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Two-Dimensional Double-Quantum Coherence Echo Correlated Spectroscopy in ^{1}H NMR

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Two-dimensional (2D) double-quantum coherence NMR spectroscopy has proved to be a useful tool for analyzing the J_{CC} connectivity in ^{13}C spectra[1] as well as the J_{HH} connectivity in ^{1}H spectra.[2] Double-quantum or multiple-quantum filter has also been proposed as a convenient technique for disentangling complex overlapping ^{1}H NMR spectra.[3–6] The present communication describes a new method for mapping the J_{HH} connectivity via double-quantum coherence echo[7] using quadrature detection in both dimensions. This method denoted as double-quantum coherence echo correlated spectroscopy (DECSY) provides the correlation map between two coupled protons as similarly as SECSY (spin–echo correlated spectroscopy)[8] and also additional important information on "remote connectivity" and "magnetic equivalence".[9]

The pulse sequence is represented as follows: $90°(0)–\tau–180°(\pi/2)–\tau–90°(0)–(t_1/2)–\alpha(\psi)–t_1$–acquisition($\Omega$). The phase ψ is cycled with 0, $\pi/2$, π, and $3\pi/2$ and Ω with 0, $3\pi/2$, π, and $\pi/2$.[10] Quadrature detection in the ω_1 direction is accomplished with a $\pi/4$ phase shift of the first three pulses of the sequence together with a $\pi/2$ shift of the receiver reference phase.[1] Total eight cycles of the pulse sequence result in selection of echo components in coherence transfer.[11]

Figure 1A shows DECSY spectrum with $\alpha = 135°$ of sucrose octaacetate in CDCl$_3$. For the purpose of comparison, the conventional SECSY spectrum is shown in Figure 1B. The cross peak in the DECSY spectrum appears at the ω_1 frequency of $\omega_{tu}/2 - \omega_{rs}$. The first term is a half of the frequency (ω_{tu}) of double-quantum coherence created by the first three pulses, and the second term is the frequency (ω_{rs}) of the detectable single-quantum coherence to which the double-quantum coherence is transferred. In the case of weakly coupled spins A and X, ω_{tu} is $\omega_A + \omega_X$ for both single-quantum frequencies ω_A and ω_X (ω_{rs}). Therefore, coordinates of cross peaks in the DECSY spectrum are $[(\omega_A - \omega_X)]/2, \omega_A]$ and $[(\omega_X - \omega_A)/2, \omega_X]$; the appearance of the spectrum is quite similar to that of SECSY spectrum except for the absence of strong auto peaks. The absence of strong auto peaks is one of the most characteristic features of DECSY. This allows one to identify easily cross peaks in the neighborhood of the ω_1-center line without interference of undesired auto peaks.[12] The situation is seen in two regions of 4.0–4.3 ppm and of 5.3–5.4 ppm if the DECSY spectrum A is compared with the SECSY spectrum B. Furthermore, the singlet peak of F1 protons is significantly suppressed because the spin system (A$_2$) does not create double-quantum coherence.

Use of $\alpha = 90°$ results in a spectrum as shown in Figure 1C. This spectrum shows a larger number of cross peaks than spectrum A. Additional cross peaks arise from "remote connectivity" and "magnetic equivalence" as described previously.[9] The appearance of these cross peaks in DECSY spectrum is schematically represented in Figure 2. For "remote connectivity" cross peak the intersection of 45° line with the ω_1-center line occurs at the midpoint between chemical shifts of two remote nuclei (A and

