Seperation and identification of an impurity from Istradefylline intermediate

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Section 1 Synthesis of Intermediate A_1

1,3-Diethylurea (1.4 g，12mmol) and 2-cyanoacetic acid (1.2 g，14mmol) were added to a solution of acetic anhydride (10ml). The reaction mixture was stirred at 90~95℃ for 1.0 h. After confirming that the reaction was complete by TLC analysis, the reddish brown oily solution was collected by concentration under reduced pressure. Purified water (10 ml) was addede to the solution at ambient temperature, adjusting to pH 14 with 40% NaOH solution, and the reaction mixture was stirred at 90~95℃ for 15 min. The white precipitate was collected by filtration and dried to give the titled compound.

Section 2.2 HPLC analysis of impurity

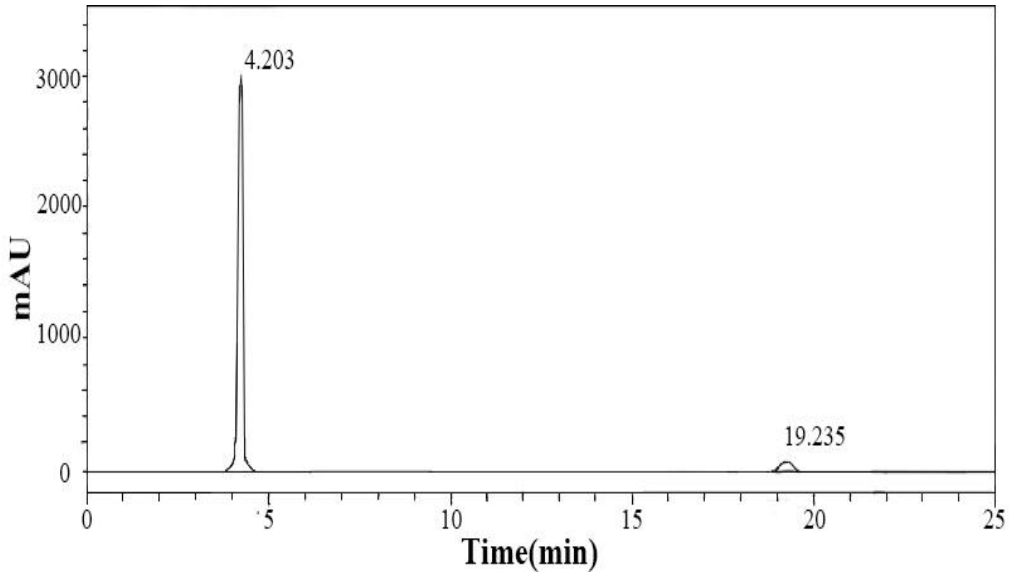

Fig.S1. HPLC analysis of impurity

Section 3.2 The spectroscopic data such ^{1}H NMR, ^{13}C NMR，IR and proton correlation spectroscopy (COSY，HMQC and HMQC) was recorded for impurity in Istradefylline intermediate A_1.

