) **4**, I_2.

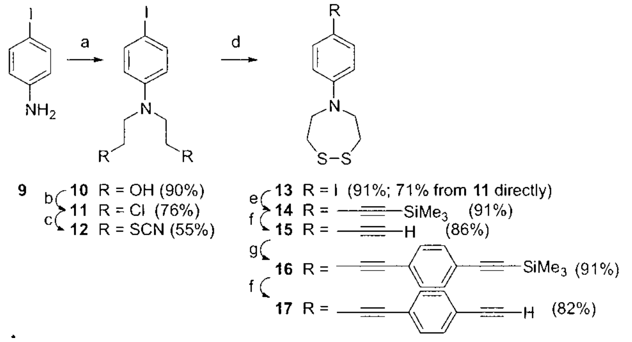
tower-shaped molecule **1** (Scheme 1) as an inroad to a series of single molecule tips for AFM applications.[10,11]

Herein, we describe the synthesis of several tetrahedrally shaped nanoscale molecules built around a 1,3,5,7-tetrasubstituted adamantane unit or else a para-substituted tetraarylmethane core.[12] Given the high affinity that thiols,[13] disulfides,[13] and thiolacetates[14] display toward gold, we included S atoms at the termini as a means to eventually anchor the molecular tip to a thin film of gold placed on a conventional AFM tip.[15] We also demonstrate that **19** is sufficiently rigid and robust to be visualized using a conventional AFM tip while laying on an atomically flat mica surface.

Tetrahedrally shaped precursors **5**[16] and **8**[17] were synthesized as follows. Tetraphenyladamantane **3** was prepared by arylation of 1-bromoadamantane in a mixture of hot benzene, *tert*-butyl bromide, and $AlCl_3$. The low solubility of **3** allows facile purification by washing with $CHCl_3$ in a Soxhlet extractor. Treatment of adamantane **3** with [bis(trifluoroacetoxy)iodo]benzene (**4**) and iodine gave tetraiodide **5**. Tetraiodide **8** was synthesized from *p*-tritylaniline (**6**), which was diazotized and reacted with KI to give iodide **7**. Further iodination of **7** with **4** in the presence of iodine gave tetraiodide **8**.

We chose a substituted [1,2,5]-dithiazepane unit for eventual binding of the tips to a gold surface. 4-Iodoaniline (**9**) was treated with ethylene oxide to give diol **10**, which was converted into dichoride **11** (Scheme 2).

Scheme 2[a]



[a] Reaction conditions: (a) Ethylene oxide, MeOH; (b) $POCl_3$, pyridine; (c) KSCN; (d) KOH; (e) TMSA, $Pd(PPh_3)_2$, CuI, THF/Et_3N; (f) K_2CO_3, MeOH; (g) (**4**-iodophenylethynyl)trimethylsilane, $Pd(PPh_3)_2$, CuI, THF/Et_3N.

Reaction of **11** with KSCN gave dithiocyanate **12**, which was converted into [1,2,5]-dithiazepane **13** upon treatment with hot KOH. Alternatively, reaction of **11** with excess KSCN afforded **13** directly. Reaction of **13** with trimethylsilylacetylene (TMSA) gave **14**. Cleavage of **14** gave alkyne **15**, which in turn was treated with (4-iodo-phenylethynyl)-trimethylsilane under Sonogashira coupling conditions to give TMS derivative **16**. Cleavage of **16** gave terminal alkyne **17**. Alkynes **15** and **17** were separately coupled to tetraiodide **8** under Sonogashira conditions to give tetraphenylmethane **18** and its larger analogue **19**, respectively (Scheme 3). Alternatively, tetraiodide **5** was coupled to alkyne **15** to give symmetrically tetrasubstituted adamantane **20**.

