2,2-Diiododimedone: a mild electrophilic iodinating agent for the selective synthesis of α-iodoketones from allylic alcohols

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Supporting Information

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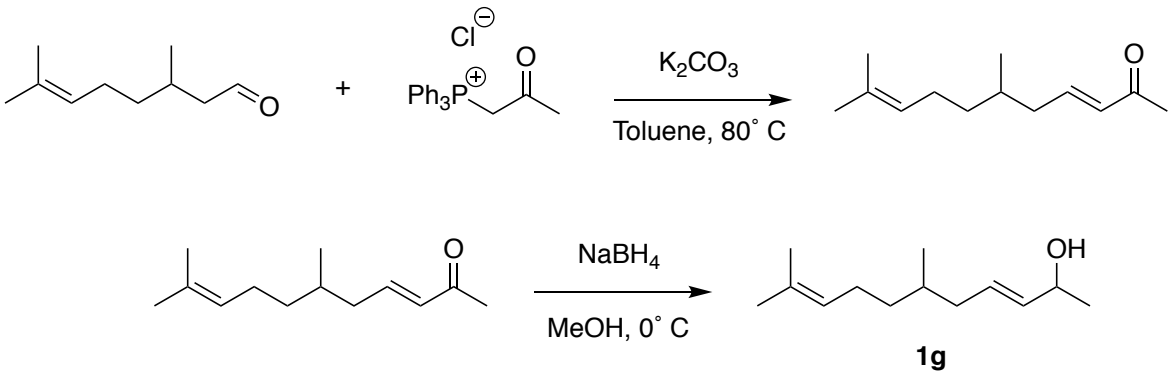
General Information:

All iridium-catalyzed reactions were carried out in closed glass-vials under an atmosphere of air. Air and moisture sensitive reactions were carried out in oven-dried glassware, under an atmosphere of dry nitrogen. Iridium-catalyzed reactions were run under air. Reagents were used as obtained from commercial suppliers without further purification. 2-methyltetrahydrofuran (2-MeTHF) was used as obtained from supplier (>97%). Flash chromatography was carried out on 60 Å (35-70 μm) silica gel (Acros Kieselgel 60) using pentane, mixtures pentane / EtOAc or mixtures pentane / Et_2O as eluent. Analytical TLC was performed on aluminum-backed plates (1.5 Å~ 5 cm) pre-coated (0.25 mm) with silica gel (Merck, Silica Gel 60 F254). Compounds were visualized by exposure to UV light or by dipping the plates in a solution of 5% $KMnO_4$ in 95% basified water (w/v). Melting points were recorded in a metal block and are uncorrected.

^1H NMR spectra were recorded at 400 MHz or 500 MHz; ^{13}C NMR spectra were recorded at 100 MHz or 125 MHz on a Bruker Advance spectrometer. ^1H and ^{13}C NMR chemical shifts (δ) are reported in ppm from tetramethylsilane using the residual solvent resonance ($CHCl_3$: δ_H 7.26 and $CDCl_3$: δ_C 77.0). Coupling constants (*J*) are given in Hz. High resolution mass spectra (HRMS) were recorded on Bruker microTOF ESI-TOF mass spectrometer. NMR yields and/or conversions were calculated using 1 equiv. of 2,3,5,6-tetrachloronitrobenzene as internal standard.

Anisole **4a**, *N,N*-dimethylaniline **4b**, oct-1-en-3-ol (**1a**), (*E*)-oct-2-en-1-ol (**1n**), cinnamyl alcohol (**1o**) and $[Cp^*IrCl_2]_2$ were used as obtained from suppliers without further purification. $[Cp^*Ir(H_2O)_3]SO_4$ and $[(Cp^*Ir)_2(OH)_3]OH \cdot 11H_2O$ were synthesized as described in the literature.[1] 1-Pivaloyl-1*H*-indole **4c**[2] and allylic alcohols **1b**,[3] **1c**,[3], **1d**,[4] **1e**,[3] **1f**,[5] **1h**,[6] **1i**,[7] **1j**,[8] **1k**,[9] **1l**,[9] **1m**,[10] **1p**,[9] **1q**,[9] **1r**,[9] were synthesized according to literature procedures.

Synthesis of (*E*)-6,10-dimethylundeca-3,9-dien-2-ol (1g):



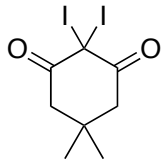
1g

(+/-)-Citronellal (5 g, 14 mmol, 1.2 equiv.), (2-oxopropyl)-triphenylphosponium chloride (2.44 g, 17 mmol, 1.5 equiv.) and K_2CO_3 (2.11 g, 11.75 mmol, 1 equiv.) were dissolved in dry toluene (100 mL) under inert atmosphere and stirred at 80 °C overnight. After that time, the reaction was quenched with aq. NH_4Cl (sat., 50 mL) and extracted with EtOAc (3 x 50 mL). The combined organic phases were dried with $MgSO_4$ and evaporated under vacuum. The resulting crude product was taken for the next reaction without further purification.

(*E*)-6,10-Dimethylundeca-3,9-dien-2-one (1.2 g, 6.18 mmol, 1 equiv.) was dissolved in dry MeOH (25 mL) under an inert atmosphere and cooled to 0 °C. $NaBH_4$ was then added (352 mg, 9.28 mmol, 1.5 equiv.) and the reaction was stirred for 2 h. The solvent was reduced under vacuum and the crude mixture was dissolved in EtOAc (25 mL). H_2O (25 mL) was added and the mixture was extracted with EtOAc (3 x 20 mL). The combined organic phases were dried over $MgSO_4$ and the solvent reduced under vacuum. The resulting product was purified by column chromatography using petroleum ether / EtOAc (9:1) mixture as eluent. Allylic alcohol **1g** was isolated as a colorless oil (780 mg, 68% yield).

^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers *ca.* 1:1) δ 5.64–5.56 (m, 1H(both diast.)), 5.53–5.47 (m, 1H(both diast.)), 5.10–5.06 (m, 1H(both diast.)), 4.26 (p, ^3J (^{1}H,^{1}H) = 6.5 Hz, 1H(both diast.)), 2.07–1.92 (m, 3H(both diast.)), 1.89–1.81 (m, 1H(both diast.)), 1.67 (s, 3H(both diast.)), 1.60 (s, 3H(both diast.)), 1.53–1.44 (m, 1H(both diast.)), 1.37–1.28 (m, 1H(both diast.)), 1.25 (d, ^3J (^{1}H,^{1}H) = 6.5 Hz, 3H(both diast.)), 1.19–1.09 (m, 1H(both diast.)), 0.86 (d, ^3J (^{1}H, ^{1}H) = 6.4 Hz, 3H(both diast.)); **^{13}C NMR (100 MHz, $CDCl_3$, mixture of diastereoisomers)** δ 135.5, 131.2, 129.50, 129.47, 124.8, 68.9, 39.5, 36.65, 36.60, 32.5, 25.7, 25.5, 23.5, 19.4, 19.3, 17.6; HRMS (ESI): m/z calcd for $[C_{13}H_{24}O+Na^+]$: 219.1719; found: 219.1711.

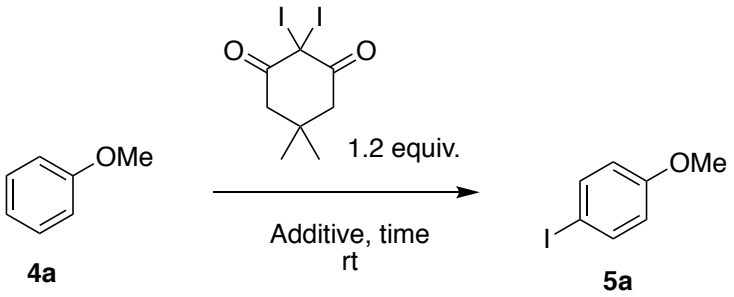
Synthesis and characterization of 2,2-diiodo-dimedone (2):



To a solution of dimedone (8.1 g, 54.89 mmol) in 1,4-dioxane (200 mL) in a 2 L bottom flask, a solution of iodine monochloride (19.4 g, 119.5 mmol, 2.1 equiv.) in 1,4-dioxane (100 mL) was added dropwise over 20 min. The reaction was stirred for 2 h at room temperature. Water was added (1 L) and a yellow-orange solid precipitated. The solid was filtered off and washed with a mixture of H_2O / 1,4-dioxane (4 : 1, 10 x 100 mL) (the solid should be washed until the mother liquids are colorless), following by H_2O (10 x 100 mL) in order to remove the traces of acids. The solid was dried under reduced pressure (0.2 mmHg), to obtain the title compound as a yellow solid (16.12 g, 41.13 mmol, 75%). The product is stable overnight at room temperature under an air atmosphere, however, it decomposes over the days. It should be kept at room temperature under vacuum, or in an atmosphere of air at −16 °C. m.p. 143-145 °C (decomp.).

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.08 (s, 4H), 0.97 (s, 6H); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 196.8, 45.9, 31.2, 27.3, 18.7; **HRMS (ESI)**: m/z calcd for $C_8H_{11}O_2I_2$: 392.8843 $[M+H]^+$; found: 392.8840.

Table S1. Optimization of the iodination of anisole by **2**.[a]

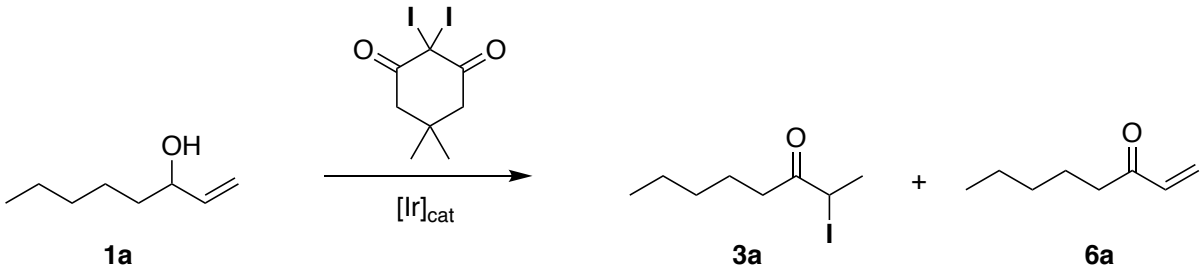


4a **5a**

Entry	Solvent	Additive (equiv.)	Time (h)	Yield [%][b]
1	Et_2O	-	16	<1
2	CH_2Cl_2	-	16	<1
3	THF	-	16	<1
4	trifluoroethanol	-	16	5
5	Hexafluoroisopropanol (HFIP)	-	16	14
6	HFIP	$BF_3{\cdot}Et_2O$ (1)	2	>99
7	HFIP	$FeCl_3$ (0.1)	2	>99
8[c]	HFIP	$FeCl_3{\cdot}H_2O$ (0.1)	2	>99(82)

[a] Reactions were performed on a 0.5 mmol scale. [**4a**] = 0.1 M. **4a** and the additive were dissolved in the corresponding solvent under argon. 2,2-Diiodo-dimedone (1.2 equiv.) were used. [b] Yield determined by ^{1}H NMR spectroscopy using 2,3,5,6-tetrachloronitrobenzene as internal standard, isolated yield in parentheses. [c] Under an atmosphere of air.

Table S2. Optimization of the iridium-catalyzed isomerization / iodination of oct-1-en-3-ol (**1a**) by **2**.[a]



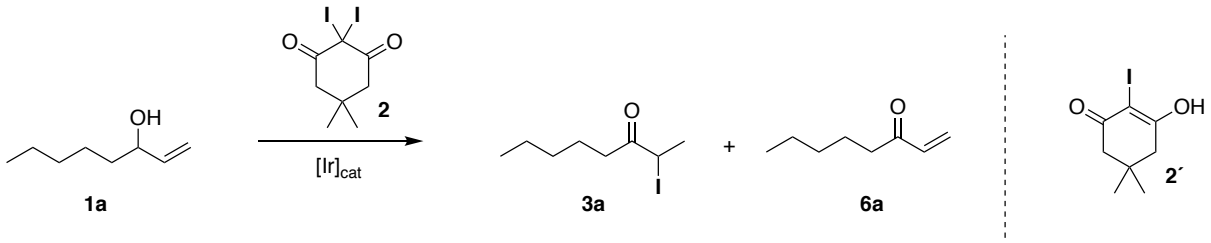
1a **3a** **6a**

Entry	Catalyst	Solvents (v/v)	Conversion [%][b]	3a/6a [%][b] [c]
1	$[IrCp^*Cl_2]_2$	Dioxane / H_2O 1:1	99	46/53
2	$[IrCp^*Cl_2]_2$	Dioxane / H_2O 5:1	23	10/13
3	$[IrCp^*Cl_2]_2$	THF / H_2O 1:1	86	58/28
4	$[IrCp^*Cl_2]_2$	THF / H_2O 5:1	51	42/9
5	$[IrCp^*Cl_2]_2$	Acetone / H_2O 1:1	>99	36/64
6	$[IrCp^*Cl_2]_2$	Acetone / H_2O 5:1	80	52/28
7	$[IrCp^*Cl_2]_2$	Acetone / H_2O 2:1	78	50/28
8	$[IrCp^*(H_2O)_3]SO_4$	Acetone / H_2O 2:1	87	59/28
9	$[(IrCp^*)_2(OH)_3]OH\ 11H_2O$	Acetone / H_2O 2:1	89	65/24
10	$[IrCp^*Cl_2]_2$	2-MeTHF / H_2O 1:1	96	85/11
11	$[IrCp^*(H_2O)_3]SO_4$	2-MeTHF / H_2O 1:1	99	93/6
12	$[(IrCp^*)_2(OH)_3]OH\ 11H_2O$	2-MeTHF / H_2O 1:1	>99	92/8
13	$[IrCp^*(H_2O)_3]SO_4$	2-MeTHF / H_2O 1:2	>99	91/9
14	$[(IrCp^*)_2(OH)_3]OH\ 11H_2O$	2-MeTHF / H_2O 1:2	>99	90/10
15	$[IrCp^*(H_2O)_3]SO_4$	2-MeTHF / H_2O 2:1	98	93/5
16	$[(IrCp^*)_2(OH)_3]OH\ 11H_2O$	2-MeTHF / H_2O 2:1	>99	94/6
17[d]	$[IrCp^*(H_2O)_3]SO_4$	2-MeTHF / H_2O 2:1	86	79/7/-
18[d]	**$[(IrCp^*)_2(OH)_3]OH\ 11H_2O$**	**2-MeTHF / H_2O 2:1**	**92**	**88/4/-**
19[e]	$[IrCp^*(H_2O)_3]SO_4$	2-MeTHF / H_2O 2:1	70	69/1/-
20[f]	$[(IrCp^*)_2(OH)_3]OH\ 11H_2O$	2-MeTHF / H_2O 2:1	27	27/-/-
21	$[IrCp^*(H_2O)_3]SO_4$	2-MeTHF / H_2O 5:1	95	91/4
22	$[(IrCp^*)_2(OH)_3]OH\ 11H_2O$	2MeTHF / H_2O 5:1	99	95/4
23	$[IrCp^*(H_2O)_3]SO_4$	2MeTHF / H_2O 20:1	94	89/5
24	$[IrCp^*(H_2O)_3]SO_4$	2-MeTHF / H_2O 20:1	97	93/4
25	$[IrCp^*(H_2O)_3]SO_4$	2-MeTHF	87	76/11
26	$[(IrCp^*)_2(OH)_3]OH\ 11H_2O$	2-MeTHF	66	54/12

[a] Unless otherwise noted: The reaction were run on a 0.5 mmol scale of **1a**; [**1a**] = 0.1 M; catalyst loading: 2 mol% of Ir; room temperature; 1.2 equiv. of 2,2-diiododimedone were used; Reaction time 16 h. [b] Determined by ^1H NMR spectroscopy using 2,3,5,6-tetrachloronitrobenzene as internal standard after quenching with an aqueous solution of $Na_2S_2O_3$. [c] Octan-3-one was not formed. [d] 1 mol% of Ir was used. [e] 0.6 equiv. of **2**. [f] 0.2 equiv. of **2**.

The solvent mixture is a critical parameter in this reaction. The mixture of solvents 2-MeTHF / H_2O was shown to be essential to afford the corresponding α-iodoketones in good yields while minimizing the amount of byproduct **6a**. The replacement of 2-MeTHF by other organic solvents (i.e. dioxane, THF or acetone) failed to provide the product in good yields and the amount of **6a** increased (entries 1-9). This could be due to the formation of a biphasic system using the mixture 2-MeTHF / H_2O, where acid species formed by the decomposition of 2,2-diiododimedone stay in the aqueous phase and the allylic alcohol in the organic phase. Over the different mixtures of 2-MeTHF / H_2O evaluated, the optimal was found to be 2:1 (entry 18).

Table S3. Control experiments of the iridium-catalyzed isomerization / iodination of oct-1-en-3-ol (**1a**) by **2**.[a]



Entry	Catalyst	Allylic alcohol	2	1a/2/3a (%)[b]	6a/2´ (%)[b]
1	Yes	Yes	No	>95/-/-	-/-
2	Yes	No	Yes	-/38/-	-/43
3	No	Yes	Yes	96/84/-	2/10
4[c]	Yes	Yes	Yes	6/15/87	7/78
5	Yes	Yes	Yes	-/nd/94	6/nd

[a] Unless otherwise noted: The reaction were run on a 0.5 mmol scale of **1a**; [**1a**] = 0.1 M; catalyst loading: 2 mol% of Ir; room temperature; 1.2 equiv. of 2,2-diiodo-dimedone were used; Reaction time 16 h. [b] Determined by ^{1}H NMR spectroscopy using 2,3,5,6-tetrachloronitrobenzene as internal standard without quenching with an aqueous solution of $Na_2S_2O_3$. [c] The catalyst and **2** were stirred for 4 h before the addition of the allylic alcohol. nd = not determined.

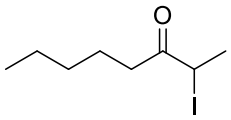
$[(IrCp^*)_2(OH)_3]OH\ 11H_2O$ is not able to react with allylic alcohol **1a** under the reaction conditions in the absence of iodinating agent **2** (entry 1). Entries 2 and 4 suggests that the decomposition of **2** is mediated by $[(IrCp^*)_2(OH)_3]OH\ 11H_2O$. Allylic alcohol **1a** does not react with the iodinating agent in the absence of the catalyst (entry 3). Entry 5 shows the optimal conditions for comparison purposes.

General procedure for the iridium-catalyzed tandem isomerization / iodination of allylic alcohols:

2,2-Diiodo-dimedone (**2**) (235 mg, 0.6 mmol, 1.2 equiv.) was dissolved in 2-MeTHF (3.3 mL) and H_2O (1.65 mL). The allylic alcohol (**1**) (0.5 mmol, 1 equiv.) and $[(IrCp^*)_2(OH)_3]OH\ 11H_2O$ (4.6 mg, 0.005 mmol, 1 mol%) were added to the mixture and the vial was closed. The reaction was stirred at room temperature for 16 h and subsequently quenched with an aqueous solution of $Na_2S_2O_3$ (1.5 mL) and extracted with Et_2O (3 x 2 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was reduced under pressure. The resulting crude was purified by column chromatography using petroleum ether / EtOAc (99:1) mixture as eluent.

Synthesis and characterization of α-iodoketones 3a-m and α-iodoaldehydes 3n-r:

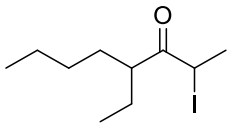
2-iodooctan-3-one (3a)



The title compound was prepared from 1-Octenol-3-ol (144 mg, 1 mmol) according to the general procedure. Purification by column chromatography (SiO_2; pentane / EtOAc, 99:1) afforded **3a** as a colorless oil (195 mg, 78%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.61 (q, $^3J(^1H,^1H)$ = 6.8 Hz, 1H), 2.89-2.83 (m, 1H), 2.63-2.58 (m, 1H), 1.88 (d, $^3J(^1H,^1H)$ = 6.8 Hz, 3H), 1.66-1.60 (m, 2H), 1.35-1.26 (m, 4H), 0.89 (t, $^3J(^1H,^1H)$ = 6.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 205.4, 38.6, 31.3, 24.9, 24.3, 22.5, 21.8, 14.0. **HRMS (ESI):** m/z calcd for $C_8H_{15}OI+Na^+$: 277.0060 $[M+Na]^+$; found: 277.0059.

4-ethyl-2-iodooctan-3-one (3b)

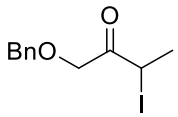


The title compound was prepared from 4-ethyloct-1-en-3-ol (156 mg, 1 mmol) according to the general procedure. Purification by column chromatography (SiO_2; pentane / EtOAc, 99:1) afforded **3b** as a colorless oil (190 mg, 68%).

^{1}H NMR (400 MHz, $CDCl_3$, mixture of 2 diastereoisomers (d.r. = 1:1.3)): δ 4.67 (q, $^3J(^1H,^1H)$ = 6.8 Hz, 1H (minor)), 4.66 ((q, $^3J(^1H,^1H)$ = 6.8 Hz, 1H (major)), 2.84–2.75 (m, 1H(both diast.)), 1.88 (d, $^3J(^1H,^1H)$ = 6.8 Hz, 3H (major)), 1.87 (d, $^3J(^1H,^1H)$ = 6.8 Hz, 3H (minor)), 1.80–1.70 (m, 1H(both diast.)), 1.58–1.18 (m, 7H(both diast.)), 0.91–0.84 (m, 6H(both diast.)). **^{13}C NMR (100 MHz, $CDCl_3$, mixture of 2 diastereoisomers (d.r. = 1:1.3)):** δ 207.75, 207.72, 50.7, 50.3, 33.1, 30.2, 29.7, 29.6,

26.5, 25.5, 25.4, 24.2, 23.0, 22.9, 21.7, 21.6, 14.1, 14.0, 12.2, 11.7. **HRMS (ESI):** m/z calcd for $C_{10}H_{19}IO+Na^+$: 305.0373 $[M+Na]^+$; found: 305.0362.

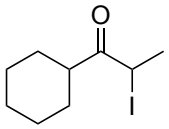
4-ethyl-2-iodooctan-3-one (3c)



The title compound was prepared from 1-(benzyloxy)but-3-en-2-ol (178 mg, 1 mmol) according to the general procedure. Purification by column chromatography (SiO_2; pentane / EtOAc, 99:1) afforded **3c** as a colorless oil (225 mg, 74%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.30 (m, 5H), 4.95 (q, $^3J(^1H,^1H)$ = 6.9 Hz, 1H), 4.60 (s, 2H), 4.48 (d, $^1J(^1H,^1H)$ = 16.6 Hz, 1H), 4.31 (d, $^1J(^1H,^1H)$ = 16.6 Hz, 1H), 1.88 (d, $^3J(^1H,^1H)$ = 6.9 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 203.3, 137.0, 128.6, 128.2, 128.1, 73.7, 71.6, 20.8, 18.8. **HRMS (ESI):** m/z calcd for $C_{11}H_{13}IO_2+Na^+$: 326.9852 $[M+Na]^+$; found: 326.9851.

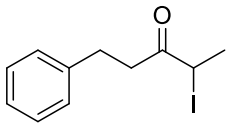
1-cyclohexyl-2-iodopropan-1-one (3d)



The title compound was prepared from 1-cyclohexylprop-2-en-1-ol (35 mg, 0.2 mmol) according to the general procedure. Purification by column chromatography (SiO_2; pentane / EtOAc, 99:1) gave **3d** as an oil (32 mg, 48%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.72 (q, $^3J(^1H,^1H)$ = 6.8 Hz, 1H), 2.83-2.76 (m, 1H), 1.87 (d, $^3J(^1H,^1H)$ = 6.8 Hz, 3H), 1.76-1.72 (m, 5H), 1.35-1.17 (m, 5H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 207.9, 47.7, 30.6, 29.2, 26.1, 25.7, 25.4, 23.7, 21.8. **HRMS (ESI):** m/z calcd for $C_9H_{15}IO+Na^+$: 289.0060. $[M+Na]^+$; found: 289.0037.

4-iodo-1-phenylpentan-3-one (3e)

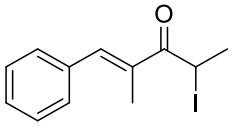


The title compound was prepared from 5-phenylpent-1-en-3-ol (162 mg, 1 mmol) according to the general procedure. Purification by column chromatography (SiO_2; pentane / EtOAc, 99:1) afforded **3e** as a yellow oil (188 mg, 67%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.25 (m, 2H), 7.23–7.19 (m, 3H), 4.53 (q, $^3J(^1H,^1H)$ = 6.8 Hz, 1H), 3.25-3.18 (m, 1H), 2.99-2.86 (m, 3H), 1.85 (d, $^3J(^1H,^1H)$ = 6.8 Hz, 3H). **^{13}C NMR (100 MHz,**

$CDCl_3$): δ 204.4, 140.7, 128.7, 128.5, 126.4, 40.4, 30.9, 24.9, 21.6. **HRMS (ESI):** m/z calcd for $C_{11}H_{13}IO+Na^+$: 310.9903 $[M+Na]^+$; found: 310.9892.

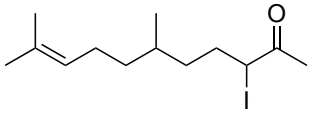
(*E*)-4-iodo-2-methyl-1-phenylpent-1-en-3-one (3f)



The title compound was prepared from (*E*)-2-methyl-1-phenylpenta-1,4-dien-3-ol (174 mg, 1 mmol) according to the general procedure. Purification by column chromatography (SiO_2; pentane / EtOAc, 99:1) afforded **3f** as a yellow solid (190 mg, 64%). m.p. 70-72 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, $^4J(^1H,^1H)$ = 1.5 Hz, 1H), 7.45–7.40 (m, 4H), 7.38–7.34 (m, 1H), 5.40 (q, $^3J(^1H,^1H)$ = 7 Hz, 1H), 2.15 (d, $^4J(^1H,^1H)$ = 1.5 Hz, 3H), 2.02 (d, $^3J(^1H,^1H)$ = 7 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 197.2, 138.8, 135.6, 133.9, 130.0, 128.9, 128.6, 22.7, 17.9, 14.1. **HRMS (ESI):** m/z calcd for $C_{12}H_{13}IO+Na^+$: 322.9912 $[M+Na]^+$; found: 322.9903.

