

# Development of Hydrogel TentaGel Shell-Core Beads for Ultra-high Throughput Solution Phase Screening of Encoded OBOC Combinatorial Small Molecule Libraries

*Hyoung Gee Baek, Ruiwu Liu, and Kit S. Lam\**

Division of Hematology and Oncology, Department of Internal Medicine, University of  
California Davis Cancer Center, 4501 X Street, Sacramento, California 95817

E-mail: Kit.lam@ucdmc.ucdavis.edu

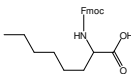
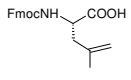
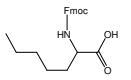
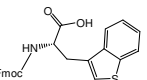
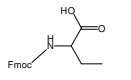
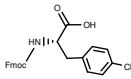
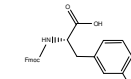
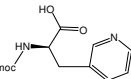
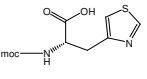
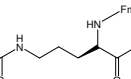
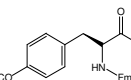
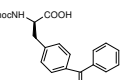
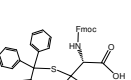
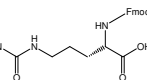
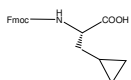
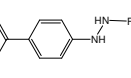
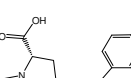
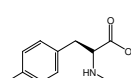
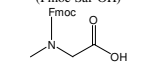
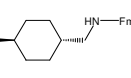
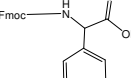
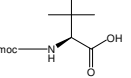
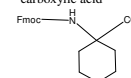
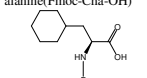
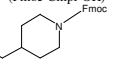
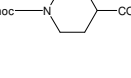
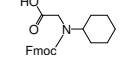
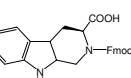
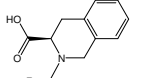
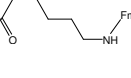
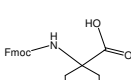
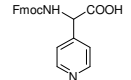
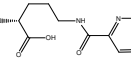
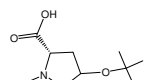
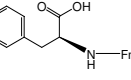
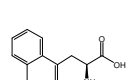
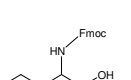
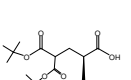
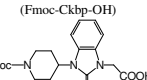
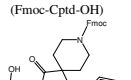
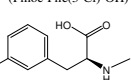
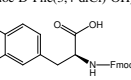
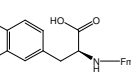
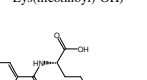
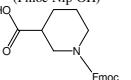
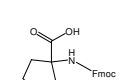
## **Supporting Information**

Table of contents .....	S2-S5
Copies of NMR and MS spectra for compounds <b>8</b> , <b>10</b> , <b>13</b> and <b>Fmoc-Ebes-OH</b> .....	S6-S17

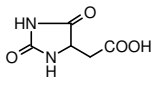
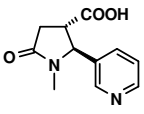
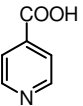
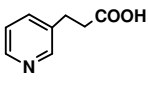
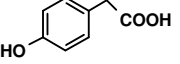
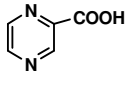
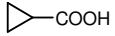
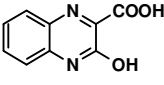
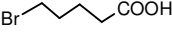
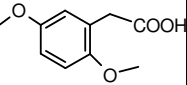
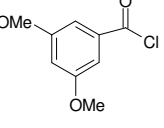
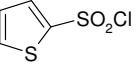
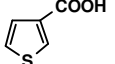
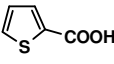
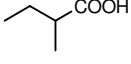
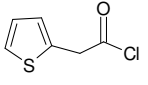
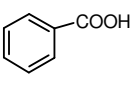
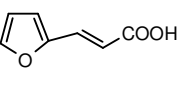
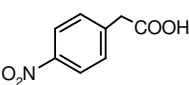
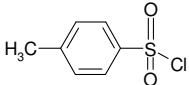
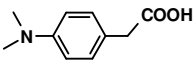
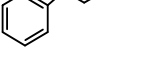
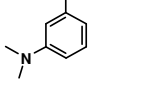
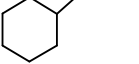
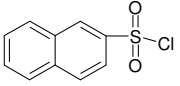
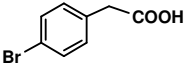
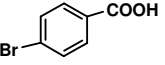
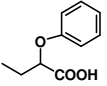
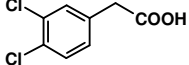
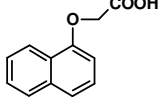
**Table 1. 96 Fmoc-amino acid used as building blocks for encoded model library**

