Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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Supplementary Information

N-Heterocyclic carbene-catalysed intermolecular Stetter reactions of acetaldehyde

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General Methods

Unless stated otherwise, reactions were carried out under a dry argon atmosphere in vacuum-flame dried glassware. Thin-layer chromatography (TLC) was performed on Merck silica gel 60 F254. Flash chromatography was performed using E. Merck silica gel (40-60 μm particle size). ^{1}H NMR spectra were recorded on a Varian at 300 MHz in $CDCl_3$ (δ 7.26 ppm) or DMSO-d_6 (δ 2.50 ppm), ^{13}C NMR spectral measurements were performed at 75 MHz using $CDCl_3$ (δ 77.16 ppm) or DMSO-d_6 (δ 39.52 ppm). The terms m, s, d, t, q, quint., and sept. represent multiplet, singlet, doublet, triplet, quadruplet, quintuplet, and septet, respectively, and the term br means a broad signal. Analytical high performance liquid chromatography (HPLC) was performed on Varian 210 using the indicated chiral column. Infrared spectra were recorded on a Bruker Vertex 70. HRMS were recorded on JEOL JMS-SX102A mass spectrometer with EI or FAB resource. Optical rotations were determined on a Perkin-Elmer Polarimeter Model 343 plus at 589 nm. Commercial grade reagents and solvents were used without further purification.

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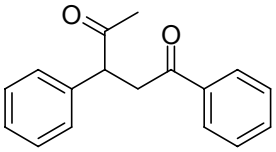
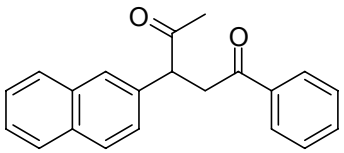
General procedure for the synthesis of 1,4-dicarbonyl compounds 4 by using thiazolium salt 1.

Anhydrous Cs_2CO_3 (0.05 mmol) was added to a suspension of Michael acceptors **3** (0.5 mmol), freshly distilled acetaldehyde (5 mmol) and thiazolium salt **1** (0.05 mmol) in 1 mL of dry THF at room temperature. The reaction was stirred for 24 h, then quenched with distilled water, and extracted with EtOAc (3 × 2 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and the filtrate was concentrated under reduced pressure. The crude product was purified by flash column chromatography (hexanes/ethyl acetate, 20:1 to 10:1) to 1,4-dicarbonyl compounds **4**.



4a

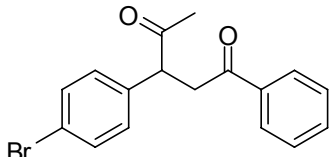
1,3-Diphenylpentane-1,4-dione (4a; Table 2, Entry 1). The physical and spectral data were identical to those previously reported for this compound.[1] By means of the general procedure described above, yield: 96%, liquid, TLC: R*f* = 0.43 (ethyl acetate/hexanes, 1:5), IR (film) ν_{max}: 1712, 1679, 1447, 1254, 1203, 1159, 1018, 755, 704, 687 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.98-7.94 (m, 2H), 7.59-7.52 (m, 1H), 7.48-7.41 (m, 2H), 7.40-7.27 (m, 5H), 4.44 (dd, *J* = 10.2, 3.9 Hz, 1H), 4.02 (dd, *J* = 18, 9.9 Hz, 1H), 3.14 (dd, *J* = 18, 3.6 Hz, 1H), 2.22 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 207.6, 198.5, 138.3, 136.8, 133.6, 129.5, 128.9, 128.7, 128.4, 128.0, 54.2, 42.6, 29.5 ppm. HRMS (FAB) ($[M + H]^+$) calcd for $C_{17}H_{17}O_2$: 253.1223, found 253.1229.



4b

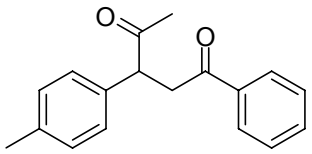
3-(Naphthalen-2-yl)-1-phenylpentane-1,4-dione (4b; Table 2, Entry 2). By means of the general procedure described above, yield: 98%, solid, Mp: 83-85 ^oC, TLC: R*f* = 0.4 (ethyl acetate/hexanes, 1:5), IR (film) ν_{max}: 1714, 1678, 1350, 1243, 999, 870, 818, 746, 691, 659 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 8.01-7.95 (m, 2H), 7.87-7.75 (m, 4H), 7.60-7.37 (m, 6H), 4.61 (dd, *J* = 9.9, 3.6 Hz, 1H), 4.12 (dd, *J* = 18, 9.9 Hz, 1H), 3.23 (dd, *J* = 18.3, 3.9 Hz, 1H),

2.26 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 207.6, 198.4, 136.7, 135.7, 133.9, 133.6, 133.0, 129.3, 128.9, 128.4, 128.1, 128.0, 127.7, 126.8, 126.5, 126.4, 54.3, 42.6, 29.7 ppm. HRMS (FAB) ($[M + H]^+$) calcd for $C_{21}H_{19}O_2$: 303.1380, found 303.1385.



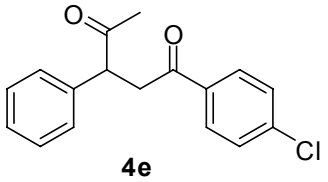
4c

3-(4-Bromophenyl)-1-phenylpentane-1,4-dione (4c; Table 2, Entry 3). By means of the general procedure described above, yield: 97%, solid, Mp: 114-116 ^{o}C, TLC: R*f* = 0.4 (ethyl acetate/hexanes, 1:5), IR (film) ν_{max}: 1710, 1679, 1489, 1251, 1202, 1160, 1001, 768, 745, 687 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.97-7.93 (m, 2H), 7.61-7.53 (m, 1H), 7.52-7.42 (m, 4H), 7.21-7.15 (m, 2H), 4.40 (dd, *J* = 9.9, 3.9 Hz, 1H), 3.97 (dd, *J* = 18, 9.6 Hz, 1H), 3.14 (dd, *J* = 18.3, 3.9 Hz, 1H), 2.22 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 207.1, 198.1, 137.2, 136.5, 133.7, 132.6, 130.3, 128.9, 128.4, 122.0, 53.5, 42.5, 29.6 ppm. HRMS (FAB) ($[M + H]^+$) calcd for $C_{17}H_{16}BrO_2$: 331.0328, found 331.0334.



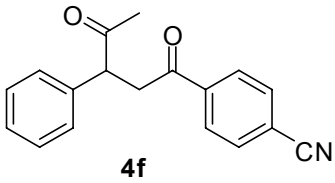
4d

1-Phenyl-3-*p*-tolylpentane-1,4-dione (4d; Table 2, Entry 4). By means of the general procedure described above, yield: 65%, solid, Mp: 65-67 ^{o}C, TLC: R*f* = 0.46 (ethyl acetate/hexanes, 1:5), IR (film) ν_{max}: 1710, 1679, 1515, 1447, 1255, 1202, 1160, 1001, 752, 687 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.99-7.93 (m, 2H), 7.59-7.52 (m, 1H), 7.48-7.40 (m, 2H), 7.18 (s, 4H), 4.40 (dd, *J* = 10.2, 3.9 Hz, 1H), 4.0 (dd, *J* = 18, 10.2 Hz, 1H), 3.12 (dd, *J* = 18, 3.6 Hz, 1H), 2.35 (s, 3H), 2.21 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 207.8, 198.6, 137.7, 136.8, 135.2, 133.5, 130.1, 128.9, 128.5, 128.4, 53.8, 42.6, 29.5, 21.4 ppm. HRMS (FAB) ($[M + H]^+$) calcd for $C_{18}H_{19}O_2$: 267.1380, found 267.1385.



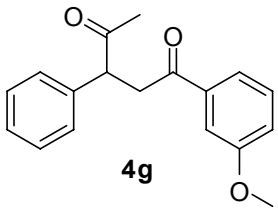
4e

1-(4-Chlorophenyl)-3-phenylpentane-1,4-dione (4e; Table 2, Entry 5). By means of the general procedure described above, yield: 99%, solid, Mp: 74-76 ^{o}C, TLC: R*f* = 0.46 (ethyl acetate/hexanes, 1:5), IR (film) ν_{max}: 1717, 1682, 1587, 1400, 1165, 1089, 977, 831, 750, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.93-7.87 (m, 2H), 7.45-7.25 (m, 7H), 4.42 (dd, *J* = 10.2, 3.6 Hz, 1H), 3.98 (dd, *J* = 18, 10.2 Hz, 1H), 3.08 (dd, *J* = 18, 3.6 Hz, 1H), 2.21 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 207.5, 197.3, 140.0, 138.0, 135.0, 129.8, 129.5, 129.2, 128.6, 128.0, 54.2, 42.4, 29.5 ppm. HRMS (FAB) ($[M + H]^+$) calcd for $C_{17}H_{16}ClO_2$: 287.0833, found 287.0839.



4f

4-(4-Oxo-3-phenylpentanoyl)benzonitrile (4f; Table 2, Entry 6). By means of the general procedure described above, yield: 99%, solid, Mp: 86-88 ^{o}C, TLC: R*f* = 0.26 (ethyl acetate/hexanes, 1:5), IR (film) ν_{max}: 2232, 1703, 1688, 1495, 1357, 1250, 1170, 1075, 842, 764, 703 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.05 (d, *J* = 8.4 Hz, 2H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.41-7.20 (m, 5H), 4.43 (dd, *J* = 9.9, 3.6 Hz, 1H), 4.0 (dd, *J* = 18, 10.2 Hz, 1H), 3.08 (dd, *J* = 18, 3.6 Hz, 1H), 2.20 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 207.0, 197.0, 139.5, 137.5, 132.6, 129.4, 128.6, 128.3, 127.9, 118.0, 116.5, 54.0, 42.4, 29.1 ppm. HRMS (FAB) ($[M + H]^+$) calcd for $C_{18}H_{16}NO_2$: 278.1176, found 278.1181.



