Electronic Supplementary Information

Facile preparation of N-*tert*-butyl amides under heat-, metal- and acid-free conditions *by using tert*-butyl nitrite (TBN) as a practical carbon source

Palani Natarajan [a,b,*], and Onder Metin [a,c,*]

[a] *Department of Chemistry, College of Sciences, Koç University, 34450, Sarıyer, Istanbul, Türkiye*

[b] *Department of Chemistry & Centre for Advanced Studies in Chemistry, Panjab University, Chandigarh - 160014, India*

[c] *Koç University Surface Science and Technology Center (KUYTAM), 34450, Sarıyer, Istanbul, Türkiye*

pnataraj@pu.ac.in (P. Natarajan) & ometin@ku.edu.tr (O. Metin)

TABLE OF CONTENTS

1. General Information

Unless otherwise specified, all substrates and reagents were obtained from reputable commercial sources and utilized without additional purification. Except when otherwise noted, all reactions were conducted in open vessels using oven-dried glassware. Unless otherwise stated, all reactions are agitated magnetically. The progress of the optimization reactions was monitored by gas chromatography. NMR spectra were used to characterize the product. Chemical shifts are expressed as δ-value in parts per million (ppm) and were calibrated using the residual protonated solvent as an internal standard. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; m, multiplet and so on. The coupling constants, J, are reported in Hertz (Hz).

2. Experimental Section

2.1. General procedure for the synthesis of N-*tert*-butyl amides (2) from nitriles (1) in liquid form

An oven-dried glass vial (10 mL) equipped with a magnetic stir bar was charged with nitrile (**1**, 3.0 mmol, 1.0 equiv), and water (3.3 mmol, 1.1 equiv., d = 1.0 g/mL). To this, TBN (6.0 mmol, 2.0 equiv., d = 0.867 g/mL) was added. Afterwards, mixture was stirred open flask at 20 ^{o}C for 16-36 h. Subsequently, the reaction mixture was diluted with ethyl acetate (5 mL), washed with saturated NaCl solution, dried over anhydrous sodium sulfate, and concentrated in vacuum. The solid/semi-solid residue obtained was passed through a short-pad of silica gel (60-120 mesh) column chromatography using 10-20% ethyl acetate in n-hexane mixture as eluent to obtain the desired pure product. This procedure has been utilized for the synthesis of **2a-2l**, **2n**, **2p**, **2x, 2y 2zc**, **2zd**, and **2zf-2zi**.

2.2. General procedure for the synthesis of N-*tert*-butyl amides (2) from nitriles (1) in solid form

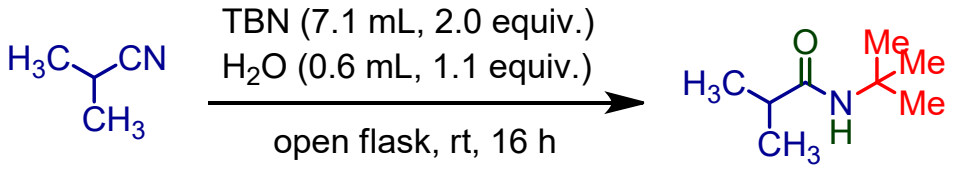
An oven-dried glass vial (10 mL) equipped with a magnetic stir bar was charged with nitrile (**1**, 3.0 mmol, 1.0 equiv), water (3.3 mmol, 1.1 equiv., d = 1.0 g/mL) and CH_2Cl_2 (3 mL). To this, TBN (6.0 mmol, 2.0 equiv., d = 0.867 g/mL) was added. Afterwards, mixture was stirred open flask at 20 ^{o}C for 24-36 h. Subsequently, the reaction mixture was diluted with additional quantity of CH_2Cl_2 (10 mL), washed with saturated NaCl solution, dried over anhydrous sodium sulfate, and concentrated in vacuum. The solid/semi-solid residue obtained was passed through a

short-pad of silica gel (60-120 mesh) column chromatography using 10-20% ethyl acetate in n-hexane mixture as eluent to obtain the desired pure product. This procedure has been utilized for the synthesis of **2m**, **2o**, **2q-2w**, **2z**, **2za**, **2zb**, and **2ze**.

2.3. Procedure for ^{1}H NMR spectroscopic monitoring experiment

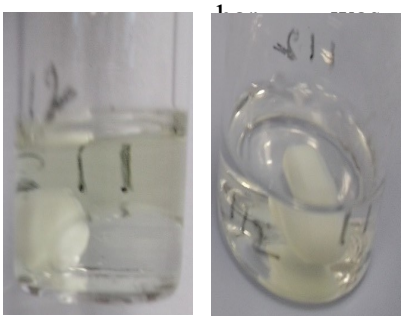
The isobutyronitrile (**1a**, 10 µl, 1.0 equiv), water (2.0 µl, 1.1 equiv.), and CD_2Cl_2 (0.5 mL) were charged into an oven-dried NMR tube. TBN (20 µl, 2.0 equiv.) was then added to the mixture. Subsequently, ^{1}H NMR was immediately measured. After that, with the aid of a tiny magnetic bar, the entire solution was stirred for 12 h. Then, the magnetic bar was removed, and NMR was once more measured. Following the NMR measurements, again the magnetic bar was introduced, and the solution was continually stirred. The same process was used for the whole experiment till 24 h.

2.4. Procedure for the scale-up synthesis of (N-(*tert*-butyl)isobutyramide (2a)



1a
(2.69 mL, 30 mmol)

2a
(3.8 g, 89%)



An oven-dried glass vial (20 mL) equipped with a magnetic stir charged with isobutyronitrile (**1a**, 2.69 mL, 30.0 mmol, 1.0 equiv), and water (0.6 mL, 33.0 mmol, 1.1 equiv., d = 1.0 g/mL). To this, TBN (7.1 mL, 60.0 mmol, 2.0 equiv., d = 0.867 g/mL) was added. Afterwards, mixture was stirred open flask at 20 °C for 16 h. Subsequently, the reaction mixture was diluted with ethyl acetate (30 mL), washed with saturated NaCl solution, dried over anhydrous sodium sulfate, and concentrated in vacuum. The semi-solid residue obtained was passed through a short-pad of silica gel (60-120 mesh) column chromatography using 10% ethyl acetate in n-hexane mixture as eluent to obtain **2a** as a colorless solid.

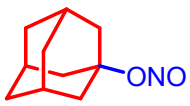
2.5. General procedure for the scale-up synthesis of 2g, 2h, and 2zh

An oven-dried glass vial (20 mL) equipped with a magnetic stir bar was charged with respective nitrile (20.0 mmol, 1.0 equiv), and water (0.4 mL, 22.0 mmol, 1.1 equiv., d = 1.0 g/mL). To this, TBN (4.75 mL, 40.0 mmol, 2.0 equiv., d = 0.867 g/mL) was added. Afterwards, mixture was stirred open flask at 20 °C for 16 h. Subsequently, the reaction mixture was diluted with ethyl acetate (30 mL), washed with saturated NaCl solution, dried over anhydrous sodium sulfate, and concentrated in vacuum. The semi-solid residue obtained was passed through a short-pad of silica gel (60-120 mesh) column chromatography using 10% ethyl acetate in n-hexane mixture as eluent to obtain the expected product.

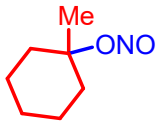
2.6. General procedure for the scale-up synthesis of 2t, 2zb, and 2ze

An oven-dried round-bottom flask (50 mL) equipped with a magnetic stir bar was charged with respective nitrile (20.0 mmol, 1.0 equiv), CH_2Cl_2 (15 mL) and water (0.4 mL, 22.0 mmol, 1.1 equiv., d = 1.0 g/mL). To this, TBN (4.75 mL, 40.0 mmol, 2.0 equiv., d = 0.867 g/mL) was added. Afterwards, mixture was stirred open flask at 20 °C for 24 h (for **2t** and **2zb**) and 36 h (for **2ze**). Subsequently, the reaction mixture was diluted with ethyl acetate (30 mL), washed with saturated NaCl solution, dried over anhydrous sodium sulfate, and concentrated in vacuum. The semi-solid residue obtained was passed through a short-pad of silica gel (60-120 mesh) column chromatography using 10% ethyl acetate in n-hexane mixture as eluent to obtain the desired product.

2.7. General procedure for the synthesis of following nitrites



adamantan-1-yl nitrite



1-methylcyclohexyl nitrite

2-methyl-4-phenylbutan-2-yl nitrite

These nitrites were readily synthesized by two methods described below.

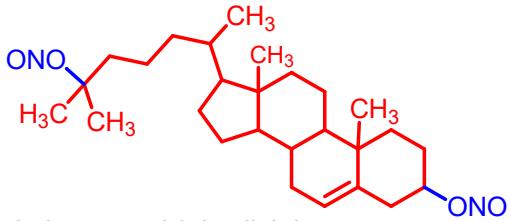
Method 1: An oven-dried conical flask (25 mL) was filled with alcohol (5 g) and 50% aqueous H_2SO_4 (10 mL) solution, and the liquid was then refrigerated to 0-5 °C in an ice bath. In a separate beaker (100 mL) equipped with a magnetic stir bar was charged with $NaNO_2$ (1.1

equiv., respect to the quantity of alcohol) and deionized water (3 mL). Afterwards, the cold acidic alcohol solution was gradually added over a period of 15 minutes to the aqueous $NaNO_2$ solution submerged in an ice bath with stirring. Subsequently, entire solution was transferred into a separating funnel and then washed three times with aqueous $NaHCO_3$ solution. The light yellow oily liquid was collected and stored over K_2CO_3 and then used for the reaction(s). It's crucial to maintain a low temperature range throughout the procedure since doing otherwise might increase the product's impurity levels.

Method 2: An oven-dried round-bottom flask (50 mL) equipped with a magnetic stir bar was charged with respective alcohol (5 g, 1.0 equiv) and pyridine (10 mL). Resultant solution was cooled to 0 °C and then nitrosylsulfuric acid (HO_3SONO, 5 equiv.) was added. Subsequently, entire reaction mixture was stirred for 0.5 h at 0 °C and then quenched with methanol. Resultant yellow solution was transferred into a separating funnel and then washed three times with aqueous $NaHCO_3$ solution. The light yellow oily liquid was collected and stored over K_2CO_3 and then used for the reaction(s). It's crucial to maintain a low temperature range throughout the procedure since doing otherwise might increase the product's impurity levels.

2.8. General procedure for the synthesis of following dinitrites

2-methylbutanyl 2,4-dinitrite



cholest-5-enyl 3,25-dinitrite

These nitrites were readily synthesized by two methods described below.

Method 1: An oven-dried conical flask (25 mL) was filled with alcohol (5 g) and 30% aqueous H_2SO_4 (10 mL) solution, and the liquid was then refrigerated to 0-5 °C in an ice bath. In a separate beaker (100 mL) equipped with a magnetic stir bar was charged with $NaNO_2$ (2.1 equiv., respect to the quantity of alcohol) and deionized water (6 mL). Afterwards, the cold acidic alcohol solution was gradually added over a period of 15 minutes to the aqueous $NaNO_2$ solution submerged in an ice bath with stirring. Subsequently, entire solution was transferred into a separating funnel and then washed three times with aqueous $NaHCO_3$ solution. The yellow oily

liquid was collected and stored over K_2CO_3 and then used for the reaction(s). It's crucial to maintain a low temperature range throughout the procedure since doing otherwise might increase the product's impurity levels.

Method 2: An oven-dried round-bottom flask (50 mL) equipped with a magnetic stir bar was charged with respective alcohol (5 g, 1.0 equiv) and pyridine (15 mL). Resultant solution was cooled to 0 ^oC and then nitrosylsulfuric acid (HO_3SONO, 8 equiv.) was added. Subsequently, entire reaction mixture was stirred for 45 minutes at 0 ^oC and then quenched with methanol. Resultant yellow solution was transferred into a separating funnel and then washed three times with aqueous $NaHCO_3$ solution. The light yellow oily liquid was collected and stored over K_2CO_3 and then used for the reaction(s). It's crucial to maintain a low temperature range throughout the procedure since doing otherwise might increase the product's impurity levels.

2.9. Procedure for control experiments

Reaction with 1,4-cyclohexadiene: A radical scavenger such as 1,4-cyclohexadiene (2.0 equiv) was added to the general procedure described in section 2.1. After 16 h, the crude reaction mixture was diluted with ethyl acetate, dried using anhydrous Na_2SO_4, filtered and analyzed by GCMS. GCMS analysis revealed that the formation of expected product 2a. The **2a** was then isolated by silica-gel column chromatography.

Reaction without TBN: An oven-dried glass vial (5 mL) equipped with a magnetic stir bar was charged with isobutyronitrile (**1a**, 3.0 mmol, 1.0 equiv), and water (3.3 mmol, 1.1 equiv.,). Resultant mixture was stirred open flask at 20 ^oC for 16 h. Subsequently, the crude reaction mixture was diluted with ethyl acetate (5 mL), dried using anhydrous Na_2SO_4, filtered and analyzed by GCMS. The results of the GCMS analysis showed that there was no product **2a** and that starting precursor **1a** was detected.

Reaction with benzamide: An oven-dried vial equipped with a magnetic stir bar was charged with benzamide (1.0 mmol). To this, DCM (2.0 mL), water (1.1 mmol), and TBN (2.0 mmol) were added. Resultant, mixture was stirred open flask at 20 ^oC for 16 h. Afterwards, the crude reaction mixture was diluted with DCM (5 mL), dried using anhydrous Na_2SO_4, filtered and

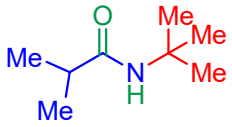
analyzed by GCMS. The results of the GCMS analysis showed that there was no product **2a**, however, trace of benzoic acid and the starting precursor benzamide were detected.

Reaction without water: An oven-dried glass vial (5 mL) equipped with a magnetic stir bar was charged with isobutyronitrile (**1a**, 3.0 mmol, 1.0 equiv), and TBN (6.0 mmol, 2.0 equiv.,). Resultant mixture was placed it in the center of a $CaCl_2$-desiccator and stirred at 20 ^oC for 16 h. Subsequently, the crude reaction mixture was diluted with ethyl acetate (5 mL), and analyzed by GCMS. The results of the GCMS analysis showed that there was only trace amount of **2a** and remaining was starting precursor **2a**.

Reaction with labeled water ($H_2{}^{18}O$, contains 97% of ^{18}O) instead of regular water (H_2O): Instead of regular water (H_2O), the labeled water (3.3 mmol, 1.1 equiv.) was added to the general procedure described in section 2.1. After 16 h, the crude reaction mixture was diluted with ethyl acetate, dried using anhydrous Na_2SO_4, filtered, passed through a silica-gel column chromatography and concentrated. An expected product as a white solid in 91% yield was obtained. The GCMS analysis of the solid indicates the 88% incorporation of labeled oxygen (^{18}O).

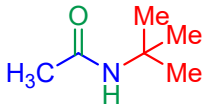
Reaction with *tert*-butyl alcohol: An oven-dried glass vial (5 mL) equipped with a magnetic stir bar was charged with isobutyronitrile (**1a**, 3.0 mmol, 1.0 equiv), water (3.3 mmol, 1.1 equiv.,) and tert-butyl alcohol (6.0 mmol, 2.0 equiv.,). Resultant mixture was stirred open flask at 20 ^oC for 16 h. Subsequently, the crude reaction mixture was diluted with ethyl acetate (5 mL), dried using anhydrous Na_2SO_4, filtered and analyzed by GCMS. The results of the GCMS analysis showed that there was no product **2a** and that starting precursor **1a** was detected.

2.10. Experimental characterization data for products



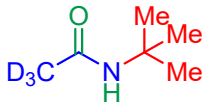
2a

N-(*tert*-Butyl)isobutyramide (2a): Synthesized with 16 hours of stirring, in accordance with the general procedure outlined in section 2.1. White solid (400 mg, 93% yield). R_f (ethyl acetate:n-hexane, 1:9): 0.3. m.p. 92-93 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.25 (bs, 1H), 2.20 (hept, J = 6.9 Hz, 1H), 1.33 (s, 9H), 1.11 (d, J = 6.9 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.5, 50.9, 36.5, 29.0, 19.8. Spectra data are consistent with those reported in the literature[1].



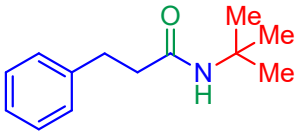
2b

N-(*tert*-Butyl)acetamide (2b): Synthesized with 16 hours of stirring, in accordance with the general procedure outlined in section 2.1. White solid (325 mg, 94% yield). R_f (ethyl acetate:n-hexane, 1:9): 0.27. m.p. 93-94 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.48 (bs, 1H), 1,88 (s, 3H), 1.32 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 51.2, 28.7, 24.5. Spectra data are consistent with those reported in the literature [2].



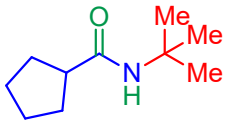
2c

N-(*tert*-Butyl)trideuteroacetamide (2c): Synthesized with 16 hours of stirring, in accordance with the general procedure outlined in section 2.1. White solid (318 mg, 92% yield). R_f (ethyl acetate:n-hexane, 1:9): 0.27. m.p. 94-95 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.47 (bs, 1H), 1.32 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 51.1, 28.7, 25.1-23.9 (m). HRMS (ESI) m/z calculated for $C_6H_{11}D_3NO$ $[(M+H)^+]$ 119.1269, found 119.1265.



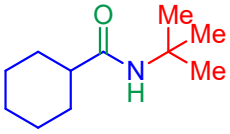
2d

N-(*tert*-Butyl)-3-phenylpropanamide (2d): Synthesized with 16 hours of stirring, in accordance with the general procedure outlined in section 2.1. White solid (554 mg, 90% yield). R_f (ethyl acetate:n-hexane, 1:9): 0.18. m.p. 88-89 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.25 (m, 2H), 7.22-7.18 (m, 3H), 5.18 (bs, 1H), 2.93 (t, J = 7.6 Hz, 2H), 2.40 (t, J = 7.6 Hz, 2H), 1.28 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 141.2, 128.6, 126.2, 51.1, 39.6, 31.9, 28.8. Spectra data are consistent with those reported in the literature [3].



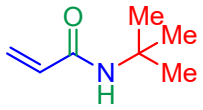
2e

N-(*tert*-Butyl)cyclopentanecarboxamide (2e): Synthesized with 16 hours of stirring, in accordance with the general procedure outlined in section 2.1. White solid (462 mg, 91% yield). R_f (ethyl acetate:n-hexane, 1:9): 0.26. m.p. 100-101 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.23 (bs, 1H), 2.46-2.36 (m, 1H), 1.85-1.78 (m, 2H), 1.76-1.70 (m, 4H), 1.57-1.52 (m, 2H), 1.34 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 50.7, 46.6, 30.5, 28.9, 25.8. Spectra data are consistent with those reported in the literature [4].



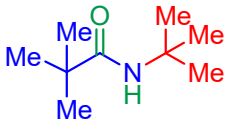
2f

N-(*tert*-Butyl)cyclohexanecarboxamide (2f): Synthesized with 16 hours of stirring, in accordance with the general procedure outlined in section 2.1. White solid (512 mg, 93% yield). R_f (ethyl acetate:n-hexane, 1:9): 0.24. m.p. 156-157 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.24 (bs, 1H), 1.95-1.89 (m, 1H), 1.84-1.70 (m, 4H), 1.62 (d, J = 7.6 Hz, 1H), 1.46-1.34 (m, 2H), 1.31 (s, 9H), 1.26-1.15 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 50.9, 46.4, 29.8, 29.0, 25.6, 25.5. Spectra data are consistent with those reported in the literature [5].



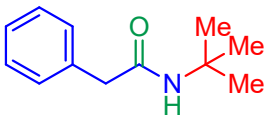
2g

N-(*tert*-Butyl)acrylamide (2g): Synthesized with 16 hours of stirring, in accordance with the general procedure outlined in section 2.1. White solid (290 mg, 76% yield). R_f (ethyl acetate:n-hexane, 1:9): 0.25. m.p. 124-125 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.22 (d, J = 16.8 Hz, 1H), 6.03 (dd, J = 16.8, 10.0 Hz, 1H), 5.82 (bs, 1H), 5.55 (d, J = 10.0 Hz, 1H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 132.2, 125.4, 51.3, 28.7. Spectra data are consistent with those reported in the literature [5].



