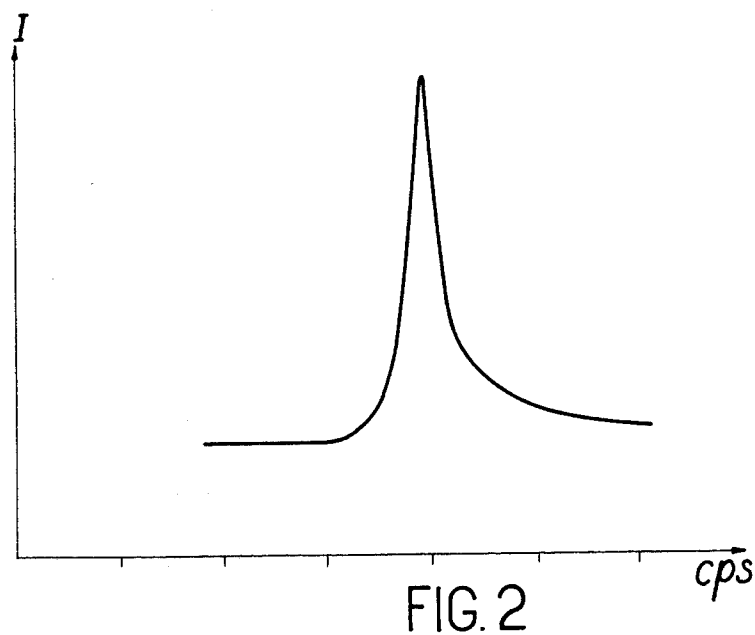
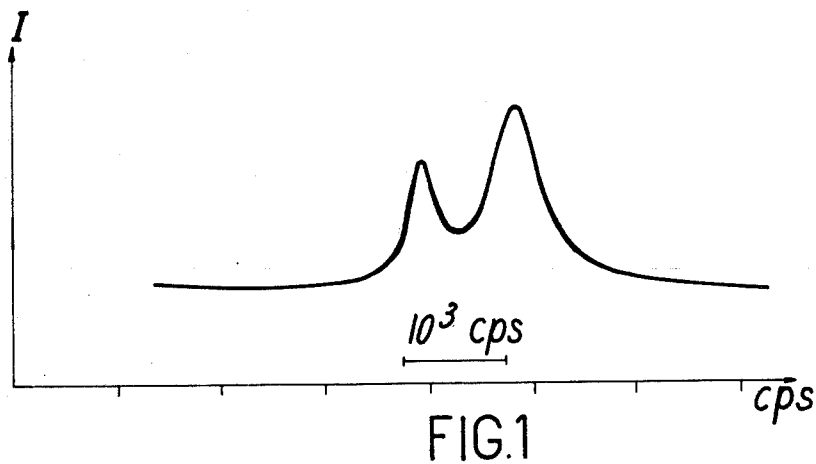


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NUCLEAR MAGNETIC RESONANCE MAGNETOMETER SOLUTIONS
CONTAINING NITROXIDE FREE RADICALS HAVING
DEUTERIUM ATOMS
Filed Oct. 12, 1970



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NUCLEAR MAGNETIC RESONANCE MAGNETOMETER SOLUTIONS CONTAINING NITROXIDE FREE RADICALS HAVING DEUTERIUM ATOMS

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5 Claims 15

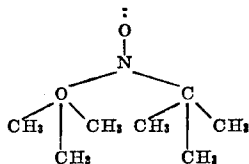
ABSTRACT OF THE DISCLOSURE

A magnetometer for measuring a weak magnetic field and its variations includes a solution which comprises a solvent with atomic nuclei (for instance protons) having non-zero magnetic moment and an organic hydrogenated free radical having unpaired electrons dissolved in the solvent. The free radical comprises a nitroxide group, the nitrogen atom of which is exclusively linked to two carbon atoms each linked with three other carbon atoms. For narrowing and enhancing the resonance lines, a major portion at least of the hydrogen atoms of the free radical are deuterium atoms. Radicals such as di-tert-butyl nitroxide (DTBN) and radicals having a hexagonal heterocycle the heteroatom of which is nitrogen (for instance tetramethyl-2-2-6-6-aza-1-cyclohexanone-3-nitroxide 1) may be used.

