SUPPLEMENTARY MATERIALS

SPECTROSCOPIC DATA

4-(2-(Cyclopropylmethoxy)ethyl)phenol (***2***)

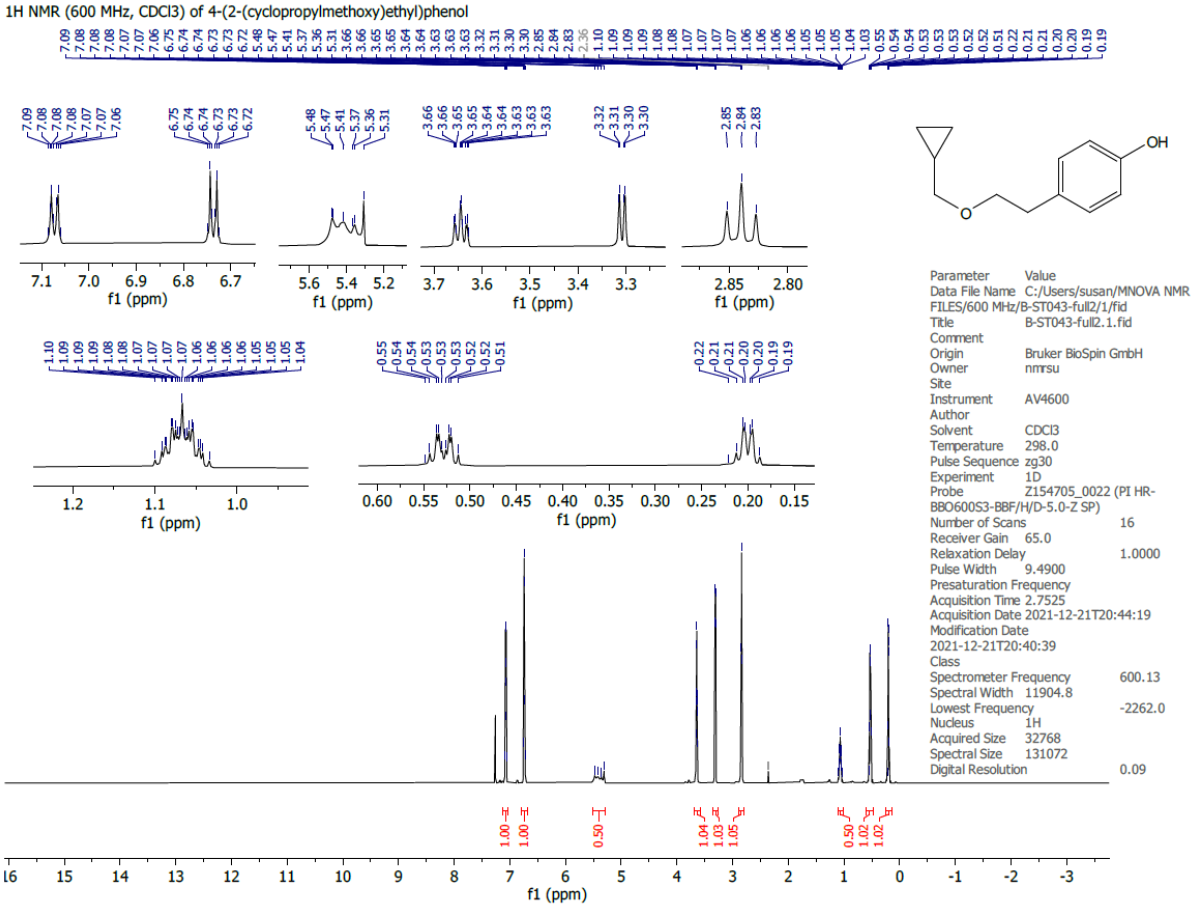


Figure S1. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of 4-(2-(cyclopropylmethoxy)ethyl)phenol (**2**).

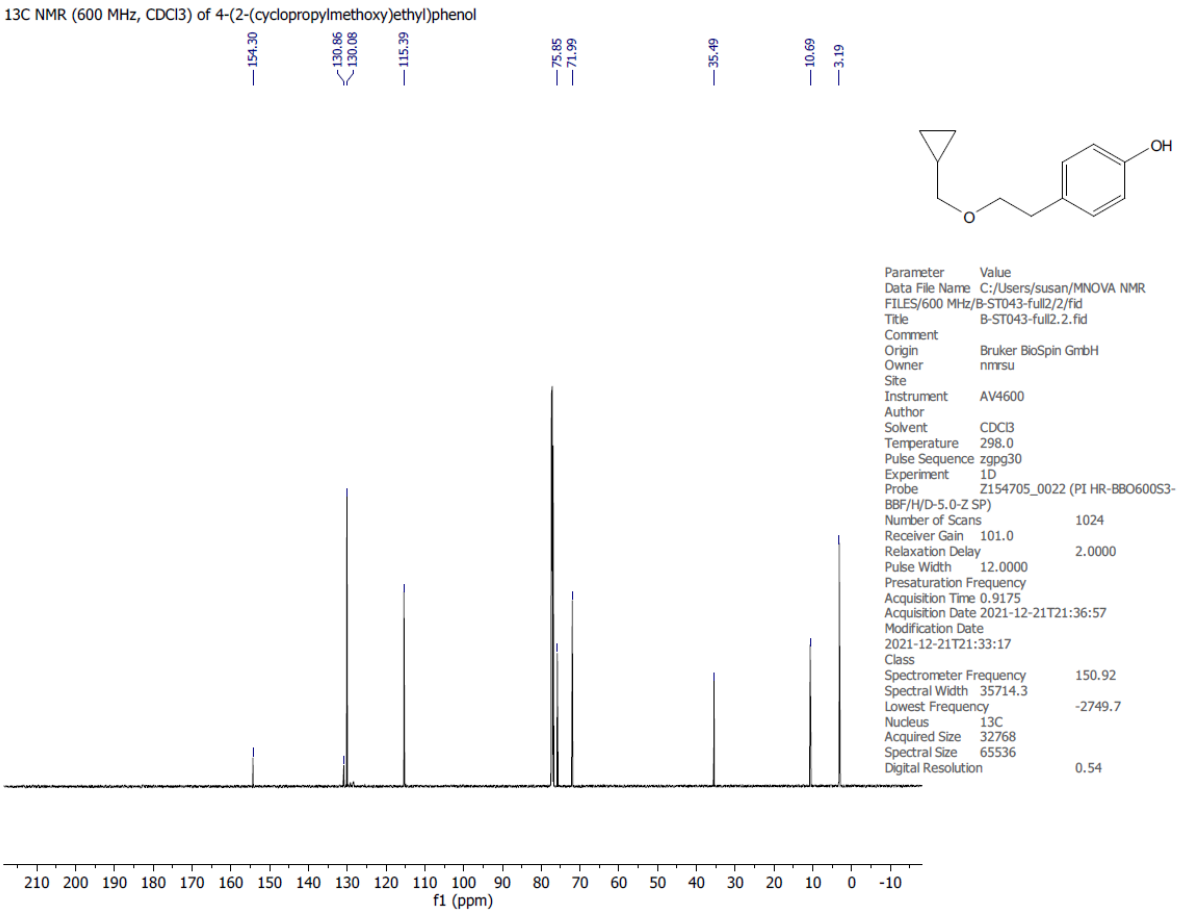


Figure S2. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of 4-(2-(cyclopropylmethoxy)ethyl)phenol (**2**).

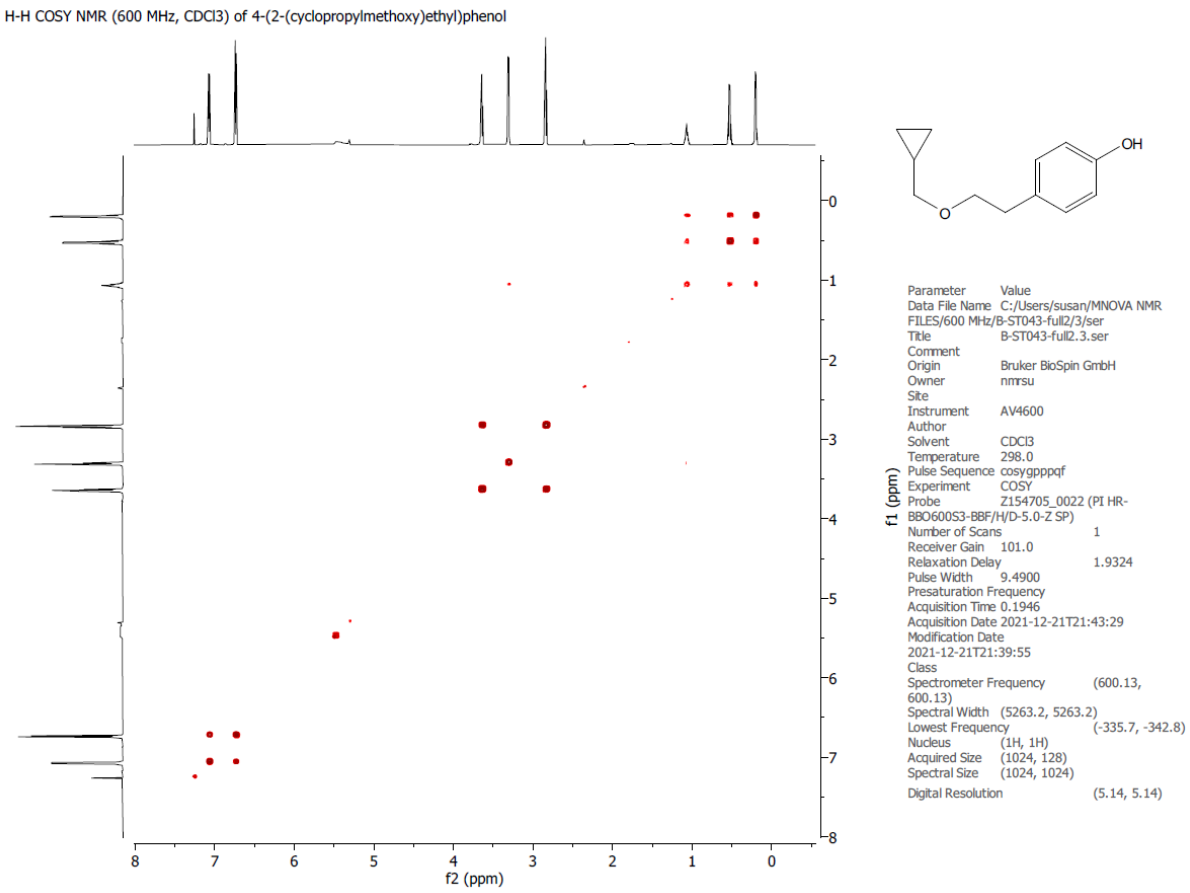


Figure S3. COSYNMR spectrum (600 MHz, $CDCl_3$) of 4-(2-(cyclopropylmethoxy)ethyl)phenol (**2**).

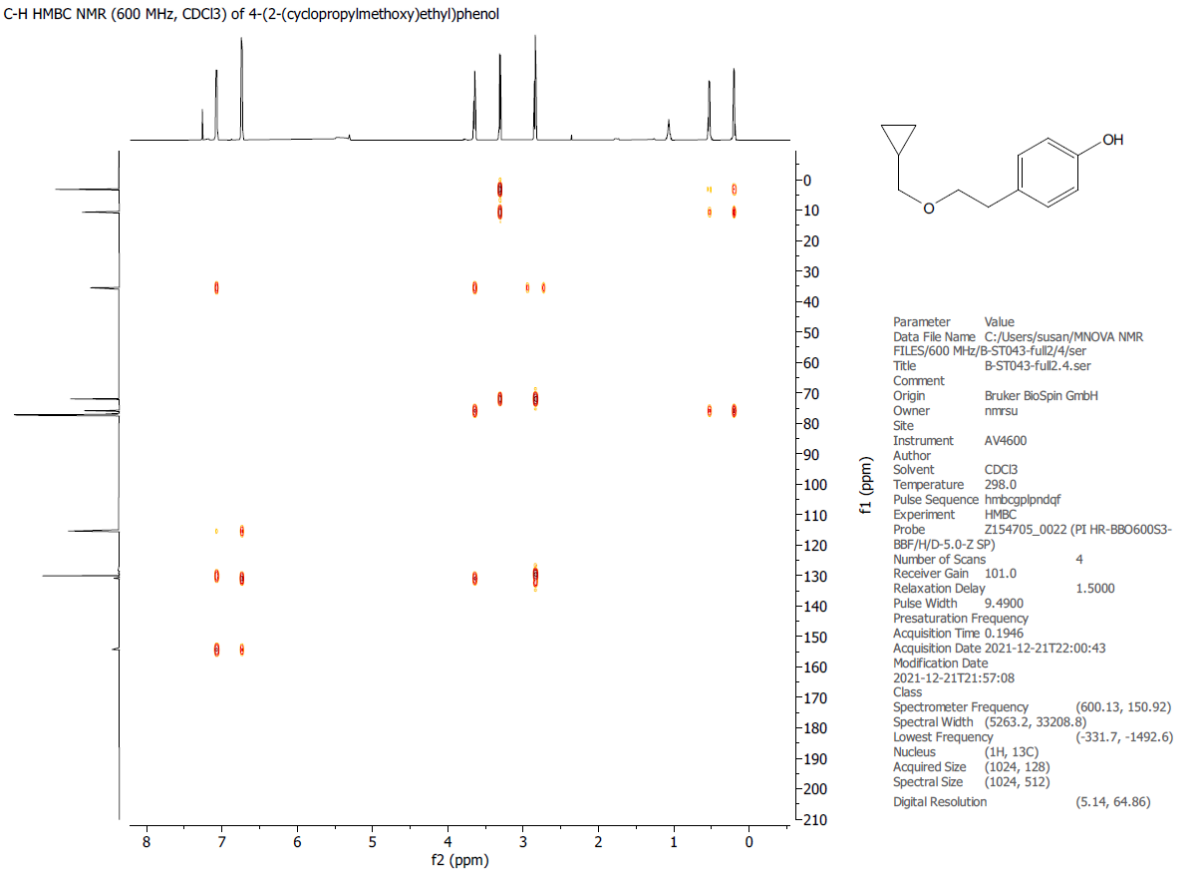


Figure S4. HMBC NMR spectrum (600 MHz, $CDCl_3$) of 4-(2-(cyclopropylmethoxy)ethyl)phenol (**2**).

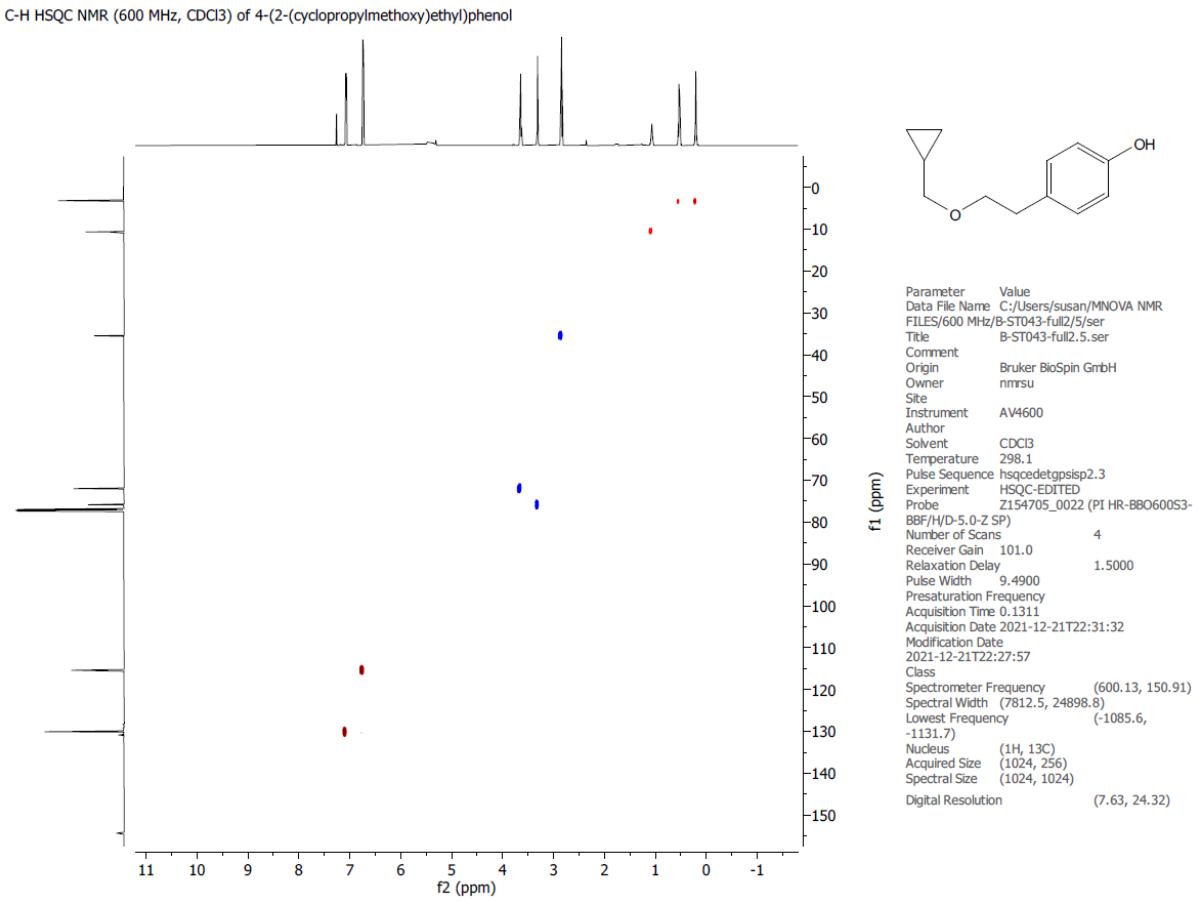


Figure S5. HSQC NMR spectrum (600 MHz, $CDCl_3$) of 4-(2-(cyclopropylmethoxy)ethyl)phenol (**2**).

