Selecting the Most Appropriate NMR Experiment to Access Weak and/or Very Long-Range Heteronuclear Correlations

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**Introduction**

Heteronuclear long-range NMR experiments are well established as essential NMR techniques for the structure elucidation of unknown natural products and small molecules. It is generally accepted that the absence of a given τ(CH) correlation in an HMBC or HSQMBC spectrum would automatically place the proton at least four bonds away from the carbon in question. This assumption can, however, be misleading in the case of a mismatch between the actual coupling constant and the delay used to optimize the experiment, which can lead to structural misassignments. Another scenario arises when an investigator, for whatever reason, needs to have access to very long-range correlations to confirm or refute a structure. In such cases, a conventional HMBC experiment will most likely fail to provide the requisite correlation, regardless of the delay optimization. Two recent methods for visualizing extremely weak or very long-range connectivities are the UR-HSQCQ and the HSQMBC-TOCSY experiments. Although they are intended to provide similar structural information, they utilize different transfer mechanisms, which differentiates the experiments, making each better suited for specific classes of compounds. In this work we have sought to examine the considerations implicit in choosing the best experiment to access weak or very long-range correlations for different types of molecules.

**Methodology**

**A)** LR-HSQMBC

**B)** HSQMBC-TOCSY

**C)** 8Hz HSQMBC

**D)** 2Hz LR-HSQMBC

**E)** 8Hz HSQMBC-TOCSY

Figure 1: Pulse schemes for the A) LR-HSQMBC and B) HSQMBC-TOCSY experiments. The delay τ is set to 1/(2τ(3CH)), all H-C 180° pulses were adiabatic CHIRP pulses for broadband inversion and refocusing, and broadband heteronuclear decoupling is applied during proton acquisition. In order to illustrate the different number of correlations observed in each experiment, the C) conventional 8-Hz optimized HSQC, D) 2-Hz optimized LR-HSQMBC and E) 8-Hz optimized HSQMBC-TOCSY (60ms) spectra of the alkaloid strychnine are shown.

**Proton-Rich Molecules**

**Proton-Deficient Molecules**

**Conclusions**

References:

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