The invention relates to polarization of atomic nuclei (protons in particular) of a solvent by electron pumping and to a nuclear magnetic resonance magnetometer of the type disclosed and claimed in U.S. Pat. specification No. 3,249,856 assigned to the assignee of the present invention. The subject matter of said U.S. patent is incorporated in the present patent application by way of reference and some aspects of that earlier patent only will be repeated here.

U.S. Pat. No. 3,249,856 provides a complete description of a method for the dynamic polarization of the atomic nuclei of a solvent in which the magnetic moment and angular momentum of said nuclei are both different from zero; this method consists in dissolving in said solvent a free radical having unpaired electrons and exhibiting a hyperfine spectral structure with at least one electron resonance line of non-zero frequency in a zero magnetic field and in saturating said electron resonance line or lines of said free radical. Said radical comprises a nitroxide group in which the nitrogen atom is additionally linked solely with two carbon atoms and these latter are each linked with three other carbon atoms.

One of the free radicals which correspond to this definition is di-tert-butyl nitroxide also known as DTBN and having the formula:

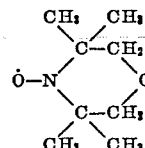


U.S. Pat. No. 3,249,856 also mentions those radicals which belong to the group comprising a hexagonal heterocycle in which the heteroatom is nitrogen and is linked

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on the one hand with an oxygen atom with which it forms nitroxide group and on the other hand solely with two carbon atoms which are adjacent thereto in the hexagonal cycle, each of these two carbon atoms being further linked with two methyl groups.

Among the above-mentioned radicals, the above-mentioned patent proposes in particular the use of triacetone amine nitroxide which is also known as tetramethyl-2-2-6-6-aza-1-cyclohexanone nitroxide-1 and abbreviated to TANO, the formula of which is:



In many applications, it is desirable to ensure that the lines of the electron paramagnetic resonance spectrum should be as fine as possible. It has become apparent to the inventors that one of the causes of widening of lines could lie in the interactions of the unpaired electron with the hydrogen nuclei when the radical is hydrogenated. In the case of TANO, it appears in particular that the coupling of the hydrogen nuclei of the methyl groups with the unpaired electron is an underlying factor, much more so in fact than that of the hydrogens which are located in the alpha position of the carbonyl nucleus.

It is an object of the invention to increase the fineness of the lines of electron paramagnetic resonance.

It is another object of the invention to provide an improved magnetometer for measuring a weak magnetic field and variations in said field (especially the earth magnetic field).

For this purpose, a hydrogenated free radical is used in which the greater part at least of the protons is replaced with deuterium nuclei.

The replacement of the hydrogenated radical by a deuterated radical results in an appreciable increase in dynamic polarization. Although the validity of this explanation does not affect the scope of the patent, it would appear that the above-mentioned increase in dynamic polarization can be attributed to a reduction in coupling within the free radical between the unpaired electron and the hydrogen nuclei which results in a higher energy transfer from the radical to the solvent nucleus (usually protons).

A better understanding of the invention will be gained from the following description of examples of application of the method according to the invention for the polarization of nuclei of a solvent by electron pumping.

Reference is made in the description to the accompanying FIGS. 1 and 2 which are curves illustrating respectively the nuclear magnetic resonance spectrum of normal TANO and that of TANO in which the methyl groups are deuterated.

By ways of first example, the preparation of deuterated TANO will be described as well as the results obtained by making use of this product; as will be seen later, these results can be extended to the cases of other hydrogenated free radicals having a hexagonal heterocycle.

The initial stage of synthetic preparation of the deuterated TANO radical consists in the preparation of deuterated ammonia. To this end, the following procedure can be adopted by way of example: 60 cm.³ of D₂O is caused to fall drop by drop onto 30 grams of magnesium nitride (approximately 0.3 mole). The reaction is highly exothermic. Ammonia which is evolved and charged with water vapor is passed into a column which is loaded with 20 g. of magnesium nitride (approximately 0.2 mole), then into two columns which are loaded with

barytes so as to eliminate the residual water. The ammonia gas is then condensed in traps which are immersed in a cooling mixture of acetone and solid carbon dioxide (-80°C.) and there are thus obtained 6 cm.³ of deuterated solid ammonia, namely approximately 4 grams (a yield of 40%).

