Supporting Information

Azobenzene-Containing Metal-Organic Framework as an Efficient Heterogeneous Catalyst for Direct Amidation of Benzoic Acids: Synthesis of Bioactive Compounds

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PART 1: SYNTHESIS AND CHARACTERIZATION OF Zr-AzoBDC

Section S1. Synthesis and Characterization of Zr-AzoBDC: Chemicals

N,*N*-dimethylformamide (DMF), sodium hydroxide, acetic acid, hydrochloric acid, zirconium(IV) oxychloride octahydrate ($ZrOCl_2 \cdot 8H_2O$), and dichloromethane (DCM) were all purchased from Sigma Aldrich Chemical Company. Glucose and 4-nitrobenzoic acid were purchased from Merck Chemical Company. All chemicals were used without further purification.

Section S2. Synthesis of Azobenzene-4,4′-dicarboxylic acid (H_2-AzoBDC)

Azobenzene-4,4′-dicarboxylic acid (H_2-AzoBDC) was synthesized, based on azo-coupling, according to a previous report [1]. In a typical synthesis, 4-nitrobenzoic acid (10.0 g, 59.9 mmol) and 50 mL water were added to a three-neck round-bottom flask attached to a reflux condenser. A 5.6 M solution of sodium hydroxide was slowly added (150 mL total) to the reaction flask and the resulting solution was heated to 50 °C. Next, a hot glucose solution (61.5 g in 200 mL water) was slowly added to the reaction that was kept at a constant 50 °C. Airflow was continuously passed through the solution. Orange precipitate initially formed and the solution's color gradually turned brown upon more addition of glucose. The solution was left to react at 50 °C overnight, which resulted in a dark-colored solution with noticeable precipitate the following day. The reaction mixture was subsequently filtered. The solid was then dissolved in water and acidified with concentrated HCl to afford an orange precipitate. The final product was filtered once again, washed with copious amounts of water, and dried at 60 °C to yield azobenzene-4,4′-dicarboxylic acid (4.53 g, 16.7 mmol, 56%). ^{1}H NMR (DMSO-d_6, 500 MHz, 25 °C): δ = 8.00 (d, 4H), 8.15 (d, 4H), 13.26 (br, 1H). ^{13}C NMR (DMSO-d_6, 125 MHz, 25 °C): δ = 122.80, 130.70, 133.2, 154.7, 166.6. ESI-MS for $C_{14}H_{16}N_2O_4$ (calculated at 270.24): found m/z = 269 ($[M-H]^+$). FT-IR (KBr, 3500-400 cm^{-1}): 3440 (br), 3086 (w), 3070 (w), 3030 (w), 2958 (br), 2879 (w), 2819 (br), 2715 (w), 2663 (m), 2544 (m), 1946 (w), 1813 (w), 1685 (s), 1602 (m), 1579 (m), 1496 (m), 1461 (w), 1425 (s), 1296 (s), 1217 (m), 1155 (w), 1126 (m), 1105 (w), 1010 (m), 962 (w), 935 (m), 871 (s), 846 (w), 781 (s), 698 (s), 640 (m), 621 (w), 559 (m), 538 (m), 511 (m).

Section S3. Synthesis, Activation, and Characterization of Zr-AzoBDC, including FT-IR Spectroscopy, Scanning Electron Microscopy Imaging, Thermal Gravimetric Analysis, and Gas Adsorption

Synthesis and Activation of $Zr_6O_4(OH)_4(4\text{-}Az)_6$, Zr-AzoBDC

Zr-AzoBDC was synthesized as follows: $ZrOCl_2 \cdot 8H_2O$ (129 mg, 0.400 mmol) and H_2-AzoBDC (108 mg, 0.400 mmol) were dissolved in a solvent mixture of DMF/acetic acid (40 mL/12 mL). The resulting solution (4 mL) was then placed into a 10 mL glass vial. The solution was subsequently heated at 85 °C for 3 days in an isothermal oven to yield orange crystalline solid. After cooling the vial to room temperature, the orange solid product was separated from the mother liquor via centrifugation.

Zr-AzoBDC as-synthesized samples were activated (removal of guest molecules from the pores) as follows: The obtained orange solid was washed three times over three days with 10 mL of DMF. After this period, the DMF was replaced with DCM and the product was washed three times over three days with fresh DCM each time. Solvent-exchanged Zr-AzoBDC was dried under vacuum at 120 °C for 12 h to yield 98 mg of activated Zr-AzoBDC (64% based on H_2-AzoBDC linker). PXRD patterns were measured on activated samples and demonstrated excellent agreement with the simulated pattern generated from a structural model. This indicated that Zr-AzoBDC was in fact synthesized.

Zr-AzoBDC was synthesized on gram scales by combining multiple products obtained from these small-scale reactions. EA of activated sample: Calcd. for $Zr_6H_{52}N_{12}O_{32}$ = $[Zr_6O_4(OH)_4(C_{14}H_8N_2O_4)_6]$: C, 44.08; H, 2.29, N, 7.34%. Found: C, 40.58; H, 2.55; N,

6.68%. Calcd. for $Zr_6H_{74}N_{12}O_{43}$ = $[Zr_6O_4(OH)_4(C_{14}H_8N_2O_4)_6]\cdot 11(H_2O)$: C, 40.57; H, 3.00; N, 6.76% [2]. FT-IR (KBr, 3500-400 cm^{-1}): 3419 (br), 1942 (w), 1699 (w), 1598 (s), 1550 (s), 1498 (w), 1417 (s), 1309 (w), 1218 (w), 1143 (w), 1099 (w), 1010 (m), 871 (m), 788 (s), 705 (m), 653 (m), 472 (w).

Scanning Electron Microscopy Imaging (SEM)

SEM images were taken on a Hitachi S-4800 scanning electron microscope operating at an accelerating voltage of 1 kV. Sample was prepared by dispersing the material onto a sticky carbon surface attached on a flat aluminum sample holder.

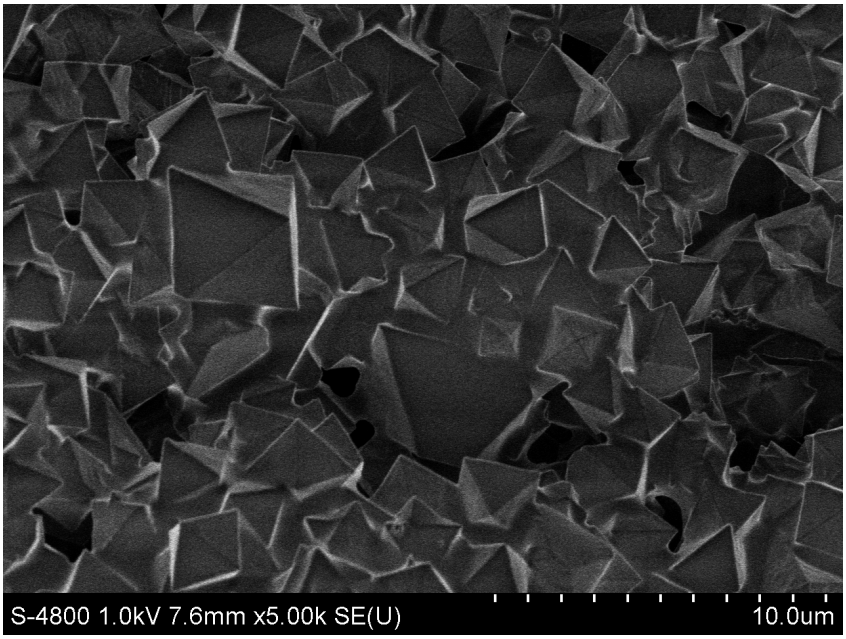


Fig. S1. SEM image of Zr-AzoBDC demonstrating the synthesized materials uniform crystal morphology as well as the relative sizes of the crystallites.

Thermal Gravimetric Analysis

In general, a ~10 mg sample of activated Zr-AzoBDC was run on a TA Instrumental Q-500 Series Thermal Gravimetric Analyzer. The sample was held in a platinum pan under a continuous air flow. During the process, the sample was heated at a constant rate of 5 °C min^{-1}. The initial weight loss is attributed to adsorbed water molecules when transferring sample to the platinum pan. It is noted that the presumably ZrO_2 residue (33.41%) in the activated sample is in satisfactory agreement with the calculated theoretical value (32.31%).

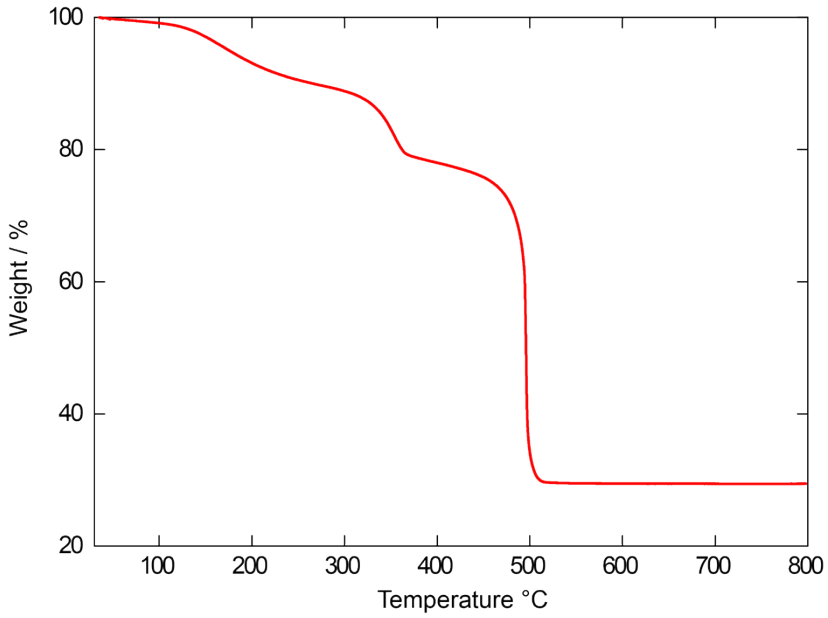


Fig. S2. Thermal gravimetric analysis trace of as-synthesized Zr-AzoBDC.

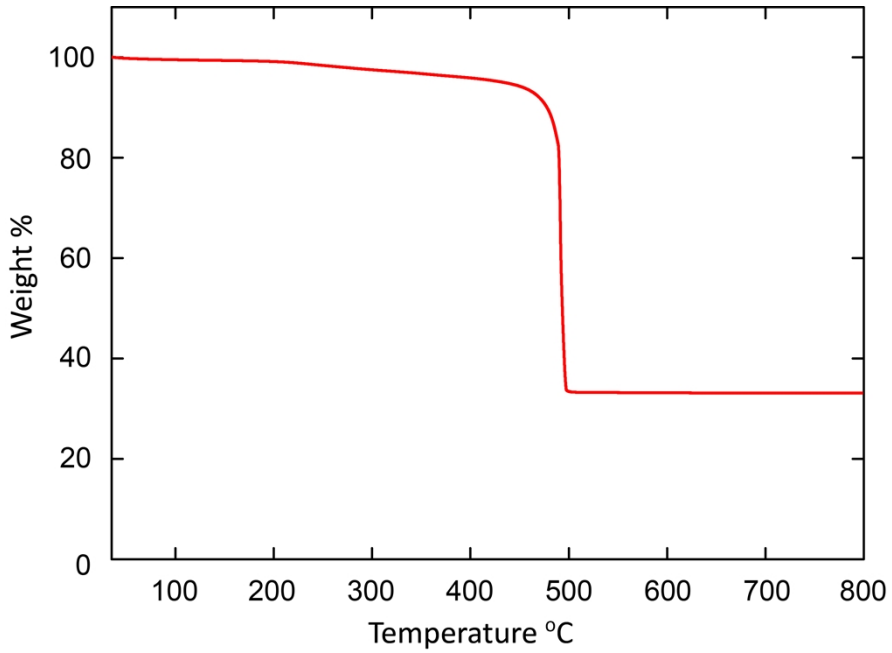


Fig. S3. Thermal gravimetric analysis trace of activated (guest-free) Zr-AzoBDC.

