

## Improved sensitivity of NMR spectroscopy probes by use of high-temperature superconductive detection coils

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**Abstract** -- High resolution nuclear magnetic resonance (NMR) spectroscopy is an important technique for the determination of molecular structures and physical properties of liquid samples. A major drawback is its low signal-to-noise ratio compared with other spectroscopic methods. The dominant source of noise in a spectrometer is often Johnson noise in the detection coils. Conductus, a leading manufacturer of superconductive electronics, and Varian, a leading manufacturer of NMR spectrometers, have successfully developed NMR sample probes using detection coils fabricated from thin films of the high temperature superconductor,  $\text{YBa}_2\text{Cu}_3\text{O}_{7-\delta}$  (YBCO) which reduce that noise and provide a sensitivity enhancement of a factor of four compared with conventional coils. The detection coils are maintained at about 25K while the sample, contained in a 5mm diameter tube, is at room temperature. The coils must carry high radio frequency currents during the excitation phase of a pulsed NMR experiment and, in order to maintain spectral quality, should cause little perturbation of the polarizing magnetic field. Characteristics of these probes and examples of spectra obtained are shown.

### I. INTRODUCTION

High resolution nuclear magnetic resonance (NMR) spectroscopy for the study of liquid samples has become a very powerful technique in the elucidation of molecular structure and dynamics. This power arises from the detailed information which can be obtained by the precise manipulation of the nuclear spins in a sample [1]. A drawback is the low sensitivity of the method compared with other spectroscopic techniques because of the small energy of the nuclear transitions.

The NMR response is excited and detected by resonant radio frequency (rf) coils within a probe situated in a polarizing magnetic field,  $B_0$ . At equilibrium the spins are represented by a single magnetization vector  $M_0$  aligned with

$B_0$ . If the magnetization is tipped away from this alignment, the resultant transverse component  $M_{xy}$  precesses around  $B_0$  at the Larmor frequency

$$\omega_0 = \gamma B_0 \quad (1)$$

where  $\gamma$ , the gyromagnetic ratio is a constant for a given nuclear species. For protons ( $^1\text{H}$ ),  $\gamma/2\pi = 42.5$  MHz/T while for  $^{13}\text{C}$ ,  $\gamma/2\pi = 10.5$  MHz/T. An rf field,  $B_1$ , perpendicular to  $B_0$  and rotating at the Larmor frequency can provide the perturbation. The magnetization precesses around  $B_1$  at a frequency

$$\omega_1 = \gamma B_1 \quad (2)$$

and the transverse magnetization is

$$M_{xy} = M_0 \sin(\gamma B_1 t) \quad (3)$$

where  $t$  is the duration of the rf excitation. A  $90^\circ$  pulse with a duration

$$t_{90} = \frac{\pi}{2\gamma B_1} \quad (4)$$

produces a maximum transverse magnetization. Following the pulse, the precessing magnetization induces a voltage in an rf coil. The same coil can be used to excite the magnetization and to detect the response. Chemical information is derived from the small variation in precession frequency with the environment of the nucleus within a molecule (chemical shift) and spin-spin and dipolar couplings to other nearby nuclei. The chemical shift range for protons is about 10 ppm while for  $^{13}\text{C}$  nuclei it is about 200 ppm. Responses from all nuclei with resonance frequencies within the chemical shift range  $\Delta\omega$  of the rf will be excited approximately uniformly if

$$B_1 = \frac{\omega_1}{\gamma} > \frac{\Delta\omega}{\gamma} \quad (5)$$

The nuclear precession signal following the rf pulse is recorded and Fourier transformed to produce the NMR spectrum.

A major motivation for the use of ever higher magnetic field strengths for NMR magnets is to improve sensitivity (signal-to-noise ratio) of the experiment, since the sign

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induced in the pick-up coil by a precessing nuclear magnetization is proportional to the square of the polarizing field strength. State of the art spectrometers operate with superconductive magnets up to 18.8 T (800 MHz for the proton resonance frequency).

