1800° to 2000°C. The samples stayed at that temperature for 10 to 20 min before being quenched by the cutting off of power to the furnace. The quench rate was measured to be ~500°C per second. The samples were subsequently decompressed at a rate of 2 to 3 GPa/hour.
17. NMR spectra described here were collected with a Varian Unity spectrometer operating at 9.4 T was a MAS probe from Doty Scientific (Columbia, SC), with 3.5-mm rotors commonly spinning at 9.3 kHz (unless otherwise specified). To make ^{27}Al analysis as straightforward as possible, a small tip angle ($<\pi/6$) was used in all cases. ^{23}Na and ^{27}Al NMR was done with the use of delay times on the order of 1 s, with a spectral band width of 2 MHz. For ^{29}Si NMR, a smaller spectral band width was used because of the limited chemical shift range in Si; however, much longer delay times were used (70 s) because of the possibility of having long relaxation times for Si species even with a small paramagnetic dopant (Gd_2O_3) [A. Abragam, *Principles of Nuclear Magnetism* (Oxford Univ. Press, New York, 1961)]. We subtracted a ^{27}Al background from the probe by collecting data on an empty rotor under conditions identical to those under which the glass samples were run. There was no probe background in the ^{23}Na and ^{29}Si spectra; however, the Si_3N_4 rotors gave a characteristic resonance at −48.8 ppm relative to tetramethyl silane at 0 ppm with spinning sidebands in the silicon NMR. This was used as an internal chemical shift calibration for ^{29}Si NMR. To reference the chemical shift of ^{23}Na and ^{27}Al, a liquid sample of 1 M NaCl (0 ppm) and 1 M $AlCl_3$ (0 ppm) was run before each spectrum, respectively.
18. We prepared the ^{29}Si-enriched $Ab_{50}NTS_{50}$ by fusing stoichiometric amounts of 92%-labeled $^{29}SiO_2$ glass (Cambridge Isotope Laboratory, Andover, MA) with sodium carbonate (Na_2CO_3), aluminum oxide (Al_2O_3), and 0.1 weight percent gadolinium oxide (Gd_2O_3) at 1200°C for 2 hours. Glass was formed upon removal of the Pt crucible containing the mixed liquid components from the furnace. We did not chemically analyze the sample because of the expense of labeled material and the proven nature of the synthesis process. Gd_2O_3 was added to shorten the spin-lattice relaxation time of Si. This sample, along with unlabeled glass made under the same conditions, was then sealed in Pt capsules for use in the high-pressure multi-anvil quenching described in (*16*).
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High-Resolution Microcoil ^1H-NMR for Mass-Limited, Nanoliter-Volume Samples

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High-resolution, proton nuclear magnetic resonance (NMR) spectra of 5-nanoliter samples have been obtained with much higher mass sensitivity [signal-to-noise ratio (S/N) per micromole] than with traditional methods. Arginine and sucrose show a mean sensitivity enhancement of 130 compared to 278-microliter samples run in a 5-millimeter tube in a conventional, commercial probe. This can reduce data acquisition time by a factor of >16,000 or reduce the needed sample mass by a factor of about 130. A linewidth of 0.6 hertz was achieved on a 300-megahertz spectrometer by matching the magnetic susceptibility of the medium that surrounds the detection cell to that of the copper coil. For sucrose, the limit of detection (defined at S/N = 3) was 19 nanograms (56 picomoles) for a 1-minute data acquisition. This technique should prove useful with mass-limited samples and for use as a detector in capillary separations.

Compared to other common spectroscopic methods of molecular characterization, NMR is by far the least sensitive (*1*). NMR is seldom the method of choice for analysis of trace level quantities, despite its strong structural identification capability and nondestructive nature. In this report, we describe an NMR radiofrequency (rf) transmission/detection coil that is more than an order of magnitude smaller than typical coils (*2*, *3*). The increase in mass sensitivity, defined as the signal-to-noise ratio (S/N) per micromole, is greater than 100-fold compared to conventional NMR. Although we previously demonstrated the feasibility of microcoil NMR spectroscopy for capillary electrophoresis (CE) and liquid chromatography (*3*), typical linewidths of 11 Hz were obtained, which were broad compared to conventional systems and prevented observation of proton scalar coupling. The approach reported here provides high-resolution NMR spectra by surrounding the coil region with a magnetic susceptibility matching fluid (Fig. 1). Efforts by others to improve sensitivity for NMR imaging have included the use of high-temperature superconducting coil materials and NMR force microscopy (*4*).

