Supplementary Information

First total synthesis and evaluation of the α-glucosidase inhibitory activity of (±)-methyl dihydromarmesinate, an anti-inflammatory phenylpropanoid from *Ficus hirta* Vahl., and related benzofurans

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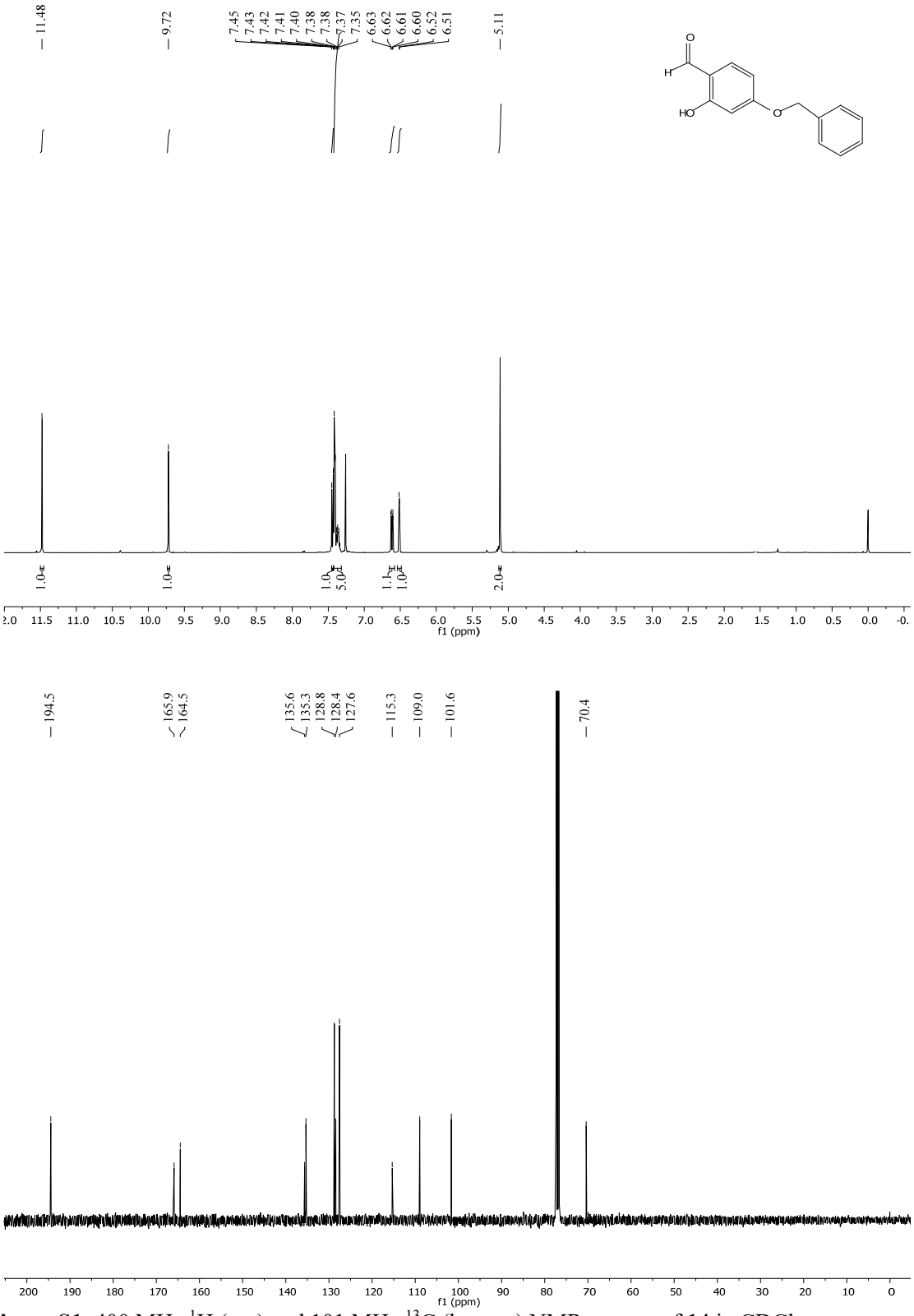


Figure S1. 400 MHz ^{1}H (top) and 101 MHz ^{13}C (bottom) NMR spectra of **14** in $CDCl_3$.

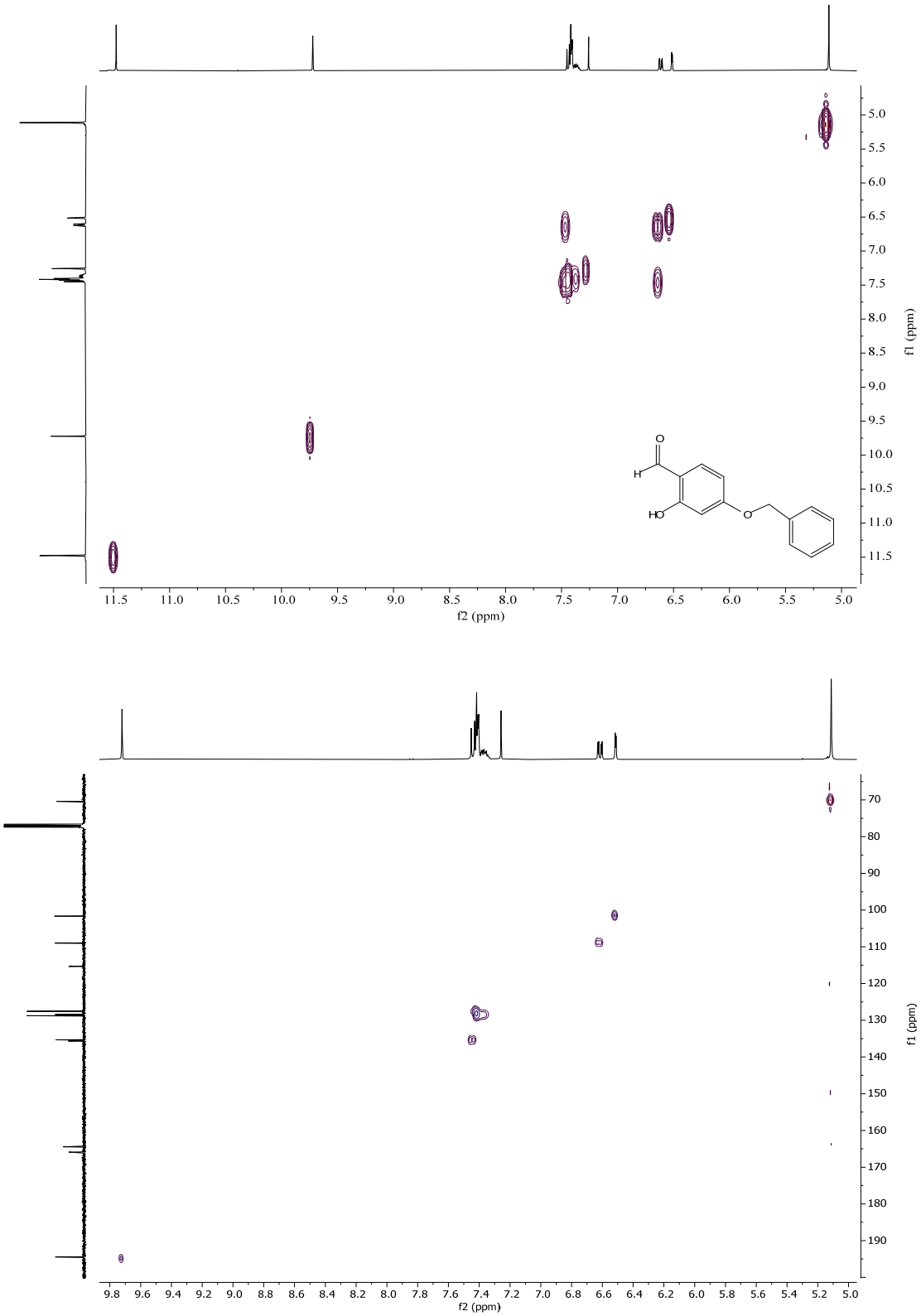


Figure S2. COSY (top) and HSQC (bottom) spectra of compound **14** in $CDCl_3$.