*2-(4-(Cyclopropylmethoxy)phenyl)ethan-1-ol (**2b**)*

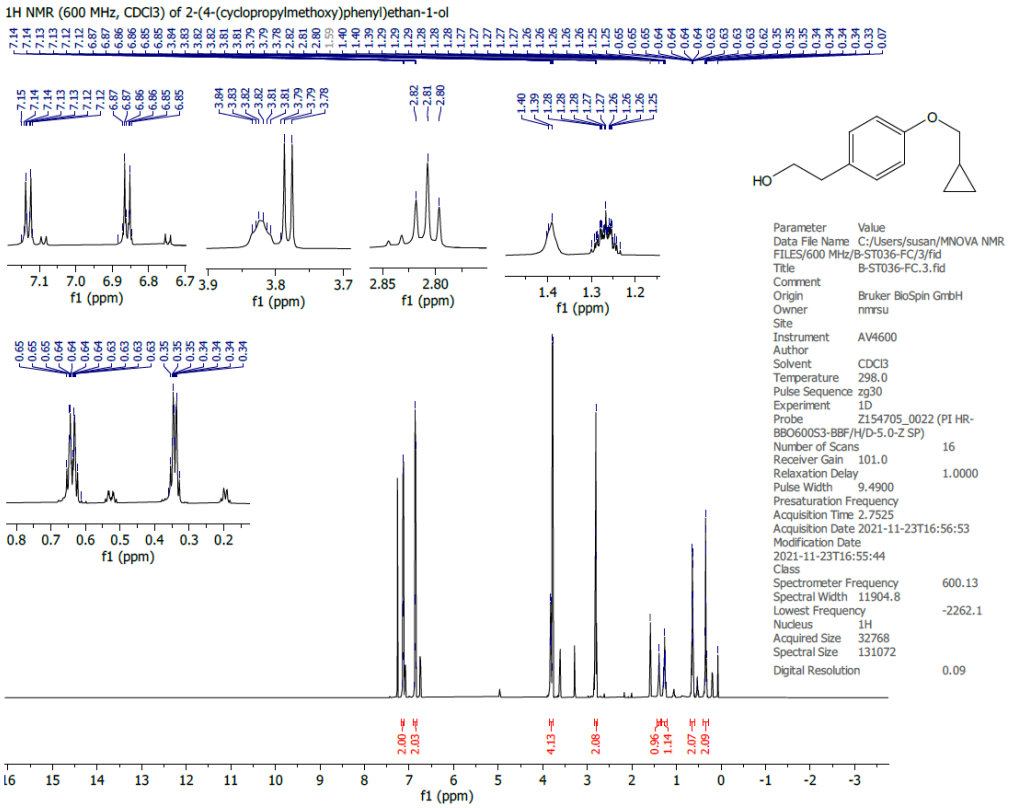


Figure S6. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of 2-(4-(cyclopropylmethoxy)phenyl)ethan-1-ol (**2b**).

*1-(Cyclopropylmethoxy)- 4-(2-(cyclopropylmethoxy)ethyl)benzene (**2c**)*

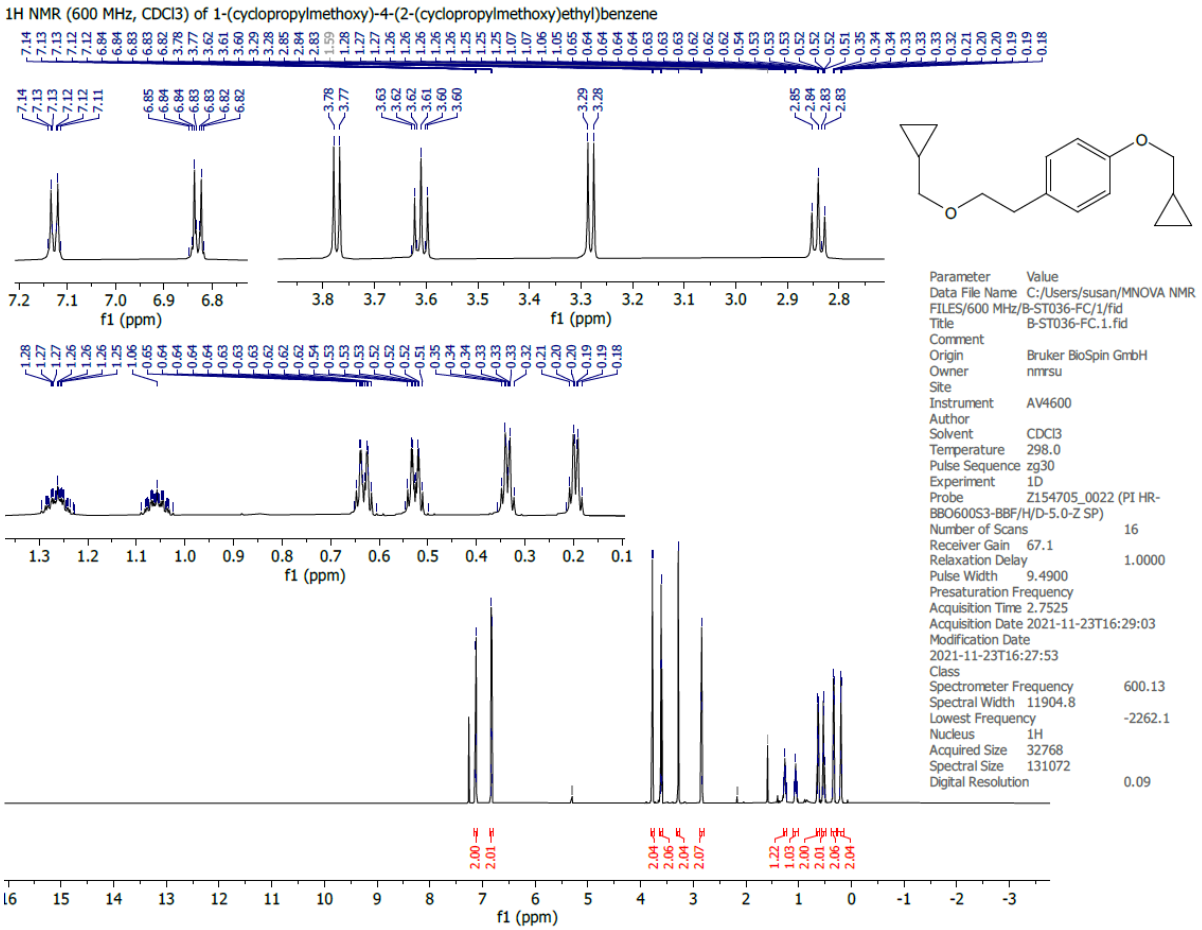


Figure S7. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of 1-(cyclopropylmethoxy)- 4-(2-(cyclopropylmethoxy)ethyl)benzene (**2c**).

*2-((4-(2-(Cyclopropylmethoxy)ethyl)phenoxy)-methyl)oxirane (**3**)*

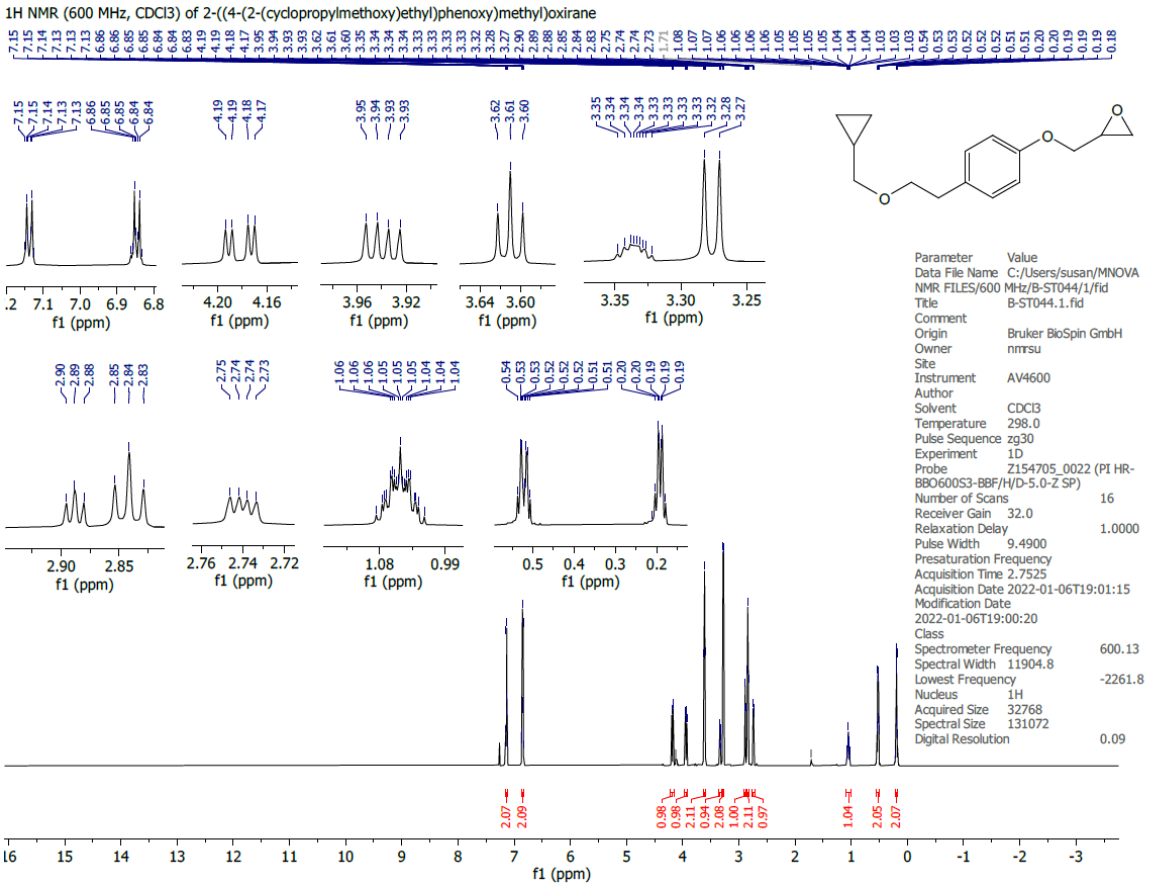


Figure S8. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of 2-((4-(2-(cyclopropylmethoxy)ethyl)phenoxy)-methyl)oxirane (**3**).

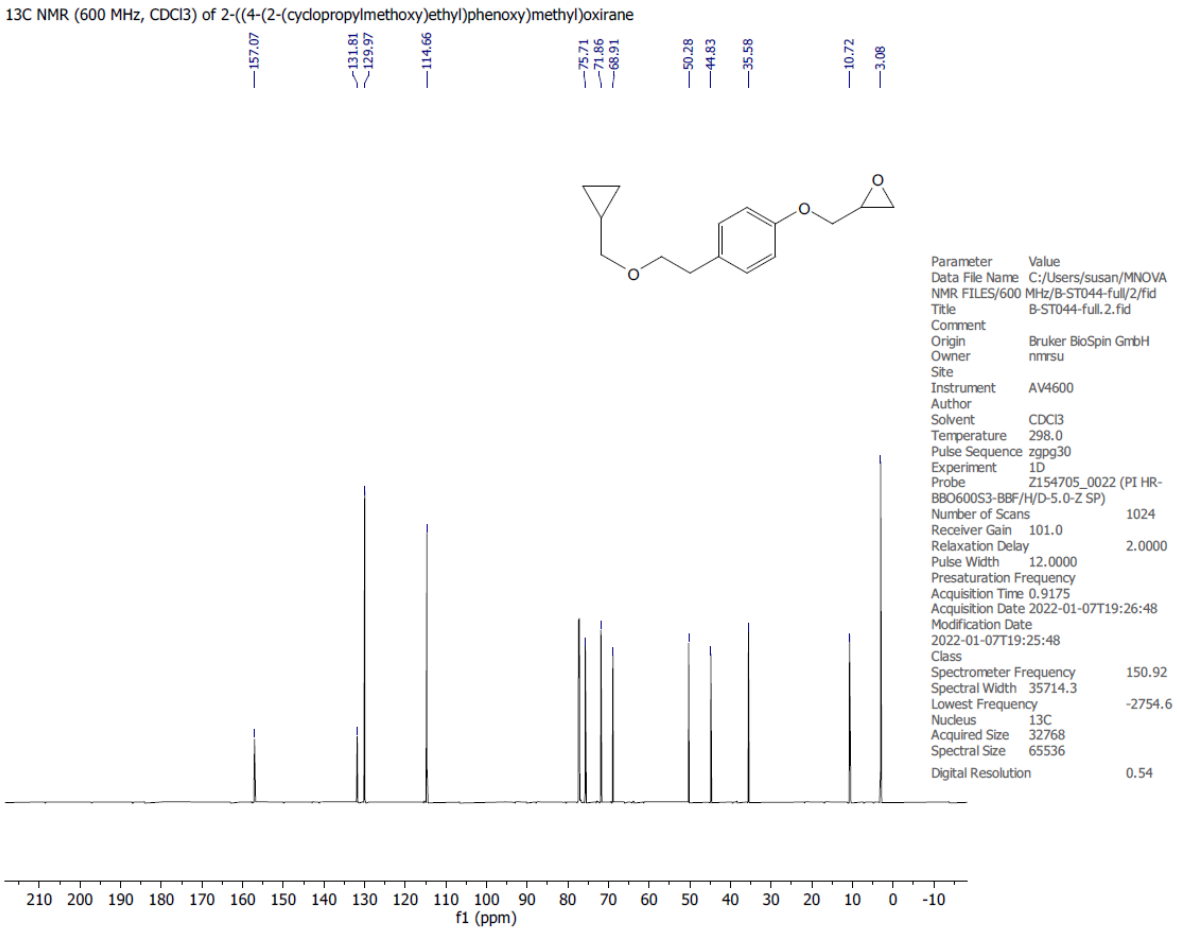


Figure S9. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of 2-((4-(2-(cyclopropylmethoxy)ethyl)phenoxy)-methyl)oxirane (**3**).

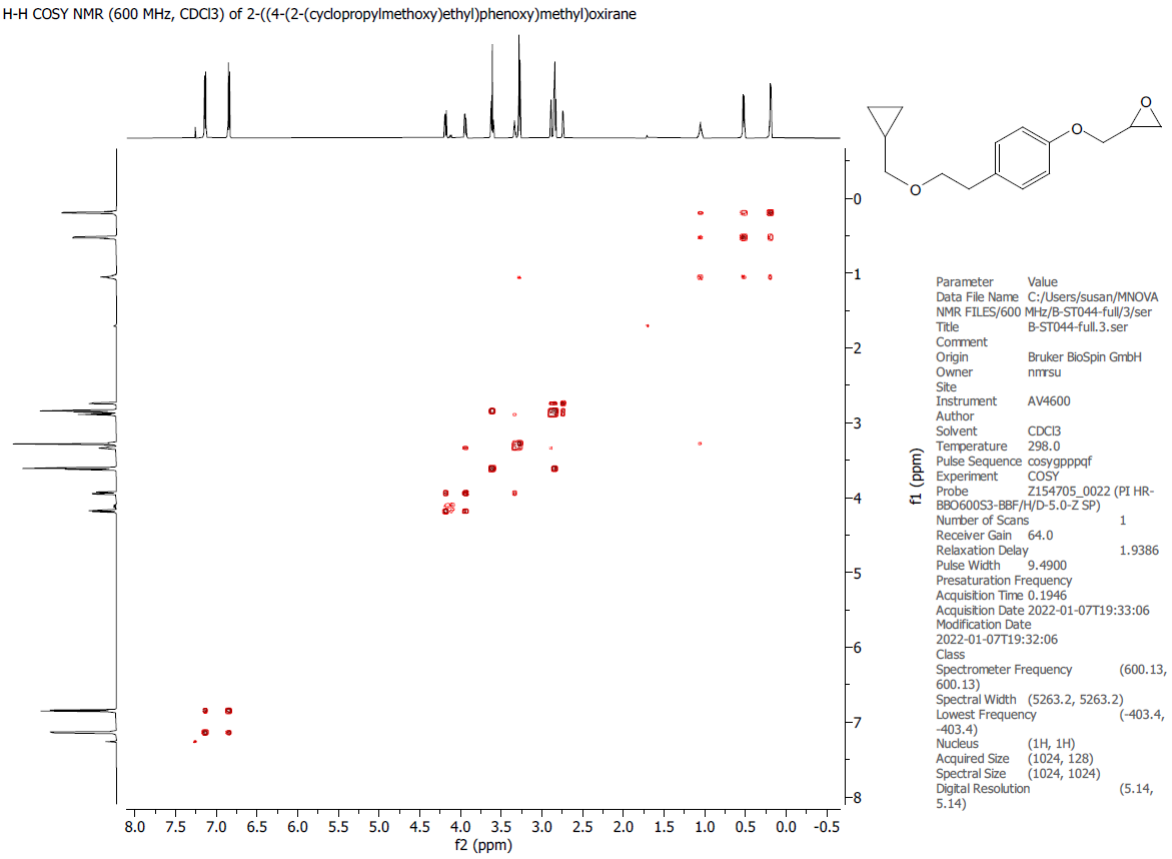


Figure S10. COSY NMR spectrum (600 MHz, $CDCl_3$) of 2-((4-(2-(cyclopropylmethoxy)ethyl)phenoxy)-methyl)oxirane (**3**).

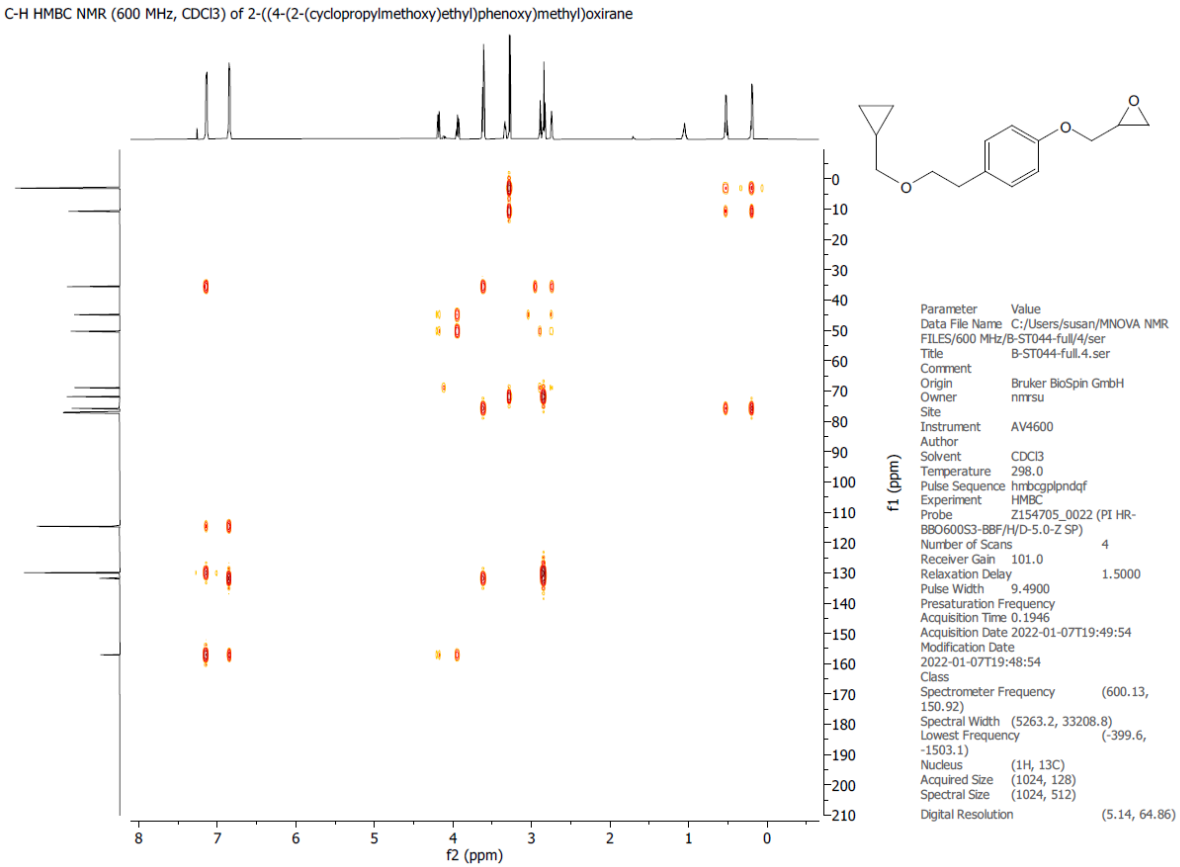


Figure S11. HMBC NMR spectrum (600 MHz, $CDCl_3$) of 2-((4-(2-(cyclopropylmethoxy)ethyl)phenoxy)-methyl)oxirane (**3**).