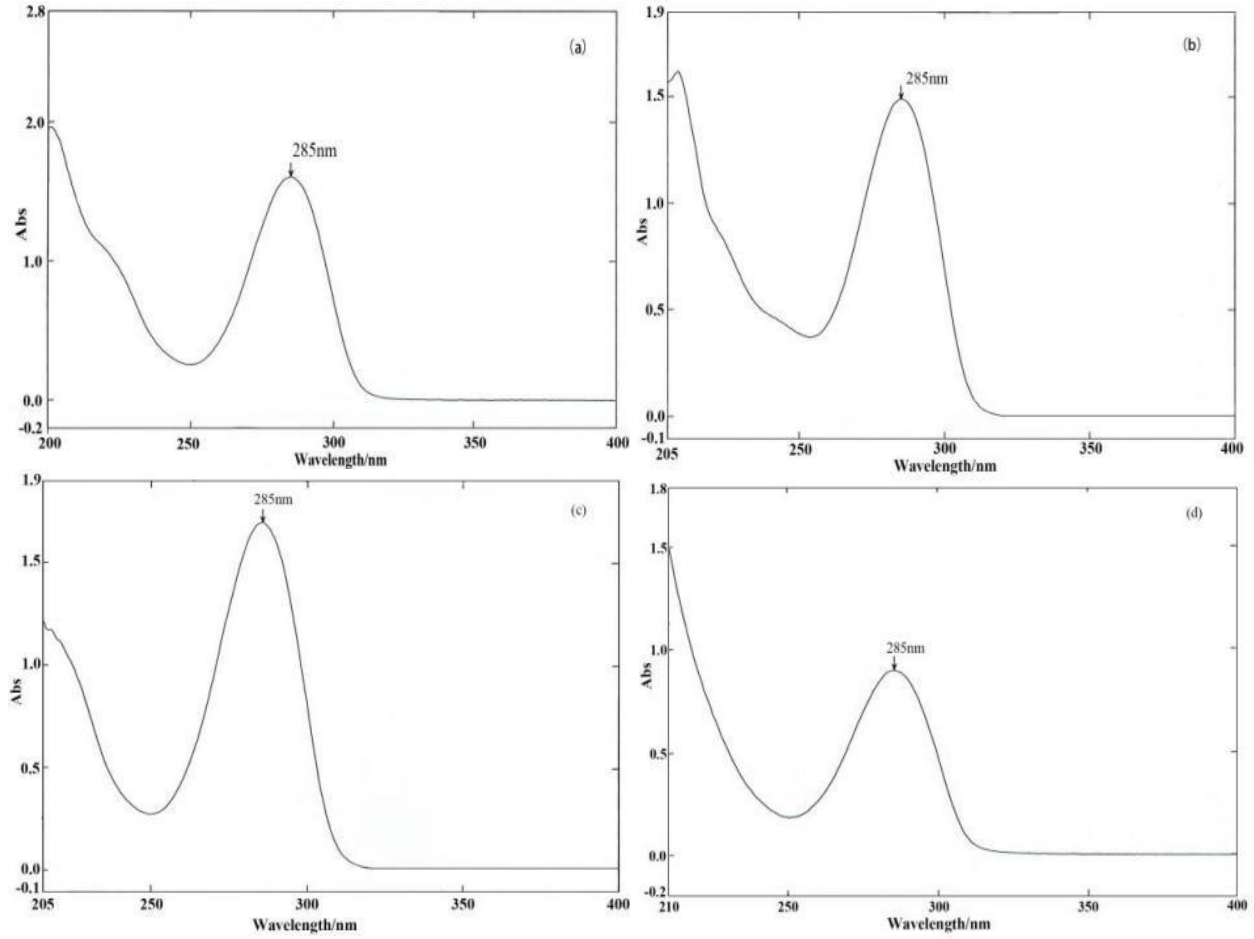

Fig.S2. UV absorption spectrum in (a) H_2O, (b) HCl solution (0.1 mol L^{-1}), (c) NaOH solution (0.1 mol L^{-1}) and (d) methnol solution

