

Supporting Information

Design, Synthesis, and Biological Evaluation of Deuterated C-Aryl Glycoside as a Potent and Long-Acting Renal Sodium-Dependent Glucose Cotransporter 2 Inhibitor for the Treatment of Type 2 Diabetes

Ge Xu,^{†,‡} Binhua Lv,[‡] Jacques Y. Roberge,[‡] Baihua Xu,[‡] Jiyan Du,[‡] Jiajia Dong,[‡] Yuanwei Chen,[‡] Kun Peng,[‡] Lili Zhang,[‡] Xinxing Tang,[‡] Yan Feng,[‡] Min Xu,[‡] Wei Fu,[†] Wenbin Zhang,[‡] Liangcheng Zhu,[‡] Zhongping Deng,[‡] Zelin Sheng,[‡] Ajith Welihinda,[§] and Xun Sun^{*,†}

[†]School of Pharmacy, Fudan University, 826 Zhangheng Road, Pudong New Area, Shanghai 201203, P. R. China

[‡]Egret Pharma (Shanghai) Co., Ltd, 4F, 1118 Halei Road, Zhangjiang Hi-Tech Park, Pudong New Area, Shanghai 201203, P. R. China

[§]Theracos Inc., 550 Del Rey Avenue, Sunnyvale, California 94805-3528, United States

HPLC-MS chromatographic metabolic monitoring for **41**: S2

Metabolic process confirmation for **41** and **5** by HPLC-MS chromatography: S3

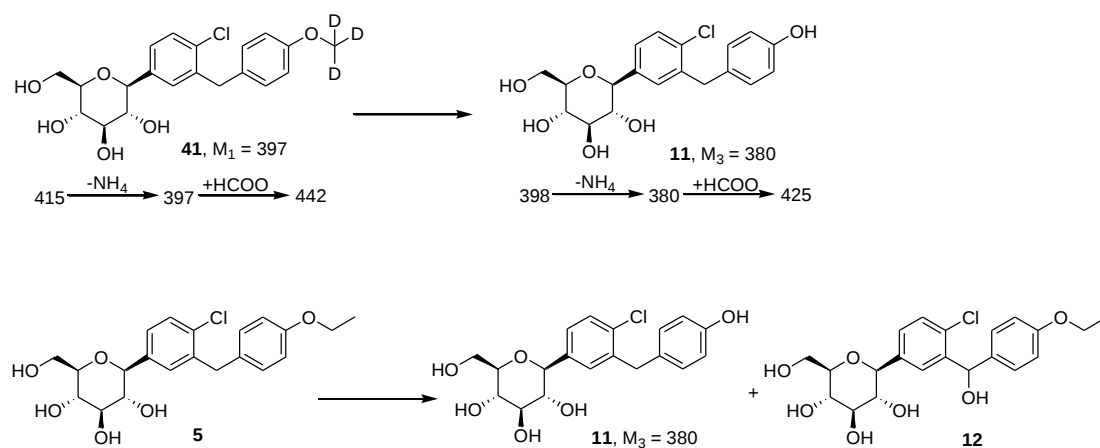
Figure 1 displays the HPLC and MS analysis of compound 11.

The top panel shows the HPLC chromatogram (AN1301220-1 5m (SG, 2x3)) with a major peak at 2.53 minutes. The chemical structure of compound 11 is shown, along with its proposed structure 41 (M₁ = 397).

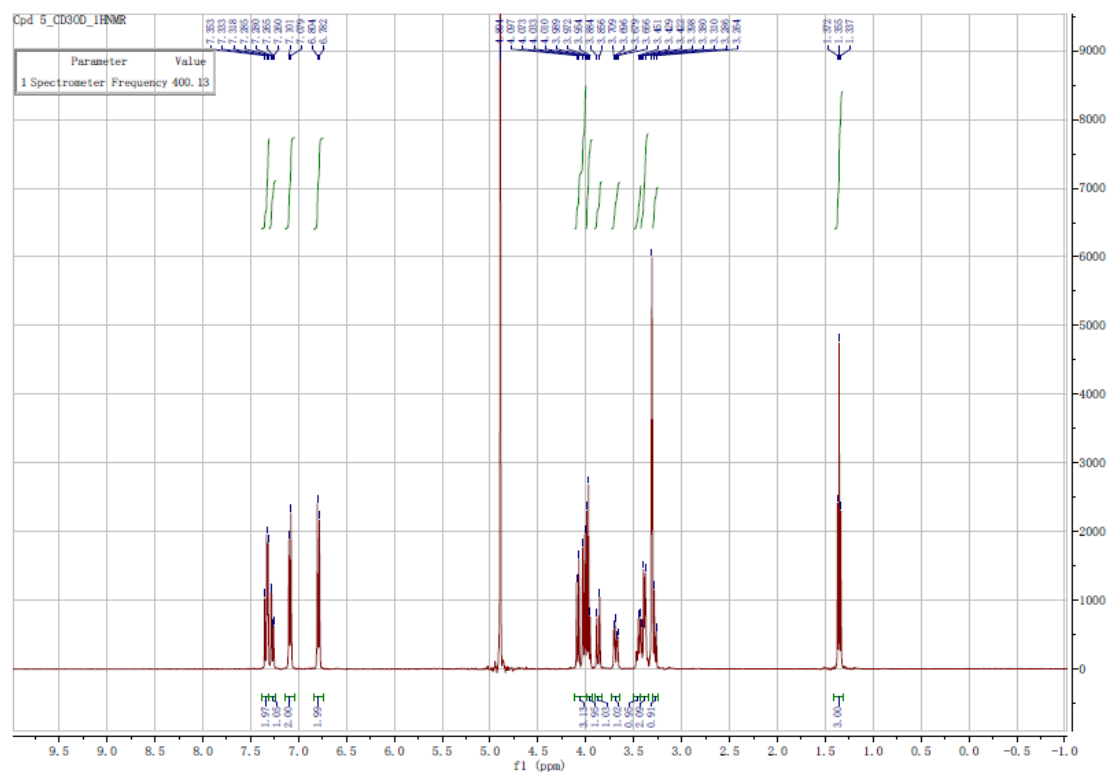
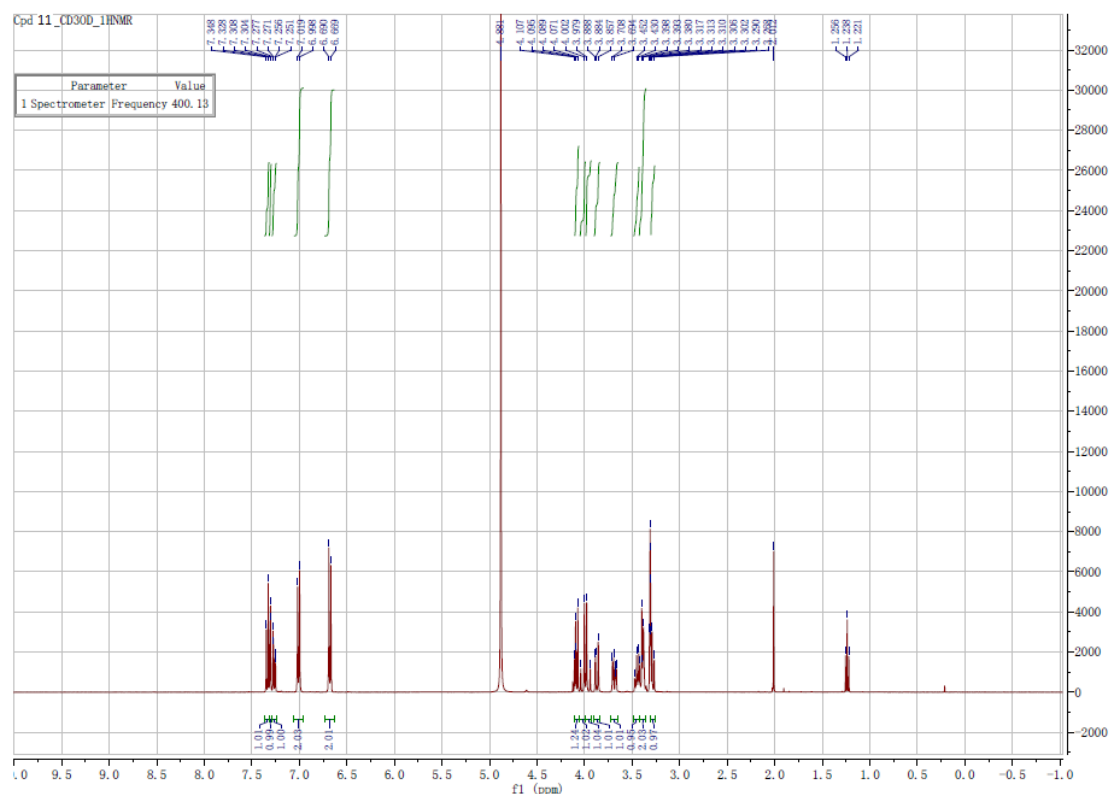
The bottom panel shows three MS spectra:

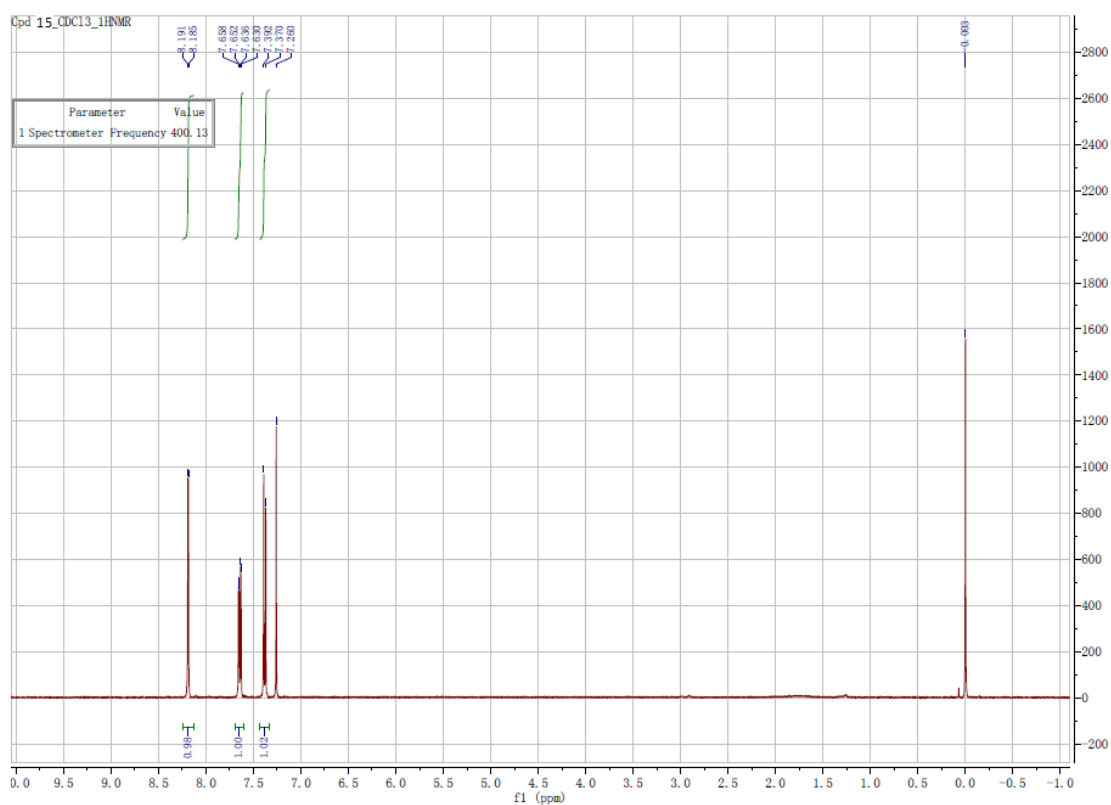
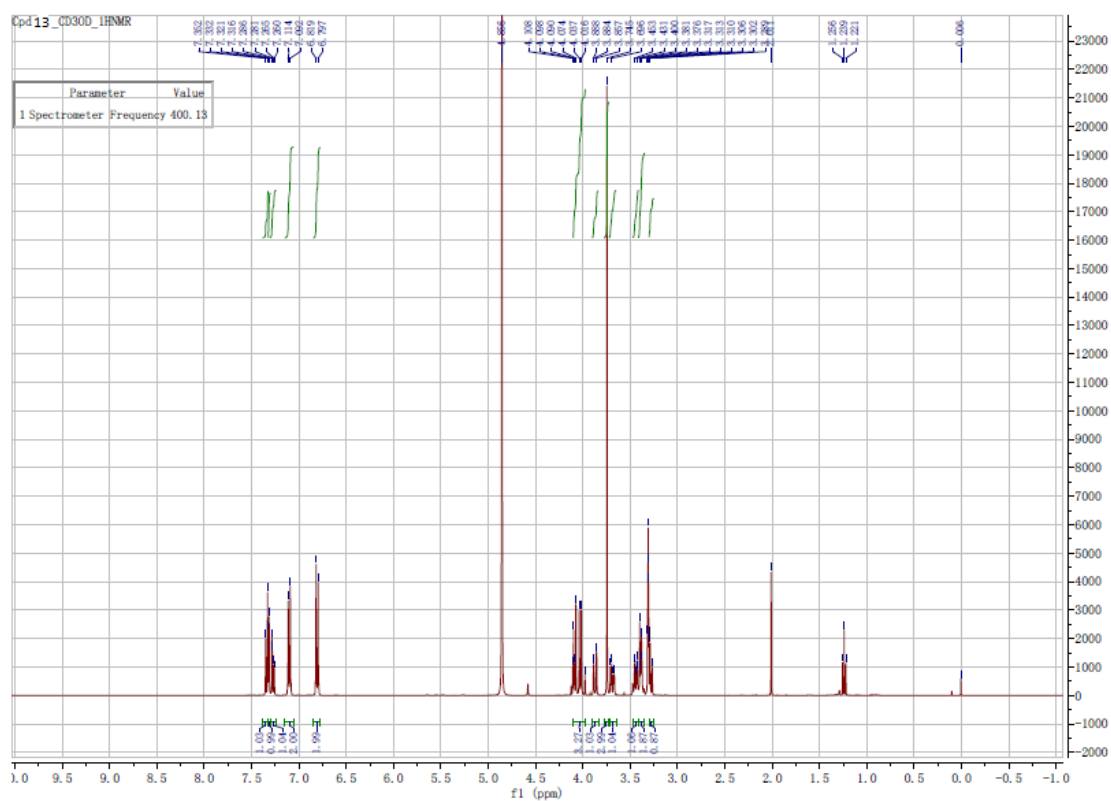
- 1: Scan ES+ (2.23e6) showing peaks for [M₃ + NH₄]⁺.
- 2: Scan ES- (1.00e6) showing peaks for [M₃ + HCOO]⁻.
- 3: Scan ES+ (6.01e6) showing peaks for [M₁ + NH₄]⁺.
- 4: Scan ES- (3.20e6) showing peaks for [M₁ + HCOO]⁻.

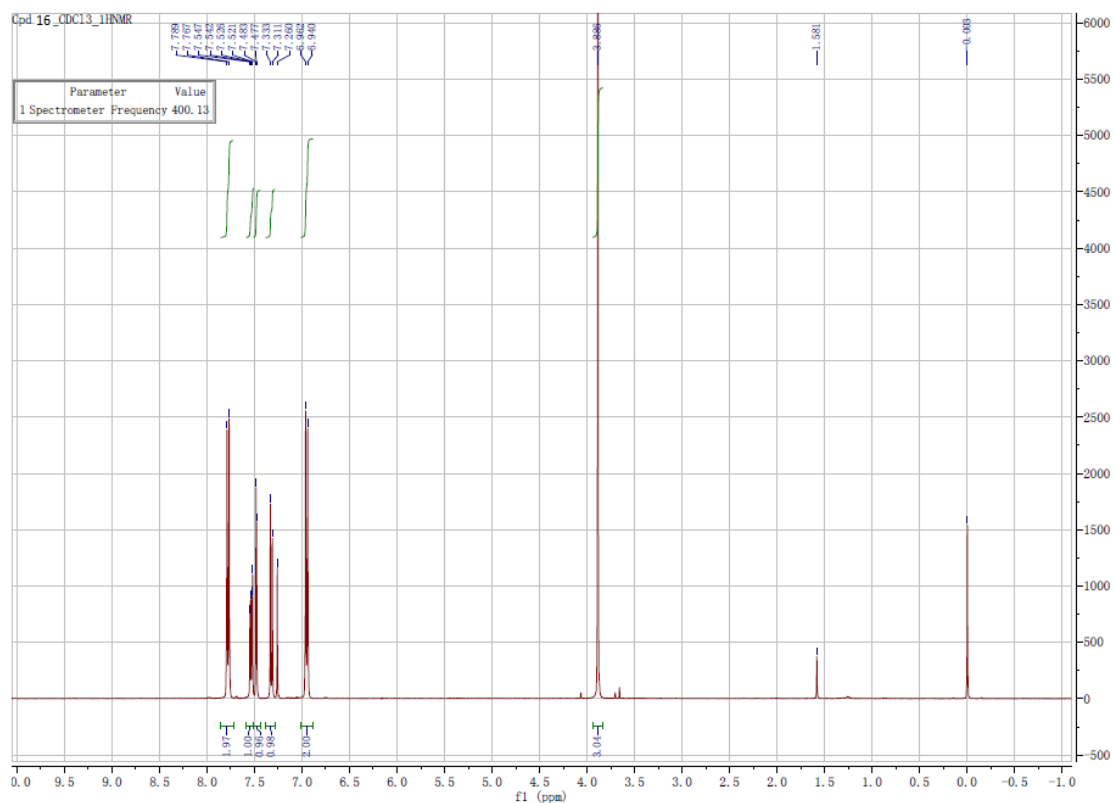
Figure S2. Metabolic process confirmation for **41** and **5** by HPLC-MS chromatography.



