Supplementary Data

Rational design, synthesis and pharmacological evaluation of a cohort of beta-adrenergic receptors ligands enables assessment of structure-activity relationships

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Table of contents

Table S1. Chemgauss4 scores from FRED docking of the selected ligand poses in the inactive and active states of the β-ARs. The stereoisomer used is indicated in parenthesis and scores are color-coded from lowest (green) to highest (red) score. Docked poses that did not exhibit a proper orientation for the ethanolamine moiety for H-bonding interactions with $D^{3.32}$ or $N^{7.39}$ are indicated with an asterisk (*). Poses that displayed a reversed orientation of the ligand within the orthosteric site are marked with ($^{\#}$), whereas *n.d.* indicates failure to find any conformation.

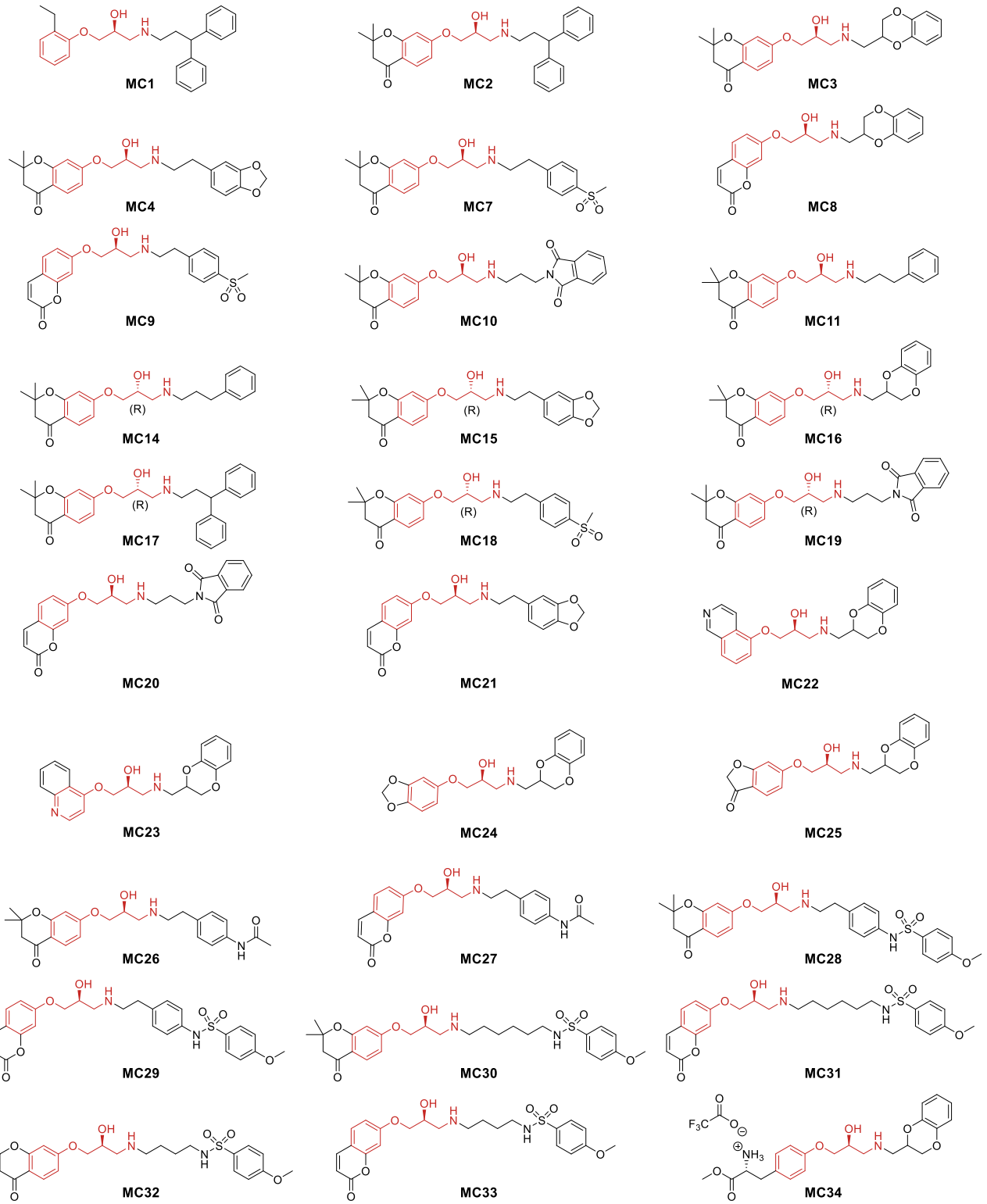
Compounds	Inactive state			Active state		
	β1	β2	β3	β1	β2	β3
SR59230A	–14.8	–14.4*	–14.4*	–14.7	–12.9	–12.3
MC1 (*S*)	–14.6	–14.8	–15.5	–14.9	–12.5	–11.1
MC2 (*S*)	–11.2	–14.3	–15.7	–11.0	*n.d.*	–2.3*
MC3 (*S*,*R*)	–13.2	–14.9	–14.3	–10.9	–6.9*	–9.3$^{\#}$
MC3 (*S*,*S*)	–15.3	–17.2	–17.4	–13.8	–9.9	–9.7$^{\#}$
MC4 (*S*)	–15.1	–16.8	–16.1	–14.2	–11.0$^{\#}$	–7.5
MC7 (*S*)	–13.1	–15.4	–15.0	–14.1	–8.6$^{\#}$	–7.3*
MC8 (*S*,*R*)	–14.3	–14.6	–14.6	–11.1	–12.1	–11.9$^{\#}$
MC8 (*S*,*S*)	–14.9	–16.1	–16.7	–14.9	–12.3	–11.2
MC9 (*S*)	–13.7	–14.8	–14.3	–15.5	–7.6	–9.8*
MC10 (*S*)	–14.5	–14.1	–17.2	–10.8	–10.7$^{\#}$	–12.2$^{\#}$
MC11 (*S*)	–14.5	–16.4	–16.6	–11.6	–8.9	–9.4
MC14 (*R*)	–12.5	–15.9	–14.3	–12.1	–8.1	–9.38*
MC15 (*R*)	–10.1*	–14.1*	–15.0*	–8.9*	–11.4$^{\#}$	–11.9$^{\#}$
MC16 (*R*,*R*)	–11.4	–12.6	–13.6*	–9.9	–8.1$^{\#}$	–11.2$^{\#}$
MC16 (*R*,*S*)	–12.2	–15.2	–15.4	–11.6	–8.4*	–8.7$^{\#}$
MC17 (*R*)	–9.4	–16.2	–14.9	–6.3*	–5.2	–6.1*
MC18 (*R*)	–9.9*	–13.5*	–13.1	–9.2*	–5.3*	–9.0*
MC19 (*R*)	–12.3	–14.5	–14.1*	–10.2	–11.8$^{\#}$	–14.4$^{\#}$
MC20 (*S*)	–14.7	–14.9	–16.8	–12.8	–12.1$^{\#}$	–12.1$^{\#}$
MC21 (*S*)	–15.5	–15.7	–15.1	–16.0	–10.0$^{\#}$	–8.5$^{\#}$
MC22 (*S*,*R*)	–16.9	–16.6	–15.2	–17.0	–11.8	–12.8
MC22 (*S*,*S*)	–17.5	–16.5	–17.0	–17.1	–13.2	–11.7
MC23 (*S*,*R*)	–15.4	–15.8	–15.7	–16.9	–13.3	–13.4
MC23 (*S*,*S*)	–17.7	–17.9	–18.7	–18.2	–13.5	–14.5
MC24 (*S*,*R*)	–14.5	–15.1	–14.6	–15.5	–13.1	–12.6
MC24 (*S*,*S*)	–15.1	–14.9	–15.4	–16.1	–12.4	–13.3
MC25 (*S*,*R*)	–14.8	–15.5	–14.2	–14.3	–10.2*	–11.9
MC25 (*S*,*S*)	–16.4	–15.5	–15.8	–16.3	–12.8	–12.6
MC26 (*S*)	–13.3	–14.2	–13.0	–13.9	–6.9	–8.5*
MC27 (*S*)	–14.9	–15.3	–14.3*	–14.7	–7.8	–8.3
MC28 (*S*)	–0.9*	–9.1*	–8.3*	–3.9	1.5$^{\#}$	–3.5*

Compounds	Inactive state			Active state		
	β1	β2	β3	β1	β2	β3
MC29 (*S*)	–5.2	–9.6*	–9.6*	–6.7	–1.6[#]	–3.8*
MC30 (*S*)	–9.7	–12.8	–10.2	–3.4*	*n.d.*	–4.1[#]
MC31 (*S*)	–10.7	–14.5	–12.3	–8.3	–2.2[#]	–5.1*
MC32 (*S*)	–10.3*	–14.1*	–13.7*	–12.0[#]	–0.1*	–7.4*
MC33 (*S*)	–11.9*	–14.0*	–14.5*	–8.6	2.0*	–5.3[#]
MC34 (*S*,*S*,*R*)	–8.3	–12.6	–11.6	–4.0	–6.2*	–9.0[#]
MC34 (*S*,*S*,*S*)	–14.6	–15.0	–14.2	–7.6	–8.6[#]	–10.5[#]

Table S2. Experimental details on the synthesis of epoxides **1**-**8**. Reaction conditions: K_2CO_3, DMF, 50°C. *: compound **4** was used directly in the next step without any further purification.

Entry	Phenol	Yield	Epoxide
a	**1p**	83%	**1**
b	**2p**	94%	**2**
c	**3p**	51%	**3**
d	**4p**	-*	**4**
e	**5p**	8%	**5**
f	**6p**	57%	**6**
g	**7p**	74%	**7**
h	**8p**	70%	**8**

Figure S1: Structures of compounds **MC1–34** presented in this work. The (*S*)-aryloxy-propanolamine scaffold of propranolol is colored red, whereas (*R*) indicates compounds with the inverse stereochemistry.



Scheme S1. Reaction conditions: *a)* **9b**, K_2CO_3, dry DMF, 50°C, 48 h, 85%; *b)* see **Table S2**

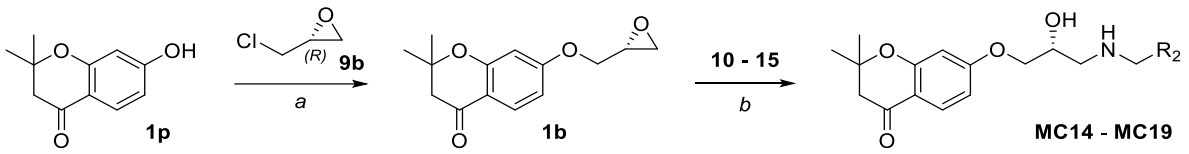


Table S3. Experimental details on the synthesis of compounds **MC14**-**17** with the (*R*) configuration. Reaction conditions: dry 2-propanol, 40–96 h, r.t.

Entry	Epoxide	Amine	Yield	MC
a	**1b**	**10**	85%	**17**
b	**1b**	**11**	58%	**16**
c	**1b**	**12**	92%	**15**
d	**1b**	**13**	75%	**18**
e	**1b**	**14**	20%	**19**
f	**1b**	**15**	73%	**14**

Figure S2: Structure of known β-AR ligands: Fenoterol, L748,337, ICI 118,551, CGP 20712A.

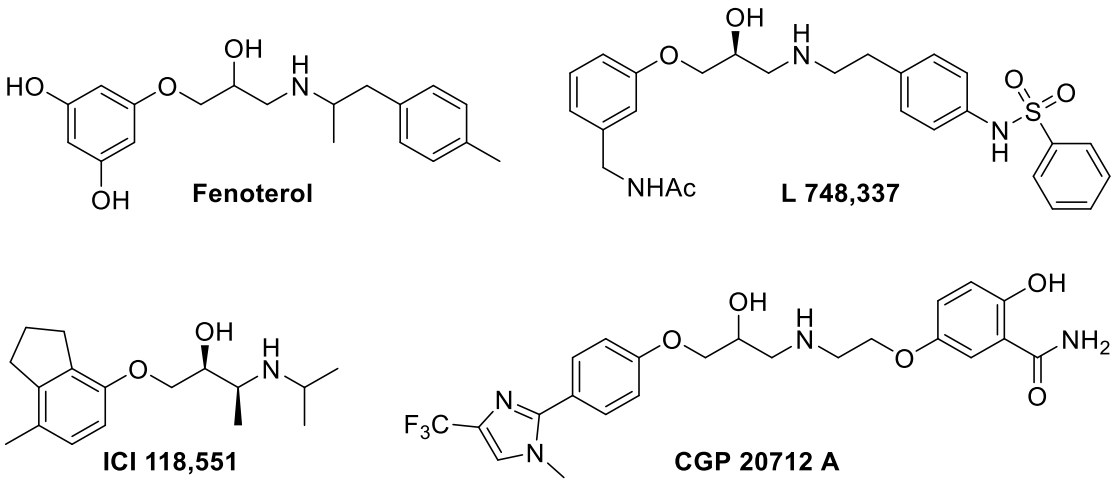


Table S1. Dihedral angle values of the central HO–CH–CH_2–O aryloxy-propanolamine moiety. Docked poses that did not exhibit a proper orientation of the ethanolamine moiety for H-bonding interactions with $D^{3.32}$ or $N^{7.39}$ are indicated with an asterisk (*).

Compound	β1	β2	β3
SR59230A	177	177*	77*
MC1 (S)	163	163	177
MC2 (S)	177	177	157
MC3 (SR)	63	63	63
MC3 (SS)	63	63	63
MC4 (S)	63	63	63
MC7 (S)	63	83	63
MC8 (SR)	63	63	63
MC8 (SS)	63	63	63
MC9 (S)	63	63	63
MC10 (S)	63	83	177
MC11 (S)	63	63	63
MC14 (R)	80	80	160
MC15 (R)	60*	60*	80*
MC16 (RR)	180	80	60*
MC16 (RS)	180	160	160
MC17 (R)	60	60	80
MC18 (R)	60*	60*	*80*
MC19 (R)	80	80	80*
MC20 (S)	63	83	83
MC21 (S)	63	63	63
MC22 (SR)	83	177	163
MC22 (SS)	83	157	177
MC23 (SR)	177	177	177
MC23 (SS)	163	157	157
MC24 (SR)	177	177	177
MC24 (SS)	163	163	163
MC25 (SR)	63	177	83
MC25 (SS)	83	163	163
MC26 (S)	63	83	83
MC27 (S)	43	77	83*
MC28 (S)	177*	177*	177*
MC29 (S)	83	177*	177*
MC30 (S)	177	177	177
MC31 (S)	177	177	177
MC32 (S)	57*	163*	163*
MC33 (S)	163*	177*	163*
MC34 (SSR)	63	63	63
MC34 (SSS)	63	63	63

Figure S3. Superimposed bound poses of the enantiomeric ligands **MC2/MC17** and **MC11/MC14** when docked in the inactive state of β2-AR.

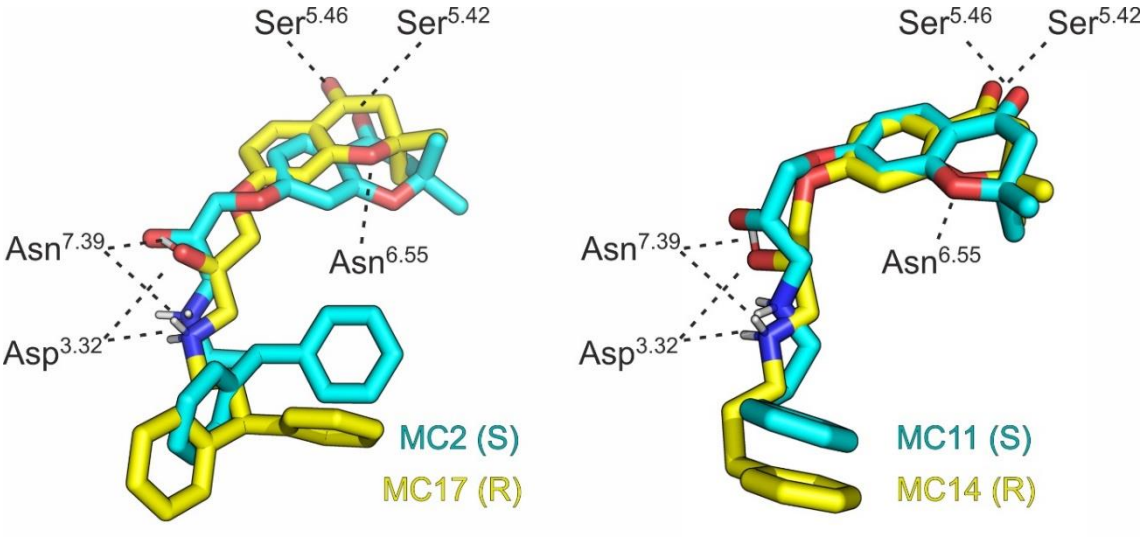


Figure S4. Superimposed poses of **MC3** (*S,S*) in the three β-ARs illustrating the position of critical residues that facilitate the variable orientation of 1,4-benzodioxane moiety.

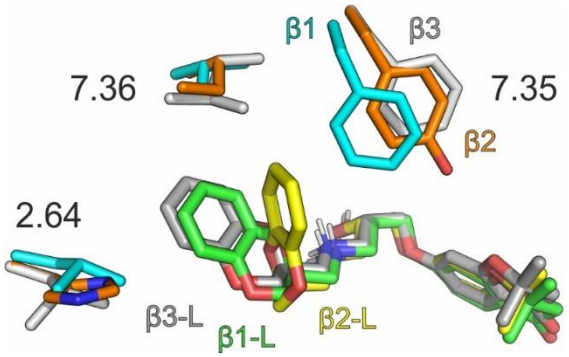


Figure S5. Bound pose of **MC3** (*S,S*) superimposed with **MC22** (*S,S*) in complex with the inactive and active states of β1-AR, illustrating the hydrogen bonding interactions of the chromanone group of **MC3** with S5.46 and between the isoquinoline ring of **MC22** and S5.42.

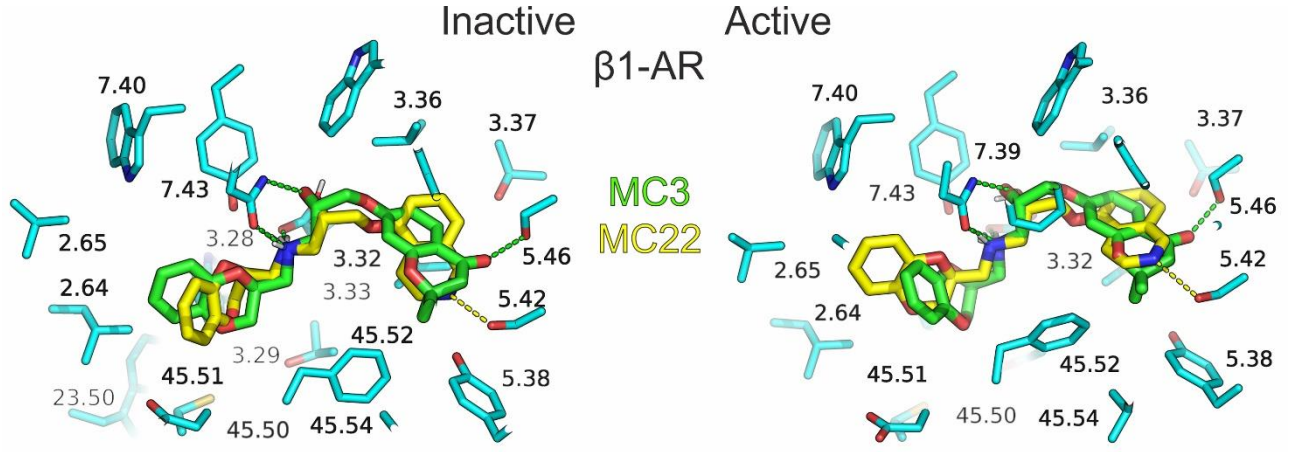


Figure S6. Bound pose of **MC24** (*S,S*) in the inactive state of β1- and β2-AR, illustrating the different network of hydrogen-bonding interactions of the dioxole moiety with critical TM5 residues.

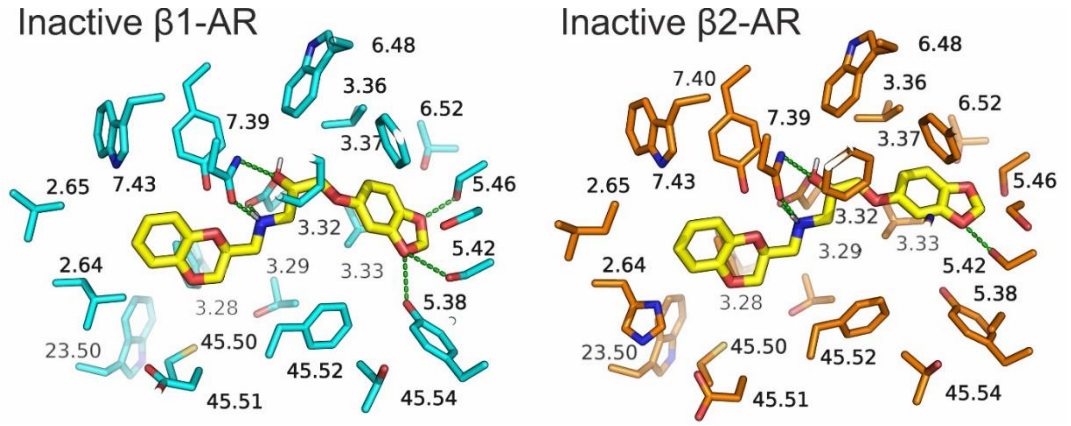


Figure S7. Surface representation of the ligand-binding site of β2-AR (A) and β3-AR (B) in the inactive state, illustrating the different shape of the cavity that affects the bound conformation of **MC11**.

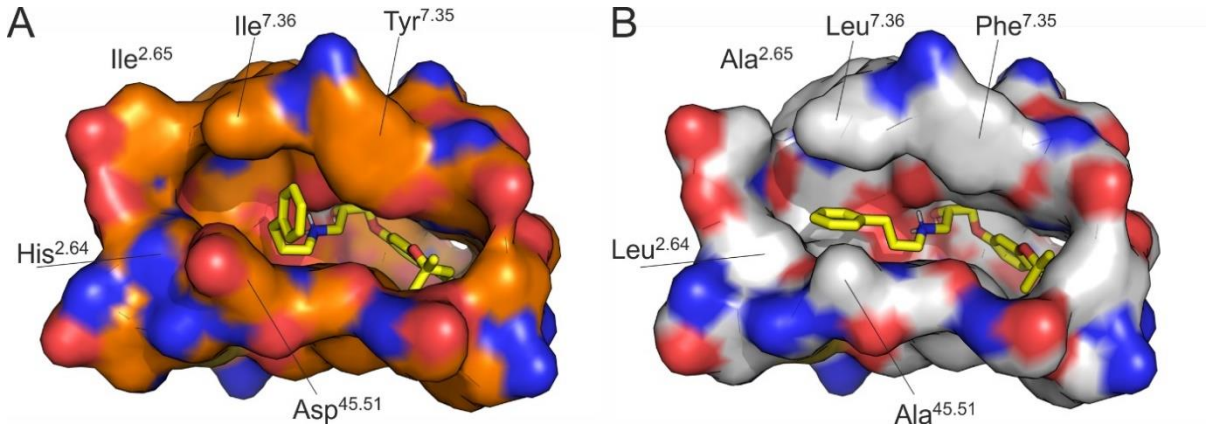
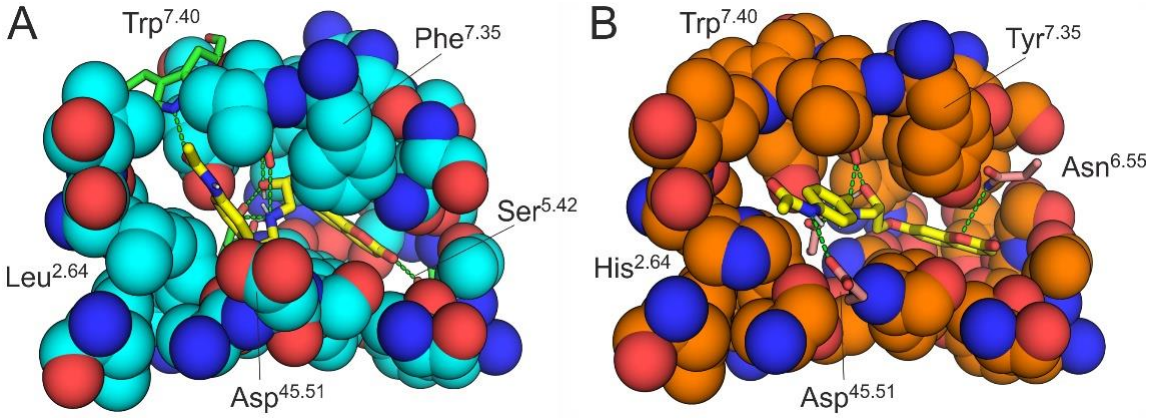
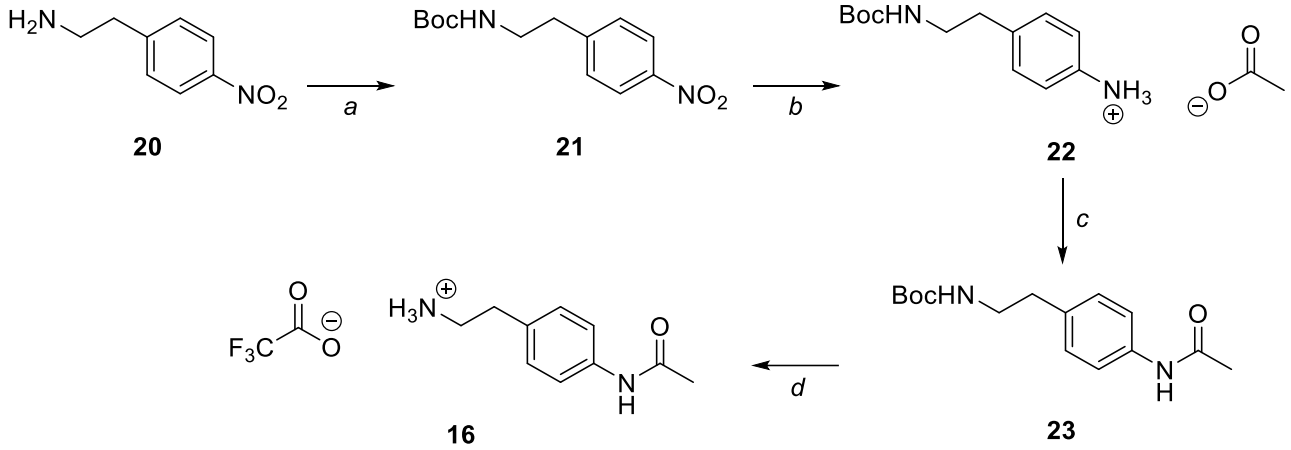


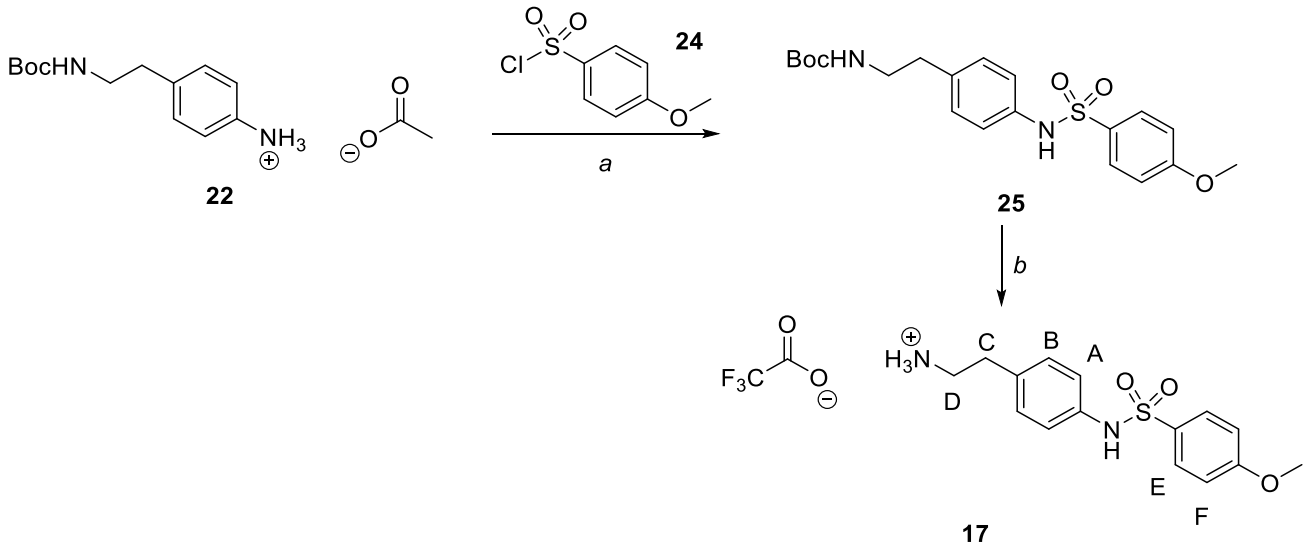
Figure S8. Bound pose of **MC27** in complex with β1-AR (A) and β2-AR in the inactive state, illustrating the difference in hydrogen-bonding interactions with key residues.



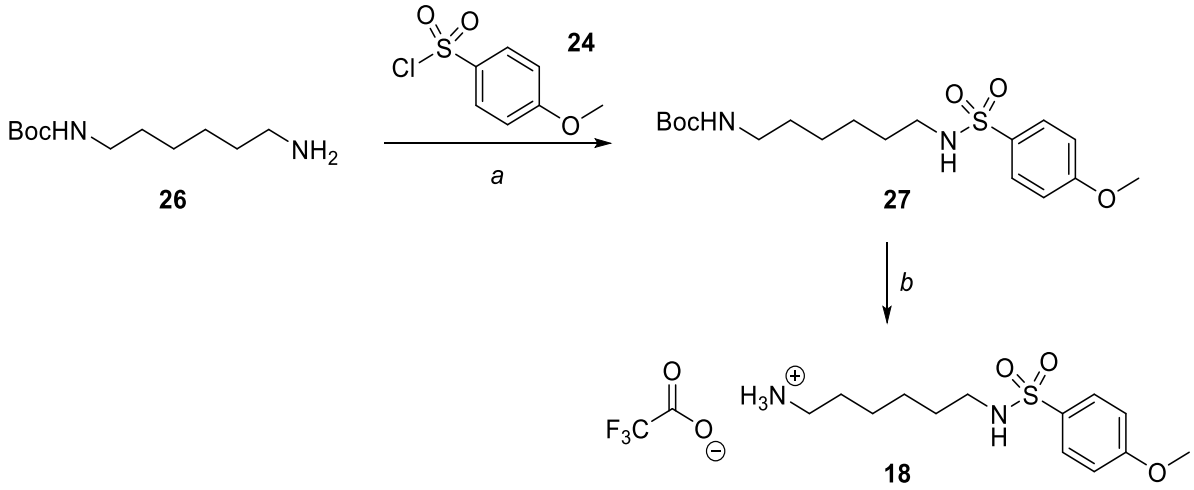
Scheme S2. Reaction conditions: *a)* Boc_2O, DCM, r.t., 2 h, 87%; *b)* Fe, acetic acid, water, ethanol, 40°C, 2 h, 91%; *c)* triethylamine, pyridine, Ac_2O, DCM, r.t., 1 h, quantitative yield; *d)* TFA, DCM, r.t., 2 h, quantitative yield.



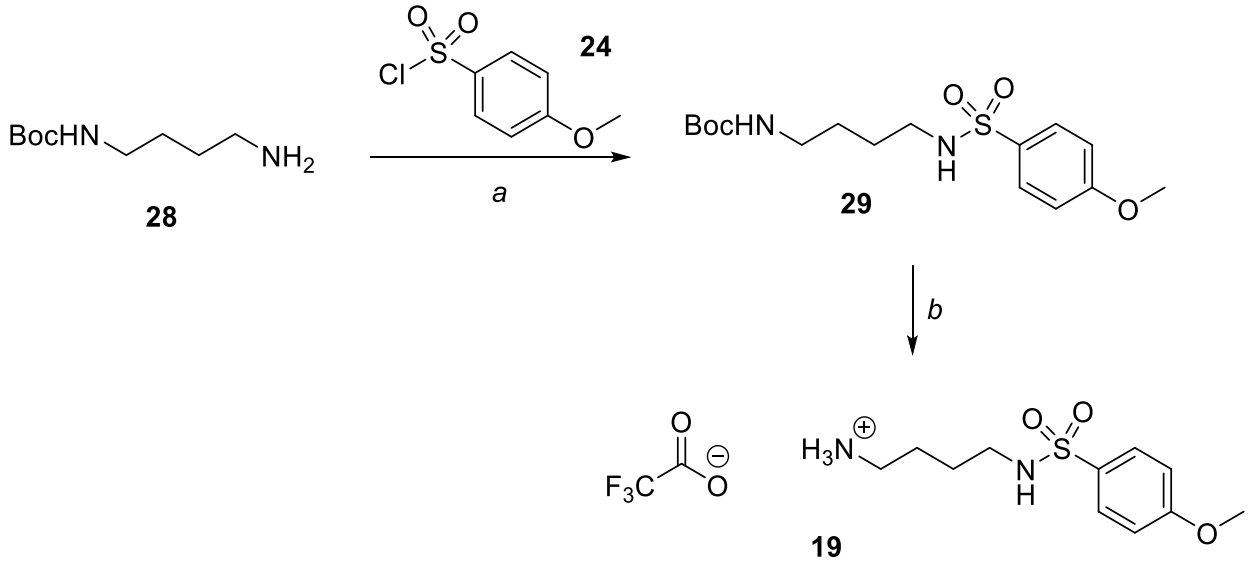
Scheme S3. Reaction conditions: *a)* **24**, triethylamine, DCM, r.t., 95 h, 88%; *b)* TFA, DCM, r.t., 2.5 h, quantitative yield.



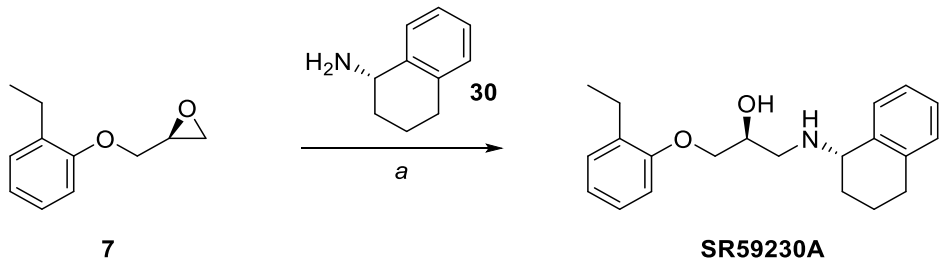
Scheme S4. Reaction conditions: *a)* **24**, triethylamine, DCM, r.t., 24 h, 85%; *b)* TFA, DCM, r.t., quantitative yield.



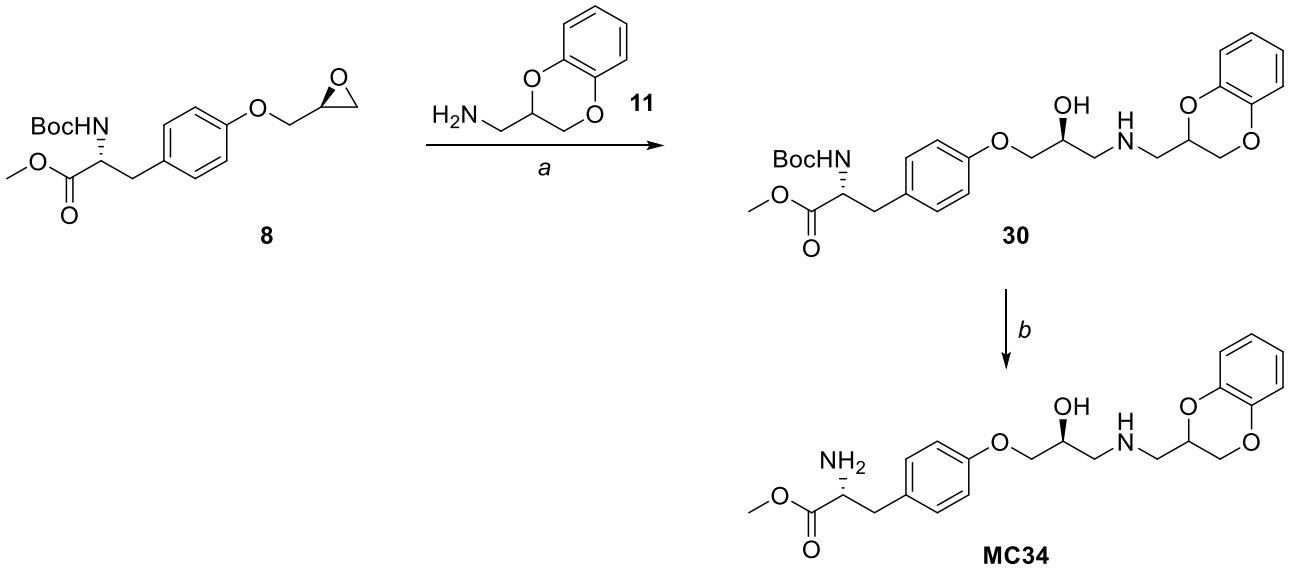
Scheme S5. Reaction conditions: *a)* **24**, triethylamine, DCM, r.t., 23 h, 81%; *b)* TFA, DCM, r.t., 2 h, quantitative yield.



Scheme S6. Reaction conditions: *a)* **30**, dry 2-propanol, r.t., 85 h, 69%



Scheme S7. reaction conditions: *a)* **11**, 2-propanol:DMSO 5:1, r.t., 68 h, 26%; *b)* TFA, DCM, r.t., 4 h, quantitative yield.



Synthesis of 1. To a stirred solution of 7-hydroxy-2,2-dimethylchroman-4-one (**1p**) (353 mg, 1.83 mmol) in dry *N*,*N*-dimethylformamide (6 mL), anhydrous K_2CO_3 was added. After 10 min, **9** (508 mg, 5.50 mmol) was added. The reaction mixture was stirred at 50° C for 23 h, then it was filtered on Celite 521 and purified by flash chromatography on silica gel (dichloromethane:acetone 50:1, Rf = 0.3) to give **1** (380 mg, 83%) as a white solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.85 (d, J_{B-C} = 8.8 Hz, 1H, H_B), 6.61 (dd, J_{C-B} = 8.8 Hz, J_{C-A} = 2.4 Hz, 1H, H_C), 6.44 (d, J_{A-C} = 2.4 Hz, 1H, H_A), 4.34-4.30 (A part of an ABX system, J_{A-B} = 11.1 Hz, J_{A-X} = 3.0 Hz, 1H, H-1), 4.02-3.98 (B part of an ABX system, J_{B-A} = 11.1 Hz, J_{B-X} = 5.8 Hz, 1H, H-1), 3.53-3.31 (m, 1H, H-2), 3.03-2.99 (m, 1H, H-3), 2.83-2.79 (B part of an ABX system, J_{B-A} = 4.8 Hz, J_{B-X} = 2.6 Hz, 1H, H-3), 2.72 (s, 2H, H_X), 1.50 (s, 6H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 191.00, 164.97, 161.90, 128.39, 114.59, 109.47, 102.05, 79.66, 68.97, 49.78, 48.63, 44.61, 26.72, 26.57. ESI-MS *m/z*: $[M+Na]^+$ calcd. for $C_{14}H_{16}NaO_4$ 271.09, found 271.14. $[\alpha]_D^{20}$ = + 20.1 (c = 0.9, $CHCl_3$).

Synthesis of 2. To a stirred solution of 7-hydroxy-2H-chromen-2-one (**2p**) (1.007 g, 6.21 mmol) in dry *N*,*N*-dimethylformamide (20 mL), anhydrous K_2CO_3 (1.716 g, 12.42 mmol) was added. After 30 min, **9** (2.43 mL, 31.05 mmol) was added. The reaction mixture was stirred at 50°C for 24 h, then it was filtered on Celite 521 and purified by flash chromatography on silica gel (dichloromethane:acetone 30:1, Rf = 0.4) to give **2** (1.28 g, 94%) as a white solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.65 (d, J_{D-E} = 9.5 Hz, 1H, H_D), 7.39 (d, J_{C-A} = 8.5 Hz, 1H, H_C), 6.91 (d, J_{B-A} = 2.4 Hz, 1H, H_B), 6.85 (dd, *J* = 6.1 Hz, *J* = 2.4 Hz, 1H, H_A), 6.28 (d, J_{E-D} = 9.5 Hz, 1H, H_E), 4.37-4.35 (A part of an ABX system, J_{A-B} = 11.0 Hz, J_{A-X} = 2.8 Hz, 1H, H-1), 3.99-3.95 (B part of an ABX system, J_{B-A} = 11.0 Hz, J_{B-X} = 6.0 Hz, 1H, H-1), 3.44-3.37 (m, 1H, H-2), 2.98-2.93 (m, 1H, H-3), 4.00-3.96 (B part of an ABX system, J_{B-A} = 11.0 Hz, J_{B-X} = 6.0 Hz, 1H, H-3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 161.52, 161.01, 155.68, 143.33, 128.87, 113.34, 112.89, 112.81, 101.61, 69.24, 49.75, 44.47. ESI-MS *m/z*: $[M+Na]^+$ calcd. for $C_{12}H_{10}NaO_4$ 241.05, found 241.09. $[\alpha]_D^{20}$ = + 8.2 (c = 0.9, $CHCl_3$).

Synthesis of 3. To a stirred solution of sesamol (**3p**) (250 mg, 1.80 mmol) in dry *N*,*N*-dimethylformamide (4 mL), anhydrous K_2CO_3 (497 mg, 3.6 mmol) was added. After 10 min,

9 (502 mg, 5.42 mmol) was added. The reaction mixture was stirred at 50° C for 50 h, then it was filtered on Celite 521 and purified by flash chromatography on silica gel (ethyl acetate:petroleum ether 1:4, Rf = 0.2) to give **3** (178 mg, 51%) as a yellow solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.69 (d, J_{A-B} = 8.5 Hz, 1H, H_A), 6.52 (d, J_{C-B} = 2.5 Hz, 1H, H_C), 6.33 (dd, J_{B-A} = 8.5 Hz, J_{B-C} = 2.5 Hz, 1H, H_B), 5.91 (s, 2H, H_D), 4.17-4.13 (A part of an ABX system, J_{A-B} = 11.0 Hz, J_{A-X} = 3.1 Hz, 1H, H-1), 3.89-3.85 (B part of an ABX system, J_{B-A} = 11.0 Hz, J_{B-X} = 5.7 Hz, 1H, H-1), 3.34-3.30 (m, 1H, H-2), 2.93-2.84 (m, 1H, H-3), 2.75-2.71 (B part of an ABX system, J_{B-A} = 4.9 Hz, J_{B-X} = 2.7 Hz, 1H, H-3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 153.95, 148.25, 142.01, 107.89, 105.82, 101.20, 98.33, 69.75, 50.15, 44.68. ESI-MS *m/z*: $[M+Na]^+$ calcd. for $C_{10}H_{10}NaO_4$ 217.05, found 217.12. $[\alpha]_D^{20}$ = + 16.0 (c = 1, $CHCl_3$).

Synthesis of 4. To a stirred solution of 5-hydroxy-2,3-dihydro-1H-inden-1-one (**4p**) (200 mg, 1.33 mmol) in dry *N*,*N*-dimethylformamide (4.5 mL), anhydrous K_2CO_3 (367 mg, 2.66 mmol) was added. After 10 min, **9** (369 mg, 3.99 mmol) was added. The reaction mixture was stirred at 50° C for 22 h, then it was filtered on Celite 521. Compound **4** is used in the nucleophilic epoxide opening reaction without further purification. $[\alpha]_D^{20}$ = + 27.7 (c = 0.9, $CHCl_3$).

Synthesis of 5. To a stirred solution of 5-hydroxyquinoline (**5p**) (317 mg, 2.18 mmol) in dry *N*,*N*-dimethylformamide (6 mL), anhydrous K_2CO_3 was added. After 10 min, **9** (605 mg, 6.54 mmol) was added. The reaction mixture was stirred at 50° C for 50 h, then it was filtered on Celite 521 and purified by flash chromatography on silica gel (ethyl acetate:petroleum ehter 3:2 → 4:1, Rf = 0.3) to give **5** (35 mg, 8%) as an orange solid. ^{1}H-NMR (400 MHz, $CDCl_3$ +5% CD_3OD) δ: 9.09 (s, 1H, H_D), 8.40 (d, J_{F-E} = 5.9 Hz, 1H, H_F), 8.02 (d, J_{E-F} = 5.9 Hz, 1H, H_E), 7.53-7.44 (m, 2H, H_C and H_B), 8.02 (d, *J* = 5.9 Hz, 1H, H_A), 4.43-4.39 (part A of ABX system, J_{A-B} = 11.1 Hz, J_{A-X} = 2.8 Hz, 1H, H-1), 4.08-4.04 (part B of ABX system, J_{B-A} = 11.1 Hz, J_{B-X} = 5.8 Hz, 1H, H-1), 3.47-3.43 (m, 1H, H-2), 2.95-2.93 (m, 1H, H-3), 2.83-2.79 (part B of ABX system, J_{B-A} = 4.8 Hz, J_{B-X} = 2.7 Hz, 1H, H-3). ^{13}C-NMR (50 MHz, $CDCl_3$ +5% CD_3OD) δ: 153.12, 151.35, 141.82, 129.37, 128.51, 127.55, 119.96, 115.43, 109.13, 69.11, 50.07, 44.55. ESI-MS *m/z*: $[M+Na]^+$ calcd. for $C_{12}H_{11}NNaO_2$ 224.07, found 224.15. $[\alpha]_D^{20}$ = + 14.7 (c = 1, $CHCl_3$).

Synthesis of 6. To a stirred solution of 4-hydroxyquinoline (**6p**) (317 mg, 2.18 mmol) in dry *N*,*N*-dimethylformamide (6 mL), anhydrous K_2CO_3 was added. After 10 min, **9** (605 mg, 6.54 mmol) was added. The reaction mixture was stirred at 50° C for 50 h, then it was filtered on Celite 521 and purified by flash chromatography on silica gel (ethyl acetate:methanol 20:1 → 10:1, Rf = 0.35) to give **6** (250 mg, 57%) as a white solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.45 (dd, *J* = 8.1, 1.5 Hz, 1H, H_B), 7.67 (ddd, *J* = 8.6 Hz, *J* = 7.1 Hz, *J* = 1.6 Hz, 1H, H_D), 7.52-7.48 (m, 2H, H_C and H_F), 7.40-7.36 (m, 1H, H_A), 6.26 (d, *J* = 7.8 Hz, 1H, H_E), 4.50-4.46 (A part of an ABX system, J_{A-B} = 15.8 Hz, J_{A-X} = 2.3 Hz, 1H, H-1), 4.16-4.12 (B part of an ABX system, J_{B-A} = 15.8 Hz, J_{B-X} = 5.4 Hz, 1H, H-1), 3.36-3.32 (m, 1H, H-2), 2.89-2.87 (m, 1H, H-3), 2.55-2.51 (B part of an ABX system, J_{B-A} = 4.5 Hz, J_{B-X} = 2.5 Hz, 1H). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 178.14, 143.39, 140.20, 132.32, 127.22, 127.07, 123.83, 115.14, 110.45, 53.64, 49.78, 45.17. ESI-MS *m/z*: $[M+Na]^+$ calcd. for $C_{12}H_{11}NNaO_2$ 224.07, found 224.13. $[\alpha]_D^{20}$ = + 35.2 (c = 1.2, $CHCl_3$).

Synthesis of 7. To a stirred solution of 2-ethylphenol (**7p**) (500 mg, 4.09 mmol) in dry *N*,*N*-dimethylformamide (1 mL), anhydrous K_2CO_3 was added. After 10 min, **9** (1.136 g, 12.28

mmol) was added. The reaction mixture was stirred at 50° C for 23 h, then it was filtered on Celite 521 and purified by flash chromatography on silica gel (ethyl acetate:petroleum ether 1:10, Rf = 0.2) to give **7** (542 mg, 74%) as a white solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.20-7.16 (m, 2H), 6.94 (at, *J* = 7.4 Hz, 1H), 6.84 (d, *J* = 8.1 Hz, 1H), 4.26 (dd, *J* = 11.0 Hz, *J* = 3.0 Hz, 1H), 3.99 (dd, *J* = 11.0 Hz, *J* = 5.5 Hz, 1H), 3.41-3.38 (m, 1H), 2.93 (at, *J* = 4.5 Hz, 1H), 2.81 (dd, *J* = 5.0 Hz, *J* = 2.7 Hz, 1H), 2.70 (q, *J* = 7.5 Hz, 2H), 1.24 (t, *J* = 7.7 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 156.20, 132.93, 129.14, 126.80, 121.06, 111.26, 68.52, 53.52, 50.40, 44.66, 23.34, 14.23. ESI-MS *m/z*: $[M+Na]^+$ calcd. for $C_{11}H_{14}NaO_2$ 201.09, found 210.13. $[\alpha]_D^{20}$ = + 7.2 (c = 0.9, $CHCl_3$).

Synthesis of 8. To a stirred solution of methyl (tert-butoxycarbonyl)tyrosine (**8p**) (300 mg, 1.01 mmol) in dry *N*,*N*-dimethylformamide (5 mL), anhydrous K_2CO_3 was added. After 10 min, **9** (239 µL, 3.07 mmol) was added. The reaction mixture was stirred at 50°C for 26h, then it was filtered on Celite 521 and purified by flash chromatography on silica gel (dichloromethane:acetone 30:1, Rf = 0.3) to give **8** (248 mg, 70%) as a white solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.02 (d, J = 8.5 Hz, 1H, H-a), 6.83 (d, J = 8.6 Hz, 1H, H-b), 4.99-4.97 (bs, 1H, H_N), 4.54-4.49 (m, 1H, H_α), 4.19-4.15 (A part of an ABX system, $J_{A\text{-}B}$ = 11.0 Hz, $J_{A\text{-}X}$ = 3.1 Hz, 1H, H-1), 3.93-3.89 (B part of an ABX system, $J_{B\text{-}A}$ = 11.0 Hz, $J_{B\text{-}X}$ = 5.7 Hz, 1H, H-1), 3.68 (s, 3H, -OCH_3), 3.34-3.30 (m, 1H, H-2), 3.06-2.94 (m, 2H, H-4), 2.88 (at, *J* = 4.5 Hz, 1H, H-3), 2.75-2.71 (B part of an ABX system, $J_{B\text{-}A}$ = 4.9 Hz, $J_{B\text{-}X}$ = 2.7 Hz, 1H, H-3), 1.40 (s, 9H, Boc). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 172.36, 157.54, 155.08, 130.30, 128.57, 115.46, 114.68, 79.88, 68.73, 54.50, 52.16, 50.11, 44.67, 37.43, 28.27. ESI-MS *m/z*: $[M+Na]^+$ calcd. for $C_{18}H_{25}NNaO_6$ 374.16, found 374.22. $[\alpha]_D^{20}$ = + 11.3 (c = 1, $CHCl_3$).

Synthesis of epoxide 1b. To a stirred solution of 7-hydroxy-2,2-dimethylchroman-4-one (**1p**) (301 mg, 1.566 mmol) in dry *N*,*N*-dimethylformamide (5 mL), anhydrous K_2CO_3 was added. After 10 min, **9b** (493 µL, 6.26 mmol) was added. The reaction mixture was stirred at 50°C for 48 h, then it was filtered on Celite 521 and purified by flash chromatography on silica gel (dichloromethane:acetone 50:1, Rf = 0.3) to give **1b** (331 mg, 85%) as a white solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.79 (d, $J_{B\text{-}C}$ = 8.8 Hz, 1H, H_B), 6.55 (dd, $J_{C\text{-}B}$ = 8.8 Hz, $J_{C\text{-}A}$ = 2.4 Hz, 1H, H_c), 6.38 (d, $J_{A\text{-}C}$ = 2.4 Hz, 1H, H_A), 4.27-4.23 (A part of an ABX system, $J_{A\text{-}B}$ = 11.1 Hz, $J_{A\text{-}X}$ = 3.0 Hz, 1H, H-1), 3.96-3.92 (B part of an ABX system, $J_{B\text{-}A}$ = 11.1 Hz, $J_{B\text{-}X}$ = 5.8 Hz, 1H, H-1), 3.37-3.33 (m, 1H, H-2), 3.37-3.33 (m, 1H, H-2), 2.94-2.90 (A part of an ABX system, $J_{A\text{-}B}$ = 4.8 Hz, $J_{A\text{-}X}$ = 4.2 Hz, 1H, H-3), 2.77-2.73 (B part of an ABX system, $J_{B\text{-}A}$ = 4.9 Hz, $J_{B\text{-}X}$ = 2.6 Hz, 1H, H-3), 2.66 (s, 2H, H_X), 1.44 (s, 6H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 191.00, 164.97, 161.90, 128.39, 109.46, 102.05, 68.96, 49.78, 48.63, 44.61, 26.71. ESI-MS *m/z*: $[M+Na]^+$ calcd. for $C_{14}H_{16}NaO_4$ 271.09, found 271.21. $[\alpha]_D^{20}$ = - 26.8 (c = 1.1, $CHCl_3$).

Synthesis of MC14. To a stirred solution of **15** (81 µL, 0.567 mmol) in 2-propanol (1 mL), **1b** (47 mg, 0.189 mmol) was added; the reaction mixture was stirred at r.t. for 40 h, then it was concentrated under vacuum. The crude was filtered on silica gel (ethyl acetate:methanol 5:1, Rf = 0.2) to give **MC14** (52 mg, 73%) as a white solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.78 (d, $J_{B\text{-}C}$ = 8.8 Hz, 1H, H_B), 7.29-7.16 (m, 5H, Ph), 6.52 (dd, $J_{C\text{-}B}$ = 8.8 Hz, $J_{C\text{-}A}$ = 2.4 Hz, 1H, H_C), 6.36 (d, $J_{A\text{-}C}$ = 2.4 Hz, 1H, H_A), 4.20-4.10 (m, 1H, H-2), 4.03-3.91 (m, 2H, H-1), 2.94-2.90 (A part of an ABX system, $J_{A\text{-}B}$ = 12.3 Hz, $J_{A\text{-}X}$ = 3.6 Hz, 1H, H-3)), 2.82 (add, J = 12.3 Hz, J = 8.6 Hz, 2H), 2.76 (q, $J_{4\text{-}5}$ = 7.0 Hz, 2H, H-4), 2.70-2.67 (m, 2H,

H-5), 2.65 (s, 2H, H_X), 1.98-1.83 (m, 2H, H-6), 1.44 (s, 6H, CH_3). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 128.54, 128.43, 128.39, 126.13, 109.52, 101.85, 70.78, 67.12, 51.25, 48.86, 48.16, 33.12, 30.54, 26.48. ESI (MS) *m/z*: for $[M-H]^-$ calcd. for $C_{23}H_{29}NO_4$ 382.21, found 382.20. $[\alpha]_D^{20}$ = - 22.8 (c = 1, $CHCl_3$).

Synthesis of MC15. To a stirred solution of **12** (68 µL, 0.493 mmol) in 2-propanol (1 mL), **1b** (48 mg, 0.197 mmol) was added; the reaction mixture was stirred at r.t. for 40 h, then it was concentrated under vacuum. The crude was filtered on silica gel (ethyl acetate:methanol 5:1, Rf = 0.3) to give **MC15** (72 mg, 92%) as a white solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.78 (d, J_{B-C} = 8.8 Hz, 1H, H_B), 6.78-6.62 (m, 3H, Ph), 6.51 (dd, J_{C-B} = 8.8 Hz, J_{C-A} = 2.3 Hz, 1H, H_C), 6.36 (d, J_{A-C} = 2.2 Hz, 1H, H_A), 5.93 (s, 2H, CH_2), 4.17-4.05 (m, 1H, H-2), 3.99 (t, J_{1-2} = 7.4 Hz, 2H), 2.98-2.89 (m, 1H, H-3), 2.85-2.76 (m, 5H, H-3 (x1), H-4 and H-5), 2.66 (s, 2H, H_X), 1.44 (s, 6H, CH_3). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 128.38, 121.66, 109.40, 109.05, 108.39, 101.84, 100.89, 70.40, 67.26, 51.10, 51.00, 48.38, 35.21, 27.28. ESI-MS *m/z*: for $[M-H]^-$ calcd. for $C_{23}H_{26}NO_6$ 412.18, found 412.11. $[\alpha]_D^{20}$ = - 13.1 (c = 0.9, $CHCl_3$).

Synthesis of MC16. To a stirred solution of **11** (93 mg, 0.563 mmol) in *2*-propanol (1 mL), **1b** (56 mg, 0.225 mmol) was added; the reaction mixture was stirred at r.t. for 80 h, then it was concentrated under vacuum. The crude was filtered on silica gel (ethyl acetate:methanol 5:1, Rf = 0.2) to give **MC16** (54 mg, 58%) as a white solid. ^{1}H-NMR (400 MHz, DMSO-d6) δ: 7.62 (d, J_{B-C} = 8.7 Hz, 1H, H_B), 6.84-6.77 (m, 4H, Ph), 6.57 (dd, J_{C-B} = 8.8 Hz, J_{C-A} = 2.3 Hz, 1H, H_c), 6.47 (d, J_{A-C} = 2.2 Hz, 1H, H_A), 5.05 (d, J = 4.9 Hz, 1H), 4.32-4.28 (A part of an ABX system, J_{A-B} = 11.4 Hz, J_{A-X} = 2.2 Hz, 1H, H-6), 4.21-4.17 (m, 1H, H-1), 4.04-4.00 (A part of an ABX system, J_{A-X} = 9.9 Hz, J_{A-B} = 4.1 Hz, 1H, H-2), 3.97-3.93 (B part of an ABX system, J_{B-X} = 11.3 Hz, J_{B-A} = 7.3 Hz, 1H, H-6), 3.91-3.86 (m, 1H, H-2), 3.86-3.83 (m, 1H, H-5), 2.83-2.75 (m, 2H, H-3), 2.68 (s, 2H, H_X), 2.67-2.65 (m, 1H, H-4), 2.62-2.57 (m, 1H, H-4), 1.35 (s, 6H, CH_3). ^{13}C-NMR (50 MHz, DMSO-d6) δ: 190.76, 165.67, 161.84, 143.55, 128.01, 121.71, 121.49, 117.49, 117.28, 114.04, 109.93, 102.17, 80.06, 73.13, 71.56, 68.37, 66.52, 49.85, 48.17, 26.58. ESI-MS *m/z*: for $[M-H]^-$ calcd. for $C_{23}H_{26}NO_6$ 412.18, found 412.31. $[\alpha]_D^{20}$ = - 23.5 (c = 1.1, $CHCl_3$).

Synthesis of MC17. To a stirred solution of **10** (104 mg, 0.493 mmol) in 2-propanol (1 mL), **1b** (49 mg, 0.197 mmol) was added; the reaction mixture was stirred at r.t. for 40 h, then it was concentrated under vacuum. The crude was filtered on silica gel (ethyl acetate, Rf = 0.3) to give **MC17** (77 mg, 85%) as a white solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.78 (d, J_{B-C} = 8.8 Hz, 1H, H_B), 7.32-7.12 (m, 10H, Ph), 6.51 (dd, J_{C-B} = 8.8 Hz, J_{C-A} = 2.1 Hz, 1H, H_C), 6.34 (d, J_{A-C} = 2.0 Hz, 1H, H_A), 4.08-3.98 (m, 2H, H-2 and H-6), 3.92 (d, J_{1-2} = 4.9 Hz, 2H, H-1), 2.87-2.83 (A part of an ABX system, J_{A-B} = 12.2 Hz, J_{A-x} = 3.3 Hz, 1H, H-3), 2.76-2.72 (B part of an ABX system, J_{B-A} = 12.8 Hz, J_{B-X} = 9.0 Hz, 1H, H-3), 2.70-2.68 (m, 2H, H-4), 2.65 (s, 2H, H_X), 2.34-2.29 (m, 2H, H-5), 1.43 (s, 6H, CH_3). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 190.97, 165.14, 161.93, 144.33, 128.60, 128.34, 127.76, 126.40, 114.52, 109.47, 102.02, 79.63, 70.49, 67.53, 51.49, 48.99, 48.66, 48.18, 35.25, 26.73. ESI (MS) *m/z*: for $[M-H]^-$ calcd. for $C_{29}H_{32}NO_4$ 458.24, found 458.21. $[\alpha]_D^{20}$ = - 35.0 (c = 1, $CHCl_3$).

Synthesis of MC18. To a stirred solution of **13** (123 mg, 0.523 mmol) in a mixture 2-propanol:MeOH 1:1 (2 mL), DIPEA (92 µL, 0.523 mmol); the reaction mixture was stirred at r.t. for 20 min. To a solution of **1b** (52 mg, 0.210 mmol) in 2-propanol (1 mL), the solution of

2-(4-(methylsulfonyl)phenyl)ethan-1-amine was added; the reaction mixture was stirred at r.t. for 72 h, then it was concentrated under vacuum. The crude was filtered on silica gel (ethyl acetate:methanol 8:1, Rf = 0.2) to give **MC18** (66 mg, 75%) as a white solid. ^{1}H-NMR (400 MHz, DMSO-d6) δ: 7.82 (d, J_{E-D} = 8.4 Hz, 2H, H_E), 7.63 (d, J_{B-C} = 8.8 Hz, 1H, H_B), 7.50 (d, J_{D-E} = 8.4 Hz, 2H, H_D), 6.57 (dd, J_{C-B} = 8.8 Hz, J_{C-A} = 2.4 Hz, 1H, H_C), 4.08-3.90 (m, 3H, H-1 and H-2), 3.16 (s, 3H, S-CH_3), 2.99-2.89 (m, 4H, H-4 and H-5), 2.88-2.84 (A part of an ABX system, J_{A-B} = 12.0 Hz, J_{A-X} = 3.2 Hz, 1H, H-3), 2.77-2.73 (B part of an ABX system, J_{B-A} = 11.8 Hz, J_{B-A} = 6.8 Hz, 1H, H-3), 2.69 (s, 2H, H_X), 1.36 (s, 6H, CH_3). ^{13}C-NMR (100 MHz, DMSO-d^6) δ: 190.77, 165.56, 161.90, 146.08, 139.35, 130.10, 128.10, 127.49, 109.95, 102.36, 80.14, 71.28, 67.17, 51.45, 49.81, 49.61, 48.30, 44.15, 26.65. ESI (MS) *m/z*: for [M-H]$^-$ calcd. for $C_{23}H_{28}NO_6S$ 447.17, found 447.12. $[\alpha]_D^{20}$ = - 19.4 (c = 0.8, $CHCl_3$).

Synthesis of MC19. To a stirred solution of **14** (76 mg, 0.314 mmol) in 2-propanol (1 mL), DIPEA (61 µL, 0.345 mmol) was added; the solution was stirred at r.t. for 30 min, then **1b** (39 mg, 0.157 mmol) was added. The reaction mixture was stirred at r.t. for 96 h, then it was concentrated under vacuum and filtered on silica gel (ethyl acetate:methanol 5:1, Rf = 0.3) to give **MC19** (14 mg, 20%) as a white solid. ^{1}H-NMR (400 MHz, CD_3OD) δ: 7.89-7.77 (m, 4H, Pht), 7.72 (d, J_{B-C} = 8.8 Hz, 1H, H_B), 6.60 (dd, J_{C-B} = 8.8 Hz, J_{C-A} = 2.4 Hz, 1H, H_C), 6.47 (d, J_{A-C} = 2.4 Hz, 1H, H_A), 4.15-4.06 (m, 1H, H-2), 4.06-3.97 (m, 2H, H-1), 3.76 (t, J_{6-5} = 6.7 Hz, 2H, H-6), 2.96-2.92 (A part of an ABX system, J_{A-B} = 12.4 Hz, J_{A-X} = 4.0 Hz, 1H, H-3), 2.86-2.82 (B part of an ABX system, J_{B-A} = 10.6 Hz, J_{B-X} = 6.5 Hz, 1H, H-3), 2.82-2.79 (m, 2H, H-4), 2.68 (s, 2H, H_X), 2.01-1.88 (m, 2H, H-5), 1.42 (s, 6H, CH_3). ^{13}C-NMR (100 MHz, DMSO-d6) δ: 190.75, 168.41, 168.46, 165.68, 161.90, 134.83, 132.20, 129.78, 128.05, 123.46, 109.96, 102.33, 80.10, 71.55, 67.76, 52.06, 48.30, 46.98, 36.16, 28.15, 26.65. ESI (MS) *m/z*: for [M-H]$^-$ calcd. for $C_{25}H_{28}N_2O_6$ 451.19, found 451.08. $[\alpha]_D^{20}$ = - 06.4 (c = 1, $CHCl_3$).

Synthesis of 21. To a dispersion of 2-(4-nitrophenyl)ethan-1-amine (**20**) (1.51 g, 7.45 mmol) in dry dichloromethane (37 mL), triethylamine (1.14 mL, 8.19 mmol) was added. After 10 min, di-tert-butyl dicarbonate (1.78 g, 8.19 mmol) was added; the reaction mixture was stirring at r.t. for 2h, then it was diluted in dichloromethane (200 mL) and washed with H_2O (2 x 20 mL) and Brine (1 x 20 mL). The organic phase was anhydrificated with Na_2SO_4, filtered and concentrated under vacuum. The crude was filtered on silica gel (ethyl acetate:petroleum ether 1:5 → ethyl acetate, Rf = 0.2) to give **21** (1.96 g, 87%) as a white solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.16 (d, J_{A-B} = 8.7 Hz, 2H, H_A), 7.35 (d, J_{B-A} = 8.6 Hz, 2H, H_B), 3.43-3.38 (m, 2H, H_D), 2.93-2.90 (m, 2H, H_C), 1.42 (s, 2H, CH_3 Boc). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 146.91, 146.70, 129.66, 123.74, 41.30, 36.21, 28.33. The NMR data agree with literature.[1]

Synthesis of 22. To a stirred dispersion of **21** (1.072g, 3.54 mmol) in H_2O (6.27 mL) and ethanol (4.13 mL), acetic acid (122 µL, 2.13 mmol) and iron powder (793 mg, 14.20 mmol) were added. The reaction mixture was stirred at 40°C for 2h, then acetic acid (101 µL, 1.77 mmol) were added and the reaction mixture was filtered on Celite 545. The crude was filtered on silica gel (ethyl acetate:methanol 10:1, Rf = 0.1) to give **22** (930 mg, 91%) as a yellow solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.97 (d, J_{A-B} = 8.2 Hz, 2H, H_A), 6.63 (d, J_{B-A} = 8.4 Hz, 2H, H_B), 4.52 (bs, 1H, H_N), 3.33-3.29 (m, 2H, H_D), 2.69-2.65 (m, 2H, H_C), 1.42 (s, 9H, CH_3

Boc). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 155.88, 144.72, 129.59, 115.34, 41.96, 35.20, 28.40. The NMR data agree with the literature.[2]

Synthesis of 23. To a stirred solution of **22** (350 mg, 1.18 mmol) in dry dichloromethane (6 mL), triethylamine (164 µL, 1.18 mmol) was added; after 30 min, pyridine (142 µL, 1.77 mmol) and acetic anhydride (164 µL, 1.77 mmol) were added. The reaction mixture was stirred at r.t. for 1 h, then it was diluted with dichloromethane (150 mL) and washed with NH_4Cl (3 x 15 mL); the organic phase was anhydrificated with Na_2SO_4, filtered and concentrated under vacuum to give **23** (328 mg, quantitative yield) as a white solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.46 (d, J_{A-B} = 8.3 Hz, 2H, H_A), 7.18 (d, J_{B-A} = 8.2 Hz, 2H, H_B), 4.56 (bs, 1H, H_N), 3.39-3.37 (m, 2H, H_D), 2.81-2.78 (m, 2H, H_C), 2.21 (s, 3H, CH_3), 1.48 (s, 9H, CH_3 Boc).[3]

Synthesis of 16. To a stirred solution of **23** (330 mg, 1.18 mmol) in dichloromethane (10 mL), trifluoroacetic acid (902 µL, 11.8 mmol) was added; the reaction mixture was stirred at r.t. for 2 h, then it was concentrated under vacuum to give **16** (292 mg, quantitative yield) as a yellow oil. ^{1}H-NMR (400 MHz, CD_3OD) δ: 7.55 (d, J_{A-B} = 8.4 Hz, 2H, H_A), 7.25 (d, J_{B-A} = 8.4 Hz, 2H, H_B), 3.20-3.16 (m, 2H, H_D), 2.96-2.93 (m, 2H, H_C), 2.14 (s, 3H, CH_3). ^{13}C-NMR (100 MHz, CD_3OD) δ: 170.46, 137.49, 132.18, 128.74, 120.57, 120.46, 40.50, 32.55, 22.35. The NMR data agree with the literature.[3]

Synthesis of 25. To a stirred solution of **22** (290 mg, 0.97 mmol) in dry dichloromethane (5 mL), triethylamine (674 µL, 4.85 mmol) was added; after 10 min, 4-methoxybenzenesulfonyl chloride (**24**) (341 mg, 1.65 mmol) was added. The reaction mixture was stirred at r.t. for 95h, then it was diluted with dichloromehane (200 mL) and washed with H2O (3 x 20 mL) and Brine (1 x 20 mL). The organic phase was anhydrificated with Na_2SO_4, filtered and concentrated under vacuum; the crude was purified by flash cromatography on silica gel (dichloromethane:acetone 30:1, Rf = 0.3) to give **25** (349 mg, 88%) as a white solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.70 (d, J_{A-B} = 8.9 Hz, 2H, H_A), 7.07-6.97 (m, 4H, Ph), 6.88 (d, J_{B-A} = 8.9 Hz, 2H, H_B), 4.54 (bs, 1H, H_N), 3.82 (s, 3H, CH_3), 3.31-3.27 (m, 2H, H_D), 2.73-2.66 (m, 2H, H_C), 1.41 (s, 9H, CH_3 Boc). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 163.03, 134.94, 130.66, 129.60, 129.37, 122.00, 114.13, 55.55, 28.38. The NMR data agree with the literature.[4]

Synthesis of 17. To a stirred solution of **24** (337 mg, 0.82 mmol) in dichloromethane (6 mL), trifluoroacetic acid (634 µL, 8.2 mmol) was added. The reaction mixture was stirred at r.t. for 2h 30 min, then it was concentrated under vacuum to give **17** (344 mg, quantitative yield) as a white solid. ^{1}H-NMR (400 MHz, CD_3OD) δ: 7.88 (s, 1H, H_N), 7.70-7.66 (m, 2H, H_E), 7.14-7.12 (m, 2H, H_A), 7.09-7.06 (m, 2H, H_F), 6.97-6.95 (m, 2H, H_B), 3.81 (s, 3H, -OMe), 3.11-3.07 (m, 2H, H_D), 2.87-2.83 (m, 2H, H_C). ^{13}C-NMR (100 MHz, solv.) δ: 163.14, 136.84, 132.61, 131.13, 129.05, 128.94, 121.10, 113.72, 54.74, 40.32, 32.42. The NMR data agree with the literature.[4]

Synthesis of 27. To a stirred solution of tert-butyl (6-aminohexyl)carbamate (**26**[5]) (253 mg, 1.17 mmol) in dry dichloromethane (6 mL), triethylamine (244 µL, 1.75 mmol) and 4-methoxybenzenesulfonyl chloride (**24**) (363 mg, 1.75 mmol) were added; the reaction mixture was stirred at r.t. for 24 h, then it was diluted with dichloromethane (150 mL) and washed with H_2O (3 x 15 mL) and Brine (1 x 15 mL). The organic phase was anhydrificated with Na_2SO_4, filtered and concentrated under vacuum. The crude was purified by flash chromatography on silica gel (ethyl acetate:petroleum ether 1:2 → 1:1, Rf = 0.3) to give **27**

(385 mg, 85%) as a white solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.80 (d, J_{A-B} = 8.9 Hz, 2H, H_A), 6.98 (d, J_{B-A} = 8.9 Hz, 2H, H_B), 3.88 (s, 3H, -OCH_3), 3.09-3.02 (m, 2H, H-6), 2.93-2.89 (m, 2H, H-1), 1.64-1.62 (m, 2H, H-5), 1.44 (s, 9H, CH_3 Boc), 1.43-1.38 (m, 2H, H-2), 1.28-1.24 (m, 4H, H-3, H-4). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 162.79, 129.17, 114.19, 55.59, 42.95, 29.89, 29.43, 28.40, 26.06, 26.02.

Synthesis of 18. To a stirred solution of **27** (376 mg, 0.97 mmol) in dichloromethane (7 mL), trifluoroacetic acid (744 µL, 9.72 mmol) was added; the reaction mixture was stirred at r.t. for 2 h, then it was concentrated under vacuum to give **18** (388 mg, quantitative yield) as a yellow solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.76 (d, J_{A-B} = 8.8 Hz, 1H, H_A), 6.97 (d, J_{B-A} = 8.8 Hz, 1H, H_B), 3.86 (s, 3H, -OCH_3), 2.93-2.75 (m, 4H, H-1, H-6), 1.65-1.59 (m, 2H, H-5), 1.48-1.34 (m, 6H, H-2, H-3, H-4). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 162.79, 131.16, 128.99, 114.20, 55.53, 49.69, 49.48, 49.26, 49.05, 48.84, 42.65, 39.46, 28.75, 26.87, 25.55, 25.43. The NMR data agree with the literature.[3]

Synthesis of 29. To a stirred solution of tert-butyl (4-aminobutyl)carbamate (**28**[6]) (260 mg, 1.5 mmol) in dry dichloromethane (7.5 mL), triethylamine (320 µL, 2.3 mmol) and 4-methoxybenzenesulfonyl chloride (**24**) (468 mg, 2.3 mmol) were added. The reaction mixture was stirred at r.t. for 23 h, then it was diluted with dichloromethane (150 mL) and washed with H_2O (3 x 15 mL) and Brine (1 x 15 mL); the organic phase was anhydrificated with Na_2SO_4, filtered and concentrated under vacuum. The crude was purified by flash chromatography on silica gel (ethyl acetate:petroleum ether 1:2 → 1:1, Rf = 0.4) to give **29** (433 mg, 81%) as a white solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.80 (d, J_{A-B} = 8.9 Hz, 1H, H_A), 6.98 (d, J_{B-A} = 8.9 Hz, 1H, H_B), 3.88 (s, 3H, -OCH_3), 3.08-3.06 (m, 2H, H-4), 2.96-2.93 (m, 2H, H-1), 1.63-1.61 (m, 2H, H-2), 1.52-1.47 (m, 2H, H-3), 1.43 (s, 9H, CH_3 Boc). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 162.85, 130.86, 128.97, 114.26, 55.51, 50.20, 49.76, 49.55, 49.34, 49.12, 48.91, 42.10, 39.31, 25.90, 24.32.

