Supplementary Material (ESI) for Chemical Communications

Electronic Supplementary Information (ESI)

A new approach to switching of enantioselectivity in NHC–Cu-catalyzed conjugate addition of alkylzincs to cyclic enones

Masaki Okamoto, Yuko Yamamoto and Satoshi Sakaguchi*

Department of Chemistry and Materials Engineering & High Technology Research Centre, Faculty of Chemistry, Materials and Bioengineering
Kansai University, Suita, Osaka 564-8680 (Japan)
Fax: (+81) 6-6339-4026
E-mail: satoshi@ipcku.kansai-u.ac.jp

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General. All chemicals were obtained from commercial sources and were used as received. Azolium chlorides **3-12** has been prepared according to our previous paper.[1] ^{1}H- and ^{13}C-NMR spectra were recorded on spectrometers at 400 and 100 MHz, respectively. Flash column chromatography was executed on silica gel 60 (Merck, mesh: 230-400; particle size: 0.040-0.063 nm).

Procedure for prepation of 9. To a flask were added N-benzylbenzimidazole[2] (4.4 mmol), 1,4-dioxane (15 mL) and α-chloroacetoaminde derived from chloroacetyl chloride and (*S*)-leucinol[3] (4 mmol). After stirring the reaction mixture at 110 ºC for 16 h, the solvent was removed under reduced pressure. The residue was dissolved in methanol, and then activated carbon (ca. 1 g) was added. After 16 h, the activated carbon was removed by filtration. The filtrate was concentrated under reduced pressure to obtain a solid, which was purified by reprecipitation using ethyl acetate and methanol to afford the corresponding coupling product as a white solid.

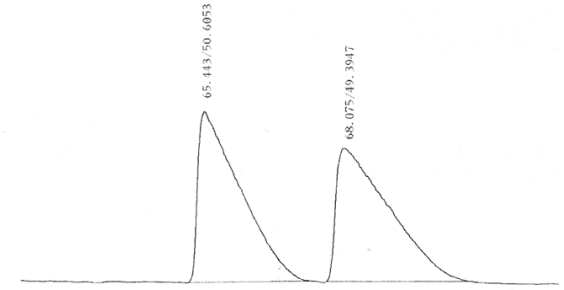
1-[2-((*S*)-1-hydroxy-4-methyl-2-pentanylamino)-2-oxoethyl]-3-benzylbenzimidazolium chloride (9): ^{1}H-NMR ($CDCl_3$): δ 10.7 (s, 1H), 9.20 (d, *J* = 8.2 Hz, 1H), 7.99 (d, *J* = 8.2 Hz, 1H), 7.57–7.27 (m, 8H), 7.42–7.32 (m, 5H), 5.86 (d, *J* = 16.0 Hz, 1H), 5.79 (d, *J* = 15.2 Hz, 1H), 5.72 (d, *J* = 15.2 Hz, 1H), 5.64 (d, *J* = 16.0 Hz, 1H), 4.72 (br, 1H), 3.97 (br, 1H), 3.65–3.54 (m, 2H), 1.61–1.50 (m, 2H), 1.27–1.24 (m, 1H), 0.83 (d, *J* = 6.4 Hz, 3H), 0.78 (d, *J* = 6.4 Hz, 3H); ^{13}C-NMR: δ 164.6, 143.6, 132.3, 132.2, 130.6, 129.3, 129.2, 127.9, 127.2, 126.9, 114.2, 113.0, 64.3, 51.5, 51.1, 49.8, 39.6, 24.8, 22.7, 22.3. Anal. Calc. for $C_{22}H_{28}ClN_3O_2$•0.25H_2O: C, 65.01; H, 7.07; N, 10.34. Found: C, 64.67; H, 6.65; N, 10.08%.

General procedure for catalytic asymmetric reaction of cyclic enone with R_2Zn. To a solution of $Cu(OTf)_2$ (0.06 mmol) in dehydrated THF (9 mL) was added **9** (0.045 mmol). Then, the reaction vessel was cooled at 0 ºC, and enone (1 mmol) followed by R_2Zn (3 mmol, 1 mol/L in hexanes for Et_2Zn or in heptane for Bu_2Zn) were added. The color immediately changed from yellow to dark brown. After stirring at room temperature for 3 h, the reaction was quenched with 10% HCl aq. (ca. 5 mL). The resulting mixture was extracted with diisopropyl ether (15 mL x 3) and dried over Na_2SO_4. The product was purifiled by silica gel column chromatography (hexane/EtOAc = 9/1). Enantiomeric excess was measured by chiral GLC. The configuration assigned through comparison with GLC data in the literature.

3-Ethylcyclohexanone (2)

Enantiomeric excess was determined by chiral GLC (Supelco γ-Dex225, 70 °C, N_2 gas, linear velocity of 27.5 cm/s, Rt = 65 min (*S*), 69 min (*R*)).[4,5]

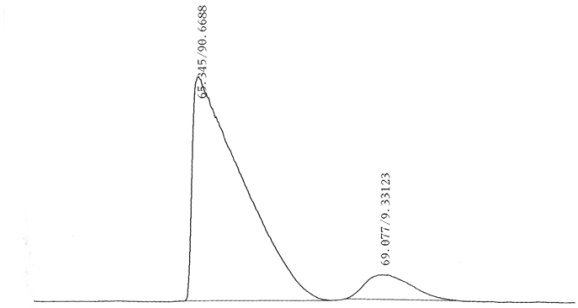
Racemic compound



** 定量計算結果 **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC	NAME
1	1	65.443	62017	1116			50.6053	
	2	68.075	60533	870			49.3947	
		TOTAL	122550	1986			100	

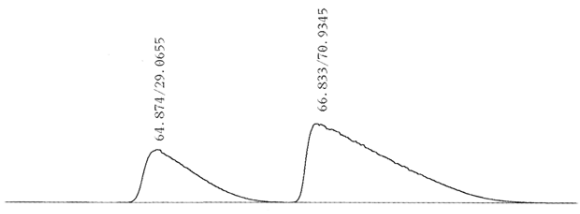
Table 1, Run 10 (*S* : *R* = 90.5 : 9.5)



** 定量計算結果 **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC	NAME
1	1	65.345	104210	1482			90.6688	
	2	69.077	10725	164			9.3312	
		TOTAL	114935	1646			100	

Table 2, Run 7 (*S* : *R* = 29.5 : 70.5)



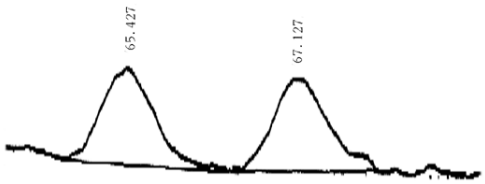
定量計算結果 **

PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC	NAME
1	64.874	76274	1796			29.0655	
2	66.833	186148	2672			70.9345	

3-Butylcyclohexanone (13)

Enantiomeric excess was determined by chiral GLC (Supelco γ-Dex225, 90 °C, N_2 gas, linear velocity of 27.5 cm/s, Rt = 65 min (*S*), 67 min (*R*)).[5]

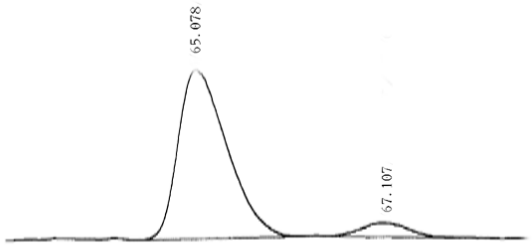
Racemic compound



定量計算結果 **

PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC
1	65.427	9718	268			49.4283
2	67.127	9943	259			50.5717
	TOTAL	19662	527			100