Sources of noise in a spectrometer are: (a) thermal noise arising from the conductivity of the sample; (b) thermal noise from the resistance of the pick-up coil and (c) noise generated in the receiver system. When the noise from the coil is dominant, as is often the case, it can be advantageous to use a coil made from a superconductor to minimize this noise because of both a lower resistance and a lower operating temperature.

The earliest proposal for the use of a superconductor as an NMR probe was made by Rollwitz [2] but was never implemented. A  $^{13}\text{C}$  probe using a cooled coil of a normal metal was constructed by Styles et al [3] [4] and demonstrated a sensitivity gain of about three compared with a conventional probe. The development of high temperature superconductive (HTS) materials sparked a renewed interest in cooled coils for NMR applications. Coils made from  $\text{YBa}_2\text{Cu}_3\text{O}_{7-\delta}$  (YBCO) for NMR imaging were described by Black et al [5] [6] and by Withers [7]. Varian, a leading manufacturer of NMR spectrometers, and Conductus, a leading manufacturer of superconductive electronics, have now collaborated to develop high sensitivity probes using YBCO coils for high resolution NMR applications.

The sensitivity of two different coils operating at the same frequency and exciting the same sample volume is given by

$$\frac{S}{N} \propto \left( \frac{\eta Q}{T_P + T_A} \right)^{1/2} \quad (6)$$

where  $\eta$  is the filling factor of the coil system, a measure of how much of the total rf field energy is within the sample volume,  $Q$  is the quality factor of the coil,  $T_P$  is the effective probe temperature and  $T_A$  is the receiver noise temperature. Table I compares the various factors for a conventional and superconductive probe with a nonconductive sample. The units for filling factor and sensitivity are normalized to the values for a conventional probe. The filling factor is lower for the HTS probe because the coils must be spaced from the sample to provide thermal isolation. Conductive samples not only lower the  $Q$  of the coil because of the additional resistance but also raise the effective coil temperature because the added resistance is at the sample temperature which is often around 300K.

## II. SPECIAL REQUIREMENTS FOR HIGH RESOLUTION NMR

In addition to the need to improve the  $Q$  and lower the probe noise temperature, high resolution NMR spectroscopy imposes some additional requirements on a probe system.

TABLE I

ESTIMATES OF SENSITIVITY IMPROVEMENT FOR  
NONCONDUCTIVE SAMPLES

FACTOR	NORMAL PROBE	HTS PROBE
$\eta$	1	0.2
$Q$	250	10000
$T_P$	300	75
$T_A$	80	80
$S/N$	1	4.5

### A. Magnetic perturbation

Natural linewidths of resonance lines in liquid samples are often less than 1 Hz while resonance frequencies may be 800 MHz or more. Inhomogeneity of the polarizing magnetic field provides a broadening mechanism which may prevent the observation of natural linewidths. The homogeneity of the magnetic field is improved by optimizing the currents in a number of orthogonal shim coils within the magnet bore. Magnetic perturbations which might be introduced by the probe are minimized by the use of cylindrically symmetric structures and, where necessary, the use of specially manufactured susceptibility compensated material. Even the susceptibility of metals like copper is too high to allow their use as coils in conventional probes so composite materials with low susceptibility are fabricated by combining diamagnetic and paramagnetic materials.

The use of a superconductor would at first sight appear to present very severe problems of magnetic perturbation arising from the Meissner effect. In practice, the use of coils made from thin superconductive films alleviates most of the problems because of several factors:

(a) the material is strongly type II so that magnetic flux is not totally excluded from the superconductor;

(b) the HTS materials are very anisotropic and, in the geometry used in this application, the copper oxide layers are parallel to the polarizing magnetic field;

(c) very thin layers can be used so the total volume of superconductor is low;

(d) the material is spaced away from the sample region by the need to provide thermal isolation.