For rf coils ≤1 mm in diameter, the noise in an NMR experiment is dominated by thermal noise from the coil and not the sample (*5*). As the coil size is reduced, the strength of the rf magnetic field per unit current increases, thereby improving mass sensitivity (*6*). The S/N per unit volume achieved by a solenoidal microcoil in an NMR experiment is proportional to the quantity of sample and inversely proportional to the coil diameter (*6*).

Fabrication of the coil shown in Fig. 2 was modified from earlier work (*3*, *7*). The microcoil is 1 mm long and encloses a sample volume of 5 nl within the capillary [76.5 μm inside diameter and 357 μm outside diameter (OD)]. The capillary functions as both the coil form and sample container and provides a flow-through means of sample loading. The sample is not spun, and sample loading through the capillary usually makes shimming between different samples unnecessary.

Compared to previous microcoil NMR results (*3*), several distinct improvements were devised to obtain the high resolution reported here. Cyanoacrylate adhesive was used to hold the coil in place instead of epoxy. This adhesive readily flows into the interface between the capillary and wire coatings and allows the matching fluid to come in close proximity to the coil material. Placement of the coil at the vertical and axial center of the shims allows rapid manual and automatic shim optimization. In addition, the capillary OD was increased from 325 to 357 μm (by leaving intact the 16-μm-thick polyimide coating).

To reduce the effects of magnetic susceptibility caused by proximity of the rf coil to the sample, Fluorinert FC-43, a perflu-

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orinated organic liquid, surrounds the coil and capillary region (*8*). Matching the volume magnetic susceptibility, χ_v, of the surrounding medium to that of the coil material lowers the static magnetic field inhomogeneities in the sample region and thus allows conventional shimming to substantially improve resolution and line shape (Figs. 3 and 4) (*9*). The signal obtained without FC-43 is similar to the line shape that results from the field perturbation caused by a cylindrical copper object placed in a magnetic field (*10*).

The resolution achievable with the microcoil was explored by using neat ethylbenzene as the sample (*11*). The linewidth is defined as the spectral peak width at half-height and is determined by the best fit of a Lorentzian curve to the data. A spectrum and Lorentzian linefit plot are shown in Fig. 4. The multipulse data acquisition ability of the microcoil is demonstrated with 1.04 μg (4.5 nmol) of a 0.9 M solution (70% w/w) of 2,3-dibromopropionic acid (DBPA) in acetone-d_6. The correlated spectroscopy (COSY) spectrum in Fig. 5 shows all expected crosspeaks (*12*) and is in excellent agreement with a spectrum from a sample in a 5-mm spinning tube.

Arginine·HCl ($C_6H_{14}N_4O_2$) and sucrose ($C_{12}H_{22}O_{11}$) (*11*) were used as model compounds to compare the sensitivity of the microcoil approach to the conventional 5-mm spinning tube method. Solutions of 500 mM in D_2O were used for the microcoil, and 5 mM solutions for the 5-mm tube, as these concentrations provided reasonable S/N ratios. The S/N was computed as the ratio of the peak signal to the root-mean-square noise level (Fig. 6) (*13*).

