Arts and Sciences Unite in Nanoput: Communicating Synthesis and the Nanoscale to the Layperson

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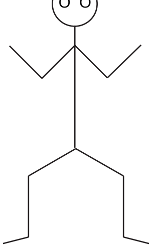
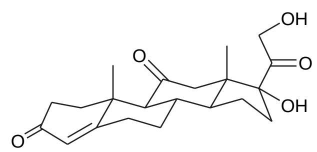
Synthetic chemists have long been fascinated by the ability to manipulate matter at the nanoscale with an atomistic precision that is unrivaled by the tools of any other profession. To the frustration of the chemist, however, the layperson often fails to appreciate the splendor within a field that builds entities that cannot be seen by the naked eye. Moreover, the structural drawings that chemists use, which themselves are simple representations of far richer quantum mechanical phenomena, hold little attraction to the unseasoned. For example, even the earth's earliest humans valued the simple communicative forms of stick figures, Figure 1a. However, a similarly drawn structure of cortisone (Figure 1b), one of the adrenicortical hormones used extensively in the treatment of rheumatoid inflammations, is not easily recognized and understood for what it represents except by the organic or medicinal chemist *(1)*. When artists and scientists intermingle, their differing codes of expression often inhibit interaction. Can the molecular sciences and the visual arts occasionally unite to the benefit of both fields? In this paper, we use the tools of the synthetic chemist, executed at the nanoscale level, to convey the art, form, and precision of the science in a venue that can be valued by the chemist and layperson alike. As the reader will see, we take some liberty in presentation only; precise chemical rigor and accuracy are maintained throughout the syntheses and characterization reported here en route to 2-nm tall molecules that resemble human figures. We therefore implore the indulgence of the chemist to see the nontraditional descriptions as a presentation to the untrained—a demonstration that would permit laypersons to appreciate the canvas of the chemical artisan. Likewise, we ask the artist to kindly endure the chemical details that are fundamental to the assurances of molecular authenticity.



a



b

Figure 1. (a) A simple stick figure structure that is immediately recognizable as a representation of a person. (b) A simple stick figure structure of the steroid cortisone.

Others have aimed to coalesce the arts and science through sculpture, canvas, pictures, images, poetry, and literature *(2–5)*. In recent micron-sized examples, Kawata et al., fashioned a 10-μm long bull-shaped sculpture from a urethane–acrylate resin *(6)*, while many other artistic structures have been created in silicon by lithographic techniques *(7)*. We take a far smaller approach by entering the truly nanoscopic regime in which each 2-nm tall figure, termed here a Nanoputian,[1] is a single molecule. Using tools of chemical synthesis, the ultimate in designed miniaturization is reached; beyond this size domain there is no conceivable entity upon which to tailor architectures that could have programmed cohesive interactions between the individual building blocks. To NanoKid, the progenitor of the Nanoputians, different "head" moieties were attached by acetal exchange under microwave irradiation (using a standard home-kitchen unit) to ultimately produce recognizable diversity among the diminutive Nanoputian populace. References to "head", "tail", "northwest region", and "warhead", for instance, are used by synthetic chemists to describe moieties or functions within a target molecule. We extend the concept to body-part-like descriptions such as "head", "neck", and "legs" in an effort to make the art and form of the nanoscale palatable to our lay-colleagues.

Nonequilibrium conformations are shown for some structures because rapid visual recognition by nonchemists is an important goal. Chemists often take the same liberties for their own benefit; for example, terpenes are routinely drawn in a nonequilibrium conformation to enhance the rapid recognition of their class *(1)*. However, liberties with the nonequilibrium conformation drawings here are only minor when representing the main-body portions; major license is taken with the Nanoputians' head dressings only.

Chemical Synthesis

NanoKid was prepared via separate syntheses of the top and bottom body portions followed by joining at the "waist", thereby constituting a convergent synthetic approach. The synthetic chemical protocol underscores the facility with which structures can be attained at the nanoscale using the tools of molecular synthesis.

The top-half of NanoKid was made as shown in Figure 2. 1,4-Dibromobenzene was iodinated in good yield *(8)*. 3,3-Dimethylbutyne was then coupled to **1** to give **2**. Formylation *(9)* of **2** was accomplished by lithium–halogen exchange followed by quenching with DMF to afford the aldehyde **3**. The aldehyde was protected as the acetal using 1,2-ethanediol in a presence of a catalytic amount of *para*-toluenesulfonic acid with azeotropic removal of the water via a Dean–Stark trap. Attempts to couple **4** to the bottom-half (vide infra) gave a low yield (9%) of the desired product due to the poor reactivity of the bromoarene in the presence of the sterically encumbering ortho-moiety. The bromide was therefore exchanged with an iodide by lithium–halogen exchange and quenching with 1,2-diiodoethane to afford **5** as the top-body portion.

