

Supplementary Materials:

Development of a Non-Hydroxamate Dual MMP-7/-13 Inhibitor

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Institute of Chemistry and Biotechnology

Center for Organic and Medicinal Chemistry

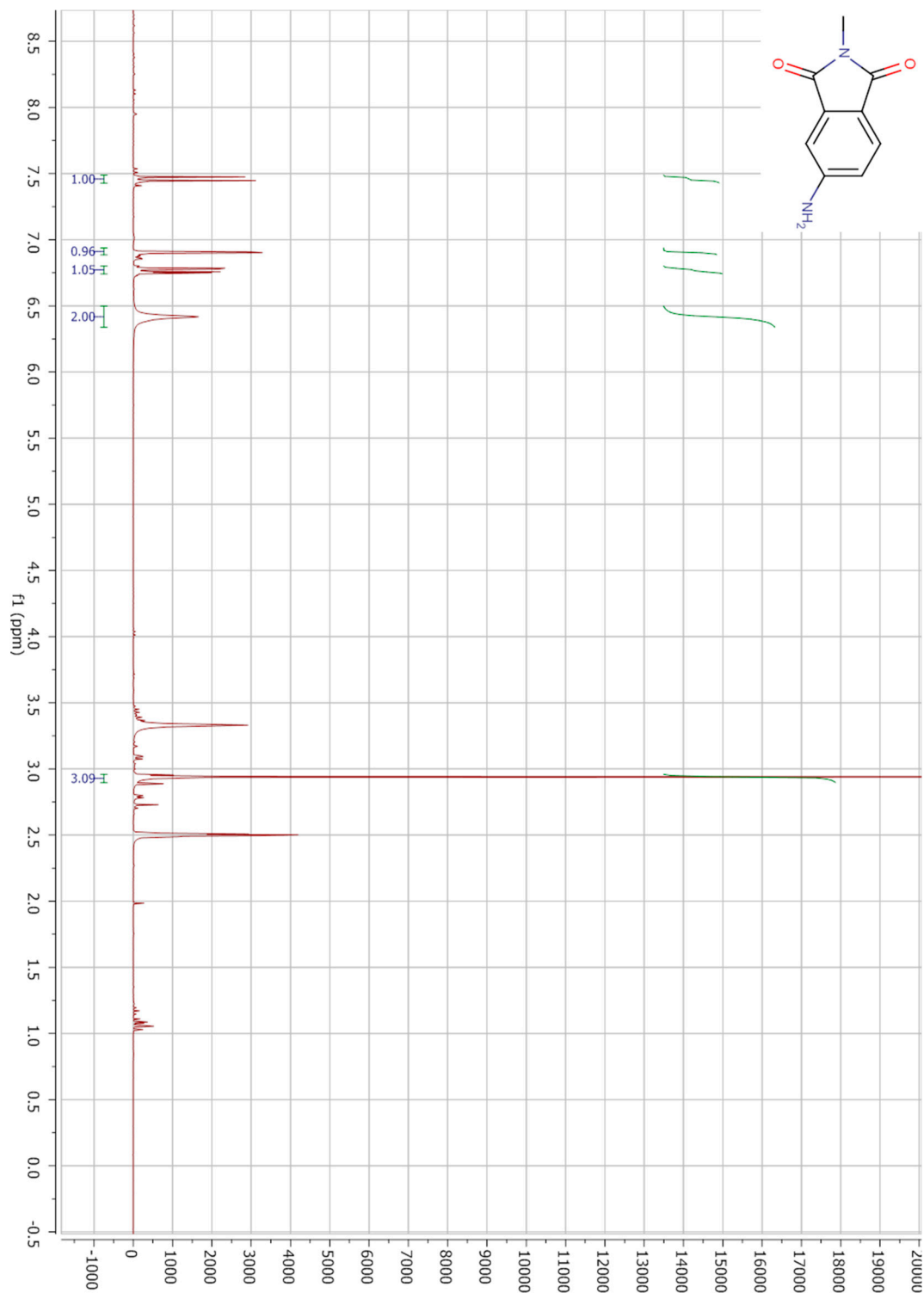
Zurich University of Applied Sciences ZHAW

Einsiedlerstrasse 31, 8820 Wädenswil, Switzerland

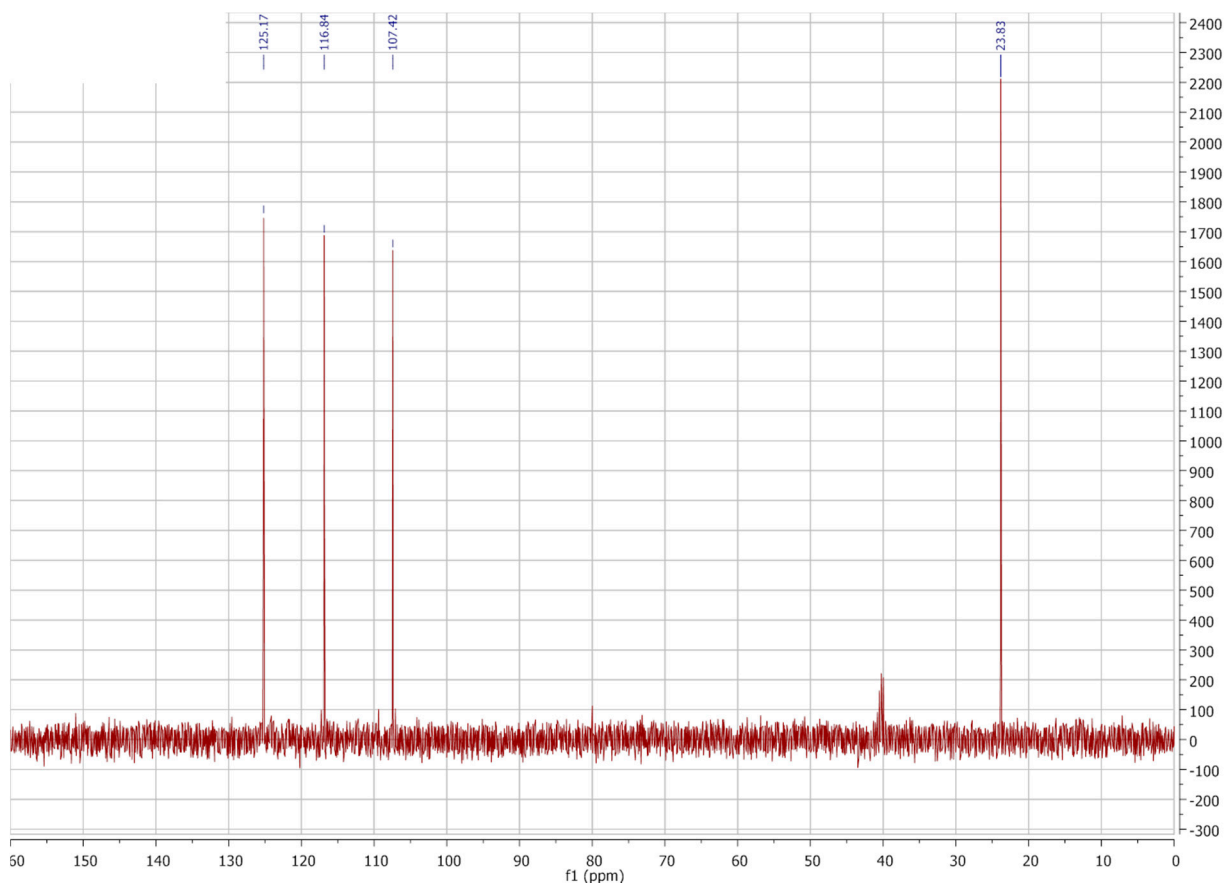
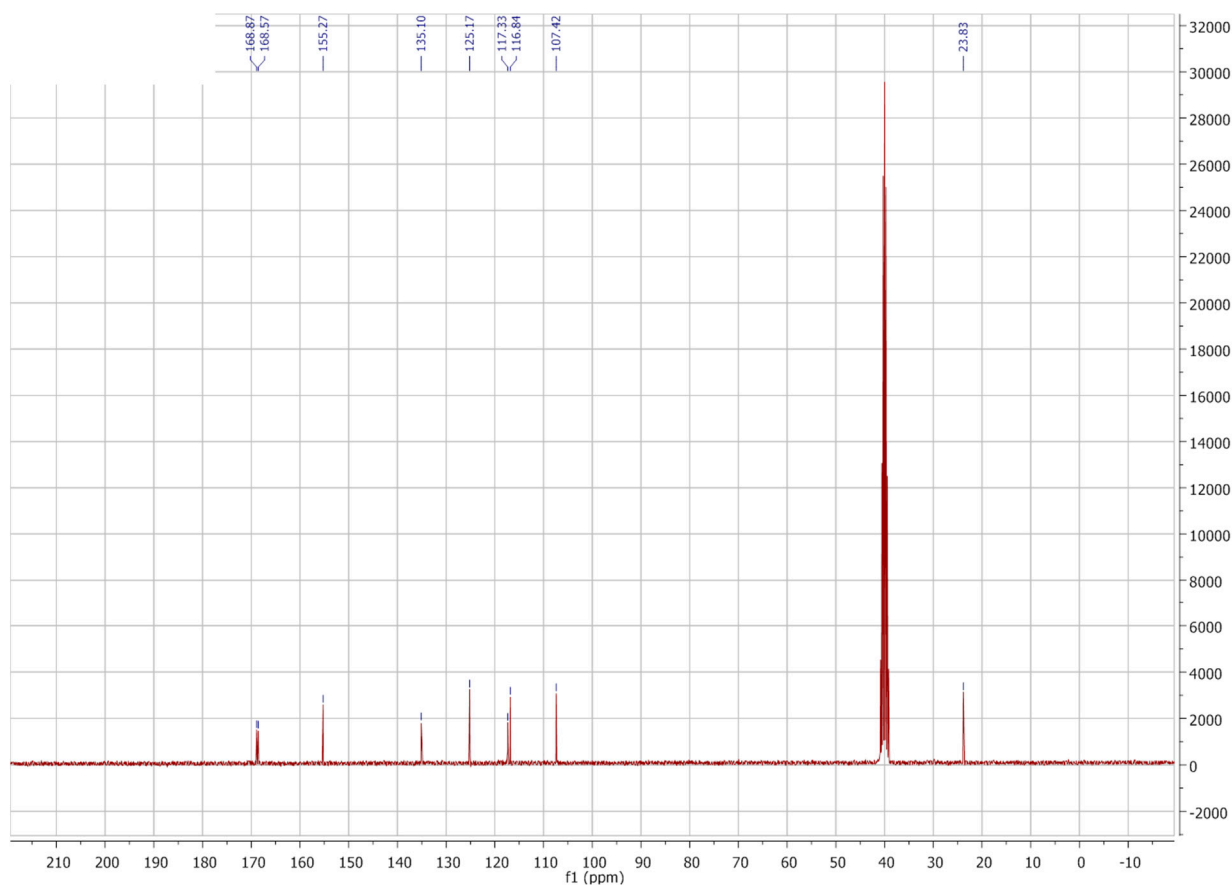
E-mail: rainer.riedl@zhaw.ch

5-amino-2-methyl-2,3-dihydro-1H-isoindole-1,3-dione (**11a**; ZHAWOC3444)

NMR

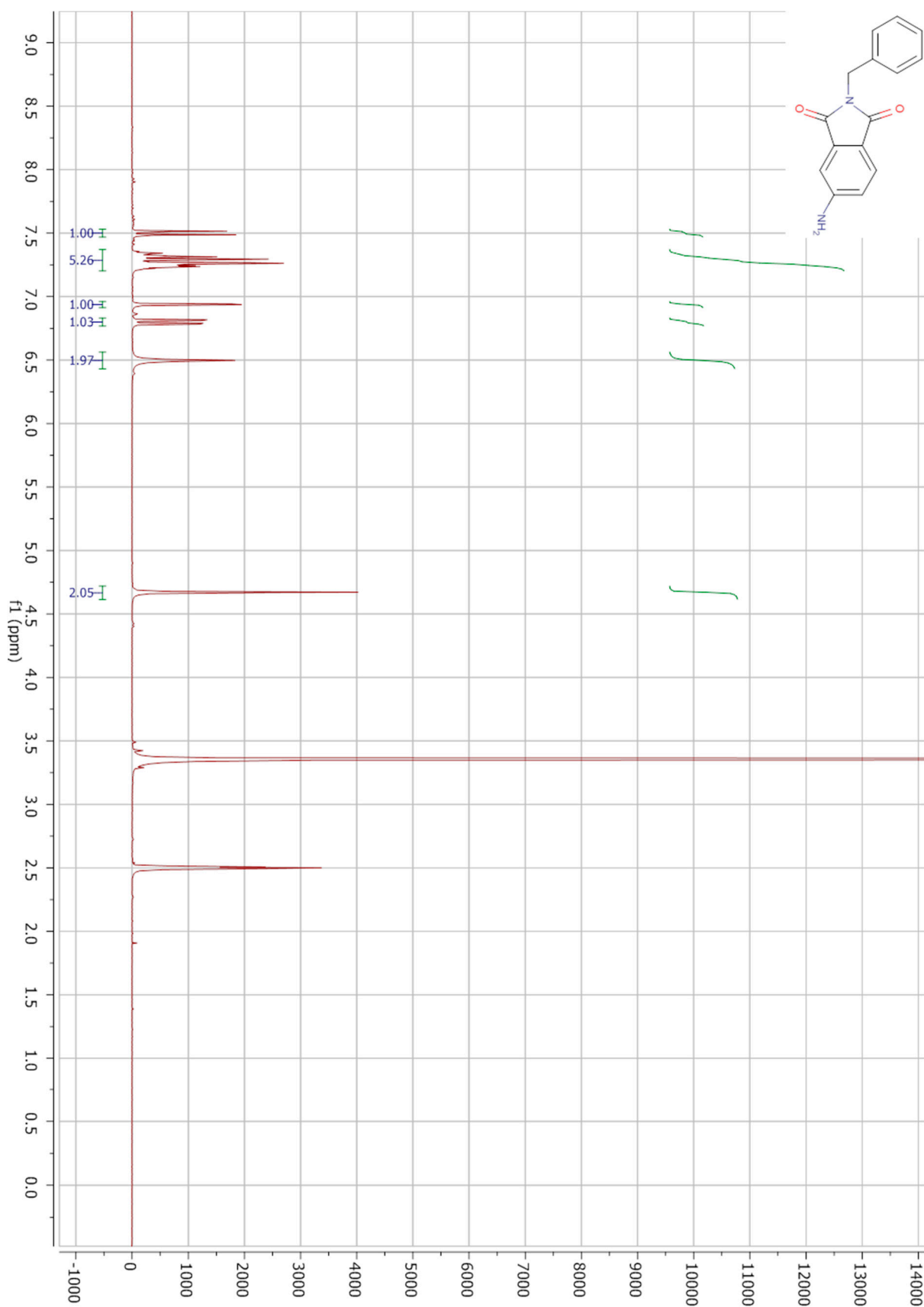


5-amino-2-methyl-2,3-dihydro-1H-isoindole-1,3-dione (11a; ZHAWOC3444)

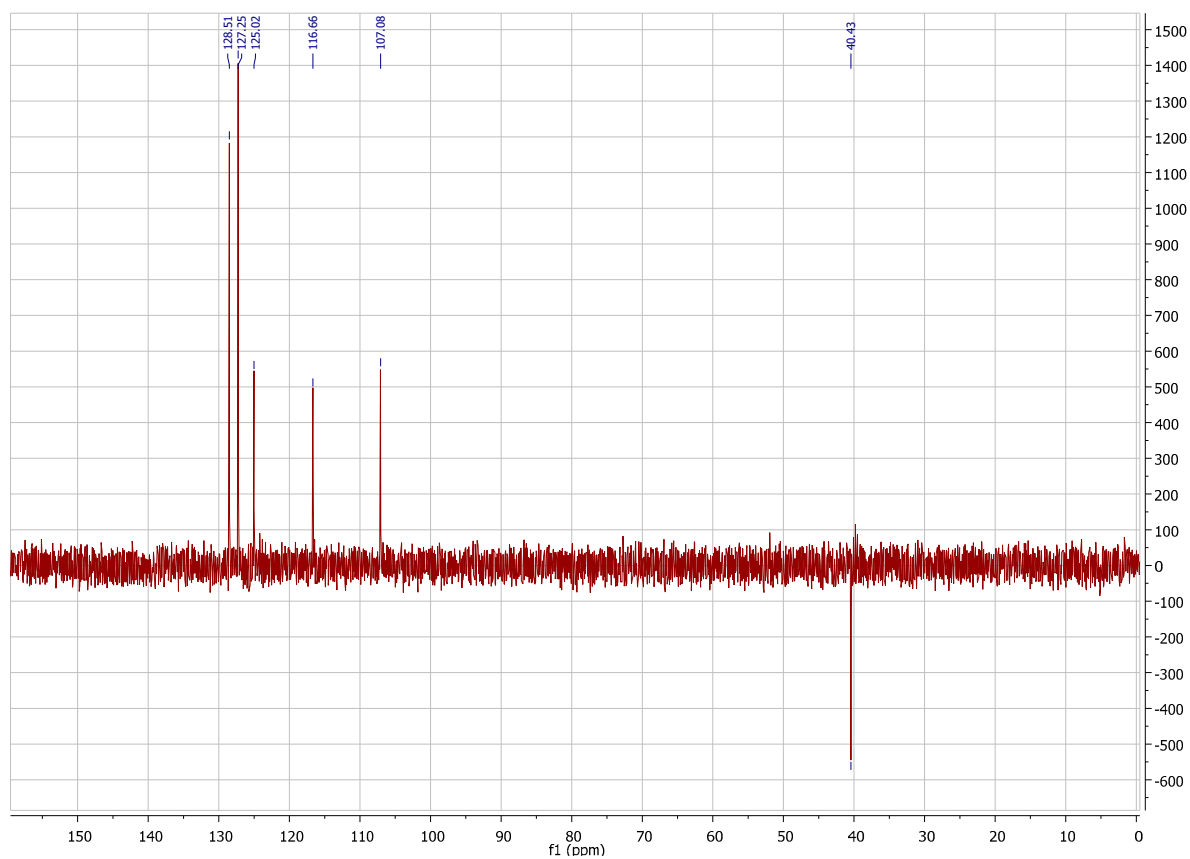
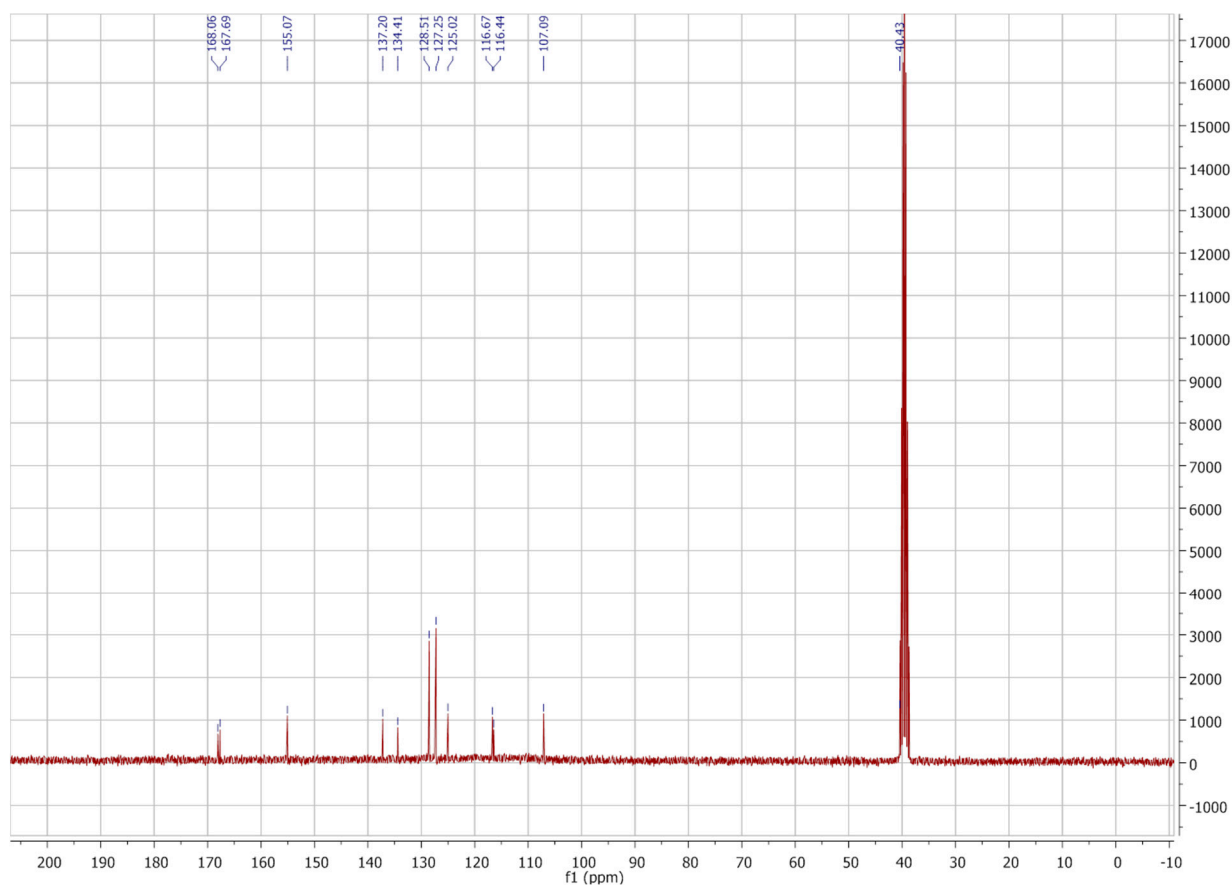


5-amino-2-benzyl-2,3-dihydro-1H-isoindole-1,3-dione (**11b**; ZHAWOC899)

NMR



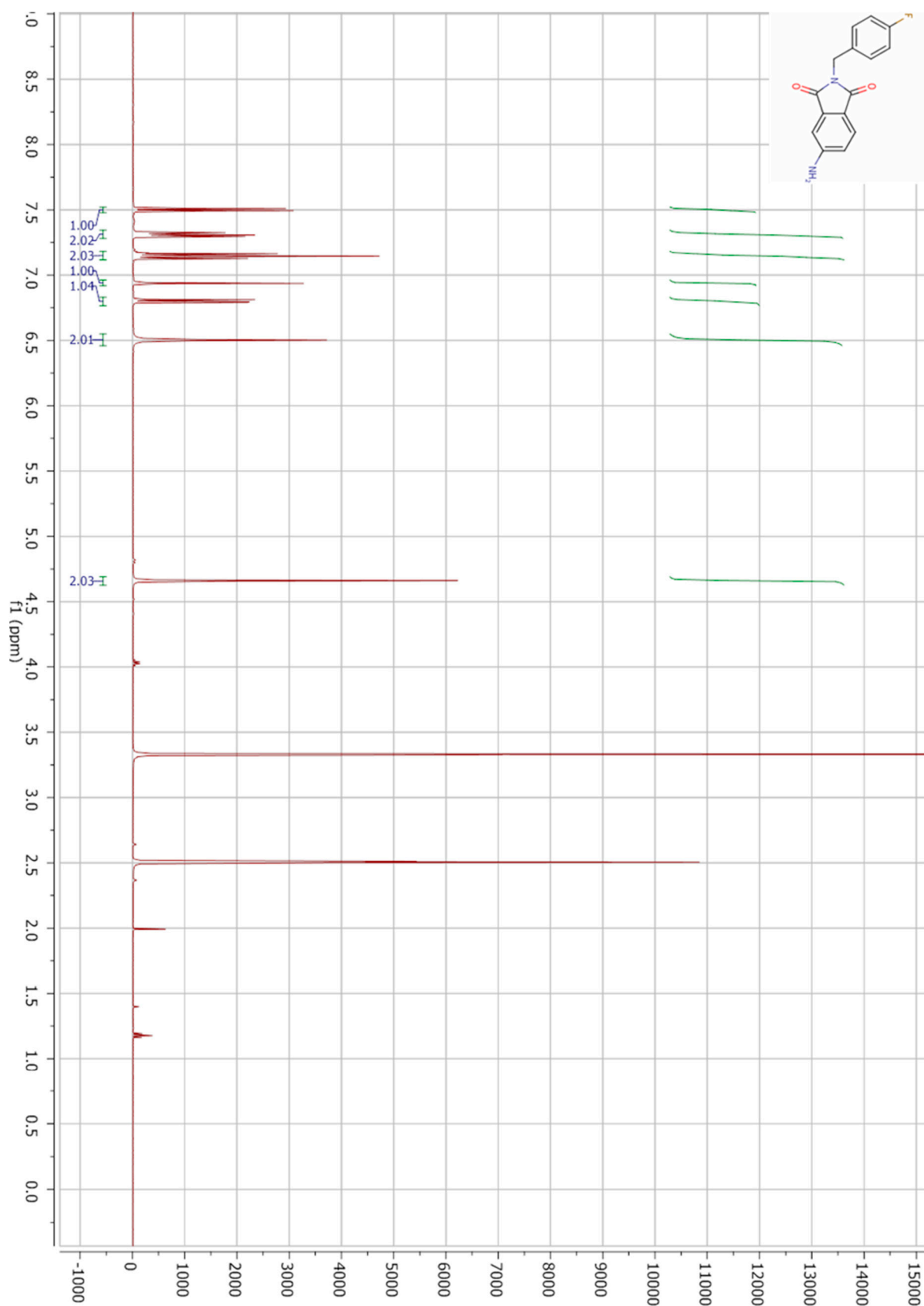
5-amino-2-benzyl-2,3-dihydro-1H-isoindole-1,3-dione (**11b**; ZHAWOC899)



5-amino-2-[(4-fluorophenyl)methyl]-2,3-dihydro-1H-isoindole-1,3-dione
ZHAWOC3199)

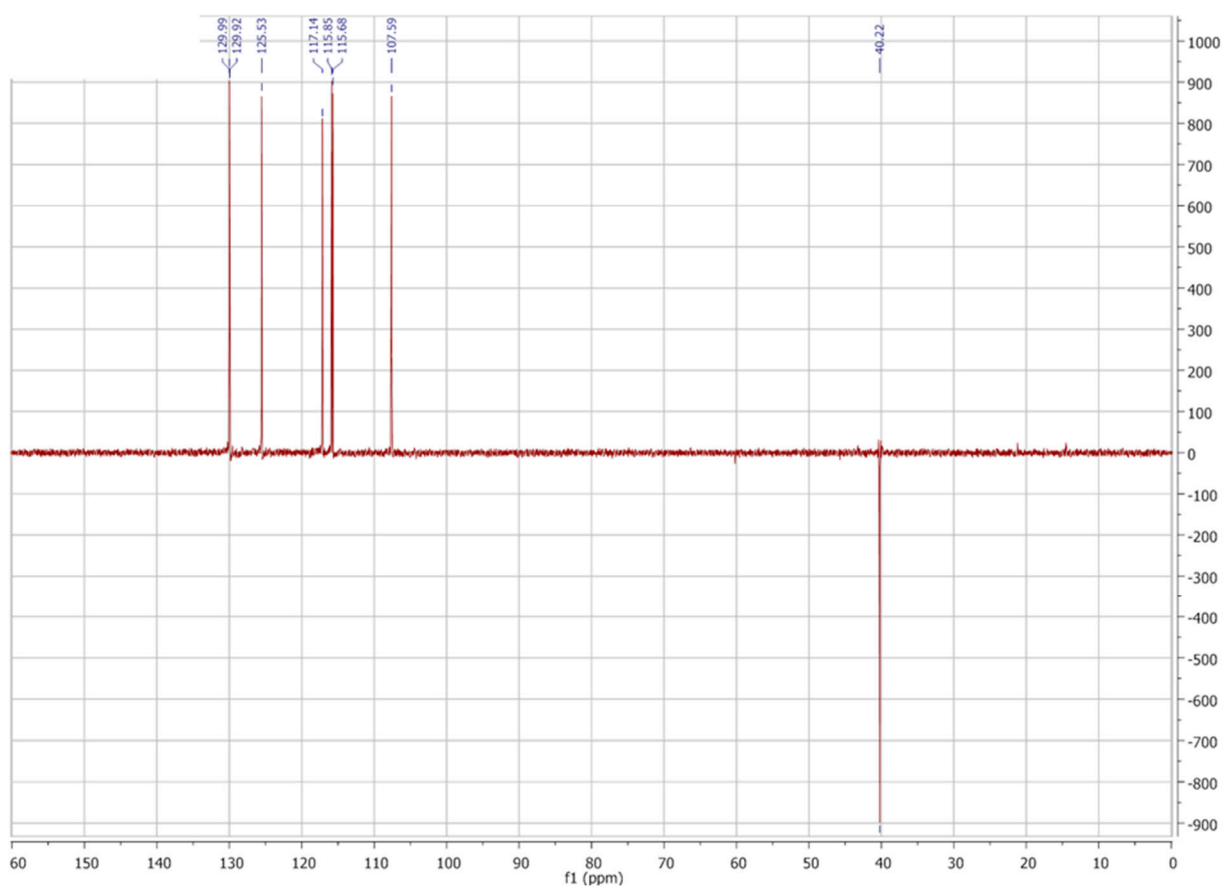
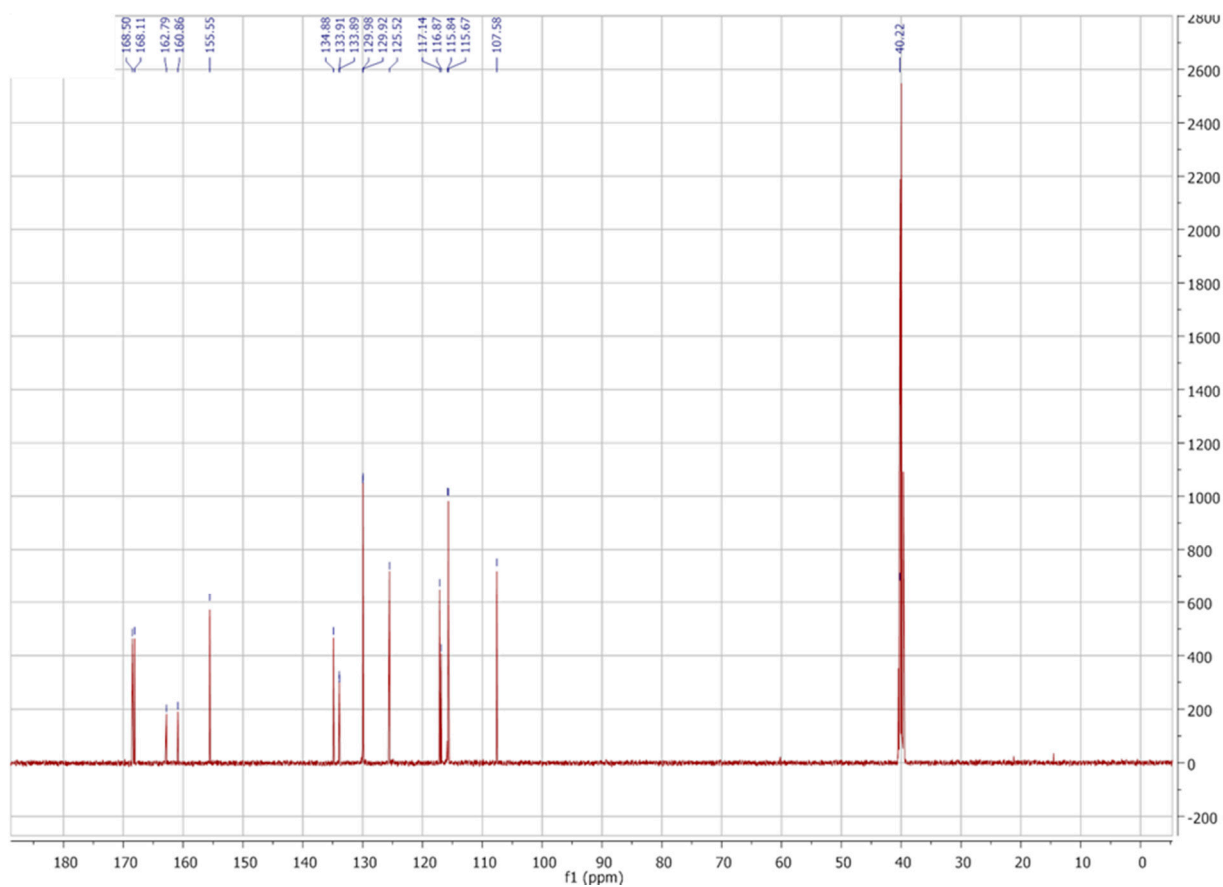
(11c;

NMR



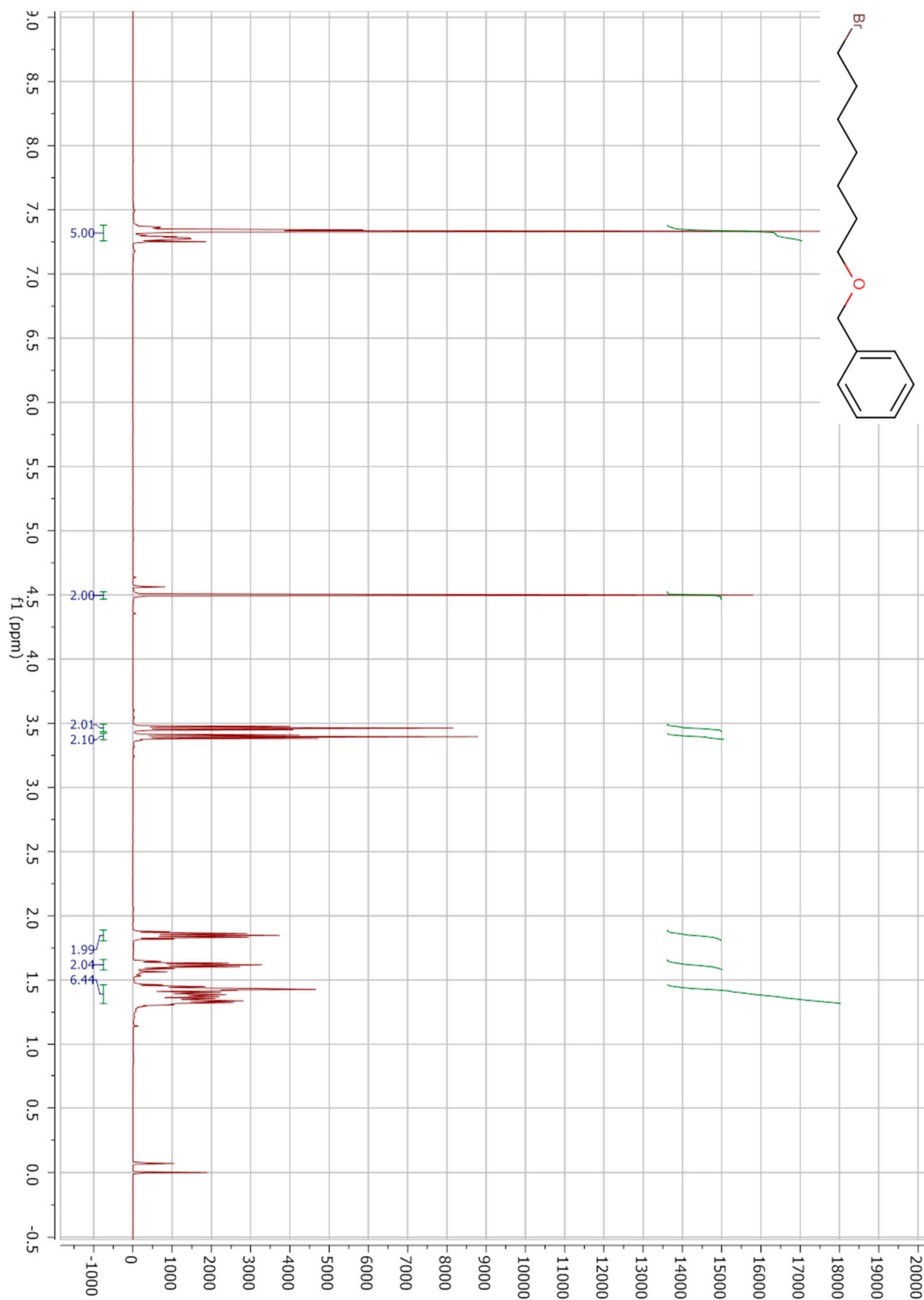
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ZHAWOC3199)

(11c;

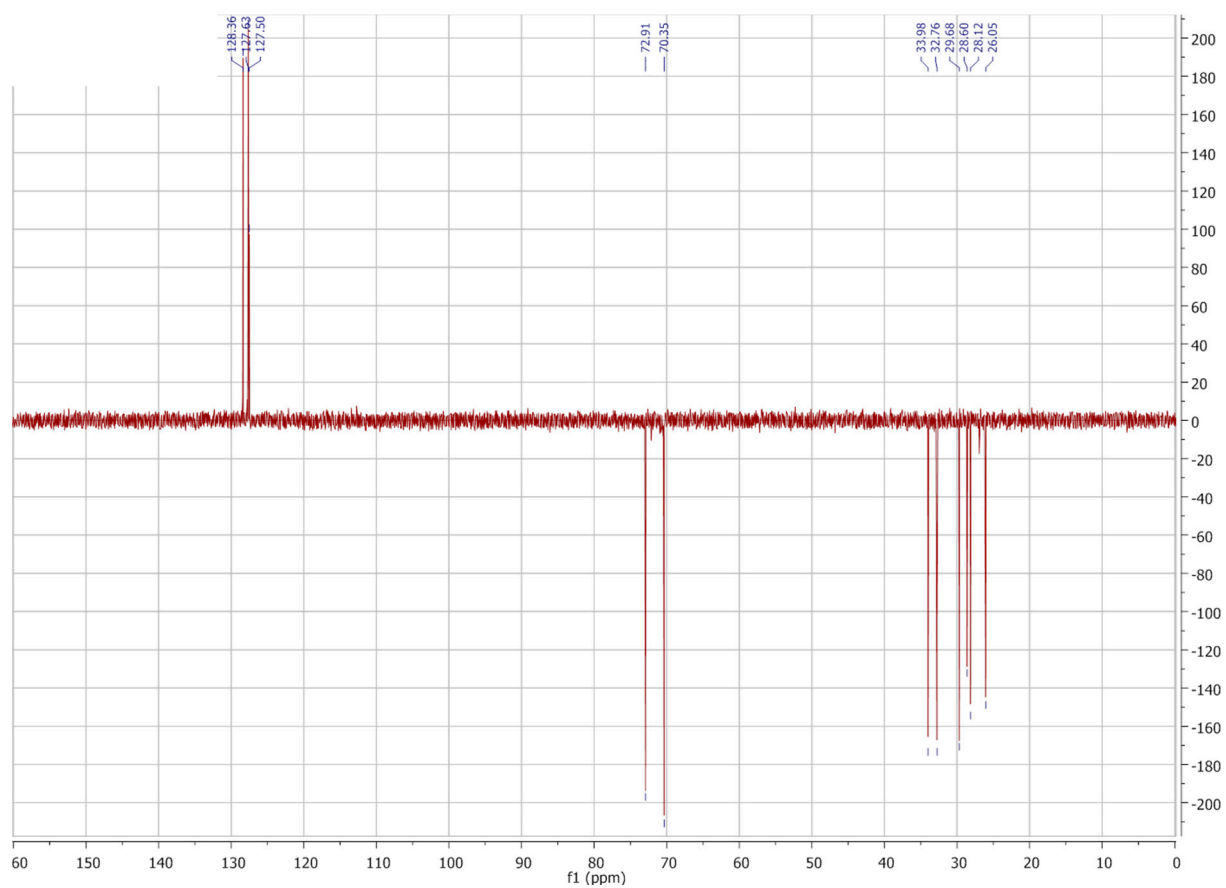
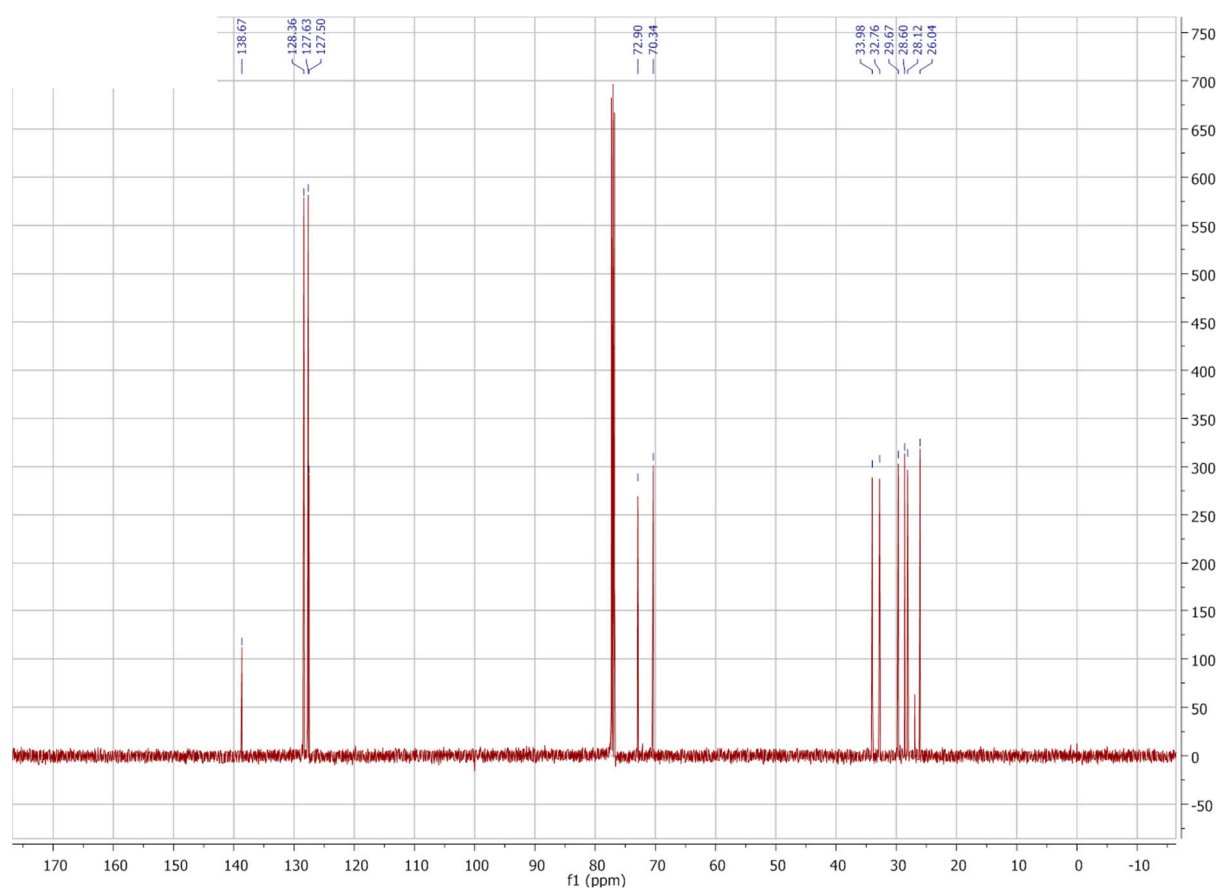


{[(7-bromoheptyl)oxy]methyl}benzene (**7a**; ZHAWOC7096)

NMR

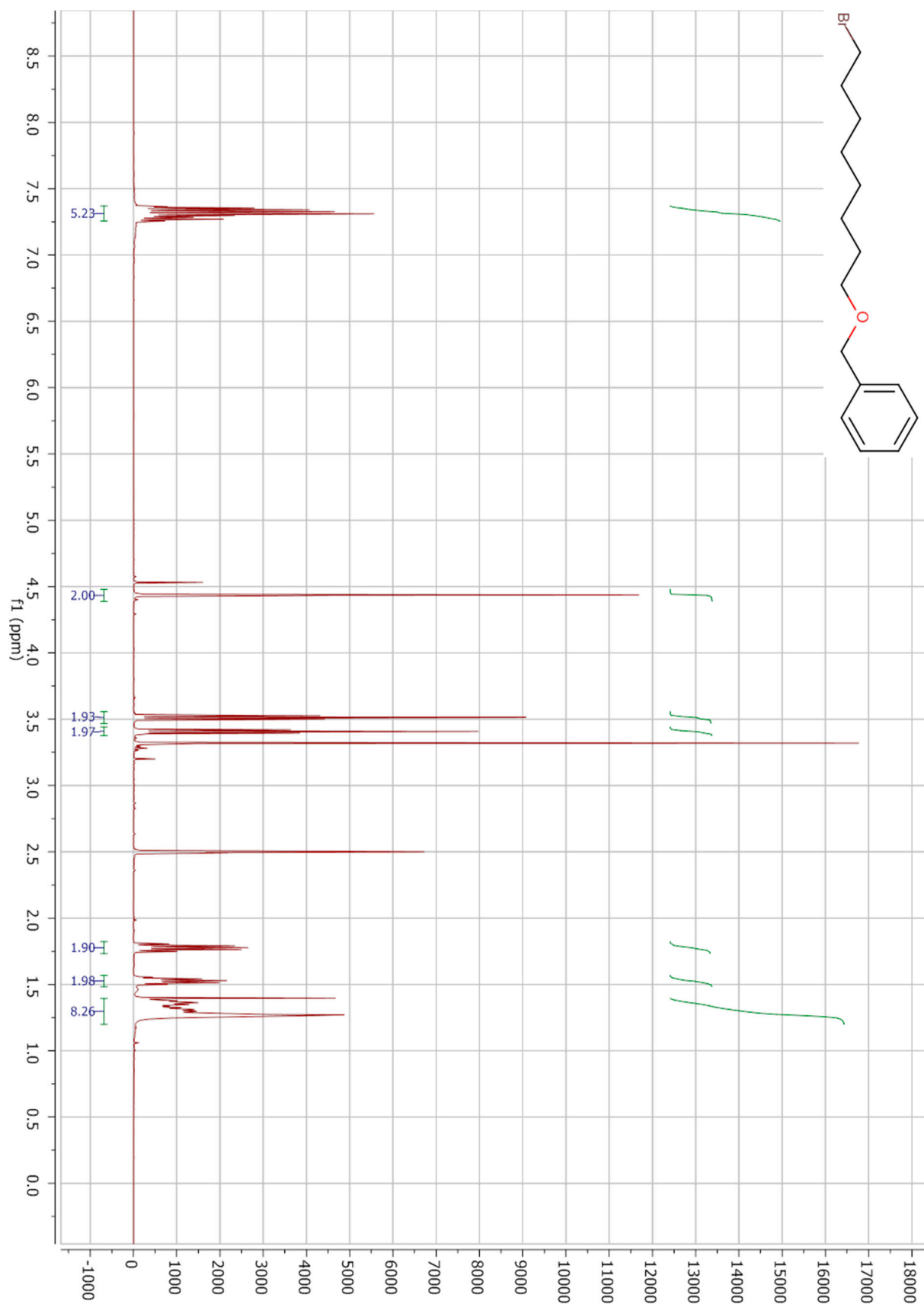


{[(7-bromoheptyl)oxy]methyl}benzene (7a; ZHAWOC7096)

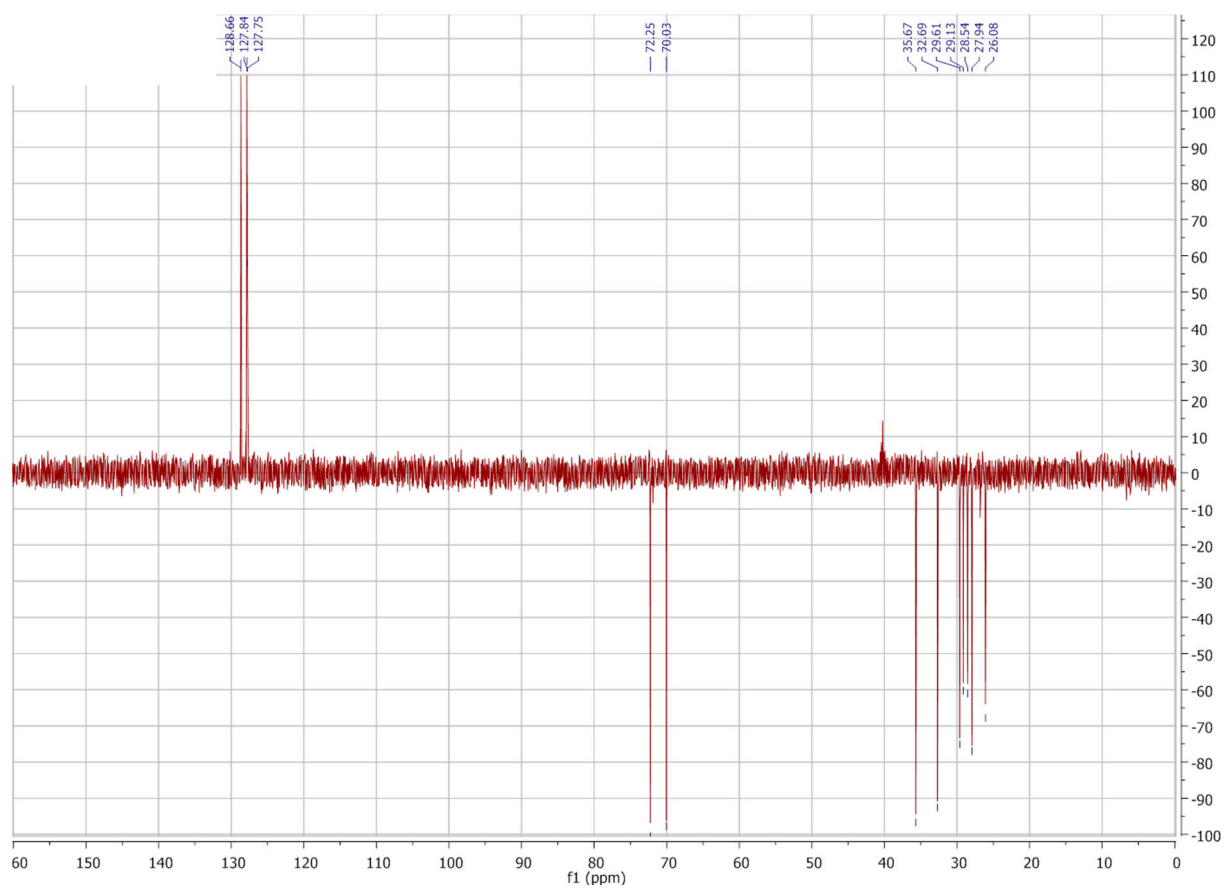
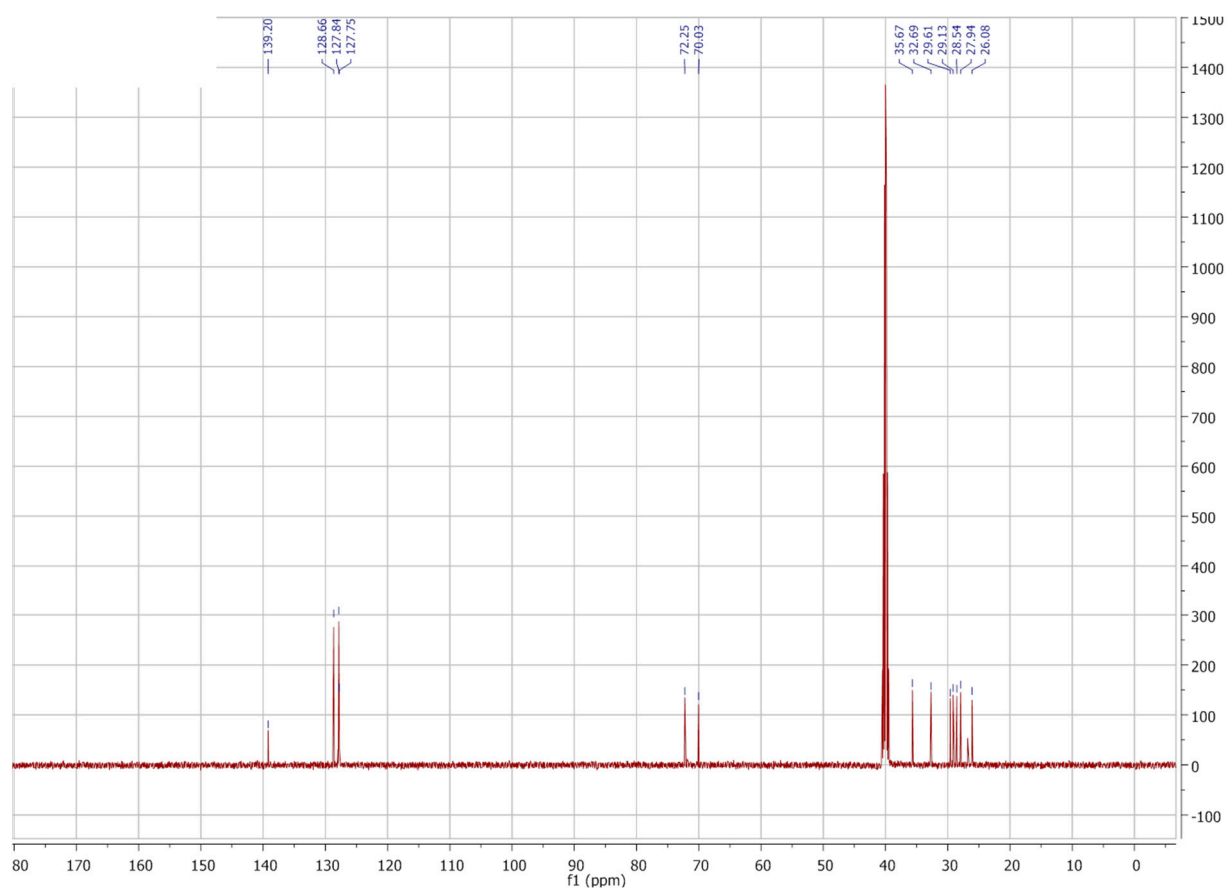


{[(8-bromooctyl)oxy]methyl}benzene (**7b**; ZHAWOC6856)

NMR

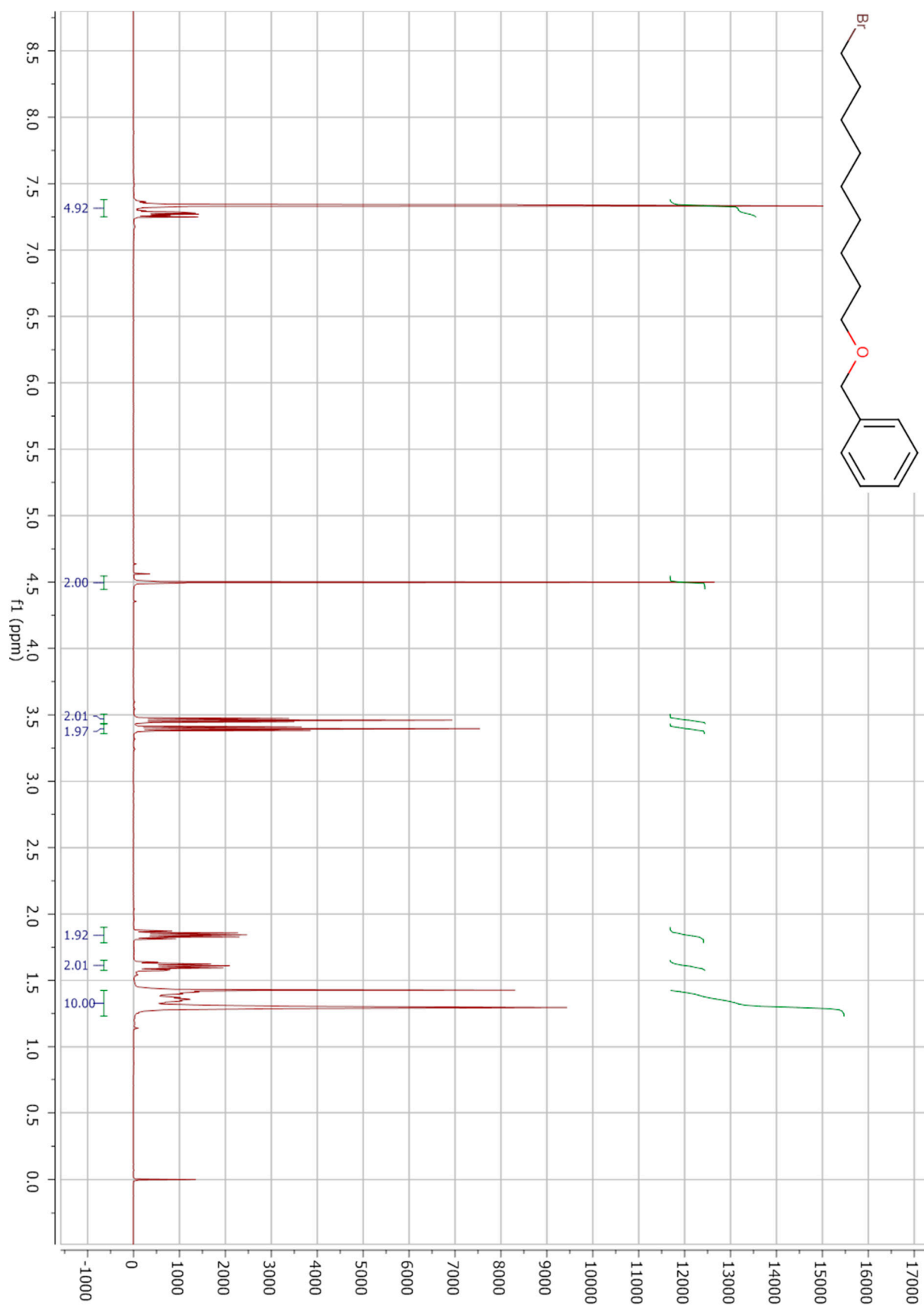


{[(8-bromooctyl)oxy]methyl}benzene (7b; ZHAWOC6856)

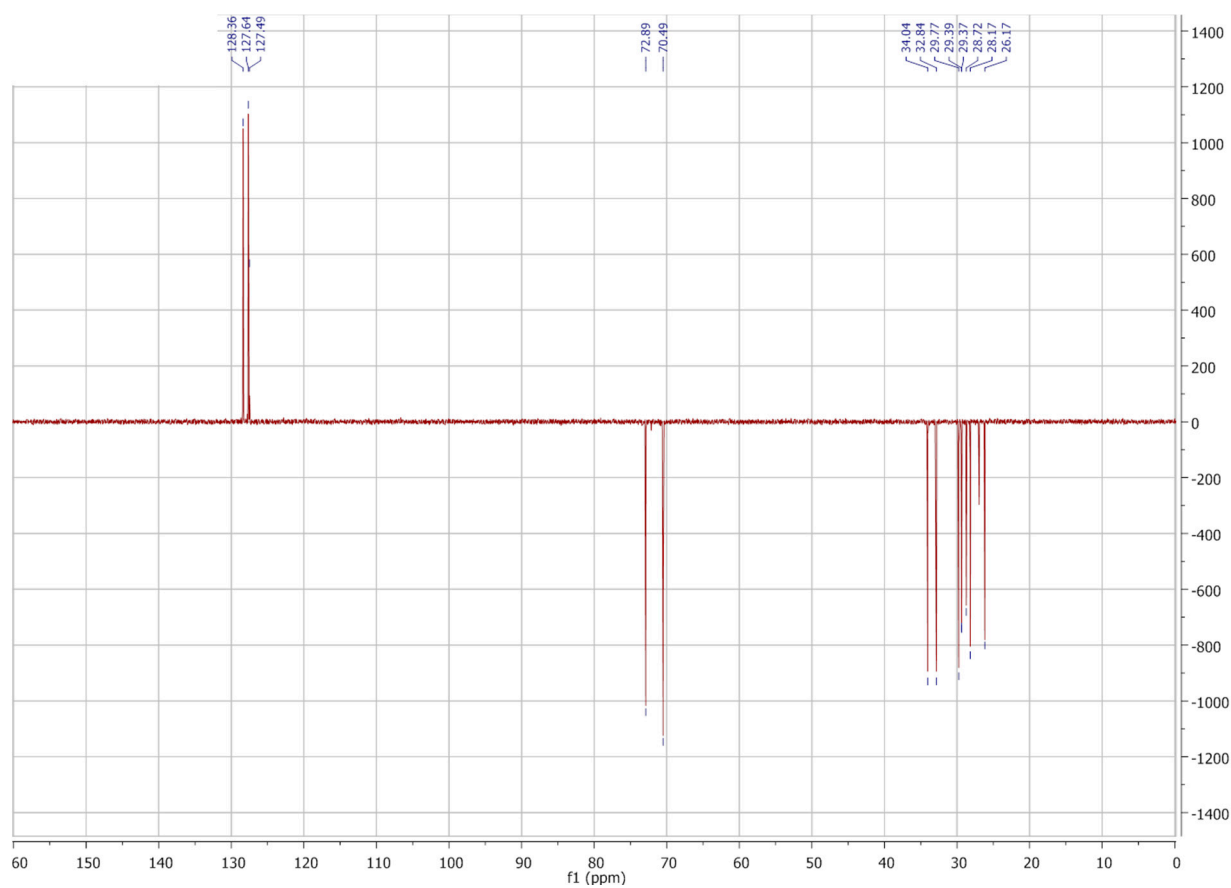
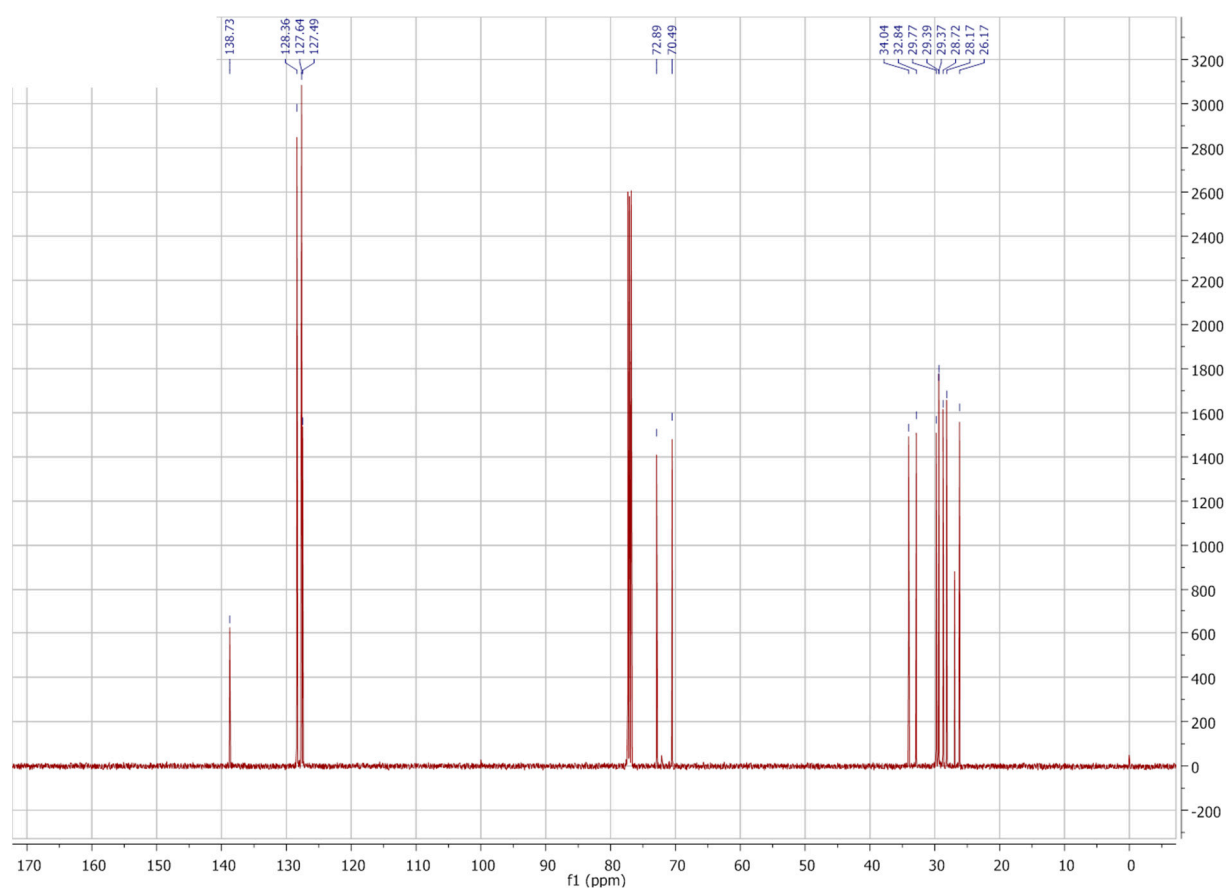


{[(9-bromononyl)oxy]methyl}benzene (**7c**; ZHAWOC6852)

NMR

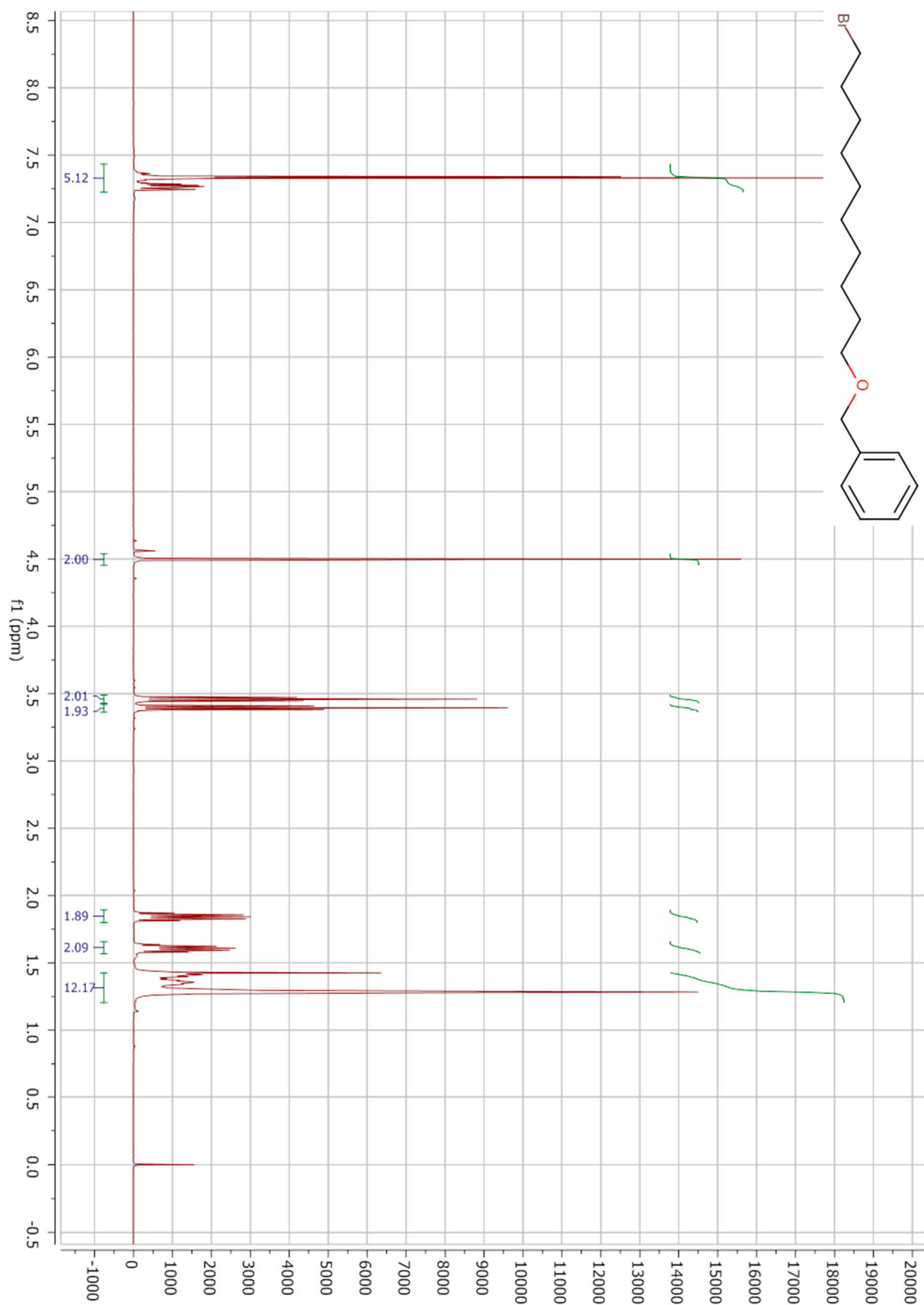


{[(9-bromononyl)oxy]methyl}benzene (7c; ZHAWOC6852)

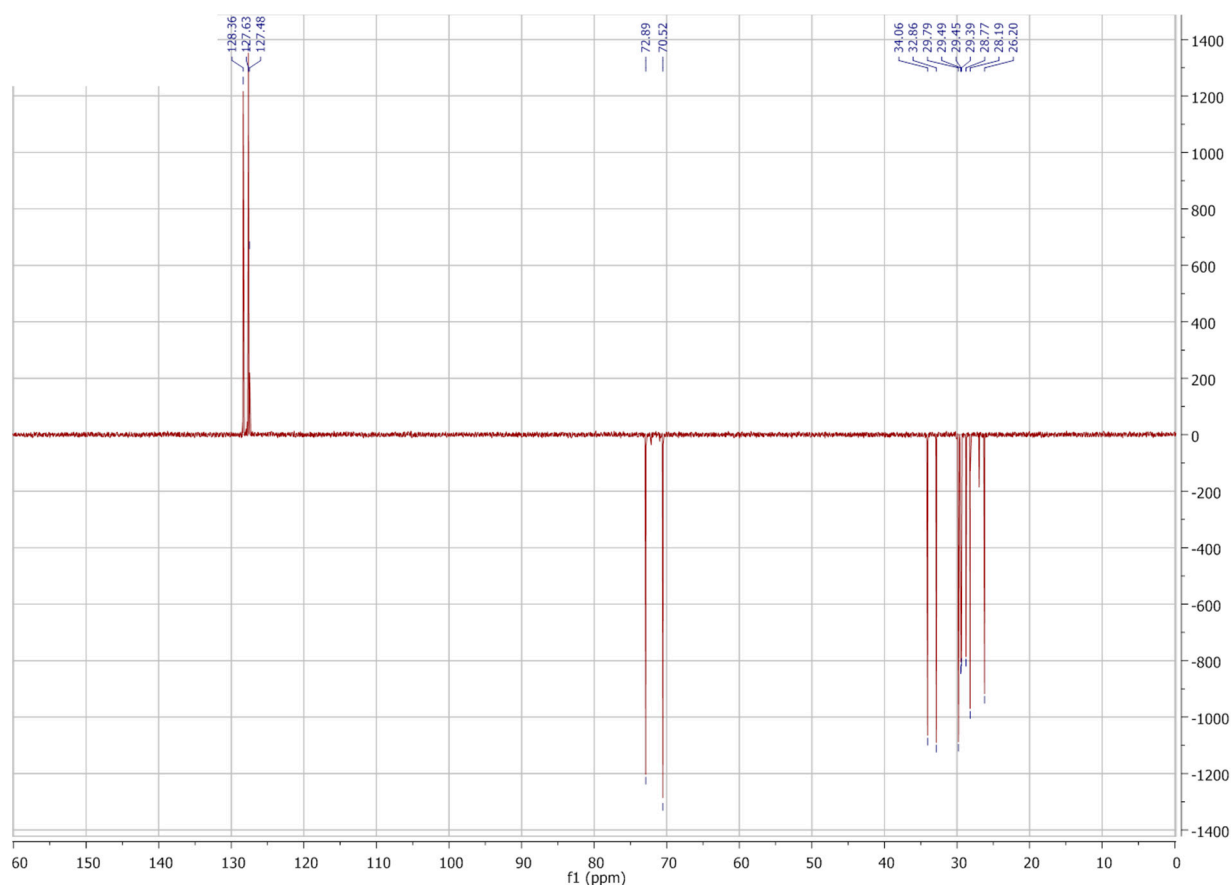
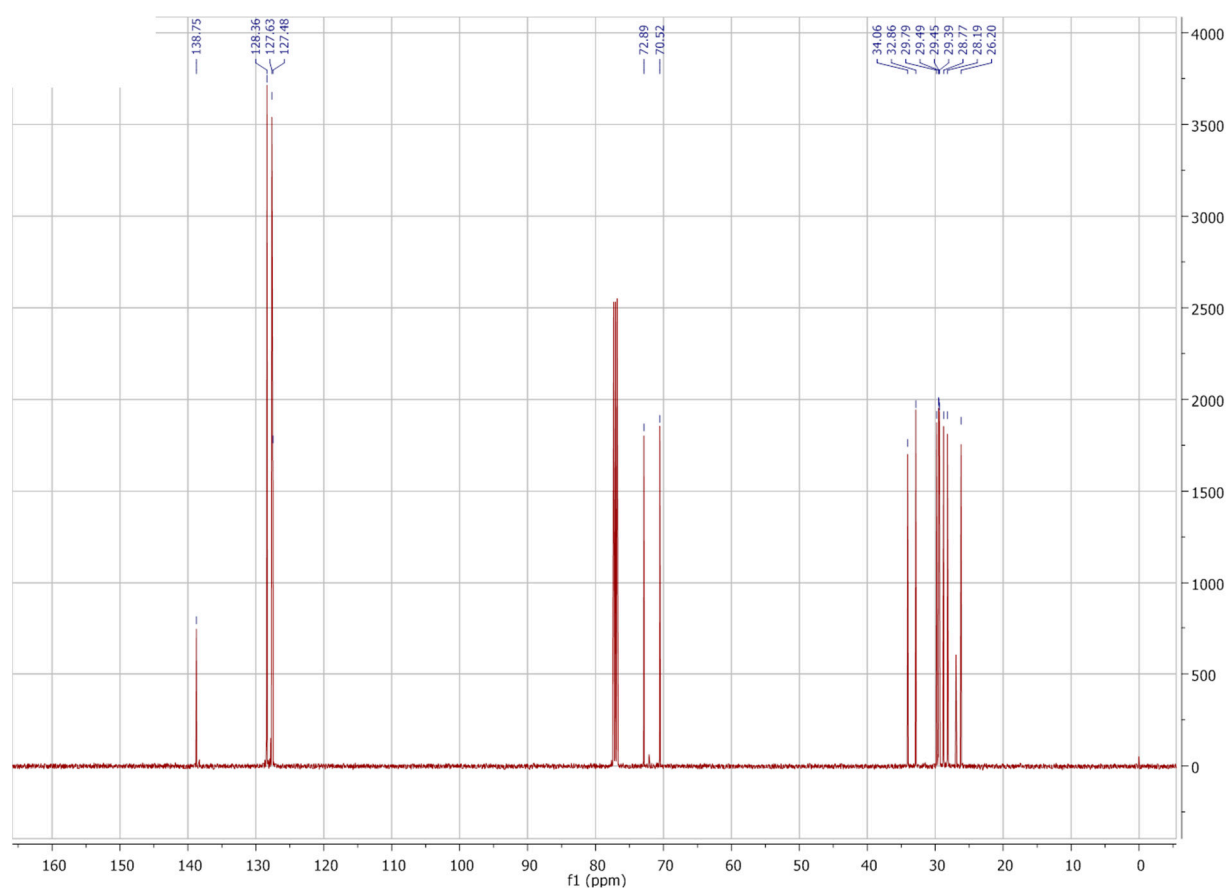


{[(10-bromodecyl)oxy]methyl}benzene (**7d**; ZHAWOC6853)

NMR

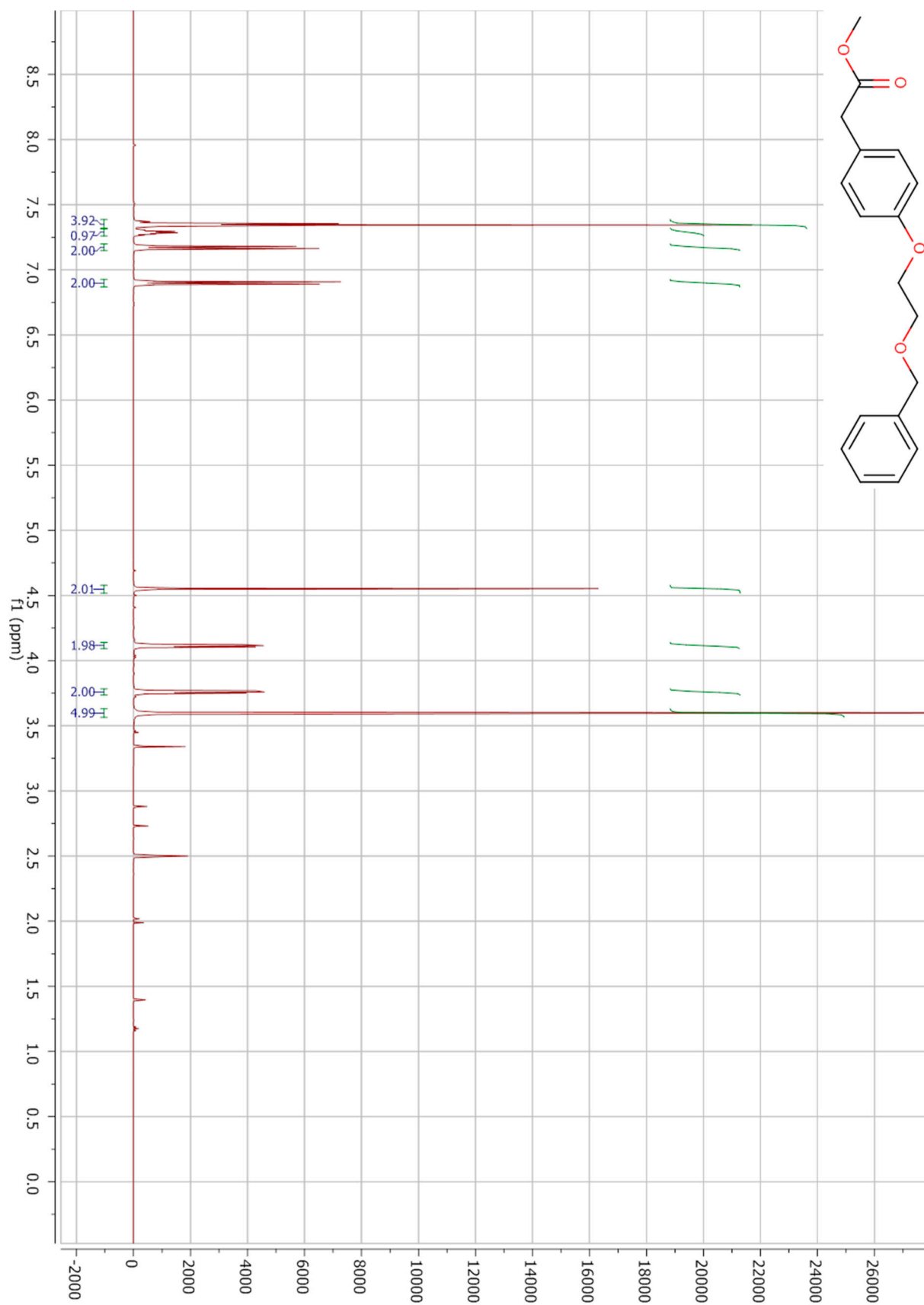


{[(10-bromodecyl)oxy]methyl}benzene (7d; ZHAWOC6853)

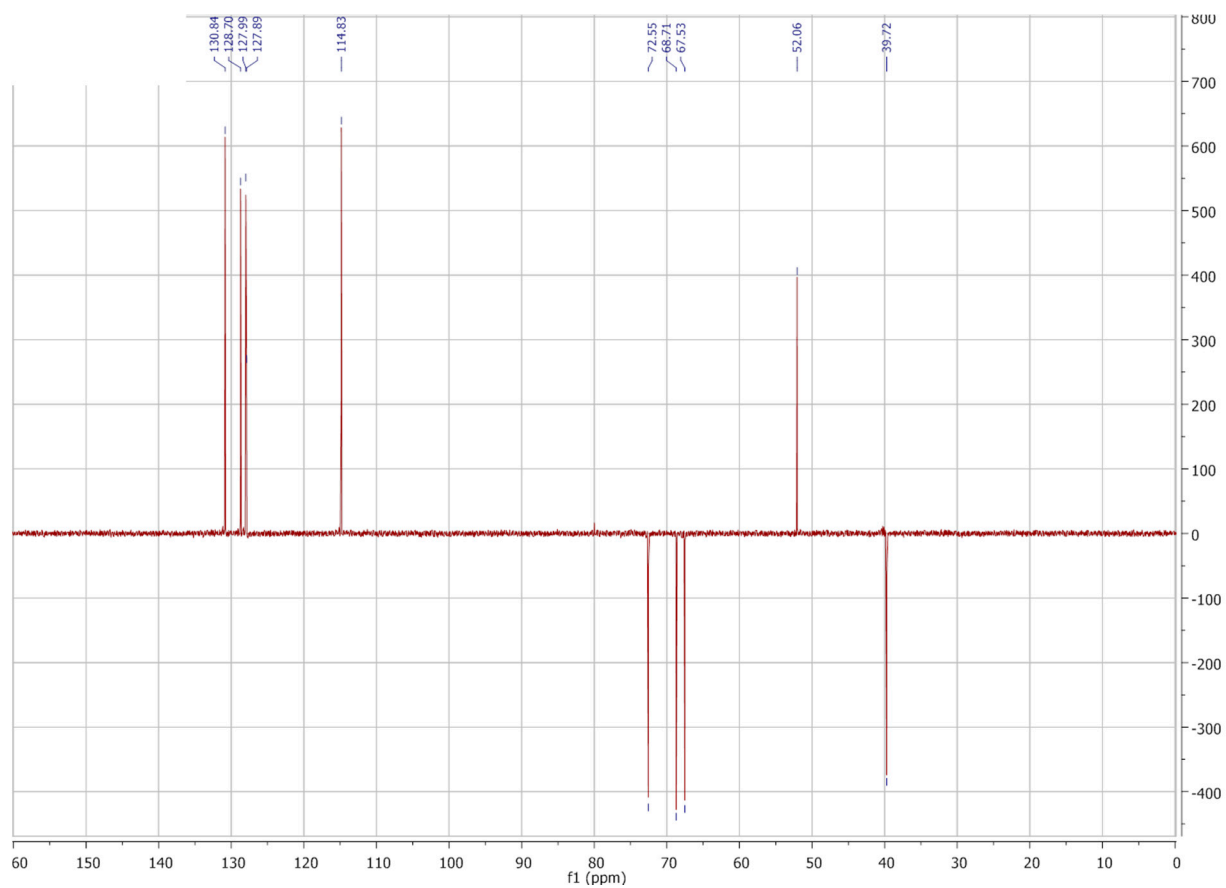
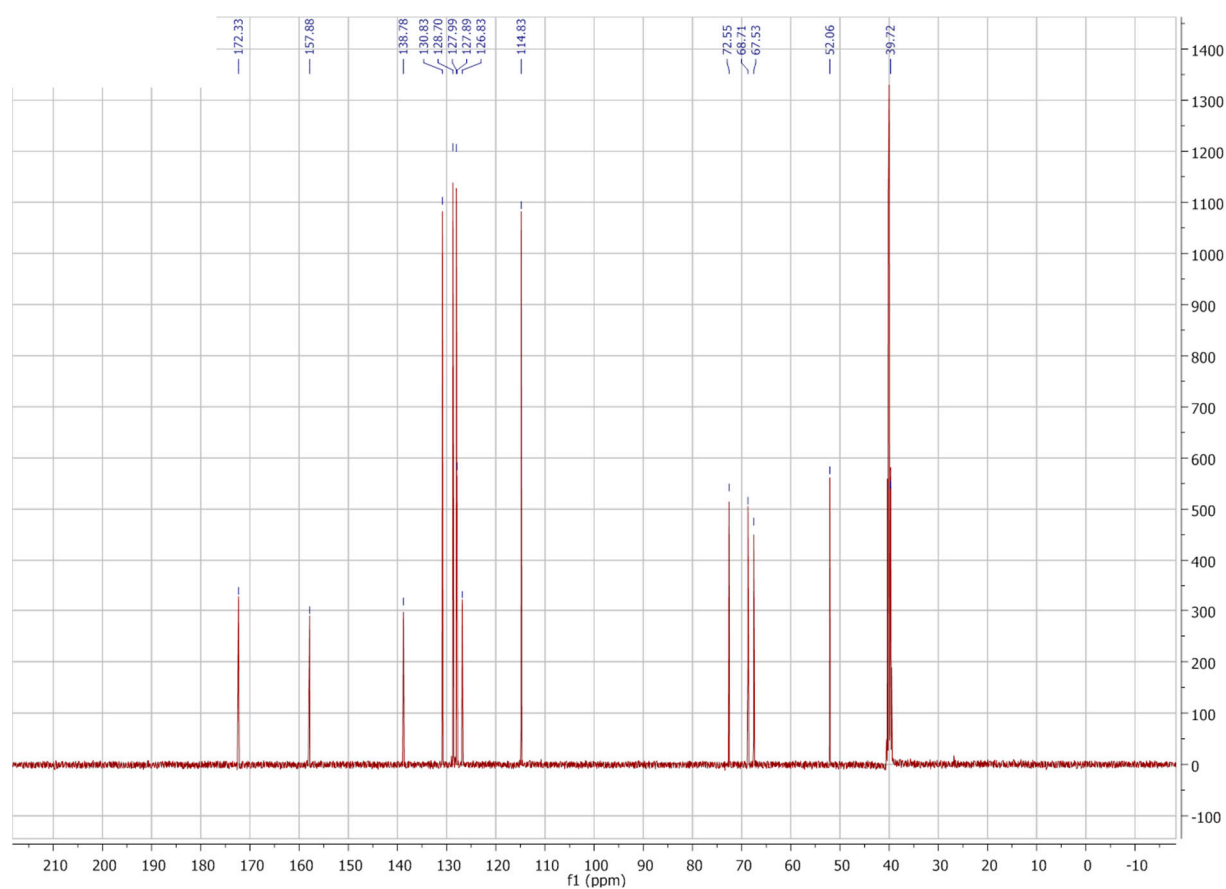


Methyl 2-{4-[2-(benzyloxy)ethoxy]phenyl}acetate (**8a**; ZHAWOC7100)

NMR

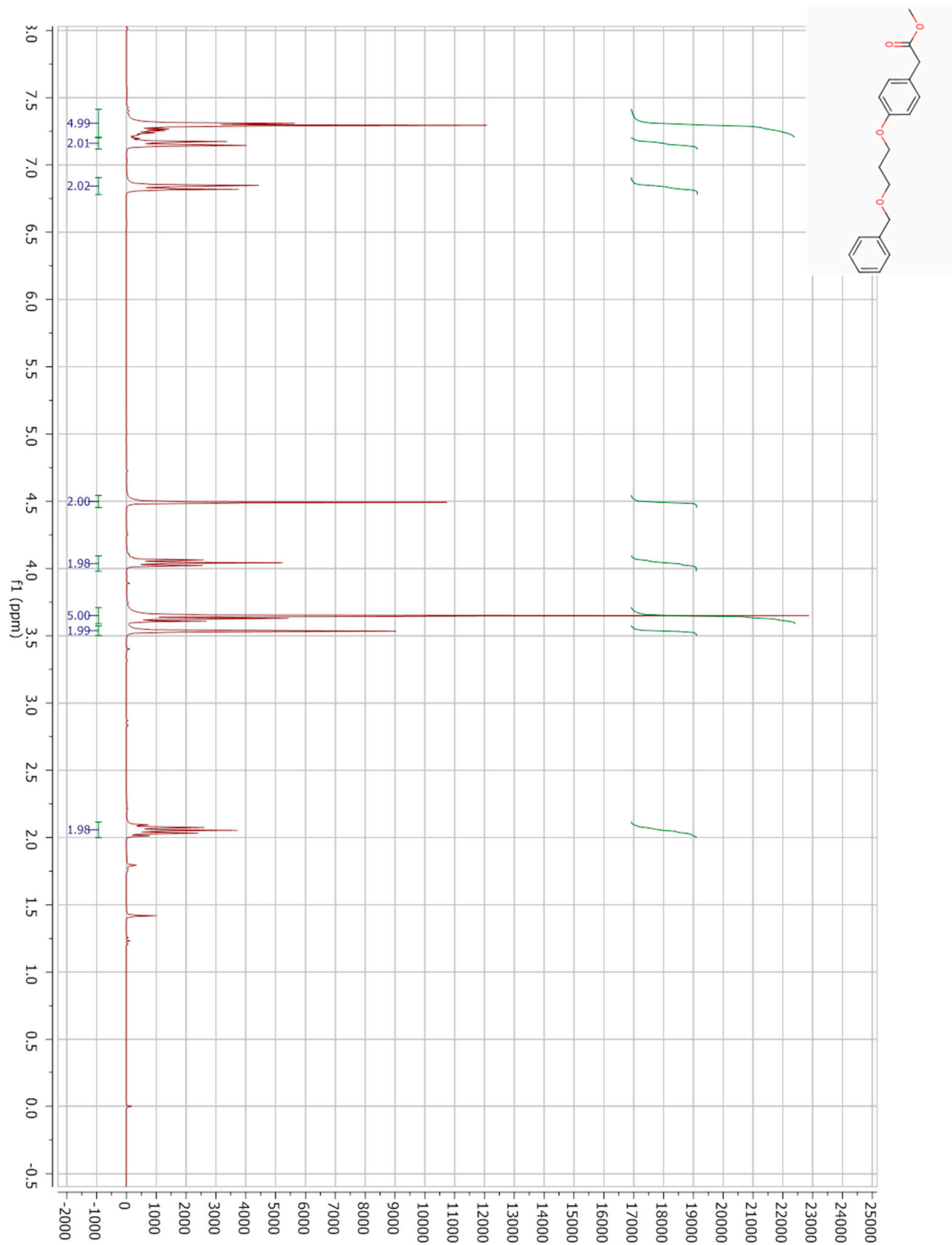


Methyl 2-{4-[2-(benzyloxy)ethoxy]phenyl}acetate (**8a**; ZHAWOC7100)

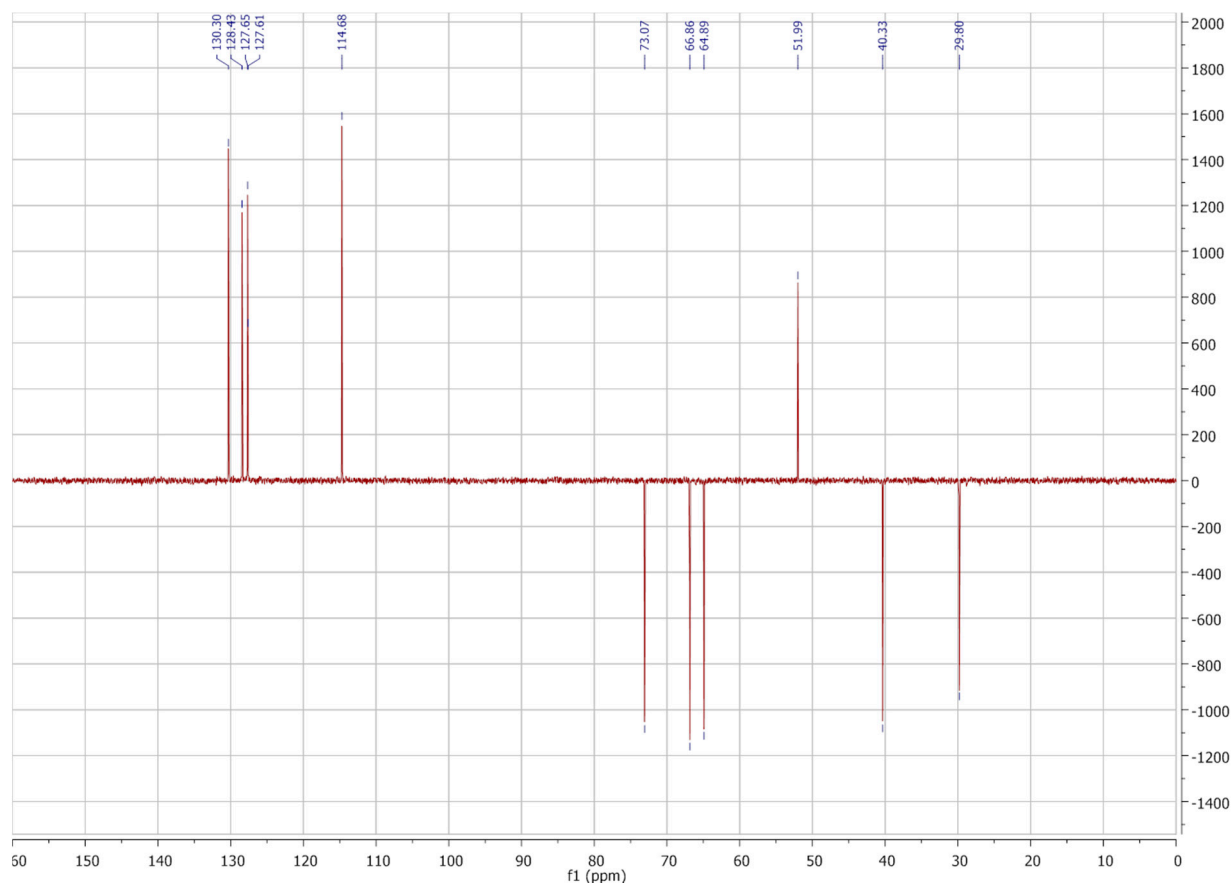
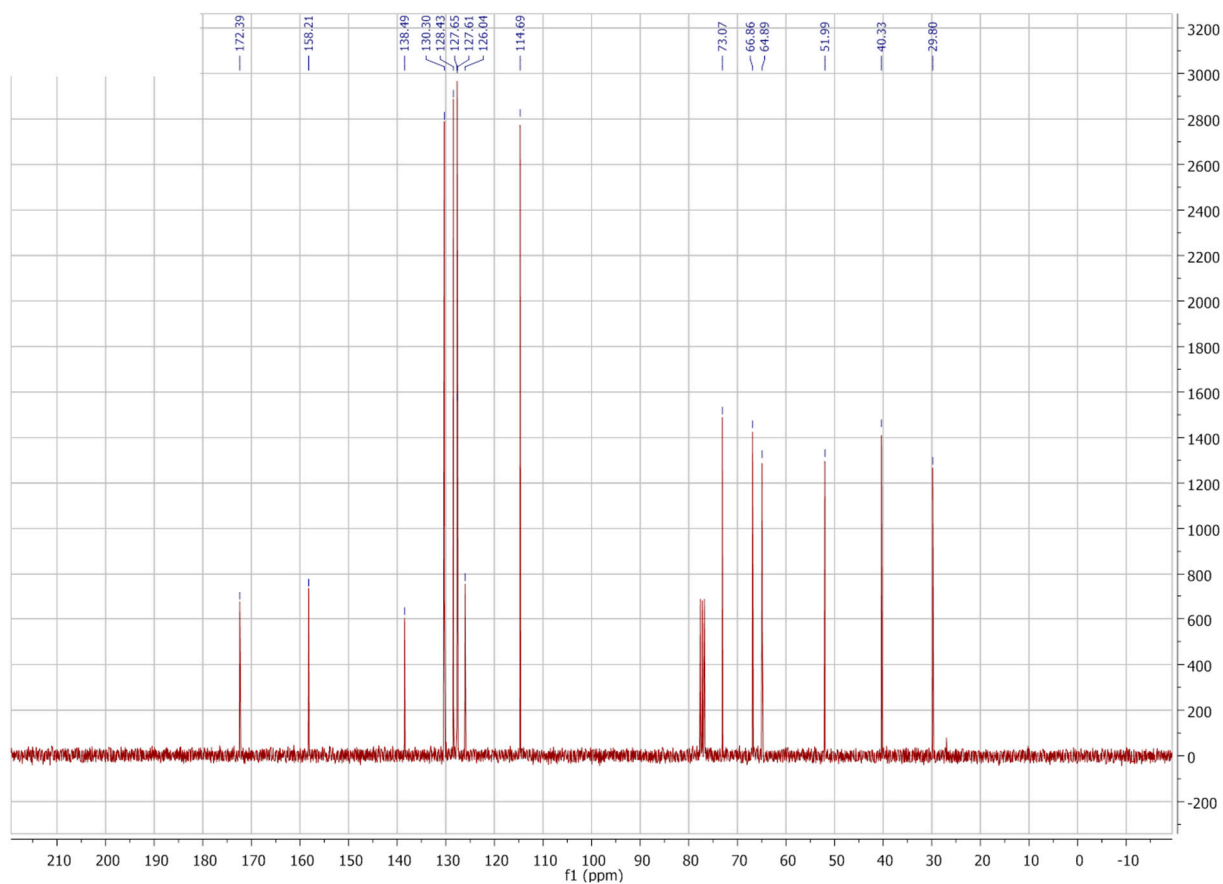


Methyl 2-{4-[3-(benzyloxy)propoxy]phenyl}acetate (**8b**; ZHAWOC4496)

NMR

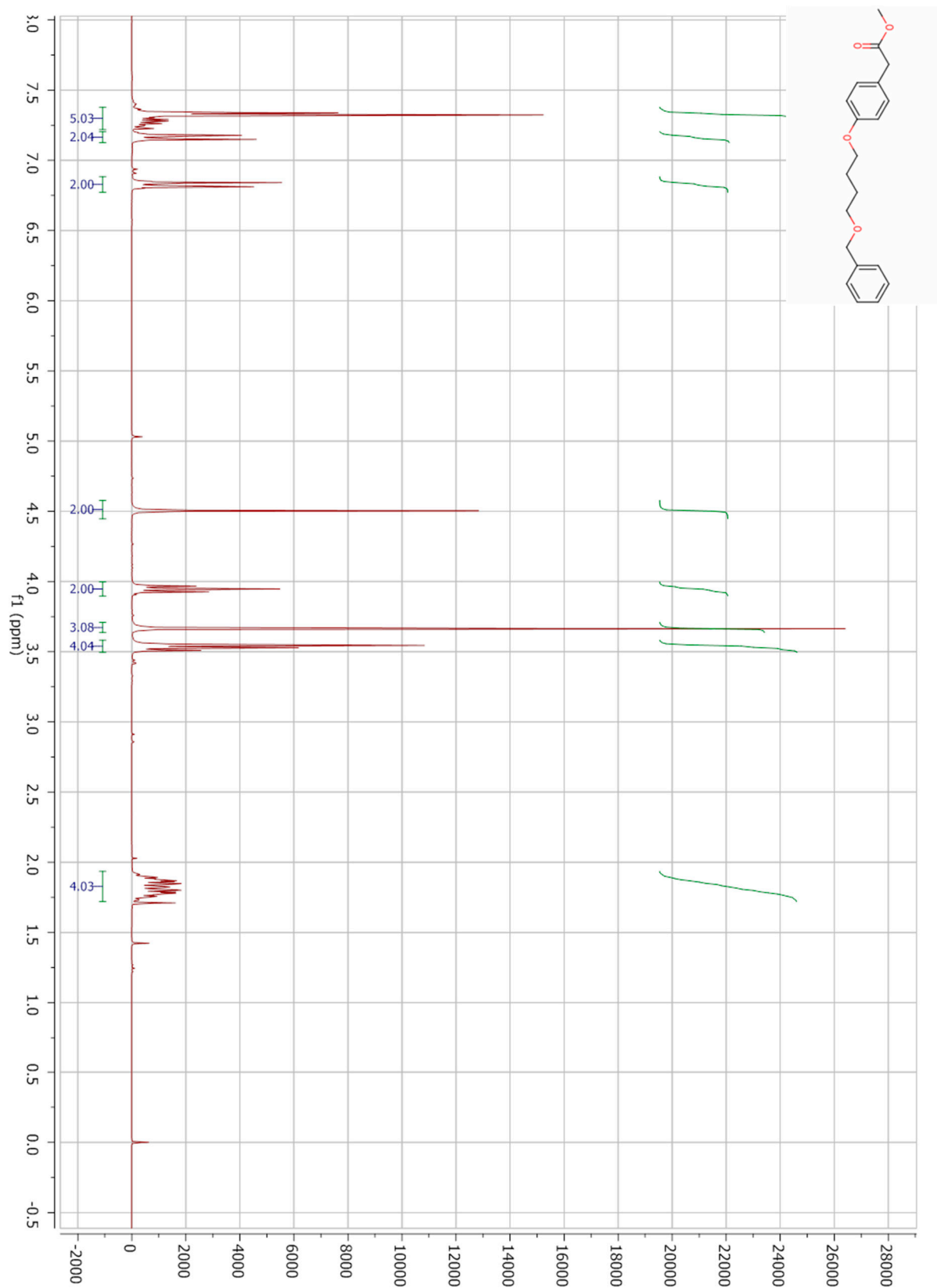


Methyl 2-{4-[3-(benzyloxy)propoxy]phenyl}acetate (**8b**; ZHAWOC4496)

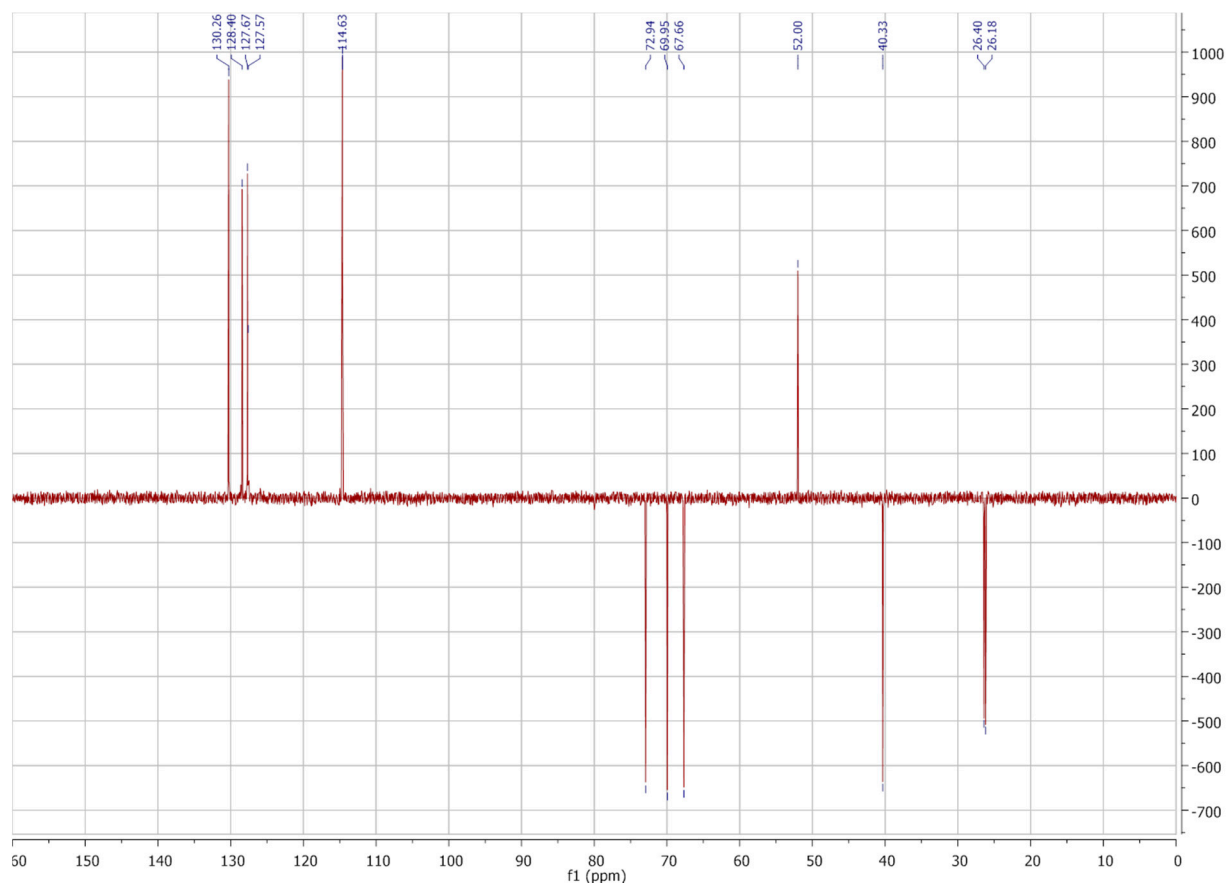
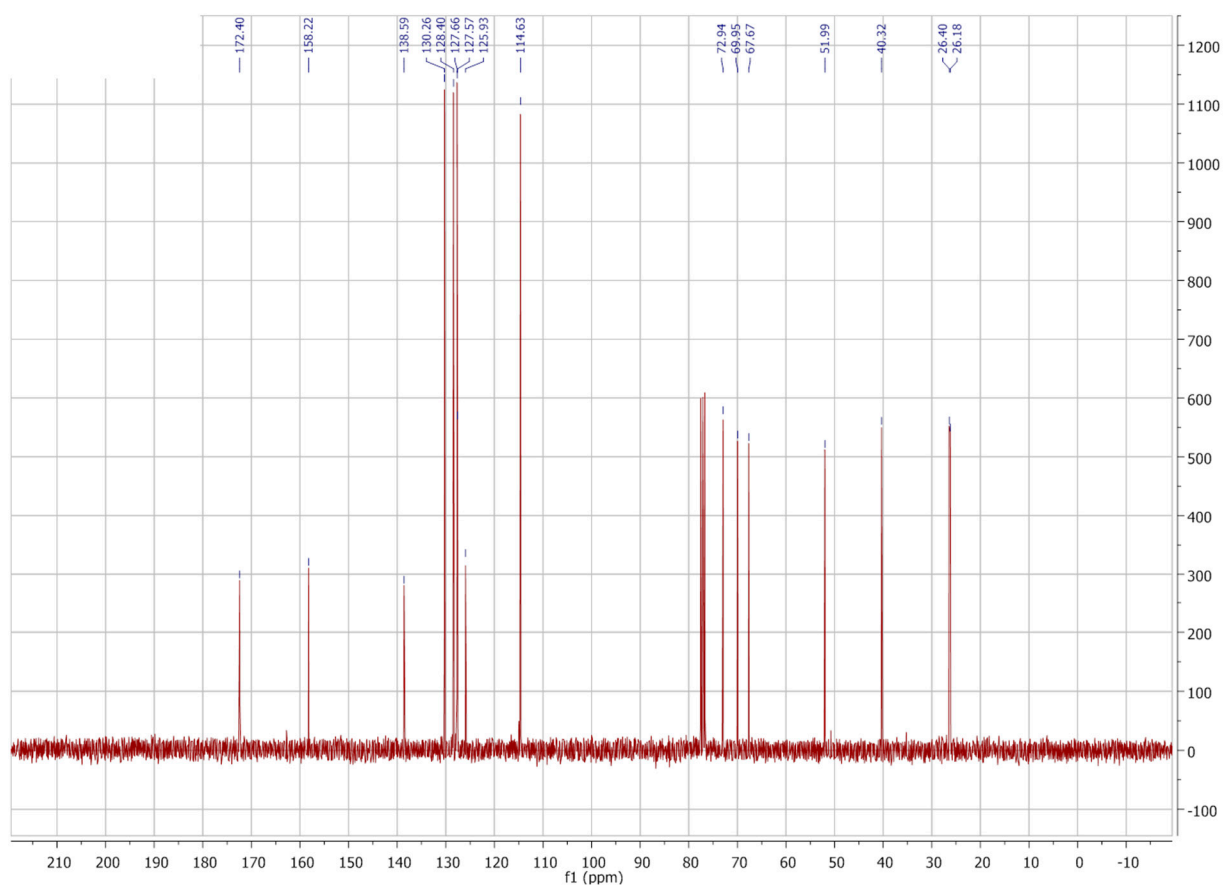