Gas Adsorption

Low-pressure N_2 adsorption measurements were carried out on a Micromeritics 3Flex Surface Characterization Analyzer. A liquid N_2 bath was used for measurements at 77 K. Helium was used as estimation of dead space. Ultrahigh-purity-grade N_2 and He (99.999% purity) were used throughout adsorption experiments.

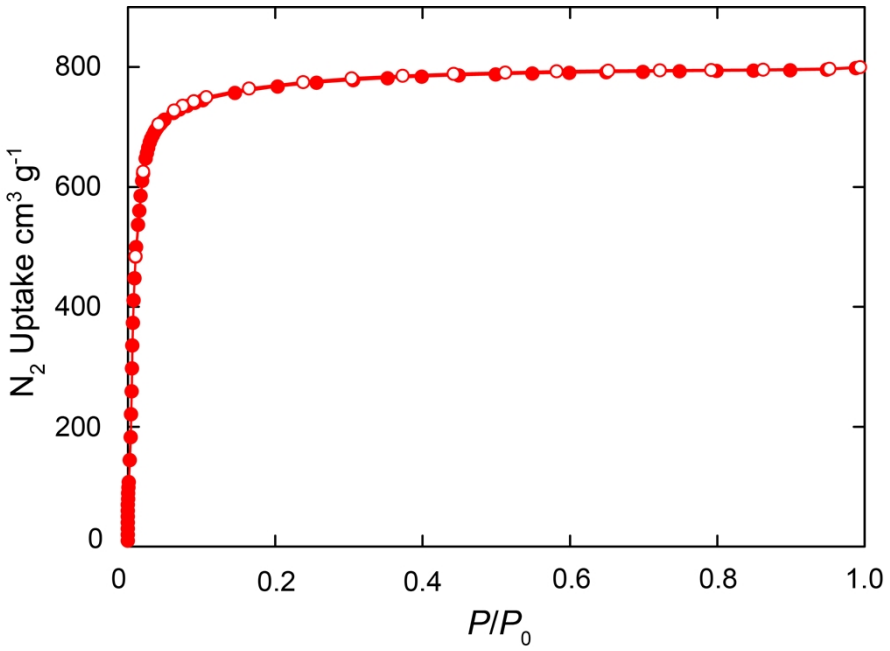


Fig. S4. N_2 isotherm of Zr-AzoBDC at 77 K. Filled and open symbols represent adsorption and desorption, respectively. The connected lines are inserted as guides for the eye.

Section S4. X-ray Crystallography

Powder X-ray diffraction data collection

Powder X-ray diffraction (PXRD) data for the activated (guest-free) sample of Zr-AzoBDC was collected on a Bruker D8-Advance θ–θ diffractometer, equipped with a *LynxEye* detector, in reflectance Bragg-Brentano geometry employing Ni filtered (0.2 mm) Cu Kα lines focused radiation (1.54059 Å, 1.54439 Å) at 1600 W (40 kV, 40 mA) power. A dried and activated powder sample of Zr-AzoBDC was mounted on a zero background holder and then leveled using a razor blade. The procedure for obtaining the best counting intensity used a measurement step scan of 0.02° 2θ from 3 – 70° with exposure time of 0.5 second per step. The measurement was performed at room temperature and atmospheric pressure.

Unit cell determination

Unit cell determinations were carried out using *TOPAS* software in the Bruker X-ray diffraction software package. A cubic lattice system (a = 29.3994 Å) with space group *Fm*-3 was selected for Zr-AzoBDC. Whole pattern profile fitting and extraction of the integrated intensities was conducted using data from 2θ = 3° – 70°. A background correction was performed using a 20-parameter Chebyschev polynomial function. The peak profile was calculated and refined by Thomson-Cox-Hasting or Pseudo-Voigt method. A Pawley refinement was then performed and converged with very low residual values (R_p = 0.0439, wR_p = 0.0561), thus demonstrating the correct cell parameters.

Section S5: Structural Modeling and Structural Determination of Zr-AzoBDC

Structural Modeling of Zr-AzoBDC

A structural model of Zr-AzoBDC was executed by using the *Materials Visualizer* module of *Materials Studio* software (Material Studio v.5.5.0.0, 2010, Accelrys Software Inc.) as follows: the inorganic secondary building unit (SBU) composition and connectivity, $Zr_6O_8(OH)_4$, was obtained from the crystal structure of UiO-66 [3]. The organic linker, AzoBDC, was then constructed in the GaussView graphical interface for *Gaussian* to identify suitable resonance geometries. The distance from the center of the azo bonding (N to N) to the carboxylate group (6.695 Å) was measured. This value was employed to determine plausible nets by connecting AzoBDC to the zirconium SBUs (points of extension or vertices). Upon completion of the structural model, an energetic minimization was performed by the universal force field implemented in the *Forcite* module of *Materials Studio*. During this process, the unit cell parameters were also optimized until proper convergence was achieved (energy convergence criteria were set at 10^{-4} kcal/mol). The PXRD pattern for the Zr-AzoBDC model was then calculated and compared to the experimental pattern obtained. A full profile pattern refinement using data from $2\theta = 3° - 70º$ was performed against the experimental powder pattern. The calculated PXRD pattern for the model achieved good agreement with the experimental PXRD pattern, as demonstrated by the refinement converging with satisfactory residual values ($R_{wp} = 11.24\%$, $R_p = 8.48\%$).

The fractional atomic coordinates and refined cell parameters for Zr-AzoBDC can be found in Table S1. Further crystal structure information is provided in Table S2.

Table S1. Refined unit cell parameters and fractional atomic coordinates for Zr-AzoBDC.

Name	Zr-AzoBDC		
Space Group	*Fm*-3 (No. 202)		
***a* (Å)**	29.3994(2)		
Unit Cell Volume (Å^3)	25410.6(3)		
Atom Name	*x*	*y*	*z*
C1	0.1041	0.0000	0.8974
C2	0.2855	0.0000	0.3018
C3	0.6413	0.0000	0.6364
C4	0.3307	0.0000	0.2858
O5	0.1168	0.0000	0.0605
C6	0.6865	0.0000	0.6209
H7	0.3377	0.0000	0.2476
H8	0.6940	0.0000	0.5829
C9	0.0000	0.1834	0.8671
O10	0.0000	0.1166	0.9379
C11	0.0000	0.8485	0.2227
H12	0.0000	0.1966	0.9036
H13	0.0000	0.8618	0.2592
O14	0.0415	0.9585	0.9585
Zr15	0.0795	0.0000	0.0000
N16	0.2715	0.7475	0.5000

Table S2. Zr-AzoBDC Crystal Structure Information

Parameters	**Zr-AzoBDC**
Empirical formula	$C_{42}H_{24}N_6O_{16}Zr_3$
Calculated density (g cm^{-3}) (dried solid)	0.5972(0)
Symmetry	Cubic
Space group	*Fm*-3
a (Å)	29.3994(2)
Unit Cell Volume ($Å^3$)	25410.6(3)
Z	8
Wavelength λ (Cu Kα)	1.54059, 1.54439
$\chi=K_{\alpha2}/K_{\alpha1}$	0.5
Temperature (K)	296
Angular range 2θ (°) (represent to Q range)	3- 70
Number of refined parameters	6
R_P	0.0848
R_{wp}	0.1124

PART 2: CATALYSIS

Section S6. Catalysis: Materials and Instrumentation

All reagents and starting materials were obtained commercially from Sigma-Aldrich and Acros, and were used as received without any further purification unless otherwise noted. Gas chromatographic (GC) analyses were performed using a Shimadzu GC 2010-Plus equipped with a flame ionization detector (FID) and an SPB-5 column (length = 30 m, inner diameter = 0.25 mm, and film thickness = 0.25 μm). The temperature program for GC analysis heated samples from 100 °C for 1 min; heated from 100 to 280 °C at 40 °C/min; held at 280 °C for 2.5 min. Inlet and detector temperature were set constant at 280 °C. Diphenyl ether was used as internal standard to calculate the yield of reaction. The ^{1}H and ^{13}C NMR were recorded on a Brucker AV 500 MHz with tetramethylsilane as standard. ICP-MS was conducted using PerkinElmer 350D ICP-MS.

Synthesis of Co-ZIF-67

ZIF-67 was prepared according to literature procedure [4]. In a typical preparation, a mixture of 2-methylimidazole (3.284 g, 40 mmol) and triethylamine (5.6 ml, 40 mmol) was dissolved in water (10 mL). A solution of $Co(NO_3)_2 \cdot 6H_2O$ (0.73 g, 2.5 mmol) in water (10 mL) was then added, and the resulting solution was stirred for 10 min at room temperature. The purple precipitates were separated by centrifugation, washed with water (3 x 10 mL) and methanol (3 x 10 mL) at room temperature. The material was evacuated under vacuum at 150 °C for 6 h, yielding 0.314 g of ZIF-67 in the form of purple crystals (56% yield).

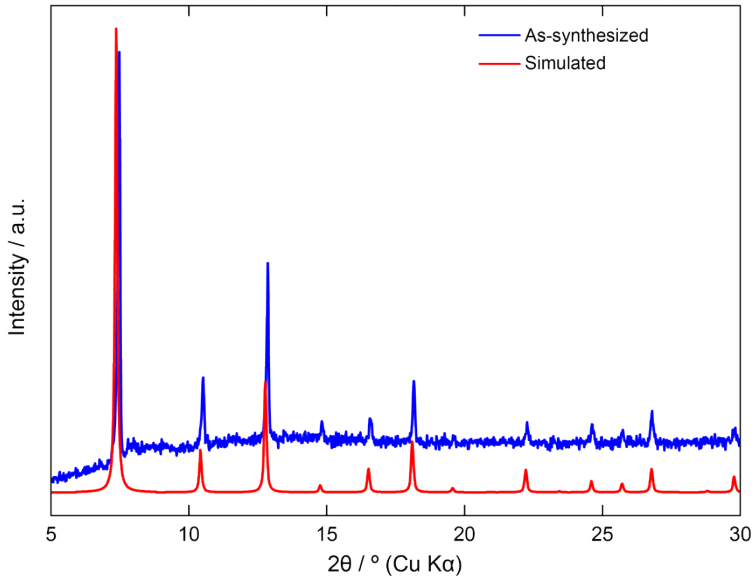


Fig. S5. PXRD comparison of as-synthesized Co-ZIF-67 and simulated patterns.

