

Supporting Information

Mild Ketone Formation via Ni-Catalyzed Reductive Coupling of Unactivated Alkyl Halides with Acid Anhydrides

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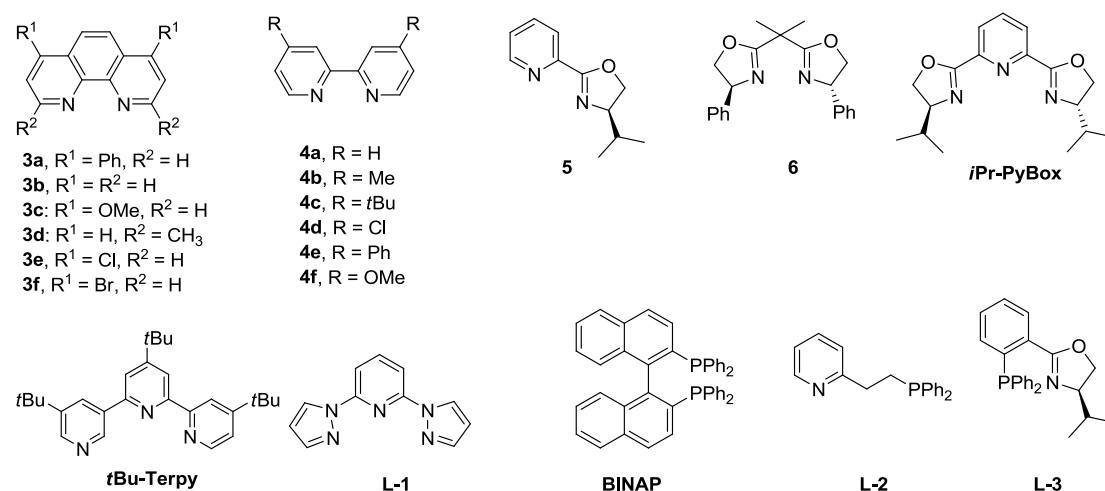
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Experimental Section

Part 1. General Information

All reagents were reagent grade quality and used as received from Aladdin Co. (China), unless otherwise indicated. All reactions were carried out under an atmosphere of nitrogen unless otherwise indicated. Anhydrous THF was distilled from sodium/benzophenone ketyl prior to use. Anhydrous DCM and MeOH were distilled over CaH₂. All other solvents were technical grade unless noted. Anhydrous DMF (Acros), DMA (anhydrous and 99.5% uLtra pure, Acros), NiCl₂ (Alfa Aesar), NiBr₂ (Alfa Aesar), NiI₂ (Alfa Aesar), Ni(COD)₂ (Aldrich), Zinc power (Aldrich), I₂ (Aldrich), CuI (anhydrous, Acros), anhydrous MgCl₂ (Alfa Aesar), *t*Bu-Terpy (Aldrich) and bathophenanthroline (Alfa Aesar),¹ 1,10-phenanthroline (Alfa Aesar), Neocuproine (TCI), P(Cy)₃ (Alfa Aesar), BINAP (Alfa Aesar) were purchased, and used as received. Ligands *i*Pr-pybox (7),² 3a, 3c, 3e,³ 3f,⁴ 4g, L-2,⁵ L-3⁶ were synthesized according to the literature procedures. Iodocyclohexane (Alfa Aesar), iodocyclopentane (Alfa Aesar), (iodomethyl)trimethylsilane (TCI), 2-iodopropane (Aldrich), 1-iodobutane (Aladdin)⁷ were used as received. The anhydrides were prepared based on reported procedures⁸ except for benzoic anhydride (Alfa Aesar). Column chromatography was performed using silica gel 300-400 mesh (purchased from Qingdao-Haiyang Co. China) as the solid support. All NMR spectra were recorded on Bruker Avance 500MHz spectrometer at STP unless otherwise indicated. ¹H NMR and ¹³C NMR chemical shifts are reported in δ units, parts per million (ppm) relative to the chemical shift of residual solvent. Reference peaks for chloroform in ¹H NMR and ¹³C NMR spectra were set at 7.26 ppm and 77.0 ppm, respectively. High-resolution mass spectra (HRMS) were obtained using a Bruker APEXIII 7.0 and Ion Spec 4.7 TESLA FTMS. Melting point was recorded on a micro melting point apparatus (X-4, YUHUA Co., Ltd, Gongyi, China).

Part 2. Details of Optimization for the reaction conditions



A. Optimization for the coupling of **1a** with benzoic anhydride

A typical procedure: To a flame-dried Schlenk tube equipped with a stir bar was loaded **1a**, benzoic anhydride, CuI (if used), followed by addition of ligand and zinc powder. The tube was moved to a dry glove box, at which point Ni(COD)₂ and MgCl₂ (if applicable) were added. The tube was capped with a rubber septum, and it was moved out of the glove box. CH₃CN were then added via a syringe. After the reaction mixture was allowed to stir for 8-12 hours under N₂ atmosphere at 25 °C, it was directly loaded onto a silica column without work-up. The residue in the reaction vessel was rinsed with small amount of DCM. Flash column chromatography provided **2**.

Table S1. Solvent screening



Entry	Solvent	Yield (%) ^a
1	DMF	32
2	CH ₃ CN	37
3	DMA	25
4	Toluene	ND ^b
5	THF	<20
6	1,4-Dioxane	17
7	DCM	ND

^a Isolated yield. ^b Not detected with more than 92% substrate being recovered.

Table S2. Screening of additives



Entry	Additives	Yield(%) ^a
1	None	38
2	MgCl ₂ (20%)	<60
3	CuI (20%)	<60
4	MgCl ₂ (20%); CuI (20%)	89
5	LiCl	73
6	MgCl ₂ (50%)	60.4
7	MgCl ₂ (100%)	80
8	MgCl ₂ (150%)	85
9	PTSA (20%)	<20
10	DMAP (20%)	<40

^a Isolated yields. PTSA = *p*-Toluenesulfonamide.

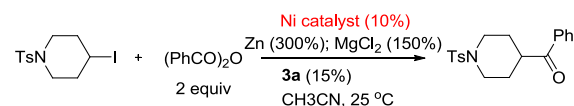
Table S3: Screening of ligands



Entry	Ligands	Yield(%) ^a	Entry	Ligands	Yield(%) ^a
1	4a	38	7	3b	58
2	3a	85	8	6	23
3	L-3	19	9	5	80
4	P(Cy) ₃	<8	10	<i>t</i> Bu-Terpy	ND ^b
5	BINAP	7	11	3c	60
6	<i>i</i> Pr-PyBox	21	12	L-1	60

^a Isolated yield. ^b Not detected.

Table S4. Screening of catalysts



Entry	Ni	Yield (%) ^a
1	Ni(COD) ₂	85
2	Ni(acac) ₂	82
3	NiI ₂	<60
4	NiBr ₂	<40
5	NiCl ₂	<40
6	None	<5

^a Isolated yield.

Table S5: Screening of reductants

Entry	Reductant	Yield (%) ^a
1	None	ND ^b
2	Zn (200%)	~60
3	Zn (300%)	85
4	Zn (400%)	85
5	Mn (300%)	~70
6	In (300%)	80

^a Isolated yield; ^b Not detected.

B. Optimization for the coupling of **1b** and benzoic anhydride

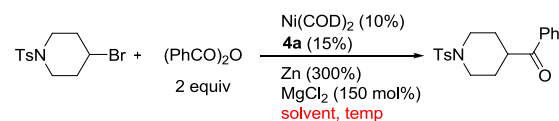
A typical procedure: To a flame-dried Schlenk tube equipped with a stir bar was loaded **1b**, benzoic anhydride, CuI (if used), followed by addition of ligand and zinc powder. The tube was moved to a dry glove box, at which point Ni(COD)₂ and MgCl₂ (if applicable) were added. The tube was capped with a rubber septum, and it was moved out of the glove box. CH₃CN and DMF (v/v, 3:7) were then added via syringe. After the reaction mixture was allowed to stir for 8-12 hours under N₂ atmosphere at 25 °C, it was directly loaded onto a silica column without work-up. The residue in the reaction vessel was rinsed with small amount of DCM. Flash column chromatography provided the product **2**.

Table S6. Ligands screening

Entry	Ligands	Yield(%) ^a	Entry	Ligands	Yield(%) ^a
1	3a	<40	7	<i>i</i> Pr-PyBox	trace
2	3b	<5	8	<i>t</i> Bu-Terpy	15
3	4a	~40	9	P(Cy) ₃	ND ^b
4	3e	<20	10	BINAP	ND ^b
5	5	~30	11	L-2	trace
6	6	<5			

^a Isolated yield. ^b Not detected.

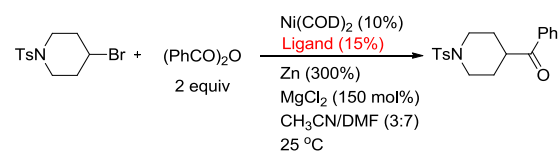
Table S7. Solvent and temperature screening



Entry	Ligands	Temp (°C)	Yield (%) ^a	Entry	Ligands	Temp (°C)	Yield (%) ^a
1	CH ₃ CN	60	<5	11	DMA: DMF(1: 1)	25	<5
2	DMF	110	<5	12	DMF: DMA(7: 3)	25	<5
3	DMF	80	<5	13	CH ₃ CN: DMF(2: 8)	25	<5
4	THF	80	<5	14	CH ₃ CN: DMF(1: 9)	25	<5
5	Toluene	80	<5	15	CH ₃ CN: DMF(3: 7)	50	46
6	DMA	80	<5	16	CH ₃ CN: DMA(3: 7)	60	trace
7	CH ₃ CN: DMA(1: 1)	25	ND	17	CH ₃ CN: DMSO(3: 7)	25	30 ^b
8	CH ₃ CN: DMF(1: 1)	25	<5	18	CH ₃ CN: 1,4-Dioxane(3: 7)	25	ND ^c
9	CH ₃ CN: DMF(7: 3)	25	19	19	CH ₃ CN: DMI(3: 7)	25	trace
10	CH₃CN: DMF(3: 7)	25	75	20	CH ₃ CN: NMP(3: 7)	25	trace

^a Isolated yield. ^b **3a** was used. ^c Not detected.

Table S8. Ligands screening using CH₃CN/DMF as co-solvent



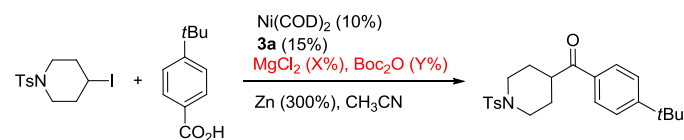
Entry	Ligands	Yield (%) ^a	Entry	Ligands	Yield (%) ^a
1	4a	75	6	3c	trace
2	4b	80	7	3b	75
3	4c	77 ^b	8	5	23
4	4e	<10	9	L-3	trace
5	4f	<10	10	None	ND ^c

^a Isolated yield. ^b 4-(*tert*-butyl)-benzoic anhydride was used. ^c Not detected.

C. Optimization for the coupling of **1a** and benzoic acid.

A typical procedure: To a flame-dried Schlenk tube equipped with a stir bar was loaded **1a**, 4-*t*Bu-benzoic acids, CuI (if used) and Boc₂O followed by addition of ligand and zinc powder. The tube was moved to a dry glove box, at which point Ni(COD)₂ and MgCl₂ (if applicable) were added. The tube was capped with a rubber septum, and it was moved out of the glove box. CH₃CN and DMF were then added via syringe. After the reaction mixture was allowed to stir for 12 hours

under N₂ atmosphere at 25 °C, it was directly loaded onto a silica column without work-up. The residue in the reaction vessel was rinsed with small amount of DCM. Flash column chromatography provided the product **10**.



Entry	Acid (mol %)	MgCl ₂ (mol %)	Boc ₂ O (mol %)	Yield (%) ^a
1	200	100	200	27
2	200	200	200	48.1
3	200	300	200	47.8
4	200	200	300	67
5	200	300	300	53
6	300	100	200	44
7	400	100	200	58
8	300	200	300	68
9	400	200	300	79

^a Isolated yields.

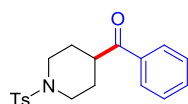
Part 3. Reductive Ketone Formation

General procedure for the preparation of ketones (GP-1). To a flame-dried Schlenk tube equipped with a magnetic stir bar was loaded alkyl iodides (0.137 mmol, 100 mol%), anhydrides (0.274 mmol, 200 mol%), **3a** (6.80 mg, 0.021 mmol, 15 mol%) and zinc powder (27.0 mg, 0.410 mmol, 300 mol%). The tube was moved into a dry glove box, at which point Ni(COD)₂ (3.80 mg, 0.014 mmol, 10 mol%) and MgCl₂ (19.6 mg, 0.210 mmol, 150 mol%) was added. After the tube was capped with a rubber septum, and was moved out of the glove box, CH₃CN (1 mL) was added *via* syringe. The mixture was allowed to stir for 12 h under N₂ atmosphere at room temperature (25°C). It was directly loaded onto a silica column without work-up (the residue was rinsed with small amount of DCM). Flash column chromatography (SiO₂: ethyl acetate in hexanes) provided the product.

General procedure for the preparation of ketones (GP-2). To a flame-dried Schlenk tube equipped with a magnetic stir bar was loaded alkyl bromide (0.137 mmol, 100 mol%), anhydride (0.274 mmol, 200 mol%), **4b** (3.80 mg, 0.021 mmol, 15 mol%) and zinc powder (27.0 mg, 0.410 mmol, 300mol%). The tube was moved into a dry glove box, at which point Ni(COD)₂ (3.80 mg, 0.0140 mmol, 10 mol%) and MgCl₂ (19.6 mg, 0.210 mmol, 150 mol%) was added. After the tube was capped with a rubber septum, and was moved out of glove box, CH₃CN and DMF (3: 7) was added *via* syringe. The mixture was allowed to stir for 12 h under N₂ atmosphere at room temperature (25°C). It was directly loaded onto a silica column without work-up (the residue was rinsed with small amount of DCM). Flash column chromatography (SiO₂: ethyl acetate in hexanes) provided the product.

General procedure for the preparation of ketones (GP-3). To a flame-dried Schlenk tube equipped with a magnetic stir bar was loaded alkyl iodides (0.137 mmol, 100 mol%), acid (300-400 mol%), **3a** (3.80 mg, 0.021 mmol, 15 mol%) and zinc powder (27.0 mg, 0.410 mmol, 300 mol%). The tube was moved into a dry glove box, at which point Ni(COD)₂ (3.80 mg, 0.014 mmol, 10 mol%) and MgCl₂ (26.1 mg, 0.270 mmol, 200 mol%) were added. After the tube was capped with a rubber septum, and was moved out of glove box, CH₃CN (1 mL) and Boc₂O (94.0 uL, 0.410 mmol, 300 mol%) were added *via* syringe. The mixture was allowed to stir for 12 h under N₂ atmosphere at room temperature (25°C). It was directly loaded onto a silica column without work-up (the residue was rinsed with small amount of DCM). Flash column

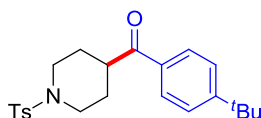
chromatography (SiO₂: ethyl acetate in hexanes) provided the product.



Phenyl(1-tosylpiperidin-4-yl)methanone (2). This compound was prepared according to the *GP-3* using **1a** (50.0 mg, 0.137 mmol, 100 mol%), benzoic acid (66.9 mg, 0.548 mmol, 200 mol%). After purification by column chromatography (SiO₂: 20% ethyl acetate in hexanes), the title compound was isolated as a white solid (37.6 mg, 0.110 mmol, 83% yield).

This compound was also prepared according to the *GP-2* using **1b** (43.6 mg, 0.137 mmol, 100 mol%), benzoic anhydride (62.0 mg, 0.274 mmol, 200 mol%). After purification by column chromatography (SiO₂: 20% ethyl acetate in hexanes), the title compound was isolated as a white solid (36.7 mg, 0.107 mmol, 78% yield).

¹H NMR (500 MHz, CDCl₃): δ 7.86 (d, *J* = 7.5 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.56 (d, *J* = 7.5 Hz, 1H), 7.45 (d, *J* = 7.5 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 3.79 (dt, *J* = 8.4, 3.4 Hz, 2H), 3.24-3.18 (m, 1H), 2.53 (td, *J* = 11.5, 2.9 Hz, 2H), 2.47 (s, 3H), 1.97-1.85 (m, 4H). ¹³C NMR (125 MHz, CDCl₃): δ 201.4, 143.7, 135.6, 133.3, 133.1, 129.7, 128.8, 128.2, 127.7, 45.6, 42.3, 27.9, 21.6. ESI-MS: Calcd for C₁₉H₂₂NO₃S (M+H)⁺: 344.1320. Found 344.2. M.p. 90-91 °C.



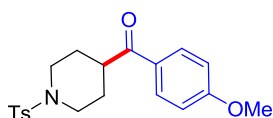
(4-(*tert*-Butyl)phenyl)(1-tosylpiperidin-4-yl)methanone (7). This compound was prepared following the *GP-1* using 4-iodo-1-tosylpiperidine **1a** (50.0 mg, 0.137 mmol, 100 mol%), 4-(*tert*-butyl)benzoic anhydride (92.7 mg, 0.274 mmol, 200 mol%). Flash column chromatography (SiO₂: 20% ethyl acetate in hexanes) gave the title compound as a white solid (52.5 mg, 0.131 mmol, 96% yield).

This compound was also prepared following the *GP-2* using 4-bromo-1-tosylpiperidine **1b** (47.5 mg, 0.137 mmol, 100 mol%), 4-(*tert*-butyl)benzoic anhydride (92.7 mg, 0.274 mmol, 200 mol%). Flash column chromatography (SiO₂: 20% ethyl acetate in hexanes) gave the title compound as a white solid (43.7 mg, 0.109 mmol, 80% yield).

This compound can also be prepared by *GP-3* using 4-iodo-1-tosylpiperidine **1a** (50.0 mg, 0.137 mmol, 100 mol%), 4-(*tert*-butyl)benzoic acid (97.8 mg, 0.548 mmol, 400 mol%), giving the

title compound in 79% yield.

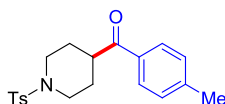
^1H NMR (500 MHz, CDCl_3): δ 7.79 (d, J = 8.5 Hz, 2H), 7.67 (d, J = 8.5 Hz, 2H), 7.44 (d, J = 8.5 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 3.76 (dt, J = 11.8, 3.4 Hz, 2H), 3.21-3.15 (m, 1H), 2.54 (td, J = 11.5, 3.4 Hz, 2H), 2.45 (s, 3H), 1.84-1.95 (m, 4H), 1.32 (s, 9H). ^{13}C NMR (125 MHz, CDCl_3): δ 201.1, 157.1, 143.7, 133.2, 133.0, 129.8, 128.2, 127.8, 125.8, 45.7, 42.2, 35.2, 31.1, 28.0, 21.7. HRMS: Calcd for $\text{C}_{23}\text{H}_{29}\text{NNaO}_3\text{S}$ ($\text{M}+\text{Na}$) $^+$: 422.1766. Found 422.1766. M.p. 167-168°C.



(4-Methoxyphenyl)(1-tosylpiperidin-4-yl)methanone (8). This compound was prepared according to the *GP-1* using 4-iodo-1-tosylpiperidine (50.0 mg, 0.137 mmol, 100 mol%), 4-methoxybenzoic anhydride (78.4 mg, 0.274 mmol, 200 mol%). After purification by column chromatography (SiO_2 : 30% ethyl acetate in hexanes), the title compound was isolated as a white solid (43.5 mg, 0.116 mmol, 83% yield).

This compound can also be prepared according to the *GP-3* using **1a** (50.0 mg, 0.137 mmol, 100 mol%), 4-methoxybenzoic acid (78.4 mg, 0.548 mmol, 400 mol%). After purification by column chromatography (SiO_2 : 20% ethyl acetate in hexanes), the title compound was isolated as a white solid (36.8 mg, 0.099 mmol, 72% yield).

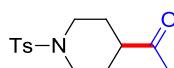
^1H NMR (500 MHz, CDCl_3): δ 7.83 (d, J = 8.5 Hz, 2H), 7.65 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 6.89 (d, J = 9.0 Hz, 2H), 3.84 (s, 3H), 3.75-3.77 (m, 2H), 3.11-3.16 (m, 1H), 2.49-2.52 (m, 2H), 2.44 (s, 2H), 1.82-1.92 (m, 4H). ^{13}C NMR (125 MHz, CDCl_3): δ 200.0, 163.7, 143.7, 133.2, 130.6, 129.8, 128.6, 127.8, 114.0, 55.6, 45.7, 42.1, 28.1, 21.6. ESI-MS ($\text{M}+\text{H}$) $^+$: Calcd for 373.13. Found 373.2. M.p. 144-145°C.



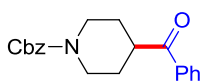
***p*-Tolyl(1-tosylpiperidin-4-yl)methanone (9).** This compound was prepared according to the *GP-1* using 4-iodo-1-tosylpiperidine **1a** (50.0 mg, 0.137 mmol, 100 mol%) and 4-methylbenzoic anhydride (69.7 mg, 0.274 mmol, 200 mol%). After purification by column chromatography (SiO_2 : 20% ethyl acetate in hexanes), the title compound was isolated as a white solid (41.6 mg, 0.116

mmol, 85% yield).

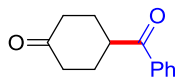
^1H NMR (500 MHz, CDCl_3): δ 7.74 (d, J = 8.5 Hz, 2H), 7.65 (d, J = 8.5 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.22 (d, J = 8.5 Hz, 2H), 3.76 (d, J = 8.0 Hz, 2H), 3.18-3.13 (m, 1H), 2.50 (td, J = 11.5, 3.5 Hz, 2H), 2.44 (s, 3H), 2.38 (s, 3H), 1.93-1.82 (m, 4H). ^{13}C NMR (125 MHz, CDCl_3): δ 201.1, 144.2, 143.7, 133.2, 133.1, 129.8, 129.6, 128.4, 127.8, 45.7, 42.3, 28.1, 21.7, 21.6. ESI-MS: Calcd for $\text{C}_{20}\text{H}_{24}\text{NO}_3\text{S}$ ($\text{M}+\text{H}$) $^+$: 358.1477. Found 358.1. M.p. 141-142°C.