The data for the microcoil and 5-mm spinning tube were compared on the same GN-300WB (wide bore) spectrometer (*13*). The S/N data were measured for the microcoil and 5-mm tube, and by using the appropriate sample concentration and detection cell volume, the micromole amounts and sensitivities were computed (Table 1). The 5-mm-tube sample volume is based on the physical dimension of the observe coil in the NMR probe and is at least 50,000

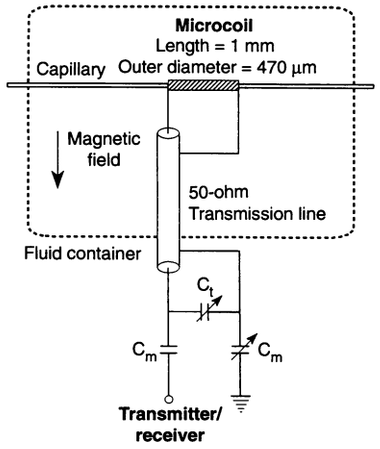

Fig. 1. Layout and circuit for microcoil NMR (*7*); C_t and C_m are the tuning and matching capacitors, respectively.

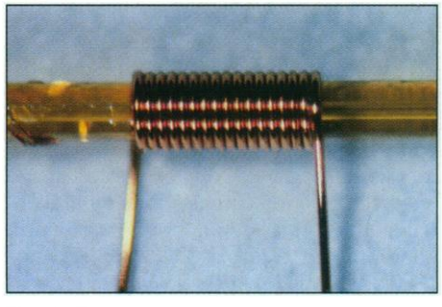

Fig. 2. Typical microcoil and polyimide-coated, fused-silica capillary. The coil is composed of 50-μm-diameter copper wire, has a length of 1 mm, and an OD of 470 μm.

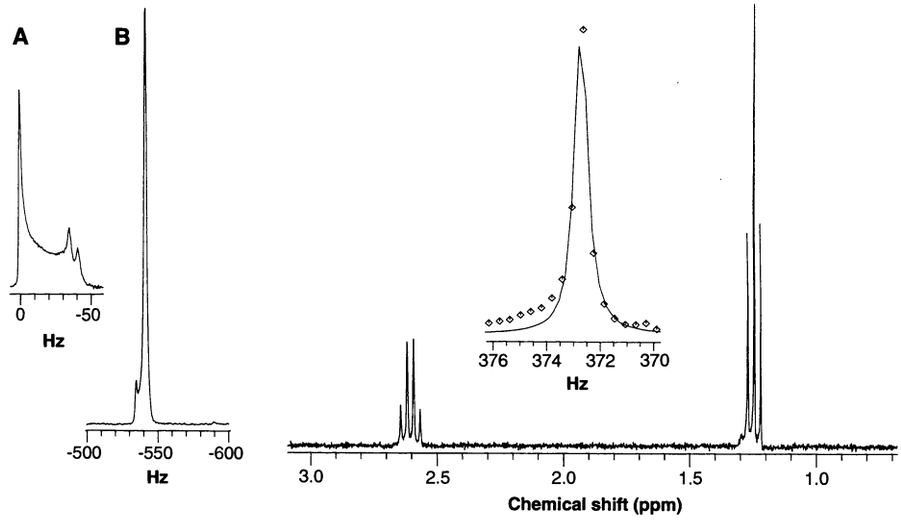

Fig. 3 (left). The effect on signal quality of Fluorinert FC-43 as a surrounding medium for the coil and capillary (*8*). The signal in (**A**) is for neat acetone in the absence of the fluid and (**B**) shows the signal with the fluid. The spectra are plotted on the same scales, and all shims are set to zero. The fluid eliminates the severe hook, shifts the signal −542 Hz, and improves the S/N by a factor of 4.5. Conditions: one scan; spectral width ±2000 Hz; 16,384 data points; and a 90° PW of 1.5 μs. **Fig. 4 (right).** Microcoil NMR spectrum of neat ethylbenzene. The phenyl region is omitted. The linewidth of the central peak of the triplet is 0.6 Hz. **Inset**: Linefit diagram for this peak. The diamonds represent the actual data, and the line is the Lorentzian fit. The mass of sample within the 5-nl capillary detection cell is 4.3 μg (41 nmol). Conditions: one scan; spectral width ±1608 Hz; 16,384 data points; and a 90° PW of 1.3 μs.