### B. Transmitter current

To satisfy (5) for proton spectra at 400 MHz requires rf fields approaching 1 mT, corresponding to a  $90^\circ$  pulse of approximately 10  $\mu$ sec. For the coil geometry used here, that requires an rf current of about 10 A. For  $^{13}\text{C}$ , with its greater chemical shift range, currents greater than 50 A are required to meet the same criterion. Using thin film superconductors, these currents translate into current densities greater than  $10^6 \text{ Acm}^{-2}$  so that very good quality films are necessary. Many NMR experiments make use of weaker rf fields to selectively excite portions of the spectrum. These weaker fields may be applied as long pulses of many msec or sometimes even as continuous irradiation. Ideally the conductor resistance should be independent of the current but a superconductor does display non-linear behavior.

### C. Multi-frequency operation

High resolution spectrometers always use more than one frequency in a probe. To maintain stability, it is customary to use an auxiliary rf channel providing continuous excitation and detection of a signal from a second nuclear species in the sample. This signal is used in a feedback circuit to stabilize the magnetic field. Most commonly, this second nuclear species is deuterium present in a deuterated solvent in the sample. In addition, the majority of NMR experiments involve the excitation of other nuclear species in the sample to exploit the couplings that exist between different nuclei in a molecule. Most NMR probes are designed to excite at least three nuclear frequencies simultaneously and it is not uncommon for an NMR probe to be able to excite four or five nuclear species at widely different resonance frequencies. This adds to the mechanical and rf complexity of the probes.

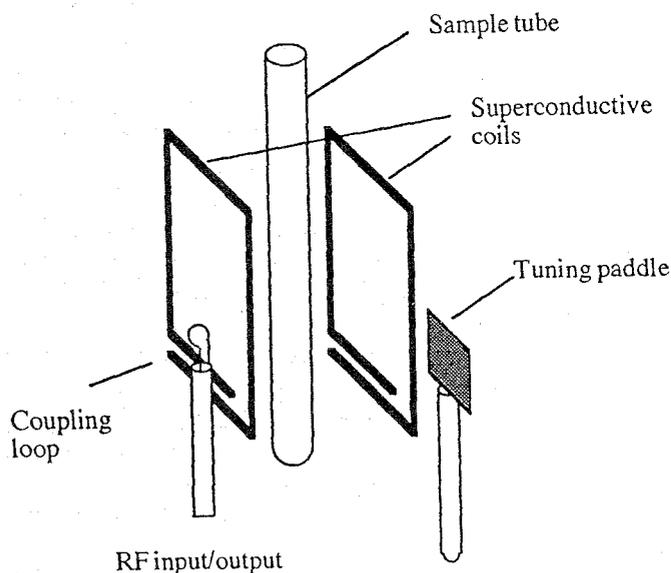


Fig. 1. The coil configuration in the superconductive probe.

### III. PROBE DESIGN

Several versions of probes designed to support two frequencies have been constructed and evaluated. A prototype probe operating at 400 MHz for protons and with a second deuterium channel has been previously described [8]. That probe is now a commercial product. Other configurations have included proton-fluorine and proton-carbon for 400 and 500 MHz spectrometers. A probe for 600 MHz is now being assembled. The configuration of a single channel is shown schematically in Fig. 1. Two coils operate as an inductively coupled system. Each coil is a self resonant circuit consisting of an inductive loop and interdigital capacitance and is etched from an epitaxial film between 300 and 650nm in thickness deposited on a planar substrate of lanthanum aluminate or sapphire. The use of a planar substrate contributes to the loss of filling factor compared with a conventional probe in which the coil system is mounted on a cylinder in close proximity to the sample. Preliminary adjustment of the resonant frequency is achieved by laser trimming of the capacitive fingers. Fine tuning in the probe is achieved by moving a conductive "paddle" close to one of the coils. Matching to the external circuit is achieved through a movable coupling loop. Typical matched Q values for a coil system of this type operating at 400 MHz are about

