Supplementary Material for Organic & Biomolecular Chemistry

Asymmetric addition of 1-ethynylcyclohexene to both aromatic and heteroaromatic ketones catalyzed by a chiral Schiff base-zinc complex

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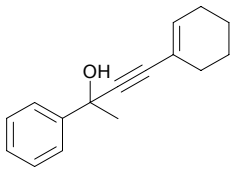
Supporting Information

1. General experimental details

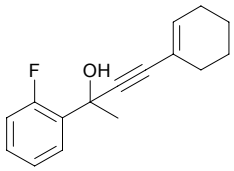
All reactions were carried out under an argon atmosphere condition and solvents were dried according to established procedures. Reactions were monitored by thin layer chromatography (TLC), column chromatography purifications were carried out using silica gel. All ketones and amino acid were purchased from Acros or Fluka. Diethylzinc was prepared from EtI with Zn and then was diluted with hexane to 1.0 M ligand **4** was prepared according to the literature method.[1] Melting points was uncorrected and recorded on X-4 melting point apparatus. ^{1}H NMR spectra were measured on a 400 MHz spectrometer (with TMS as an internal standard). ^{13}C NMR spectra were measured on a 100 MHz spectrometer with $CDCl_3$ as the solvent. IR spectra were obtained on Nicolet NEXUS 670 FT-IR. Optical rotations were recorded on a Perkin-Elmer 341 polarimeter. HR-MS was measured with an APEX II 47e mass spectrometer and the ESI-MS was recorded on a Mariner biomassspectrometer. The ee value determination was carried out using chiral HPLC with a Daicel Chiracel OD-H column on Waters with a 996 UV-detector.

2. Typical procedure for catalytic asymmetric addition of 1-ethynylcyclohexene to both aromatic and heteroaromatic ketones.

Under argon, ligand **4** (1.068mg, 0.0025 mmol) was mixed in dry hexane (1.0 mL) at room temperature. Then Et_2Zn in hexane (1.0 M, 0.75 ml) was added and stirred for 10 minutes at the same temperature. After that, 1-ethynylcyclohexene (86.5ul) was added. After the mixture was stirred at room temperature for another 6 hours, the solution was cooled to 0 °C and treated with ketone (0.25 mmol). The resulting mixture was stirred for 48 hours at -18 °C. After the reaction was complete (monitoring by TLC), it was quenched with aqueous HCl (5%). Then the mixture was extracted with ether. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated under vacuum. The residue was purified by flash column chromatography to give the product.

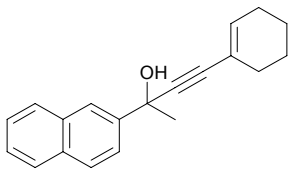


4-cyclohexenyl-2-phenylbut-3-yn-2-ol （7a）55% yield isolated after 48 hours reaction. 79% ee determined by HPLC analysis (Chiralcel OD-H column, IPA: hexane = 1: 120, 228.5 nm). Retention time: t_{major} = 17.6 and t_{minor} = 20.1 min; $[\alpha]^{15}_{D}$ + 3 (c 1.21, CH_2Cl_2); ^{1}H NMR (400MHz, $CDCl_3$, ppm): 7.67-7.65 (m, 2H), 7.37-7.25 (m, 3H), 6.16-6.15 (m, 1H), 2.40 (s, 1H), 2.16-2.09 (m, 4H), 1.77 (s, 3H), 1.67-1.57 (m, 4H); ^{13}C NMR (100MHz, $CDCl_3$, ppm): δ= 145.9, 135.3, 128.1, 127.5, 124.9, 120.0, 89.7, 86.7, 70.2, 33.4, 29.1, 25.5, 22.2, 21.4; IR (KBr): 3384, 3060, 3027, 2930, 2859, 2217, 1600, 1490, 1445, 1363, 1240, 1085, 763, 699 cm^{-1}.



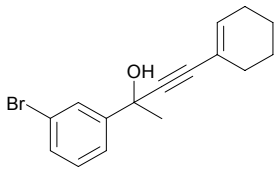
4-cyclohexenyl-2-(2-fluorophenyl)but-3-yn-2-ol (7b)

62% yield isolated after 48 hours reaction. 81% ee determined by HPLC analysis (Chiralcel OD-H column, IPA: hexane = 1: 400, 228.5nm). Retention time: t_{major} = 43.3 and t_{minor} = 48.8 min; $[\alpha]^{15}_{D}$ +6 (c 1.61, CH_2Cl_2); ^{1}H NMR (400MHz, $CDCl_3$, ppm): 7.69-7.65 (m, 1H), 7.30-7.24 (m, 1H), 7.14-7.03 (m, 2H), 6.14-6.13 (m, 1H), 2.79 (s, 1H), 2.14-2.04 (m, 4H), 1.88 (s, 3H), 1.65-1.53 (m, 4H); ^{13}C NMR (100MHz, $CDCl_3$, ppm): δ= 158.9**,** 135.4**,** 132.2, 129.3, 126.8, 123.7, 119.9, 116.1, 88.7, 86.1, 68.0, 30.6, 28.9, 25.5, 22.1, 21.3; IR (KBr): 3394, 3079, 3029, 2931, 2860, 2220, 1612, 1582, 1485, 1447, 1364, 1220, 1073, 759, 620 cm^{-1}.



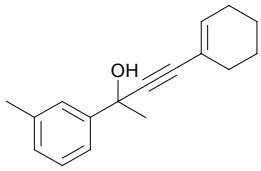
4-cyclohexenyl-2-(naphthalen-3-yl)but-3-yn-2-ol (7c)

63% yield isolated after 48 hours reaction. 83% ee determined by HPLC analysis (Chiralcel OD-H column, IPA: hexane = 1: 120, 225nm). Retention time: t_{major} = 36.3 and t_{minor} = 46.4 min; $[\alpha]^{15}_{D}$ +1 (c 0.80, CH_2Cl_2); ^{1}H NMR (400MHz, $CDCl_3$, ppm): 8.11(s, 1H), 7.84-7.72 (m, 4H), 7.47-7.42 (m, 2H), 6.17 (s, 1H), 2.71 (s, 1H), 2.17-2.08 (m, 4H), 1.85 (s, 3H), 1.66-1.54 (m, 4H); ^{13}C NMR (100MHz, $CDCl_3$, ppm): δ= 143.2, 135.3, 132.9, 132.7, 128.2, 127.9, 127.4, 126.0, 125.9, 123.5, 123.2, 120.0, 89.7, 86.8, 70.3, 33.2, 29.1, 25.5, 22.1, 21.3; IR (KBr): 3395, 3055, 3024, 2930, 2858, 2218, 1673, 1599, 1437, 1360, 1124, 819, 748 cm^{-1}.



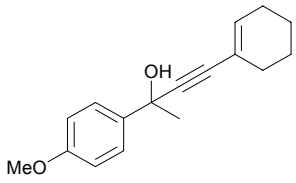
2-(3-bromophenyl)-4-cyclohexenylbut-3-yn-2-ol (7d)

59% yield isolated after 48 hours reaction. 75% ee determined by HPLC analysis (Chiralcel OD-H column, IPA: hexane = 1: 400, 225nm). Retention time: t_{major} = 37.3 and t_{minor} = 42.4 min; $[\alpha]^{15}_{D}$ +4 (c 1.10, CH_2Cl_2); ^{1}H NMR (400MHz, $CDCl_3$, ppm): 7.80-7.79 (m, 1H), 7.58-7.56 (m, 1H), 7.41-7.39 (m, 1H), 7.25-7.19 (m, 1H), 6.16-6.14 (m, 1H), 2.57 (s, 1H), 2.15-2.07 (m, 4H), 1.74 (s, 3H), 1.67-1.55 (m, 4H); ^{13}C NMR (100MHz, $CDCl_3$, ppm): δ= 148.3, 135.7, 130.5, 129.7, 128.2, 123.7, 122.3, 119.8, 89.0, 87.0, 69.7, 33.4, 29.0, 25.5, 22.1, 21.3; IR (KBr): 3378, 3062, 3026, 2930, 2859, 2218, 1591, 1567, 1469, 1237, 1074, 922, 784, 693 cm^{-1}.



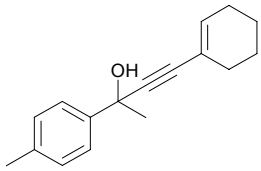
4-cyclohexenyl-2-m-tolylbut-3-yn-2-ol (7e)

63% yield isolated after 48 hours reaction. 80% ee determined by HPLC analysis (Chiralcel OD-H column, IPA: hexane = 1: 1000, 225nm). Retention time: t_{major} = 58.5 and t_{minor} = 65.1 min; $[\alpha]^{15}_{D}$ +5 (c 0.90, CH_2Cl_2); ^{1}H NMR (400MHz, $CDCl_3$, ppm): 7.48-7.46 (m, 2H), 7.27-7.23 (m, 1H), 7.11-7.09 (m, 1H), 6.17-6.15 (m, 1H), 2.47 (s, 1H), 2.38 (s, 3H), 2.18-2.10(m, 4H), 1.77 (s, 3H), 1.68-1.58 (m, 4 H); ^{13}C NMR (100MHz, $CDCl_3$, ppm): δ= 145.8, 137.8, 135.2, 128.2, 128.0, 125.5, 122.0, 120.0, 89.8, 86.5, 70.2, 33.3, 29.1, 25.5, 22.2, 21.5, 21.4; IR (KBr): 3389, 3025, 2929, 2859, 2218, 1606, 1484, 1440, 1362, 1126, 1081, 921, 787 cm^{-1}.



4-cyclohexenyl-2-(4-methoxyphenyl)but-3-yn-2-ol (7f)

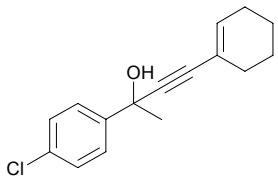
63% yield isolated after 48 hours reaction. 82% ee determined by HPLC analysis (Chiralcel OD-H column, IPA: hexane = 1: 120, 228.5nm). Retention time: t_{major} = 33.3 and t_{minor} = 41.1 min; $[\alpha]^{15}_{D}$ +8 (c 0.60, CH_2Cl_2); ^{1}H NMR (400MHz, $CDCl_3$, ppm): 7.59-7.56 (m, 2H), 6.89-6.85 (m, 2H), 6.16-6.14 (m, 1H), 3.80 (s, 3H), 2.52 (s, 1H), 2.17-2.07 (m, 4H), 1.75 (s, 3H), 1.67-1.55 (m, 4H); ^{13}C NMR (100MHz, $CDCl_3$, ppm): δ= 158.8, 138.1, 135.1, 126.2, 126.1, 120.0, 113.3, 89.8, 86.5, 69.8, 55.1, 33.2, 29.1, 25.5, 22.1, 21.3; IR (KBr): 3417, 3063, 3026, 2931, 2216, 1609, 1509, 1247, 1176, 1033, 920, 833, 590 cm^{-1}.