Methyl 2-{4-[4-(benzyloxy)butoxy]phenyl}acetate (**8c**; ZHAWOC4534)

NMR

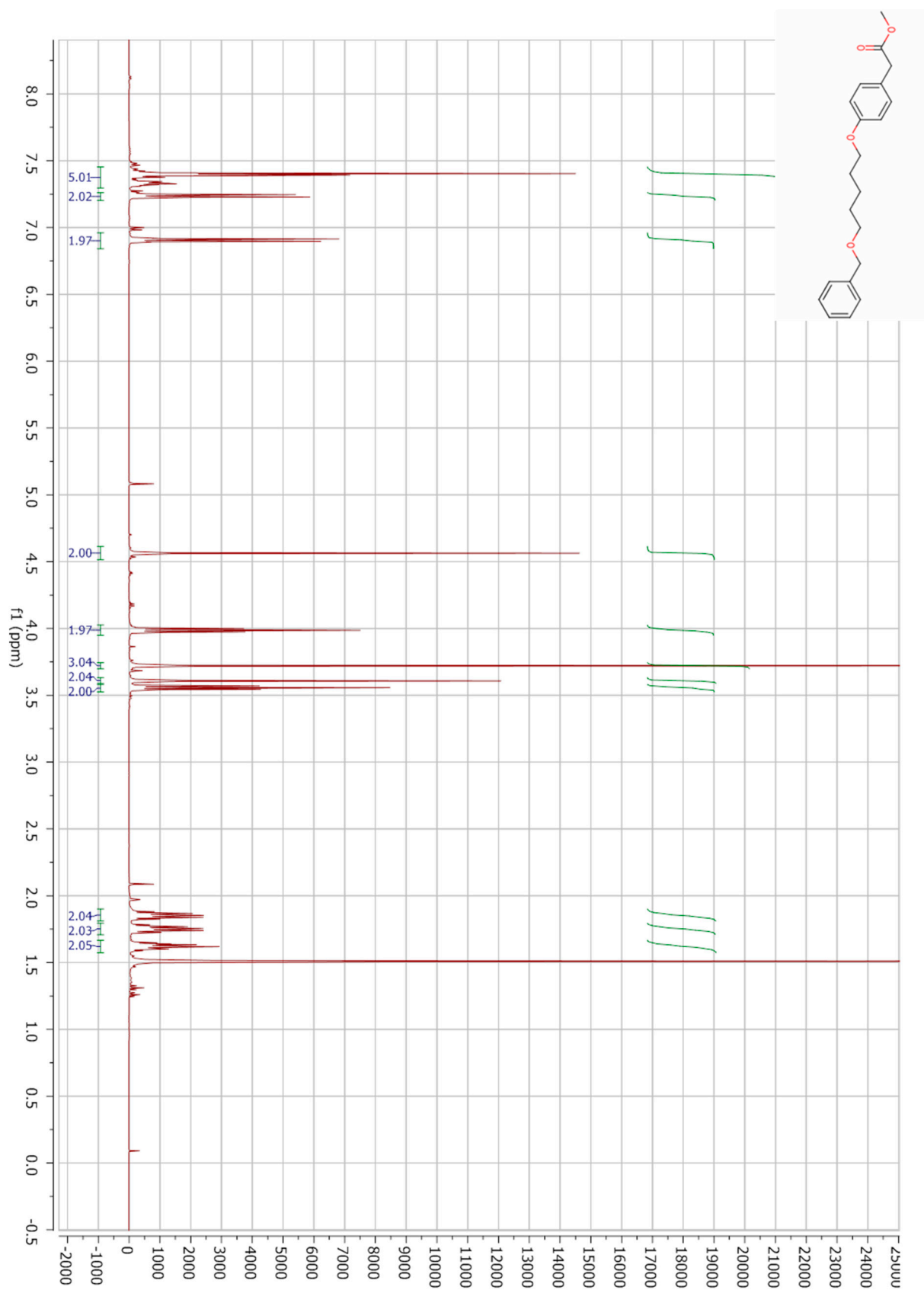


Methyl 2-{4-[4-(benzyloxy)butoxy]phenyl}acetate (**8c**; ZHAWOC4534)

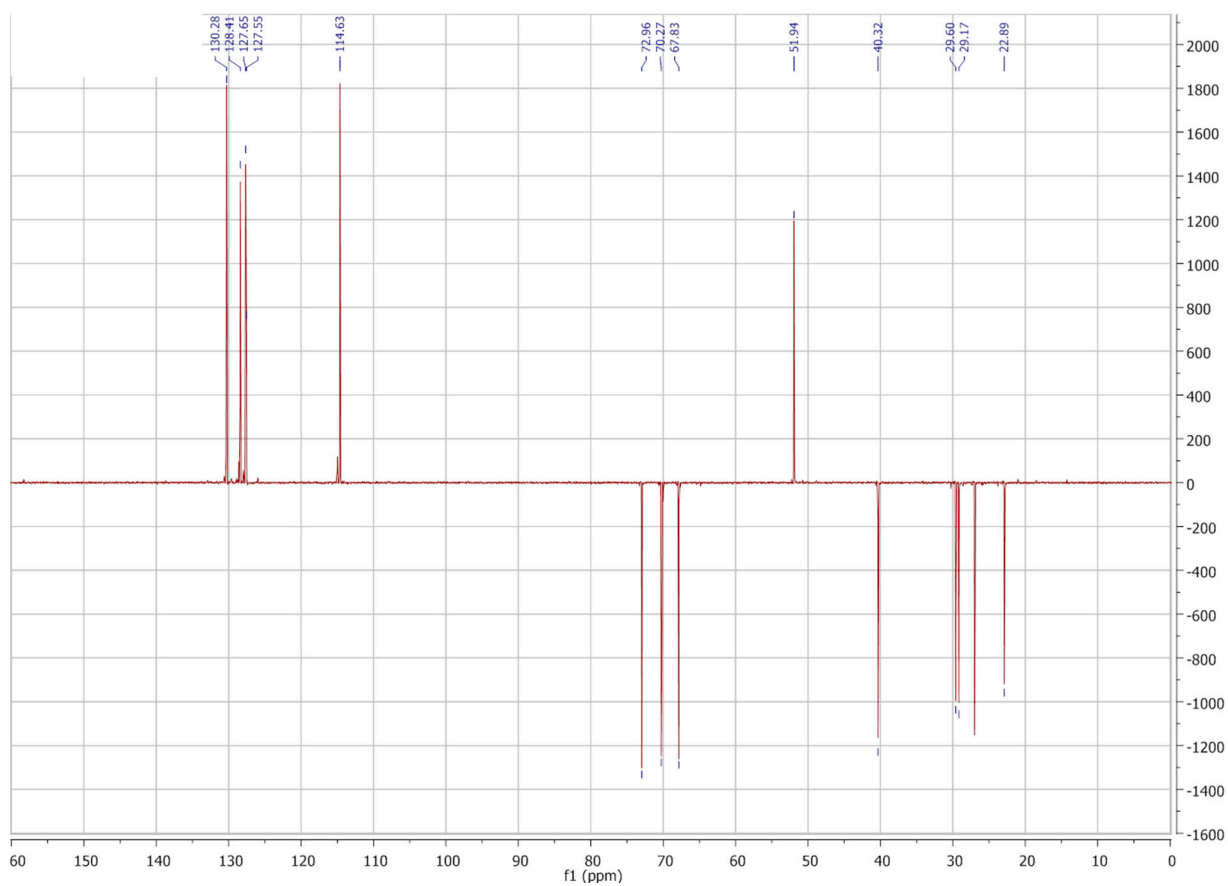
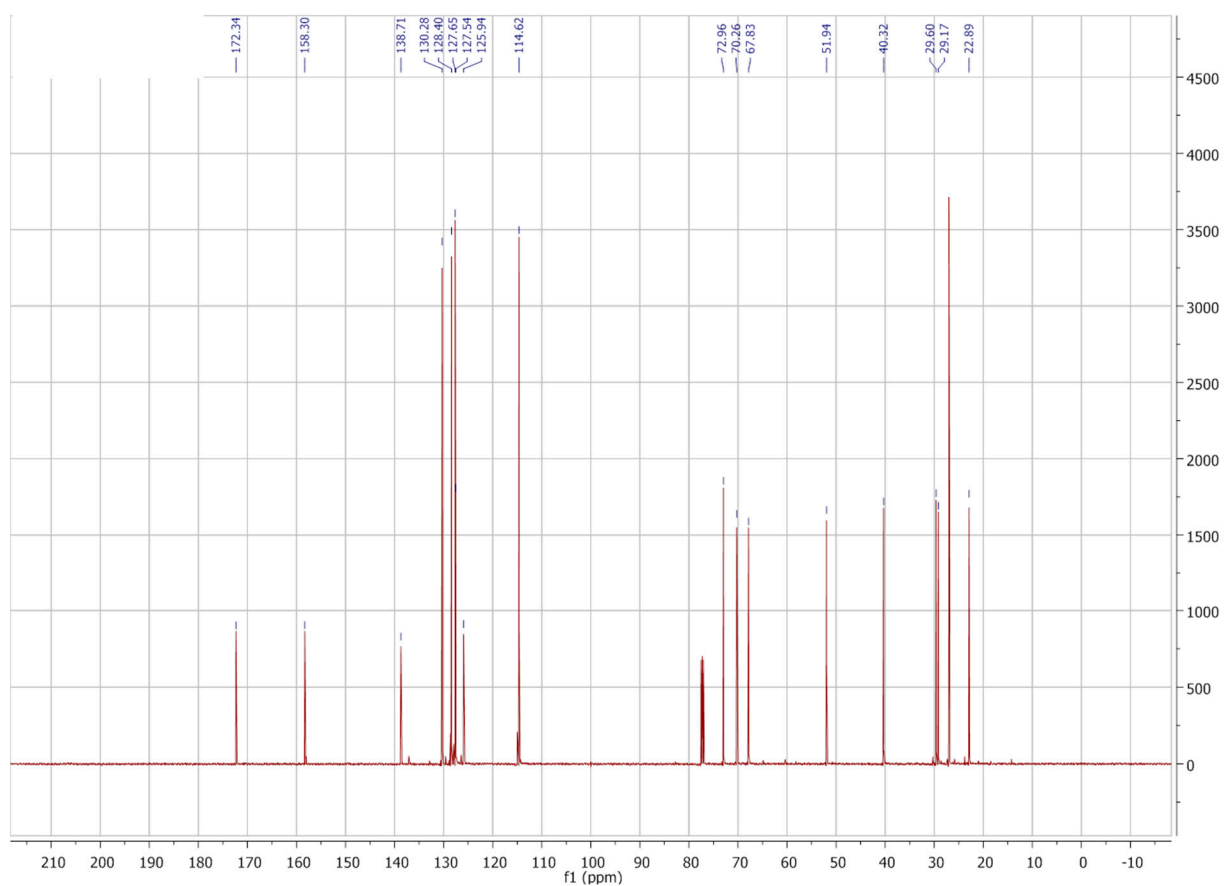


Methyl 2-(4-[[5-(benzyloxy)pentyl]oxy}phenyl)acetate (**8d**; ZHAWOC5921)

NMR

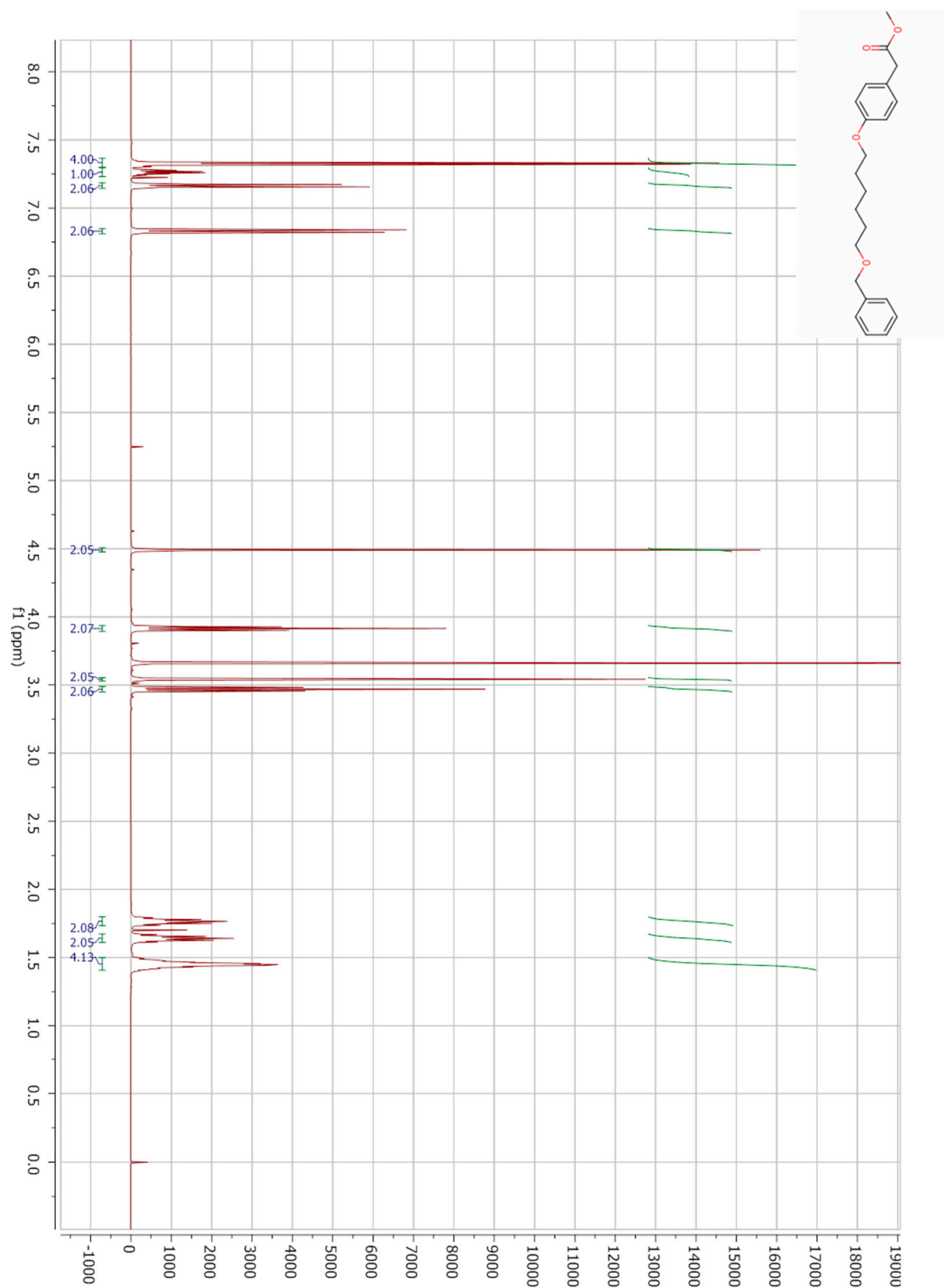


Methyl 2-(4-([5-(benzyloxy)pentyl]oxy)phenyl)acetate (**8d**; ZHAWOC5921)

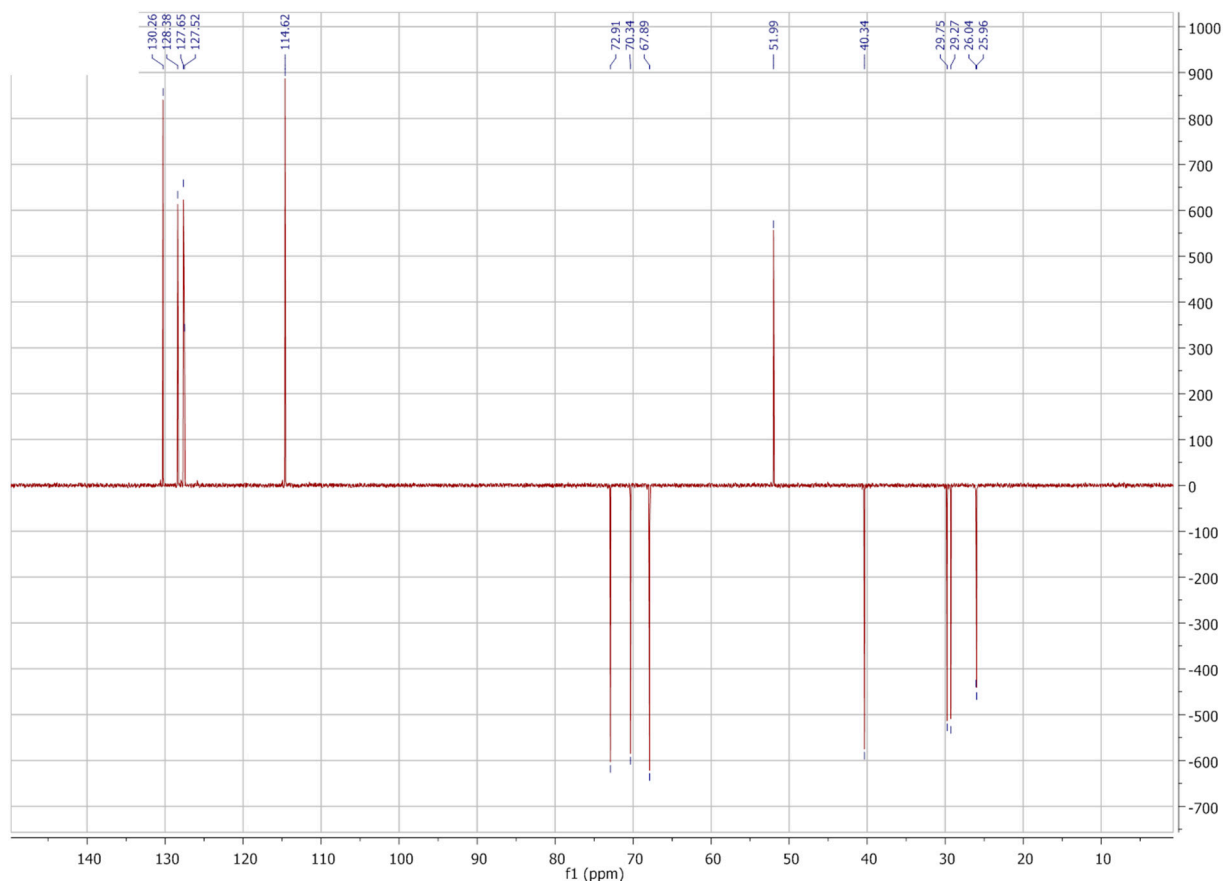
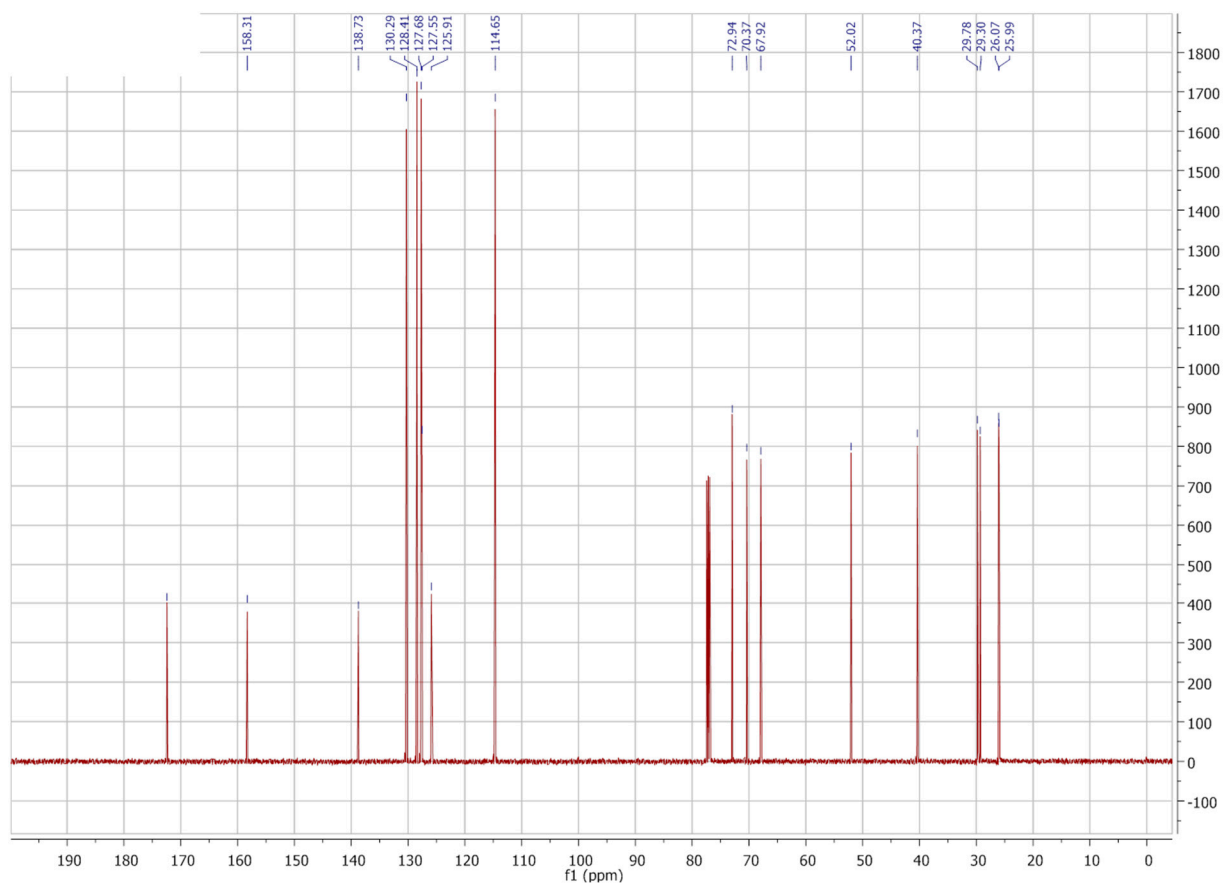


Methyl 2-(4-[[6-(benzyloxy)hexyl]oxy}phenyl)acetate (**8e**; ZHAWOC5946)

NMR

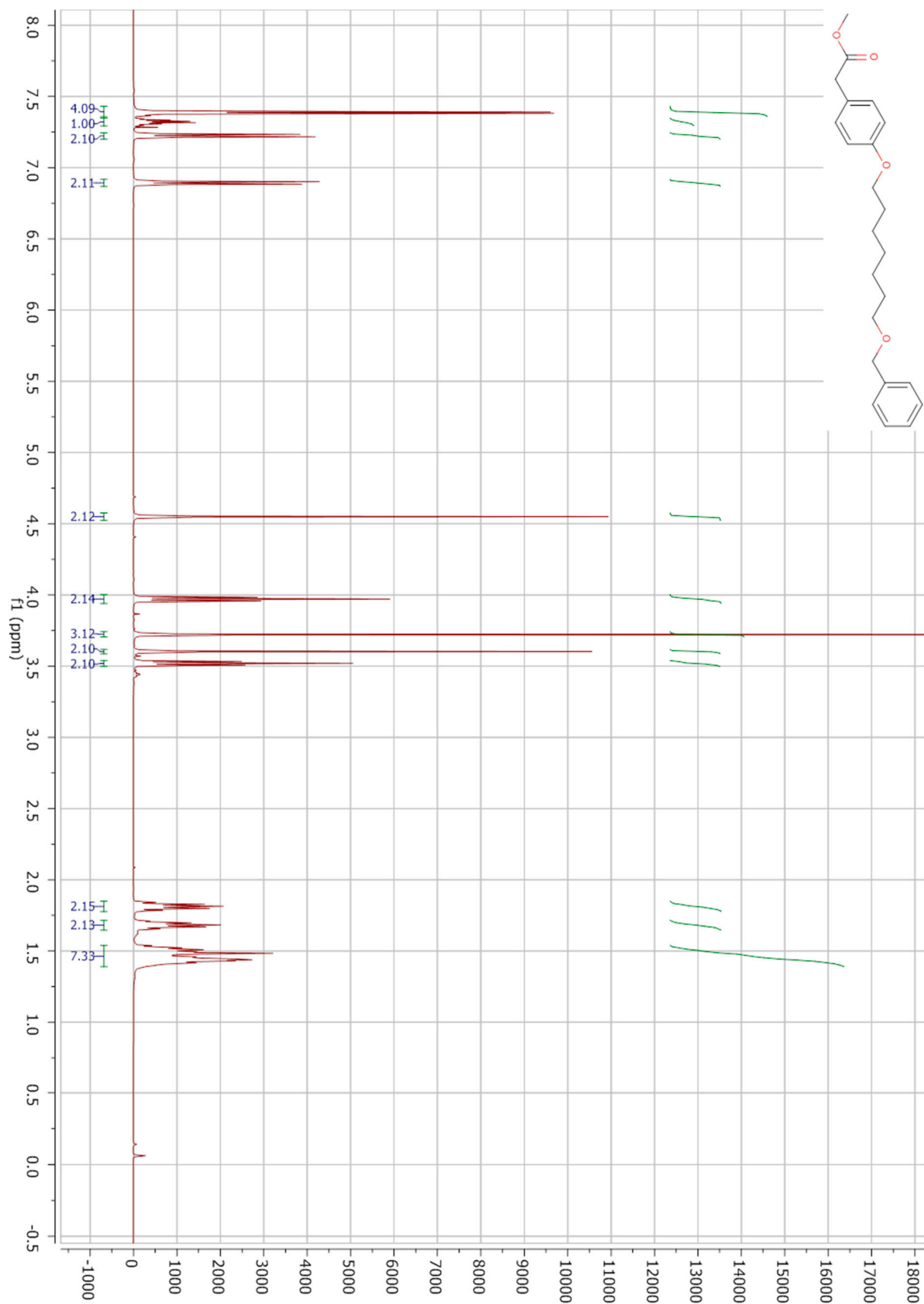


Methyl 2-(4-([6-(benzyloxy)hexyl]oxy)phenyl)acetate (**8e**; ZHAWOC5946)

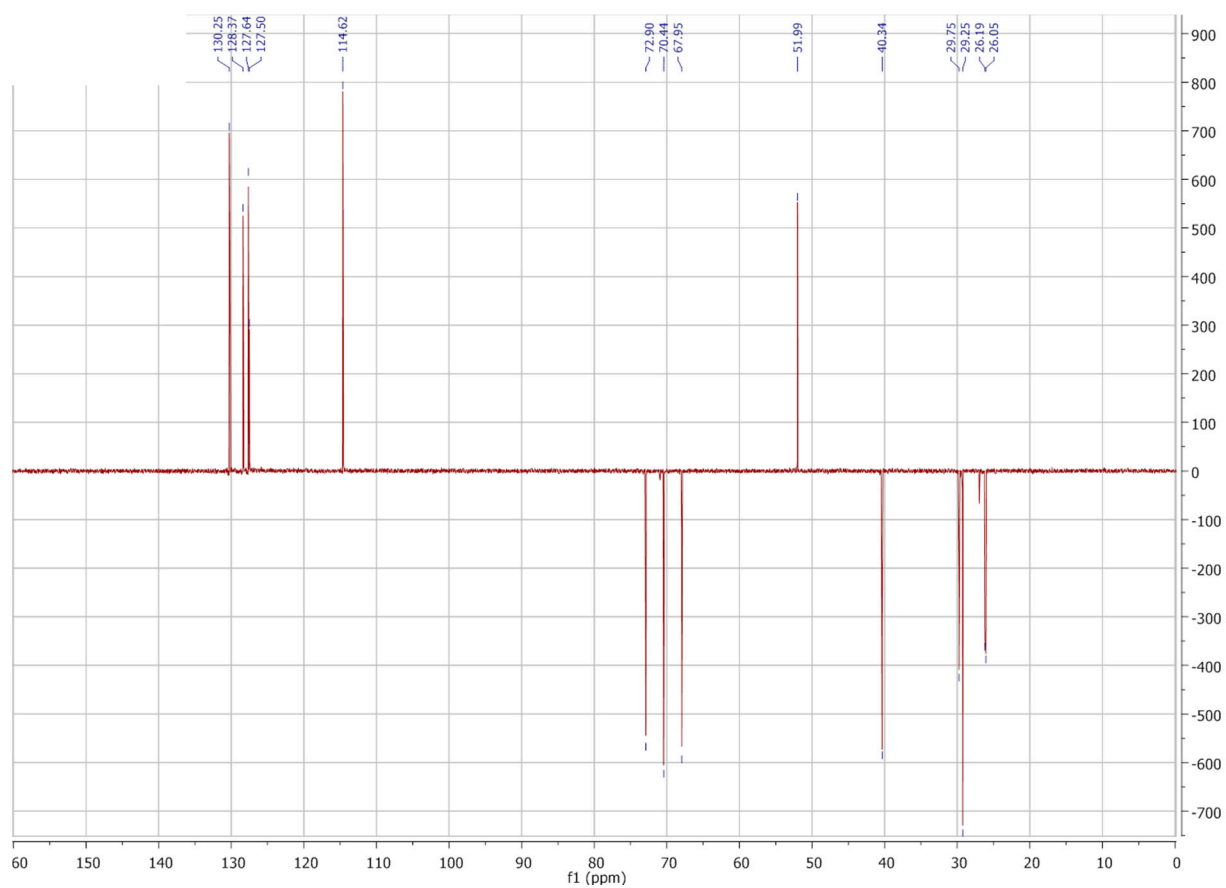
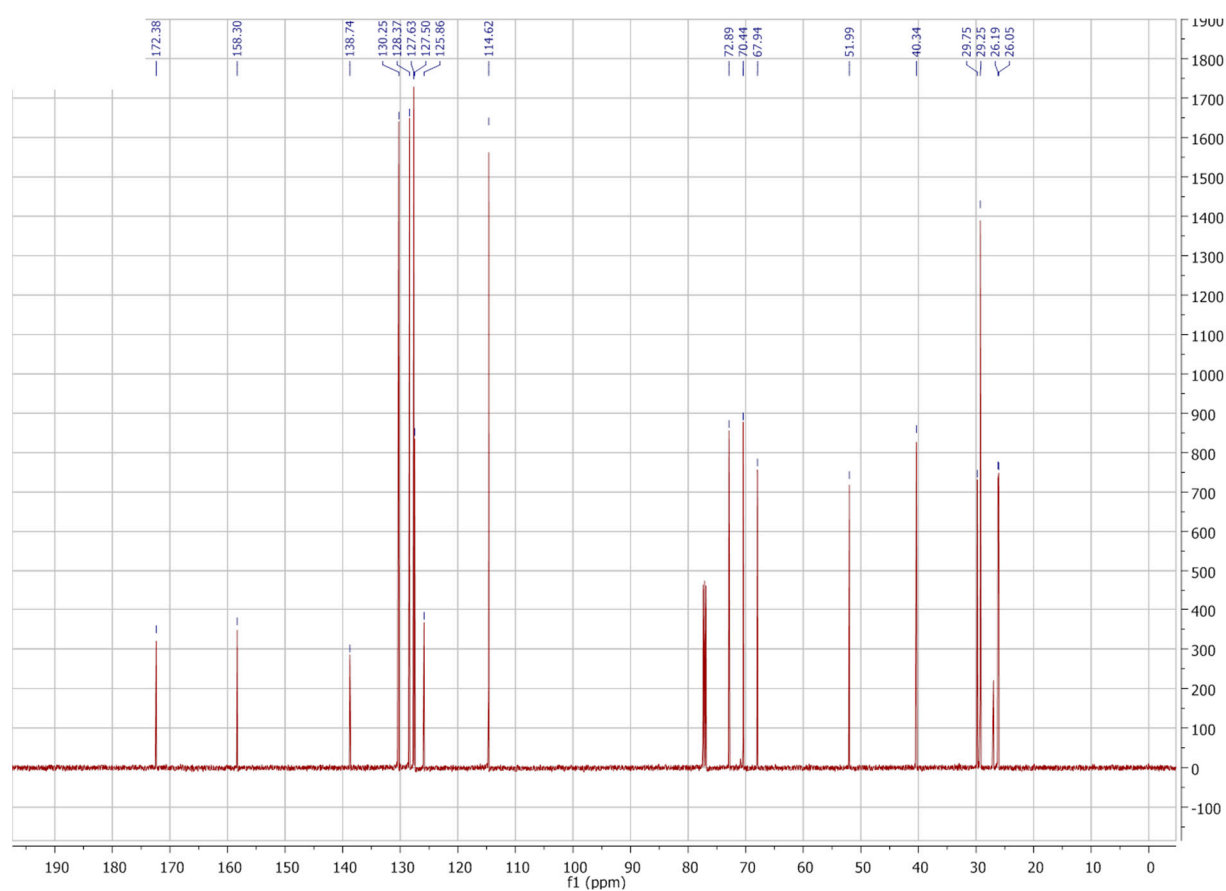


Methyl 2-(4-([7-(benzyloxy)heptyl]oxy)phenyl)acetate (**8f**; ZHAWOC7097)

NMR

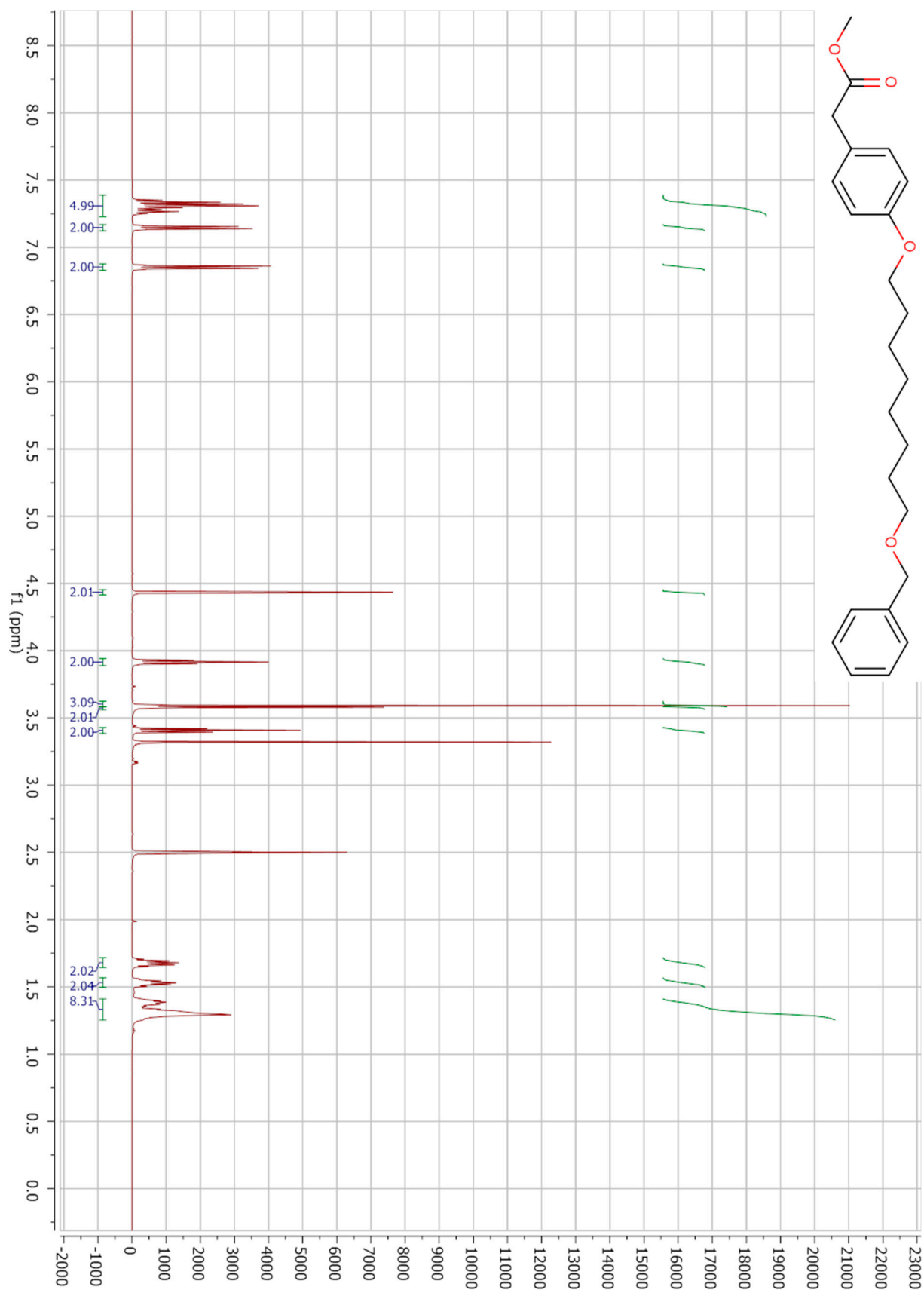


Methyl 2-(4-{[7-(benzyloxy)heptyl]oxy}phenyl)acetate (**8f**; ZHAWOC7097)

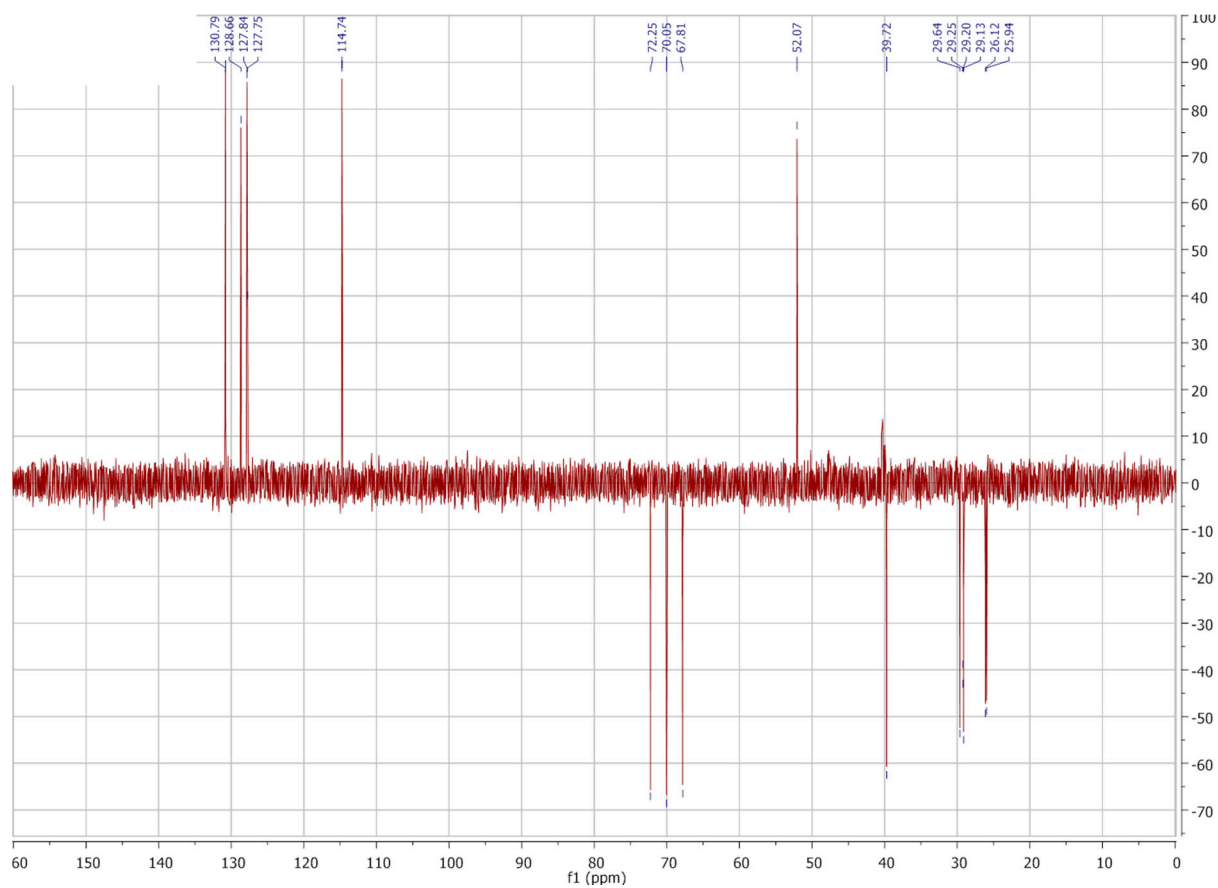
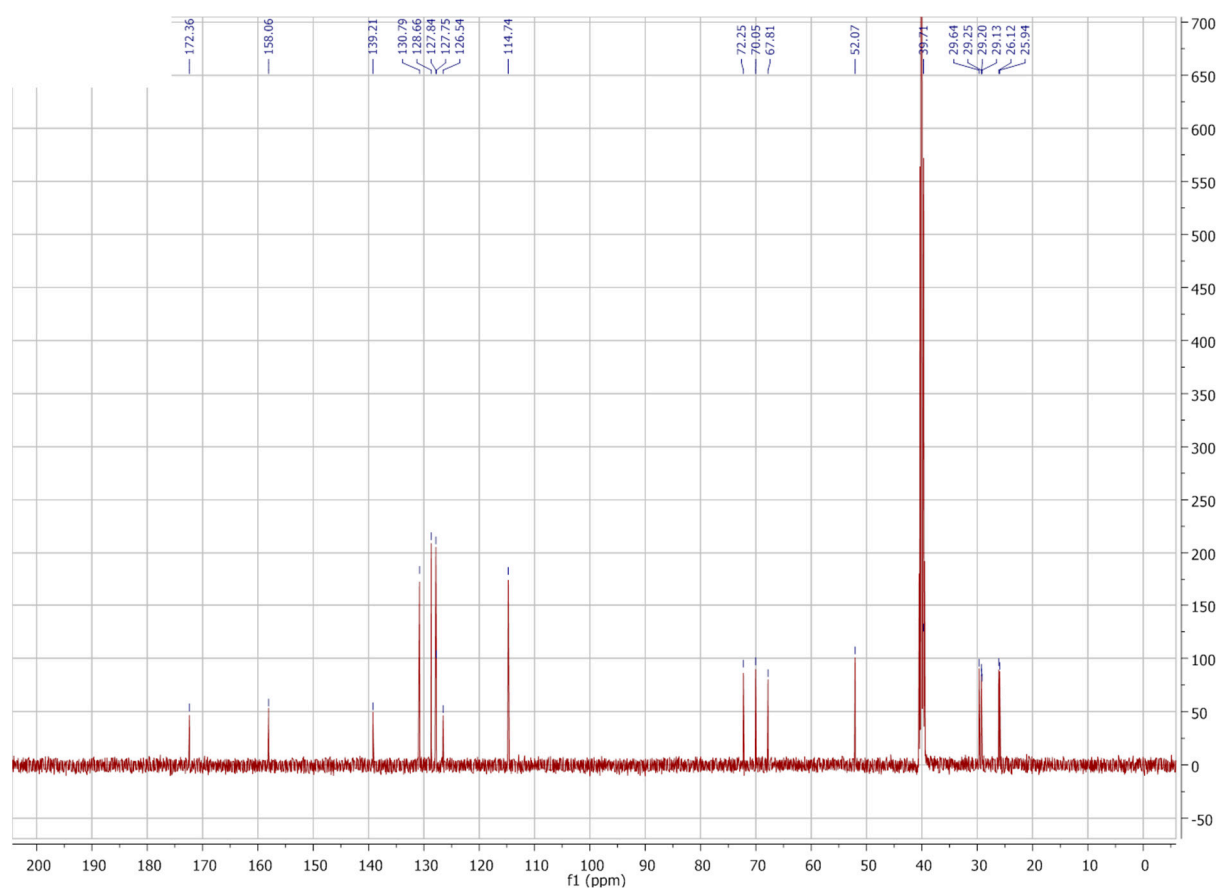


Methyl 2-(4-([8-(benzyloxy)octyl]oxy)phenyl)acetate (**8g**; ZHAWOC6857)

NMR

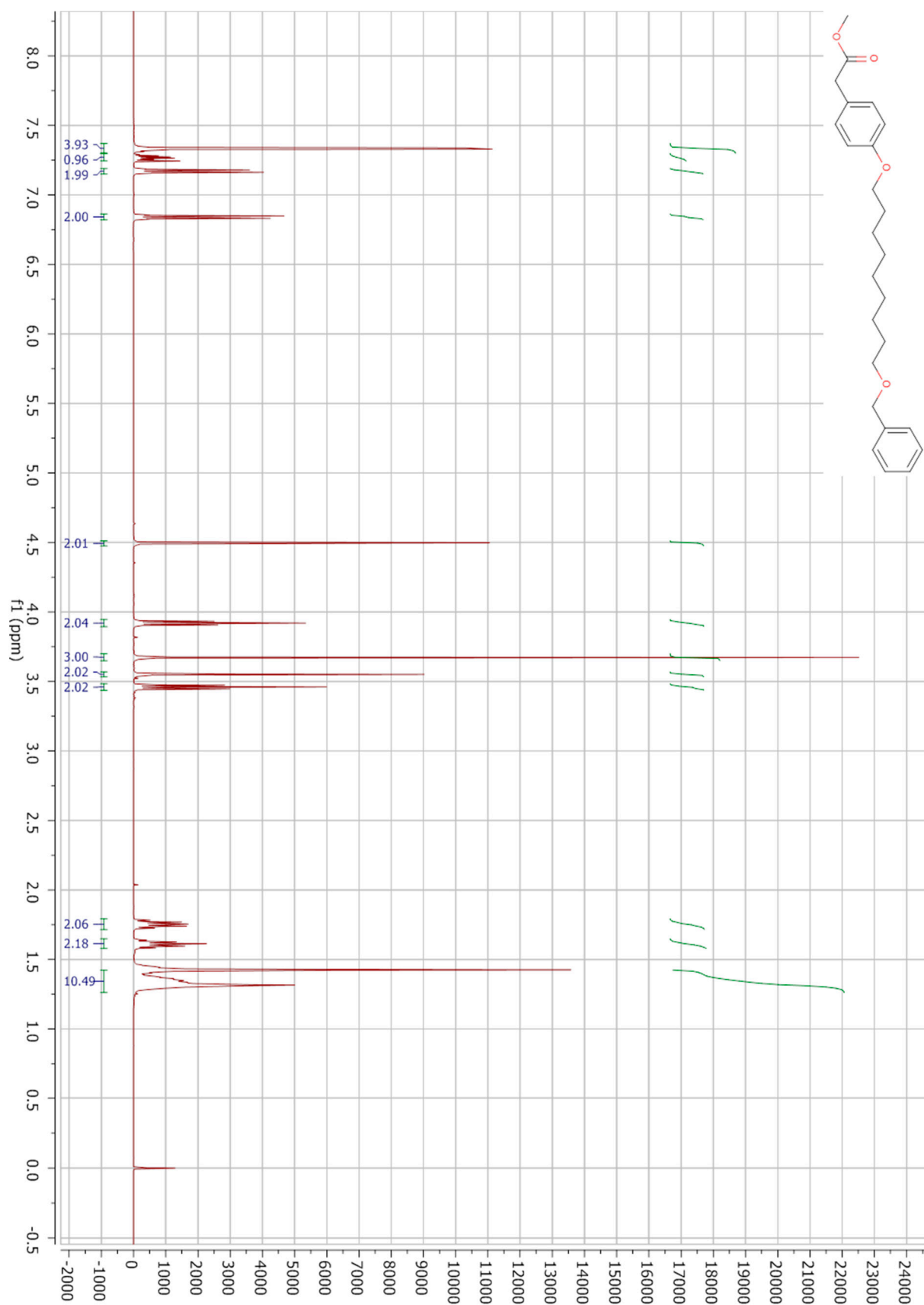


Methyl 2-(4-([8-(benzyloxy)octyl]oxy)phenyl)acetate (8g; ZHAWOC6857)

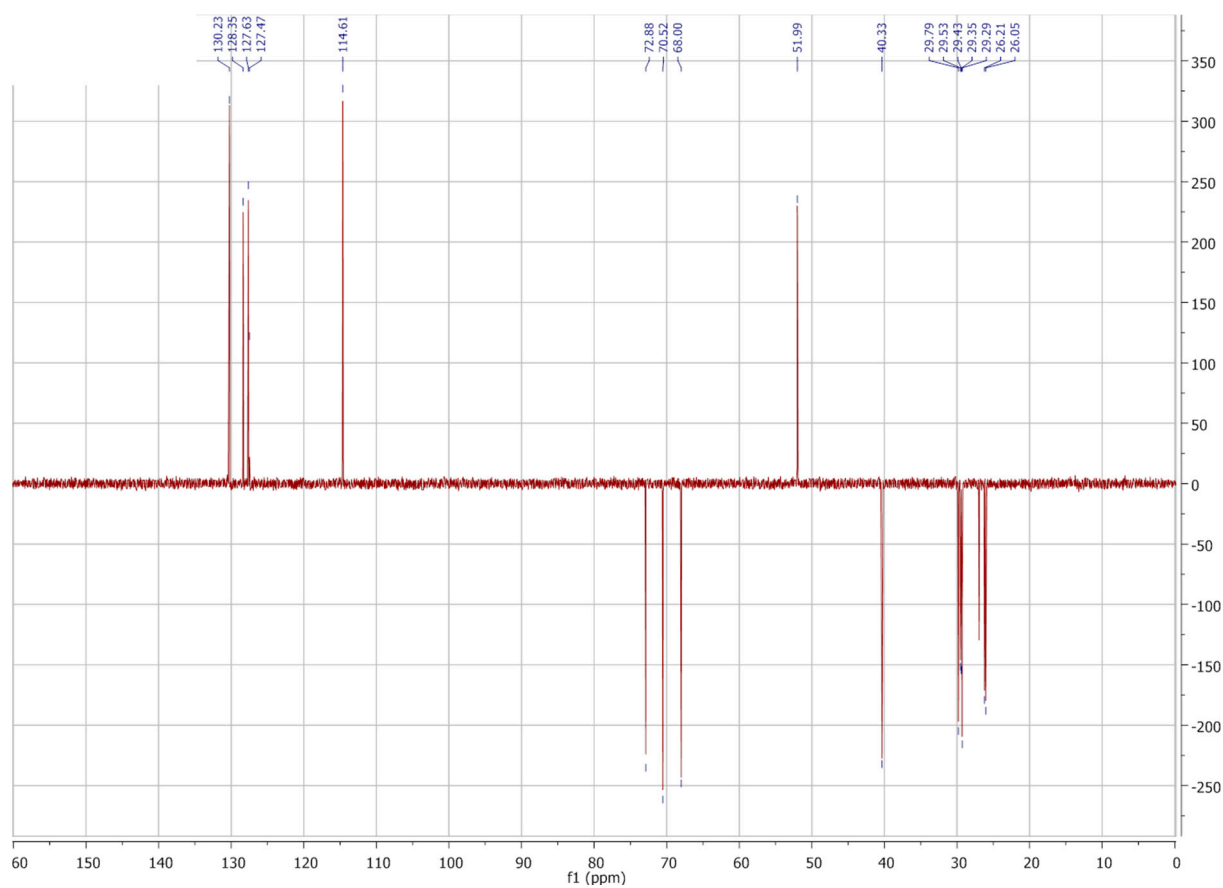
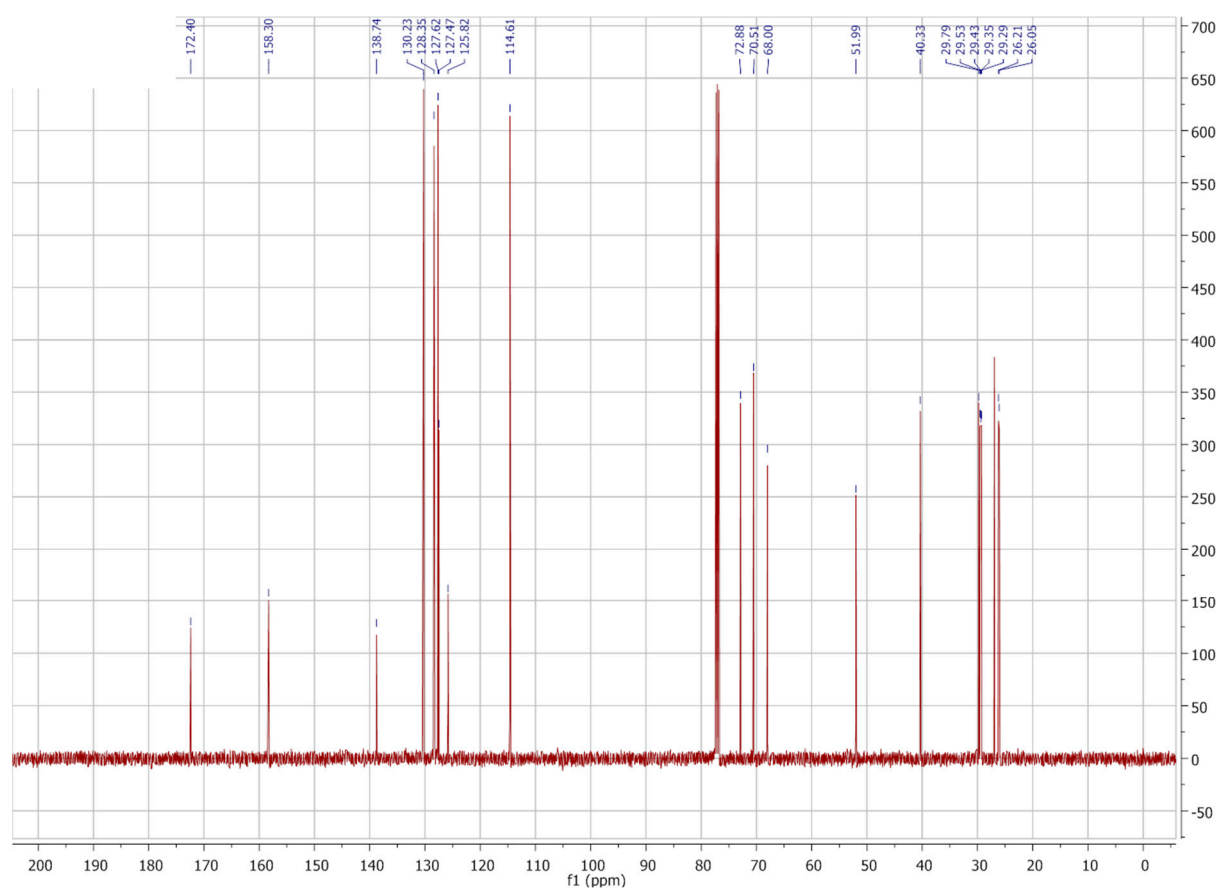


Methyl 2-(4-([9-(benzyloxy)nonyl]oxy}phenyl)acetate (**8h**; ZHAWOC6854)

NMR

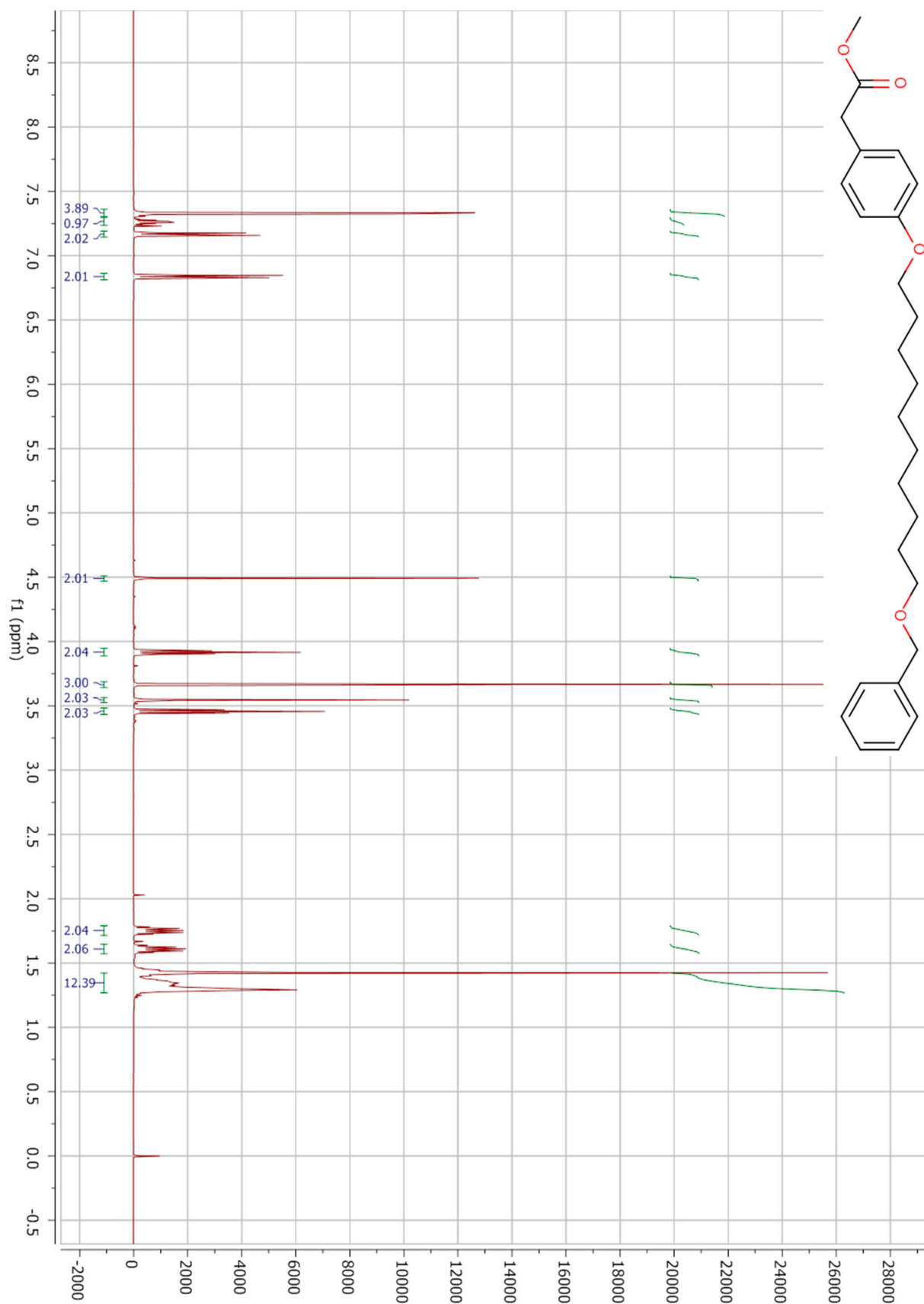


Methyl 2-(4-([9-(benzyloxy)nonyl]oxy)phenyl)acetate (**8h**; ZHAWOC6854)

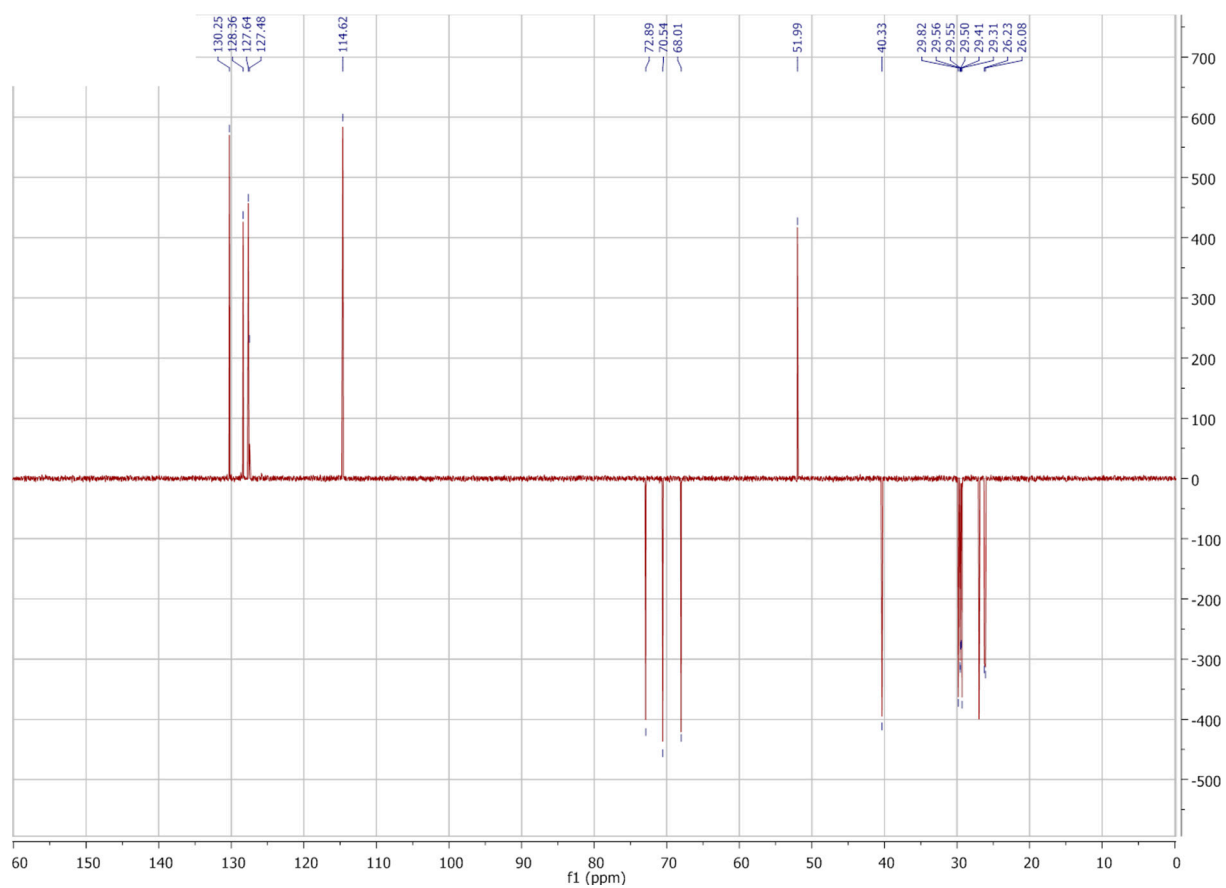
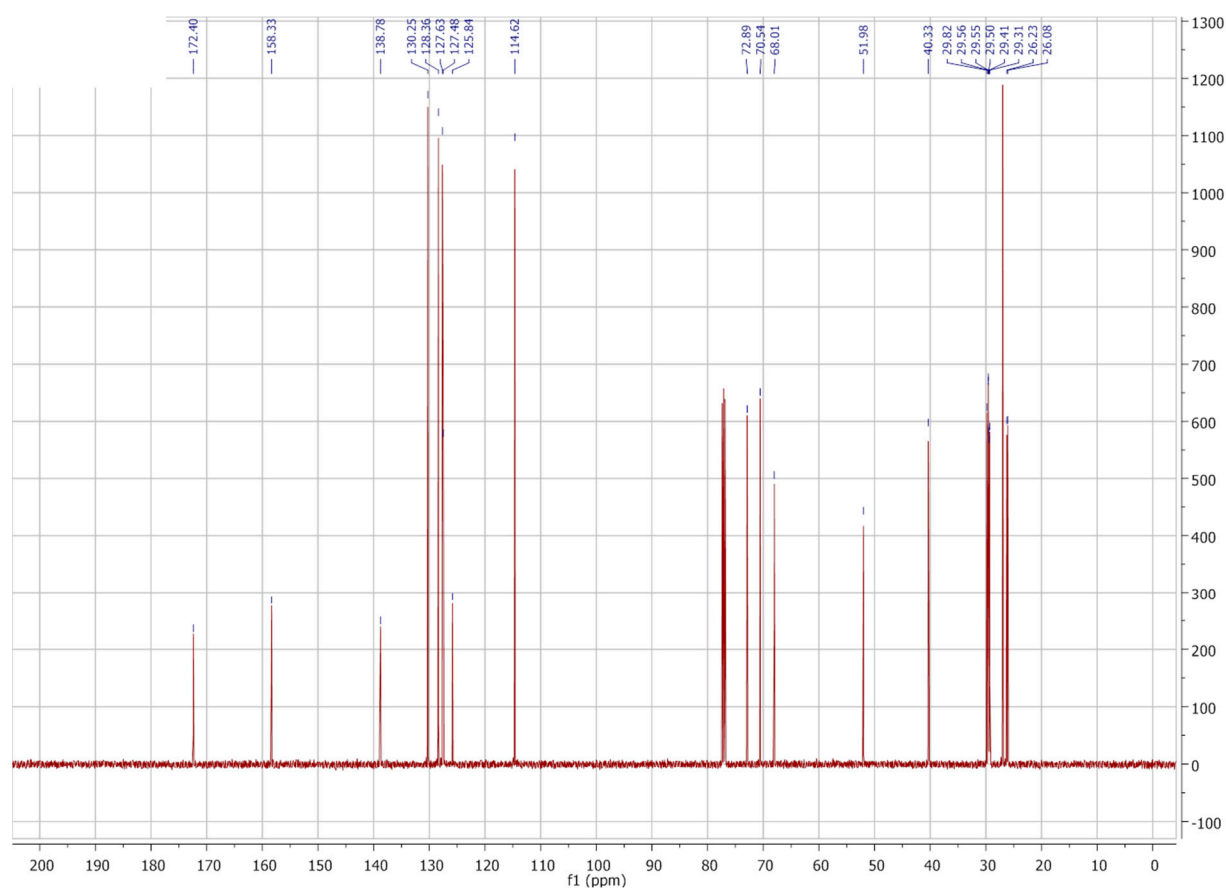


Methyl 2-(4-[[10-(benzyloxy)decyl]oxy]phenyl)acetate (**8i**; ZHAWOC6855)

NMR

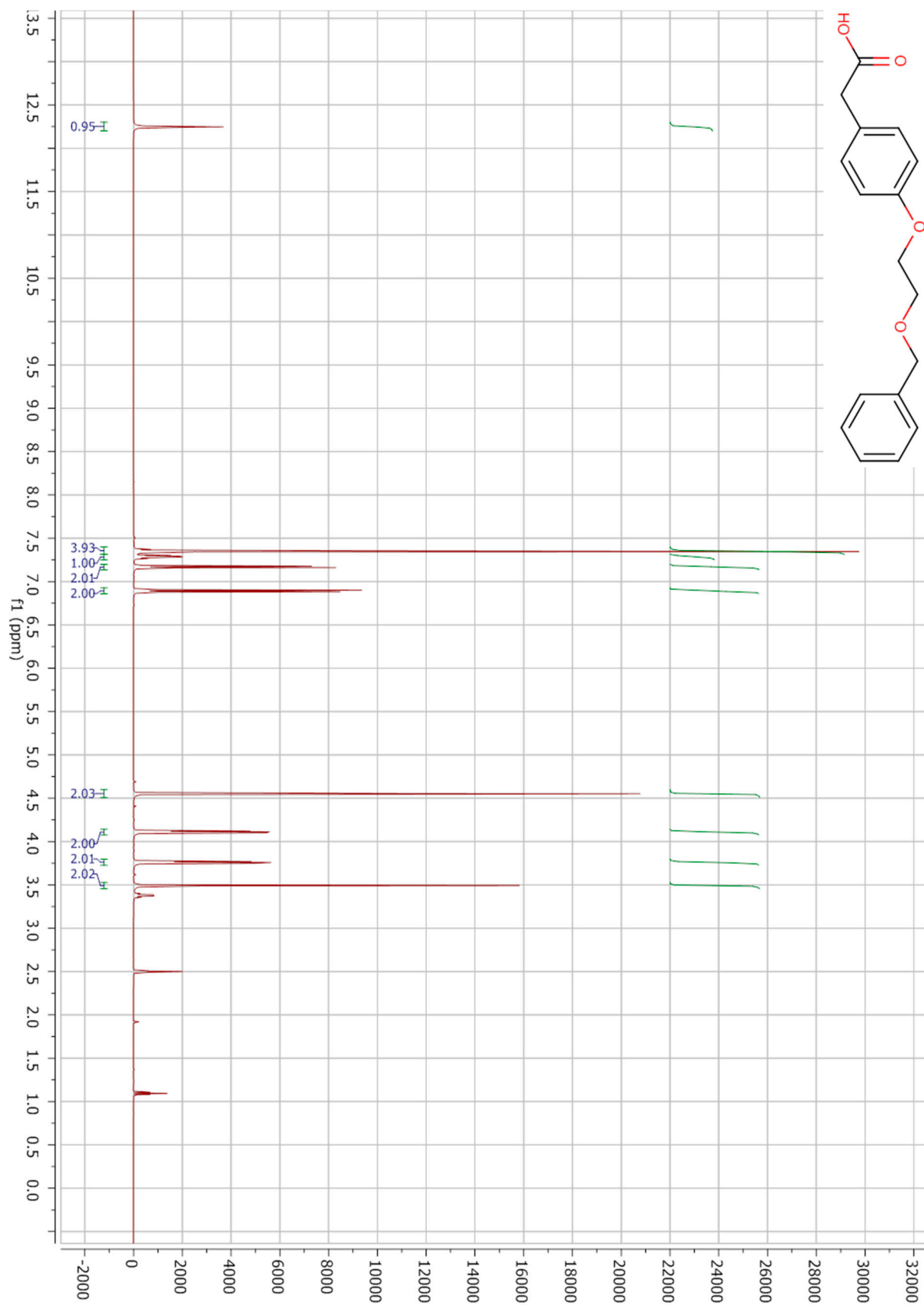


Methyl 2-(4-([10-(benzyloxy)decyl]oxy)phenyl)acetate (**8i**; ZHAWOC6855)

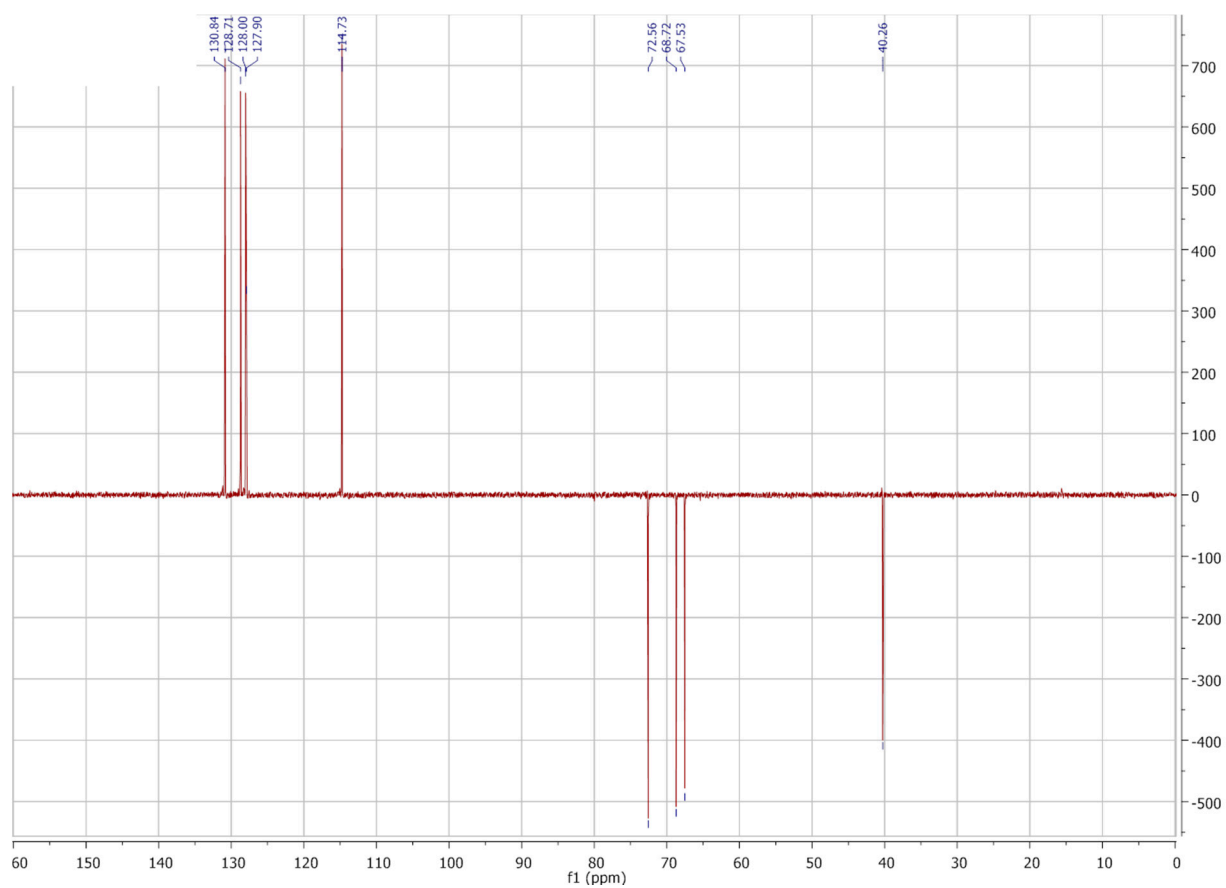
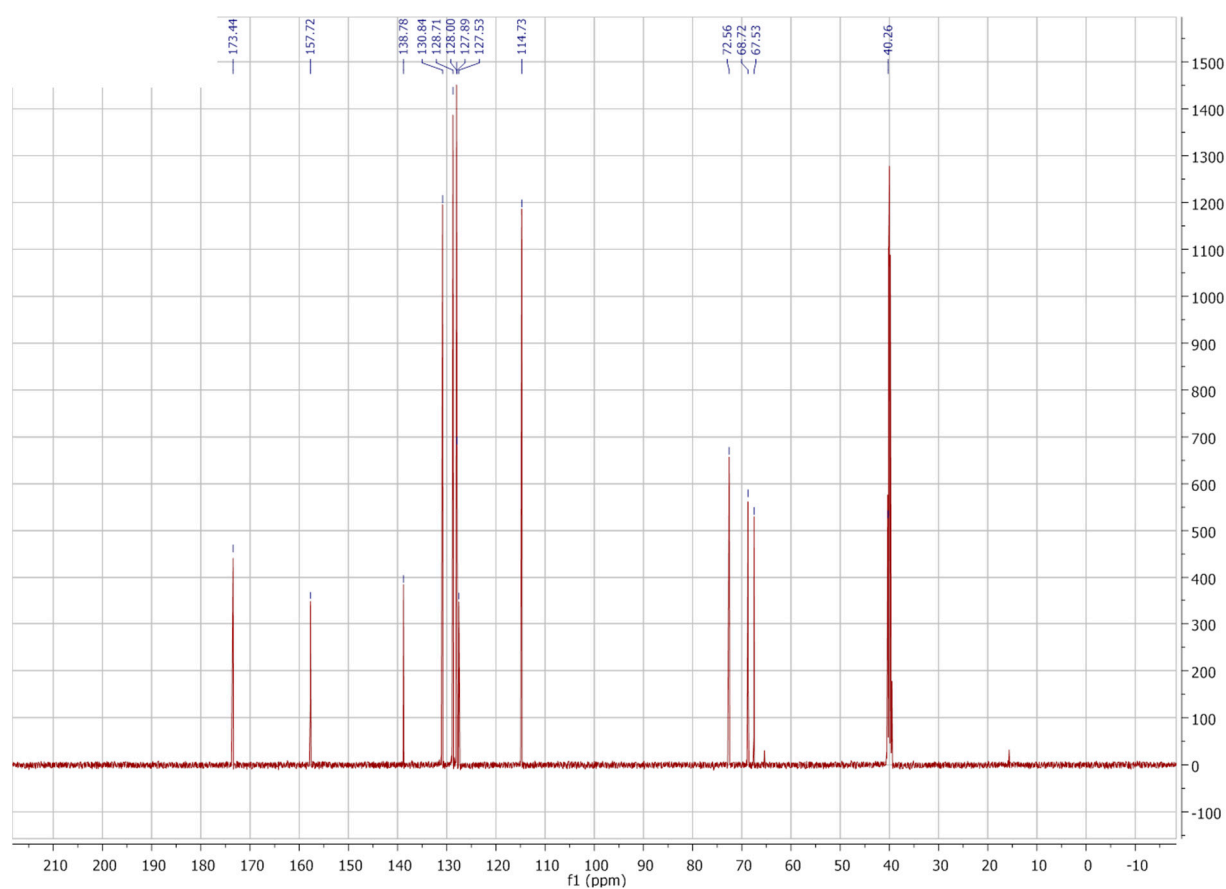


2-{4-[2-(benzyloxy)ethoxy]phenyl}acetic acid (**9a**; ZHAWOC7101)

NMR

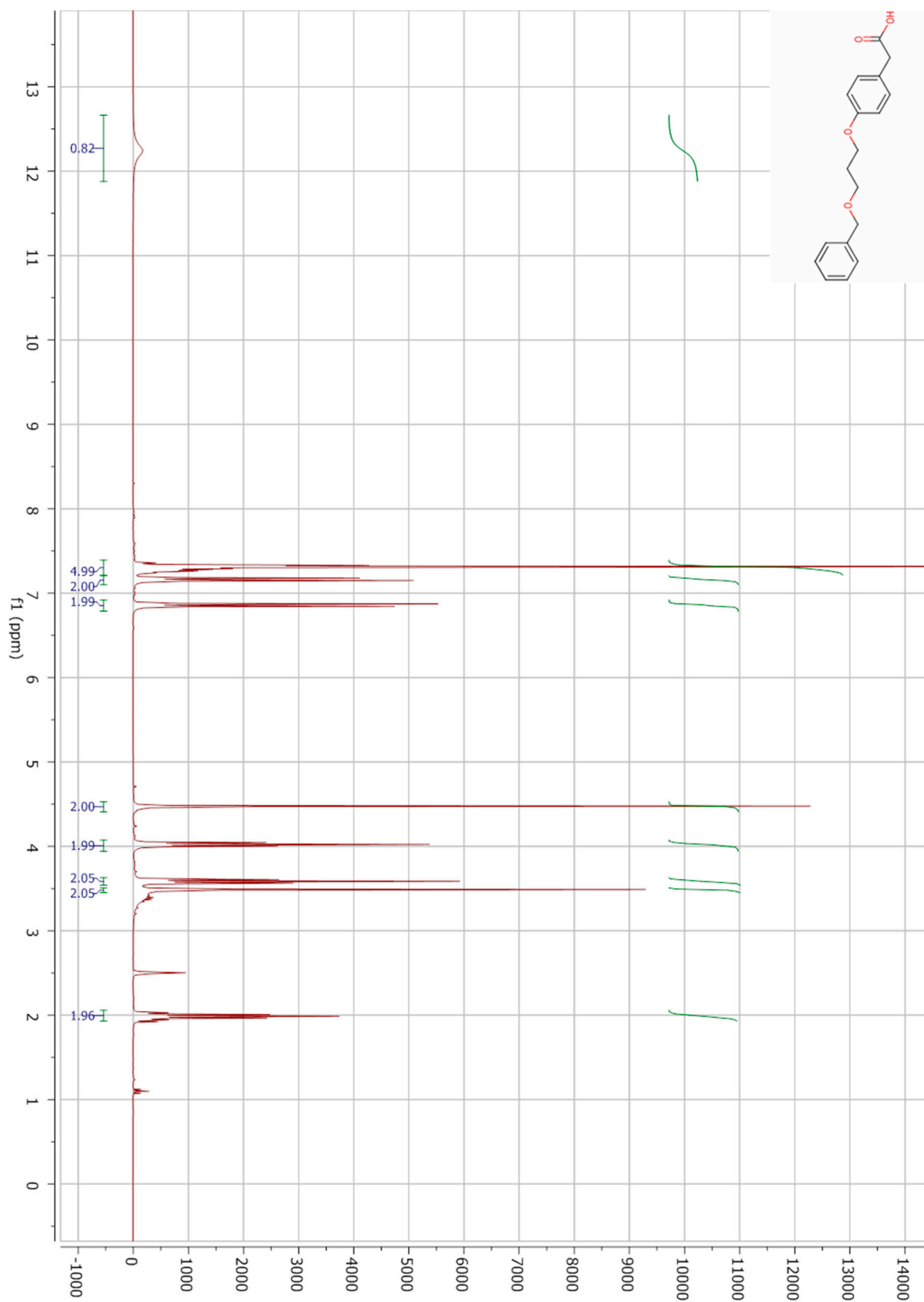


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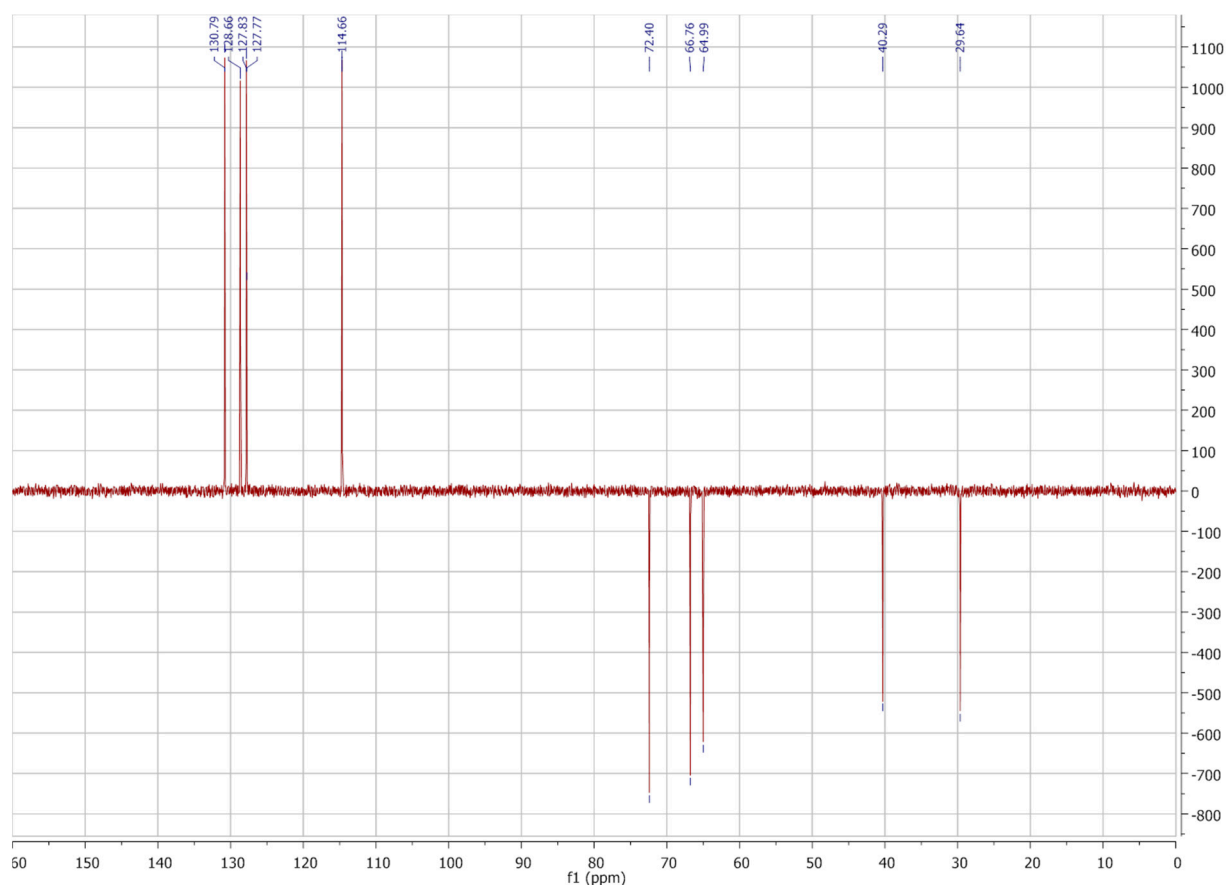
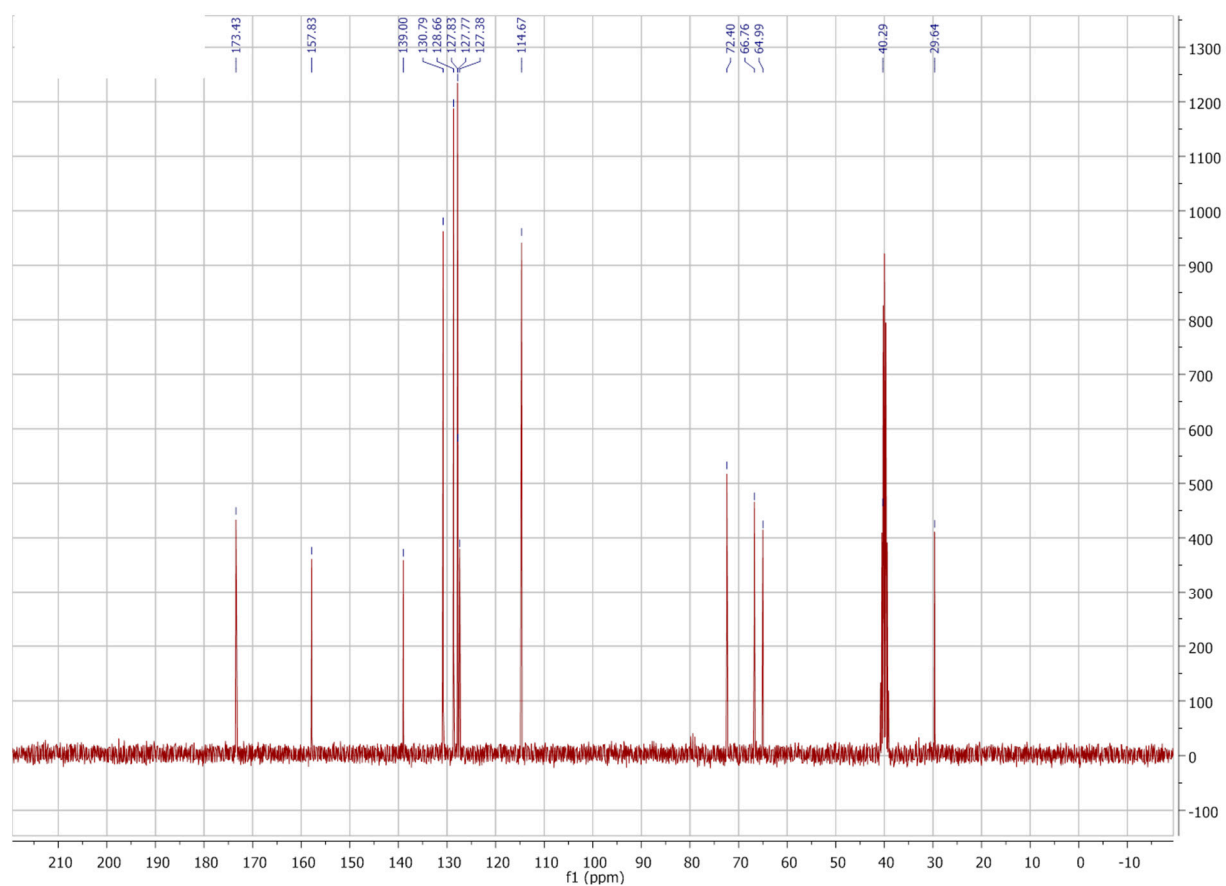


2-{4-[3-(benzyloxy)propoxy]phenyl}acetic acid (**9b**; ZHAWOC4497)

NMR

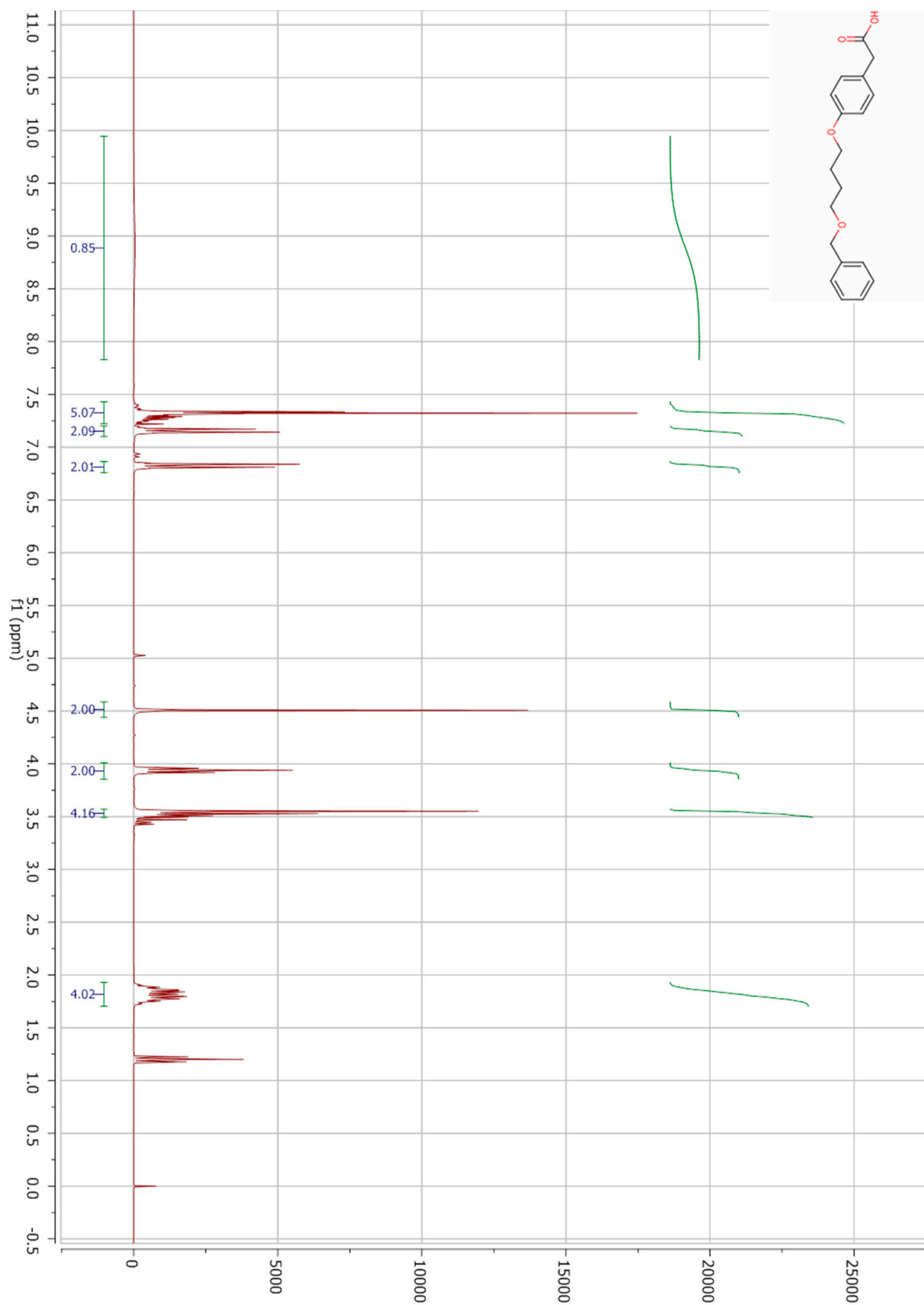


2-{4-[3-(benzyloxy)propoxy]phenyl}acetic acid (**9b**; ZHAWOC4497)

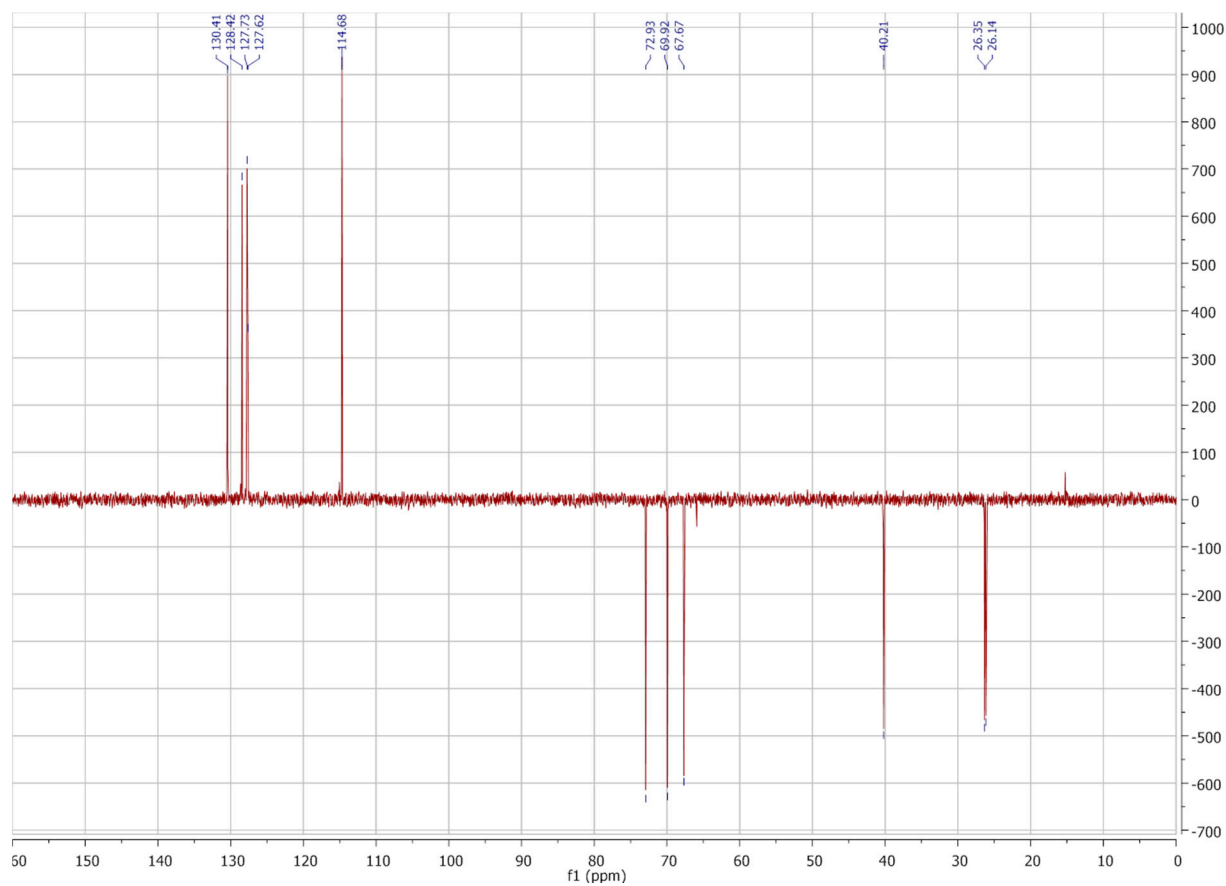
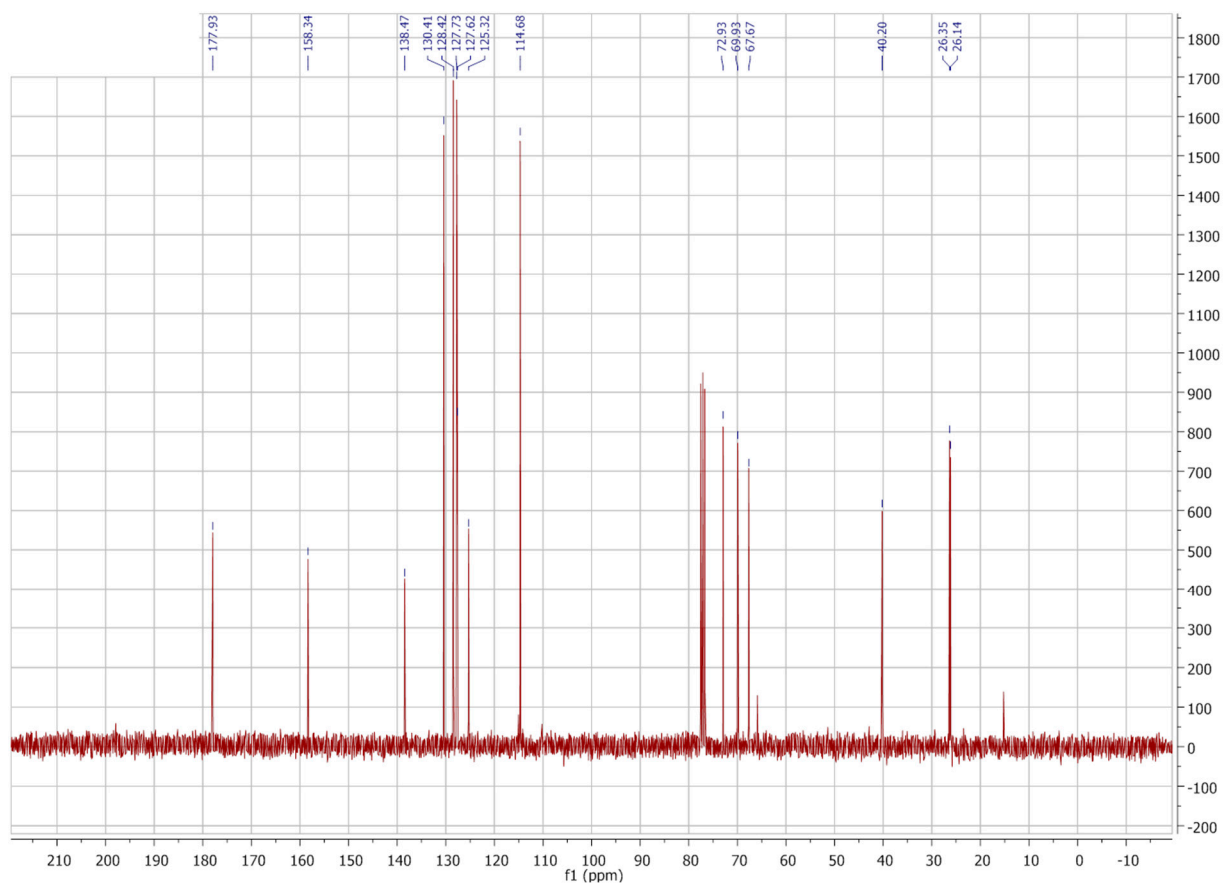


2-{4-[4-(benzyloxy)butoxy]phenyl}acetic acid (**9c**; ZHAWOC4535)

NMR

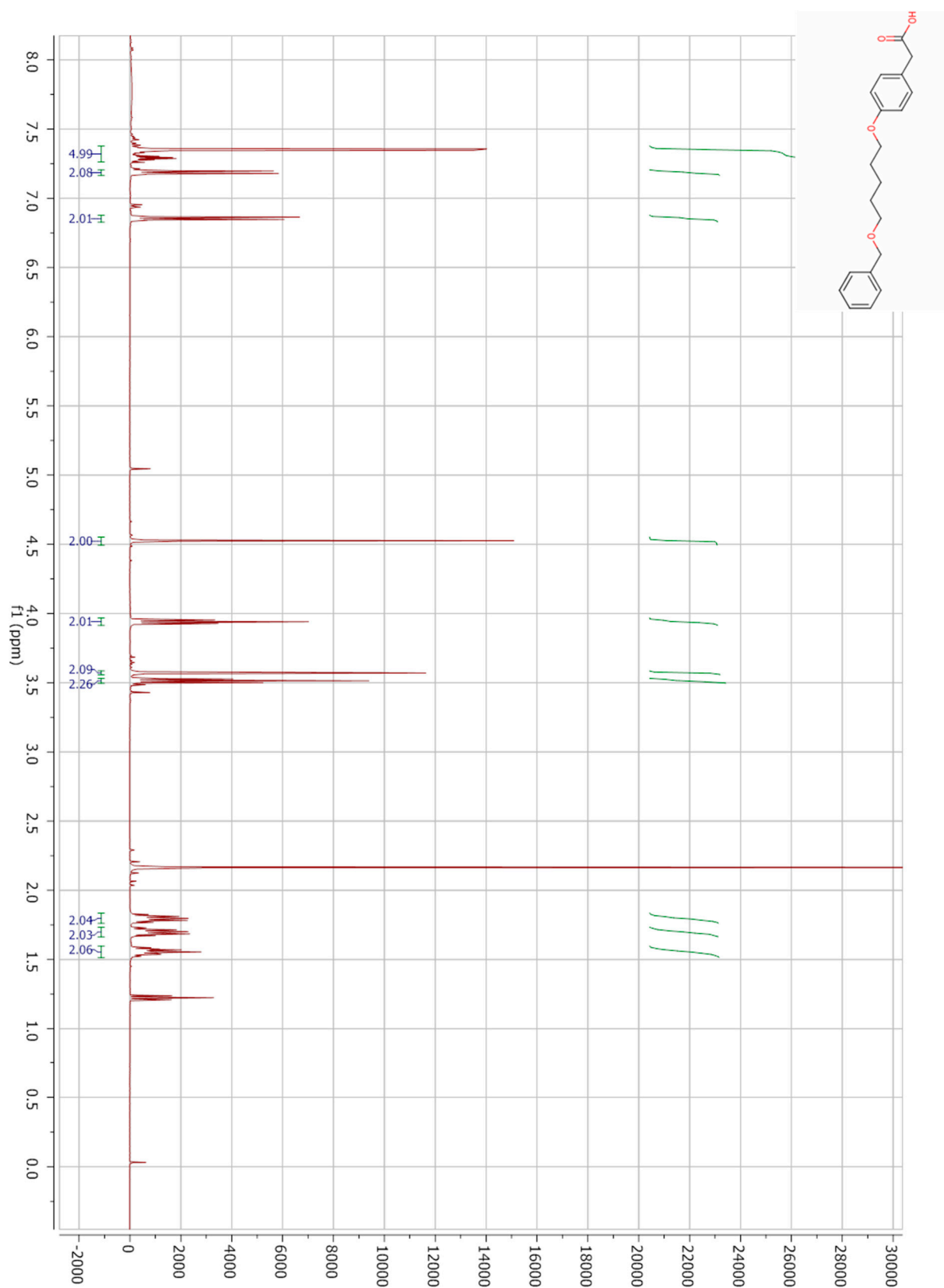


2-{4-[4-(benzyloxy)butoxy]phenyl}acetic acid (**9c**; ZHAWOC4535)

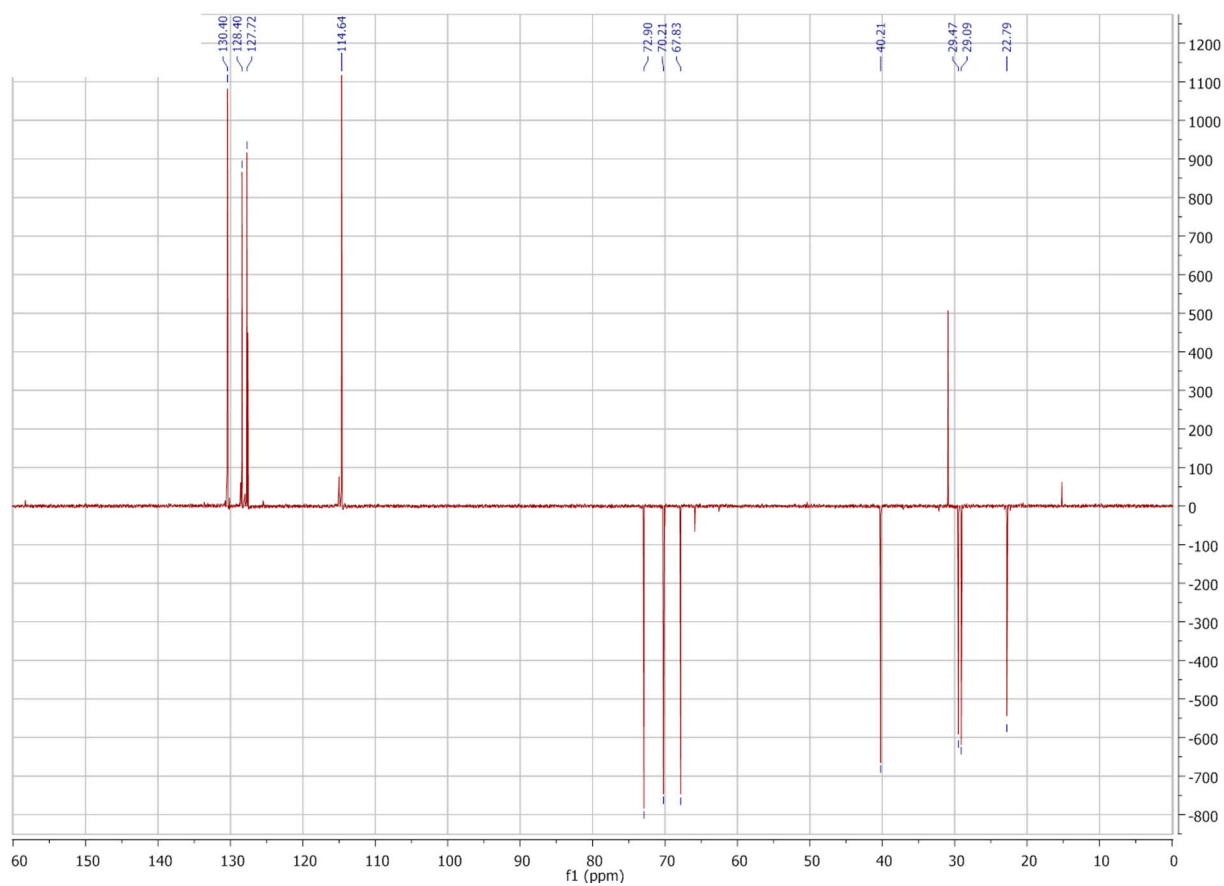
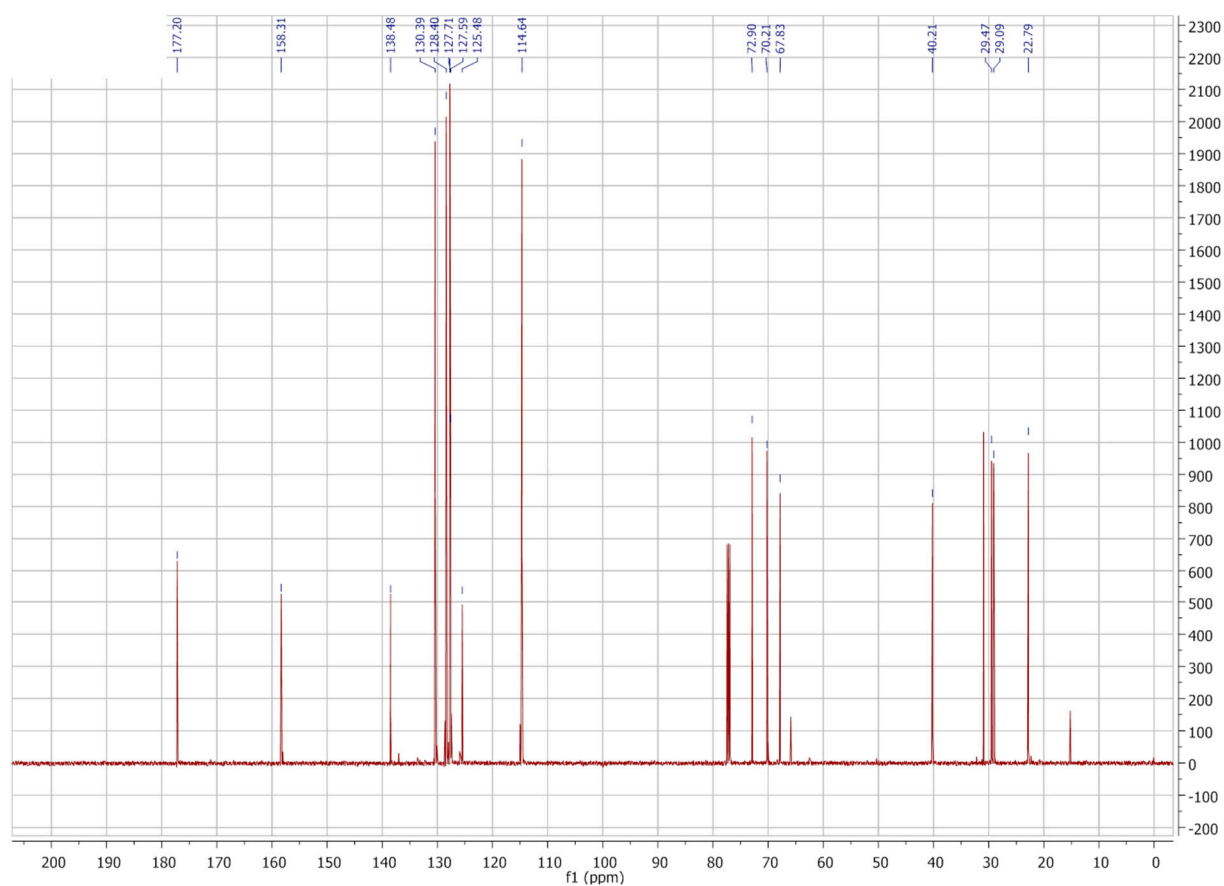


