Lewis-Acid Catalysed One Pot Synthesis of Substituted Xanthenes

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Supporting Information

Experimental details

Unless otherwise indicated, all reagents and solvents were purchased from commercial distributors and used as received. Solvents (toluene, hexanes, ethyl acetate, dichloromethane, methanol) used for column chromatography were of technical grade and used after distillation in a rotary evaporator. TLC was used to check the reactions for full conversion and was performed on Macherey-Nagel Polygram Sil G/UV_{254} thin layer plates. TLC spots were visualized by UV-light irradiation. Flash column chromatography was carried out using Merck Silica Gel 60 (40-63 μm). Yields refer to pure isolated compounds. ^{1}H and ^{13}C NMR spectra were measured with Bruker AV 500 and AV 600 spectrometers. All chemical shifts are given in ppm downfield relative to TMS and were referenced to the solvent residual peaks.[7] ^{1}H NMR chemical shifts are designated using the following abbreviations as well as their combinations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad signal. High resolution mass spectra were recorded with a Bruker APEX III FTICR-MS or a Finnigan SSQ 7000 quadrupole MS or a Finnigan MAT 95 double focusing sector field MS instrument. Infrared spectra were measured with a PerkinElmer Spectrum 100 FT-IR spectrometer on a diamond ATR unit. High performance liquid chromatography (HPLC) was performed on a Shimadzu LC-20A HPLC-System. Microwave reactions were carried out in a CEM Discover Microwave with up to 300W. The reaction temperature (IR surface flask, air cooling upon heating), pressure (non-invasive pressure transducer) and microwave power were remotely controlled.

General Procedure A – oil bath heating

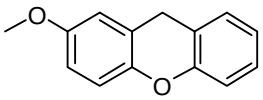
Representative procedure: 5-Methoxysalicylaldehyde 1 (138.32μL, 1.1 mmol) and 2-cyclohexene-1-one 2 (96.81μL, 1.0 mmol) was quickly added to a suspension of scandium(III) triflate (24.61 mg, 0.05 mmol) in chlorobenzene (4.0 mL). The reaction mixture was refluxed for 24 hours and allowed to cool to room temperature. DCM (20 mL) and saturated aqueous $NaHCO_3$ (20 mL) were added to the reaction mixture and the two layers separated. The aqueous phase was extracted with DCM (3× 20 mL) and the combined organic layers were dried over $MgSO_4$, filtered and solvent was removed by rotary evaporator. The crude product **3a** was purified with flash chromatography using mixtures of pentane and ethyl acetate.

General Procedure B – microwave heating

Representative procedure: 5-Methoxysalicylaldehyde 1 (138.32μL, 1.1 mmol) and 2-cyclohexene-1-one 2 (96.81μL, 1.0 mmol) was quickly added to a suspension of scandium(III) triflate (24.61 mg, 0.05 mmol) in chlorobenzene (4.0 mL). The reaction mixture was heated in a microwave tube at 180 °C for 30 minutes. After compressed air cooling to room temperature, DCM (20 mL) and saturated aqueous $NaHCO_3$ (20 mL) were added to the reaction mixture and the two layers separated. The aqueous phase was extracted with DCM (3× 20 mL) and the combined organic layers were dried over $MgSO_4$, filtered and solvent was removed by rotary evaporator. The crude product **3a** was purified with flash chromatography using mixtures of pentane and ethyl acetate.

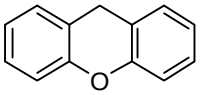
Characterisation of products

2-methoxy-9*H*-xanthene **3a**



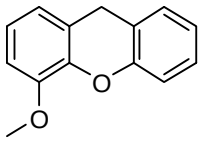
Synthesized according to general procedure A. Yield: 134 mg, 63%; Synthesized according to general procedure B. Yield: 174 mg, 82%; Yellowish solid, ^{1}H NMR (500 MHz, DMSO): δ 7.25-7.18 (m, 2H), 7.06-6.98 (m, 3H), 6.83-6.77 (m, 2H), 4.01 (s, 2H), 3.73 (s, 3H); ^{13}C NMR (125 MHz, DMSO): δ 155.0, 151.6, 145.2, 129.1, 127.7, 122.9, 121.4, 120.1, 116.8, 116.0, 113.5, 113.3, 55.4, 27.3; HRMS-(EI) (*m/z*): M^+ calcd for $C_{14}H_{12}O_2$, 212.083728; found 212.083561.

9*H*-xanthene **3b**



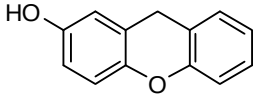
Synthesized according to general procedure A. Yield: 91 mg, 50%; Synthesized according to general procedure B. Yield: 102 mg, 56%; White solid, ^{1}H NMR (500 MHz, DMSO): δ 7.27-7.20 (m, 4H), 7.09-7.04 (m, 4H), 4.04 (s, 2H); ^{13}C NMR (125 MHz, DMSO):151.31, 129.17, 127.75, 123.23, 120.61, 116.04, 26.90; HRMS-(EI) (*m/z*): M^+ calcd for $C_{13}H_{10}O_1$, 182.073166; found 182.072975.

4-methoxy-9*H*-xanthene **3c**



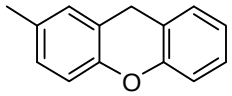
Synthesized according to general procedure A. Yield: 115 mg, 54%; Synthesized according to general procedure B. Yield: 132 mg, 62%;Yellowish oil, ^{1}H NMR (500 MHz, DMSO): δ 7.26-7.19 (m, 2H), 7.10-7.04 (m, 2H), 7.02-6.97 (m, 1H), 6.94-6.90 (m, 1H), 6.83-6.79 (m, 1H), 4.02 (s, 2H), 3.83 (s, 3H); ^{13}C NMR (125 MHz, DMSO): 151.2, 147.6, 140.6, 129.1, 127.7, 123.3, 122.9, 121.3, 120.5, 120.4, 116.2, 110.5, 55.6, 27.0; HRMS-(EI) (*m/z*): M^+ calcd for $C_{14}H_{12}O_2$, 212.083730; found 212.083684.

9H-xanthen-2-ol **3d**



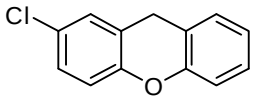
Synthesized according to general procedure A. Yield: 59 mg, 30%; Synthesized according to general procedure B. Yield: 109 mg, 55%;White solid, ^{1}H NMR (500 MHz, DMSO): δ 9.18 (s, 1H), 7.25-7.17 (m, 2H), 7.06-6.99 (m, 2H), 6.90-6.89 (m, 1H), 6.64-6.59 (m, 2H), 3.96 (s, 2H); ^{13}C NMR (125 MHz, DMSO): 153.03, 151.74, 144.08, 129.10, 127.61, 122.74, 121.22, 120.24, 116.68, 115.94, 114.64, 114.48, 27.30; HRMS-(EI) (*m/z*): M^+ calcd for $C_{13}H_{10}O_2$, 198.068079; found 198.067949

2-methyl-9*H*-xanthene **3e**



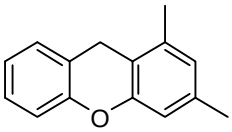
Synthesized according to general procedure A. Yield: 134 mg, 63%; Synthesized according to general procedure B. Yield: 187 mg, 88%;White solid, ^{1}H NMR (500 MHz, DMSO): δ 7.26-7.19 (m, 2H), 7.07-6.99 (m, 4H), 6.97-6.93 (m, 1H), 4,00 (s, 2H), 2.26 (s, 3H); ^{13}C NMR (125 MHz, DMSO): δ 151.4, 149.2, 132.1, 129.4, 129.2, 128.2, 127.7, 123.1, 120.5, 120.2, 116.0, 115.8, 26.9, 20.2 ; HRMS-(EI) (*m/z*): M^+ calcd for $C_{14}H_{12}O_1$, 196.088811; found 196.088659.

2-chloro-9*H*-xanthene **3f**



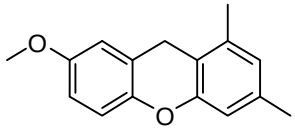
Synthesized according to general procedure A. Yield: 39 mg, 18%; Synthesized according to general procedure B. Yield: 65 mg, 30%; White solid, ^{1}H NMR (500 MHz, DMSO): δ 7.34-7.32 (m, 1H), 7.27-7.21 (m, 3H), 7.09-7.04 (m, 3H), 4.04 (s, 2H); ^{13}C NMR (125 MHz, DMSO): δ 150.9, 150.1, 129.1, 128.7, 127.9, 127.6, 126.7, 123.5, 122.8, 119.9, 117.8, 116.1, 26.7; HRMS-(EI) (*m/z*): M^+ calcd for $C_{13}H_9O_1Cl_1$, 216.034193; found 216.034201.

1,3-dimethyl-9*H*-xanthene **3g**



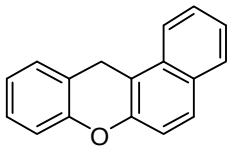
Synthesized according to general procedure A. Yield: 126 mg, 60%; Synthesized according to general procedure B. (at 200°C) Yield: 118 mg, 56%;White solid, ^{1}H NMR (500 MHz, DMSO): δ 7.26-7.17 (m, 2H), 7.05-6.98 (m, 2H), 6.73 (s, 1H), 6.68 (s, 1H), 3.88 (s, 2H), 2.22 (s, 6H); ^{13}C NMR (125 MHz, DMSO): 150.95, 150.80, 136.88, 136.45, 129.49, 127.71, 125.04, 122.93, 120.06, 115.83, 115.81, 113.94, 24.53, 20.56, 18.64; HRMS-(EI) (*m/z*): M^+ calcd for $C_{15}H_{14}O_1$, 210.104467; found 210.104383.

7-methoxy-1,3-dimethyl-9*H*-xanthene **3h**



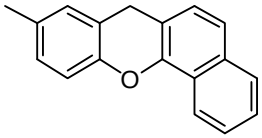
Synthesized according to general procedure A. Yield: 149 mg, 62%; Synthesized according to general procedure B. (at 200°C) Yield: 166 mg, 69%;White solid, ^{1}H NMR (500 MHz, DMSO): 6.96-6.92 (m, 1H), 6.84-6.81 (m, 1H), 6.79-6.75 (m, 1H), 6.72 (s, 1H), 6.66 (s, 1H), 3.88 (s, 2H), 3.72 (s, 3H), 2.22 (s, 6H); ^{13}C NMR (125 MHz, DMSO): 154.78, 151.07, 144.87, 136.81, 136.39, 124.79, 120.80, 116.59, 115.36, 113.87, 113.59, 55.36, 24.99, 20.58, 18.70; HRMS-(EI) (*m/z*): M^+ calcd for $C_{16}H_{16}O_2$, 240.115026; found 240.115225.

12*H*-benzo[*a*]xanthene **3i**



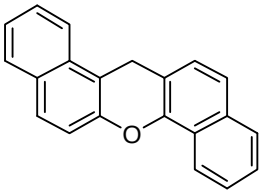
Synthesized according to general procedure A. Yield: 207 mg, 89%; Synthesized according to general procedure B. Yield: 221 mg, 95%;White solid, ^{1}H NMR (500 MHz, DMSO): δ 7.97-7.93 (m, 2H), 7.88-7.85 (m, 1H), 7.66-7.61 (m, 1H), 7.52-7.48 (m, 1H),7.43-7.39 (m, 1H), 7.35-725 (m, 2H), 7.17-7.11 (m, 1H), 4.41 (s, 2H); ^{13}C NMR (125 MHz, DMSO): 150.33, 147.95, 131.57, 129.81, 129.68, 128.35, 128.33, 127.87, 126.90, 124.34, 123.42, 122.49, 119.49, 117.51, 116.06, 111.68, 23.87; HRMS-(EI) (*m/z*): M^{+} calcd for $C_{17}H_{12}O_1$, 232.088813; found 232.088790.

9-methy-7*H*-benzo[*c*]xanthene **3j**



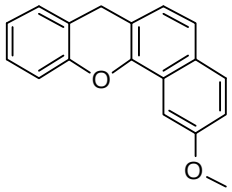
Synthesized according to general procedure A. Yield: 207 mg, 84%; Synthesized according to general procedure B. (at 200 °C) Yield: 190 mg, 77%;White solid, ^{1}H NMR (500 MHz, DMSO) δ 8.30-8.26 (m, 1H), 7.92-7.88 (m, 1H), 7.62-7.51 (m, 3H), 7.36-7.30 (m, 1H), 7.17-7.12 (m, 1H), 7.10-7.04 (m, 2H), 4.13 (s, 2H), 2.27 (s, 3H); ^{13}C NMR (125 MHz, DMSO): 149.00, 145.64, 132.90, 132.43, 129.43, 128.29, 127.67, 127.00, 126.11, 123.40, 122.29, 120.73, 119.91, 116.07, 114.47, 27.13, 20.27; HRMS-(EI) (*m/z*): M^{+} calcd for $C_{18}H_{14}O_1$, 246.104468; found 246.104376.

14*H*-dibenzo[*a*,*h*]xanthene **3k**



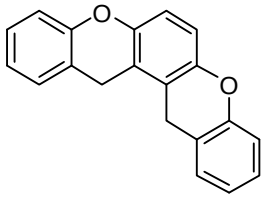
Synthesized according to general procedure A. Yield: 234 mg, 83%; Synthesized according to general procedure B. Yield: 271 mg, 96%;White solid, ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.46-8.42 (m, 1H), 7.94-7.78 (m, 4H), 7.64-7.56 (m, 3H), 7.54-7.43 (m, 3H), 7.40-7.37 (m, 1H), 4.51 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): 148.70, 145.73, 133.53, 132.23, 130.44, 128.57, 128.41, 127.69, 127.14, 126.85, 126.19, 126.08, 124.35, 124.28, 122.75, 122.53, 121.53, 118.14, 113.61, 111.79, 25.46; HRMS-(EI) (*m/z*): M^{+} calcd for $C_{21}H_{14}O_1$, 282.104462; found 282.104546.

2-methoxy-7*H*-benzo[*c*]xanthene **3l**



Synthesized according to general procedure A. Yield: 210 mg, 80%; Synthesized according to general procedure B. Yield: 252 mg, 96%;White solid, ^{1}H NMR (500 MHz, DMSO): δ 7.84-7.80 (m, 1H), 7.62-7.52 (m, 2H), 7.32-7.26 (m, 3H), 7.21-7.15 (m, 2H), 7.13-7.08 (m, 1H), 4.16 (s, 2H), 3.94 (s, 3H); ^{13}C NMR (125 MHz, DMSO): 157.64, 151.18, 144.83, 129.41, 129.22, 128.32, 127.75, 124.47, 124.30, 123.47, 122.32, 120.43, 118.34, 116.41, 115.21, 99.45, 55.23, 27.24; HRMS-(EI) (*m/z*): M^+ calcd for $C_{18}H_{14}O_2$, 262.099378; found 262.099142.

13,14-dihydrochromeno[*3,2a*]xanthene **5**



Synthesized according to general procedure A. Yield: 20 mg, 7%; Synthesized according to general procedure B. Yield: 14 mg, 5%;White solid, ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22-7.15 (m, 4H), 7.05-6.98 (m, 4H), 6.88 (s, 2H), 3.96 (s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): 151.61, 147.12, 129.21, 127.98, 122.92, 118.84, 118.69, 116.40, 115.50, 25.6; HRMS-(EI) (*m/z*): M^+ calcd for $C_{20}H_{14}O_2$, 286.099377, found 286.099179.

The structure was assigned based on an INEPT-INADEQUATE spectrum which was recorded as described in Weigelt and Otting[1] on a Bruker AV600 spectrometer equipped with a 5-mm H/C/N triple-resonance cryogenically-cooled probehead, with 16 scans per increment, TD(F2) = 1k, TD(F1) = 2k, and 2 s of relaxation delay for acquisition. (Sample amount was 12mg of **5** in CDCl3).

[1] J. Weigelt and G. Otting, *J. Magn. Reson. A*, 1995, **113**, 128.