4g

1-(3-Methoxyphenyl)-3-phenylpentane-1,4-dione (4g; Table 2, Entry 7). By means of the general procedure described above, yield: 80%, solid, Mp: 65-67 ^{o}C, TLC: R*f* = 0.34 (ethyl acetate/hexanes, 1:5), IR (film) ν_{max}: 1708, 1681, 1439, 1256, 1160, 1020, 1008, 769, 702, 682

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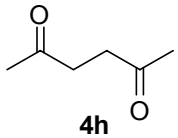
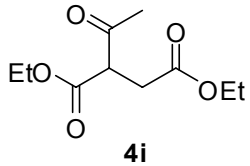
cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.58-7.53 (m, 1H), 7.49-7.45 (m, 1H), 7.40-7.27 (m, 6H), 7.14-7.07 (m, 1H), 4.42 (dd, *J* = 9.9, 3.6 Hz, 1H), 4.0 (dd, *J* = 18, 9.9 Hz, 1H), 3.84 (s, 3H), 3.14 (dd, *J* = 18.3, 3.9 Hz, 1H), 2.22 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 207.6, 198.3, 160.1, 138.2, 138.1, 129.9, 129.5, 128.7, 128.0, 121.1, 120.2, 112.4, 55.7, 54.2, 42.7, 29.5 ppm. HRMS (FAB) ($[M + H]^+$) calcd for $C_{18}H_{19}O_3$: 283.1329, found 283.1334.



4h

Hexane-2,5-dione (4h; Table 2, Entry 8). The physical and spectral data were identical to those previously reported for this compound.[2] yield: 95%, TLC: R*f* = 0.1 (ethyl acetate/hexanes, 1:5), ^1H NMR (300 MHz, $CDCl_3$) δ: 2.71 (s, 4H), 2.20 (s, 6H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 207.6, 37.2, 30.3 ppm.



4i

Diethyl 2-acetylsuccinate (4i; Table 2, Entry 9). The physical and spectral data were identical to those previously reported for this compound.[3] yield: 40%, TLC: R*f* = 0.31 (ethyl acetate/hexanes, 1:5), ^1H NMR (300 MHz, $CDCl_3$) δ: 4.26-4.08 (m, 4H), 4.02-3.96 (m, 1H), 2.97 (dd, *J* = 17.7, 8.1 Hz, 1H), 2.82 (dd, *J* = 17.7, 6.6 Hz, 1H), 2.36 (s, 3H), 1.32-1.22 (m, 6H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 202.1, 171.6, 168.7, 62.1, 61.3, 54.9, 32.6, 30.2, 14.4, 14.3 ppm.

General procedure for the synthesis of (*R*)-1,4-diketones 8 by using chiral triazolium salt 7a.

Anhydrous Cs_2CO_3 (0.05 mmol) was added to a suspension of Michael acceptors **3** (0.5 mmol), freshly distilled acetaldehyde (5 mmol) and chiral triazolium salt **7a** (0.05 mmol) in 1 mL of dry THF or $CHCl_3$ at 20 ^oC. The reaction was stirred for 24 h, then quenched with distilled water, and extracted with EtOAc (3 × 2 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and the filtrate was concentrated under reduced pressure. The crude product was purified by flash column chromatography (hexanes/ethyl acetate, 20:1 to 10:1) to

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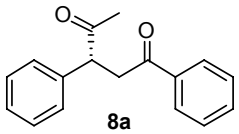
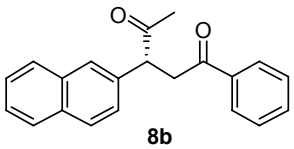
1,4-dicarbonyl compounds **8**.



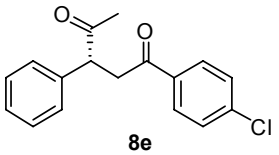
8a

(8a; Table 4, Entry 1) yield: 42%, ee: 57%, $[\alpha]_D^{20}$ = -197.5 (*c* 1.0, $CHCl_3$). The enantiomeric purity was determined by HPLC analysis (Daicel Chiralcel OJ-H, hexanes/2-propanol = 92:8, 0.7 mL/min, t_R(R) = 29.98 min (major) and t_R(S) = 36.0 min (minor).



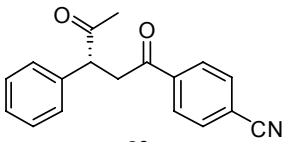
8b

(8b; Table 4, Entry 2) yield: 62%, ee: 76%, $[\alpha]_D^{20}$ = -229.3 (*c* 1.0, $CHCl_3$). The enantiomeric purity was determined by HPLC analysis (Daicel Chiralcel OJ-H, hexanes/2-propanol = 85:15, 1.0 mL/min, t_R(R) = 30.28 min (major) and t_R(S) = 46.89 min (minor).



8e

(8e; Table 4, Entry 3) yield: 78%, ee: 62%, $[\alpha]_D^{20}$ = -183.4 (*c* 1.0, $CHCl_3$). The enantiomeric purity was determined by HPLC analysis (Daicel Chiralcel OJ-H, hexanes/2-propanol = 92:8, 1.0 mL/min, t_R(R) = 25.10 min (major) and t_R(S) = 22.19 min (minor)



8f

(8f; Table 4, entry 4) yield: 85%, ee: 60%, $[\alpha]_D^{20}$ = -172.4 (*c* 1.0, $CHCl_3$). The enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak AD-H, hexanes/2-propanol = 92:8, 1.0 mL/min, t_R(R) = 32.52 min (major) and t_R(S) = 40.39 min (minor).

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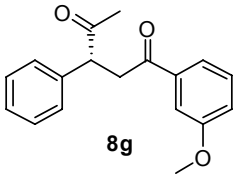

8g

(8g; Table 4, Entry 5) yield: 43%, ee: 58%, $[\alpha]_D^{20}$ = -174.9 (*c* 1.0, $CHCl_3$). The enantiomeric purity was determined by HPLC analysis (Daicel Chiralcel OJ-H, hexanes/2-propanol = 92:8, 0.7 mL/min, t_R(R) = 29.30 min (major) and t_R(S) = 41.90 min (minor).

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1. C. Dresen, M. Richter, M. Pohl, S. Lüdeke and M. Müller, *Angew. Chem., Int. Ed*., 2010, **49**, 6600.
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3. I. Kádas, V. Morvai, G. Árvai, L. Tőke, Á. Szöllősy, G. Tóth and M. Bihari, *Monatsh Chem*, 1995, **126**, 107.

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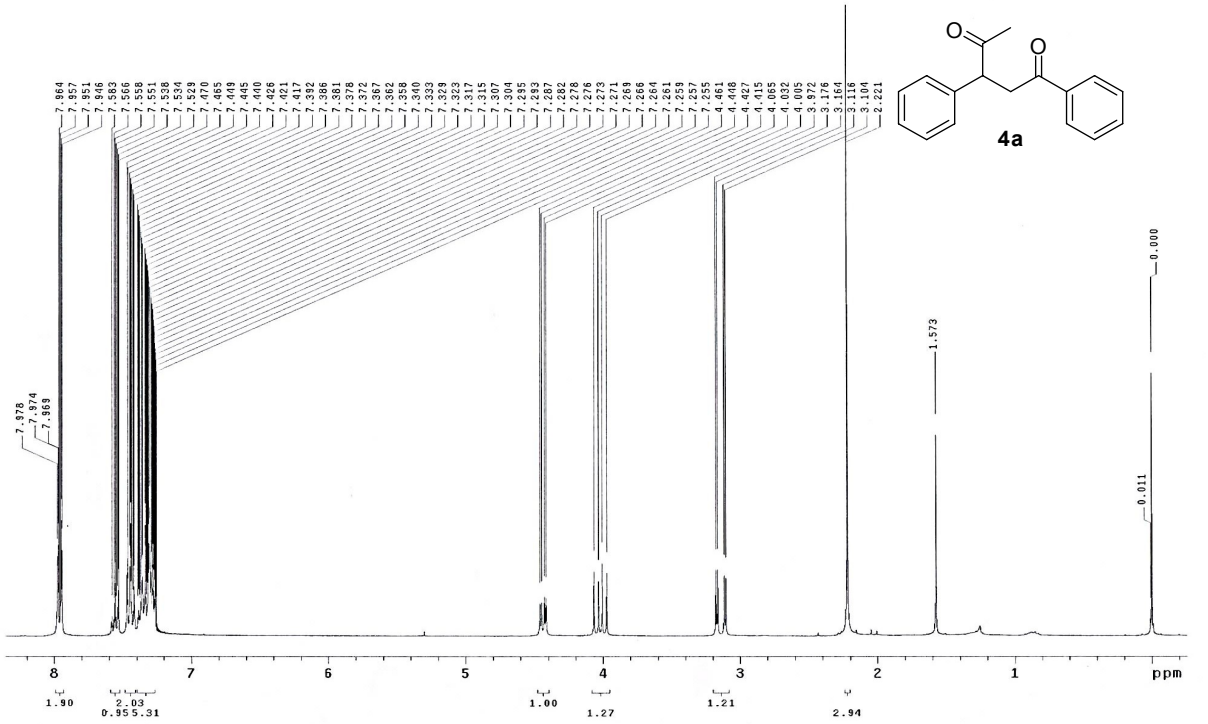

