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Heterogeneous C–H Alkenylations in Continuous-Flow: Oxidative Palladium-Catalysis in a Biomass-Derived Reaction Medium

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ELECTRONIC SUPPORTING INFORMATION

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General Information

Unless otherwise stated, all solvents and reagents were used as obtained from commercial sources without further purification. GC analyses were performed by using a Hewlett-Packard HP 5890A equipped with a capillary column DB-35MS (30 m, 0.53 mm), a FID detector and hydrogen as gas carrier. GC-EIMS analyses were carried out using a Hewlett-Packard HP 6890N Network GC system/5975 Mass Selective Detector equipped with an electron impact ionizer at 70 eV. NMR spectra were recorded on a Bruker DRX-ADVANCE 400 MHz (^1H at 400 MHz, ^{13}C at 100.6 MHz and ^{19}F at 376 MHz) in DMSO-d_6 using TMS as the internal standard. Elemental Analyses were conducted on a Fisons EA1108CHN. Melting points were measured on a Büchi 510. The amount of palladium leached in solution was measured with an Inductive Coupled Plasma – Optical Emission Spectrometer ICP-OES 710 from Agilent Technology. Flow procedures were performed using a Jasco PU-2080 pump and an Omnifit Glass Column as reservoir.

Typical Procedure for the Fujiwara-Moritani Reaction in Batch

A screw capped vial equipped with a magnetic stirrer was loaded, in the given order, with *p*-benzoquinone (1 mmol, 2 eq), PS-TsOH (0.5 mmol, 1 eq), acetanilide (0.5 mmol, 1 eq), Pd/C 10 wt. % (2.5 mol % of Pd), 1 mL of GVL and the alkene (0.55 mmol, 1.1 eq). The resulting solution was stirred at 85 °C for 24h. The reaction was left cooling to r.t and filtered through a pad of celite. A 0.5 M solution of $NaHCO_3$ (2 mL) was added and the aqueous layer was extracted with ethyl acetate (2 mL). The organic layer was then washed with deionized water (3 x 20 mL), dried over anhydrous Na_2SO_4 and evaporated under vacuum. The products were isolated by flash chromatography using a 4:1 mixture of petroleum ether and ethyl acetate as eluent.

Procedure for Catalyst Recovery and Recycling

After stirring at 85 °C for 24h, the reaction mixture was filtered and the combined solids were washed with GVL (5 mL). New substrates (**1a** and **2a**), benzoquinone and solvent were added (without the need of fresh PS-TsOH) and left under stirring for 24 h at 85 °C. The mixture of Pd/C and PS-TsOH could be used for four consecutive reaction runs without appreciable loss in reactivity.

Procedure for the Fujiwara-Moritani Reaction in Flow

Preparation of the reactor

A PTFE tube (2 m, 5 mm internal diameter) was packed with 2 g of Pd/C 10 wt. % (1.88 mmol) mixed with 55.2 g of glass beads (0.5 mm diameter). The terminations of the reactor were sealed with custom made Derlin® septa with appropriate connections.

Procedure for Fujiwara-Moritani reaction in flow at 85 °C

A pre-mixed mixture of acetanilide (1 eq), acrylate (1.1 eq), *p*-benzoquinone (2 eq), *p*-toluenesulfonic acid monohydrate (1 eq) in GVL was charged into a glass column functioning as a reservoir. The equipment was connected, by using the appropriate valves, to a pump and installed into a box thermostated at 85 °C. The reaction mixture was continuously pumped (flow rate: 0.5 $mL \cdot min^{-1}$; residence time: 40 min) through the catalyst column and the reaction was monitored by GC. Product was collected in fractions and palladium content of the GVL solution was periodically measured by ICP-OES analysis. The GVL solution was poured in 0.2 M NaOH, and extracted with EtOAc. Evaporating the organic phase under vacuum afforded a solid compound, which was washed with 0.2 M NaOH. Drying of the solid under vacuum afforded the pure products as white crystals.

Hot-filtration test

Two reactions between substrates **1a** and **2a** were run in parallel, in the optimized batch conditions. After 2 hours, one of the two reactions was removed from the heating and immediately subjected to filtration through a pad of Celite. The required amount of fresh PS-TsOH was added and the reaction was allowed to stir at the reaction conditions for additional 22 hours. The two reactions were monitored by GC analysis.

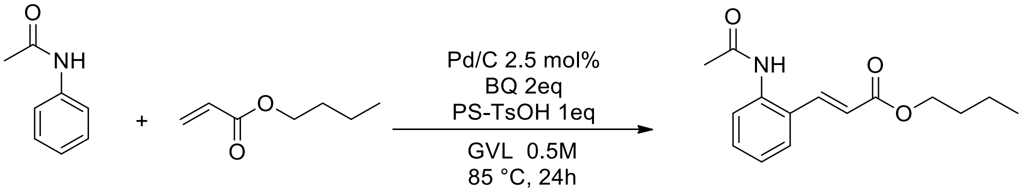
	2h	3h	6h	24h
Control reaction	46%	68%	74%	95%
Filtered reaction	43%	45%	45%	46%

Hg-poisoning test

Two reactions between substrates **1a** and **2a** were run in parallel, in the optimized batch conditions. After 2 hours, in one of the two reactions 100 equivalents (relative to the catalyst) of Hg(0) were added and the reaction was allowed to stir at the reaction conditions for additional 22 hours. The two reactions were monitored by GC analysis.

	2h	3h	6h	24h
Control reaction	46%	68%	74%	95%
Hg-poisoned reaction	47%	51%	50%	51%

Chem. Name	**Butyl (*E*)-3-(2-acetamidophenyl)acrylate (3a)**
Lit. Ref.	*J. Am. Chem. Soc.*, **2002**, *124*, 1586-1587



Mol.Wt.: 261.13

METHOD:
A screw capped vial equipped with a magnetic stirrer was loaded with *p*-benzoquinone (1 mmol, 108.1 mg), PS-TsOH (0.5 mmol, 150 mg), acetanilide (0.5 mmol, 67.6 mg), Pd/C (2.5 mol %, 13.3 mg), 1 mL of GVL and butyl acrylate (0.55 mmol, 76 µL). The resulting solution was stirred at 85 °C for 24h. The reaction was left cooling to r.t and filtered through a pad of celite. A 0.5 M solution of $NaHCO_3$ (2 mL) was added and the aqueous layer was extracted with ethyl acetate (2 mL). The organic layer was then washed with deionized water (3 x 20 mL), dried over anhydrous Na_2SO_4 and evaporated under vacuum. Chromatography of the crude product (PE/EtOAc 4:1) afforded the pure product as a white solid, 124 mg (95%).

Mol Formula	$C_{15}H_{19}NO_3$	**m.p.**	82-85 °C

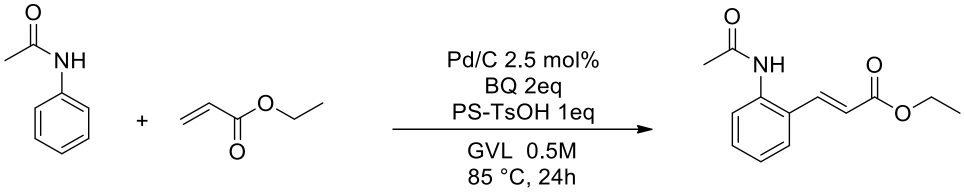
Elemental Analysis: Calc.: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.96; H, 7.32; N, 5.35.

^{1}H NMR **400 MHz** **DMSO**	**δ value**	**No. H**	**Mult.**	**J value/Hz**
	0.93	3	*t*	7.6
	1.44-1.36	2	*m*	
	1.67-1.60	2	*m*	
	2.08	3	*s*	
	4.16	2	*t*	6.4
	6.57	1	*d*	16.0
	7.30-7.20	1	*m*	
	7.55-7.45	2	*m*	
	7.77	1	*d*	16.0
	7.83	1	*d*	8.0
	9.85	1	*s*	

^{13}C NMR (100.6 MHz, DMSO) δ : 14.1, 19.1, 23.6, 30.7, 64.2, 119.1, 126.2, 127.1, 127.3, 129.1, 131.0, 137.5, 140.7, 166.8, 169.2

GC-EIMS (m/z, %): 90 (15), 117 (45), 118 (77), 128 (20), 146 (100), 219 (16), 261 (18)

Chem. Name	**Ethyl (*E*)-3-(2-acetamidophenyl)acrylate (3b)**
Lit. Ref.	*Org. Lett.*, **2012**, *14*, 728-731



Mol.Wt.: 233.10

METHOD:
A screw capped vial equipped with a magnetic stirrer was loaded with *p*-benzoquinone (1 mmol, 108.1 mg), PS-TsOH (0.5 mmol, 150 mg), acetanilide (0.5 mmol, 67.6 mg), Pd/C (2.5 mol %, 13.3 mg), 1 mL of GVL and ethyl acrylate (0.55 mmol, 60 µL). The resulting solution was stirred at 85 °C for 24h. The reaction was left cooling to r.t and filtered through a pad of celite. A 0.5 M solution of $NaHCO_3$ (2 mL) was added and the aqueous layer was extracted with ethyl acetate (2 mL). The organic layer was then washed with deionized water (3 x 20 mL), dried over anhydrous Na_2SO_4 and evaporated under vacuum. Chromatography of the crude product (PE/EtOAc 4:1) afforded the pure product as a white solid, 113 mg (97%).

Mol Formula	$C_{13}H_{15}NO_3$	**m.p.**	140-143 °C

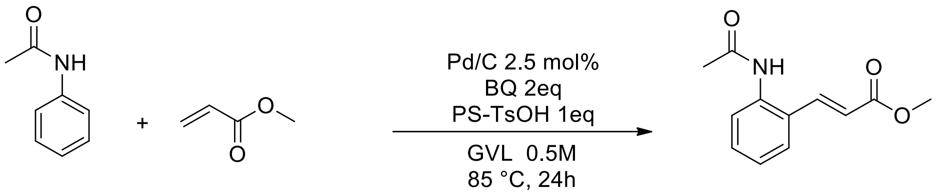
Elemental Analysis: Calc.: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.91; H, 6.48; N, 6.02.

^{1}H NMR 400 MHz DMSO	**δ value**	**No. H**	**Mult.**	**J value/Hz**
	1.25	3	*t*	7.2
	2.08	3	*s*	
	4.19	2	*q*	7.2
	6.56	1	*d*	16.0
	7.30-7.15	1	*m*	
	7.50-7.33	2	*m*	
	7.90-7.70	2	*m*	
	9.86	1	*s*	

^{13}C NMR (100.6 MHz, DMSO) δ : 14.6, 23.6, 60.5, 119.1, 126.2, 127.1, 127.2, 128.9, 131.0, 137.5, 140.7, 166.7, 169.2

GC-EIMS (m/z, %): 117 (45), 118 (59), 128 (22), 146 (100), 191 (25), 233 (23)

Chem. Name	**Methyl (*E*)-3-(2-acetamidophenyl)acrylate (3c)**
Lit. Ref.	*Tetrahedron Lett.*, **2007**, *48*, 5449–5453



Mol.Wt.: 219.23

METHOD:
A screw capped vial equipped with a magnetic stirrer was loaded with *p*-benzoquinone (1 mmol, 108.1 mg), PS-TsOH (0.5 mmol, 150 mg), acetanilide (0.5 mmol, 67.6 mg), Pd/C (2.5 mol %, 13.3 mg), 1 mL of GVL and methyl acrylate (0.55 mmol, 50 µL). The resulting solution was stirred at 85 °C for 24h. The reaction was left cooling to r.t and filtered through a pad of celite. A 0.5 M solution of $NaHCO_3$ (2 mL) was added and the aqueous layer was extracted with ethyl acetate (2 mL). The organic layer was then washed with deionized water (3 x 20 mL), dried over anhydrous Na_2SO_4 and evaporated under vacuum. Chromatography of the crude product (PE/EtOAc 4:1) afforded the pure product as a white solid, 87 mg (80%).

Mol Formula	$C_{12}H_{13}NO_3$	**m.p.**	136-138 °C

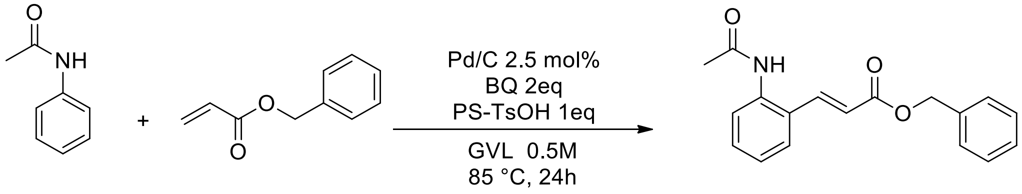
Elemental Analysis: Calc.: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.72; H, 5.99; N, 6.37.

^{1}H NMR 400 MHz DMSO	**δ value**	**No. H**	**Mult.**	**J value/Hz**
	2.09	3	*s*	
	3.74	3	*s*	
	6.58	1	*d*	16.0
	7.28-7.18	1	*m*	
	7.44-7.35	2	*m*	
	7.83-7.76	2	*m*	
	9.84	1	*s*	

^{13}C NMR (100.6 MHz, DMSO) δ : 23.6, 52.0, 118.8, 126.2, 127.0, 127.3, 128.8, 131.0, 137.5, 140.8, 167.2, 169.2

GC-EIMS (m/z, %): 89 (24), 90 (26), 118 (74), 128 (31), 146 (100), 160 (24), 176 (27), 177 (30), 219 (27)

Chem. Name	**Benzyl (*E*)-3-(2-acetamidophenyl)acrylate (3d)**
Lit. Ref.	*Angew. Chem. Int. Ed.*, **2015**, *54*, 7414–7417



Mol.Wt.: 295.33

METHOD:
A screw capped vial equipped with a magnetic stirrer was loaded with *p*-benzoquinone (1 mmol, 108.1 mg), PS-TsOH (0.5 mmol, 150 mg), acetanilide (0.5 mmol, 67.6 mg), Pd/C (2.5 mol %, 13.3 mg), 1 mL of GVL and benzyl acrylate (0.55 mmol, 84 µL). The resulting solution was stirred at 85 °C for 24h. The reaction was left cooling to r.t and filtered through a pad of celite. A 0.5 M solution of $NaHCO_3$ (2 mL) was added and the aqueous layer was extracted with ethyl acetate (2 mL). The organic layer was then washed with deionized water (3 x 20 mL), dried over anhydrous Na_2SO_4 and evaporated under vacuum. Chromatography of the crude product (PE/EtOAc 4:1) afforded the pure product as a white solid, 99 mg (67%).

Mol Formula	$C_{18}H_{17}NO_3$	**m.p.**	105-107 °C

Elemental Analysis: Calc.: C, 73.20; H, 5.80; N, 4.74. Found: C, 73.19; H, 5.78; N, 4.75.