1-(1-Tosylpiperidin-4-yl)ethanone (10). This compound was prepared according to the *GP-1* using 4-iodo-1-tosylpiperidine (50.0 mg, 0.137 mmol, 100 mol%) and acetic anhydride (25.7 μL , 0.274 mmol, 200 mol%). After purification by column chromatography (SiO_2 : 10% ethyl acetate in hexanes), the title compound was isolated as a solid (28.1 mg, 0.1 mmol, 68% yield).



Benzyl 4-benzoylpiperidine-1-carboxylate (11). This compound was prepared according to the *GP-1* using benzyl 4-iodopiperidine-1-carboxylate (47.3 mg, 0.137 mmol, 100 mol%) and benzoic anhydride (62.0 mg, 0.274 mmol, 200 mol%). After purification by column chromatography (SiO_2 : 20% ethyl acetate in hexanes), the title compound was isolated as a white solid (36.8 mg, 0.114 mmol, 83% yield).⁹

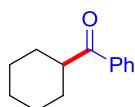


4-Benzoylcyclohexanone (12). This compound was prepared according to the *GP-1* using 4-iodocyclohexanone (30.7 mg, 0.137 mmol, 100 mol%) and benzoic anhydride (62.0 mg, 0.274 mmol, 200 mol%). After purification by column chromatography (SiO_2 : 20% ethyl acetate in hexanes), the title compound was isolated as a white solid (22.5 mg, 0.111 mmol, 81% yield).

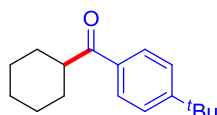
This compound can also be prepared according to the *GP-2* using 4-bromocyclohexanone (24.3 mg, 0.137 mmol, 100 mol%), benzoic anhydride (62.0 mg, 0.274 mmol, 200 mol%). After purification by column chromatography (SiO_2 : 20% ethyl acetate in hexanes), the title compound

was isolated as a white solid (15.4 mg, 0.076 mmol, 55% yield).

^1H NMR (500 MHz, CDCl_3): δ 7.99 (d, $J = 7.5$ Hz, 2H), 7.61 (t, $J = 7.0$ Hz, 1H), 7.51 (t, $J = 7.5$ Hz, 2H), 3.76-3.71 (m, 1H), 2.59-2.55 (m, 2H), 2.50-2.44 (m, 2H), 2.26-2.22 (m, 2H), 2.10-2.02 (m, 2H). ^{13}C NMR (125 MHz, CDCl_3): δ 210.2, 210.1, 135.8, 133.4, 128.9, 128.3, 42.7, 39.9, 28.8. M.p. 73-74°C.



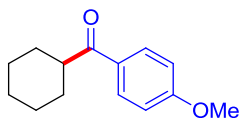
Cyclohexyl(phenyl)methanone (13). This compound was prepared according to the *GP-1* using iodocyclohexane (18 μL , 0.139 mmol, 100 mol%) and benzoic anhydride (62.0 mg, 0.278 mmol, 200 mol%). After purification by column chromatography (SiO_2 : 5% ethyl acetate in hexanes), the title compound was isolated as a colorless oil (13.3 mg, 0.071 mmol, 51% yield).¹⁰



(4-(tert-Butyl)phenyl)(cyclohexyl)methanone (14). This compound was prepared according to the *GP-1* using iodocyclohexane (18.0 μL , 0.139 mmol, 100 mol%) and 4-(tert-butyl)benzoic anhydride (92.7 mg, 0.274 mmol, 200 mol%). After purification by column chromatography (SiO_2 : 5% ethyl acetate in hexanes), the title compound was isolated as a colorless oil (31.3 mg, 0.128 mmol, 92% yield).

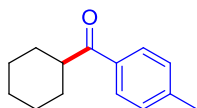
This compound can also be prepared according to *GP-3* using iodocyclohexane (18 μL , 0.139 mmol, 100 mol%) and 4-(tert-butyl)benzoic acid (99.0 mg, 0.56 mmol, 400 mol%). After purification by column chromatography (SiO_2 : 5% ethyl acetate in hexanes), the title compound was isolated as a colorless oil (24.1 mg, 0.098 mmol, 71% yield).

^1H NMR (500 MHz, CDCl_3): δ 7.92 (d, $J = 8.4$ Hz, 2H), 7.49 (d, $J = 8.4$ Hz, 2H), 3.28 (tt, $J = 11.2, 3.0$ Hz, 1H), 1.92-1.85 (m, 4H), 1.77-1.74 (m, 1H), 1.56-1.28 (m, 5H), 1.36 (s, 9H). ^{13}C NMR (125 MHz, CDCl_3): δ 203.5, 156.4, 133.7, 128.2, 125.5, 45.6, 35.1, 31.1, 29.5, 26.0, 25.9. EI-MS (70 eV) M^+ : 244, 187, 161, 83.

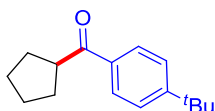


Cyclohexyl(4-methoxyphenyl)methanone (15). This compound was prepared according to the *GP-1* using iodocyclohexane (18 μ L, 0.139 mmol, 100 mol%), and 4-methoxybenzoic anhydride (79.6 mg, 0.278 mmol, 200 mol%). After purification by column chromatography (SiO₂: 5% ethyl acetate in hexanes), the title compound was isolated as a colorless oil (20.6 mg, 0.094 mmol, 68% yield).

This compound can also be prepared according to the *GP-3* using iodocyclohexane (18 μ L, 0.139 mmol, 100 mol%), and 4-methoxybenzoic acid (84.6 mg, 0.456 mmol, 400 mol%). After purification by column chromatography (SiO₂: 5% ethyl acetate in hexanes), the title compound was isolated as a colorless oil (19.7 mg, 0.09 mmol, 65% yield).¹¹

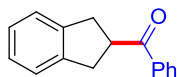


Cyclohexyl(*p*-tolyl)methanone (16). This compound was prepared according to the *GP-1* using iodocyclohexane (18 μ L, 0.139 mmol, 100 mol%), and 4-methylbenzoic anhydride (70.7 mg, 0.278 mmol, 200 mol%). After purification by column chromatography (SiO₂: 5% ethyl acetate in hexanes), the title compound was isolated as a colorless oil (21.4 mg, 0.106 mmol, 76% yield).¹²



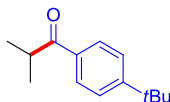
(4-(*tert*-Butyl)phenyl)(cyclopentyl)methanone (17). This compound was prepared according to the *GP-1* using iodocyclopentane (16 μ L, 0.134 mmol, 100 mol%) and 4-(*tert*-butyl)benzoic anhydride (90.8 mg, 0.268 mmol, 200 mol%). After purification by column chromatography (SiO₂: 5% ethyl acetate in hexanes), the title compound was isolated as a colorless oil (29.4 mg, 0.128 mmol, 95% yield).

¹H NMR (500 MHz, CDCl₃): δ 7.95 (d, J = 8.5 Hz, 2H), 7.50 (d, J = 8.5 Hz, 2H), 3.76-3.70 (m, 1H), 1.96-1.92 (m, 4H), 1.79-1.64 (m, 4H), 1.37 (s, 9H). ¹³C NMR (125 MHz, CDCl₃): δ 202.5, 156.4, 134.3, 128.4, 125.5, 46.3, 35.1, 31.1, 30.0, 26.3.

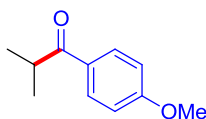


(2,3-Dihydro-1H-inden-2-yl)(phenyl)methanone (18). This compound prepared according to the *GP-I* using 2-iodo-2,3-dihydro-1H-indene (33.4 mg, 0.137 mmol, 100 mol%) and benzoic anhydride (62.0 mg, 0.274 mmol, 200 mol%). After purification by column chromatography (SiO₂: 10% ethyl acetate in hexanes), the title compound was isolated as a white solid (22.2 mg, 0.100 mmol, 73% yield).

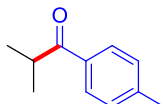
¹H NMR (500 MHz, CDCl₃): δ 8.05 (d, *J* = 7.5 Hz, 2H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 2H), 7.26-7.24 (m, 2H), 7.22-7.20 (m, 2H), 4.38- 4.31 (m, 1H), 3.43 (dd, *J* = 16.0, 7.5 Hz, 2H), 3.31 (dd, *J* = 16.0, 7.5 Hz, 2H). ¹³C NMR (125 MHz, CDCl₃): δ 200.9, 141.7, 136.4, 133.1, 128.7, 128.6, 126.7, 124.4, 46.3, 36.3.



1-(4-*tert*-Butylphenyl)-2-methylpropan-1-one (19). This compound was prepared according to the *GP-I* using 2-iodopropane (14 uL, 0.140 mmol, 100 mol%), 4-*tert*-butylbenzoyl anhydride (94.9 mg, 0.280 mmol, 200 mol%). After purification by column chromatography (SiO₂: 5% ethyl acetate in hexanes), the title compound was isolated as a colorless oil (23.3 mg, 0.114 mmol, 76% yield).¹³

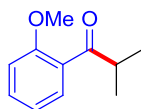


1-(4-Methoxyphenyl)-2-methylpropan-1-one (20). This compound was prepared according to the *GP-I* using 2-iodopropane (14 uL, 0.140 mmol, 100 mol%), and 4-methoxybenzoic anhydride (80.1 mg, 0.280 mmol, 200 mol%). After purification by column chromatography (SiO₂: 5% ethyl acetate in hexanes), the title compound was isolated as a colorless oil (12.5 mg, 0.07 mmol, 50% yield).¹⁴



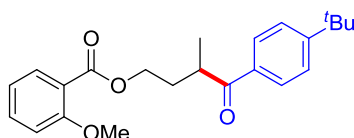
2-Methyl-1-(p-tolyl)propan-1-one (21). This compound was prepared according to the *GP-I* using 2-iodopropane (14 uL, 0.140 mmol, 100 mol%), and 4-methylbenzoic anhydride (71.3 mg, 0.280 mmol, 200 mol%). After purification by column chromatography (SiO₂: 5% ethyl acetate in

hexanes), the title compound was isolated as a colorless oil (14.5 mg, 0.090 mmol, 64% yield).¹⁵



1-(2-Methoxyphenyl)-2-methylpropan-1-one (22). This compound was prepared according to the *GP-1* using 2-iodopropane (23.3 mg, 0.137 mmol, 100 mol%) and 2-methoxybenzoic anhydride (78.4 mg, 0.254 mmol, 200 mol%). After purification by column chromatography (SiO₂: 7% ethyl acetate in hexanes), the title compound was isolated as a liquid (11.7 mg, 0.066 mmol, 48% yield).

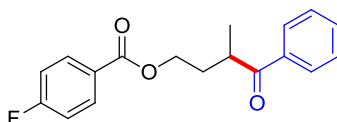
¹H NMR (500 MHz, CDCl₃): δ 7.50 (d, *J* = 1.5 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 1H), 6.99 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 8.5 Hz, 1H), 3.88 (s, 3H), 3.45-3.50 (m, 1H), 1.14, (d, *J* = 7.0 Hz, 6H). ¹³C NMR (125 MHz, CDCl₃): δ 208.3, 157.7, 132.6, 130.0, 129.0, 120.7, 111.3, 55.5, 40.1, 18.6. ESI-MS: Calcd for C₁₁H₁₄O₂ (M+H)⁺: 178.1 Found 178.0.



4-(4-(*tert*-Butyl)phenyl)-3-methyl-4-oxobutyl 2-methoxybenzoate (23). This compound was prepared following the *GP-1* using 3-iodobutyl 2-methoxybenzoate (47.5 mg, 0.137 mmol, 100 mol%), 4-(*tert*-butyl)benzoic anhydride (92.7 mg, 0.274 mmol, 200 mol%). Flash column chromatography (SiO₂: 20% ethyl acetate in hexanes) gave the title compound as a white solid (89% yield).

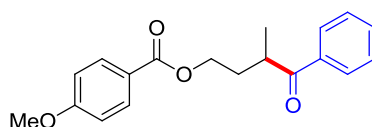
This compound can also be prepared following the *GP-2* using 3-bromobutyl 2-methoxybenzoate (39.3 mg, 0.137 mmol, 100 mol%), 4-(*tert*-butyl)benzoic anhydride (92.7 mg, 0.274 mmol, 200 mol%) which get 60% yield.

¹H NMR (500 MHz, CDCl₃): δ 7.92 (d, *J* = 8.5 Hz, 2H), 7.73 (dd, *J* = 7.7 and 1.8 Hz, 1H), 7.46 (td, *J* = 8.0 and 1.9 Hz, 1H), 7.44 (d, *J* = 8.5 Hz, 2H), 6.96 (t, *J* = 8.1 Hz, 2H), 4.36-4.42 (m, 1H), 4.28-4.34 (m, 1H), 3.88 (s, 3H), 3.68-3.76 (h, *J* = 6.9 Hz, 1H), 2.29-2.36 (m, 1H), 1.84-1.90 (m, 1H), 1.33 (s, 9H), 1.27 (d, *J* = 7.0 Hz, 1H). ¹³C NMR (125 MHz): δ 203.1, 166.2, 159.1, 156.7, 133.6, 133.5, 131.6, 128.4, 125.6, 120.1, 112.0, 62.9, 55.9, 37.3, 35.1, 32.4, 31.1, 17.6. M.p. = 92°C-93°C, ESI-MS: Calcd for C₂₃H₂₈O₄ (M+H)⁺: 391.1885. Found 391.1.



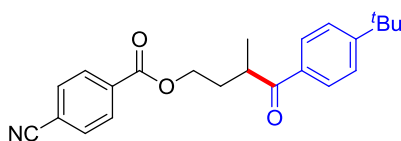
3-Methyl-4-oxo-4-phenylbutyl 4-fluorobenzoate (24). This compound was prepared according to the *GP-I* using 3-iodobutyl 4-fluorobenzoate (44.1 mg, 0.137 mmol, 100 mol%) and benzoic anhydride (62.0 mg, 0.274 mmol, 200 mol%). After purification by column chromatography (SiO₂: 20% ethyl acetate in hexanes), the title compound was isolated as a liquid (31.3 mg, 0.104 mmol, 76% yield).

¹H NMR (500 MHz, CDCl₃): δ 7.95 (t, *J* = 5.0 Hz, 4H), 7.55 (t, *J* = 7.3 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.07 (t, *J* = 8.5 Hz, 2H), 4.32-4.42 (m, 2H), 3.67-3.71 (m, 1H), 2.34-2.40 (m, 1H), 1.89-1.96 (m, 1H), 1.29 (d, *J* = 7.0 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 203.2, 166.7, 165.5, 136.1, 133.1, 132.1, 132.0, 128.7, 128.3, 115.6, 115.4, 63.3, 37.6, 32.3, 17.9. ESI-MS: Calcd for C₁₈H₁₇O₂ (M+H)⁺: 300.12. Found 300.1.



3-Methyl-4-oxo-4-phenylbutyl 4-methoxybenzoate (25). This compound was prepared according to the *GP-I* using 3-iodobutyl 4-methoxybenzoate (47.5 mg, 0.137 mmol, 100 mol%) and benzoic anhydride (62.0 mg, 0.274 mmol, 200 mol%). After purification by column chromatography (SiO₂: 20% ethyl acetate in hexanes), the title compound was isolated as a colorless liquid (55% yield).

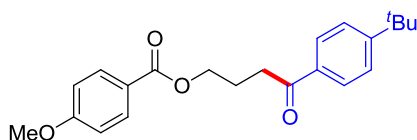
¹H NMR (500 MHz, CDCl₃): δ 7.98 (d, *J* = 7.5 Hz, 2H), 7.94 (d, *J* = 8.8 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.50-7.47 (t, *J* = 7.8 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 4.43-4.38 (m, 1H), 4.37-4.31 (m, 1H), 3.88 (s, 3H), 3.75-3.69 (m, 1H), 2.41-2.34 (m, 1H), 1.96-1.89 (m, 1H), 1.30 (d, *J* = 7.0 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 200.4, 166.2, 163.4, 136.2, 133.1, 131.6, 128.7, 128.4, 122.6, 113.6, 62.8, 55.4, 37.6, 32.4, 17.8. HRMS: Calcd for C₁₉H₂₀NaO₄ (M+Na)⁺: 335.1259. Found 335.1248. M.p. 52-53°C.



4-(4-(*tert*-Butyl)phenyl)-3-methyl-4-oxobutyl 4-cyanobenzoate (26). This compound was

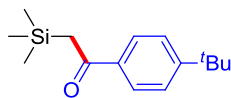
prepared according to the *GP-I* using 3-iodobutyl 4-cyanobenzoate (45.1 mg, 0.137 mmol, 100 mol%), 4-(*tert*-butyl)benzoic anhydride (92.7 mg, 0.274 mmol, 200 mol%). After purification by column chromatography (SiO₂: 20% ethyl acetate in hexanes), the title compound was isolated as a white liquid (33.8 mg, 0.093 mmol, 68%).

¹H NMR (500 MHz, CDCl₃): δ 8.01 (d, *J* = 8.0 Hz, 2H), 7.88 (d, *J* = 8.5 Hz, 2H), 7.68 (d, *J* = 8.5 Hz, 2H), 7.44 (d, *J* = 8.5 Hz, 2H), 4.35-4.45 (m, 2H), 3.64-3.68 (m, 1H), 2.37-2.45 (m, 1H), 1.90-1.96 (m, 1H), 1.32 (s, 3H), 1.28 (d, *J* = 7.0 Hz, 2H). ¹³C NMR (125 MHz, CDCl₃): δ 202.6, 164.8, 157.0, 133.9, 133.4, 132.13, 130.0, 128.3, 125.7, 118.0, 116.3, 64.2, 37.6, 35.1, 32.2, 31.1, 18.3. ESI-MS: Calcd for C₂₃H₂₅NO₃(M+H)⁺: 363.1. Found 363.1.



4-(4-(*tert*-Butyl)phenyl)-4-oxobutyl 4-methoxybenzoate (27). This compound was prepared following the *GP-I* using 3-iodopropyl 4-methoxybenzoate (43.8 mg, 0.137 mmol, 100 mol%), 4-(*tert*-butyl)benzoic anhydride (92.7 mg, 0.274 mmol, 200 mol%). Flash column chromatography (SiO₂: 20% ethyl acetate in hexanes) gave the title compound as a white solid (30.6 mg, 0.086 mmol, 63% yield).

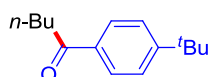
¹H NMR (500 MHz, CDCl₃): δ 7.97 (d, *J* = 9.0 Hz, 2H), 7.91 (d, *J* = 8.5 Hz, 2H), 7.47 (d, *J* = 8.0 Hz, 2H), 6.91 (d, *J* = 9.0 Hz, 2H), 4.39 (t, *J* = 6.5 Hz, 2H), 3.86 (s, 3H), 3.13 (t, *J* = 7.5 Hz, 2H), 2.23 (m, 2H), 1.34 (s, 9H). ¹³C NMR (125 MHz, CDCl₃): δ 198.9, 166.3, 163.3, 156.9, 134.3, 131.6, 128.0, 125.6, 122.7, 113.6, 64.1, 55.4, 35.1, 34.9, 31.1, 23.5. ESI-MS: Calcd for C₁₁H₁₃IO₃(M+H)⁺: 354.5. Found 354.1. M.p. 61-62 °C.



1-(4-(*tert*-Butyl)phenyl)-2-(trimethylsilyl)ethanone (28). This compound was prepared according to the *GP-I* using (iodomethyl)trimethylsilane (21.0 uL, 0.137 mmol, 100 mol%) and 4-(*tert*-butyl)benzoic anhydride (92.7 mg, 0.274 mmol, 200 mol%). After purification by column chromatography (SiO₂: 5% ethyl acetate in hexanes), the title compound was isolated as a colorless oil (25.6 mg, 0.103 mmol, 75% yield).

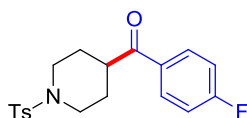
This compound can also be prepared according to *GP-3* using (iodomethyl)trimethylsilane (21.0 uL, 0.137 mmol, 100 mol%) and 4-(*tert*-butyl)benzoic acid (97.8 mg, 0.548 mmol, 400 mol%). The title compound was isolated as a colorless oil (25.6 mg, 0.103 mmol, 75% yield).

¹H NMR (500 MHz, CDCl₃): δ 7.86 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 2.74 (s, 2H), 3.16 (s, 9H), 0.11 (s, 9H). ¹³C NMR (125 MHz, CDCl₃): δ 199.3, 156.2, 135.6, 128.3, 125.3, 35.0, 33.5, 31.1, -0.9. ESI-MS: Calcd for C₁₅H₂₅OSi (M+H)⁺: 249.1675. Found 249.2.



1-(4-*tert*-Butylphenyl)pentan-1-one (29). This compound was prepared according to the *GP-1* using 1-iodobutane (16 uL, 0.136 mmol, 100 mol%), 4-*tert*-butylbenzoyl anhydride (92.2 mg, 0.300 mmol, 200 mol%). After purification by column chromatography (SiO₂: 8% ethyl acetate in hexanes), the title compound was isolated as a colorless oil (21.3 mg, 0.098 mmol, 65% yield).

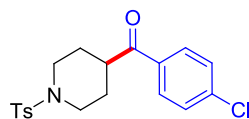
¹H NMR (500 MHz, CDCl₃): δ 7.93 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 2.97 (t, *J* = 7.5 Hz, 2H), 1.77-1.71 (m, 2H), 1.47-1.39 (m, 2H), 1.36 (s, 9H), 0.97 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 200.3, 156.5, 134.5, 128.1, 125.5, 38.3, 35.1, 31.1, 26.6, 22.5, 14.0. HRMS: Calcd for C₁₅H₂₂NaO (M+Na)⁺: 241.1568. Found 241.1562.



