PROGRESSOS RECENTES EM RMN ORGÂNICA

(WORKSHOP)

CAMPINAS 7 - 11 JULHO 1986

INSTITUTO DE QUÍMICA
UNIVERSIDADE ESTADUAL DE CAMPINAS

PROGRAMA, RELATÓRIO FINAL E RESUMOS

PROGRESSOS RECENTES EM RMN ORGÂNICA

A Reunião de Trabalho ("Workshop") sobre Progressos Recentes em Ressonância Magnética Nuclear Orgânica/ "Recent Developments in Organic Nuclear Magnetic Resonance" foi realizada no Centro de Convenções da Universidade Estadual de Campinas, Campinas, SP, no período de 7 a 11 de julho de 1986.

Comissão Organizadora

Joseph B. Lambert – Northwestern University, Evanston, Illinois, EUA.
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Entidades e Agências de Financiamento

A Comissão Organizadora deseja expressar os seus sinceros agradecimentos pelo auxílio concedido para a realização desta Reunião de Trabalho, às seguintes Entidades:

Universidade Estadual de Campinas – UNICAMP
Fundação de Amparo a Pesquisa do Estado de São Paulo – FAPESP
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Consejo Nacional de Investigaciones Científicas y Técnicas – CONICET
Food and Drug Administration – FDA
International Business Machines Corporation – IBM

Apoio Recebido para a Realização do WORKSHOP

Colaboradores

Banco do Estado de São Paulo S/A – BANESPA
Companhia Paulista de Força e Luz – CPFL
Sociedade Brasileira de Química – SBQ
Universidade Estadual de Campinas – UNICAMP
- Assessoria de Apoio a Eventos – APEU
- Instituto de Química – IQ
- Laboratório Interdisciplinar para a Melhoria da Comunicação – LIMEC
- Reitoria

Expositores

Bruker Analytische Messtechnik GMBH.
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Varian Indústria e Comércio Ltda.

RELATÓRIO FINAL

O texto apresentado a seguir é a versão integral do Relatório enviado às Agências de Financiamento, resumindo as conclusões da sessão de encerramento do "Workshop".
"FINAL REPORT ON THE US-LATIN AMERICAN WORKSHOP ON RECENT DEVELOPMENTS IN ORGANIC NMR"

Objectives

Nuclear magnetic resonance (NMR) is the principal spectroscopic method for the determination of molecular structure and conformation. Recent advances have increased dramatically the size of molecules that can be studied. Natural products in particular are well suited for study by NMR, and Brazil is one of the richest sources in the world for natural products. Equipment and expertise, however, have not flowed into Brazil easily for the pursuit of modern NMR methods. The objective of a one week workshop held on the UNICAMP campus in Campinas from July 7 to July 11, 1986, was to explore methods for enhancing NMR capabilities in Brazil.

Organization

Participation by U.S. scientists was organized by Joseph B. Lambert of Northwestern University. Participation by Brazilian scientists was organized by Roberto Rittner of UNICAMP, who also took care of all local arrangements.

One hour talks were given by each of 19 scientists, including 9 from the US, 7 from Brazil, 1 from Argentina, 1 from Belgium, and 1 from West Germany. The talks by the U.S. and European scientists provided a survey of the current status of the field of NMR, and the talks by the Brazilians provided an overview of NMR activities in Brazil. In addition to the speakers, there were about 100 registrants from universities throughout Brazil. Other acivities during the week included a cocktail party, two poster sessions, a dinner party, a panel discussion on instrumentation, a summary session, and an ongoing display by four commercial companies. Expenses for the U.S. speakers were provided by NSF; expenses for the Brazilian speakers were provided by CNPq and FAPESP; expenses for the other three speakers were provided by CONICET (Contreras), FNRS (Laszlo) and DAAD (Fischer). Support for individual speakers was provided by the FDA (Mazzola) and by IBM-Brazil (Yannoni). Additional support was provided by UNICAMP and Northwestern University.

Scientific Program

Outstanding talks were given by the speakers. These talks provided a minicourse in NMR for the registrants. The two poster sessions attracted almost 30 posters. The panel discussion on Tuesday provided further insight into the problems of obtaining and maintaining NMR instrumentation in Brazil. The summary session on Friday was attended by more than 40 individuals and provided the opportunity for all participants to comment on the proceedings of the week.

Attached with this report is the booklet given to all participants at the Workshop. It includes abstracts for the talks and posters, a list of speakers and participants, and an outline of the program.

Results and Recommendations

A. Personnel

1. *Collaborations.* One of the most important results was the initiation of specific collaborations between U.S. and Brazilian scientists who attended the workshop. These collaborations may envolve into complete research projects and should provide opportunities for the Brazilian scientists to use NMR instrumentation in the U.S., either personally or by mail.

2. *Short-term visits.* In some cases, existing Brazilian NMR instruments are underused because the technical personnel is not fully trained on all available capabilities. A short-term visit in the laboratory of a U.S. NMR spectroscopist who has the same instrumentation therefore can be of considerable benefit. Travel and subsistence funds will be needed by the Brazilian scientists. Short-term visits also will enhance scientific collaborations that are or will be underway.

3. *Ph.D.s from U.S. universities.* Ph. D. programs in the United States accept foreign students with a good knowledge of English, provided the student has an excellent university record and is highly recommended. Applications are most likely to meet success when the professors at the U.S. and Brazilian institutions know each other personally. Letters of recommentation then carry more weight. Brazilian students can obtain support from the Brazilian government and directly from the U.S. university. The mechanics of applying work most smoothly when a U.S. scientist takes a personal interest. The Workshop provided the opportunity for many U.S. and Brazilian chemists to get to know each other and hence to provide a good environment for applications to U.S. programs. A Ph. D. in the U.S. provides the Brazilian student with access to state-of-the art instrumentation.

4. *Postdoctoral fellowships.* A fellowship of one or two years in the United States also can provide training. Applications are made directly to specific professors. Competition is keen for such positions in good U.S. universities, so a good knowledge of English is essential and previous contact between the respective U.S. and Brazilian professors is important.

5. *Instrument maintenance.* Brazilian NMR laboratories need a substantial supply of electrical engineers (bachelor's level) who can maintain NMR spectrometers. These people might be able to be hired from one's own university. The jobs should be long term. Only with the availability of a large corps of engineers throughout Brazil can NMR spectrometers he used optimally and be kept in operating condition as much of the time as possible. Eventually these people also will be able to upgrade existing instruments and to install improvements (such as new pulse sequences) as they appear in the literature. Such people are needed not only at laboratories doing physical chemistry NMR but also at laboratories interested primarily in routine structural analysis. Such people will be needed not only at chemistry laboratories but also in biotechnology laboratories that plan to utilize NMR.

6. *The vendor's role.* Training of Brazilian personnel by the vendor of the NMR spectrometer at the time of instrument purchase is very important. If a lobartory is relatively inexperienced in the field of NMR spectroscopy, not one, but two people should be sent to the vendor's facility for training, included in the purchase price of the instrument.

7. *Meetings.* Continued contact within the Brazilian NMR community is important, in order to discuss problems of common interest (including maintenance), to present current research results, and to maintain personal acquaintance with NMR spectroscopists at other institutions. Such goals can be fulfilled by an annual meeting that moves from one university to another. A follow-up workshop also was suggested, in 3-5 years, between U.S. and Brazilian NMR spectroscopists. If the annual NMR meeting develops, it can provide an alternative to a future workshop, since 2 or 3 foreign scientists could be invited each year. In this way continued personal contact between Brazilian scientists and their counterparts in other countries can be maintained.

B. Instrumentation

1. *New spectrometers.* New spectrometrs are urgently

needed, of the routine (80-90 MHz iron core), of the advanced (200-300 MHz), and of the state-of-the-art (400-500 MHz). Each year, one or two 80-90 MHz and one or two 200-300 MHz instruments should be added in the country. A 400-500 MHz machine should be added every 3-4 years. Institutions to receive these spectrometers should be chosen on the basis of (1) the quality of the faculty and their research, (2) their ability to obtain liquid helium on a regular basis, and (3) their ability to maintain the instrument and utilize it most fully. In the third area, universities with personnel (such as electrical engineers) who can maintain instrumentation should be given preference.

2. *Used instruments and spare parts.* A spare parts and maintenance kit should be purchased with any new instrument and shipped as part of that instrument's purchase. For existing instruments, it is possible that excess instruments in the U.S. can be used for spare parts. Although shipment of an entire used spectrometer, including the magnet, is probably prohibitive and may not always result in a working spectrometer, the acquisition of the electronics (other than the magnet) can provide an excellent source for spare parts. Used instruments are frequently advertised in the TAMUNMR Newsletter, and Brazilians can advertise their needs in this same journal.

3. *Customs regulations.* Since all NMR spectrometers must be imported, greater flexibility in importation is needed. In particular, acquisition of replacement parts should not be held up by complex customs regulations. It is not in the best Brazilian interests for a machine that costs several hundred thousand dollars to be out of service for weeks or months because a small part is held up by customs regulations. A university research environment should be able to obtain exceptions.

4. *Buying protocol.* During the process of choosing a spectrometer, the following ideal procedure is recommended. (a) Run your own samples on the prospective machine. Do not let the vendor use only their samples. The samples may be mailed to the vendor or taken personally. (b) Include the test spectra as a specification in the purchase order for the new spectrometer. The vendor must fulfill not only their published specifications but also be able to achieve the same results on the new spectrometer in its home site as was obtained on the vendor's spectrometer. (c) Do not pay in full for the spectrometer until all parts are installed and all specifications met. Normally, a certain amount is paid at the time of placing the order, a second amount on delivery of the spectrometer, and a final amount when all specifications are fulfilled. It is extremely important that government funding sources realize that it is in Brazil's best interests to make payment in stages. Only when final payment is contingent on fulfilling the sales contract are vendors fully motivated to complete the installation satisfactorily. (d) Return damaged equipment immediately. (e) Write down all specifications and agreements. (f) Purchase should include training of one or two individuals on the instrument.

Conclusions

The most urgent current need is an infusion of new NMR spectrometers at a range of field strengths. Brazilian institutions must be committed to providing good professional maintenance through the training of individuals with a background in electrical engineering. Continued contact between U.S. and Brazilian NMR spectroscopists with a few international visitors will provide a means for discussing new results, comparing maintenance problems, and maintaining contact with international scientists.

PROGRAMA CIENTÍFICO

SEGUNDA-FEIRA –.7 DE JULHO

09:30 – 10:30: Sessão de Abertura
11:00 – 12:00: Conferência
J.A. Vanin, Universidade de São Paulo.
"Twenty Years of NMR Spectroscopy in Brazil".
14:00 – 16:00: Sessão de Painéis I
16:00 – 17:00: Conferência
A.A. Bothner-By, Carnegie-Mellon University.
"The Production of Very High Fields for High Resolution NMR: Progress and Prospects".
17:00 – 18:00: Conferência
N. Zanatta, Universidade Federal de Santa Maria.
"NMR of Nucleic Acids".

TERÇA-FEIRA – 8 DE JULHO

08:30 – 09:30: Conferência
W.S. Brey, University of Florida.
"Principles of Pulse Experiments".
09:30 – 10:30: Conferência
D.E. Wemmer, University of Washington.
"Two-Dimensional NMR Studies of Biomolecular Structures".
11:00 – 12:00: Conferência
H.C. Panepucci, Instituto de Física e Química de São Carlos (USP).
"NMR Imaging".
14:00 – 15:30: Mesa Redonda
J.B. Grutzner (Coordenador), A.A. Bothner-By,
J.A. Vanin, C.S. Yannoni e C. Rettori.
"Construção e Manutenção de Espectrômetros de RMN".
16:00 – 17:00: Conferência
P.R. Seidl, Instituto Militar de Engenharia.
"Applications of Carbon-13 NMR Spectroscopy to the Analysis of Oleaginous Seeds".

QUARTA-FEIRA – 9 DE JULHO

08:30 – 09:30: Conferência
R. Rittner, UNICAMP.
"Substituent Effects of α-Heteroatoms. Stereochemical Consequences".
09:30 – 10:30: Conferência
P. Fischer, Universitat Stuttgart.
"Applications of 2D-NMR in Organic Structural Elucidation – A Practical Survey".