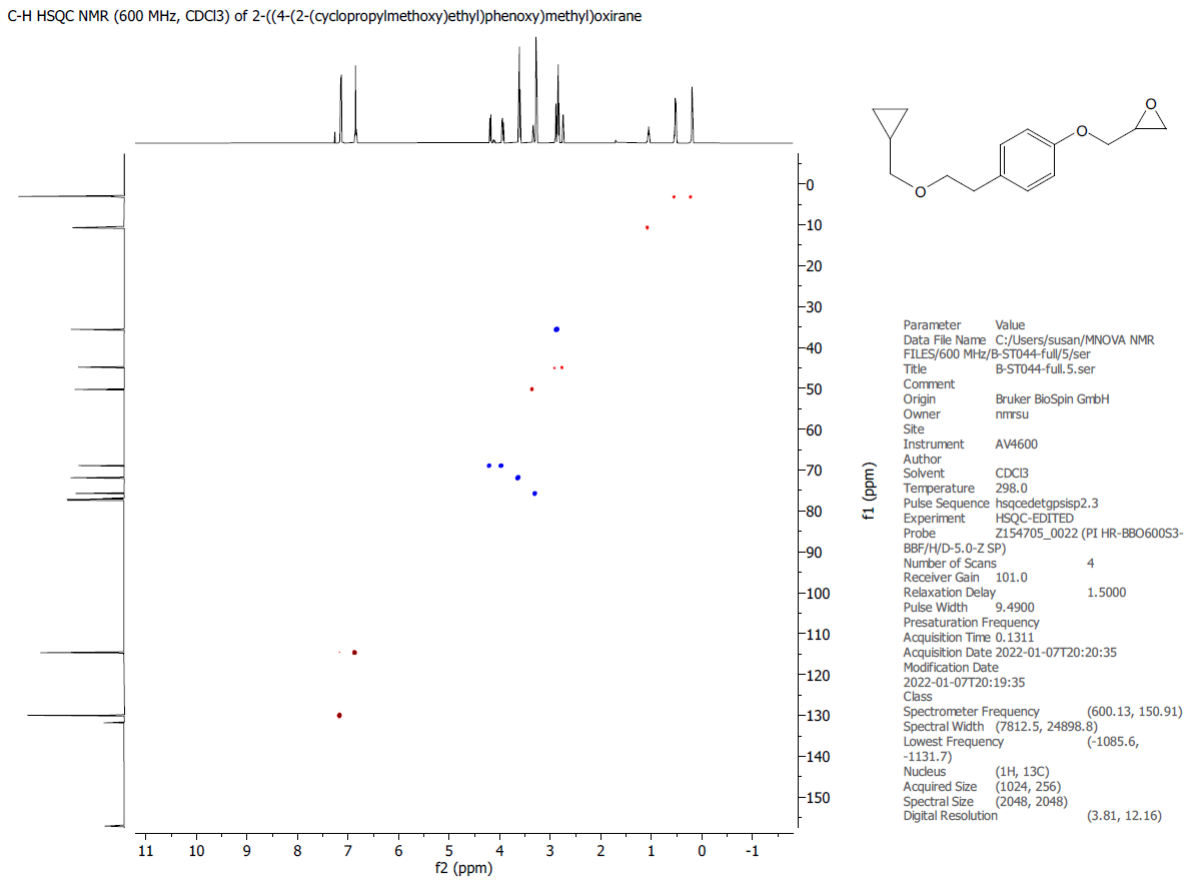


Figure S12. HSQC NMR spectrum (600 MHz, $CDCl_3$) of 2-((4-(2-(cyclopropylmethoxy)ethyl)phenoxy)-methyl)oxirane (**3**).

*2-(4-(oxiran-2-ylmethoxy)phenyl)ethan-1-ol (**4**)*

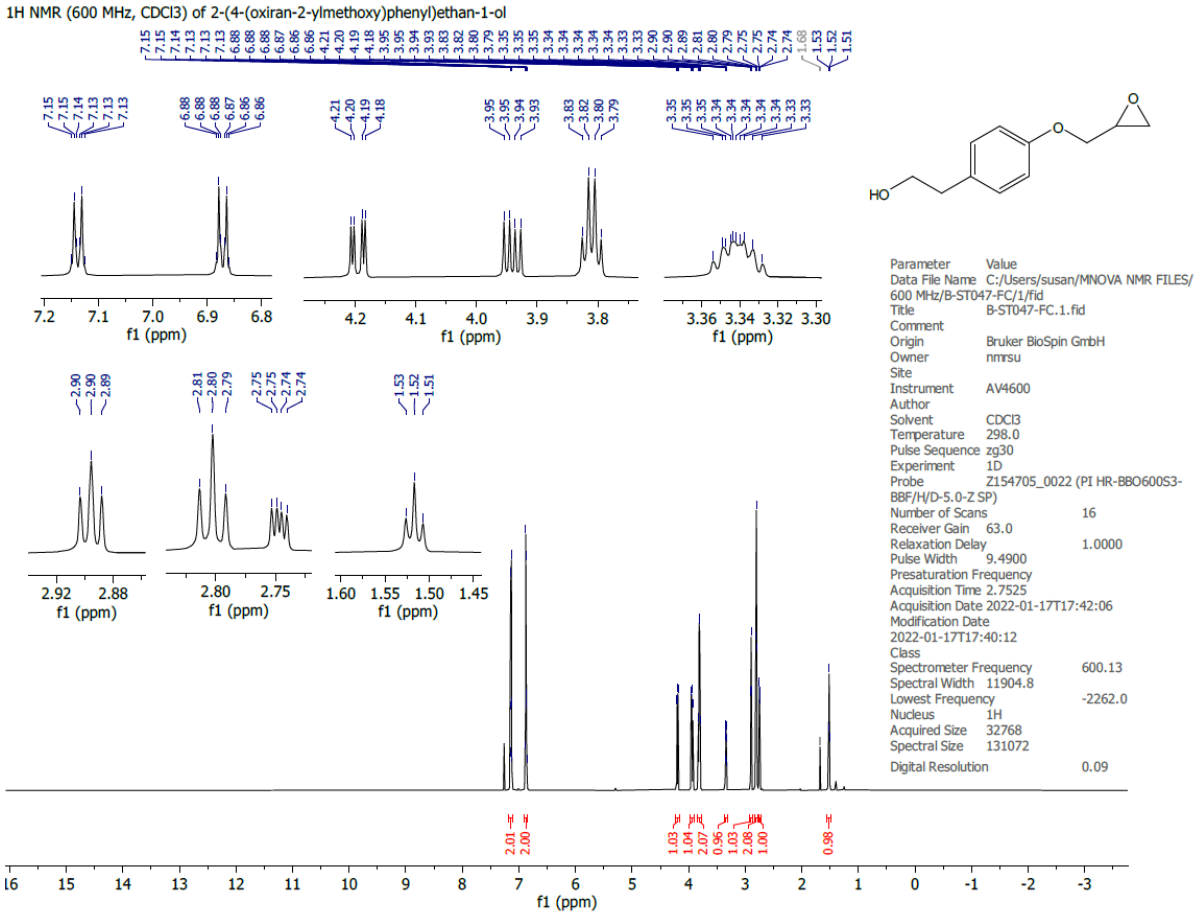


Figure S13. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of 2-(4-(oxiran-2-ylmethoxy)phenyl)ethan-1-ol (**4**).

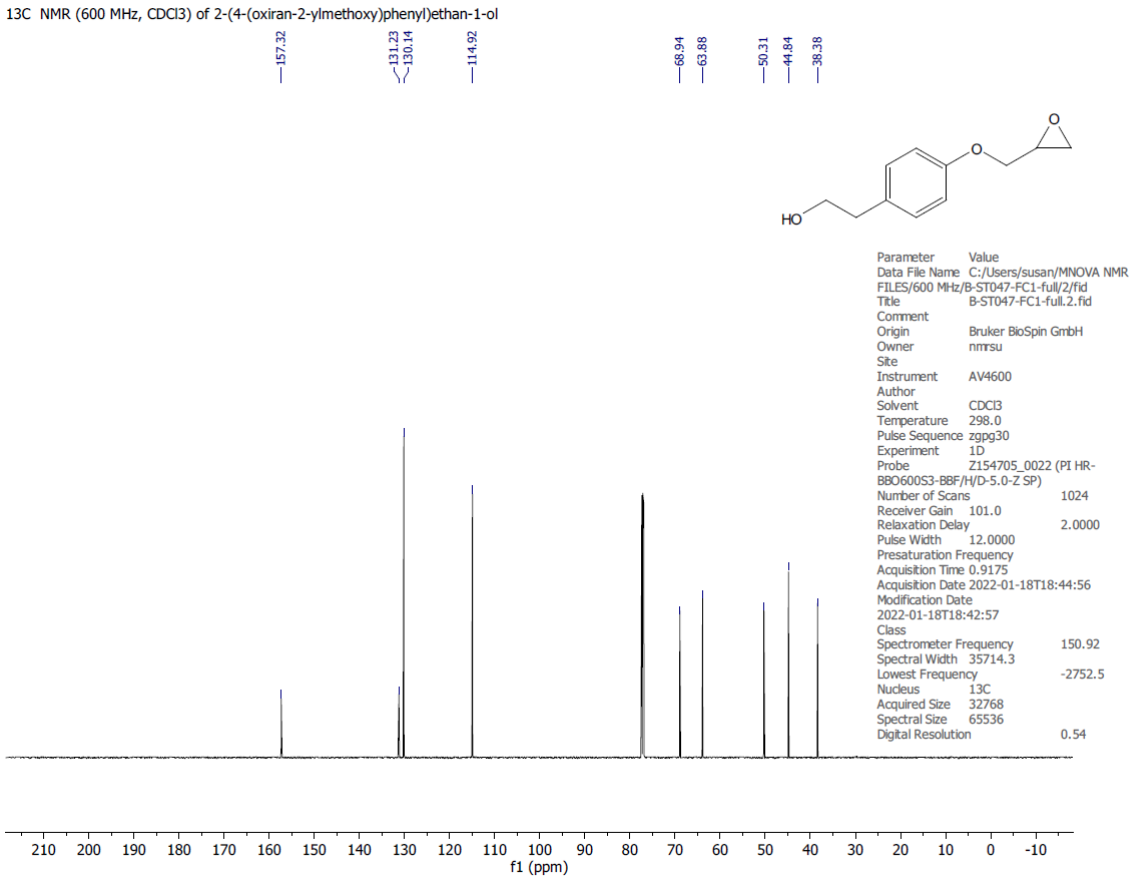


Figure S14. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of 2-(4-(oxiran-2-ylmethoxy)phenyl)ethan-1-ol (**4**).

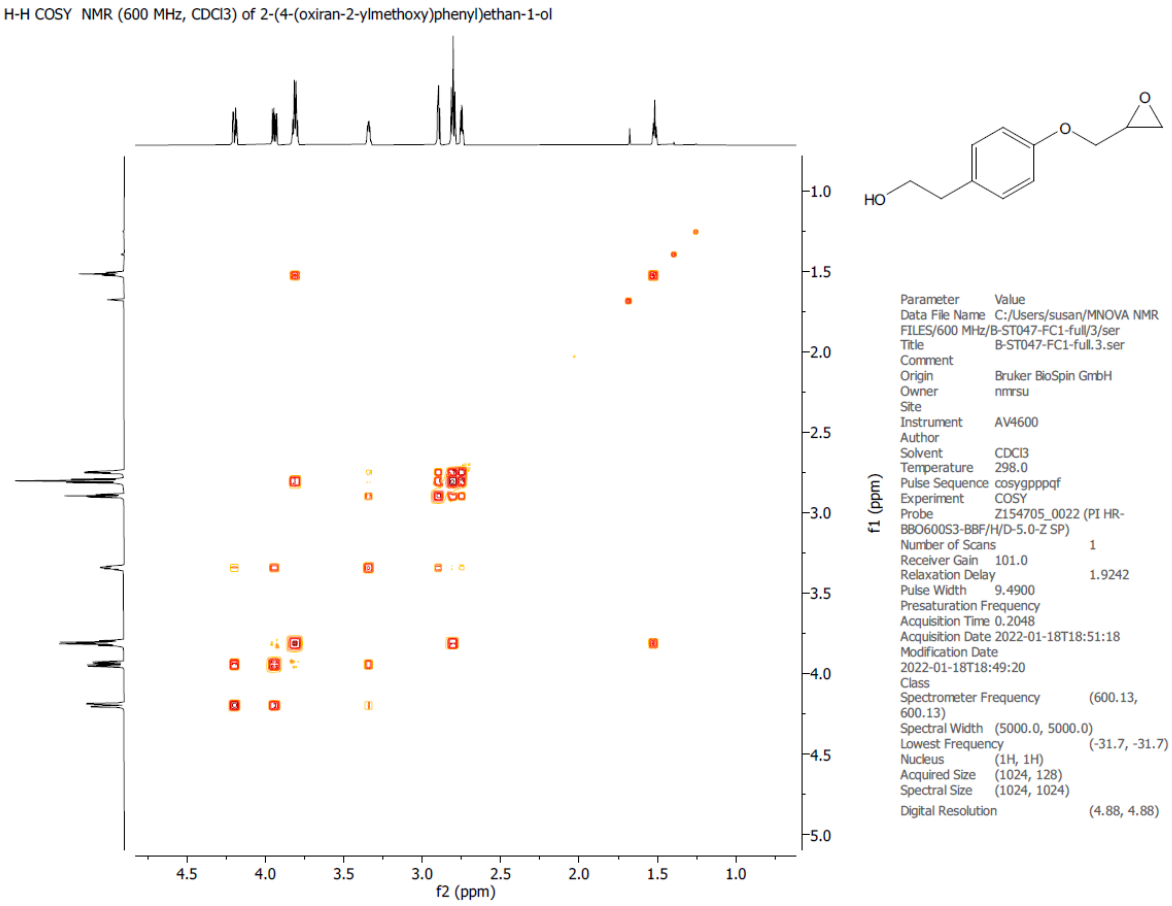


Figure S15. COSY NMR spectrum (600 MHz, $CDCl_3$) of 2-(4-(oxiran-2-ylmethoxy)phenyl)ethan-1-ol (**4**).

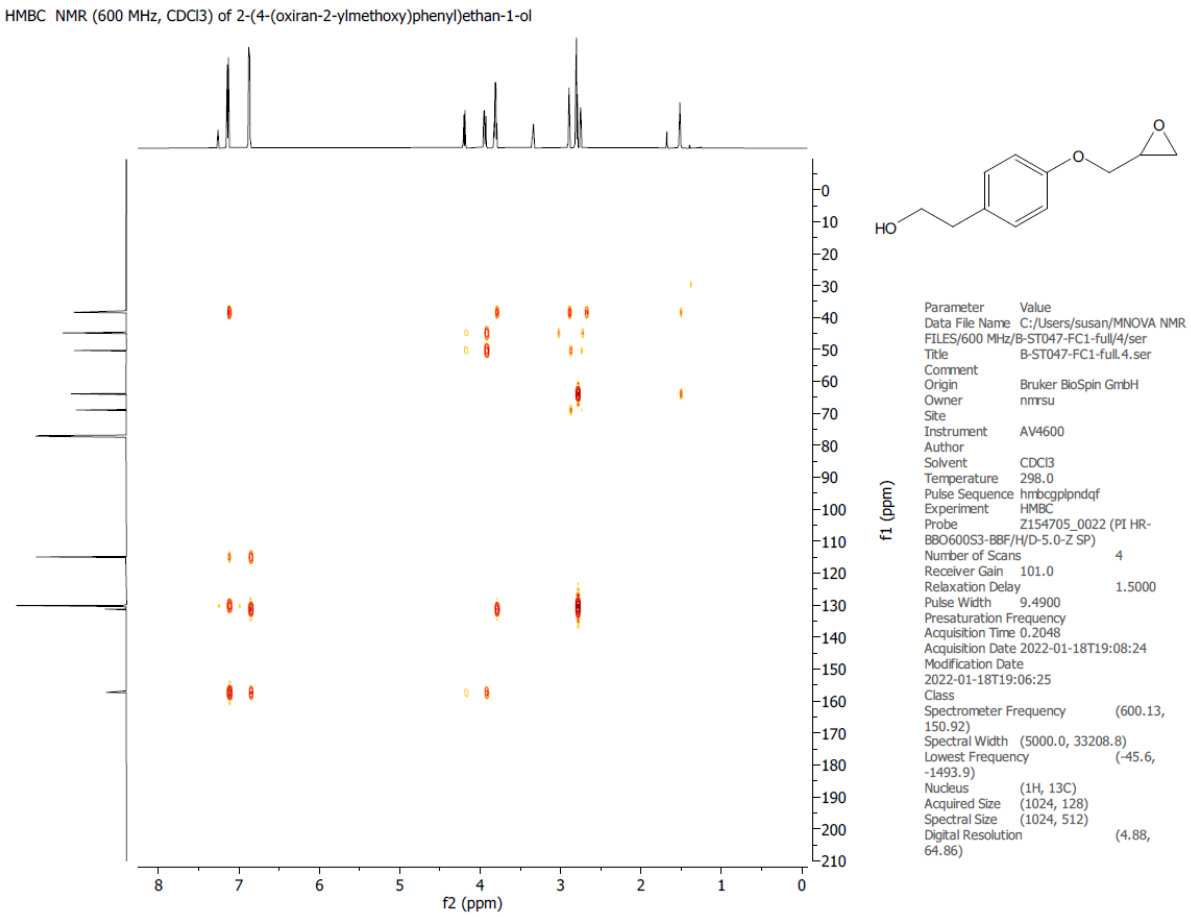


Figure S16. HMBC NMR spectrum (600 MHz, $CDCl_3$) of 2-(4-(oxiran-2-ylmethoxy)phenyl)ethan-1-ol (**4**).