Fig. 5. Microcoil COSY spectrum of 2,3-dibromopropionic acid in acetone-d_6. The 5-nl detection cell contains 1.0 μg (4.5 nmol) of 0.9 M sample, and the data were acquired in 2.2 hours. Conditions: a 90° PW of 1.3 μs; recycle delay of 300 ms; 1024 data points; 16 acquisitions per block; 256 blocks; spectral width ±197 Hz in both dimensions. Processing: One zero fill was used for the first Fourier transform (FT), and two zero fills for the second FT; two unshifted sine bell apodizations were applied to each FT. Projections appear along the respective axes. The one-dimensional spectrum appears on top; conditions: 16 scans; and 4096 data points.

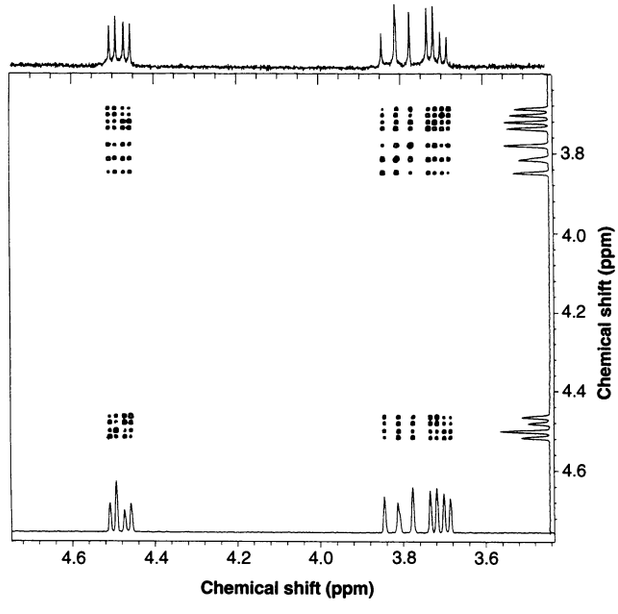

Table 1. NMR sensitivity study for microcoil (500 mM, 5-nl samples) versus 5-mm spinning tube (5 mM, 278-μl samples). Sensitivity is S/N per micromole of sample (mean enhancement is 129). Sample conditions for arginine: 527 ng (2.5 nmol) for the microcoil and 293 μg (1.39 μmol) for the 5-mm tube. Sample conditions for sucrose: 856 ng (2.5 nmol) for the microcoil and 476 μg (1.39 μmol) for the 5-mm tube.

Sample	Sensitivity		Enhancement	Limits of detection (S/N = 3)					
	Microcoil	5-mm tube		Microcoil			5-mm tube		
				ng	pmol	mM	ng	pmol	mM
Arginine									
1 min	10,200	84.9	120	34.2	162	32.4	5,990	28,400	0.101
10 min	31,800	232	137	10.9	51.9	10.4	1,890	8,980	0.033
Sucrose									
1 min	23,200	181	128	19.3	56.3	11.3	4,560	13,300	0.049
10 min	69,200	523	132	6.44	18.8	3.8	1,580	4,630	0.017

times greater than the corresponding volume within the microcoil. The sensitivity enhancement is defined as the ratio of the microcoil sensitivity to the sensitivity of the 5-mm tube for a given compound. The mean sensitivity enhancement for arginine and sucrose is 129 and is independent of observation time. An exactly analogous set of 5-mm-tube experiments were conducted on the GN-300NB to compare differences between 300-MHz spectrometers. The sensitivities of the wide-bore and narrow-bore spectrometers were within 2%.

