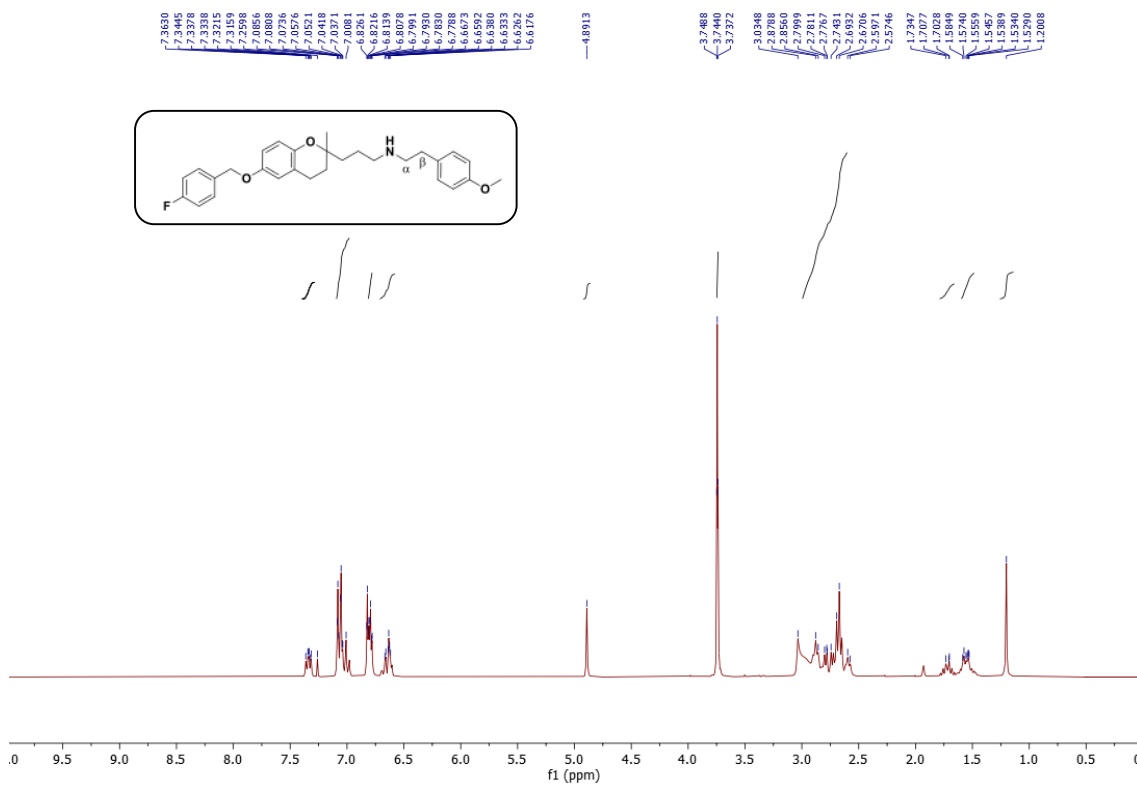


Supplementary Information of
Synthesis of 2-aminopropyl benzopyran derivatives as potential agents against
triple negative breast cancer

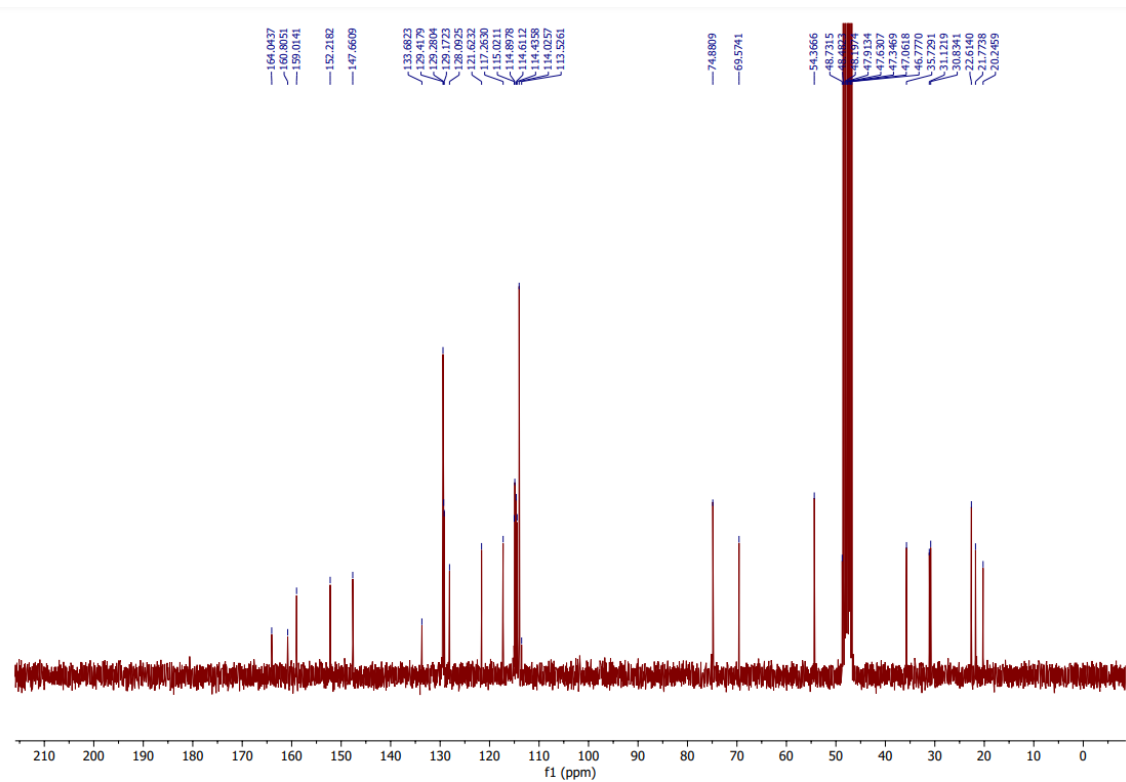
Ainhoa García^{a,b}, Sandra Torres-Ruiz^b, Laura Vila^b, Carlos Villarroel-Vicente^{a,b},
Álvaro Bernabeu^a, Pilar Eroles^{b,c,d,*}, Nuria Cabedo^{a,b,*}, Diego Cortes^a

NMR spectra of all final compounds.

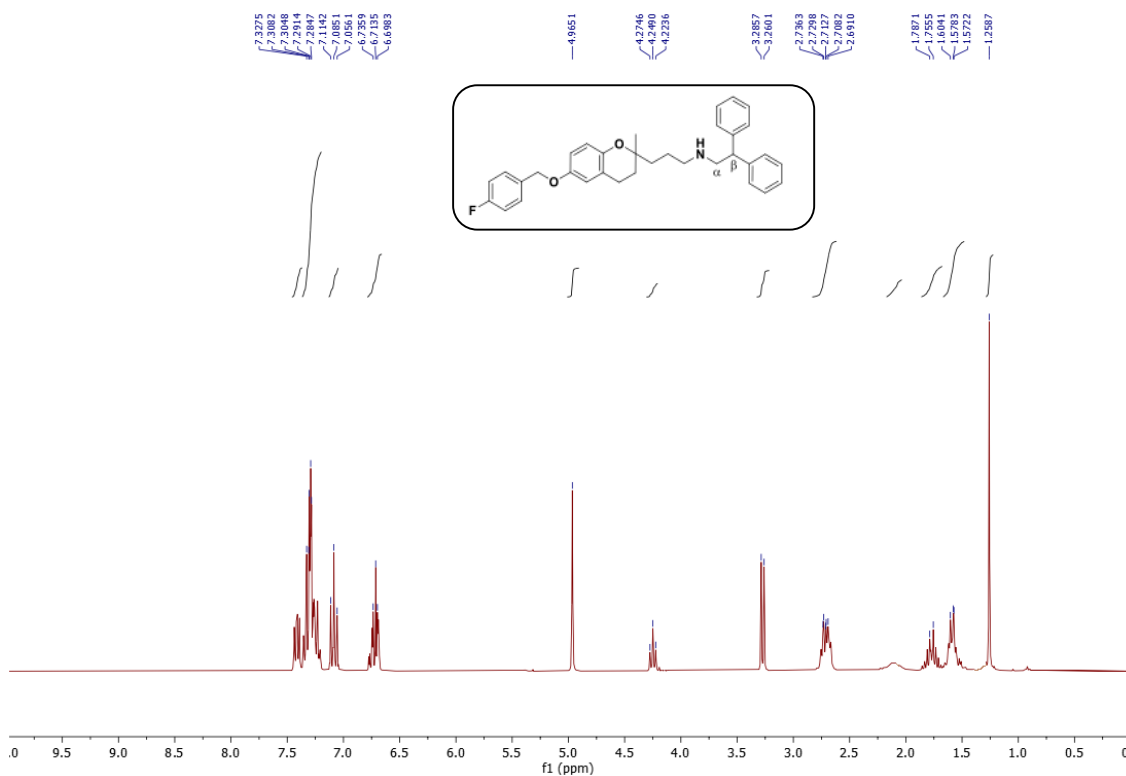
3-(6-(<i>p</i> -Fluorobenzyloxy)-2-methyldihydrobenzopyran-2-yl)- <i>N</i> -(<i>p</i> -methoxyphenethyl)propanamine (5).	S2
<i>N</i> -(2,2-Diphenylethyl)-3-(6-(<i>p</i> -fluorobenzyloxy)-2-methyldihydrobenzopyran-2-yl)propanamine (6).	S3
1-(2-(6-((<i>p</i> -Fluorobenzyl)oxy)-2-methyldihydrobenzopyran-2-yl)ethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (7).	S4
3-(6-Hydroxy-2-methyldihydrobenzopyran-2-yl)- <i>N</i> -(<i>p</i> -methoxyphenethyl)propanamine (5a).	S5
2-(3-((2,2-Diphenylethyl)amino)propyl)-2-methyldihydrobenzopyran-6-ol (6a).	S6
2-(2-(6,7-Dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl)ethyl)-2-methyldihydrobenzopyran-6-ol (7a).	S7
3-(6-(<i>p</i> -Fluorobenzyloxy)-2-methyldihydrobenzopyran-2-yl)- <i>N</i> -(<i>p</i> -methoxyphenethyl)- <i>N</i> -methyl-propanamine (5b).	S8
<i>N</i> -(2,2-Diphenylethyl)-3-(6-((<i>p</i> -fluorobenzyl)oxy)-2-methyldihydrobenzopyran-2-yl)- <i>N</i> -methylpropan-1-amine (6b).	S9
1-(2-(6-((<i>p</i> -Fluorobenzyl)oxy)-2-methyldihydrobenzopyran-2-yl)ethyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (7b).	S10
3-(6-(<i>p</i> -Fluorobenzyloxy)-2-methyldihydrobenzopyran-2-yl)- <i>N</i> -(<i>p</i> -methoxyphenethyl)- <i>N,N</i> -dimethylpropan-1-aminium (5c).	S11
<i>N</i> -(2,2-Diphenylethyl)-3-(6-((<i>p</i> -fluorobenzyl)oxy)-2-methyldihydrobenzopyran-2-yl)- <i>N,N</i> -dimethylpropan-1-aminium (6c).	S12
1-(2-(6-((<i>p</i> -Fluorobenzyl)oxy)-2-methyldihydrobenzopyran-2-yl)ethyl)-6,7-dimethoxy-2,2-dimethyl-1,2,3,4-tetrahydroisoquinolin-2-ium (7c).	S13
3-(<i>p</i> -Chlorophenyl)- <i>N</i> -(3-(6-((<i>p</i> -fluorobenzyl)oxy)-2-methyldihydrobenzopyran-2-yl)propyl)- <i>N</i> -(<i>p</i> -methoxyphenethyl)urea (5d).	S14
3-(<i>p</i> -Chlorophenyl)- <i>N</i> -(2,2-diphenylethyl)- <i>N</i> -(3-(6-((<i>p</i> -fluorobenzyl)oxy)-2-methyldihydrobenzopyran-2-yl)propyl)urea (6d).	S15
<i>N</i> -(<i>p</i> -Chlorophenyl)-1-(2-(6-((<i>p</i> -fluorobenzyl)oxy)-2-methyldihydrobenzopyran-2-yl)ethyl)-6,7-dimethoxy-3,4-dihydroisoquinoline-2(1 <i>H</i>)-carboxamide (7d).	S16