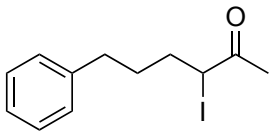
3-iodo-6,10-dimethylundec-9-en-2-one (3g)



The title compound was prepared from (*E*)-6,10-dimethylundeca-3,9-dien-2-ol (39 mg, 0.2 mmol) according to the general procedure. Purification by column chromatography (SiO_2; pentane / EtOAc, 99:1) gave **3g** as an oil (22 mg, 34%).

^{1}H NMR (400 MHz, $CDCl_3$, mixture of 2 diastereoisomers (d.r. = 1:1)): δ 5.10-5.06 (m, 1H(both diast.)), 4.41 (t, $^3J(^1H,^1H)$ = 7.5 Hz, 1H(both diast.)), 2.41 (s, 3H(both diast.)), 2.04-1.86 (m, 4H(both diast.)), 1.68 (s, 3H(both diast.)), 1.60 (s, 3H(both diast.)), 1.47-1.10 (m, 5H(both diast.)), 0.90-0.87 (m, 3H(both diast.)). **^{13}C NMR (100 MHz, $CDCl_3$, mixture of 2 diastereoisomers (d.r. = 1:1)):** δ 202.63, 202.61, 131.4, 124.6, 36.9, 36.7, 36.6, 36.4, 33.9, 33.7, 32.4, 32.2, 32.1, 25.97, 25.95, 25.8, 25.5, 25.4, 19.6, 19.4, 17.7. **HRMS (ESI):** m/z calcd for $C_{13}H_{23}IO+Na^+$: 345.0686. $[M+Na]^+$; found: 345.0689.

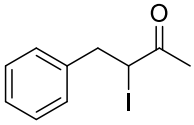
3-iodo-6-phenylhexan-2-one (3h)



The title compound was prepared from (*E*)-6-phenylhex-3-en-2-ol (176 nmg, 1 mmol) according to the general procedure. Purification by column chromatography (SiO_2; pentane / EtOAc, 99:1) afforded **3h** as a colorless oil (199 mg, 66%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.26 (m, 2H), 7.21–7.16 (m, 3H), 4.45 (t, $^3J(^1H,^1H)$ = 7.4 Hz, 1H), 2.69–2.61 (m, 2H), 2.38 (s, 3H), 1.99–1.94 (m, 2H), 1.83–1.74 (m, 1H), 1.67–1.58 (m, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 202.5, 141.5, 128.6, 128.5, 126.2, 35.2, 34.1, 33.1, 31.2, 26.1. **HRMS (ESI):** m/z calcd for $C_{12}H_{15}IO+Na^+$: 325.0060 [*M*+Na]$^+$; found: 325.0070.

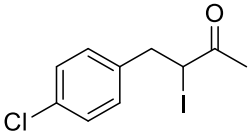
3-iodo-4-phenylbutan-2-one (3i)



The title compound was prepared from (*E*)-4-phenylbut-3-en-2-ol (148 mg, 1 mmol) according to the general procedure. Purification by column chromatography (SiO_2; pentane / EtOAc, 99:1) afforded **3i** as a yellow oil (125mg, 55%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.25 (m, 3H), 7.19–7.17 (m, 2H), 4.72-4.68 (m, 1H), 3.48-3.43 (m, 1H), 3.22-3.17 (m, 1H), 2.36 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 202.1, 138.9, 129.1, 128.8, 127.2, 40.8, 32.3, 26.8. **HRMS (ESI):** m/z calcd for $C_{10}H_{11}IO+Na^+$: 296.9747 [*M*+Na]$^+$; found:297.9745.

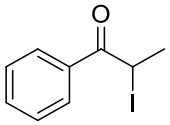
4-(4-chlorophenyl)-3-iodobutan-2-one (3j)



The title compound was prepared from (*E*)-4-(4-chlorophenyl)but-3-en-2-ol (180 mg, 1 mmol) according to the general procedure. Purification by column chromatography (SiO_2; pentane / EtOAc, 99:1) afforded **3j** as a colorless oil (170 mg, 55%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29–7.26 (m, 2H), 7.14–7.11 (m, 2H), 4.68–4.64 (m, 1H), 3.42 (dd, $^1J(^1H,^1H)$ = 14.5 Hz, $^3J(^1H,^1H)$ = 8 Hz, 1H), 3.15 (dd, $^1J(^1H,^1H)$ = 14.5 Hz, $^3J(^1H,^1H)$ = 7 Hz, 1H), 2.37 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 201.8, 137.3, 133.1, 130.5, 128.9, 40.0, 31.7, 26.9. **HRMS (ESI):** m/z calcd for $C_{10}H_{10}{}^{35}ClIO+Na^+$: 330.9357 [*M*+Na]$^+$; found: 330.9350.

2-iodo-1-phenylpropan-1-one (3k)

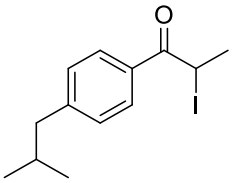


The title compound was prepared from 1-phenylprop-2-en-1-ol (134 mg, 1 mmol) according to the general procedure. Purification by column chromatography (SiO_2; pentane / EtOAc, 99:1) afforded **3k** as a colorless oil (189 mg, 72%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02–7.99 (m, 2H), 7.59–7.55 (m, 1H), 7.49–7.44 (m, 2H), 5.50 (q, $^3J(^1H,^1H)$ = 6.7 Hz, 1H), 2.08 (d, $^3J(^1H,^1H)$ = 6.7 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 194.8, 133.7, 133.6, 128.83, 128.78, 22.2, 18.2.

For complete characterization see: M. M. Reddy, P. Swamy, M. Naresh, K. Srujana, C. Durgaiah, T. V. Rao, N. Narender, *RSC advances* **2015**, *5*, 12186.

2-iodo-1-(4-isobutylphenyl)propan-1-one (3l)

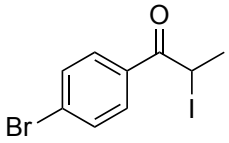


The title compound was prepared from 1-(4-isobutylphenyl)prop-2-en-1-ol (190 mg, 1 mmol) according to the general procedure. Purification by column chromatography (SiO_2; pentane / EtOAc, 99:1) afforded **3l** as a colorless oil (230 mg, 74%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, $^3J(^1H,^1H)$ = 8.5 Hz, 2H), 7.24 (d, $^3J(^1H,^1H)$ = 8.5 Hz, 2H), 5.48 (q, $^3J(^1H,^1H)$ = 6.7 Hz, 1H), 2.54 (d, $^3J(^1H,^1H)$ = 7.2 Hz, 2H), 2.07 (d, $^3J(^1H,^1H)$ = 6.7 Hz, 3H), 1.91 (m, 1H), 0.92 (m, 6H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 194.5, 148.2, 131.3, 129.5, 128.7, 45.5, 30.1, 22.4, 22.1, 18.2.

For complete characterization see: H. Sonawane, N. Bellur, D. G. Kulkarni, N. R. Ayyangar, *Tetrahedron* **1994**, *4*, 1243.

1-(4-bromophenyl)-2-iodopropan-1-one (3m)

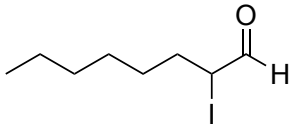


The title compound was prepared from 1-(4-bromophenyl)prop-2-en-1-ol (213, 1 mmol) according to the general procedure. Purification by column chromatography (SiO_2; pentane / EtOAc, 99:1) afforded **3m** as a yellow solid (186 mg, 55%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, $^3J(^1H,^1H)$ = 8.7 Hz, 2H), 7.61 (d, $^3J(^1H,^1H)$ = 8.7 Hz, 2H), 5.42 (q, $^3J(^1H,^1H)$ = 6.7 Hz, 1H), 2.07 (d, $^3J(^1H,^1H)$ = 6.7 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 193.9, 132.5, 132.2, 130.3, 128.8, 22.0, 17.9.

For complete characterization see: T. Yamauchi, K. Hattori, K. Nakao, K. Tamaki, *J. Org. Chem.* **1988**, *53*, 4859.

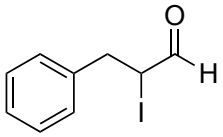
2-iodooctanal (3n)



The title compound was prepared from (*E*)-oct-2-en-1-ol (128 mg, 1 mmol) according to the general procedure. Purification by column chromatography (SiO_2; pentane / EtOAc, 99:1) afforded **3n** as a colorless oil (53 mg, 21%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.26 (d, $^3J(^1H,^1H)$ = 3.2 Hz, 1H), 4.45 (ddd, $^3J(^1H,^1H)$ = 7.7 Hz, $^3J(^1H,^1H)$ = 7.0 Hz, $^3J(^1H,^1H)$ = 3.2 Hz, 1H), 1.98–1.87 (m, 2H), 1.52–1.45 (m, 1H), 1.34–1.29 (m, 7H), 0.90–0.87 (m, 3H) **^{13}C NMR (100 MHz, $CDCl_3$)** δ 192.0, 36.9, 32.3, 31.6, 29.5, 28.7, 22.6, 14.1. **HRMS (ESI):** m/z calcd for $C_8H_{15}IO{\cdot}MeOH+Na^+$: 309.0322 $[M+MeOH+Na]^+$; found: 309.0314.

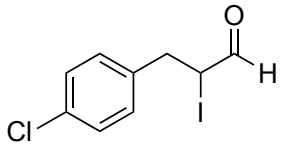
2-iodo-3-phenylpropanal (3o)



The title compound was prepared from (*E*)-3-phenylprop-2-en-1-ol (134 mg, 1 mmol) according to the general procedure. Purification by column chromatography (SiO_2; pentane / EtOAc, 99:1) afforded **3o** as a colorless oil (50 mg, 37%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.30 (d, $^3J(^1H,^1H)$ = 2.7 Hz, 1H), 7.36-7.26 (m, 3H), 7.22-7.18 (m, 2H), 4.71 (td, $^3J(^1H,^1H)$ = 7.5, 2.7 Hz, 1H), 3.50 (dd, $^1J(^1H,^1H)$ = 14.7, $^3J(^1H,^1H)$ = 7.5 Hz, 1H), 3.21 (dd, $^1J(^1H,^1H)$ = 14.7, $^3J(^1H,^1H)$ = 7.5 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 191.1, 138.2, 129.0, 128.9, 127.4, 38.6, 36.0. **HRMS (ESI):** m/z calcd for $C_9H_9IO{\cdot}H_2O+Na^+$: 300.9696 $[M+H_2O+Na]^+$; found: 300.9695.

3-(4-chlorophenyl)-2-iodopropanal (3p)

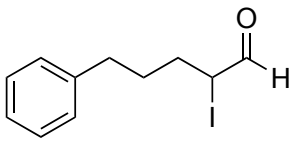


The title compound was prepared from (*E*)-3-(4-chlorophenyl)prop-2-en-1-ol (168 mg, 1 mmol) according to the general procedure. Purification by column chromatography (SiO_2; pentane / EtOAc, 99:1) afforded **3p** as a colorless oil (57 mg, 34%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.30 (d, $^3J(^1H,^1H)$ = 2.2 Hz, 1H), 7.30-7.28 (m, 2H), 7.15-7.13 (m, 2H), 4.66 (td, $^3J(^1H,^1H)$ = 7.5, 2.2 Hz, 1H), 3.46 (dd, $^1J(^1H,^1H)$ = 14.7, $^3J(^1H,^1H)$ = 7.5 Hz, 1H), 3.16 (dd, $^1J(^1H,^1H)$ = 14.7, $^3J(^1H,^1H)$ = 7.5 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 190.9, 136.7, 133.3,

130.5, 129.0, 37.8, 35.6. **HRMS (ESI):** m/z calcd for $C_9H_8{}^{35}ClIO{\cdot}MeOH{+}Na^+$: 348.9463 [*M*+MeOH+Na]$^+$; found: 348.9472.

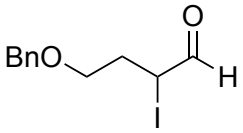
2-iodo-5-phenylpentanal (3q)



The title compound was prepared from (*E*)-5-phenylpent-2-en-1-ol (162 mg, 1 mmol) according to the general procedure. Purification by column chromatography (SiO_2; pentane / EtOAc, 99:1) afforded **3p** as a colorless oil (68 mg, 42%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.25 (d, $^3J(^1H,^1H)$ = 3 Hz, 1H), 7.31-7.28 (m, 2H), 7.22-7.17 (m, 3H), 4.47 (ddd, $^3J(^1H,^1H)$ = 7.8, 6.8, 2.2 Hz, 1H), 2.72-2.62 (m, 2H), 2.03-1.66 (m, 4H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 191.6, 141.3, 128.6, 128.5, 126.2, 36.6, 35.2, 31.7, 31.2. **HRMS (ESI):** m/z calcd for $C_{11}H_{13}IO{\cdot}MeOH{+}Na^+$: 343.0165 [*M*+MeOH+Na]$^+$; found: 343.0177.

4-(benzyloxy)-2-iodobutanal (3r)

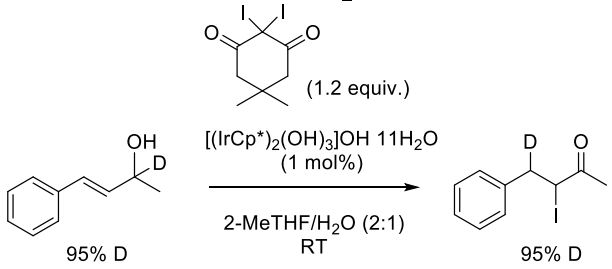


The title compound was prepared from (*Z*)-4-(benzyloxy)but-2-en-1-ol (178 mg, 1 mmol) according to the general procedure. Purification by column chromatography (SiO_2; pentane / EtOAc, 99:1) afforded **3r** as a colorless oil (70 mg, 23%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.28 (d, $^3J(^1H,^1H)$ = 2.7 Hz, 1H), 7.38–7.26 (m, 5H), 4.75 (ddd, $^3J(^1H,^1H)$ = 7.8 Hz, $^3J(^1H,^1H)$ = 6.7 Hz, $^3J(^1H,^1H)$ = 2.7 Hz, 1H), 4.50 (s, 2H), 3.66–3.61 (m, 1H), 3.55–3.50 (m, 1H), 2.38–2.30 (m, 1H), 2.19–2.12 (m, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 191.6, 138.0, 128.6, 128.0, 127.9, 73.4, 68.6, 33.7, 33.0. **HRMS (ESI):** m/z calcd for $C_{11}H_{13}IO_2{\cdot}H_2O{+}Na^+$: 344.9958 [*M*+H_2O+Na]$^+$; found: 344.9950.

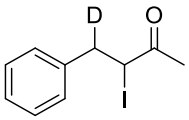
Deuterium labelling studies:

Iridium-catalyzed isomerization / iodination of 1i-*d*$_1$



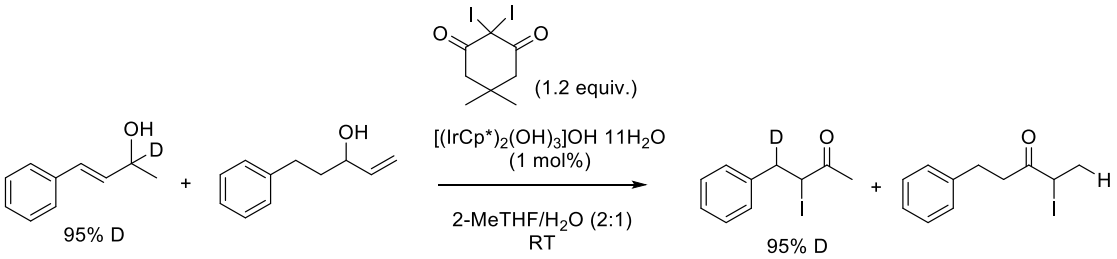
Deuterated allylic alcohol 2-*d*-(*E*)-4-phenylbut-3-en-2-ol (**1i-*d*$_1$**) (95% deuterium) (0.5 mmol) was reacted according to the general procedure using 1 mol% [(IrCp*)$_2$(OH)$_3$]OH 11H$_2$O and 1.2 equiv. of 2,2-diodo-dimedone (16 h reaction time). **3i-*d*$_1$** (79 mg, 58% isolated yield) was obtained as colorless oil after purification with column chromatography (SiO_2; pentane / EtOAc, 99:1). ^{1}H, ^{13}C and HRMS showed 95% of deuterium content in **3i-*d*$_1$** evidencing a 1,3-H shift pathway in these reaction conditions.

4-d-3-iodo-4-phenylbutan-2-one (3i-*d*$_1$)



^{1}H NMR (400 MHz, $CDCl_3$, mixture of 2 diastereoisomers (d.r. = 1:1)): δ 7.32–7.26 (m, 3H(both diast.)), 7.20–7.17 (m, 2H(both diast.)), 4.70 (d, $^3J(^1H,^1H)$ = 7.7 Hz, 1H(both diast.)), 3.45–3.20 (m, 1H(both diast.)), 2.36 (s, 3H(one diast.)), 2.35 (s, 3H(one diast.)). **^{13}C NMR (100 MHz, $CDCl_3$, mixture of 2 diastereoisomers (d.r. = 1:1)):** δ 202.1, 138.8, 129.1, 128.8, 127.2, 40.6 (t, $^1J(^1H,^2H)$ = 19.9 Hz), 40.5 (t, $^1J(^1H,^2H)$ = 19.9 Hz), 32.3, 32.1, 26.8. **HRMS (ESI):** m/z calcd for $C_{10}H_{10}DIO+Na^+$: 297.9810 [*M*+Na]$^+$; found: 297.9808

Crossover experiment between 1i-*d*$_1$ *and* 1e



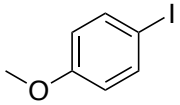
Deuterated allylic alcohol 2-*d*-(*E*)-4-phenylbut-3-en-2-ol (**1i-*d*$_1$**) (95% deuterium) (0.25 mmol) and allylic alcohol 5-phenylpent-1-en-3-ol (**1e**) were reacted according to the general procedure using 1 mol% [(IrCp*)$_2$(OH)$_3$]OH 11H$_2$O and 1.2 equiv. of 2,2-diodo-dimedone (16 h reaction time). The mixture showed a 95% of deuterium content in **3i-*d*$_1$** and no deuterium in **3e** as determined by ^{1}H, ^{13}C and HRMS, suggesting an intramolecular process operating in this reaction.

General procedure for synthesis of iodoarenes using 2

2,2-Diiodo-dimedone (**2**) (235 mg, 0.6 mmol, 1.2 equiv.), the corresponding arene (0.5 mmol, 1 equiv.) and $FeCl_3$ H_2O (0.05 mmol, 10 mol%) were dissolved in HFIP (5 mL) and the mixture was stirred at room temperature under an air atmosphere for 2 h. The reaction was quenched by the addition of sat. aqueous solution of $Na_2S_2O_3$ (2 mL) and the product was extracted with CH_2Cl_2 (3x10 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The product was purified by column chromatography using petroleum ether / EtOAc (98:2) mixture as eluent.

Synthesis and characterization of iodoarenes 5a-c

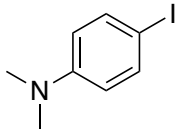
1-iodo-4-methoxybenzene (5a)



The title compound was prepared from anisole **4a** (108 μL, 1 mmol,) according to the general procedure affording **5a** as a yellow solid (193 mg, 82%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64–7.53 (m, 2H), 6.78–6.66 (m, 2H), 3.80 (s, 3H).**^{13}C NMR (100 MHz, $CDCl_3$)**: δ 159.5, 138.2, 116.4, 82.7, 55.3.

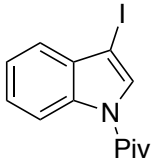
4-iodo-*N*,*N*-dimethylaniline (5b)



The title compound was prepared from *N,N*-dimethylaniline **4b** (127 μL, 1 mmol) according to the general procedure affording **5b** as a white solid (169 mg, 68%).

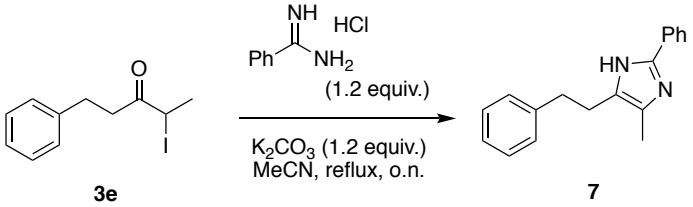
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56–7.42 (m, 2H), 6.60–6.45 (m, 2H), 2.94 (s, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 150.0, 137.6, 114.7, 77.4, 40.4.

1-(3-iodo-1*H*-indol-1-yl)-2,2-dimethylpropan-1-one (5c)



The title compound was prepared from pivaloyl-1*H*-indole **4c** (201 mg, 1 mmol) according to the general procedure affording **5c** as a yellow solid (266 mg, 81%).**^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.53–8.47 (m, 1H), 7.88 (s, 1H), 7.47–7.35 (m, 3H), 1.55 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 176.2, 136.2, 131.0, 129.7, 126.2, 124.2, 121.2, 117.2, 67.3, 41.4, 28.7. **HRMS (ESI):** m/z calcd for $C_{13}H_{14}NI+Na^+$: 350.0012 $[M+Na]^+$; found: 349.9997.

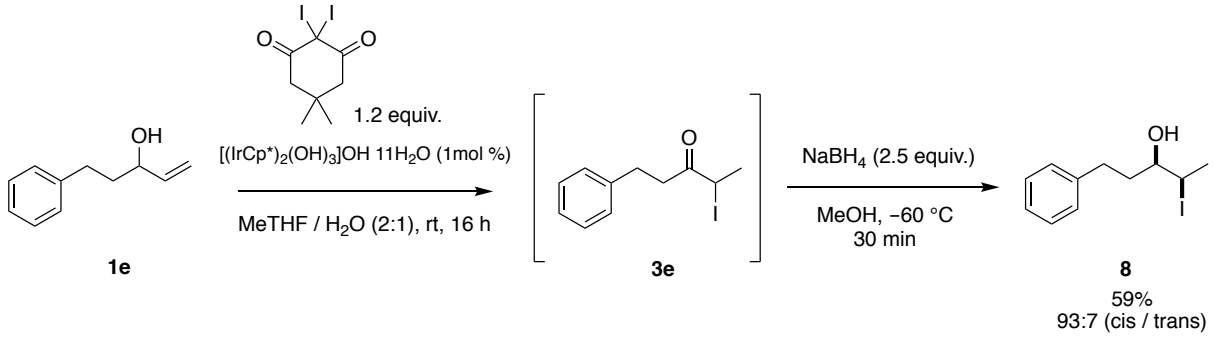
Procedure for the synthesis and characterization of imidazole 7



α-iodoketone **6e** (52 mg, 0.18 mmol, 1 equiv.) was dissolved in MeCN (2 mL). Benzamidine hydrochloride (35 mg, 0.225 mmol, 1.2 equiv.) and K_2CO_3 (31 mg, 0.225 mmol, 1.2 equiv.) were added and the reaction mixture was heated to reflux overnight. The reaction was subsequently quenched with H_2O (1.5 mL) and extracted with EtOAc (3 x 2 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was reduced under pressure. 4-methyl-5-phenethyl-2-phenyl-1*H*-imidazole (**7**) was isolated in 95% yield as a white oil/foam.

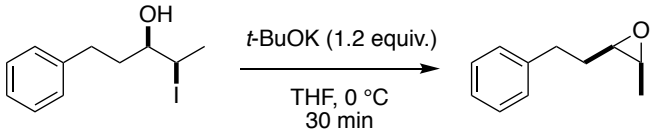
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, $^3J(^1H,^1H)$ = 7.0 Hz, 2H), 7.32–7.15 (m, 6H), 7.02 (d, $^3J(^1H,^1H)$ = 7.0 Hz, 2H), 2.85–2.79 (m, 4H), 1.98 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 144.6, 141.7, 132.0, 130.7, 128.85 , 128.85, 128.6, 128.4, 127.9, 126.0, 125.0, 36.5, 28.0, 1 0.6. **HRMS (ESI):** m/z calcd for $C_{18}H_{18}N_2$+H^+: 263.1543 $[M+H]^+$; found: 263.1548.

One-pot synthesis and characterization of halohydrin 8 and synthesis of epoxide 9



2,2-Diiodo-dimedone (**2**) (92 mg, 0.24 mmol, 1.2 equiv.) was dissolved in 2-MeTHF (1.33 mL) and H_2O (0.66 mL). Allylic alcohol (**1e**) (33 mg, 0.2 mmol, 1 equiv.) and $[(IrCp^*)_2(OH)_3]OH$ $11H_2O$ (2 mg, 0.002 mmol, 1 mol%) were added to the mixture and the vial was closed and stirred at room temperature for 16 h. After that, MeOH (4 mL) was added and the mixture was cooled to −60 °C. $NaBH_4$ (20 mg, 0.5 mmol, 2.5 equiv.) was incorporated in small portions and the reaction stirred for 30 minutes at −60 °C. The volatiles were reduced under vacuum and the residue was then carefully quenched with H_2O (2 mL) and extracted with EtOAc (3 x 2 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was reduced under pressure. Purification by column chromatography (SiO_2; pentane / EtOAc, 90:10) afforded 4-iodo-1-phenylpentan-3-ol (**8**) with 59% isolated yield and a diastereomeric ratio of 93:7 (cis/trans).