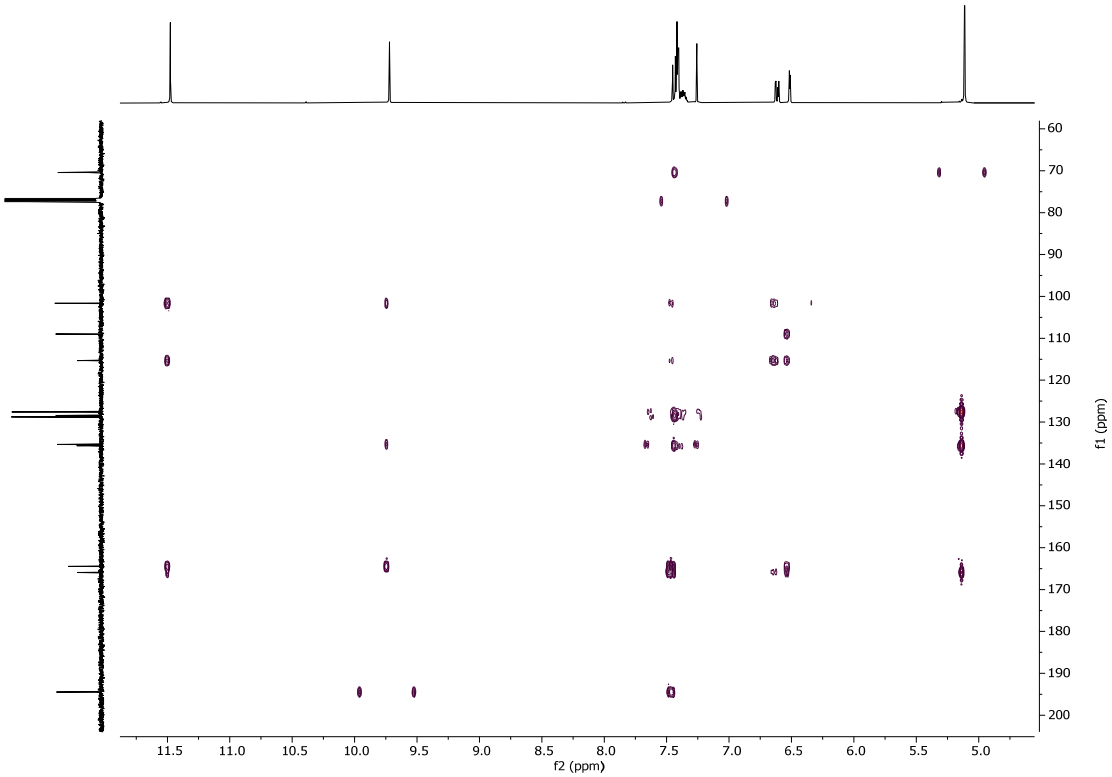


Figure S3. HMBC spectrum of compound **14** in $CDCl_3$.

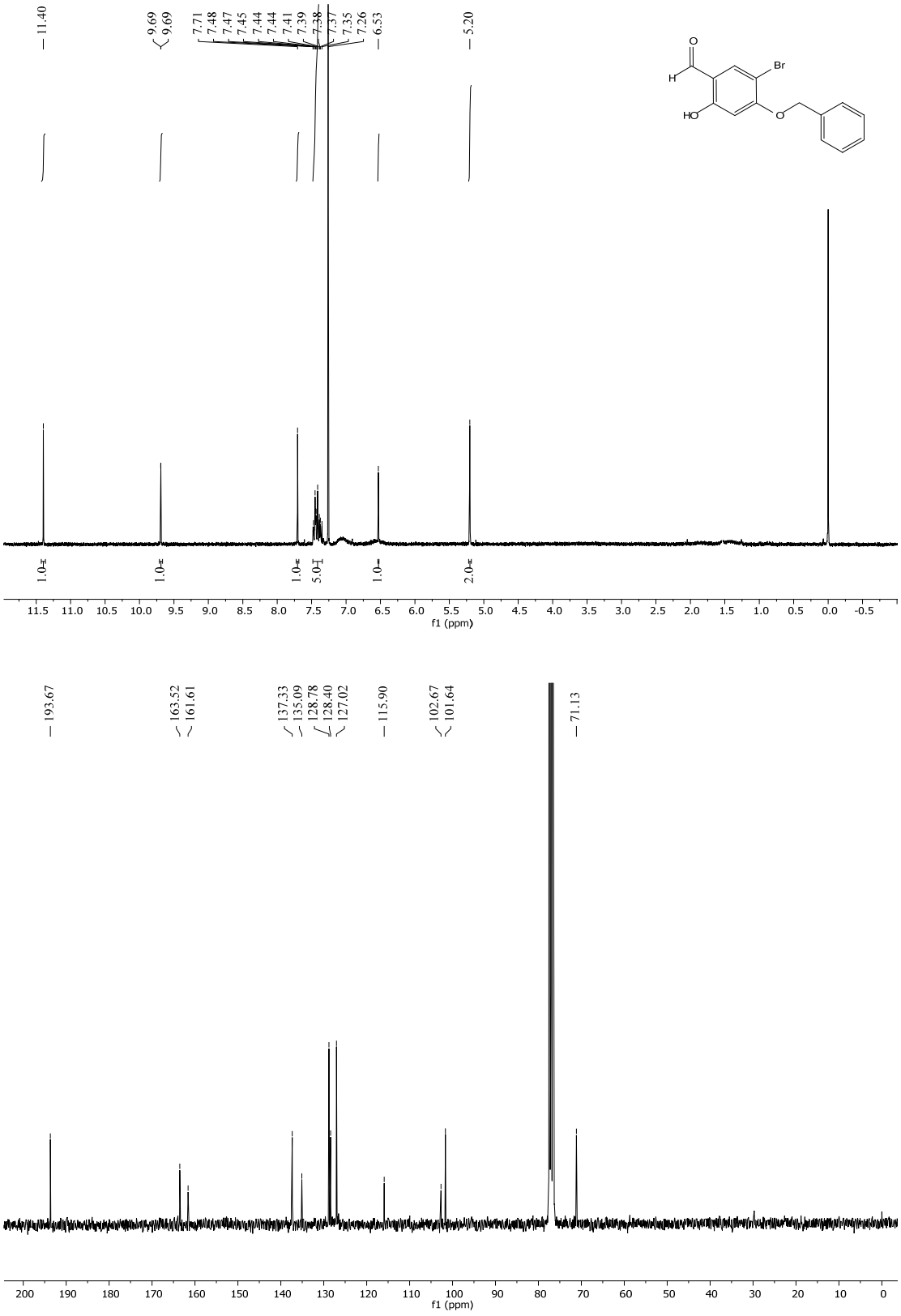


Figure S4. 300 MHz ^{1}H (top) and 75 MHz ^{13}C (bottom) NMR spectra of **17** in $CDCl_3$.