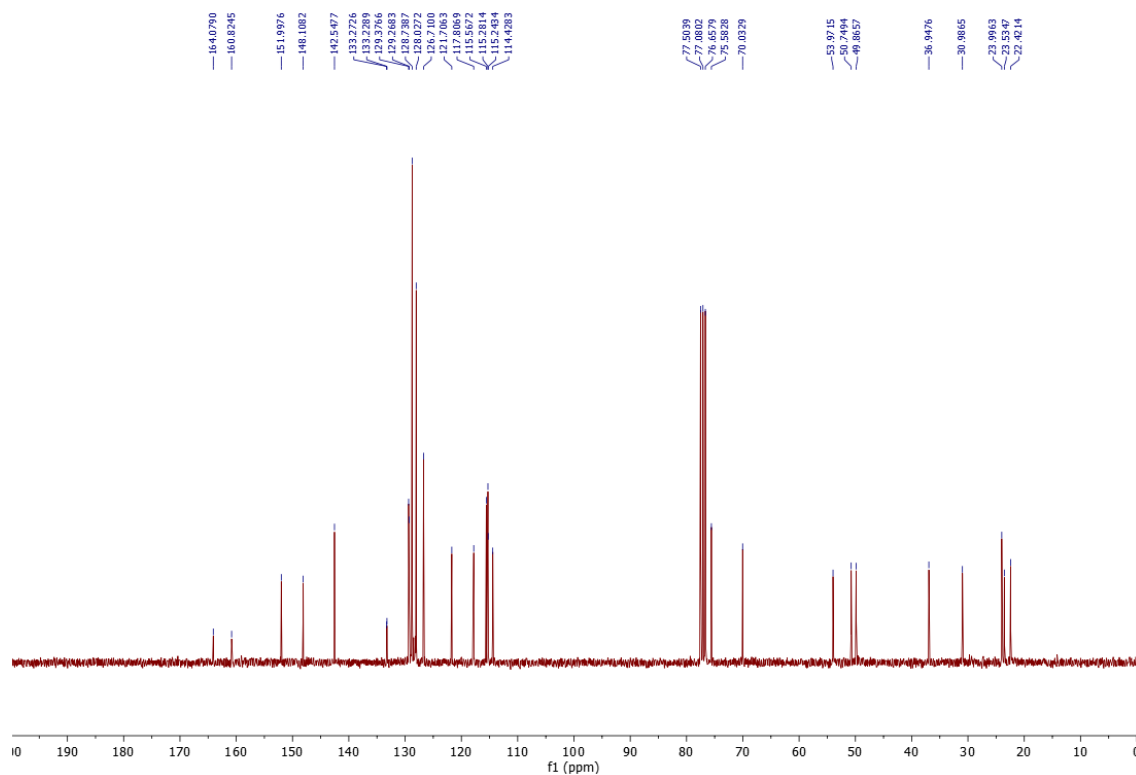
¹H NMR (300 MHz, CDCl₃) of 3-(6-(p-Fluorobenzyloxy)-2-methyldihydrobenzopyran-2-yl)-N-(p-methoxyphenethyl)propanamine (5).



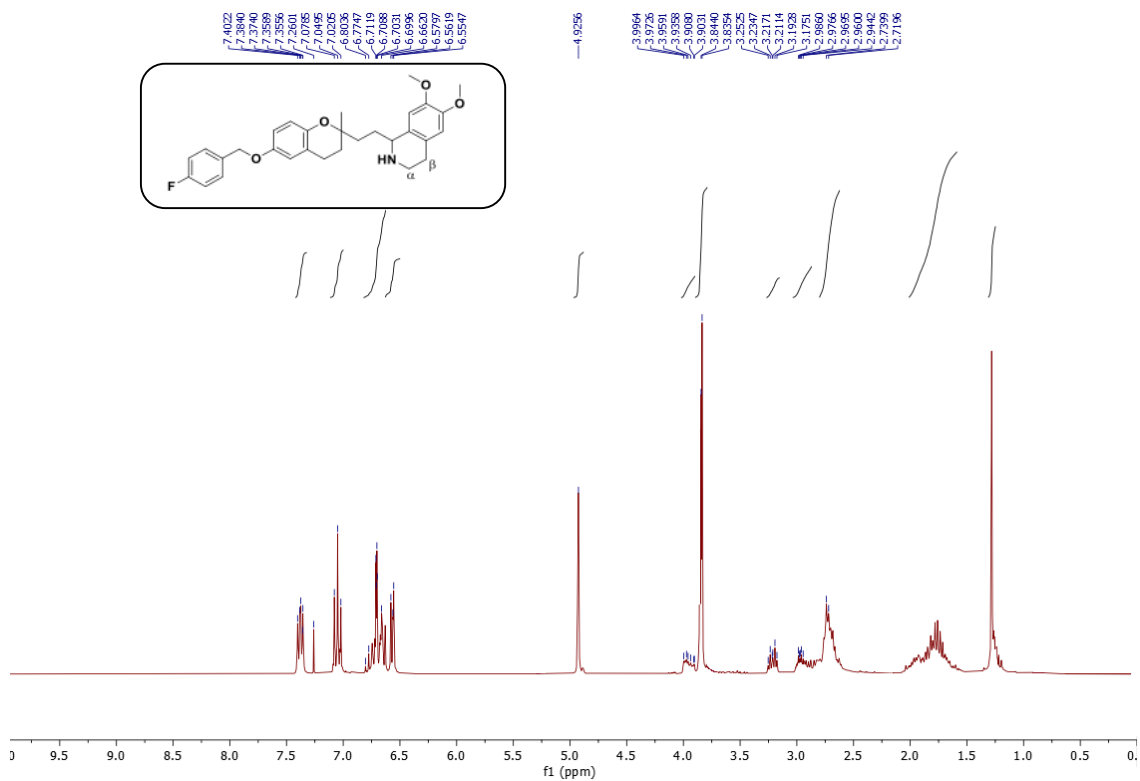
¹³C NMR (75 MHz, CD₃OD) of 3-(6-(p-Fluorobenzyloxy)-2-methyldihydrobenzopyran-2-yl)-N-(p-methoxyphenethyl)propanamine (5).



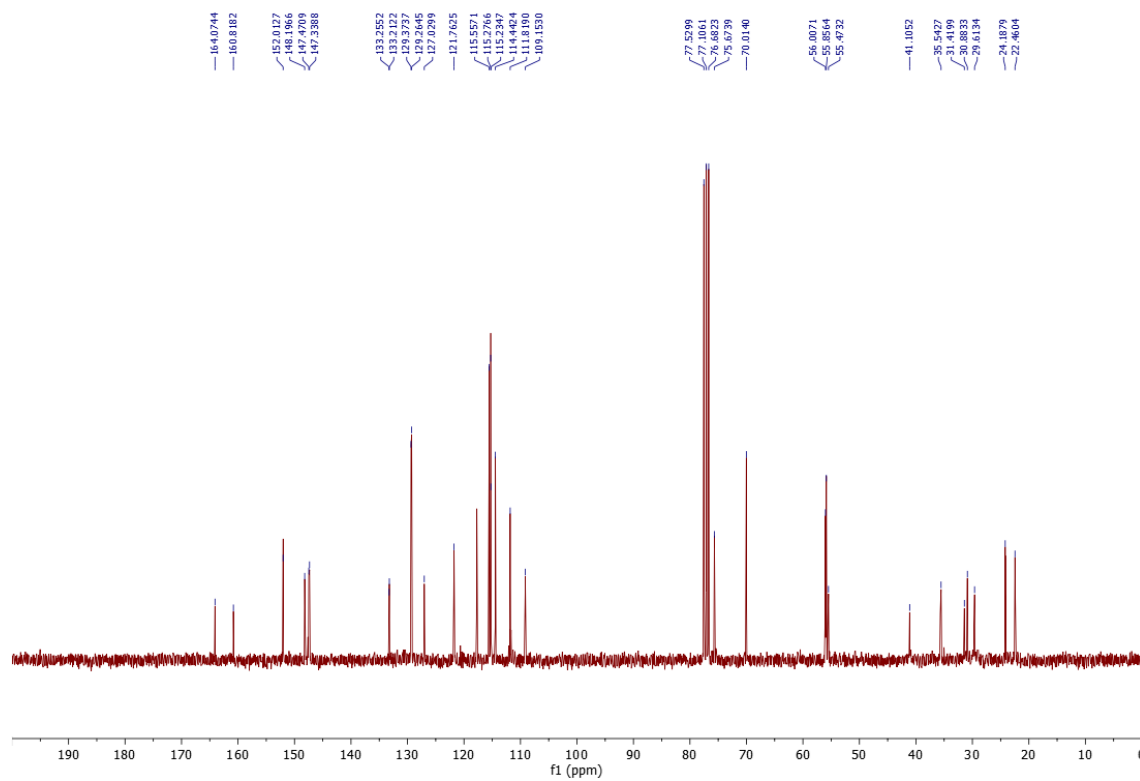
¹H NMR (300 MHz, CDCl₃) of *N*-(2,2-Diphenylethyl)-3-(6-(*p*-fluorobenzyloxy)-2-methyl-dihydrobenzopyran-2-yl)propanamine (**6**).



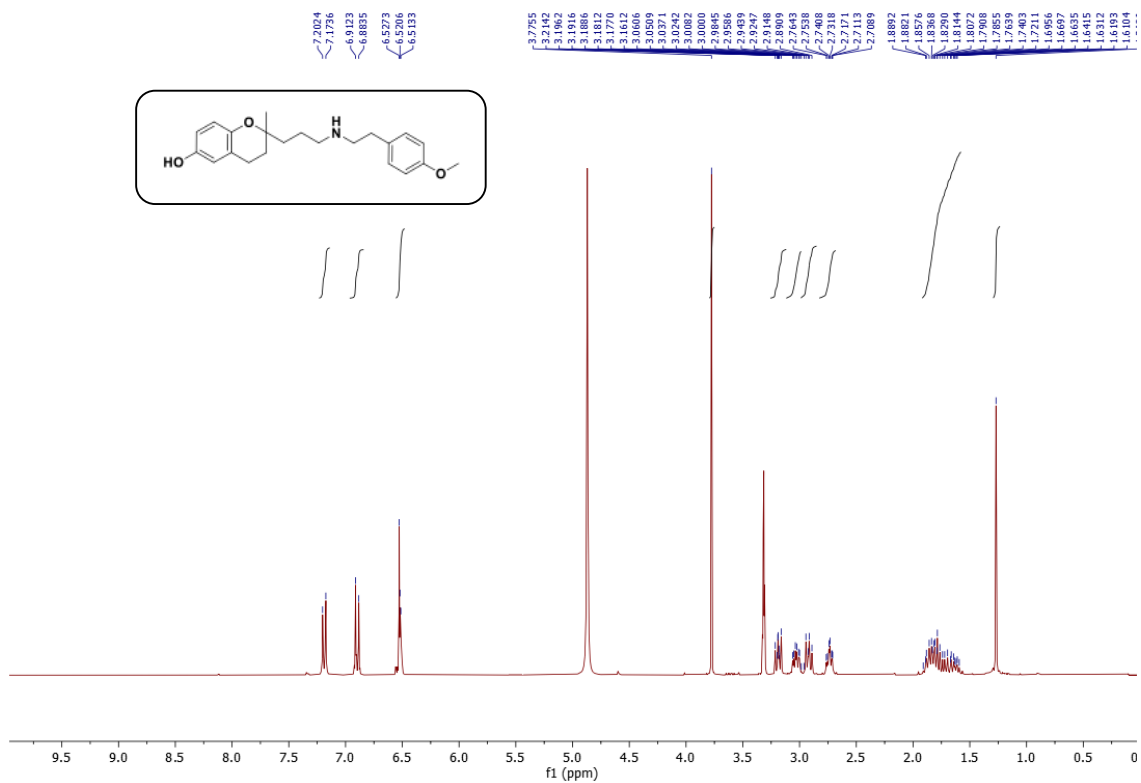
¹³C NMR (75 MHz, CDCl₃) of *N*-(2,2-Diphenylethyl)-3-(6-(*p*-fluorobenzyloxy)-2-methyl-dihydrobenzopyran-2-yl)propanamine (**6**).