	A	B	C	D	E
1	Fmoc-D,L-3-amino-3-(pyridyl)-propionic acid 	Fmoc-3-amino-2-benzylpropionic acid 	Fmoc-Ala-OH 	Fmoc-Arg(Pmc)-OH 	Fmoc-Asn-OH 
2	Fmoc-Asp(OtBu)-OH 	Fmoc-Cys(Trt)-OH 	Fmoc-Glu(OtBu)-OH 	Fmoc-Gln-OH 	Fmoc-Gly-OH 
3	Fmoc-His(Trt)-OH 	Fmoc-Ile-OH 	Fmoc-Leu-OH 	Fmoc-Lys(Boc)-OH 	Fmoc-Ser(tBu)-OH 
4	Fmoc-Met-OH 	Fmoc-Phe-OH 	Fmoc-Pro-OH 	Fmoc-Tyr(tBu)-OH 	Fmoc-Thr(tBu)-OH 
5	Fmoc-Val-OH 	Fmoc-Trp-OH 	Fmoc-D-Ala-OH 	Fmoc-D-Arg(Pmc)-OH 	Fmoc-D-Asn-OH 
6	Fmoc-D-Asp(OtBu)-OH 	Fmoc-D-Cys(Trt)-OH 	Fmoc-D-Glu(OtBu)-OH 	Fmoc-D-Gln-OH 	Fmoc-D-His(Trt)-OH 
7	Fmoc-D-Ile-OH 	Fmoc-D-Leu-OH 	Fmoc-D-Lys(Boc)-OH 	Fmoc-D-Ser(tBu)-OH 	Fmoc-D-Met-OH 
8	Fmoc-D-Phe-OH 	Fmoc-D-Pro-OH 	Fmoc-D-Tyr(tBu)-OH 	Fmoc-D-Thr(tBu)-OH 	Fmoc-D-Val-OH 
9	Fmoc-D-Trp-OH 	Fmoc-glycine 	Fmoc-L-Norleucine 	Fmoc-Bpa-OH 	Fmoc-L-2-Naphthyl alanine 
10	Fmoc-4-phenyl piperidine-4-carboxylic acid 	Fmoc-L-pipecolic acid 	N-Fmoc-Amino-(4-t-butoxycyclohexyl) carboxylic acid(Fmoc-Ahch-OH) 	Fmoc-1-amino-cyclohexan acetic acid 	Fmoc-3-aminocyclohexane carboxylic acid 

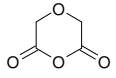
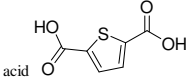
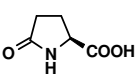
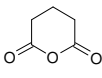

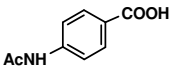
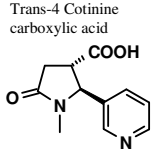
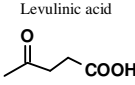
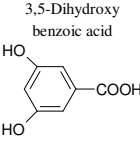
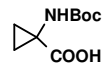
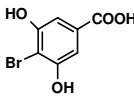
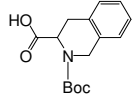
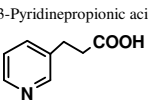
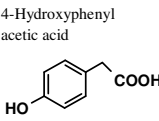
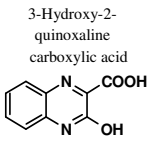
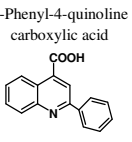
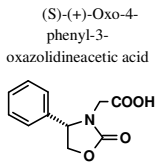
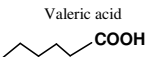
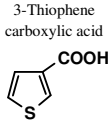
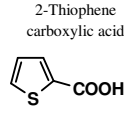
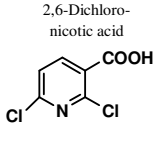
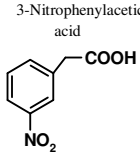
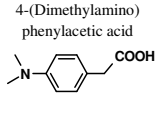
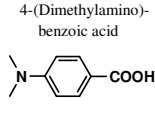
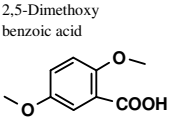
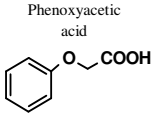
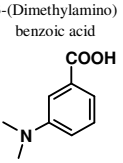
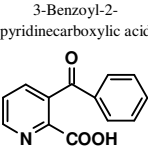
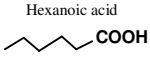
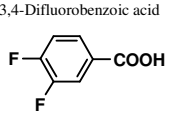
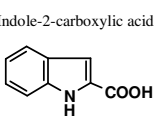
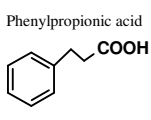
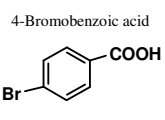
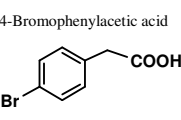
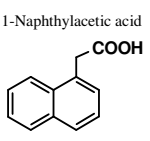
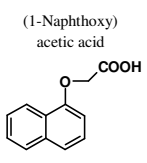
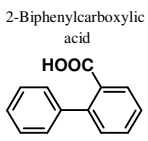
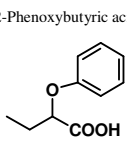
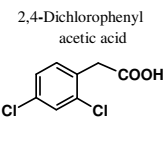
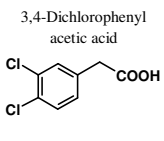
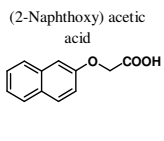
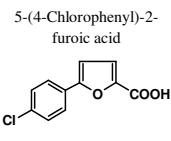
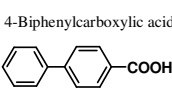
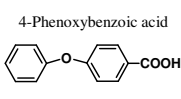
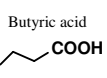
**Table 1. (Continued)**