NMR spectra of products

2-methoxy-9*H*-xanthene **3a**

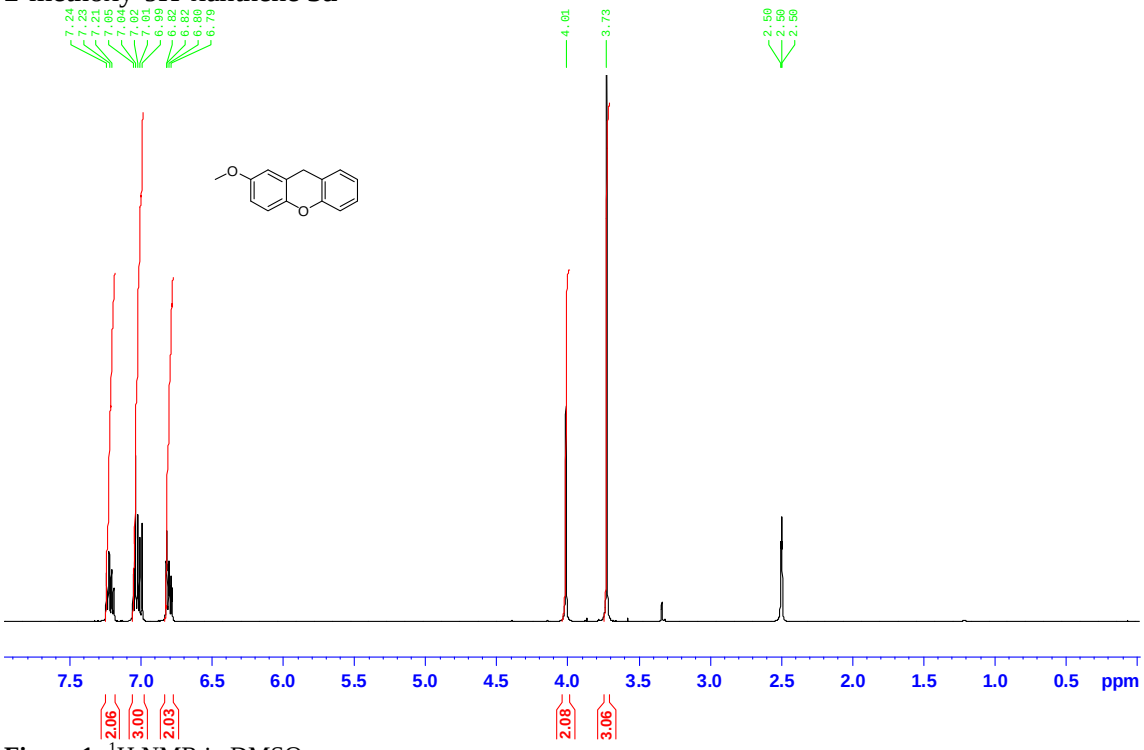


Figure 1: ^{1}H NMR in DMSO

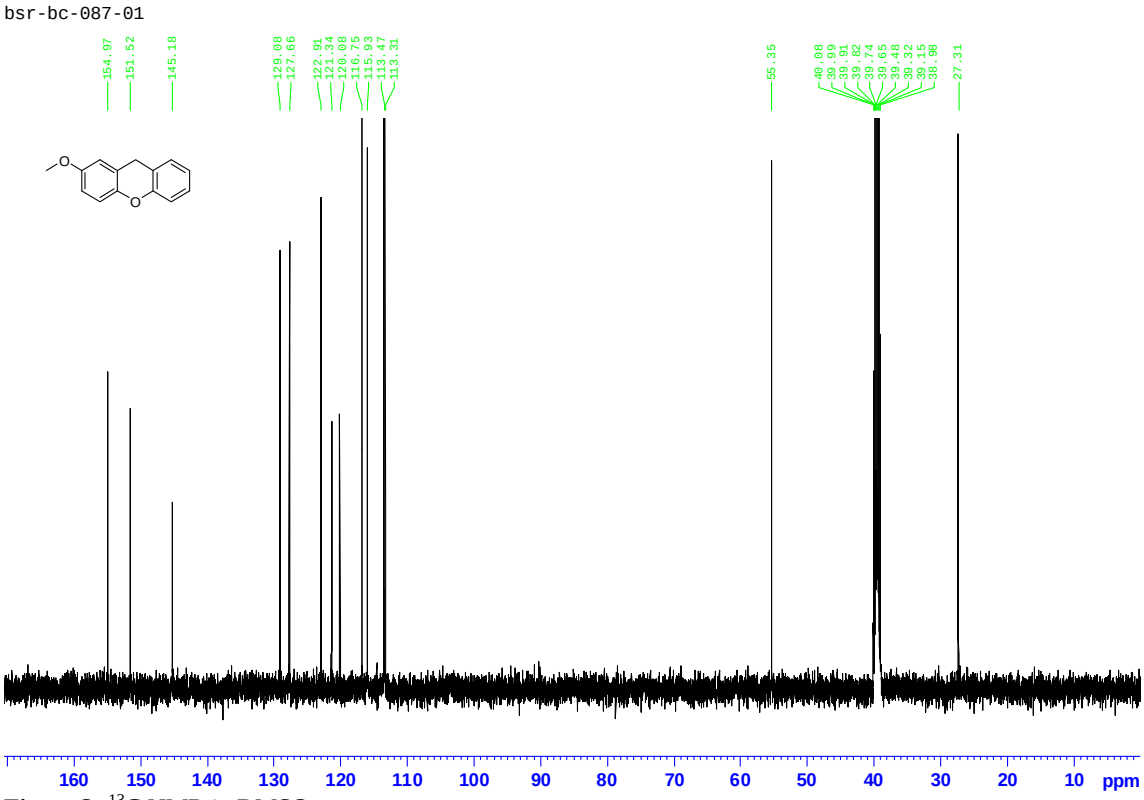


Figure 2: ^{13}C NMR in DMSO

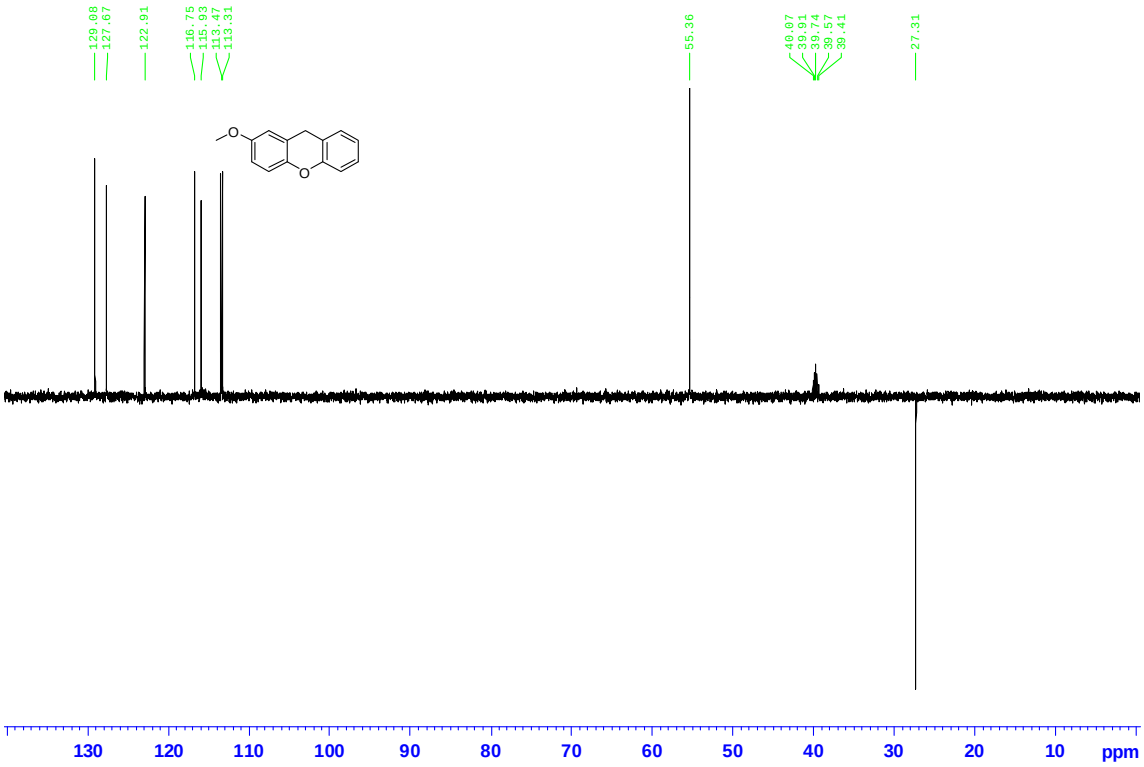


Figure 3: dept135 NMR in DMSO

9*H*-xanthene **3b**

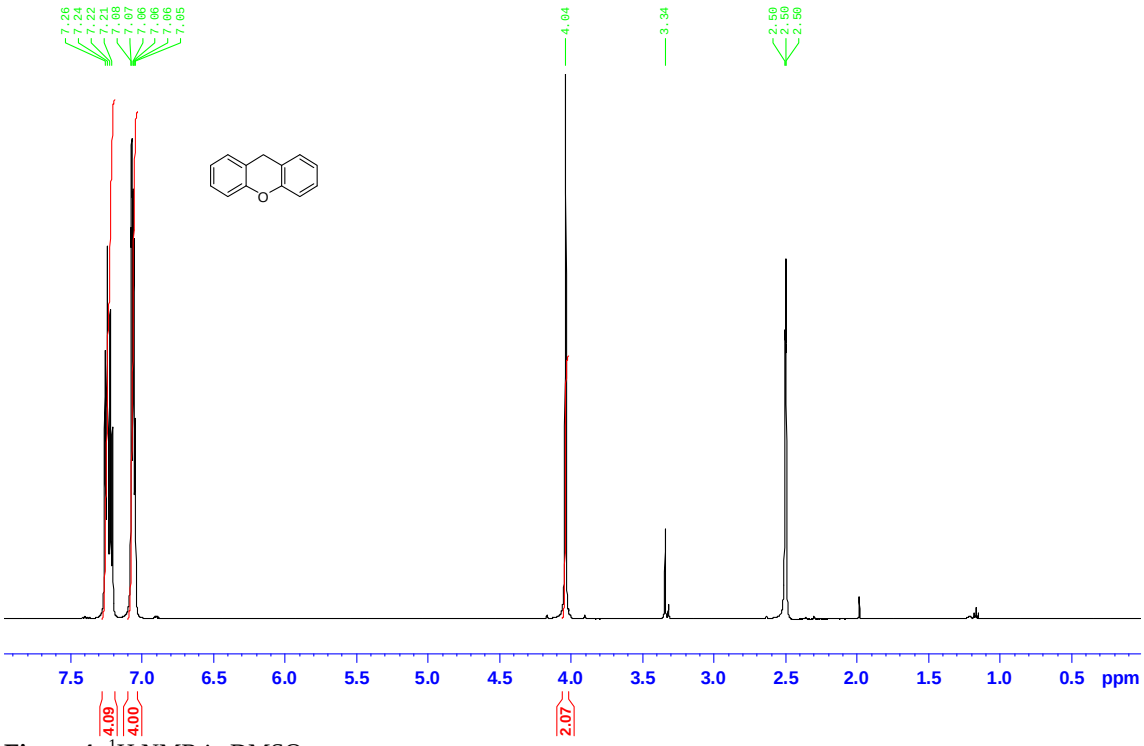


Figure 4: ^{1}H NMR in DMSO

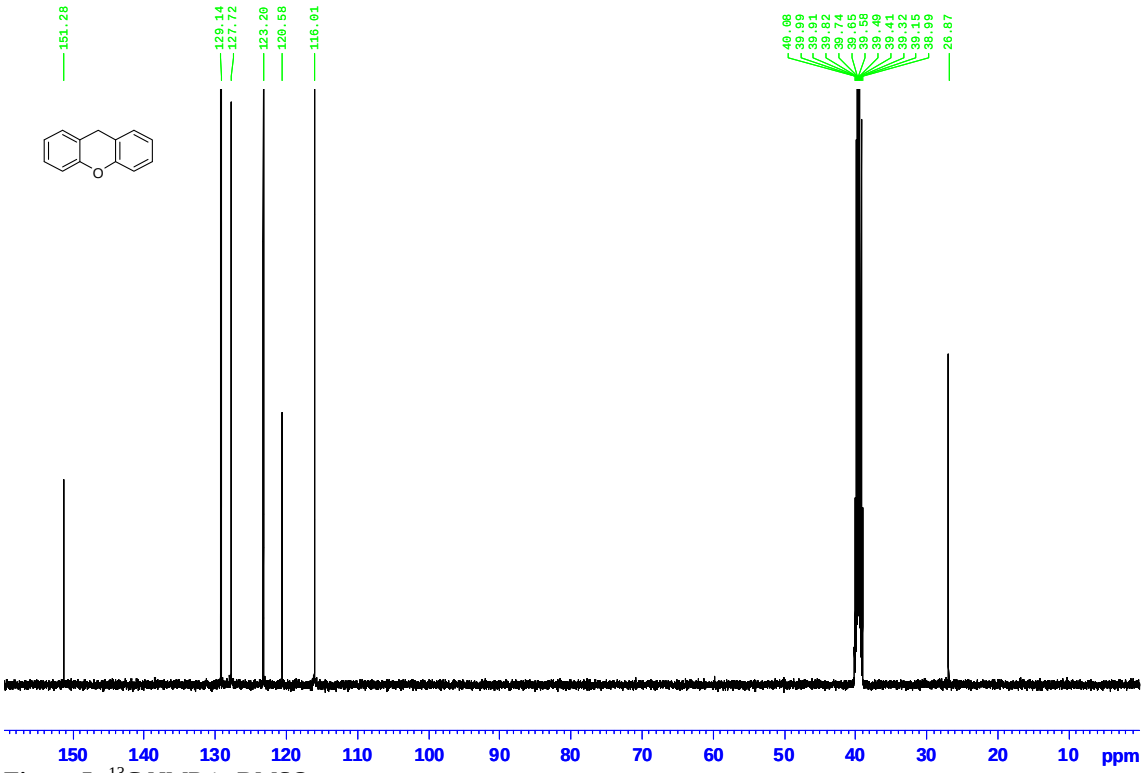


Figure 5: ^{13}C NMR in DMSO

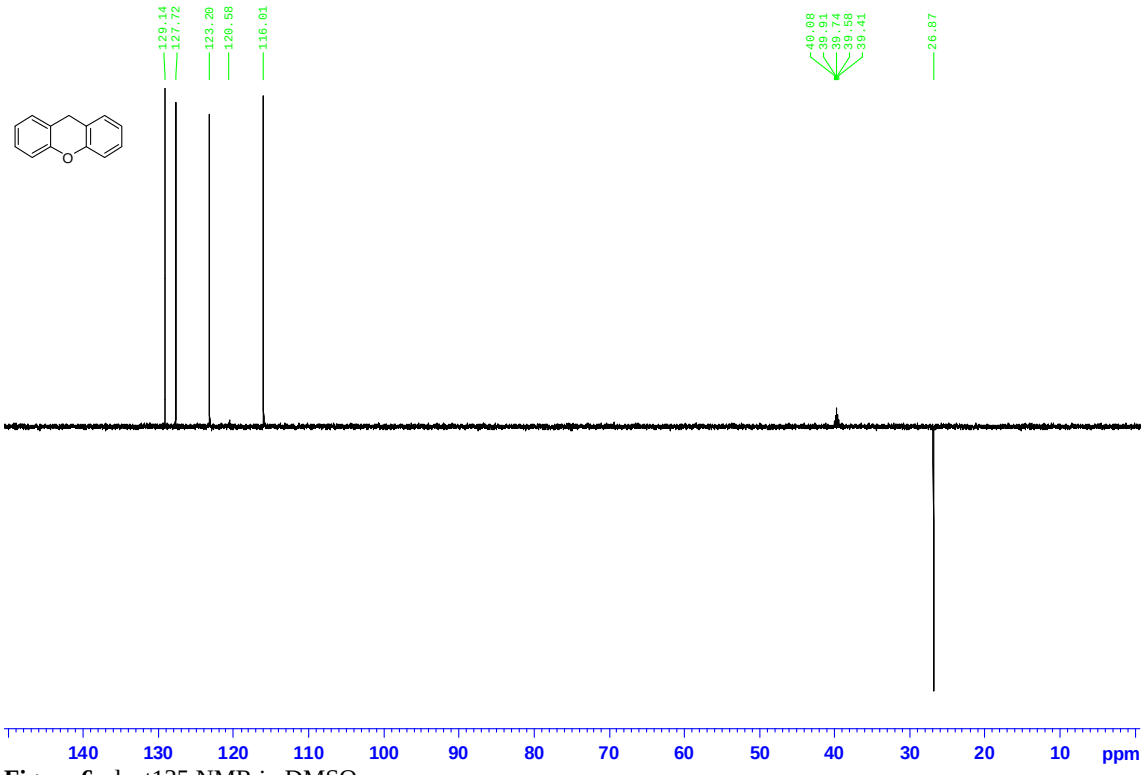


Figure 6: dept135 NMR in DMSO

4-methoxy-9*H*-xanthene **3c**

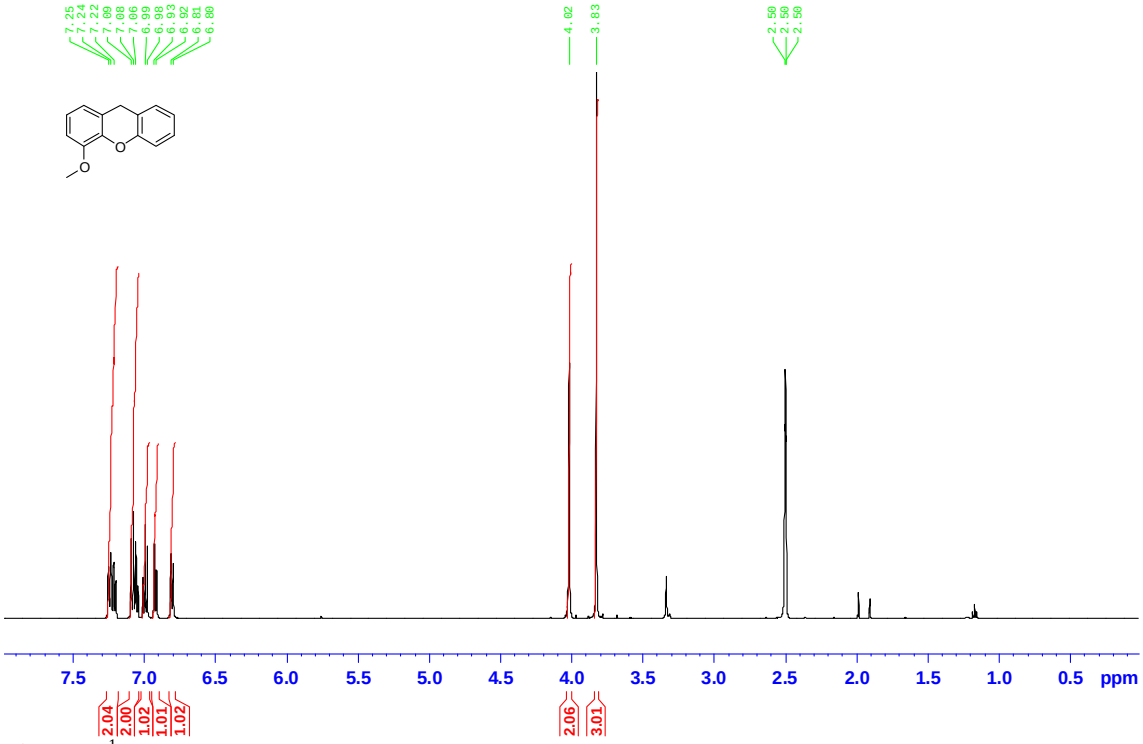


Figure 7: ^{1}H NMR in DMSO

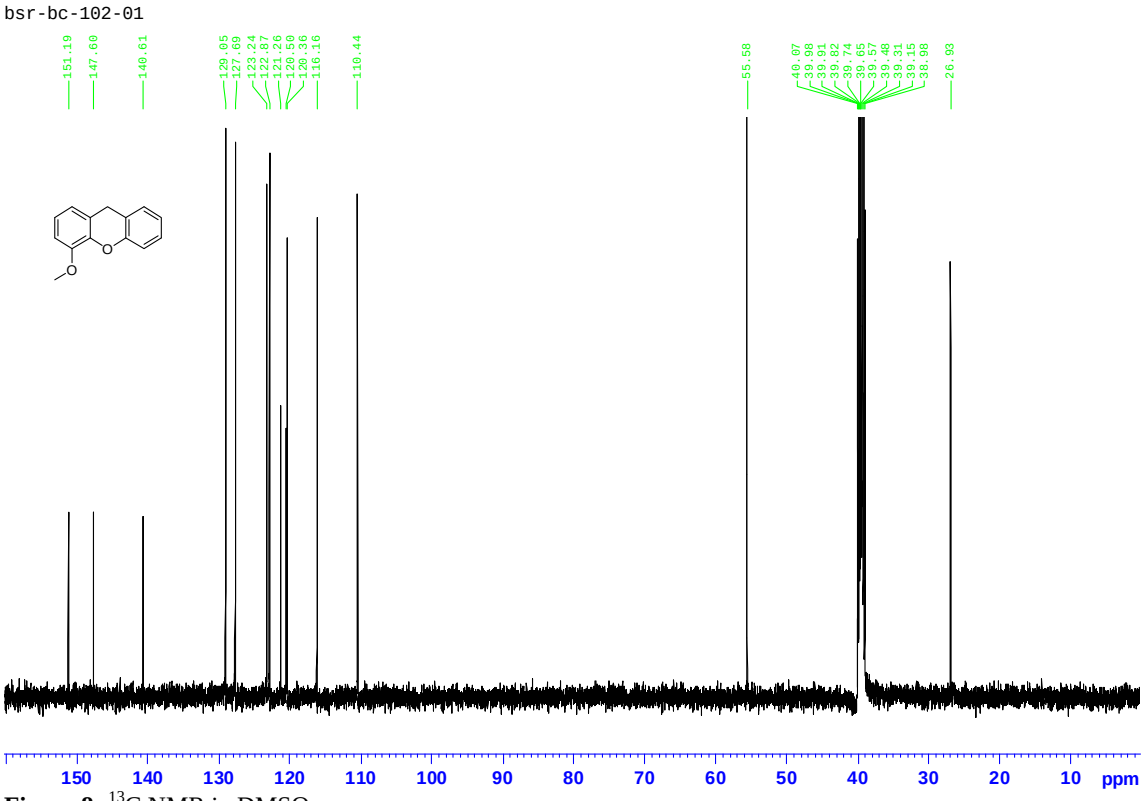


Figure 8: ^{13}C NMR in DMSO

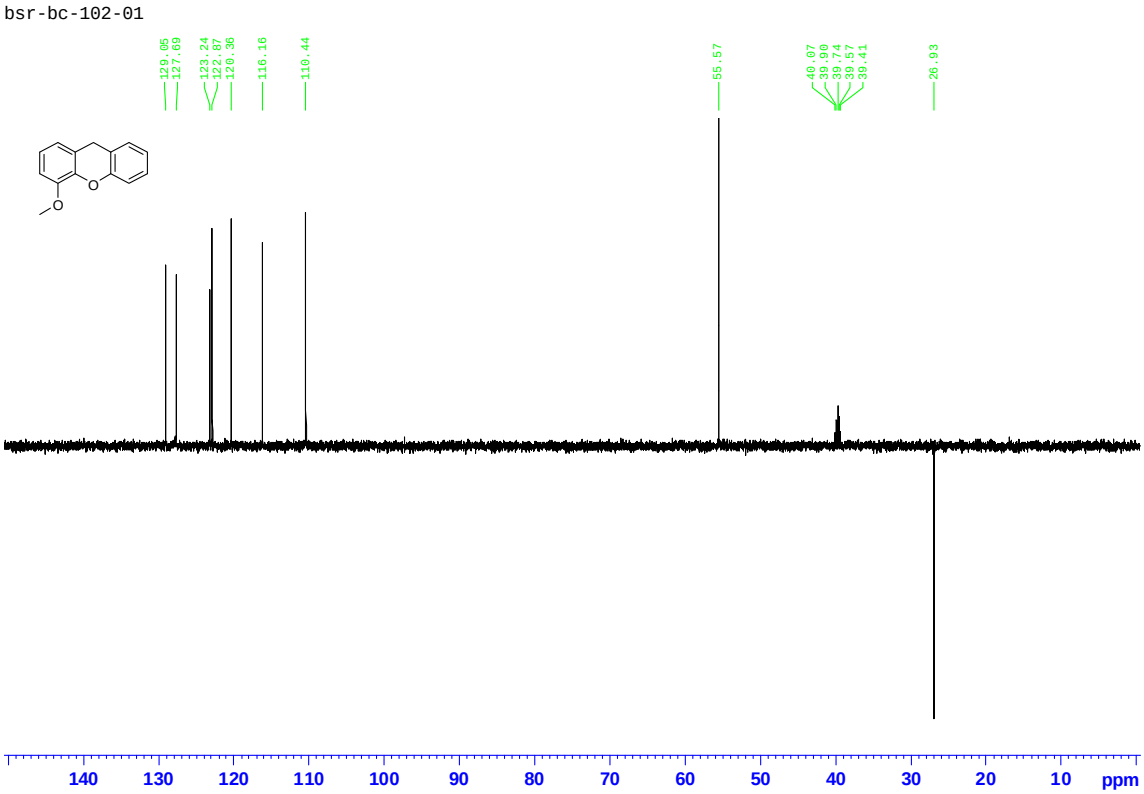


Figure 9: dept135 NMR in DMSO

9H-xanthen-2-ol **3d**

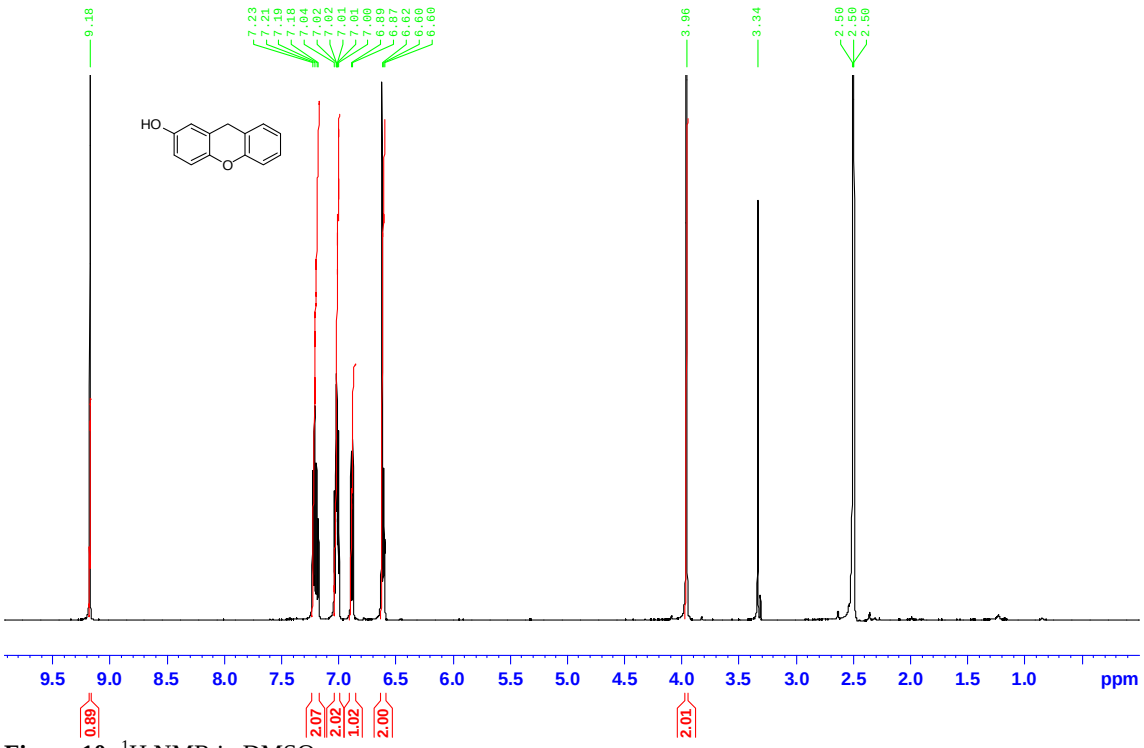


Figure 10: ^{1}H NMR in DMSO

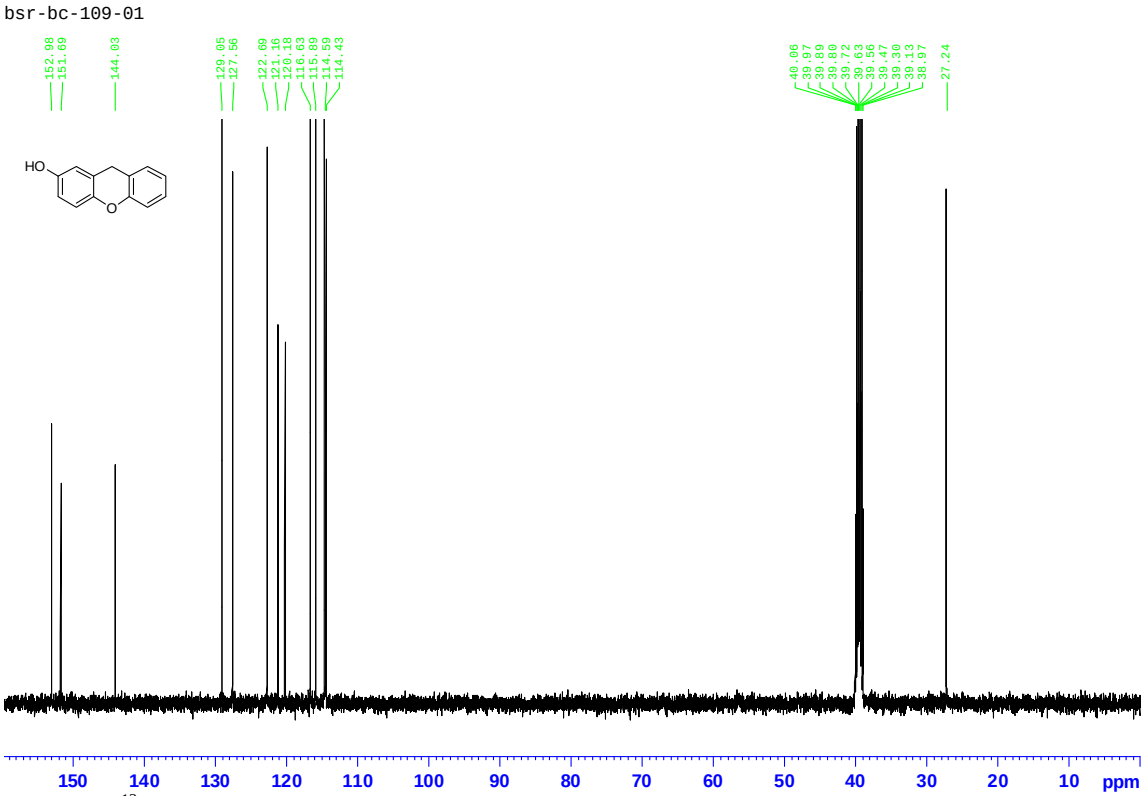


Figure 11: ^{13}C NMR in DMSO

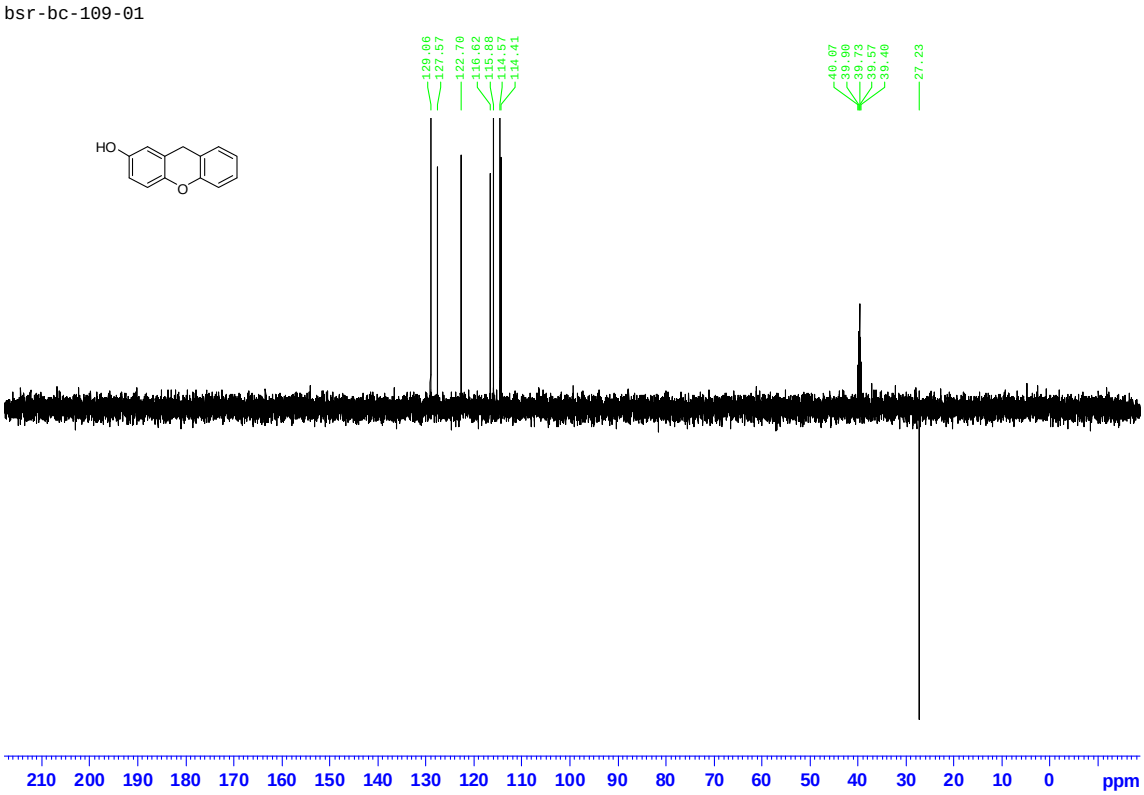


Figure 12: dept135 NMR in DMSO

2-methyl-9*H*-xanthene **3e**