(4-Fluorophenyl)(1-tosylpiperidin-4-yl)methanone (30). This compound was prepared following the *GP-3* using 4-iodo-1-tosylpiperidine **1a** (50.0 mg, 0.137 mmol, 100 mol%), 4-fluorobenzoic acid (76.8 mg, 0.548 mmol, 400 mol%). Flash column chromatography (SiO₂: 20% ethyl acetate in hexanes) gave the title compound as a white solid (28.7 mg, 0.0795 mmol, 58% yield).

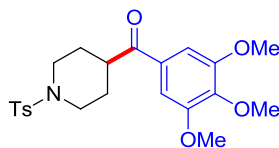
¹H NMR (500 MHz, CDCl₃): δ 7.90 (dd, *J* = 8.5, 5.0 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.12 (t, *J* = 8.5 Hz, 2H), 3.79 (dt, *J* = 8.4, 3.4 Hz, 2H), 3.19-3.14 (m, 1H), 2.52 (td, *J* = 11.3, 3.2 Hz, 2H), 2.47 (s, 3H), 1.95-1.85 (m, 4H). ¹³C NMR (125 MHz, CDCl₃): δ 199.8, 164.8, 143.7, 130.9, 130.8, 129.7, 127.7, 116.0, 115.8, 45.6, 42.3, 27.9, 21.6. HRMS: Calcd for

$C_{19}H_{20}FNNaO_3S$ ($M+Na$)⁺: 384.1046. Found 384.1048. M.p. 147-148°C.



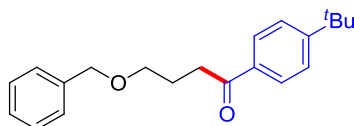
(4-Chlorophenyl)(1-tosylpiperidin-4-yl)methanone (31). This compound was prepared according to the *GP-3* using 4-iodo-1-tosylpiperidine (50.0 mg, 0.137 mmol, 100 mol%) and 4-chlorobenzoic acid (85.8 mg, 0.548 mmol, 400 mol%). After purification by column chromatography (SiO_2 : 20% ethyl acetate in hexanes), the title compound was isolated as a colorless solid (15.5 mg, 0.0411 mmol, 30% yield).

1H NMR (500 MHz, $CDCl_3$): δ 7.80 (d, J = 8.5 Hz, 2H), 7.67 (d, J = 8.0 Hz, 2H), 7.42 (d, J = 8.5 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 3.79 (dt, J = 8.4, 3.4 Hz, 2H), 3.18-3.12 (m, 1H), 2.53 (td, J = 11.5, 3.0 Hz, 2H), 2.47 (s, 3H), 1.95-1.83 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.2, 143.7, 139.7, 133.8, 133.0, 129.7, 129.6, 129.1, 127.7, 45.5, 42.3, 27.8, 21.6. HRMS: Calcd for $C_{19}H_{20}ClNNaO_3S$ ($M+Na$)⁺: 400.0750. Found 400.0762. M.p. 155-156°C.



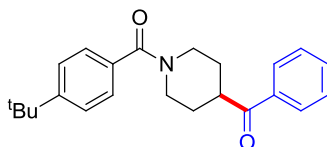
(1-Tosylpiperidin-4-yl)(3,4,5-trimethoxyphenyl)methanone (33). This compound was prepared according to the *GP-3* using 4-iodo-1-tosylpiperidine **1a** (50.0 mg, 0.137 mmol, 100 mmol%) and 3,4,5-trimethoxybenzoic acid (116.3 mg, 0.548 mmol, 400 mol%). After purification by column chromatography (SiO_2 : 30% ethyl acetate in hexanes), the title compound was isolated as a white solid (23.8 mg, 0.055 mmol, 40% yield).

1H NMR (500 MHz, $CDCl_3$): δ 7.67 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 8.5 Hz, 2H), 7.09 (s, 2H), 3.92 (s, 3H), 3.90 (s, 6H), 3.78-3.80 (m, 2H), 3.15-3.19 (m, 1H), 2.53-2.58 (m, 2H), 2.48 (s, 3H), 1.90-1.95 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.3, 153.2, 143.6, 142.9, 133.2, 130.8, 129.7, 127.8, 105.9, 60.9, 56.4, 45.5, 41.9, 28.1, 21.6. ESI-MS: Calcd for $C_{22}H_{27}NO_6S$ ($M+H$)⁺: 433.2. Found 433.2. M.p. 108-110°C.



4-(Benzyloxy)-1-(4-(tert-butyl)phenyl)butan-1-one (34). This compound was prepared according to the *GP-3* using (3-iodopropoxy)methylbenzene (37.8 mg, 0.137 mmol, 100 mol%) and 4-(tert-butyl)benzoic acid (97.7 mg, 0.548 mmol, 400 mol%). After purification by column chromatography (SiO₂: 20% ethyl acetate in hexanes), the title compound was isolated as a colorless liquid (17.9 mg, 0.058 mmol, 42%).

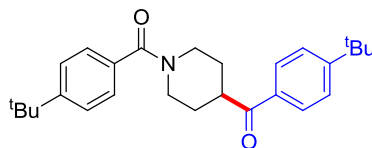
¹H NMR (500MHz, CDCl₃): δ 7.91 (d, *J* = 8.5 Hz, 2H), 7.47 (d, *J* = 8.0Hz, 2H), 7.32-7.33 (m, 4H), 7.27-7.29 (m, 1H), 4.51 (s, 2H), 3.58 (t, *J* = 6.0 Hz, 2H), 3.08 (t, *J* = 7.0 Hz, 2H), 2.04-2.09 (m, 2H), 1.35 (s, 9H). ¹³C NMR (125MHz, CDCl₃): δ 199.8, 156.8, 138.6, 134.6, 128.5, 128.2, 127.8, 125.6, 73.0, 69.6, 35.2, 31.2, 24.5. ESI-MS: Calcd for C₂₁H₂₆O₂ (M+H)⁺: 310.2. Found 310.2.



(4-Benzoylpiperidin-1-yl)(4-(tert-butyl)phenyl)methanone (35). This compound was prepared according to the *GP-2* using (4-bromopiperidin-1-yl)(4-*tert*-butylphenyl)methanone (44.4 mg, 0.137 mmol, 100 mol%), benzoic anhydride (62.0 mg, 0.274 mmol, 200 mol%). After purification by column chromatography (SiO₂: 20% ethyl acetate in hexanes), the title compound was isolated as a white solid (34.3 mg, 0.108 mmol, 79% yield). This compound can also be prepared by *GP-1* using (4-(tert-butyl)phenyl)(4-iodopiperidin-1-yl)methanone (50.8 mg, 0.137 mmol, 100 mol%) and benzoic anhydride (62.0 mg, 0.274 mmol, 200 mol%). After purification by column chromatography (SiO₂: 20% ethyl acetate in hexanes), the title compound was isolated as a white solid (40.2 mg, 0.115 mmol, 84% yield).

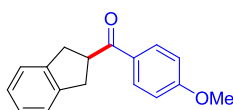
¹H NMR (500MHz, CDCl₃): δ 7.96 (d, *J* = 8.0 Hz, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.42 (d, *J* = 7.5 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 4.72 (br, 1H), 3.95 (br, 1H), 3.59-3.54 (m, 1H), 3.15-3.08 (m, 2H), 2.03 (br, 1H), 1.86-1.80 (m, 3H), 1.37 (s, 9H). ¹³C NMR (125 MHz, CDCl₃): δ 201.7, 170.7, 152.9, 135.7, 133.3, 133.0, 128.8, 128.3, 126.8, 125.4, 43.4,

34.8, 31.2, 28.7. ESI-MS: Calcd for $C_{23}H_{28}NO_2$ ($M+H$)⁺: 350.2. Found 350.2.



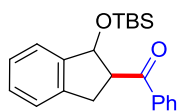
Piperidine-1,4-diylbis((4-(tert-butyl)phenyl)methanone) (36). This compound was prepared according to the *GP-2* using (4-bromopiperidin-1-yl)(4-tert-butylphenyl)methanone (44.4 mg, 0.137 mmol, 100 mol%), 4-*tert*-butylbenzoic anhydride (92.7 mg, 0.274 mmol, 200 mol%). After purification by column chromatography (SiO₂: 20% ethyl acetate in hexanes), the title compound was isolated as a white solid (38.9 mg, 0.096 mmol, 70% yield).

¹H NMR (500 MHz, CDCl₃): δ 7.92 (d, *J* = 8.5 Hz, 2H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.37 (d, *J* = 8.5 Hz, 2H), 4.71 (br, 1H), 3.95 (br, 1H), 3.59-3.53 (m, 1H), 3.16-3.09 (m, 2H), 2.03 (br, 1H), 1.86-1.81 (m, 3H), 1.36 (s, 9H), 1.34 (s, 9H). ¹³C NMR (125 MHz, CDCl₃): δ 201.3, 170.6, 157.0, 152.8, 133.0, 128.2, 126.7, 125.7, 125.3, 43.2, 35.1, 34.8, 31.2, 31.0, 28.7. ESI-MS: Calcd for $C_{27}H_{36}NO_2$ ($M+H$)⁺: 406.2746. Found 406.3. M.p. 132-133 °C.



(2,3-Dihydro-1H-inden-2-yl)(4-methoxyphenyl)methanone (37). This compound was prepared according to the *GP-2* using 2-bromo-2,3-dihydro-1H-indene (33.4 mg, 0.137 mmol, 100 mol%), 4-methoxybenzoyl anhydride (78.4 mg, 0.274 mmol, 200 mol%). After purification by column chromatography (SiO₂: 10% ethyl acetate in hexanes), the title compound was isolated as a white solid (21.4 mg, 0.085 mmol, 70% yield).

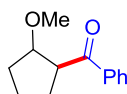
¹H NMR (500 MHz, CDCl₃): δ 8.45 (d, *J* = 8.6 Hz, 2H), 7.26-7.19 (m, 4H), 7.01 (d, *J* = 8.7 Hz, 2H), 4.33-4.26 (m, 1H), 3.92 (s, 3H), 3.42 (dd, *J* = 16.0, 7.5 Hz, 2H), 3.28 (dd, *J* = 16.0, 7.5 Hz, 2H). ¹³C NMR (125 MHz, CDCl₃): δ 199.5, 163.5, 141.8, 130.8, 129.4, 126.6, 124.4, 113.9, 55.5, 46.1, 36.4. HRMS: Calcd for $C_{17}H_{16}NaO_2$ ($M+Na$)⁺: 275.1048. Found 275.1053. M.p. 109-110 °C.



(1-((*tert*-Butyldimethylsilyl)oxy)-2,3-dihydro-1H-inden-2-yl)(phenyl)methanone (38).

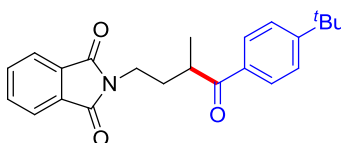
This compound was prepared according to the *GP-2* using (2-bromo-2,3-dihydro-1H-inden-1-yl)oxy(*tert*-butyl)dimethylsilane (44.8 mg, 0.137 mmol, 100 mol%), benzoic anhydride (62.0 mg, 0.274 mmol, 200 mol%). After purification by column chromatography (SiO₂: 5% ethyl acetate in hexanes), the title compound was isolated as a white solid (38.6 mg, 0.110 mmol, 80% yield).

¹H NMR (500 MHz, CDCl₃): δ 8.09 (d, *J* = 7.3 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 2H), 7.35 (d, *J* = 7.0 Hz, 1H), 7.32-7.26 (m, 2H), 7.19 (d, *J* = 7.0 Hz, 1H), 5.83 (d, *J* = 7.0 Hz, 1H), 4.30 (td, *J* = 9.2, 7.1 Hz, 1H), 3.34 (dd, *J* = 15.7, 8.9 Hz, 1H), 3.08 (dd, *J* = 16.0, 9.5 Hz, 1H), 0.92 (s, 9H), 0.21 (s, 3H), -0.08 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 201.2, 144.4, 139.6, 137.2, 133.4, 128.8, 128.7, 128.2, 127.2, 124.5, 124.2, 79.0, 57.2, 35.5, 25.9, 18.0, -4.4, -4.5. ESI-MS: Calcd for C₂₂H₂₈NaO₂Si (M+Na)⁺: 375.17. Found 375.1. M.p. 79-81 °C.



(2-Methoxycyclopentyl)(phenyl)methanone (39). This compound was prepared according to the General procedure 2 using 1-bromo-2-methoxycyclopentane (24.5 mg, 0.137 mmol, 100 mol%), benzoic anhydride (62.0 mg, 0.274 mmol, 200 mol%). After purification by column chromatography (SiO₂: 10% ethyl acetate in hexanes), the title compound was isolated as a colorless oil (11.2 mg, 0.055 mmol, 40% yield).

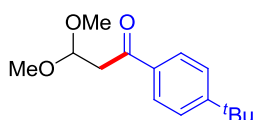
¹H NMR (500 MHz, CDCl₃): δ 8.05 (d, *J* = 7.3 Hz, 2H), 7.58 (d, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 2H), 4.20-4.17 (m, 1H), 3.79-3.75 (m, 1H), 2.17-2.11 (m, 1H), 1.94-1.90 (m, 1H), 1.86-1.76 (m, 4H), ¹³C NMR (125 MHz, CDCl₃): δ 201.7, 136.6, 133.1, 128.6, 85.1, 57.1, 53.3, 32.0, 29.5, 24.0.



2-(4-(4-(*tert*-Butyl)phenyl)-3-methyl-4-oxobutyl)isoindoline-1,3-dione (40). This

compound was prepared according to the *GP-2* using 2-(3-bromobutyl)isoindoline-1,3-dione (38.6

mg, 0.137 mmol, 100 mmol%) and 4-(tert-butyl)benzoic anhydride (92.7 mg, 0.268 mmol, 200 mol%). After purification by column chromatography (SiO₂: 15% ethyl acetate in hexanes), the title compound was isolated as a white solid contaminated with inseparable homocoupling product of the starting alkyl bromide (26.5 mg, 0.086 mmol, 63% yield based on NMR). ¹H NMR (500 MHz, CDCl₃): δ 7.85 (d, *J* = 8.3 Hz, 2H), 7.82 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.71 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.45 (d, *J* = 8.3 Hz, 2H), 3.84-3.71 (m, 2H), 3.57-3.50 (m, 1H), 2.37-2.30 (m, 1H), 1.84-1.78 (m, 1H), 1.35 (s, 9H), 1.28 (d, *J* = 7.0 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 202.5, 168.3, 156.6, 134.1, 133.9, 132.1, 128.3, 125.6, 123.2, 38.4, 36.2, 35.1, 31.8, 31.1, 18.0. ESI-MS: Calcd for C₂₂H₂₄NO₃ (M+H)⁺ : 350.1756. Found 350.1. M.p. 93-94°C.



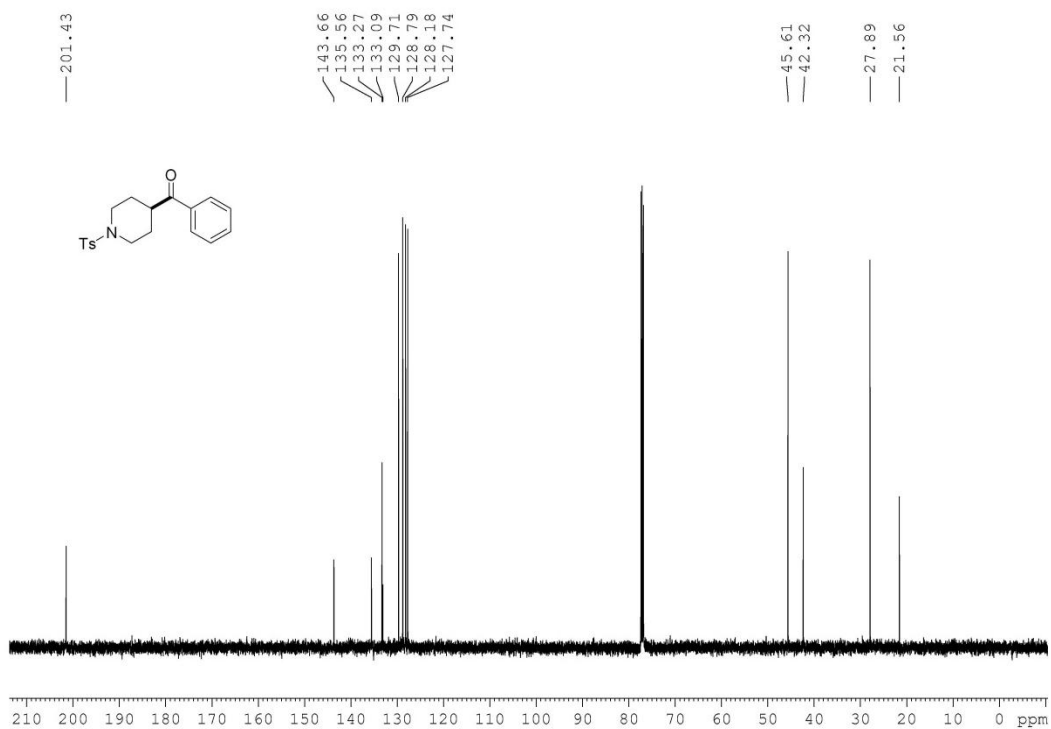
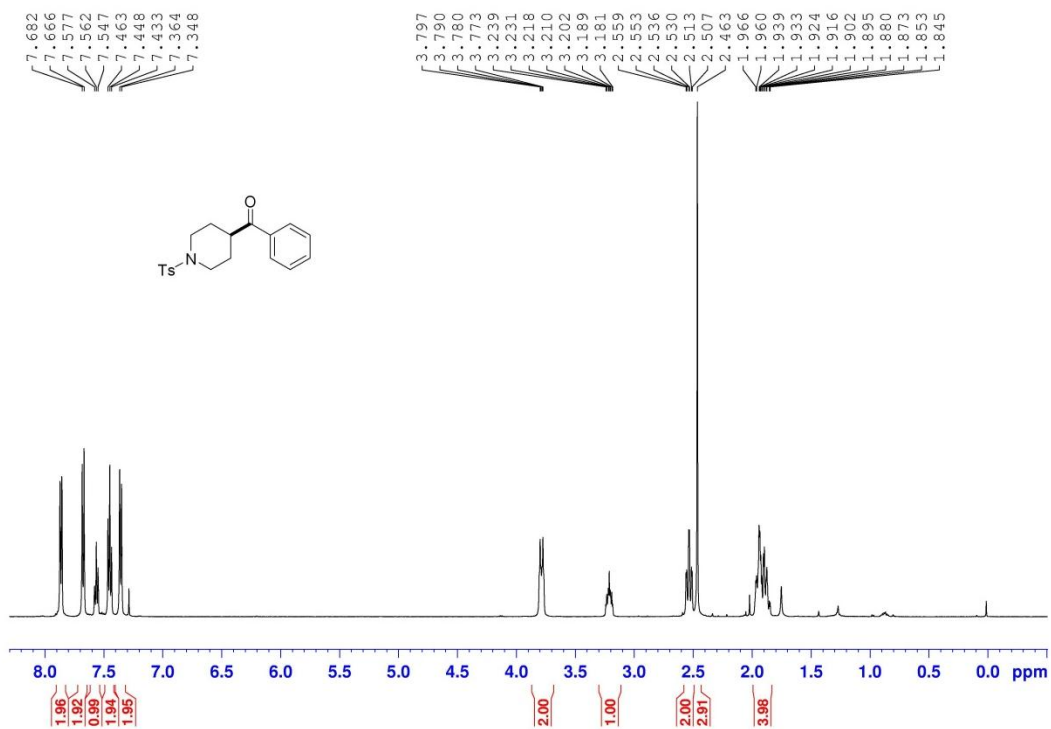
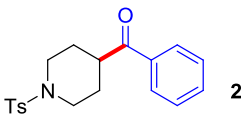
1-(4-tert-Butylphenyl)-3,3-dimethoxypropan-1-one (41). This compound was prepared according to the *GP-2* using 2-bromo-1,1-dimethoxyethane (23.1 mg, 0.137 mmol, 100 mol%) and 4-(tert-butyl)benzoic anhydride (92.7 mg, 0.268 mmol, 200 mol%). After purification by column chromatography (SiO₂: 10% ethyl acetate in hexanes), the title compound was isolated as a colorless oil (29.1 mg, 0.116 mmol, 85% yield).