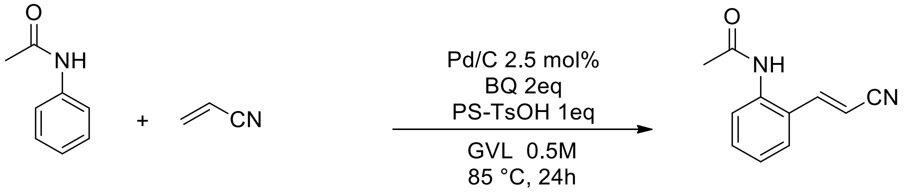
^{1}H NMR 400 MHz DMSO

δ value	No. H	Mult.	J value/Hz
2.08	3	*s*	
5.24	2	*s*	
6.64	1	*d*	16.0
7.26-7.20	1	*m*	
7.50-7.30	7	*m*	
7.85-7.80	2	*m*	
9.86	1	*s*	

^{13}C NMR (100.6 MHz, DMSO) δ : 23.6, 66.1, 118.8, 126.2, 127.1, 127.3, 128.51, 128.55, 128.9, 131.1, 136.7, 137.6, 141.2, 166.6, 169.2

GC-EIMS (m/z, %): 65 (16), 91 (100), 117 (29), 118 (44), 145 (15), 146 (44), 160 (15), 162 (21), 204 (20), 295 (10)

Chem. Name	**(*E*)-*N*-(2-(2-cyanovinyl)phenyl)acetamide (3e)**
Lit. Ref.	*Org. Lett.*, **2009**, *11*, 269–271



Mol.Wt.: 186.20

METHOD:
A screw capped vial equipped with a magnetic stirrer was loaded with *p*-benzoquinone (1 mmol, 108.1 mg), PS-TsOH (0.5 mmol, 150 mg), acetanilide (0.5 mmol, 67.6 mg), Pd/C (2.5 mol %, 13.3 mg), 1 mL of GVL and acrylonitrile (0.55 mmol, 38 µL). The resulting solution was stirred at 85 °C for 24h. The reaction was left cooling to r.t and filtered through a pad of celite. A 0.5 M solution of $NaHCO_3$ (2 mL) was added and the aqueous layer was extracted with ethyl acetate (2 mL). The organic layer was then washed with deionized water (3 x 20 mL), dried over anhydrous Na_2SO_4 and evaporated under vacuum. Chromatography of the crude product (PE/EtOAc 4:1) afforded the pure product as a white solid, 61 mg (66%).

Mol Formula	$C_{11}H_{10}N_2O$	**m.p.**	171-174 °C

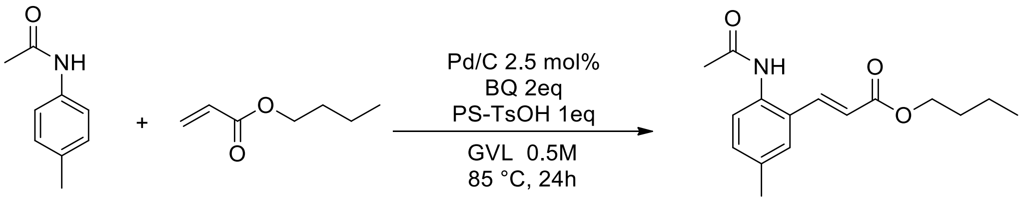
Elemental Analysis: Calc.: C, 70.95; H, 5.41; N, 15.04. Found: C, 70.93; H, 5.40; N, 15.05.

	δ value	**No. H**	**Mult.**	**J value/Hz**
^{1}H NMR **400 MHz** **DMSO**	2.10	3	*s*	
	6.41	1	*d*	16.8
	7.24	1	*t*	7.6
	7.44	1	*t*	7.6
	7.50	1	*d*	8.0
	7.69	1	*d*	16.4
	7.75	1	*d*	7.6
	9.76	1	*s*	

^{13}C NMR (100.6 MHz, DMSO) δ : 23.8, 97.6, 119.5, 125.9, 126.4, 126.6, 127.8, 131.7, 137.2, 146.9 169.3

GC-EIMS (m/z, %):90 (15), 117 (62), 144 (100), 171 (18), 186 (22)

Chem. Name	**Butyl (*E*)-3-(2-acetamido-5-methylphenyl)acrylate (3f)**
Lit. Ref.	*Org. Lett.*, **2012**, *14*, 728–731



Mol.Wt.: 275.34

METHOD:
A screw capped vial equipped with a magnetic stirrer was loaded with *p*-benzoquinone (1 mmol, 108.1 mg), PS-TsOH (0.5 mmol, 150 mg), 4'-methylacetanilide (0.5 mmol, 74.6 mg), Pd/C (2.5 mol %, 13.3 mg), 1 mL of GVL and butyl acrylate (0.55 mmol, 76 µL). The resulting solution was stirred at 85 °C for 24h. The reaction was left cooling to r.t and filtered through a pad of celite. A 0.5 M solution of $NaHCO_3$ (2 mL) was added and the aqueous layer was extracted with ethyl acetate (2 mL). The organic layer was then washed with deionized water (3 x 20 mL), dried over anhydrous Na_2SO_4 and evaporated under vacuum. Chromatography of the crude product (PE/EtOAc 4:1) afforded the pure product as a white solid, 107 mg (78%).

Mol Formula	$C_{16}H_{21}NO_3$	**m.p.**	127-129 °C

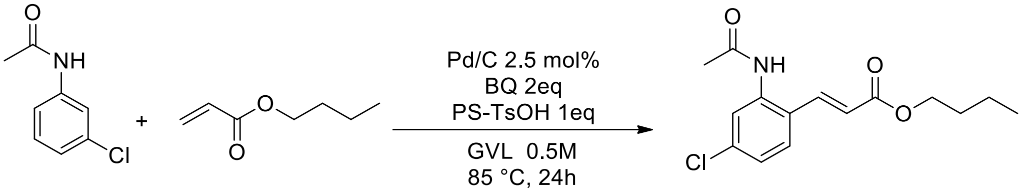
Elemental Analysis: Calc.: C, 69.79; H, 7.69; N, 5.09. Found: C, 69.81; H, 7.69; N, 5.07.

^{1}H NMR 400 MHz DMSO	**δ value**	**No. H**	**Mult.**	**J value/Hz**
	0.93	3	*t*	7.2
	1.44-1.34	2	*m*	
	1.66-1.59	2	*m*	
	2.06	3	*s*	
	2.31	3	*s*	
	4.15	2	*t*	6.4
	6.55	1	*d*	16.0
	7.27-7.20	2	*m*	
	7.67	1	*s*	
	7.73	1	*d*	16.0
	9.74	1	*s*	

^{13}C NMR (100.6 MHz, DMSO) δ : 14.1, 19.1, 20.9, 23.6, 30.7, 64.2, 118.8, 127.1, 127.4, 128.9, 131.8, 135.1, 135.6, 140.8, 166.8, 169.2

GC-EIMS (m/z, %): 130 (26), 131 (22), 132 (65), 142 (15), 160 (100), 233 (18), 275 (25)

Chem. Name	**Butyl (*E*)-3-(2-acetamido-4-chlorophenyl)acrylate (3g)**
Lit. Ref.	*Adv. Synth. Catal.*, **2005**, *347*, 1921–1924



Mol.Wt.: 295.76

METHOD:
A screw capped vial equipped with a magnetic stirrer was loaded with *p*-benzoquinone (1 mmol, 108.1 mg), PS-TsOH (0.5 mmol, 150 mg), 3’-chloroacetanilide (0.5 mmol, 84.8 mg), Pd/C (2.5 mol %, 13.3 mg), 1 mL of GVL and butyl acrylate (0.55 mmol, 76 µL). The resulting solution was stirred at 85 °C for 24h. The reaction was left cooling to r.t and filtered through a pad of celite. A 0.5 M solution of $NaHCO_3$ (2 mL) was added and the aqueous layer was extracted with ethyl acetate (2 mL). The organic layer was then washed with deionized water (3 x 20 mL), dried over anhydrous Na_2SO_4 and evaporated under vacuum. Chromatography of the crude product (PE/EtOAc 4:1) afforded the pure product as a white solid, 118 mg (80%).

Mol Formula	$C_{15}H_{18}ClNO_3$	**m.p.**	152-155 °C

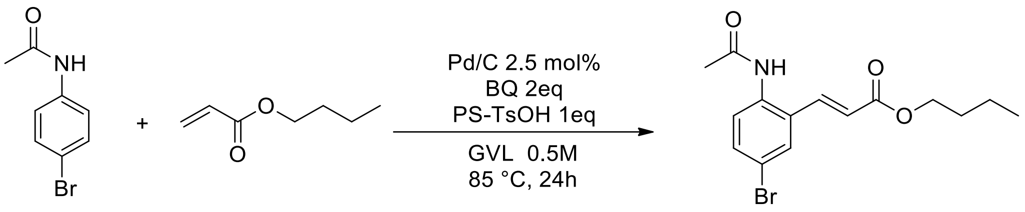
Elemental Analysis: Calc.: C, 60.91; H, 6.13; N, 4.74. Found: C, 60.93; H, 6.12; N, 4.75.

^{1}H NMR 400 MHz DMSO	**δ value**	**No. H**	**Mult.**	**J value/Hz**
	0.92	3	*t*	7.6
	1.43-1.34	2	*m*	
	1.67-1.59	2	*m*	
	2.10	3	*s*	
	4.16	2	*t*	6.4
	6.61	1	*d*	16.0
	7.28	1	*dd*	8.4; 2.0
	7.59	1	*d*	2.0
	7.75	1	*d*	16.0
	7.86	1	*d*	8.4
	9.97	1	*s*	

^{13}C NMR (100.6 MHz, DMSO) δ : 14.1, 19.1, 23.7, 30.7, 64.3, 120.0, 125.9, 126.1, 127.3, 129.0, 135.0, 138.7, 139.4, 166.6, 169.4

GC-EIMS (m/z, %): 89 (17), 117 (18), 151 (40), 152 (81), 153 (22), 154 (26), 162 (17), 180 (100), 182 (33), 253 (22), 295 (17)

Chem. Name	**Butyl (*E*)-3-(2-acetamido-5-bromophenyl)acrylate (3h)**
Lit. Ref.	



Mol.Wt.: 340.21

METHOD:
A screw capped vial equipped with a magnetic stirrer was loaded with *p*-benzoquinone (1 mmol, 108.1 mg), PS-TsOH (0.5 mmol, 150 mg), 4’-bromoacetanilide (0.5 mmol, 106.5 mg), Pd/C (2.5 mol %, 13.3 mg), 1 mL of GVL and butyl acrylate (0.55 mmol, 76 µL). The resulting solution was stirred at 85 °C for 24h. The reaction was left cooling to r.t and filtered through a pad of celite. A 0.5 M solution of $NaHCO_3$ (2 mL) was added and the aqueous layer was extracted with ethyl acetate (2 mL). The organic layer was then washed with deionized water (3 x 20 mL), dried over anhydrous Na_2SO_4 and evaporated under vacuum. Chromatography of the crude product (PE/EtOAc 4:1) afforded the pure product as a white solid, 129 mg (76%).

Mol Formula	$C_{15}H_{18}BrNO_3$	**m.p.**	120-123 °C

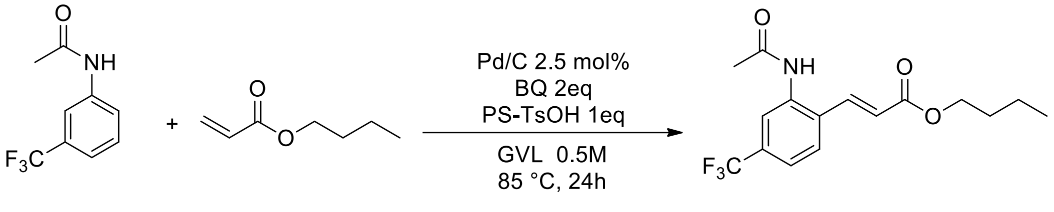
Elemental Analysis: Calc.: C, 52.96; H, 5.33; N, 4.12. Found: C, 52.96; H, 5.32; N, 4.13.

^{1}H NMR **400 MHz** **DMSO**	**δ value**	**No. H**	**Mult.**	**J value/Hz**
	0.92	3	*t*	7.2
	1.41-1.34	2	*m*	
	1.66-1.59	2	*m*	
	2.09	3	*s*	
	4.15	2	*t*	6.8
	6.70	1	*d*	16.0
	7.39	1	*d*	8.4
	7.57	1	*d*	8.4
	7.67	1	*d*	16.0
	8.05	1	*s*	
	9.91	1	*s*	

^{13}C NMR (100.6 MHz, DMSO) δ : 14.0, 19.1, 23.6, 30.7, 64.3, 118.6, 120.7, 128.8, 129.7, 131.0, 133.5, 136.7, 139.1, 166.6, 169.2

GC-EIMS (m/z, %): 89 (20), 116 (22), 117 (44), 195 (18), 196 (28), 197 (21), 198 (28), 224 (100), 225 (22), 226 (97), 297 (25), 299 (25), 339 (19), 341 (19)

Chem. Name	**Butyl (*E*)-3-(2-acetamido-4-(trifluoromethyl)phenyl)acrylate (3i)**
Lit. Ref.	*Adv. Synth. Catal.*, **2011**, *353*, 2988–2998



Mol.Wt.: 329.31

METHOD:
A screw capped vial equipped with a magnetic stirrer was loaded with *p*-benzoquinone (1 mmol, 108.1 mg), PS-TsOH (0.5 mmol, 150 mg), 3'-trifluoromethylacetanilide (0.5 mmol, 101.5 mg), Pd/C (2.5 mol %, 13.3 mg), 1 mL of GVL and butyl acrylate (0.55 mmol, 76 µL). The resulting solution was stirred at 85 °C for 24h. The reaction was left cooling to r.t and filtered through a pad of celite. A 0.5 M solution of $NaHCO_3$ (2 mL) was added and the aqueous layer was extracted with ethyl acetate (2 mL). The organic layer was then washed with deionized water (3 x 20 mL), dried over anhydrous Na_2SO_4 and evaporated under vacuum. Chromatography of the crude product (PE/EtOAc 4:1) afforded the pure product as a white solid, 122 mg (74%).

Mol Formula	$C_{16}H_{18}F_3NO_3$	**m.p.**	160-162 °C

Elemental Analysis: Calc.: C, 58.35; H, 5.51; N, 4.25. Found: C, 58.33; H, 5.50; N, 4.24.

^{1}H NMR 400 MHz DMSO

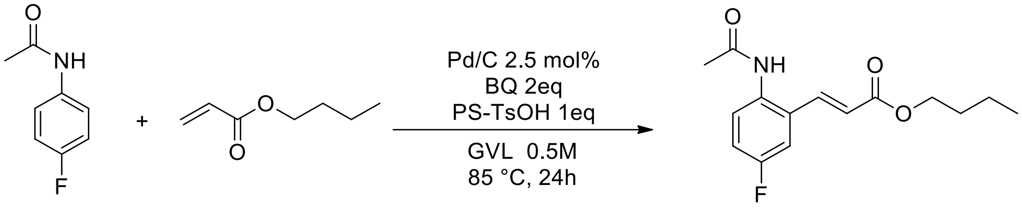
δ value	No. H	Mult.	J value/Hz
0.92	3	*t*	7.2
1.43-1.35	2	*m*	
1.67-1.59	2	*m*	
2.11	3	*s*	
4.17	2	*t*	6.8
6.72	1	*d*	16.0
7.54	1	*d*	8.0
7.79	1	*d*	16.0
7.86	1	*s*	
8.04	1	*d*	8.0
10.08	1	*s*	

^{13}C NMR (100.6 MHz, DMSO) δ : 14.0, 19.1, 23.7, 30.7, 64.5, 122.0, 122.2, 122.9, 124.2 ($J_{C\text{-}F}$ = 271 Hz), 128.7, 130.5 ($J_{C\text{-}F}$ = 32 Hz), 132.2, 137.9, 139.1, 166.4, 169.6

^{19}F NMR (376 MHz, DMSO) δ : -61.50

GC-EIMS (m/z, %):57 (19), 166 (31), 185 (68), 186 (100), 187 (18), 196 (35), 213 (29), 214 (100), 215 (31), 228 (28), 287 (30), 329 (23)

Chem. Name	**Butyl (*E*)-3-(2-acetamido-5-fluorophenyl)acrylate (3j)**
Lit. Ref.	*Org. Lett.*, **2012**, *14*, 728–731



Mol.Wt.: 279.30

METHOD:
A screw capped vial equipped with a magnetic stirrer was loaded with *p*-benzoquinone (1 mmol, 108.1 mg), PS-TsOH (0.5 mmol, 150 mg), 4'-fluoroacetanilide (0.5 mmol, 76.5 mg), Pd/C (2.5 mol %, 13.3 mg), 1 mL of GVL and butyl acrylate (0.55 mmol, 76 µL). The resulting solution was stirred at 85 °C for 24h. The reaction was left cooling to r.t and filtered through a pad of celite. A 0.5 M solution of $NaHCO_3$ (2 mL) was added and the aqueous layer was extracted with ethyl acetate (2 mL). The organic layer was then washed with deionized water (3 x 20 mL), dried over anhydrous Na_2SO_4 and evaporated under vacuum. Chromatography of the crude product (PE/EtOAc 4:1) afforded the pure product as a white solid, 114 mg (82%).