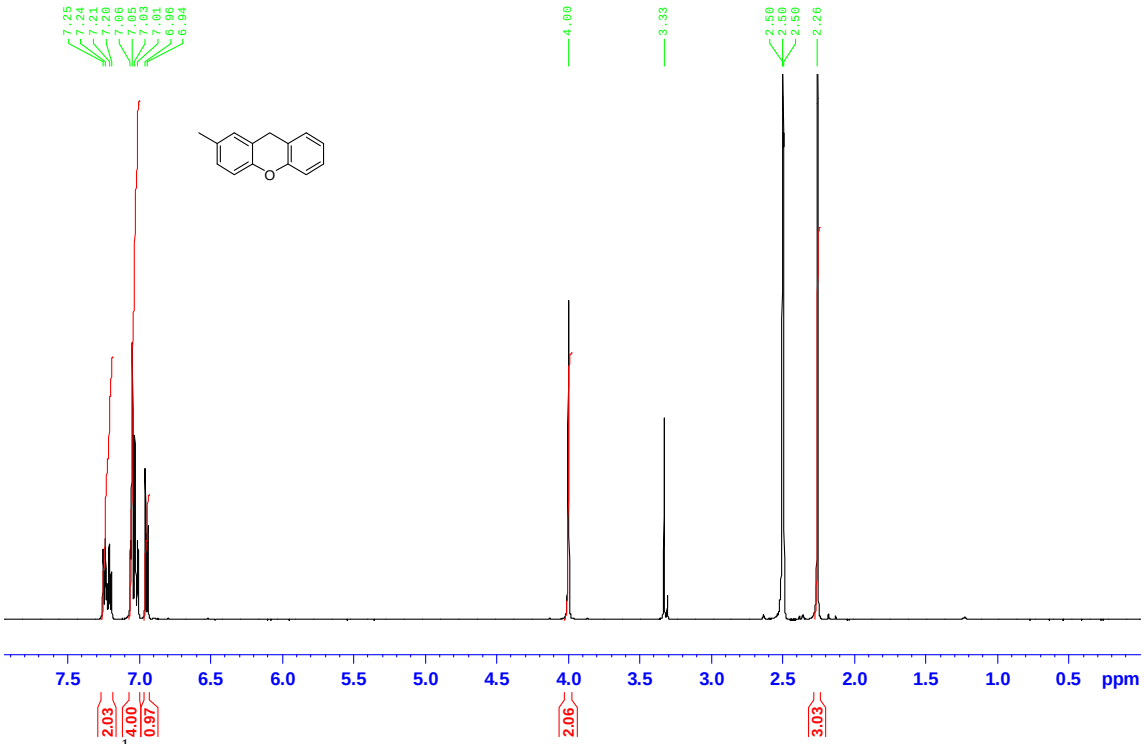


Figure 13: ^{1}H NMR in DMSO

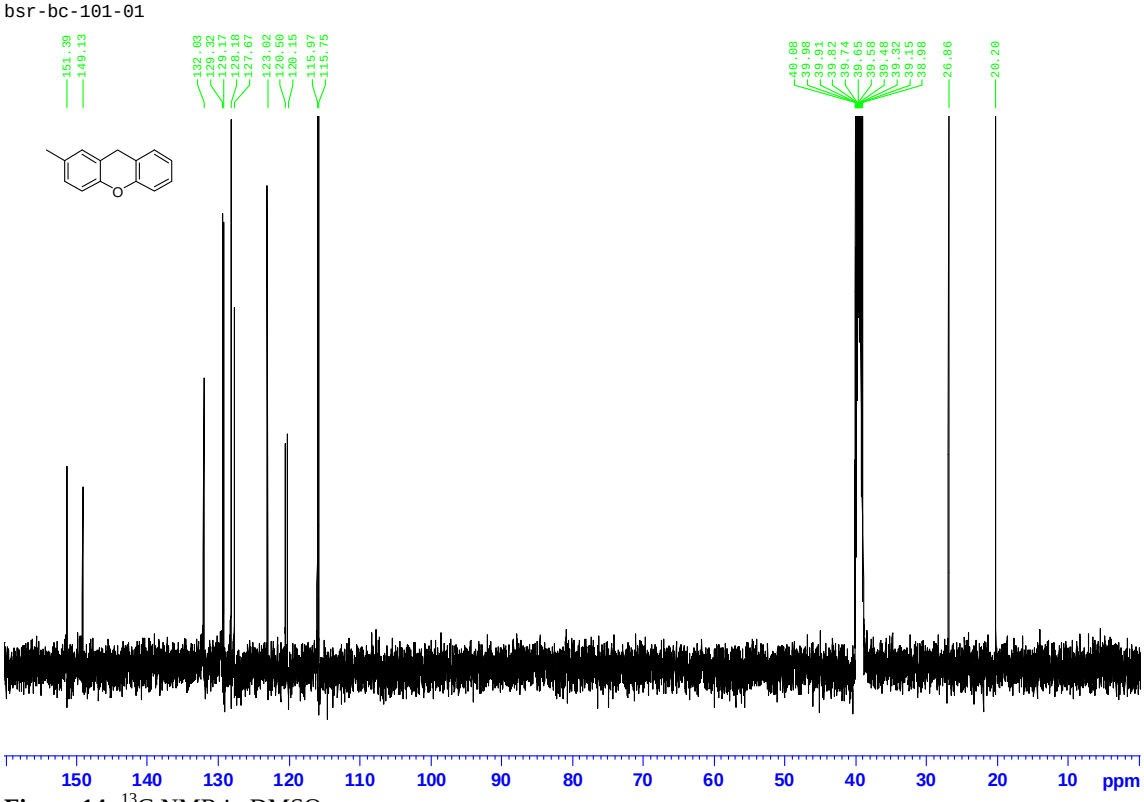


Figure 14: ^{13}C NMR in DMSO

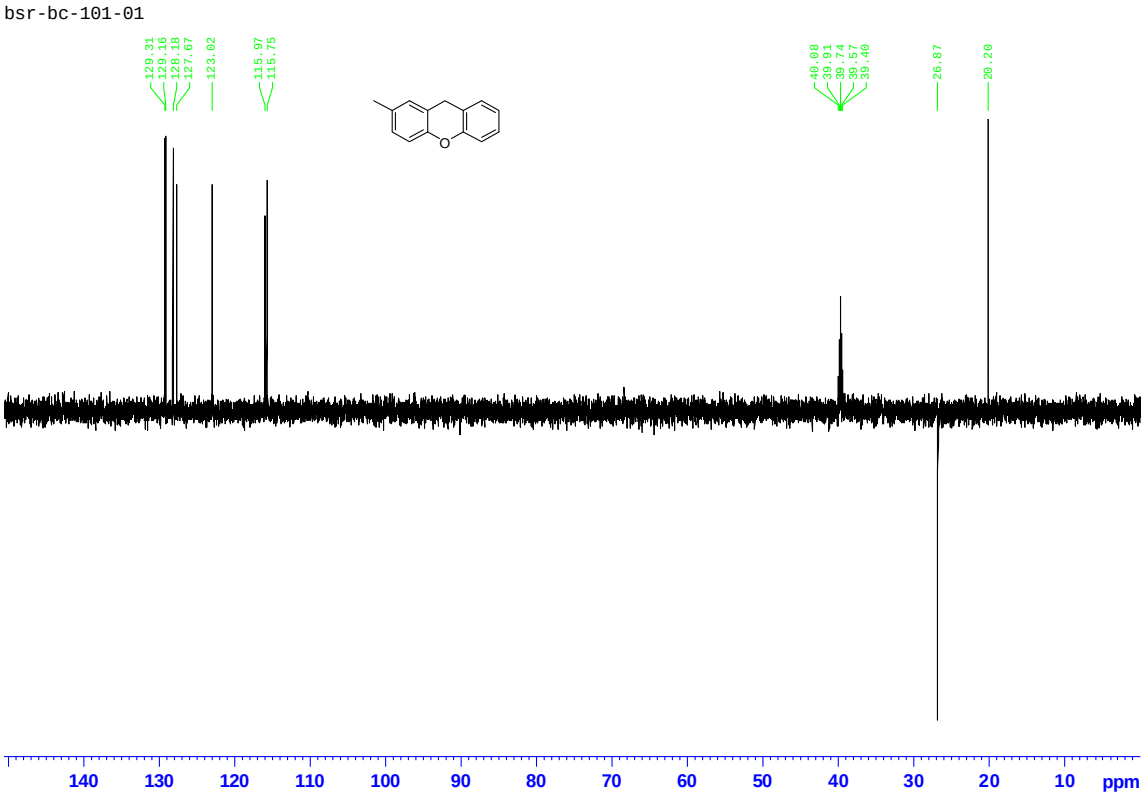


Figure 15: dept135 NMR in DMSO

2-chloro-9*H*-xanthene **3f**

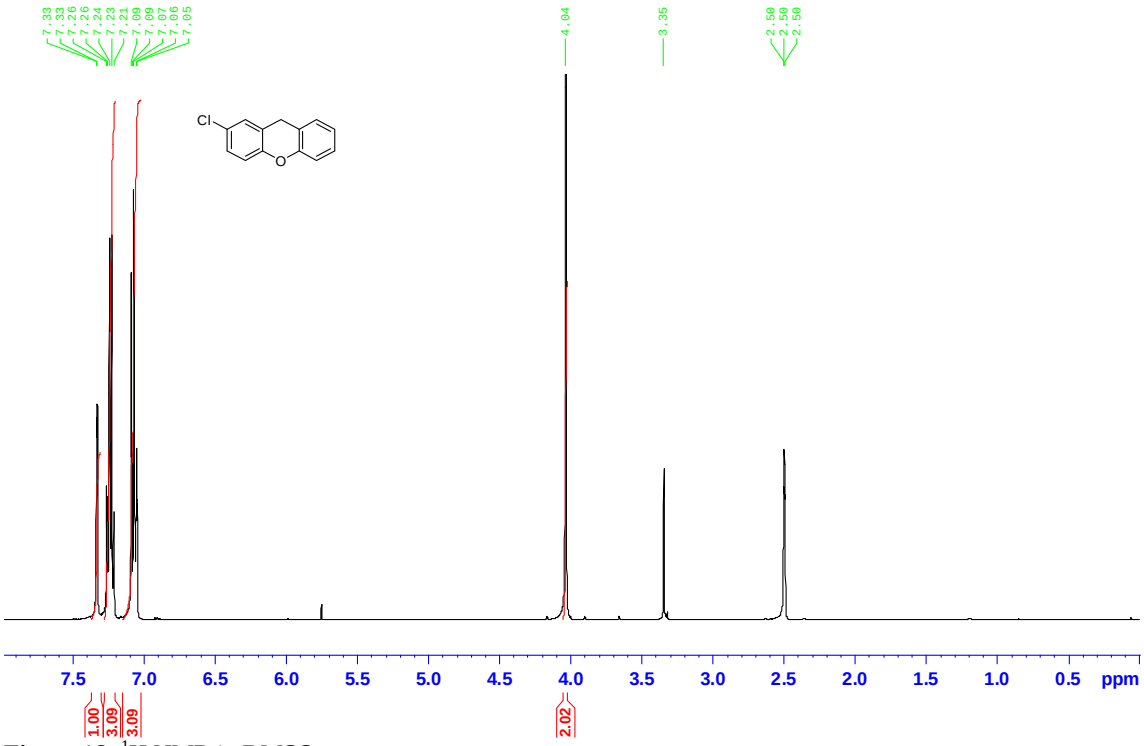


Figure 16: ^{1}H NMR in DMSO

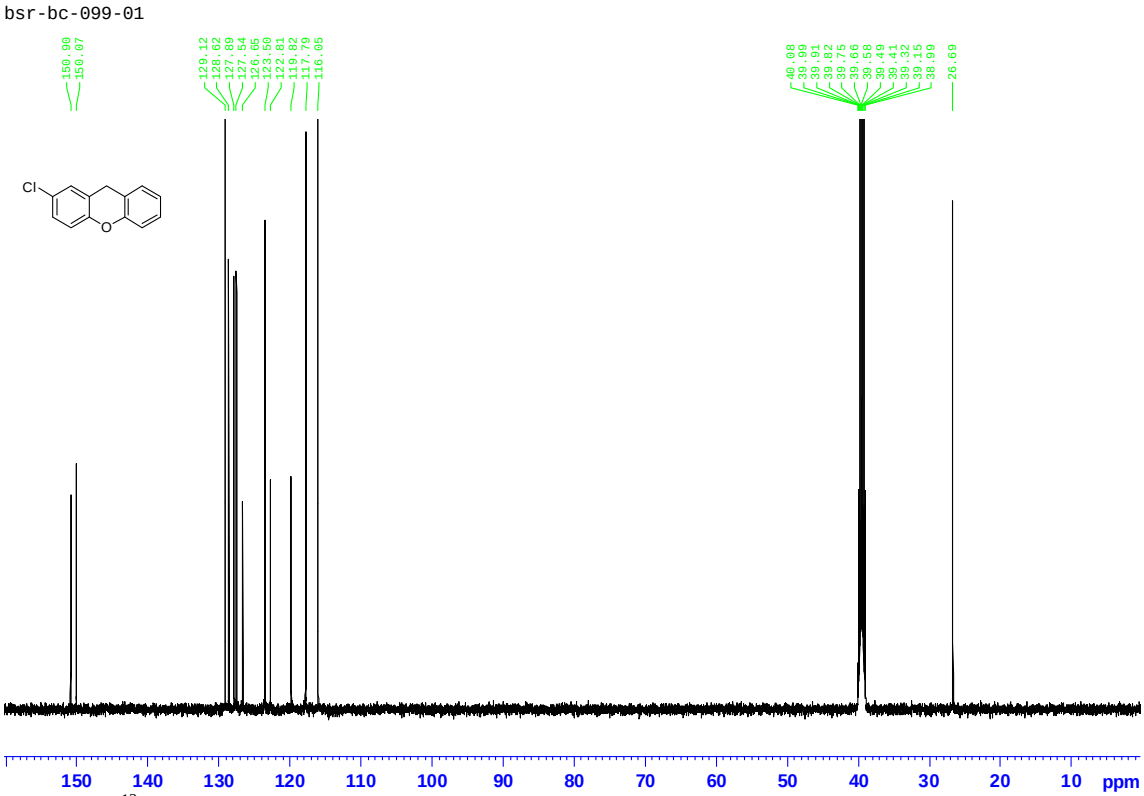


Figure 17: ^{13}C NMR in DMSO

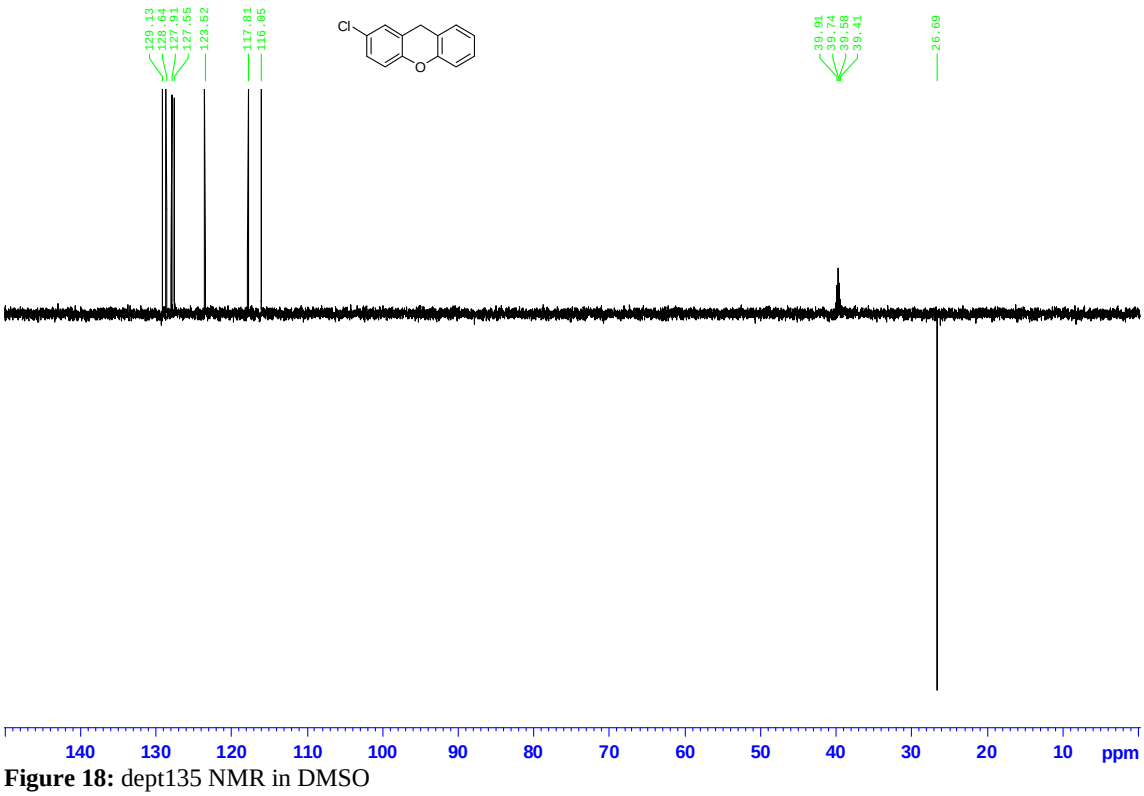


Figure 18: dept135 NMR in DMSO

1, 3-dimethyl-9*H*-xanthene **3g**

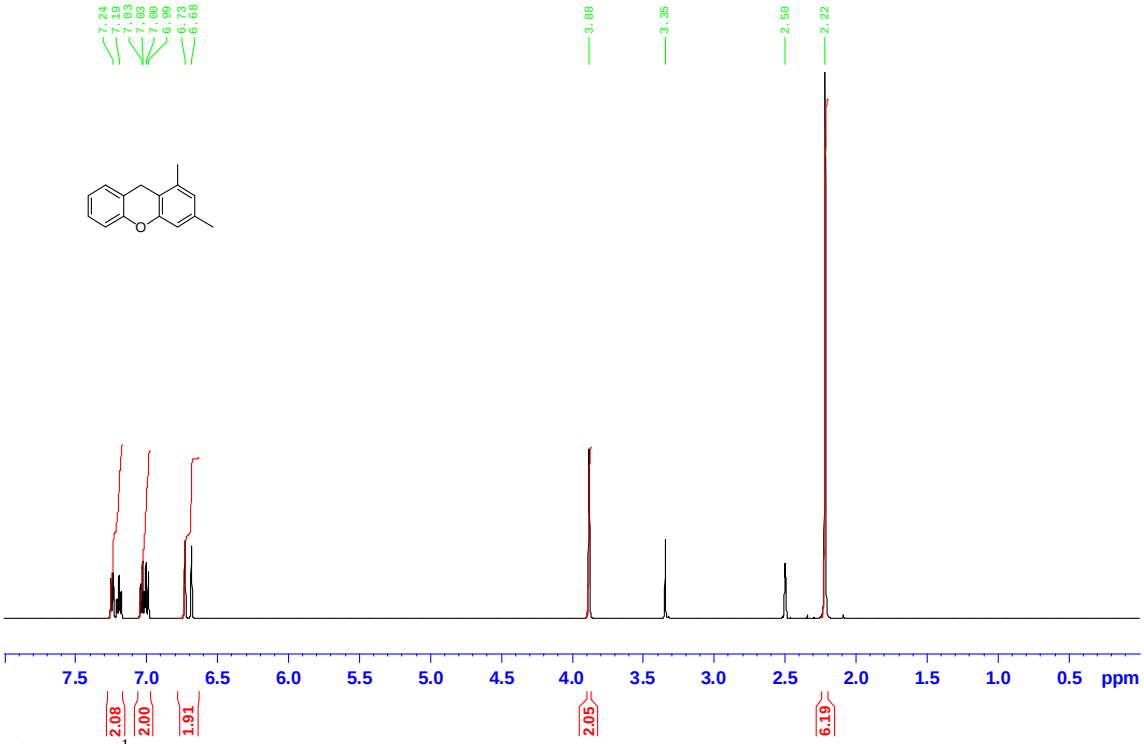


Figure 19: ^{1}H NMR in DMSO

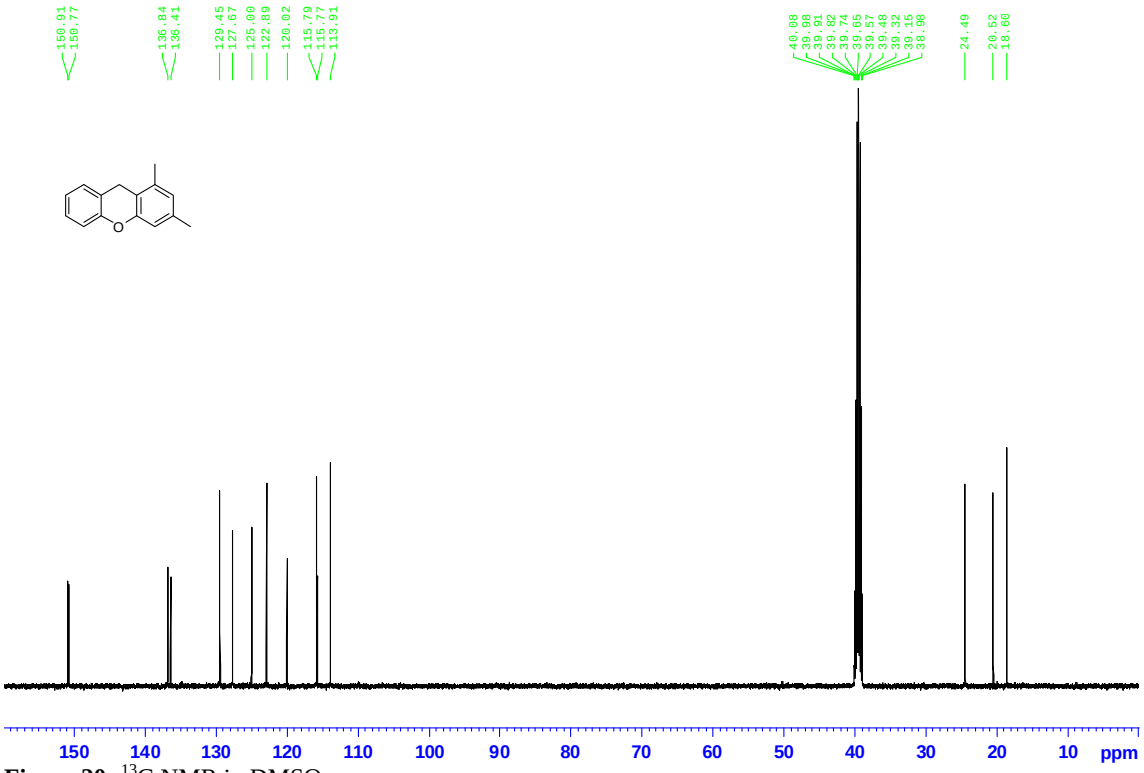


Figure 20: ^{13}C NMR in DMSO

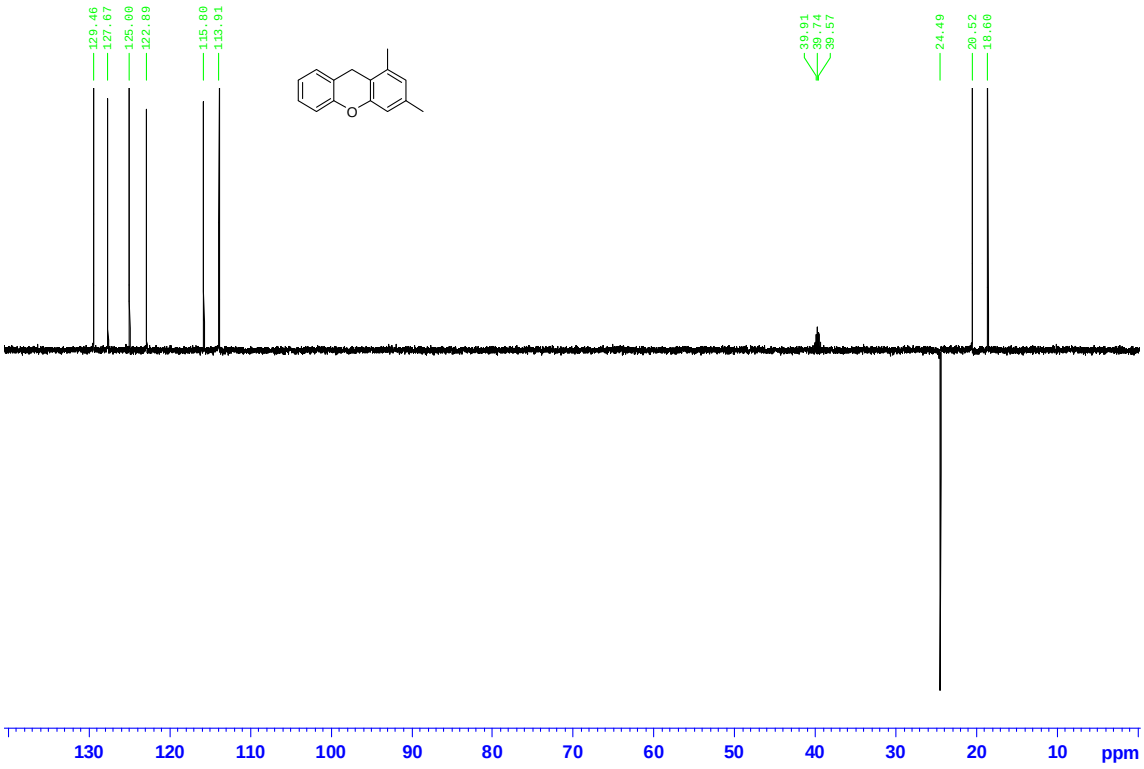


Figure 21: dept135 NMR in DMSO

7-methoxy-1, 3-dimethyl-9*H*-xanthene **3h**

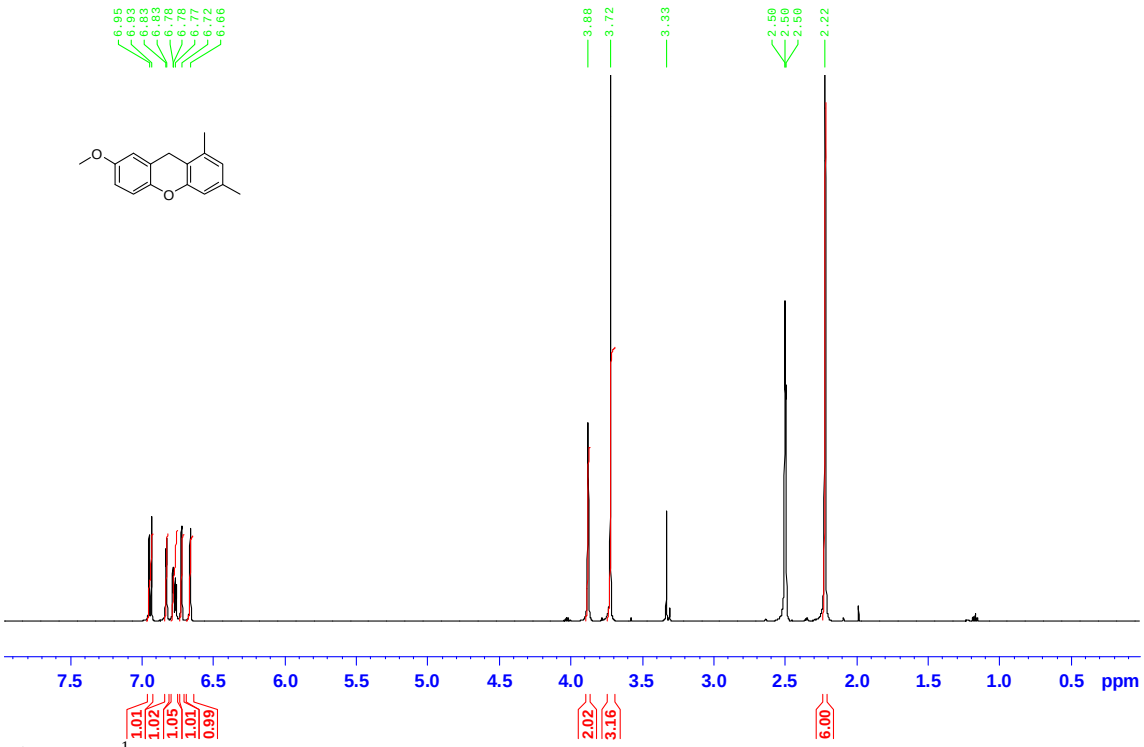


Figure 22: ^{1}H NMR in DMSO

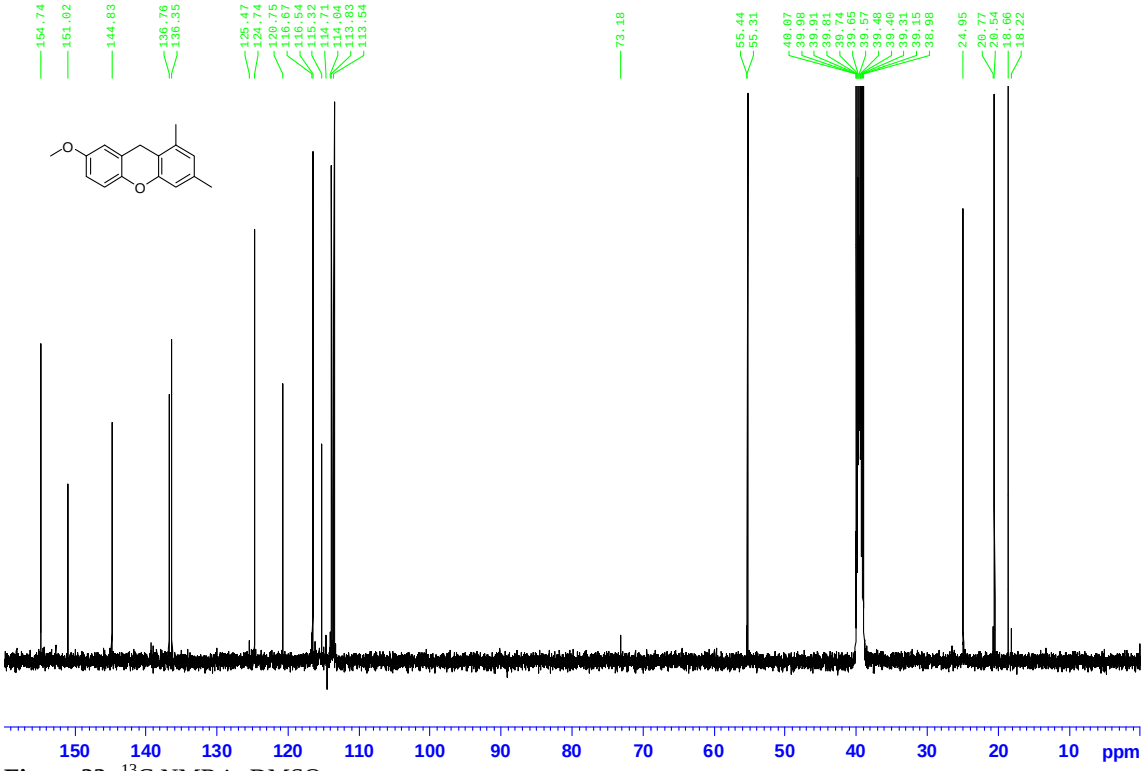


Figure 23: ^{13}C NMR in DMSO

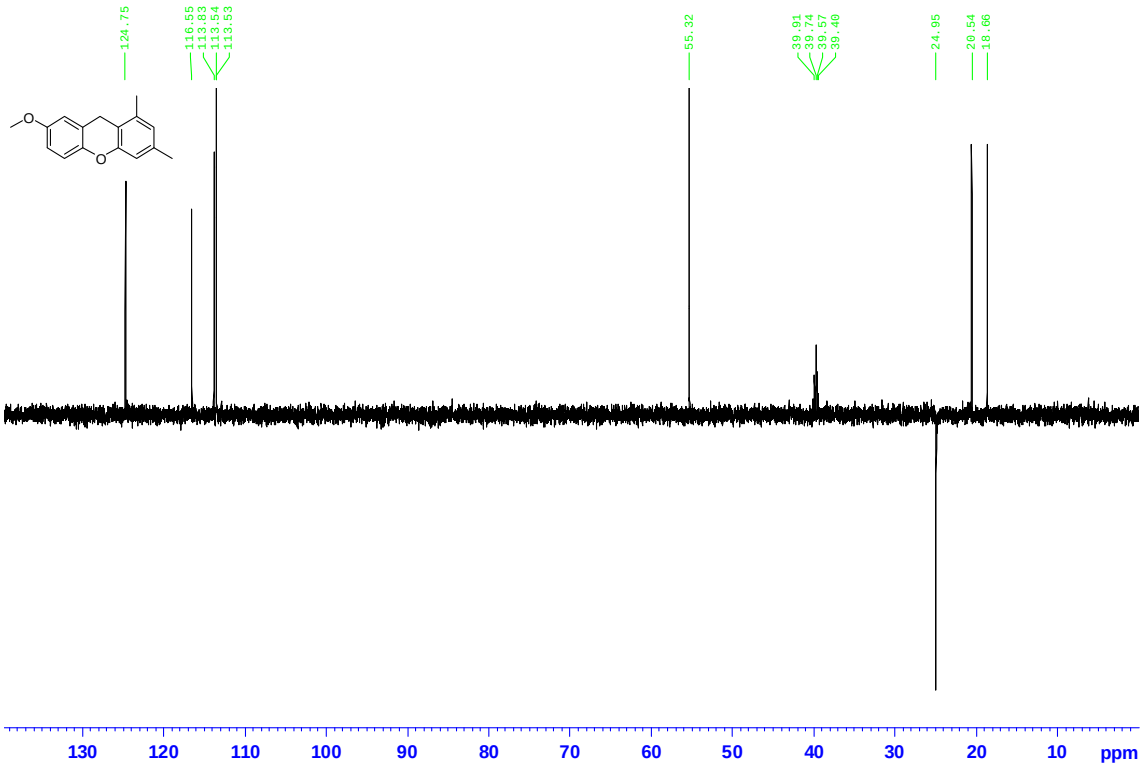


Figure 24: dept135 NMR in DMSO

12*H*-benzo[*a*]xanthene **3i**