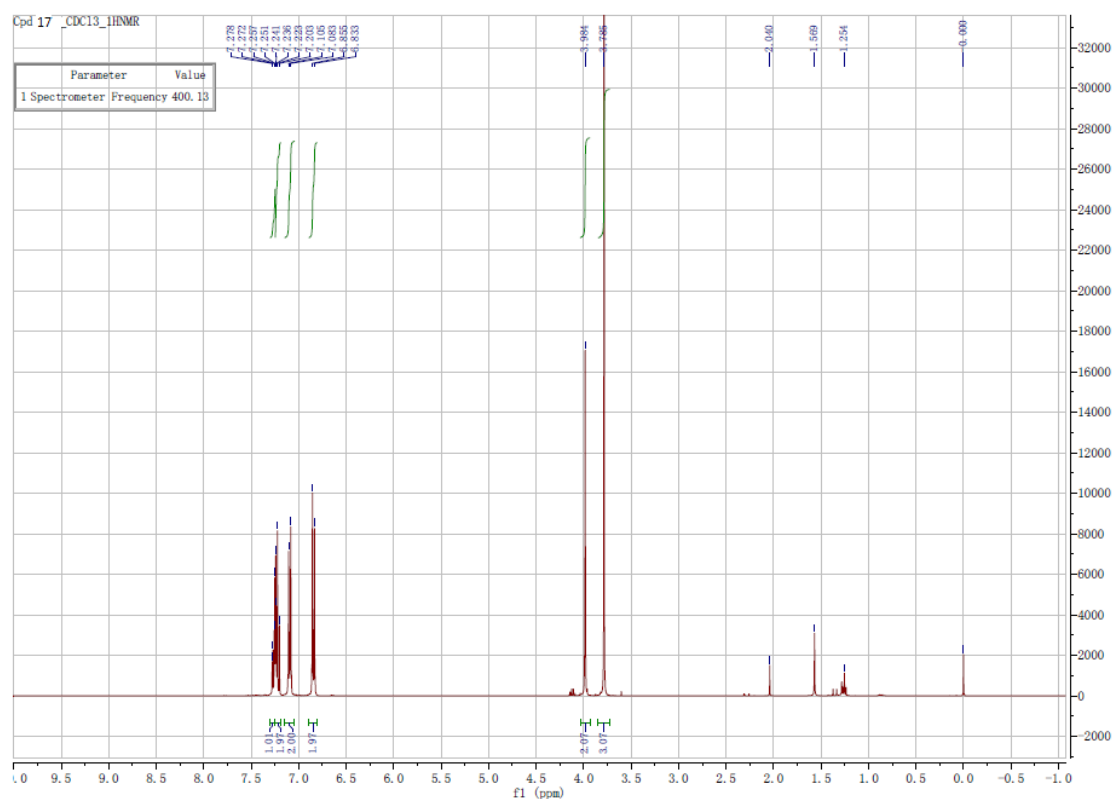
Analytical Data

¹H NMR¹H-NMR of 5¹H-NMR of **11**

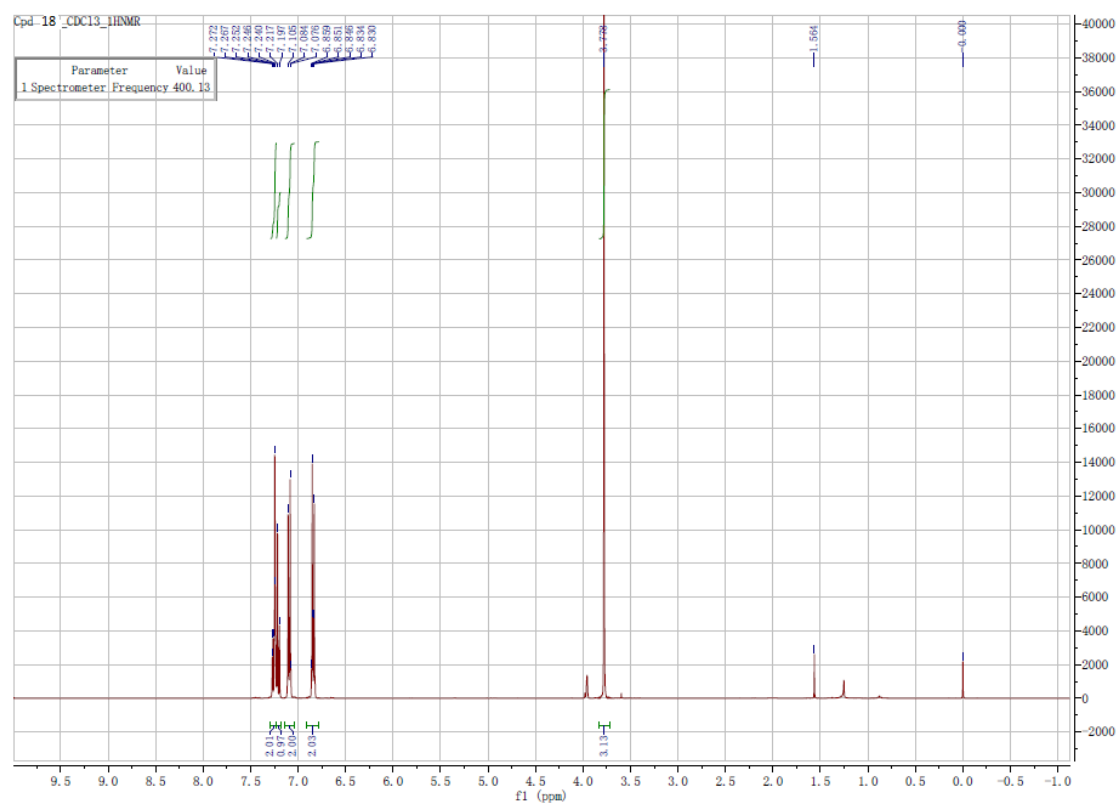
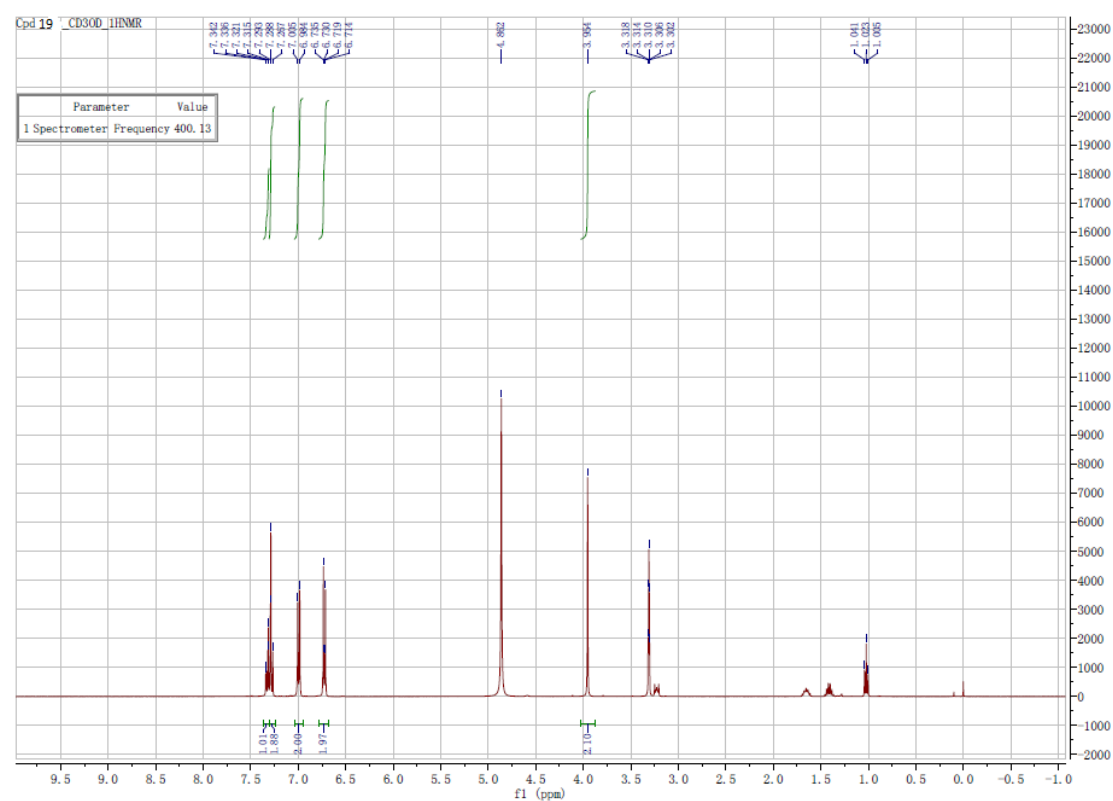


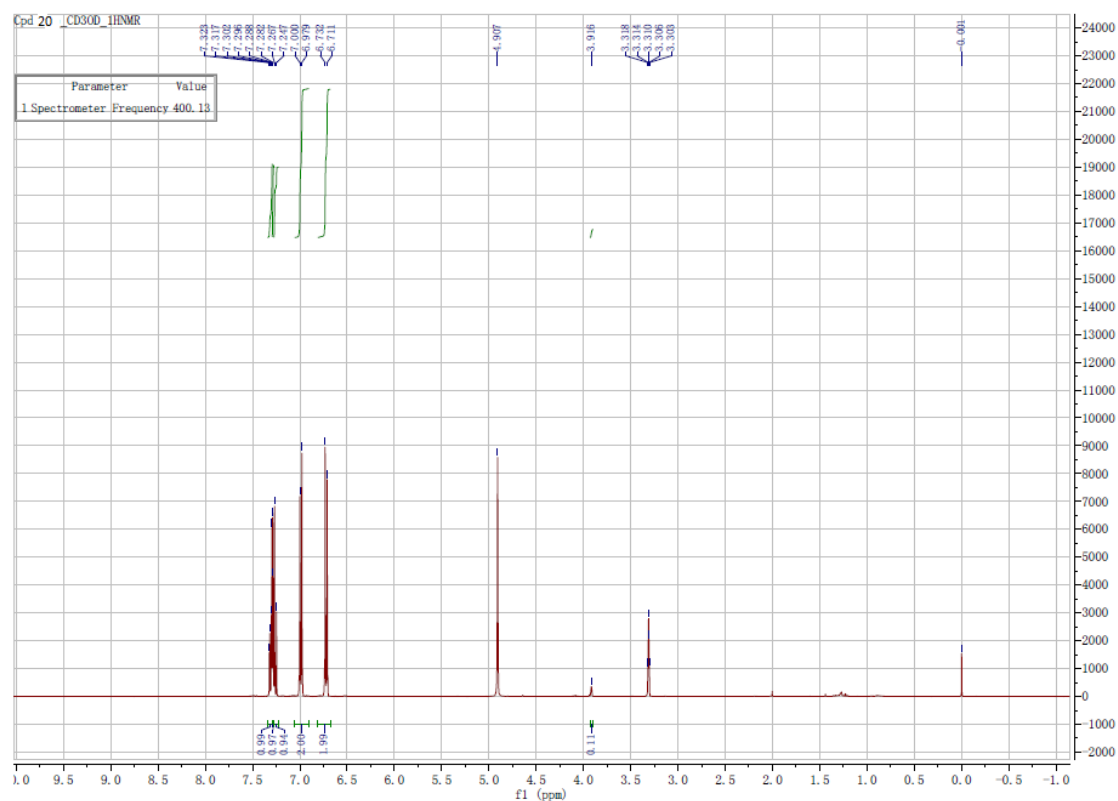


^1H -NMR of 16

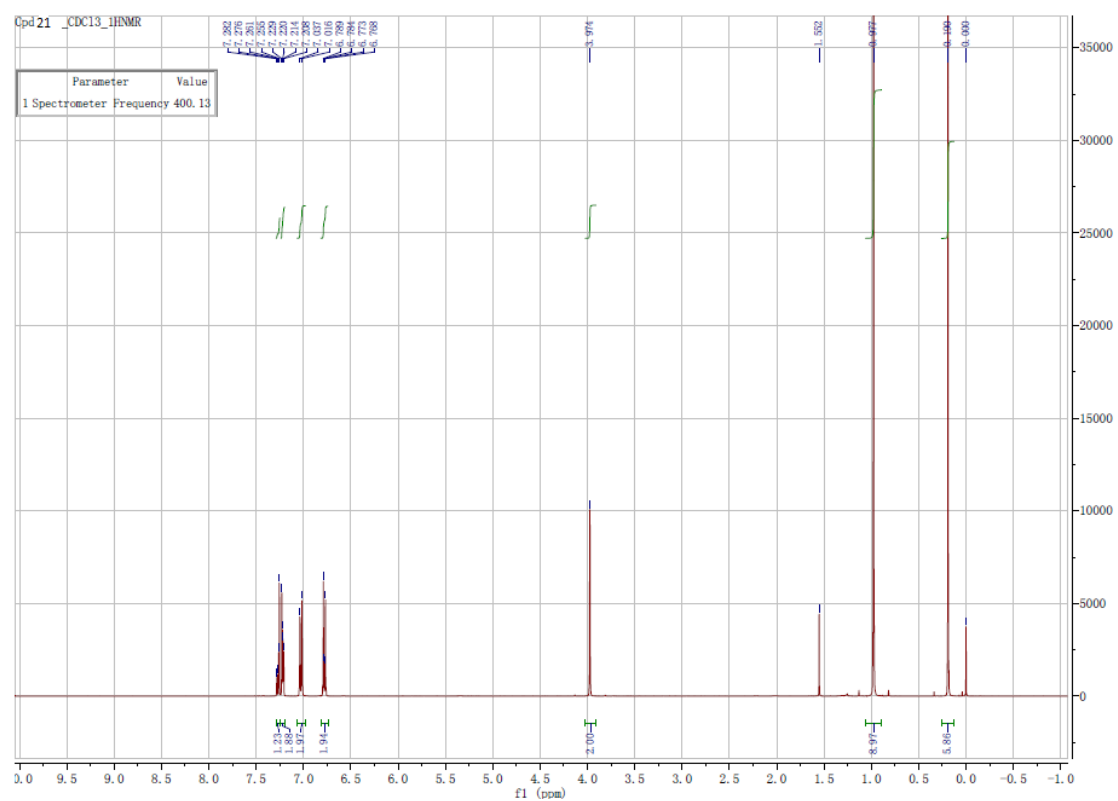


^1H -NMR of 17

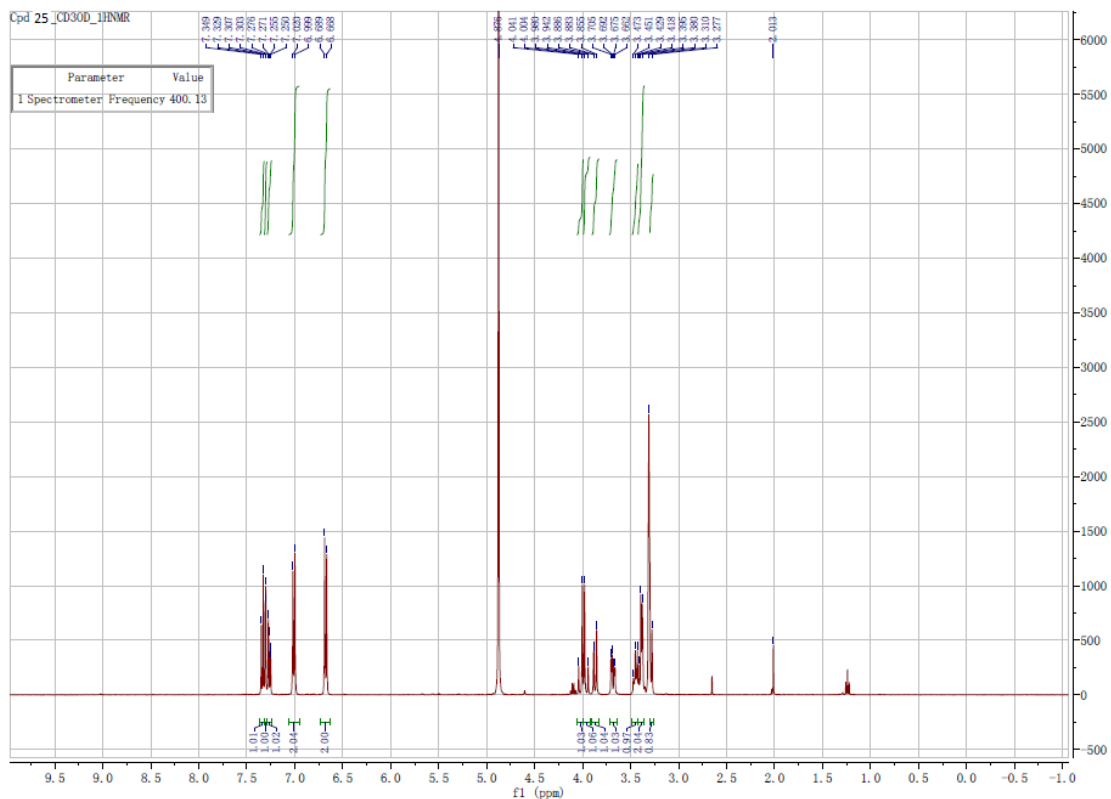
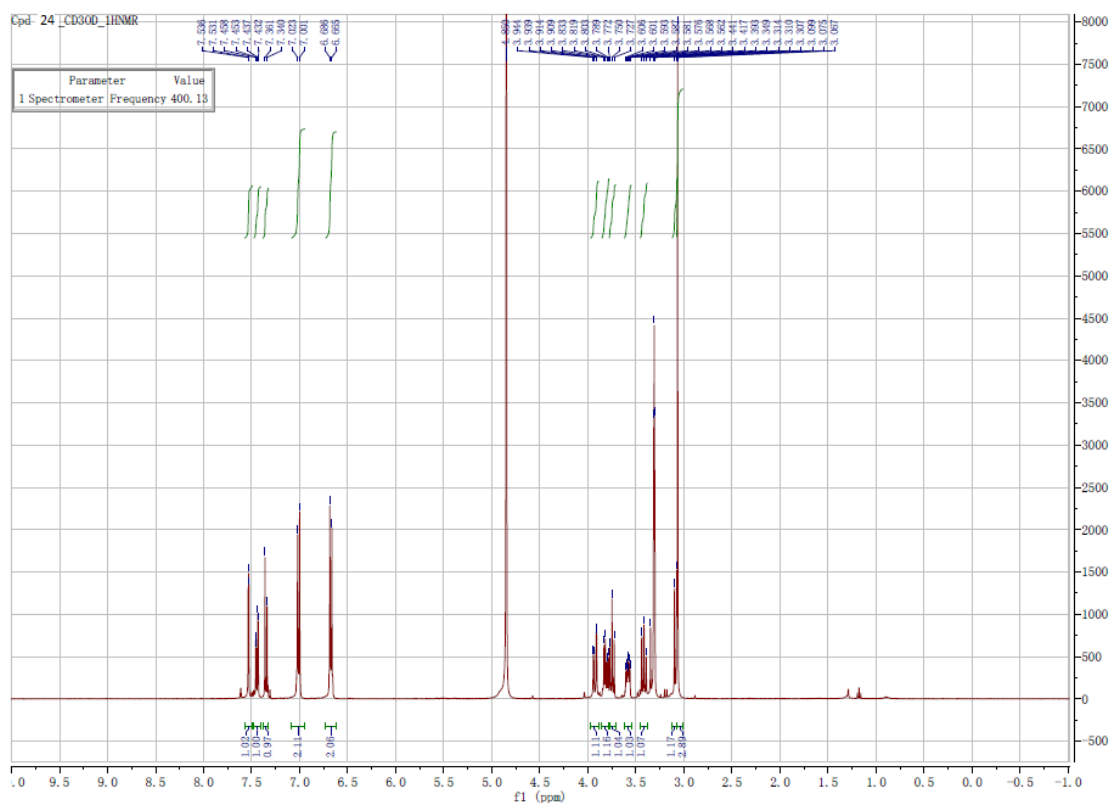
¹H-NMR of **18**¹H-NMR of **19**