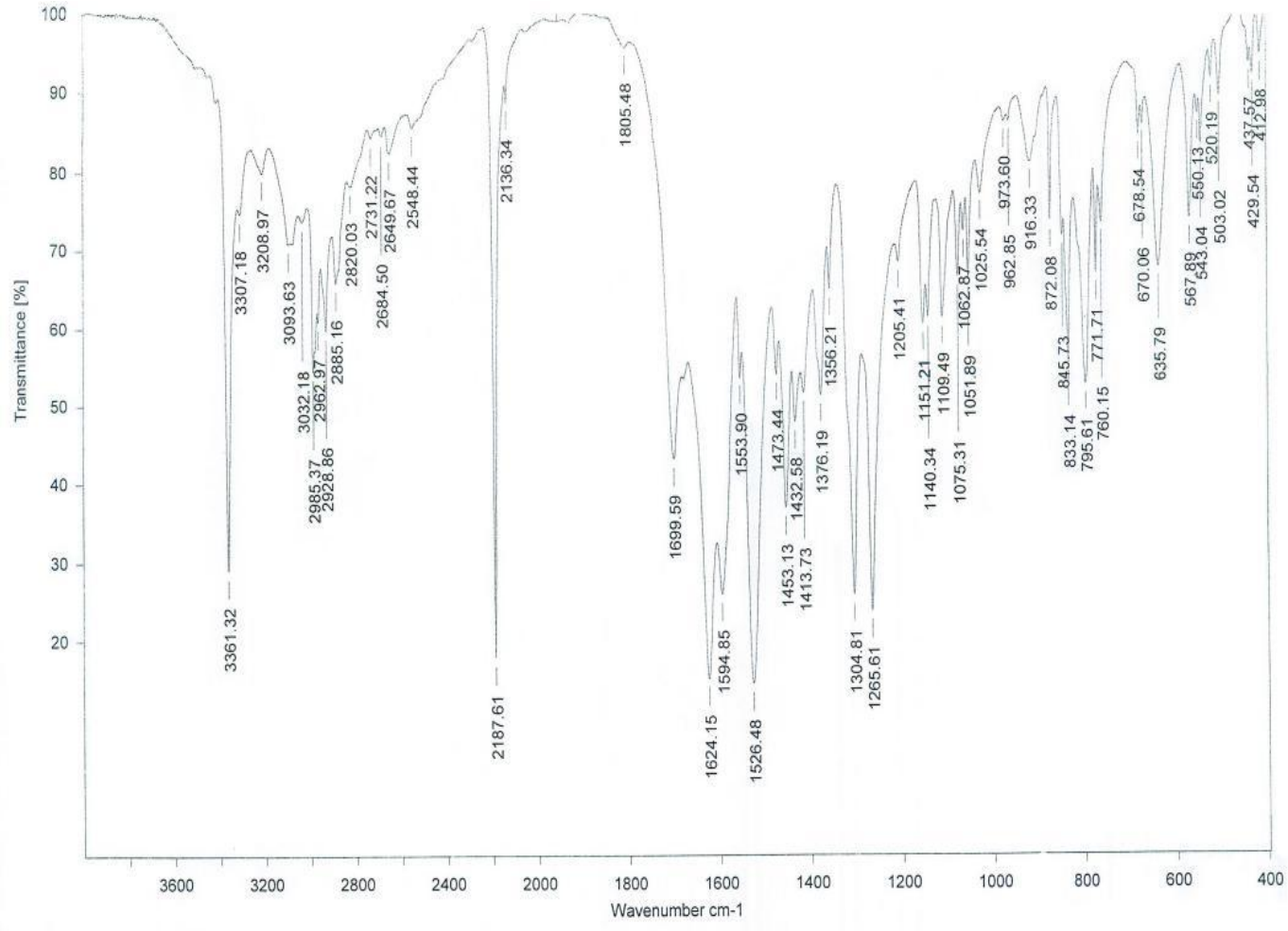

Fig.S3. IR absorption spectrum of impurity

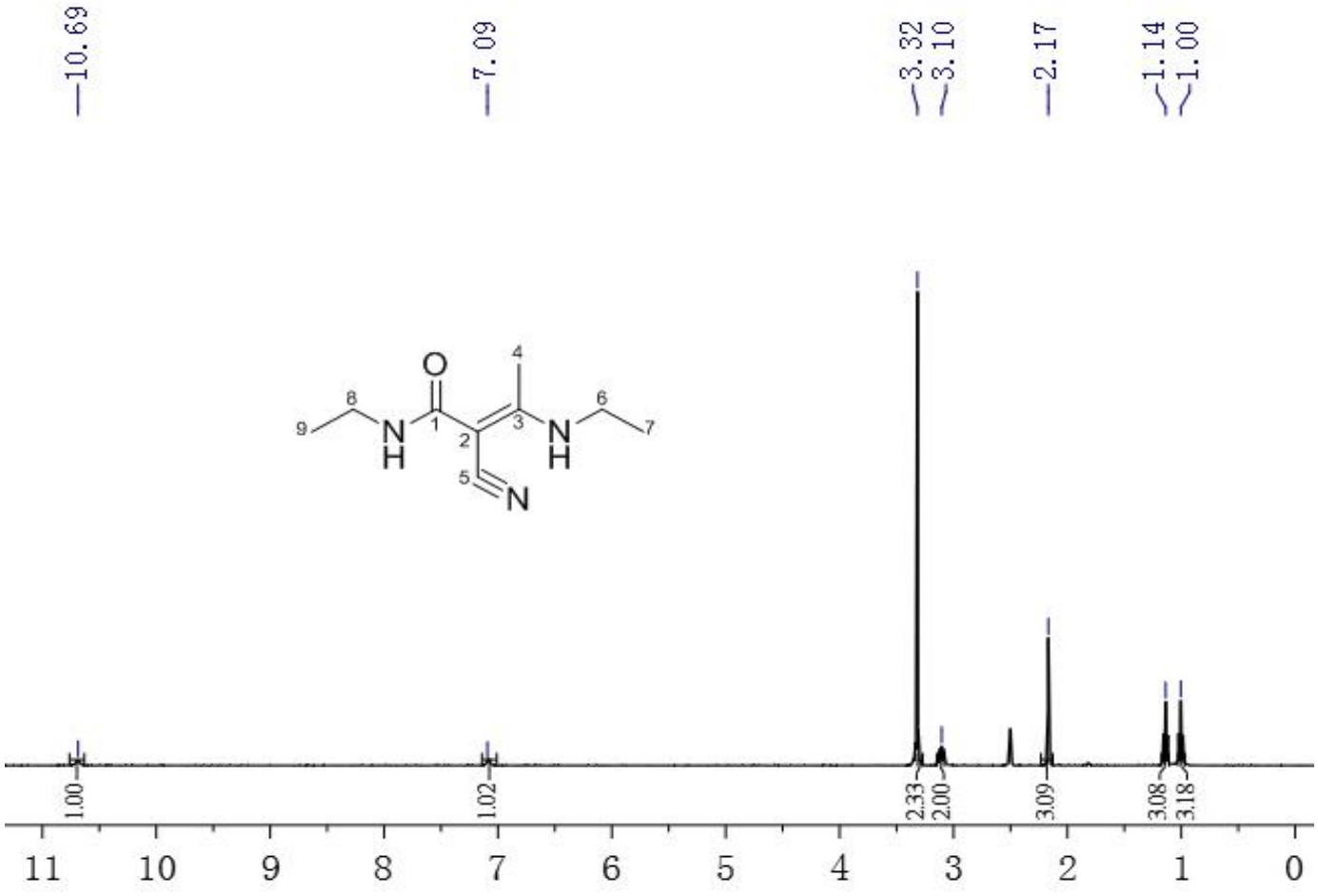