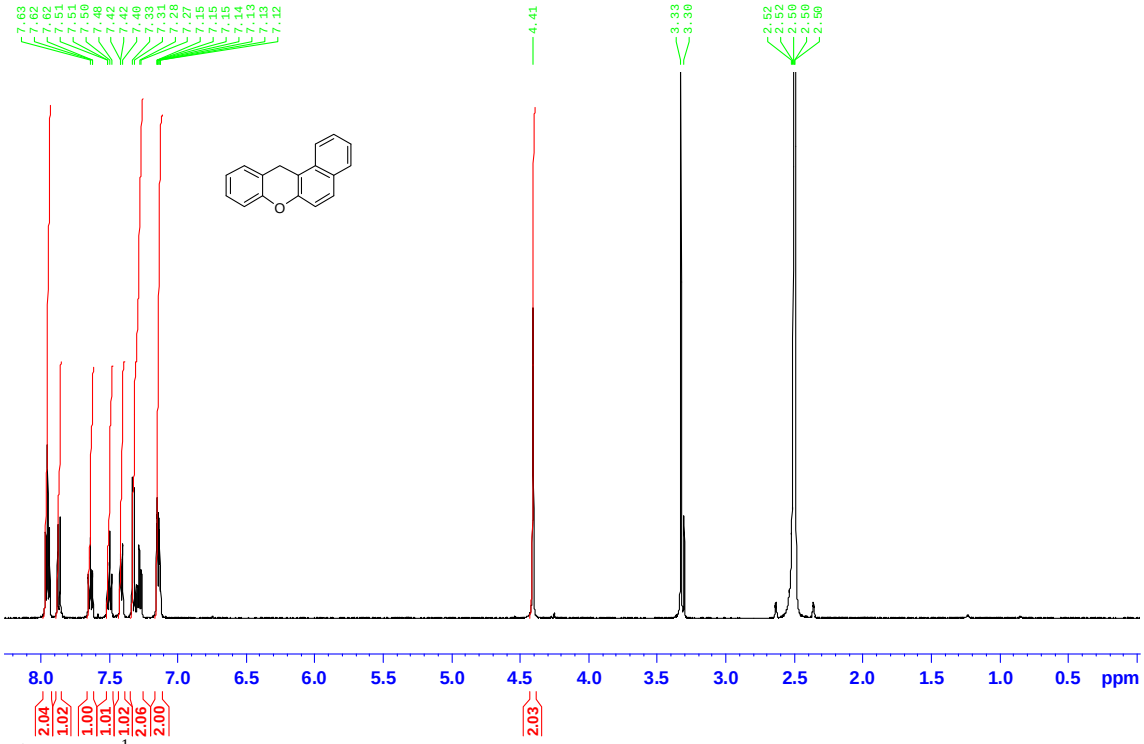


Figure 25: ^{1}H NMR in DMSO

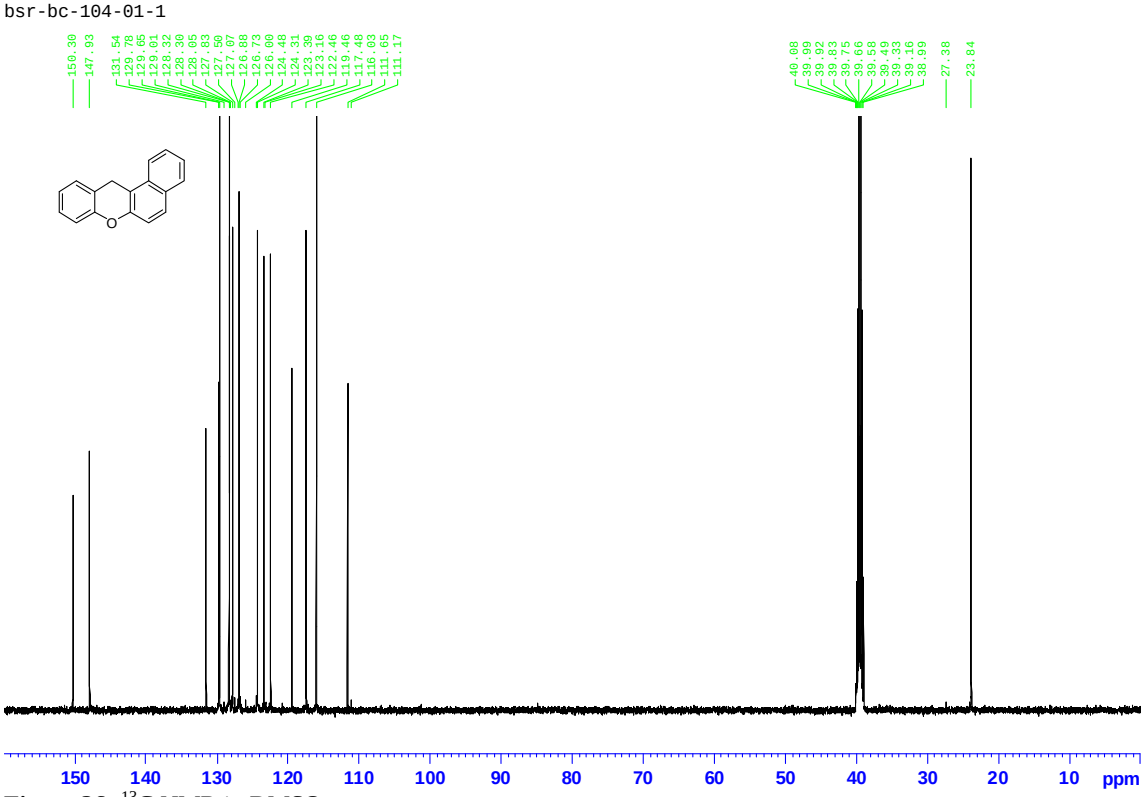


Figure 26: ^{13}C NMR in DMSO

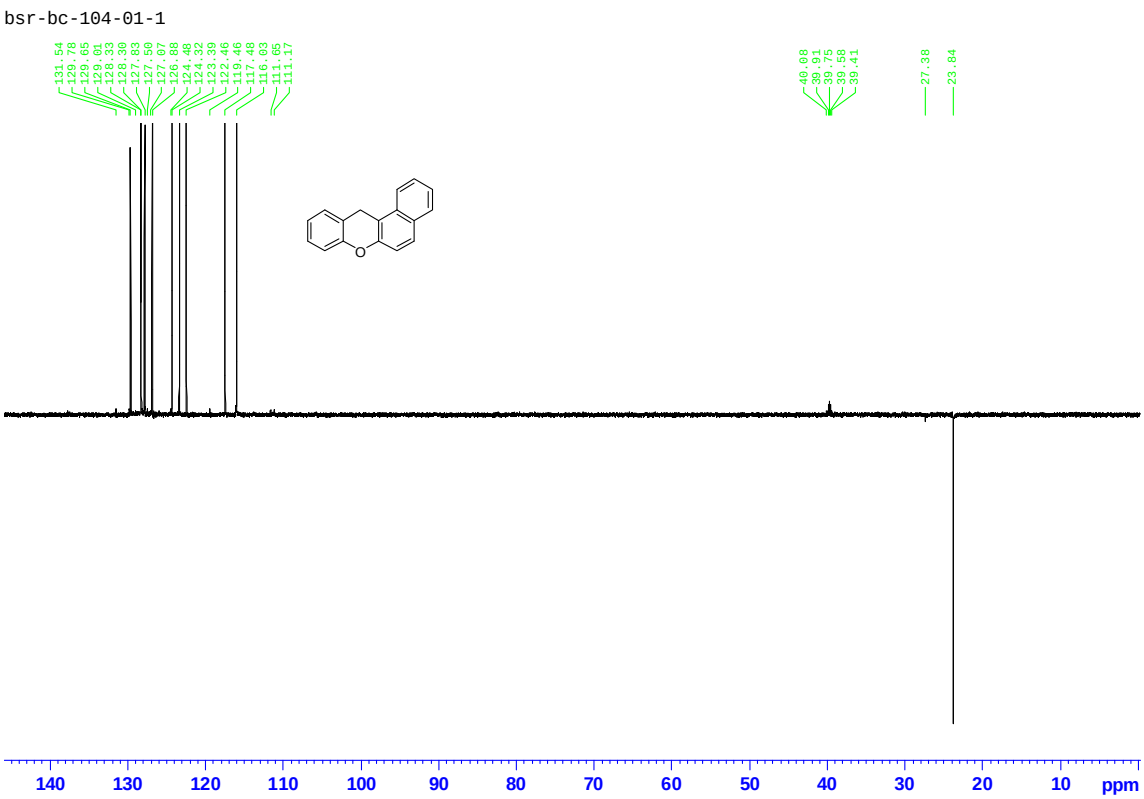


Figure 27: dept135 NMR in DMSO

9-methy-7*H*-benzo[*c*]xanthene **3j**

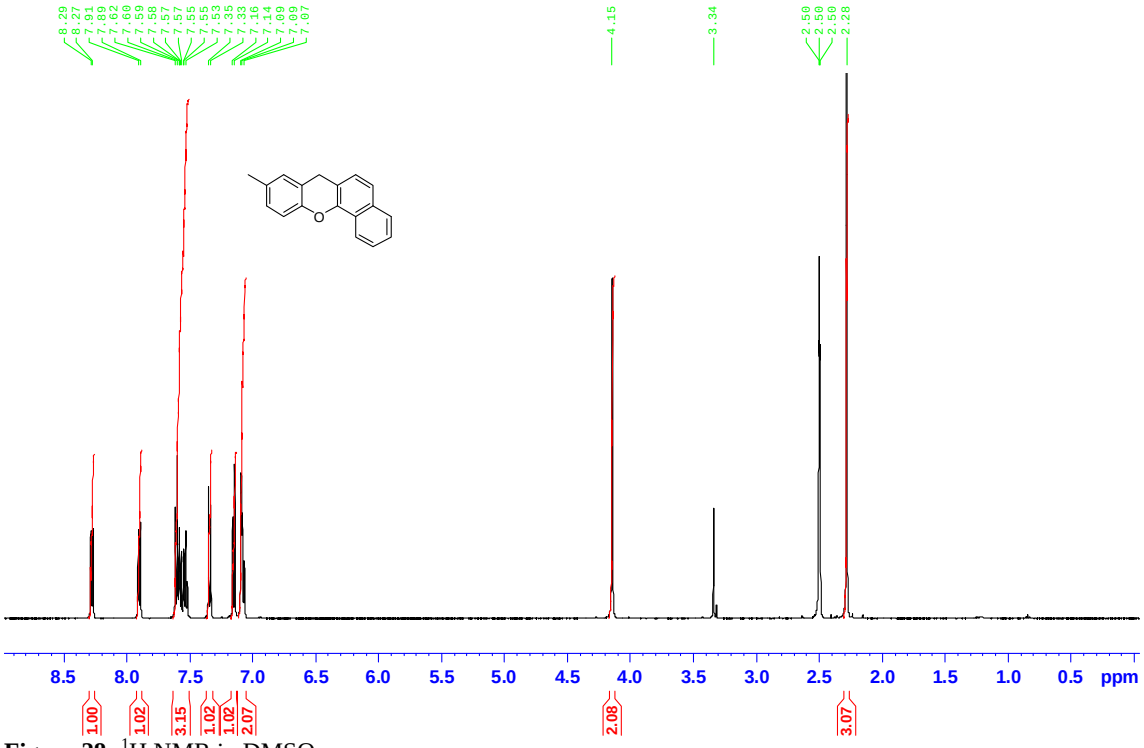


Figure 28: ^{1}H NMR in DMSO

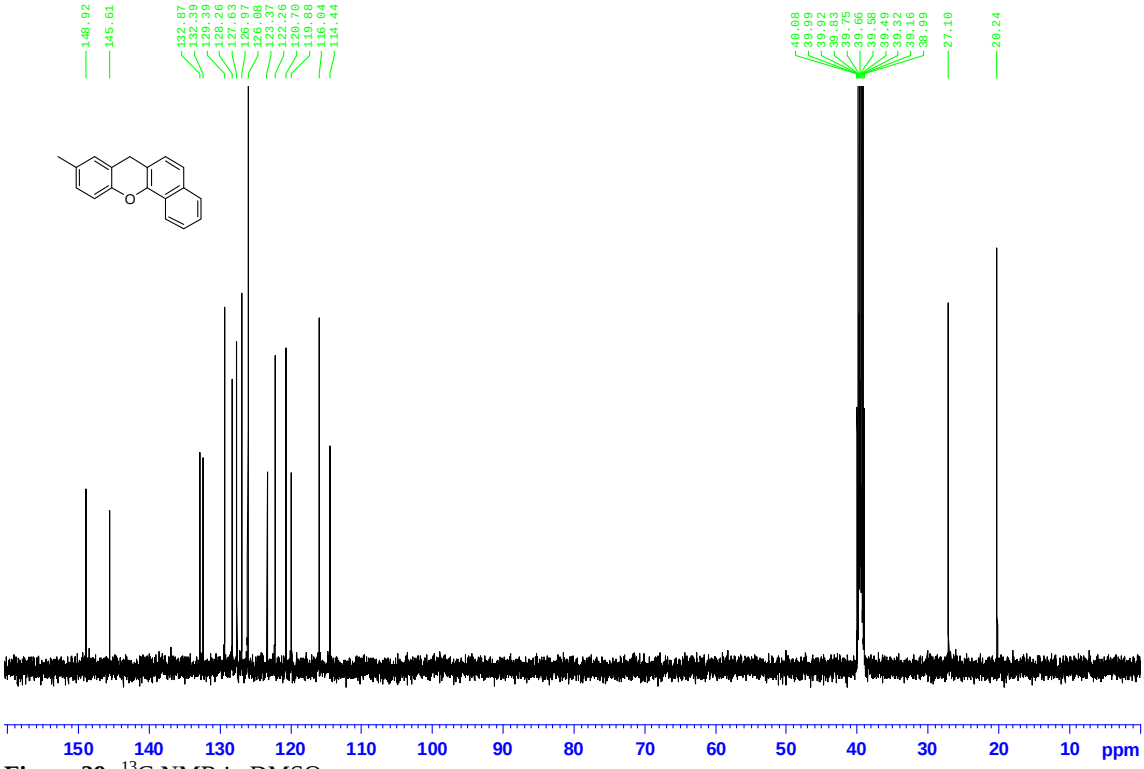


Figure 29: ^{13}C NMR in DMSO

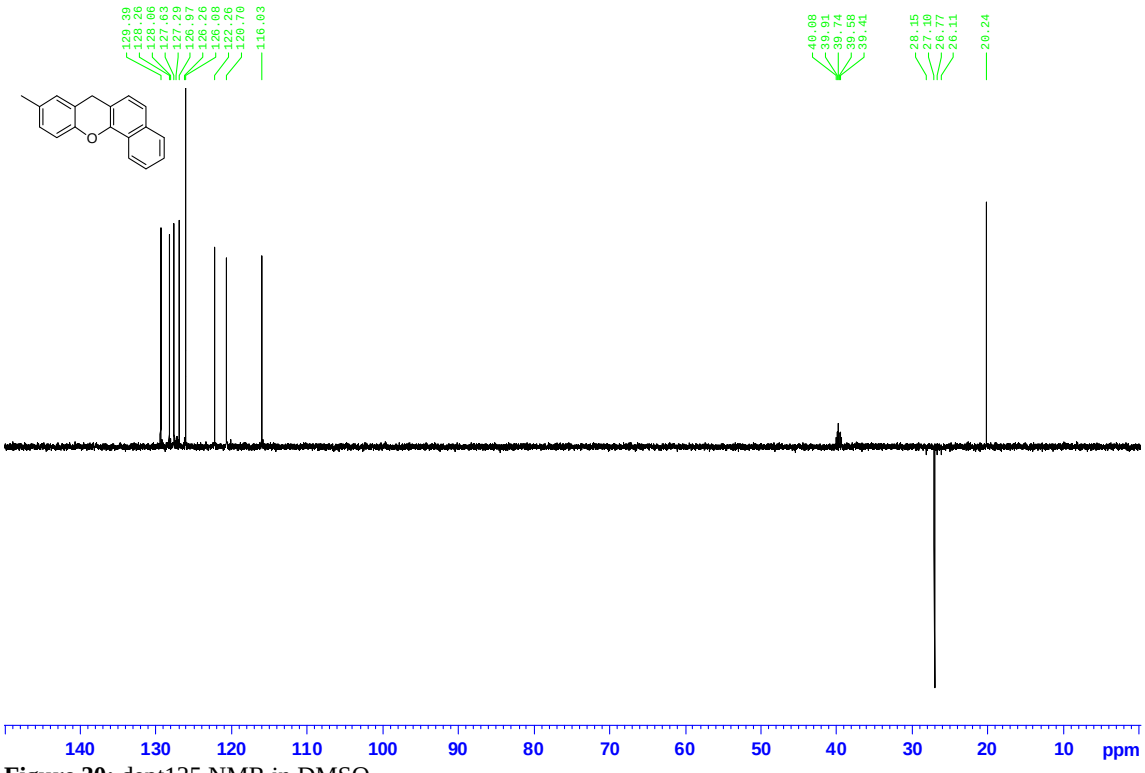


Figure 30: dept135 NMR in DMSO

14*H*-dibenzo[*a*,*h*]xanthene **3k**

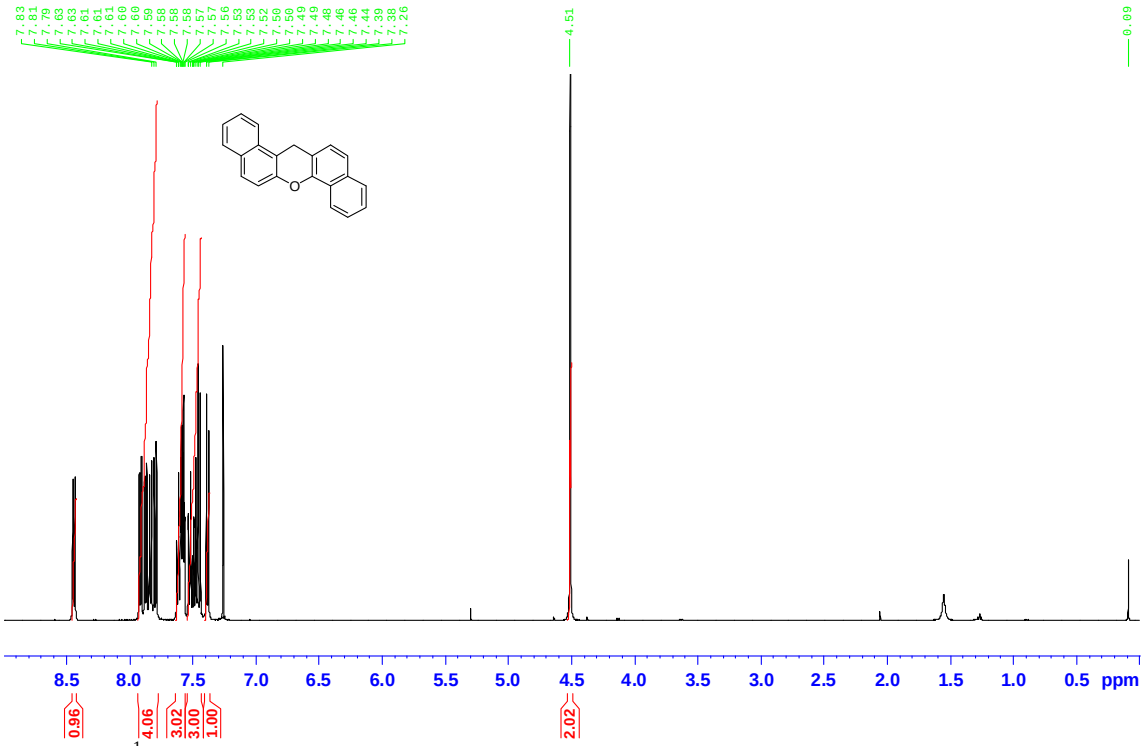


Figure 31: ^{1}H NMR in $CDCl_3$

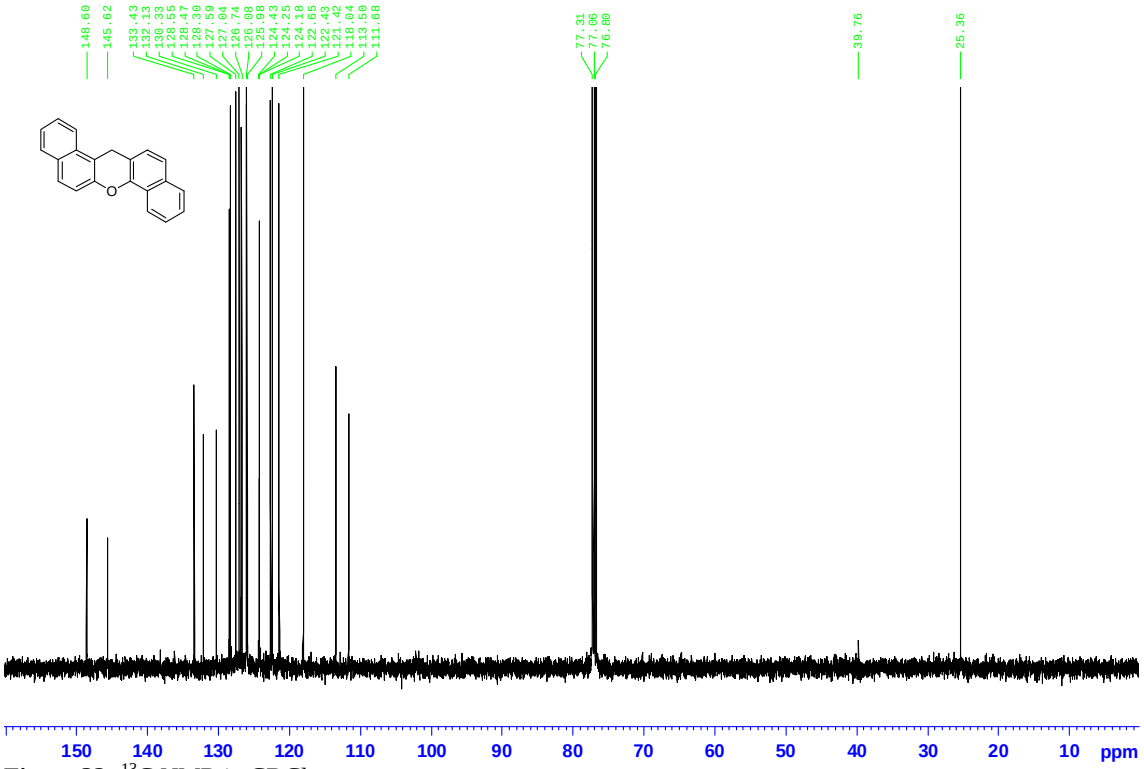


Figure 32: ^{13}C NMR in $CDCl_3$

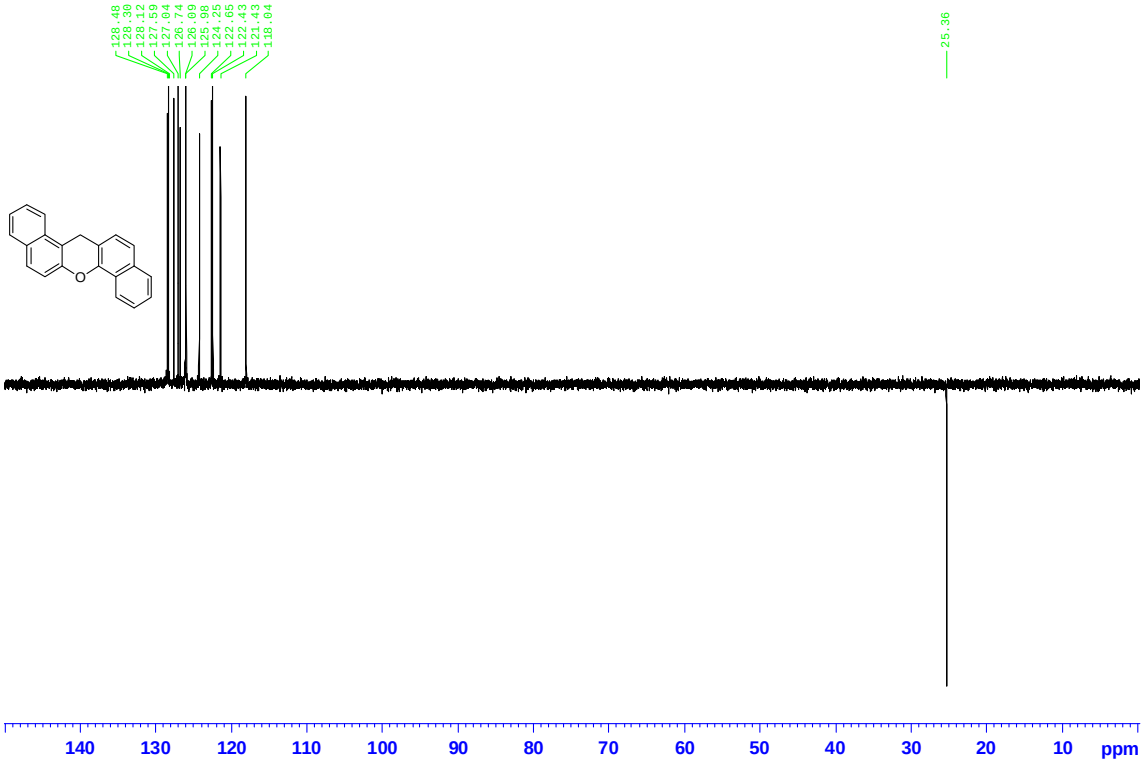


Figure 33: dept135 NMR in $CDCl_3$

2-methoxy-7*H*-benzo[*c*]xanthene **3l**

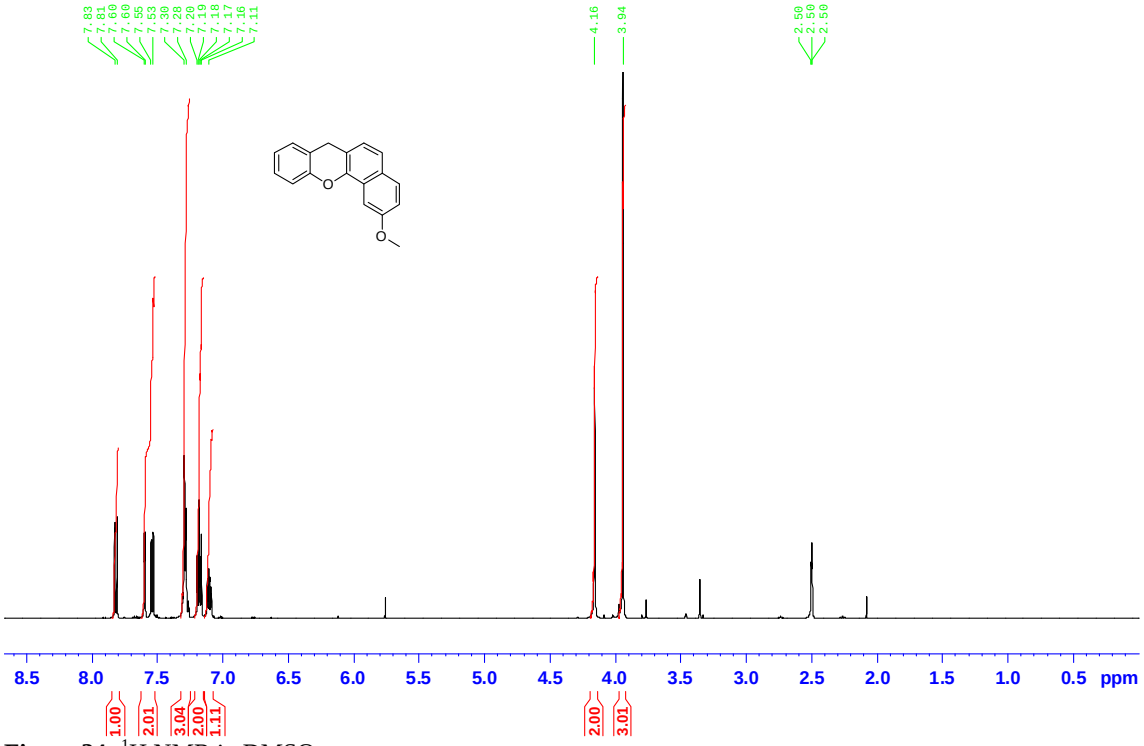


Figure 34: ^{1}H NMR in DMSO

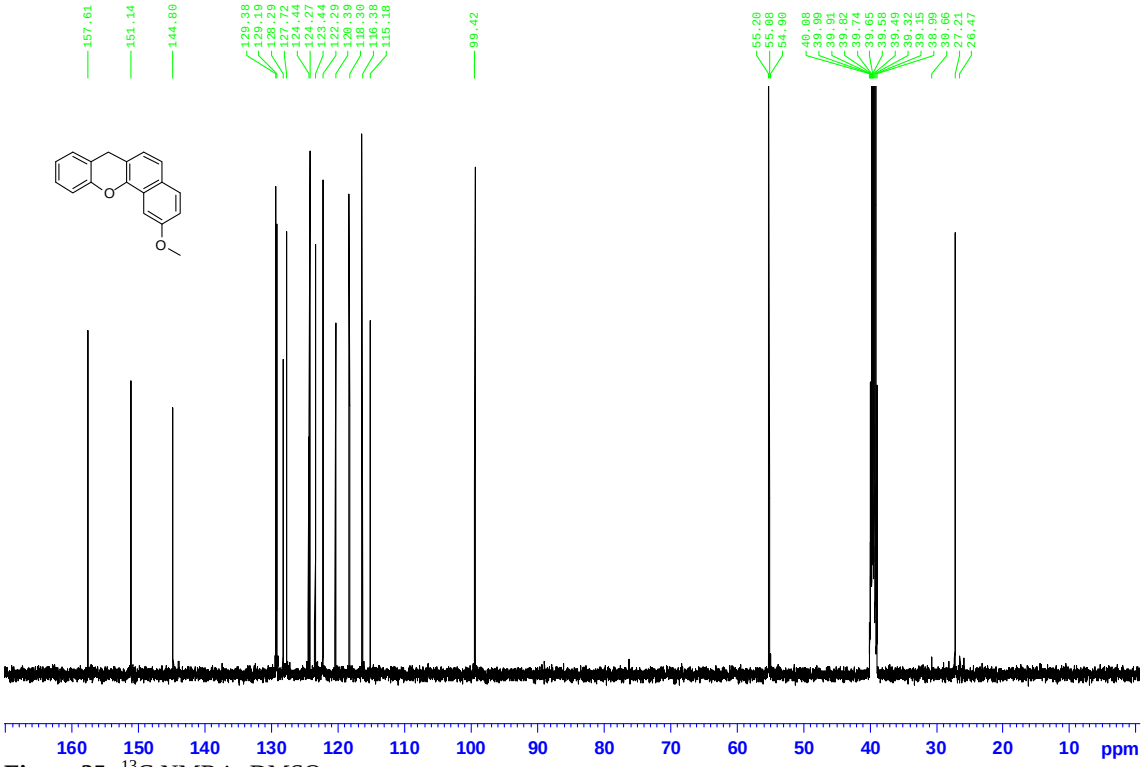


Figure 35: ^{13}C NMR in DMSO

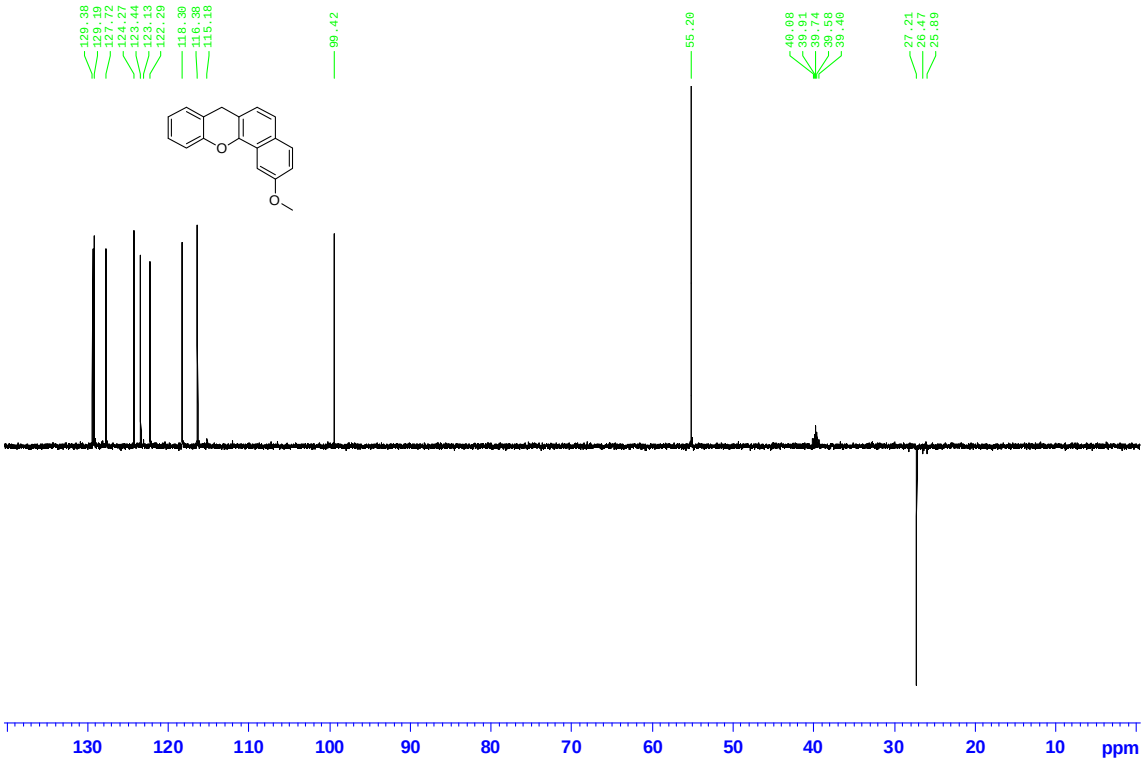


Figure 36: dept135 NMR in DMSO