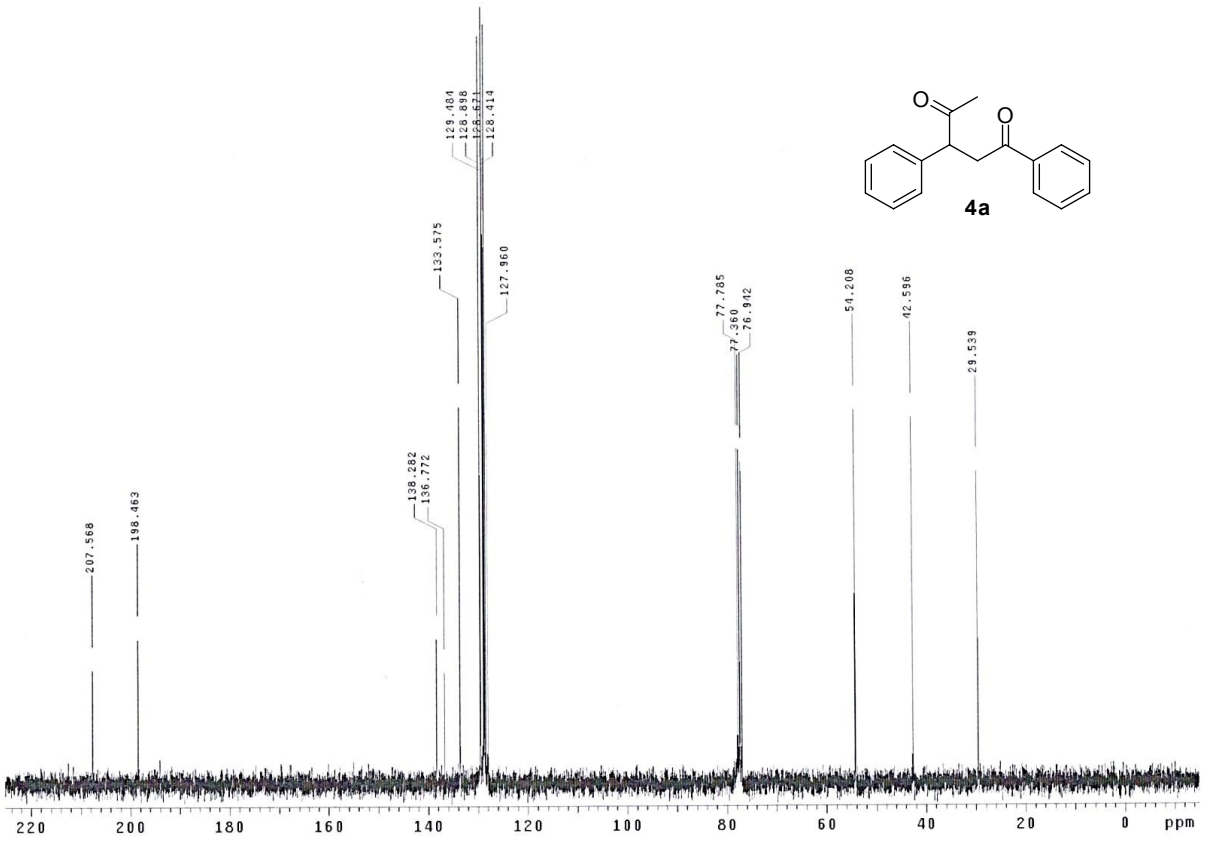

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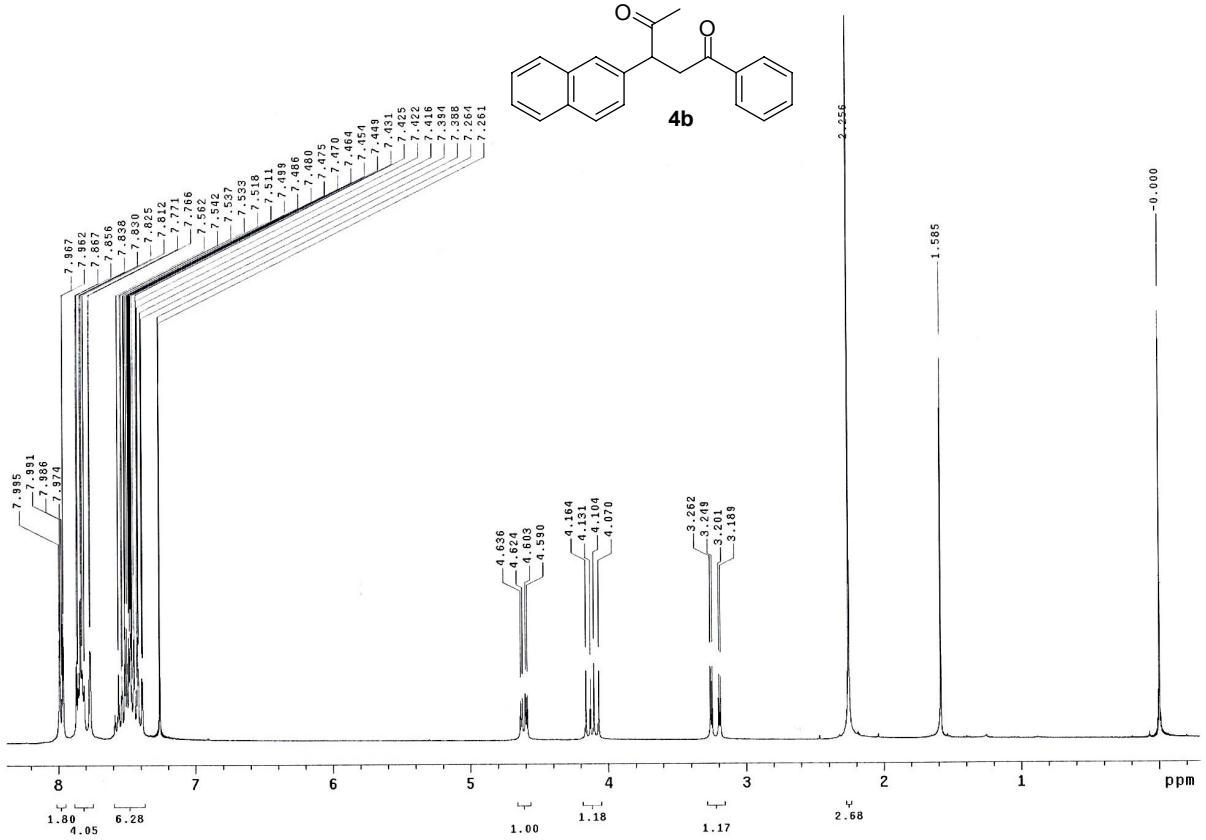

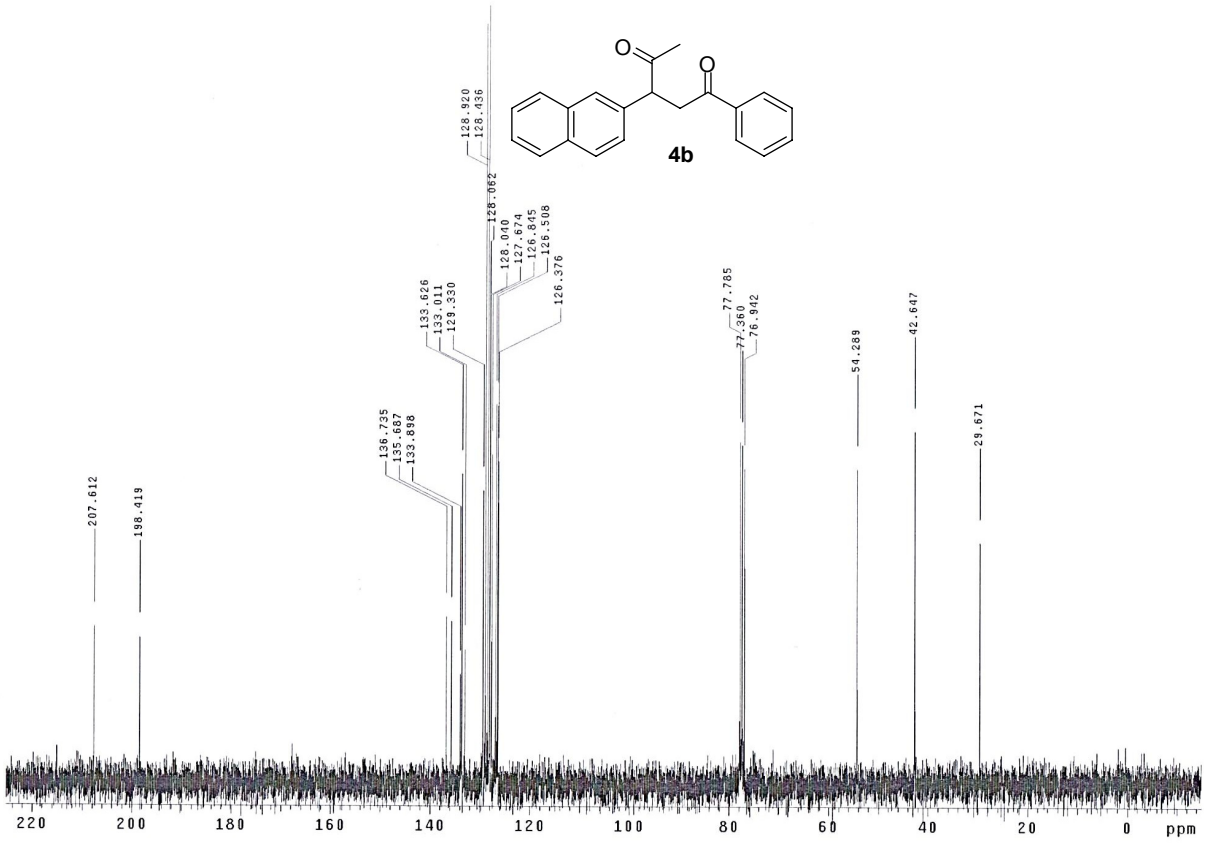

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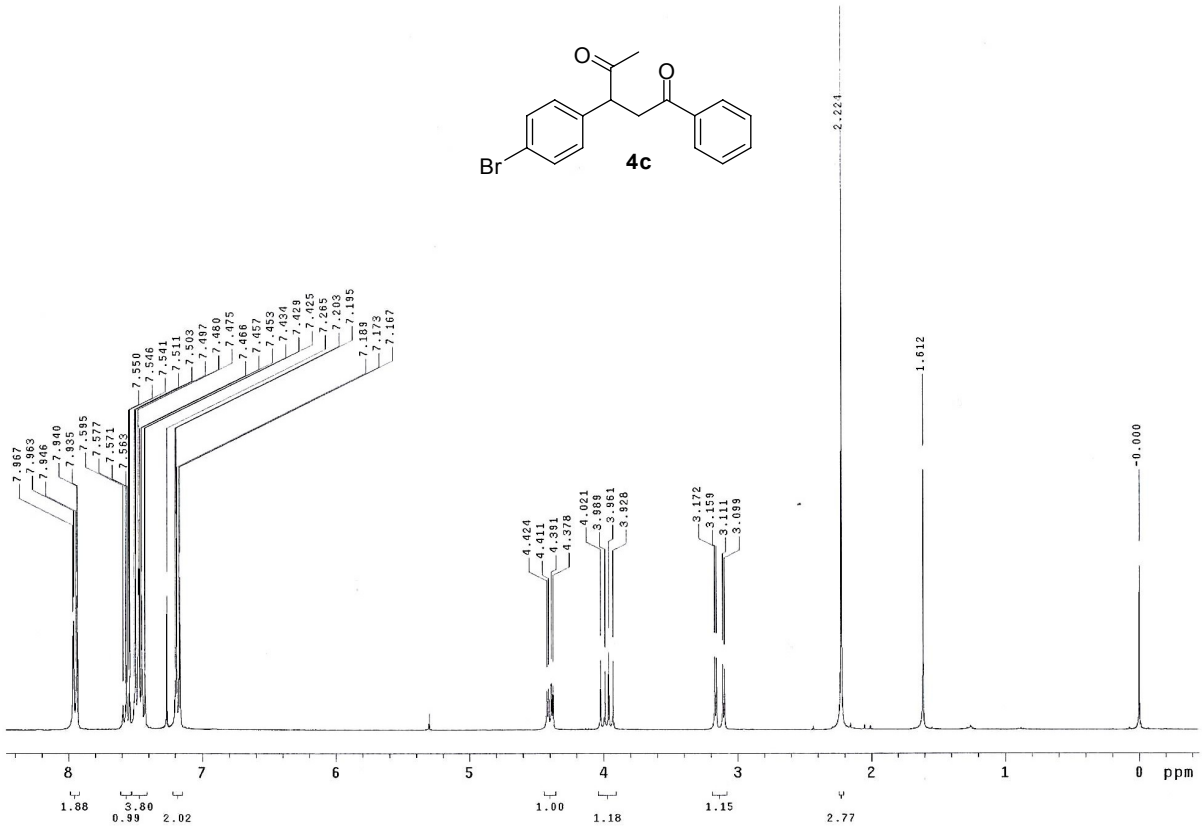