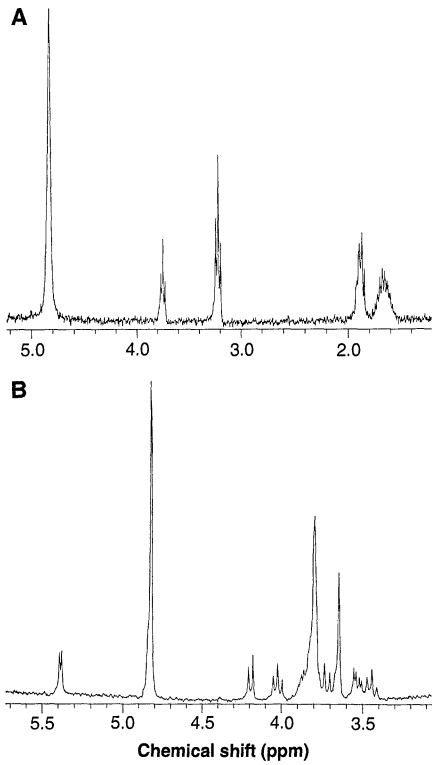

Fig. 6. (**A**) Arginine•HCl and (**B**) sucrose microcoil NMR spectra. The data acquisition time was 1 min and line broadening was used. The arginine spectrum has 0.53 μg (2.5 nmol) of sample in the 5-nl capillary detection cell. The sucrose spectrum has 0.86 μg (2.5 nmol) of sample in the cell. The LODs appear in Table 1, and data acquisition parameters are in (*13*).

To a first approximation for a given transmission power level on the same magnet, the ratio of the 90° pulse widths (PWs) for two coils is inversely proportional to the sensitivity enhancement (*14*). For the 90° PWs of the commercial coil and microcoil used here, $PW_{tube}/PW_{microcoil} = 210/1.6 = 131$, which is in good agreement with the mean sensitivity enhancement obtained.

The sensitivity enhancement values in Table 1 for the microcoil are remarkably high. Compared to the 5-mm tube, the mean enhancement of 129 represents a decrease in data acquisition time of 16,600 (129^2) or the ability to perform an experiment in the same amount of time with 0.8% (1/129) of the sample mass. The 5-mm tube in the 10-mm probe was used as a reference because this combination is commonly used in routine NMR. The sensitivity enhancement of the microcoil changes if compared to a smaller diameter probe. For instance, in the 10-mm probe, the diameter of the observe coil is estimated at 13 mm (*15*). If a probe with a 3-mm observe coil (one of the smallest commercially available) is used instead, the expected sensitivity enhancement would be less. If we use the approximation S/N ∝ 1/(coil diameter) (*6*), the enhancement would be about 30-fold, which is still a dramatic increase.

The limits of detection (LOD) shown in Table 1 indicate that picomole samples can be analyzed with the microcoil in reasonable observation times. The concentration LODs are in the millimolar range for 1- and 10-min data, and although these seem high, they correspond to nanogram (picomole) amounts of sample. For structural identification, an amount 10 times the LOD is generally needed. Solubility may be a limiting factor in using the microcoil for analysis of low-solubility compounds or in the study of phenomena that require low concentrations.

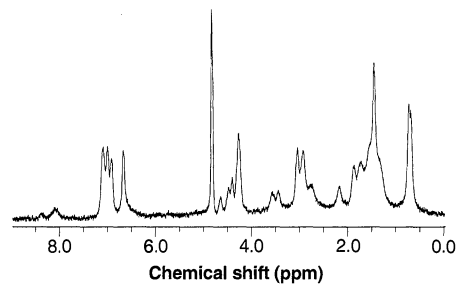

Fig. 7. A 300-MHz microcoil NMR spectrum of *Aplysia californica* α-bag cell peptide (residues 1-7). The 5-nl detection cell contains 3.0 μg (3.3 nmol) of peptide. The LOD is 112 ng (124 pmol). Data acquisition parameters are as in (*13*).

The ability to acquire high-resolution spectra on 5-nl samples with improved mass sensitivity enables a variety of uses for microscale NMR. Biological applications will greatly benefit from the ability to structurally identify molecules with submicrogram LODs. As an example, a microcoil NMR spectrum of a seven–amino acid peptide (*11*) is shown in Fig. 7. The feasibility of microcoil NMR for on-line CE detection has been shown (*3*). The work presented here can allow the acquisition of high-resolution NMR electropherograms and chromatograms when the improved microcoil NMR cell is coupled to capillary separations. Use of capillary flow injection systems, electrokinetic sample introduction, and direct nanoliter-volume injection (*16*) will allow routine analysis of small-volume samples. High-quality NMR data will also permit the examination of electrophoretic mobility, diffusion coefficients (*17*), and vesicle composition (*18*) in biological regimes, especially in relation to cellular environments.