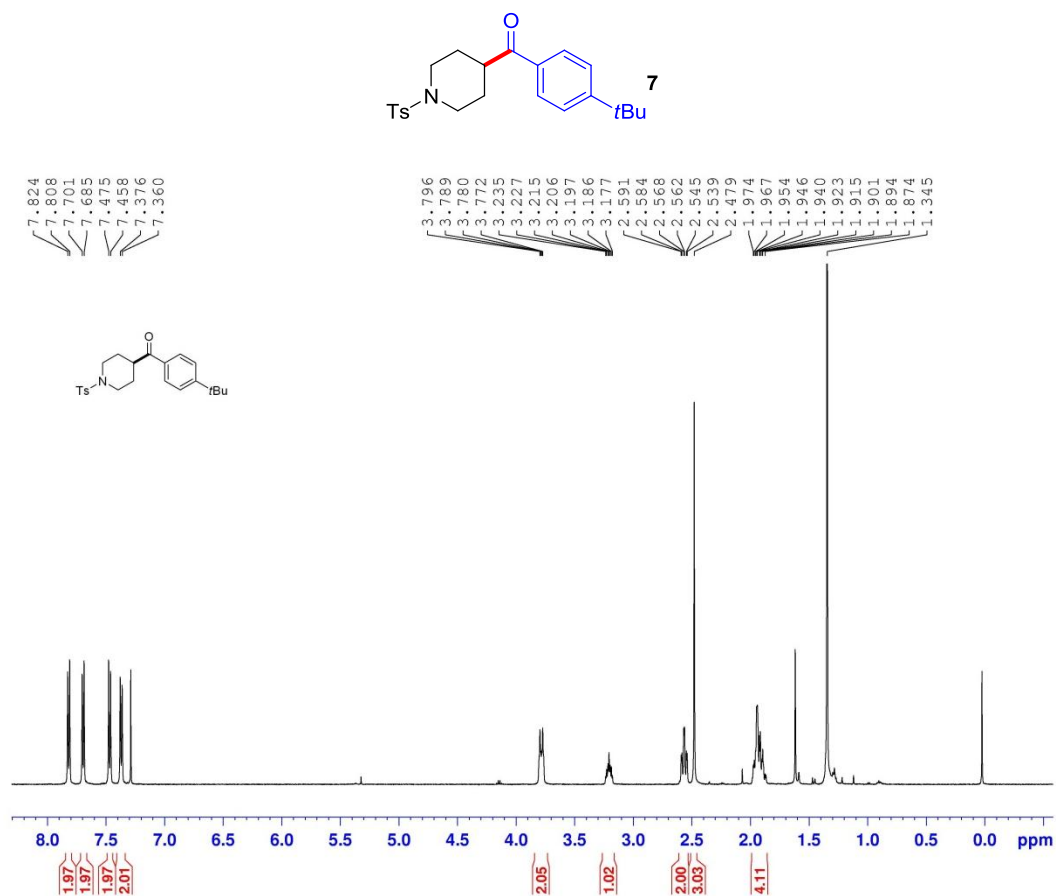
¹H NMR (500 MHz, CDCl₃): δ 7.92 (d, *J* = 8.5 Hz, 2H), 7.50 (d, *J* = 8.5 Hz, 2H), 5.03 (t, *J* = 5.5 Hz, 1H), 3.44 (s, 6H), 3.29 (d, *J* = 5.5 Hz, 2H), 1.36 (s, 9H). ¹³C NMR (125 MHz, CDCl₃): δ 196.6, 157.0, 134.5, 128.3, 125.6, 102.3, 54.2, 42.5, 35.1, 31.1. ESI-MS: Calcd for C₁₅H₂₃O₃ (M+H)⁺ : 251.1647. Found 251.2.

References

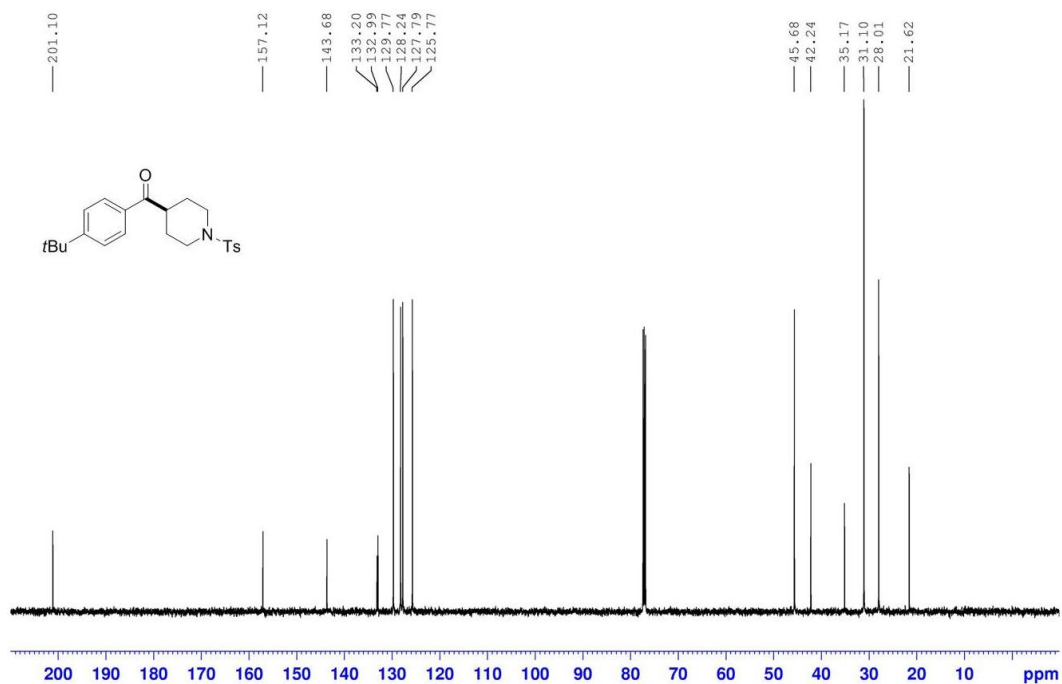
- (1) Cai, L.; Zhao, H.; Zhang, W.; Dai, L. *PCT Int. Appl.* **2010**, WO 2010127574.
- (2) (a) Nishiyama, H.; Kondo, M.; Nakamura, T.; Itoh, K. *Organometallics* **1991**, *10*, 500-508. (b) Nishiyama, H.; Soeda, N.; Naito, T.; Motoyama, Y. *Tetrahedron Asym.* **1998**, *9*, 2865-2869. (c) Müller, P.; Chappellet, S. *Helv. Chim. Acta* **2005**, *88*, 1010.
- (3) Altman, R. A.; Koval, E. D.; Buchwald, S. L. *J. Org. Chem.* **2007**, *72*, 6190.
- (4) Kawashima, T.; Takao, T.; Suzuki, H. *J. Am. Chem. Soc.* **2007**, *129*, 11006.
- (5) Kermagoret, A.; Braunstein, P. *Organometallics* **2008**, *27*, 88.
- (6) Stangeland, E. L.; Sammakia, T. *Tetrahedron* **1997**, *53*, 16503.
- (7) The reagent was distilled at 40 °C, 0.1 Mpa.
- (8) Bartoli, G.; Bosco, M.; Carlone, A. *Synthesis* **2007**, *22*, 3489.
- (9) Chang, M.-Y.; Kung, Y.-H.; Ma, C.-C., *Tetrahedron Lett.* **2007**, *48*, 199.
- (10) (a) Schneider, H. J.; *J. Org. Chem.* **1978**, *43*, 3866. (b) Lewis, F.D.; *J. Am. Chem. Soc.* **1974**, *96*, 6090.
- (11) Takemiya, A. *J. Am. Chem. Soc.* 2006, *128*, 14800
- (12) Rao, M. L. N. *Tetrahedron* **2007**, *63*, 12917
- (13) Kondo, T. *J. Org. Chem.* **1990**, *55*, 1286.
- (14) (a) Spectral data were obtained from Wiley Subscription Services. (b) Dohner, Brent R.; *J. Am. Chem. Soc.* **1986**, *108*, 245.
- (15) (a) West, J. D.; *J. Am. Chem. Soc.* **2008**, *130*, 7816; (b) Lee, S. W.; *J. Org. Chem.* **2004**, *69*, 4852.

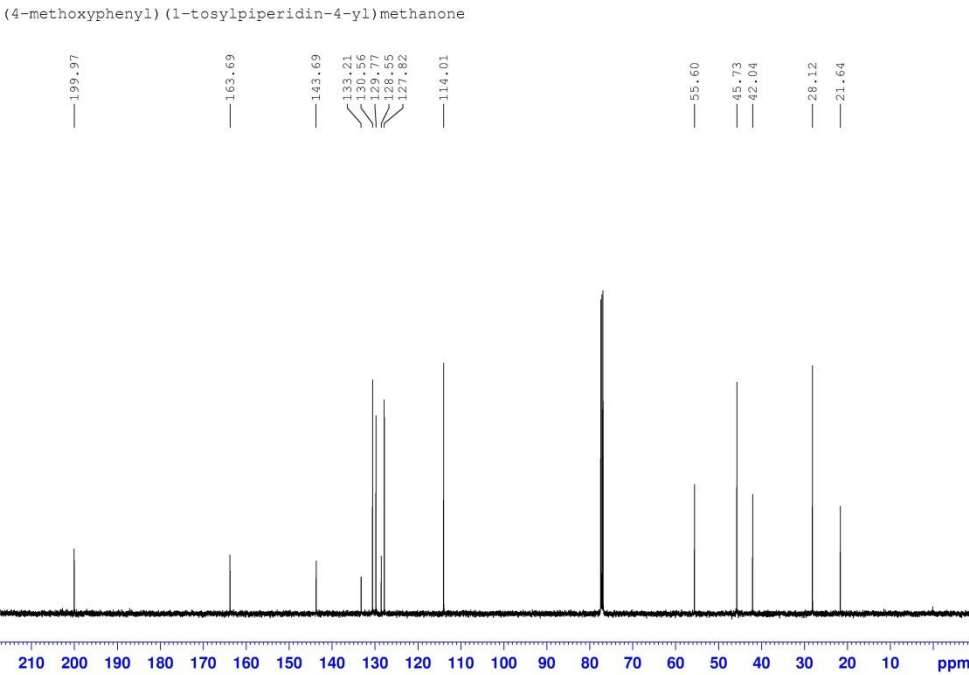
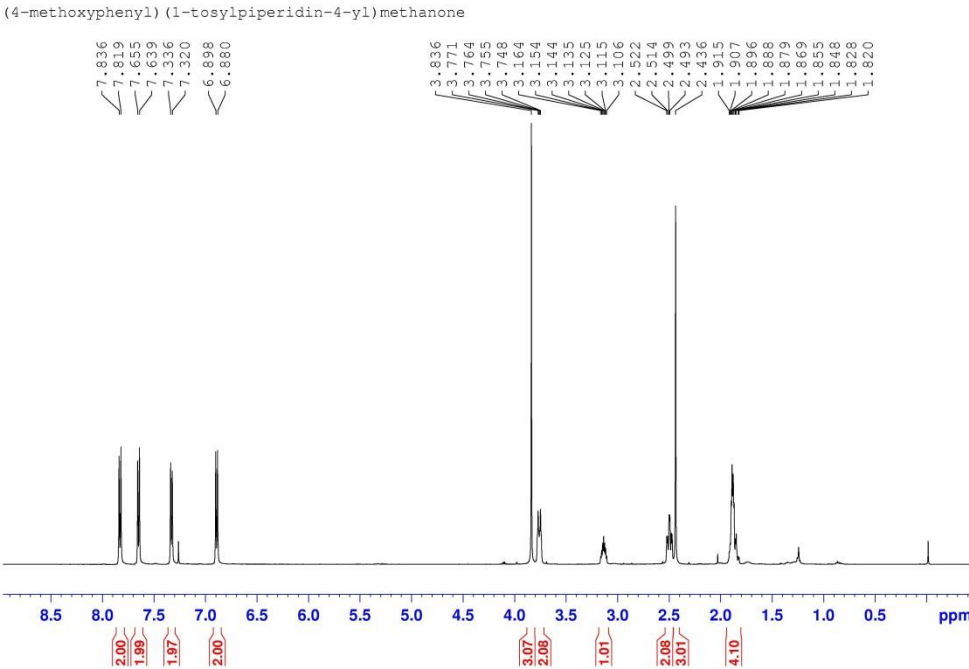
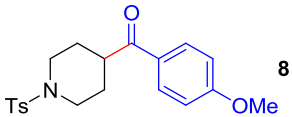
II. Spectral Data for New Compounds

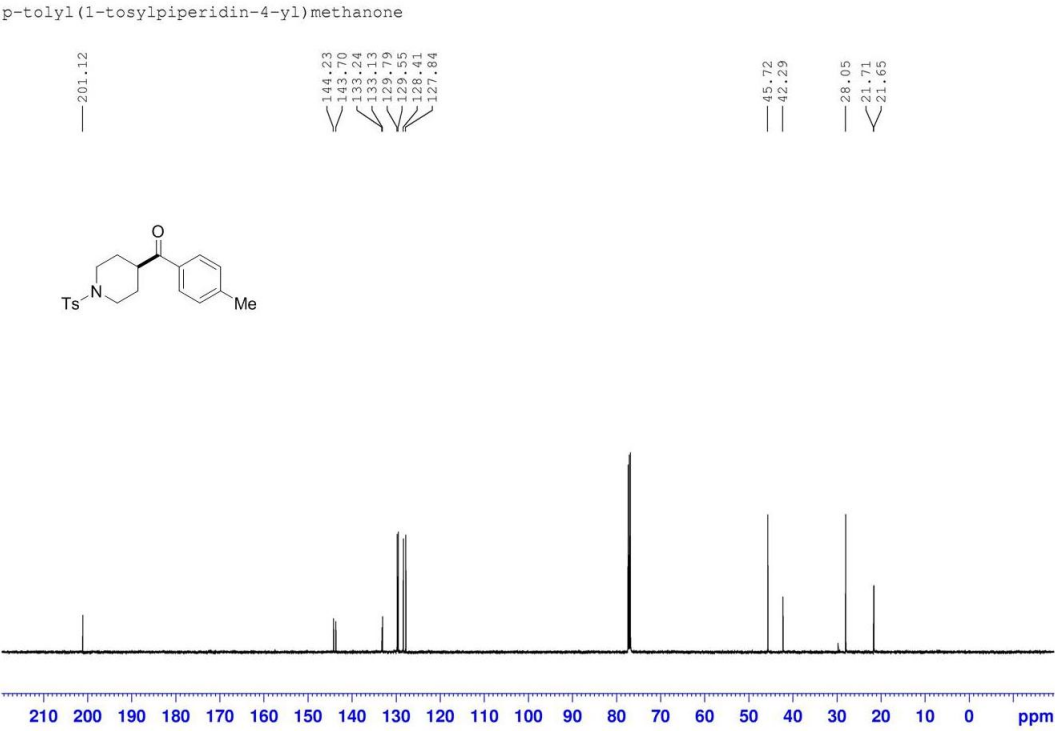
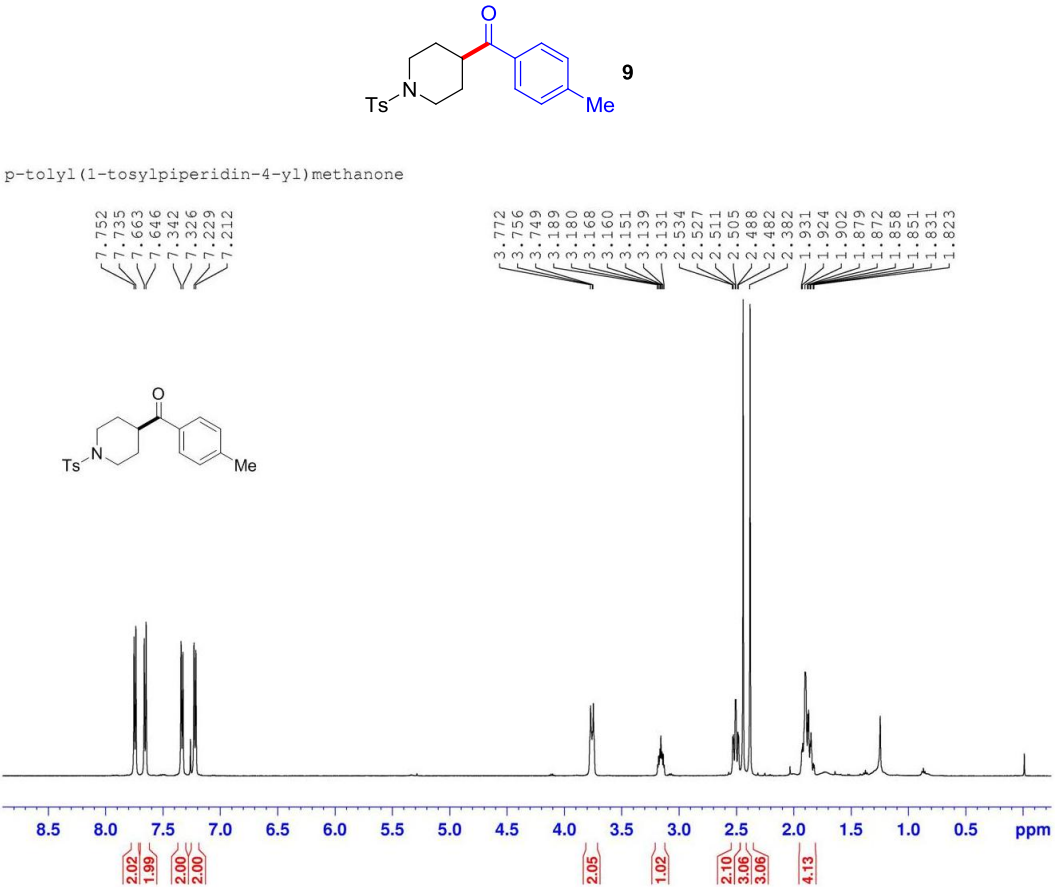


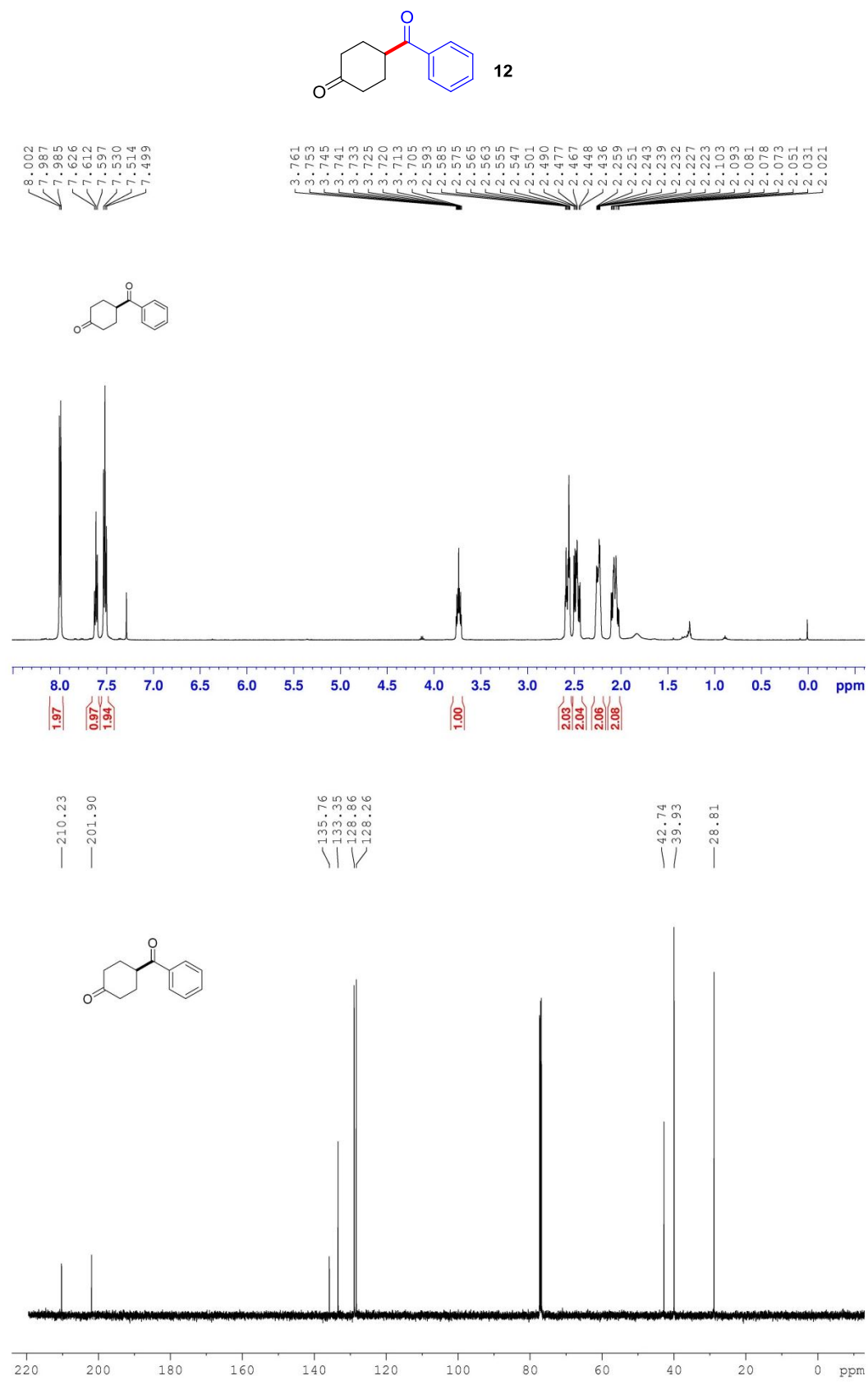


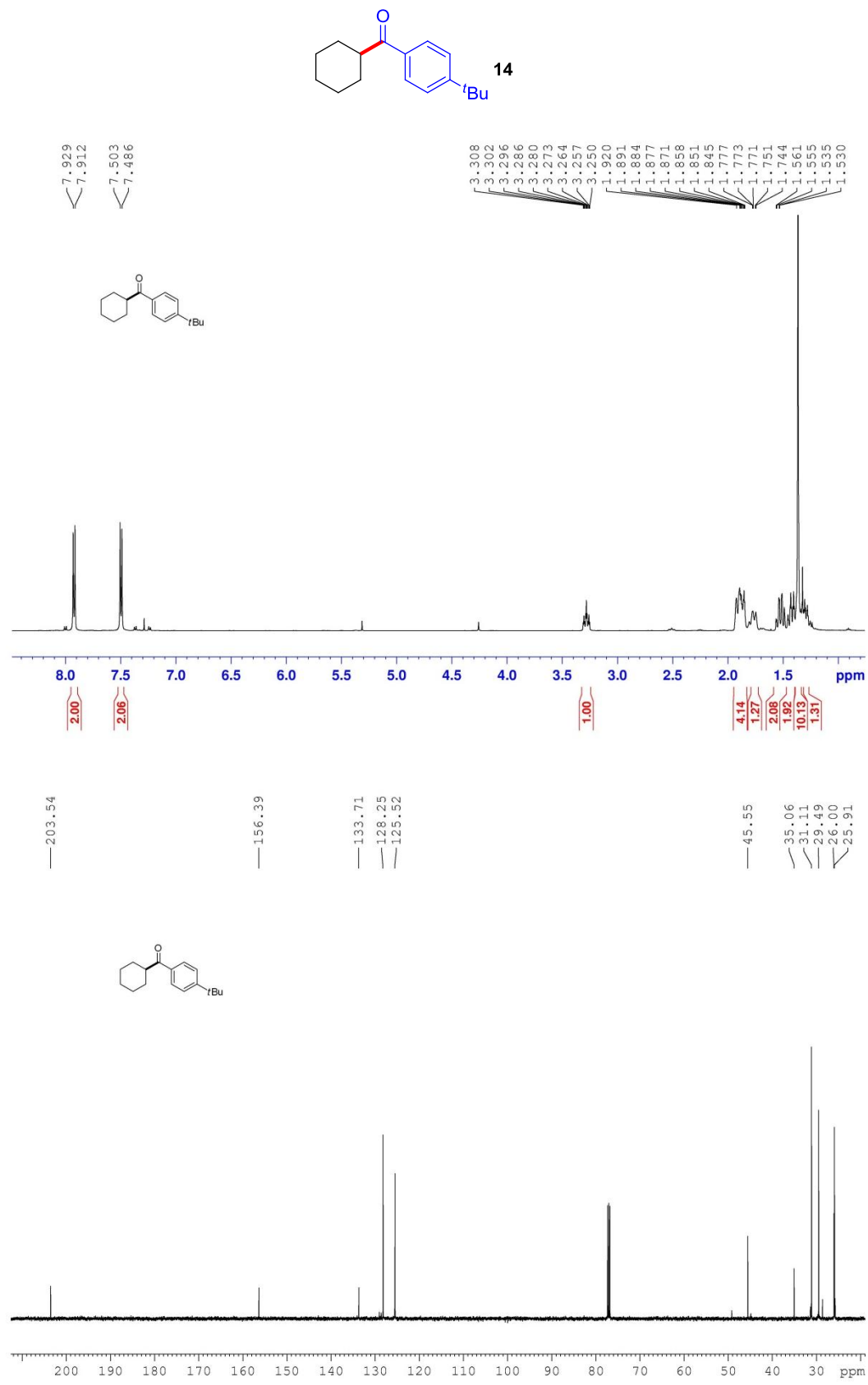
(4-(tert-butyl)phenyl) (1-tosylpiperidin-4-yl)methanone