2-(4-[[5-(benzyloxy)pentyl]oxy]phenyl)acetic acid (**9d**; ZHAWOC5922)

NMR

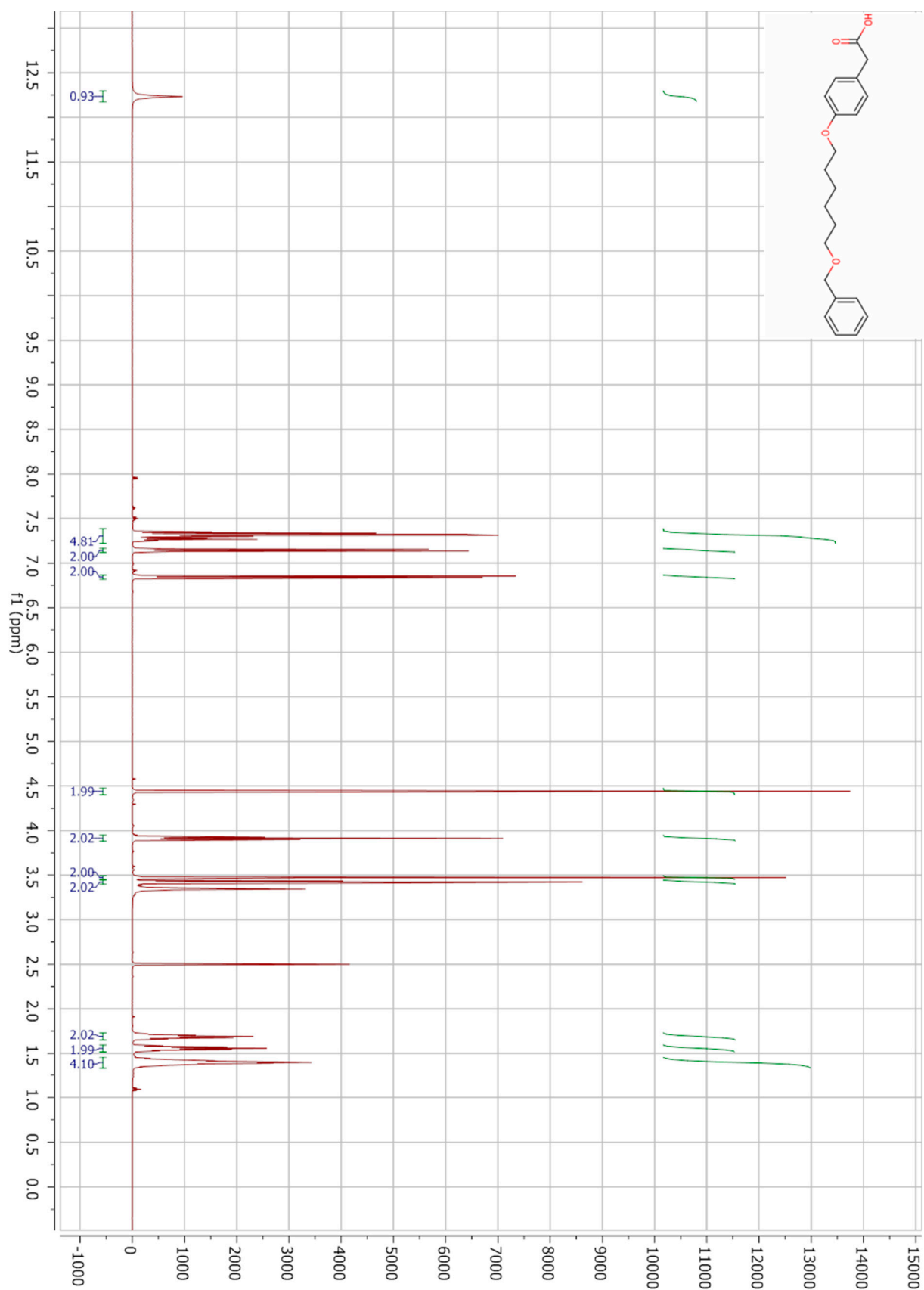


2-(4-{[5-(benzyloxy)pentyl]oxy}phenyl)acetic acid (**9d**; ZHAWOC5922)

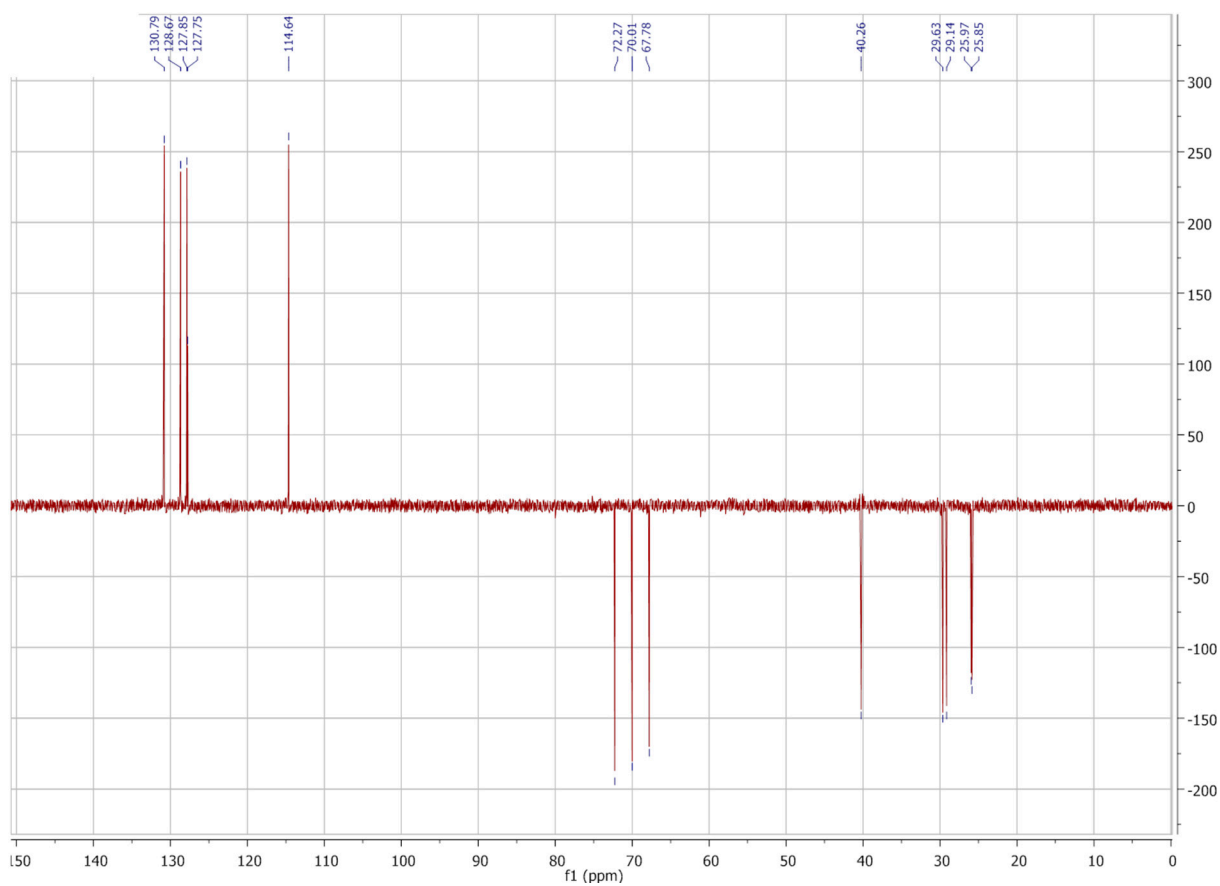
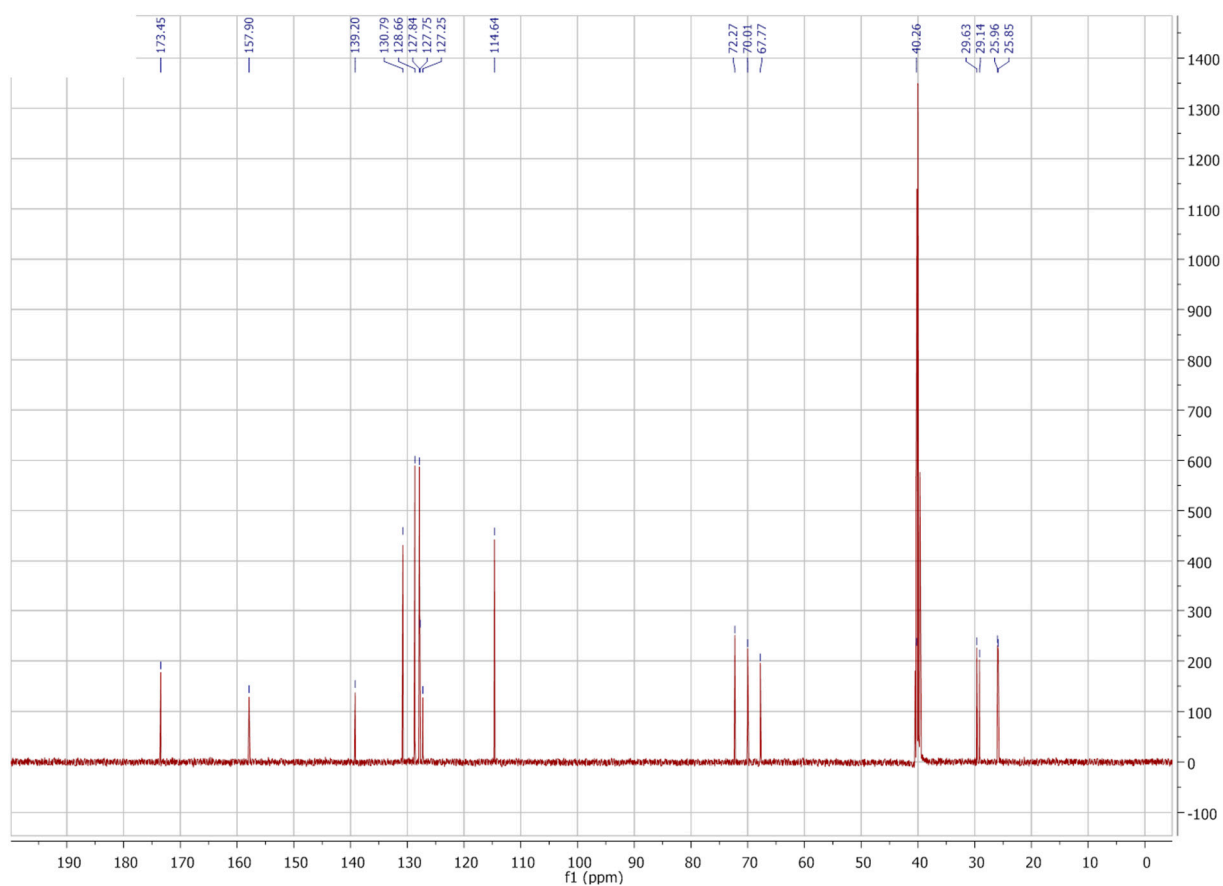


2-(4-{{6-(benzyloxy)hexyl}oxy}phenyl)acetic acid (**9e**; ZHAWOC5947)

NMR

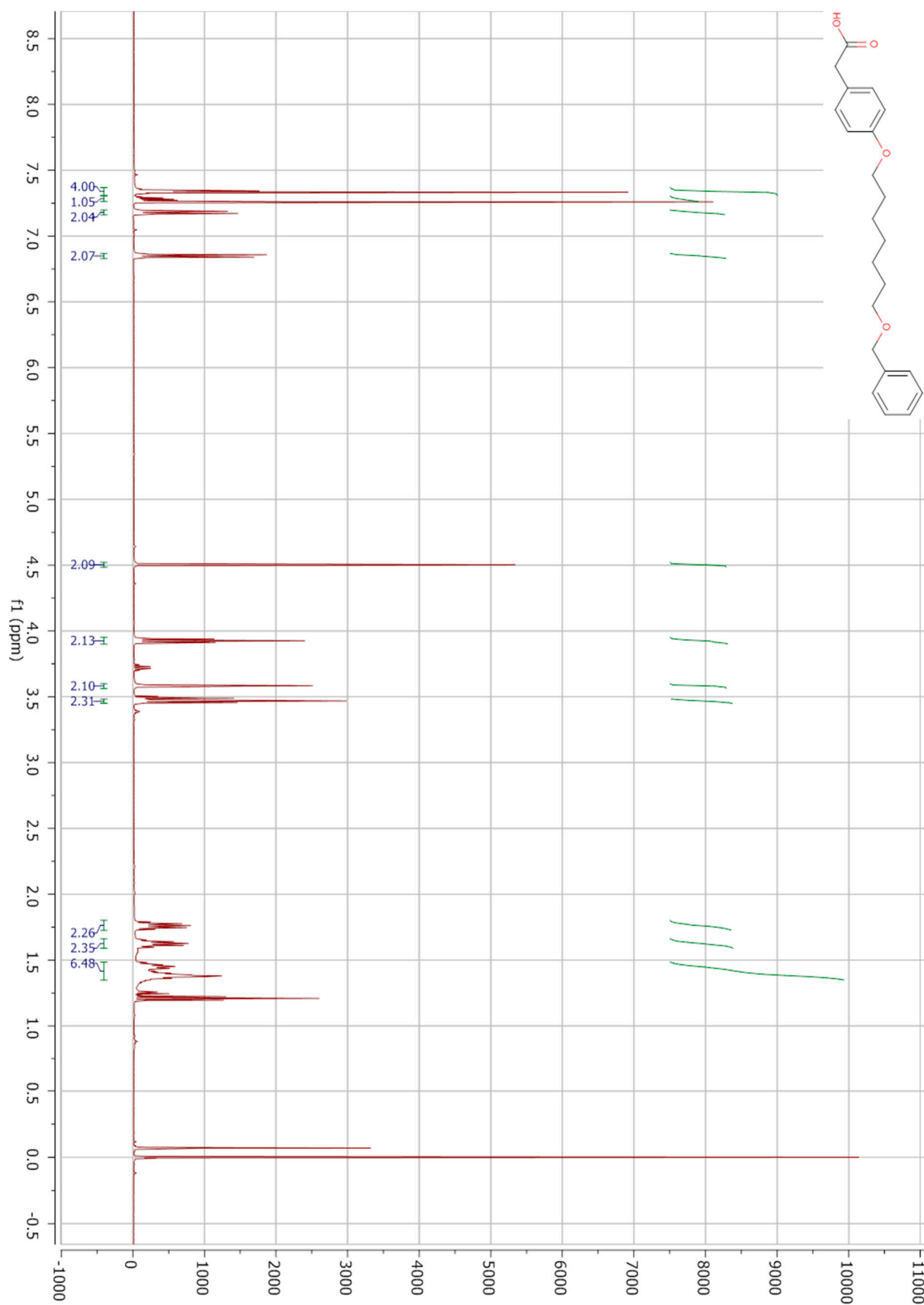


2-(4-{{6-(benzyloxy)hexyl}oxy}phenyl)acetic acid (**9e**; ZHAWOC5947)

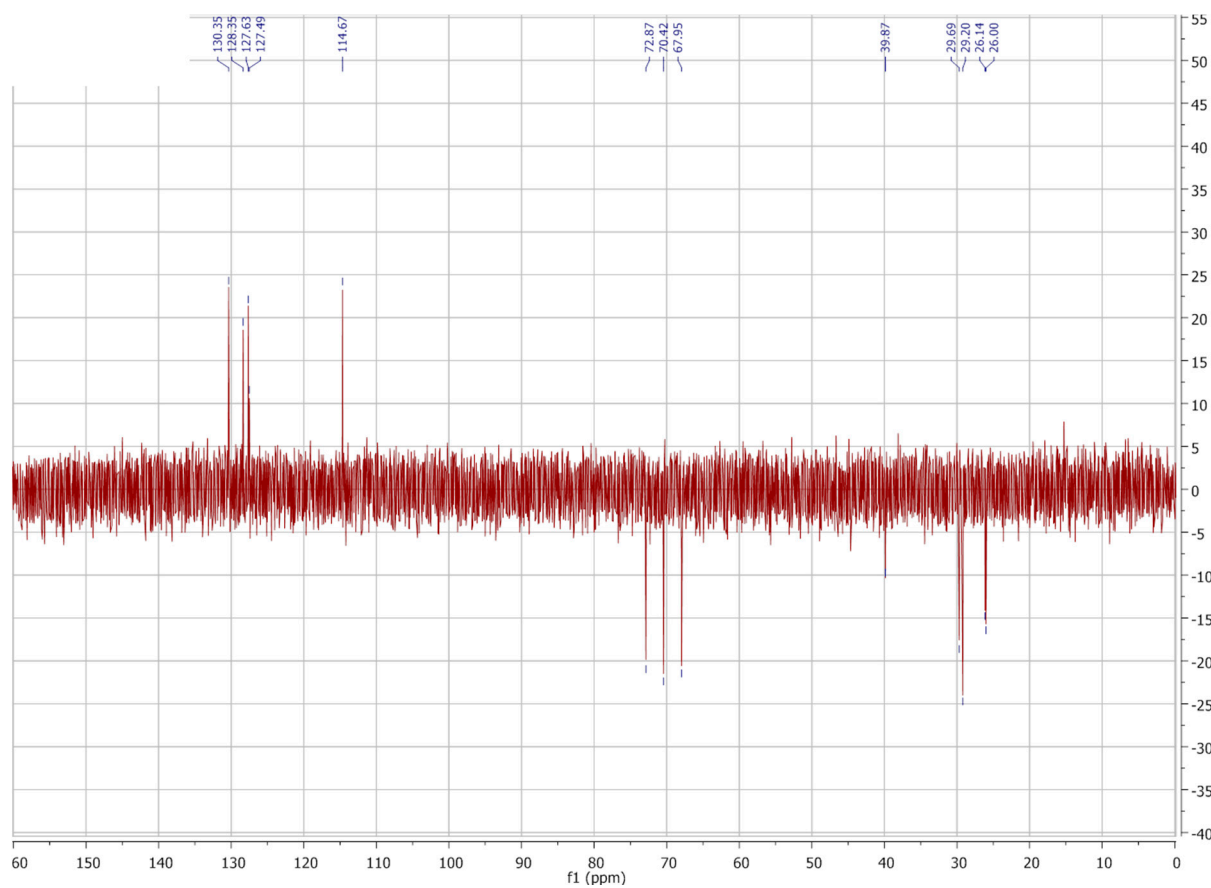
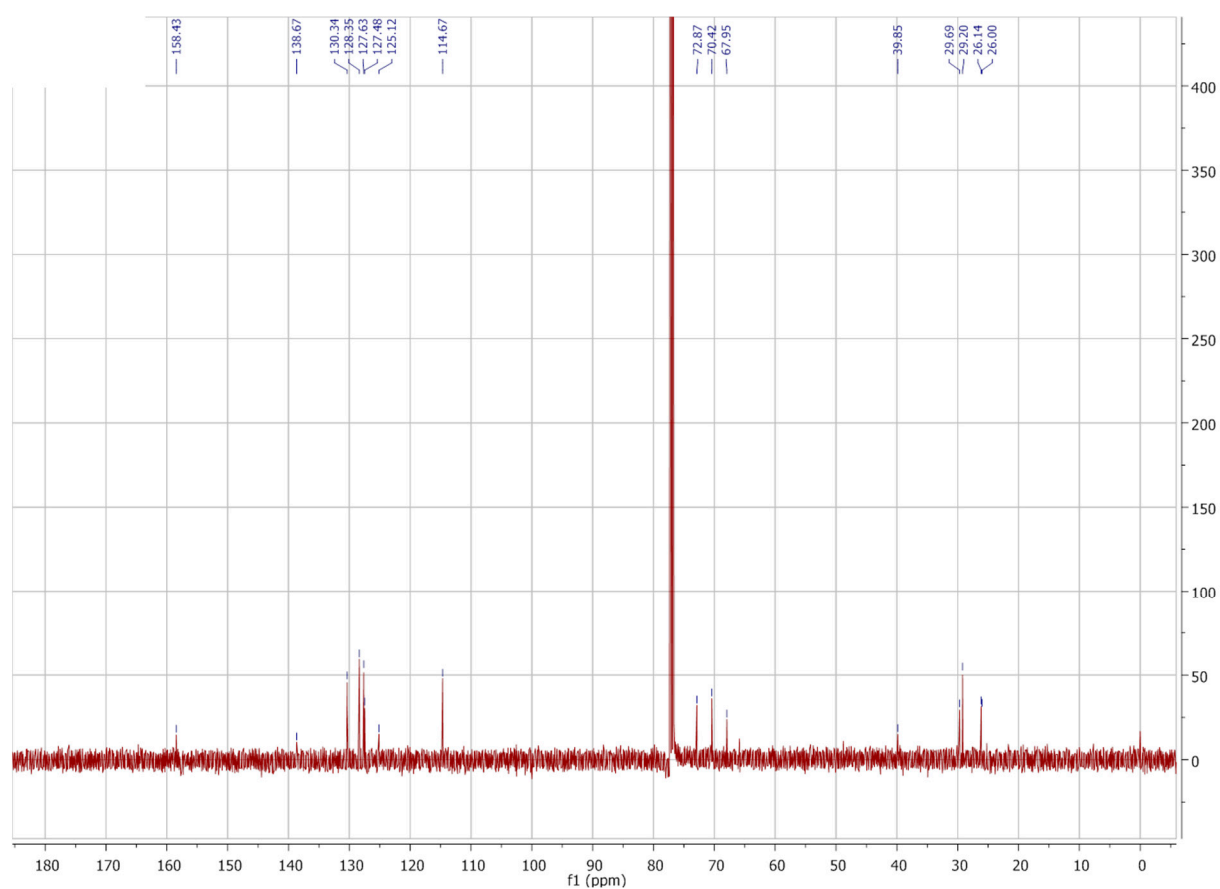


2-(4-[[7-(benzyloxy)heptyl]oxy]phenyl)acetic acid (**9f**; ZHAWOC7098)

NMR

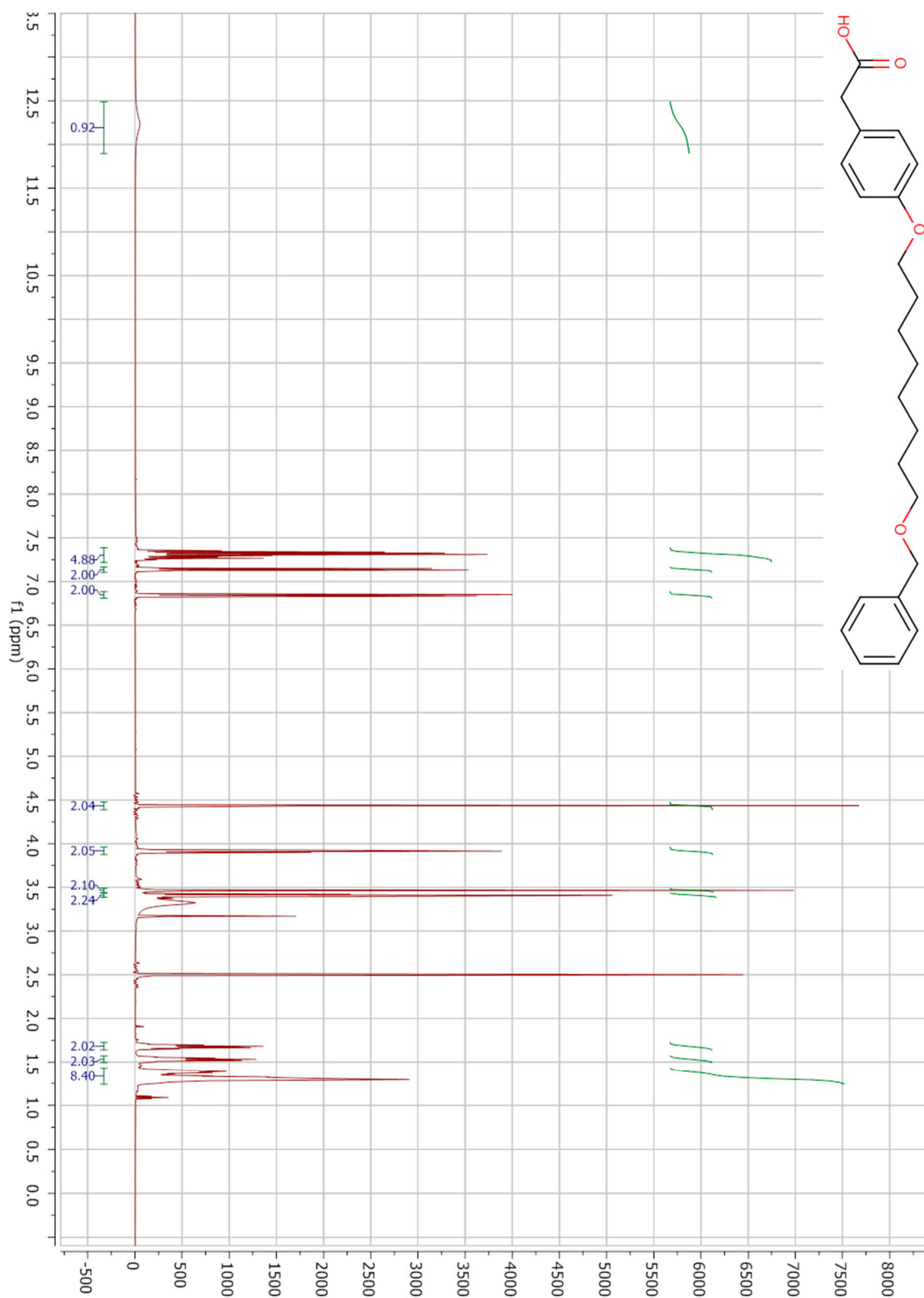


2-(4-{[7-(benzyloxy)heptyl]oxy}phenyl)acetic acid (**9f**; ZHAWOC7098)

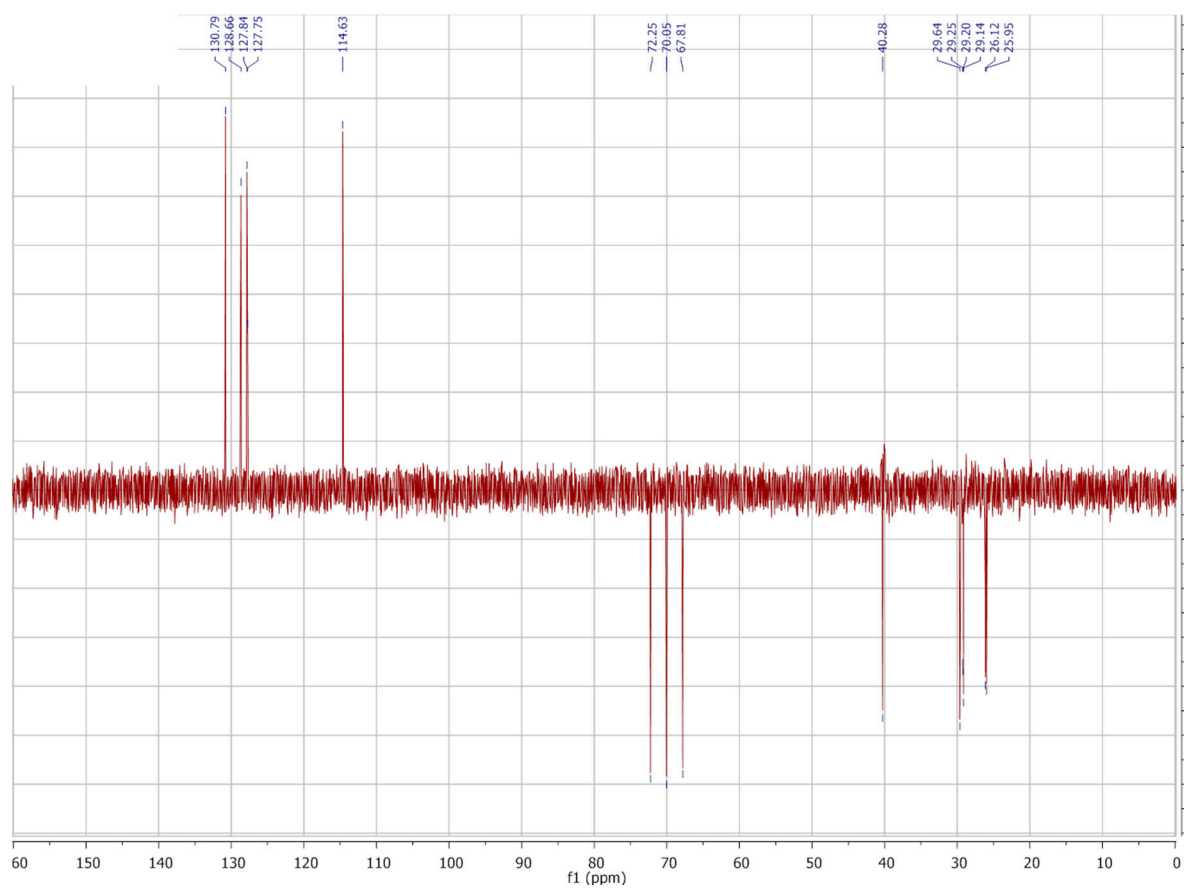
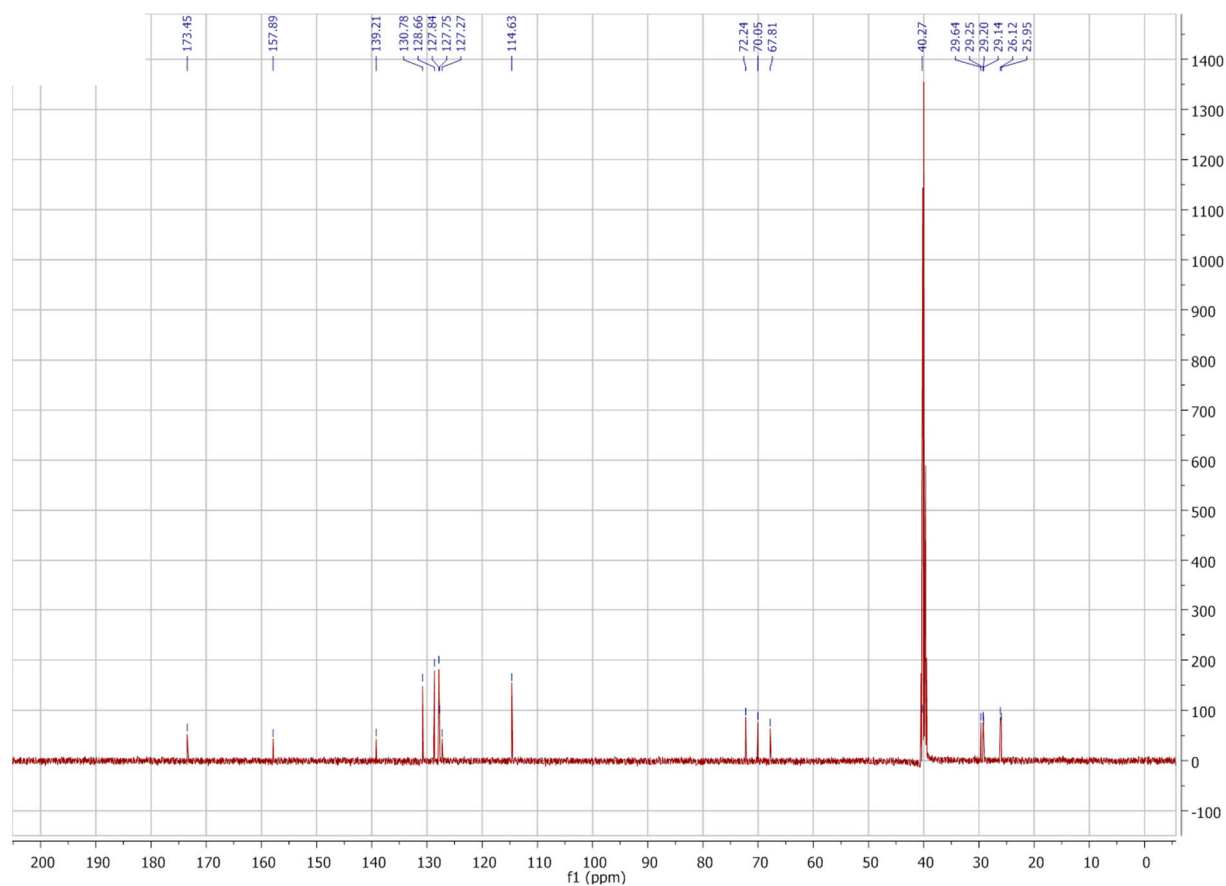


2-(4-{{[8-(benzyloxy)octyl]oxy}phenyl}acetic acid (**9g**; ZHAWOC6858)

NMR

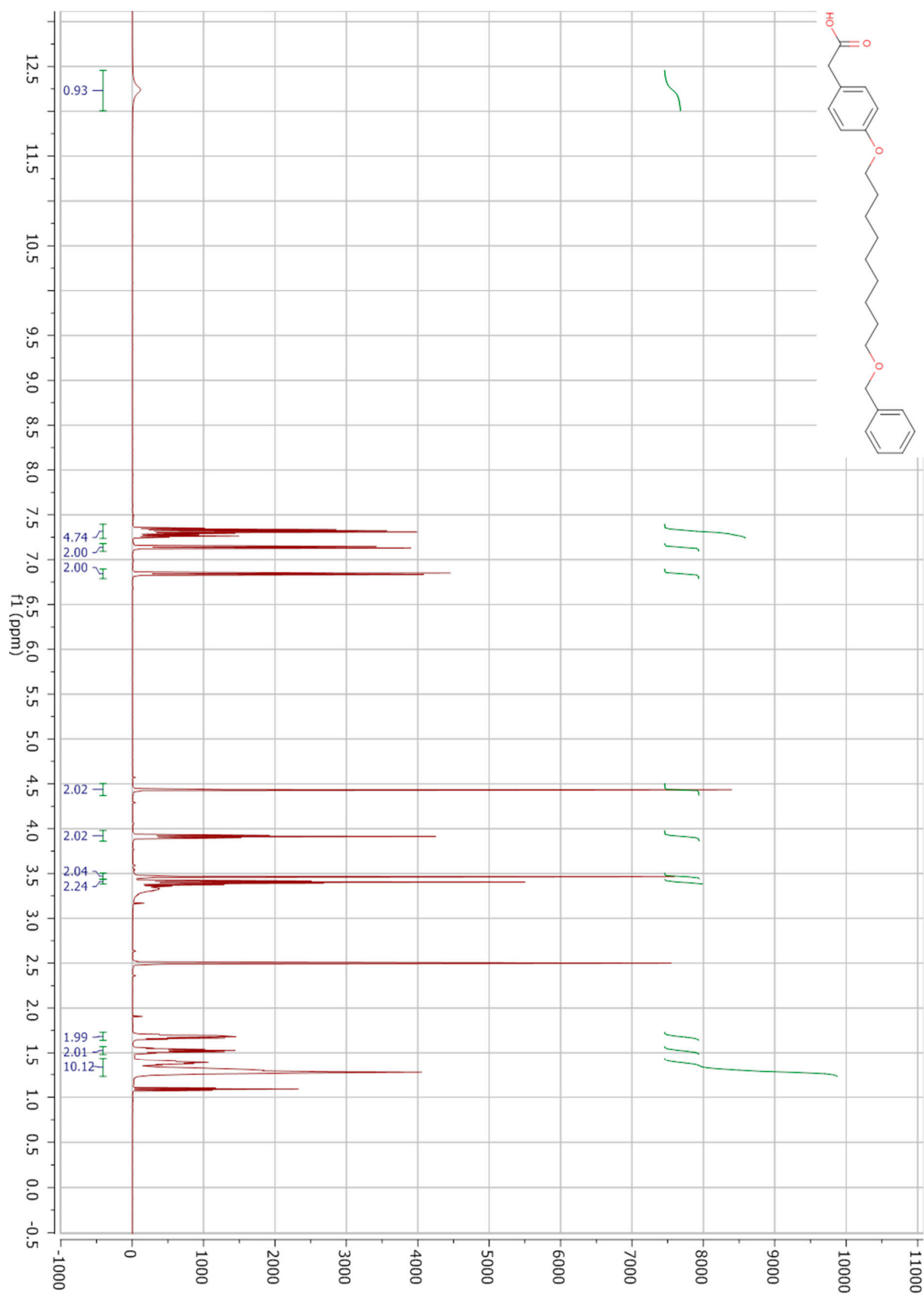


2-(4-{[8-(benzyloxy)octyl]oxy}phenyl)acetic acid (**9g**; ZHAWOC6858)

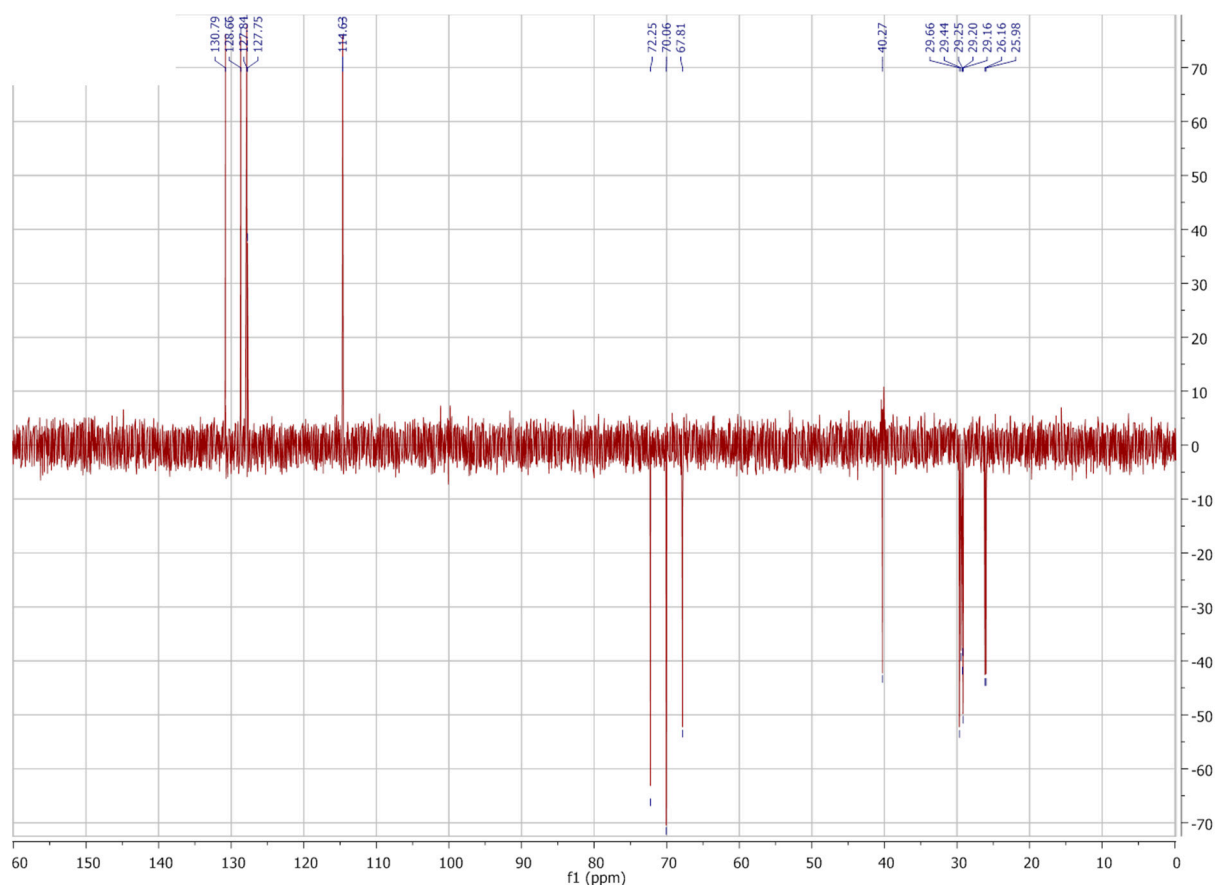
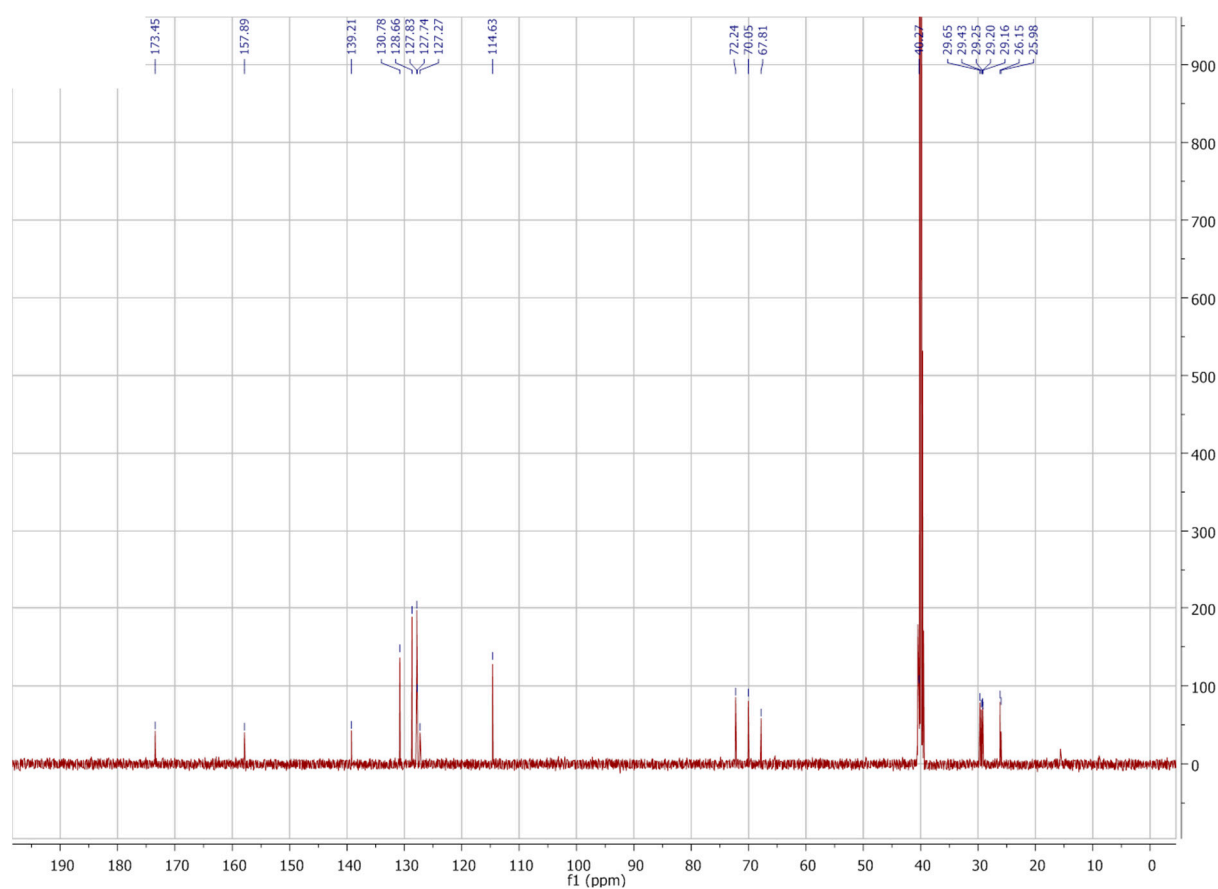


2-(4-{{9-(benzyloxy)nonyl}oxy}phenyl)acetic acid (**9h**; ZHAWOC6861)

NMR

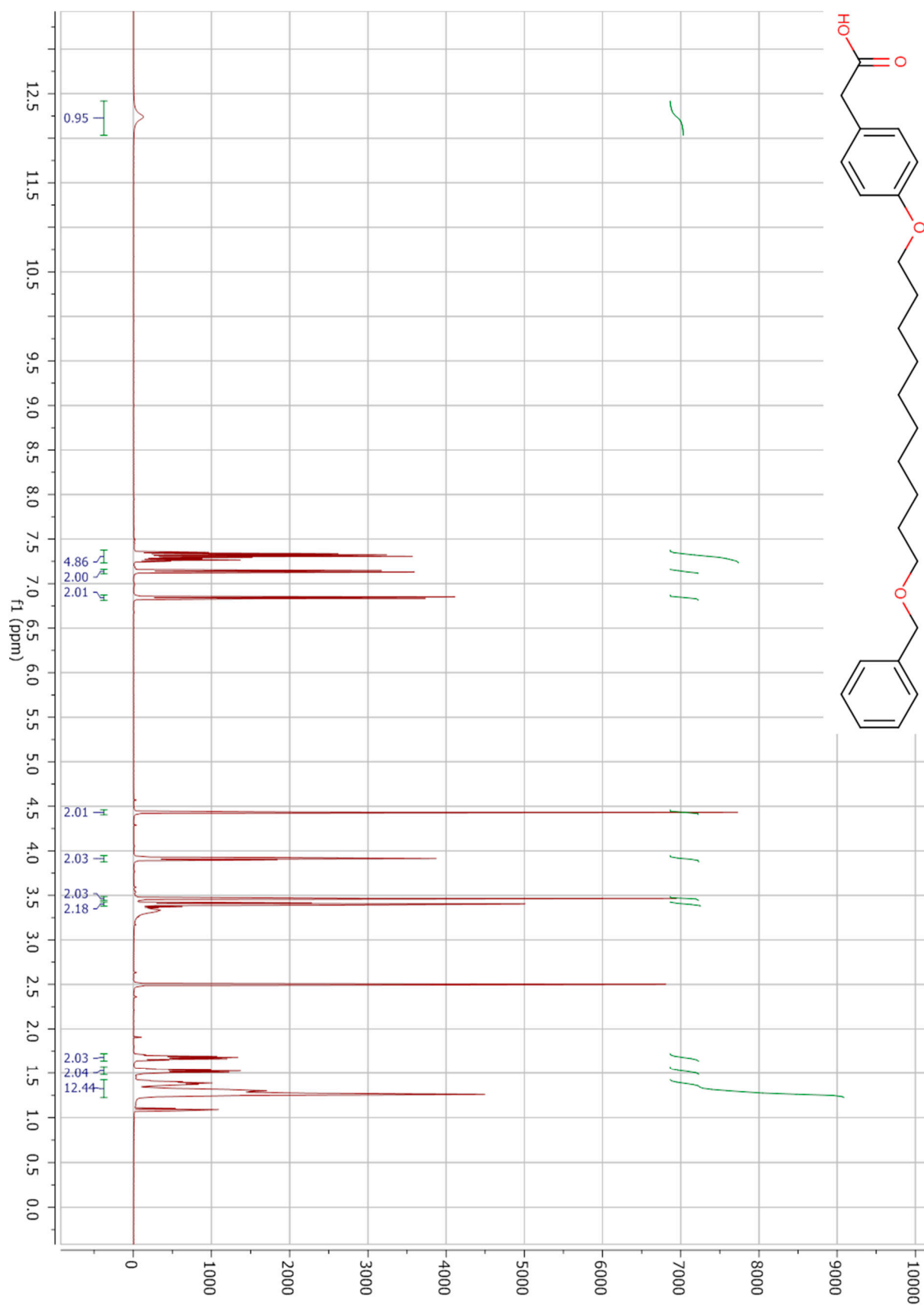


2-(4-{[9-(benzyloxy)nonyl]oxy}phenyl)acetic acid (**9h**; ZHAWOC6861)

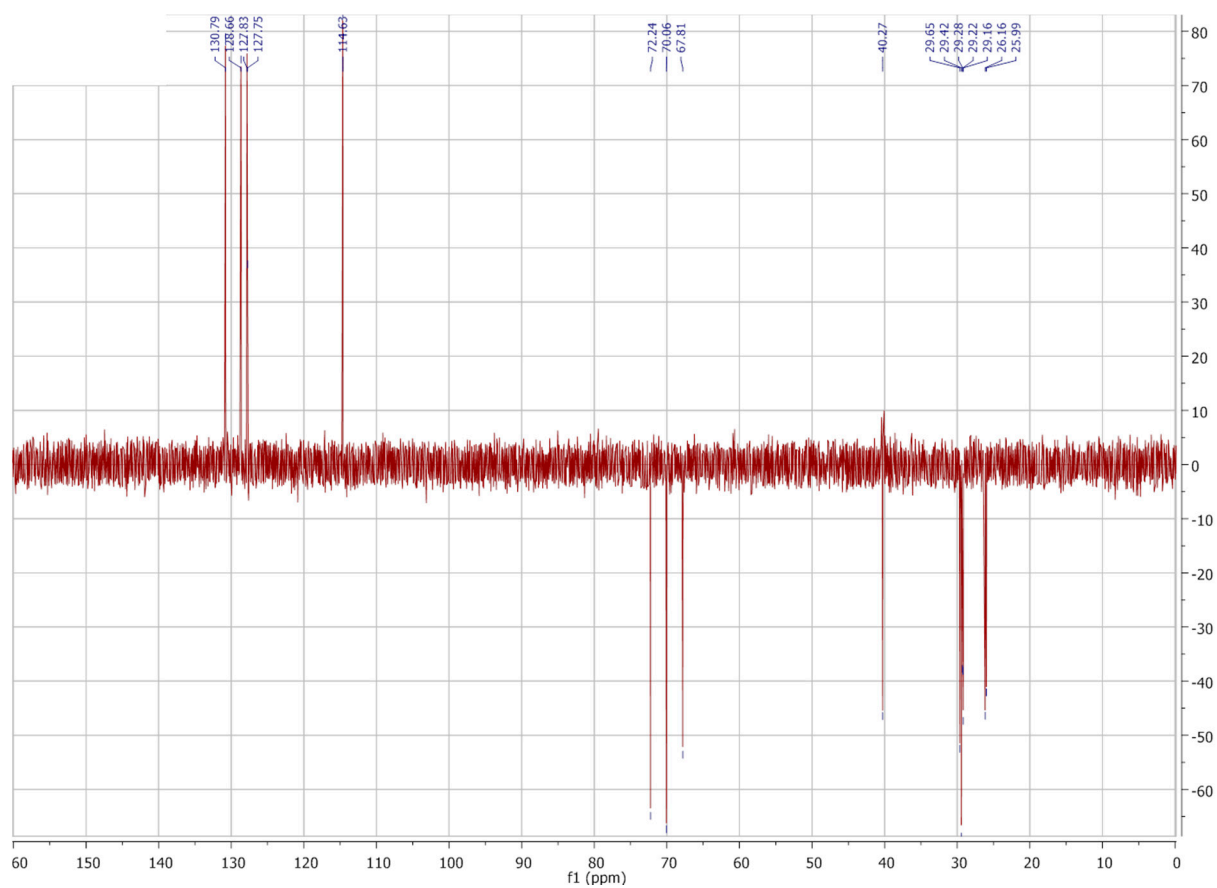
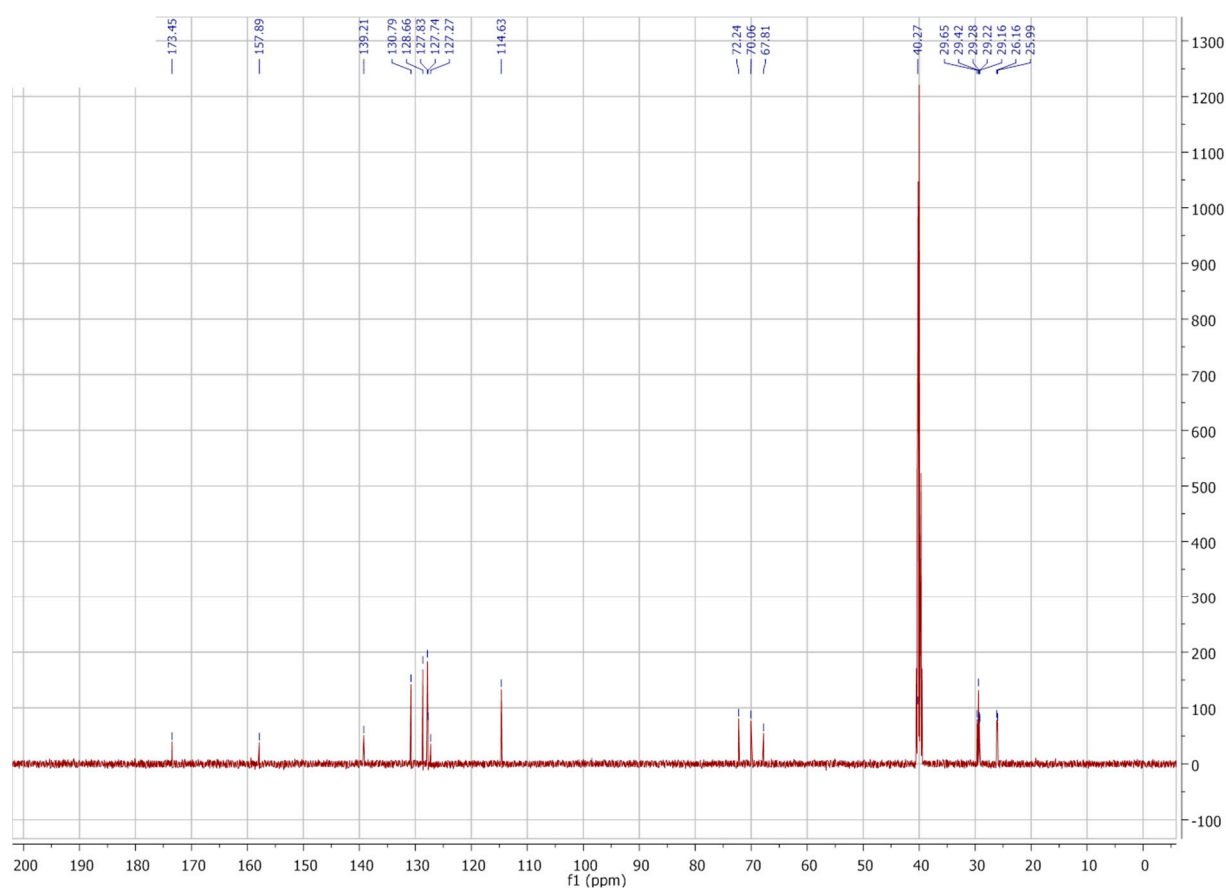


2-(4-{{10-(benzyloxy)decyl}oxy}phenyl)acetic acid (**9i**; ZHAWOC6862)

NMR

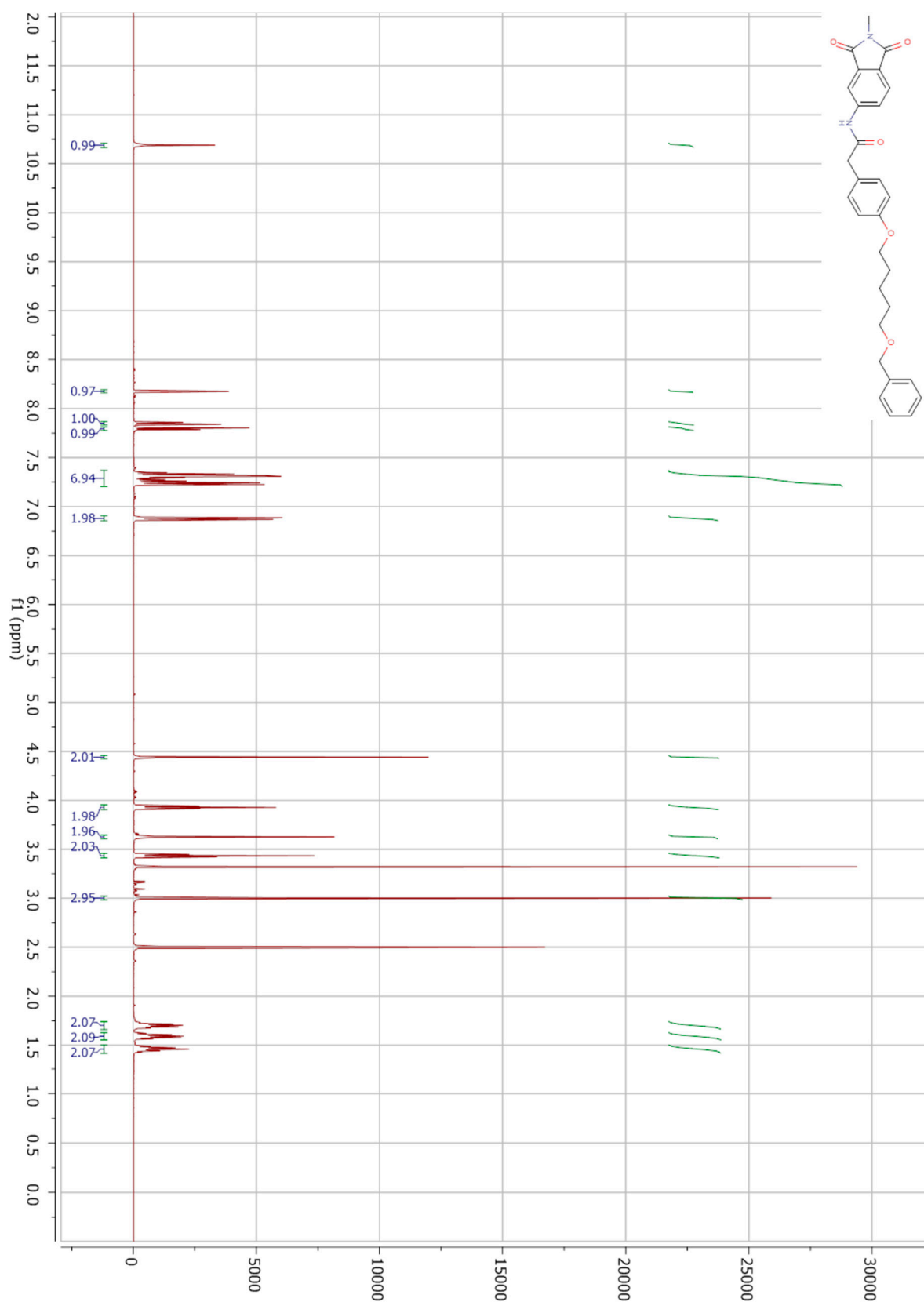


2-(4-{{[10-(benzyloxy)decyl]oxy}phenyl}acetic acid (**9i**; ZHAWOC6862)

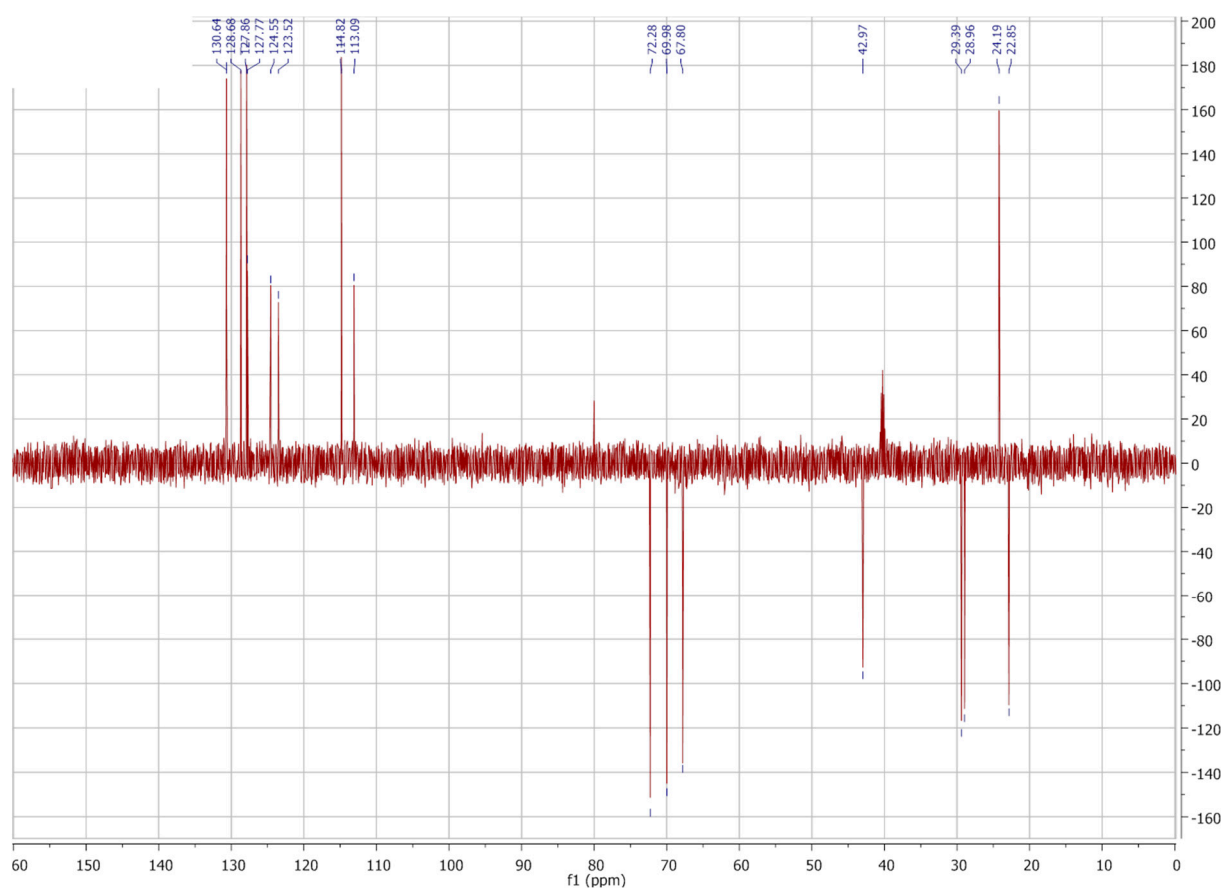
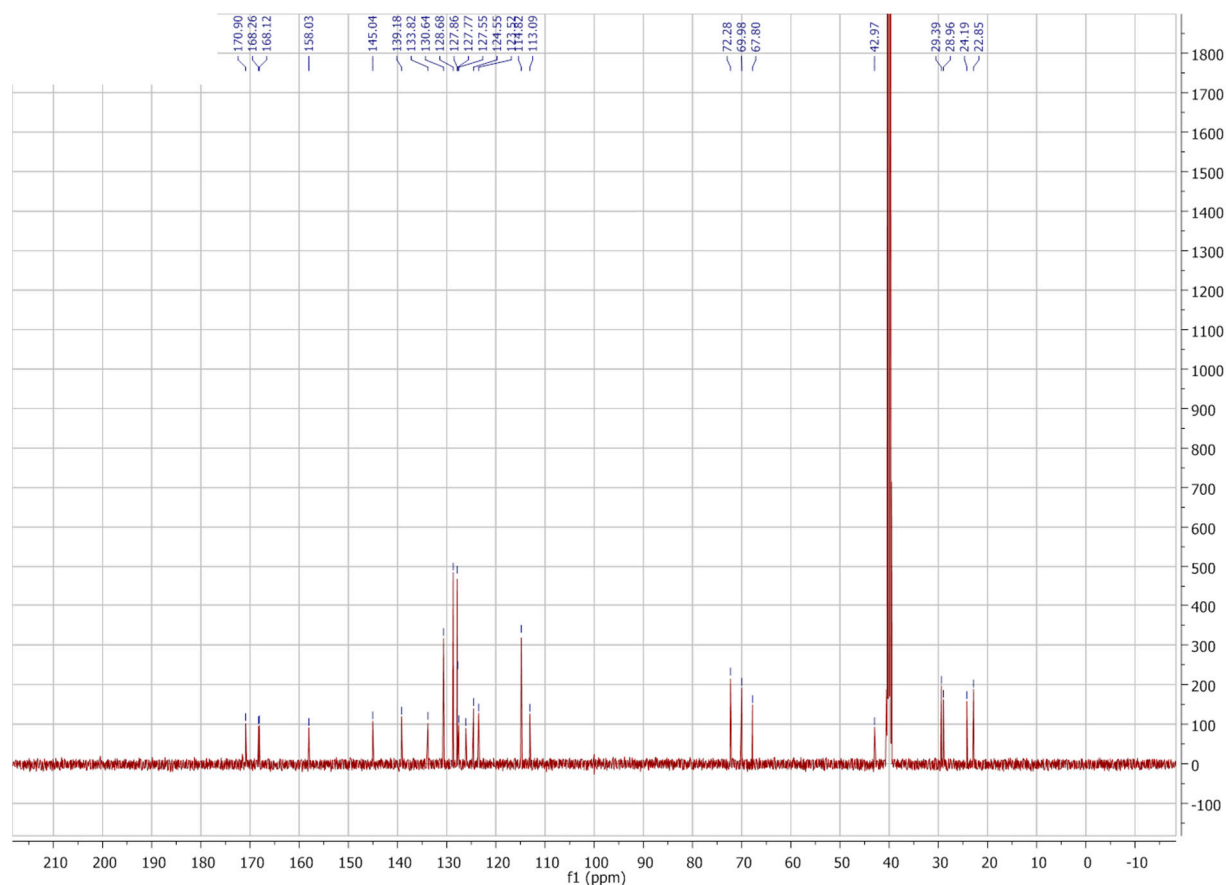


2-(4-{[5-(benzyloxy)pentyl]oxy}phenyl)-N-(2-methyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)acetamide (**12a**; ZHAWOC6647)

NMR

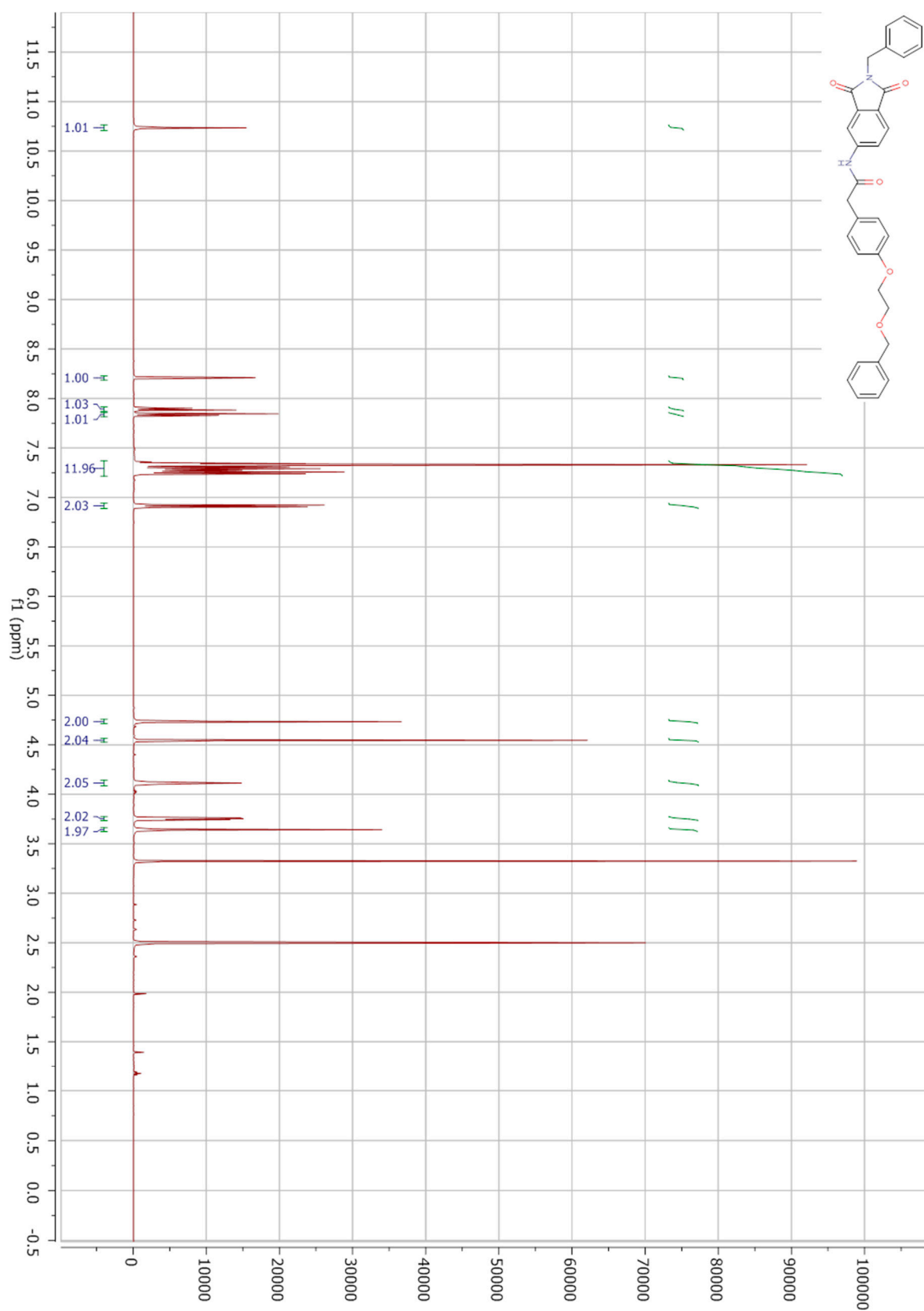


2-(4-{[5-(benzyloxy)pentyl]oxy}phenyl)-N-(2-methyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)acetamide (**12a**; ZHAWOC6647)

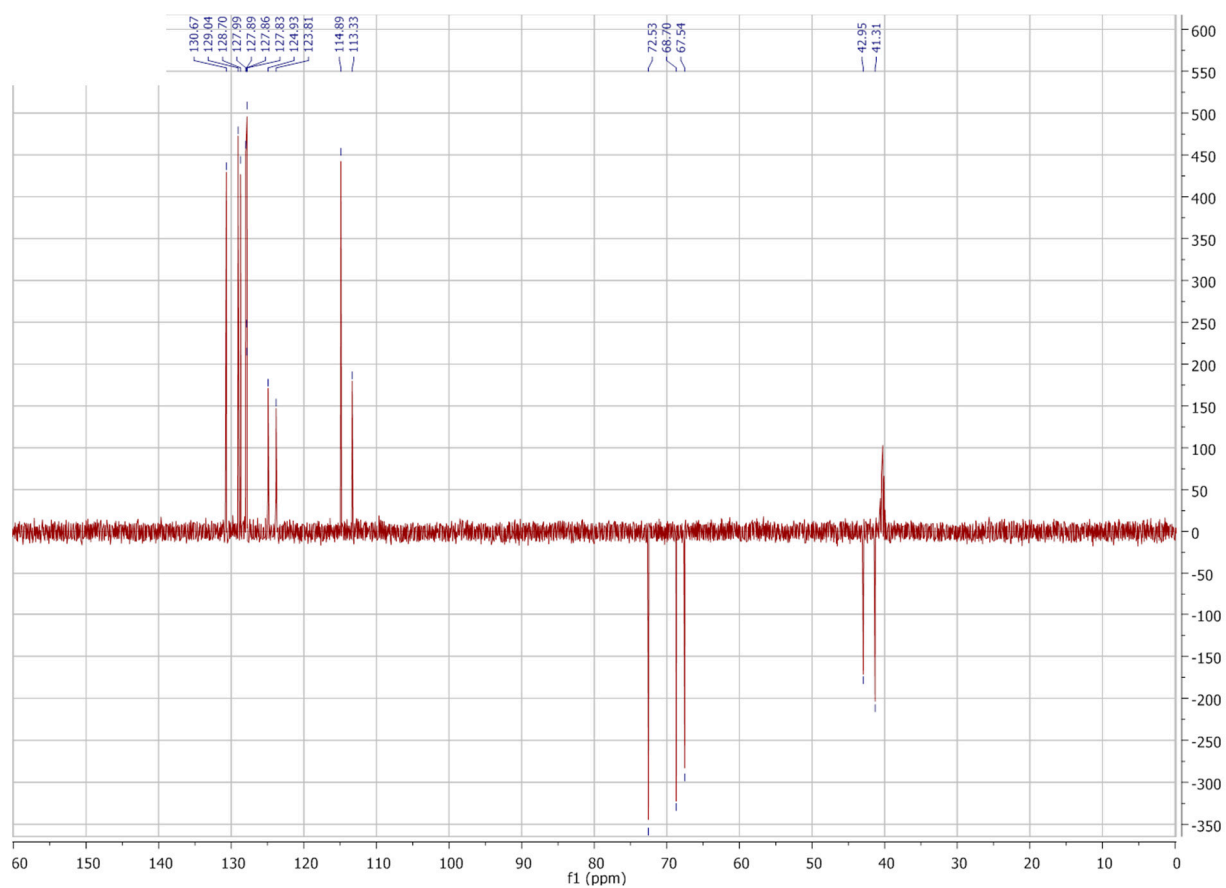
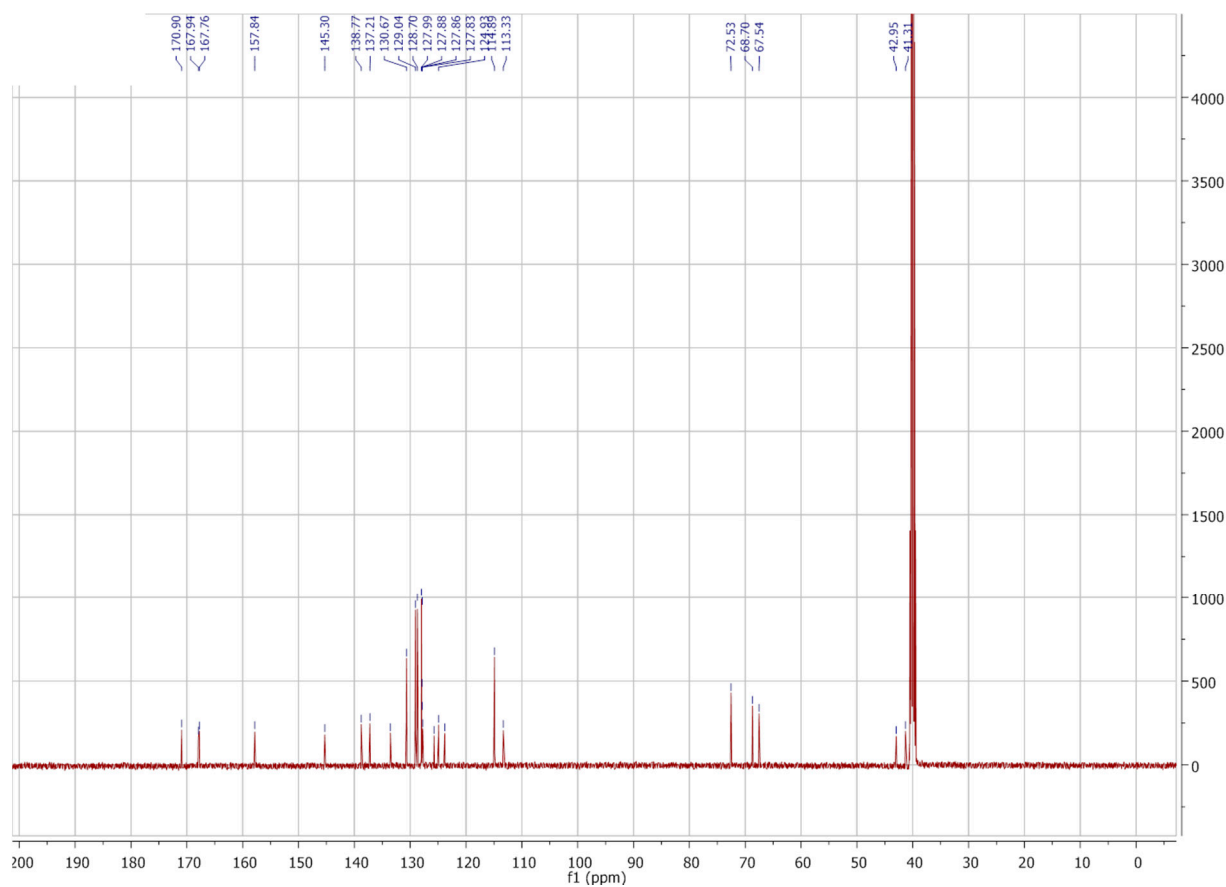


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-{4-[2-(benzyloxy)ethoxy]phenyl}acetamide (**12b**; ZHAWOC5467)

NMR

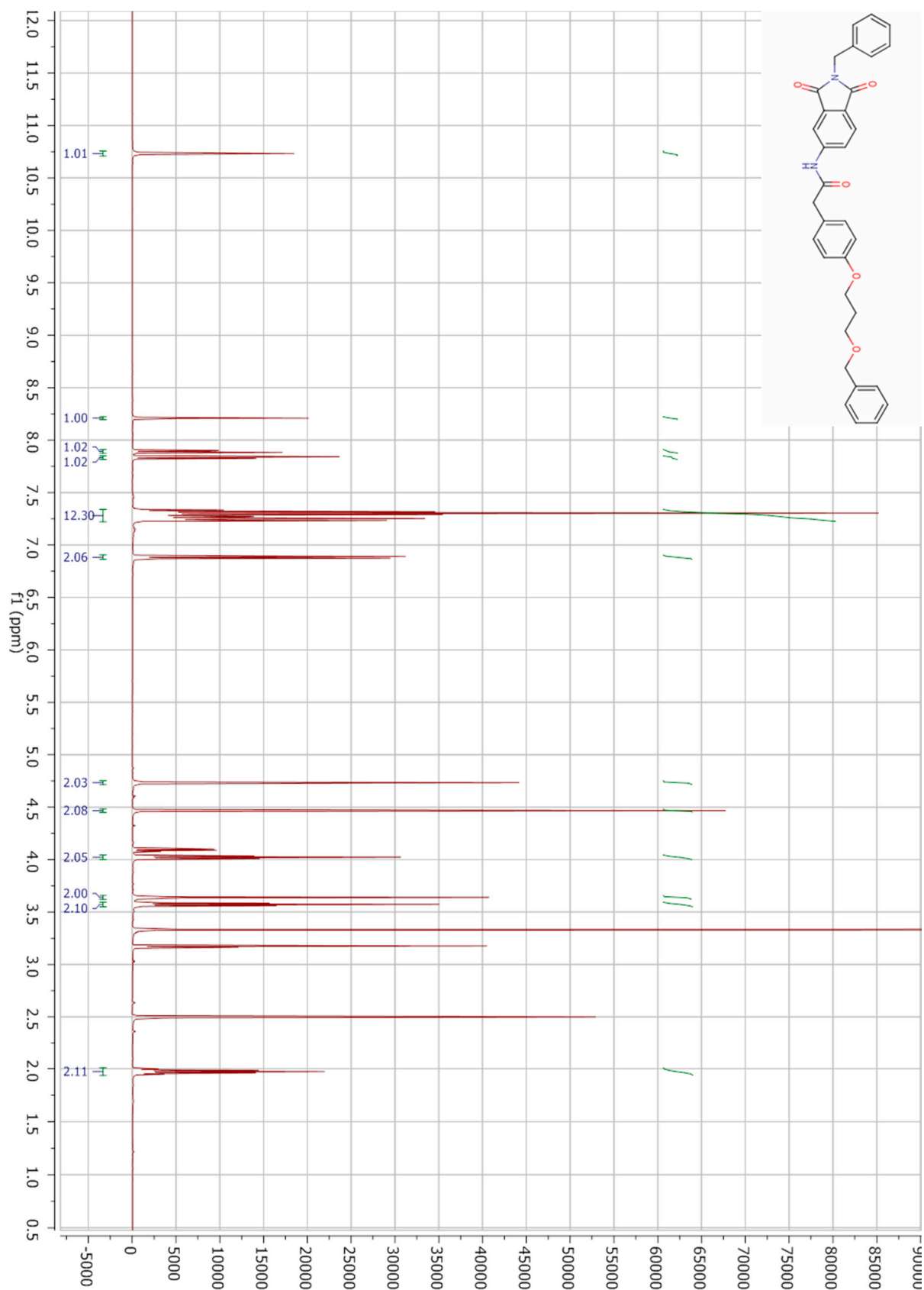


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-{4-[2-(benzyloxy)ethoxy]phenyl}acetamide (**12b**; ZHAWOC5467)

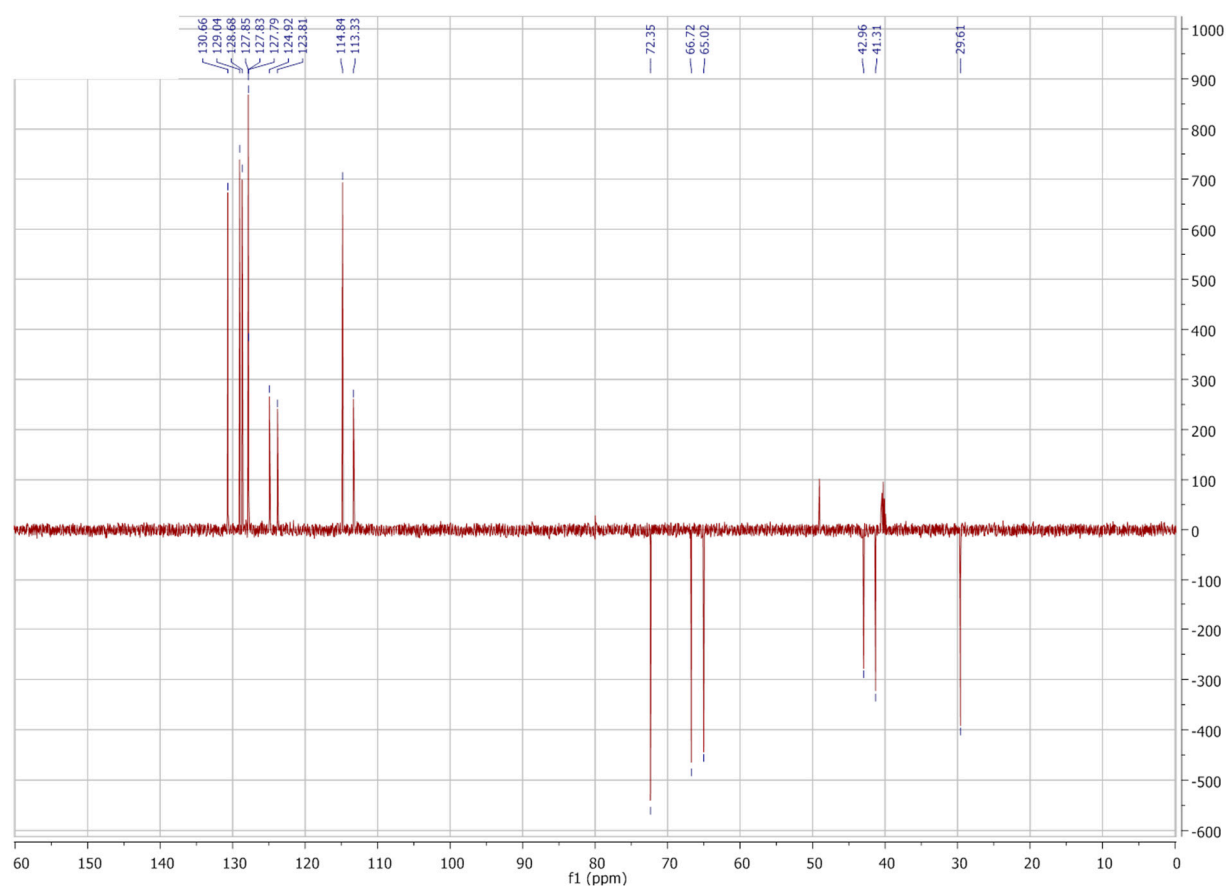
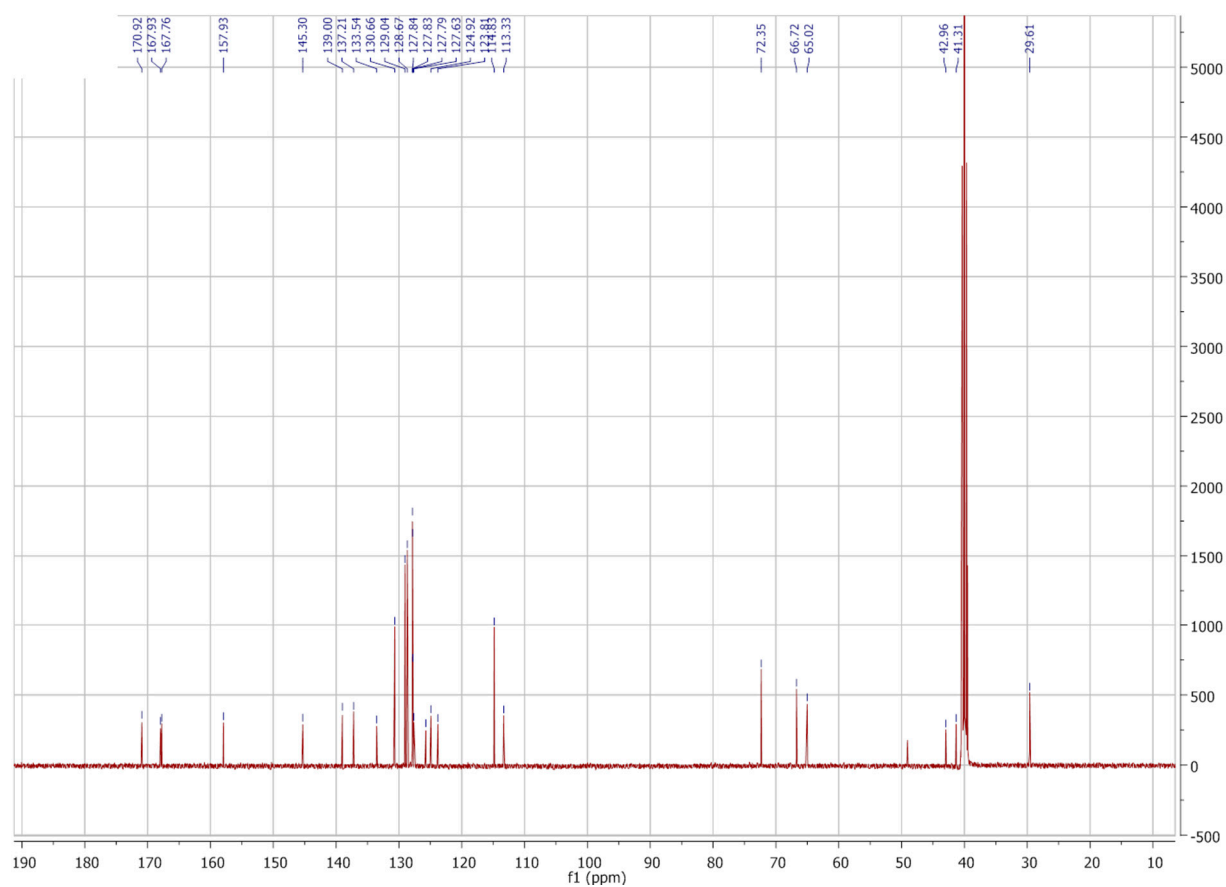


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-{4-[3-(benzyloxy)propoxy]phenyl}acetamide (**12c**; ZHAWOC4511)

NMR

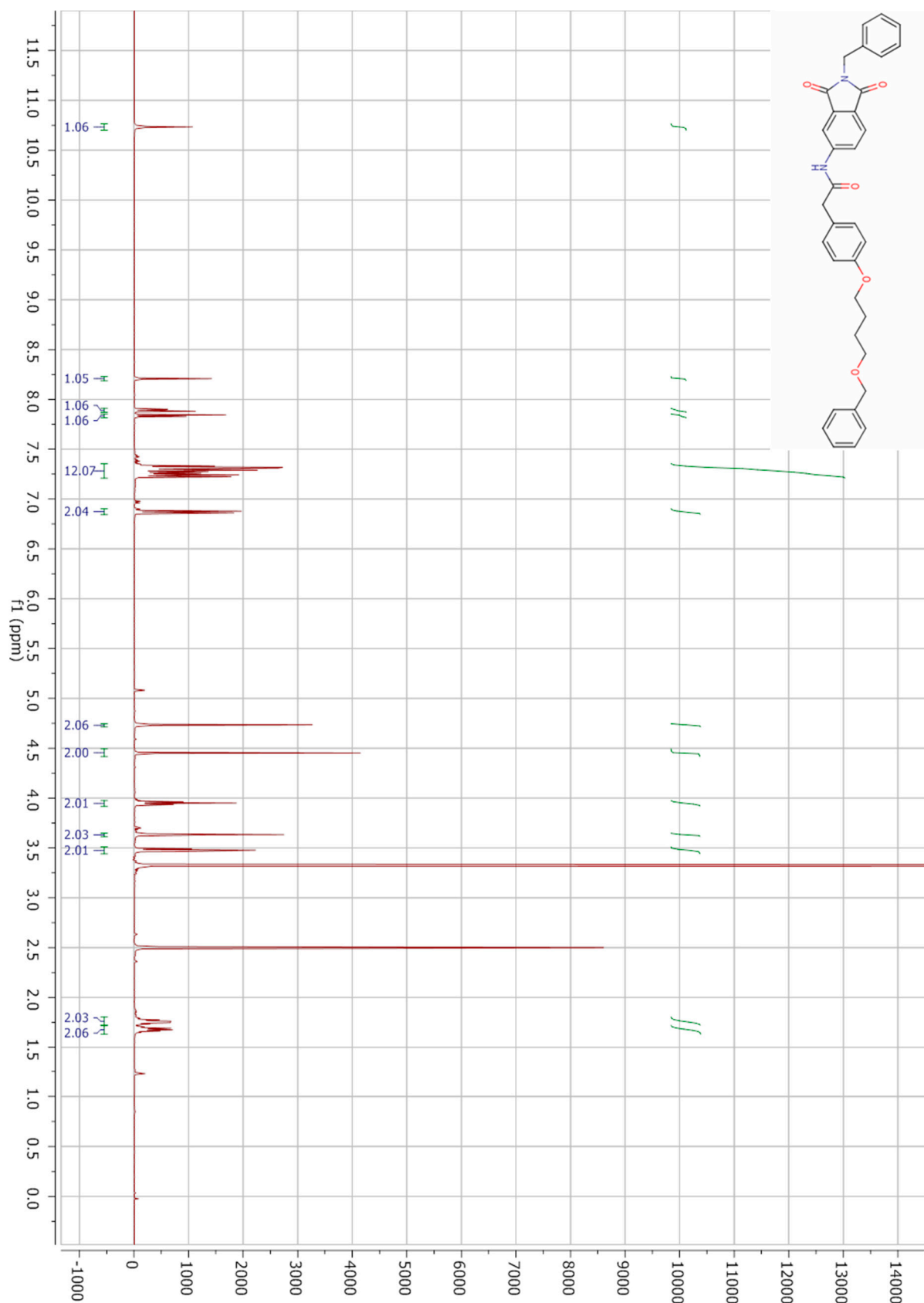


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-{4-[3-(benzyloxy)propoxy]phenyl}acetamide (**12c**; ZHAWOC4511)

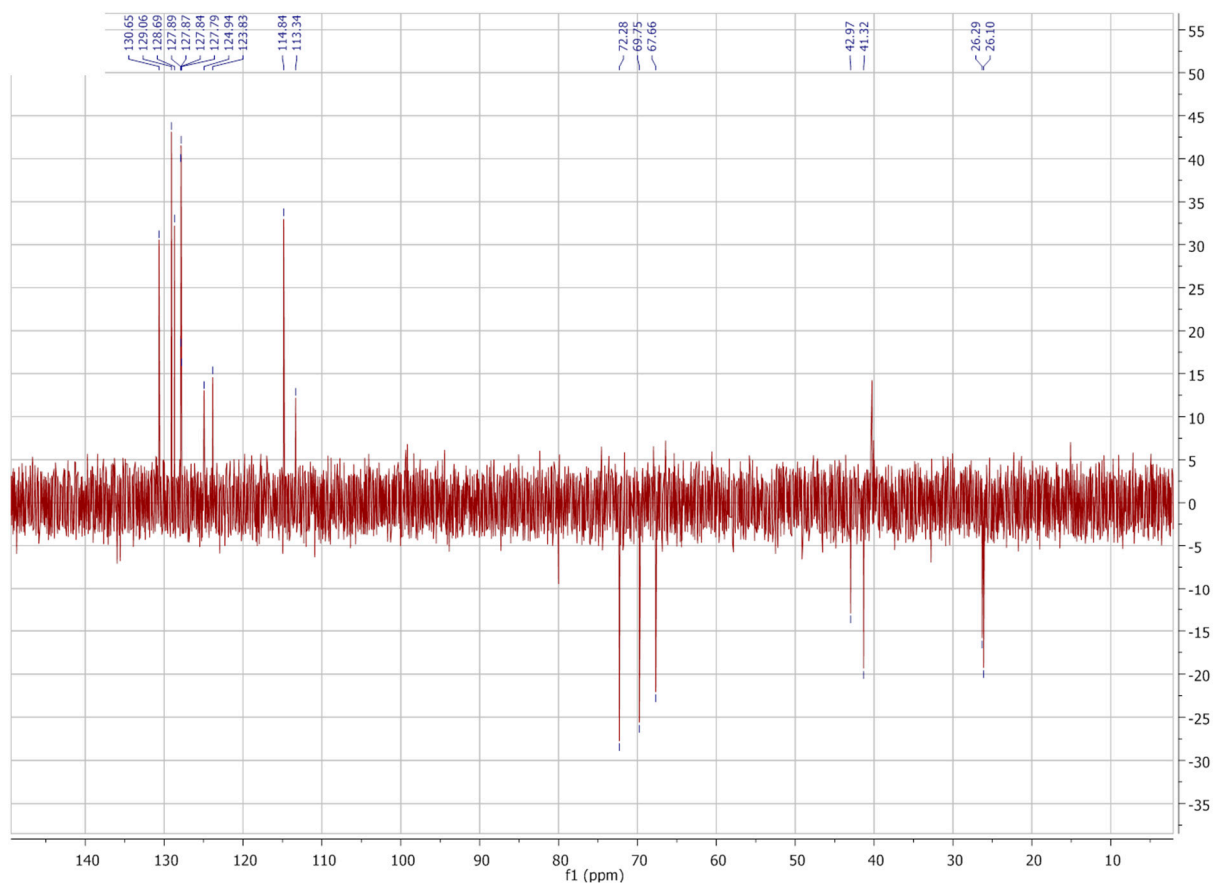
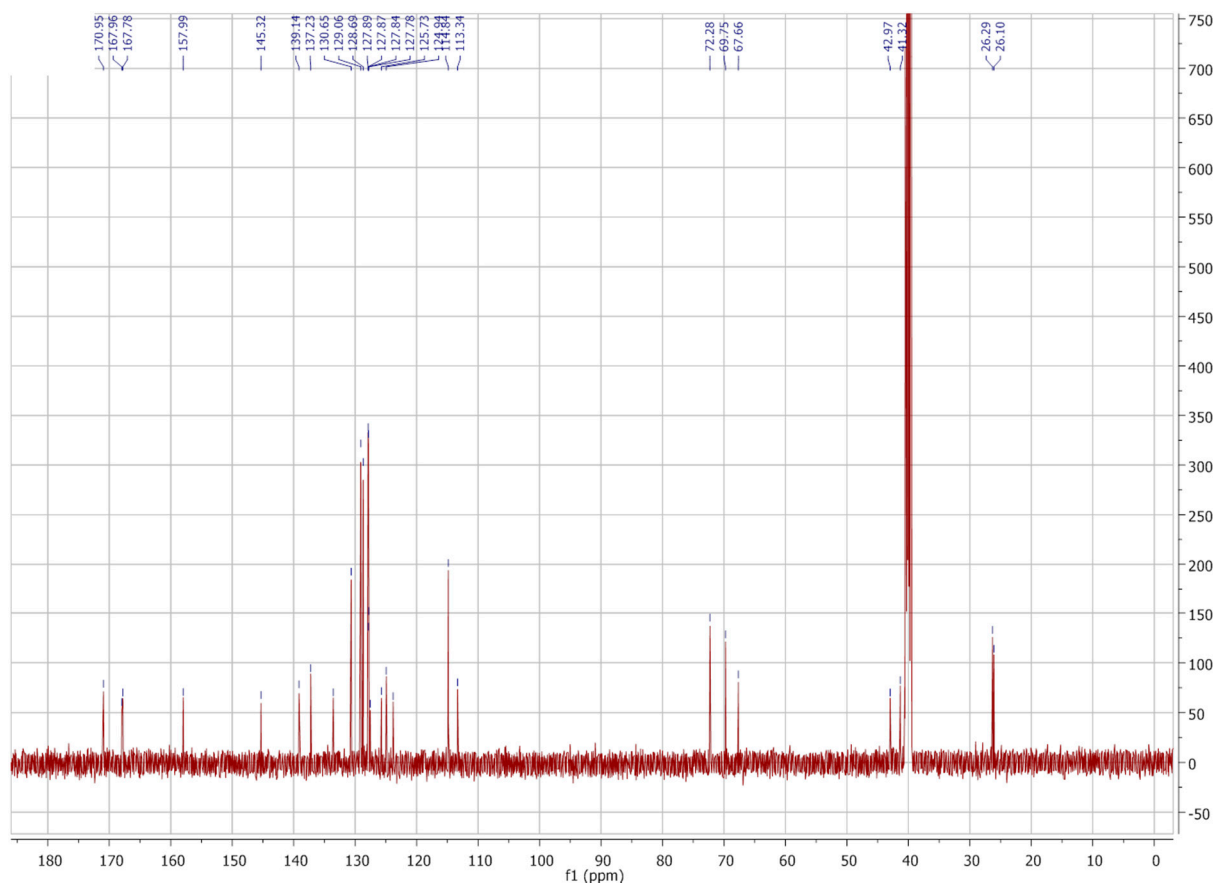


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-{4-[4-(benzyloxy)butoxy]phenyl}acetamide (**12d**; ZHAWOC4752)

NMR

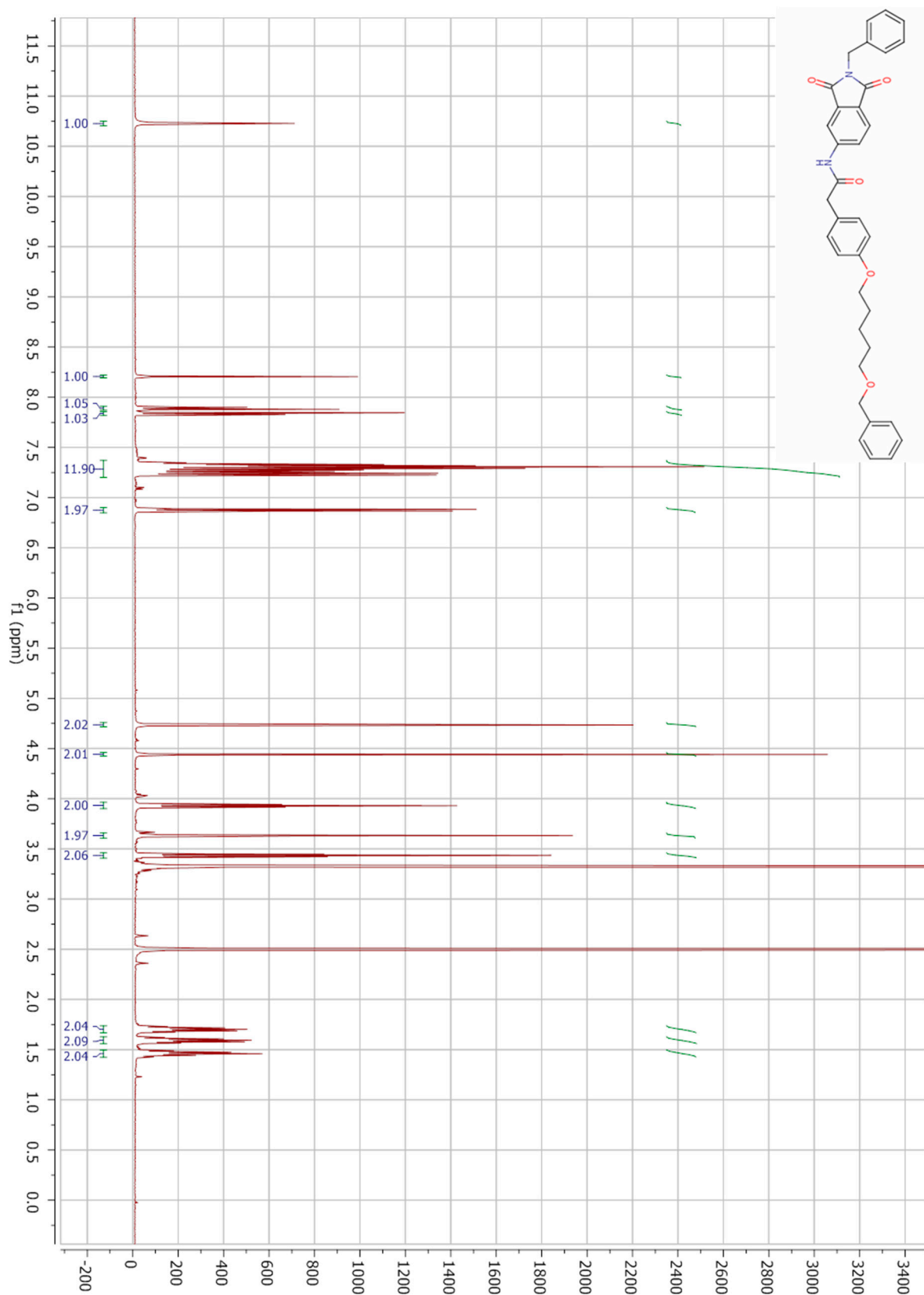


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-{4-[4-(benzyloxy)butoxy]phenyl}acetamide (**12d**; ZHAWOC4752)