Mol Formula	$C_{15}H_{18}FNO_3$	**m.p.**	137-140 °C

Elemental Analysis: Calc.: C, 64.50; H, 6.50; N, 5.01. Found: C, 64.52; H, 6.50; N, 5.00.

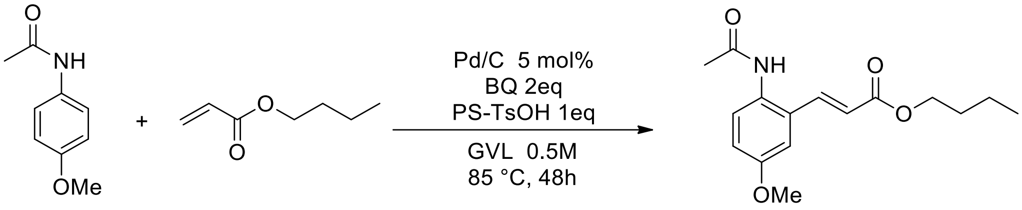
^{1}H NMR 400 MHz DMSO	**δ value**	**No. H**	**Mult.**	**J value/Hz**
	0.93	3	*t*	7.2
	1.44-1.34	2	*m*	
	1.67-1.60	2	*m*	
	2.07	3	*s*	
	4.16	2	*t*	6.4
	6.68	1	*d*	16.0
	7.29-7.24	1	*m*	
	7.42-7.38	1	*m*	
	7.68	1	*d*	16.0
	7.76-7.72	1	*m*	
	9.83	1	*s*	

^{13}C NMR (100.6 MHz, DMSO) δ : 14.0, 19.1, 23.5, 30.7, 64.3, 113.3 (J_{C-F} = 23 Hz), 117.9 (J_{C-F} = 23 Hz), 120.6, 129.4 (J_{C-F} = 8 Hz), 131.3 (J_{C-F} = 8 Hz), 133.8, 139.5, 160.2 (J_{C-F} = 241 Hz), 166.6, 169.3

^{19}F NMR (376 MHz, DMSO) δ : -116.2 (m)

GC-EIMS (m/z, %): 135 (29), 136 (44), 164 (100), 237 (22), 279 (15)

Chem. Name	**Butyl (*E*)-3-(2-acetamido-5-methoxyphenyl)acrylate (3k)**
Lit. Ref.	*J. Am. Chem. Soc.*, **2002**, *124*, 1586-1587



Mol.Wt.: 291.34

METHOD:
A screw capped vial equipped with a magnetic stirrer was loaded with *p*-benzoquinone (1 mmol, 108.1 mg), PS-TsOH (0.5 mmol, 150 mg), 4'-methoxyacetanilide (0.5 mmol, 82.6 mg), Pd/C (5 mol %, 26.6 mg), 1 mL of GVL and butyl acrylate (1 mmol, 143 µL). The resulting solution was stirred at 85 °C for 48h. The reaction was left cooling to r.t and filtered through a pad of celite. A 0.5 M solution of $NaHCO_3$ (2 mL) was added and the aqueous layer was extracted with ethyl acetate (2 mL). The organic layer was then washed with deionized water (3 x 20 mL), dried over anhydrous Na_2SO_4 and evaporated under vacuum. Chromatography of the crude product (PE/EtOAc 95:5) afforded the pure product as a white solid, 106 mg (73%).

Mol Formula	$C_{16}H_{21}NO_4$	**m.p.**	128-130 °C

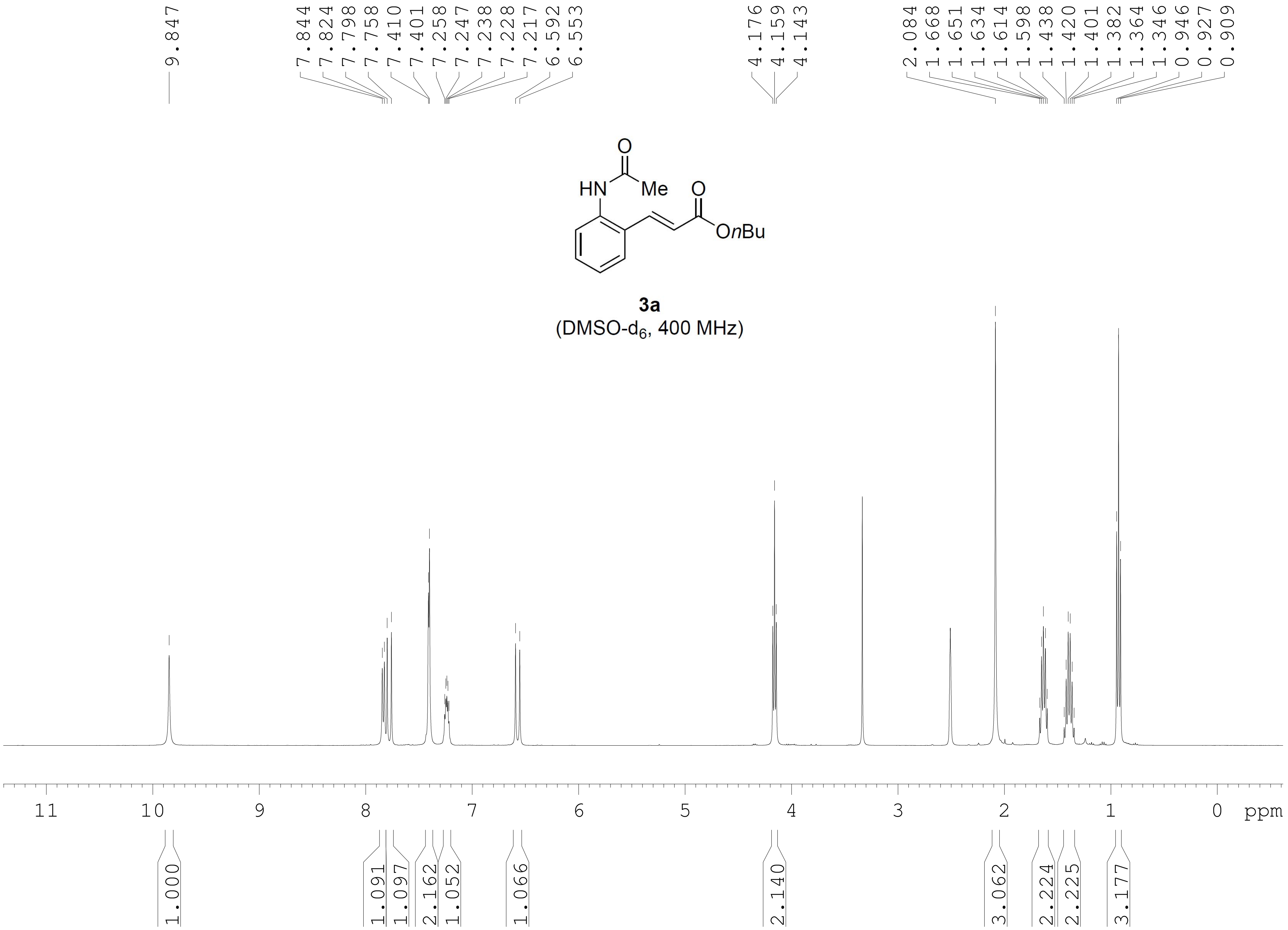
Elemental Analysis: Calc.: C, 65.96; H, 7.27; N, 4.81. Found: C, 65.99; H, 7.25; N, 4.83.

^{1}H NMR 400 MHz DMSO	**δ value**	**No. H**	**Mult.**	**J value/Hz**
	0.93	3	*t*	7.6
	1.45-1.30	2	*m*	
	1.67-1.59	2	*m*	
	2.05	3	*s*	
	3.80	3	*s*	
	4.16	2	*t*	6.8
	6.66	1	*d*	16.0
	6.99	1	*dd*	8.8; 2.8
	7.23	1	*d*	8.8
	7.34	1	*d*	2.8
	7.70	1	*d*	15.6
	9.67	1	*s*	

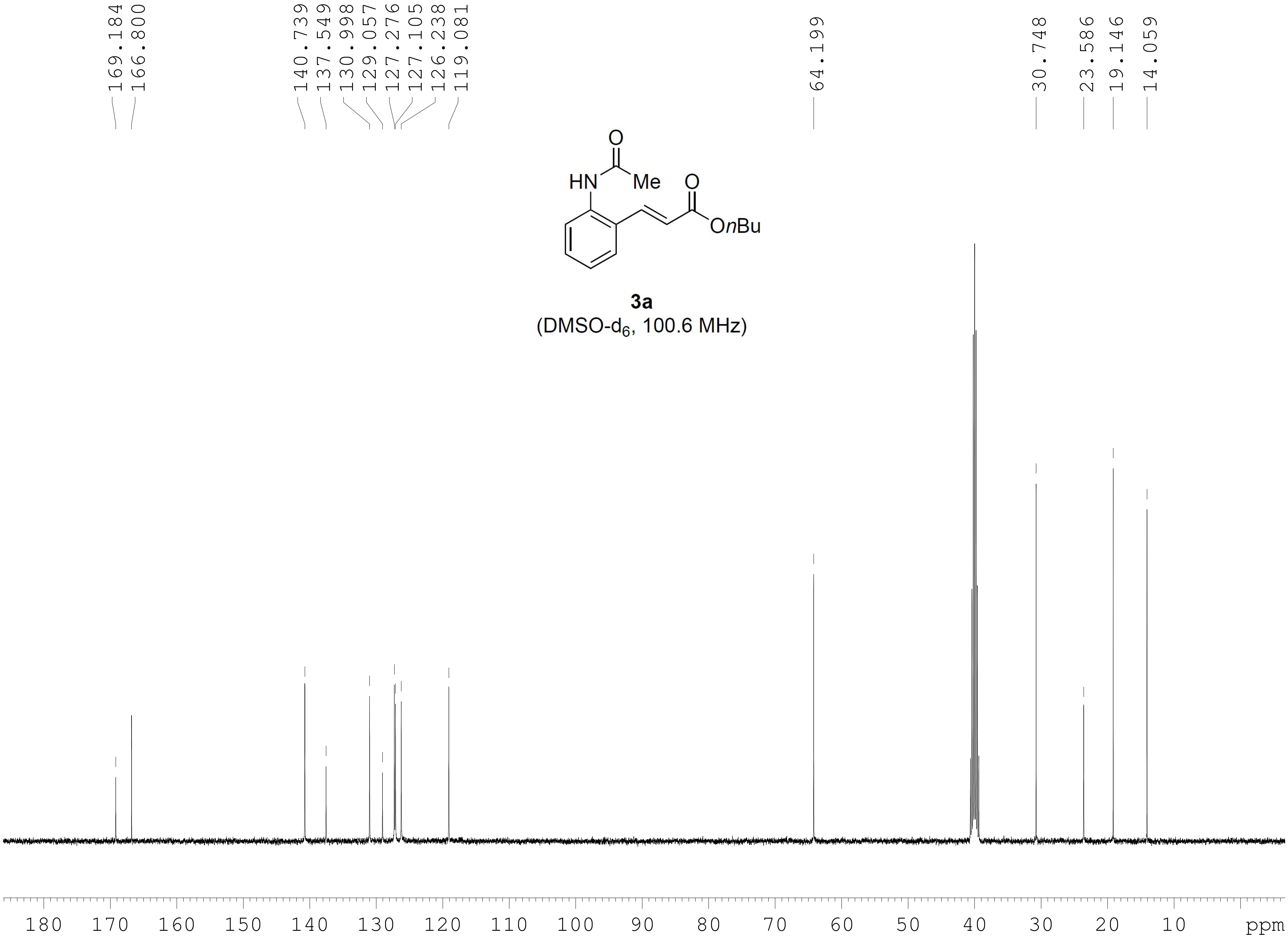
^{13}C NMR (100.6 MHz, DMSO) δ : 14.1, 19.1, 23.4, 30.7, 56.0, 64.2, 110.7, 117.8, 119.5, 129.0, 130.6, 130.7, 140.6, 157.6, 166.8, 169.3

GC-EIMS (m/z, %): 132 (17), 148 (36), 176 (100), 249 (20), 291 (37)

Butyl (E)-3-(2-acetamidophenyl)acrylate (3a)



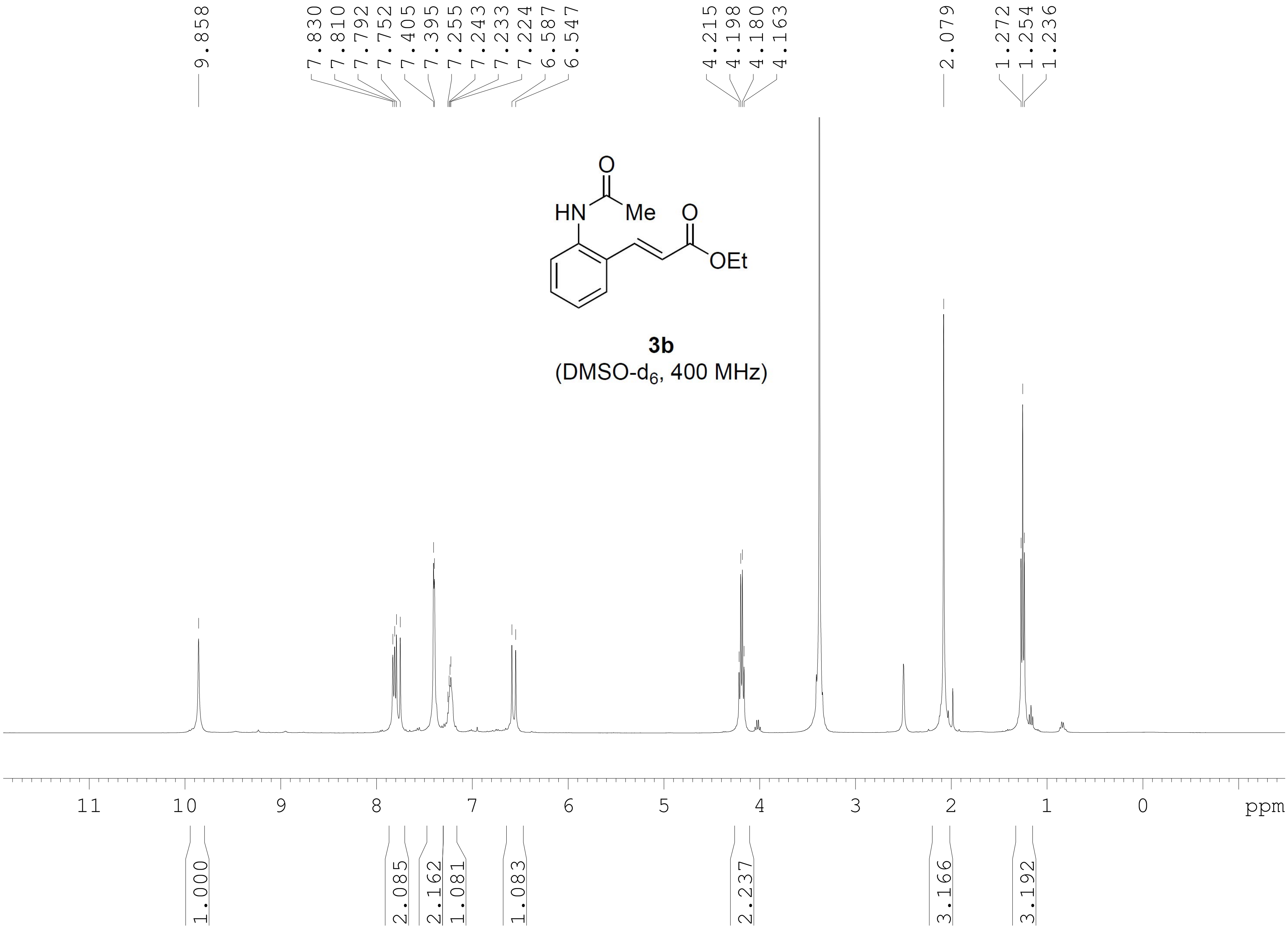
Butyl (E)-3-(2-acetamidophenyl)acrylate (3a)