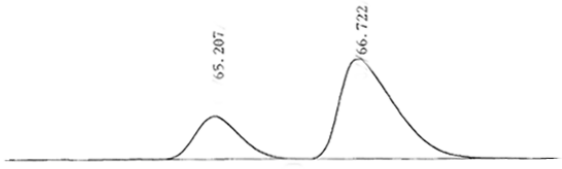
Table 3, Run 1 (*S* : *R* = 92 : 8)



** 定量計算結果 **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC
2	1	65.078	97579	2650			92.225
	2	67.107	8226	229			7.775
		TOTAL	105806	2880			100

Table 3, Run 2 (*S* : *R* = 26 : 74)



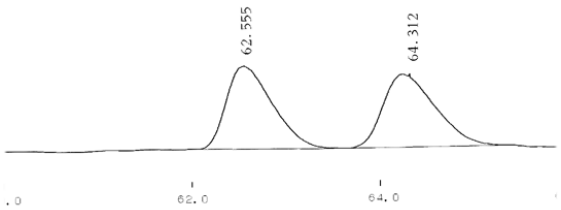
** 定量計算結果 **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC
2	1	65.207	42774	1313			25.6504
	2	66.722	123984	3075			74.3496
		TOTAL	166758	4389			100

4,4-Dimethyl-3-ethlcyclohexanone

Enantiomeric excess was determined by chiral GLC (Supelco γ-Dex225, 85 °C, N_2 gas, linear velocity of 27.5 cm/s, Rt = 62 min (*R*), 64 min (*S*)).[5]

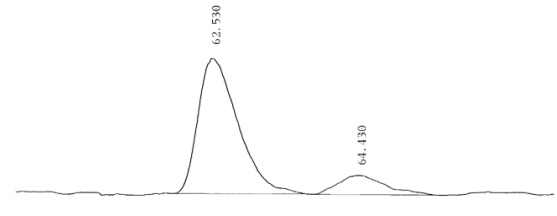
Racemic compound



定量計算結果 **

PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC
1	62.555	60377	1782			50.1376
2	64.312	60045	1575			49.8624
	TOTAL	120422	3356			100

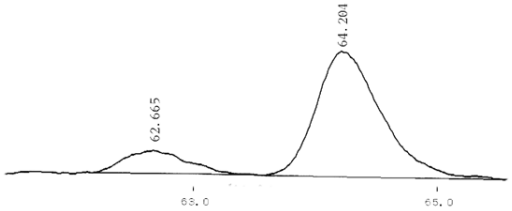
Table 3, Run 3 (*R : S* = 86 : 14)



** 定量計算結果 **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC	NAME
2	1	62.53	64086	1783			85.6034	
	2	64.43	10778	255			14.3966	
		TOTAL	74864	2038			100	

Table 3, Run 4 (*R : S* = 15 : 85)



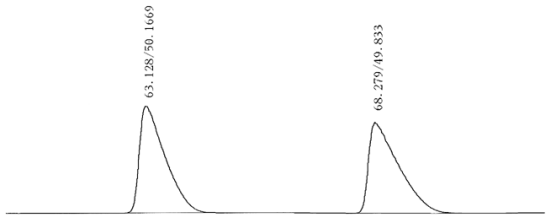
算結果 **

TIME	AREA	HEIGHT	MK	IDNO	CONC
62.665	5047	142			14.9283
64.204	28761	768			85.0717
TOTAL	33808	909			100

3-Ethylcycloheptanone (16)

Enantiomeric excess was determined by chiral GLC (Supelco β-Dex225, 80 °C, N_2 gas, linear velocity of 27.5 cm/s, Rt = 63 min (*S*), 69 min (*R*)).[5]

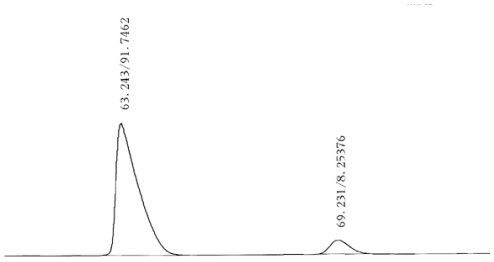
Racemic compound



** 定量計算結果 **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC	NAME
1	1	63.128	56373	1417			50.17	
	2	68.279	55998	1208			49.83	
		TOTAL	112370	2624			100	

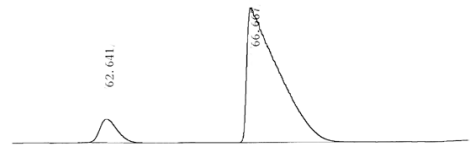
Table 3, Run 5 (*S* : *R* = 92 : 8)



** 定量計算結果 **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC
1	1	63.243	75067	1752			91.75
	2	69.231	6753	180			8.25
		TOTAL	81820	1932			100

Table 3, Run 6 (*S* : *R* = 9 : 91)



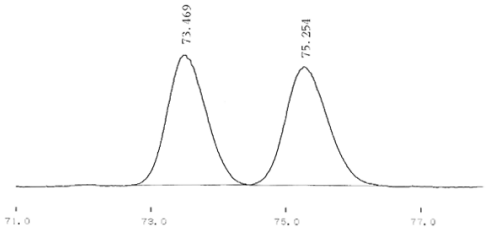
** 定量計算結果 **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC
1	1	62.641	15080	447			8.8592
	2	66.667	155142	2546			91.1408
		TOTAL	170222	2993			100

3-Butylccloheptanone (17)

Enantiomeric excess was determined by chiral GLC (Agilent J&W Cyclodex-B, 100 °C, N_2 gas, linear velocity of 27.5 cm/s, Rt = 73 min (*S*), 75 min (*R*)).[6]

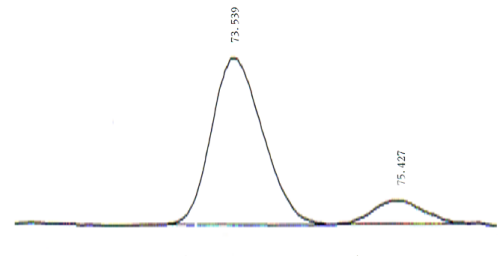
Racemic compound



** 定量計算結果 **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC
1	1	73.469	17281	431			50.1764
	2	75.254	17160	394			49.8236
		TOTAL	34441	825			100

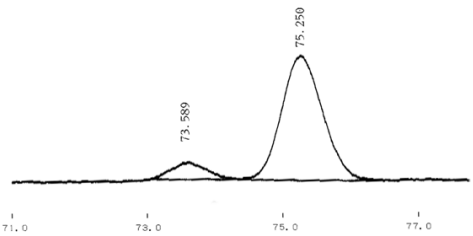
Table 3, Run 7 (*S* : *R* = 88 : 12)



** 定量計算結果 **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC	NAME
1	1	73.539	18684	449			87.9572	
	2	75.427	2558	63			12.0428	

Table 3, Run 8 (*S* : *R* = 11 : 89)



** 定量計算結果 **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC
1	1	73.589	1289	36			10.6466
	2	75.25	10814	256			89.3534
		TOTAL	12103	292			100