4-cyclohexenyl-2-p-tolylbut-3-yn-2-ol (7g)

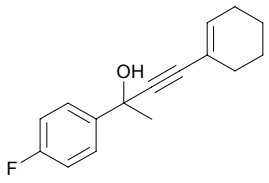
51% yield isolated after 48 hours reaction. 74% ee determined by HPLC analysis (Chiralcel OD-H column, IPA: hexane = 1: 120, 228.5 nm). Retention time: t_{major} = 15.9 and t_{minor} = 18.3 min; $[\alpha]^{15}_{D}$ +2 (c 0.62, CH_2Cl_2); ^{1}H NMR (400MHz, $CDCl_3$, ppm): 7.55-7.52 (m, 2H), 7.16-7.14 (m, 2H), 6.16-6.13 (m, 1H), 2.43 (s, 1H), 2.34 (s, 3H), 2.16-2.07 (m, 4H), 1.75 (s, 3H), 1.66-1.55 (m, 4H); ^{13}C NMR (100MHz, $CDCl_3$,

ppm): δ= 143.1, 137.1, 135.1, 128.8, 124.8, 120.1, 89.9, 86.5, 70.0, 33.2, 29.1, 25.5, 22.1, 21.4, 20.9; IR (KBr): 3388, 3025, 2929, 2859, 2217, 1509, 1440, 1362, 1240, 1082, 921, 818, 593 cm^{-1}.



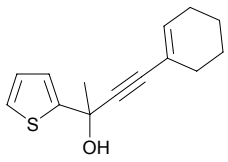
2-(4-chlorophenyl)-4-cyclohexenylbut-3-yn-2-ol (7h)

49% yield isolated after 48 hours reaction. 74% ee determined by HPLC analysis (Chiralcel OD-H column, IPA: hexane = 1: 400, 226.2nm). Retention time: t_{major} = 37.4 and t_{minor} = 41.7 min; $[\alpha]^{15}_{D}$ +3 (c 0.71, CH_2Cl_2); ^{1}H NMR (400MHz, $CDCl_3$, ppm): 7.59-7.56 (m, 2H), 7.32-7.25 (m, 2H), 6.15-6.13 (m, 1H), 2.54 (s, 1H), 2.14-2.09 (m, 4H), 1.73 (s, 3H), 1.66-1.56 (m, 4H); ^{13}C NMR (100MHz, $CDCl_3$, ppm): δ= 144.5, 135.6, 133.2, 128.2, 126.5, 126.4, 119.9, 89.2, 86.9, 69.8, 33.4, 29.0, 25.5, 22.1, 21.3; IR (KBr): 3361, 3027, 2931, 2859, 2218, 1632, 1488, 1398, 1363, 1093, 1013, 922, 828, 590 cm^{-1}.



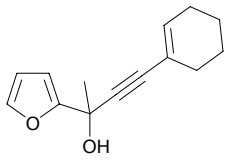
4-cyclohexenyl-2-(4-fluorophenyl)but-3-yn-2-ol (7i)

45% yield isolated after 48 hours reaction. 71% ee determined by HPLC analysis (Chiralcel OD-H column, IPA: hexane = 1: 1000, 228.5nm). Retention time: t_{major} = 51.5 and t_{minor} = 58.0 min; $[\alpha]^{15}_{D}$ +4 (c 0.32, CH_2Cl_2); ^{1}H NMR (400MHz, $CDCl_3$, ppm): 7.63-7.60 (m, 2H), 7.03-6.99 (m, 2H), 6.16-6.14 (m, 1H), 2.53 (s, 1H), 2.15-2.07 (m, 4H), 1.74 (s, 3H), 1.67-1.56(m, 4 H); ^{13}C NMR (100MHz, $CDCl_3$, ppm): δ= 163.8, 141.7, 135.5, 126.8, 126.7, 119.9, 114.9, 114.7, 89.4, 86.8, 69.8, 33.5, 29.1, 25.5, 22.2, 21.4; IR (KBr): 3373, 3027, 2931, 2860, 2218, 1602, 1506, 1440, 1227, 1158, 1082, 922, 837, 575 cm^{-1}.



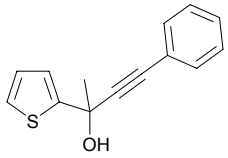
4-cyclohexenyl-2-(thiophen-2-yl)but-3-yn-2-ol (7j)

88% yield isolated after 48 hours reaction. 80% ee determined by HPLC analysis (Chiralcel OD-H column, IPA: hexane = 1: 120, 232 nm). Retention time: t_{major} = 24.4 and t_{minor} = 29.7 min; $[\alpha]^{15}_{D}$ +4 (c 0.48, CH_2Cl_2); ^{1}H NMR (400MHz, $CDCl_3$, ppm): 7.25-7.16 (m, 2H), 6.95-6.92(m, 1H), 6.18-6.15 (m, 1H), 2.63 (s, 1H), 2.15-2.03(m, 4H), 1.88 (s, 3H), 1.66-1.55 (m, 4H); ^{13}C NMR (100MHz, $CDCl_3$, ppm): δ= 150.9, 135.7, 128.0, 126.4, 124.8, 123.7, 89.0, 86.0, 67.5, 33.2, 28.9, 25.5, 22.1, 21.3; IR (KBr): 3398, 3072, 2930, 2858, 2217, 1630, 1436, 1355, 1233, 1071, 920, 700, 619 cm^{-1}.



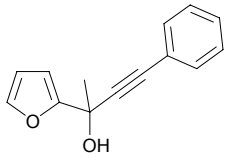
4-cyclohexenyl-2-(furan-2-yl)but-3-yn-2-ol (7k)

85% yield isolated after 48 hours reaction. 65% ee determined by HPLC analysis (Chiralcel OD-H column, IPA: hexane = 1: 120, 228.5nm). Retention time: t_{major} = 28.7 and t_{minor} = 39.9 min; $[\alpha]^{15}_{D}$ +6 (c 0.22, CH_2Cl_2); ^{1}H NMR (400MHz, $CDCl_3$, ppm): 7.30-7.29 (m, 1H), 6.30-6.22 (m, 2H), 6.08-6.06 (m, 1H), 2.70 (s, 1H), 2.09-2.00(m, 4H), 1.76(s, 3H), 1.59-1.46 (m, 4H); ^{13}C NMR (100MHz, $CDCl_3$, ppm): δ= 156.5, 142.4, 135.6, 119.7, 110.0, 105.5, 87.5, 85.6, 65.0, 28.9, 28.7, 25.5, 22.1, 21.3; IR (KBr): 3403, 3026, 2932, 2860, 2219, 1640, 1586, 1440, 1362, 1155, 1009, 920, 738, 595 cm^{-1}.



4-phenyl-2-(thiophen-2-yl)but-3-yn-2-ol (7l)

66% yield isolated after 48 hours reaction. 83% ee determined by HPLC analysis (Chiralcel OD-H column, IPA: hexane = 5: 95, 241.5nm). Retention time: t_{major} = 12.4 and t_{minor} = 15.7 min; $[\alpha]^{15}_{D}$ +5 (c 0.35, CH_2Cl_2); ^{1}H NMR (400MHz, $CDCl_3$, ppm): 7.51-7.50 (m, 2H), 7.35-7.27 (m, 5H), 7.00-6.98 (m, 1H), 3.03 (s, 1H), 2.01 (s, 3 H); ^{13}C NMR (100MHz, $CDCl_3$, ppm): δ= 150.4, 131.6, 128.5, 128.2, 126.5, 124.9, 123.8, 122.1, 91.6, 84.2, 67.5, 33.0; IR (KBr): 3402, 3074, 2985, 2857, 2233, 1663, 1489, 1443, 1367, 1130, 1070, 934, 756, 694 cm^{-1}.

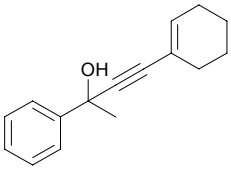


2-(furan-2-yl)-4-phenylbut-3-yn-2-ol (7m)

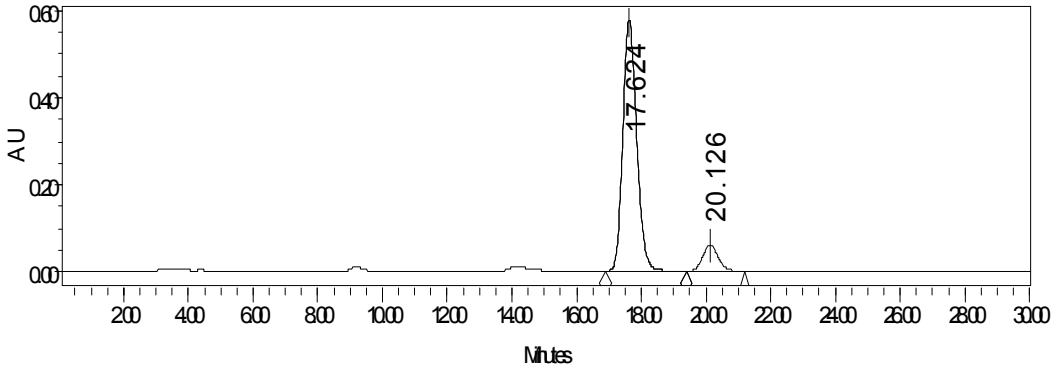
70% yield isolated after 48 hours reaction. 67% ee determined by HPLC analysis (Chiralcel OD-H column, IPA: hexane = 5: 95, 241.5 nm). Retention time: t_{major} = 13.5 and t_{minor} = 17.5 min; $[\alpha]^{15}_{D}$ +5 (c 0.35, CH_2Cl_2); ^{1}H NMR (400MHz, $CDCl_3$, ppm): 7.44-7.33 (m, 3H), 7.27-7.18 (m, 3H), 6.39-6.38 (m, 1H), 6.29-6.28 (m, 1H), 2.57 (s, 1H), 1.89 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$, ppm): δ= 156.2, 142.3, 131.6, 128.4, 128.1, 122.2, 116.2, 115.1, 110.1, 105.7, 90.2, 85.7, 65.1, 28.6; IR (KBr): 3382, 3058, 2991, 2931, 2236, 1597, 1490, 1443, 1366, 1156, 1074, 935, 755, 691 cm^{-1}.