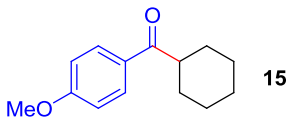




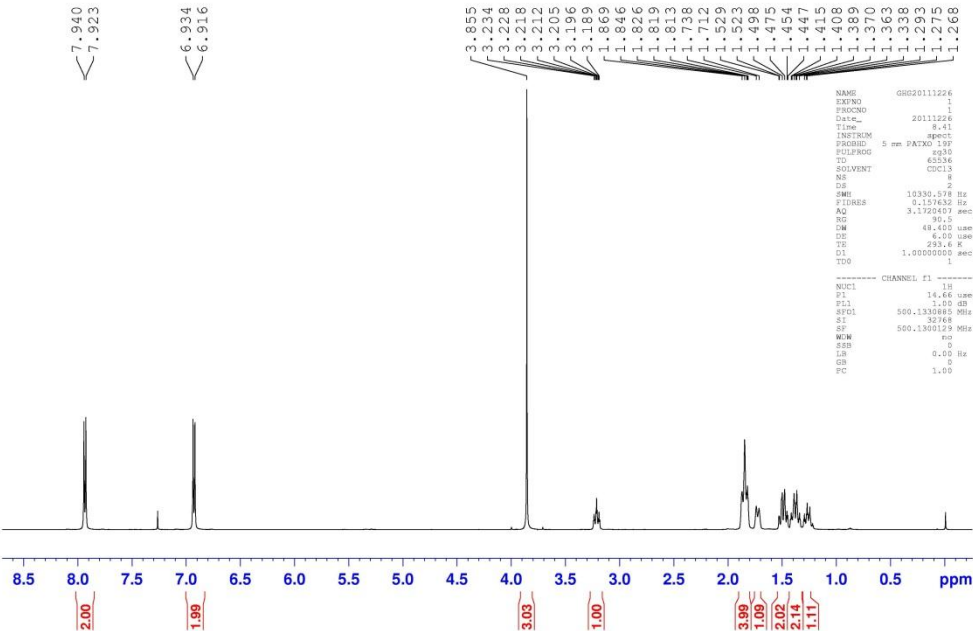




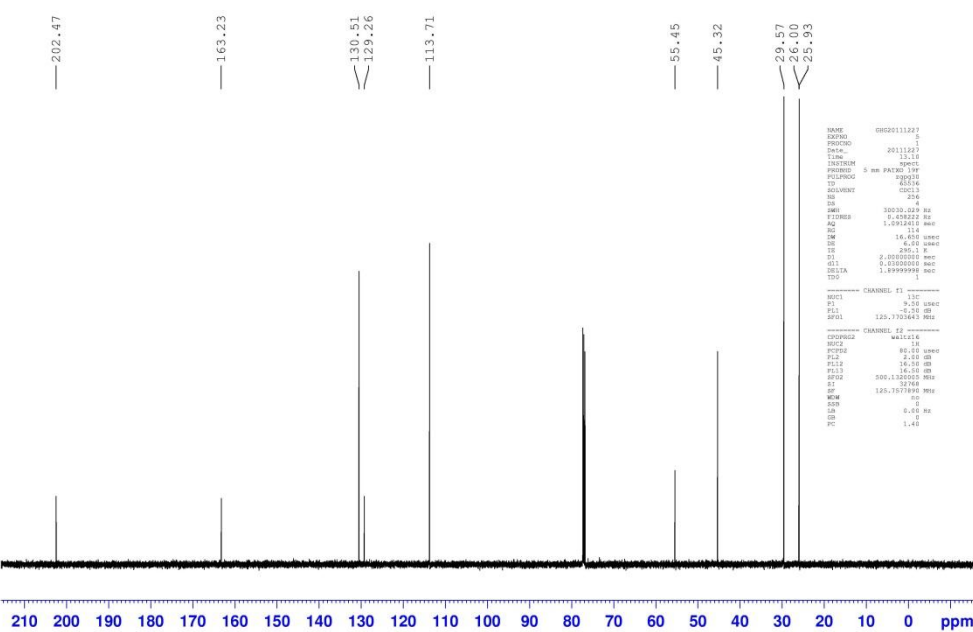


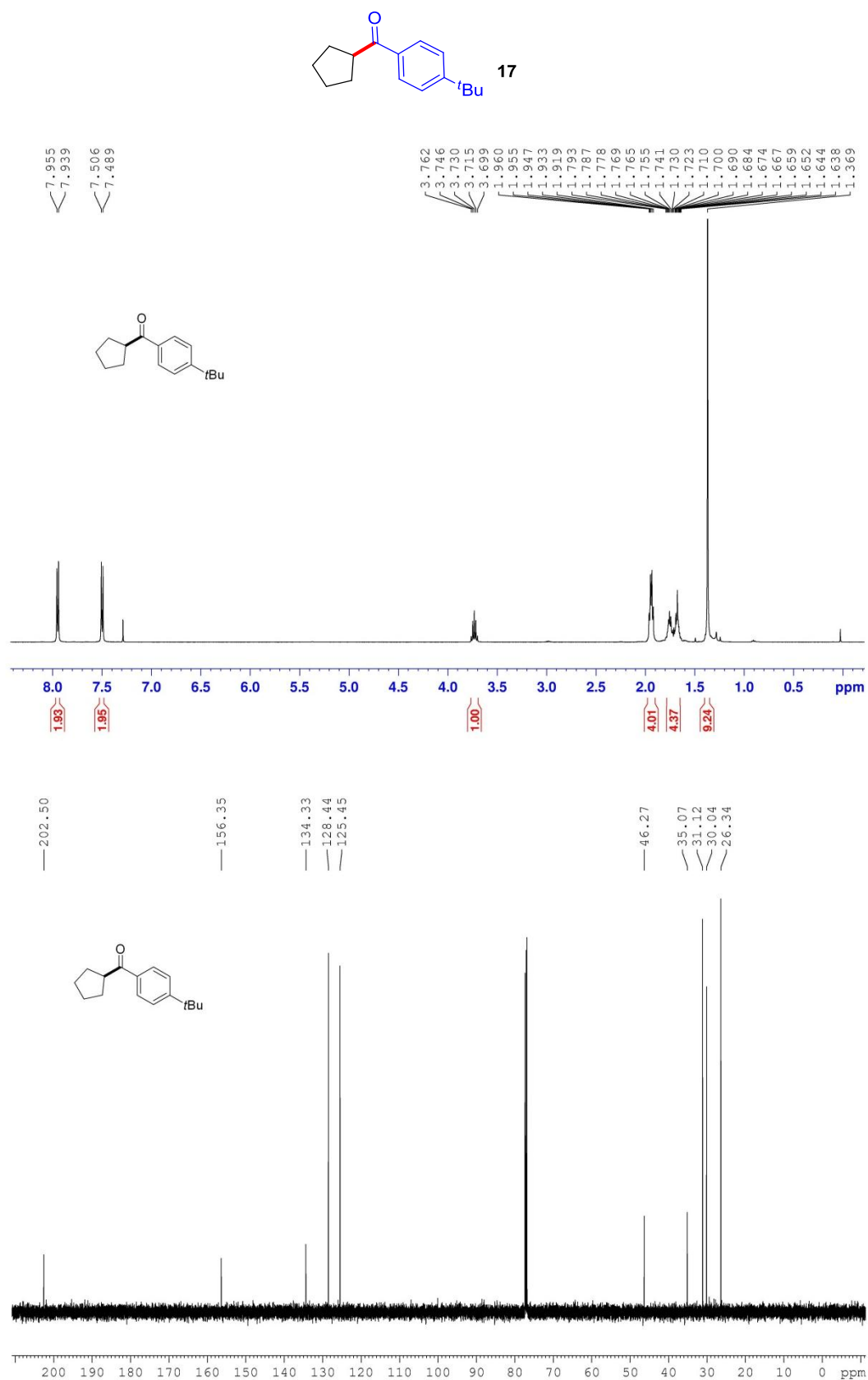


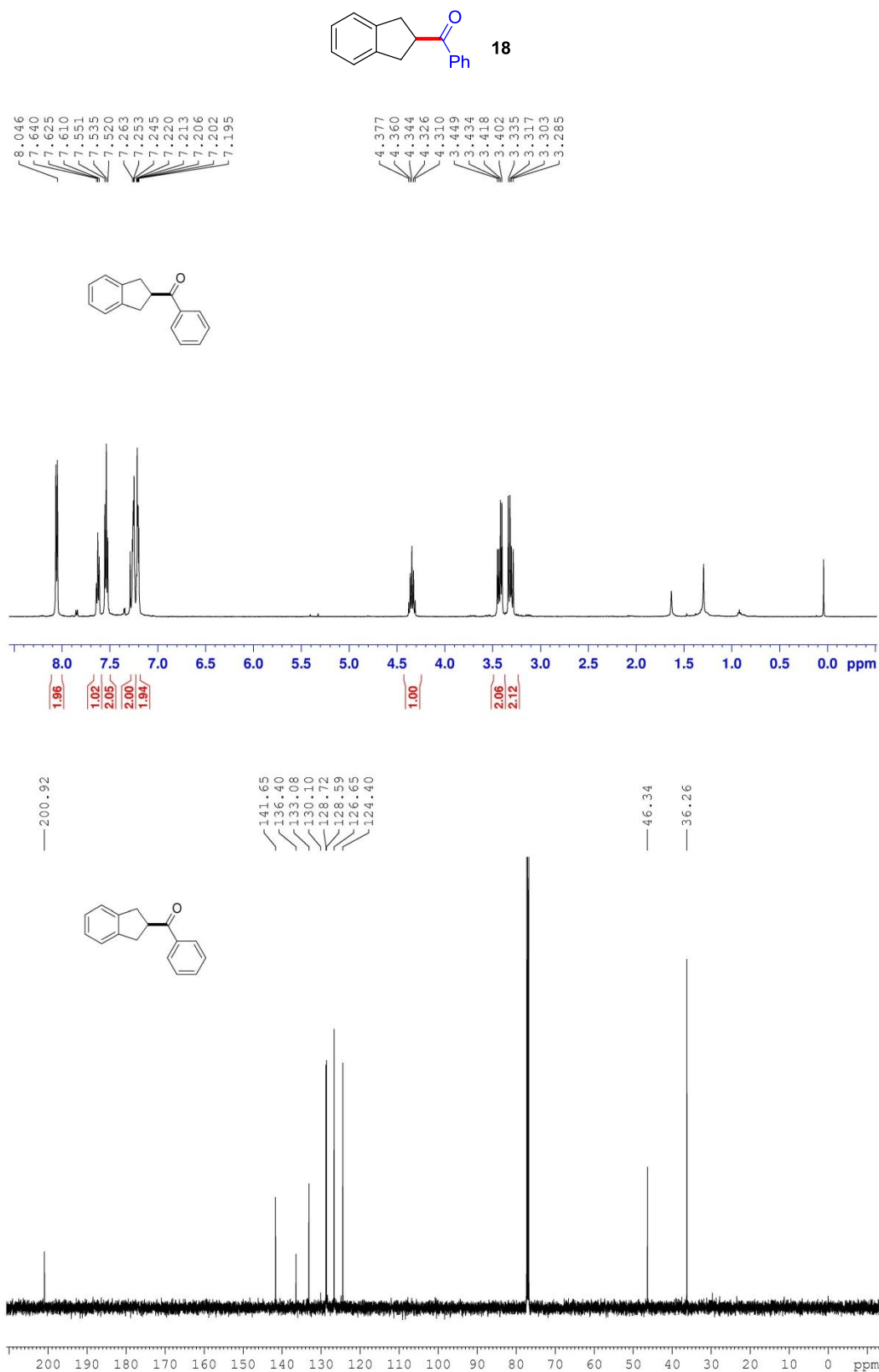
cyclohexyl (4-methoxyphenyl) methanone

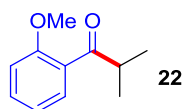


cyclohexyl (4-methoxyphenyl) methanone

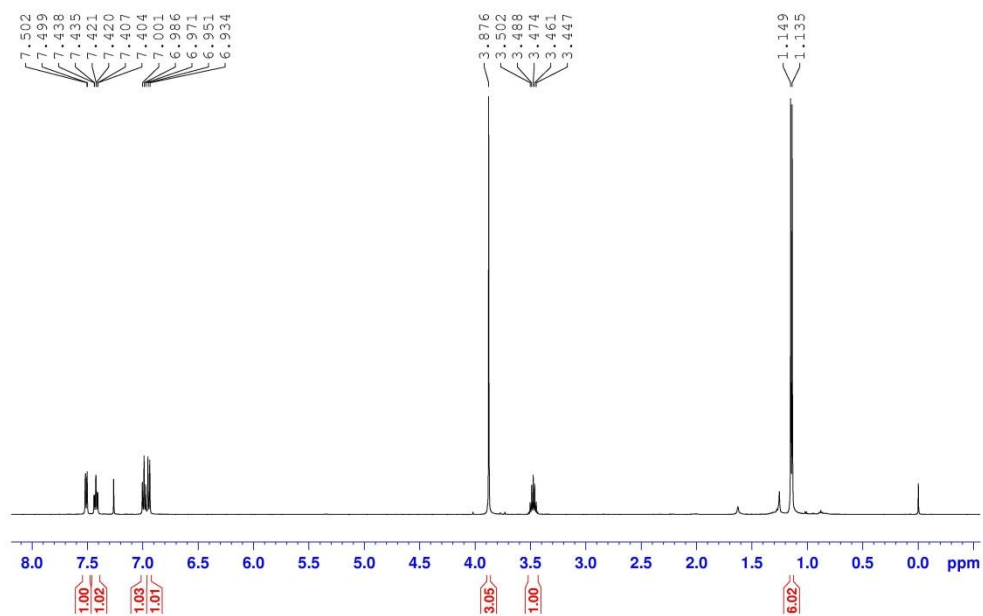




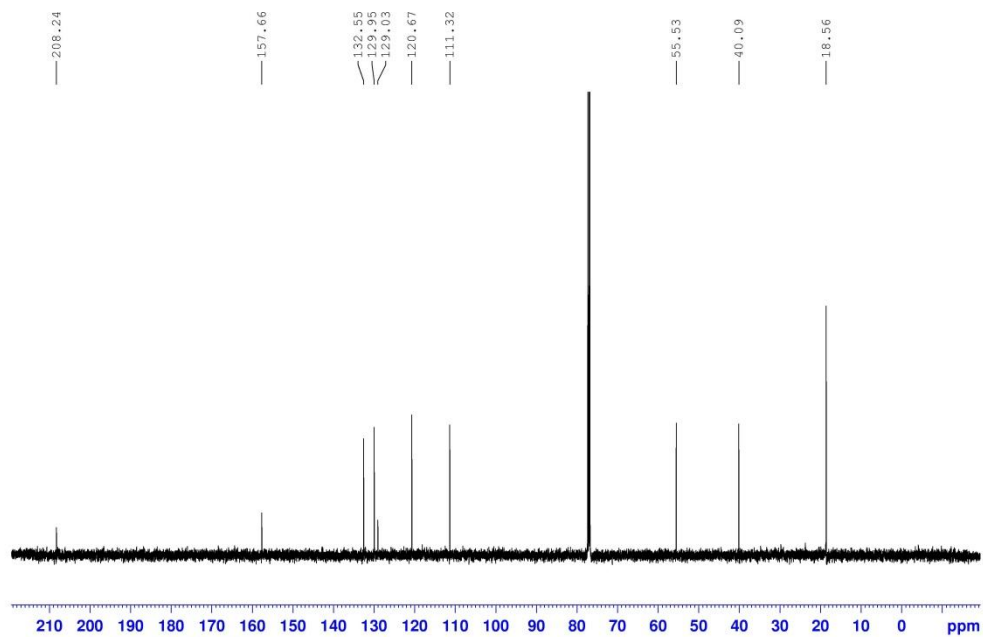


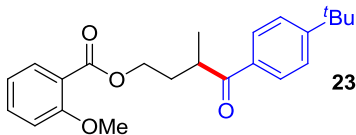


1-(2-methoxyphenyl)-2-methylpropan-1-one

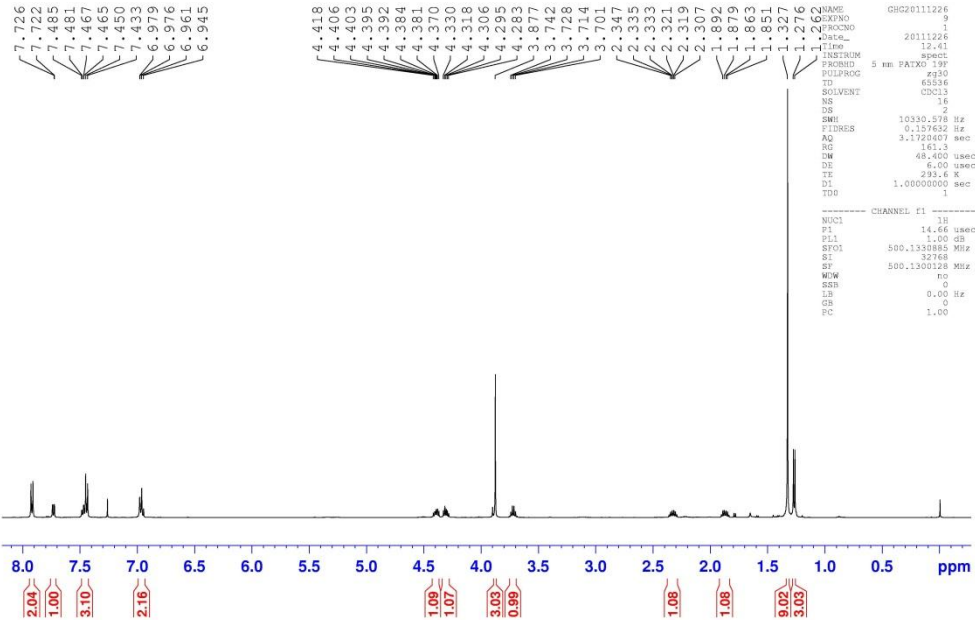