2,2'-(((2-Hydroxypropane-1,3-diyl)bis(oxy))bis(4,1-phenylene))bis(ethan-1-ol)

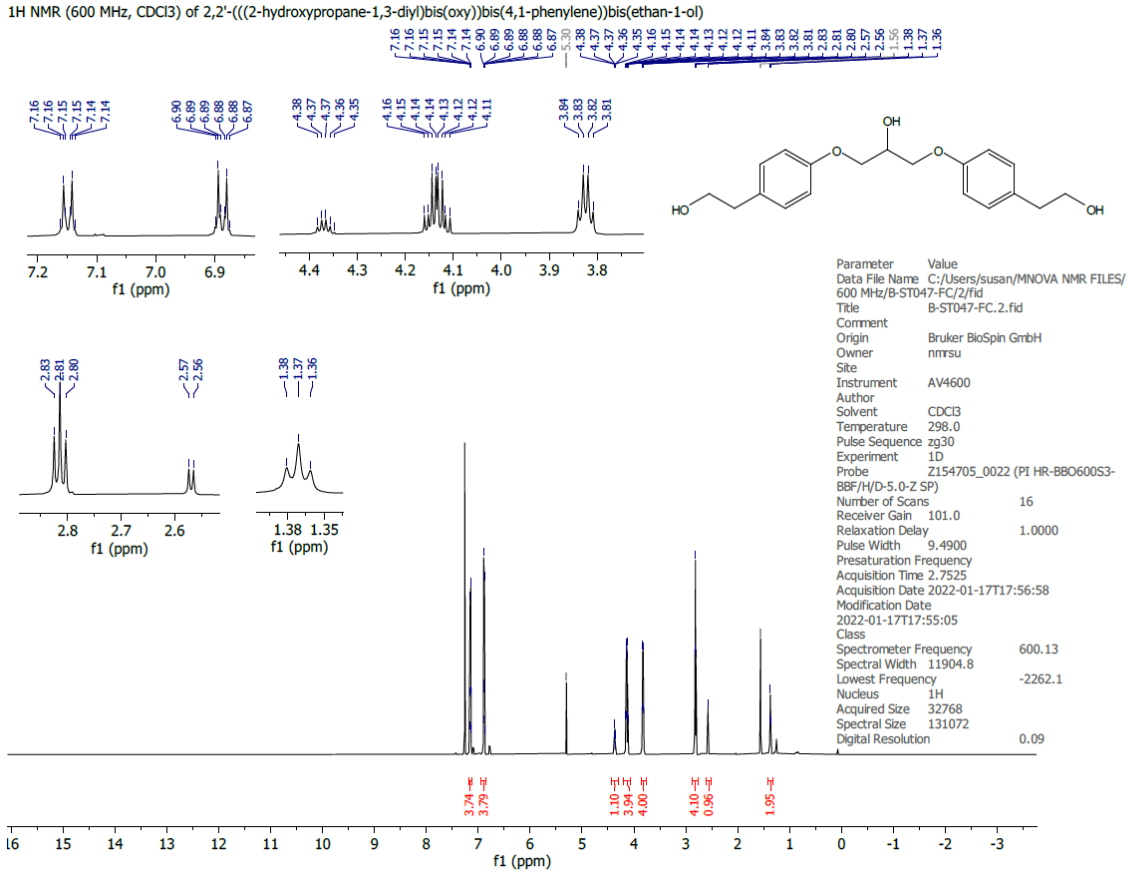


Figure S17. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of 2,2'-(((2-hydroxypropane-1,3-diyl)bis(oxy))bis(4,1-phenylene))bis(ethan-1-ol.

*1-chloro-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-ol (**5a**)*

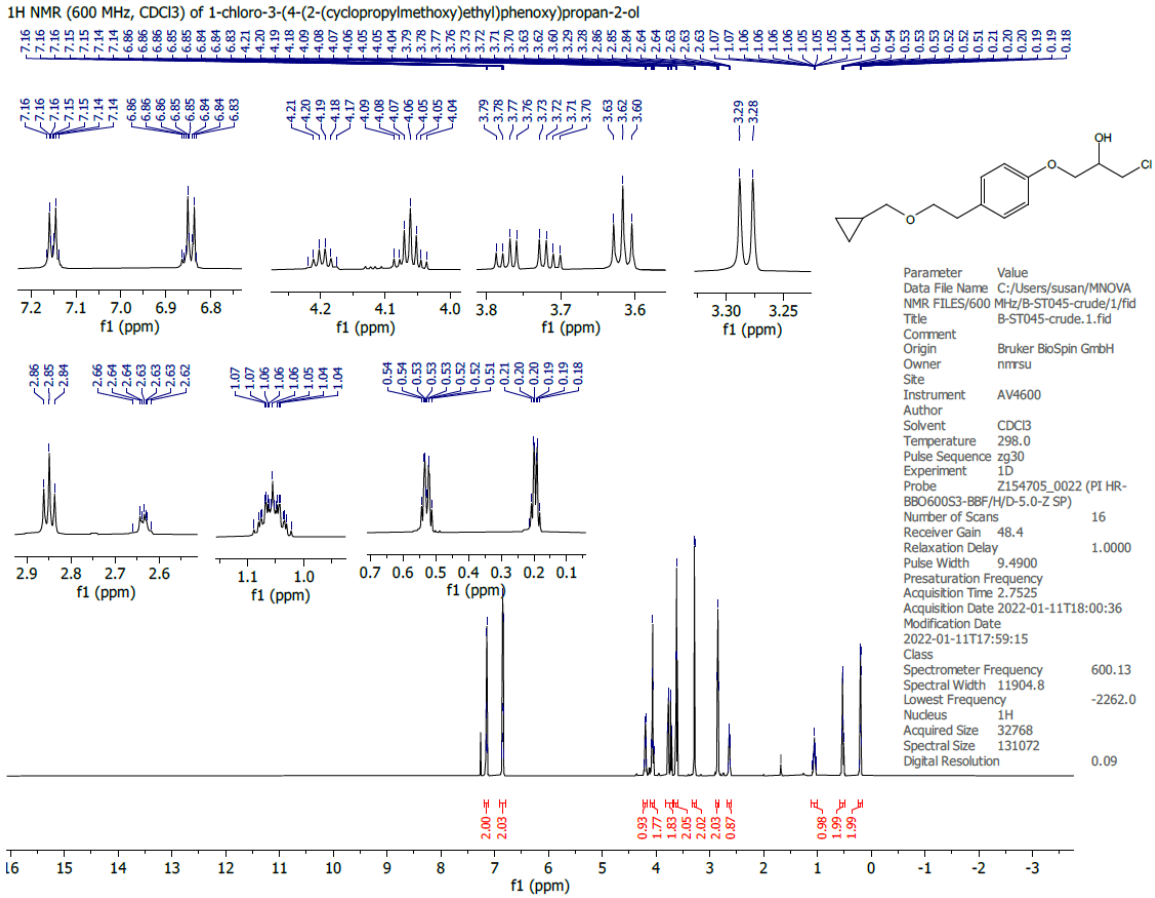


Figure S18. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of 1-chloro-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-ol (**5a**).

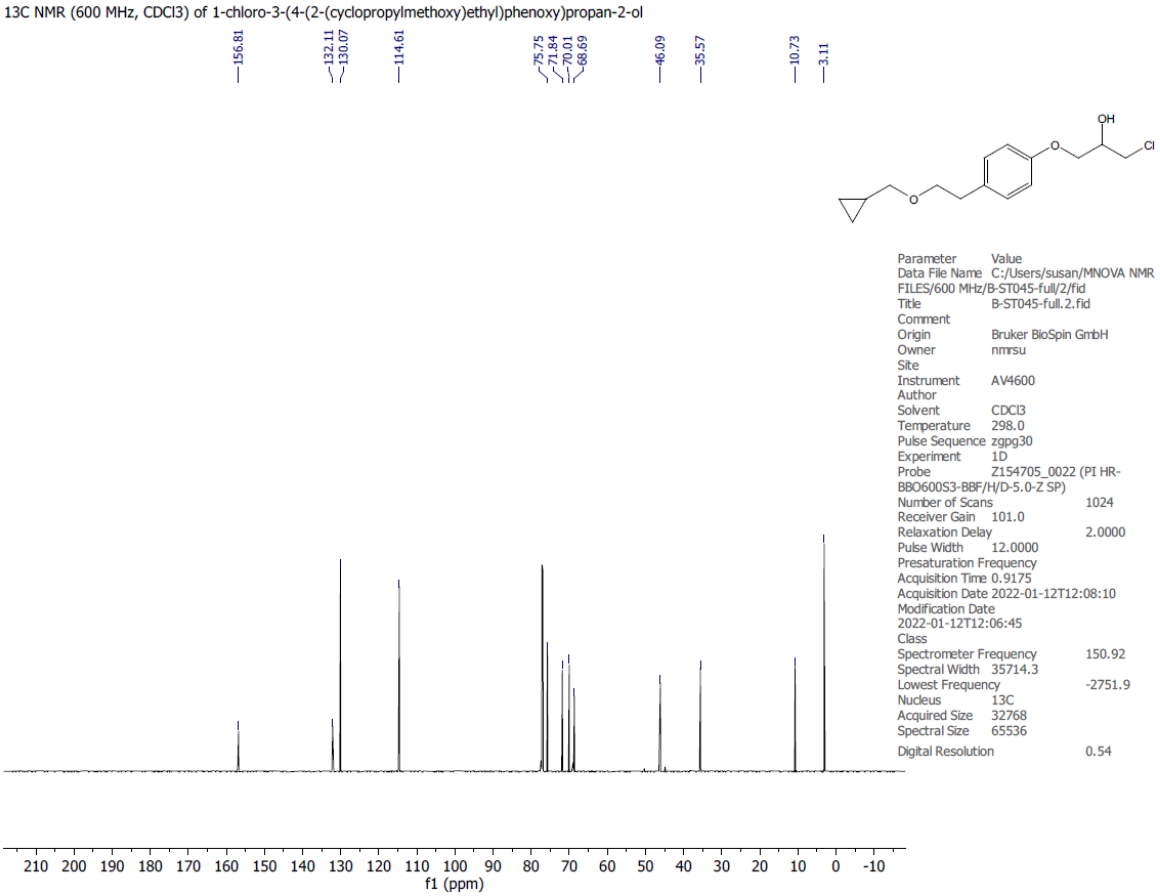


Figure S19. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of 1-chloro-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-ol (**5a**).

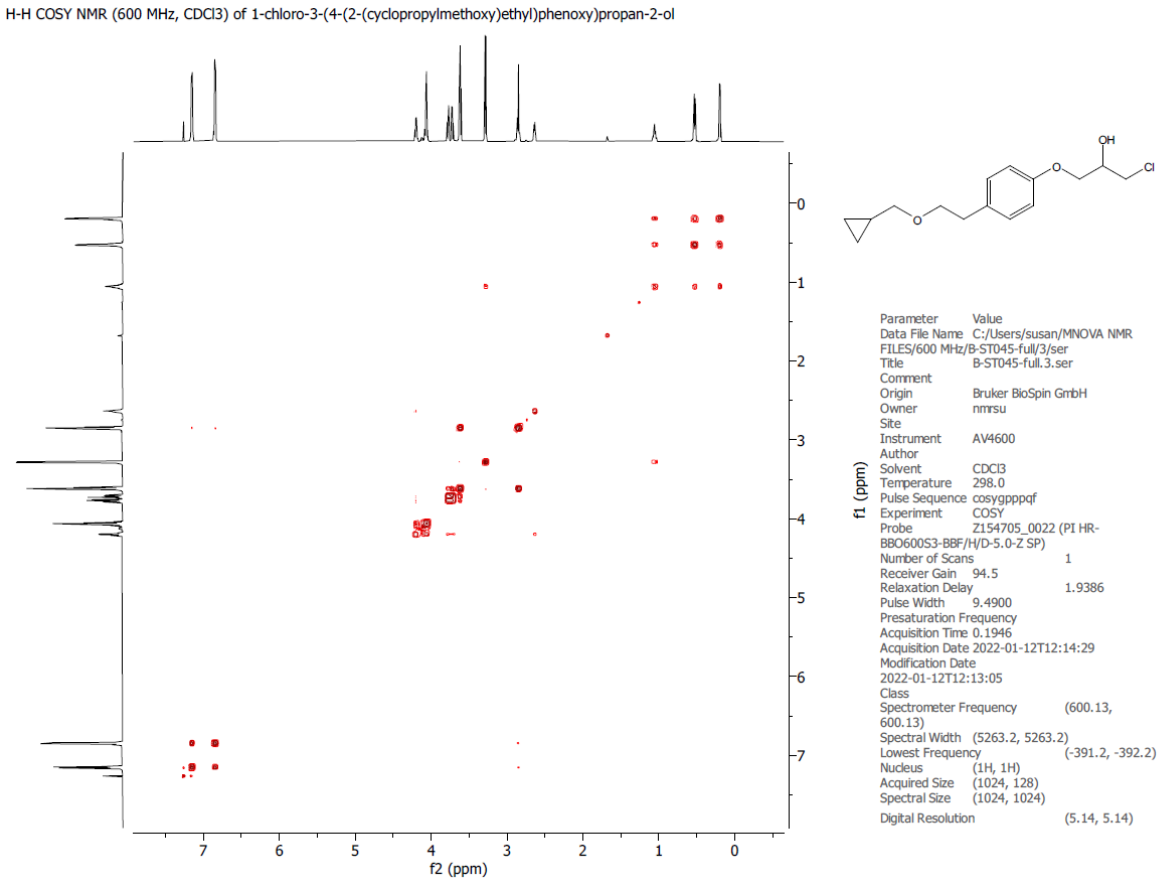


Figure S20. COSY NMR spectrum (600 MHz, $CDCl_3$) of 1-chloro-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-ol (**5a**).

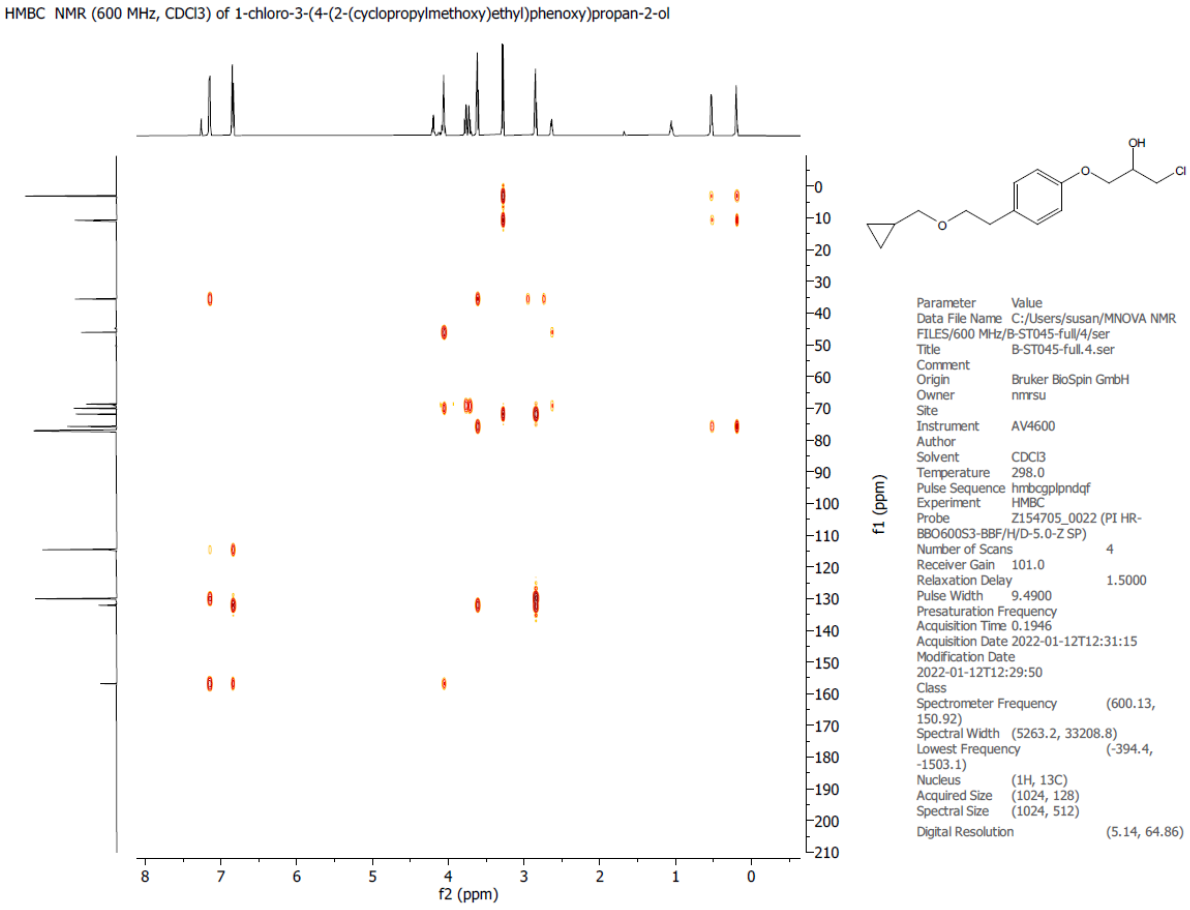


Figure S21. HMBC NMR spectrum (600 MHz, $CDCl_3$) of 1-chloro-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-ol (**5a**).

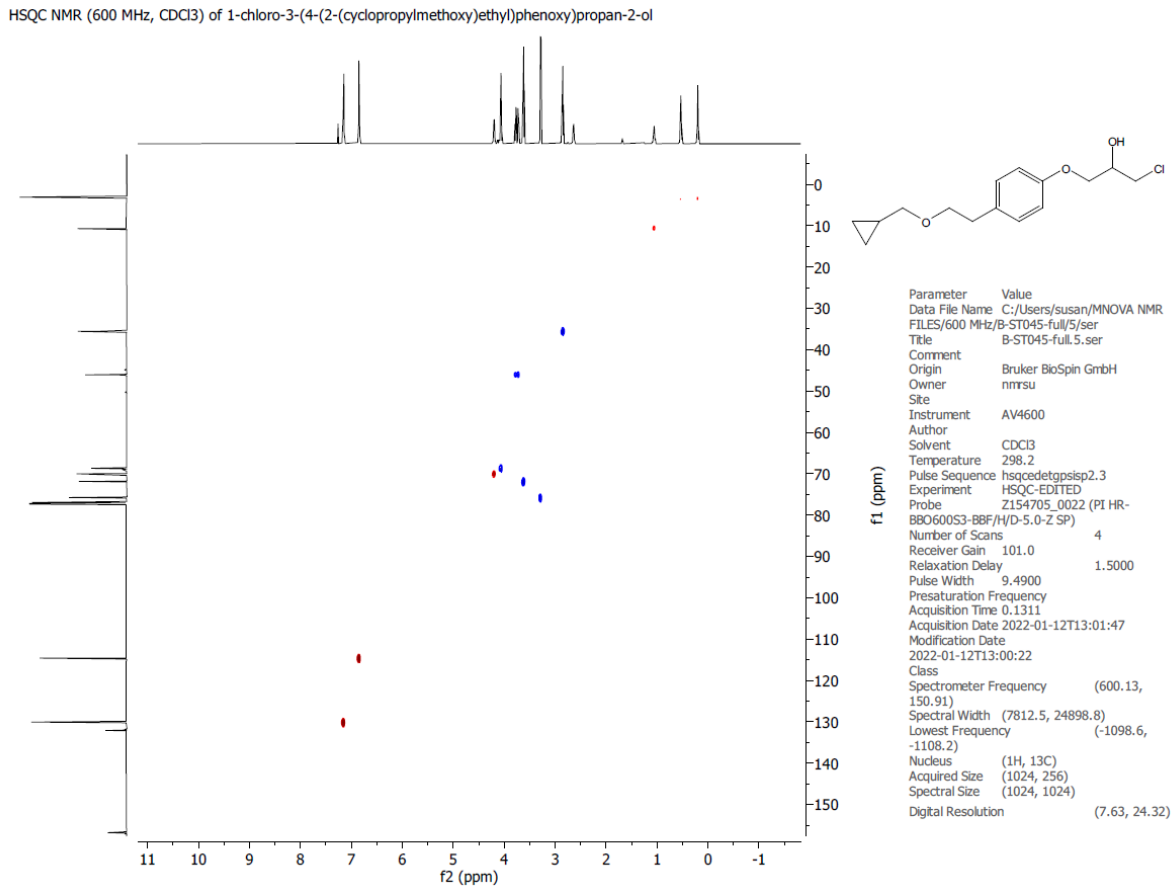


Figure S22. HSQC NMR spectrum (600 MHz, $CDCl_3$) of 1-chloro-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-ol (**5a**).