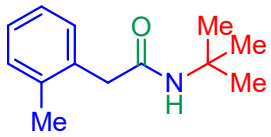
2h

N-(*tert*-Butyl)pivalamide (2h): Synthesized with 16 hours of stirring, in accordance with the general procedure outlined in section 2.1. Colorless semi-solid (396 mg, 84% yield). R_f (ethyl acetate:n-hexane, 1:9): 0.25. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.27 (bs, 1H), 1.34 (s, 9H), 1.22 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.4, 51.0, 38.4, 28.8, 27.6. HRMS (ESI) m/z calculated for $C_9H_{20}NO$ $[(M+H)^+]$ 158.1549, found 158.1543.



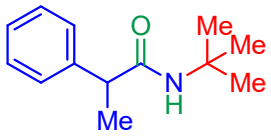
2i

N-(*tert*-Butyl)-2-phenylacetamide (2i): Synthesized with 24 hours of stirring, in accordance with the general procedure outlined in section 2.1. White solid (510 mg, 89% yield). R_f (ethyl acetate:n-hexane, 1:4): 0.52. m.p. 110-111 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.32 (m, 2H), 7.31-7.24 (m, 3H), 5.19 (bs, 1H), 3.46 (s, 2H), 1.27 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 135.4, 129.2, 128.9, 127.2, 51.2, 44.9, 28.6. Spectra data are consistent with those reported in the literature [6].



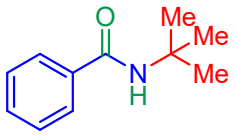
2k

N-(*tert*-Butyl)-2-(*o*-tolyl)acetamide (2k): Synthesized with 36 hours of stirring, in accordance with the general procedure outlined in section 2.1. White solid (406 mg, 66% yield). R_f (ethyl acetate:n-hexane, 1:4): 0.48. m.p. 107-109 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.14 (m, 4H), 5.07 (bs, 1H), 3.49 (s, 2H), 2.28 (s, 3H), 1.26 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 137.2, 134.0, 130.7, 130.3, 127.5, 126.7, 51.1, 43.2, 28.6, 19.3. Spectra data are consistent with those reported in the literature [5].



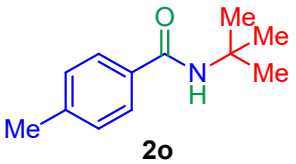
2l

N-(*tert*-Butyl)-2-phenylpropanamide (2l): Synthesized with 24 hours of stirring, in accordance with the general procedure outlined in section 2.1. White solid (524 mg, 85% yield). R_f (ethyl acetate:n-hexane, 1:4): 0.47. m.p. 103-104 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.27 (m, 5H), 5.19 (bs, 1H), 3.52-3.48 (m, 1H), 1.49 (d, J = 6.2 Hz, 3H), 1.27 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 142.1, 128.9, 127.6, 127.2, 51.1, 47.8, 28.7, 18.8. Spectra data are consistent with those reported in the literature [4].



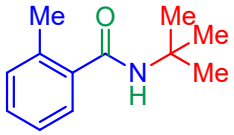
2n

N-(*tert*-Butyl)benzamide(2n): Synthesized with 24 hours of stirring, in accordance with the general procedure outlined in section 2.1. White solid (462 mg, 87% yield). R_f (ethyl acetate:n-hexane, 1:4): 0.38. m.p. 135-136 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74-7.70 (m, 2H), 7.48-7.44 (m, 1H), 7.42-7.38 (m, 2H), 5.98 (bs, 1H), 1.47 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 136.0, 131.0, 128.5, 126.6, 51.6, 28.8. Spectra data are consistent with those reported in the literature [2].



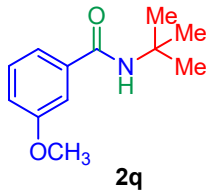
2o

N-(*tert*-Butyl)-4-methylbenzamide (2o): Synthesized with 24 hours of stirring, in accordance with the general procedure outlined in section 2.2. White solid (516 mg, 90% yield). R_f (ethyl acetate:n-hexane, 1:4): 0.36. m.p. 113-114 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.0 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 5.91 (bs, 1H), 2.38 (s, 3H), 1.47 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 141.3, 133.1, 129.2, 126.7, 51.5, 28.9, 21.4. Spectra data are consistent with those reported in the literature [3].



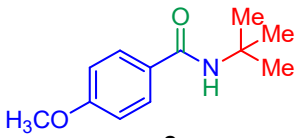
2p

N-(*tert*-Butyl)-2-methylbenzamide (2p): Synthesized with 36 hours of stirring, in accordance with the general procedure outlined in section 2.1. White solid (275 mg, 48% yield). R_f (ethyl acetate:n-hexane, 1:4): 0.37. m.p. 78-79 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.26 (m, 2H), 7.21-7.15 (m, 2H), 5.61 (bs, 1H), 2.43 (s, 3H), 1.47 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 137.9, 135.4, 130.7, 129.3, 126.4, 125.5, 51.7, 28.8, 19.6. Spectra data are consistent with those reported in the literature [5].



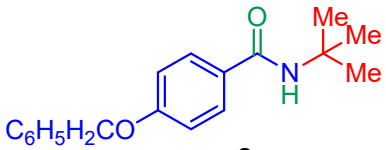
2q

N-(*tert*-Butyl)-3-methoxybenzamide (2q): Synthesized with 24 hours of stirring, in accordance with the general procedure outlined in section 2.2. White solid (528 mg, 85% yield). R_f (ethyl acetate:n-hexane, 1:4): 0.29. m.p. 102-103 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.21 (m, 3H), 7.02-6.99 (m, 1H), 5.95 (bs, 1H), 3.84 (s, 3H), 1.47 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 159.9, 137.5, 129.6, 118.5, 117.5, 112.4, 55.6, 51.6, 28.9. Spectra data are consistent with those reported in the literature [1].



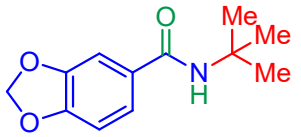
2r

N-(*tert*-Butyl)-4-methoxybenzamide (2r): Synthesized with 24 hours of stirring, in accordance with the general procedure outlined in section 2.2. White solid (565 mg, 91% yield). R_f (ethyl acetate:n-hexane, 1:4): 0.27. m.p. 117-118 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 8.4 Hz, 2H), 6.89 (d, J = 8.4 Hz, 2H), 5.88 (bs, 1H), 3.83 (s, 3H), 1.47 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 161.9, 128.3, 128.2, 113.6, 55.3, 51.4, 28.9. Spectra data are consistent with those reported in the literature [4].



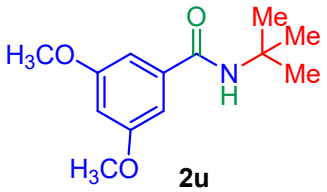
2s

4-(Benzyloxy)-N-(*tert*-butyl)benzamide (2s): Synthesized with 24 hours of stirring, in accordance with the general procedure outlined in section 2.2. Pale yellow solid (748 mg, 88% yield). R_f (ethyl acetate:n-hexane, 1:4): 0.18. m.p. 108-109 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.66 (m, 2H), 7.46-7.31 (m, 5H), 6.99-6.89 (m, 2H), 5.89 (bs, 1H), 5.15 (s, 2H), 1.45 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 161.0, 136.4, 128.7, 128.5, 128.4, 128.2, 127.5, 114.5, 70.0, 51.5, 29.0. Spectra data are consistent with those reported in the literature [7].



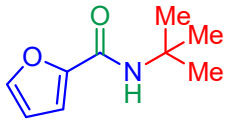
2t

N-(*tert*-Butyl)benzo[d][1,3]dioxole-5-carboxamide (2t): Synthesized with 24 hours of stirring, in accordance with the general procedure outlined in section 2.2. Pale yellow solid (610 mg, 92% yield). R_f (ethyl acetate:n-hexane, 1:4): 0.17. m.p. 106-107 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.21 (m, 2H), 6.81-6.76 (m, 1H), 6.01 (s, 2H), 5.84 (bs, 1H), 1.45 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 149.9, 147.9, 130.3, 121.2, 107.8, 107.5, 101.6, 51.6, 28.9. Spectra data are consistent with those reported in the literature [7].



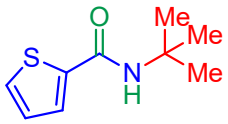
2u

N-(*tert*-Butyl)-3,5-dimethoxybenzamide (2u): Synthesized with 24 hours of stirring, in accordance with the general procedure outlined in section 2.2. Pale yellow solid (633 mg, 89% yield). R_f (ethyl acetate:n-hexane, 1:4): 0.18. m.p. 112-113 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (d, J = 2.1 Hz, 2H), 6.53 (t, J = 2.1 Hz, 1H), 5.93 (bs, 1H), 3.79 (s, 6H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 160.9, 138.2, 104.7, 103.2, 55.6, 51.6, 28.9. Spectra data are consistent with those reported in the literature [3].



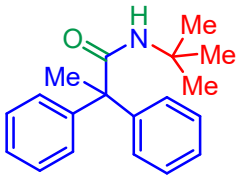
2x

N-(*tert*-Butyl)furan-2-carboxamide (2x): Synthesized with 24 hours of stirring, in accordance with the general procedure outlined in section 2.1. White solid (421 mg, 84% yield). R_f (ethyl acetate:n-hexane, 1:4): 0.34. m.p. 98-99 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.37 (m, 1H), 7.04 (d, J = 3.4 Hz, 1H), 6.48-6.46 (m, 1H), 5.98 (bs, 1H), 1.45 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 148.7, 143.2, 113.4, 112.1, 51.4, 28.9. Spectra data are consistent with those reported in the literature [7].



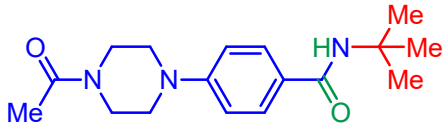
2y

N-(*tert*-Butyl)thiophene-2-carboxamide (2y): Synthesized with 24 hours of stirring, in accordance with the general procedure outlined in section 2.1. Pale yellow solid (494 mg, 90% yield). R_f (ethyl acetate:n-hexane, 1:4): 0.33. m.p. 142-144 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.41 (m, 2H), 7.05-7.03 (m, 1H), 5.86 (bs, 1H), 1.46 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 140.5, 129.4, 127.5, 127.4, 52.0, 28.9. Spectra data are consistent with those reported in the literature [7].



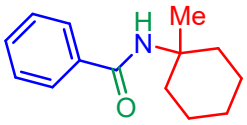
2za

N-(*tert*-Butyl)-2,2-diphenylpropanamide (2za): Synthesized with 36 hours of stirring in accordance with the general procedure outlined in section 2.2. White solid (481 mg, 57% yield). R_f (ethyl acetate:n-hexane, 1:4): 0.24. m.p. 78-79 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.34 (m, 4H), 7.33-7.26 (m, 2H), 7.25-7.20 (m, 4H), 5.46 (bs, 1H), 2.03 (s, 3H), 1.46 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 145.2, 128.6, 128.2, 127.1, 57.0, 51.9, 28.9, 27.2. HRMS (ESI) m/z calculated for $C_{19}H_{24}NO$ $[(M+H)^+]$ 282.1852, found 282.1861.



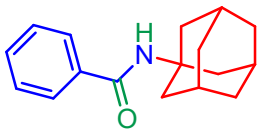
2zb

4-(4-Acetylpiperazin-1-yl)-N-(*tert*-butyl)benzamide (2zb): Synthesized with 24 hours of stirring, in accordance with the general procedure outlined in section 2.2. Pale yellow semi-solid (737 mg, 81% yield). R_f (ethyl acetate:n-hexane, 1:4): 0.13. ^{1}H NMR (400 MHz, $CDCl_3$+DMSO-d_6) δ 7.78 (d, J = 8.6 Hz, 2H), 6.97 (d, J = 8.6 Hz, 2H), 5.84 (bs, 1H), 3.59-3.55 (m, 4H), 3.38-3.33 (m, 4H), 2.04 (s, 3H), 1.45 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$+DMSO-d_6) δ 168.4, 166.3, 150.9, 129.4, 128.5, 113.8, 57.3, 51.6, 46.7, 28.8, 21.2. HRMS (ESI) m/z calculated for $C_{17}H_{26}N_3O_2$ $[(M+H)^+]$ 304.2028, found 304.2031.



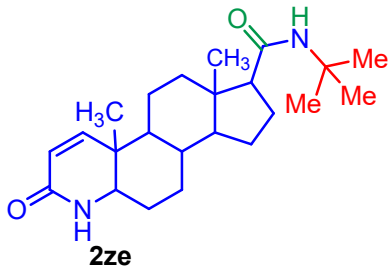
2zc

N-(1-Methylcyclohexyl)benzamide (2zc): Synthesized with 24 hours of stirring, in accordance with the general procedure outlined in section 2.1. Colorless oil (554 mg, 85% yield). R_f (ethyl acetate:n-hexane, 1:4): 0.26. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.66 (m, 2H), 7.43-7.34 (m, 3H), 5.85 (bs, 1H), 2.15-1.84 (m, 2H), 1.60-1.16 (m, 11H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 136.1, 131.0, 128.4, 126.7, 53.3, 36.7, 26.1, 25.5, 22.0. HRMS (ESI) m/z calculated for $C_{14}H_{20}NO$ $[(M+H)^+]$ 218.1547, found 218.1551.



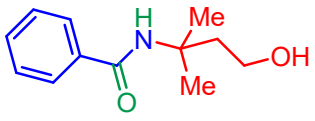
2zd

N-((3s,5s,7s)-Adamantan-1-yl)benzamide (2zd): Synthesized with 24 hours of stirring, in accordance with the general procedure outlined in section 2.1. White solid (551 mg, 72% yield). R_f (ethyl acetate:n-hexane, 1:4): 0.39. m.p. 126-127 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 7.4 Hz, 2H), 7.41 (t, J = 7.2 Hz, 1H), 7.35 (t, J = 7.4 Hz, 2H), 5.87 (bs, 1H), 2.08 (s, 9H), 1.68 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 136.0, 130.9, 128.4, 126.7, 52.3, 41.6, 36.3, 29.5. Spectra data are consistent with those reported in the literature [8].



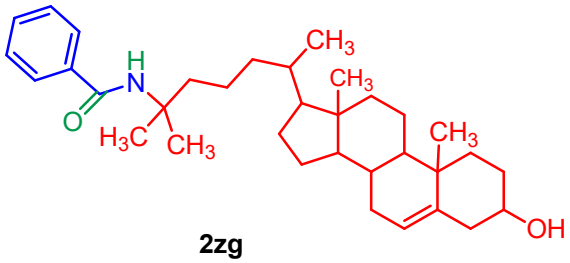
2ze

N-(*tert*-Butyl)-4a,6a-dimethyl-2-oxo-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-1H-indeno[5,4-f]quinoline-7-carboxamide (2ze): Synthesized with 36 hours of stirring, in accordance with the general procedure outlined in section 2.2. Colorless oil (882 mg, 84% yield). R_f (ethyl acetate:n-hexane, 1:4): 0.14. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (d, J = 9.8 Hz, 1H), 5.82 (d, J = 9.8, 1H), 5.43 (bs, 1H), 5.09 (bs, 1H), 3.41-3.25 (m, 1H), 2.28-2.12 (m, 1H), 2.09-1.96 (m, 2H), 1.84-1.68 (m, 4H), 1.63-1.58 (m, 2H), 1.54-1.42 (m, 2H), 1.38 (s, 9H), 1.32-1.23 (m, 2H), 1.20-1.03 (m, 3H), 1.00 (s, 3H), 0.72 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 166.4, 150.8, 123.1, 59.7, 57.6, 55.7, 51.1, 47.6, 44.0, 39.5, 38.5, 35.4, 29.5, 29.1, 26.1, 24.3, 23.4, 21.3, 13.3, 12.0. Spectra data are consistent with those reported in the literature [9].



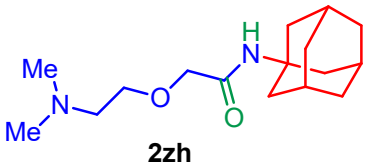
2zf

N-(4-Hydroxy-2-methylbutan-2-yl)benzamide (2zf): Synthesized with 24 hours of stirring, in accordance with the general procedure outlined in section 2.1. Colorless oil (503 mg, 81% yield). R_f (ethyl acetate:n-hexane, 1:4): 0.27. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74-7.72 (m, 2H), 7.52-7.48 (m, 1H), 7.43-7.40 (m, 2H), 5.79 (bs, 1H), 4.46 (t, J = 5.2 Hz, 2H), 2.11 (t, J = 5.2 Hz, 2H), 1.62 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.0, 136.4, 132.7, 128.6, 128.4, 64.4, 58.0, 38.1, 27.6. Spectra data are consistent with those reported in the literature [10].



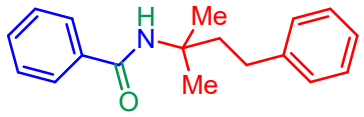
2zg

N-(6-(3-Hydroxy-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-17-yl)-2-methylheptan-2-yl)benzamide (2zg): Synthesized with 24 hours of stirring, in accordance with the general procedure outlined in section 2.1. White solid (956 mg, 63% yield). R_f (ethyl acetate:n-hexane, 1:4): 0.11. m.p. 102-103 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.66 (m, 2H), 7.42-7.39 (m, 1H), 7.38-7.34 (m, 2H), 5.87 (bs, 1H), 5.37 (d, J = 5.0 Hz, 1H), 3.66-3.64 (m, 1H), 3.24-3.22 (m, 1H), 2.45-2.42 (m, 1H), 2.27-2.24 (m, 1H), 2.06-2.04 (m, 1H), 1.99-1.96 (m, 2H), 1.88-1.84 (m, 2H), 1.65-1.61 (m, 2H), 1.59-1.23 (m, 13H), 1.18 (s, 6H), 1.14-1.10 (m, 2H), 1.08-1.02 (m, 5H), 0.98-0.94 (m, 4H), 0.73 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 141.9, 136.1, 130.9, 128.4, 126.6, 122.5, 71.4, 58.2, 57.5, 51.6, 45.1, 43.4, 41.1, 39.4, 38.5, 37.8, 37.6, 37.0, 33.2, 33.0, 30.6, 29.2, 29.1, 29.0, 25.2, 22.1, 21.8, 19.7, 19.1, 12.2. HRMS (ESI) m/z calculated for $C_{34}H_{52}NO_2$ $[(M+H)^+]$ 506.3999, found 506.4014.



2zh

N-((3s,5s,7s)-Adamantan-1-yl)-2-(2-(dimethylamino)ethoxy)acetamide (2zh): Synthesized with 24 hours of stirring, in accordance with the general procedure outlined in section 2.1. Due to the limited stability, compound was precipitated as its hydrochloric acid. White solid (513 mg, 54% yield). m.p. 140-141 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.27 (s, 1H), 3.82 (t, J = 5.0 Hz, 2H), 3.32 (s, 2H), 3.21 (t, J = 5.0 Hz, 2H), 2.73 (s, 6H), 1.97-1.93 (m, 9H), 1.57 (s, 6H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.6, 70.5, 65.1, 55.9, 51.5, 42.8, 41.6, 36.5, 29.4. Spectra data are consistent with those reported in the literature [11].



2zi

N-(2-Methyl-4-phenylbutan-2-yl)benzamide (2zi): Synthesized with 24 hours of stirring, in accordance with the general procedure outlined in section 2.1. Colorless semi-solid (714 mg, 89% yield). R_f (ethyl acetate:n-hexane, 1:4): 0.41. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.64 (m, 2H), 7.50-7.46 (m, 1H), 7.45-7.35 (m, 2H), 7.29-7.24 (m, 2H), 7.21-7.12 (m, 3H), 5.87 (bs, 1H), 2.67 (t, J = 5.0 Hz, 2H), 2.19 (t, J = 5.0 Hz, 2H), 1.52 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 142.1, 135.2, 131.0, 128.6, 128.4, 128.1, 126.7, 125.8, 54.3, 46.5, 30.8, 27.3. Spectra data are consistent with those reported in the literature [12].

