^{17}O NMR and ^{15}N NMR Chemical Shifts of Sterically-Hindered Amides: Ground-State Destabilization in Amide Electrophilicity

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Electronic Supplementary Information

Table of Contents 1

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Additional Data Referred to from the Manuscript

To gain additional information, we next decided to analyze three series of control compounds (Table ESI-1). First, since adamantyl group represents one of the most sterically-hindered C-substituents,[5b] we prepared and analyzed a series of representative C-adamantyl amides (entries 1-5). As expected, the presence of an adamantyl results in strong deshielding of the carbonyl oxygen, which is attributed to increased rotation around the N–C(O) bond (up to 8 ppm, a plot of ^{17}O NMR(adamantyl) vs. ^{17}O NMR(pivaloyl) gives a linear correlation, R^2 = 0.98). Along the same lines, N-TMP is the most sterically-hindered alkyl substituent that has been used to twist amide bonds.[16] We found that the use of a simple C-primary substituent in combination with N-TMP group results in a highly electrophilic carbonyl (entry 6, 398.2 ppm). This can be compared with the analogous N-Et_2 amide (entries 7-8), which shows a remarkable $\Delta\sigma^{17}$O of 66.8 ppm. Indeed, the unique electrophilic reactivity of N-TMP amides has been well demonstrated, and future studies will likely expand the growing utility of this class of sterically-destabilized amides.

Table ESI-1. ^{17}O NMR and ^{15}N NMR Chemical Shifts for Amides in Series **5-7**.

Entry	Amide	Series	$\delta(^{17}O)^a$ ppm	$\delta(^{15}N)^b$ ppm
1	**5a**	Ad	350.3	93.9
2	**5b**	Ad	347.6	123.7
3	**5c**	Ad	348.1	116.9
4	**5d**	Ad	350.5	133.0
5	**5e**	Ad	393.0	132.6
6	**6**	TMP	398.2	146.3
7	**7a**	$PhCH_2$	344.1	126.1
8	**7b**	$Ph(CH_2)_2$	331.4	126.1

[a]Recorded at 54.1 MHz in C_6D_6. Chemical shifts are referenced to external H_2O. [a]Recorded at 40.4 MHz in C_6D_6. Chemical shifts are referenced to external CH_3NO_2. Ad = adamantyl; TMP = 2,2,6,6-tetramethylpiperidinyl.

^{17}O NMR Chemical Shift Measurement

^{17}O NMR spectra were recorded on Bruker Avance III 400 spectrometer (400 MHz for ^{1}H, 54.1 MHz for ^{17}O) from approximately 1.0 M C_6D_6 solutions at 297 K using a "directly" detecting broadband observe (BBFO) probe, unless stated otherwise. Referencing was performed against external H_2O (0 ppm, coaxial capillary) by measuring the difference between the water ^{17}O shift and the spectrometer values. For the ^{17}O NMR spectra 10 000 to 300 000 scans were accumulated (pulse width 90°, acquisition time 0.15 s, relaxation delay 0.2 s, spectral width 500 ppm) and Fourier transformed after a 200 Hz line broadening by exponential multiplication. To decrease acoustic ringing a pre-scan delay DE = 100 μs was used in the pulse sequence.

^{15}N NMR Chemical Shift Measurement

^{15}N NMR spectra were recorded on Bruker Avance III 400 spectrometer (400 MHz for ^{1}H, 40.4 MHz for ^{15}N) from approximately 1.0 M C_6D_6 solutions at 297 K using a "directly" detecting broadband observe (BBFO) probe, unless stated otherwise. The spectra were either taken via one-pulse experiments (inverse gated decoupling, digital resolution 1 Hz/data point, 15 s relaxation delay, 8192 scans) or via gradient-selected ^{15}N,^{1}H HMBC spectra (2048×32 data matrix, 16 ppm spectral width for ^{15}N). Referencing was performed against neat, external nitromethane (0 ppm, coaxial capillary) by measuring the difference between the nitromethane ^{15}N shift and the spectrometer values. The reported values are referenced against nitromethane and given according to IUPAC by adding -380.5 ppm to the referenced spectrometer value for C_6D_6.

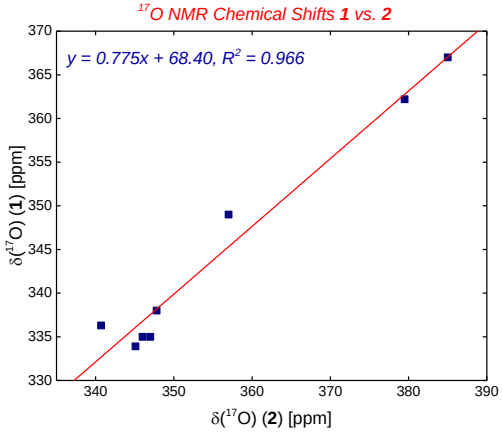

Chart ESI-1. Plot of ^{17}O NMR chemical shifts in amide series **1** vs. amide series **2**. Outlier: **1d**, δ(^{17}O) = 327 ppm.

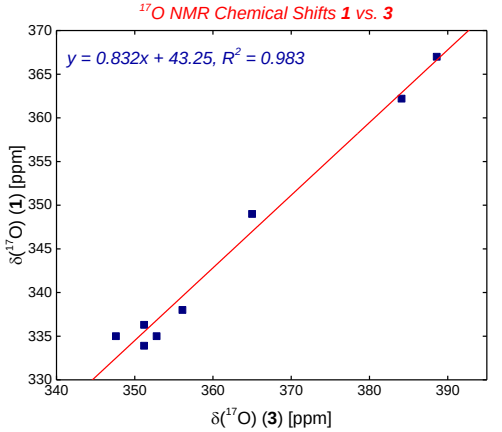

Chart ESI-2. Plot of ^{17}O NMR chemical shifts in amide series **1** vs. amide series **3**. Outlier: **1d**, δ(^{17}O) = 327 ppm.

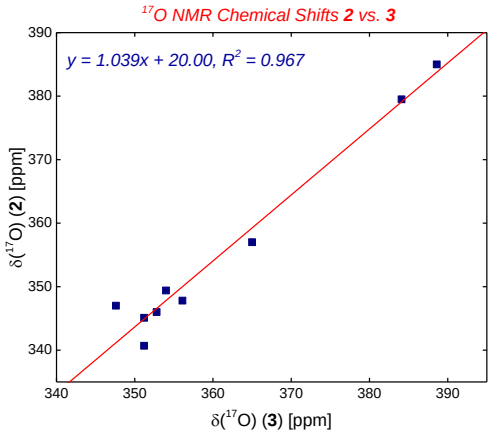

Chart ESI-3. Plot of ^{17}O NMR chemical shifts in amide series **2** vs. amide series **3**.