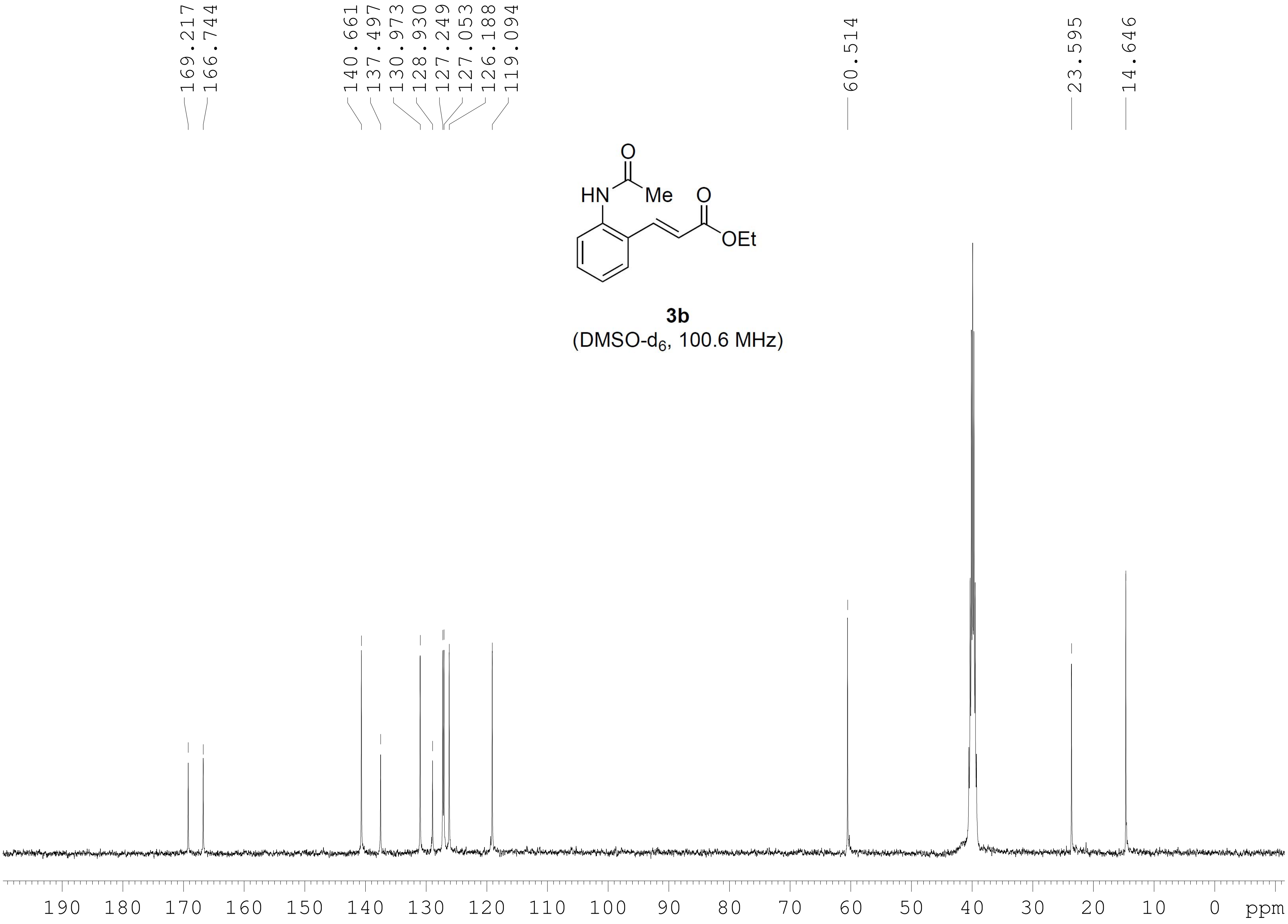
3a

(DMSO-d_6, 100.6 MHz)

Ethyl (E)-3-(2-acetamidophenyl)acrylate (3b)

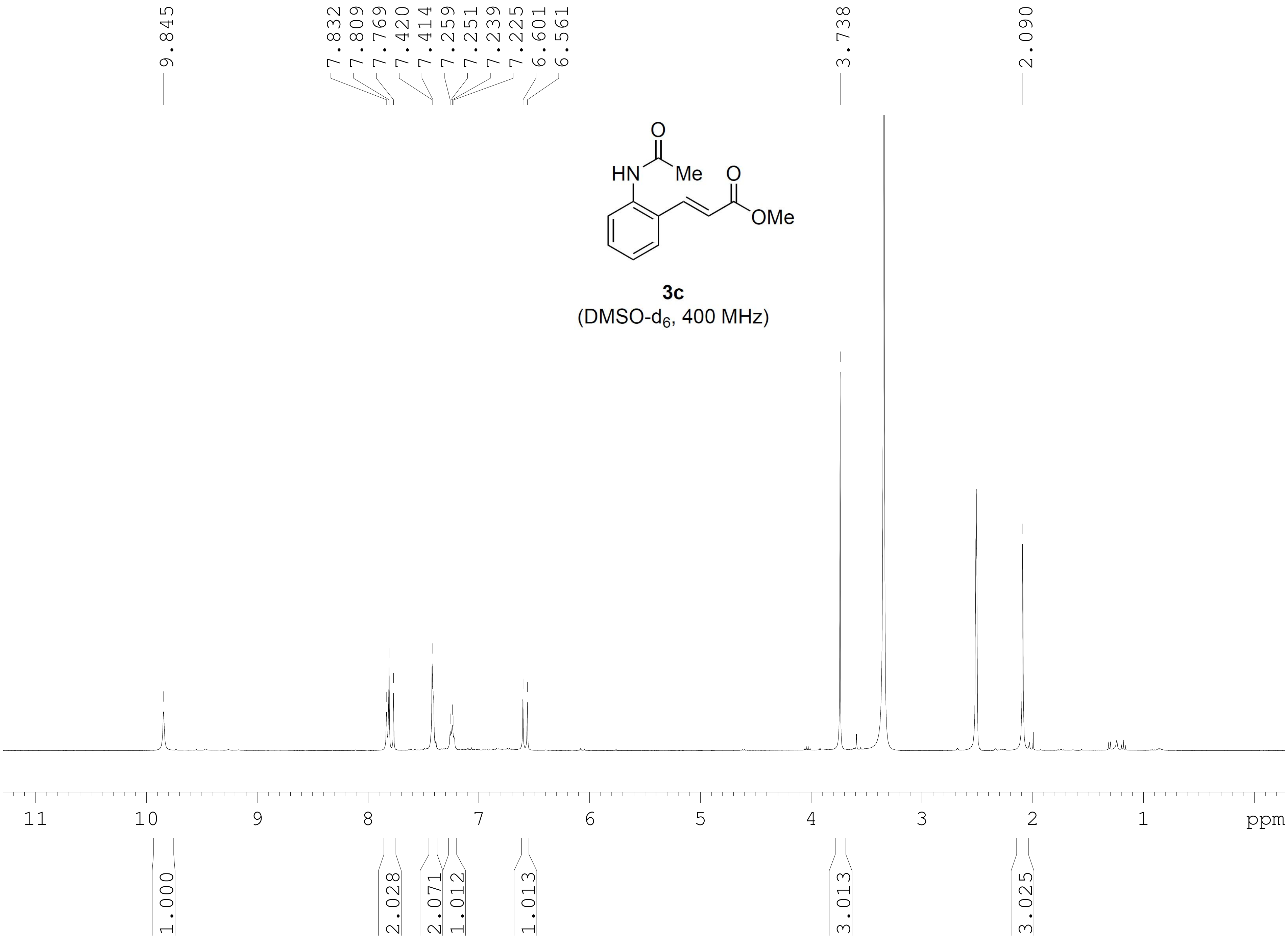


Ethyl (E)-3-(2-acetamidophenyl)acrylate (3b)

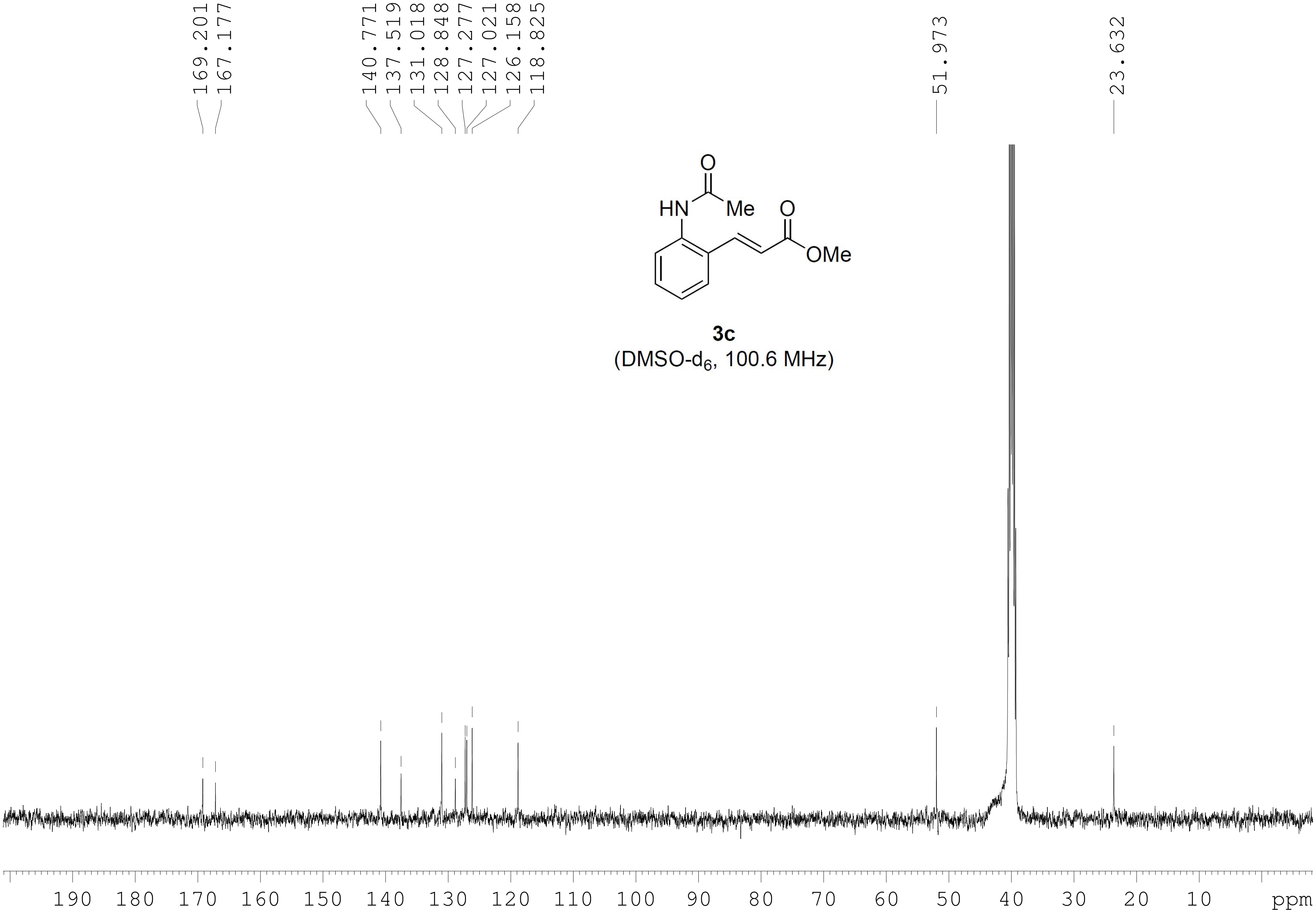


3b
(DMSO-d_6, 100.6 MHz)

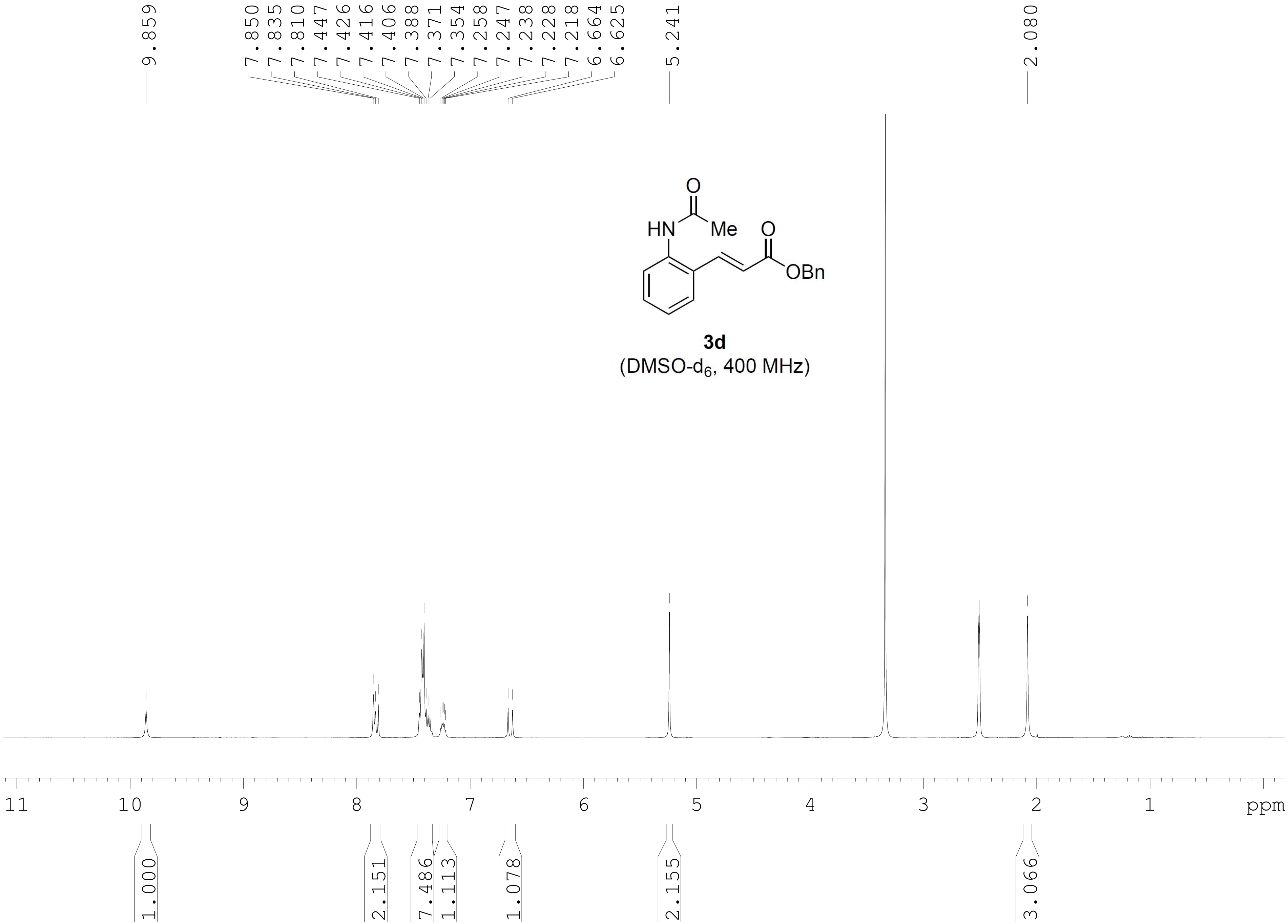
Methyl (E)-3-(2-acetamidophenyl)acrylate (3c)