References

1. S. Sakaguchi, M. Kawakami, J. O'Neill, K. S. Yoo and K. W. Jung, J. Organomet. Chem., in press.

2. G. Guillemot, M. Neuburger and A. Pfaltz, *Chem. Eur. J.*, 2007, **13**, 8960.

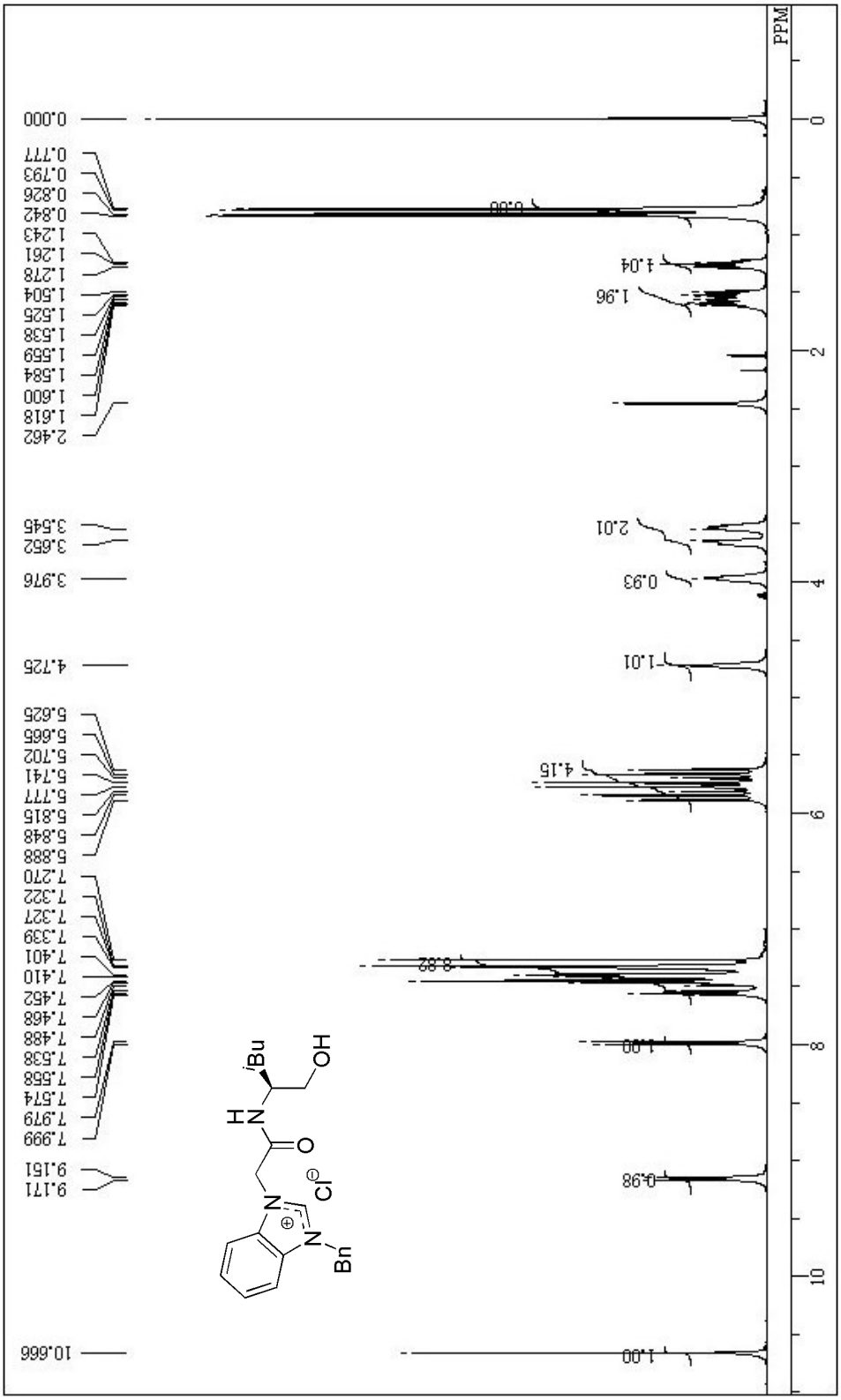
3. W.-C. Shieh, M. Lozanov, M. Loo, O. Repic and T. J. Blacklock, *Tetrahedron Lett.*, 2003, **44**, 4563.

4. Y. Matsumoto, K.-I. Yamada and K. Tomioka, *J. Org. Chem.*, 2008, **73**, 4578.

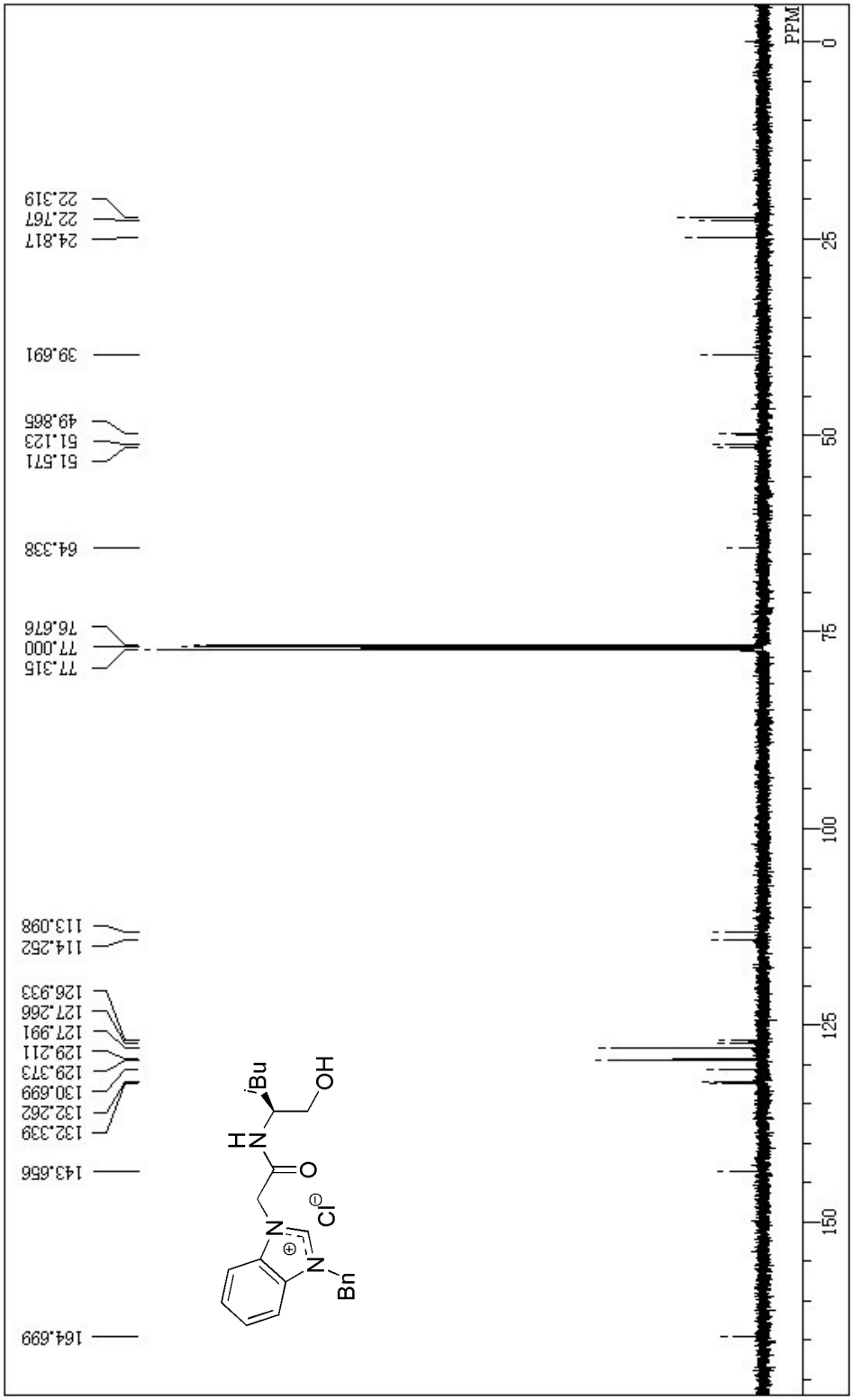
5. K. Kawamura, H. Fukuzawa and M. Hayashi, *Org. Lett.*, 2008, **10**, 3509.