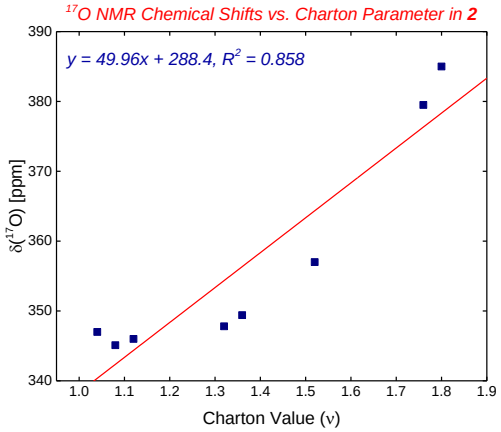

Chart ESI-4. Plot of ^{17}O NMR chemical shifts in amide series **2** vs. Charton Value (ν). Outlier: **2f**, δ(^{17}O) = 340.7 ppm.

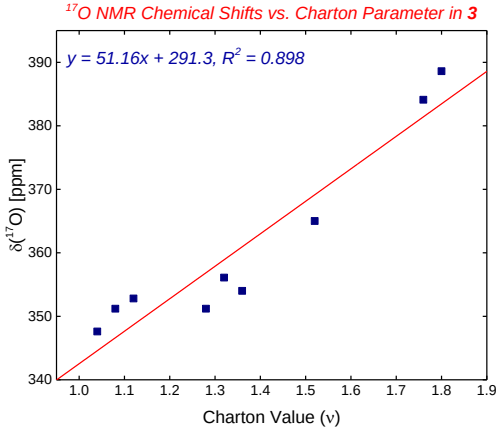

Chart ESI-5. Plot of ^{17}O NMR chemical shifts in amide series **3** vs. Charton Value (ν).

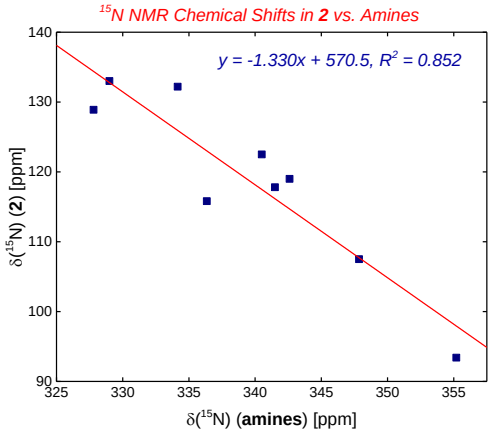

Chart ESI-6. Plot of ^{15}N NMR chemical shifts in amide series **2** vs. ^{15}N NMR chemical shifts in amines.

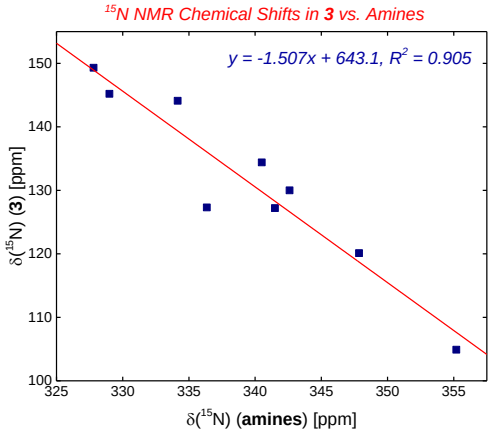

Chart ESI-7. Plot of ^{15}N NMR chemical shifts in amide series **3** vs. ^{15}N NMR chemical shifts in amines.

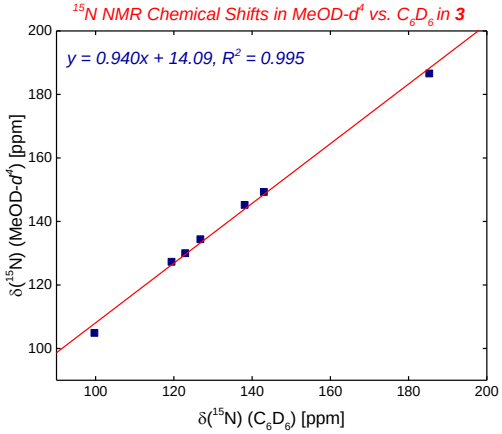

Chart ESI-8. Plot of ^{15}N NMR chemical shifts in MeOD-*d*^{4} vs. C_6D_6 in **3**.