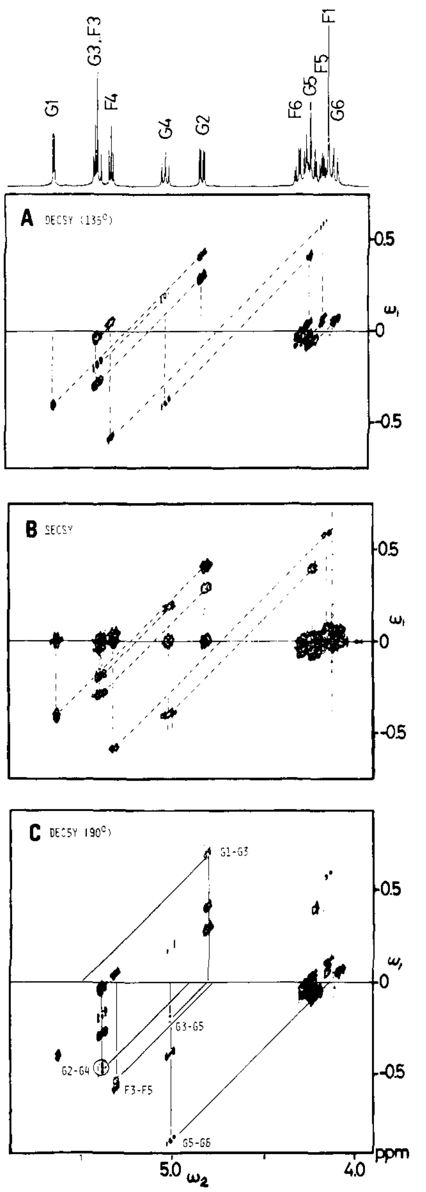

Figure 1. 2D 500-MHz ^{1}H NMR spectra of sucrose octaacetate in CDCl$_3$ and at 25 °C. (A) DECSY spectrum with $\alpha = 135°$ (1000 Hz(ω_2) × 750 Hz(ω_1), 512 × 128 data points); (B) conventional SECSY spectrum (1000 Hz(ω_2) × 750 Hz(ω_1), 512 × 128 data points); (C) DECSY spectrum with $\alpha = 90°$ (1000 Hz(ω_2) × 1000 Hz(ω_1), 512 × 256 data points). Methyl resonances of acetyl group are out of range and filtered. The corresponding region of the one-dimensional ^{1}H NMR spectrum is shown at the top, and the assignments of the protons are indicated. Direct connectivities are labeled by broken lines in spectra A and B. Remote connectivities are labeled by solid lines in spectrum C. The spectra were taken with a JEOL GX-500 spectrometer.

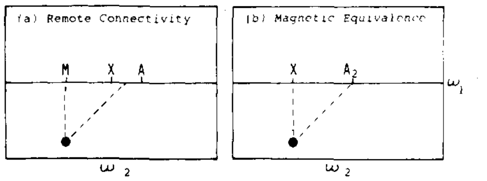

Figure 2. Schematic representation of two types of connectivities in 2D DECSY spectrum with $\alpha = 90°$. (a) Remote connectivity in AMX spin system; (b) magnetic equivalance in A$_2$X spin system.

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X), and for "magnetic equivalance" cross peak the same intersection coincides with the chemical shift of equivalent nuclei (A_2). In the SECSY spectrum B, we cannot decide connectivities between G3 and G4 and between F3 and F4 due to severe overlap of G3 and F3. However, the circled cross peak shown in DECSY spectrum C indicates that the resonance at about 5 ppm is remote connected with G2 resonance and is thus assigned to G4 proton. The combined use of two DECSY spectra A and C is expedient to facilitate the analysis of complex spectra.

We should emphasize that DECSY is superior to conventional double-quantum coherence spectroscopy with respect to narrower spectral width in the ω_1 dimension and to conventional SECSY with respect to the absence of strong auto peaks. Furthermore, valuable information about remote connectivity and magnetic equivalence can be obtained. These characteristics will take advantage in studying large molecules such as proteins.[13,14]

In addition, DECSY can be modified to a COSY-type data presentation, which is accomplished by the following pulse sequence: 90°–τ–180°–τ–90°–t_1–α–t_1–acquisition. Extension to higher order multiple-quantum coherence echo spectroscopy will be possible using the selective excitation and detection phase cyclings.[10]

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X-ray Crystal Structure of *N*-(2-Lithiocyclohexenyl)-*N*,*N'*,*N'*-trimethyl-1,3-propanediamine: A Pentavalent Lithium?

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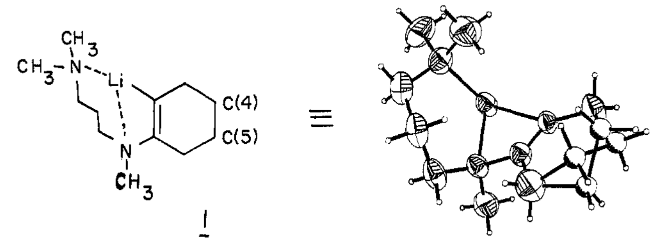
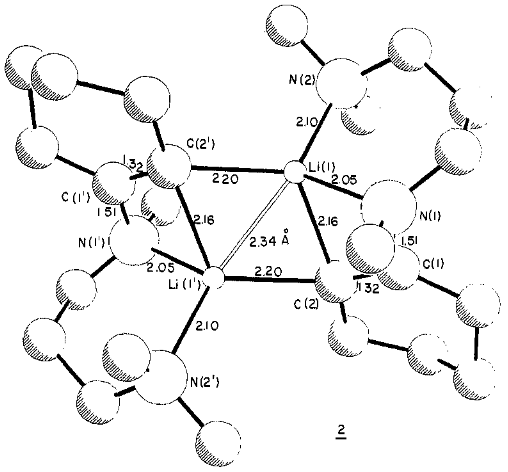
Vinyllithium derivatives are useful tools for the synthesis of organic molecules. Due to a complete lack of structural information about this important class of compounds, we were stimulated to obtain the X-ray crystal structure of the vinyllithium reagent **1**.[1] This is the first X-ray crystal structure of an organovinyllithium derivative.[2,3]

Pure crystalline **1** is easily handled in an inert atmosphere of argon. These crystals are stable over a month in a sealed vial in the presence of solvent (cyclohexane) but undergo a gradual decomposition over a period of weeks in the absence of solvent. A single crystal of **1** sealed in a 0.5-mm glass capillary under argon was utilized for x-ray diffraction analysis.[4]



1

Figure 1.