^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers (93:7)): δ 7.32–7.28 (m, 2H(both diast.)), 7.22–7.19 (m, 3H(both diast.)), 4.42–4.36 (m, 1H(minor)), 4.32–4.26 (m, 1H(major)), 2.89–2.68 (m, 3H(both diast.)), 1.96 (d, $^3J(^1H,^1H)$ = 7.0 Hz, 3H(both diast.)), 1.88–1.82 (m, 2H(both diast.)), 1.76 (d, $^3J(^1H,^1H)$ = 7.4 Hz, 1H(both diast.)). **^{13}C NMR (100 MHz, $CDCl_3$ mixture of diastereoisomers (93:7)):** δ 141.6, 128.62, 128.58, 126.2, 75.5, 40.4, 39.0, 31.9, 25.5. **HRMS (ESI):** m/z calcd for $C_{11}H_{15}IO+Na^+$: 313.0060 $[M+Na]^+$; found: 313.0045.



8

93:7 (cis / trans)

9

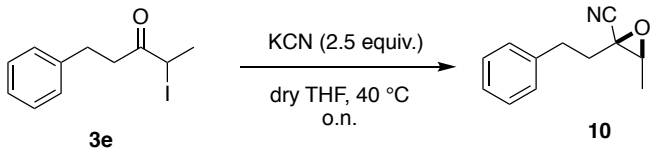
70%
93:7 (cis / trans)

t-BuOK (16 mg, 0.14 mmol, 1.2 equiv.) was dissolved in dry THF (1.5 ml) under an inert atmosphere at 0 °C. 4-iodo-1-phenylpentan-3-ol (34 mg, 0.12 mmol, 1 equiv.) was added dissolved in in dry THF (1 ml) drop by drop and the reaction was stirred at 0 °C for 30 minutes. After that, the reaction was then carefully quenched with H_2O (2 mL) and extracted with EtOAc (3 x 2 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was reduced under pressure. Purification by column chromatography (SiO_2; pentane / EtOAc, 90:10) afforded 2-methyl-3-phenethyloxirane (**9**) with 70% isolated yield and a diastereomeric ratio of 93:7 (cis/trans).

^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers (93:7)): δ 7.31–7.28 (m, 2H(both diast.)), 7.22–7.18 (m, 3H(both diast.)), 3.06–3.01 (m, 1H(both diast.)), 2.98–2.93 (m, 1H(both diast.)), 2.89–2.69 (m, 2H(both diast.)), 1.93–1.75 (m, 2H(both diast.)), 1.26 (d, $^3J(^1H,^1H)$ = 5.5 Hz, 3H(minor)), 1.19 (d, $^3J(^1H,^1H)$ = 5.5 Hz, 3H(major)). **^{13}C NMR (100 MHz, $CDCl_3$ mixture of diastereoisomers (93:7)):** δ 141.5, 128.57, 128.57, 126.2, 56.7, 53.0, 32.9, 29.6, 13.3.

For complete characterization see: S.K. Taylor, M. E. Davisson, B. R. Hisson, S. L. Brown, H. A. Pristach, S. B. Schramm, S. M. Harvey. *J. Org. Chem.* **1987**, *52*, 425.

Procedure for the synthesis and characterization of cyanoepoxide 10



3e

10

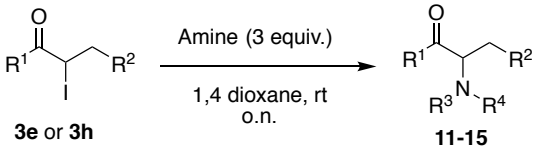
74%
80:20 d.r.

α-iodoketone **3e** (39 mg, 0.13 mmol, 1 equiv.) was dissolved in 2 mL of THF. KCN (22 mg, 0.337 mmol, 2.5 equiv.) and the reaction mixture was heated at 40 °C overnight. The volatiles were removed under vacuum and the crude was purified directly by column chromatography (SiO_2; pentane

/ EtOAc, 90:10) affording 3-methyl-2-phenethyloxirane-2-carbonitrile (**10**) with 74% isolated yield and a diastereomeric ratio of 80:20.

^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereisomers 80:20): δ 7.35–7.25 (m, 2H(both diast.)), 7.25–7.21 (m, 3H(both diast.)), 3.40 (q, $^3J(^1H,^1H)$ = 5.5 Hz, 1H(minor), 3.00–2.86 (m, 2H(both diast.)), 2.83 (q, $^3J(^1H,^1H)$ = 5.5 Hz, 1H(major), 2.24–2.11 (m, 1H(both diast.)), 1.98–1.92 (m, 1H(both diast.)), 1.41 (d, $^3J(^1H,^1H)$ = 5.5 Hz, 3H(major), 1.13 (d, $^3J(^1H,^1H)$ = 5.5 Hz, 3H(minor). **^{13}C NMR (100 MHz, $CDCl_3$, mixture of diastereisomers 80:20):** δ 140.6, 139.6, 128.8, 128.80, 128.6, 128.5, 126.8, 126.7, 118.9, 117.3, 59.6, 59.5, 54.1, 52.0, 36.0, 31.4, 31.2, 30.4, 15.5, 12.8. **HRMS (ESI):** m/z calcd for $C_{12}H_{13}NO+Na^+$: 210.0889 $[M+Na]^+$; found: 210.0887.

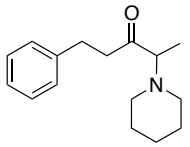
Procedure for the synthesis and characterization of α-aminoketones 11-15



3e or **3h** — **11-15**

The corresponding α-iodoketone (0.16 mmol, 1 equiv.) and the amine (0.486 mmol, 3 equiv.) were dissolved in 2 mL of 1,4 dioxane. The reaction mixture was stirred at room temperature overnight and then quenched with $NaHCO_3$ sat. aqueous solution and extracted with EtOAc. The organic phases were dried with $MgSO_4$ and the volatiles were removed under vacuum. The crude was purified by column chromatography (SiO_2; pentane / EtOAc, 90:10).

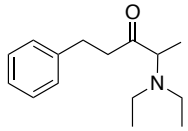
1-phenyl-4-(piperidin-1-yl)pentan-3-one (11)



The title compound was prepared from **3e** (47 mg, 0.16 mmol) and piperidine (48 μL, 0.486 mmol), according to the procedure described above. Purification by column chromatography (SiO_2; pentane / EtOAc, 90:10) afforded **12** as a yellow oil (40 mg, 89%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29–7.26 (m, 2H), 7.21–7.17 (m, 3H), 3.08 (q, $^3J(^1H,^1H)$ = 6.8 Hz, 1H), 2.99–2.85 (m, 4H), 2.41–2.29 (m, 4H), 1.57–1.49 (m, 4H), 1.43–1.39 (m, 2H), 1.06 (d, $^3J(^1H,^1H)$ = 6.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 221.7, 141.6, 128.51, 128.46, 126.0, 69.8, 51.2, 40.8, 30.0, 26.4, 24.4, 10.0. **HRMS (ESI):** m/z calcd for $C_{16}H_{23}NO+H^+$: 246.1852 $[M+H]^+$; found: 246.1855.

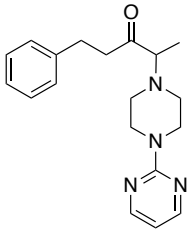
4-(diethylamino)-1-phenylpentan-3-one (12)



The title compound was prepared from **3e** (47 mg, 0.16 mmol) and diethylamine (50 μL, 0.486 mmol), according to the procedure described above. Purification by column chromatography (SiO_2; pentane / EtOAc, 90:10) afforded **12** as an oil (20 mg, 51%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.28 (m, 2H), 7.23–7.18 (m, 3H), 3.37 (q, $^3J(^1H,^1H)$ = 6.7 Hz, 1H), 3.08–2.86 (m, 4H), 2.54–2.37 (m, 4H), 1.06–1.00 (m, 9H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 213.2, 141.7, 128.53, 128.52, 126.1, 64.3, 44.4, 40.9, 30.3, 13.7, 8.5. **HRMS (ESI):** m/z calcd for $C_{15}H_{23}NO+H^+$: 234.1852 $[M+H]^+$; found: 234.1837.

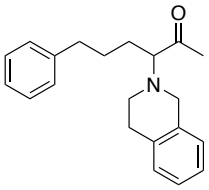
1-phenyl-4-(4-(pyrimidin-2-yl)piperazin-1-yl)pentan-3-one (13)



The title compound was prepared from **3e** (47 mg, 0.16 mmol) and 2-(piperazin-1-yl)pyrimidine (70 μL, 0.486 mmol), according to the procedure described above. Purification by column chromatography (SiO_2; pentane / EtOAc, 90:10) afforded **13** as a yellow oil (40 mg, 73%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (d, $^3J(^1H,^1H)$ = 4.7 Hz, 2H), 7.29–7.25 (m, 2H), 7.21–7.16 (m, 3H), 6.46 (t, $^3J(^1H,^1H)$ = 4.7 Hz, 1H), 3.82–3.72 (m, 4H), 3.15 (q, $^3J(^1H,^1H)$ = 6.8 Hz, 1H), 3.03–2.87 (m, 4H), 2.51–2.38 (m, 4H), 1.09 (d, $^3J(^1H,^1H)$ = 6.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 211.6, 161.7, 157.8, 141.4, 128.54, 128.52, 126.2, 110.0, 69.1, 49.7, 44.0, 40.9, 29.9, 10.4. **HRMS (ESI):** m/z calcd for $C_{19}H_{24}NO+H^+$: 325.2023 $[M+H]^+$; found: 325.2020.

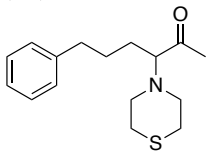
3-(3,4-dihydroisoquinolin-2(1*H*)-yl)-6-phenylhexan-2-one (14)



The title compound was prepared from **3h** (32 mg, 0.11 mmol) and tetrahydroisoquinoline (40 μL, 0.32 mmol), according to the procedure described above. Purification by column chromatography (SiO_2; pentane / EtOAc, 90:10) afforded **14** as a yellow oil (25 mg, 77%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30–7.27 (m, 2H), 7.21–7.17 (m, 3H), 7.15–7.09 (m, 3H), 7.01–7.00 (m, 1H), 3.79 (d, $^2J(^1H,^1H)$ = 14.7 Hz, 1H), 3.68 (d, $^2J(^1H,^1H)$ = 14.7 Hz, 1H), 3.21–3.18 (m, 1H), 2.88–2.76 (m, 4H), 2.68–2.65 (m, 2H), 2.20 (s, 3H), 1.80–1.58 (m, 4H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 210.3, 142.0, 134.9, 134.5, 128.9, 128.52, 128.47, 126.6, 126.2, 126.0, 125.8, 73.8, 52.7, 47.8, 36.0, 29.8, 28.4, 28.0, 25.7. **HRMS (ESI):** m/z calcd for $C_{21}H_{25}NO+H^+$: 308.2009 [*M* +H]$^+$; found: 308.2006.

6-phenyl-3-thiomorpholinohexan-2-one (15)



The title compound was prepared from **3h** (32 mg, 0.11 mmol) and thiomorpholine (30 μL, 0.32 mmol), according to the procedure described above. Purification by column chromatography (SiO_2; pentane / EtOAc, 90:10) afforded **15** as a yellow oil (26 mg, 88%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29–7.26 (m, 2H), 7.20–7.15 (m, 3H), 3.05–3.01 (m, 1H), 2.80–2.78 (m, 4H), 2.63–2.60 (m, 6H), 2.16 (s, 3H), 1.70–1.50 (m, 4H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 209.5, 142.1, 128.5, 128.5, 126.0, 74.8, 52.3, 36.0, 28.9, 28.7, 24.85, 24.85. **HRMS (ESI):** m/z calcd for $C_{16}H_{23}NOS+H^+$: 278.1573 [*M* +H]$^+$; found: 278.1584.

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[1] a) N. A. Owston, A. J. Parker, J. M. J. Williams, *Org. Lett.* **2007**, *9*, 73. b) S. Ogo, N. Makihara, Y. Watanabe, *Organometallics* **1999**, *18*, 5470. c) A. Nutton, P. M. Bailey, P. M. Maitlis, *J. Chem. Soc., Dalton Trans.* **1981**, 9, 1997.

[2] D. R. Stuart, E. Villemure, K. Fagnou, *J. Am. Chem. Soc.* **2007**, *129*, 12072.

[3] N. Ahlsten, B. Martín-Matute, *Chem- Commun.* **2011**, *47*, 8331.

[4] M. J. Fuchter, J. N. Levy. *Org. Lett.*, **2008**, *10*, 4919.

[5] D. Xing, D. Yang, *Org. Lett.* **2010**, *12*, 1068.

[6] D. R. Li, A. He, J. R. Falck, *Org. Lett*. **2010**, *12*, 1756.

[7] M. B. Onaran, C. T. Seto. *J. Org. Chem.* **2003**, *68*, 8136.

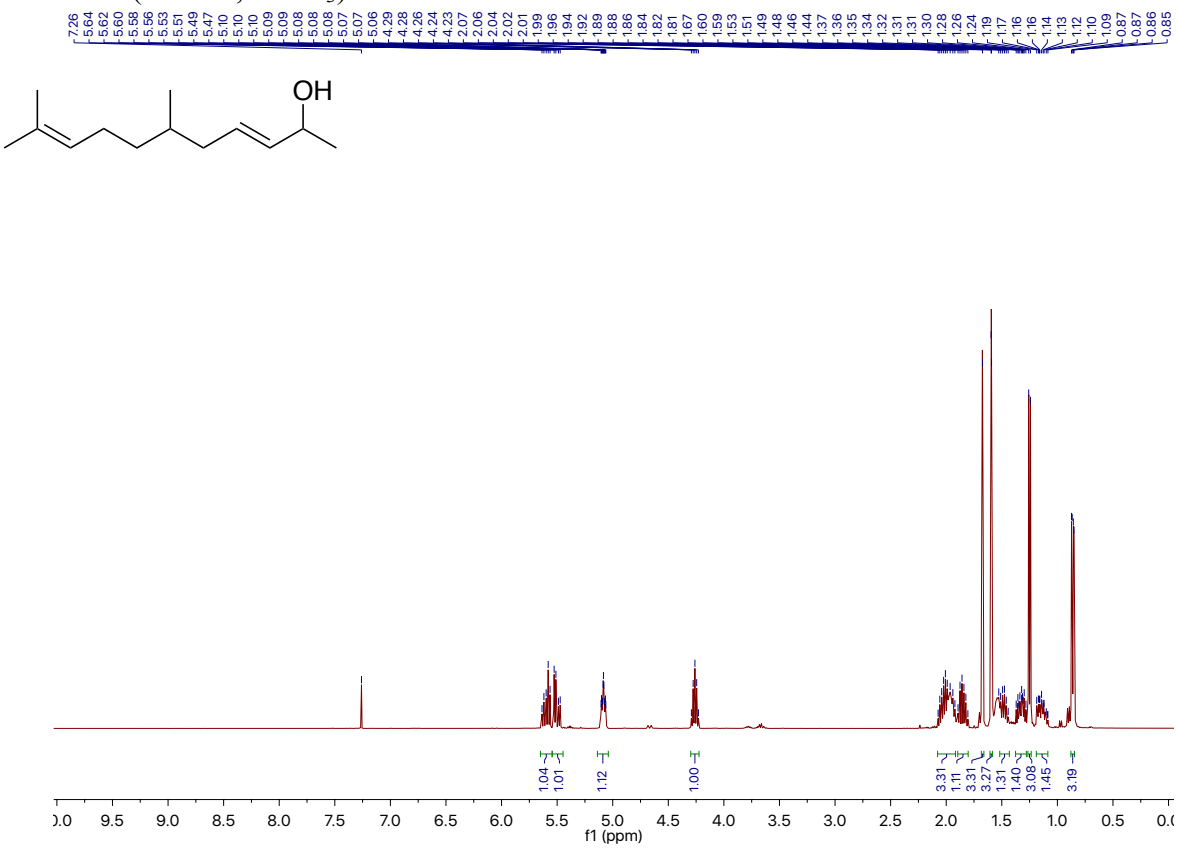
[8] S. Akai, R. Hanada, N. Fujiwara, Y. Kita, M. Egi, *Org. Lett.*, **2010**, 12, 4900.

[9] N. Ahlsten, A. Bermejo Gómez, B. Martín-Matute, *Angew. Chem. Int. Ed.* **2013**, *52*, 6273, *Angew. Chem.* **2013**, *125*, 6393.

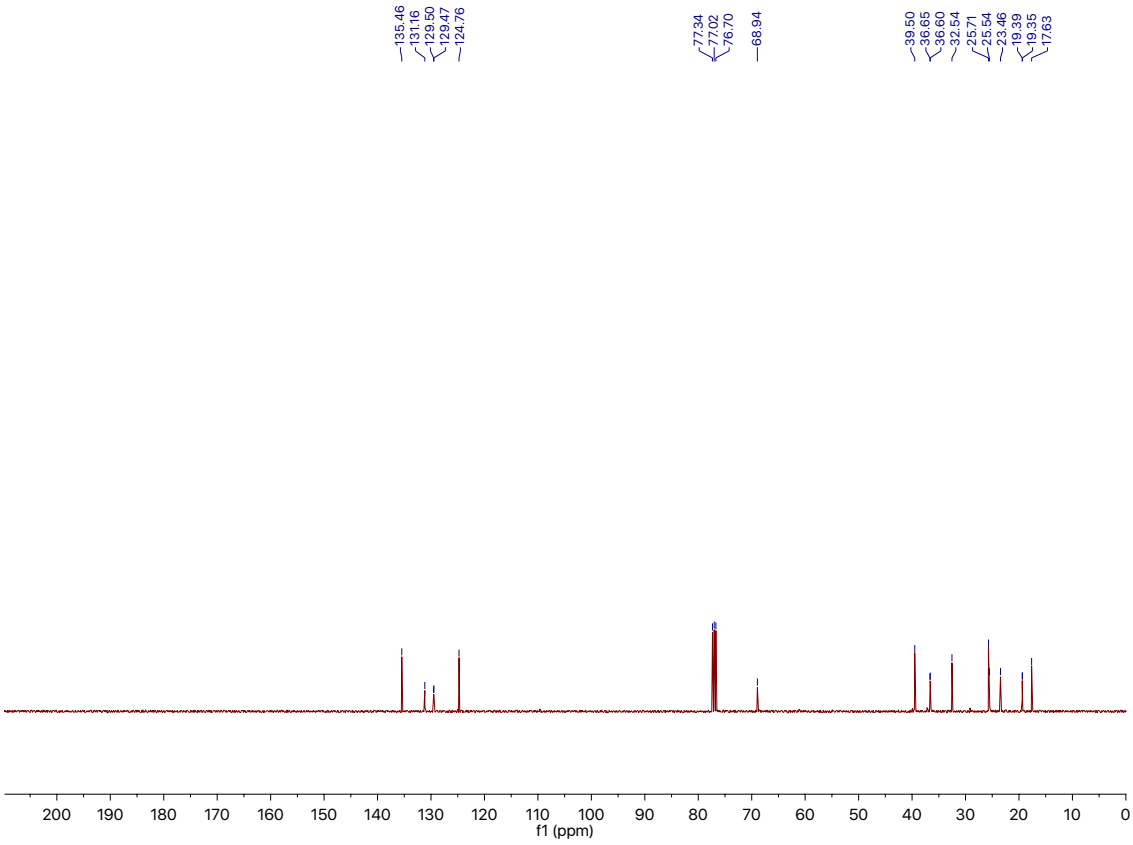
[10] J. Stambasky, A. V. Malkov, P. Kocovsky, *J. Org. Chem.* **2008**, *73*, 9148.

^{1}H-NMR and ^{13}C-NMR spectra of (*E*)-6,10-dimethylundeca-3,9-dien-2-ol (1g)

^{1}H NMR (400 Hz, $CDCl_3$)

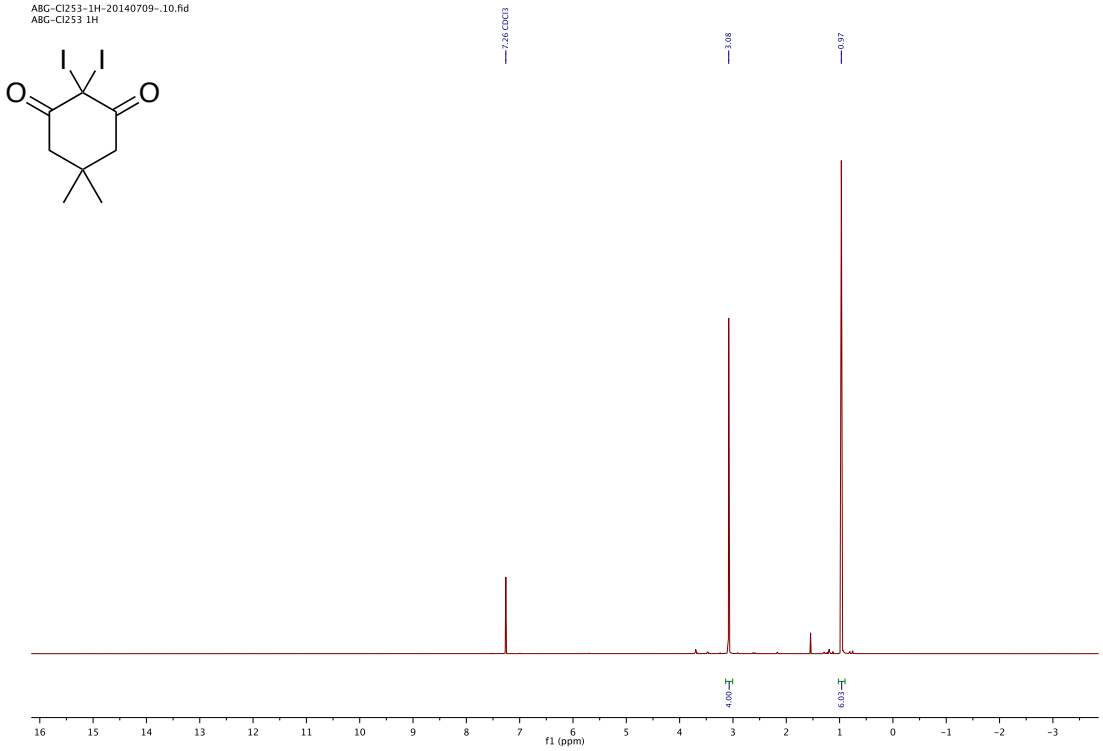


^{13}C NMR (100 Hz, $CDCl_3$)

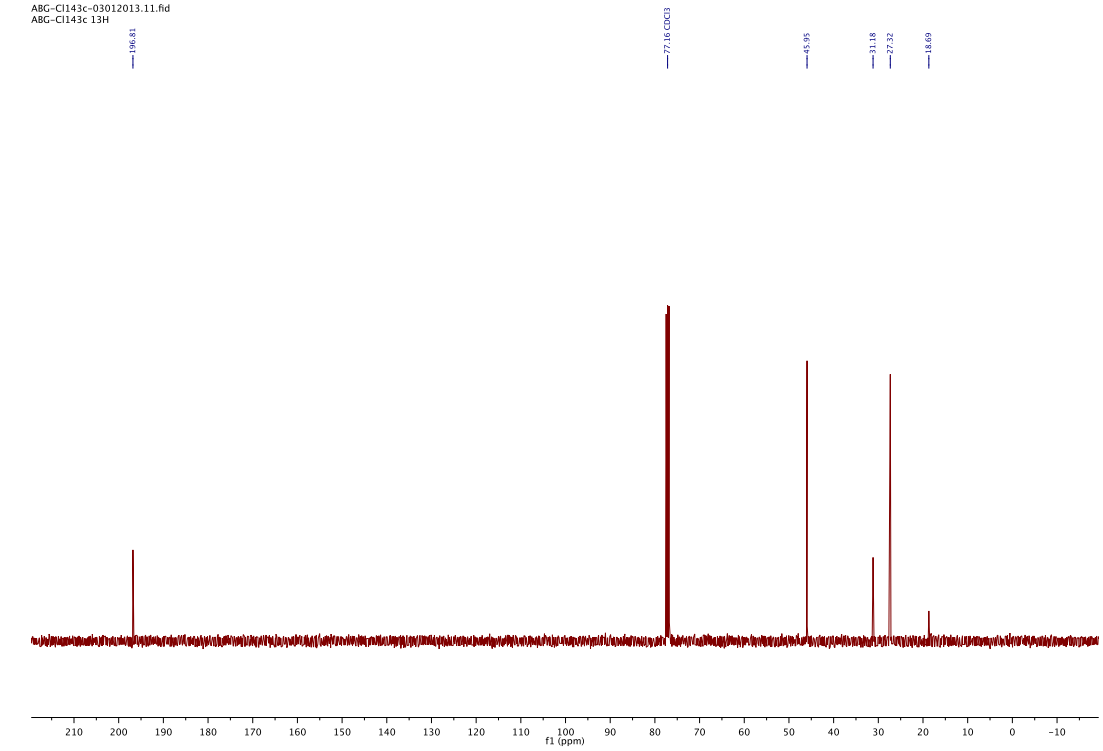


^{1}H-NMR and ^{13}C-NMR spectra of 2,2-diiodo-5,5-dimethylcyclohexane-1,3-dione 2,2-diiodo-5,5-dimethylcyclohexane-1,3-dione (2)

^{1}H NMR (400 Hz, $CDCl_3$)