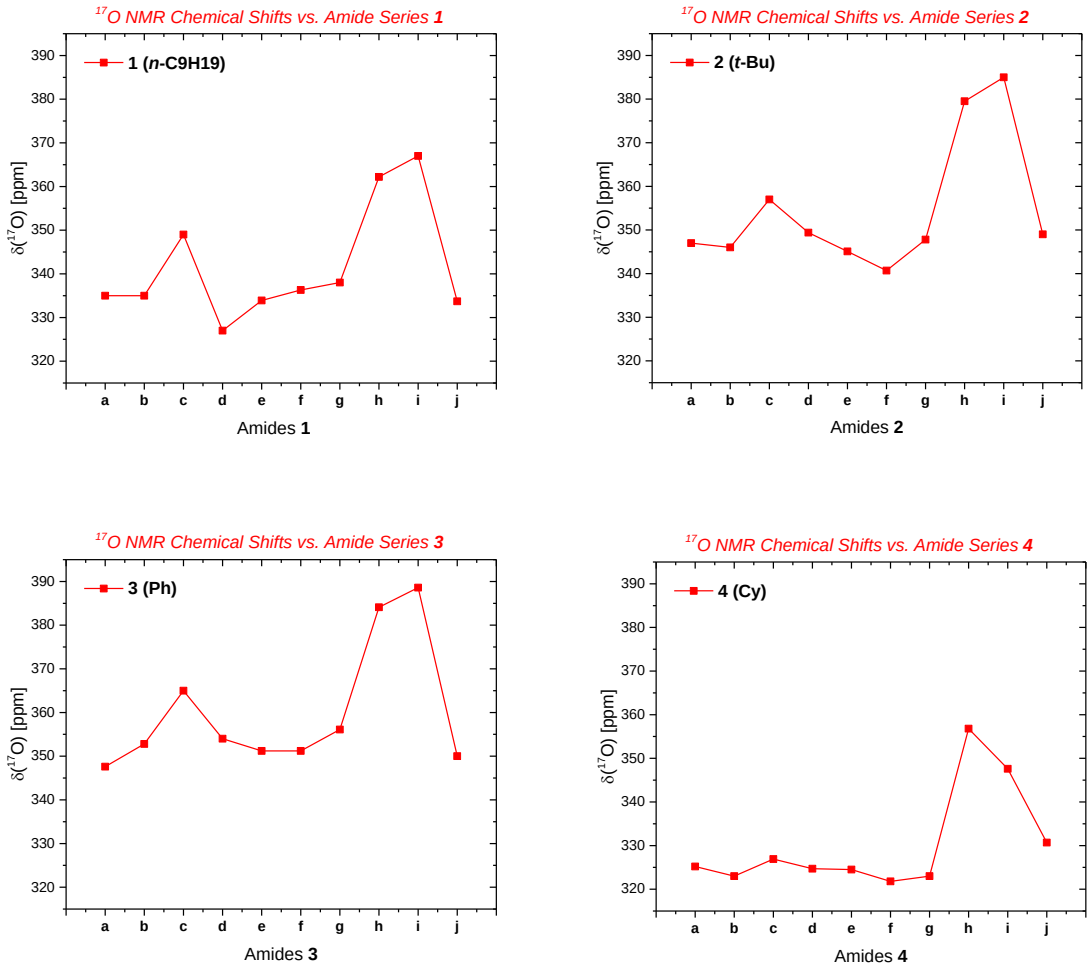

Chart ESI-9. Plots of ^{17}O NMR chemical shifts vs. amide series **1-4** showing δ(^{17}O) as a function of individual amides **1-4**.

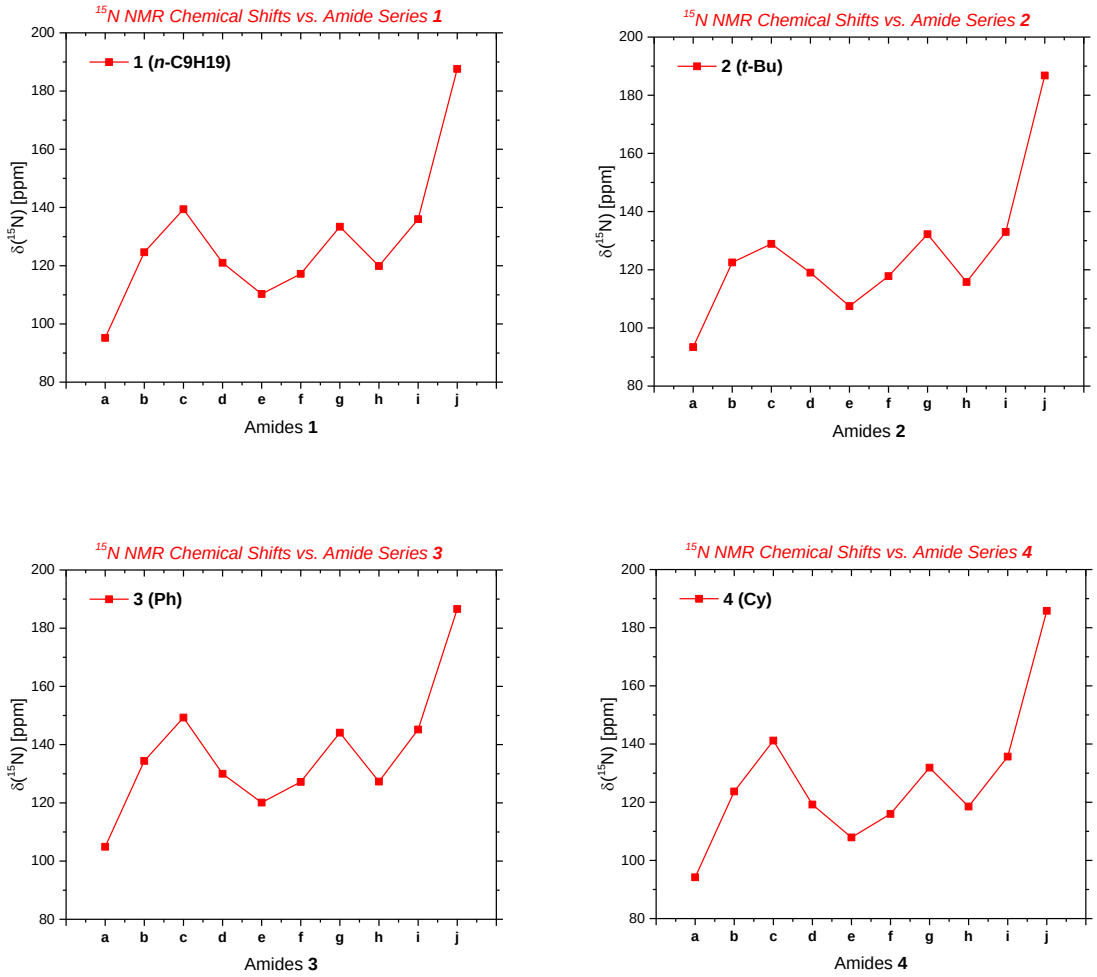

Chart ESI-10. Plots of ^{15}O NMR chemical shifts vs. amide series **1-4** showing δ(^{15}O) as a function of individual amides **1-4**.

