

Using microcontact printing to fabricate microcoils on capillaries for high resolution proton nuclear magnetic resonance on nanoliter volumes

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This letter describes a method for producing conducting microcoils for high resolution proton nuclear magnetic resonance (¹H-NMR) spectroscopy on nanoliter volumes. This technique uses microcontact printing and electroplating to form coils on microcapillaries. Nuclear magnetic resonance spectra collected using these microcoils, have linewidths less than 1 Hz for model compounds and a limit of detection (signal-to-noise ratio=3) for ethylbenzene of 2.6 nmol in 13 min. © 1997 American Institute of Physics. [S0003-6951(97)00818-8]

Nuclear magnetic resonance (NMR) spectroscopy is an indispensable tool for determining dynamical and structural properties of molecules. Previous studies showed that the use of microcoils for excitation and detection of NMR signals from analyte contained in microcapillaries (357 μm o.d., 75 μm i.d.) increased the signal-to-noise ratio per mole of analyte by a factor greater than 100.¹ Such coils are particularly useful for examination of mass-limited samples and for detection in microseparations.² The microcoils used in initial experiments were formed by wrapping wire with a diameter of 50 μm around a capillary. In this report, we describe an alternate means for forming conducting microcoils suitable for collecting NMR data from nanoliter volumes; the method uses microcontact printing (μCP)³ and electroplating to generate thick, conducting, metallic coils on capillaries. The ease of producing microcoils with this method may allow for

automation of the construction of the coils. In addition, the flexibility afforded by μCP allows the geometries of the coils to be adjusted over a range that is difficult or impossible to access with other means of fabrication. In this letter, we demonstrate that μCP allows formation of microcoils with geometries similar to those used in previous work and we demonstrate that these microcoils can be used for high resolution ¹H-NMR spectroscopy.

The scheme for fabricating conducting microcoils for NMR uses μCP to print lines onto capillaries^{4,5} (Fig. 1). The capillaries (324 μm o.d., 75 μm i.d., Polymicro Technologies, Inc., Phoenix, AZ) were prepared for printing by first stripping their polyimide coating using a moderate butane flame. The stripped capillaries were then coated with titanium ($\sim 25 \text{ \AA}$) and silver ($\sim 500 \text{ \AA}$) using an electron beam evaporator. Mounting the samples on stages that rotated the

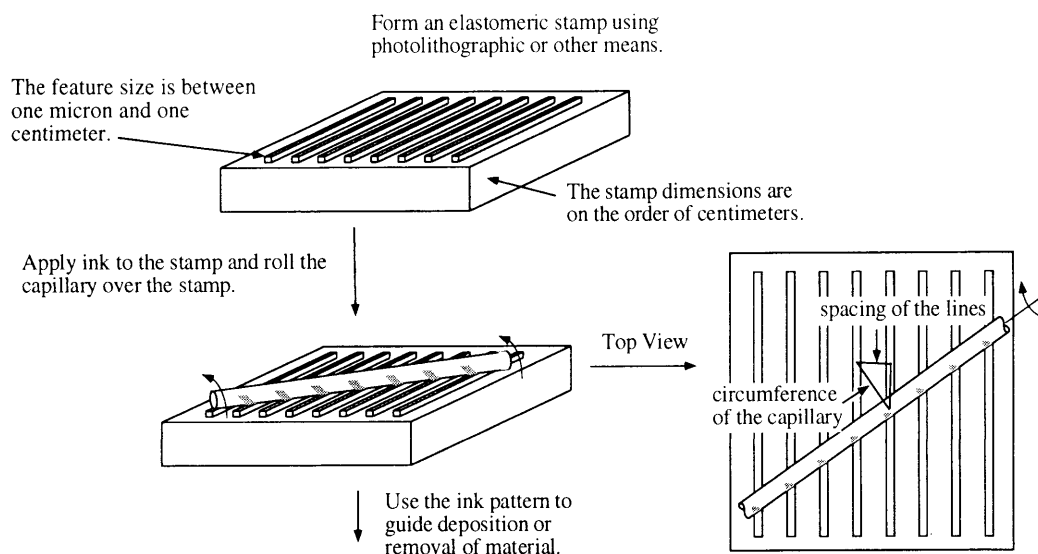


FIG. 1. Scheme for fabricating helical microcoils using microcontact printing. An inked elastomeric stamp consisting of raised lines formed using photolithographic or other means, delivers ink to selected locations on a sample. When the sample is a cylinder and the orientation between the axis of the cylinder and the lines of the stamp is properly related to the spacing of the lines and the circumference of the cylinder, then rolling the cylinder over the stamp once generates a coil on the surface of the cylinder. The ink either initiates deposition of material or prevents its removal.