11:00 – 12:00: Conferência
E.L. Eliel, University of North Carolina at Chapel Hill
"Applications of Oxygen-17 and Carbon-13 in Conformational Analysis".
14:00 – 16:00: Sessão de Painéis II
16:00 – 17:00: Conferência
J.B. Grutzner, Purdue University.
"Chemical Shift Theory: Orbital Symmetry and Charge Effects on Chemical Shifts".
17:00 – 18:00: Conferência
R.H. Contreras, Universidad de Buenos Aires.
"New Perspectives in Using Spin-Spin Coupling Constants as Probes to Obtain Molecular Information".

QUINTA-FEIRA – 10 DE JULHO

08:30 – 09:30: Conferência
F.Y. Fujiwara, UNICAMP.
"Molecular Structure Determinations by NMR Liquid Crystals".
09:30 – 10:30: Conferência
M. Barfield, University of Arizona
"Spin-Spin Coupling in Peptides".
11:00 – 12:00: Conferência
P. Laszlo, Université de Liege.
"NMR of Newly Acessible Nuclei".
14:00 – 15:00: Conferência
J.B. Lambert, Northwestern University.
"Applications of Spin-Lattice Relaxation to Organic Chemistry".
15:30 – 16:30: Conferência
C.S. Yannoni, IBM, California
"High Resolution NMR of Organic Materials in the Solid State: Structure and Dynamics".

SEXTA-FEIRA – 11 DE JULHO

08:30 – 09:30: Conferência
A.J. Marsaioli, UNICAMP.
"NMR Studies of Natural Products".
09:30 – 10:30: Conferência
E.P. Mazzola, Food and Drug Administration, Washington
"Structure and NMR Characterization of Trichothecenes".

11:00 – 12:00: Encerramento do "Workshop"

ÍNDICE DOS RESUMOS

CONFERÊNCIAS — Página

PAINÉIS

CONFERÊNCIAS*

THE PRODUCTION OF VERY HIGH FIELDS FOR HIGH RESOLUTION NMR: PROGRESS AND PROSPECTS

Aksel A. Bothner-By

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Pittsburgh, Pennsylvania 15213, USA

The history of NMR has been one of ever increasing magnetic field strengths. The most obvious and often-cited reason for this is that chemical shifts are more widely dispersed in the frequency domain, allowing spectra of more complicated molecules to be fully resolved and analyzed. However, other equally important advantages accrue, often as the square, rather than as the first power of the field strength. Examples include spectral dispersion in 2D spectra; line narrowing as a result of the spectrometer frequency exceeding the mean molecular rotational frequency; narrowing of the $+1/2 \rightarrow -1/2$ transition in the solid-state spectra of quadrupolar nuclei; detection of more rapid chemical exchange; and appearance of effects arising from molecular orientation by the magnetic field. Sensitivity increases at higher field, but only relatively slowly. Examples of each effect will be presented.

Currently, magnets permitting proton magnetic resonance observation as high as 630 MHz are in operation. The problems to be faced in constructing such magnets and magnets for yet higher fields include development of superconductors which will carry high currents when exposed to such intense fields; design of the magnet structure to withstand the large magnetostatic stresses generated during operation; and design to produce highly homogeneous and stable fields (1 part in 10^{10}) at the sample. A practical and economic cryostat should also be provided. The magnet must be protected against thermal quench. The r.f. circuitry, amplifiers, detectors, and computer acquisition and processing are well within current technology. It seems reasonable to expect NMR spectrometers to be operational at 900-1000 MHz in the next few years.

^{13}C-NMR ASSIGNMENT, STRUCTURE, AND DYNAMICS OF DEOXYOLIGONUCLEOTIDES

Nilo Zanatta*, Philip N. Borer⁺, and George C. Levy⁺

**Departamento de Química, Universidade Federal de Santa Maria, Santa Maria, RS, Brasil.*
⁺Chemistry Department, Syracuse University, Syracuse, NY, USA.

High resolution ^{13}C-NMR spectra, T_1 relaxation times and NOEs were measured for duplex of the self-complementary oligo-DNAs: $d(CG)_3$ and d(GGTATACC). The target of this study is to develop a systematic ^{13}C-NMR spectral assignment and to investigate the structure and dynamics of these two sequences by this technique. Assignments were made, in part, by comparisson between the duplexes and with mononucleotides spectra. Nearly half of the profiles for the base carbons exhibit transitions opposit to the expectation from ring current predictions. These shielding increases on duplex melting are apparently due to hydrogen-bonding. The Cl' carbons all become less shielded upon duplex melting. However, only half of the C2', C3', C4', and C5' carbons exhibit shielding decreases whereas the remaining carbons display shielding increases upon duplex melting. T_1 and NOE values were measured for all protonated carbons of the duplexes, at different temperatures and magnetic fields. Dynamic modeling of the T_1 and NOE values supplied information about the frequencies of overall and internal (localized) motion of the duplexes.

PRINCIPLES OF PULSE EXPERIMENTS

Wallace S. Brey

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Gainesville, Florida 32611, USA

The talk will be presented at an introductory level to develop certain principles and techniques related to spin-echo and polarization transfer methods which are incorporated into more complex experiments, including two-dimensional methods. The following topics will be included.

(1) Modulation of spin echoes by spin-spin coupling.
(2) Methods of multiplicity determination and editing of carbon-13 spectra, using less sophisticated instruments; the ESCORT experiment.
(3) J spectroscopy, homonuclear and heteronuclear, and applications in two-dimensional experiments.
(4) Polarization transfer methods and use of selective decoupling.
(5) Some extensions of the INEPT sequence.
(6) Use of INEPT and DEPT as preliminaries to 2D experiments.
(7) The flip-angle effect.
(8) Combination of J spectroscopy and correlation spectroscopy in three dimensions.

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* Nota: Os Resumos das Conferências 1 e 6 não foram enviados à Comissão Organizadora.

TWO DIMENSIONAL NMR STUDIES OF BIOMOLECULAR STRUCTURE

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Analysis of complex NMR spectra from biopolymers has been difficult due to the problems of assigning resonances, relatively low sensitivity, and poor resolution. All of these problems have been alleviated by the development of 2D NMR methods. Wüthrich developed the sequential approach for reliably obtaining resonance assignments in proteins, which are crucial for analysis of the spectra. Since that time a similar method has been developed for nucleic acids, and some work has been done with oligosaccharides as well. The sequential method first uses correlated spectra to identify spin systsems (and thus residue type), then NOE spectra to connect neighboring residues following the primary structure. We will present examples of such sequential assignments for nucleic acids and proteins. In complex molecules, experiments for obtaining extended correlations (RELAY and MQ) are of particular importance in identifying the spin systems; examples of their use will be given. Structural information is derived from the NMR data in several ways. Most important of these is through estimated distances based on NOE cross-peak intensities or build-up rates. Large numbers of reasonably accurate distances can be determined from a single spectrum, when care is taken to assure that the cross-relaxation is still in its linear phase. Analysis of NOEs involving backbone protons provides information about the secondary structure, while side-chain proton NOEs characterize the tertiary folding. Additional structural information comes from measurements of coupling constants (giving dihedral angles) and identification of hydrogen bonds through retardation of amide proton exchange. Longer distances may be determined through analysis of relaxation contributions from spin labels attached to the molecule at specific points.

The distances determined from NOE spectra, relaxation, or other sources can be used to develop a structure in several ways. Mechanical models are useful for an initial qualitative analysis, but are not transportable, and are difficult to refine. Several computational methods are now available for generating structures including distance geometry (Crippen, Kuntz, Havel, Wüthrich); molecular dynamics/energy minimization (Kaptein, van Gunsteren); and local-global sequential folding (Go, Braun, Wüthrich). These methods are automated, can give information about the quality of the structure determined, and provide coordinates, which can easily be communicated to others. The principles of these methods will be presented, with some examples, and the quality of the structures thus determined will be discussed.

APPLICATIONS OF CARBON-13 NMR SPECTROSCOPY TO THE ANALYSIS OF OILSEEDS

Peter Rudolf Seidl and Luiz Alberto Colnago

Instituto Militar de Engenharia, Rio de Janeiro, RJ

Oilseeds have been important souces of food, fuel and raw material since early times. They are grown today on a large scale, contributing significantly to the economy of many regions of the world. The oil, or fluid constituent of the seed, constitutes its energy reserve and is consumed during germination.

Vegetable oils are normally made up of triglicerides of fatty acids. Although a large number of these compounds is found in nature, most of their esters result from the combination of a few C_8-C_{13} straight chain acids (which may contain double bonds or other functional groups) and glycerol.

Until recently these compounds were analyzed by methods which require destruction of the seed and chemical work-up. Carbon-13 NMR, however, can be used identify the main constituents of the liquid or water soluble compounds found in oilseeds. We have adapted this technique to a large number of oilseeds that are grown in Brazil and have investigated the factors that affect chemical shifts. Changes in relative proportions of constituents can be followed in a continuous way on the same seed during seed development and germination.

SUBSTITUENT EFFECTS OF α-HETEROATOMS STEREOCHEMICAL CONSEQUENCES

Roberto Rittner

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Campinas, SP, Brasil

Substituent effects on chemical shifts are widely studied by organic chemists to gain insight on their effects in the eletronic structure of organic compounds.

Carbonyl carbon chemical shift does vary in an apparently random way and it defies one to correlate the observed upfield shifts to any other structural property, throught either a linear or a multilinear relationship, or even to advance a qualitative explanation for the observed results. The α-methylene carbon exhibits also an upfield shift, when compared to the expected chemical shift, estimated by a simple additivity rule.

Experimental data for α-heterosubstituted aliphatic ketones, esters and amides are masked by the conformational equilibria, which depend upon the substituents and on the classes of compounds studied. However, both the substituent effects as the conformation equilibria reveal a similar trend for the above mentioned carbonyl compounds.

Mono- and bicyclic ketones allow to fix a given stereochemical relationship between the carbonyl group and the α-substituent. Preliminary work has shown the substituent effects can be better understood in the light of orbital interactions in the CO-CH_2-Z system. Therefore, theoretical calculations and photoelectron spectroscopy data should be used in conjunction with Carbon-13 NMR data to elucidate the substituent effects on such α-heterosubstituted systems.

APPLICATION OF 2D-NMR IN ORGANIC STRUCTURAL ELUCIDATION. A PRACTICAL SURVEY

Peter Fischer

Institut für Organische Chemie, Biochemie und Isotopenforschung, Universität Stuttgart, D-7000 Stuttgart 80

Application of polarization transfer experiments (2D sequences) to structural elucidation of small to medium sized organic molecules is described. For a number of specific strucutural problems, the individual procedures employed and the practical analysis of the 2D plots will be demonstrated. The following analytical problems will be stressed specifically.

i) identification of individual spin systems (J-correlated spins: homonuclear COSY), as contrasted with conventional selective decoupling sequences, and also with straightforward numerical analysis.
ii) correlation of directly coupled H and C nuclei (H, X-COSY), especially for the case of two diastereotopic, anisochronic CH_2 protons.
iii) correlation of long-range coupled H and C nuclei (COLOC).
iv) determination of spatial relation of two nuclei (difference NOE, NOESY).
v) differentiation between spectral multiplicity, arising from the presence of either configurational isomers (diastereoisomers), or of rotamers, i.e. configurationally homogeneous molecules in different conformations – as contrasted to temperature dependent line form analysis (coalescence).

APPLICATION OF OXYGEN-17 AND CARBON-13 IN CONFORMATIONAL ANALYSIS

Ernest L. Eliel

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^{13}C NMR has long been used in conformational analysis of ring compounds: cf. the classical work of Grant extensively cited in Stothers's 1972 book and work in saturated heterocycles cited by Eliel and Pietrusiewicz in *Topics in Carbon-13 NMR Spectroscopy, 3,* 171-282 (1979). It is less convenient for acyclic compounds because of their conformational complexity and the need to fathom conformational distribution about each bond before ^{13}C shifts can be calculated from first principles.