Synthesis of 19. To a stirred solution of **29** (424 mg, 1.18 mmol) in dry dichloromethane (9 mL), trifluoroacetic acid (906 µL, 11.8 mmol) was added. The reaction mixture was stirred at r.t. for 2 h, then it was concentrated under vacuum to give **19** (439 mg, quantitative yield) as a white solid. ^{1}H-NMR (400 MHz, solv.) δ: 7.75 (d, J_{A-B} = 8.9 Hz, 2H, H_A), 6.96 (d, J_{B-A} = 8.8 Hz, 1H, H_B), 3.85 (s, 3H, -OCH_3), 2.94-2.85 (m, 4H, H-1, H-4), 1.78-1.68 (m, 2H, H-2), 1.63-1.50 (m, 2H, H-3). NMR data agree with the literature.[7]

Synthesis of SR59230A. To a stirred solution of **30** (806 mg, 5.47 mmol) in dry 2-propanol, **7** (542 mg, 3.04 mmol) was added; the reaction mixture was stirred at r.t. for 85 h, then it was concentrated under vacuum. The crude was filtered on silica gel (ethyl acetate:methanol 15:1, Rf = 0.3) to give **SR59230A** (650 mg, 69%) as a pink solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.44-7.39 (m, 1H), 7.18-7.13 (m, 4H), 7.10-7.06 (m, 1H), 6.90 (at, *J* = 7.4 Hz, 1H), 6.83 (d, *J* = 8.5 Hz, 1H), 4.11-4.03 (m, 2H), 4.00-3.96 (m, 1H), 3.87-3.85 (m, 1H), 3.12-3.02 (m, 1H), 2.98-2.88 (m, 1H), 2.85-2.70 (m, 2H), 2.61 (q, *J* = 7.5 Hz, 2H), 1.98-1.89 (m, 3H), 1.79-1.74 (m, 1H), 1.16 (t, J = 7.5 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 156.26, 137.44, 132.58, 129.21, 129.14, 129.05, 128.99, 128.97, 128.88, 126.98, 126.85, 125.88, 120.83, 111.07, 70.24, 68.62, 68.13, 55.82, 55.21, 49.52, 48.98, 29.35, 29.31, 28.58, 28.21, 23.38, 23.34, 18.95, 18.91, 14.20. NMR data agree with the literature.[8]

Synthesis of 30. To a stirred solution of **11** (48 µL, 0.34 mmol) in 2-propanol (1 mL) and DMSO (0.2 mL), **8** (60 mg, 0.17 mmol) was added. The reaction mixture was stirred at r.t.

for 68h, then it was concentrated under vacuum. The crude was filtered on silica gel (ethyl acetate:methanol 5:1, Rf = 0.1) to give **30** (22 mg, 26%) as a yellow solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.03 – 7.01 (m, 2H, H_A), 6.89 – 6.81 (m, 6H, H_D, H_B, H_C), 5.00 – 4.97 (m, 1H, H_{NBOC}), 4.55 – 4.50 (m, 1H, H-7), 4.35 – 4.30 (m, 1H, H-2), 4.28-4.24 (A part of an ABX system, J_{A-B} = 11.3 Hz, J_{A-X} = 2.2 Hz, 1H, H-1), 4.11 – 4.07 (m, 1H,H-5), 4.05-4.01 (B part of an ABX system, J_{B-A} = 6.8 Hz, J_{B-X} = 4.6 Hz, 1H, H-1), 3.97 – 3.96 (m, 2H, H-6), 3.70 (s, 3H, -OMe), 3.04 – 2.98 (m, 2H, H-7), 2.97 – 2.92 (m, 3H, H-3, H-4), 2.87-2.83 (B part of an ABX system, J_{B-A} = 12.2 Hz, J_{B-X} = 7.9 Hz, 1H, H4). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 172.40, 157.60, 155.09, 143.12, 142.88, 142.80, 130.33, 128.44, 121.63, 121.61, 121.49, 117.32, 117.16, 114.56, 79.92, 72.31, 70.22, 68.29, 66.25, 54.49, 52.23, 51.93, 49.78, 37.42, 28.30.

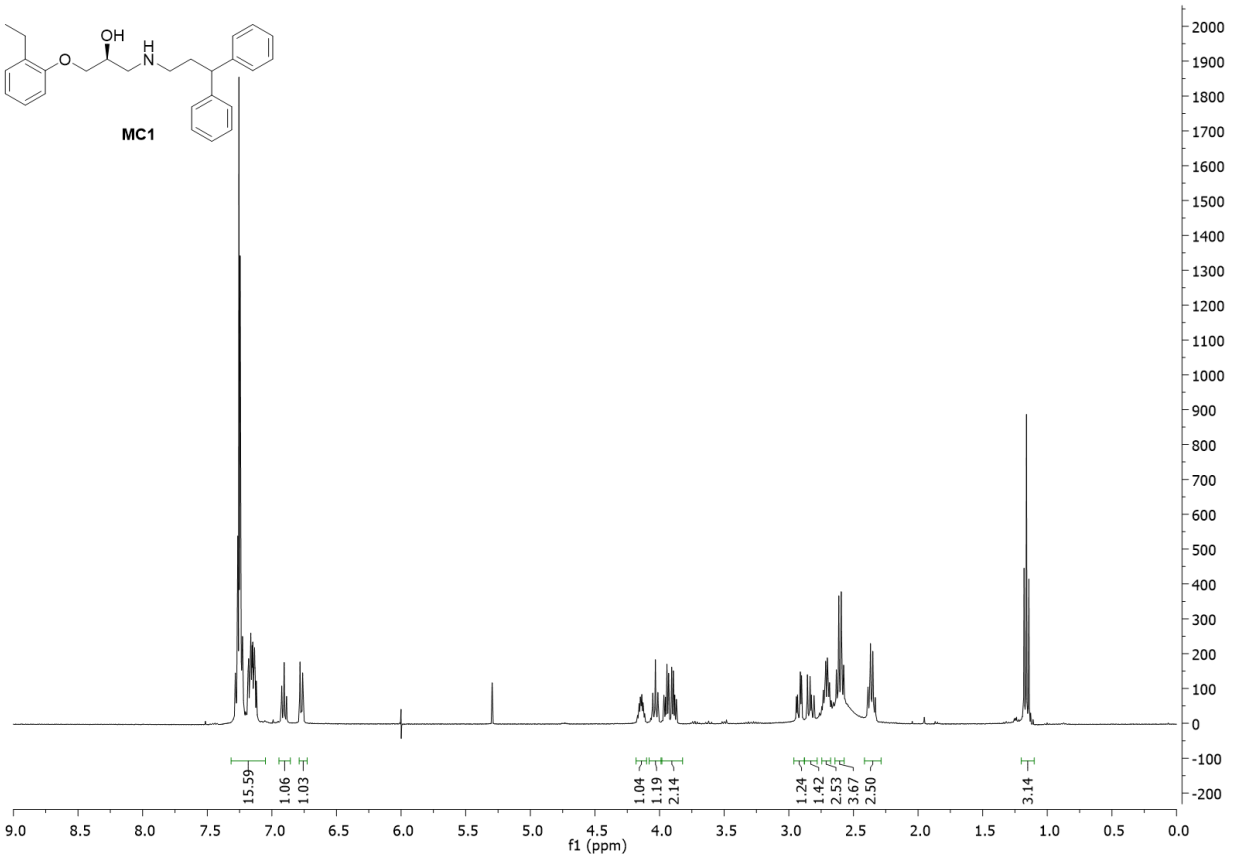


Figure S 9. ^{1}H-NMR of **MC1** (400 MHz, $CDCl_3$)

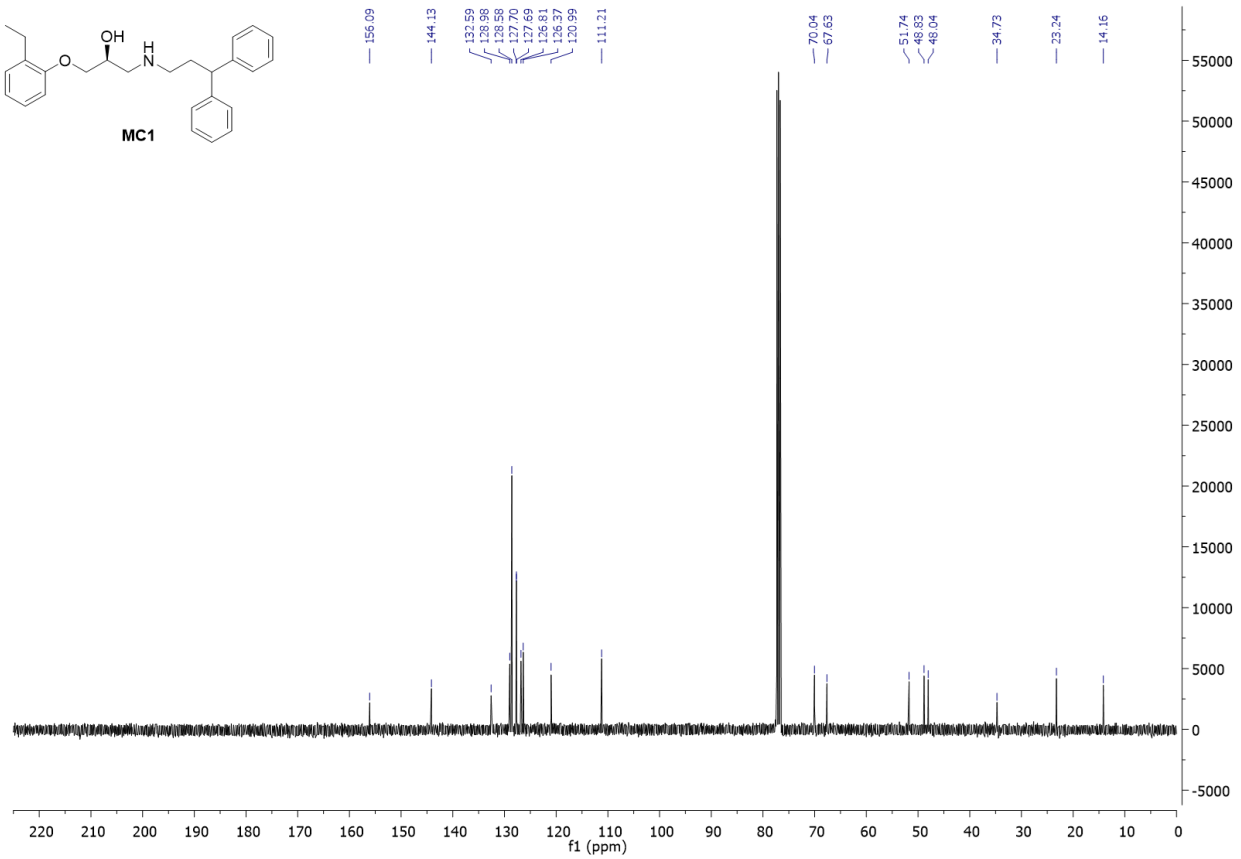


Figure S 10. ^{13}C-NMR of **MC1** (100 MHz, $CDCl_3$)

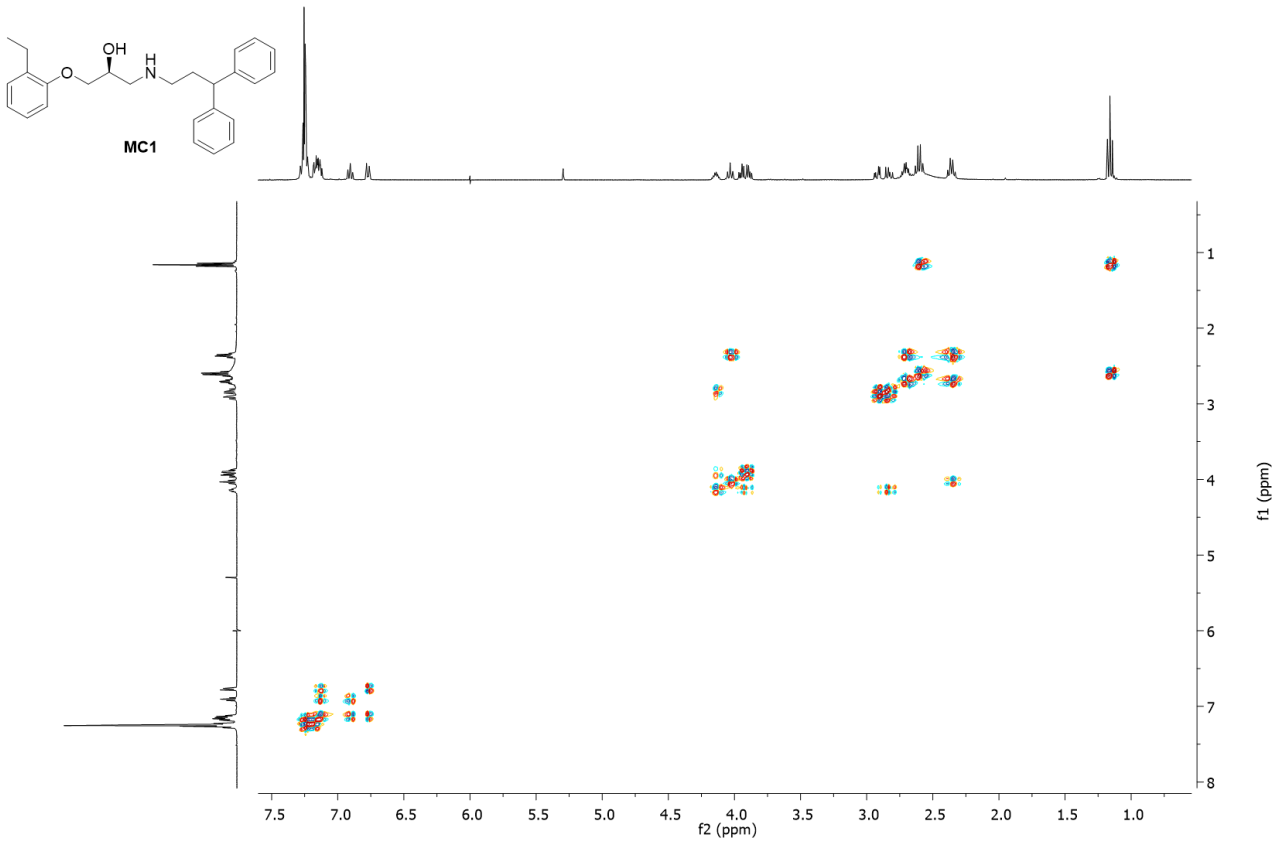


Figure S 11. gDQCOSY-NMR of **MC1** (400 MHz, $CDCl_3$)

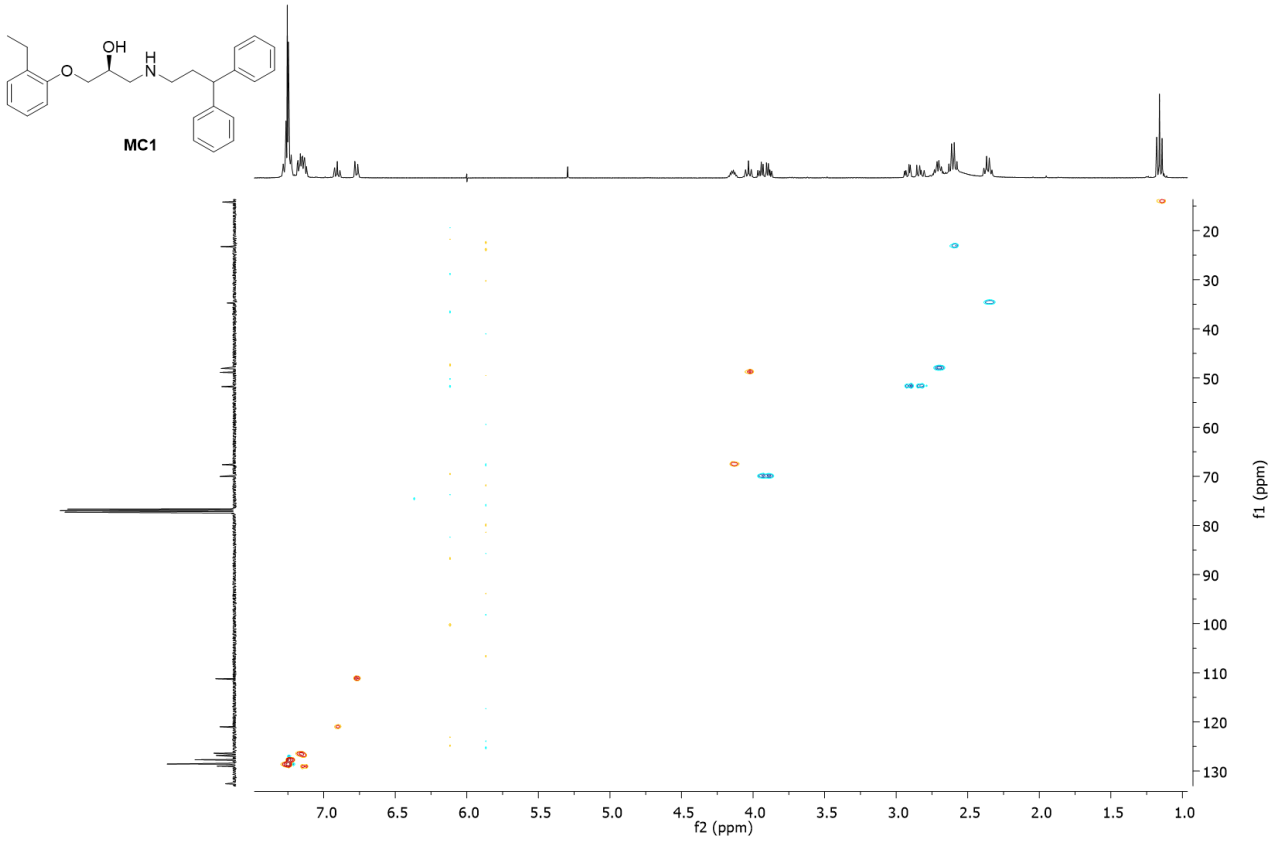


Figure S 12. gHSQC-NMR of **MC1** (400 MHz, $CDCl_3$)

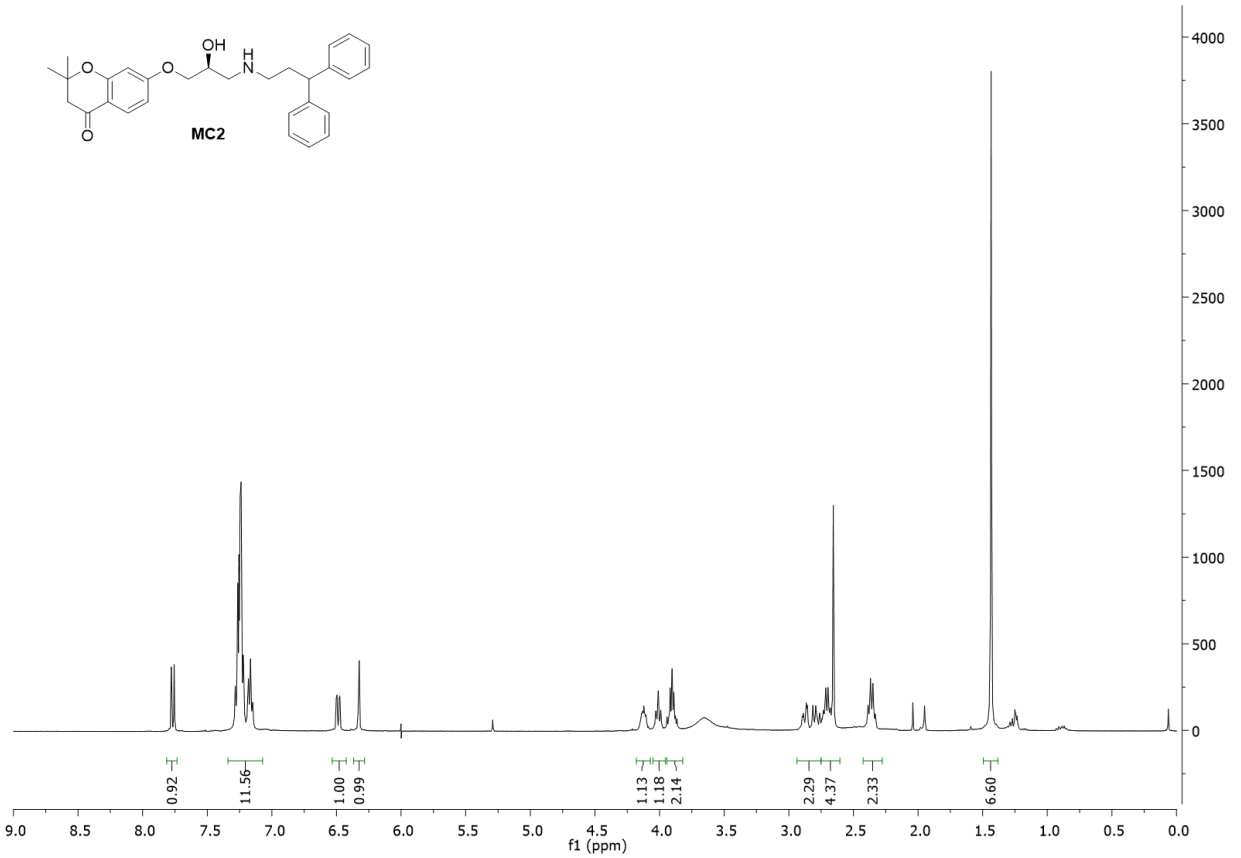


Figure S 13. ^{1}H-NMR of **MC2** (400 MHz, $CDCl_3$)

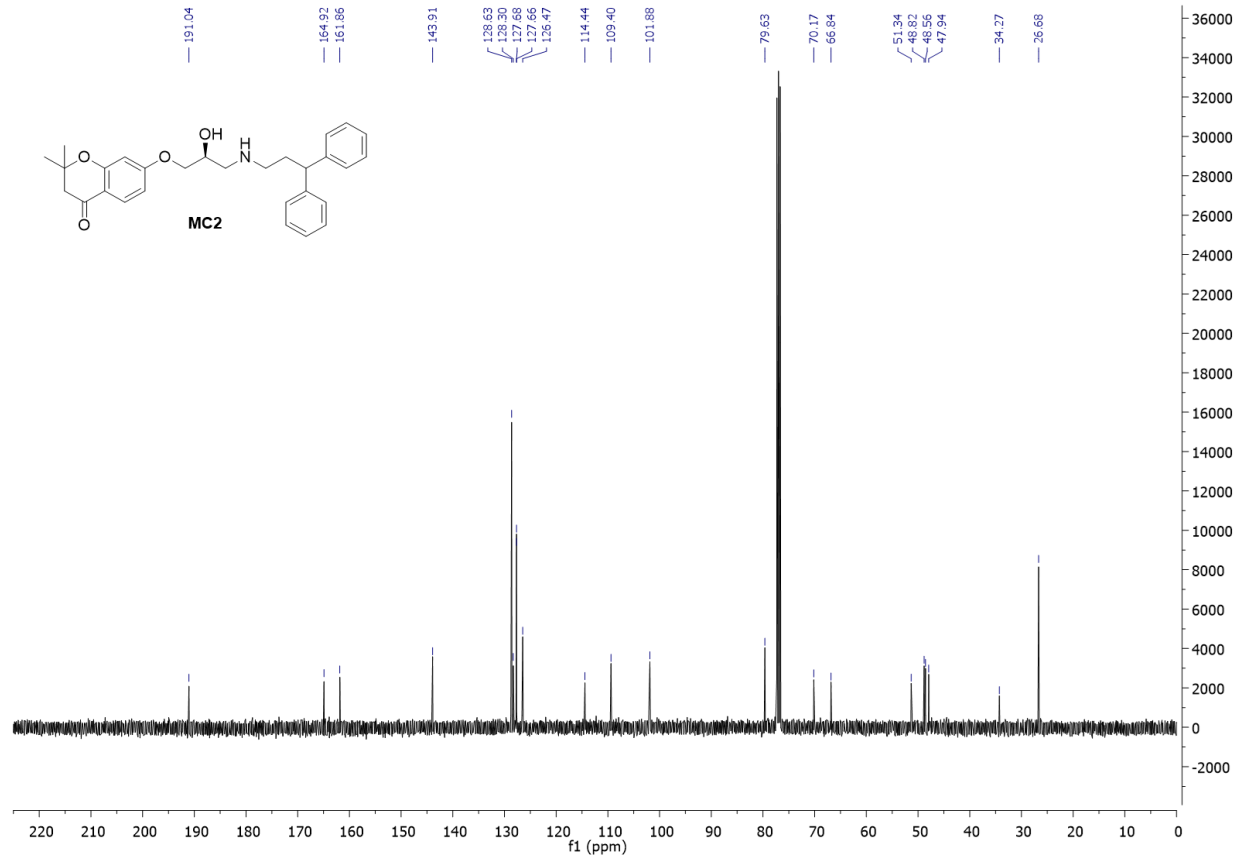


Figure S 14. ^{13}C-NMR of **MC2** (100 MHz, $CDCl_3$)

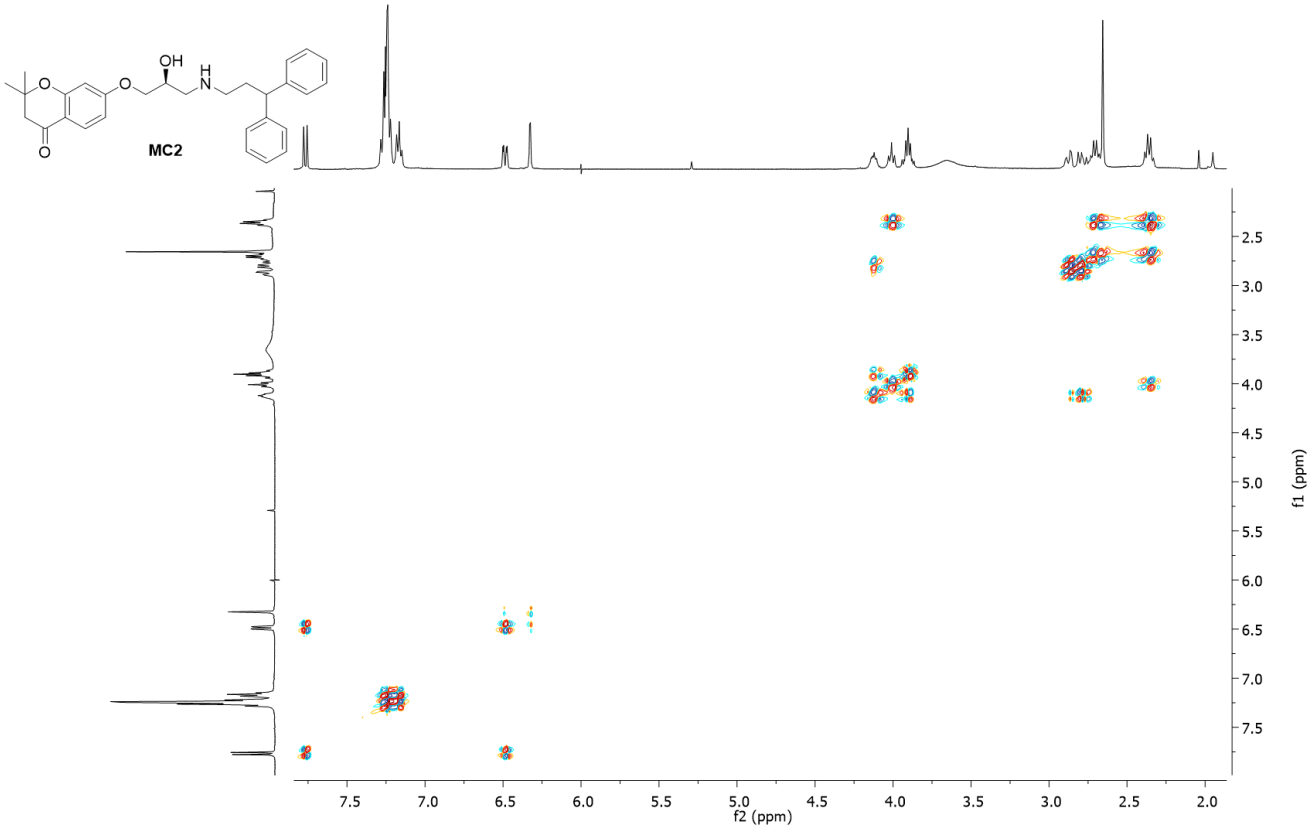


Figure S 15: gDQCOSY-NMR of **MC2** (400 MHz, $CDCl_3$)

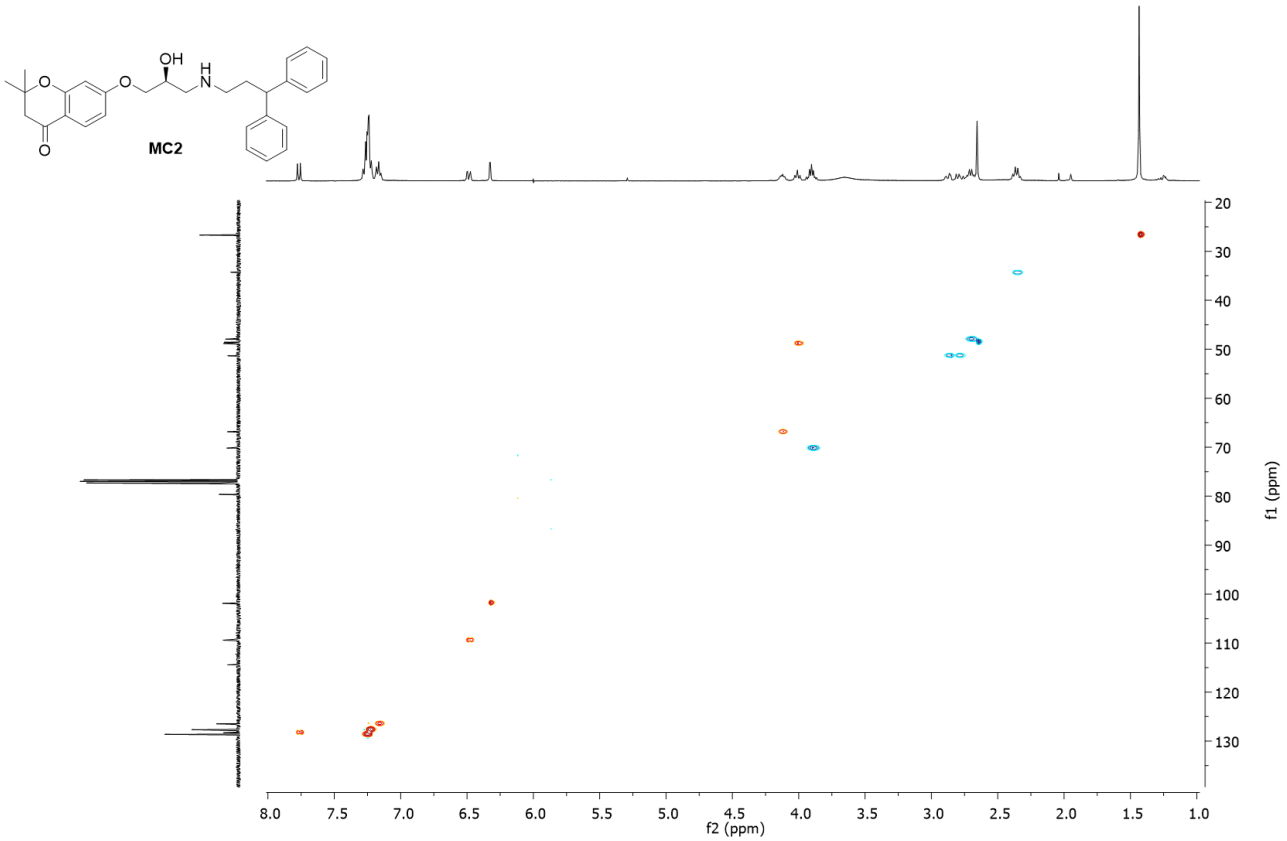


Figure S 16: gHSQC-NMR of **MC2** (400 MHz, $CDCl_3$)

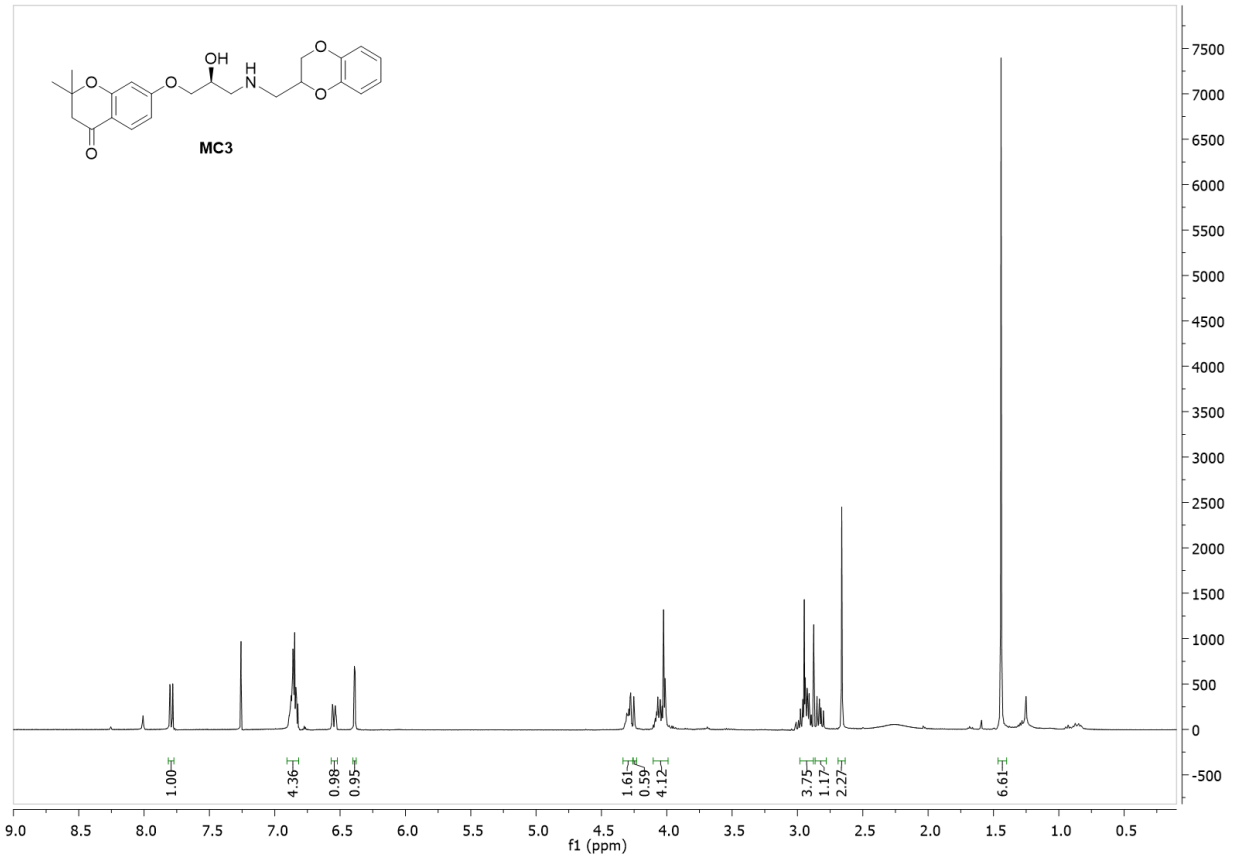


Figure S 17. ^{1}H-NMR of **MC3** (400 MHz, $CDCl_3$ +1% CD_3OD)

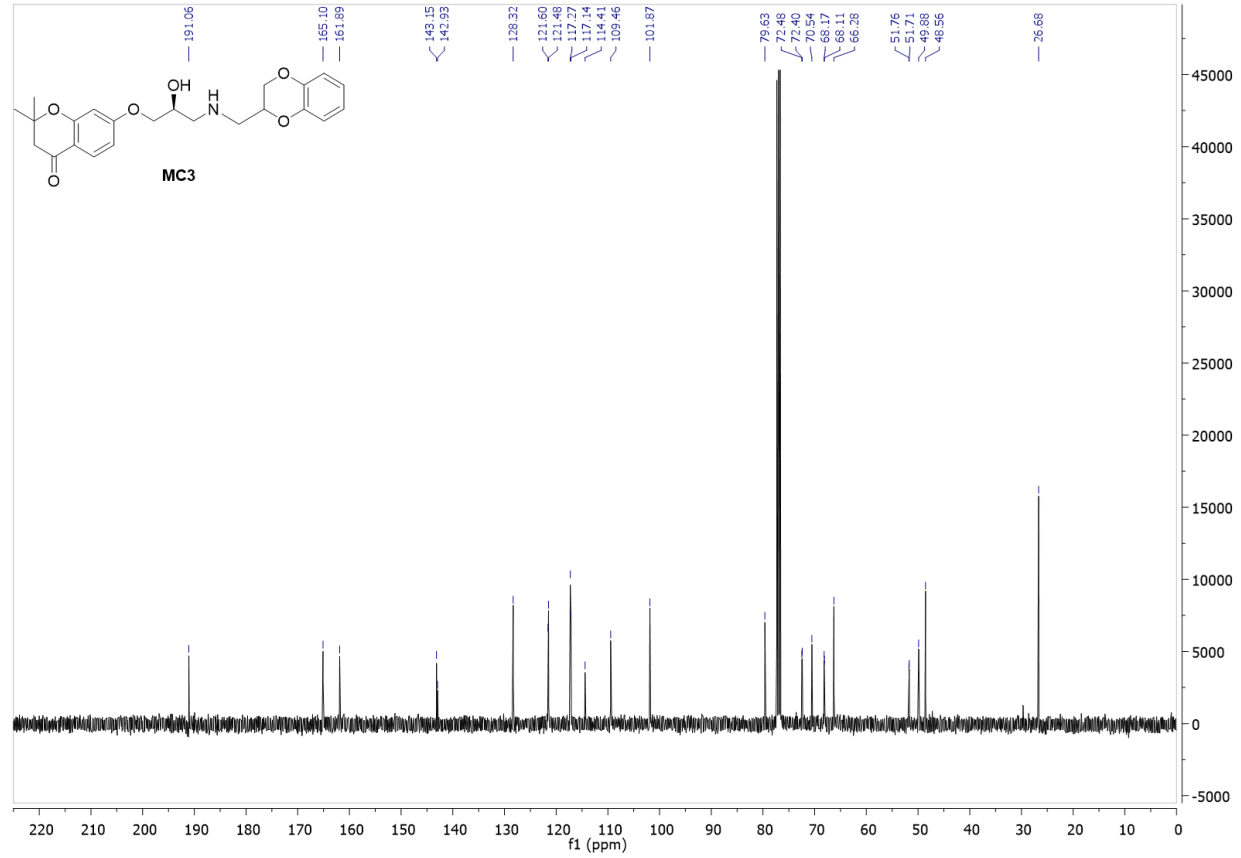


Figure S 18. ^{13}C-NMR of **MC3** (100 MHz, $CDCl_3$ +1% CD_3OD)

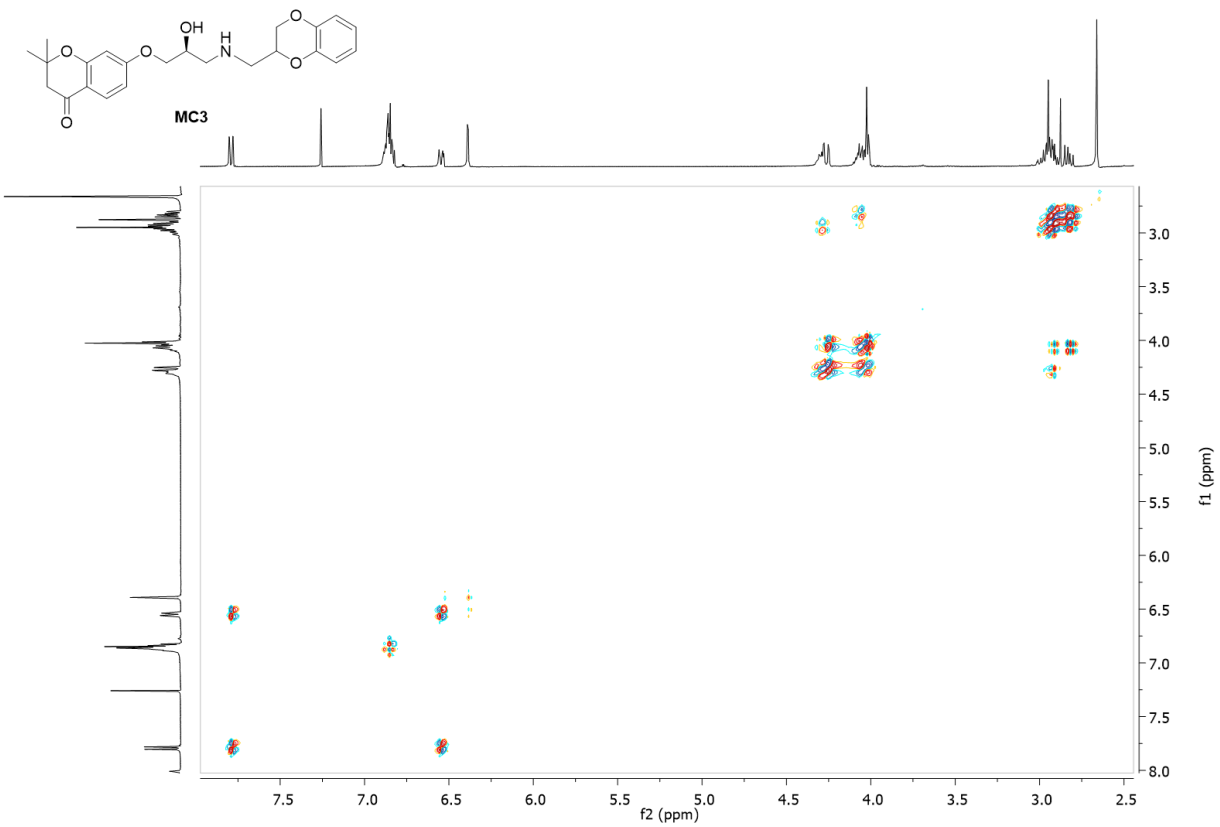


Figure S 19: gDQCOSY-NMR of **MC3** (400 MHz, $CDCl_3$ +1% CD_3OD)

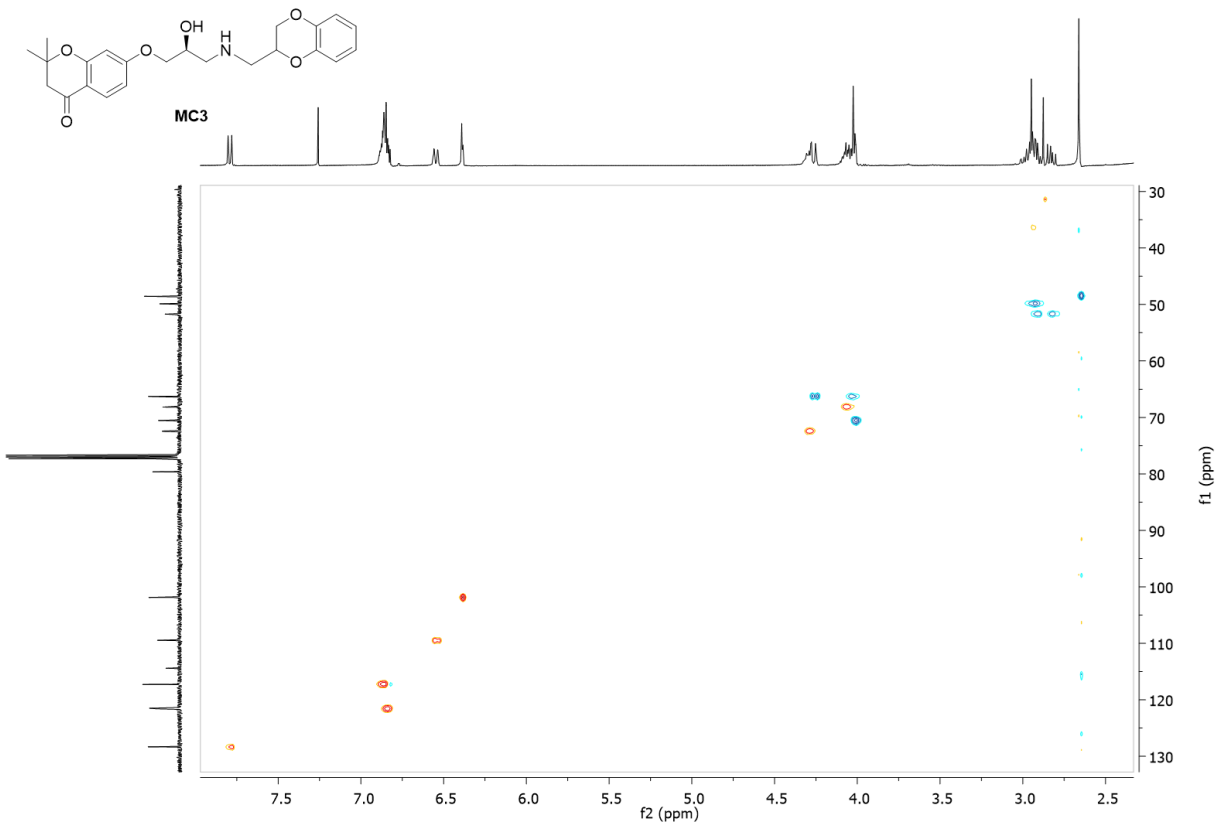


Figure S 20: gHSQC-NMR of **MC3** (400 MHz, $CDCl_3$ +1% CD_3OD)

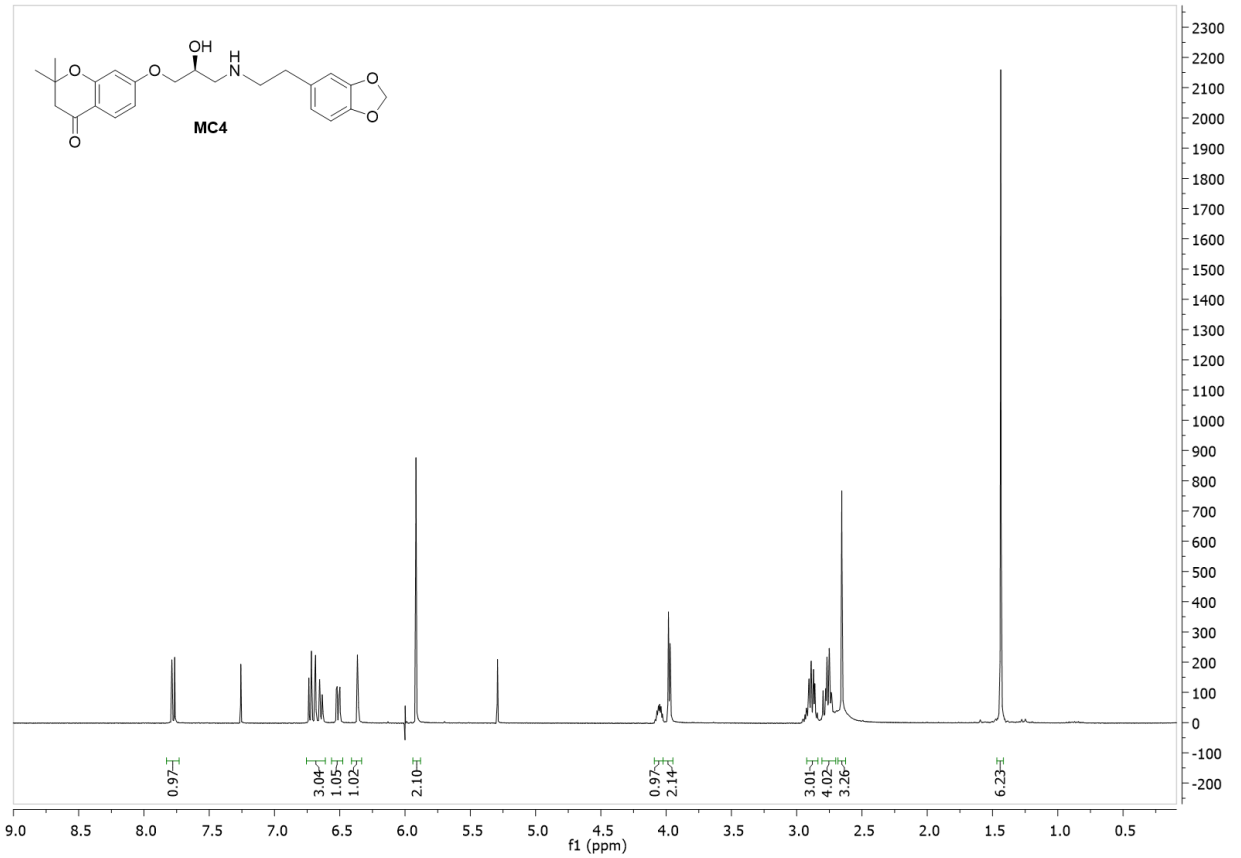


Figure S 21. ^{1}H-NMR of **MC4** (400 MHz, $CDCl_3$)

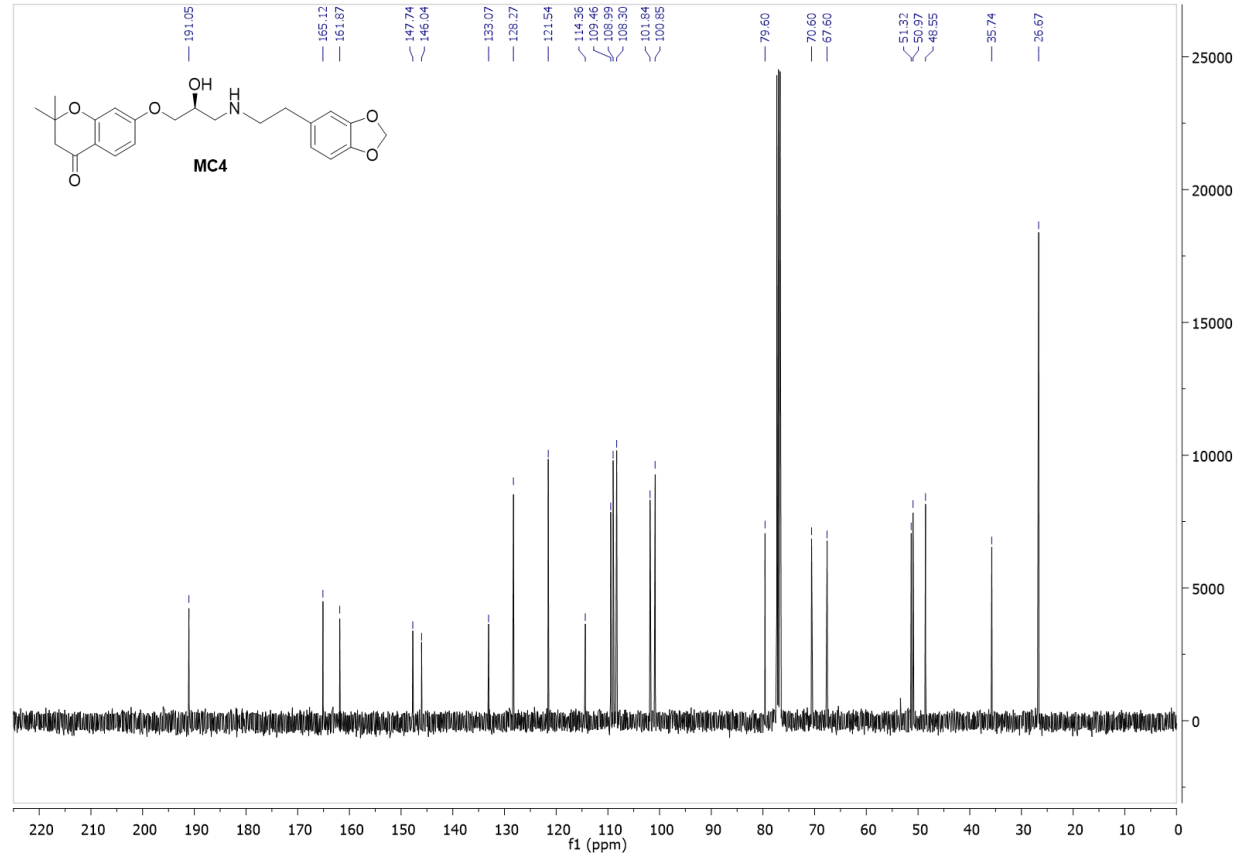


Figure S 22. ^{13}C-NMR of **MC4** (100 MHz, $CDCl_3$)

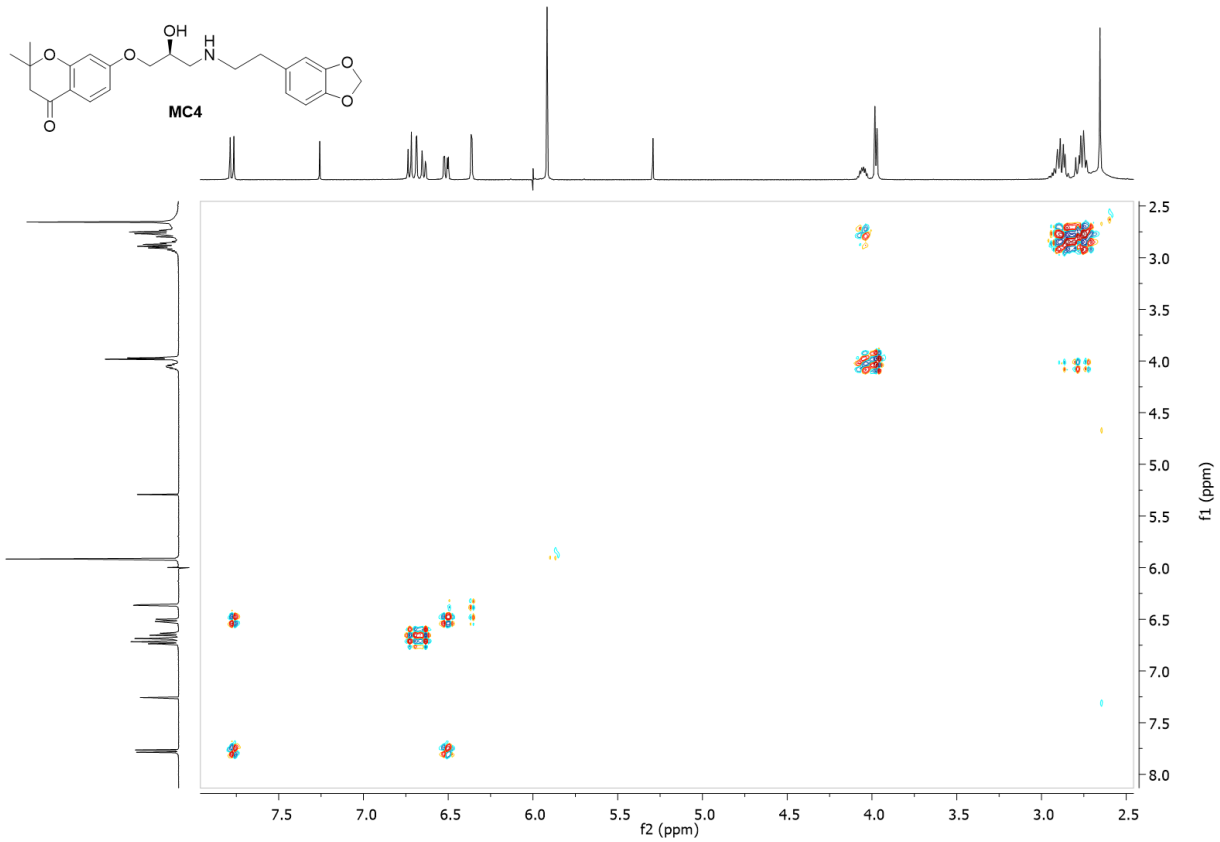


Figure S 23: gDQCOSY-NMR of **MC4** (400 MHz, $CDCl_3$)

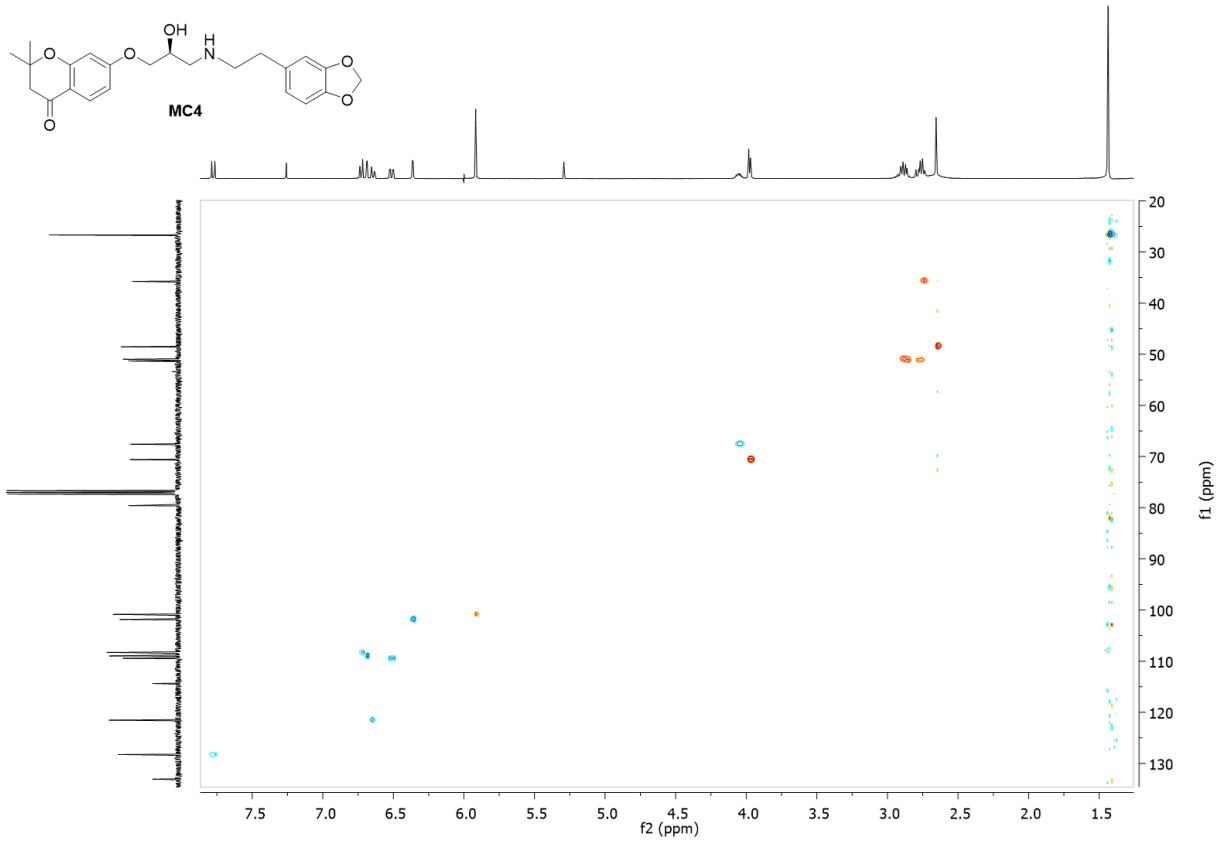


Figure S 24: gHSQC-NMR of **MC4** (400 MHz, $CDCl_3$)

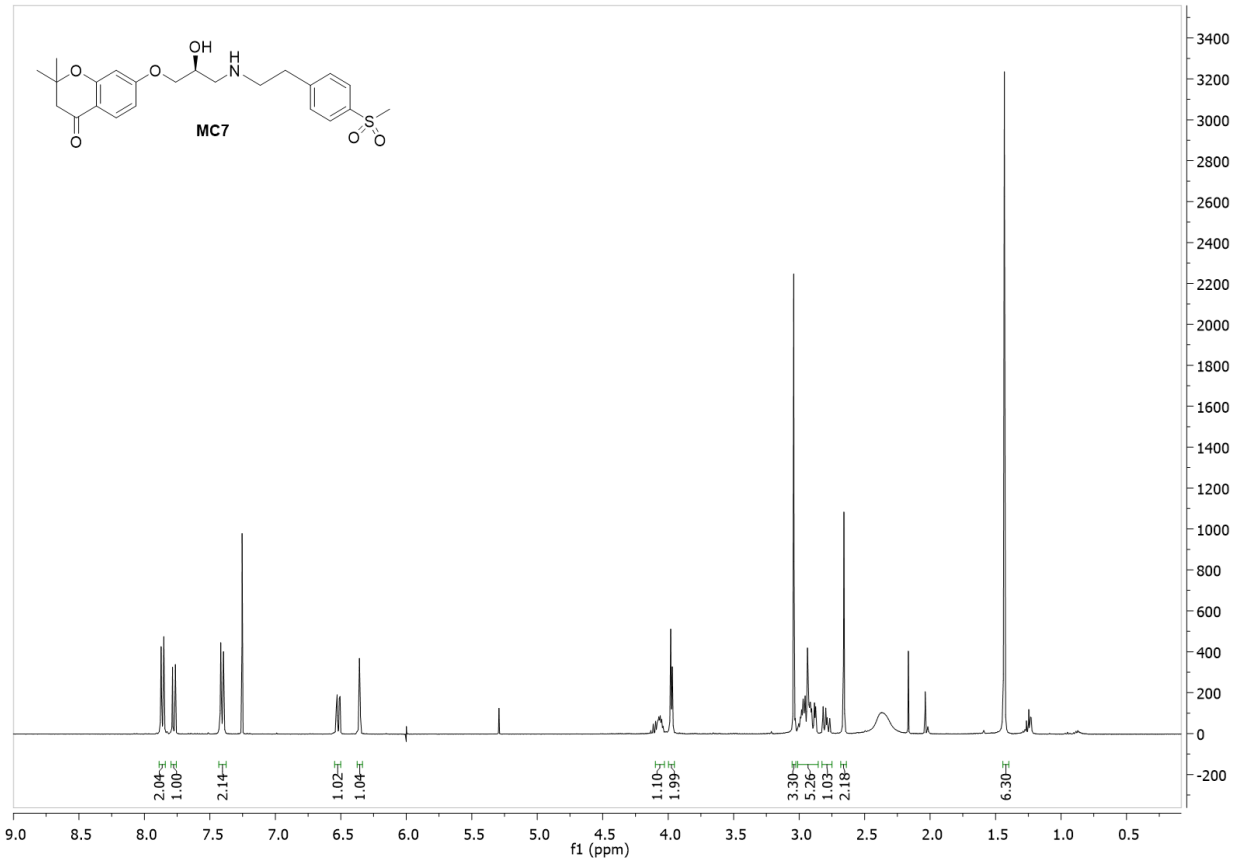


Figure S 25. ^{1}H-NMR of **MC7** (400 MHz, $CDCl_3$)

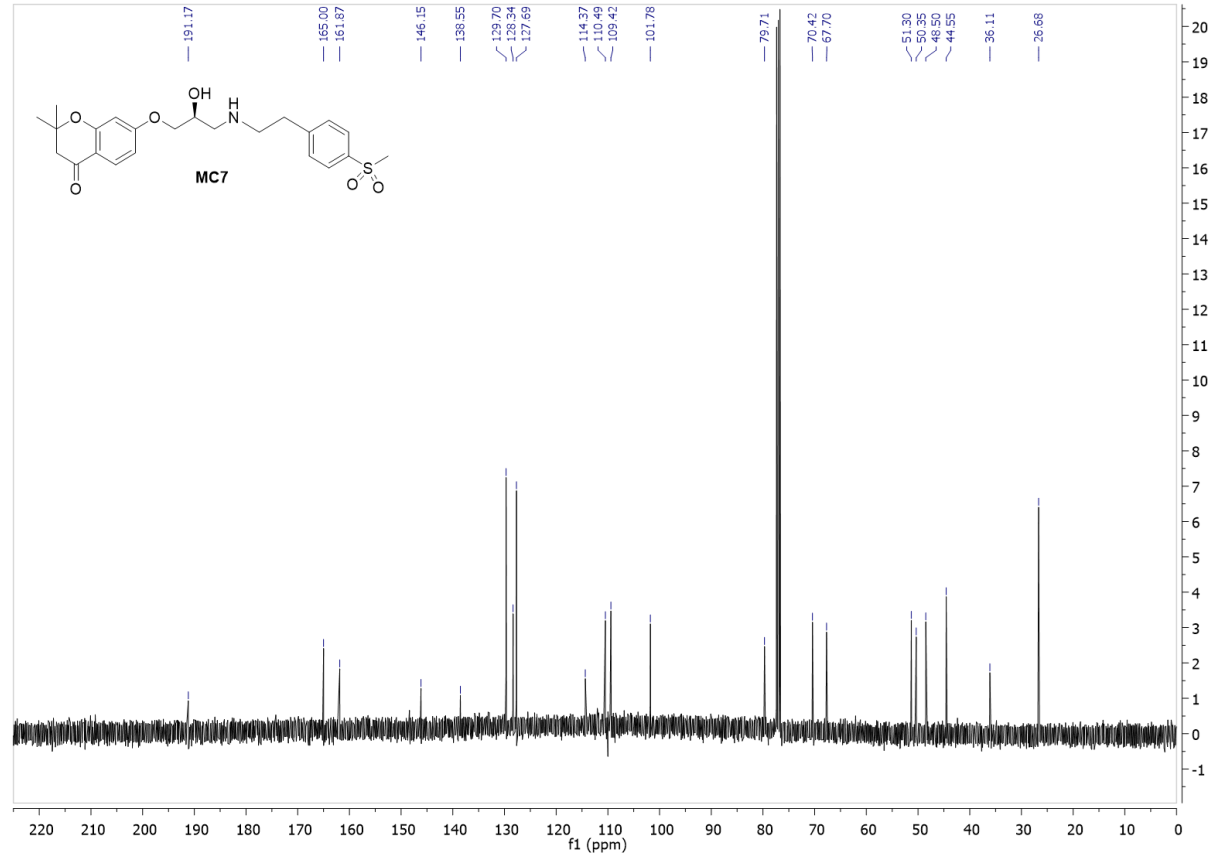


Figure S 26. ^{13}C-NMR of **MC7** (100 MHz, $CDCl_3$)

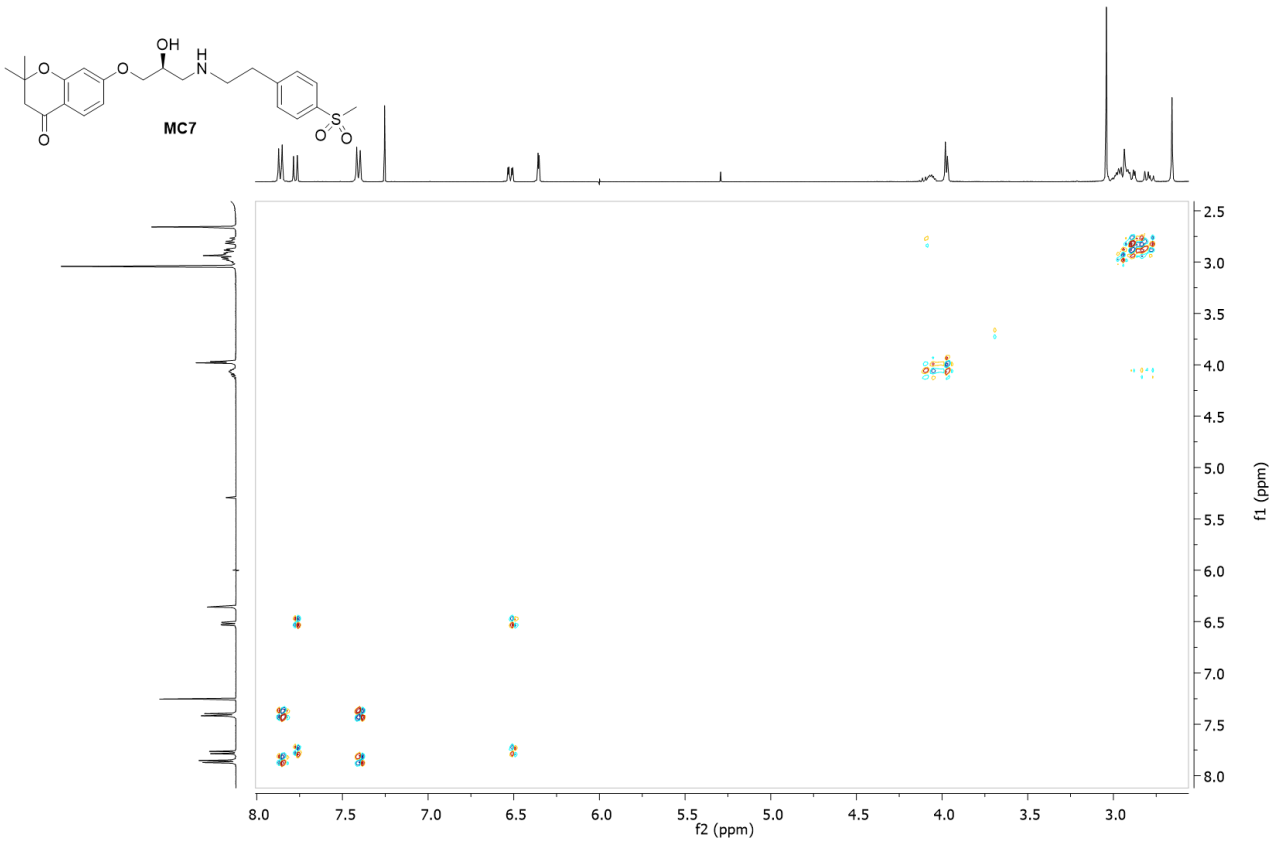


Figure S 27: gDQCOSY-NMR of **MC7** (400 MHz, $CDCl_3$)

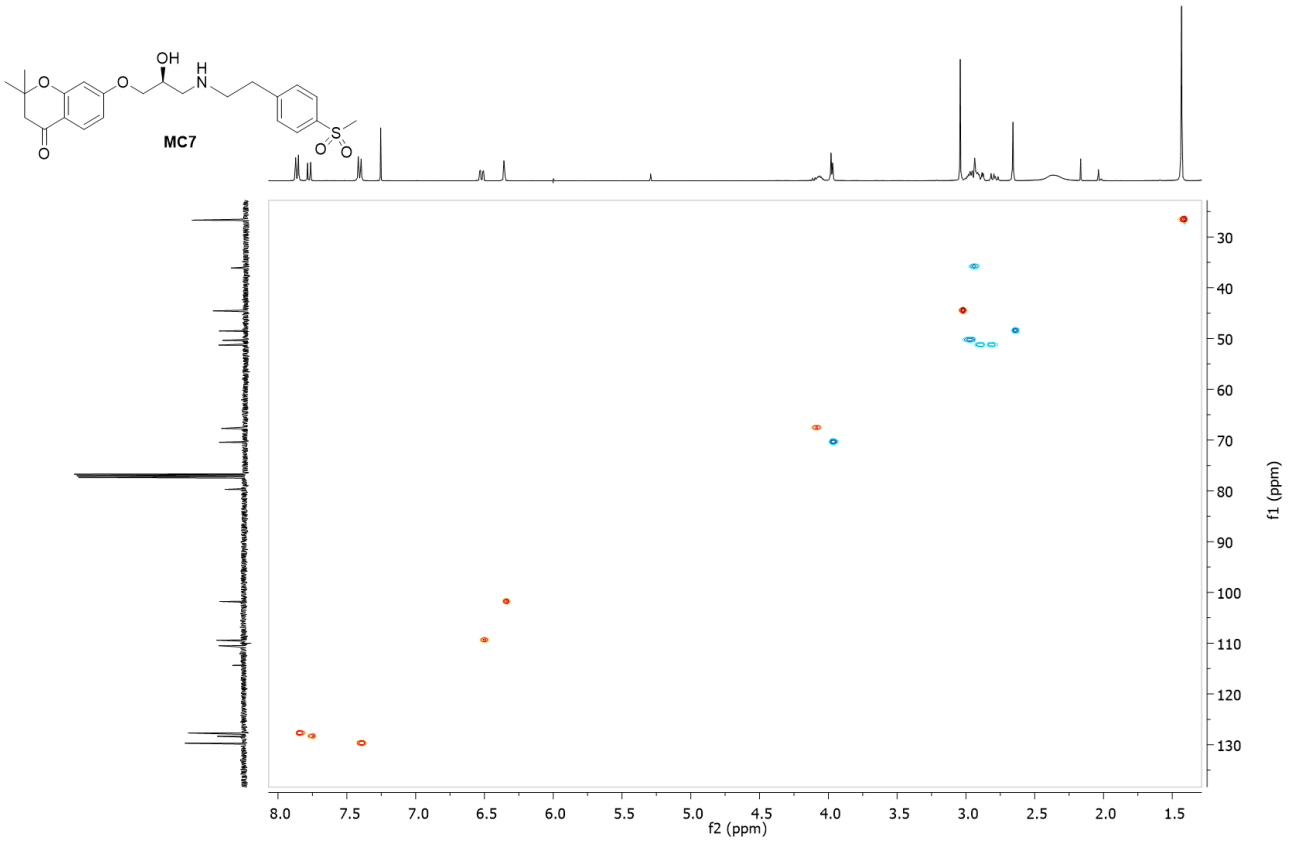


Figure S 28: gHSQC-NMR of **MC7** (400 MHz, $CDCl_3$)

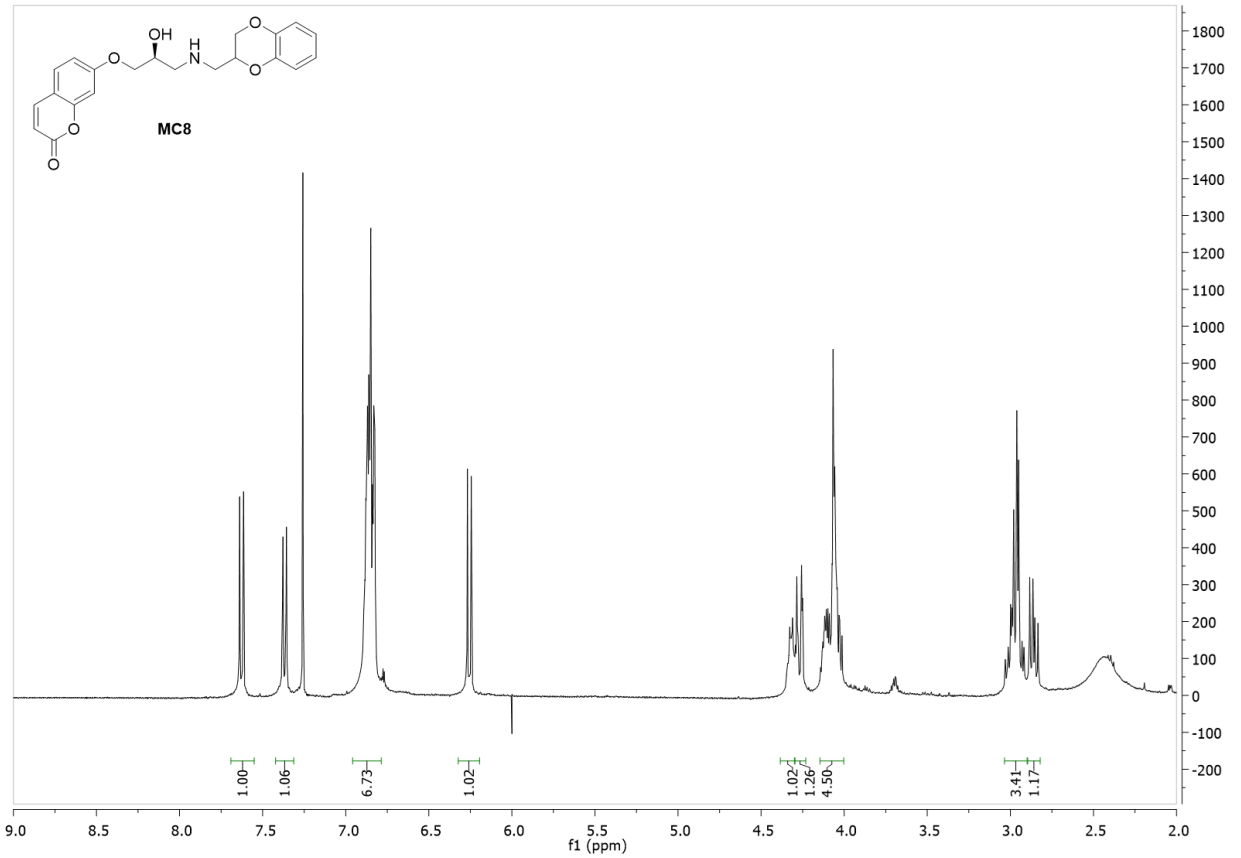


Figure S 29. ^{1}H-NMR of **MC8** (400 MHz, $CDCl_3$)