Fig.S4. [1]H NMR spectrum of impurity

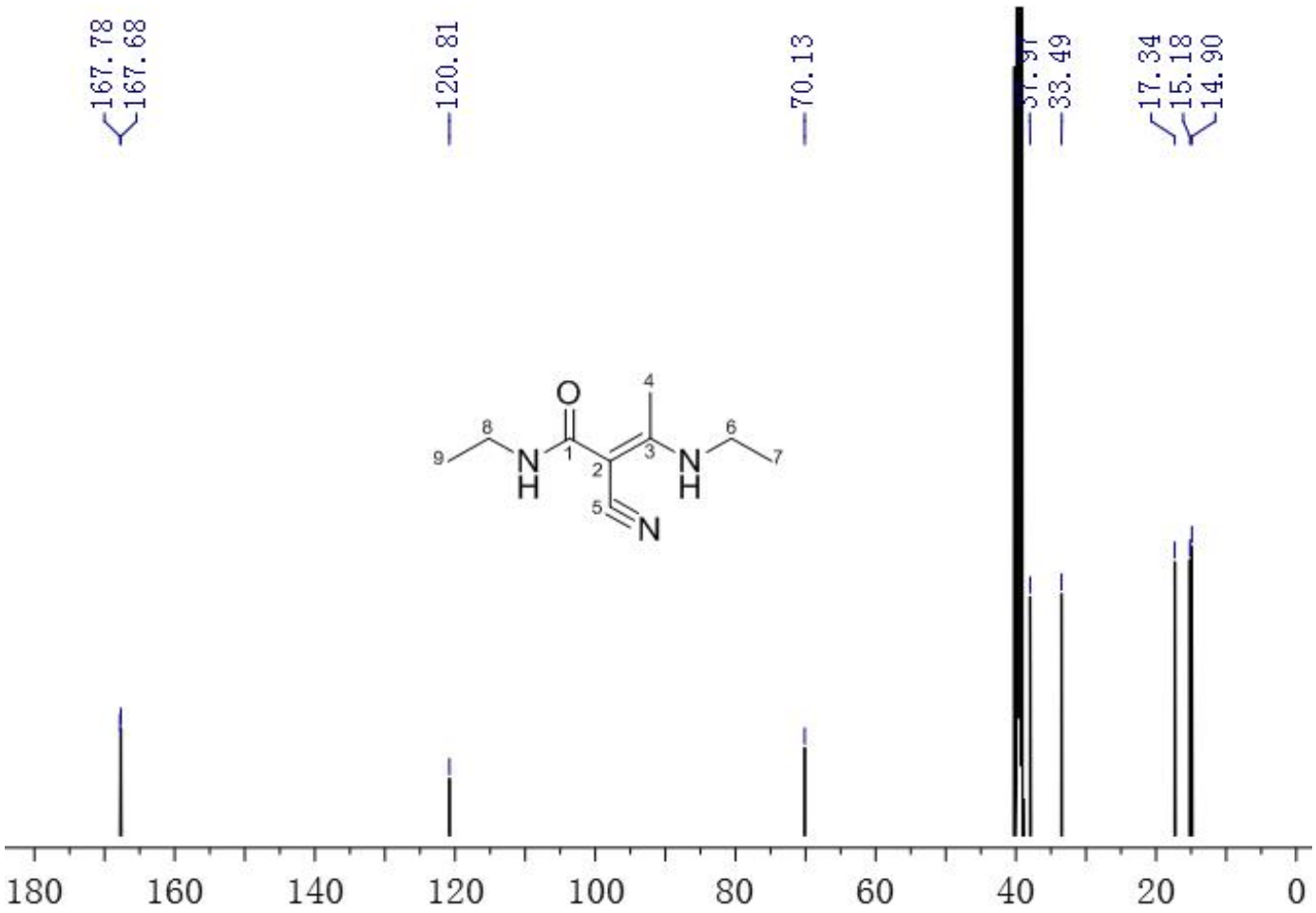

Fig.S5. ^{13}C NMR spectrum of impurity