An important but neglected aspect relates to "intermolecular conformational analysis" – the effect of intermolecular interactions such as solvation, hydrogen bonding, dipole association, etc., on conformation and hence on NMR spectra. Following a background discussion of conformational analysis and ^{13}C spectroscopy in saturated oxygen, sulfur, and nitrogen heterocycles and salts of the latter, ^{13}C results for such systems bearing polar substitutents will be presented. Dipole-dipole interactions, intra- and intermolecular hydrogen bonding effects and solute-solvent interactions in some cases affect conformation- and hence ^{13}C spectra-profoundly. The case of *cis*-3-hydroxythiane S- oxide will be shown in which the conformational equilibrium changes from nearly all e-e to nearly all a-a as the concentration is lowered from 3 M to 0.002 M. As a result, ^{13}C NMR spectra of this substance cannot be reproduced unless the concentration (in a nonpolar solvent) is precisely stated. (The concentration effect disappears in a polar, associating solvent.)

^{17}O NMR of oxygen-containing heterocycles and heterocycles with oxygen-bearing substituents can now readily be recorded at natural abundance (0.037%) in sensitive, high-field instruments. The very rapid quadrupole relaxation of the ^{17}O nucleus allows for acqusition times of the order of 10 μsec, so that 200,000-300,000 transients can be observed in one hour. Of course, there is serious quadrupole broadening. Several examples of ^{17}O spectra in ring systems of defined conformation will be shown and discussed. The results are so far interpreted only empirically and, in some instances, are rather surprising.

CHEMICAL SHIFT THEORY: ORBITAL SYMMETRY AND CHARGE EFFECTS ON CHEMICAL SHIFTS

John B. Grutzner

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The influence of charge and orbital symmetry on NMR chemical shifts will be developed within the original Ramsey formulation. A simplified orbital model will be presented which accounts for the common notion that chemical shift and charge are linearly related AND the many examples where this naive relationship fails. The model is based on the Ramsey theory as explicithy developed by Cornwell. The following are basic features.

1. The chemical shift observed in solution is the average of the three principal shielding tensors which may be measured directly in the solid, $\sigma = (\sigma_{XX} + \sigma_{yy} + \sigma_{ZZ})/3$.

2. Shielding arises from electron circulation induced by the applied magnetic field in the plane perpendicular to the applied field. σ_{XX} arises from electron circulation in the yz plane.

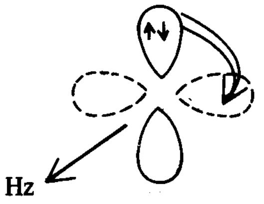
3. Electron orbital momentum (p electrons, d electrons, etc., but not s electrons) is the major contributor to shielding through the paramagnetic term of the Ramsey equation.

$$\sigma_{xx} = \sigma_{xx}{}^{d} + \sigma_{xx}{}^{p} = \frac{e^2}{2mc^2} \langle 0 | \sum_i \frac{(y_{ki}{}^2 + z_{ki}{}^2)}{r_{ki}{}^3} | 0 \rangle + \frac{e^2}{2m^2c^2} \sum_{k>0} \times \left[\frac{\langle 0 | \sum \frac{(L_{ki})_x}{r_{ki}{}^3} | k \rangle \langle k | L_x | 0 \rangle + \langle 0 | L_x | k \rangle \langle k | \sum_i \frac{(L_{ki})_x}{r_i{}^3} | 0 \rangle}{E_0 - E_k} \right]$$

4. Orbital symmetry has a major effect on shielding through the orbital angular momentum term. For example, linear molecules have zero orbital angular momentum about the molecular axis and show anomalous high field shifts as a result.

5. Charge acts only as a scaling factor for the orbital angular momentum contribution.

6. The Ramsey-Cornwell model may be represented pictorially.



$$\equiv \langle n | L_z | 0 \rangle$$

The following so-called anomalous chemical shifts will be used to illustrate the application of the model.

(a) F_2 resonates 720 ppm downfield of F^- yet FCl resonates 160 ppm upfield.

(b) The oxygen shift of $NO_2{}^+$ is 250 ppm upfield of $NO_2{}^-$. Similarly, CO_2 resonates upfield of $CO_3{}^{2-}$, which in turn is upfield of carboxylate oxygens.

(c) sp-Hybridized carbon in acetylene occurs 130 ppm to high field of the sp carbon in allene, whereas the sp^2 carbon in allene resonates 50 ppm to high field of that in an alkene.

(d) π-Conjugated cations, anions, and neutrals give a linear relationship between charge and chemical shift, with cationic carbons occuring at lowest field. Yet C1 in phenyllithium resonates downfield of a benzene carbon and a number of carbocations are known in which the formally cationic carbon resonates to highfield of TMS.

THE IPPP METHOD AS A COMPLEMENTARY TOOL FOR HIGH RESOLUTION NMR SPECTROSCOPY

Rubén H. Contreras, Claudia G. Giribet, Martín C. Ruiz de Azúa and Agustín C. Diz

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In the present work several applications of the IPPP (Inner Projections of the Polarization Propagator) tecnique for studying spin-spin coupling constants are presented. This technique is specially suited to study different electronic contributions to spin-spin coupling constants and to chemical shifts. It can be implemented with different degrees of sophistication. Its basic ideas can be summarized as follows: 1) the ground state wave function of the molecule under study is calculated; 2) unitary transformations to both occupied and virtual molecular orbitals are applied; 3) the polarization propagator is inner projected onto the chosen localized molecular orbitals; 4) local contributions are calculated using the projected polarization propagator and the perturbators defining the studied interactions (the Fermi contact, the paramgnetic spin-orbital, and the spin-dipolar terms).

Examples presented in this work intend to show both the usefulness of this approach and the easiness with which an experimentalist can use it. Three different kinds of problems are discussed, namely, a) the decomposition on σ- and π-transmitted components, b) the through-space transmission of couplings, and c) the analysis of the multipath transmission in cyclic and multicyclic compounds. In all three cases the approach used is the IPPP-RPA-INDO one, which means that the molecular ground state wave function is obtained using the INDO approximation, and that the polarization propagator is evaluated at the RPA (Random Phase Approximation) level. As this perturbative approach is equivalent to the CHF (Coupled Hartree-Fock) one, total couplings quoted in this work are exactly the same as those obtained with other schemes to obtain the CHF approximation.

Local contributions from a given molecular fragment to the coupling constant between a pair of nuclei N and N' can be expressed as a sum of terms involving the projected polarization propagator and the perturbators which define the studied interaction between nuclei and electrons. Each term depends on two occupied and two vacant localized molecular orbitals which are chosen to represent chemical functions (bonds, antibonding orbitals and lone-pairs). The analysis of these terms yields an intuitive picture about the way in which the coupling is transmitted. This pictorial representation is complemented with plots of the localized molecular orbitals involved in the analysed term.

MOLECULAR STRUCTURE DETERMINATIONS BY NMR USING LIQUID CRYSTALS

Fred Y. Fujiwara

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Some twenty years ago, small molecules dissolved in nematic liquid crystals were observed to present well-resolved spectra from which intermolecular dipole-dipole coupling constants could be obtained. Since these couplings depend on the inter-nuclear distances, the structure of molecules in solution can be obtained, apparently with a high precision. During the last twenty years the applications of this technique for structural determinations has been explored. A review of the advantages and limitations of this method will be presented. Other applications of NMR using liquid crystal solvents, such as the determination of quadrupole coupling constants and anisotropies of chemical shielding tensors, and studies of internal motion and fluxional behavior of organic molecules, will be presented.

SPIN-SPIN COUPLING IN PEPTIDES

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Conformational studies of peptides in solution make use of NOE close contact data and spin-spin coupling constants, primarily vicinal H-N-C-H values. A number of homonuclear and heteronuclear coupling constants, having potential for conformational information in the peptide backbone, are being investigated in these laboratories. Great care must be exercised in the inference of conformational dependencies for apparently related moieties. Our approach emphasizes the need for measurements in appropriate model compounds, which include the relevant conformational and substituent features; e.g., lactam-constrained systems. Several types of ^{13}C-^{1}H coupling constants which have been investigated can be used to reduce conformational ambiguities in the coupling constant data. Of particular interest is the possibility of using these data to obtain the elusive ψ angles. Alghough some of this work involves the use of labeled compounds, recent developments in selective 2D INEPT techniques will probably make it possible to carry out this work on small peptides in natural abundance.

NMR OF NEWLY ACCESSIBLE NUCLEI

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To begin, the natural abundances, the sensitivities, the electric quadrupole moments, and the corresponding IQ terms will be surveyed for the various nuclides in the Periodic Table. In order to focus the talk, and so that it will be complementary with the other lectures in the workshop, most of the illustrations will be taken from deuterium NMR.

It is enlightening to consider the recent shift from deuterium in NMR (deuterium isotope shifts, multiplicities, and lineshapes for spin 1/2 resonances scalar coupled to deuterons) to deuterium NMR. The attendant spectral simplification with respect to proton NMR will be stressed. Applications will be given to detection of diastereotopic deuterons. The question of single-versus double-well potentials for hydrogen-bonded systems, such as acetylacetone, will be addressed.

Deuterium NMR at natural abundance reveals the isotopic distribution in organic molecules. This is a truly unique trace of the chemical history of the sample. It reflects kinetic isotope effects in the steps (synthetic, natural C_3 cycle, or C_4 cycle photosynthetic) having led to this particular molecule. Several applications of such natural abundance labeling will be discussed, including the detection of wine frauds.

Deuterium relaxation rates, alone or in conjunction with carbon-13 relaxation measurements, provide one of the best handles onto molecular dynamics. Applications mentioned in this section will include enzymatic kinetics and the extent of local mobility in biological membranes. They will include also the determination of ultrafast rate constants (10^8-10^{10} s^{-1}), allowing for the clear delineation of collision complexes from longer-lived complexes.

Our concluding topic will be the removal of the quadrupolar interaction between spin states differing only in sign. A nice example is the double quantum coherence for a deuteron. This allows easy determination of the principal components for the chemical shielding anisotropy tensor for a solid as a powder. A description will be given of the corresponding 2D experiment.

Support by Fonds National de la Recherche Scientifique, Brussels.

APPLICATIONS OF SPIN-LATTICE RELAXATION TO ORGANIC CHEMISTRY

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The spin-lattice relaxation time (T_1) is one of the four fundamental parameters of NMR, the others being chemical shift, coupling constant, and exchange rate constants. Spin-lattice or longitudinal relaxation is the return of magnetization to equilibrium along the z direction. The relaxation time is best measured by the inversion recovery pulse sequence. The primary mechanism of spin-lattice relaxation for spin 1/2 nuclei is the dipole-dipole interaction of the resonating nucleus with a nearby magnetic nucleus in motion. Spin rotation, chemical shielding anisotropy, and scalar coupling also contribute. Nuclear quadrupole relaxation provides the dominant mechanism for nuclei of spins greater than 1/2. Mechanisms of spin-lattice relaxatiom may be separated by measurement of nuclear Overhauser effects, the temperature dependence of T_1, and the field dependence of T_1. When the dipolar relaxation is dominant, T_1 is inversely proportional to a correlation time for molecular rotation and is directly proportional to the distance between the resonating and relaxing nuclei and to the number of nearest neighbor magnetic nuclei. Spin-lattice relaxation is used to study molecular motion and structure. Applications include the examination of anisotropy of motion, segmental motion, partially relaxed spectra, peak suppresion, structu-

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Germany

ral determination, and the determination of rate constants for fast or slow processes not amenable to lineshape analysis.

HIGH RESOLUTION NMR OF ORGANIC MATERIALS IN THE SOLID STATE: STRUCTURE AND DYNAMICS

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High resolution NMR is the most diagnostic spectroscopic technique for studying molecular structure in liquids, and cross polarization magic angle spinning (CPMAS) has made it possible to obtain well-resolved spectra of certain nuclei (e.g., ^{13}C, 29$_{\mathrm{Si}}$, ^{15}N) in solids. We have used ^{13}C CPMAS for a variety of dynamic and structural studies in which the molecule of interest undergoes a degenerate rearrangement with a very low activation energy ($E_a > 1.5$ kcal mol^{-1}). This has required the development of a magic angle spinning apparatus for temperatures as low as 15K, which will be described along with some of the more general magnetic resonance ideas underlying the CPMAS method.