References

(1) Park, J.; Park, S.; Jang, G. S.; Kim, R. H.; Jung, J.; Woo, S. K. Weak base-promoted selective rearrangement of oxaziridines to amides via visible-light photoredox catalysis. *Chem. Commun.* **2021**, *57*, 9995-9998.

(2) Ölmez, N. A.; Osman, B. P(HEMA)-SO3H catalyst: preparation, characterization and its catalytic activity in Ritter reaction. *Res. Chem. Intermed.* **2022**, *48*, 4987-5001.

(3) Baum, J. C.; Milne, J. E.; Murry, J. A.; Thiel, O. R. An Efficient and Scalable Ritter Reaction for the Synthesis of tert-Butyl Amides. *J. Org. Chem.* **2009**, *74*, 2207-2209.

(4) Feng, C. L.; Yan, B.; Zhang, M.; Chen, J.-Q.; Ji, M. An efficient synthesis of N-tert-butyl amides by the reaction of tert-butyl benzoate with nitriles catalyzed by Zn(ClO4)2·6H2O. *Chem. Pap.* **2019**, *73*, 535-542.

(5) Yang, W.; Feng, C.; Tang, Y.; Ji, M.; Chen. J. A convenient synthesis of N-tert-butyl amides by the reaction of di-tert-butyl dicarbonate and nitriles catalyzed by Cu(OTf)2. *J. Chem. Res.* **2020**, *44*, 602–608.

(6) Gore, B. S.; Senadi, G. C.; Garkhedkar, A. M.; Wang, J.-J. Efficient Approach to Amide Bond Formation with Nitriles and Peroxides: One-Pot Access to Boronated b-Ketoamides. *Adv. Synth. Catal.* **2017**, *359*, 3014-3021.

(7) Hazarika, N.; Baishya, G. One-Pot Sequential Schmidt and Ritter Reactions for the Synthesis of N-tert-Butyl Amides. *Eur. J. Org. Chem.* **2014**, 5686–5690.

(8) Ramkumar, R.; Chandrasekaran, S. Catalyst-Free, Metal-Free, and Chemoselective Transamidation of Activated Secondary Amides. *Synthesis* 2019, *51*, 921–932.

(9) Gauthier, Jr. D. R.; Rivera, N. R.; Yang, H.; Schultz, D. M.; Shultz, C. S. Palladium-Catalyzed Carbon Isotope Exchange on Aliphatic and Benzoic Acid Chlorides. *J. Am. Chem. Soc.* 2018, 140, 15596-15600.

(10) Zhang, S.; Zhang, J.; Zou, H. C(sp3)–H oxygenation via alkoxypalladium(II) species: an update for the mechanism. *Chem. Sci*., 2022, 13, 1298–1306.

(11) Klimochkin, Y. N.; Ivleva, E. A. Synthesis and Chemical Transformations of *N*-Adamantylated Amides. *Russ. J. Org. Chem.,* 2022, 58, 669–678.

(12) Xu, Y.; Young, M. C.; Wang, C.; Magness, D. M.; Dong, G. Catalytic C(sp3)H Arylation of Free Primary Amines with an exo Directing Group Generated In Situ. *Angew. Chem. Int. Ed*. 2016, 55, 9084 –9087.

Copies of NMR Spectra of products

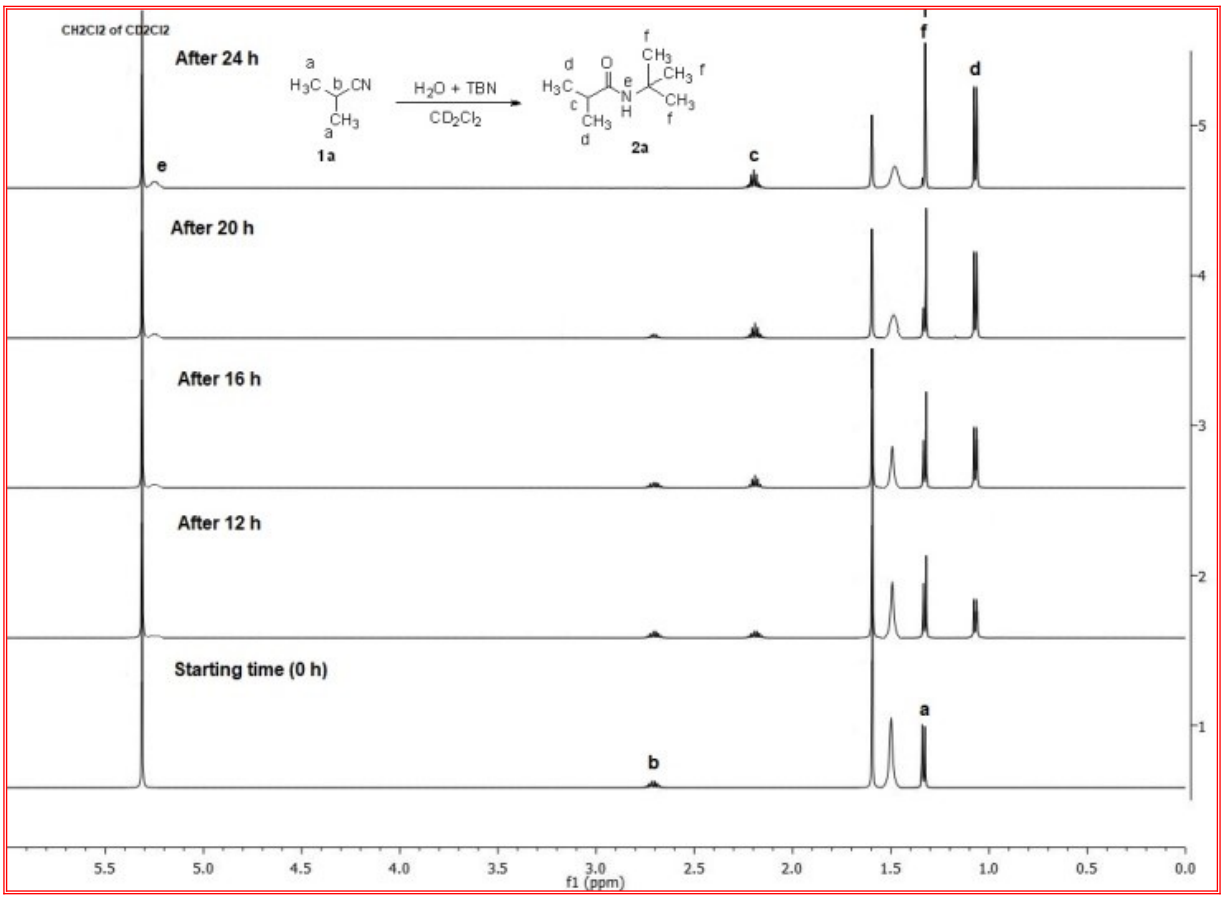


Figure S1. ^{1}H NMR spectroscopic monitoring (0-24 h) of conversion of **1a** into **2a** in CD_2Cl_2 solution. Notice that new peaks (correspond to isopropyl unit of **2a**) gradually appeared at 1.1 ppm (d) and 2.2 ppm (c), while signals at 1.3 ppm (a) and 2.7 ppm (b) of **1a** have disappeared over time.

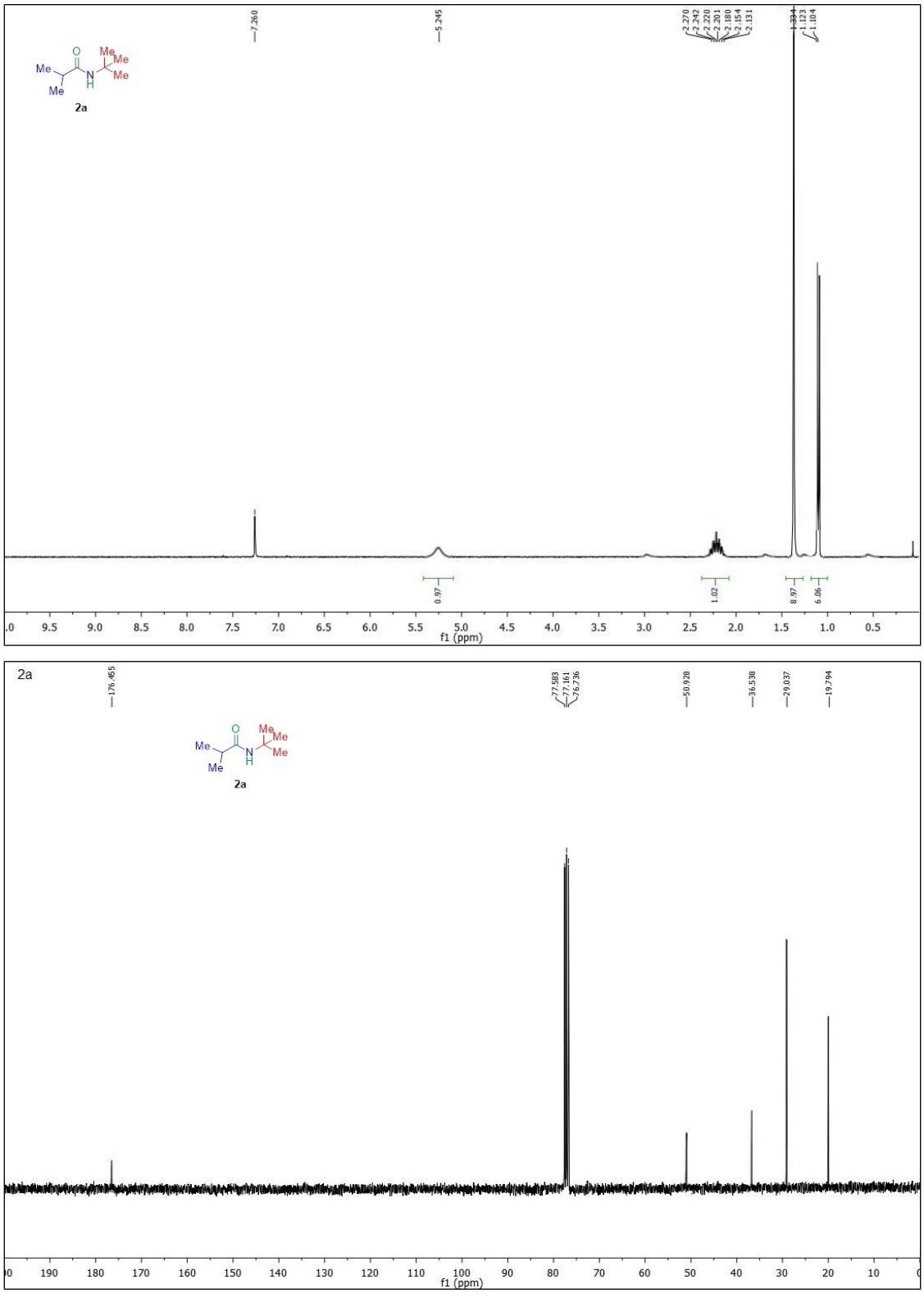


Figure S2. ^{I}H (top) and ^{13}C (bottom) spectra of **2a** in $CDCl_3$.

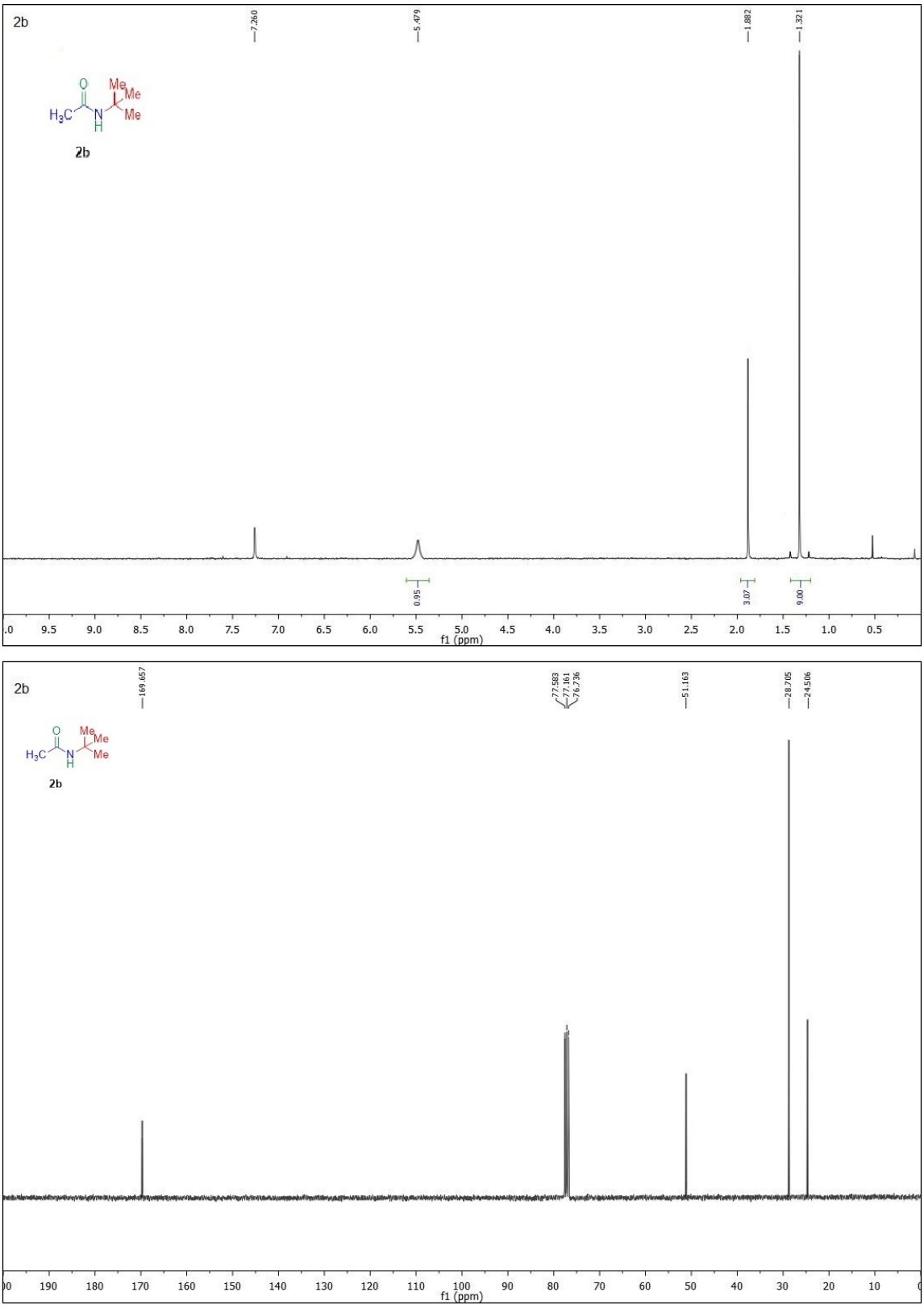


Figure S3. ^{1}H (top) and ^{13}C (bottom) spectra of **2b** in $CDCl_3$.

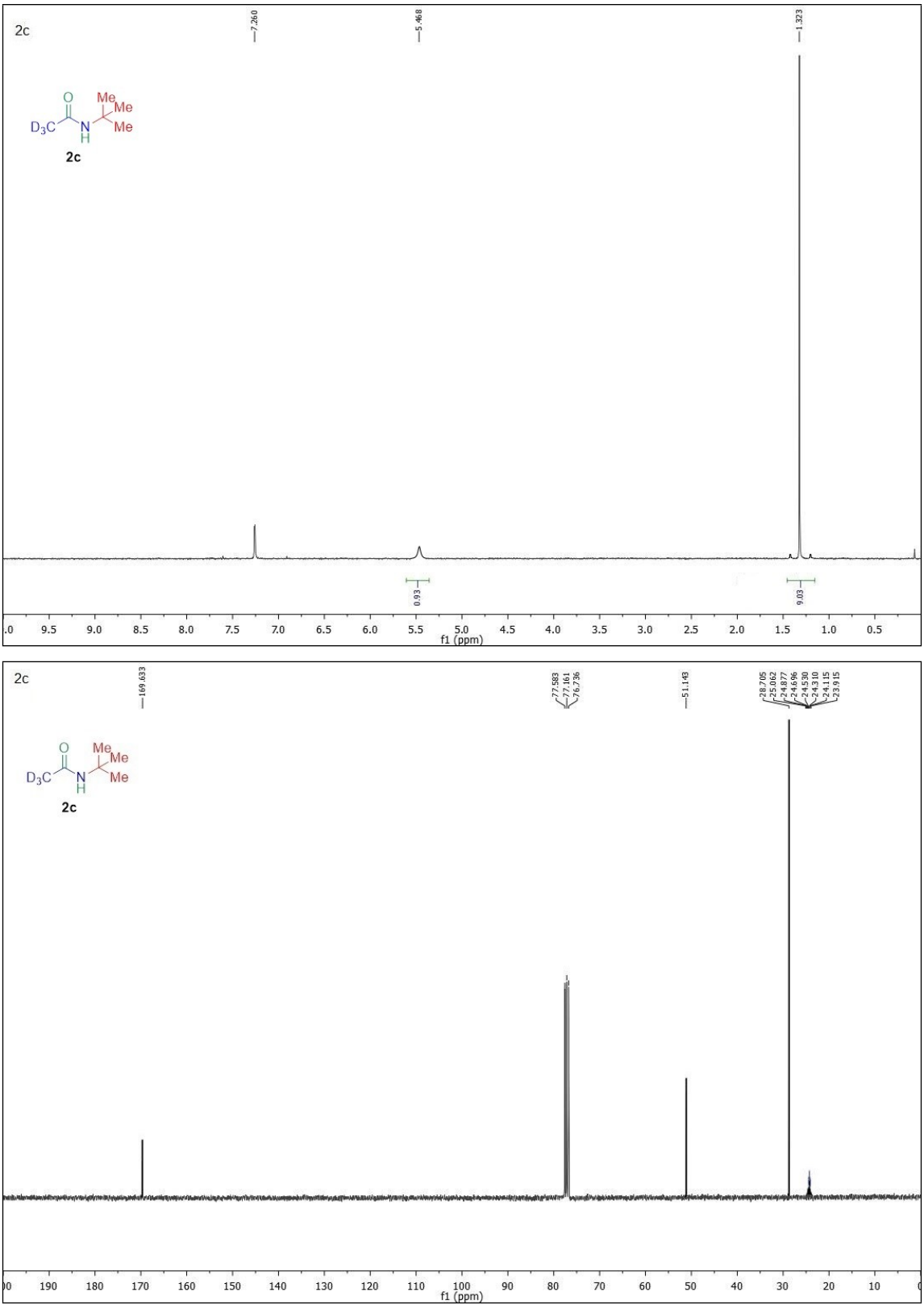


Figure S4. ^{1}H (top) and ^{13}C (bottom) spectra of **2c** in $CDCl_3$.