*1-Bromo-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-ol (**5b**)*

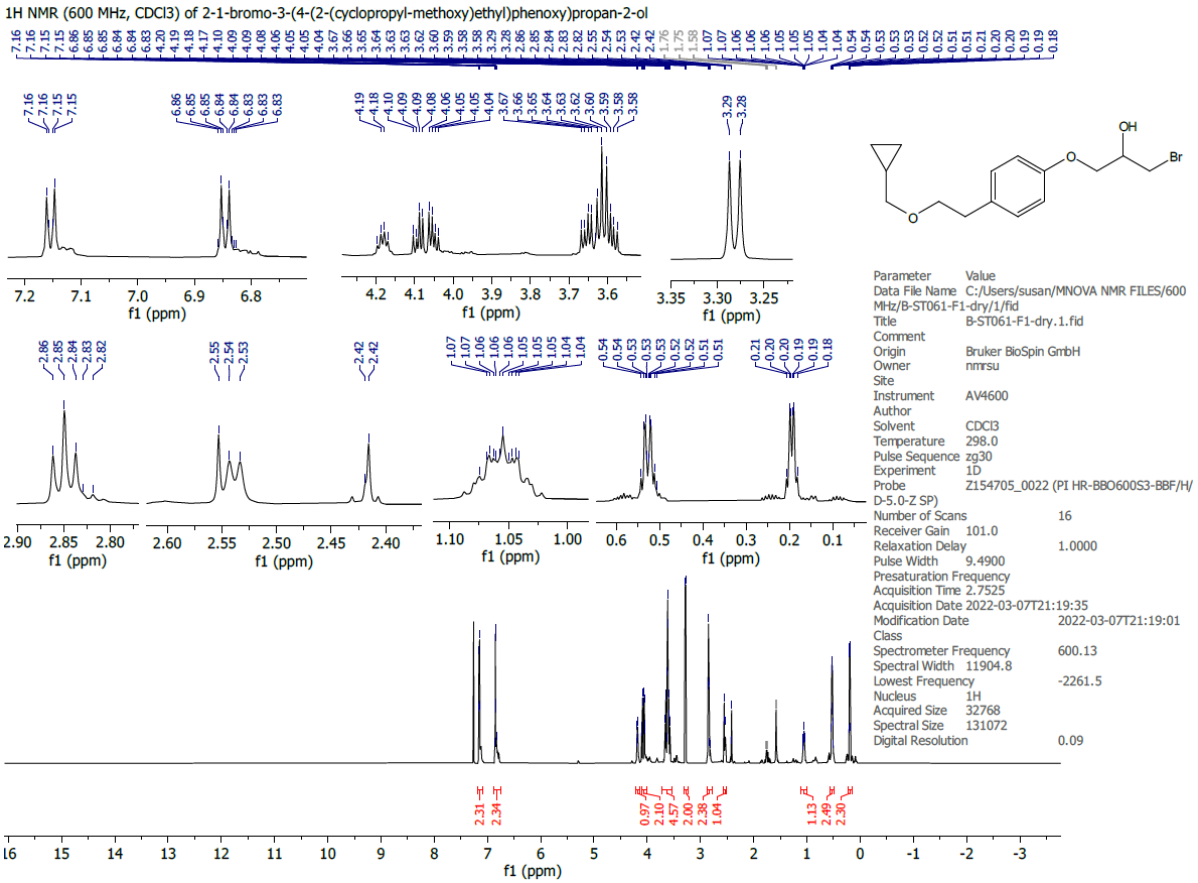


Figure S23. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of 1-bromo-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-ol (**5b**).

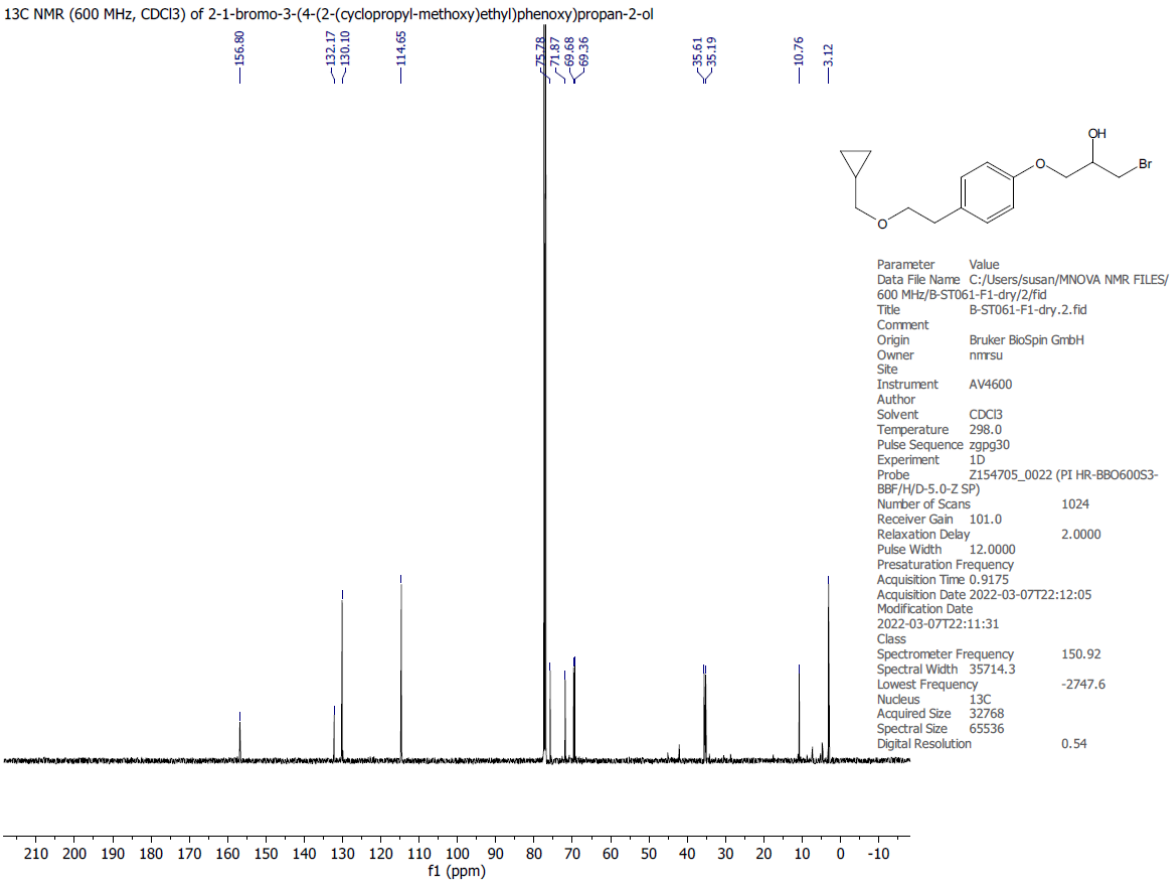


Figure S24. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of 1-bromo-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-ol (**5b**).

1-chloro-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-yl butanoate, ***6a***

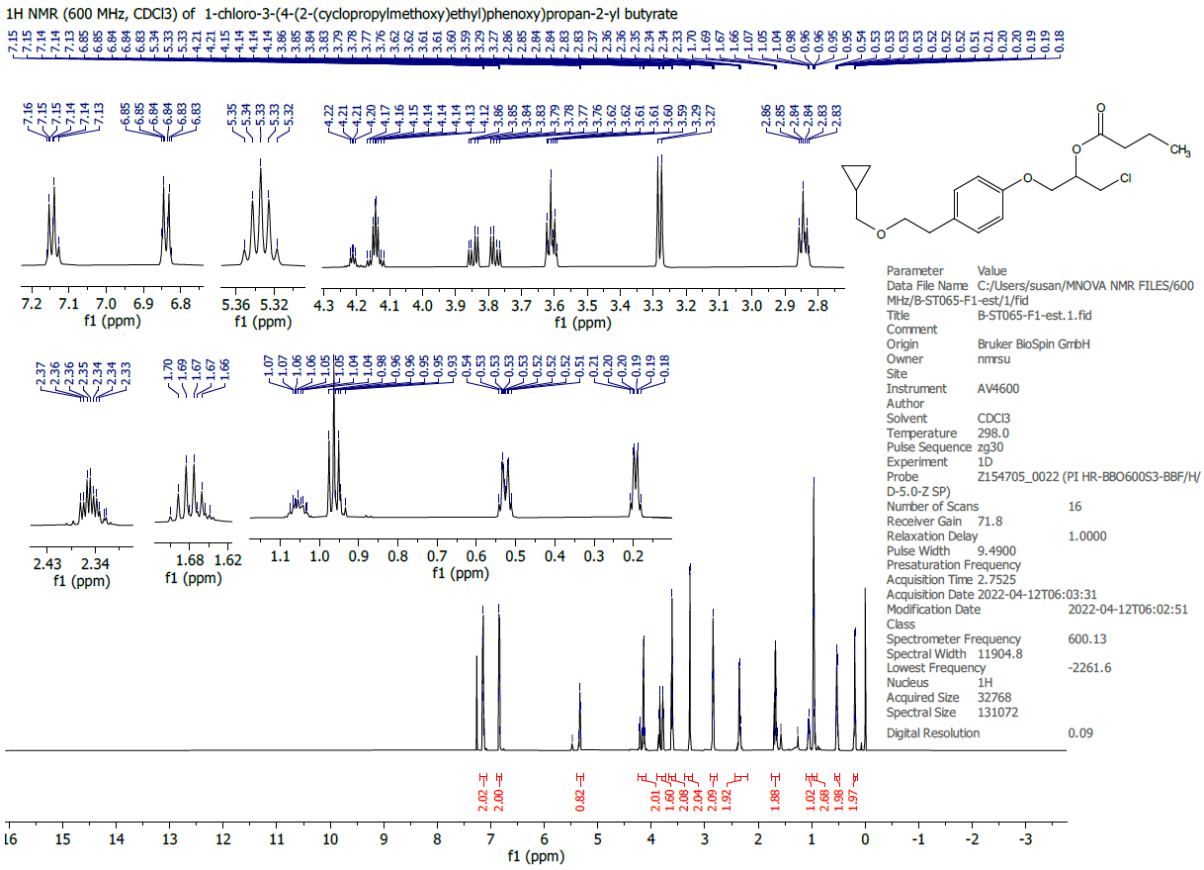


Figure S25. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of 1-chloro-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-yl butanoate (**6a).**

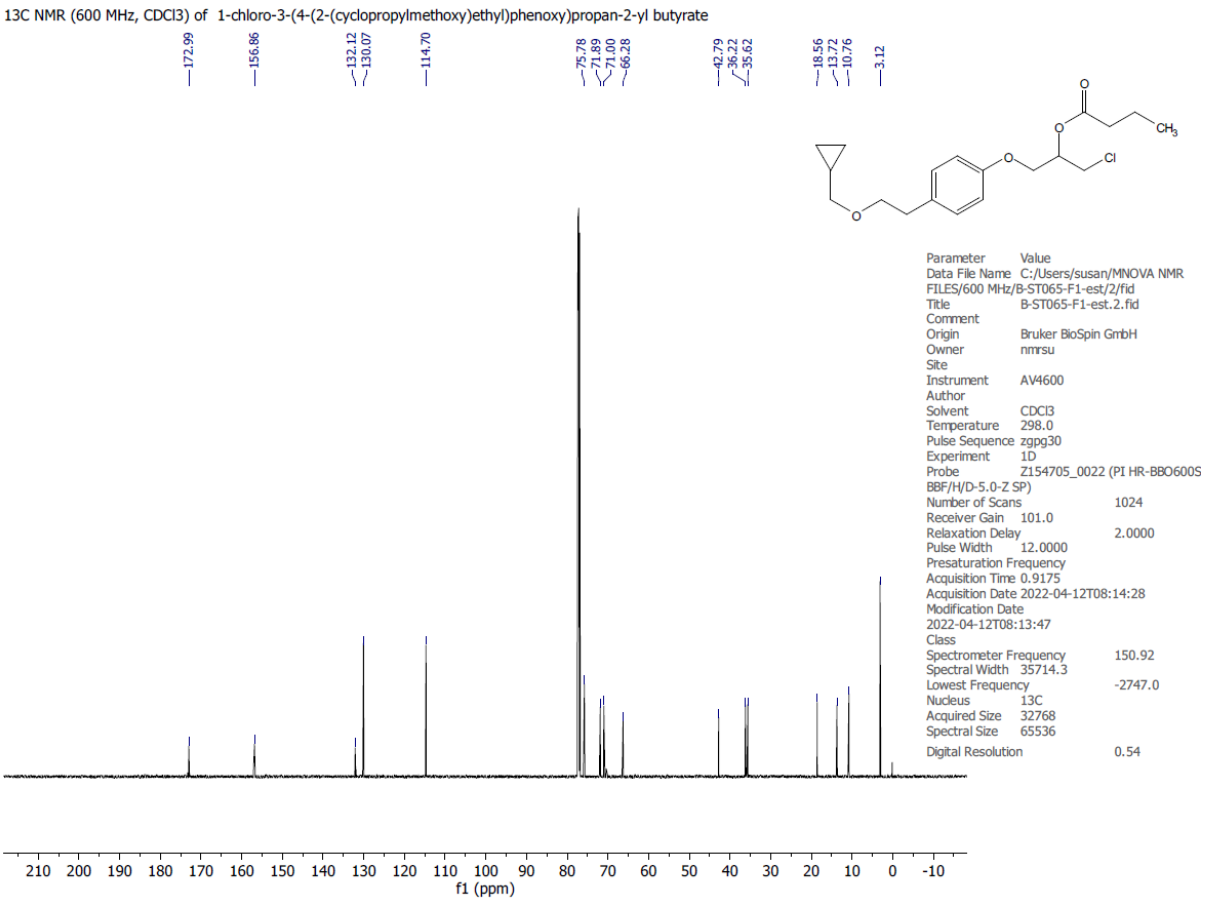


Figure S26. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of 1-chloro-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-yl butanoate (**6a).**

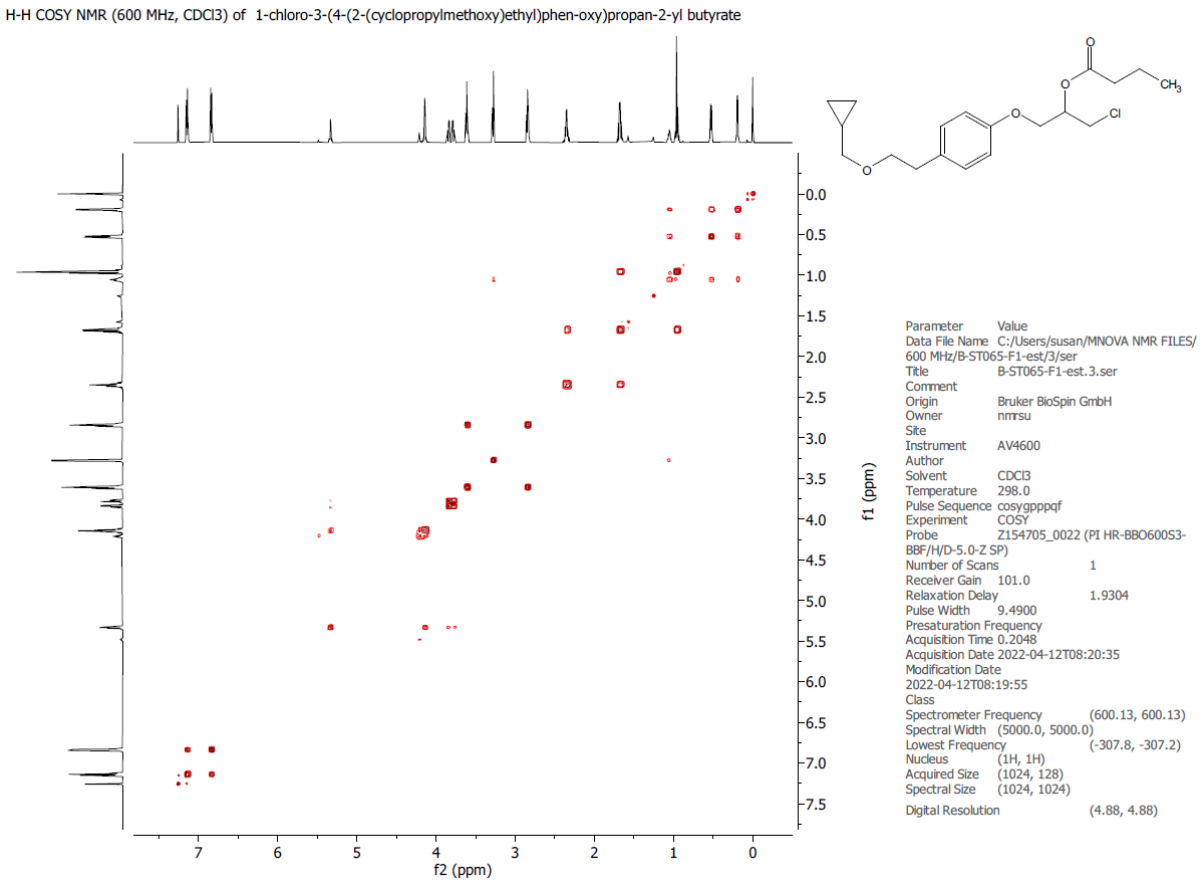


Figure S27. COSY NMR spectrum (600 MHz, $CDCl_3$) of 1-chloro-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-yl butanoate (**6a).**