The technique has been applied to several systems including (1) the degenerate hydride shifts in carbonium ions (*sec*-butyl and 2-norbornyl), (2) the morphology-dependent electrocyclic rearrangement of semibullvalene, (3) the very low barrier rearrangement in cyclooctatetraene diironpentacarbonyl, and (4) methyl group tunneling.

^{13}C N.M.R. SPECTROSCOPY IN NATURAL PRODUCTS CHEMISTRY

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^{13}C N.M.R. spectroscopy has been used in natural products chemistry as a complementary technique in the various stage of the structure elucidation process. The ever increasing magnetic field strength and development of new techniques in N.M.R. spectroscopy has enabled the detection of stereoisomers and other closely related compounds as well as the assignment of rather complex structures, isolated in minute amounts.

It is worthwhile mentioning that the availability of spectral data in the literature greatly facilitates the analysis of new carbon skeletons.

Our attention was particulary attracted to the application of ^{13}C NMR spectroscopy to detect conformational aspects of natural products in solution.

We have thus studied the berbamine, curine and daphonoline – repandine class of bis (benzylisoquinoline) alkaloids revealing some interesting conformational aspects of their benzylisoquinoline moieties. To support the shift assignments of the above series several isoquinoline alkaloids were studied systematically with the objective of rationalizing the shielding effects exerted by the various substituents. ^{13}C N.M.R. spectroscopy revealed itself as a straightforward method for the determination of the oxygenated functions in the oxoaporphine and aporphine alkaloids, and for the determination of the relative configuration of two novel erythrine N-oxides.

A completely different line began with the study of the isocopalane and podocarpane class of diterpenes when we suçessfully applied the inversion-recovery and spin-echo techniques in conjunction with SFORD spectra to support unambiguous assignments. Application of the semiempirical derivation of ^{13}C N.M.R. chemical shifts supported the ^{13}C data of the isocopalane and isocopalanol.

Finally, we are now dealing with naturally occuring acetylenes, conscious that ^{13}C data have not been exploited for determining structures in this class of compounds.

STRUCTURE AND NMR CHARACTERIZATION OF TRICHOTHECENES

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The structures of many simple and macrocyclic trichothecenes have been elucidated in our labortories almost entirely by proton and carbon-13 NMR spectroscopy. Some interesting relationships between chemical shifts, primarily carbon, and the molecular conformation and configuration of both side chains and macrocyclic rings have emerged from these studies. The macrocyclic systems, in particular, have proved to be intriguing in a number of respects. First, these macrolides are situated much more closely to certain nuclei of the trichothecene moiety than Dreiding stereo models would suggest. Minor changes, such as epoxidation, in the structure of the macrocyclic ring have profound effects on both the proton and carbon-13 NMR spectra. The dienic side chains of the nonmacrocyclic trichothecenes also display anomalous behavior. The chemical shifts of one distinctly deshielded proton (due to proximity to oxygen) are, for instance, similar to those of the macrocyclic congeners despite the fact that the former protons are located in side chains which would be expected to exhibit greater mobility. Moreover, in diastereomeric pairs of nonmacrocyclic trichothecenes, a provocative correlation exists between the site of epimerization and the chemical shifts of neighboring carbon atoms. Unfortunately, this relationship does not appear to be applicable to analogous diastereomeric pairs of macrocyclic trichothecenes. Proton homonuclear Overhauser effects have been critical in establishing the configurations and relative geometries of many groups in these compounds.

The subject trichothecenes have been primarily isolated by liquid chromatographic techniques, and many are metabolites of the molds *M. verrucaria* and *M. roridum.* Both of these fungi coexist nicely with the plant *B. megapotamica,* which grows in southern Brazil.

^{1}H-NMR CHARACTERIZATION OF THE OIL FRACTIONS PRODUCED BY DIRECT LIQUEFACTION OF SUGAR CANE BAGASSE.

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Instituto de Química - UNICAMP - C.P. 6154
13.083 - Campinas - SP - Brasil

Sugar cane bagasse, available in large quantities in Brazil, can be liquefied with formate and water under argon pressure furnishing heavy oils in 60 to 70% yield [Schuchardt, U. and Pereira Matos, F.A., Fuel (1982) 61, 106]. We have developed methods for the distillation, liquid-liquid extraction and column chromatography of these oils which allow their separation into volatile (120 ºC/1 mm Hg), phenolic, acidic, neutral polar and non-polar components. The yields are 17.3%, 21.6%, 11.9%, 5.0% and 6.3%, respectively [Cotrim, A.R., Schuchardt, U. and Rodrigues, J.A.R., Quím. Nova (1985) 8, 219].

These fractions are highly oxygenated and easily characterized by IR and ^{1}H-NMR spectroscopy. The IR spectra show intensive absorptions of hydroxyl, carbonyl, and ester groups. Since the signals of the ^{1}H-NMR spectra are usually broad, we have defined five intervals of chemical shift according to the main types of protons: methyl (0- 1.2 ppm); methylene and methine (1.2 - 3.4 ppm); hydrogen, methyl and methylene attached to oxygen (3.4 - 5.0 ppm); vinyl (5.0 - 6.0 ppm) and aromatic and phenolic (6.0 - 8.0 ppm). The signals of the hydroxy and phenolic protons are sensitive to the sample concentration and normally vary within the interval. The percentages of the different types of protons, determined by integration over the interval, are shown in Table 1.

Table 1: Percentage of the Different Protons.

Range of C.S. [ppm]	Volatiles [%]	Phenolics [%]	Acidics [%]	Neutral Polars [%]	Non-Polars [%]
0 -1.2	16.5	12.7	11.7	13.8	23.8
1.2-3.4	38.9	44.9	51.9	57.8	55.4
3.4-5.0	15.6	26.4	10.7	16.5	10.7
5.0-6.0	6.3	2.2	2.1	3.2	6.1
6.0-8.0	22.6	13.7	23.5	8.7	3.9

From these data we can see that the volatile fraction shows a different profile with a high content in aromatic, phenolic, methoxy and vinyl protons. It is mainly composed of guaicols, phenols, cyclohexenes, and substituted furanes. The phenolic fraction has a high ether content, with 26.4% of protons α to an oxygen atom, as it contains guaiacyl and syringyl type components. The acidic fraction shows à high content of aromatics (11.5%) and phenolics (12.0%) but a low content of methoxy protons, due to its highly condensed structure. The neutral polar components are mostly aliphatic with an increased percentage of hydroxy protons, indicating a high content in aliphatic alcohols. The drastic reduction of aromatic protons and increased percentages of methyl and vinyl protons in the non-polar components suggests that this fraction is composed of aliphatic ketones and ethers with a high degree of unsaturation (6.1% of vinyl protons).

Financial support from FINEP, FAPESP and CNPq is gratefully acknowledged.

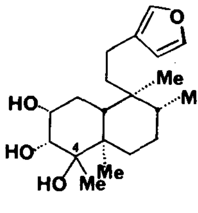
TWO-DIMENSIONAL NMR OF A NOVEL CLERODANE DITERPENE FROM *Croton sonderianus* Muell.Arg.

Edilberto R. Silveira*, James D. McChesney and James N. Shoolery[1].
Dept⁰ de Química Orgânica e Inorgânica, Universidade Federal do Ceará, 60.000, Fortaleza,Ceará,Brasil.
1.VARIAN Instrument Group, 611 Hansey Way, Palo Alto, California 94303.

A survey of the literature revealed that bitter taste and interesting biological activities such as insect repellant, antiviral, piscicidal, antitumour,and antifeedant have been related to clerodane diterpenes or plant material containing these as principal constituents.

The ethanol extract from the roots of *Croton sonderianus*, popularly known as marmeleiro preto, showed antimicrobial activity in qualitative biological assays, and yielded an active clerodane diterpene whose final structure, <u>1</u>, except for the stereochemistry at C-4, has been determined by using the most recent NMR spectroscopy techniques.

Multiplicities of all observed lines in the PND spectrum of <u>1</u> were determined by the DEPT experiment (distortionless enhancement by polarization transfer) and the carbon-carbon connectivity through the 2D-INADEQUATE pulse technique (incredible natural abundance double quantum transfer experiment).Additional information about the bonding pathway establishment was obtained by analysis of the direct and long range C/H correlated spectra.



(1)

NMR SUPERCONDUCTOR MAG AND NATIONAL SUPPLY OF LHe#

D.G.Pinatti(1,2), C.A.Baldan(2)*, C.Y.Shigue(2)
(1)IFGW-UNICAMP,(2)FTI-DMAR Polo Urbo Industrial, Gleba AI-6, 12.600 - Lorena - SP - Brazil

<u>NMR Superconductor Magnets</u> - A NMR system is composed of 3 parts: RF acquisition, computer and magnet.Software, probes, data print, storage system and accessories are coupled to these 3 parts.The present paper is related to superconductor magnet and a LHe supply facility.The magnet is composed of a main coil and a correction coil system.The distortion of the fields is due to the tolerance in the mechanical construction of the winding and iron closé to the magnet.The homogeneity is given in a sphere by (Bmax - Bmin/Bcentral).Eq(1) expresses the magnet field in terms of Legendre polynomial series in spherical polar coordinates. A_n^m and B_n^m are magnitudes of the particular types of field distortion, which values have been determined over a reference sphere of radius ρ_o

$$B(\rho,\Theta,\phi)=\sum_{n=0}\left(\frac{\rho}{\rho_o}\right)^n\sum_{m=0} P_n^m(\cos\ \Theta)(A_n^m\cos m\phi + B_n^m \sin m\phi) \quad (1)$$

The following shorthand notation is used to label each type of distortion:$A_o^o=z_o$, $A_1^o=z_1$, $A_2^o=z_2$, $A_3^o=z_3$, $A_4^o=z_4$, $A_5^o=z_5$,$A_1^1=x$, $B_1^1=y$, $A_2^1=zx$, $B_2^1=zy$, $A_3^1=z^2x$, $B_3^1=z^2y$, $A_2^2=x^2-y^2$, $B_2^2=xy$.

If rigorous knowledge of a particular distortion is requered we must return to eq(1).Usually thirteen sets of coil winding are mounted in a surface of a tube over or under the main magnet.Shimming of the magnet is made by a NMR field measuring equipment with resolution of 5 parts in 10^7.The probe is located in various points in a surface of a sphere in the useful diameter of the magnet.The fields are measured and they are analyzed by a Fourier fitting routine so that the coefficients of eq(1) are given unique values.For correction, the strength (ppm/amp) of each shim set is determined during construction. The shimming is repeated many times in order to reach the best adjustment of the magnet.

<u>Construction of Superconductor Magnets</u>-For magnets fabrication, superconductor cables are being imported but national cable will be used in a near future.Cables of NbTi and Nb_3Sn ϕ 0.4, ϕ 0.6, ϕ 0.8 are used.The structure of the magnets is made of stainless steel or aluminum alloy.The last one is preferred due to higher contraction of the cable with respect to aluminum.Motion of wire is deleterious to homogeneity of the magnet and two techniques are used to maintain the stability of the magnet: resin bounding and pre-stressed winding.NMR magnets

demand high precision on the windings. Calculation is made with computer programmes which take into consideration geometry of the magnets and cables, electrical characteristics, stress-strain relation and thermal properties during cyclic cooling to 4.2 K. Horizontal or vertical cryostats are made of stainless steel or aluminum. Depending on the size of the magnet, losses range from 0.05 to 1 ℓ/h for nitrogen (20 day refill) and from 0.1 to 4 ℓ/h for helium (40 day refill). The current leads are of dismountable type in order to extend refilling time and this demands that the magnet operates in persistent mode. Magnetic field scanning increases helium consumption. Magnets of NbTi are highly safe but magnets of Nb_3Sn are still on development. Field stability is 0.1 ppm/h and field homogeneity in a sphere with one half the bore of the magnet is in the range of 100 to 10 ppm, depending on the precision of construction and number of shims. Cost for 10 ppm is 3 to 5 times larger than a 100 ppm precision magnet. The FTI-DMAR development aims to reduce the cost of NMR magnet.