Synthesis of Zn-ZIF-8

ZIF-8 was prepared according to literature procedure [4]. In a typical preparation, a mixture of 2-methylimidazole (3.284 g, 40 mmol) and triethylamine (5.6 ml, 40 mmol) was dissolved in water (10 mL). A solution of $Zn(NO_3)_2 \cdot 6H_2O$ (0.74 g, 2.5 mmol) in water (10 mL) was then added, and the resulting solution was stirred for 10 min at room temperature. The white precipitates were separated by centrifugation, washed with water (3 x 10 mL) and methanol (3 x 10 mL) at room temperature. The material was evacuated under vacuum at 150 °C for 6 h, yielding 0.356 g of ZIF-8 in the form of white crystals (62% yield).

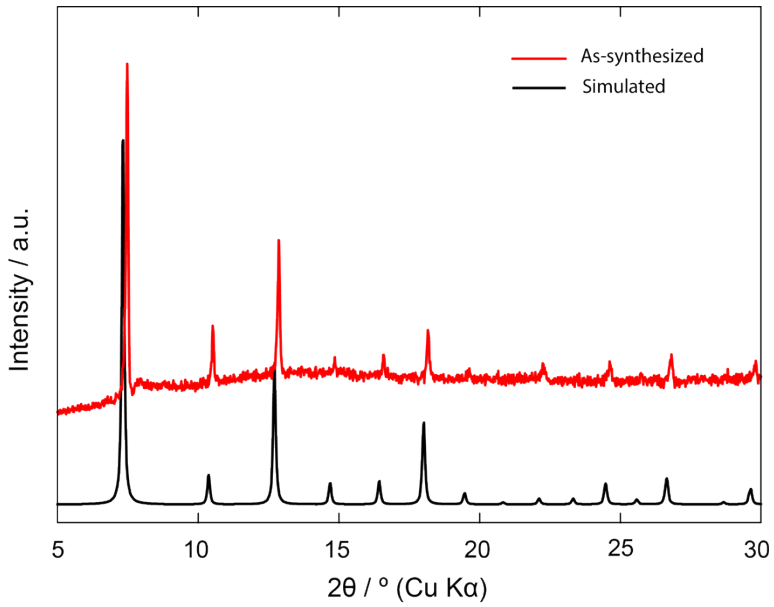


Fig. S6. PXRD comparison of as-synthesized Zn-ZIF-8 and simulated patterns.

Synthesis of $Cu_2(BDC)_2(DABCO)$

$Cu_2(BDC)_2(DABCO)$ was prepared according to literature procedure [5]: a mixture of H_2BDC (H_2BDC = 1,4-benzenedicarboxylic acid; 0.506 g, 3.1 mmol), DABCO (DABCO = 1,4-diazabicyclo[2.2.2]octane; 0.188 g, 1.67 mmol), and $Cu(NO_3)_2 \cdot 3H_2O$ (0.8 g, 3.3 mmol) was dissolved in DMF (DMF = *N*,*N*'-dimethylformamide, 80 mL). The mixture was stirred for 2 h, and the resulting solution was then distributed to eight 10 mL vials. The vial was heated at 120 °C in an isothermal oven for 48 h, forming blue crystals. After cooling the vial to room temperature, the solid product was removed by decanting with mother liquor and washed with DMF (3 x 10 mL). Solvent exchange was carried out with methanol (3 x 10 mL) at room temperature. The product was then dried at 140 °C for 6 h under vacuum, yielding 0.57 g of the metal–organic framework $Cu_2(BDC)_2(DABCO)$ as light blue crystals (66% yield).

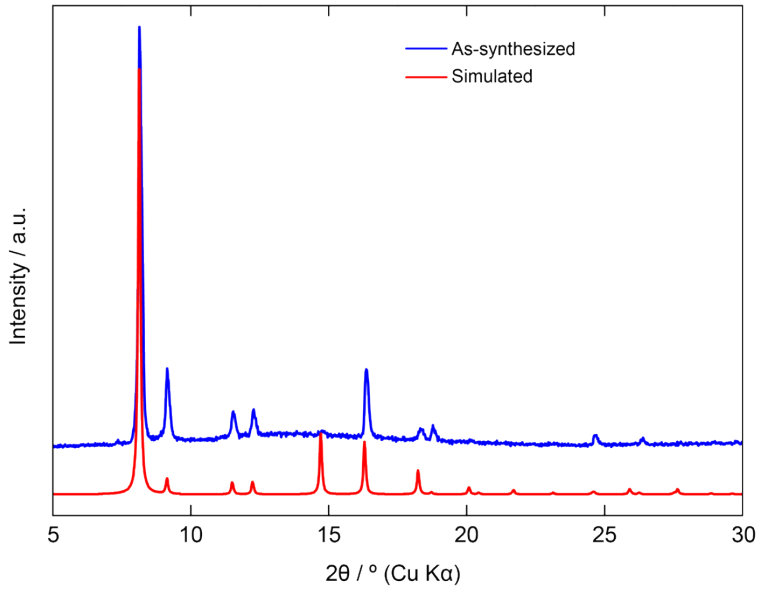


Fig. S7. PXRD comparison of as-synthesized $Cu_2(BDC)_2(DABCO)$ and simulated patterns.

Synthesis of $Ni_2(BDC)_2(DABCO)$

$Ni_2(BDC)_2(DABCO)$ was prepared according to literature procedure [5]: a solid mixture of H_2BDC (H_2BDC = 1,4-benzenedicarboxylic acid; 0.415 g, 2.5 mmol), DABCO (DABCO = 1,4-diazabicyclo[2.2.2]octane; 0.168 g, 1.5 mmol), and $Ni(NO_3)_2{\cdot}6H_2O$ (0.58 g, 2 mmol) was dissolved in DMF (DMF = *N,N'*-dimethylformamide; 15 mL). The resulting solution was distributed to two 20 ml vials. The vials were then heated at 100 °C in an isothermal oven for 48 h. After cooling the vials to room temperature, the solid product was removed by decanting with mother liquor and washed in DMF (3 x 10 mL) for 3 days. Solvent exchange was carried out with methanol (3 x 10 ml) at room temperature for 3 days. The material was then evacuated under vacuum at 140 °C for 6 h, yielding 0.425 g of $Ni_2(BDC)_2(DABCO)$ in the form of green crystals (76% yield).

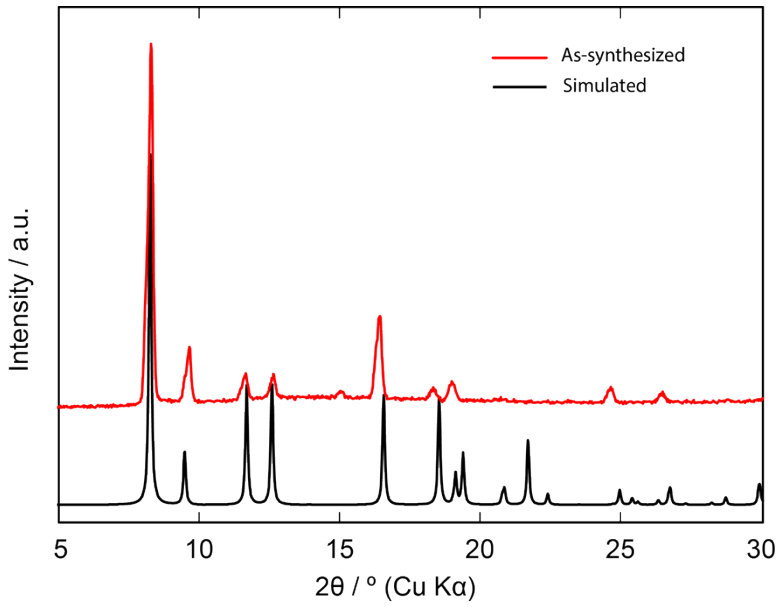


Fig. S8. PXRD comparison of as-synthesized $Ni_2(BDC)_2(DABCO)$ and simulated patterns.

Synthesis of UiO-66

The UiO-66 was prepared according to literature procedure [6]: $ZrCl_4$ (0.125 g, 0.54 mmol) was dissolved in a mixture of DMF (DMF = *N,N'*-dimethylformamide; 5 mL) and concentrated HCl (1mL) before being sonicated for 20 min. Linker H_2BDC (H_2BDC = 1,4-benzenedicarboxylic acid, 0.123 g, 0.75 mmol) and an additional amount of DMF (10 mL) were then added. The resulting solution was distributed to two 20 ml vials. The vials were then heated at 80 °C in an isothermal oven for 48 h. After cooling the vials to room temperature, the solid product was removed by decanting with mother liquor and washed in DMF (3 x 10 mL) for 3 days. Solvent exchange was carried out with ethanol (3 x 10 ml) at room temperature for 3 days. The material was then evacuated under vacuum at 150 °C for 3 h, yielding 0.084 g of UiO-66 in the form of white crystals (57 % yield).

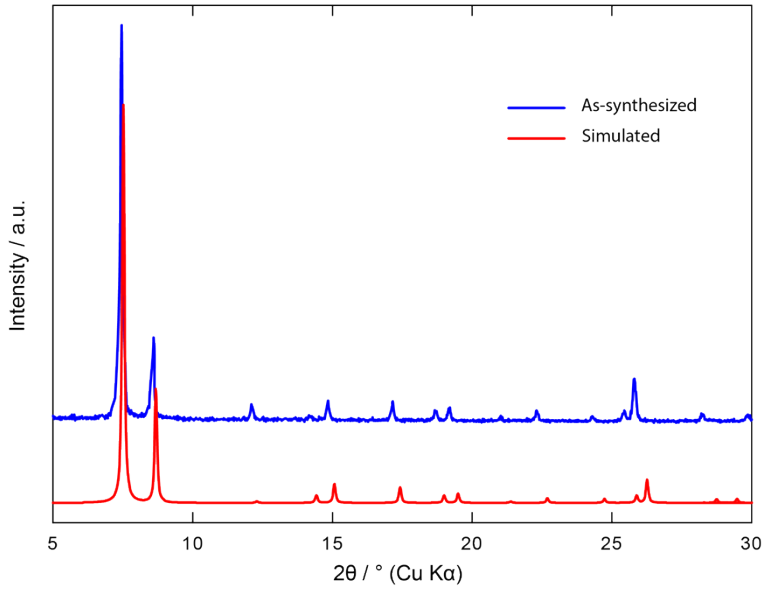


Fig. S9. PXRD comparison of as-synthesized UiO-66 and simulated patterns.

Synthesis of UiO-67

UiO-67 was prepared according to literature procedure [6]: $ZrCl_4$ (0.067 g, 0.27 mmol) was dissolved in a mixture of DMF (DMF = *N,N'*-dimethylformamide; 5 mL) and concentrated HCl (0.5 mL) before being sonicated for 20 min. Linker H_2BPDC (H_2BPDC = biphenyl-4,4'-dicarboxylic acid, 0.09 g, 0.38 mmol) and an additional amount of DMF (10 mL) were then added. The resulting solution was distributed to two 20 ml vials. The vials were then heated at 80 °C in an isothermal oven for 48 h. After cooling the vials to room temperature, the solid product was removed by decanting with mother liquor and washed in DMF (3 x 10 mL) for 3 days. Solvent exchange was carried out with ethanol (3 x 10 ml) at room temperature for 3 days. The material was then evacuated under vacuum at 150 °C for 3 h, yielding 0.059 g of UiO-67 in the form of white crystals (57 % yield).