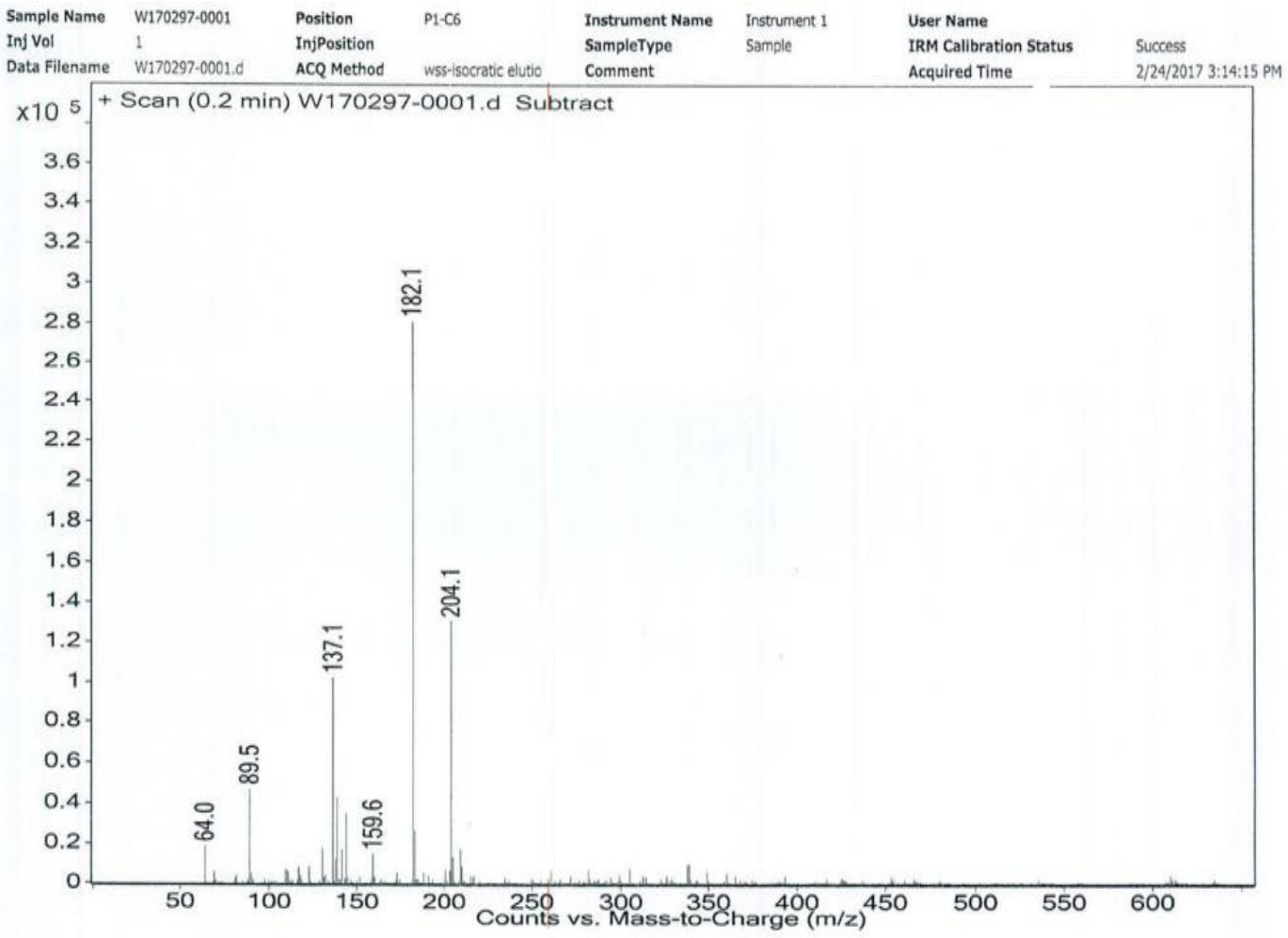

Fig.S6. ESI mass spectrum of impurity

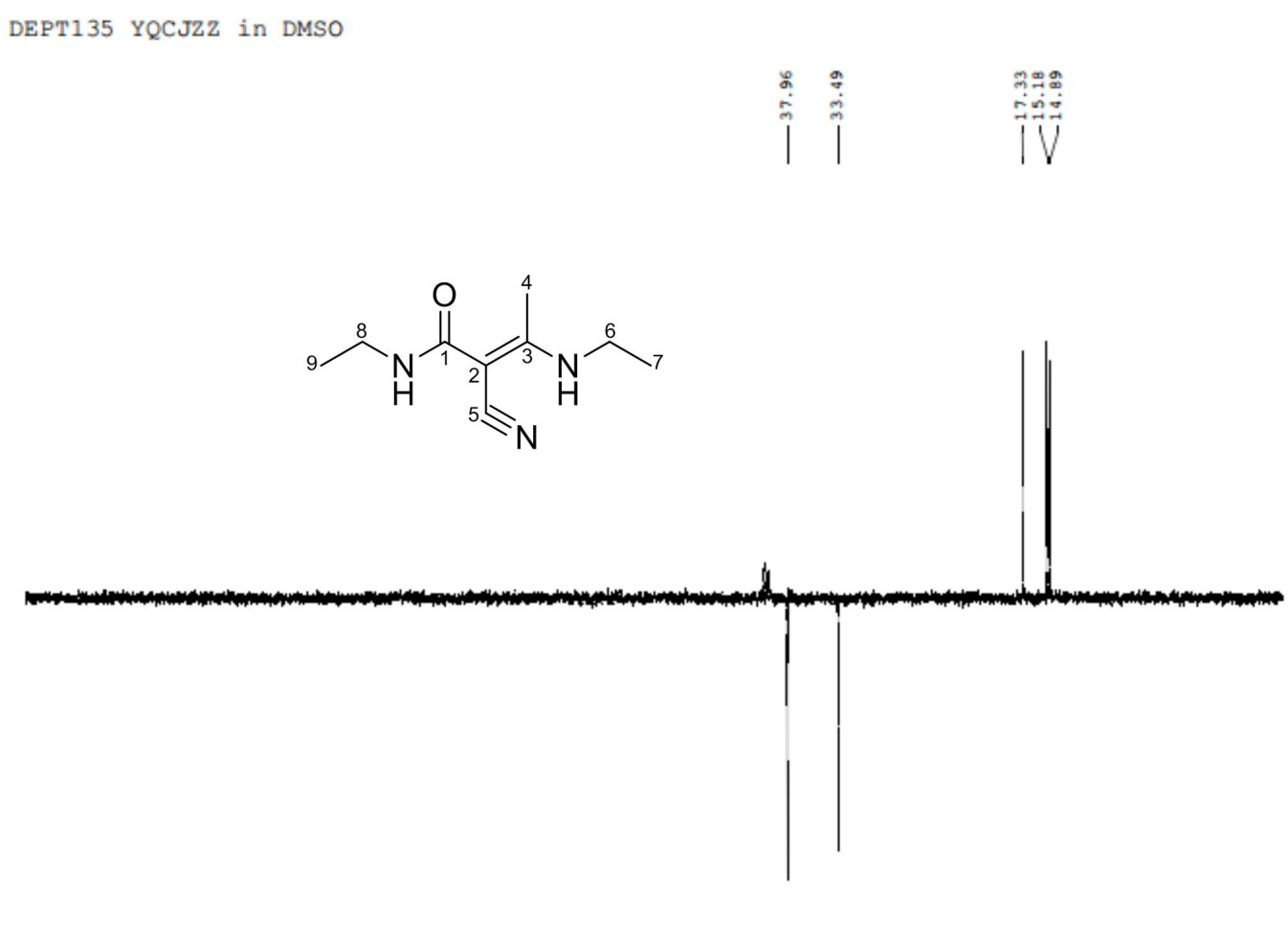

Fig.S7. DEPT spectrum