Methyl (E)-3-(2-acetamidophenyl)acrylate (3c)



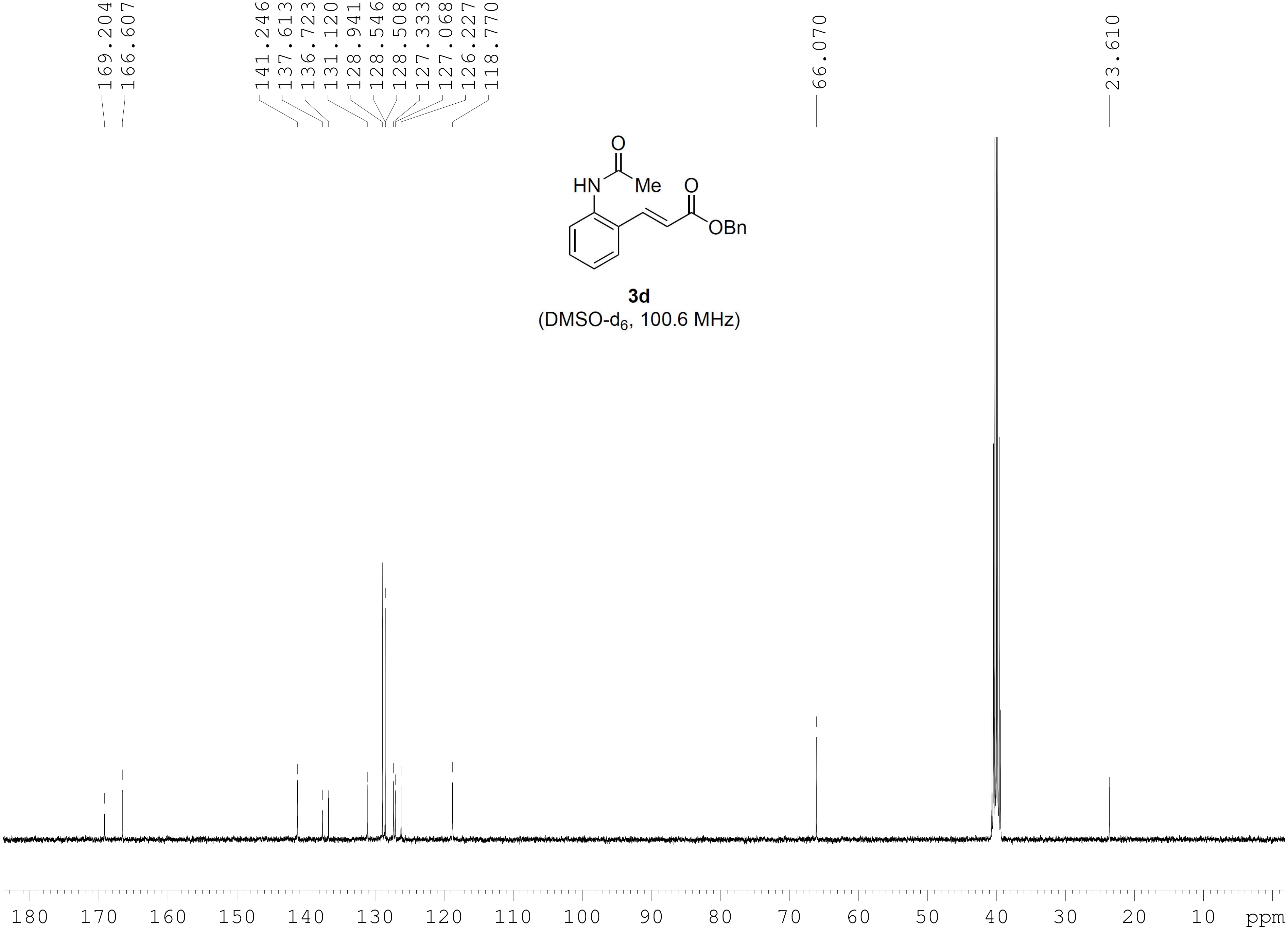
Benzyl (E)-3-(2-acetamidophenyl)acrylate (3d)



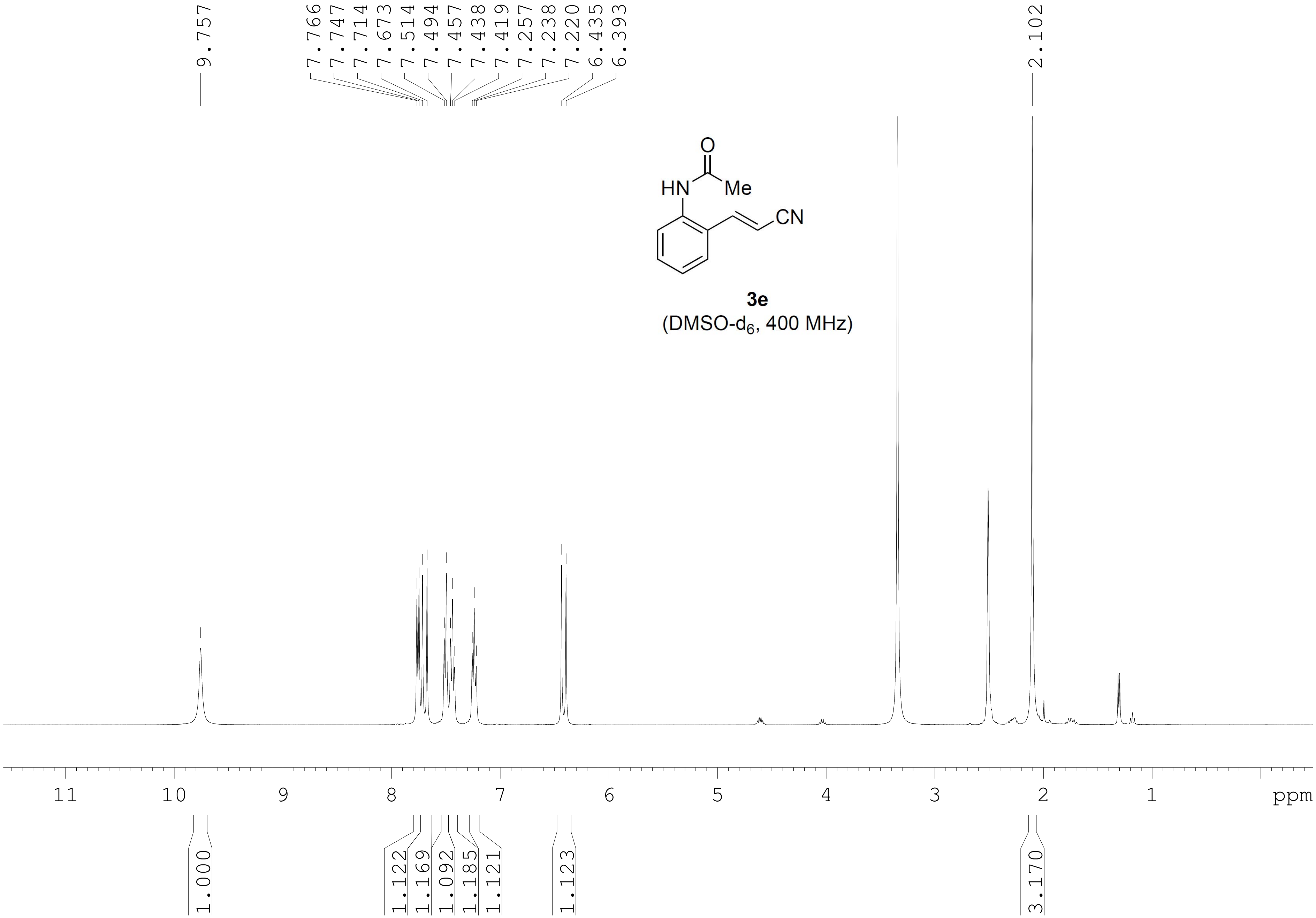
3d

(DMSO-d_6, 400 MHz)

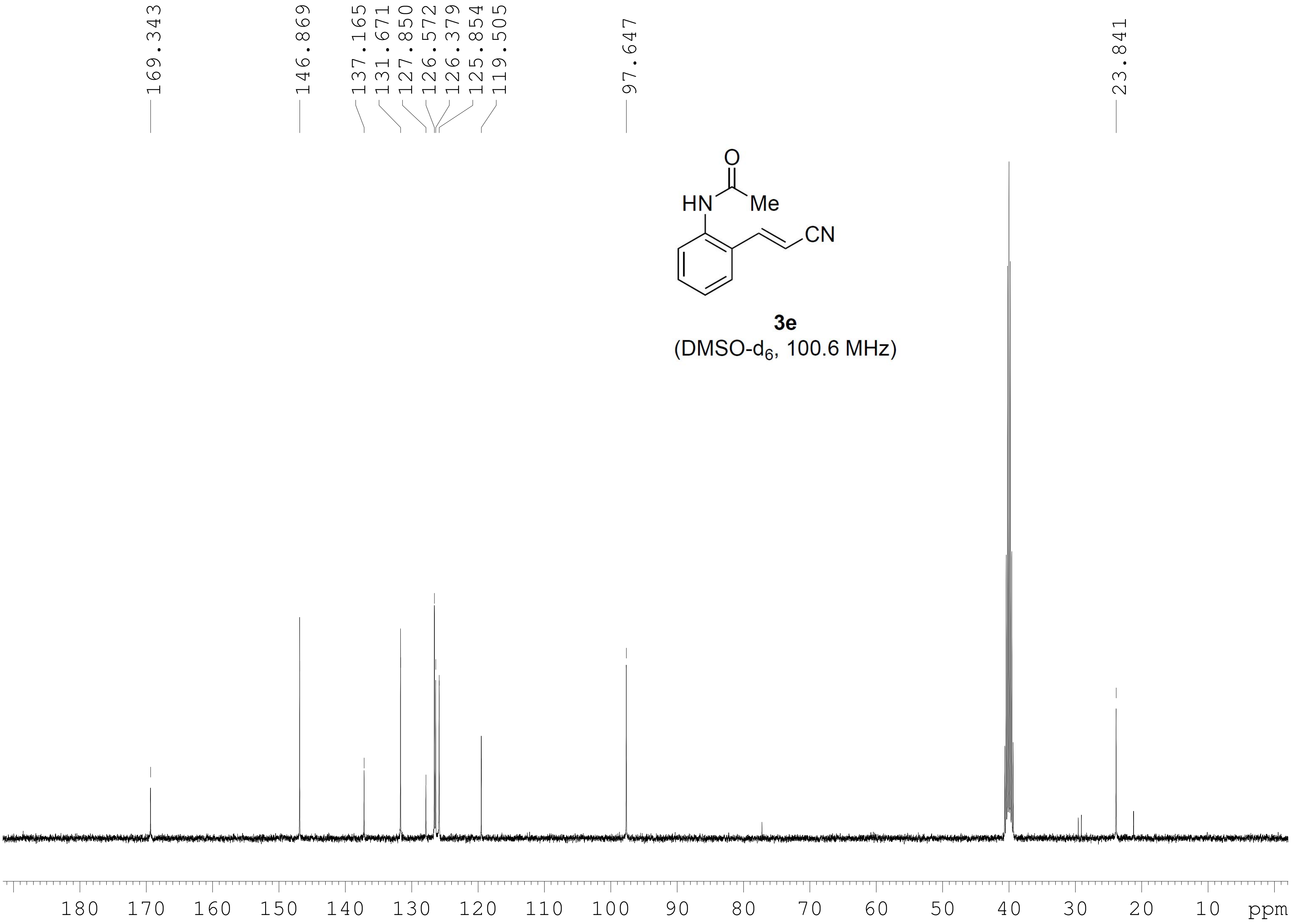
Benzyl (E)-3-(2-acetamidophenyl)acrylate (3d)


3d
(DMSO-d_6, 100.6 MHz)

(E)-N-(2-(2-cyanovinyl)phenyl)acetamide (3e)

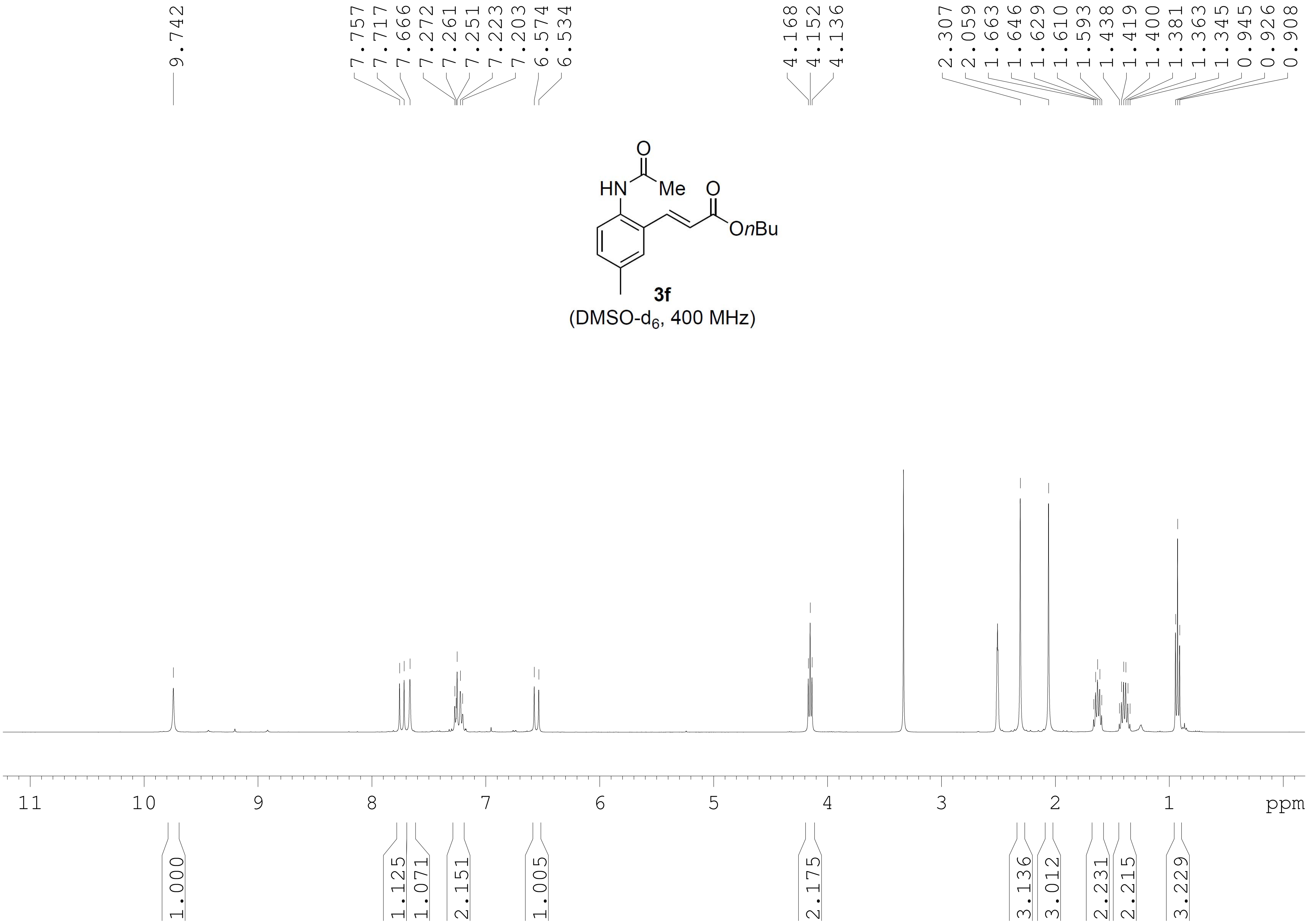


(E)-N-(2-(2-cyanovinyl)phenyl)acetamide (3e)

