Solid–state NMR crystallography analysis of Lorlatinib, an active pharmaceutical ingredient

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A NMR crystallography study is presented for Lorlatinib, an active pharmaceutical ingredient (API) used in the treatment of lung cancer. Various one-dimensional and two-dimensional solid-state magic-angle spinning (MAS) NMR experiments have been performed that provide the ^{1}H and ^{13}C chemical shifts as well as the ^{14}N shifts. A ^{1}H(DQ)-^{1}H(SQ) MAS NMR spectrum was obtained with BaBa recoupling that reveals proton-proton proximities interactions between the ^{1}H nuclei that are typically within 3.5 Å of each other. A ^{14}N-^{1}H HMQC MAS NMR spectrum reveals that one of the NH_2 ^{1}H resonances has a significantly low ^{1}H chemical shift; this is interpreted in terms of differences in intermolecular hydrogen bonding. Enhanced resolution is observed in two-dimensional ^{1}H-^{13}C heteronuclear MAS NMR experiments at 1 GHz.

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