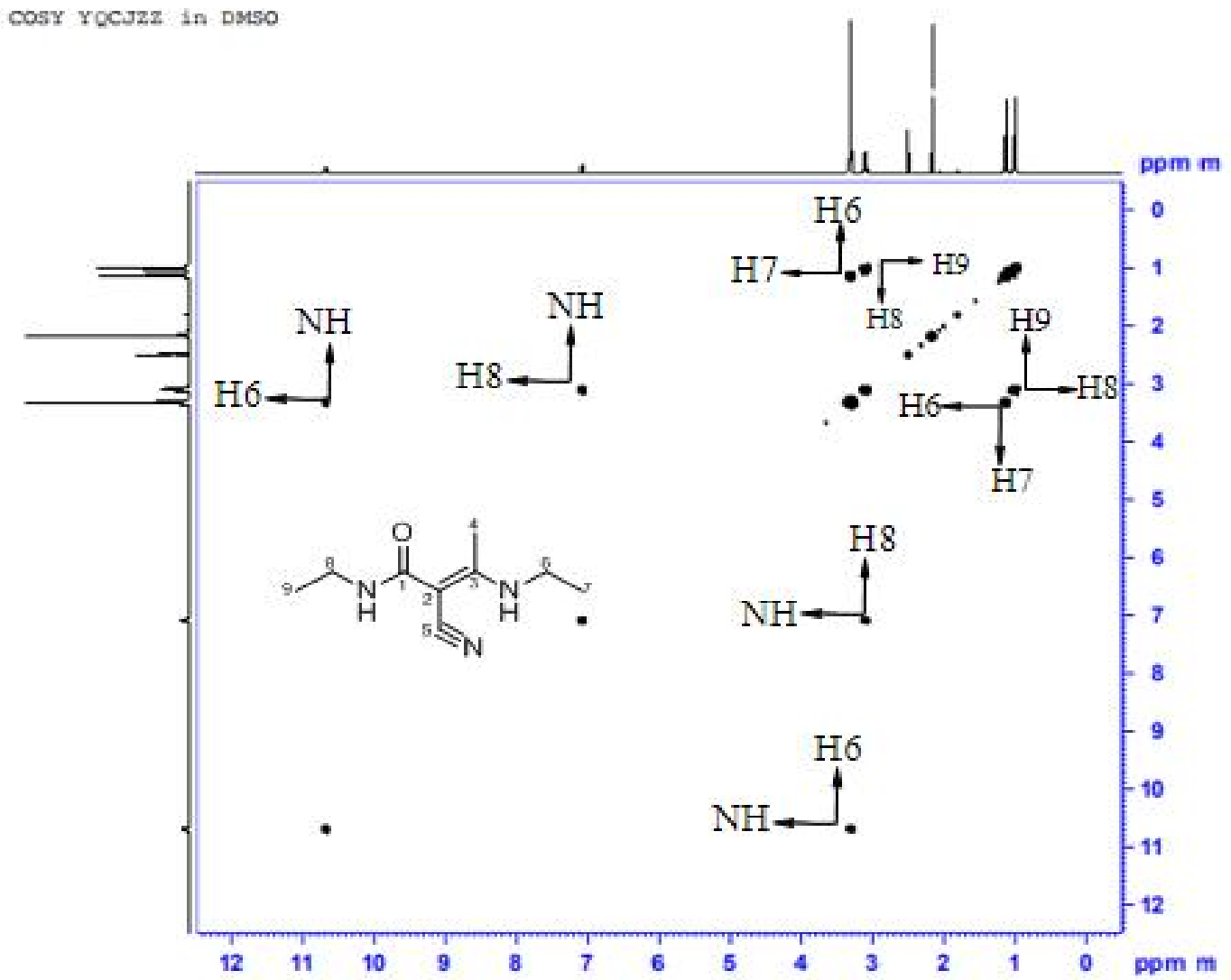

Fig.S8. ^{1}H-^{1}H COSY correlation spectrum

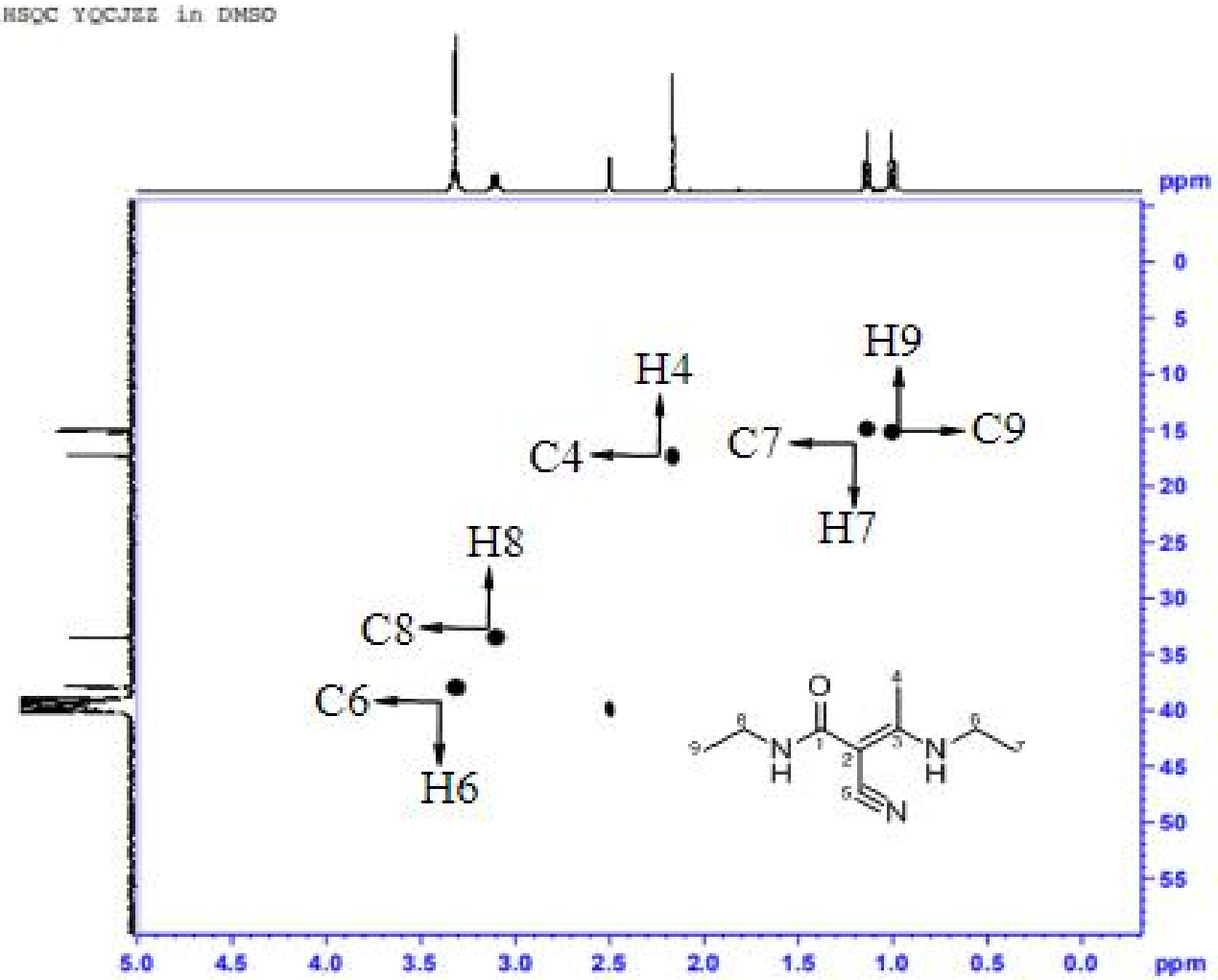