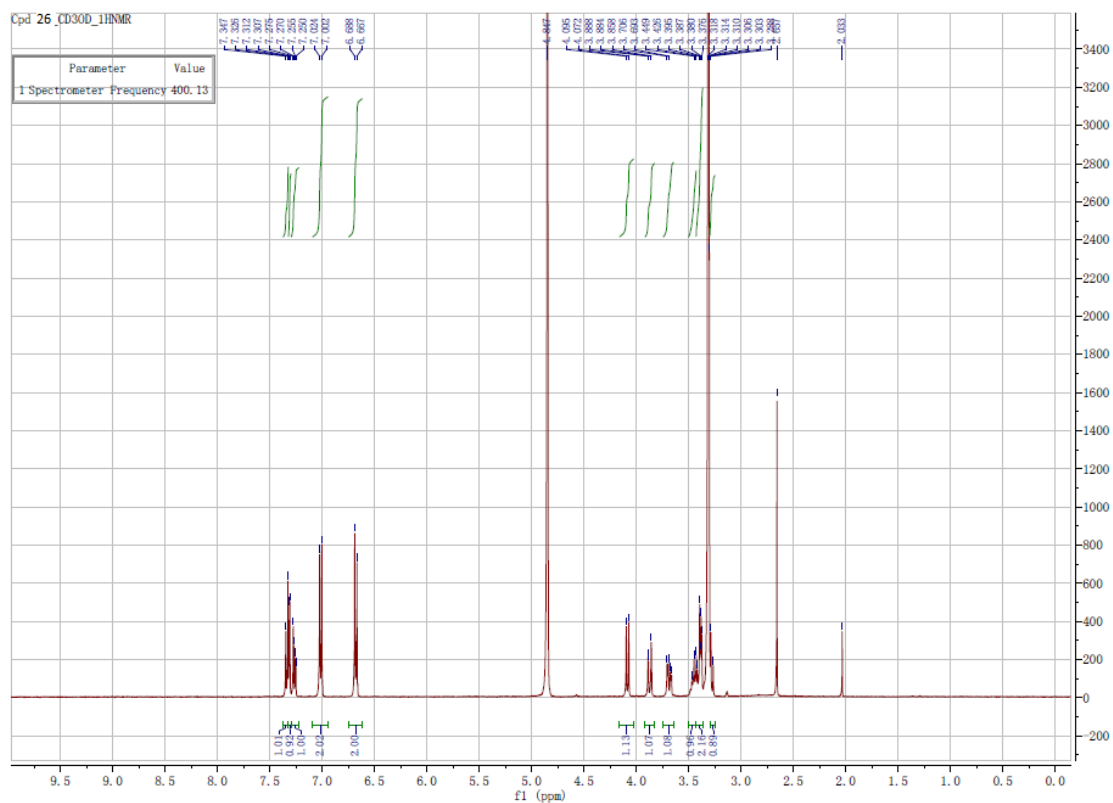


$^1\text{H-NMR}$ of 20

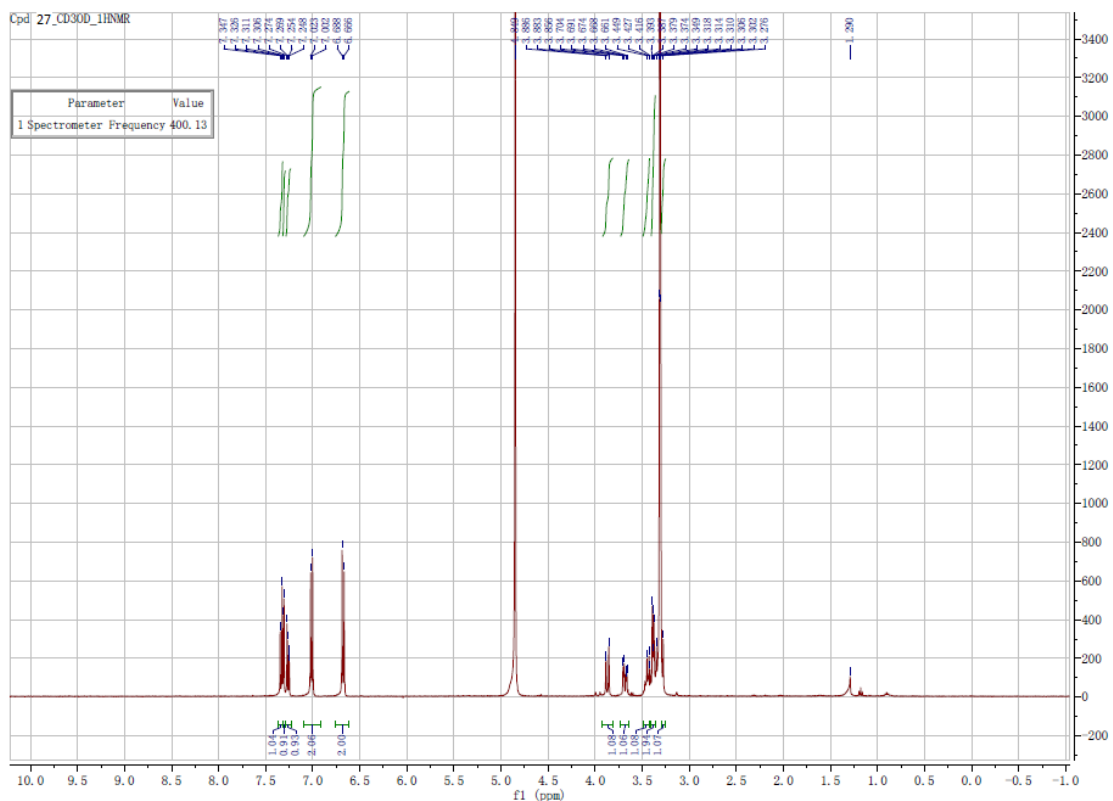


$^1\text{H-NMR}$ of 21

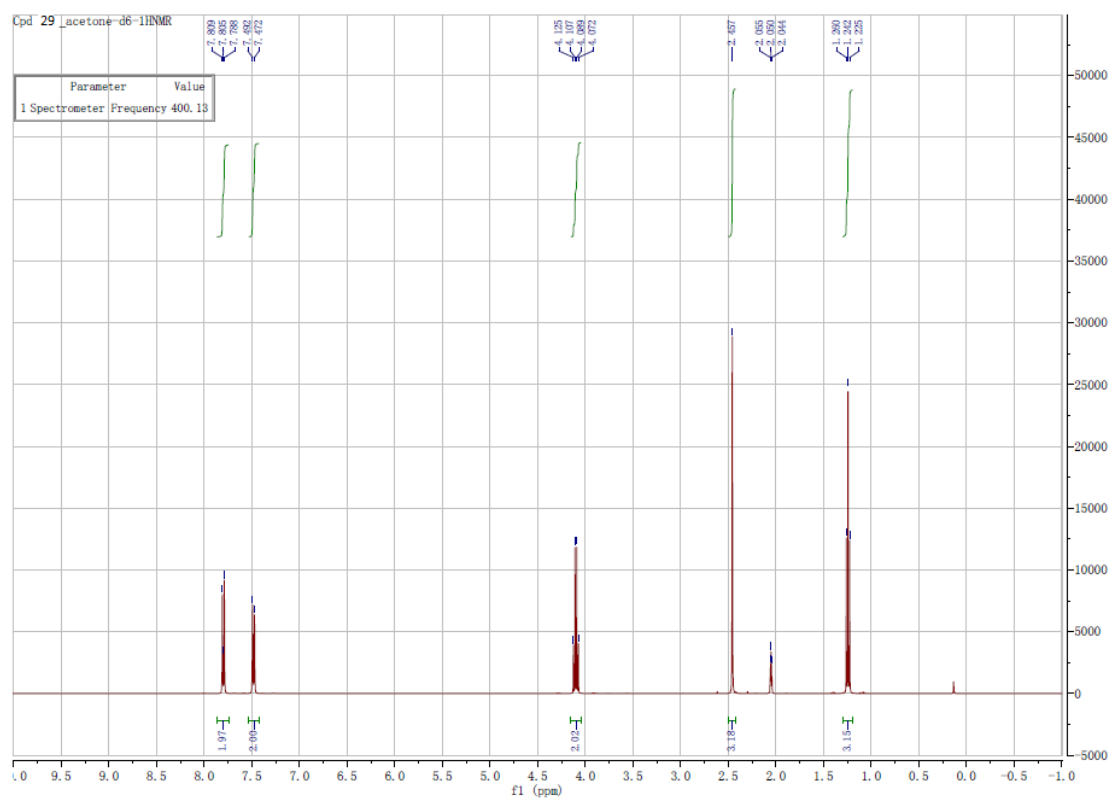




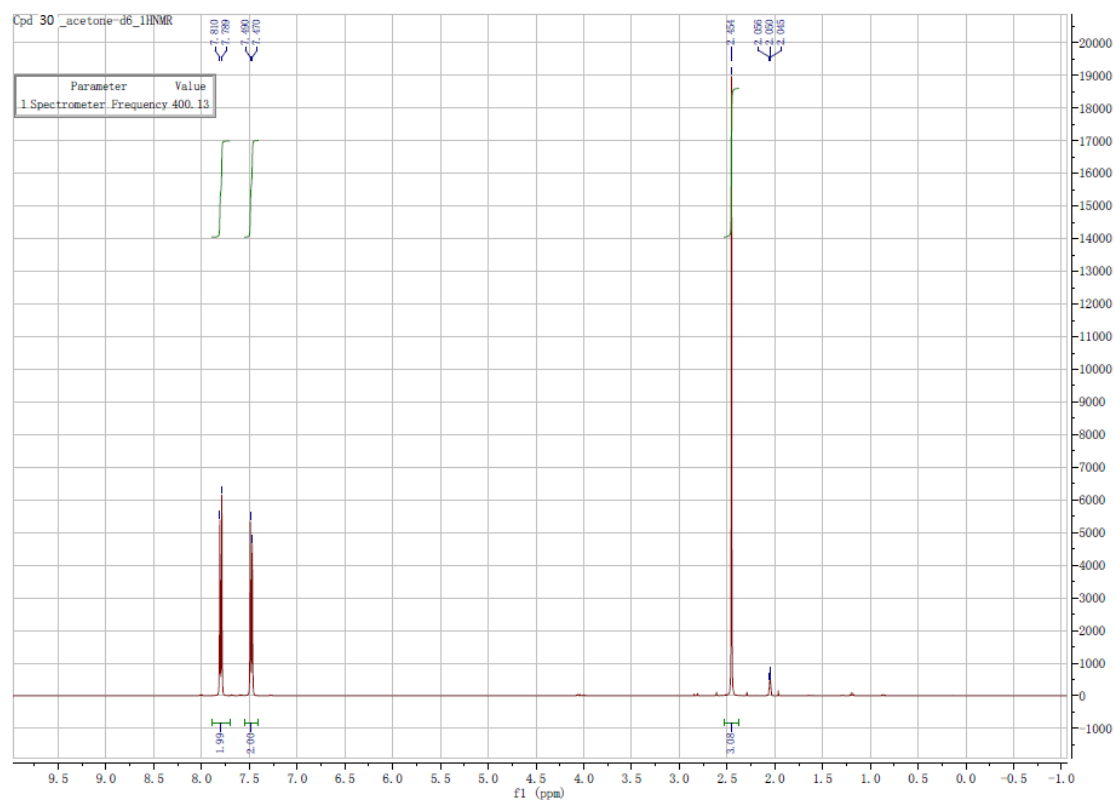
^1H -NMR of 26



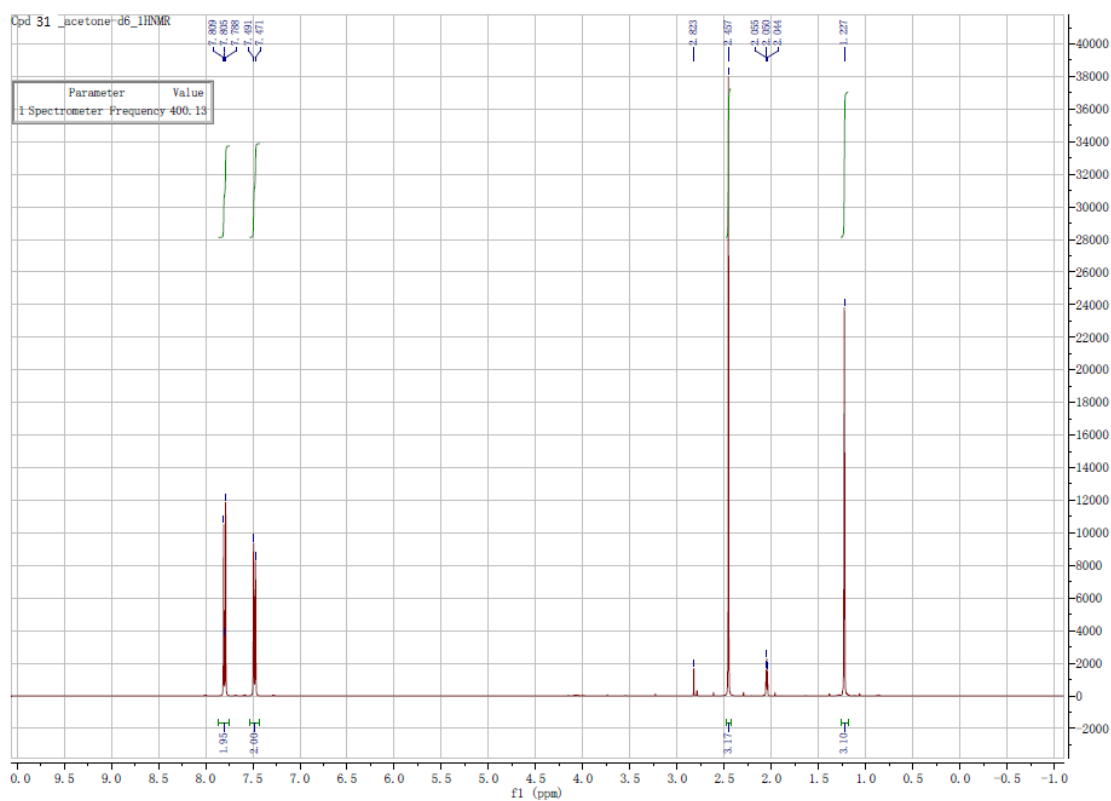
^1H -NMR of 27



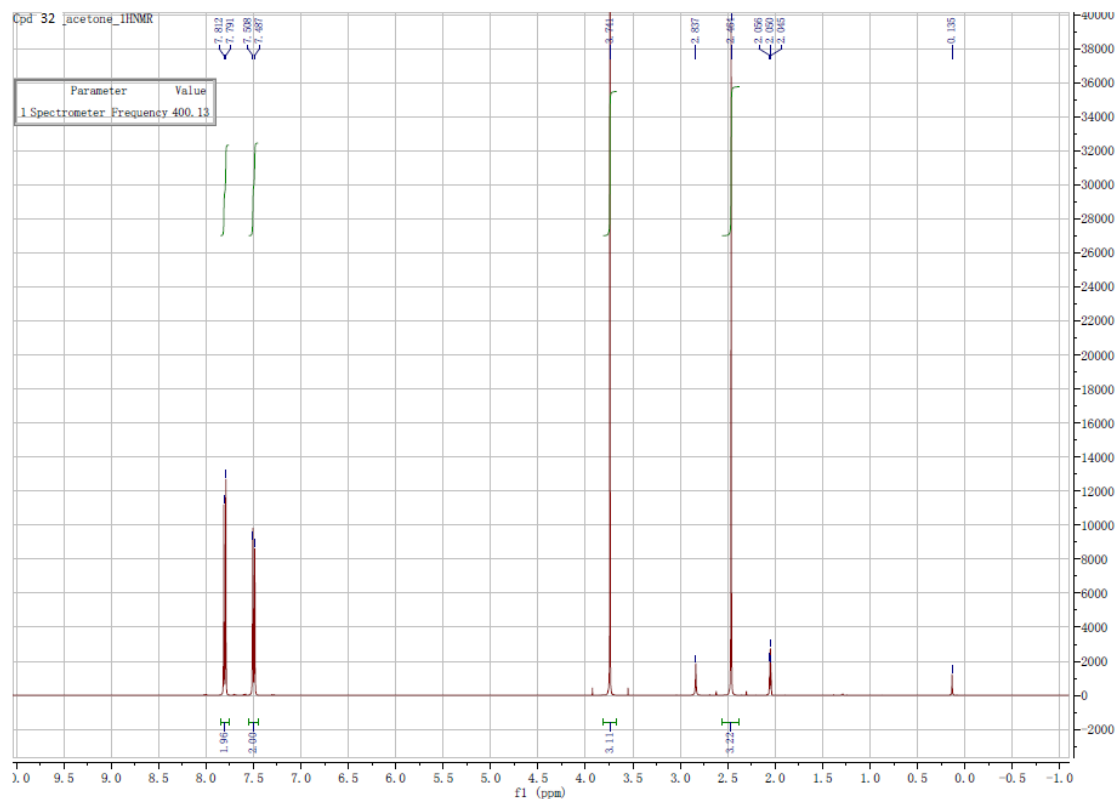
^1H -NMR of 29



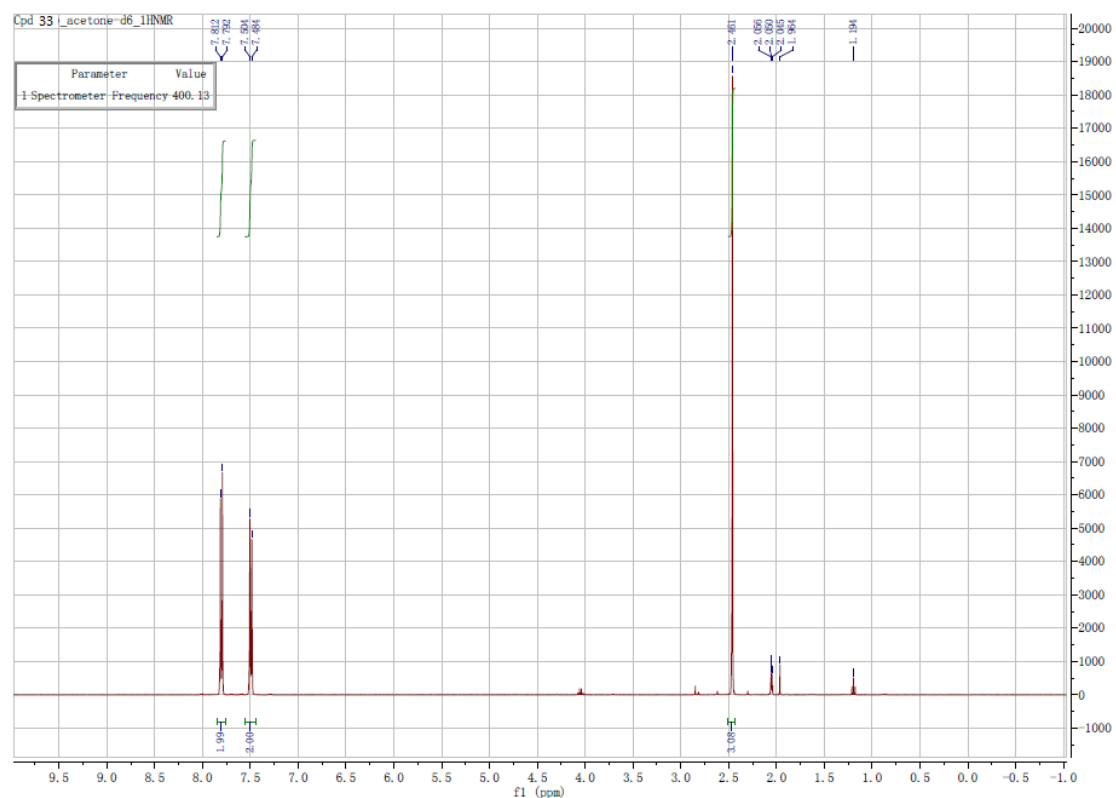
^1H -NMR of 30



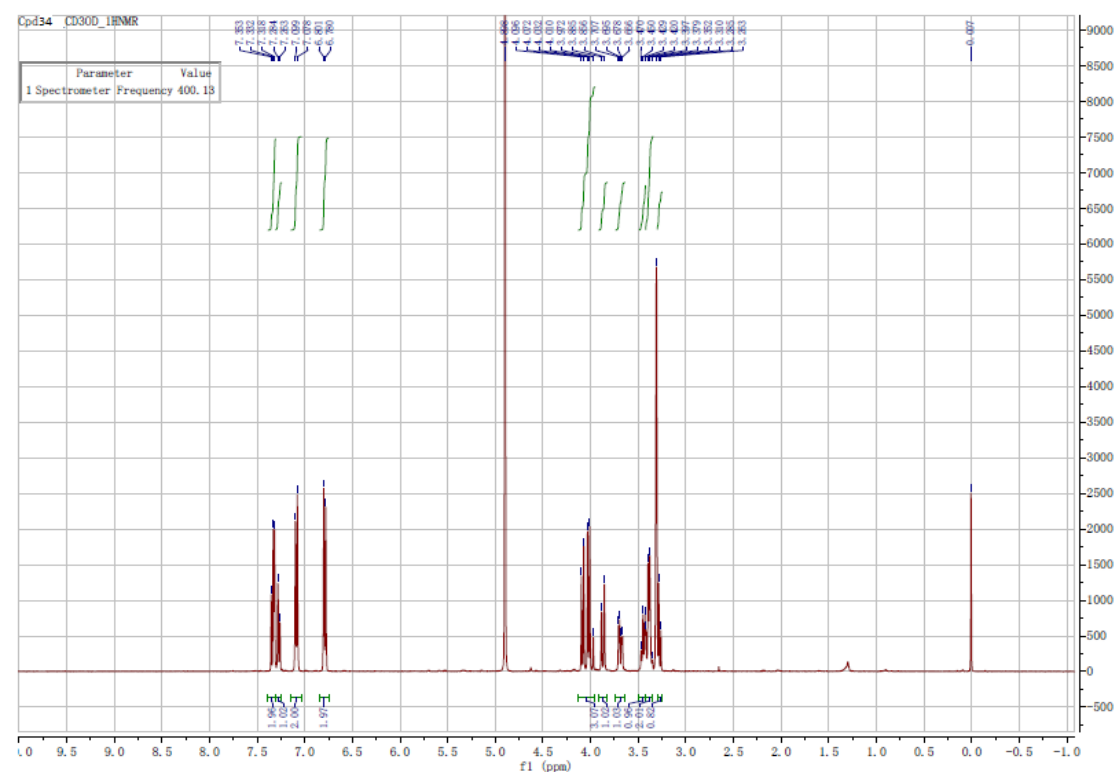
^1H -NMR of 31



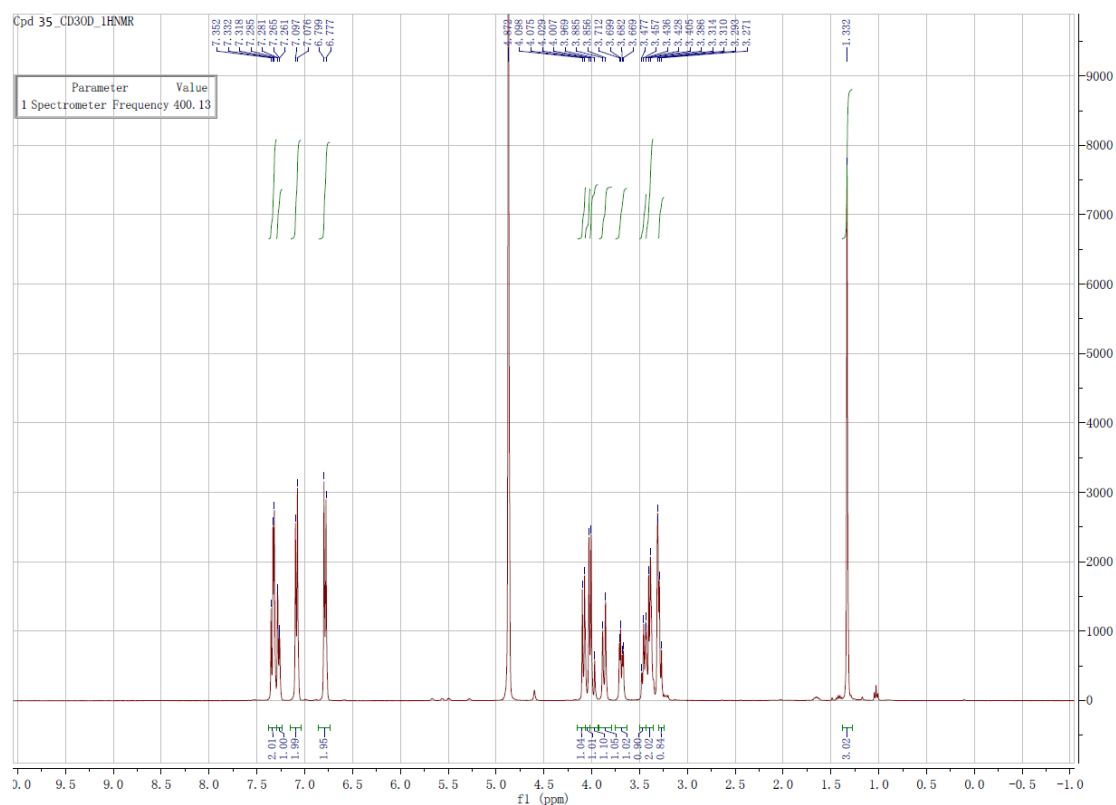