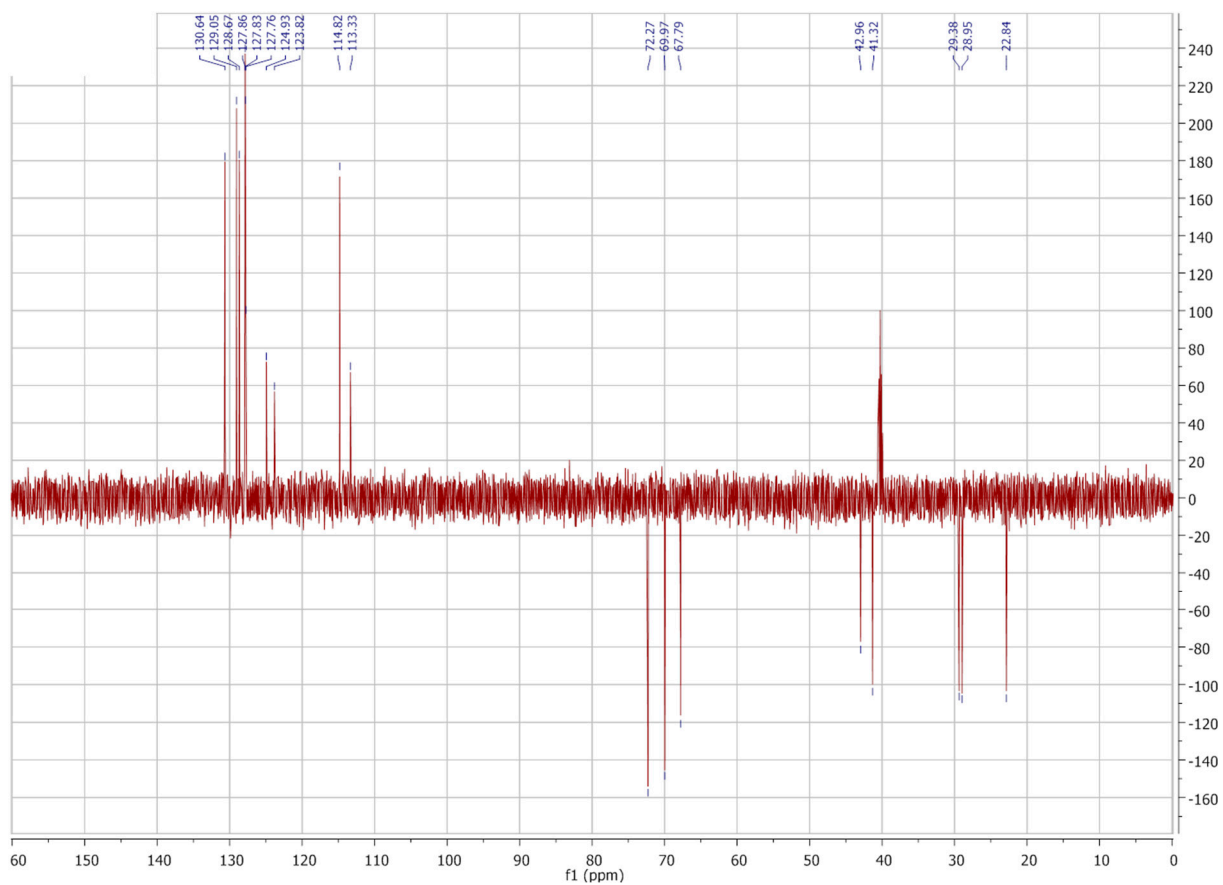
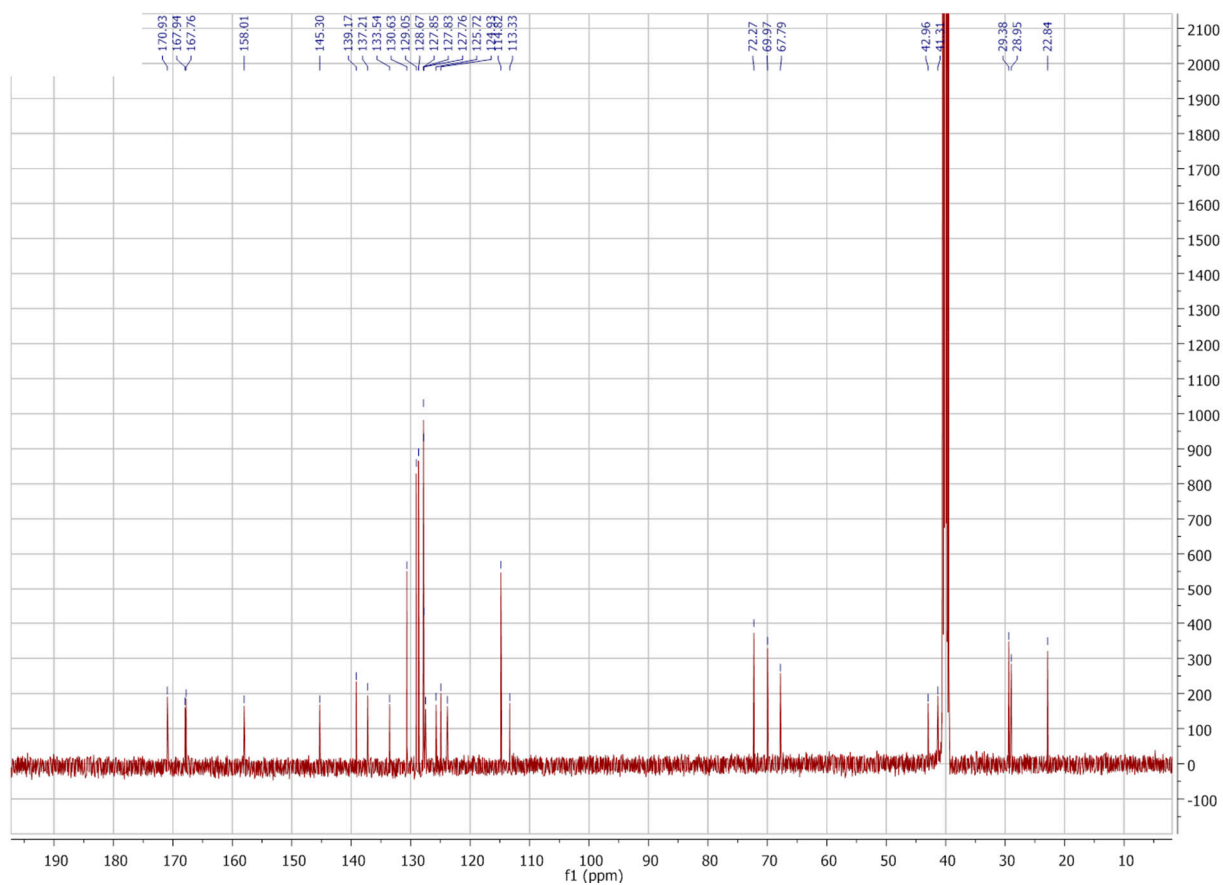


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-(4-{{[5-(benzyloxy)pentyl]oxy}phenyl)acetamide (**12e**; ZHAWOC5979)

NMR

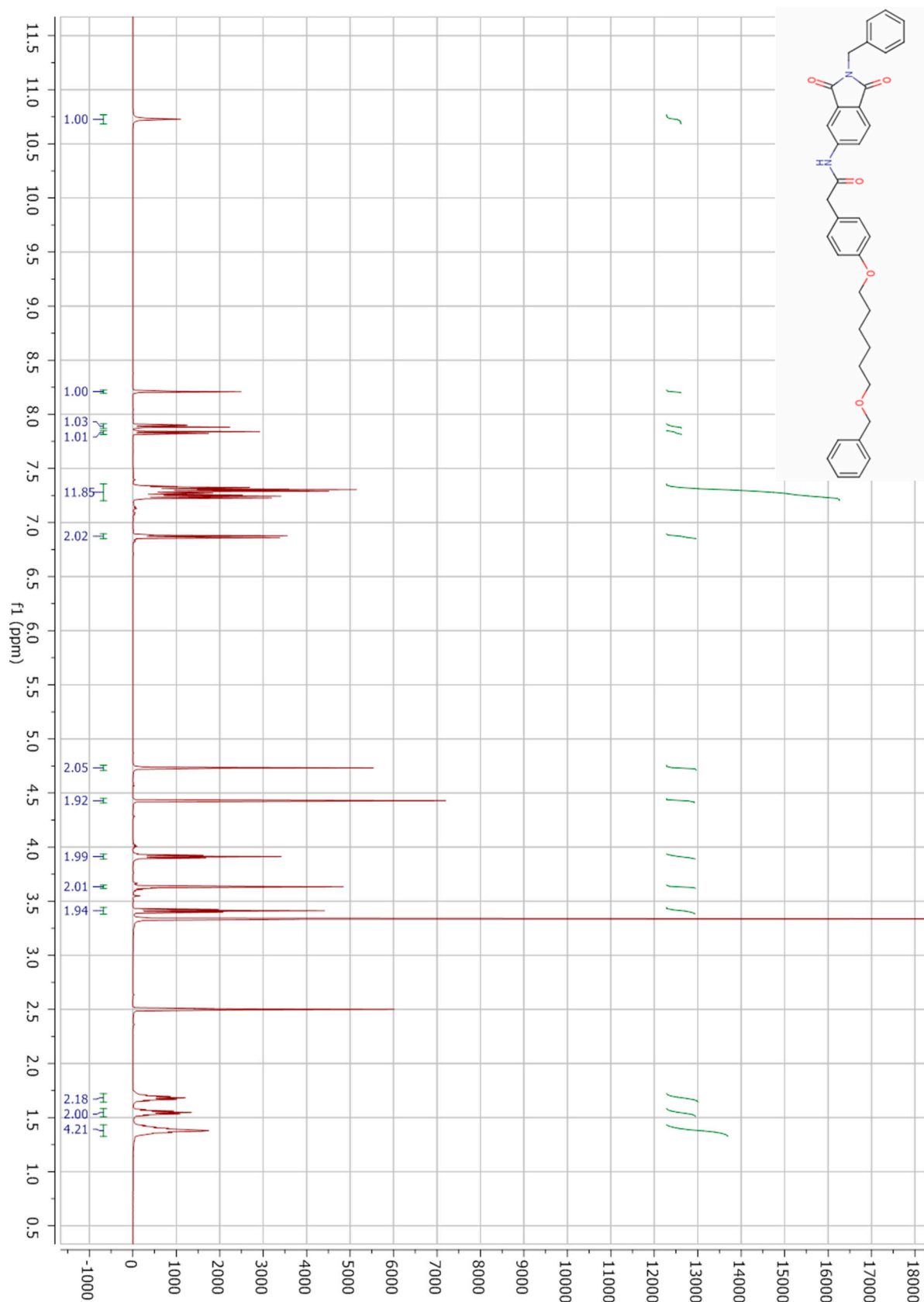


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-(4-{[5-(benzyloxy)pentyl]oxy}phenyl)acetamide (**12e**; ZHAWOC5979)

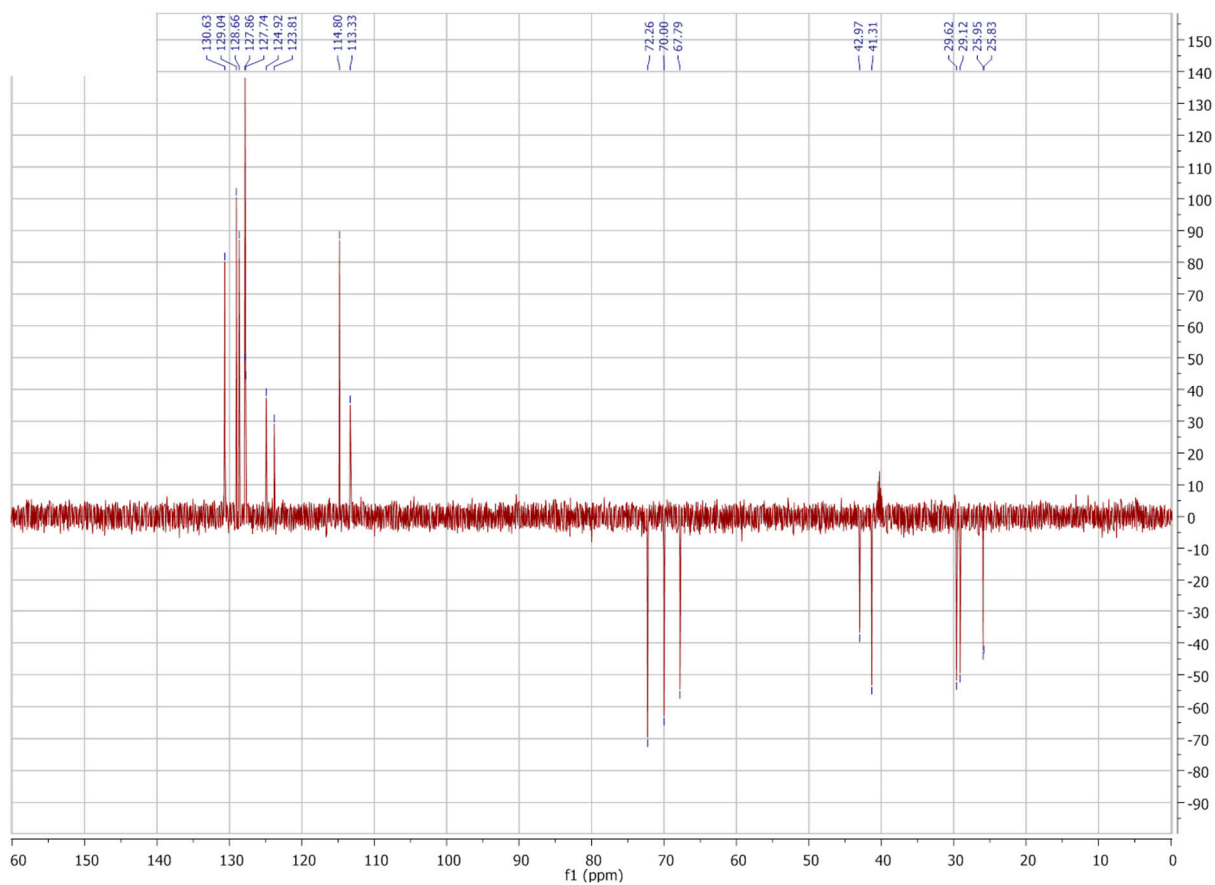
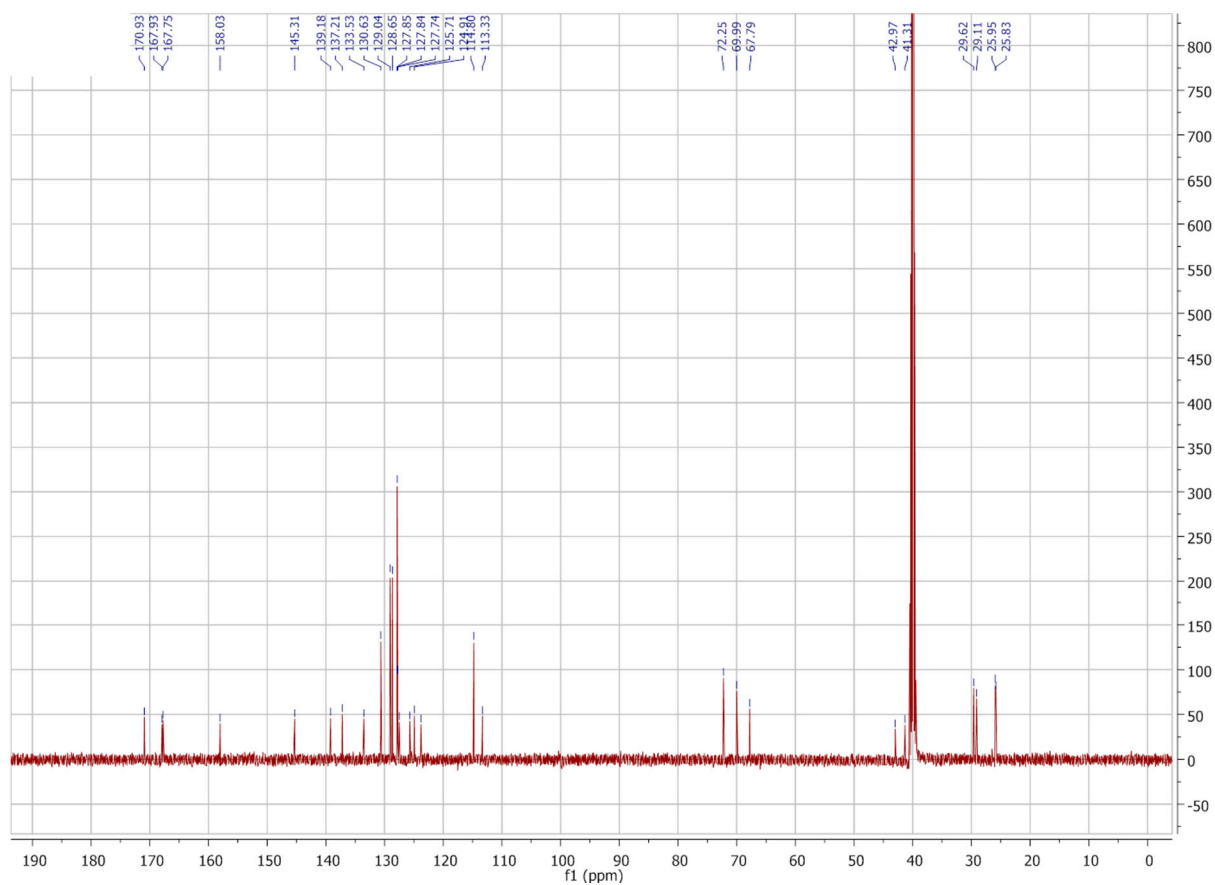


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-(4-{{[6-(benzyloxy)hexyl]oxy}phenyl}acetamide) (**12f**; ZHAWOC5980)

NMR

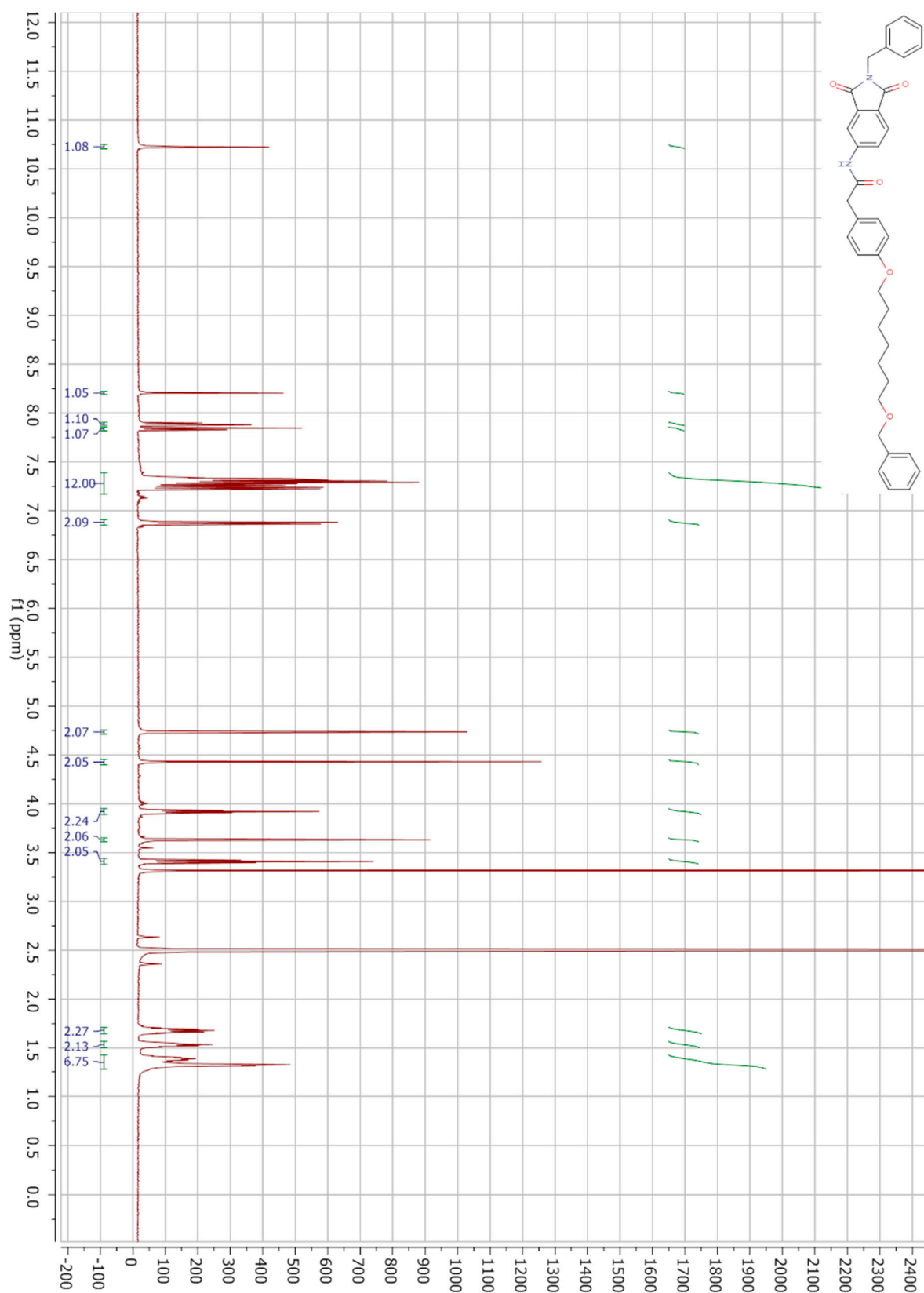


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-(4-([6-(benzyloxy)hexyl]oxy}phenyl)acetamide (**12f**; ZHAWOC5980)

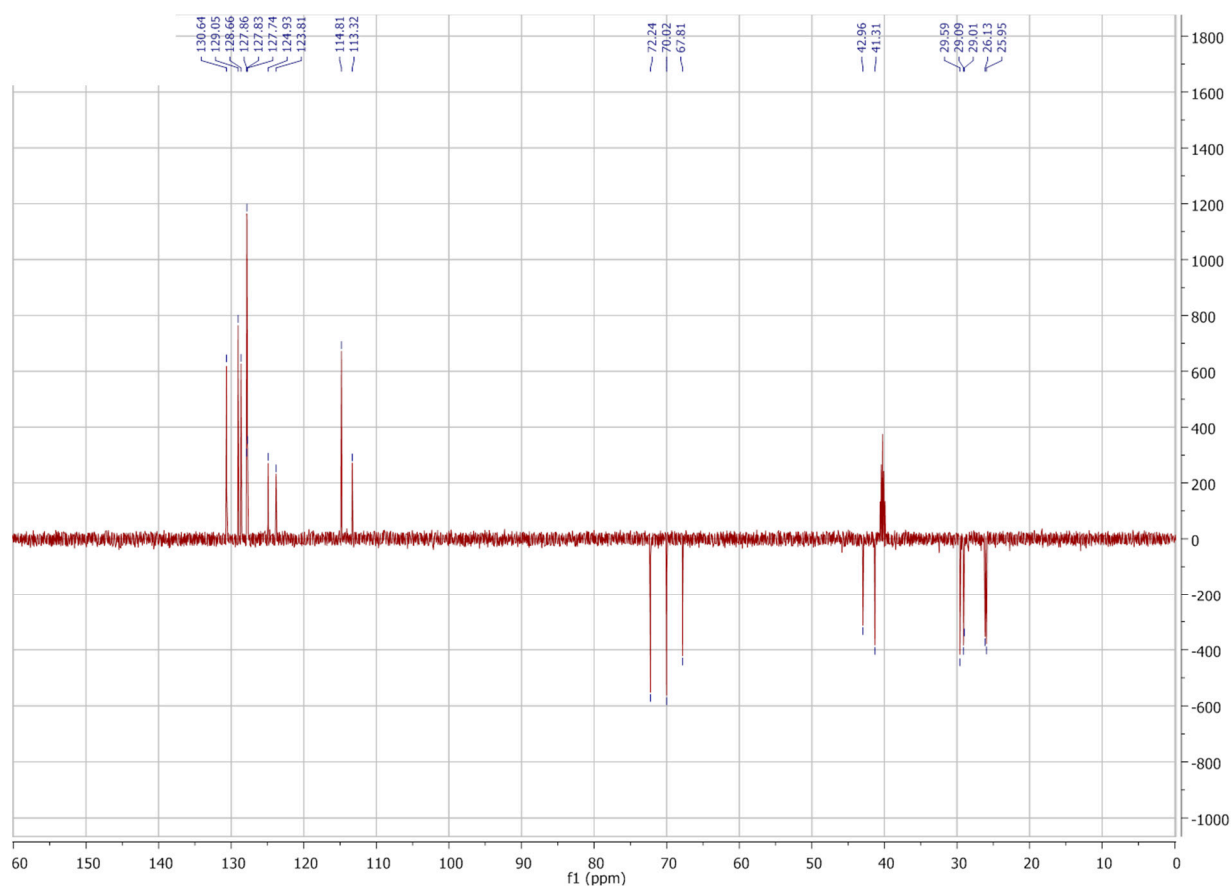
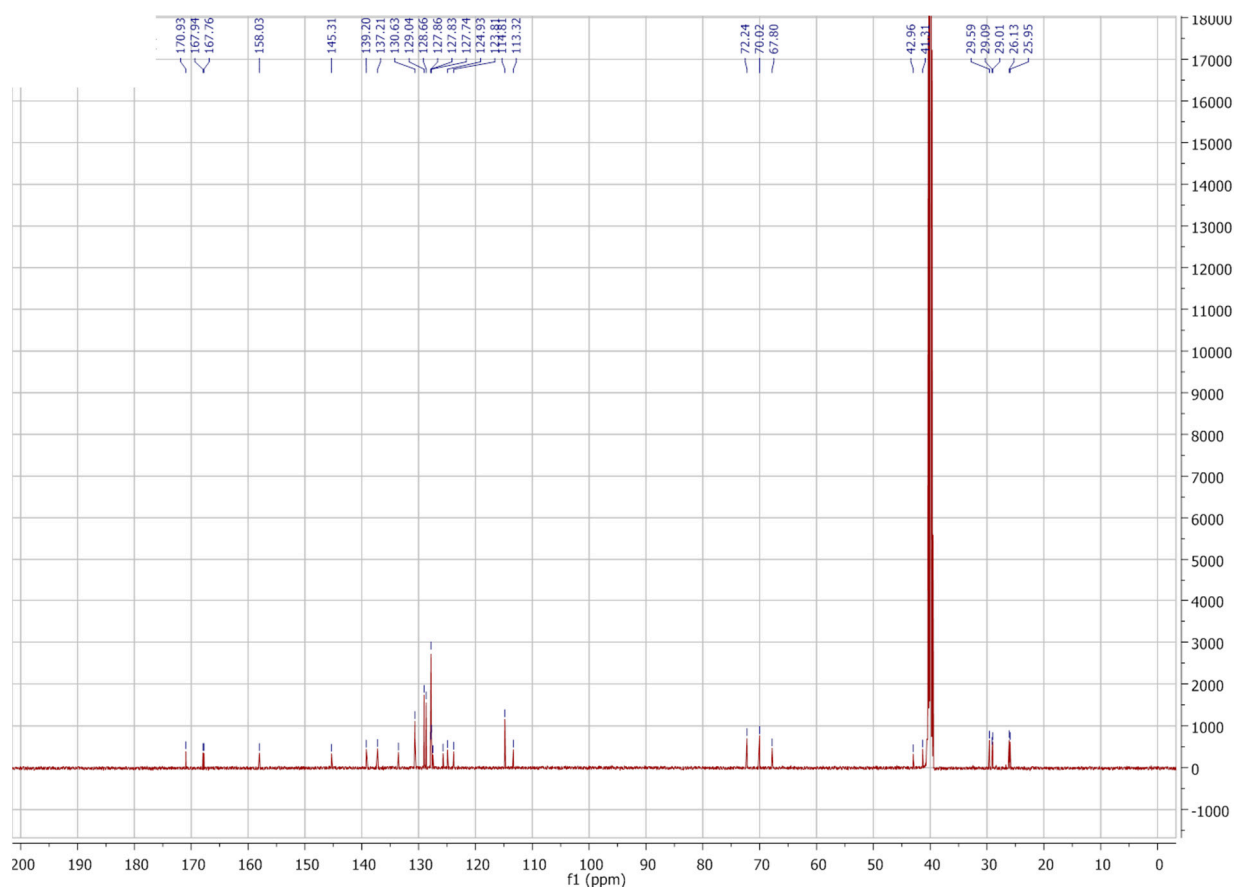


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-(4-([7-(benzyloxy)heptyl]oxy}phenyl)acetamide (**12g**; ZHAWOC7099)

NMR

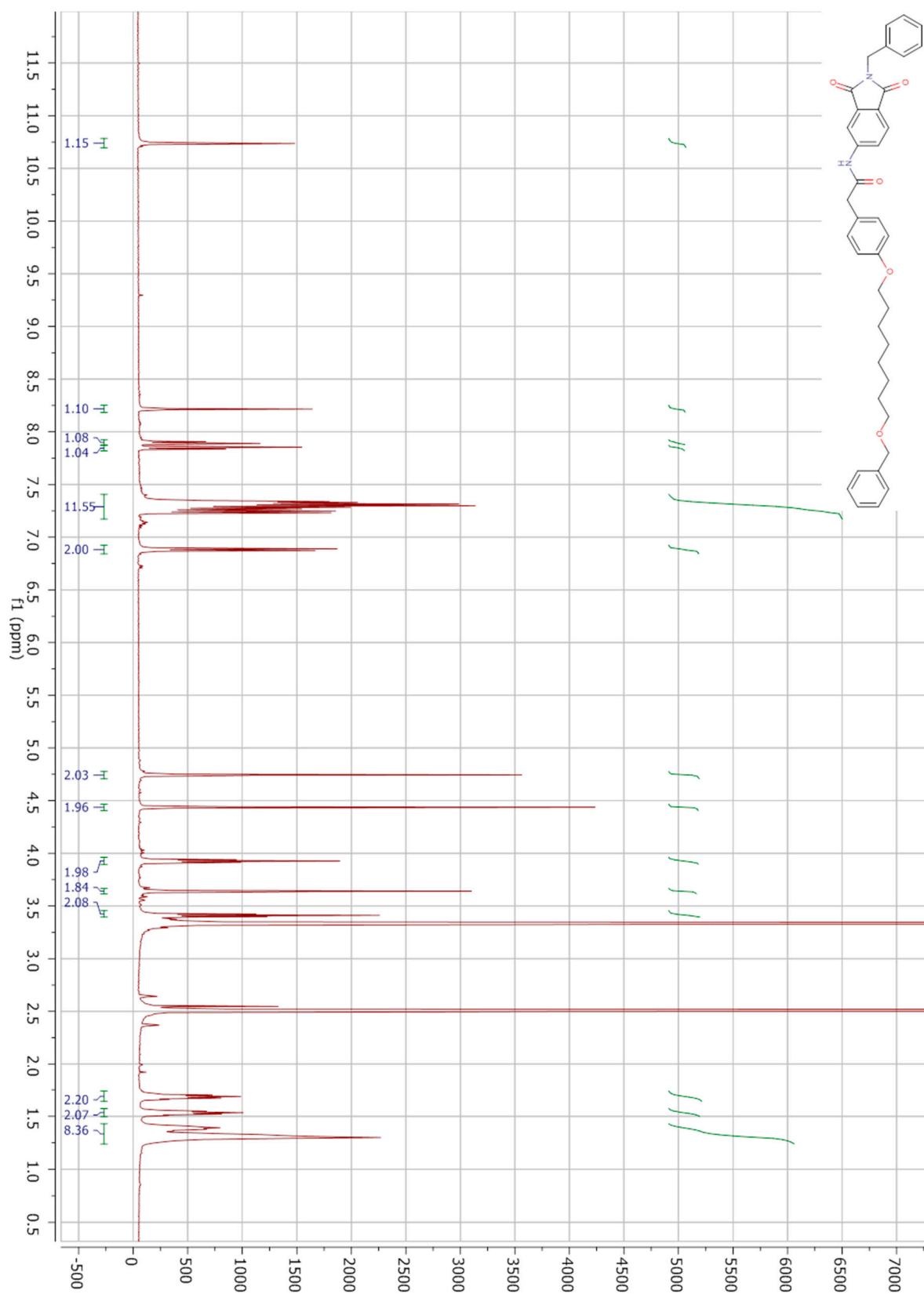


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-(4-{[7-(benzyloxy)heptyl]oxy}phenyl)acetamide (**12g**; ZHAWOC7099)

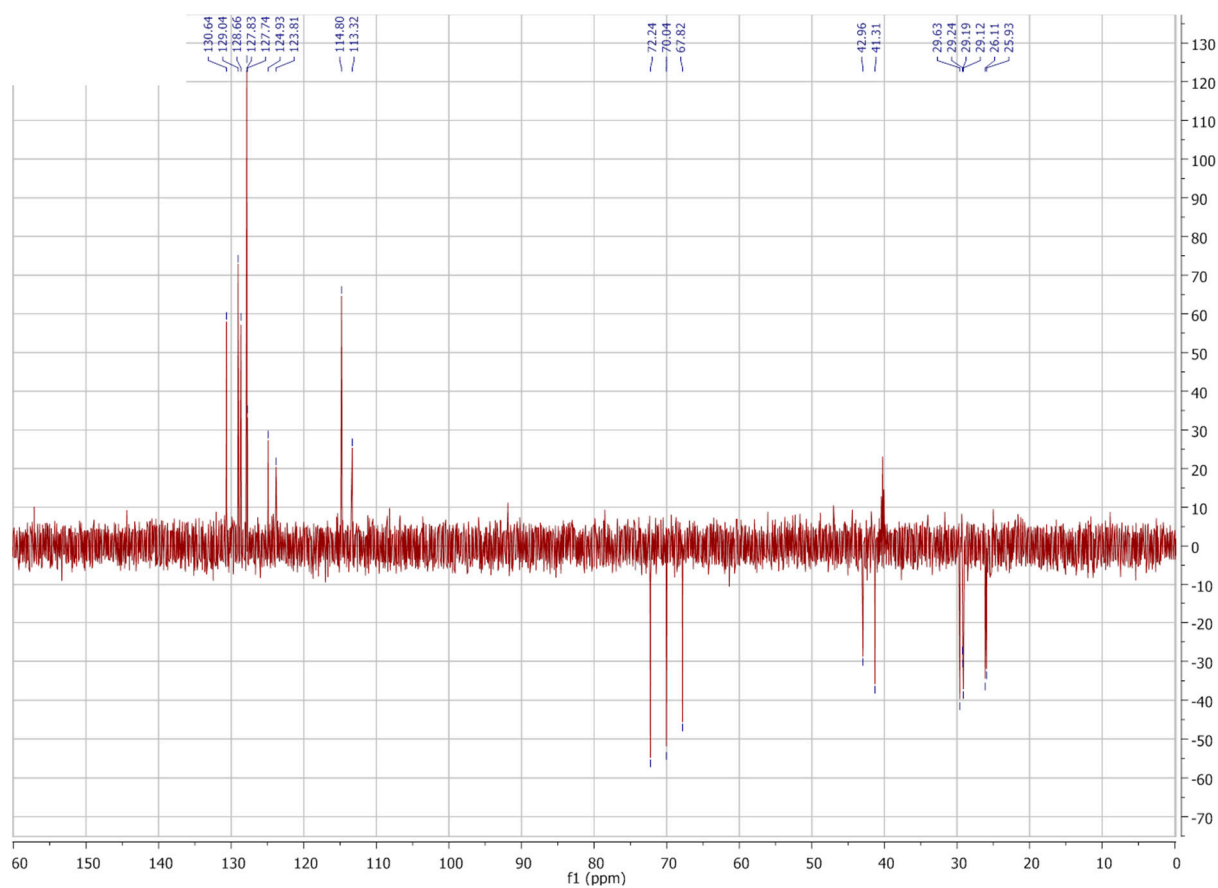
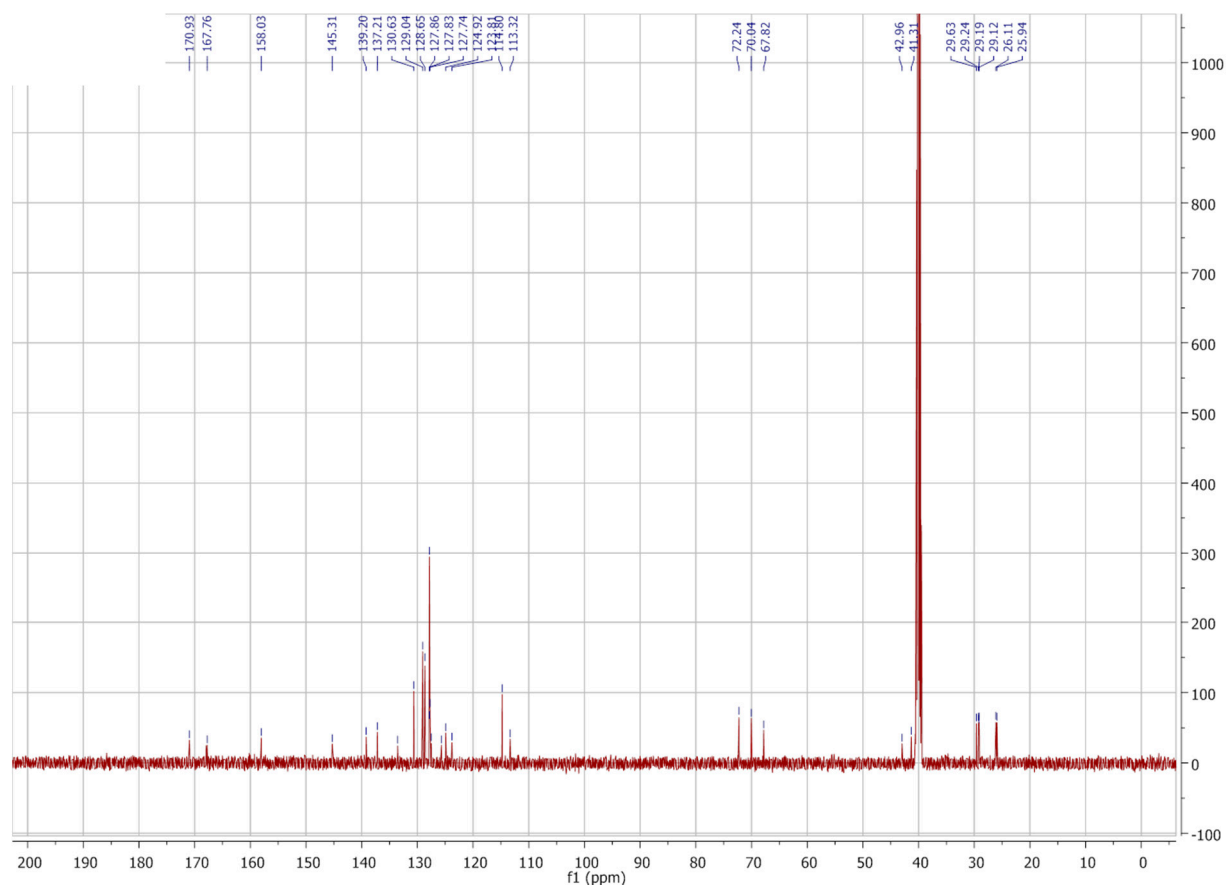


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-(4-([8-(benzyloxy)octyl]oxy}phenyl)acetamide (**12h**; ZHAWOC7095)

NMR

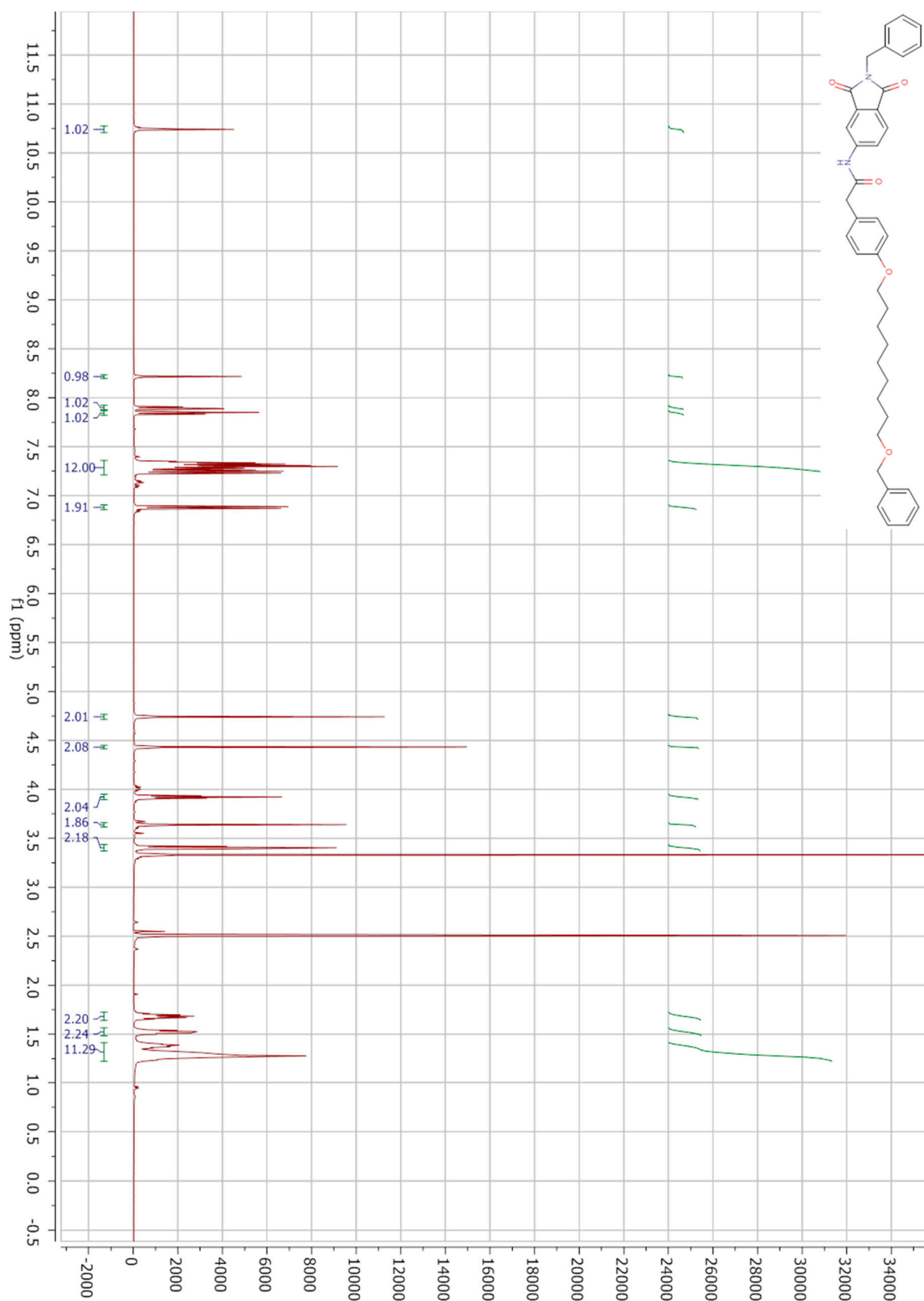


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-(4-([8-(benzyloxy)octyl]oxy}phenyl)acetamide (**12h**; ZHAWOC7095)

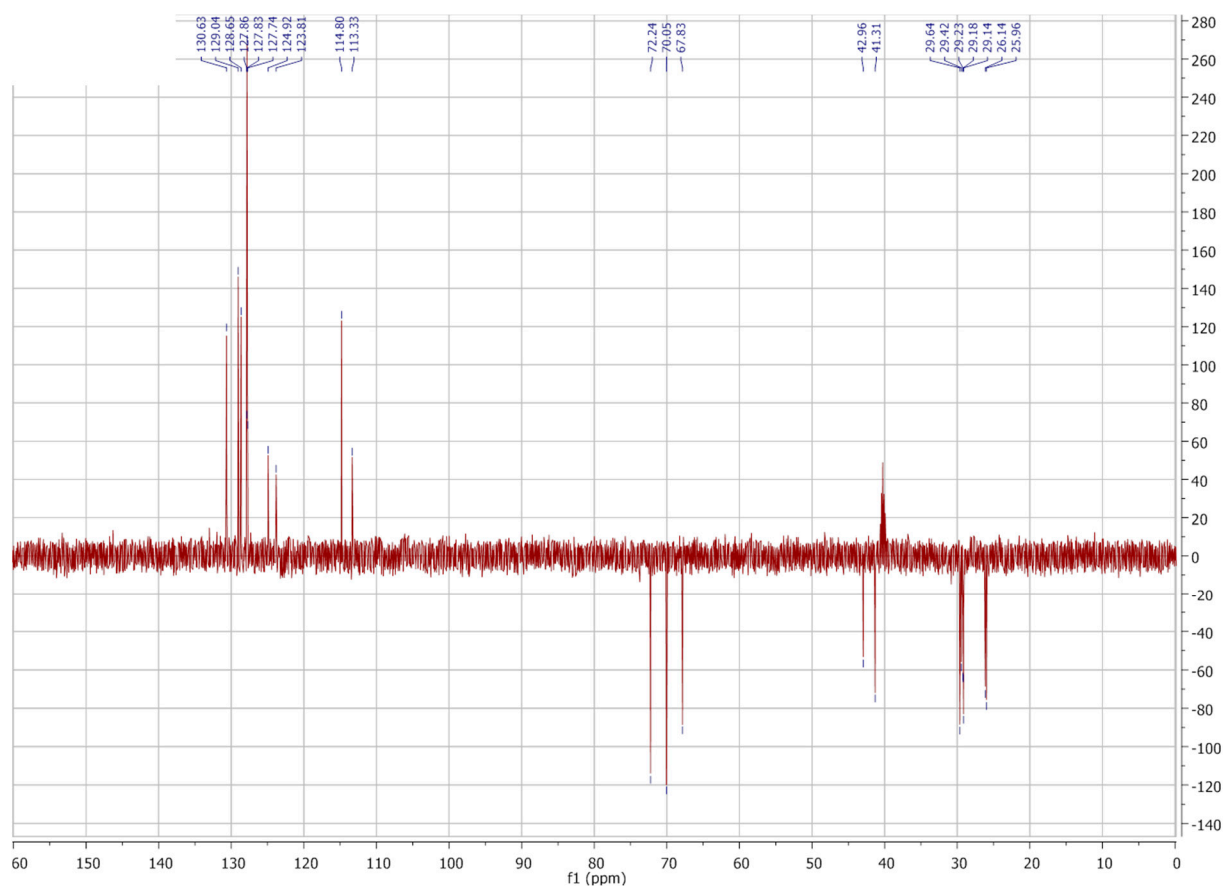
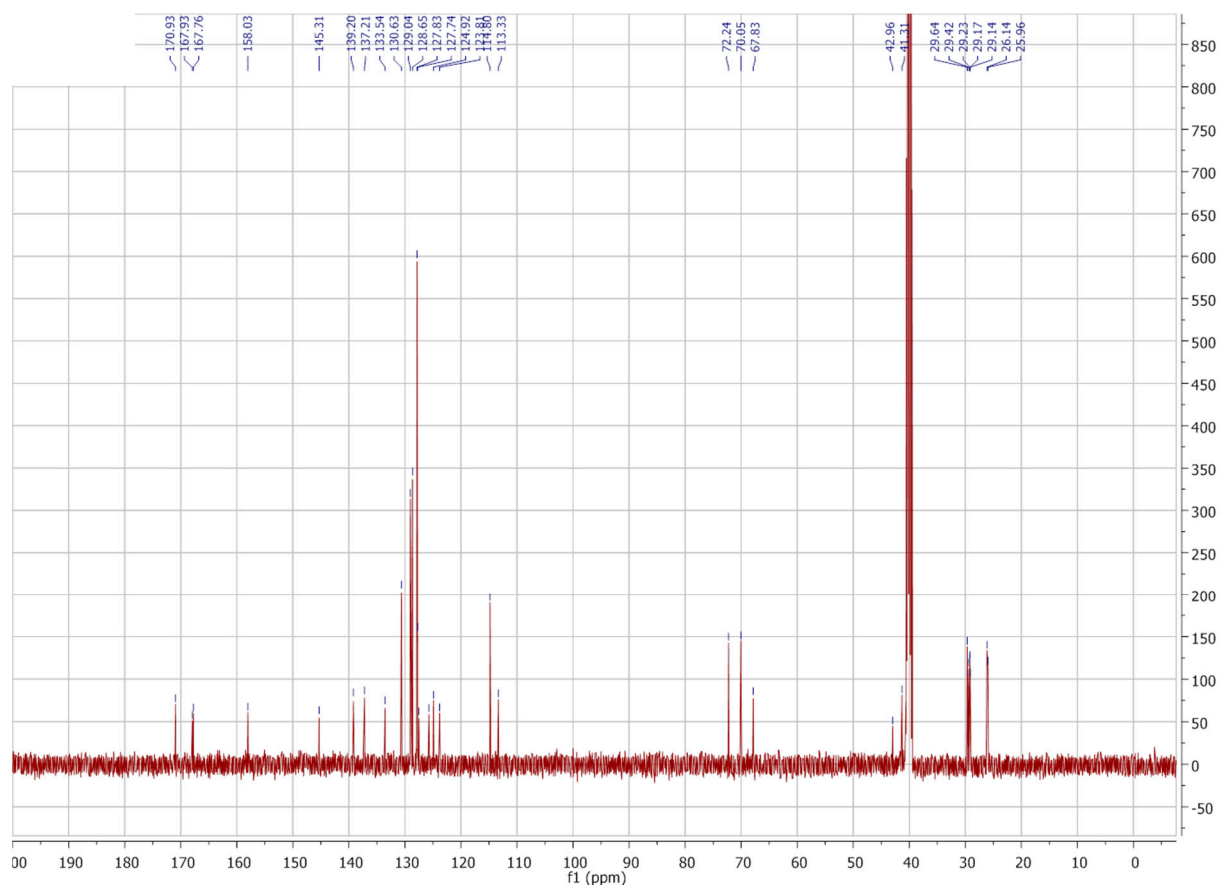


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-(4-([9-(benzyloxy)nonyl]oxy)phenyl)acetamide (**12i**; ZHAWOC6931)

NMR

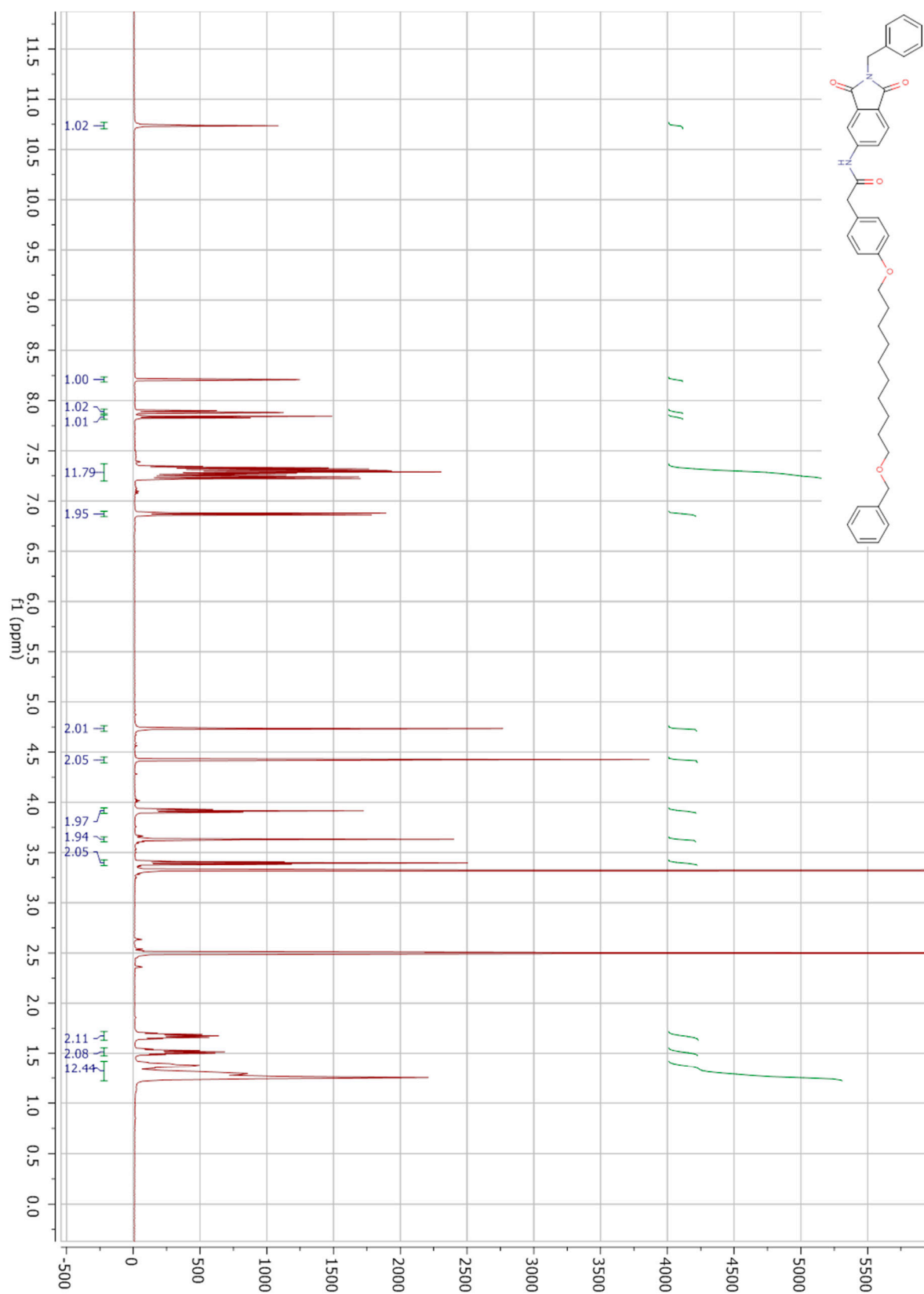


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-(4-{[9-(benzyloxy)nonyl]oxy}phenyl)acetamide (**12i**; ZHAWOC6931)

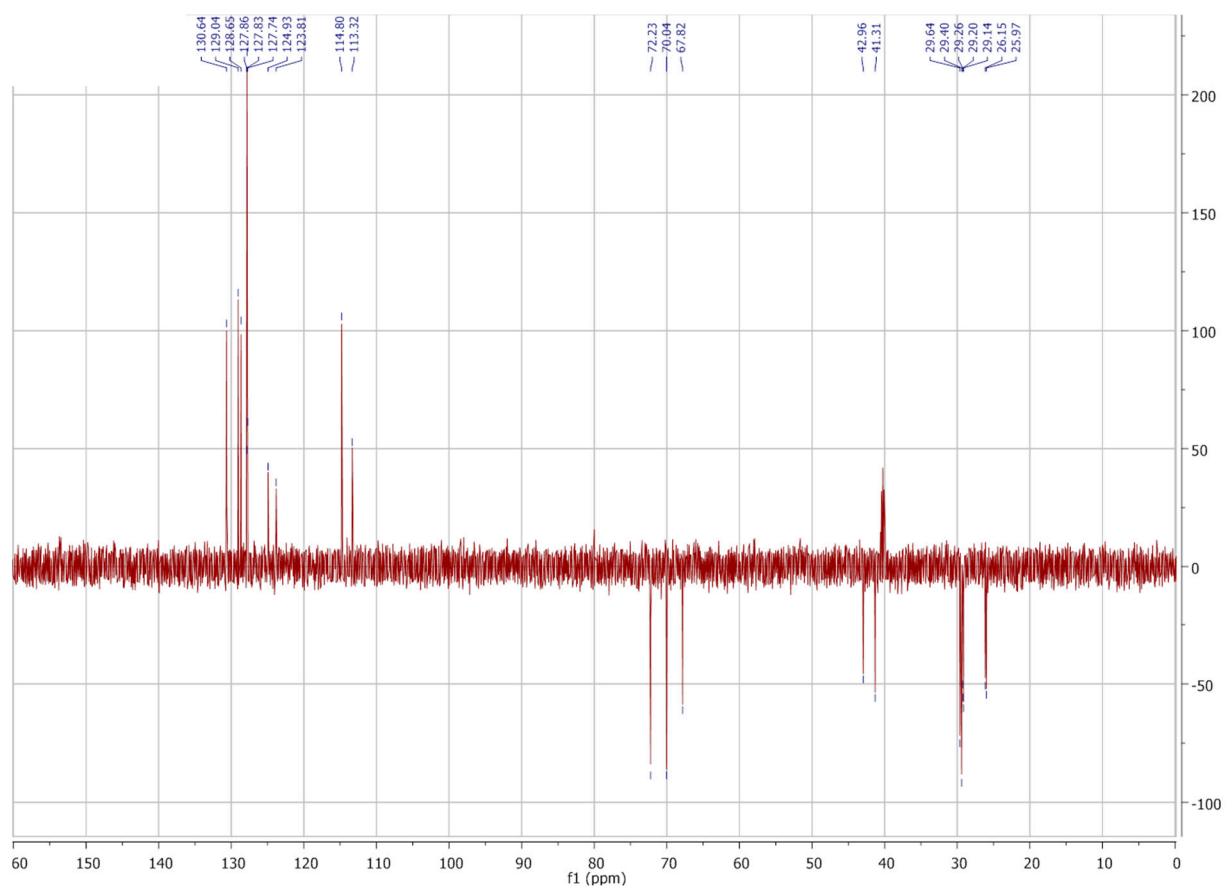
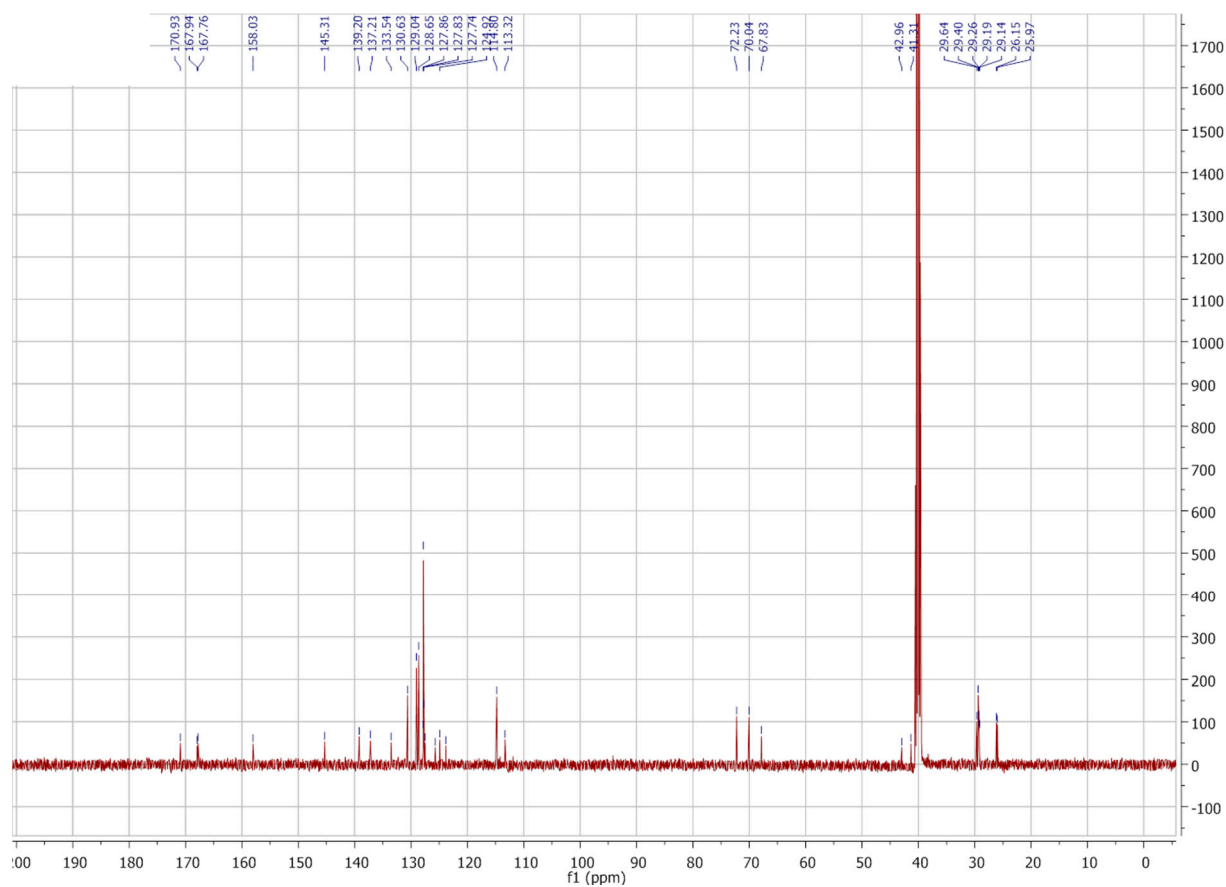


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-(4-[[10-(benzyloxy)decyl]oxy}phenyl)acetamide (**12j**; ZHAWOC6932)

NMR

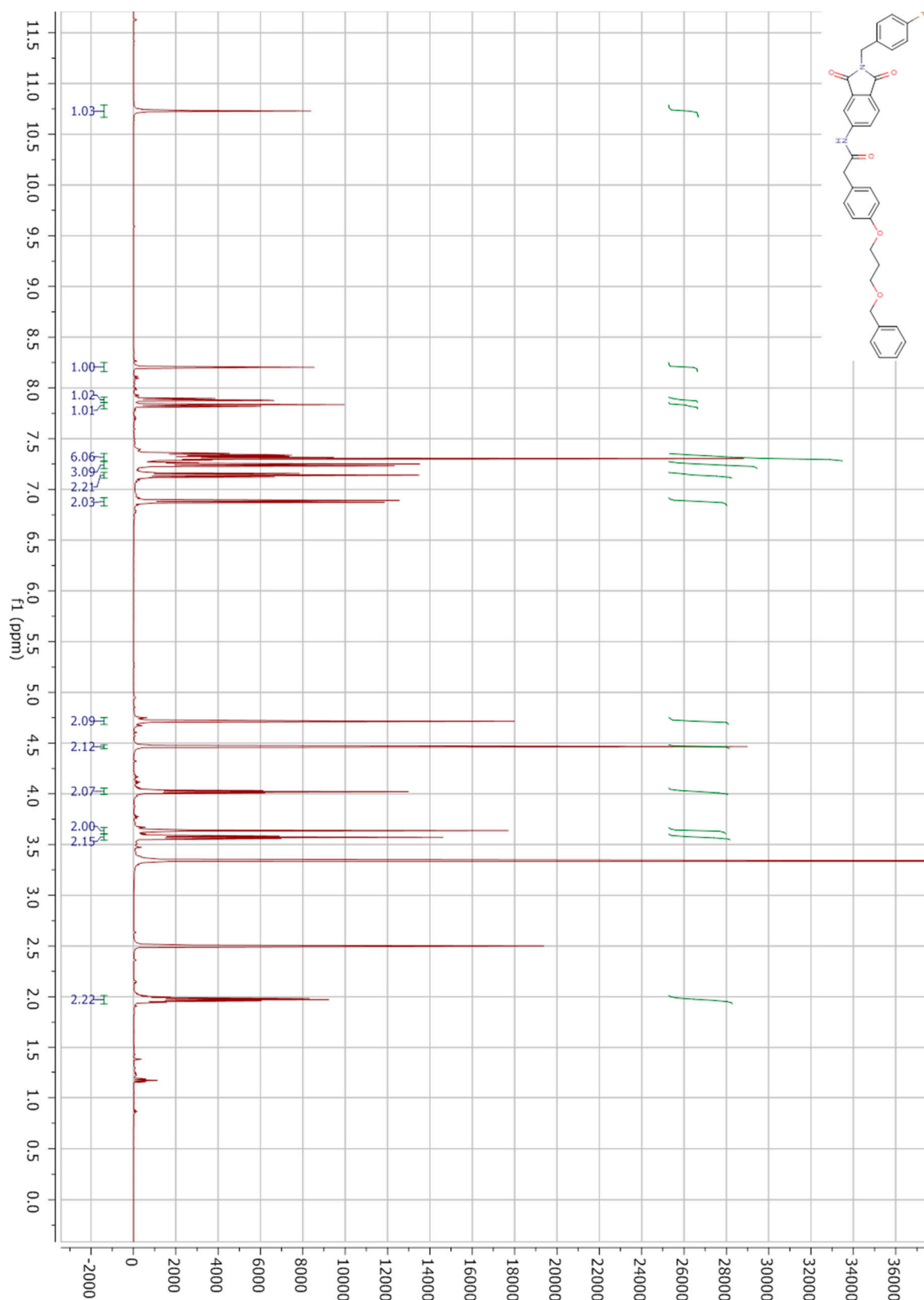


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-(4-([10-(benzyloxy)decyl]oxy}phenyl)acetamide (**12j**; ZHAWOC6932)

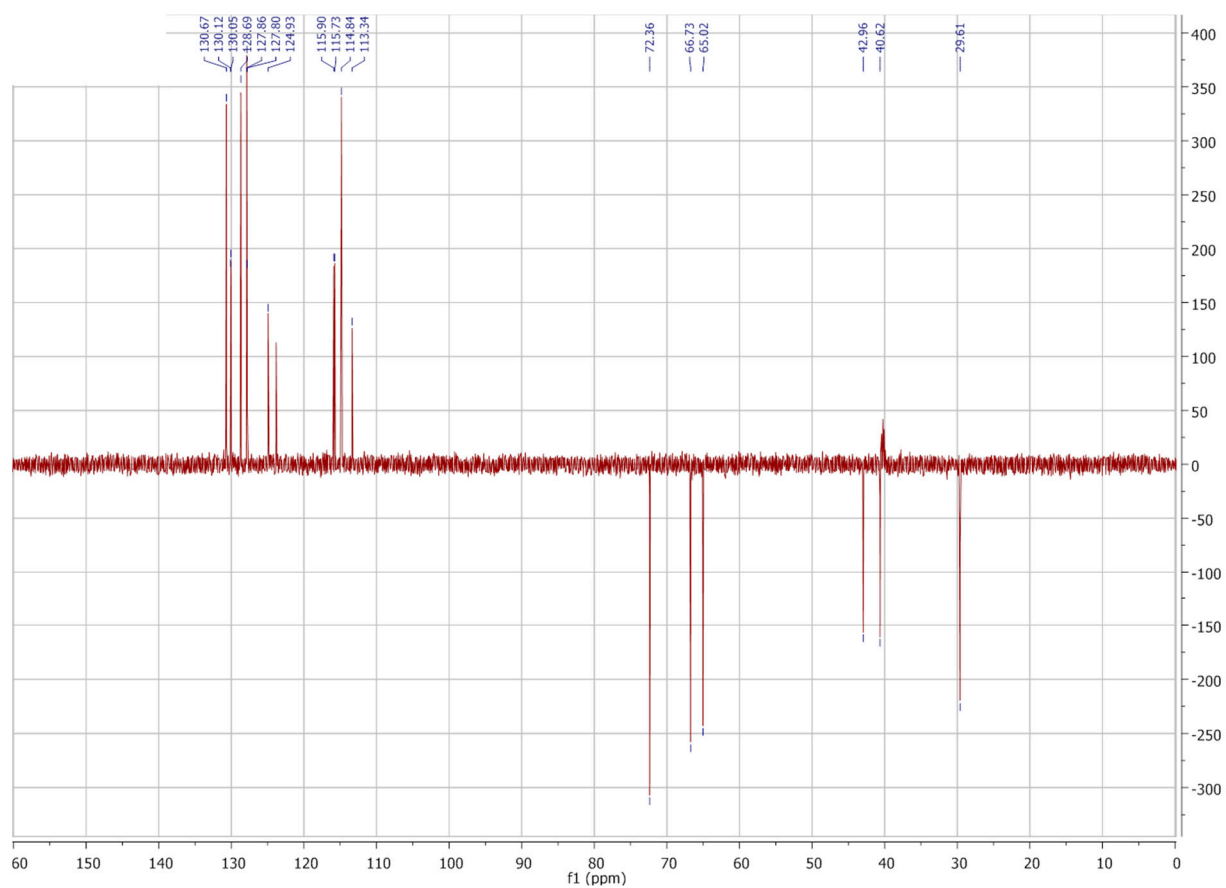
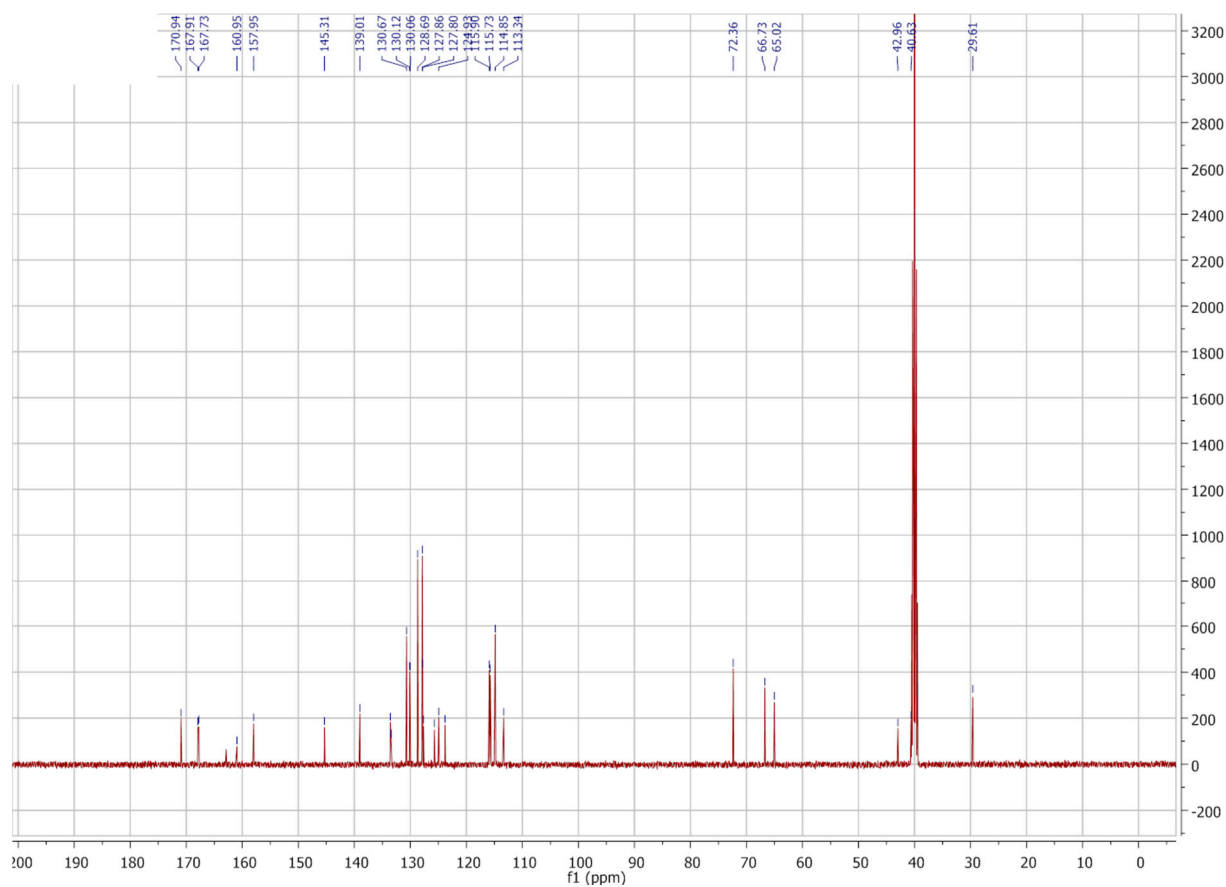


2-{4-[3-(benzyloxy)propoxy]phenyl}-N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl}acetamide (**12k**; ZHAWOC6641)

NMR

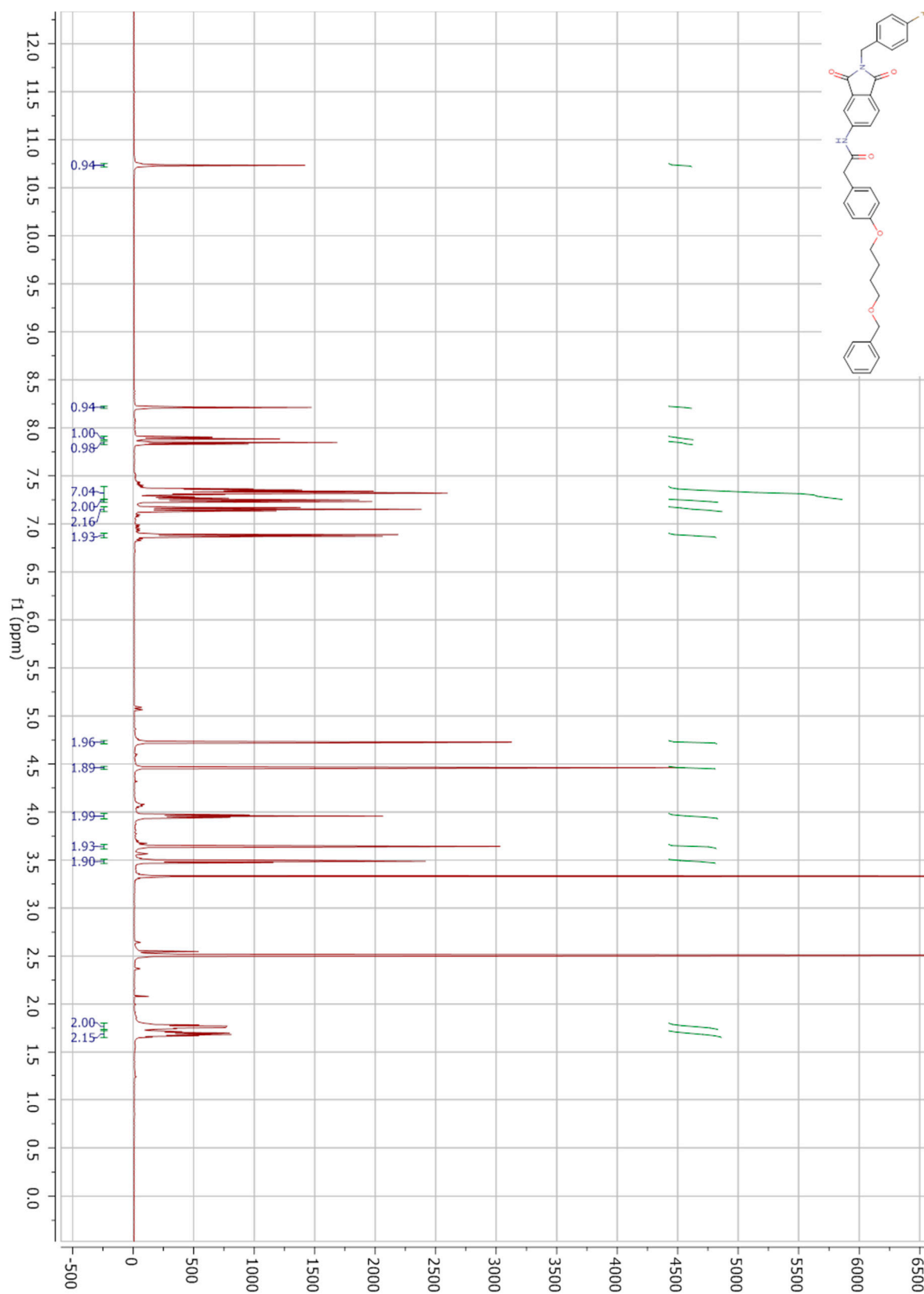


2-{4-[3-(benzyloxy)propoxy]phenyl}-N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl}acetamide (**12k**; ZHAWOC6641)

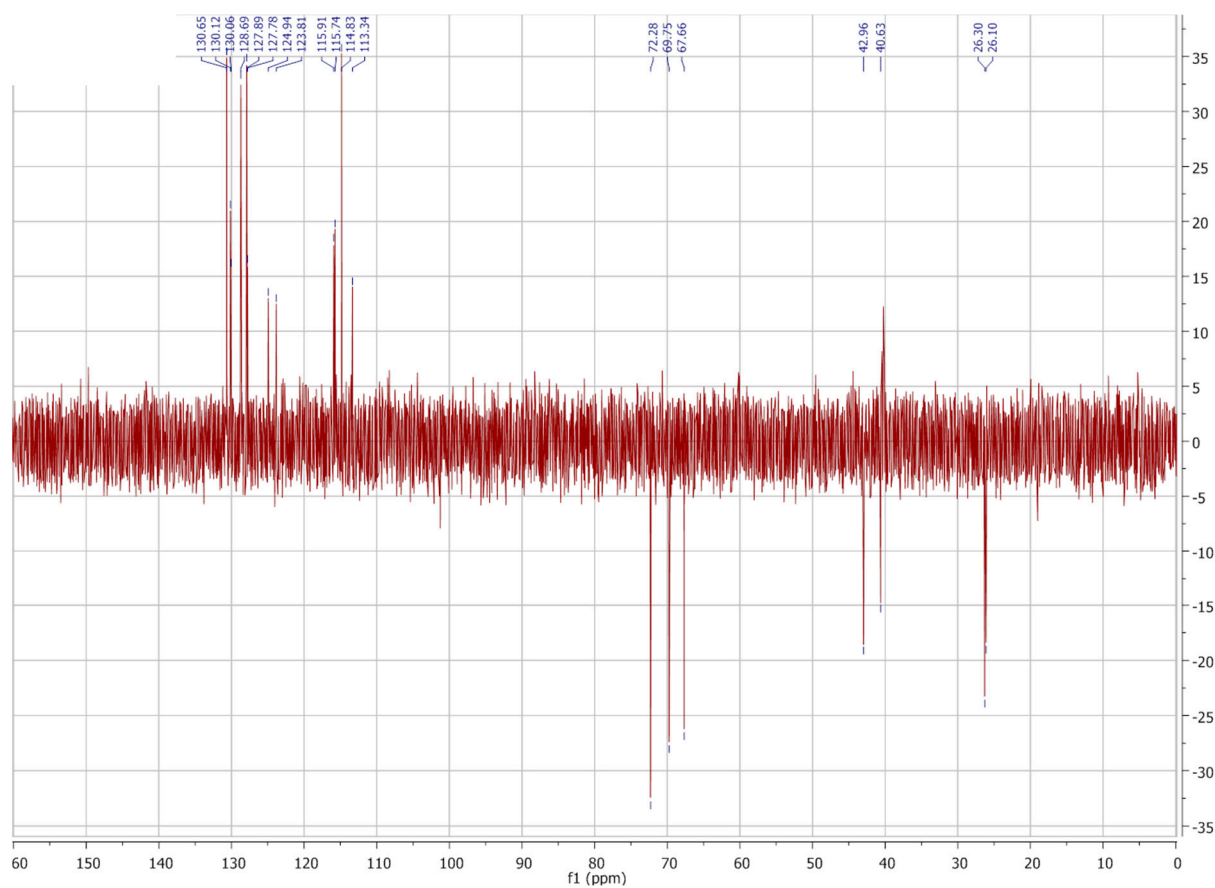
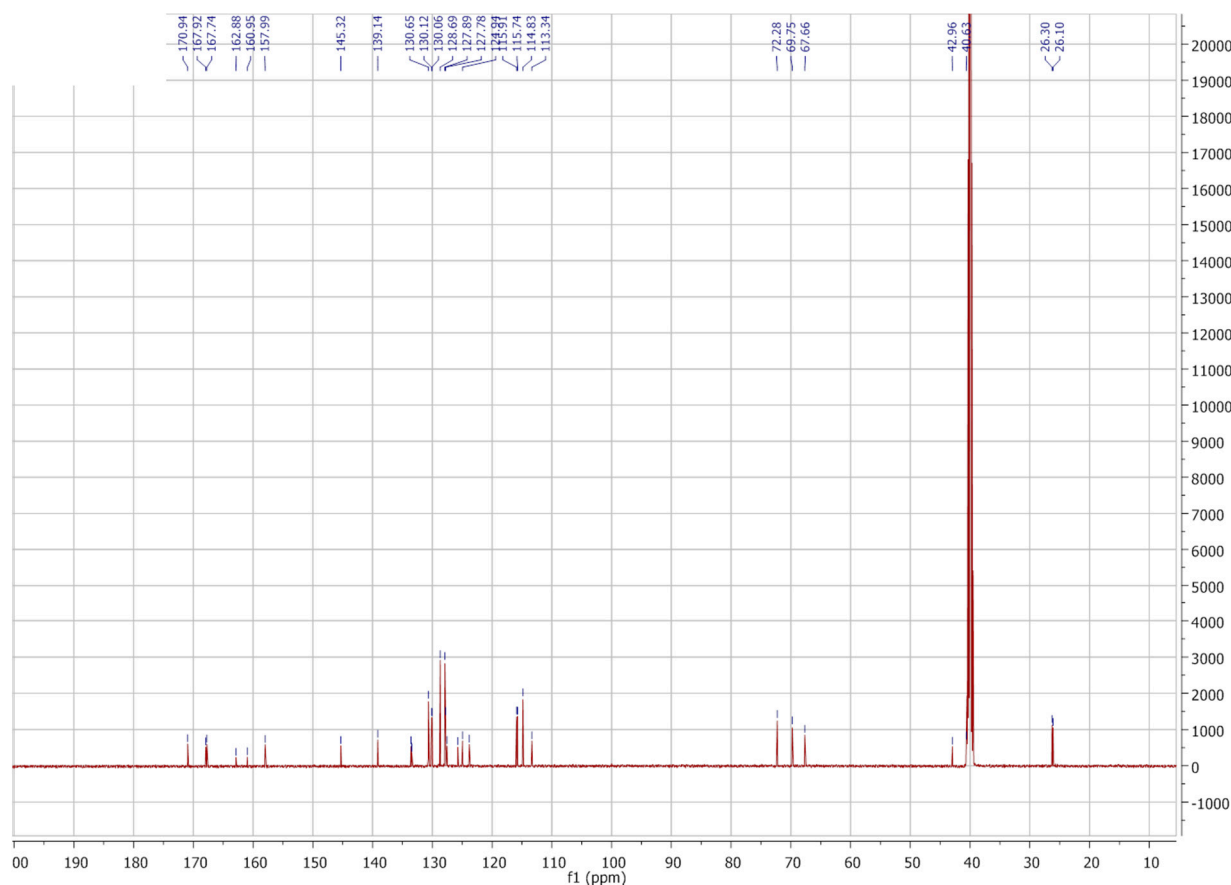


2-{4-[4-(benzyloxy)butoxy]phenyl}-N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl}acetamide (**12l**; ZHAWOC7102)

NMR

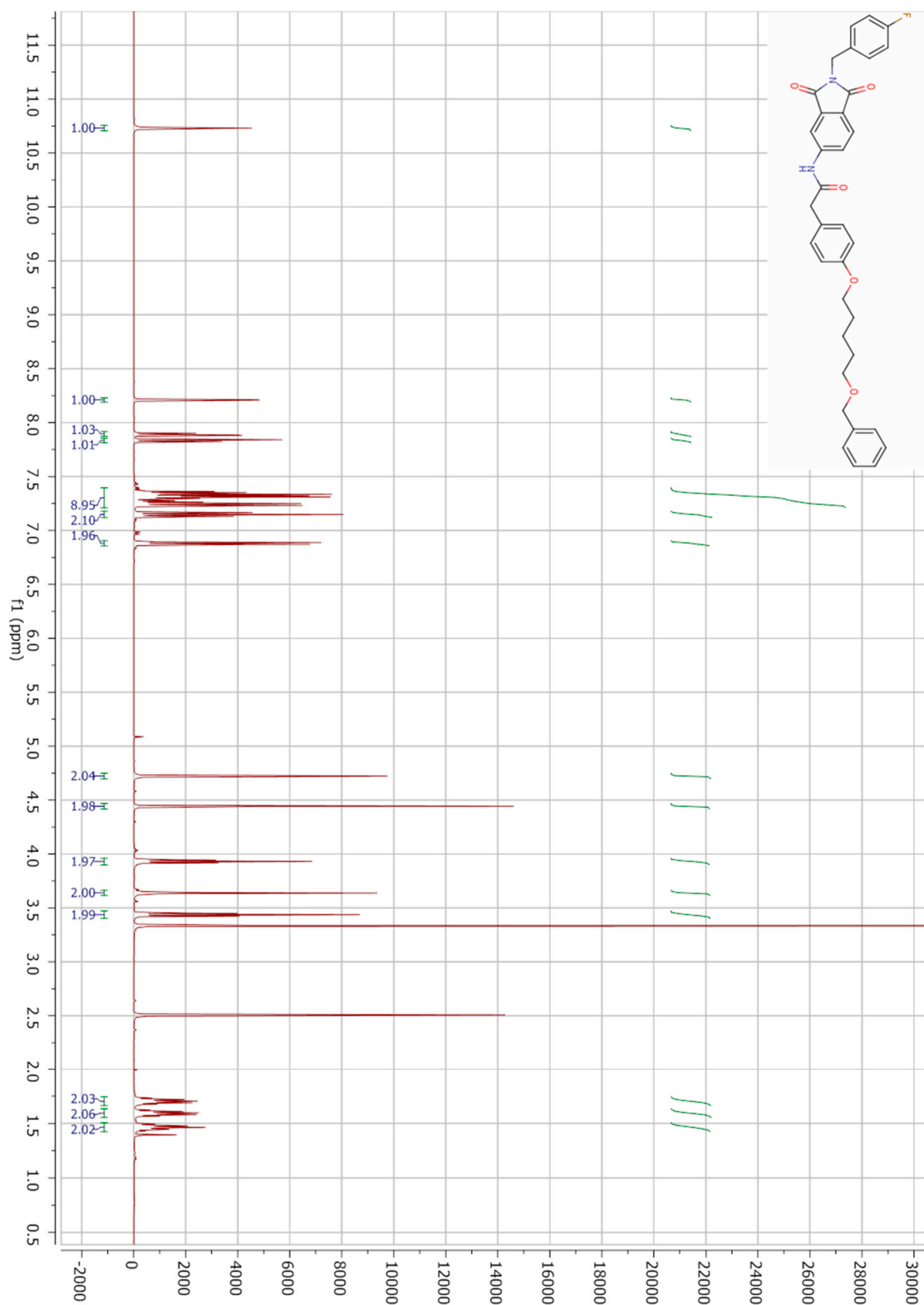


2-{4-[4-(benzyloxy)butoxy]phenyl}-N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl}acetamide (**12l**; ZHAWOC7102)

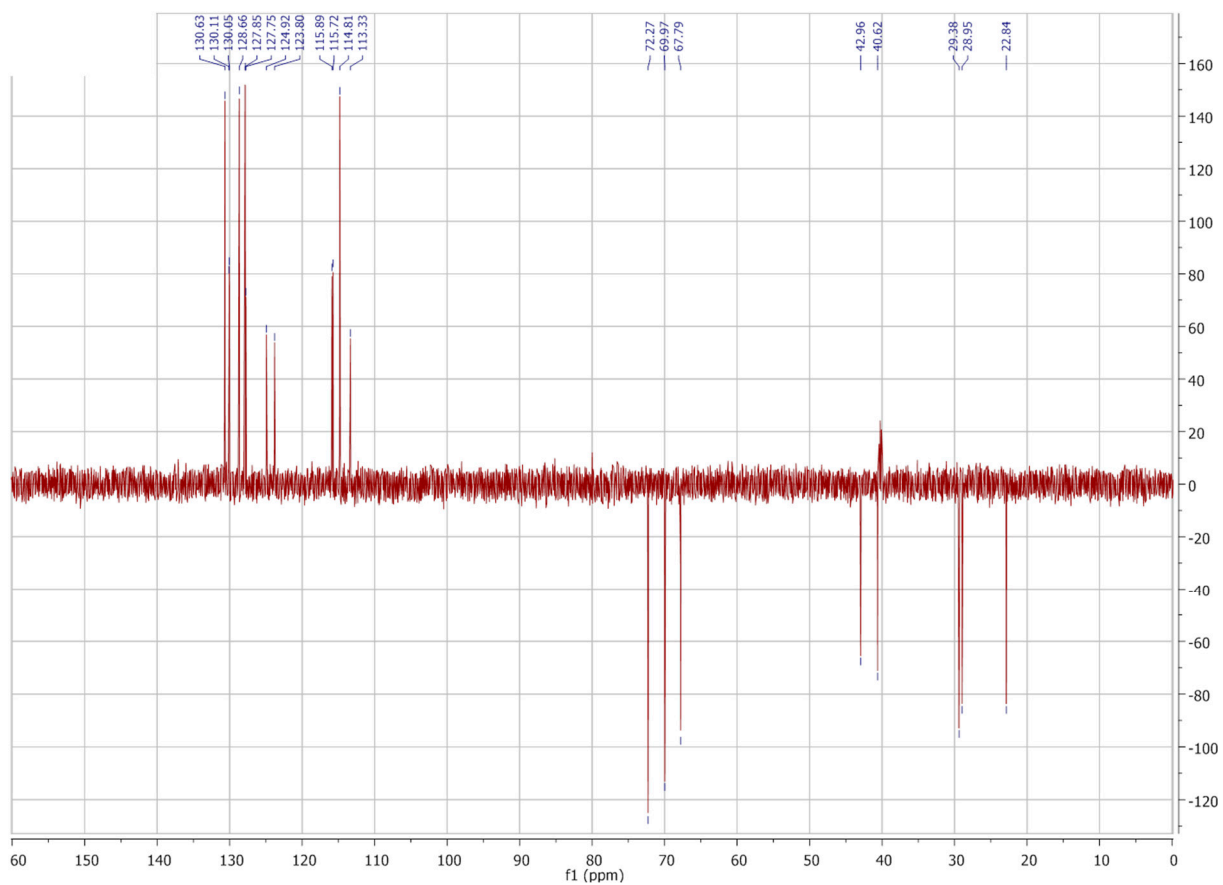
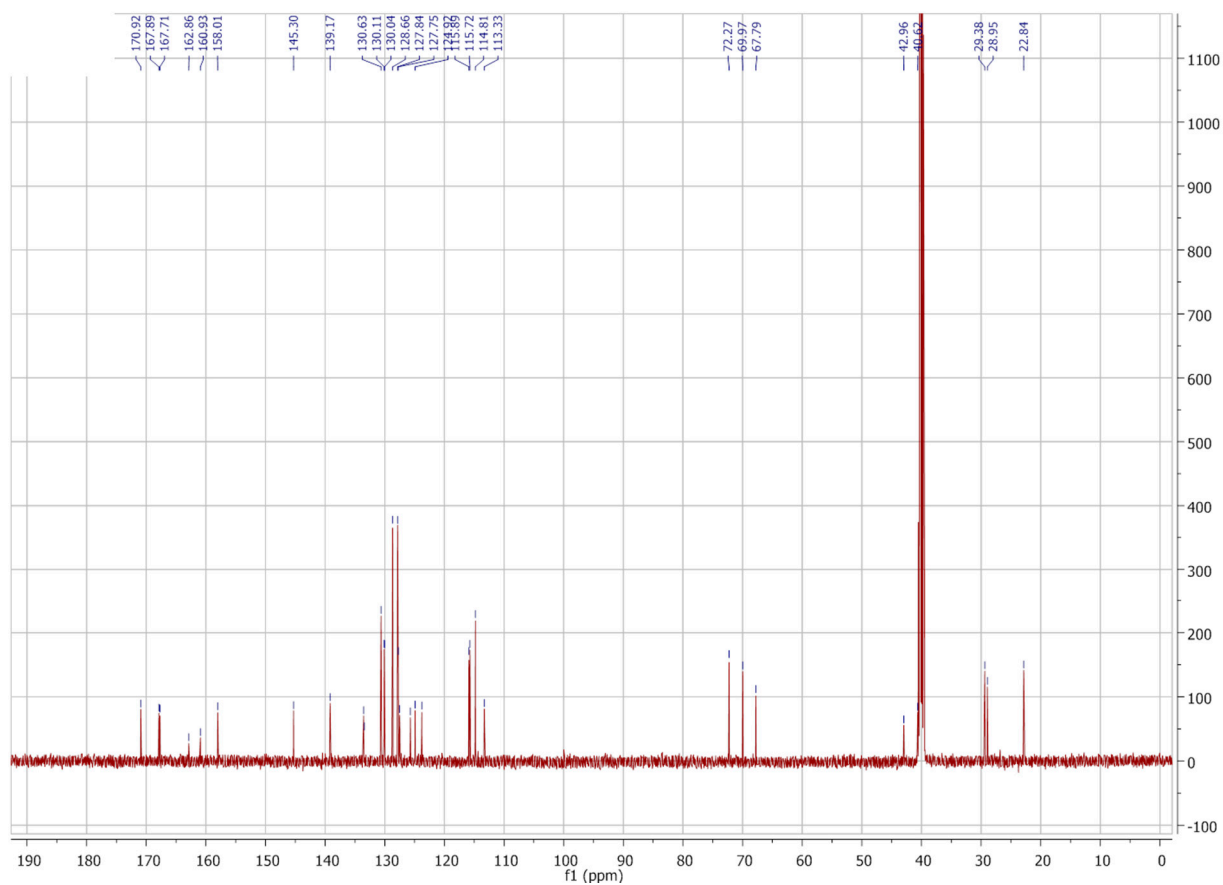


2-(4-{{5-(benzyloxy)pentyl}oxy}phenyl)-N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl}acetamide (**12m**; ZHAWOC5682)

NMR

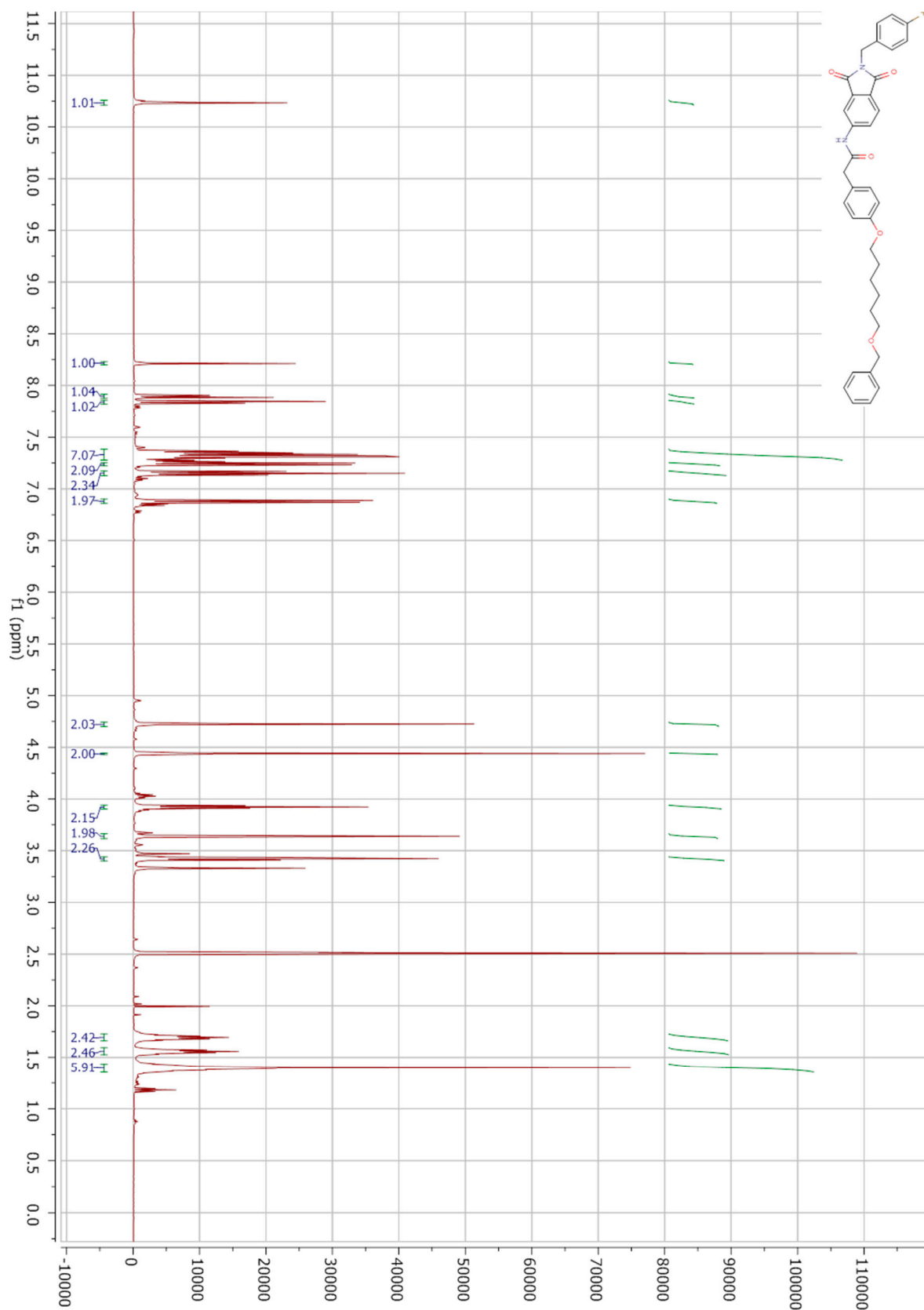


2-(4-{[5-(benzyloxy)pentyl]oxy}phenyl)-N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl}acetamide (**12m**; ZHAWOC5682)

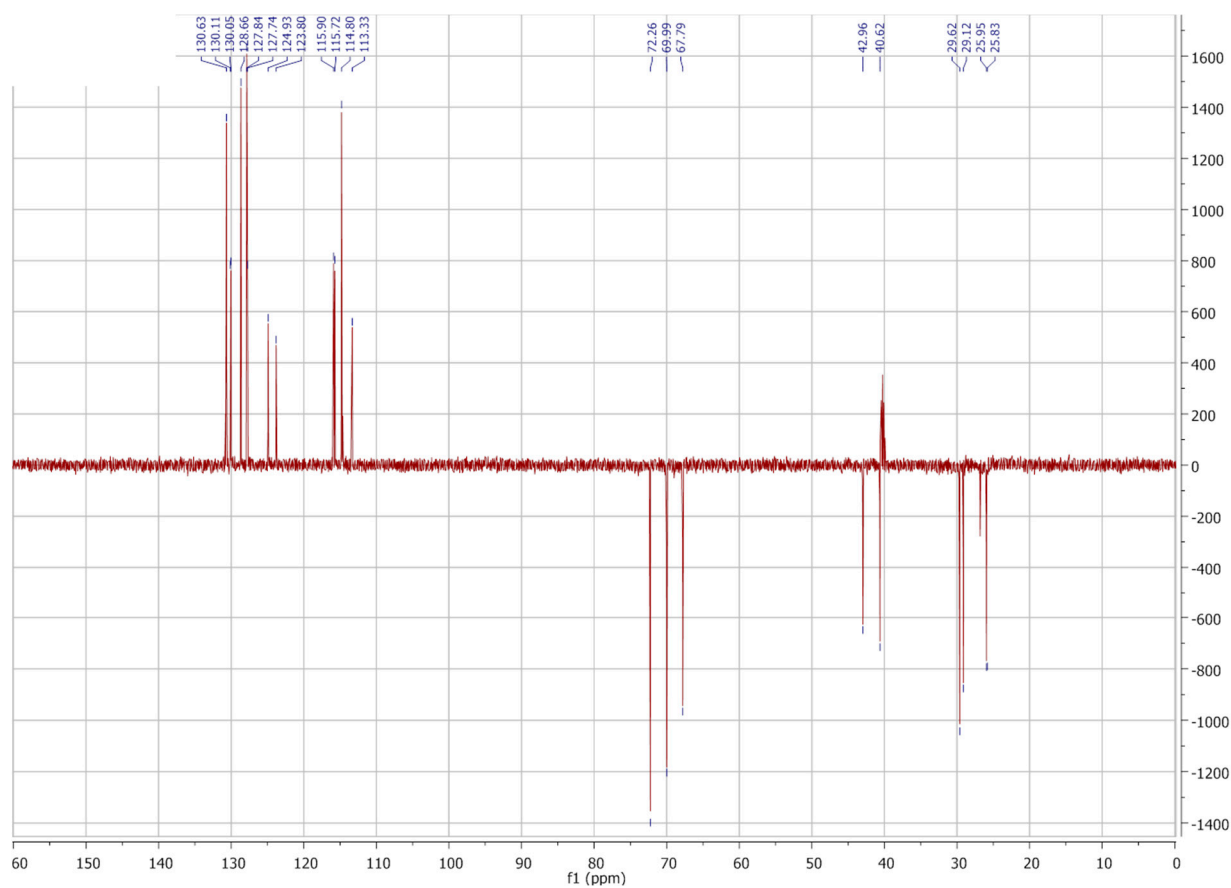
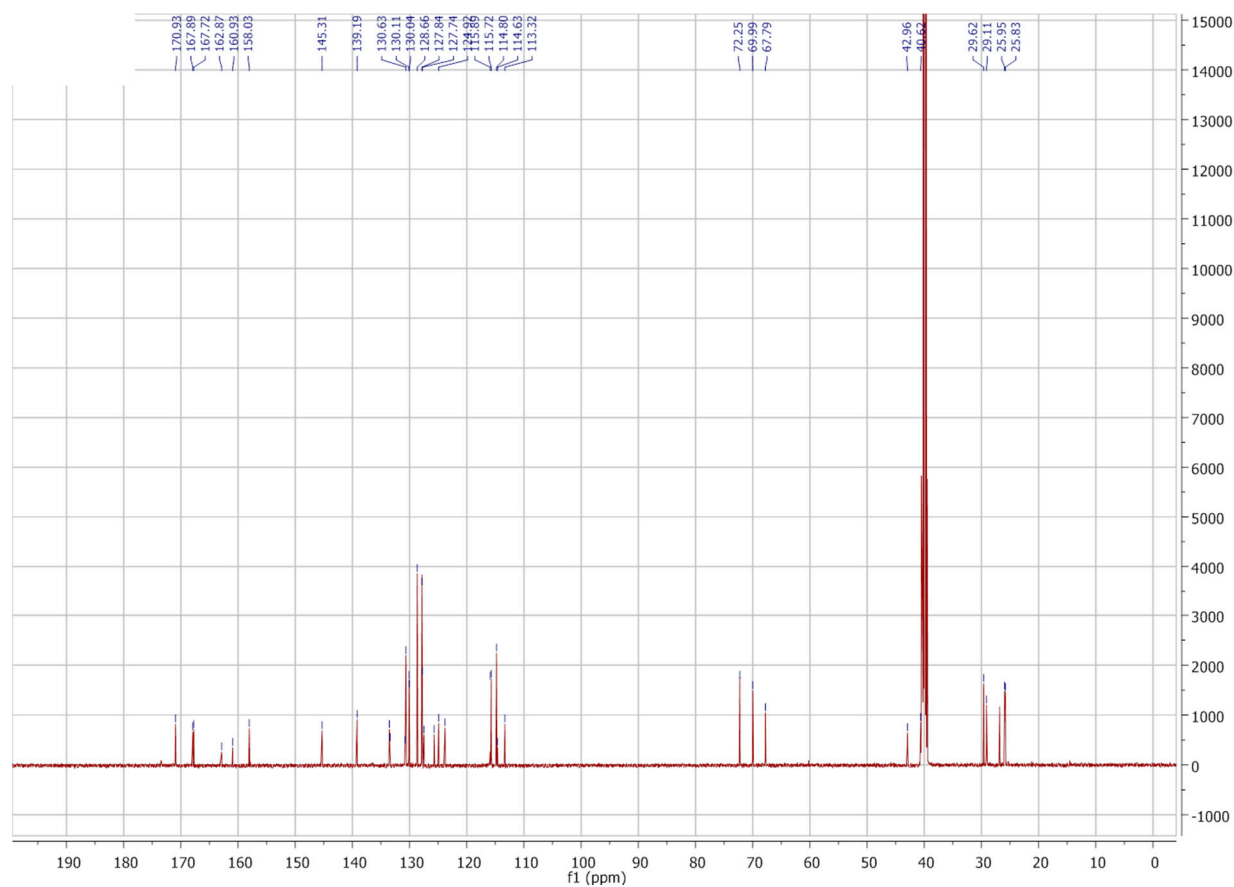


2-(4-{[6-(benzyloxy)hexyl]oxy}phenyl)-N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl}acetamide (**12n**; ZHAWOC6640)

NMR

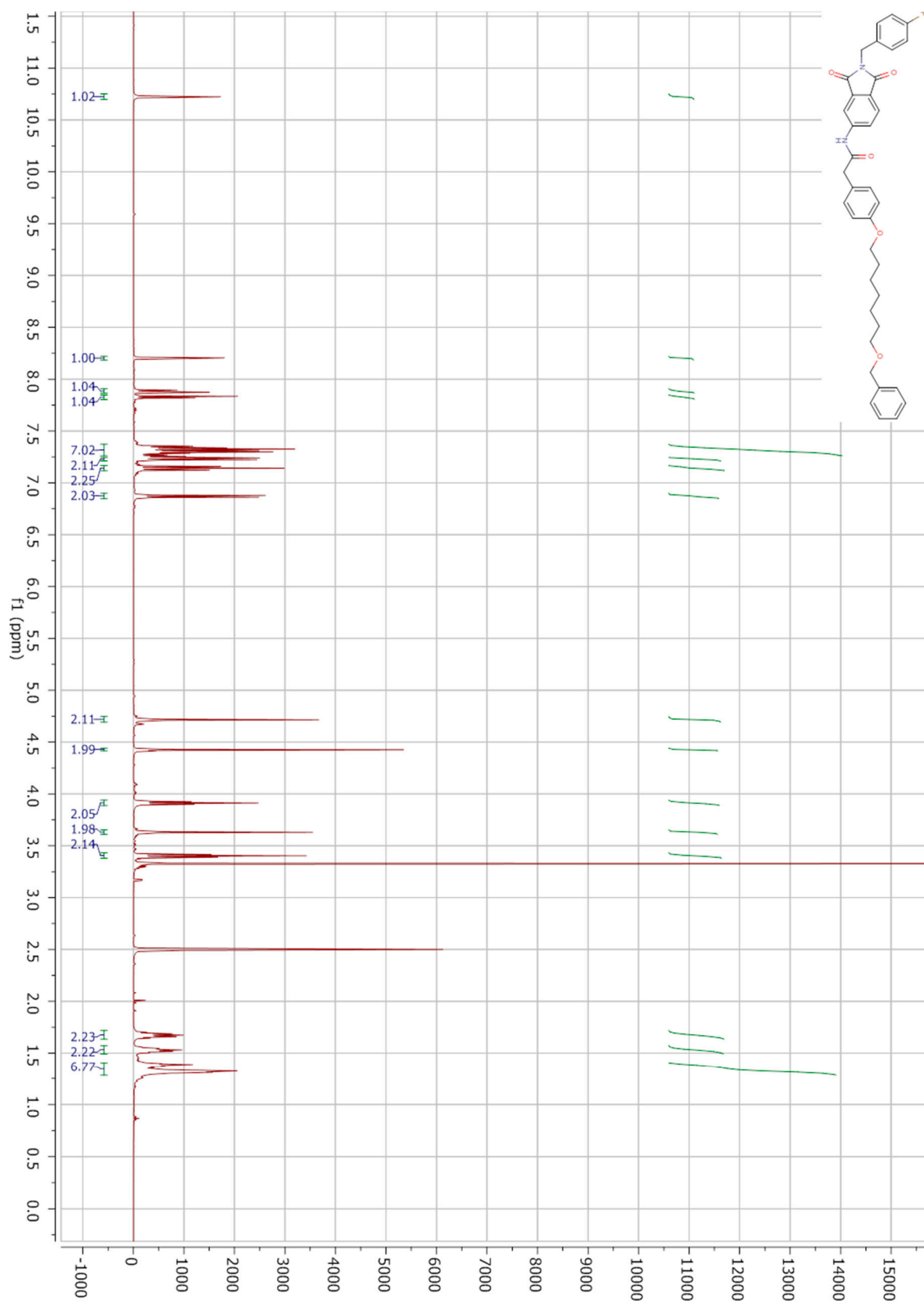


2-(4-{[6-(benzyloxy)hexyl]oxy}phenyl)-N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl}acetamide (**12n**; ZHAWOC6640)