	F	G	H	I	J
11	Fmoc-(+,-)-2-aminooctanoic acid 	Fmoc-4,5-dehydro-L-leucine 	Fmoc-2-aminoheptanoic acid(2-Ahe) 	Fmoc-D-3-Benzothienyl alanine 	Fmoc-D-2-Aminobutyric acid 
12	Fmoc-D-4-Chlorophenyl alanine 	Fmoc-D-2-Fluorophenyl alanine 	Fmoc-D-3-Pyridyl alanine 	Fmoc-D-4-Thiazolyl alanine 	Fmoc-D-Citruline 
13	Fmoc-D-Tyr(Me)-OH 	Fmoc-D-Bpa-OH 	Fmoc-penicillamine(trt)-OH(Fmoc-Pen(Trt)-OH) 	Fmoc-Citruline(Fmoc-Cit-OH) 	Fmoc-β-cyclopropyl-alanine 
14	Fmoc-4-Hydrazinobenzoic acid 	Fmoc-Hyp(Bzl)-OH 	Fmoc-Tyr(Me)-OH 	Fmoc-sarcosine, (Fmoc-Sar-OH) 	Fmoc-Tranexamic acid 
15	Fmoc-Phenylglycine(Fmoc-Phg-OH) 	Fmoc-Tert-Leucine,(Fmoc-Tle-OH) 	Fmoc-4-Amino-tetrahydropyran-4-carboxylic acid 	Fmoc-β-Cyclohexyl-L-alanine(Fmoc-Cha-OH) 	Fmoc-4-Carboxymethylpiperidine (Fmoc-Cmpi-OH) 
16	Fmoc-Isonipetic acid, (Fmoc-Inp-OH) 	Fmoc-Nchg-OH 	Fmoc-L-1,2,3,4-Tetrahydronorhaman-3-carboxylic acid 	Fmoc-Tetrahydroisoquinoline-3-carboxylic acid(Fmoc-L-Tic-OH) 	Fmoc-ε-Aminocaproic acid 
17	N-Fmoc-aminocyclohexyl Carboxylic acid 	Fmoc-α-amino-(4-pyridyl)acetic acid Fmoc-Apa-OH 	Fmoc-Orn(pyrazinylcarbonyl)-OH 	Fmoc-Hydroxyproline(But)OH, (Fmoc-Hyp(tBu)-OH) 	Fmoc-L-3,4-Dichlorophenylalanine 
18	Fmoc-L-1-Naphthylalanine(Fmoc-Nal-1) 	Fmoc-L-2-Aminovaleric acid(Fmoc-Nva-OH) 	Fmoc-γ-carboxyl-L-glutamic acid-γ-di-t-butyl ester 	Fmoc-4-(3-carboxymethyl-2-keto-1-benzimidazolyl-piperidine, (Fmoc-Ckbp-OH) 	Fmoc-3-carboxymethyl-1-phenyl-1,3,8-triazaspiro(4,5)decane-4-one, (Fmoc-Cptd-OH) 
19	Fmoc-3-chloro-L-phenylalanine, (Fmoc-Phe(3-Cl)-OH) 	Fmoc-3,4-dichloro-D-phenylalanine, (Fmoc-D-Phe(3,4-diCl)-OH) 	Fmoc-3-Iodo-L-tyrosine 	Fmoc-N-Nicotinoyl-L-lysine(Fmoc-Lys(nicotinoyl)-OH) 	Fmoc-nipetic acid (Fmoc-Nip-OH) 
20	Fmoc-1-Amino-1-cyclopentane carboxylic acid(Fmoc-Acp-OH) 				