6. S. J. Degrado, H. Mizutani and A. H. Hoveyda, *J. Am. Chem. Soc.*, 2001, **123**, 755.

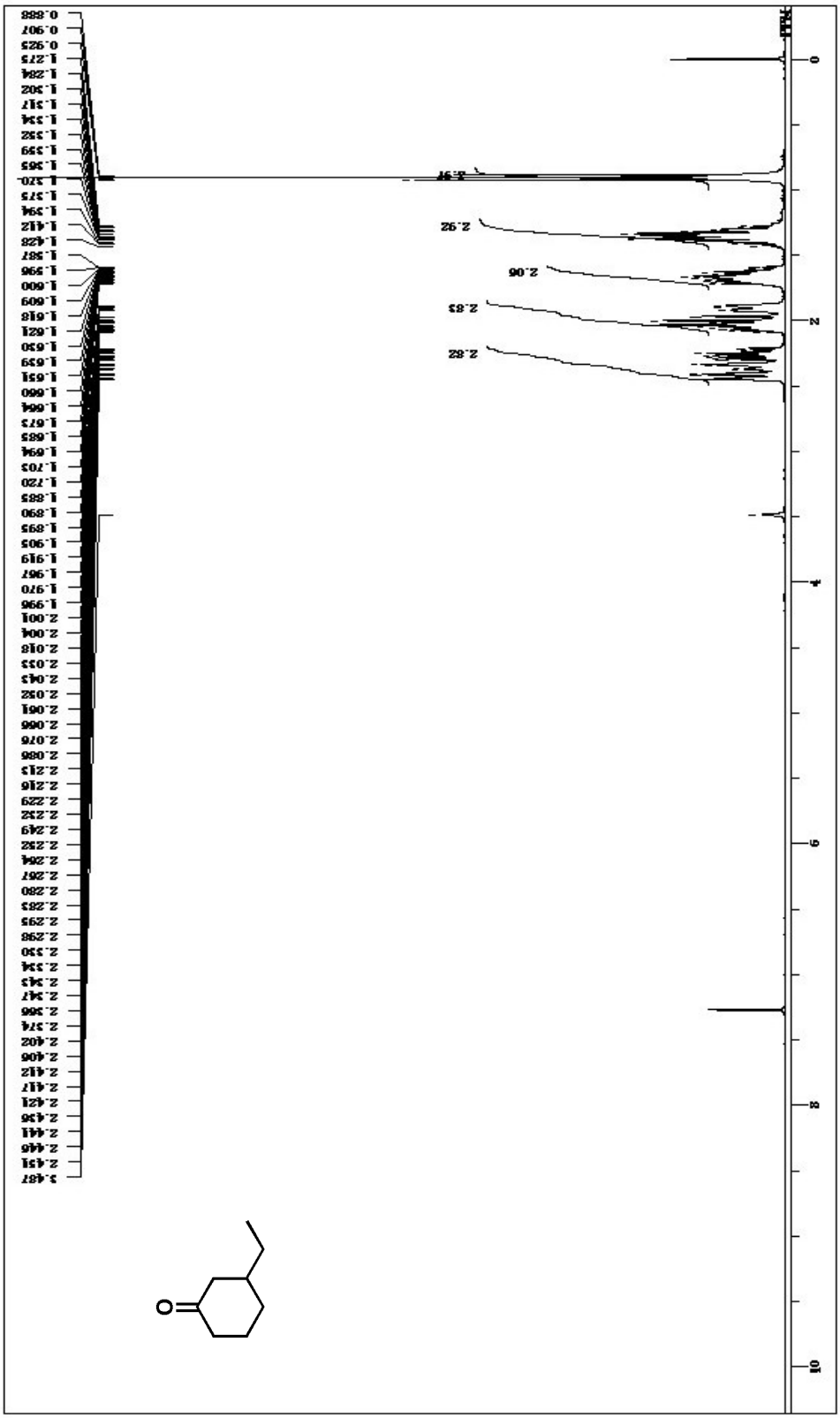
[1]H-NMR Spectra for **9**



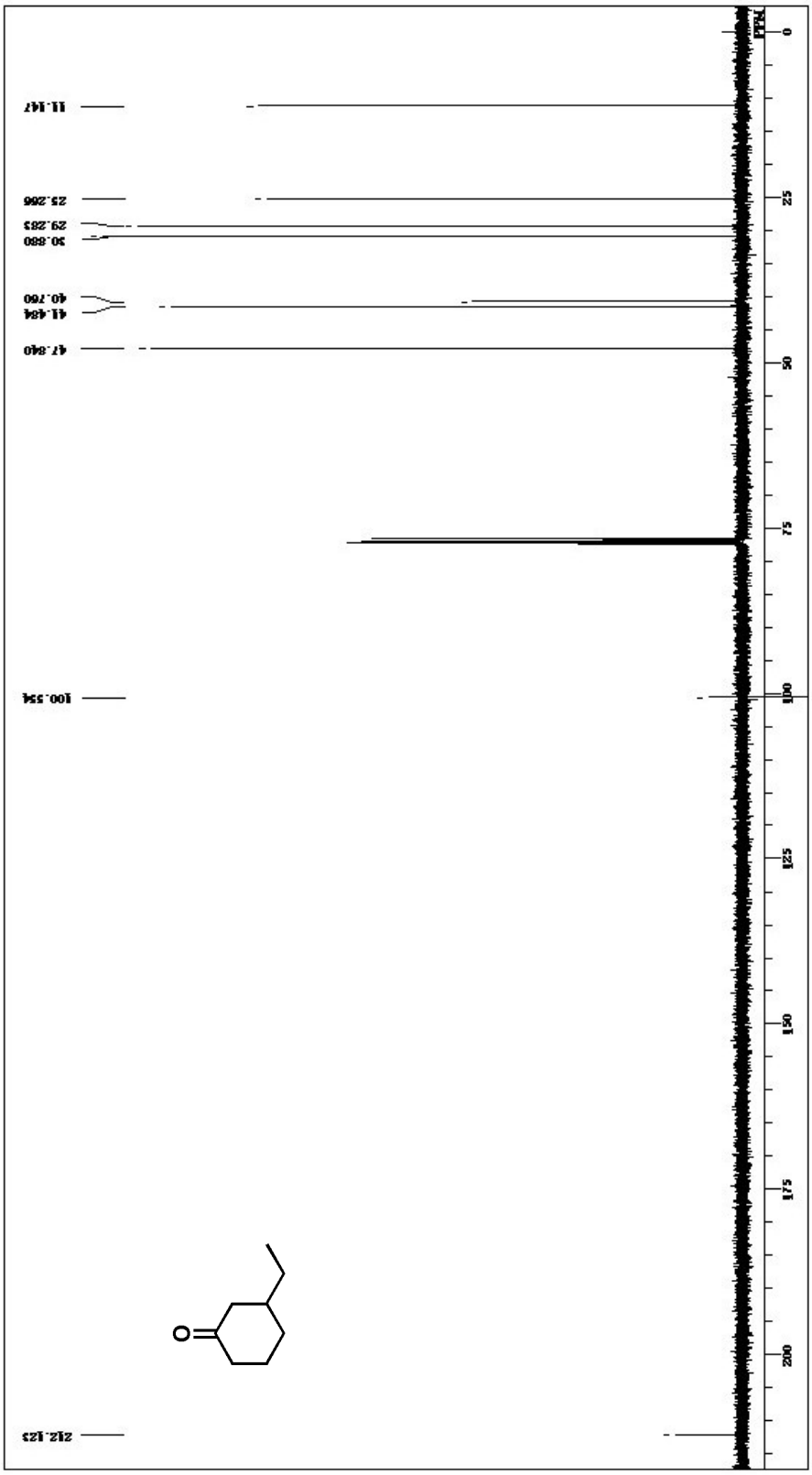
^{13}C-NMR Spectra for **9**