References

1 C. Chen, L. Hong, Z. Q. Xu, L. Liu and R. Wang, *Org. Lett.*, 2006, **8**, 2277.



4-cyclohexenyl-2-phenylbut-3-yn-2-ol （7a）



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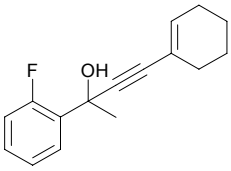
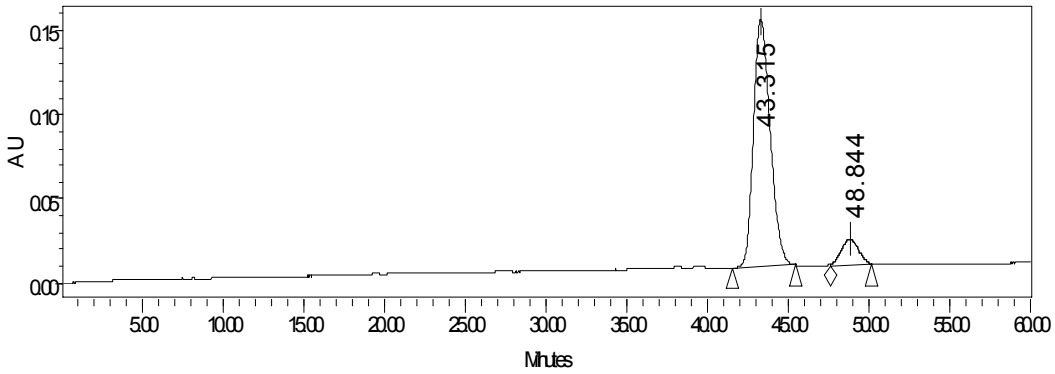


4-cyclohexenyl-2-(2-fluorophenyl)but-3-yn-2-ol (7b)



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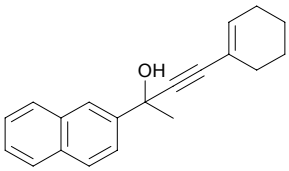
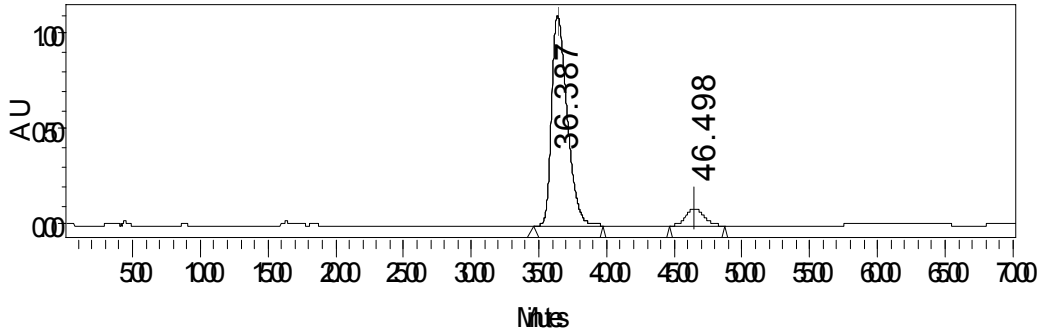


4-cyclohexenyl-2-(naphthalen-3-yl)but-3-yn-2-ol (7c)



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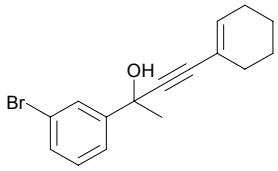
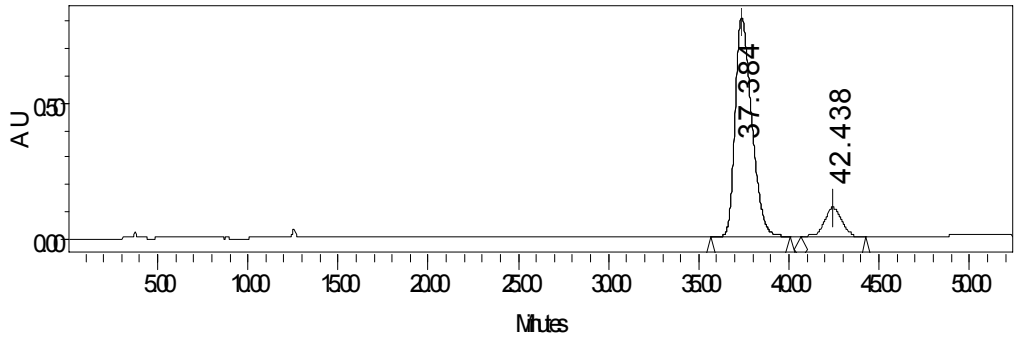
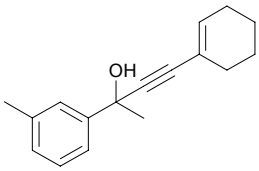


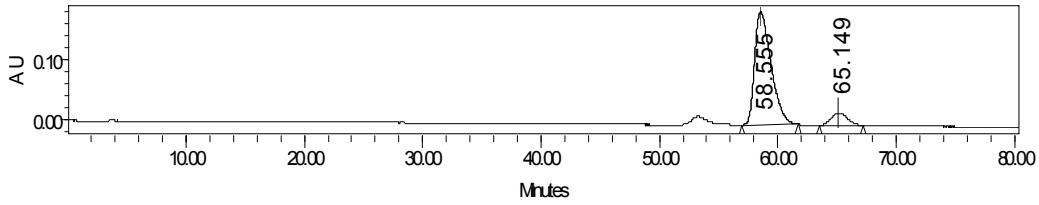
2-(3-bromophenyl)-4-cyclohexenylbut-3-yn-2-ol (7d)



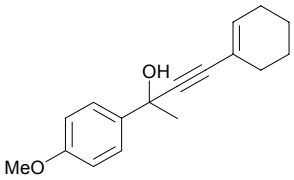
	Name	Retention Time	Area	% Area	Height	Int Type	Amount	Units	Peak Type	Peak Codes
1		37.384	51442737	87.59	803837	BB			Unknown	
2		42.438	7291402	12.41	106347	VB			Unknown	



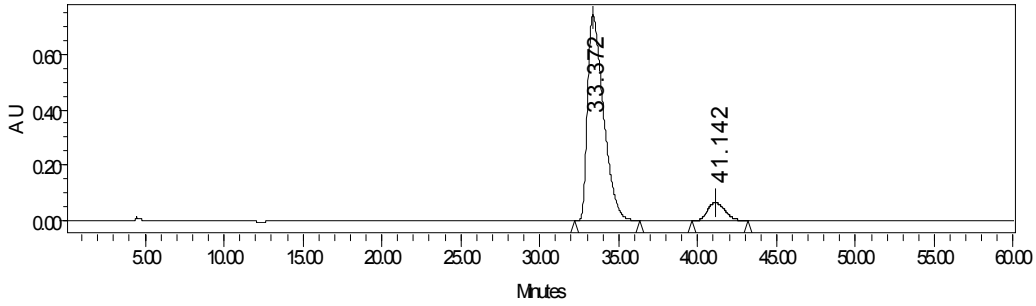
4-cyclohexenyl-2-m-tolylbut-3-yn-2-ol (7e)



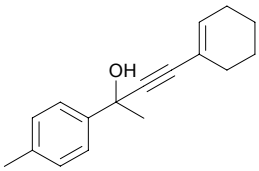
	Name	Retention Time	Area	% Area	Height	Int Type	Amount	Units	Peak Type	Peak Codes
1		58.555	18071445	90.15	187226	BB			Unknown	
2		65.149	1974724	9.85	20701	BB			Unknown	



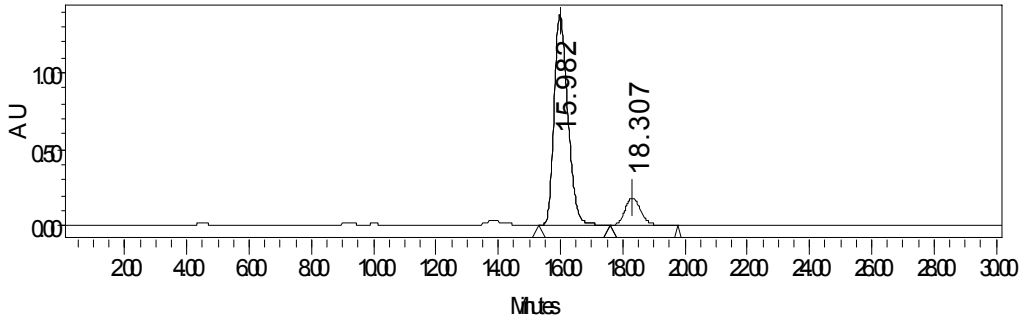
4-cyclohexenyl-2-(4-methoxyphenyl)but-3-yn-2-ol (7f)



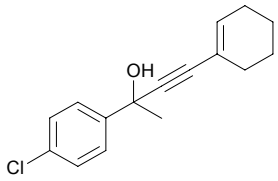
	Name	Retention Time	Area	% Area	Height	Int Type	Amount	Units	Peak Type	Peak Codes
1		33.372	52395303	90.90	741462	BB			Unknown	
2		41.142	5244958	9.10	66994	BB			Unknown	



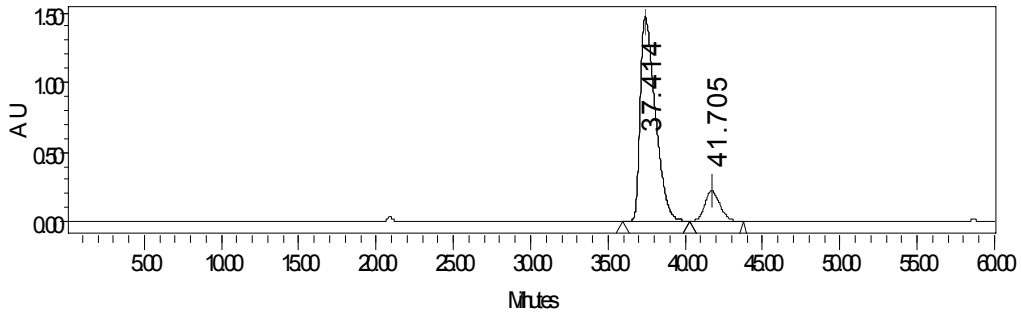
4-cyclohexenyl-2-p-tolylbut-3-yn-2-ol (7g)



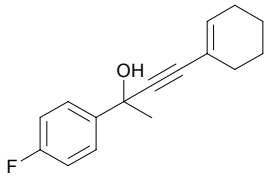
	Name	Retention Time	Area	% Area	Height	Int Type	Amount	Units	Peak Type	Peak Codes
1		15.982	42236614	87.00	1370287	VV			Unknown	
2		18.307	6313136	13.00	181773	VB			Unknown	



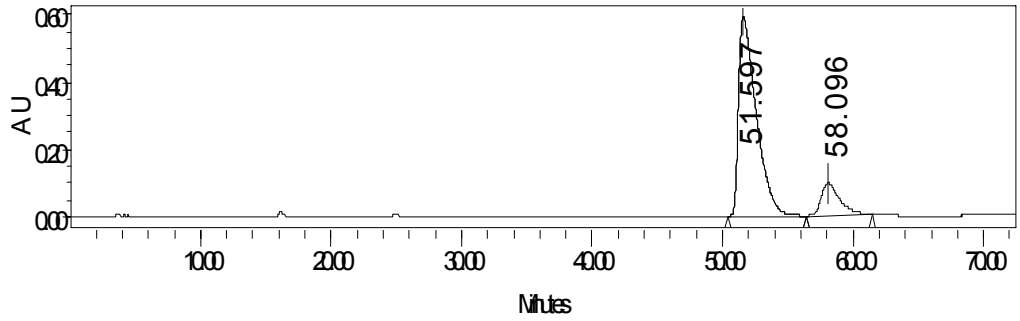
2-(4-chlorophenyl)-4-cyclohexenylbut-3-yn-2-ol (7h)



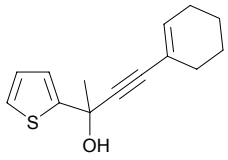
	Name	Retention Time	Area	% Area	Height	Int Type	Amount	Units	Peak Type	Peak Codes
1		37.414	99695709	87.07	1463081	VV			Unknown	
2		41.705	14800877	12.93	216479	VB			Unknown	