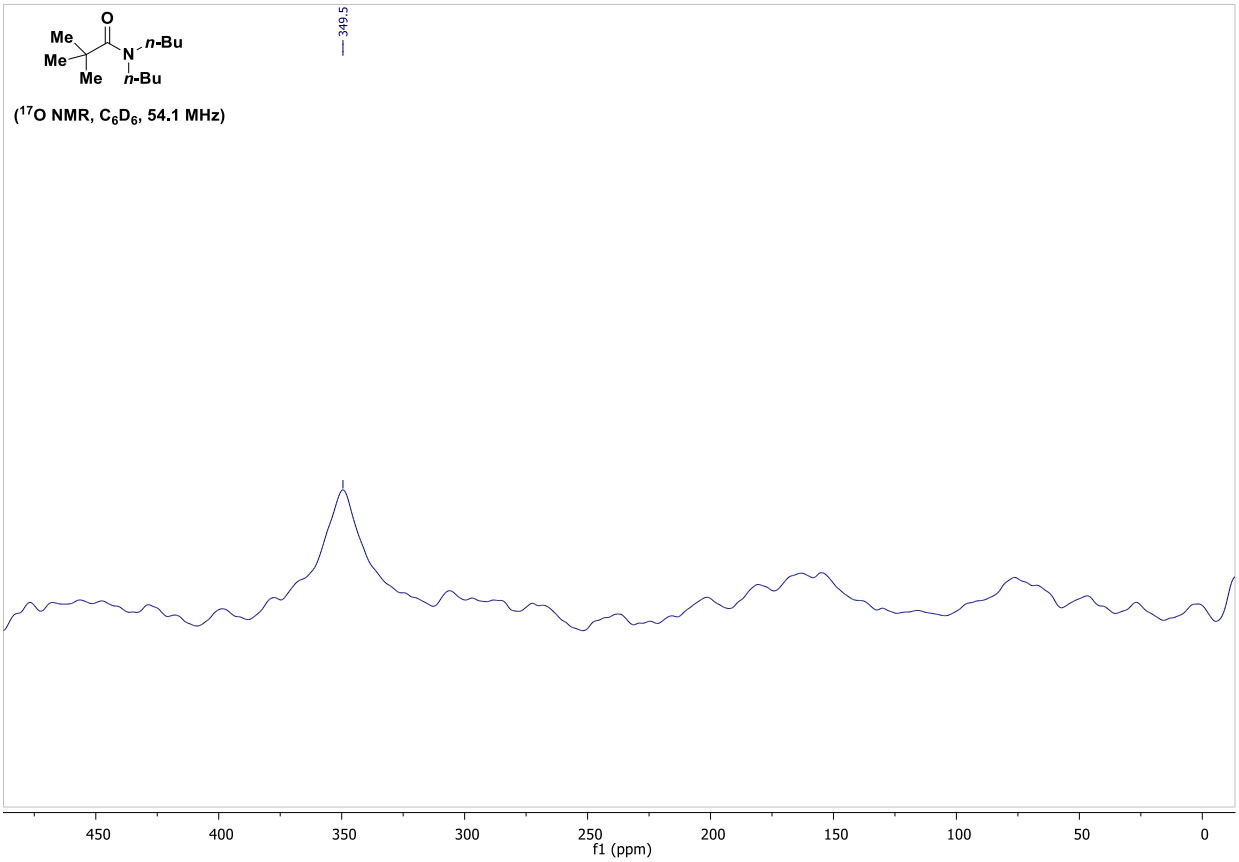

Figure ESI-1. ^{17}O NMR Spectrum of *N*,*N*-Dibutyl-2,2-dimethylpropanamide.

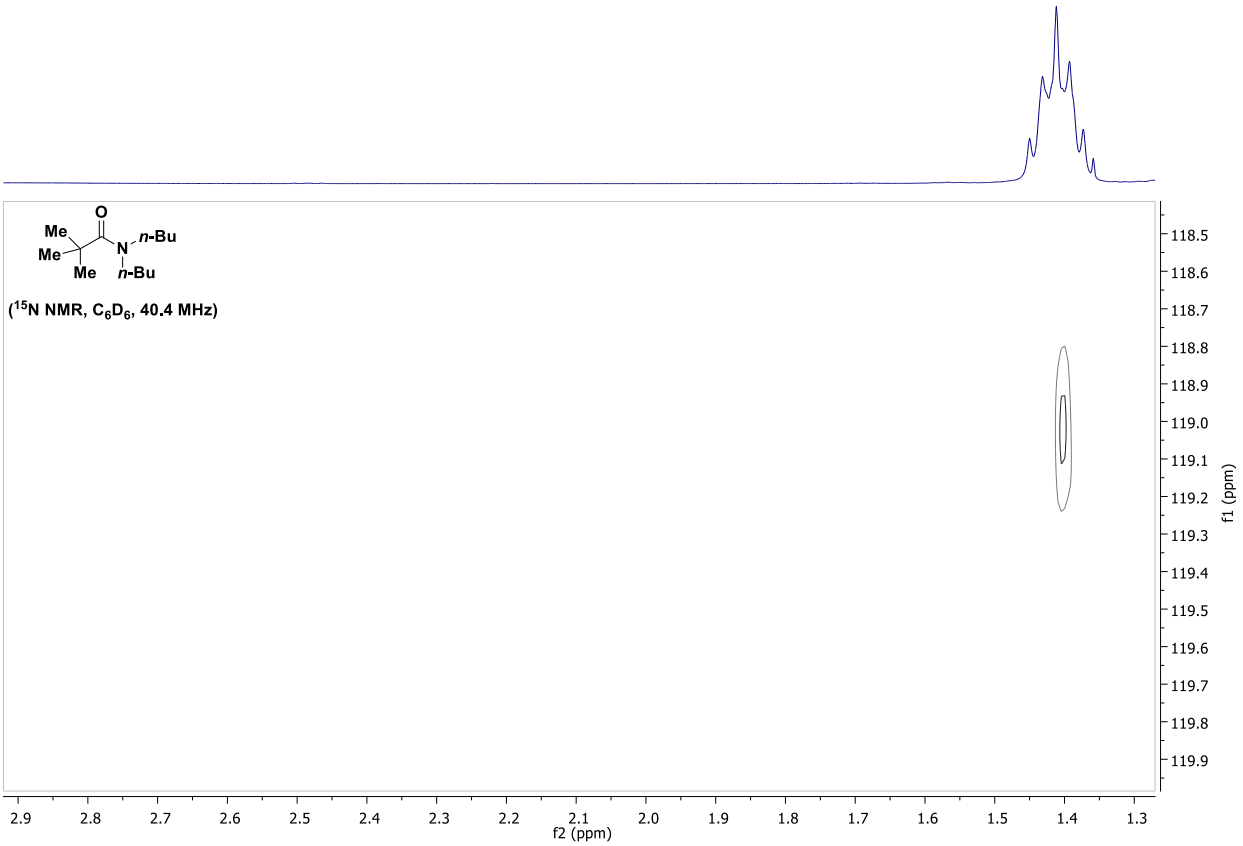

Figure ESI-2. ^{15}N NMR Spectrum of *N*,*N*-Dibutyl-2,2-dimethylpropanamide.