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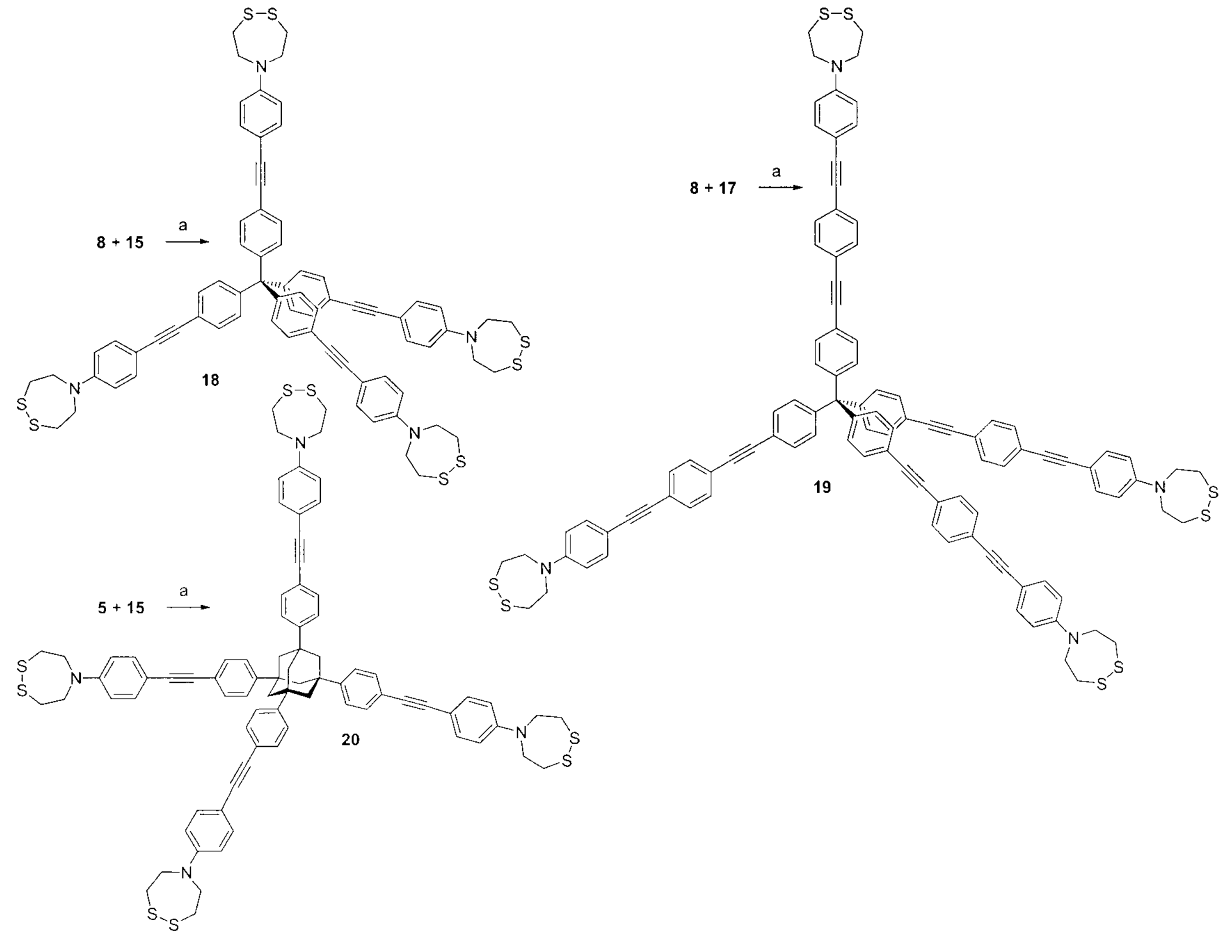
Scheme 3[a]



[a] Reaction conditions: (a) $Pd(PPh_3)_2$, CuI, THF/Et_3N.

Visualization of Molecule 19 Using a Conventional AFM Tip. Freshly cleaved mica was separately spin-coated with 0.06, 0.25, and 1.00 μM solutions of molecule **19** in CH_2Cl_2 and then examined by AFM in air and ambient humidity using a conventional tip with tapping mode (Figure 1B−D). The light spots are images of individual molecules[18] laying on the mica surface. The observed heights[19] of the molecules in Figures 1B−D are 0.8 ± 0.1 nm, 1.0 ± 0.2 nm, and 0.5 ± 0.1 nm.[20] The variation in height likely stems from day to day differences in humidity[21] and set up parameters (drive amplitude A_0 and set point amplitude A_{sp}[22,23]). The height determined by AFM is lower than the calculated height based on molecular modeling. This is consistent with similar differences observed for DNA[24] and C_{60}[18] and may be due to molecular deformations caused by the AFM tip. As a control, freshly cleaved mica was separately spin-coated with the CH_2Cl_2 used as the solvent (Figure 1A) and a 1 μM solution of segment **17** (Figure 1E) in CH_2Cl_2 and then examined by AFM. Segment **17** is much smaller than **19** and can lay flat on the mica surface. As expected, only the mica surface is seen in both control images, absent features analogous to those observed with **19**.

Figure 1F shows images of **19** in the presence of DNA fragments, which were deposited onto mica from aqueous buffer and washed extensively prior to spin-coating a 0.25 μM solution of **19** in CH_2Cl_2. The observed height (0.6 ± 0.1 nm) of **19** is similar to that of the DNA fragments (0.7 ± 0.1 nm), as expected. Images B−D demonstrate that the number of individual molecules of **19** appearing in the images is concentration dependent.

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(18) Individual fullerene molecules (C_{60}) on a Si(111) surface have been imaged by AFM in a noncontact mode in an ultrahigh vacuum. See: Kobayashi, K.; Yamada, H.; Horiuchi, T.; Matsushige, K. *Appl. Surf. Sci.* **1999**, *140*, 281.