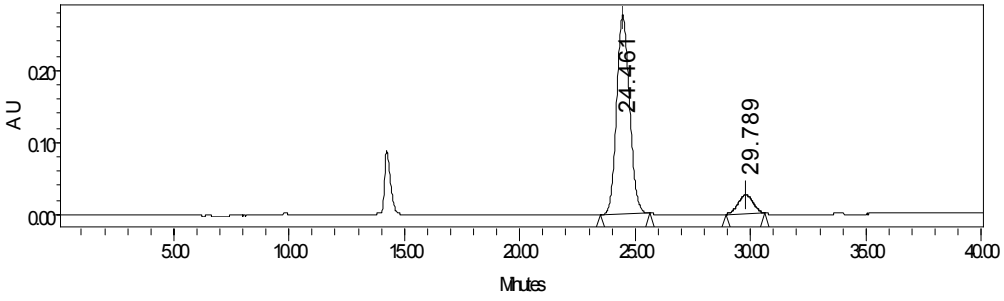
4-cyclohexenyl-2-(4-fluorophenyl)but-3-yn-2-ol (7i)



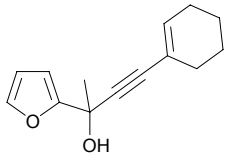
	Name	Retention Time	Area	% Area	Height	Int Type	Amount	Units	Peak Type	Peak Codes
1		51.597	55624559	85.35	595379	BB			Unknown	
2		58.096	9550649	14.65	95785	BB			Unknown	



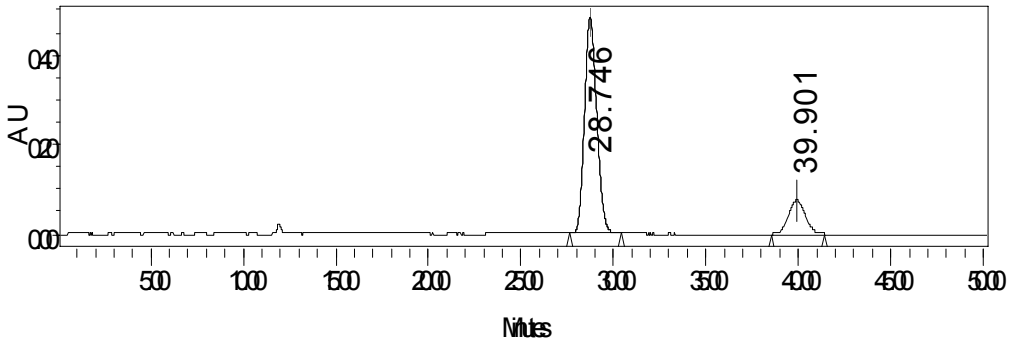
4-cyclohexenyl-2-(thiophen-2-yl)but-3-yn-2-ol (7j)



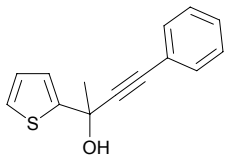
	Name	Retention Time	Area	% Area	Height	Int Type	Amount	Units	Peak Type	Peak Codes
1		24.461	10782560	90.17	276419	bb			Unknown	
2		29.789	1175318	9.83	26107	bb			Unknown	



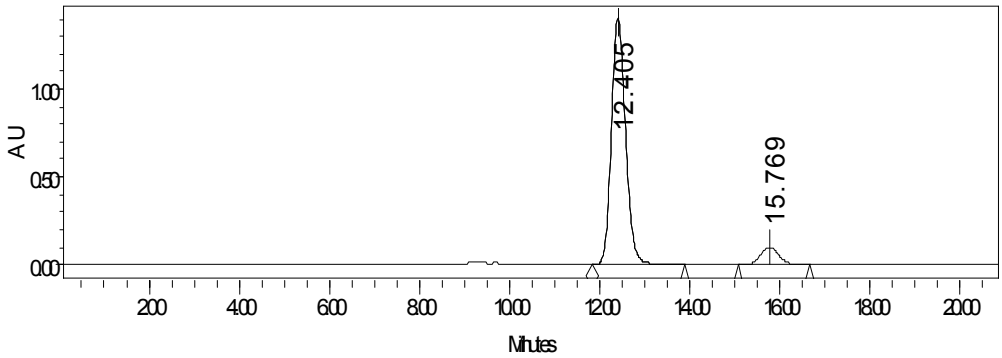
4-cyclohexenyl-2-(furan-2-yl)but-3-yn-2-ol (7k)



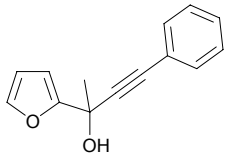
	Name	Retention Time	Area	% Area	Height	Int Type	Amount	Units	Peak Type	Peak Codes
1		28.746	22273285	82.63	483542	BB			Unknown	
2		39.901	4682643	17.37	74811	BB			Unknown	



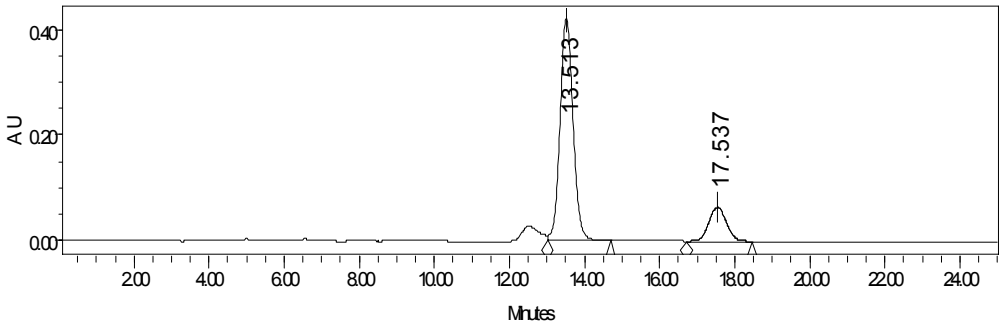
4-phenyl-2-(thiophen-2-yl)but-3-yn-2-ol (7l)



	Name	Retention Time	Area	% Area	Height	Int Type	Amount	Units	Peak Type	Peak Codes
1		12.405	30632272	91.65	1402839	VB			Unknown	
2		15.769	2791580	8.35	99135	BB			Unknown	



2-(furan-2-yl)-4-phenylbut-3-yn-2-ol (7m)



	Name	Retention Time	Area	% Area	Height	Int Type	Amount	Units	Peak Type	Peak Codes
1		13.513	10274725	83.30	422680	VB			Unknown	
2		17.537	2059258	16.70	64683	VB			Unknown	

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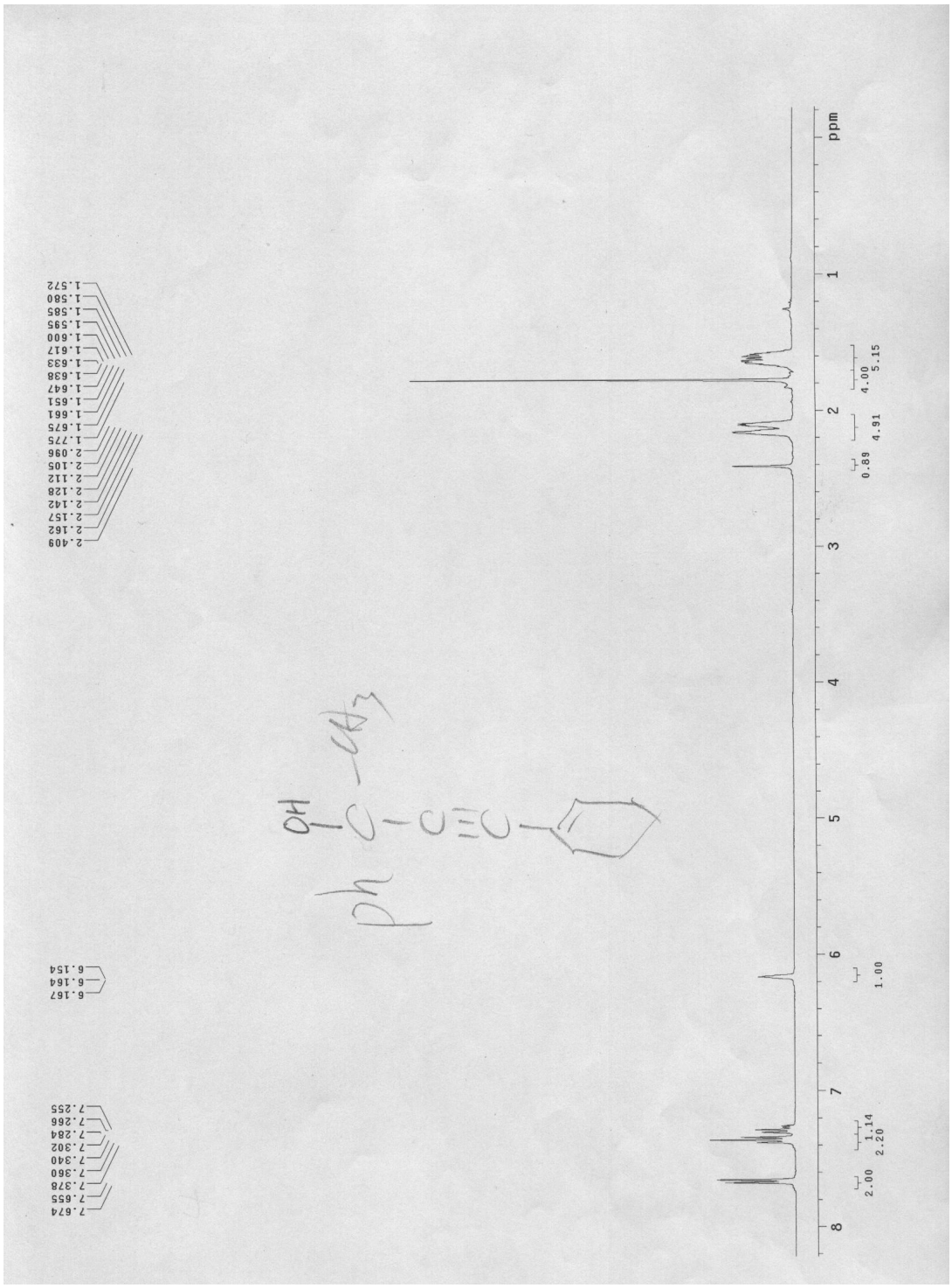
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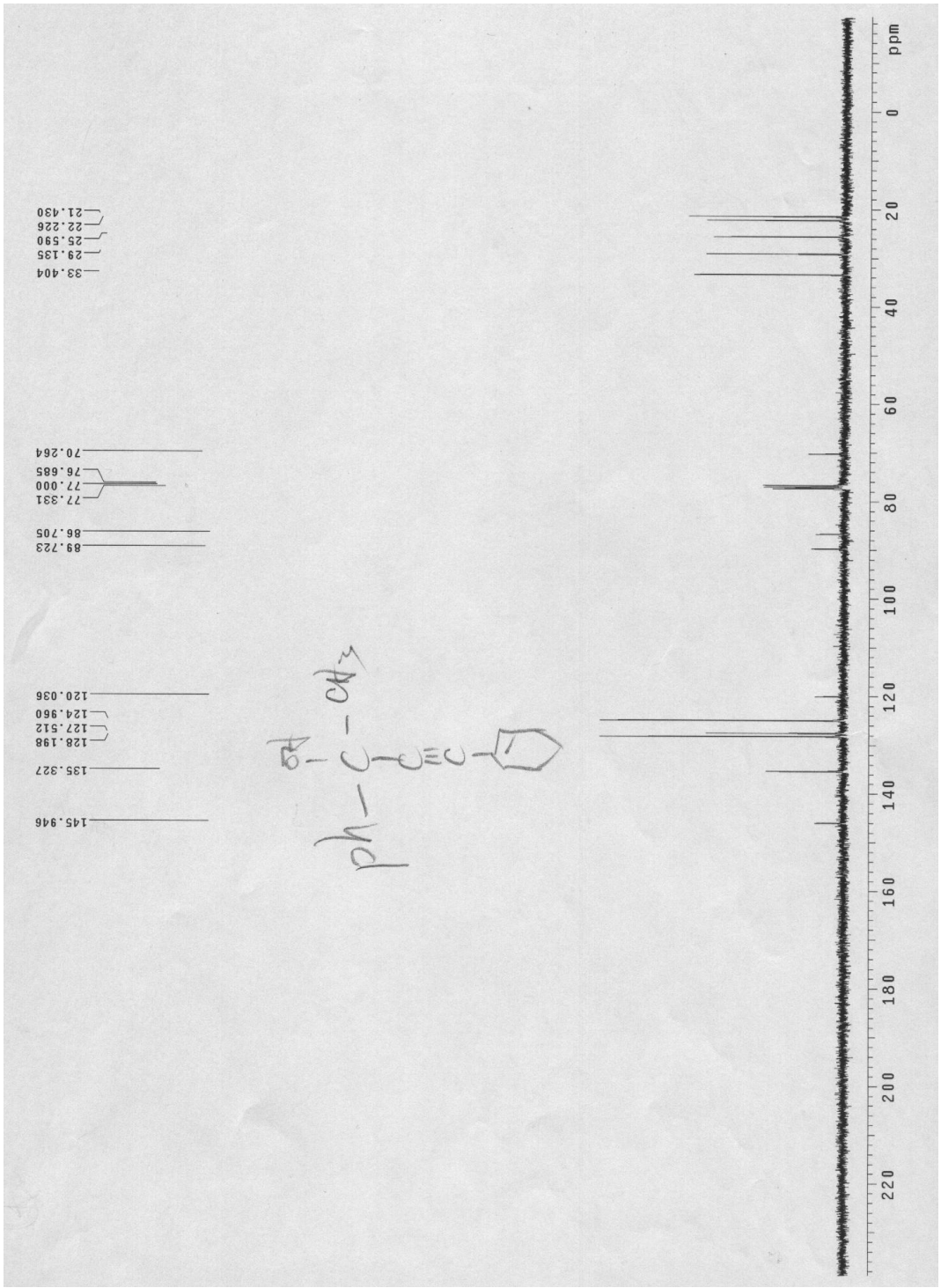