^1H -NMR of 32



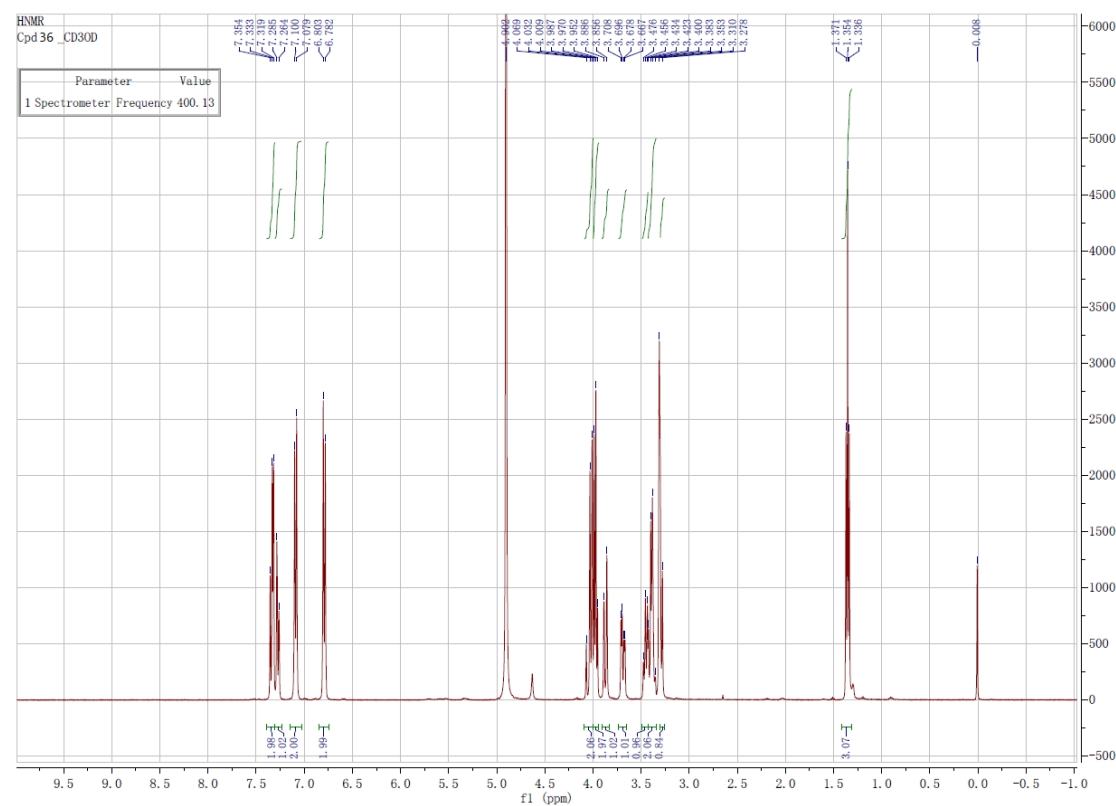
¹H-NMR of 33



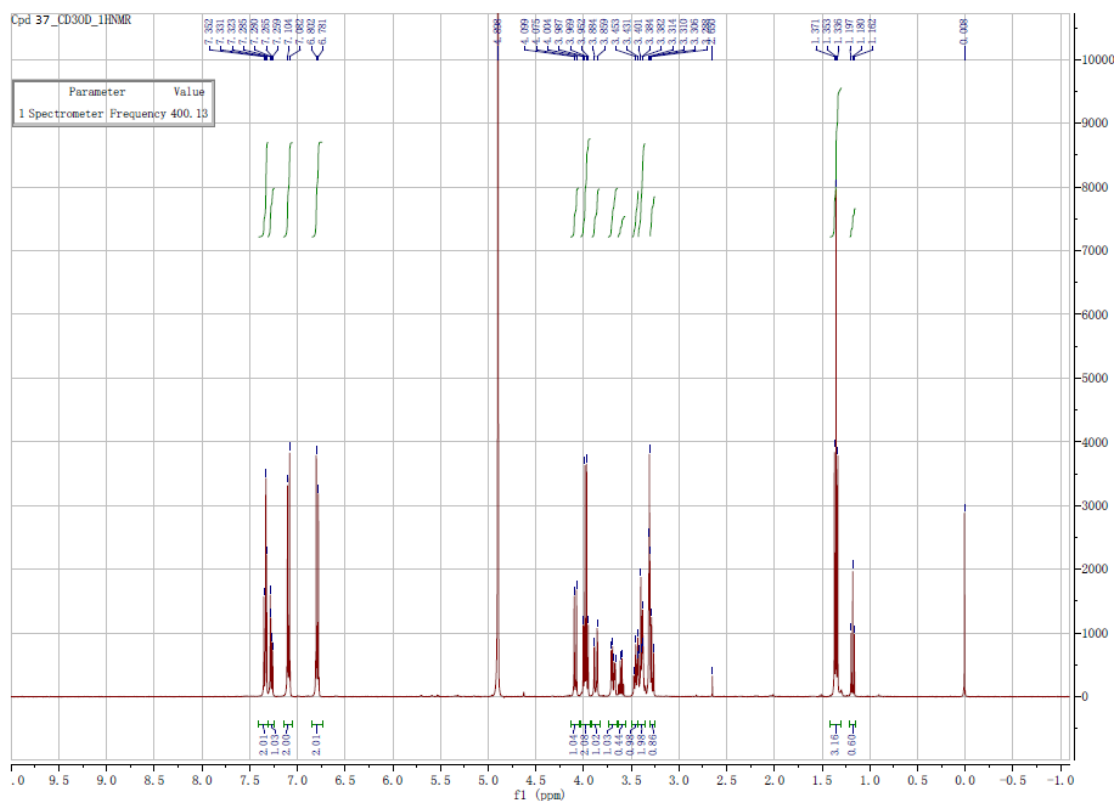
¹H-NMR of 34



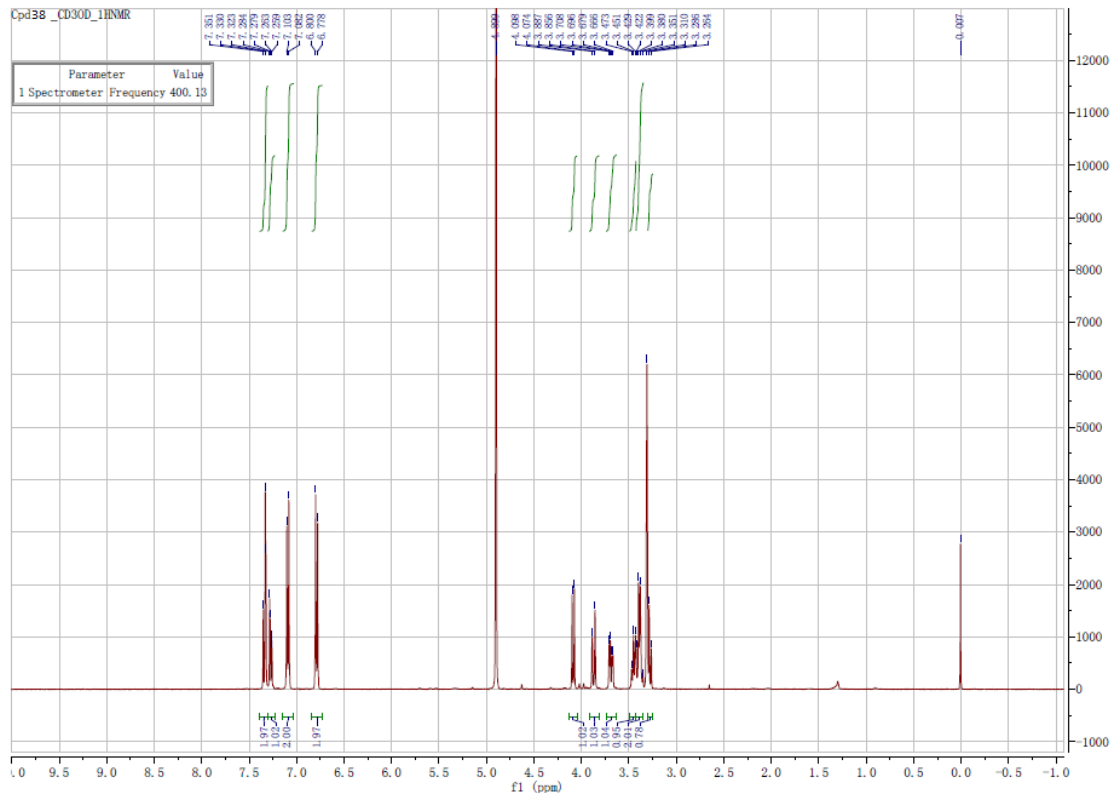
$^1\text{H-NMR}$ of 35



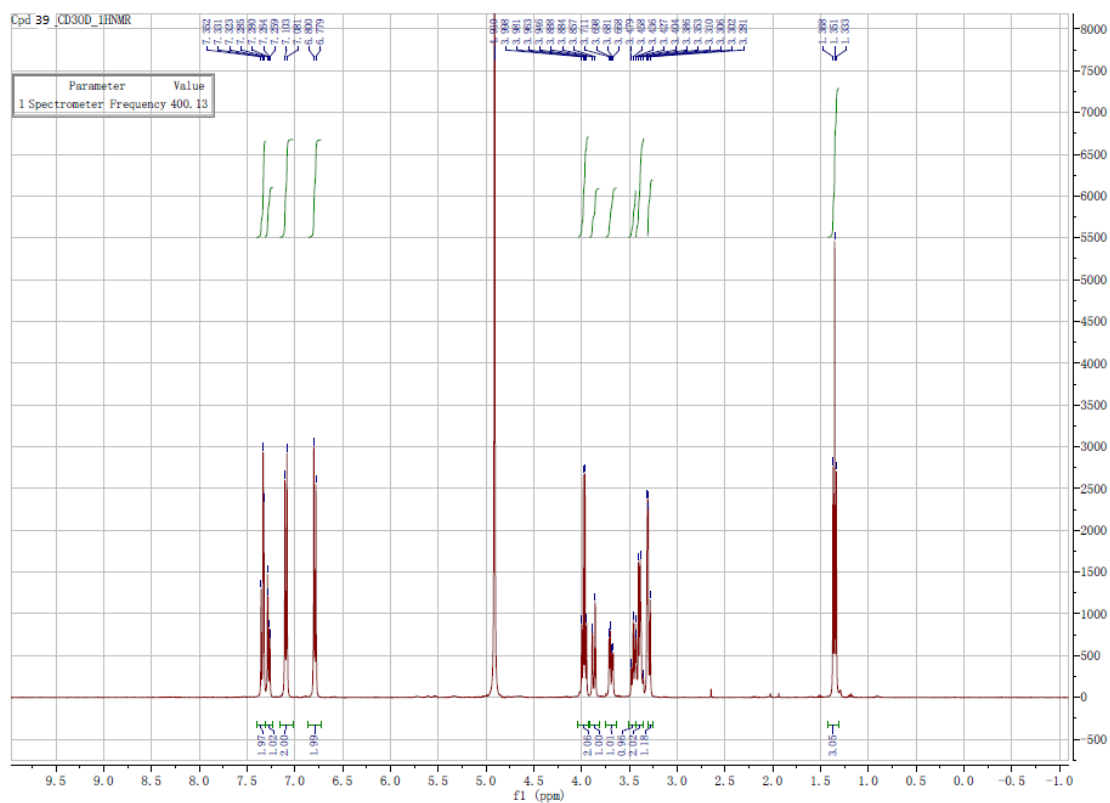
$^1\text{H-NMR}$ of 36



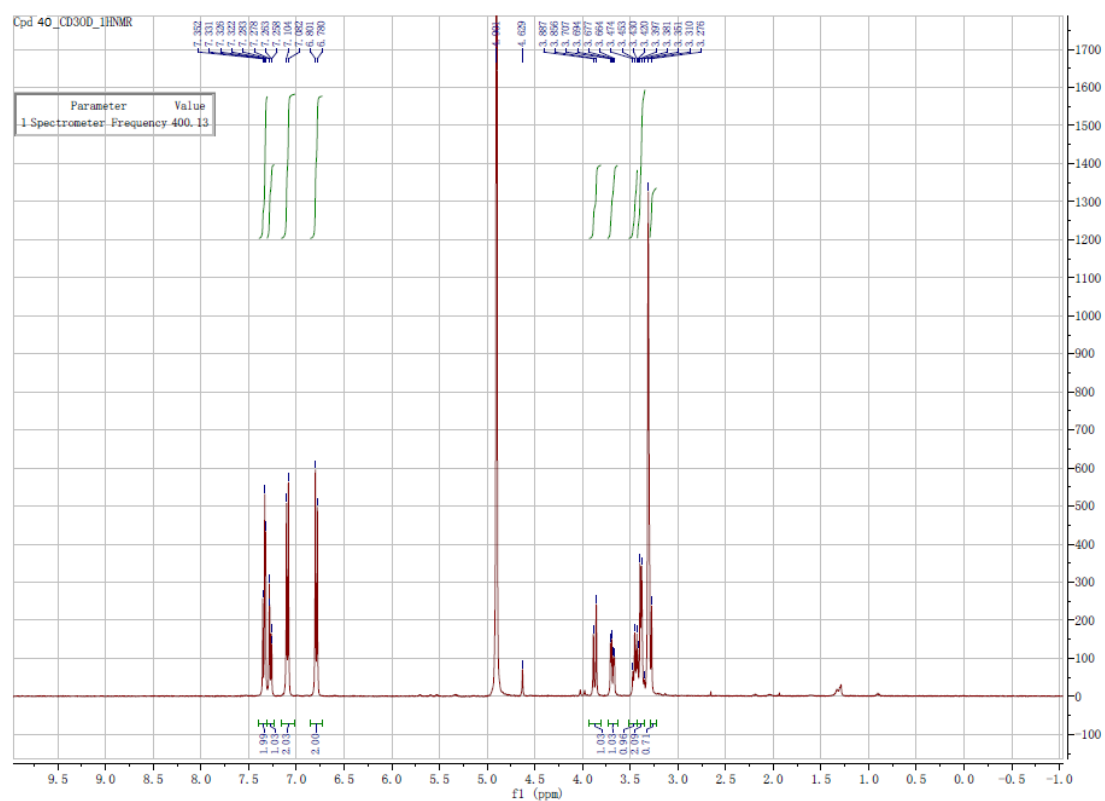
^1H -NMR of 37



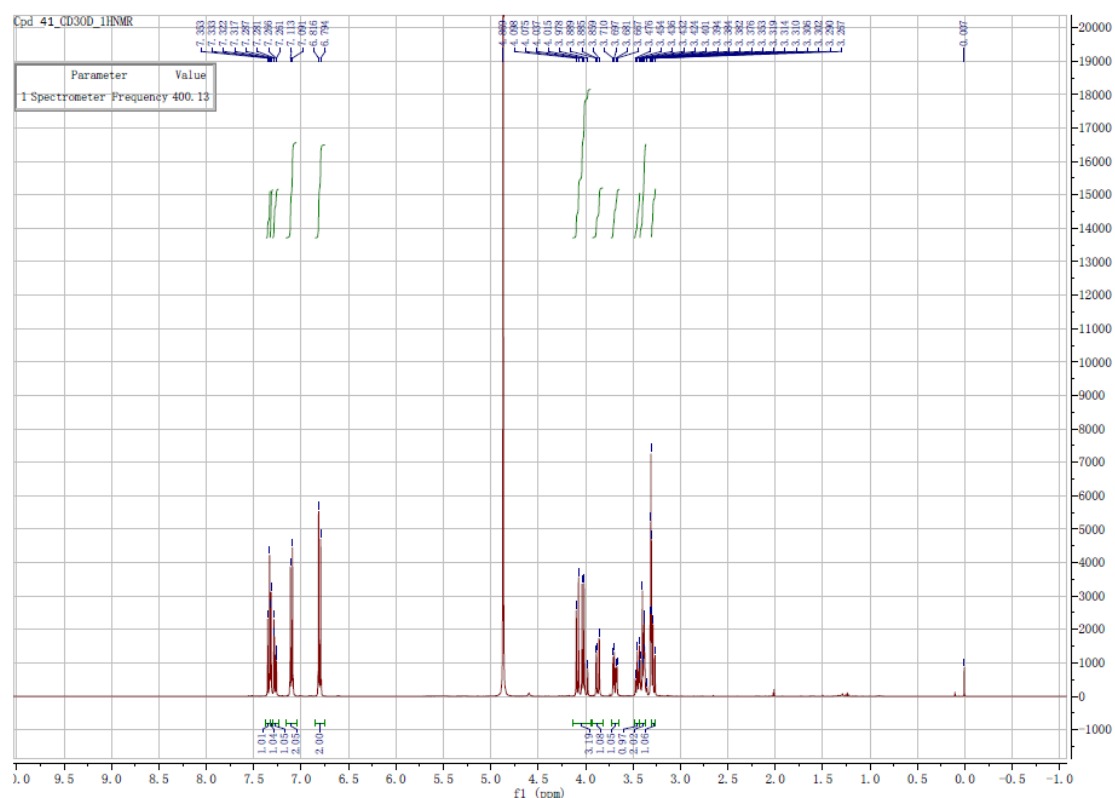
^1H -NMR of 38



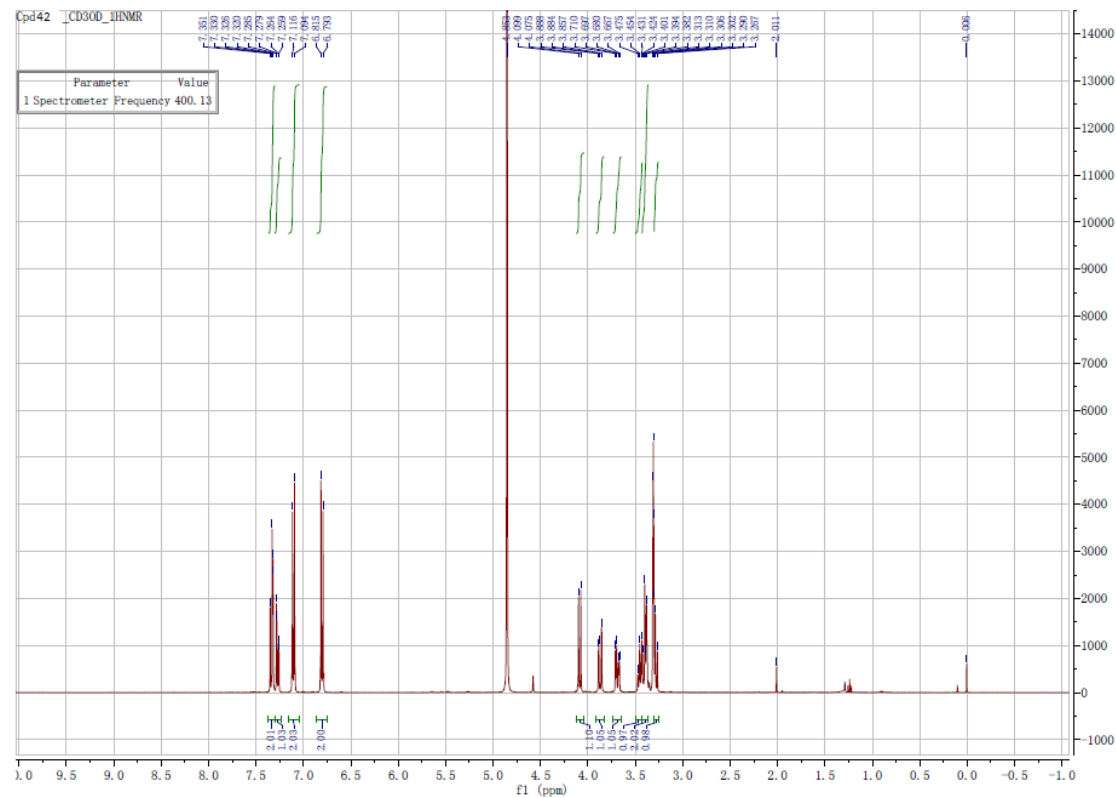
^1H -NMR of 39



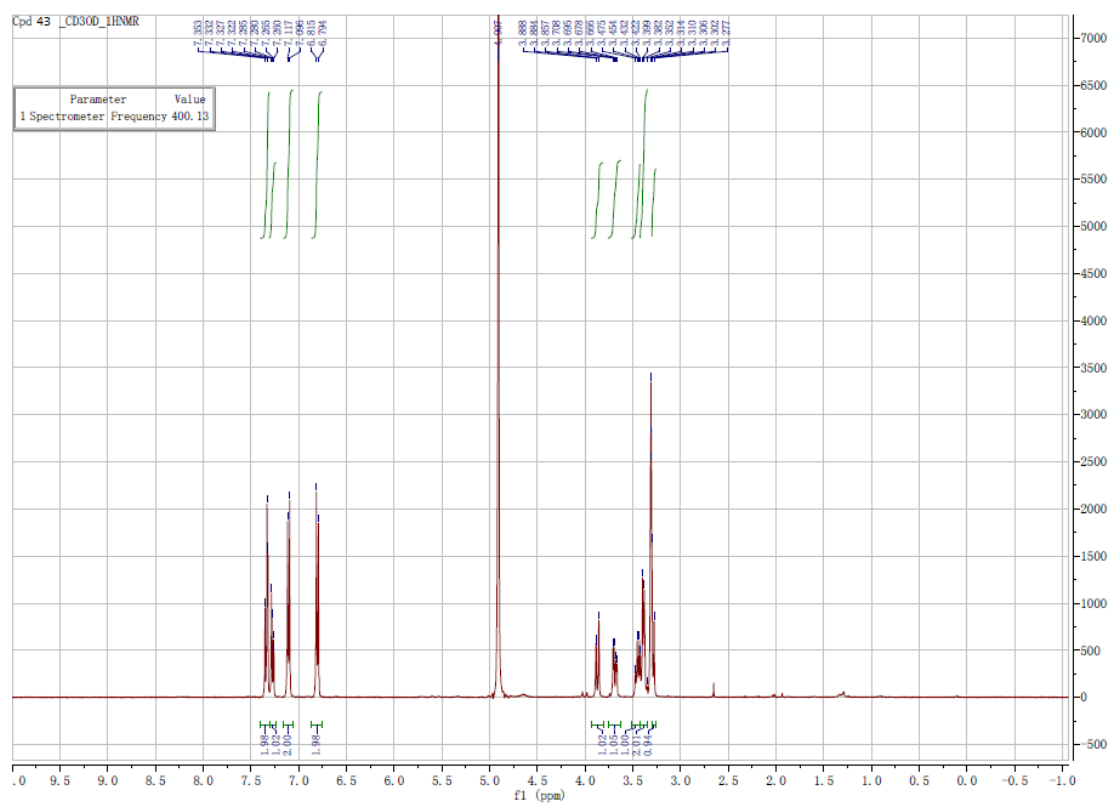
^1H -NMR of 40



$^1\text{H-NMR}$ of 41