The following stage, that is to say the synthesis of the deuterated triacetoneamine, is then carried out as follows: 25 ml. (20 grams, 0.31 mole) of 99.7% deuterated acetone and 8 g. of a dehydrating and complexing agent such as calcium chloride are introduced in an autoclave which is then cooled in liquid nitrogen. There are then added 3.5 cm.³ of liquid ammonia ND₃ (≈ 0.12 mole). The calcium chloride assists the absorption of ammonia and, as a result of dehydration, the condensation of the acetone molecules.

The reaction product is then placed within a flask provided with a coolant. This product consists of two phases: a reddish liquid phase and a whitish phase of more or less pasty consistency. This mixture is then heated to 70°C. for a period of five hours until the ammonia is completely evolved. The two phases are now well separated from each other and the brown liquid phase is collected. After addition of 0.5 cm.³ of heavy water and freezing to -15°C. (mixture of ice and salt), the triacetoneamine hydroate precipitates.

The triacetoneamine which is thus synthesized is purified by recrystallization followed by sublimation in vacuum, with the result that 5.1 g. of deuterated triacetoneamine are finally obtained. The yield was 30% as calculated with respect to the starting acetone.

Finally, the last stage of the process is the preparation of triacetoneamine nitroxide in the deuterated form and this is carried out as follows: the 5.1 g. of deuterated triacetoneamine are dissolved in a few cm.³ of water or heavy water. There are then added 5.5 cm.³ of hydrogen peroxide having a strength of 110 volumes and approximately 100 mg. of phosphotungstic acid.

When the reaction has proceeded for a period of two hours, the reaction product is extracted with ether, washed with dilute sulphuric acid and then with water, then dried on sodium sulphate. The ether is evaporated in vacuum. The deuterated triacetoneamine nitroxide is then recrystallized in petroleum ether; the quantity obtained is 3.3 grams (yield: 60% as calculated with respect to the starting triacetoneamine).

Since the α positions of the carbonyl group are capable of rehydrogenating during oxidation by H₂O₂, it is preferable to carry out on the substance obtained two consecutive isotopic exchanges in heavy water in a basic medium.

An analysis of the product thus obtained has been carried out by means of a mass spectrograph and has served to determine its composition as summarized in the table below:

Molecular mass	Formula	Percentage
183.....	C ₆ H ₃ D ₁₁ O ₂ N	7.5
184.....	C ₆ H ₂ D ₁₂ O ₂ N	23.1
185.....	C ₆ H ₁ D ₁₃ O ₂ N	41.4
186.....	C ₆ D ₁₄ O ₂ N	28.0

It is apparent that, in the mixture thus obtained, the degree of deuteration is remarkably high since 100% of the molecules which constitute the mixture have at least 14 atoms of deuterium.

Complete deuteration of the methyl groups can be checked by obtaining a nuclear magnetic resonance spectrum of the product in which the α positions of the carbonyl group are hydrogenated; in this case, there is only one visible peak which corresponds to the resonance of the protons in the α position of the carbonyl group.

FIG. 1 shows the nuclear magnetic resonance spectrum of normal TANO. There are shown in these figures two peaks which correspond respectively to the hydrogens in

the α position of the carbonyl group and to the hydrogens of the methyl groups.

FIG. 2 shows the nuclear magnetic resonance spectrum of deuterated TANO which is rehydrogenated in the α positions of the carbonyl group. There is now only one peak which corresponds to resonance of the protons which are present in the molecule.

In these figures, the number of cycles per second (c.p.s.) has been plotted as abscissae and the peak intensity (I) has been plotted as ordinates.

Accordingly, if the electron paramagnetic resonance spectra of the triacetoneamine nitroxide radical are studied on the one hand in the ordinary form and on the other hand in the deuterated form in solution at M/1000 in different solvents (methanol, ethanol, dimethoxyethane), a table is consequently obtained as given below, the line widths being expressed in gauss. In order to carry out these measurements, the solutions employed were placed in calibrated glass tubes 1 mm. in diameter and were deoxidized in a vacuum of 10^{-6} mm. of mercury.