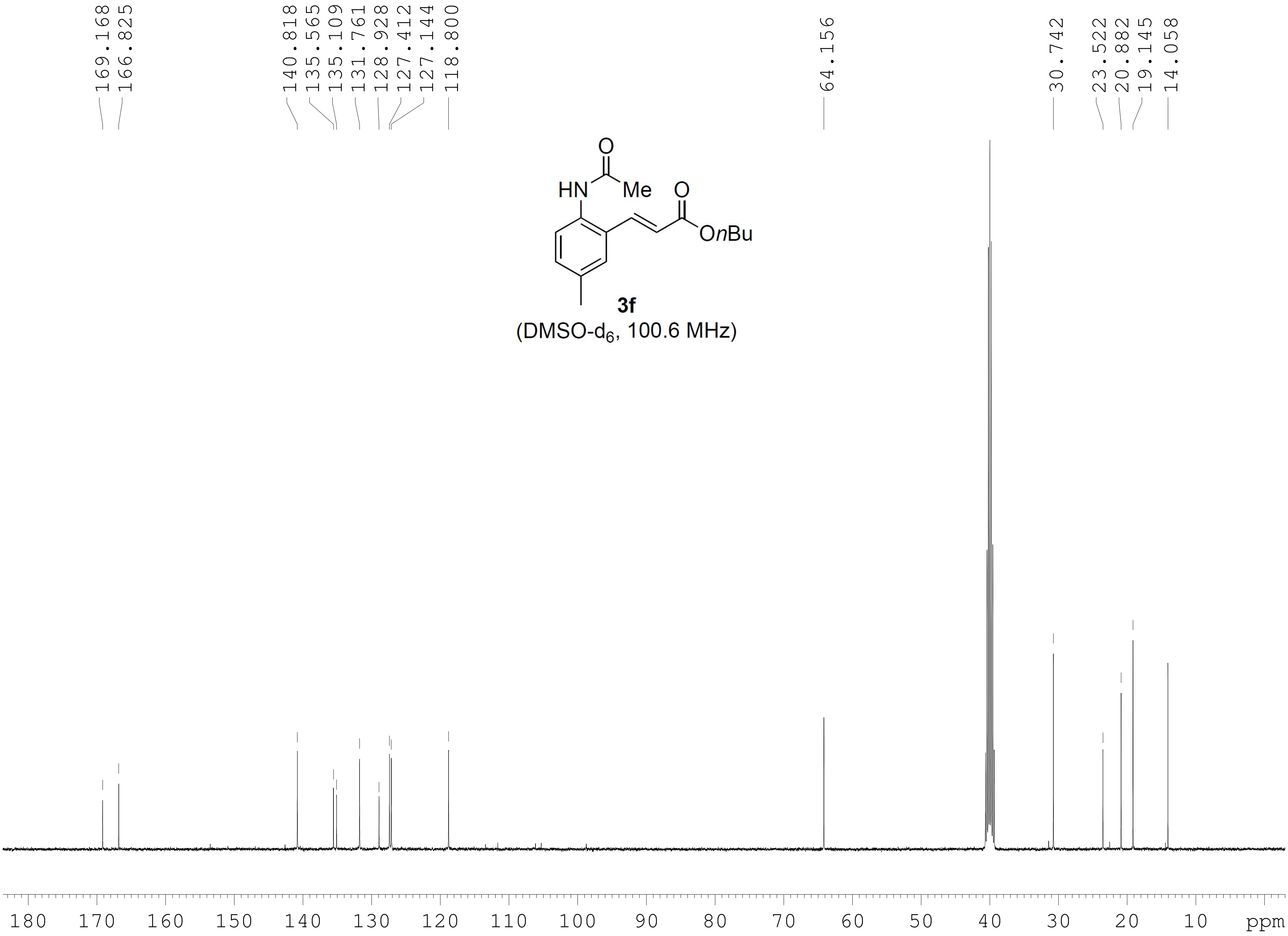


3e
(DMSO-d_6, 100.6 MHz)

Butyl (E)-3-(2-acetamido-5-methylphenyl)acrylate (3f)



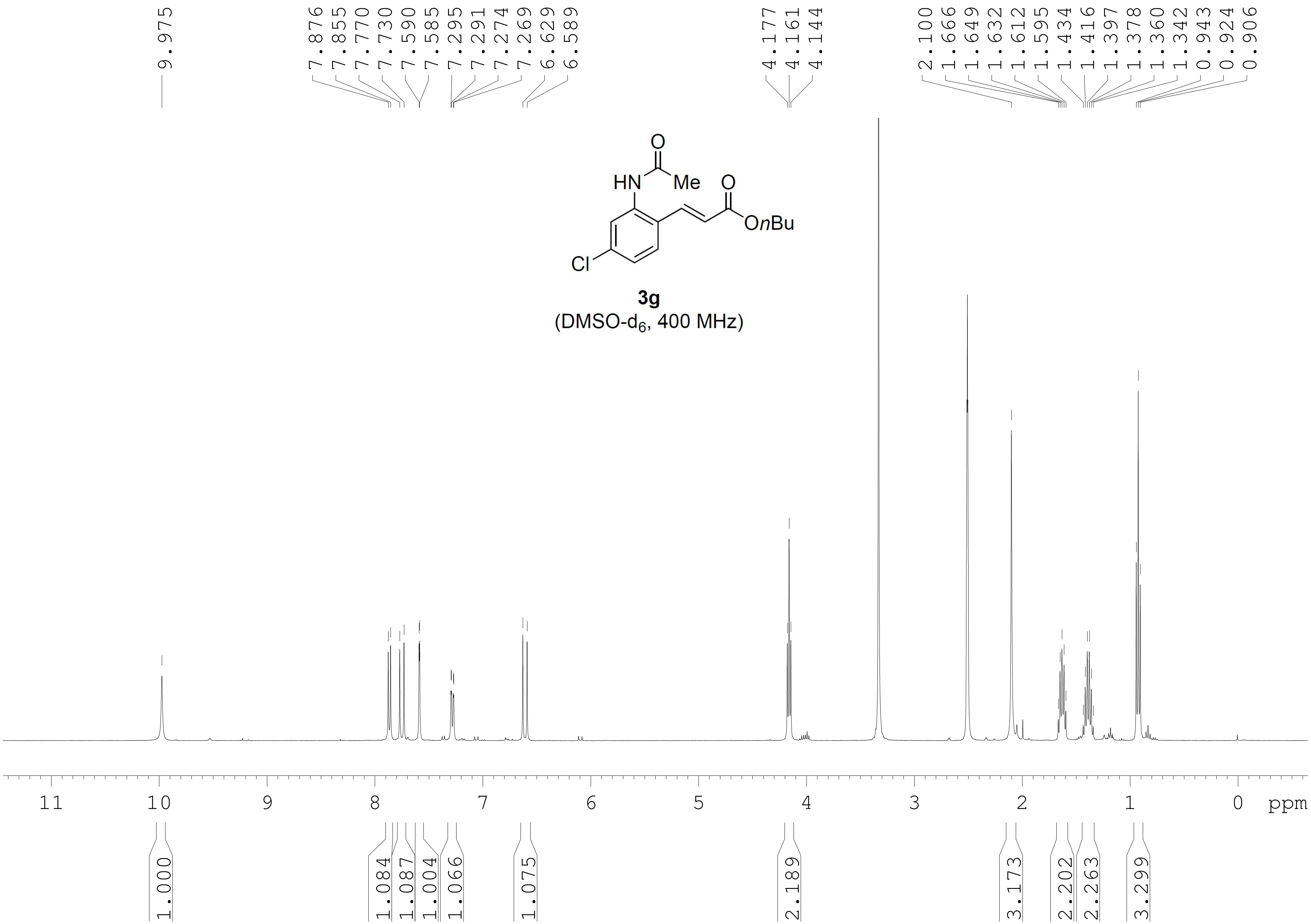
Butyl (E)-3-(2-acetamido-5-methylphenyl)acrylate (3f)



3f

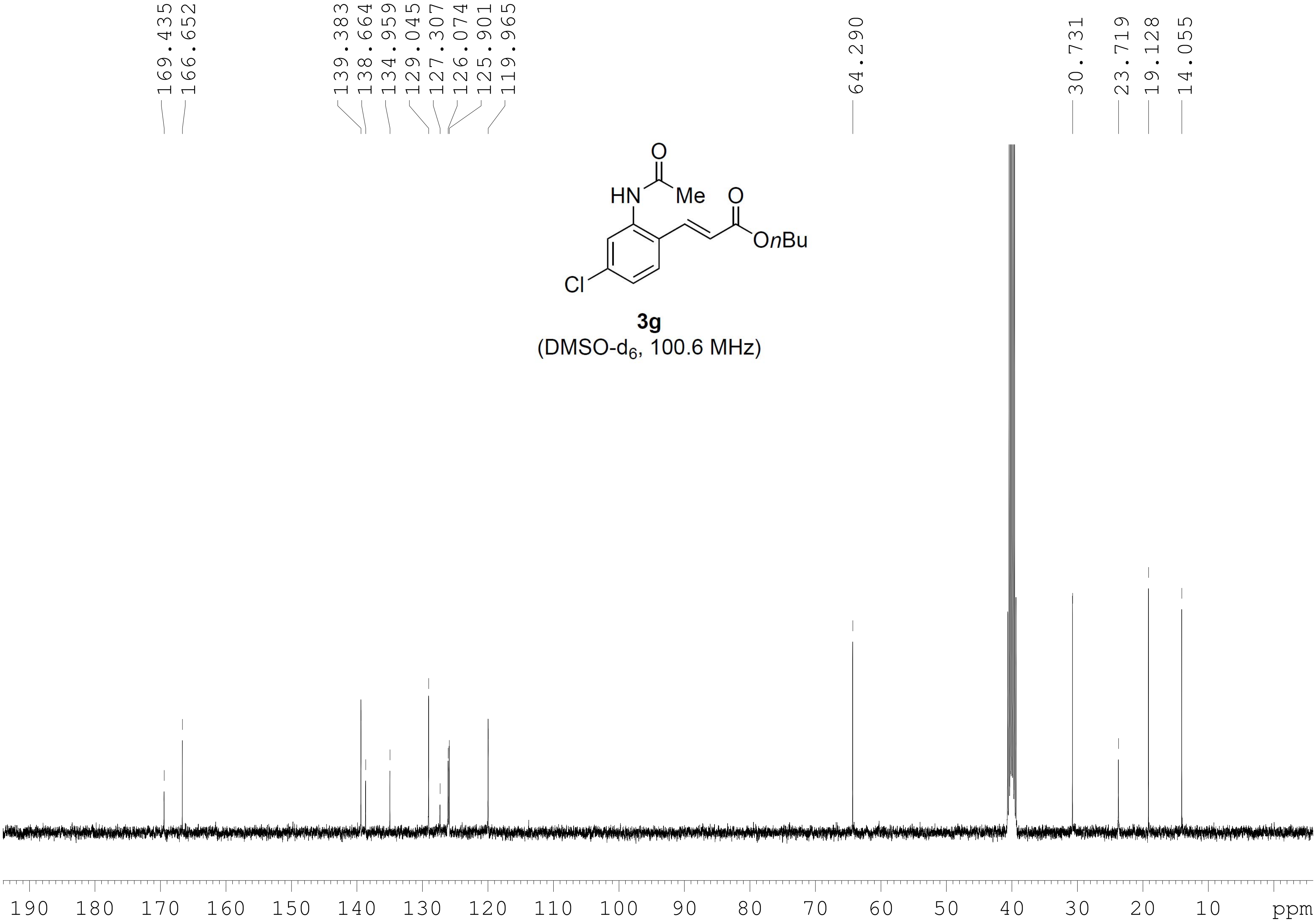
(DMSO-d_6, 100.6 MHz)

Butyl (E)-3-(2-acetamido-4-chlorophenyl)acrylate (3g)

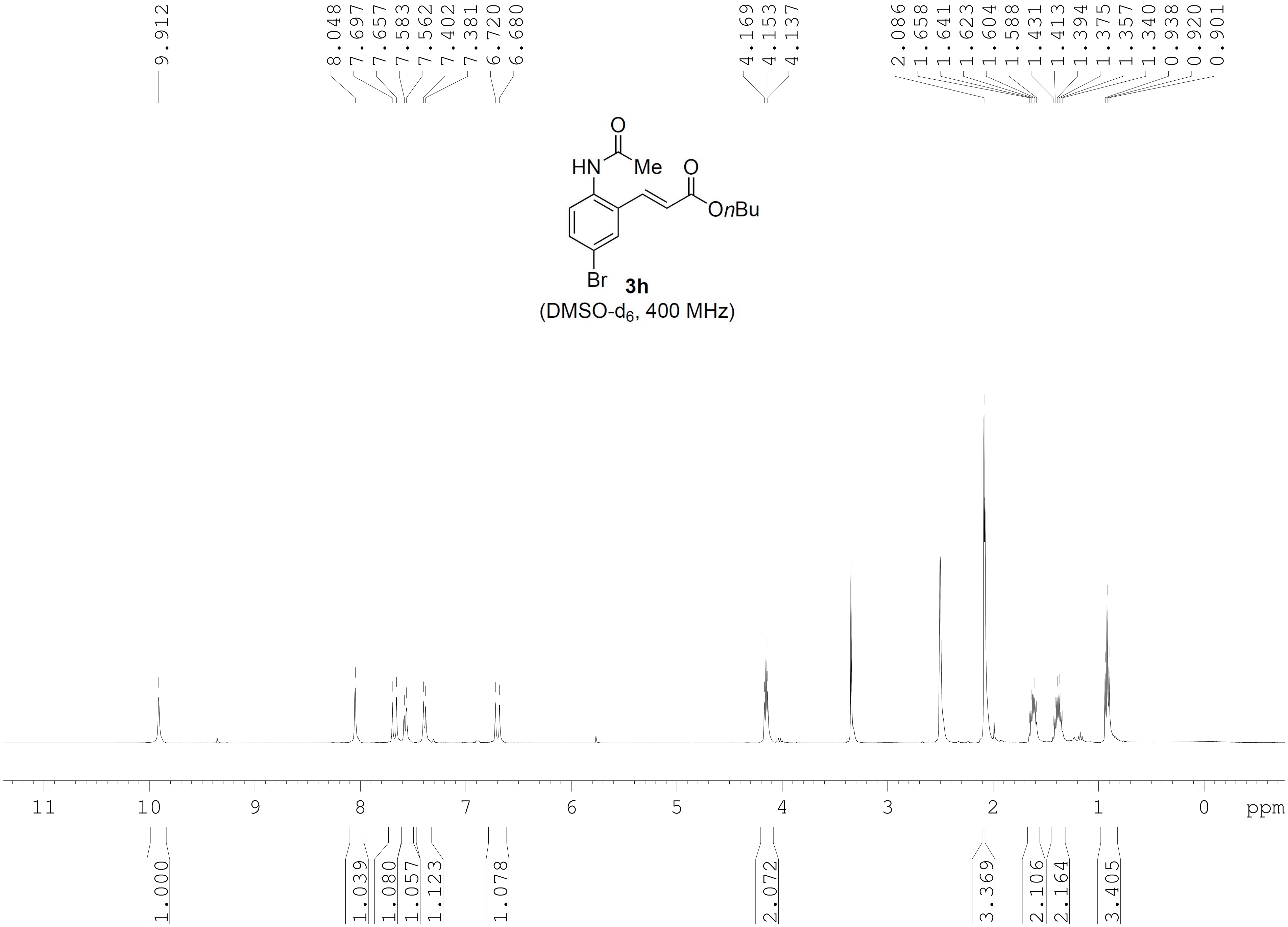


3g
(DMSO-d_6, 400 MHz)