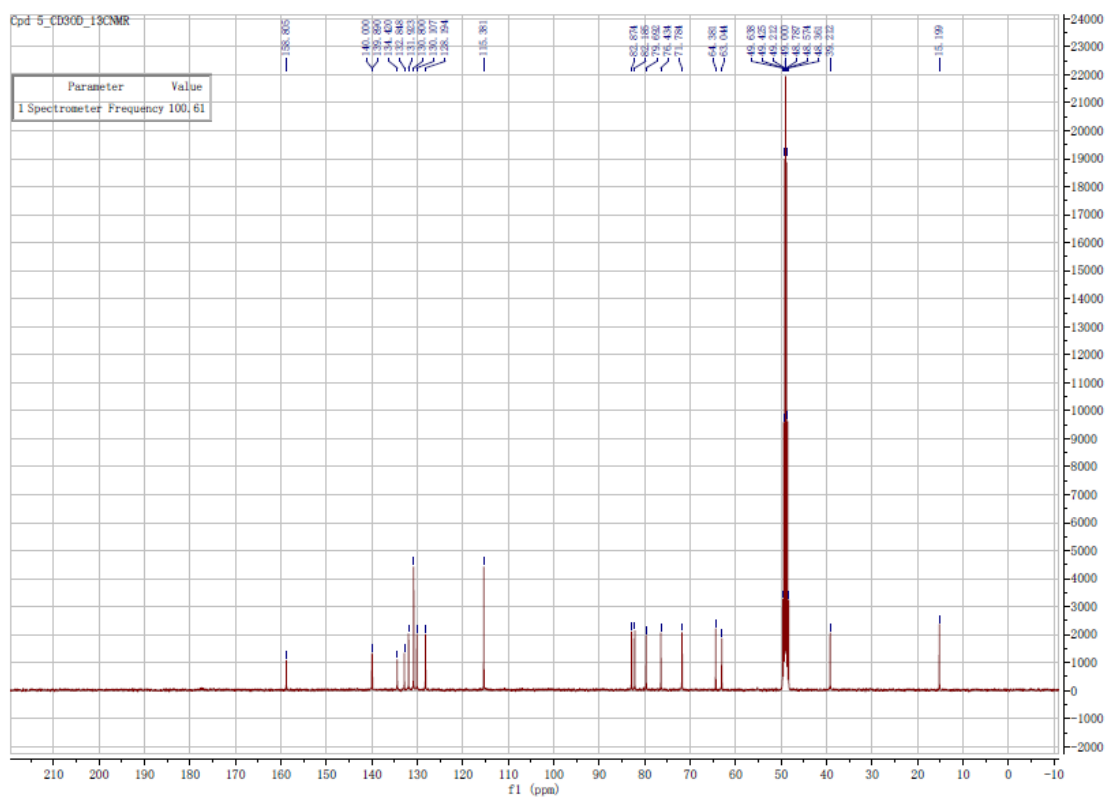


$^1\text{H-NMR}$ of 42

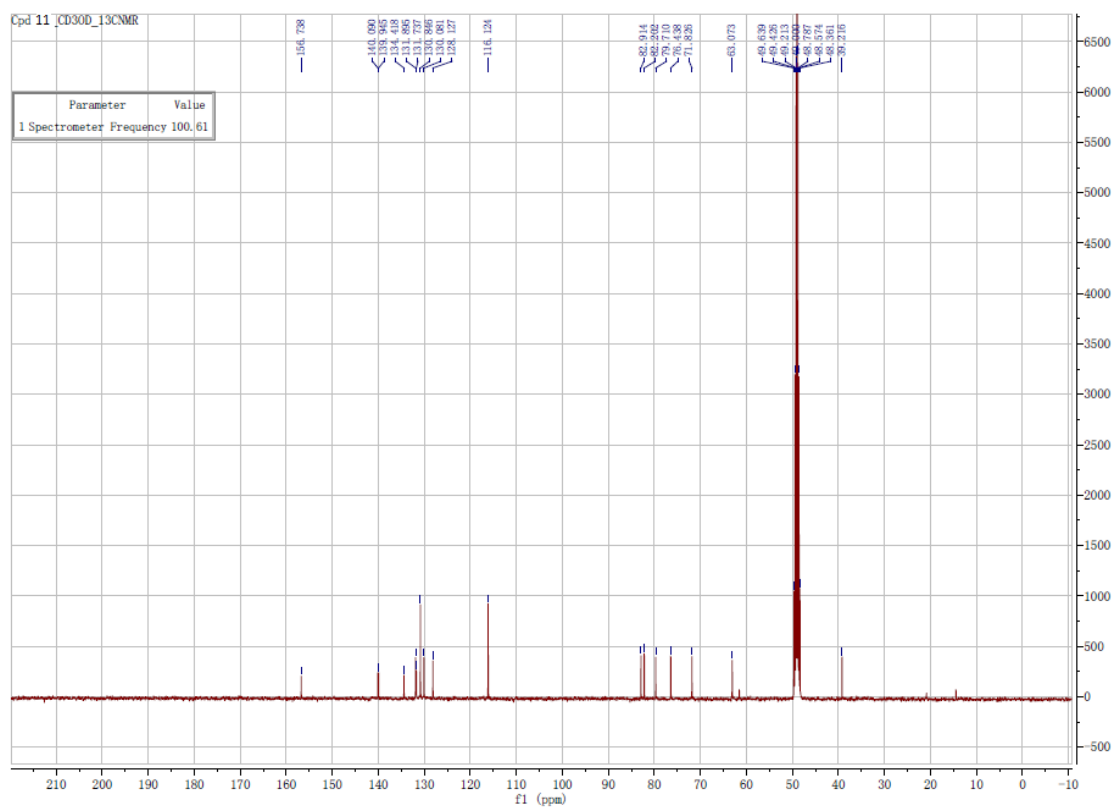
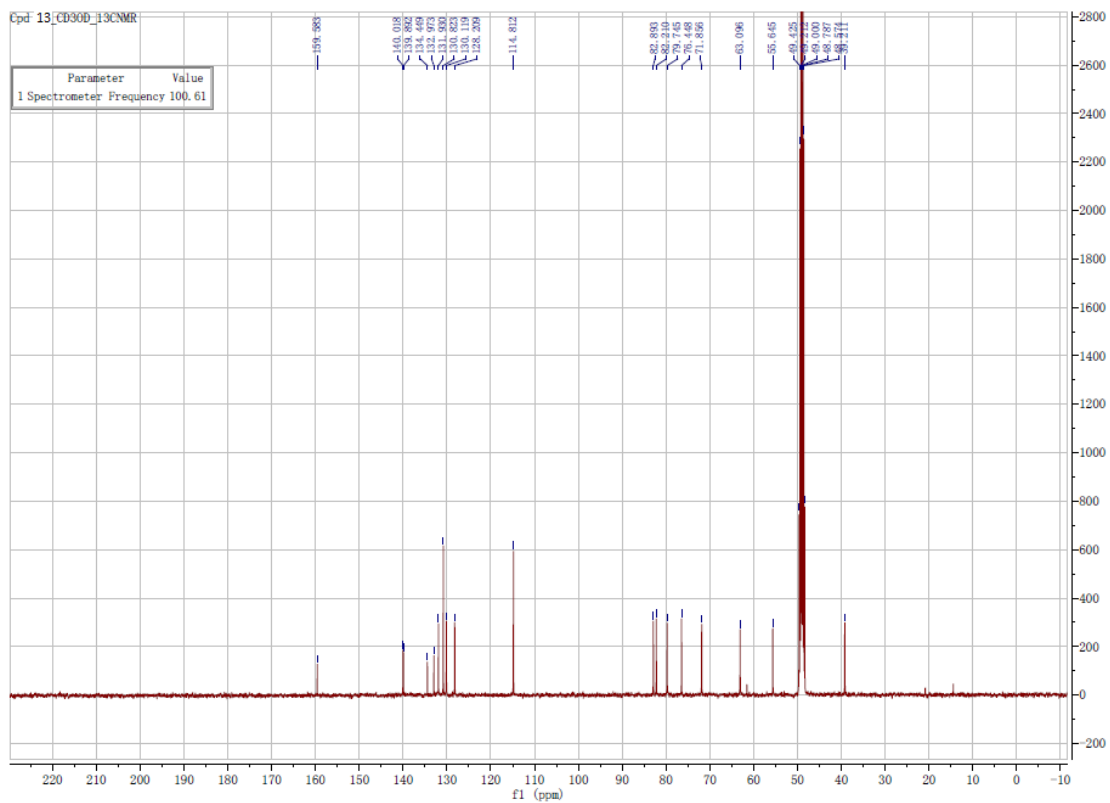


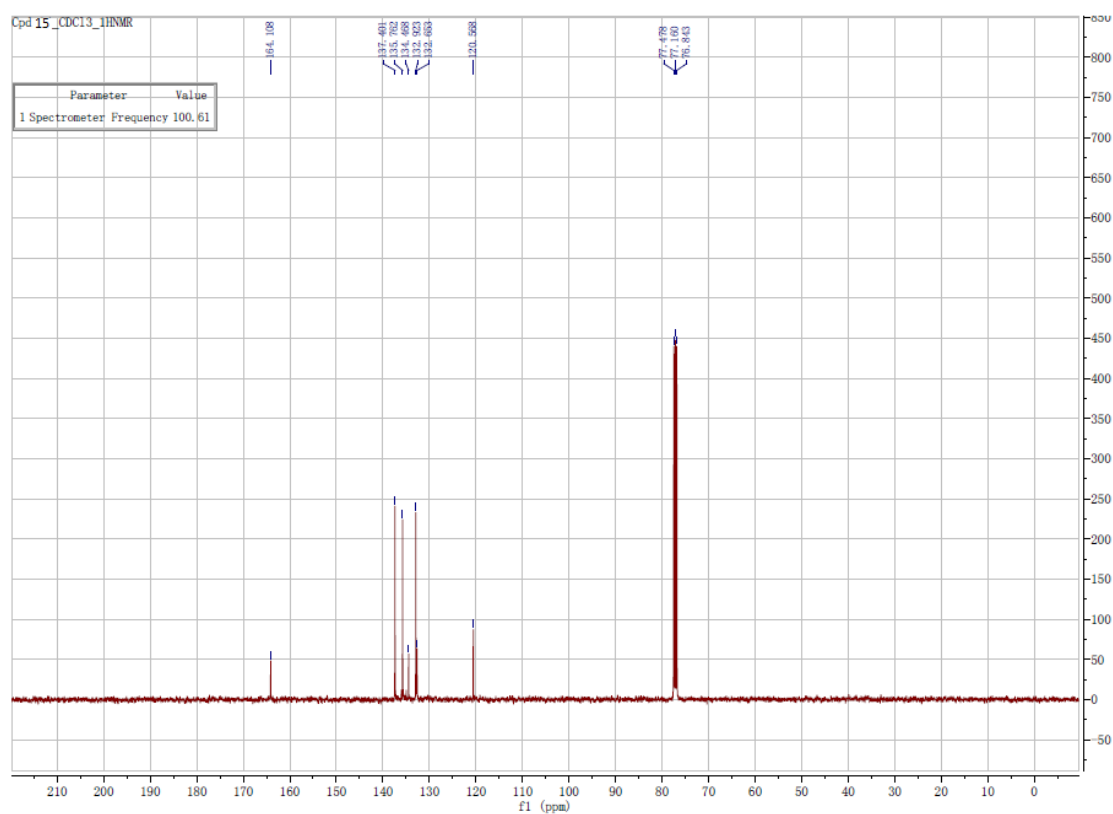
^1H -NMR of 43

^{13}C NMR

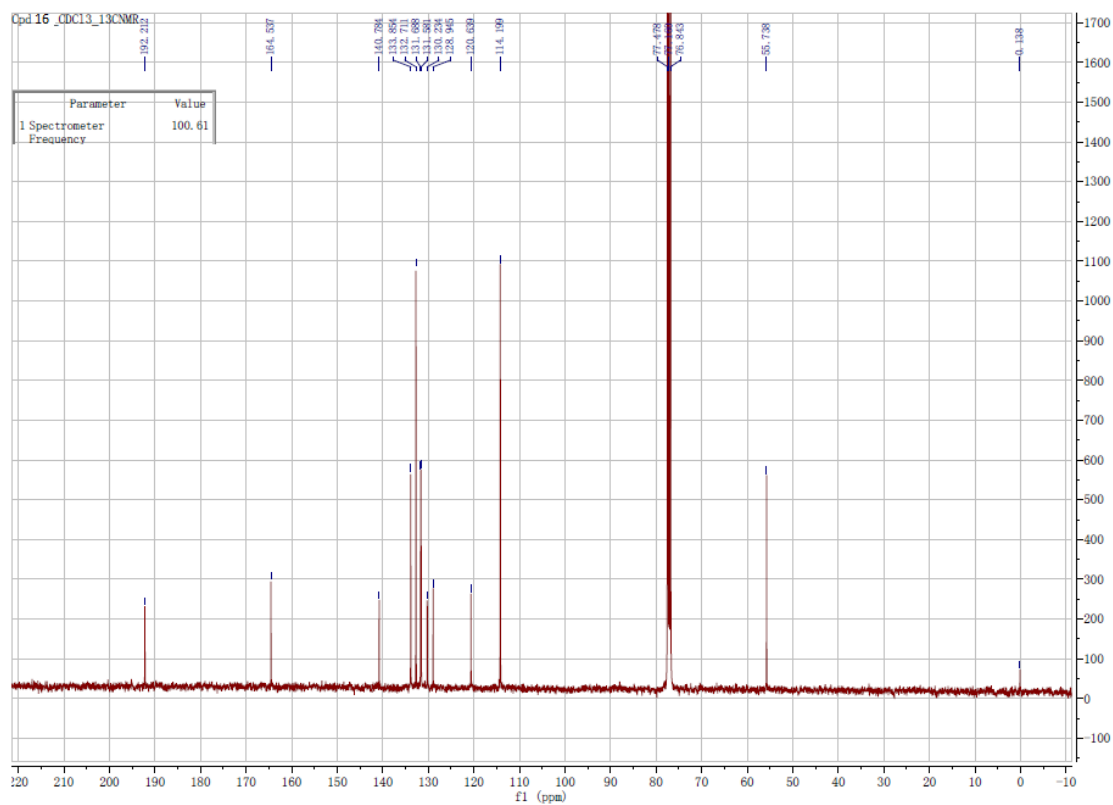


^{13}C -NMR of 5

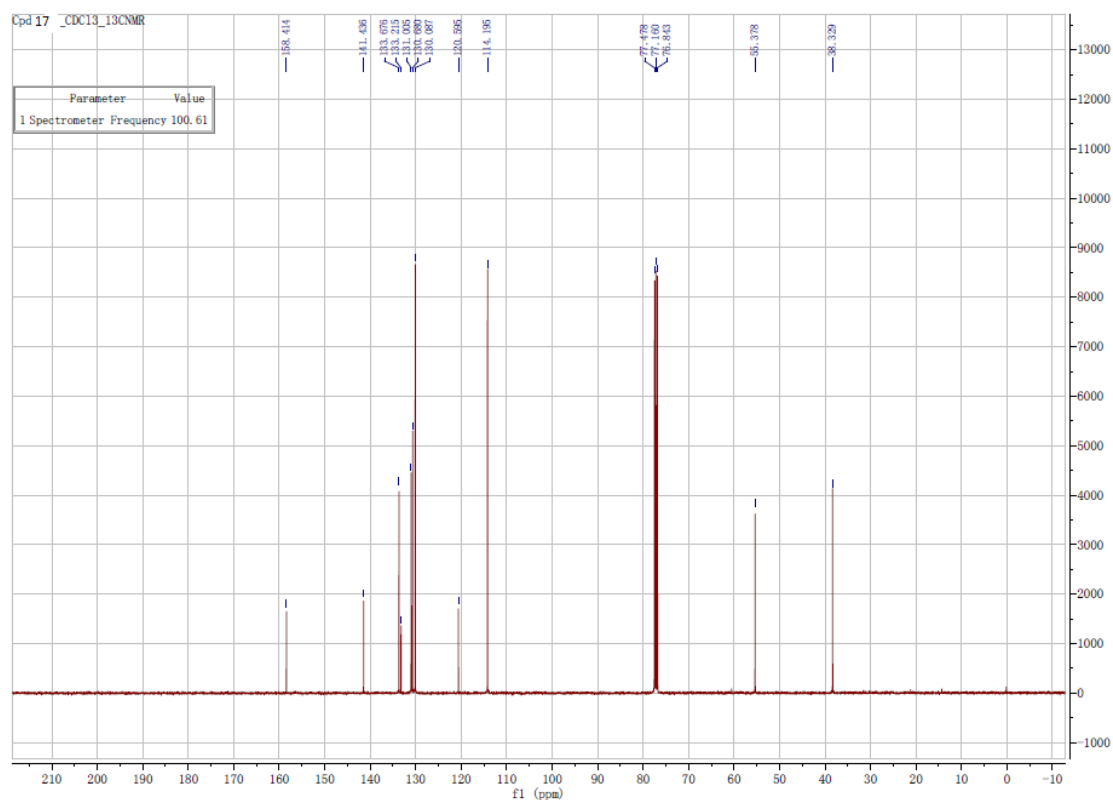
 ^{13}C -NMR of **11**¹³C-NMR of **13**



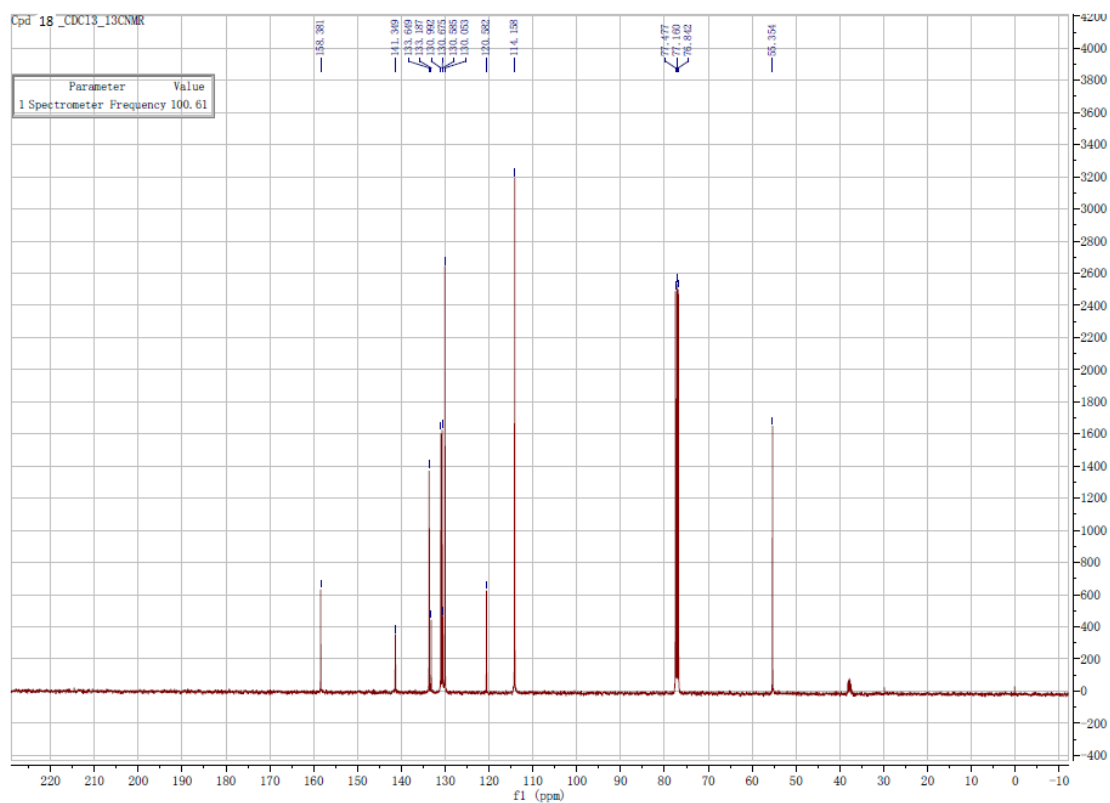
^{13}C -NMR of 15



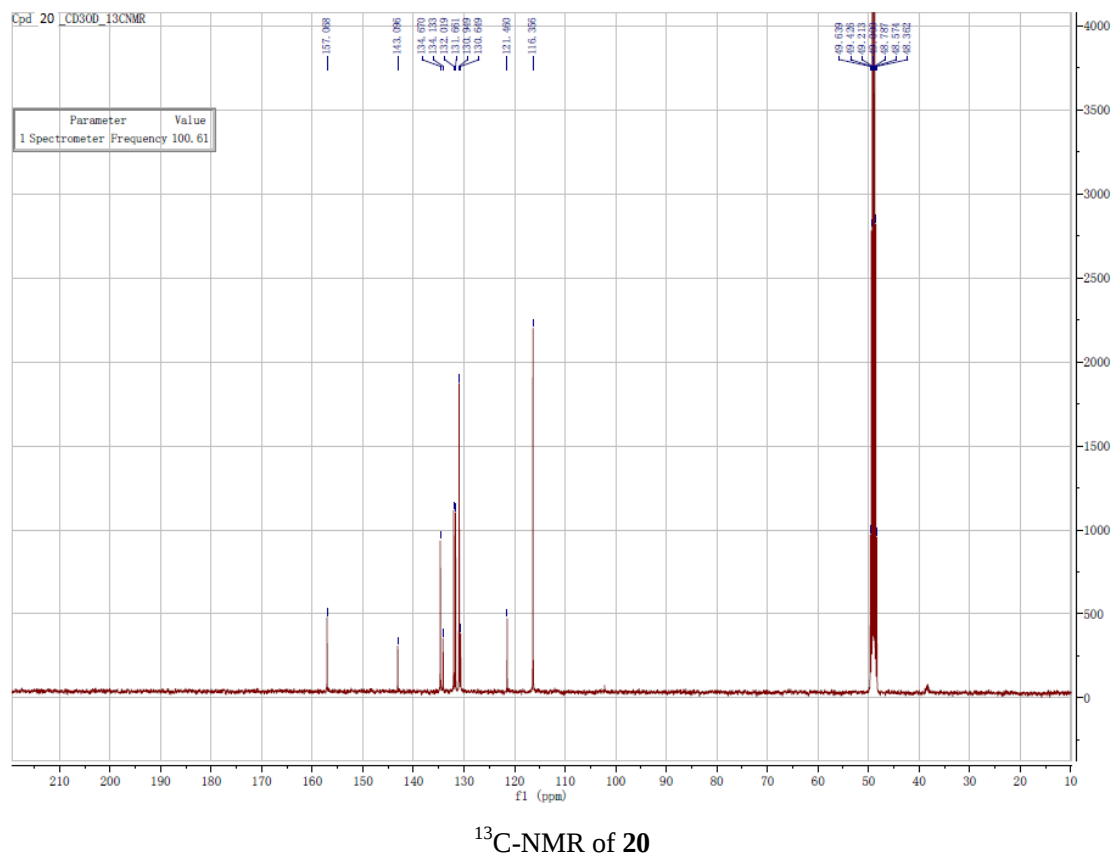
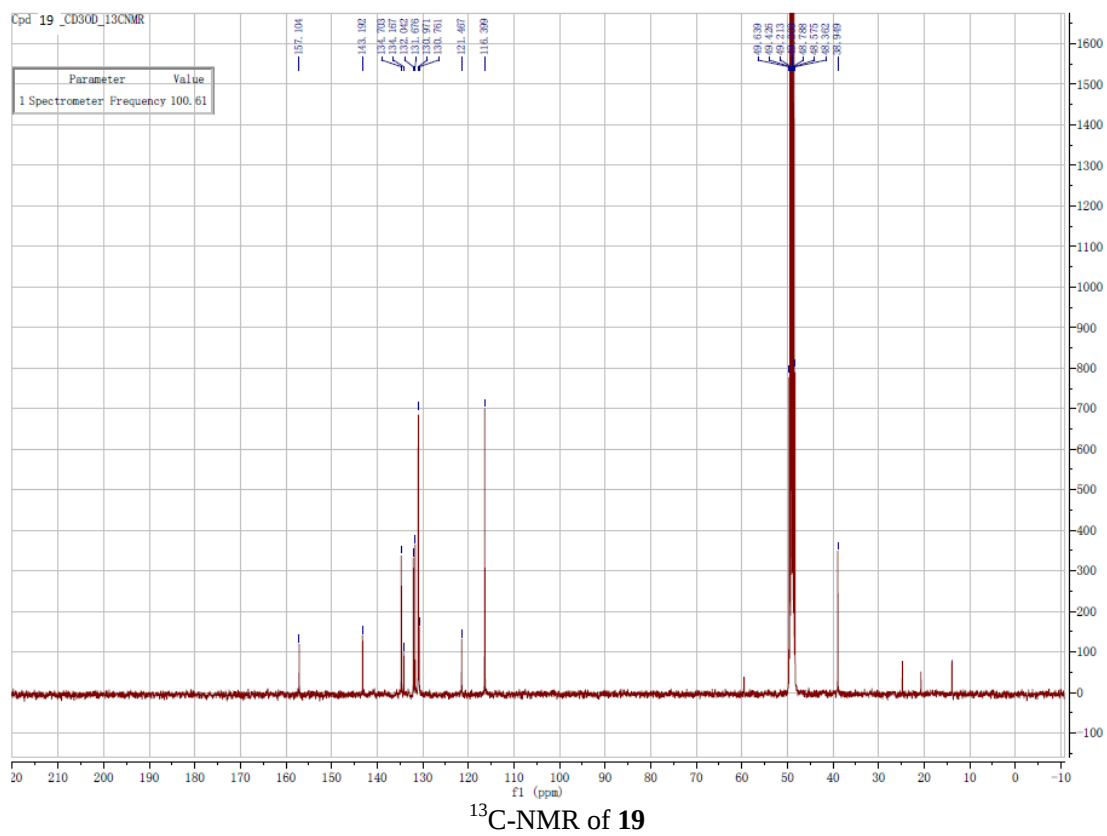
^{13}C -NMR of 16