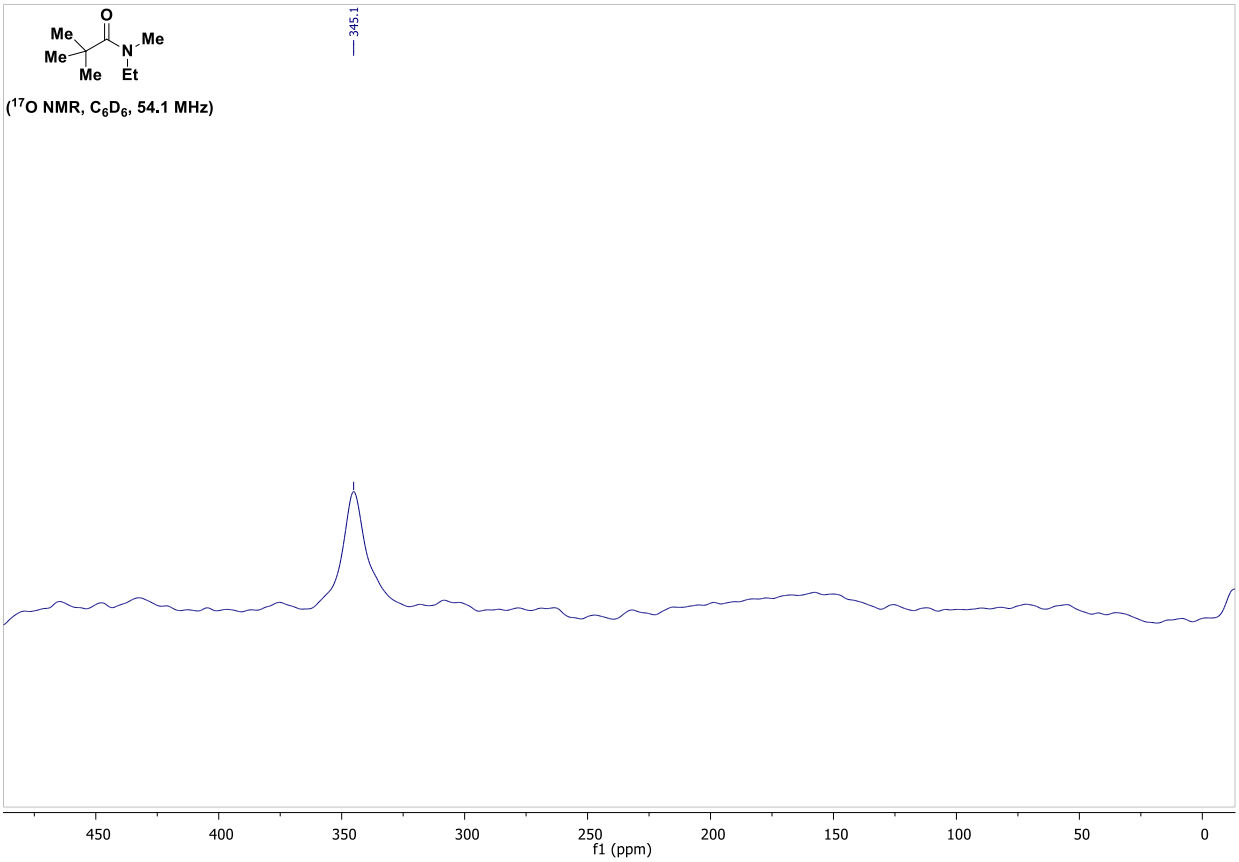

Figure ESI-3. ^{17}O NMR Spectrum of *N*-Ethyl-*N*,2,2-trimethylpropanamide.

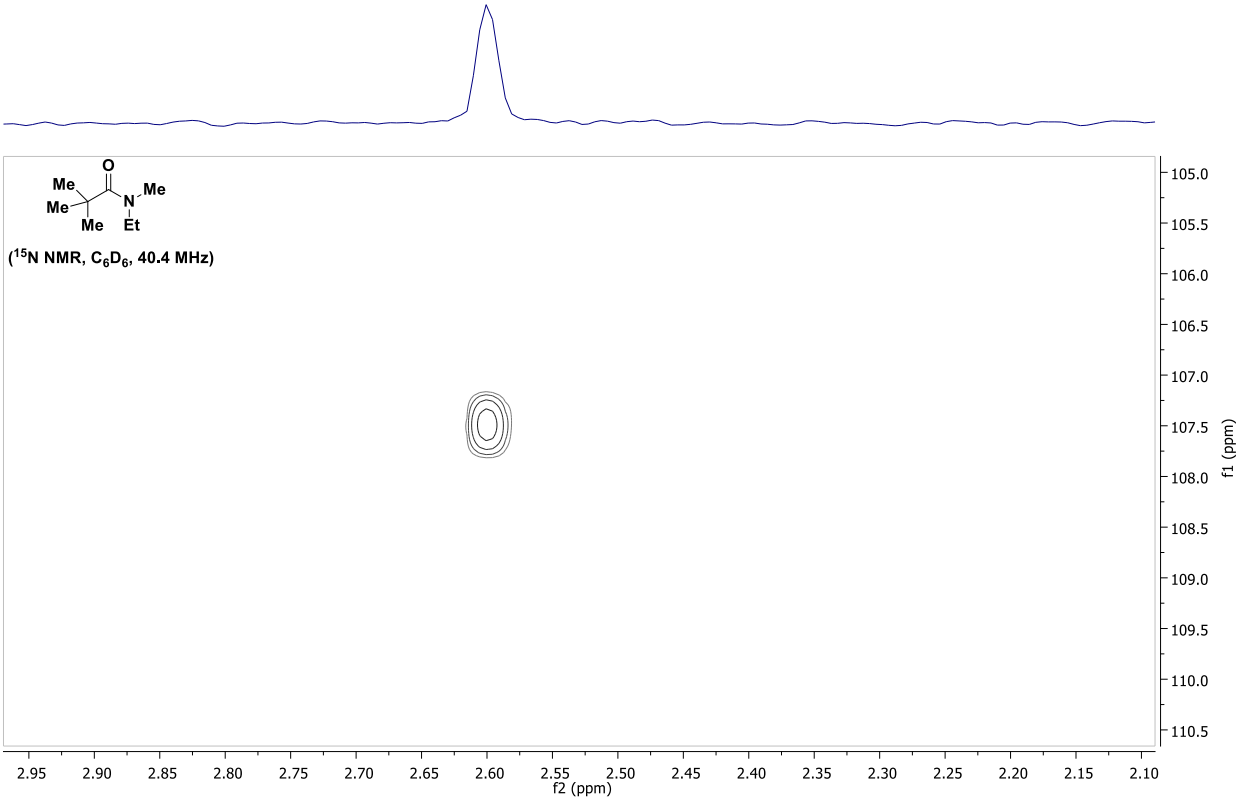

Figure ESI-4. ^{15}N NMR Spectrum of *N*-Ethyl-*N*,2,2-trimethylpropanamide.