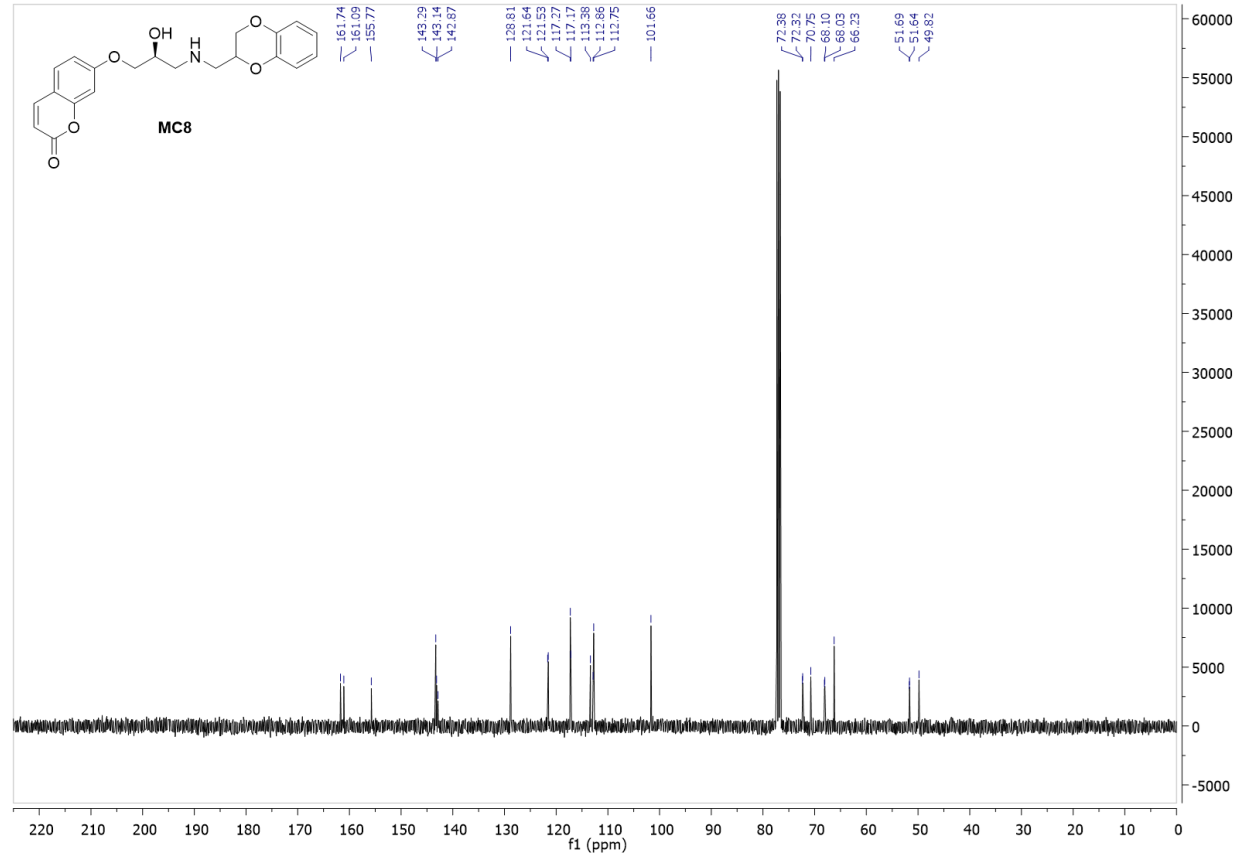


Figure S 30. ^{13}C-NMR of **MC8** (100 MHz, $CDCl_3$)

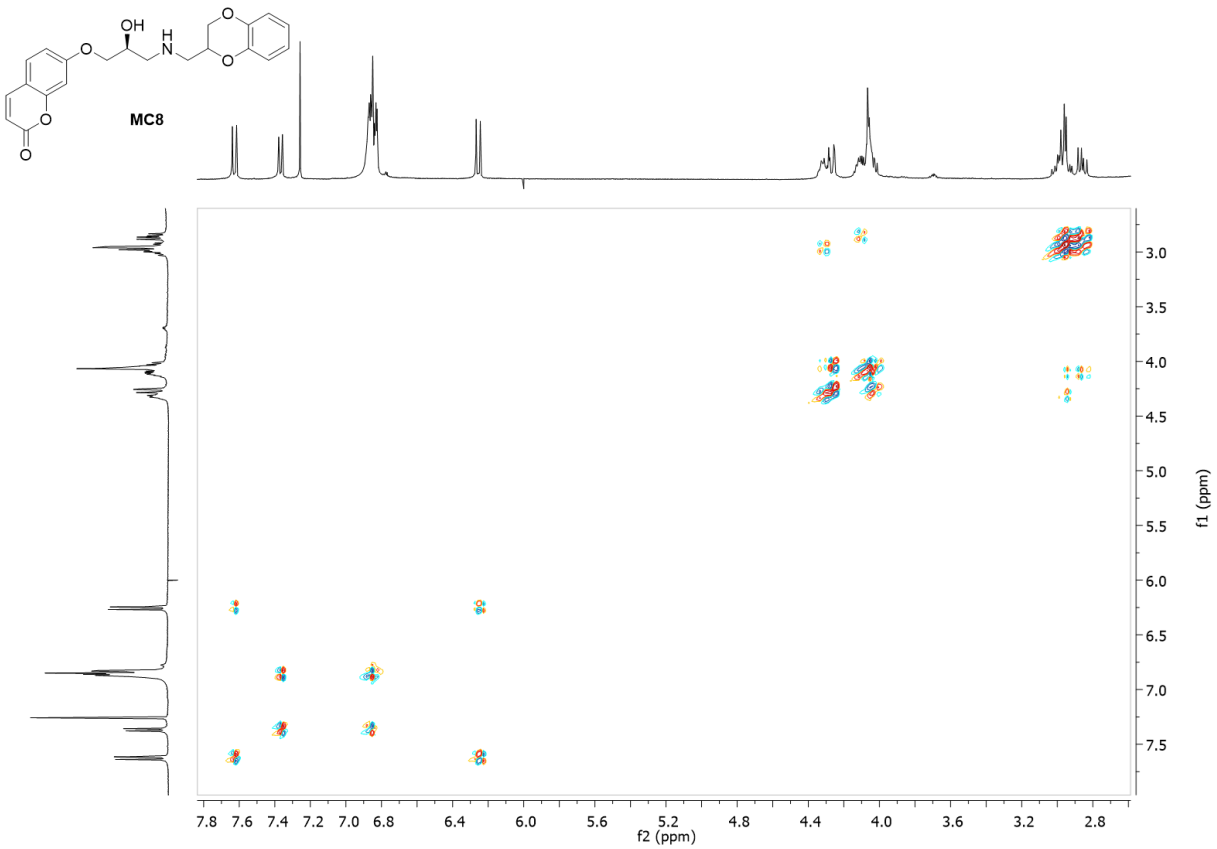


Figure S 31: gDQCOSY-NMR of **MC8** (400 MHz, $CDCl_3$)

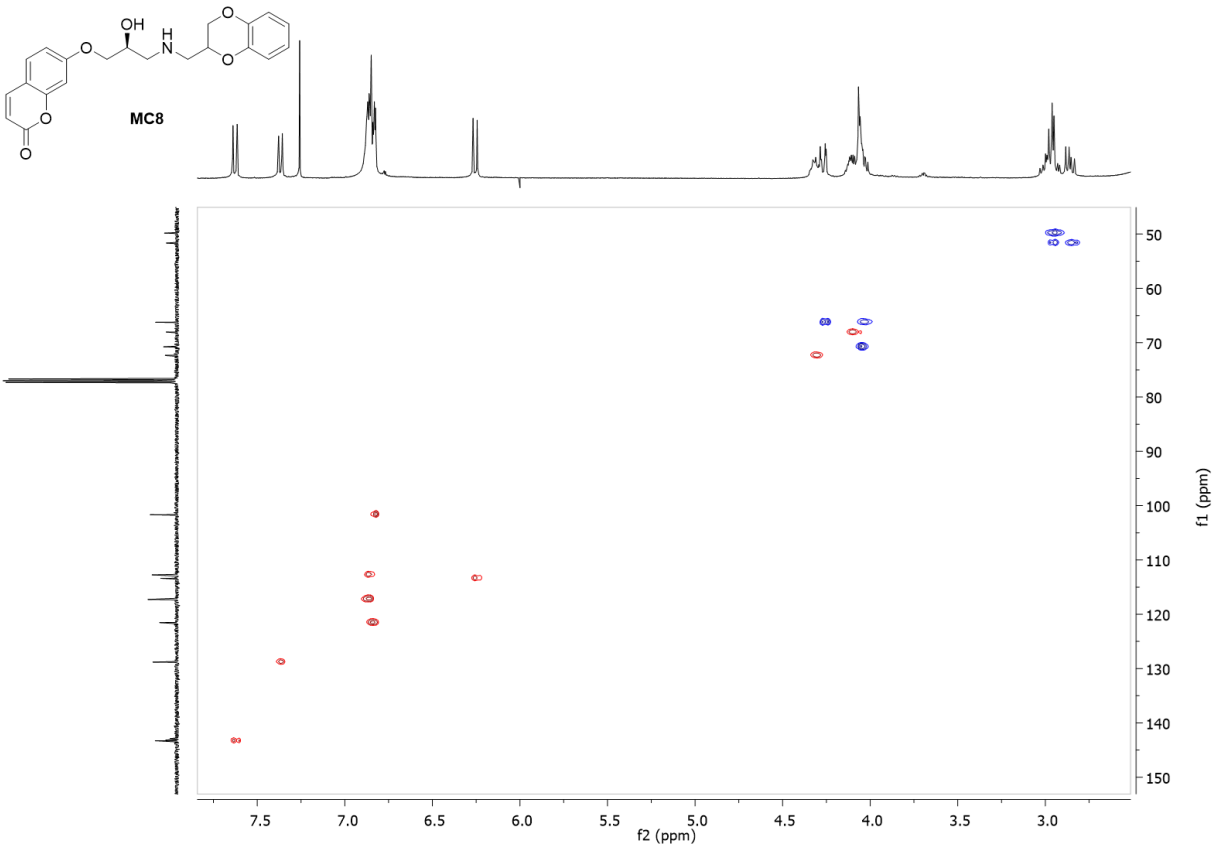


Figure S 32: gDQCOSY-NMR of **MC8** (400 MHz, $CDCl_3$)

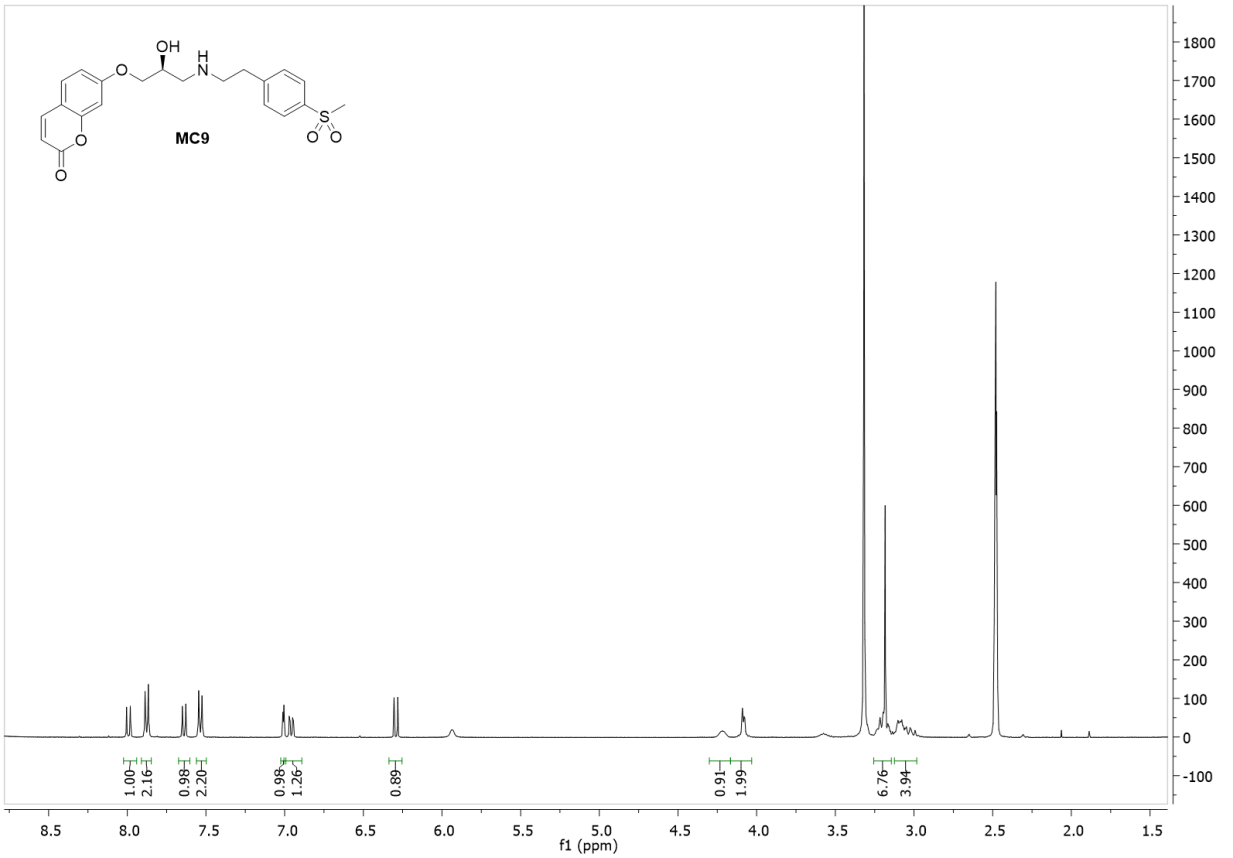


Figure S 33. ^{1}H-NMR of **MC9** (400 MHz, DMSO-d^{6})

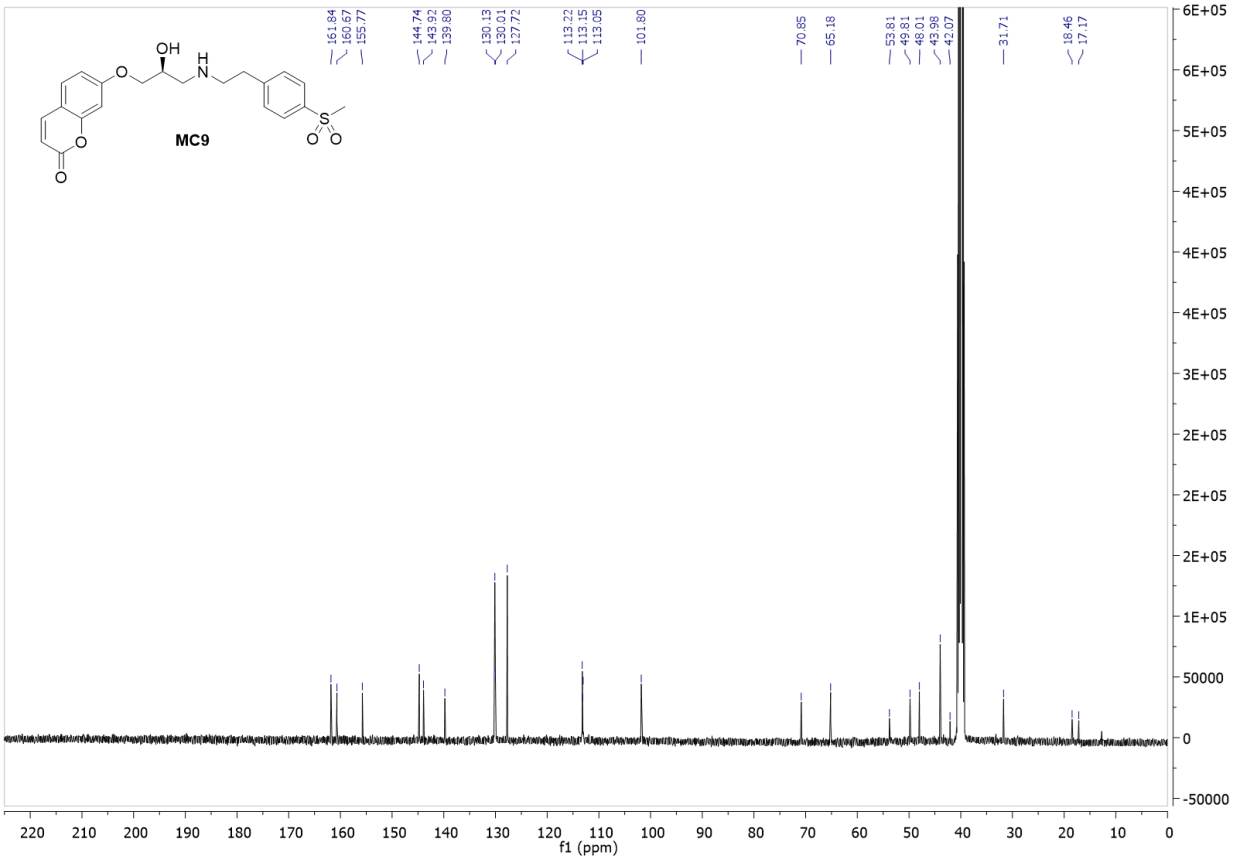


Figure S 34. ^{13}C-NMR of **MC9** (100 MHz, DMSO-d^{6})

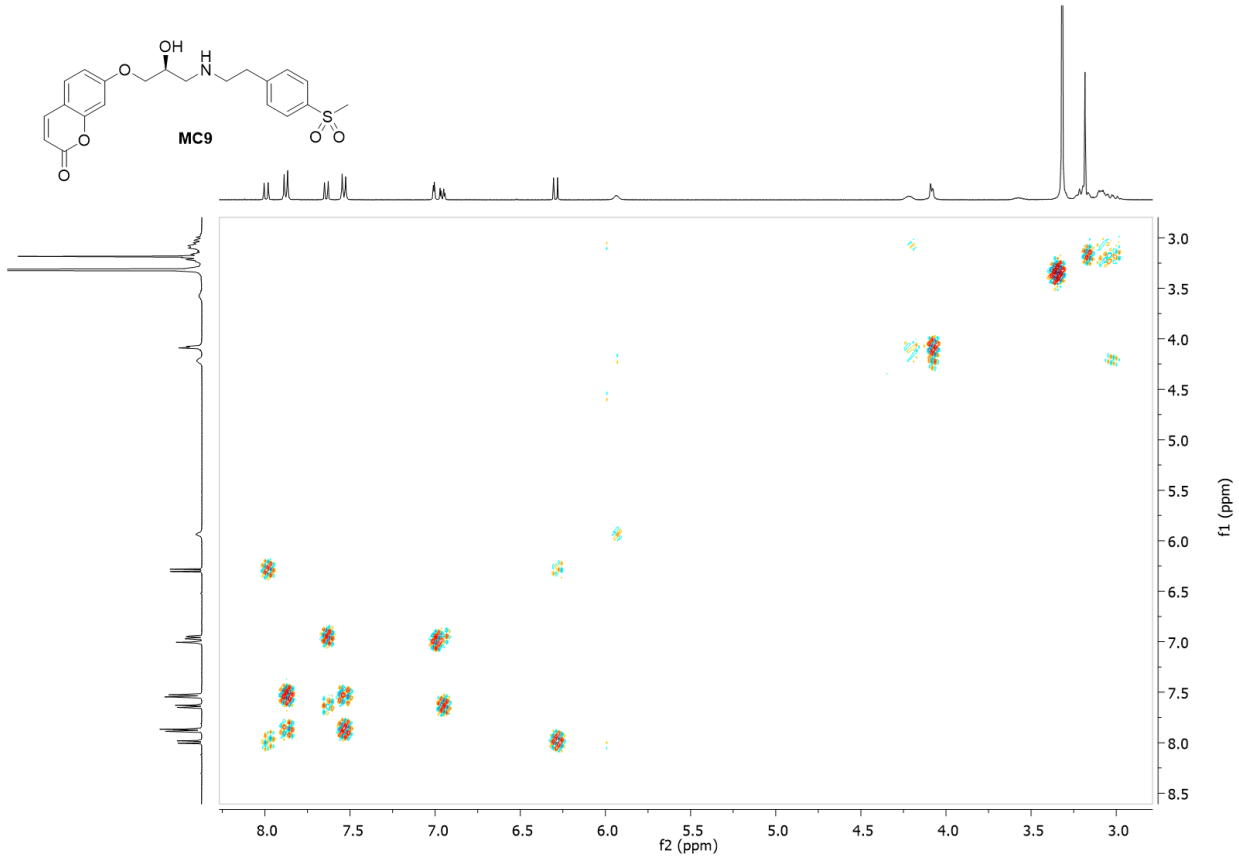


Figure S 35: gDQCOSY-NMR of **MC9** (400 MHz, DMSO-d^6)

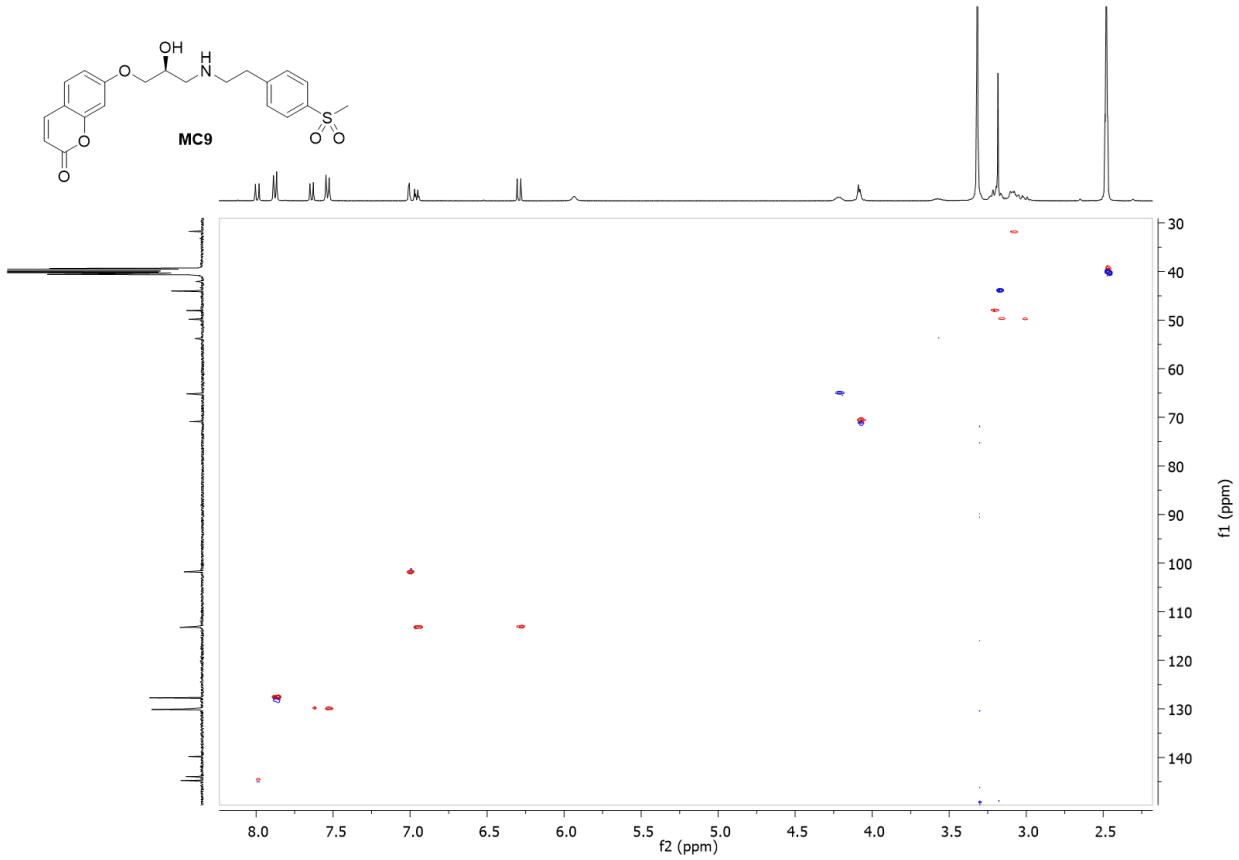


Figure S 36: gHSQC-NMR of **MC9** (400 MHz, DMSO-d^6)

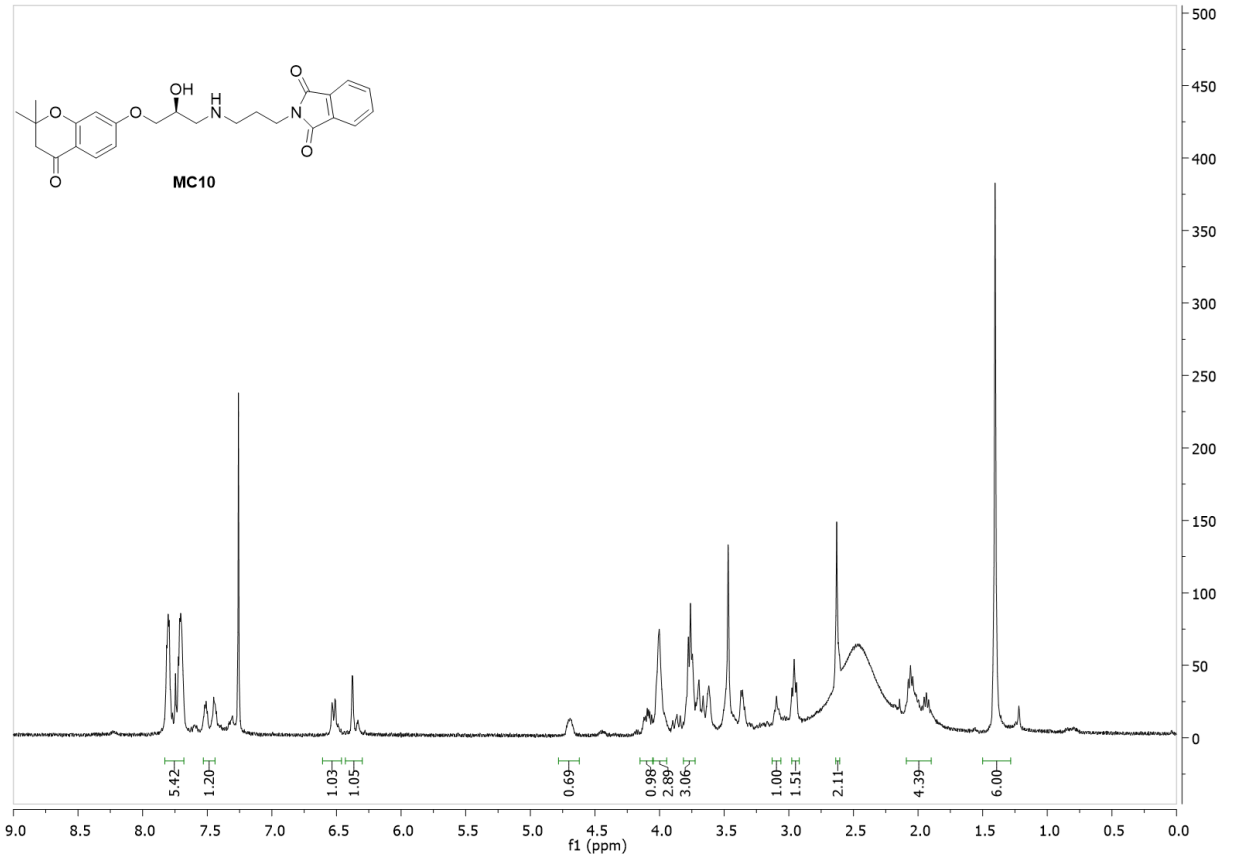


Figure S 37. ^{1}H-NMR of **MC10** (400 MHz, $CDCl_3$ +5% CD_3OD)

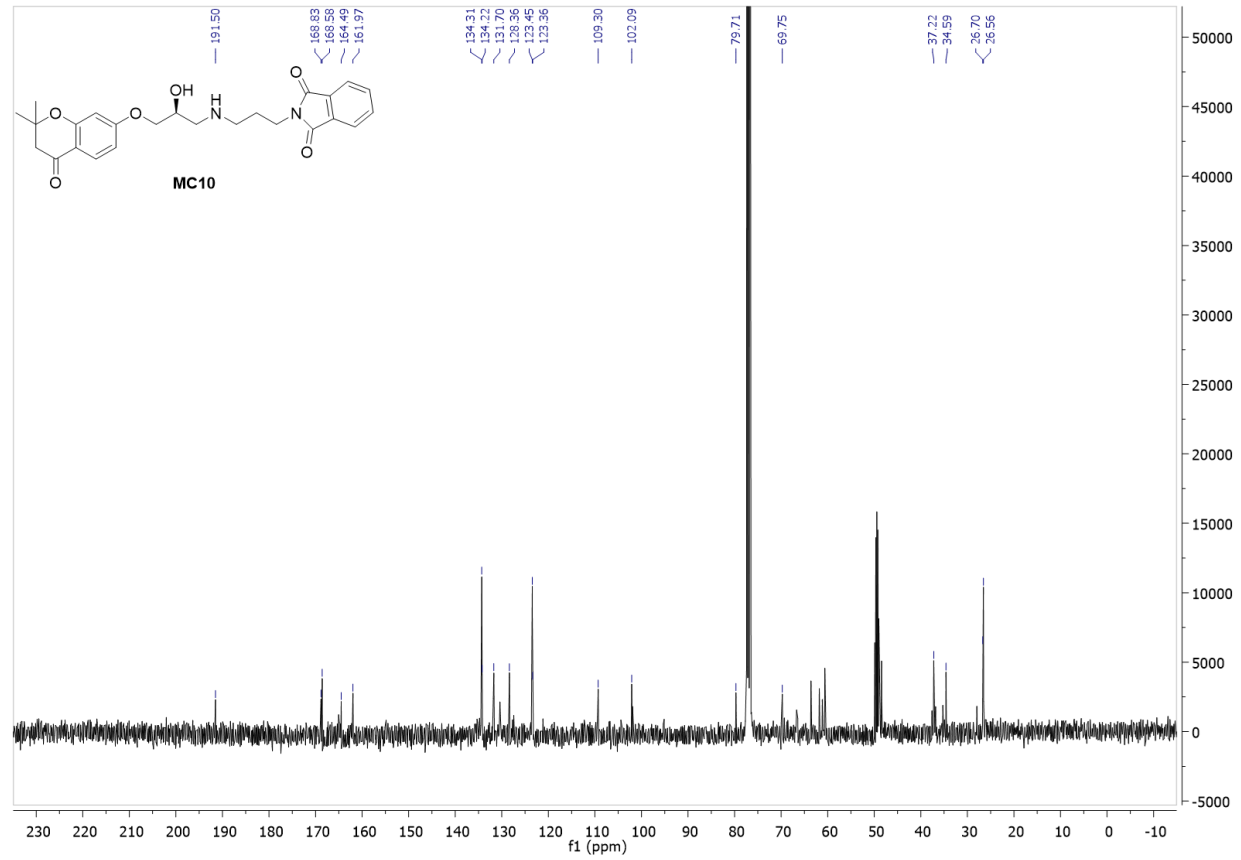


Figure S 38. ^{13}C-NMR of **MC10** (100 MHz, $CDCl_3$ +5% CD_3OD)

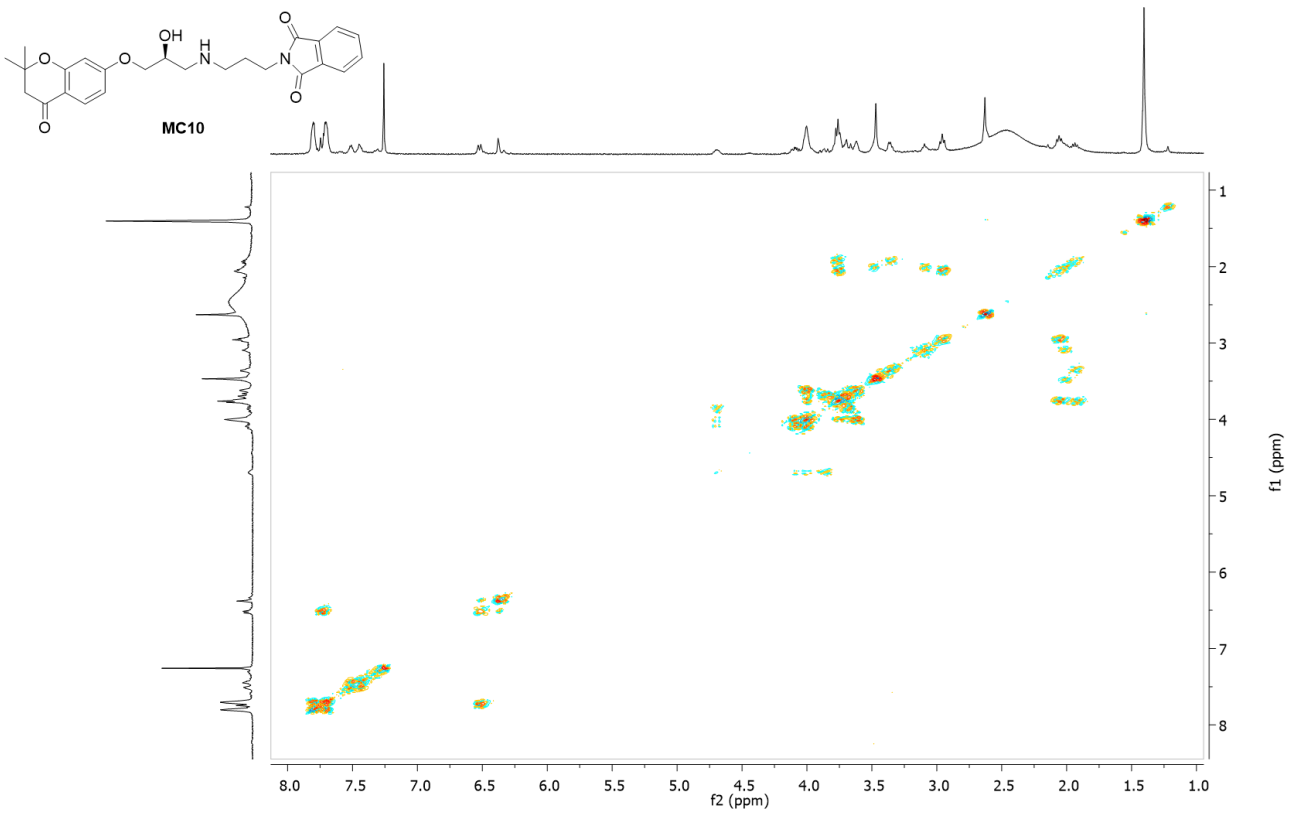


Figure S 39: gDQCOSY-NMR of **MC10** (400 MHz, $CDCl_3$ +5% CD_3OD)

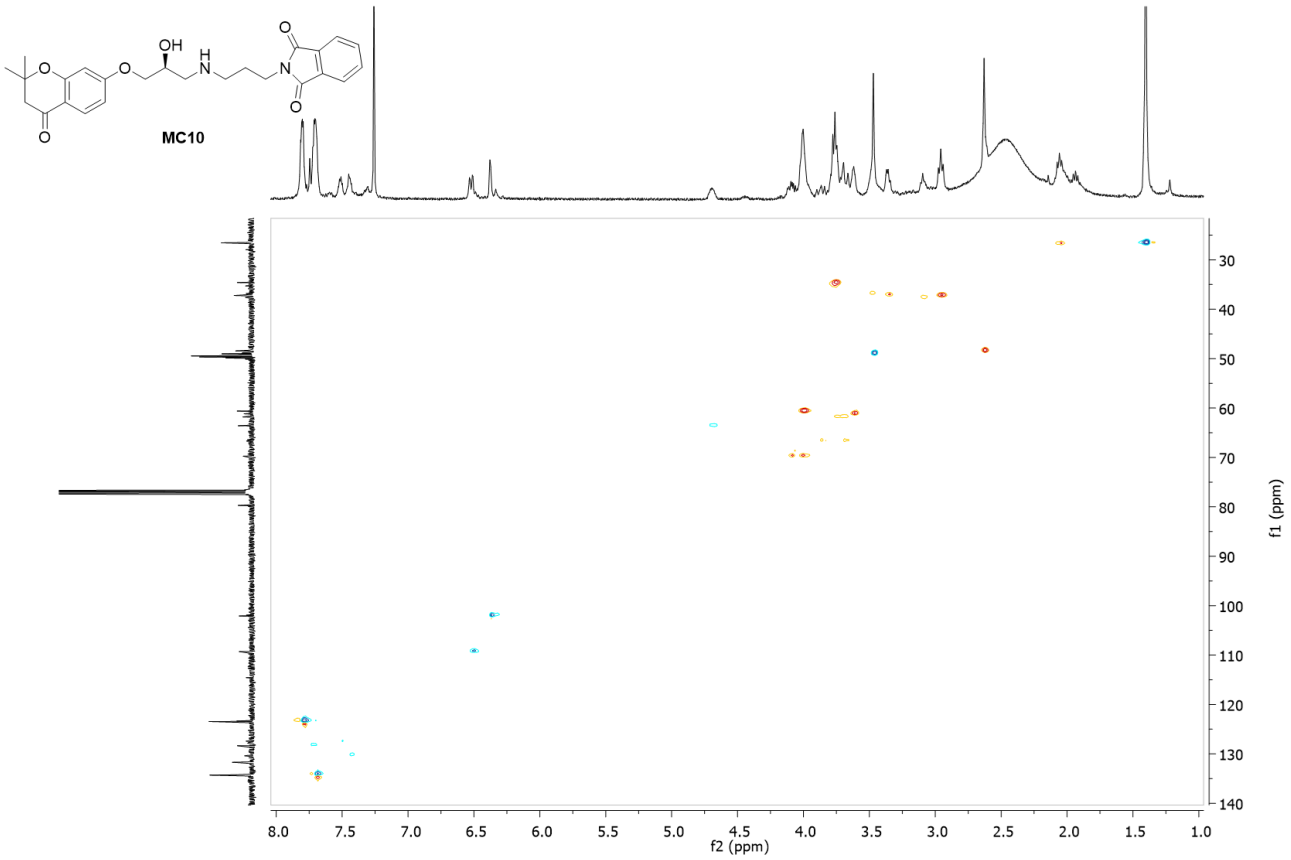


Figure S 40: gHSQC-NMR of **MC10** (400 MHz, $CDCl_3$ +5% CD_3OD)

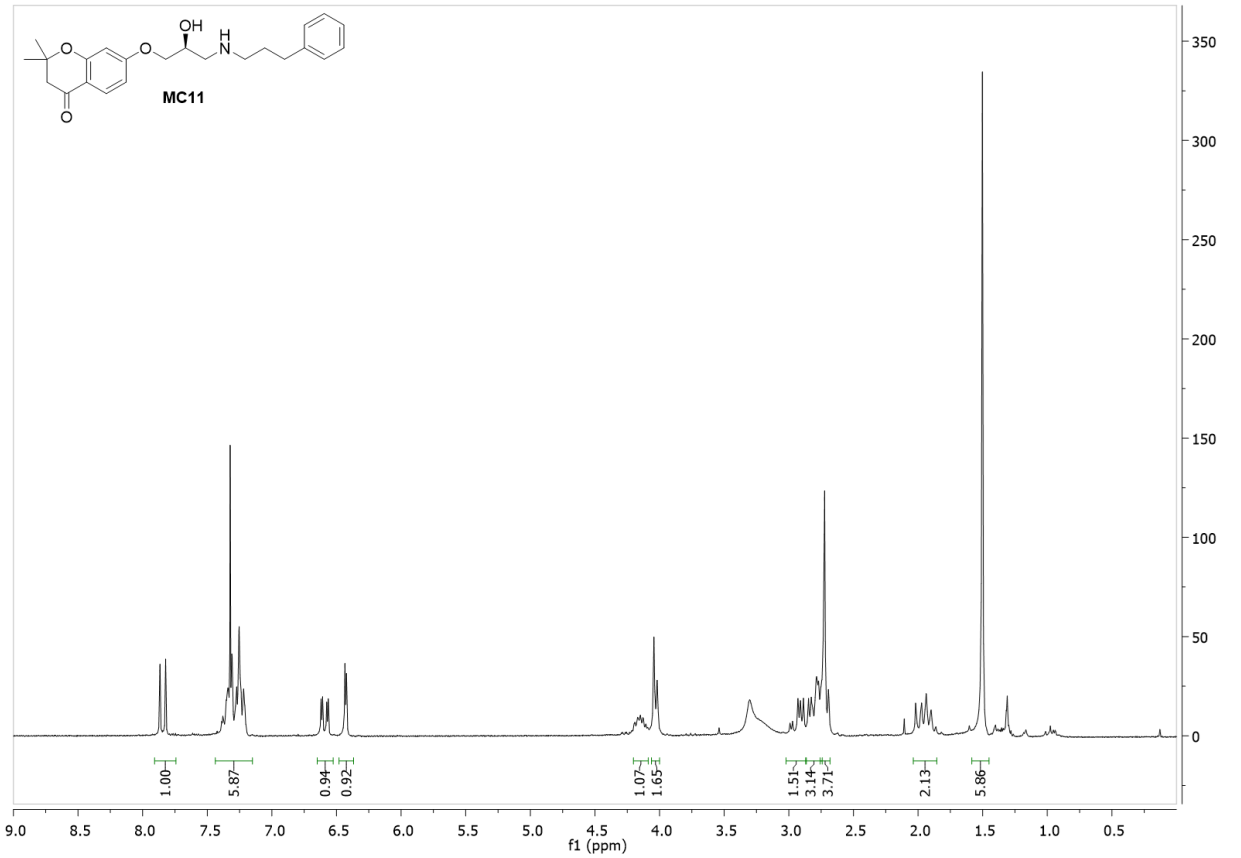


Figure S 41. ^{1}H-NMR of **MC11** (400 MHz, $CDCl_3$)

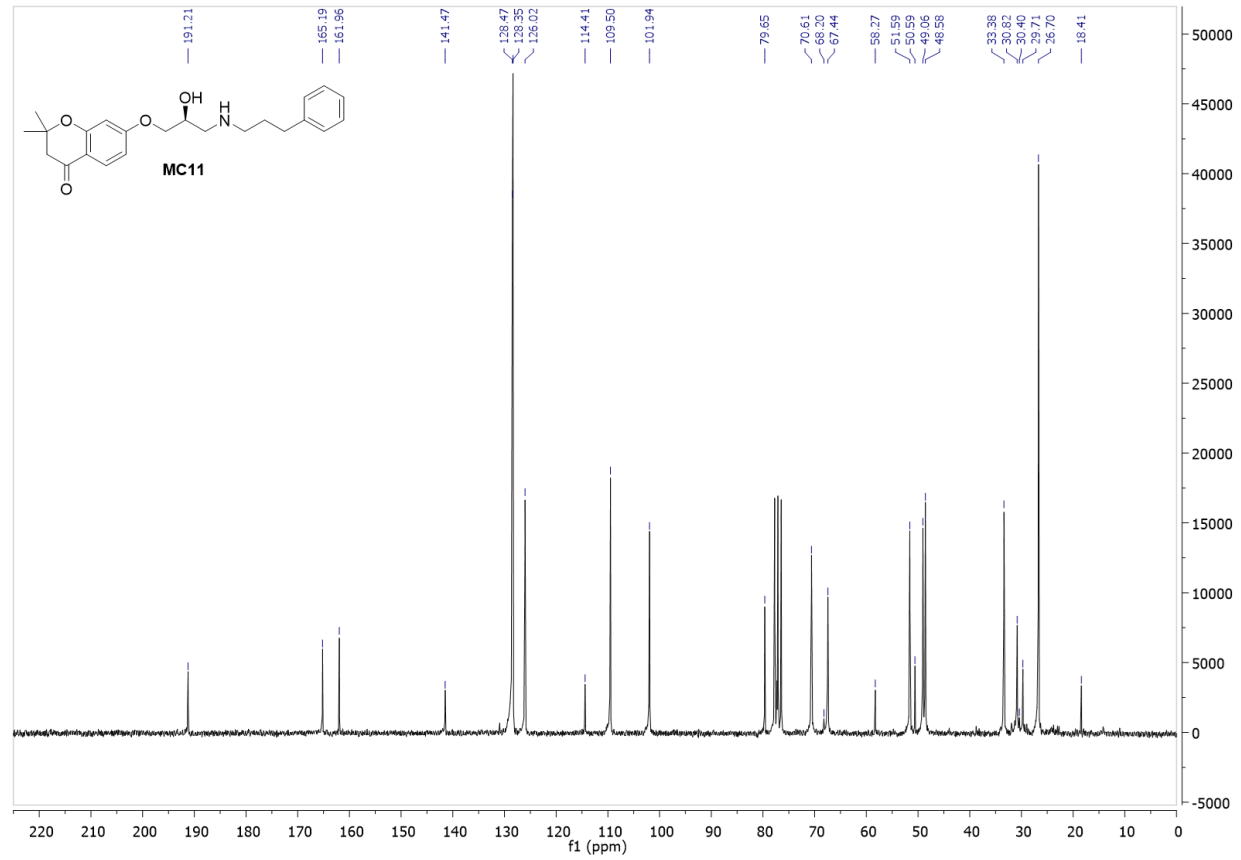


Figure S 42. ^{13}C-NMR of **MC11** (100 MHz, $CDCl_3$)

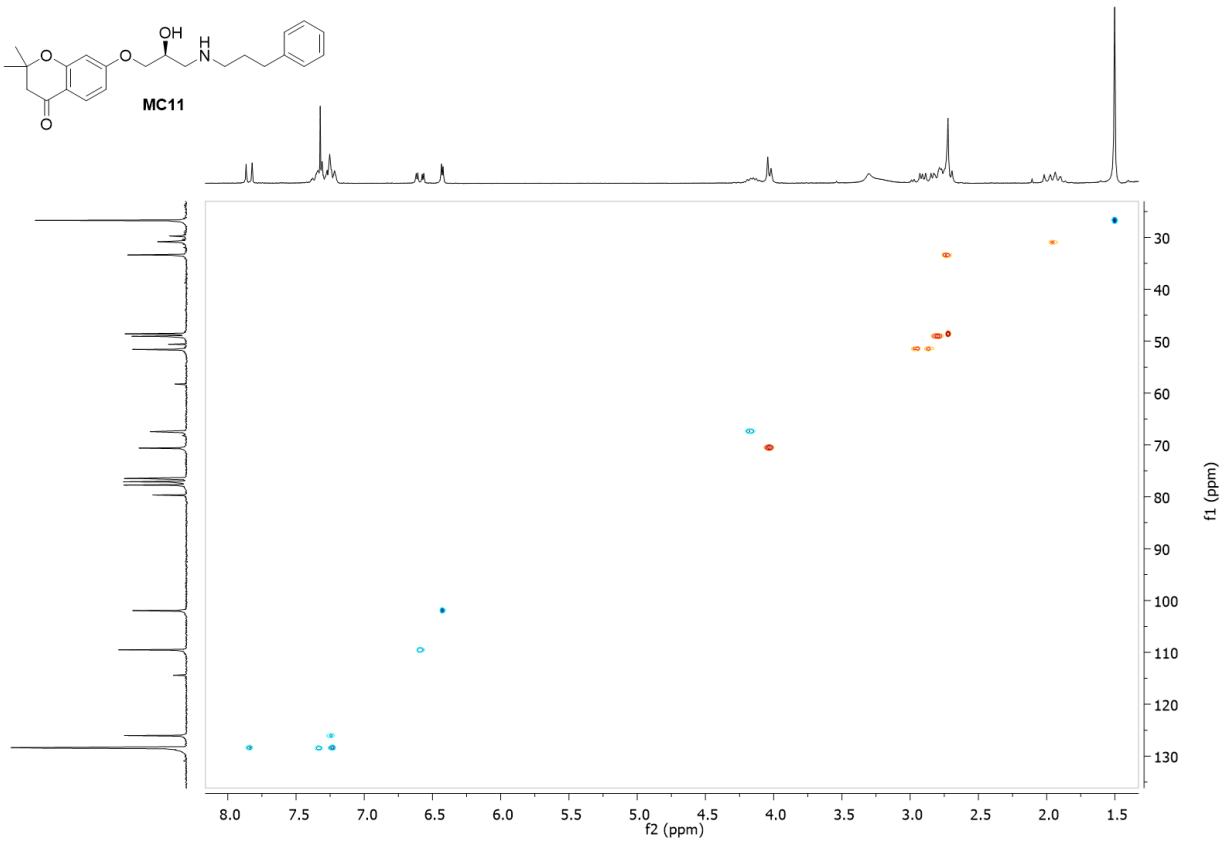


Figure S 43: gHSQC-NMR of **MC11** (400 MHz, $CDCl_3$)

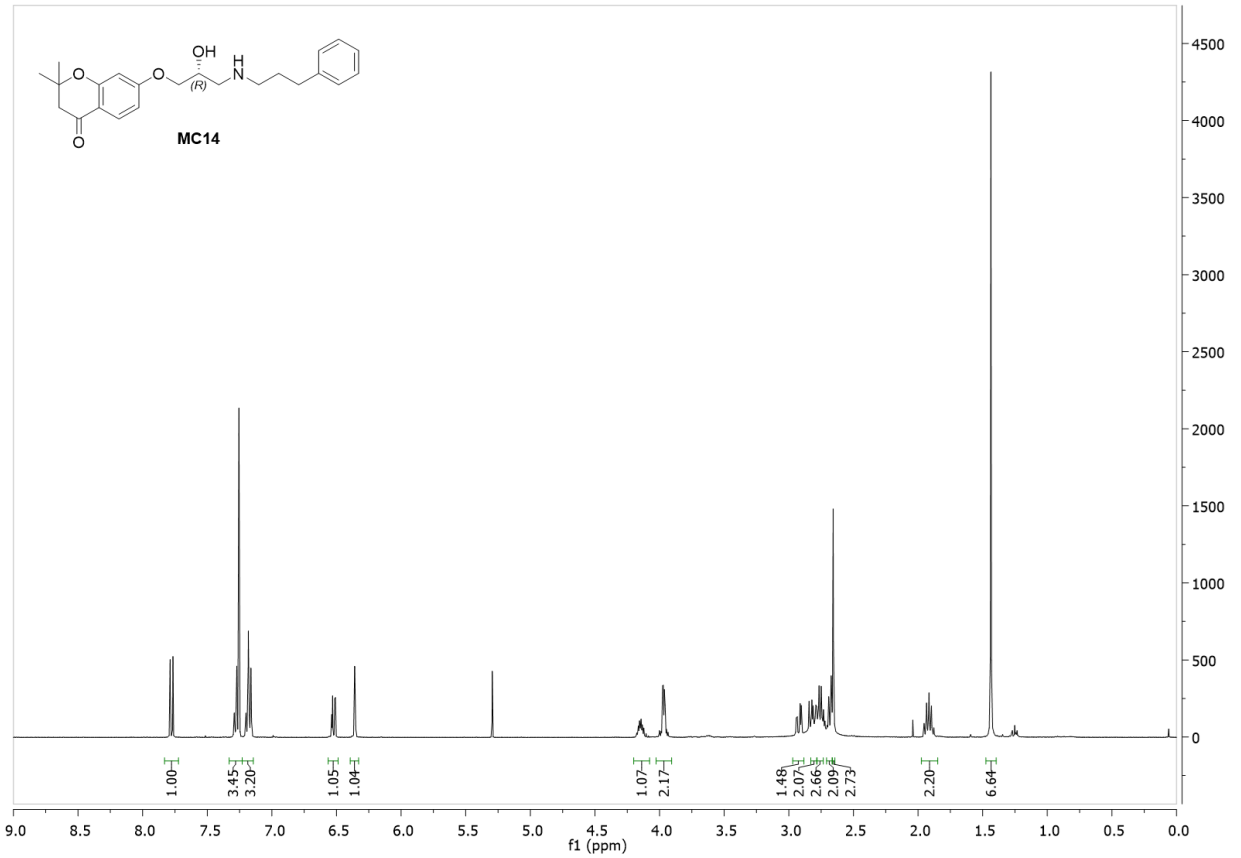


Figure S 44: ^{1}H-NMR of **MC14** (400 MHz, $CDCl_3$)

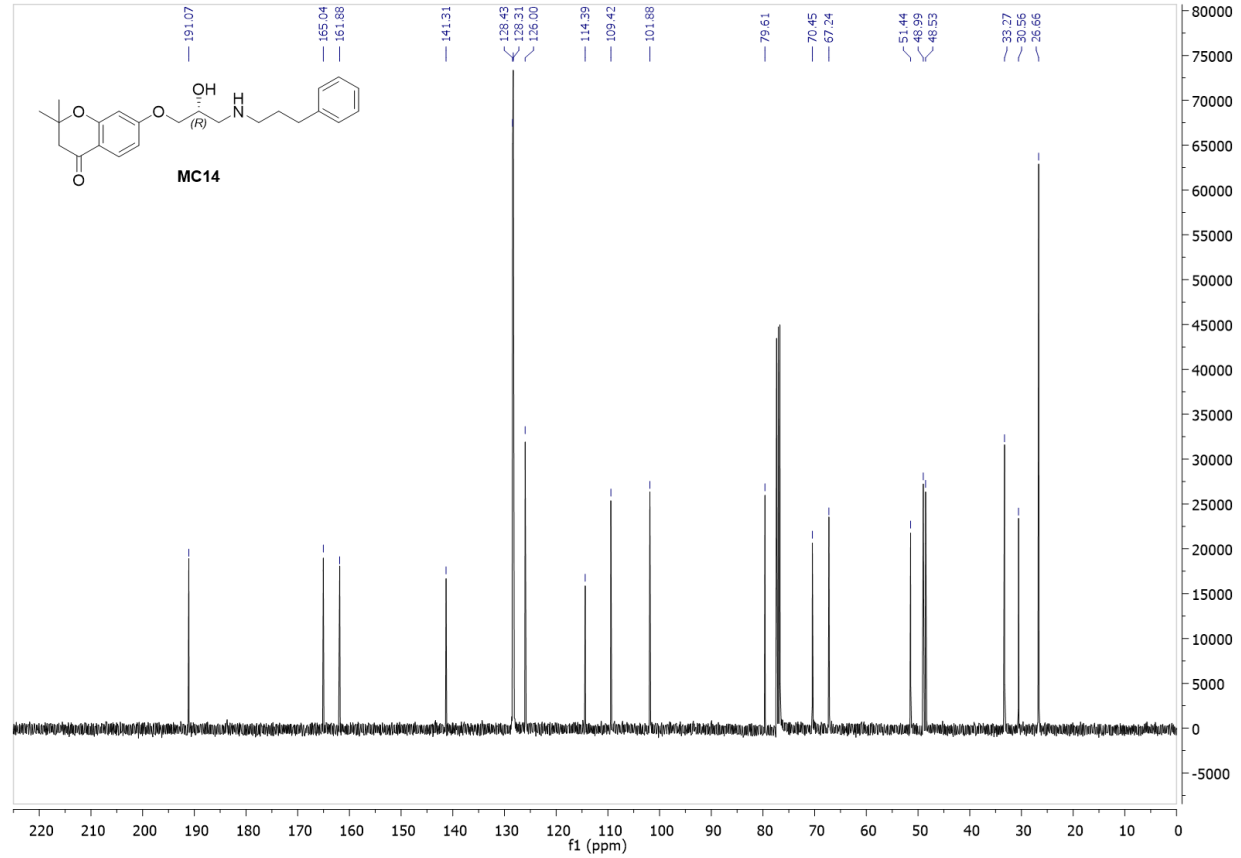


Figure S 45. ^{13}C-NMR of **MC14** (100 MHz, $CDCl_3$)

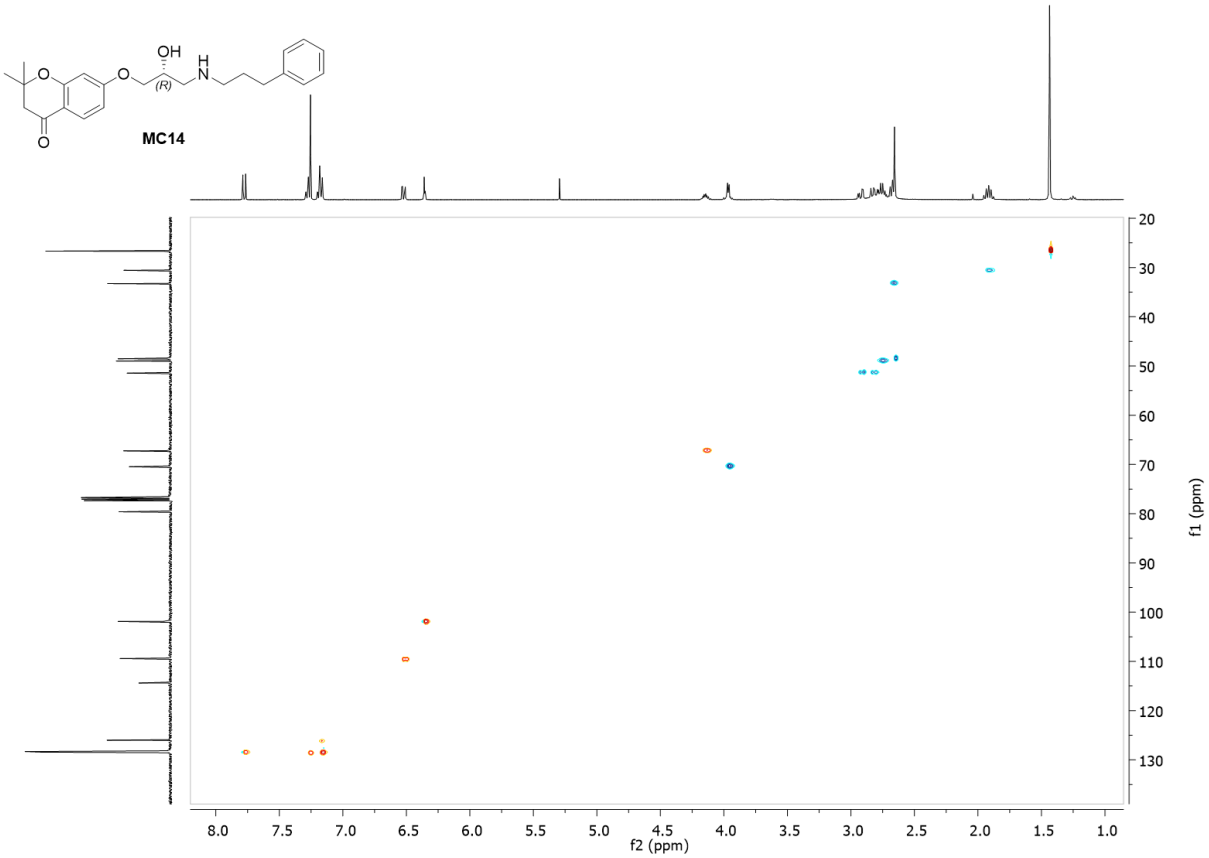


Figure S 46. gHSQC-NMR of **MC14** (400 MHz, $CDCl_3$)

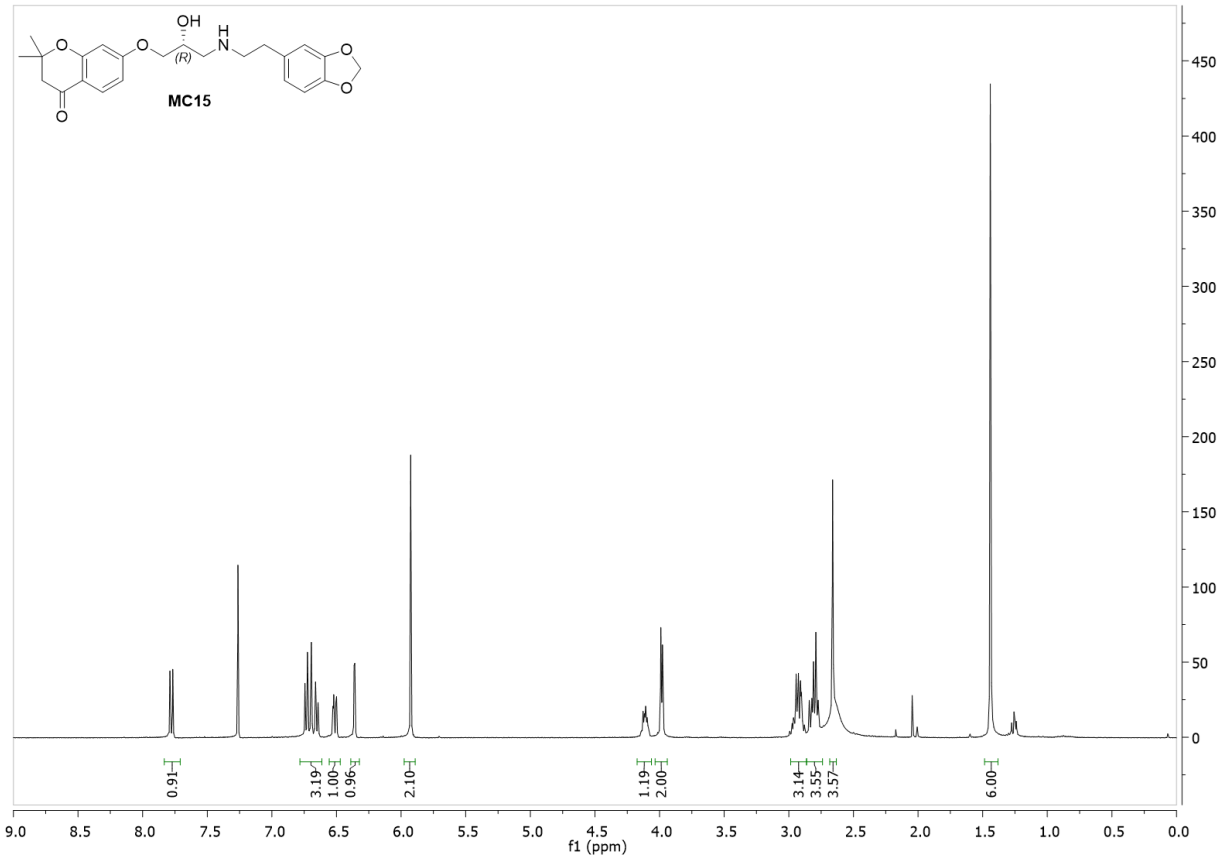


Figure S 47: ^{1}H-NMR of **MC15** (400 MHz, $CDCl_3$)

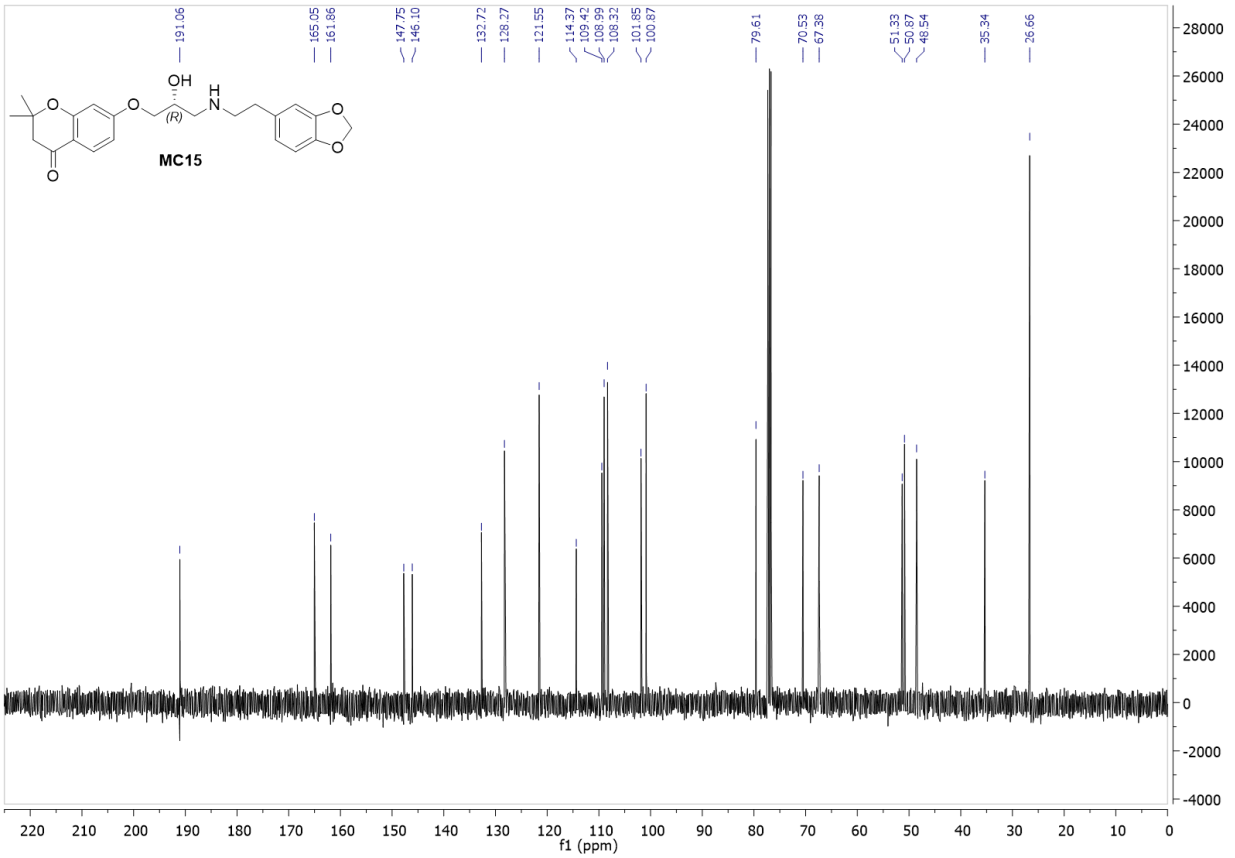


Figure S 48: ^{13}C-NMR of **MC15** (100 MHz, $CDCl_3$)

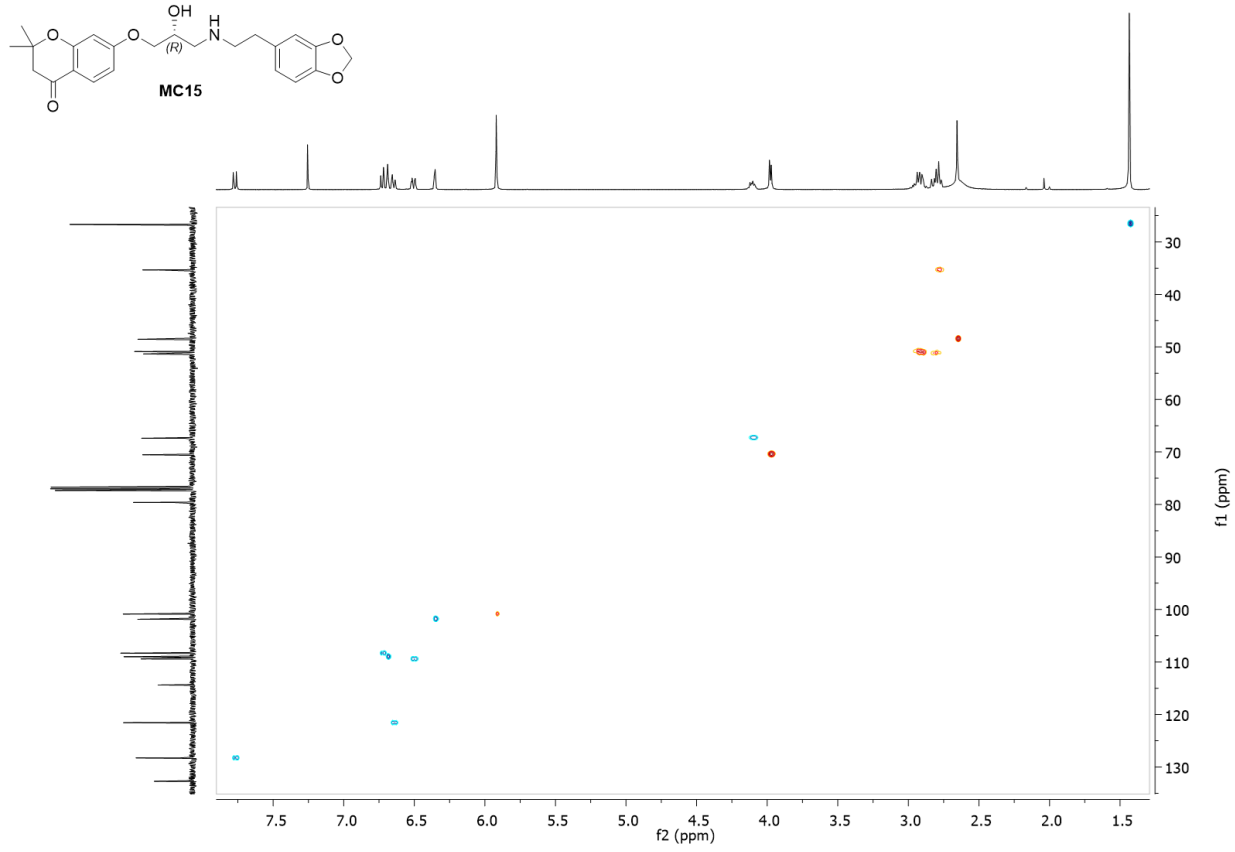


Figure S 49. gHSQC-NMR of **MC15** (400 MHz, $CDCl_3$)

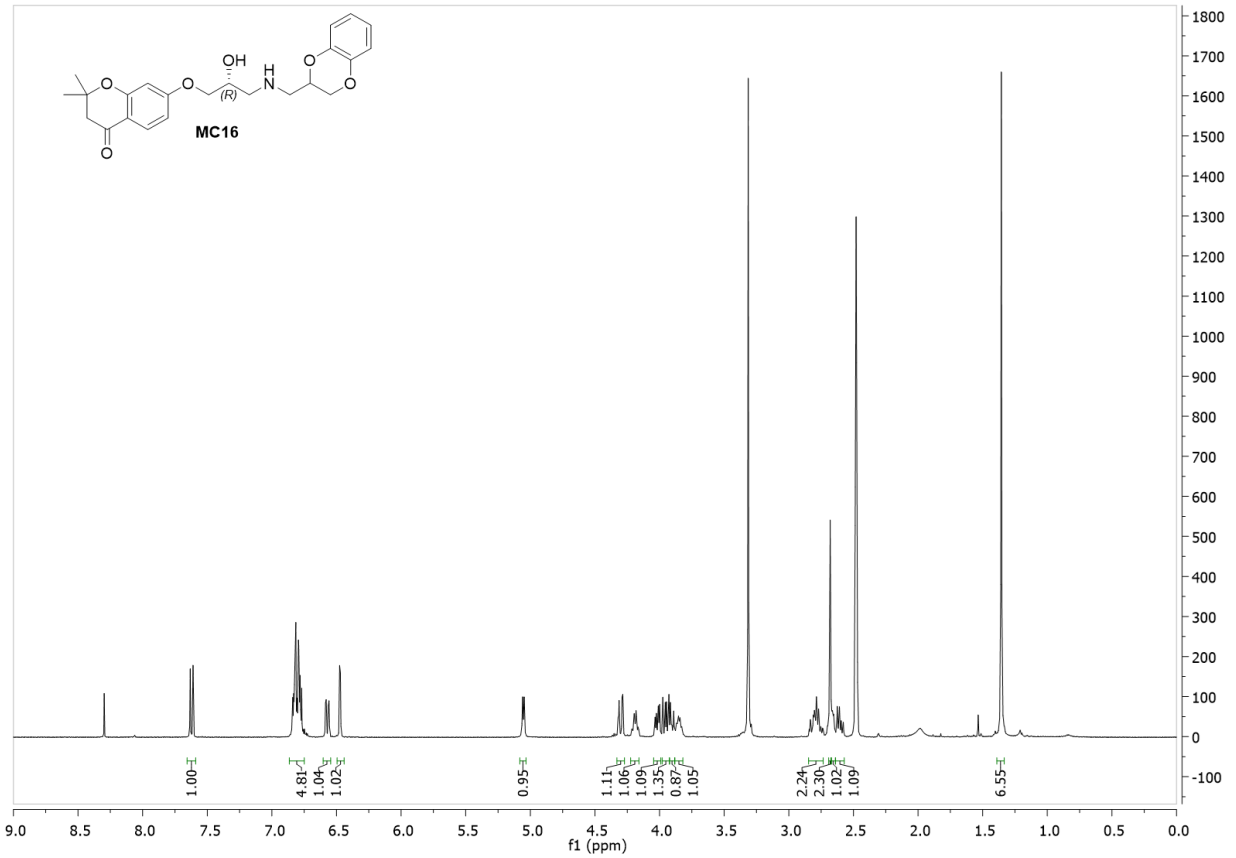


Figure S 50. ^{1}H-NMR of **MC16** (400 MHz, DMSO-d^{6})

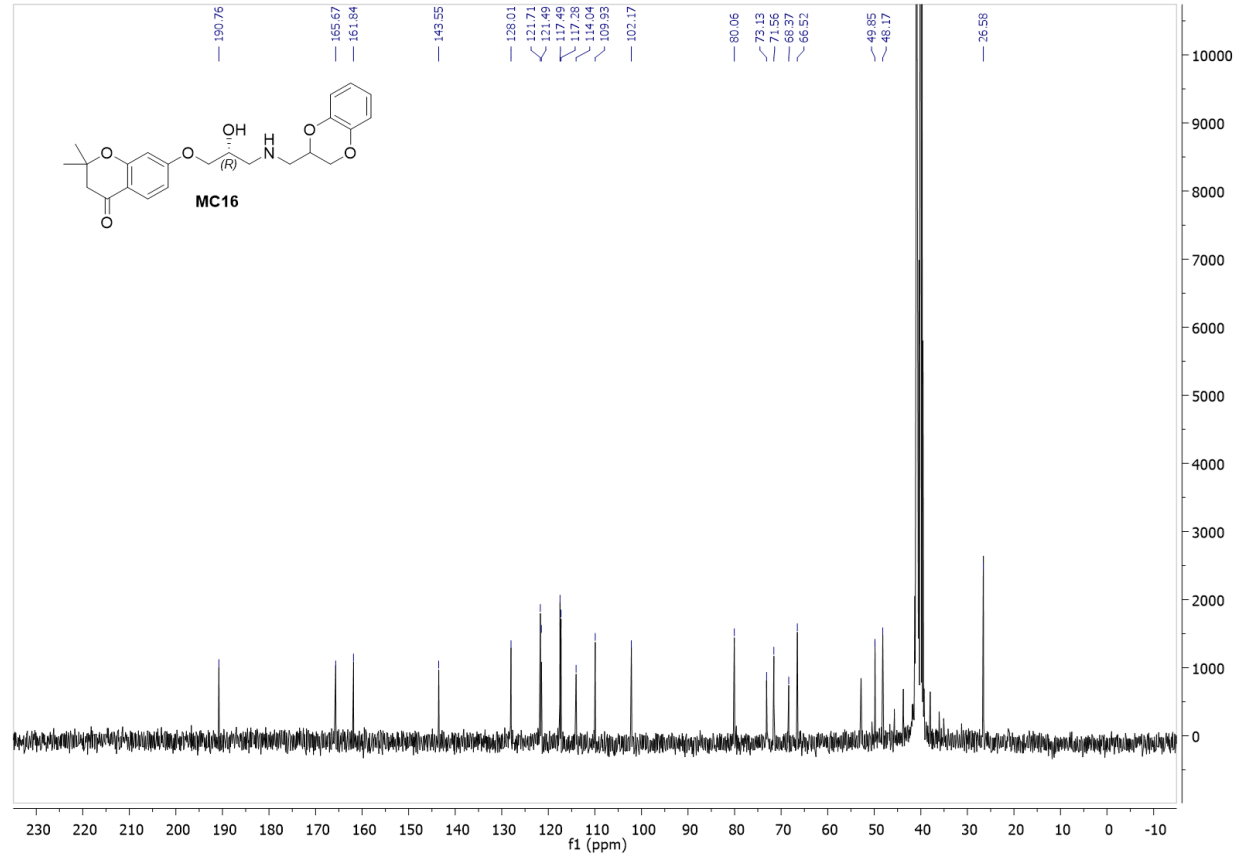


Figure S 51: ^{13}C-NMR of **MC16** (100 MHz, DMSO-d^{6})