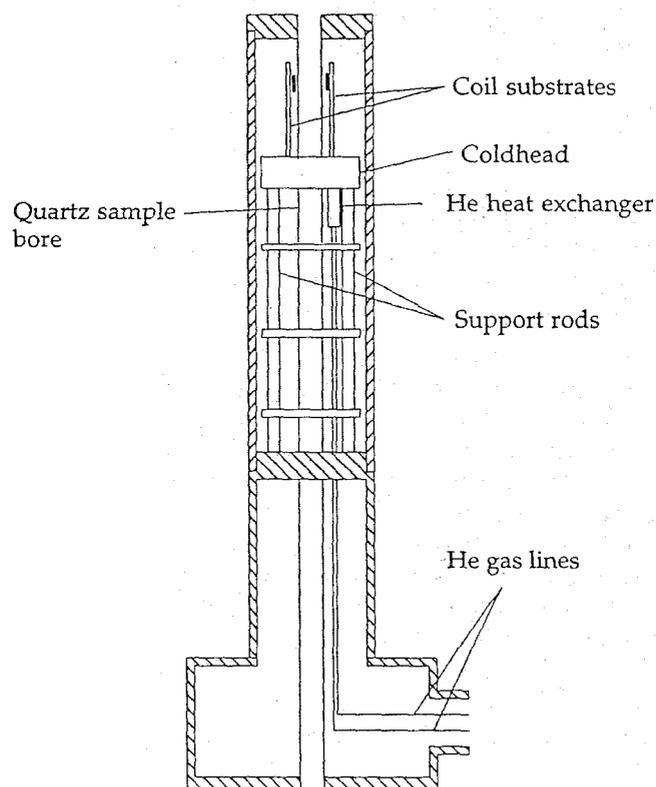


Fig. 2. The internal structure of the superconductive probe

15000 in zero magnetic field and 10000 in a field of 9.4 T.

The second channel uses a similar configuration with the coil pair mounted orthogonally to those of the first channel. When this second channel is used for field frequency lock, sufficient sensitivity is realized by using normal metal coils. For other applications, both coil pairs are made from superconductors.

A sketch of the probe is shown in Fig. 2. The coil substrate is thermally anchored to a cold head which is cooled to about 25 K by flowing helium gas. The temperature of the coils is controlled within a few tens of mK by a heater, thermometer and conventional feedback controller. This degree of temperature control is required to avoid variations in phase of the NMR signal from the temperature coefficient of the resonant circuit. The probe body is evacuated so that

With greatly reduced noise from the probe, the preamplifier may become the dominant noise source in the system unless it, too, is improved. Use of a GaAs FET preamplifier cooled in liquid nitrogen [9] can achieve a noise temperature of approximately 20 K. The probes described here include rf connections at room temperature so that contributions from cable losses limit the probe noise temperature to about 60 K. A GaAs FET preamplifier operating at room temperature can achieve a noise temperature also of about 60 K so that, by cooling the preamplifier, approximately a 25% improvement in sensitivity could be realized. However, by incorporating a cooled preamplifier into the body of the probe and maintaining all rf cables and connections at low temperature, an improvement of about 75% might be achieved.

#### IV. PROBE PERFORMANCE

Probes built to observe proton or fluorine resonances at 400 MHz and 500 MHz have achieved sensitivity improvements of greater than a factor of four when compared with the best that can be achieved with a conventional probe. With this sensitivity improvement, a 400 MHz spectrometer has greater sensitivity than a much more expensive 750 MHz spectrometer.

Measured linewidths with a non-spinning sample of 1% chloroform in deuterio-acetone are less than 1 Hz, 10 Hz and 20 Hz at 50%, 0.55% and 0.11% of the peak signal amplitude, respectively. (This apparently odd choice of intensities for the lineshape specification was made because  $^{13}\text{C}$  has a natural abundance of 1.1%. The signal from a proton attached to a carbon nucleus is flanked by a pair of  $^{13}\text{C}$  satellites with an intensity of 0.55% of the main peak.) This performance is not as good as a conventional probe but is still quite respectable and demonstrates that the magnetization effects of the superconductor are manageable.

Typical  $90^\circ$  pulse times for  $^1\text{H}$  and  $^{19}\text{F}$  are less than 15  $\mu\text{sec}$ . For the geometries used this requires about 10 A of rf current on the coils.