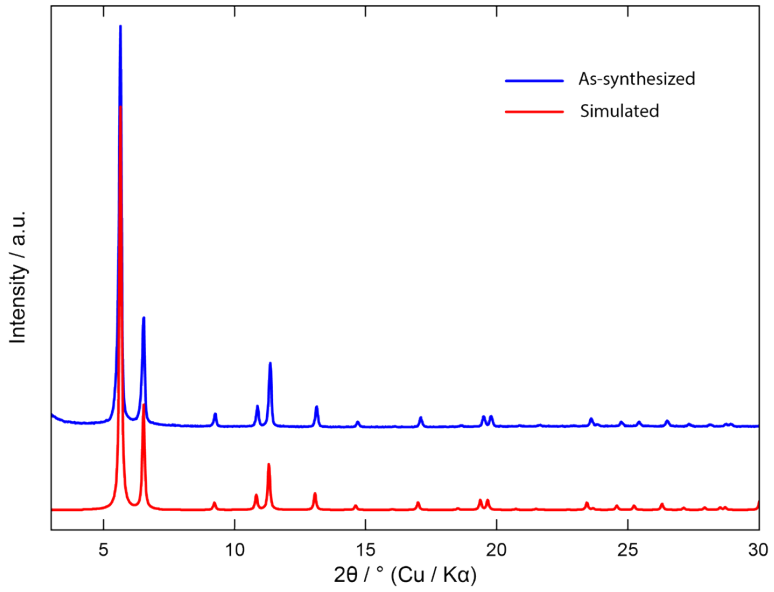


Fig. S10. PXRD comparison of as-synthesized UiO-67 and simulated patterns.

Section S7. Catalysis: Optimization

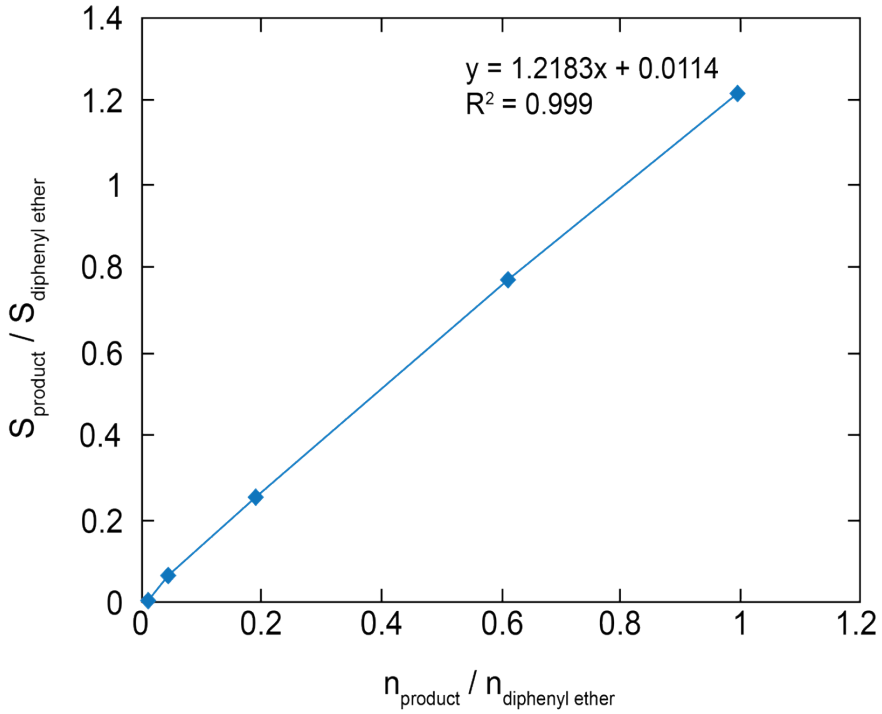


Fig. S11. Calibration curve to determine the GC yield.

GC yield was calculated as equation:

$$Y\% = \frac{\frac{S_{product}}{S_{diphenylether}} - 0.0114}{1.2183} \times \frac{n_{diphenylether}}{n_{SM}} \times 100$$

In which:

$S_{product}$: peak area of product *N*-benzylbenzamide.

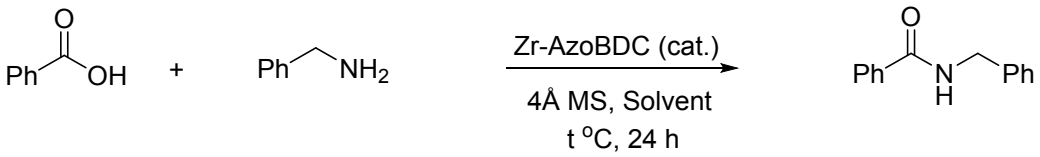
$S_{diphenyl\ ether}$: peak area of standard diphenyl ether.

$n_{diphenylether:}$ mole of standard diphenyl ether.

n_{SM}: mole of starting material.

Catalytic procedure: In a typical experiment, a mixture of benzoic acid (1 mmol), benzylamines (1.5 mmol), THF (Tetrahydrofuran, 2 mL), and 4Å MS (MS = molecular sieves, 0.5 g) was added into a 25 mL pressure vessel containing Zr-AzoBDC catalyst. The reaction mixture was stirred at 70 °C for 24h. After the completion of reaction, catalyst was filtered off. The solution was washed with an aqueous Na_2CO_3 solution (5%, 3 x 20 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic phase was then dried over Na_2SO_4 and concentrated under vacuum. After chromatography (ethyl acetate:hexane:triethylamine = 1:2:0.05), pure products were obtained.

Table S3. Optimization of reaction conditions[a]



Entry	Temperature (°C)	Solvent	Catalyst loading	GC yield
1	70	THF	10	82 (76)
2	70	1,4-dioxane	10	6
3	70	Toluene	10	19
4	70	Acetonitrile	10	3
5	70	THF	7.5	43
6	70	THF	5	10
7	60	THF	10	50
8	80	THF	10	83
9[b]	70	THF	0	trace
10[c]	70	THF	10	7
11[d]	70	THF	10	<2
12[d]	110	THF	10	42

[a]Reaction conditions: benzoic acid (1 mmol), benzylamine (1.5 mmol), activated 4Å molecular sieves (0.5 g), anhydrous solvent in a sealed tube under a Ar atmosphere. [b]Reaction without catalyst. [c]benzoic acid (1.5 mmol), benzylamine (1.0 mmol).[d]Reactions without molecular sieve. Numbers in parenthesis indicated the isolated yields.

Section S8. Catalysis: Leaching Test and Recycling Studies

To investigate the recyclability of Zr-AzoBDC, the catalyst was separated from the reaction mixture by simple filtration, washed with copious amounts of THF and methanol, dried 150 °C under vacuum in 8 h, and reused under identical conditions with previous runs. For the leaching test, a catalytic reaction was stopped after 6 h, analyzed by GC, and filtered to remove the solid catalyst. The reaction solution was then stirred for a further 18 h. Reaction progress, if any, was monitored by GC as previously described.

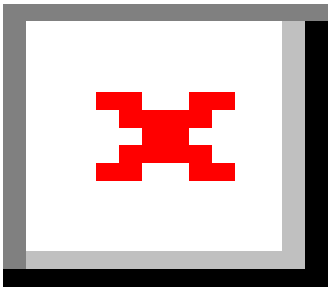


Fig S12. Inductively-coupled plasma mass spectra of possible leached Zr^{4+}.

Table S4. Leaching test with removal of catalyst after 6h.

Reaction time	6 h	12 h	18 h	20 h	22 h	24 h
GC Yields (Reaction with catalyst)	9.2 %	24.6 %	62.3 %	74.1%	81.8%	82.0 %
GC Yields (Reaction with catalyst removed	8.9%	8.4%	8.3%	8.6%	8.3%	8.4%

after 6 h)						

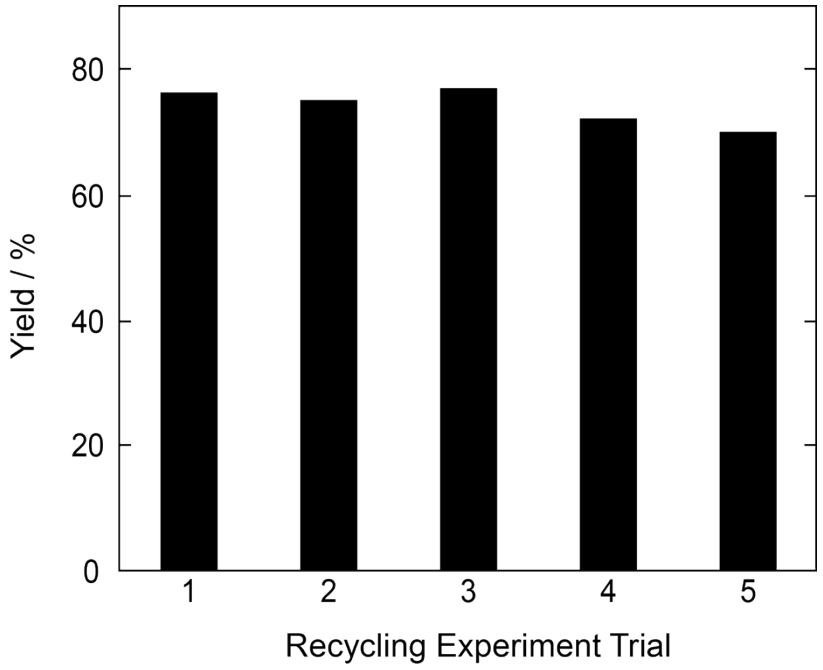


Fig S13. Recycling studies.

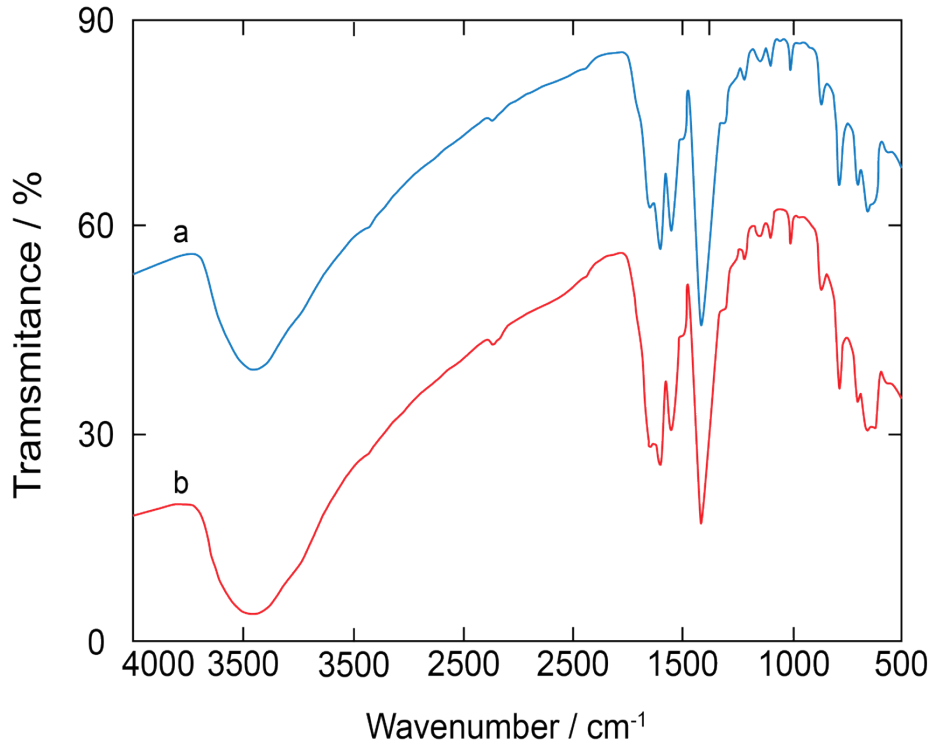


Fig. S14. FT-IR of (a) fresh Zr-AzoBDC and (b) 5th used Zr-AzoBDC.

