NMR Structure Elucidation of Small Organic Molecules and Natural Products: Choosing ADEQUATE vs HMBC

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Long-range heteronuclear shift correlation methods have served as the cornerstone of modern structure elucidation protocols for several decades. The ¹H-¹³C HMBC experiment provides a versatile and relatively sensitive means of establishing predominantly ³JCH connectivity with the occasional ²JCH or ⁴JCH correlation being observed. The two-bond and four-bond outliers must be identified specifically to avoid spectral and/or the structural misassignment. Despite the versatility and extensive applications of the HMBC experiment, it can fail to elucidate structures of molecules that are highly proton-deficient. In such cases, recourse to the ADEQUATE experiments should be considered. The current study was undertaken to facilitate a better understanding of situations where it might be beneficial to apply 1,1- or 1,n-ADEQUATE vs HMBC experiments to proton-rich and/or proton-deficient molecules. Strychnine (1) and cervinomycin A₂ (2) were employed as model compounds for each of these structural classes, respectively. DFT methods were employed to calculate the relevant heteronuclear proton-carbon ⁶JCH and homonuclear carbon-carbon ⁸JCC coupling constants for this study.