Fig.S9. ^{13}C-$^{1}HSQC$ correlation spectrum

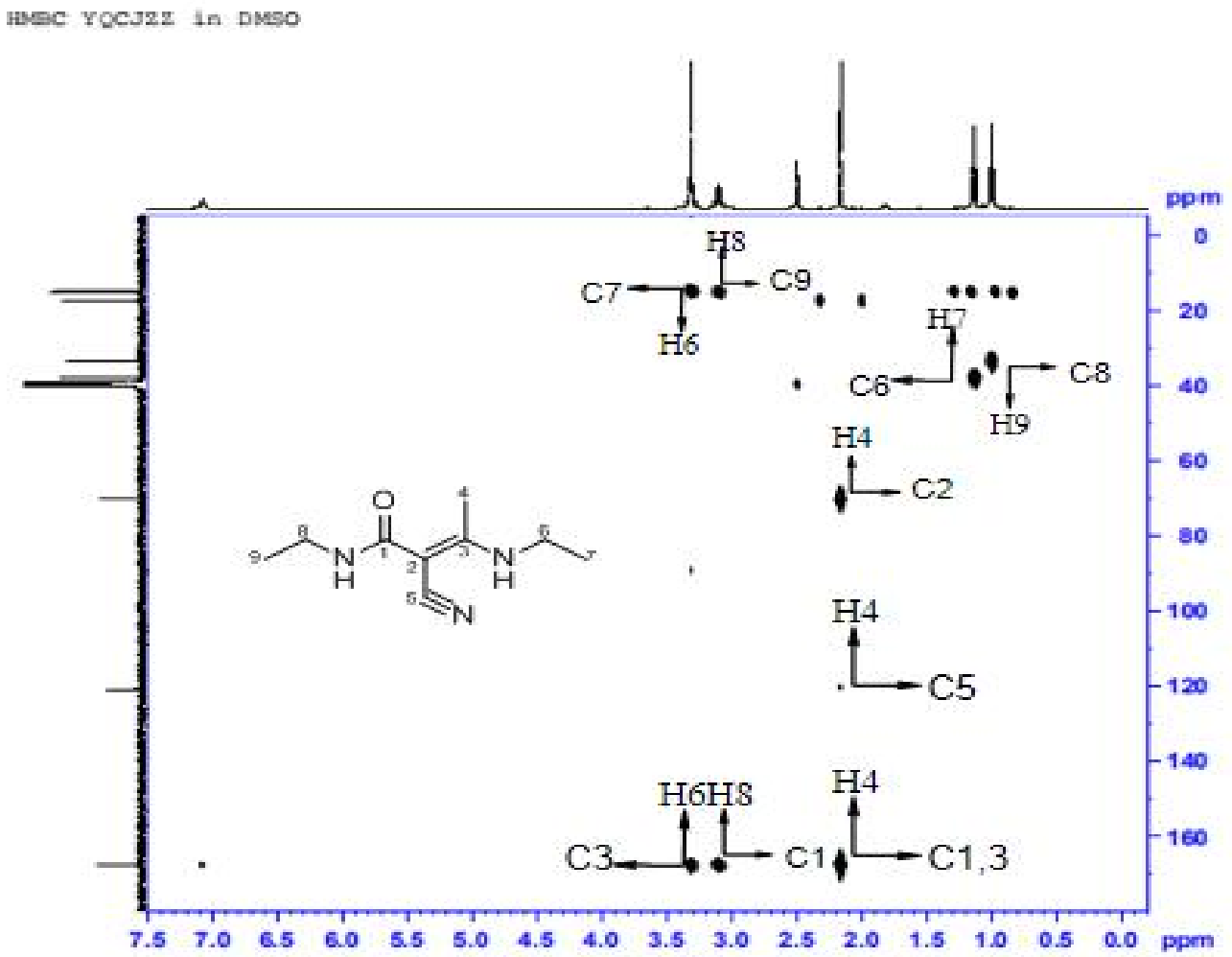

Fig.S10. The remote ^{13}C-^{1}H HMBC correlation spectrum

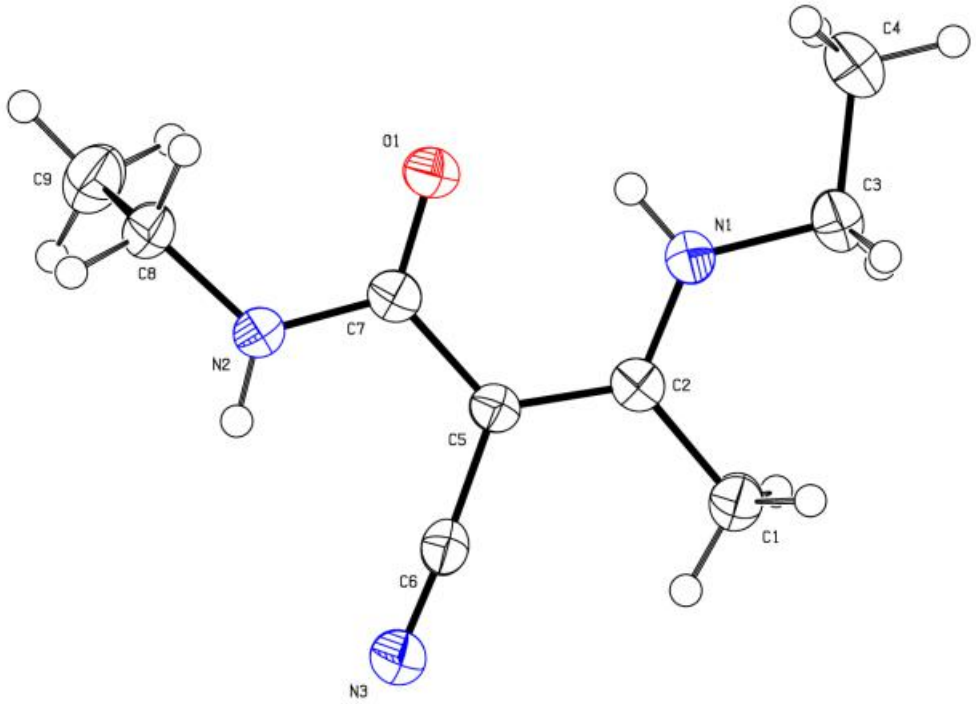

Fig.S11. Single crystal X-ray diffractometer spectrum