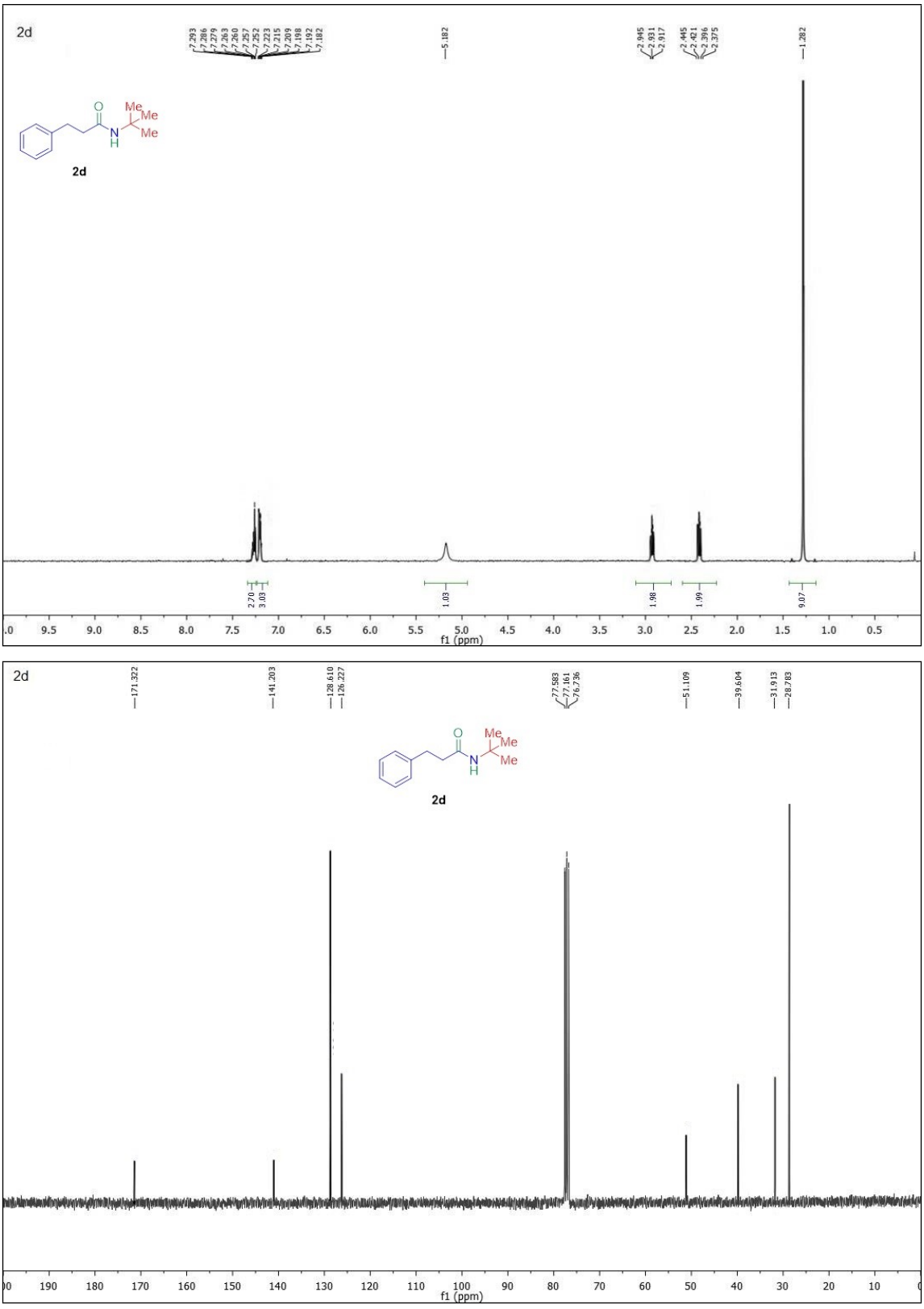


Figure S5. ^{1}H (top) and ^{13}C (bottom) spectra of **2d** in $CDCl_3$.

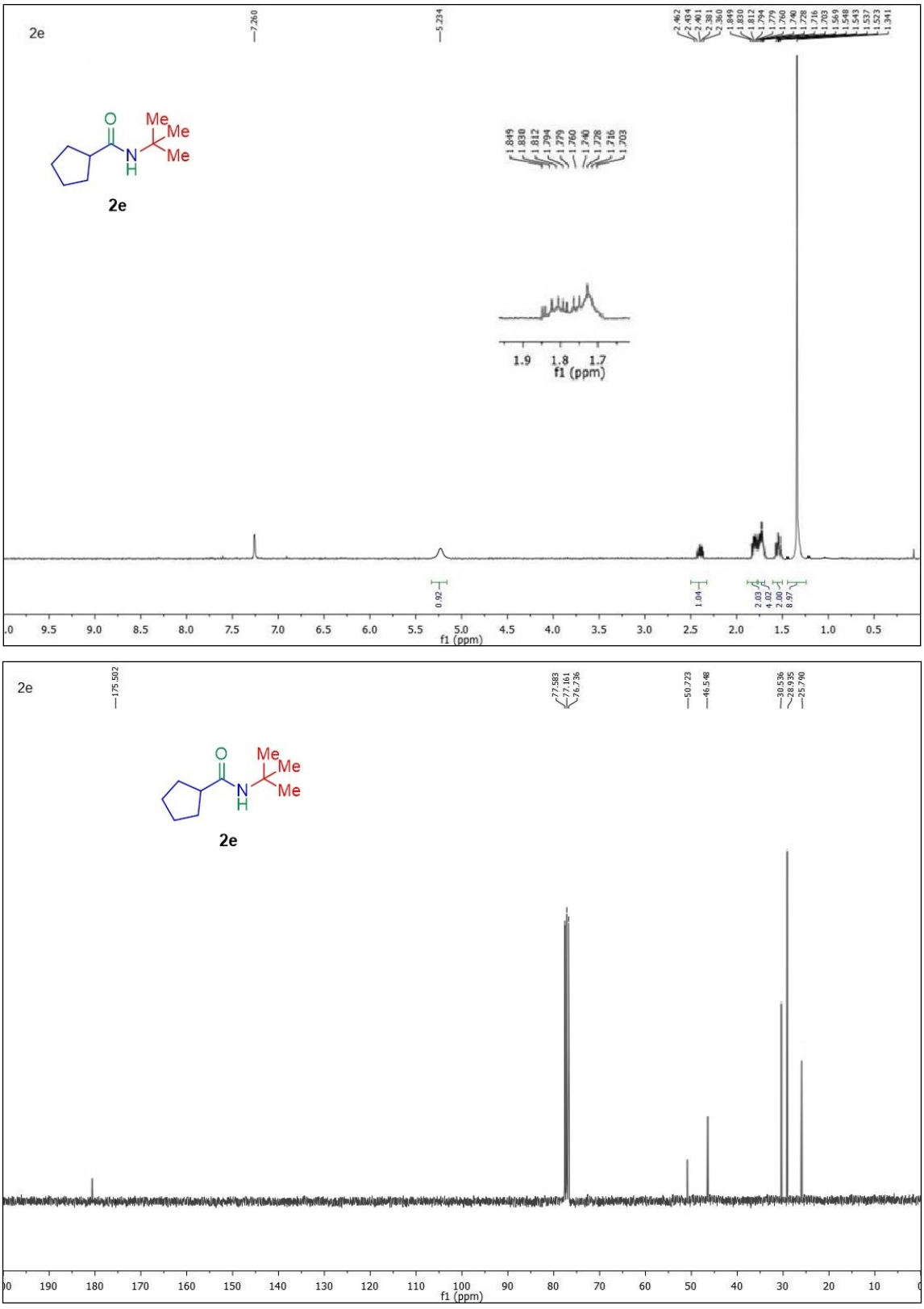


Figure S6. ^{1}H (top) and ^{13}C (bottom) spectra of **2e** in $CDCl_3$.

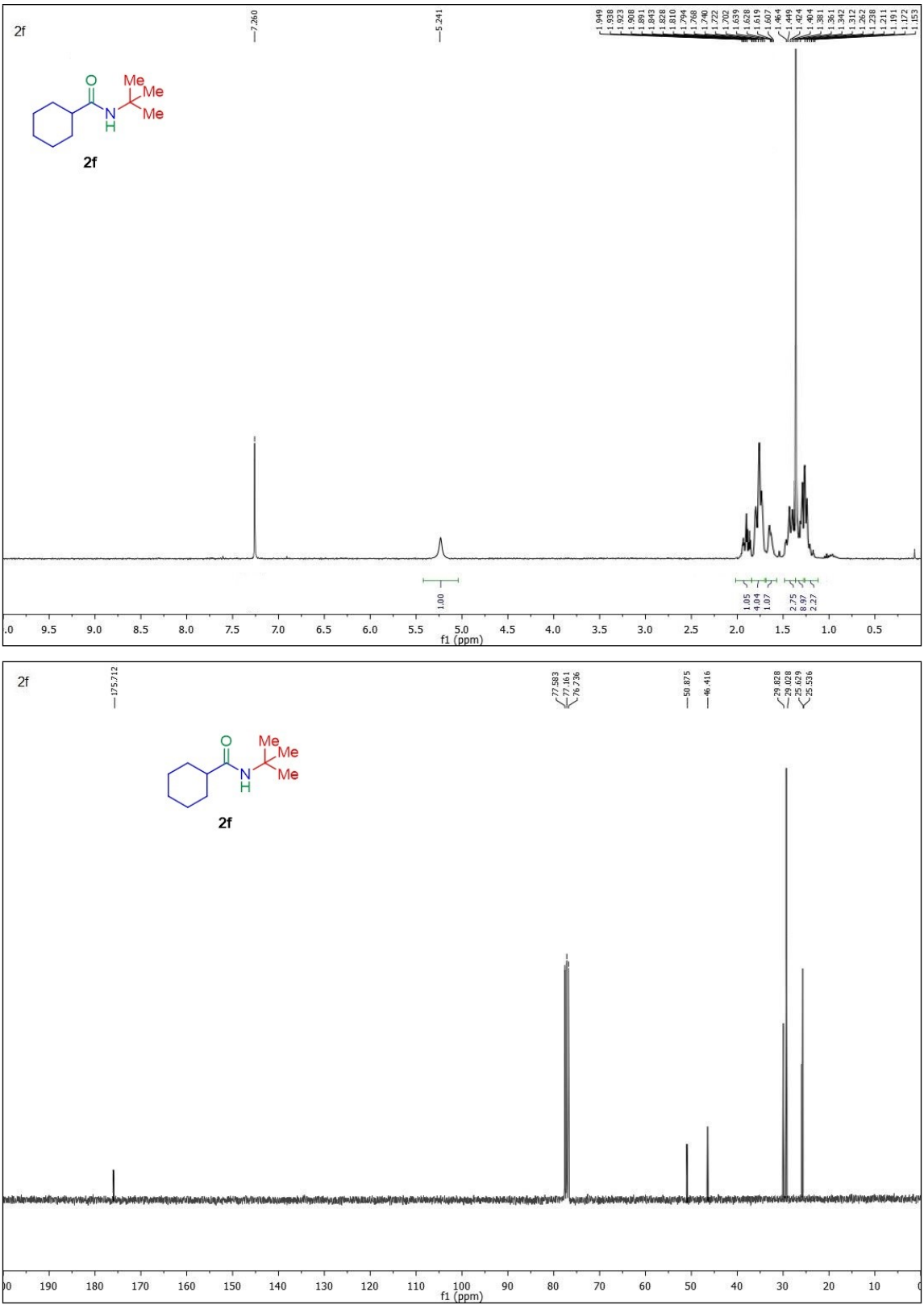


Figure S7. ^{1}H (top) and ^{13}C (bottom) spectra of **2f** in $CDCl_3$.

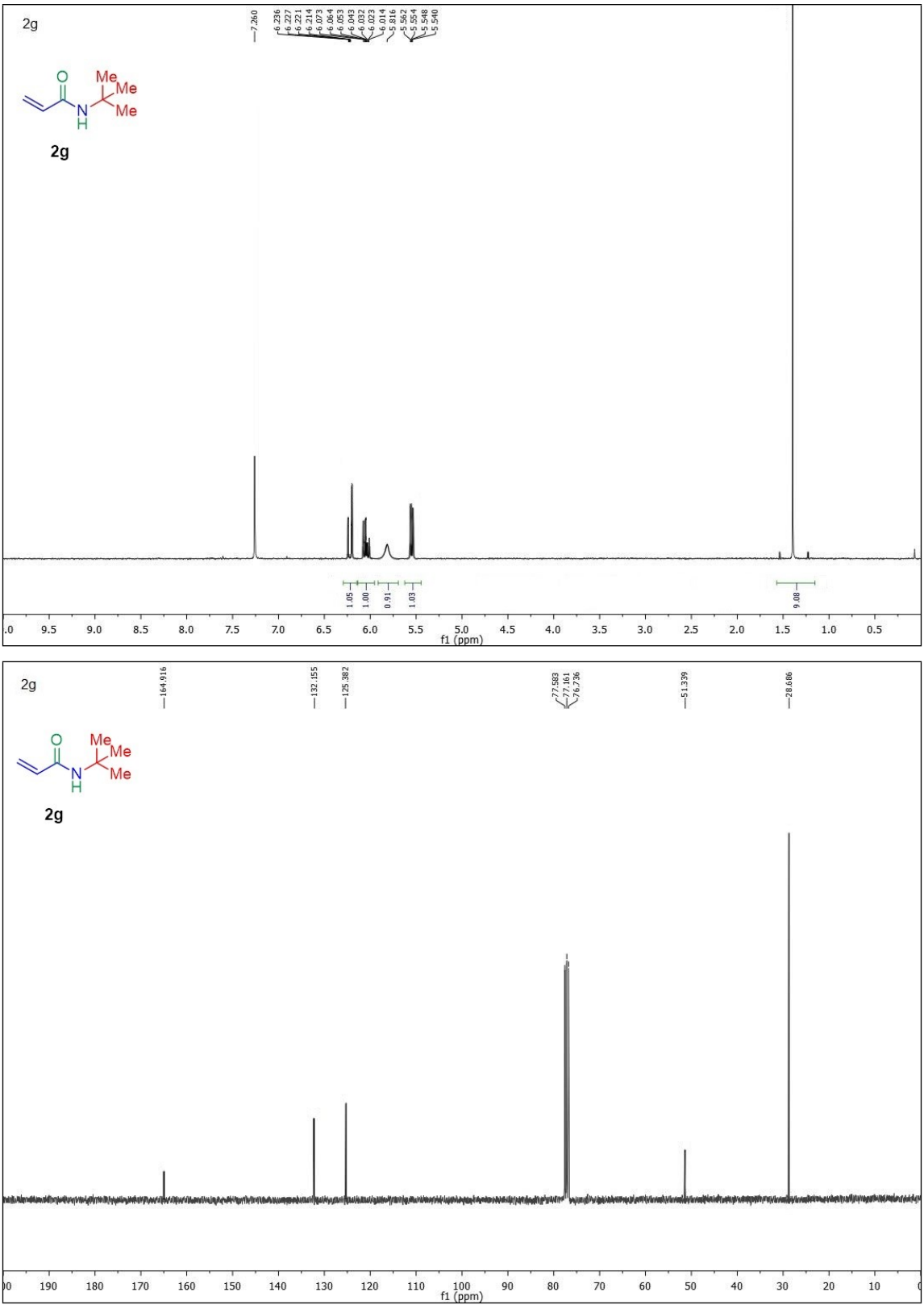


Figure S8. ^{1}H (top) and ^{13}C (bottom) spectra of **2g** in $CDCl_3$.

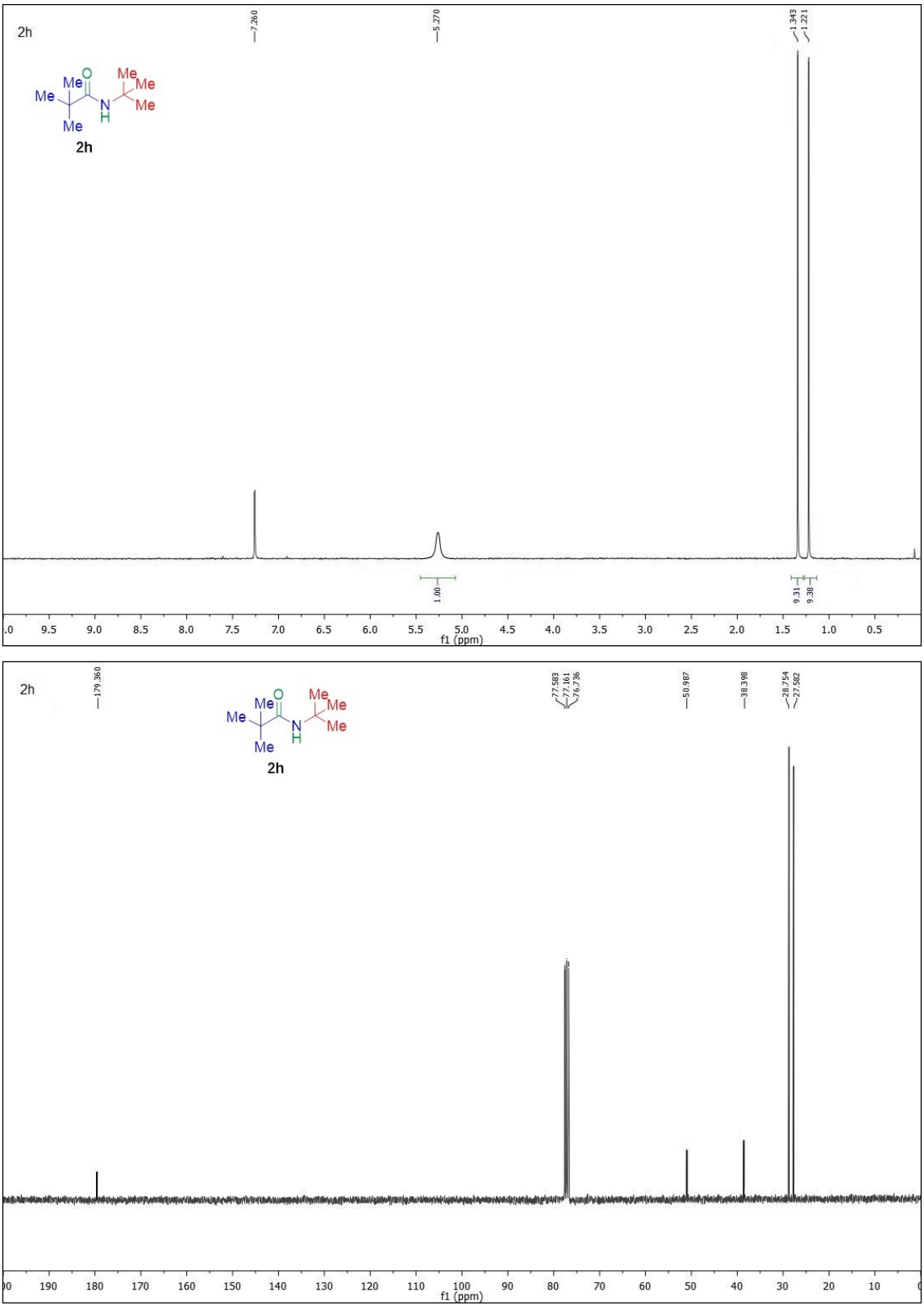


Figure S9. ^{1}H (top) and ^{13}C (bottom) spectra of **2h** in $CDCl_3$.