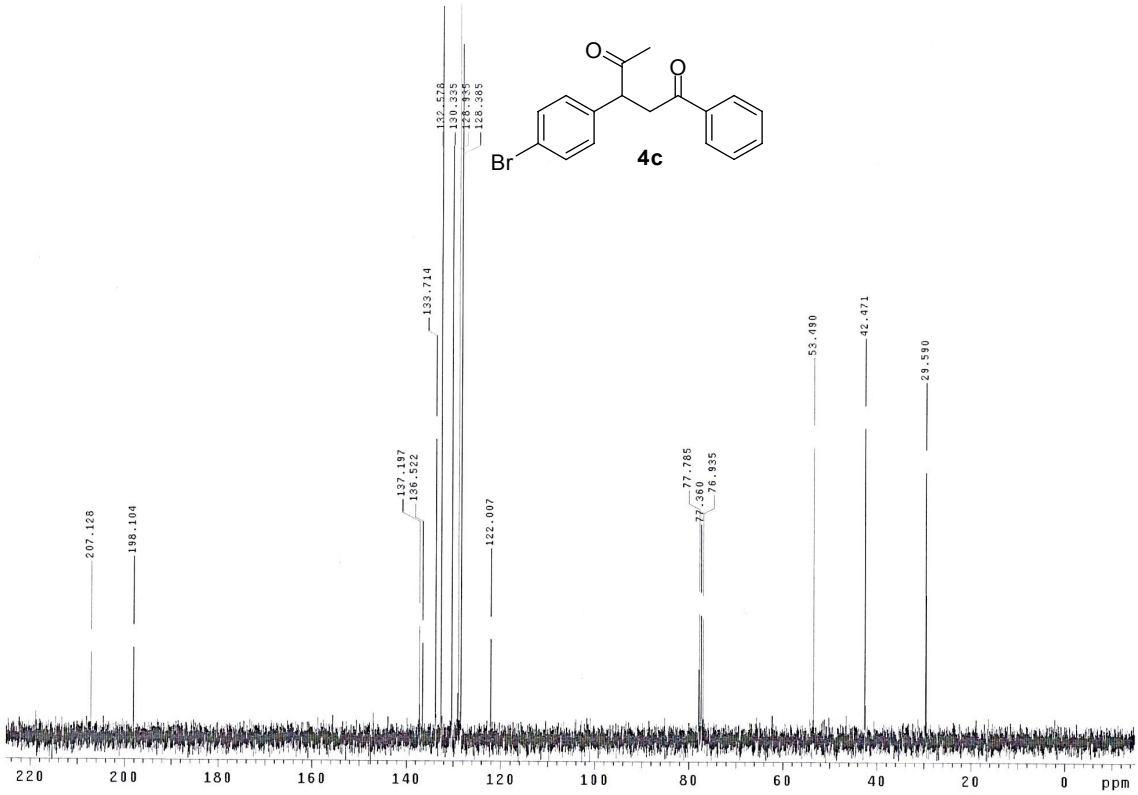

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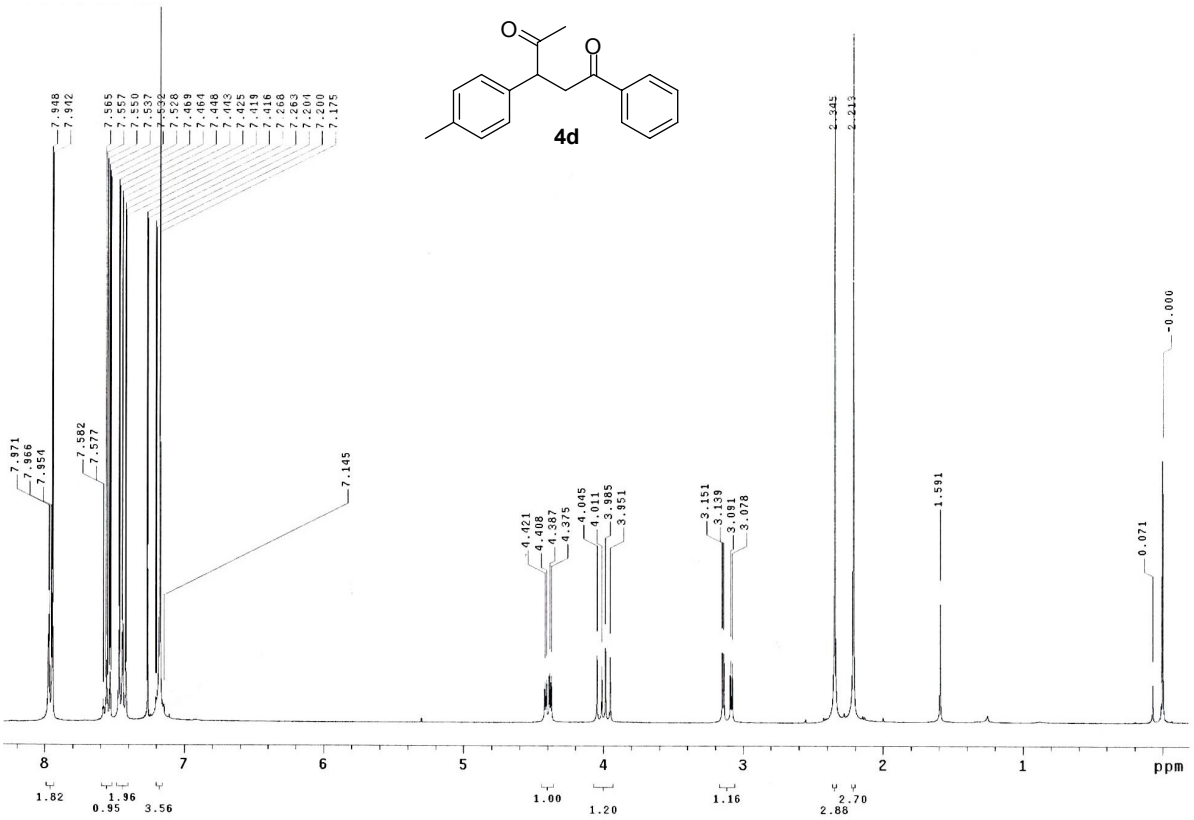