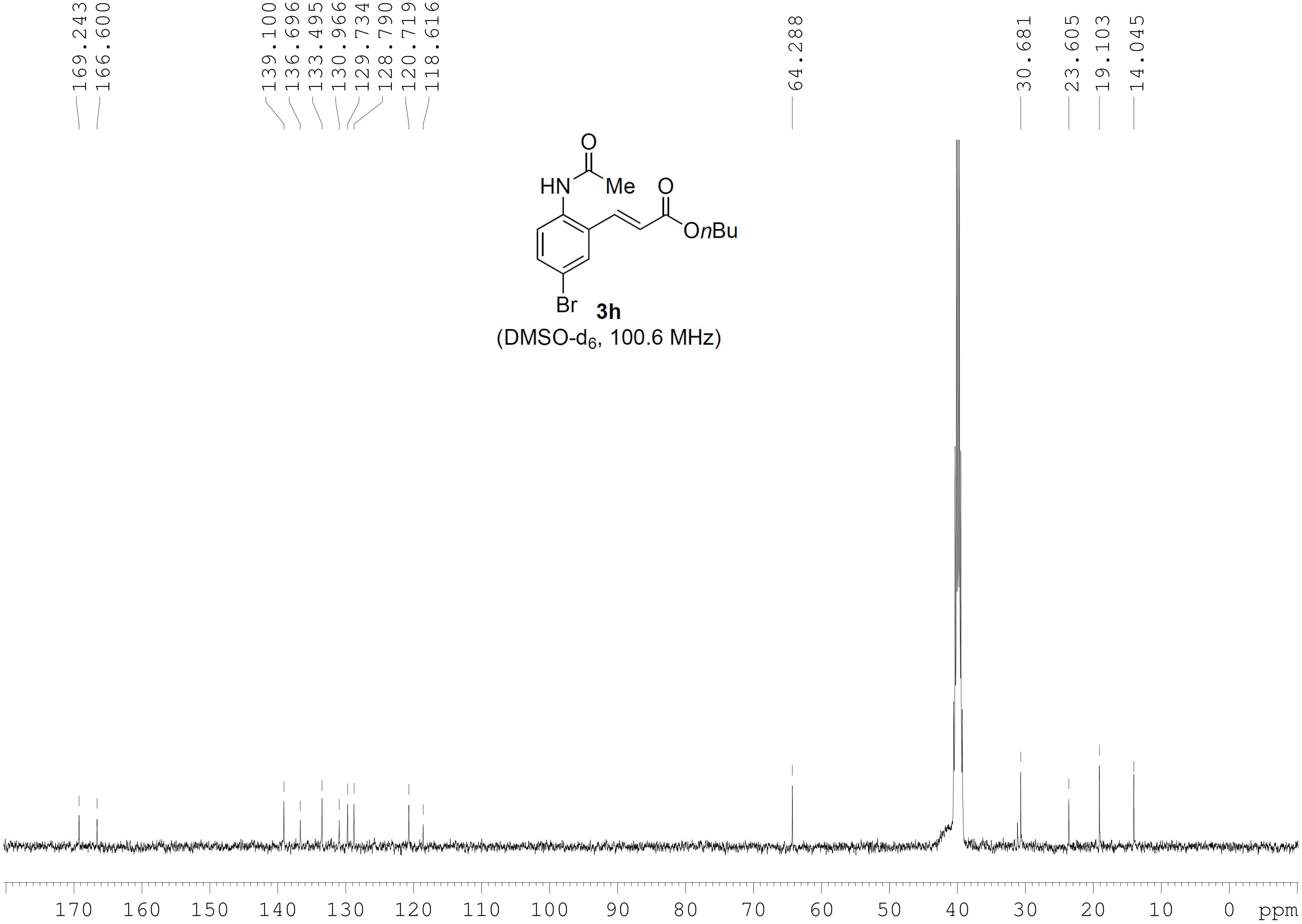
Butyl (E)-3-(2-acetamido-4-chlorophenyl)acrylate (3g)



Butyl (E)-3-(2-acetamido-5-bromophenyl)acrylate (3h)



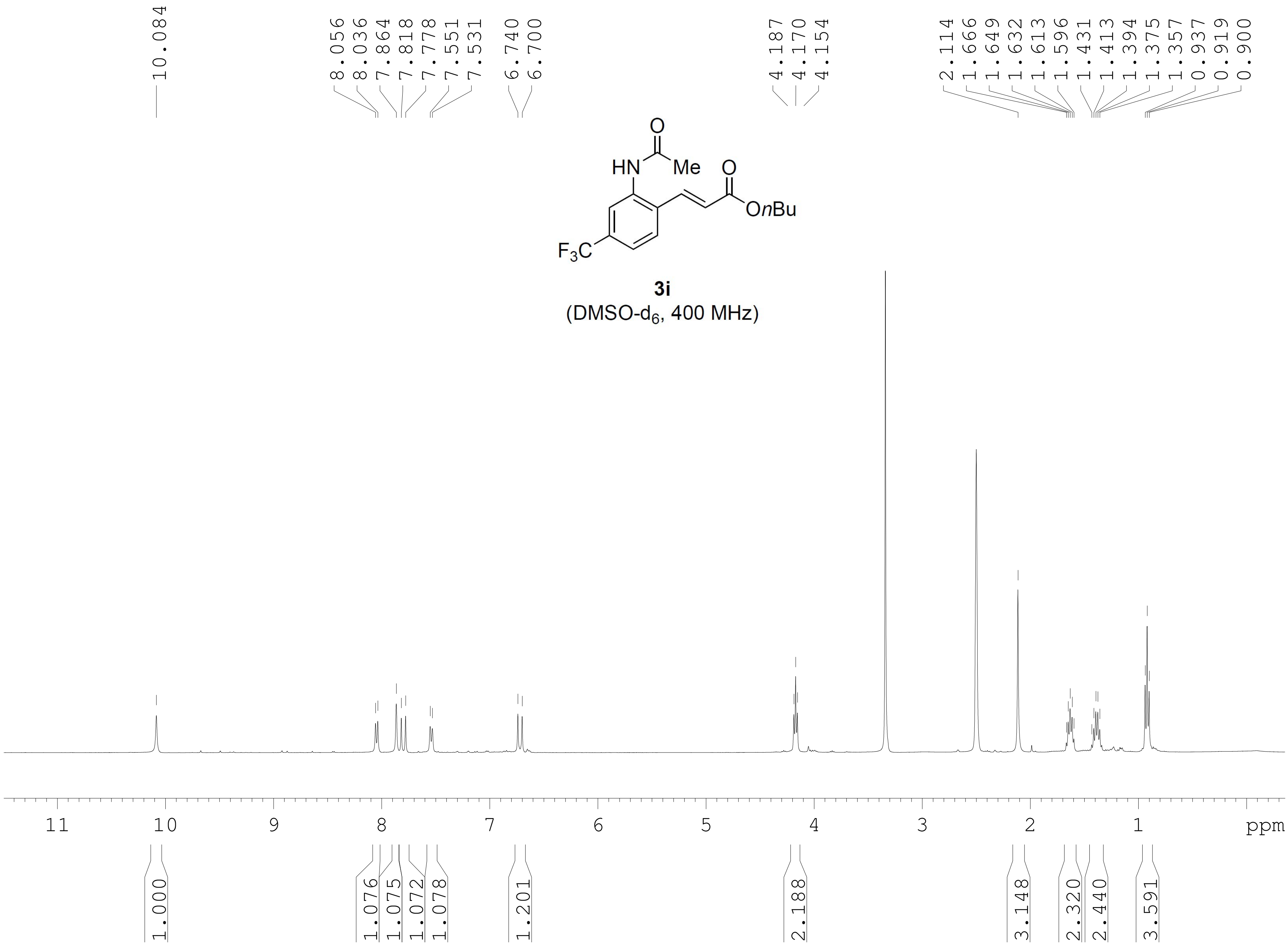
Butyl (E)-3-(2-acetamido-5-bromophenyl)acrylate (3h)



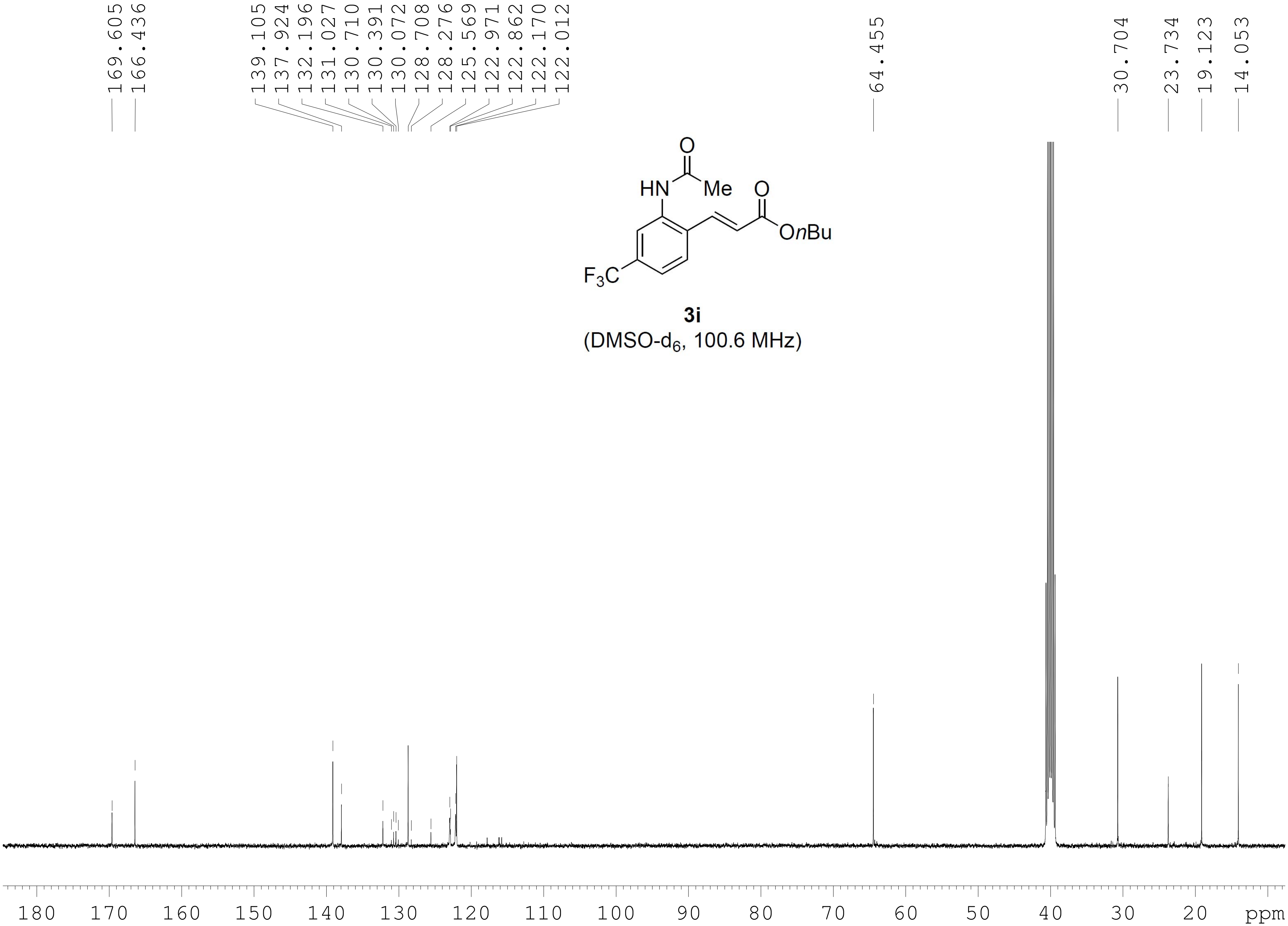
3h

(DMSO-d_6, 100.6 MHz)

Butyl (E)-3-(2-acetamido-4-(trifluoromethyl)phenyl)acrylate (3i)



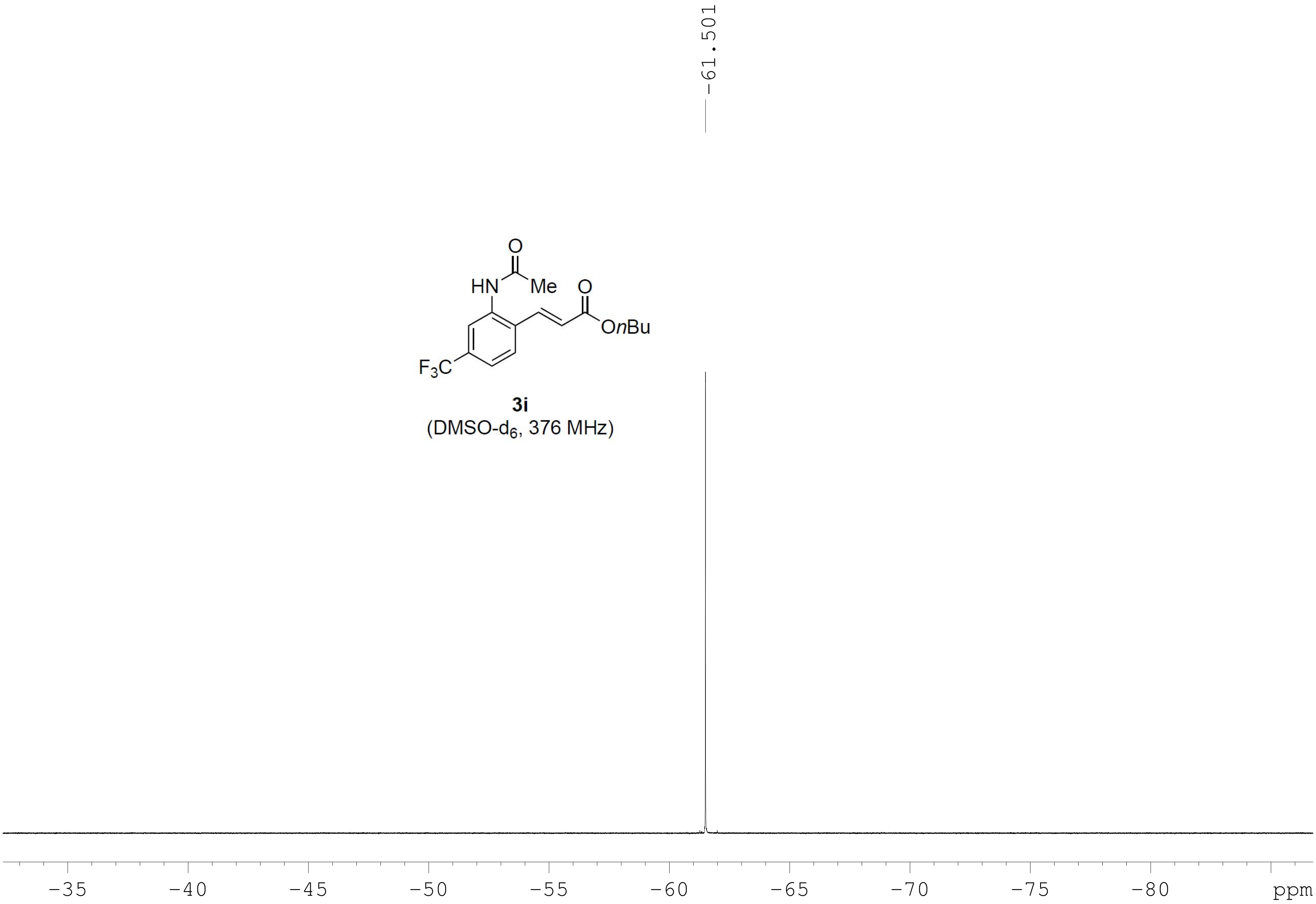
Butyl (E)-3-(2-acetamido-4-(trifluoromethyl)phenyl)acrylate (3i)