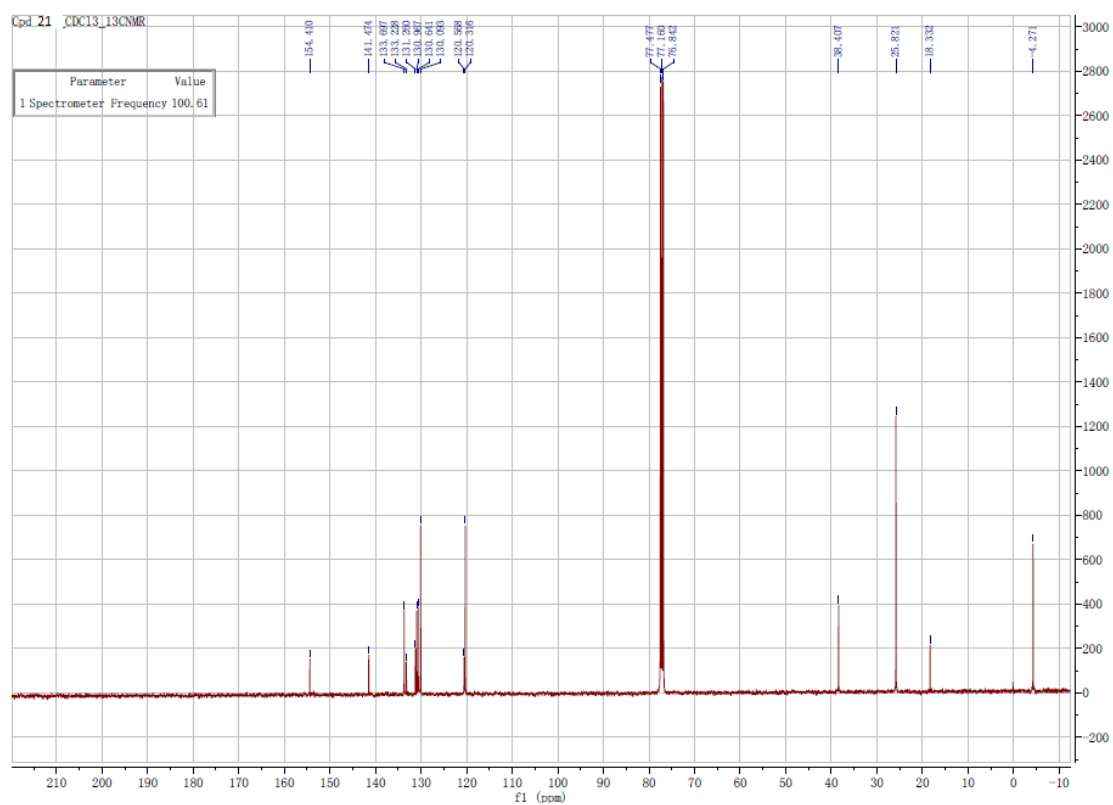


¹³C-NMR of 17

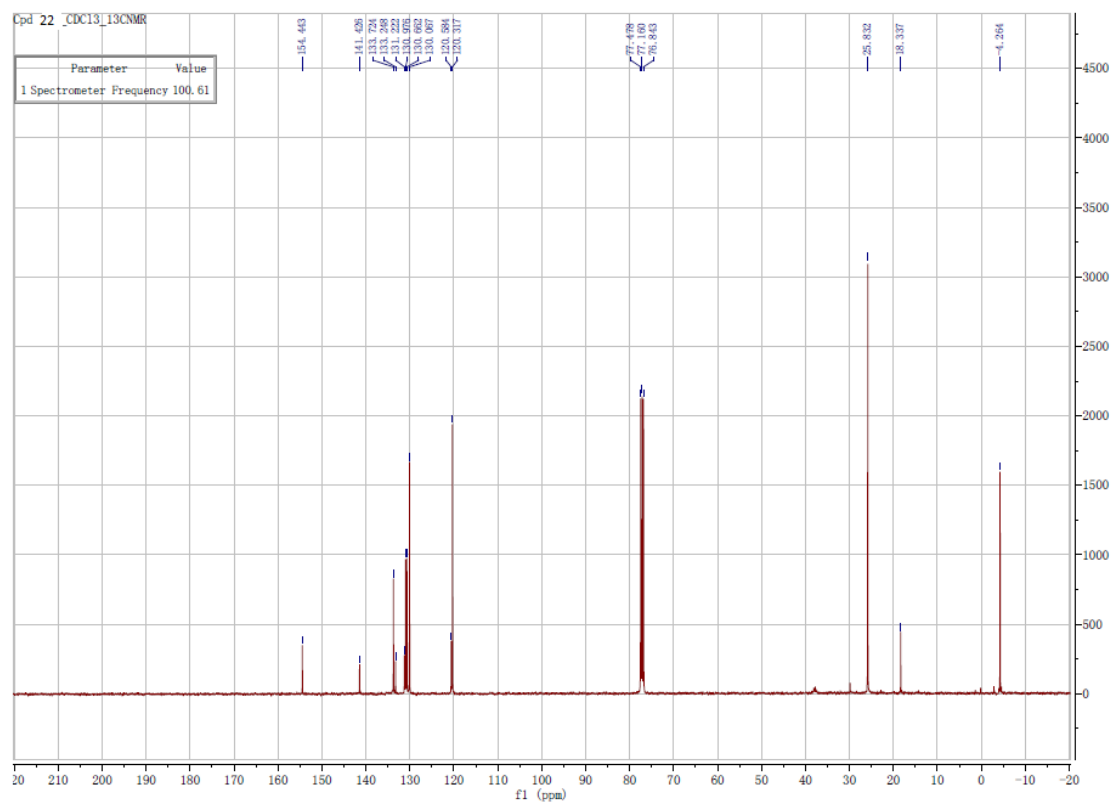


¹³C-NMR of 18

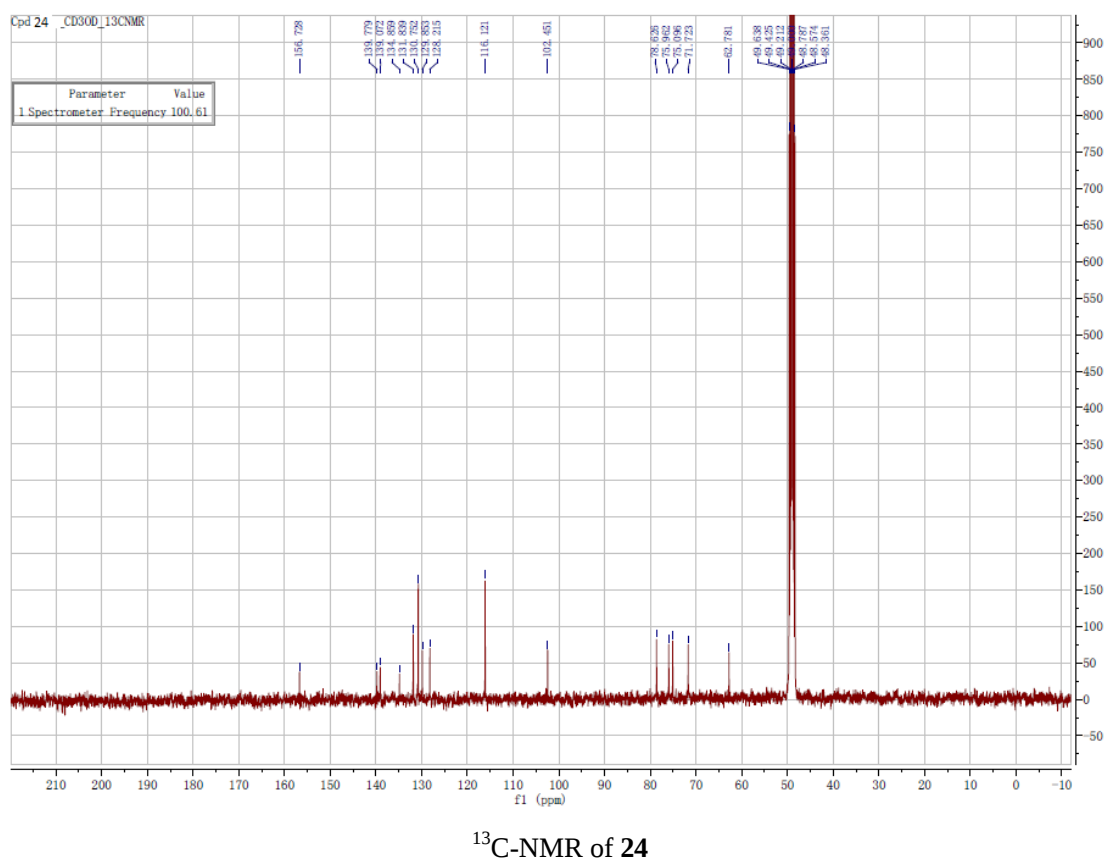
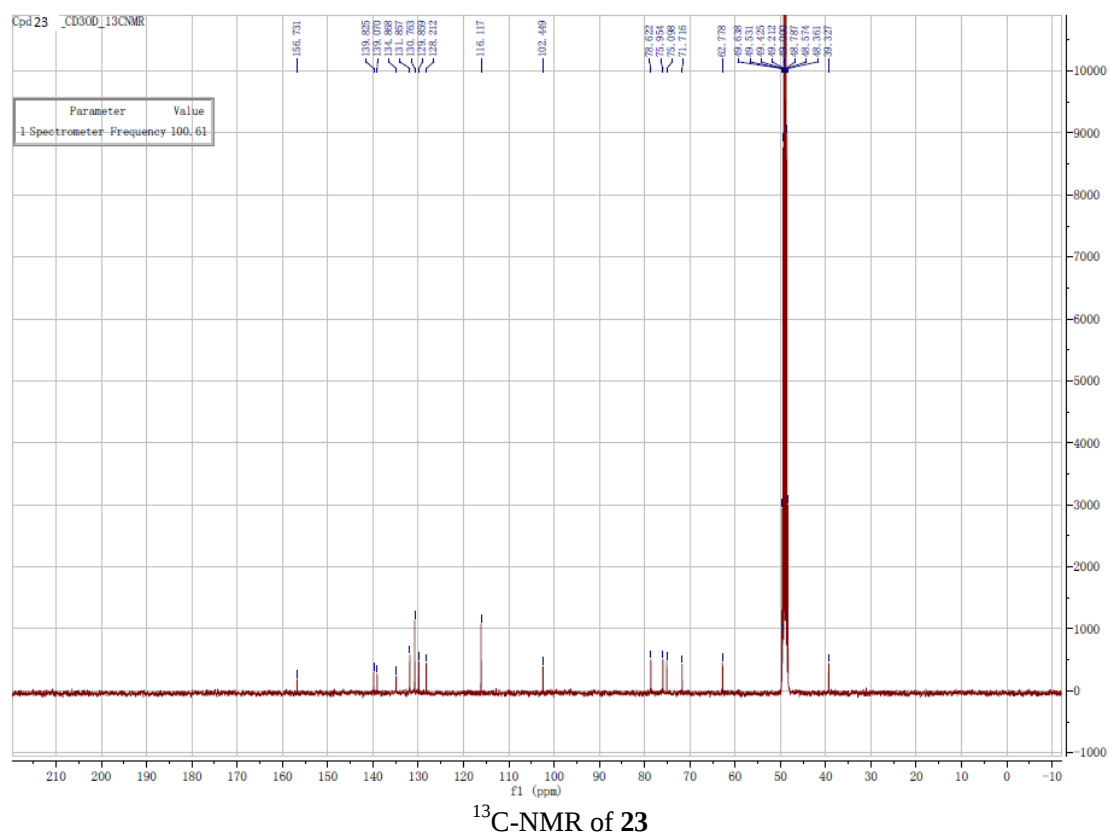