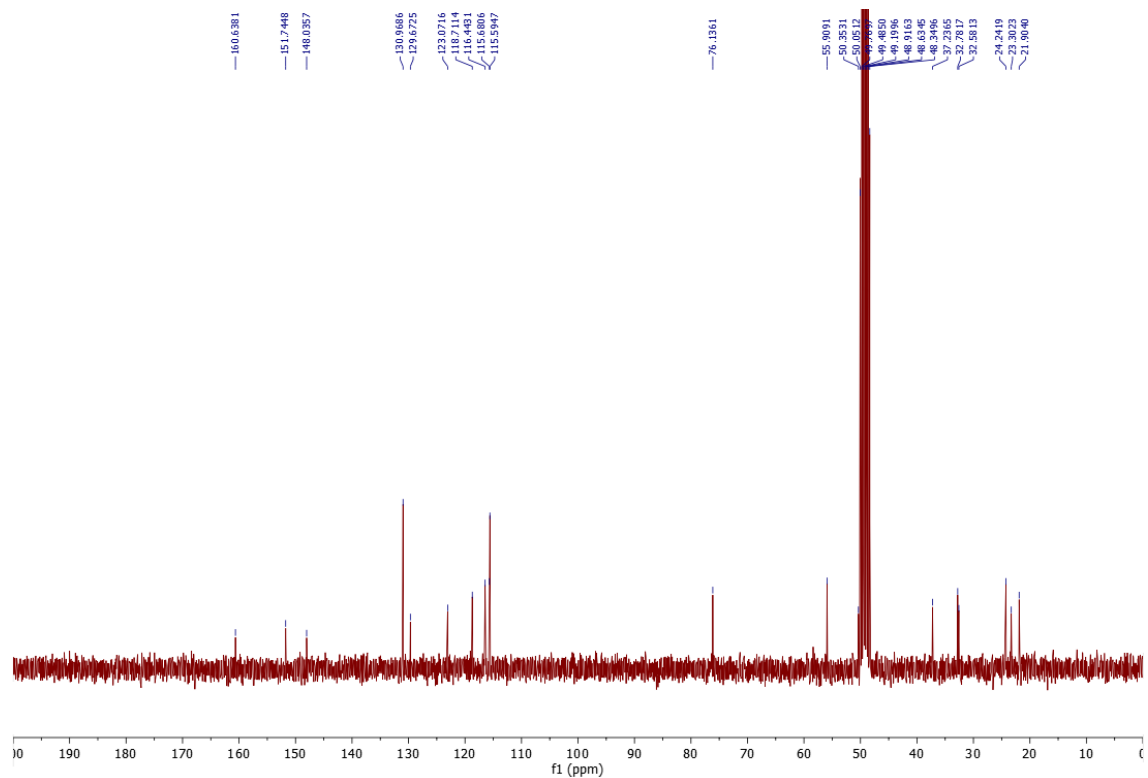
¹H NMR (300 MHz, CDCl₃) of 1-(2-(6-((p-Fluorobenzyl)oxy)-2-methyldihydro benzopyran-2-yl)ethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (7).



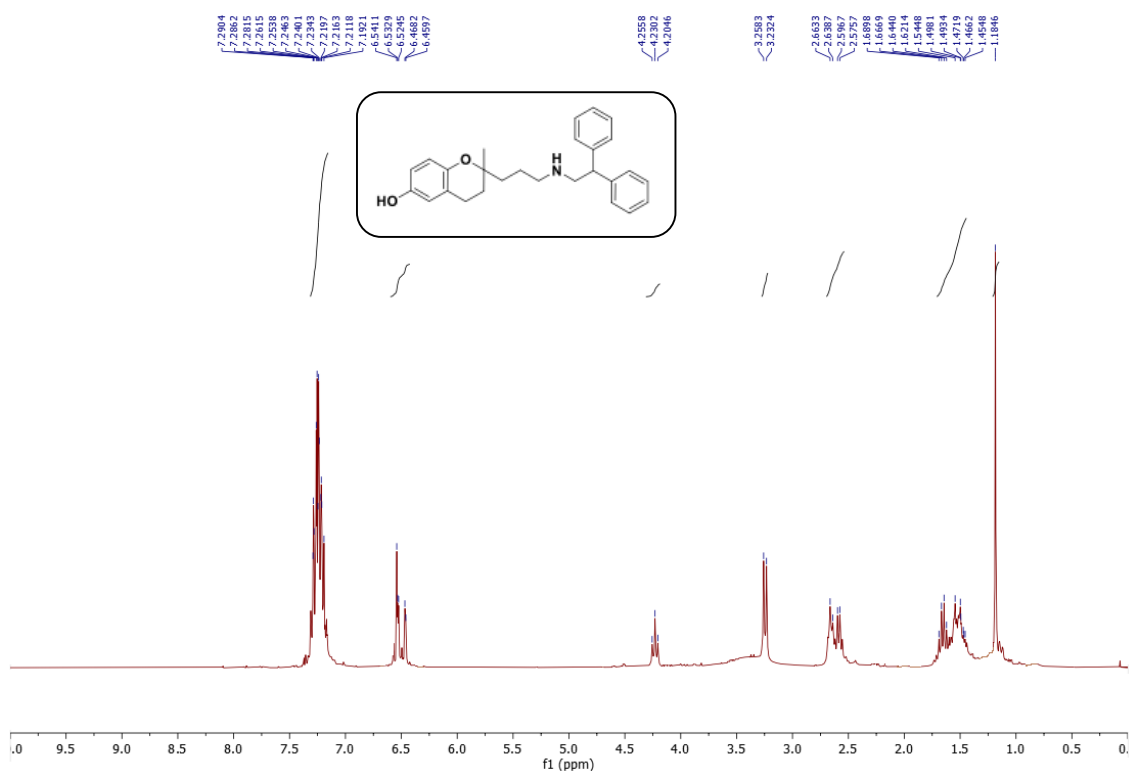
¹³C NMR (75 MHz, CDCl₃) of 1-(2-(6-((p-Fluorobenzyl)oxy)-2-methyldihydro benzopyran-2-yl)ethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (7).



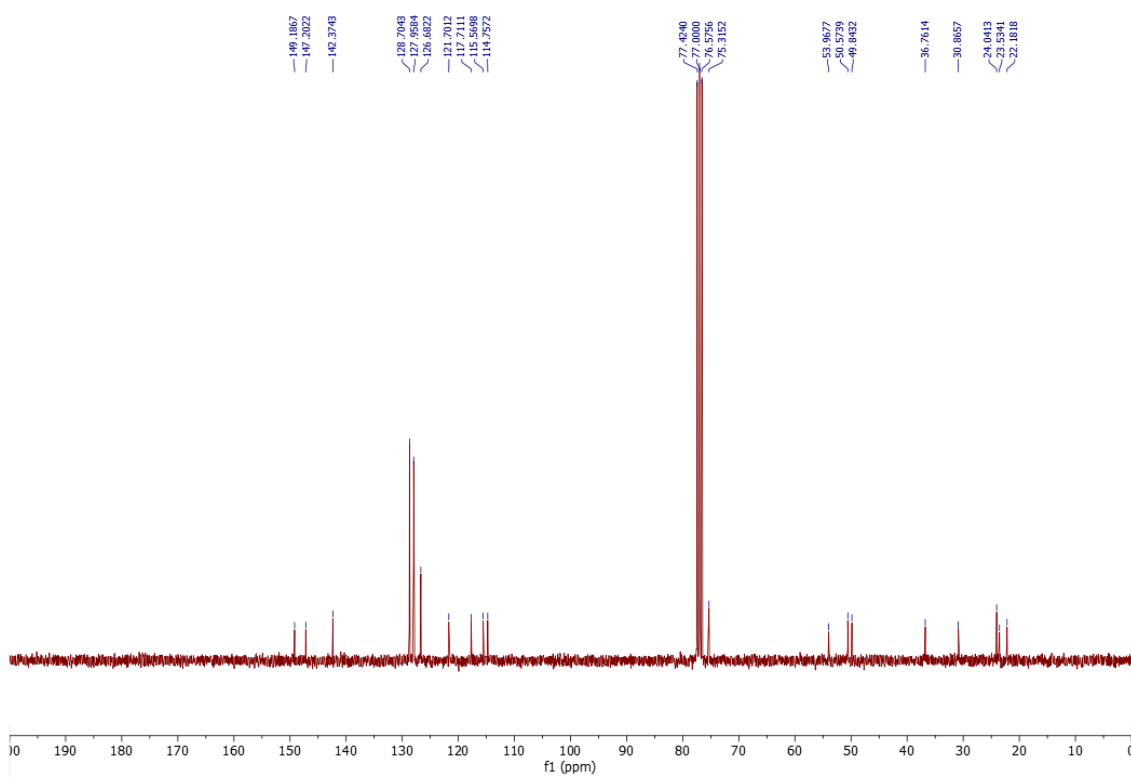
¹H NMR (300 MHz, CD₃OD) of 3-(6-Hydroxy-2-methylidihydrobenzopyran-2-yl)-N-(p-methoxyphenethyl)propanamine (**5a**).



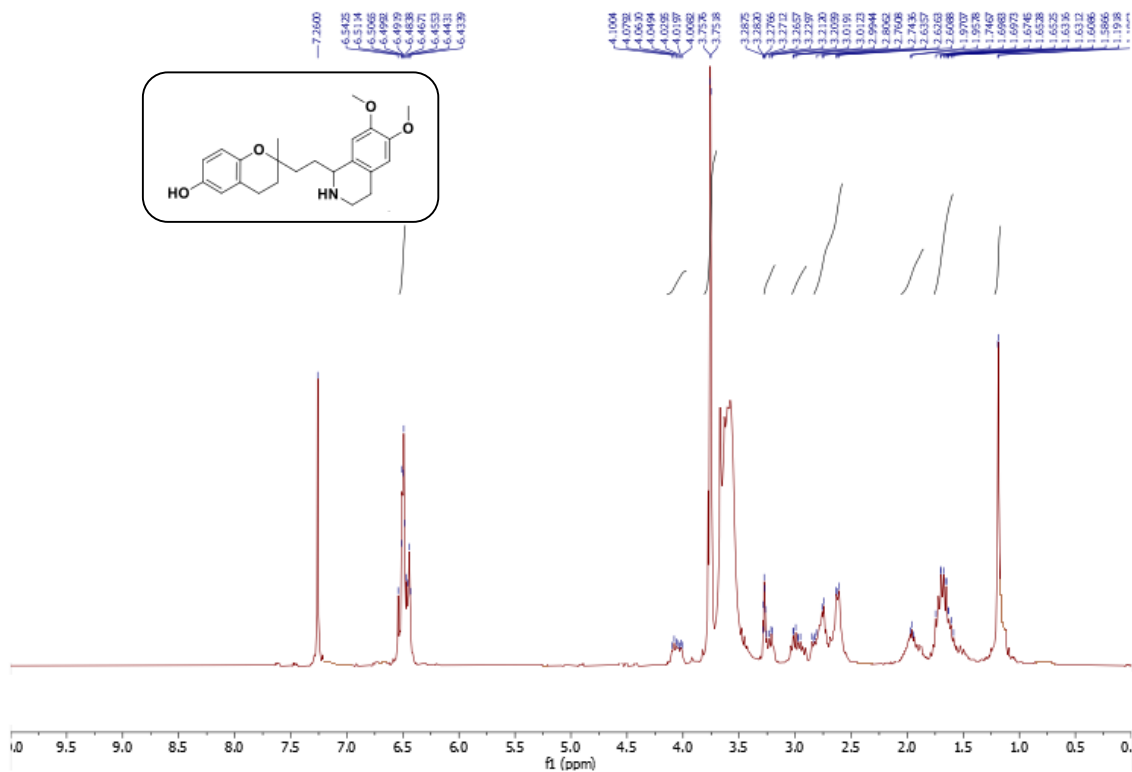
¹³C NMR (75 MHz, CD₃OD) of 3-(6-Hydroxy-2-methylidihydrobenzopyran-2-yl)-N-(p-methoxyphenethyl)propanamine (**5a**).