3i

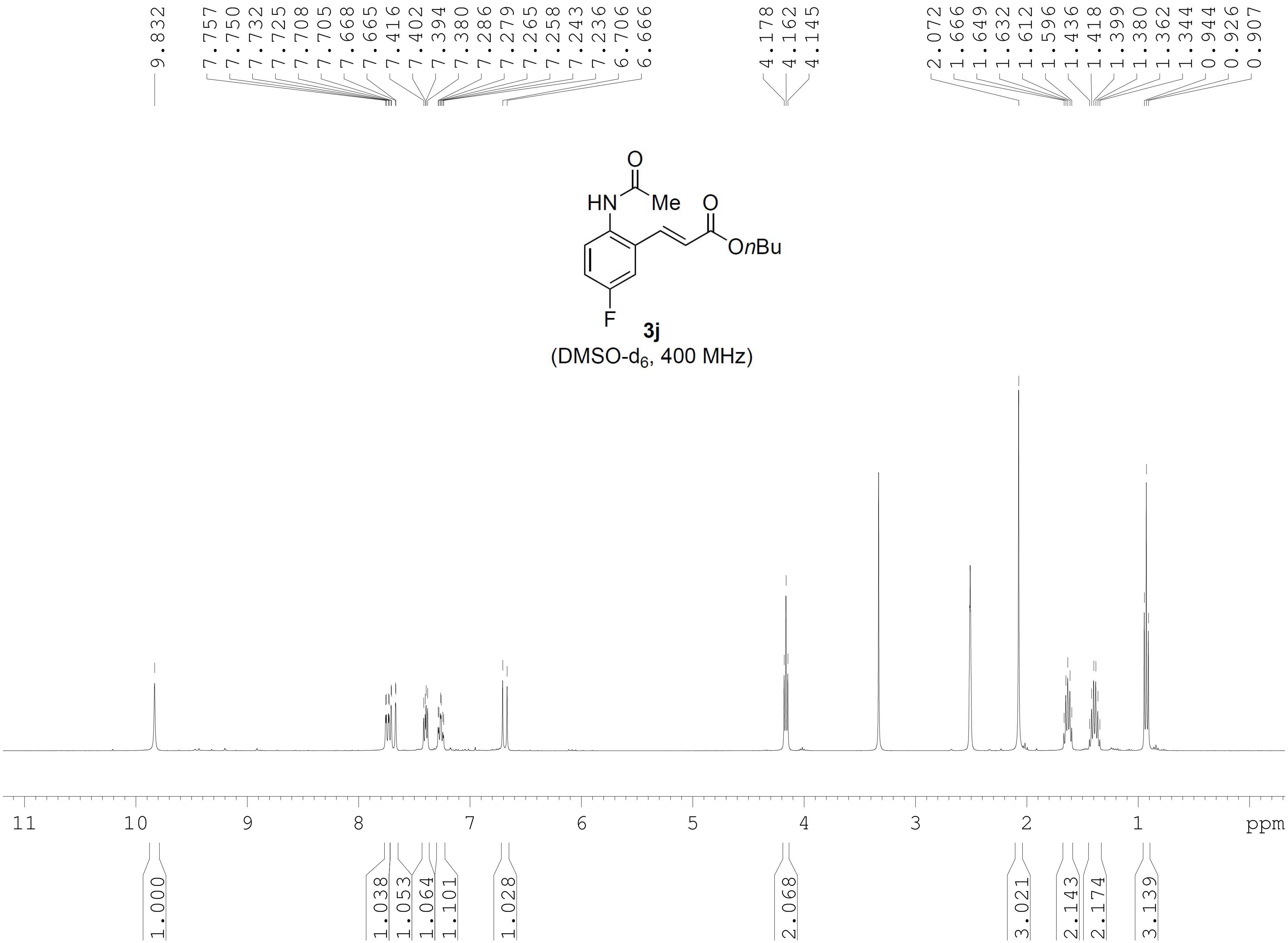
(DMSO-d_6, 100.6 MHz)

Butyl (E)-3-(2-acetamido-4-(trifluoromethyl)phenyl)acrylate (3i)

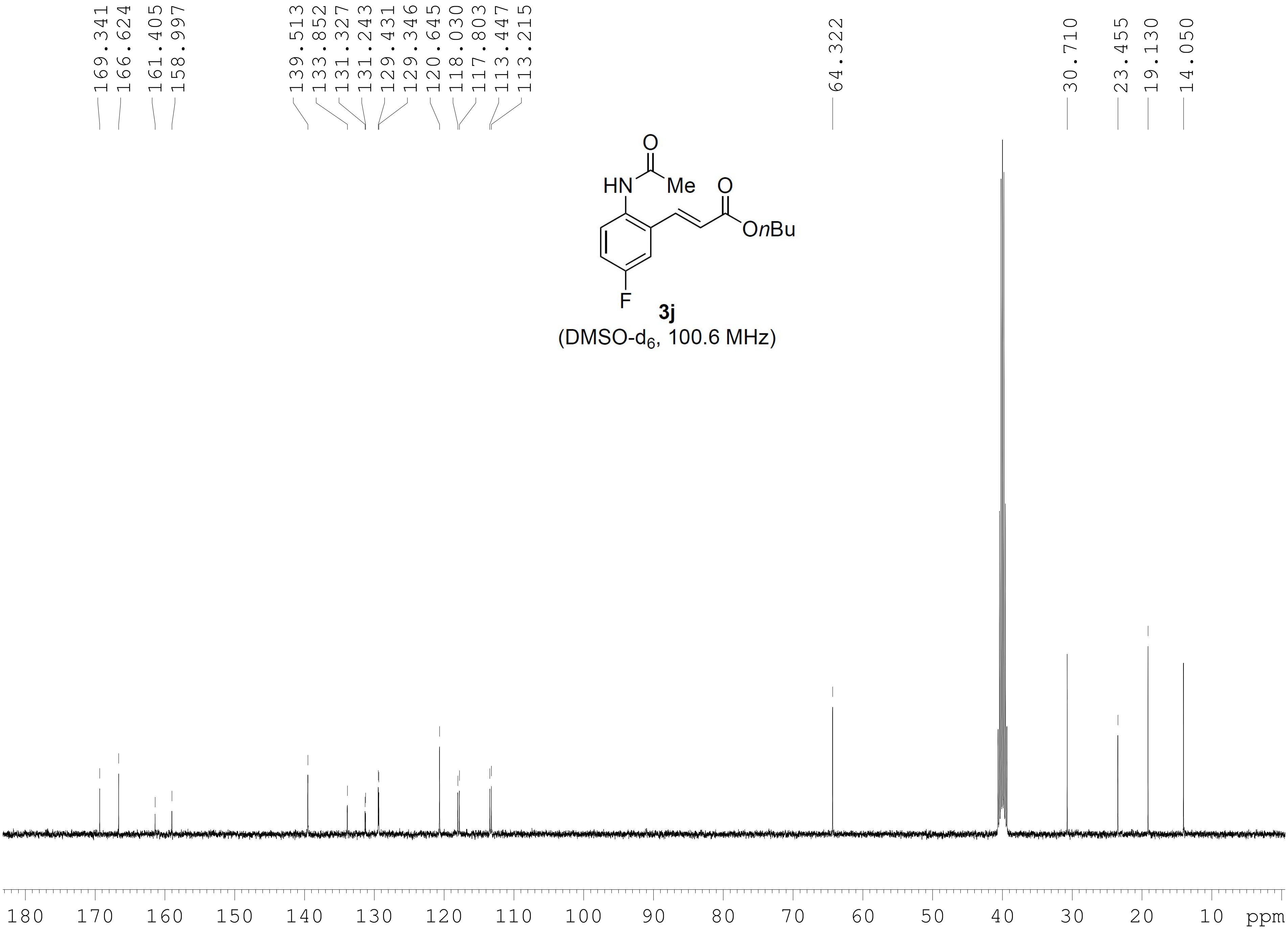


3i
(DMSO-d_6, 376 MHz)

Butyl (E)-3-(2-acetamido-5-fluorophenyl)acrylate (3j)


3j
(DMSO-d_6, 400 MHz)

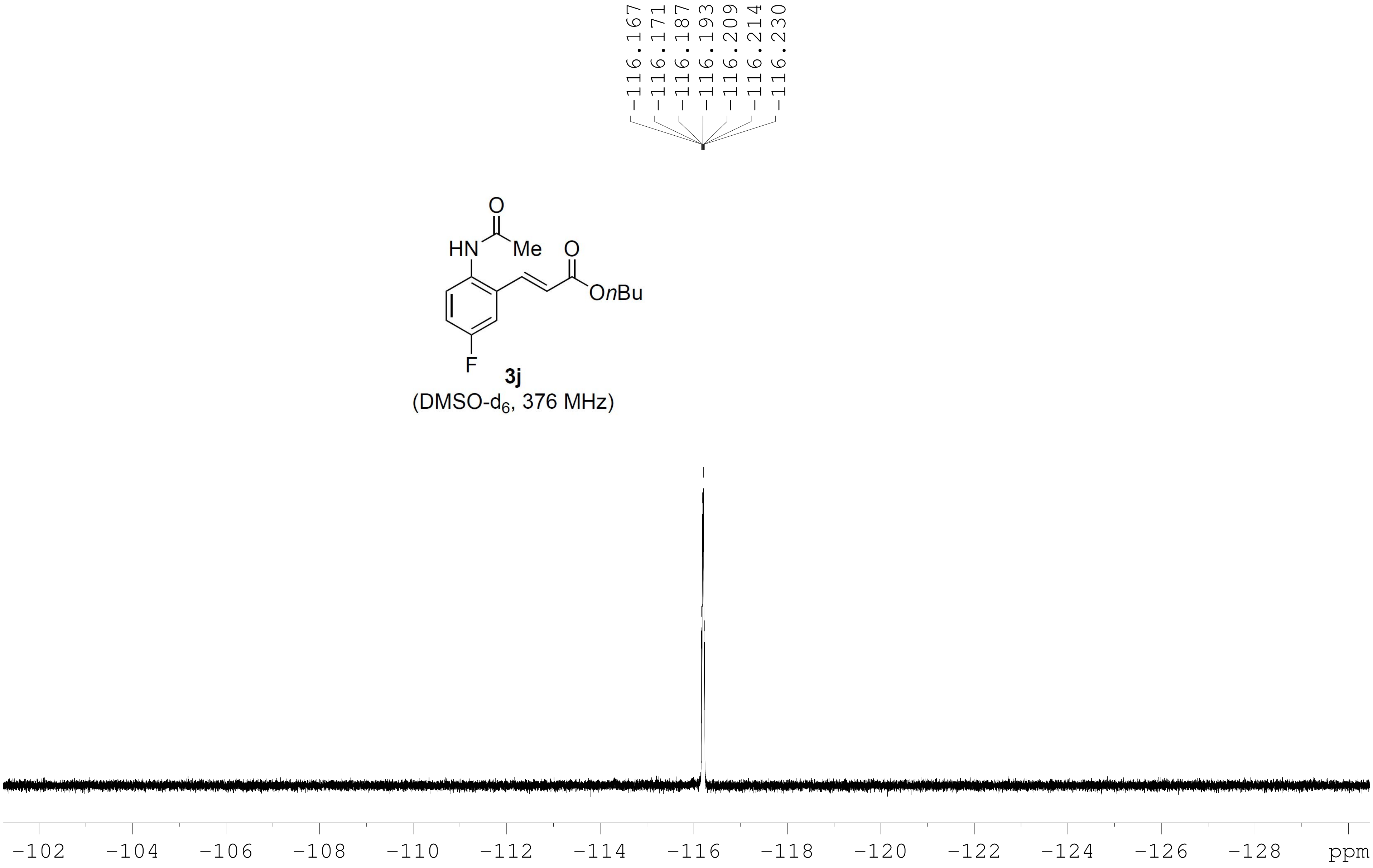
Butyl (E)-3-(2-acetamido-5-fluorophenyl)acrylate (3j)



3j

(DMSO-d_6, 100.6 MHz)

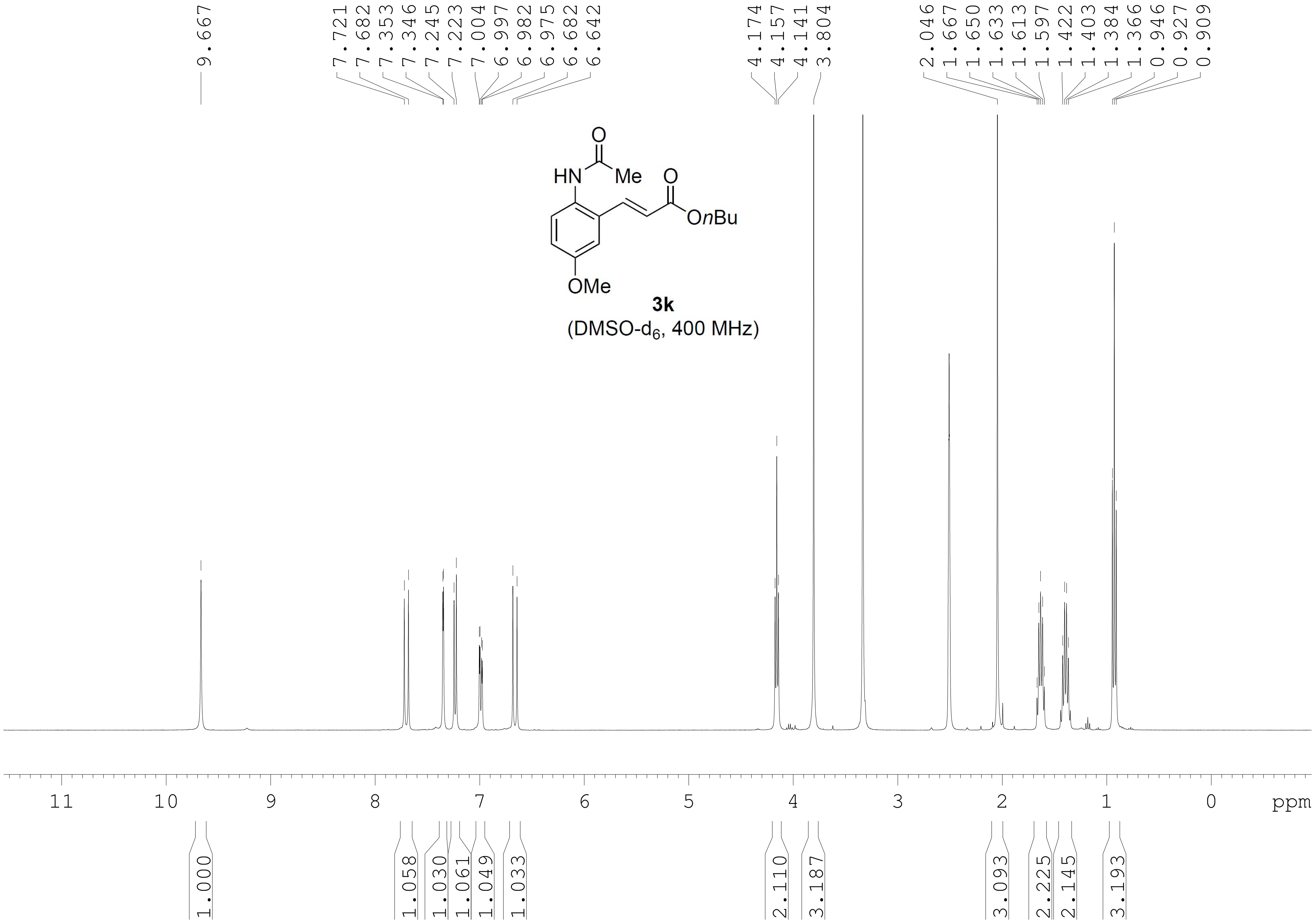
Butyl (E)-3-(2-acetamido-5-fluorophenyl)acrylate (3j)



3j

(DMSO-d_6, 376 MHz)

Butyl (E)-3-(2-acetamido-5-methoxyphenyl)acrylate (3k)



Butyl (E)-3-(2-acetamido-5-methoxyphenyl)acrylate (3k)