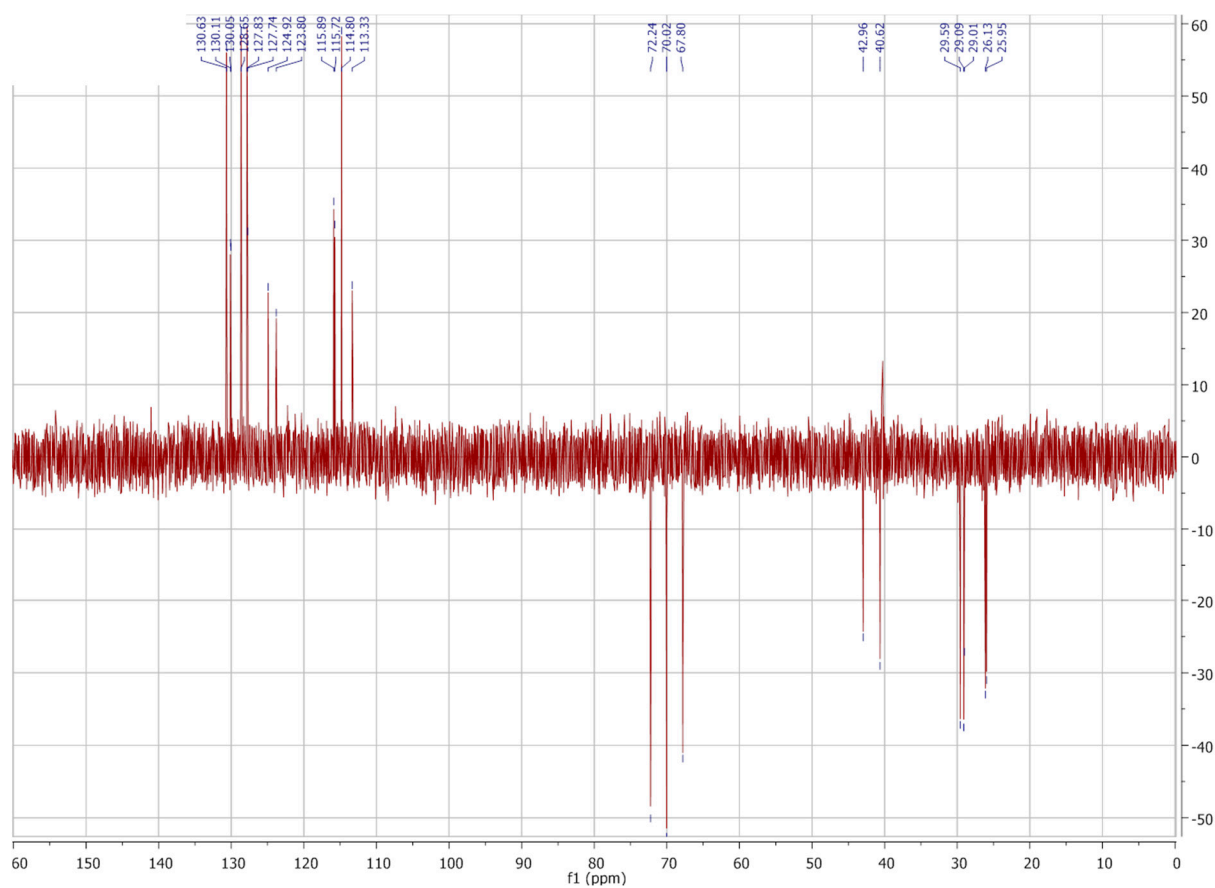
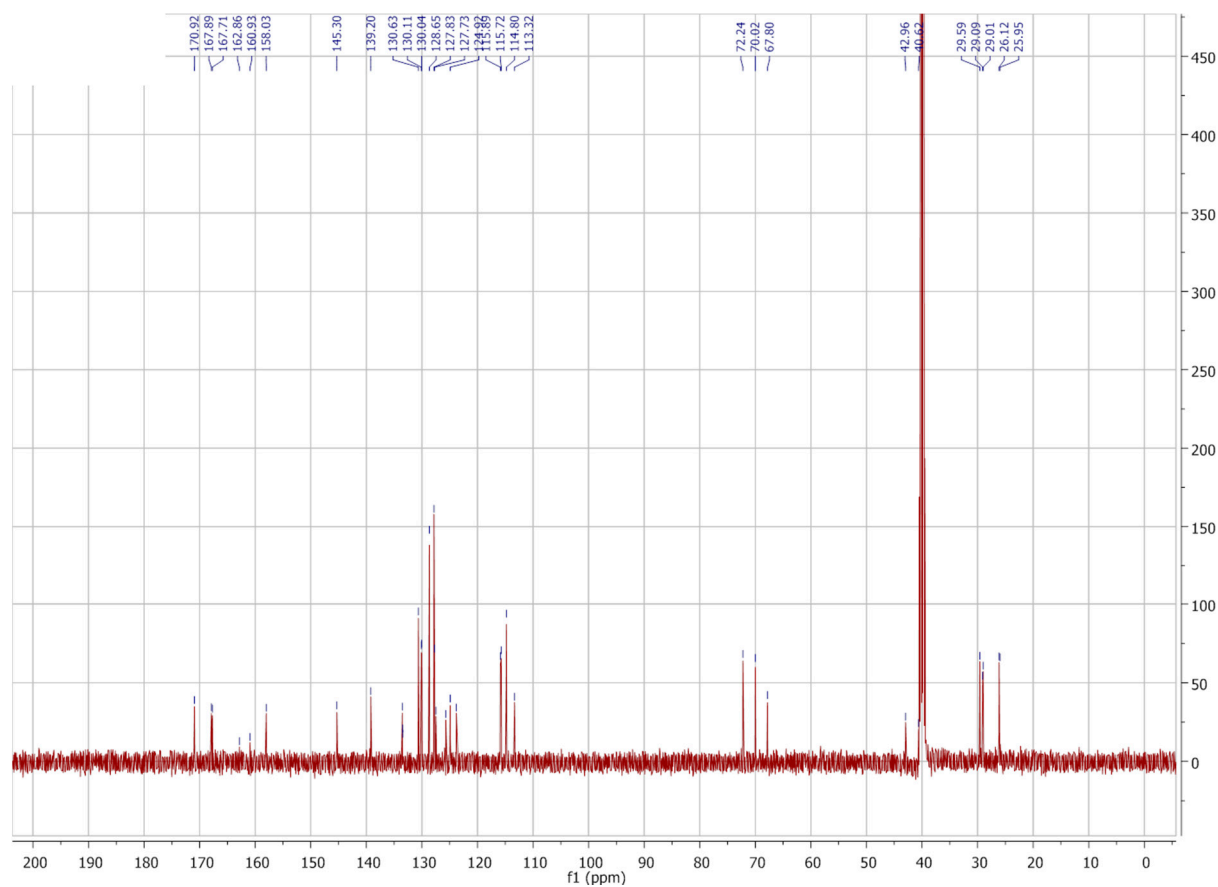


2-(4-{[7-(benzyloxy)heptyl]oxy}phenyl)-N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl}acetamide (**12o**; ZHAWOC6635)

NMR

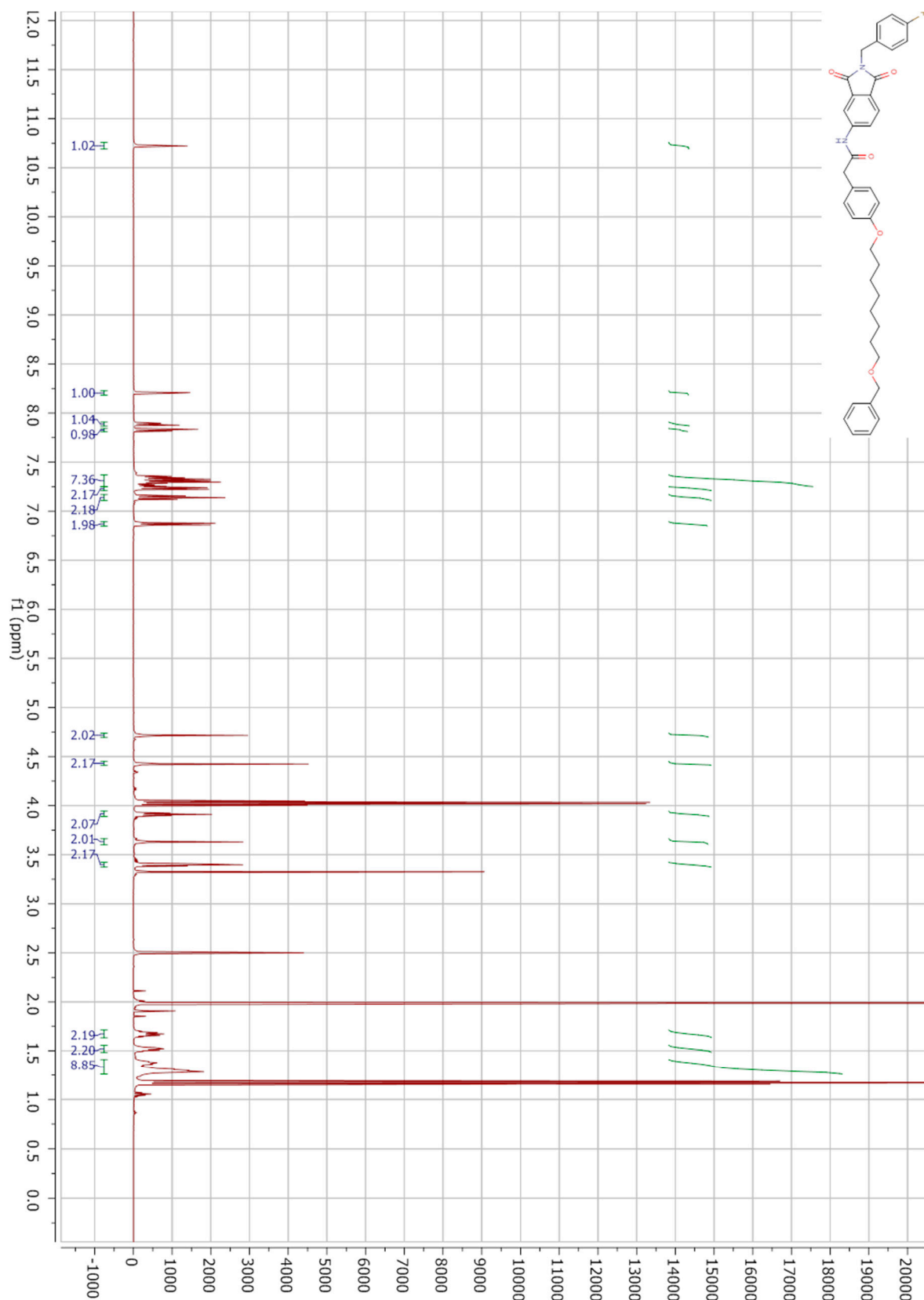


2-(4-{[7-(benzyloxy)heptyl]oxy}phenyl)-N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl}acetamide (**12o**; ZHAWOC6635)

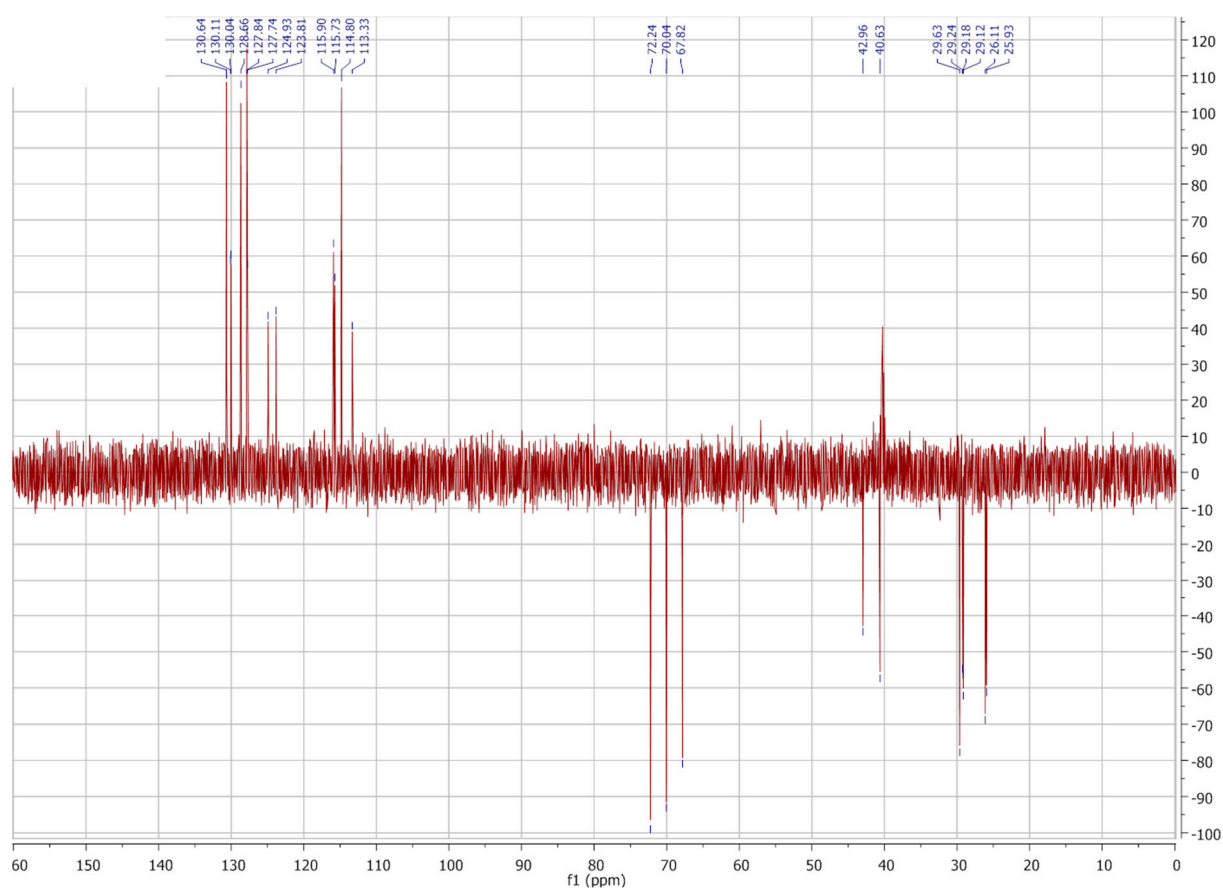
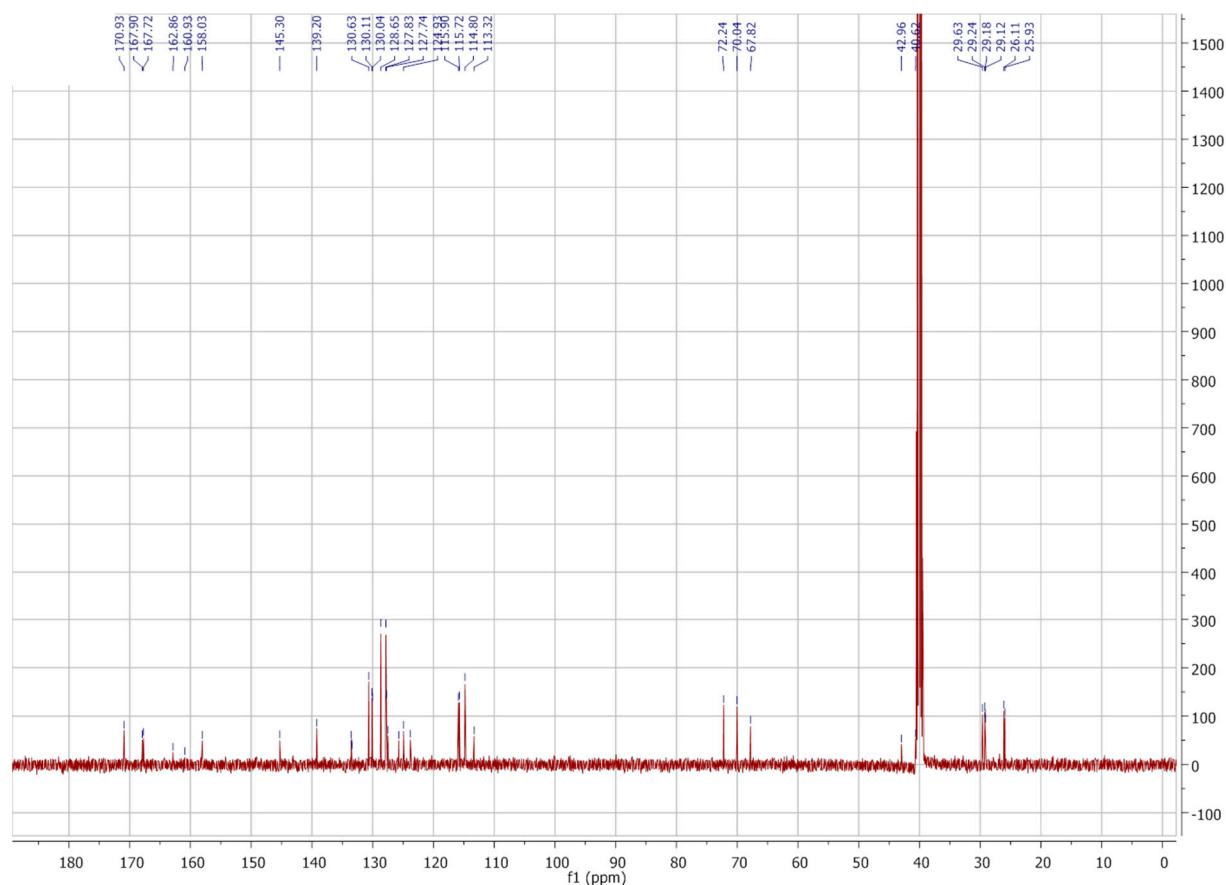


2-(4-{[8-(benzyloxy)octyl]oxy}phenyl)-N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl}acetamide (**12p**; ZHAWOC6638)

NMR

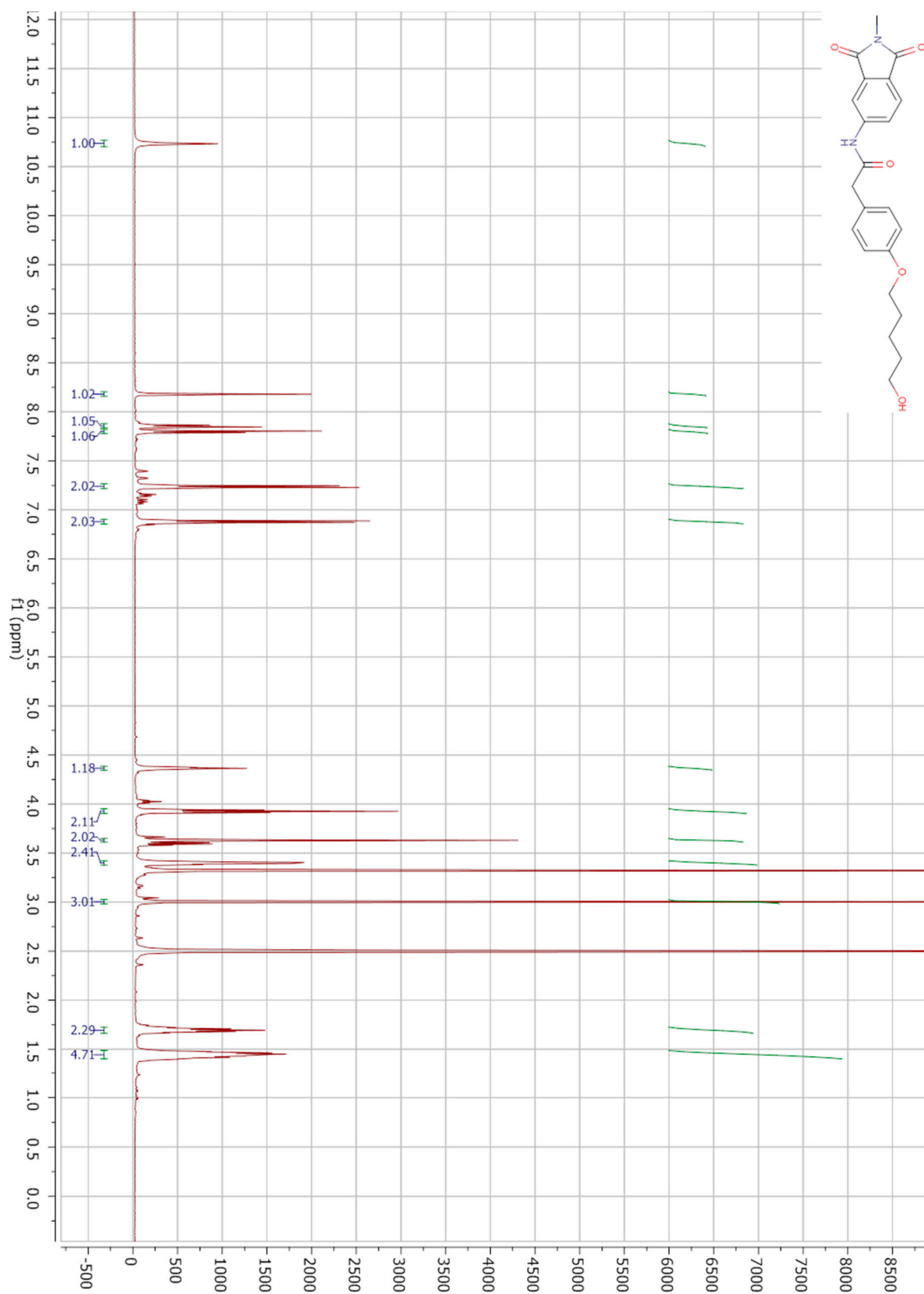


2-(4-{[8-(benzyloxy)octyl]oxy}phenyl)-N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl}acetamide (**12p**; ZHAWOC6638)

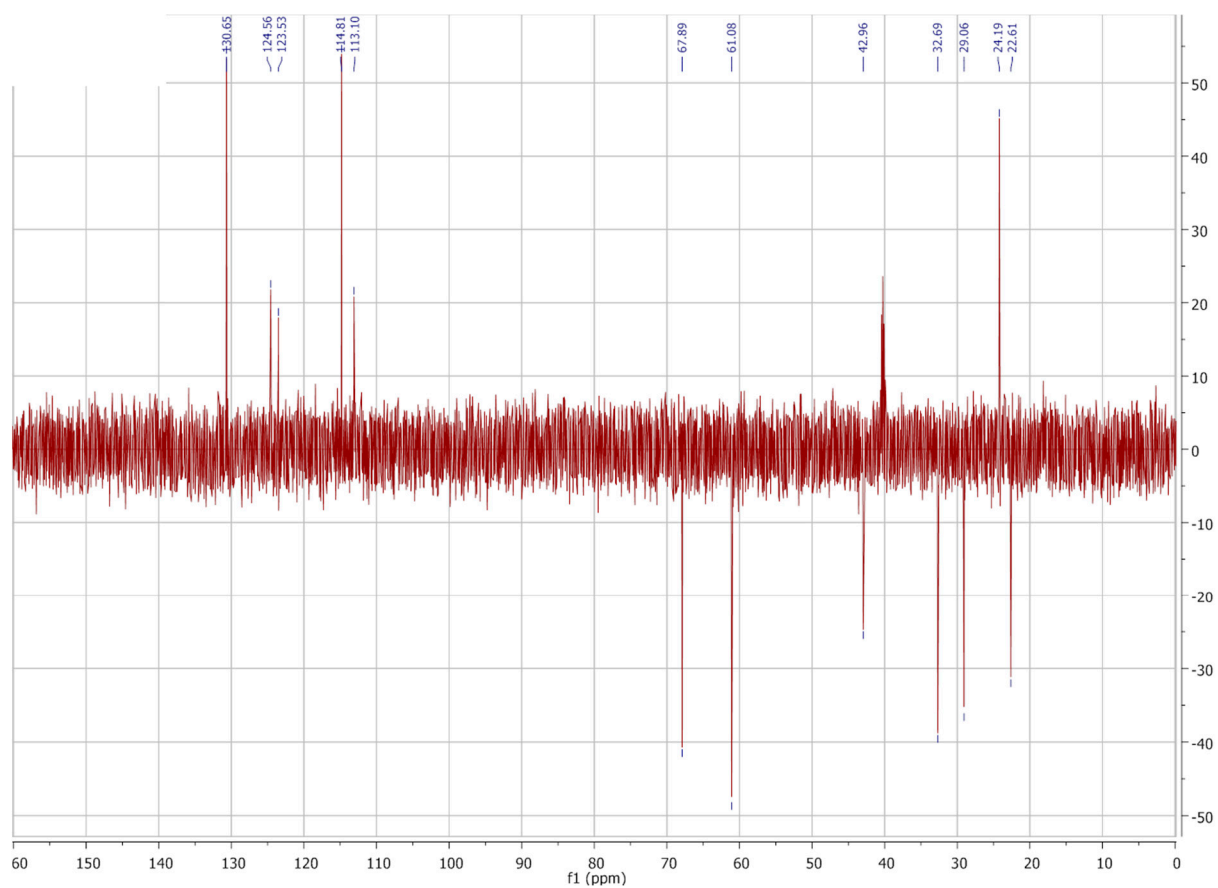
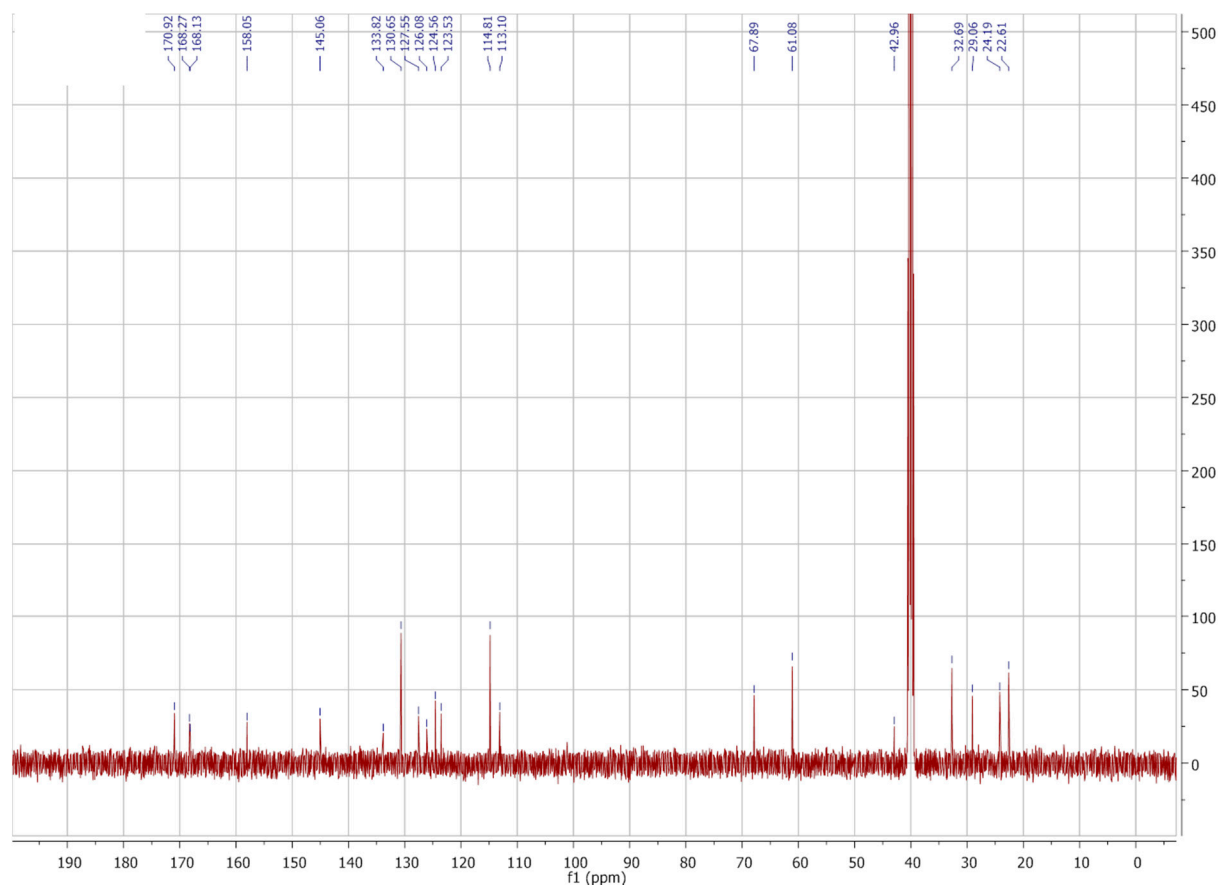


2-{4-[(5-hydroxypentyl)oxy]phenyl}-N-(2-methyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)acetamide (**13a**; ZHAWOC6648)

NMR

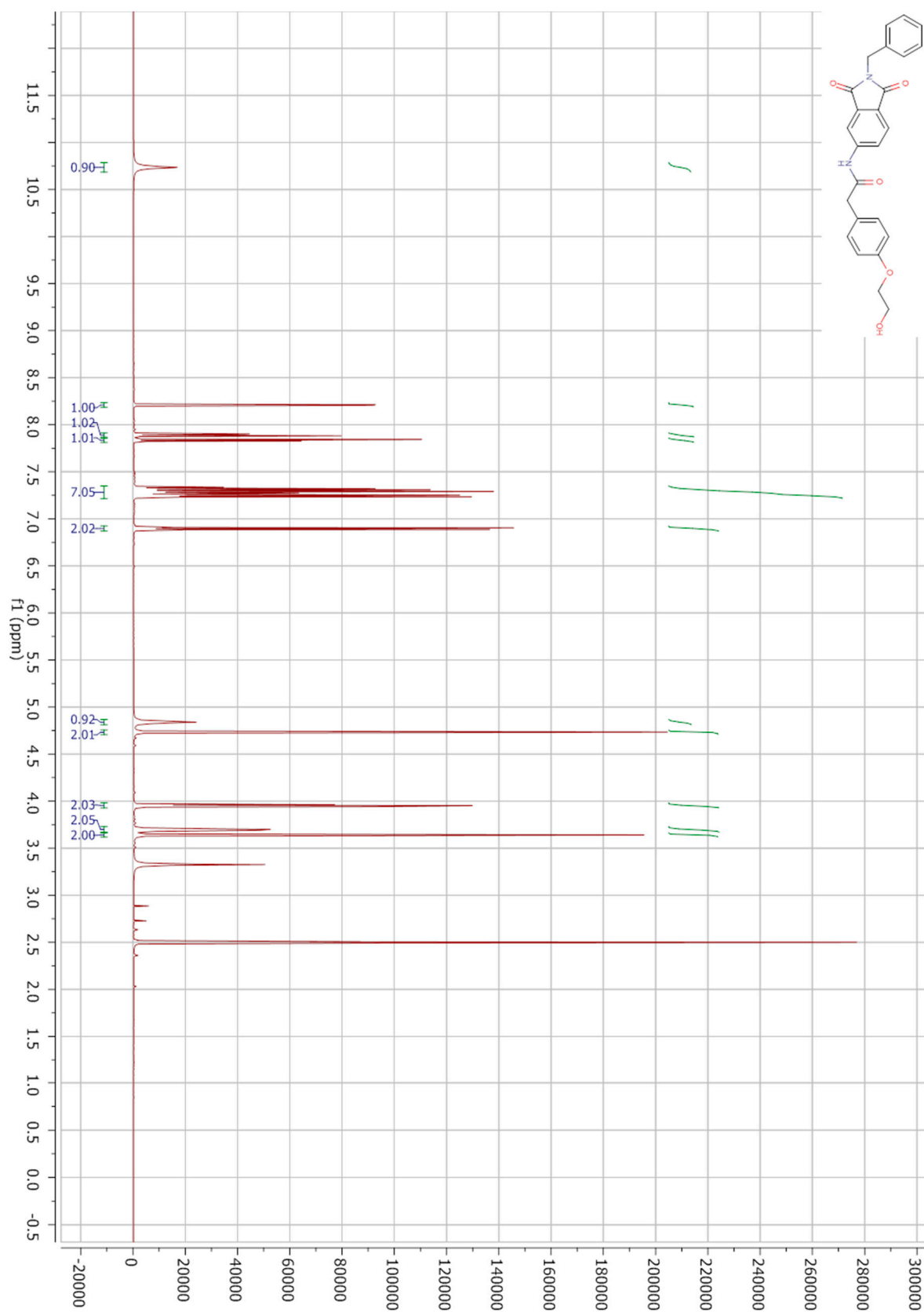


2-{4-[(5-hydroxypentyl)oxy]phenyl}-N-(2-methyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)acetamide (**13a**; ZHAWOC6648)

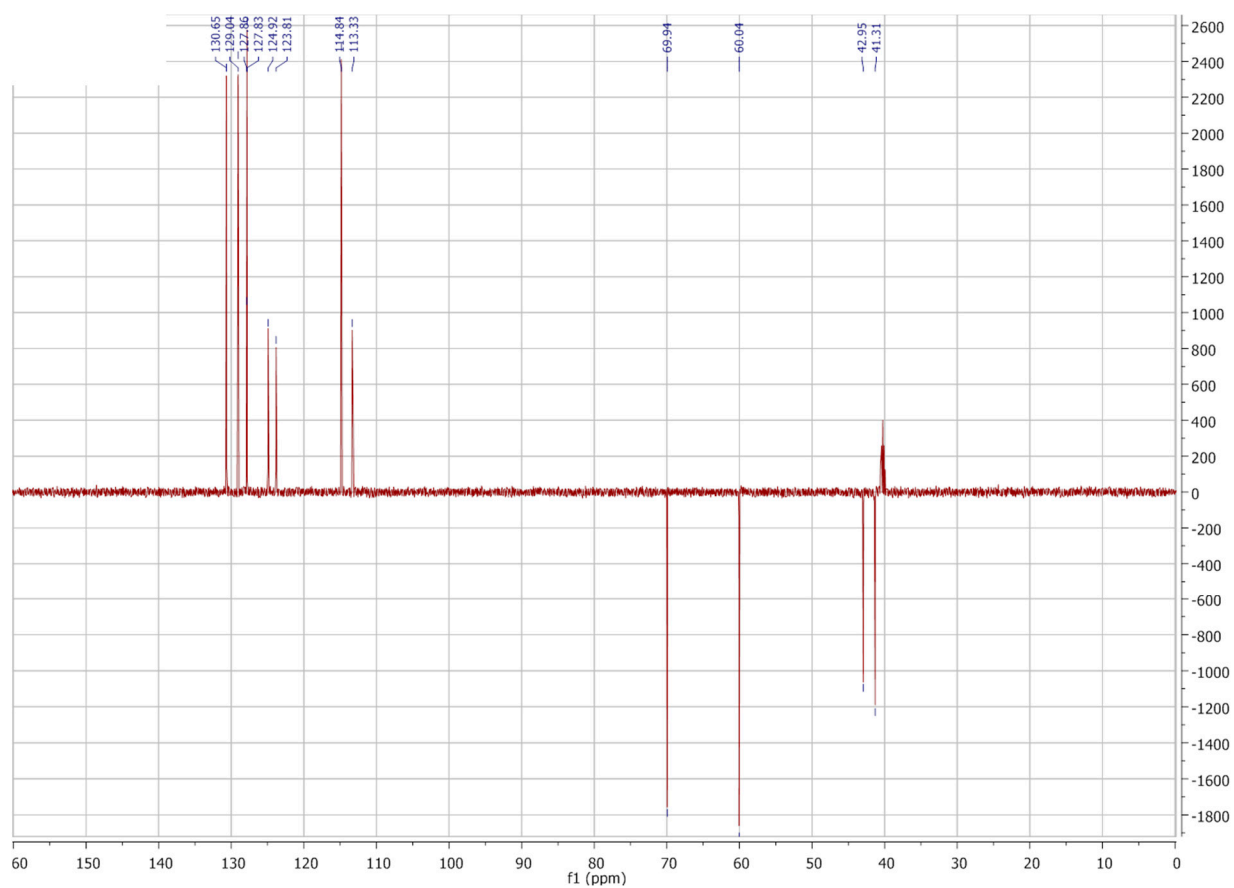
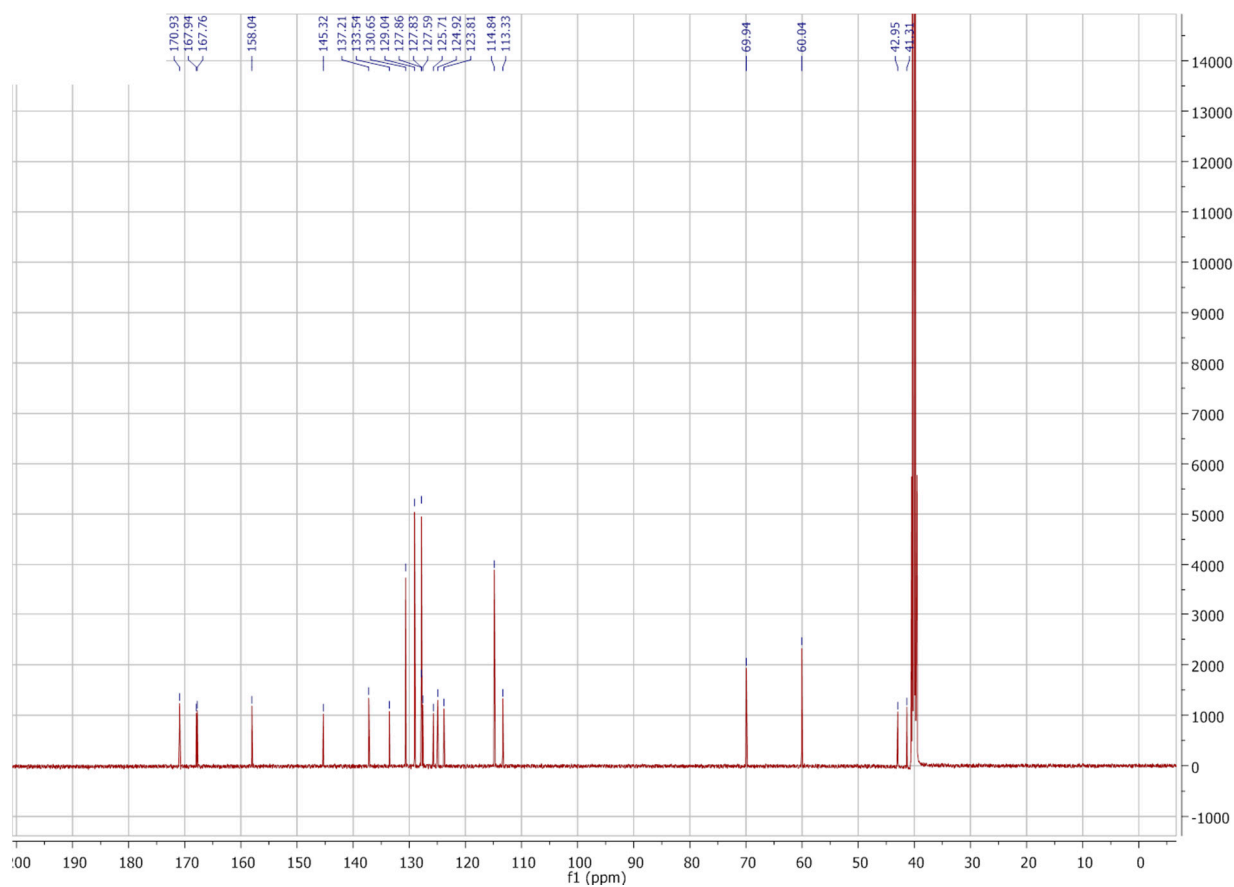


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-[4-(2-hydroxyethoxy)phenyl]acetamide (**13b**; ZHAWOC5473)

NMR

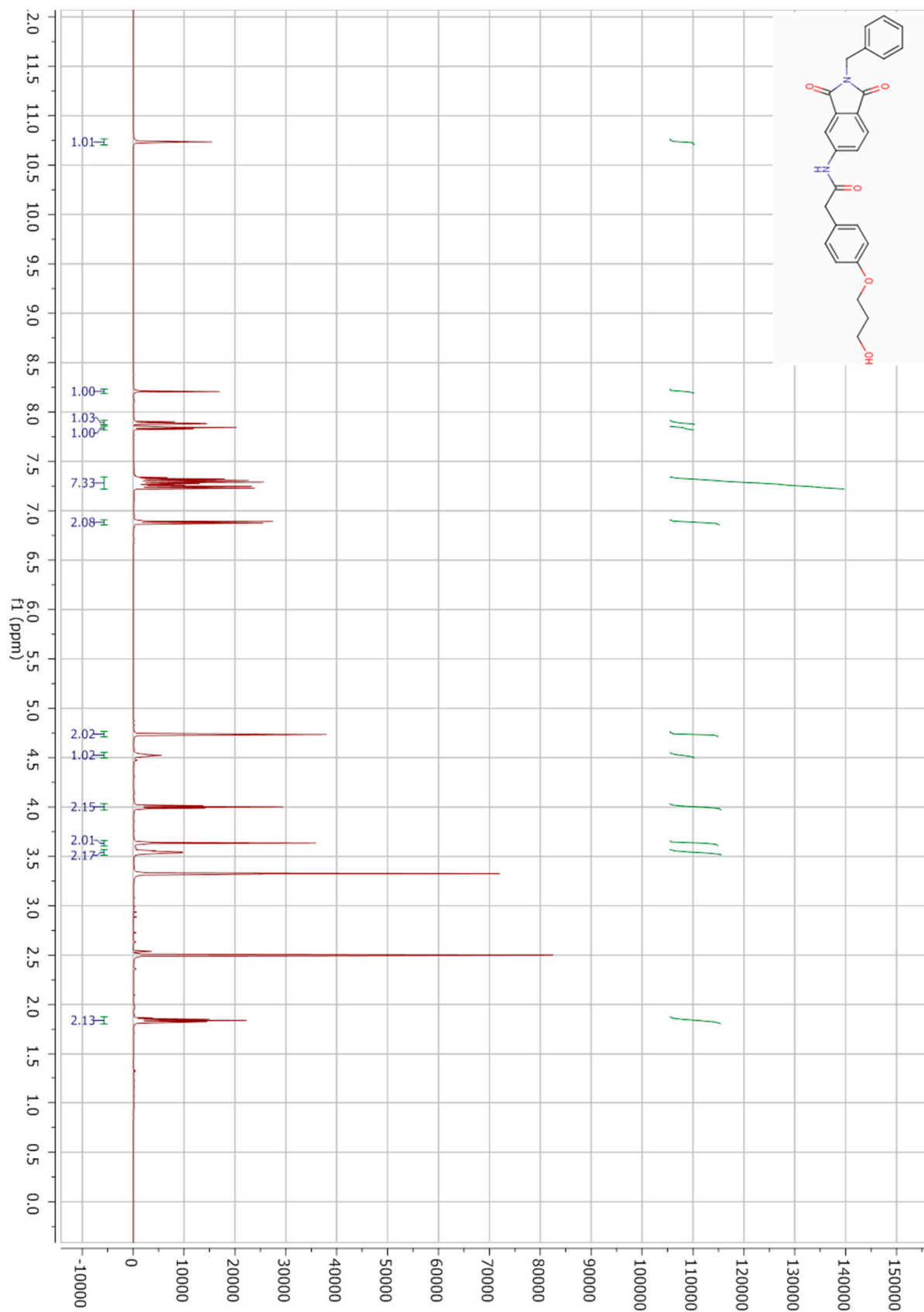


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-[4-(2-hydroxyethoxy)phenyl]acetamide (**13b**; ZHAWOC5473)

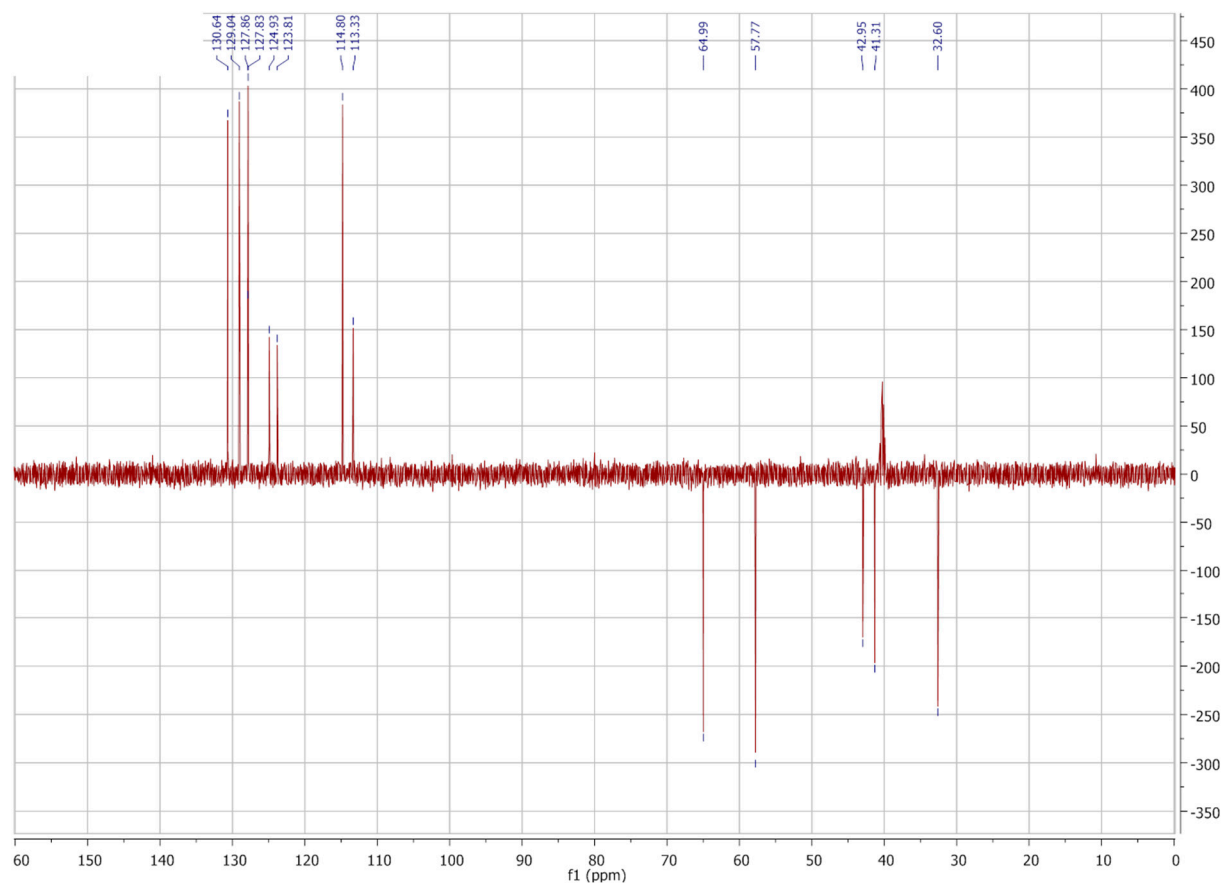
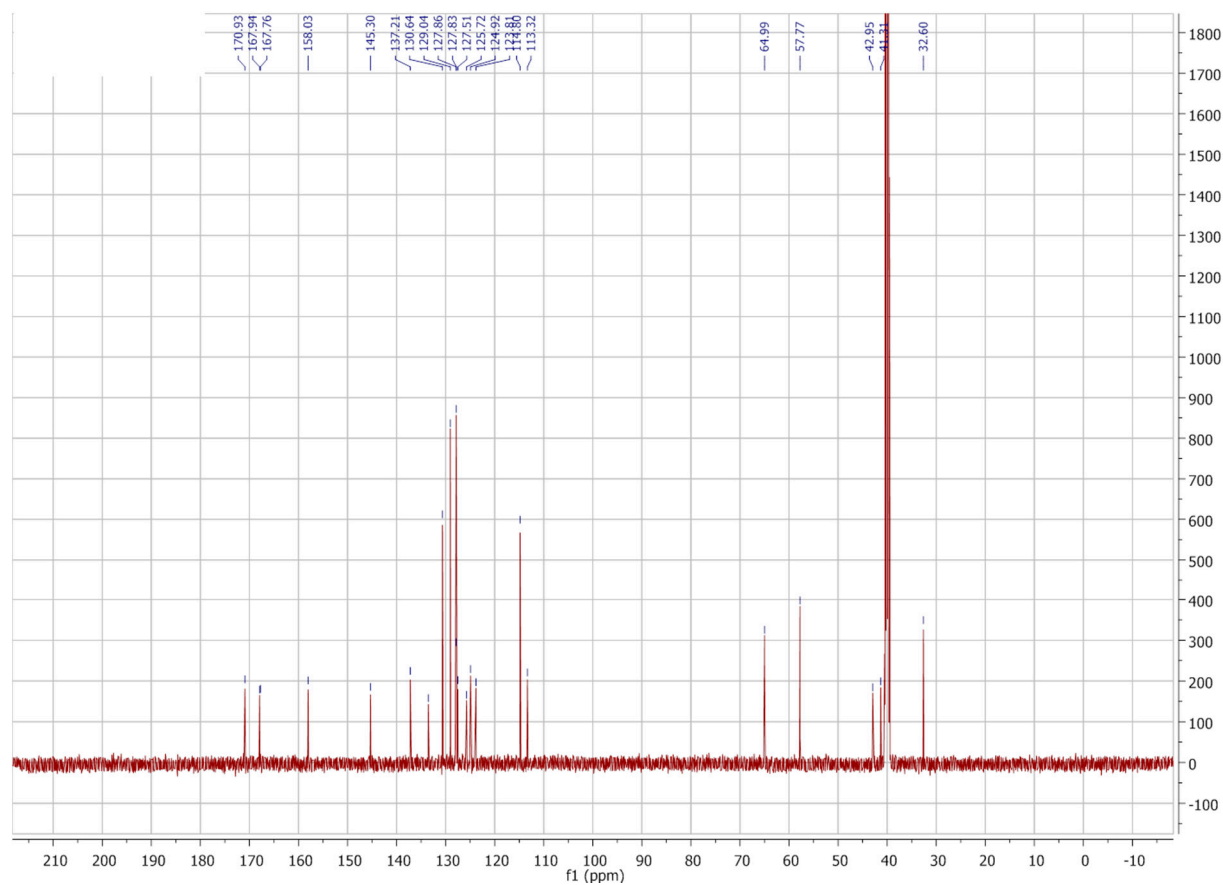


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-[4-(3-hydroxypropoxy)phenyl]acetamide (**13c**; ZHAWOC4512)

NMR

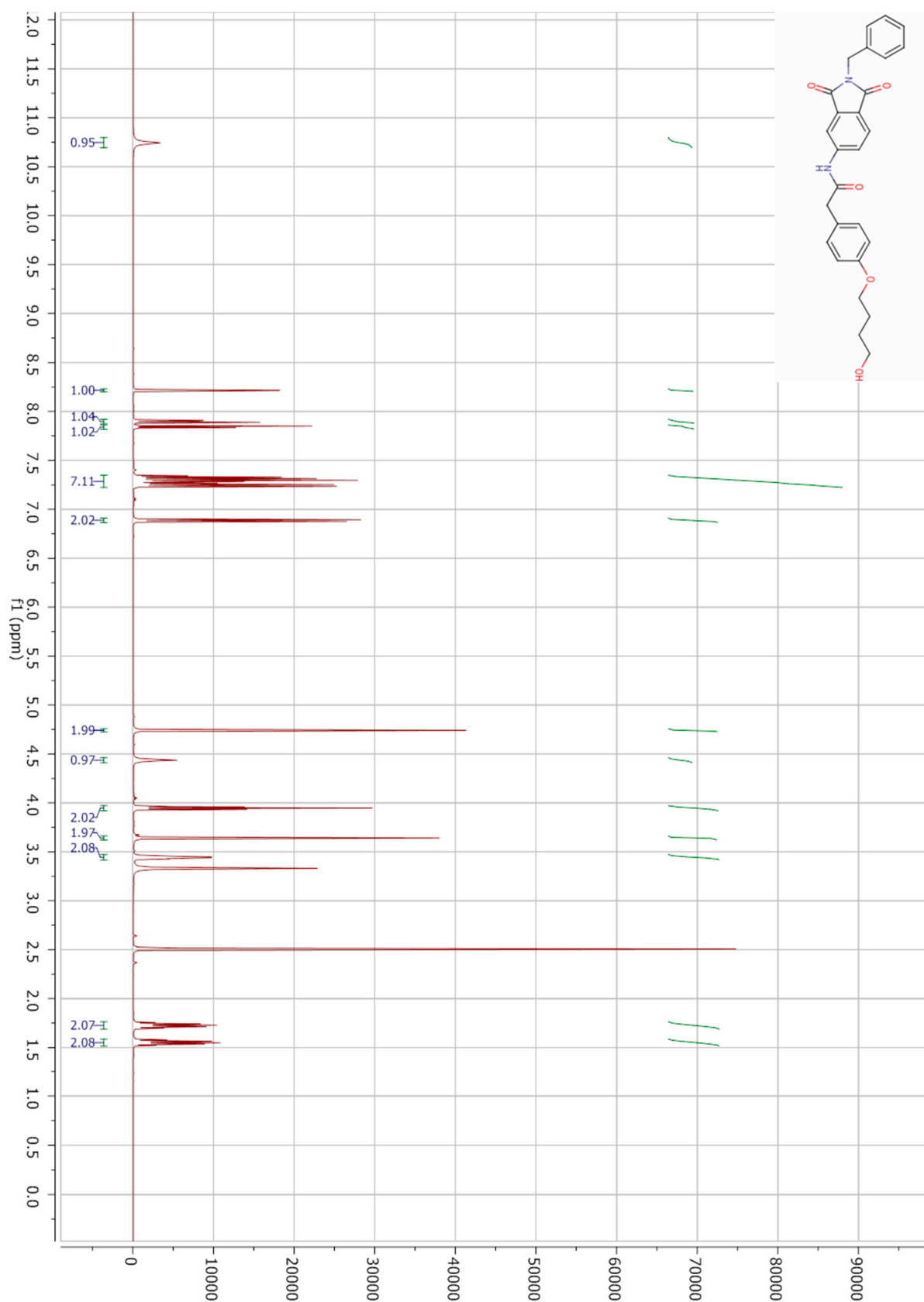


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-[4-(3-hydroxypropoxy)phenyl]acetamide (**13c**; ZHAWOC4512)

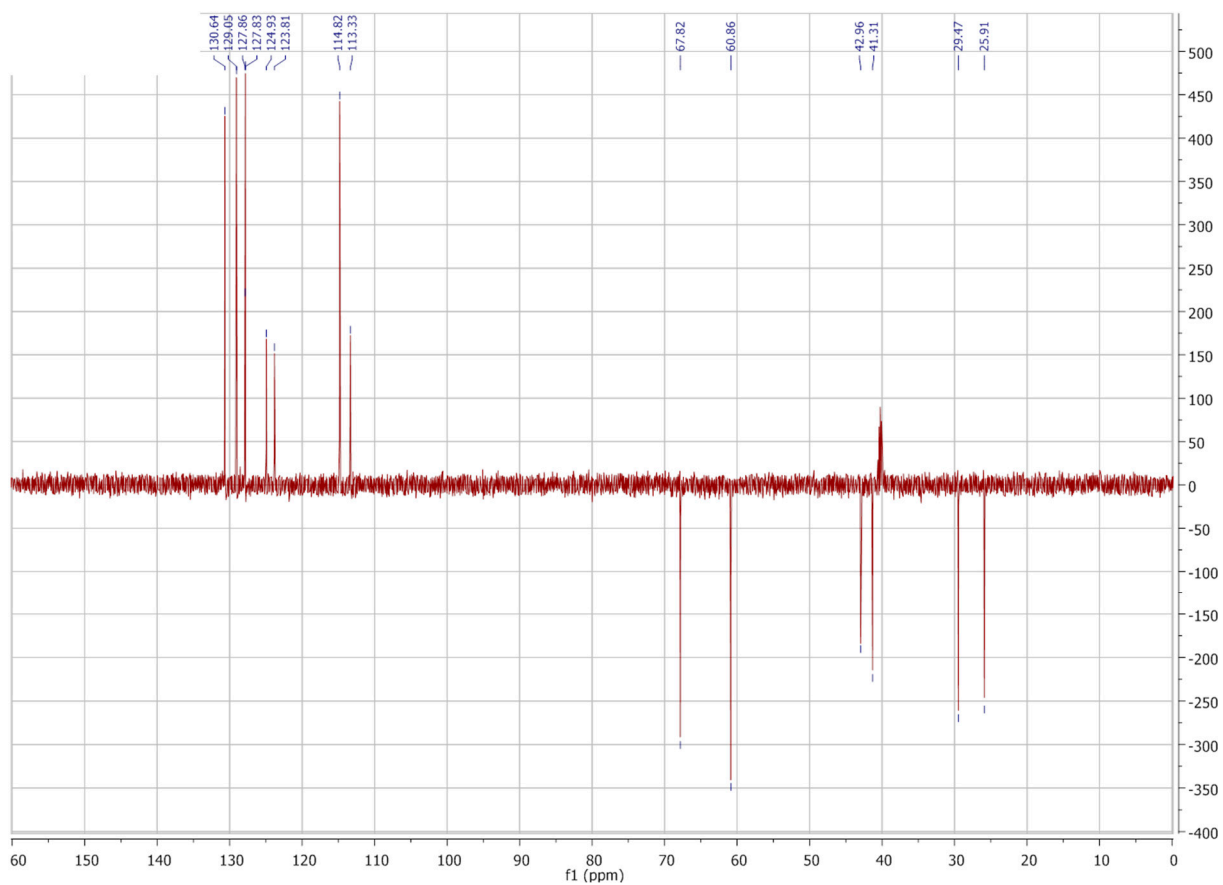
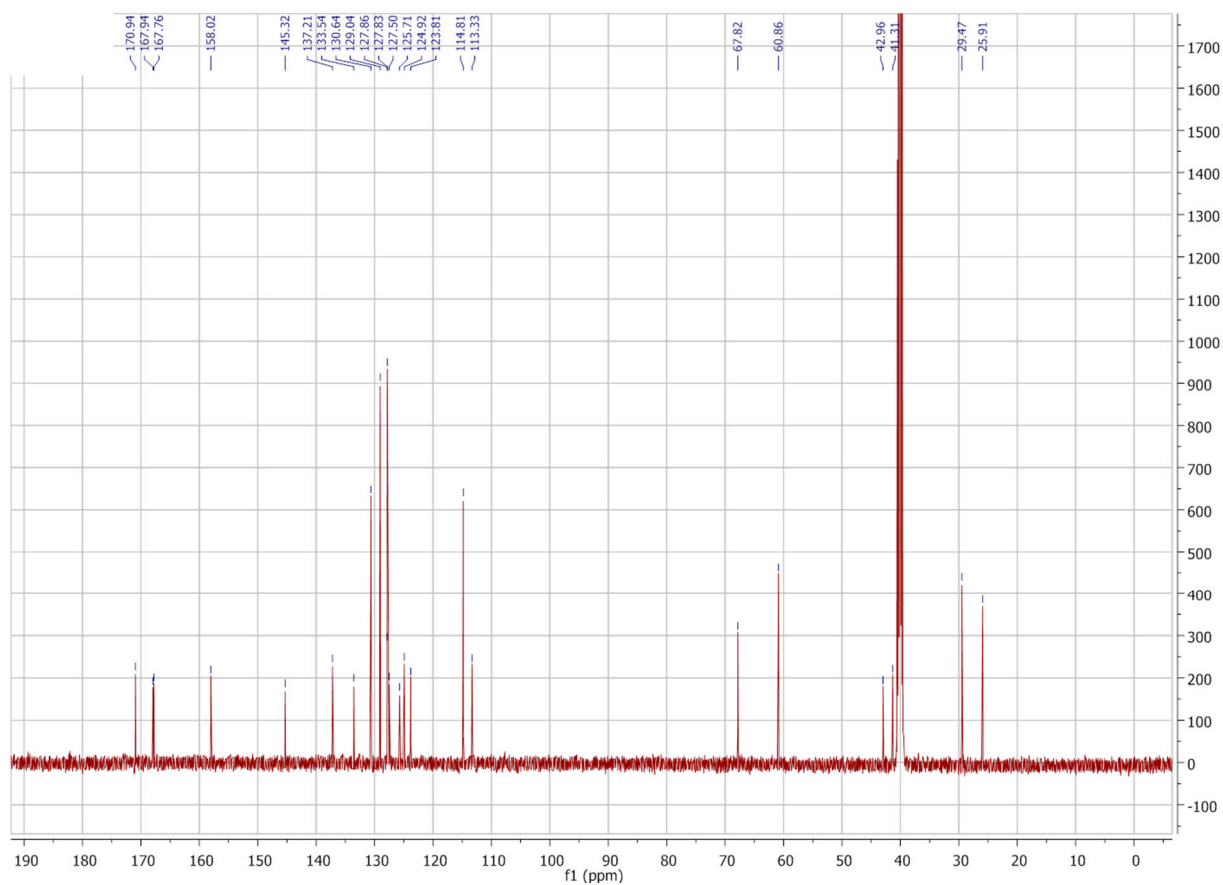


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-[4-(4-hydroxybutoxy)phenyl]acetamide (**13d**; ZHAWOC4753)

NMR

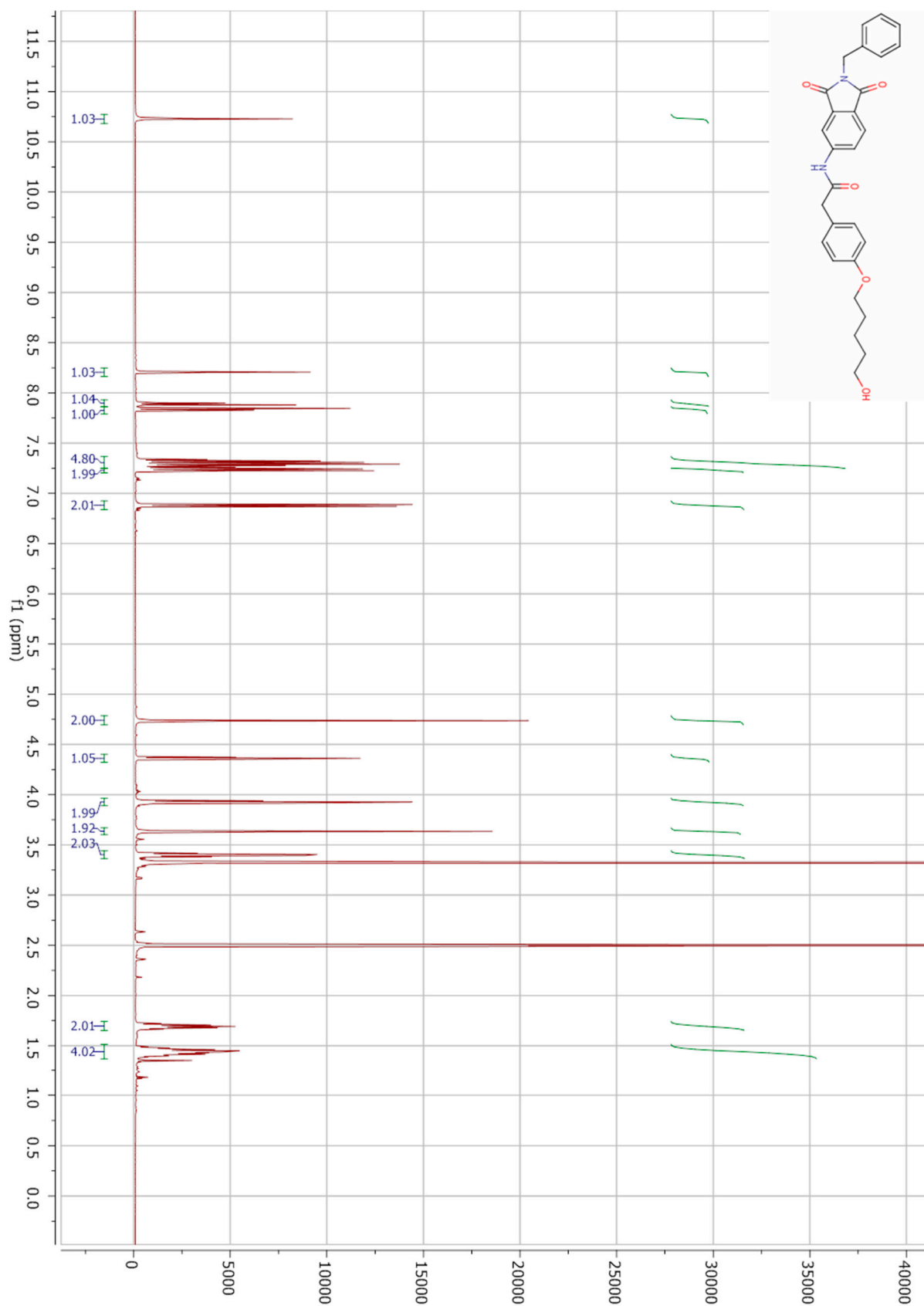


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-[4-(4-hydroxybutoxy)phenyl]acetamide (**13d**; ZHAWOC4753)

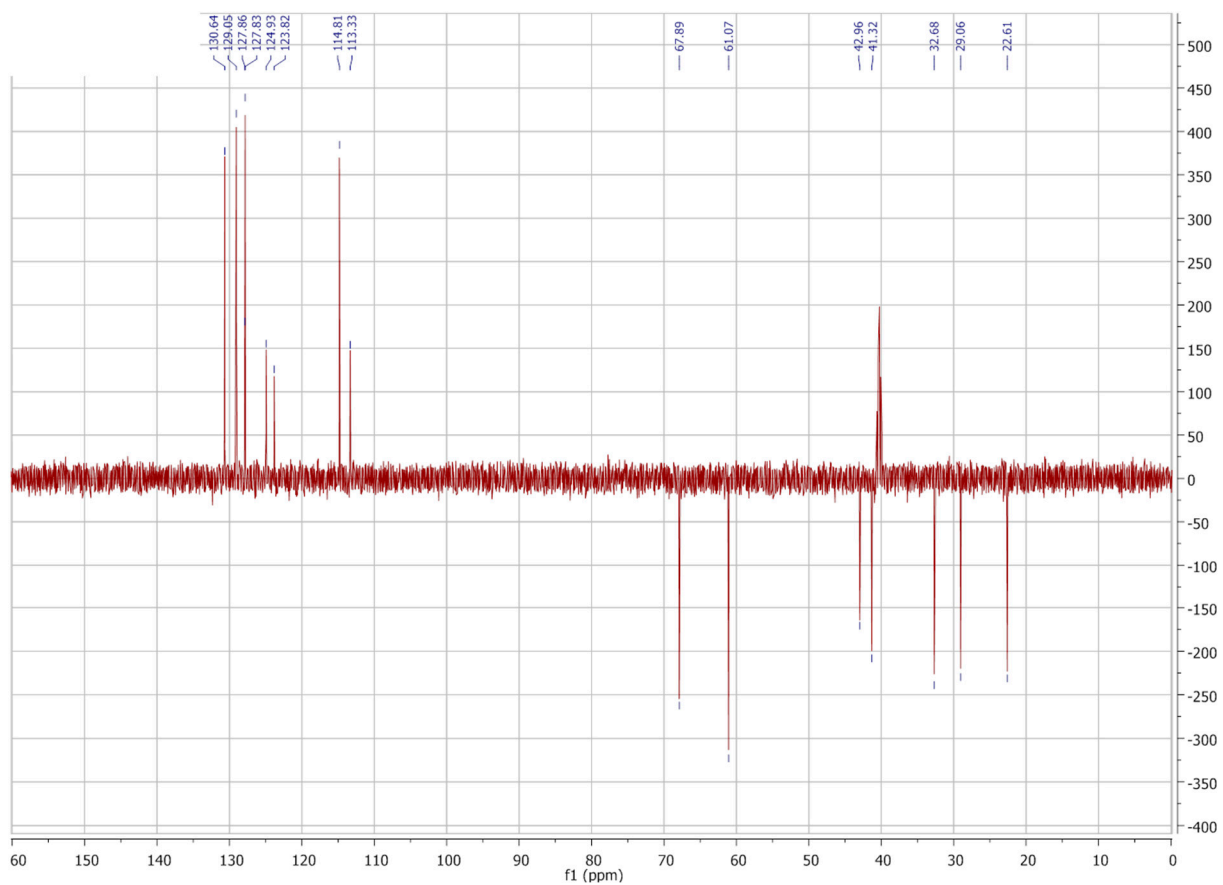
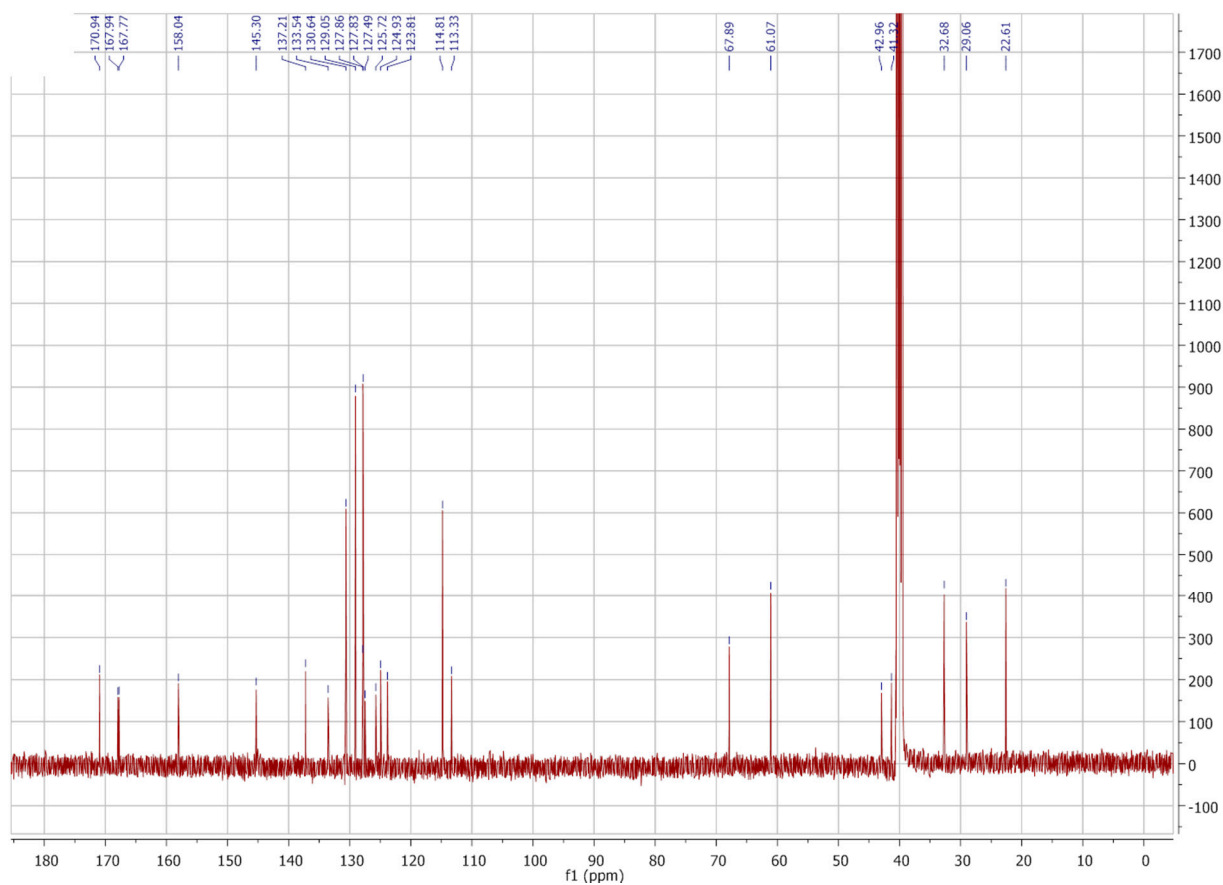


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-{4-[(5-hydroxypentyl)oxy]phenyl}acetamide (**13e**; ZHAWOC5130)

NMR

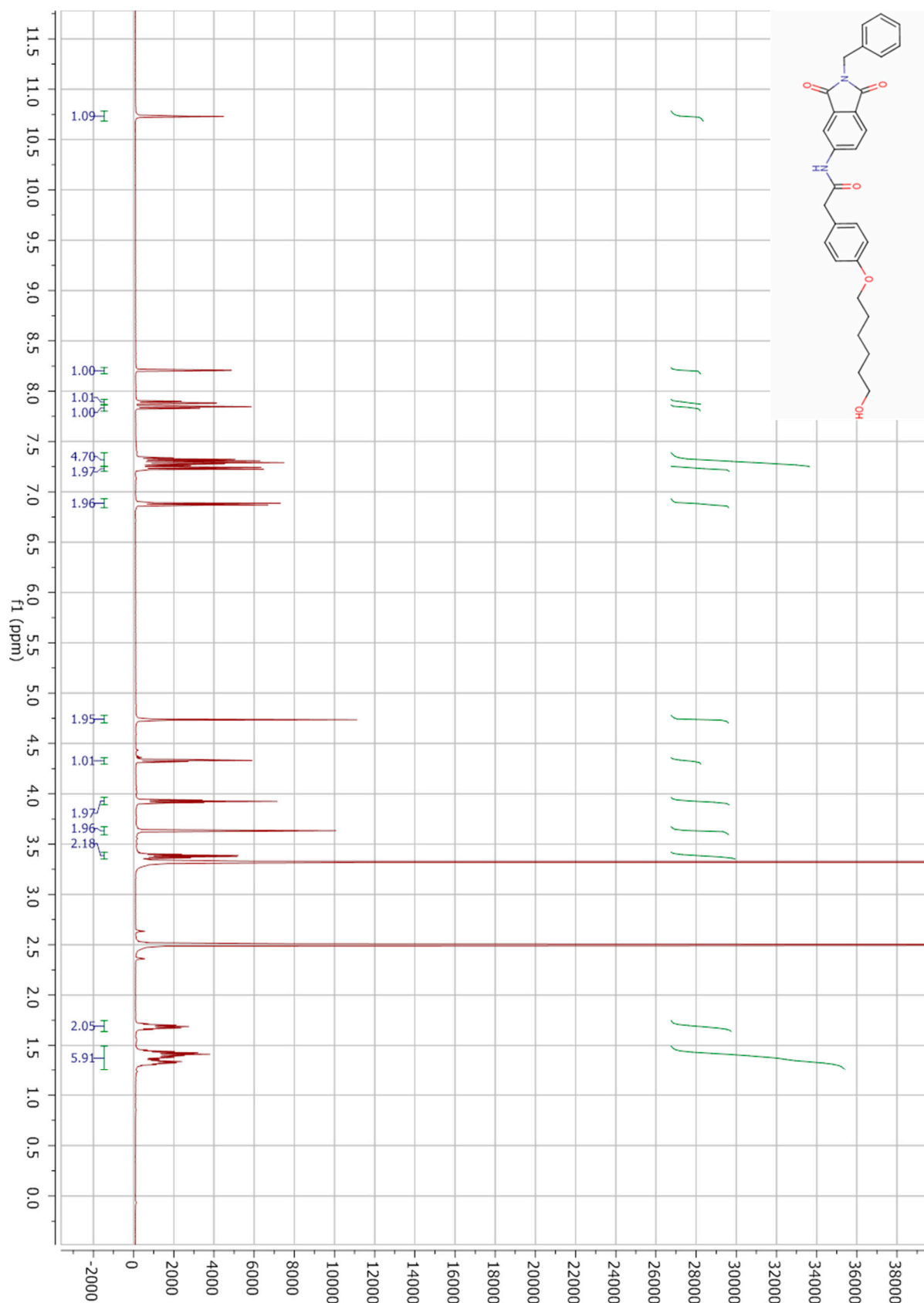


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-{4-[(5-hydroxypentyl)oxy]phenyl}acetamide (**13e**; ZHAWOC5130)

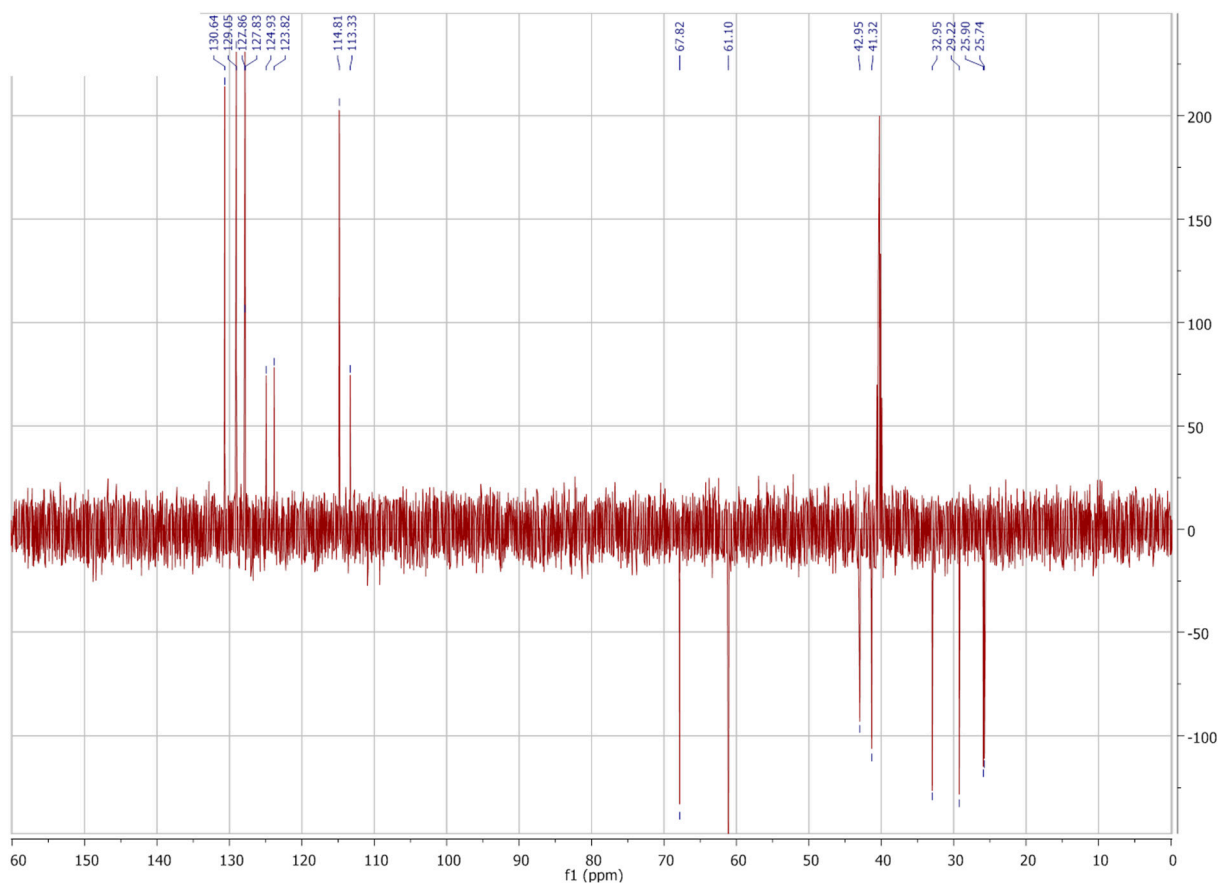
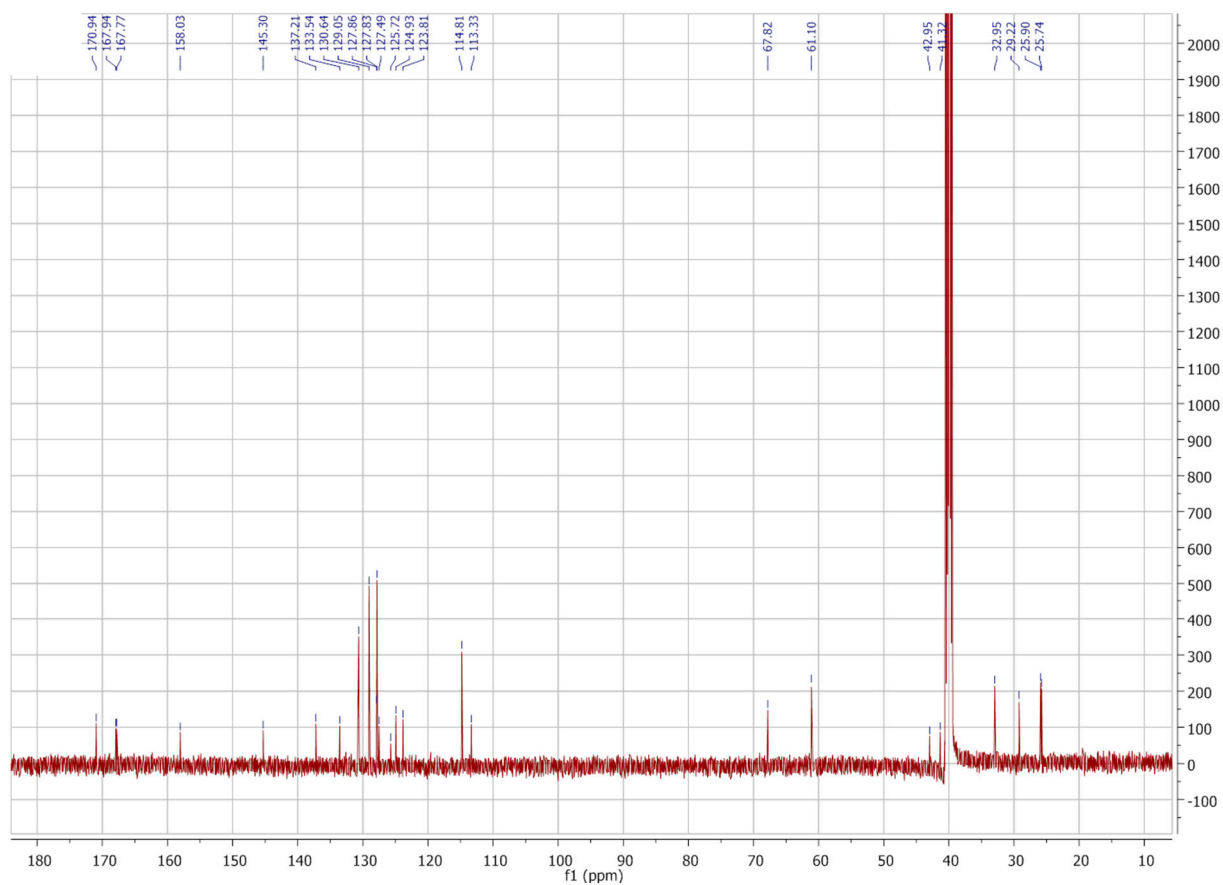


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-{4-[(6-hydroxyhexyl)oxy]phenyl}acetamide (**13f**; ZHAWOC5132)

NMR

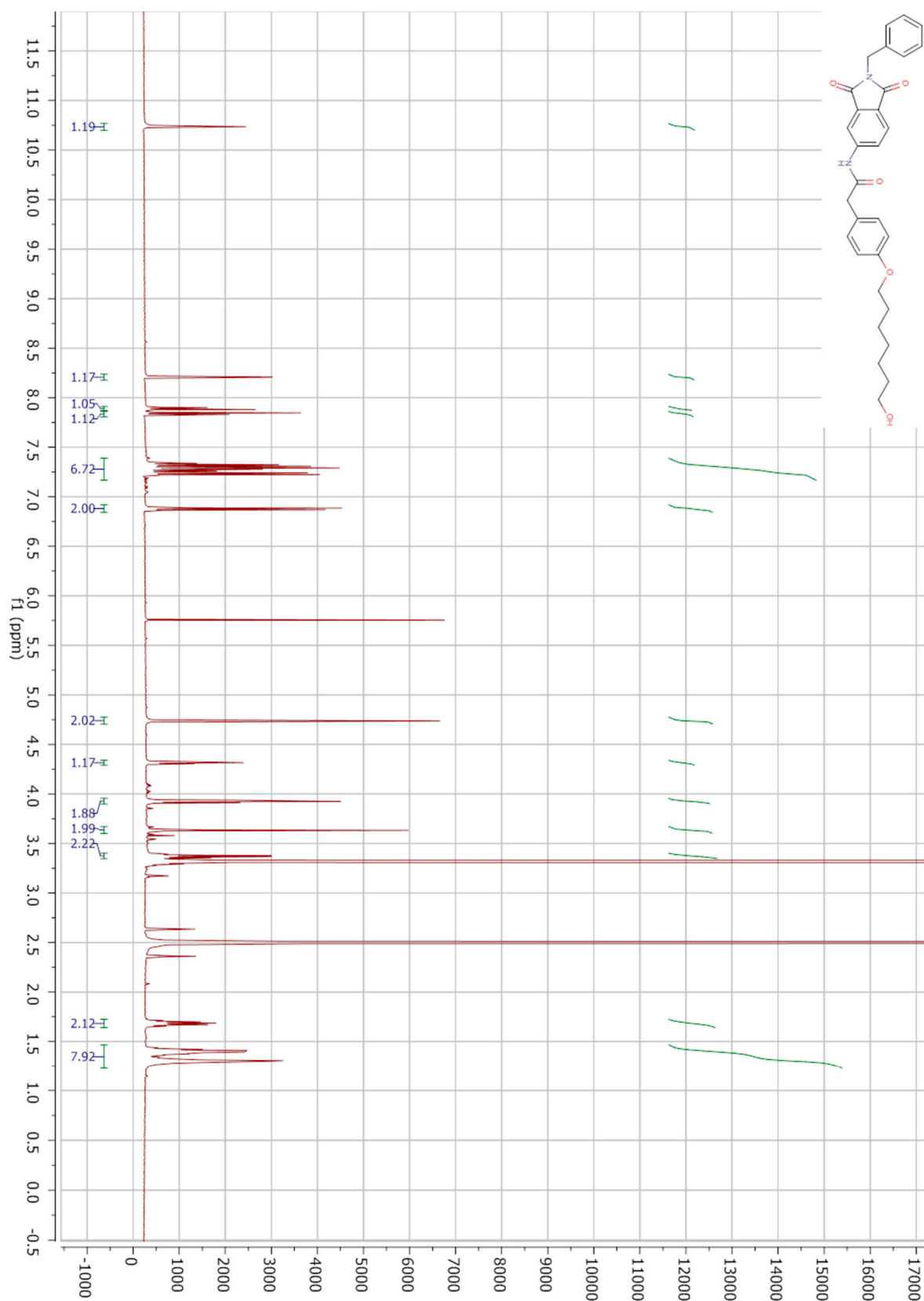


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-{4-[(6-hydroxyhexyl)oxy]phenyl}acetamide (**13f**; ZHAWOC5132)

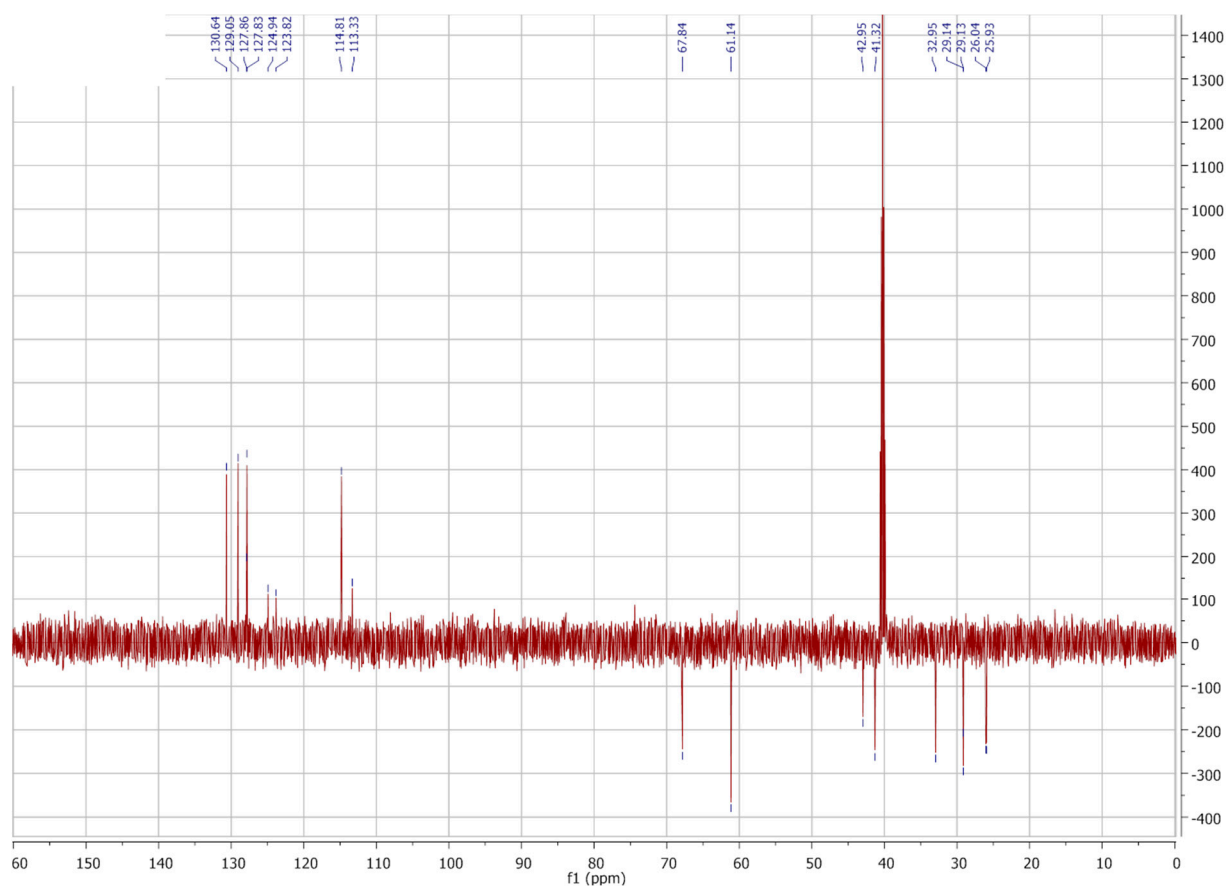
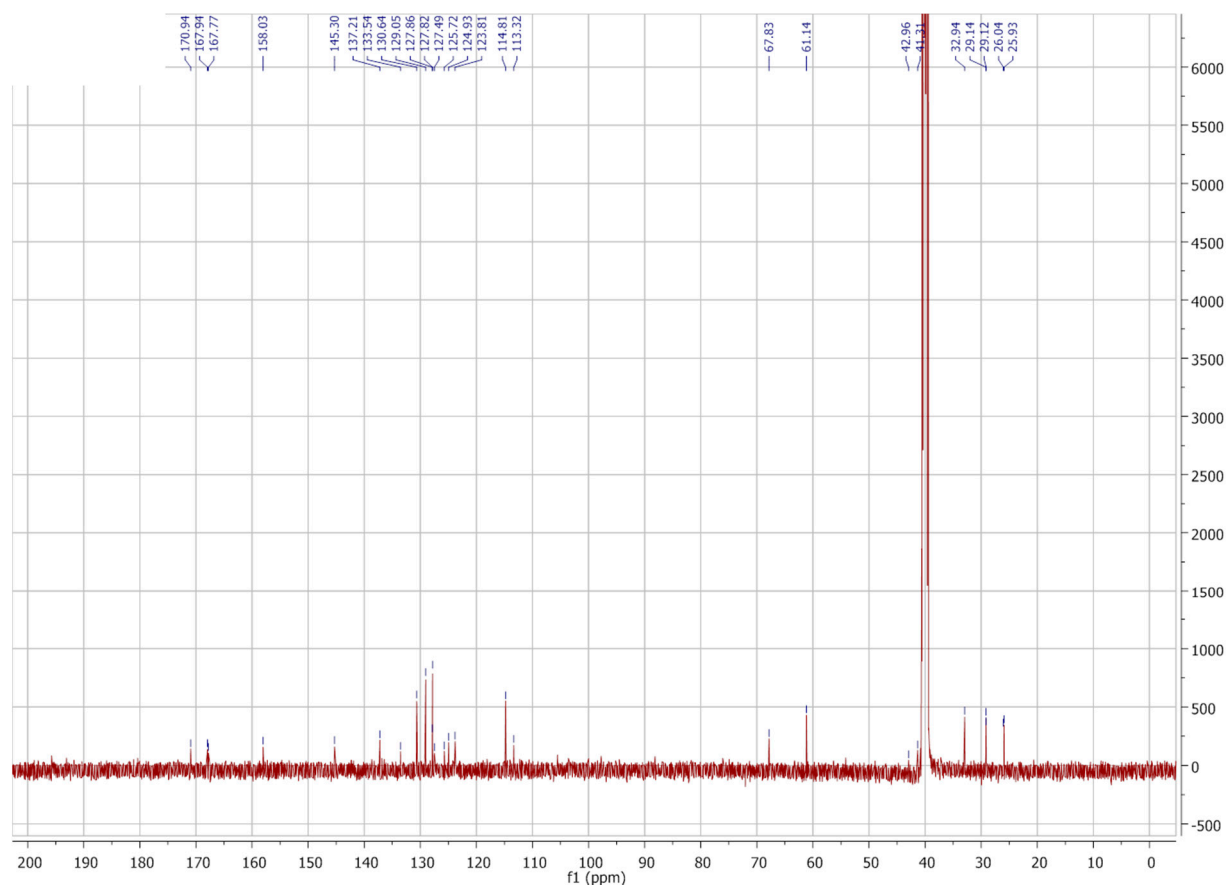


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-{4-[(7-hydroxyheptyl)oxy]phenyl}acetamide (**13g**; ZHAWOC7103)

NMR

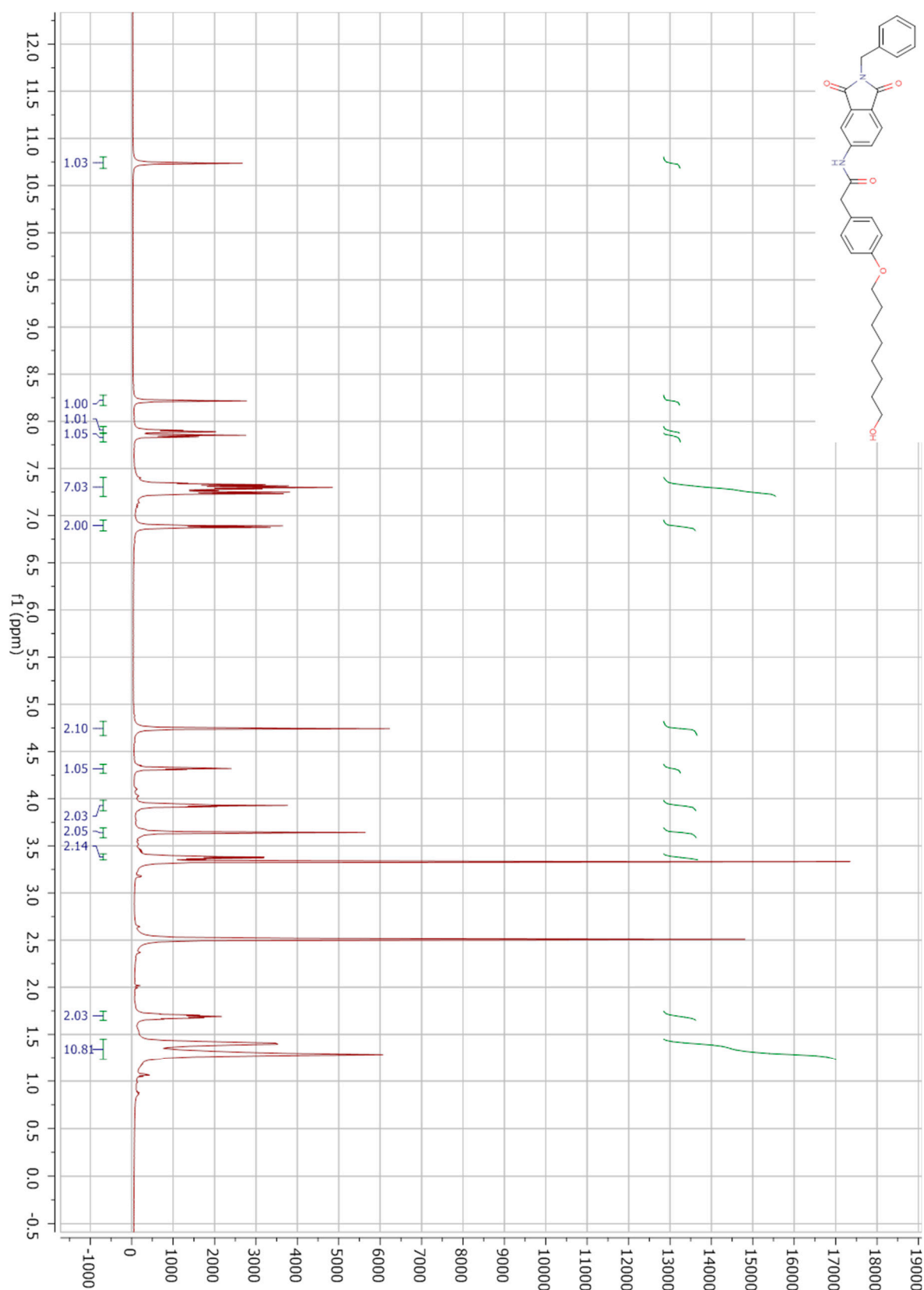


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-{4-[(7-hydroxyheptyl)oxy]phenyl}acetamide (**13g**; ZHAWOC7103)

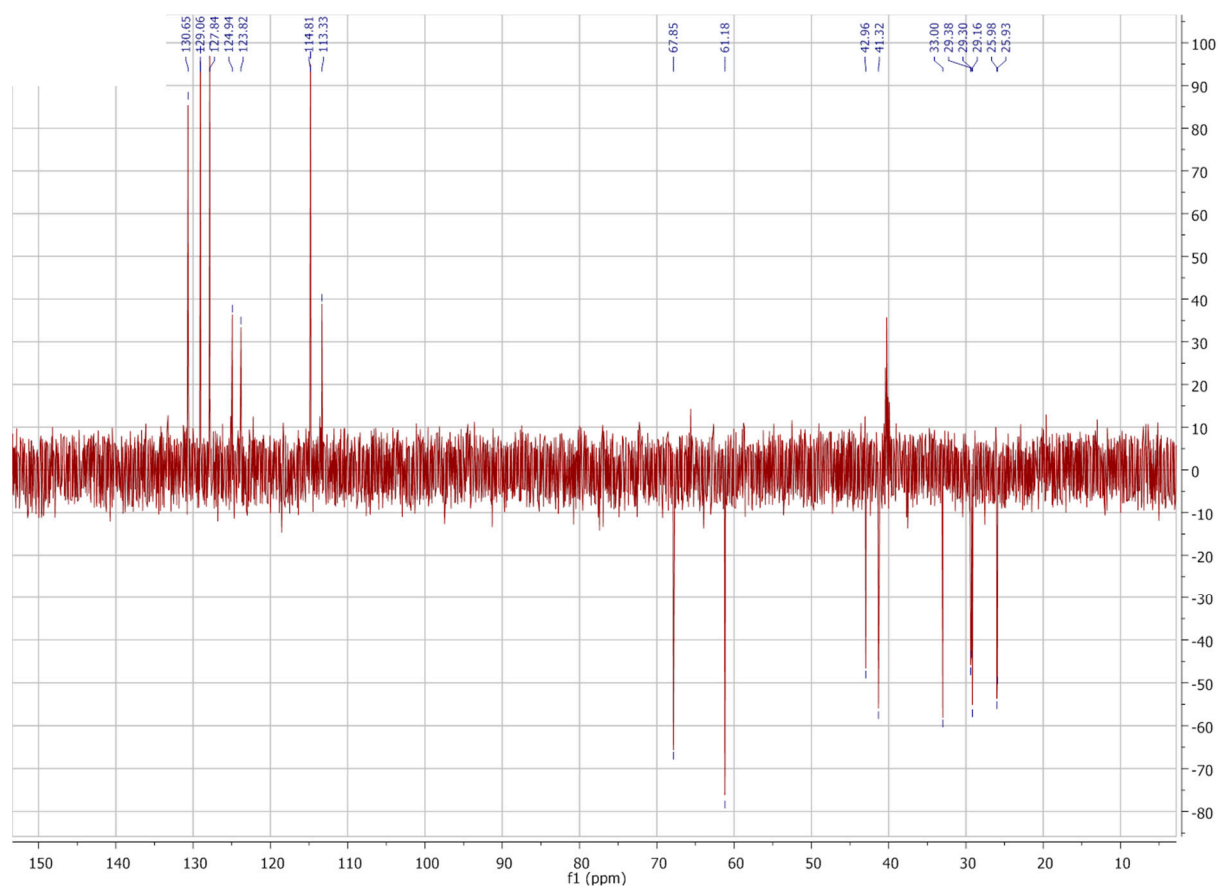
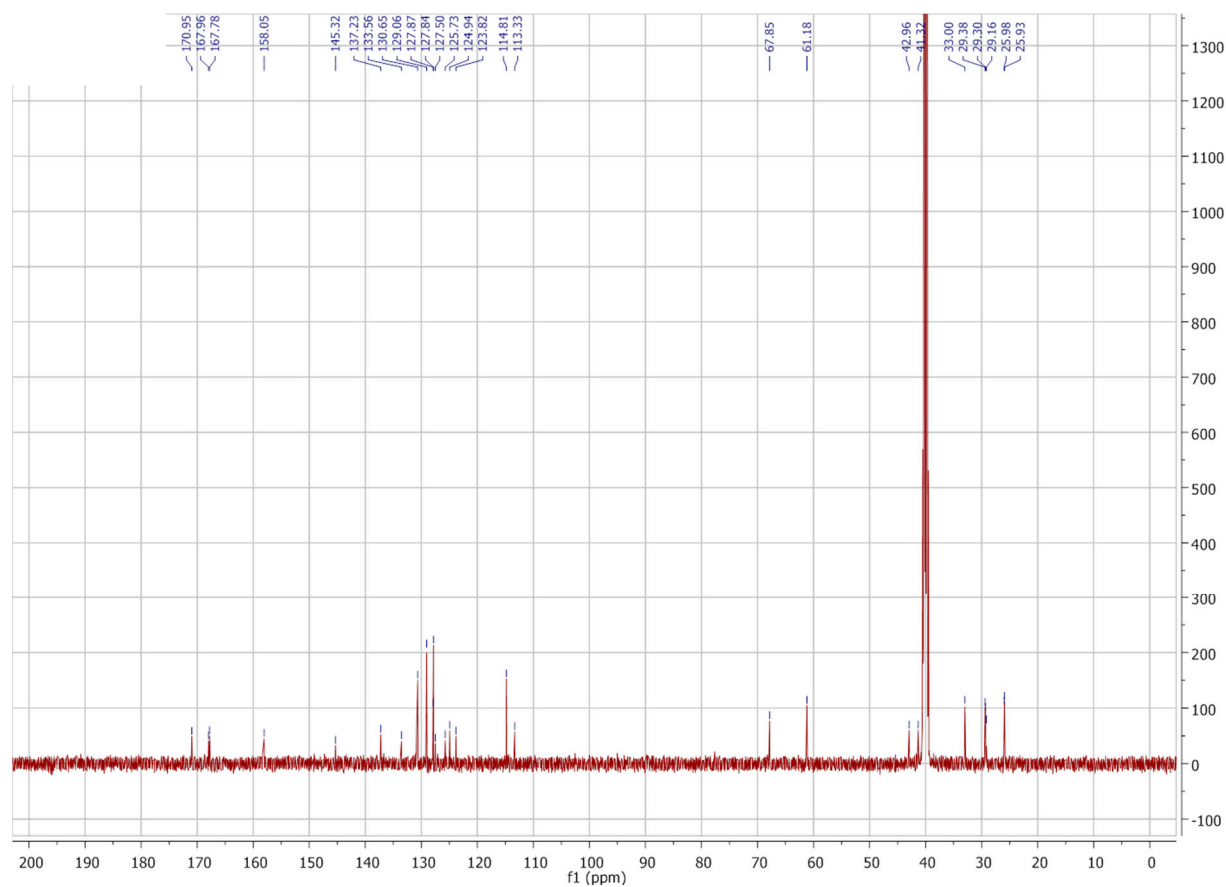


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-{4-[(8-hydroxyoctyl)oxy]phenyl}acetamide (**13h**: ZHAWOC7137)