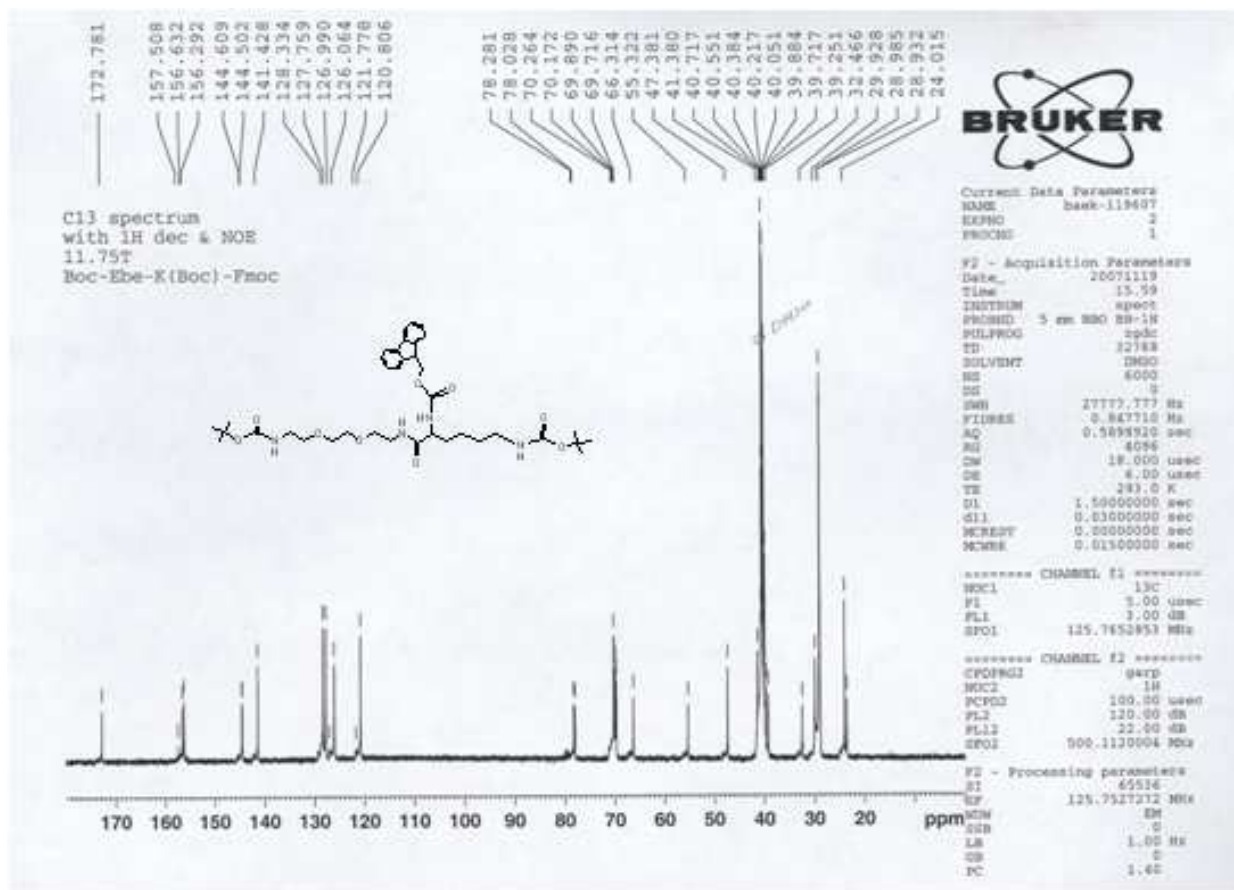
**Table 2. Thirty acylation reagents used for making library :  $R_1\text{COOH}$ ,  $R_1\text{COCl}$ , or  $R_1\text{SO}_2\text{Cl}$**

	A	B	C	D	E
1	5-Hydantoinacetic acid 	Trans-4Cotinine-carboxylic acid 	Isonicotinic acid 	3-Pyridinepropionic acid 	4-Hydroxyphenylacetic acid 
2	2-Pyrazinecarboxylic acid 	Cyclopropane carboxylic acid 	3-Hydroxy-2-quinox-aline carboxylic acid 	5-Bromovaleric acid 	2,5-Dimethoxyphenyl acetic acid 
3	3,4-Dimethoxybenzoyl chloride 	2-Thiophenesulfonyl chloride 	3-Thiophene carboxylic acid 	2-Thiophenecarboxylic acid 	2-Methylbutyric acid 
4	2-Thiophenacetyl chloride 	Benzoic acid 	Furylacrylic acid 	4-Nitrophenyl acetic acid 	p-Toluenesulfonyl chloride 
5	4-(Dimethylamino) phenylacetic acid 	Phenoxyacetic acid 	3-(Dimethylamino) benzoic acid 	Cyclohexane carboxylic acid 	2-Naphthalenesulfonyl chloride 
6	4-Bromophenylacetic acid 	4-Bromobenzoic acid 	2-Phenoxybutyric acid 	3,4-Dichlorophenylacetic acid 	(1-Naphthoxy)acetic acid 