For the preparation of the lower-body segment, nitroaniline was brominated to afford **6**, which was further converted to the diazonium salt and reduced to remove the diazo moiety as shown in Figure 3. Conversion of the nitro group to the amine afforded **8** *(10).* Sandmeyer reaction was then used to make a diazonium salt followed by iodination *(11)* to afford the dibromoiodobenzene **9**. This latter compound was coupled to trimethylsilylacetylene via a Pd/Cu mixed catalyst *(12)* to give **10.** Analogous coupling of the dibromoarene **10** to two equivalents of 1-pentyne afforded **11**, that was desilylated in alkaline methanol to yield the lower half, **12**, of NanoKid.

The last step in the NanoKid synthesis involves the coupling of the top and bottom portions. This was accomplished by once again using the Pd/Cu-catalyzed protocol *(12)* to afford 4.6 billion trillion NanoKids, **13**, each with the structure shown in Figure 4. For an interesting size comparison, Kawata's micro-bull is 5,000 times longer and 200 billion times the volume of NanoKid *(6)*.[2]

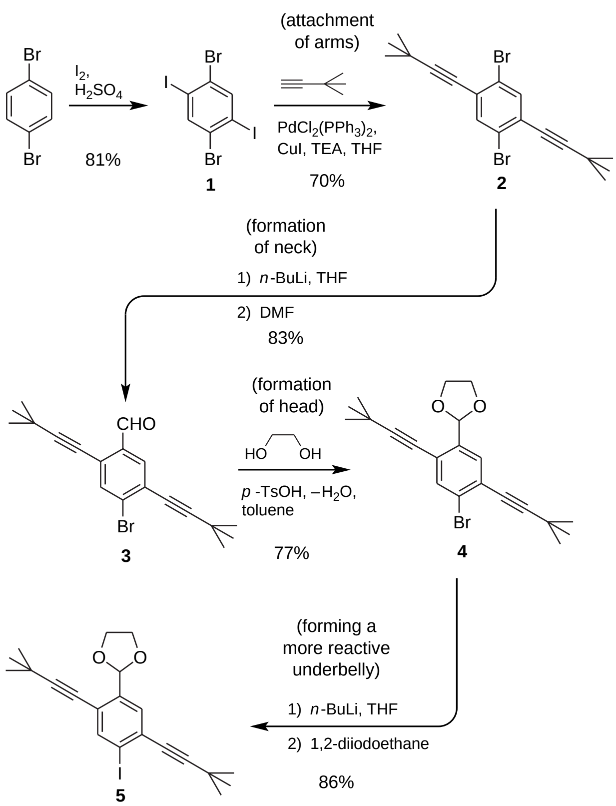


Figure 2. Synthesis of NanoKid's upper-body (TEA = triethylamine).

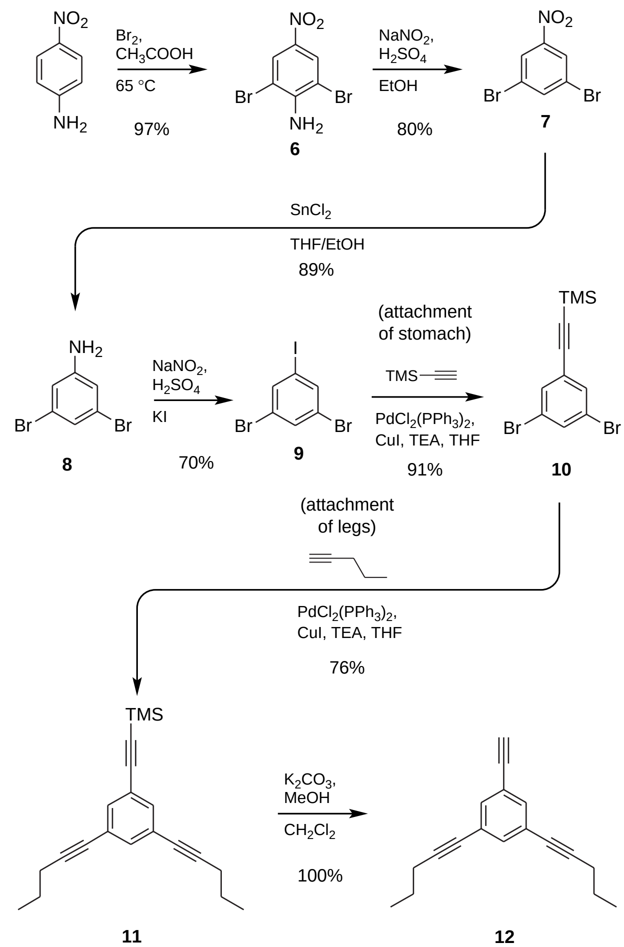


Figure 3. Synthesis of NanoKid's lower-body.