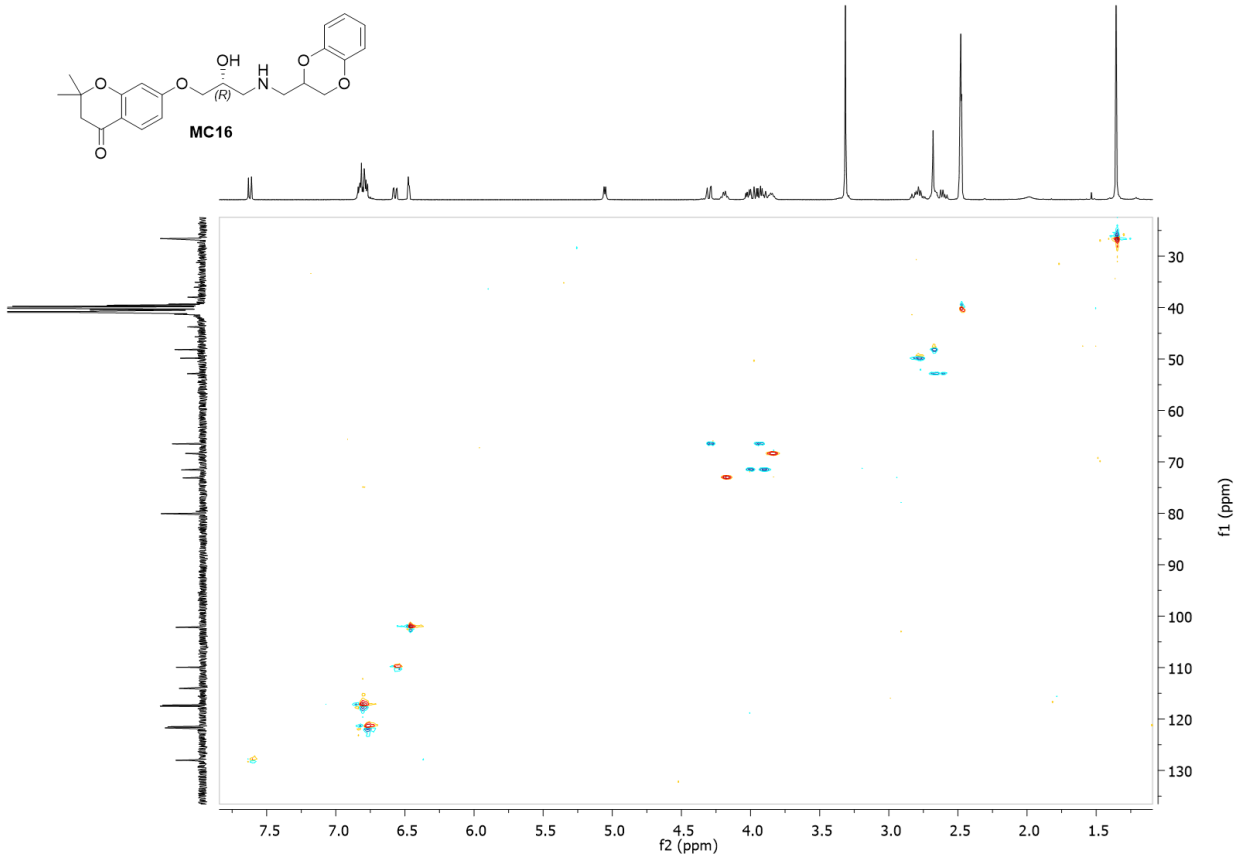


Figure S 52: gHSQC-NMR of **MC16** (400 MHz, DMSO-d^6)

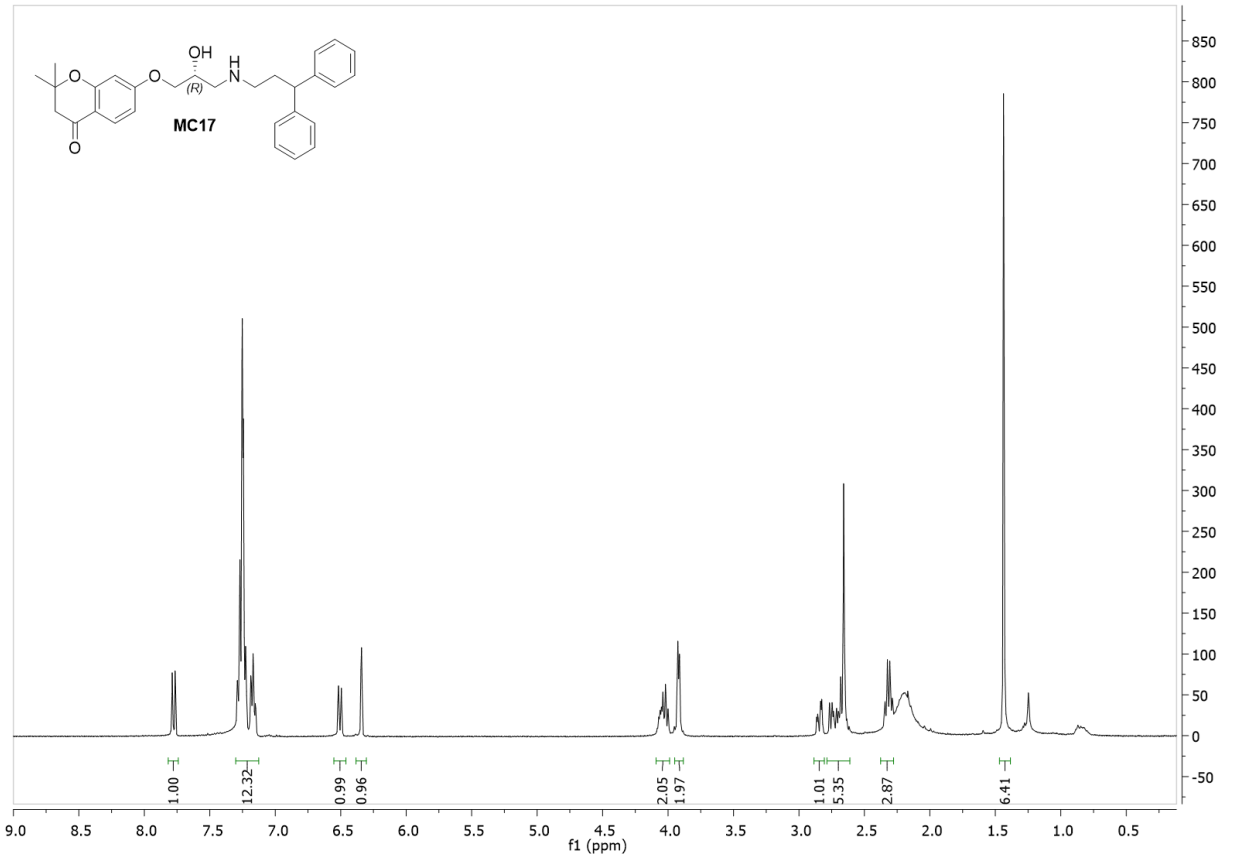


Figure S 53. ^{1}H-NMR of **MC17** (400 MHz, $CDCl_3$)

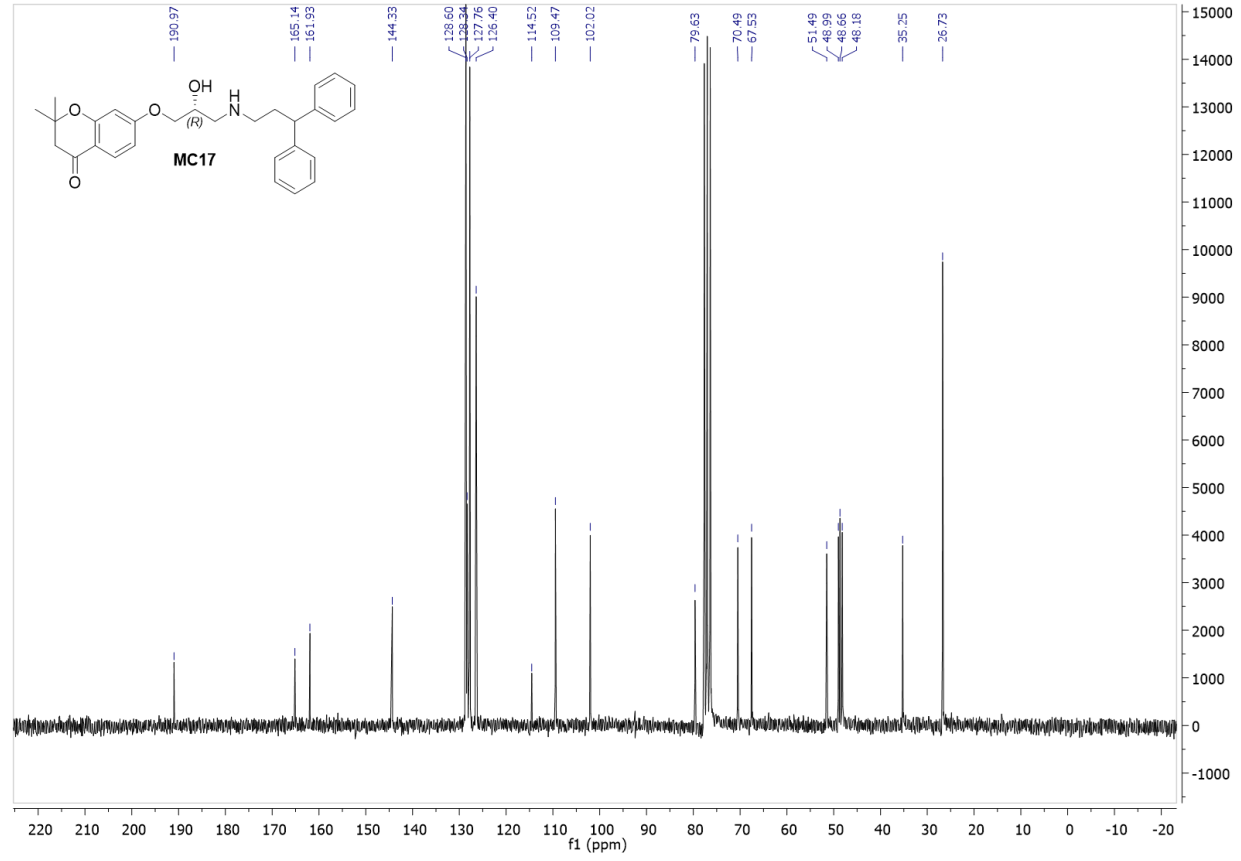


Figure S 54. ^{13}C-NMR of **MC17** (100 MHz, $CDCl_3$)

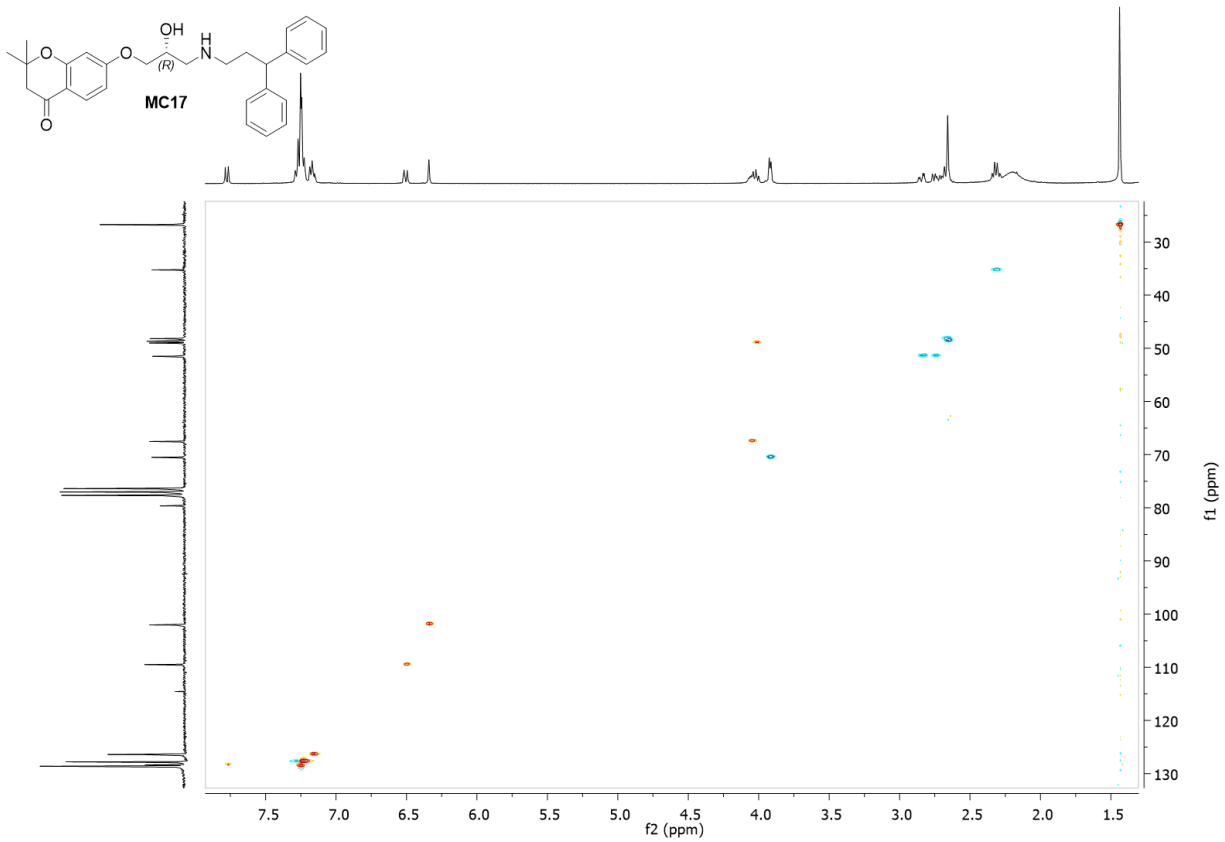


Figure S 55: gHSQC-NMR of **MC17** (400 MHz, $CDCl_3$)

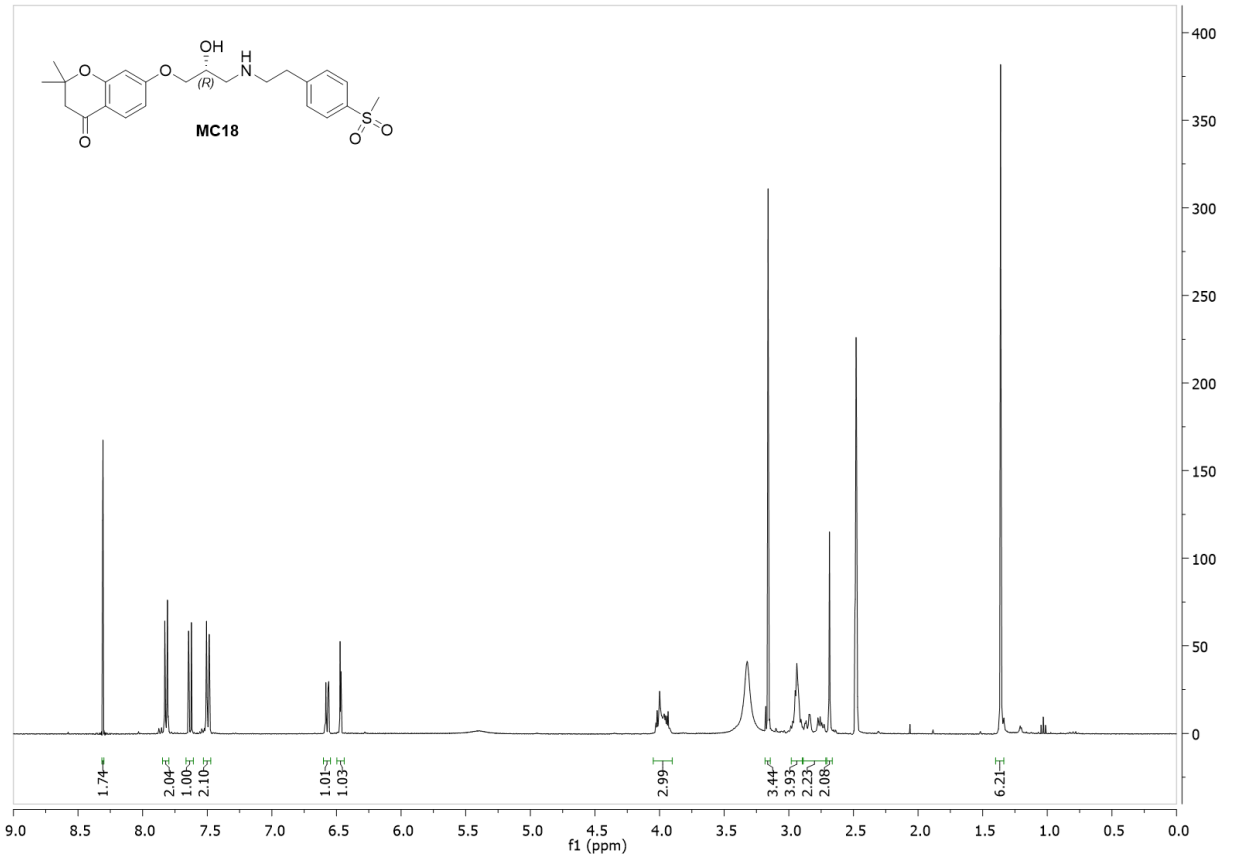


Figure S 56: ^{1}H-NMR of **MC18** (400 MHz, DMSO-d^{6})

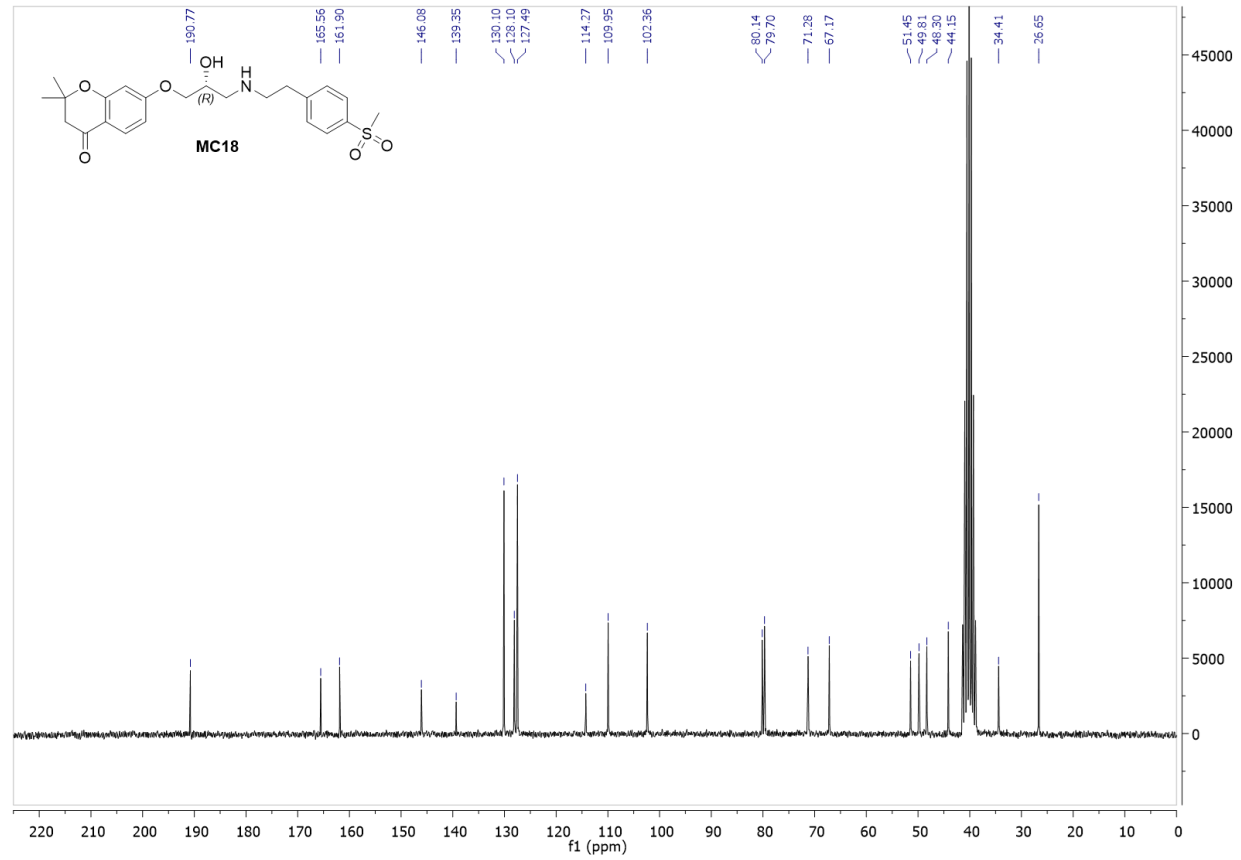


Figure S 57. ^{13}C-NMR of **MC18** (100 MHz, DMSO-d^{6})

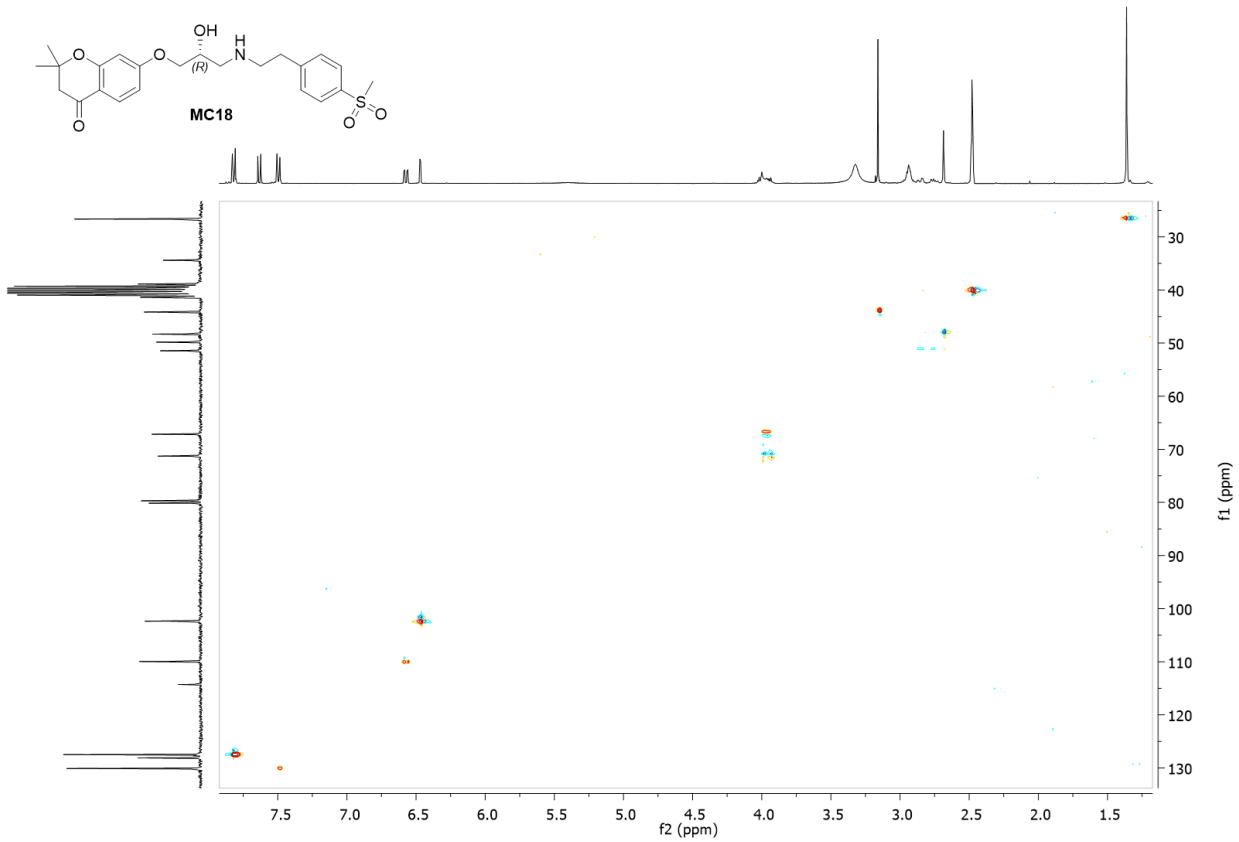


Figure S 58. gHSQC-NMR of **MC18** (400 MHz, DMSO-d^6)

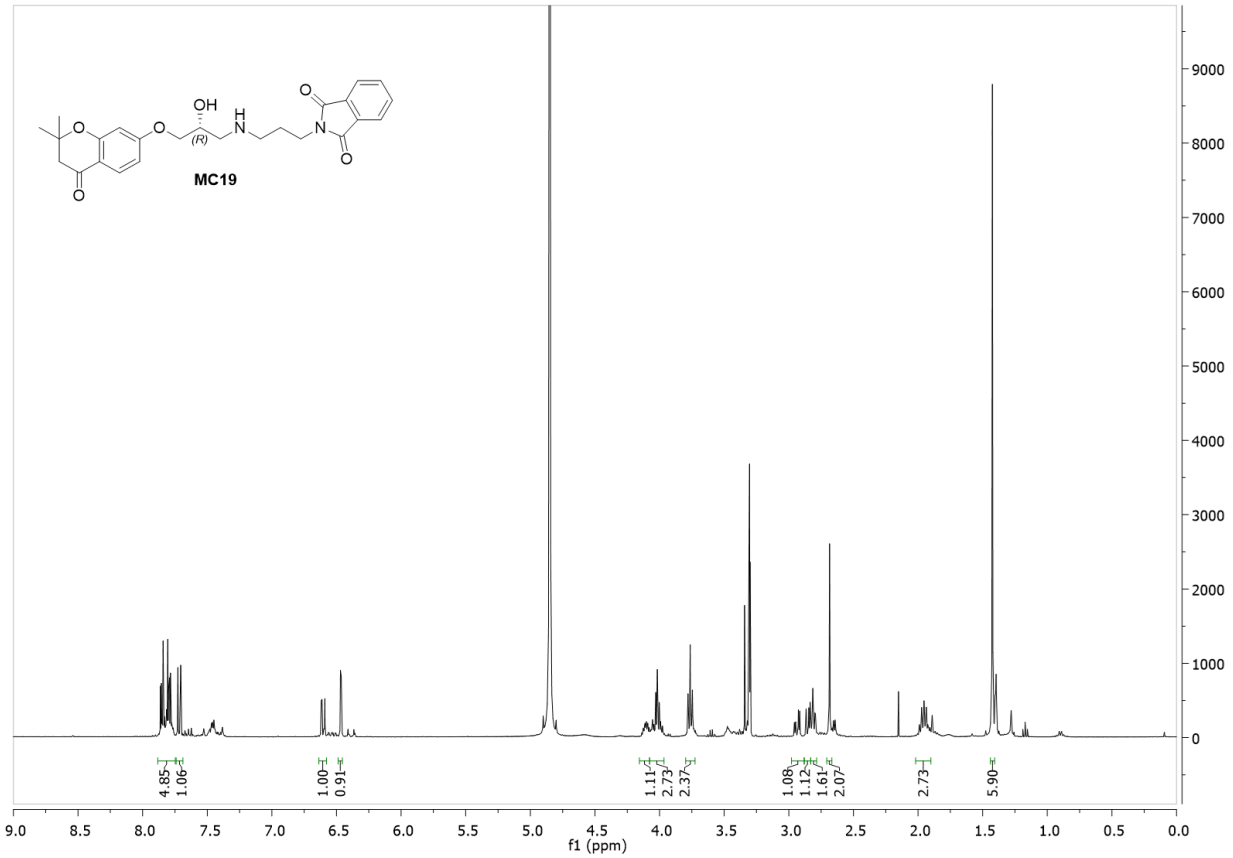


Figure S 59. ^{1}H-NMR of **MC19** (400 MHz, CD_3OD)

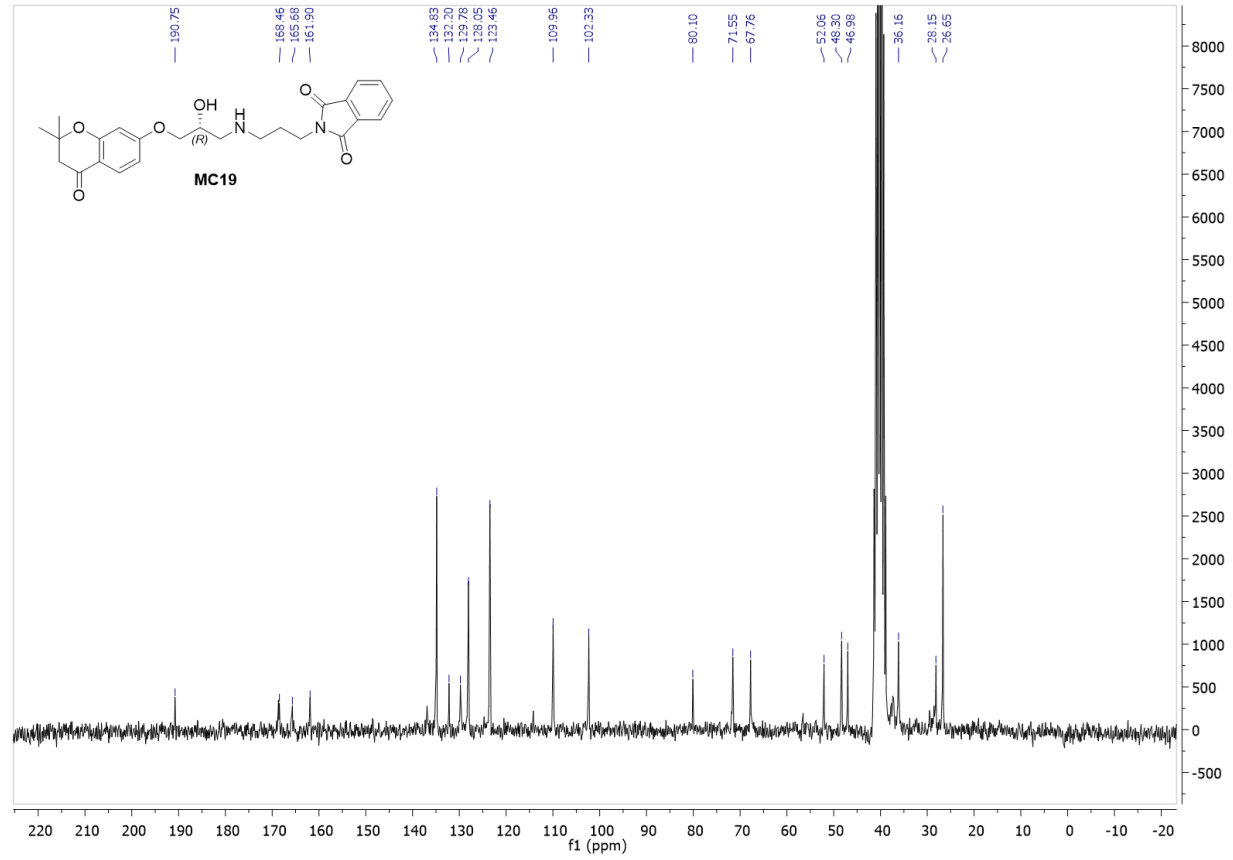


Figure S 60. ^{13}C-NMR of **MC19** (100 MHz, CD_3OD)

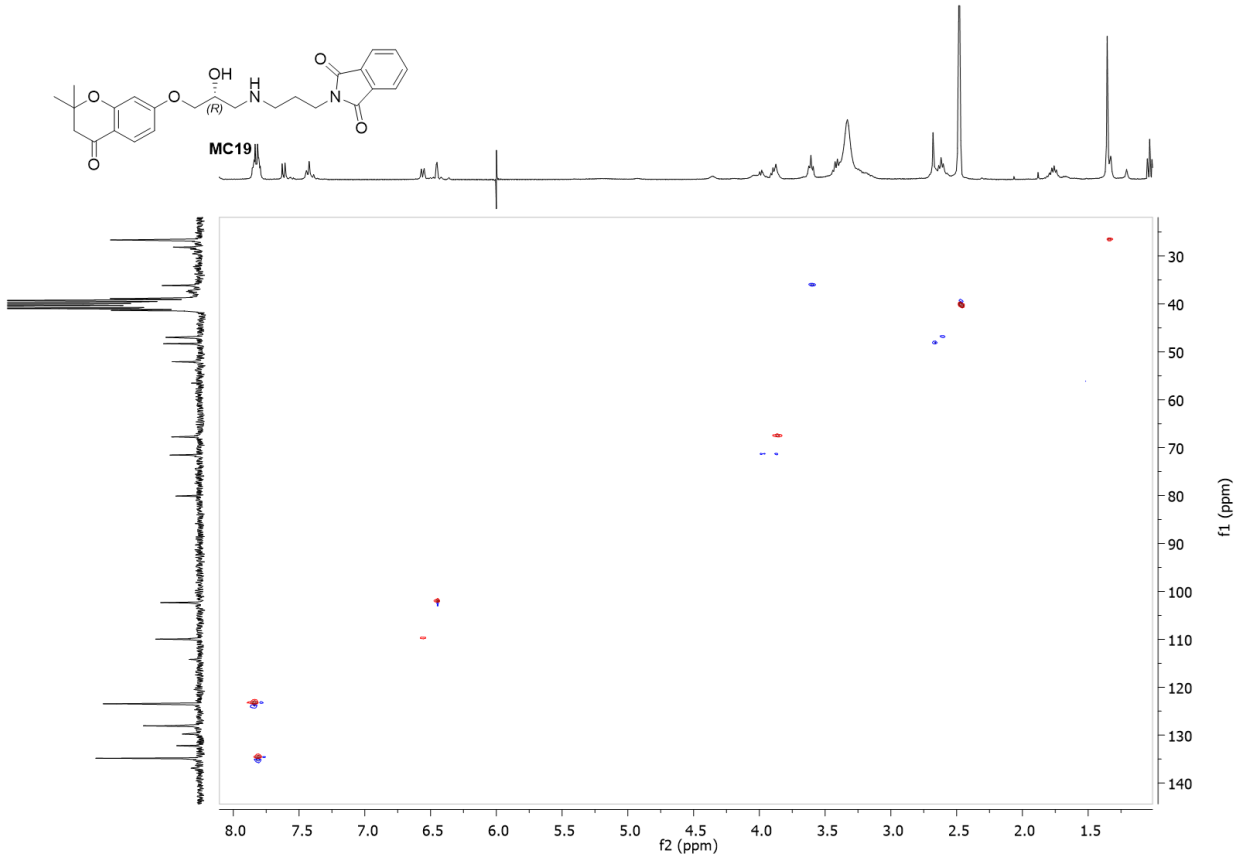


Figure S 61. gHSQC-NMR of **MC19** (400 MHz, DMSO-d^6)

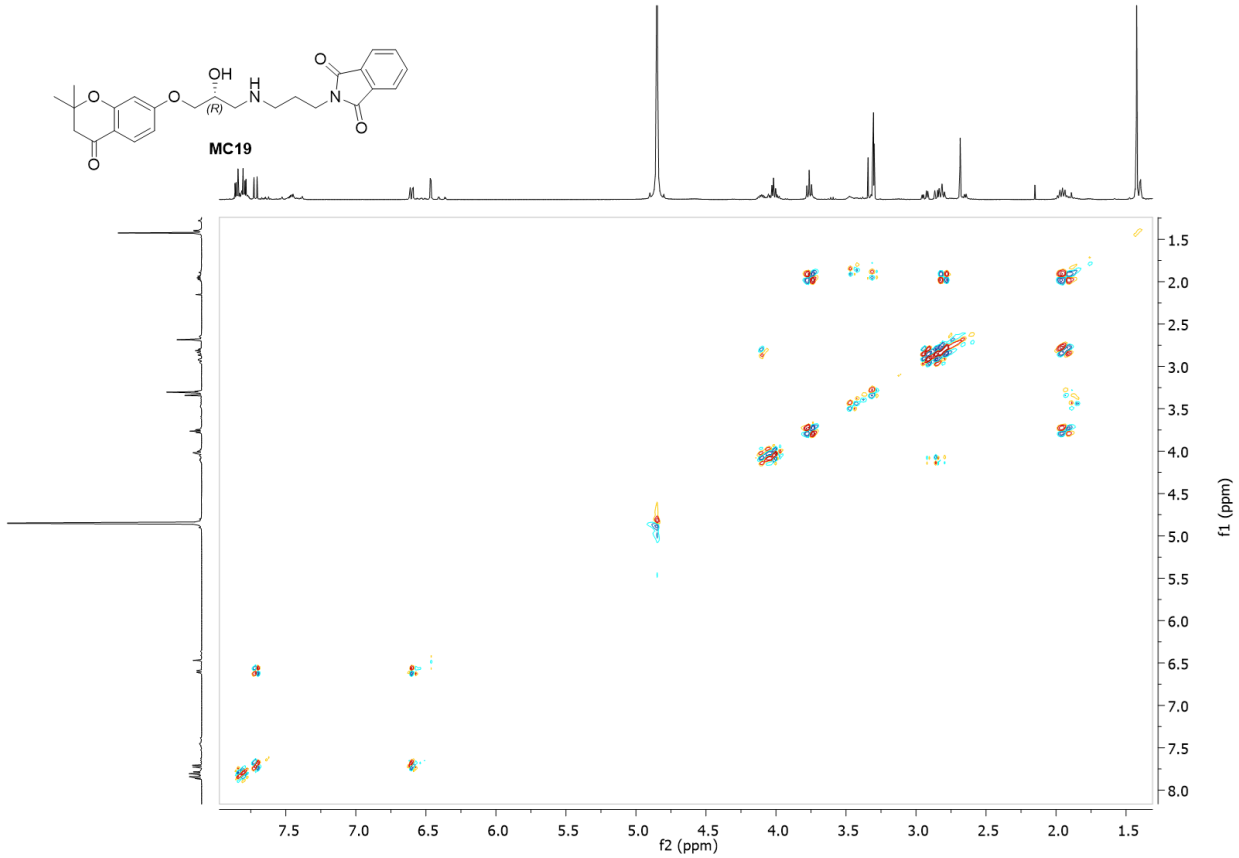


Figure S 62. gDQCOSY-NMR of **MC19** (400 MHz, CD_3OD)

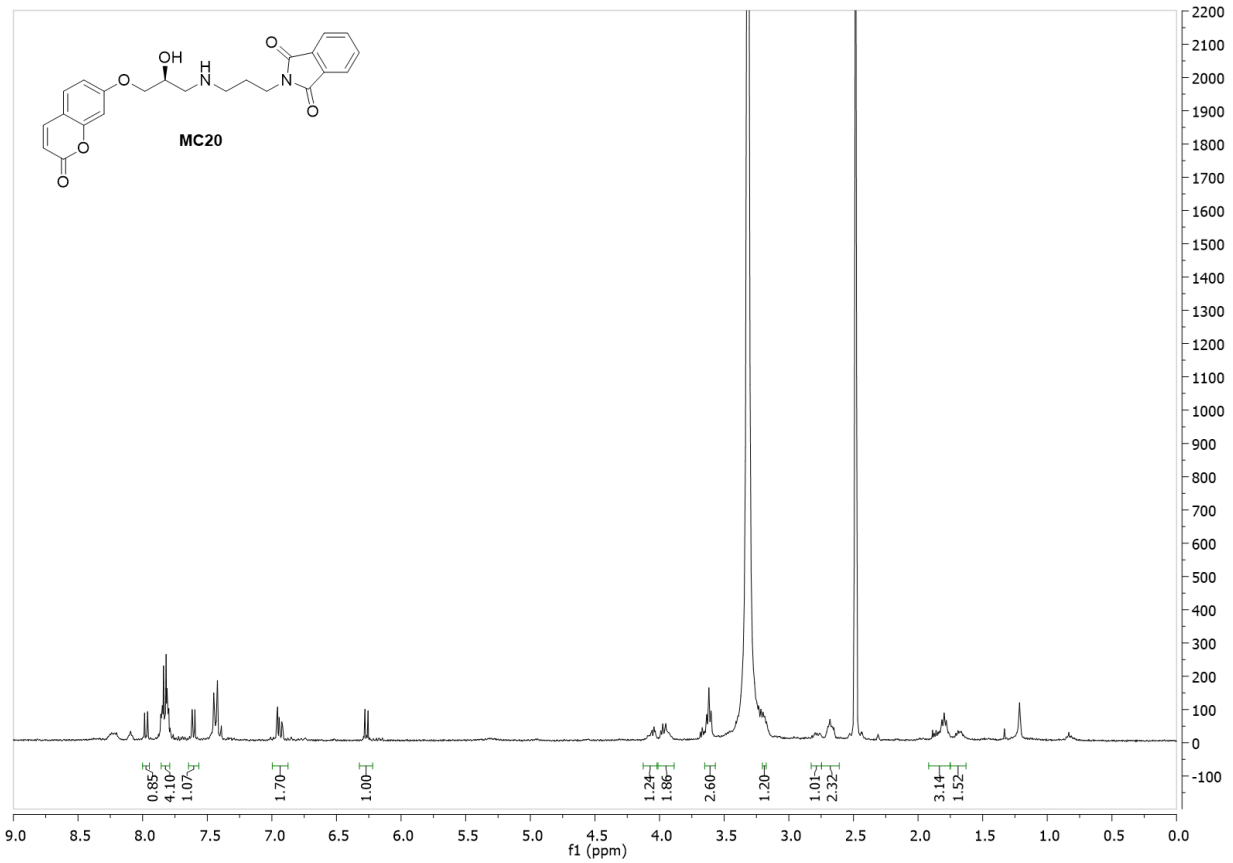


Figure S 63: ^{1}H-NMR of **MC20** (400 MHz, DMSO-d^{6})

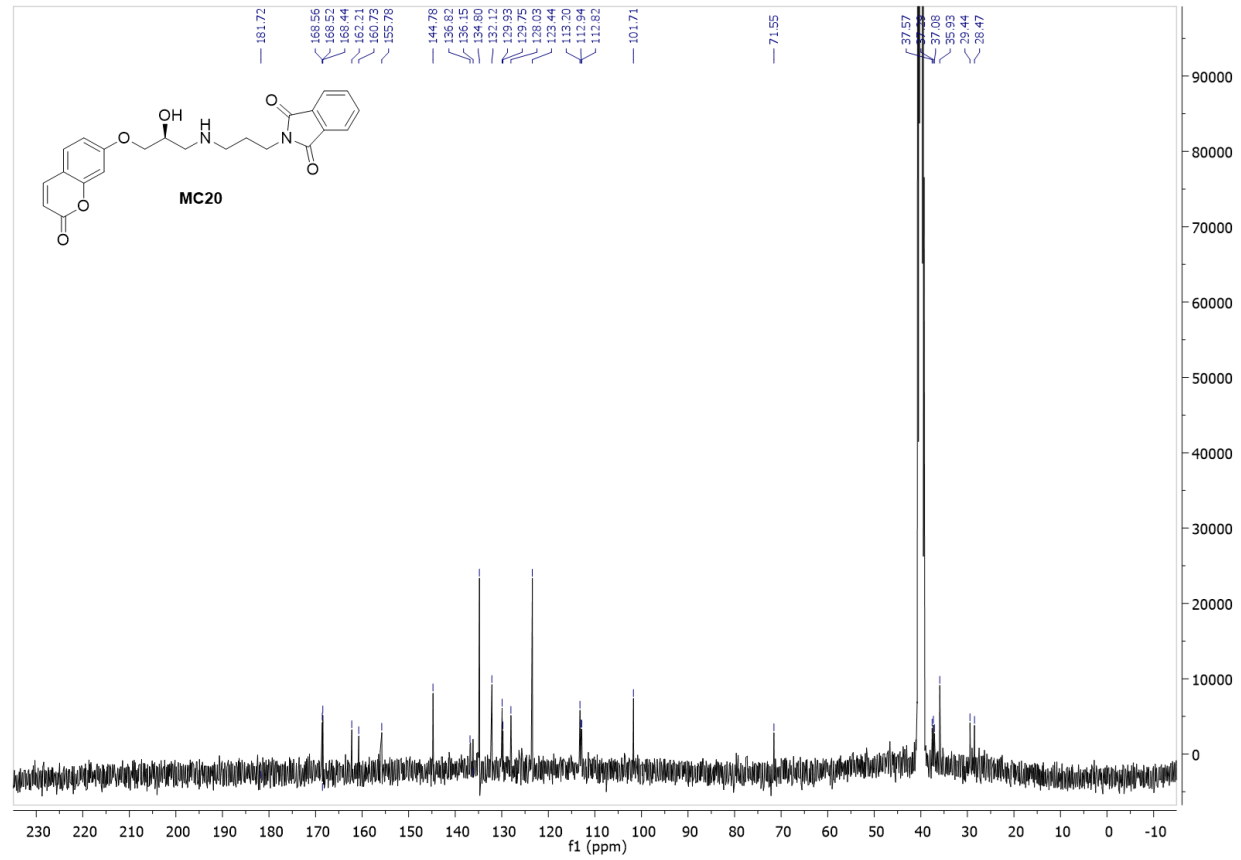


Figure S 64: ^{13}C-NMR of **MC20** (100 MHz, DMSO-d^{6})

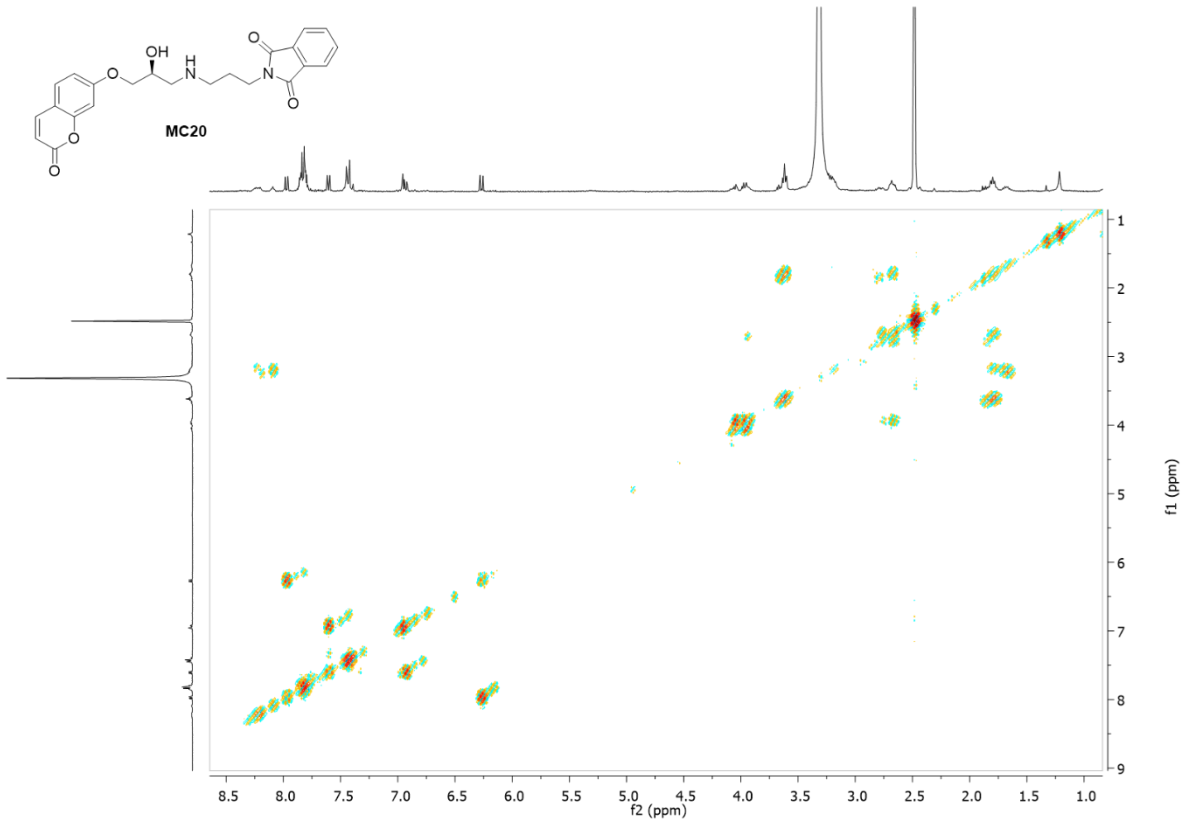


Figure S 65. gCOSY-NMR of **MC20** (400 MHz, DMSO-d^6)

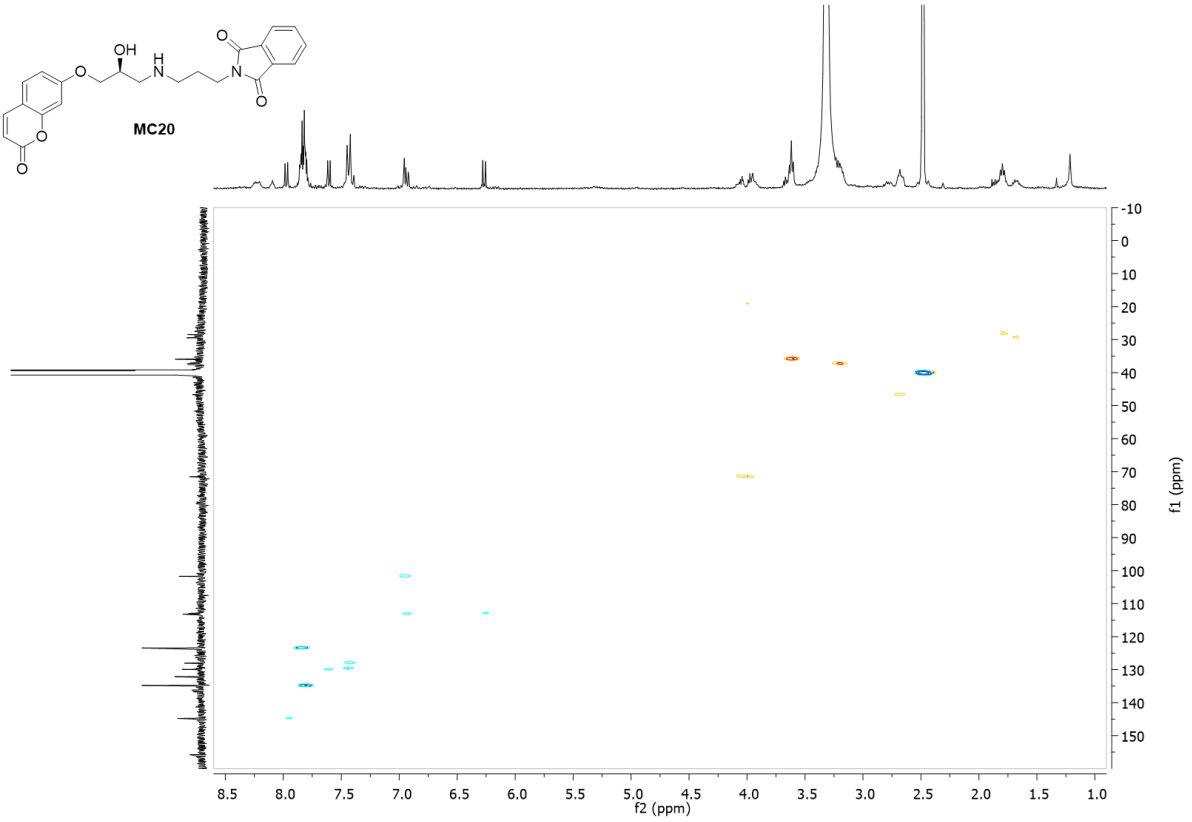


Figure S 66. gHSQC-NMR of MC20 (400 MHz, DMSO-d6)

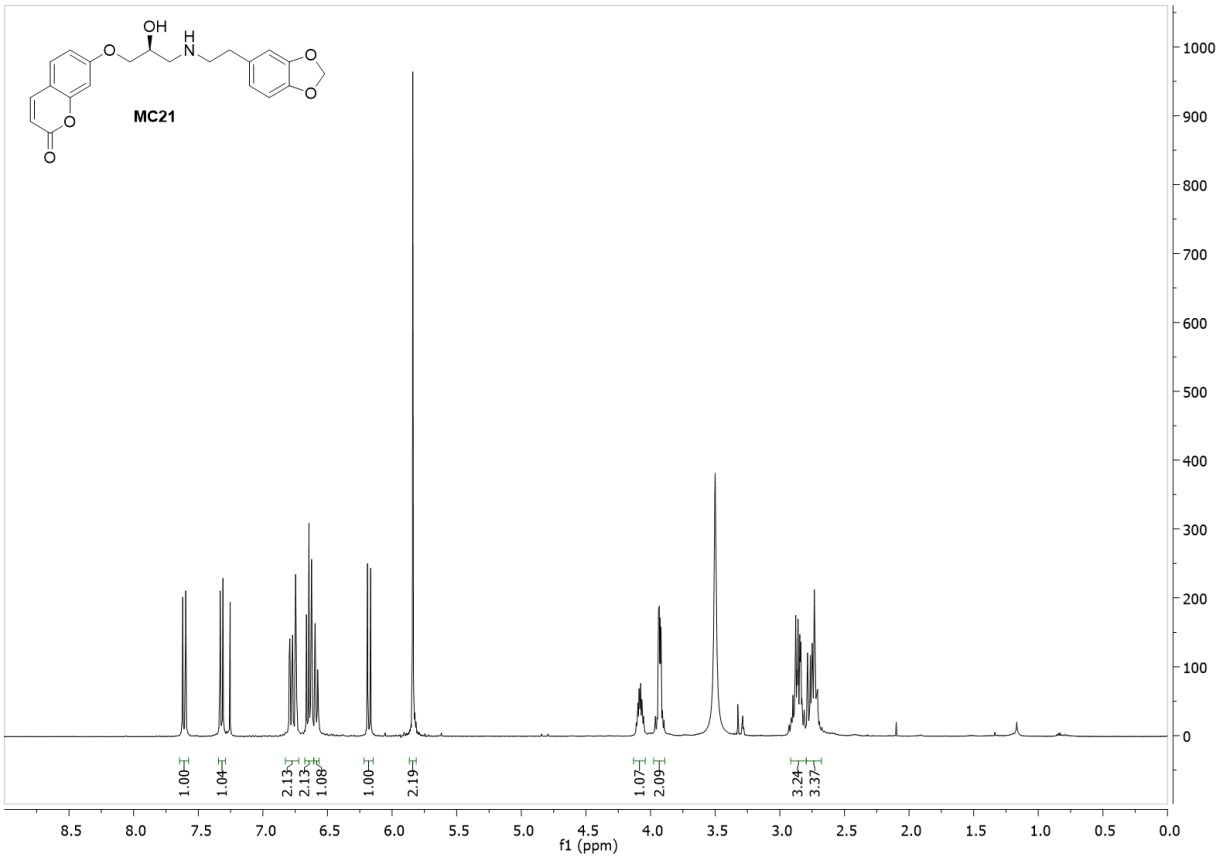


Figure S 67. ^{1}H-NMR of **MC21** (400 MHz, $CDCl_3$ +5% CD_3OD)

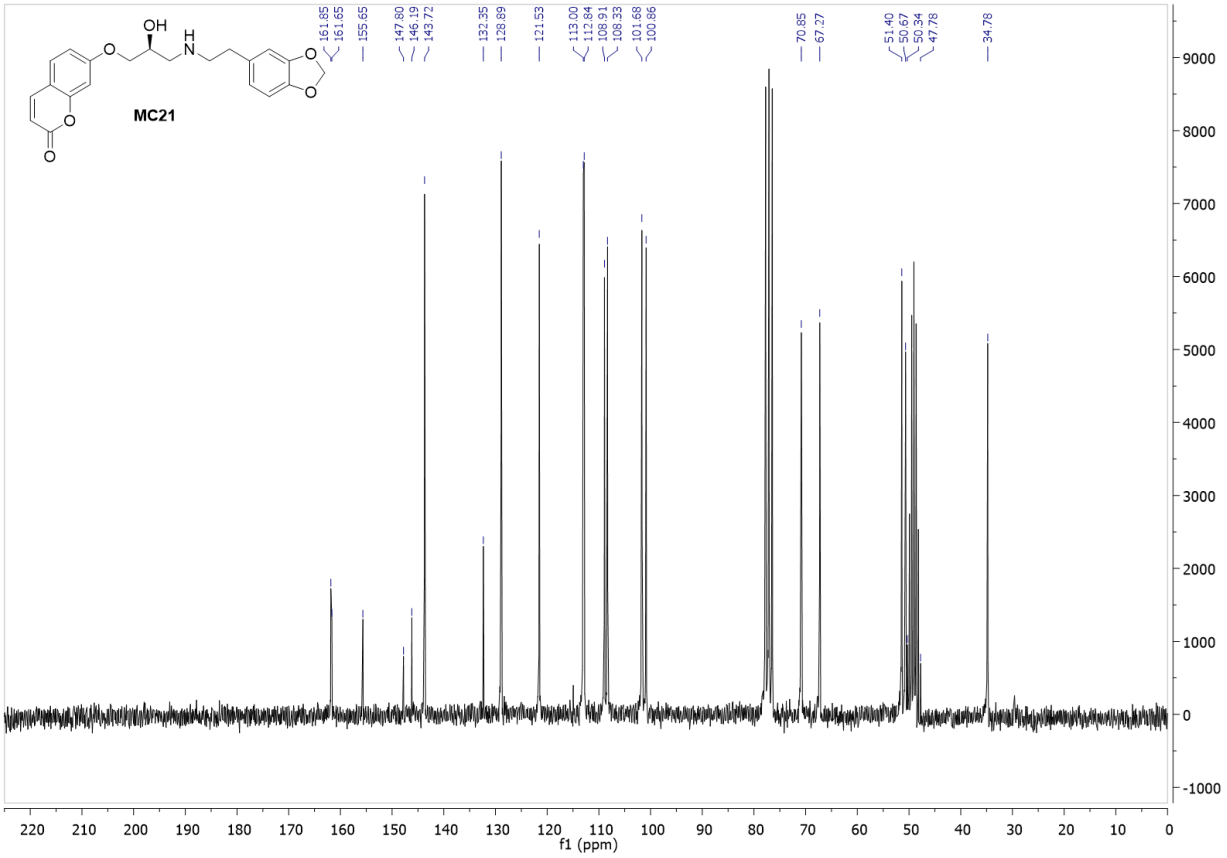


Figure S 68. ^{13}C-NMR of **MC21** (100 MHz, $CDCl_3$ +5% CD_3OD)

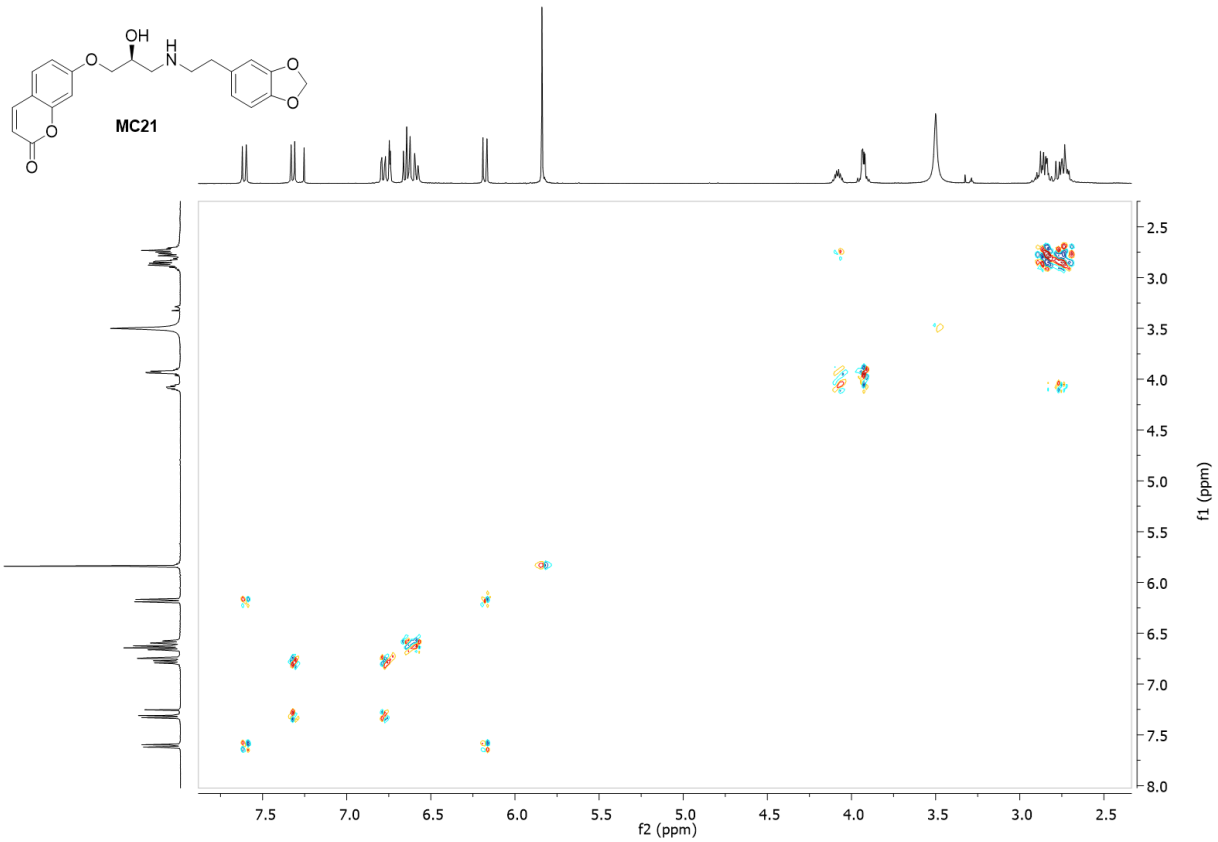


Figure S 69. gDQCOSY-NMR of **MC21** (400 MHz, $CDCl_3$ +5% CD_3OD)

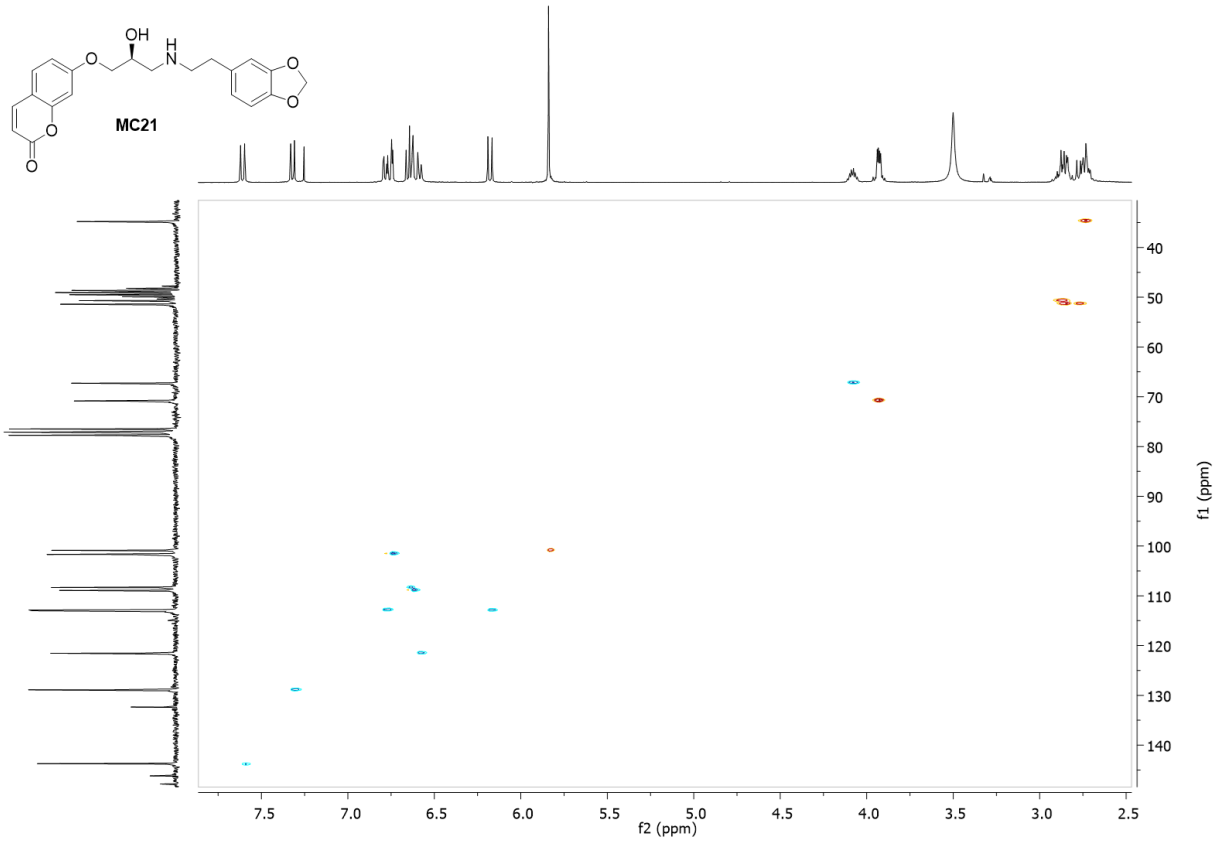


Figure S 70. gHSQC-NMR of **MC21** (400 MHz, $CDCl_3$ +5% CD_3OD)

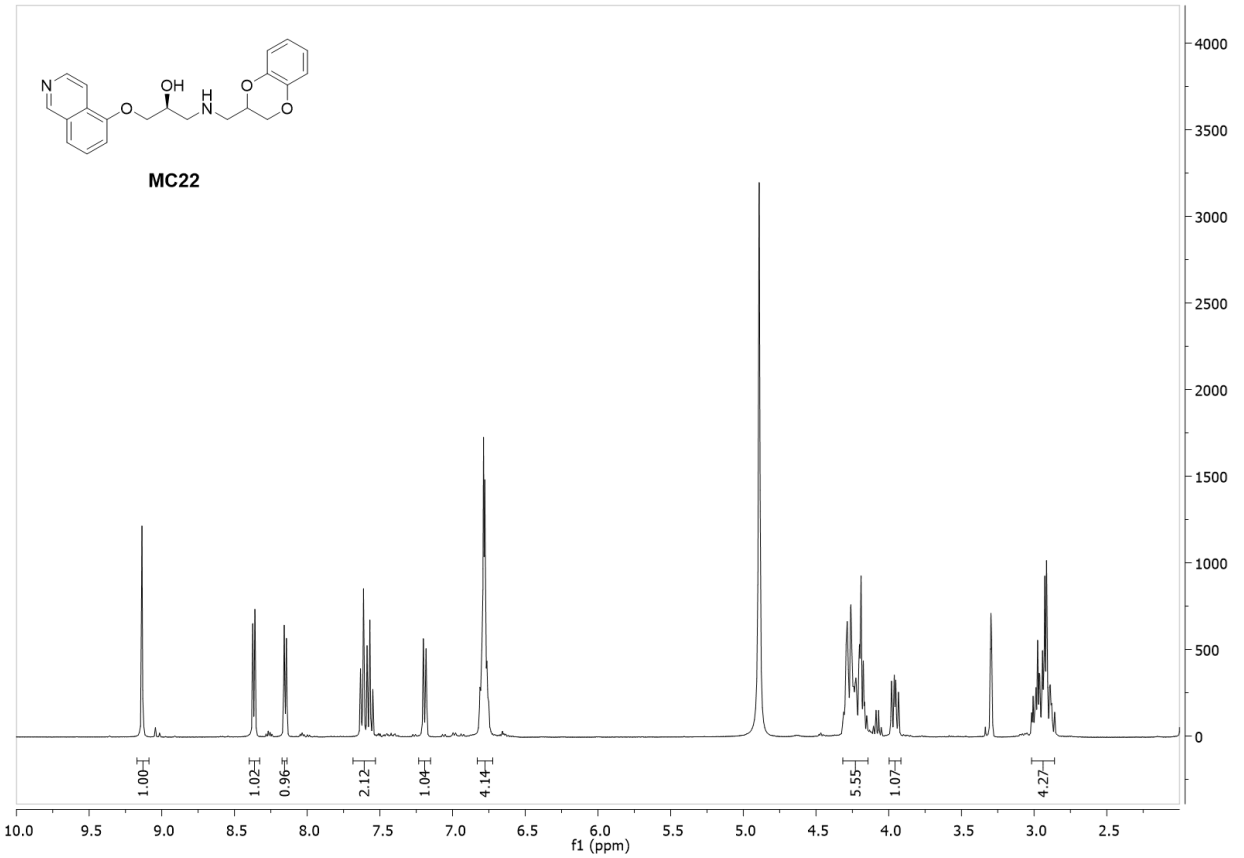


Figure S 71. ^{1}H-NMR of **MC22** (400 MHz, CD_3OD)

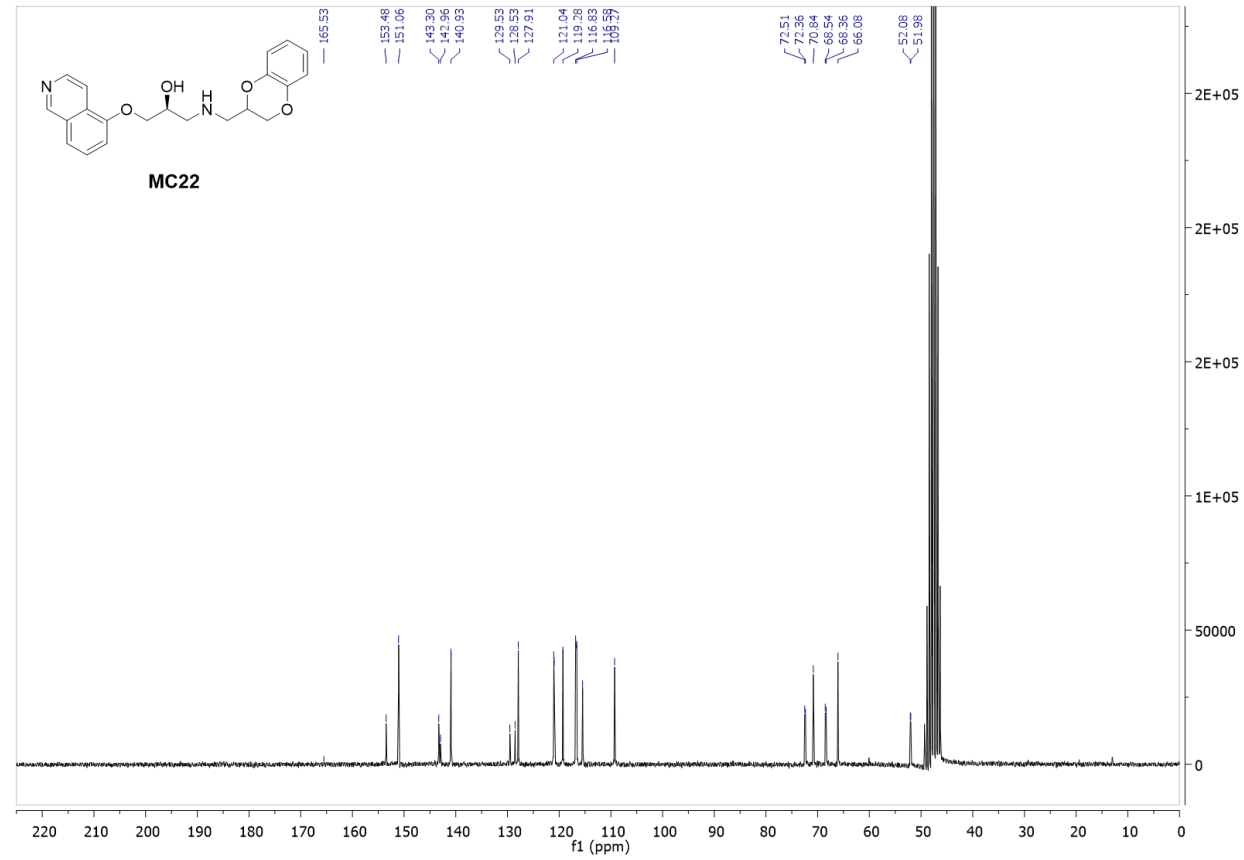


Figure S 72. ^{13}C-NMR of **MC22** (400 MHz, CD_3OD)

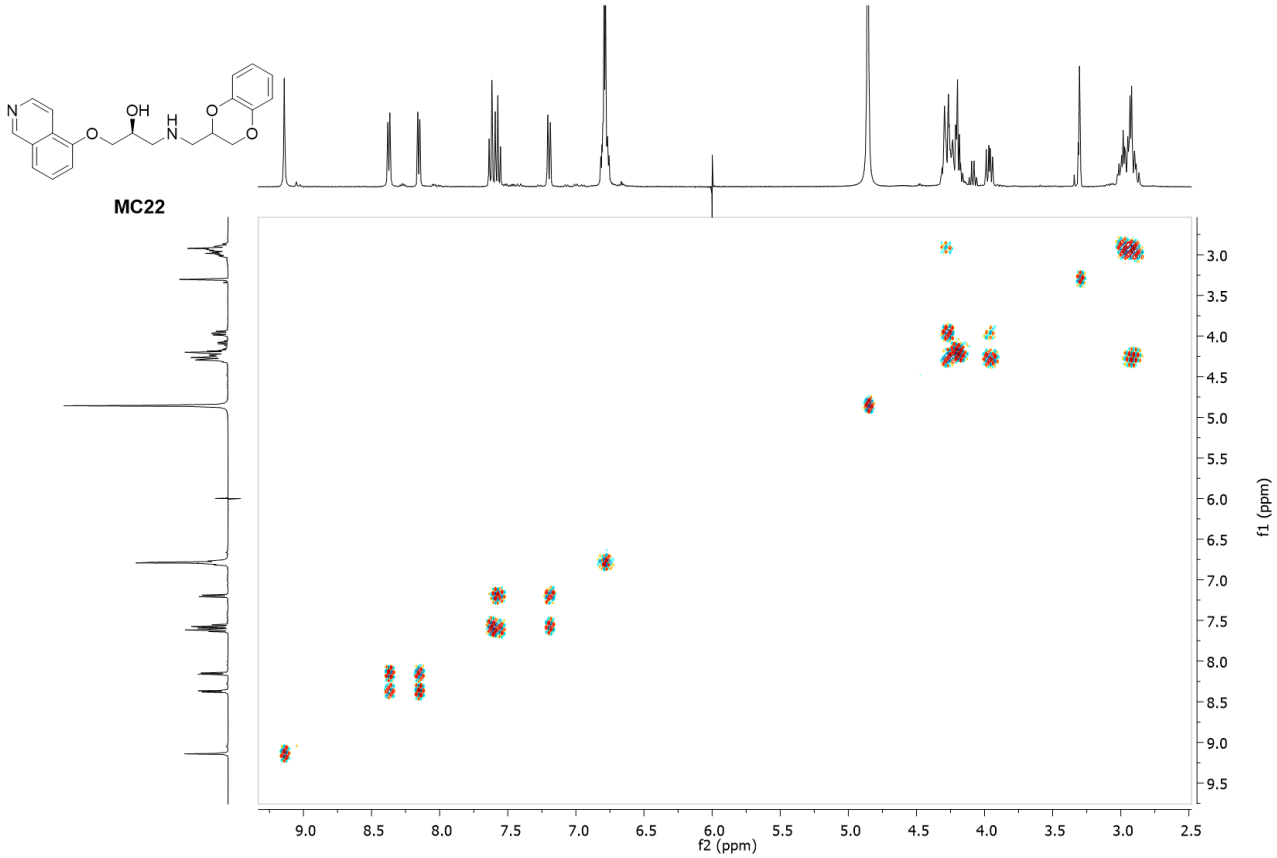


Figure S 73. gDQCOSY-NMR of **MC22** (400 MHz, CD_3OD)