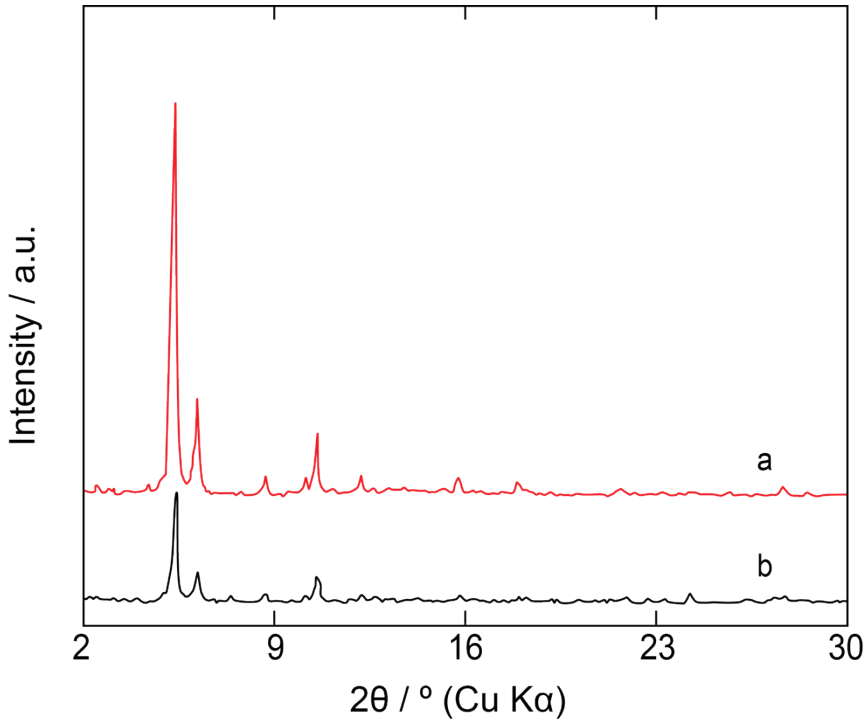


Fig. S15. PXRD of (a) fresh Zr-AzoBDC and (b) 5th used Zr-AzoBDC.

***N*-benzylbenzamide:** a white solid. This compound is known [7]. ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ (ppm) = 4.65 (d, J = 5.5 Hz, 2H), 6.43 (bs, 1H), 7.29-7.36 (m, 5H), 7.41-7.44 (m, 2H), 7.48-7.52 (m, 1H), 7.78-7.80 (m, 2H). ^{13}C NMR (125MHz, $CDCl_3$, TMS): δ (ppm) = 44.2, 126.9, 127.6, 127.9, 128.6, 128.8, 131.5, 134.4, 138.2, 167.3.

***N*-benzyl-4-nitrobenzamide:** a yellow solid. This compound is known [7]. ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ (ppm) = 4.67 (d, J = 5.5 Hz, 2H), 6.45 (bs, 1H), 7.31-7.39 (m, 5H), 7.94-7.96 (m, 2H), 8.27-8.29 (m, 2H). ^{13}C NMR (125MHz, $CDCl_3$, TMS): δ (ppm) = 44.5, 123.8, 128.0, 128.0, 128.1, 128.9, 137.4, 139.9, 149.7, 165.2.

***N*-benzyl-4-methoxybenzamide:** a white solid. This compound is known [7]. ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ (ppm) = 3.84 (s, 3H), 4.64 (d, J = 5.5 Hz, 2H), 6.29 (bs, 1H), 6.90-6.93 (m, 2H), 7.27-7.31 (m, 1H), 7.33-7.35 (m, 4H), 7.74-7.77 (m, 2H). ^{13}C NMR (125MHz, $CDCl_3$, TMS): δ (ppm) = 44.1, 55.42, 113.8, 126.6, 127.6, 127.9, 128.7, 128.7, 138.4, 162.2, 166.8.

***N*-(4-methoxybenzyl)benzamide:** a white solid. This compound is known [8]. ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ (ppm) = 3.77 (s, 3H), 4.53 (d, J = 5.5 Hz, 2H), 6.59 (bs, 1H), 6.84-6.86 (m, 2H), 7.24-7.26 (m, 2H), 7.37-7.40 (m, 2H), 7.45-7.48 (m, 1H), 7.76-7.77 (m, 2H). ^{13}C NMR (125MHz, $CDCl_3$, TMS): δ (ppm) = 43.5, 55.3, 114.1, 126.9, 128.5, 129.2, 130.3, 131.4, 134.4, 159.0, 167.3.

***N*-(4-chlorobenzyl)benzamide:** a white solid. This compound is known [8]. ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ (ppm) = 4.58 (d, J = 6.0 Hz, 2H), 6.60 (bs, 1H), 7.25-7.30 (m, 4H),

7.40-7.43 (m, 2H), 7.48-7.51 (m, 1H), 7.77-7.78 (m, 2H). ^{13}C NMR (125MHz, $CDCl_3$, TMS): δ (ppm) = 43.3, 126.9, 128.6, 128.8, 129.1, 131.6, 133.3, 134.1, 136.8, 167.4.

***N*-benzylpentanamide:** a yellow solid. This compound is known [7]. ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ (ppm) = 0.91 (t, J = 7.3 Hz, 3H), 1.32-1.39 (m, 2H), 1.61-1.67 (m, 2H), 2.21 (t, J = 7.5, 2H), 4.43 (d, J = 5.5, 2H), 5.723 (bs, 1H), 7.26-7.34 (m, 5H). ^{13}C NMR (125MHz, $CDCl_3$, TMS): δ (ppm) = 13.7, 22.4, 27.8, 36.5, 43.6, 127.4, 127.8, 128.7, 138.4, 172.9.

***N*-benzyl-2-(4-chlorophenoxy)acetamide:** a white solid. This compound is known [7]. ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ (ppm) = 4.5 (s, 2H), 4.53 (d, J = 5.5, 2H), 6.81-6.84 (m, 2H), 6.87 (bs, 1H), 7.23-7.35 (m, 7H). ^{13}C NMR (125MHz, $CDCl_3$, TMS): δ (ppm) = 43.0, 67.6, 115.9, 127.1, 127.6, 127.7, 128.7, 129.6, 137.6, 155.7, 167.6.

***N*-(2-chlorobenzyl)benzamide:** a white solid. This compound is known [8]. ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ (ppm) = 4.69 (d, J = 6.0 Hz, 2H), 6.84 (bs, 1H), 7.19-7.23 (m, 2H), 7.34-7.42 (m, 4H), 7.46-7.49 (m, 1H), 7.76-7.78 (m, 2H). ^{13}C NMR (125MHz, $CDCl_3$, TMS): δ (ppm) = 42.0, 127.0, 127.1, 128.6, 128.9, 129.6, 130.2, 131.6, 133.6, 134.3, 135.7, 167.5.

***N*-(2-aminobenzyl)benzamide:** a yellow solid. This compound is known [10]. ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ (ppm) = 4.32 (s, br, 2H), 4.55 (d, J = 6.0 Hz, 2H), 6.61 (bs, 1H), 6.64-6.69 (m, 2H), 7.08-7.12 (m, 2H), 7.36-7.39 (m, 2H), 7.44-7.48 (m, 1H), 7.72-7.74 (m, 2H). ^{13}C NMR (125MHz, $CDCl_3$, TMS): δ (ppm) = 41.4, 115.8, 117.8, 121.8, 127.0, 128.6, 129.3, 130.7, 131.7, 134.1, 145.7, 167.9.

Procainamide: light brown solid. This compound is known [11]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, J = 8.6 Hz, 2H), 6.80 (br, 1H), 6.65 (d, J = 8.6 Hz, 2H), 3.95 (br, 2H) , 3.41 – 3.55 (m, 2 H), 2.64 (t, J=6.2 Hz, 2 H), 2.54 (q, J=7.0 Hz, 4 H), 1.03 (t, J=7.0 Hz, 6 H).

Paracetamol: white solid. This compound is known [12]. ^{1}H NMR (400 MHz; DMSO-d_6): 9.63 (br, 1H), 9.12 (s, 1H), 7.33 (d, 2H, J = 8.2 Hz), 6.67 (d, 2H, J = 8.3 Hz) 1.96 (s, 3H).

Flutamide: tan solid. This compound is known [13]. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 8.38 (s, 1H), 8.12 (s, 1H), 7.87 – 7.96 (m, 2H), 2.48 – 2.68 (m, 1H), 1.25 (d, J = 2.8 Hz, 6H).