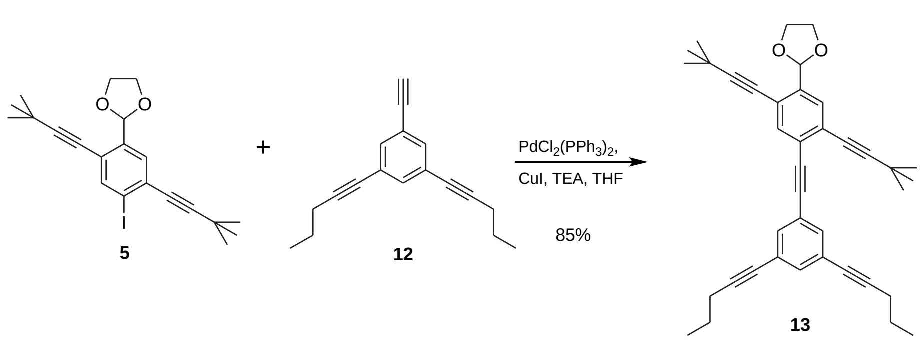


Figure 4. Coupling of NanoKid's upper- and lower-body to form the complete NanoKid.

NanoKid **13** can serve as the progenitor of many other Nanoputians. A facile procedure using microwave[3] irradiation *(13–15)* was used for the head-conversion reactions. NanoKid **13** with an excess of a 1,2- or 1,3-diol, in the presence of a catalytic amount of *para*-toluenesulfonic acid, was irradiated for a few minutes, after which each new Nanoputian was "born" (Figure 5 and Table 1). These include NanoAthlete **14**, NanoPilgrim **15**, NanoGreenBeret **16**, NanoJester **17**, NanoMonarch **18**, NanoTexan **19**, NanoScholar **20**, and NanoBaker **21**. By using this microwave-irradiation method, conventional solvents such as benzene and long reaction times were obviated. Decomposition resulted when the NanoChef **22** synthesis was attempted under the microwave conditions (Table 1, entry 9). This was probably the result of polymerization involving the electron-rich catechol and the aldehyde-based oxonium intermediate. Thus an alternate procedure employing catechol and chlorotrimethylsilane was used *(16),* albeit low yielding; only 23 billion billion NanoChefs were formed.

There are no microscopy tools, including scanning probe microscopy, currently available that could assess chemical structure at these dimensions; one would see only an ill-defined mass (for example, the aliphatic portions are rarely resolved with these methods). But the Nanoputians were unequivocally characterized using routine spectroscopic (NMR and FTIR) and mass spectrometric analysis.

In a separate combinatorial experiment, we sought to make the entire Nanoputian population at once by starting with NanoKid **13** and adding the appropriate diols (except catechol) in a single flask to generate **14–21** in one microwave oven reaction. Indeed, the conversion proceeded as planned in 4 min and the formation of **14–21** was confirmed by mass spectrometric analysis of the reaction mixture where the mass of each Nanoputian was detected. However, since a few of the figures have the same molecular weight, further confirmation was obtained using ^{1}H NMR peak matching of the mixture against the individual Nanoputian spectra that had previously been obtained.

Visual recognition can be enhanced (Figure 6) by adding color to some of the atoms, although chemists routinely use color with rigorous uniformity for each atom type. Artistic liberty has been taken to promote the rapid recognition of the Nanoputians. Note the comparison of the stick figure drawn for **13** in Figure 4 to a molecular mechanics energy-minimized form of **13** in Figure 7. Interestingly, the rigidity of the backbone molecular structure causes the conformation in Figure 7 to be quite similar to the visually recognizable form drawn for **13** in Figure 4, although the energy-minimized structure gives the appearance of a walking or strutting NanoKid.