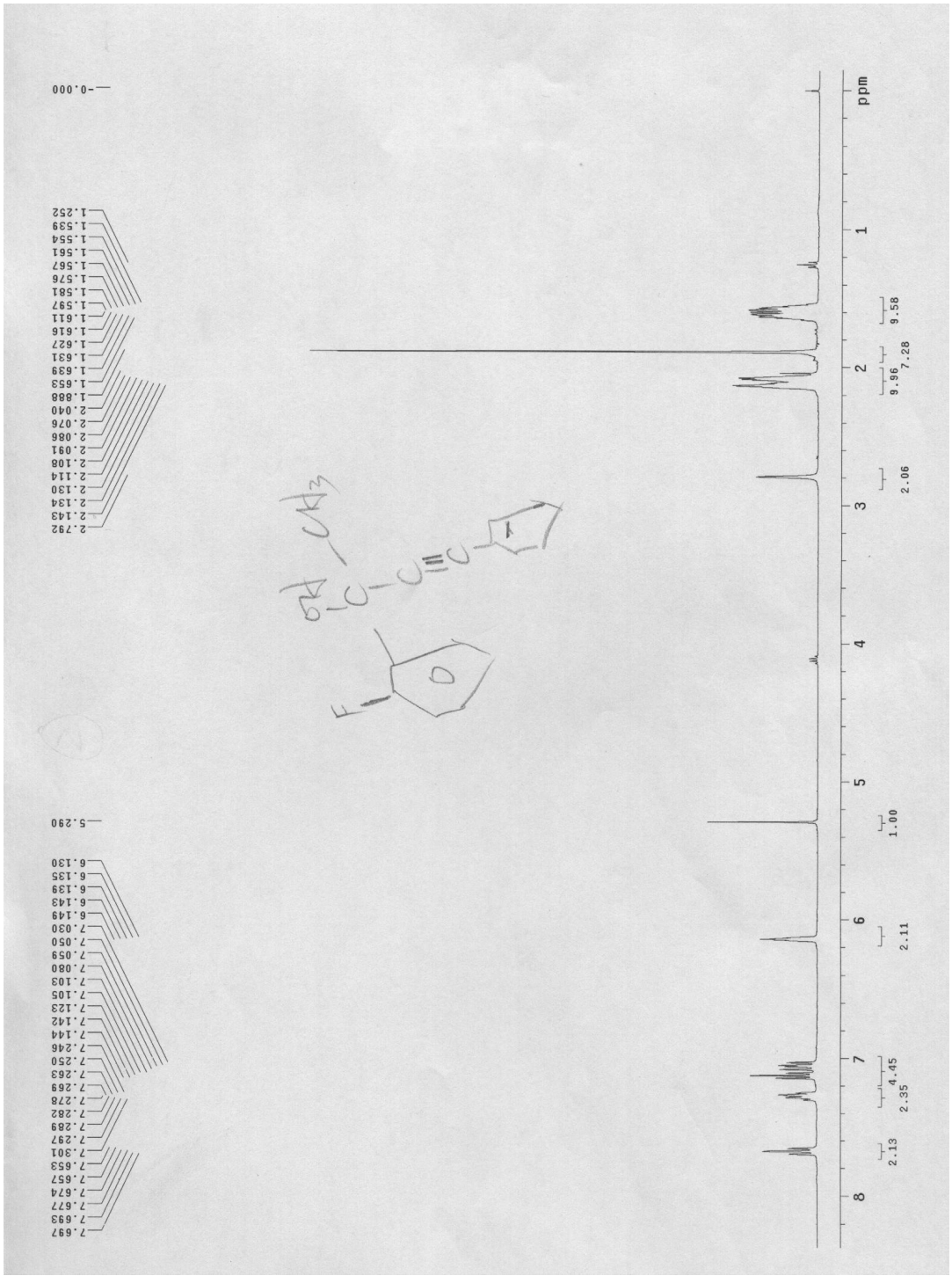

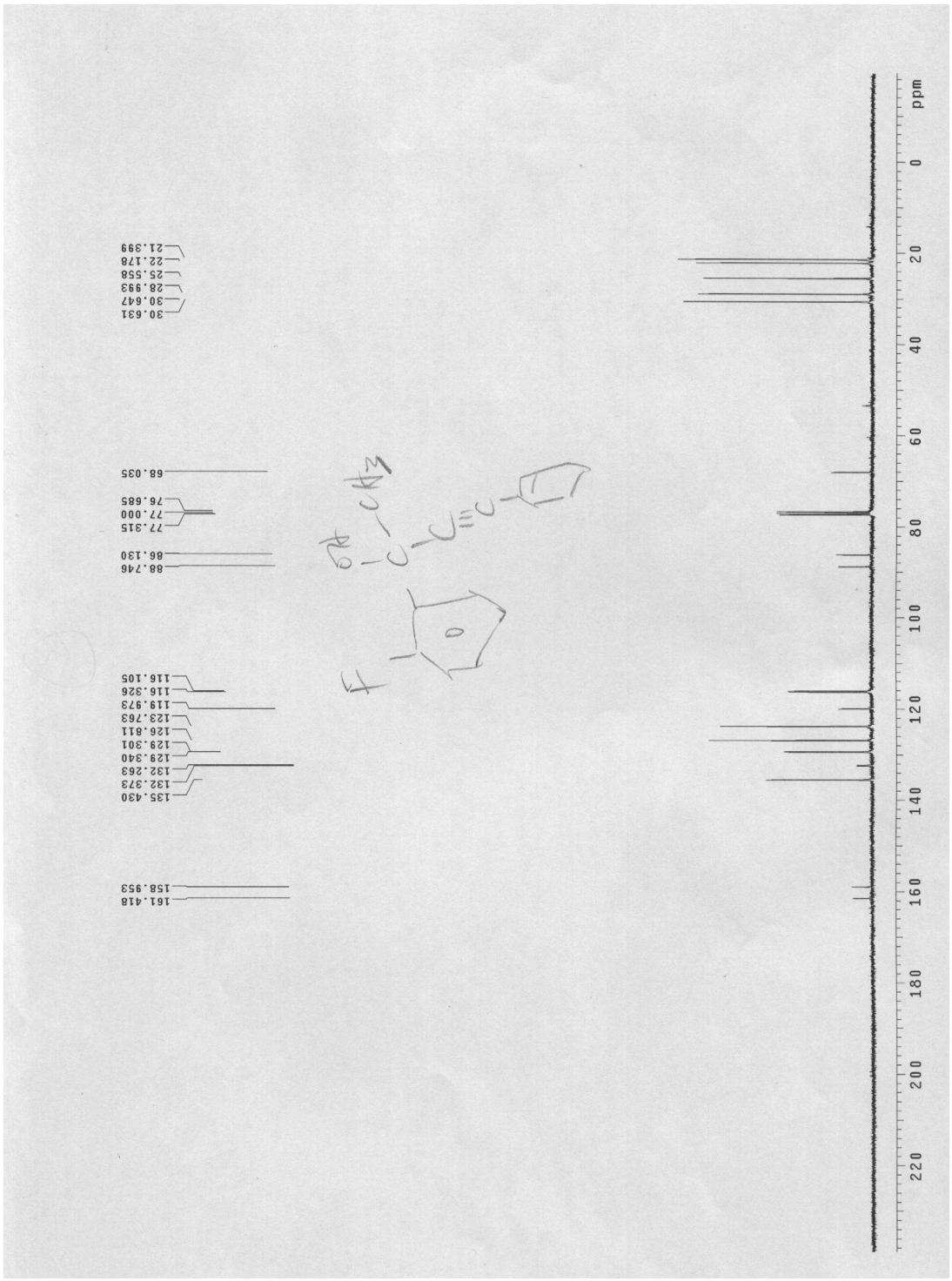

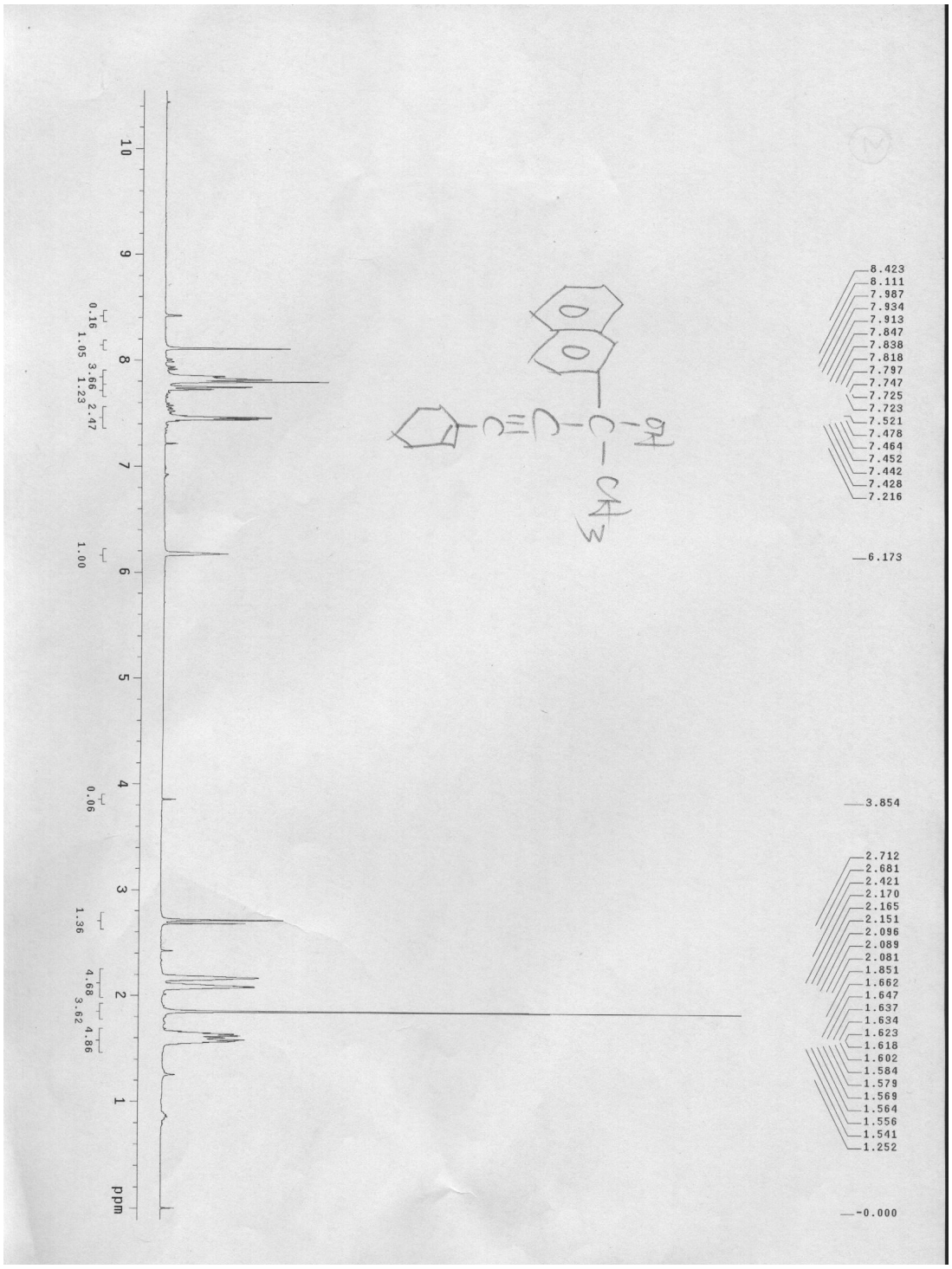