NMR

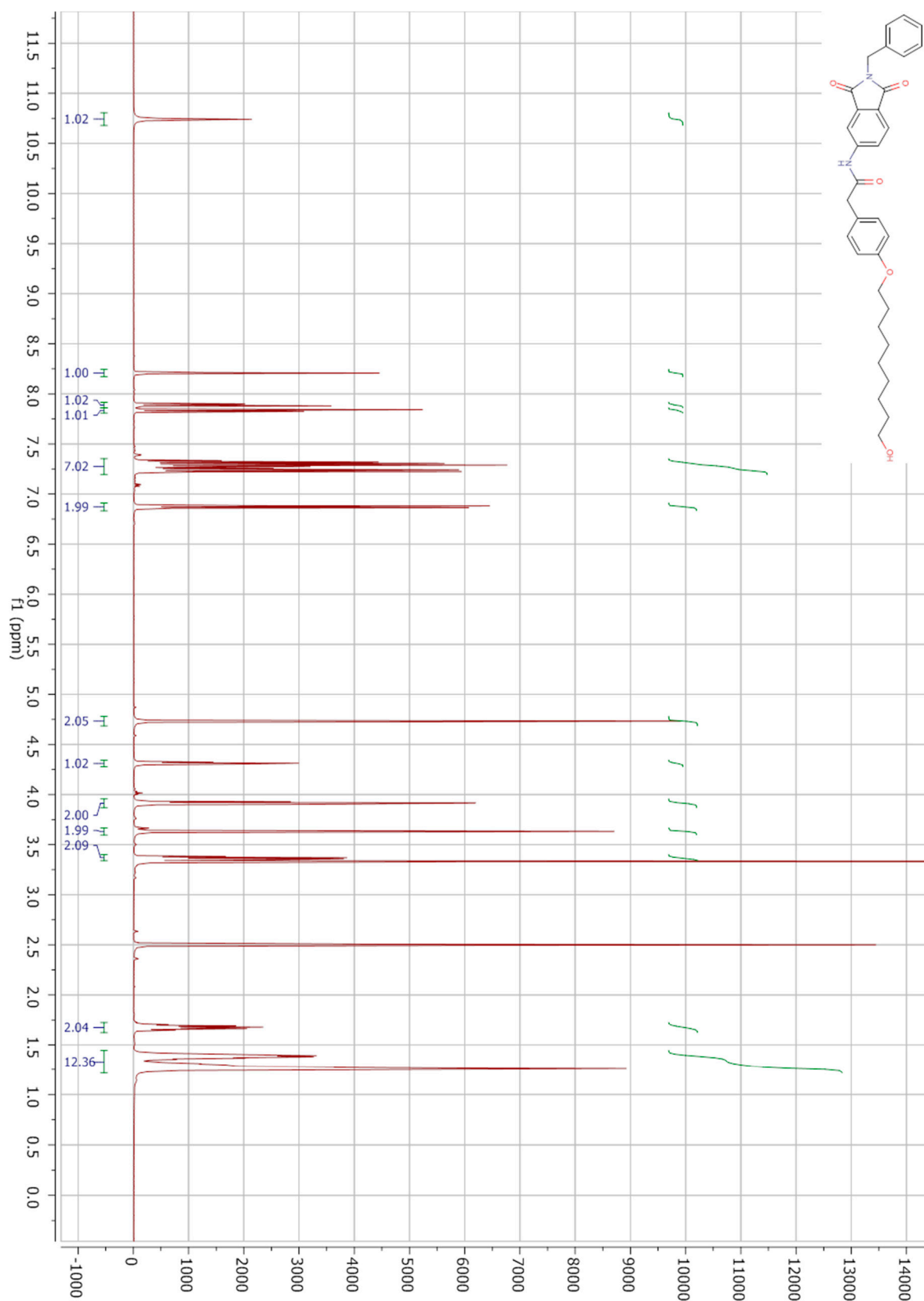


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-{4-[(8-hydroxyoctyl)oxy]phenyl}acetamide (**13h**: ZHAWOC7137)

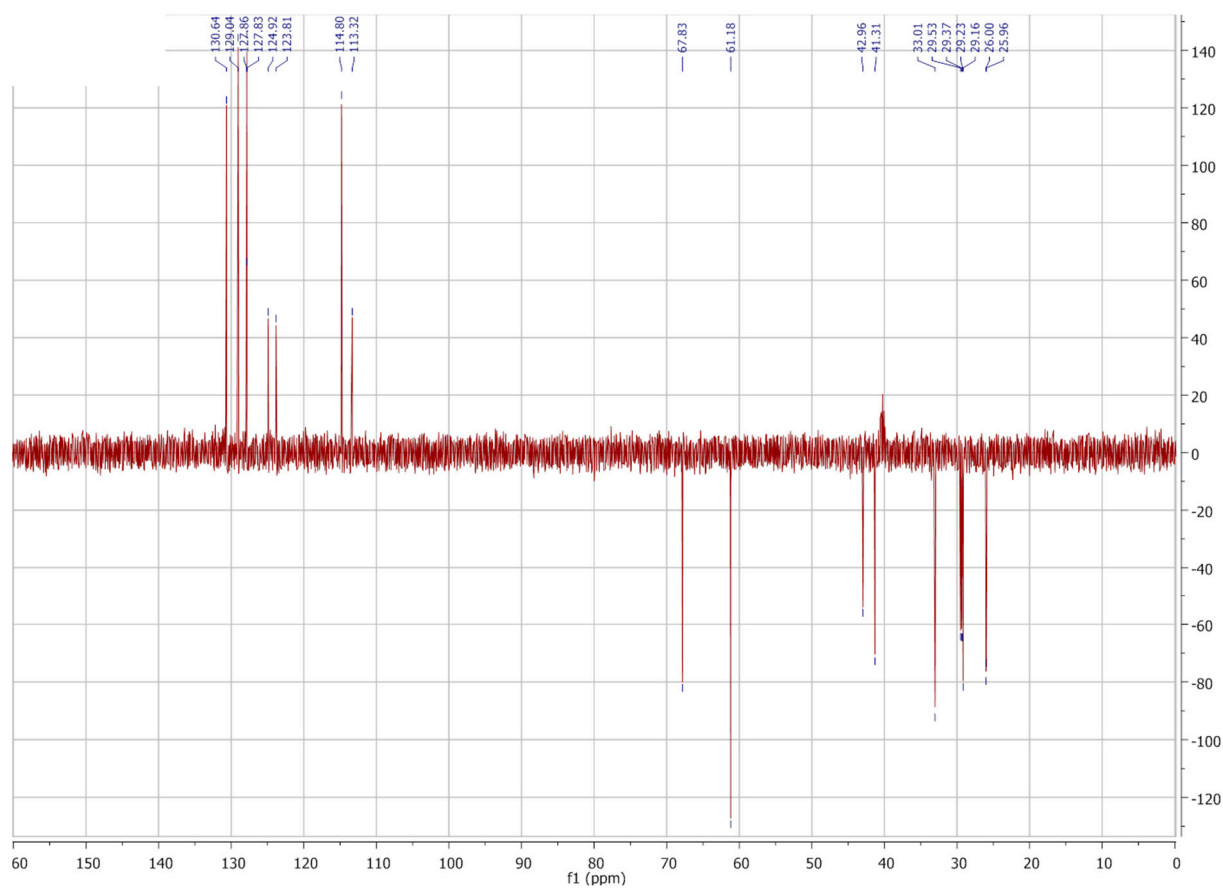
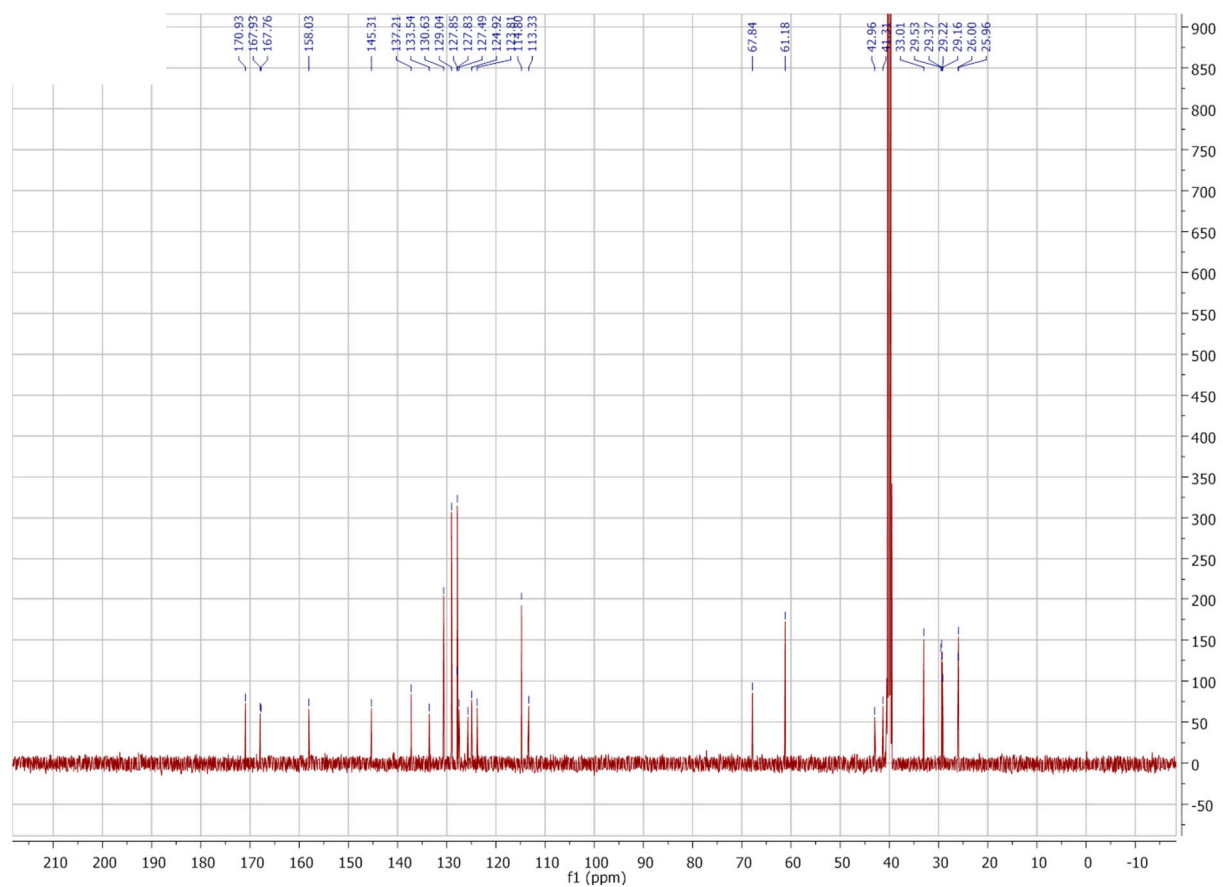


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-{4-[(9-hydroxynonyl)oxy]phenyl}acetamide (**13i**; ZHAWOC6936)

NMR

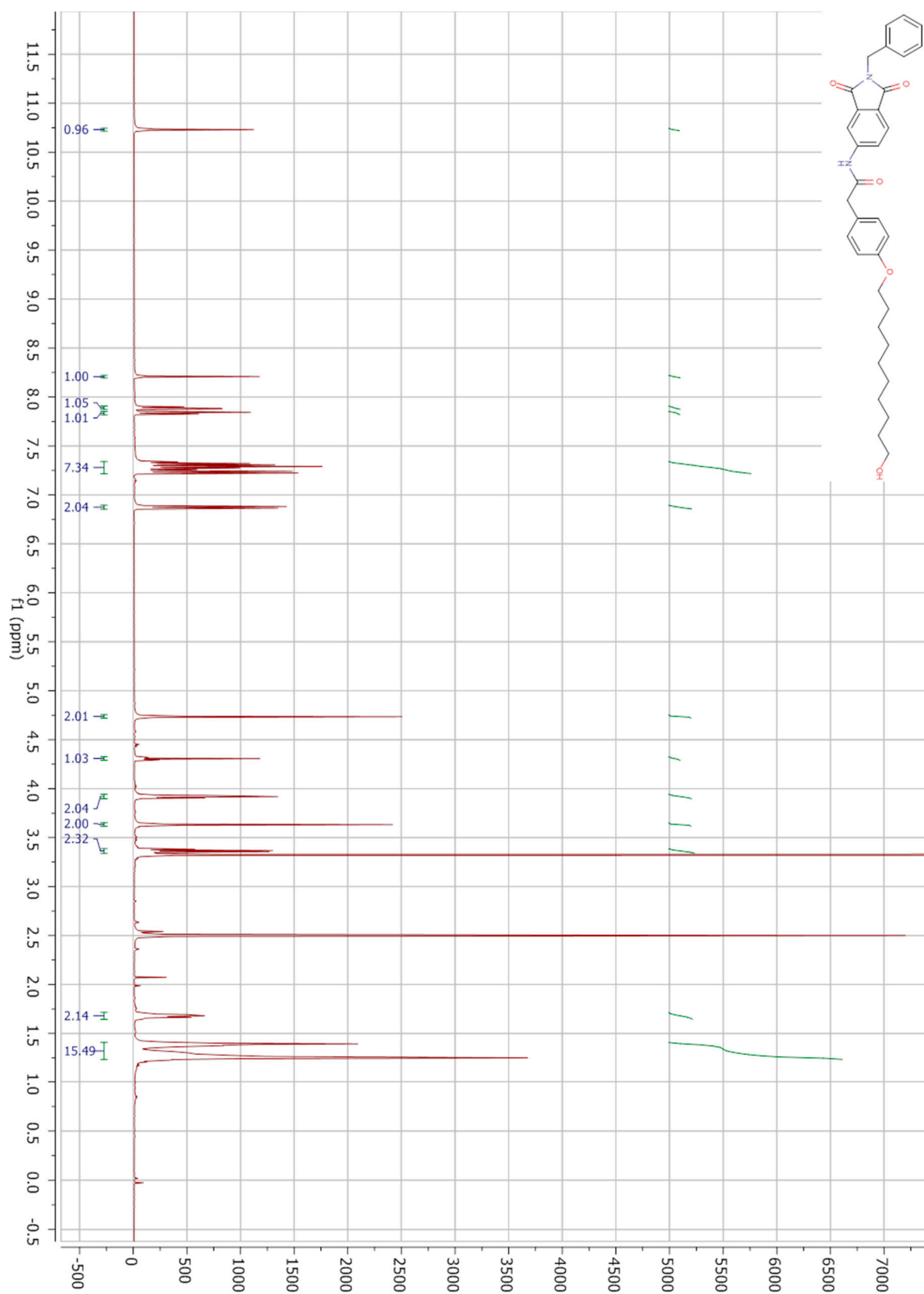


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-{4-[(9-hydroxynonyl)oxy]phenyl}acetamide (**13i**; ZHAWOC6936)

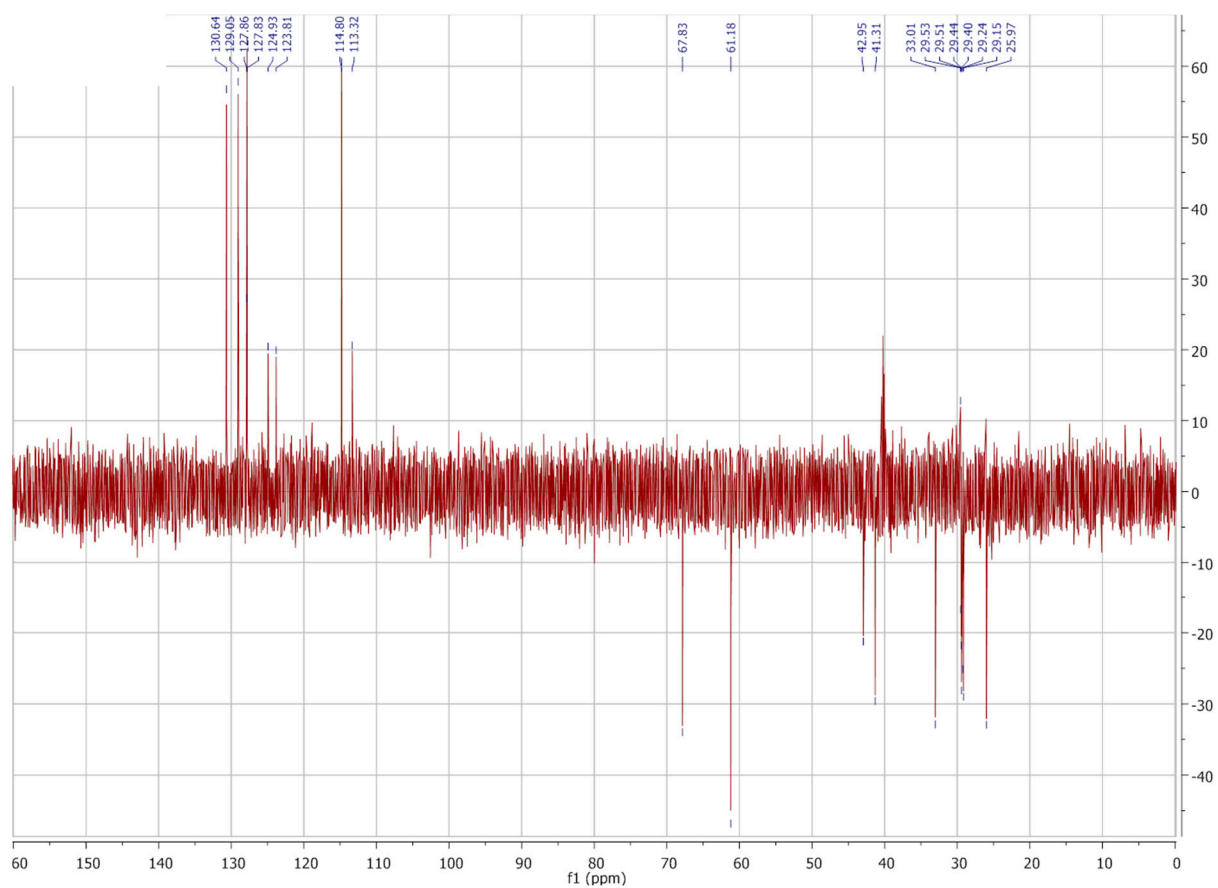
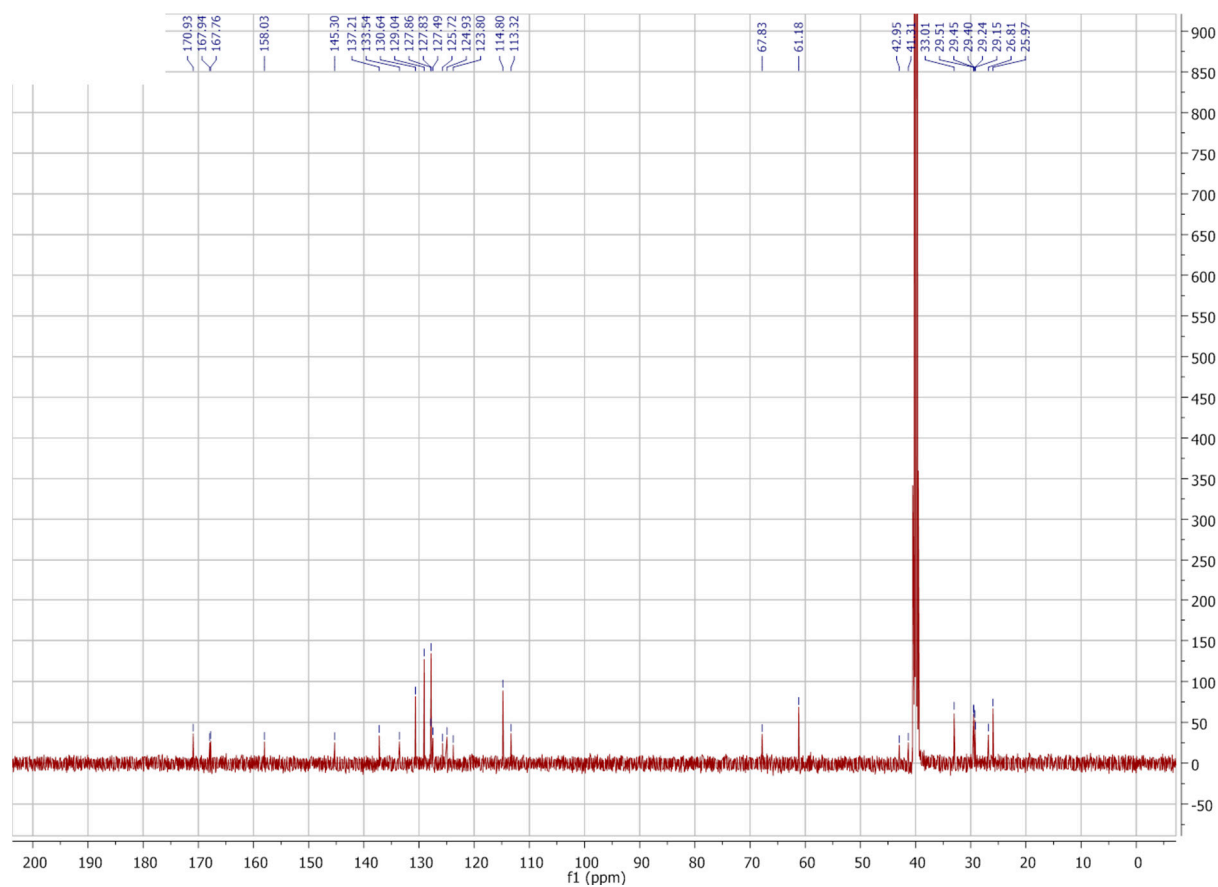


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-{4-[(10-hydroxydecyl)oxy]phenyl}acetamide (**13j**; ZHAWOC6937)

NMR

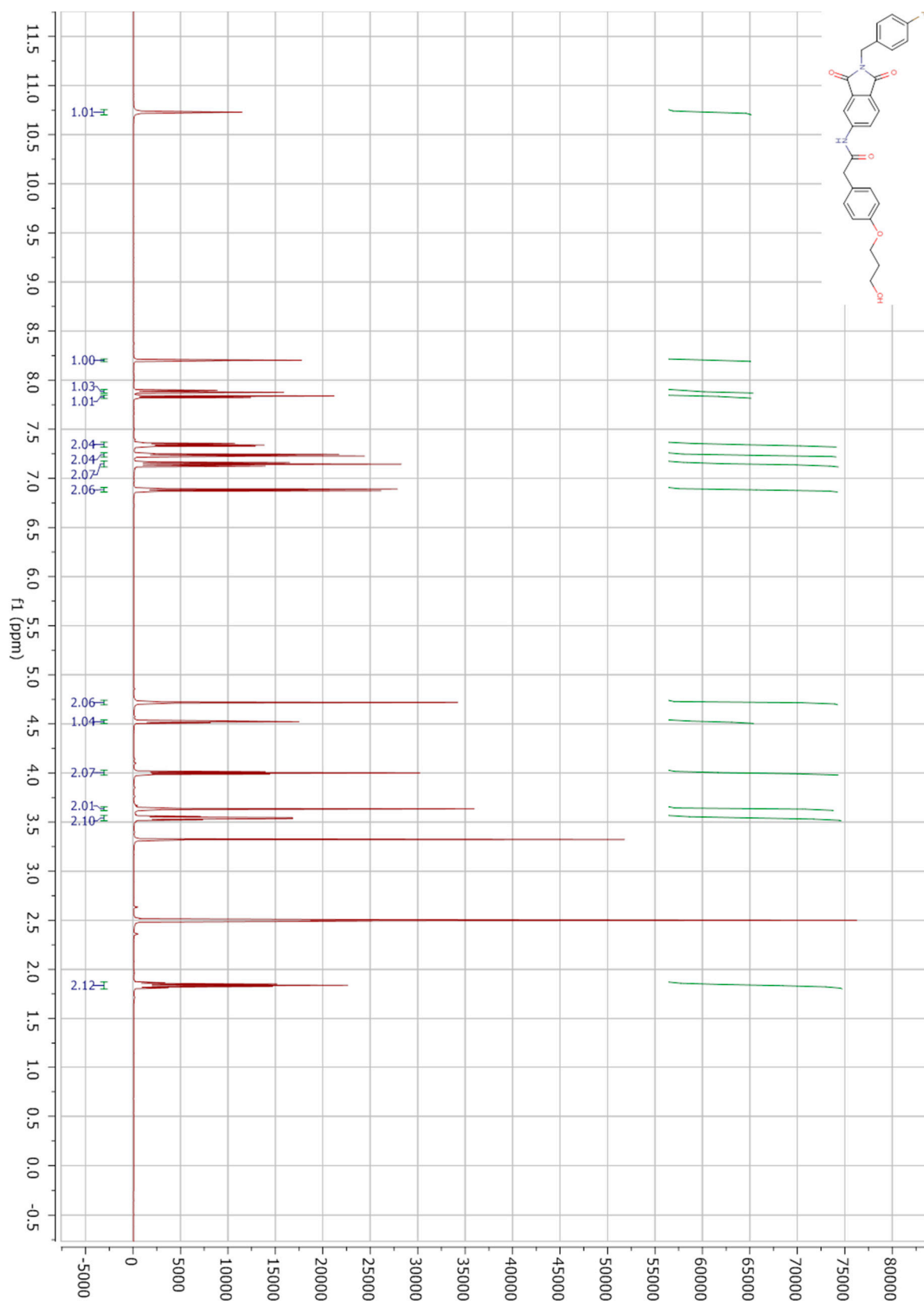


N-(2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)-2-{4-[(10-hydroxydecyl)oxy]phenyl}acetamide (**13j**; ZHAWOC6937)

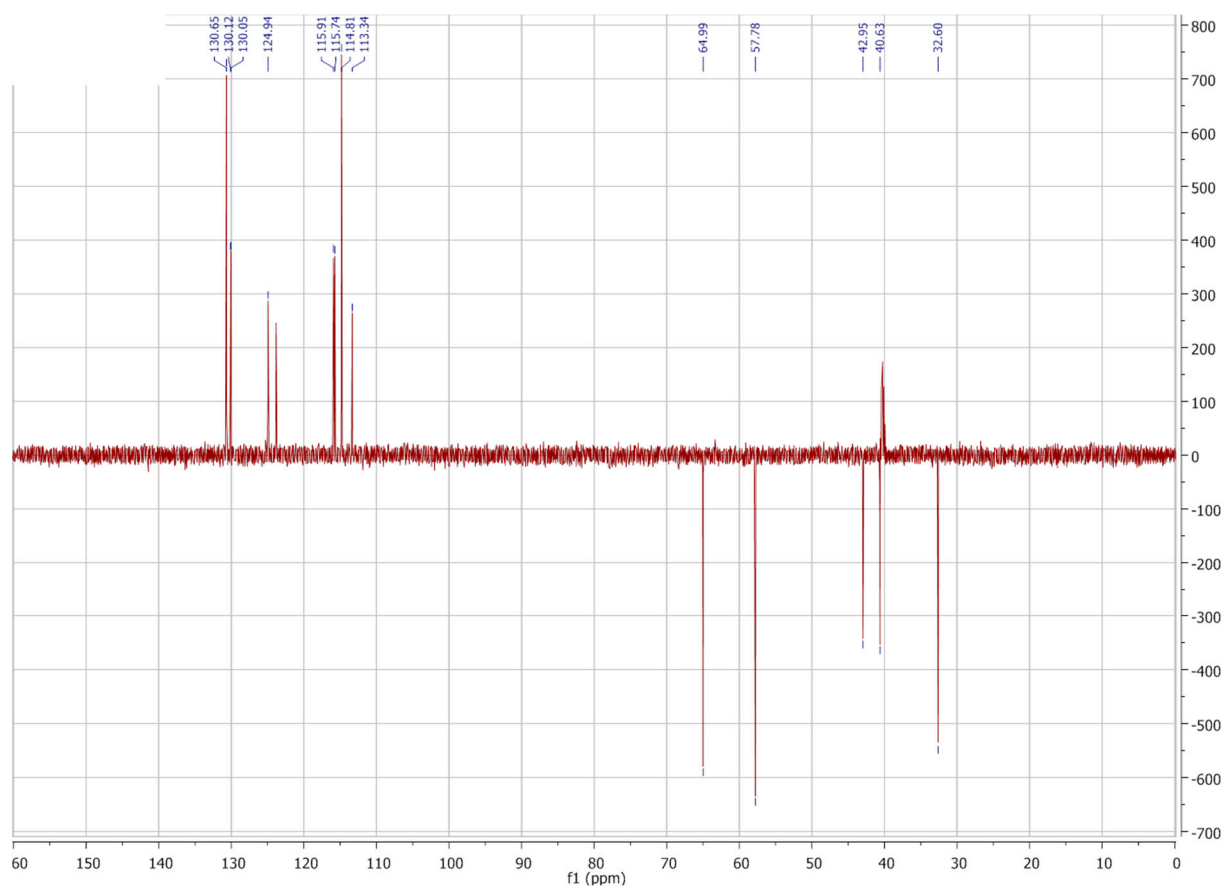
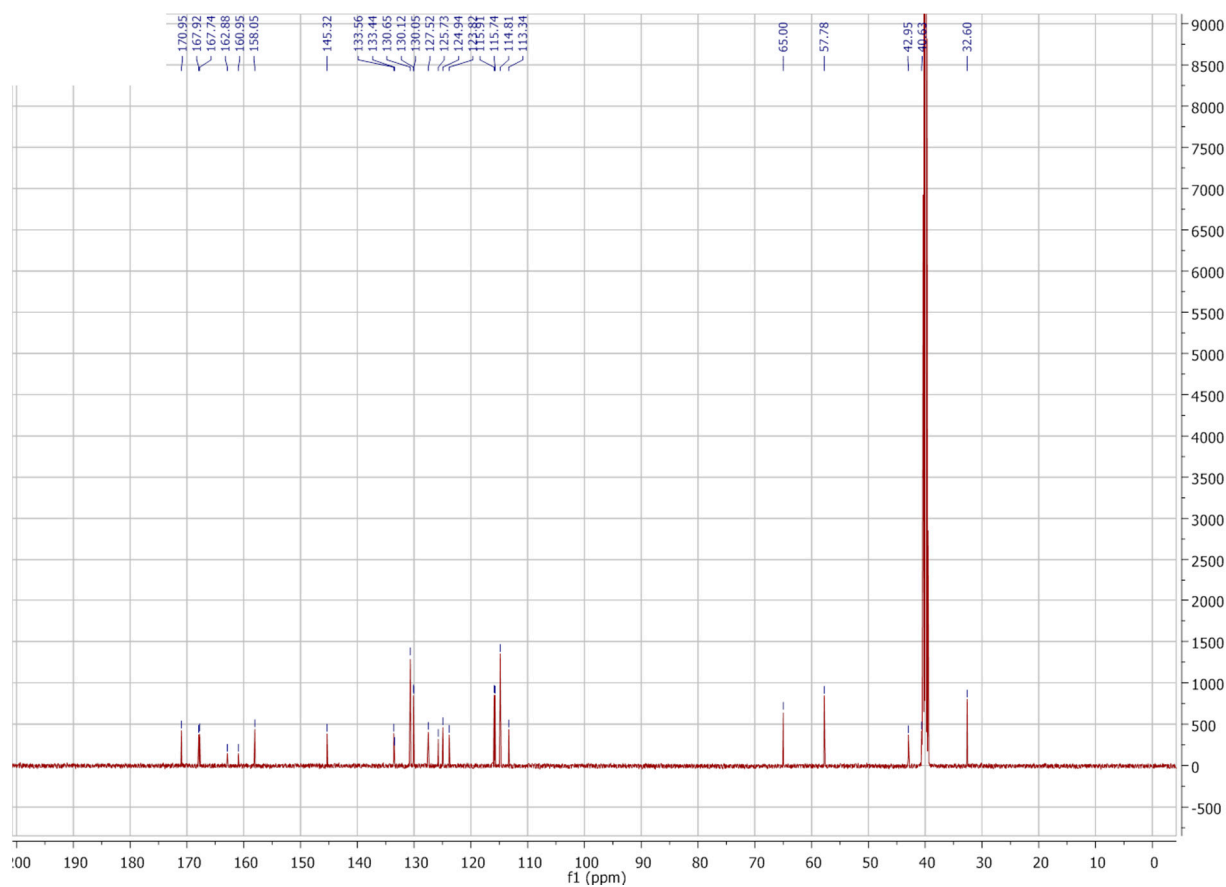


N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl}-2-[4-(3-hydroxypropoxy)phenyl]acetamide (**13k**; ZHAWOC6642)

NMR

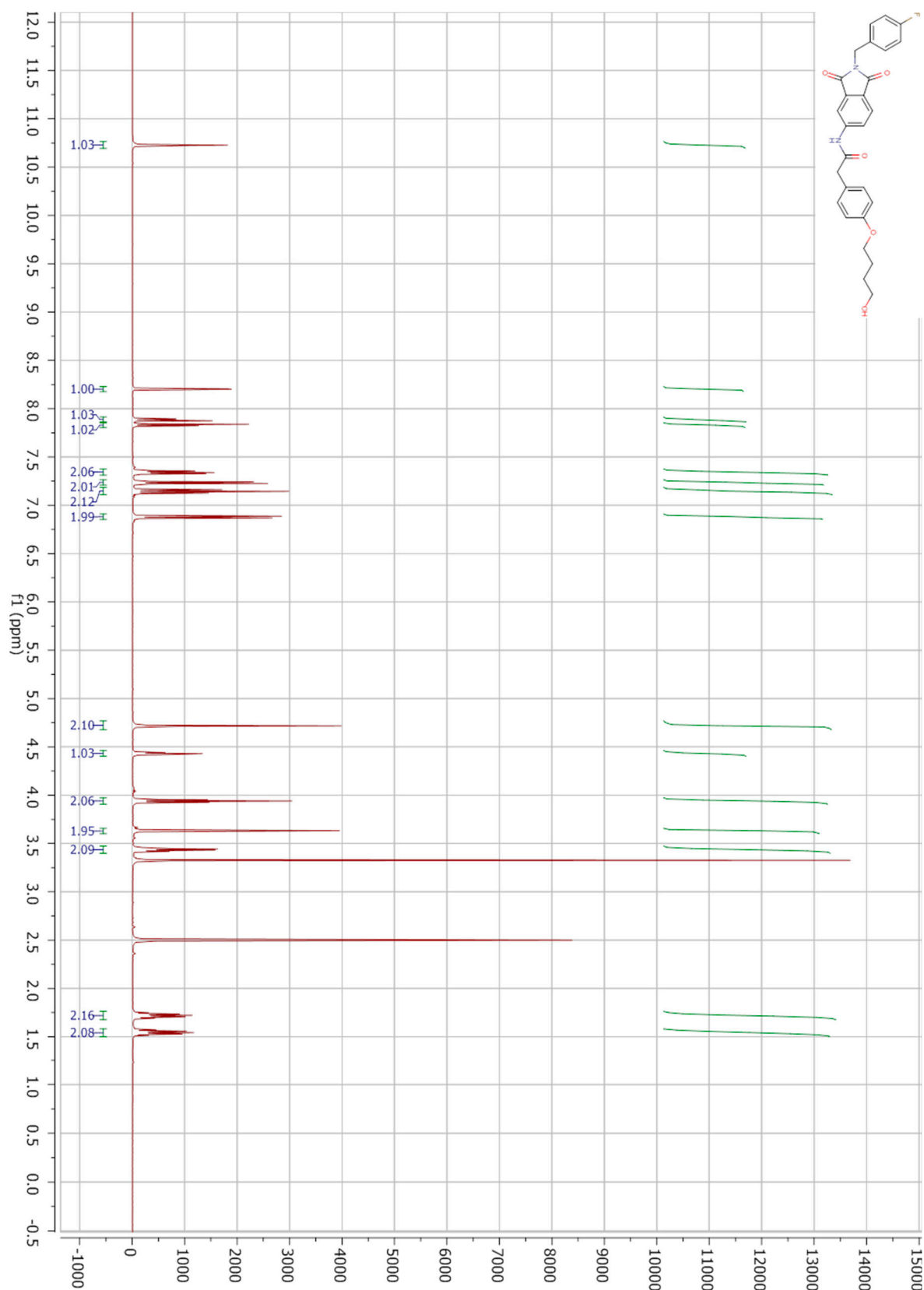


N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl}-2-[4-(3-hydroxypropoxy)phenyl]acetamide (**13k**; ZHAWOC6642)

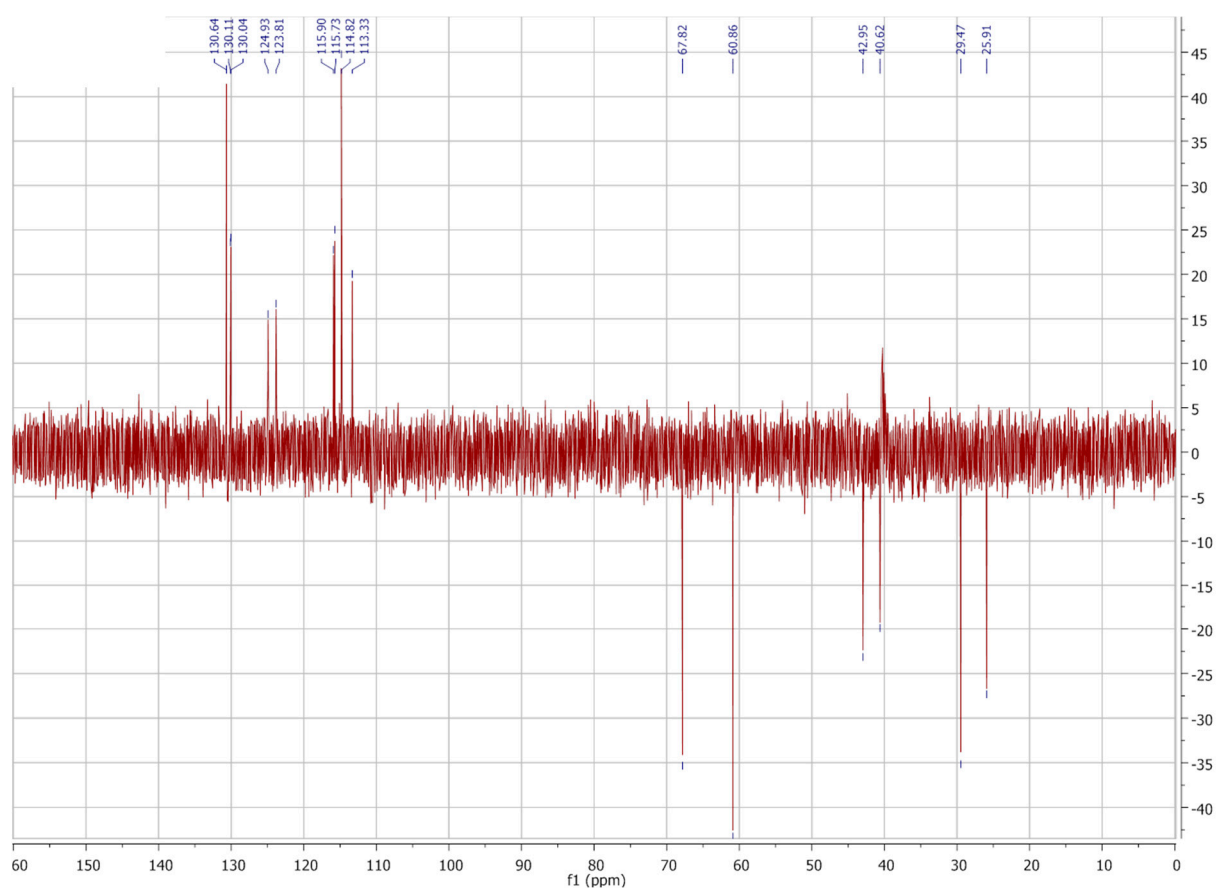
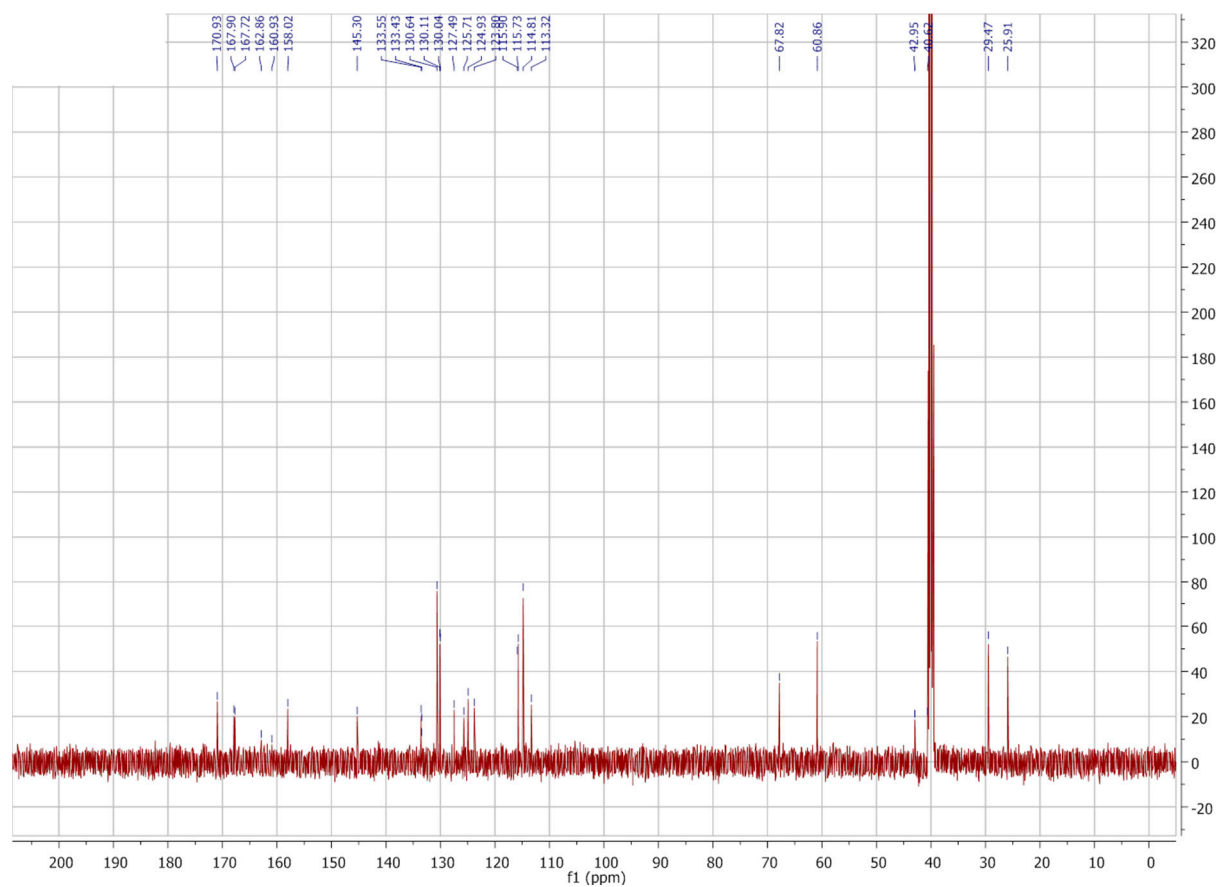


N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl}-2-[4-(4-hydroxybutoxy)phenyl]acetamide (**13l**; ZHAWOC5462)

NMR

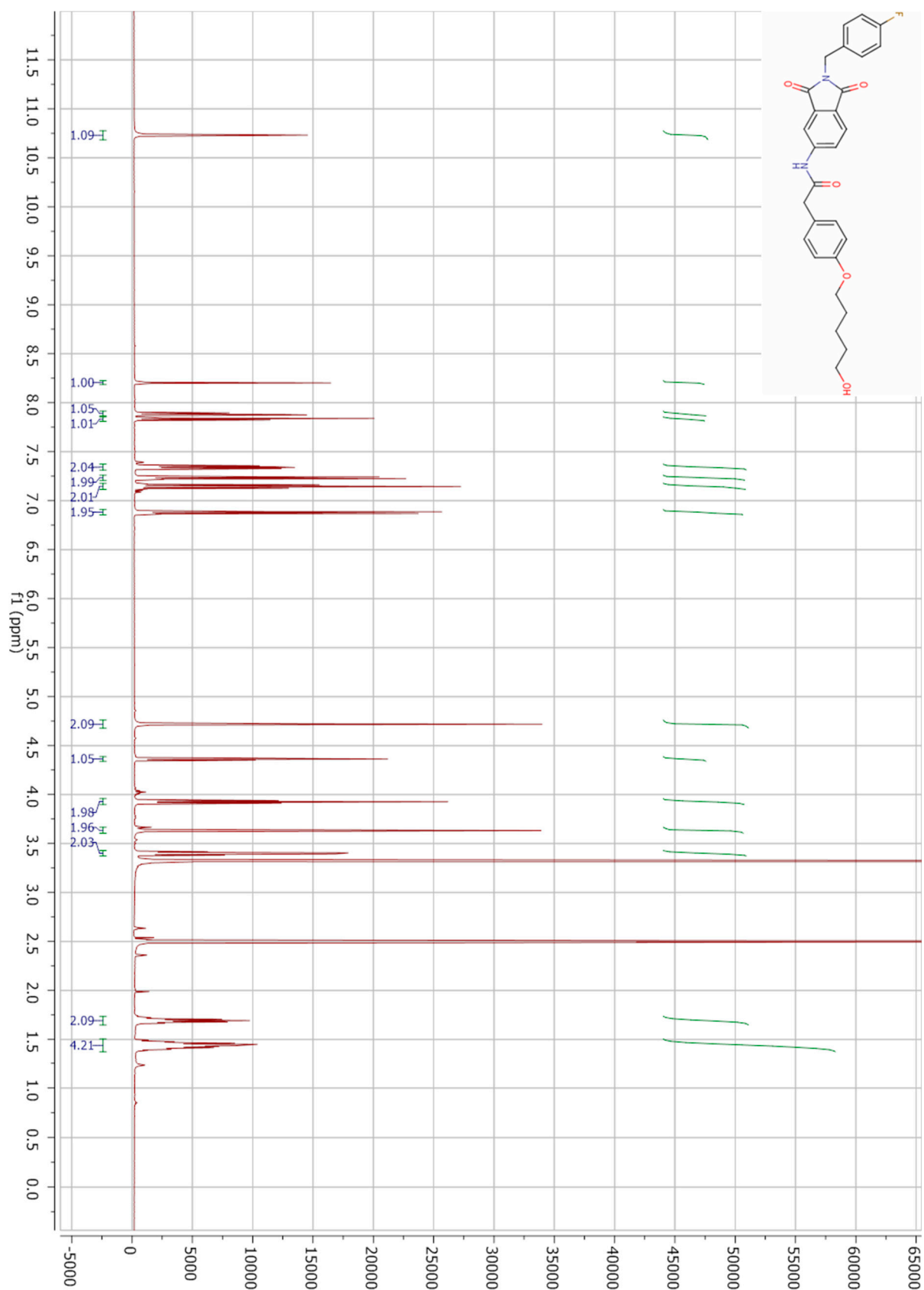


N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl}-2-[4-(4-hydroxybutoxy)phenyl]acetamide (**13l**; ZHAWOC5462)

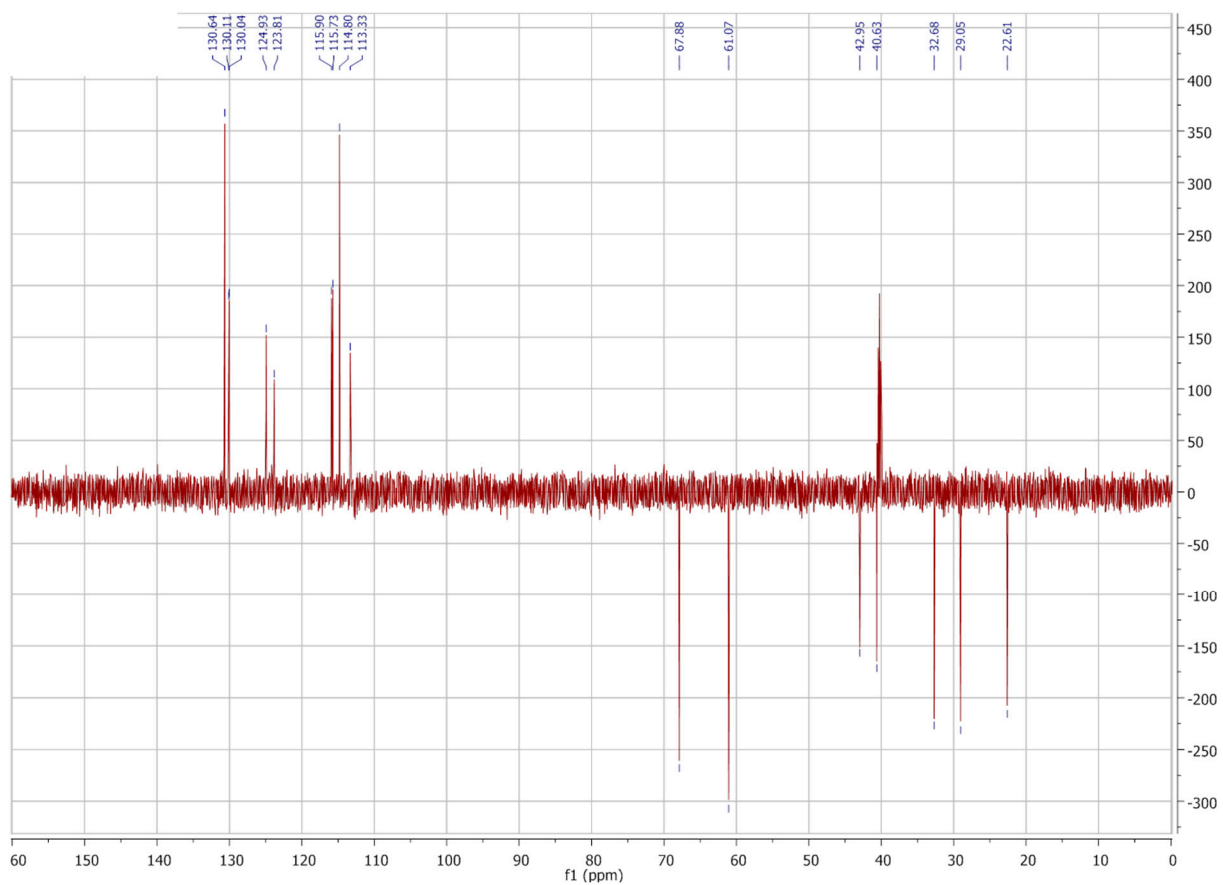
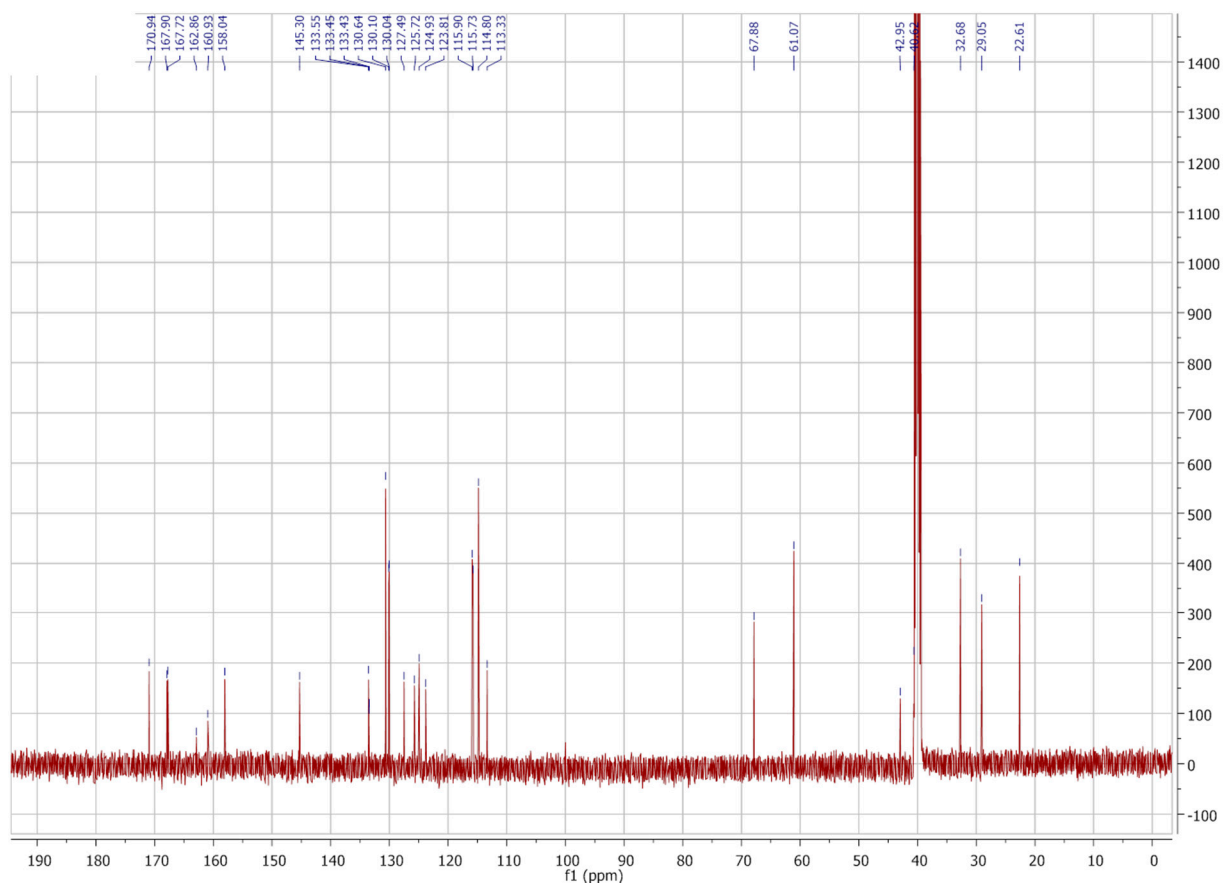


N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl}-2-{4-[(5-hydroxypentyl)oxy]phenyl}acetamide (**13m**; ZHAWOC5683)

NMR

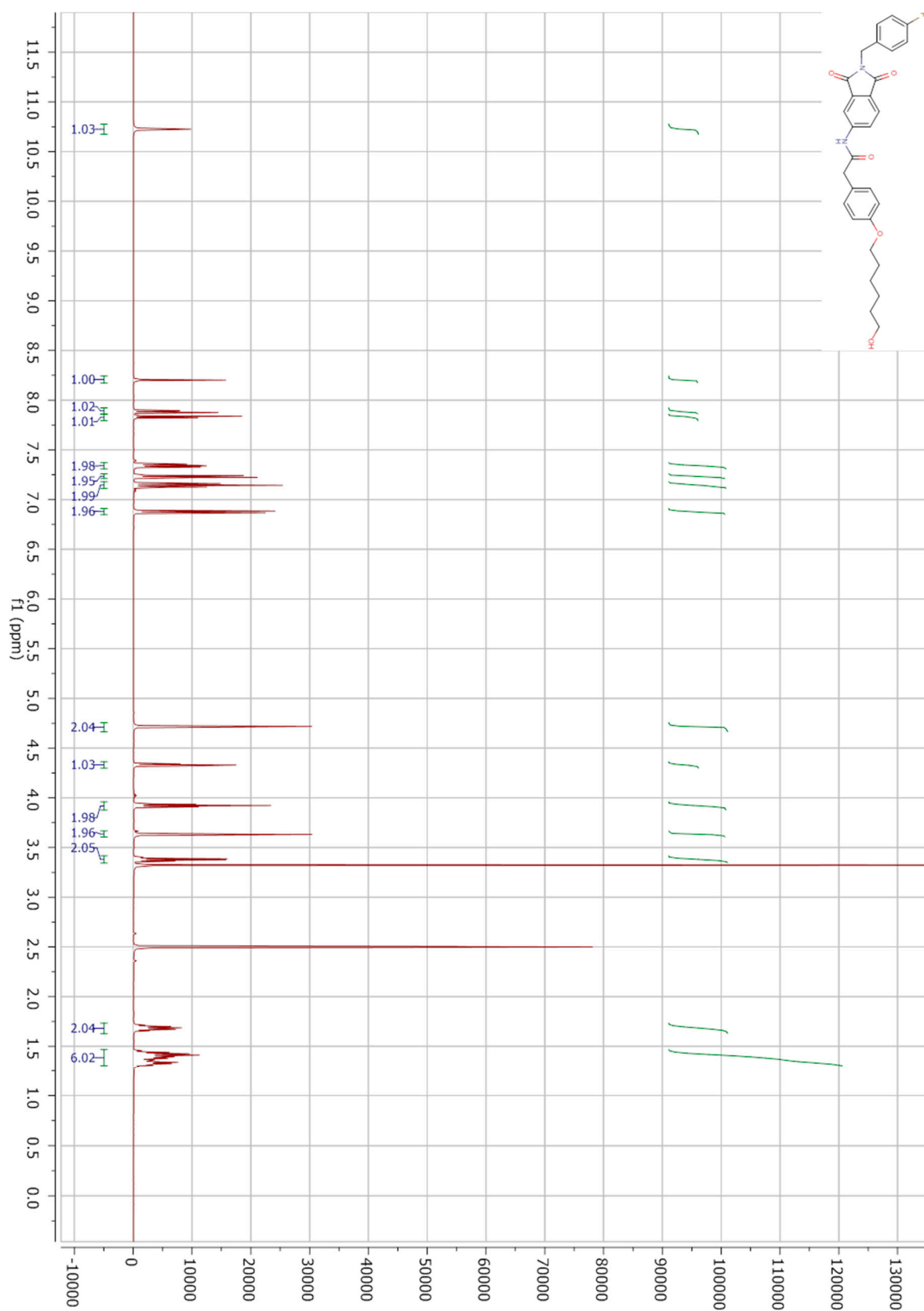


N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl}-2-{4-[(5-hydroxypentyl)oxy]phenyl}acetamide (**13m**; ZHAWOC5683)

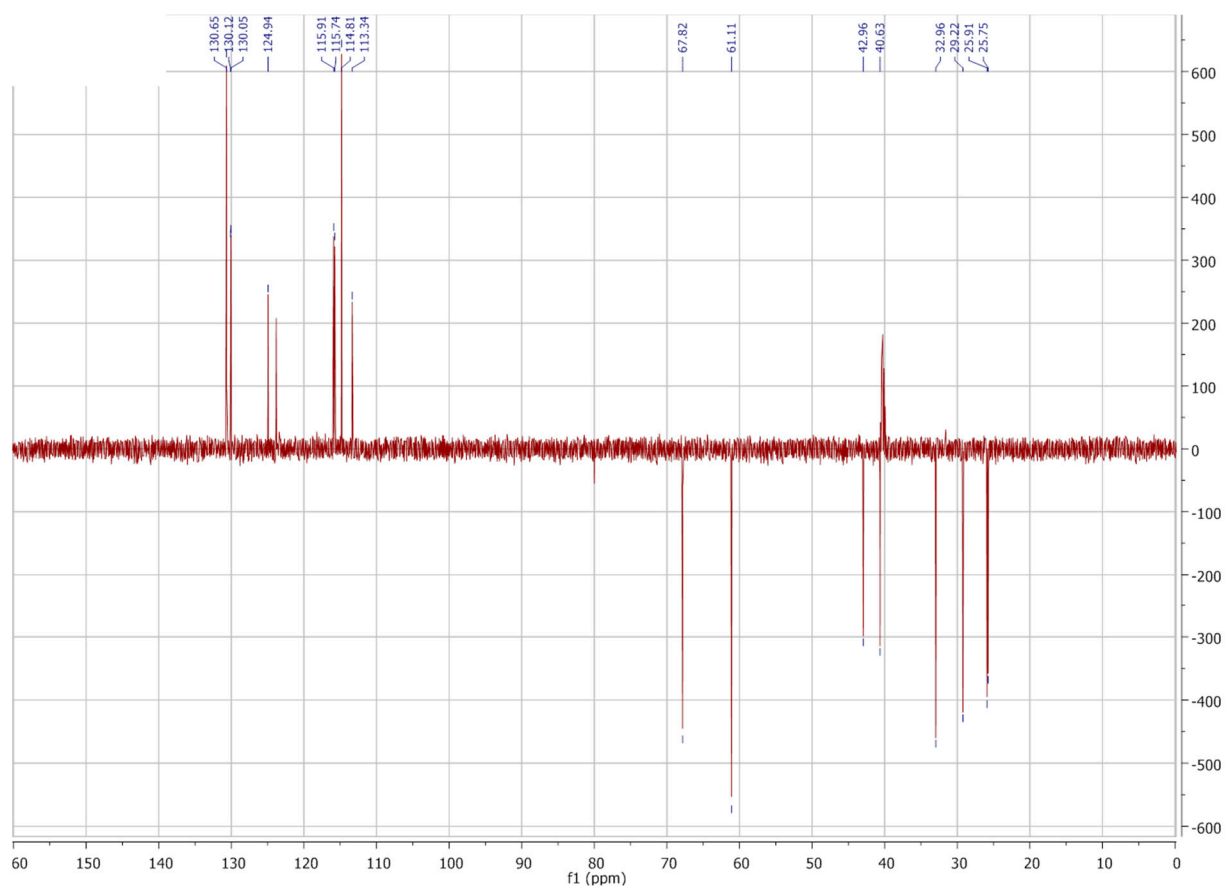
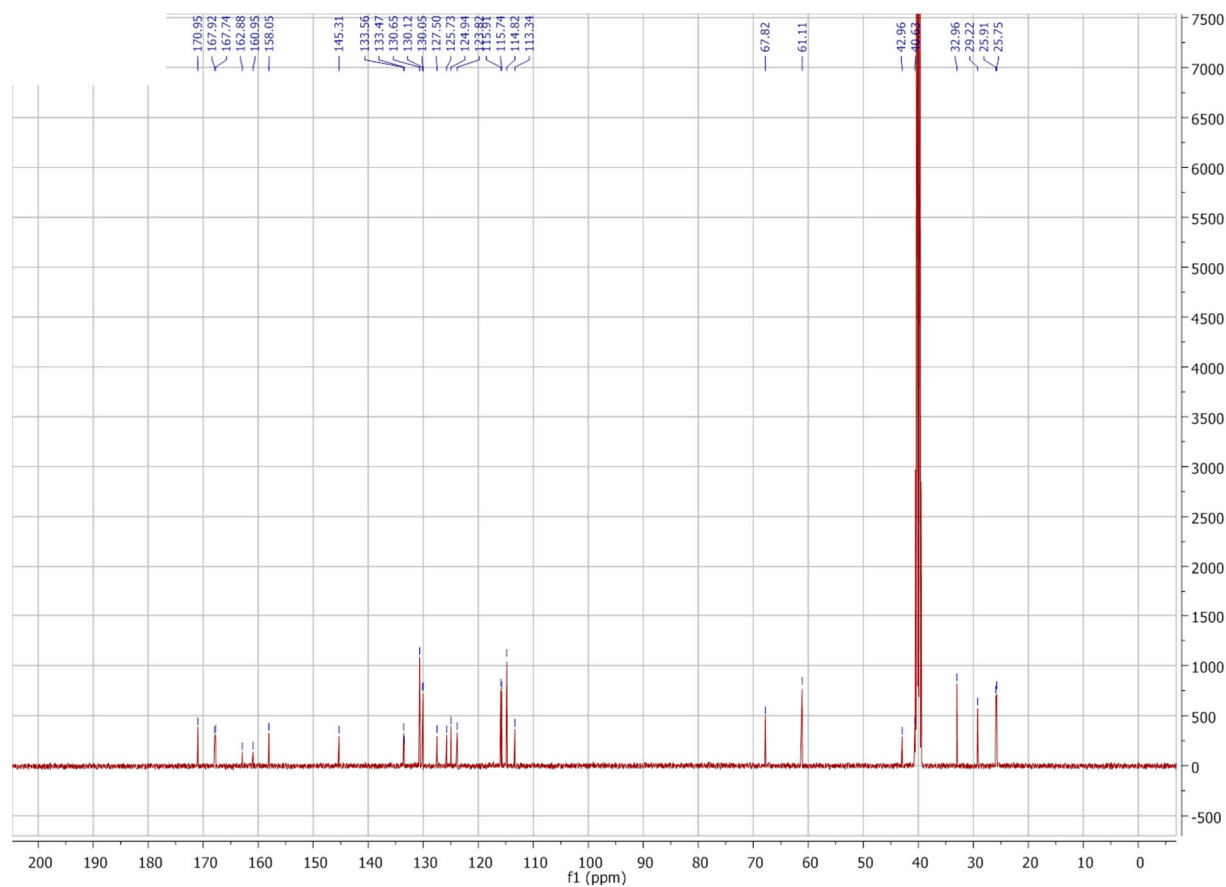


N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl}-2-{4-[(6-hydroxyhexyl)oxy]phenyl}acetamide (**13n**; ZHAWOC6643)

NMR

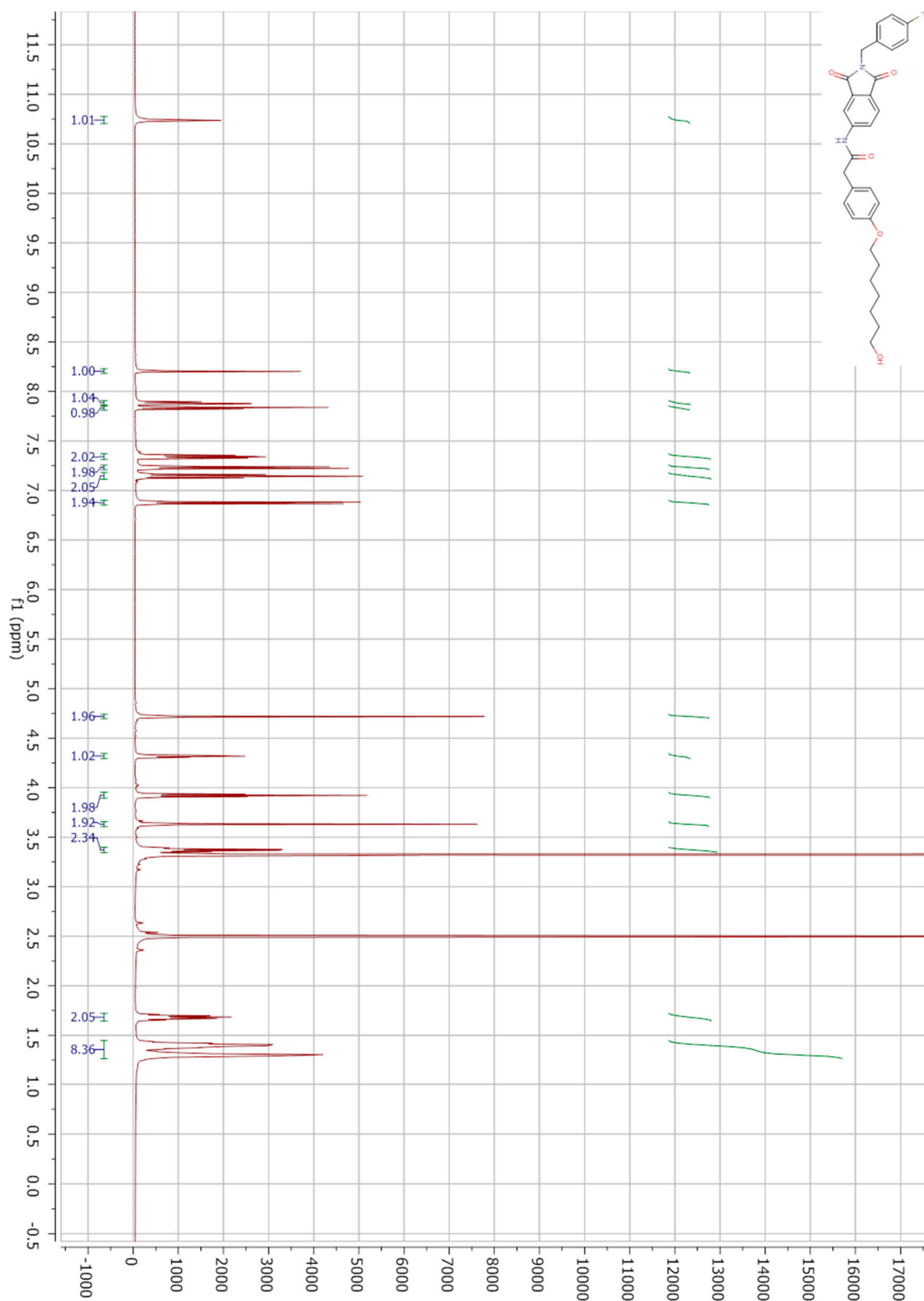


N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl}-2-{4-[(6-hydroxyhexyl)oxy]phenyl}acetamide (**13n**; ZHAWOC6643)

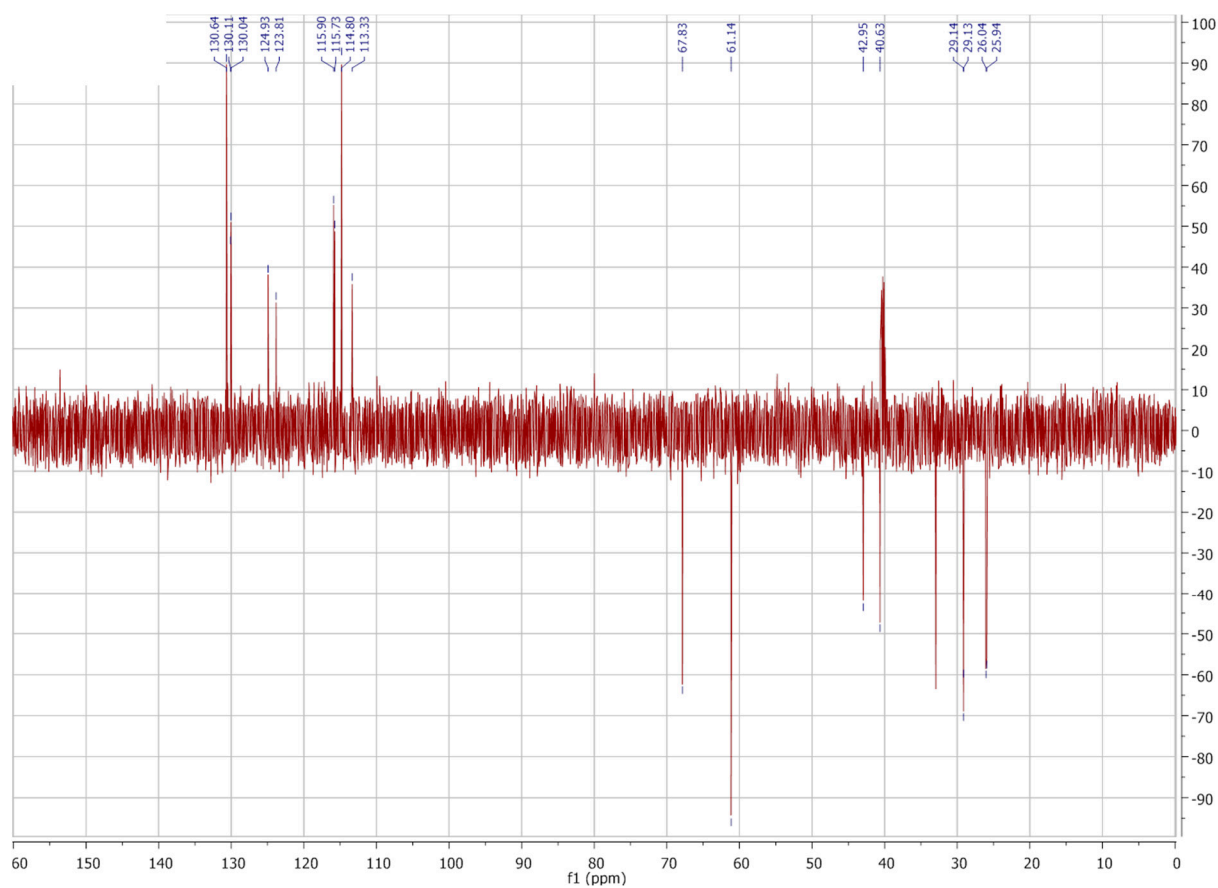
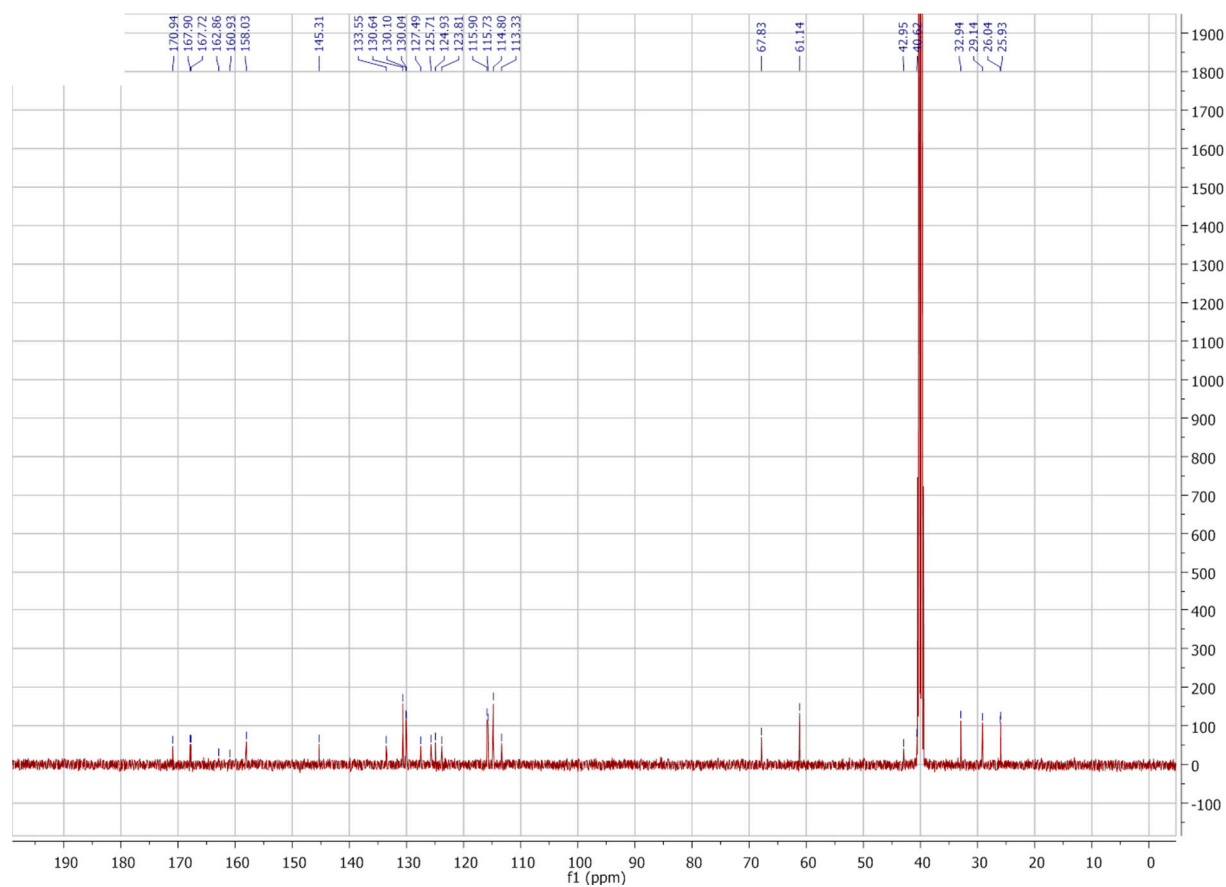


N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl}-2-{4-[(7-hydroxyheptyl)oxy]phenyl}acetamide (**13o**; ZHAWOC6636)

NMR

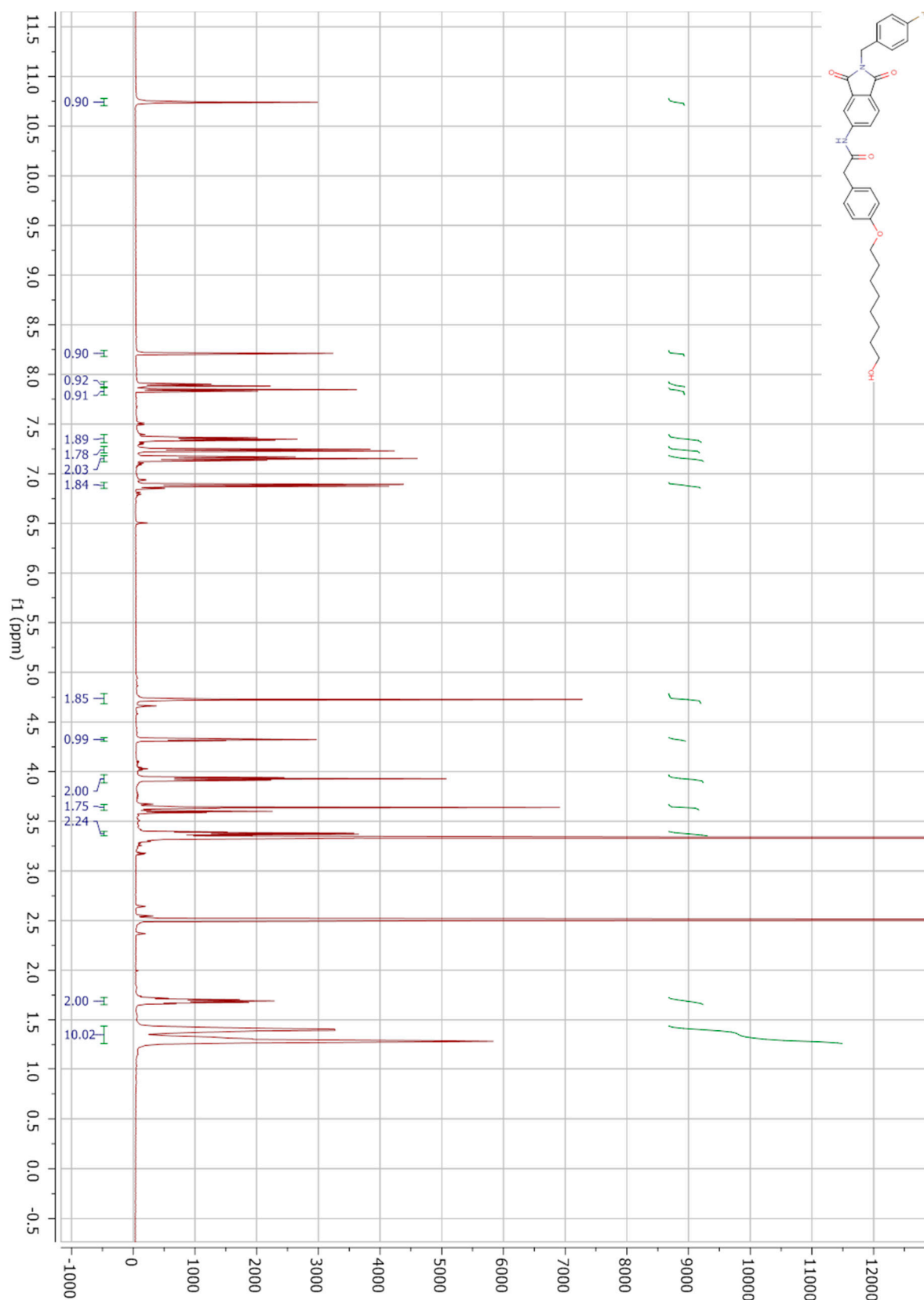


N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl}-2-{4-[(7-hydroxyheptyl)oxy]phenyl}acetamide (**13o**; ZHAWOC6636)

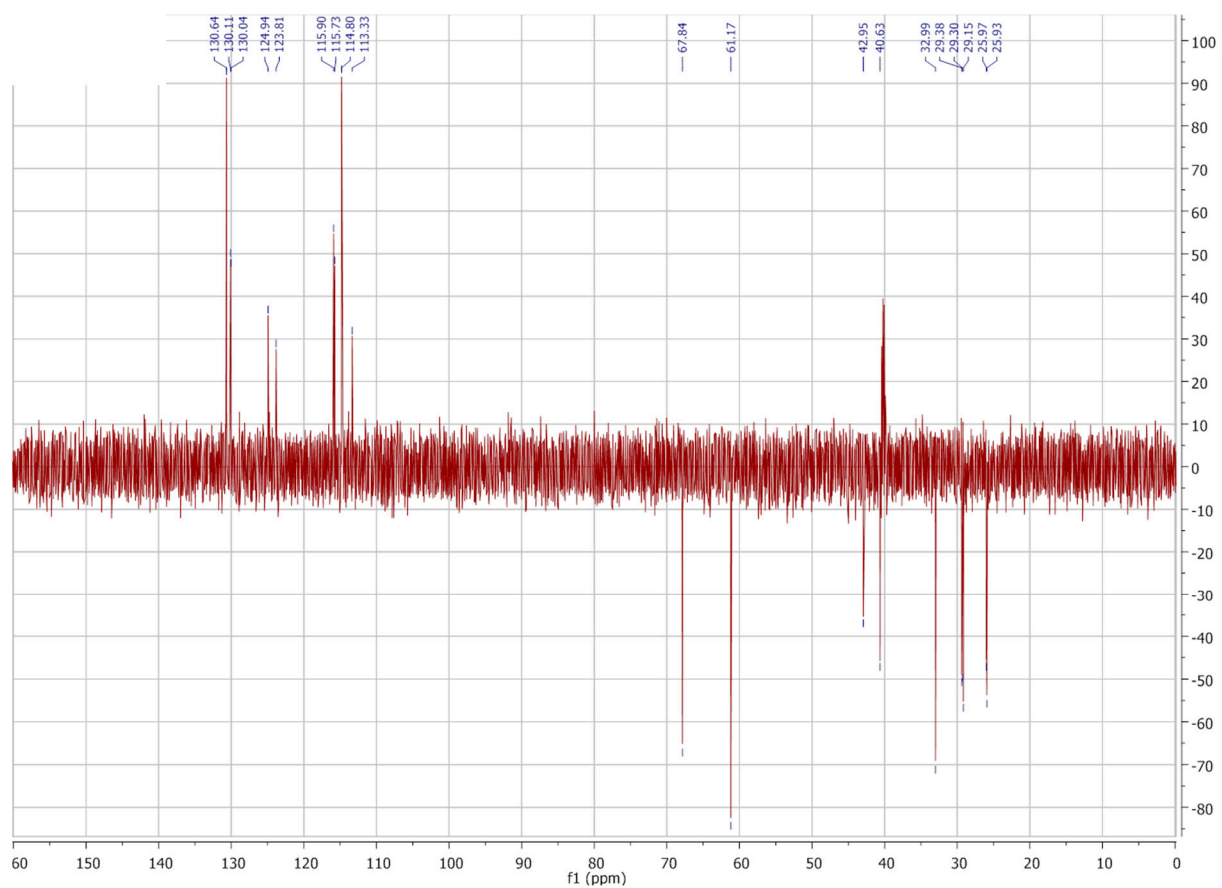
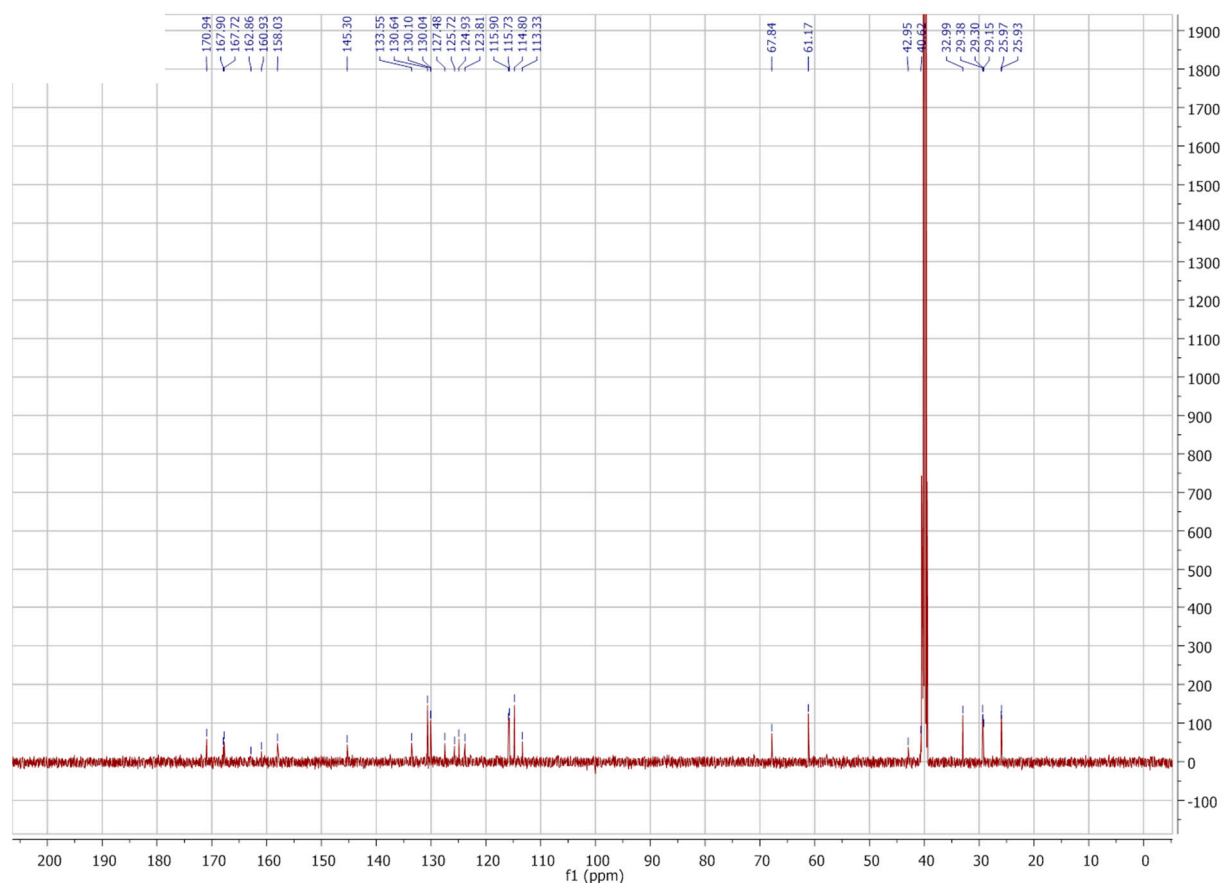


N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl}-2-{4-[(8-hydroxyoctyl)oxy]phenyl}acetamide (**13p**; ZHAWOC6639)

NMR

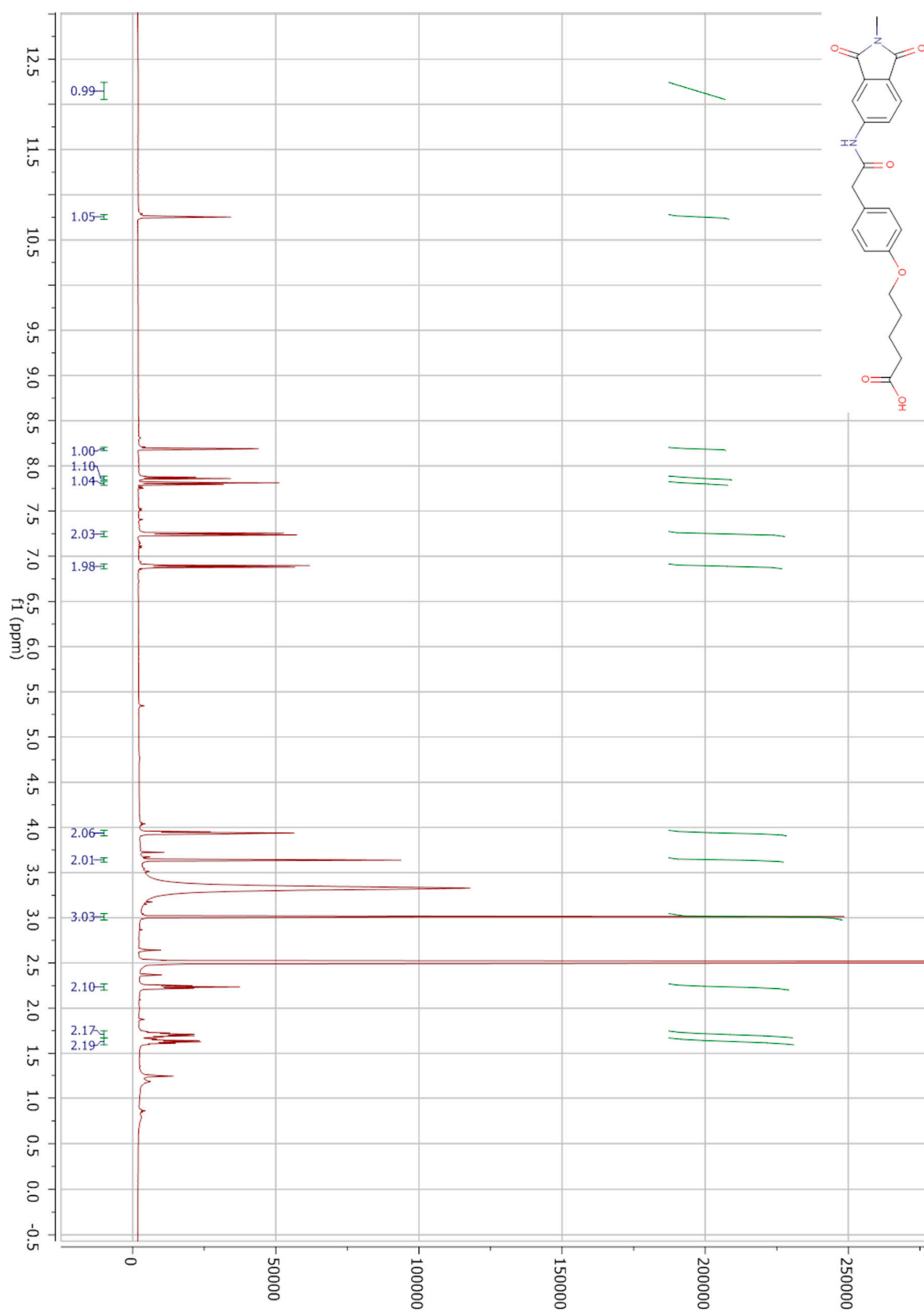


N-{2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl}-2-{4-[(8-hydroxyoctyl)oxy]phenyl}acetamide (**13p**; ZHAWOC6639)

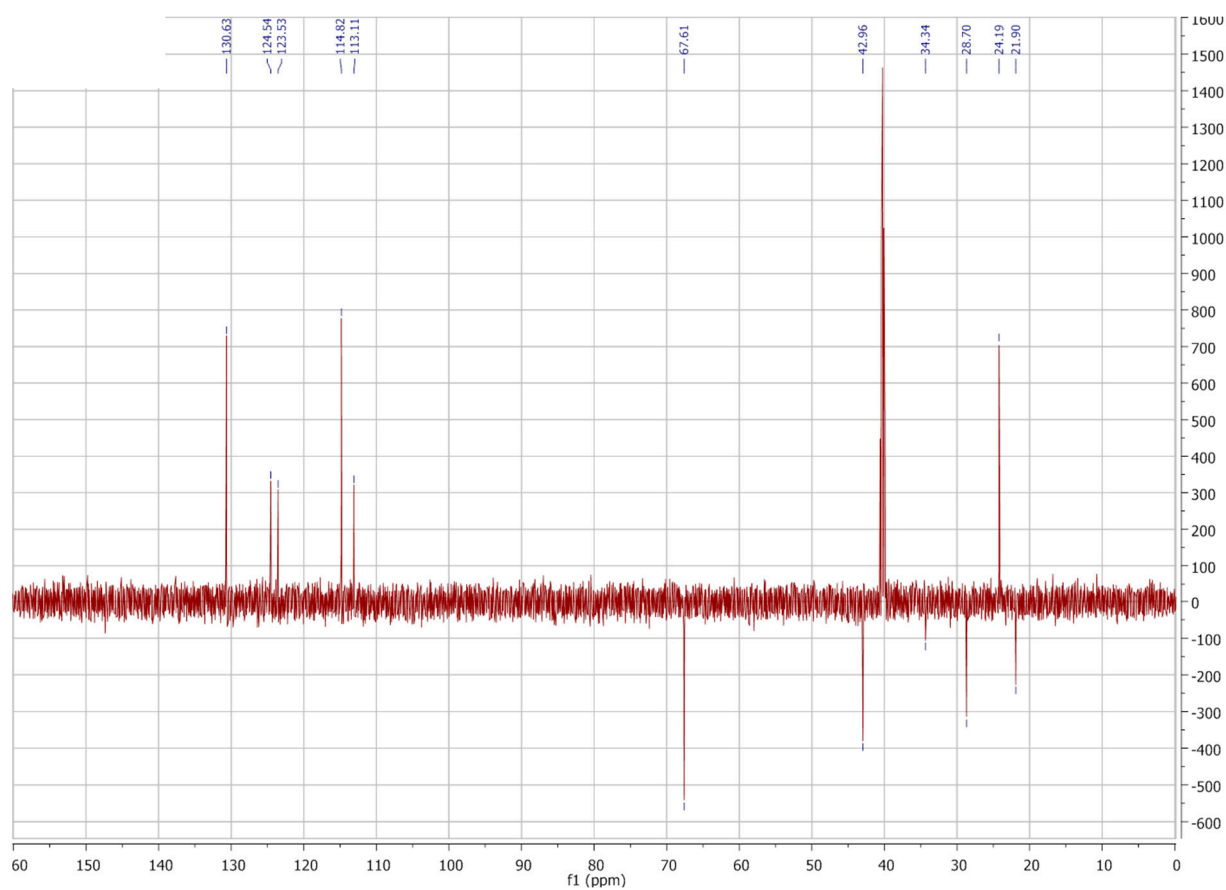
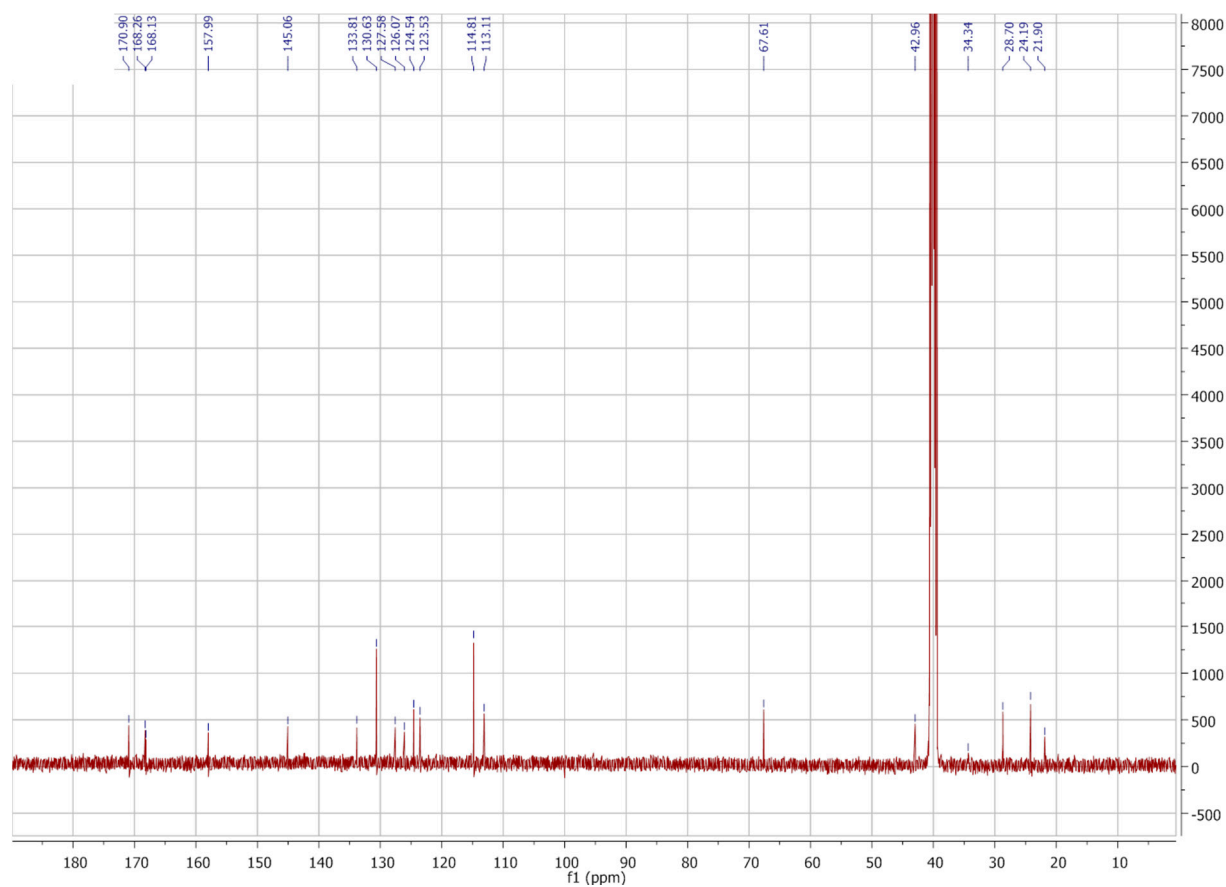


5-(4-[(2-methyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)pentanoic acid (**14a**; ZHAWOC6649)

NMR

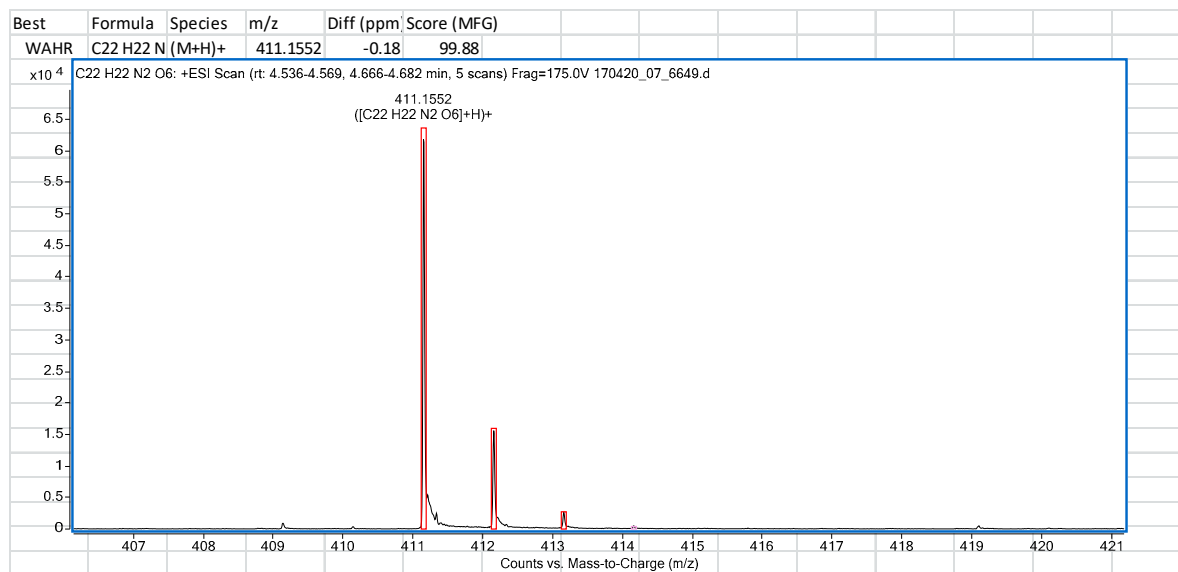


5-(4-[(2-methyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)pentanoic acid (**14a**; ZHAWOC6649)



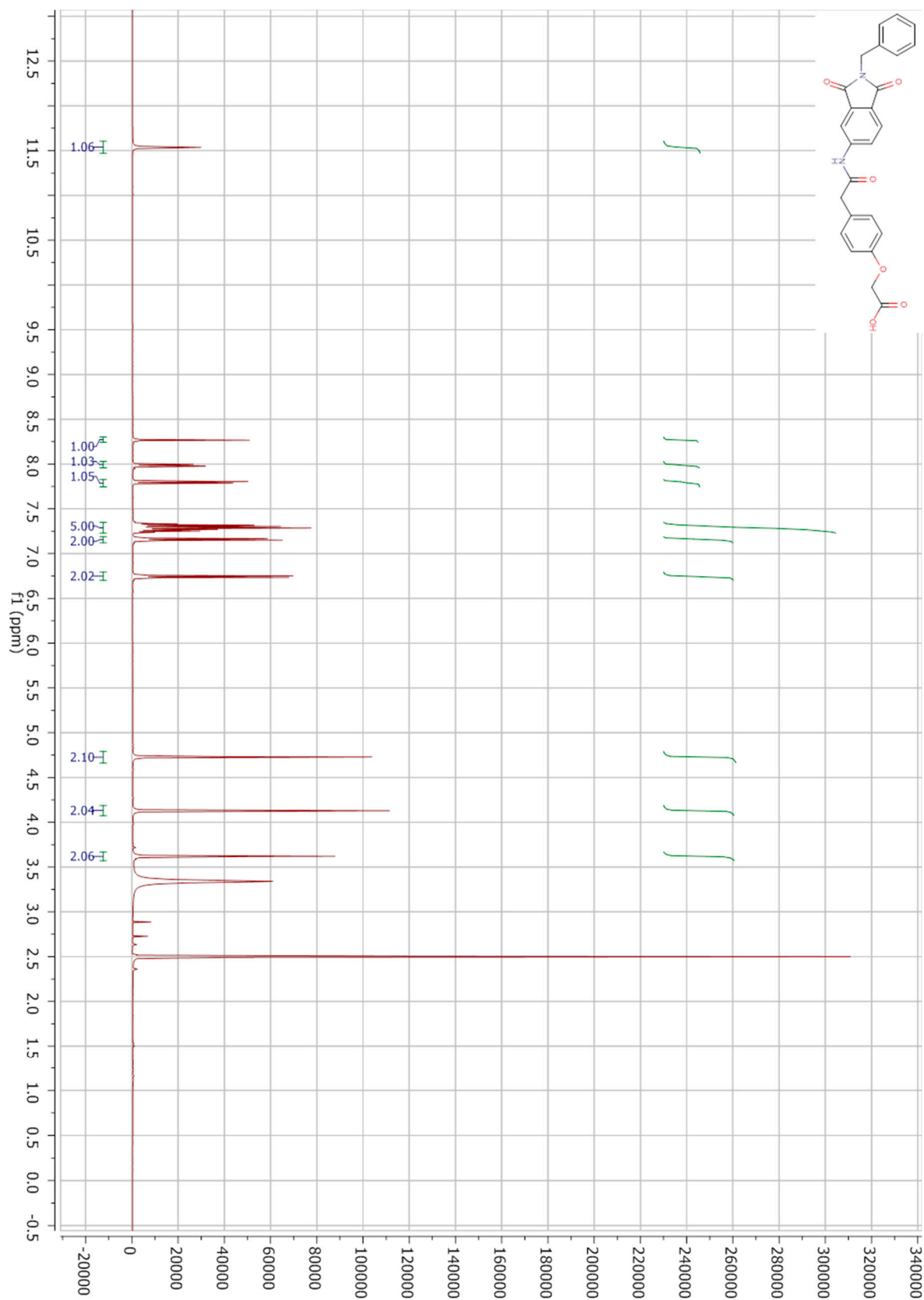
5-(4-[(2-methyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)pentanoic acid (14a; ZHAWOC6649)

HRMS

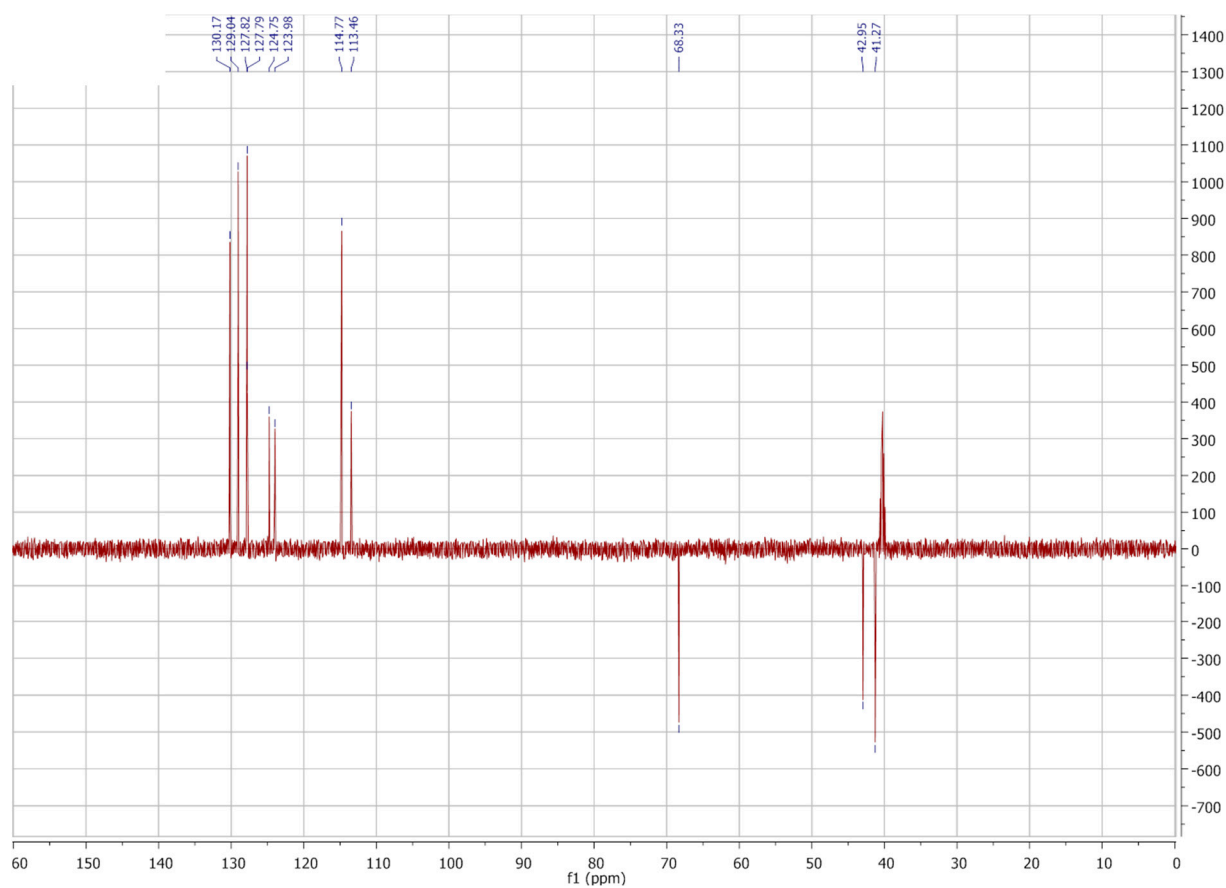
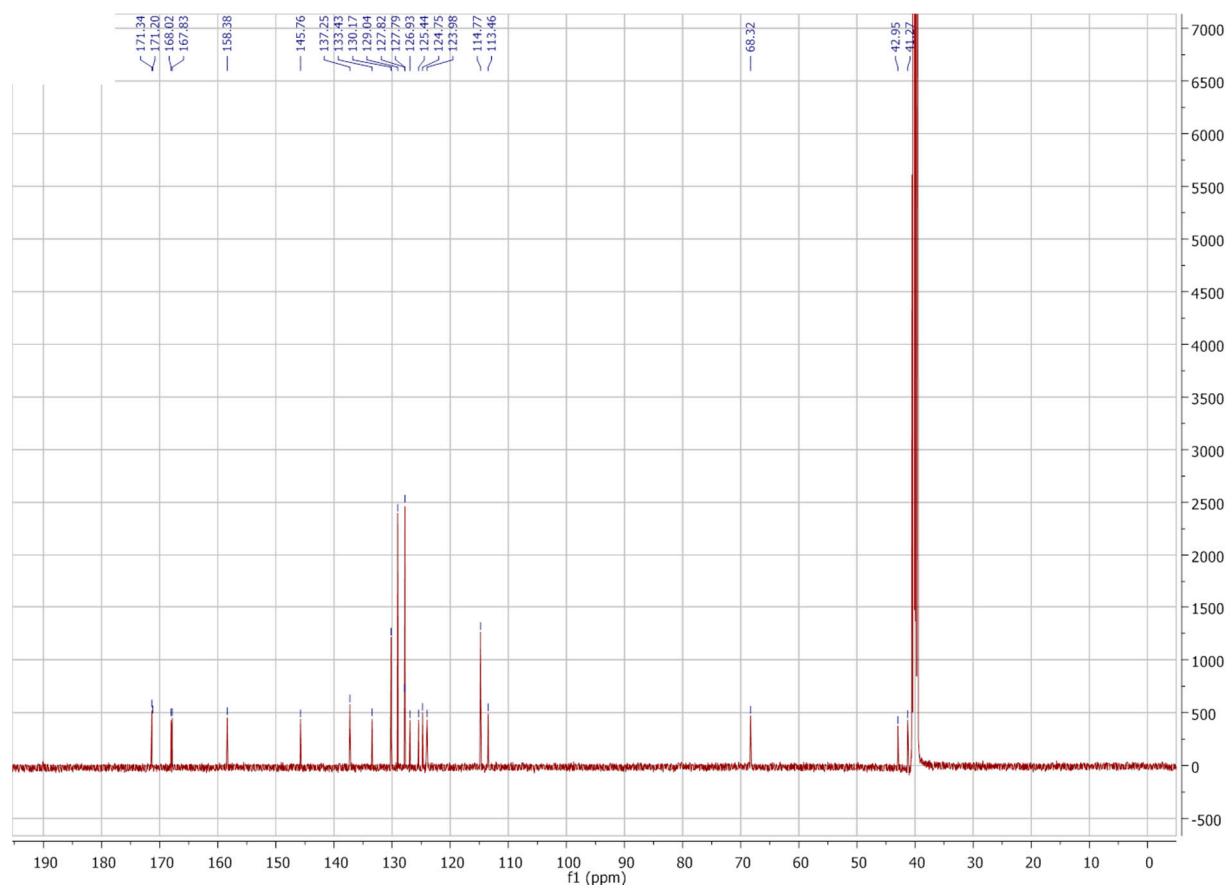