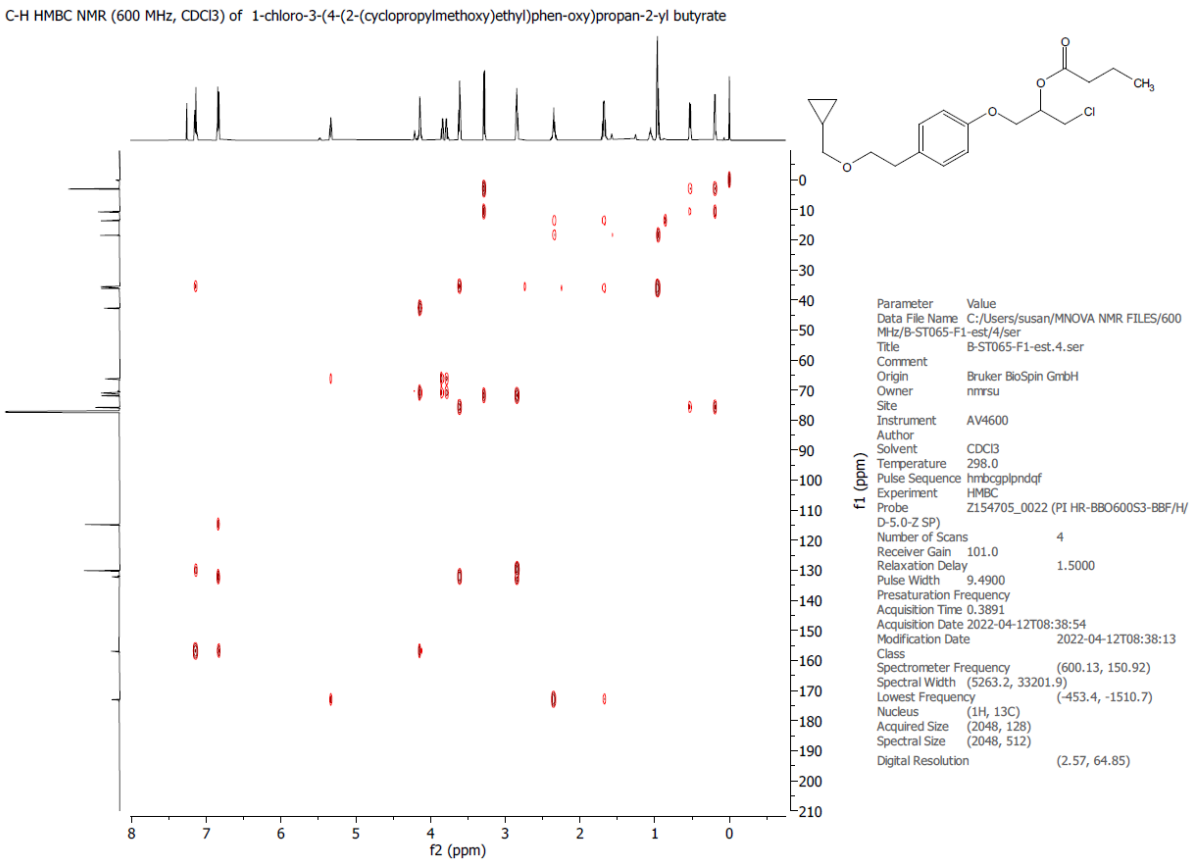


Figure S28. HMBC NMR spectrum (600 MHz, $CDCl_3$) of 1-chloro-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-yl butanoate (**6a).**

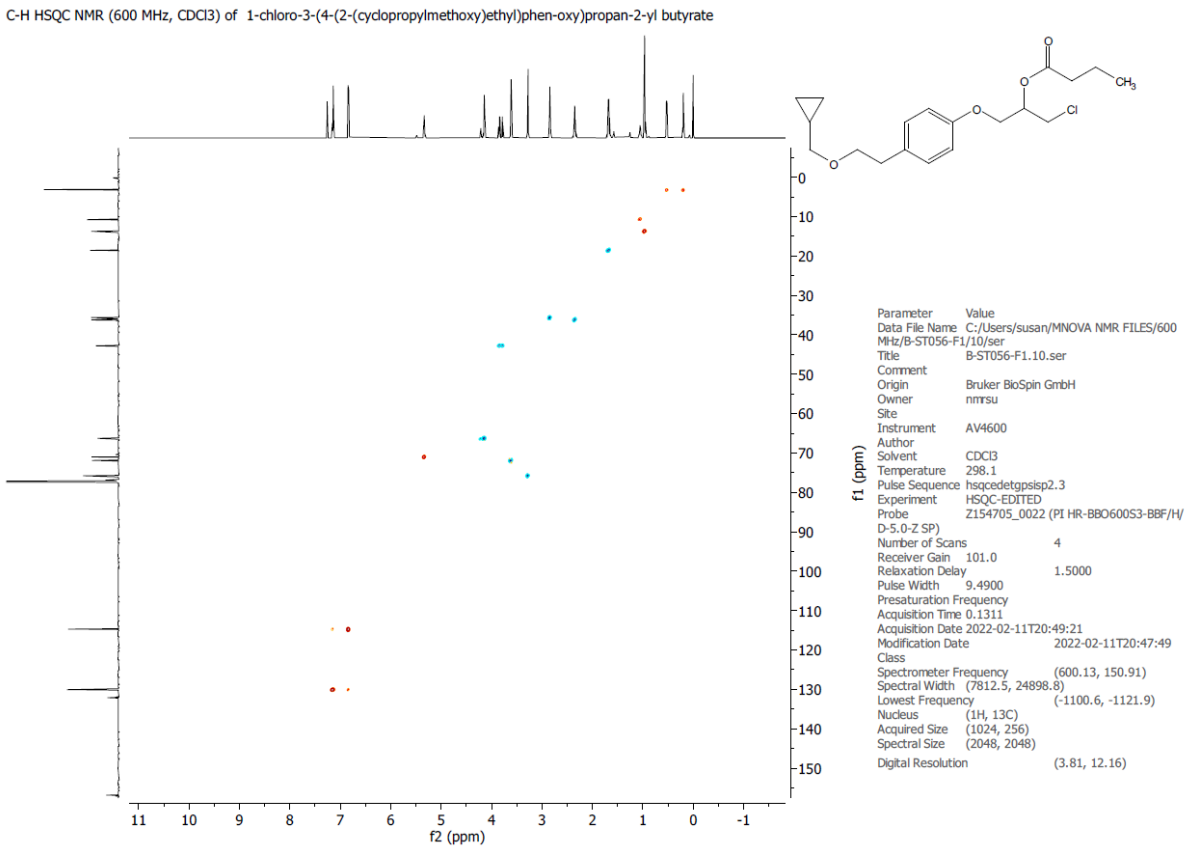


Figure S29. HSQC NMR spectrum (600 MHz, $CDCl_3$) of 1-chloro-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-yl butanoate (**6a).**

*Betaxolol (**7**)*

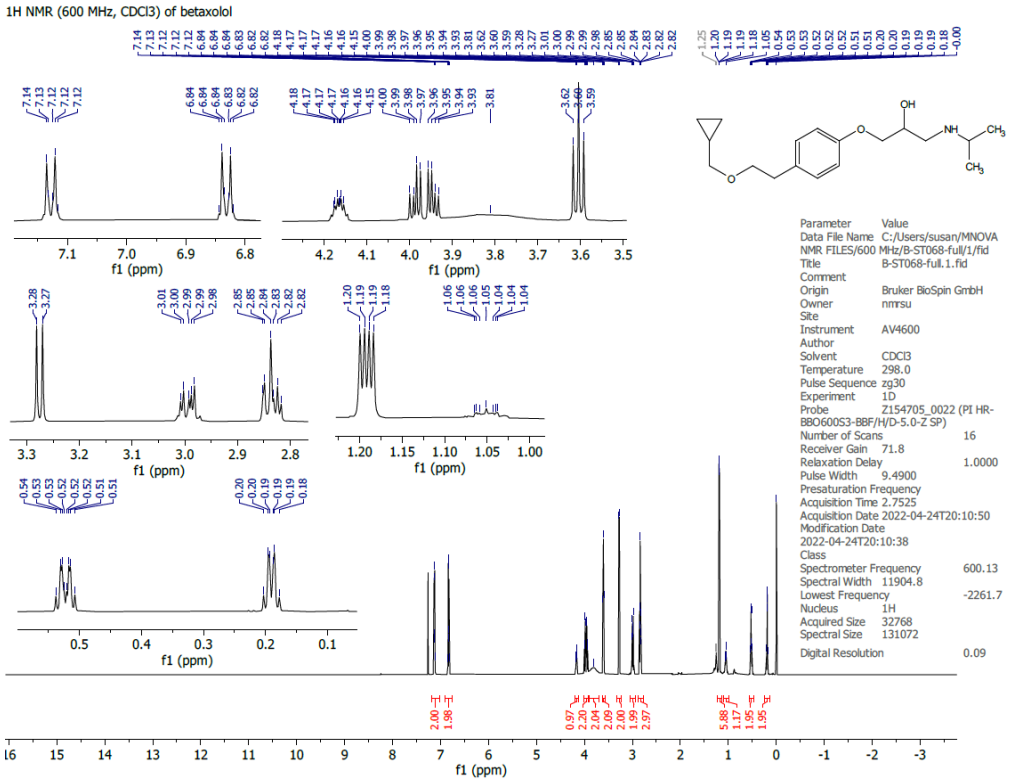


Figure S30. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of betaxolol (**7**).

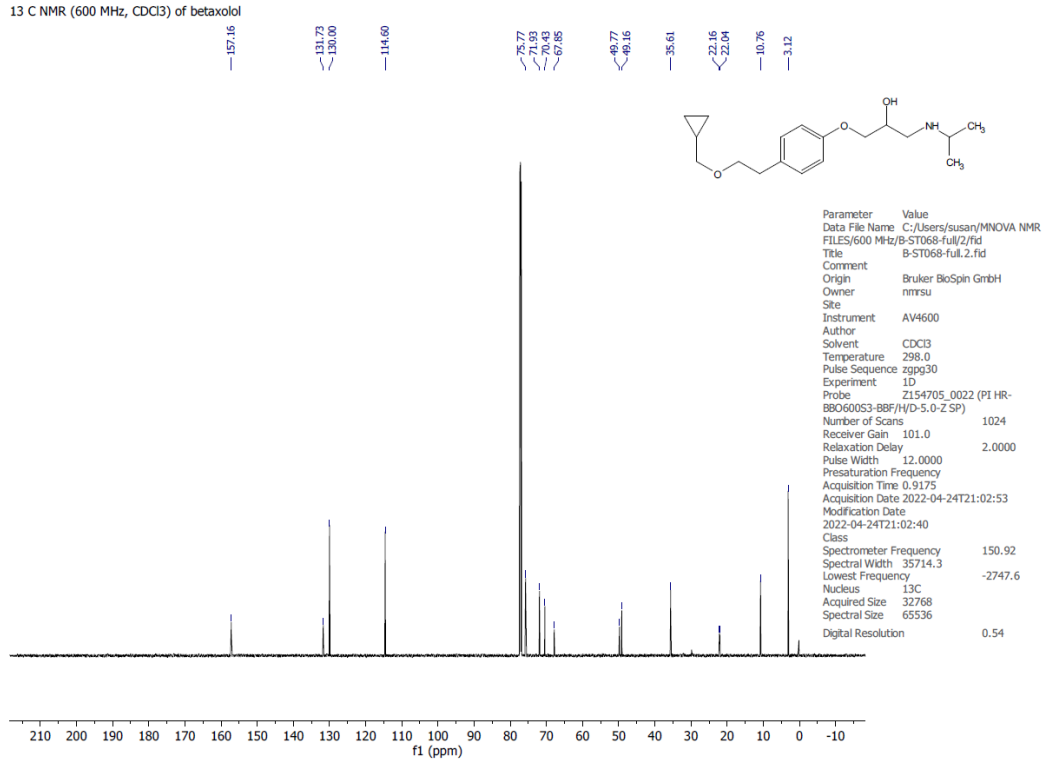


Figure S31. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of betaxolol (**7**).

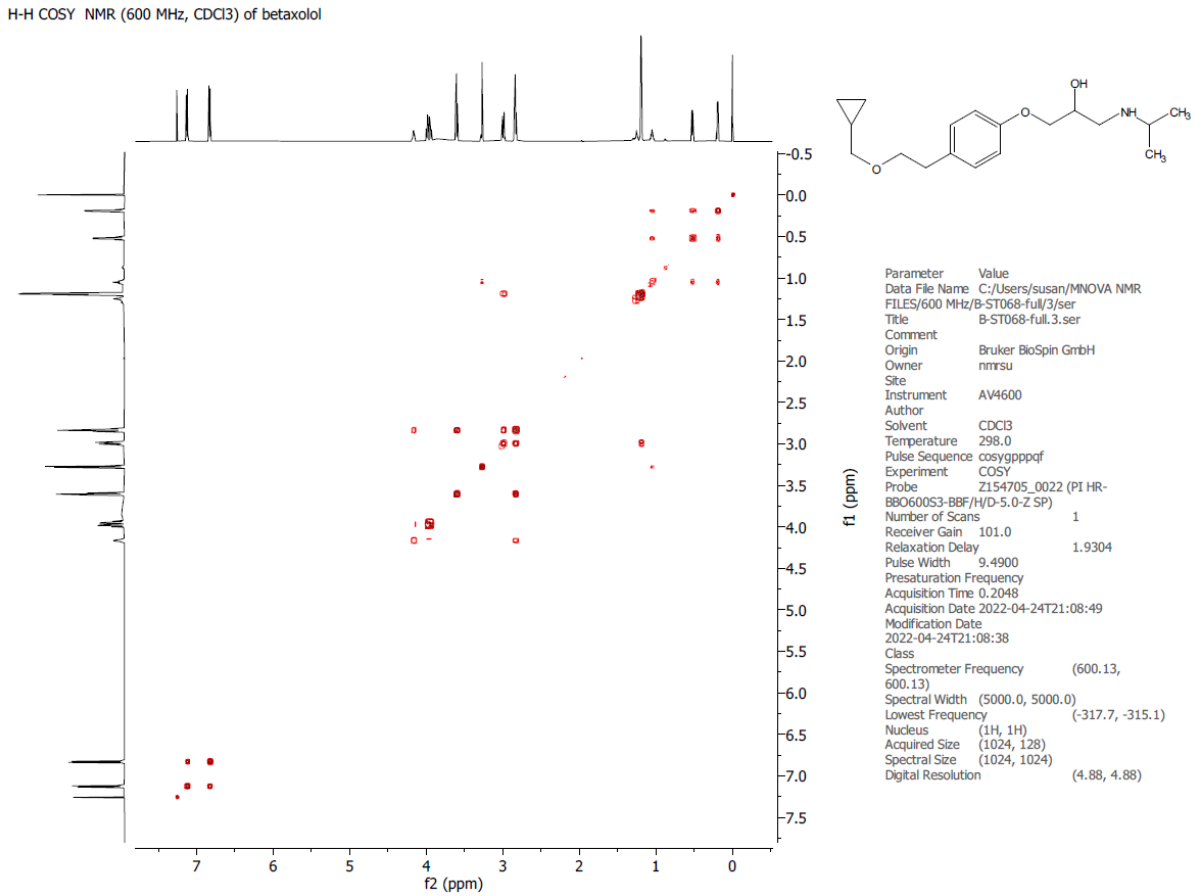


Figure S32. COSY NMR spectrum (600 MHz, $CDCl_3$) of betaxolol (**7**).

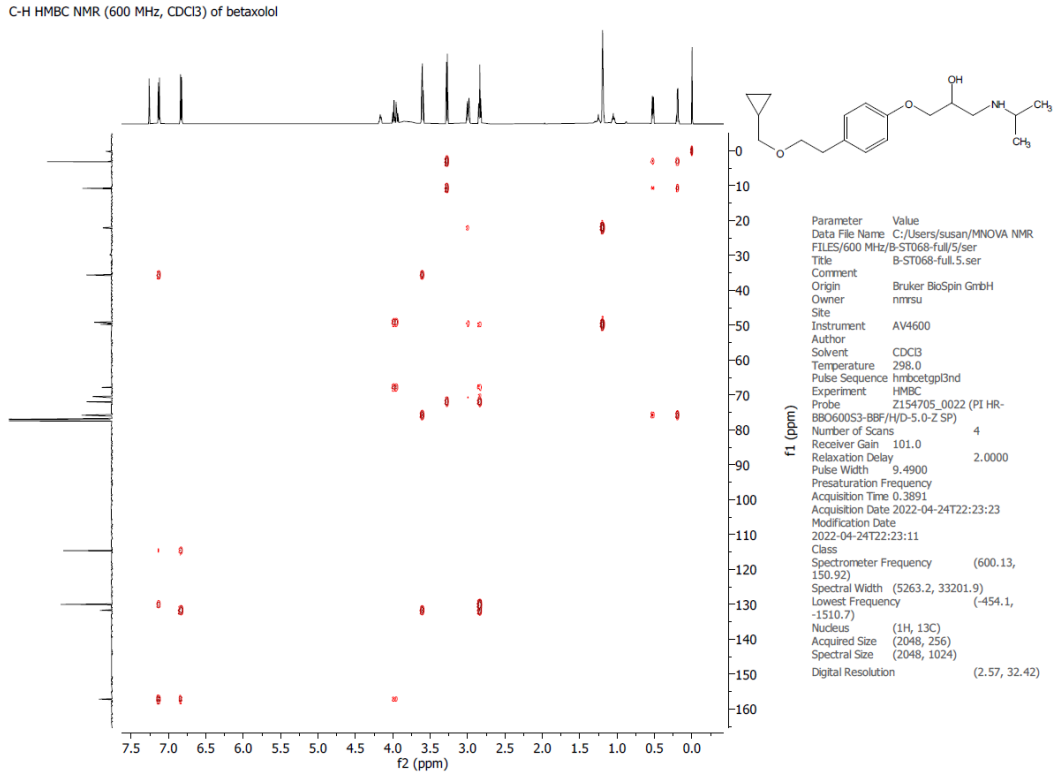


Figure S33. HMBC NMR spectrum (600 MHz, $CDCl_3$) of betaxolol (**7**).

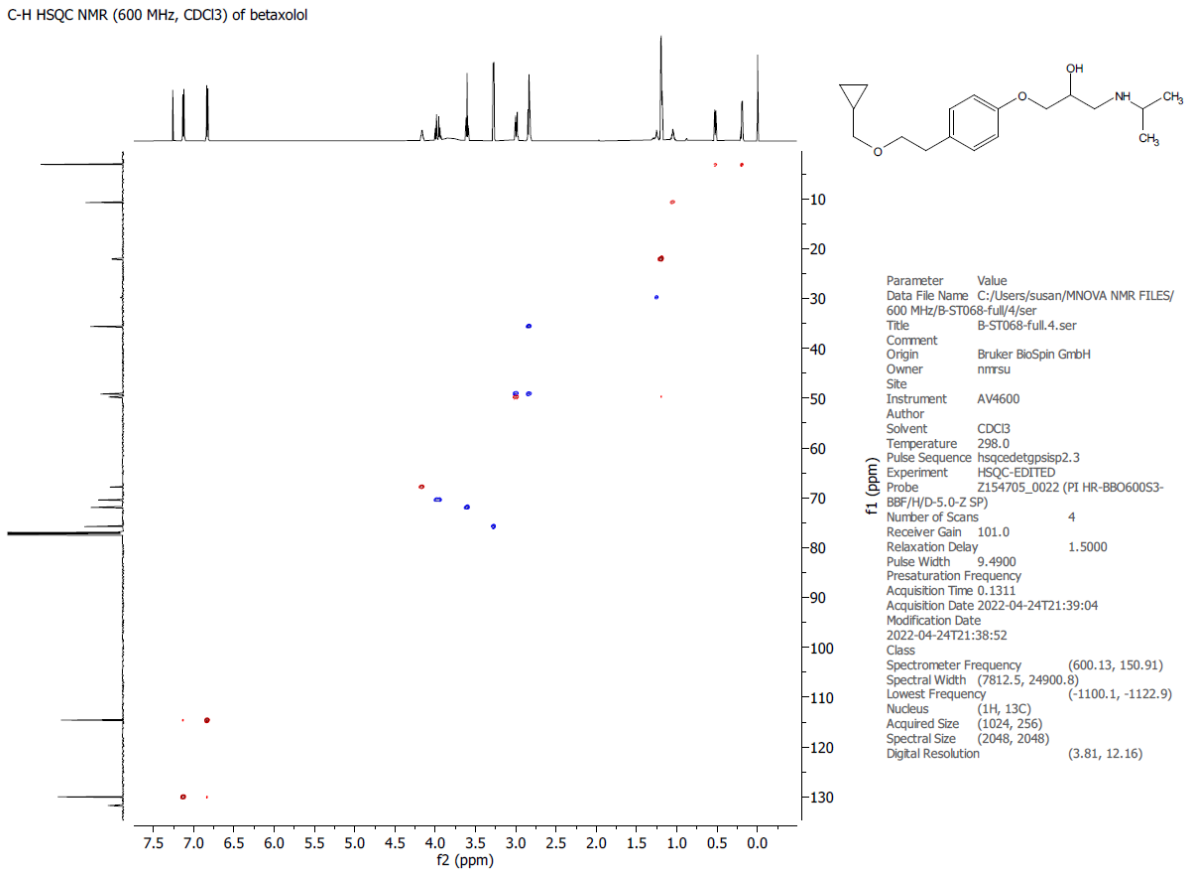


Figure S34. HSQC NMR spectrum (600 MHz, $CDCl_3$) of betaxolol (**7**).