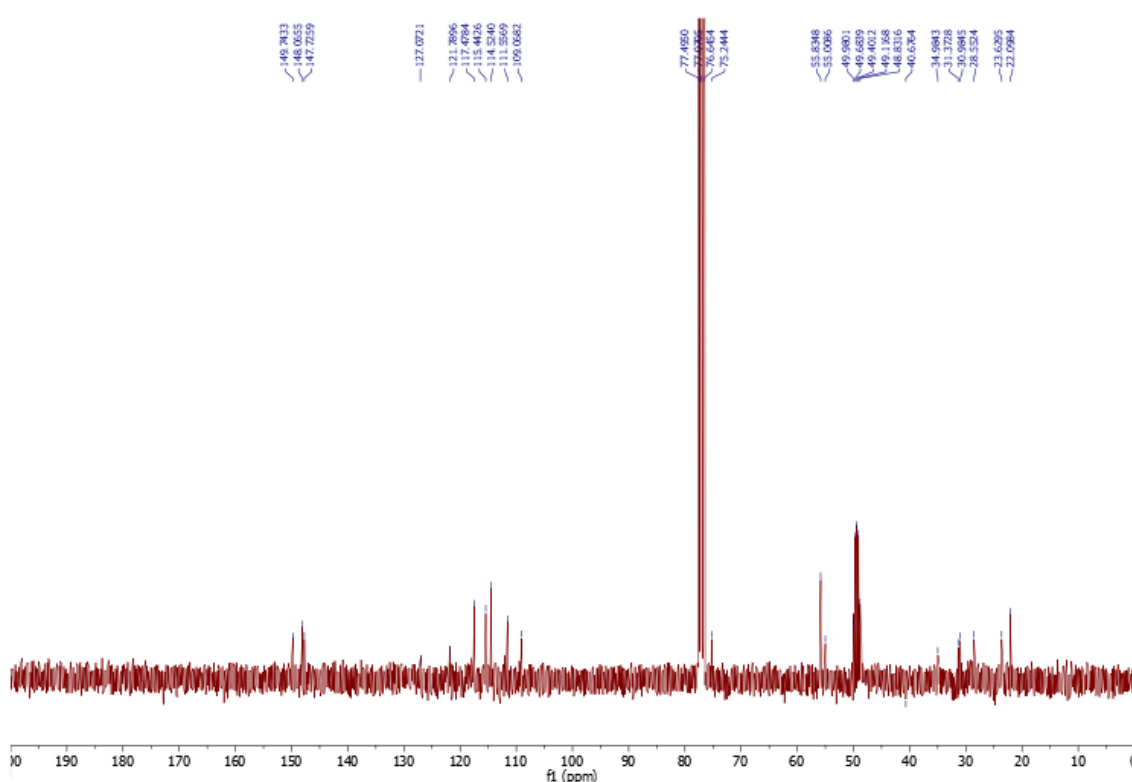
¹H NMR (300 MHz, CDCl₃) of 2-(3-((2,2-Diphenylethyl)amino)propyl)-2-methyl dihydrobenzopyran-6-ol (**6a**).



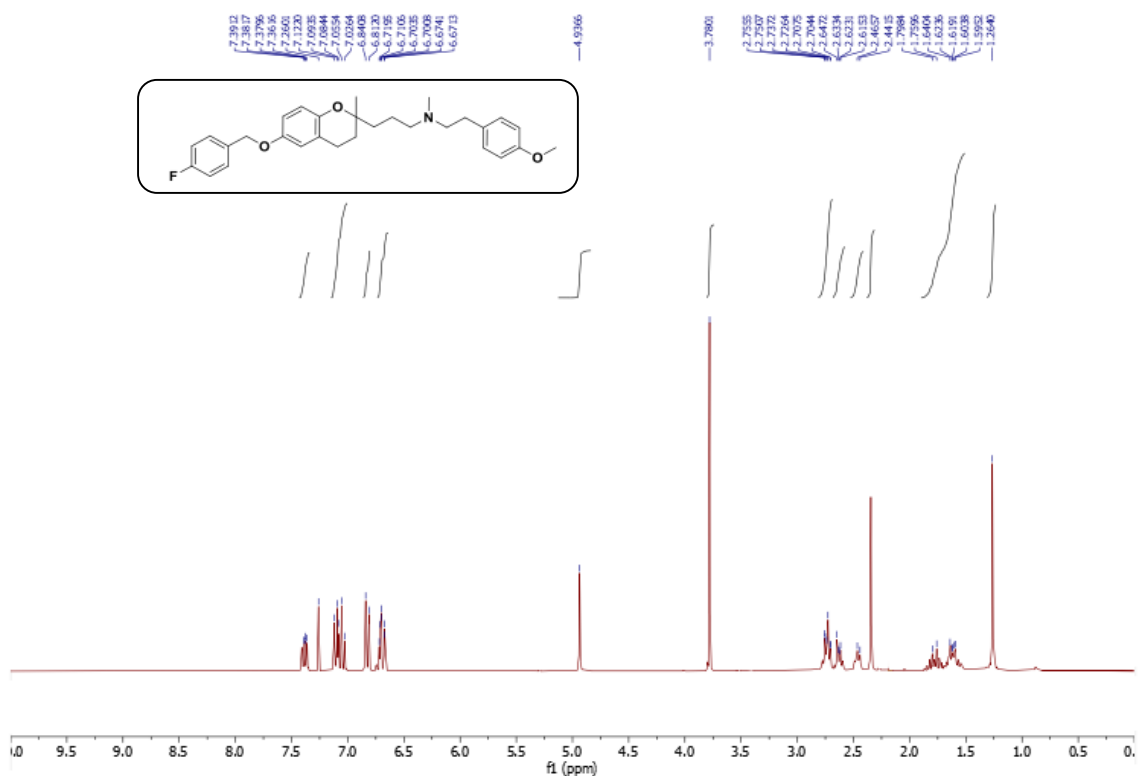
¹³C NMR (75 MHz, CDCl₃) of 2-(3-((2,2-Diphenylethyl)amino)propyl)-2-methyl dihydrobenzopyran-6-ol (**6a**).



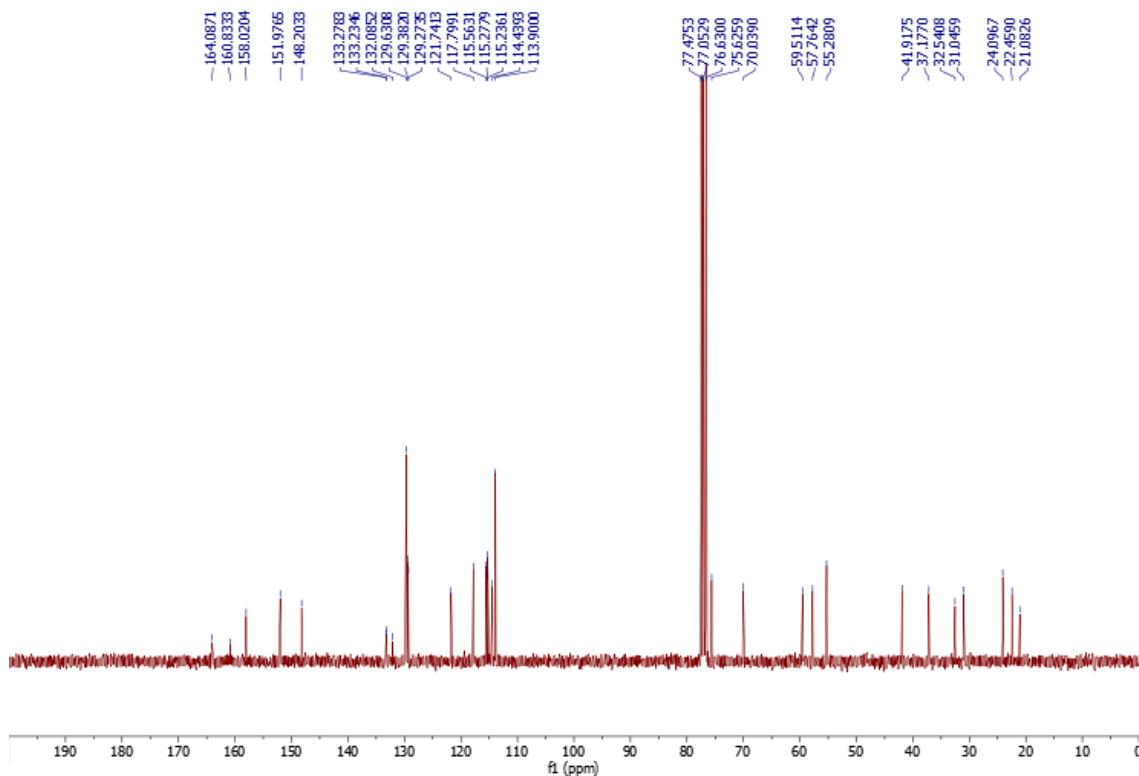
^1H NMR (300 MHz, CDCl_3 + 1 drop CD_3OD) of 2-(2-(6,7-Dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl)ethyl)-2-methyldihydrobenzopyran-6-ol (**7a**).



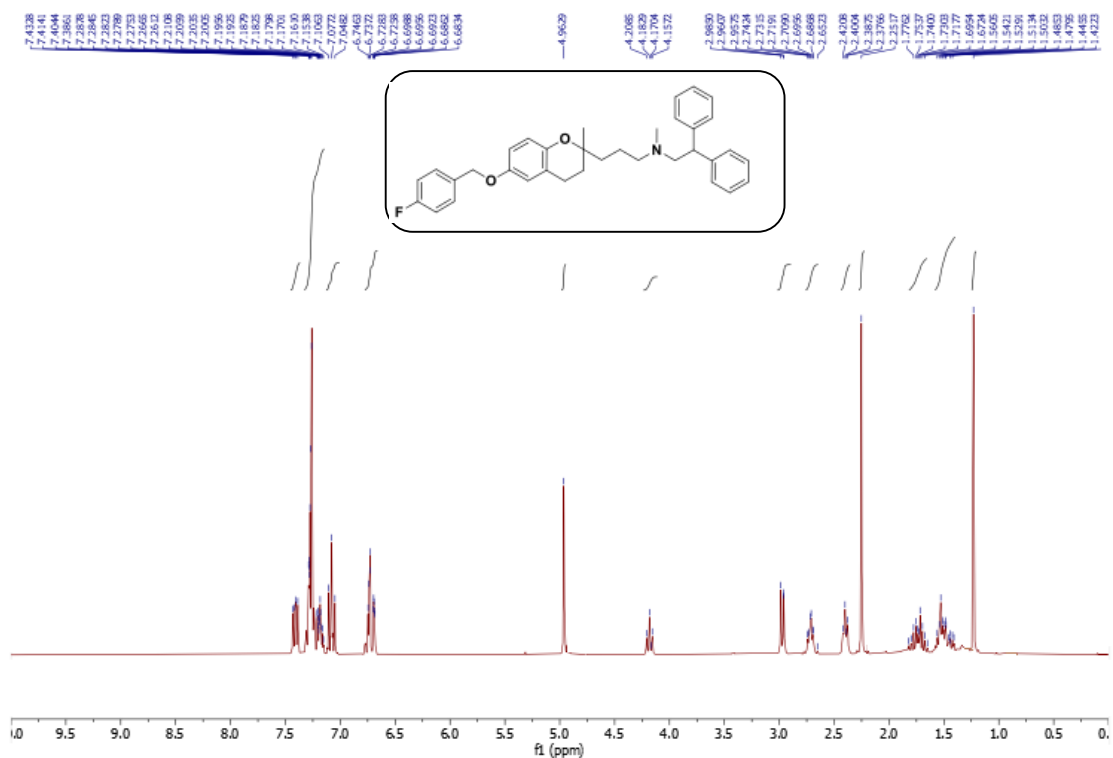
^{13}C NMR (75 MHz, CDCl_3 + 1 drop CD_3OD) of 2-(2-(6,7-Dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl)ethyl)-2-methyldihydrobenzopyran-6-ol (**7a**).