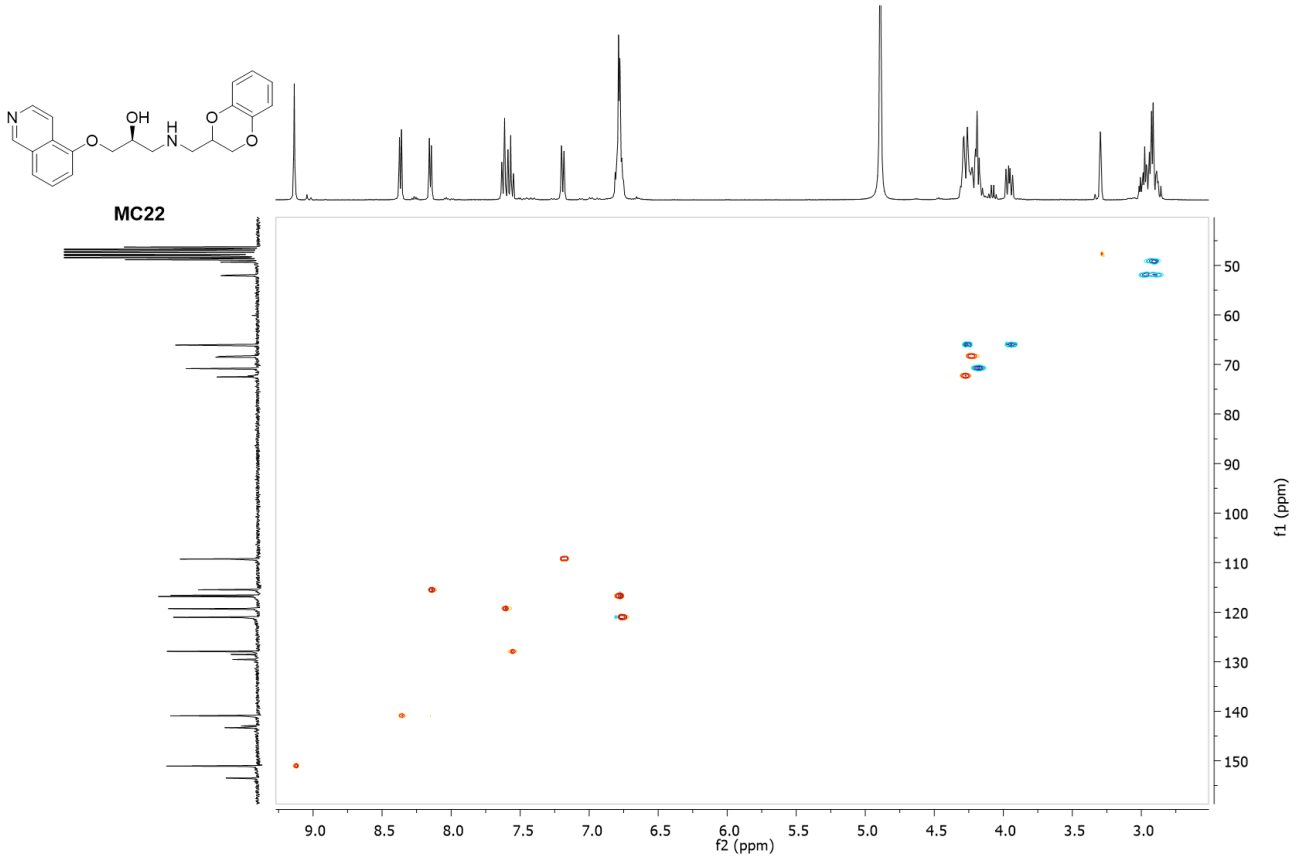


Figure S 74. gDQCOSY-NMR of **MC22** (400 MHz, CD_3OD)

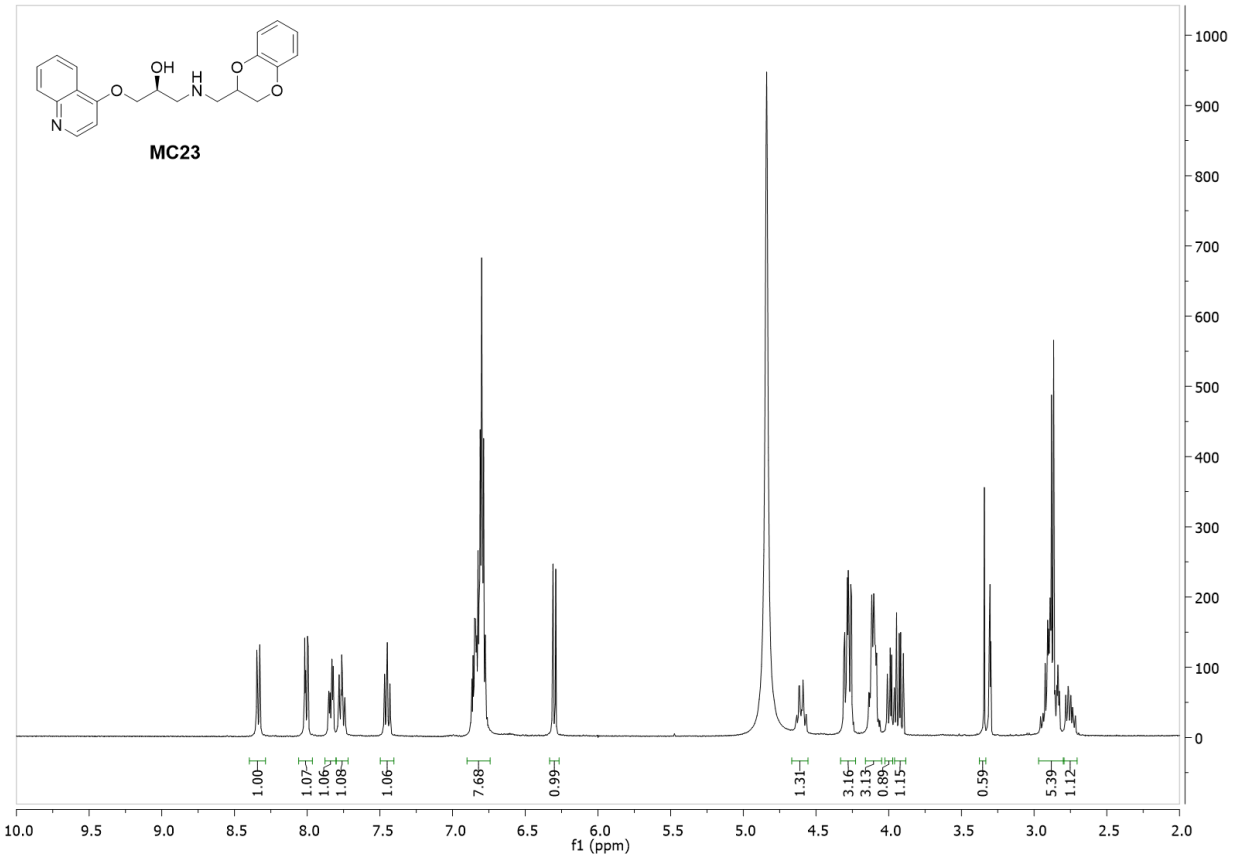


Figure S 75: ^{1}H-NMR of **MC23** (400 MHz, CD_3OD)

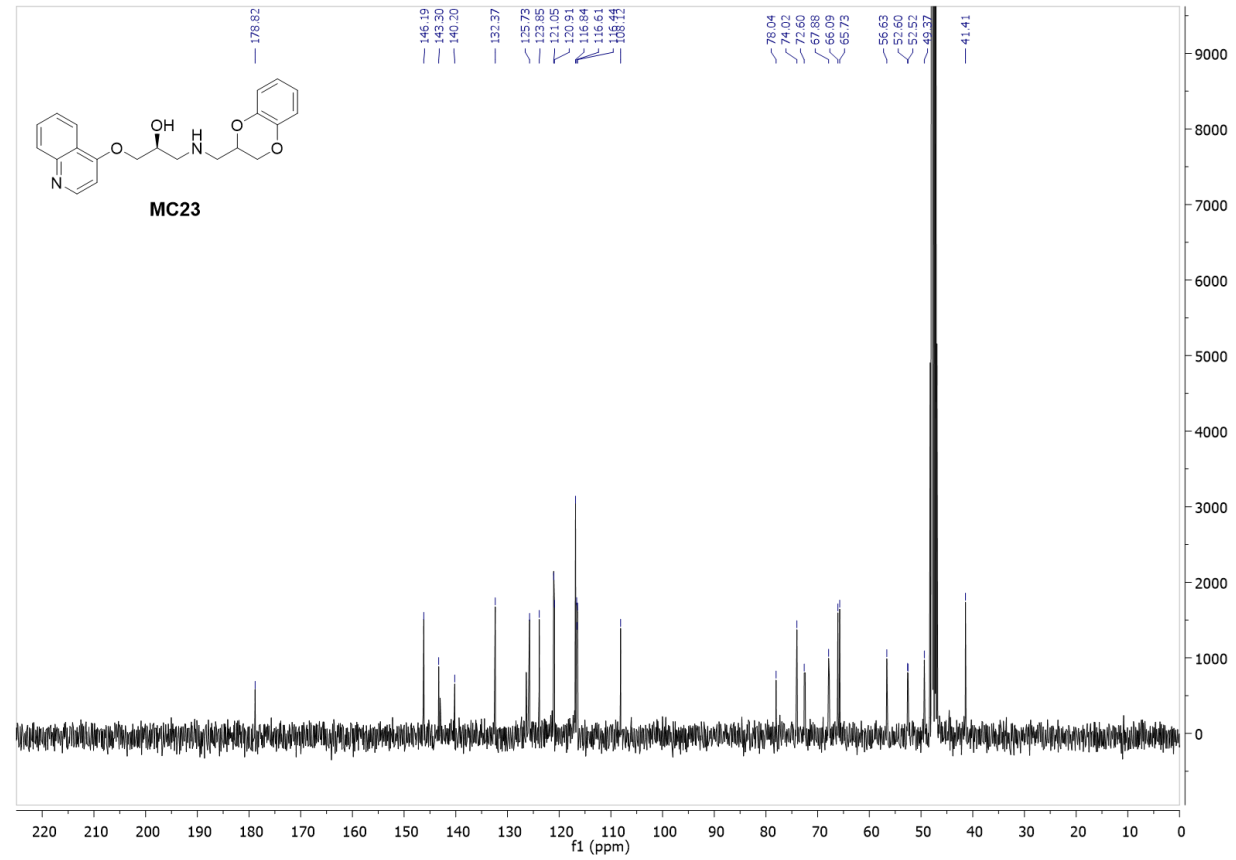


Figure S 76: ^{13}C-NMR of **MC23** (100 MHz, CD_3OD)

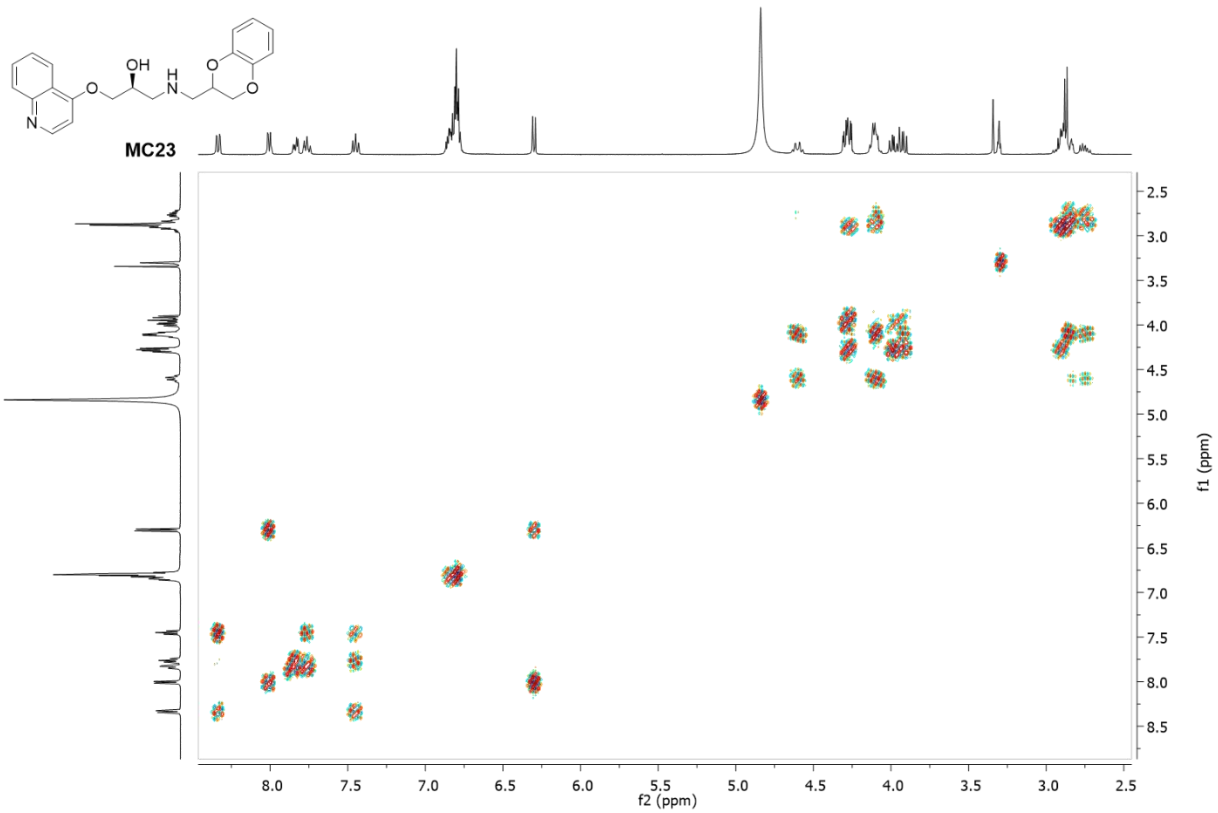


Figure S 77. gDQCOSY-NMR of **MC23** (400 MHz, CD_3OD)

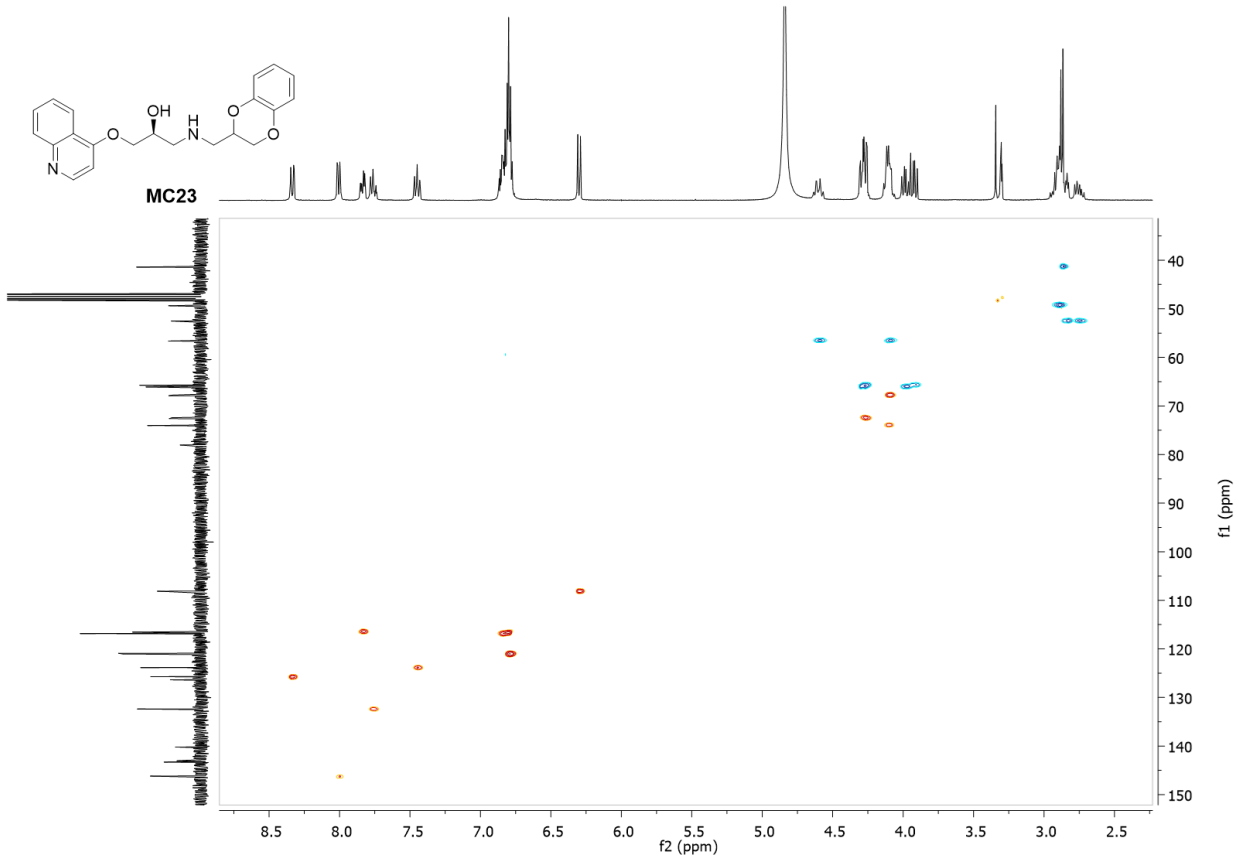


Figure S 78. gHSQC-NMR of **MC23** (400 MHz, CD_3OD)

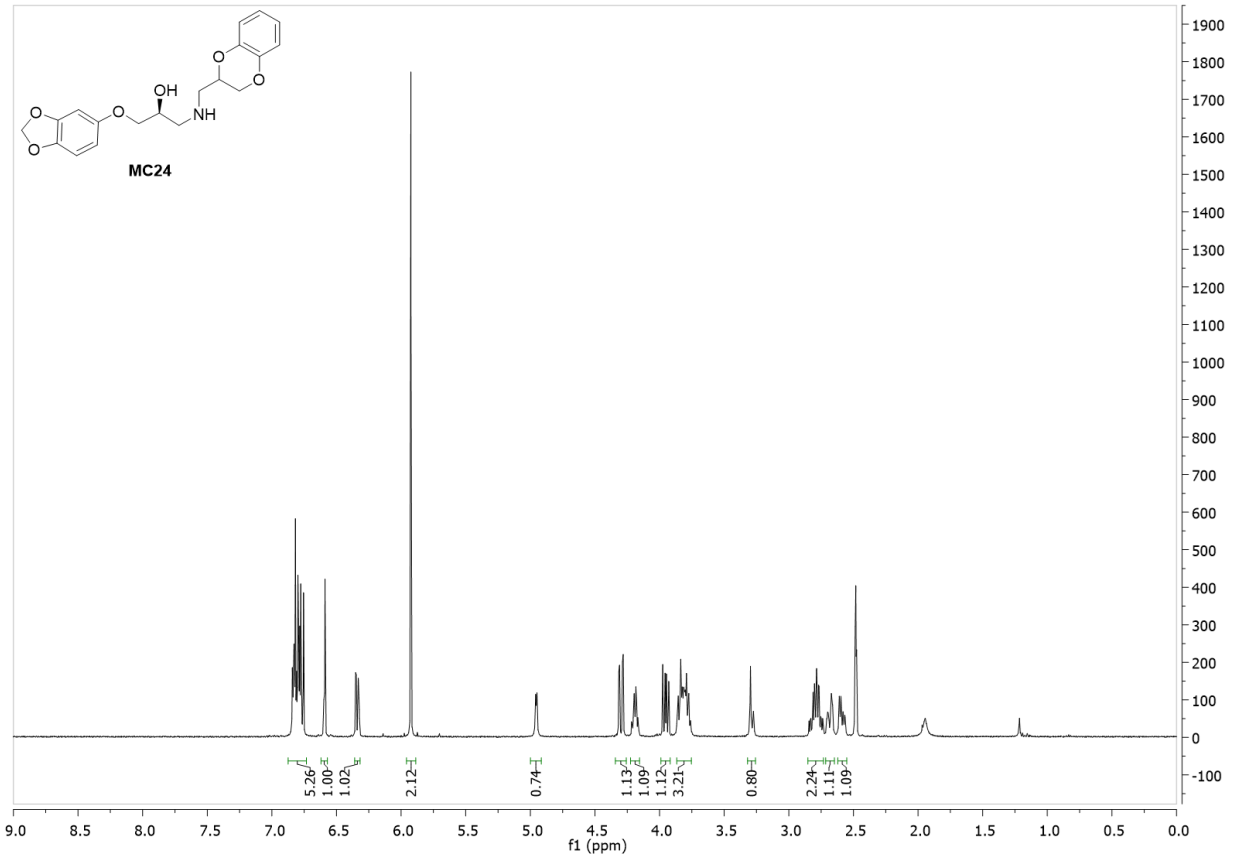


Figure S 79. ^{1}H-NMR of **MC24** (400 MHz, DMSO-d^{6})

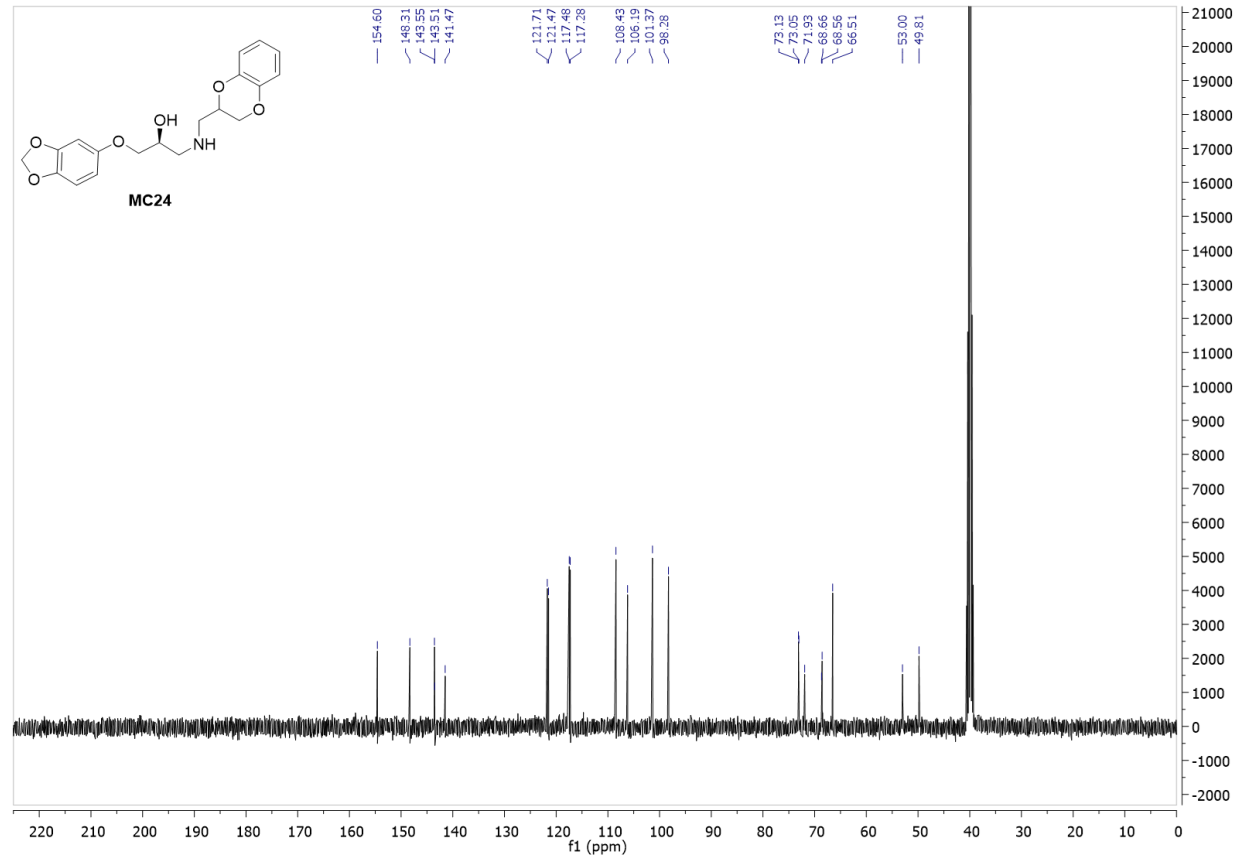


Figure S 80. ^{13}C-NMR of **MC24** (100 MHz, DMSO-d^{6})

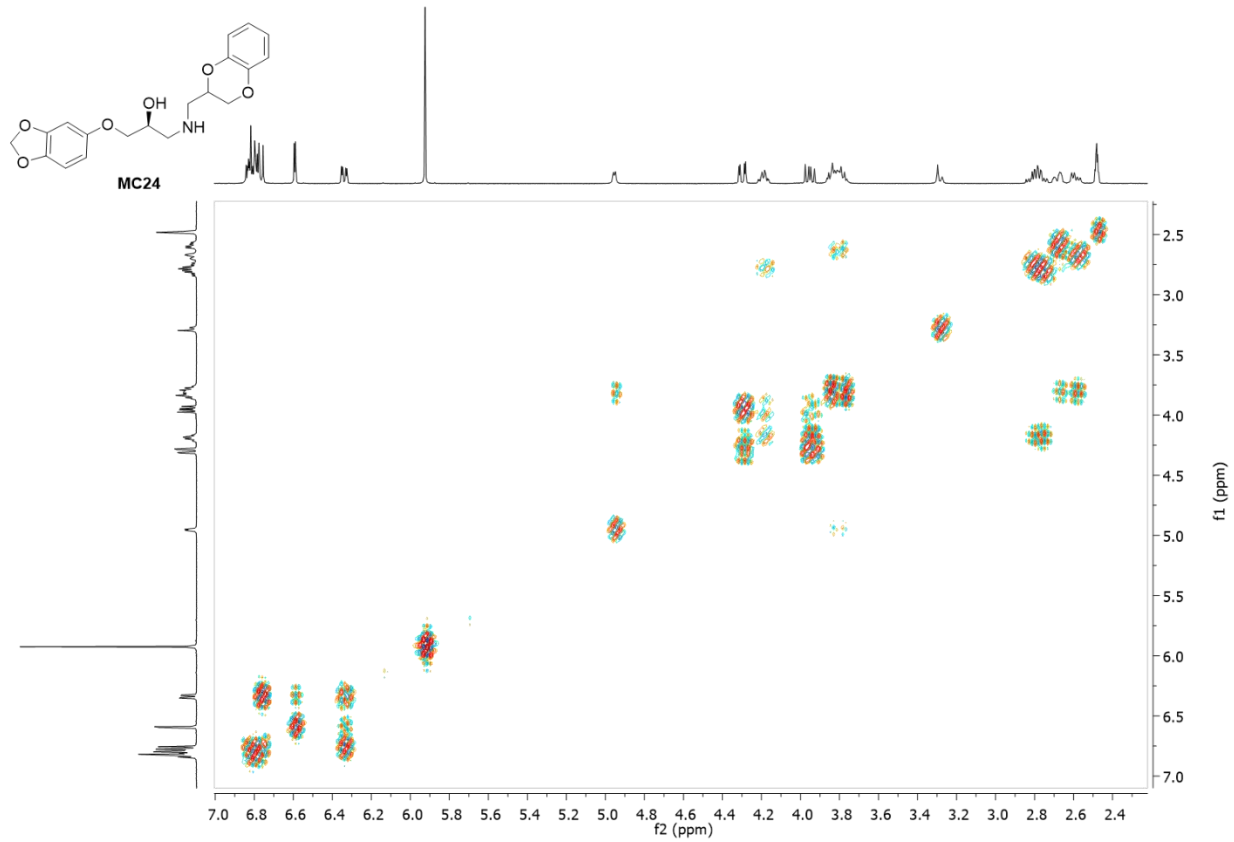


Figure S 81. gDQCOSY-NMR of **MC24** (400 MHz, DMSO-d^6)

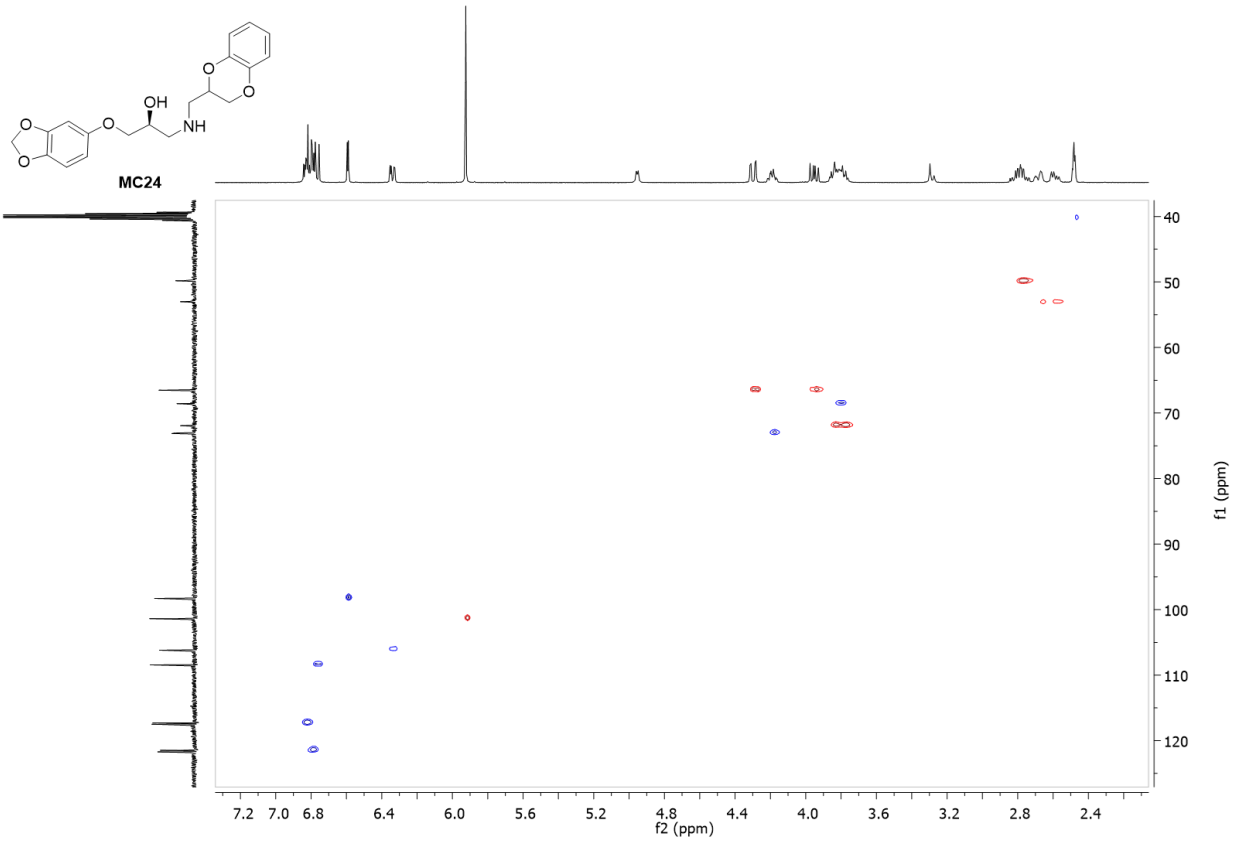


Figure S 82. gHSQC-NMR of **MC24** (400 MHz, DMSO-d^6)

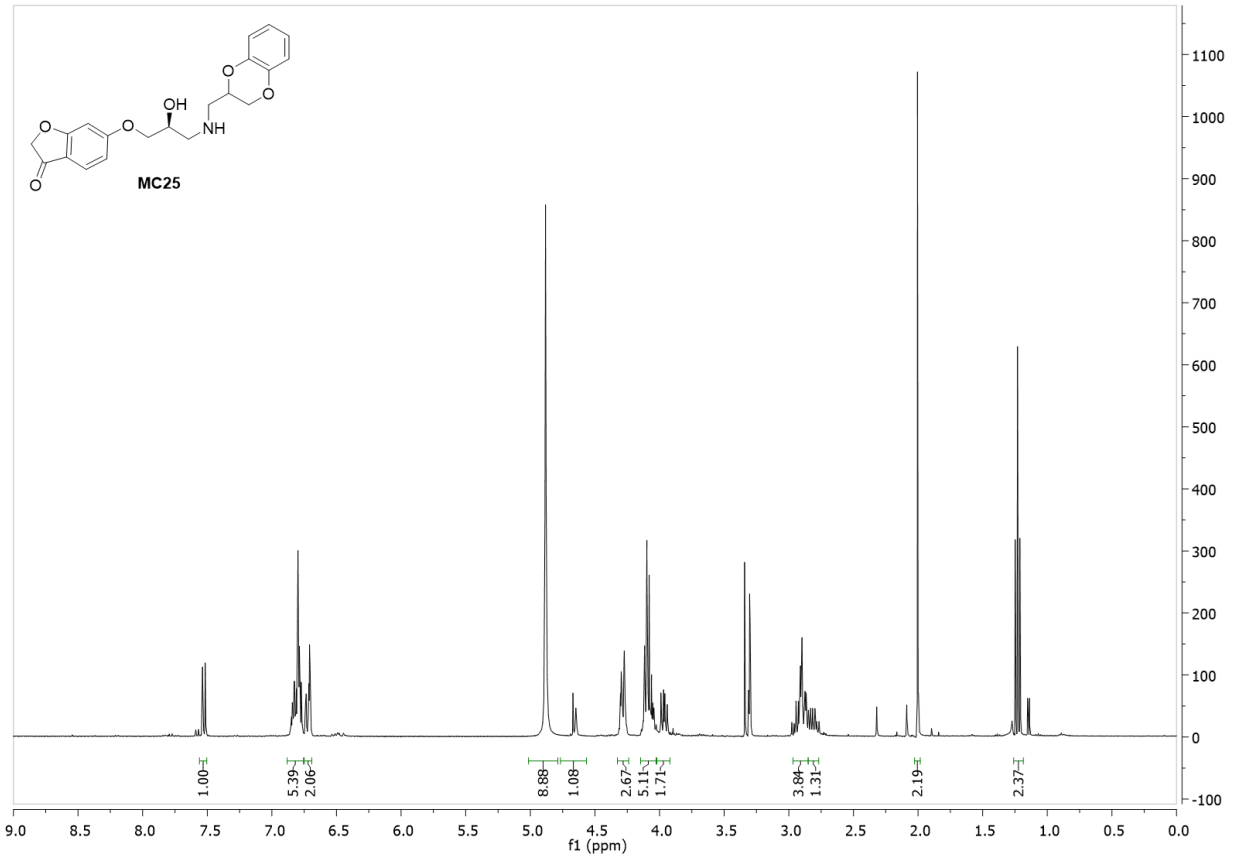


Figure S 83. ^{1}H-NMR of **MC25** (400 MHz, CD_3OD)

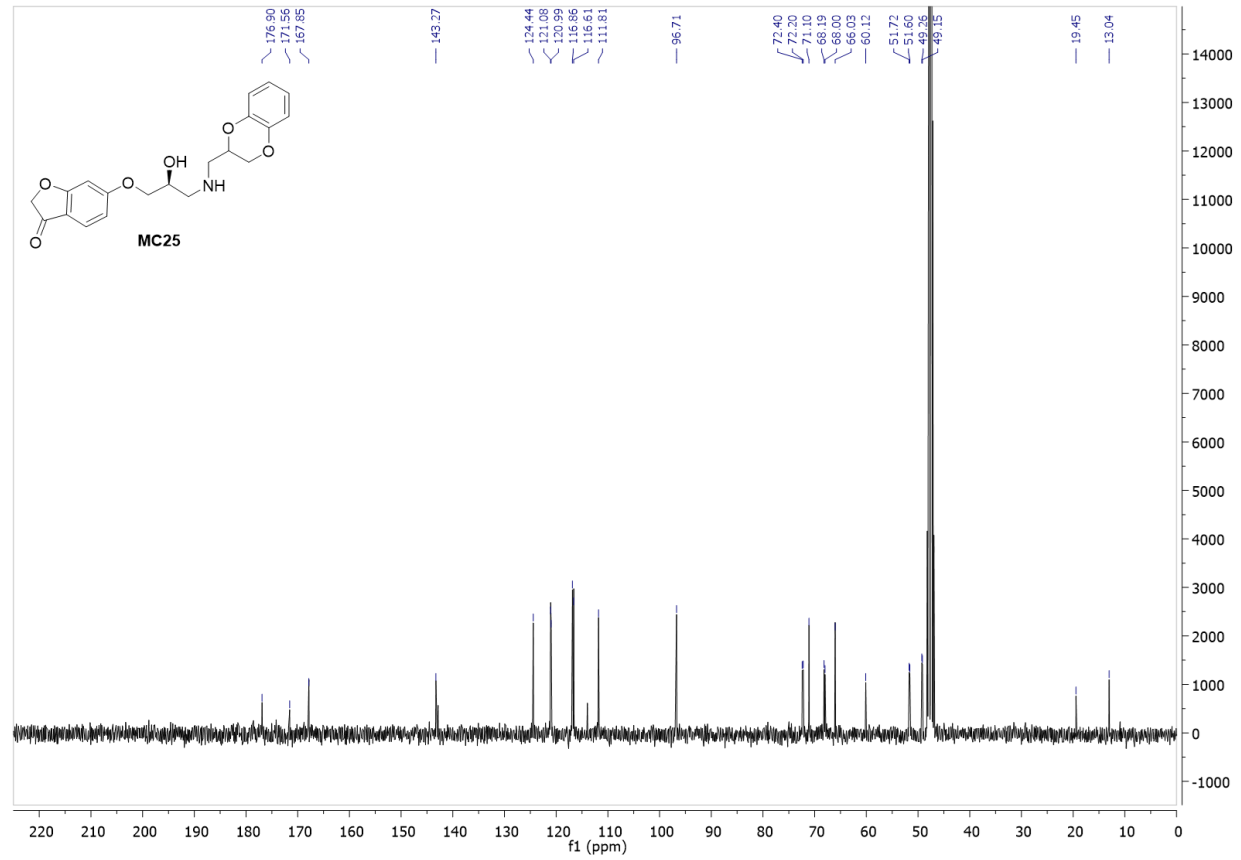


Figure S 84. ^{13}C-NMR of **MC25** (100 MHz, CD_3OD)

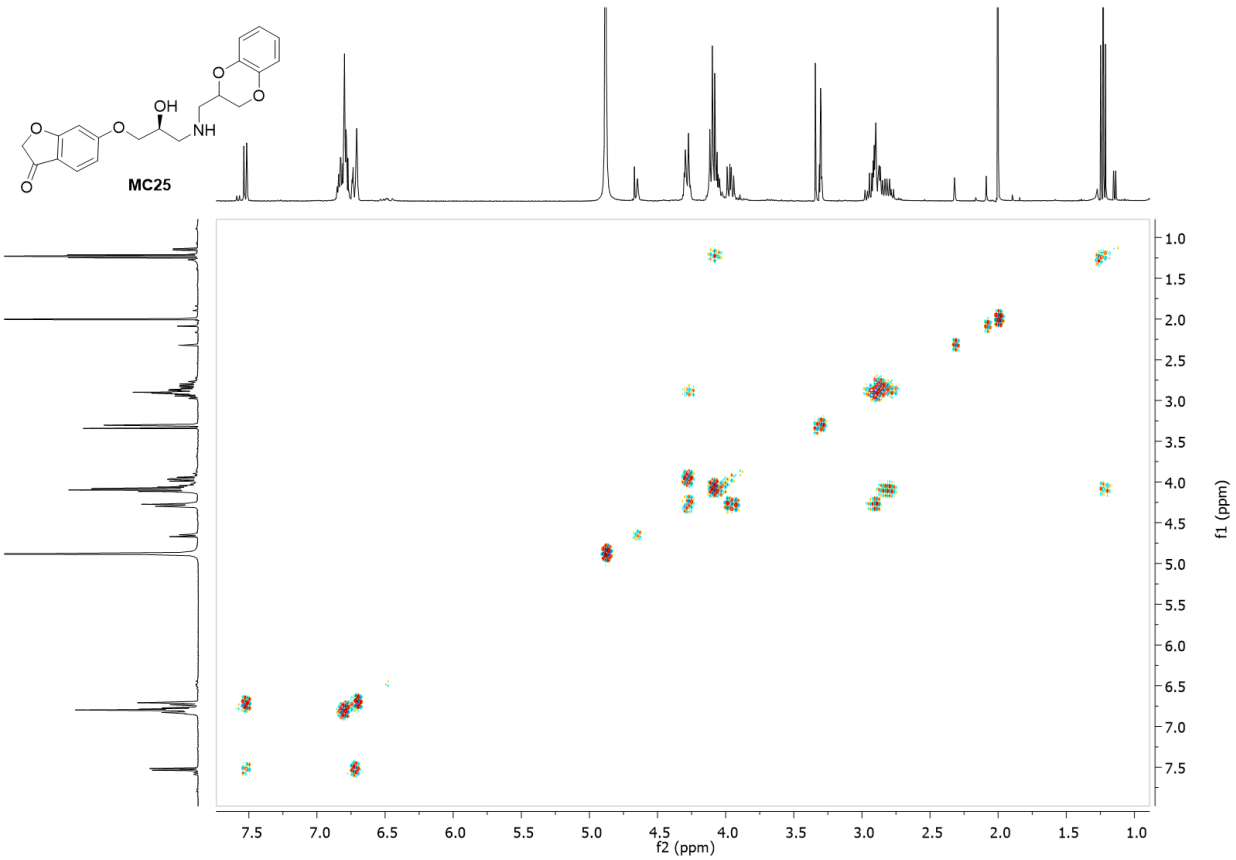


Figure S 85. gDQCOSY-NMR of **MC25** (400 MHz, CD_3OD)

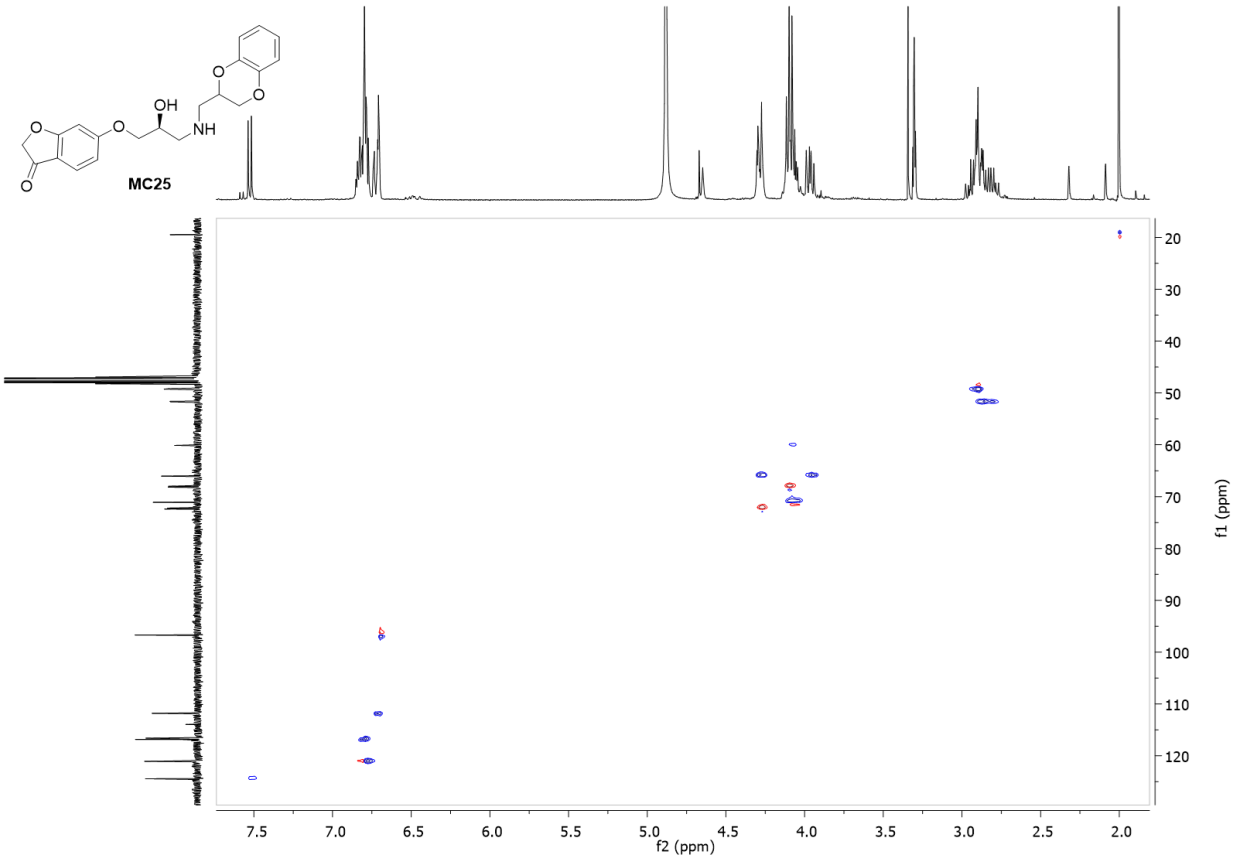


Figure S 86. gHSQC-NMR of **MC25** (400 MHz, CD_3OD)

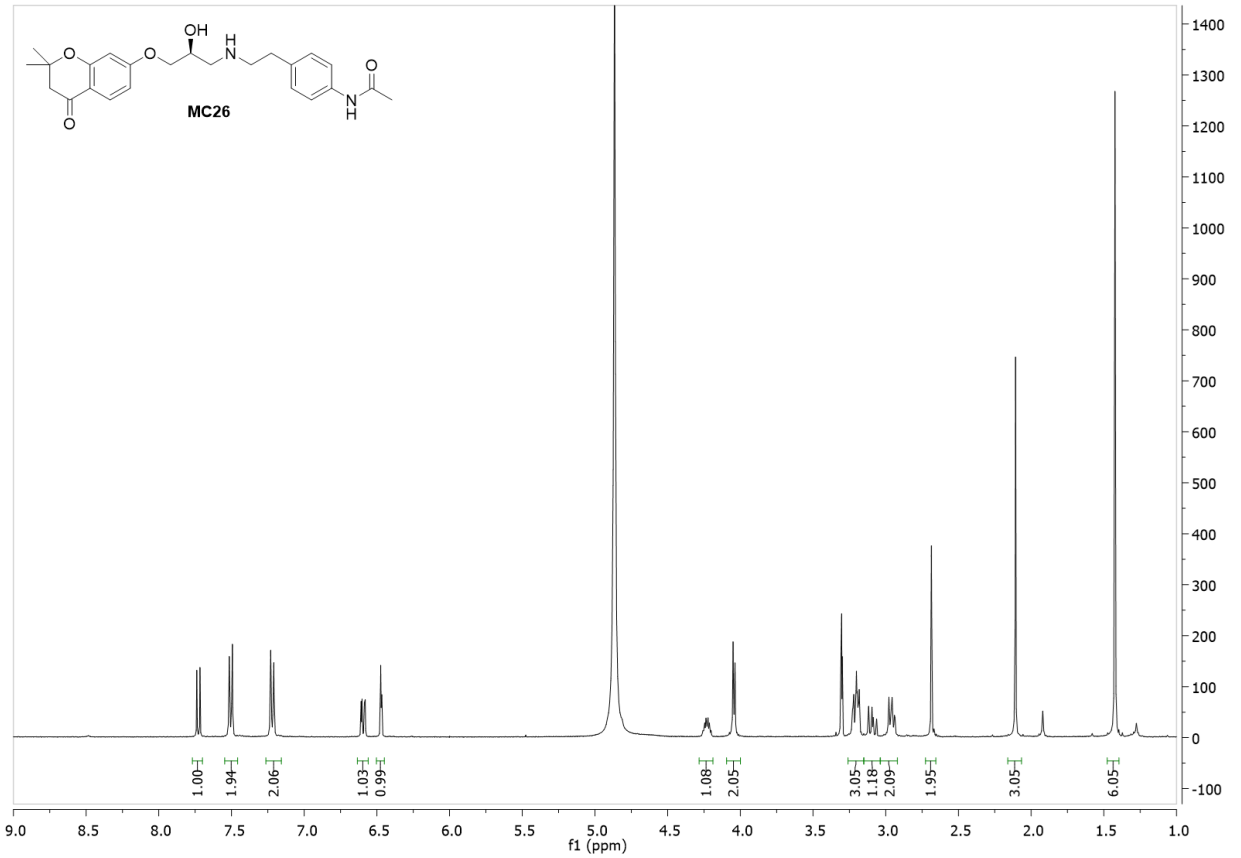


Figure S 87. ^{1}H-NMR of **MC26** (400 MHz, CD_3OD)

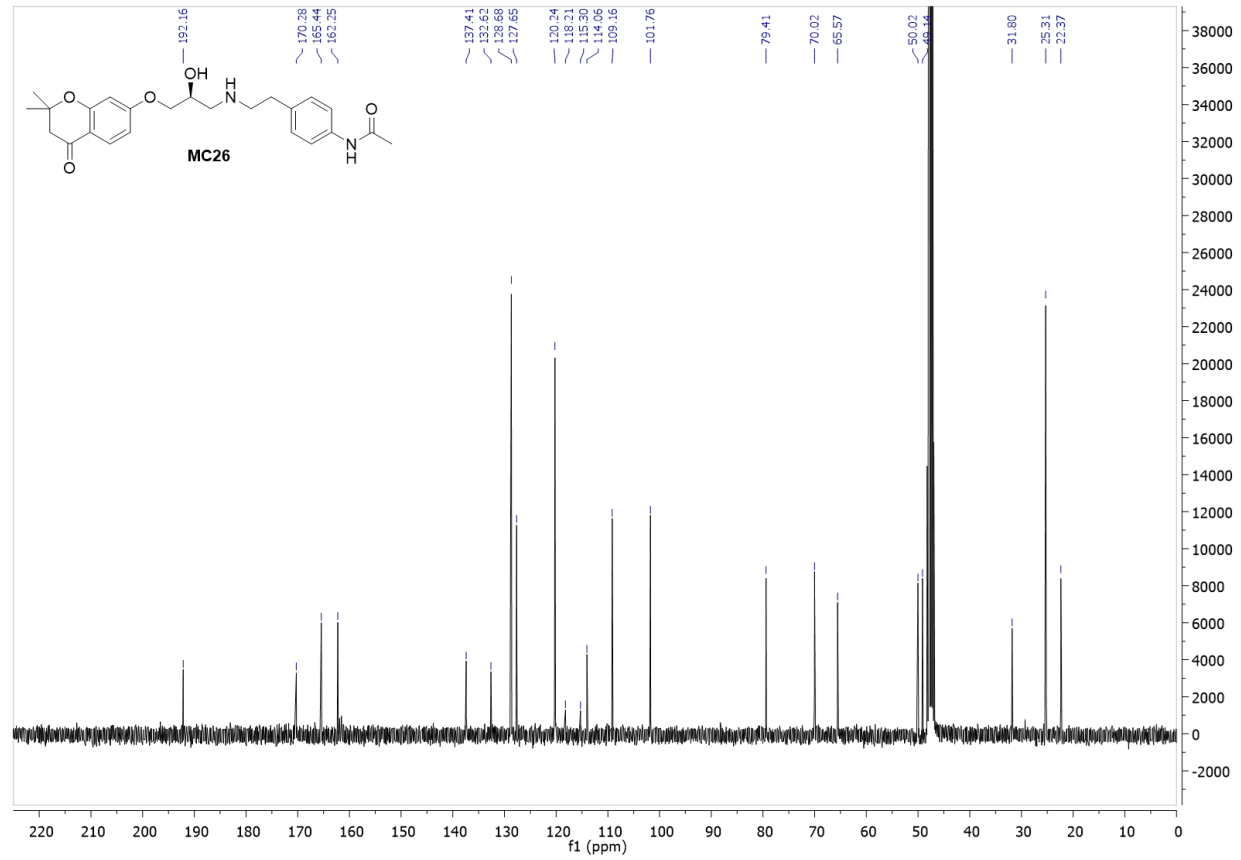


Figure S 88. ^{13}C-NMR of **MC26** (100 MHz, CD_3OD)

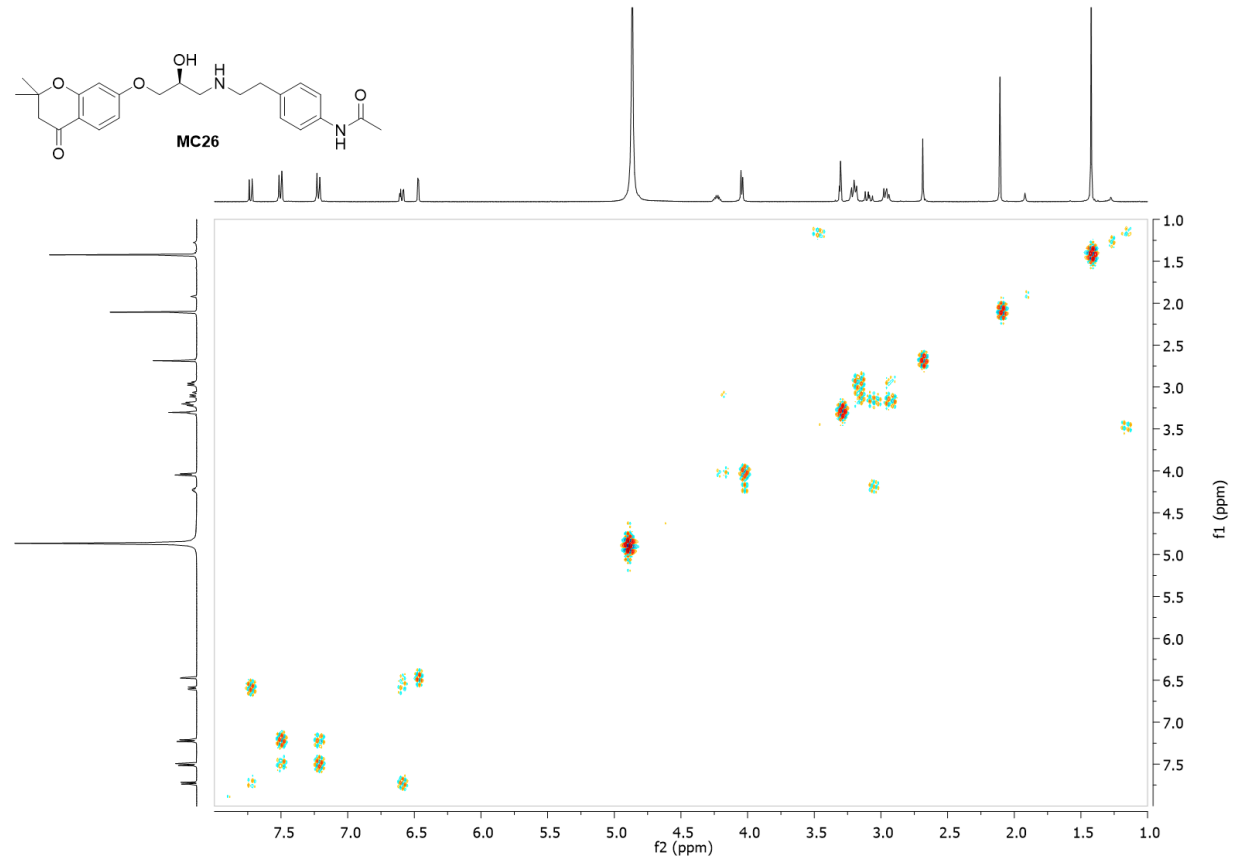


Figure S 89. gDQCOSY-NMR of **MC26** (400 MHz, CD_3OD)

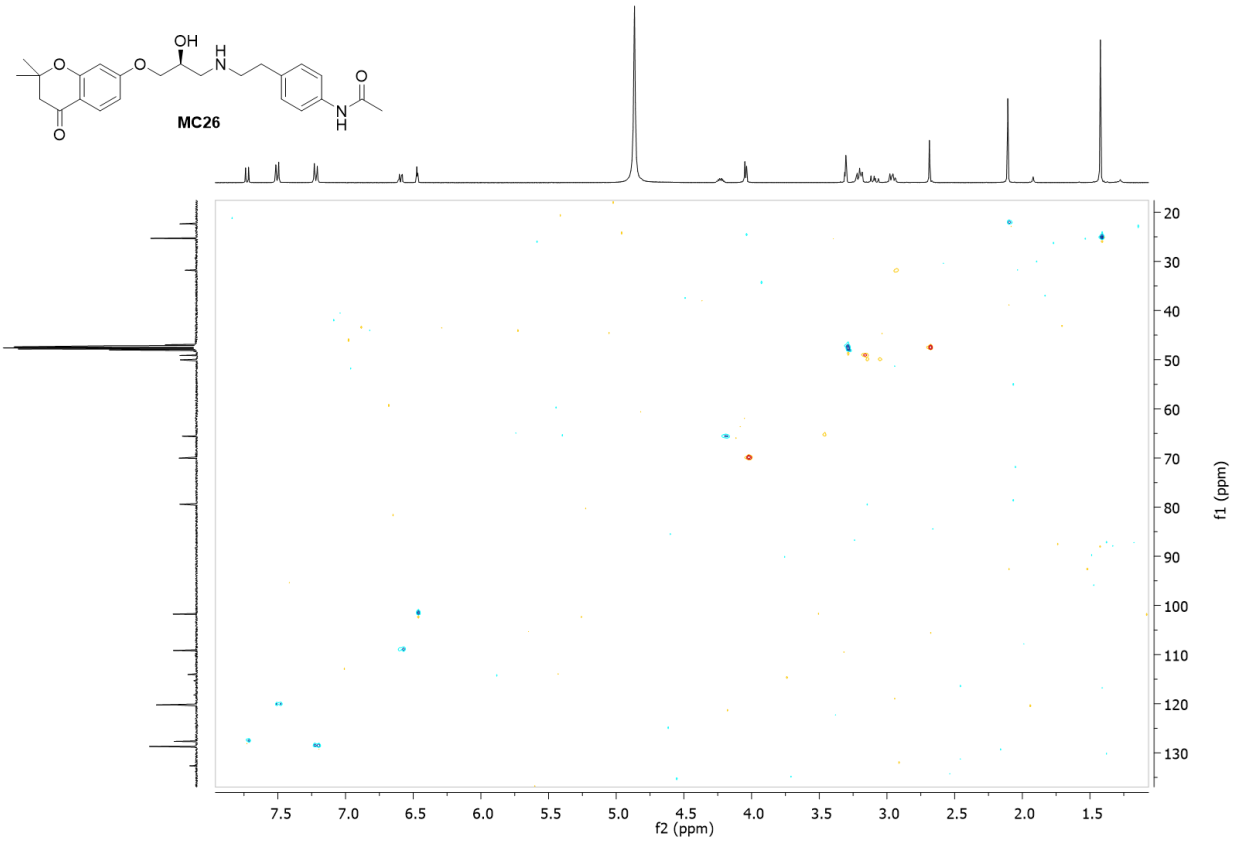


Figure S 90. gHSQC-NMR of **MC26** (400 MHz, CD_3OD)

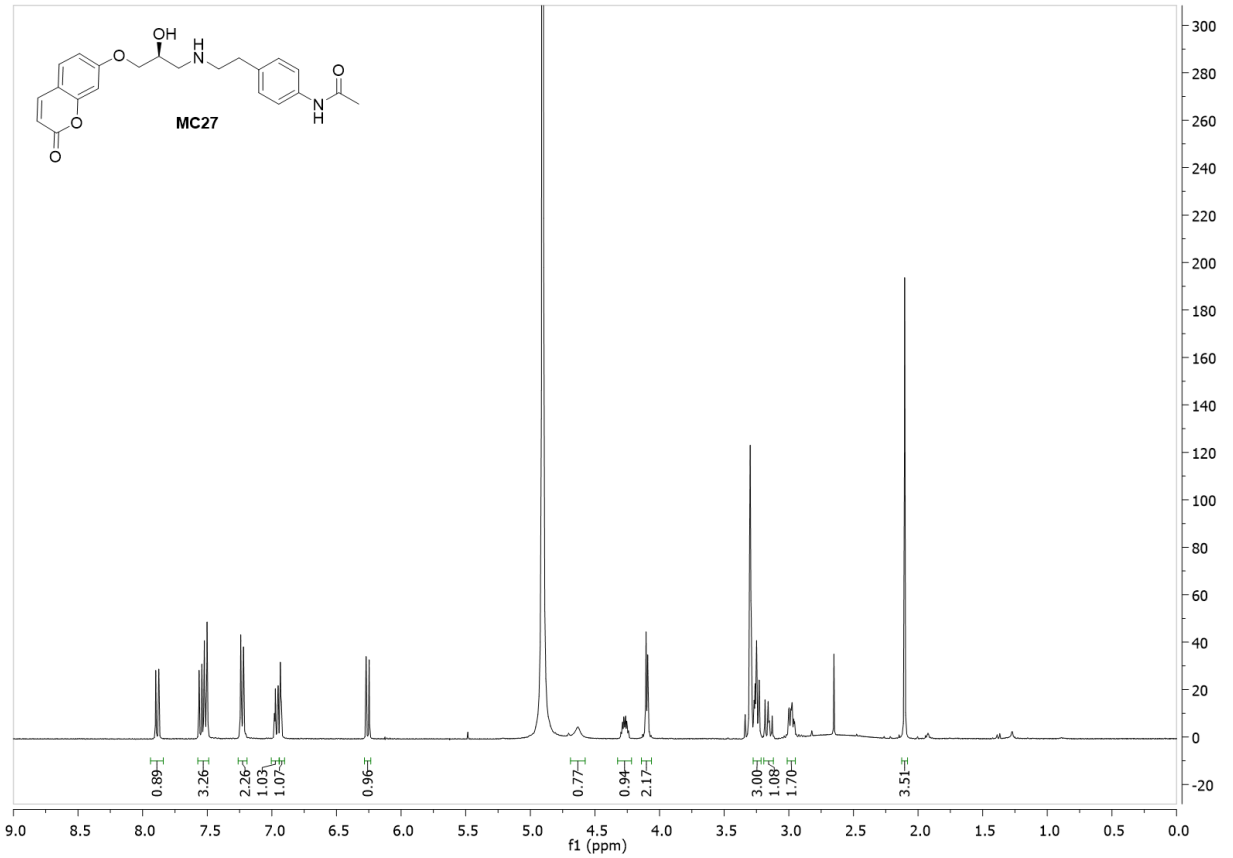


Figure S 91. ^{1}H-NMR of **MC27** (400 MHz, CD_3OD +5% DMSO-d^6)

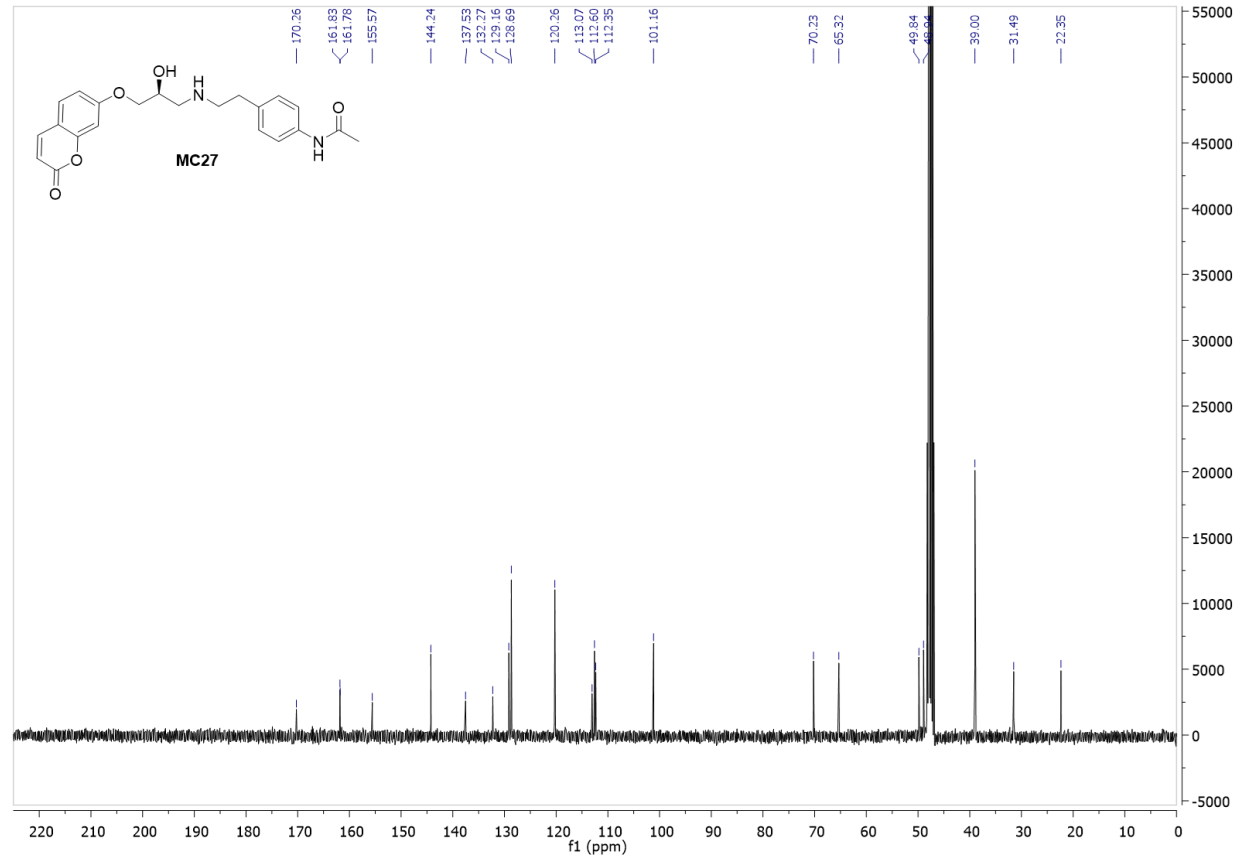


Figure S 92. ^{13}C-NMR of **MC27** (100 MHz, CD_3OD +5% DMSO-d^6)

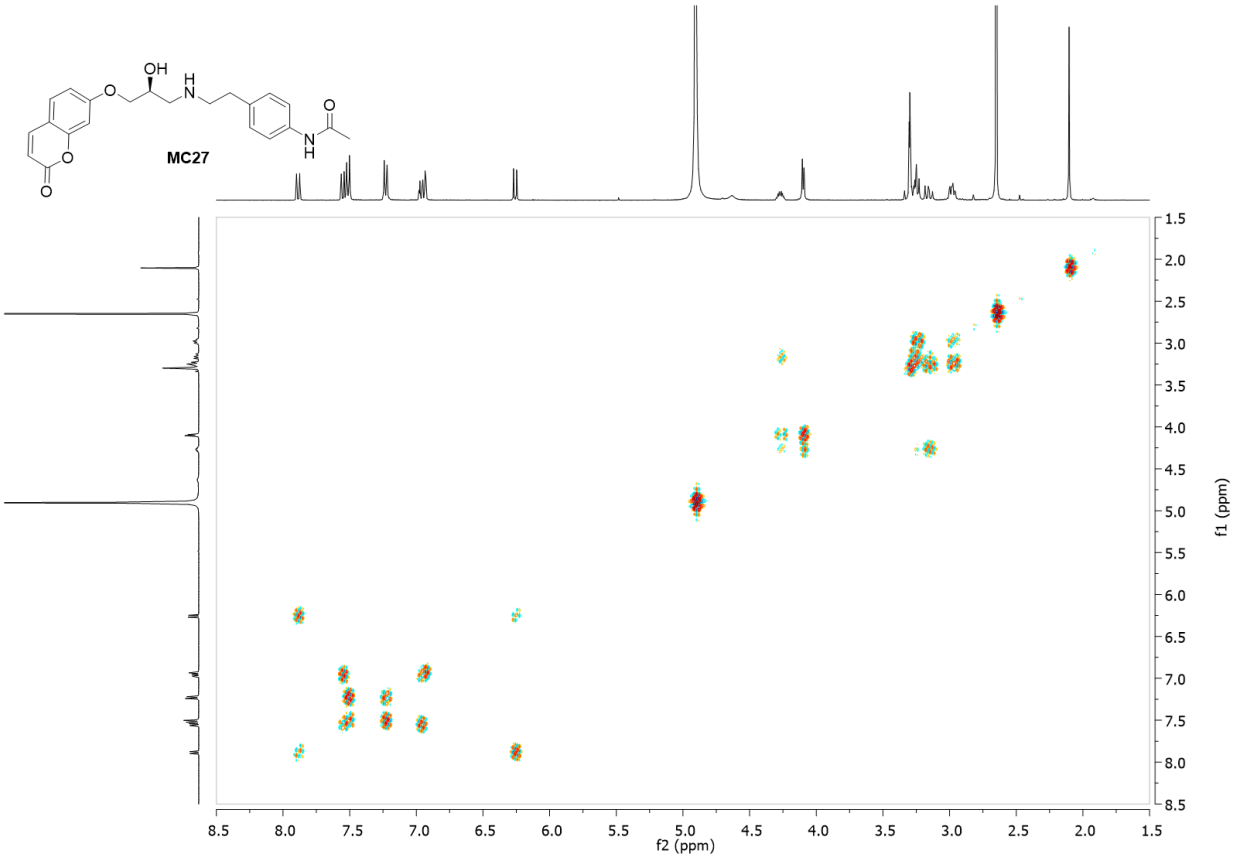


Figure S 93. gDQCOSY-NMR of **MC27** (400 MHz, CD_3OD +5% DMSO-d^6)

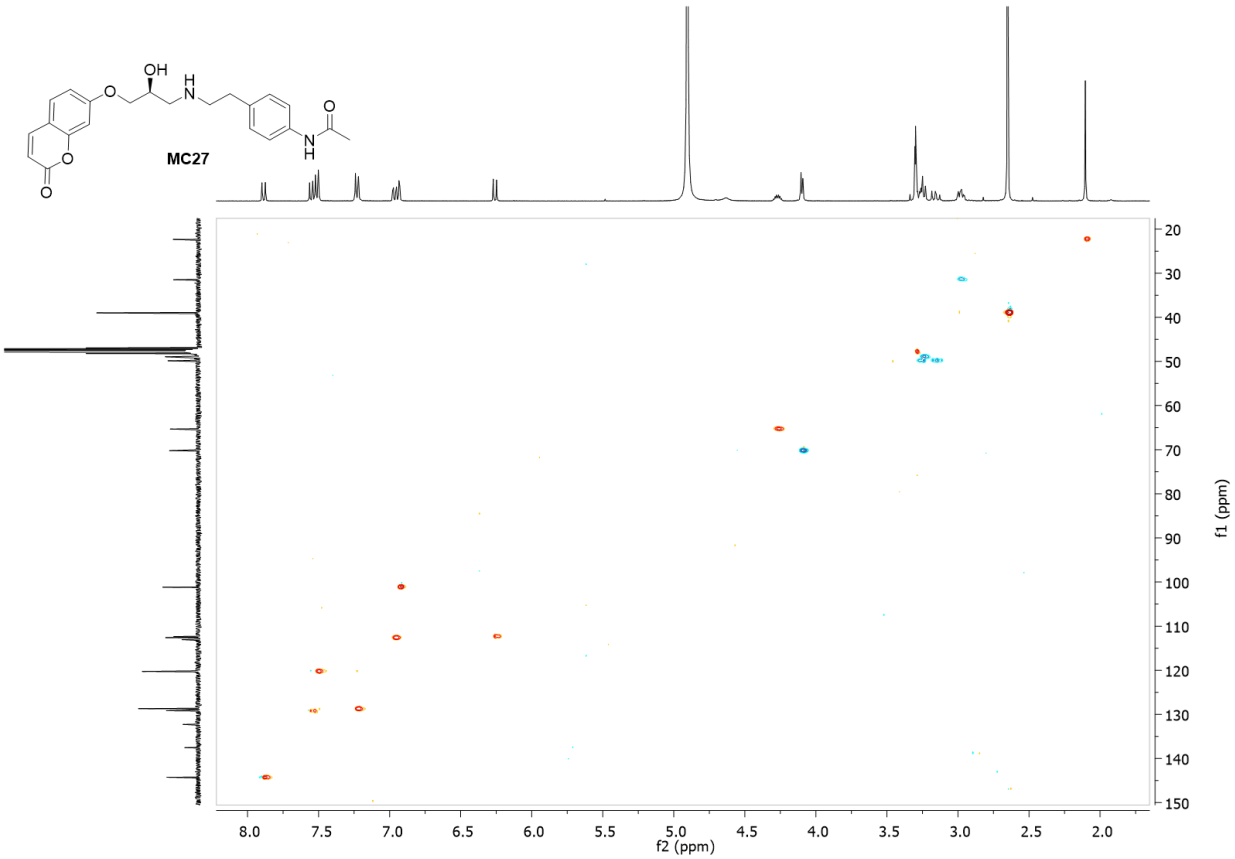


Figure S 94. gHSQC-NMR of **MC27** (400 MHz, CD_3OD +5% DMSO-d^6)

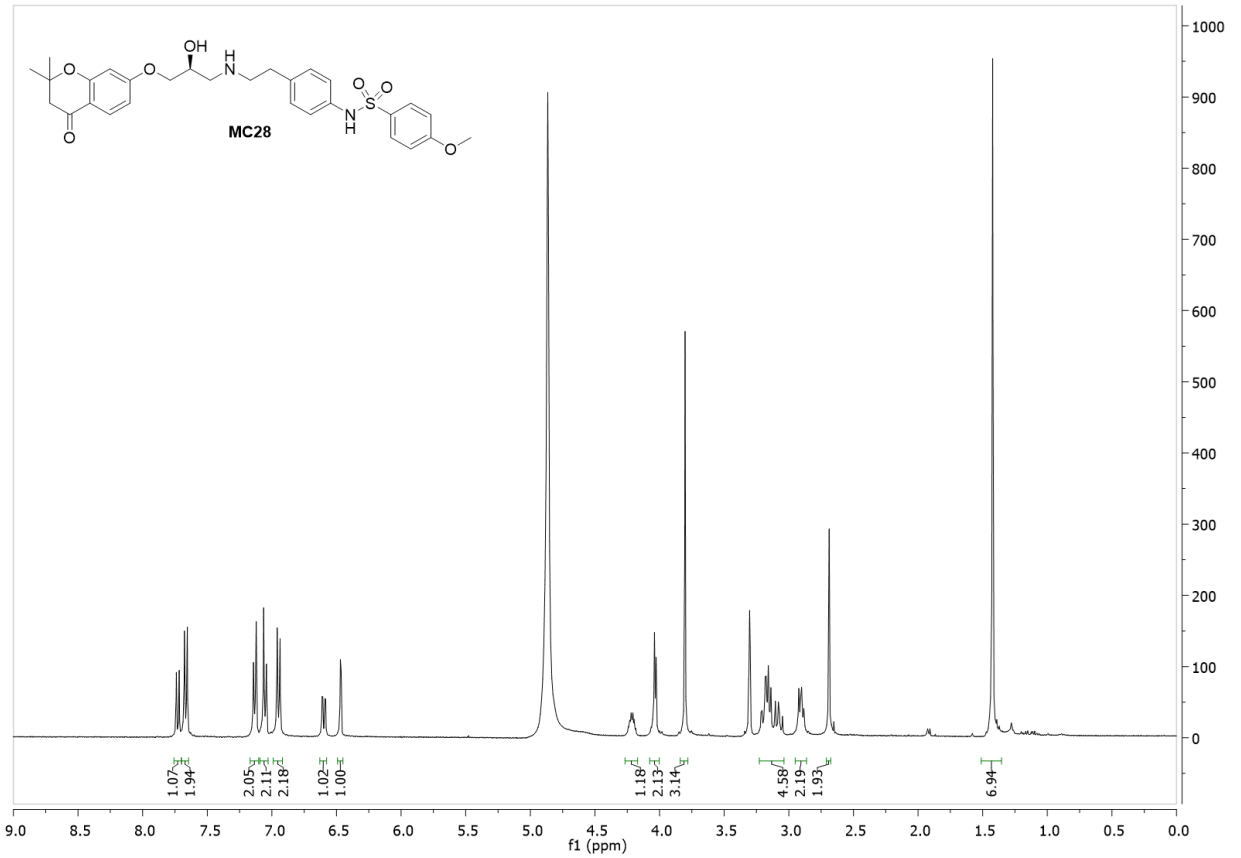


Figure S 95. ^{1}H-NMR of **MC28** (400 MHz, CD_3OD +5% DMSO-d^6)