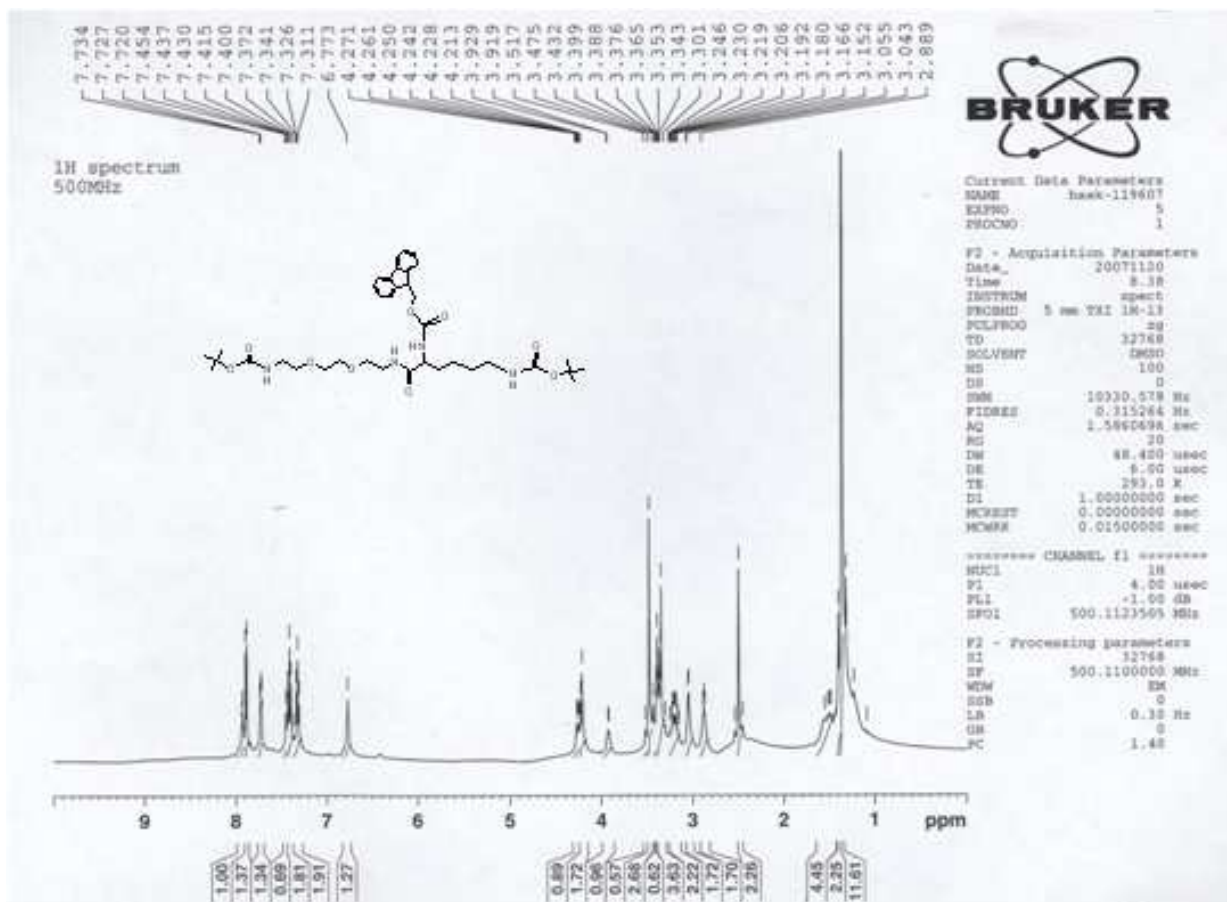
**Table 3. 45 Carboxylic acids used for library synthesis : R<sub>2</sub>COOH, R<sub>2</sub>COCl, or R<sub>2</sub>SO<sub>2</sub>Cl**

