LR-HSQMBC: A Highly Sensitive NMR Technique to Probe Very Long-Range Heteronuclear Coupling Pathways

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HMBC is one of the most often used and vital NMR experiments for structure elucidation. We have developed a new, high sensitivity NMR pulse sequence that overcomes the typical 2JCH, 3JCH limitation of HMBC by extending the visualization of long-range correlation to 4-, 5-, and even 6-bond long-range 4JCH heteronuclear couplings. This technique should prove to be an effective experiment to complement HMBC for probing the structures of proton-deficient molecules. The LR-HSQMBC NMR experiment can, in effect, extend the range of HMBC to provide data similar to that afforded by the 1,n-ADEQUATE experiment even in limited sample situations. This is accomplished by optimizing responses for very small 4JCH couplings as opposed to relying on the markedly less sensitive detection of long-range coupled 13C-13C homonuclear pairs at natural abundance. DFT calculations were employed to determine whether the very long-range correlations observed for cervinomycin A2 were reasonable.