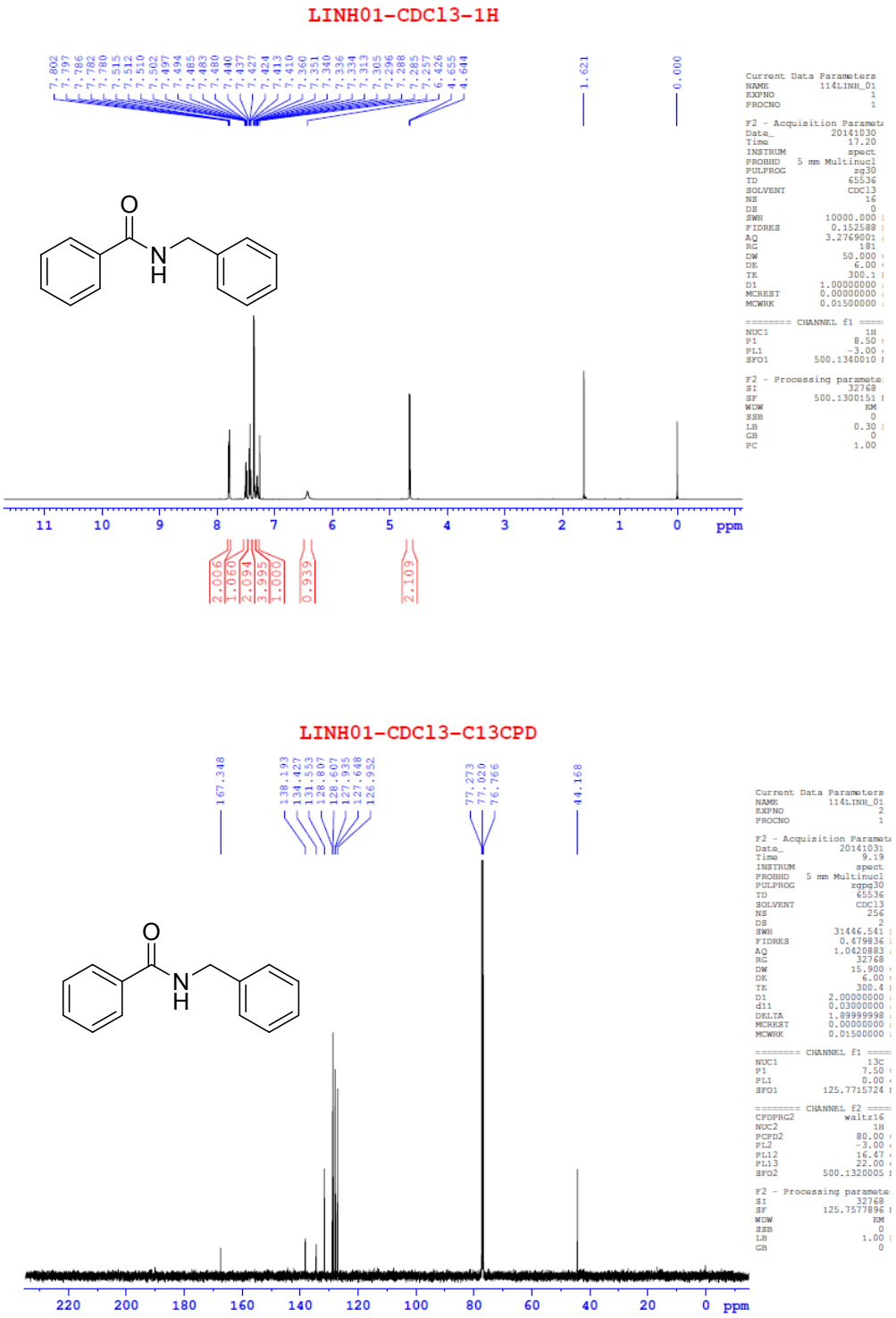


Fig. S16. ^{1}H NMR spectra and ^{13}C NMR of *N*-benzylbenzamide in $CDCl_3$.

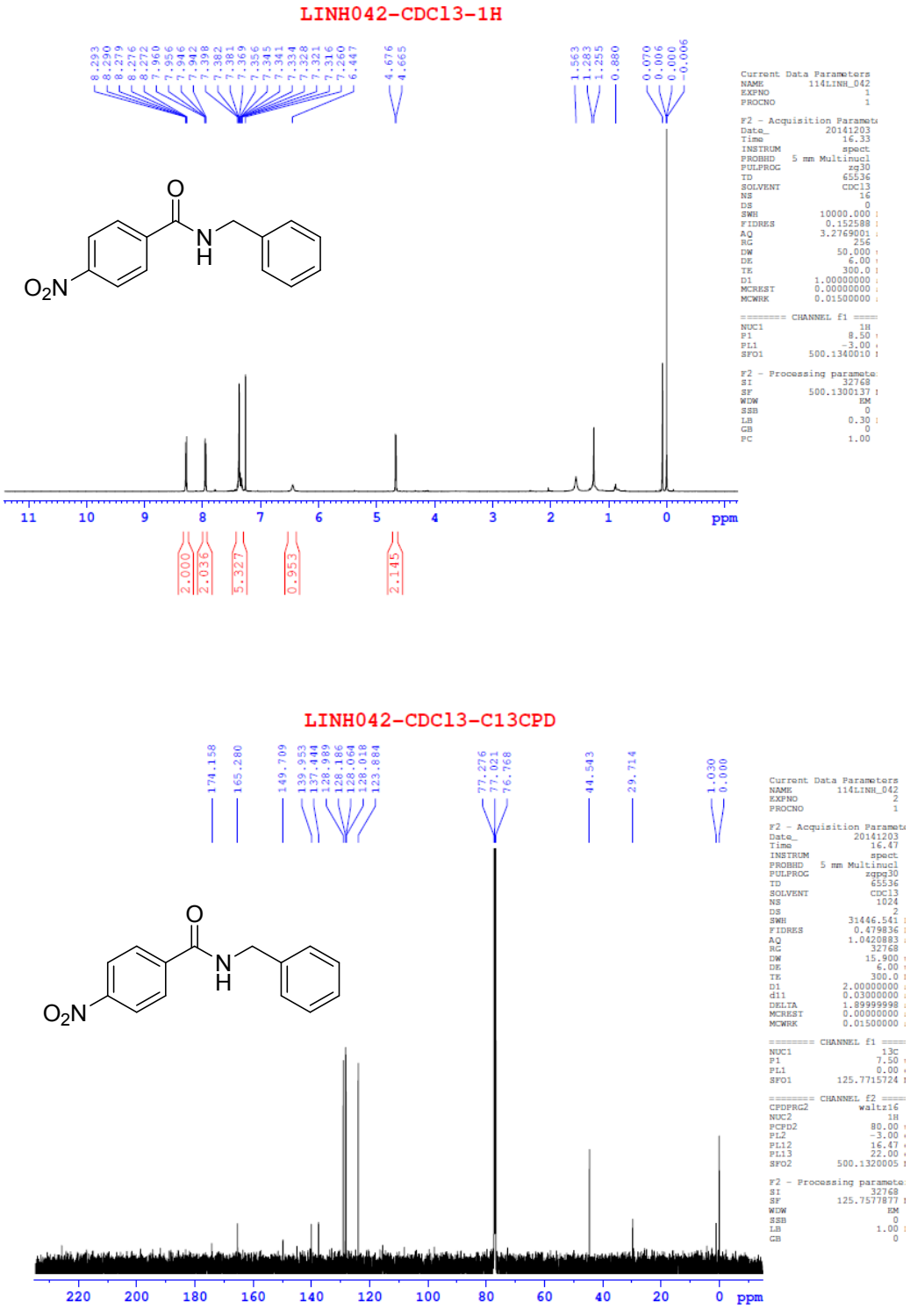


Fig. S17. ^{1}H NMR spectra and ^{13}C NMR of *N*-benzyl-4-nitrobenzamide in $CDCl_3$.

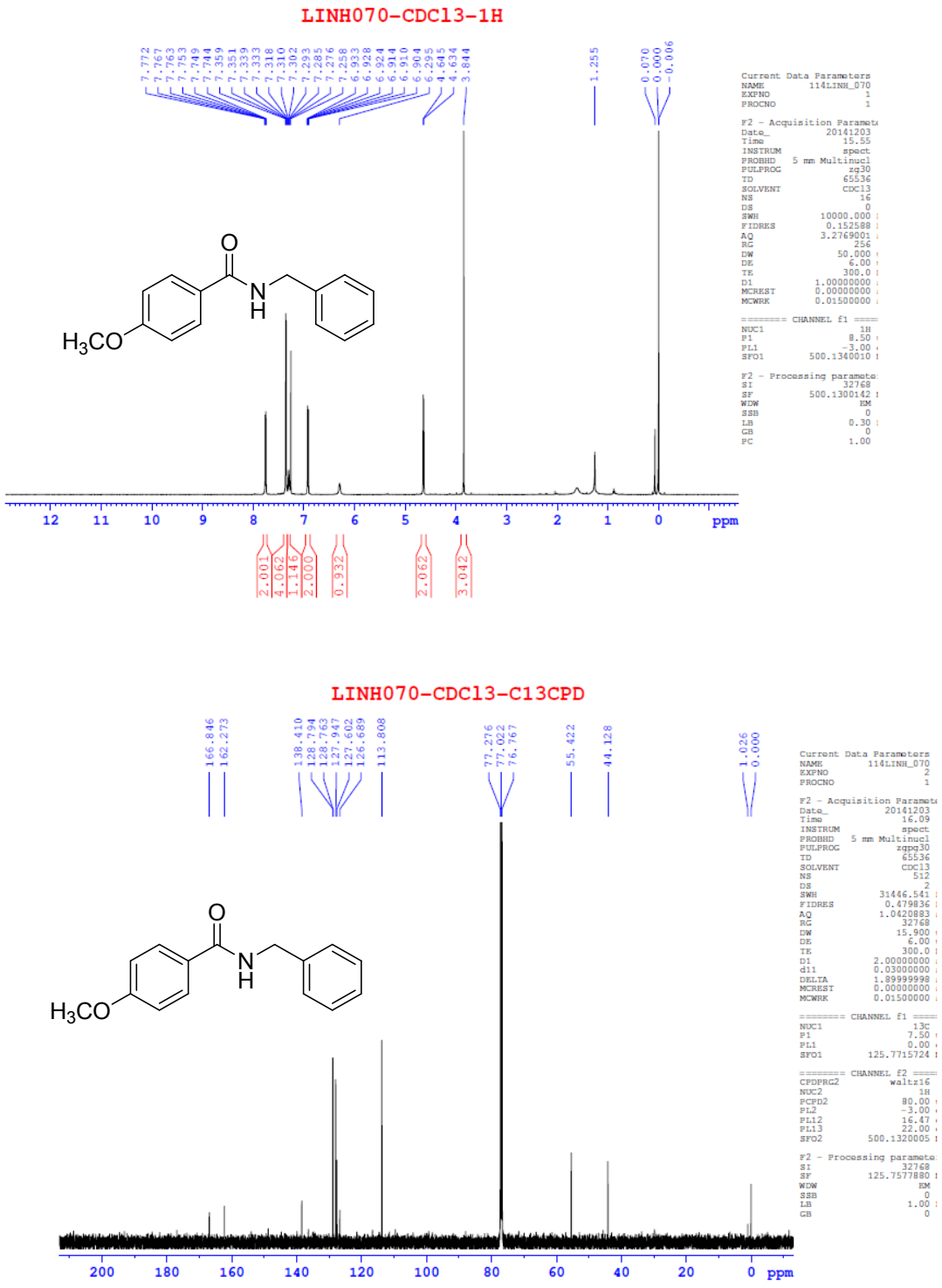


Fig. S18. ^{1}H NMR spectra and ^{13}C NMR of *N*-benzyl-4-methoxybenzamide in $CDCl_3$.