	A	B	C	D	E	F
1	Diglycolic anhydride 	2,5-Thiophenedicarboxylic acid 	L-Pyroglutamic acid 	Glutaric anhydride 	Malonic acid 	4-Acetamidobenzoic acid 
2	Trans-4 Cotinine carboxylic acid 	Levulinic acid 	3,5-Dihydroxy benzoic acid 	Boc-1-aminocyclopropane-1-carboxylic acid 	4-Bromo-3,5-dihydroxy benzoic acid 	Boc-D-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid(Boc-D-Tic- OH) 
3	3-Pyridinepropionic acid 	4-Hydroxyphenyl acetic acid 	3-Hydroxy-2-quinoxaline carboxylic acid 	2-Phenyl-4-quinoline carboxylic acid 	(S)-(+)-Oxo-4-phenyl-3-oxazolidinoneacetic acid 	Valeric acid 
4	3-Thiophene carboxylic acid 	2-Thiophene carboxylic acid 	2,6-Dichloro-nicotinic acid 	3-Nitrophenylacetic acid 	4-(Dimethylamino) phenylacetic acid 	4-(Dimethylamino)-benzoic acid 
5	2,5-Dimethoxy benzoic acid 	Phenoxyacetic acid 	3-(Dimethylamino) benzoic acid 	3-Benzoyl-2-pyridinecarboxylic acid 	Hexanoic acid 	3,4-Difluorobenzoic acid 
6	Indole-2-carboxylic acid 	Phenylpropionic acid 	4-Bromobenzoic acid 	4-Bromophenylacetic acid 	1-Naphthylacetic acid 	(1-Naphthoxy) acetic acid 
7	2-Biphenylcarboxylic acid 	2-Phenoxybutyric acid 	2,4-Dichlorophenyl acetic acid 	3,4-Dichlorophenyl acetic acid 	(2-Naphthoxy) acetic acid 	5-(4-Chlorophenyl)-2-furoic acid 
8	4-Biphenylcarboxylic acid 	4-Phenoxybenzoic acid 	Butyric acid 			