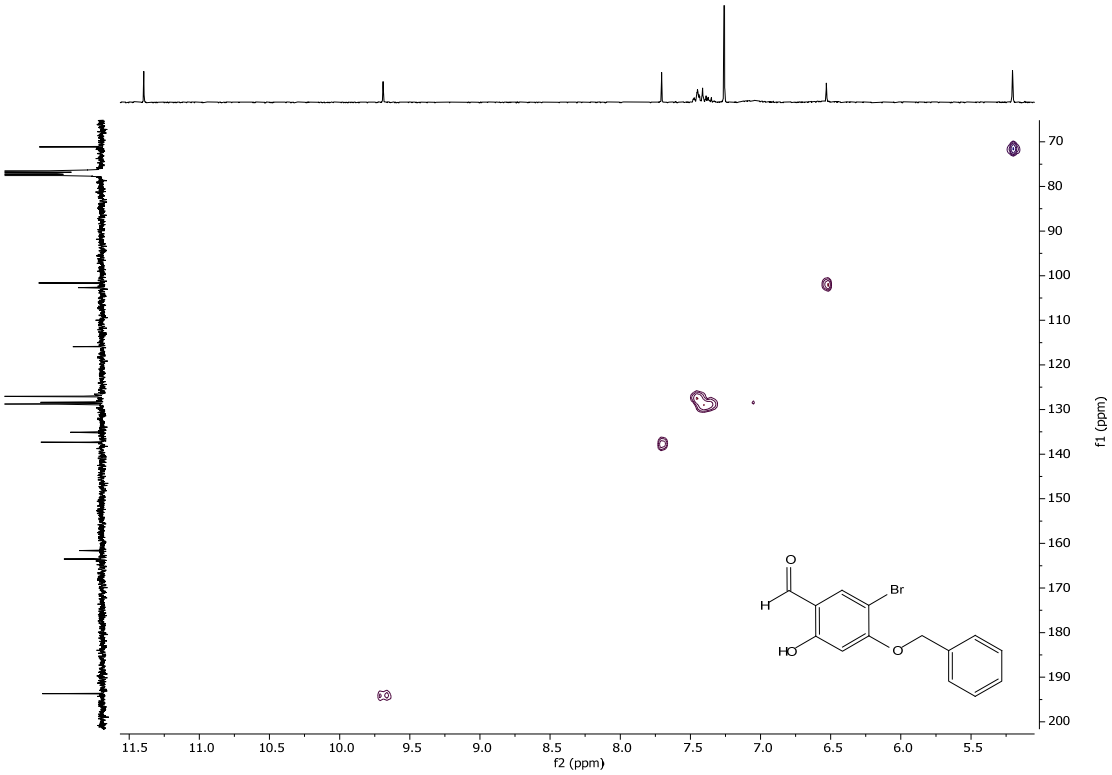


Figure S5. HSQC spectrum of compound **17** in $CDCl_3$.

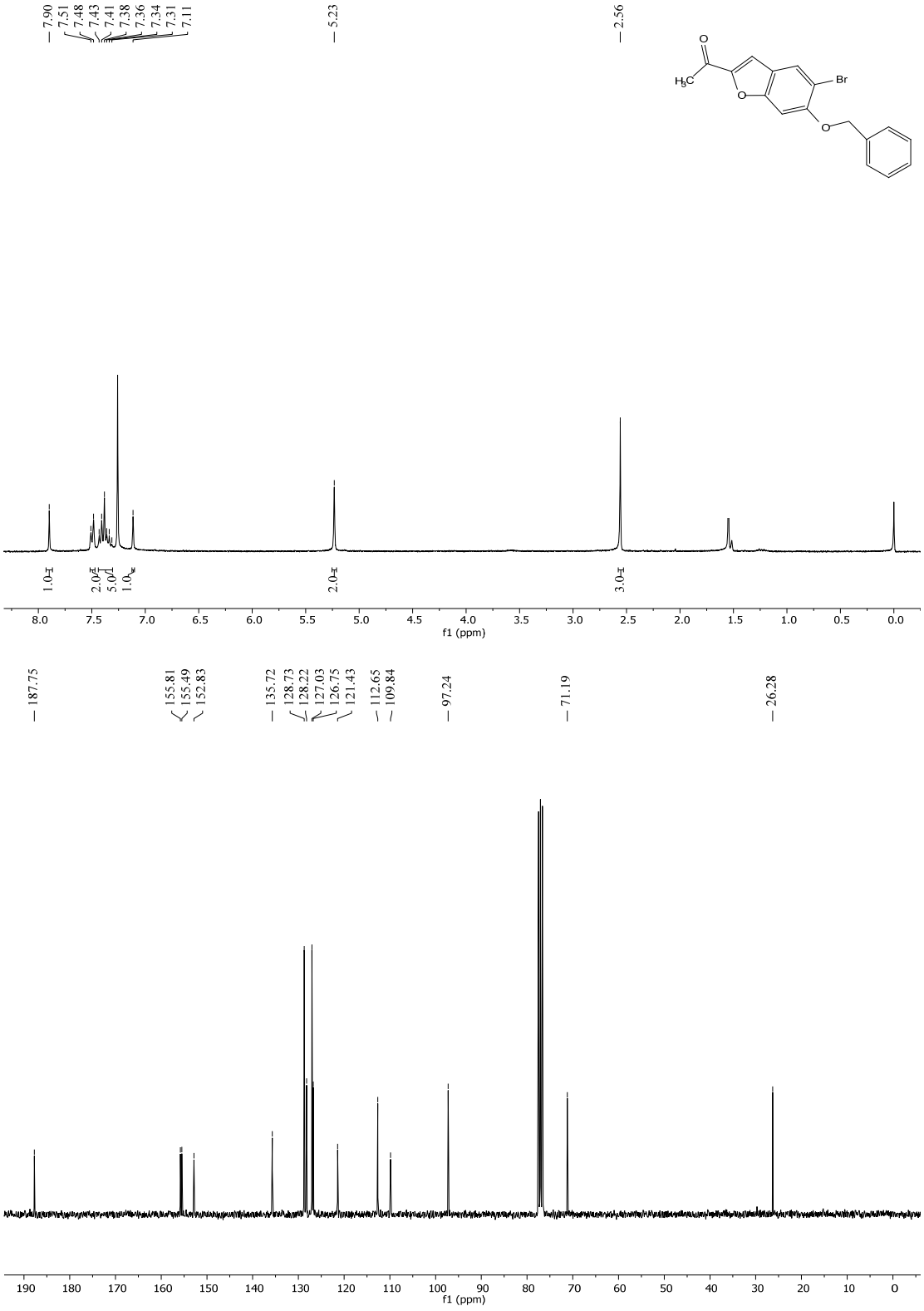


Figure S6. 300 MHz ^{1}H (top) and 75 MHz ^{13}C (bottom) NMR spectra of **19** in $CDCl_3$.

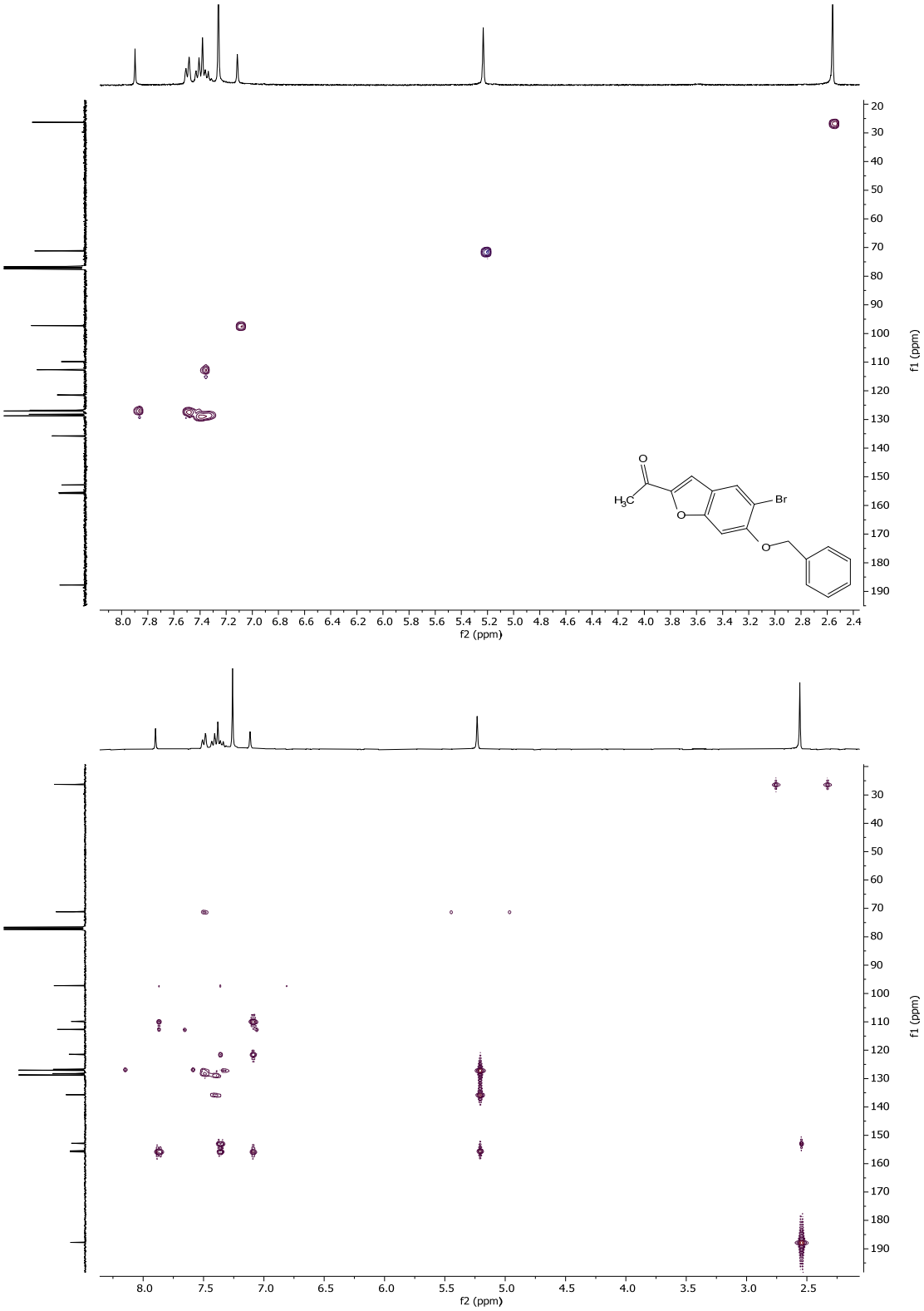


Figure S7. HSQC (top) and HMBC (bottom) spectra of compound **19** in $CDCl_3$.