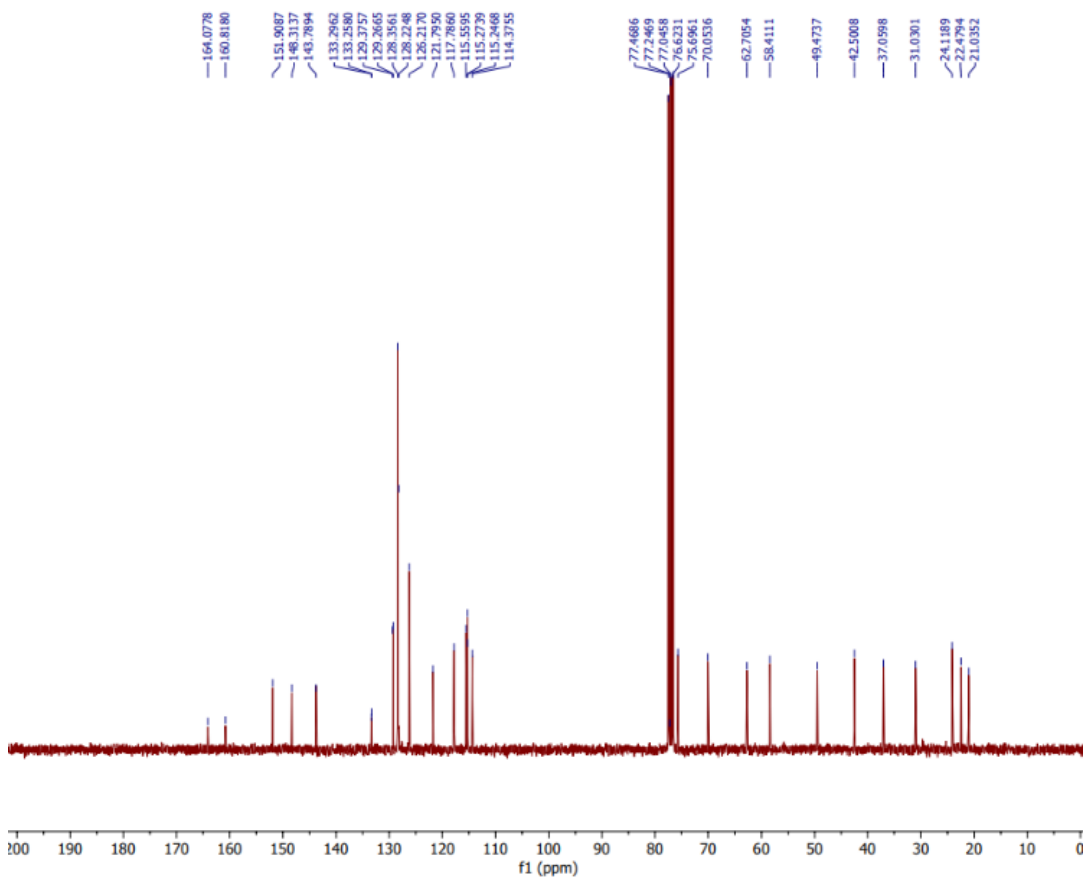
¹H NMR (300 MHz, CDCl₃) of 3-(6-(*p*-Fluorobenzoyloxy)-2-methyl-dihydrobenzopyran-2-yl)-*N*-(*p*-methoxyphenethyl)-*N*-methyl-propanamine (**5b**).



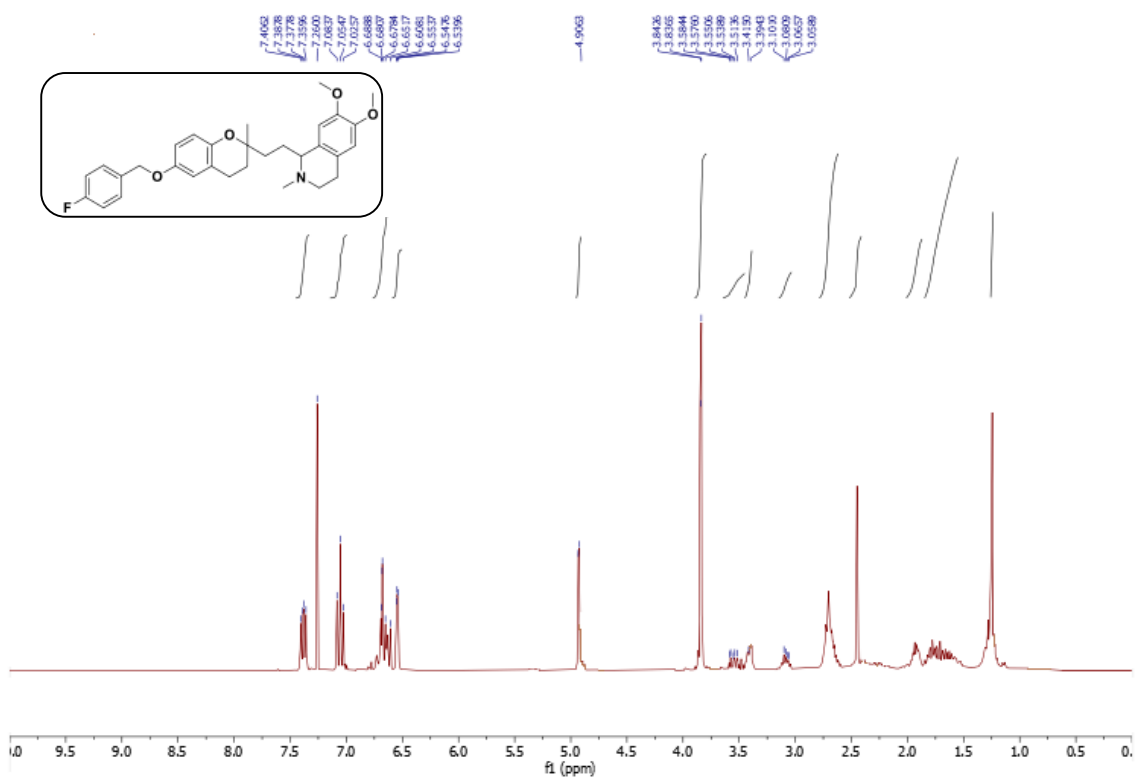
¹³C NMR (75 MHz, CDCl₃) of 3-(6-(*p*-Fluorobenzoyloxy)-2-methyl-dihydrobenzopyran-2-yl)-*N*-(*p*-methoxyphenethyl)-*N*-methyl-propanamine (**5b**).



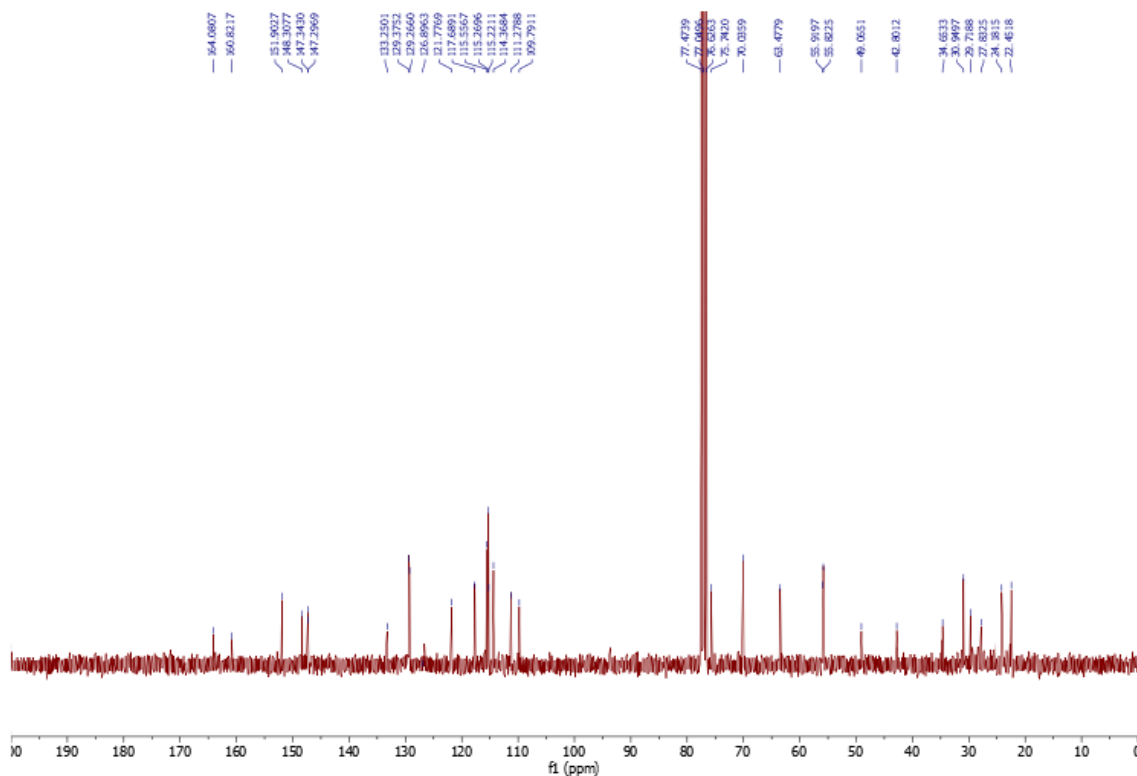
¹H NMR (300 MHz, CDCl₃) of *N*-(2,2-Diphenylethyl)-3-(6-((*p*-fluorobenzyl)oxy)-2-methyl-dihydrobenzopyran-2-yl)-*N*-methylpropan-1-amine (**6b**).



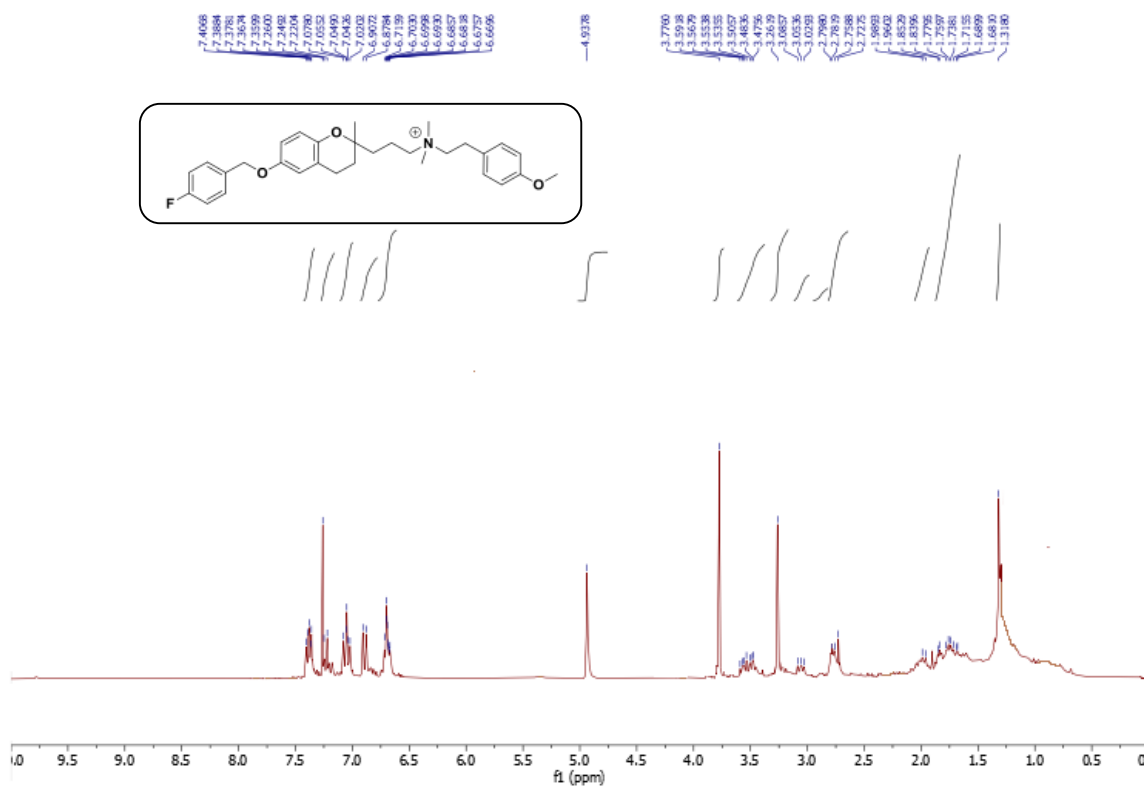
¹³C NMR (75 MHz, CDCl₃) of *N*-(2,2-Diphenylethyl)-3-(6-((*p*-fluorobenzyl)oxy)-2-methyl-dihydrobenzopyran-2-yl)-*N*-methylpropan-1-amine (**6b**).