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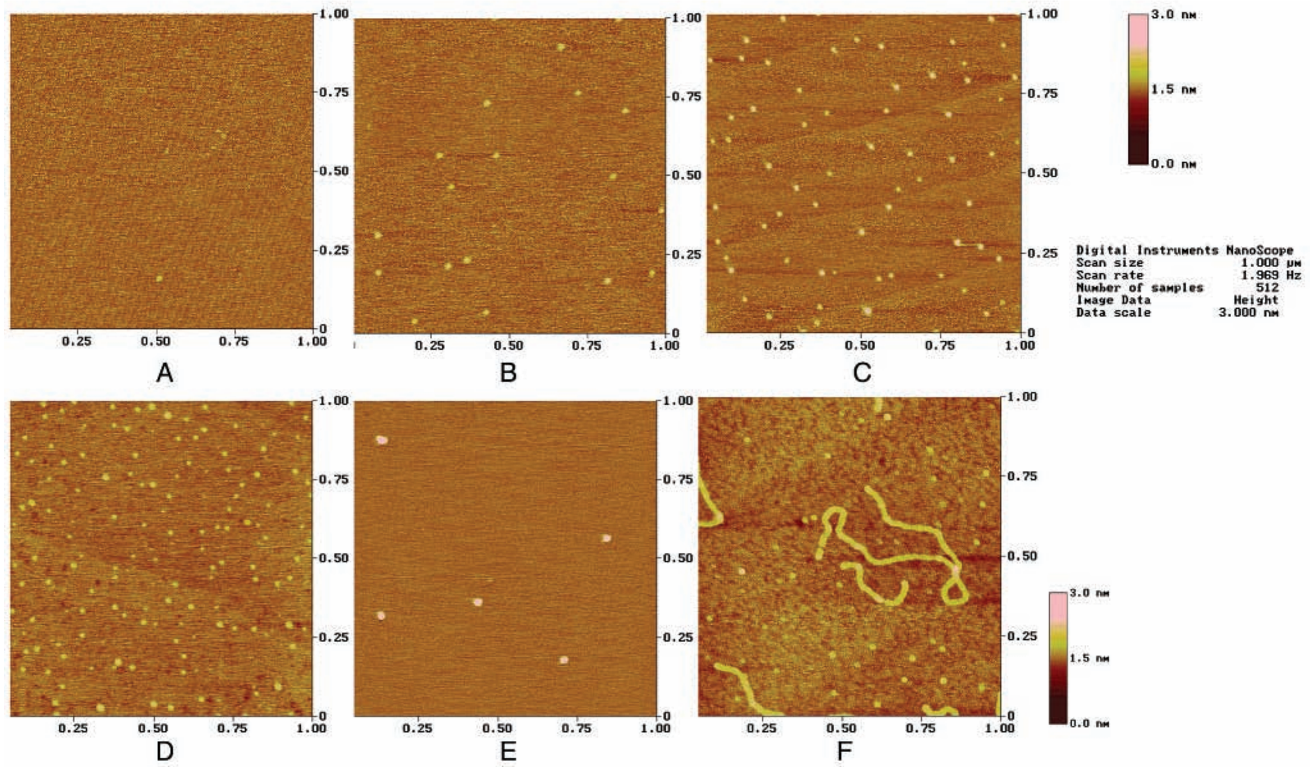

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Digital Instruments NanoScope
Scan size                 1.000 μm
Scan rate                 1.969 Hz
Number of samples           512
Image Data               Height
Data scale             3.000 nm
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Figure 1. AFM images (1.00 × 1.00 μm) of freshly cleaved mica after spin-coating with the following: A, CH_2Cl_2 used as the solvent (control image); B, 0.06 μM solution of **19** in CH_2Cl_2; C, 0.25 μM solution of **19** in CH_2Cl_2; D, 1 μM solution of **19** in CH_2Cl_2; E, 1 μM solution of segment **17** in CH_2Cl_2 (control image). For image F, DNA was applied to the mica prior to spin-coating a 0.25 μM solution of **19** in CH_2Cl_2. Note the dependence of molecule **19** image density on concentration (B−D). Nanofeatures such as those in control images A (observed height, 0.6 nm) and E (observed height, 2.1 ± 0.1 nm) are occasionally seen on certain regions of the surface when imaging freshly cleaved mica and may represent mica particulates produced as a result of the cleavage.[23]

In summary, we have synthesized three tetrahedrally shaped nanoscale molecules **18**−**20**. These molecules are designed to serve as molecular tips for AFM and may also find application as chemically well-defined objects for calibration of commercial AFM tips. AFM images of **19** demonstrate that the molecule is sufficiently large and rigid to be imaged by a conventional AFM tip. Efforts to attach the molecules to commercial AFM tips are underway.

Acknowledgment. This work was supported by a grant from the National Institutes of Health (GM 27137).

Supporting Information Available: Experimental procedures and AFM conditions, ^{1}H NMR spectra for **5**, **7**, **8**, and **10**−**20**, and ^{13}C NMR spectra for **5** and **10**−**20**. This material is available free of charge via the Internet at http://pubs.acs.org.

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