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7. The solenoidal microcoil was made from 50-μm diameter wire composed of 99.99% Cu (California Fine Wire, Grover Beach, CA) and coated with ~6.4 μm of polyurethane. The fused silica capillary (Polymicro, Phoenix, AZ) was used without removing its polyimide coating. Coil fabrication was monitored with a dissecting stereomicroscope. By using a procedure modified from a previous approach (*3*), the coil was wound (with no gap between turns) past the number of turns desired (17 here), and cyanoacrylate adhesive (Ross, Conros Corp., Taylor, MI) was applied at points 17 turns apart. After the glue dried, excess turns were removed from each end to yield the final 17-turn coil. The polyurethane coating on the coil leads was removed with Strip-X (GC Electronics, Rockford, IL) followed by concentrated H_2SO_4. The leads were soldered to a 3-cm long, semirigid coaxial cable (UT85SS; Rosenberger Micro-coax, Collegeville, PA) and wired to the circuit as shown in Fig. 1. The nonmagnetic, tuning and matching variable capacitors (1 to 30 pF, Johansen 5641; Boonton, NJ) and the fixed capacitor (2.2 pF; Non-Mag 100 B 2R2 PN; American Technical Ceramics, Huntington Station, NY) complete the transmit/receive circuit. The unit was connected to the NMR by using a low-magnetic, coaxial cable (Belden MIL-C-17G; Richmond, IN). Both transmission line and cable have a 50-ohm impedance. The coil and capillary are situated horizontally in the static magnetic field (Fig. 1) and are housed in an Al tube inserted into the wide-bore magnet.
8. Fluorinert FC-43 (3M, St. Paul, MN) was contained in a 20-ml, low-density polyethylene bottle fitted and epoxied to the circuit board. Once the fluid was applied to the coil region, the NMR signal took about 3 hours to stabilize. Shimming was performed only after application of the FC-43 yielded a stable signal. Teflon tubing (30 gauge) was attached to the capillary with a shrink-melt Teflon sleeve (Small Parts, Inc., Miami Lakes, FL). Samples were injected into the capillary via the Teflon tubing by using a syringe and needle connection. For data acquisition, the syringe was left in place and the outlet end of the tubing was closed off with another needle attached to a cutoff valve. All spectra and NMR data were obtained and analyzed on General Electric 300-MHz (7.05 T) spectrometers. The 89-mm wide-bore (WB) magnet (GN-300WB) and a custom probe stand (made in-house) were used for all microcoil experiments. The GN-300WB and a similar narrow-bore (NB) unit (GN-300NB) were both used for studies with 5-mm spinning tubes (Wilmad 528-PP, Buena, NJ). Both spectrometers are equipped with their own 10-mm, high-resolution, broad-band solution probes. The WB probe has an observe coil length of 20 mm that encloses within a 5-mm tube a sample volume of 278 μl; the NB probe has a coil length of 18 mm that encloses a volume of 250 μl within a 5-mm tube (*15*). All experiments were run at ~18.5°C within the magnet bore. Neither NMR magnet was vibrationally isolated, nor were the magnet, console, or software modified to accommodate the microcoil probe. The 5-mm spinning tube was shimmed in a conventional manner with a deuterated lock solvent. The microcoil, however, was shimmed on the free induction decay (FID) signal of a protonated compound, usually neat acetone, or the compound of interest in a particular experiment. Solvent locking was not used for the microcoil, as the present circuit was only designed for tuning to protons at 300 MHz. Tuning and matching was performed with the circuit board and microcoil outside the magnet; otherwise, the procedure was conventional. A new microcoil is automatically placed in the axial center of the shims by the design of the probe stand. The probe was moved to the vertical shim center by adjustment of the vertical position until a significant change in the Z1 coarse shim shifted the position of a reference peak less than 1 Hz [W. W. Conover, in *Topics in C-13 NMR Spectroscopy*, G. C. Levy, Ed. (Wiley-Interscience, New York, 1984), vol. 4, p. 37]. The microcoil was then manually shimmed by using the five coarse adjustments for Z1, Z2, Z3, X, and Y. A simplex-based, Conover-derived macro optimized the remaining fine shim settings. After manual and auto shimming, Z2 and Z4 sometimes require manual adjustment based on the appearance of the final signal. A new microcoil is shimmed in <3 hours. The sample injection arrangement allows samples to be loaded without moving the probe.
9. The volume magnetic susceptibility of FC-43, $\chi_v = -0.655 \times 10^{-6}$, is within 15% of the χ_v for Cu of -0.768×10^{-6} and within 7% of the χ_v for D_2O of -0.705×10^{-6}, compared to $\chi_v = +0.030 \times 10^{-6}$ for air and $\chi_v = -1.084 \times 10^{-6}$ for silica. The magnetic susceptibility of FC-43 was measured on a 1.0 T magnetometer (Quantum Design, Model MPMS, San Diego, CA). Other values from D. R. Lide, Ed., *CRC Handbook of Chemistry and Physics* (CRC Press, Ann Arbor, MI, ed. 74, 1993). All χ_v values are dimensionless but computed using cgs units.
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13. The 90° pulse width (PW) for both arginine and sucrose was 1.6 μs for the capillary and 210 μs for the 5-mm tube for the same transmission power setting. Data acquisition parameters were established by adjustment of the spectral width and number of data points to yield an FID that was nearly completely relaxed in the first half of the pulse repetition time (T_p). The spectral resolution, $1/T_p$, was always <1 Hz per data point. Data were acquired for 1 and 10 min for both compounds. The line broadening value was set equal to the linewidth (*12*) but used only for the determination of S/N ratios in the computation of LODs. For the microcoil, the line broadening was 0.6 Hz, and for the 5-mm tube, 0.3 Hz. Data acquisition parameters for arginine·HCl (60 scans/min): data points, 4096; spectral width, ±1004 Hz; pulse repetition time, 1.02 s; resolution, 0.98 Hz per point. For sucrose (48 scans per minute): data points, 2048; spectral width, ±400 Hz; pulse repetition time, 1.28 s; resolution, 0.78 Hz per point. For peptide: 256 scans in 11.8 min; data points, 8192; spectral width, ±2674 Hz; pulse repetition time, 0.77 s; 1.3 Hz per point; recycle delay, 1.0 s; line broadening 0.6 Hz; the water signal at 4.8 ppm was presaturated for 1.0 s per scan.
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Unusually Mild and Selective Hydrocarbon C–H Bond Activation with Positively Charged Iridium(III) Complexes