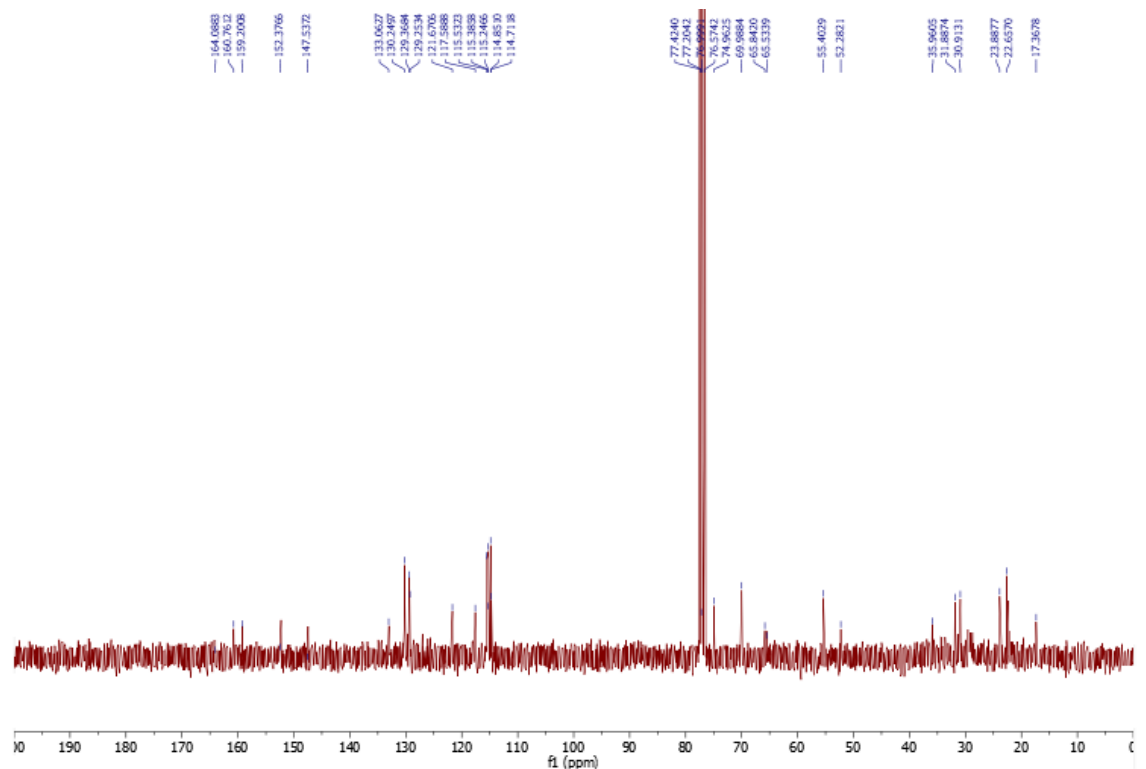
¹H NMR (300 MHz, CDCl₃) of 1-(2-(6-(*p*-Fluorobenzyl)oxy)-2-methyldihydrobenzopyran-2-yl)ethyl-6,7-dimethoxy-2-methyl-1,2,3,4-THIQ (**7b**).



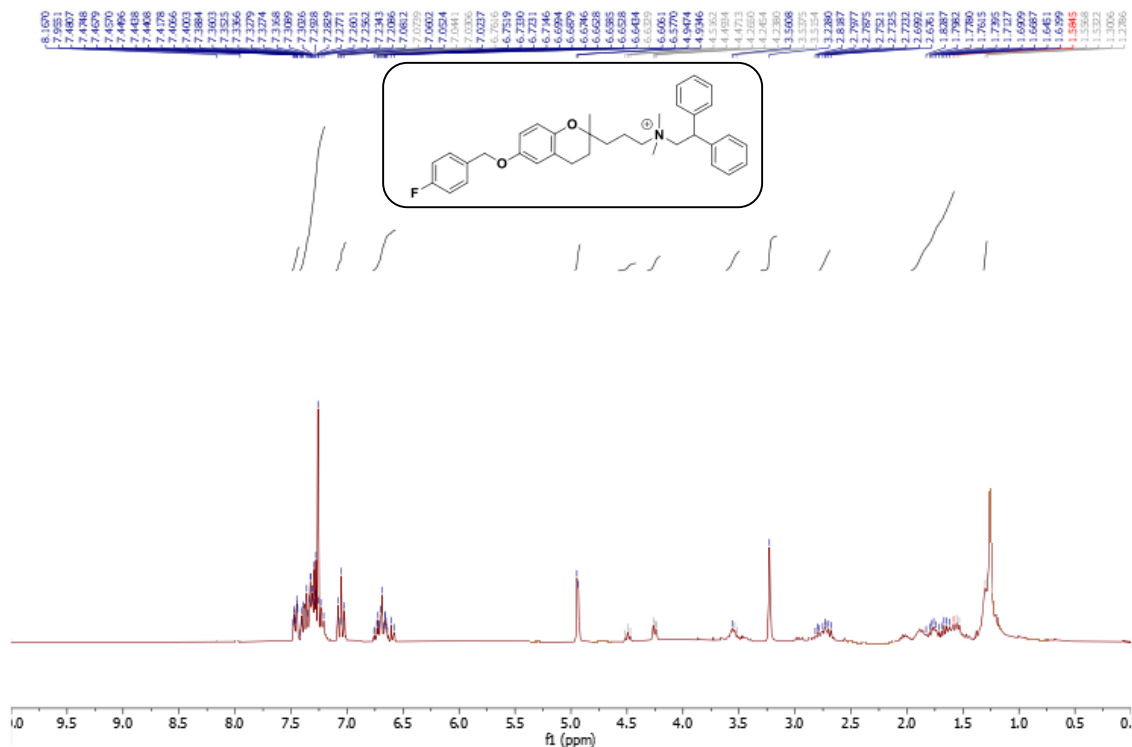
¹³C NMR (75 MHz, CDCl₃) of 1-(2-(6-(*p*-Fluorobenzyl)oxy)-2-methyldihydrobenzopyran-2-yl)ethyl-6,7-dimethoxy-2-methyl-1,2,3,4-THIQ (**7b**).



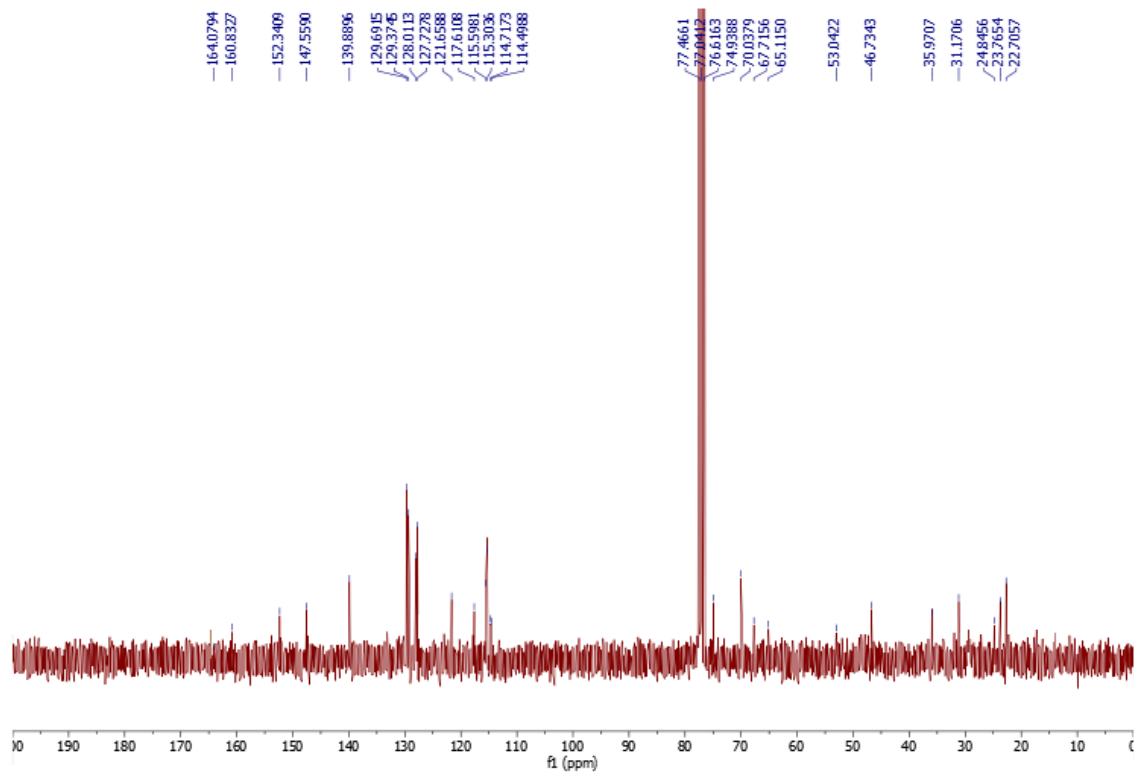
¹H NMR (300 MHz, CDCl₃) of 3-(6-(*p*-Fluorobenzoyloxy)-2-methyldihydrobenzopyran-2-yl)-*N*-(*p*-methoxyphenethyl)-*N,N*-dimethylpropan-1-aminium (**5c**).



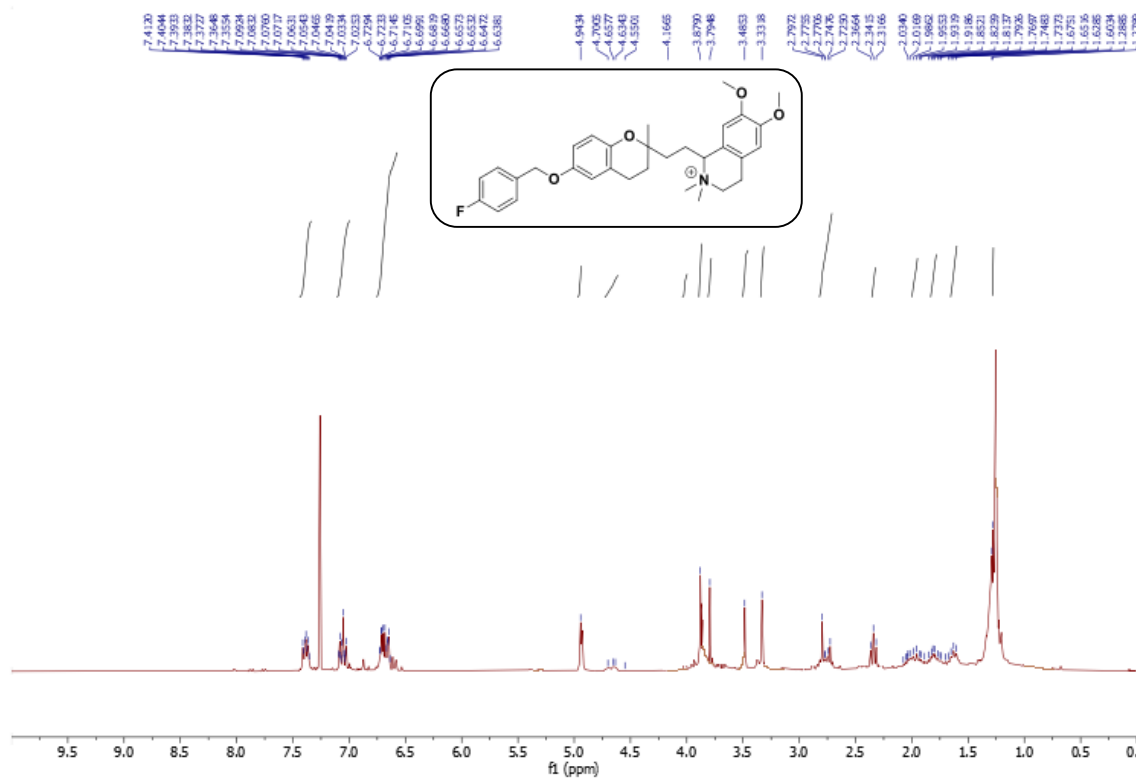
¹³C NMR (75 MHz, CDCl₃) of 3-(6-(*p*-Fluorobenzoyloxy)-2-methyldihydrobenzopyran-2-yl)-*N*-(*p*-methoxyphenethyl)-*N,N*-dimethylpropan-1-aminium (**5c**).