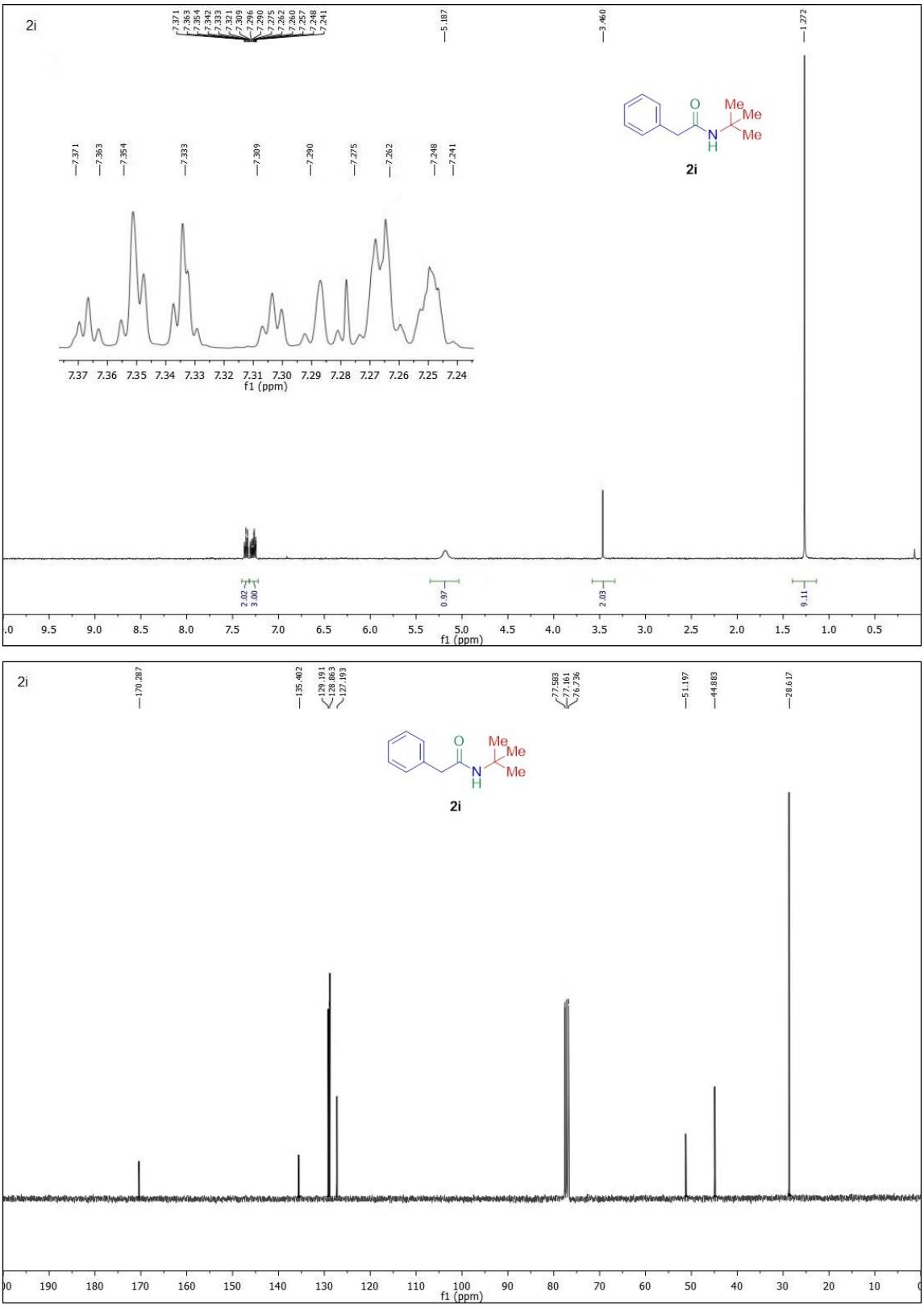


Figure S10. ^{1}H (top) and ^{13}C (bottom) spectra of **2i** in $CDCl_3$.

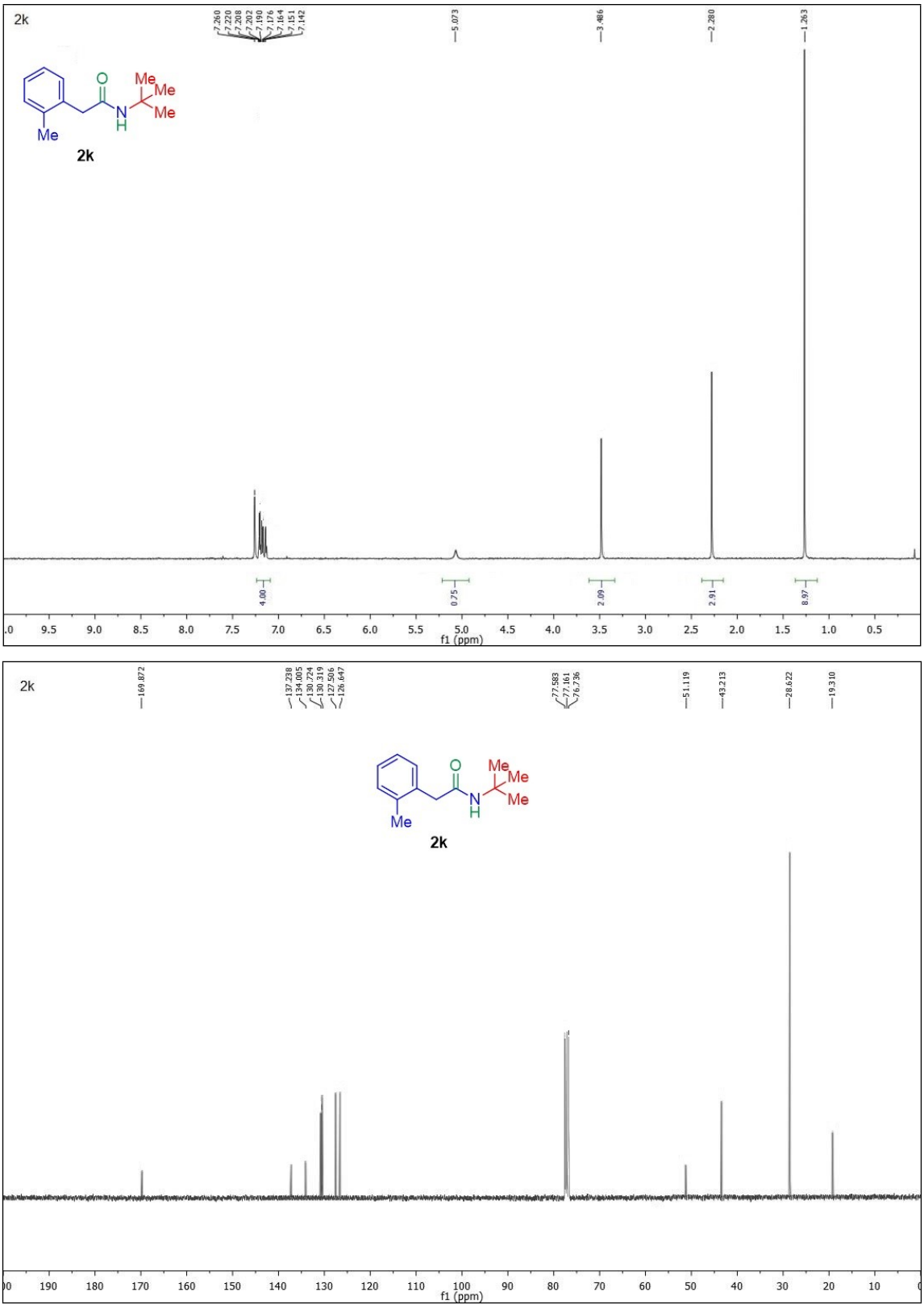


Figure S11. ^{1}H (top) and ^{13}C (bottom) spectra of **2k** in $CDCl_3$.

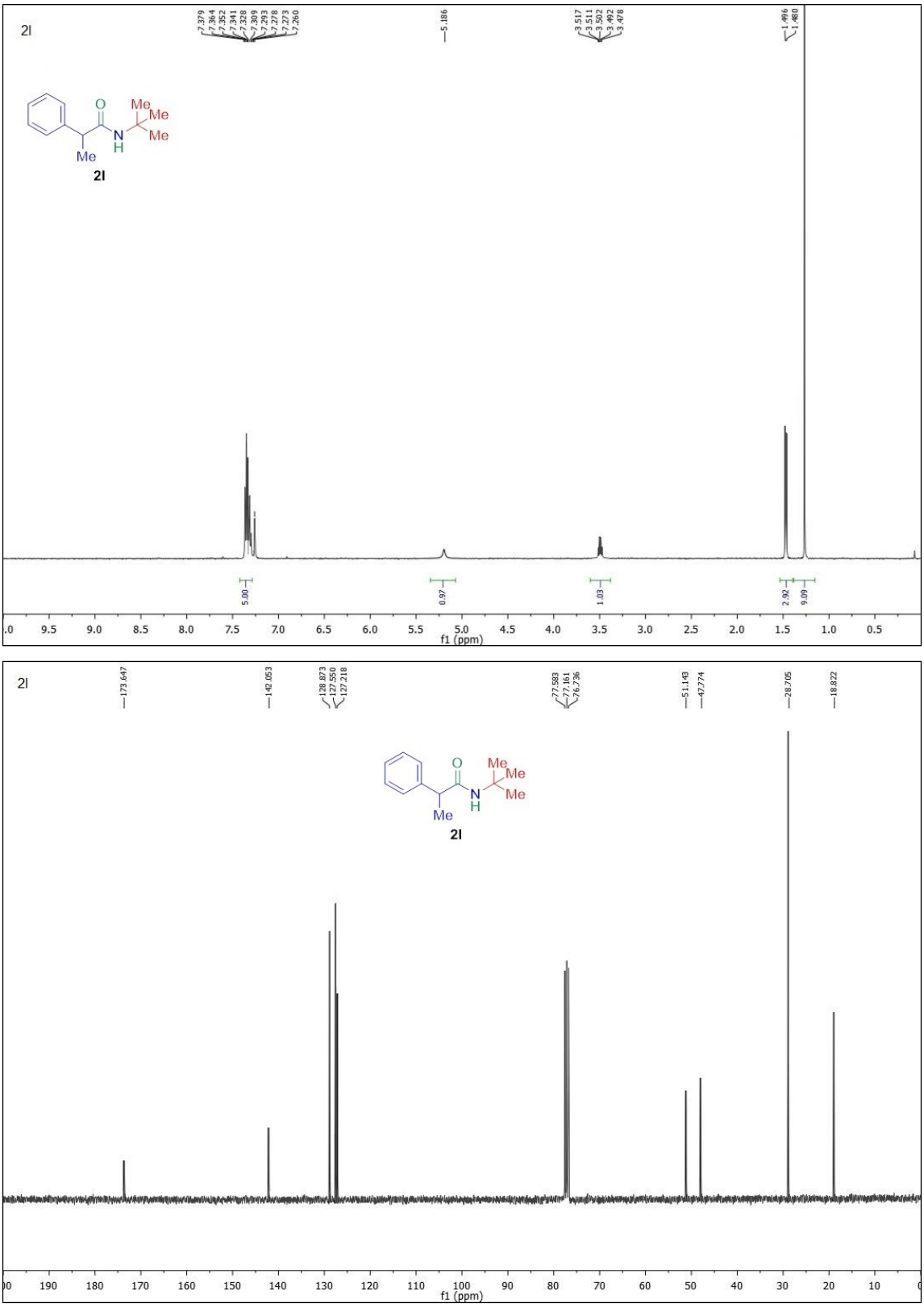


Figure S12. ^{1}H (top) and ^{13}C (bottom) spectra of **2l** in $CDCl_3$.

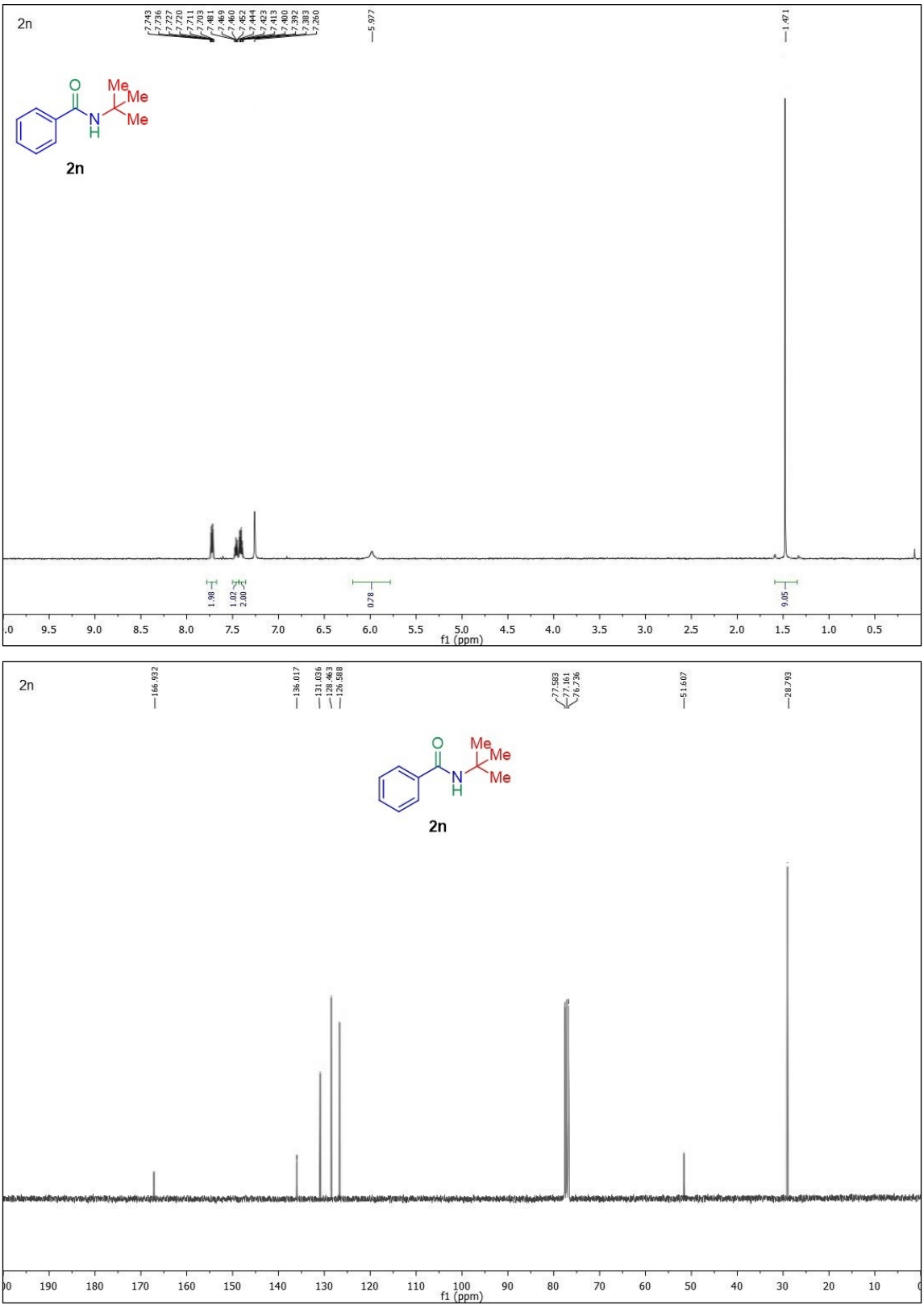


Figure S13. ^{1}H (top) and ^{13}C (bottom) spectra of **2n** in $CDCl_3$.

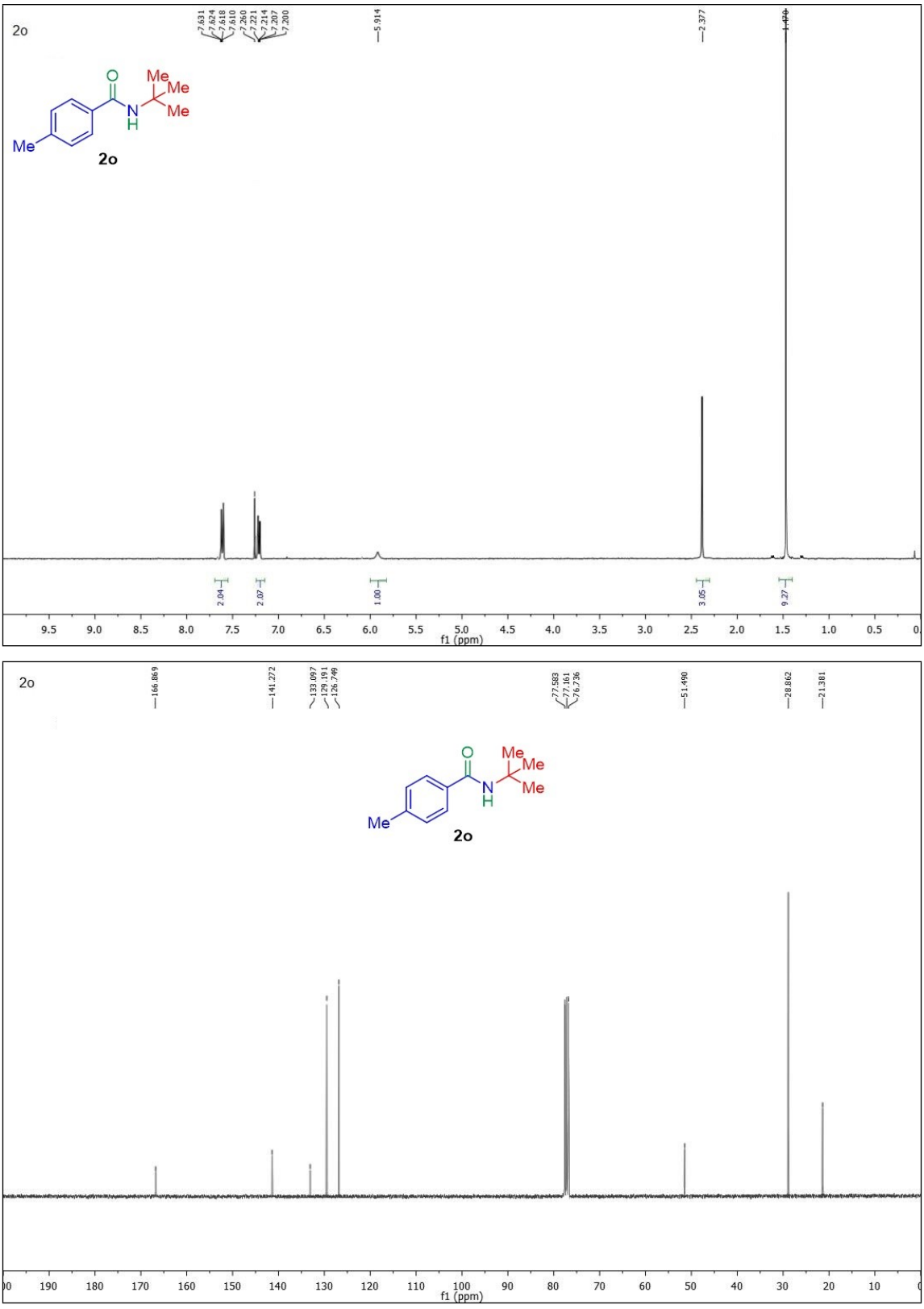


Figure S14. ^{1}H (top) and ^{13}C (bottom) spectra of **2o** in $CDCl_3$.

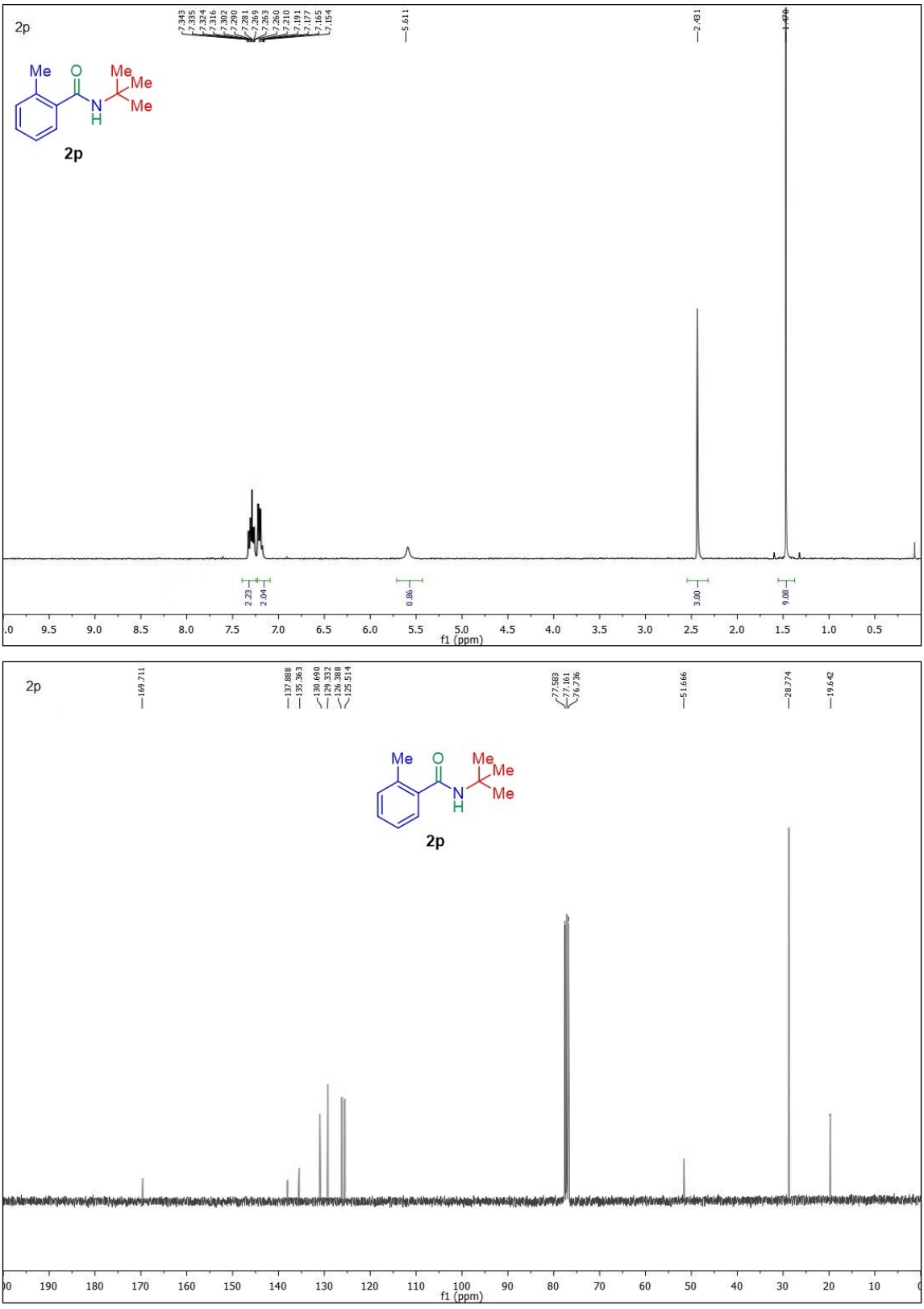


Figure S15. ^{1}H (top) and ^{13}C (bottom) spectra of **2p** in $CDCl_3$.