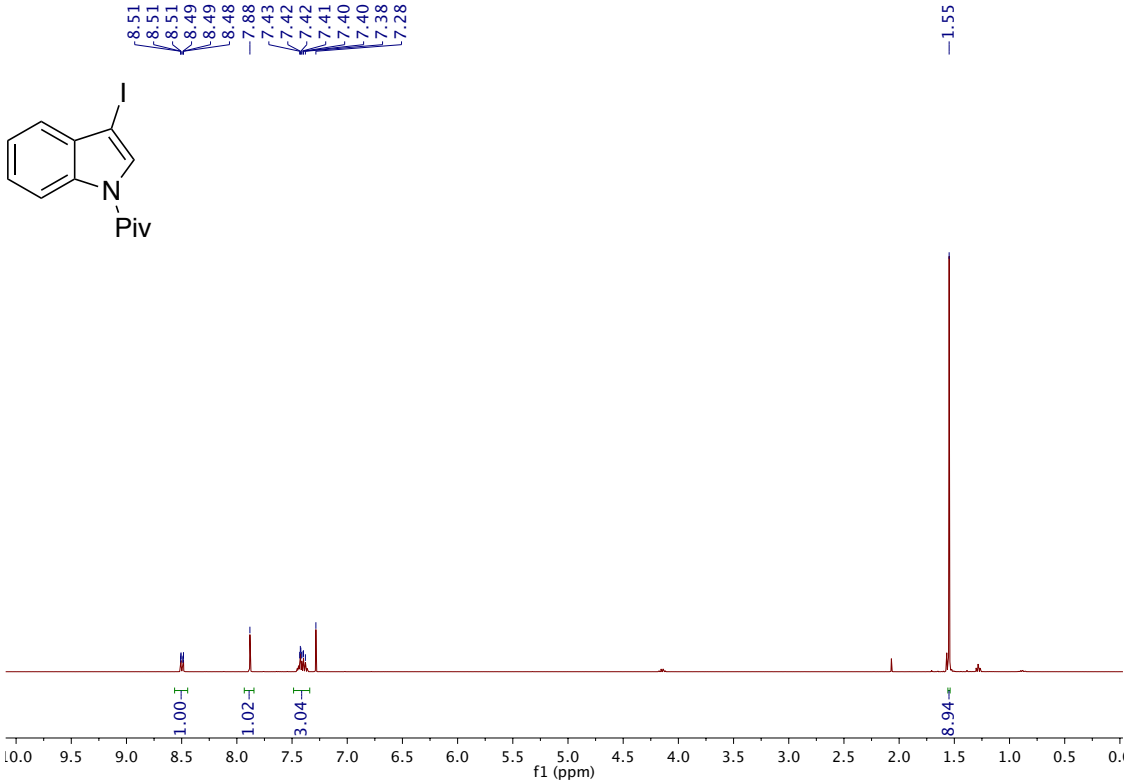


^{13}C NMR (100 Hz, $CDCl_3$)

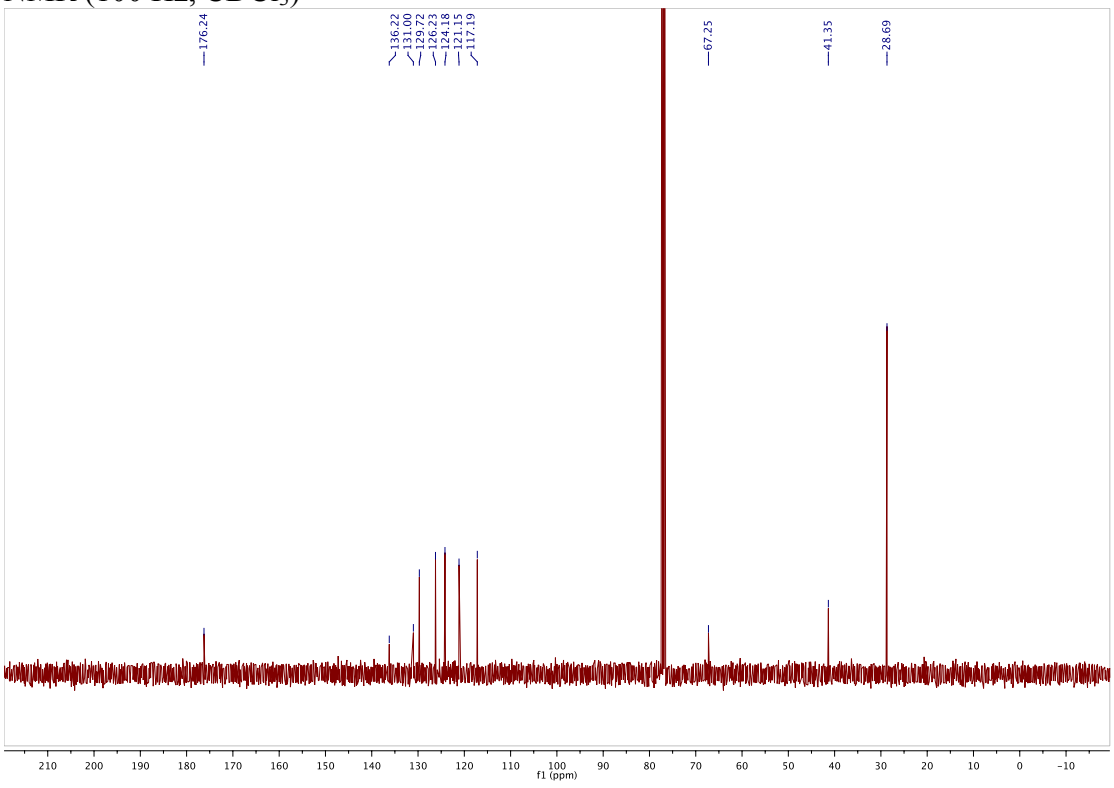


^{1}H-NMR and ^{13}C-NMR spectra of 1-(3-iodo-1*H*-indol-1-yl)-2,2-dimethylpropan-1-one (5c)

^{1}H NMR (400 Hz, $CDCl_3$)



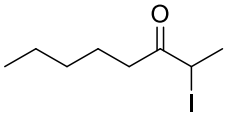
^{13}C NMR (100 Hz, $CDCl_3$)



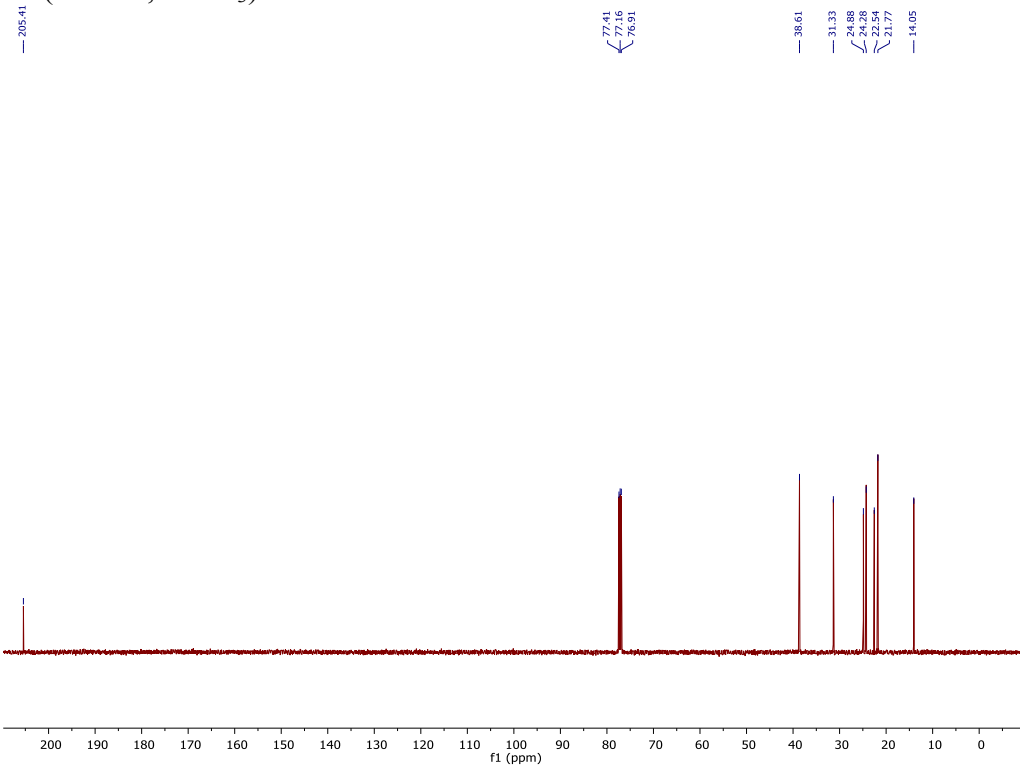
^{1}H and ^{13}C NMR of of α-iodoketones 3a-j and α-iodoaldehydes 3n-r

2-iodooctan-3-one (3a)

^{1}H NMR (400 Hz, $CDCl_3$)

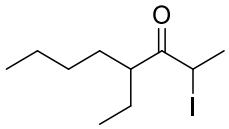


^{13}C NMR (100 Hz, $CDCl_3$)

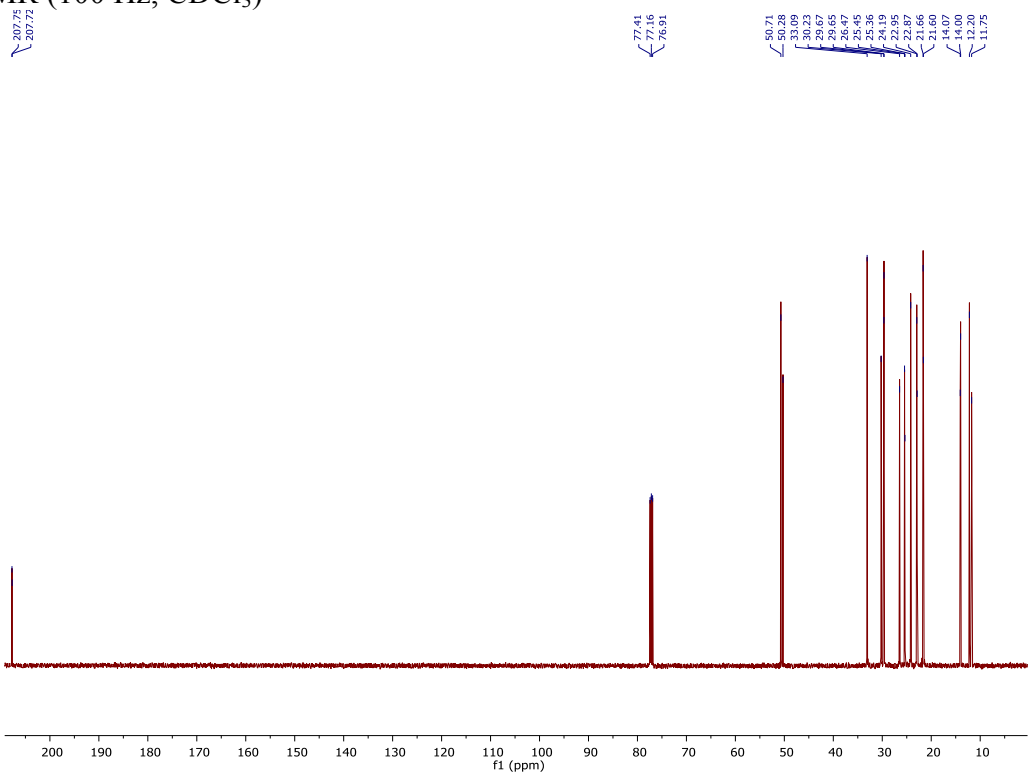


4-ethyl-2-iodooctan-3-one (3b)

^{1}H NMR (400 Hz, $CDCl_3$)

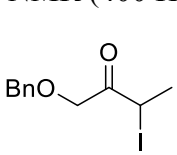


^{13}C NMR (100 Hz, $CDCl_3$)

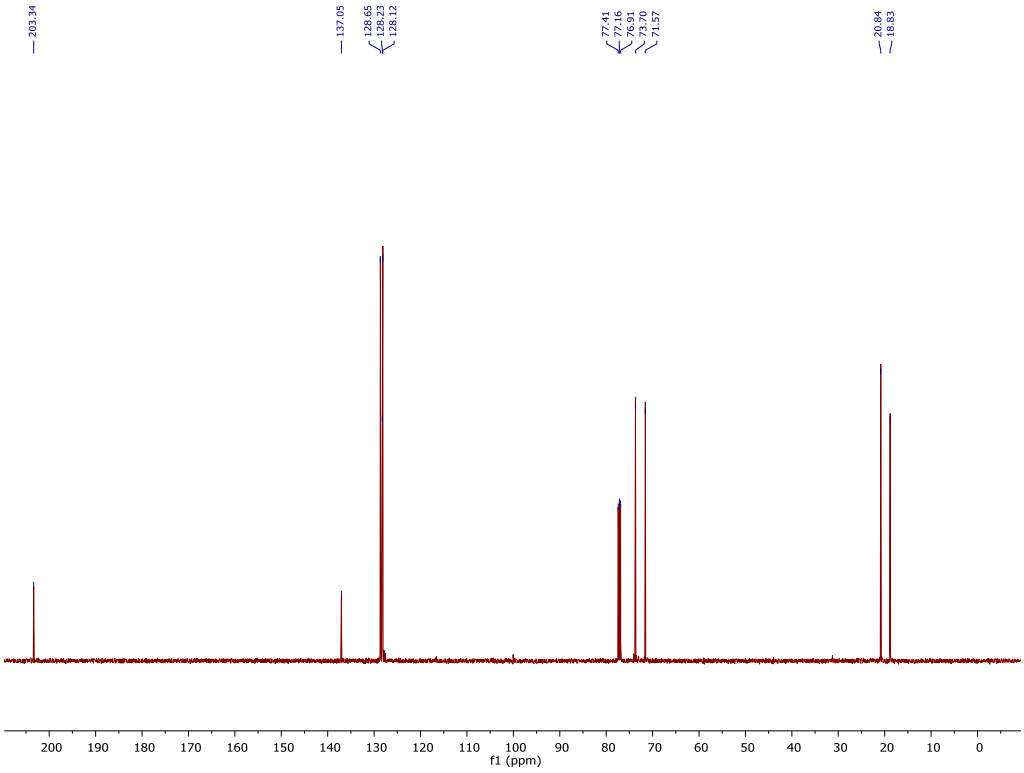


4-ethyl-2-iodooctan-3-one (3c)

^{1}H NMR (400 Hz, $CDCl_3$)

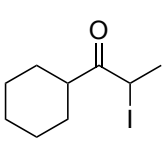


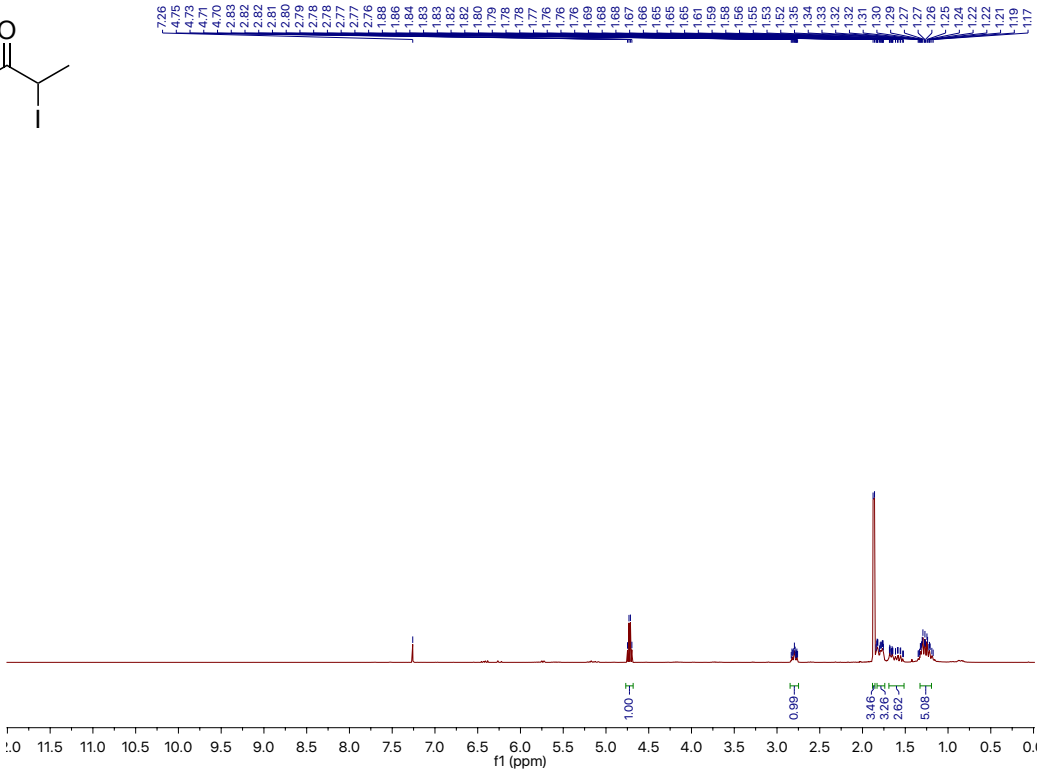
^{13}C NMR (100 Hz, $CDCl_3$)



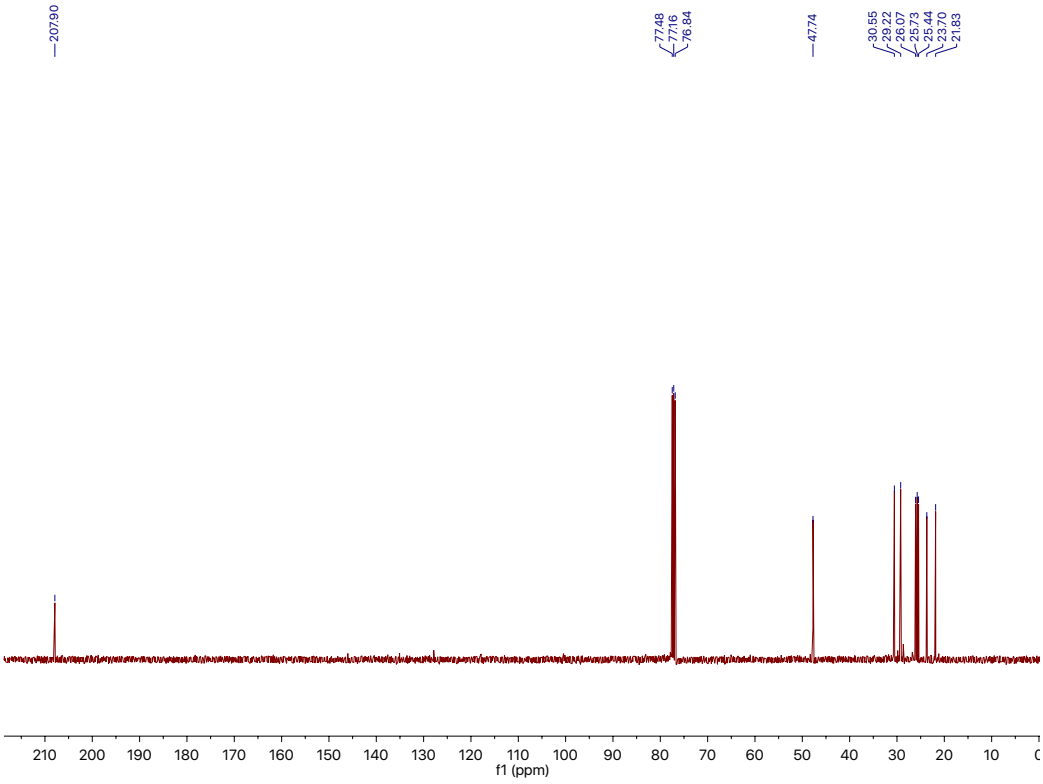
1-cyclohexyl-2-iodopropan-1-one (3d)

^{1}H NMR (400 Hz, $CDCl_3$)



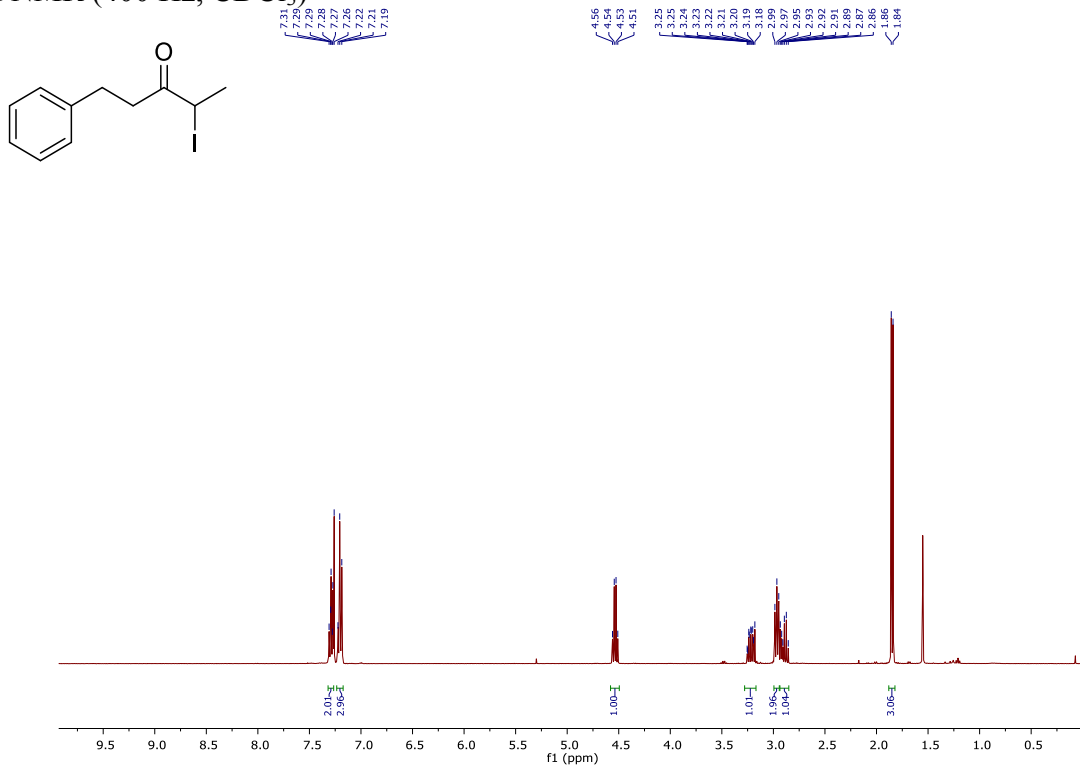


^{13}C NMR (100 Hz, $CDCl_3$)

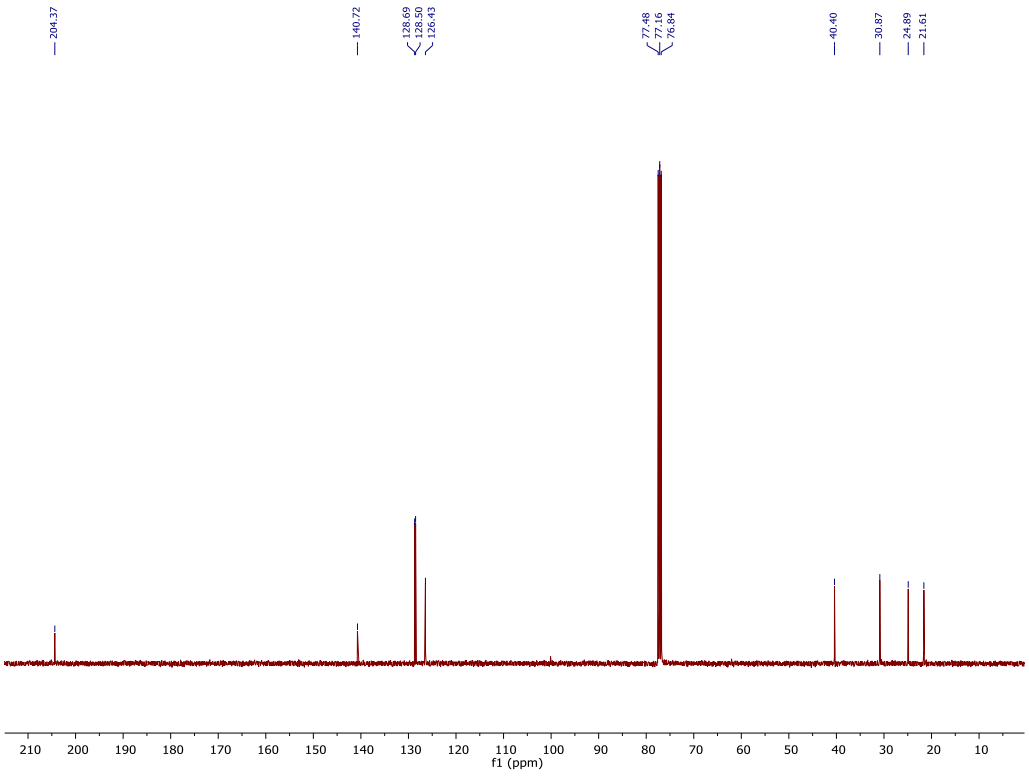


4-iodo-1-phenylpentan-3-one (3e)

^{1}H NMR (400 Hz, $CDCl_3$)