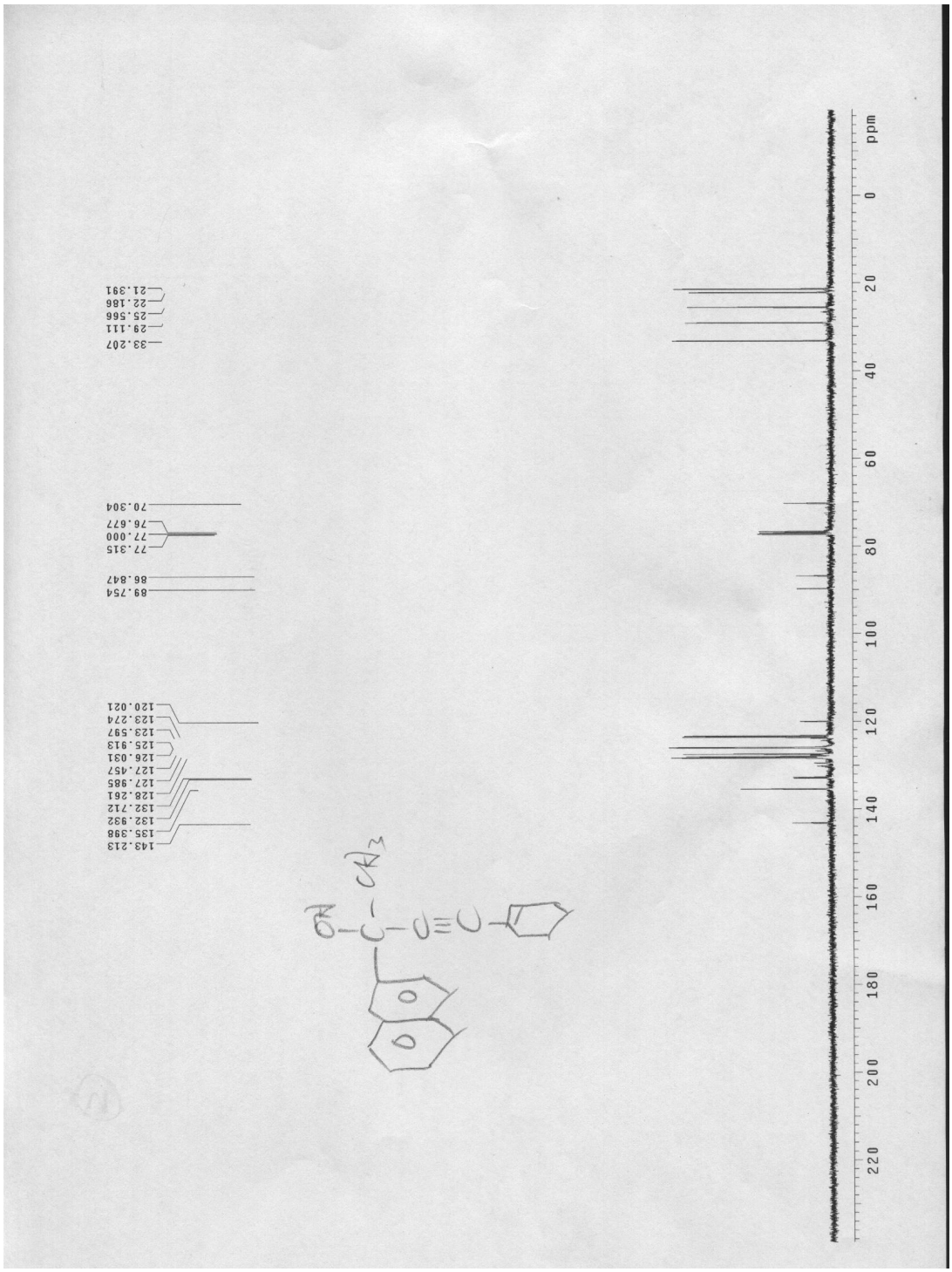

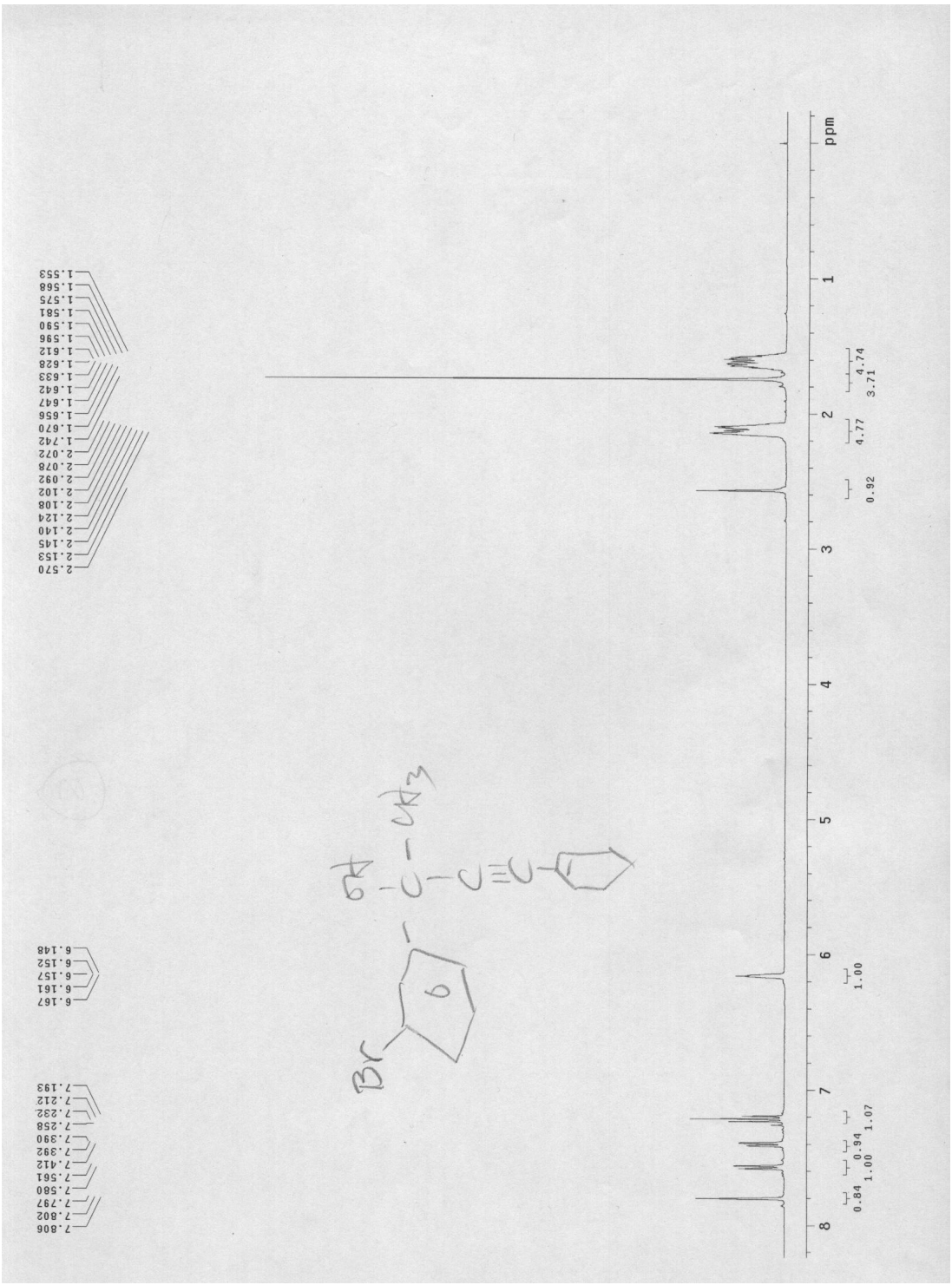

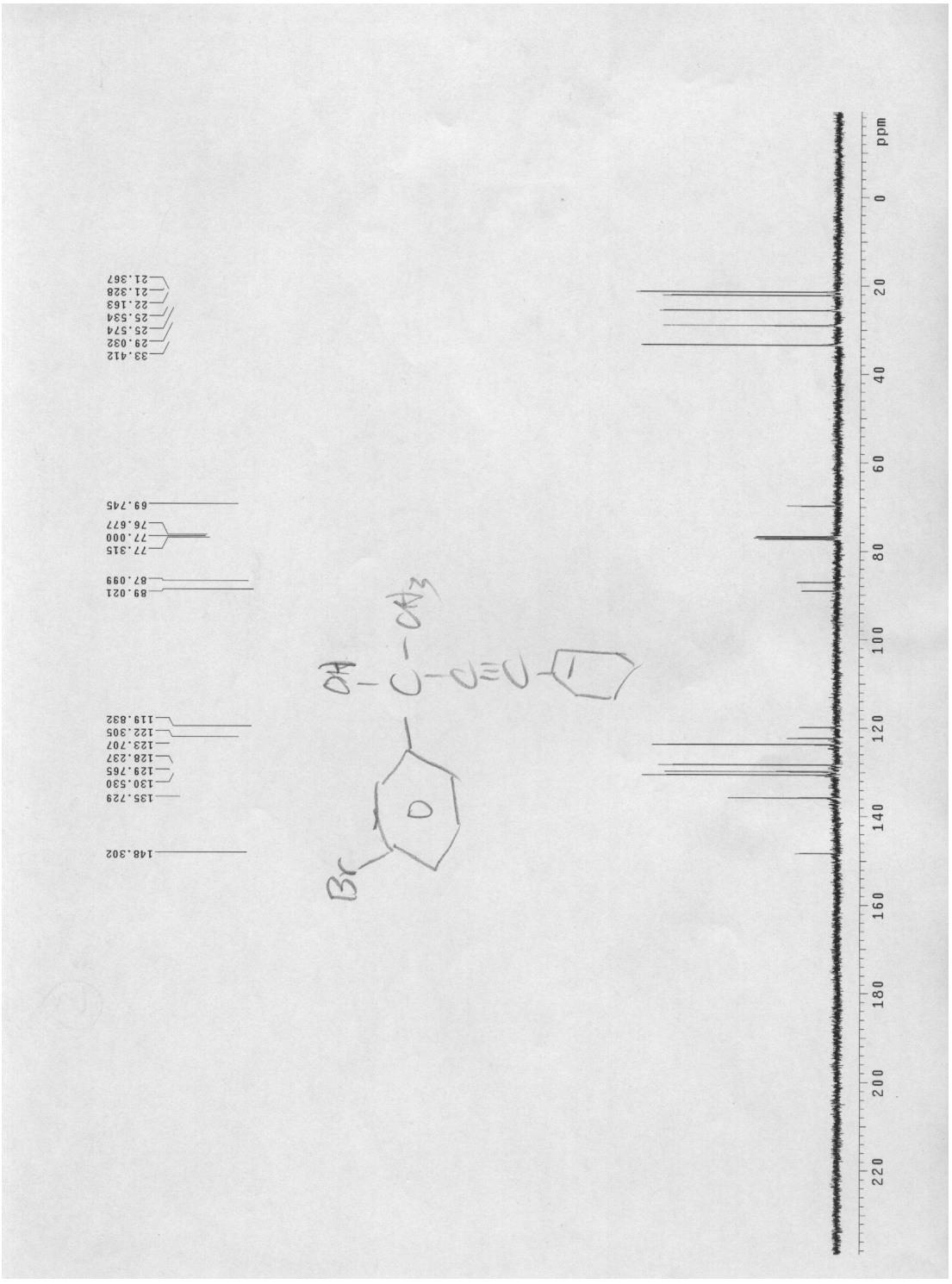