Most NMR experiments use more complex excitation than a single  $90^\circ$  pulse and often require time averaging for long periods. Two-dimensional Fourier transform spectroscopy is a particularly powerful technique. The inclusion of a variable delay in a series of excitations of the spins provides a second time dimension. The running time variable of the precession signal is the first time dimension. Data stored as a matrix of these two time variables is transformed to give frequency domain data as a function of two frequencies. Spectral intensity is represented by a surface in three dimensional space and is often displayed as a contour plot. Many different experiments are possible, some involving a single nuclear species and others involving two different nuclear species.

Fig. 4. shows a two-dimensional  $^1\text{H}$  total correlation

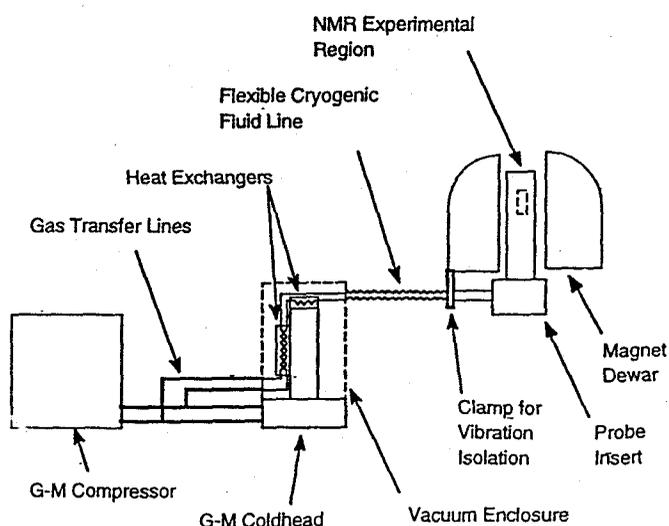


Fig. 3. Superconductive probe with closed cycle cryogenic system

only a single nonconductive wall separates the coil from the sample space which is designed to accommodate a 5 mm diameter sample tube. The sample temperature is controlled around room temperature by flowing air or nitrogen using the standard variable temperature system of the NMR spectrometer. The probe interfaces to the normal bore equipment of a high resolution spectrometer so that sample insertion and ejection and, if necessary, sample spinning is the same as with a conventional probe.

The source of cold helium gas is either a pressurized liquid helium storage vessel in an open cycle configuration or by recirculating helium cooled by a closed cycle refrigerator. The closed cycle system using a commercial Gifford McMahon cooler is shown in Fig. 3. An important feature of this system is the removal of mechanical vibrations by the use of a flexible coupling from the cooler to the probe and by clamping the probe inlet arm to the magnet. Without these measures, vibrations up to about 30 Hz severely distort the baseline around spectral peaks.

spectroscopy (TOCSY) spectrum [10] recorded with a 400MHz superconductive proton probe. The experiment includes a spin-locking rf field with a strength of about  $2.4 \times 10^{-4}$  T ( $\omega_1=10$  kHz) applied for 60 msec, and two weak selective presaturation rf fields to suppress unwanted resonances. The off-diagonal peaks in the spectrum provide information about spin-spin coupling between the protons of