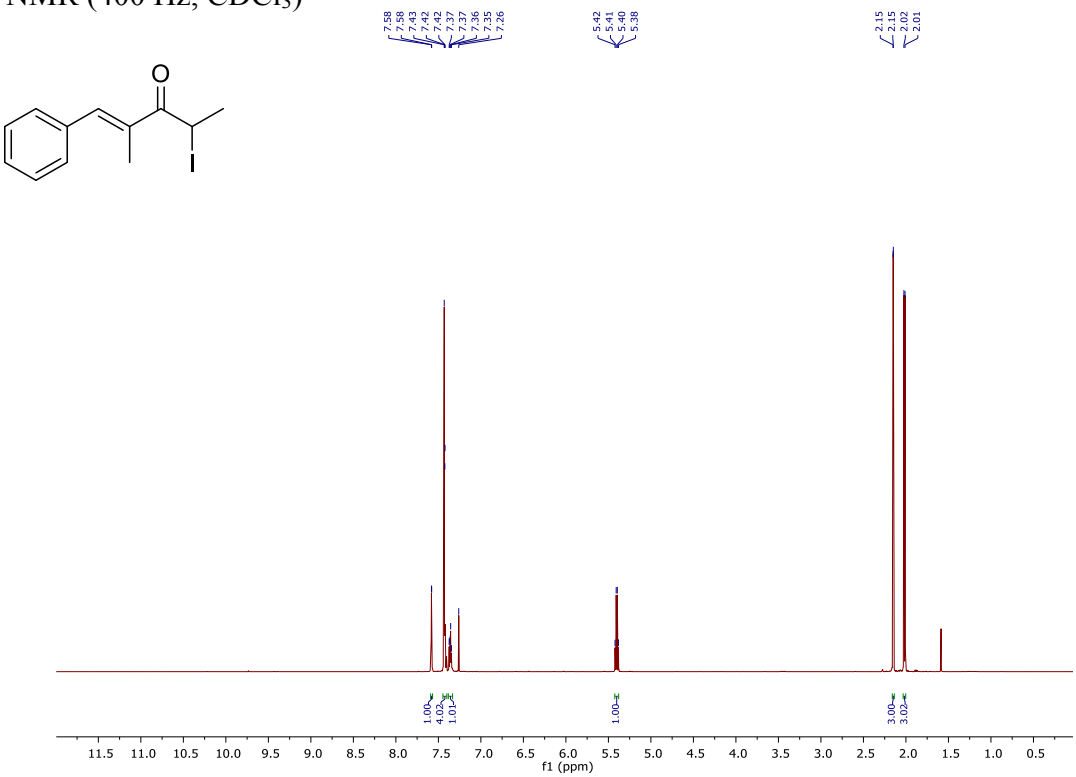


^{13}C NMR (100 Hz, $CDCl_3$)

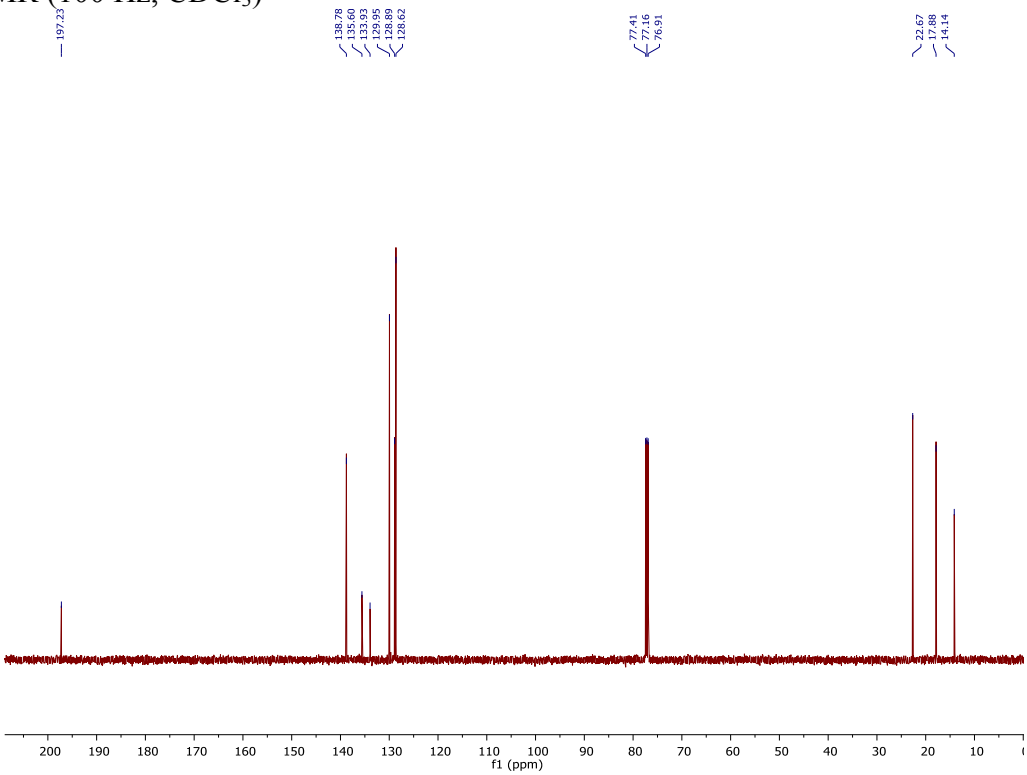


(*E*)-4-iodo-2-methyl-1-phenylpent-1-en-3-one (3f)

^{1}H NMR (400 Hz, $CDCl_3$)

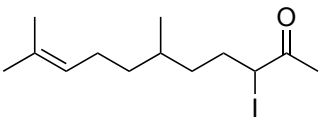


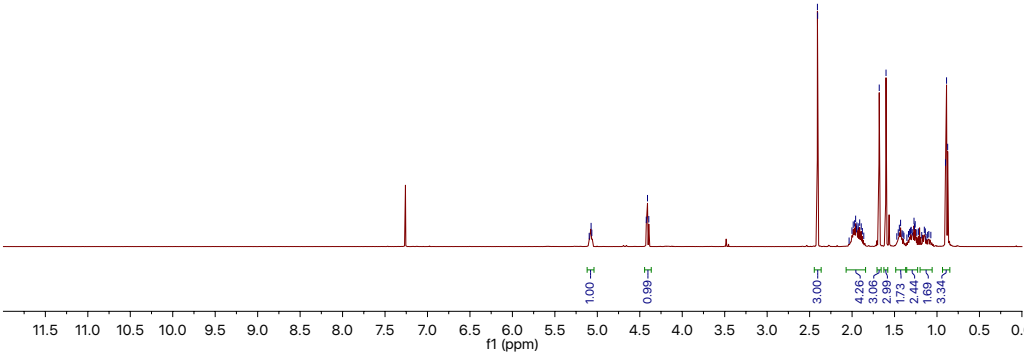
^{13}C NMR (100 Hz, $CDCl_3$)



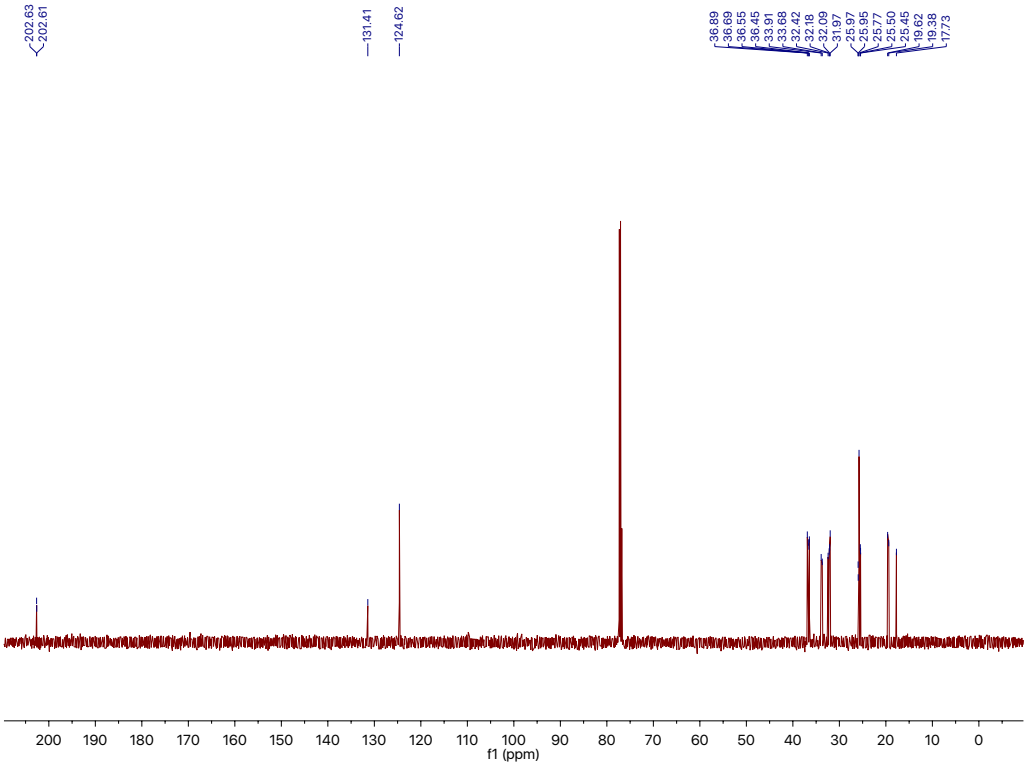
3-iodo-6,10-dimethylundec-9-en-2-one (3g)

^{1}H NMR (400 Hz, $CDCl_3$)



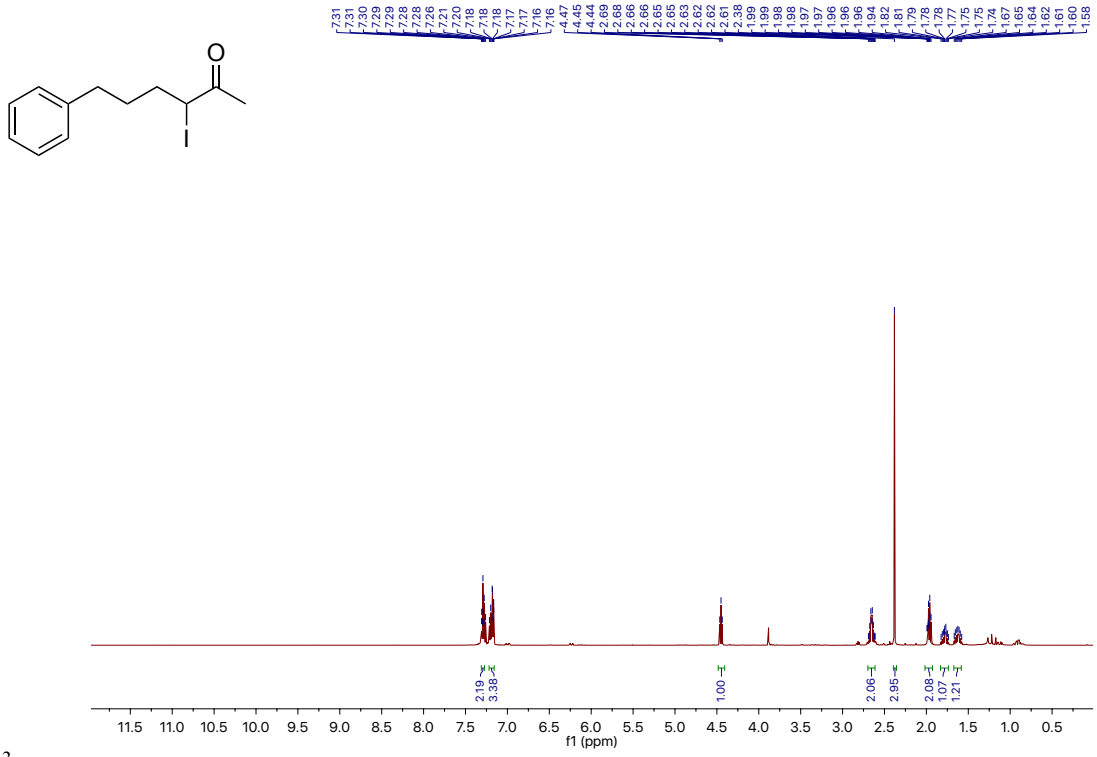


^{13}C NMR (100 Hz, $CDCl_3$)

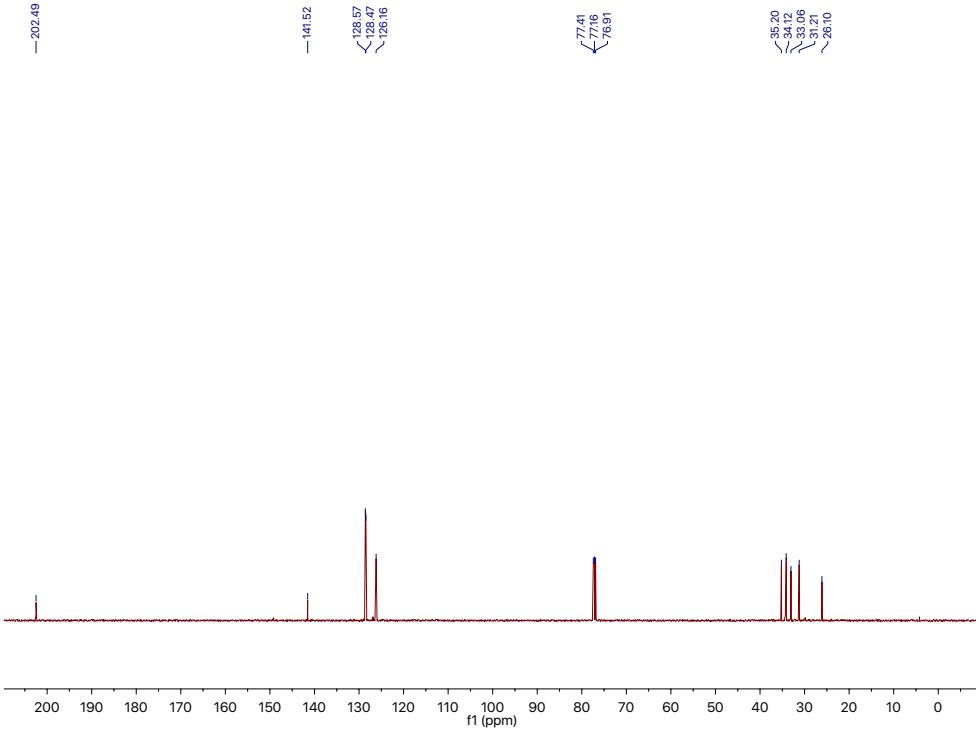


3-iodo-6-phenylhexan-2-one (3h)

^{1}H NMR (400 Hz, $CDCl_3$)

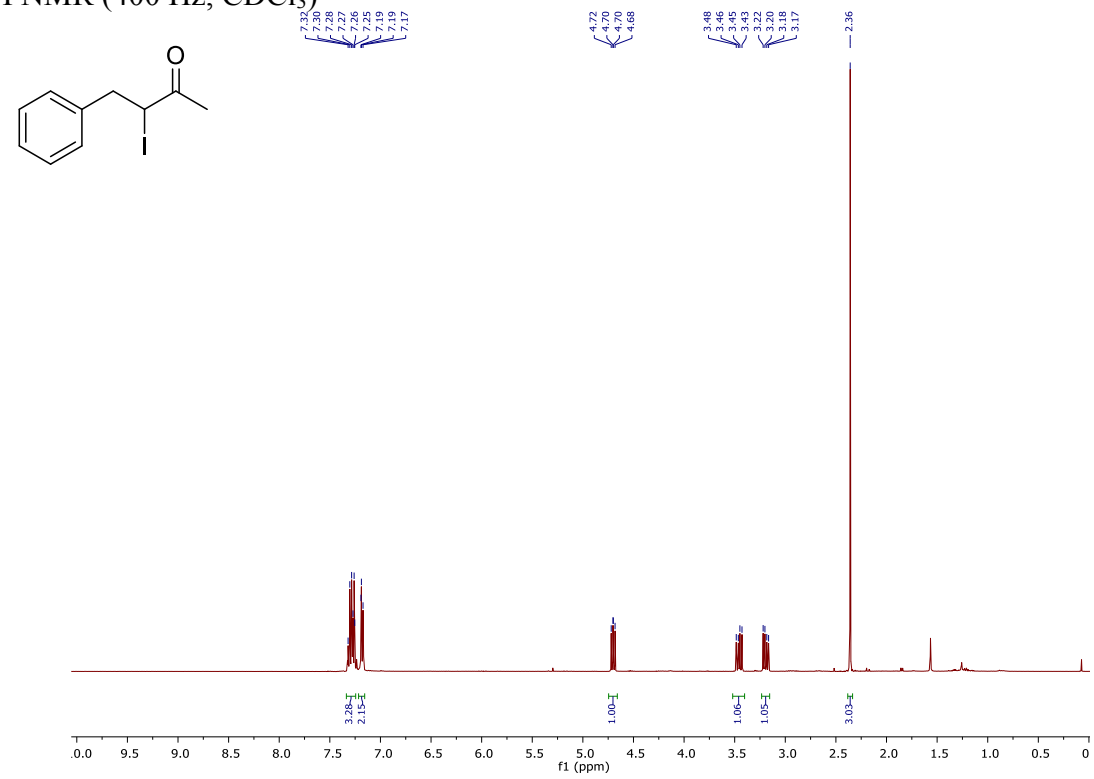


^{13}C NMR (100 Hz, $CDCl_3$)

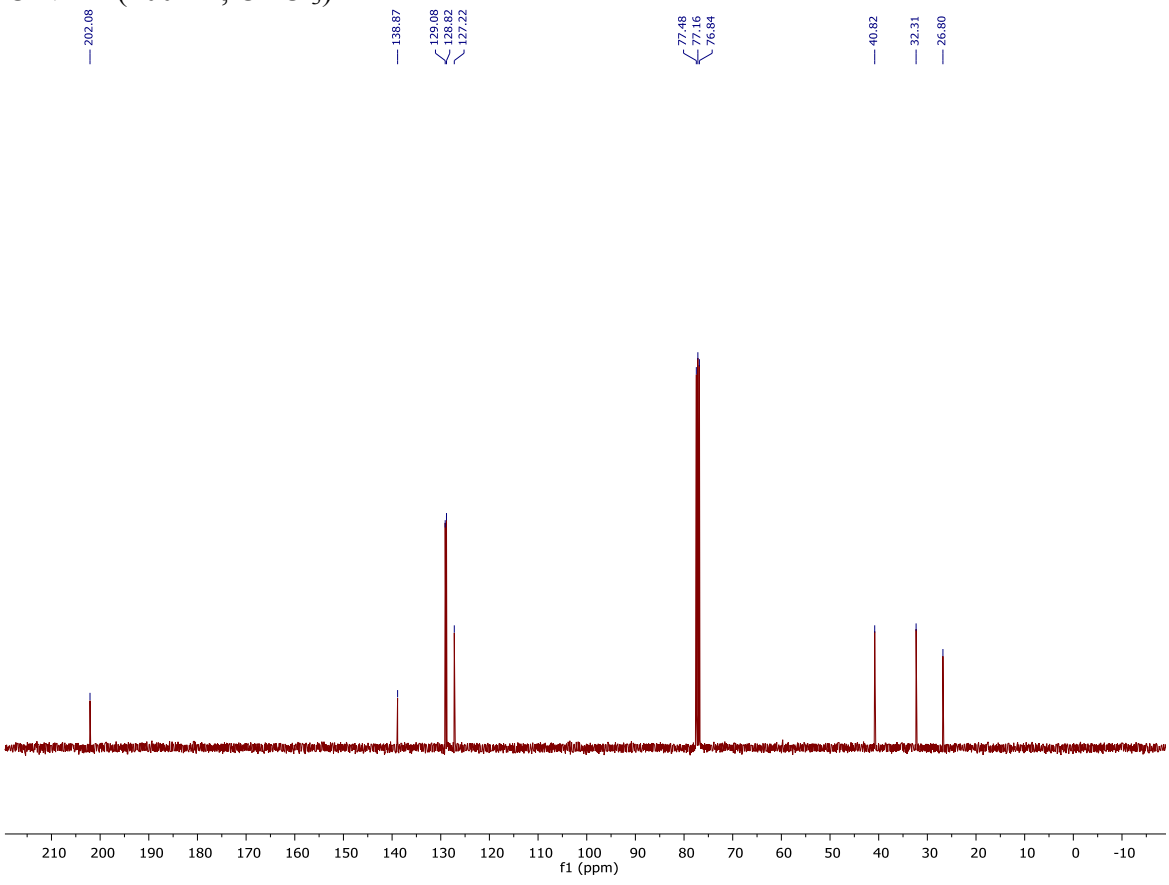


3-iodo-4-phenylbutan-2-one (3i)

^{1}H NMR (400 Hz, $CDCl_3$)

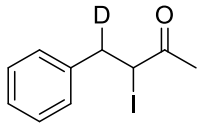


^{13}C NMR (100 Hz, $CDCl_3$)

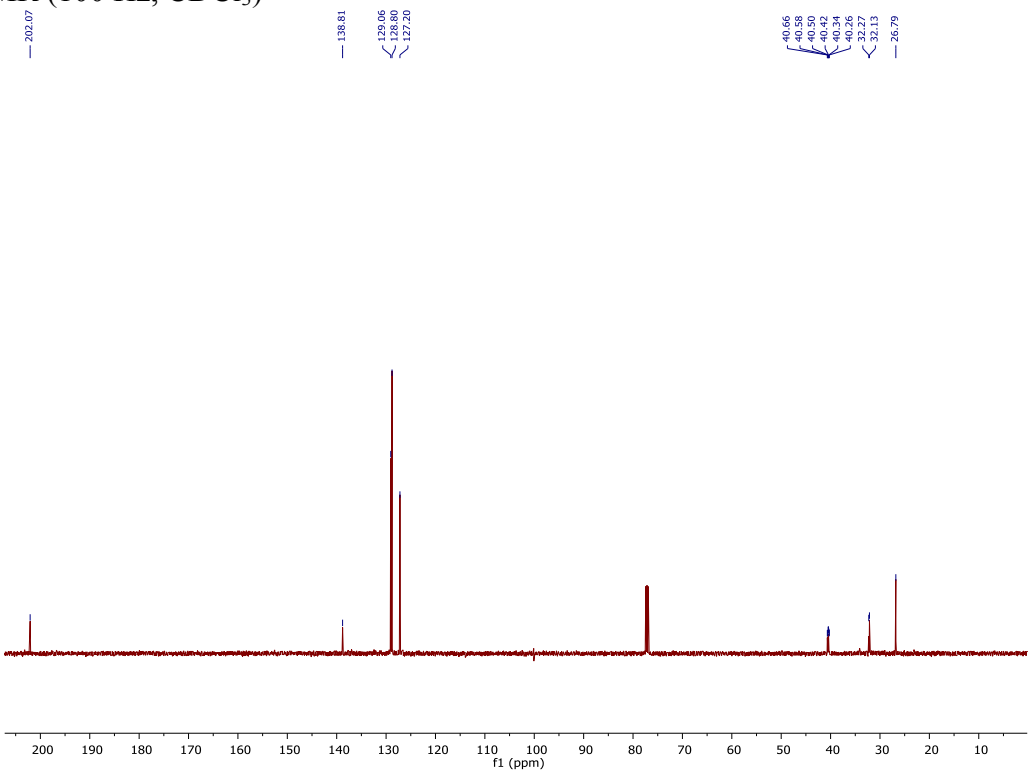


4-*d*-3-iodo-4-phenylbutan-2-one (3i-d_1)

^{1}H NMR (400 Hz, $CDCl_3$)

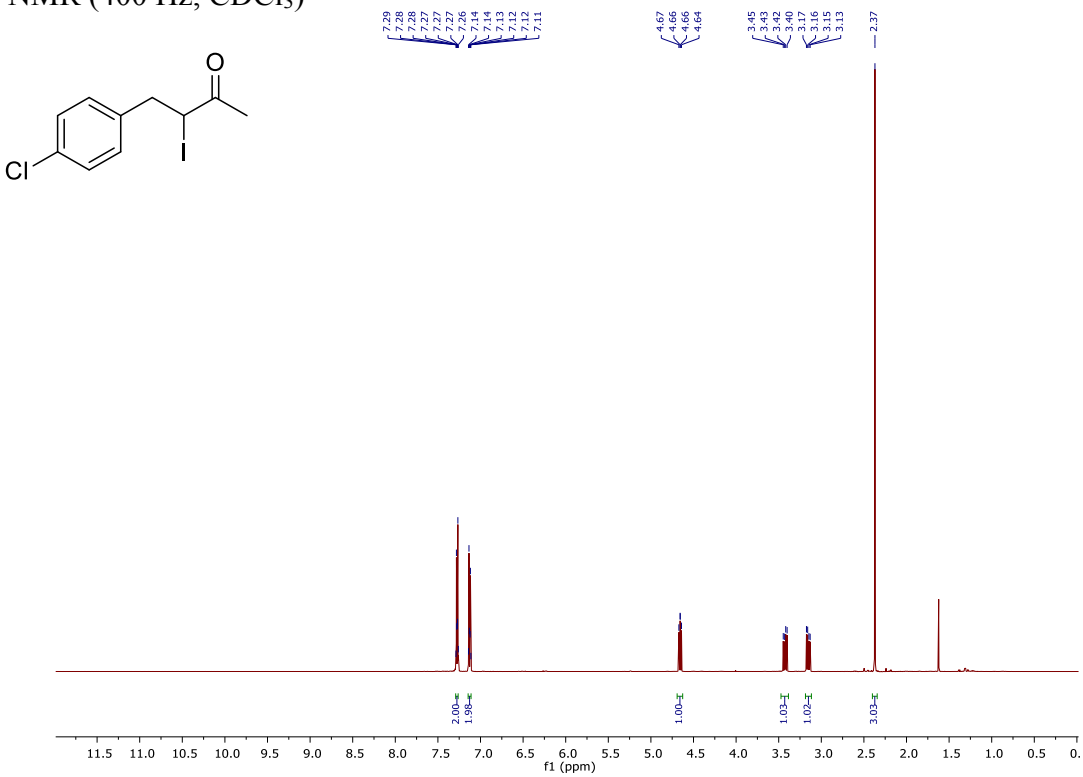


^{13}C NMR (100 Hz, $CDCl_3$)