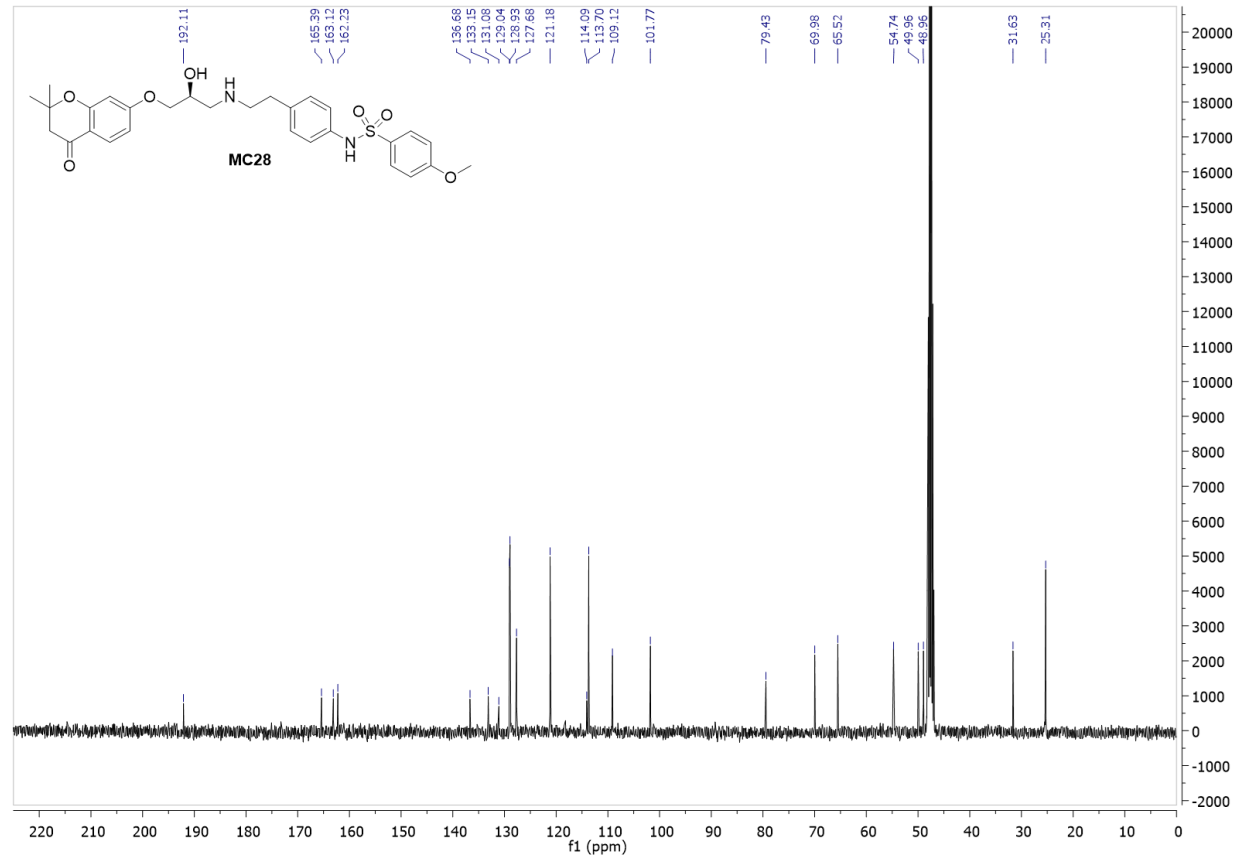


Figure S 96. ^{13}C-NMR of **MC28** (100 MHz, CD_3OD +5% DMSO-d^6)

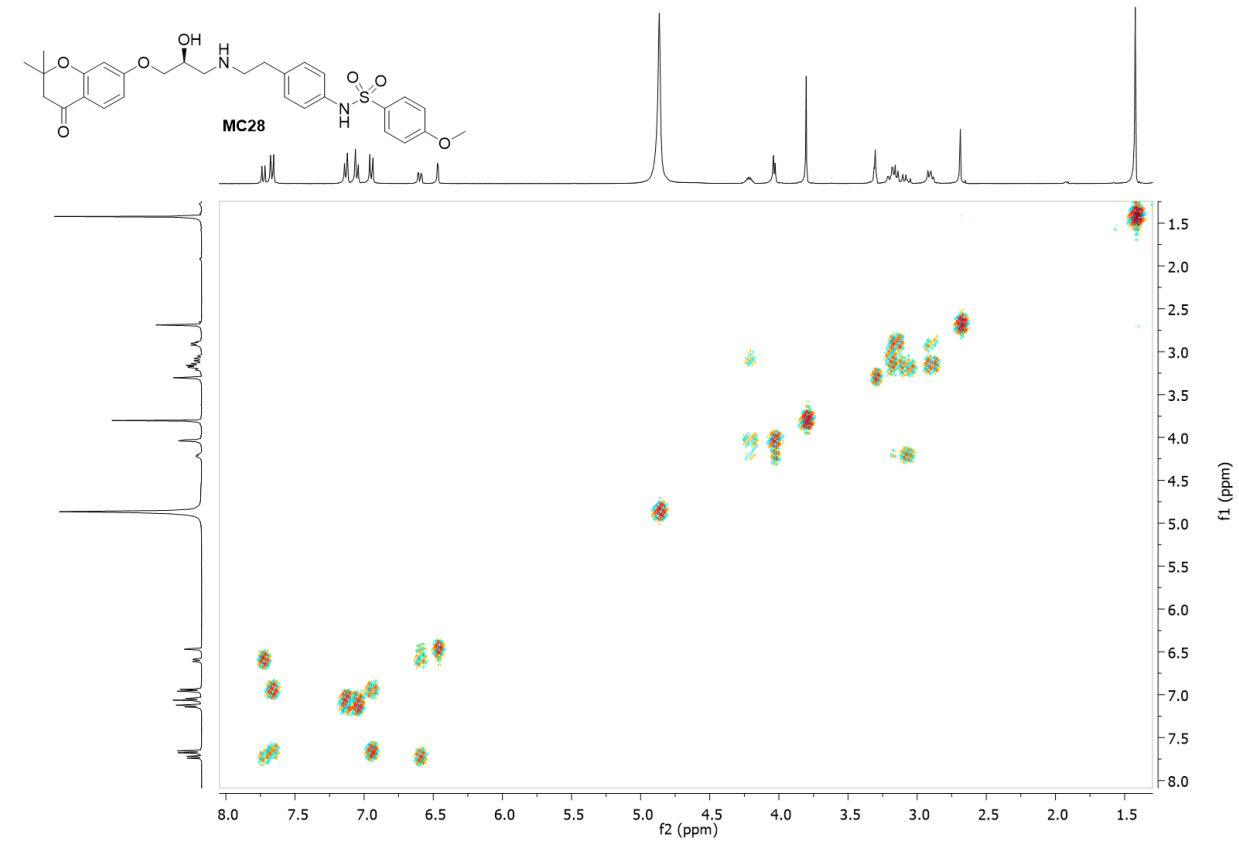


Figure S 97. gCOSY-NMR of **MC28** (400 MHz, CD_3OD +5% DMSO-d^6)

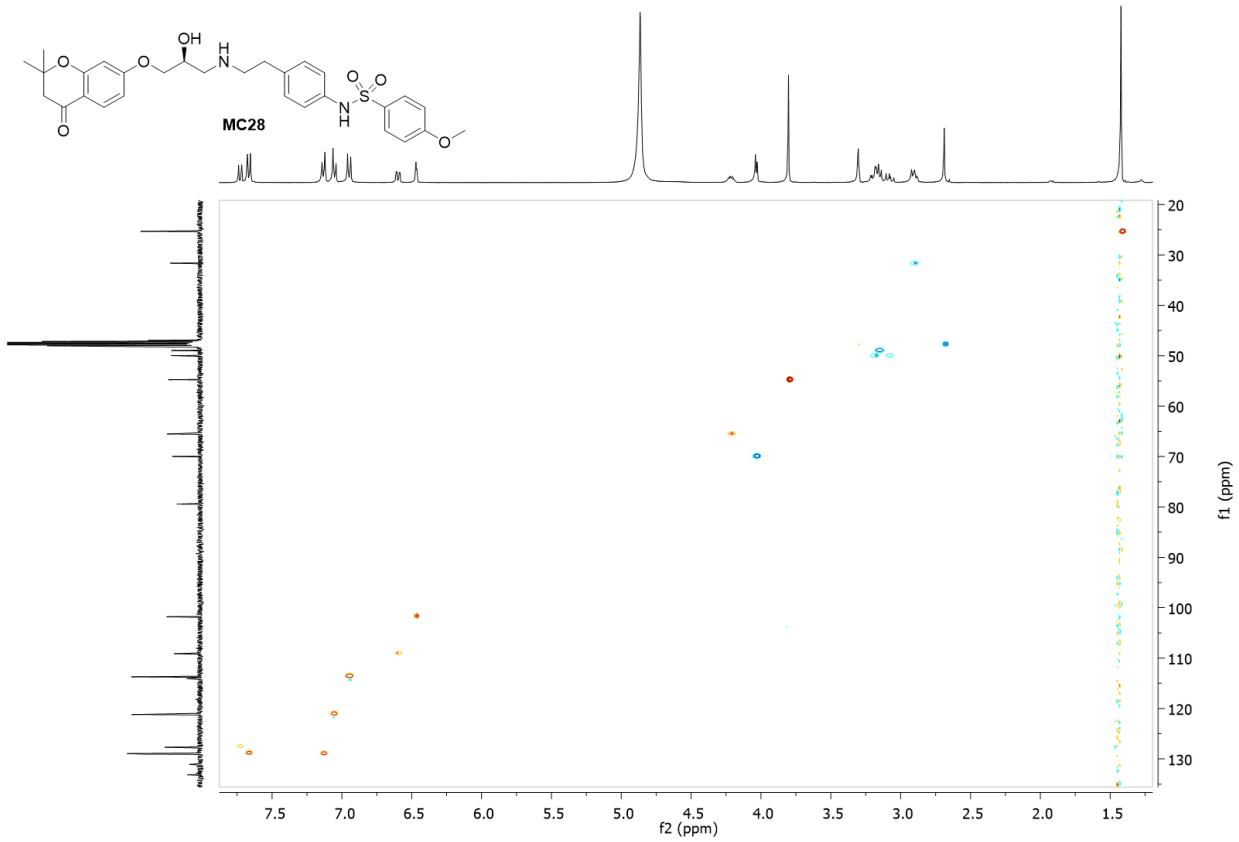


Figure S 98. gHSQC-NMR of **MC28** (400 MHz, CD_3OD +5% DMSO-d^6)

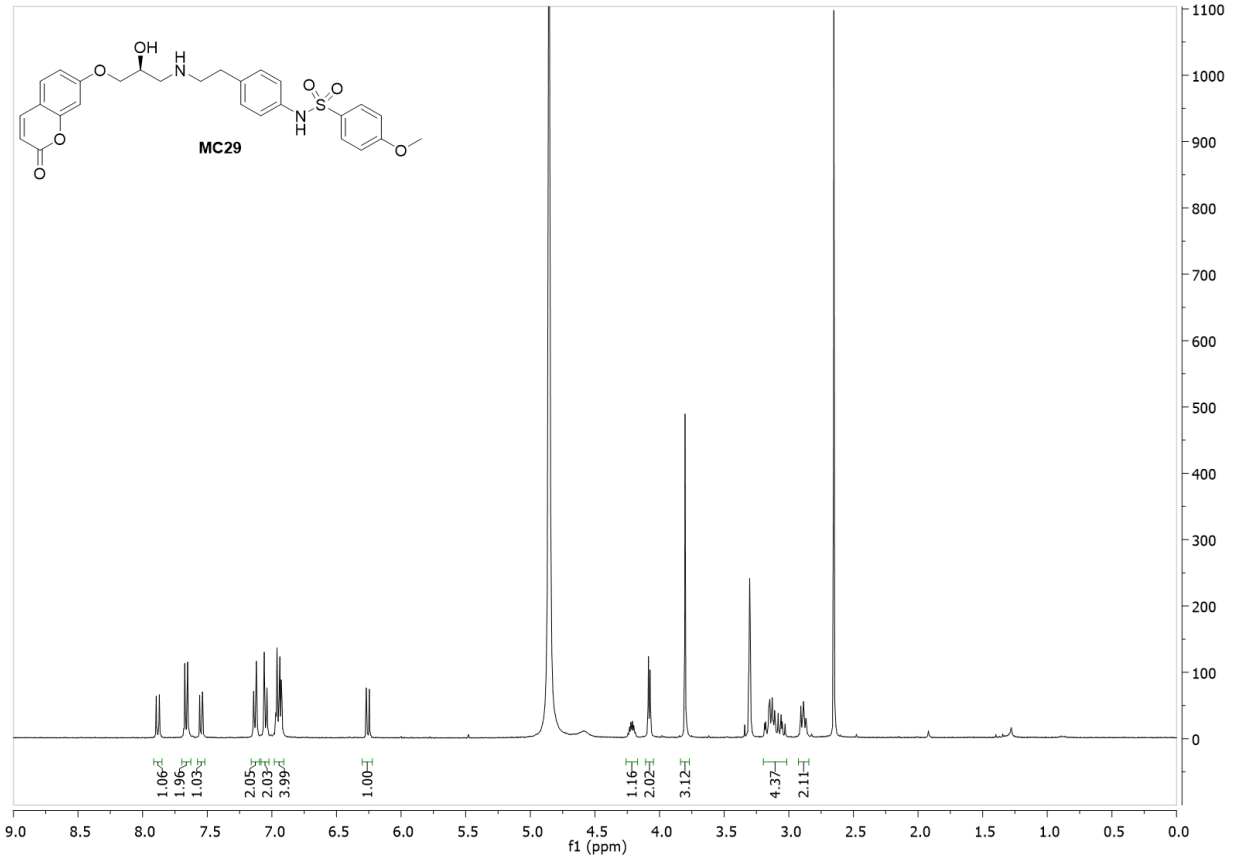


Figure S 99. ^{1}H-NMR of **MC29** (400 MHz, CD_3OD +5% DMSO-d^6)

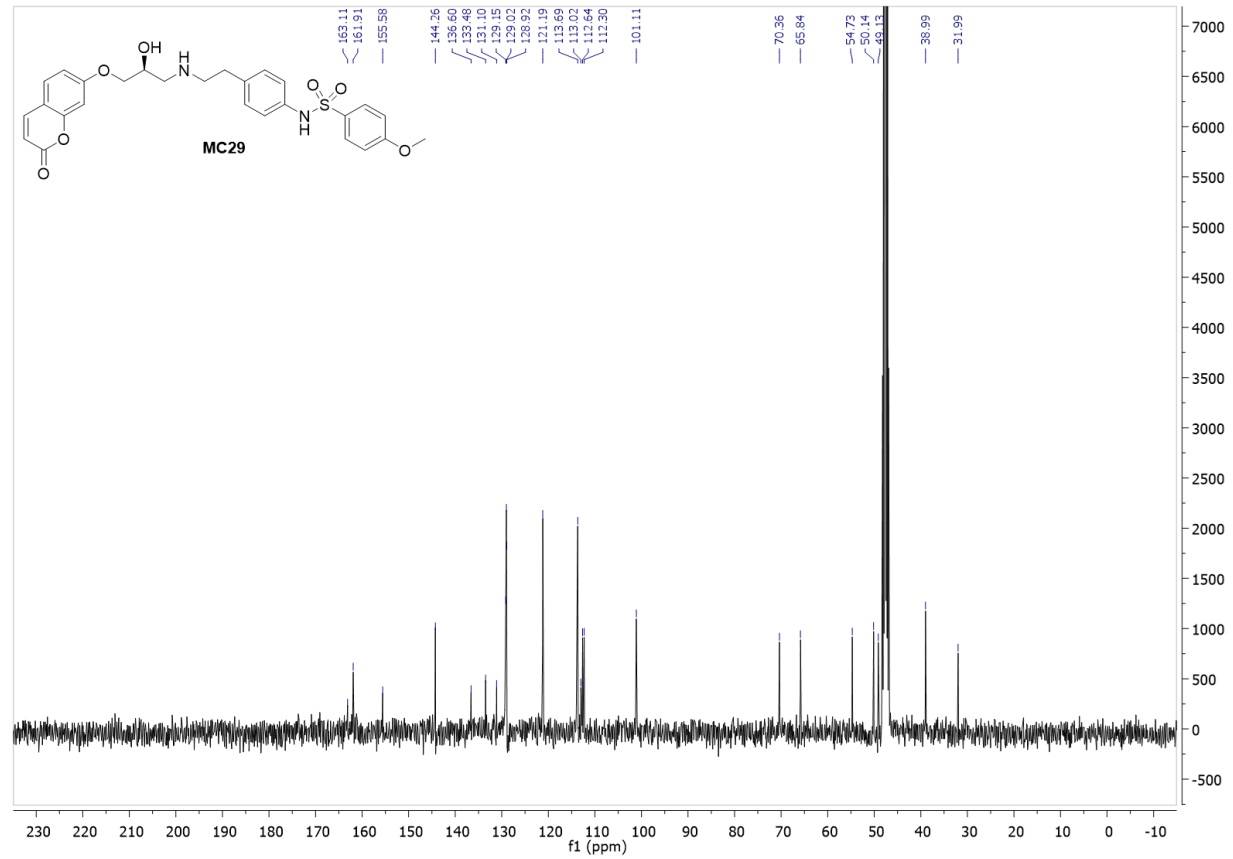


Figure S 100. ^{13}C-NMR of **MC29** (100 MHz, CD_3OD +5% DMSO-d^6)

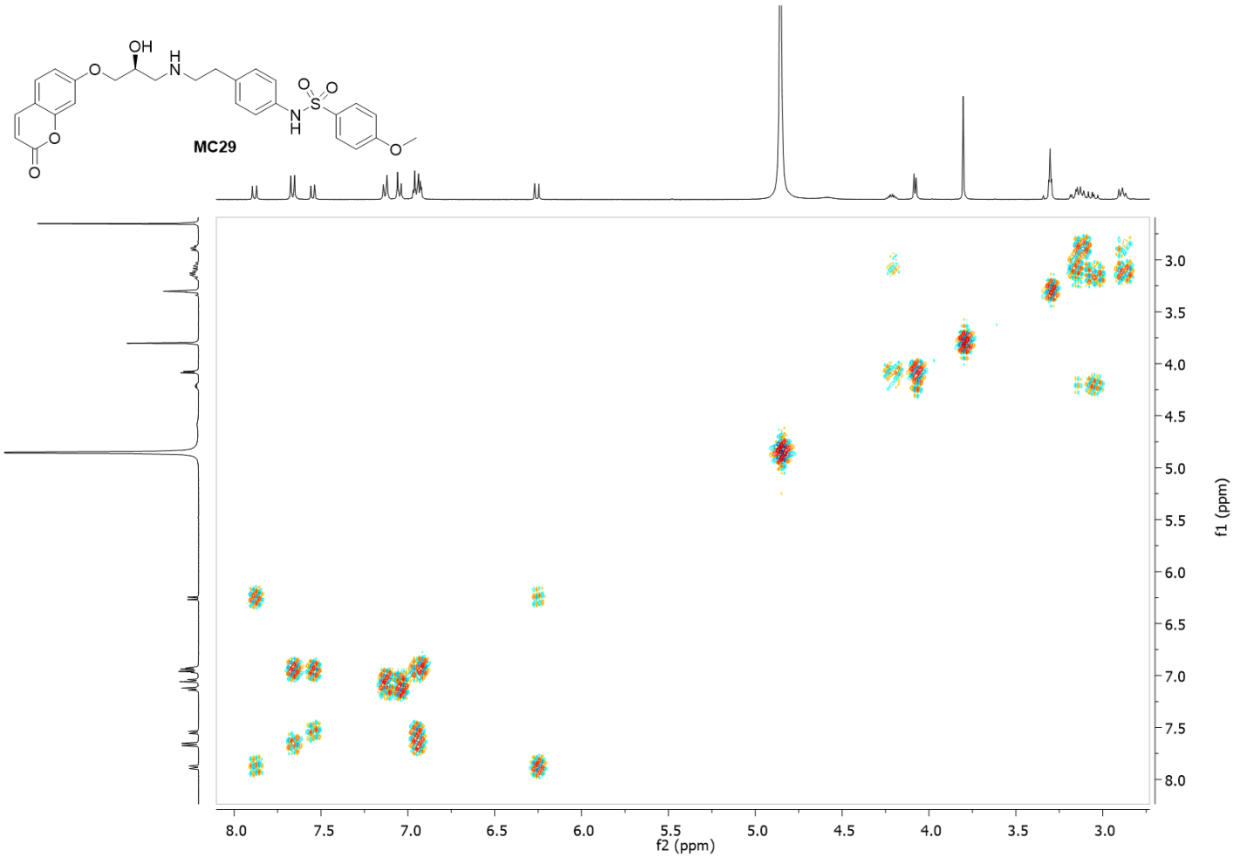


Figure S 101. gCOSY-NMR of **MC29** (400 MHz, CD_3OD +5% DMSO-d^6)

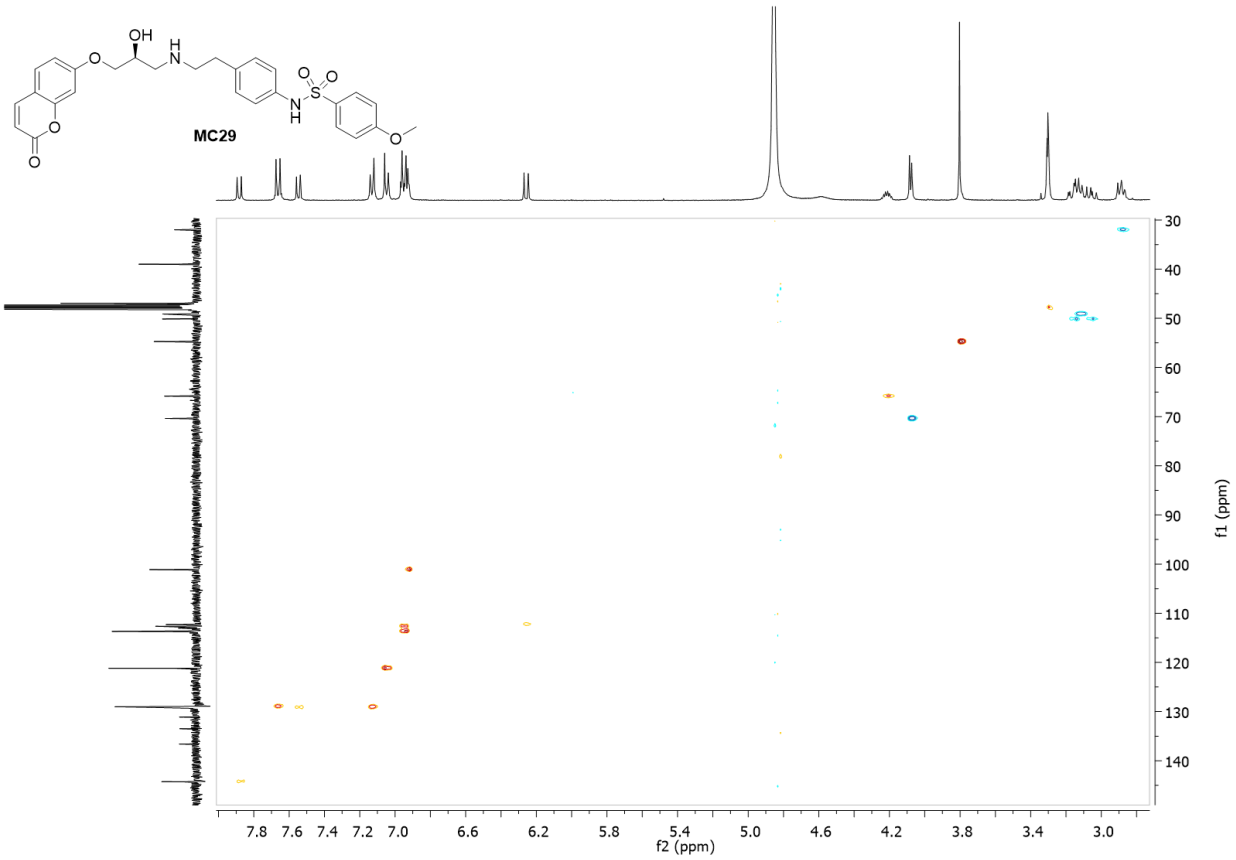


Figure S 102. gHSQC-NMR of **MC29** (400 MHz, CD_3OD +5% DMSO-d^6)

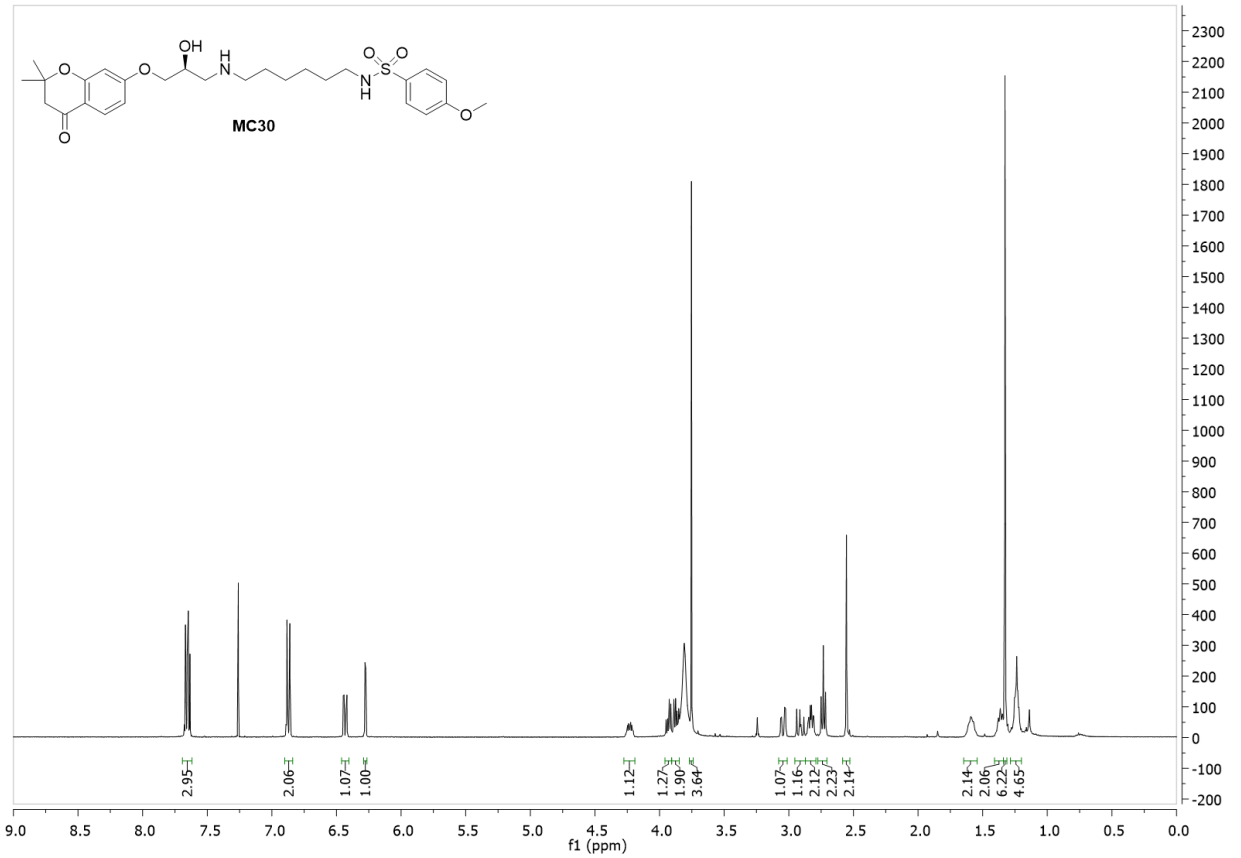


Figure S 103. ^{1}H-NMR of **MC30** (400 MHz, $CDCl_3$ +1% CD_3OD)

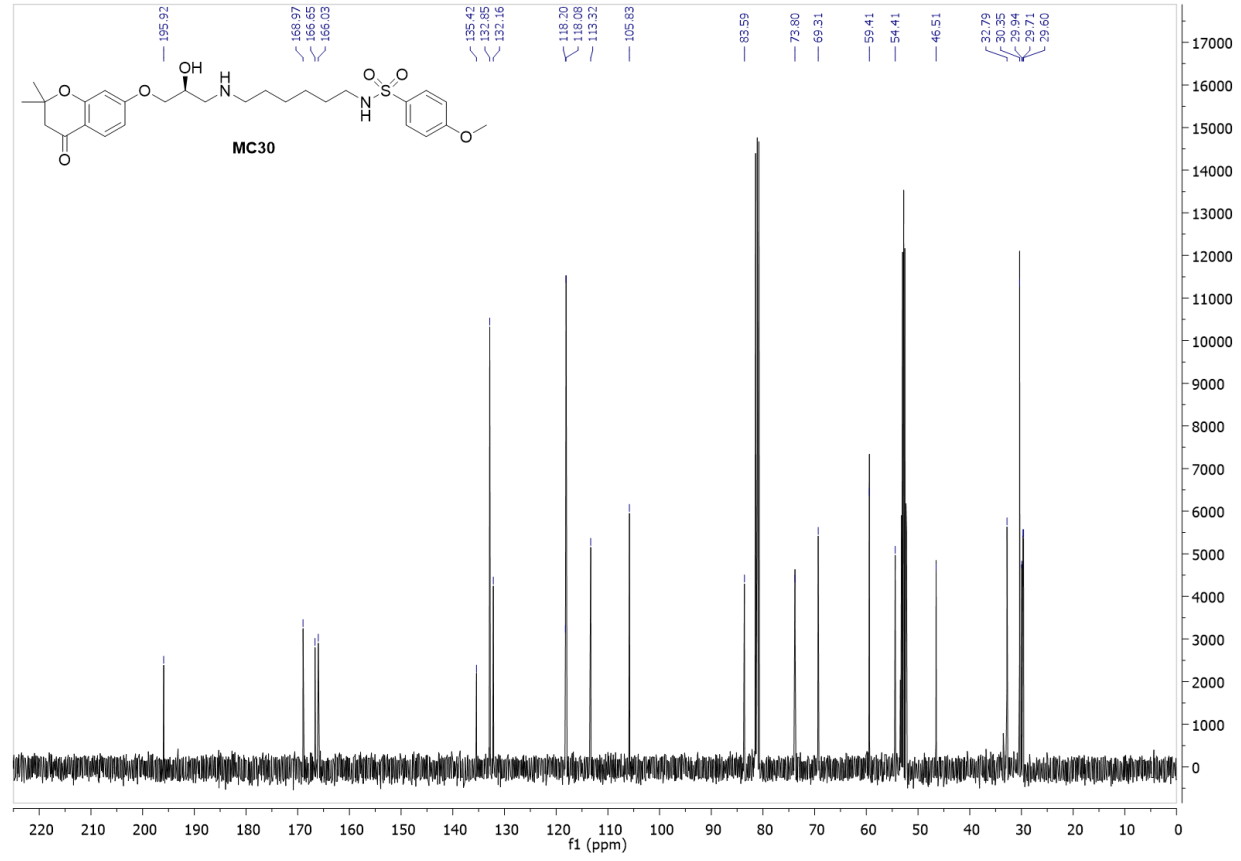


Figure S 104. ^{13}C-NMR of **MC30** (100 MHz, $CDCl_3$ +1% CD_3OD)

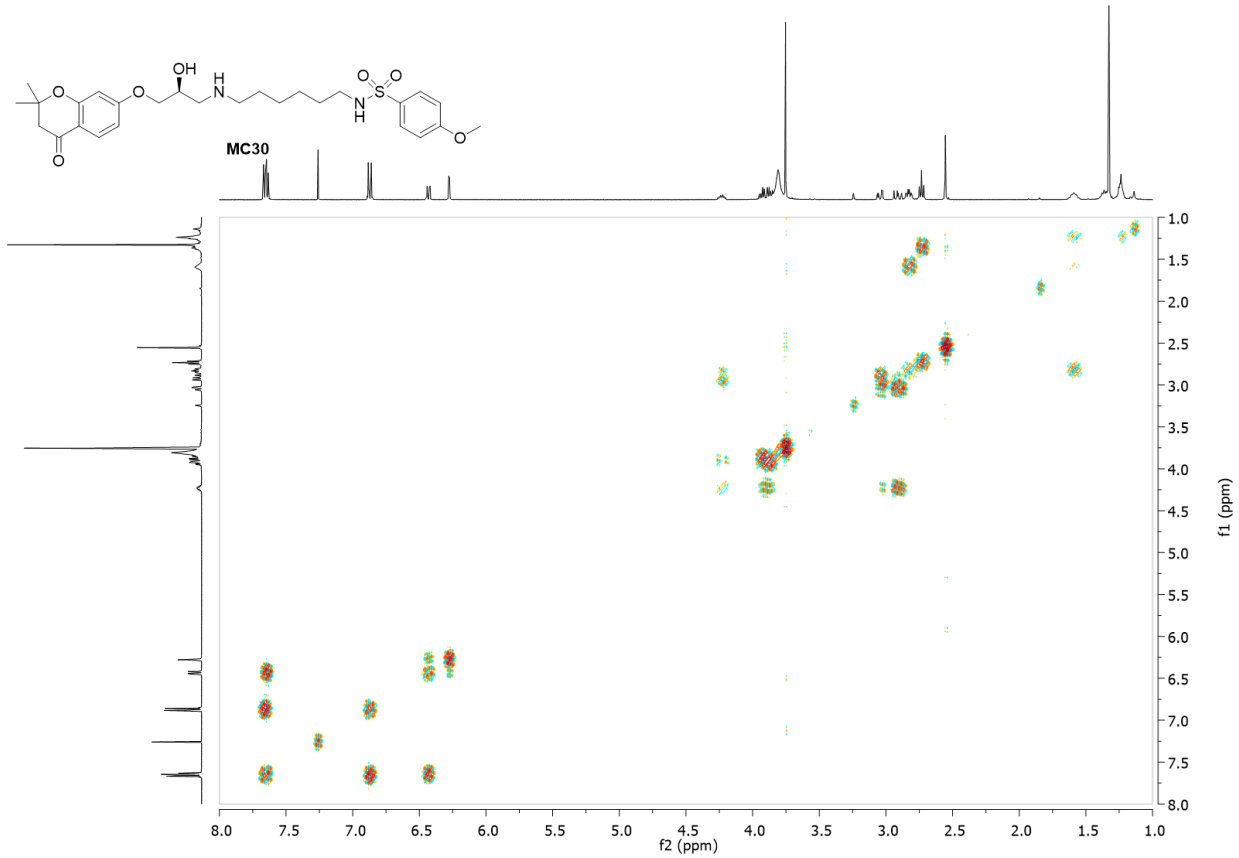


Figure S 105. gCOSY-NMR of **MC30** (400 MHz, $CDCl_3$ +1% CD_3OD)

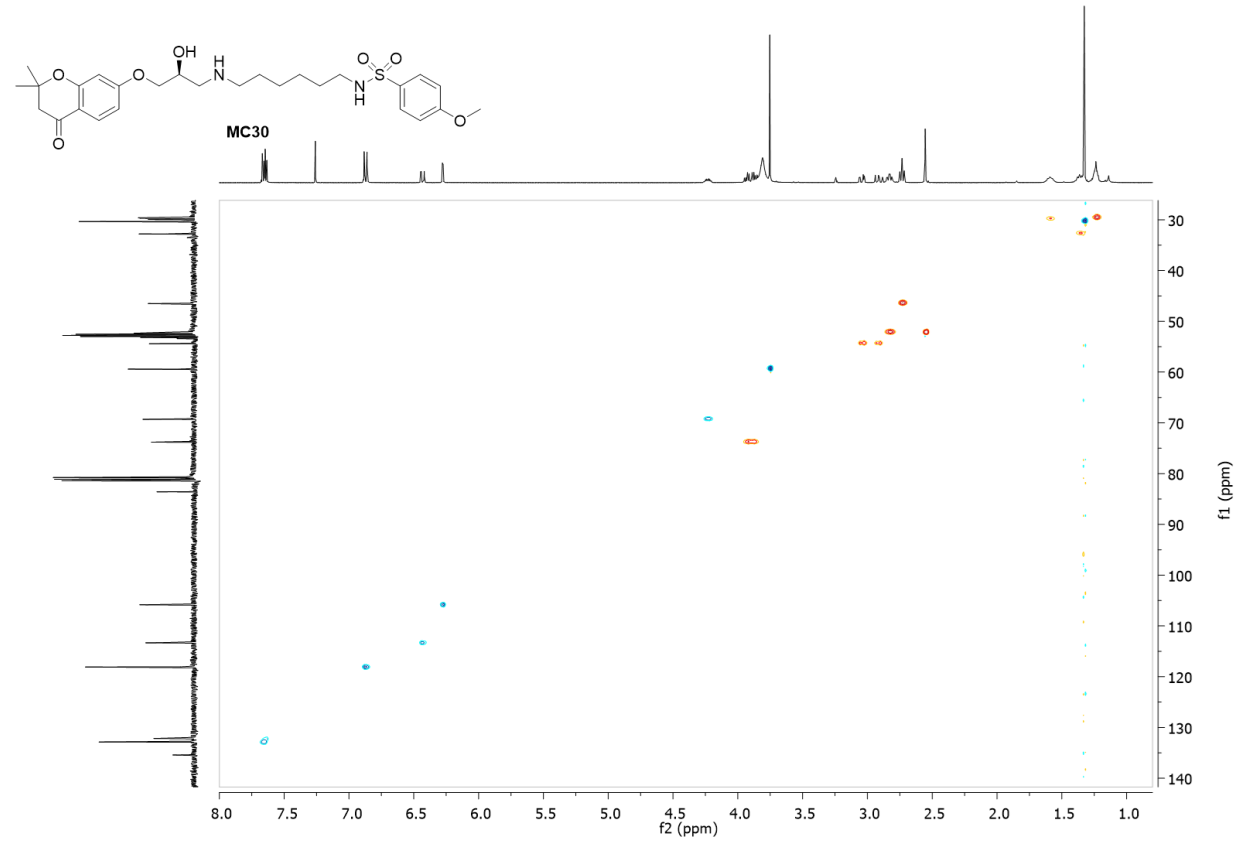


Figure S 106. gHSQC-NMR of **MC30** (400 MHz, $CDCl_3$ +1% CD_3OD)

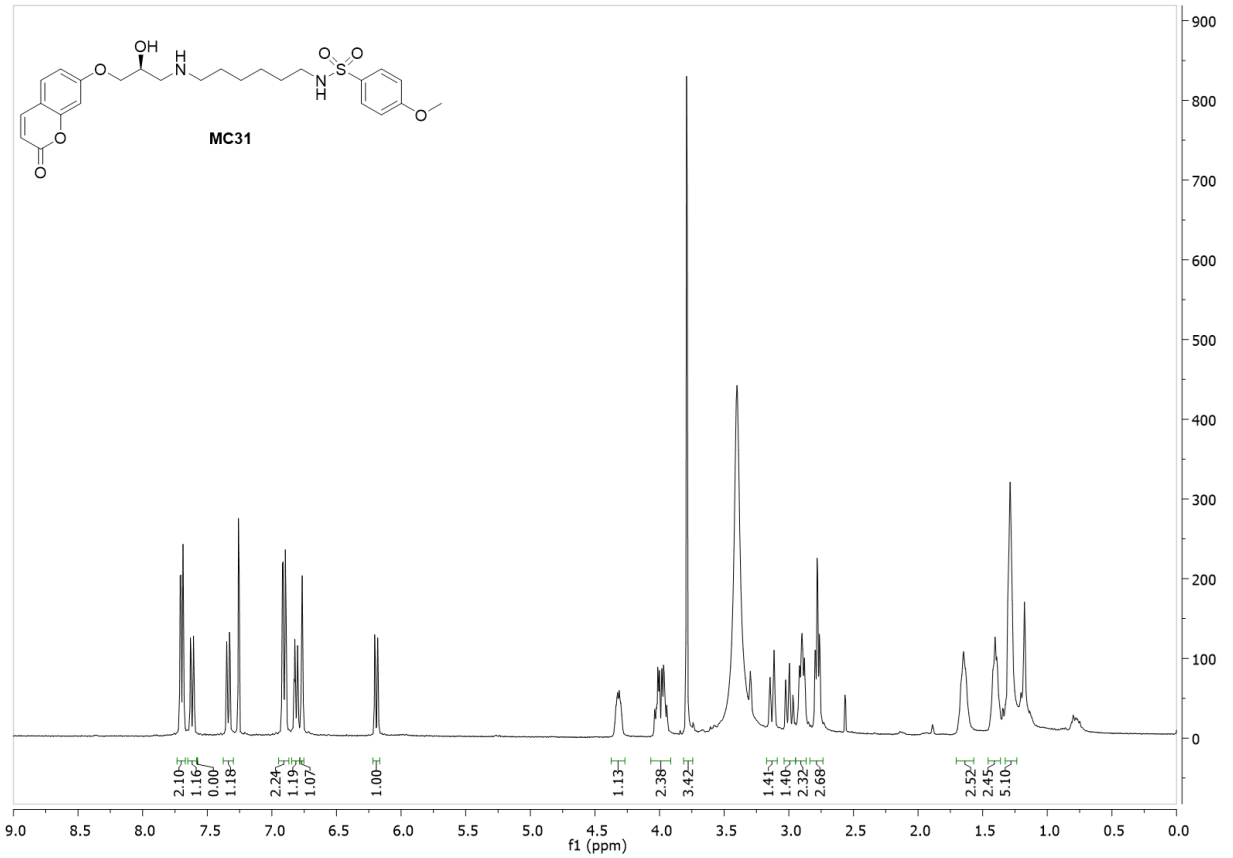


Figure S 107. ^{1}H-NMR of **MC31** (400 MHz, $CDCl_3$)

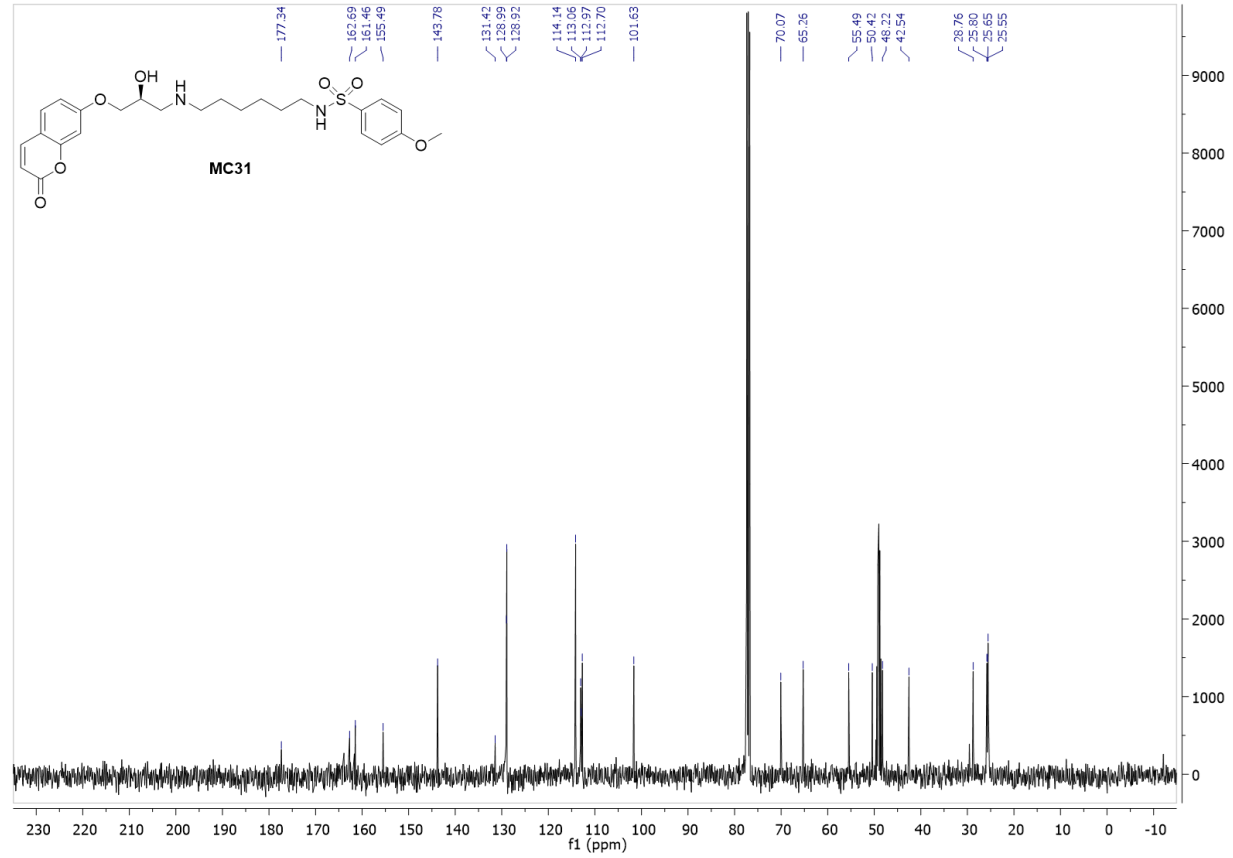


Figure S 108. ^{13}C-NMR of **MC31** (100 MHz, $CDCl_3$)

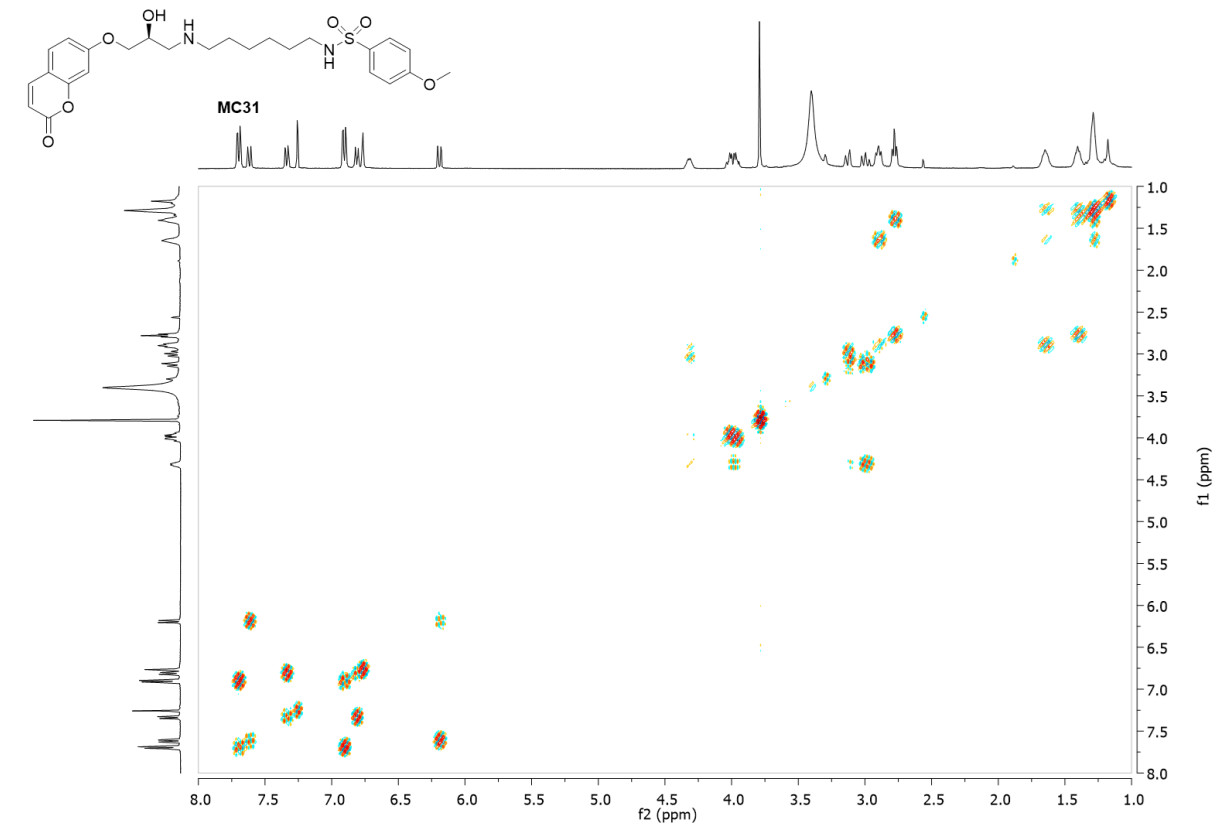


Figure S 109. gCOSY-NMR of **MC31** (400 MHz, $CDCl_3$)

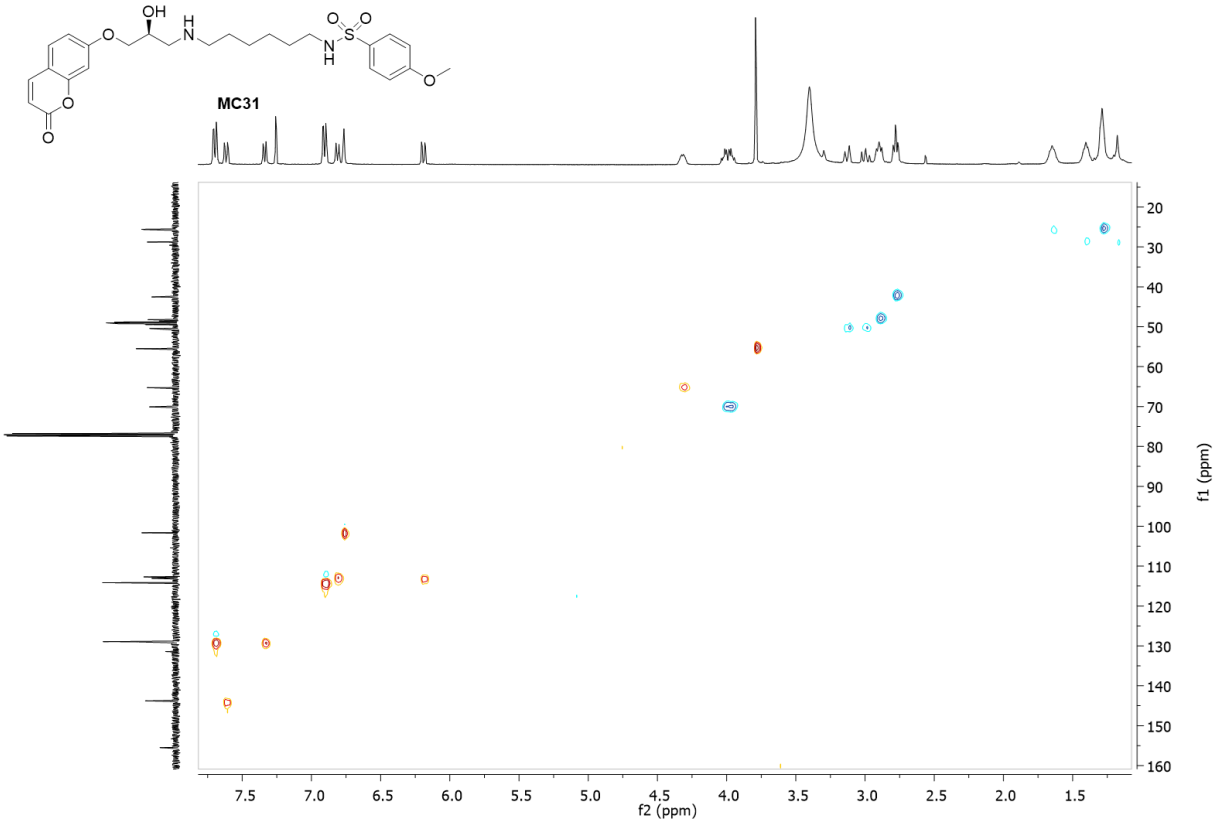


Figure S 110. gHSQC-NMR of **MC31** (400 MHz, $CDCl_3$)

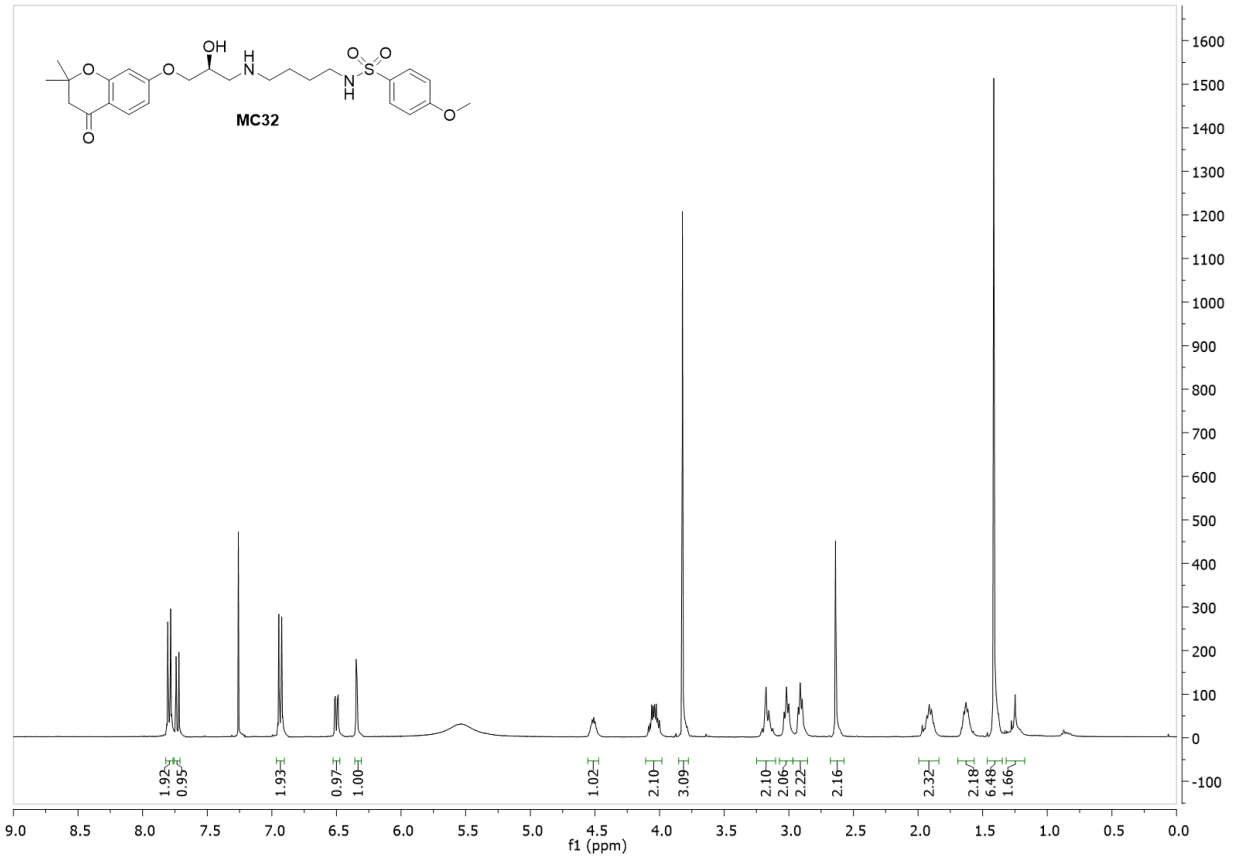


Figure S 111. ^{1}H-NMR of **MC32** (400 MHz, $CDCl_3$)

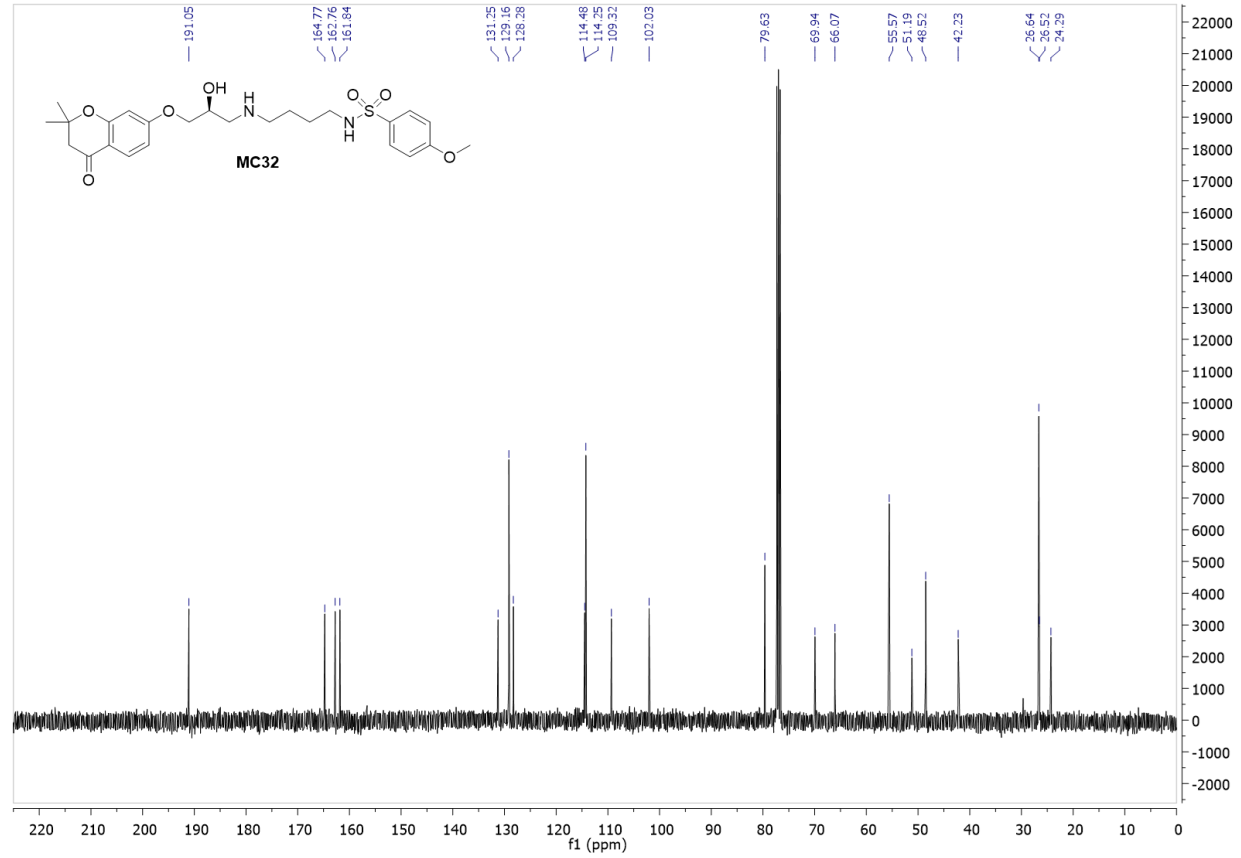


Figure S 112. ^{13}C-NMR of **MC32** (100 MHz, $CDCl_3$)

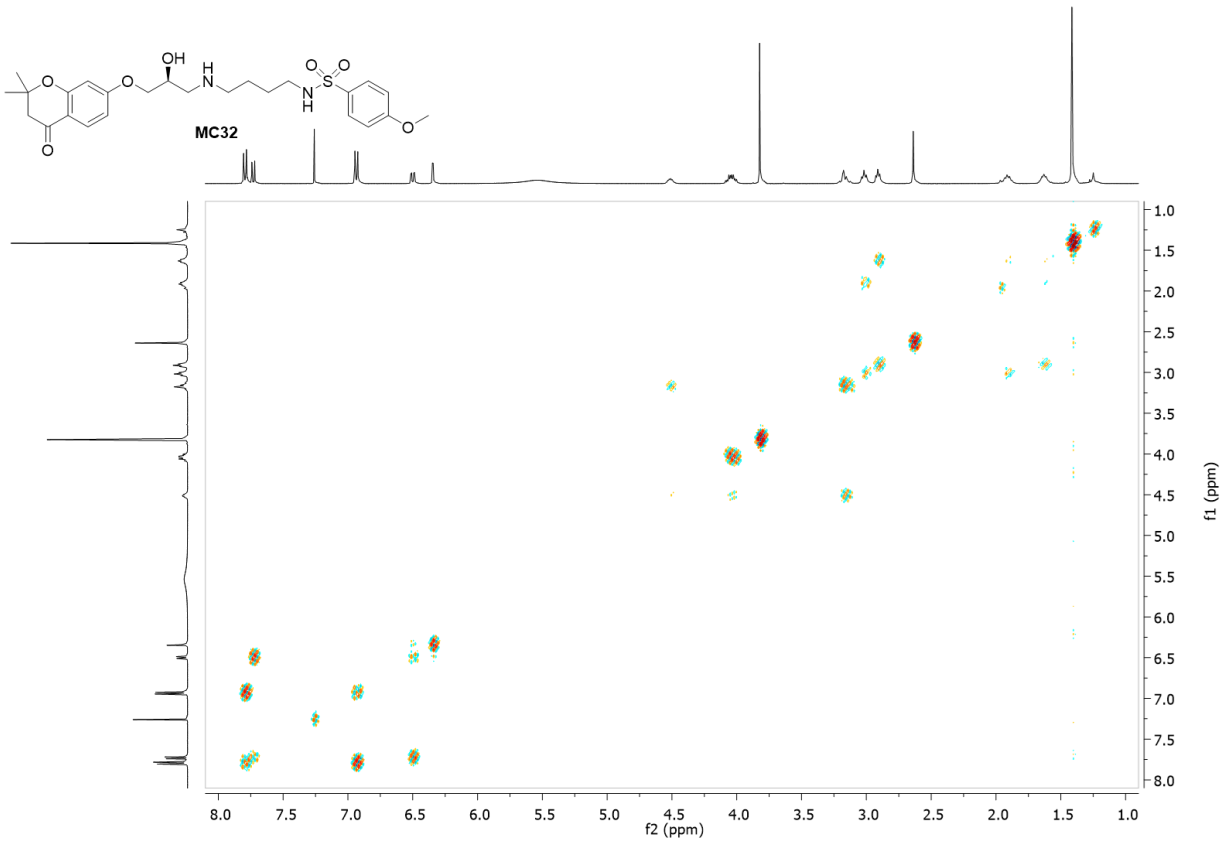


Figure S 113. gCOSY-NMR of **MC32** (400 MHz, $CDCl_3$)

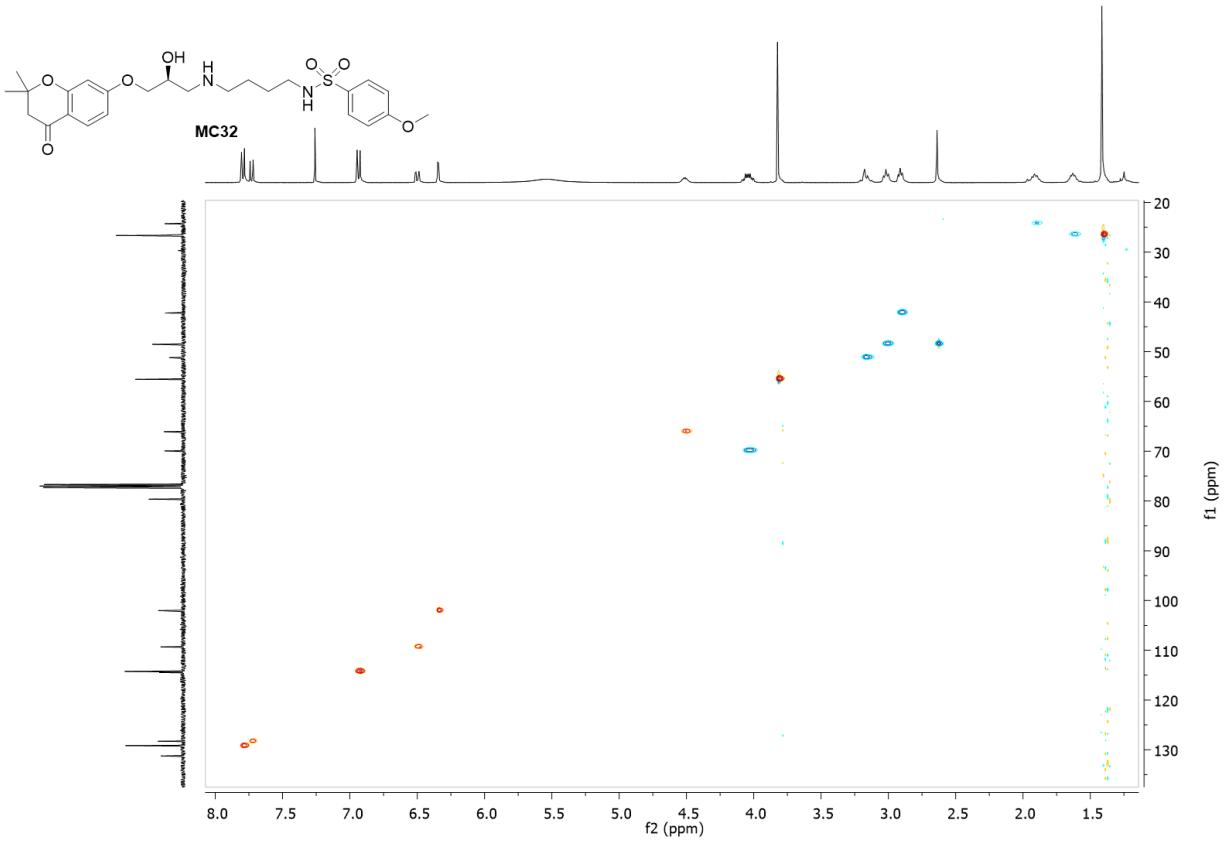


Figure S 114. gHSQC-NMR of **MC32** (400 MHz, $CDCl_3$)

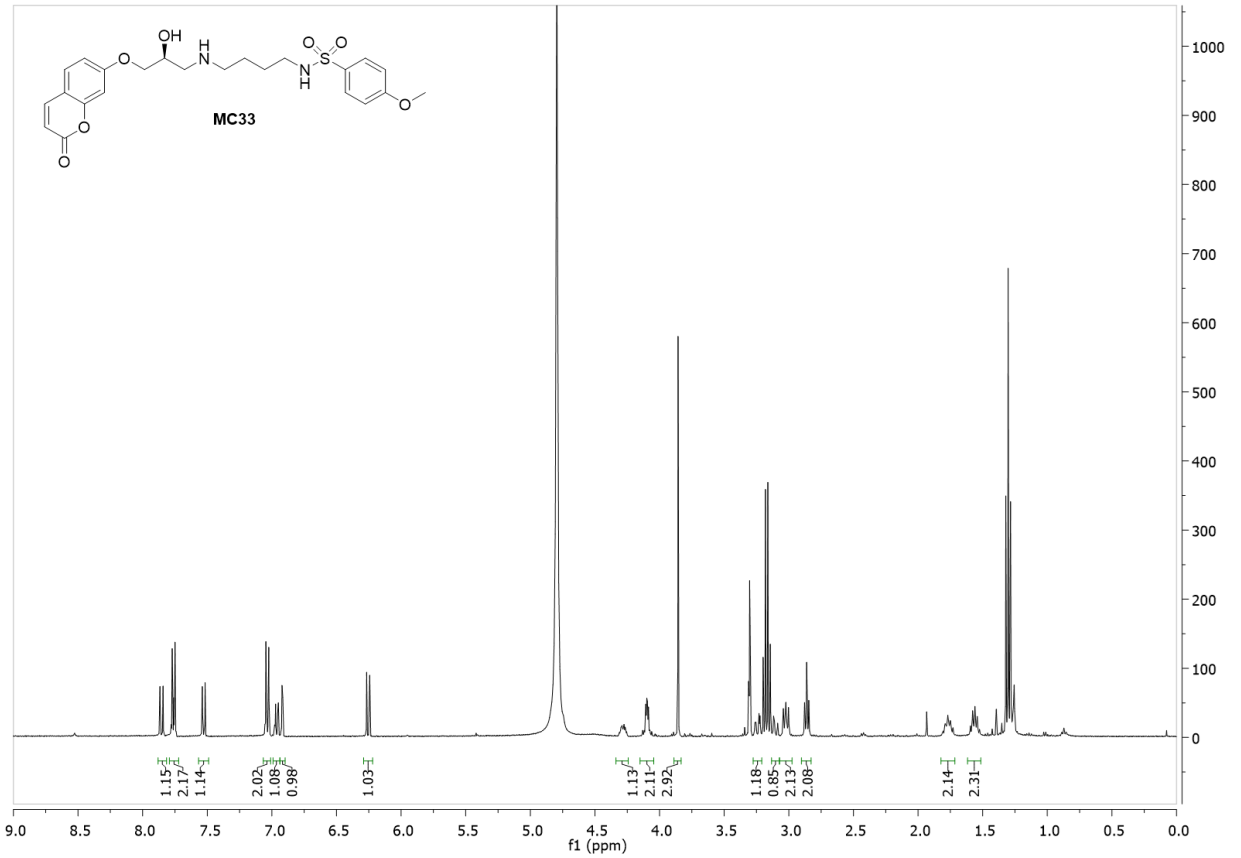


Figure S 115. ^{1}H-NMR of **MC33** (400 MHz, CD_3OD)

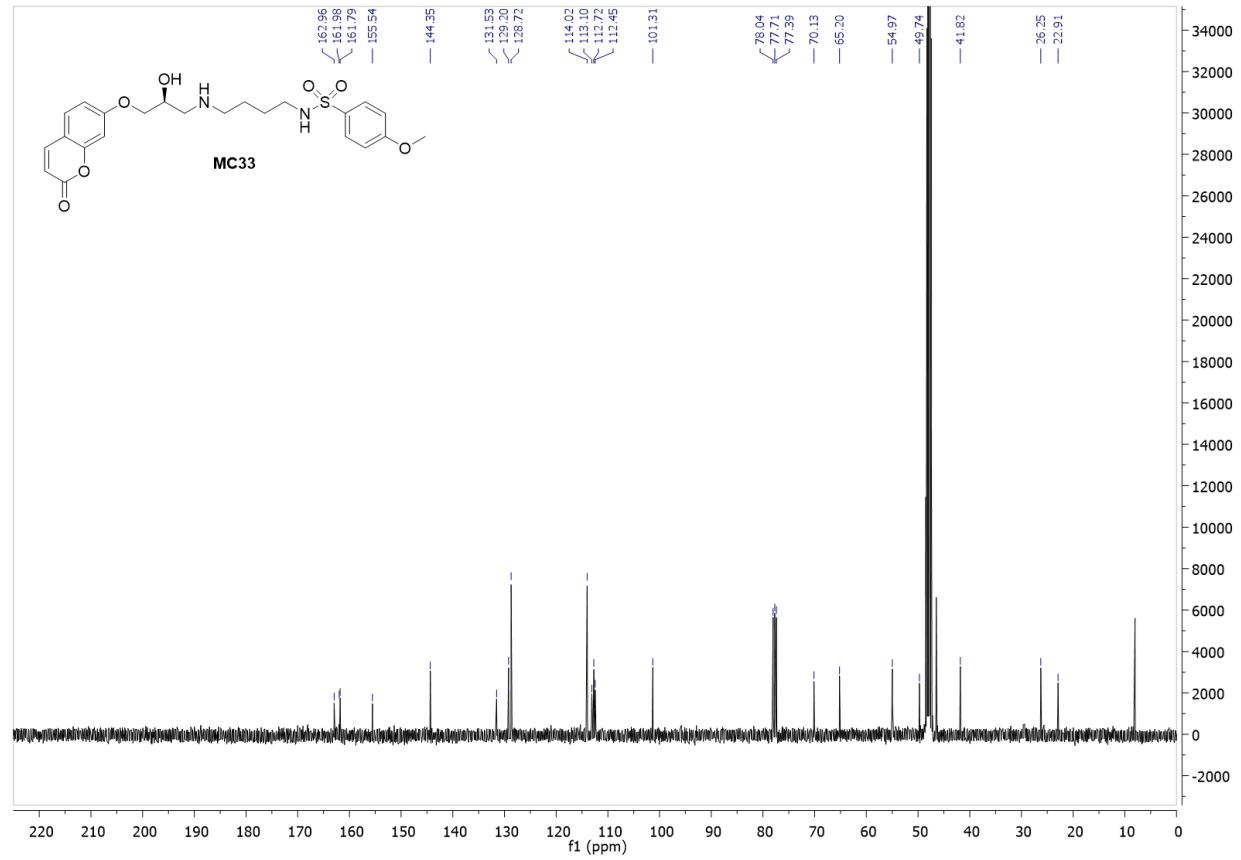


Figure S 116. ^{13}C-NMR of **MC33** (100 MHz, CD_3OD)

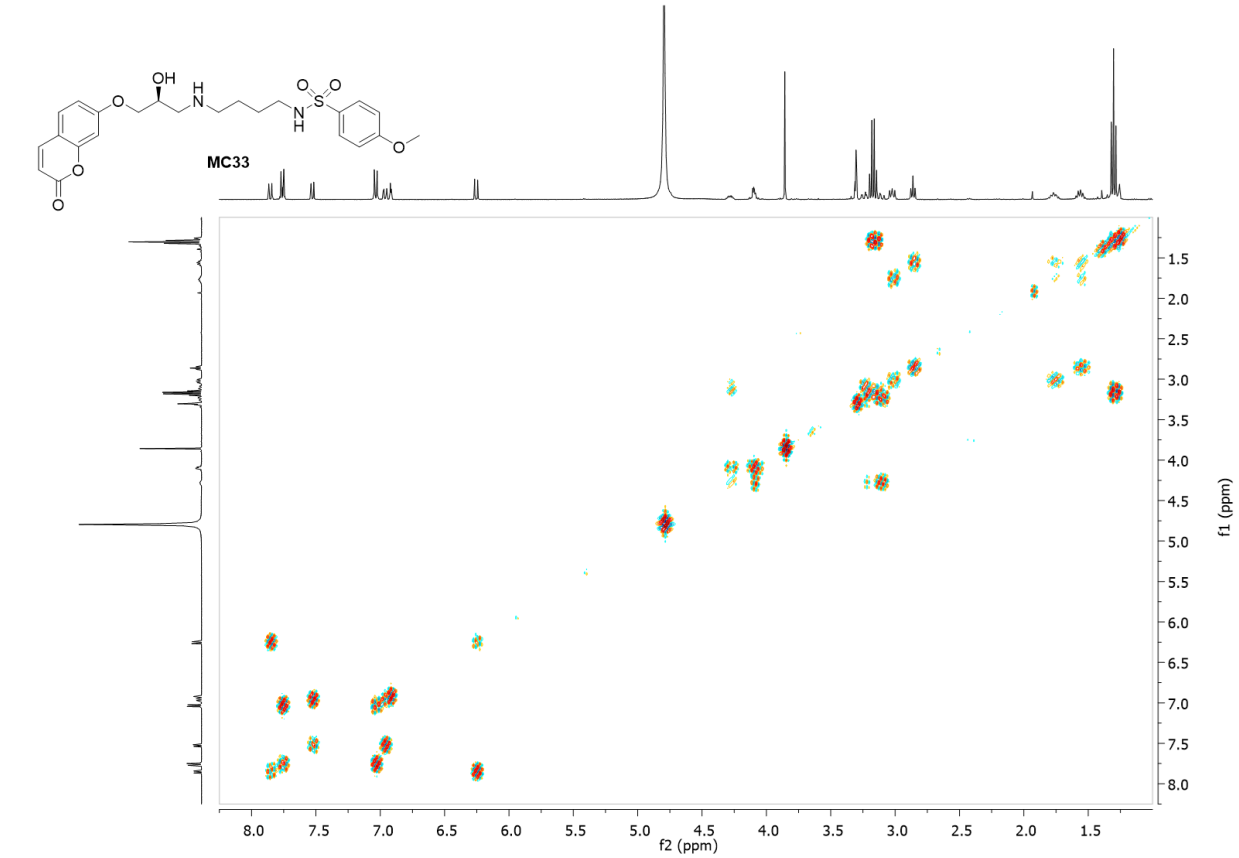


Figure S 117. gCOSY-NMR of **MC33** (400 MHz, CD_3OD)