1-(2-methoxyphenyl)-2-methylpropan-1-one

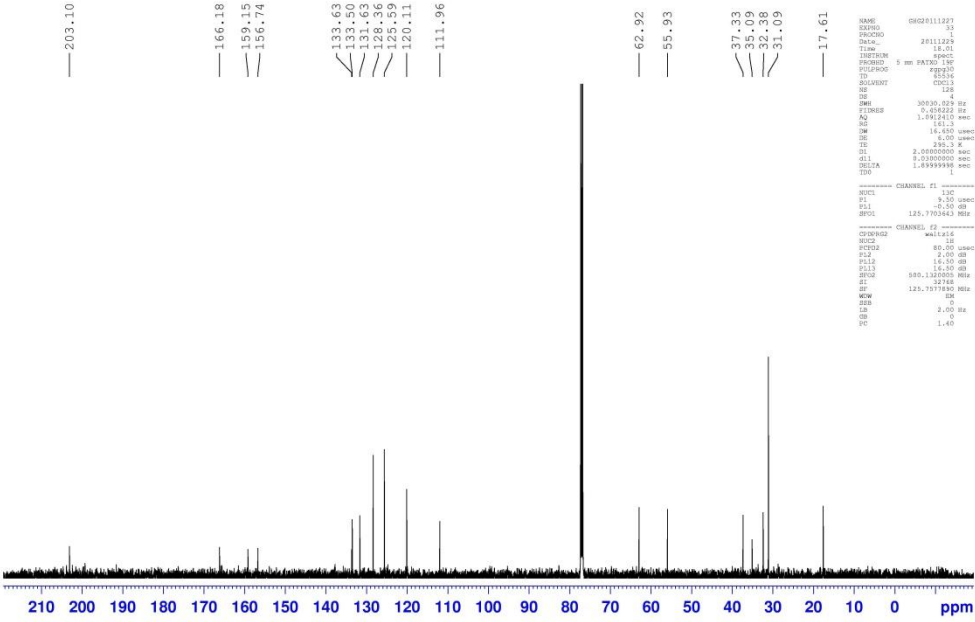


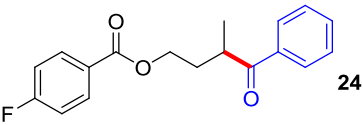


4-(4-(tert-butyl)phenyl)-3-methyl-4-oxobutyl 2-methoxybenzoate

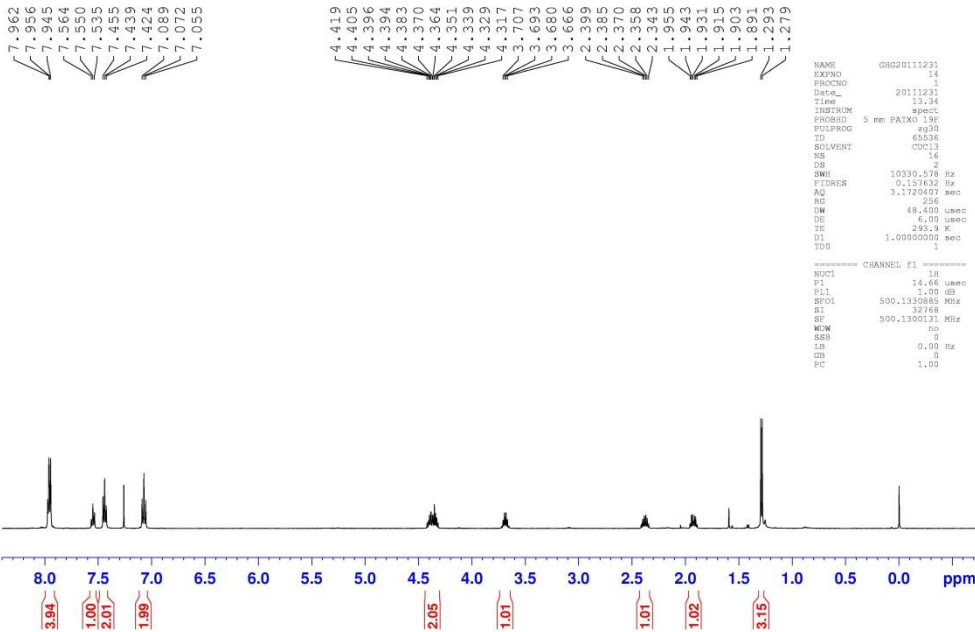


4-(4-(tert-butyl)phenyl)-3-methyl-4-oxobutyl 2-methoxybenzoate

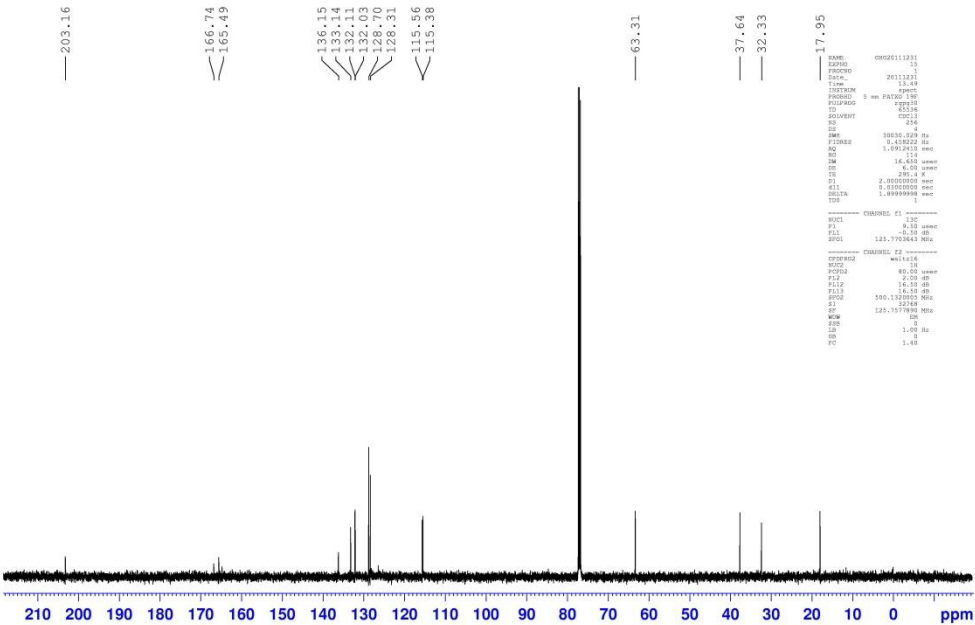


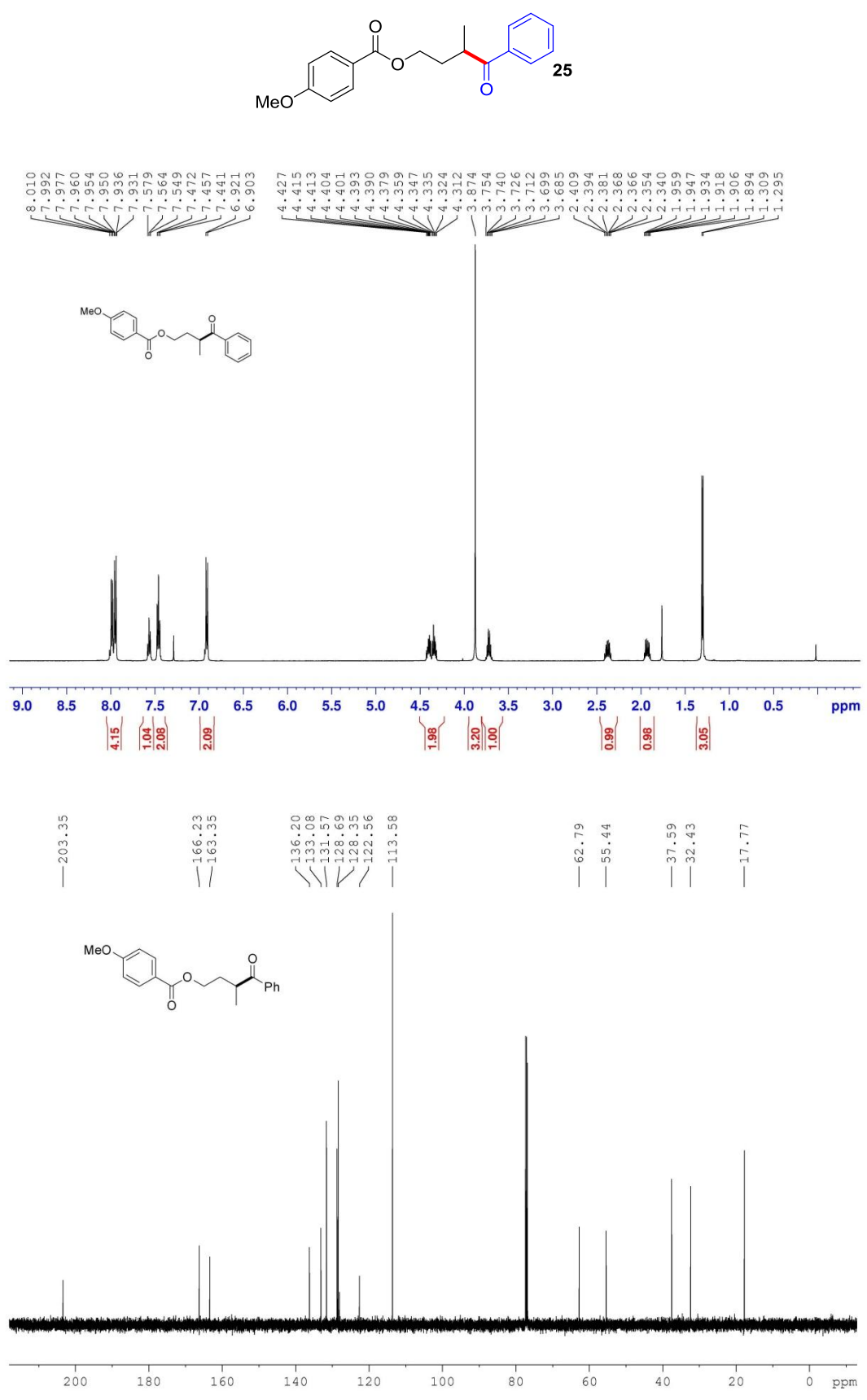


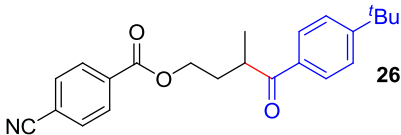
3-methyl-4-oxo-4-phenylbutyl 4-fluorobenzoate



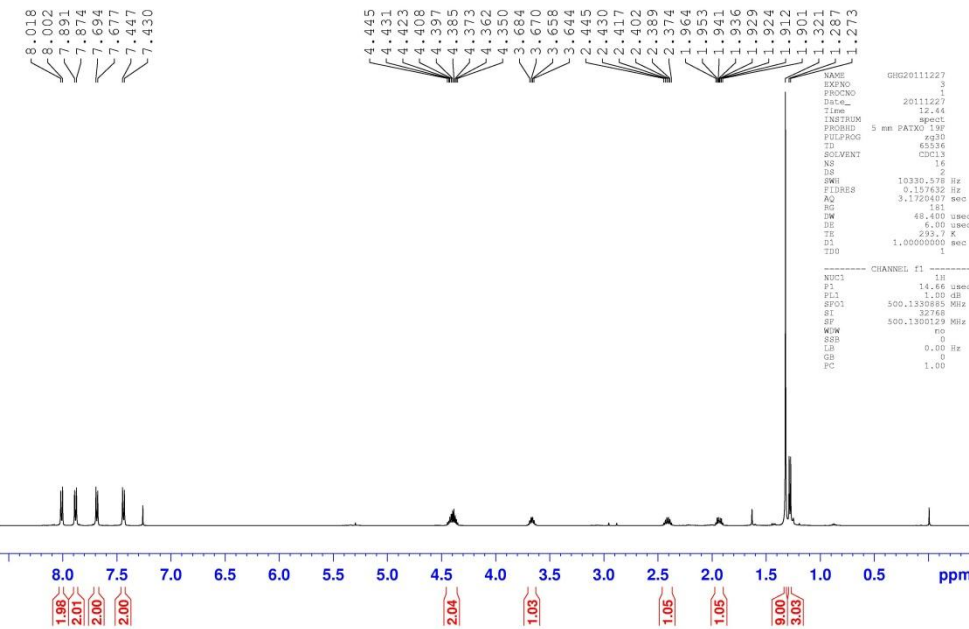
3-methyl-4-oxo-4-phenylbutyl 4-fluorobenzoate