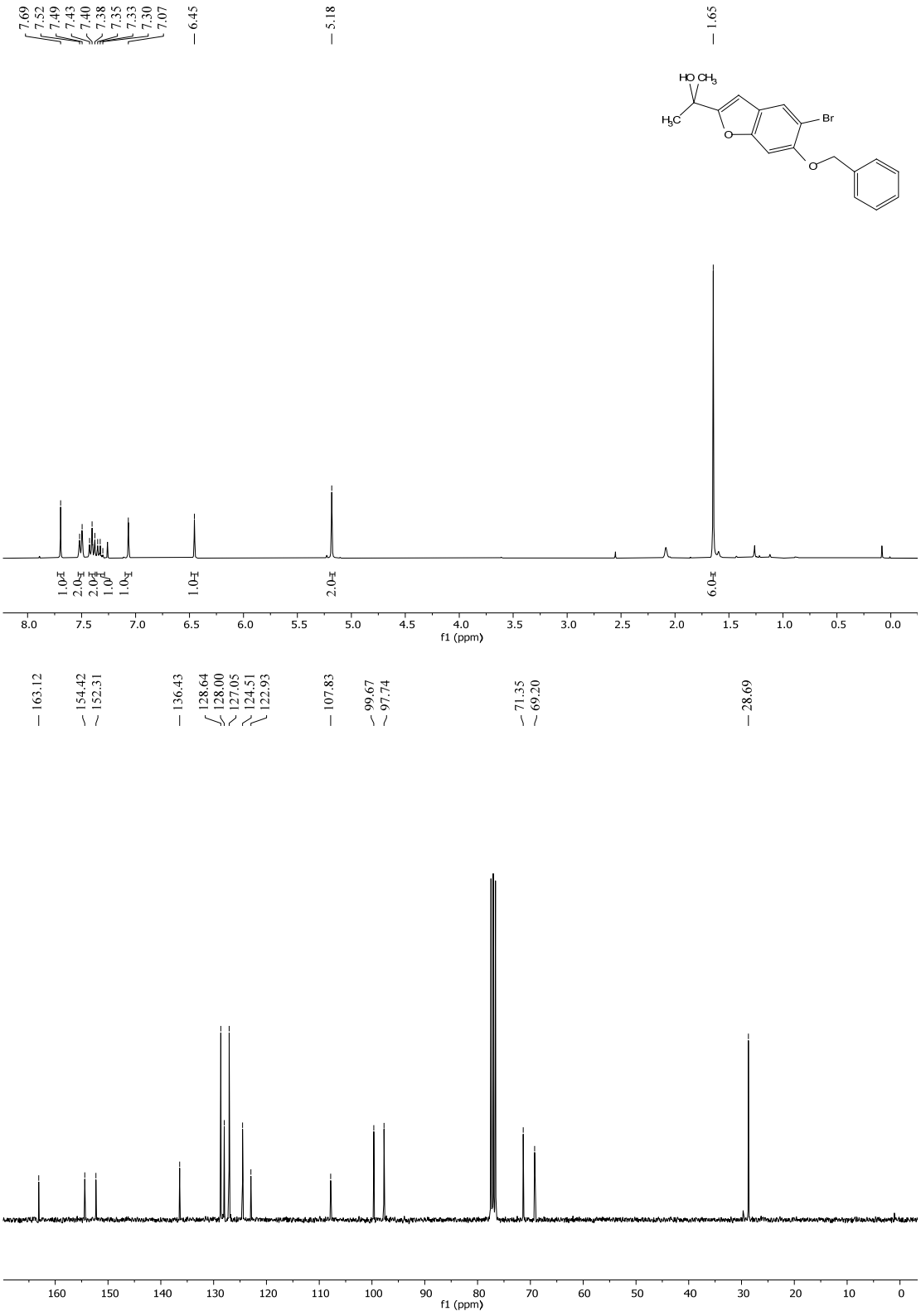


Figure S8. 300 MHz ^{1}H (top) and 75 MHz ^{13}C (bottom) NMR spectra of **22** in $CDCl_3$.

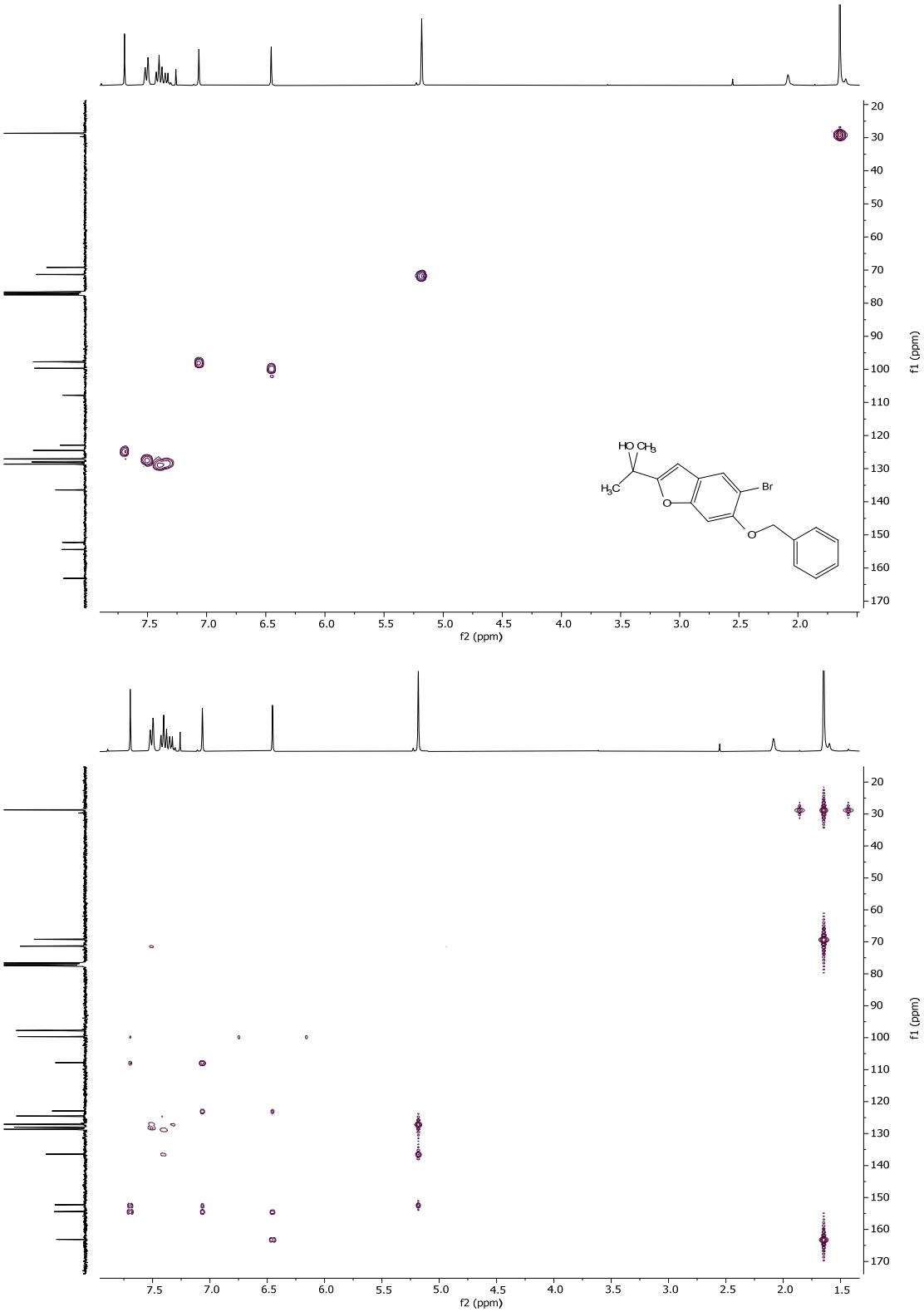


Figure S9. HSQC (top) and HMBC (bottom) spectra of compound **22** in $CDCl_3$.