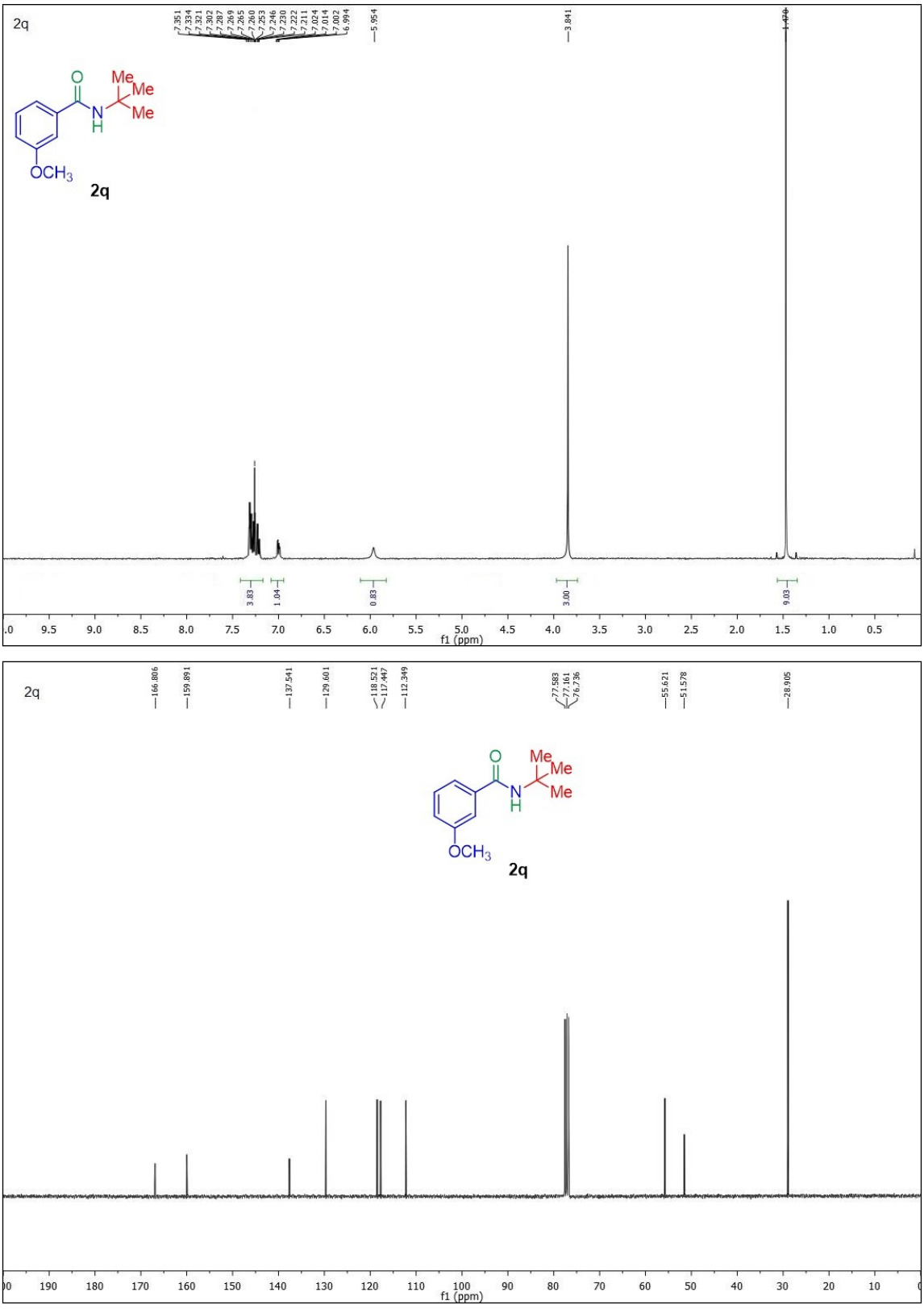


Figure S16. ^{1}H (top) and ^{13}C (bottom) spectra of **2q** in $CDCl_3$.

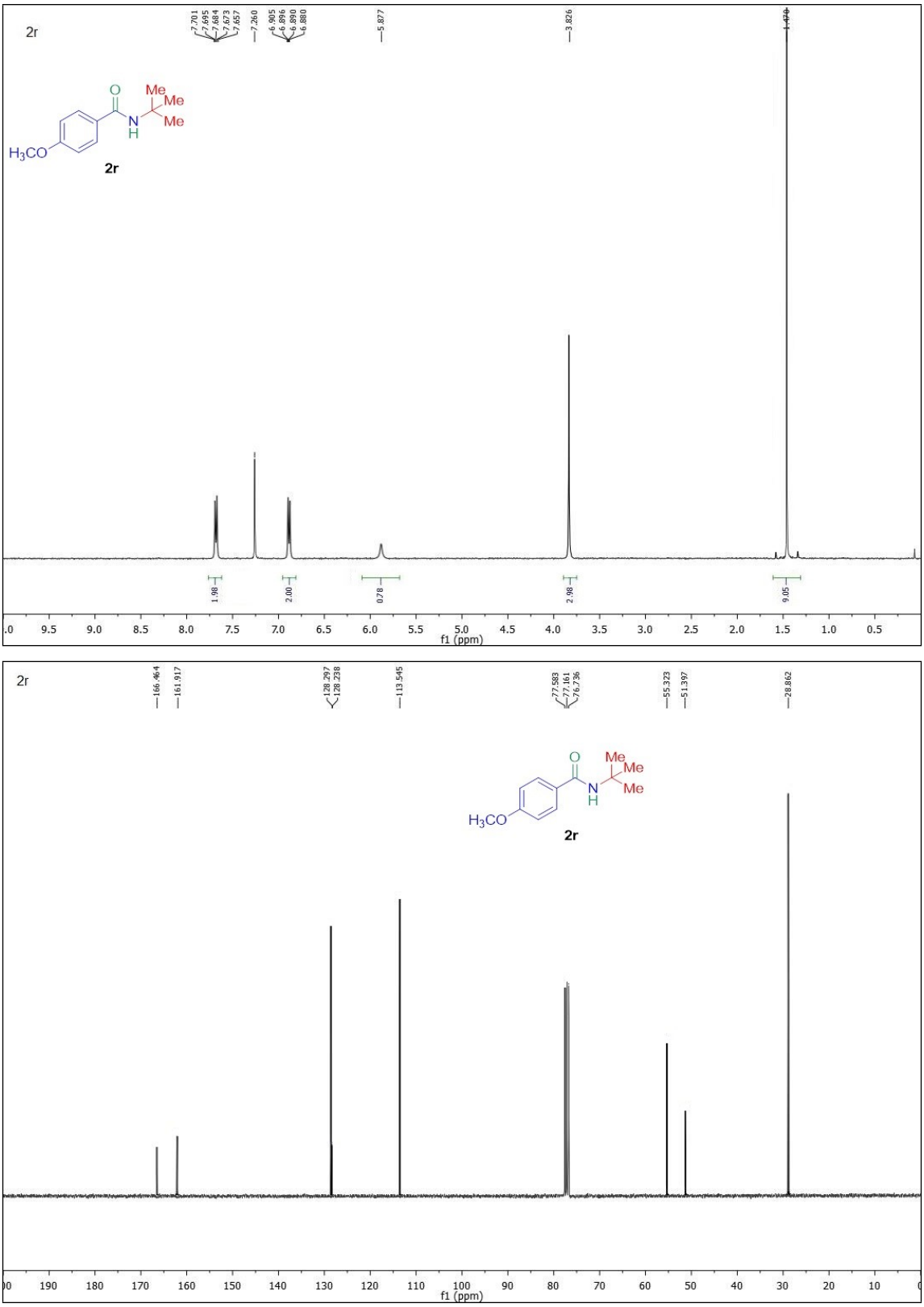


Figure S17. ^{1}H (top) and ^{13}C (bottom) spectra of **2r** in $CDCl_3$.

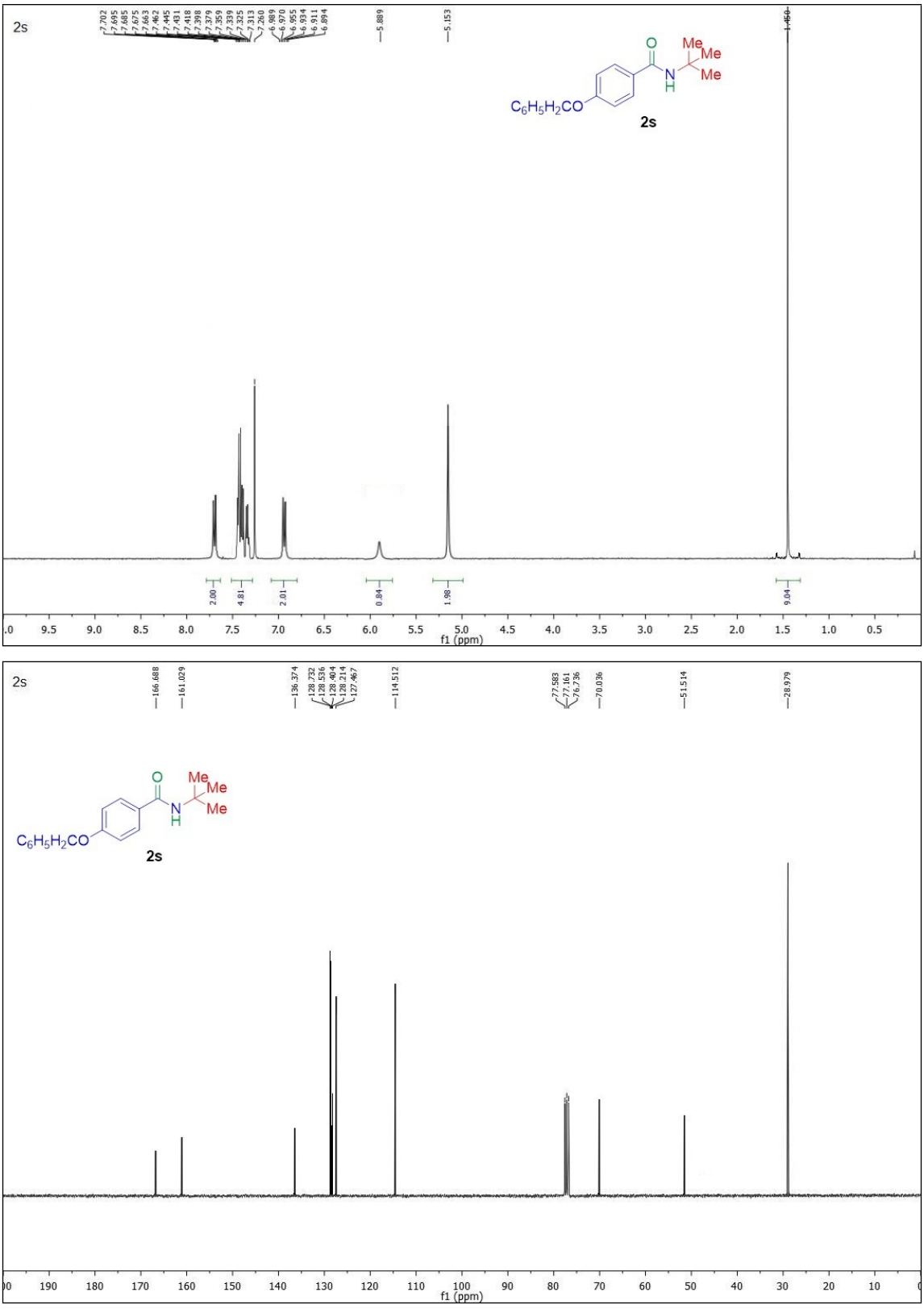


Figure S18. ^{1}H (top) and ^{13}C (bottom) spectra of **2s** in $CDCl_3$.

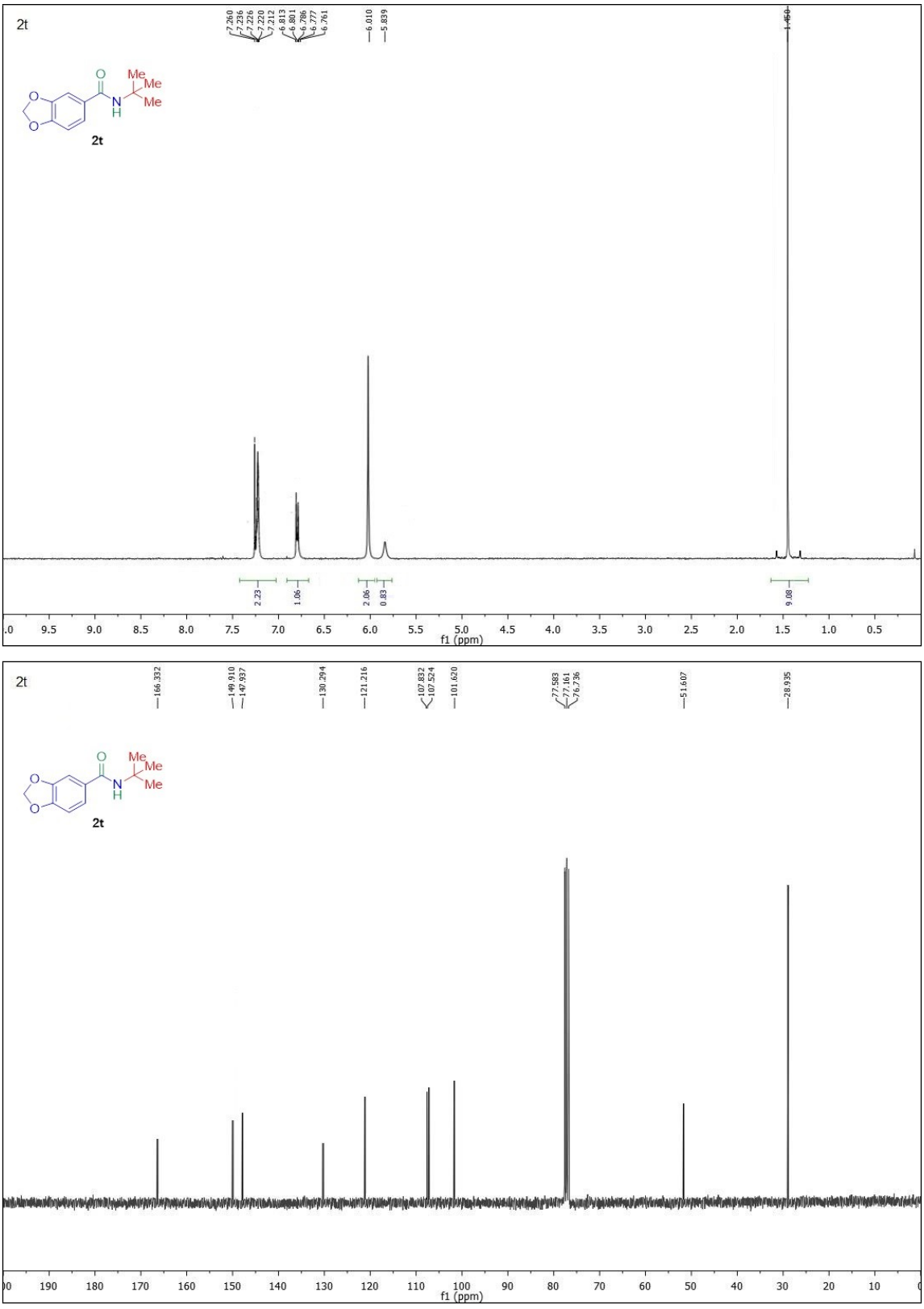


Figure S19. ^{1}H (top) and ^{13}C (bottom) spectra of **2t** in $CDCl_3$.

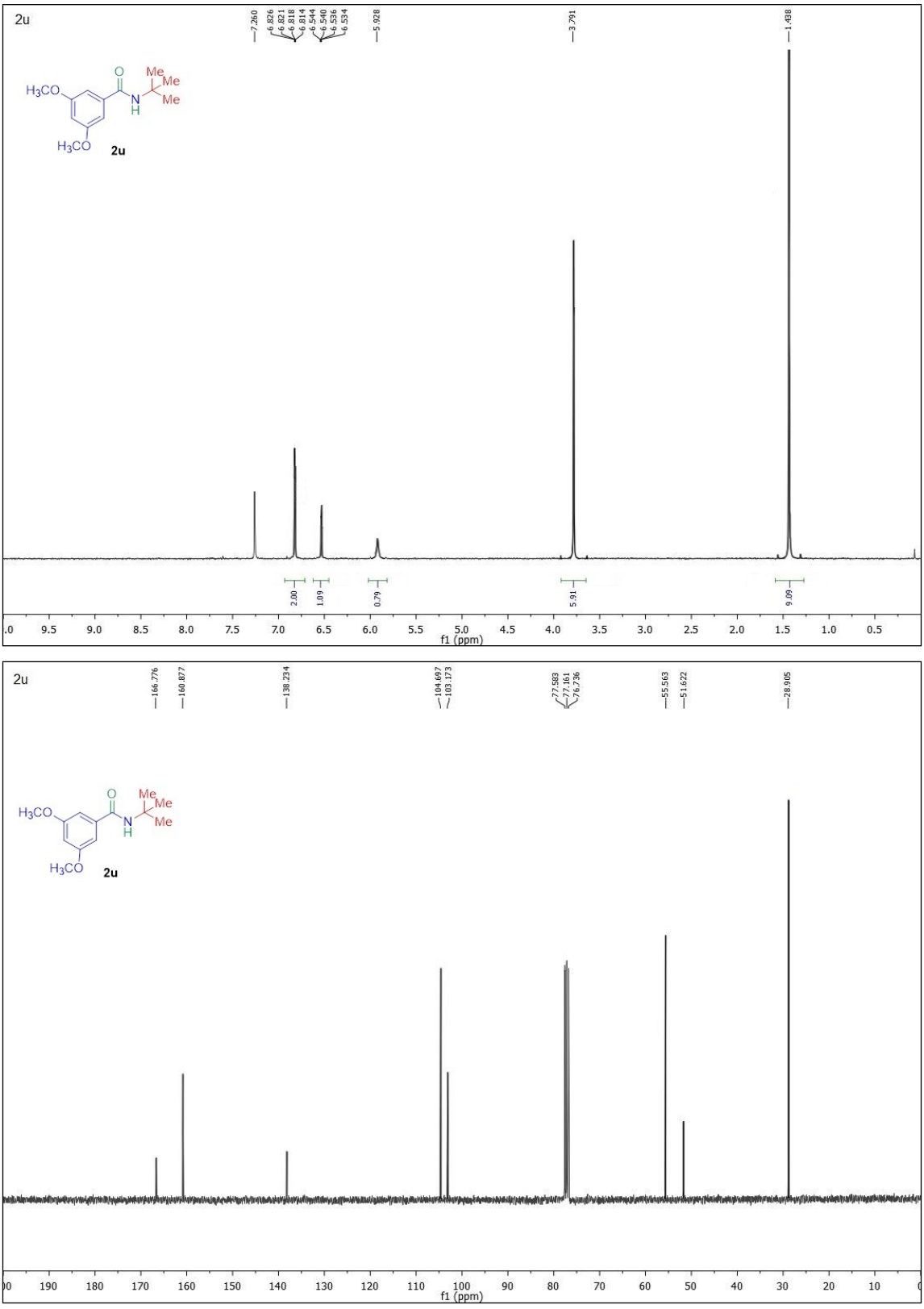


Figure S20. ^{1}H (top) and ^{13}C (bottom) spectra of **2u** in $CDCl_3$.