13,14-dihydrochromeno[*3,2a*]xanthene **5**

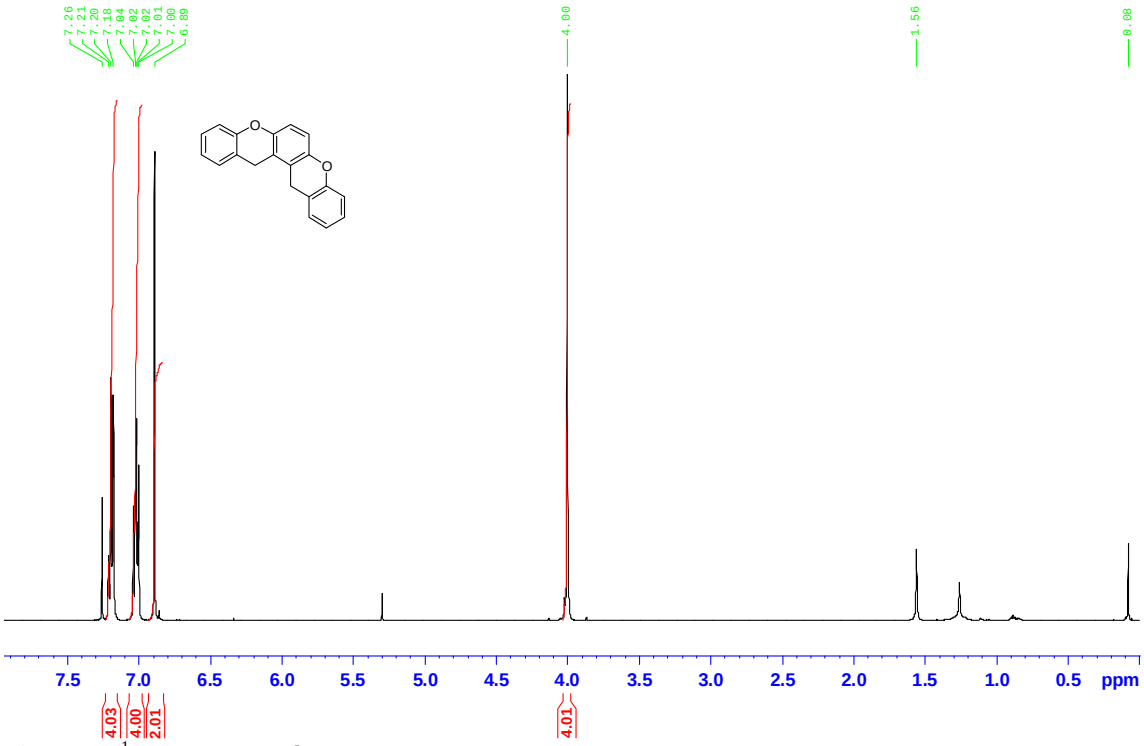


Figure 37: ^{1}H NMR in $CDCl_3$

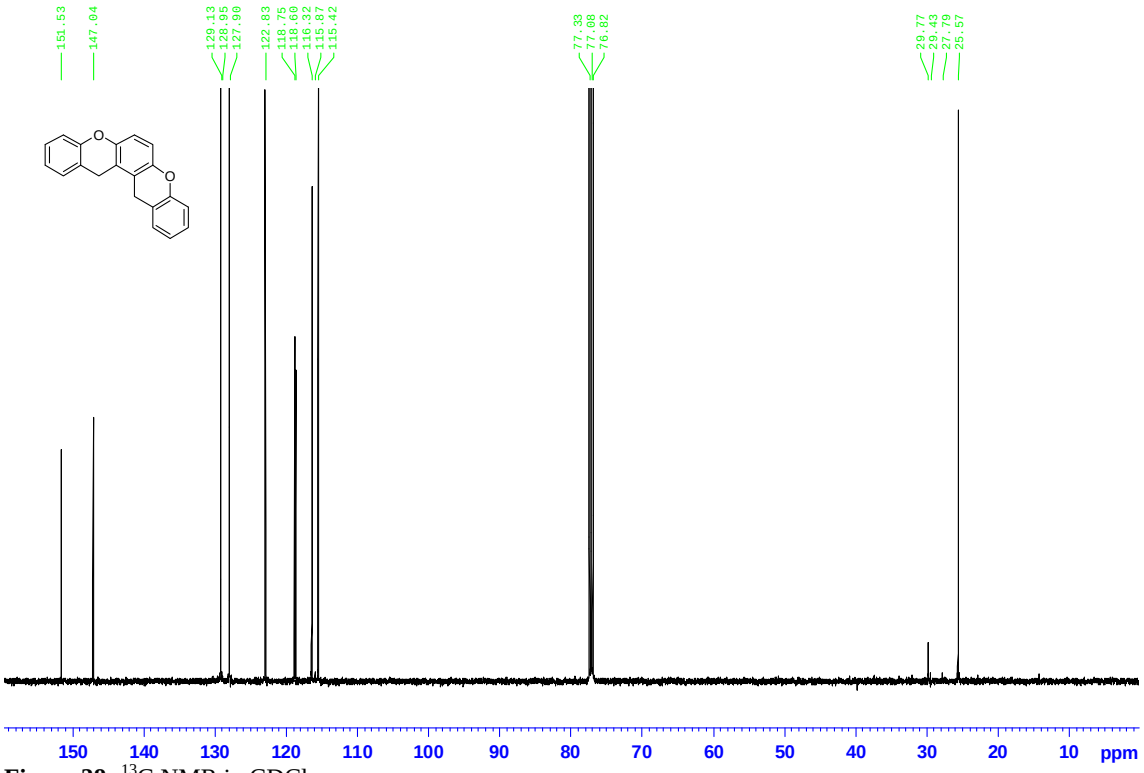


Figure 38: ^{13}C NMR in $CDCl_3$

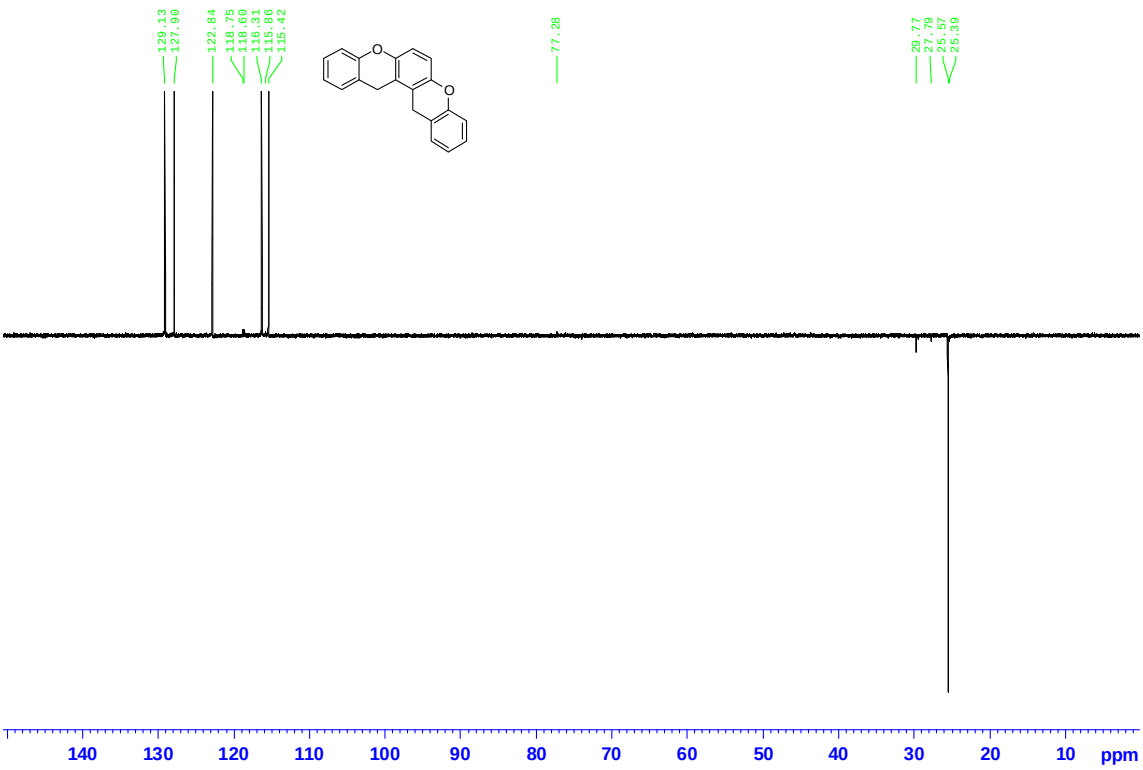
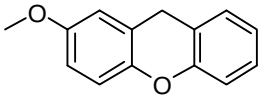
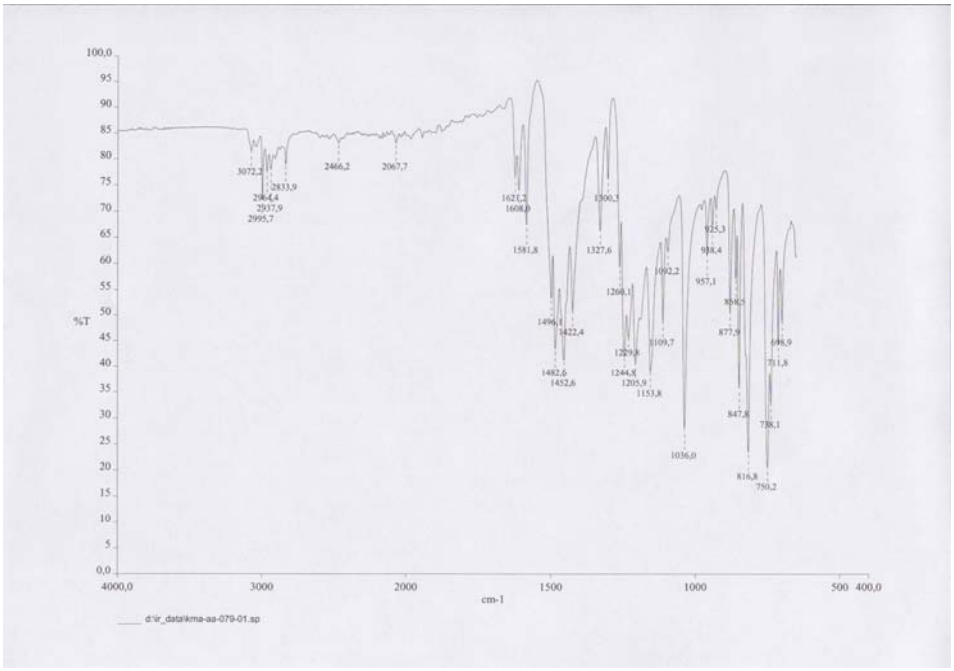
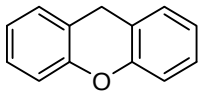


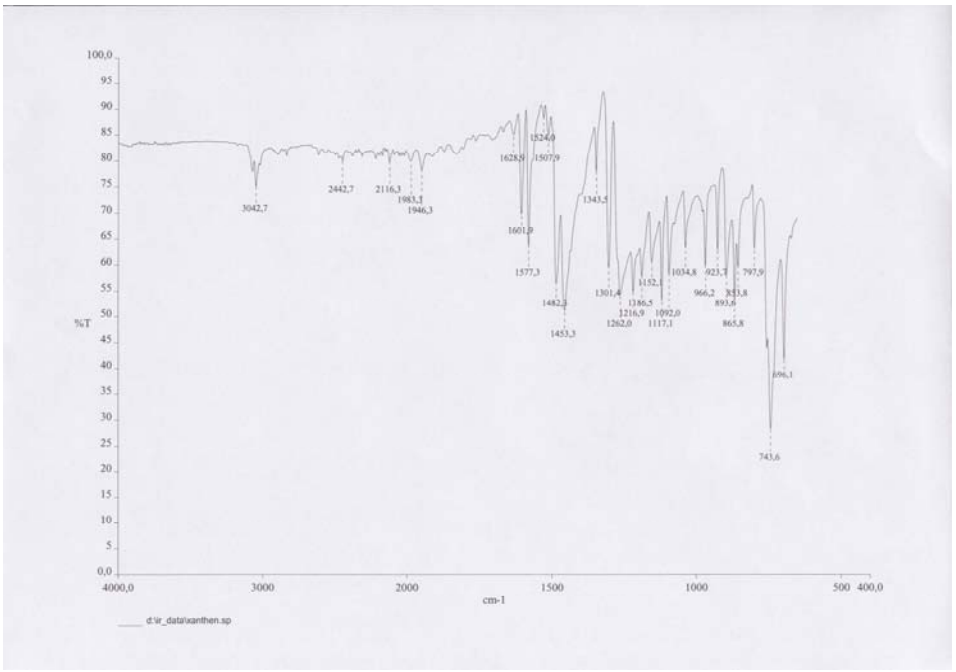
Figure 39: dept135 NMR in $CDCl_3$

IR spectra of products





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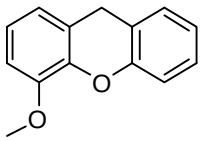

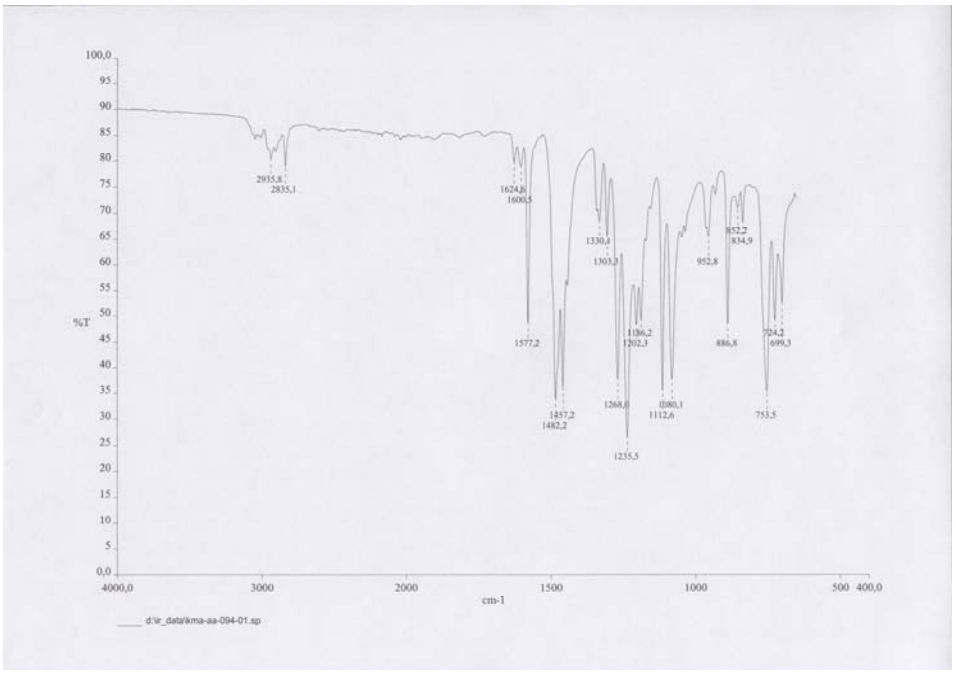
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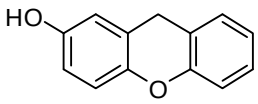
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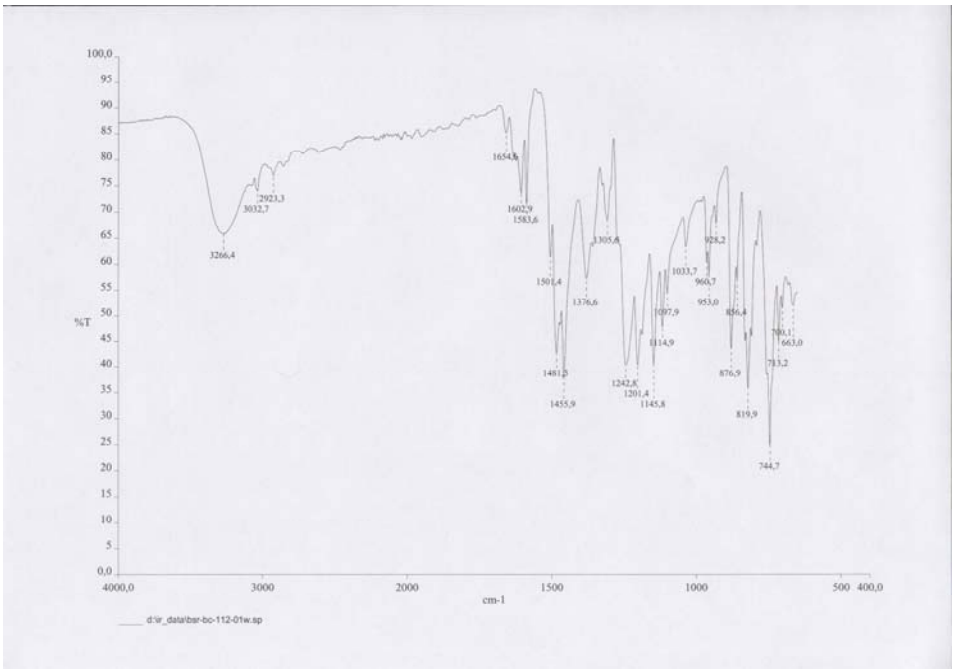
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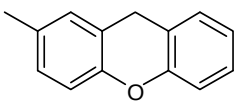
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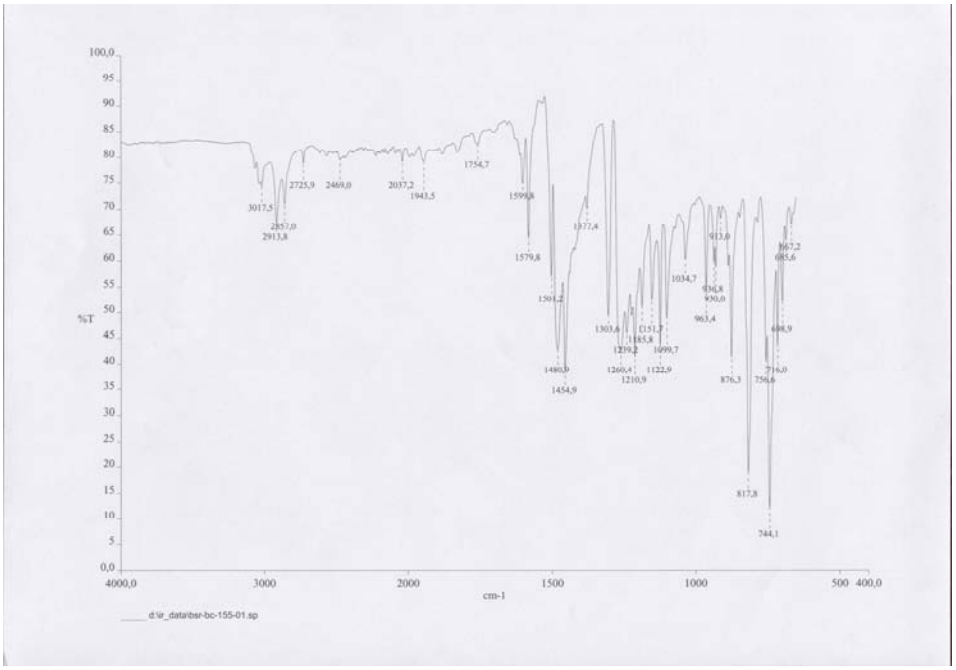