2-(4-[[[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl]phenoxy)acetic acid (**14b**; ZHAWOC5474)

NMR

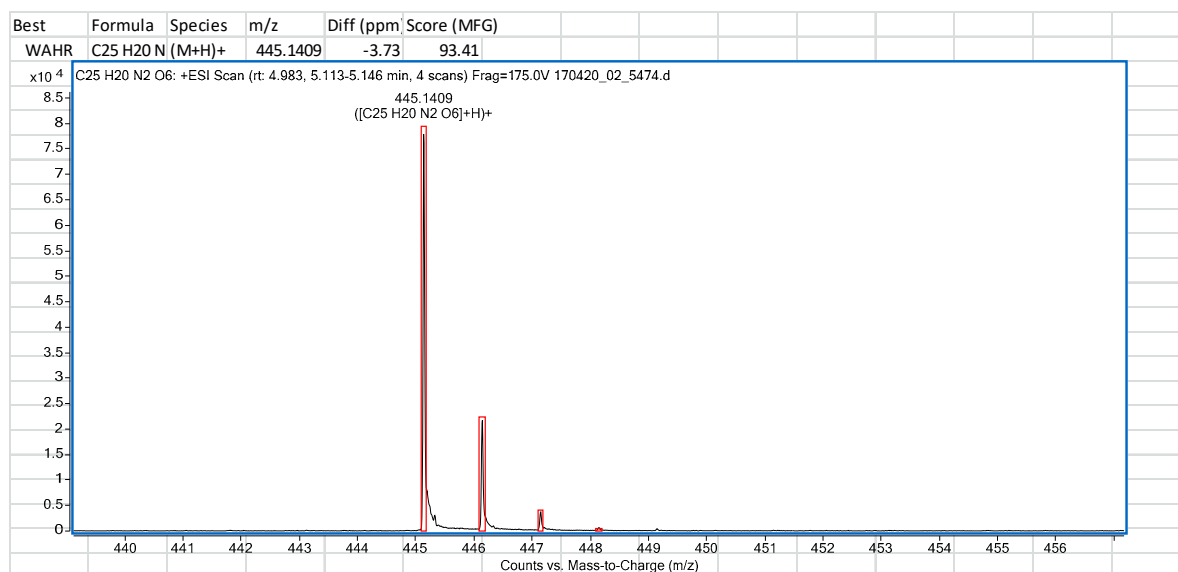


2-(4-[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)acetic acid (**14b**; ZHAWOC5474)



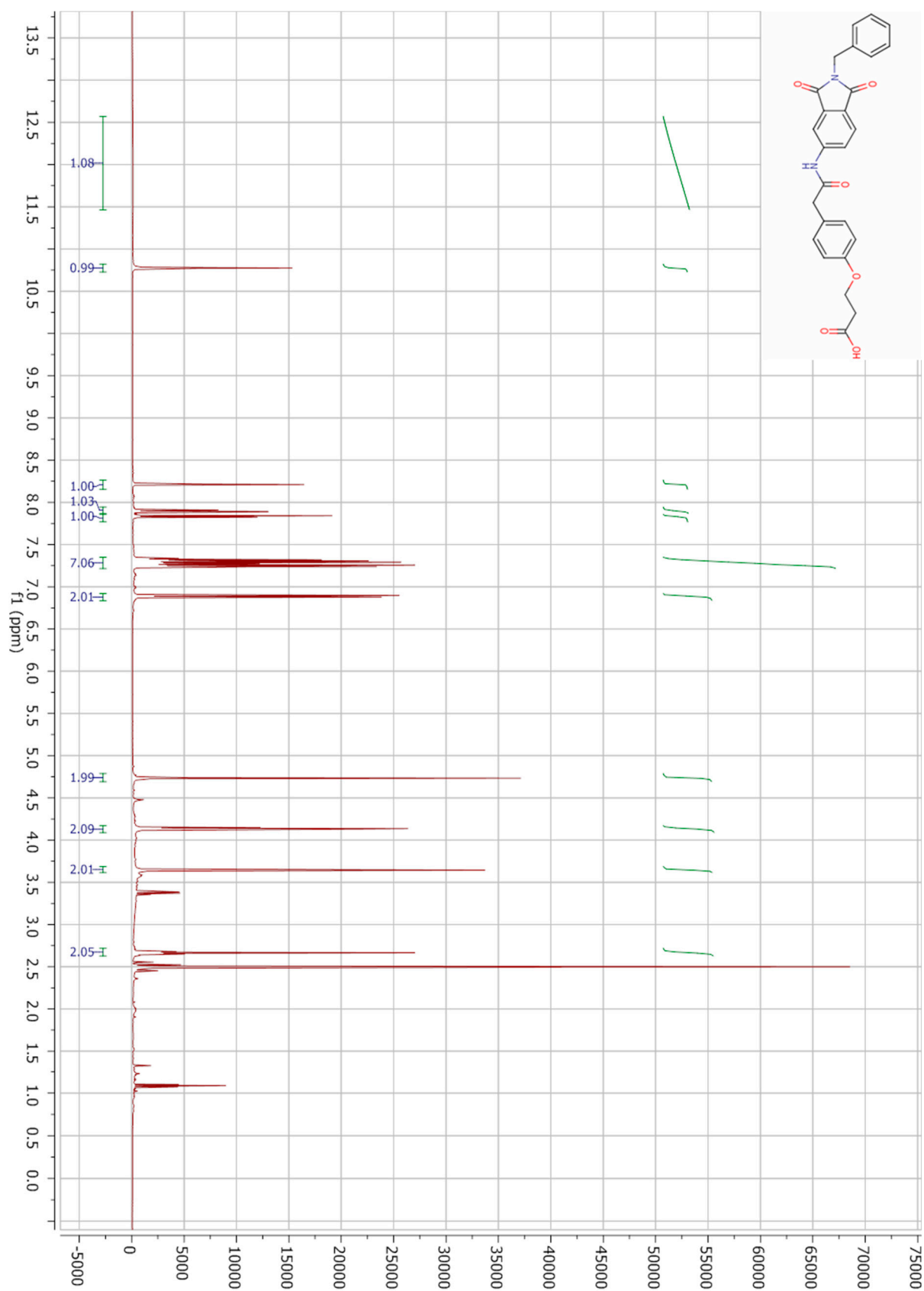
2-(4-[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)acetic acid (**14b**; ZHAWOC5474)

HRMS

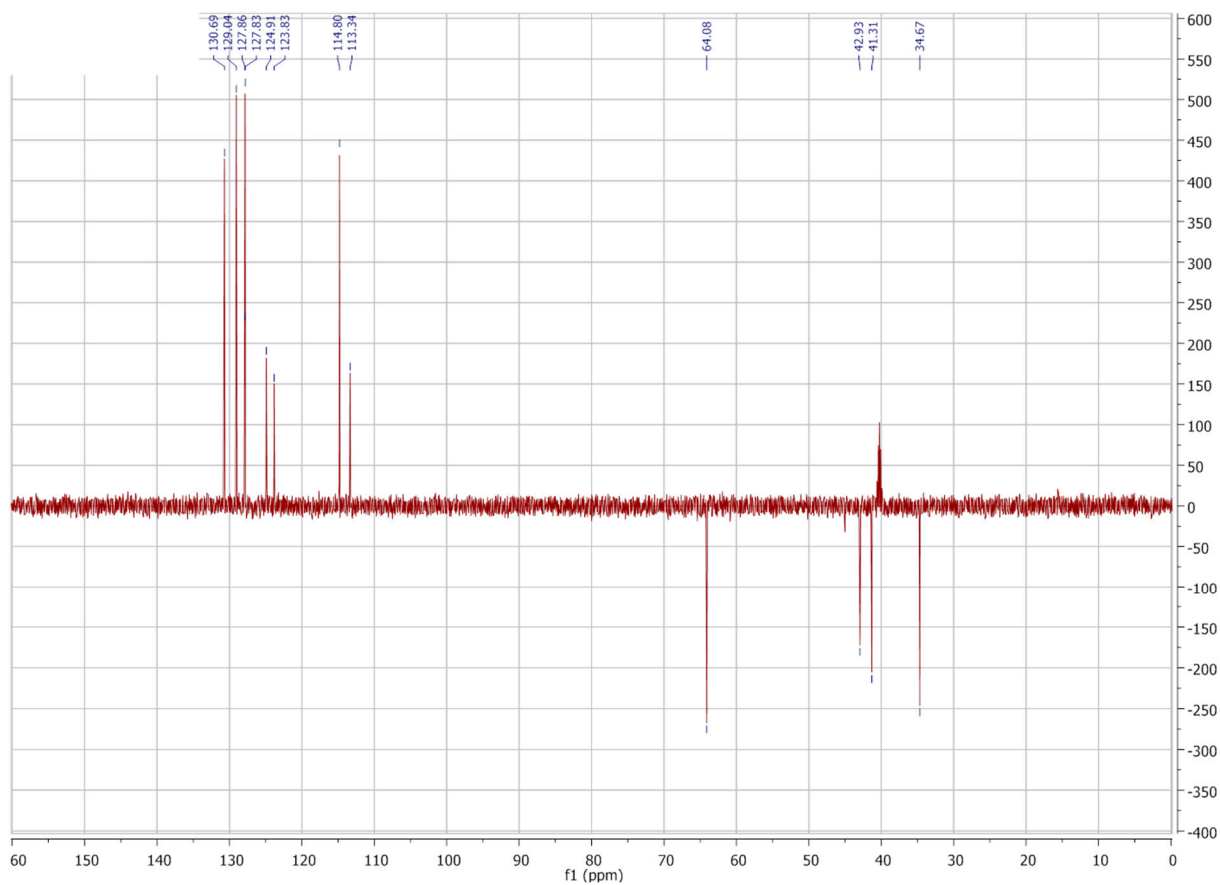
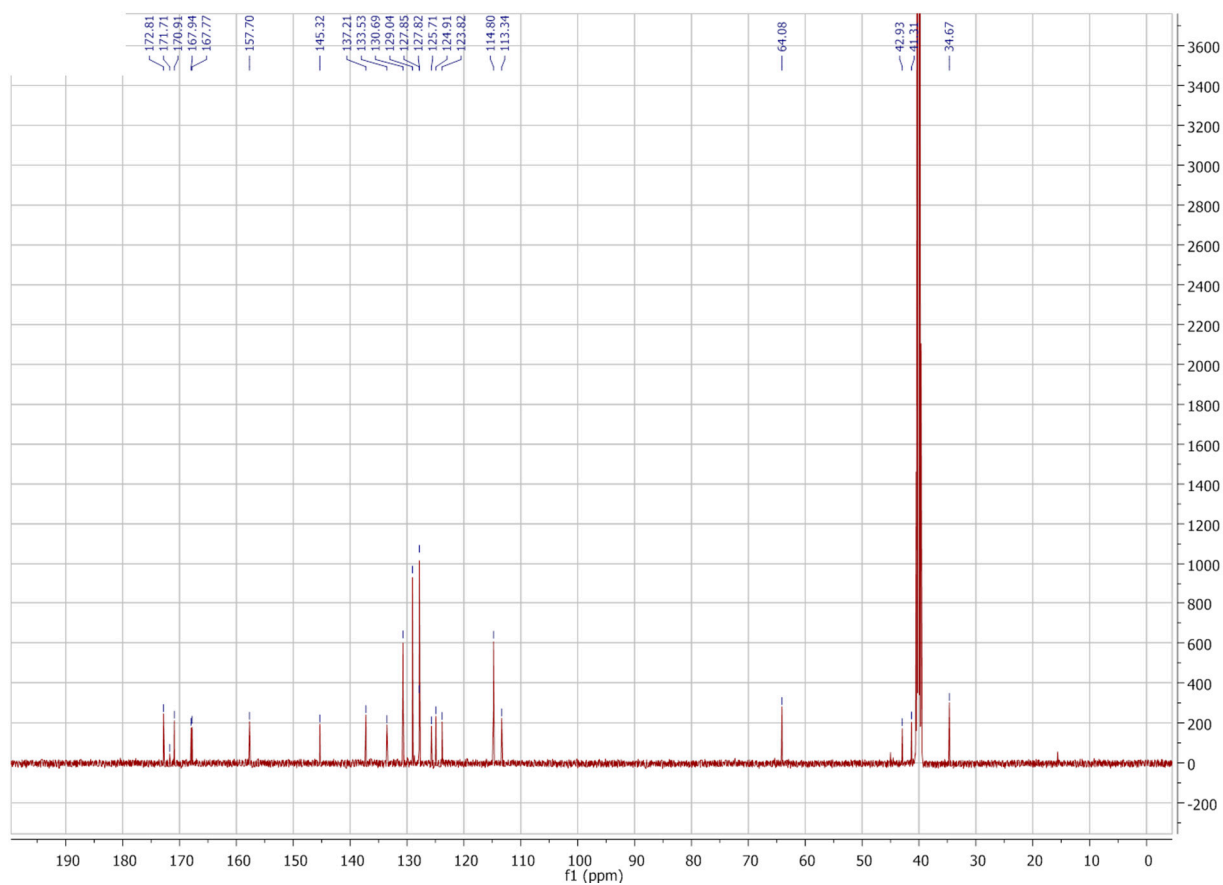


3-(4-[[[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl]phenoxy]propanoic acid (**14c**; ZHAWOC4765)

NMR

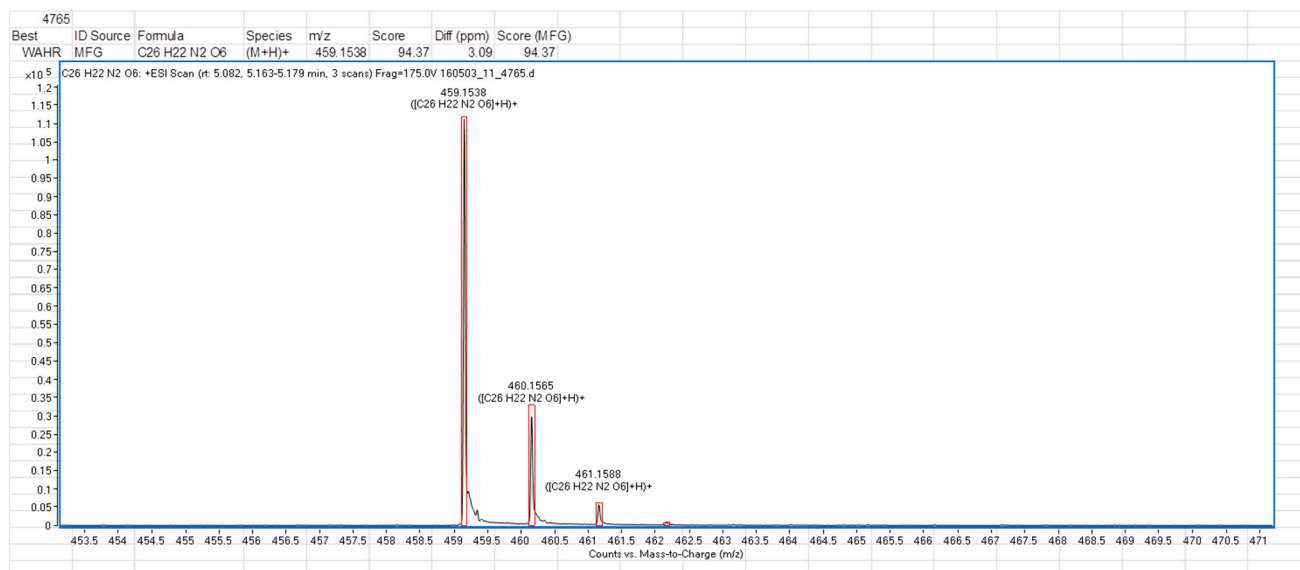


3-(4-[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)propanoic acid (**14c**; ZHAWOC4765)

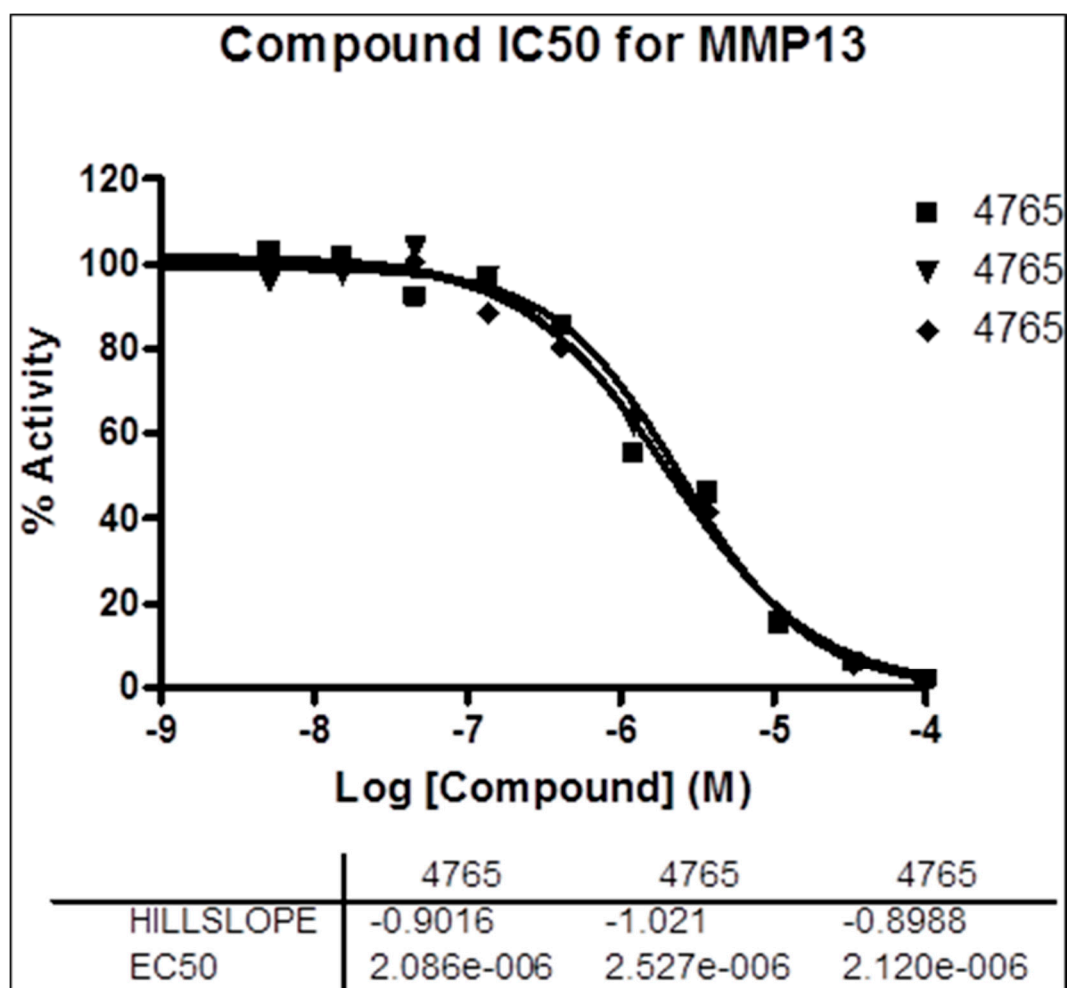


3-(4-[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)propanoic acid (**14c**; ZHAWOC4765)

HRMS

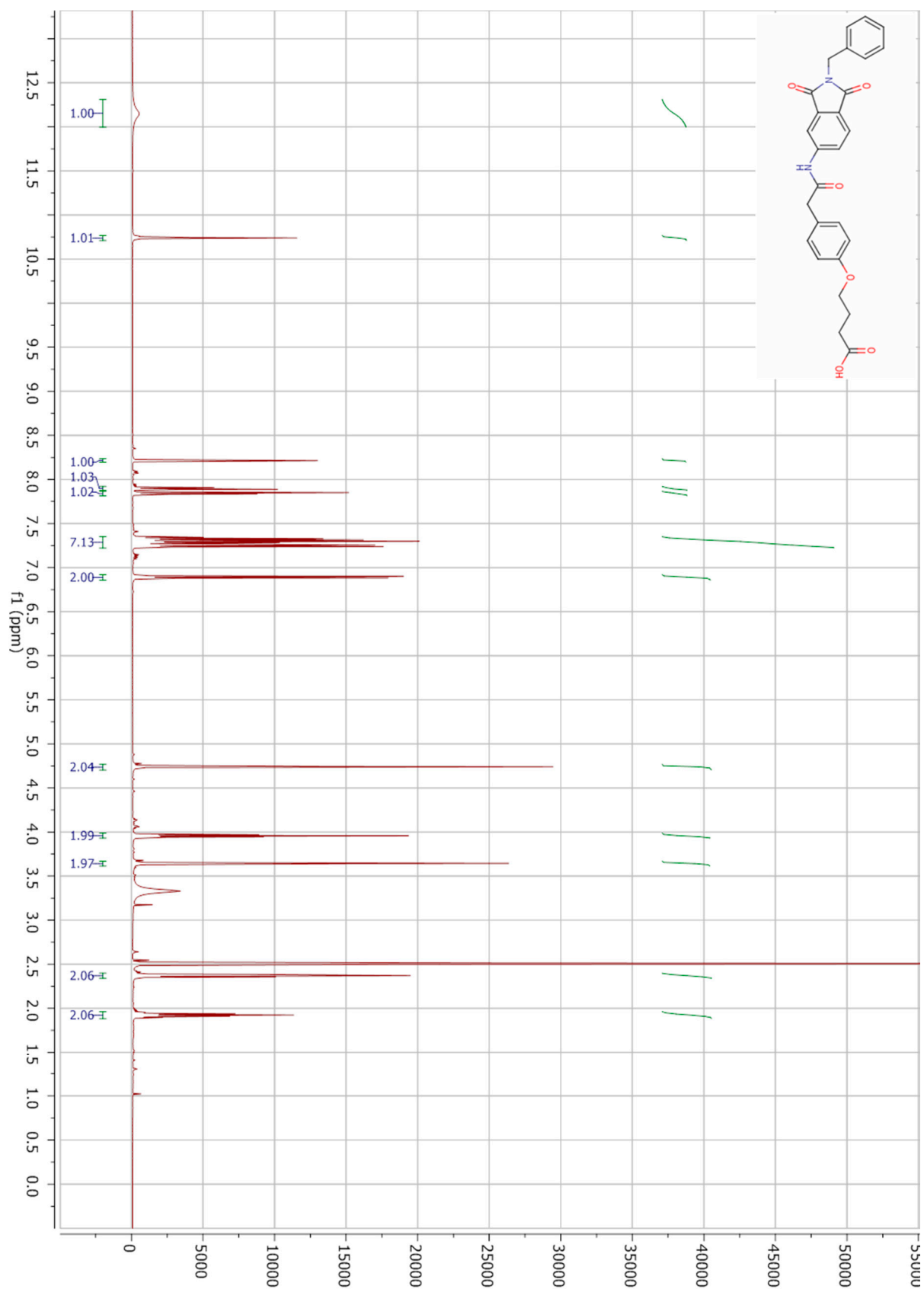


IC₅₀

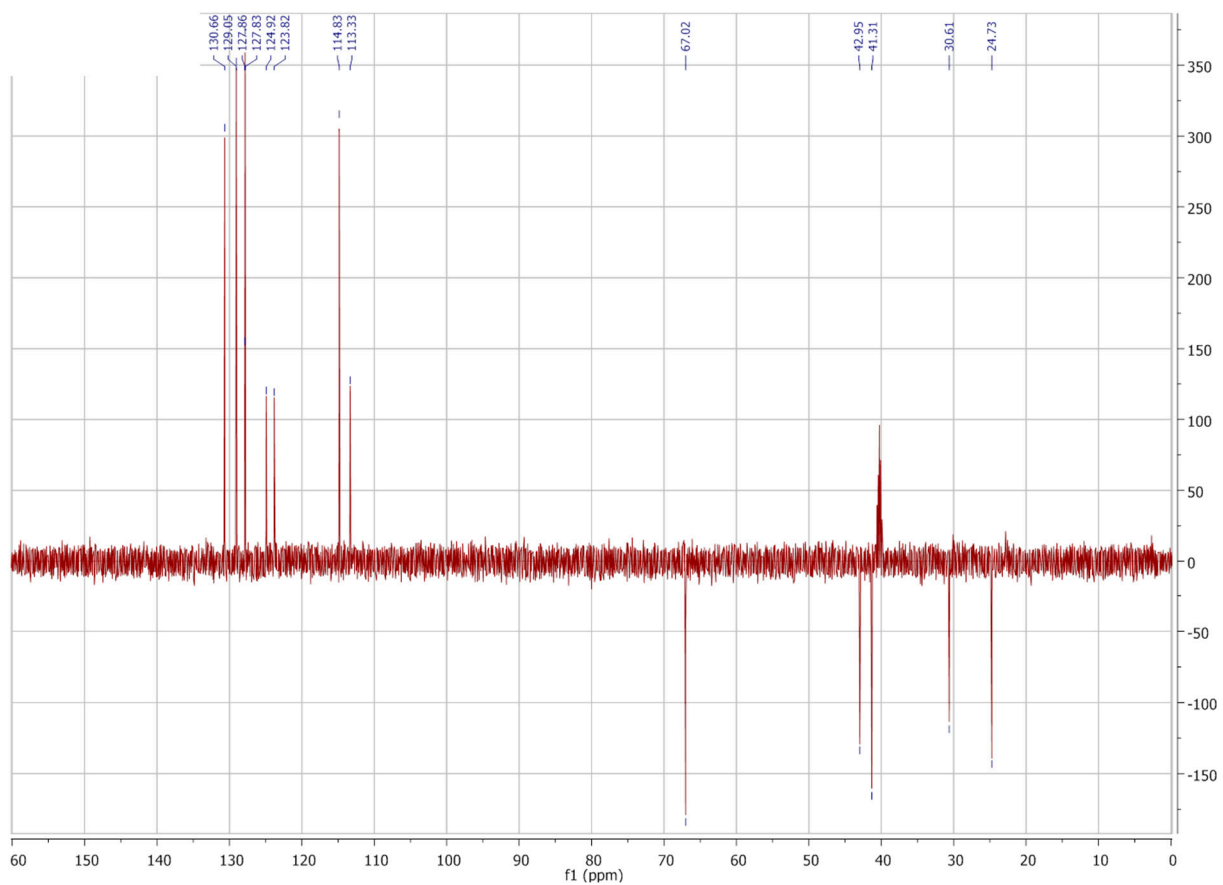
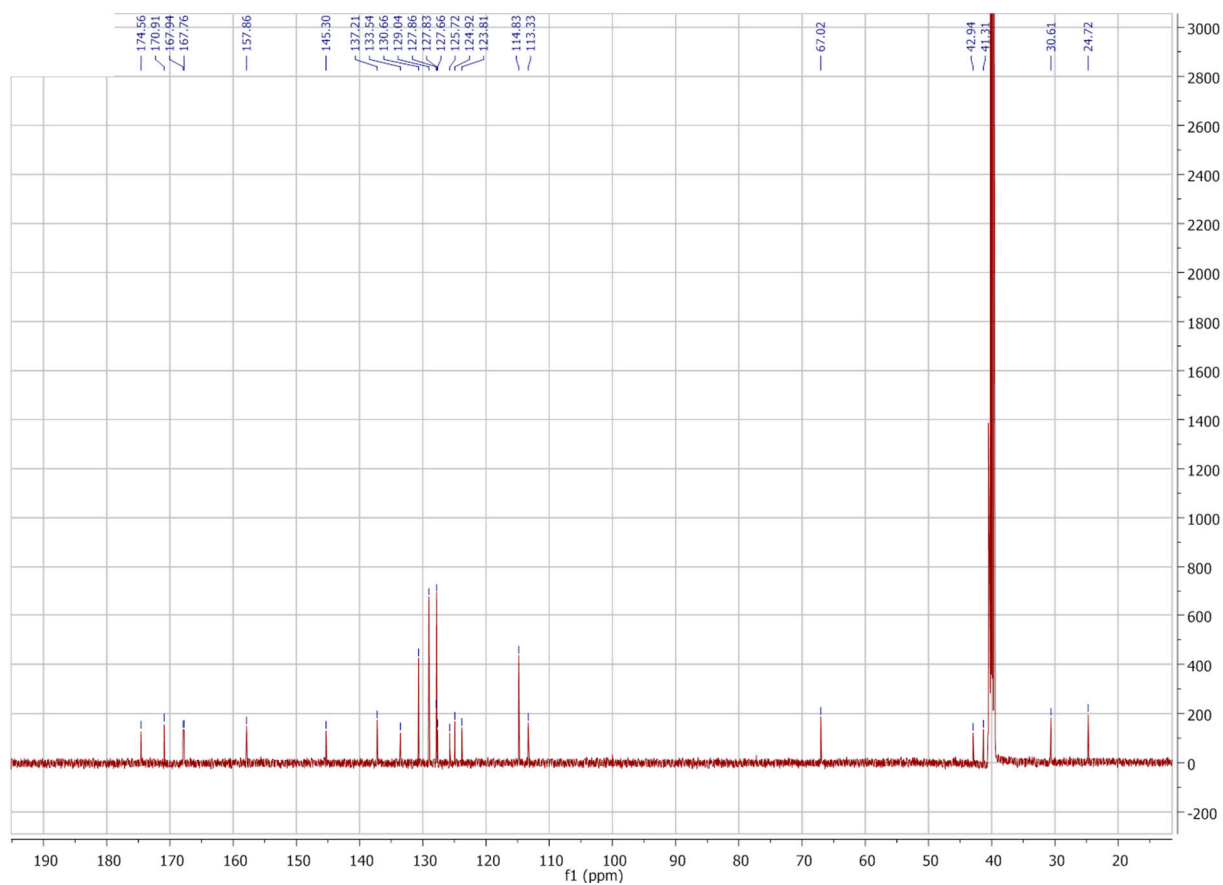


4-({[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)butanoic acid (**14d**; ZHAWOC4766)

NMR

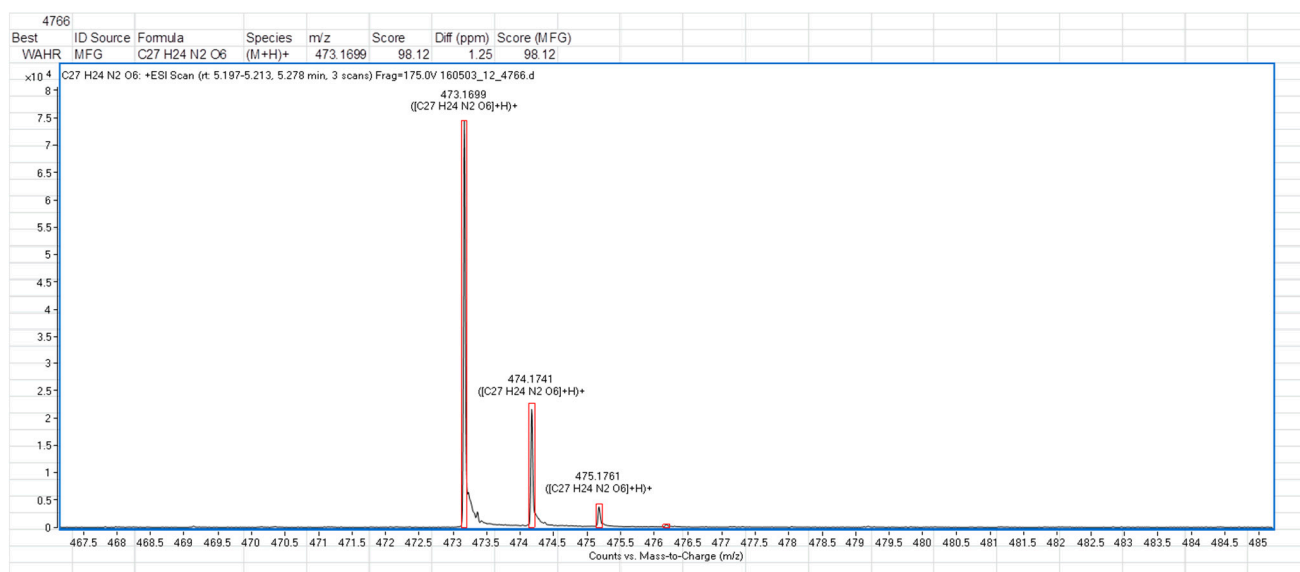


4-(4-[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)butanoic acid (**14d**; ZHAWOC4766)

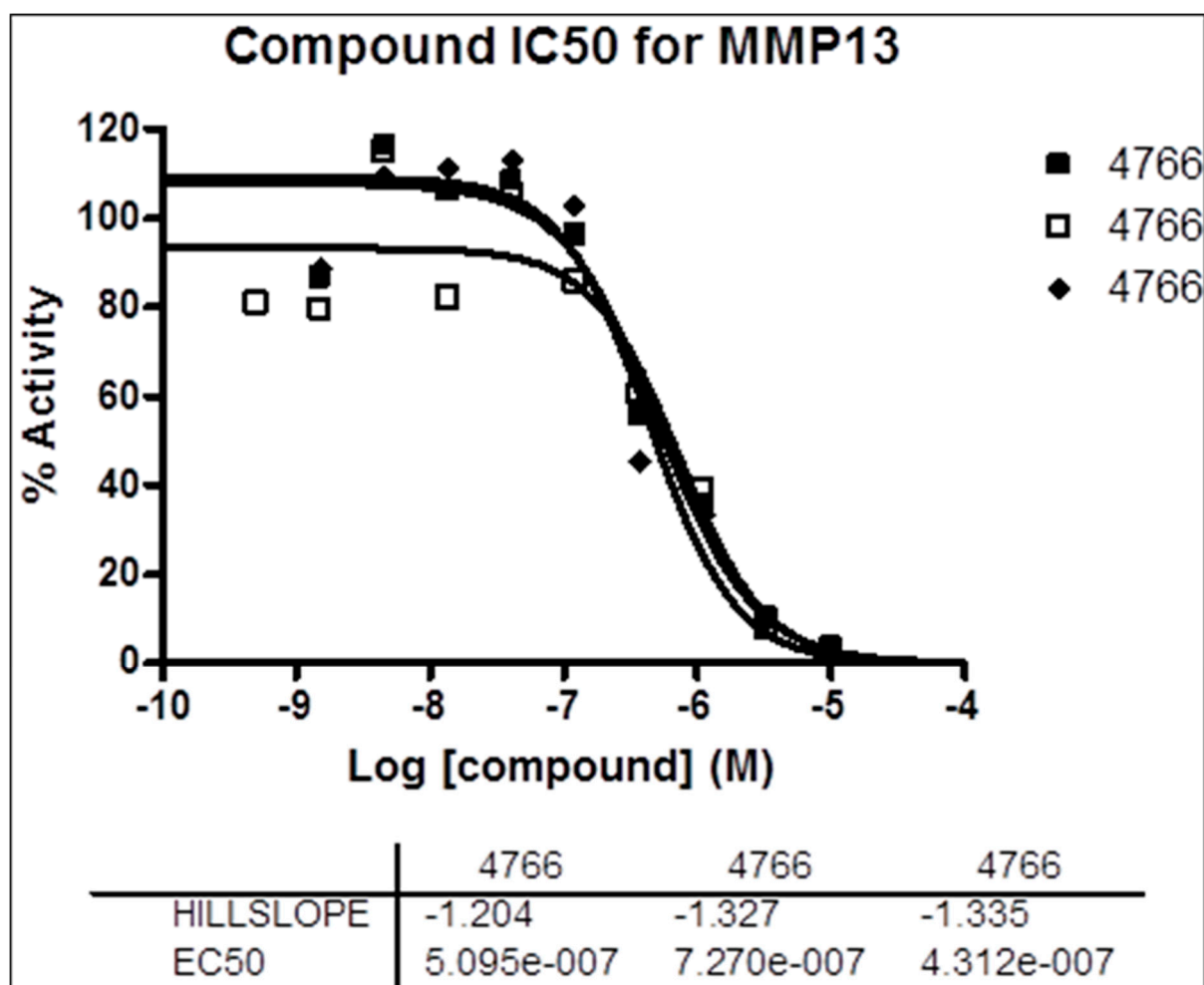


4-(4-[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)butanoic acid (**14d**; ZHAWOC4766)

HRMS

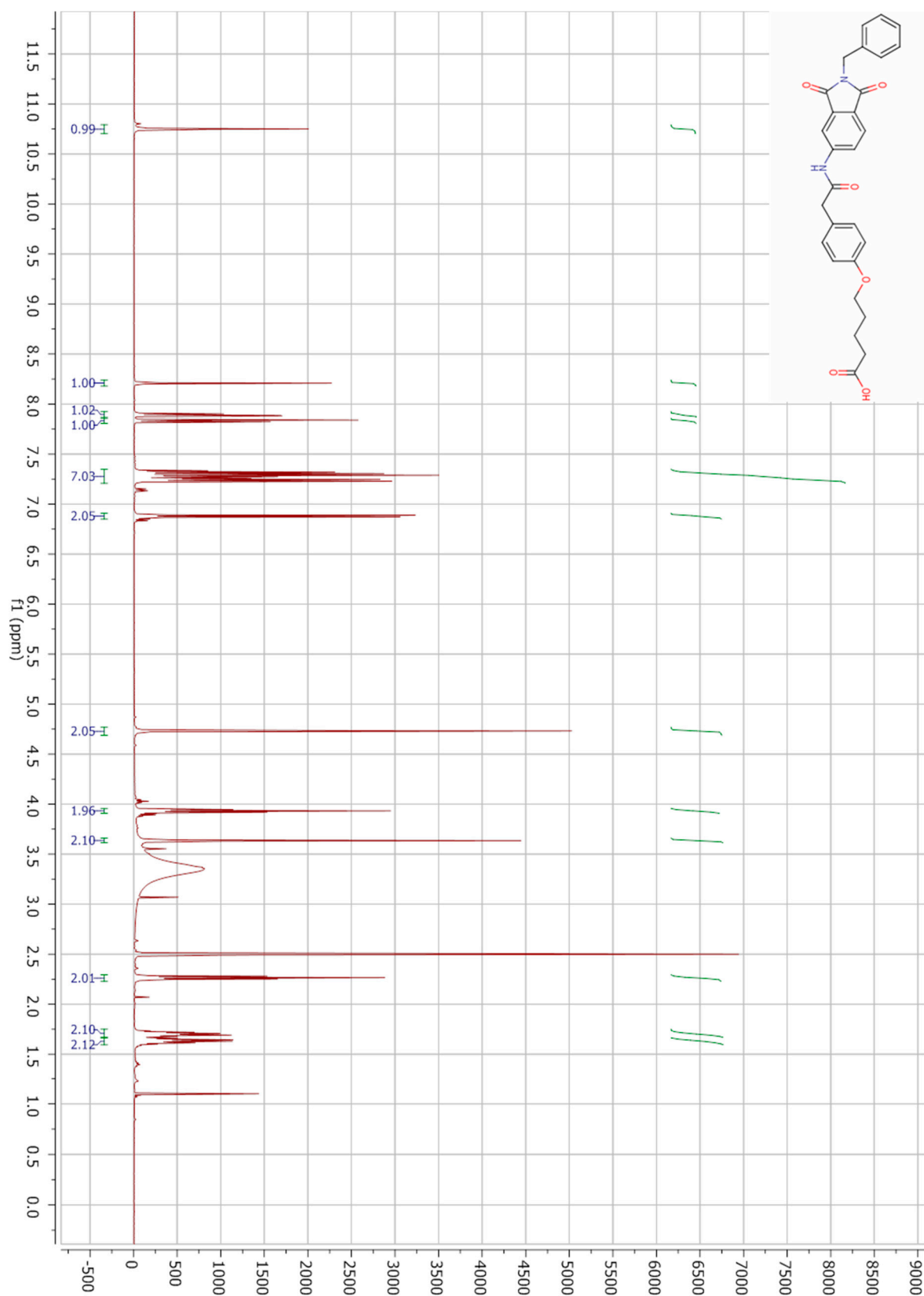


IC₅₀

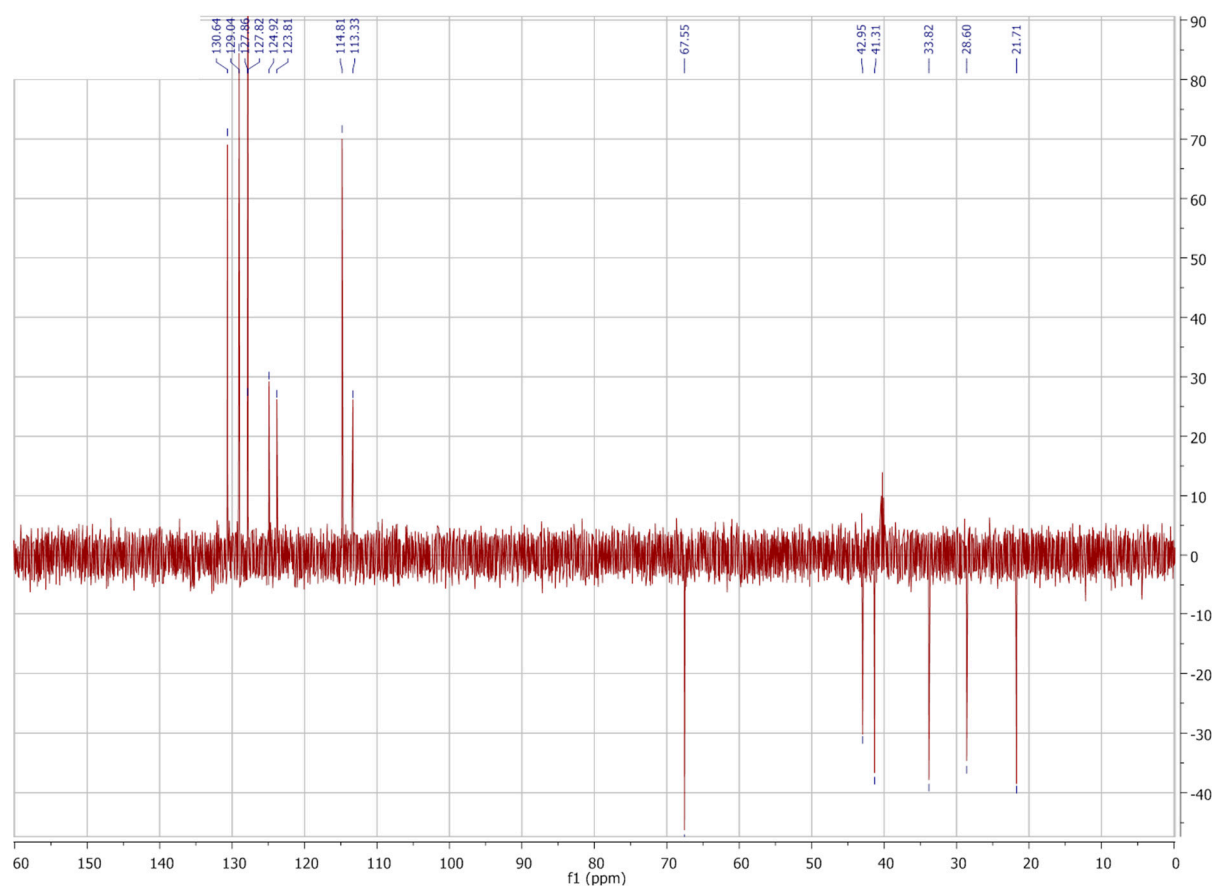
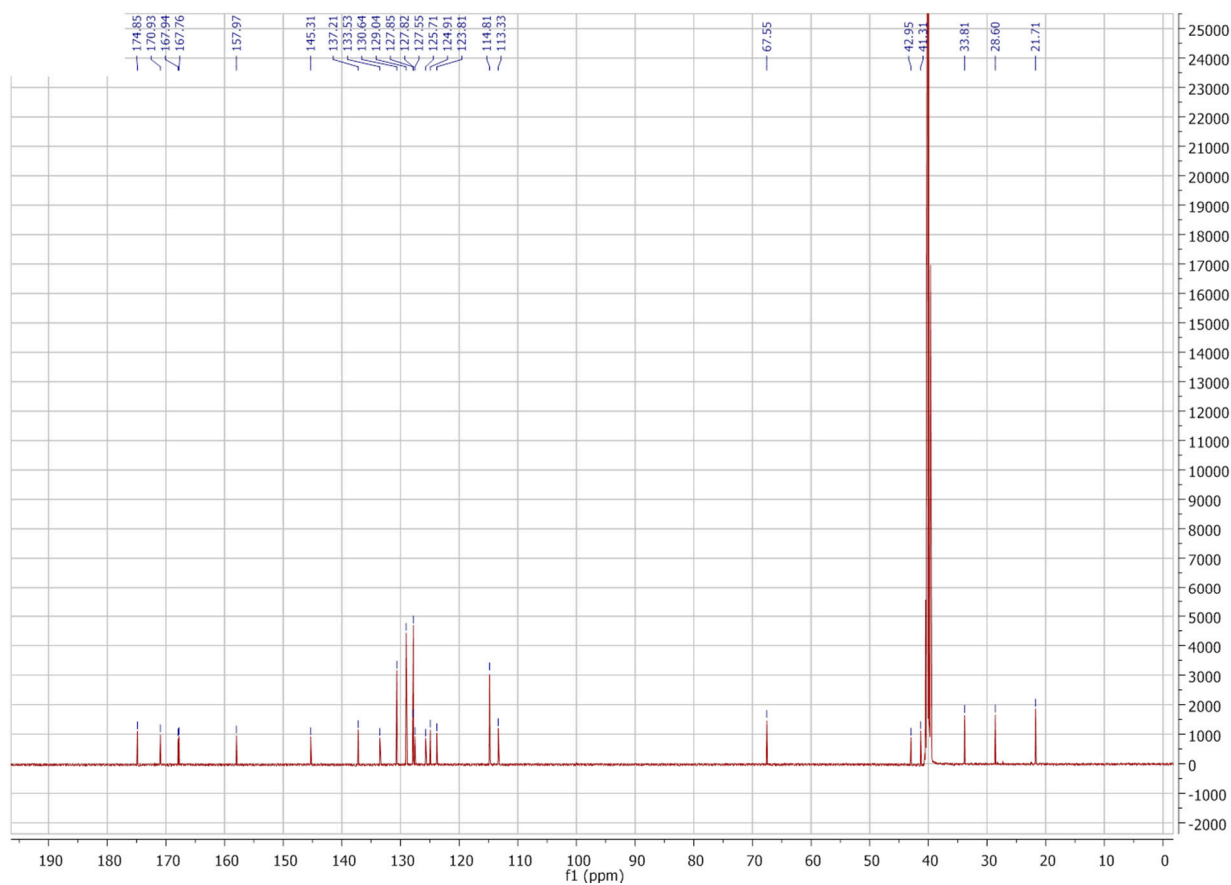


5-(4-[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)pentanoic acid (**14e**; ZHAWOC5131)

NMR

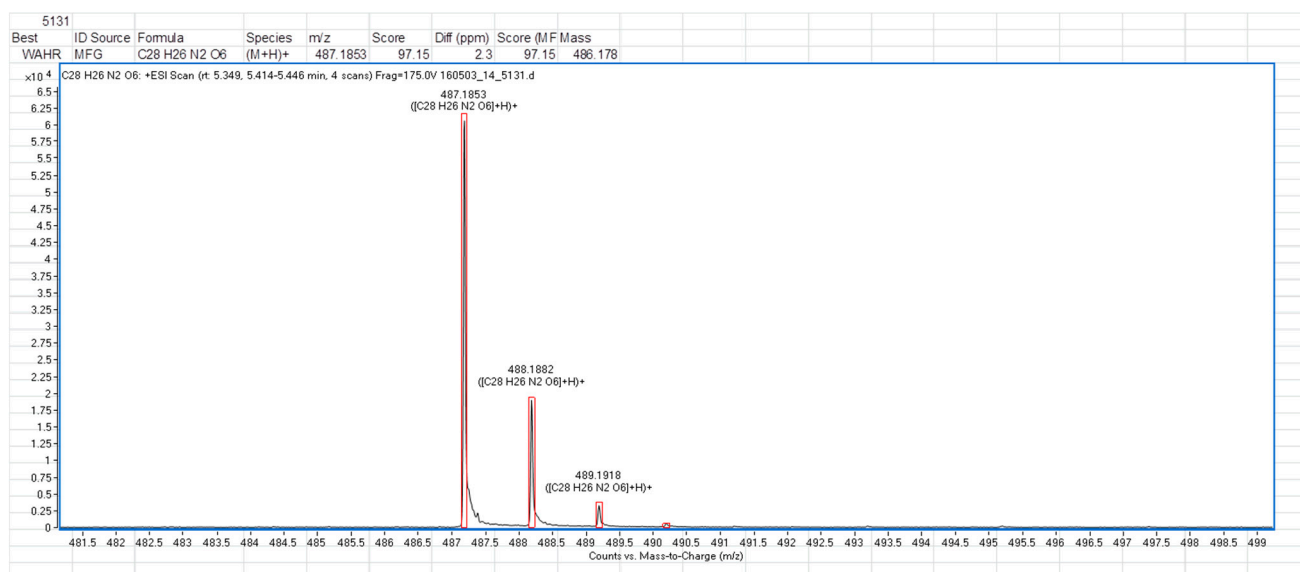


5-(4-[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)pentanoic acid (**14e**; ZHAWOC5131)

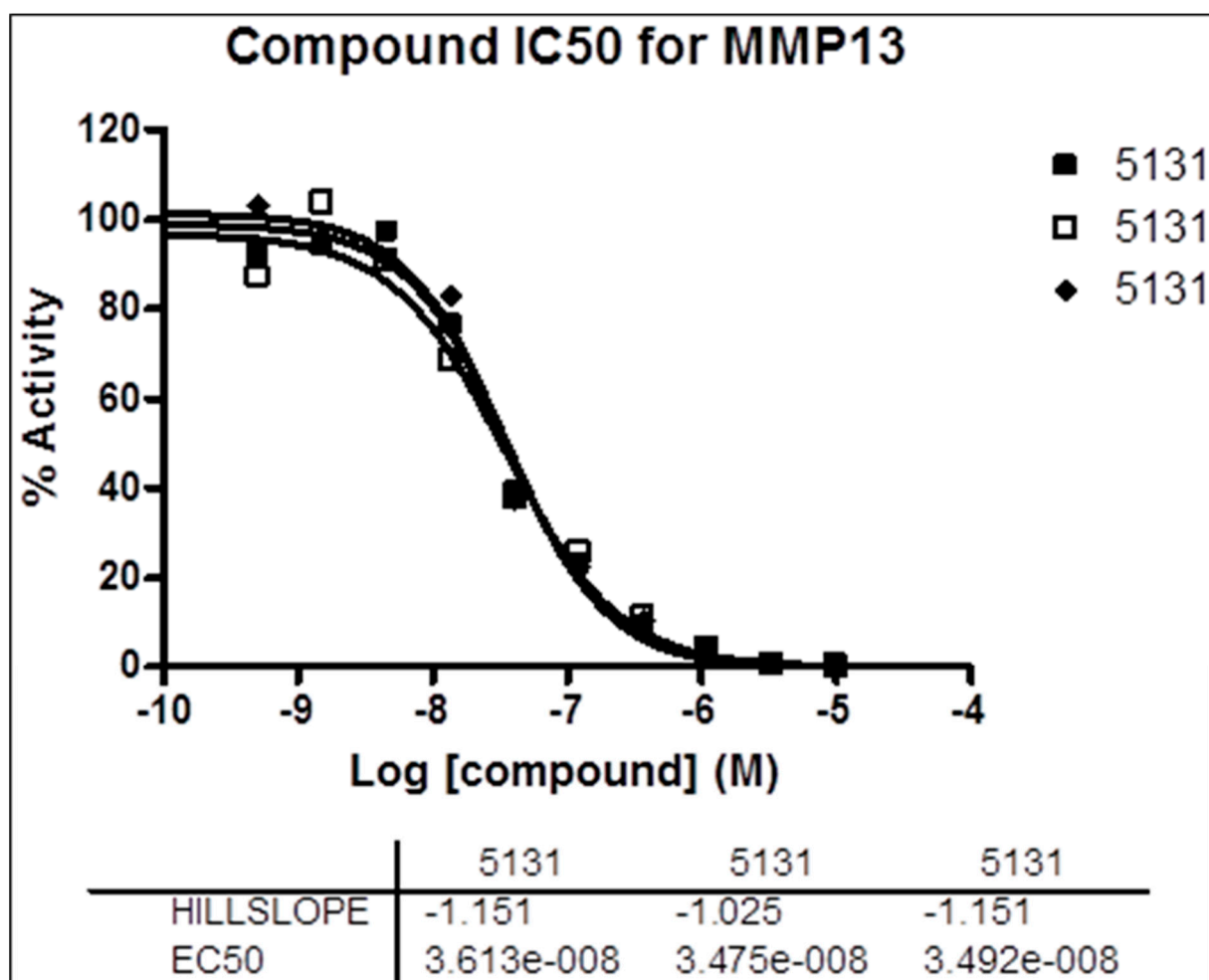


5-(4-[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)pentanoic acid (**14e**; ZHAWOC5131)

HRMS

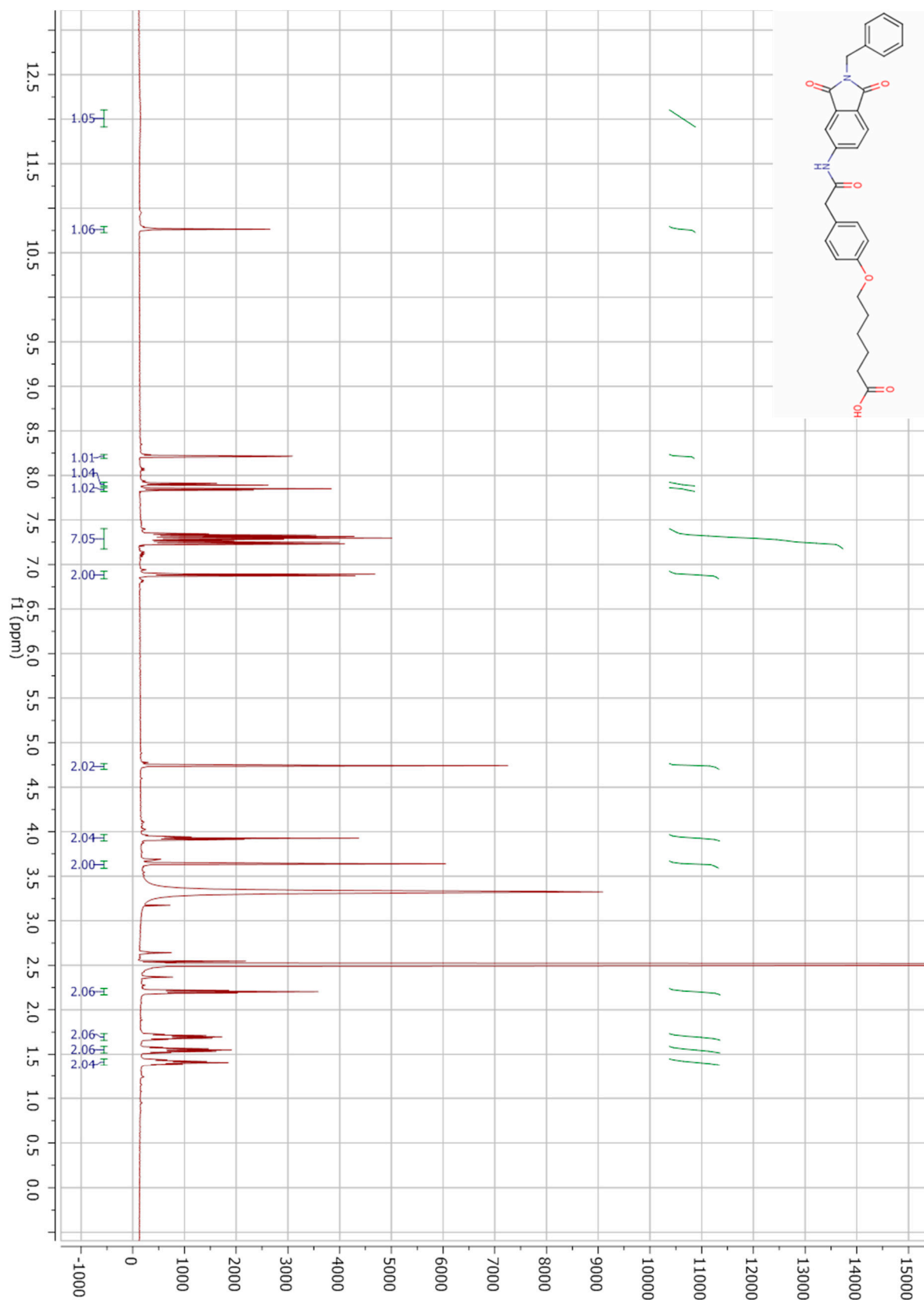


IC₅₀

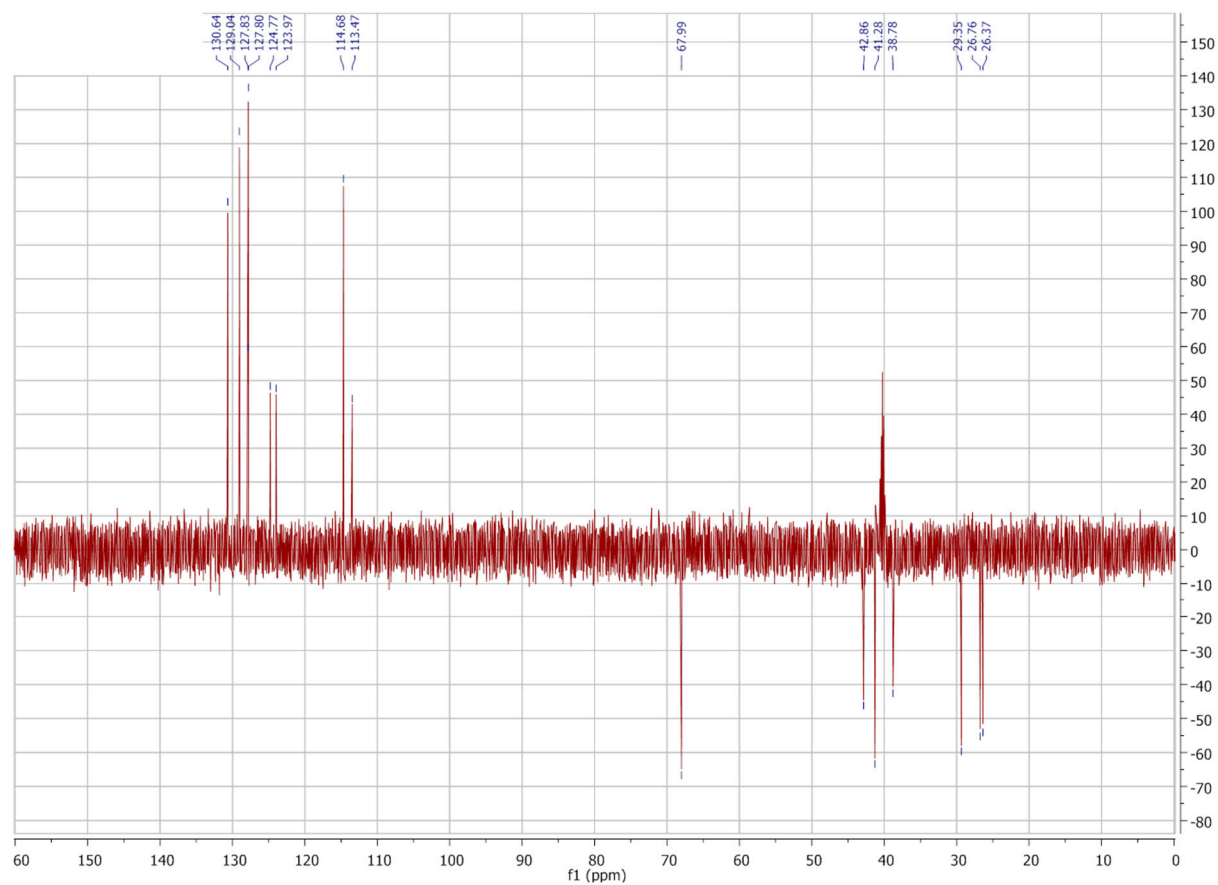
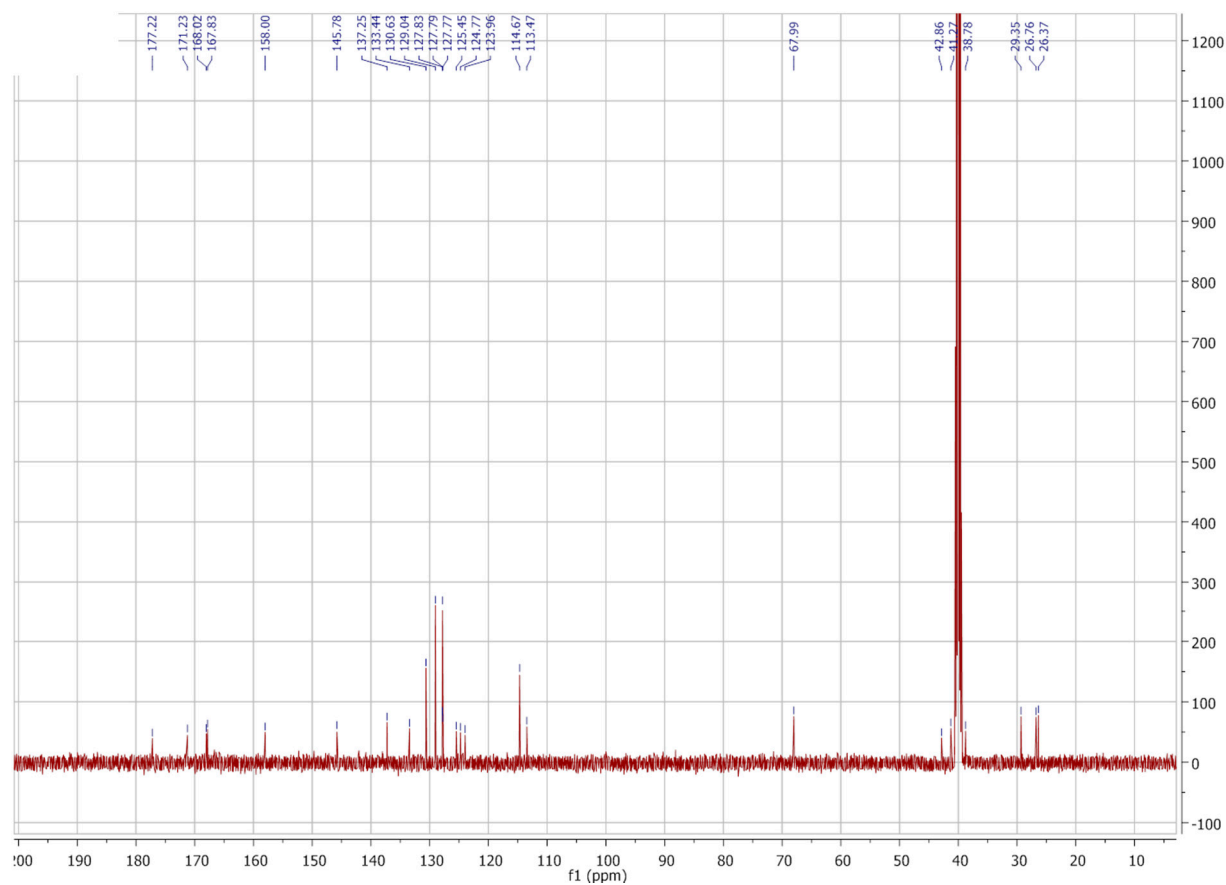


6-({[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)hexanoic acid (**14f**; ZHAWOC5133)

NMR

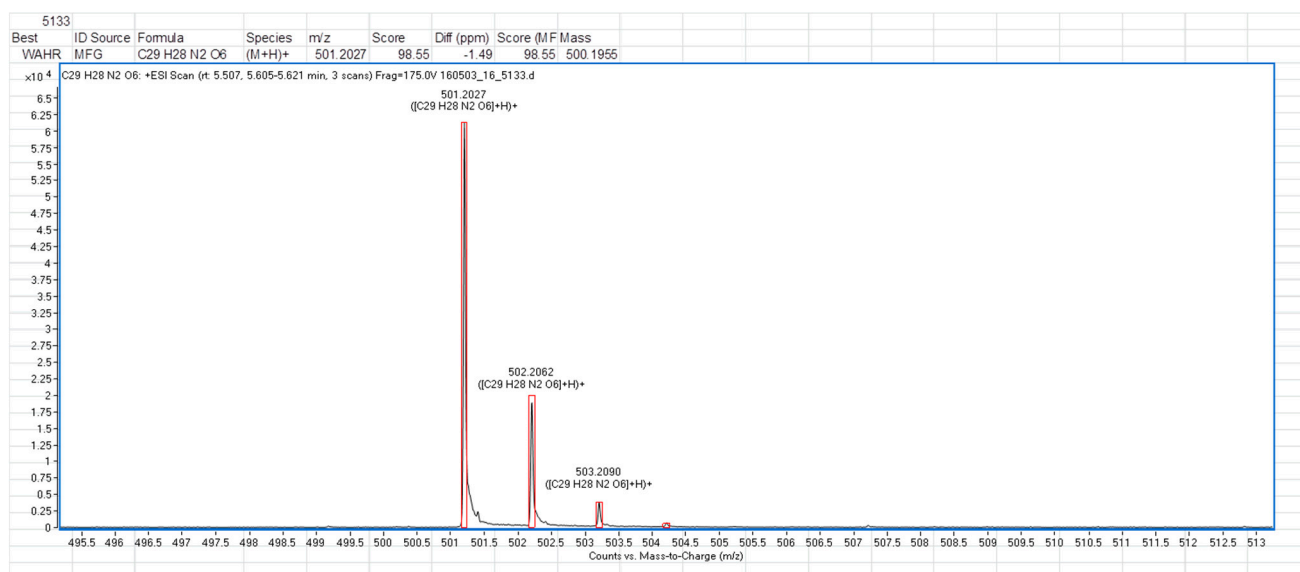


6-(4-[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)hexanoic acid (**14f**; ZHAWOC5133)

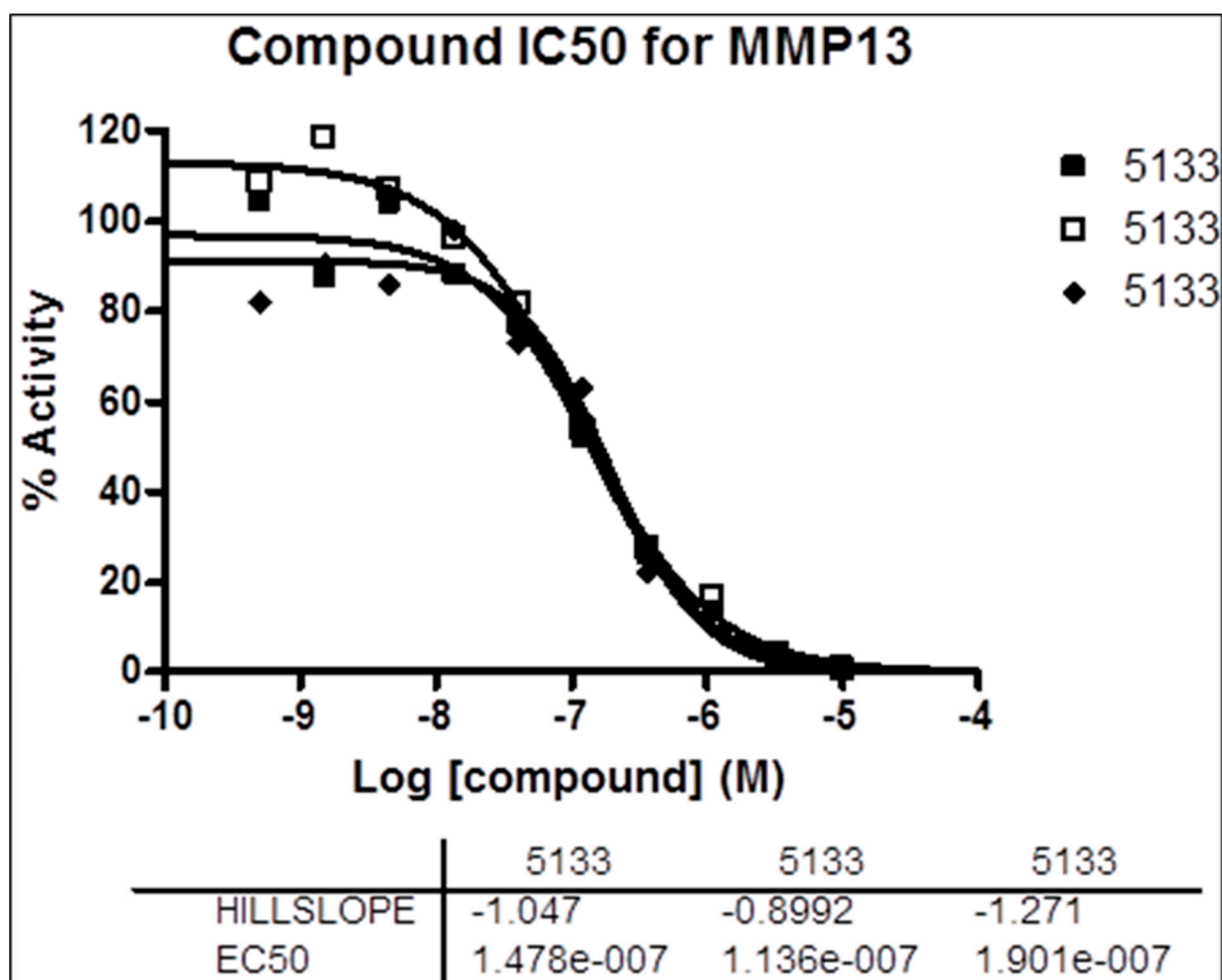


6-(4-[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)hexanoic acid (**14f**; ZHAWOC5133)

HRMS

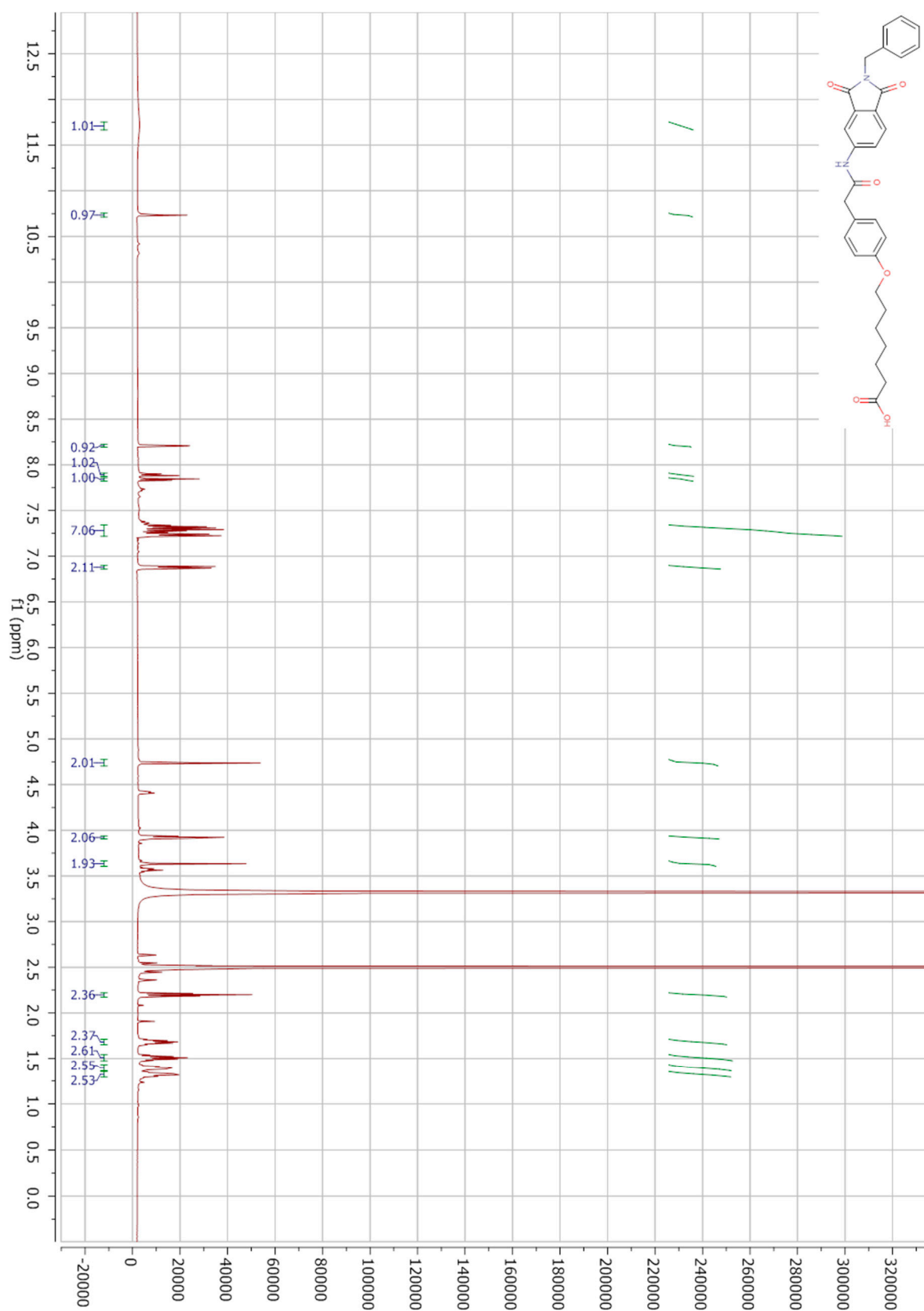


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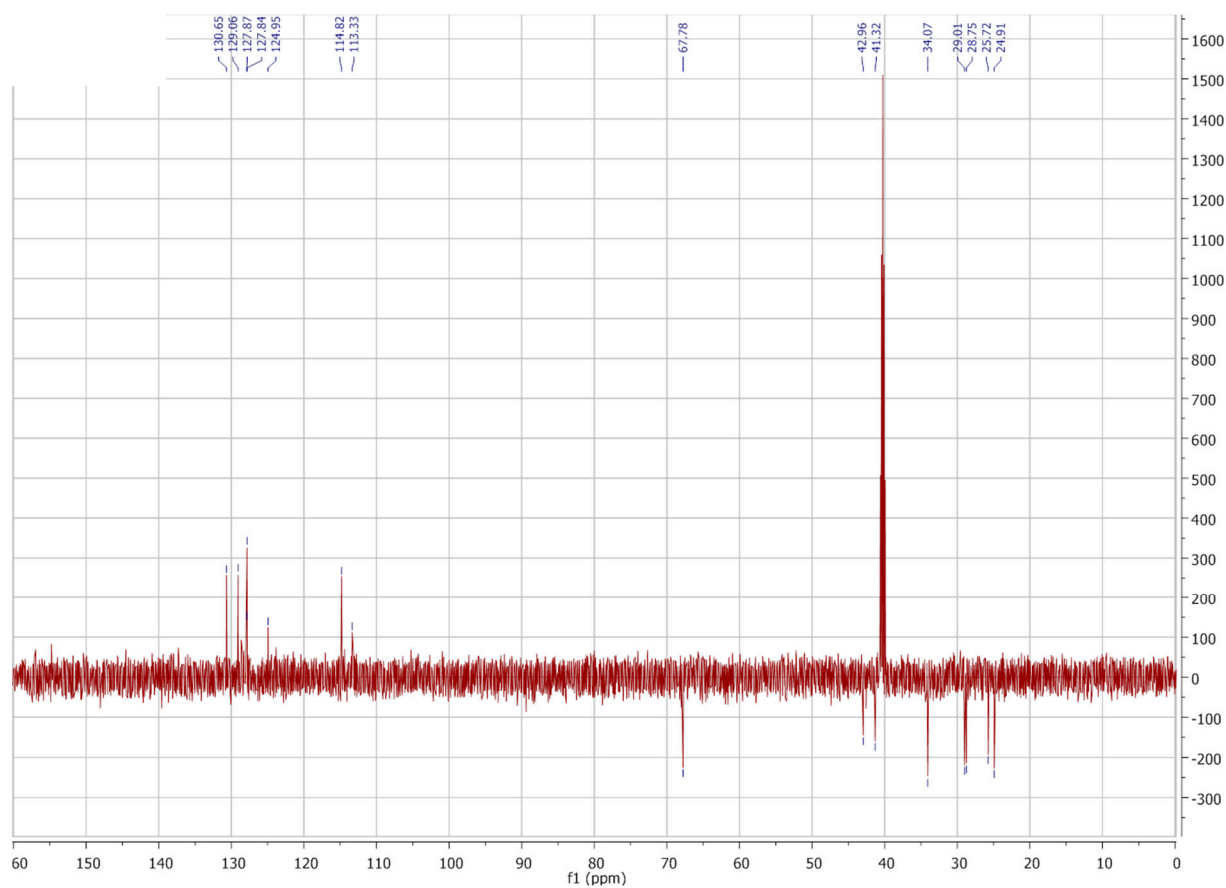
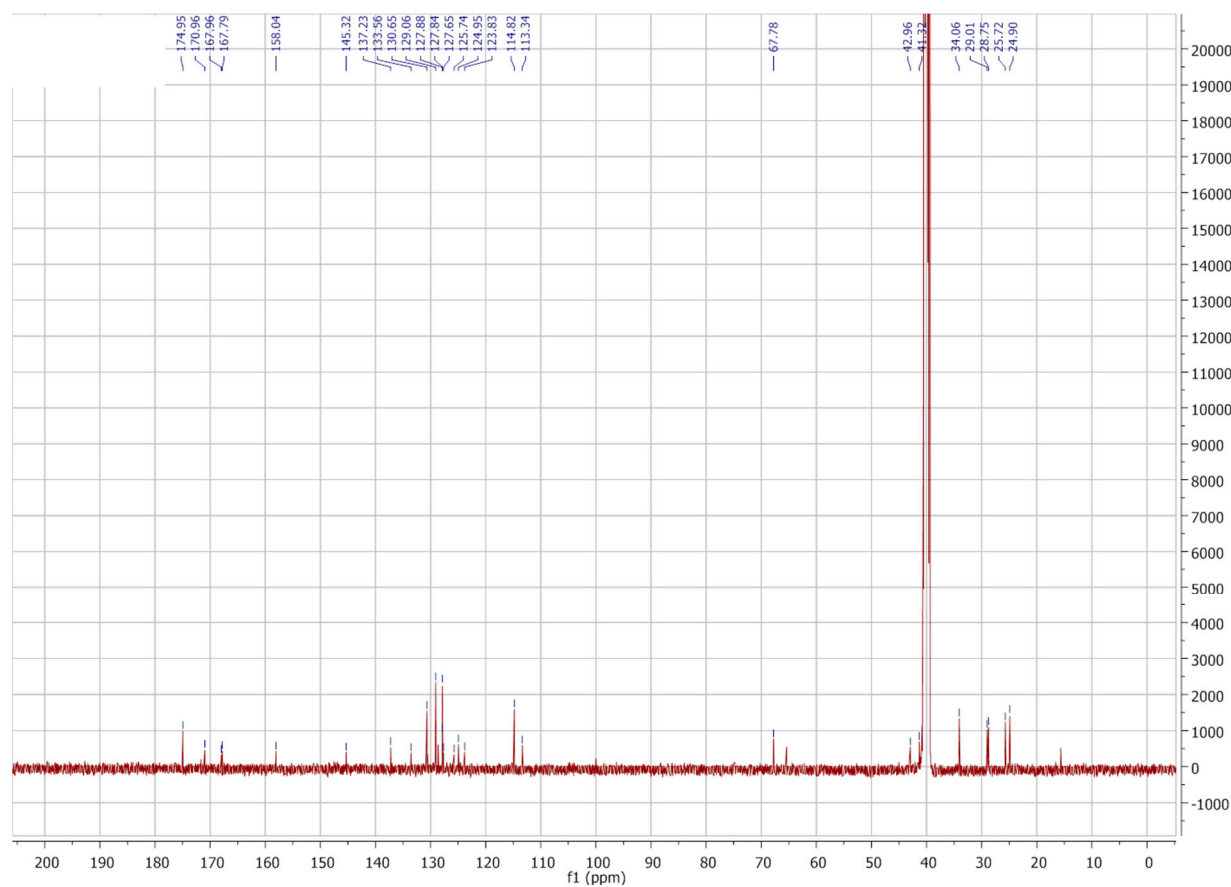


7-(4-[[[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl]phenoxy]heptanoic acid (**14g**; ZHAWOC6650)

NMR

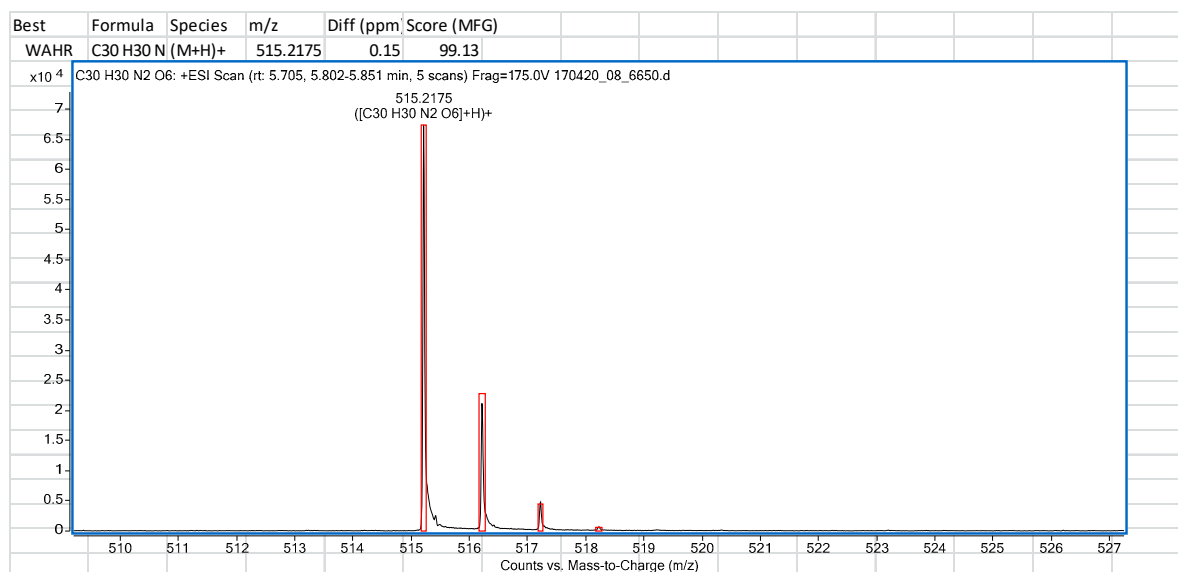


7-(4-[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)heptanoic acid (**14g**; ZHAWOC6650)



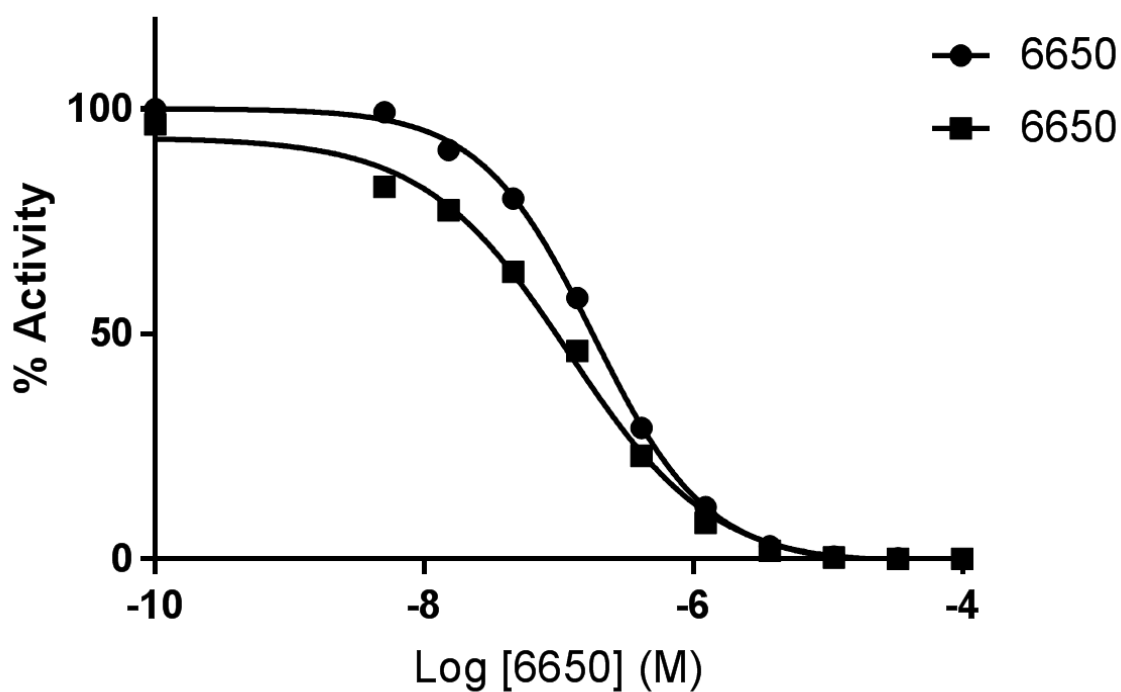
7-(4-[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)heptanoic acid (**14g**; ZHAWOC6650)

HRMS



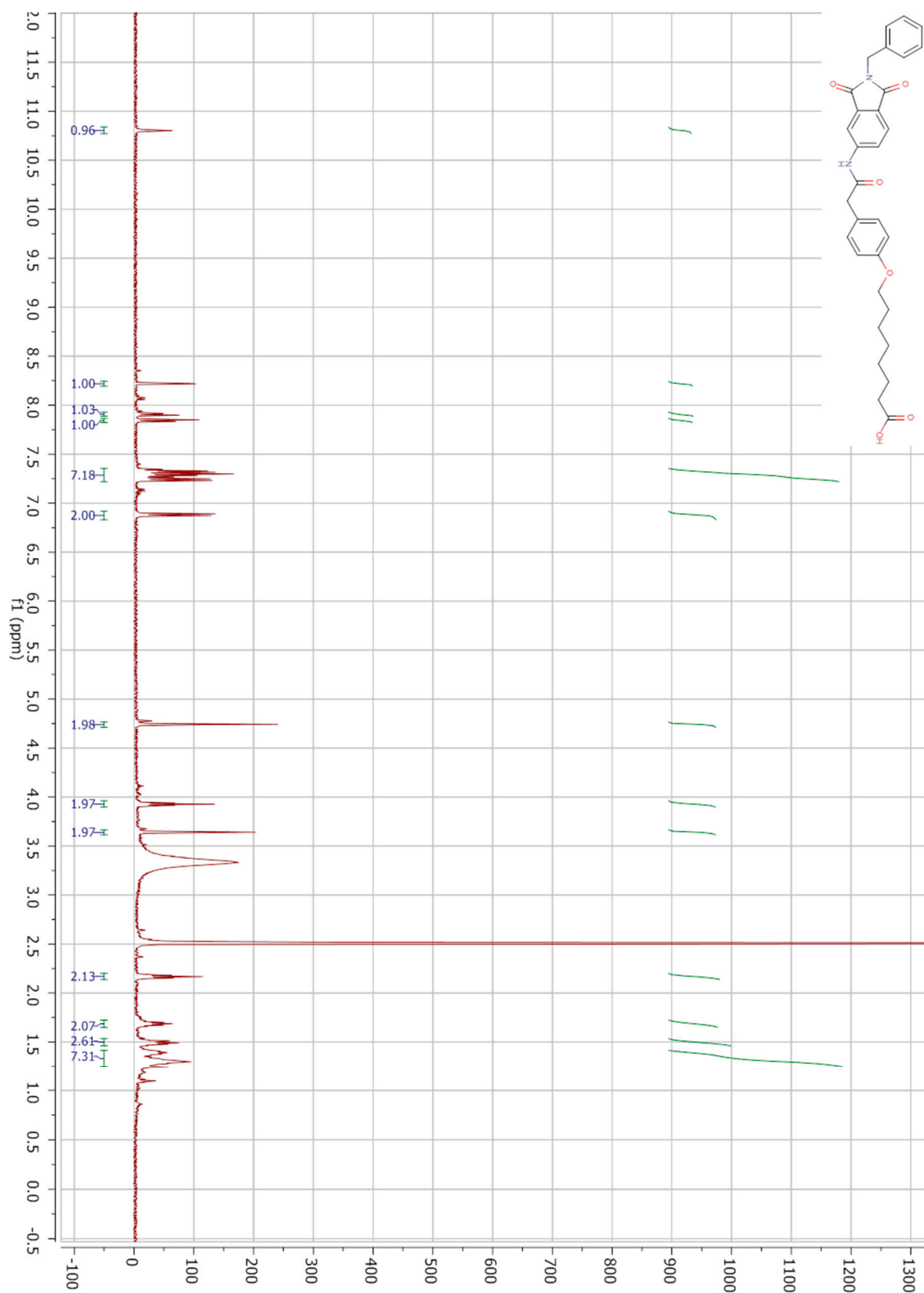
IC₅₀

6650 IC₅₀ for MMP13

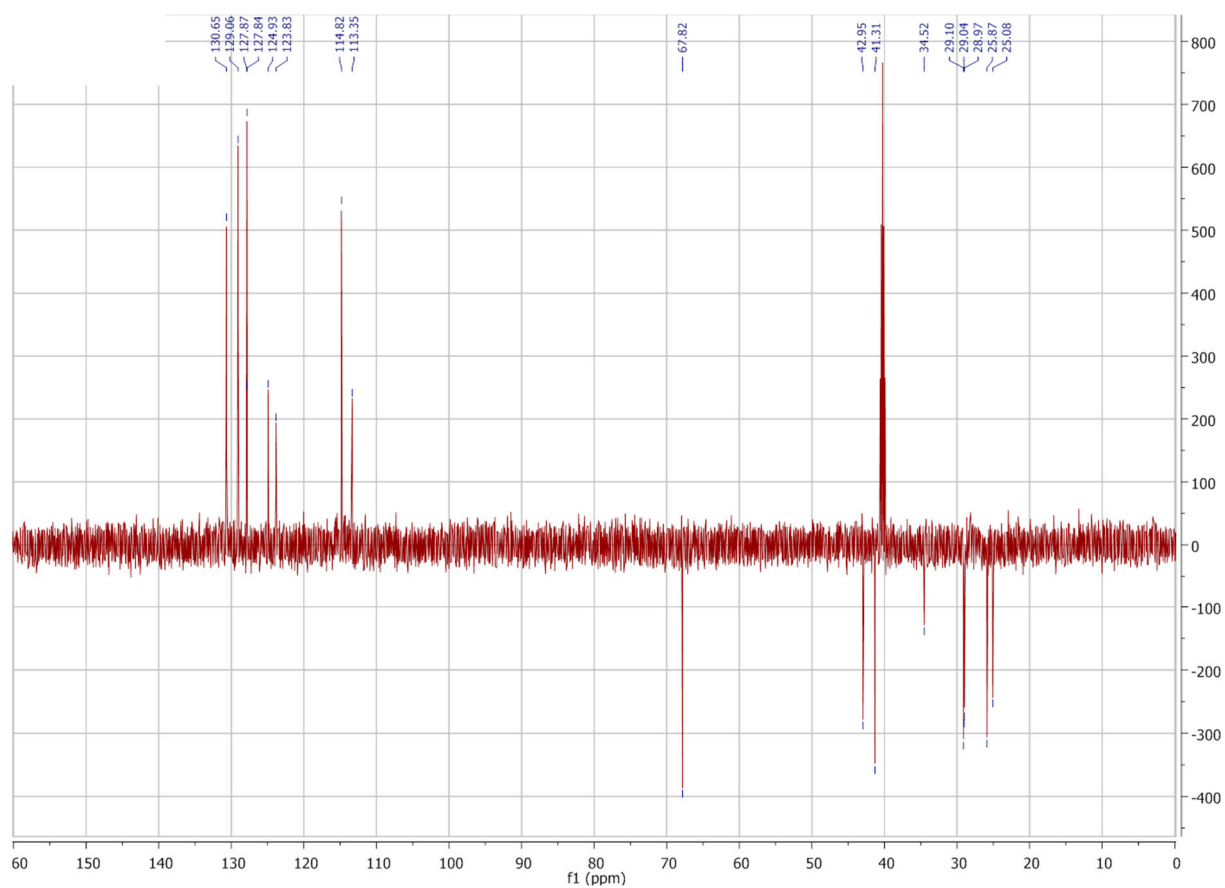
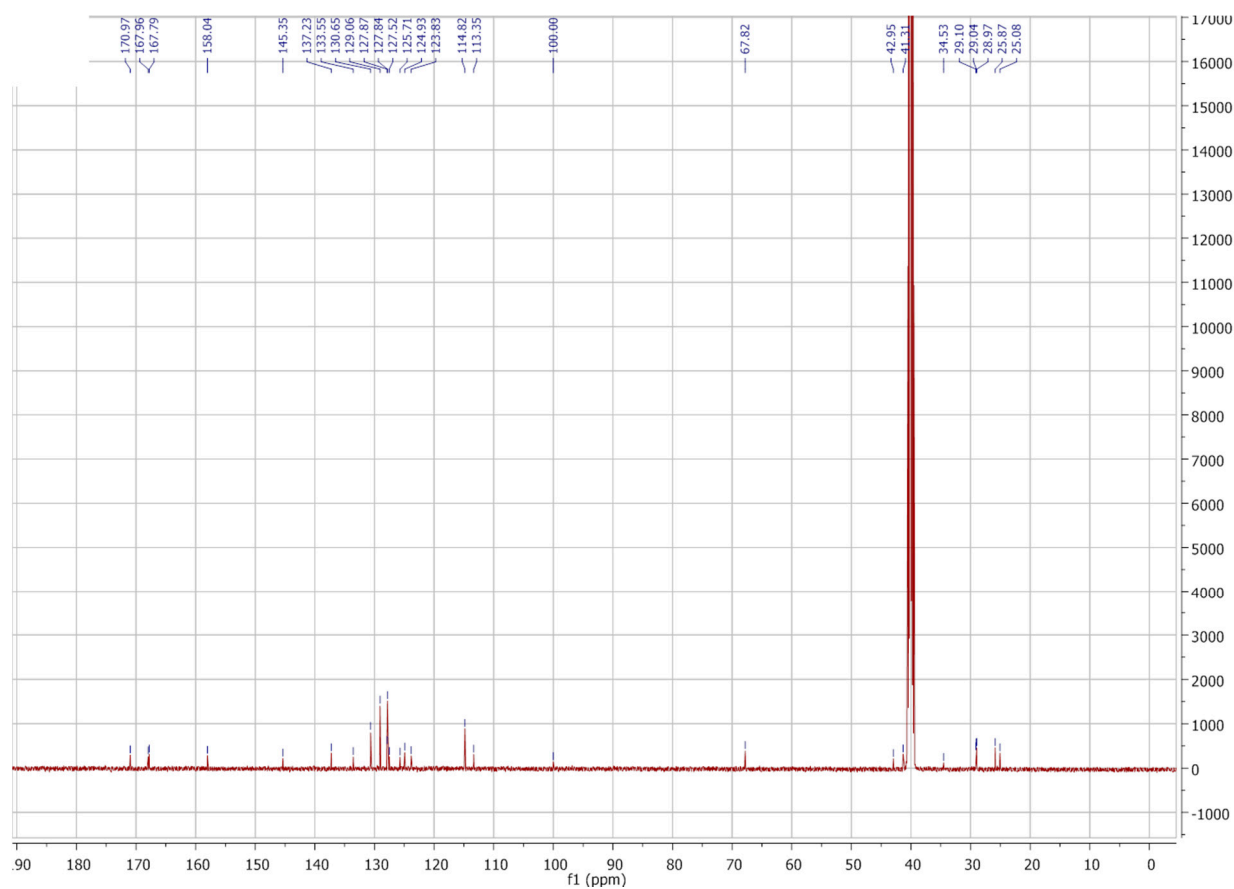


8-({[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)octanoic acid (**14h**; ZHAWOC6651)

NMR

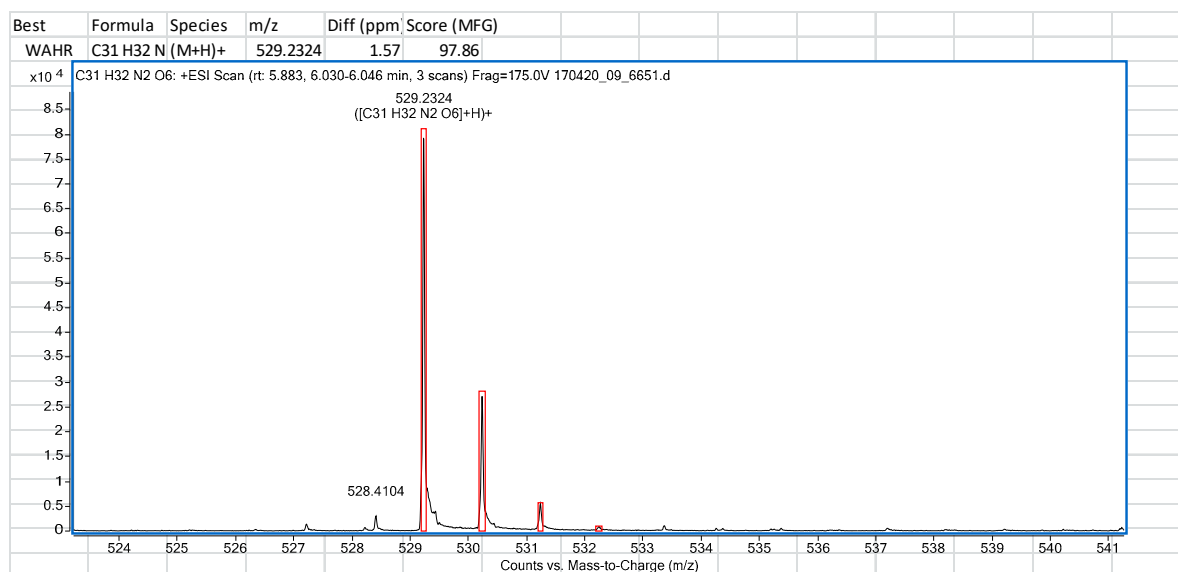


8-(4-[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)octanoic acid (**14h**; ZHAWOC6651)



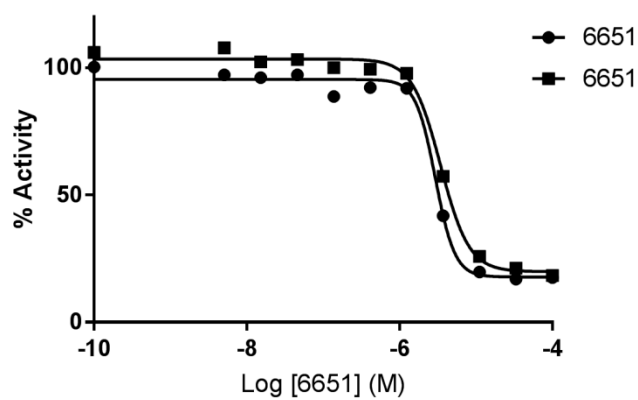
8-(4-[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)octanoic acid (14h; ZHAWOC6651)

HRMS

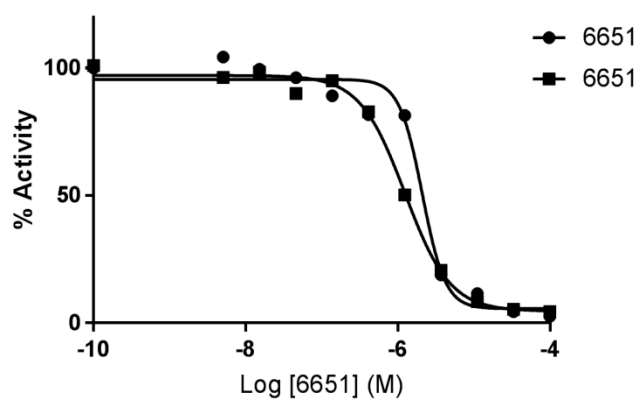


IC50

6651 IC50 for MMP7

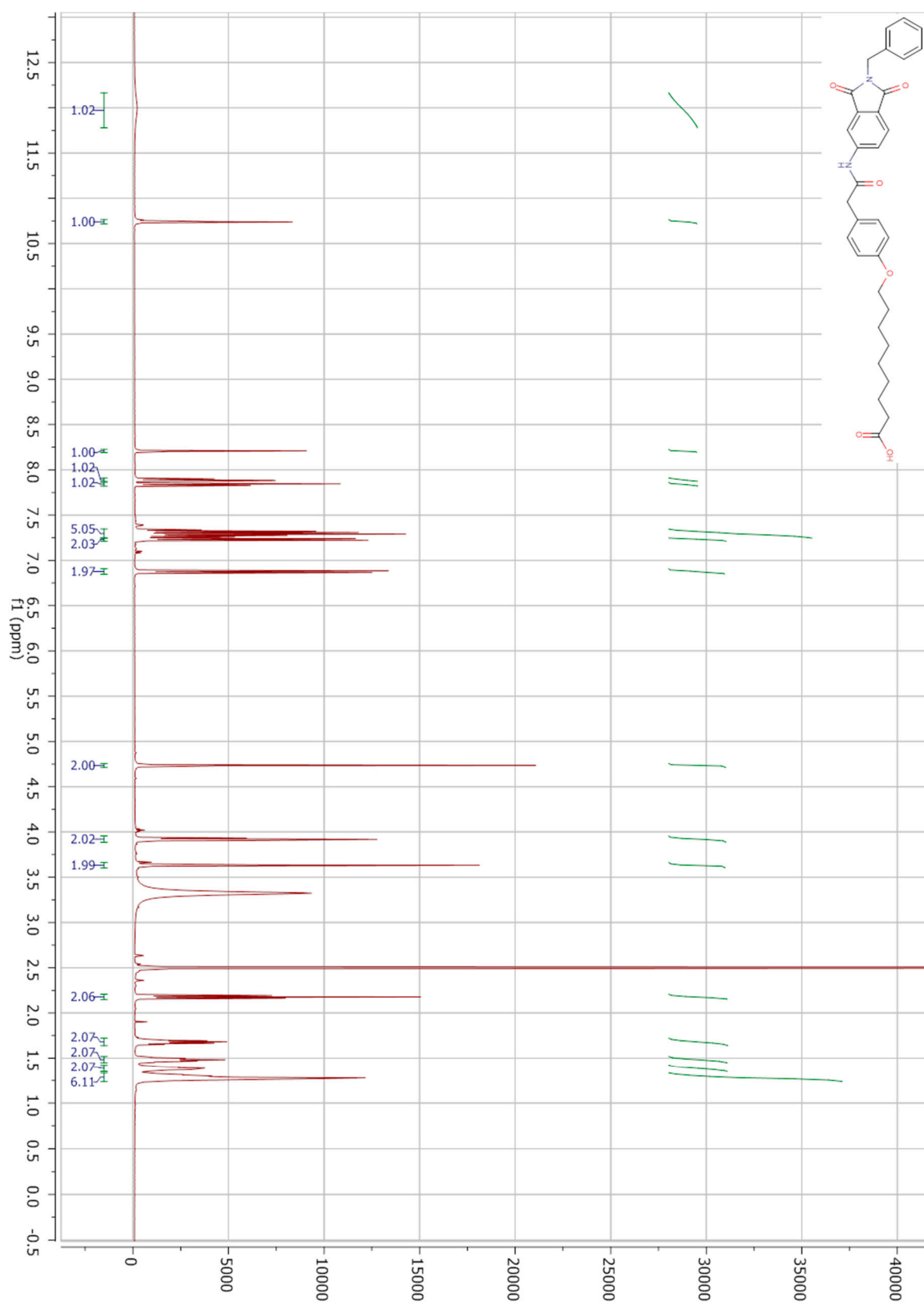


6651 IC50 for MMP13

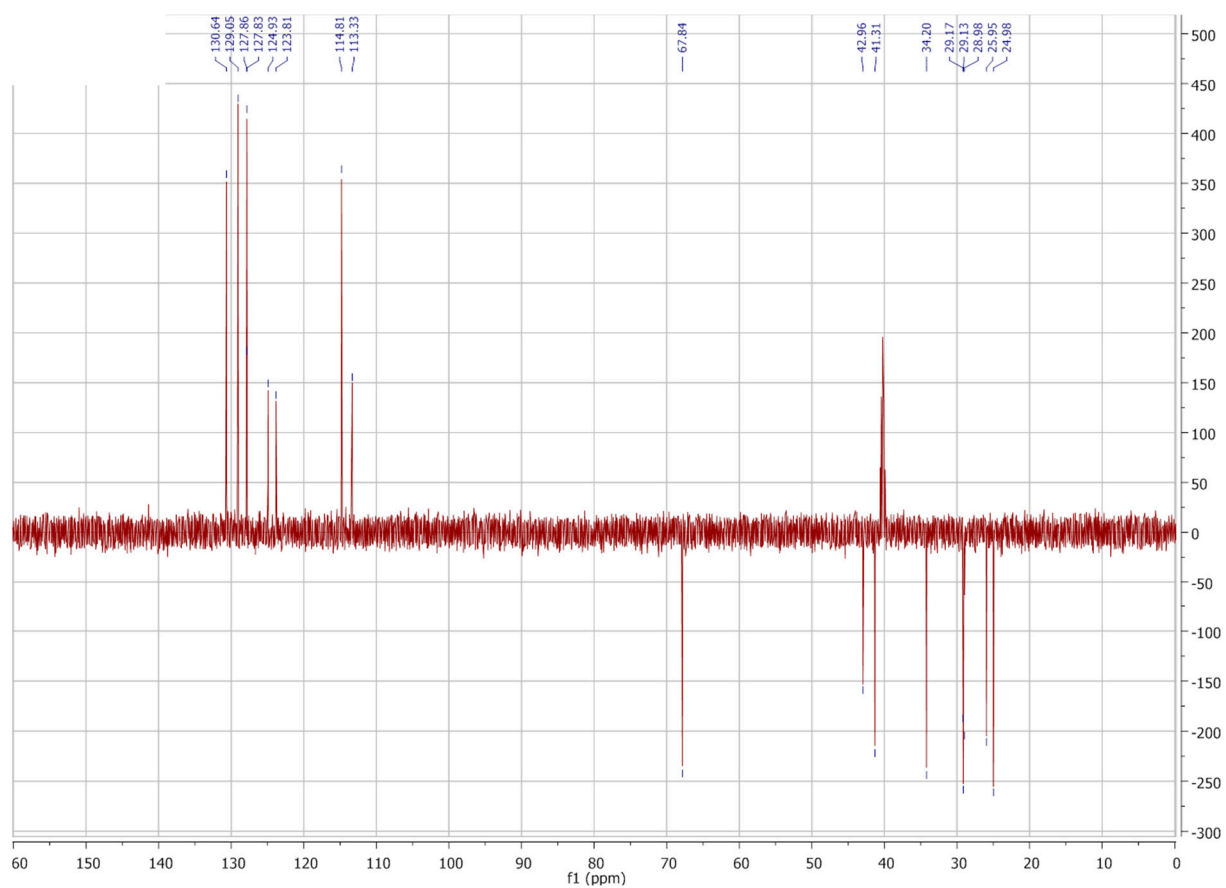
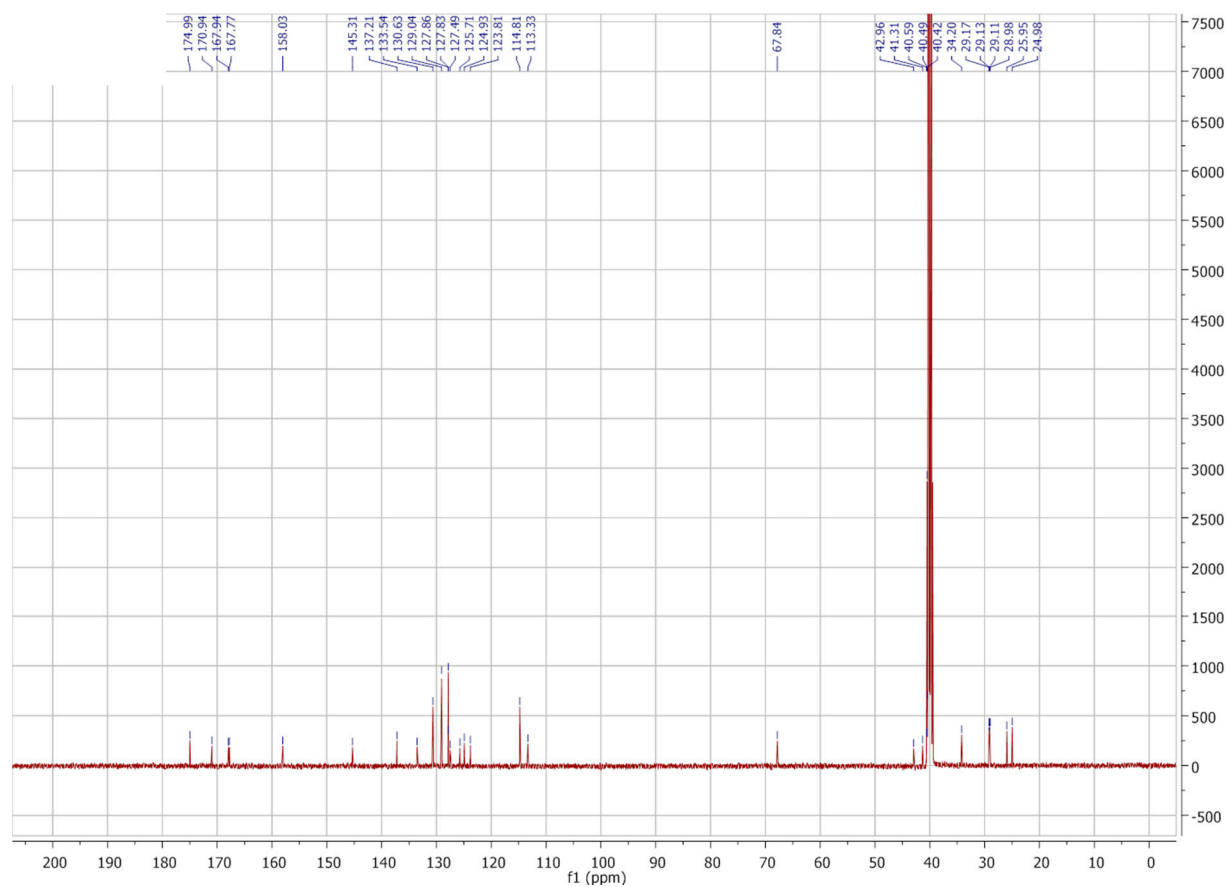


9-(4-[[[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl]phenoxy]nonanoic acid (**14i**; ZHAWOC6941)

NMR

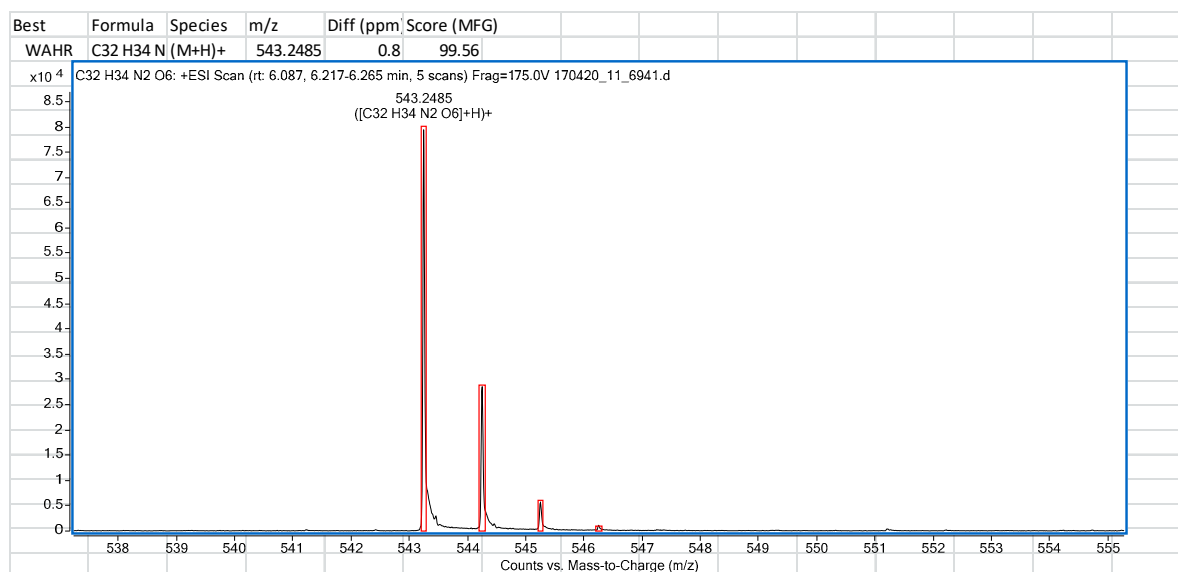


9-(4-[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)nonanoic acid (**14i**; ZHAWOC6941)



9-(4-[[2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl]carbamoyl]methyl}phenoxy)nonanoic acid (**14i**; ZHAWOC6941)

HRMS



IC₅₀

6941 IC₅₀ for MMP7

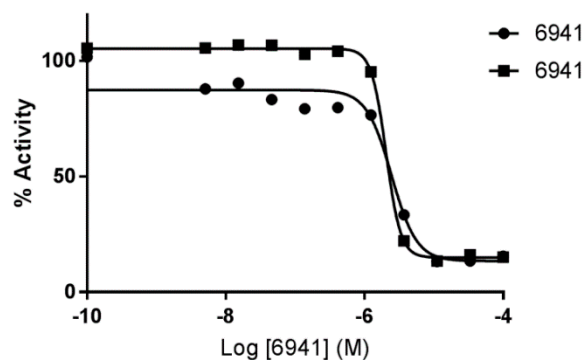


Figure S1a: Determination of the IC₅₀-value for compound **14i** against MMP-7.