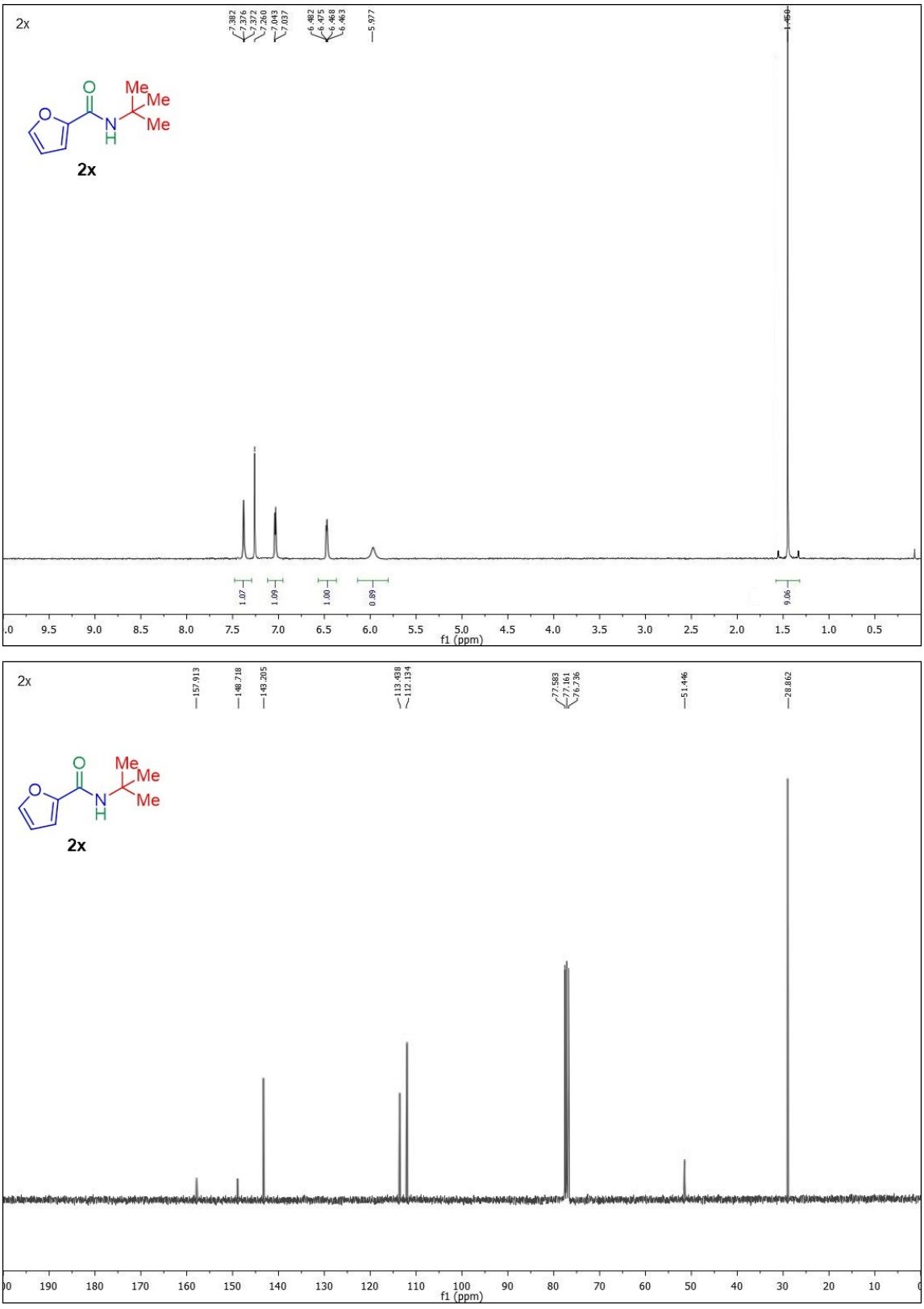


Figure S21. ^{1}H (top) and ^{13}C (bottom) spectra of **2x** in $CDCl_3$.

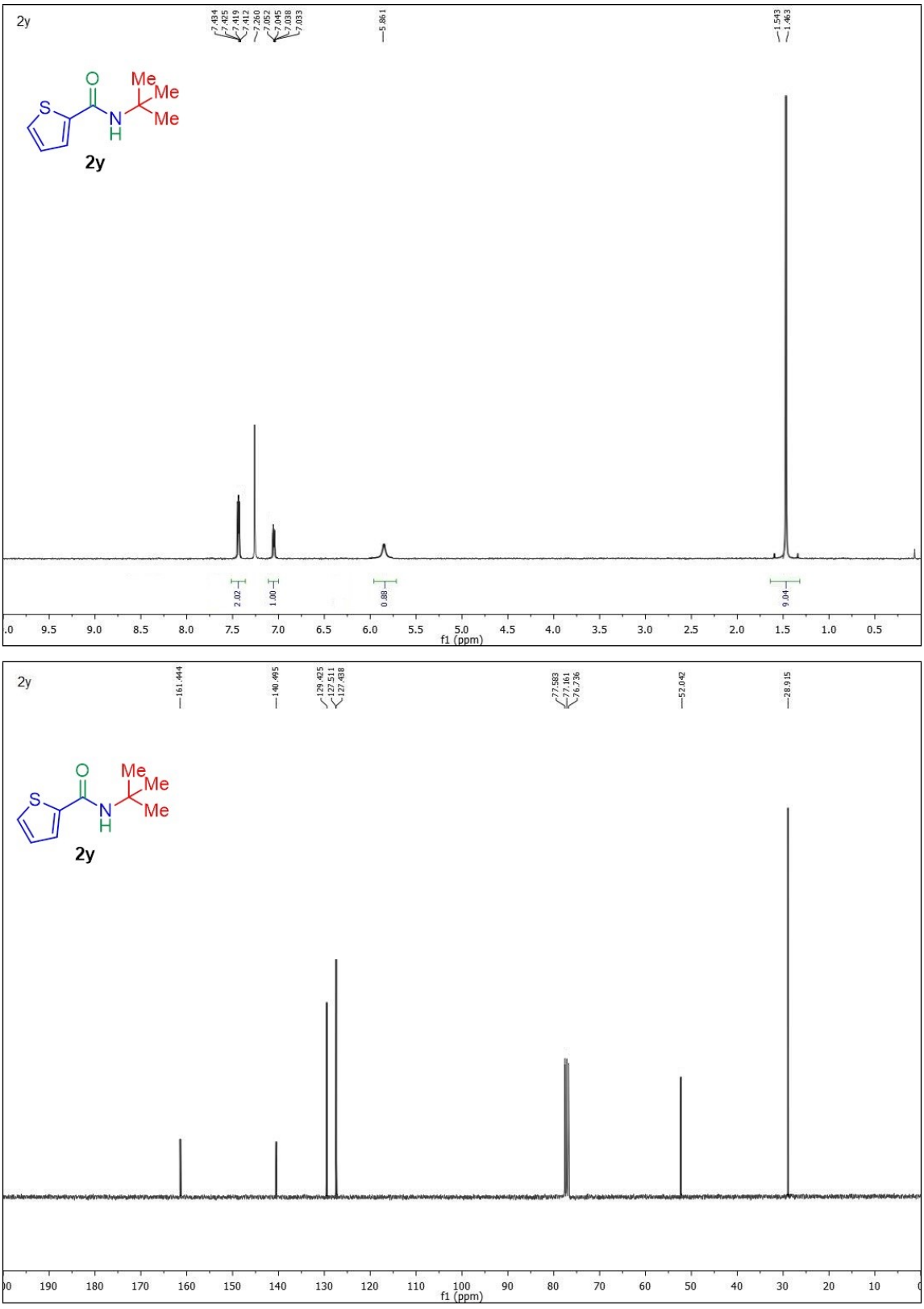


Figure S22. ^{1}H (top) and ^{13}C (bottom) spectra of **2y** in $CDCl_3$.

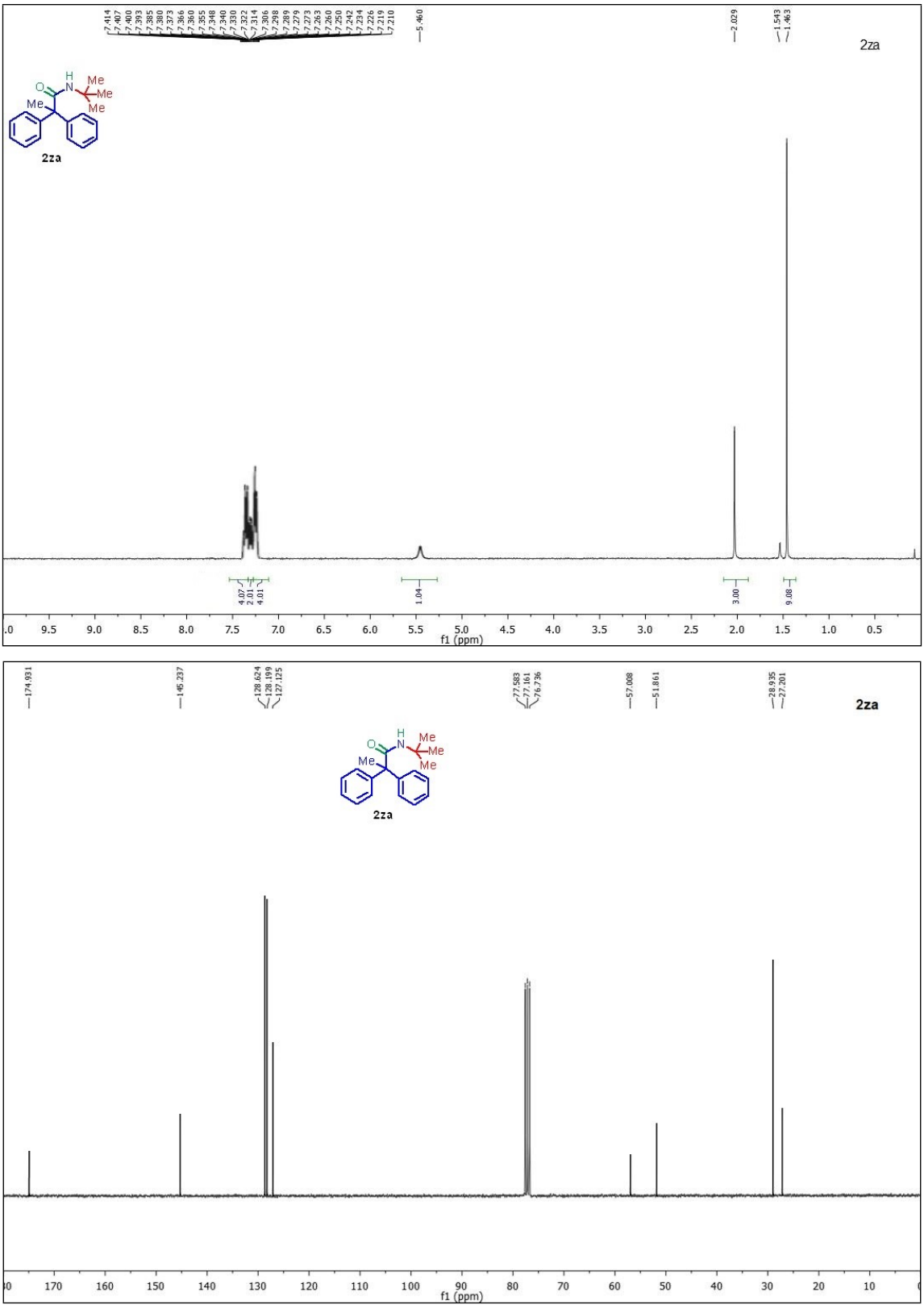


Figure S23. ^{1}H (top) and ^{13}C (bottom) spectra of **2za** in $CDCl_3$.

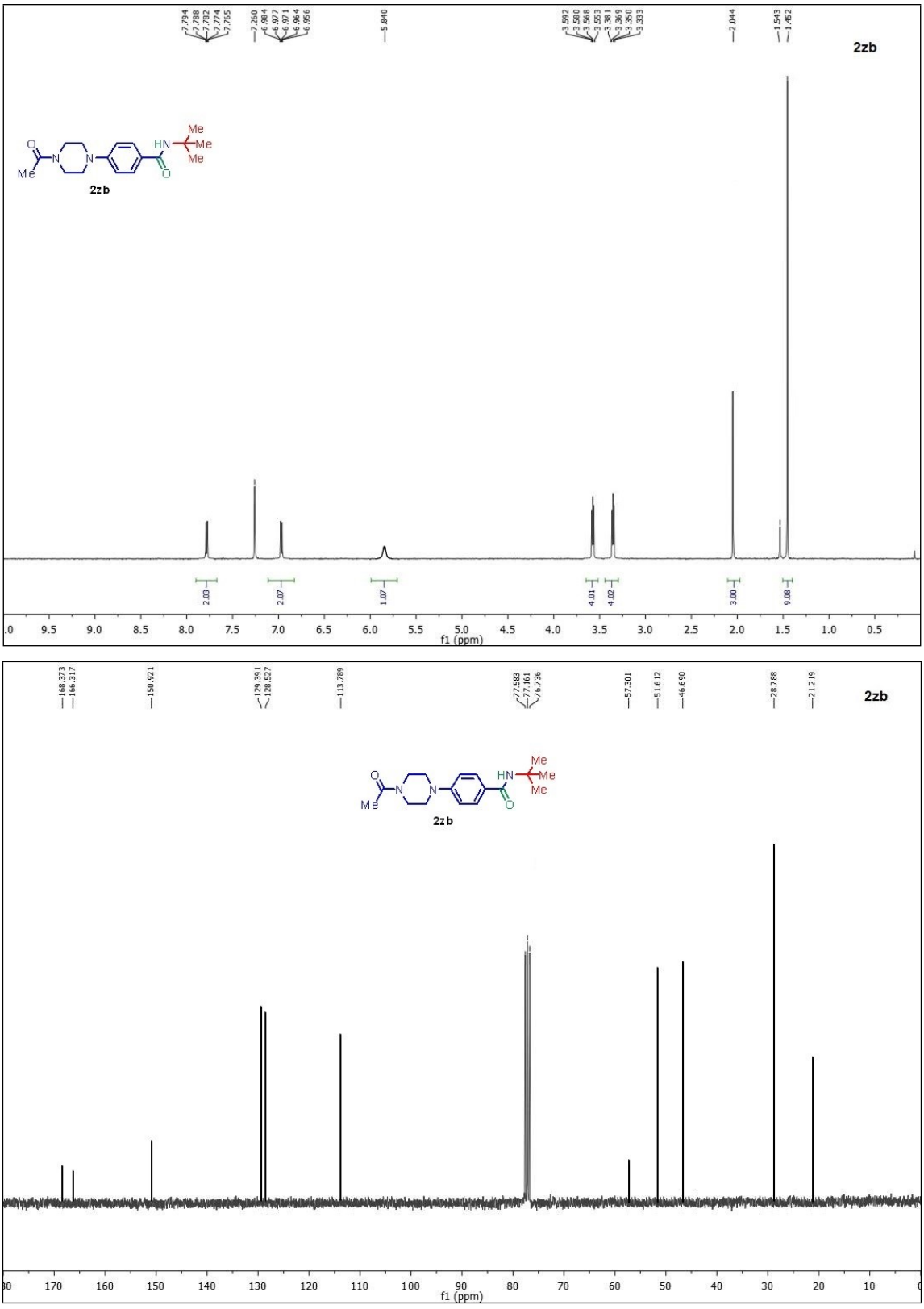


Figure S24. ^{1}H (top) and ^{13}C (bottom) spectra of **2zb** in $CDCl_3$.

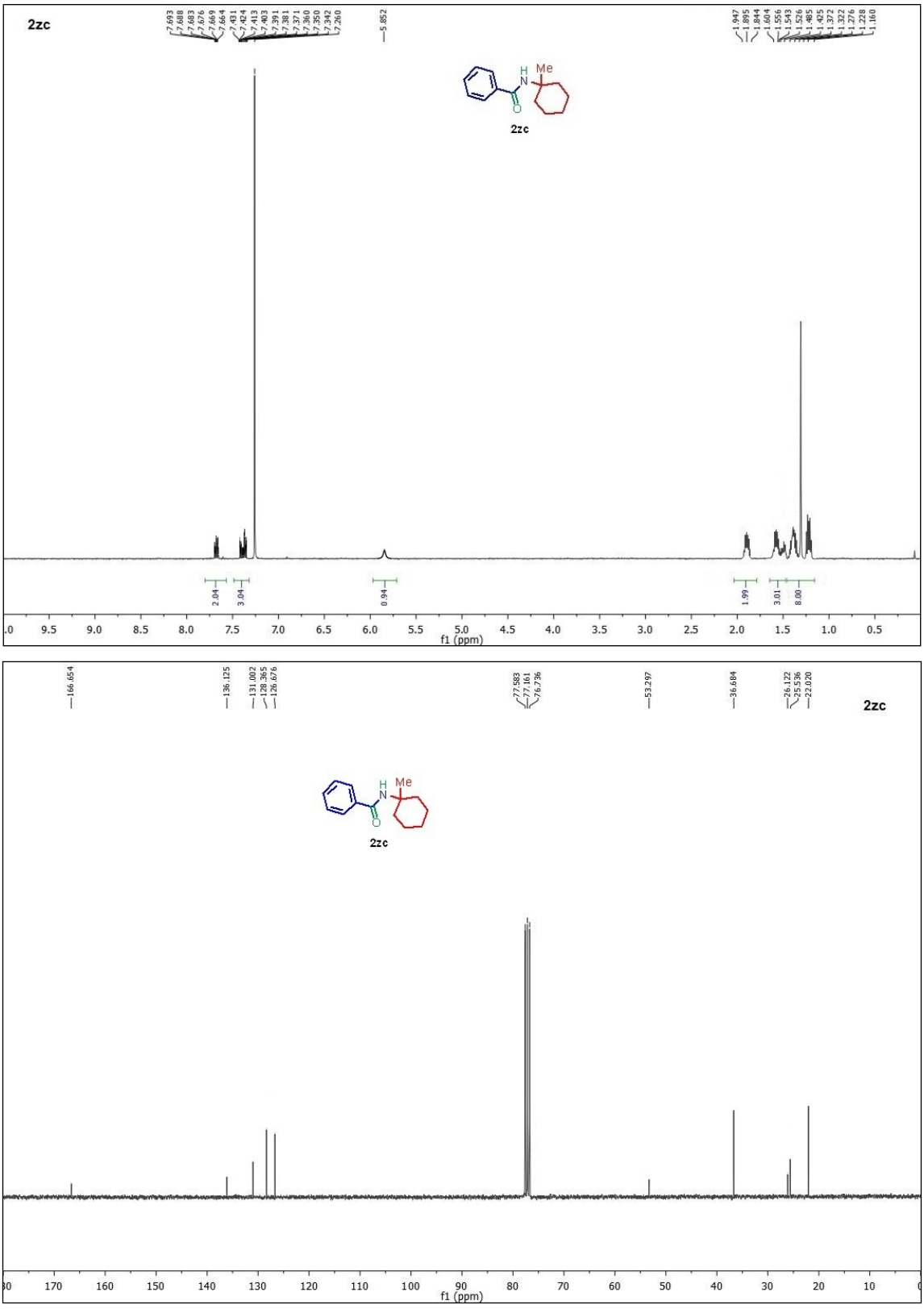


Figure S25. ^{1}H (top) and ^{13}C (bottom) spectra of **2zc** in $CDCl_3$.