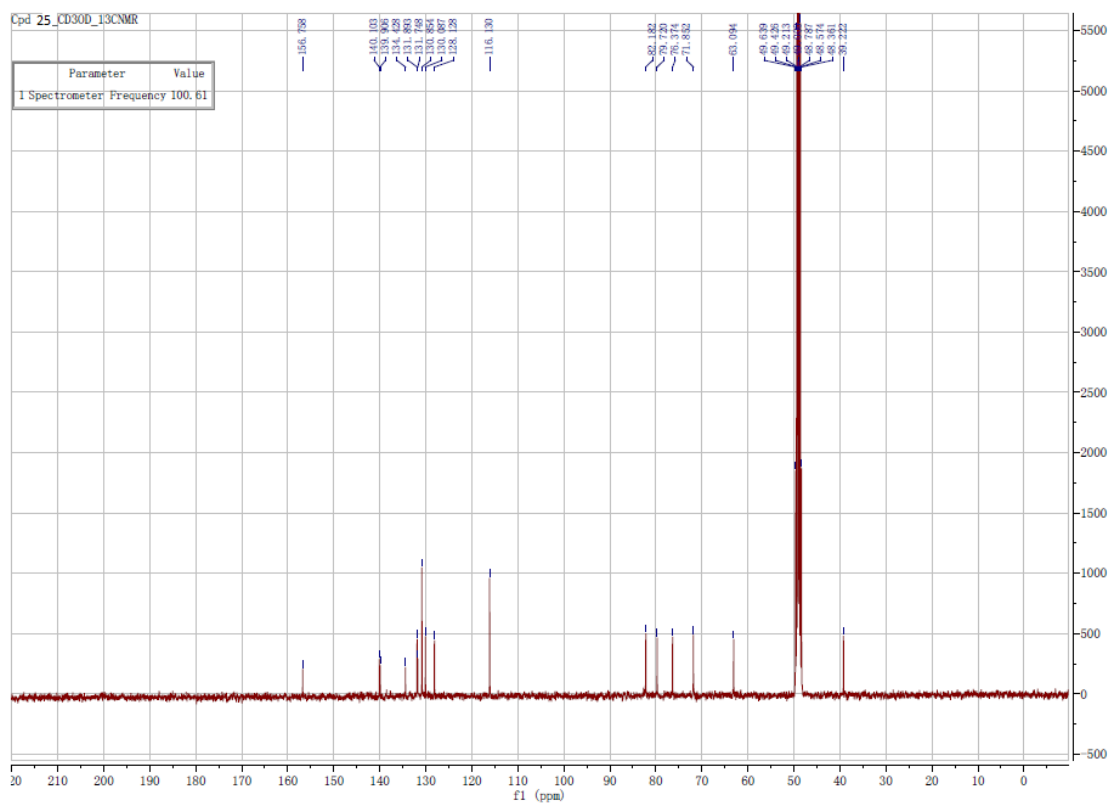


^{13}C -NMR of 21

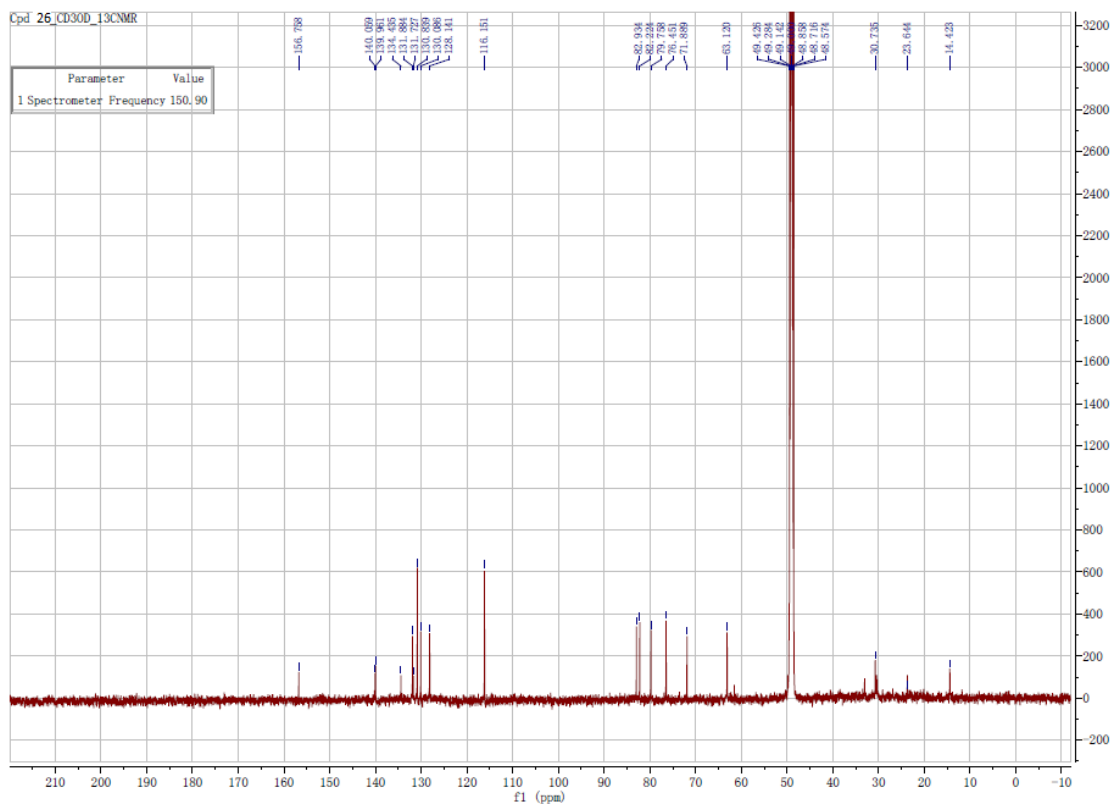


^{13}C -NMR of 22

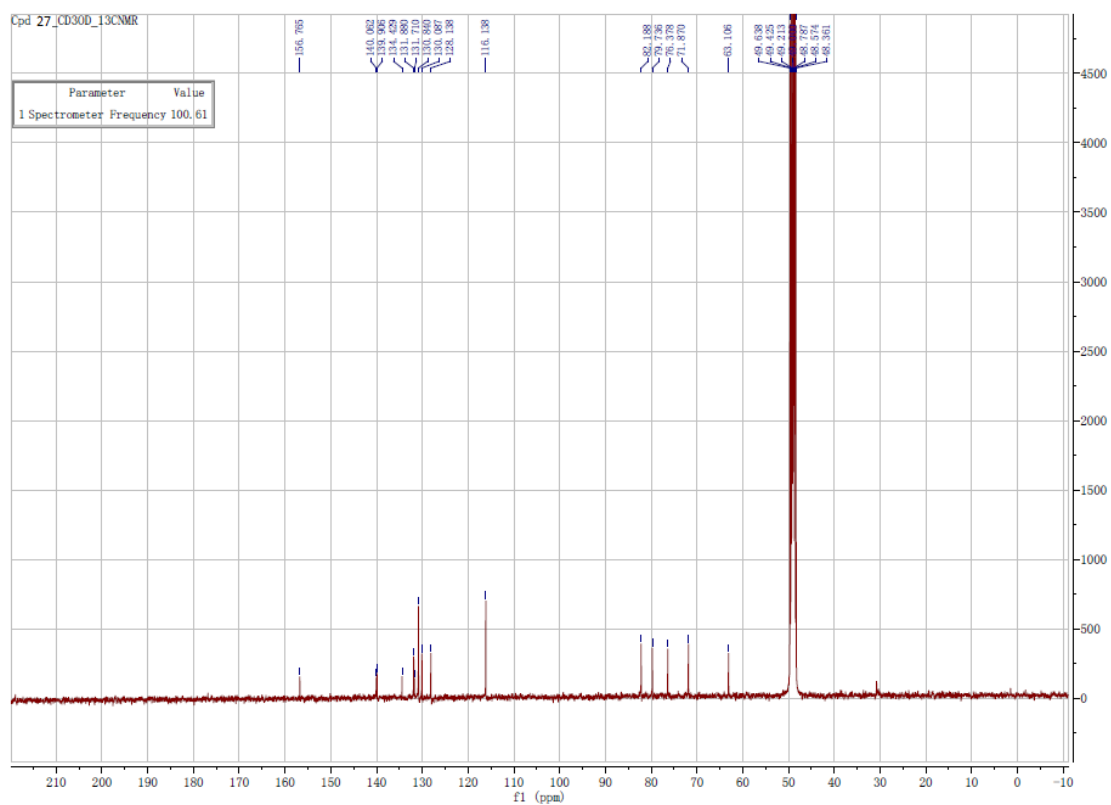




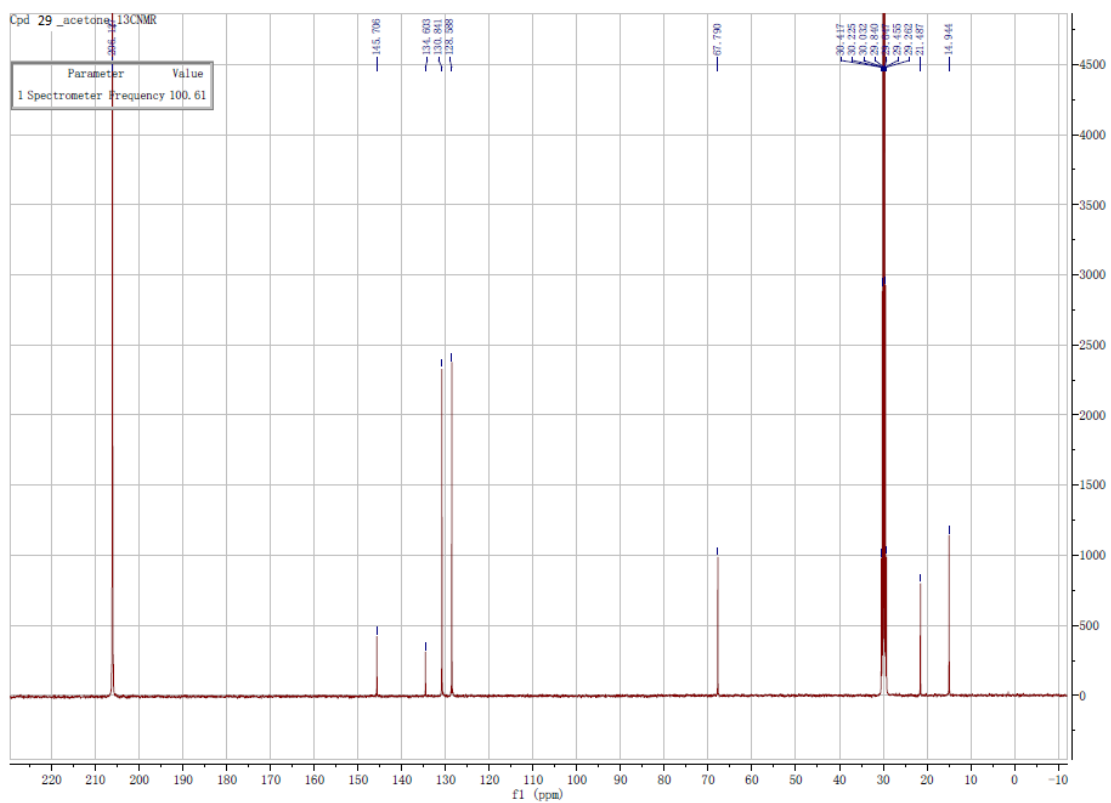
^{13}C -NMR of 25



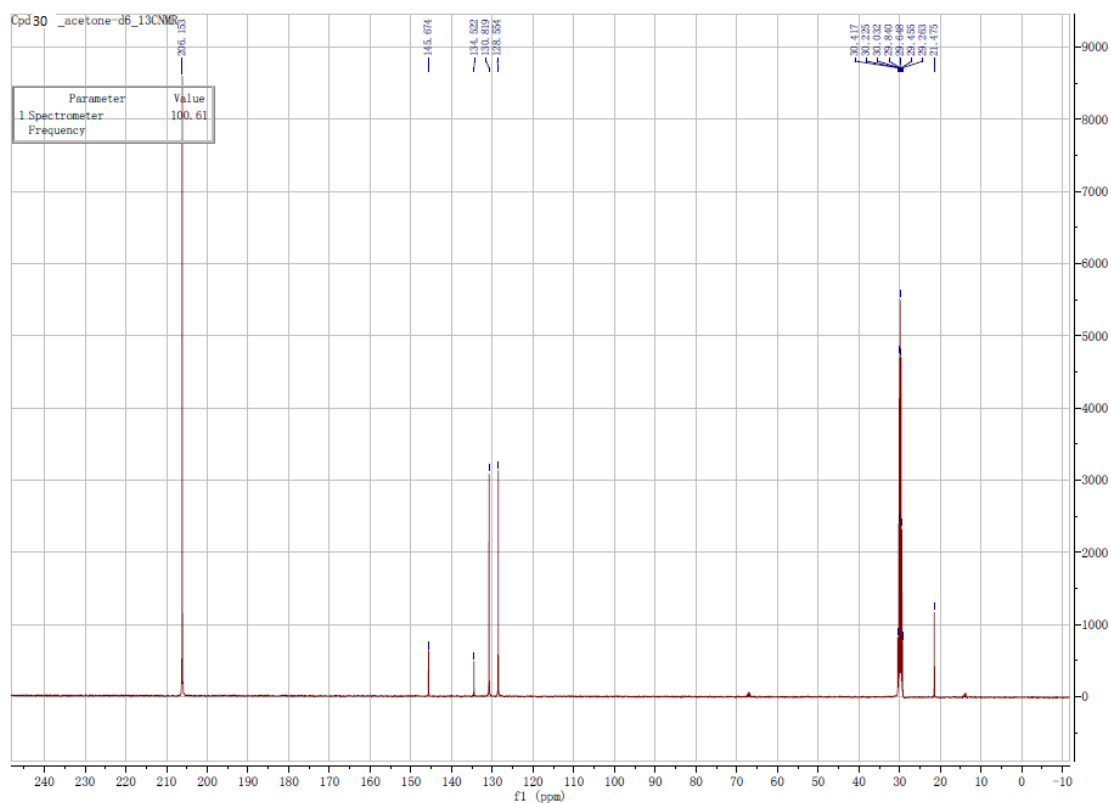
^{13}C -NMR of 26



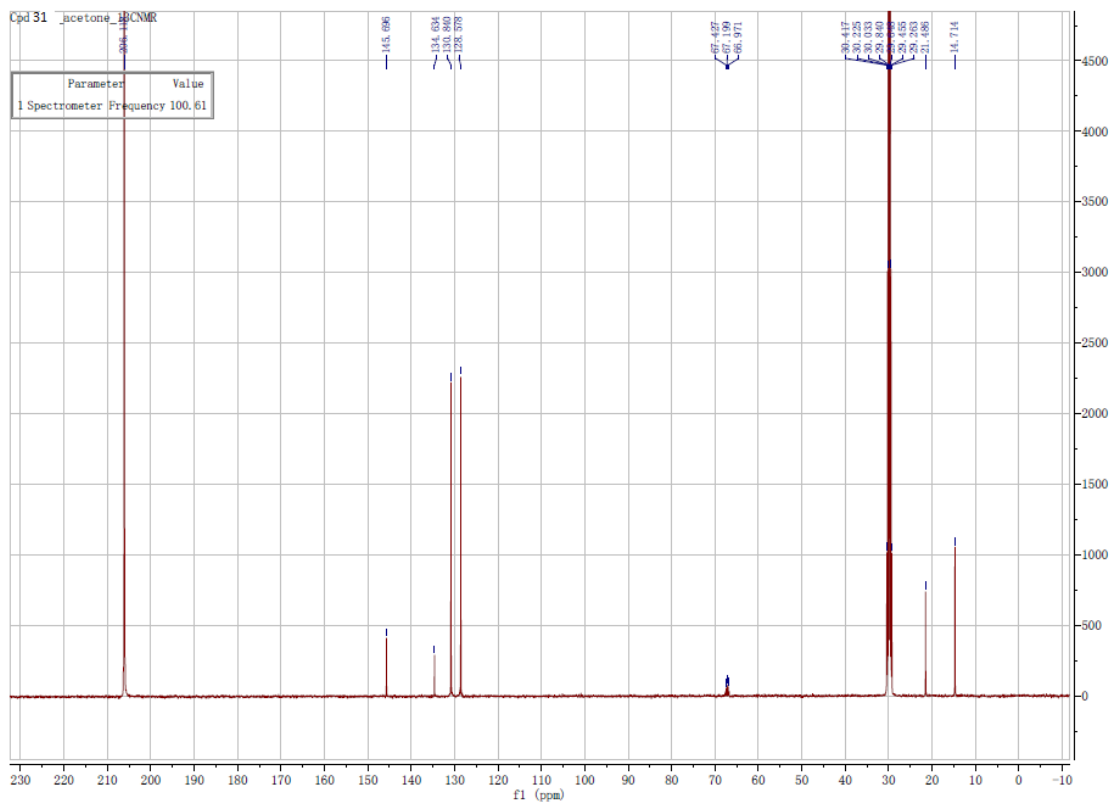
^{13}C -NMR of 27



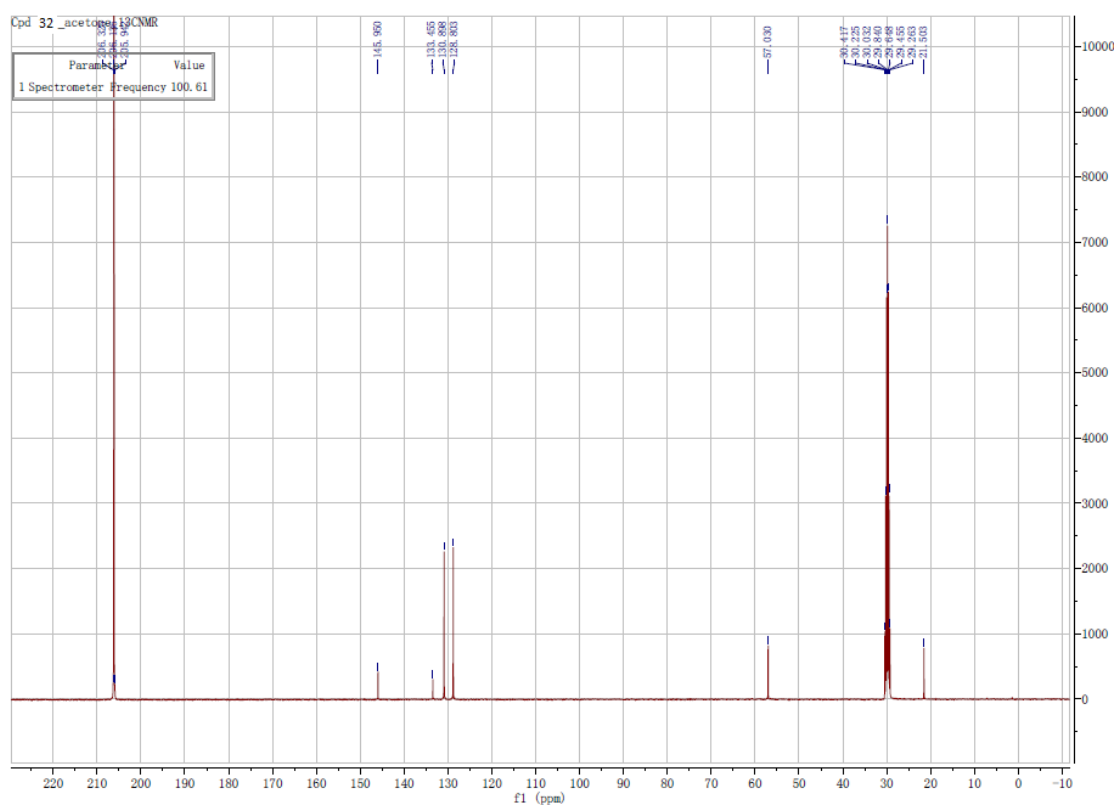
^{13}C -NMR of 29



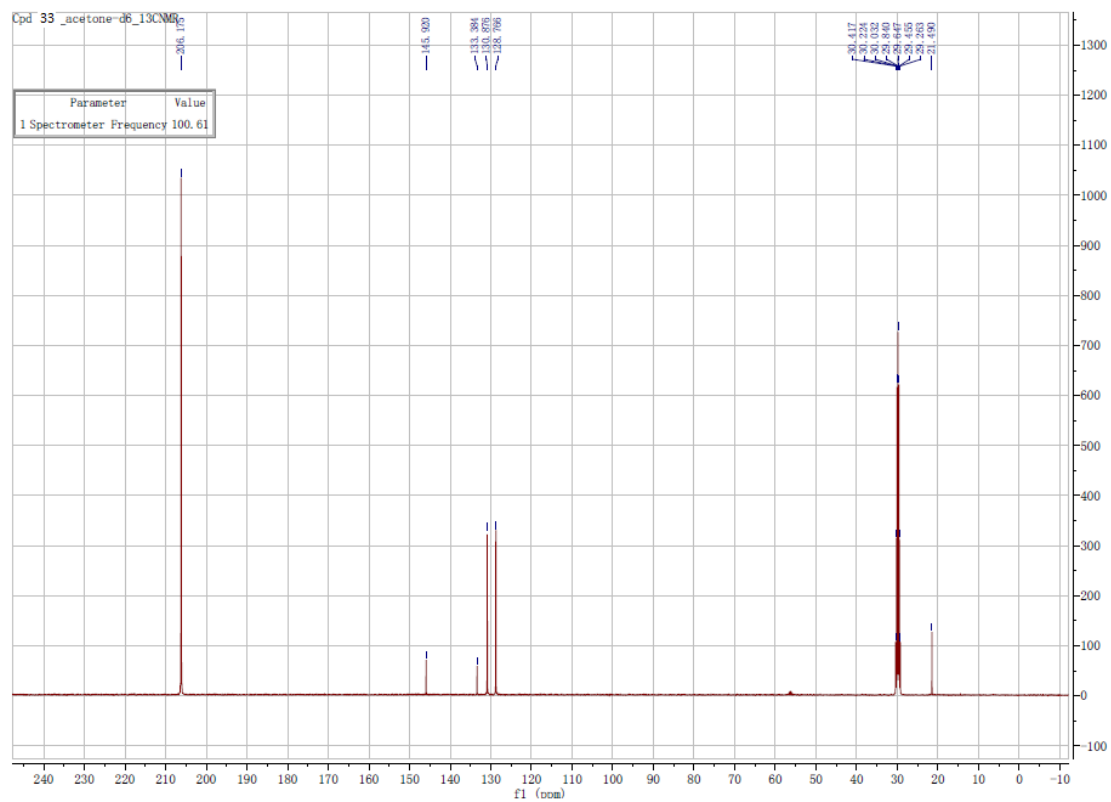
^{13}C -NMR of **30**



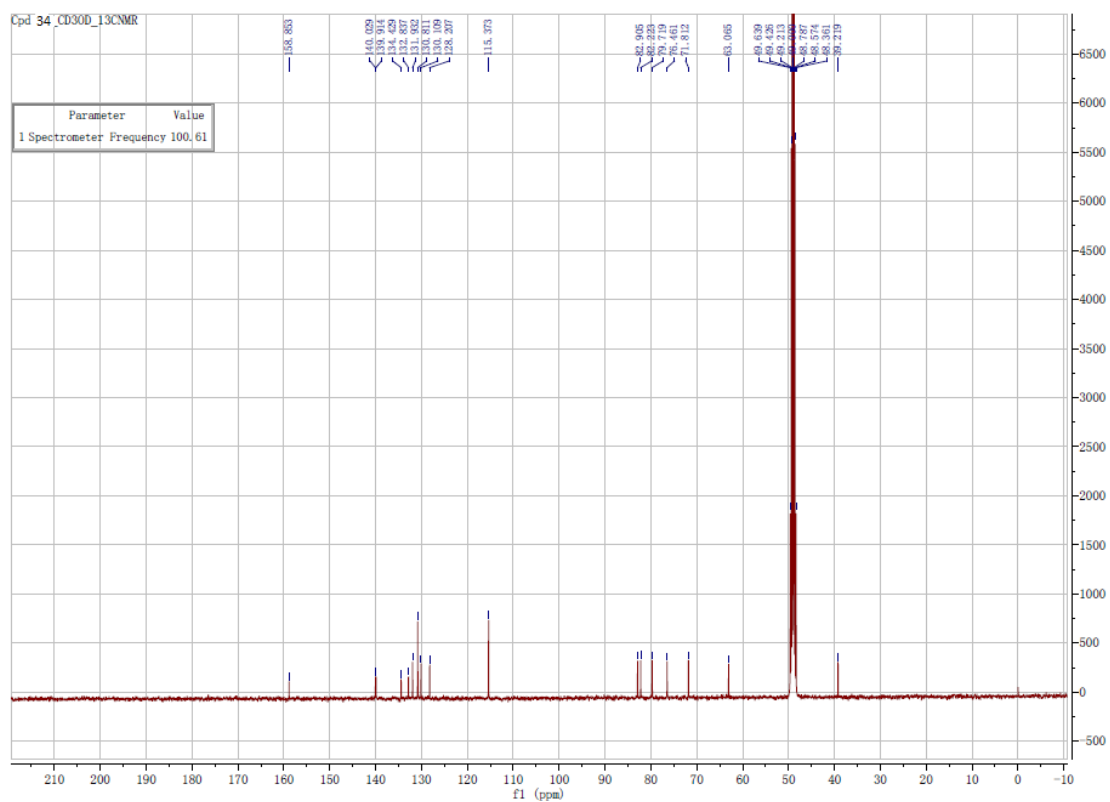
^{13}C -NMR of **31**



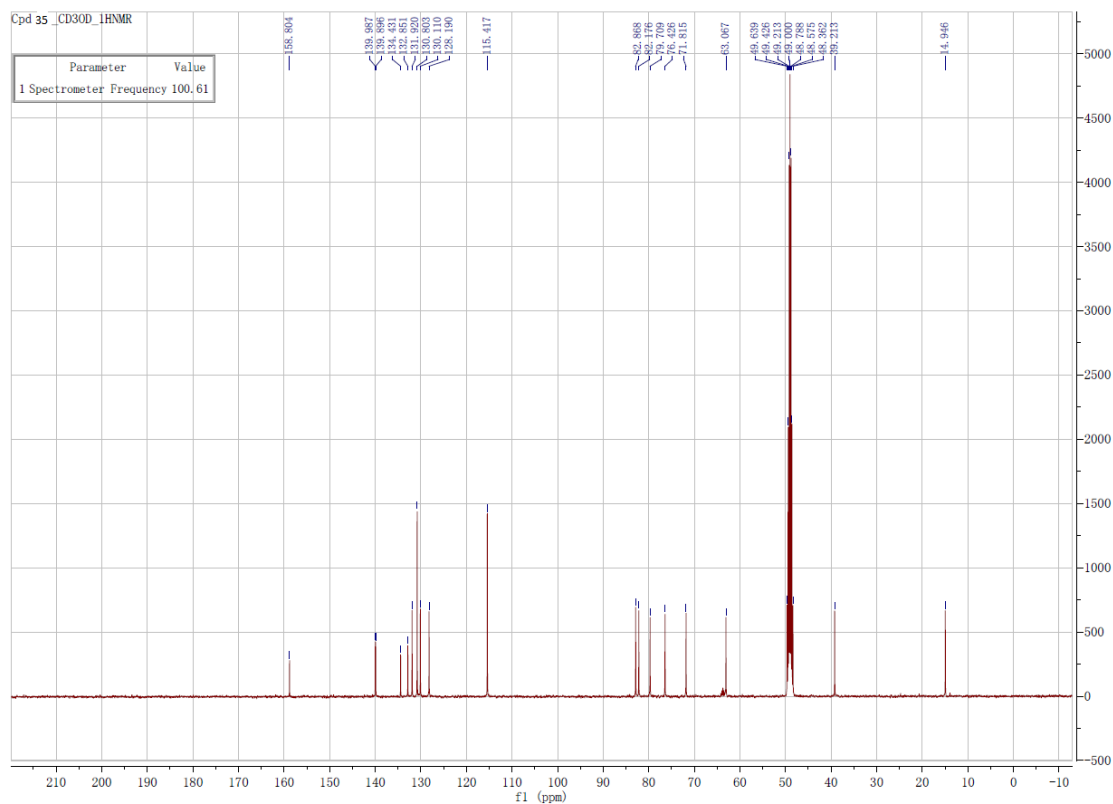