Copy of <sup>13</sup>C-NMR for compound 8



Copy of <sup>1</sup>H-NMR for compound 8





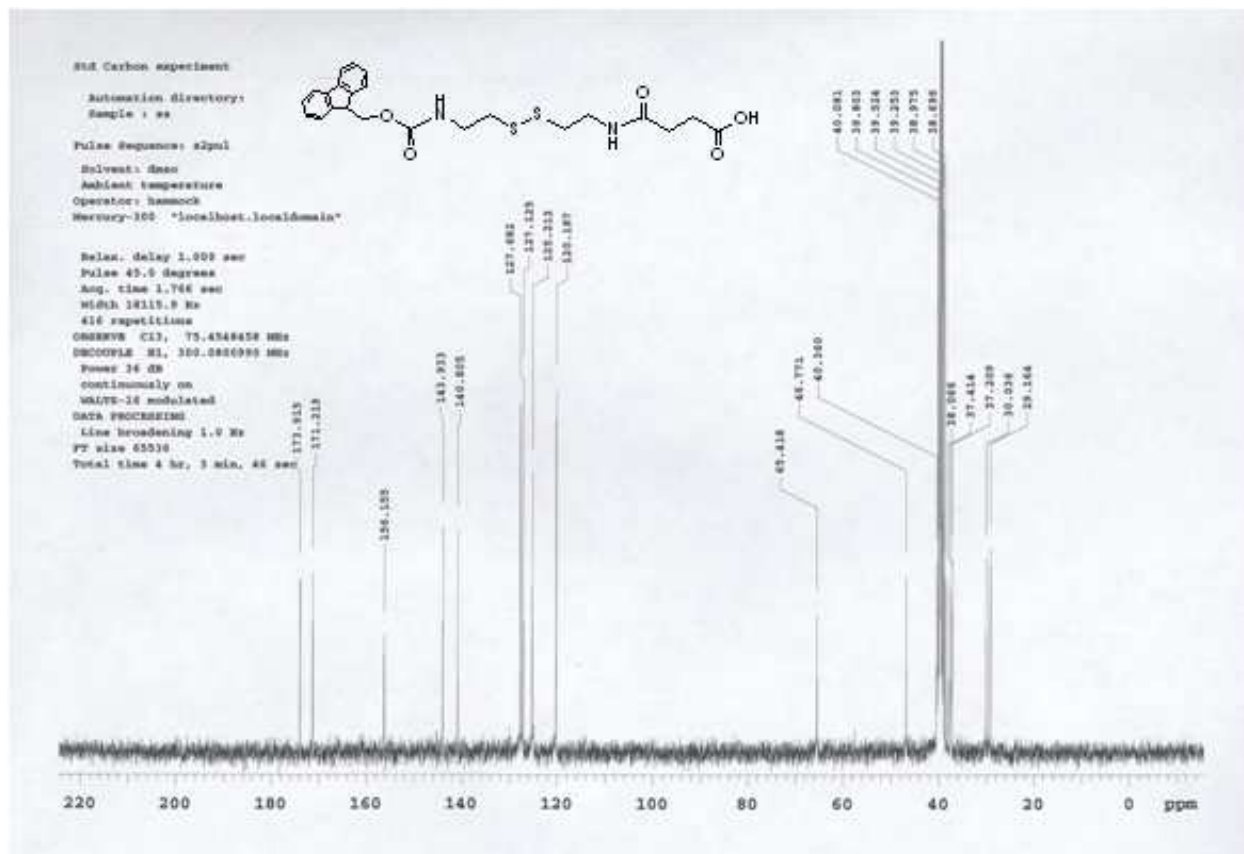






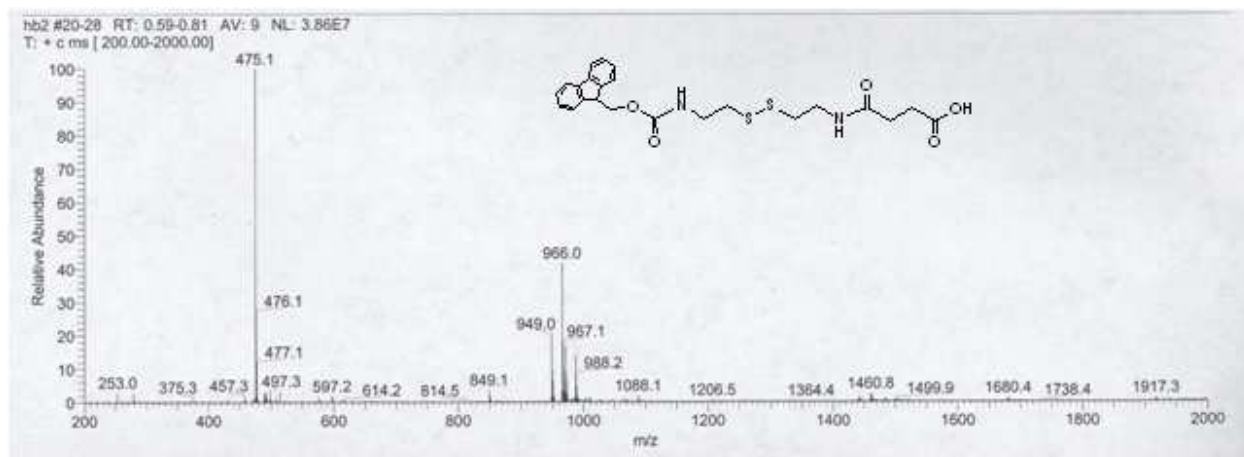


# Copy of $^{13}\text{C}$ -NMR for compound 13

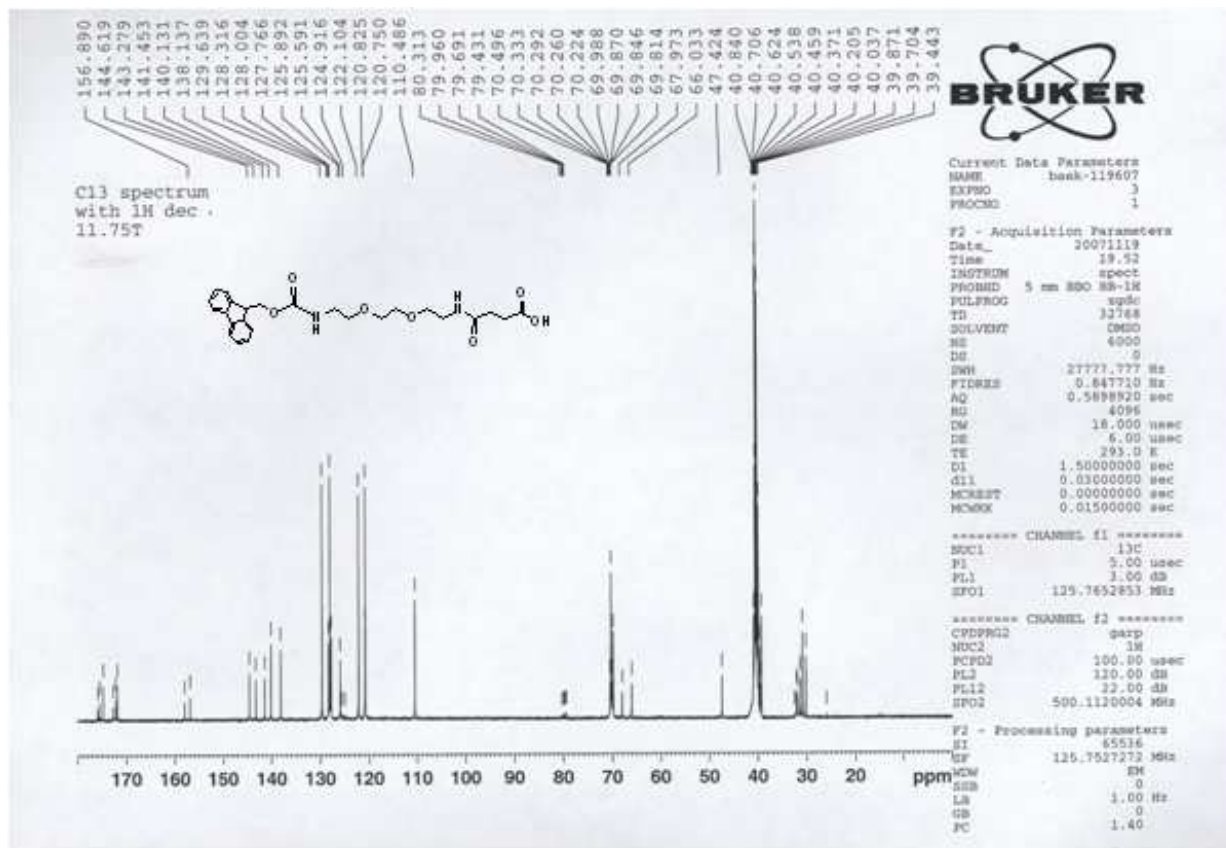