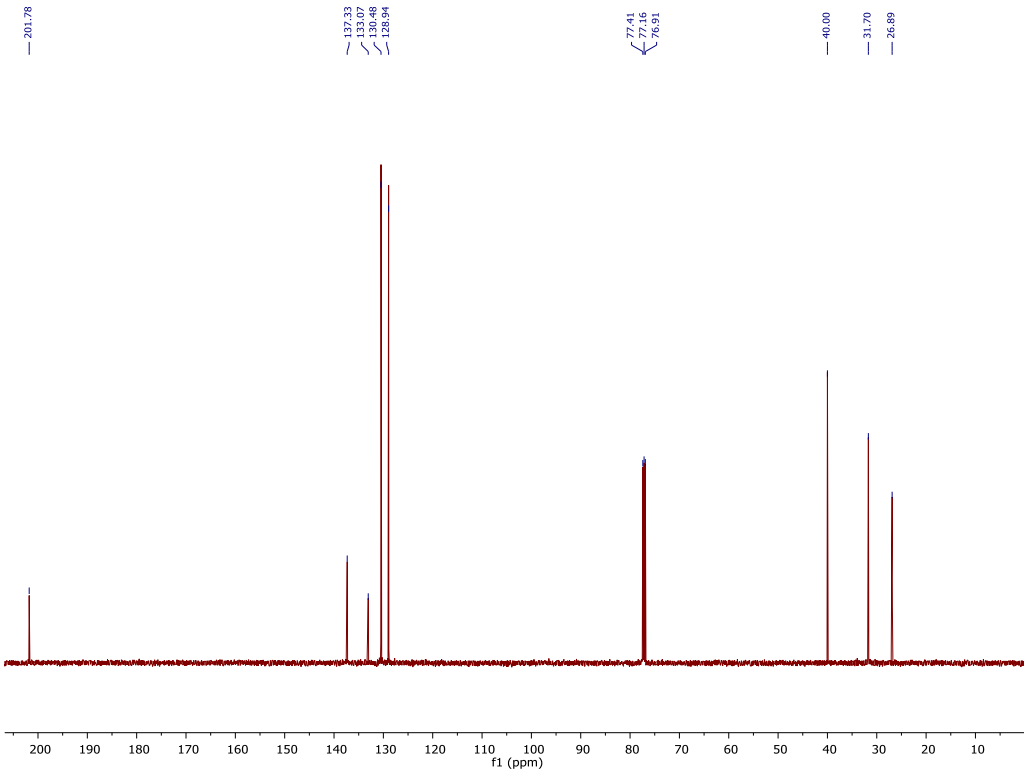


4-(4-chlorophenyl)-3-iodobutan-2-one (3j)

^{1}H NMR (400 Hz, $CDCl_3$)

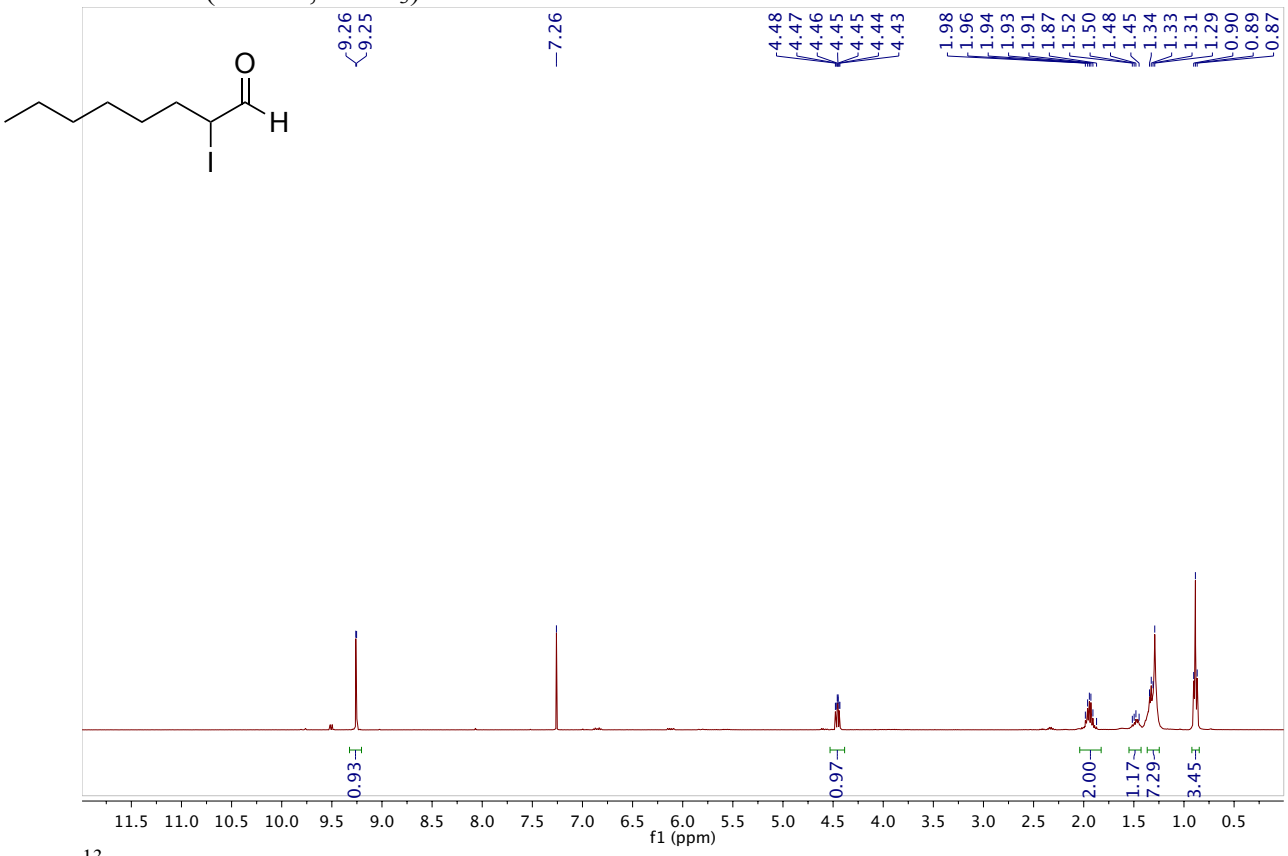


^{13}C NMR (100 Hz, $CDCl_3$)

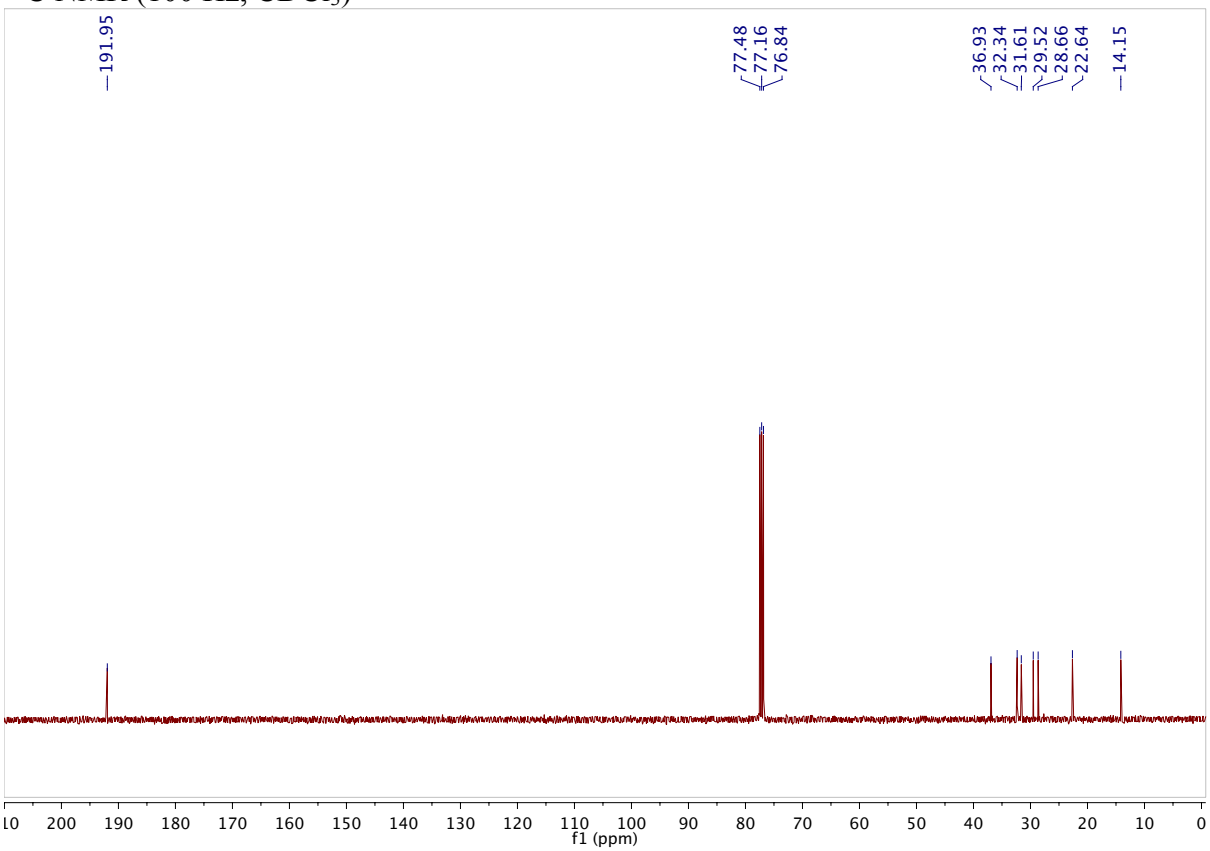


2-iodooctanal (3n)

^{1}H NMR (400 Hz, $CDCl_3$)

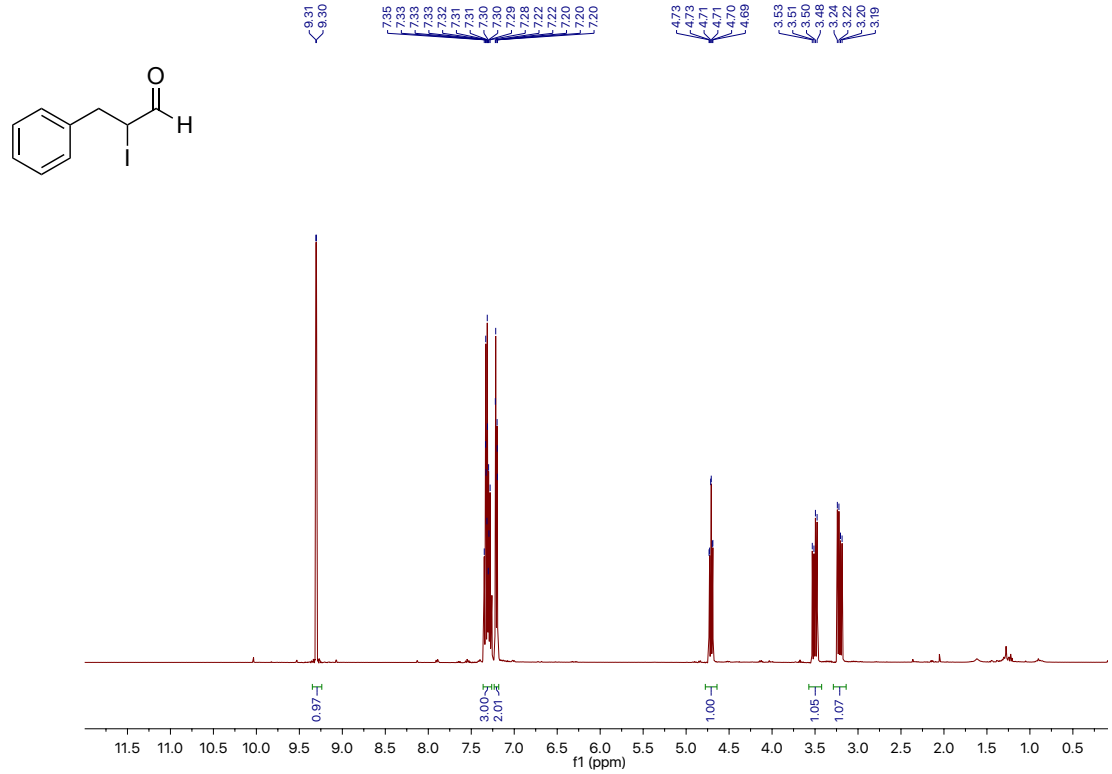


^{13}C NMR (100 Hz, $CDCl_3$)

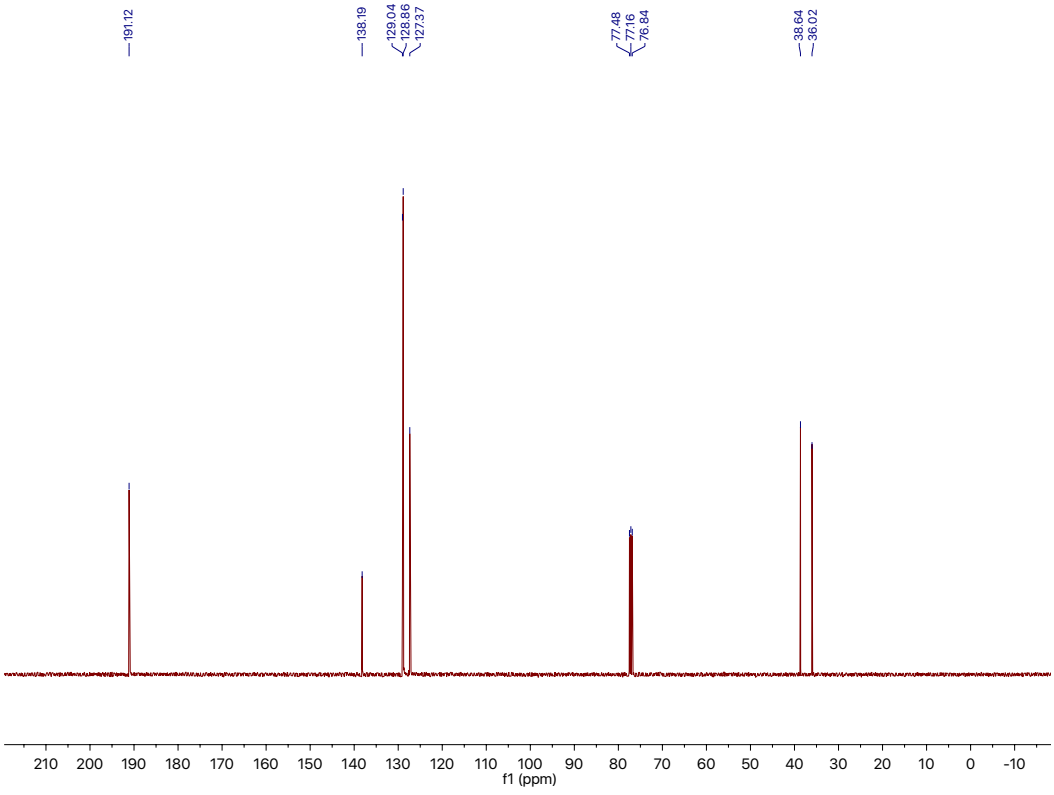


2-iodo-3-phenylpropanal (3o)

^{1}H NMR (400 Hz, $CDCl_3$)

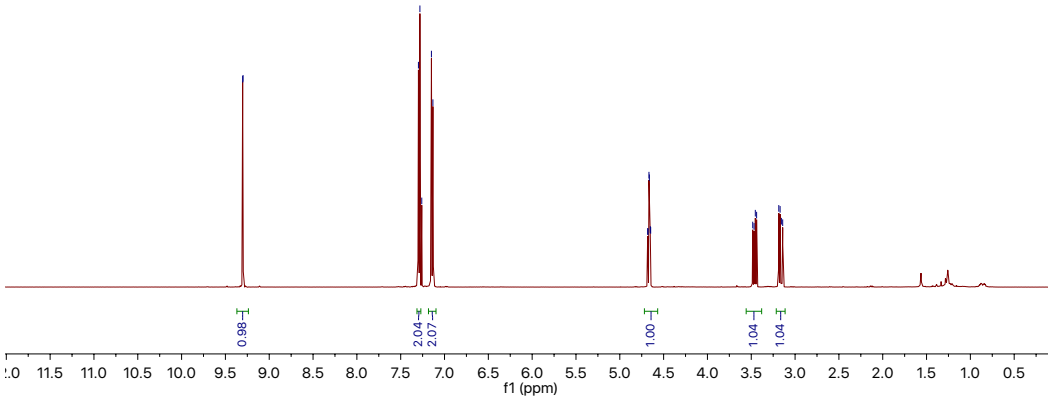


^{13}C NMR (100 Hz, $CDCl_3$)

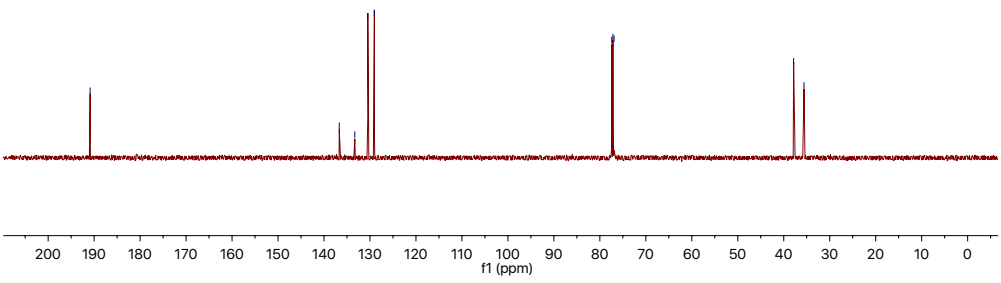


3-(4-chlorophenyl)-2-iodopropanal (3p)

^{1}H NMR (400 Hz, $CDCl_3$)

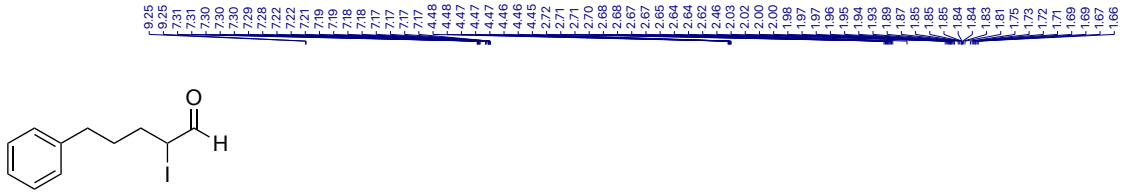


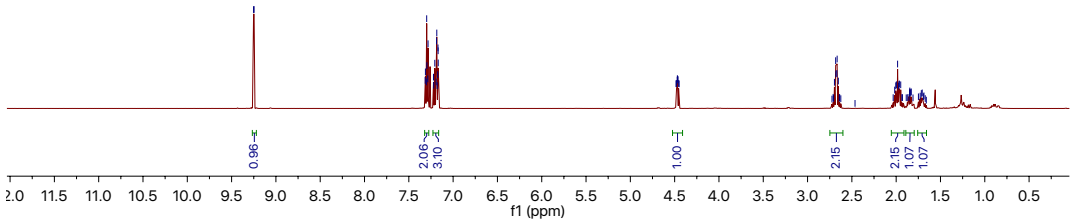
^{13}C NMR (100 Hz, $CDCl_3$)



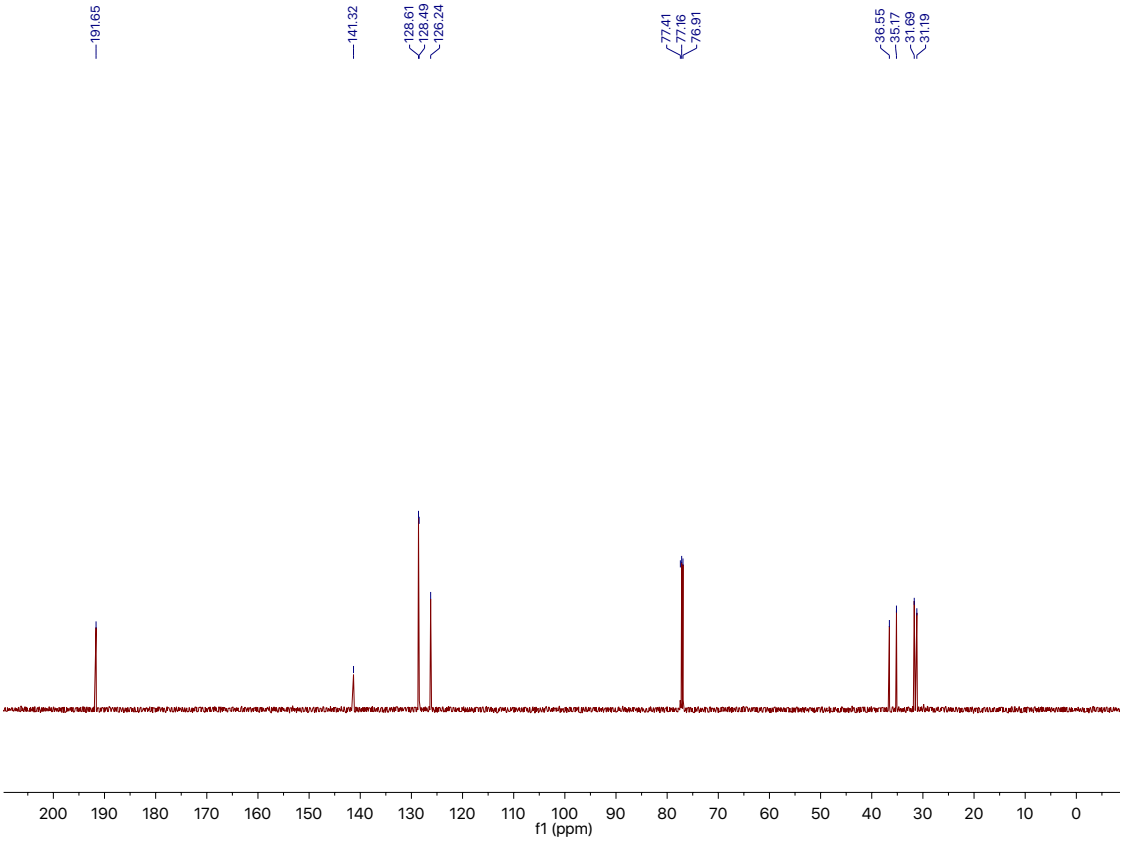
2-iodo-5-phenylpentanal (3q)

^{1}H NMR (400 Hz, $CDCl_3$)



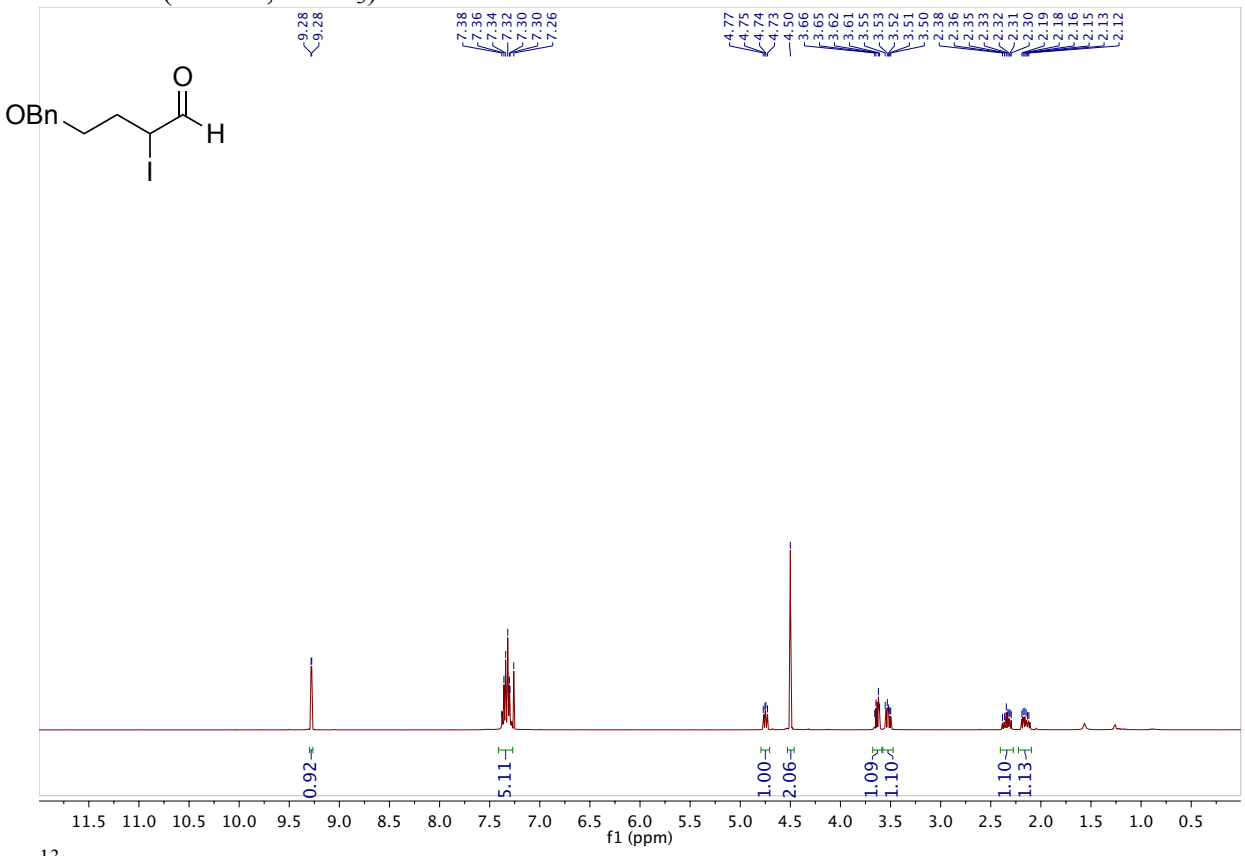


^{13}C NMR (100 Hz, $CDCl_3$)