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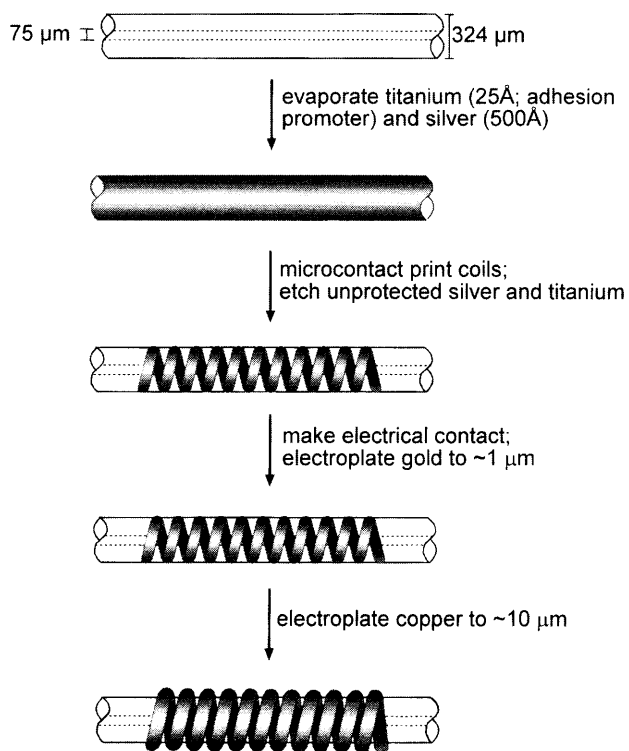


FIG. 2. Procedures for fabricating conducting microcoils for NMR spectroscopy. Glass capillaries, stripped of their polyimide coating, were coated on all sides with titanium ($\sim 25 \text{ \AA}$) and silver ($\sim 500 \text{ \AA}$) using an electron beam evaporator. Microcontact printing hexadecanethiol using a stamp with parallel lines oriented at the appropriate angle to the glass capillary formed a continuous spiral structure. Wet chemical etching removed silver not protected by hexadecanethiol. Immersion of the etched capillary in 1% HF solution removed exposed titanium leaving a conducting coil. We electrodeposited layers of gold ($\sim 1 \mu\text{m}$) and copper ($\sim 10 \mu\text{m}$) onto the silver coils.

capillaries allowed metal to be deposited on all sides of the capillaries in a single evaporation.⁵

We used μCP to generate continuous coils of a hexadecanethiolate (HDT) monolayer on the silver-coated capillaries. The features on the stamp and the orientation between the stamp and the capillary defined the geometry of the coils (Fig. 1). The stamps used for this work consisted of raised lines $50 \mu\text{m}$ wide, separated by $50 \mu\text{m}$. After printing HDT,

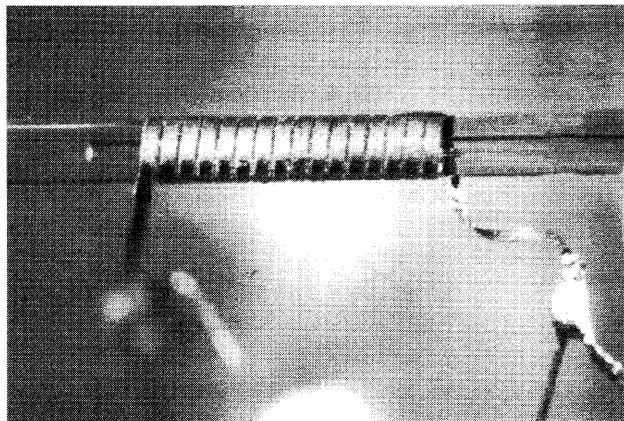


FIG. 3. Optical micrograph of a microcoil (16 turns of $70 \mu\text{m}$ wire separated by $\sim 30 \mu\text{m}$) printed on a capillary ($324 \mu\text{m}$ o.d., $75 \mu\text{m}$ i.d.). The length of the coil is 1.6 mm with an enclosed volume of 8 nl. Strips of printed wire 2 to 3 mm long were peeled back and used for connecting the microcoil to a NMR data acquisition circuit.