^{13}C -NMR of 32



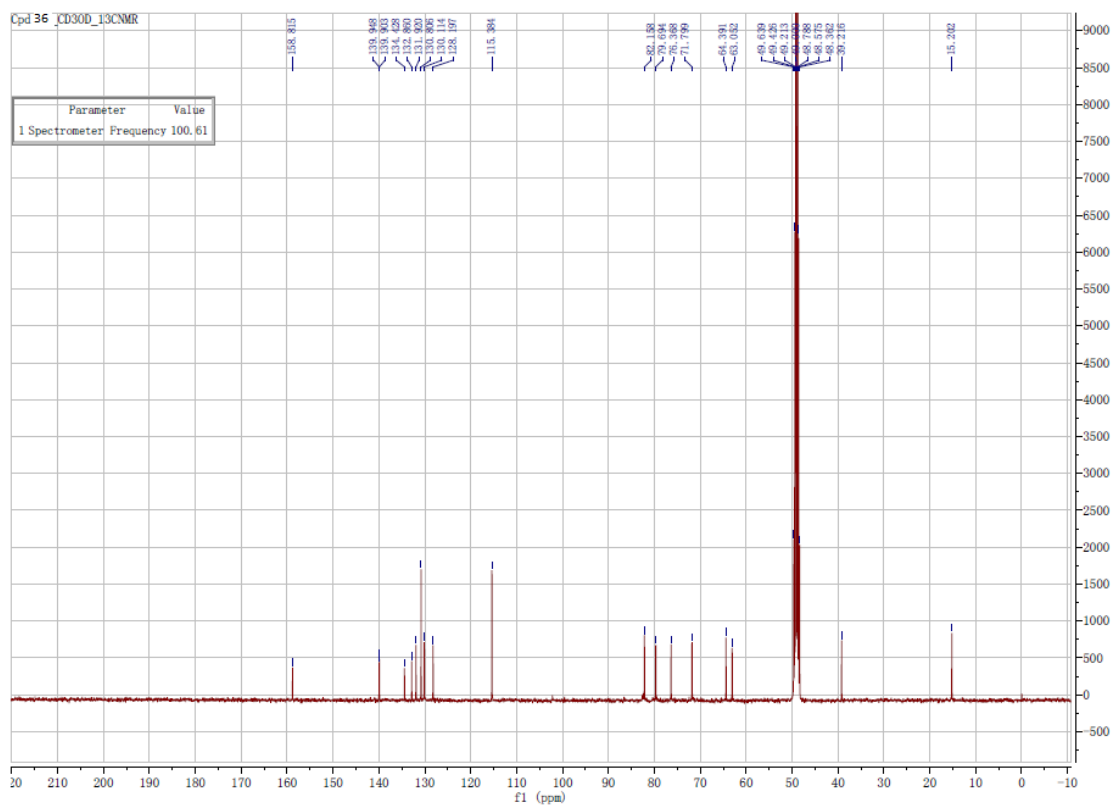
^{13}C -NMR of 33



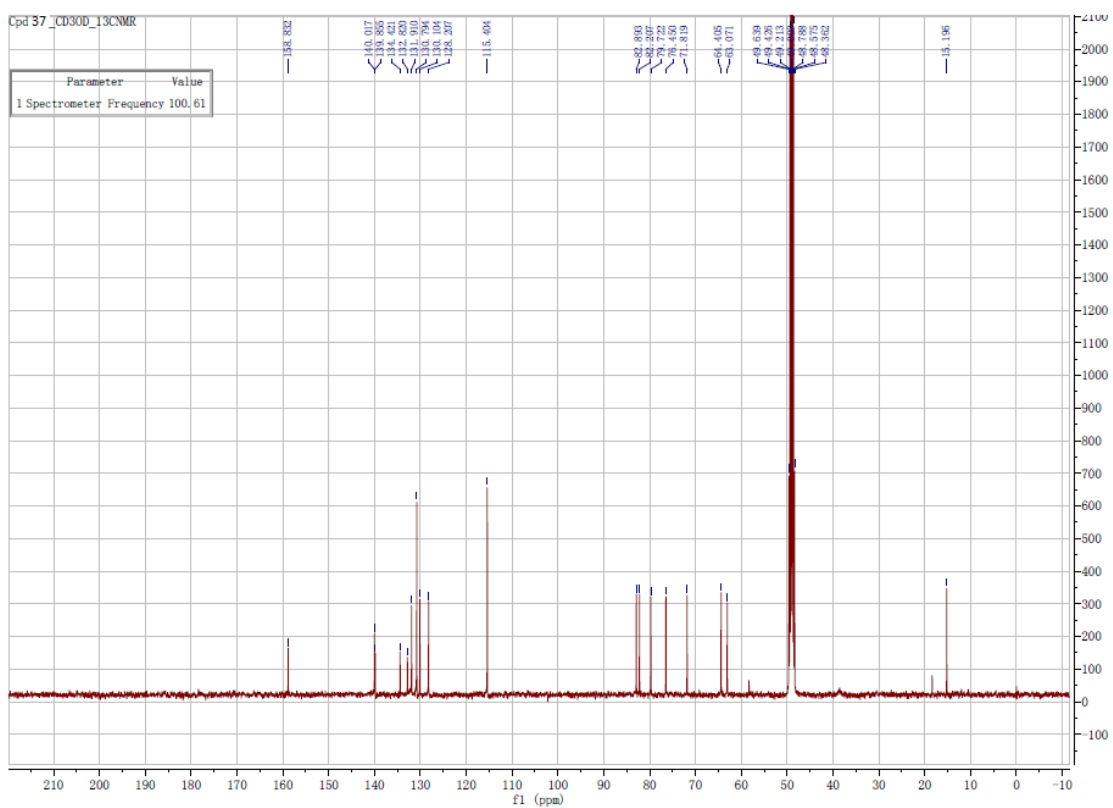
^{13}C -NMR of **34**



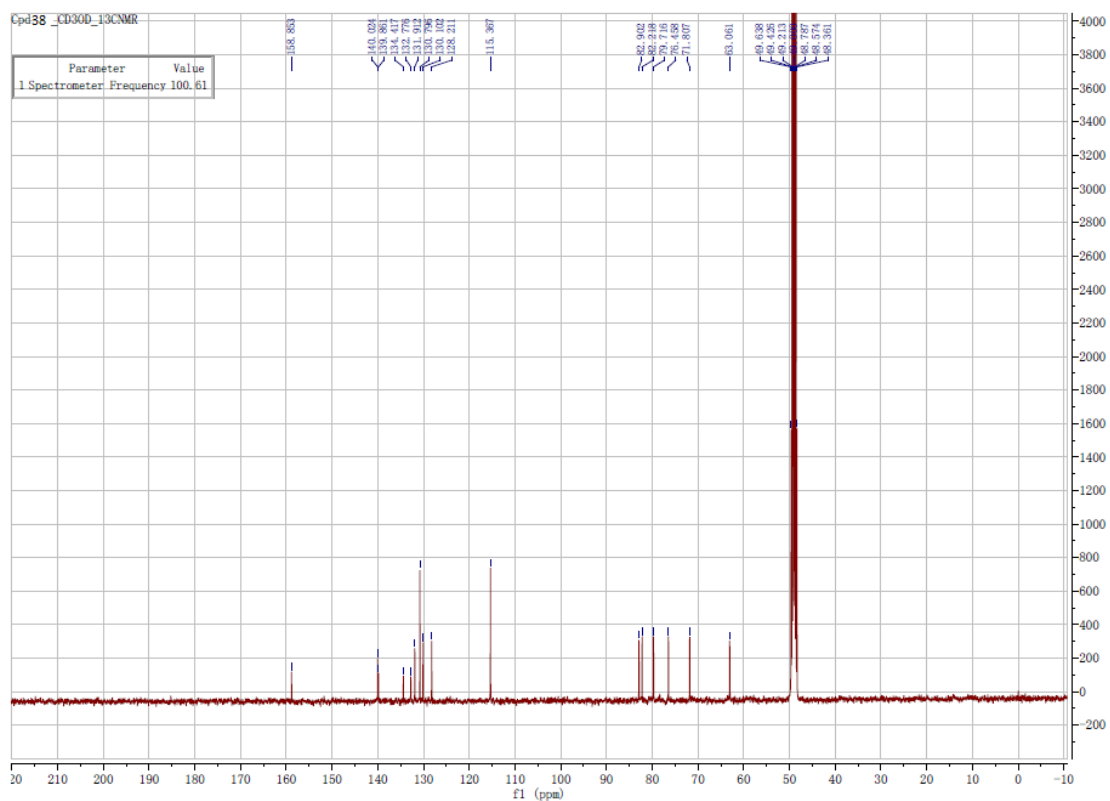
^{13}C -NMR of **35**



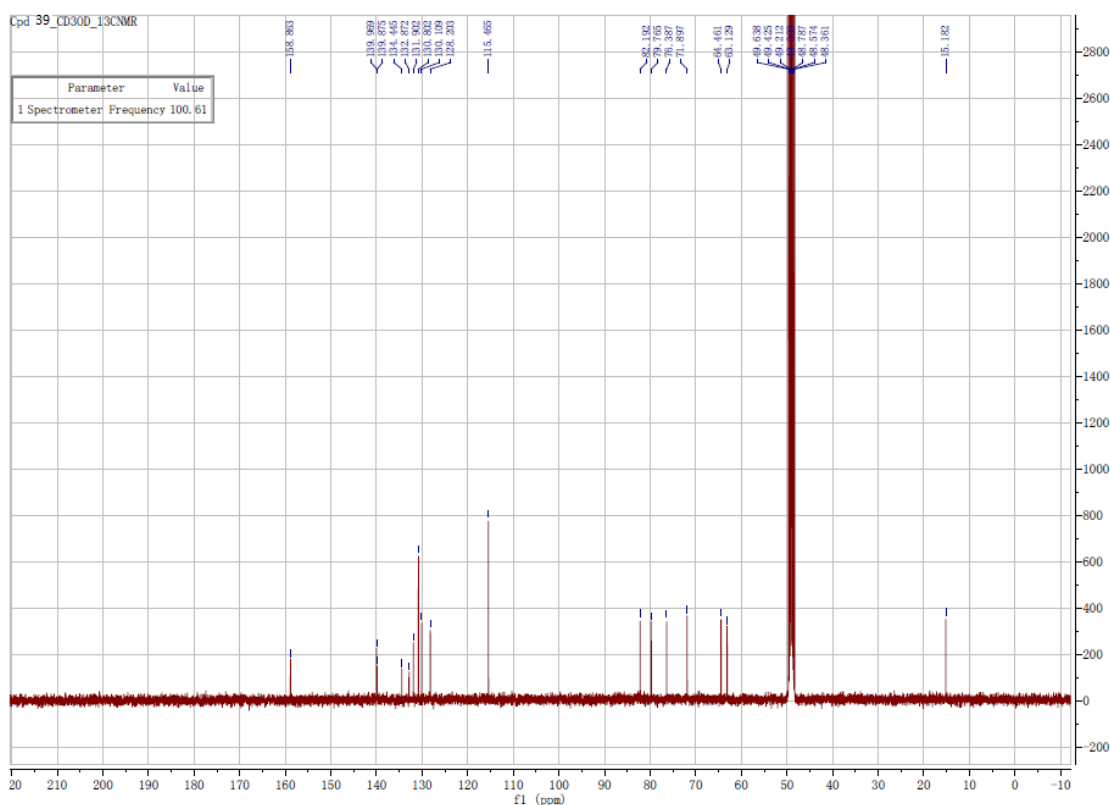
^{13}C -NMR of **36**



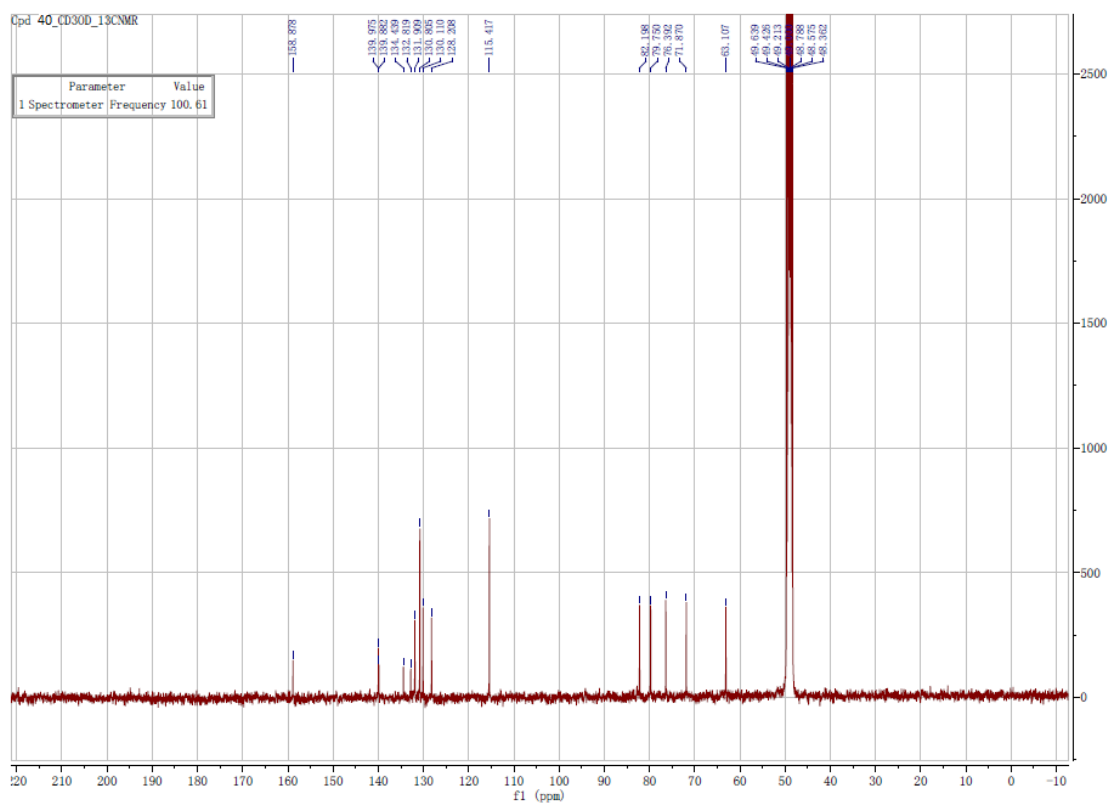
^{13}C -NMR of **37**



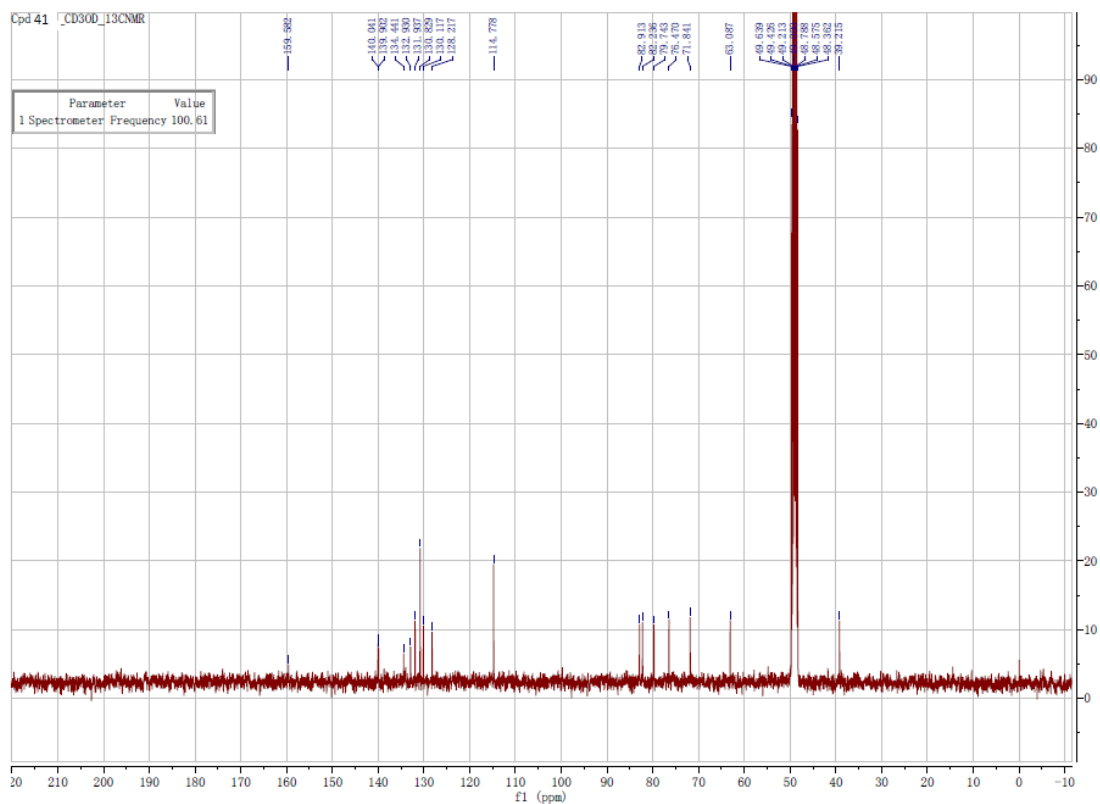
^{13}C -NMR of **38**



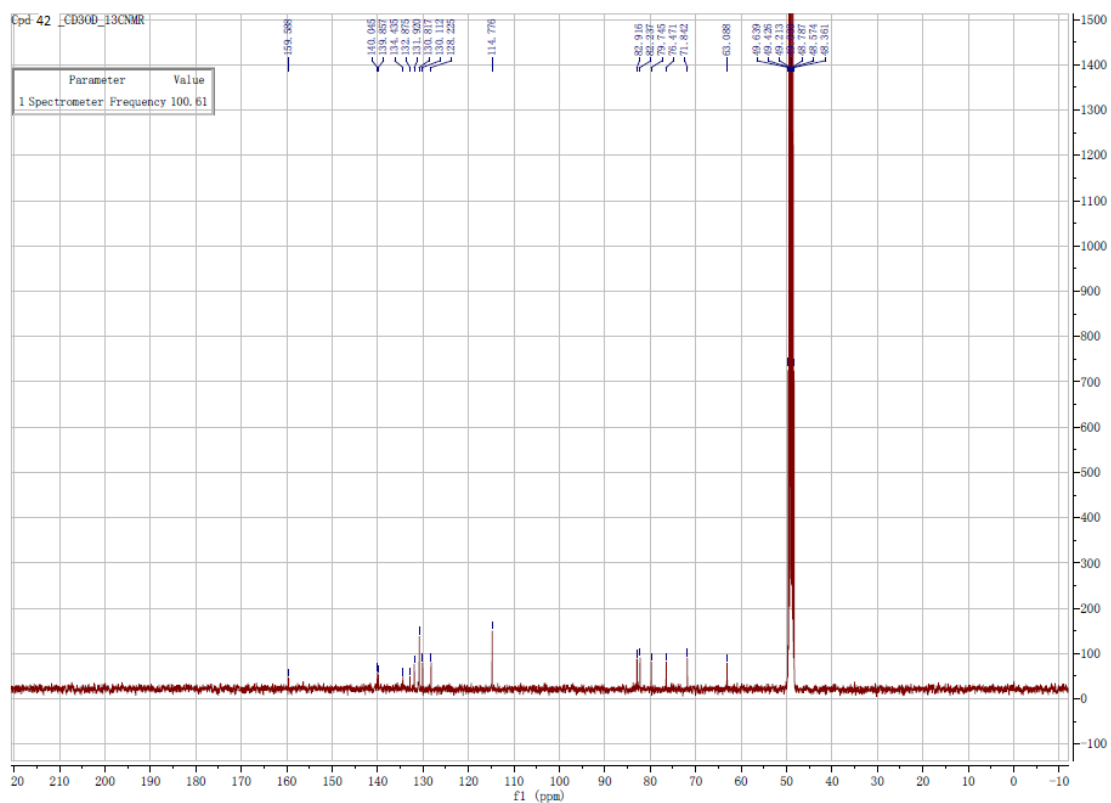
^{13}C -NMR of **39**



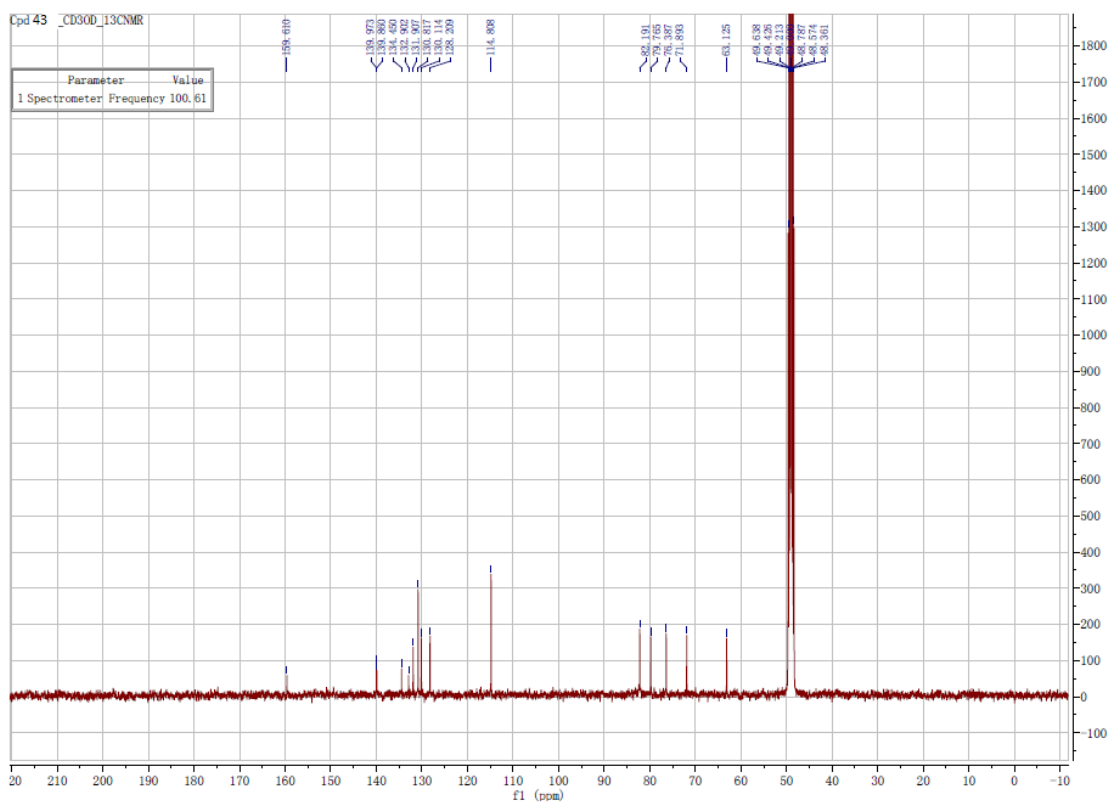
^{13}C -NMR of 40



^{13}C -NMR of 41



^{13}C -NMR of 42



^{13}C -NMR of 43