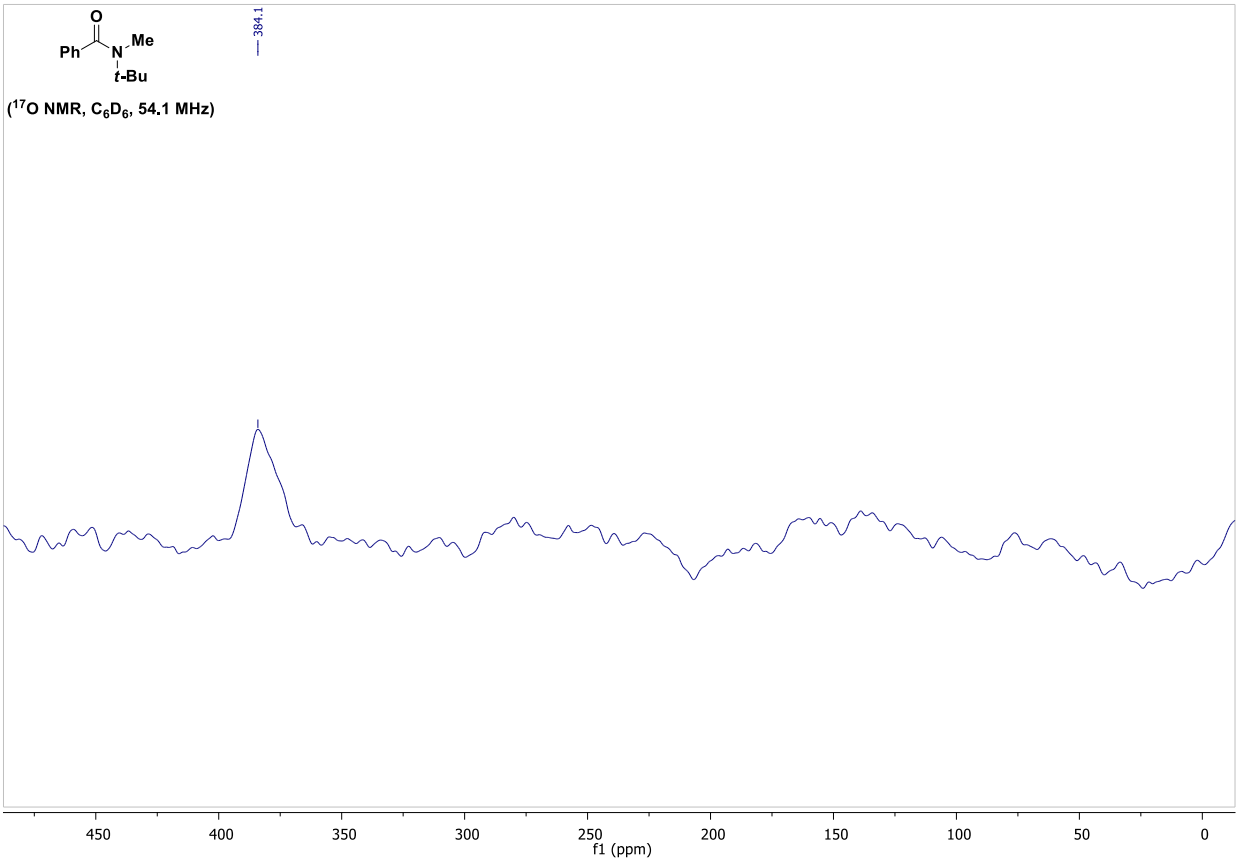

Figure ESI-5. ^{17}O NMR Spectrum of *N*-*tert*-Butyl-*N*-methylbenzamide.

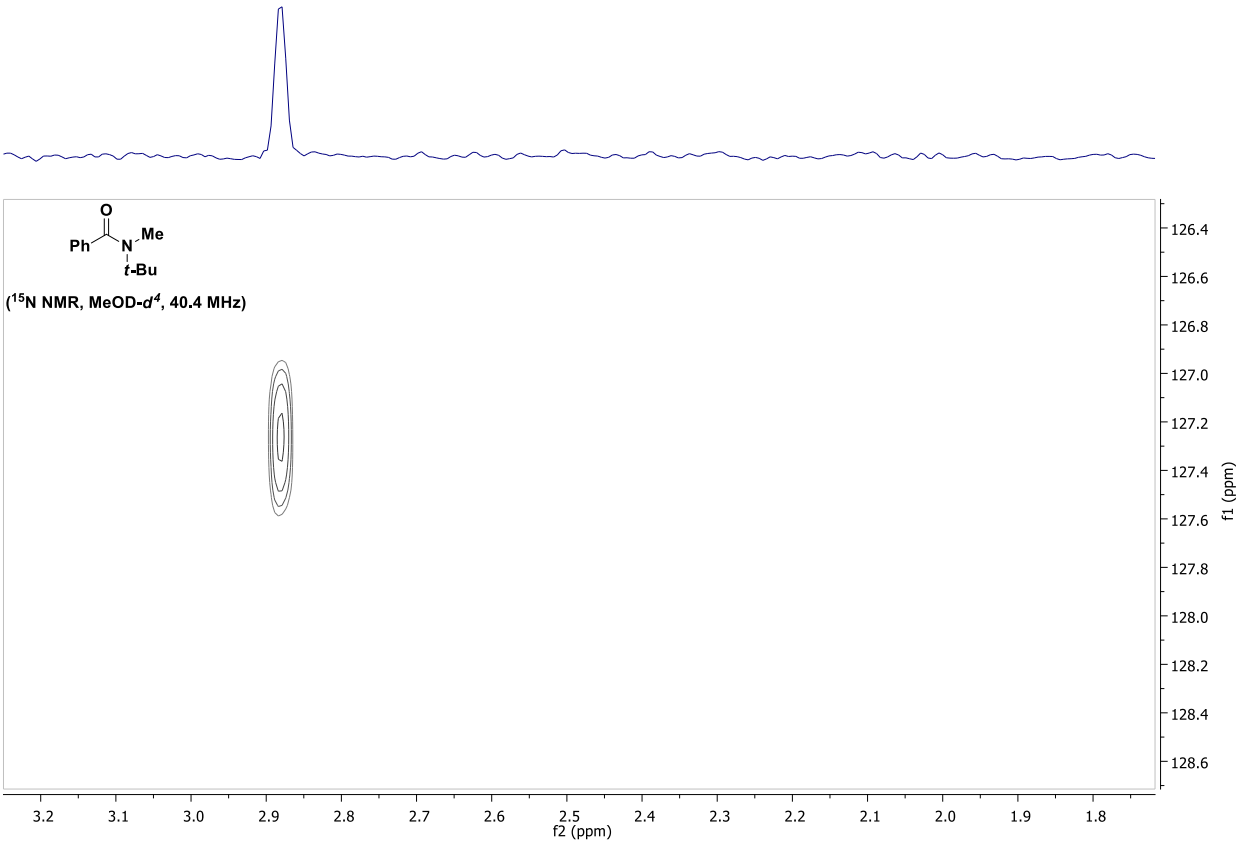

Figure ESI-6. [15]N NMR Spectrum of *N*-*tert*-Butyl-*N*-methylbenzamide.