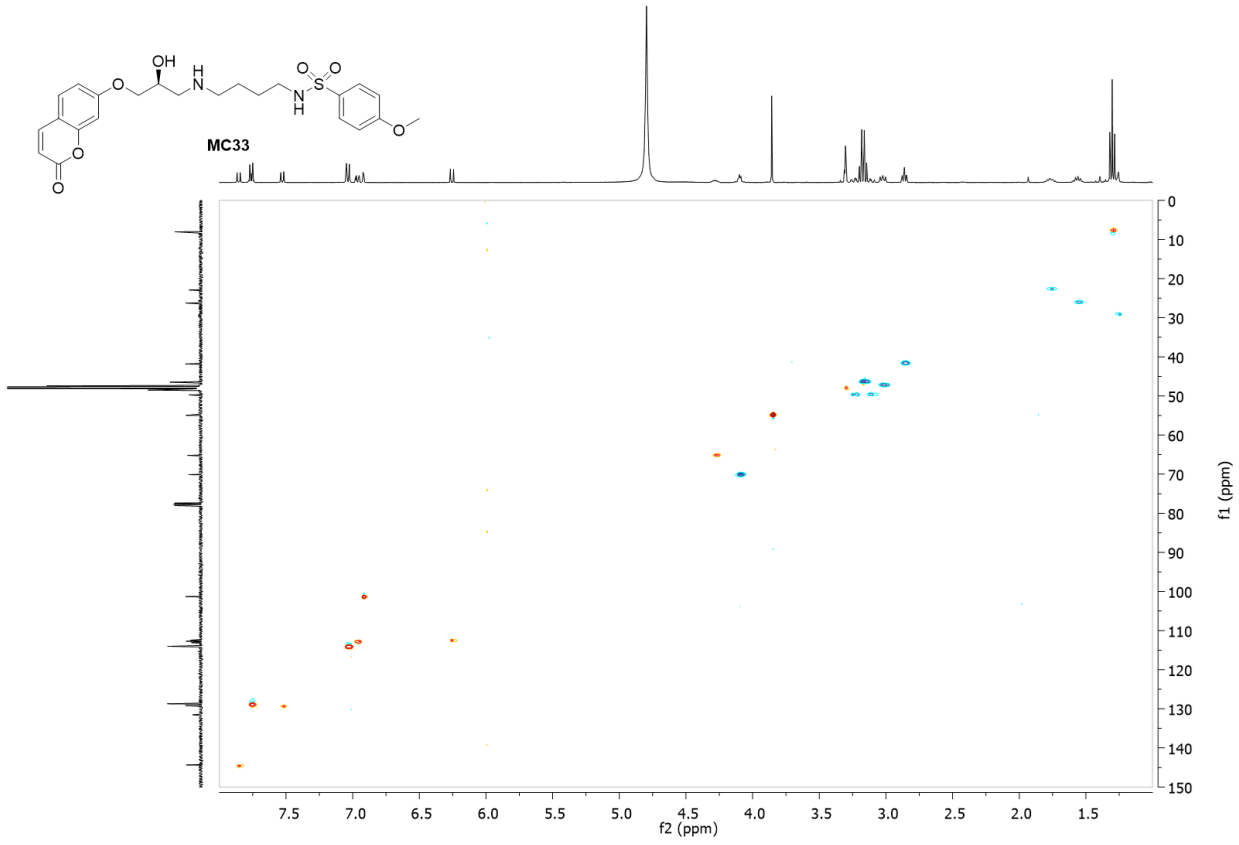


Figure S 118. gHSQC-NMR of **MC33** (400 MHz, CD_3OD)

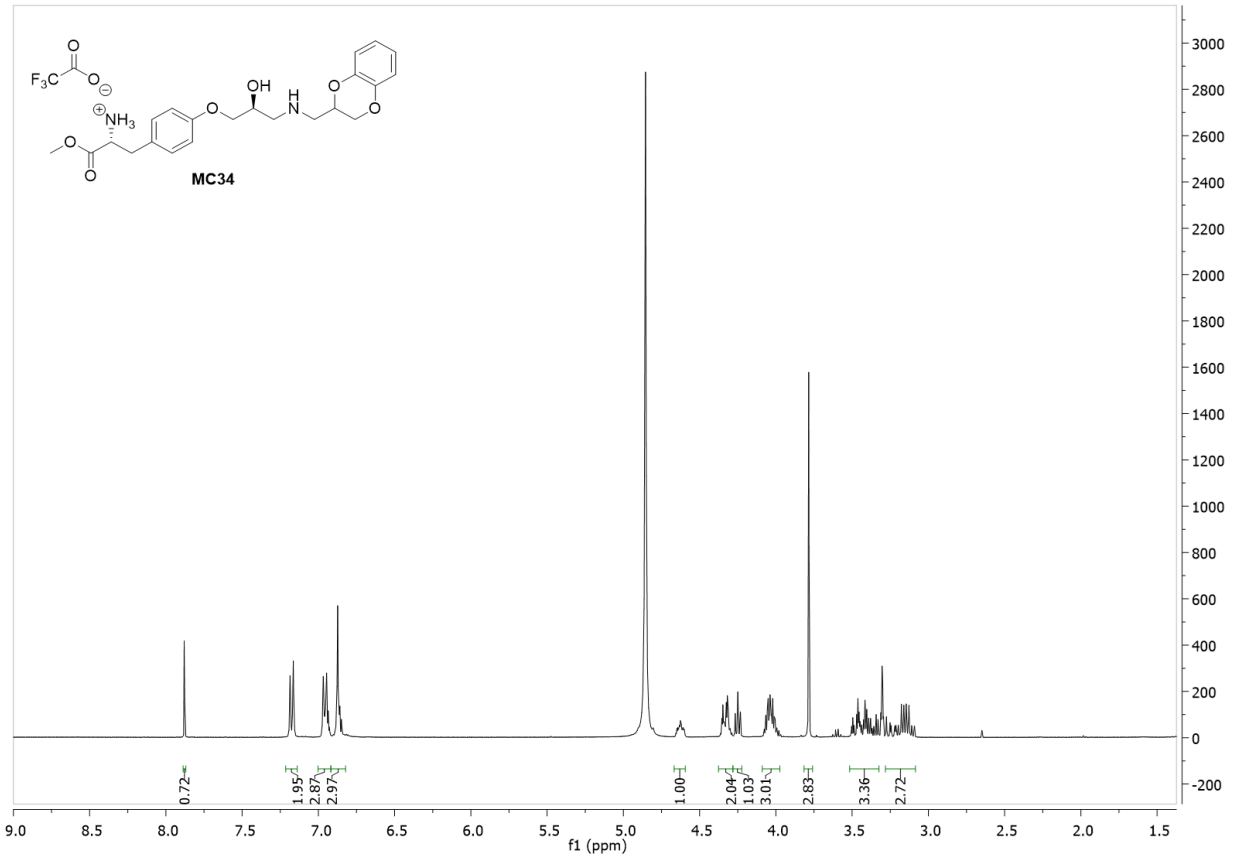


Figure S 119. ^{1}H-NMR of **MC34** (400 MHz, CD_3OD)

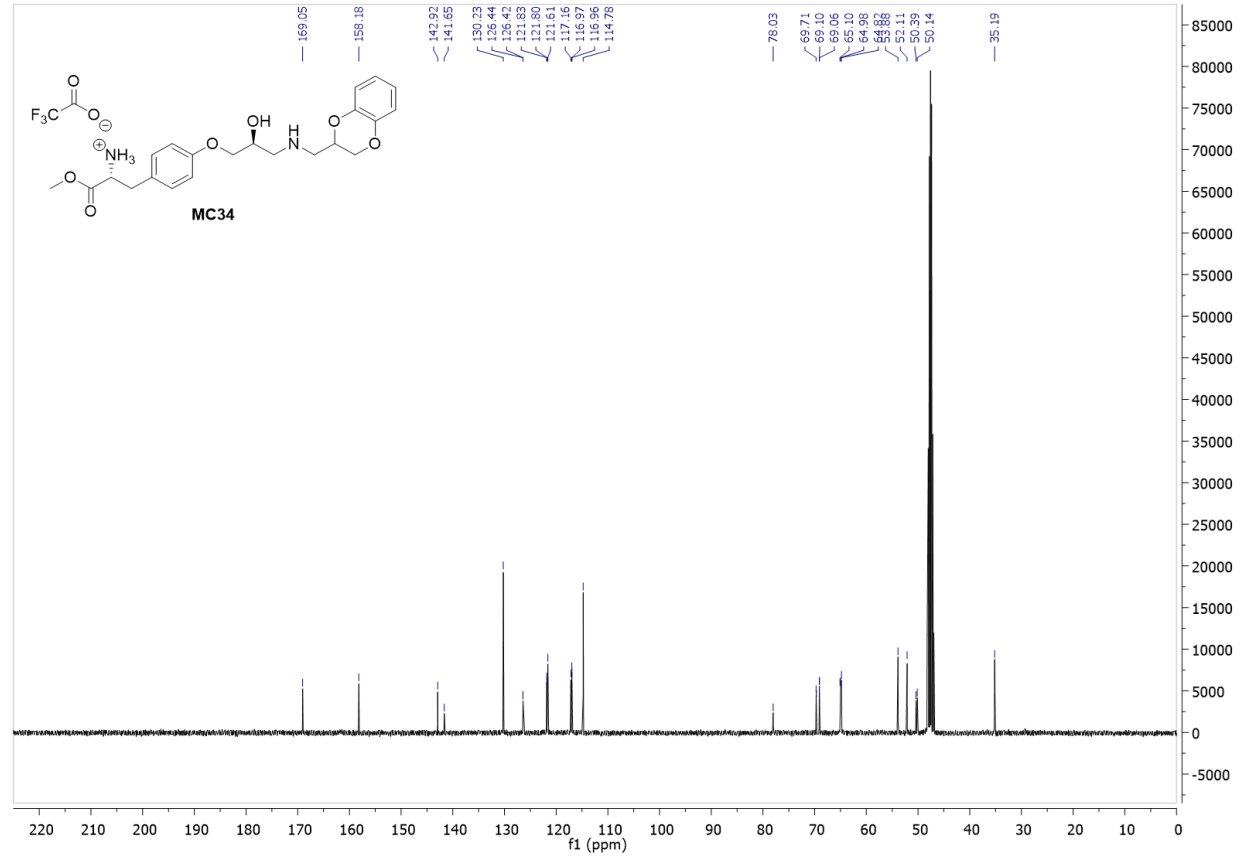


Figure S 120. ^{13}C-NMR of **MC34** (100 MHz, CD_3OD)

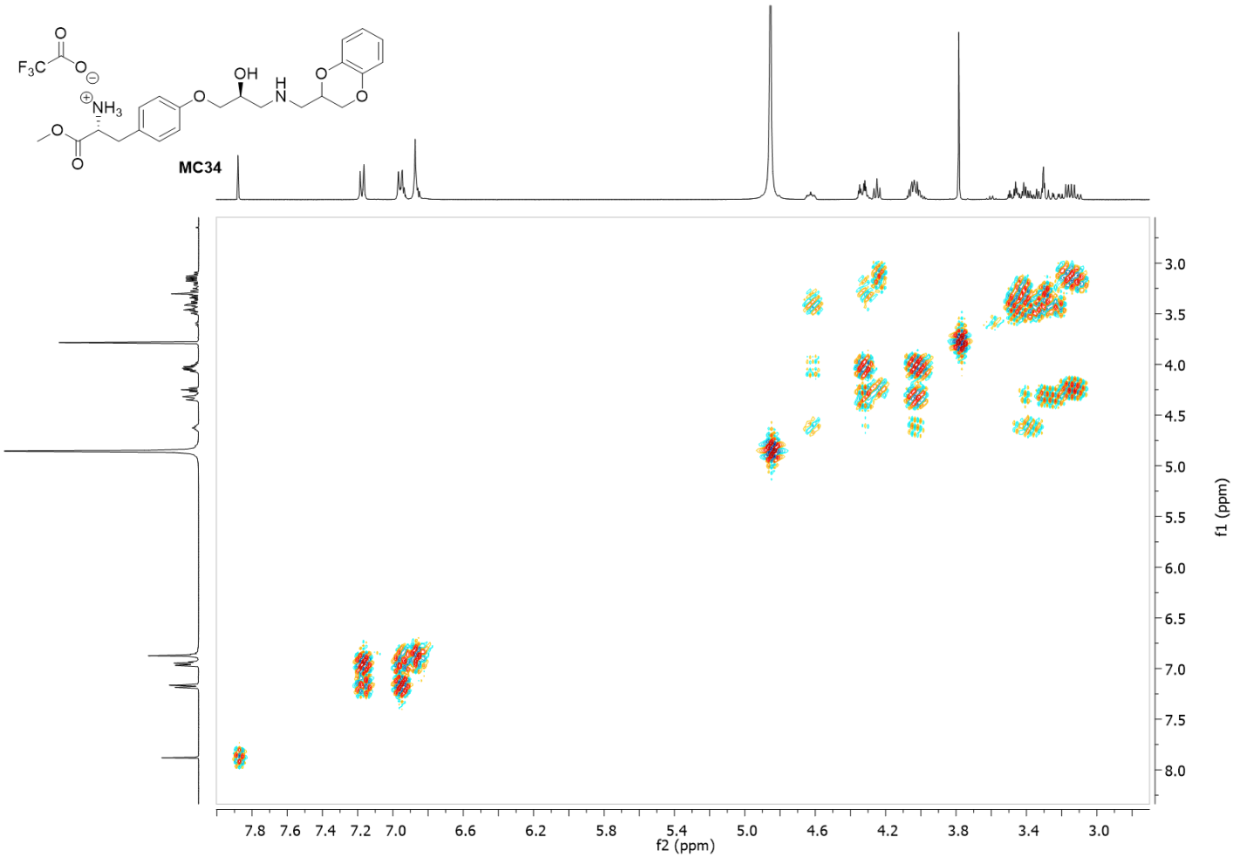


Figure S 121. gCOSY-NMR of **MC34** (400 MHz, CD_3OD)

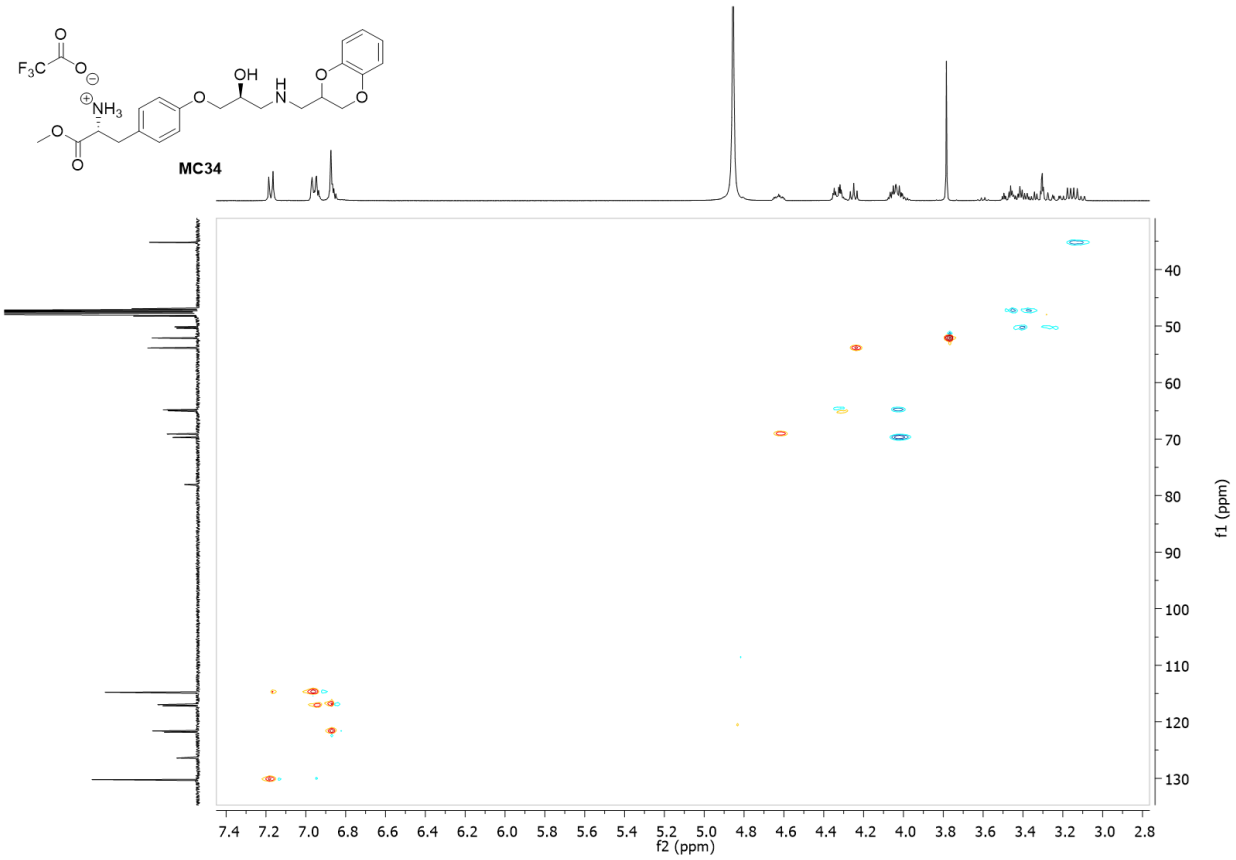


Figure S 122. gHSQC-NMR of **MC34** (400 MHz, CD_3OD)

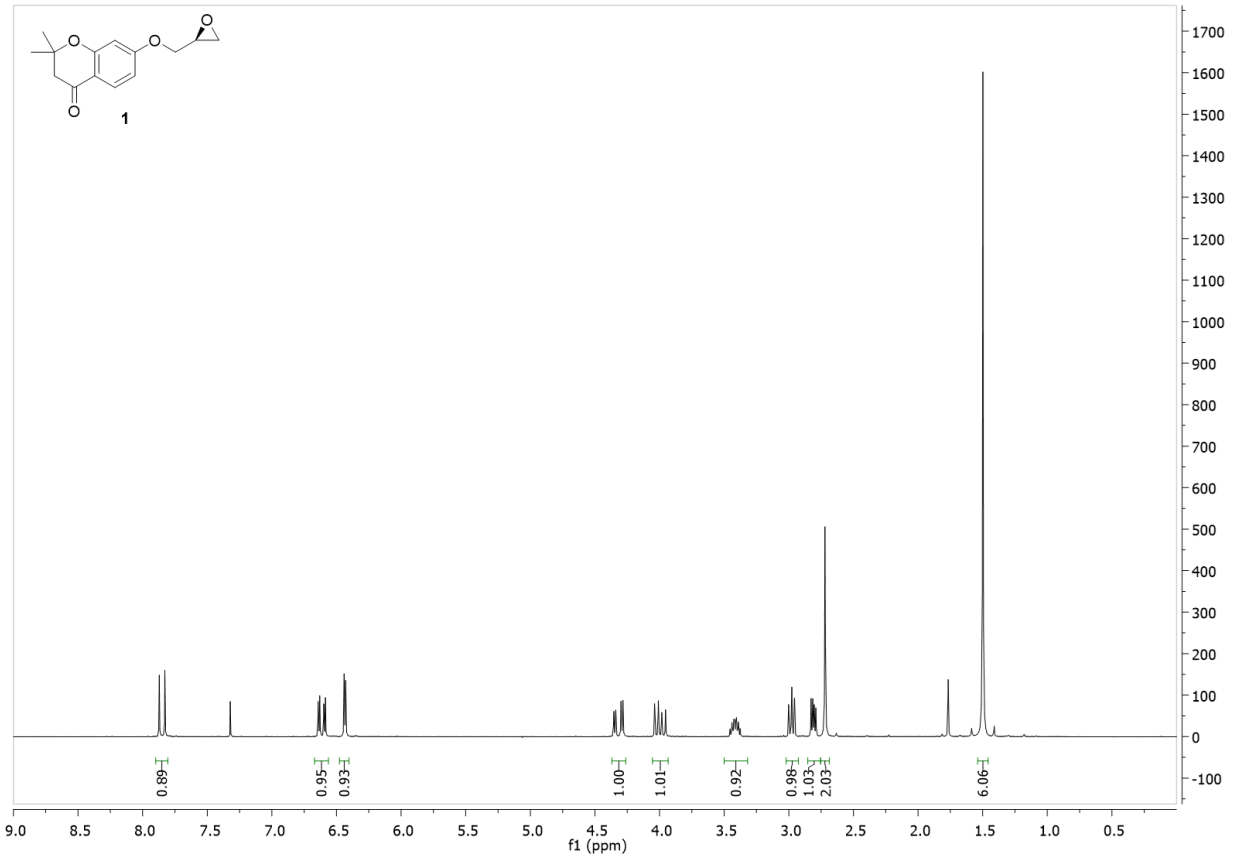


Figure S 123. ^{1}H-NMR of **1** (400 MHz, $CDCl_3$).

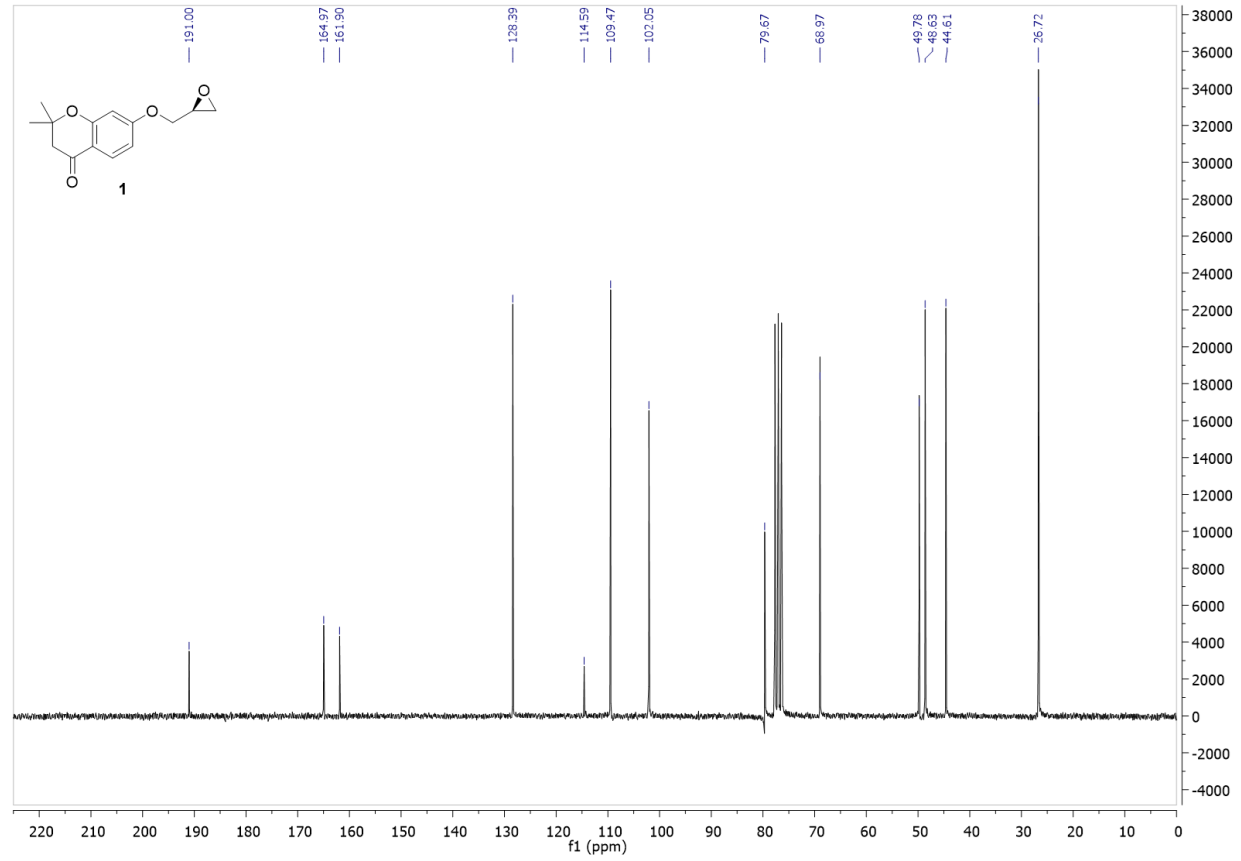


Figure S 124. ^{13}C-NMR of **1** (100 MHz, $CDCl_3$).

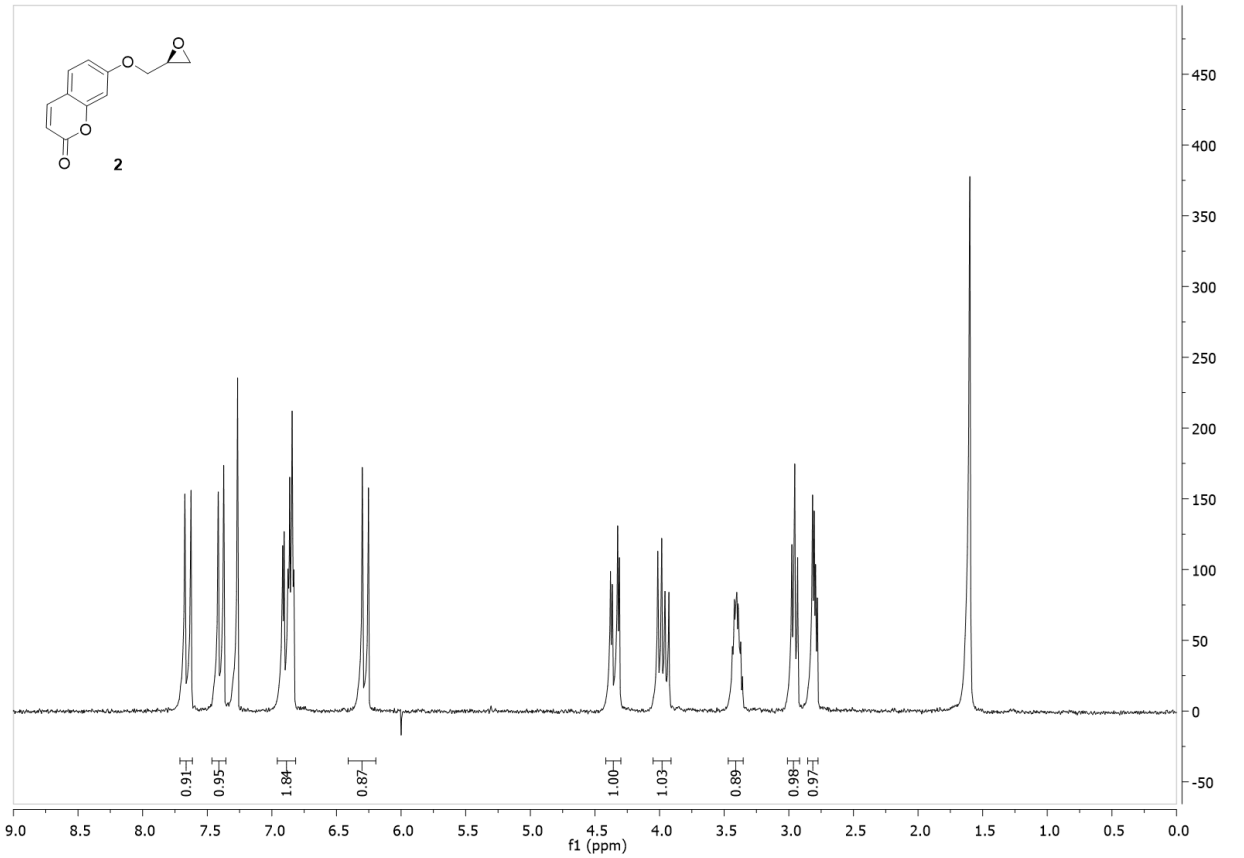


Figure S 125. ^{1}H-NMR of **2** (400 MHz, $CDCl_3$).

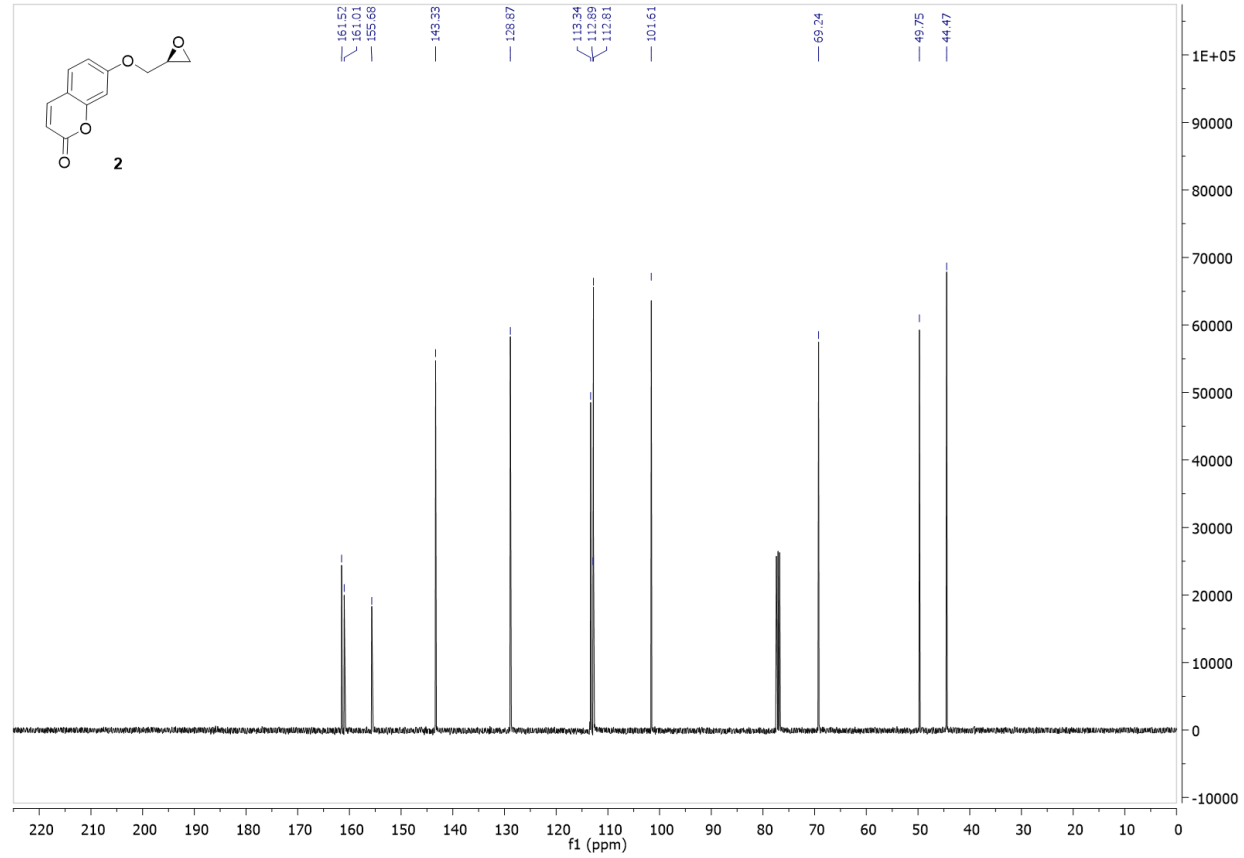


Figure S 126. ^{13}C-NMR of **2** (100 MHz, $CDCl_3$).

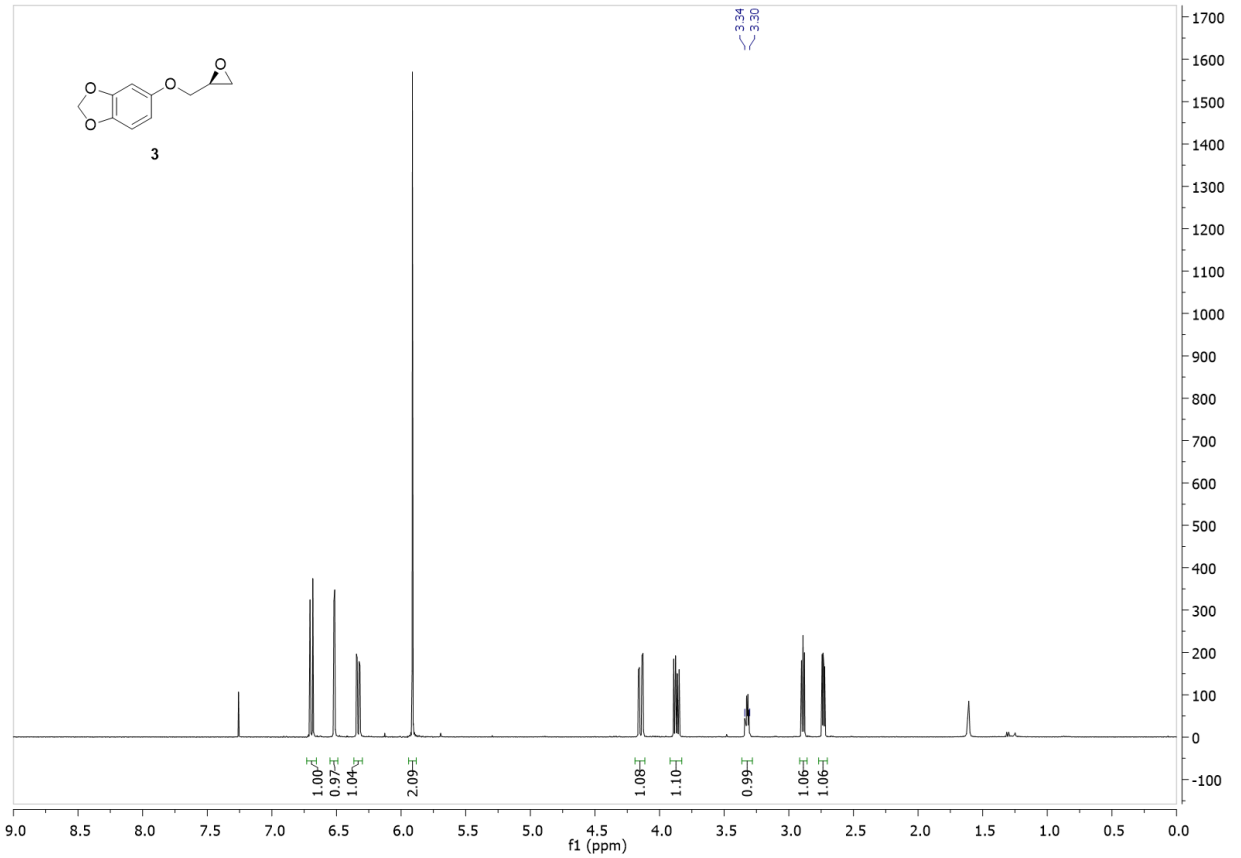


Figure S 127. ^{1}H-NMR of **3** (400 MHz, $CDCl_3$)

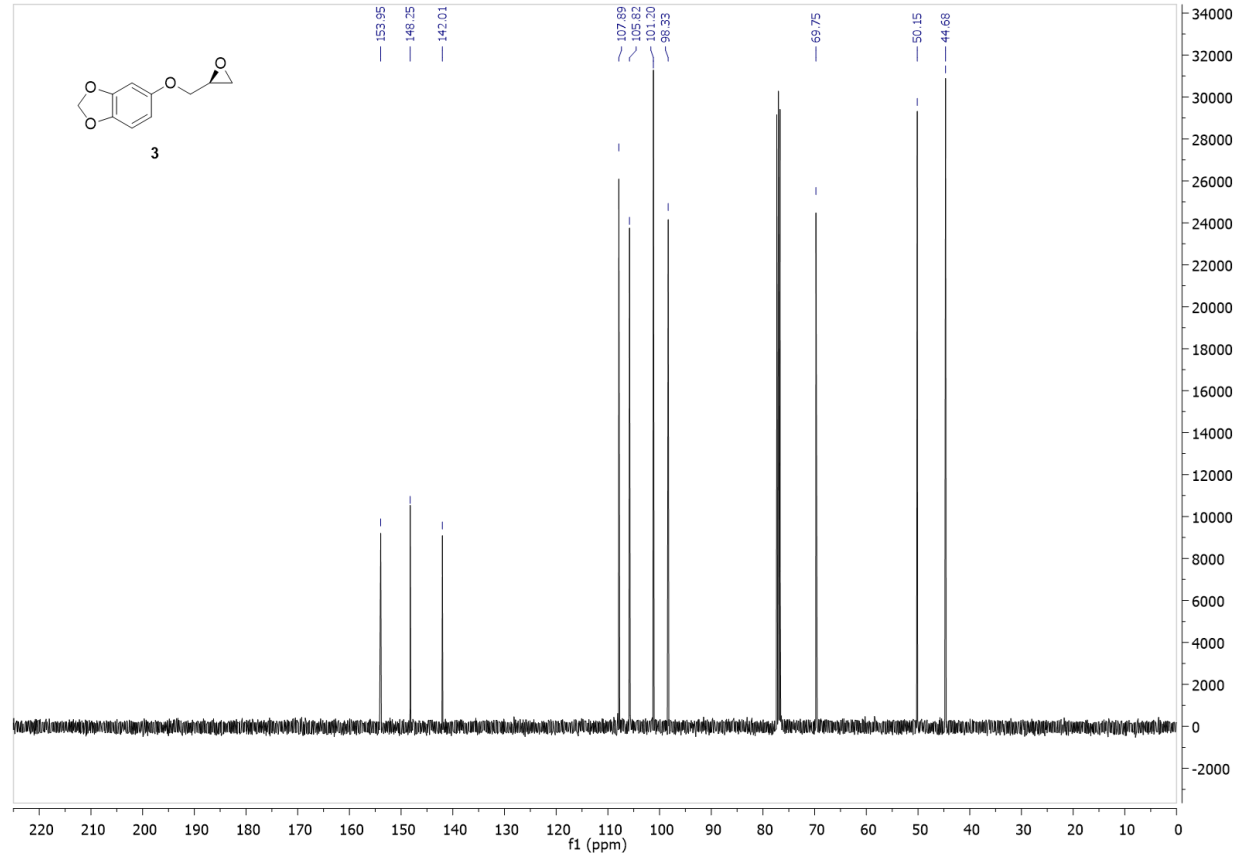


Figure S 128. ^{13}C-NMR of **3** (100 MHz, $CDCl_3$)

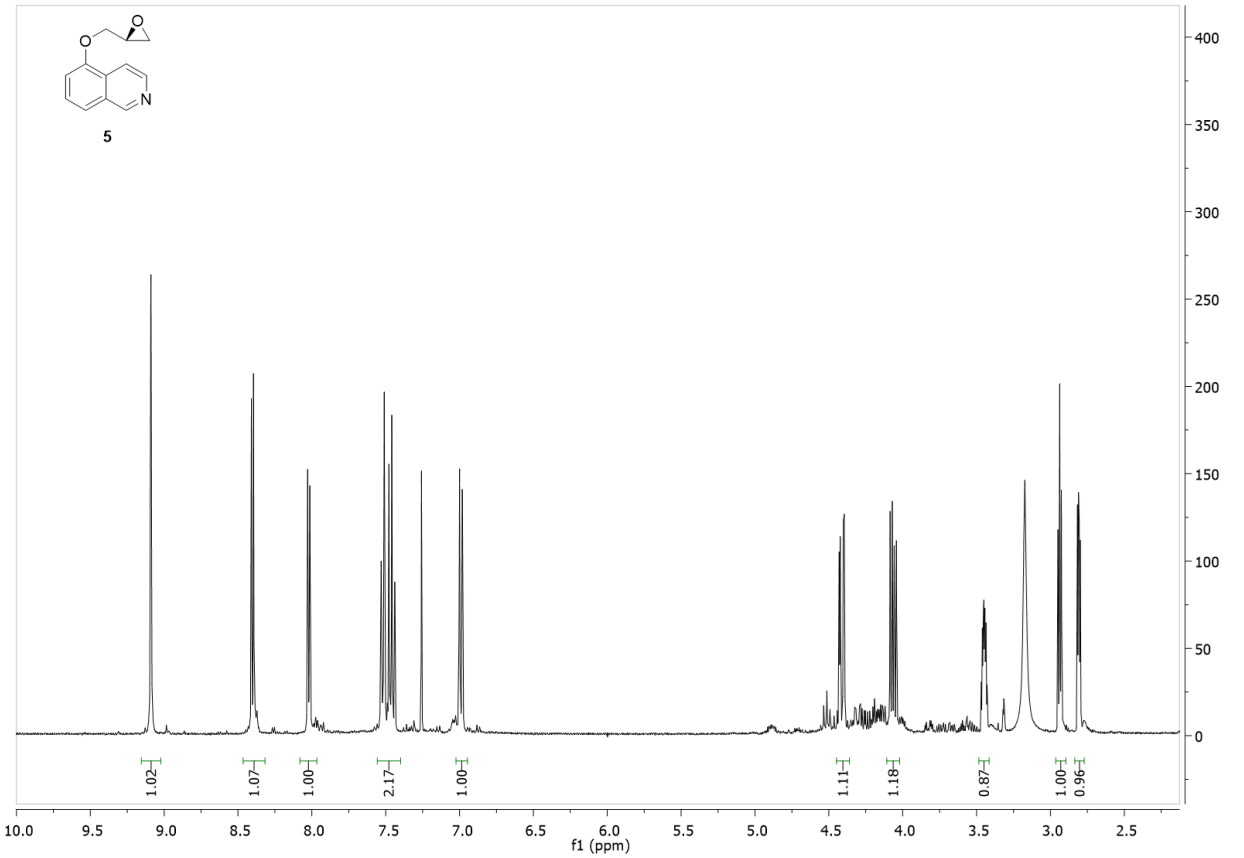


Figure S 129. ^{1}H-NMR of **5** (400 MHz, $CDCl_3$ +5% CD_3OD)

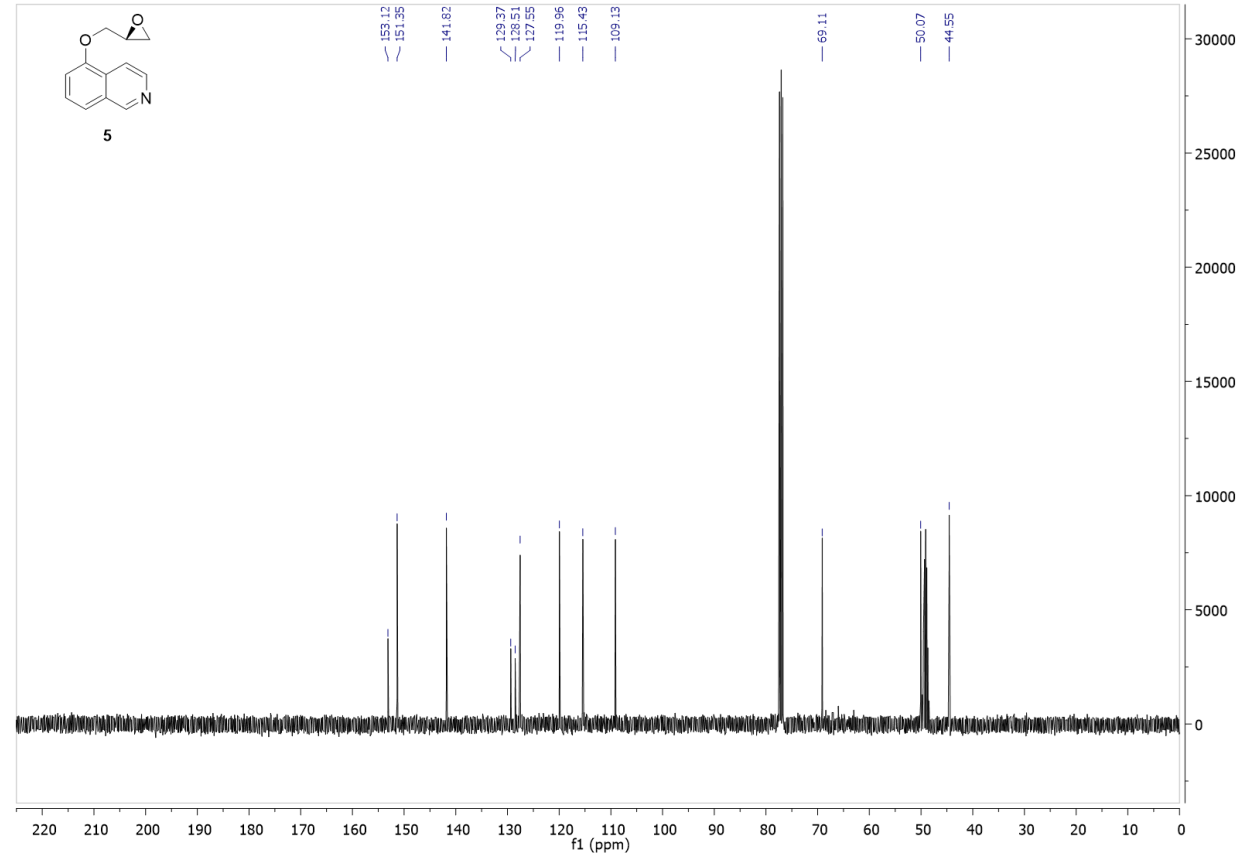


Figure S 130. ^{13}C-NMR of **5** (50 MHz, $CDCl_3$ +5% CD_3OD)

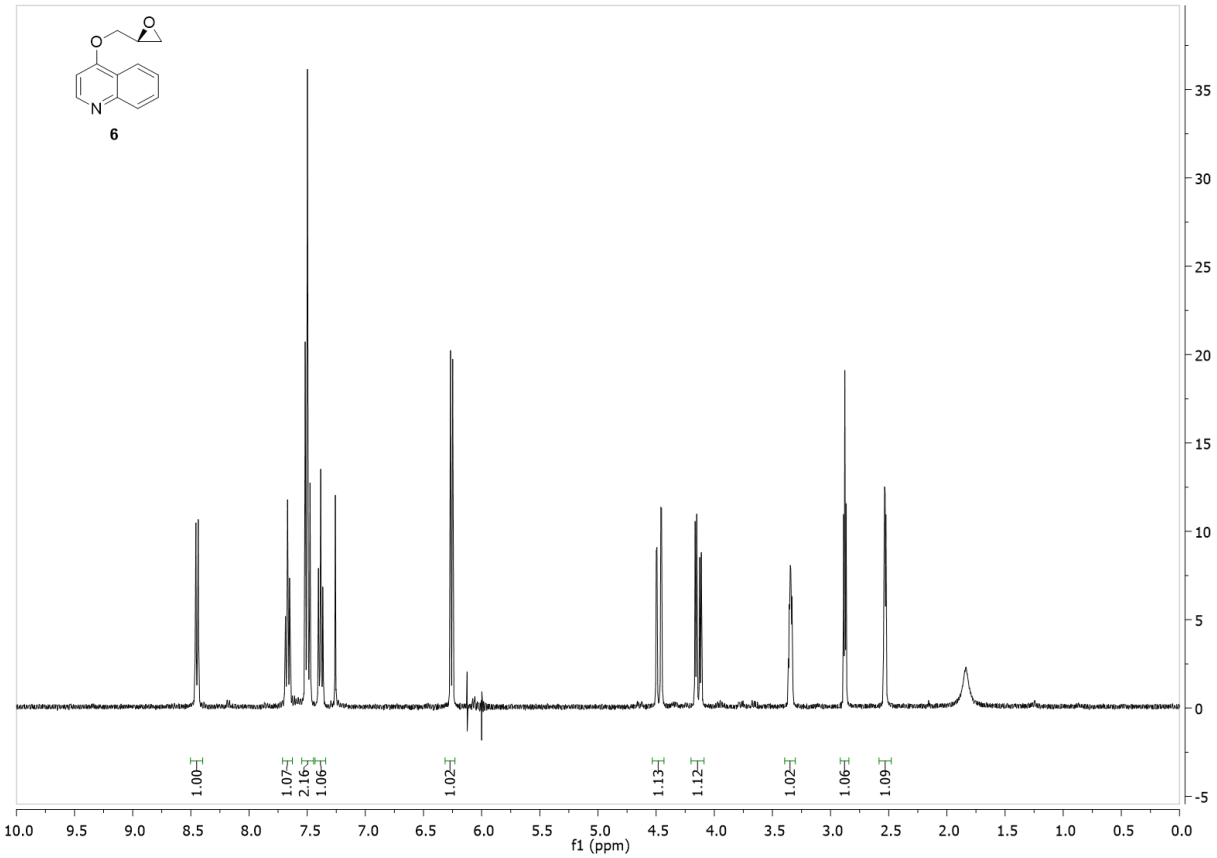


Figure S 131. ^{1}H-NMR of **6** (400 MHz, $CDCl_3$)

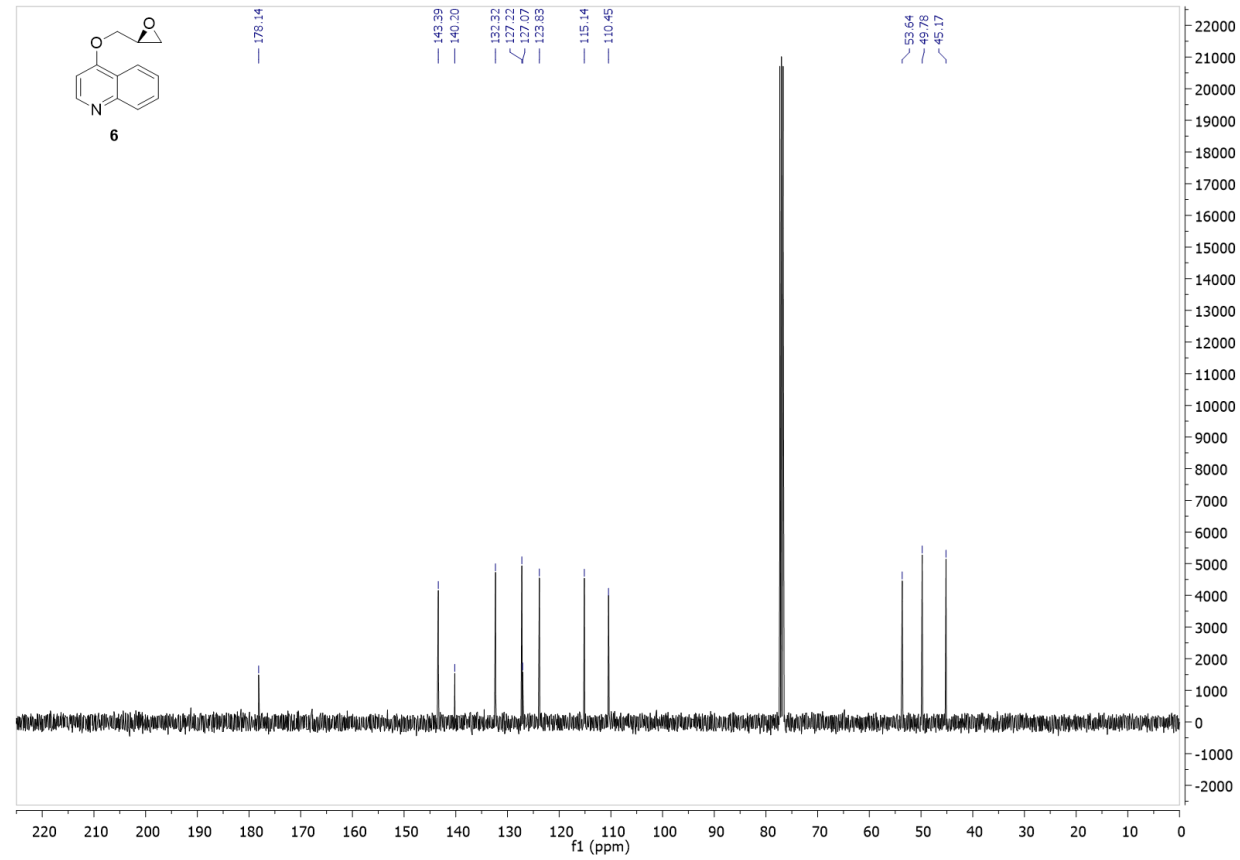


Figure S 132. ^{13}C-NMR of **6** (400 MHz, $CDCl_3$)

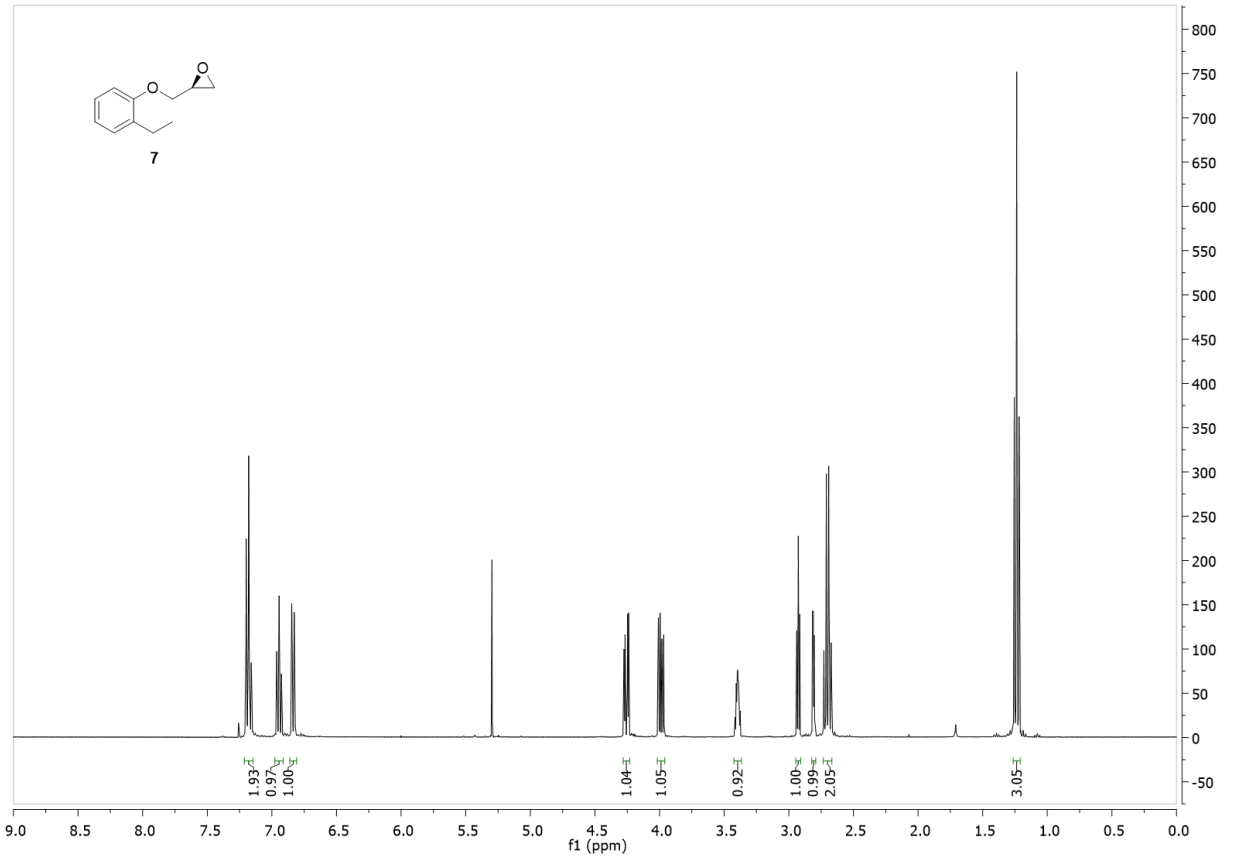


Figure S 133. ^{1}H-NMR of **7** (400 MHz, $CDCl_3$)

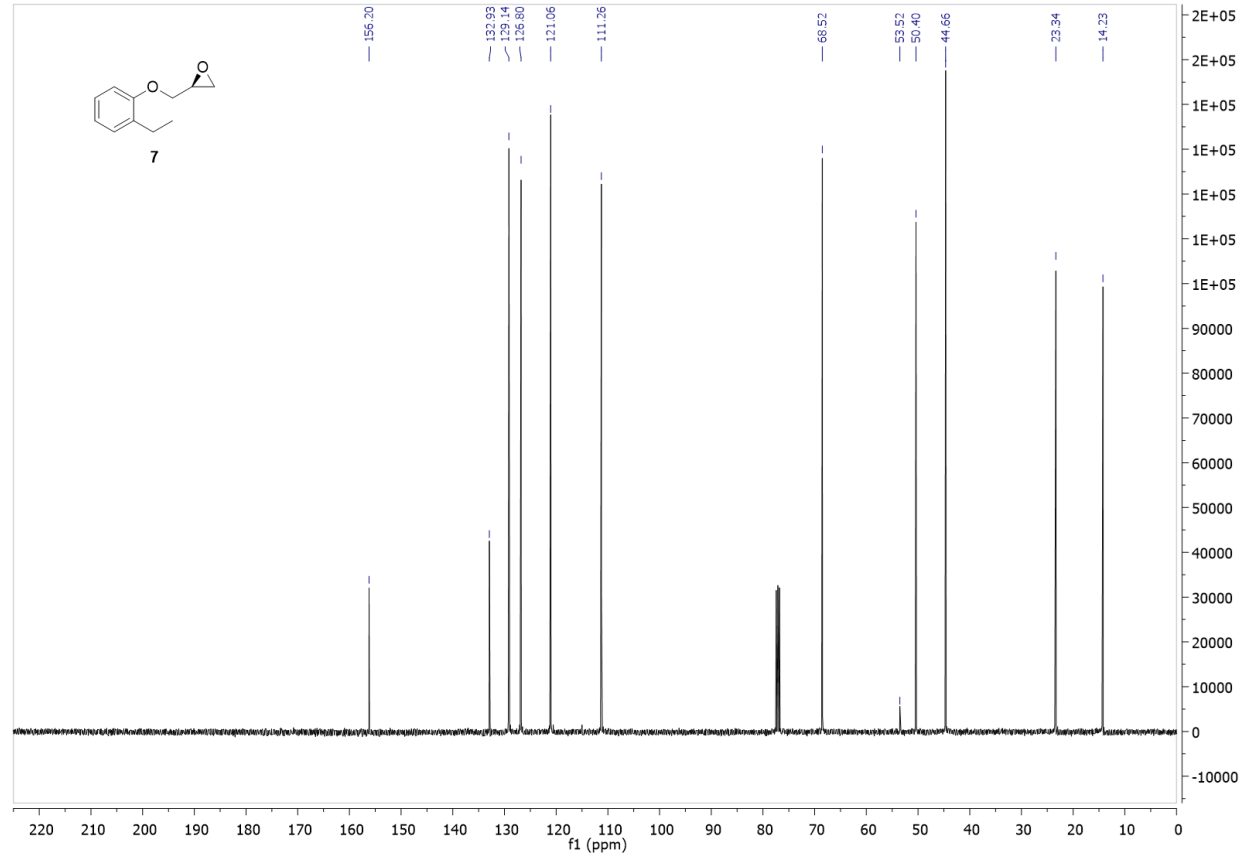


Figure S 134. ^{13}C-NMR of **7** (100 MHz, $CDCl_3$)

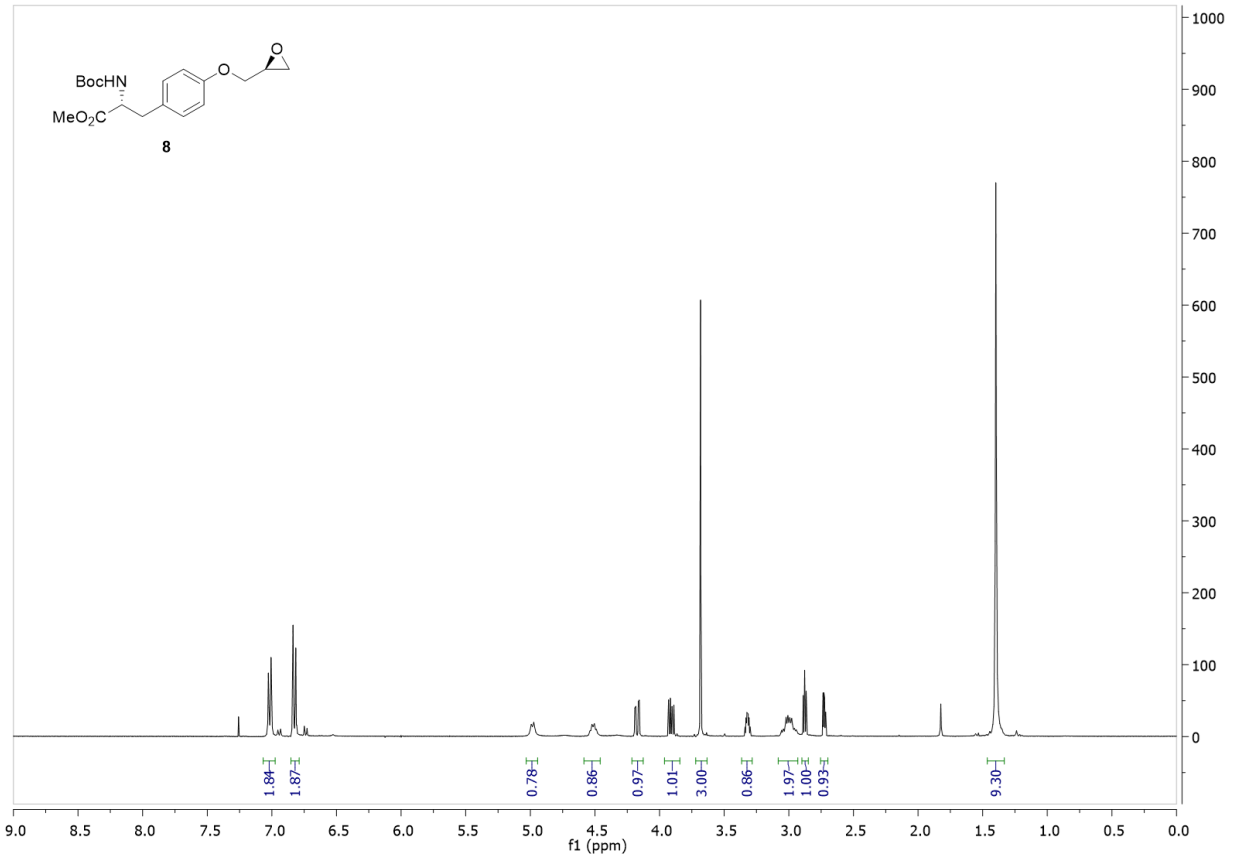


Figure S 135. ^{1}H-NMR of **8** (400 MHz, $CDCl_3$)

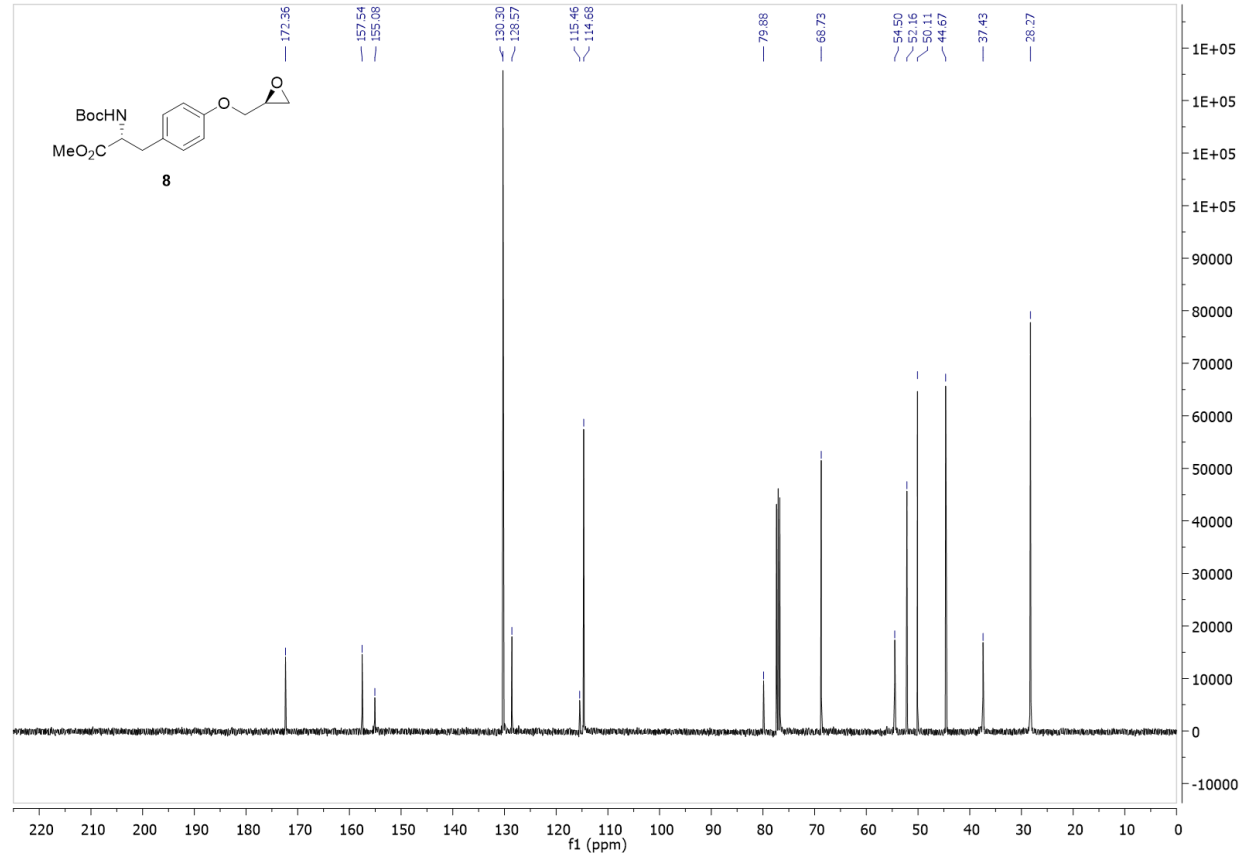


Figure S 136. ^{13}C-NMR of **8** (100 MHz, $CDCl_3$)

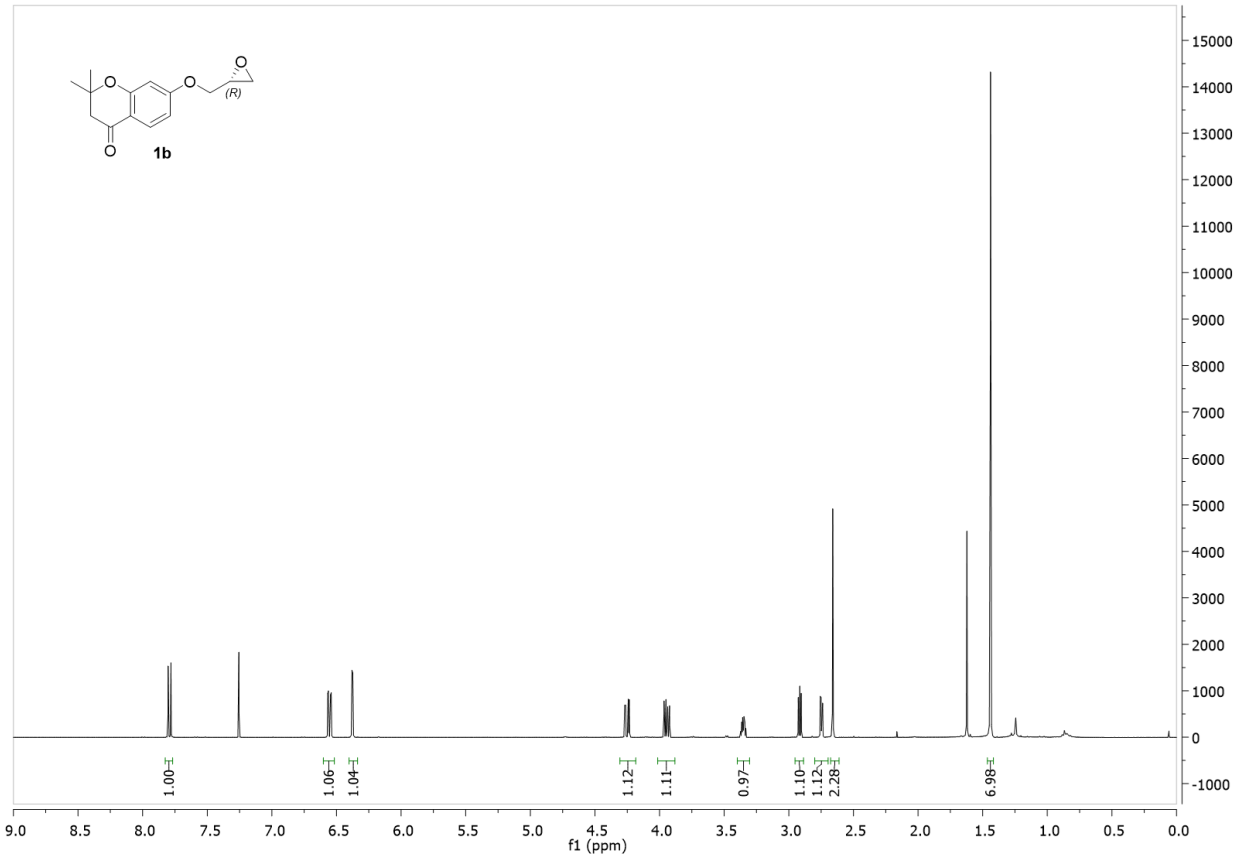


Figure S 137. ^{1}H-NMR of ***1b*** (400 MHz, *$CDCl_3$*).

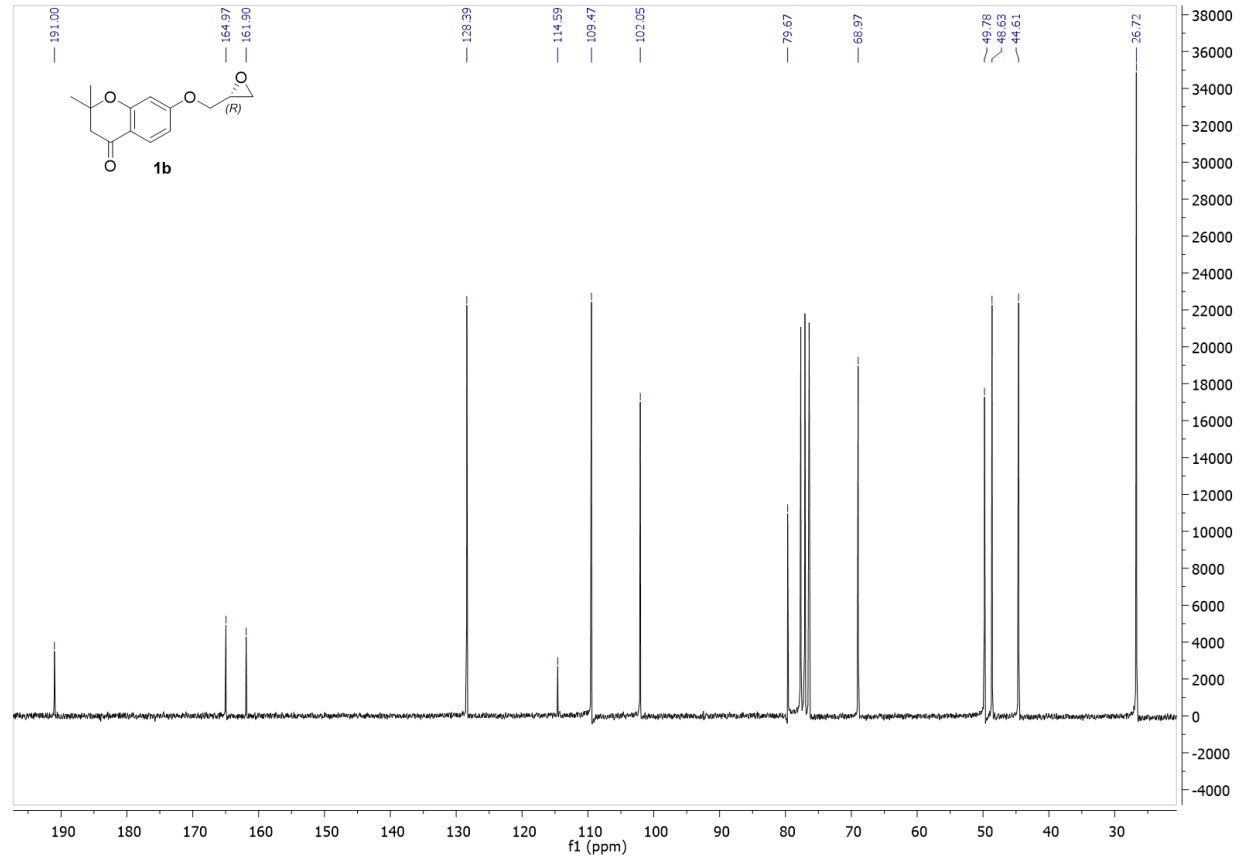


Figure S 138. *^{13}C*-NMR of ***1b*** (*100* MHz, *$CDCl_3$*).