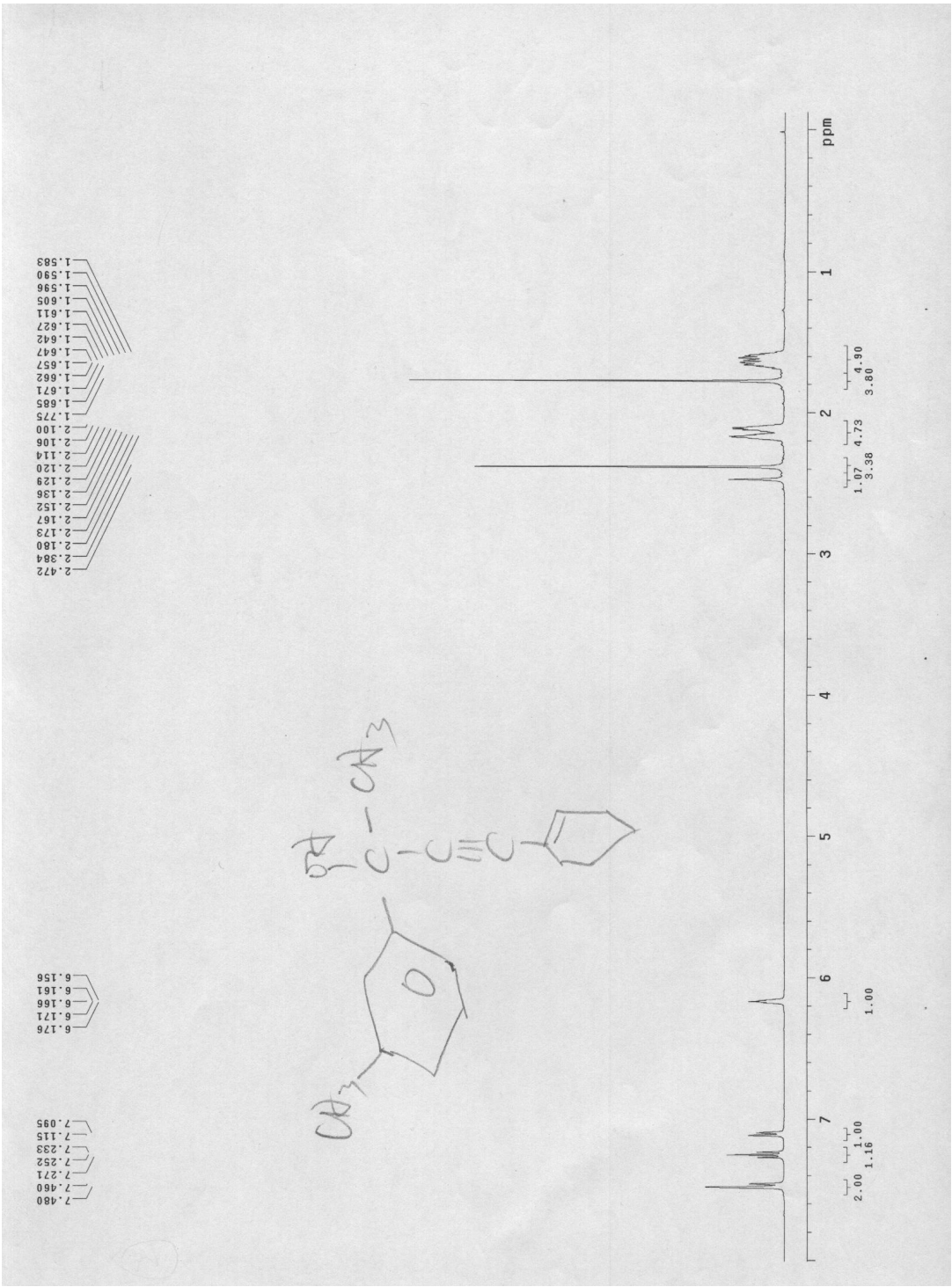

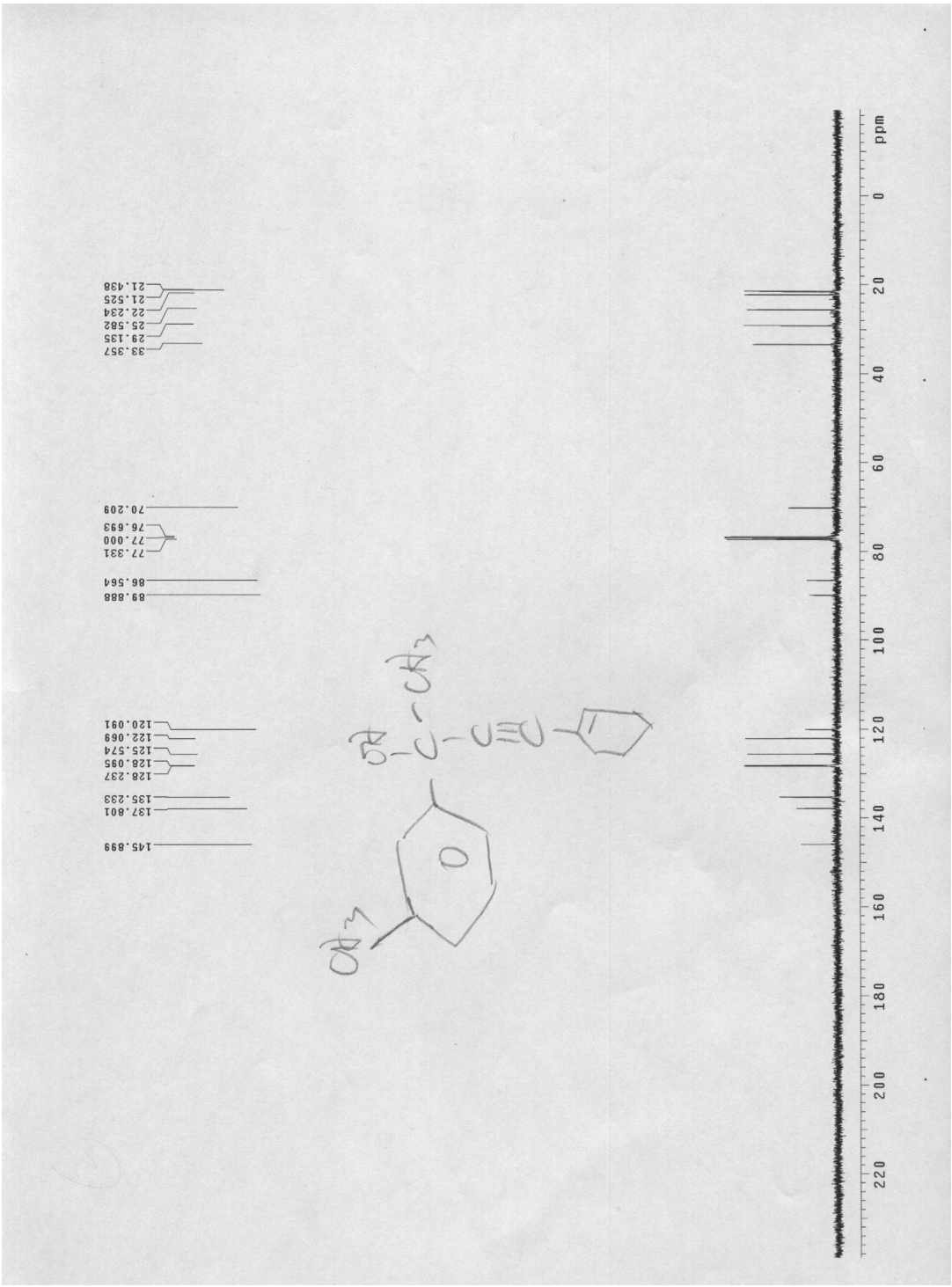

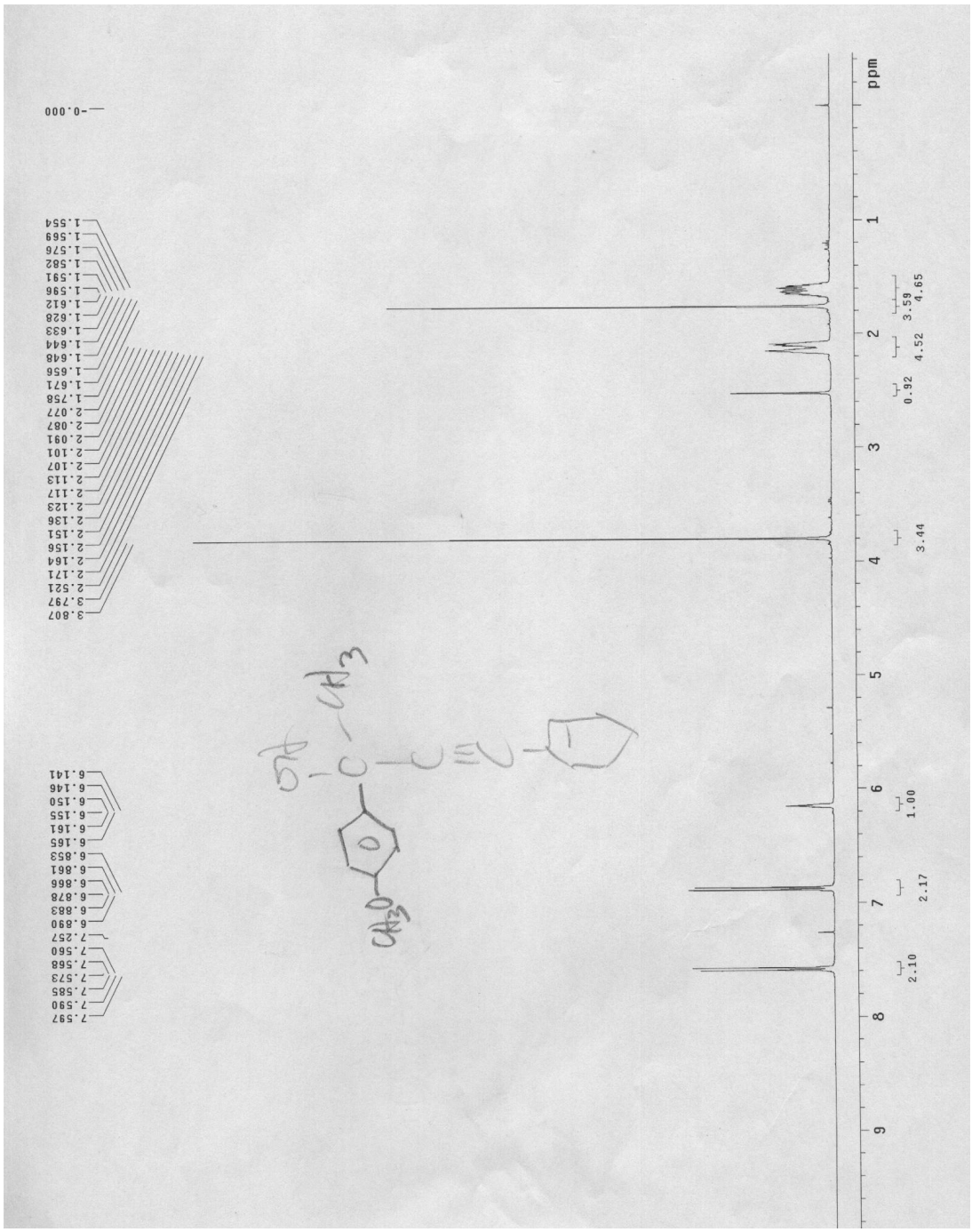