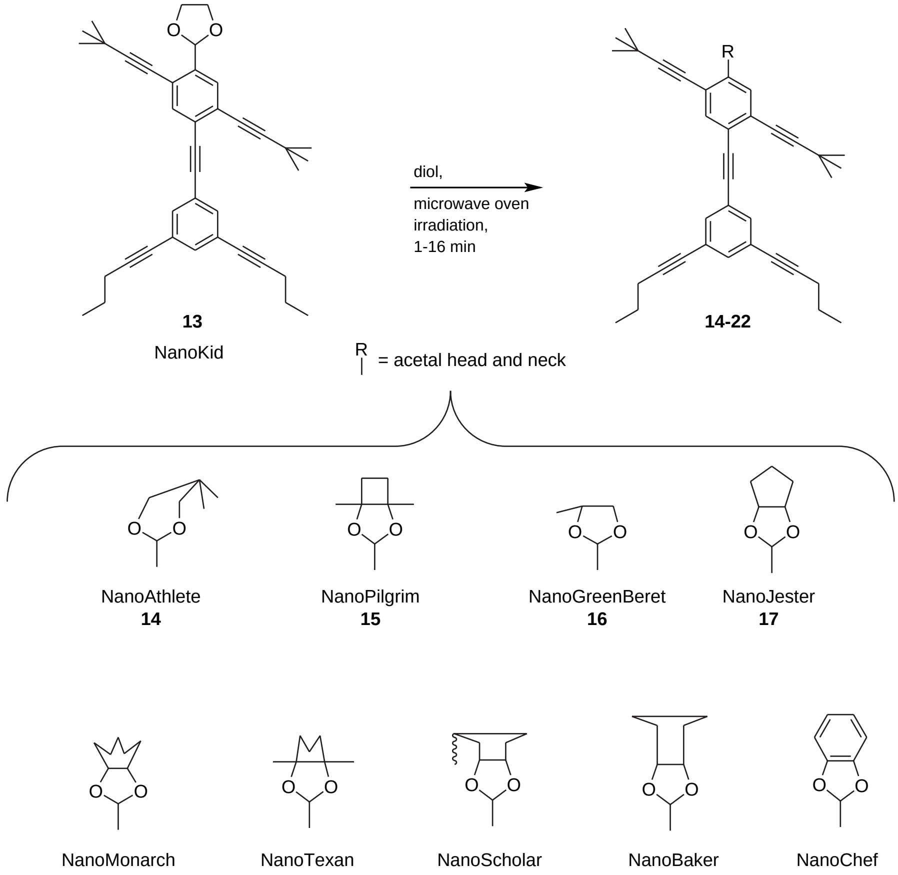
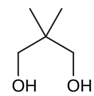
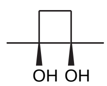
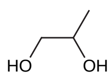
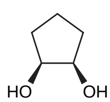
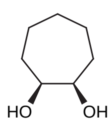
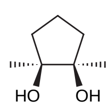
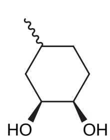
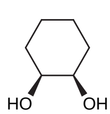
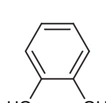


Figure 5. NanoKid can be treated with a series of 1,2- or 1,3-diols in the presence of catalytic acid and microwave oven irradiation to effect acetal exchange and hence head conversion to afford a series of other Nanoputians. See Table 1 for the specific diol used and the yield for each head conversion.

Table 1. Conversion of NanoKid 13 **into Nanoputians** 14–22
Using Microwave Irradiation in the Presence of Selected Diols

Entry	Diol[a]	Equiv. of Diol	Irradiation /min	Nanoputian	Yield (%)
1		20	7	**14**	91
2		11	13	**15**	25[c]
3		100	1	**16**	85
4		20	7	**17**	94
5		5	10	**18**	87
6		9	9	**19**	24[c]
7		20	16	**20**	90
8		15	10	**21**	84
9[b]		22	—	**22**	9[c]

[a]The cyclic diols for entries 5 and 7 were prepared by catalytic OsO_4 dihydroxylation of the corresponding alkenes. The diols for entries 2 and 6 were prepared by reductive pinacol coupling of the 1,4- and 1,5-diketones with SmI_2 and $Mg/TiCl_4$, respectively.

[b]NanoChef, **22**, was synthesized using chlorotrimethylsilane (5 equivalents) in dichloromethane.

[c]Yields based on recovered NanoKid, **13**, for entries 2, 6, and 9 were 33%, 58%, and 20%, respectively.

Figure 6. Electron cloud-based space-filling model programs were color-modified[W] to enhance the visual recognition of the Nanoputians (Copyright 2002 James M. Tour, all rights reserved).