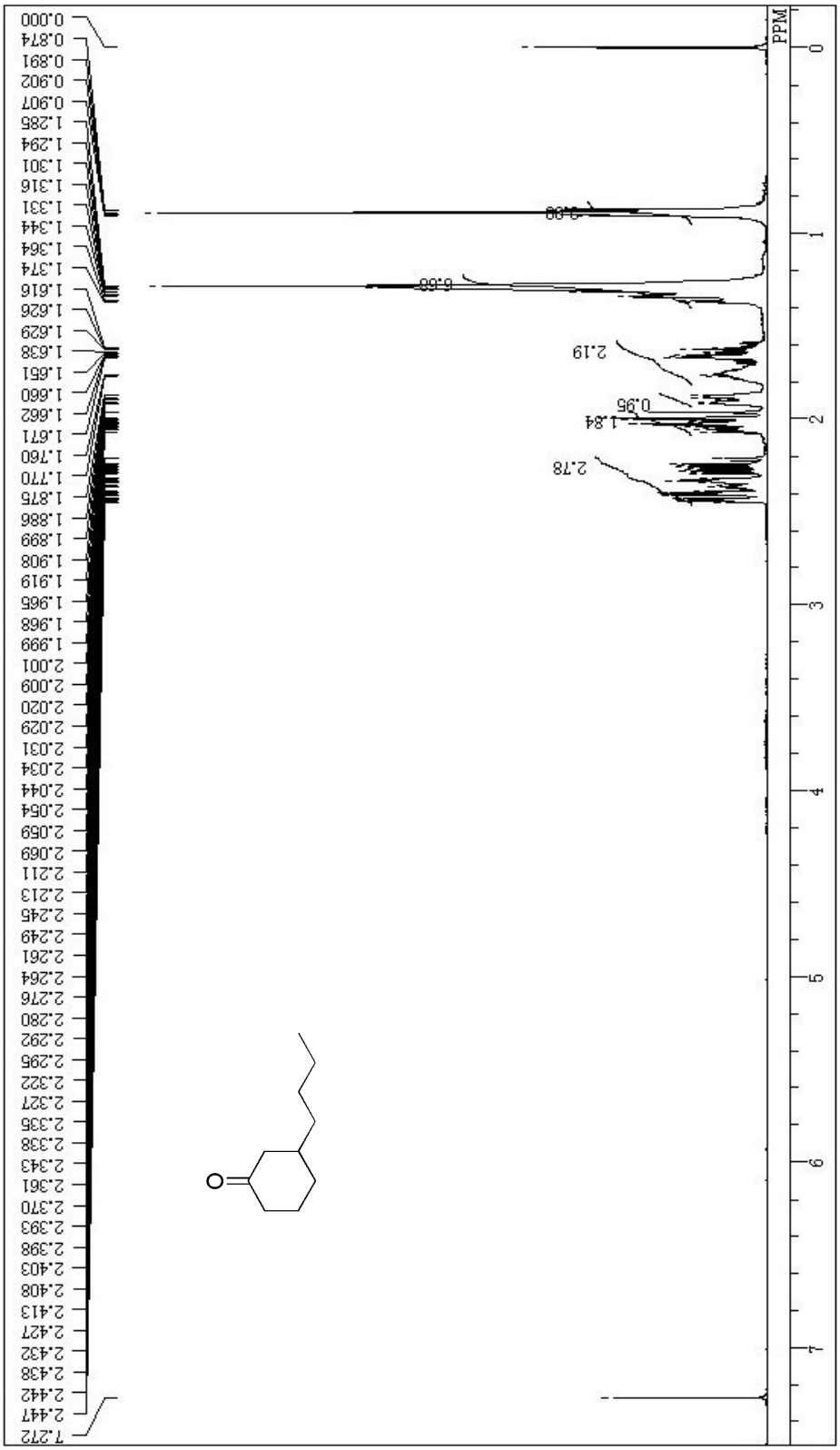
^{1}H-NMR Spectra for 3-ethylcyclohexanone (**2**)



^{13}C-NMR Spectra for for 3-ethylcyclohexanone (**2**)



[1]H-NMR Spectra for 3-butylcyclohexanone (**13**)