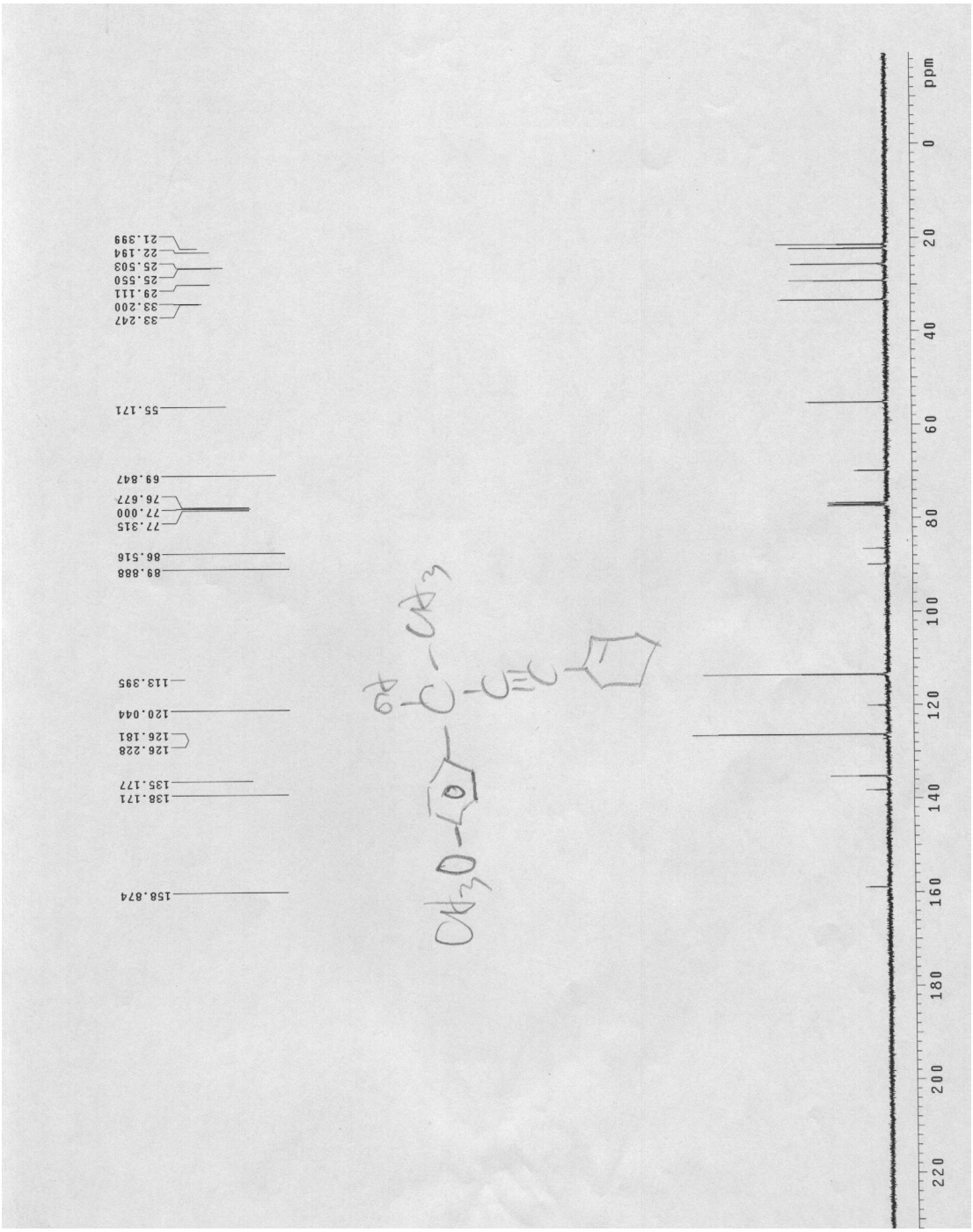

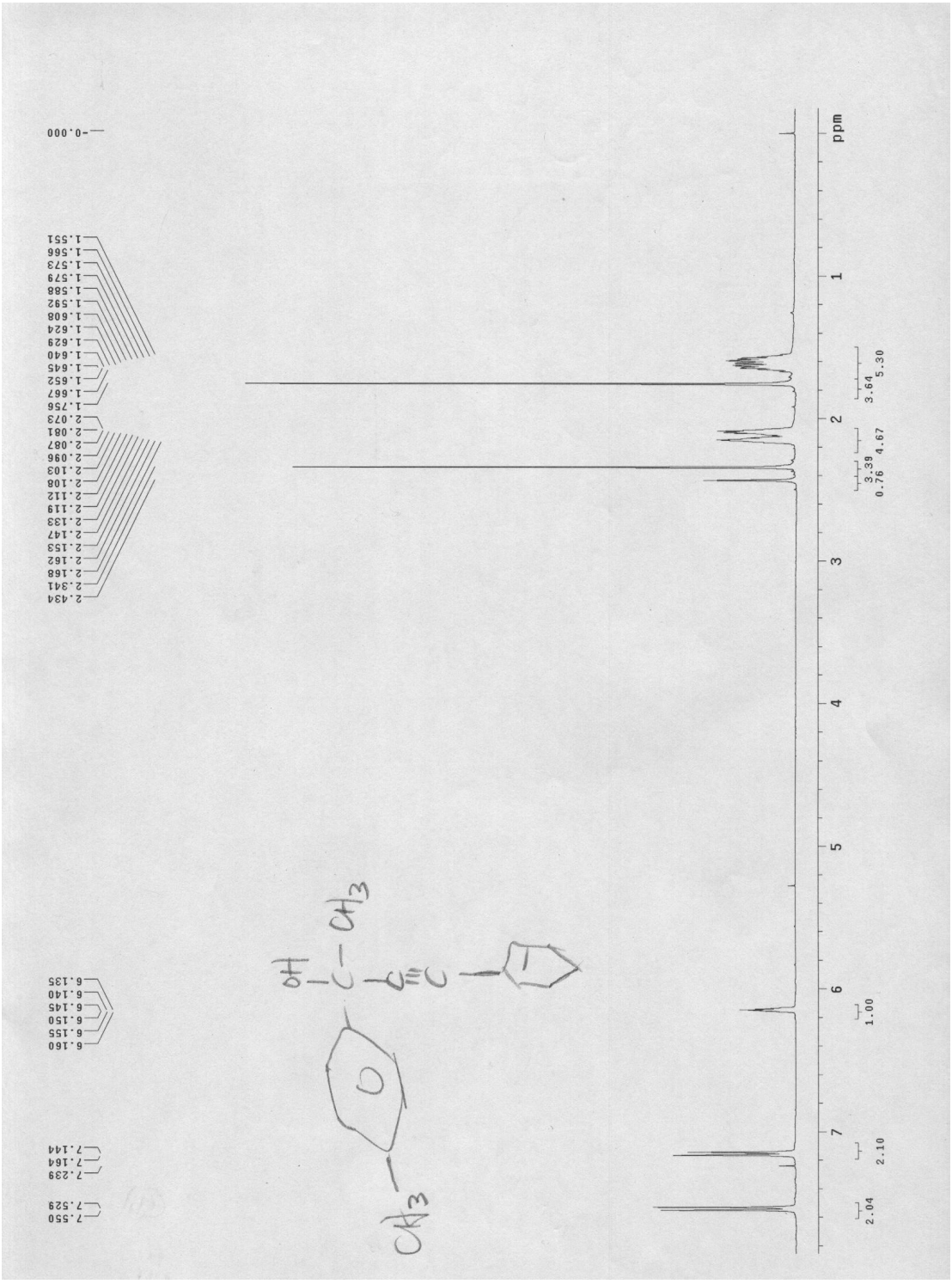
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