National Facility in LHe - This supply is being established in FTI-DMAR sponsored by FINEP-PADCT. It will be established in 3 steps based on: a) importation of helium in high pressure gas cylinders; b) importation of helium in liquid cryogenic tanks and c) helium recovery from brazilian natural gas sources. The programme begin in 1985 and in March 1987 the national distribution of the LHe will start. The initial capacity of the plant is 40 ℓ/h of LHe reaching 240 ℓ/h in the first module. Distribution will be made in a special truck with a 500 LHe tank, mobile recovery compressor and high pressure cylinders. The present cost is US$ 18,00/ℓ of LHe collected in the cryostat of the user; the objective is to reach US$ 8,00/ℓ. The cryogenic and high pressure equipment start with 80% nationalization and will reach 100% in a near future. Besides the construction of the superconductor magnet the capability of construction, maintenance, technical assistance and training in the whole field of magnets and LHe are being developed. The areas which will be attendend are: Superconductor Magnet Construction, Low Temperature Physics, NMR Spectroscopy, MRI Imaging (hospitals), Space Science, Materials Research and Analytical Chemistry.

Work supported by FINEP and PADCT.

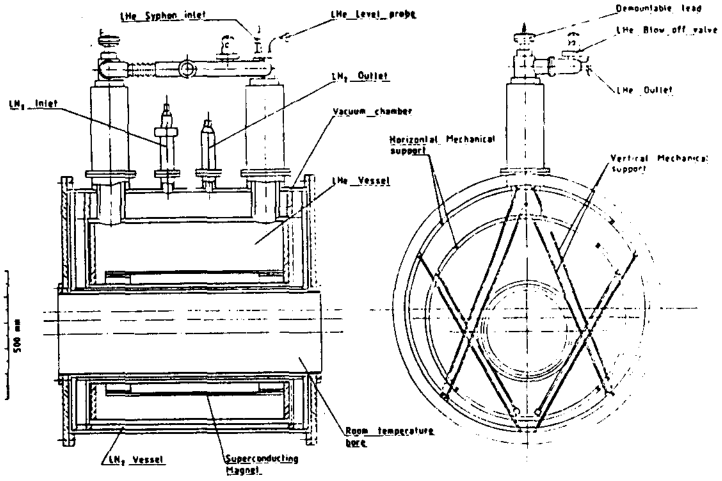
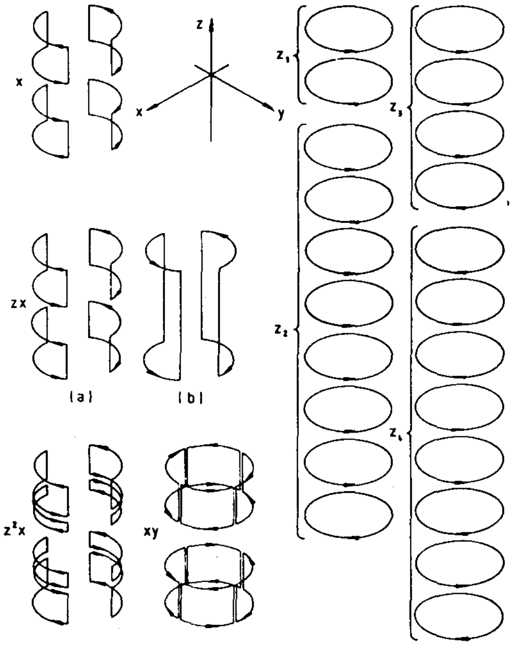


FIG. 1 - HORIZONTAL NMR MAGNET

FIG. 2 - SCHEMATIC LAYOUT OF SHIM COILS.



NMR IMAGING WITH THE STIMULATED ECHO PULSE SEQUENCE.

Beckmann, N.*, Bonagamba, T.J., Tannús,A.,Panepucci,H.
*Instituto de Física e Química de São Carlos,USP, Caixa Postal 369, 13560-São Carlos, SP, Brasil.

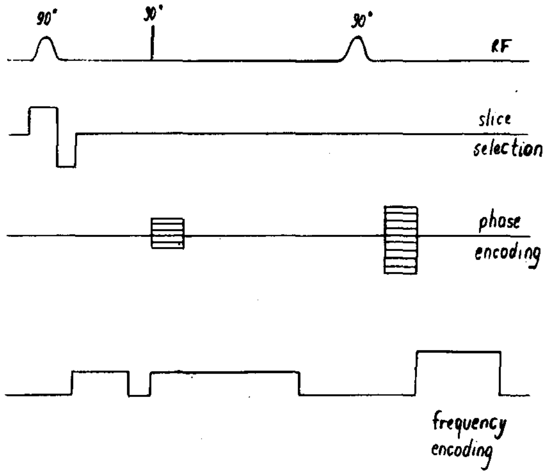
Spin-echo and inversion-recovery techniques have been extensively used in NMR imaging for the generation of respectively T_2- and T_1- weighted images, that are important for medical diagnostic purposes. A drawback of these techniques is that for obtaining the weighted images, it is necessary to change the RF pulse sequence

An imaging technique is described that allows the obtention of simultaneous T_1- and T_2-weighted images, without altering the pulse sequence parameters. This technique is based on the application of three 90° pulses(1), following the scheme $90°-\tau-90°-(T-\tau)-90°$. If $T \gg 2\tau$, five echoes are in general produced, the HAHN's echo ($t = 2\tau$), the stimulated echo ($t = T + \tau$) and three secondary echoes ($t=2T-2\tau$, $t=2T-\tau$, $t=2T$). The amplitudes of HAHN's and secondary echoes possess T_2 dependence, while that of the stimulated echo has a particular dependence on T_1 and T_2. These echoes may than be used for the generation of images with different T_1 and T_2 contrasts.

The image sequence that codifies spatially the phase and frequency components of the echoes is depicted below(2). In this sequence, the stimulated echo is not affected by the gradients applied between the second and third 90° pulses, because it results from the longitudinal component of magnetization stored during this time interval. The other echoes, but the secondary one at $t = 2T - \tau$, which depends only on the gradients applied after the second 90° pulse, are affected by all the gradients applied prior to their formation. This behavior permits the obtention of images with different spatial resolutions when the gradients applied have differing maximum amplitudes.

(1) HAHN,E.L., Spin Echoes. Phys. Review, vol. 80, nº 4, pages 580-594 (1950).

(2) FRAHM, J., MERBOLDT,K.D., HANICKE,W., HAASE, A.- J. Magnetic Resonance 64, pages 81-93 (1985).



ARCHYTECTURE OF THE SÃO CARLOS 2.0 TESLA NMR TOMOGRAPH

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A Nuclear Magnetic Resonance (NMR) tomograph is a sophisticated and versatile pulsed NMR Fourier spectrometer being more and more used for Medical diagnostic purpose. We developed in São Carlos (IFQSC/USP) an NMR spectrometer and a control system based on modules destinated to: generate RF and field gradient taylored pulse shapes; event synchronism; data acquisition, digitalization and averaging of NMR signals; devices for image viewing; generation and detection of RF signals; NMR probes. The system has enough flexibility to operate under control of a great variety of computers.

At present, the control system works with the Z80-based microcomputer MicroLIE (developed in our labs) and is being tested with a spectrometer prototype developed to operate with a VARIAN 12" iron core resistive magnet at 0.6 Tesla.

The system we describe in this paper is designed to operate later with a solenoidal superconductive magnet, with 31 cm bore and magnetic field strenght up to 2.0 Tesla, with a gradient coil set fully time and gradient orientation controlled.

With the resistive prototype we obtained our first images of phantoms, small fruits and vegetables limited to about 3 cm diameter. The techniques used for image reconstruction are two-dimensional convolution/retroprojection and 2DFT, both with slice selection of less than 9 mm thickness. The images obtained will be shown in poster exposition.

CARBON-PROTON COUPLING CONSTANTS AND CARBON SHIELDING CONFORMATIONAL EFFECTS IN VERATROLE AND METHYLENEDIOXYBENZENE DERIVATIVES

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Marta B. Ferraro y Rubén H. Contreras*

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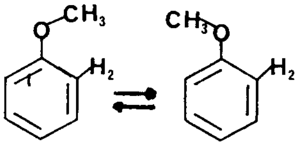
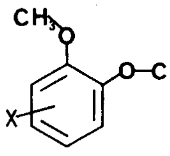
The barrier to inner rotation about the $C(sp_2)$-O bond in anisole in solution is known to be notably larger than kT at room temperature but not large enough to prevent rapid interconversion between the two coplanar rotamers |J. Goulon, D. Canet. M. Evans. and G.J. Davies. Mol. Phys. 30. 973 (1975)|.



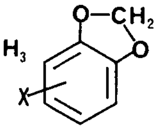
In ortho-substituted anisoles the steric hindrance between the two adjacent groups defines a methoxy group conformation which is cis to the proton in ring position 6.

The consequences of this preferred conformation on ^{13}C-NMR parameters are being studied both from an empirical and a theoretical viewpoints.

For this purpose several veratrole (I) and methylenedioxybenzene (II) derivatives were synthetized and their proton coupled and decoupled spectra were analysed in order to determine C-H spin-spin couplings as well as carbon chemical shifts.



I



II

The effect of the conformational change of the methoxy group on ^1J(CH) was studied and results thus obtained were compared with similar effects of the methoxy group in vinyl derivatives |N.J. Koole. M.J. A. de Bie. P.E. Hansen, Org. Magn. Reson. 22 (3). 146 (1984)|.

In order to obtain a deeper understanding of factors originating the ^1J(CH) cis/trans difference, IPPP-INDO calculations were carried out |A.R. Engelmann and R.H. Contreras, Int. J. Quantum.Chem. 23. 1033 (1983)|.

Empirically, the additivity rule of substituent effects was applied looking for a quantitative estimation of the influence of a side-chain conformational change on carbon shieldings.

In order to correlate ^{13}C chemical shifts to atomic electron densities, MNDO calculations were performed in the studied compounds. Mulliken population analyses were carried out at the MNDO optimized geometries.

ANALYSIS OF NON-LINEAR EFFECTS ON SLICE SELECTION IN MR IMAGING.

Bonagamba*, T.J., Magon, C.J., Beckmann, N., Tannús, A., Panepucci, H. - *Instituto de Física e Química de São Carlos,USP, Caixa Postal 369, 13560-São Carlos,SP

Slice selection in magnetic resonance tomography is achieved by selective excitation with a radiofrequency (RF) pulse which spectral width is much narrower than the Larmor frequency distribution produced by the applied selection gradient. Ideally, one wishes to obtain a transverse magnetization which is zero everywhere, except for the selected region, for which $M_x = 0$ and M_y = constant. This requires the use of some spin refocalization technique following the excitation. The non-linear response of the spin system plus the finite lenght of the RF pulses are the main difficulties in achieving the above ideal result. Here we make an analysis of the various possible alternatives to handle this problem and point out the most convenient pulse sequences for 2D image generation.

HETERO-SUBSTITUTED CYCLOBUTANES – A ^{13}C INVESTIGATION OF CONFIGURATION / CONFORMATION

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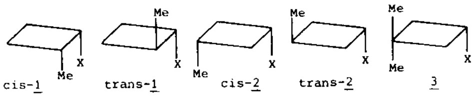
Substituent effects on cyclobutane ^{13}C chemical shifts (SCS) are investigated for the following series of cyclobutane derivatives, and the SCS values, determined experimentally, evaluated in terms of established physical and/or empirical models.



X = H, Me, Cl, Br, I, CN, OH, OMe, NH_2

Even more informative, however, are the relative trends of individual SCS in these five, configurationally different cyclobutane structures. Thus, *e*,*e*-conformation and virtually identical angle of ring puckering can be established for both the cyclobutane and the *cis*-3-methylcyclobutane compounds.

In the *trans*-3- and *cis*-2-methyl derivatives, the hetero substituent occupies the same quasi-equatorial position as in the cyclobutane derivatives, thus forcing the CH_3 moiety into a quasi-axial position. Since, moreover, the γ high field shift on the *cis* CH_3 carbon in 1-X-substituted *cis*-2-methylcyclobutanes parallels that observed for the corresponding 1-X-substituted *cis*-2-methylcyclopropanes, ring puckering must be severly abated in the substituted cyclobutanes.

An inspection of the individual shifts in polymethylcyclobutanes indicates that neither β nor γ effect of a CH_3 substituent vary with the relative orientation of the methyl group (*e* vs. *a*), i.e. configurational assignment on the basis of ^{13}C n.m.r. data is not feasible for four-membered rings (as already stated by *Eliel et al.*). However, in *cis*- and *trans*-1-halo-3-methylcyclobutanes, the halogen-bearing carbon displays a very clear stereochemical shift ($\Delta\delta$ 4.6 ppm).