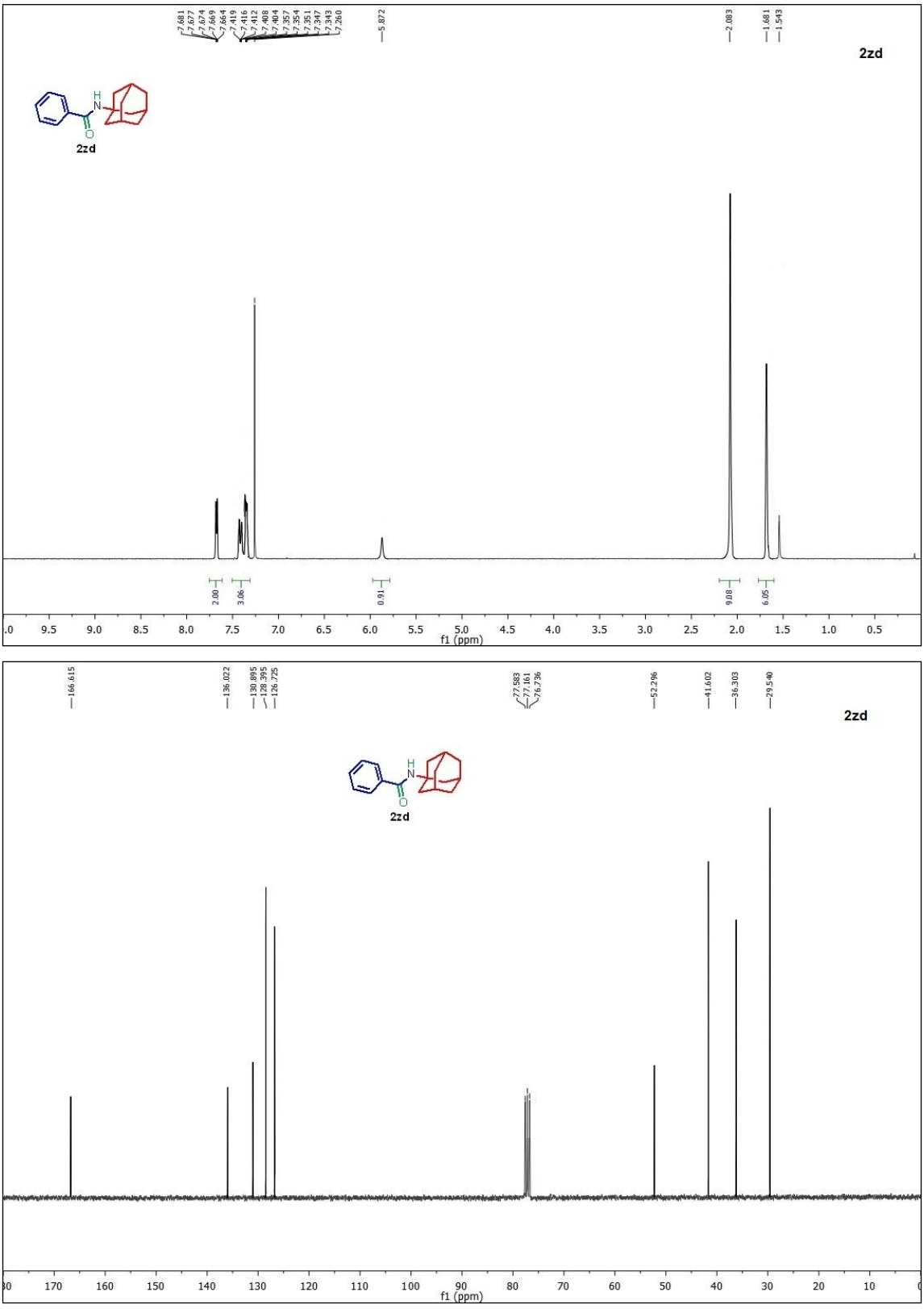


Figure S26. ^{1}H (top) and ^{13}C (bottom) spectra of **2zd** in $CDCl_3$.

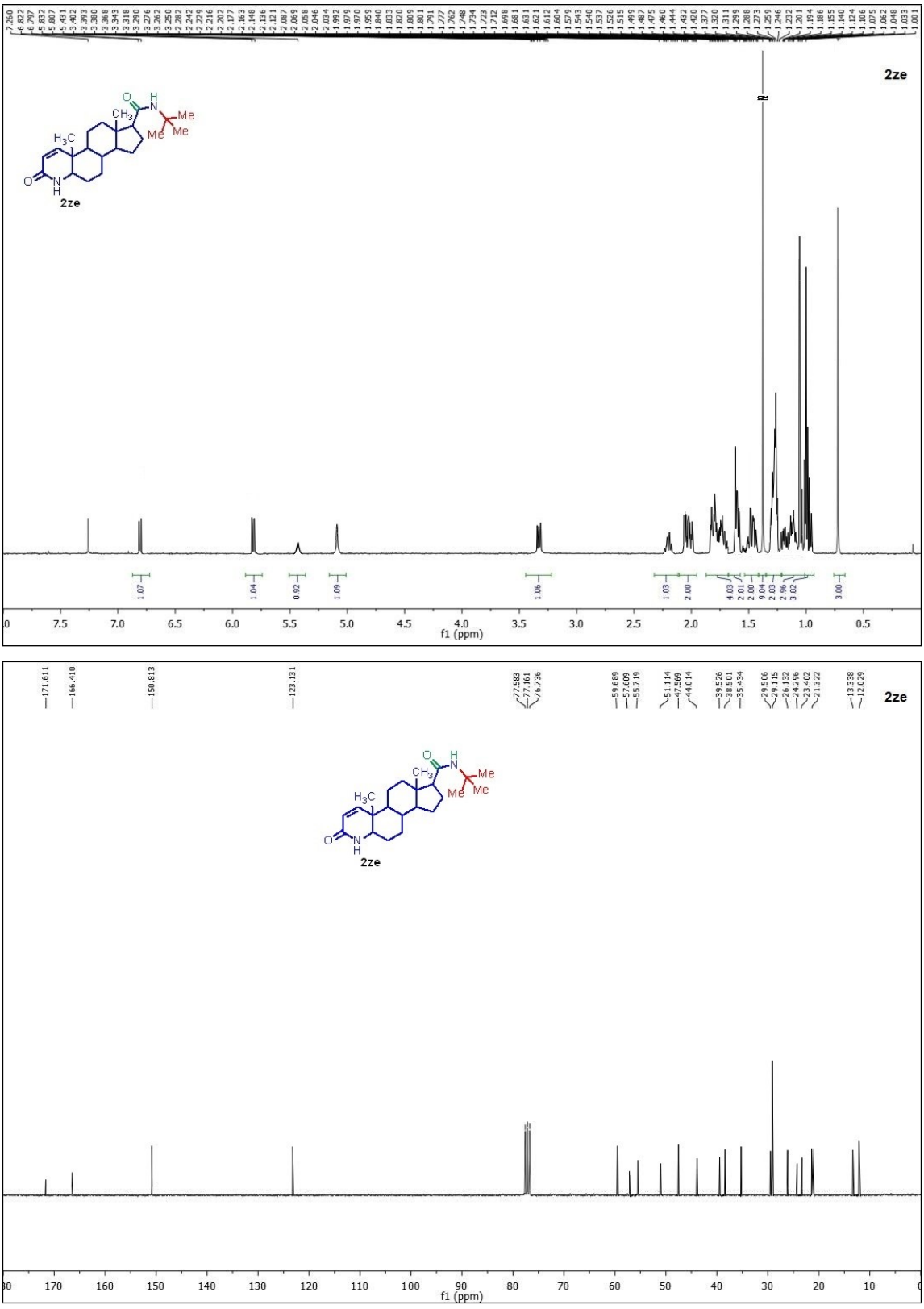


Figure S27. ^{1}H (top) and ^{13}C (bottom) spectra of **2ze** in $CDCl_3$.

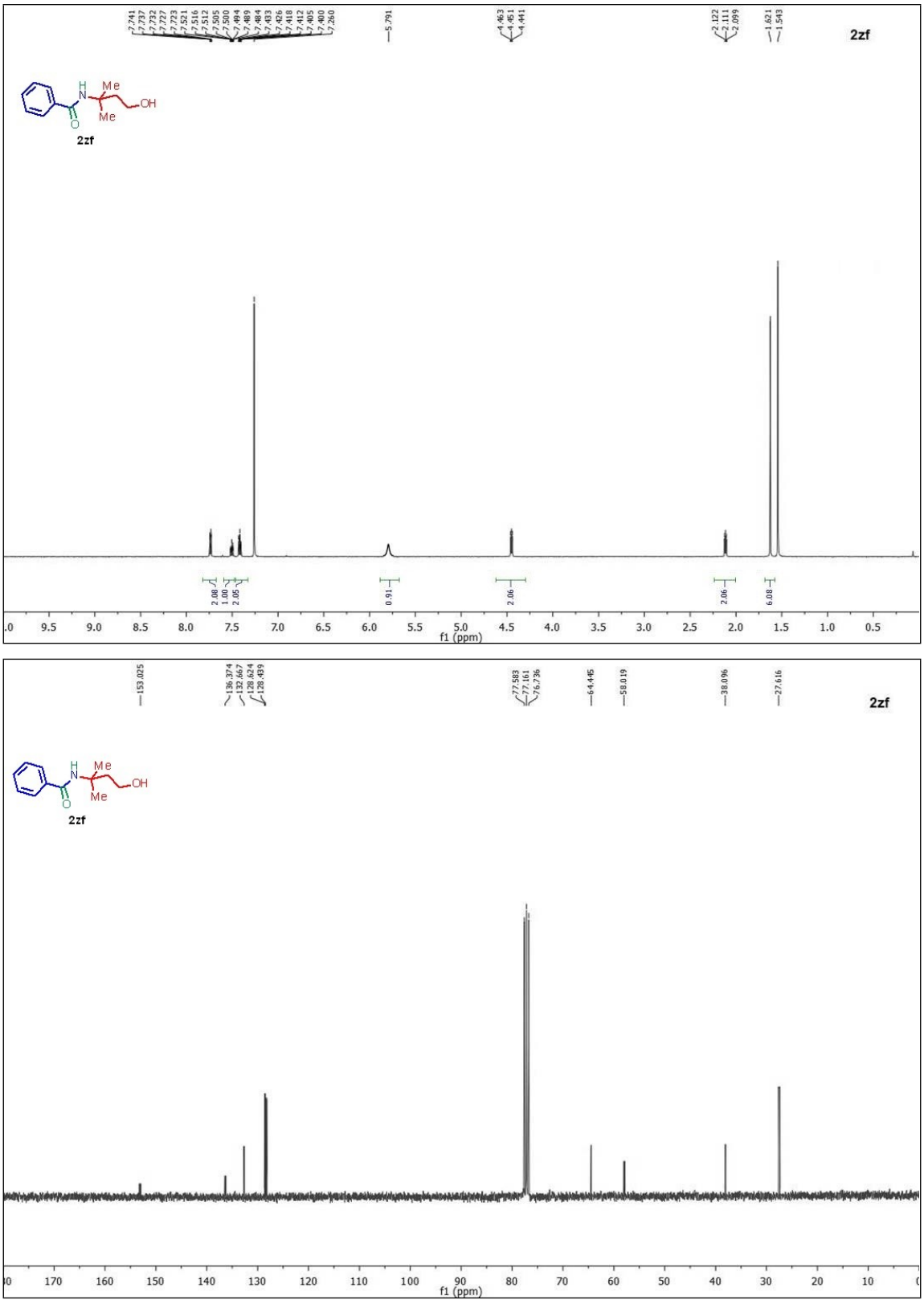


Figure S28. ^{1}H (top) and ^{13}C (bottom) spectra of **2zf** in $CDCl_3$.

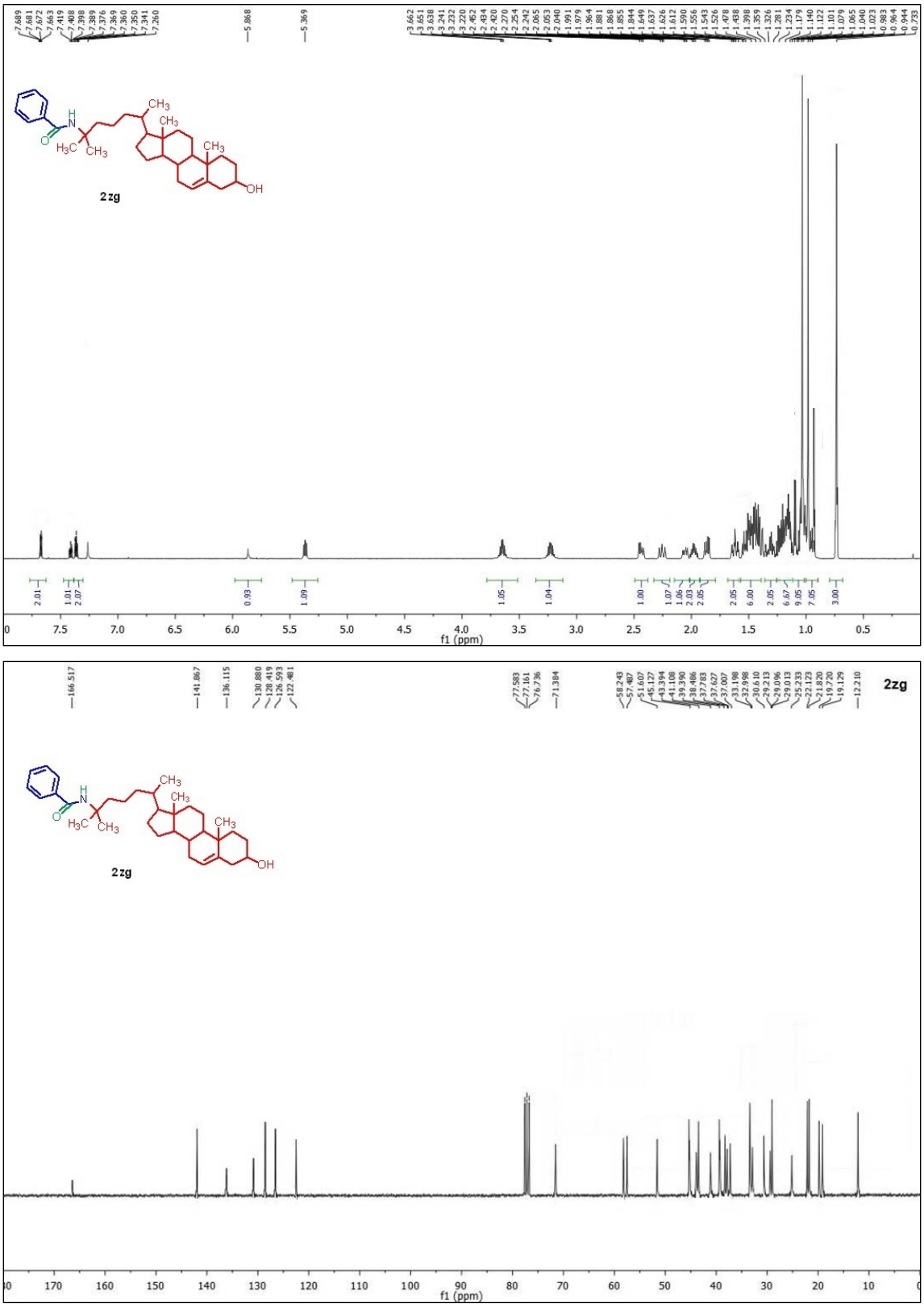


Figure S29. ^{1}H (top) and ^{13}C (bottom) spectra of **2zg** in $CDCl_3$.

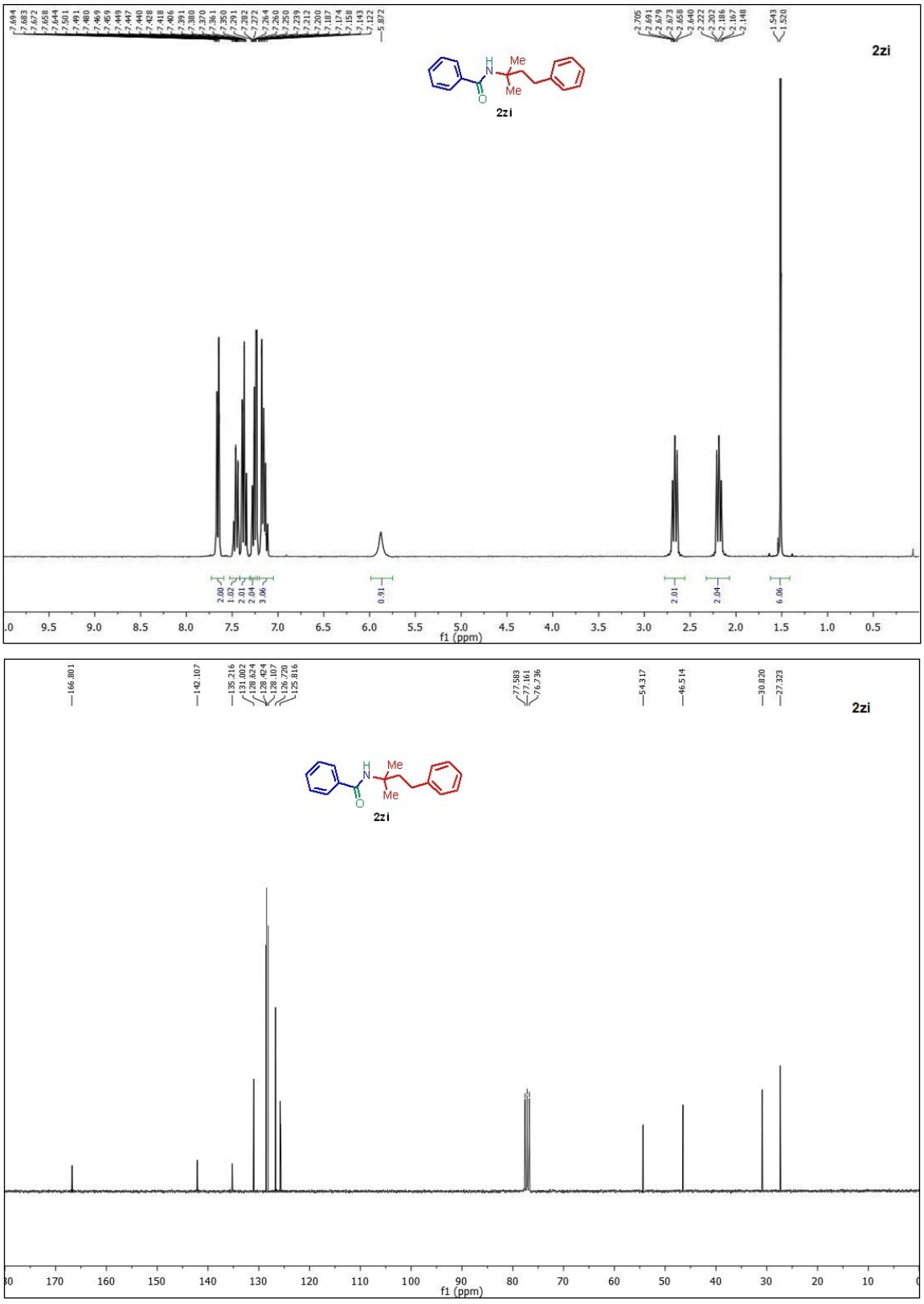


Figure S30. ^{1}H (top) and ^{13}C (bottom) spectra of **2zi** in $CDCl_3$.