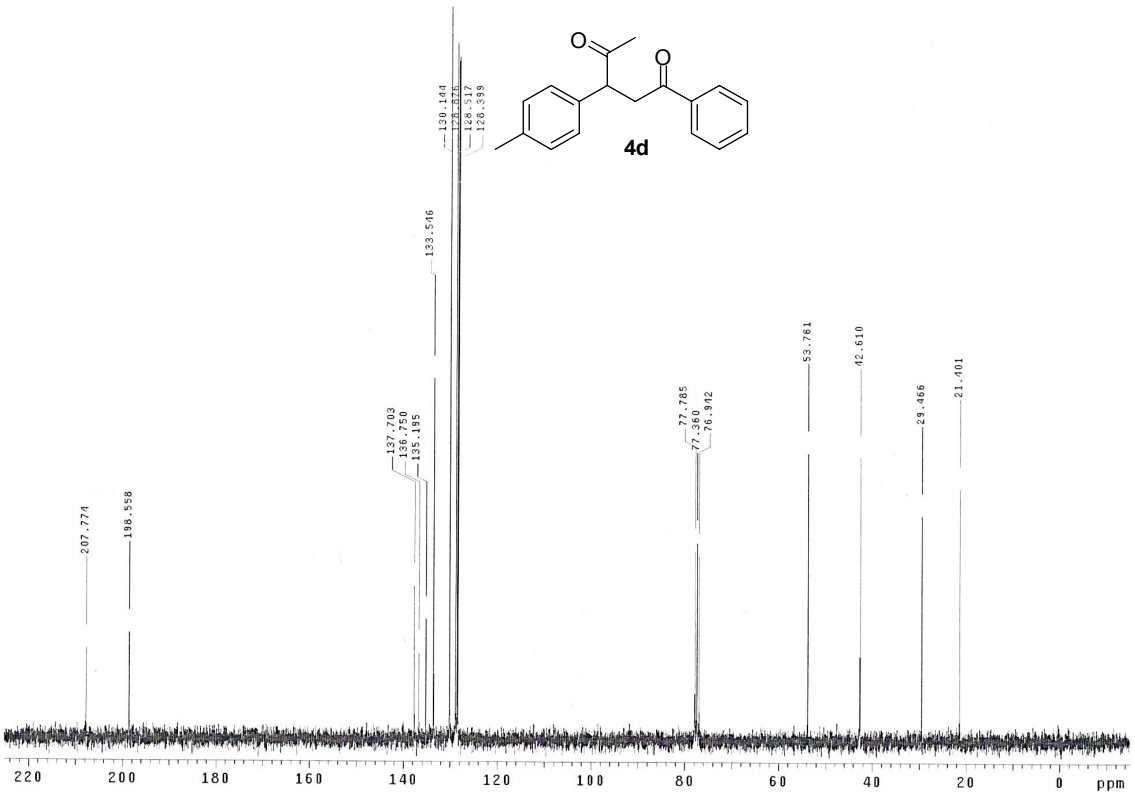

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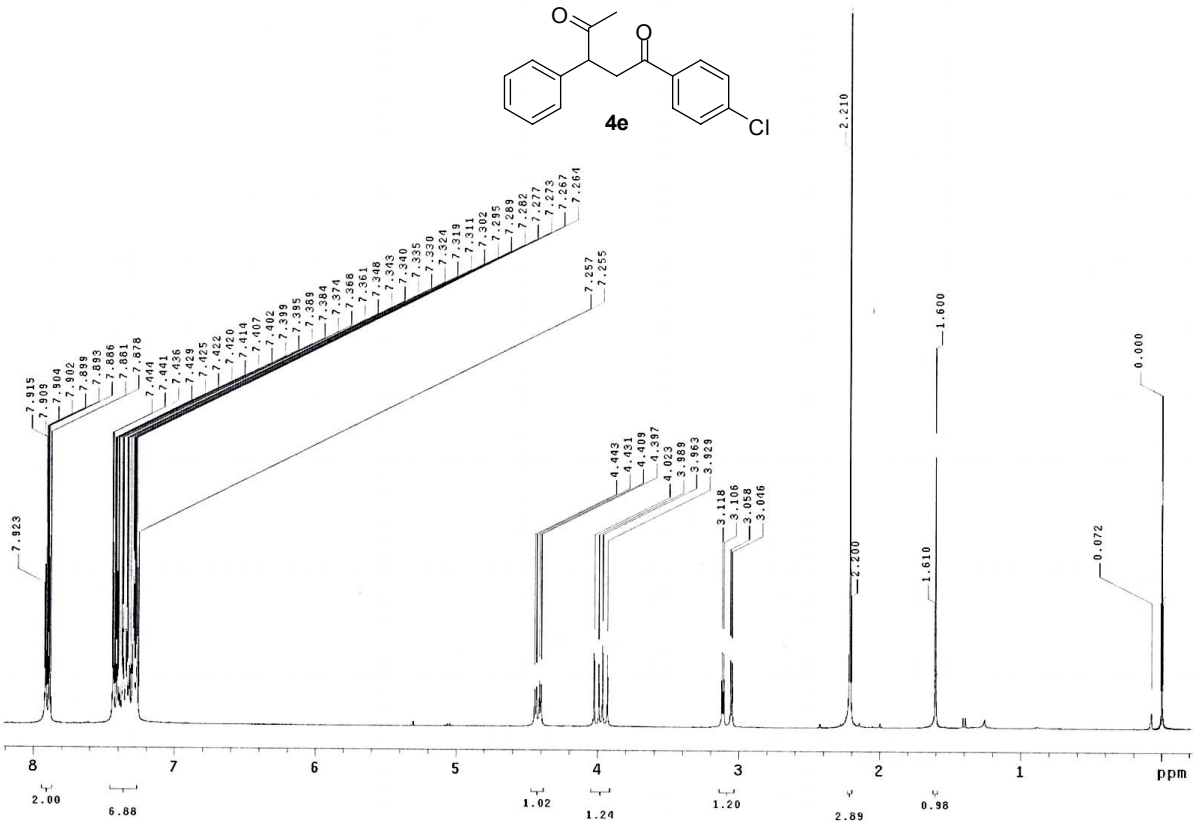

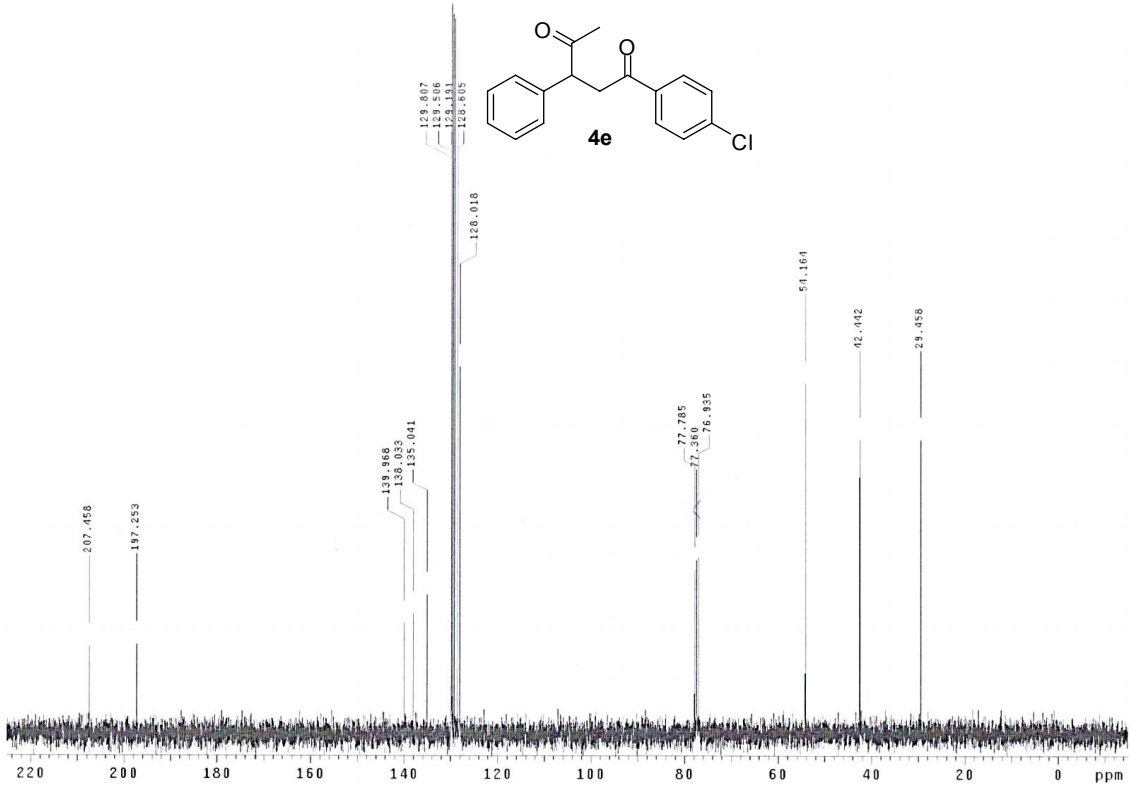

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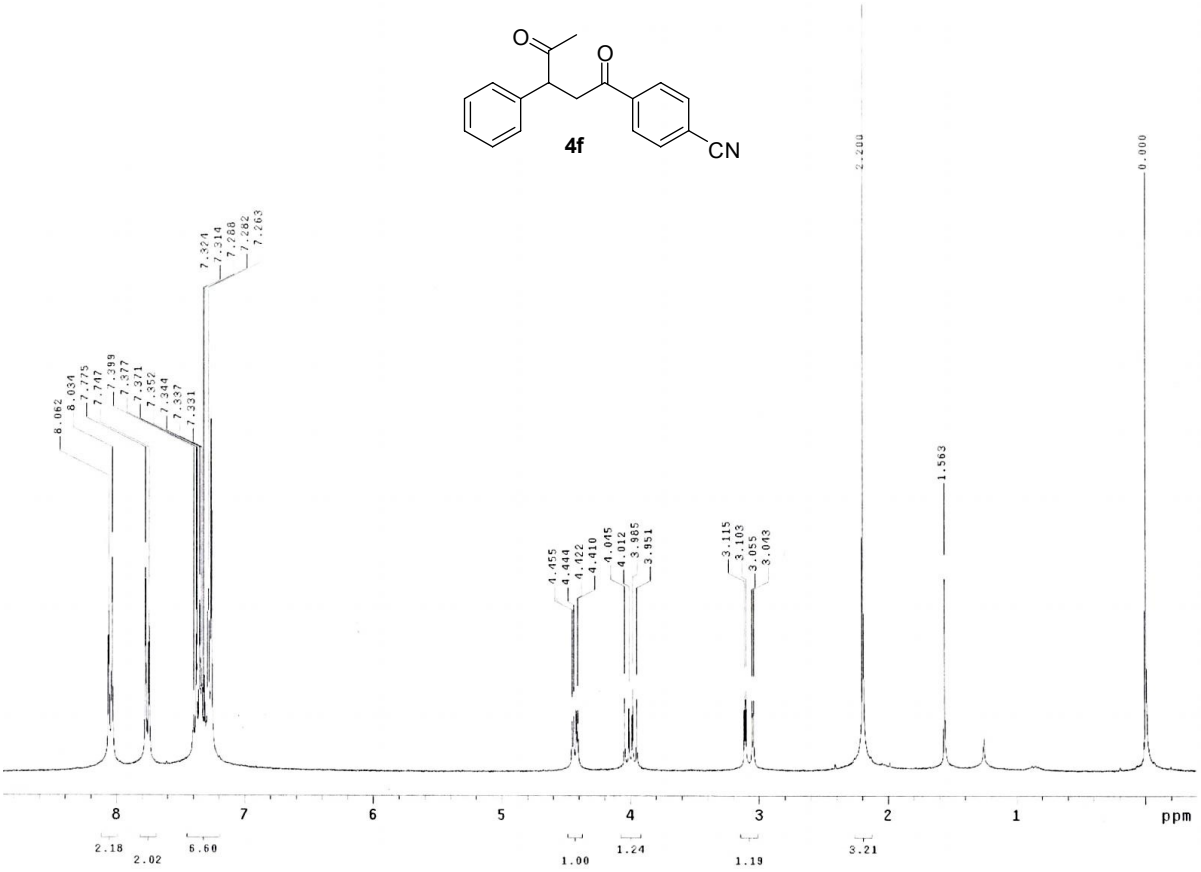