LC-MS DATA

*1-bromo-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-ol (**5b**)*

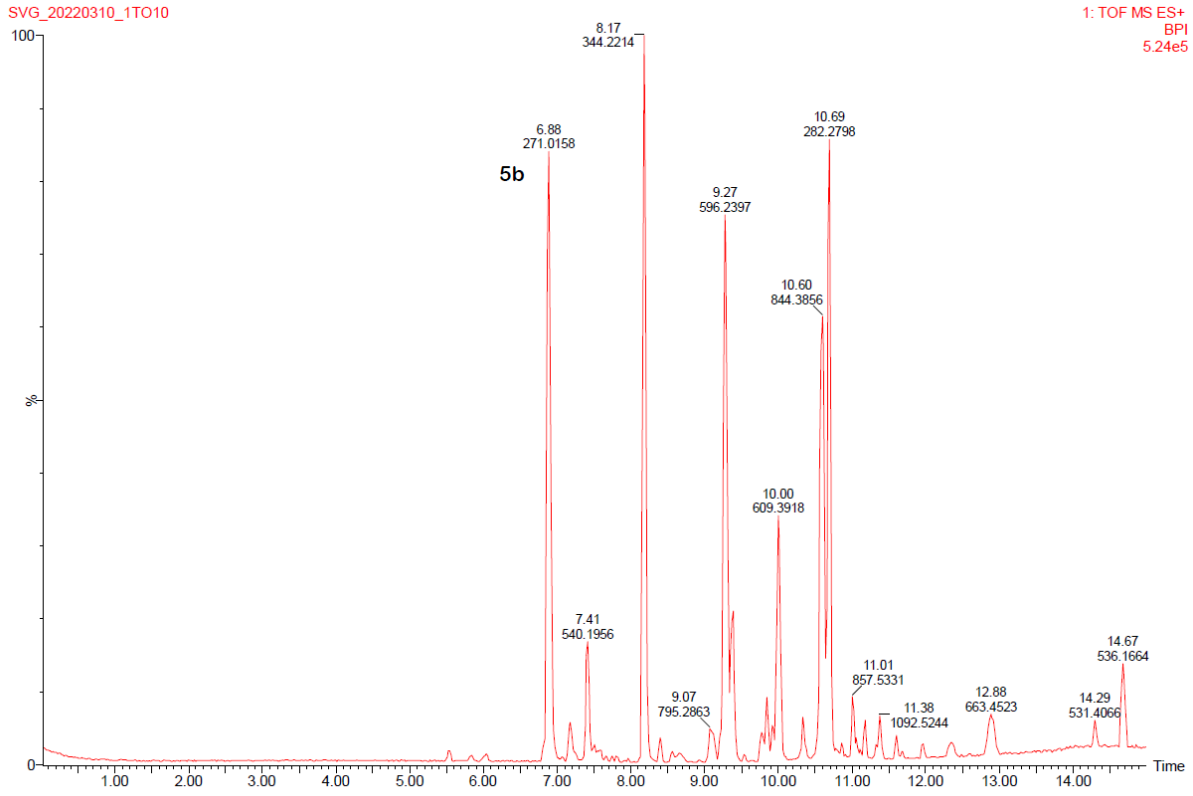
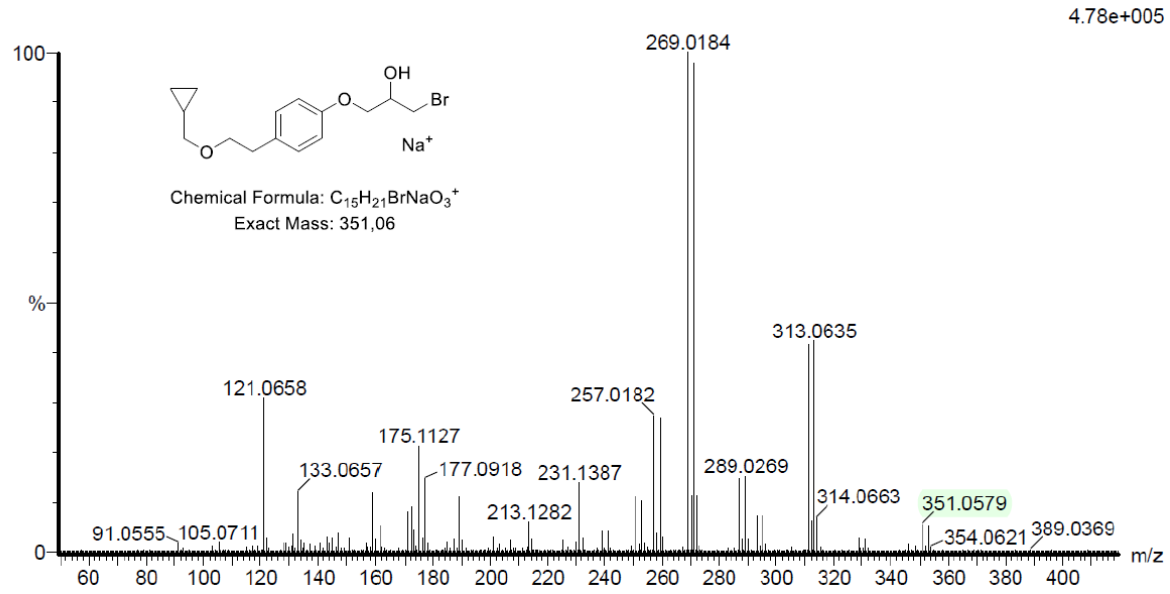


Figure S35. LC-MS chromatogram of 1-bromo-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-ol (**5b**). Performed on an ACQUITY UPLC HSS T3 column (100 mm x2.1 mm ID, 100 Å x 1.8 µm film thickness) with a mobile phase of A: water with 0.12% NH4OH and B: MeCN, flow rate: 0.25 mL min−1. The analyses were run with a gradient of 10-100% B for 12 min, 2 min hold, then 100-10% B for 1 min. Total time 15.0 min. Quadrouple time of flight mass analyzer (QTOF; SYNAPT-G2S) with a ZSpray EIS ion source (Waters, Milford, USA).



Minimum:				-1.5				
Maximum:		5.0	3.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
351.0579	351.0572	0.7	2.0	4.5	974.5	0.080	92.32	C15 H21 O3 Na Br
	351.0569	1.0	2.8	8.5	977.0	2.566	7.68	C13 H16 N6 O Br

Figure S36. TOF MS ES+ spectrum for 5b with m/z = 351.0572 $[M+Na]^+$, from LC-MS analysis shown in Figure S18, at t_R = *6.9 min.*

CHIRAL HPLC DATA

*2-((4-(2-(Cyclopropylmethoxy)ethyl)phenoxy)-methyl)oxirane (**3**)*

```
Data File C:\CHEM32\...SEN TROØYEN\20220214_B-ST056_B-ST044 2022-02-14 11-38-40\001-0101.D
Sample Name: B-ST044-epoxide
    ======================================================================
    Acq. Operator   : Susanne                       Seq. Line :   1
    Acq. Instrument : Instrument 1                   Location : Vial 1
    Injection Date  : 14.02.2022 11:58:53                 Inj :   1
                                                  Inj Volume : 10 µl
    Acq. Method     : C:\Chem32\1\DATA\SUSANNE HANSEN TROØYEN\20220214_B-ST056_B-ST044 2022-02-14
                      11-38-40\KIRAL_SHT_1.M
    Last changed    : 14.02.2022 11:38:23  by Susanne
    Analysis Method : C:\CHEM32\1\DATA\SUSANNE HANSEN TROØYEN\20220214_B-ST056_B-ST044 2022-02-14
                      11-38-40\001-0101.D\DA.M (KIRAL_SHT_1.M)
    Last changed    : 05.04.2022 05:27:00  by Lucas
    Method Info     : Kiral separasjon med Chiralcel OD-H kolonne 250x4.6mm, 5um
                      Solventer: Heksan + ipa

    ======================================================================
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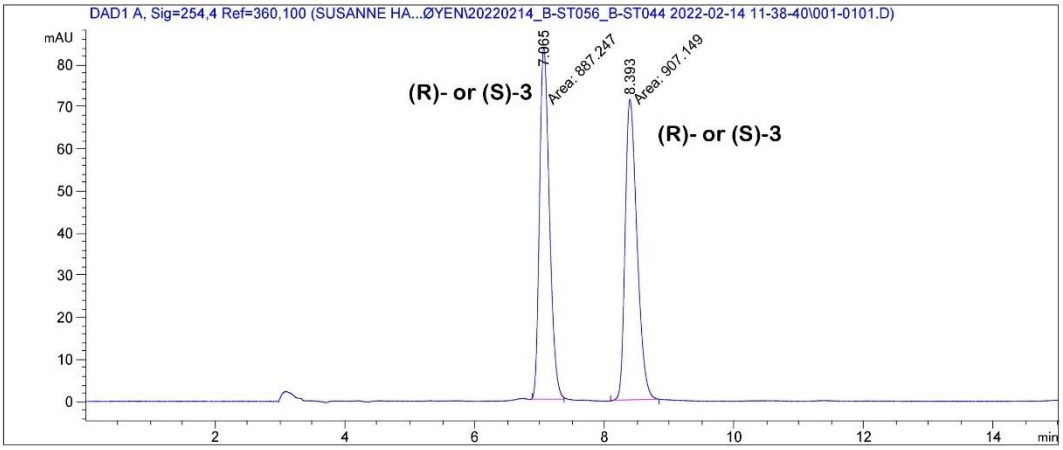


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    ======================================================================
                              Area Percent Report
    ======================================================================

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    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1   7.065 MM    0.1769  887.24689   83.58057  49.4454
       2   8.393 MM    0.2115  907.14948   71.47255  50.5546

    Totals :                  1794.39636  155.05312


    ======================================================================
                              *** End of Report ***

Instrument 1 05.04.2022 05:27:26  Lucas                          Page   1 of 1
```
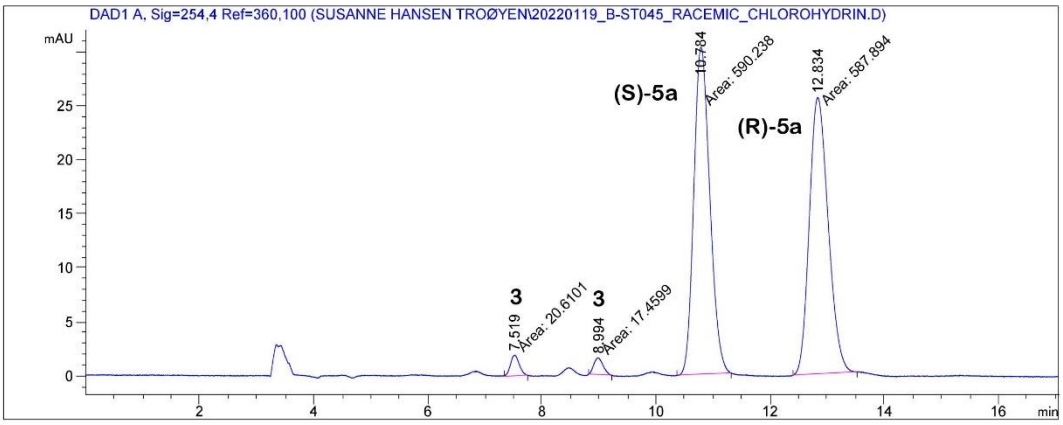

Figure S37. Chiral HPLC chromatogram of **3**. The analysis was performed on a Chiralcel OD-H column with *n*-hexane and *i*-PrOH (90:10) as eluent and 1 mL/min flow, and with a

detection wavelength of 254 nm. The retention times obtained are t_R((*S*)-**3**) = 9.4 min and t_R((*R*)-**3**) = 7.1 min.

*1-Chloro-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-ol (**5a**)*

```
Data File C:\CHEM32\1\DATA\SUSANNE HANSEN TROØYEN\20220119_B-ST045_RACEMIC_CHLOROHYDRIN.D
Sample Name: Racemic chlorohydrin
    ======================================================================
    Acq. Operator   : Susanne
    Acq. Instrument : Instrument 1                    Location : Vial 3
    Injection Date  : 19.01.2022 11:17:33
                                                    Inj Volume : 10 µl
    Acq. Method     : C:\CHEM32\1\METHODS\ELISABETH JACOBSEN\KIRAL_SHT_1.M
    Last changed    : 19.01.2022 10:42:03  by Susanne
                      (modified after loading)
    Analysis Method : C:\CHEM32\1\DATA\SUSANNE HANSEN TROØYEN\20220119_B-ST045_RACEMIC_
                      CHLOROHYDRIN.D\DA.M (KIRAL_SHT_1.M)
    Last changed    : 05.04.2022 05:29:44  by Lucas
    Method Info     : Kiral separasjon med Chiralcel OD-H kolonne 250x4.6mm, 5um
                      Solventer: Heksan + ipa

    Sample Info     : 90% n-hexane 10% IPA 1mL/min


    ======================================================================
```

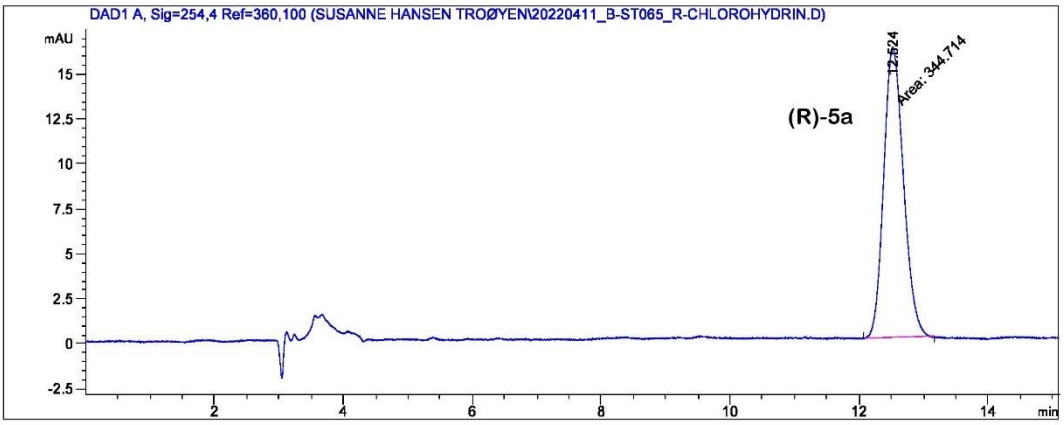



```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1   7.519 MM    0.1778   20.61008    1.93238   1.6946
       2   8.994 MM    0.1877   17.45990    1.55045   1.4356
       3  10.784 MM    0.3249  590.23779   30.28229  48.5312
       4  12.834 MM    0.3828  587.89429   25.59438  48.3385

    Totals :                  1216.20205   59.35949


    ======================================================================
                               *** End of Report ***


Instrument 1 05.04.2022 05:30:09  Lucas                          Page   1 of 1
```

Figure S38. Chiral HPLC chromatogram of **5a**. The analysis was performed on a Chiralcel OD-H column with *n*-hexane and *i*-PrOH (90:10) as eluent and 1 mL/min flow, and with a detection wavelength of 254 nm. The retention times obtained are t_R((*S*)-**5a**) = 10.8 min, t_R((*R*)-**5a**) = 12.8 min.

*(R)-1-Chloro-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-ol, (R)-**5a***

```
Data File C:\CHEM32\1\DATA\SUSANNE HANSEN TROØYEN\20220411_B-ST065_R-CHLOROHYDRIN.D
Sample Name: B-ST065-F2-chlorohydr
    ======================================================================
    Acq. Operator   : Susanne
    Acq. Instrument : Instrument 1                    Location : Vial 2
    Injection Date  : 11.04.2022 03:10:18
                                                    Inj Volume : 10 µl
    Acq. Method     : C:\CHEM32\1\METHODS\ELISABETH JACOBSEN\KIRAL_SHT_1.M
    Last changed    : 11.04.2022 03:10:01  by Susanne
    Analysis Method : C:\CHEM32\1\DATA\SUSANNE HANSEN TROØYEN\20220411_B-ST065_R-CHLOROHYDRIN.D\
                      DA.M (KIRAL_SHT_1.M)
    Last changed    : 11.04.2022 04:23:38  by Lucas
    Method Info     : Kiral separasjon med Chiralcel OD-H kolonne 250x4.6mm, 5um
                      Solventer: Heksan + ipa

    Sample Info     : 90% hexane 10% IPA CALB chlorohydrin after FC


    ======================================================================
```

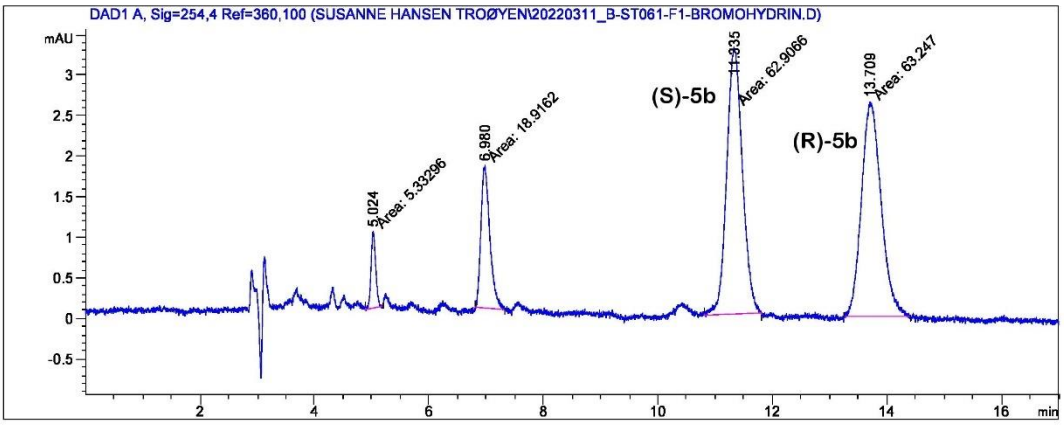



```
    ======================================================================
                              Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  12.524 MM    0.3556  344.71445   16.15702 100.0000

    Totals :                   344.71445   16.15702

    ======================================================================
                              *** End of Report ***


Instrument 1 11.04.2022 04:24:01  Lucas                          Page   1 of 1
```

Figure S39. Chiral HPLC chromatogram of (*R*)-**5a**. The analysis was performed on a Chiralcel OD-H column with *n*-hexane and *i*-PrOH (90:10) as eluent and 1 mL/min flow, and with a detection wavelength of 254 nm. The retention time is t_R((*R*)-**5a**) = 12.5 min.