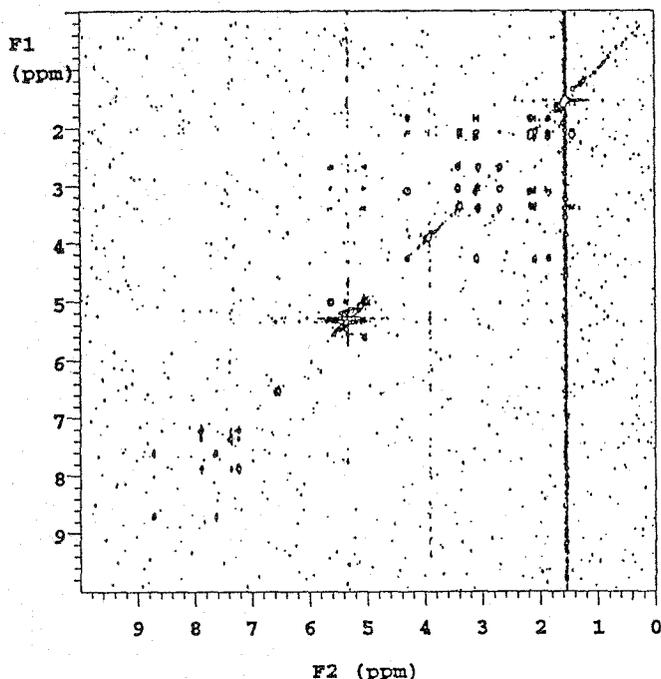


Fig. 4. 400 MHz  $^1\text{H}$  TOCSY spectrum of 13.7  $\mu\text{g}$  quinine in  $\text{CD}_2\text{Cl}_2$ . The total acquisition time was 1.5 hours.

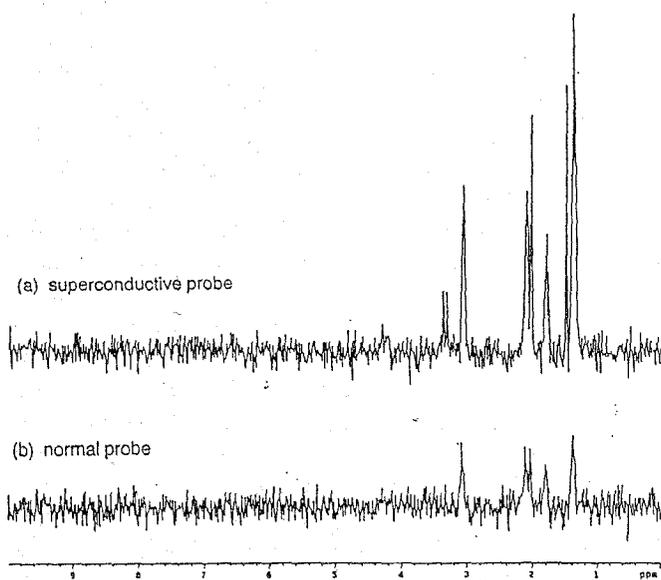


Fig. 5. Corresponding traces through TOCSY spectra of 13.7  $\mu\text{g}$  quinine recorded under the same conditions with (a) a superconductive probe and (b) a conventional probe.

the molecule. Comparison of corresponding traces from this spectrum and one recorded in the same total time on a conventional probe in Fig. 5 shows that the sensitivity improvement is maintained for this more demanding but fairly typical experiment.

With a Q of 10000, the bandwidth of the probe is approximately 100 ppm and, at 400 MHz, the transient rise-time is about 4  $\mu\text{sec}$ . These values are not of great concern for proton spectroscopy with its chemical shift range of about 10 ppm.

Because of the low natural abundance of  $^{13}\text{C}$  and its low gyromagnetic ratio, carbon NMR spectroscopy is much less sensitive than proton spectroscopy but can provide direct information about the backbone structure of organic molecules. The improved sensitivity of a superconductive probe to  $^{13}\text{C}$  spectroscopy is an obvious application. Magnetic perturbations are less of a problem with a lower gyromagnetic ratio nucleus, but the wider spectral range of 200ppm means that higher  $B_1$  field strengths are needed to satisfy (5) and the coil Q cannot be too high without causing serious spectral distortion. A  $^{13}\text{C}$  spectrum of deuterobenzene

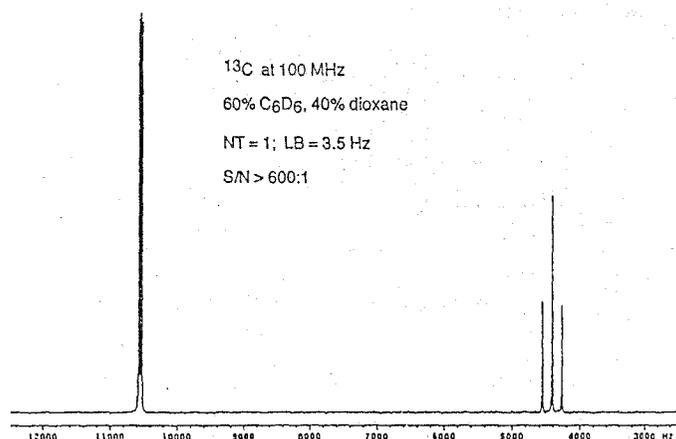


Fig. 6. A 100 MHz  $^{13}\text{C}$  spectrum of the ASTM sensitivity standard showing a sensitivity improvement of about a factor of four compared with a conventional probe.