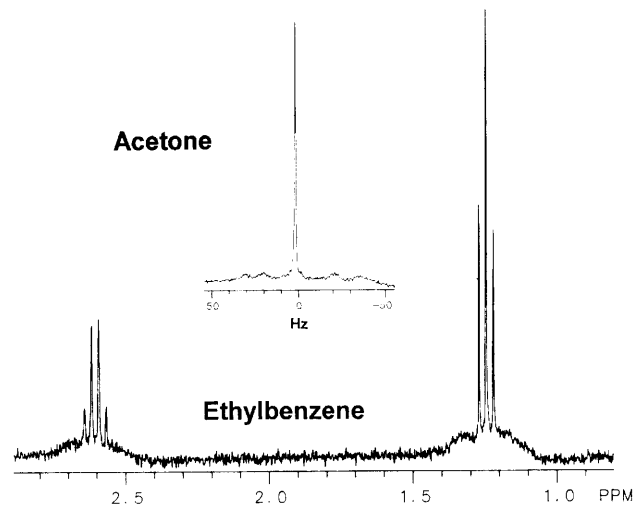


FIG. 4. NMR spectra collected from ethylbenzene and acetone using a microcoil printed on a capillary. The spectrum from acetone represents 16 co-added scans, each collected with 90° pulses (width = $14.0 \mu\text{s}$), spectral width of $\pm 2000 \text{ Hz}$ and 16 384 points. The signal-to-noise ratio of this data is 138 and its linewidth is 0.7 Hz. The spectrum from ethylbenzene represents 256 scans in 13 min. All other settings were identical to those used for acetone. The linewidth of the triplet in ethylbenzene is 0.9 Hz and the signal-to-noise ratio is 76. The microcoil was carefully placed in the center of the shims, but all shim settings were set to zero for data acquisition, and line broadening was not used in data analysis.

wet chemical etching [$0.001 \text{ M K}_4\text{Fe(CN)}_6$, $0.01 \text{ M K}_3\text{Fe(CN)}_6$, $0.1 \text{ M Na}_2\text{S}_2\text{O}_3$] removed silver not protected by the monolayer resist.⁶ Immersion of the capillary in 1% HF for 10 s removed exposed titanium, and left a conducting microcoil of silver consisting of wires $50 \mu\text{m}$ wide and separated by approximately $50 \mu\text{m}$. We electroplated a thin ($\sim 1 \mu\text{m}$) layer of gold (Orotemp 24, Technic Inc., Providence, RI) and then a thick ($\sim 10 \mu\text{m}$) layer of copper (Copper C RTU, Technic Inc., Providence, RI) onto the silver coils. The gold protected the underlying silver from etching induced by the copper plating bath. After electroplating, the wires of the coils were approximately $70 \mu\text{m}$ wide, separated by $30 \mu\text{m}$. Figure 2 illustrates the procedure for fabrication, and Fig. 3 shows an optical micrograph of one of the microcoils as configured for NMR measurements.

The printed microcoils were connected to a tank circuit¹ using $50 \mu\text{m}$ wire (99.99% Cu, California Fine Wire, Grover Beach, CA) and silver conductive epoxy (Epo-tek 410E, Epoxy Technology, Billerica, MA). Spectra were acquired using the microcoils and a General Electric 300 MHz (7.05 T) wide-bore NMR spectrometer. To position the microcoils in the center of the Z1 shim field, a signal from neat acetone was obtained at $\pm 10\%$ of the Z1 coarse shim range, and the height of the probe was adjusted until the signal position shifted by less than 1 Hz.

Figure 4 shows typical spectral collected from neat acetone and neat ethylbenzene. For 16 co-added scans, the signal-to-noise ratio (S/N) and the linewidth of the signal from acetone were 138 and 0.7 Hz, respectively. For ethylbenzene, with 256 scans, we observed a S/N of 76 and a linewidth of 0.9 Hz. From a comparison of the widths of radio frequency pulses needed to cause a ninety degree rotation of the proton spin magnetization, we estimate that the sensitivity of the printed microcoil is 15 times larger than

that of conventional 5 mm spinning tube probes.^{1,7} Although this increase in sensitivity is considerable, it is smaller than the increase observed previously using wound microcoils. We believe that the sensitivity of the printed microcoil is lower than that of the wound microcoil primarily because its resistance is higher.⁸ (For example, we found that the dc resistance of the printed microcoil was ~ 8 times higher than the resistance of the wound microcoil.) The resistance of the printed microcoil is higher than the wound microcoil partly because its cross sectional area is smaller and because our electrodeposited copper may have a slightly higher resistivity than annealed copper. It is also possible that the silver epoxy further increases the resistance of the circuit, particularly at high frequencies. We are exploring means for reducing this resistance.

In this letter, we described a method for fabricating conducting microcoils on capillaries and we showed how these microcoils can be used for high resolution ¹H-NMR spectroscopy of nanoliter samples. Since μ CP can produce features with sizes as small as 0.2 μ m, we anticipate that our scheme for fabrication will allow for NMR microcoils consisting of wire with widths less than one micron, more than an order of magnitude smaller than what is currently achieved by winding. This capability may allow for NMR measurements on smaller volumes of samples. Also, μ CP

may allow for construction of coils with specialized geometries that improve sensitivity and line shape,⁹ but are difficult to fabricate by conventional approaches.

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