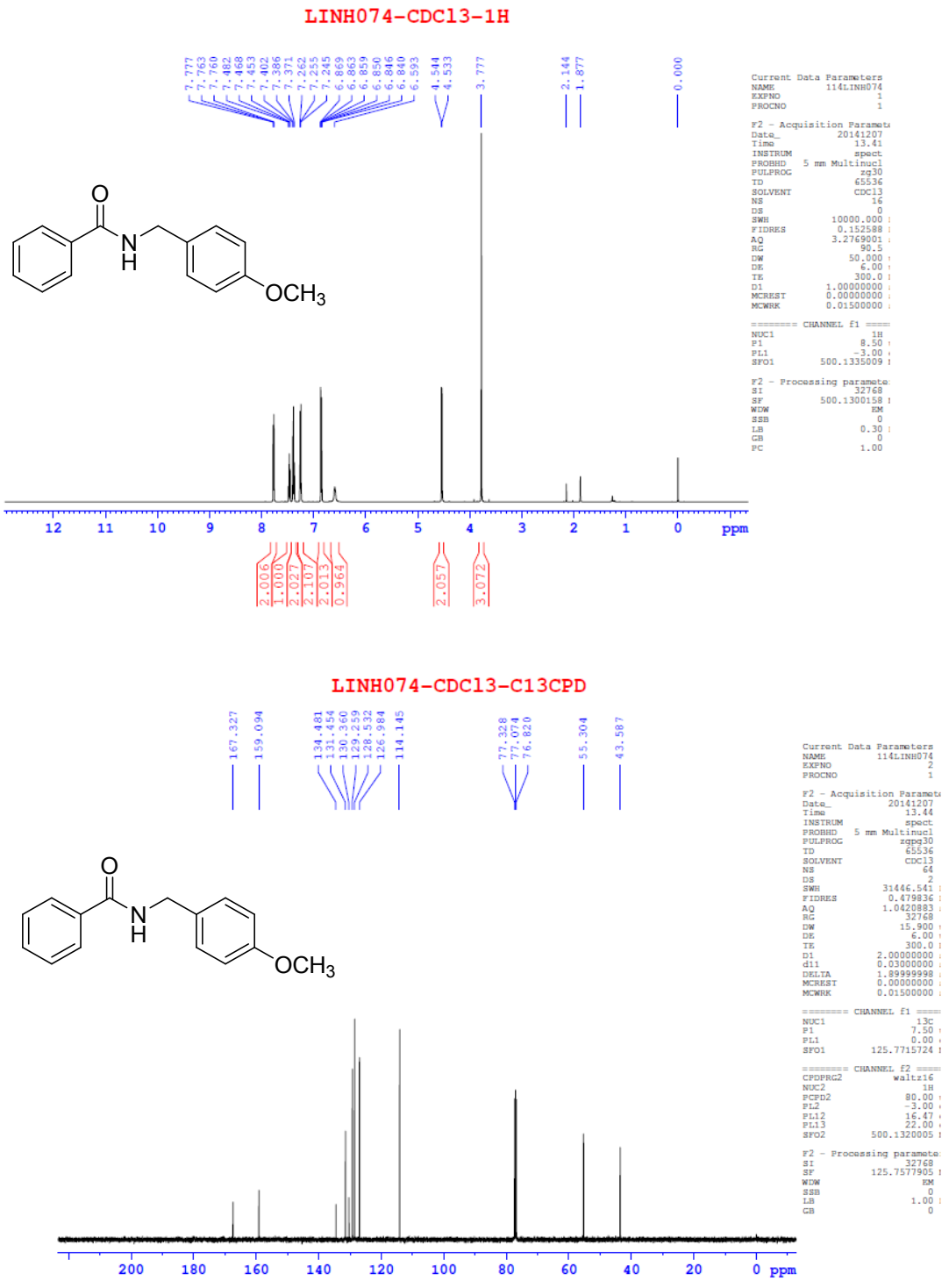


Fig. S19. ^{1}H NMR spectra and ^{13}C NMR of *N*-(4-methoxybenzyl)benzamide in $CDCl_3$.

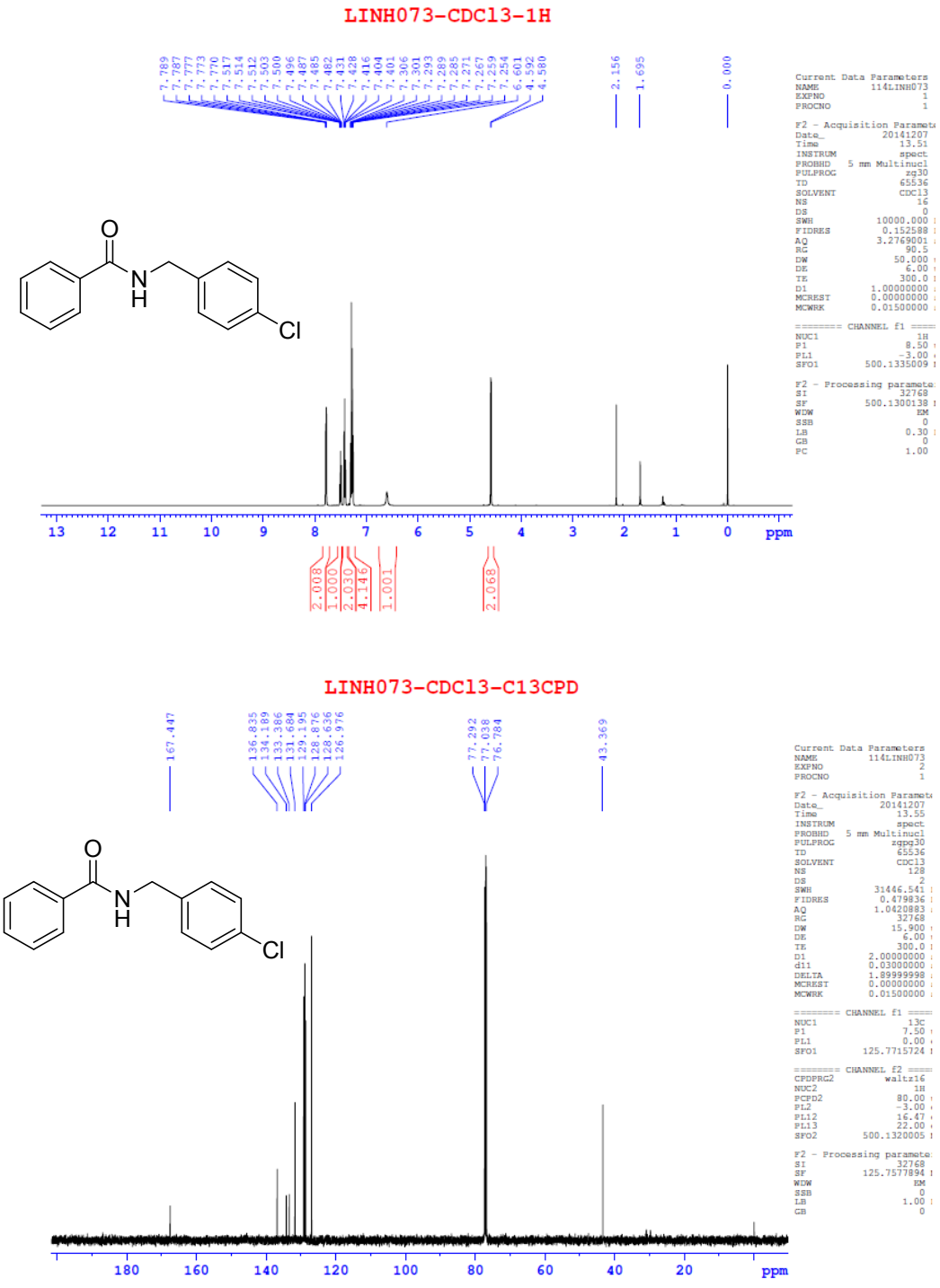


Fig. S20. ^{1}H NMR spectra and ^{13}C NMR of *N*-(4-chlorobenzyl)benzamide in $CDCl_3$.

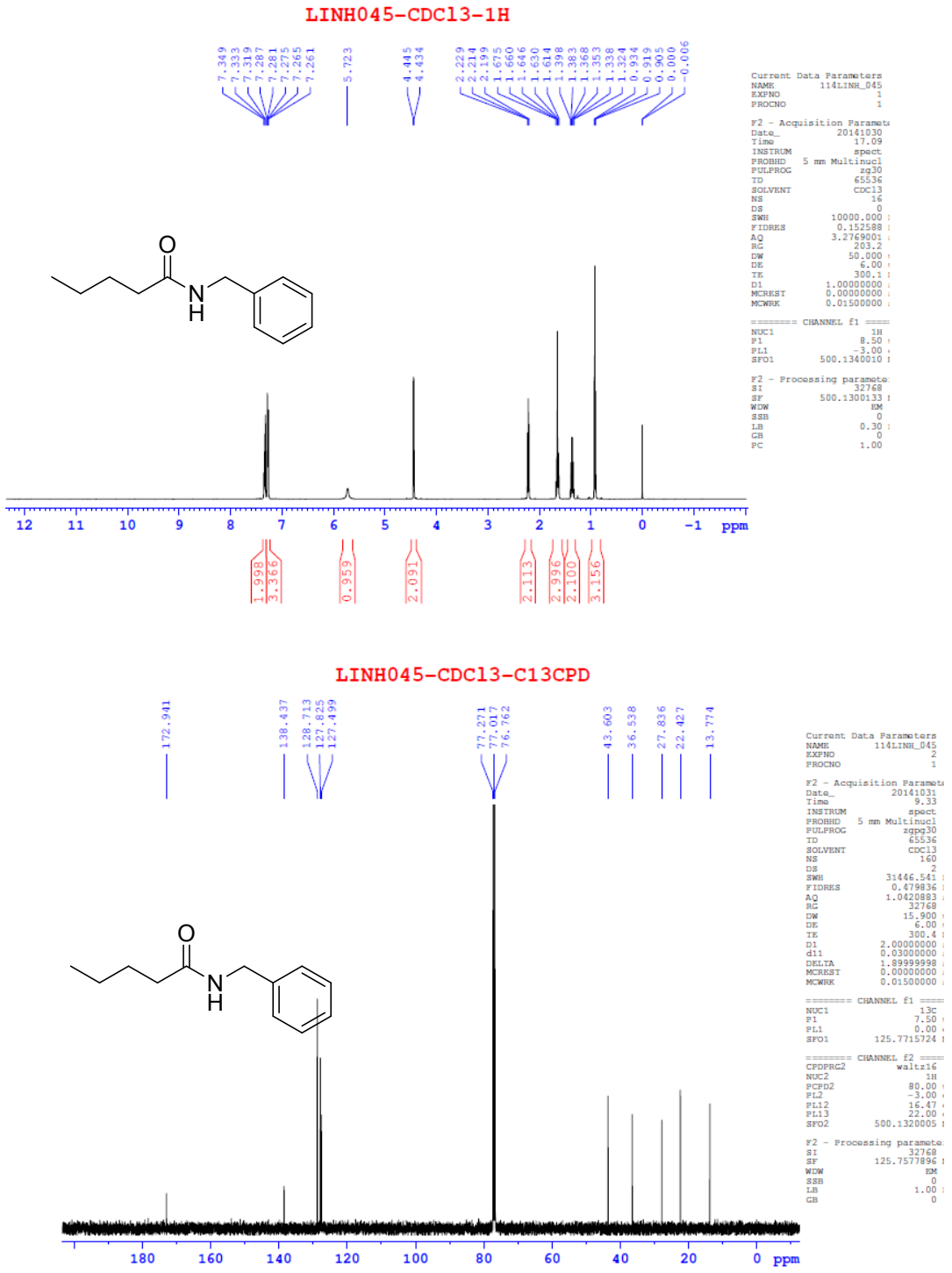


Fig. S21. ^{1}H NMR spectra and ^{13}C NMR of *N*-benzylpentanamide in $CDCl_3$.