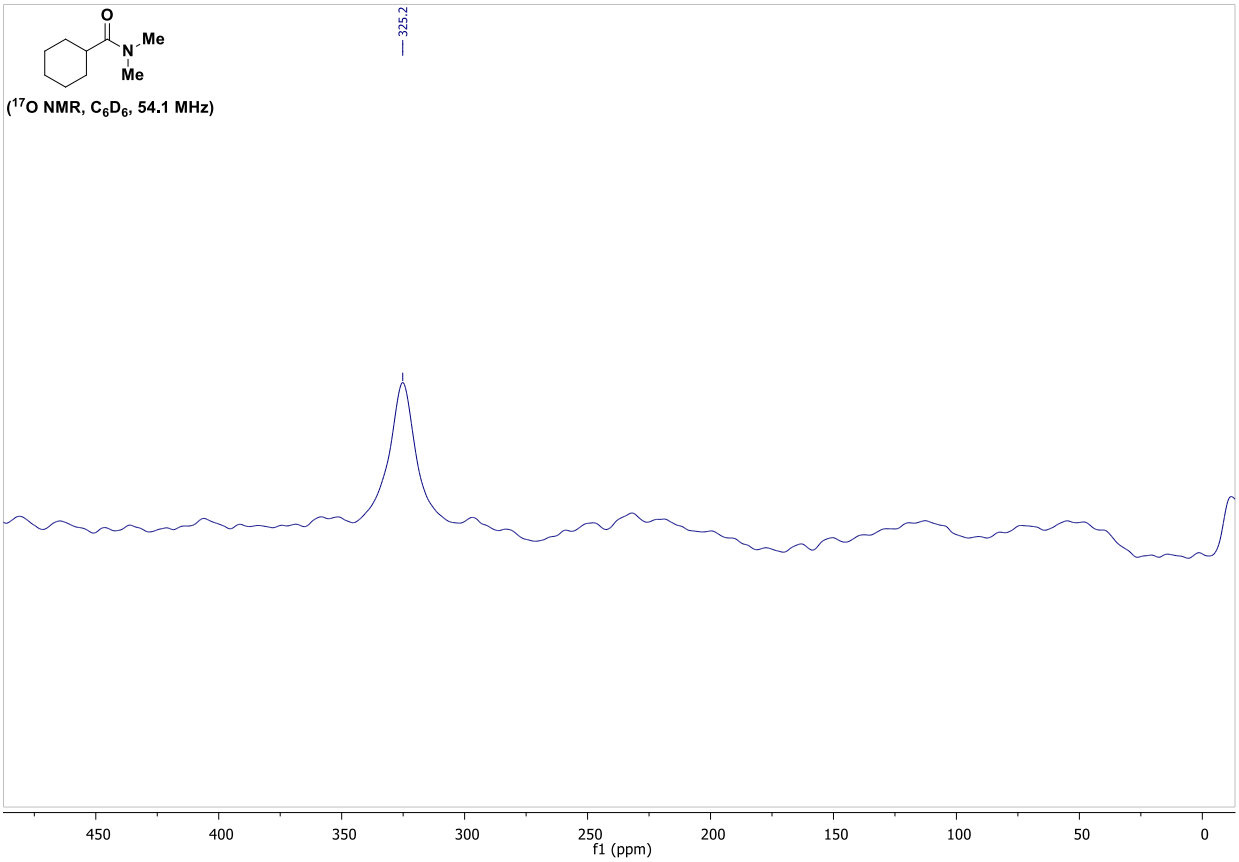

Figure ESI-7. ^{17}O NMR Spectrum of *N*,*N*-Dimethylcyclohexanecarboxamide.

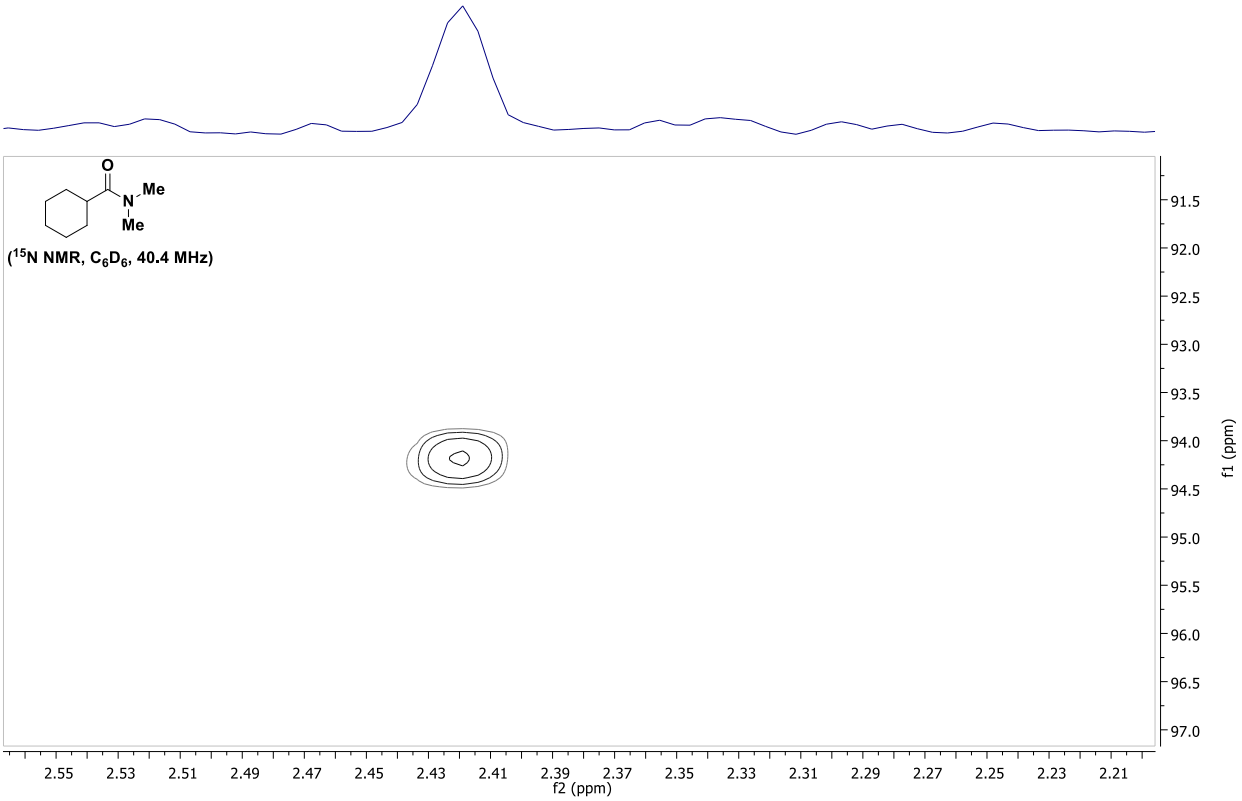

Figure ESI-8. ^{15}N NMR Spectrum of *N*,*N*-Dimethylcyclohexanecarboxamide.