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Certain transition metal complexes can react to break normally inert carbon-hydrogen (C–H) bonds, but these metal-based processes typically require photochemistry or elevated temperatures. In addition, most are unselective toward complicated functionalized substrates, which has limited their synthetic usefulness. The cationic iridium complex $Cp^*(P(CH_3)_3)Ir(CH_3)(ClCH_2Cl)^+BAr_f^-$ [$Cp^* = \eta^5$-$C_5(CH_3)_5$, $BAr_f = B(3,5\text{-}C_6H_3(CF_3)_2)_4$] can thermally activate methane and terminal alkanes at unprecedentedly mild temperatures (10°C). This complex will also induce C–H activation reactions in various functionalized substrates at ambient temperatures. High steric and electronic selectivity is observed, leading invariably to only one reaction product; the initial C–H activation reaction is typically followed by rapid metal-based rearrangements (that is, functionalization).

In synthetic chemistry, methods exist to transform nearly every organic functional group into another, thereby making many natural and unnatural compounds accessible to laboratory synthesis. Perhaps the most glaring exceptions to this rule involve saturated carbon-hydrogen (C–H) and carbon-carbon (C–C) bonds in alkanes or alkyl groups, where current techniques typically require these groups to be considered untouchable to selective synthetic reagents. Although the necessity for transforming these compounds and groups can sometimes be avoided by altering the choice of starting materials, the ubiquitous nature of saturated C–H bonds (in hydrocarbon fuels and the alkyl groups of useful organic molecules) implies that the ability to

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