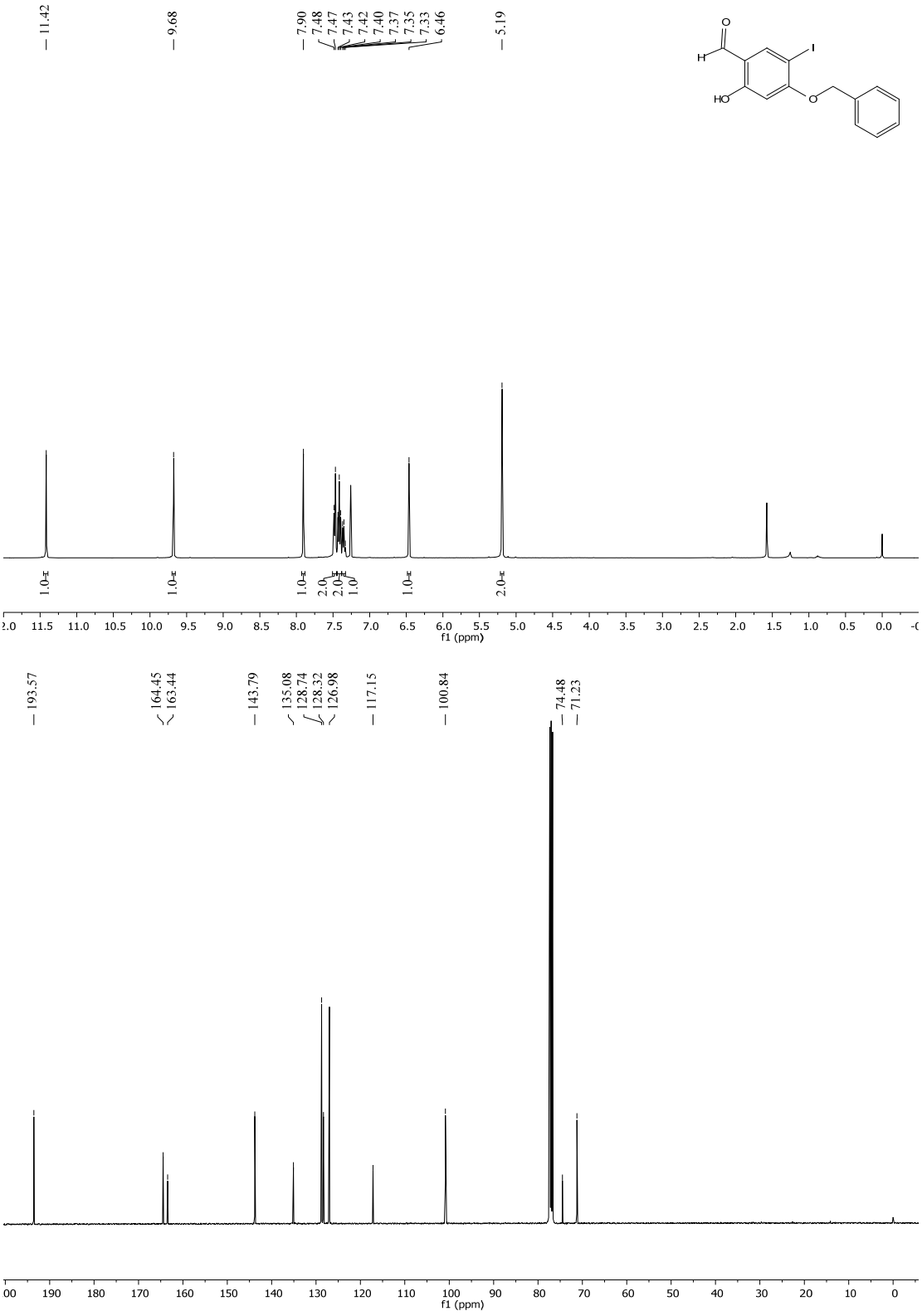


Figure S10. 400 MHz 1H (top) and 101 MHz ^{13}C (bottom) NMR spectra of **24** in $CDCl_3$.

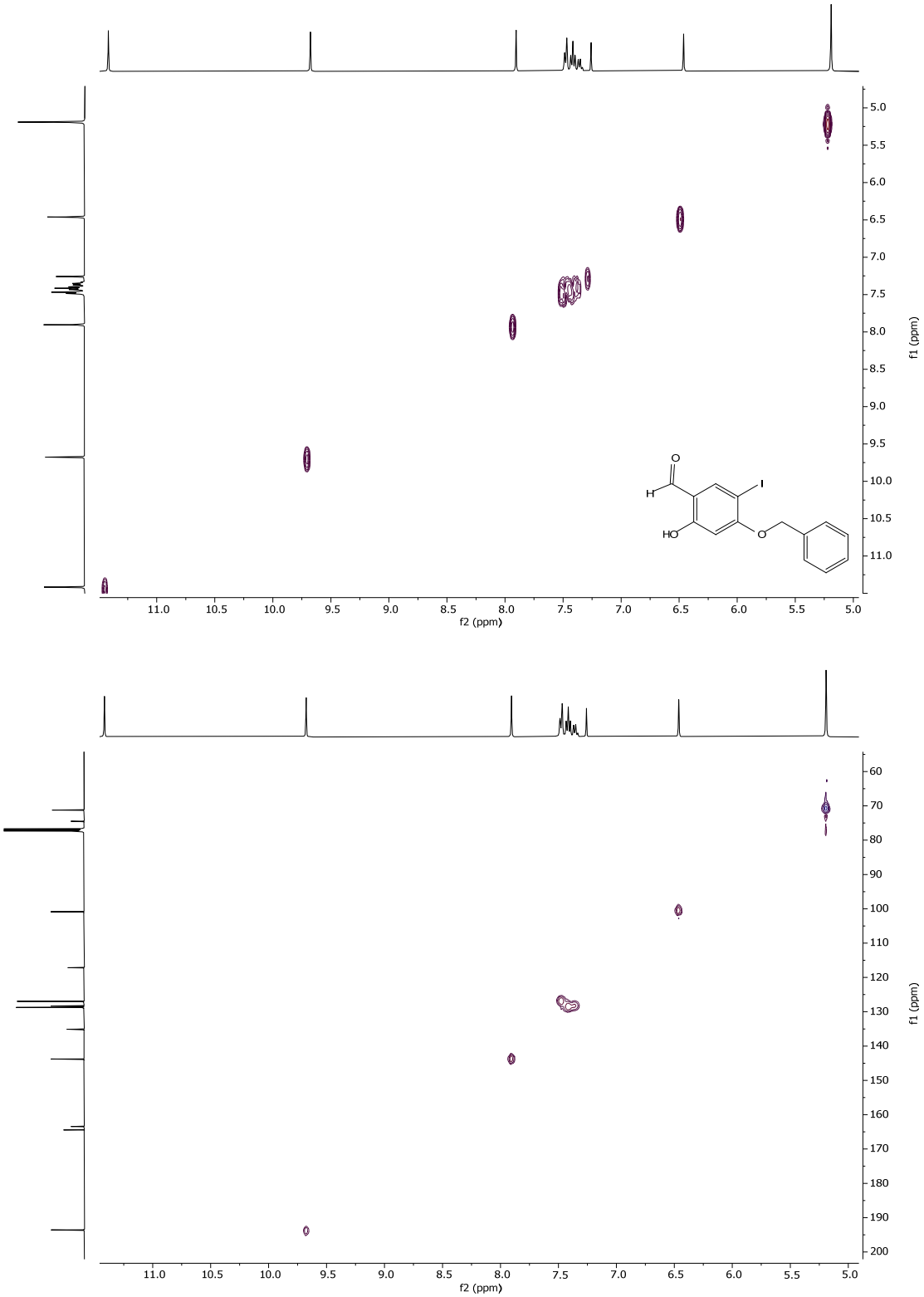


Figure S11. COSY (top) and HSQC (bottom) spectra of compound **24** in $CDCl_3$.