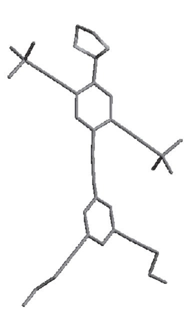


Figure 7. NanoKid **13** in the energy-minimized conformation that was determined using molecular mechanics (Spartan). The atomic placement is shown for the most stable energy conformation that would exist in a vacuum where **13** is the only molecule present. Hydrogen atoms and multiple bonds are not shown.

Hazards

All reactions should be conducted in an efficient fume hood using safety protocols (i.e., eye and skin protection) that are standard when conducting syntheses of compounds with undetermined toxicity levels *(17).*

Art within Art

The artwork of the Nanoputians was moved into a new medium by incorporating Nanoputian molecules directly into a visual arts presentation. NanoKid **13**, 85 mg, was dissolved in 800 µL of 2-propanol and injected into the red-ink cartridge of an HP 895 Inkjet printer. Then 60 copies of the NanoTexan **16** were printed to occupy the full area of an 8.5 × 11 inch sheet of paper using the same color scheme as shown in Figure 6. Hence, each picture of NanoTexan contained millions of molecules of NanoKid **13**. This was confirmed by rinsing the NanoTexan-covered papers with acetone, concentrating the solution, and obtaining the mass spectrometric analysis data to verify the existence of NanoKid (542.3 atomic mass units) within the NanoTexan print. There was no compound of the same mass detected in the prints of NanoTexan when a fresh print cartridge was used as a control. Similarly, NanoKid **13** was injected into the blue-ink cartridge and used to print copies of NanoKid using the same color scheme as shown in Figure 6. There is nothing surprising here to the chemist; it is merely a matter of mass balance. However, to generate an art form wherein the macroscopic view includes millions of the nanoscopic entities constitutes an unprecedented approach that can capture the students' imaginations, as they envision, in their mind's eye, the movements of the Nanoputians within the static macroscopic structure. When these pictures were shown to nonchemists, they seemed absorbed in the viewing as they tried to comprehend the fact that there were millions of moving NanoKids within the prints.

Finally, this concept has been extended to using the arts to aid in teaching of the physical sciences by producing a three-dimensionally rendered animation of the NanoKid synthesis starring NanoKid itself. In this animation, NanoKid immediately draws one's attention through the visual and musical arts.[4] NanoKid helps one to understand the scale of the nanoworld by comparing its size, for example, to that of a white blood cell, which is billions of times larger. The detailed synthesis of NanoKid ensues via appendage of body parts in a mechanistically correct fashion, yet in an attractive setting for all ages by giving character roles to the individual atoms. The more precise chemical stick figures are shown alongside to lead the viewer into bona fide organic chemical structure appreciation and recognition. In this manner, all age groups can gain a new appreciation for the beauty of chemical design and synthesis in a friendly and entertaining venue.

Summary

The standard tools of synthetic chemistry are displayed in a manner that both the chemical artisan and layperson might enjoy. Although an expert from either the arts or sciences might have difficulty with this nonstandard presentation, we believe that it can attract and interest the nonexpert without sacrificing the rigor characteristic of science.

[W]Supplemental Material

Details of the synthesis and characterization of all substances are available in this issue of *JCE Online*. The pdf version of this article contains Figure 6 in color; the Nanoputians are shown on the cover.

Acknowledgments

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Notes

1. The name “Nanoputian” is derived from the inch-sized Lilliputians, the people of Lilliput, in Jonathan Swift’s classic, *Gulliver’s Travels.*

2. The final step in the NanoKid synthesis yielded 4.17 g = 7.69 mmoles = 4.6×10^{21} (4.6 billion trillion) NanoKids. Kawata’s micro-bull *(6)* is about 10-μm long while NanoKid is 2-nm long, or 5,000 times shorter in length. With estimated dimensions of 10-μm long, 7-μm high, and 3-μm thick, the micro-bull has a volume of 210 $\mu m^3 = 2.1 \times 10^{11}$ nm^3. NanoKid’s dimensions are approximately 2-nm in length, 1-nm in width, and 0.5-nm thick, for a volume of 1 nm^3. Therefore the “micro-bull” is approximately 2×10^{11} times the volume of NanoKid.

3. A Sharp Carousel microwave oven (model R510C) was used.

4. For previews of educational animations involving the NanoKids concept, see: *http://www.NanoArtworks.com* (accessed Jan 2003).

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