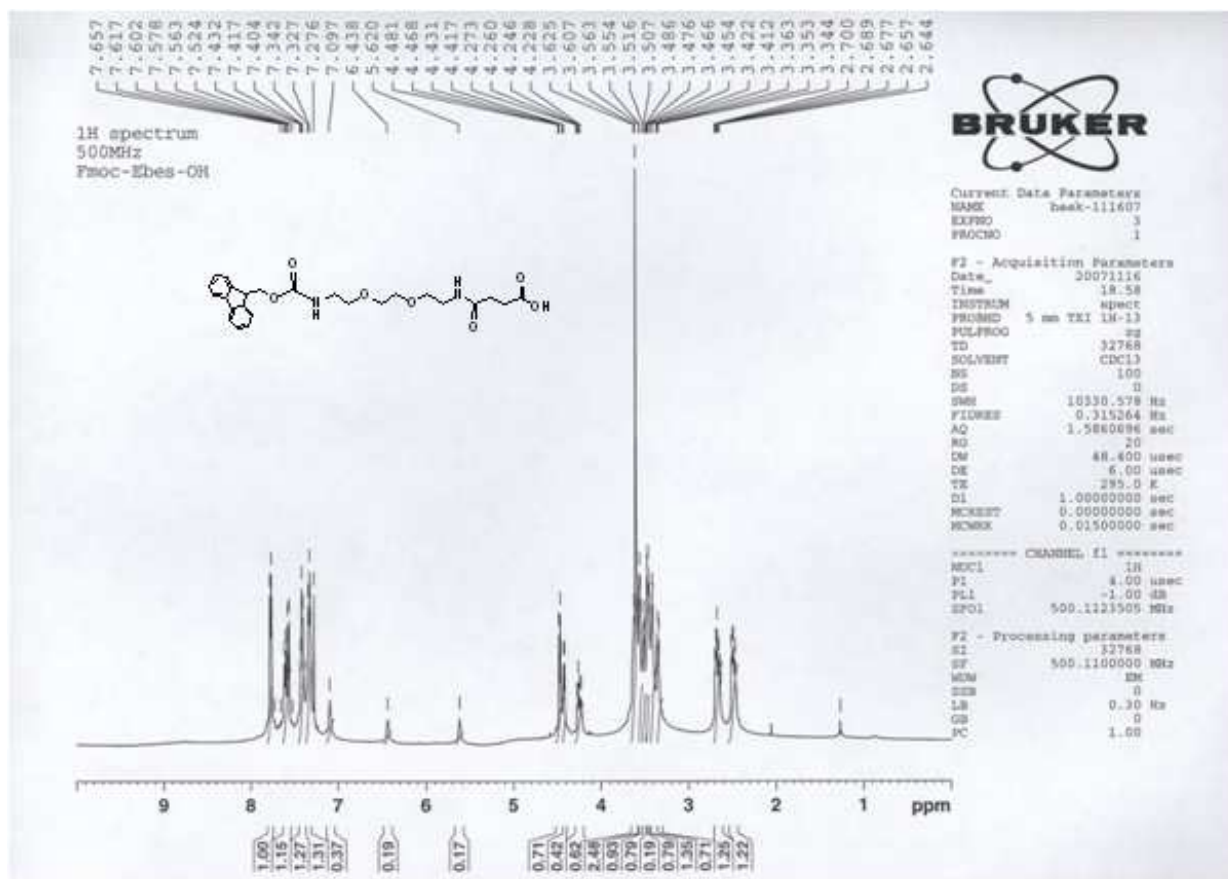
# Copy of MS for compound 13



Copy of <sup>13</sup>C-NMR for compound Fmoc-Ebes-OH



Copy of <sup>1</sup>H-NMR for compound Fmoc-Ebes-OH





# Copy of MS for compound Fmoc-Ebes-OH