^{1}H-NMR APPLICATIONS TO THE STUDY OF UNSATURATED POLYESTER RESINS (USPR) AND OTHER INDUSTRIAL PRODUCTS

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It is described the applications of ^{1}H-NMR spectroscopy to the study of commercial USPR, giving information about cualitative and cuantitative results from 20 polyester systems for future references.

USPR are lineal polymers derived from condensation of some dicarboxylic acids with di or polyhydroxilated alcohols; a polymerizable monomer gives up the crosslinking unities, and also may act as a solvent.

Identificaton of USPR alcohols and acids was made by comparison of the sample spectra with model compound spectra, chemical shift Tables and some reference spectra from well-known composition resins.

Molar relations of acids and alcohols from USPR were obtained from cuantitative analysis. Interferences caused by terminal hidroxyl groups and those from non reactant alcohols were eliminated by the use of trichloroacetyl isocyanate (derivatization reactive) as they introduce errors in alcohols relation calculus.

Procedure described was applied to structural studies of these resins extracting information about composition, isomerization and monomer sequence. With these and previously published data, chemical shift Tables from 19 acids and 14 alcohols of potential use were elaborated, generating 20 polyester systems with a broad diversity of final properties.

^{1}H-NMR spectroscopy has been found to be the best and fastest technique for USPR characterization, giving answers to industrial requeriments about this important group of resins whose principal application lies on reinforced plastics field.

In a similar way other industrial products, i.e. elastomers and surface-active agents were studied. Dealing with elastomers ^{1}H-NMR spectroscopy was able to determine the composition of vulcanizated and non vulcanizated elastomers assigning microstructures of homopolymers, copolymers and blends. About surface active agents, the determination of their chemical structure made possible to connect this information with superficial activity, HLB value and biodegradability.

THE STUDY BY ^{13}C-NUCLEAR MAGNETIC RESONANCE OF - N-ALKYL-2-MERCAPTO-1-ALKYLAMINE HYDROCHLORIDES

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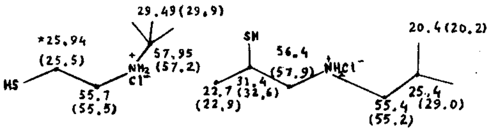
Derivatives of N-alkyl-2-mercapto-1-alkylamines have presented schistosomocide activity in mice previously infected with S.mansoni (Nelson & Pellegrino, Rev. Inst. Med. Trop. São Paulo, 18: 264, 1976). One path for the synthesis of these substances involves the opening of epithioalkanes by primary amines (Pilõ-Veloso & Prado, Ciência e Cultura, Supl. 36:481, 1984). Under conditions which favor bimolecular nucleophilic substitution, the products which resulted contained the RNH amino group bound to methylenic carbon 1 of the main chain and the SH group bound to the methynyl carbon. An interesting technique for verifying the formation of these products is ^{13}C NMR, which permits the distinction in relation to the isomers containing RNH bound to the methynyl carbon and SH bound to the methylenic carbon. This distinction may be confirmed by empirical calculation of the δ values for ^{13}C, taking into consideration the Δδ increment due to the relative position of the substituents on the molecule. Thus by applying the tabulated values for the SH and RNH contributions (Wehrli & Wirthlin, "Interpretation of Carbon-13 NMR Spectra Heyden, 1978, Chapt. 3), it is possible to encounter agreement between the experimental and calculated δ values for the proposed structures (eventhough the tabulated empirical values for RNH were used for RNH_2^+) :



* Observed ^{13}C shift values;( ) calculated ^{13}C shift values.

(CNPq, FINEP).

SPECTROSCOPIC ANALYSIS OF COPOLYMER BETWEEN GLUTARIC ANHYDRIDE AND 2-METHYL-2-OXAZOLINE

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In the last few years we have been working in "non catalyst copolymerization" between electrophilic (ME) and nucleophilic monomers (MN).(Makromol. Chem. 187, 71(1986);Eur. Polym. J. 21, 939(1985); Polymer Bulletin 13, 519(1985); ibid 11, 465(1984); An. Quim. 79, 62(1983).

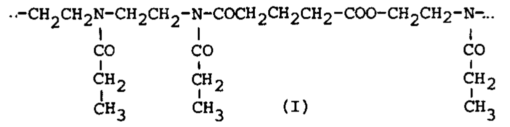
Spontaneous copolymerization of 2-ethyl-2-oxazoline(ETOX) as MN with glutaric anhydride (GLU) as ME was studied. The copolymerization reaction was carried out in bulk without initiator at different feed compositions of the comonomers, but keeping constant the total amount of substance (0.03 mol)(see Table 1).

Table 1.- Copolymerization of GLU/ETOX at 45°C in bulk by 14 h.

Copolymer	GLU/ETOX ratio	Yield (g)	Yield (%)
GLU/ETOX 1	1:2	1.70	54.4
GLU/ETOX 2	1:1	2.03	63.4
GLU/ETOX 3	2:1	2.09	63.8

The IR spectra of the GLU/ETOX copolymer sample show the disappearance of the characteristic absorption band at 1830 cm^{-1}, corresponding to the $\nu_{C=O}$ of the anhydride group which indicates the opening of the glutaric anhydride ring.

When the copolymerization proceeds through opening of the oxazoline ring and anhydride ring the following structure(I) could be expected:


$$\ldots\text{-}CH_2CH_2\underset{\underset{\underset{CH_3}{|}}{\underset{CH_2}{|}}}{\underset{CO}{\underset{|}{N}}}\text{-}CH_2CH_2\text{-}\underset{\underset{\underset{CH_3}{|}}{\underset{CH_2}{|}}}{\underset{CO}{\underset{|}{N}}}\text{-}COCH_2CH_2CH_2\text{-}COO\text{-}CH_2CH_2\text{-}\underset{\underset{\underset{CH_3}{|}}{\underset{CH_2}{|}}}{\underset{CO}{\underset{|}{N}}}\text{-}\ldots \qquad (I)$$

Though, the structure of the resulting product disagrees with the corresponding one for the proposed compound I. It was found that the CH_2/CH_3 ratio obtained from the proton NMR spectrum is smaller than the expected value for structure I. Fig.1 shows the complex 400MHz proton NMR spectrum of the GLU/ETOX copolymer 1.

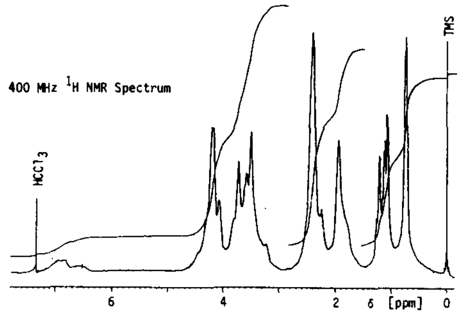


Fig.1

Double resonance 400 MHz proton NMR and INDOR techniques confirm the complex structure of the obtained copolymer.

The 100MHz ^{13}C NMR spectra of GLU/ETOX copolymers show more signals than expected for structure (I). On the other hand, ^{13}C NMR spectra recorded by spin-echo techniques show the signals for methyl and methylene carbons besides the signals corresponding to methine and quaternary aliphatic carbons, which are not present in structure I.

Proton NMR spectrum of acid hydrolysis products of GLU/ETOX copolymer, did not show the presence of CH_3CH_2COOH as expected for a structure containing amide or imide ($-\underset{|}{N}COCH_2CH_3$) groups.

Possible copolymer structures are analyzed according to the spectroscopic data.

We thank the "Dirección de Investigación", Universidad de Concepción for financial support (grant N°20.13.16 and 20.13.39-A).

AIDS IN INTERPRETING CARBON-13 NMR SPECTRA OF SUBSTITUED EXO,ENDO TETRACYCLO [6,2,1,1^{3,6},0^{2,7}] DODECANES.

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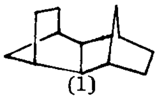
Praça General Tibúrcio,80- Rio de Janeiro RJ - 22.290).



(1)

Carbon-13 NMR spectra of a number of exo, endo - tetracyclo [6,2,1,1^{3,6},0^{2,7}] dodecanes (1) have been recently reported in the literature. With the exception of heavily chlorinated derivatives,however, no interpretation of respective spectra is offered. We have assigned chemical shifts of two monounsaturated hydoxyl derivatives and propose some types of substituent and additivity effects that may aid in the interpretation of other members of the series.

(CNPq, FINEP, FAPERGS).

AN EMPIRICAL METHOD FOR CONFIGURATIONAL ASSIGNMENT AT THE BRANCHING POINT OF ACETAMIDO SUGARS BY PROTON NUCLEAR MAGNETIC RESONANCE

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In connection with our synthetic studies on branched nitro sugars of antibiotics, we have searched for a convenient technique to ascertain the configuration at the tertiary carbon-3 of compounds 1 to 6. It has been demonstrated by Lukacs and coworkers that ^{13}C NMR analysis can be used to assign this configuration, but nothing has been mentioned concerning the more accessible ^{1}H NMR method.

The evaluation of the ^{1}H NMR substituent resonance at the branching point for assignment of configuration seemed particularly attractive in this present series of compounds due to the fact that we were dealing with a methylene group (H-2) vicinal to the quaternary center which was easily assigned in the spectra.

On the basis of H-4 and H-2 resonances of three pairs of compounds 1/2, 3/4 and 5/6 we found that in those with equatorially oriented acetamido group the hydrogens located on vicinal carbons are deshielded, when compared to the same sites of the compounds with axially oriented tertiary acetamido group.

The variations of the H-2 and H-4 resonances will depend on: a) the orientations of the methyl group on carbon-3 (the change of a methyl group from the axial to the equatorial position in cyclohexanes with fixed chair conformation induces an upfield shift of c.a. 0.5 ppm on the axial hydrogen and a downfield shift of c.a. 0.2 ppm on the equatorial hydrogen of the vicinal carbon) b) the 1,3 syn or anti relationship with the carbonyl and the magnetic anisotropy of the acetamido group.

The latter has been extensively studied by Paulsen, but mainly in connection with amides where the rotation process about N-CO bond leads to a doubling up of signals. In our case the signals in the ^{1}H NMR spectra of 1 to 6 were sharp and no doubling up of signals could be detected. We have thus assumed that only one of the most probable rotamers was present for each compound (depicted in structures 1 to 6).

The change in chemical shift due to the magnetic anisotropy of the acetamido group can be explained by the angle variation between the vicinal hydrogens (H-2, H-4) and the N-CO π system. The axial protons are more strongly deshielded than the equatorial ones in 2 and 4 because both anisotropy of the acetamido and methyl orientation effects lead to downfield shifts while in the equatorial protons these effects oppose one another.

The weaker deshielding effect of the acetamido group on H-2 of 6 when compared to that of 4 and 2 corresponds to a change in the N-CO rotamer due to the hidrogen bonding between the hydroxyl and the acetamido group changing from syn to anti the relationship between the carbonyl and carbon-2. (The OH resonance at 5.96 ppm is indicative of an internal hydrogen bonding).

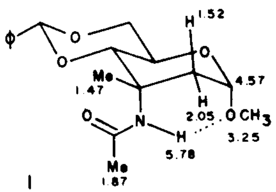
It is worthwhile mentioning that Lichtenthaler in an earlier attempt to determine the configuration of tertiary acetamido groups in pyranose acetates by ^{1}H NMR has suggested that the methyl of tertiary acetamido resonances are 0.1 ppm more deshielded than those of the secondary unbranched counterparts.

Application of this method to 5/6 where both methyls of the acetamido group show equivalent chemical shifts would certainly lead to doubtful assignments.

Finally the effects observed for these compounds are limited to tertiary acetamido groups and cannot be extrapolated to their secondary counterparts due to different rotamer population.

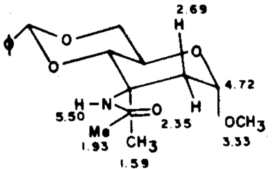
Acknowledgement

The authors are indebted to FAPESP and CNPq for financial support.