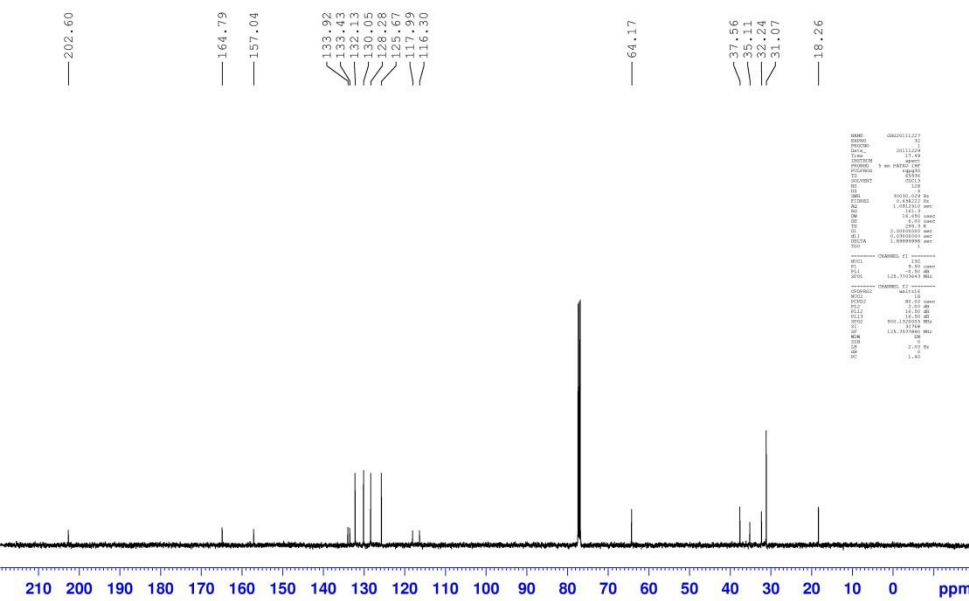


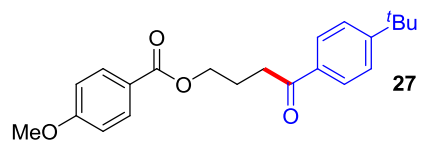


4-(4-(tert-butyl)phenyl)-3-methyl-4-oxobutyl 4-cyanobenzoate

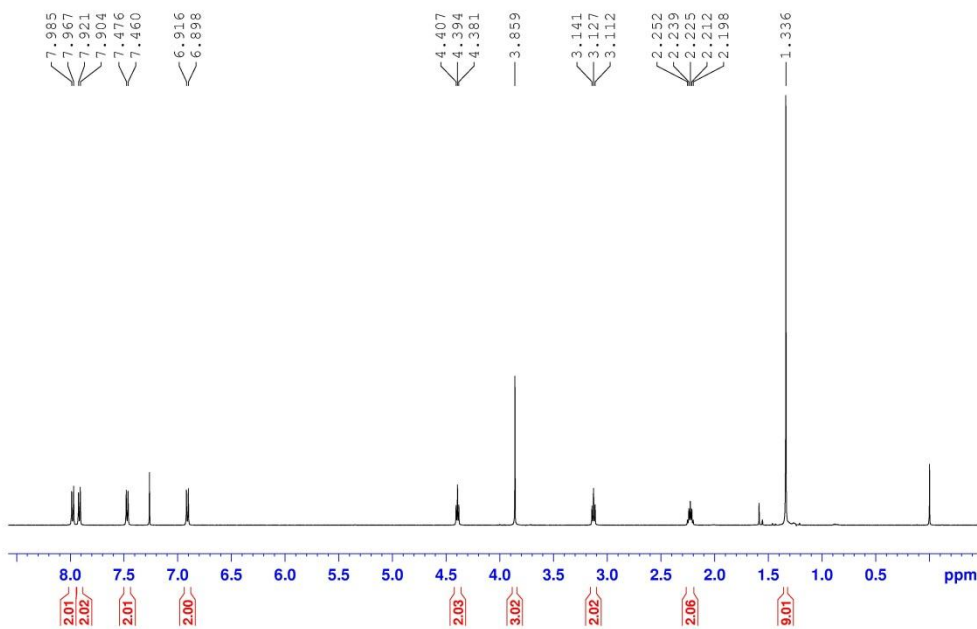


4-(4-(tert-butyl)phenyl)-3-methyl-4-oxobutyl 4-cyanobenzoate

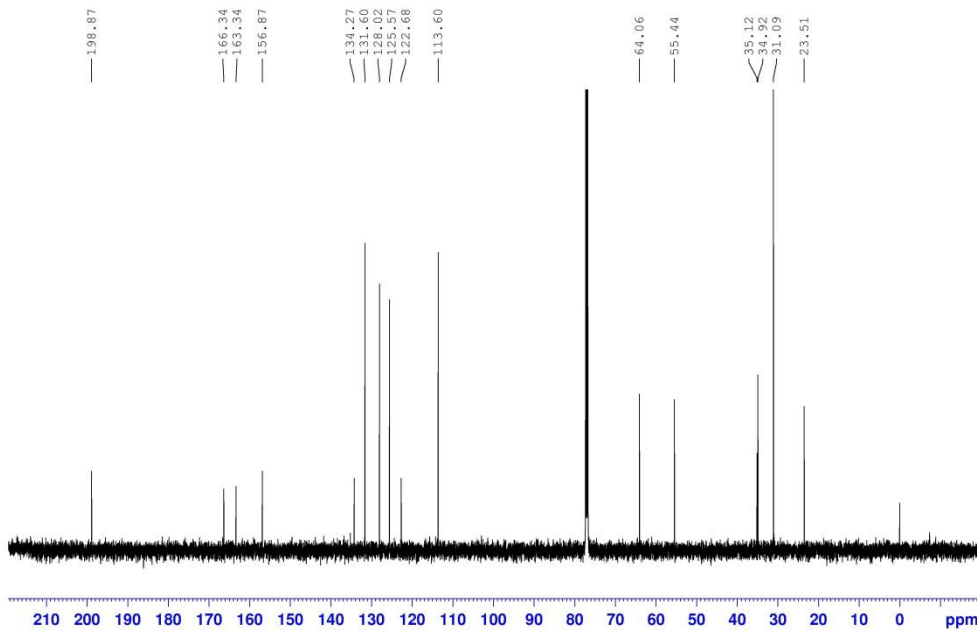


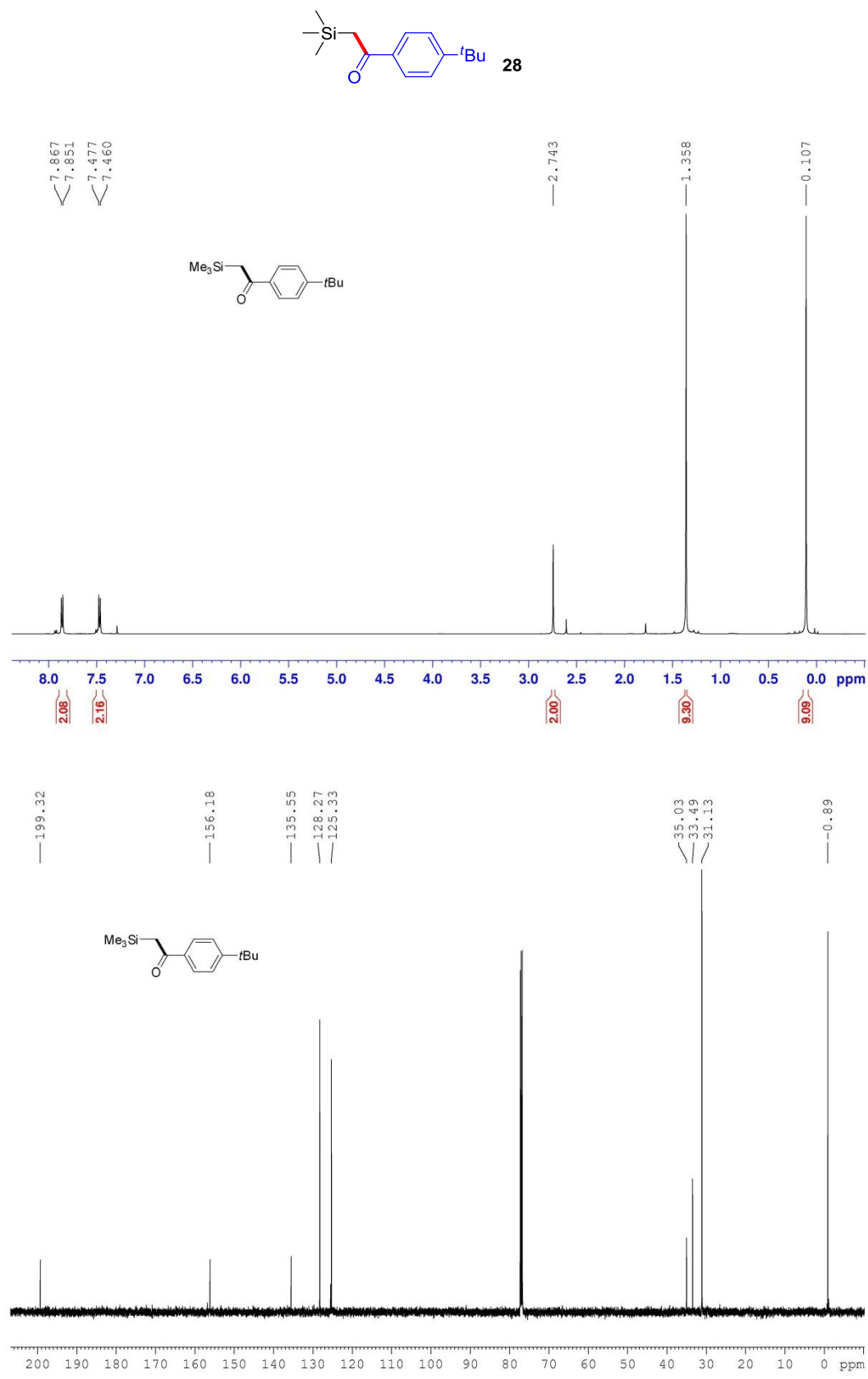


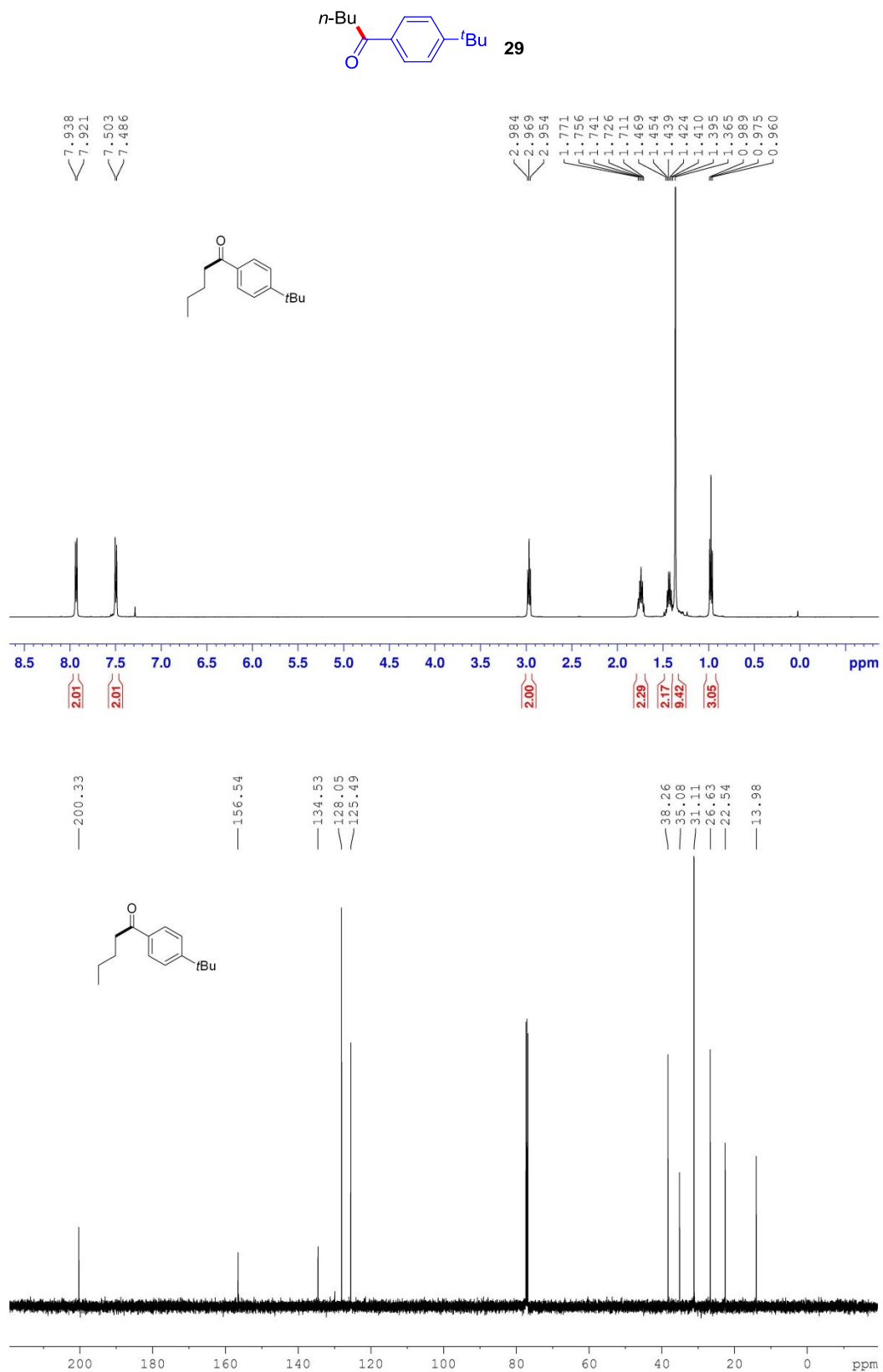
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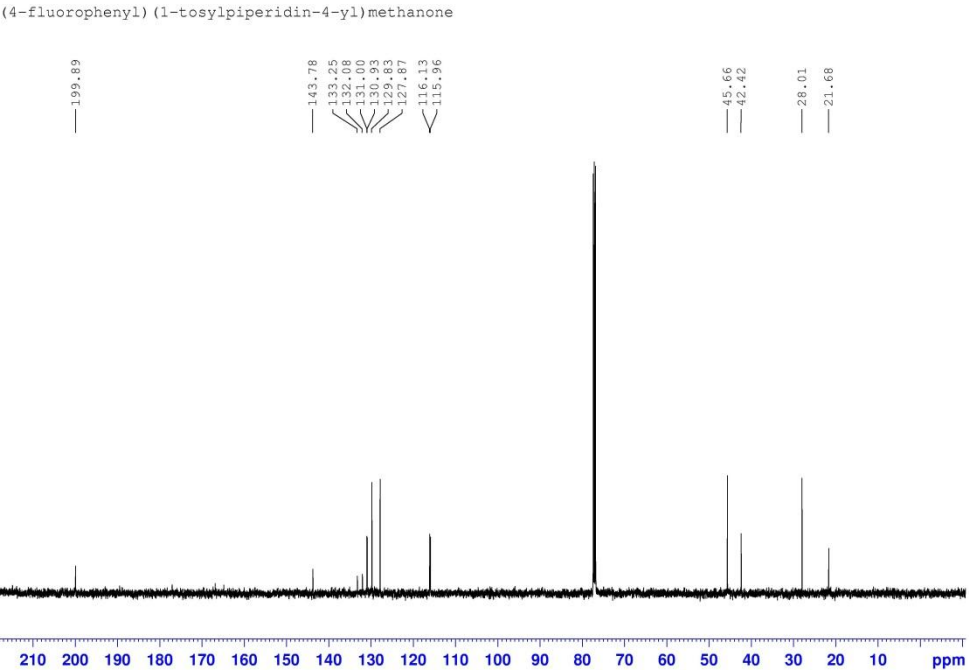
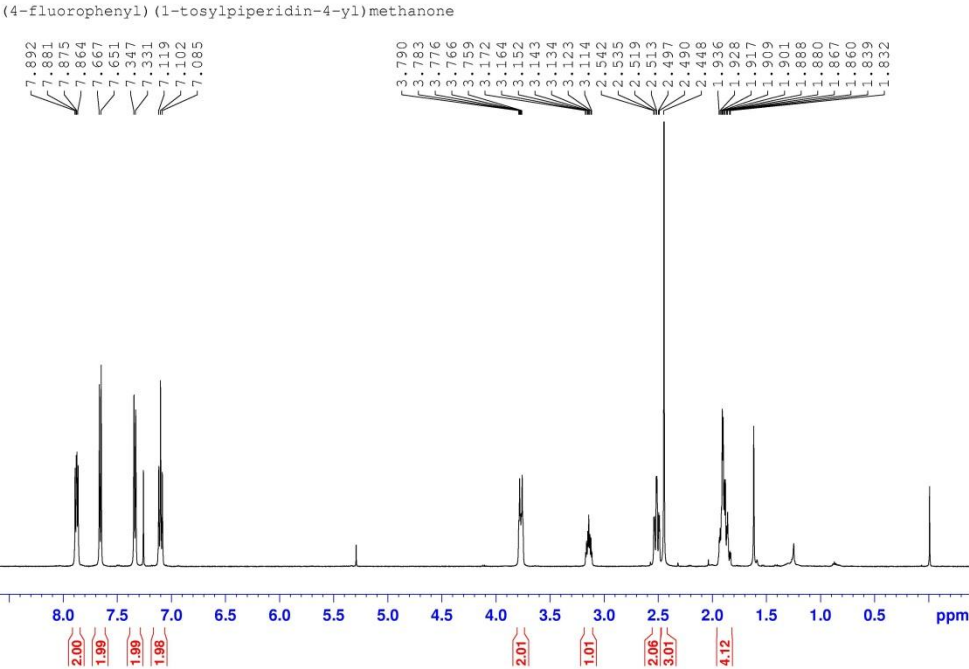
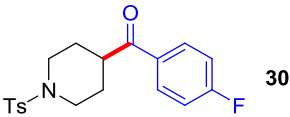


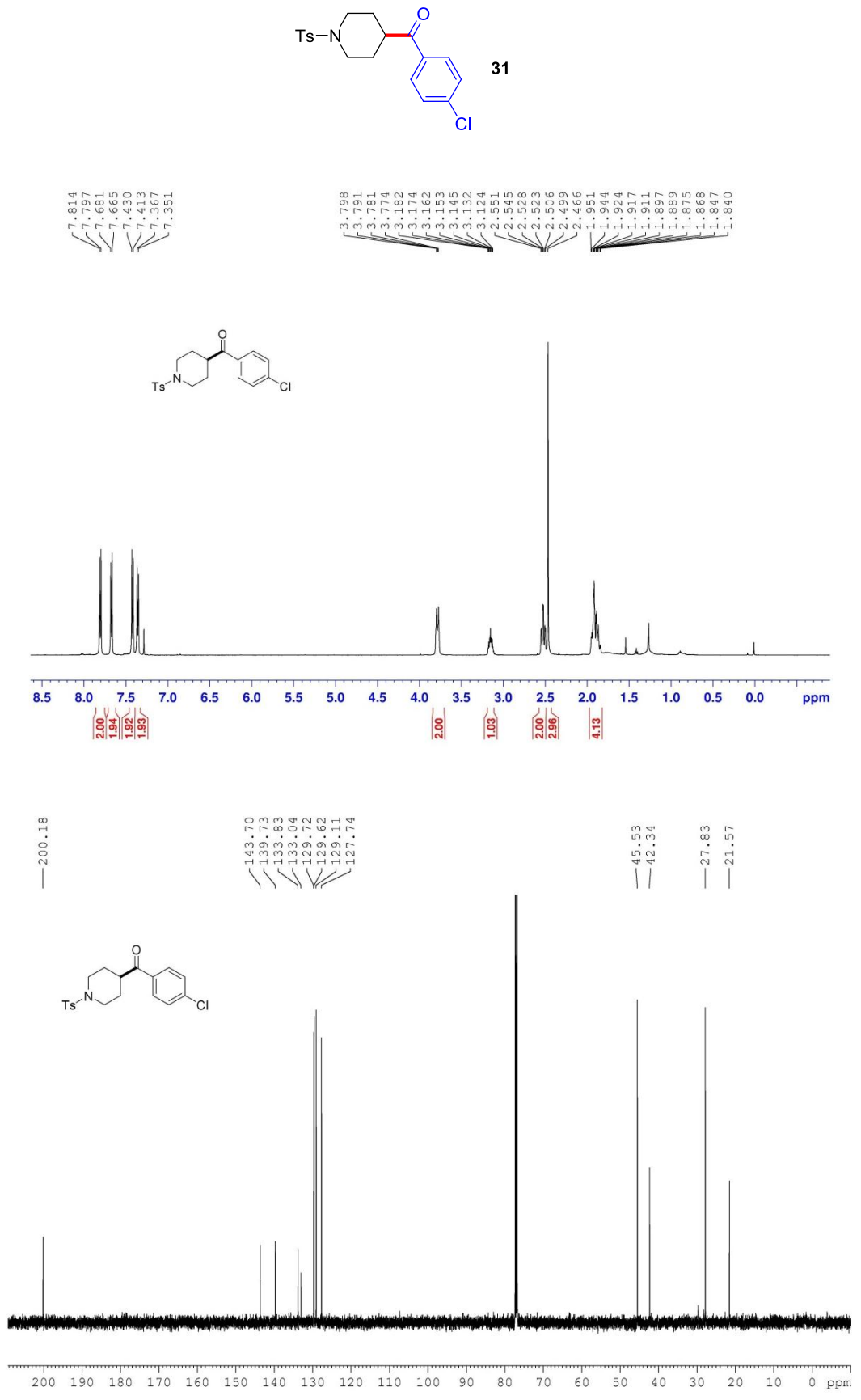
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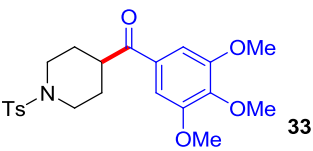




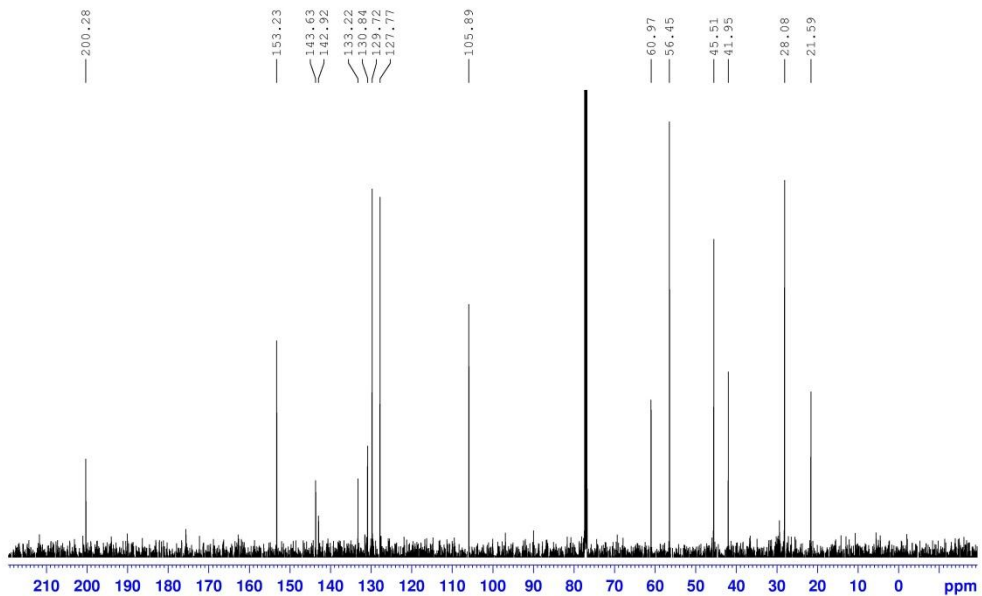
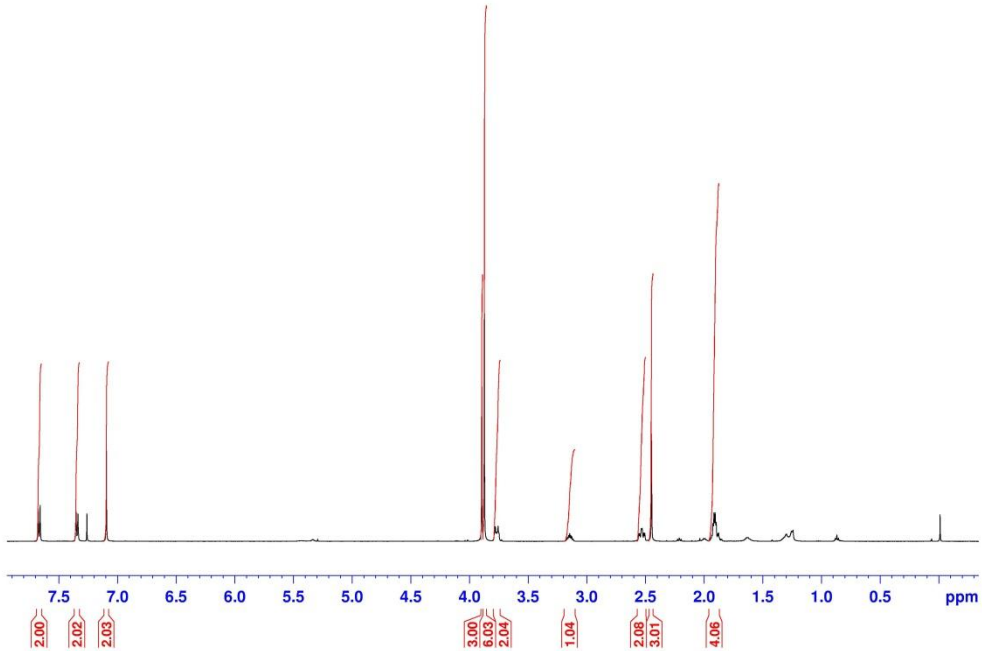