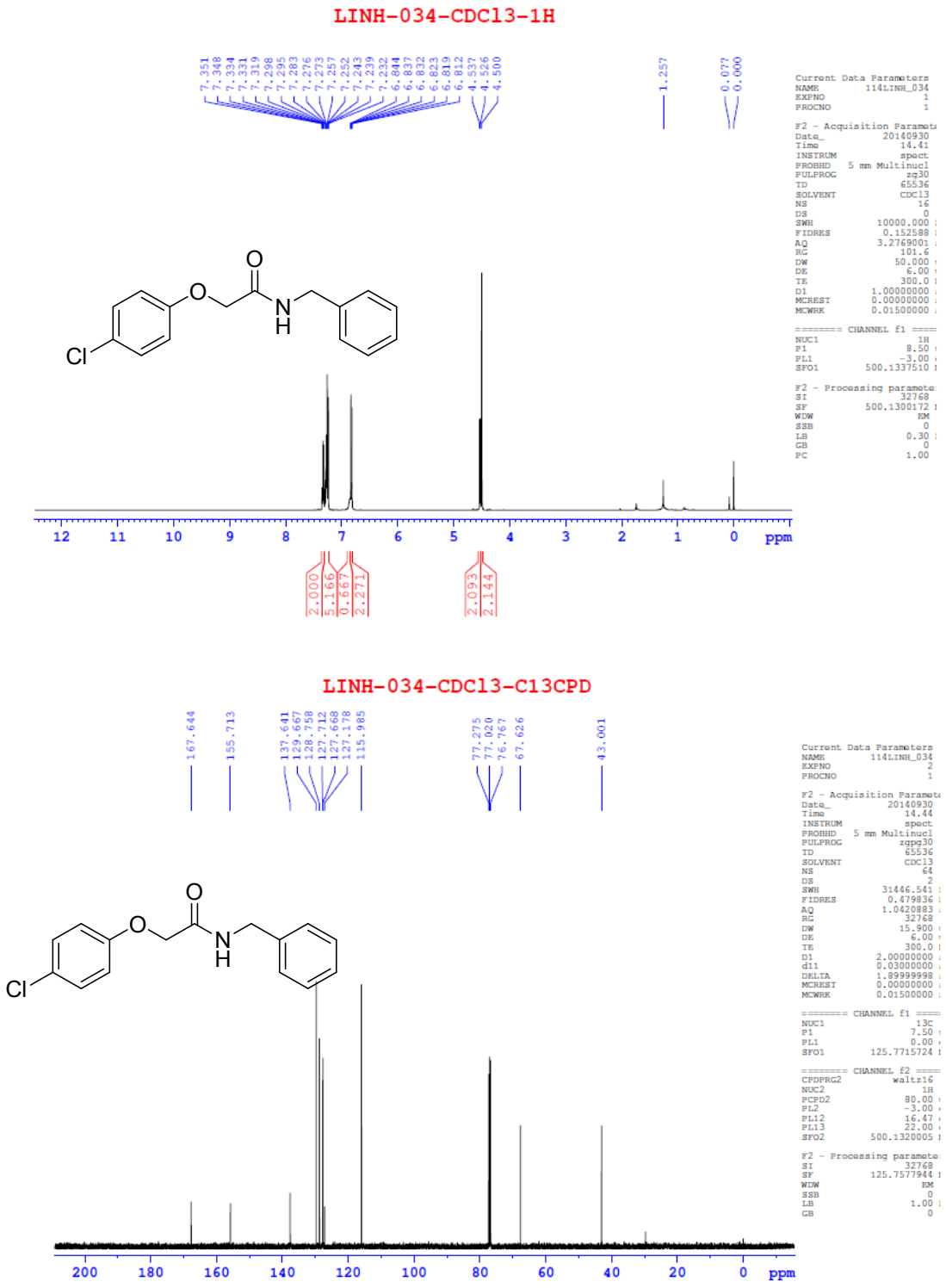


Fig. S22. ^{1}H NMR spectra and ^{13}C NMR of *N*-benzyl-2-(4-chlorophenoxy)acetamide in $CDCl_3$.

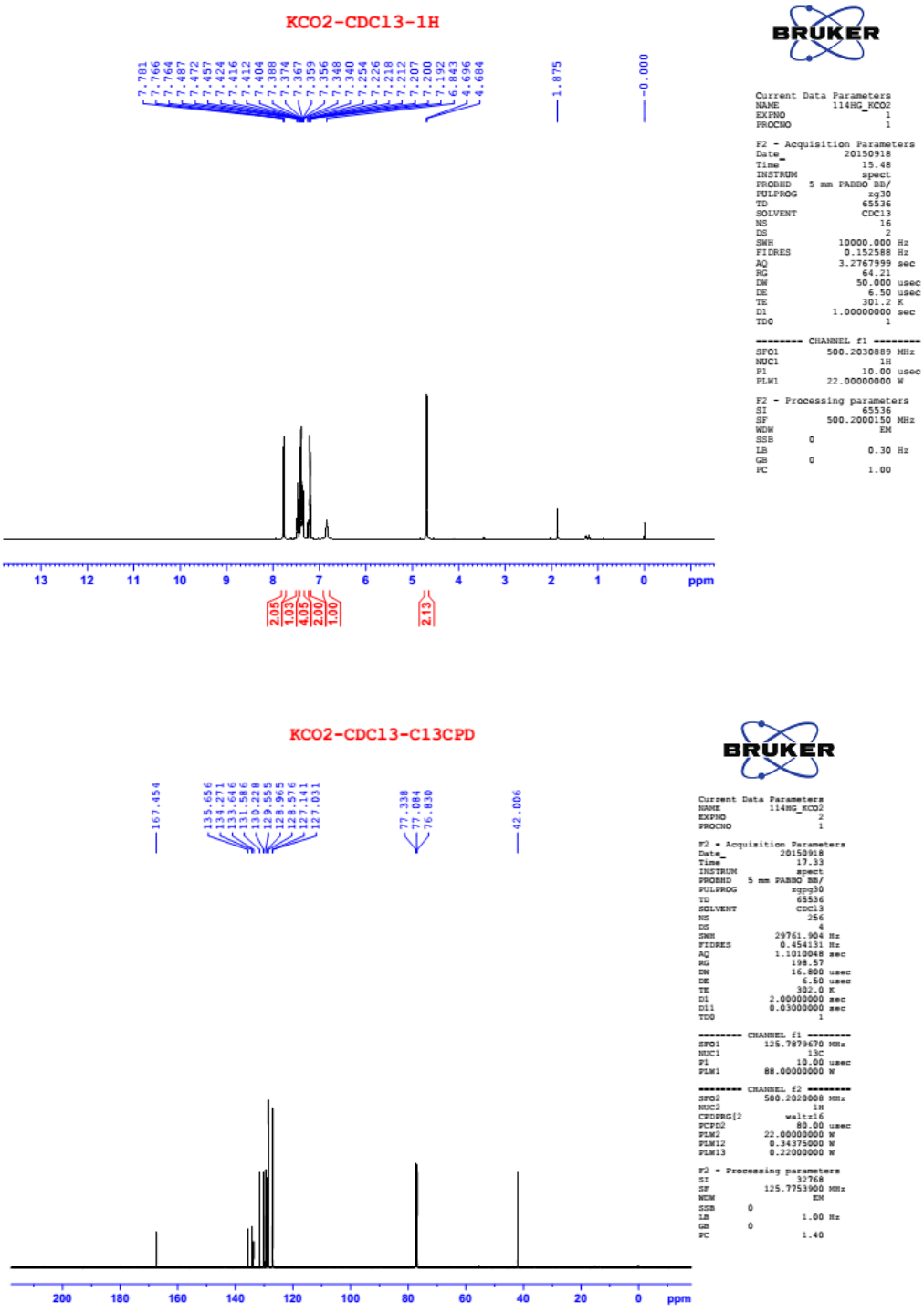


Fig. S23. ^{1}H NMR spectra and ^{13}C NMR of N-(2-chlorobenzyl)benzamide in $CDCl_3$.

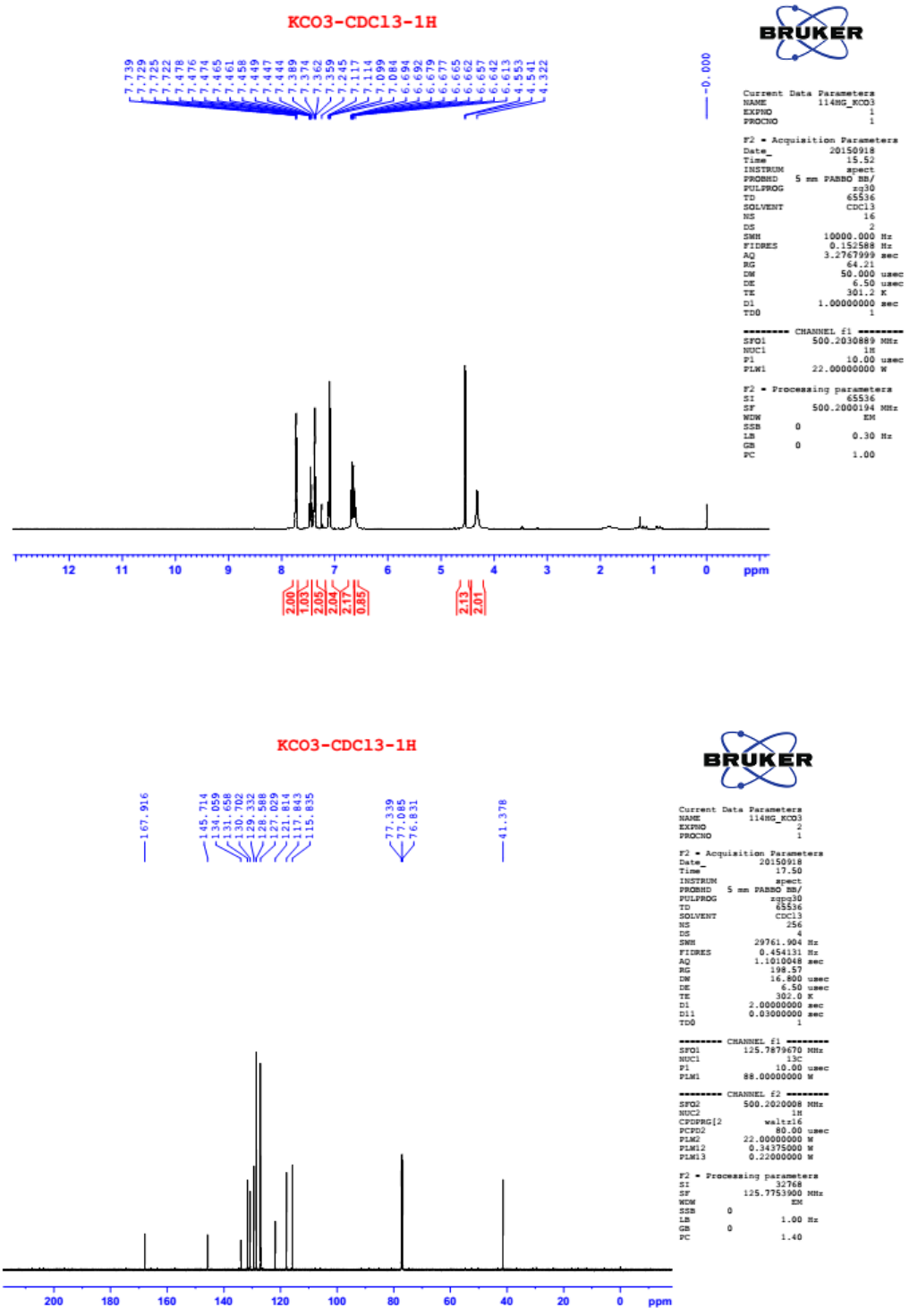


Fig. S24. ^{1}H NMR spectra and ^{13}C NMR of N-(2-aminobenzyl)benzamide in $CDCl_3$.

Section S9. References

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