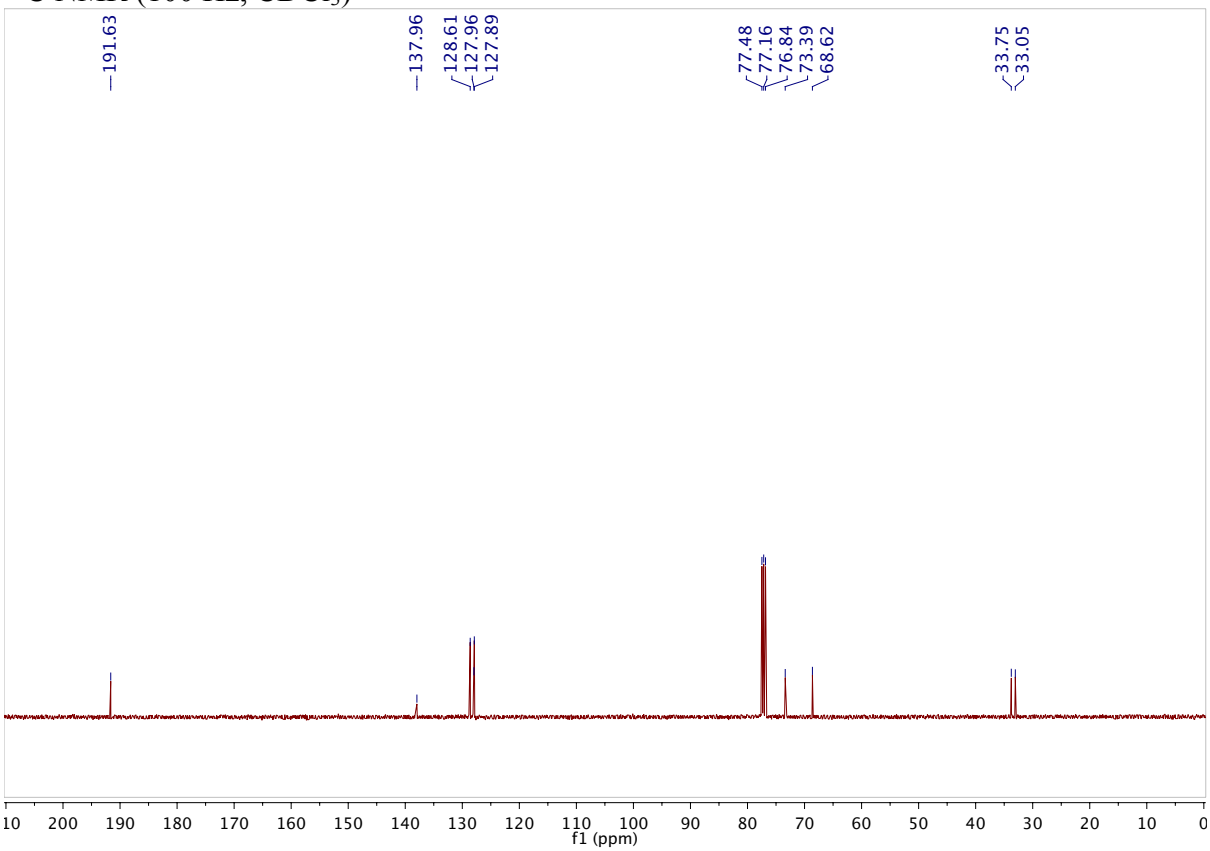


4-(benzyloxy)-2-iodobutanal (3r)

^{1}H NMR (400 Hz, $CDCl_3$)

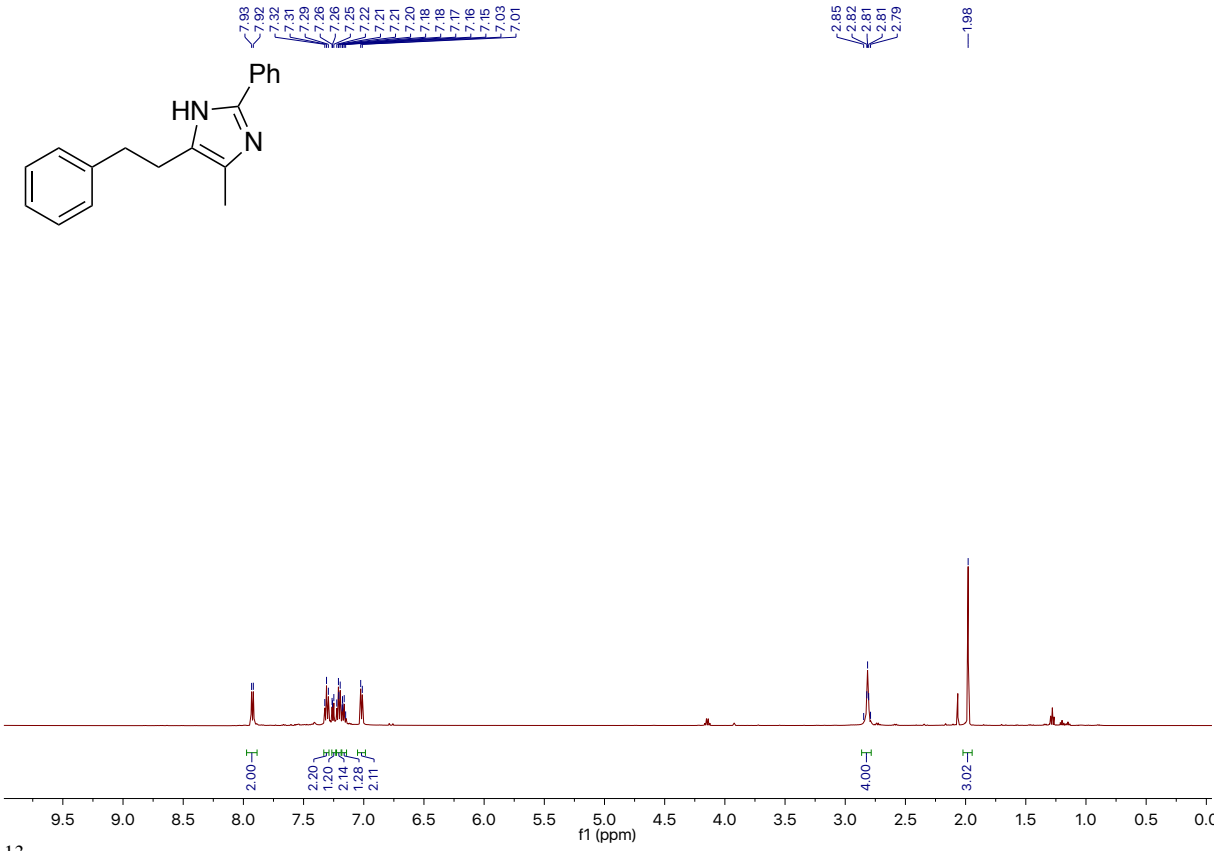


^{13}C NMR (100 Hz, $CDCl_3$)

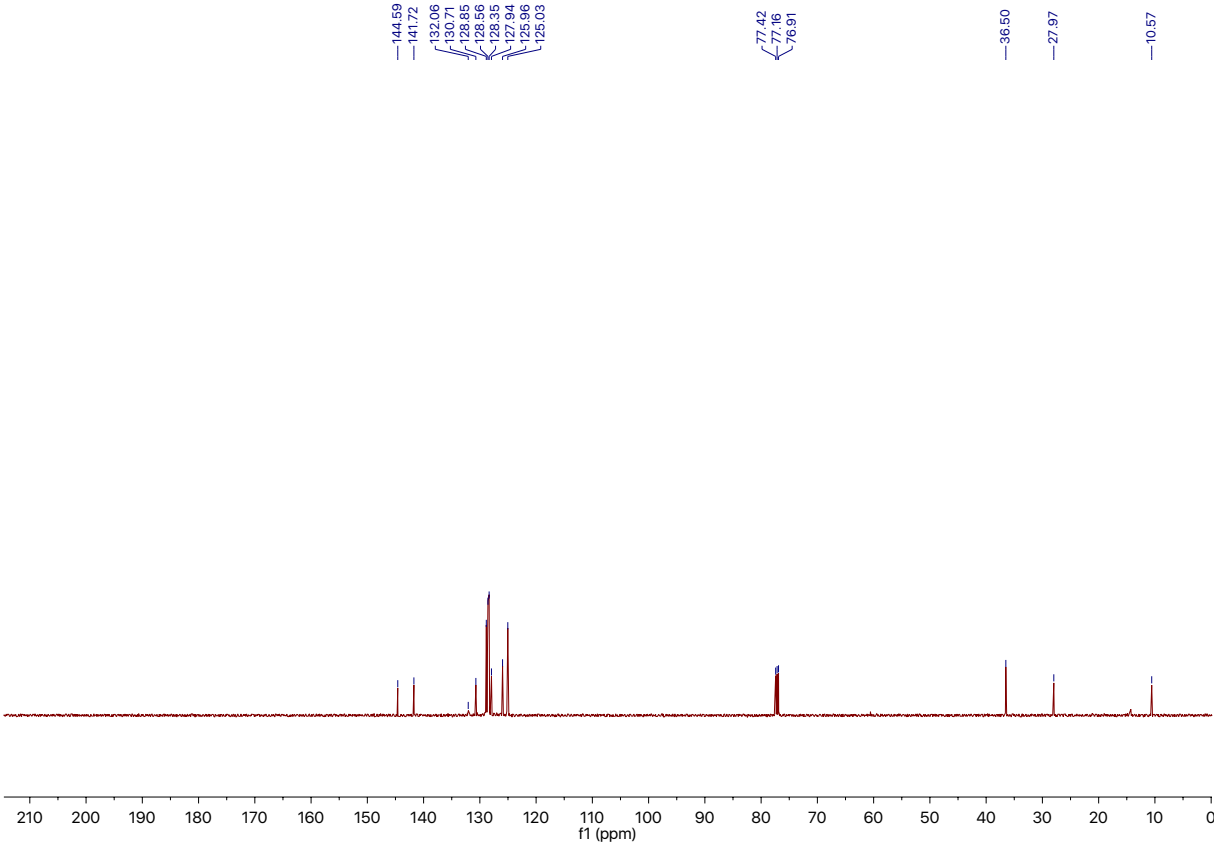


^{1}H-NMR and ^{13}C-NMR spectra of 4-methyl-5-phenethyl-2-phenyl-1*H*-imidazole (7)

^{1}H NMR (400 Hz, $CDCl_3$)

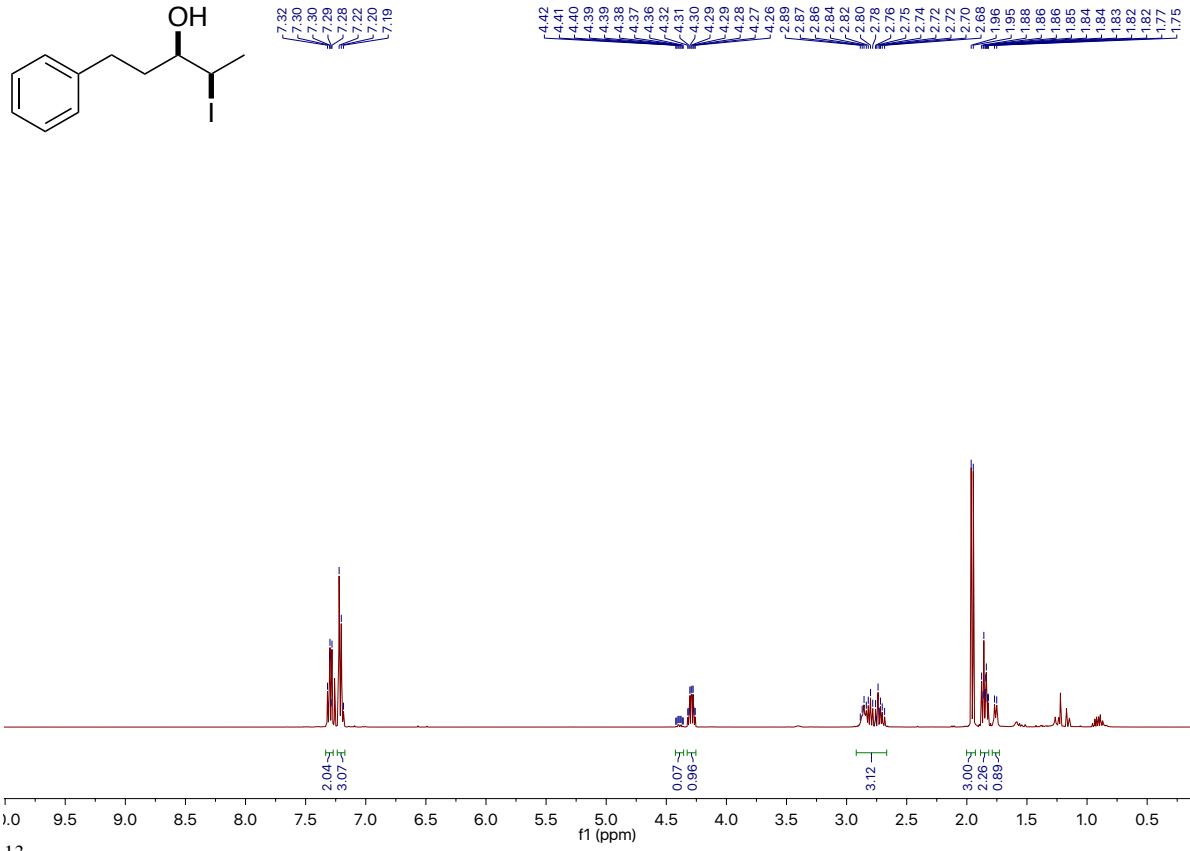


^{13}C NMR (100 Hz, $CDCl_3$)

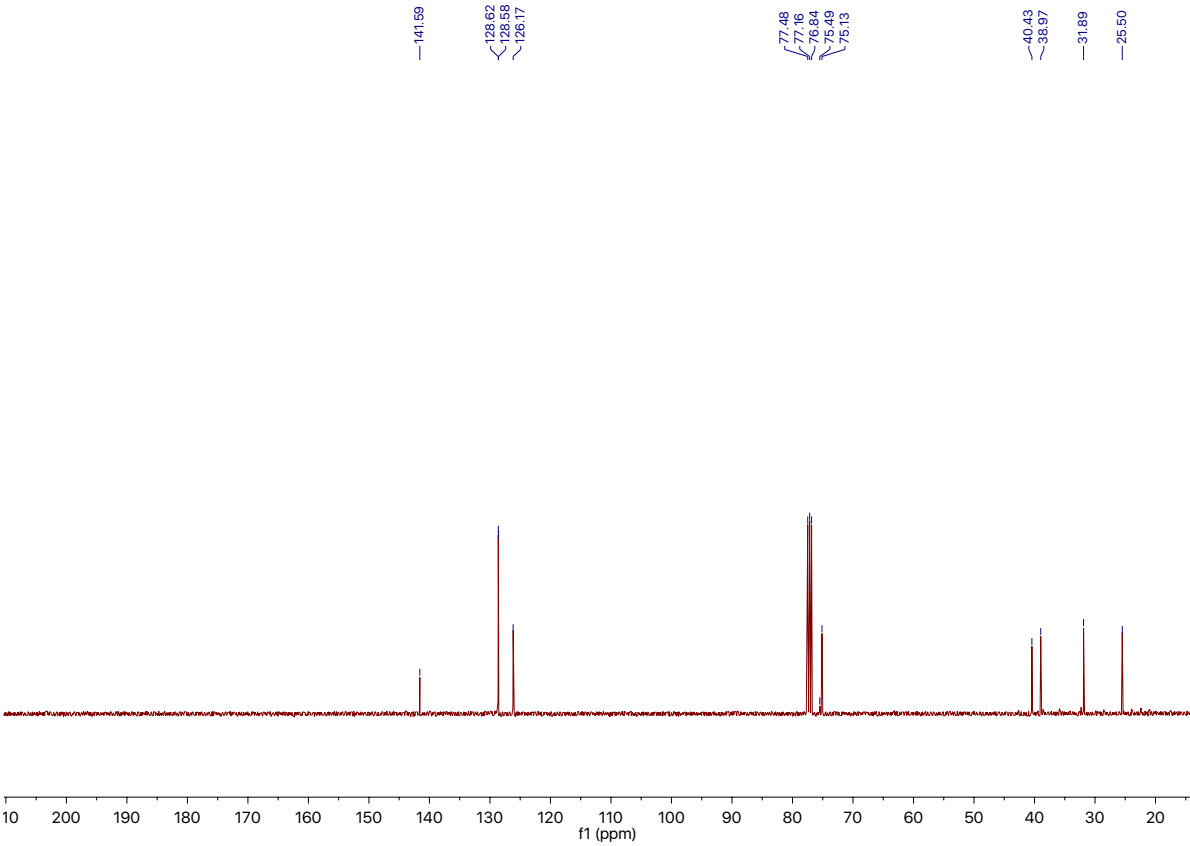


^{1}H-NMR and ^{13}C-NMR spectra of 4-iodo-1-phenylpentan-3-ol (8)

^{1}H NMR (400 Hz, $CDCl_3$)

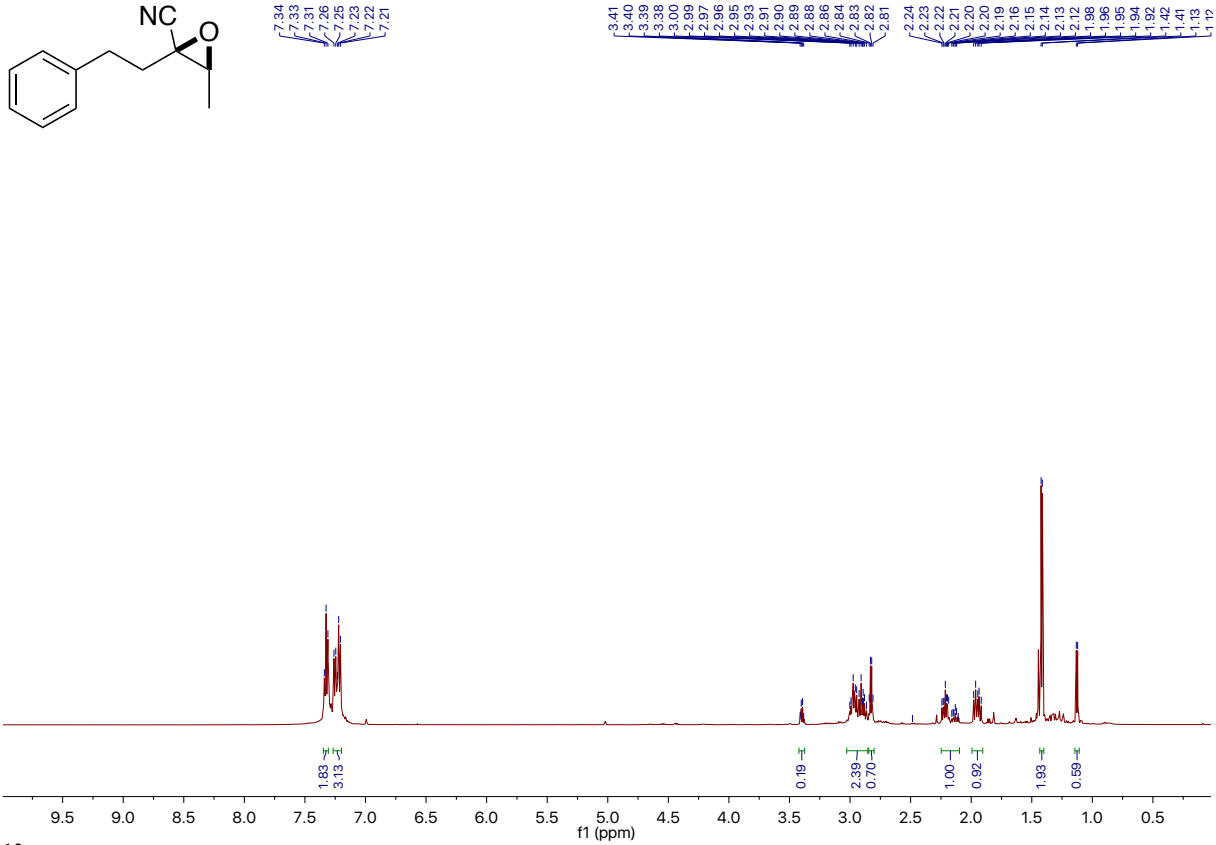


^{13}C NMR (100 Hz, $CDCl_3$)

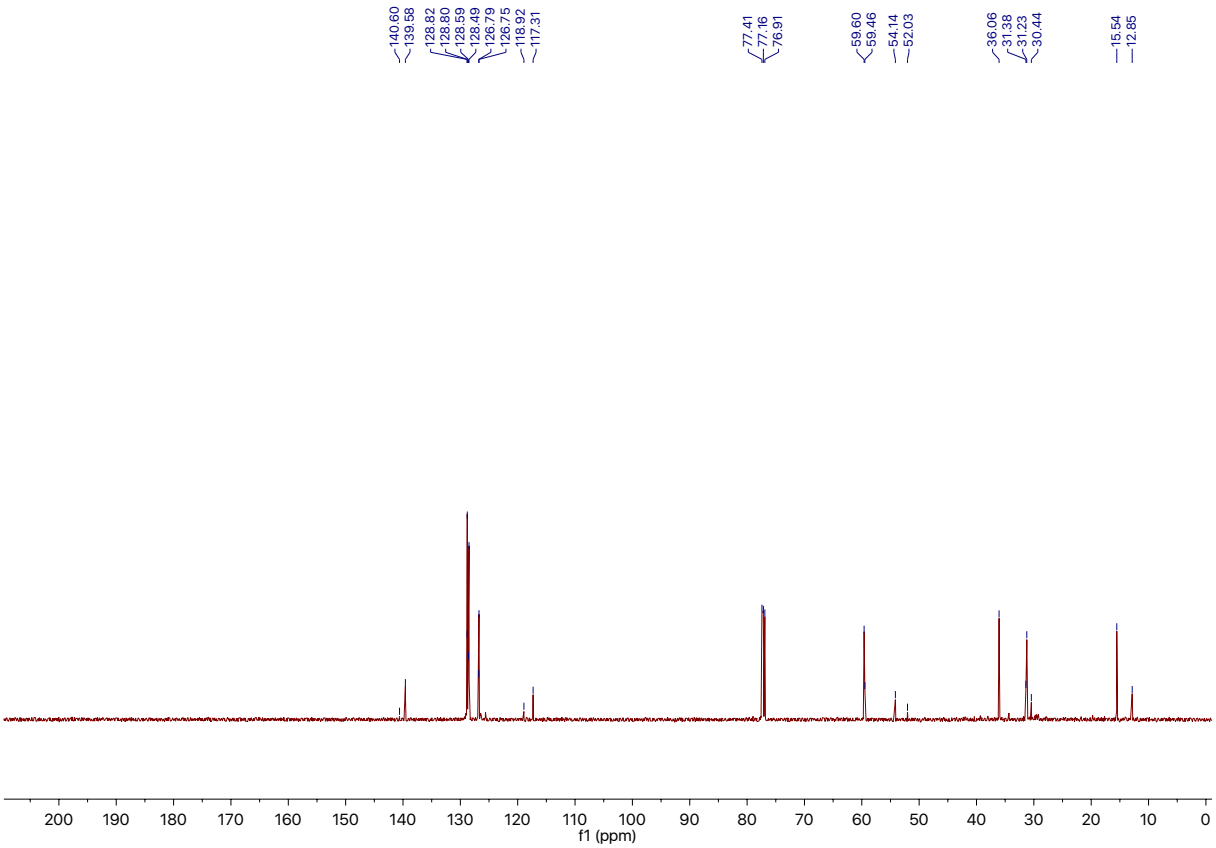


^{1}H-NMR and ^{13}C-NMR spectra of 3-methyl-2-phenethyloxirane-2-carbonitrile (10)

^{1}H NMR (400 Hz, $CDCl_3$)



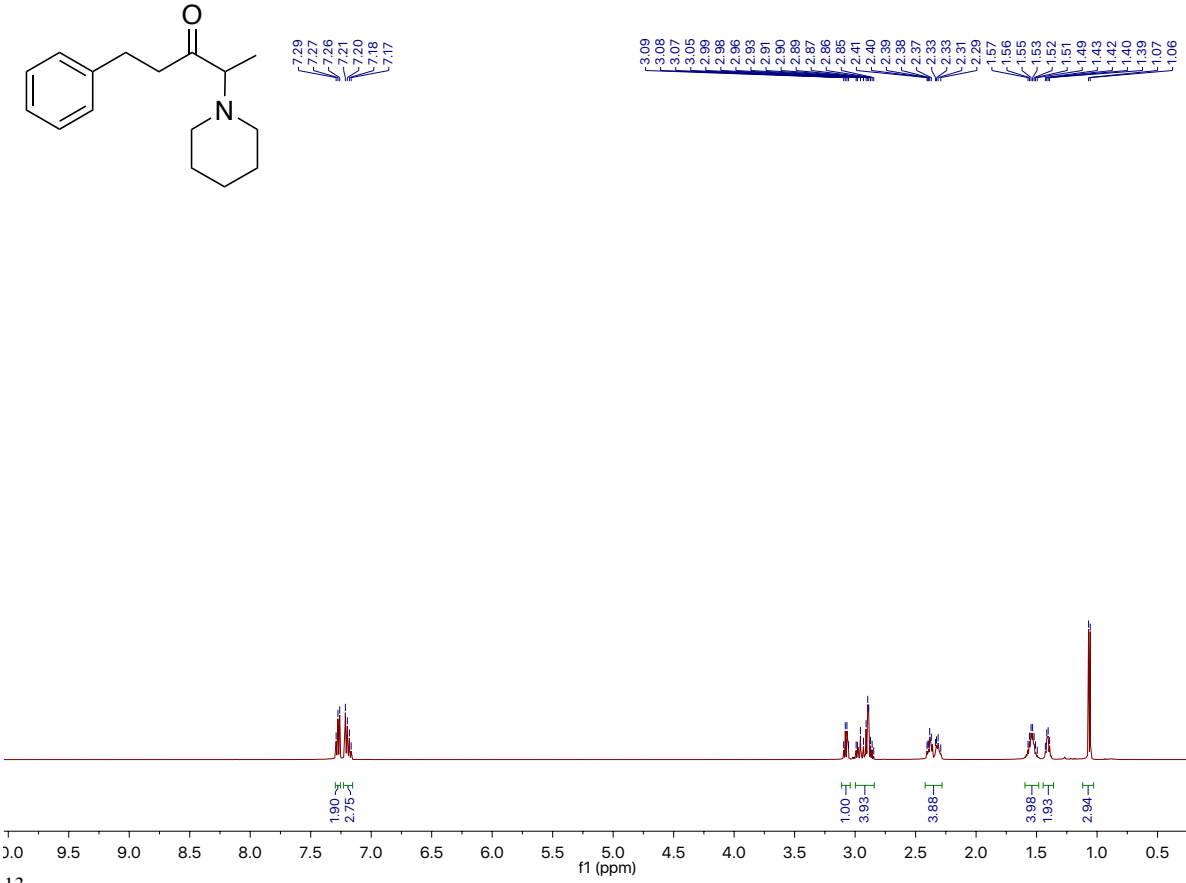
^{13}C NMR (100 Hz, $CDCl_3$)