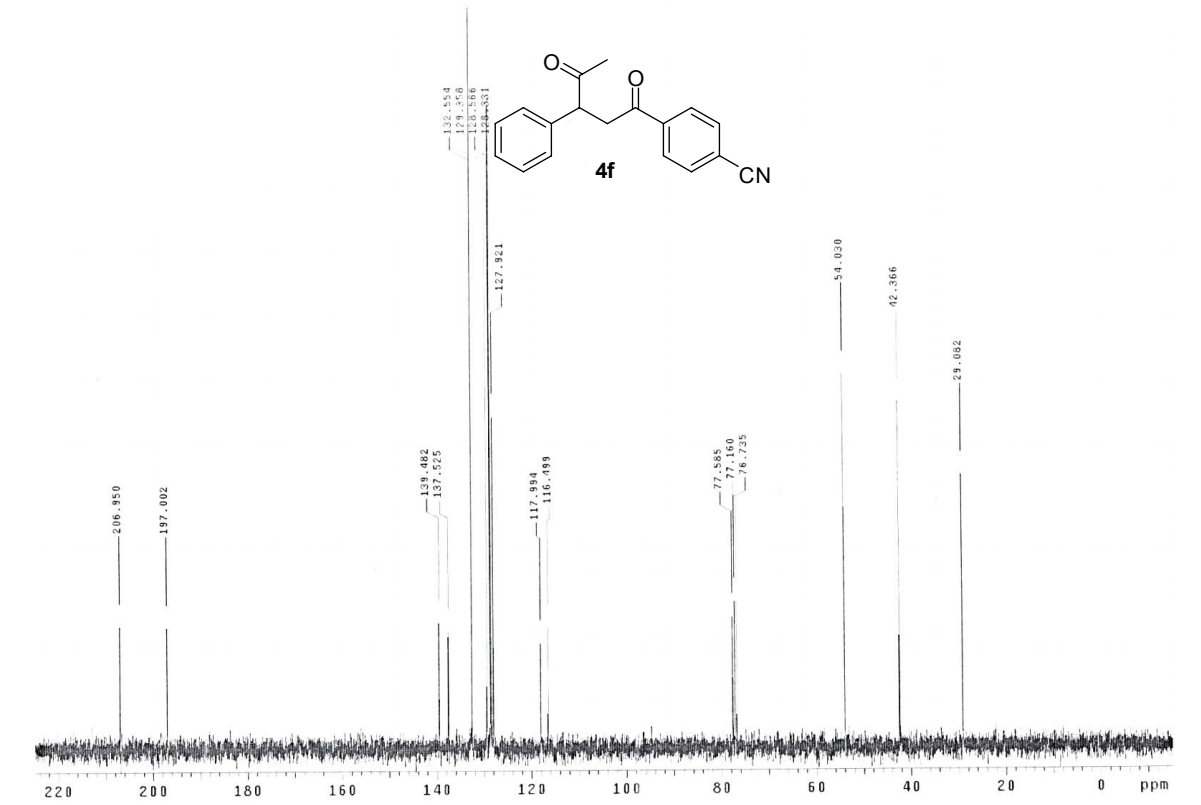

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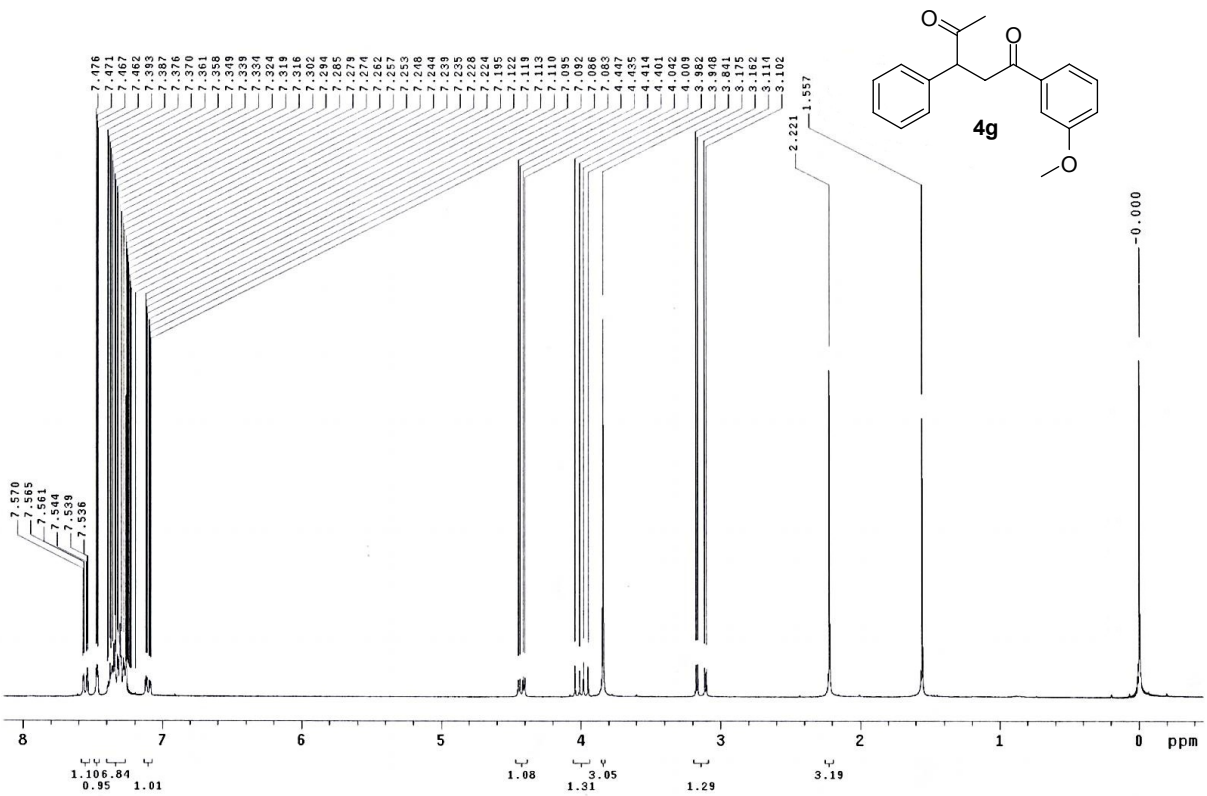