Solvents	Line widths		Gain, percent
	Ordinary radical	Deuterated radical	
Methanol (CH ₃ OH).....	0.71	0.45	38
Ethanol (CH ₃ CH ₂ OH).....	0.60	0.36	40
Dimethoxyethane (CH ₃ OCH ₂ CH ₂ OCH ₃)....	0.73	0.46	37

It is apparent that, in the most favourable case, namely that of a deuterated triacetoneamine nitroxide solution in ethanol, the gain in fineness of line is 40%. This gain consequently represents a very considerable advantage so far as the electronic equipment of the magnetometer is concerned since it results in a gain in energy of the same order of magnitude. Moreover, the deuterated triacetoneamine nitroxide proves to be as stable as normal triacetoneamine nitroxide and there has not been shown any evidence of variation in the electron paramagnetic resonance spectra obtained in the same sample tube over a six-month interval.

The magnetometer in which the apparatus can be employed will not be described here since said magnetometer can be of the type described in the main patent or, better still, of the type which is contemplated in French patent application No. EN 7027099 of July 22, 1970, to which reference may usefully be made.

The proportions to be adopted in the case of the radicals are of the same order as in the case of non-deuterated radicals.

Results similar to those mentioned above can be obtained by means of various radicals of the same family, namely of the hexagonal heterocycle type, and especially by means of Tanol-6 and Tanane-6. These radicals are soluble in water and in many organic solvents having low viscosity which can be employed in magnetometry by virtue of their solidification point which is lower than that of water.

Similar results are also obtained with free radicals which do not have a hexagonal heterocycle and especially with DTBN. Deuterated DTBN is prepared by synthesis of deuterated nitro-tert-butane followed by action of metallic sodium on nitro-tert-butane in solution in dimethoxyethane (Hoffmann method). The synthesis comprises four stages:

Synthesis of the deuterated tert-butyl alcohol by reaction of deuterated magnesium methyl iodide with deuterated acetone (Grignard method); the alcohol yield is of the order of 60%;

Preparation of tert-butyl formamide (according to the Ritter method) respectively by action of acetonitrile on alcohol and action of sodium cyanide on alcohol;

Preparation of tert-butylamine by hydrolysis of the formamide (yield of approximately 80%);

Preparation of nitro-tert-butane by oxidation of the amine in accordance with the Kornblum method (yield of approximately 85%).

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The deuterated DTBN which is obtained in solution in methanol, ethanol or dimethoxyethane exhibits a resonance line which has been made finer by 30 to 40% with respect to that of normal DTBN. This gain is all the more advantageous since DTBN already has a resonance line width which is substantially smaller than that of the most widely employed radicals and especially TANO.

We claim:

1. In a magnetometer for measuring a weak magnetic field and its variations, of the type including a solution which comprises a solvent with atomic nuclei having non-zero magnetic moment and dissolved in said solvent, an organic hydrogenated free radical having unpaired electrons, comprising a nitroxide group, the nitrogen atom of which is exclusively linked to two carbon atoms each linked with three other carbon atoms, the improvement consisting in that a major portion at least of the hydrogen atoms of the free radicals are deuterium atoms.

2. The improvement according to claim 1, wherein said radical is ditertiobutyl nitroxide.

3. The improvement according to claim 1, wherein said radical includes a hexagonal heterocycle the heteroatom of which is nitrogen and is linked, on the one hand, to an oxygen atom with which it constitutes a nitroxide

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group and, on the other hand, exclusively with the two carbon atoms adjacent thereto in the hexagonal cycle, each of these two carbon atoms being linked on the other hand with two methyl groups.

4. The improvement according to claim 3, wherein the hexagonal heterocycle radical is tetramethyl-2-2-6-6-azal-1-cyclohexanone-3-nitroxide 1.

5. An improvement according to claim 4, wherein the solvent is selected from the group consisting of CH_3OH , $\text{CH}_3\text{CH}_2\text{OH}$, $\text{CH}_3\text{OCH}_2\text{CH}_2\text{OCH}_3$ and mixtures thereof.

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23—230 R; 324—0.5 E