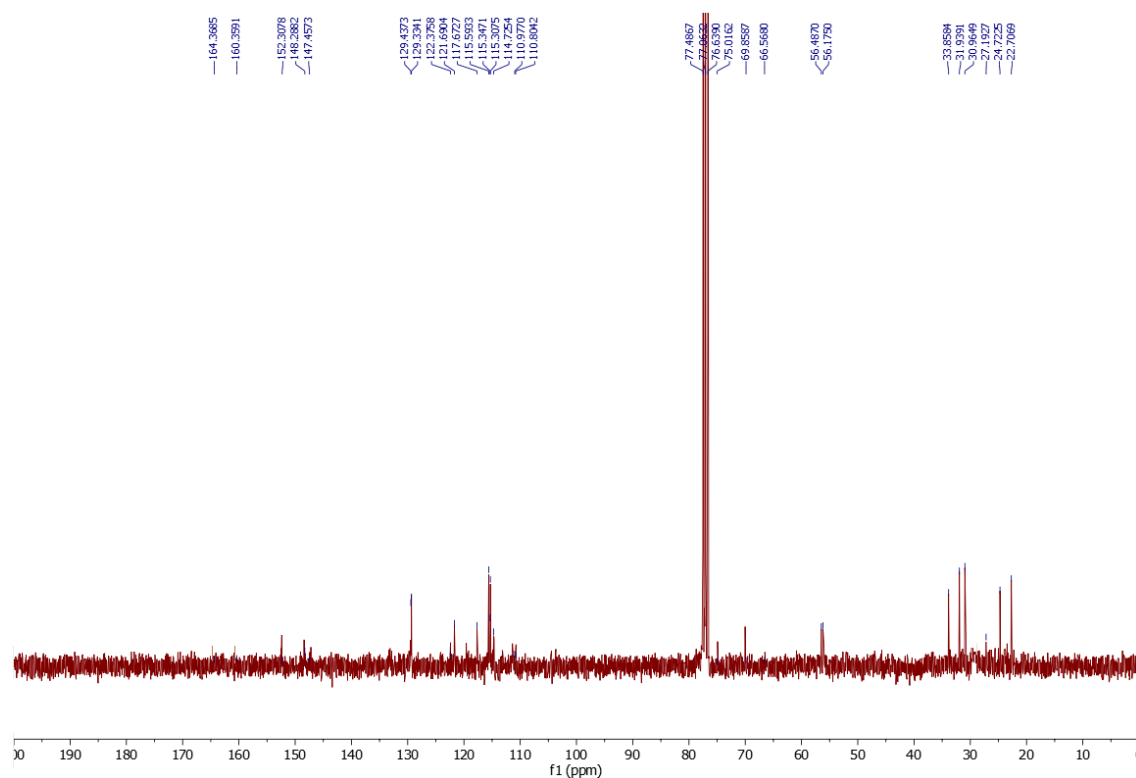
¹H NMR (300 MHz, CDCl₃) of *N*-(2,2-Diphenylethyl)-3-(6-((*p*-fluorobenzyl)oxy)-2-methyldihydrobenzopyran-2-yl)-*N,N*-dimethylpropan-1-aminium (**6c**).



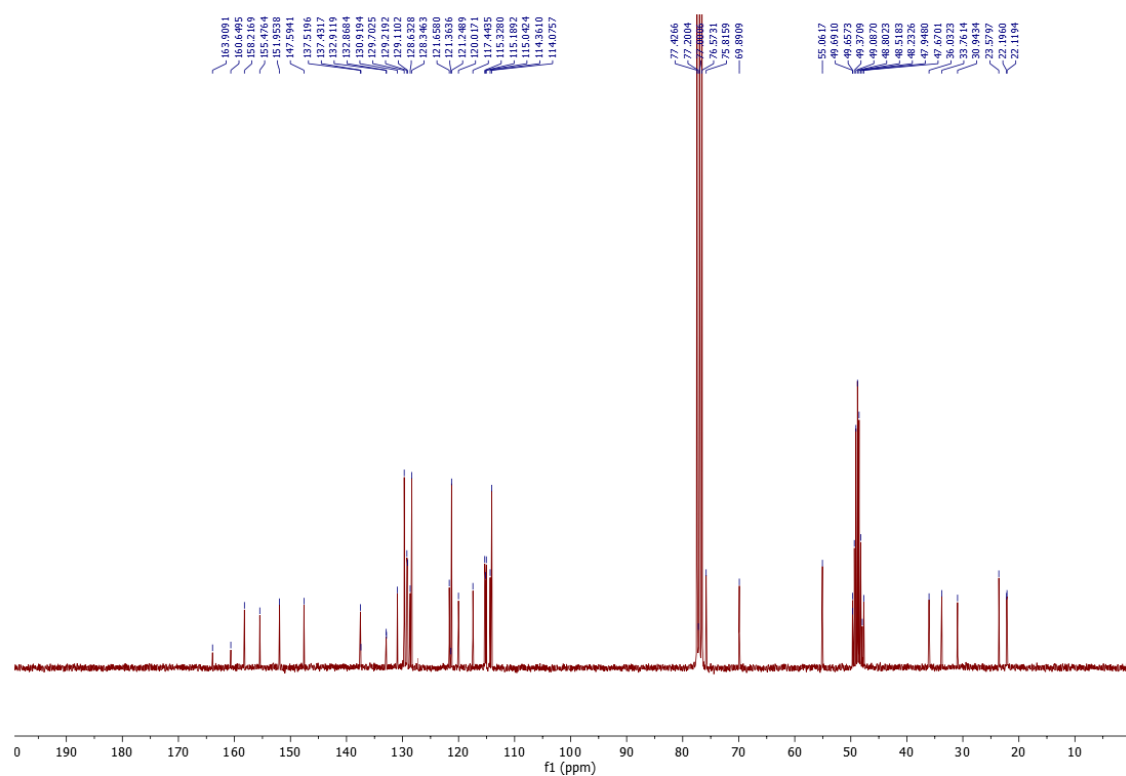
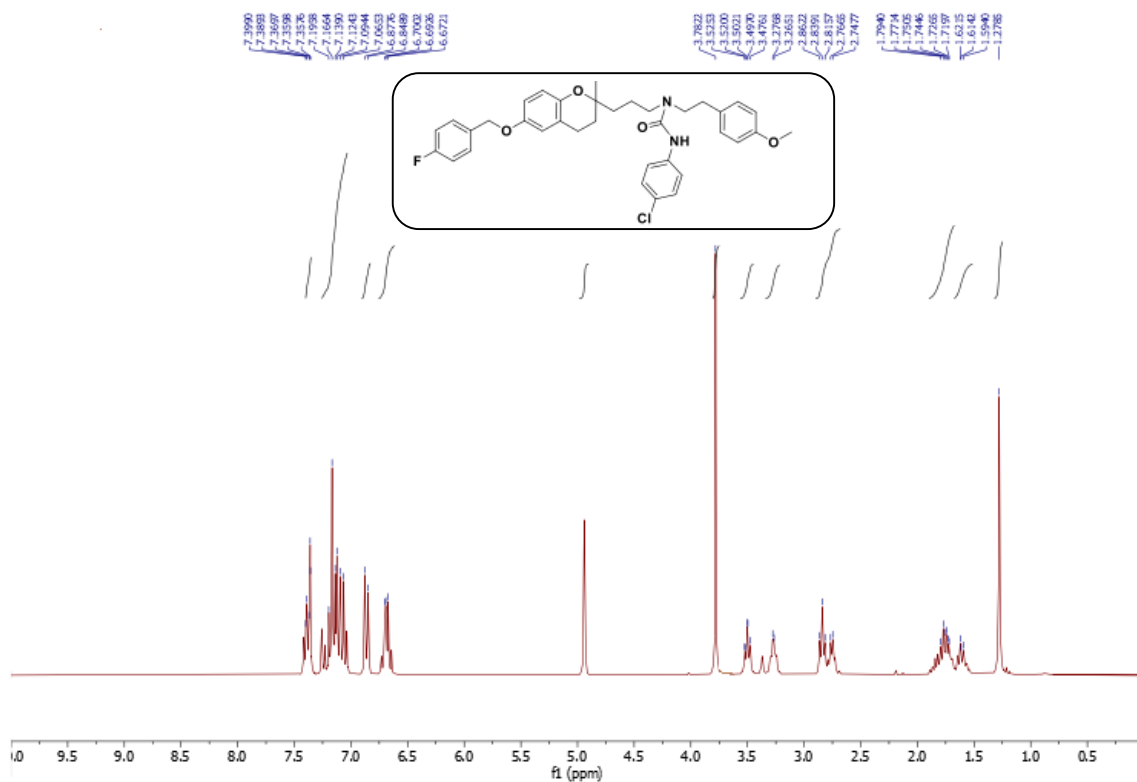
¹³C NMR (75 MHz, CDCl₃) of *N*-(2,2-Diphenylethyl)-3-(6-((*p*-fluorobenzyl)oxy)-2-methyldihydrobenzopyran-2-yl)-*N,N*-dimethylpropan-1-aminium (**6c**).