*1-Bromo-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-ol (**5b**)*

```
Data File C:\CHEM32\1\DATA\SUSANNE HANSEN TROØYEN\20220311_B-ST061-F1-BROMOHYDRIN.D
Sample Name: B-ST061-F1-bromohydrin
    ======================================================================
    Acq. Operator   : Susanne
    Acq. Instrument : Instrument 1                    Location : Vial 2
    Injection Date  : 11.03.2022 11:06:03
                                                    Inj Volume : 10 µl
    Acq. Method     : C:\CHEM32\1\METHODS\ELISABETH JACOBSEN\KIRAL_SHT_1.M
    Last changed    : 11.03.2022 11:05:48  by Susanne
    Analysis Method : C:\CHEM32\1\DATA\SUSANNE HANSEN TROØYEN\20220311_B-ST061-F1-BROMOHYDRIN.D\
                      DA.M (KIRAL_SHT_1.M)
    Last changed    : 05.04.2022 05:32:26  by Lucas
                      (modified after loading)
    Method Info     : Kiral separasjon med Chiralcel OD-H kolonne 250x4.6mm, 5um
                      Solventer: Heksan + ipa

    Sample Info     : 90% n-hexane 10% IPA sep bromohydrin (betaxolol)


    ======================================================================
```

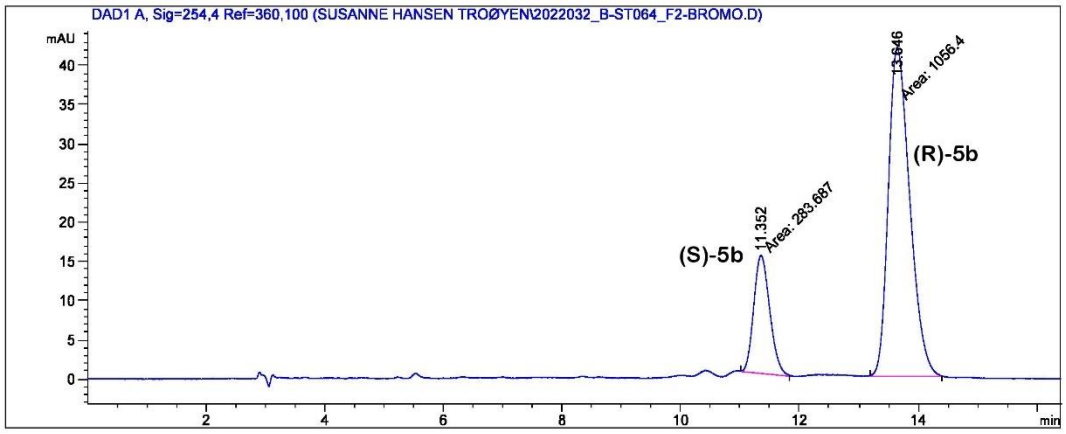



```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1   5.024 MM    0.0940    5.33296 9.45676e-1   3.5458
       2   6.980 MM    0.1792   18.91615    1.75959  12.5770
       3  11.335 MM    0.3189   62.90660    3.28753  41.8254
       4  13.709 MM    0.3981   63.24703    2.64774  42.0518

    Totals :                   150.40274    8.64054


    ======================================================================
                              *** End of Report ***


Instrument 1 05.04.2022 05:32:28  Lucas                          Page   1 of 1
```

Figure S40. Chiral HPLC chromatogram of **5b**. The analysis was performed on a Chiralcel OD-H column with *n*-hexane and *i*-PrOH (90:10) as eluent and 1 mL/min flow, and with a detection wavelength of 254 nm. The retention times are t_R((*S*)-**5b**) = 11.3 min, t_R((*R*)-**5b**) = 13.7 min.

*(R)-1-Bromo-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-ol, (R)-**5b***

```
Data File C:\CHEM32\1\DATA\SUSANNE HANSEN TROØYEN\2022032_B-ST064_F2-BROMO.D
Sample Name: B-ST064-bromohydrin
    ======================================================================
    Acq. Operator   : Susanne
    Acq. Instrument : Instrument 1                    Location : Vial 2
    Injection Date  : 06.04.2022 02:15:03
                                                   Inj Volume : 10 µl
    Acq. Method     : C:\CHEM32\1\METHODS\ELISABETH JACOBSEN\KIRAL_SHT_1.M
    Last changed    : 06.04.2022 02:13:47  by Susanne
    Analysis Method : C:\CHEM32\1\DATA\SUSANNE HANSEN TROØYEN\2022032_B-ST064_F2-BROMO.D\DA.M
    Last changed    : 06.04.2022 02:35:35  by Lucas
    Method Info     : Kiral separasjon med Chiralcel OD-H kolonne 250x4.6mm, 5um
                      Solventer: Heksan + ipa

    Sample Info     : 90% n-hexane 10% IPA bromohydrin after purification fro
                      m calb

    ======================================================================
```

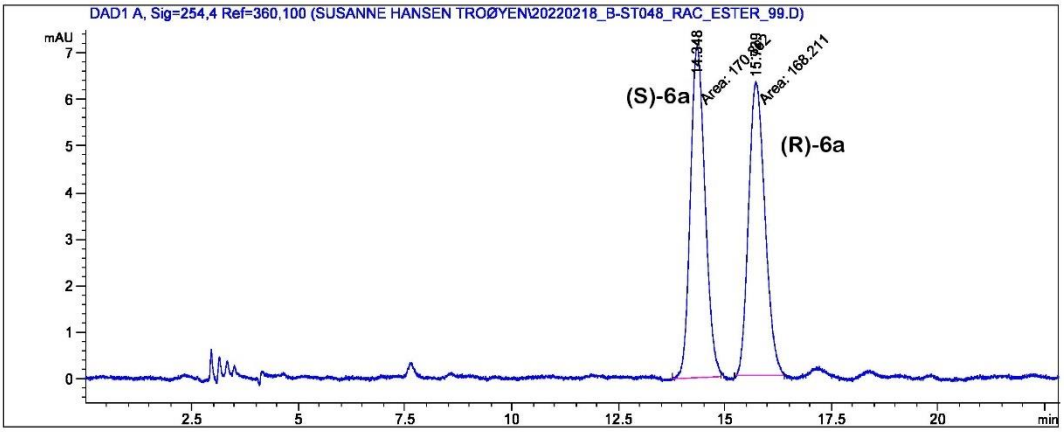



```
    ======================================================================
                            Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  11.352 MM    0.3137  283.68704   15.07188  21.1694
       2  13.646 MM    0.4198 1056.39661   41.94152  78.8306

    Totals :                  1340.08365   57.01341

    ======================================================================
                              *** End of Report ***


Instrument 1 06.04.2022 02:35:59  Lucas                          Page   1 of 1
```

Figure S41. Chiral HPLC chromatogram of enantiomerically enriched (*R*)-**5b**. The analysis was performed on a Chiralcel OD-H column with *n*-hexane and *i*-PrOH (90:10) as eluent and 1 mL/min flow, and with a detection wavelength of 254 nm. The retention times are t_R((*S*)-**5b**) = 11.3 min, t_R((*R*)-**5b**) = 13.6 min.

*1-chloro-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-yl butanoate (**6a**)*

```
Data File C:\CHEM32\1\DATA\SUSANNE HANSEN TROØYEN\20220218_B-ST048_RAC_ESTER_99.D
Sample Name: B-ST048_rac_ester
    ======================================================================
    Acq. Operator   : Susanne
    Acq. Instrument : Instrument 1                    Location : Vial 1
    Injection Date  : 18.02.2022 10:28:50
                                                    Inj Volume : 10 µl
    Acq. Method     : C:\CHEM32\1\METHODS\ELISABETH JACOBSEN\KIRAL_SHT_CALB_GRAD_2.M
    Last changed    : 18.02.2022 10:07:37  by Susanne
    Analysis Method : C:\CHEM32\1\DATA\SUSANNE HANSEN TROØYEN\20220218_B-ST048_RAC_ESTER_99.D\DA.
                      M (KIRAL_SHT_CALB_GRAD_2.M)
    Last changed    : 05.04.2022 05:33:10  by Lucas
    Method Info     : Kiral separasjon med Chiralcel OD-H kolonne 250x4.6mm, 5um
                      Solventer: Heksan + ipa

    Sample Info     : 99% hexane 1% IPA betaxolol racemic ester separation.


    ======================================================================
```

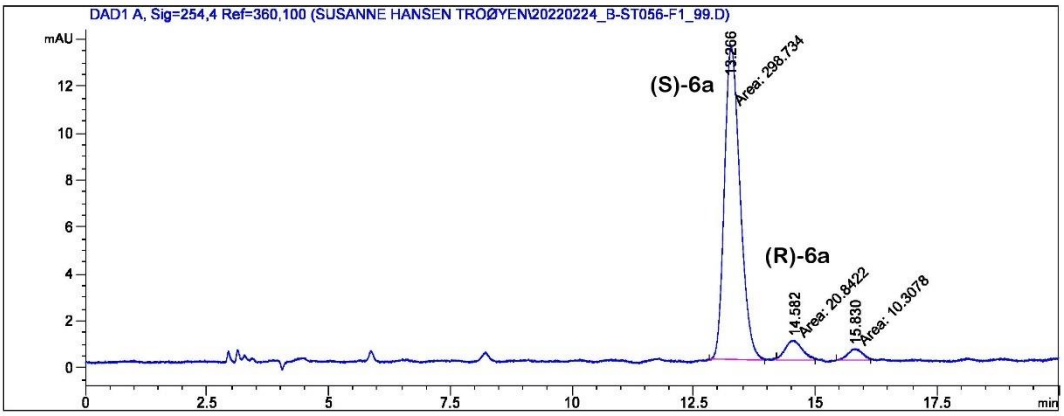



```
    ======================================================================
                              Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  14.348 MM    0.3991  170.36200    7.11436  50.3177
       2  15.729 MM    0.4442  168.21086    6.31114  49.6823

    Totals :                   338.57286   13.42550


    ======================================================================
                              *** End of Report ***


    Instrument 1 05.04.2022 05:33:37  Lucas                          Page   1 of 1
```

Figure S42. Chiral HPLC chromatogram of **6a**. The analysis was performed on a Chiralcel OD-H column with *n*-hexane and *i*-PrOH (99:1) as eluent and 1 mL/min flow, and with a detection wavelength of 254 nm. The retention times are t_R((*S*)-**6a**) = 14.4 min, t_R((*R*)-**6a**) = 15.7 min.

*(S)-1-Chloro-3-(4-(2-(cyclopropylmethoxy)ethyl)phenoxy)propan-2-yl butanoate, (S)-**6a***

```
Data File C:\CHEM32\1\DATA\SUSANNE HANSEN TROØYEN\20220224_B-ST056-F1_99.D
Sample Name: B-ST056-ester
    ======================================================================
    Acq. Operator   : Susanne
    Acq. Instrument : Instrument 1                    Location : Vial 1
    Injection Date  : 24.02.2022 09:20:30
                                                    Inj Volume : 10 µl
    Acq. Method     : C:\CHEM32\1\METHODS\ELISABETH JACOBSEN\KIRAL_SHT_CALB_GRAD.M
    Last changed    : 24.02.2022 08:50:42  by Susanne
    Analysis Method : C:\CHEM32\1\DATA\SUSANNE HANSEN TROØYEN\20220224_B-ST056-F1_99.D\DA.M (
                      KIRAL_SHT_CALB_GRAD.M)
    Last changed    : 13.04.2022 10:35:51  by Lucas
                      (modified after loading)
    Method Info     : Kiral separasjon med Chiralcel OD-H kolonne 250x4.6mm, 5um
                      Solventer: Heksan + ipa

    Sample Info     : 99% n-hexane 1% IPA sep of ester from CALB kinetic res
                      (gradient)

    ======================================================================
```

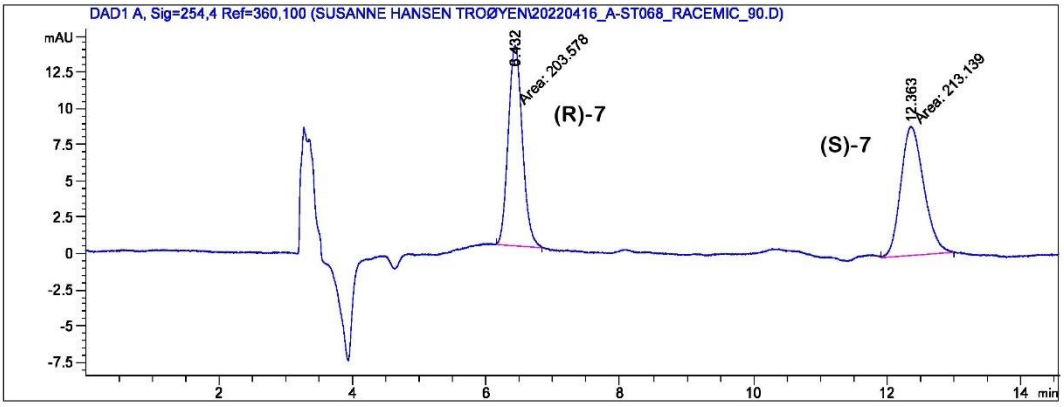



```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  13.266 MM    0.3738  298.73386   13.31897  90.5573
       2  14.582 MM    0.4106   20.84216 8.45972e-1   6.3180
       3  15.830 MM    0.3478   10.30780 4.93923e-1   3.1247

    Totals :                   329.88381   14.65887


    ======================================================================
                              *** End of Report ***


Instrument 1 13.04.2022 10:35:55  Lucas                          Page   1 of 1
```

Figure S43. Chiral HPLC chromatogram of enantiomerically enriched (*S*)-**6a**. The analysis was performed on a Chiralcel OD-H column with *n*-hexane and *i*-PrOH (99:1) as eluent and 1 mL/min flow, and with a detection wavelength of 254 nm. The retention times are t_R((*S*)-**6a**) = 13.3 min, t_R((*R*)-**6a**) = 14.6 min.

*Betaxolol (**7**)*

```
Data File C:\CHEM32\1\DATA\SUSANNE HANSEN TROØYEN\20220416_A-ST068_RACEMIC_90.D
Sample Name: B-68-rac
    ======================================================================
    Acq. Operator   : Susanne
    Acq. Instrument : Instrument 1                    Location : Vial 3
    Injection Date  : 16.04.2022 05:26:23
                                                    Inj Volume : 10 µl
    Acq. Method     : C:\CHEM32\1\METHODS\ELISABETH JACOBSEN\KIRAL_3_DEA.M
    Last changed    : 16.04.2022 05:25:46  by Susanne
    Analysis Method : C:\CHEM32\1\DATA\SUSANNE HANSEN TROØYEN\20220416_A-ST068_RACEMIC_90.D\DA.M
                      (KIRAL_3_DEA.M)
    Last changed    : 16.04.2022 05:42:44  by Lucas
    Method Info     : Kiral separasjon med Chiralcel OD-H kolonne 250x4.6mm, 5um
                      Solventer: Heksan + ipa

    Sample Info     : 90% hexane 10% IPA  w 2% DEA betaxolol sep, in IPA
```

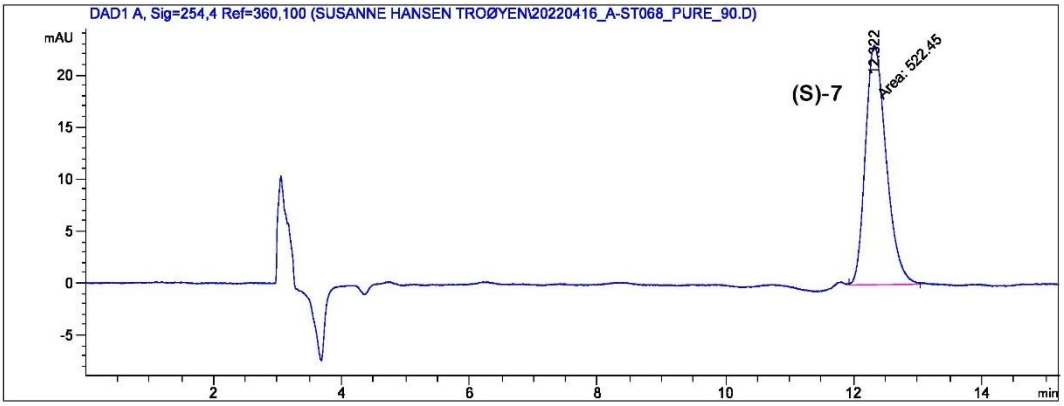



```
    ======================================================================
                              Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1   6.432 MM    0.2452  203.57849   13.83809  48.8529
       2  12.363 MM    0.3992  213.13907    8.89915  51.1471

    Totals :                   416.71756   22.73724


    ======================================================================
                              *** End of Report ***

Instrument 1 16.04.2022 05:42:58  Lucas                          Page   1 of 1
```

Figure S44. Chiral HPLC chromatogram of **7**. The analysis was performed on a Chiralcel OD-H column with *n*-hexane:*i*-PrOH:diethylamine (90:9.8:0.2) as eluent and 1 mL/min flow, and with a detection wavelength of 254 nm. The retention times are t_R((*R*)-**7**) = 6.4 min, t_R((*S*)-**7**) = 12.4 min.

*(S)-Betaxolol, (S)-**7***

```
Data File C:\CHEM32\1\DATA\SUSANNE HANSEN TROØYEN\20220416_A-ST068_PURE_90.D
Sample Name: B-68
    ======================================================================
    Acq. Operator   : Susanne
    Acq. Instrument : Instrument 1                    Location : Vial 2
    Injection Date  : 16.04.2022 04:49:28
                                                    Inj Volume : 10 µl
    Acq. Method     : C:\CHEM32\1\METHODS\ELISABETH JACOBSEN\KIRAL_3_DEA.M
    Last changed    : 16.04.2022 04:48:38  by Susanne
    Analysis Method : C:\CHEM32\1\DATA\SUSANNE HANSEN TROØYEN\20220416_A-ST068_PURE_90.D\DA.M (
                      KIRAL_3_DEA.M)
    Last changed    : 16.04.2022 05:57:49  by Lucas
    Method Info     : Kiral separasjon med Chiralcel OD-H kolonne 250x4.6mm, 5um
                      Solventer: Heksan + ipa

    Sample Info     : 90% hexane 10% IPA  w 2% DEA betaxolol sep, in IPA
```




```
    ======================================================================
                            Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  12.322 MM    0.3781  522.44952   23.03251 100.0000

    Totals :                   522.44952   23.03251


    ======================================================================
                              *** End of Report ***


Instrument 1 16.04.2022 05:58:03  Lucas                          Page   1 of 1
```

Figure S45. Chiral HPLC chromatogram of (*S*)-**7**. The analysis was performed on a Chiralcel OD-H column with *n*-hexane:*i*-PrOH:diethylamine (90:9.8:0.2) as eluent and 1 mL/min flow, and with a detection wavelength of 254 nm. The retention time is t_R((*S*)-**7**) = 12.3 min.