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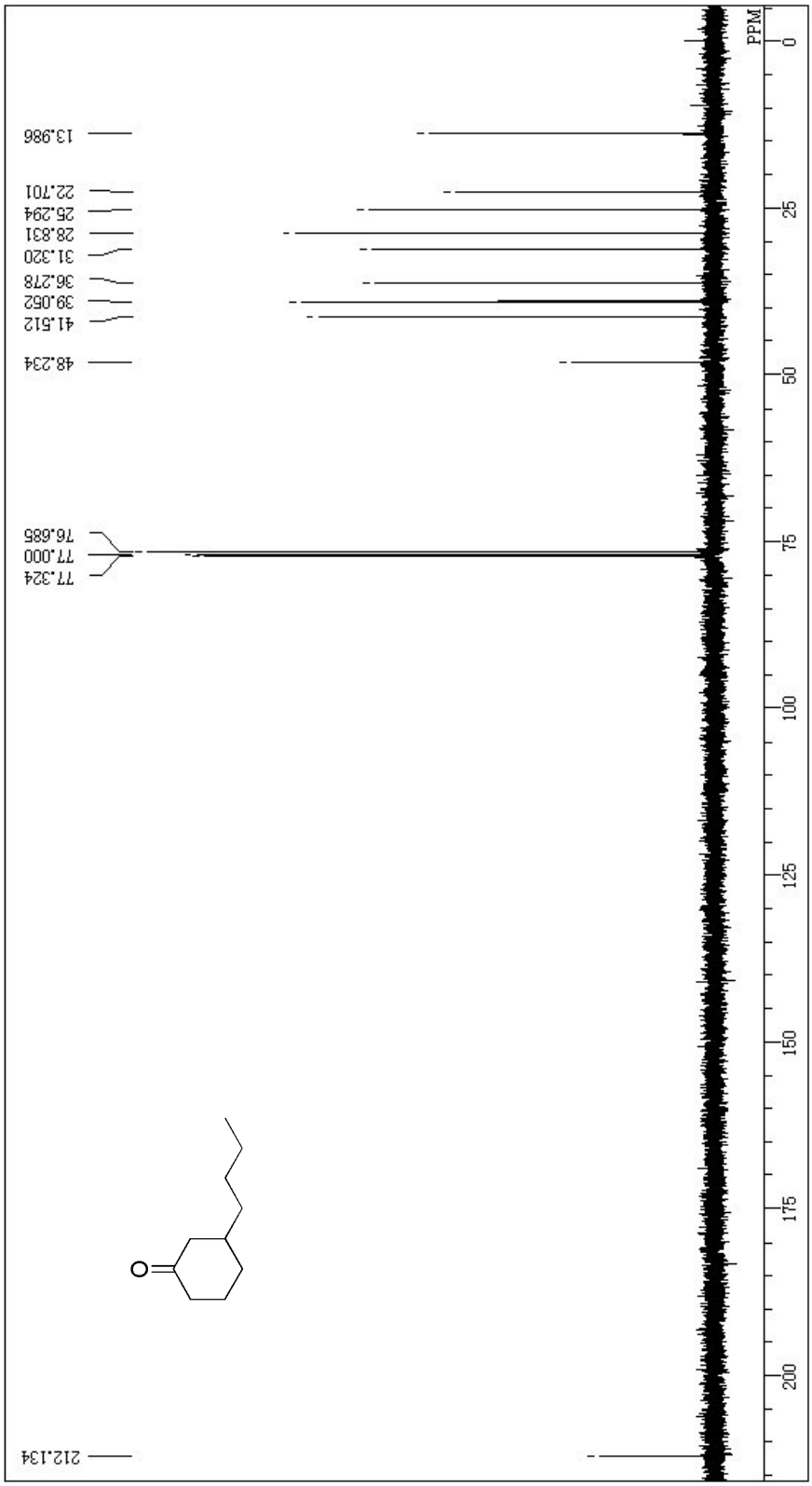
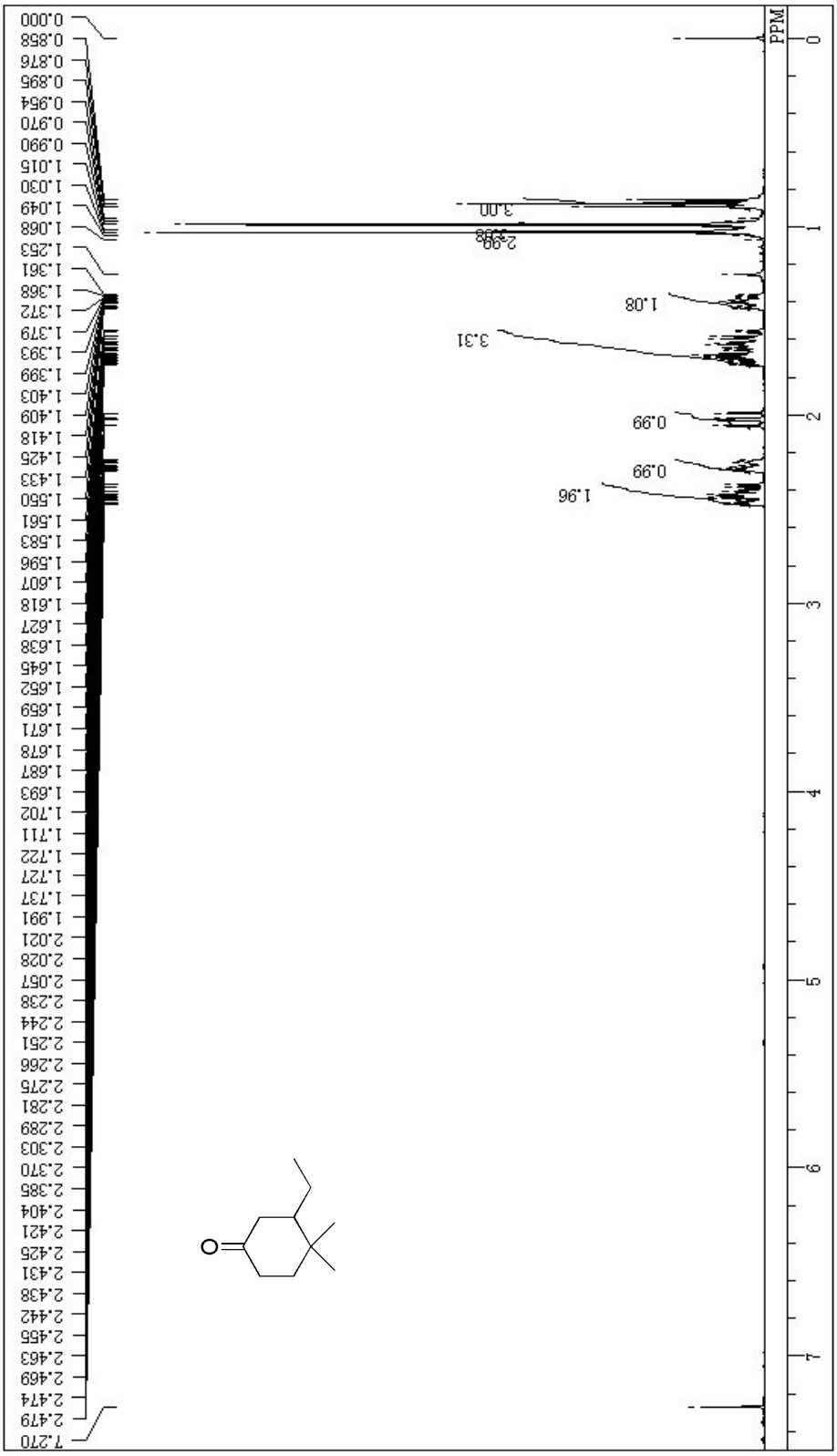
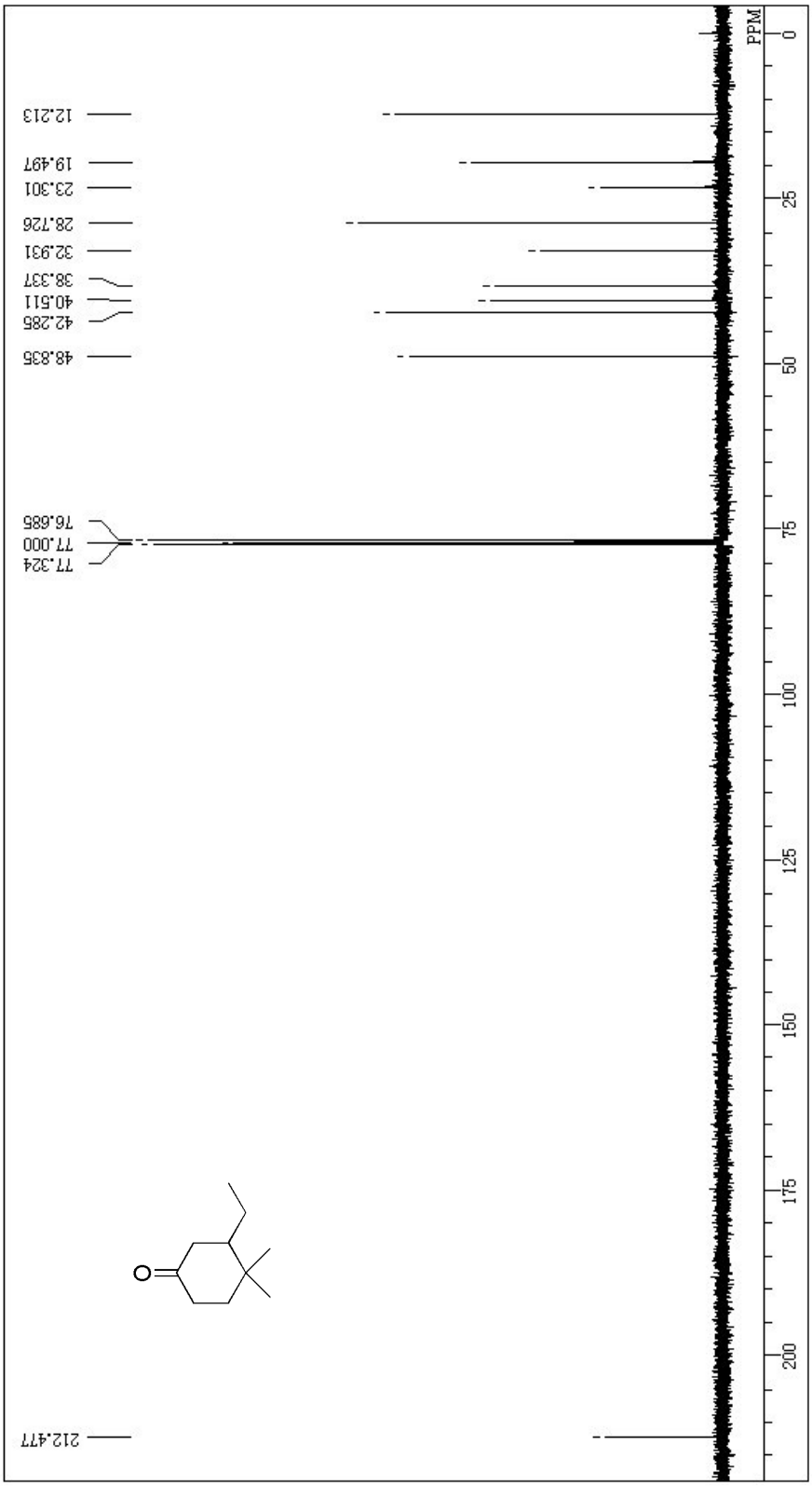