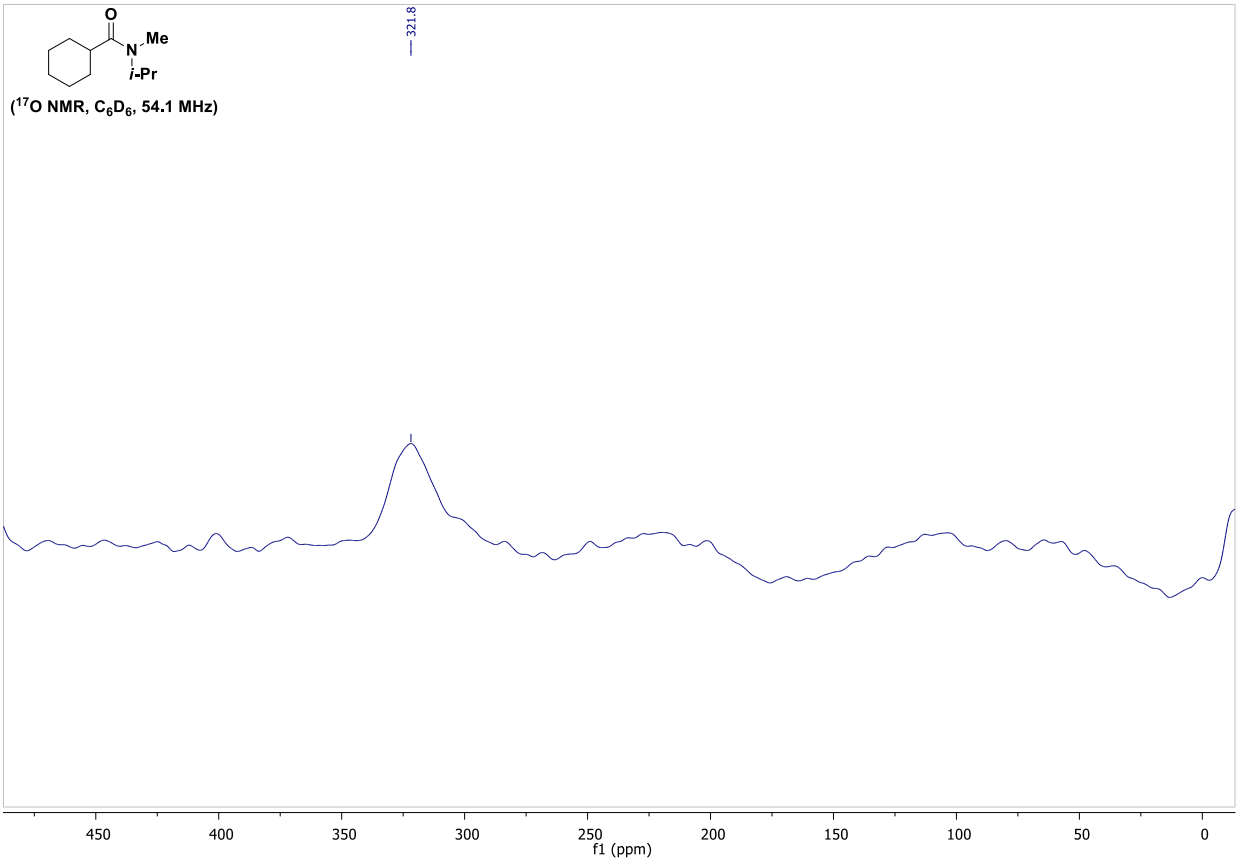

Figure ESI-9. ^{17}O NMR Spectrum of *N*-Methyl-*N*-(propan-2-yl)cyclohexanecarboxamide.

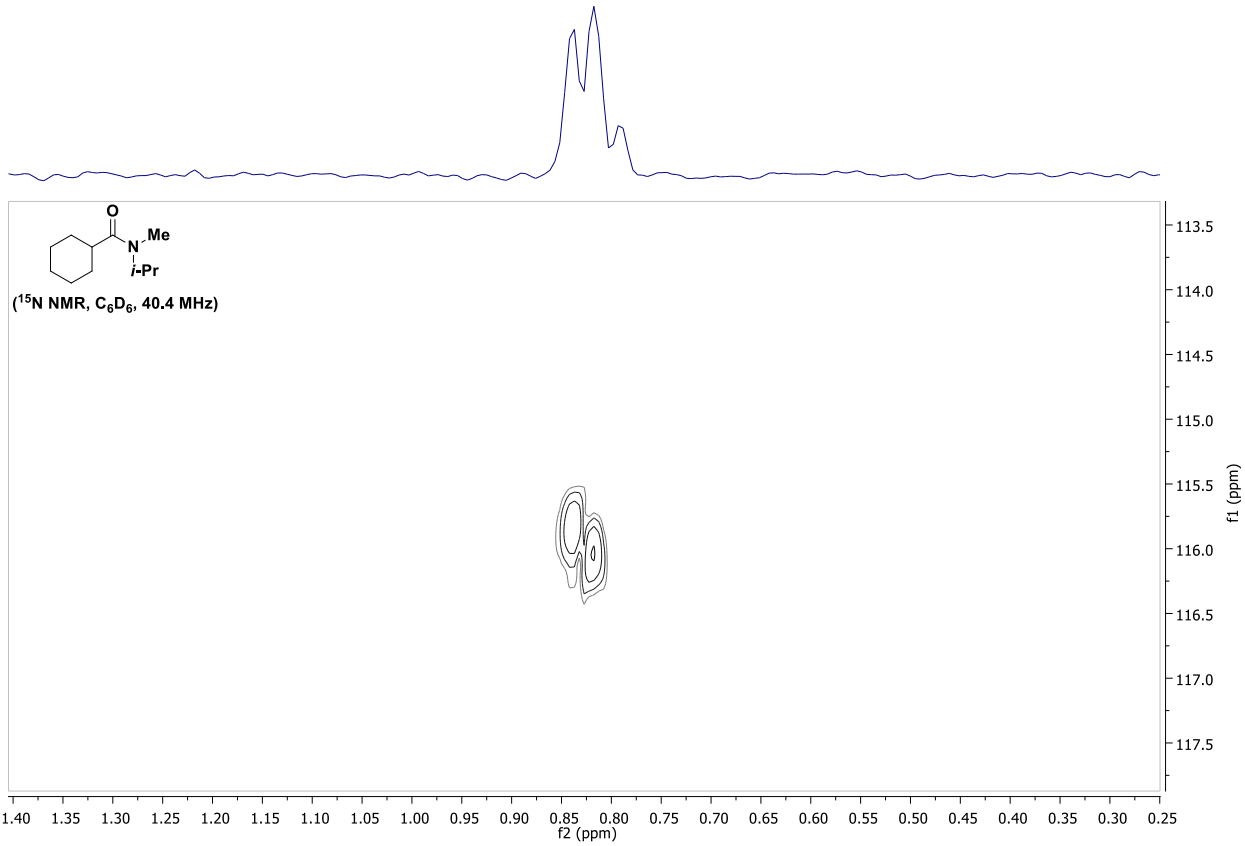

Figure ESI-10. ^{15}N NMR Spectrum of *N*-Methyl-*N*-(propan-2-yl)cyclohexanecarboxamide.