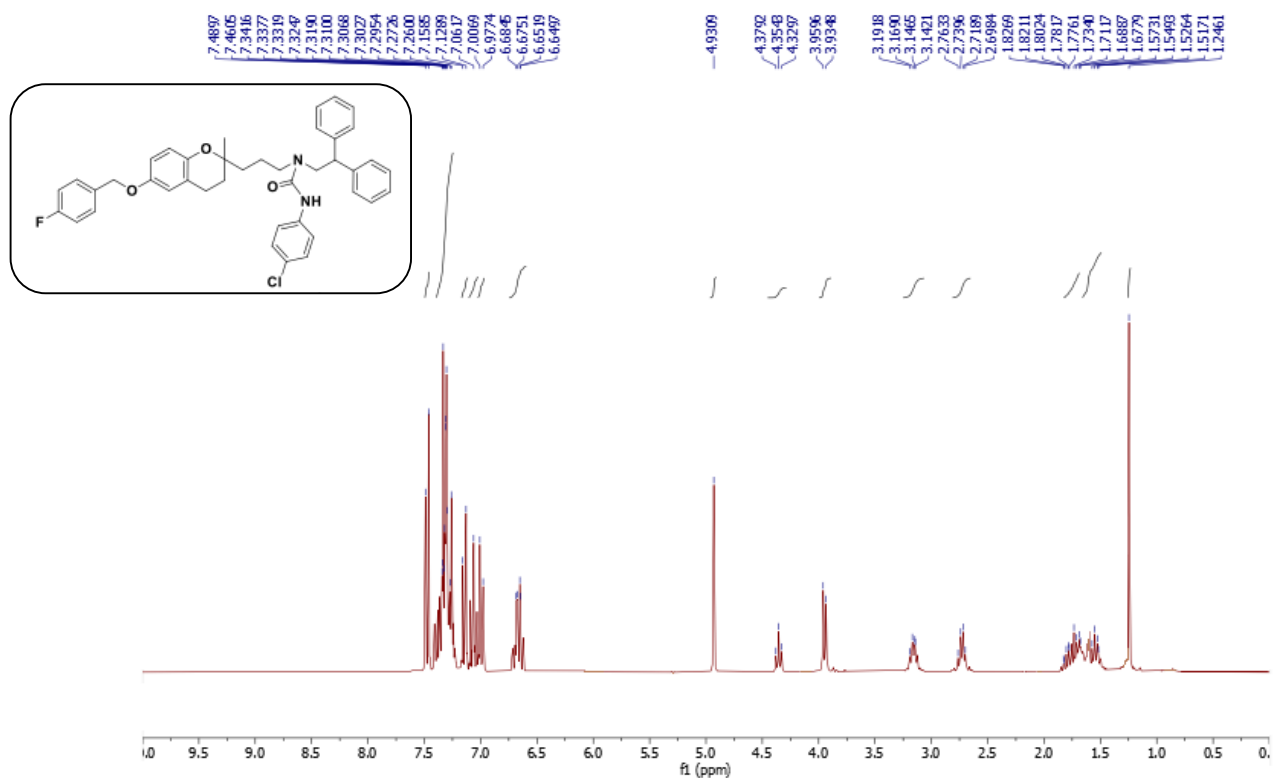


¹H NMR (300 MHz, CDCl₃) of 1-(2-(6-((*p*-Fluorobenzyl)oxy)-2-methyldihydrobenzopyran-2-yl)ethyl)-6,7-dimethoxy-2,2-dimethyl-1,2,3,4-tetrahydroisoquinolin-2-ium (7c).

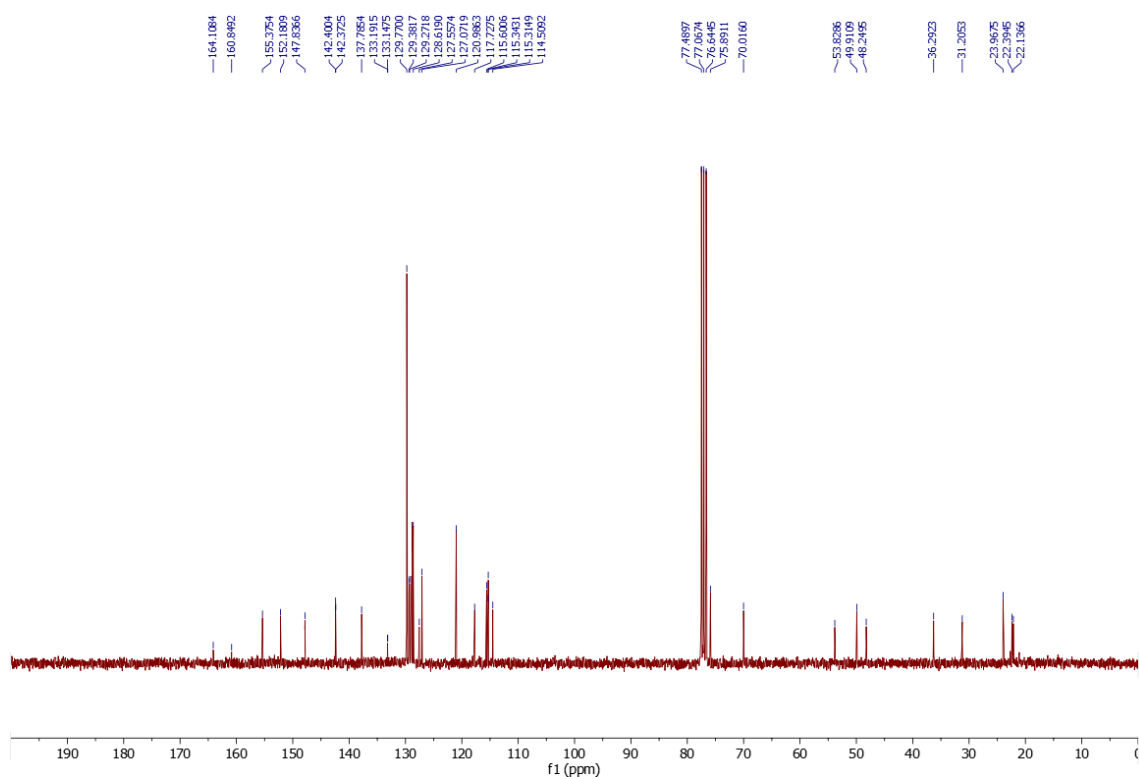


¹³C NMR (75 MHz, CDCl₃) of 1-(2-(6-((*p*-Fluorobenzyl)oxy)-2-methyldihydrobenzopyran-2-yl)ethyl)-6,7-dimethoxy-2,2-dimethyl-1,2,3,4-tetrahydroisoquinolin-2-ium (7c).

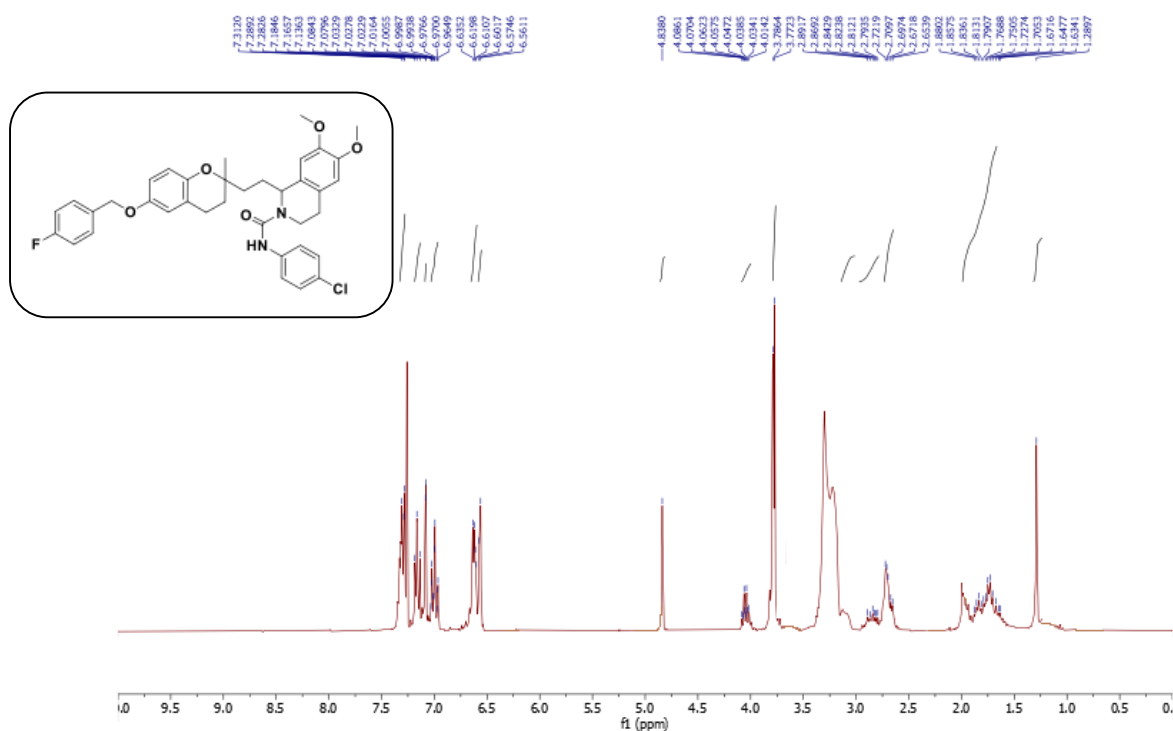




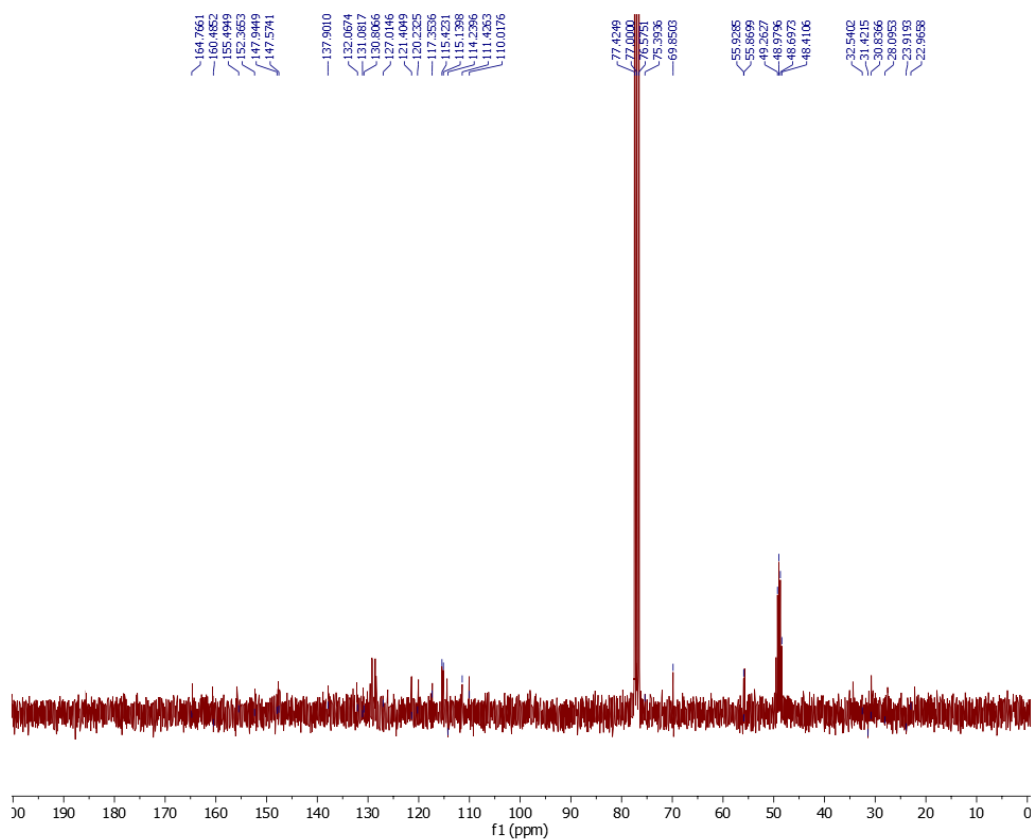
¹H NMR (300 MHz, CDCl₃) of 3-(*p*-Chlorophenyl)-*N*-(2,2-diphenylethyl)-*N*-(3-(6-((*p*-fluorobenzyl)oxy)-2-methyl-dihydrobenzopyran-2-yl)propyl)urea (**6d**).



¹³C NMR (75 MHz, CDCl₃) 3-(*p*-Chlorophenyl)-*N*-(2,2-diphenylethyl)-*N*-(3-(6-((*p*-fluorobenzyl)oxy)-2-methyl-dihydrobenzopyran-2-yl)propyl)urea (**6d**).



¹H NMR (300 MHz, CDCl₃ +1 drop CD₃OD) of *N*-(*p*-Chlorophenyl)-1-(2-(6-(*p*-fluorobenzyl)oxy)-2-methyldihydrobenzopyran-2-yl)ethyl)-6,7-dimethoxy-3,4-dihydroisoquinoline-2(*1H*)-carboxamide (**7d**).



¹³C NMR (75 MHz, CDCl₃ +1 drop CD₃OD) of *N*-(*p*-Chlorophenyl)-1-(2-(6-(*p*-fluorobenzyl)oxy)-2-methyldihydrobenzopyran-2-yl)ethyl)-6,7-dimethoxy-3,4-dihydroisoquinoline-2(*1H*)-carboxamide (**7d**).