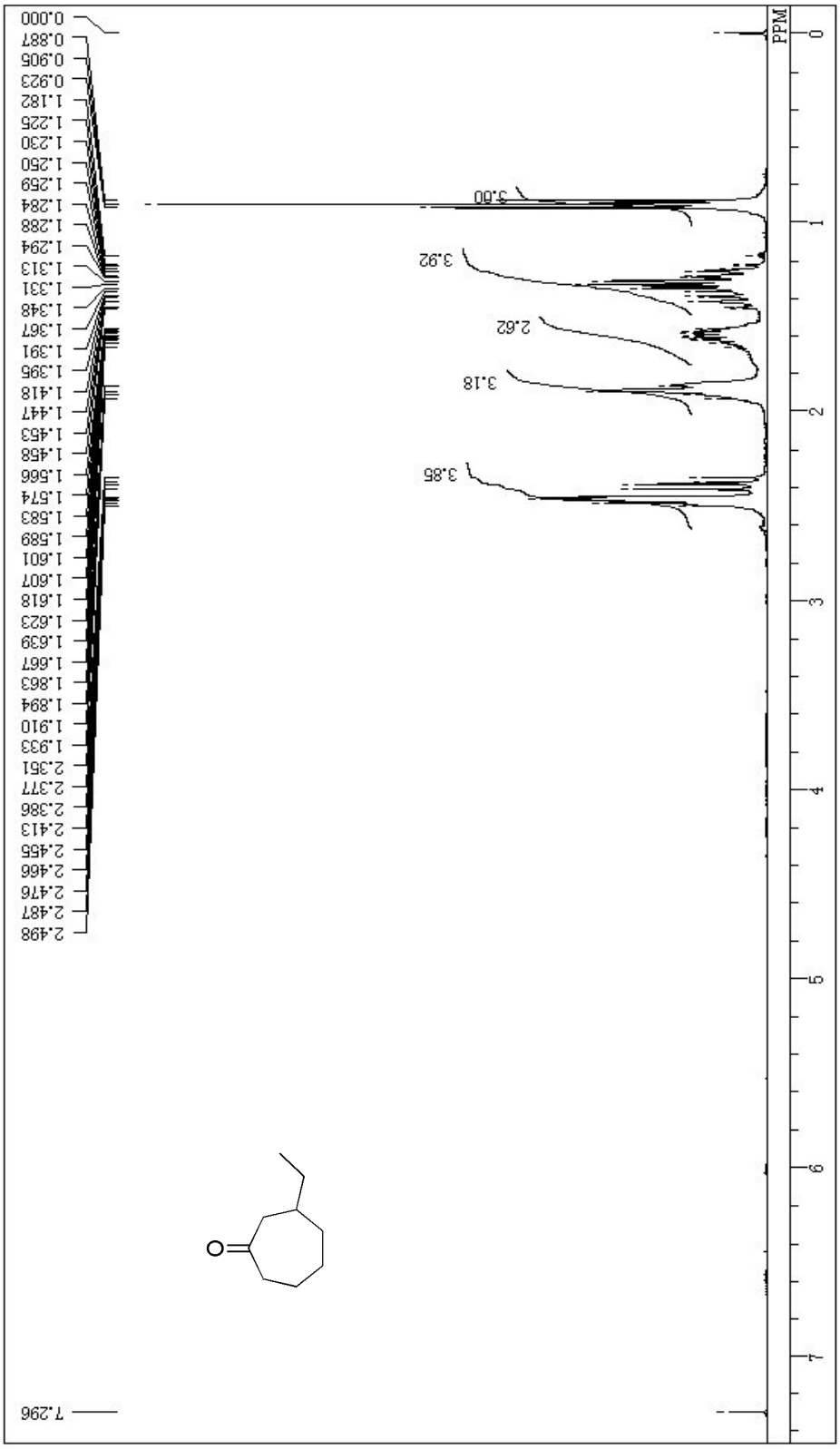
^{1}H-NMR Spectra for 4,4-dimethyl-3-ethlcyclohexanone