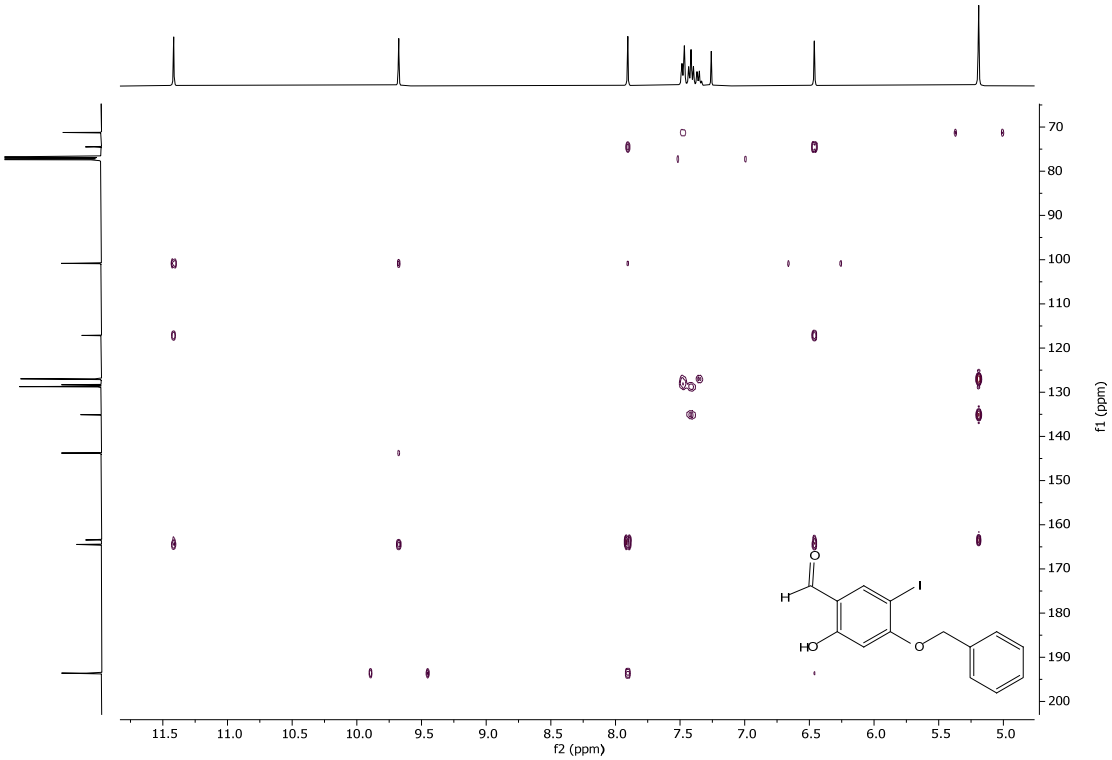


Figure S12. HMBC spectrum of compound **24** in $CDCl_3$.

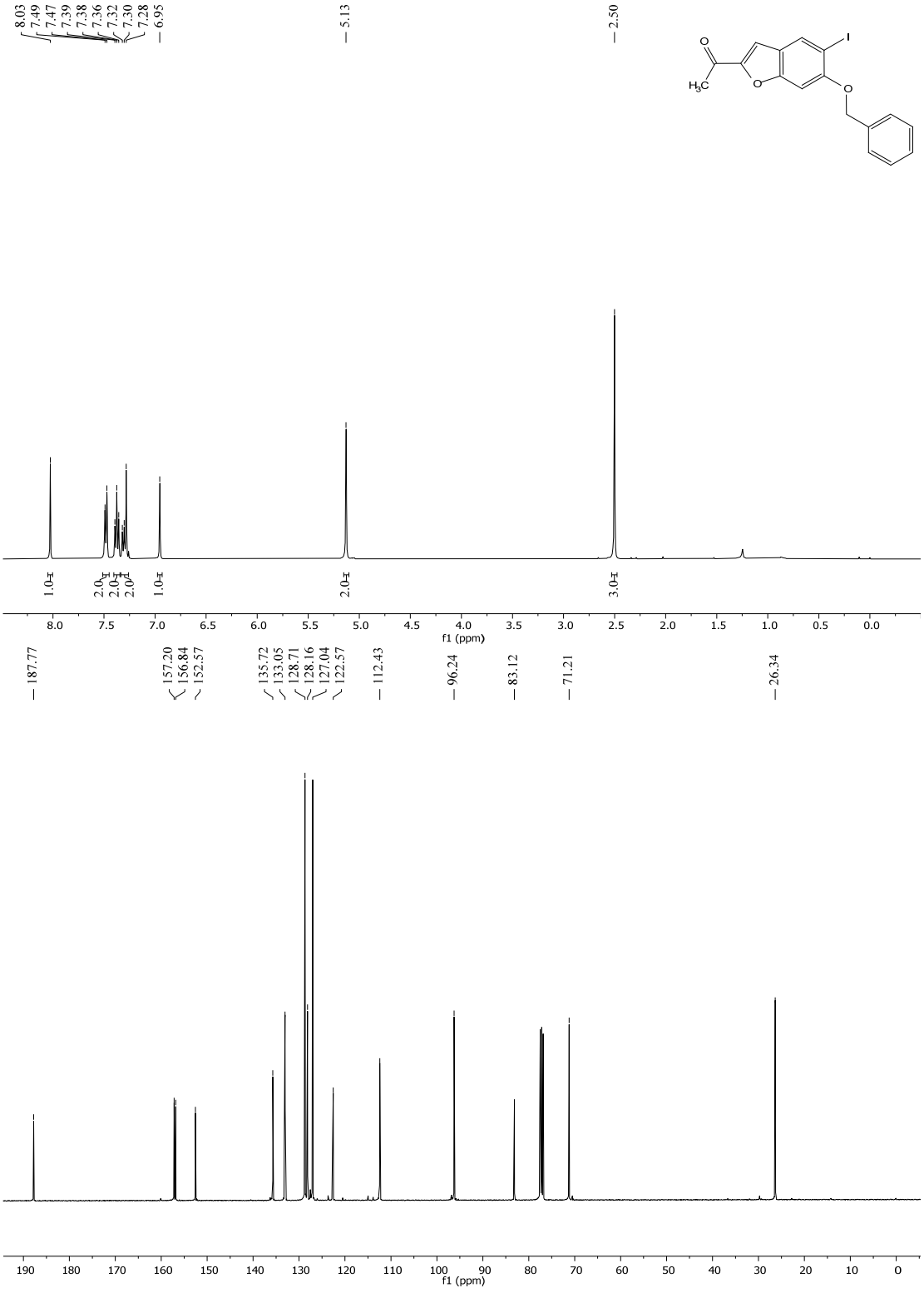


Figure S13. 400 MHz ^{1}H (top) and 101 MHz ^{13}C (bottom) NMR spectra of **27** in $CDCl_3$.