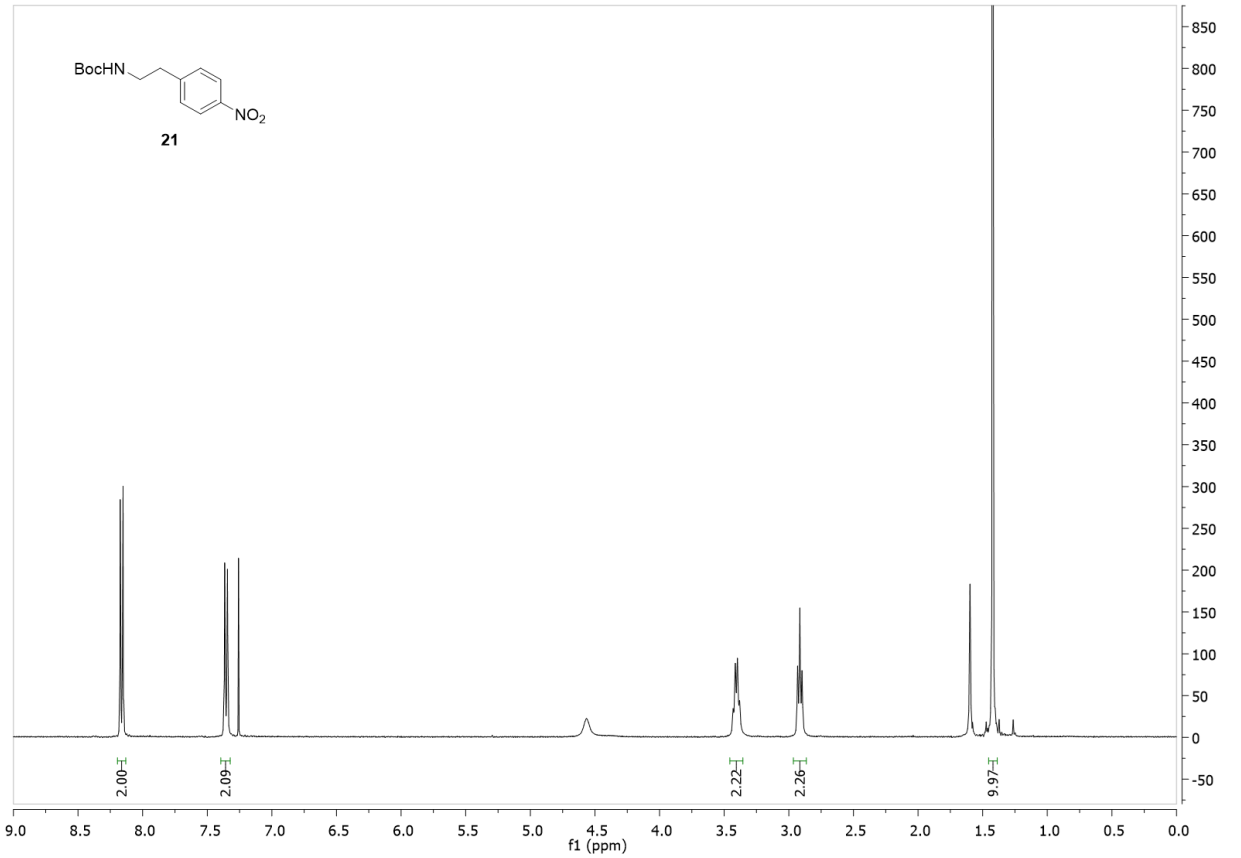


Figure S 139. ^{1}H-NMR of **21** (400 MHz, $CDCl_3$)

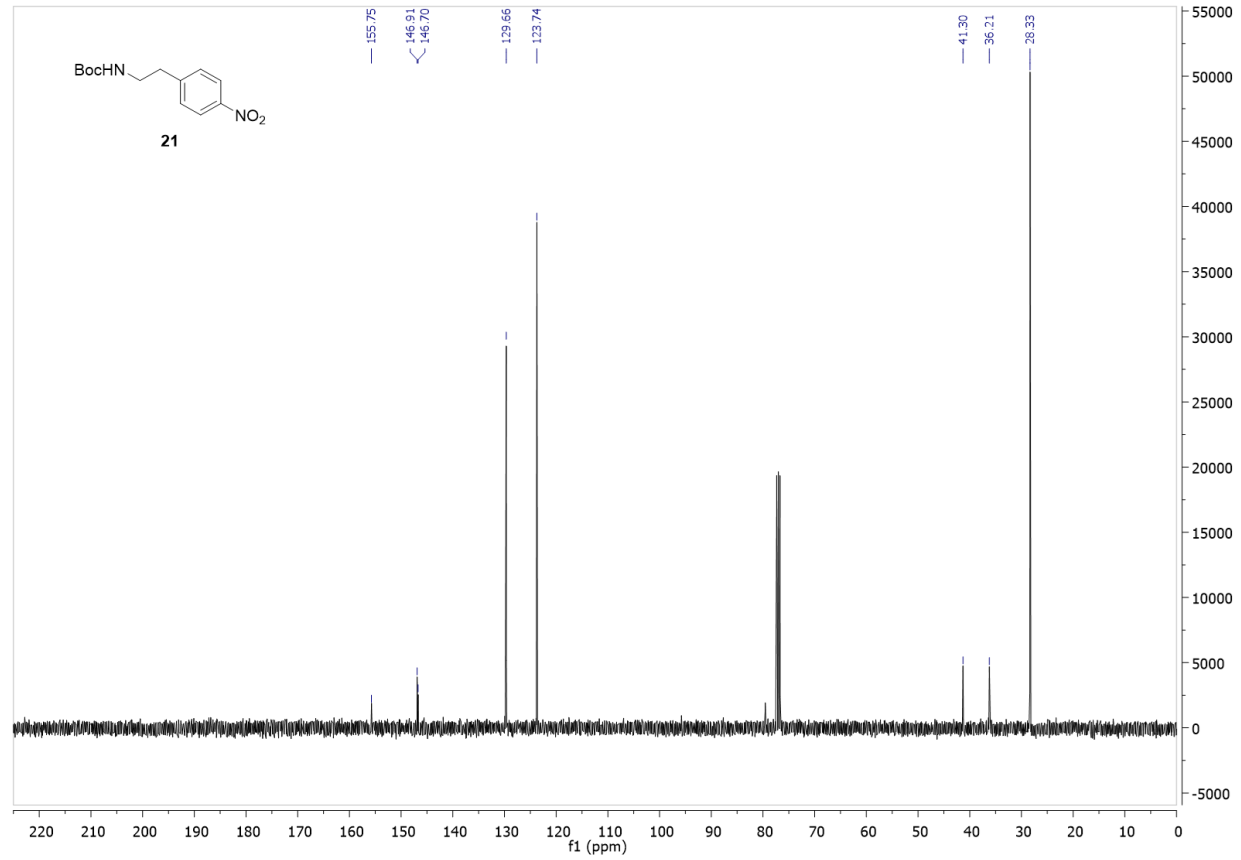


Figure S 140. ^{13}C-NMR of **21** (100 MHz, $CDCl_3$)

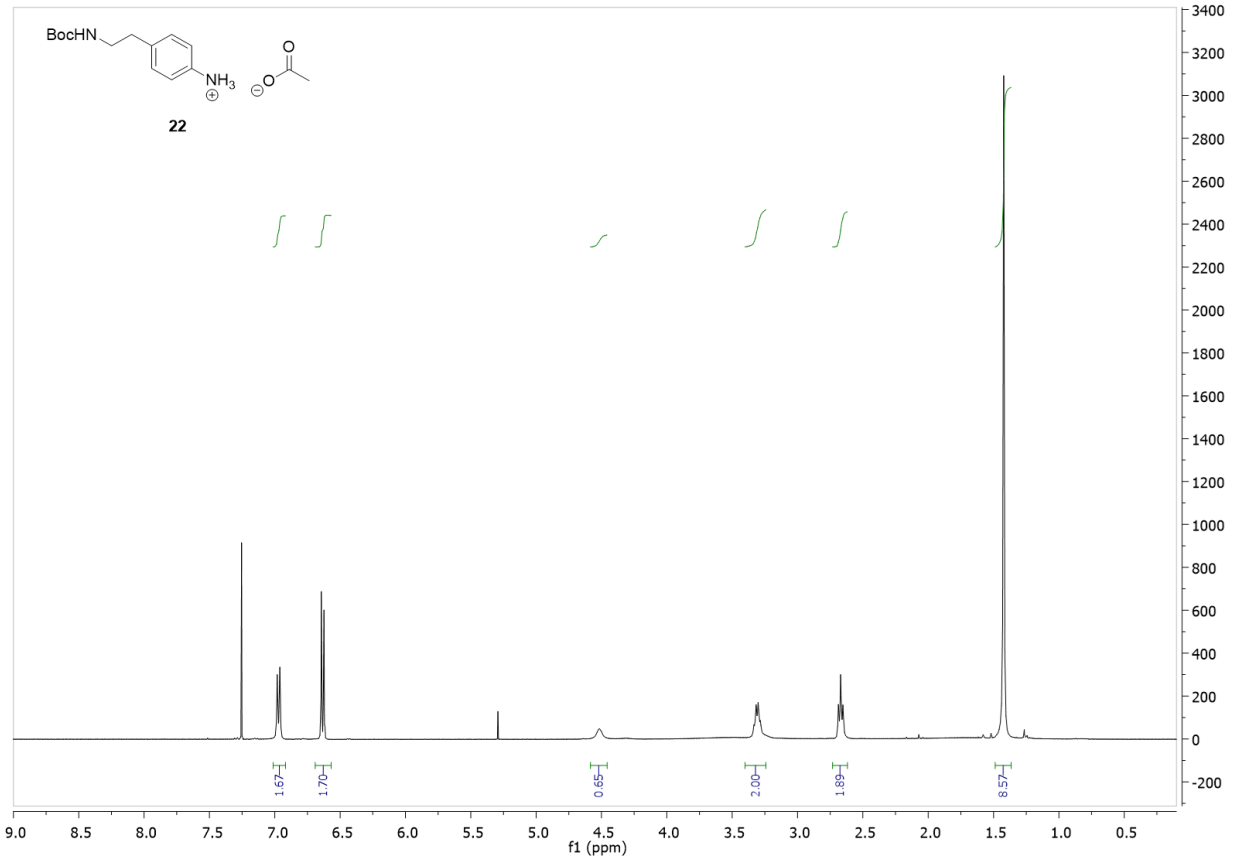


Figure S 141. ^{1}H-NMR of **22** (400 MHz, $CDCl_3$)

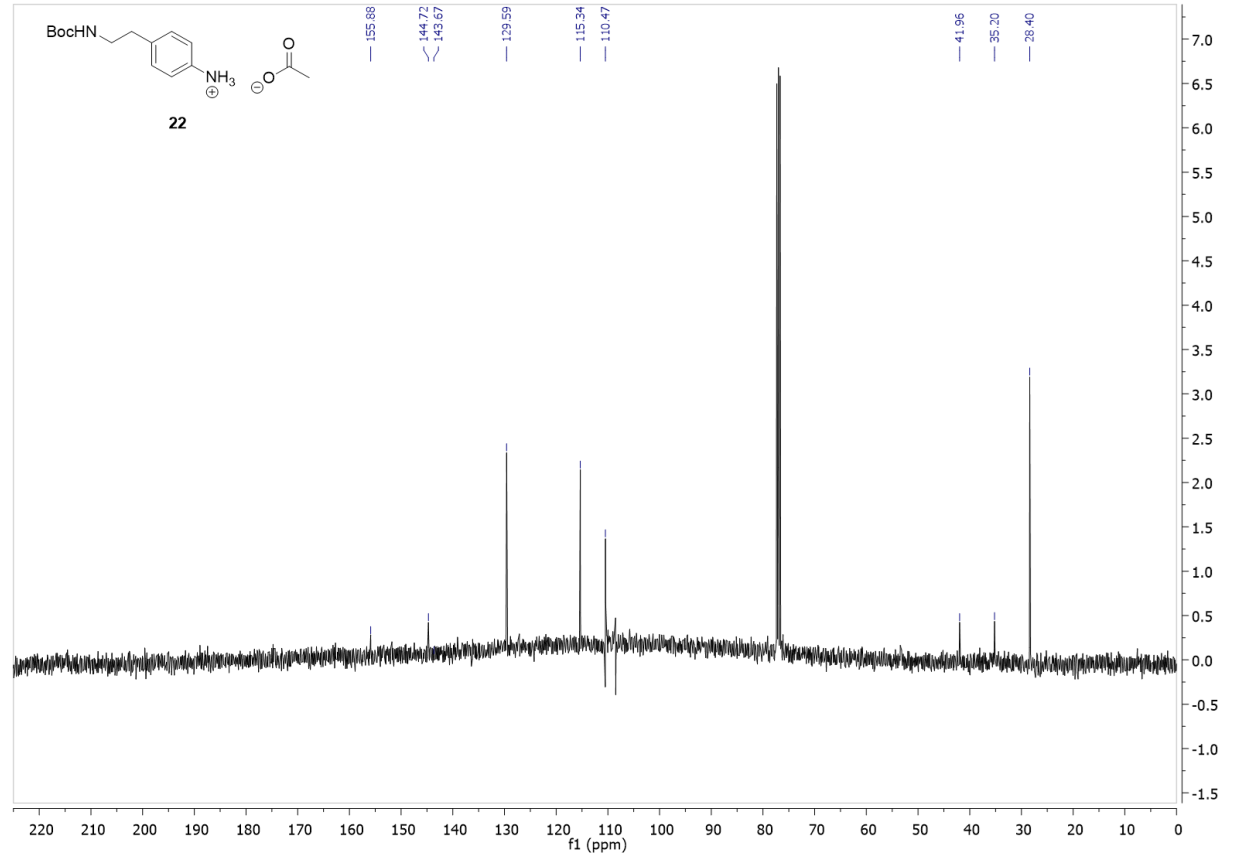


Figure S 142. ^{13}C-NMR of **22** (100 MHz, $CDCl_3$)

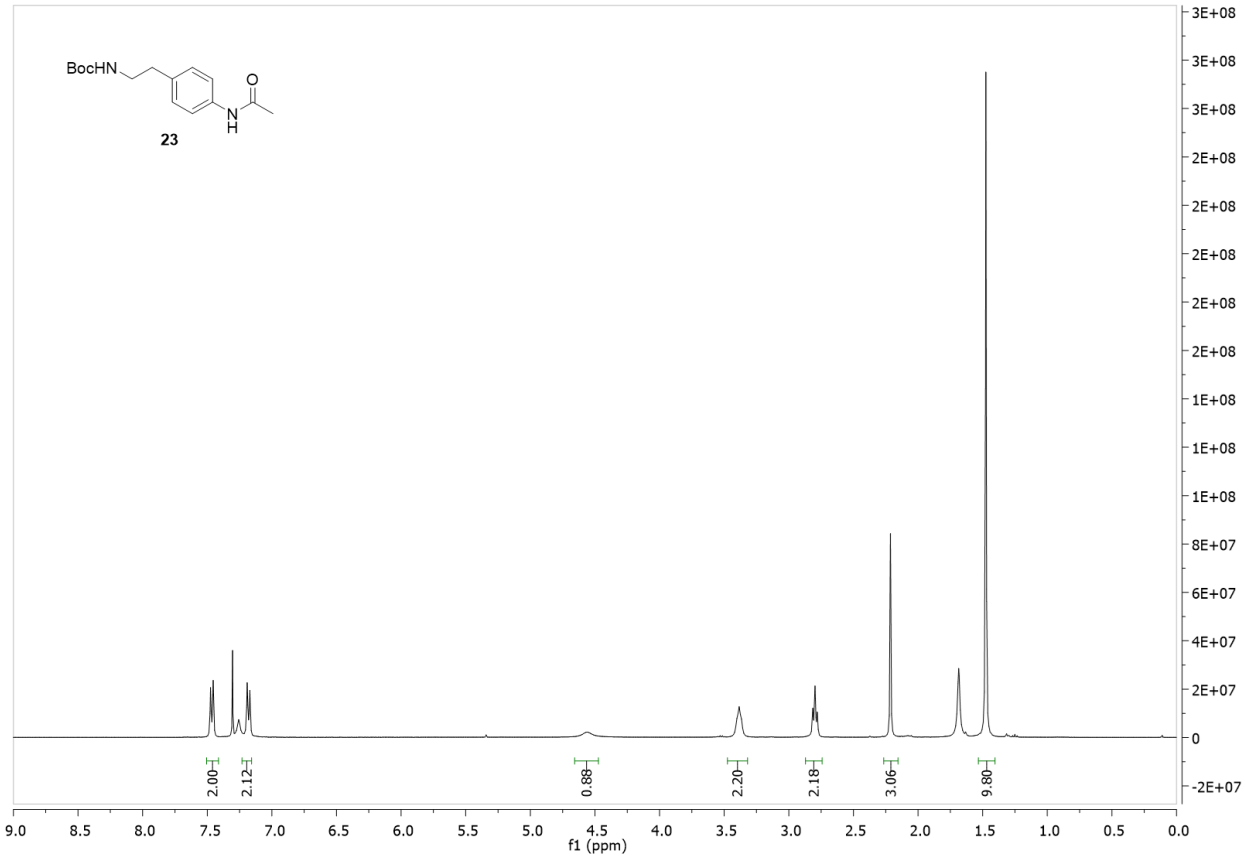


Figure S 143. ^{1}H-NMR of **23** (400 MHz, $CDCl_3$)

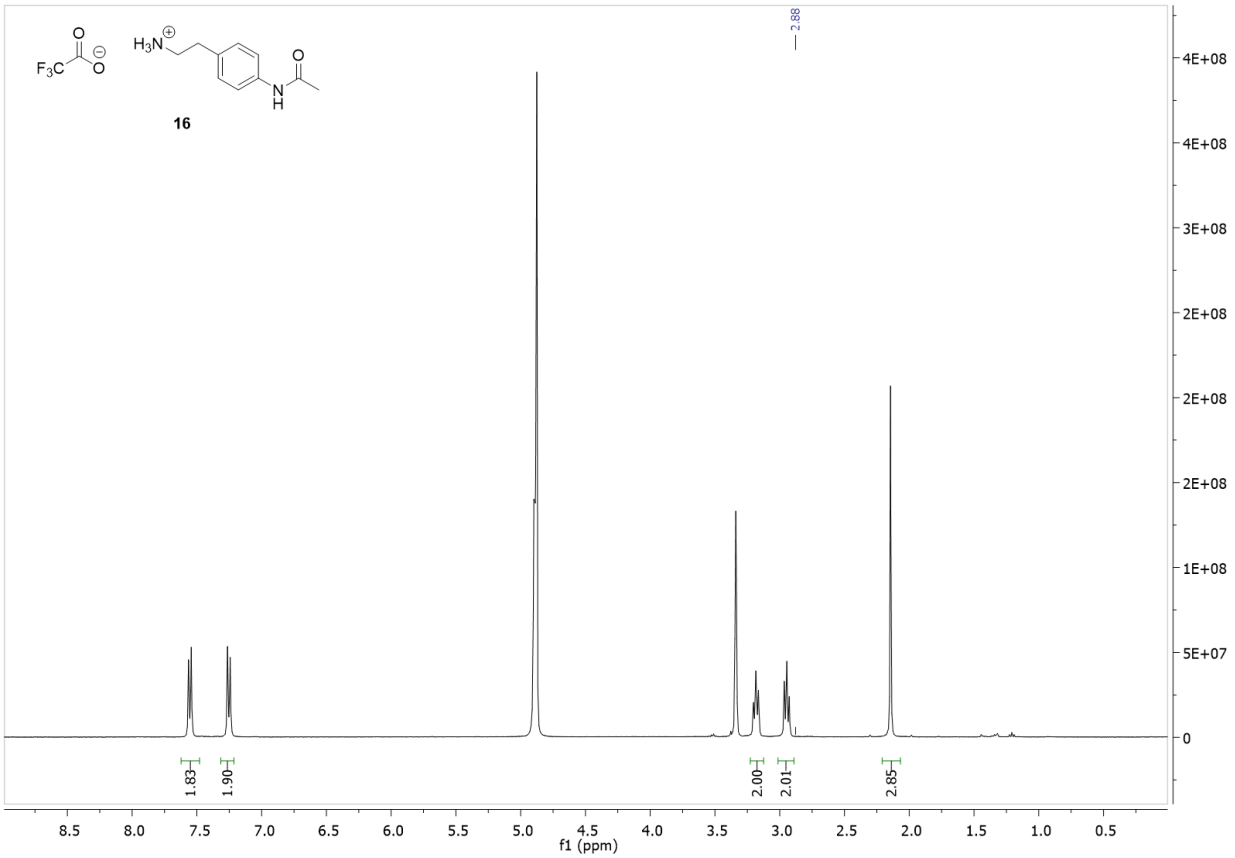


Figure S 144. ^{1}H-NMR of **16** (400 MHz, CD_3OD)

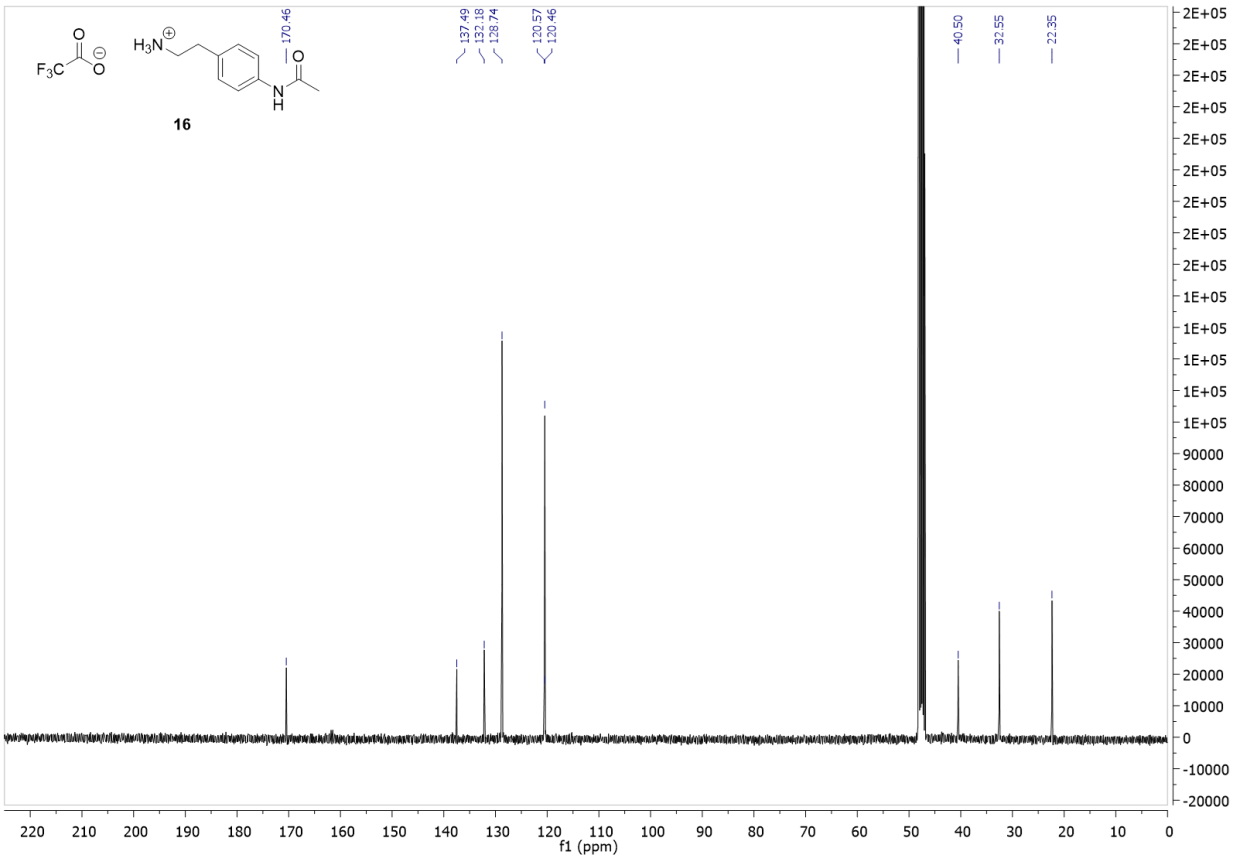


Figure S 145. ^{13}C-NMR of **16** (100 MHz, CD_3OD)

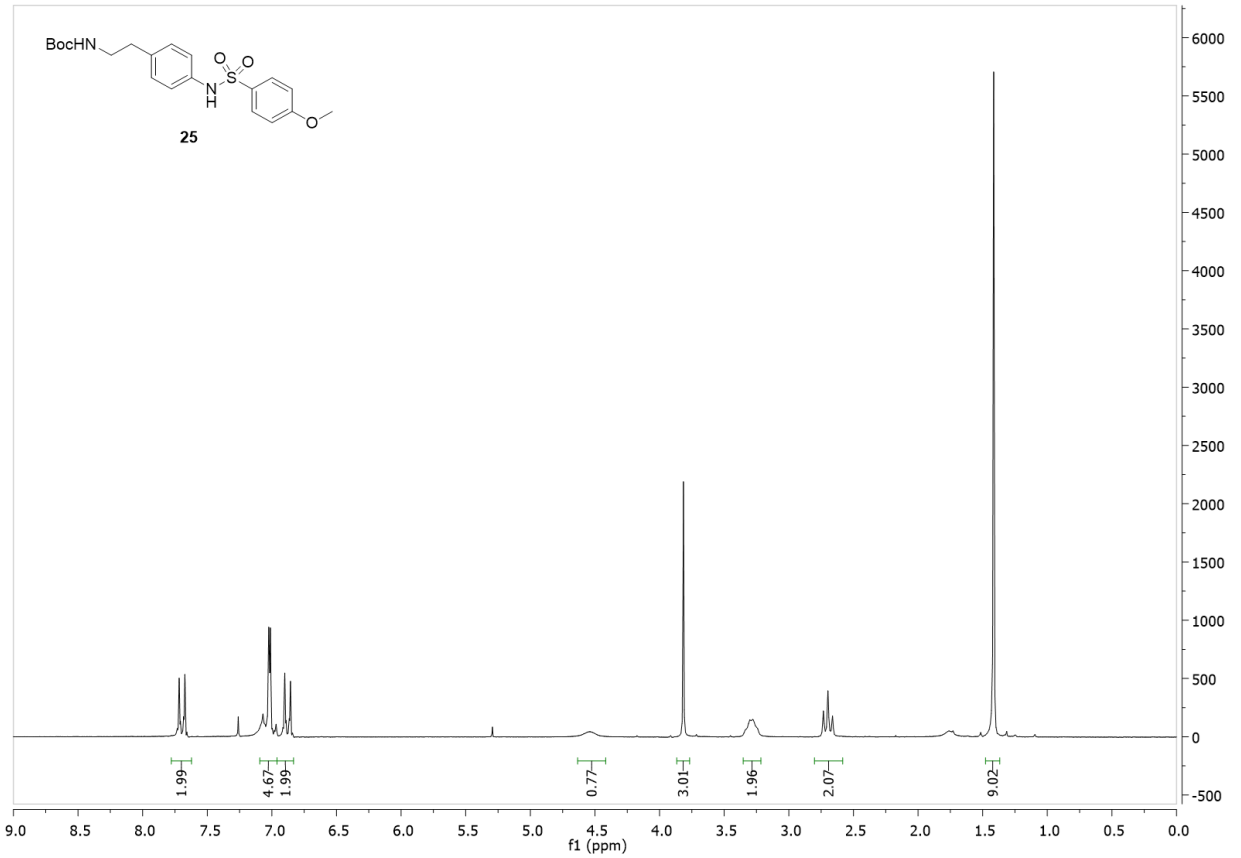


Figure S 146. ^{1}H-NMR of **25** (400 MHz, $CDCl_3$)

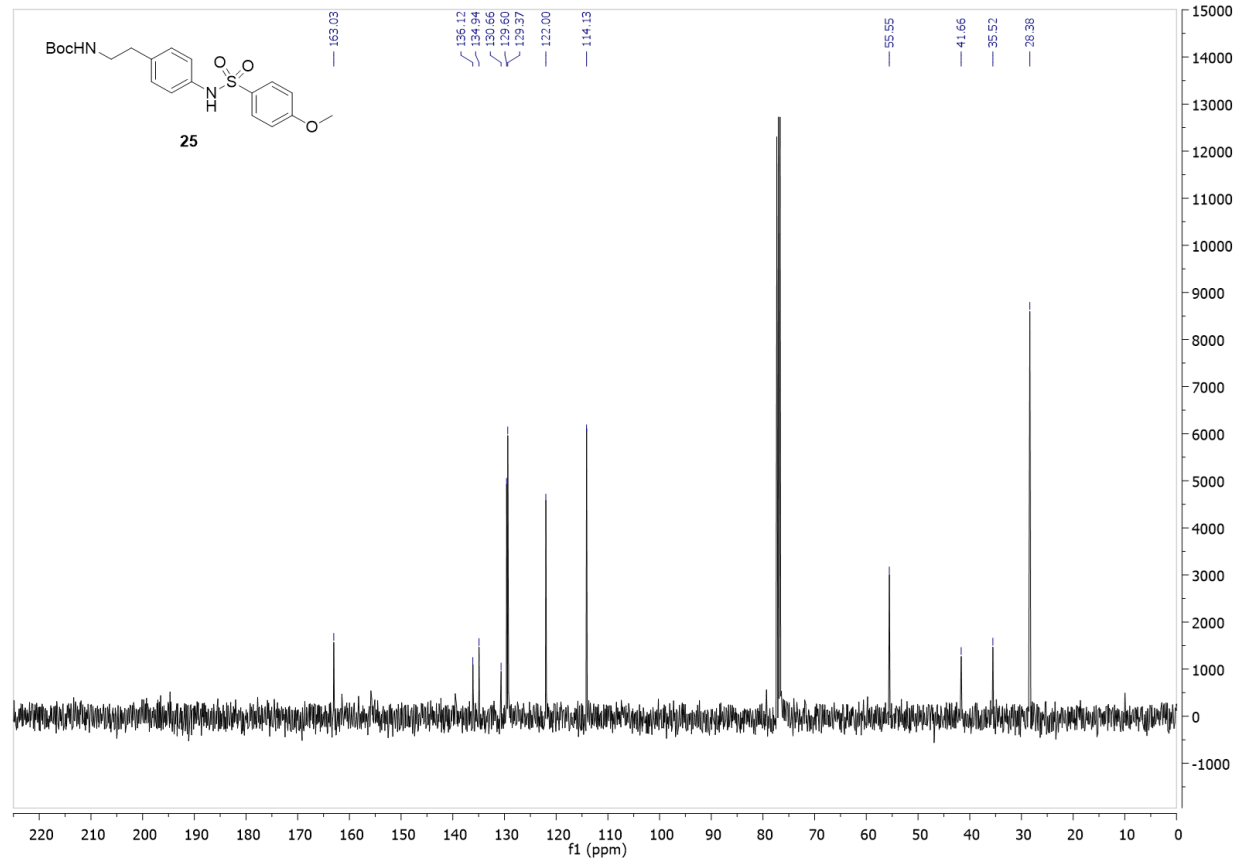


Figure S 147. ^{13}C-NMR of **25** (50 MHz, $CDCl_3$)

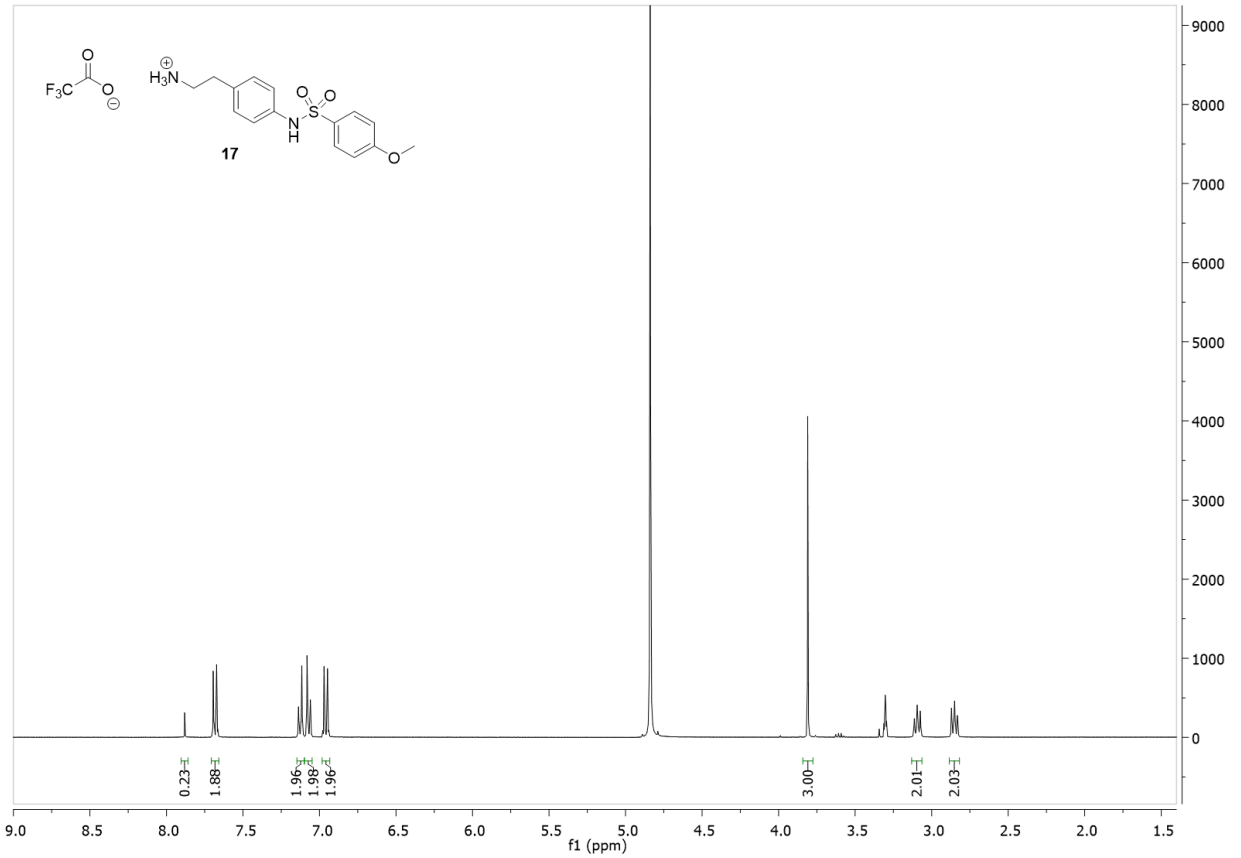


Figure S 148. ^{1}H-NMR of **17** (400 MHz, CD_3OD)

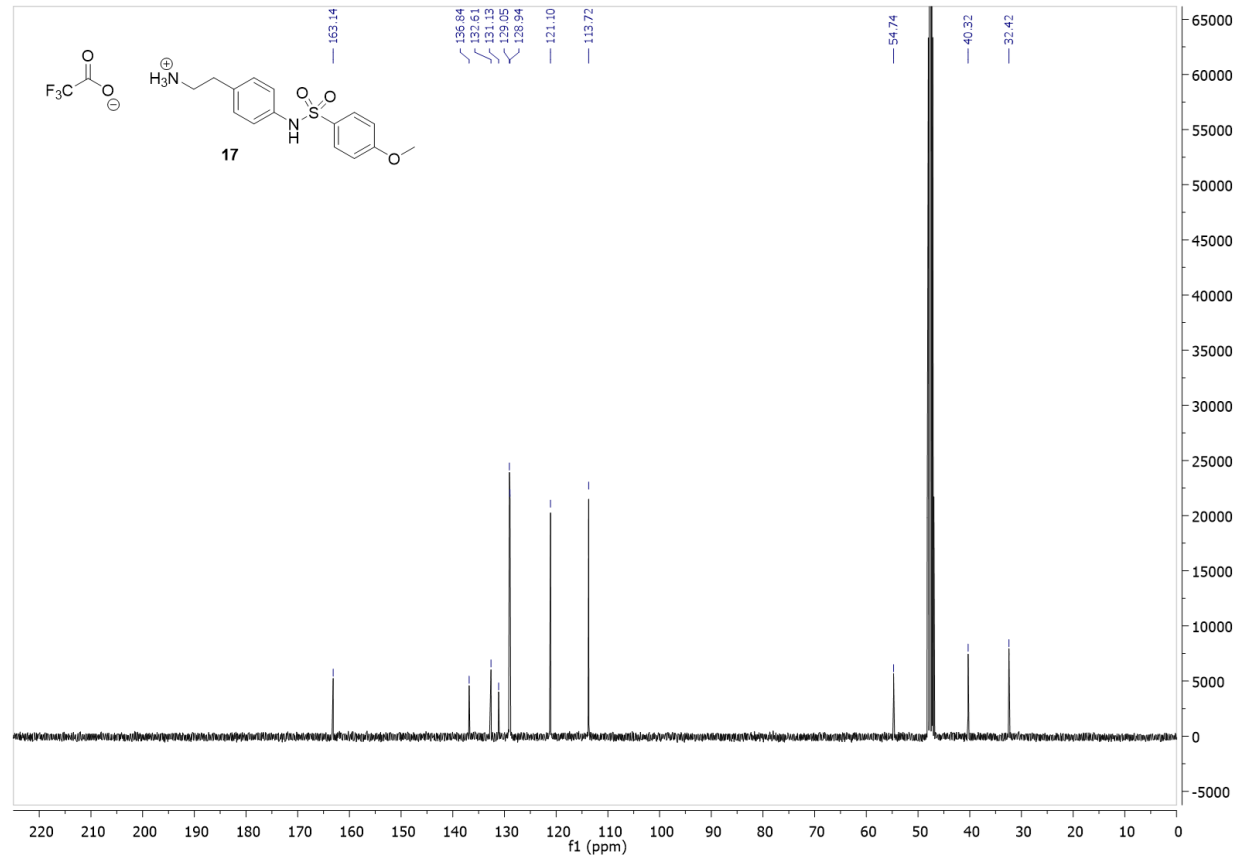


Figure S 149. ^{13}C-NMR of **17** (100 MHz, CD_3OD)

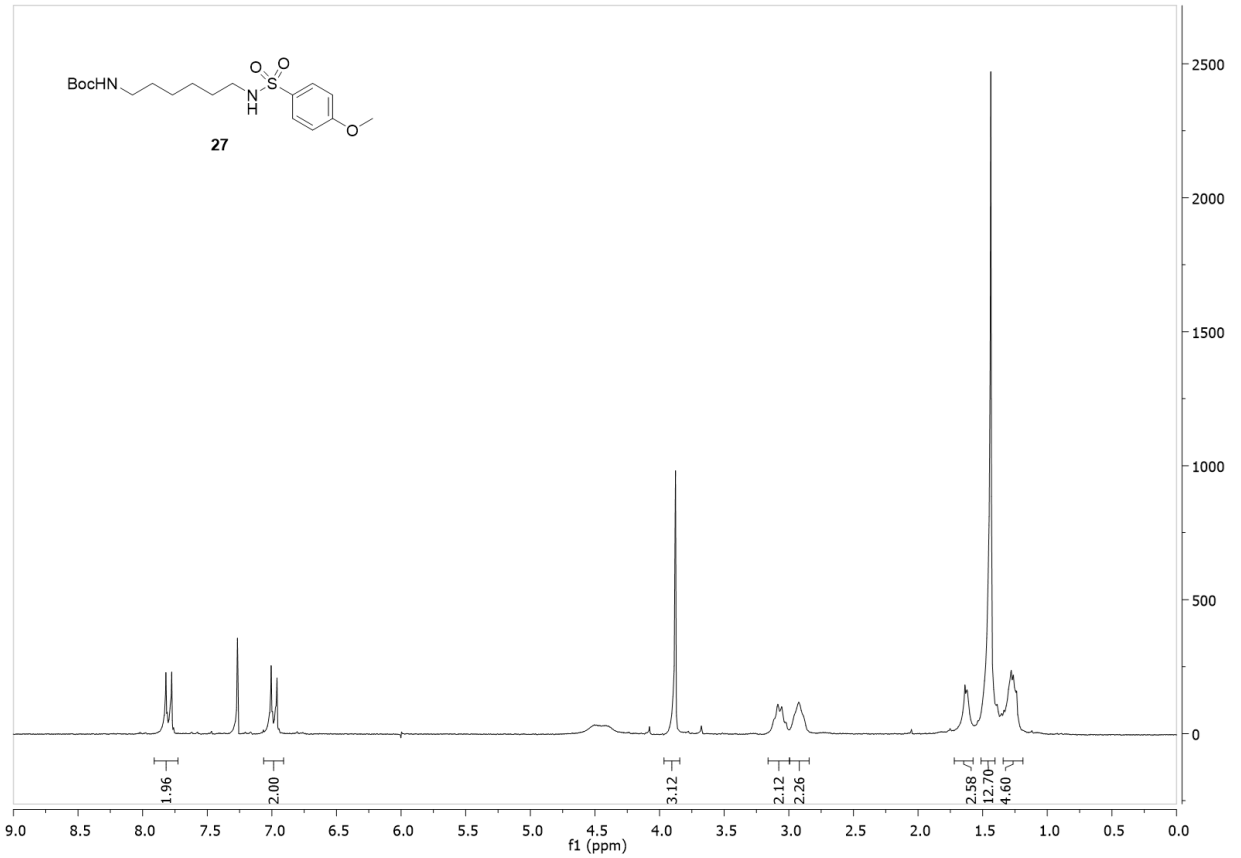


Figure S 150. ^{1}H-NMR of **27** (200 MHz, $CDCl_3$)

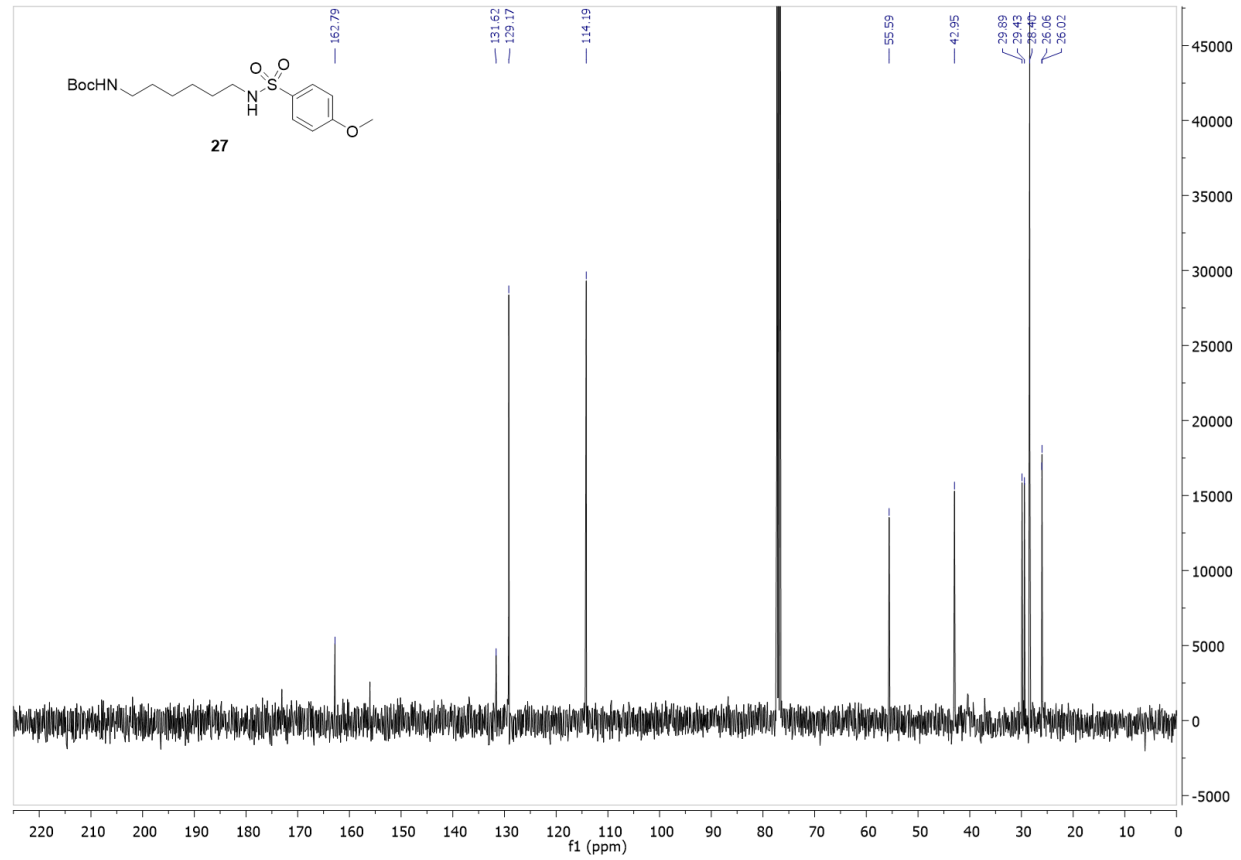


Figure S 151. ^{13}C-NMR of **27** (50 MHz, $CDCl_3$)

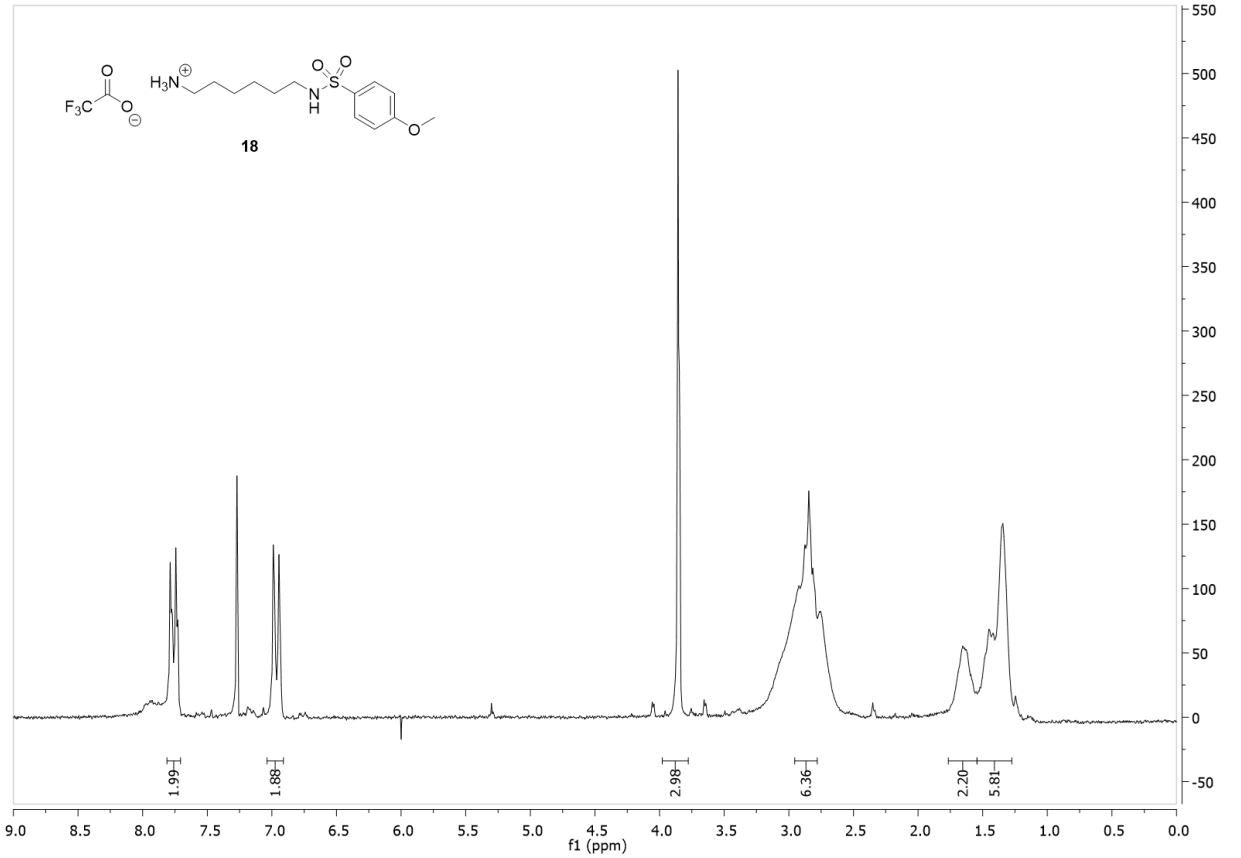


Figure S 152. ^{1}H-NMR of **18** (200 MHz, $CDCl_3$ +5% CD_3OD)

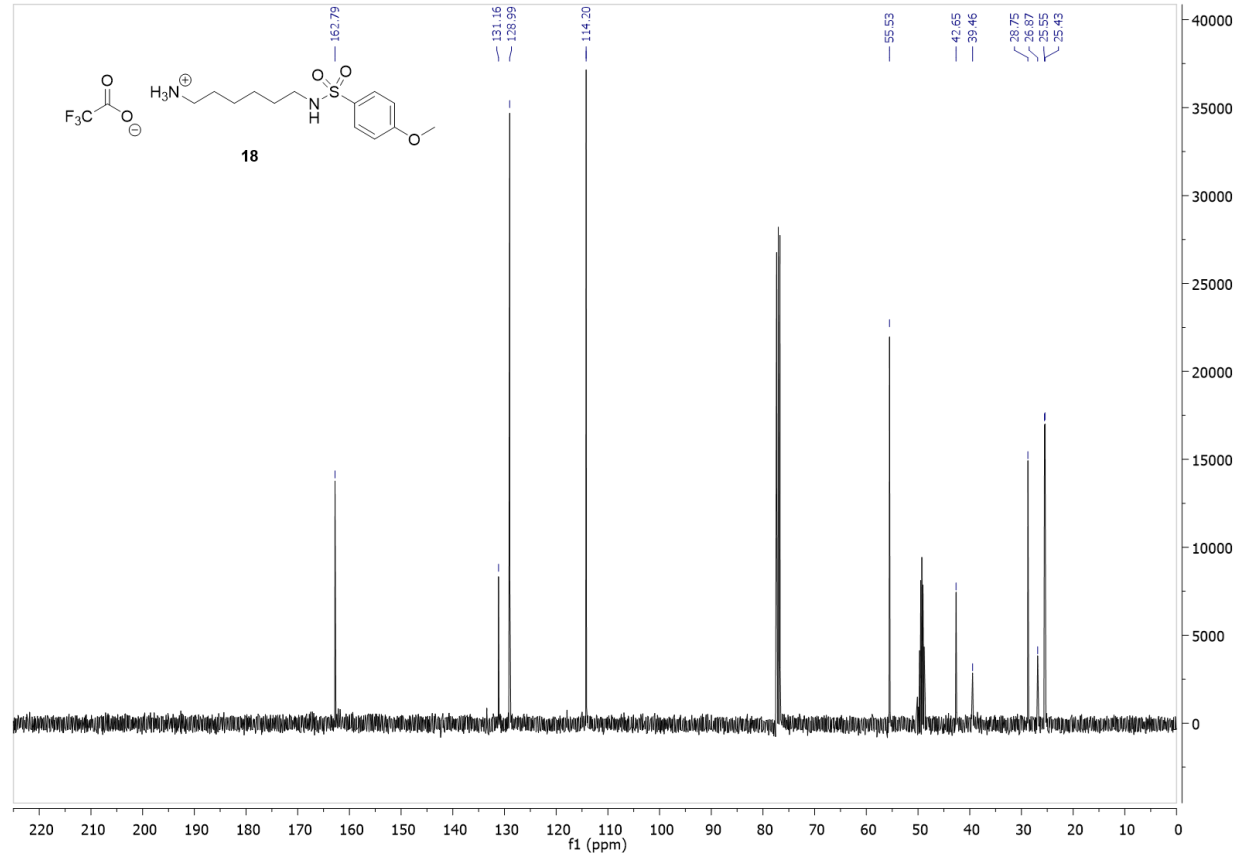


Figure S 153. ^{13}C-NMR of **18** (50 MHz, $CDCl_3$ +5% CD_3OD)

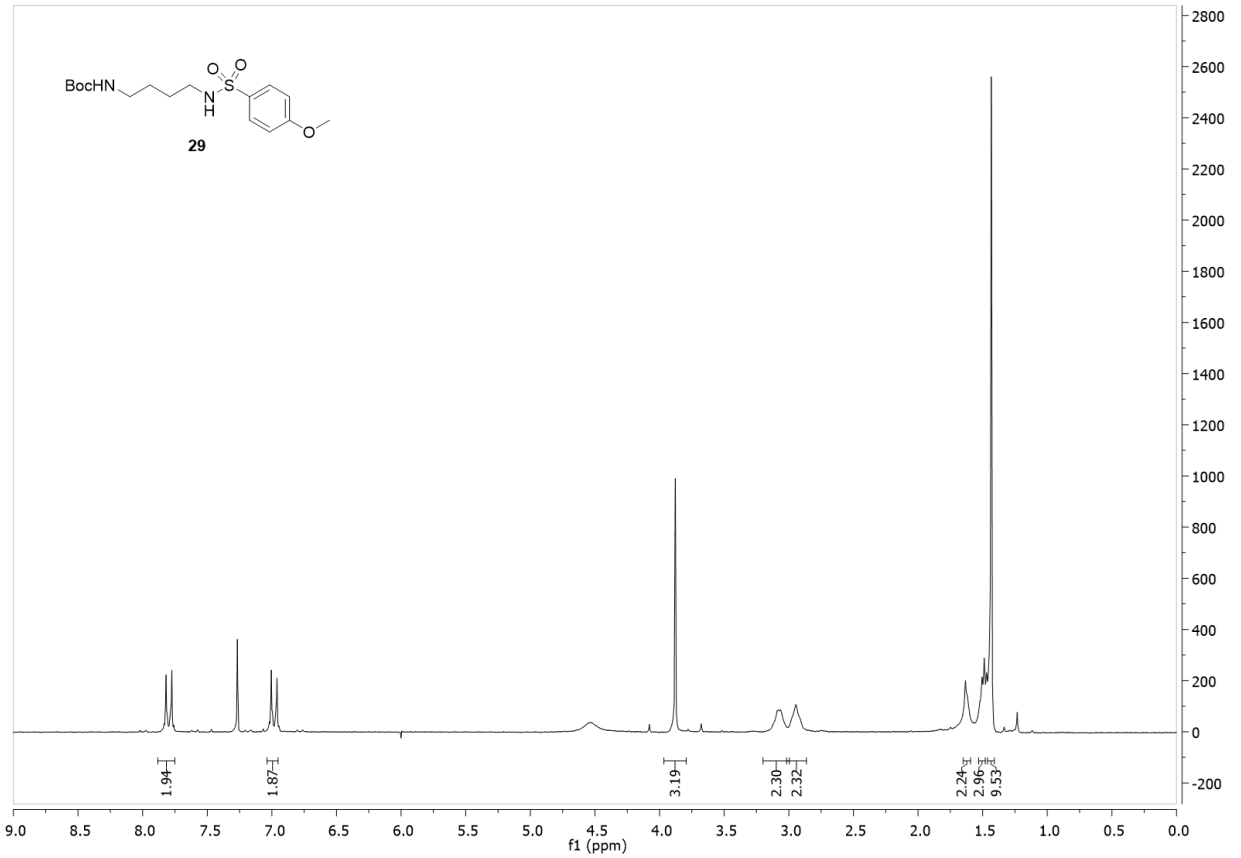


Figure S 154. ^{1}H-NMR of **29** (400 MHz, $CDCl_3$)

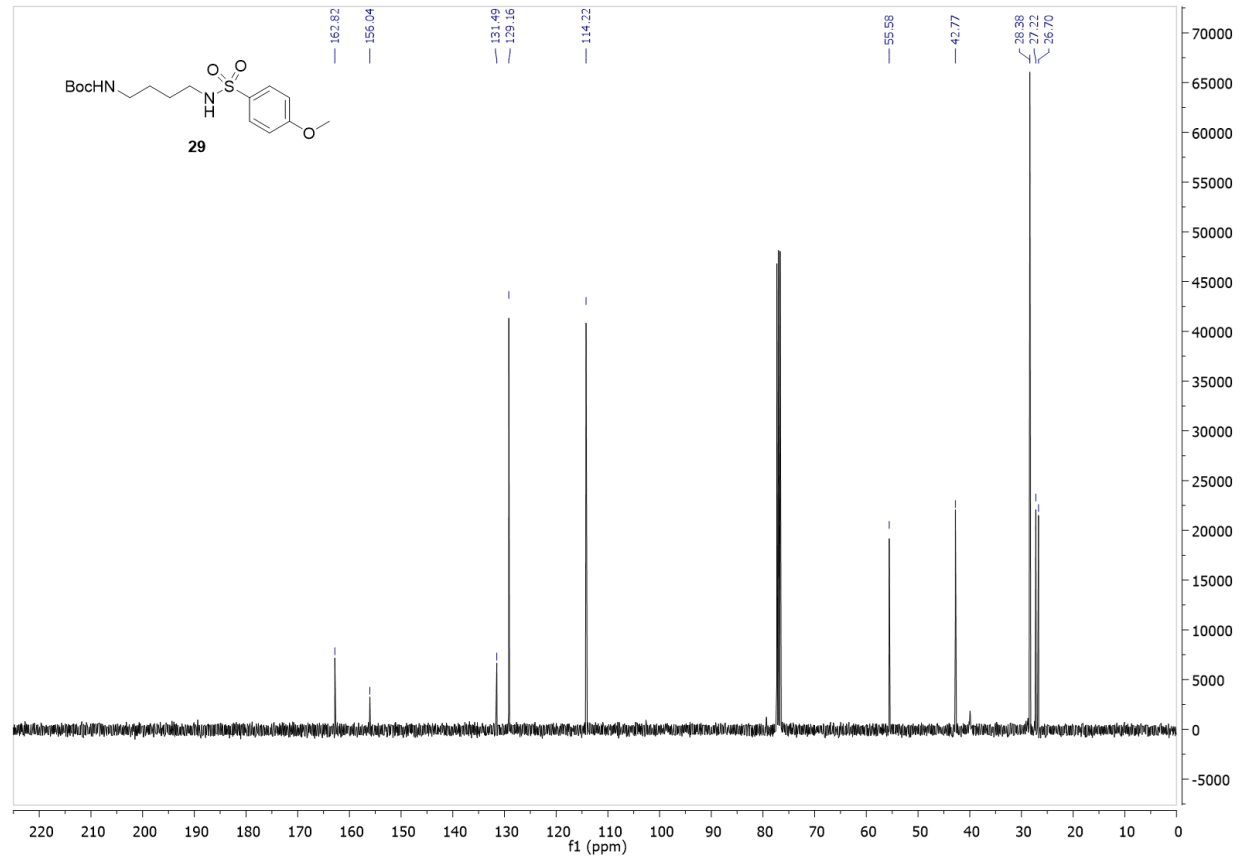


Figure S 155. ^{13}C-NMR of **29** (100 MHz, $CDCl_3$)

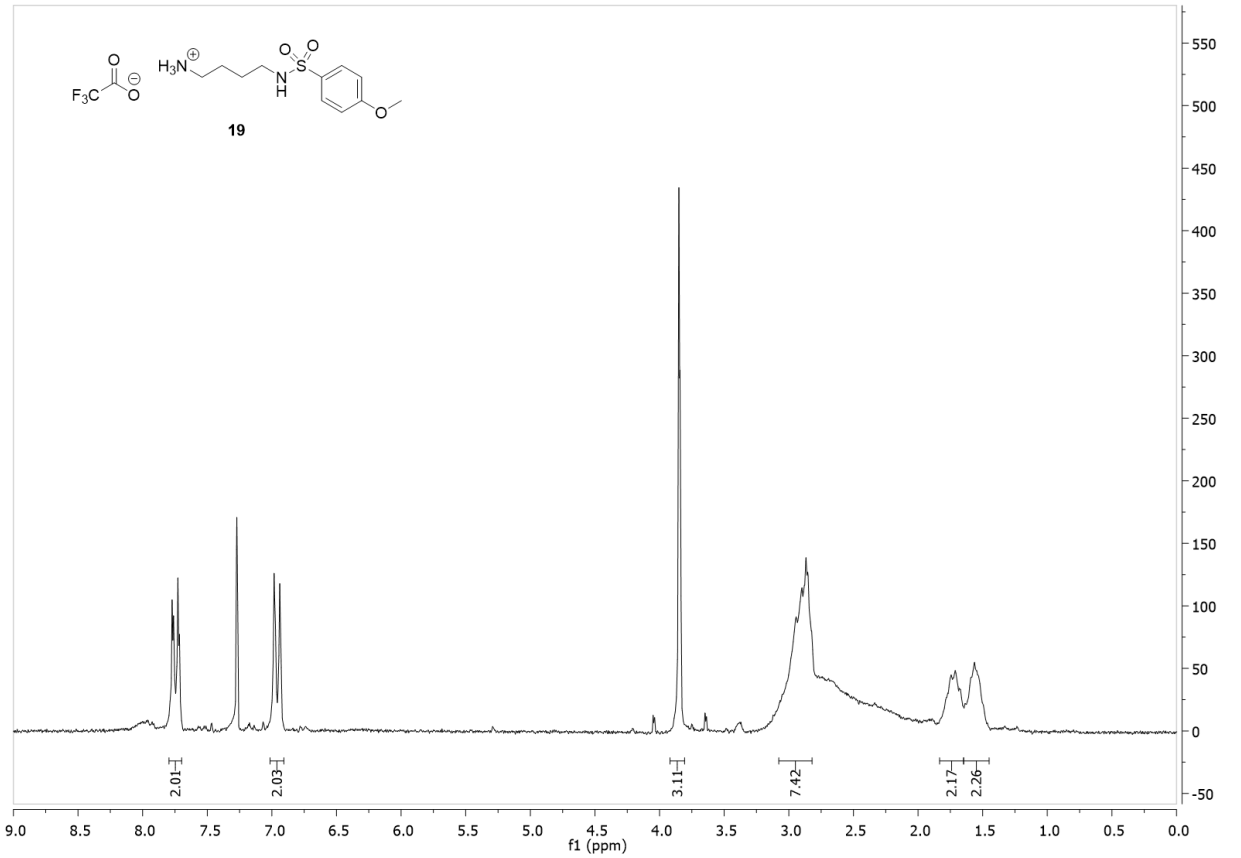


Figure S 156. ^{1}H-NMR of **19** (200 MHz, $CDCl_3$ +5% CD_3OD)

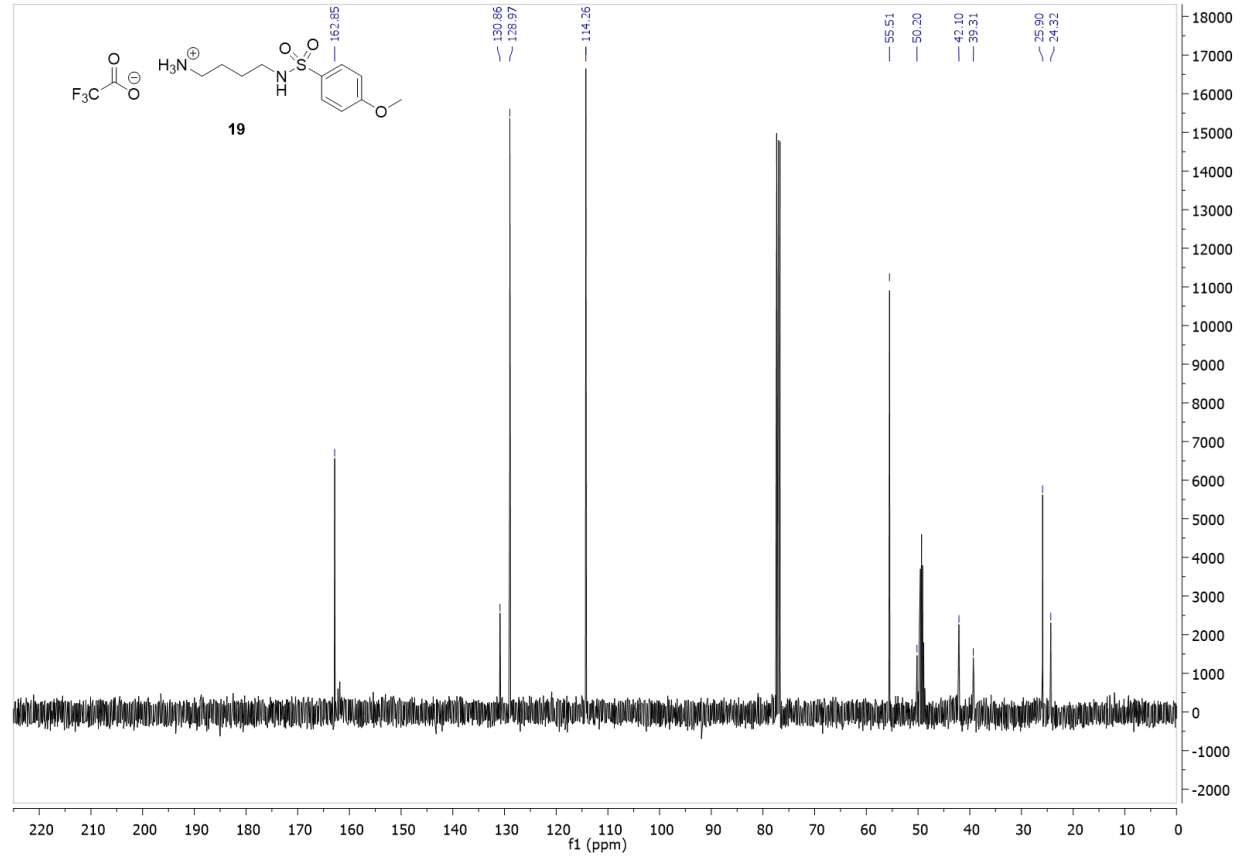


Figure S 157. ^{13}C-NMR of **19** (50 MHz, $CDCl_3$ +5% CD_3OD)

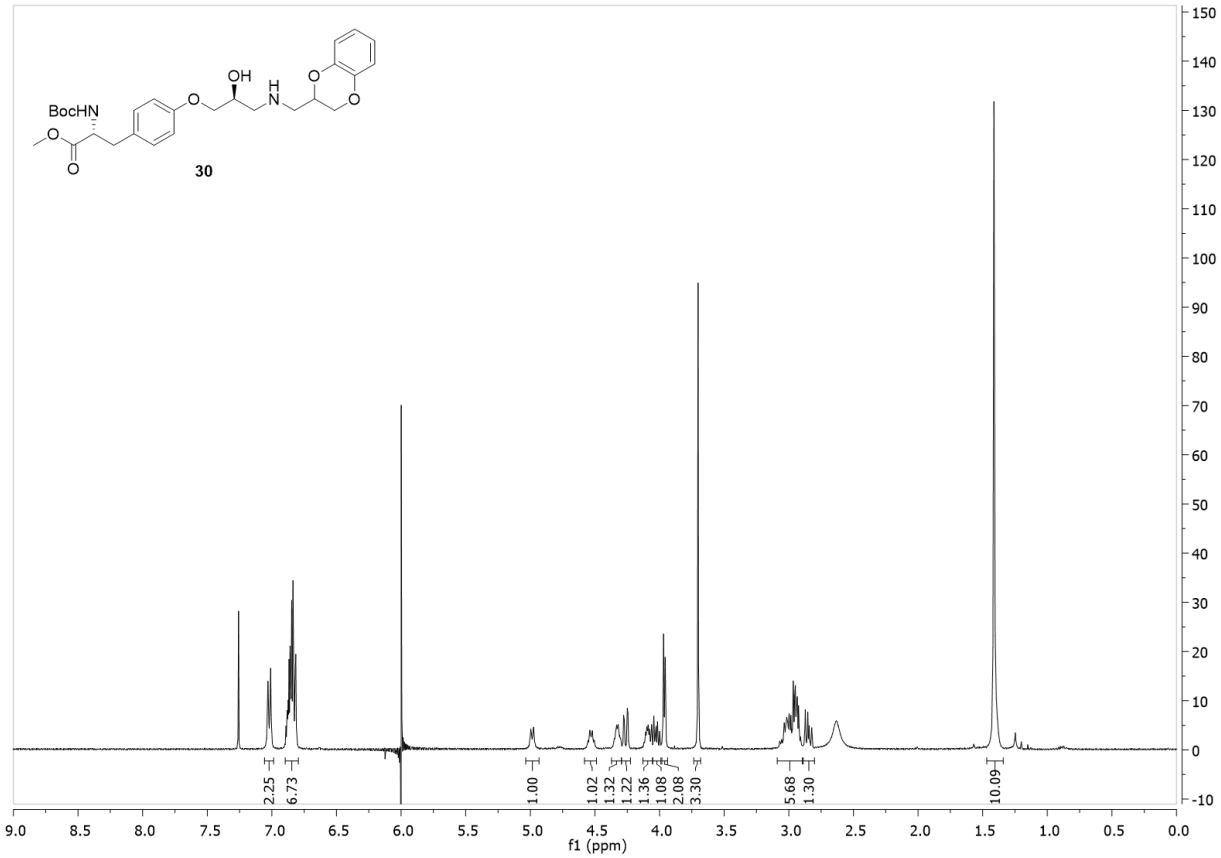


Figure S 158. ^{1}H-NMR of **30** (400 MHz, $CDCl_3$)

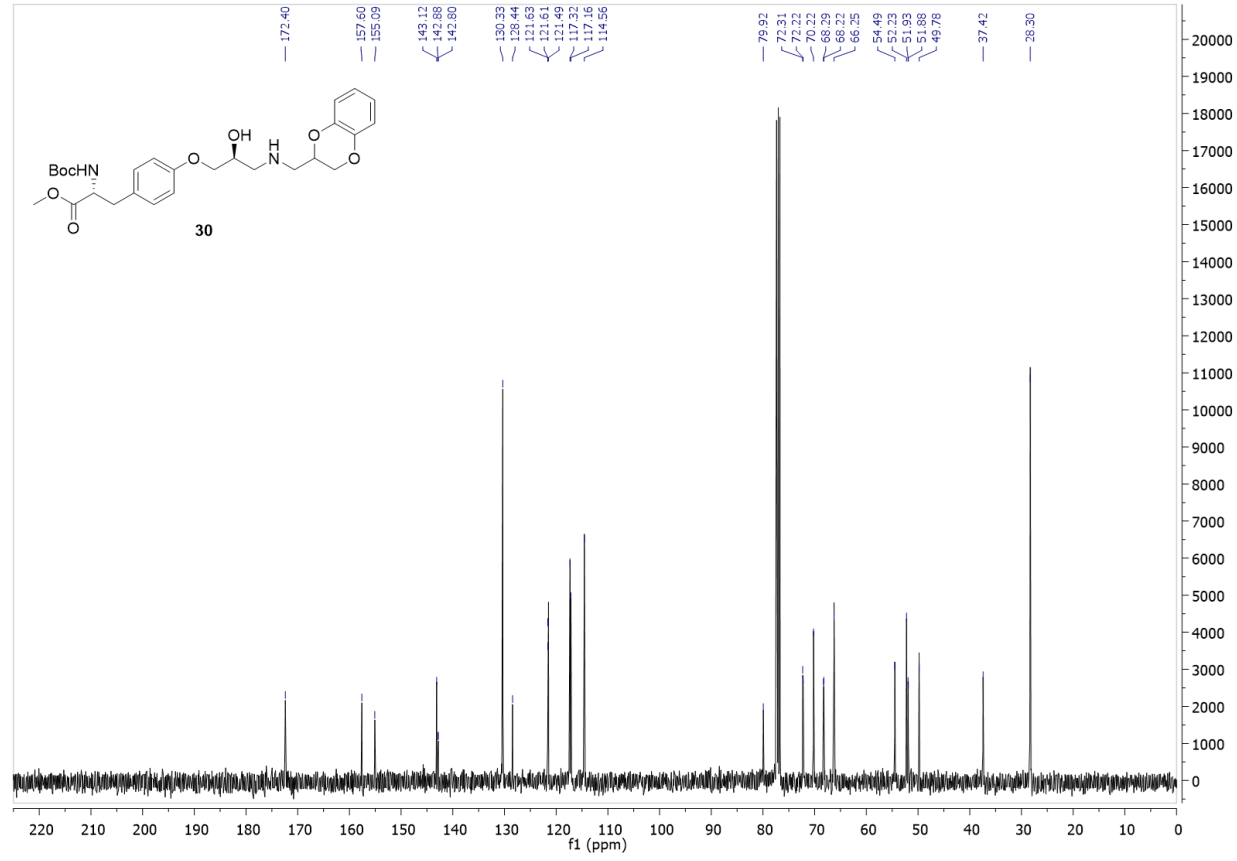


Figure S 159. ^{13}C-NMR of **30** (100 MHz, $CDCl_3$)

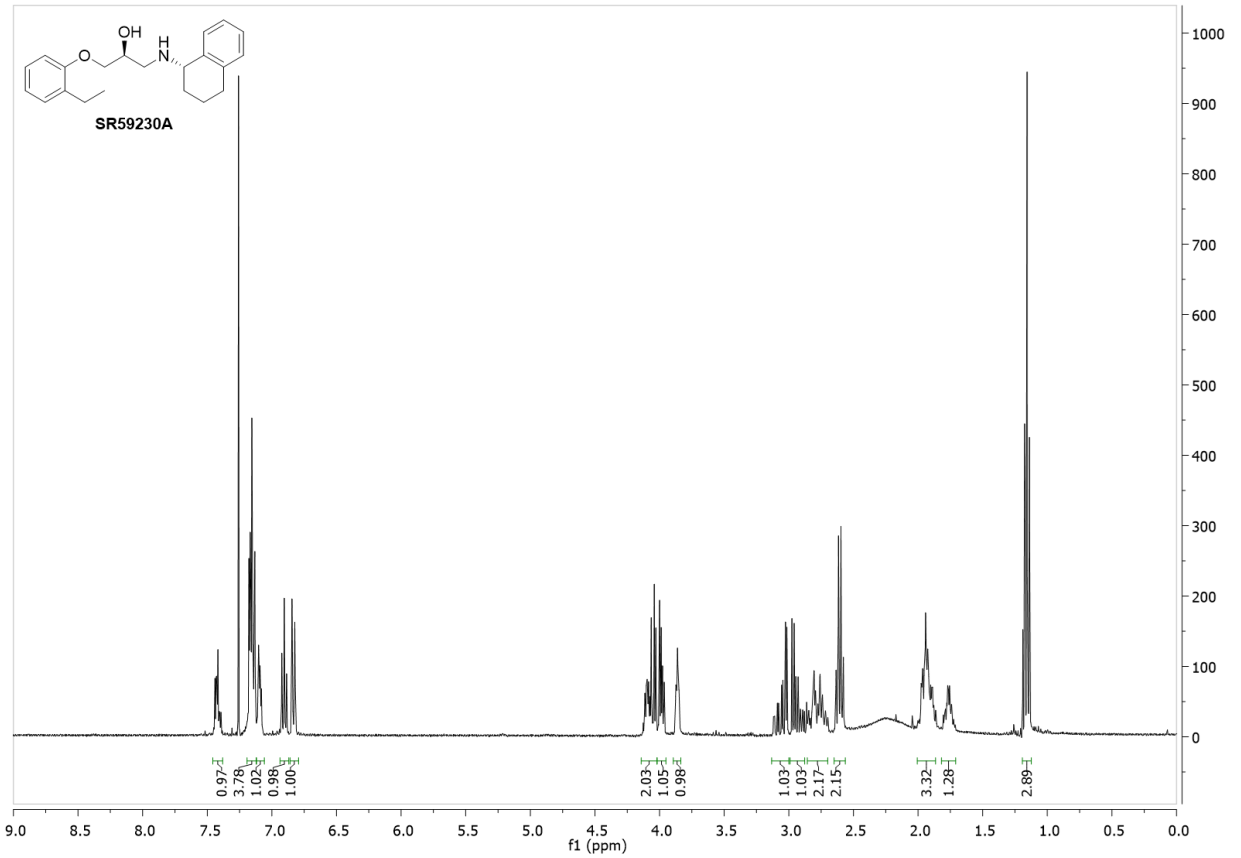


Figure S 160. ^{1}H-NMR of **SR59230A** (400 MHz, $CDCl_3$)

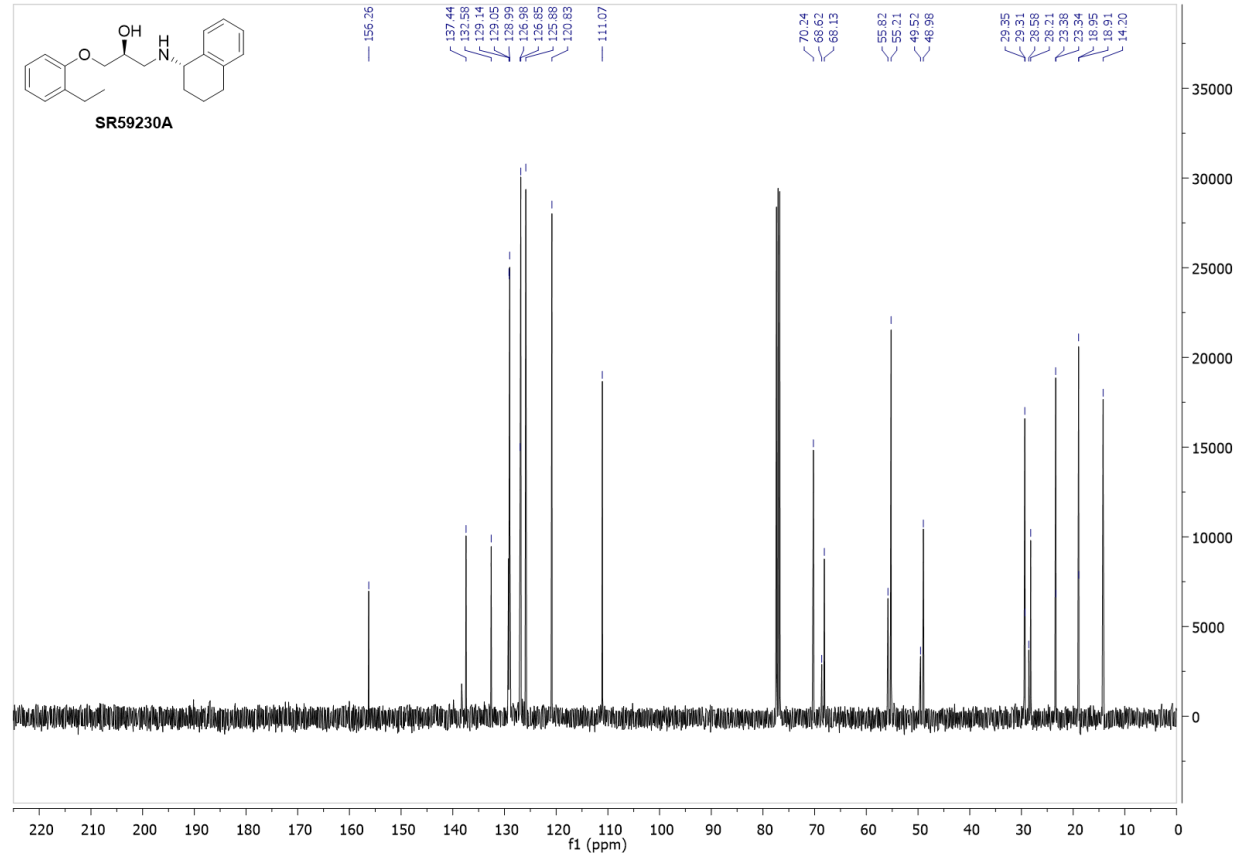


Figure S 161. ^{13}C-NMR of **SR59230A** (100 MHz, $CDCl_3$)

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