6941 IC₅₀ for MMP13

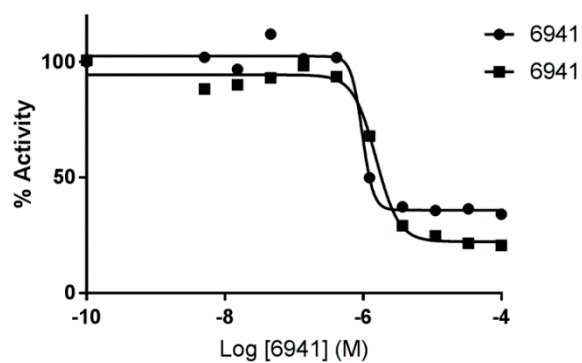
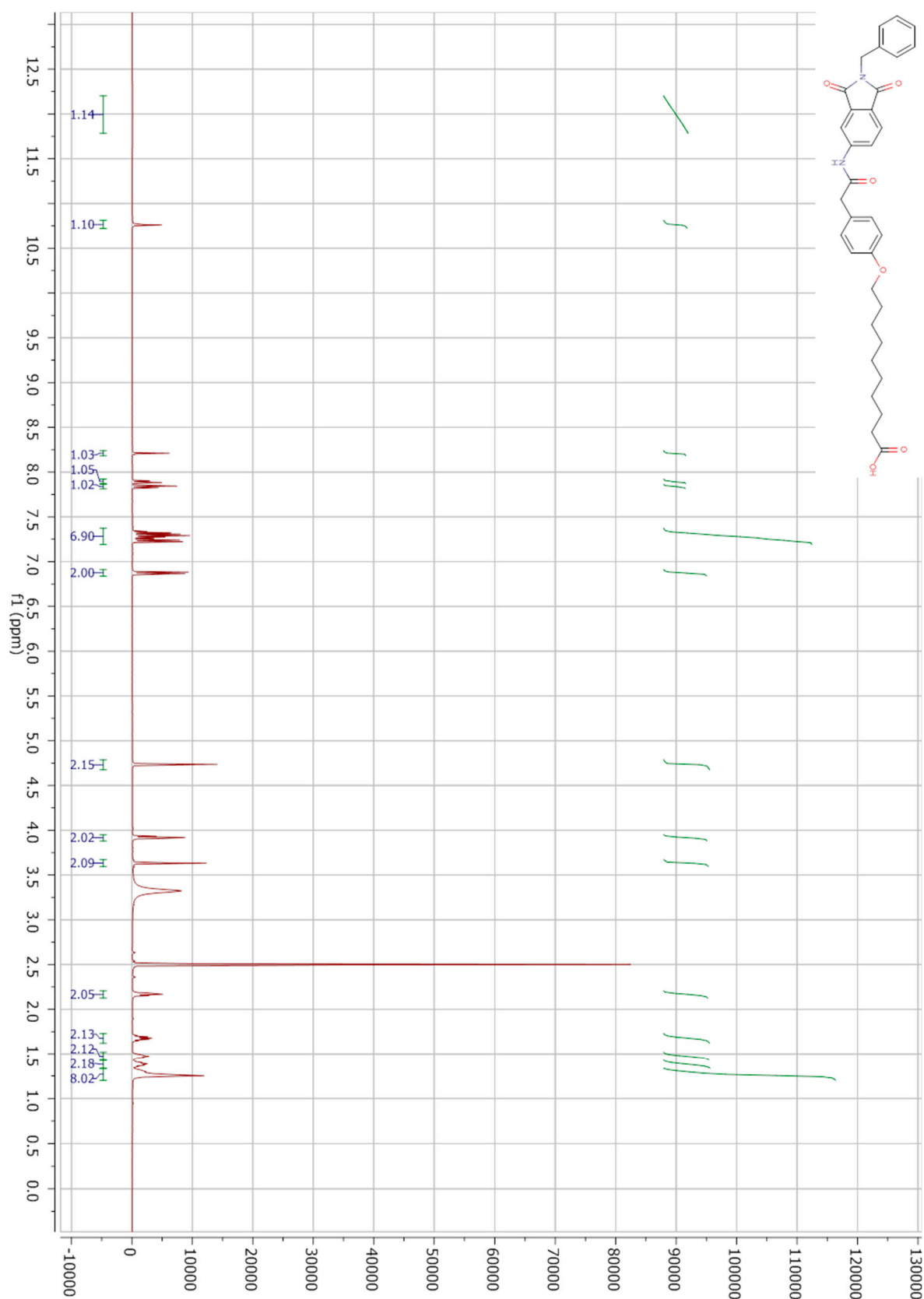


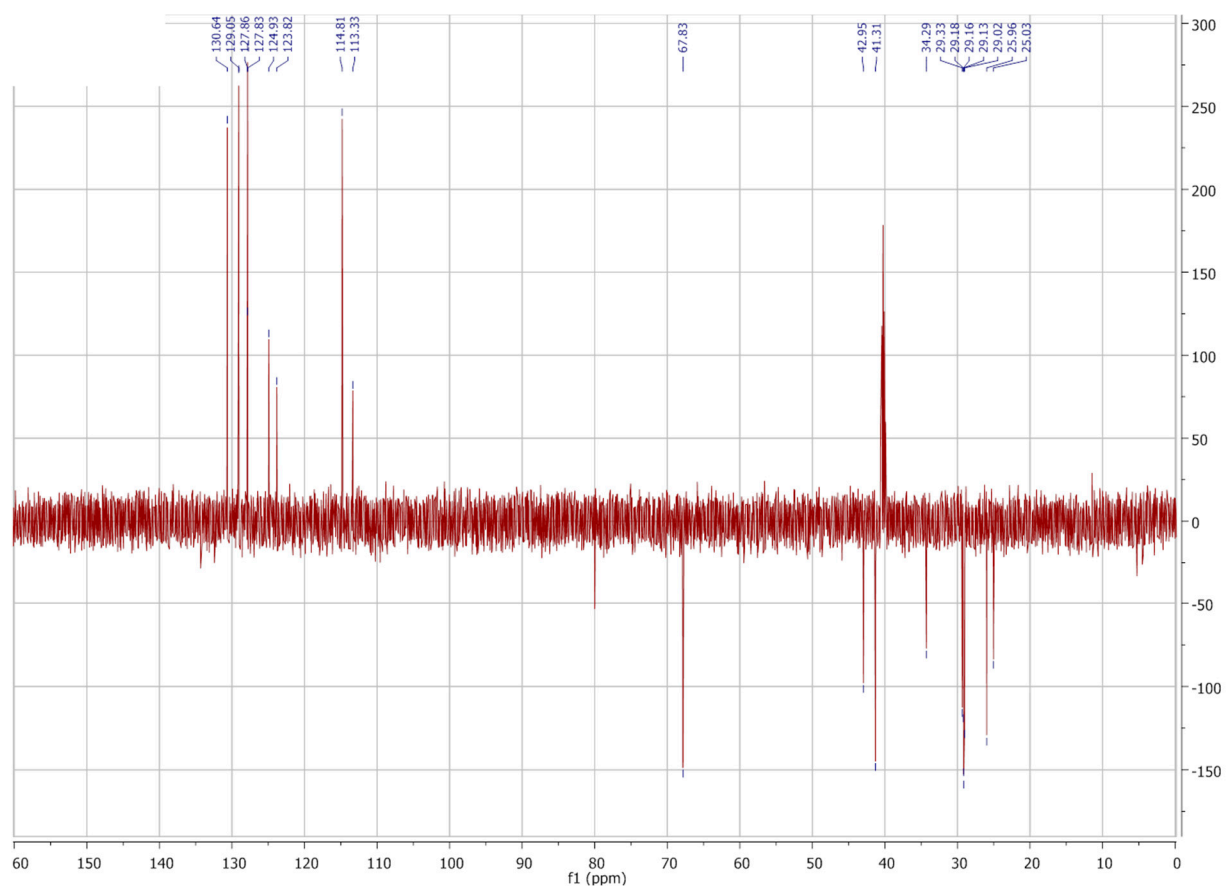
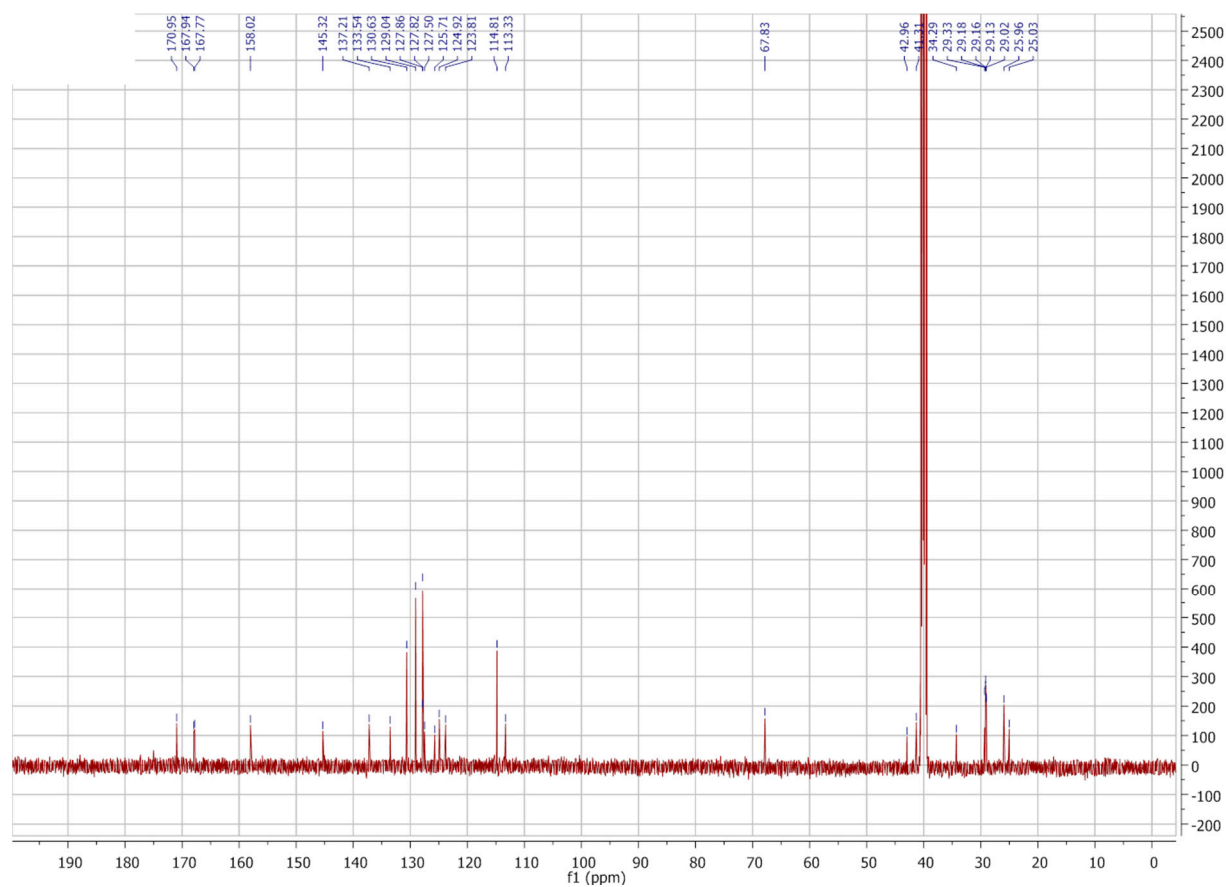
Figure S1b: Determination of the IC₅₀-value for compound **14i** against MMP-13.

10-(4-[[[(2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl]methyl}phenoxy)decanoic acid (**14j**; ZHAWOC6942)

NMR

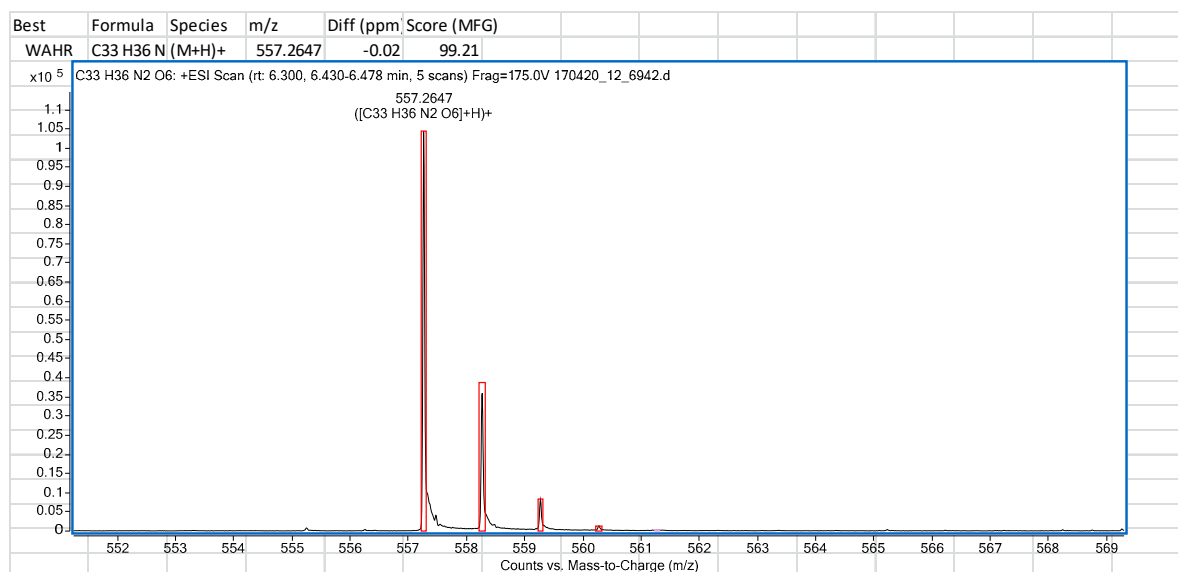


10-(4-[[2-benzyl-1,3-dioxo-2,3-dihydro-1*H*-isoindol-5-yl)carbamoyl]methyl}phenoxy)decanoic acid (**14j**; ZHAWOC6942)



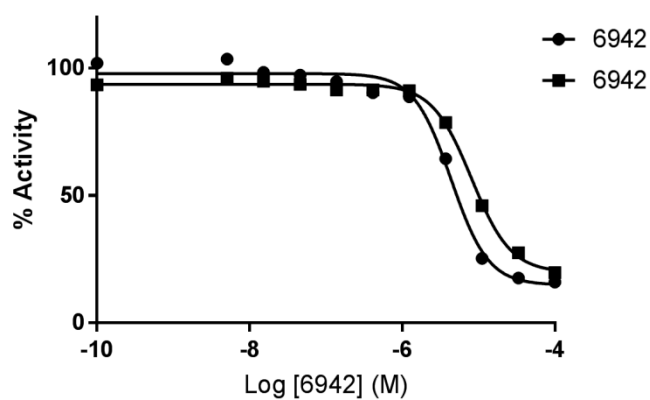
10-(4-[[2-benzyl-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbonyl]methyl}phenoxy)decanoic acid (**14j**; ZHAWOC6942)

HRMS

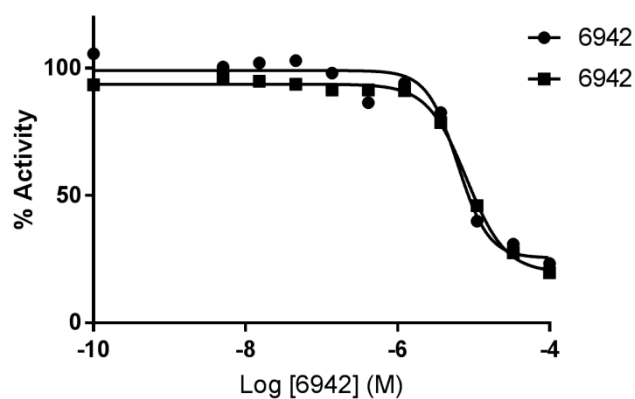


IC₅₀

6942 IC₅₀ for MMP7

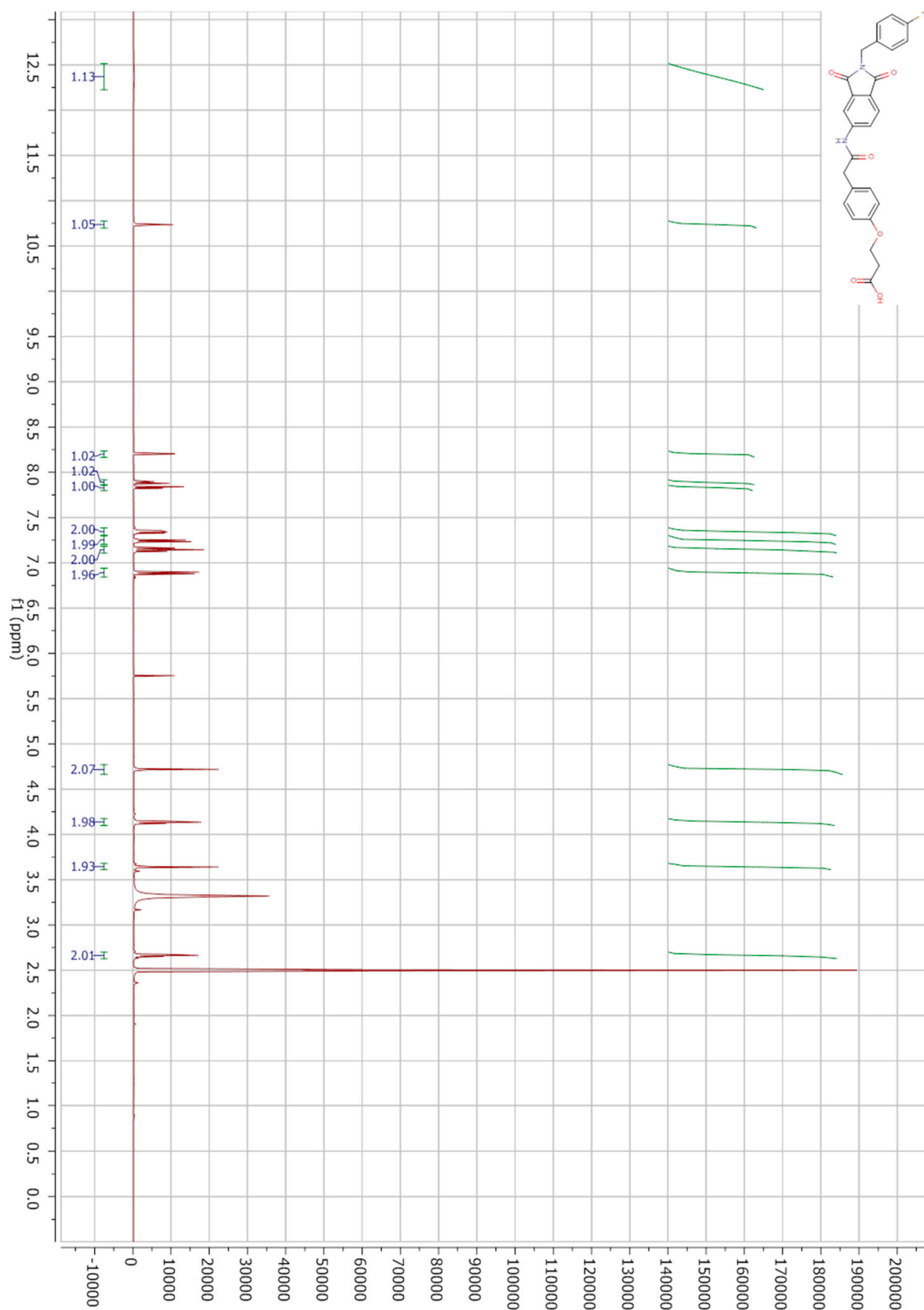


6942 IC₅₀ for MMP13

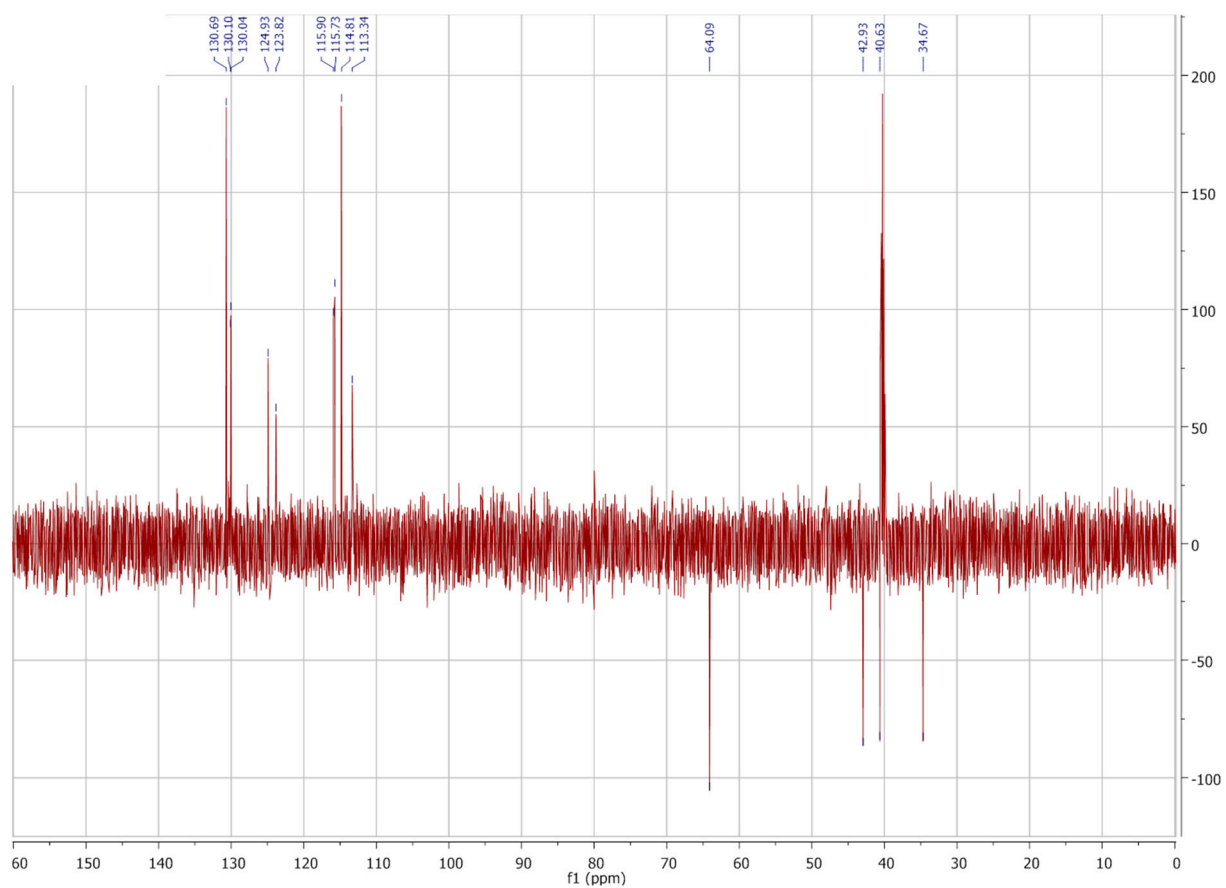
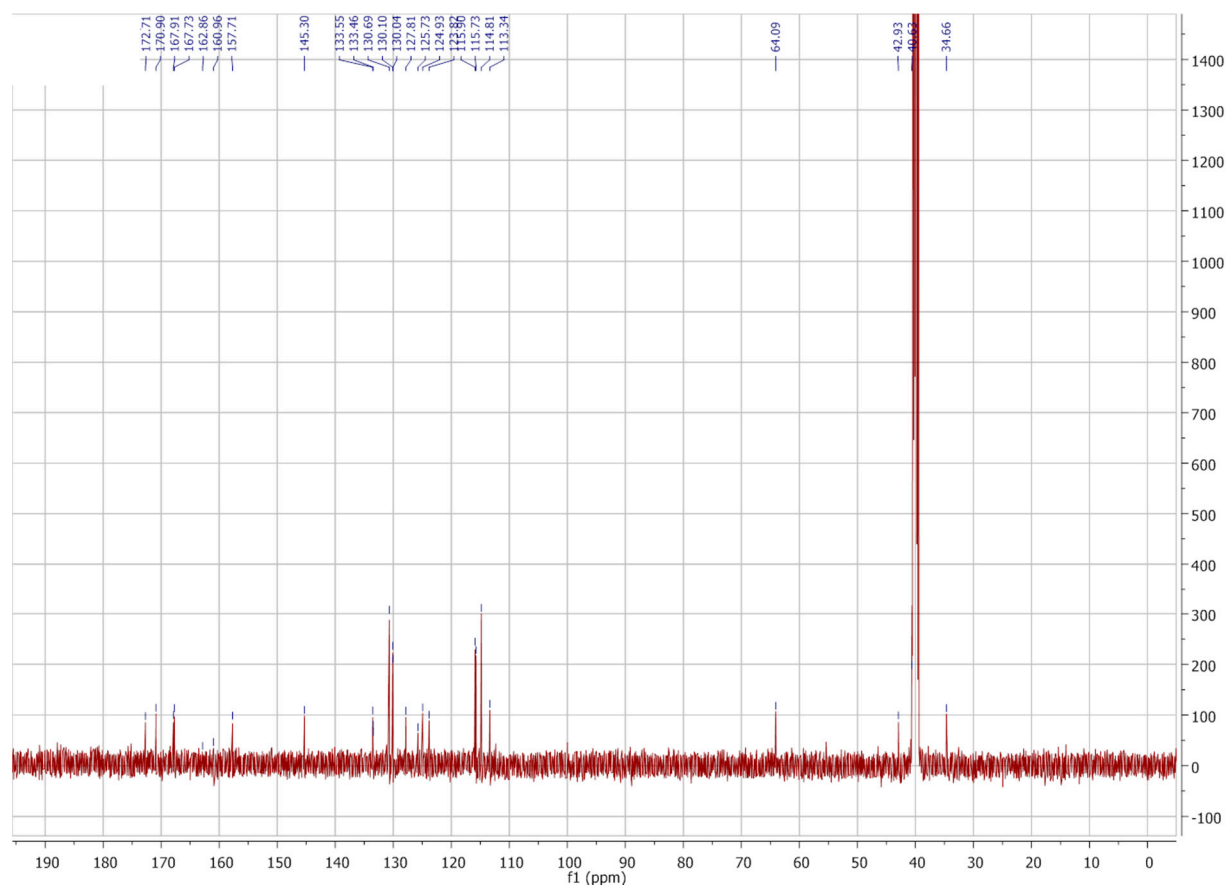


3-{4-[(2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbonyl)methyl]phenoxy}propanoic acid (**14k**; ZHAWOC6644)

NMR

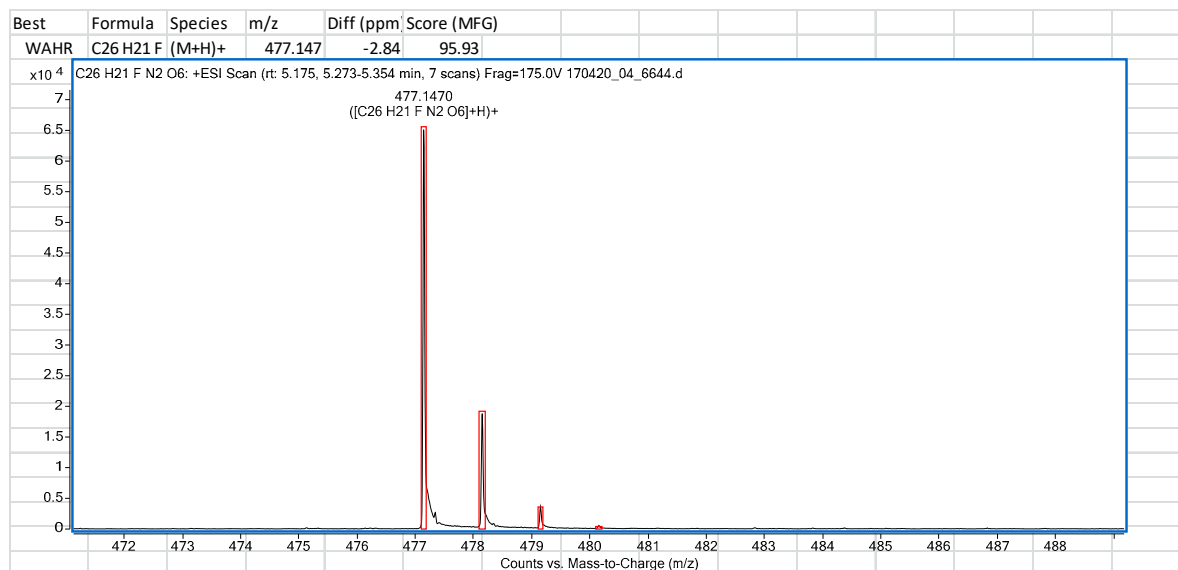


3-{4-[(2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl)methyl]phenoxy}propanoic acid (14k**; ZHAWOC6644)**



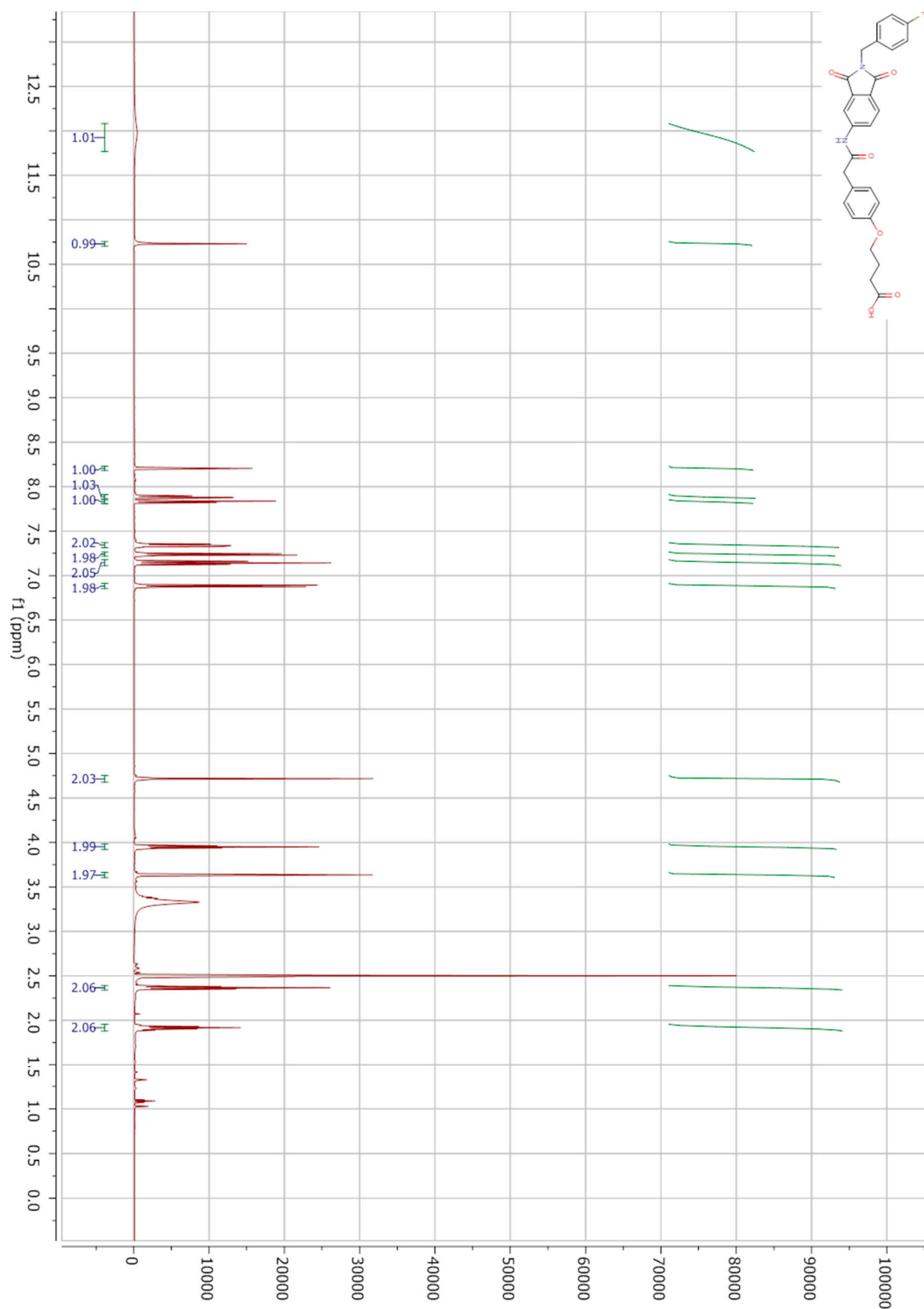
3-{4-[(2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl)methyl]phenoxy}propanoic acid (14k**; ZHAWOC6644)**

HRMS

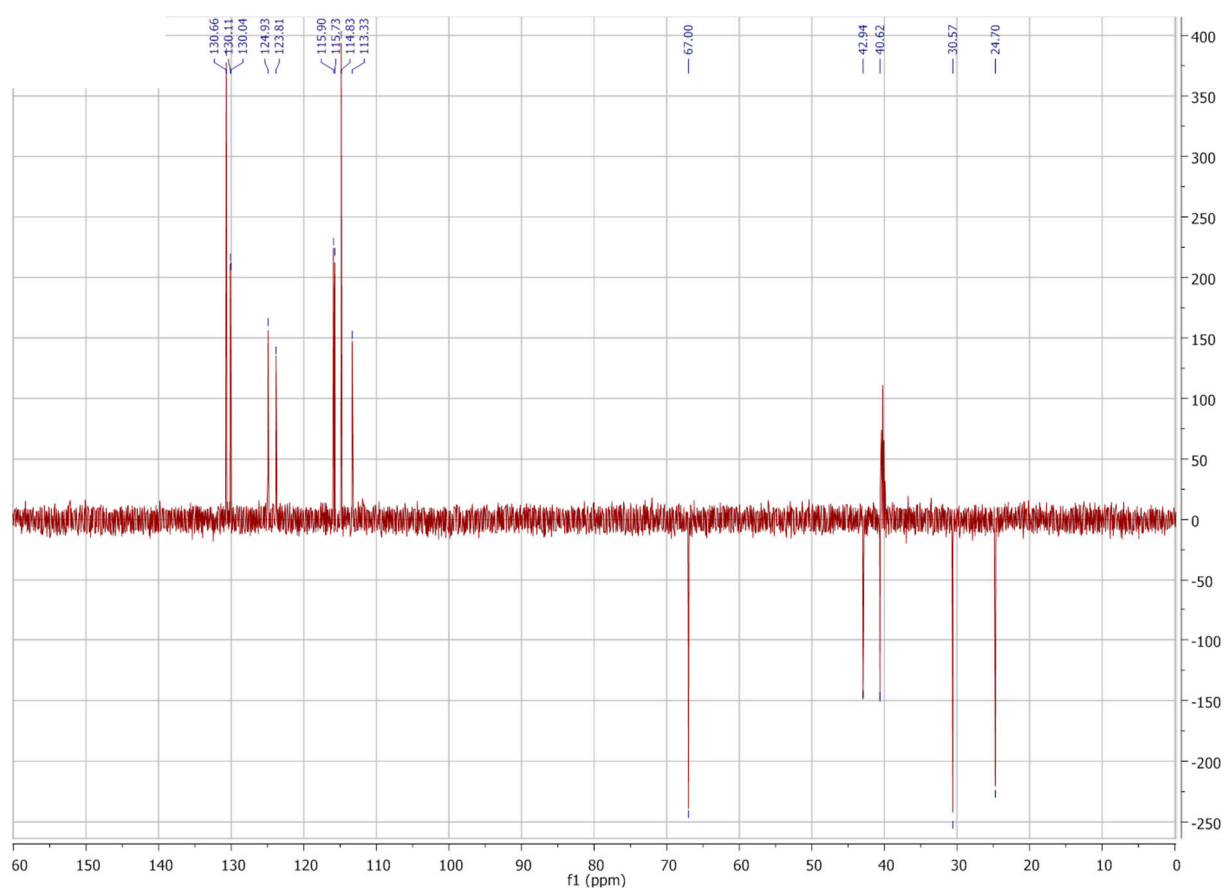
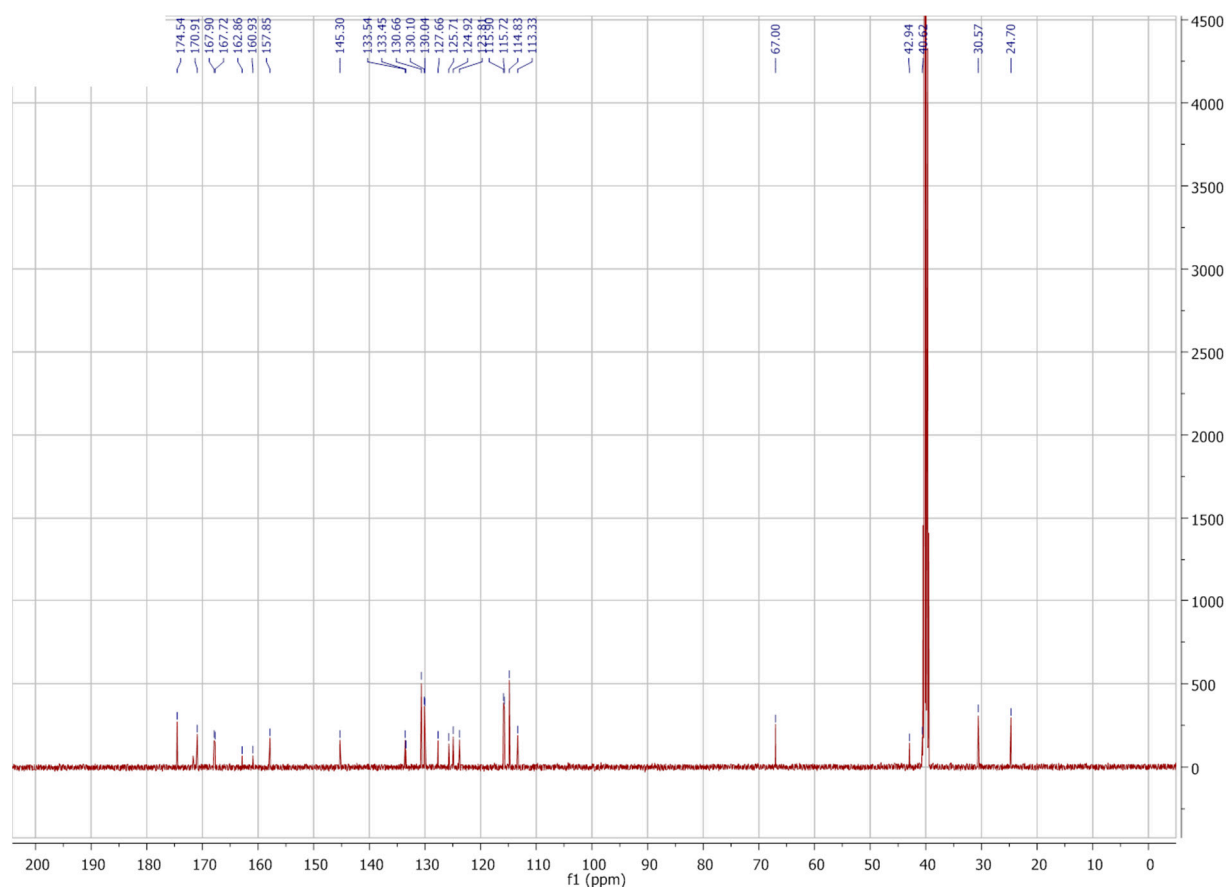


4-{4-[(2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbonyl)methyl]phenoxy}butanoic acid (**14I**; ZHAWOC5463)

NMR

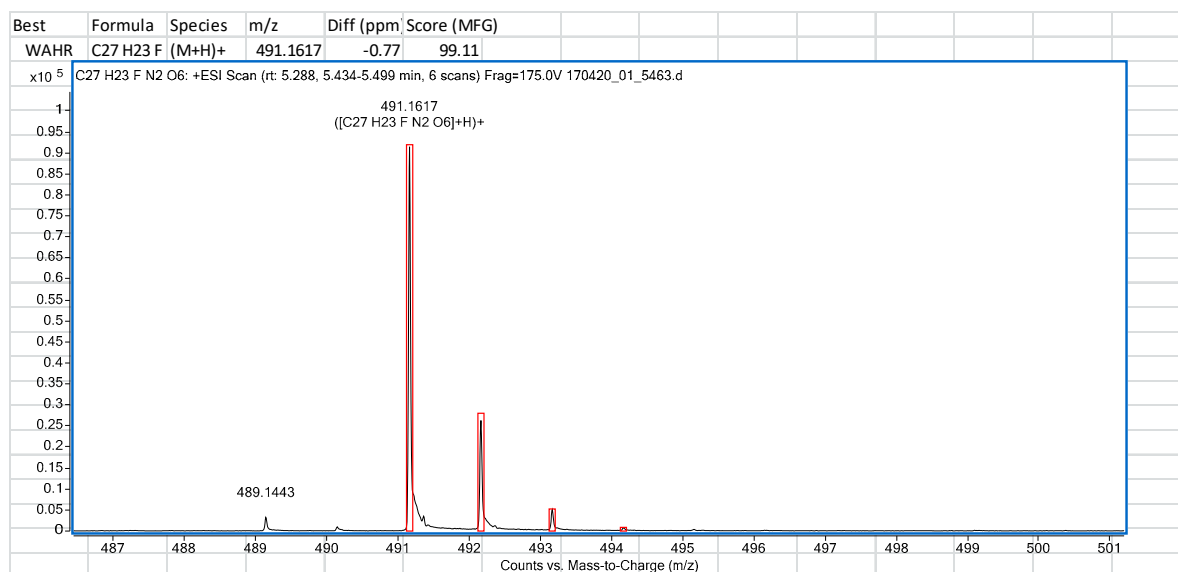


4-{4-[(2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbonyl)methyl]phenoxy}butanoic acid (**14i**; ZHAWOC5463)



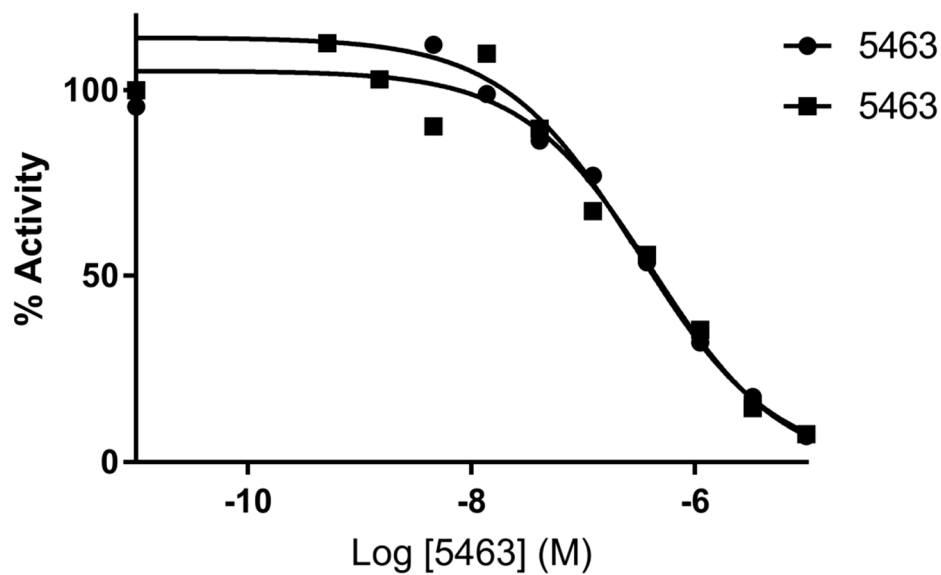
4-{4-[(2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl)methyl]phenoxy}butanoic acid (**14I**; ZHAWOC5463)

HRMS



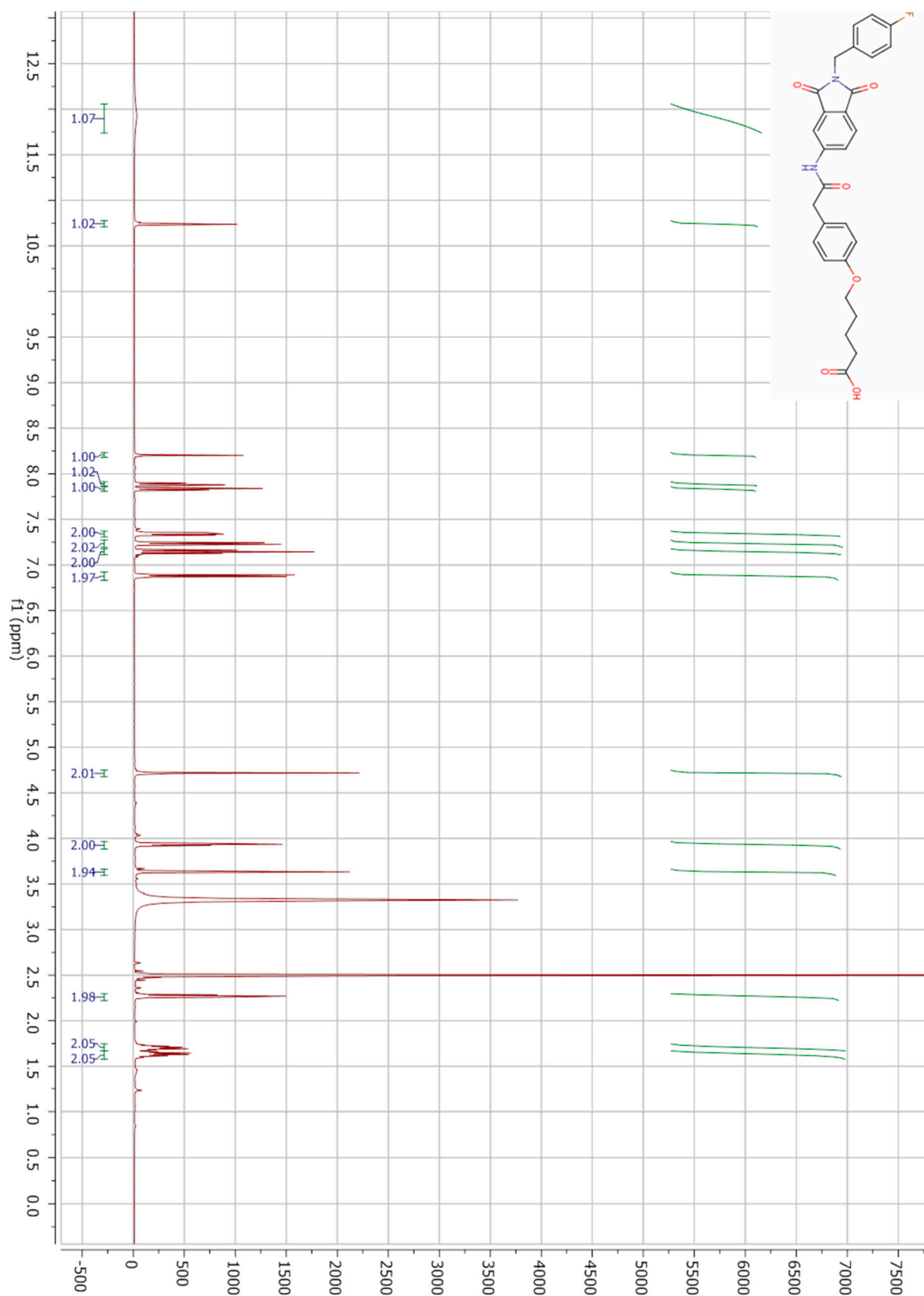
IC₅₀

5463 IC₅₀ for MMP13

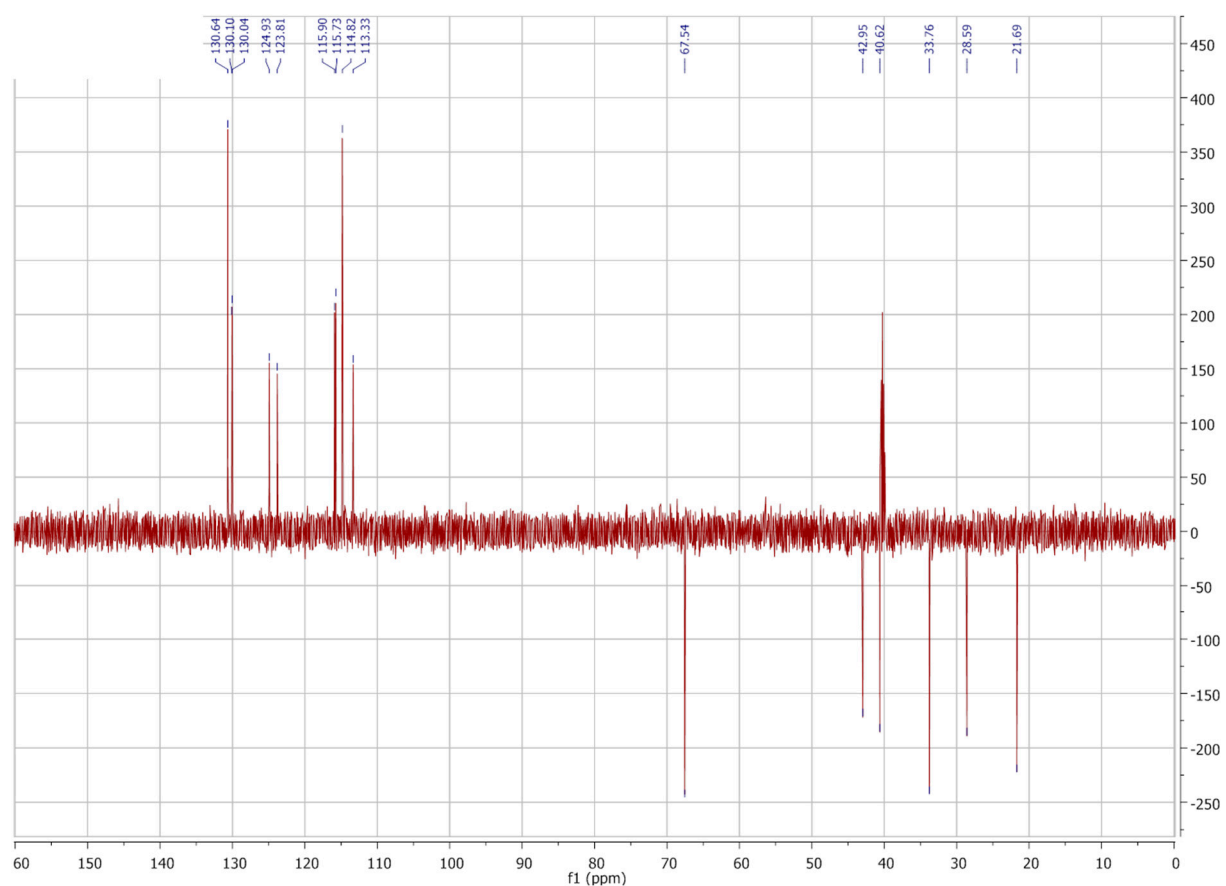
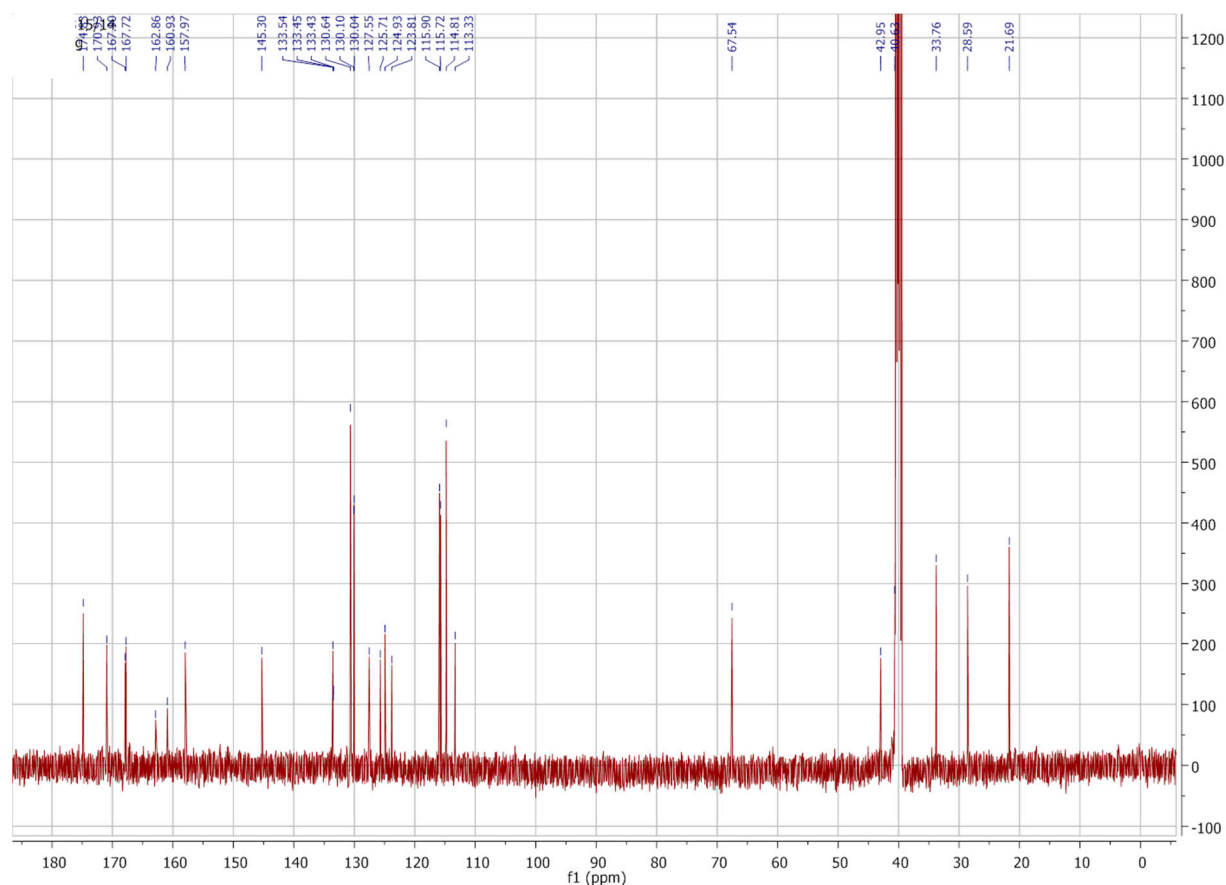


5-{4-[(2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbonyl)methyl]phenoxy}pentanoic acid (**5**; ZHAWOC5684)

NMR

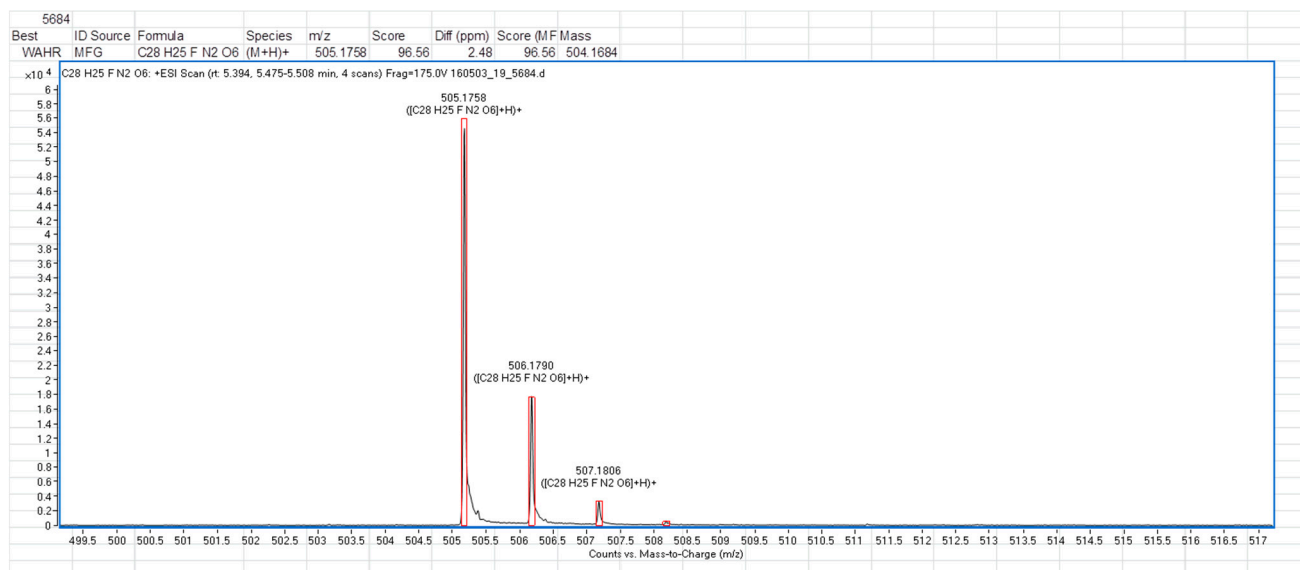


5-{4-[(2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl)methyl]phenoxy}pentanoic acid (5**; ZHAWOC5684)**



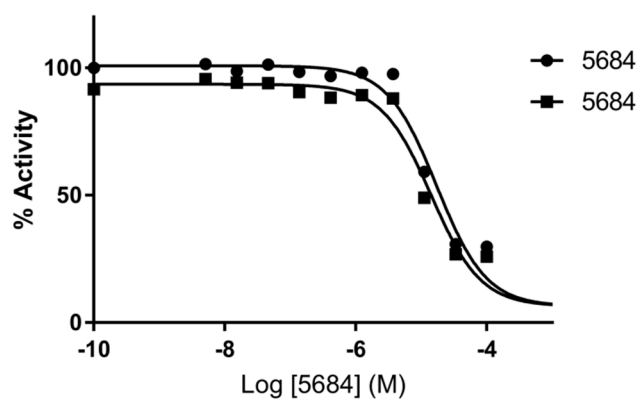
5-{4-[(2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl)methyl]phenoxy}pentanoic acid (5; ZHAWOC5684)

HRMS

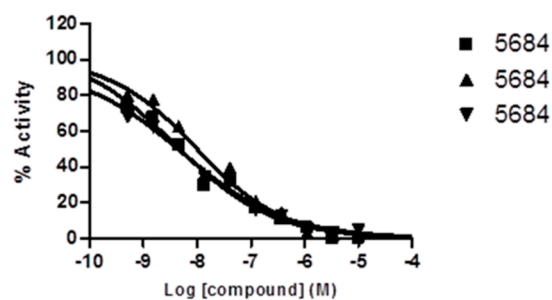


IC₅₀

5684 IC₅₀ for MMP7



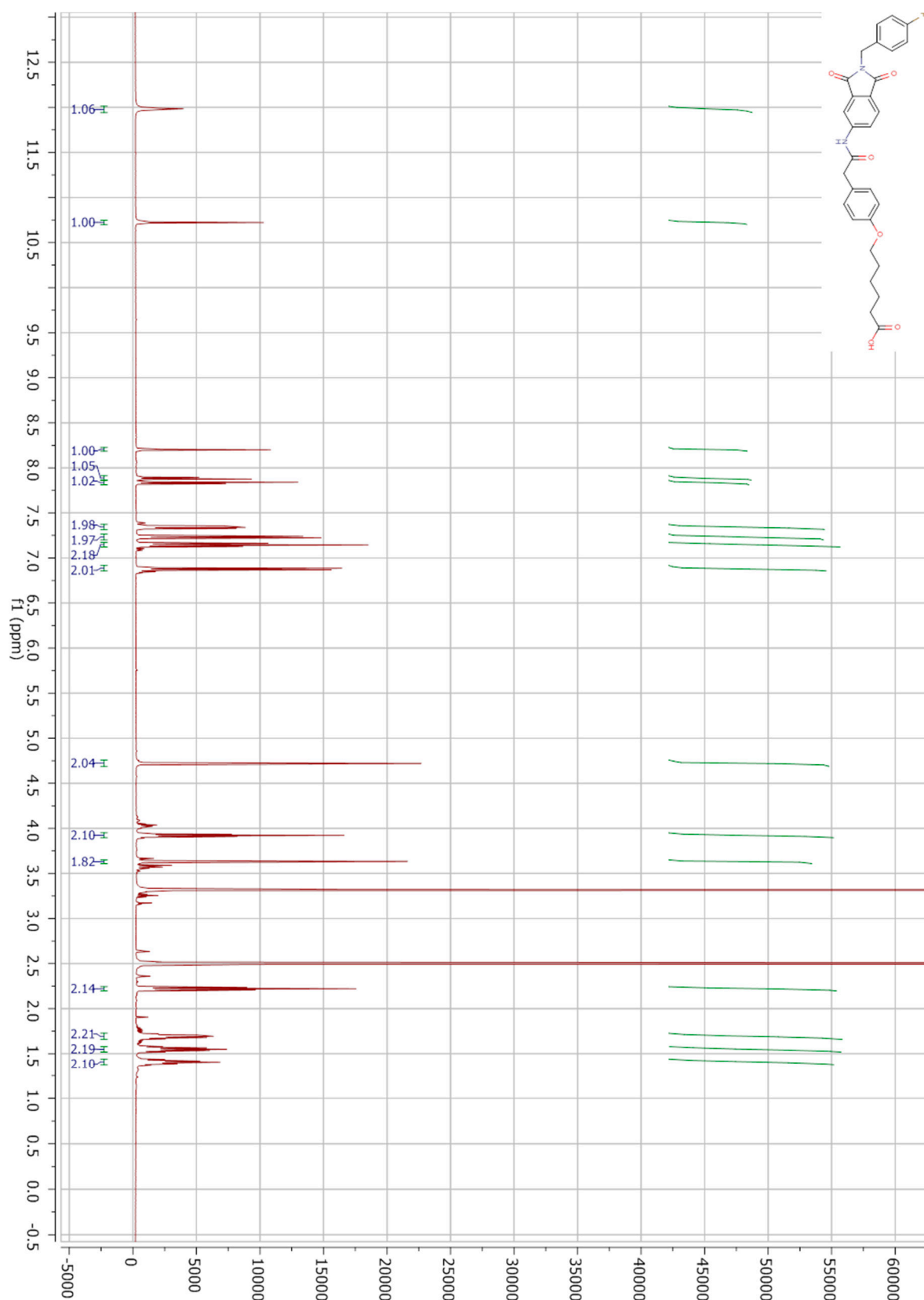
Compound IC₅₀ for MMP 13



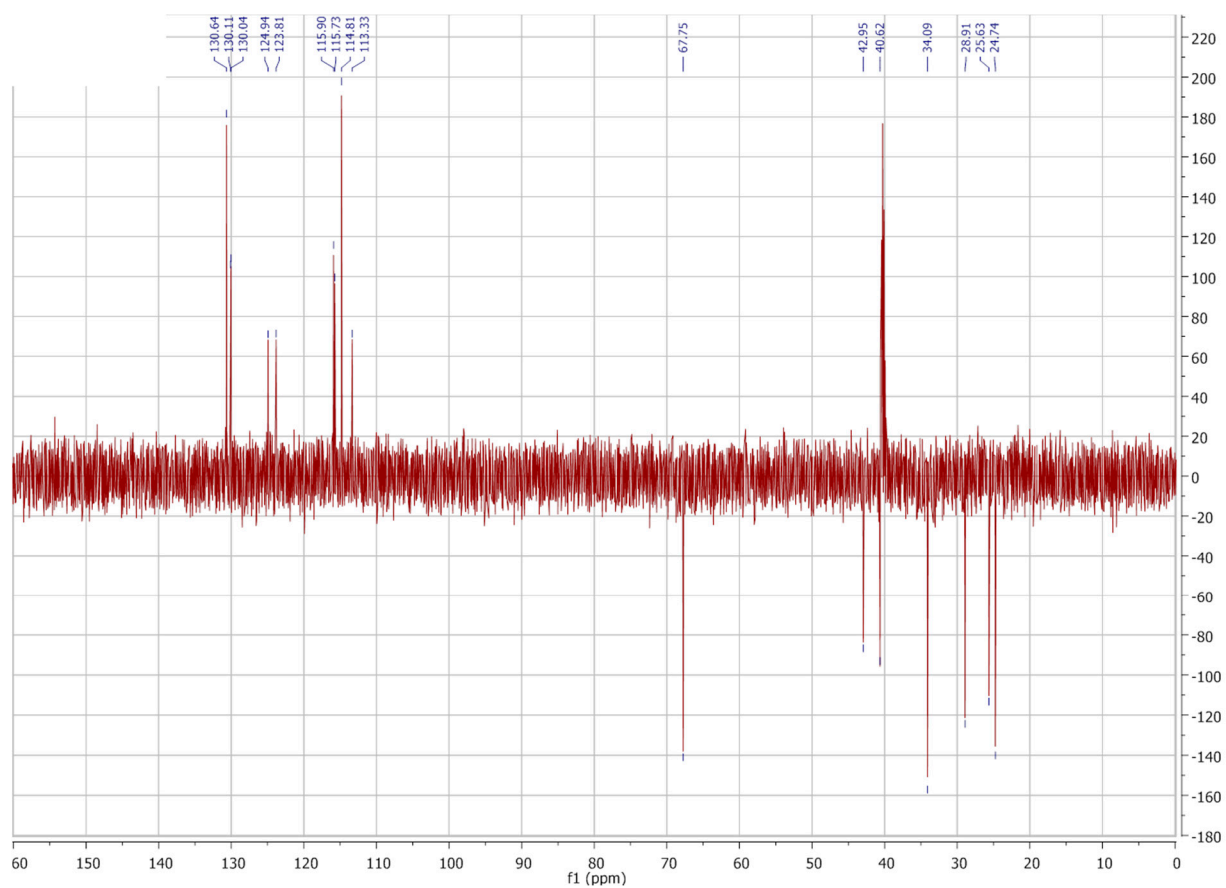
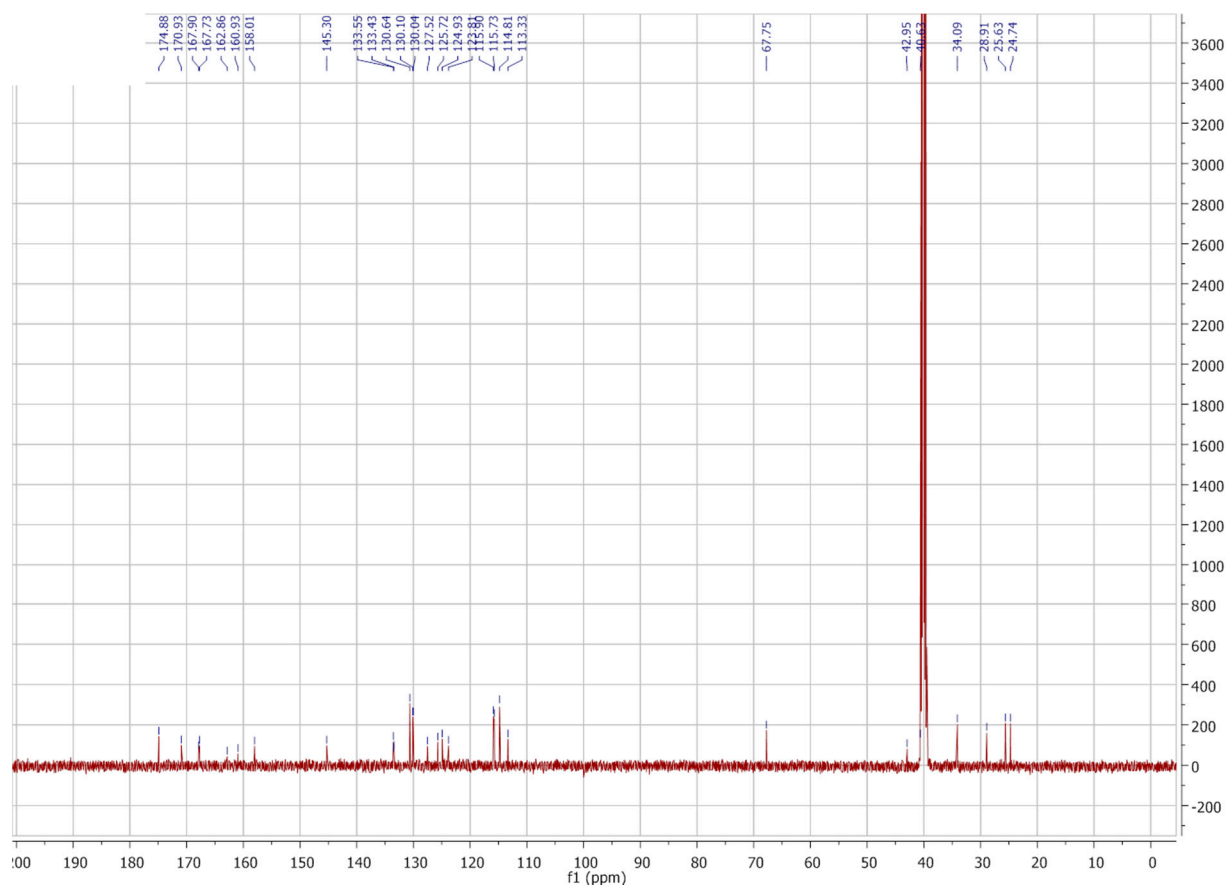
	5684	5684	5684
HILLSLOPE	-0.4789	-0.5361	-0.4540
EC50	3.835e-009	9.790e-009	5.316e-009

6-{4-[(2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbonyl)methyl]phenoxy}hexanoic acid (**14m**; ZHAWOC6645)

NMR

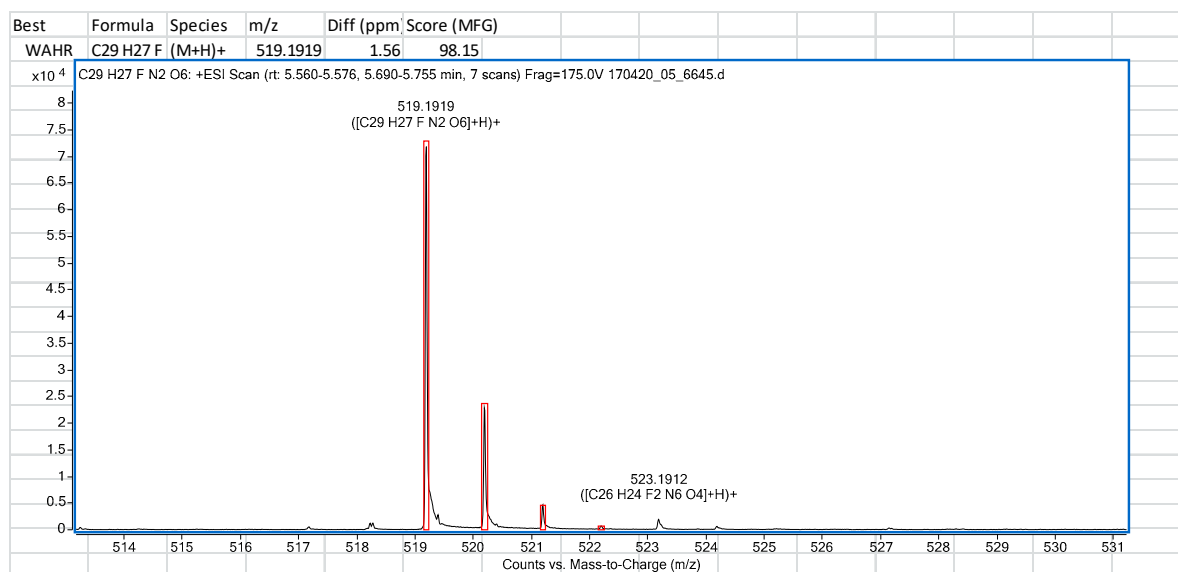


6-{4-[(2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl)methyl]phenoxy}hexanoic acid (**14m**; ZHAWOC6645)



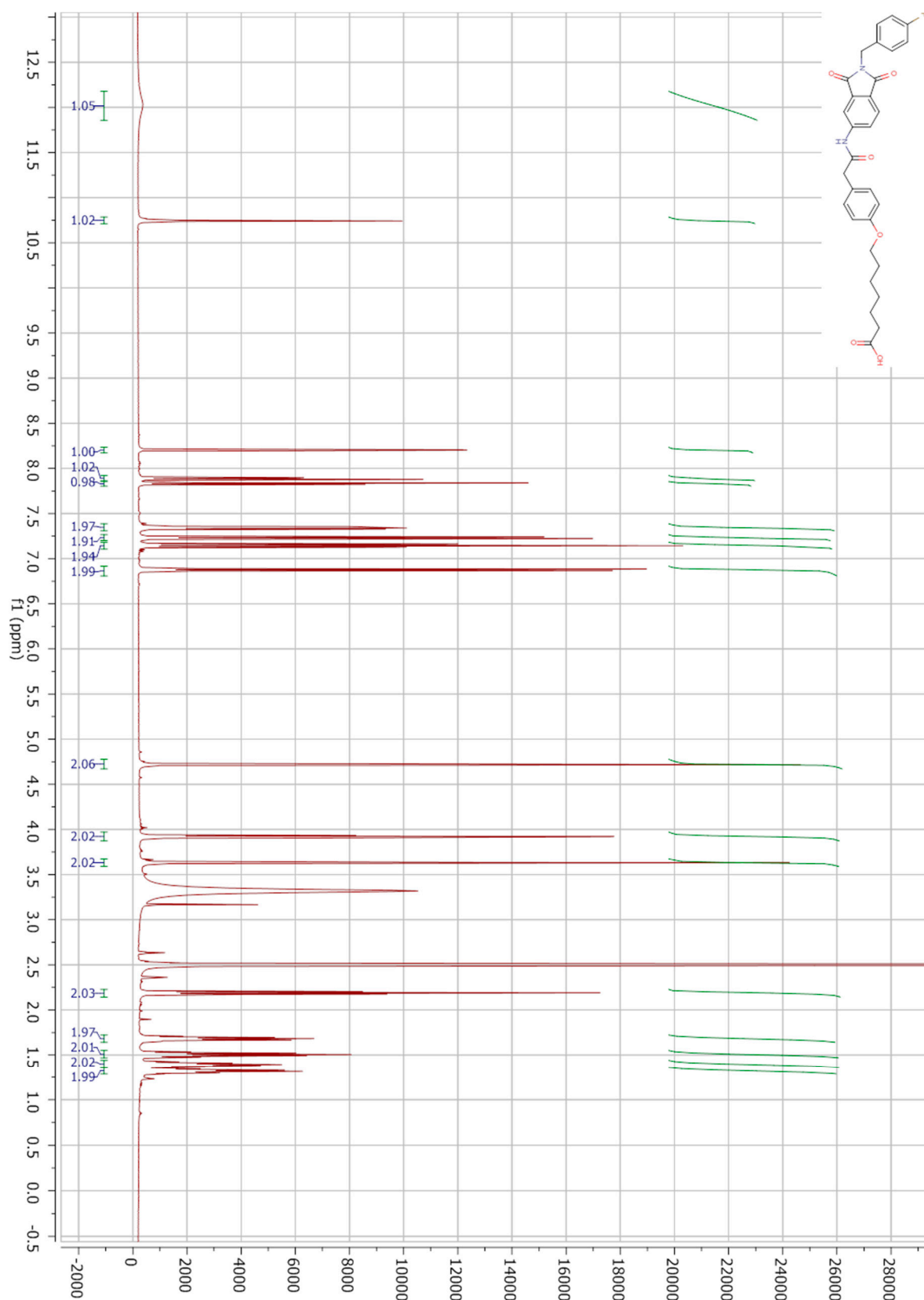
6-{4-[(2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl)methyl]phenoxy}hexanoic acid (**14m**; ZHAWOC6645)

HRMS

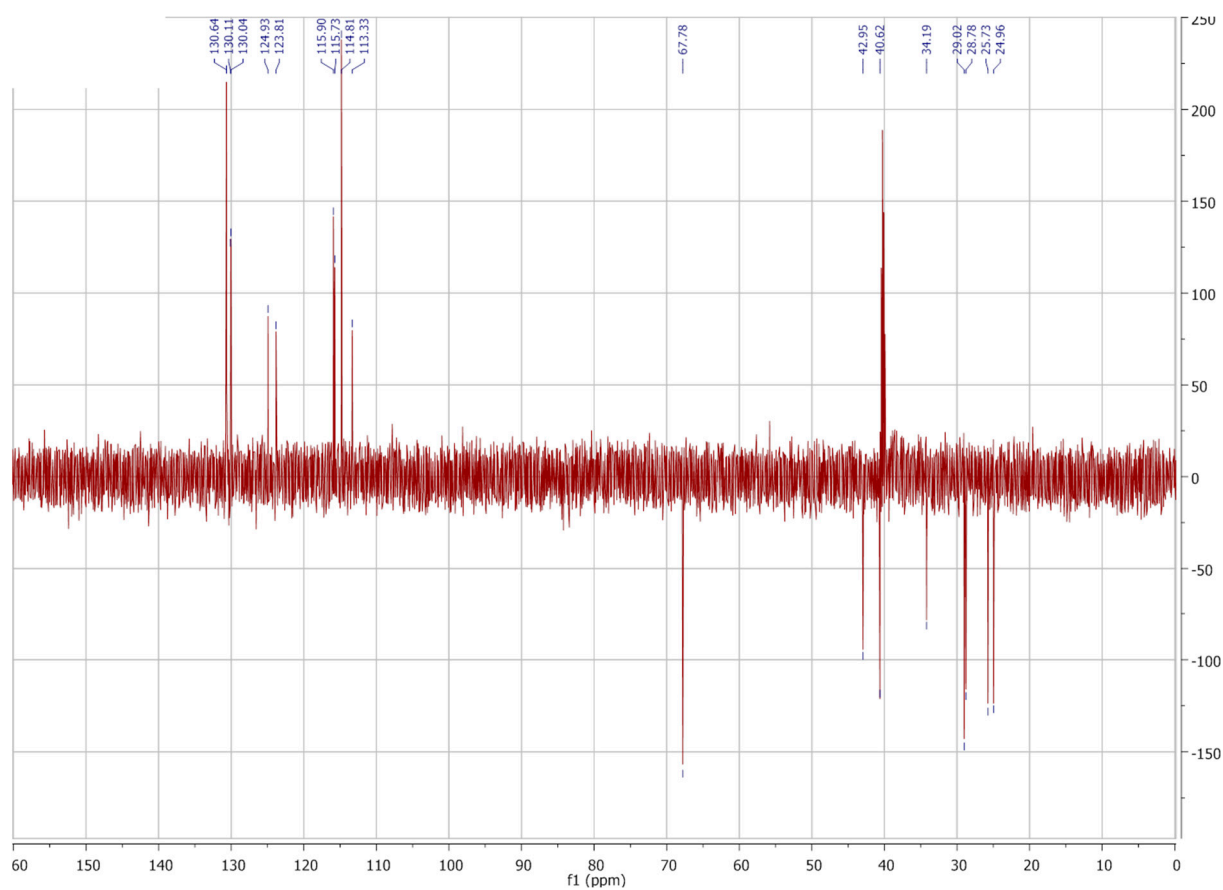
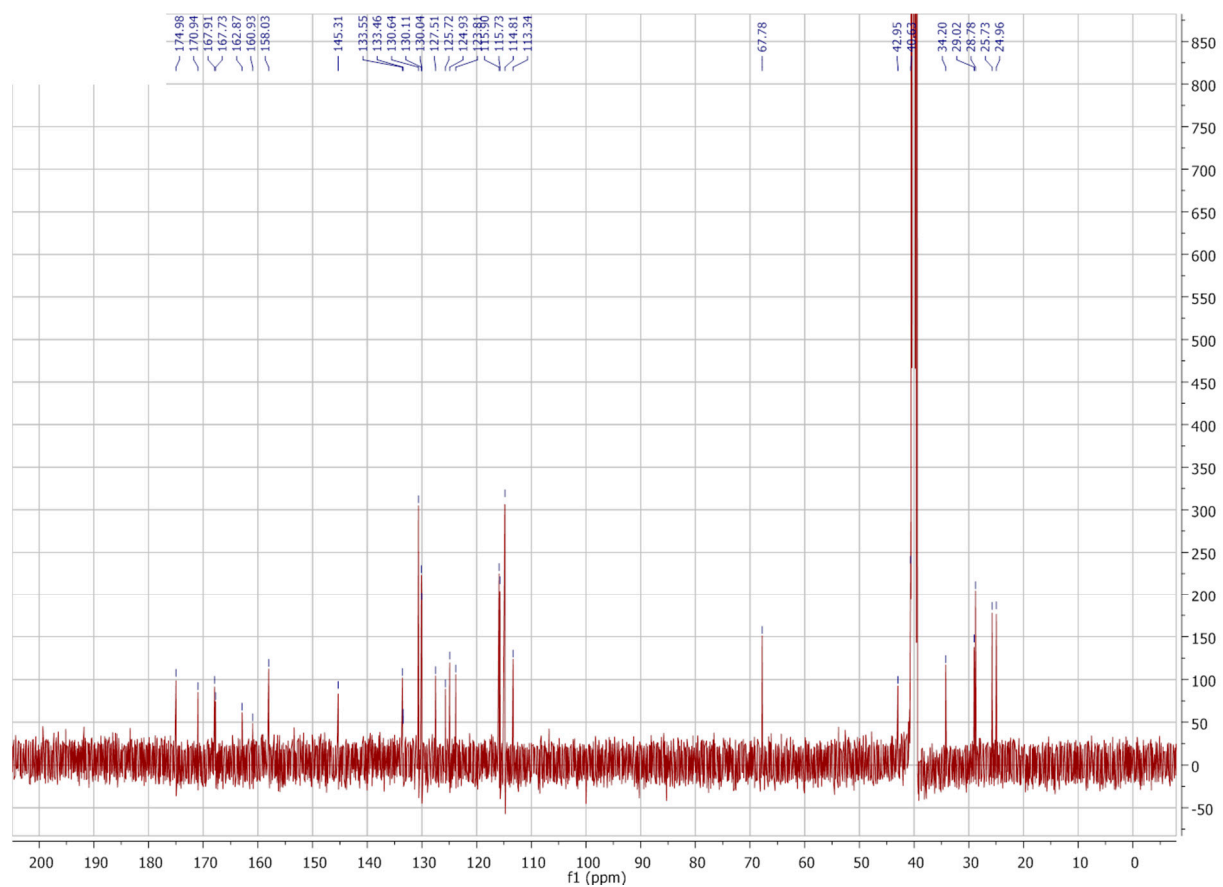


7-{4-[(2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbonyl)methyl]phenoxy}heptanoic acid (**14n**; ZHAWOC6637)

NMR

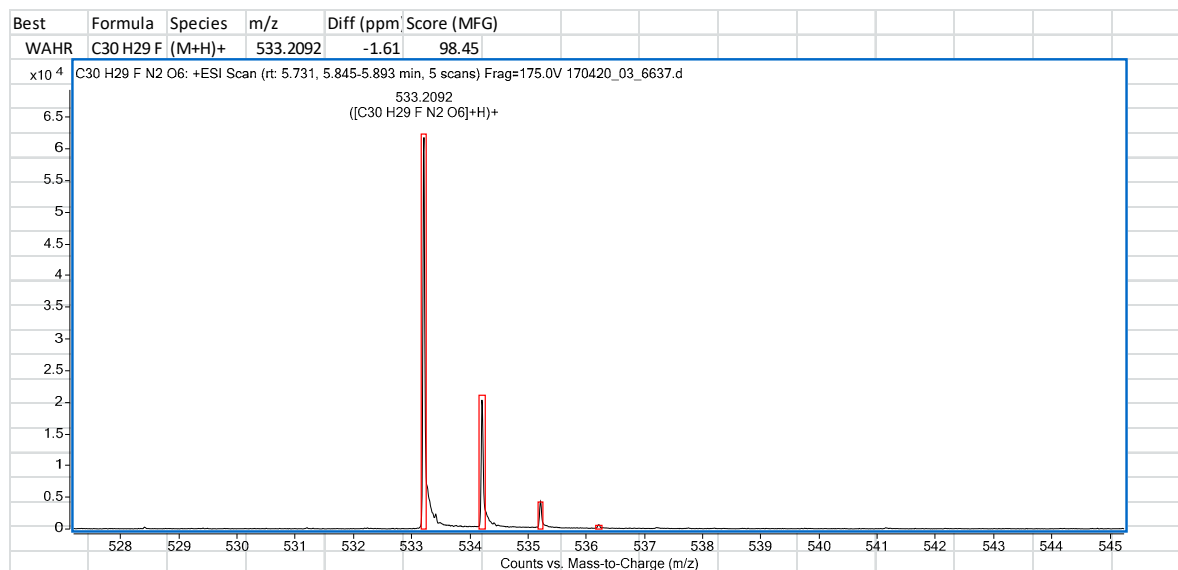


7-{4-[(2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl)methyl]phenoxy}heptanoic acid (**14n**; ZHAWOC6637)



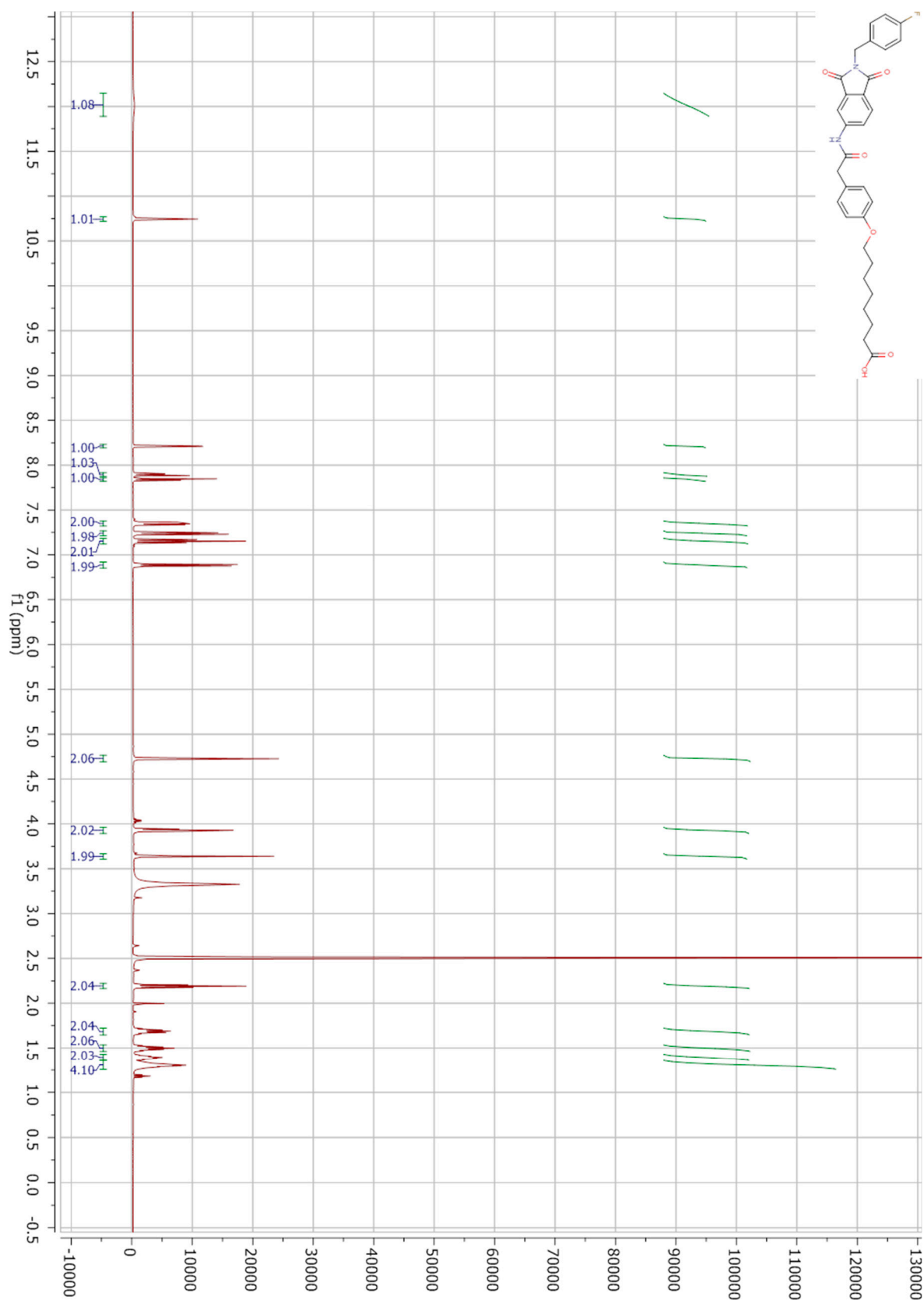
7-{4-[(2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl)methyl]phenoxy}heptanoic acid (**14n**; ZHAWOC6637)

HRMS

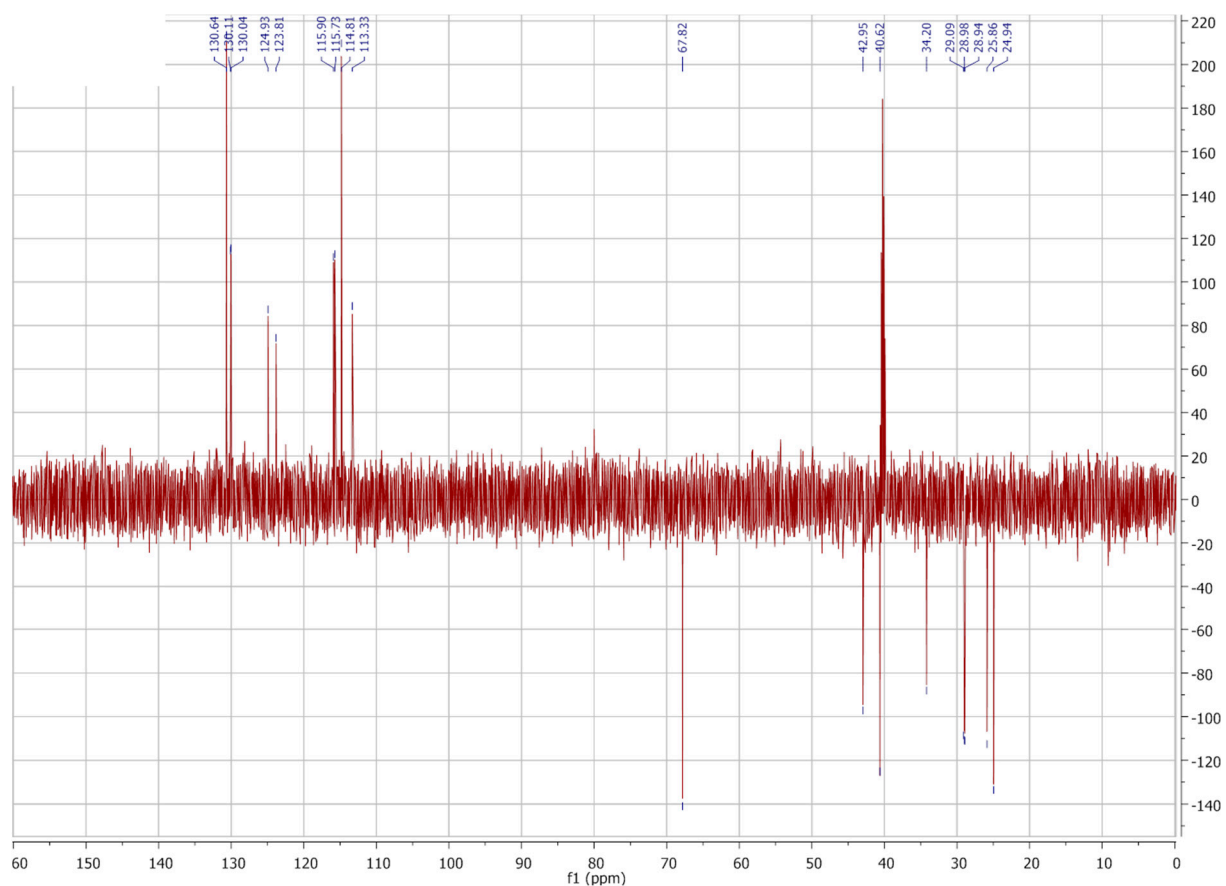
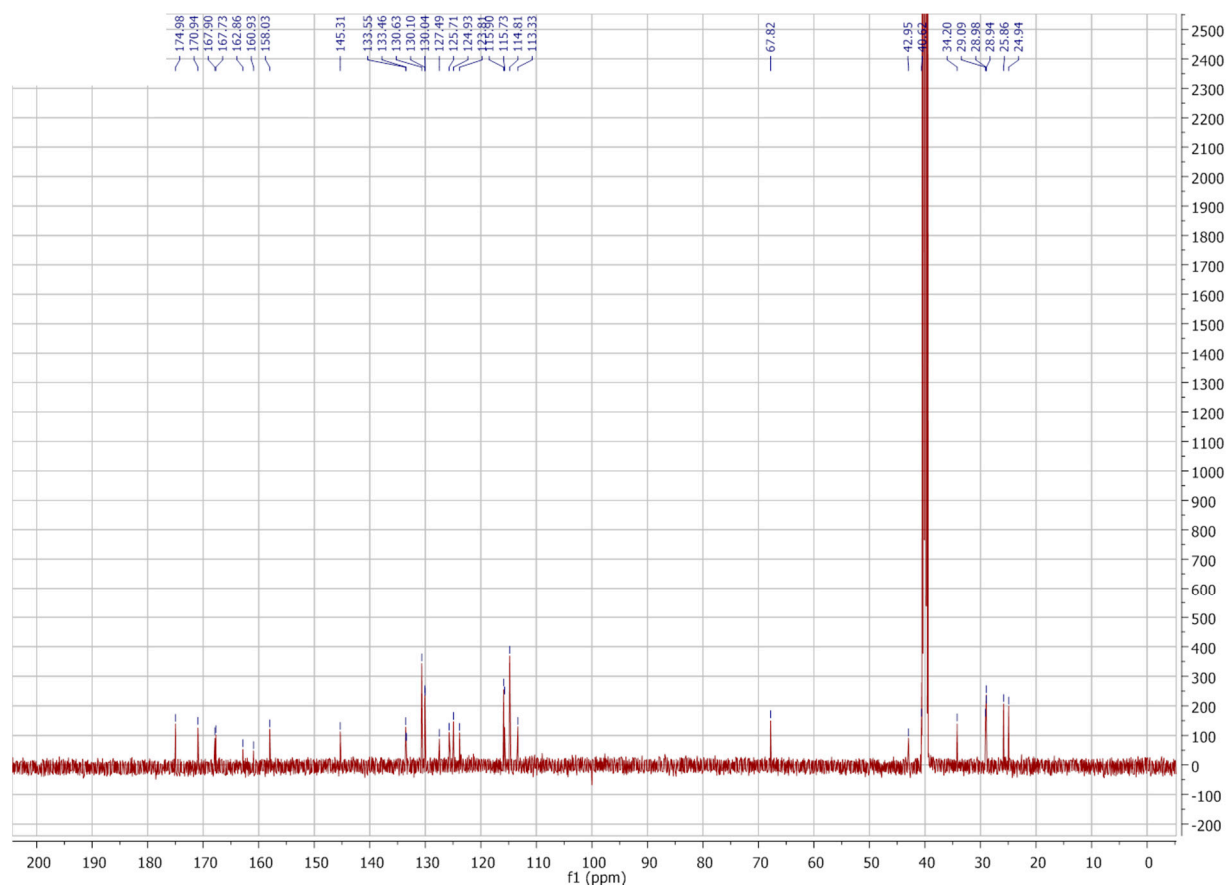


8-{4-[(2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbonyl)methyl]phenoxy}octanoic acid (**14o**; ZHAWOC6646)

NMR



8-{4-[(2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl)methyl]phenoxy}octanoic acid (**14o**; ZHAWOC6646)



8-{4-[(2-[(4-fluorophenyl)methyl]-1,3-dioxo-2,3-dihydro-1H-isoindol-5-yl)carbamoyl)methyl]phenoxy}octanoic acid (14o**; ZHAWOC6646)**

HRMS