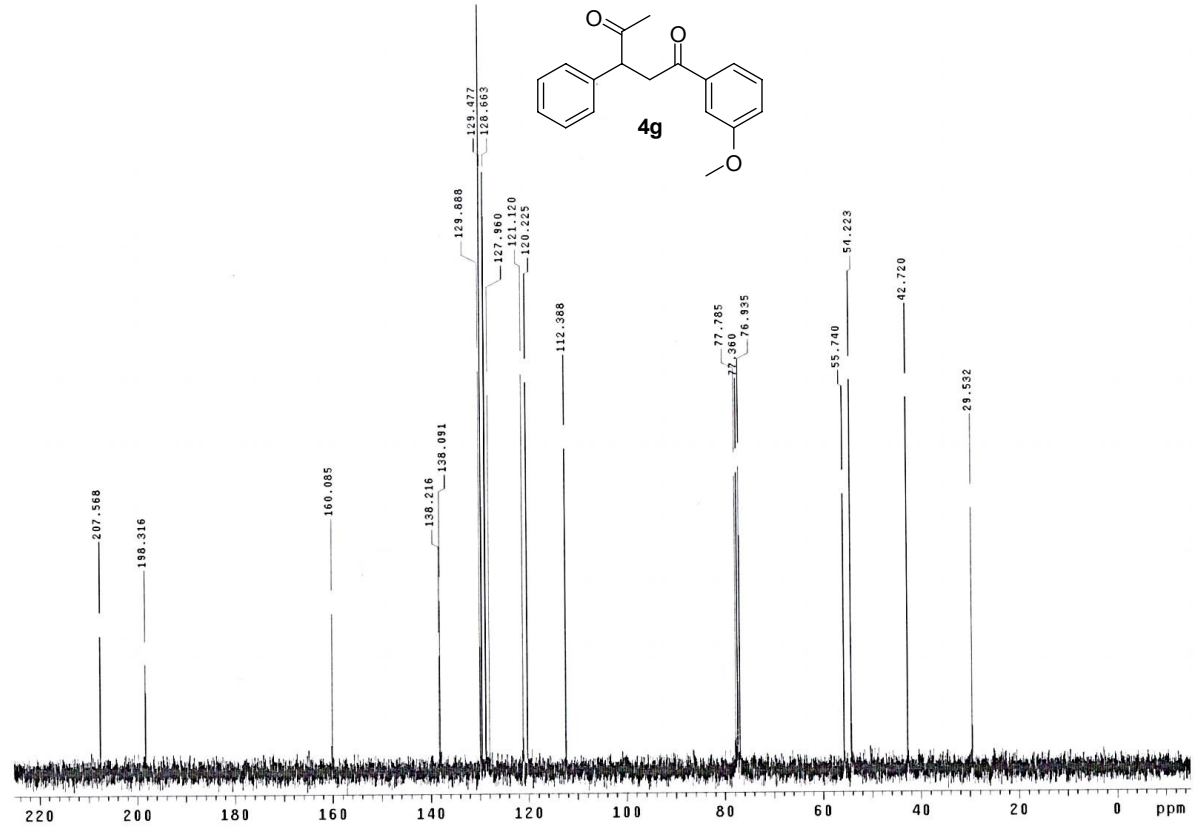

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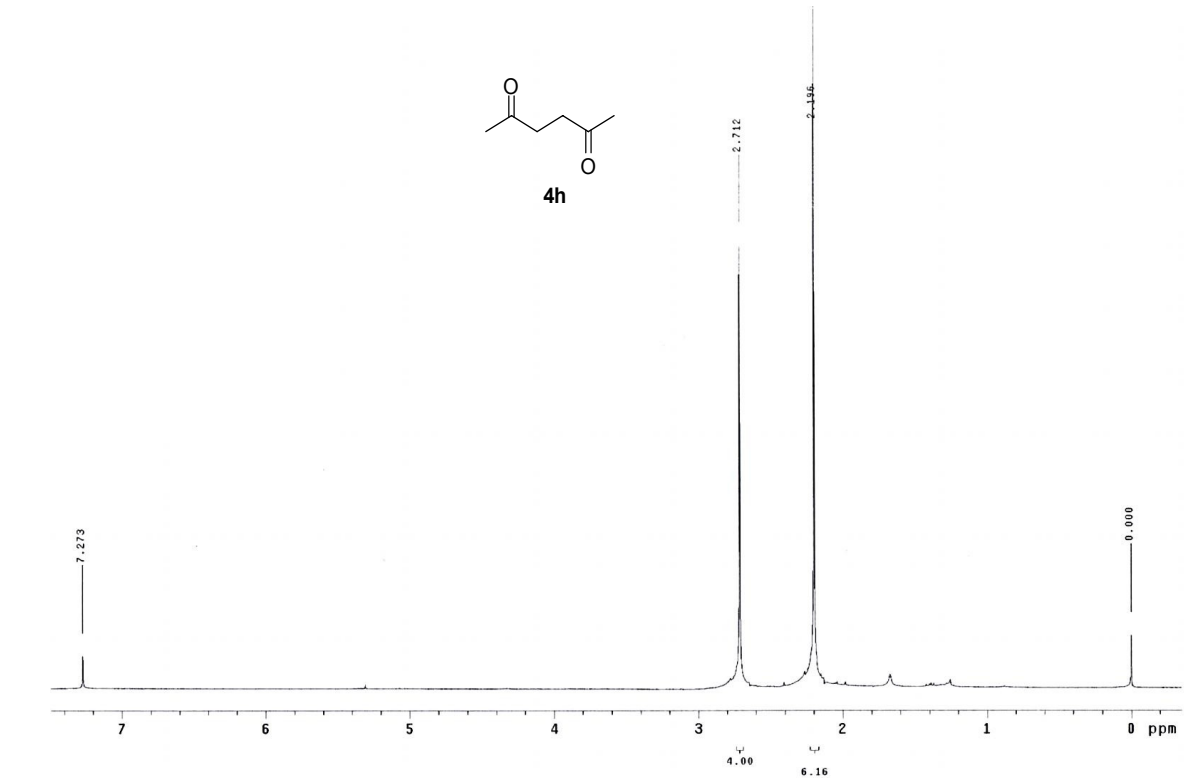

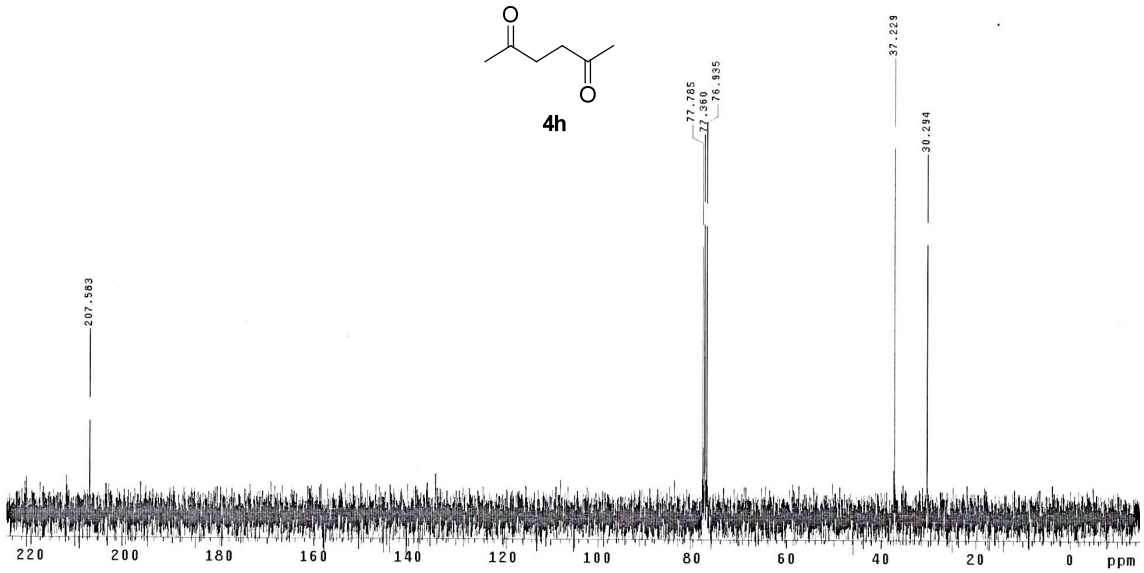

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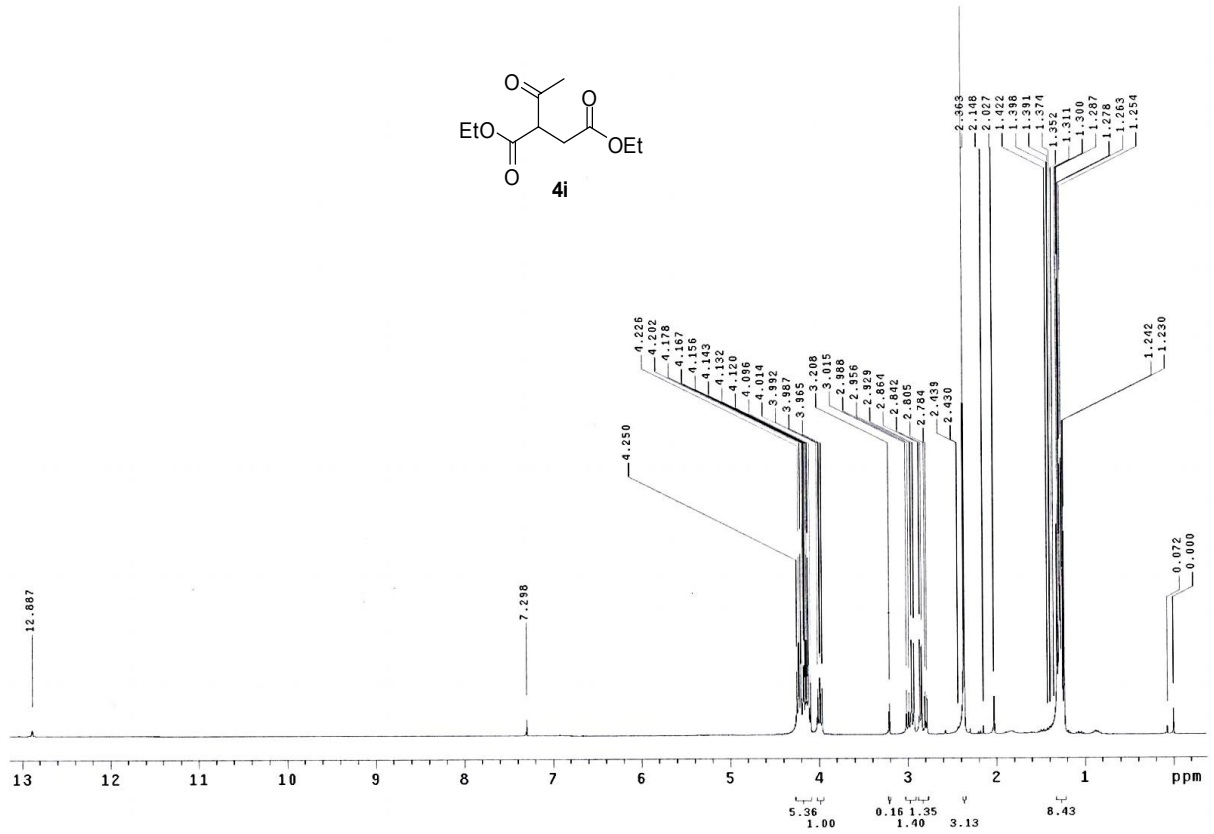
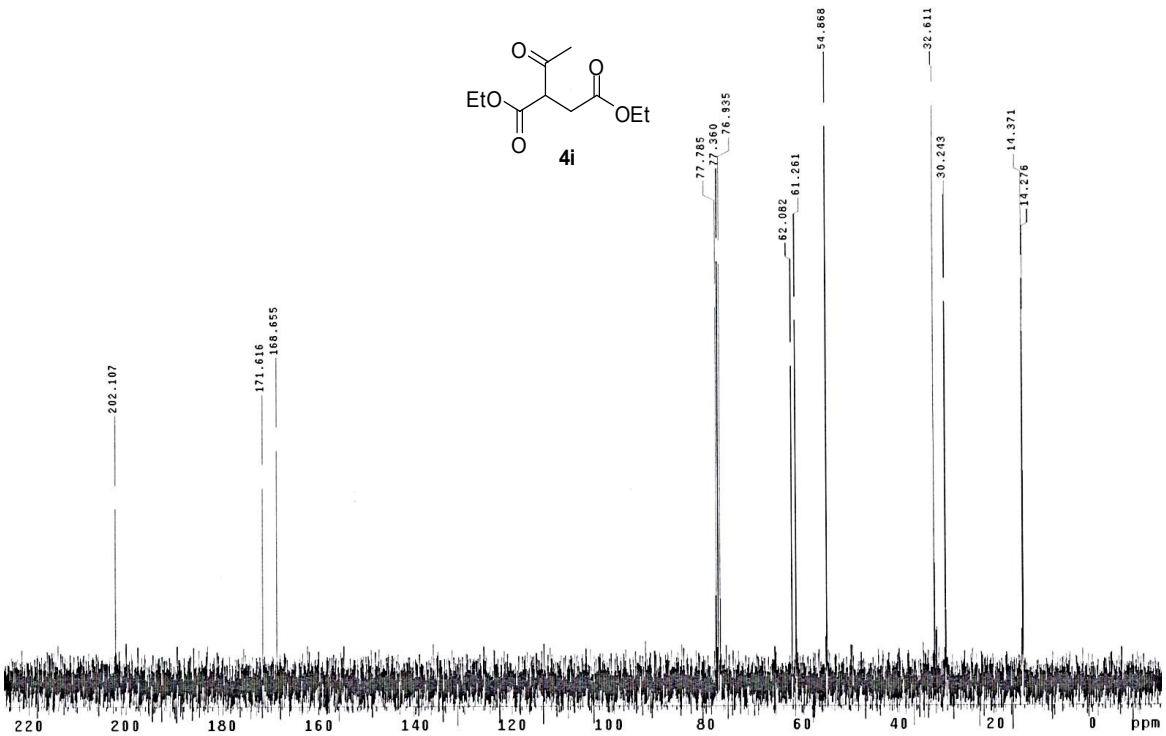
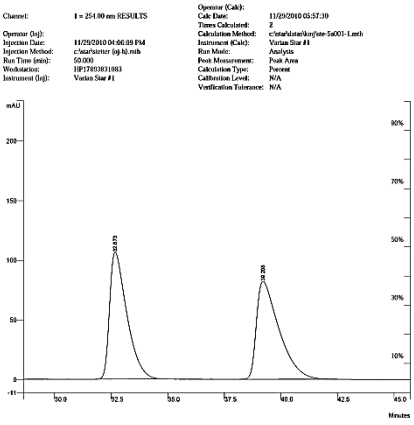
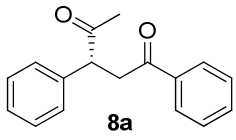




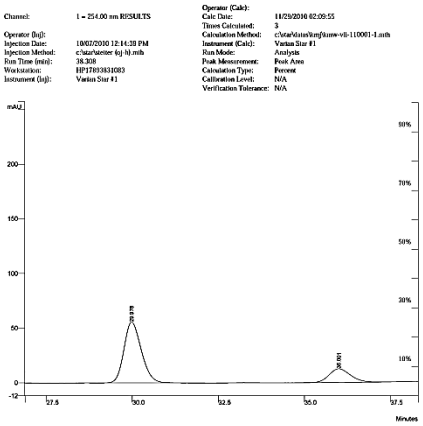
HPLC Chromatograms of the Chiral Compounds 8a, 8b, 8e, 8f, 8g.