2

Figure 2. Bond Angles for the Dimer **2**: N(1)–Li(1)–N(2) 103.0, N(1)–Li(1)–C(2) 69.3, N(1)–Li(1)–Li(1') 105.5, N(1)–Li(1)–C(2') 129.2, N(2)–Li(1)–C(2) 114.7, N(2)–Li(1)–Li(1') 144.4, N(2)–Li(1)–C(2') 117.1, C(2)–Li(1)–C(2') 115.0, C(2)–Li(1)–Li(1') 58.3.

The crystallographic asymmetric unit of **1** is the monomeric species illustrated in Figure 1. The initial refinement of this structure ($R_w = 0.083$)[5] leads to a planar cyclohexene ring with a shortened σ bond between C(4) and C(5). These two carbon atoms also exhibited elongated thermal parameters in a direction perpendicular to the plane of the cyclohexene ring. This situation is indicative either of a dynamic equilibrium between two half-chair conformations or of an analogous static disorder in the crystal. In either case a more realistic description and better agreement ($R_w = 0.0702$)[5] was obtained by refinement of a model with four half-methylene groups (site occupation factor = 0.50)[6] shown together in the computer generated plot of **1** in Figure 1.

The asymmetric units of **1** are sufficiently close to the crystallographic inversion centers so that two of these units form an associated dimer shown in Figure 2 as **2**. Dimeric association allows for coordination of a single lithium atom with four donor ligands (e.g., Li(1) with N(1), N(2), C(2), and C(2')). It is not clear whether this dimer remains associated in solution. Other solution-phase dimeric species have been proposed on the basis of NMR studies for two aryllithium derivatives which are internally chelated.[7] Cryoscopic experiments also indicate that an alkenyllithium derivative of stilbene is dimeric in benzene solution.[8] Hence there is reason to believe that **1** remains associated in solution.

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(1) A series of α-heteroatom substituted β-lithiated vinyl reagents have been prepared by exchange of halogen or Sn with lithium. To data none of these reagents have been isolated as crystalline solids, cf.: (a) Ficini, J.; Falou, S.; Touzin, A.-M.; d'Angelo, J. *Tetrahedron Lett.* **1977**, 3589 (b) Wollenberg, R. H.; Albizati, K. F.; Peries, R. *J. Am. Chem. Soc.* **1977**, *99*, 7365. (c) Lou, K. S. Y.; Schlosser, M. *J. Org. Chem.* **1978**, *43*, 1595. (d) Kowalski, C. J.; O'Dowd, M. L.; Burke, M. C.; Fields, K. W. *J. Am. Chem. Soc.* **1980**, *102*, 5411. (e) Duhamel, L; Poirier, J.-M. *Bull. Chem. Soc. Fr.* **1982**, *9-10* (2), 297.

(2) For a comprehensive review of the few crystal structures of aliphatic and aryllithium derivatives, see: Wardell, J. L. in "Comprehensive Organometalic Chemistry"; Wilkinson, G., Stone, F.G.A., Abel, E. W., Eds.; Pergamon Press: Oxford, 1982; Vol. I, p 65, 84.

(3) Recently, the X-ray crystal structures of two THF-solvated lithium enolates have been described; cf.: Amstutz, R.; Schweizer, W. B.; Seebach, D.; Dunitz, J. D. *Helv. Chem. Acta.* **1981**, *64*, 2617. It is clear that there is no sp^2 C–Li bonding in these solvated enolates.

(4) Crystallographic parameters along with a summary of the structure solution can be found in the supplementary material.

(5) The weighting scheme used was the following: $R_w = [\sum(\text{weight}\cdot\nabla^2)/\sum(\text{weight}\cdot F_o^2)]^{1/2}$ where $\nabla = |F_o - F_c|$ and weight $= 1/[\sigma^2(F_o) + 0.0004F_o^2]$.

(6) The site occupation factors (sof) of the two disordered methylene groups were initially refined as independent variables. However, these values did not differ significantly from 0.5 so they were fixed at this value in the final stages of refinement.

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