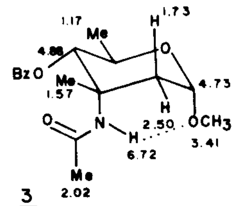
1

$Ø\pi - H_{2a} \cong 90°$
$Ø\pi - H_{2e} \cong 0°$



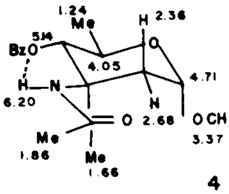
2

$Ø\pi - H_{2a} \cong 0°$
$Ø\pi - H_{2e} \cong 120°$



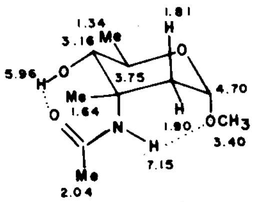
3

$Ø\pi - H_{2a} \cong 90°$
$Ø\pi - H_{2e} \cong 0°$



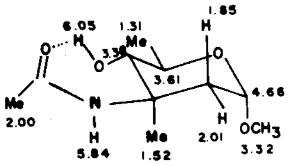
4

$Ø\pi - H_{2e} \cong 0°$
$Ø\pi - H_{2e} \cong 120°$



$Ø\pi - H_{2e} \cong 60°$
$Ø\pi - H_{2e} \cong 60°$

5



$Ø\pi - H_{2e} \cong 0°$
$Ø\pi - H_{2e} \cong 120°$

6

DETERMINATION OF ASSOCIATION CONSTANTS OF N,N - DIALKYLAMIDE-BENZENE COMPLEXES BY NMR SPECTROSCOPY.

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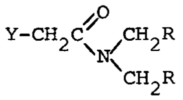
The association constants for a series of N,N-dialkylamide complexes I and II with benzene have been determined in carbon tetrachloride as solvent, with benzene concentration in large excess. The values of the association constant were determined by measuring the ^1H chemical shift of the electron acceptor specie as the concentration of the electron donnor is altered.



R= (I) Me and
(II) i-Pr
Y= H,Me,Cl,Br,and I

The association constants have been determined by multiple linear regression by using an appropriate expression (Eq.1), derived from Bittrich-Kirsch Equation (*Z.Phys. Chem.(Leipzig)*,*257*,893,1976).

$$\Delta_i{}^2 = \Delta_{AB}\Delta_i.Mr - K\Delta_{AB}{}^2/K+1.Mr + C \qquad (1)$$

Here Δ_i is the observed induced shift difference between the *anti* N-CH_2 protons and the *syn* N-CH_2 protons resonances, Mr is the (benzene)/(amide) molar ratio, Δ_{AB} is the maximum shift for the pure complex, K is the association constant of the complex, and C is a constant.

Plots of K against substituent electronegativities shows substituent effect dependence for the serie I, but no dependence for the serie II. Plots of K against pKa values of the corresponding carboxylic acids shows the same behavior. Another interesting correlation was found when K was plotted against the variation of ^{13}C chemical shift between the *anti*- and *syn*-N-CH2 resonances. In this case, the slopes of the profiles of K *versus* $\Delta\delta^{13}C$ of the two series (I and II), correlate with opposit sign.

^{13}C-NMR ASSIGNMENT, STRUCTURE, AND DYNAMICS OF DEOXYOLIGONUCLEOTIDES.

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^{13}C-NMR has been used for the first time to study short fragments of synthetic deoxyoligonucleotide duplexes in low salt aqueous solution. The target of this study is to develop a systematic ^{13}C-NMR spectral assignment and to investigate the structure and dynamics of oligonucleotides, by this technique.

Attention has been centered on two short oligonucleotide fragments, $[d(CG)_3]_2$ and $[d(GGTATACC)]_2$. In the duplex condition most of the spectral lines are resolvable and they were assigned, in part, by comparison between the duplexes and with mononucleotide spectra. Nearly half of the chemical shift *versus* temperature profiles for the base carbons exhibit transition opposit to the expectation from ring current predictions. These shielding increases on duplex melting are apparently due to hydrogen bonding. It is possible that such changes can be used to determine the hydrogen-bonding network in drug-nucleic acid and protein-nucleic acid complexes. The 1'-carbons of internal residues become less shielded upon duplex melting. This phenomenon is also displayed by the internal pyrimidine C4' nucleotides. 2'-, 3'-, and 5'-carbons of internal nucleotides, however, exhibit opposit trends which may be an indication of a heterogeneity of the sugar pucker conformations. As the duplex melts, 3'-, 4'-, and 5'-carbons show melting profiles that converge to a common point within a given carbon region. This indicates that the fast conformational motion of the backbone structure in the coil state (high temperature), average out the chemical shift. For both base and sugar carbons, the variation of the chemical shift as a function of the temperature was empirically analyzed in terms of steric and electronic effects acting in each carbon.

Determination of the spin-lattice relaxation times and nuclear Overhauser enhancements in 0.1M NaCl indicate that both duplexes tumble almost isotropically. At 30°C both molecules exhibit frequencies of overall motion around the minimum point of the T_1 versus correlation time curve. However, the hexamer presents frequency of overall motion toward the left side and the octamer slightly on the right side of the T_1 versus correlation time curve. At temperatures below the melting point, the bases have local motion on the same range of the overall motion. The sugar carbons experience more local motion than do the bases under conditions where the double helix is the predominant specie. The relaxation data is also consistent with the most rapid local motion occuring at the chain terminals.

"CARBON-13 SPECTRA AND MOLECULAR MOTIONS IN A CONSTITUENT OF CASHEW-NUT SHELL LIQUID (CNSL)"

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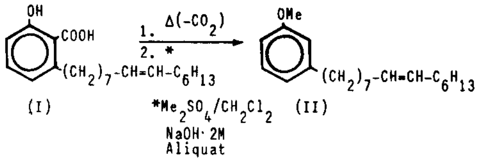
The plant "Cajueiro" (Anacardium occidentale L.) grows native in Brazil northeastern coast. From its nut is extracted a viscous oil. This oil called Cashew-Nut Shell Liquid (CNSL) whose composition is a mixture of phenolic olefinic compounds that contain a long side chain with 15 carbon atoms attached to the phenolic ring. The principal constituents of this mixture are: anacardic acid, cardanol, cardol and 2-methylcardol.

The following study was performed in one of the constituents of CNSL, the methyl ether of cardanol-$\Delta^{8'}$ (II) which was prepared from anacardic acid (I) by decarboxylation on heating followed by methylation with dimethyl sulfate according to Lehman.



The crude Carbon-13 spectrum can be partly assigned using the usual methods. However, along the carbon chain most carbons appear around 29 ppm and cannot be distinguished. In particular the position of the double bond cannot be determined. In order to do so, relaxation measurements were performed on the compound. Due to internal rotations around C - C bonds, motion increase along the carbon chain and so do the T_1's. The phenyl ring itself is animated by a rather fast rotation around the 1' 2' bond and therefore carbons 2,3,4 and 5 show a longer T_1 than carbon 6. The position of the double bond can be quite easily determined by the T_1 measurements. The 2 alpha carbons have a caracteristic chemical shift of 27 ppm. Their T_1's should be respectively longer than the T_1's of carbons 1' to 6' and shorter than carbons 11' to 15'. In fact, and this is a general observation, the T_1 of these carbons is always slightly higher than expected. This is of course due to the restricted motion imparted by the double bond. In our case consideration of the spectra run in $CDCl_3$ inequivocally asserts the position of the double bond. Similar results were obtained in benzene.

Finally, we tried to complex the double bond with a silver cation in order to modify the molecular motion along the chain. The reagent used was AgFOD, |(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octadionato)| silver, which is soluble in $CDCl_3$. Complexation introduces a extra weight (around 400 mass units) close to the double bond preventing the movement. This should in turn decrease the T_1's. The experiment confirms this hypothesis and corroborates the location of the double bond.

(UFC, CAPES)

^{13}C NMR STUDY OF 3,4-BENZO-2-AZABICYCLO |3.2.0|HEPTA-3,6-DIENES AND BENZAZEPINES

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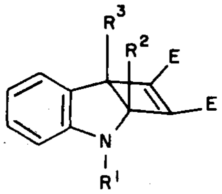
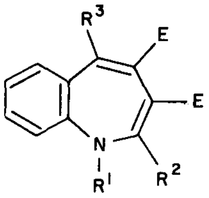
The 3,4-benzo-2-azabicyclo |3.2.0| hepta-3,6-diene derivatives obtained from the reaction of indoles and dimethyl acetylenedicarbexylate (DMAD) are thermally unstable. This instability makes structural determination difficult and only ^{1}H NMR data have been previously reported. Five bicyclo-hepta-3,6-diene (I) derivatives were isolated from rections of various indoles with DMAD carried out at low temperatures and catalysed by boron trifluoride etherate. ^{13}C NMR was used in determining their structures. Two singlets at 68.4-73.3 ppm and 53.8-57.6 ppm were attributed to C-1 and C-5, respectively. The relative intensities of signals allowed the attribution of C-6 and C-7. The other carbons were assigned by comparison with know alkaloides using the β, γ and δ effects and previously reported chemical shifts. The cycloadducts (I) were thermal isomerized to benzazepines (II) which were also studied by ^{13}C NMR. The totally substituted seven membered rings, such as 1,2,5-trimethyl-6,7-benzo-1H-1-benzazepine, have six carbons without hydrogen. The attribution of these carbons was made by considering the benzazepines as a derivative of cinnamic acid and enaminones.



(I)



E = CO_2CH_3

(II)

(We thank CNPq and FAPESP for financial support.)

^{1}H- AND ^{13}C-NMR ASSIGNMENT OF PEPTIDE ALKALOIDS.

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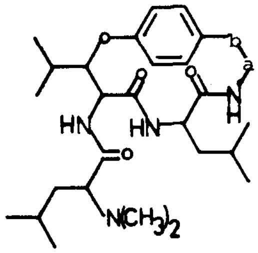
Franganine 1 has been isolated from the extract of Rhamnus frangula (rhamnaceae), by Tschesche et al. (Tetrahedron Lett., 2993 (1968)). It was found that the alcaloid 1 exist in this plant in very small amounts.

In this communication we report the isolation of the compound 1 from the extract of Discaria febrifuga Mart from R.S., Brazil, as the major alcaloid existing in this plant.

The structural assignment of the alcaloid 1 was confirmed by exhaustive ^{1}H- and ^{13}C-NMR studies. The 400 MHz ^{1}H-NMR spectrum of 1, in $CDCl_3$, exhibit alpha- and beta-methyne signal of the common beta-oxyleucine unit at =4.46 and 4.98 ppm respectively. Both alpha- and beta-methyne signals appear as doublet of doublets. The alpha-methyne has $^{3}J_{H-H}$=8 and 2 Hz. The coupling constant of 8 Hz reflects a alpha-H/beta-H dihedral angle relationship of 0-20 or 150-180°. Since the 14-membered ring of Franganine is fairly rigid, only the latter geometry (erithro configuration) is possible for the beta-Oxyleucine portion of the alcaloid.



1-Franganine: a-b -- c=c

2-Dihydrofranganine: a-b -- c-c

In this work, we are introducing more sofisticated ^{13}C-NMR techniques to help on the elucidation of the structure and stereochemistry of this alcaloid. We used techniques such as: (i) J-Modulated Spin-Eco Experiment which distinguishes between primary and tertiary carbons (with negative signal), from the secundary and quaternary (with positive signal); (ii) DEPT (Distortionless Enhancement by Polarization Transfer), which differentiates carbons by the number of ^1H attached to them; (iii) 2D-Heteronuclear shift correlated spectroscopy which permits the direct conection between carbons and their respective attached protons.

With the aid of these advanced techniques, plus the NMR spectral data of the Dihydrogenated compound 2 was possible to achieve an unambigous ^1H- and ^{13}C-NMR spectral assignment of the Franganine 1.

NMR CHEMICAL SHIFTS SUBSTITUENT EFFECTS
α- HETEROSUBSTITUTED METHYL ACETATES

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Recent data on substituent effects, in the carbonyl and α-methylene carbon chemical shifts of some α-substituted ketones and amides, can hardly be explained by the classical theories of Organic Chemistry.