and dioxane (the ASTM sensitivity standard) obtained with a superconducting probe with a matched Q of 5000 is shown in Fig. 6. The sensitivity of this spectrum is still almost a factor of four greater than that which can be obtained using a conventional probe.

A very powerful but extremely insensitive technique [11] exploits the coupling between neighboring  $^{13}\text{C}$  nuclei in a molecule to provide the connectivities of the various carbon nuclei. This is often sufficient to give an unambiguous molecular structure. This experiment is known by the acronym INADEQUATE (Incredible Natural Abundance Double Quantum Transfer Experiment). It is a demanding experiment because only signals from  $^{13}\text{C}$  nuclei coupled to neighboring  $^{13}\text{C}$  nuclei, occurring in  $1.2 \times 10^{-4}$  of the

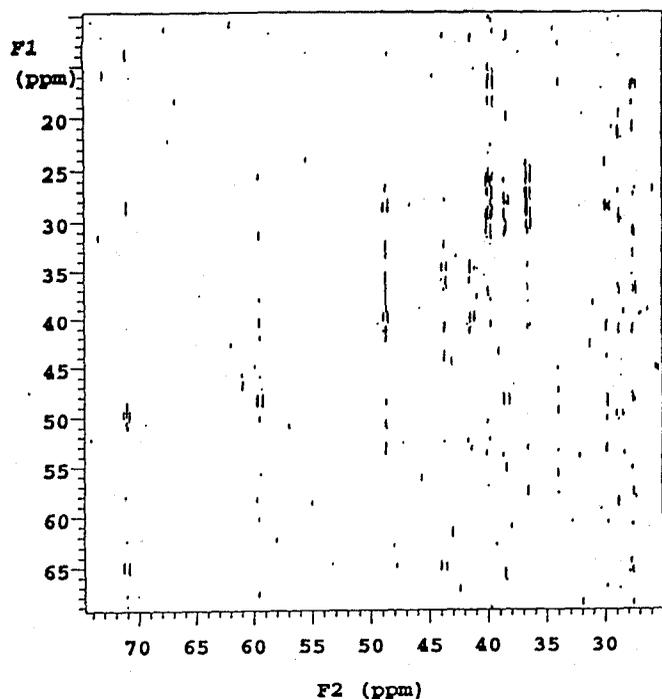


Fig. 7. 100 MHz  $^{13}\text{C}$  INADEQUATE spectrum of 18mg sucrose in 300  $\mu\text{l}$   $\text{D}_2\text{O}$  with broadband proton decoupling recorded in 11 hours with a superconductive probe.

molecules in the sample, are recorded. The almost 100 times stronger signals from  $^{13}\text{C}$  nuclei coupled to  $^{12}\text{C}$  are suppressed by exploiting the different behavior of the two types of signals to the phase of the rf excitation. To be successful, this requires stable operation over a long period of time. An example of an INADEQUATE spectrum recorded using a superconductive probe at 100 MHz is shown in Fig. 7. The pairs of doublets appearing at a fixed value of F1 show carbons which are directly bonded. Although this spectrum required 11 hours of data accumulation it is still shows much greater sensitivity than that from the same sample in a conventional probe.

## V. CONCLUSIONS AND FUTURE WORK

A practical probe for high resolution NMR has been demonstrated to improve sensitivity by approximately a factor of four. This factor is realized without the benefit of cooling the system preamplifier. Additional gains in sensitivity should be possible by incorporating a cooled preamplifier into the probe assembly. Greater usefulness of this type of probe will be realized by extending the capability to include at least three nuclear frequencies. Work to achieve this is in progress.

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