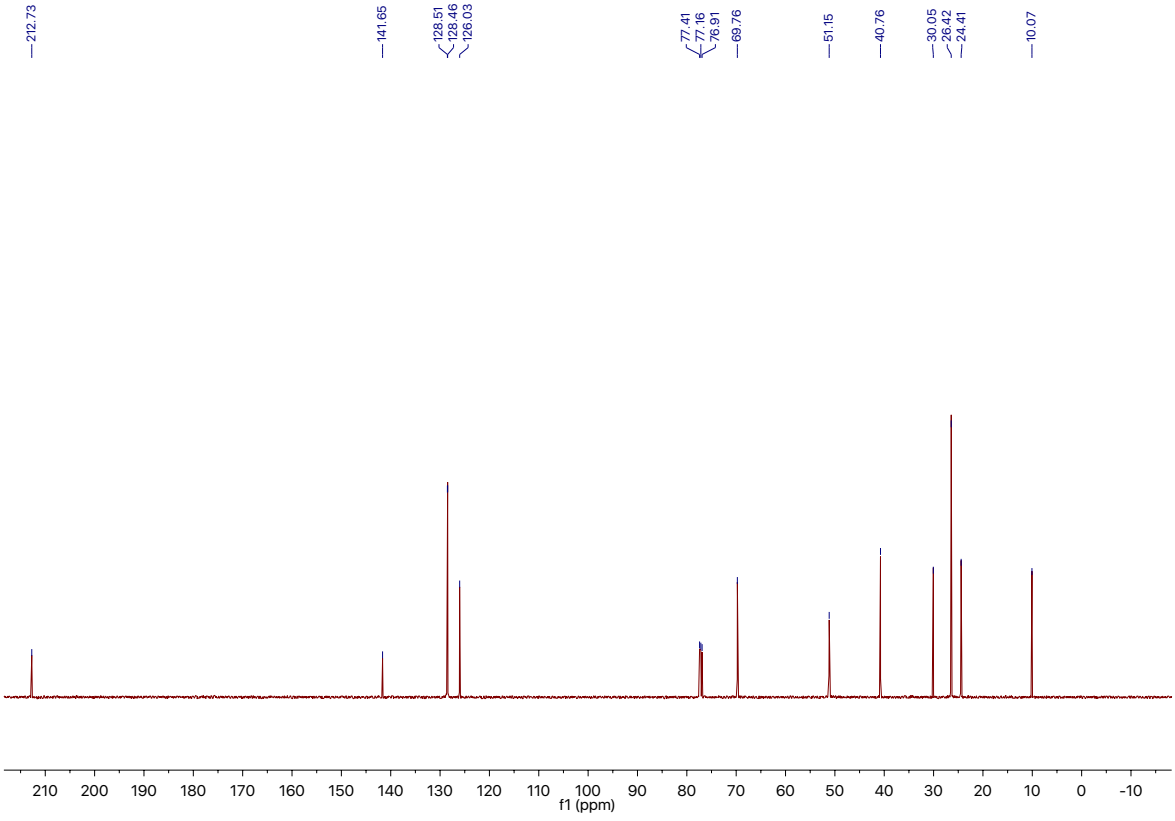
^{1}H-NMR and ^{13}C-NMR spectra of α-aminoketones 11-15

1-phenyl-4-(piperidin-1-yl)pentan-3-one (11)

^{1}H NMR (400 Hz, $CDCl_3$)

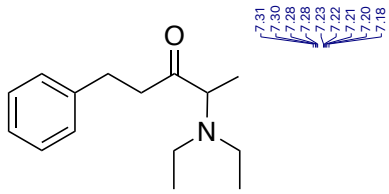


^{13}C NMR (100 Hz, $CDCl_3$)

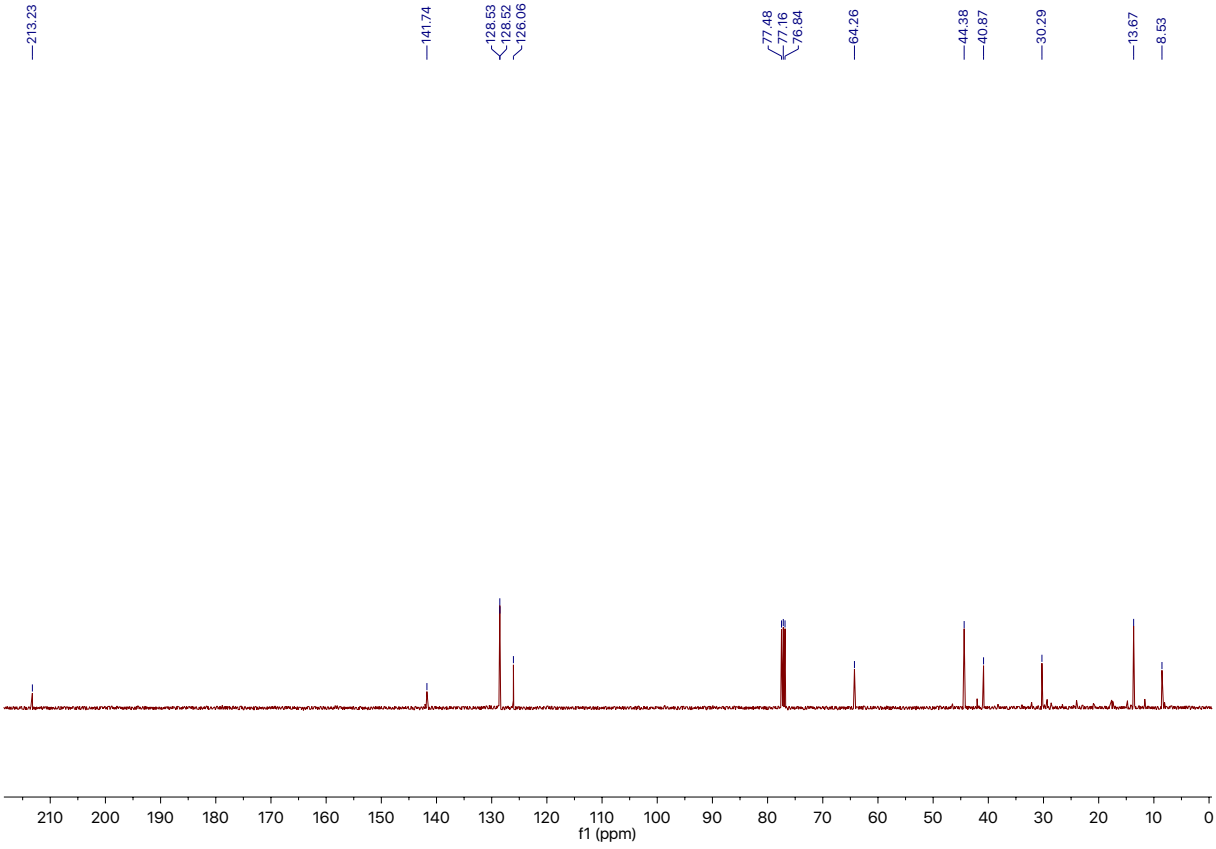


4-(diethylamino)-1-phenylpentan-3-one (12)

^{1}H NMR (400 Hz, $CDCl_3$)

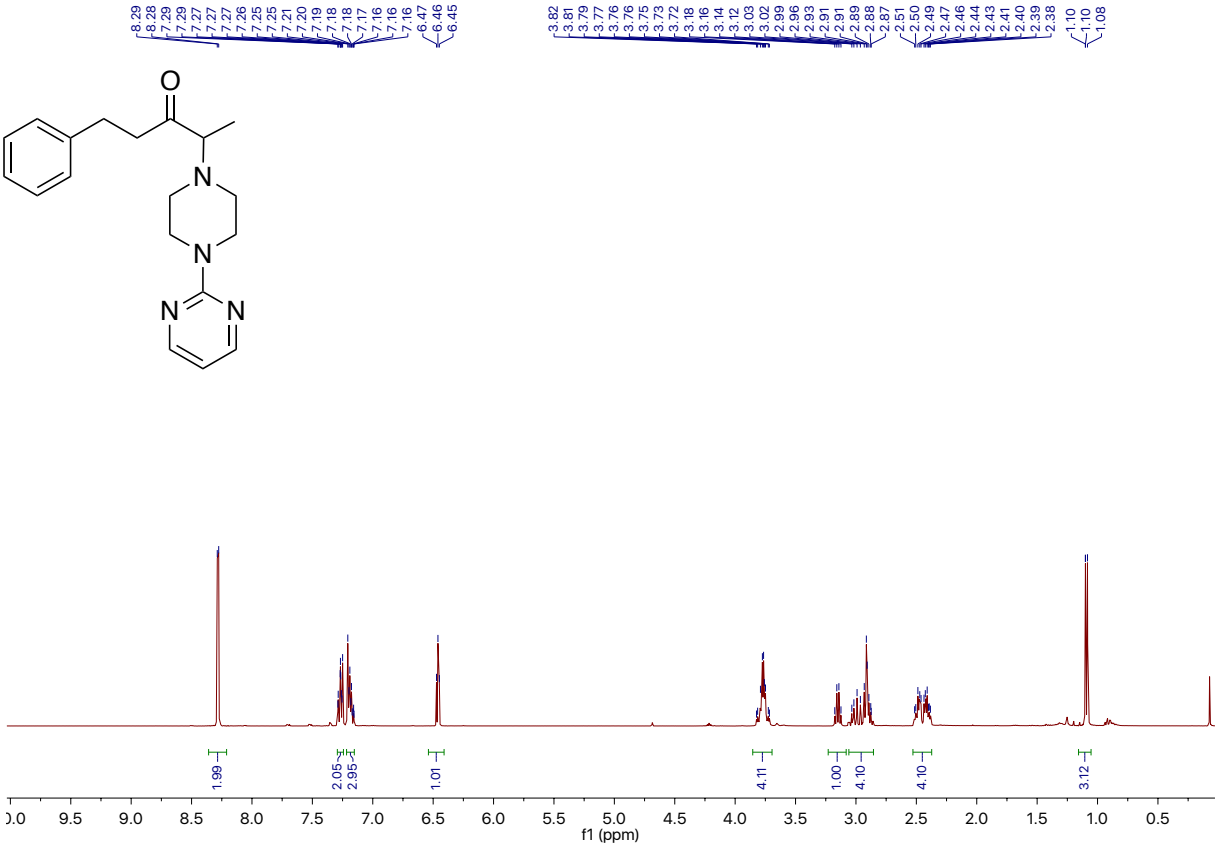


^{13}C NMR (100 Hz, $CDCl_3$)

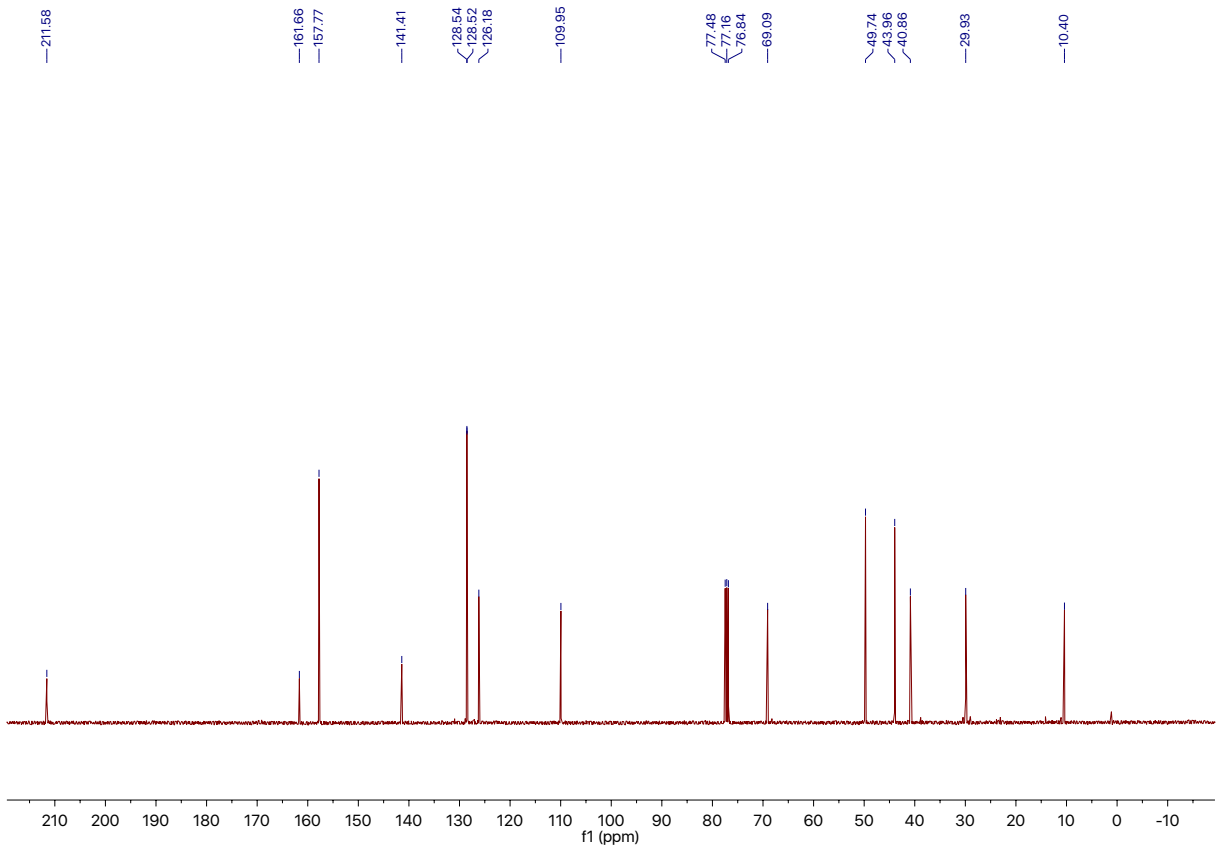


1-phenyl-4-(4-(pyrimidin-2-yl)piperazin-1-yl)pentan-3-one (13)

^{1}H NMR (400 Hz, $CDCl_3$)

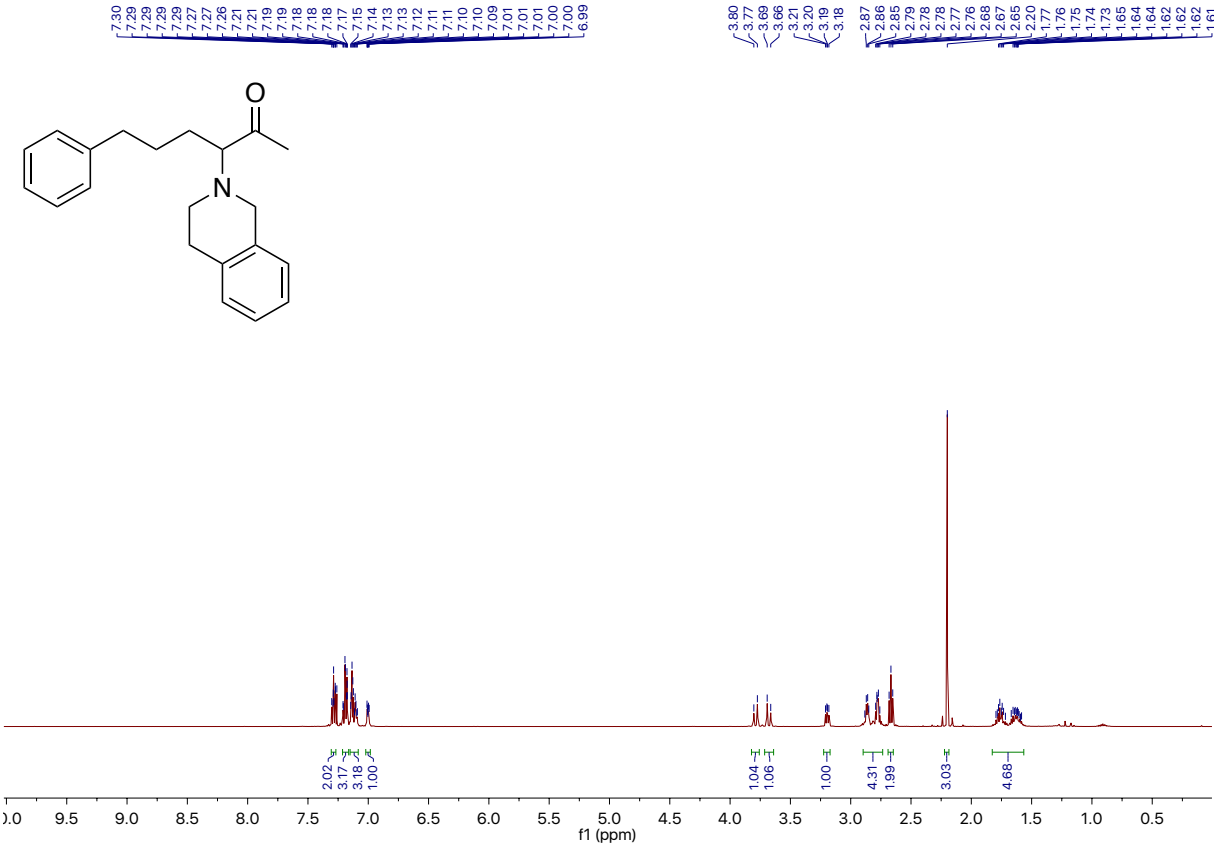


^{13}C NMR (100 Hz, $CDCl_3$)

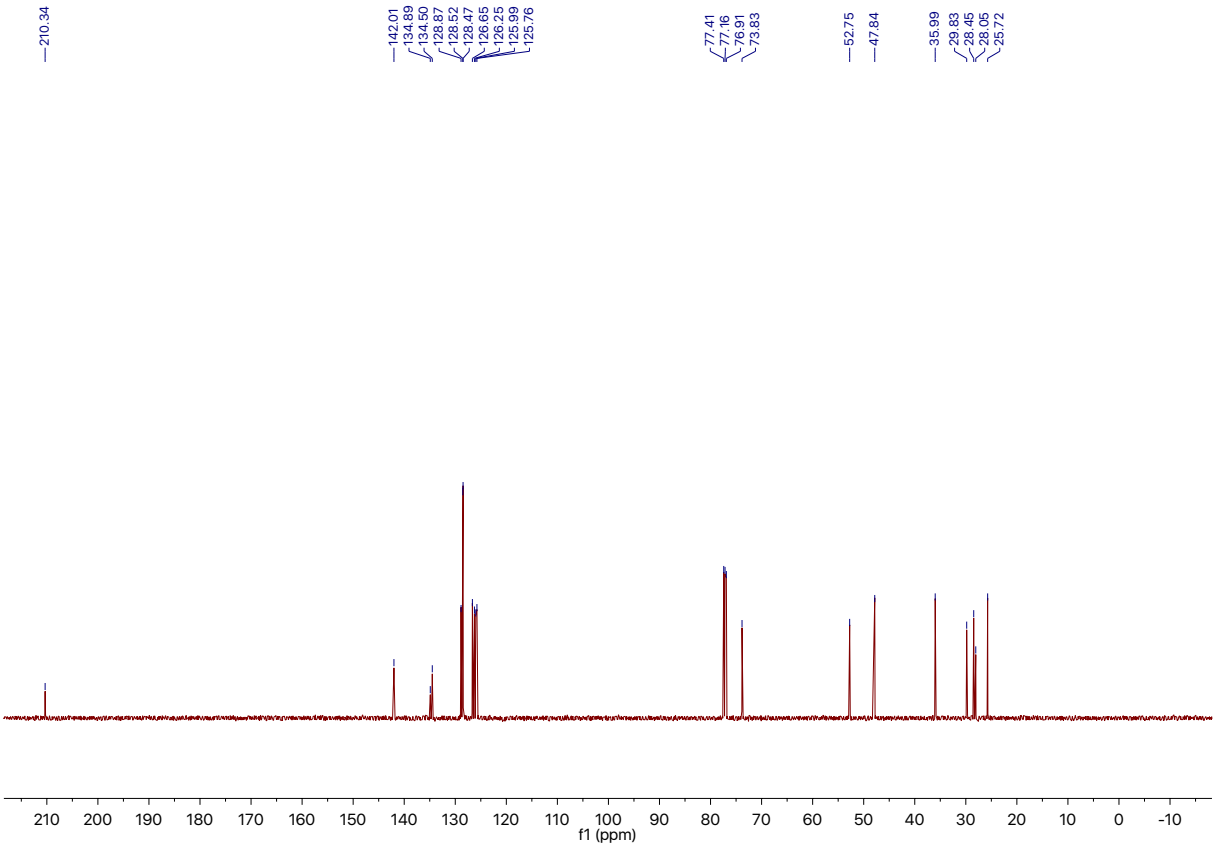


3-(3,4-dihydroisoquinolin-2(1*H*)-yl)-6-phenylhexan-2-one (14)

^{1}H NMR (400 Hz, $CDCl_3$)

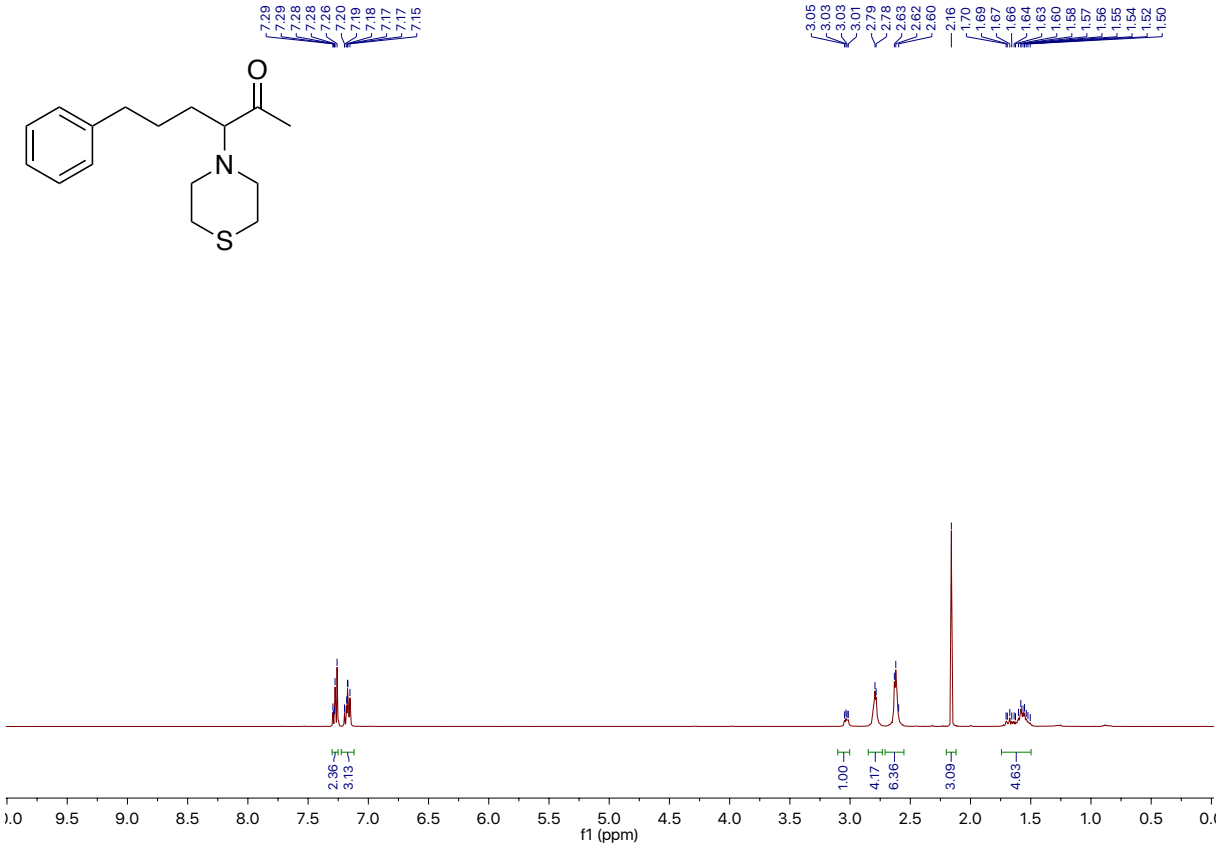


^{13}C NMR (100 Hz, $CDCl_3$)



6-phenyl-3-thiomorpholinohexan-2-one (15)

^{1}H NMR (400 Hz, $CDCl_3$)



^{13}C NMR (100 Hz, $CDCl_3$)