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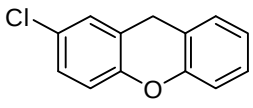
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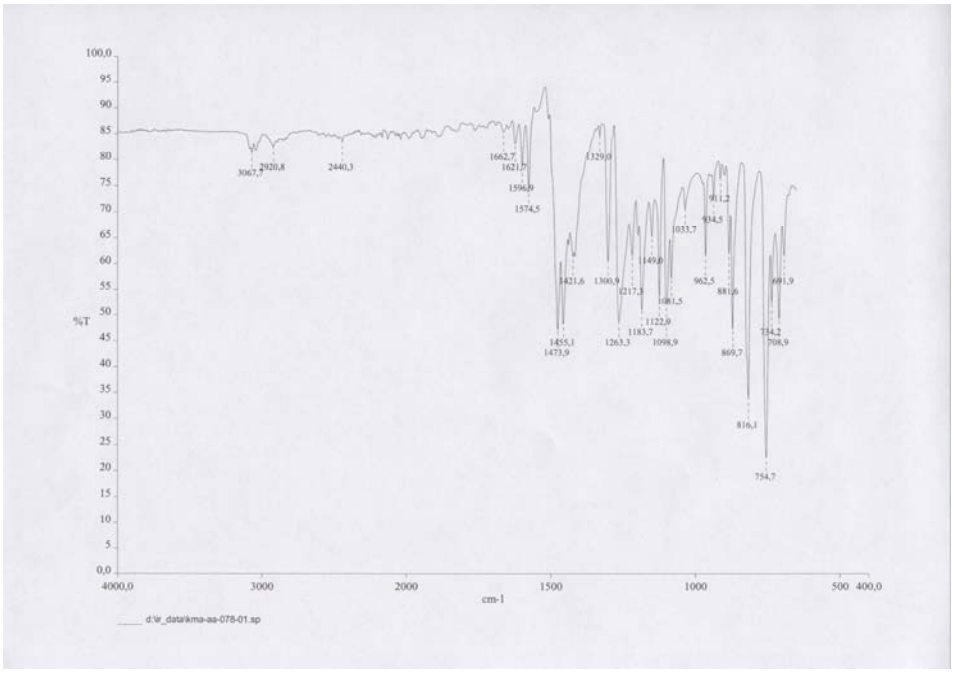
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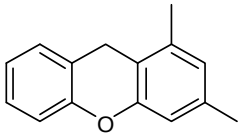
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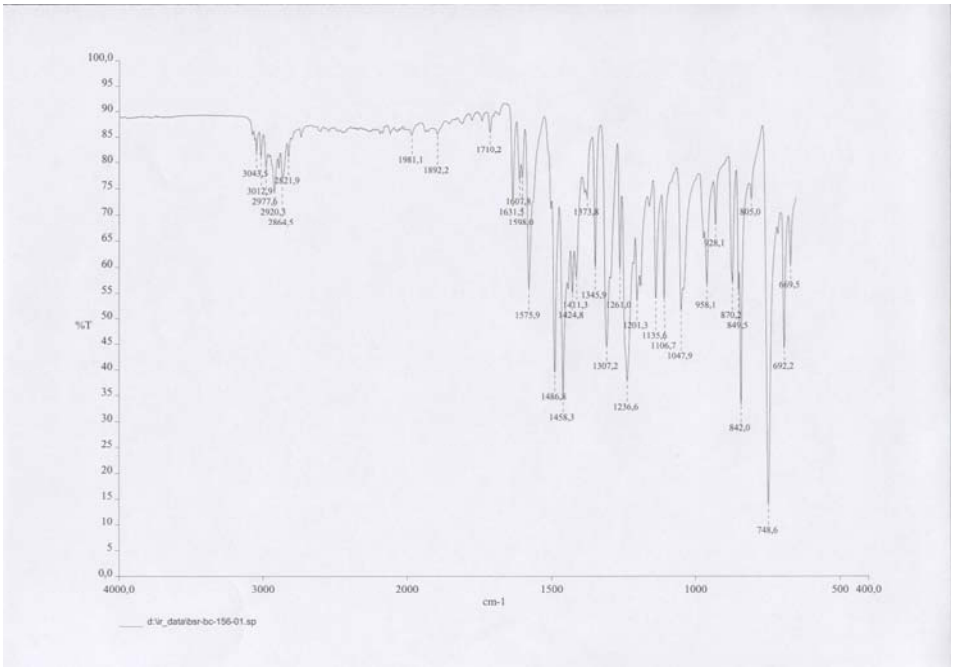
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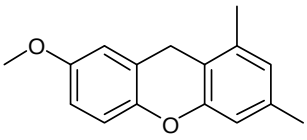

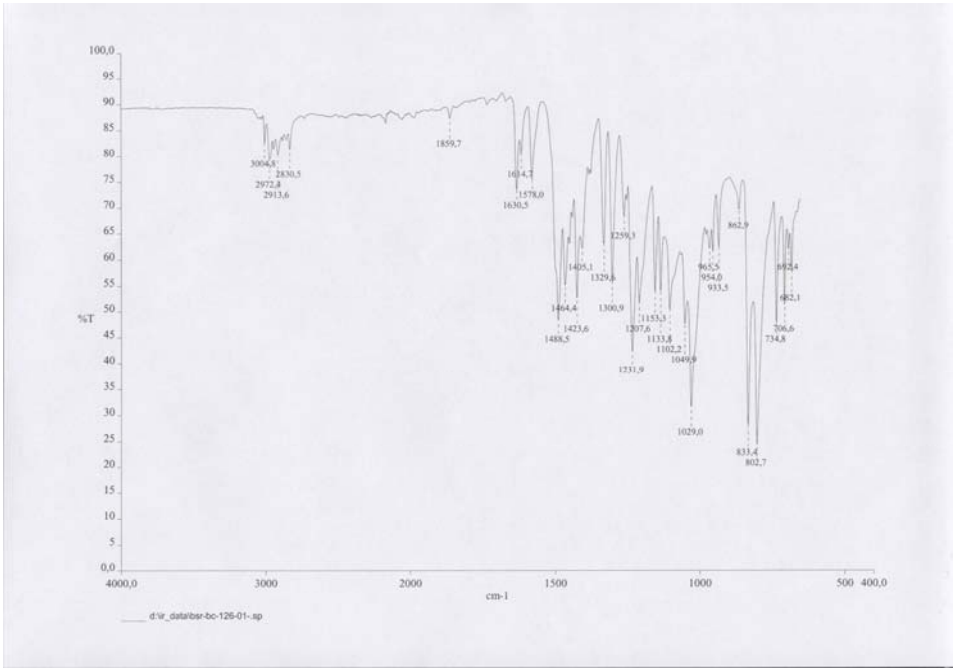
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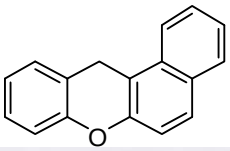

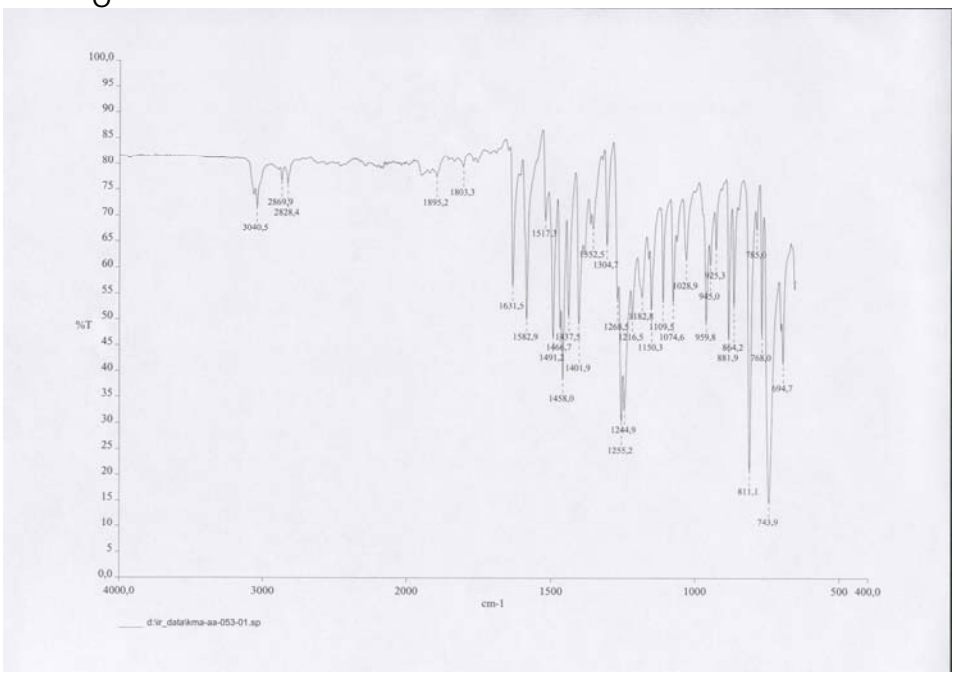
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1109,5
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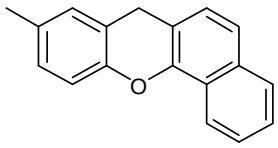

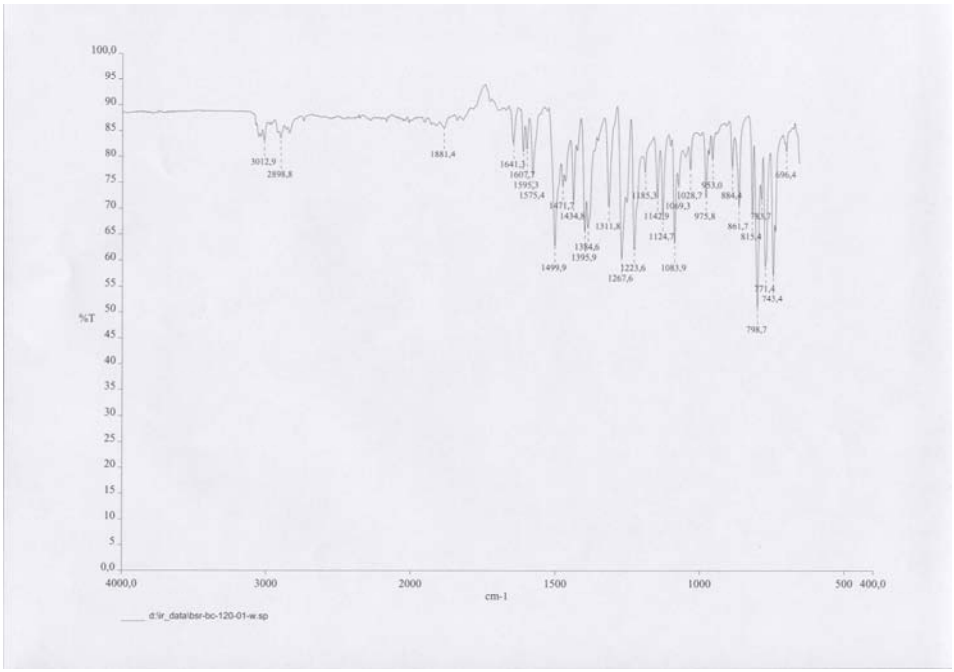
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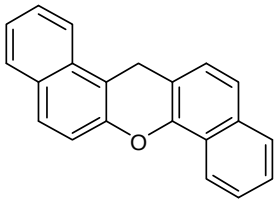

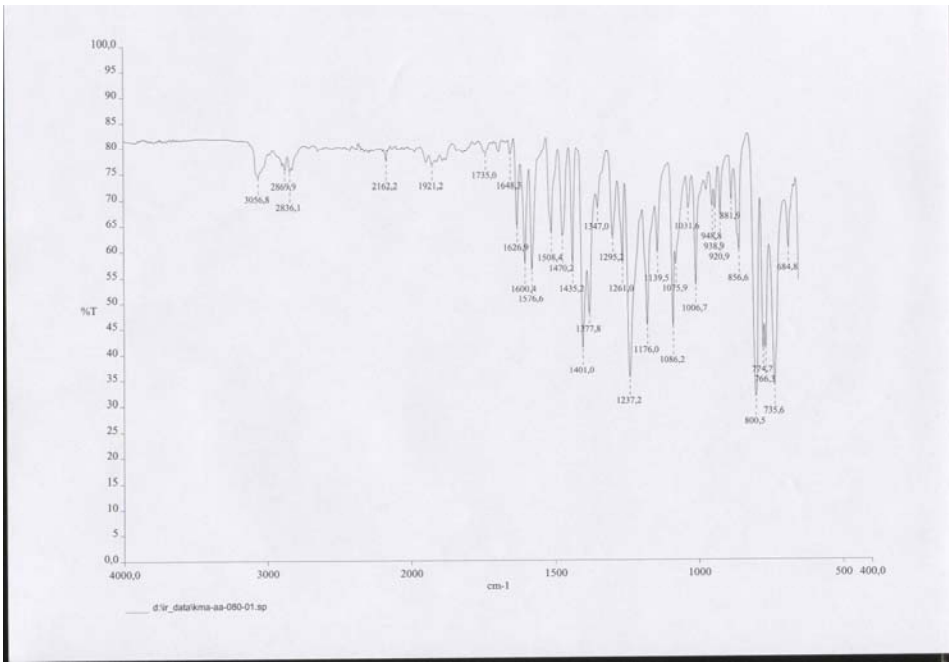
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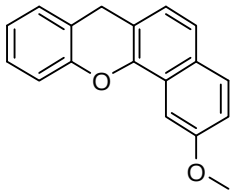