The present work on α-heterosubstituted methyl acetates has lead to similar results. The carbonyl carbon chemical shifts seem to change in a random way. Some substituents (e.g.Cl) lead to an upfield shift, while for other substituents (e.g. O) no shift is observed. The carbonyl carbon chemical shifts for esters and ketones (or amides) are not linearly related, but the same trend is observed.

Simple additivity calculations for the α-methyllene carbons showed deviations of up to 16 ppm, in relation to the experimental shifts. A new parameter for the effects of heteroatoms (α^*_Z) is thus suggested, which could be used for all kinds of α-substituted carbonyl compounds. On applying this new set of substituent constants, empirical calculations for ca. 30 compounds has lead to a predicted value better than 1 ppm.

(FAPESP, CNPq, FINEP).

NMR CHEMICAL SHIFTS SUBSTITUENT EFFECTS:
3-SUBSTITUTED 2-METILPROPENES;

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The present work reports substituent chemical shifts (SCS) on some heterosubstituted methallyl compounds. They were prepared mostly by nucleophilic substitution of the chlorine atom by the corresponding nucleophile.

α-Methylene carbon chemical shifts have been estimated by simple additivity rules. Deviations of ca. 4 ppm were observed for the α-halo (Cl and Br) and for the α-oxygen (OH, OMe and OEt) derivatives.

Substituent chemical shifts (SCS) for heteroatoms on sp^2 carbons were not available and have been estimated from allyl derivatides. Correction terms due to α-branching have also been determined. Calculated chemical shifts for olefinic carbons of the title compounds were obtained by the Robert's empirical method (J.Org. Chem. 36, 2757 (1971)). An excellent agreement between both the calculated and experimental data was found.

Both sp^2 carbons are shielded for most substituents. The conformational equilibria may be responsible for some exceptions which were noted (e.g. OR).

^{13}C NMR OF SOME PODOCARPIC ACID DERIVATIVES

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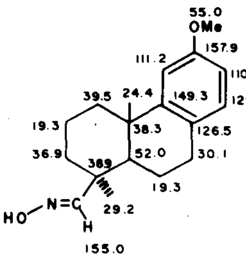
Systematic studies of substituent effects have already been carried out on a series of podocarpatriene and unequivocal assignments were made with the aid of joint application of various techniques. The data were found to be sufficiently characteristic to allow stereochemical conclusions concerning the axial or equatorial function at C_{19} or C_{18} respectively.

Our interest in podocarpic acid derivates was directed toward the introduction of a fourth ring containing a nitrogen group in order to build up a series of diterpene alkaloid analoges, to be tested as analgesic compounds. Although the synthetic part of this work has not been concluded yet we are now reporting the ^{13}C n.m.r study of podocarpic acid derivatives 1 to 6. These data were conclusive in the structure elucidation of compound 6 which was obtained from the photolisis of 4. The signal at δ 40.3, in the spectrum of 6, was assigned to C_4 based on its long range coupling to phosphorus (d, J^3 =7,3 Hz) which was analogous to C-4 of 5 (δ 37.5,d, $J^3_{C_4-P}$=7,2 Hz) and 4 (δ 37.2,d, $J^3_{C_4-P}$=8.0 Hz). The two doublets at δ 55.7 and δ 56.5 were assigned to C-5 and to C-6 respectively, taking into consideration the $J^2_{C_6-P}$=2.5 Hz and $J^3_{C_5-P}$=10 Hz. Carbon-19 also showed a $J^2_{C_{19}-P}$=3.5 Hz. It is interesting to mention that the ring closure on C_6 produced a δ shielding effect on C_{20}(Δδ(6-4)=4.2ppm) and C_1 (Δδ(6-4)=5.3ppm). Normally the 1,3-synaxial interactions (δs.a) lead to down field shifts, and only in some cases when the nonbonded distances between these δ groups are somewhat larger, an upfield shift is observed at the δ position. Thus through drieding models of 4 and 6 we could observe that the introduction of the fourth ring in 6 produced a change in the conformation of ring B from half chair in 4 to skew boat in 6, leading to an increase in the distance between C-20 and C-19 (in 6). The distance between the nitrogen atom on C-6 and C-20 is also larger than normal 1,3 synaxial interactions in chair conformation cydohexanes. Both facts can explain the shielding of C-20 in 6 when compared to 4 and 5. The change in conformation of ring B of 6 is probably responsible for the shielding effect observed on C-1.

Acknowledgement

The authors are indebted to FAPESP and CNPq for financial support and scholarship to M.A.C.O.



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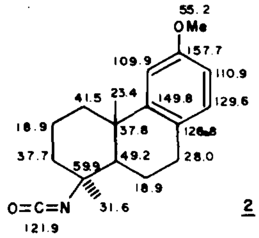

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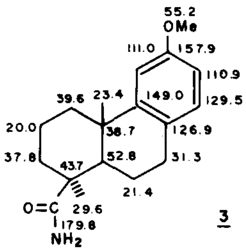

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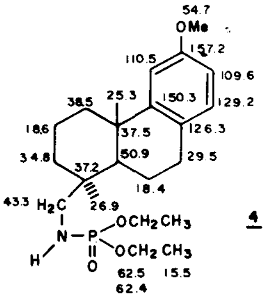

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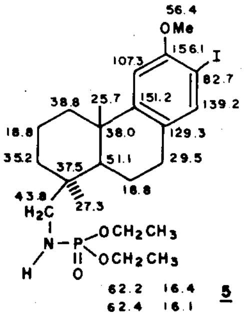

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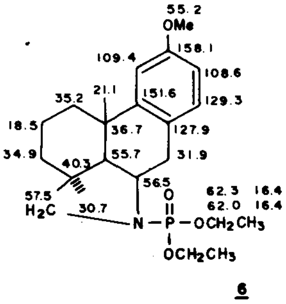

6

STRUCTURE OF THE LITHIUM ENOLATE OF ACETALDEHYDE IN THF

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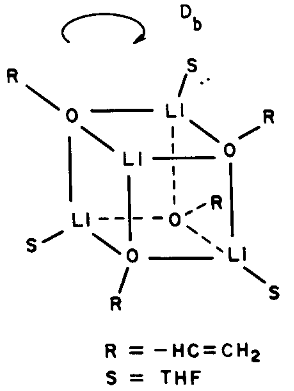
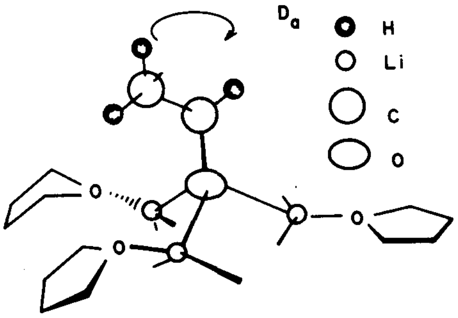
The lithium enolate of acetaldehyde in THF solution has been shown to be tetrameric by NMR T_1 relaxation studies. The vinyl group of the enolate is rotating more rapidly about the C-O axis than the tetramer tumbles in solution (E_{rot} = 6.6 Kjoule/mole). The formula for the enolate is best represented as $(CH_2{=}CHOLi)_4$.





LITHIUM NORBORNENONE ENOLATE: STEREOCHEMICAL CONTROL OF ALKYLATION BY AGGREGATION

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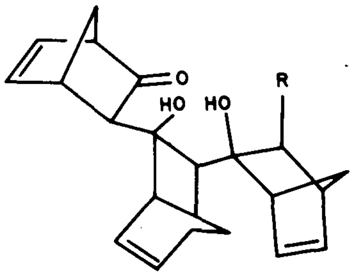
The lithium enolate of norbornenone gives low yields of 3-alkyl norbornenone when alkylated in THF with a series of alkylating agents (MeI, $C_6H_{13}I$, $C_6H_5CH_2Cl$, $C_2H_3CH_2Br$). The major product is the mono-alkylated RSR-trimer. NMR techniques, including COSY, NOE and T_1 relaxation, were used to establish the structure. The specific formation of this trimeric product (128 stereoisomers of the trimer are possible) is accounted for by reaction in a specifically aggregated enolate. The reaction is contrasted with that of norbornanone and substituted norbornenones which are alkylated in good yield.



VISCOSITY MEASUREMENT BY NMR:

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A new method for measuring kinematic viscosity in nmr samples is introduced. The method is based on the detection of the coherent motion associated with the onset of Taylor vortex flow in concentric tubes. The method was applied to pure liquids and to mixtures and shown to give viscosities within 2% of those obtained by traditional methods. A mixture of Carbowax 600 (MW $\sim$ 600) and DMSO gave the same apparent bulk viscosity when measured with the signals from either component. The experimental requirements and the scope and limitations of the method will be presented. It relies on the generation of spinning sideband images of coherent rotational flow in the presence of an axial field gradient. The method is readily implemented on standard spectrometers with minimal instrumental modification. A range of flow images will be presented.

SIDEBANDS FROM ROTATIONAL FLOW:

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Spinning sidebands are ubiquitous in high resolution nmr. Their position and intensities have been understood since the fundamental work of Williams and Gutowsky (Phys. Rev. 104, 278, 1956). In this presentation, sideband patterns from coherent but non-uniform rotational flow will be shown. The flow pattern used to demonstrate the phenomenon is Couette flow between concentric cylinders. The fluid velocity varies between the spinning frequency at the wall of the spinning tube to zero at the stationary tube according to

$$F(r) = F_o(a^2/r^2)(b^2-r^2)/(b^2-a^2)$$

where a and b are the radii of the inner and outer cylinders and F_o and F(r) are the rotational frequencies of the spinning tube and the fluid rotational frequency at radius r. Experimentally observed sideband patterns and calculated simulations will be shown, together with their dependence on rotational frequency and field gradient. The data show that any coherent rotational flow will produce a characteristic (and calculable) nmr sideband pattern.

A NMR STUDY OF THE BENZENESULFONATE ION IN MICELLAR SYSTEMS.

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In order to study the interaction of the benzenesulfonate ion with the charged interface in micellar systems, the partial orientation and the carbon-13 relaxation times of the solute were determined. The order parameters, which describe the partial orientation, were determined from the dipolar couplings obtained from the proton NMR spectra of N_C and N_D nematic mesophases prepared using several cationic and anionic surfactants. In all cases the results indicate that the symmetry axis of the benzenesulfonate ion is oriented on the average perpendicular to the micelle interface and a comparison with the degrees of order of the initial segments of the surfactant hydrocarbon chains, determined from the H-2 quadrupole splittings, indicate that the solute is located predominantly in the interfacial region of the micelle. In anionic surfactant sys

NMR STUDIES OF α-N,N-DIALKYLAMINOKETONES

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Preliminary data has shown that the replacement of an hydrogen atom by a *N,N*-dimethylamino group does not lead to any shift in the carbonyl carbon chemical shifts of some aliphatic carbonyl compounds.

Previous work on some α-heterosubstituted cyclohexanones has also shown that the substituent effects of α-heteroatoms are strongly dependent on the stereochemical relationship between the later and the carbonyl group.

α-*N,N*-Dimethylamino- and α-*N,N*-diethylaminocyclohexanone and the corresponding 4-*t*-butyl compounds were prepared. Their Carbon-13 NMR spectra have presented some difficulties in the chemical shifts assignments. Spin-echo, noise decoupled and SFORD NMR spectra were used to identify the carbons signals for the *cis*- and *trans* diastereoisomers.

Attempts to estimate the axial/equatorial ratio for the α-*N,N*-dimethylaminocyclohexanone, from the Carbon-13 chemical shifts, were performed and compared to the α-chloro-, α-bromo- and α-methoxycyclohexanone calculated and experimental ratios.

(FAPESP, FINEP).

tems, the the solute present a small anisotropy of the static ordering; small diferences in the degree of order of the two axes perpendicular to the symmetry axis were observed in contrast to the behavior in cationic systems in which the solute presented an extreme anisotropy in the partial orientation.

The ratios of the spin-lattice relaxation times, determined in isotropic micellar solutions, of the *para* carbon to that of the *ortho* and *meta* carbons of the benzenesulfonate ion were used to characterize the anisotropy of the rotational diffusion. A significantly larger anisotropy of the rotational diffusion was observed for the solute in anionic surfactant systems. In the cationic micellar systems, the anisotropy was only slightly greater than that in non-micellar aqueous solutions.