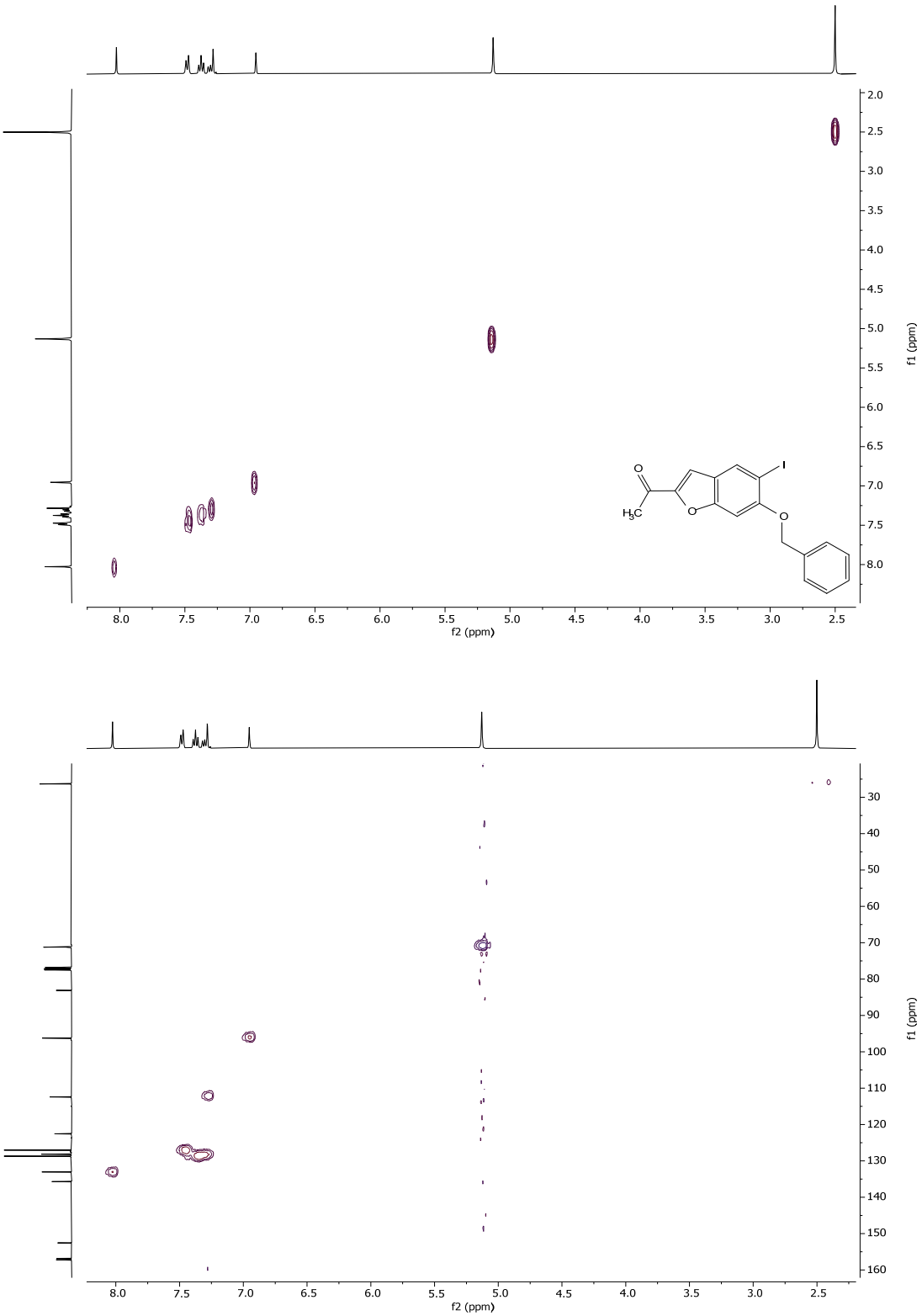


Figure S14. COSY (top) and HSQC (bottom) spectra of compound **27** in $CDCl_3$.

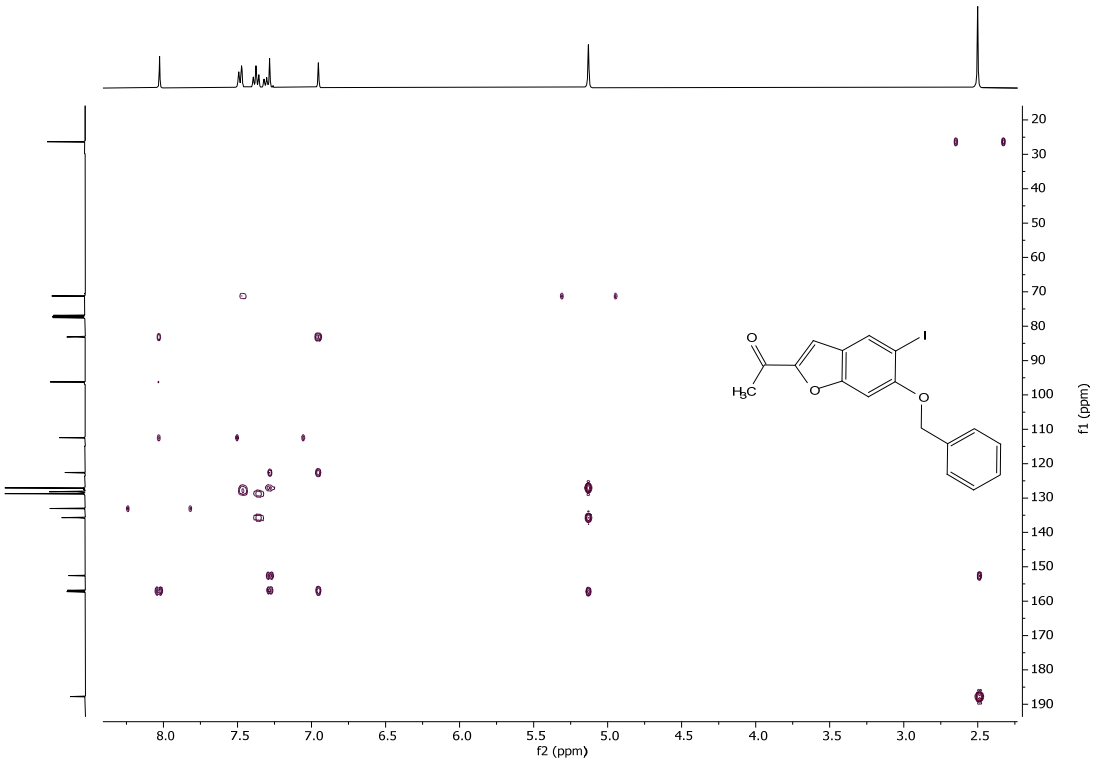


Figure S15. HMBC spectrum of compound **27** in $CDCl_3$.