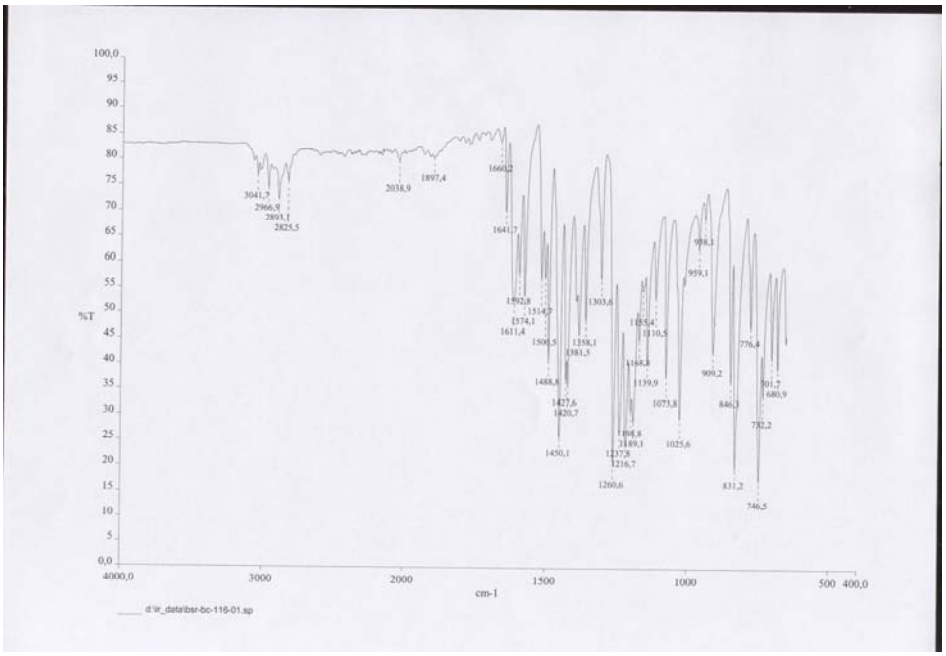
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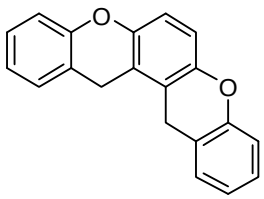

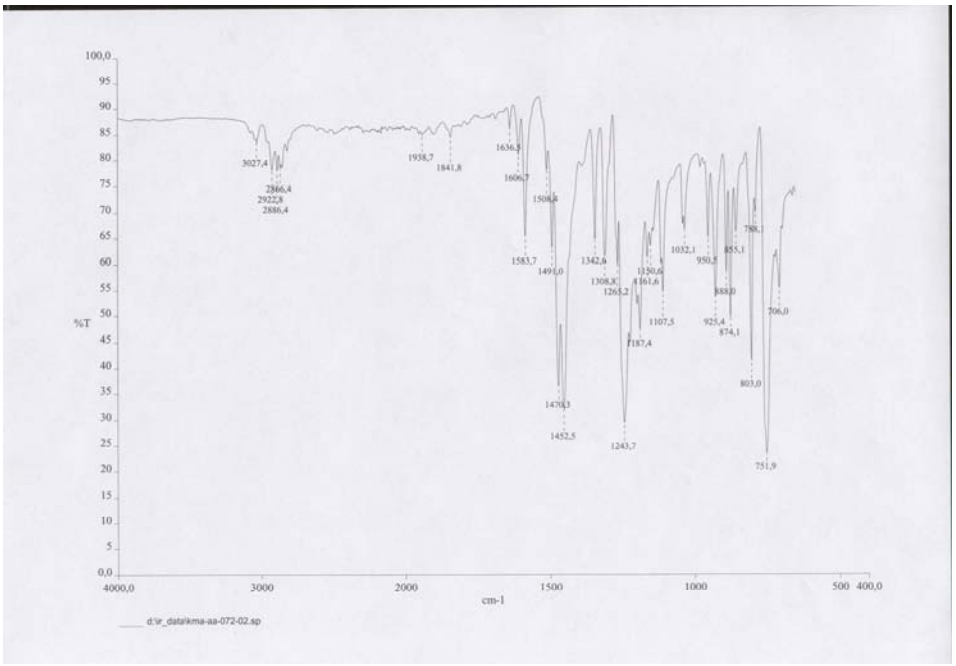
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751,9
706,0
d:\ir_data\kma-aa-072-02.sp

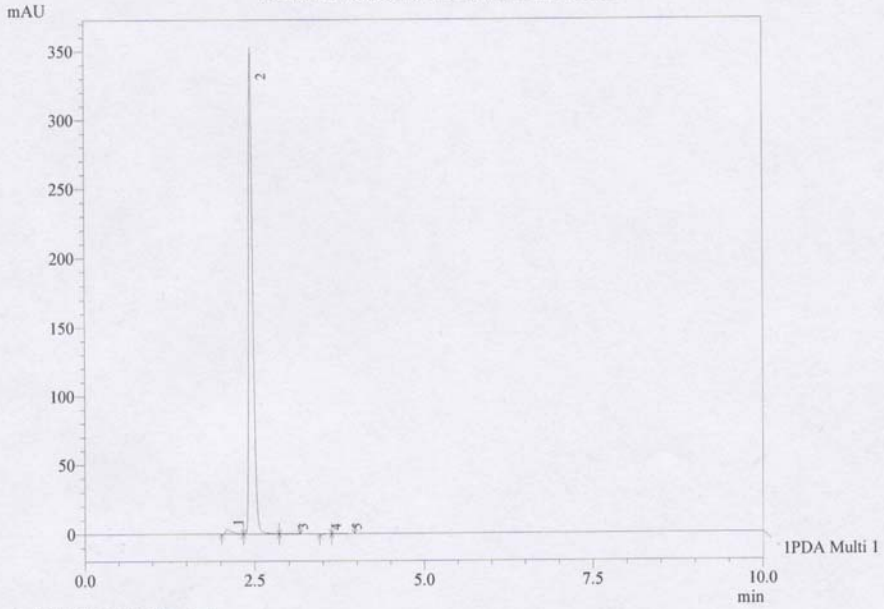
HPLC analysis

150 mm Chiralpak IC-3 4.6 mm i. D.
n-Heptan/2-Propanol 95:5, 1.0mL/min, 4.9 MPa, 305K

Sample Information

Acquired by	: Admin
Sample Name	: xanthen
Sample ID	:
Tray#	: 1
Vail#	: 11
Injection Volume	: 1 uL
Data Filename	: xanthen01.lcd
Method Filename	: xanthen.lcm
Batch Filename	:
Report Filename	: Default.lcr
Date Acquired	: 26.11.2010 09:14:08
Data Processed	: 26.11.2010 09:24:11

Chromatogram
xanthen C:\LabSolutions\Data\Esther\xanthen01.lcd

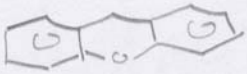


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area %	Theoretical Plate#
1	2.094	20921	1.376	2127.056
2	2.448	1489905	98.024	6090.633
3	3.041	4808	0.316	1813.501
4	3.531	1260	0.083	3400.517
5	3.837	3040	0.200	51.392
Total		1519933	100.000	

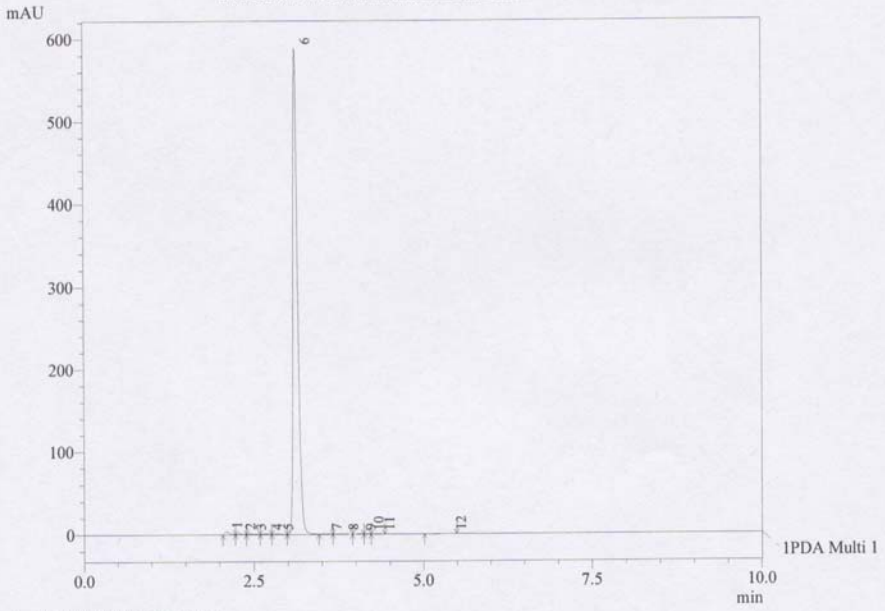


Sample Information

Acquired by	: Admin
Sample Name	: kma-aa-079-01
Sample ID	:
Tray#	: 1
Vail#	: 9
Injection Volume	: 1 uL
Data Filename	: kma-aa-079-02.lcd
Method Filename	: xanthen.lcm
Batch Filename	:
Report Filename	: Default.lcr
Date Acquired	: 26.11.2010 08:39:28
Data Processed	: 26.11.2010 08:49:31

Chromatogram

kma-aa-079-01 C:\LabSolutions\Data\Esther\kma-aa-079-02.lcd

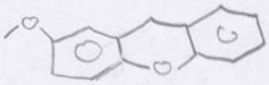


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area %	Theoretical Plate#
1	2.089	18438	0.630	3262.376
2	2.283	9400	0.321	3044.159
3	2.439	9375	0.320	2469.871
4	2.678	8843	0.302	2006.206
5	2.840	8799	0.301	1973.620
6	3.114	2861127	97.746	7350.210
7	3.548	2333	0.080	3723.186
8	3.797	2550	0.087	1355.906
9	4.051	1998	0.068	5541.350
10	4.171	1050	0.036	980.766
11	4.328	1176	0.040	3671.823
12	5.394	2003	0.068	2977.878
Total		2927091	100.000	

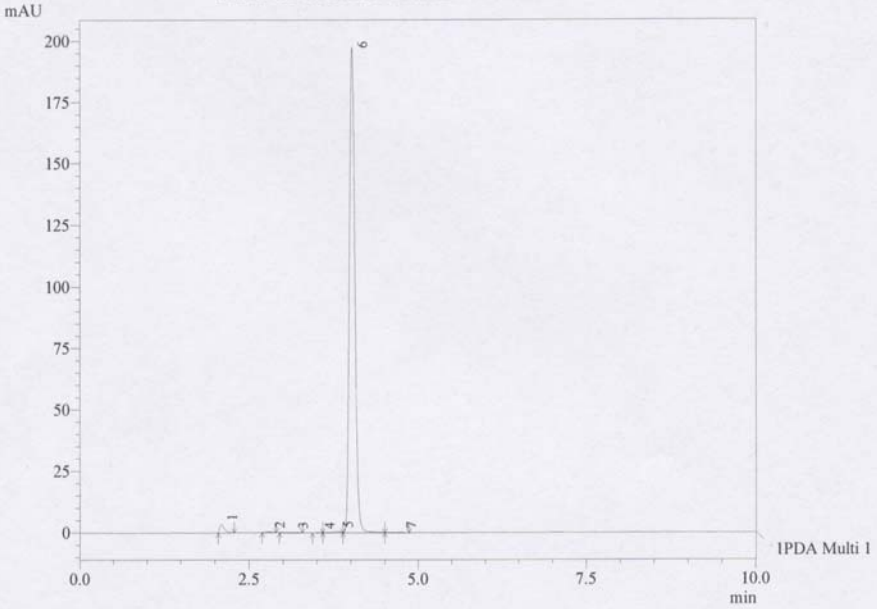


Sample Information

Acquired by	: Admin
Sample Name	: kma-aa-100-01
Sample ID	:
Tray#	: 1
Vail#	: 10
Injection Volume	: 1 uL
Data Filename	: kma-aa-100-02.lcd
Method Filename	: xanthen.lcm
Batch Filename	:
Report Filename	: Default.lcr
Date Acquired	: 26.11.2010 09:02:35
Data Processed	: 26.11.2010 09:12:37

Chromatogram

kma-aa-100-01 C:\LabSolutions\Data\Esther\kma-aa-100-02.lcd

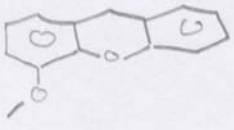


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area %	Theoretical Plate#
1	2.087	16961	1.467	3640.697
2	2.786	3478	0.301	1966.750
3	3.129	3423	0.296	1037.539
4	3.520	1171	0.101	1587.348
5	3.794	6075	0.525	3814.866
6	4.012	1121559	97.013	9534.361
7	4.731	3422	0.296	1483.458
Total		1156089	100.000	

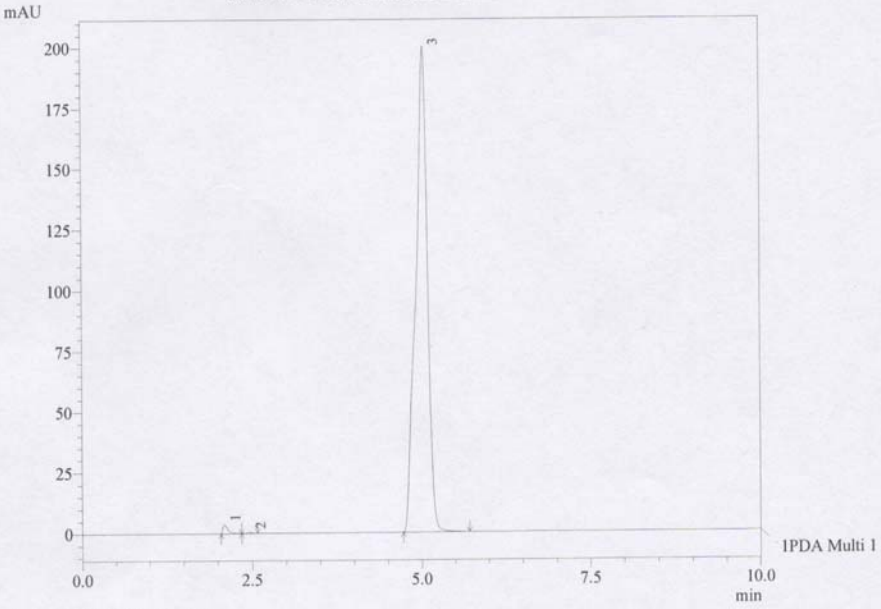


Sample Information

Acquired by	: Admin
Sample Name	: bsr-bc-112-01
Sample ID	:
Tray#	: 1
Vail#	: 2
Injection Volume	: 1 uL
Data Filename	: bsr-bc-112-01.lcd
Method Filename	: xanthen.lcm
Batch Filename	:
Report Filename	: Default.lcr
Date Acquired	: 23.11.2010 10:10:47
Data Processed	: 23.11.2010 10:20:50

Chromatogram

bsr-bc-112-01 C:\LabSolutions\Data\Esther\bsr-bc-112-01.lcd

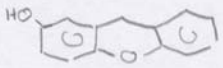


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area %	Theoretical Plate#
1	2.088	19288	0.796	3526.559
2	2.457	2443	0.101	4385.284
3	5.037	2402160	99.103	4145.897
Total		2423891	100.000	

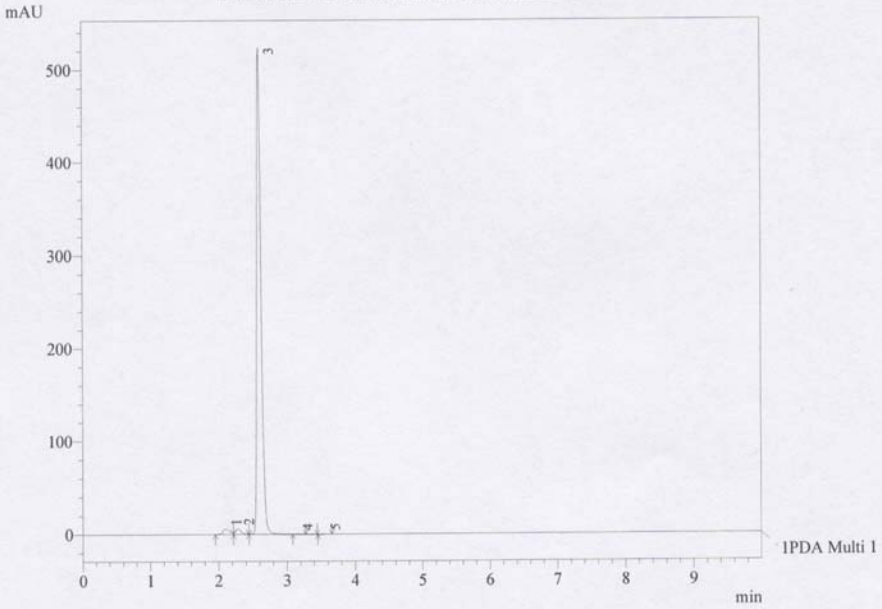


Sample Information

Acquired by	: Admin
Sample Name	: kma-aa-101-01
Sample ID	:
Tray#	: 1
Vail#	: 12
Injection Volume	: 1 uL
Data Filename	: kma-aa-101-03.lcd
Method Filename	: xanthen.lcm
Batch Filename	:
Report Filename	: Default.lcr
Date Acquired	: 26.11.2010 10:00:29
Data Processed	: 26.11.2010 10:10:31

Chromatogram

kma-aa-101-01 C:\LabSolutions\Data\Esther\kma-aa-101-03.lcd



1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

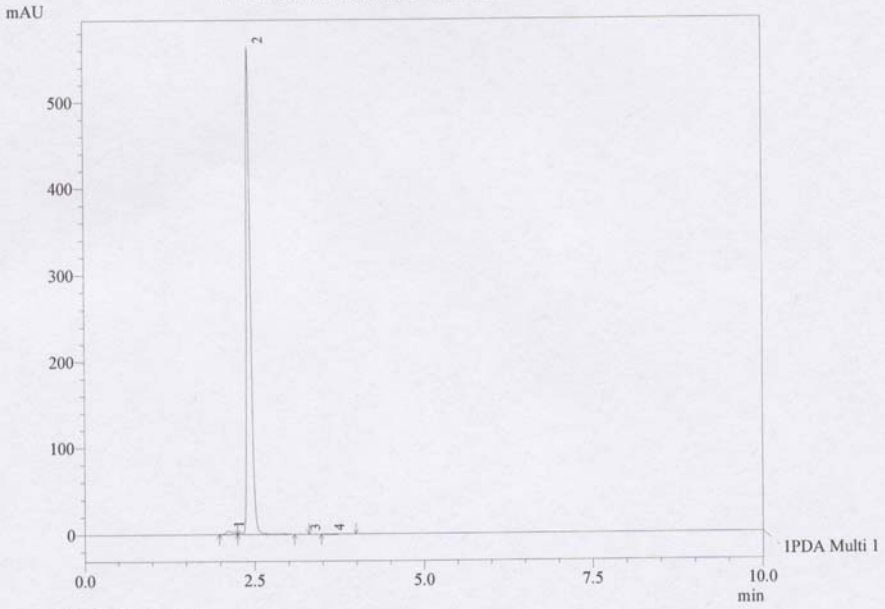
Peak#	Ret. Time	Area	Area %	Theoretical Plate#
1	2.096	41722	1.738	1437.512
2	2.279	33844	1.410	3151.143
3	2.594	2321725	96.742	5922.510
4	3.140	1295	0.054	4498.726
5	3.544	1327	0.055	6017.288
Total		2399913	100.000	

Sample Information

Acquired by	: Admin
Sample Name	: kma-aa-102-01
Sample ID	:
Tray#	: 1
Vail#	: 15
Injection Volume	: 1 uL
Data Filename	: kma-aa-102-01.lcd
Method Filename	: xanthen.lcm
Batch Filename	:
Report Filename	: Default.lcr
Date Acquired	: 27.11.2010 11:09:09
Data Processed	: 27.11.2010 11:19:11

Chromatogram

kma-aa-102-01 C:\LabSolutions\Data\Esther\kma-aa-102-01.lcd

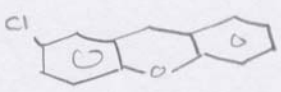


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area %	Theoretical Plate#
1	2.105	27694	1.121	1481.754
2	2.420	2437694	98.668	5524.062
3	3.221	1095	0.044	3138.598
4	3.576	4112	0.166	800.854
Total		2470595	100.000	

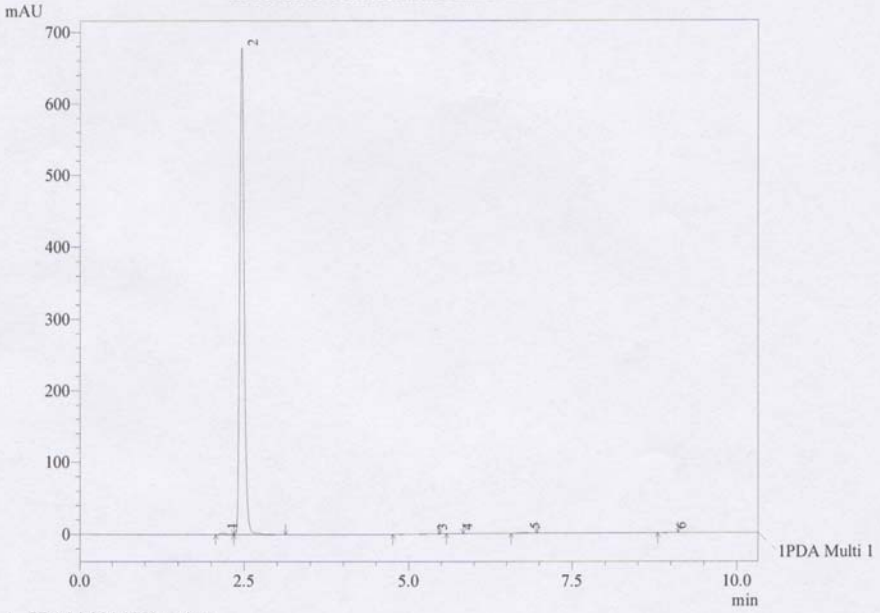


Sample Information

Acquired by	: Admin
Sample Name	: bsr-bc-125-01
Sample ID	:
Tray#	: 1
Vail#	: 1
Injection Volume	: 1 uL
Data Filename	: bsr-bc-125-09.lcd
Method Filename	: xanthen.lcm
Batch Filename	:
Report Filename	: Default.lcr
Date Acquired	: 23.11.2010 09:48:02
Data Processed	: 23.11.2010 09:58:22

Chromatogram

bsr-bc-125-01 C:\LabSolutions\Data\Esther\bsr-bc-125-09.lcd

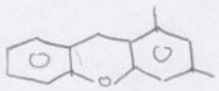


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area %	Theoretical Plate#
1	2.153	12876	0.403	3016.295
2	2.454	3169188	99.171	4923.919
3	5.344	4944	0.155	1777.846
4	5.728	1068	0.033	549.442
5	6.764	5693	0.178	12404.289
6	8.985	1909	0.060	16183.923
Total		3195679	100.000	