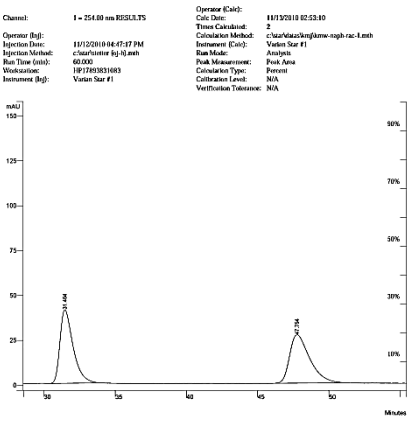
Peak No	Ret. Time (min)	Result (%)	Area (counts)
1	32.673	49.7713	56307084
2	39.208	50.2287	56824560
		100.0000	113131648



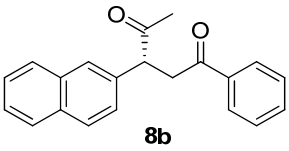
8a



Peak No	Ret. Time (min)	Result (%)	Area (counts)
1	29.978	78.5854	19376470
2	36.001	21.4146	5334912
		100.0000	24911082



Peak No	Ret. Time (min)	Result (%)	Area (counts)
1	31.464	49.8846	26281368
2	47.754	50.1154	26402952
		100.0000	52684320



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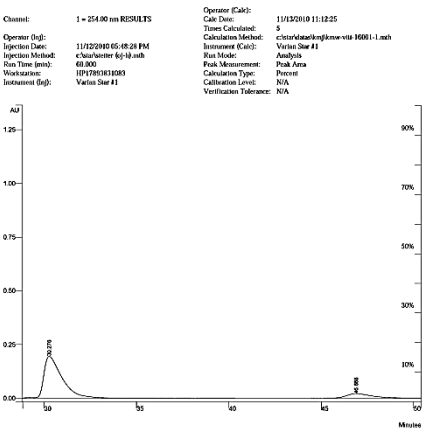
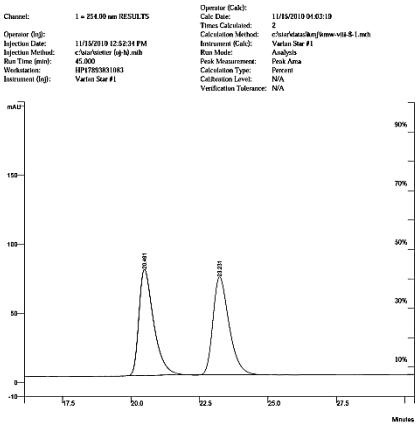
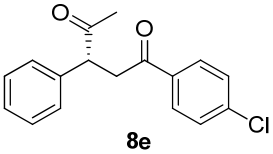


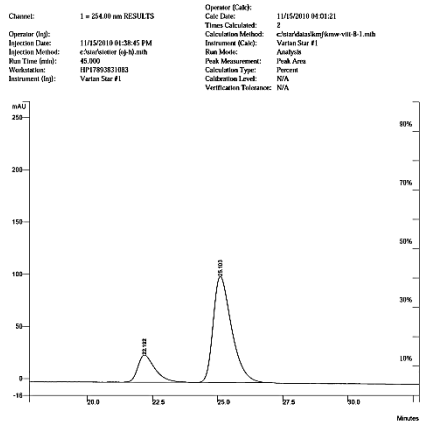
Peak No	Ret. Time (min)	Result (%)	Area (counts)
1	30.276	87.4364	130445120
2	48.888	12.5636	18743456
		100.0000	149188576



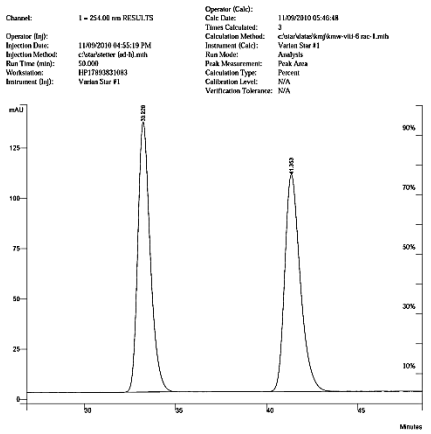
Peak No	Ret. Time (min)	Result (%)	Area (counts)
1	20.491	49.7203	28648936
2	23.231	50.2711	28961200
		100.0000	57610036



8e



Peak No	Ret. Time (min)	Result (%)	Area (counts)
1	22.162	19.0323	11773525
2	25.103	80.9677	50087252
		100.0000	61860776



Channel:	1 = 254.00 nm RESULTS	Operator (Calc):	
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Operator (Inj):		Times Calculated:	2
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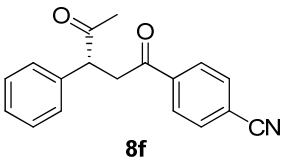
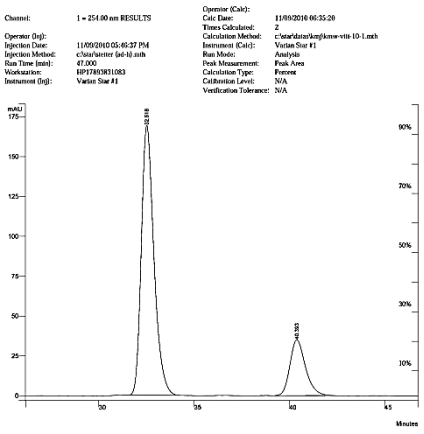
Injection Method:	c:\star\setter (ed-h).mth	Instrument (Calc):	Varian Star #1
Run Time (min):	50.000	Run Mode:	Analysis
Worksation:	HP17893831083	Peak Measurement:	Peak Area
Instrument (Inj):	Varian Star #1	Calculation Type:	Percent
		Calibration Level:	N/A
		Verification Tolerance:	N/A

Peak No	Ret. Time (min)	Result (%)	Area (counts)
1	33.226	49.8817	63515288
2	41.353	50.1183	63816592
		100.0000	127331880



8f



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Operator (Inj):		Times Calculated:	2
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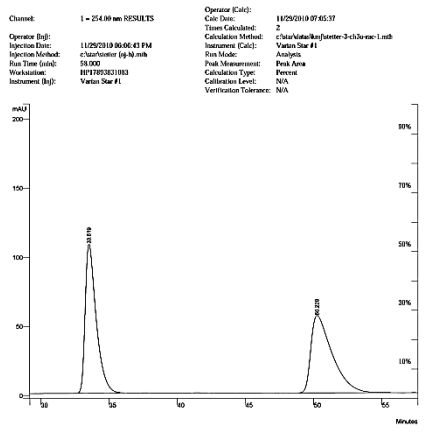
Injection Method:	c:\star\setter (ed-h).mth	Instrument (Calc):	Varian Star #1
Run Time (min):	47.000	Run Mode:	Analysis
Worksation:	HP17893831083	Peak Measurement:	Peak Area
Instrument (Inj):	Varian Star #1	Calculation Type:	Percent
		Calibration Level:	N/A
		Verification Tolerance:	N/A

Peak No	Ret. Time (min)	Result (%)	Area (counts)
1	32.516	79.6890	77895588
2	40.393	20.3110	19853968
		100.0000	97749636



Channel:	1 = 254.00 nm RESULTS	Operator (Calc):	
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Operator (Inj):		Times Calculated:	2
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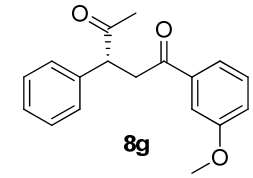
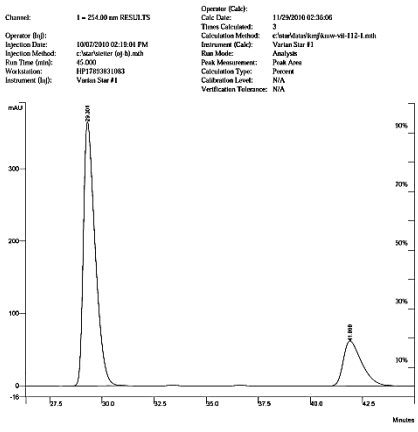
Injection Method:	c:\star\setter (ej-h).mth	Instrument (Calc):	Varian Star #1
Run Time (min):	58.000	Run Mode:	Analysis
Worksation:	HP17893831083	Peak Measurement:	Peak Area
Instrument (Inj):	Varian Star #1	Calculation Type:	Percent
		Calibration Level:	N/A
		Verification Tolerance:	N/A

Peak No	Ret. Time (min)	Result (%)	Area (counts)
1	33.519	49.9248	60287116
2	50.229	50.0752	60468792
		100.0000	120755904



8g



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Operator (Inj):		Times Calculated:	3
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Run Time (min):	45.000	Run Mode:	Analysis
Worksation:	HP17893831083	Peak Measurement:	Peak Area
Instrument (Inj):	Varian Star #1	Calculation Type:	Percent
		Calibration Level:	N/A
		Verification Tolerance:	N/A

Peak No	Ret. Time (min)	Result (%)	Area (counts)
1	29.304	78.9611	142293024
2	41.896	21.0389	37867912
		100.0000	180160928