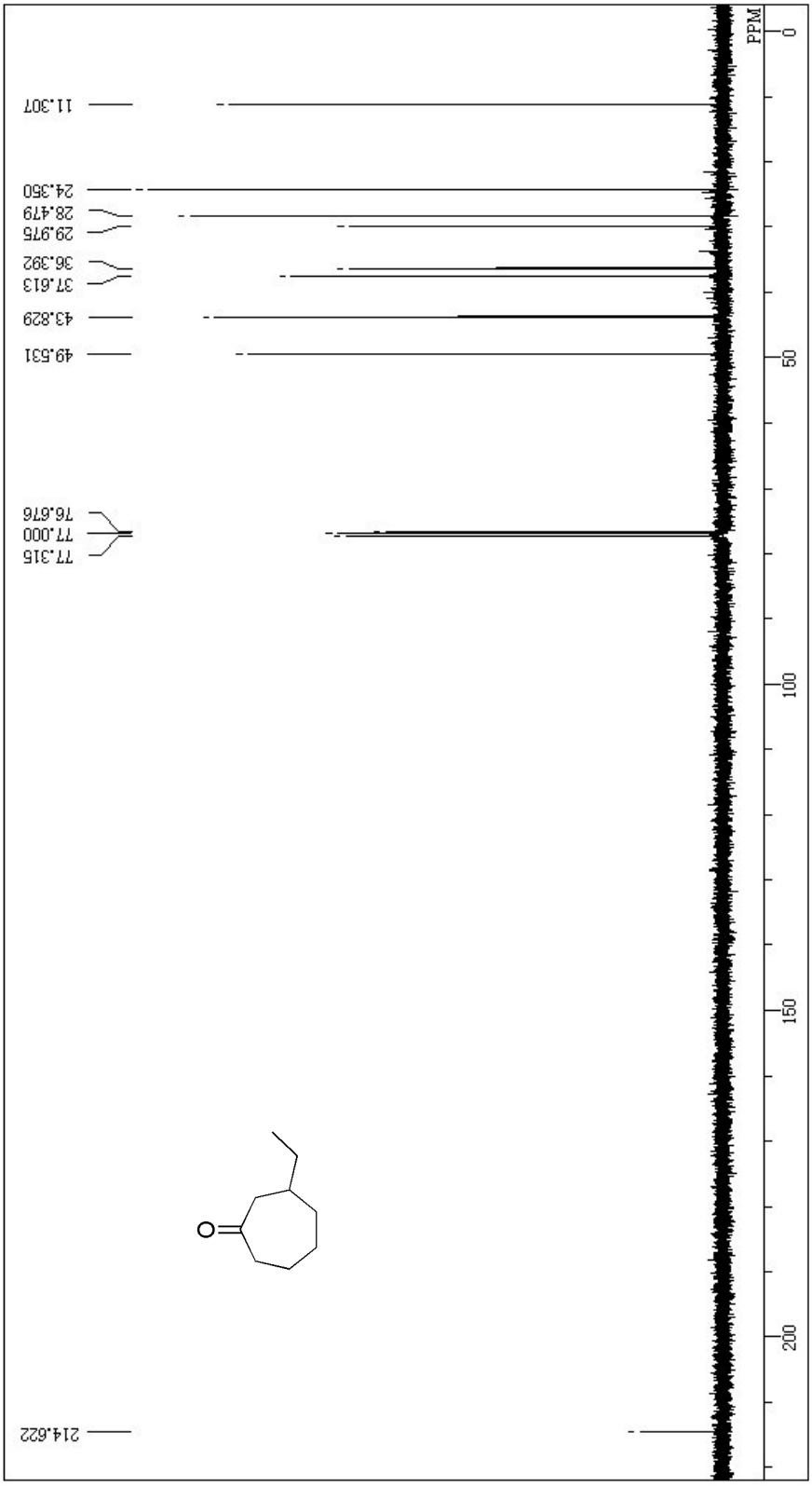
^{13}C-NMR Spectra for for 4,4-dimethyl-3-ethlcyclohexanone



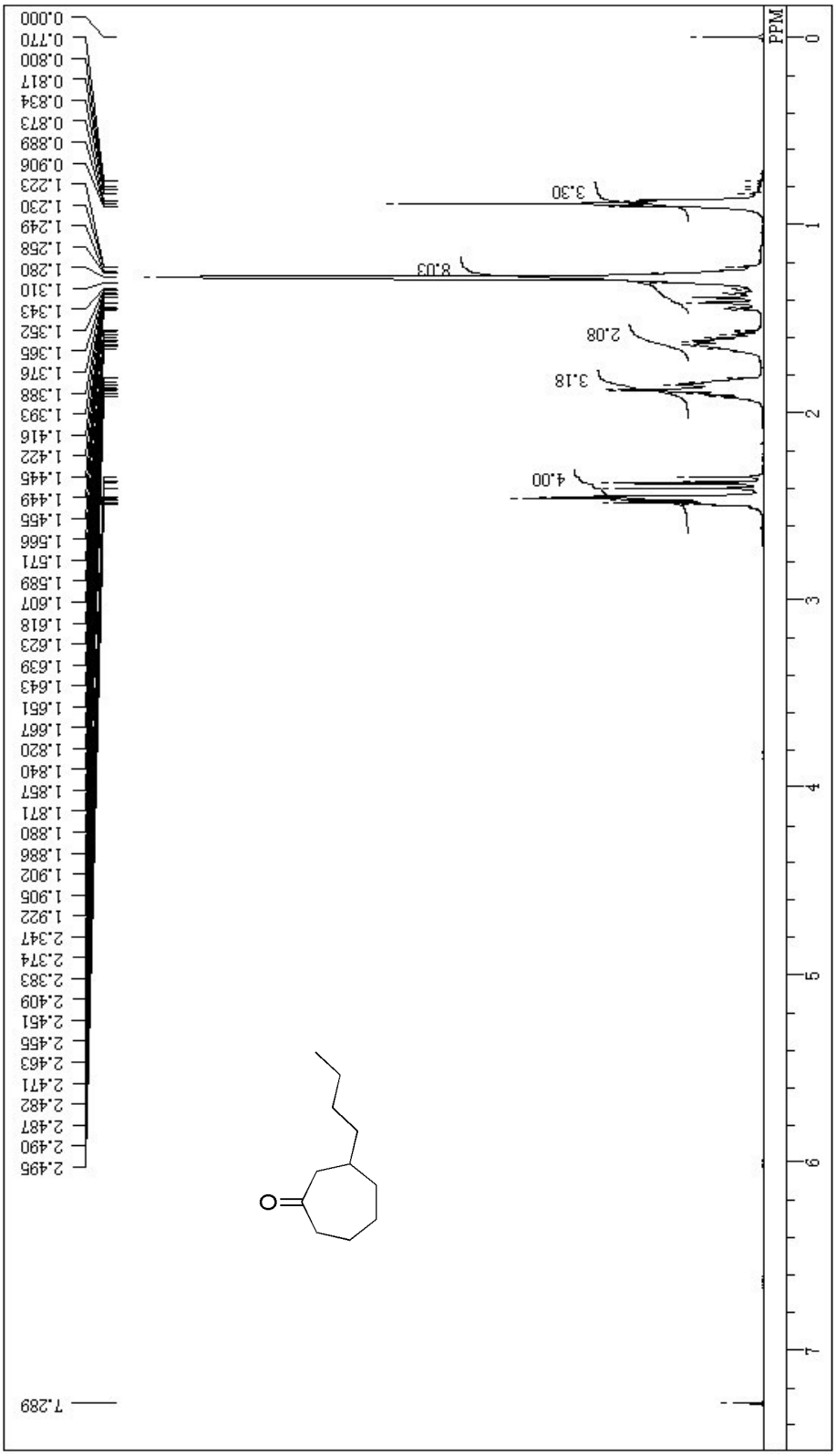
^{1}H-NMR Spectra for 3-ethylcycloheptanone **(16)**



^{13}C-NMR Spectra for for 3-ethylcycloheptanone **(16)**



[1]H-NMR Spectra for 3-butylcycloheptanone **(17)**



^{13}C-NMR Spectra for 3-butylcycloheptanone **(17)**