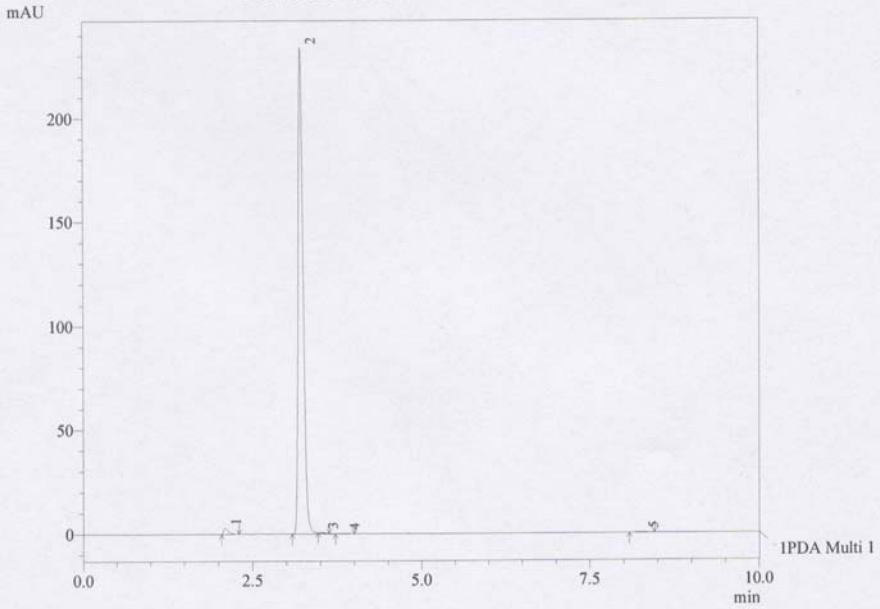


Sample Information

Acquired by	: Admin
Sample Name	: bsr-bc-126-01
Sample ID	:
Tray#	: 1
Vail#	: 3
Injection Volume	: 1 uL
Data Filename	: bsr-bc-126-03.lcd
Method Filename	: xanthen.lcm
Batch Filename	:
Report Filename	: Default.lcr
Date Acquired	: 26.11.2010 04:06:06
Data Processed	: 26.11.2010 04:16:08

Chromatogram

bsr-bc-126-01 C:\LabSolutions\Data\Esther\bsr-bc-126-03.lcd

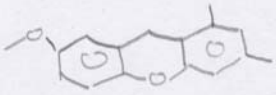


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area %	Theoretical Plate#
1	2.095	14330	1.184	3565.707
2	3.210	1192019	98.474	7372.247
3	3.522	1328	0.110	9252.920
4	3.838	1164	0.096	4844.160
5	8.273	1653	0.137	12704.892
Total		1210493	100.000	

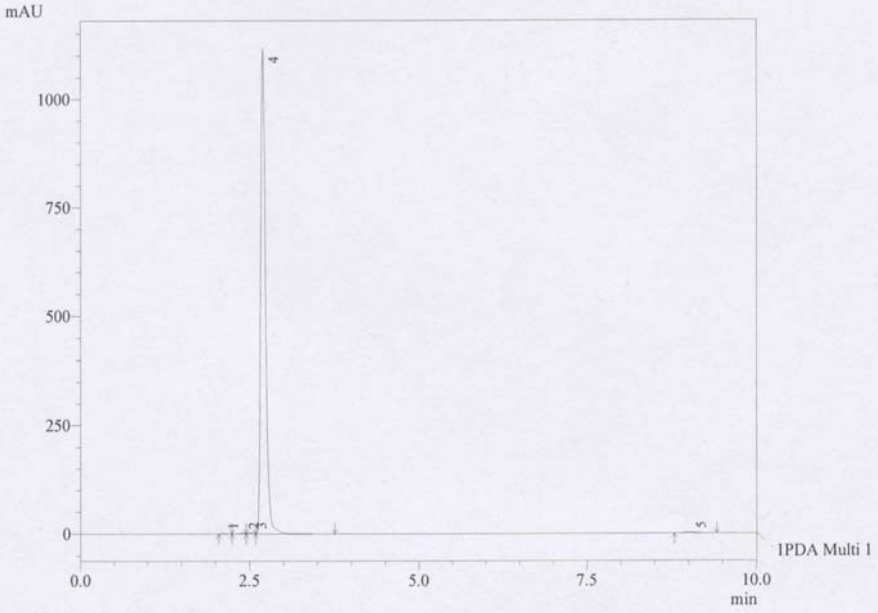


Sample Information

Acquired by	: Admin
Sample Name	: kma-aa-045-01
Sample ID	:
Tray#	: 1
Vail#	: 5
Injection Volume	: 1 uL
Data Filename	: kma-aa-045-02.lcd
Method Filename	: xanthen.lcm
Batch Filename	:
Report Filename	: Default.lcr
Date Acquired	: 26.11.2010 05:06:07
Data Processed	: 26.11.2010 05:16:09

Chromatogram

kma-aa-045-01 C:\LabSolutions\Data\Esther\kma-aa-045-02.lcd

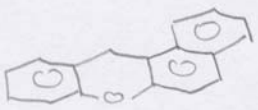


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area %	Theoretical Plate#
1	2.095	13184	0.230	3123.960
2	2.397	15537	0.271	3235.936
3	2.510	20534	0.358	2940.275
4	2.692	5651135	98.619	5450.934
5	9.019	29901	0.522	11836.294
Total		5730291	100.000	

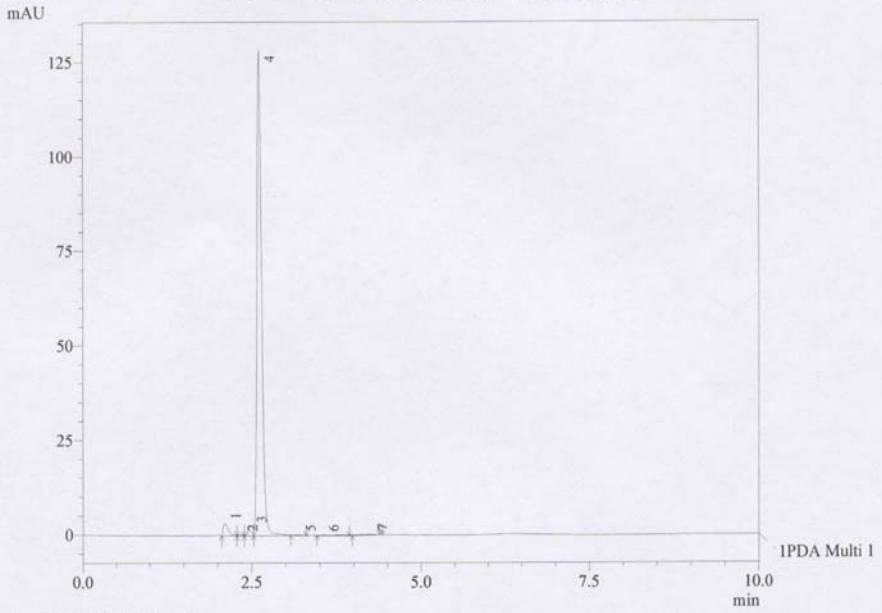


Sample Information

Acquired by	: Admin
Sample Name	: bsr-bc-120-01
Sample ID	:
Tray#	: 1
Vail#	: 1
Injection Volume	: 1 uL
Data Filename	: bsr-bc-120-04.lcd
Method Filename	: xanthen.lcm
Batch Filename	:
Report Filename	: Default.lcr
Date Acquired	: 28.11.2010 09:26:24
Data Processed	: 28.11.2010 09:36:28

Chromatogram

bsr-bc-120-01 C:\LabSolutions\Data\Esther\bsr-bc-120-04.lcd

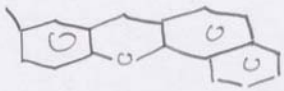


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area %	Theoretical Plate#
1	2.098	17164	2.725	3559.678
2	2.347	1289	0.205	14.364
3	2.480	11539	1.832	4613.327
4	2.606	592441	94.043	5687.182
5	3.200	1009	0.160	3648.293
6	3.540	3759	0.597	53.051
7	4.260	2766	0.439	14.774
Total		629968	100.000	

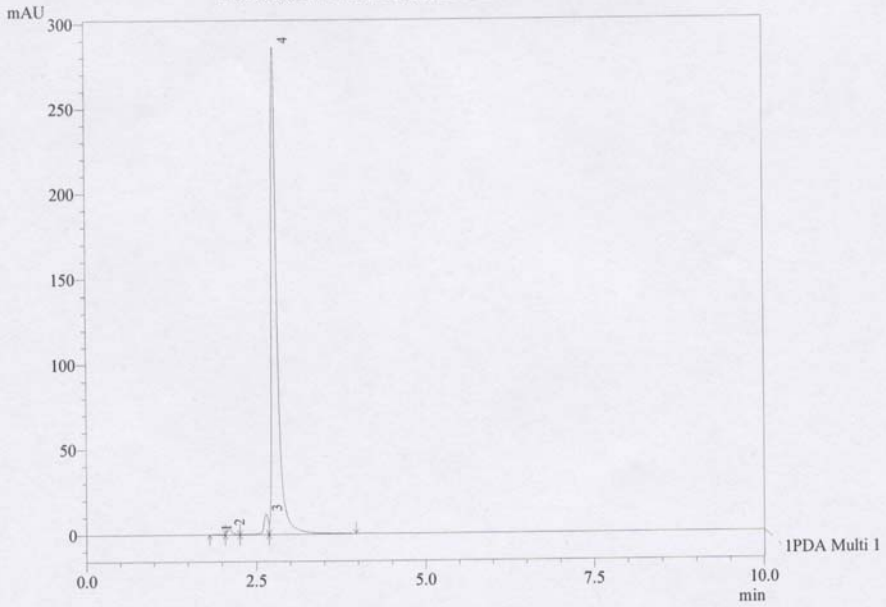


Sample Information

Acquired by	: Admin
Sample Name	: kma-aa-082-01
Sample ID	:
Tray#	: 1
Vail#	: 14
Injection Volume	: 1 uL
Data Filename	: kma-aa-082-02.lcd
Method Filename	: xanthen.lcm
Batch Filename	:
Report Filename	: Default.lcr
Date Acquired	: 27.11.2010 08:50:49
Data Processed	: 27.11.2010 09:00:51

Chromatogram

kma-aa-082-01 C:\LabSolutions\Data\Esther\kma-aa-082-02.lcd

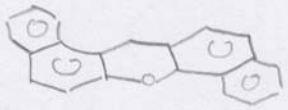


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area %	Theoretical Plate#
1	1.899	1878	0.109	1065.489
2	2.090	17416	1.011	3438.231
3	2.640	59358	3.444	5204.090
4	2.773	1644690	95.436	5136.476
Total		1723342	100.000	

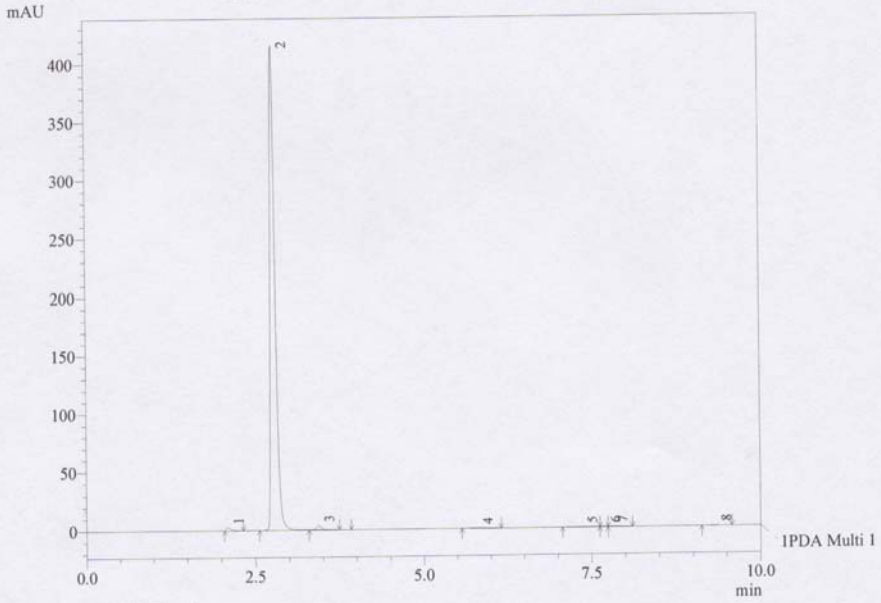


Sample Information

Acquired by	: Admin
Sample Name	: bsr-bc-116-01
Sample ID	:
Tray#	: 1
Vail#	: 4
Injection Volume	: 1 uL
Data Filename	: bsr-bc-116-01.lcd
Method Filename	: xanthen.lcm
Batch Filename	:
Report Filename	: Default.lcr
Date Acquired	: 26.11.2010 04:29:03
Data Processed	: 26.11.2010 04:39:05

Chromatogram

bsr-bc-116-01 C:\LabSolutions\Data\Esther\bsr-bc-116-01.lcd

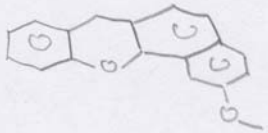


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area %	Theoretical Plate#
1	2.088	14047	0.654	3455.316
2	2.775	2093345	97.448	5755.101
3	3.428	19224	0.895	8234.586
4	5.792	6186	0.288	2499.159
5	7.349	5419	0.252	0.289
6	7.691	1799	0.084	338.878
7	7.795	5292	0.246	2412.304
8	9.330	2862	0.133	10422.033
Total		2148175	100.000	

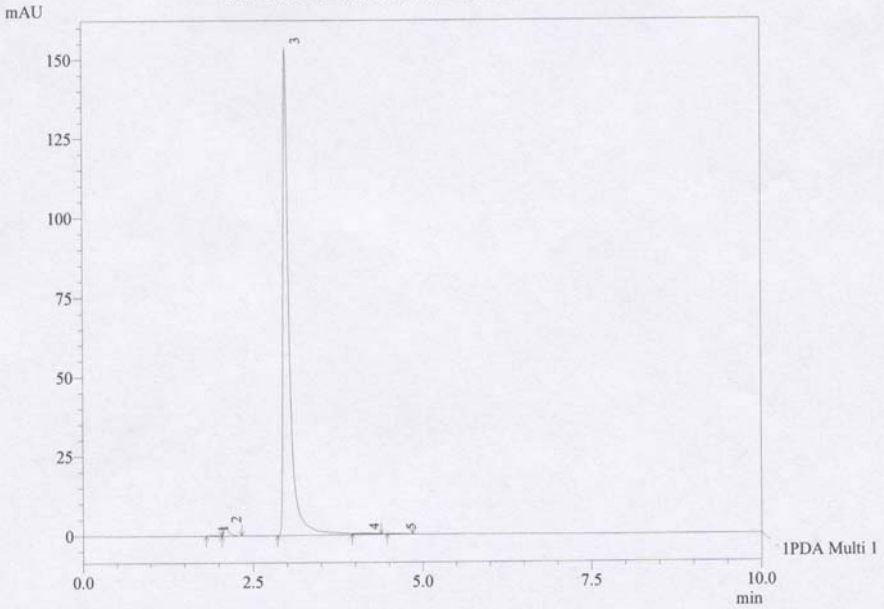


Sample Information

Acquired by	: Admin
Sample Name	: kma-aa-088-01
Sample ID	:
Tray#	: 1
Vail#	: 16
Injection Volume	: 1 uL
Data Filename	: kma-aa-088-01.lcd
Method Filename	: xanthen.lcm
Batch Filename	:
Report Filename	: Default.lcr
Date Acquired	: 28.11.2010 08:42:04
Data Processed	: 28.11.2010 08:52:08

Chromatogram

kma-aa-088-01 C:\LabSolutions\Data\Esther\kma-aa-088-01.lcd

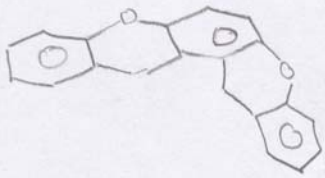


1 PDA Multi 1 / 254nm 4nm

PeakTable

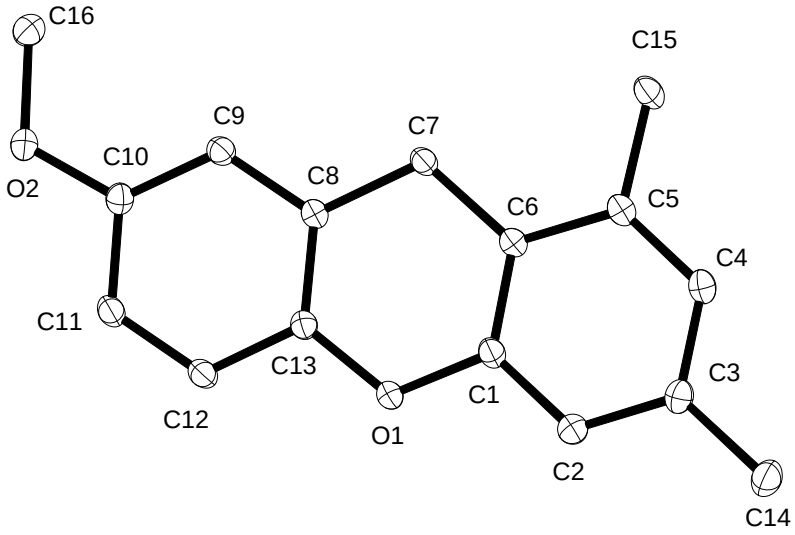
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area %	Theoretical Plate#
1	1.899	1993	0.197	636.979
2	2.089	15666	1.548	3541.543
3	2.983	989004	97.697	5110.708
4	4.112	3782	0.374	907.281
5	4.661	1868	0.185	14.454
Total		1012313	100.000	

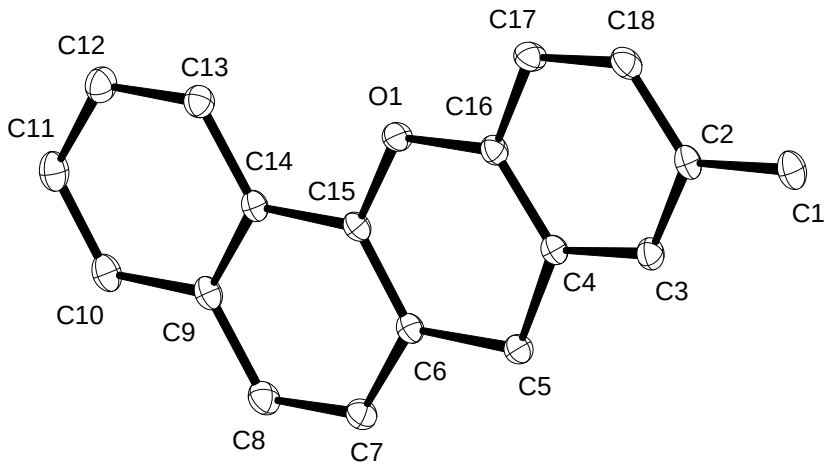


X-ray analysis

Single crystals of **3h** and **3j** were recrystallised from Et_2O / pentane, mounted in inert oil and transferred to the cold gas stream of the diffractometer.



[b] Crystal data for **3h**: $C_{16}H_{16}O_2$, M = 240.29, triclinic, a = 7.3745(19) Å, b = 8.763(3) Å, c = 10.395(2) Å, α = 99.79(2)°, β = 110.27(2)°, γ = 98.47(3)°, V = 605.3(3) Å^3, T = 100 K, space group $P\bar{1}$, Z = 2, μ(MoK$_\alpha$) = 0.086 mm^{-1}, 11977 reflections measured, 4896 independent reflections (R_{int} = 0.0273). The final R_1 values were 0.046 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.134 (all data). The goodness of fit on F^2 was 1.043. CCDC reference number: 797429.

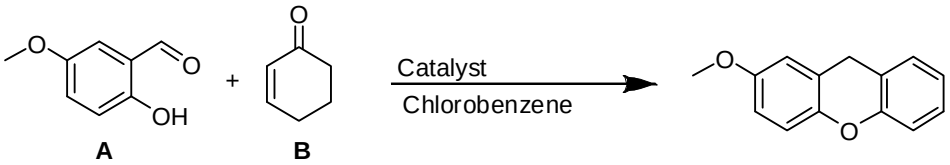


[a] Crystal data for **3j**: $C_{18}H_{14}O$, M = 246.29, monoclinic, a = 4.7615(5) Å, b = 11.9406(12) Å, c = 21.373(2) Å, β = 93.296(2)°, V = 1213.1(2) Å^3, T = 100 K, space group $P2_1/c$, Z = 4, μ(Mo-Kα) = 0.082 mm^{-1}, 69156 reflections measured, 5495 independent reflections (R_{int} = 0.0768). The final R_1 values were 0.045 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.136 (all data). The goodness of fit on F^2 was 1.037. CCDC reference number: 797428.

Optimization studies

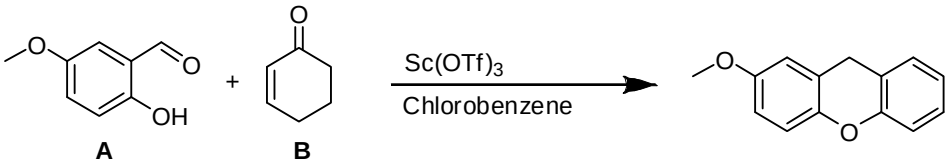
Given are isolated yields. All reactions were performed by refluxing in an oil bath for 24 hours unless noted otherwise.

Screening of catalysts



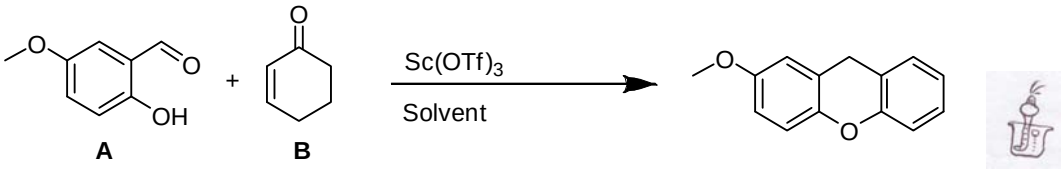
Run	Catalyst loading	Catalyst	Solvent	Equivalents A : B	Yield %
1	20 mol %	-	chlorobenzene	1 : 1	0
2	20 mol %	$ZnCl_2$	chlorobenzene	1 : 1	50
3	20 mol %	$Zn(OTf)_2$	chlorobenzene	1 : 1	23
4	20 mol %	$Sc(OTf)_3$	chlorobenzene	1 : 1	55
5	20 mol %	$Yb(OTf)_3$	chlorobenzene	1 : 1	40
6	20 mol %	$Y(OTf)_3$	chlorobenzene	1 : 1	22
7	20 mol %	$Er(OTf)_3$	chlorobenzene	1 : 1	42
8	20 mol %	$Sm(OTf)_3$	chlorobenzene	1 : 1	23
9	20 mol %	$Cu(OTf)_2$	chlorobenzene	1 : 1	23
10	20 mol %	CF_3SO_3H	chlorobenzene	1 : 1	9

Optimization of catalyst loading



Run	Catalyst loading	Solvent	Equivalents A : B	Yield %
1	5 mol %	chlorobenzene	1 : 1	59
2	10 mol %	chlorobenzene	1 : 1	47
3	15 mol %	chlorobenzene	1 : 1	55
4	3 mol %	chlorobenzene	1 : 1	48
5	20 mol %	chlorobenzene	1 : 1	55

solvent screening



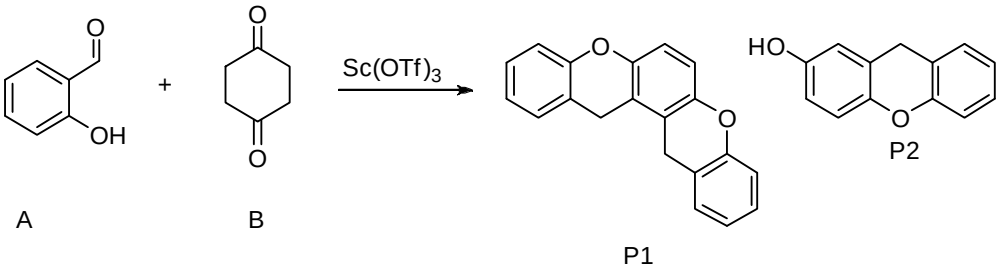
Run	Catalyst loading	Solvent	Equivalents A : B	Yield %
1	5 mol %	chlorobenzene	1 : 1	59
2	5 mol %	toluene	1 : 1	40
3	5 mol %	iso-hexane	1 : 1	7
4	5 mol %	dichloroethane	1 : 1	9

Equivalents Screening

Run	Catalyst loading	Solvent	Equivalents A : B	Yield %
1	5 mol %	chlorobenzene	1.5 : 1	61
2	5 mol %	chlorobenzene	1 : 1.5	54
3	5 mol %	chlorobenzene	1.25 : 1	59
4	5 mol %	chlorobenzene	1.10 : 1	63

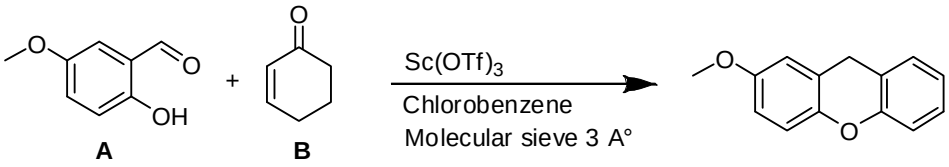
Optimal conditions for the Xanthene derivative synthesis are 5 mol % catalyst loading using chlorobenzene as solvent and a slight excess of the aldehyde.

Reaction with 1,4-cyclohexanedione



Equivalents A : B	Catalyst loading	Solvent	Yield % GP A (oil bath)	Yield % GP B (microwave)
1.1 :1	5 mol %	chlorobenzene	P1 (7) P2 (25)	P1 (5) P2 (51)

Effect of molecular sieves



* Using reactions conditions of general procedure **A**, plus addition of molecular sieves (3A, 0.5 g). Isolated yield after 24 h was 6 %.