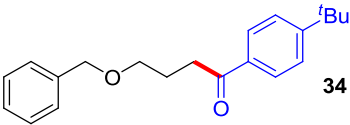




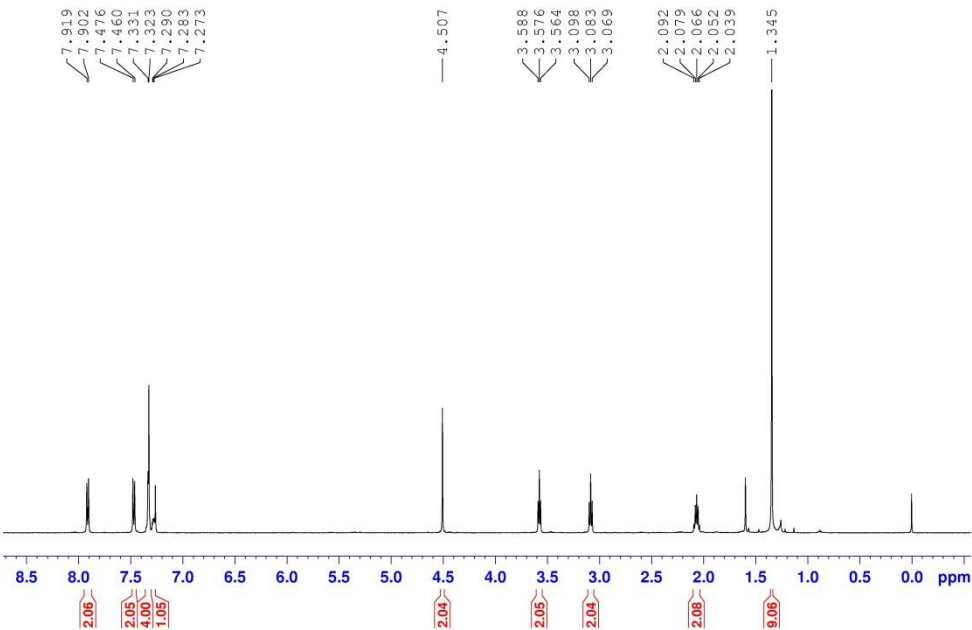


(1-tosylpiperidin-4-yl) (3,4,5-trimethoxyphenyl)methanone

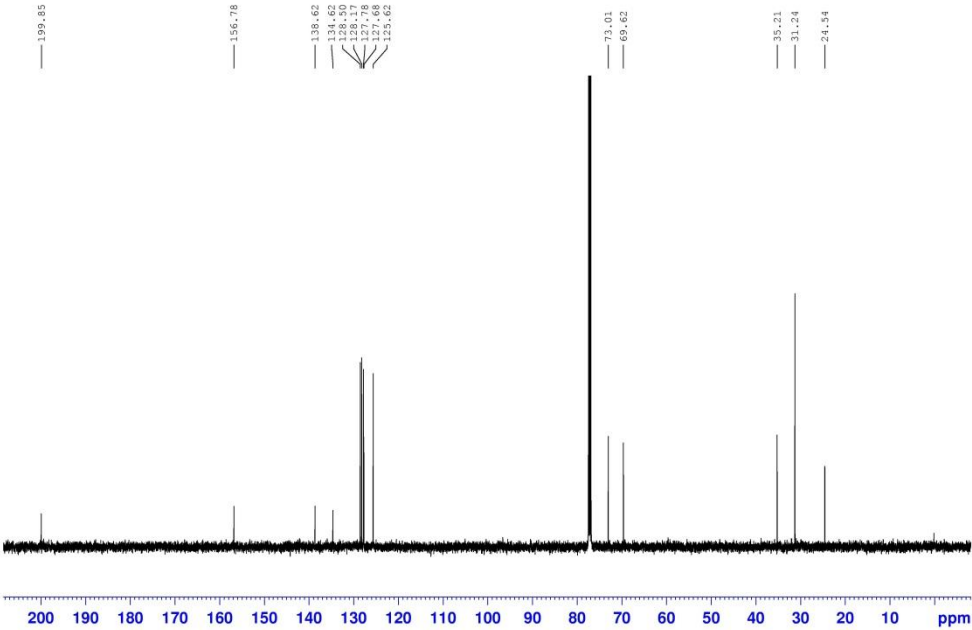


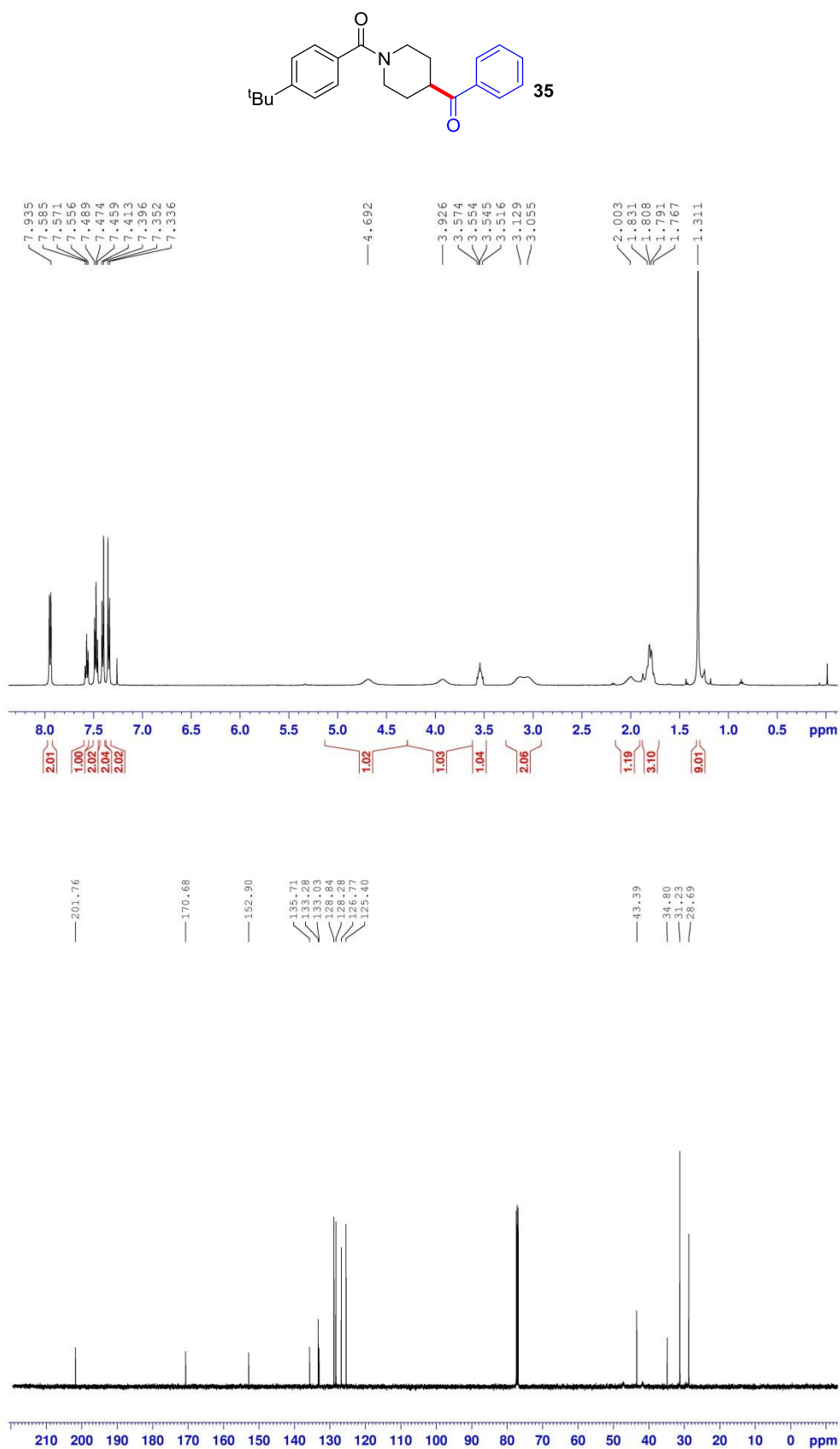


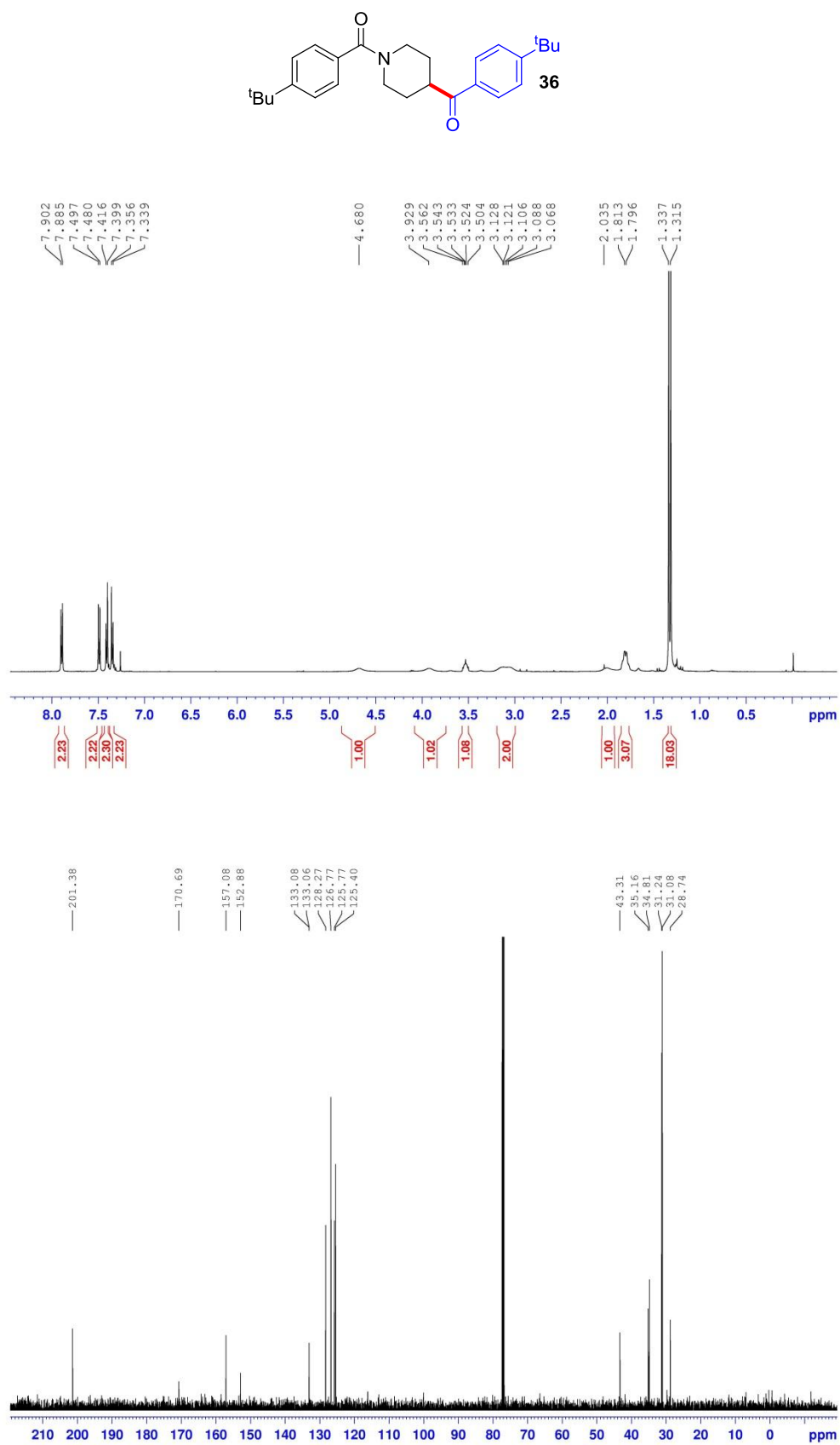
4-(benzyloxy)-1-(4-(tert-butyl)phenyl)butan-1-one

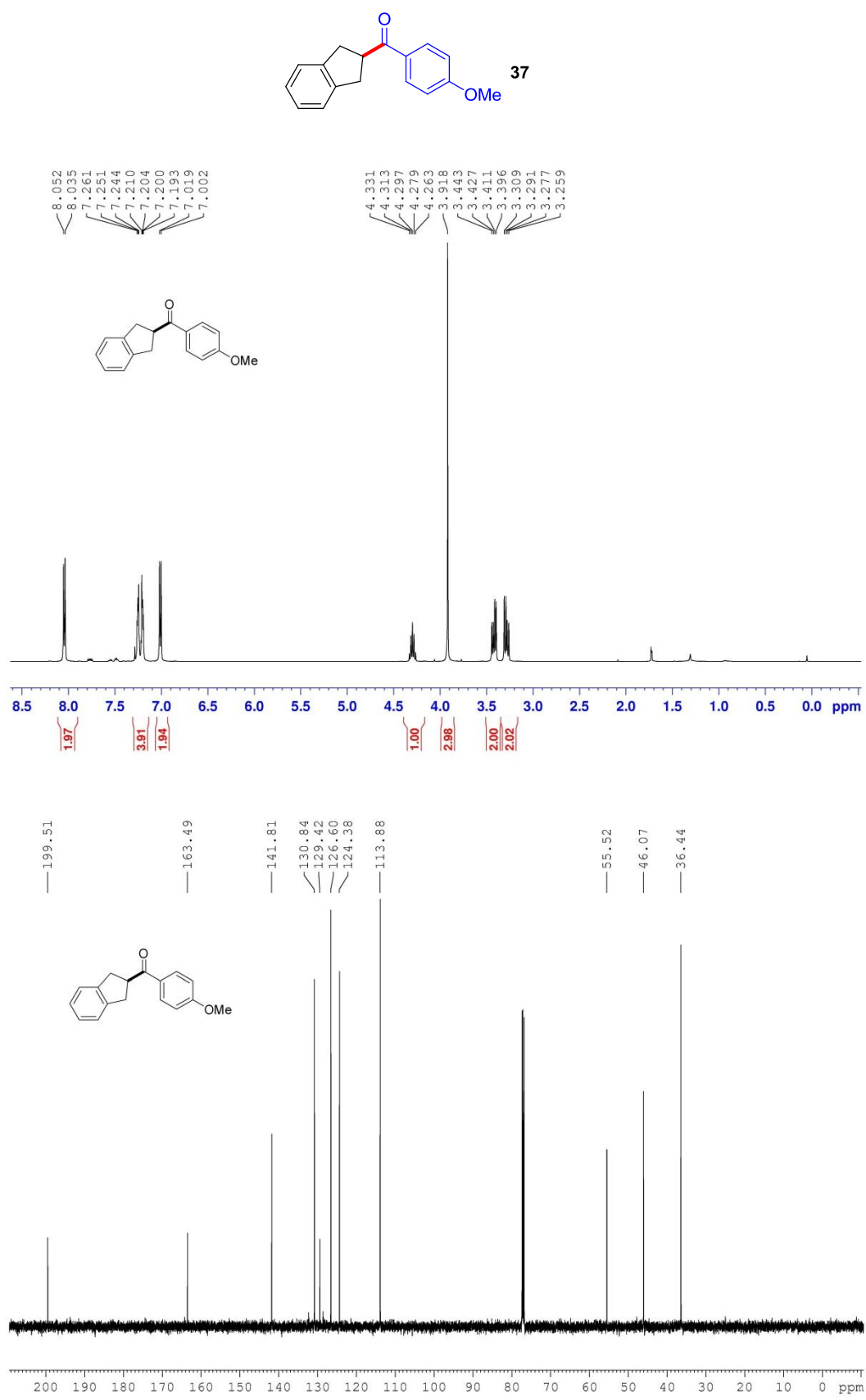


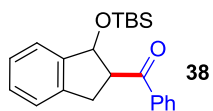
4-(benzyloxy)-1-(4-(tert-butyl)phenyl)butan-1-one



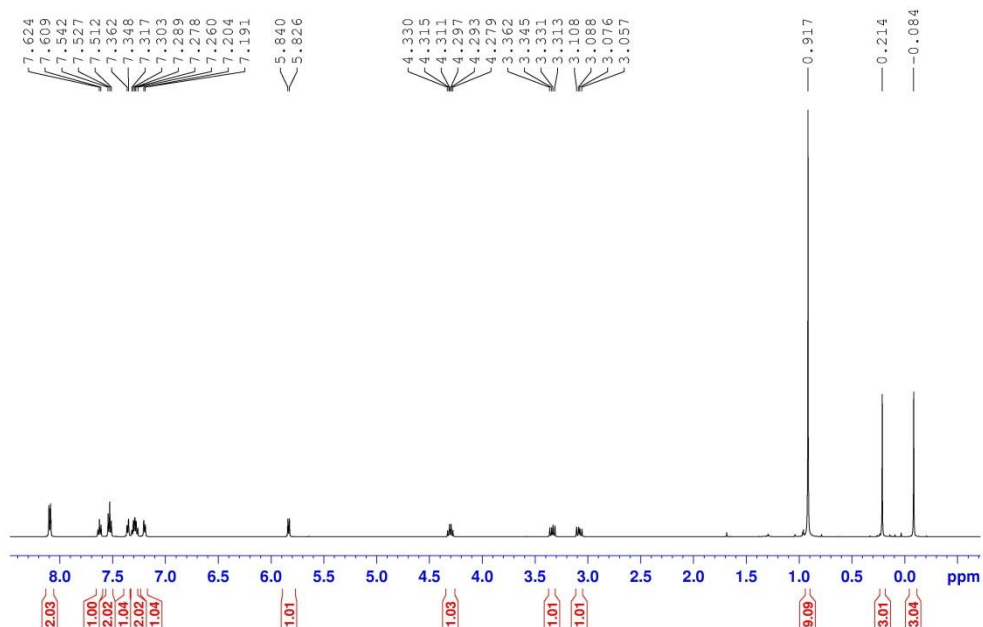




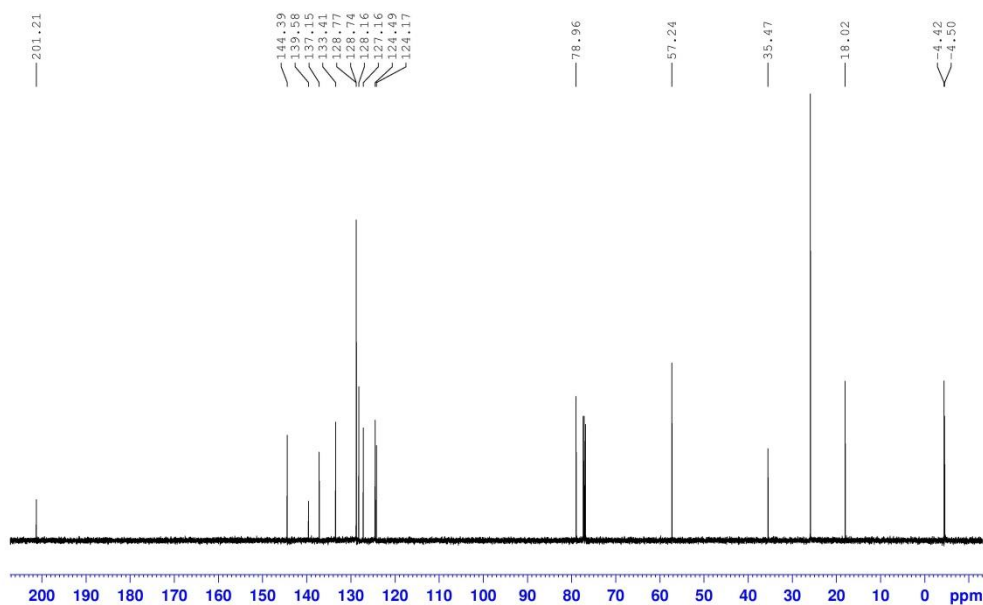


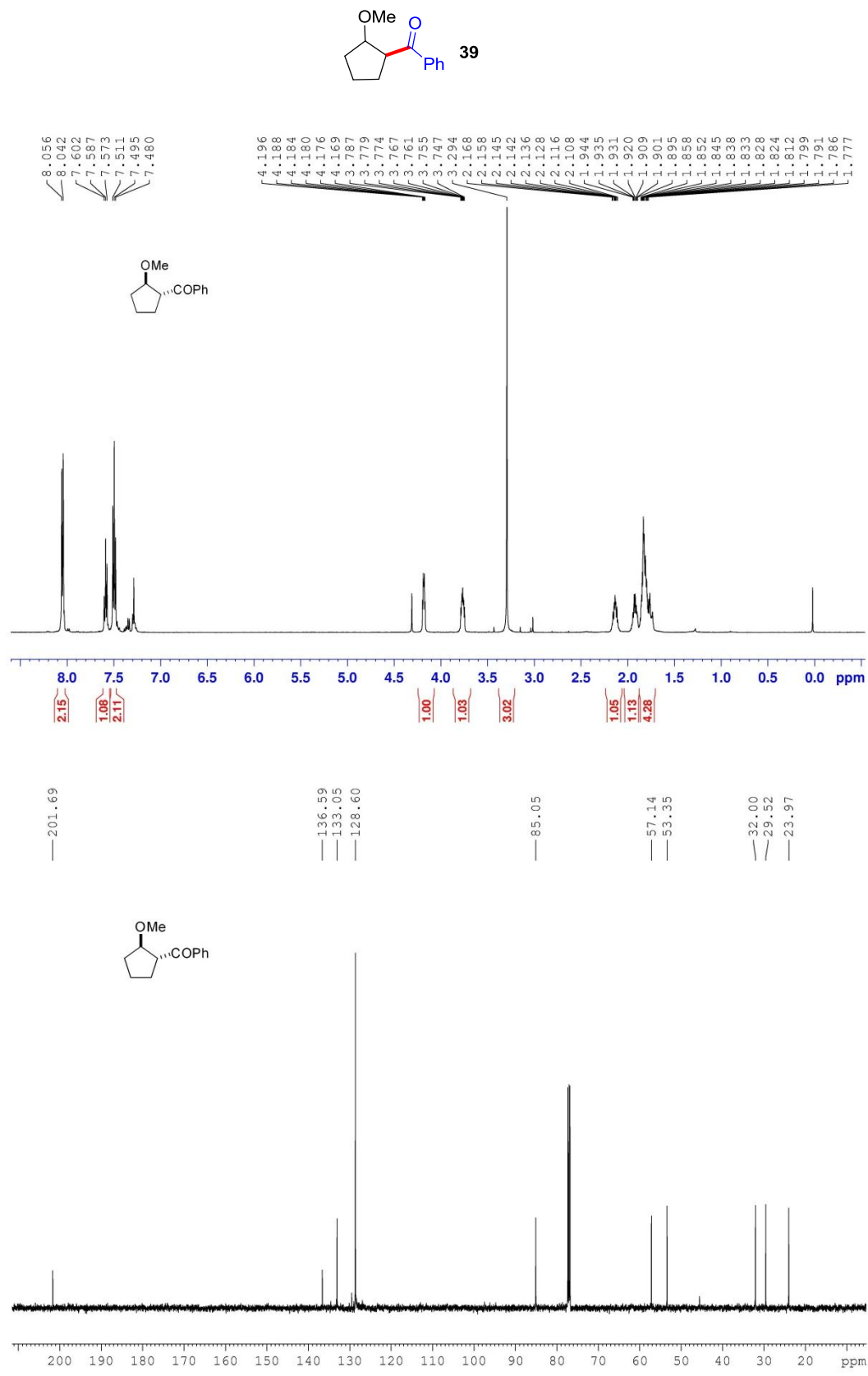


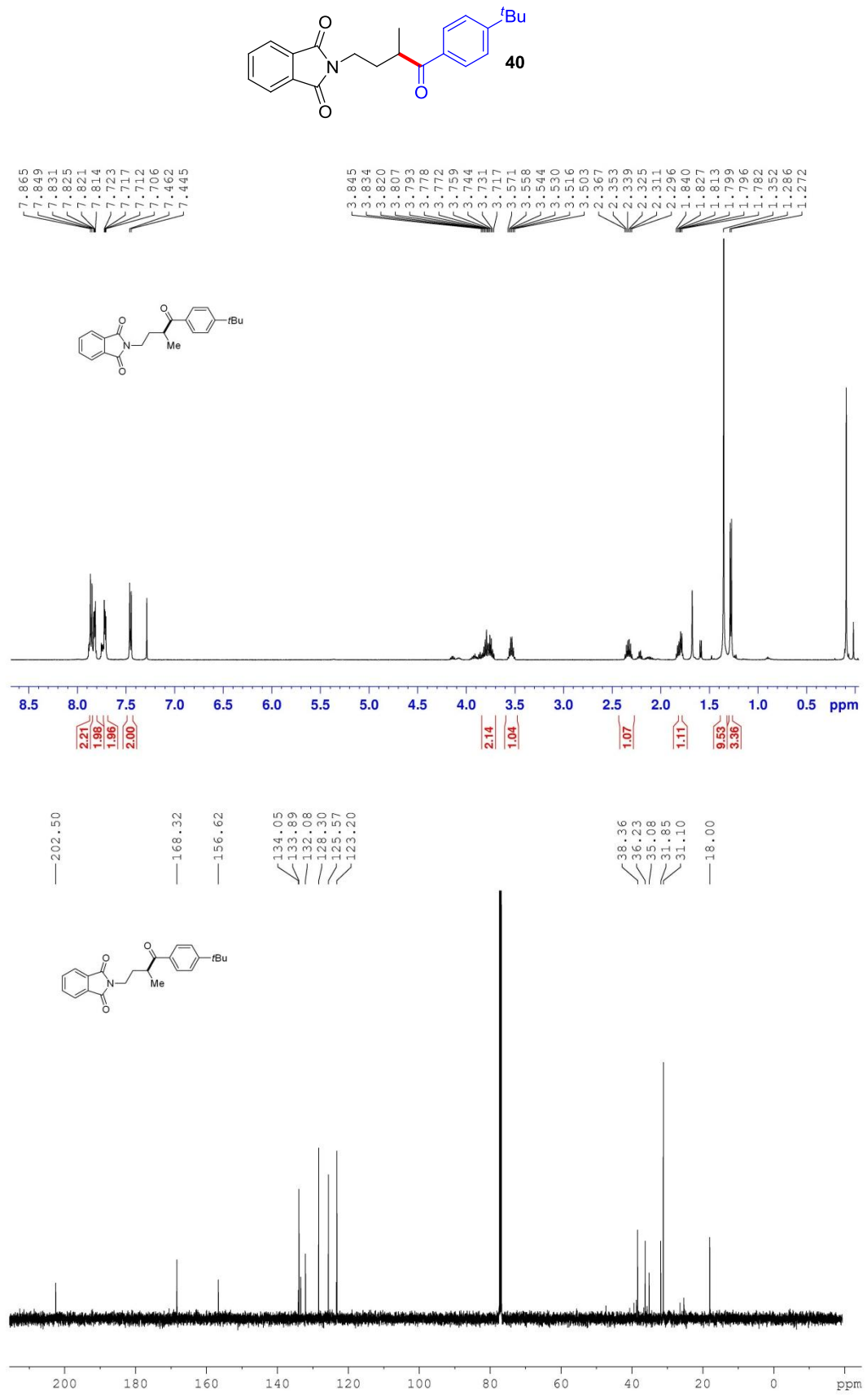
(1-((tert-butyldimethylsilyl)oxy)-2,3-dihydro-1H-inden-2-yl) (phenyl)methanone

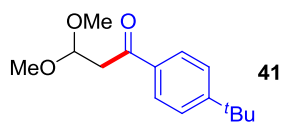


(1-((tert-butyldimethylsilyl)oxy)-2,3-dihydro-1H-inden-2-yl) (phenyl)methanone

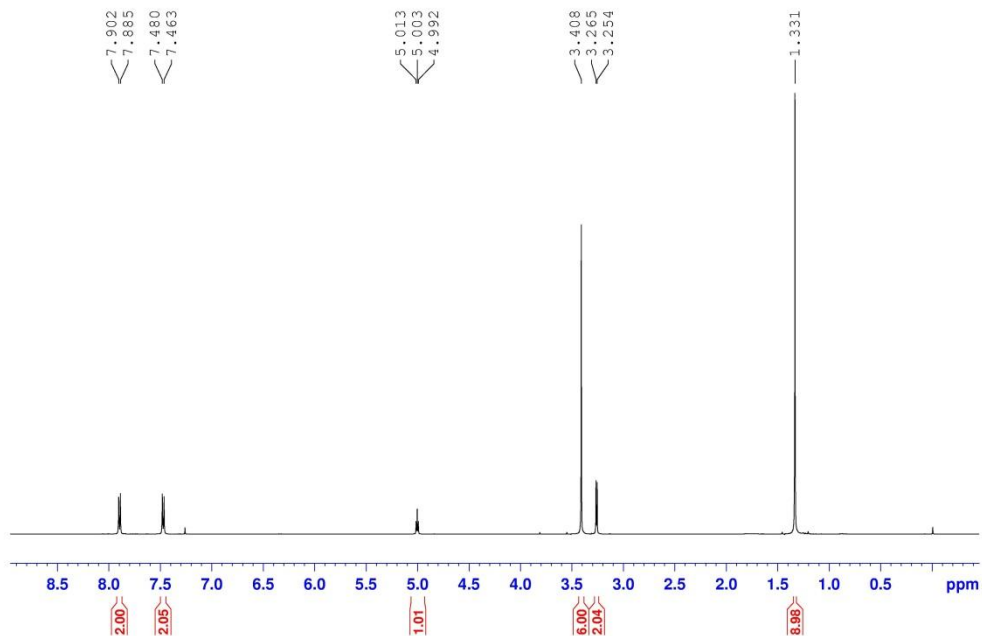








1-(4-(tert-butyl)phenyl)-3,3-dimethoxypropan-1-one



1-(4-(tert-butyl)phenyl)-3,3-dimethoxypropan-1-one