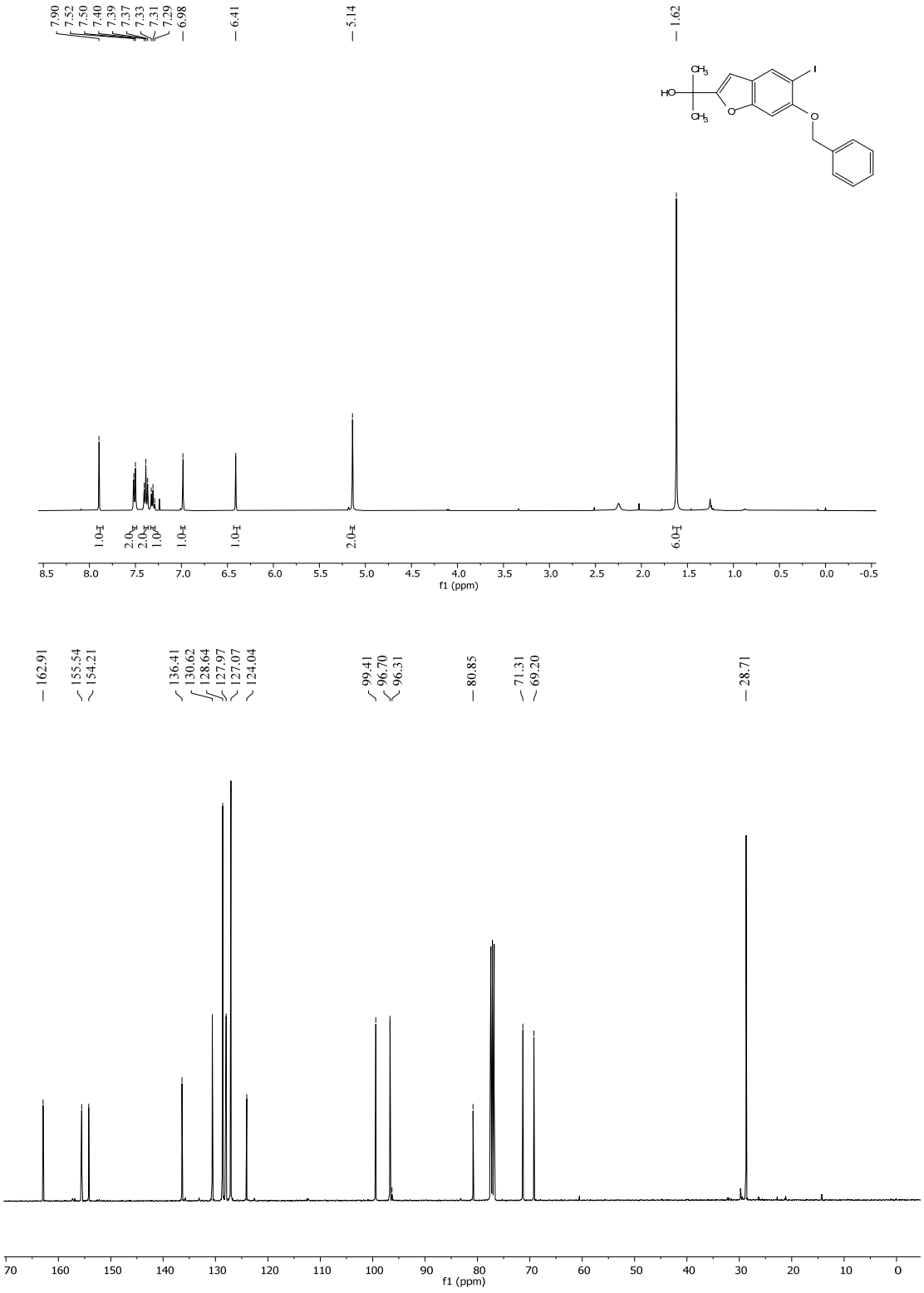


Figure S16. 400 MHz ^{1}H (top) and 101 MHz ^{13}C (bottom) NMR spectra of **28** in $CDCl_3$.

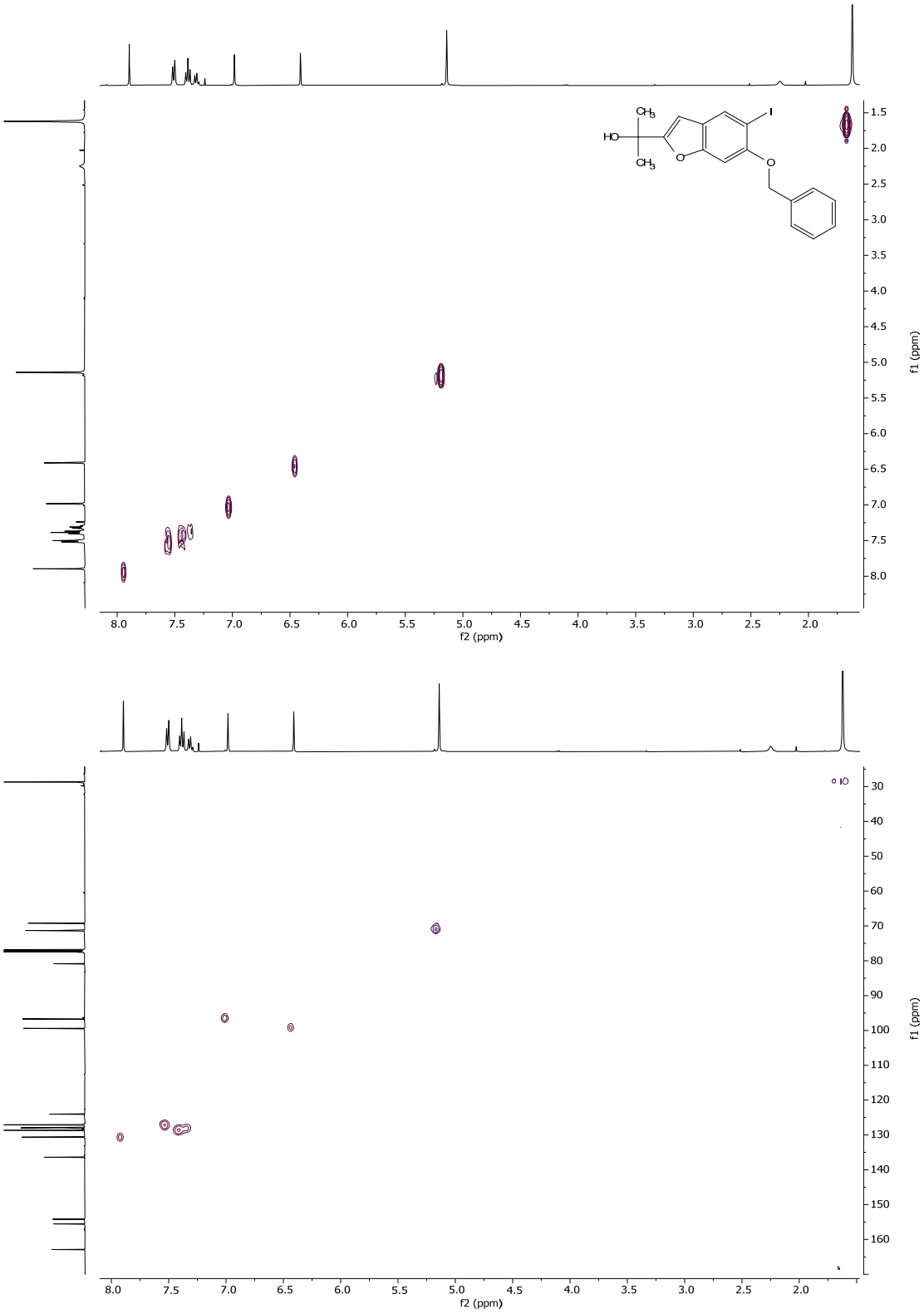


Figure S17. COSY (top) and HSQC (bottom) spectra of compound **28** in $CDCl_3$.

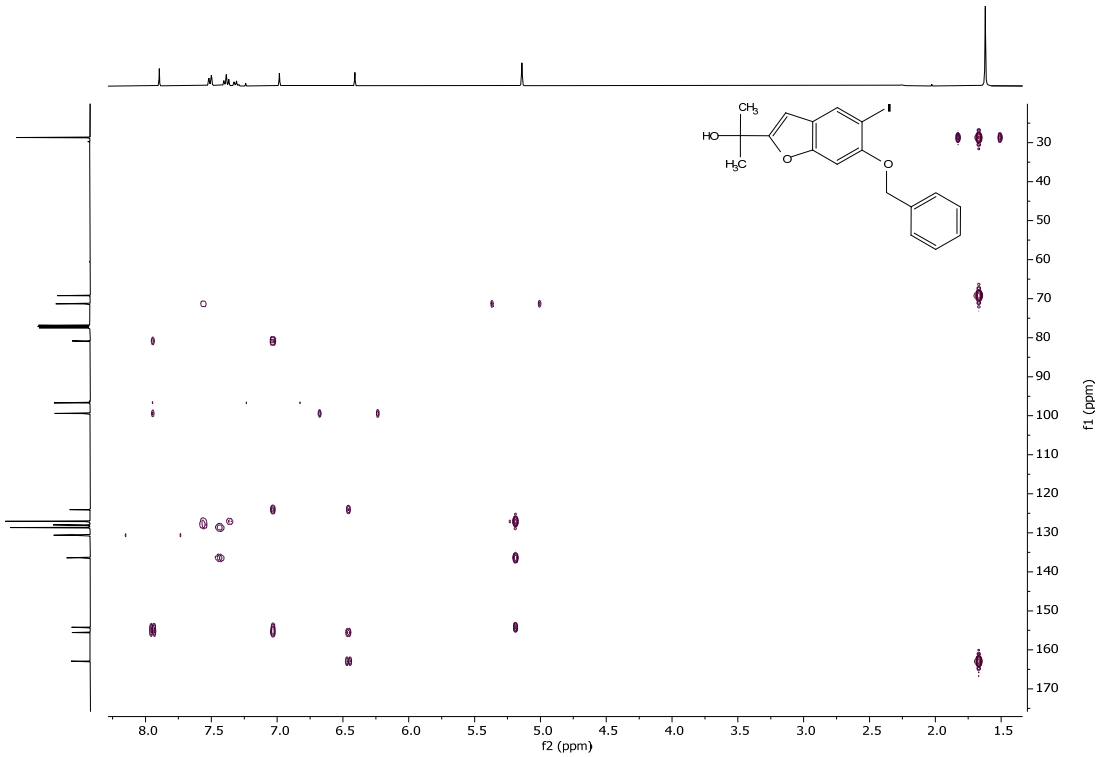


Figure S18. HMBC spectrum of compound **28** in $CDCl_3$.

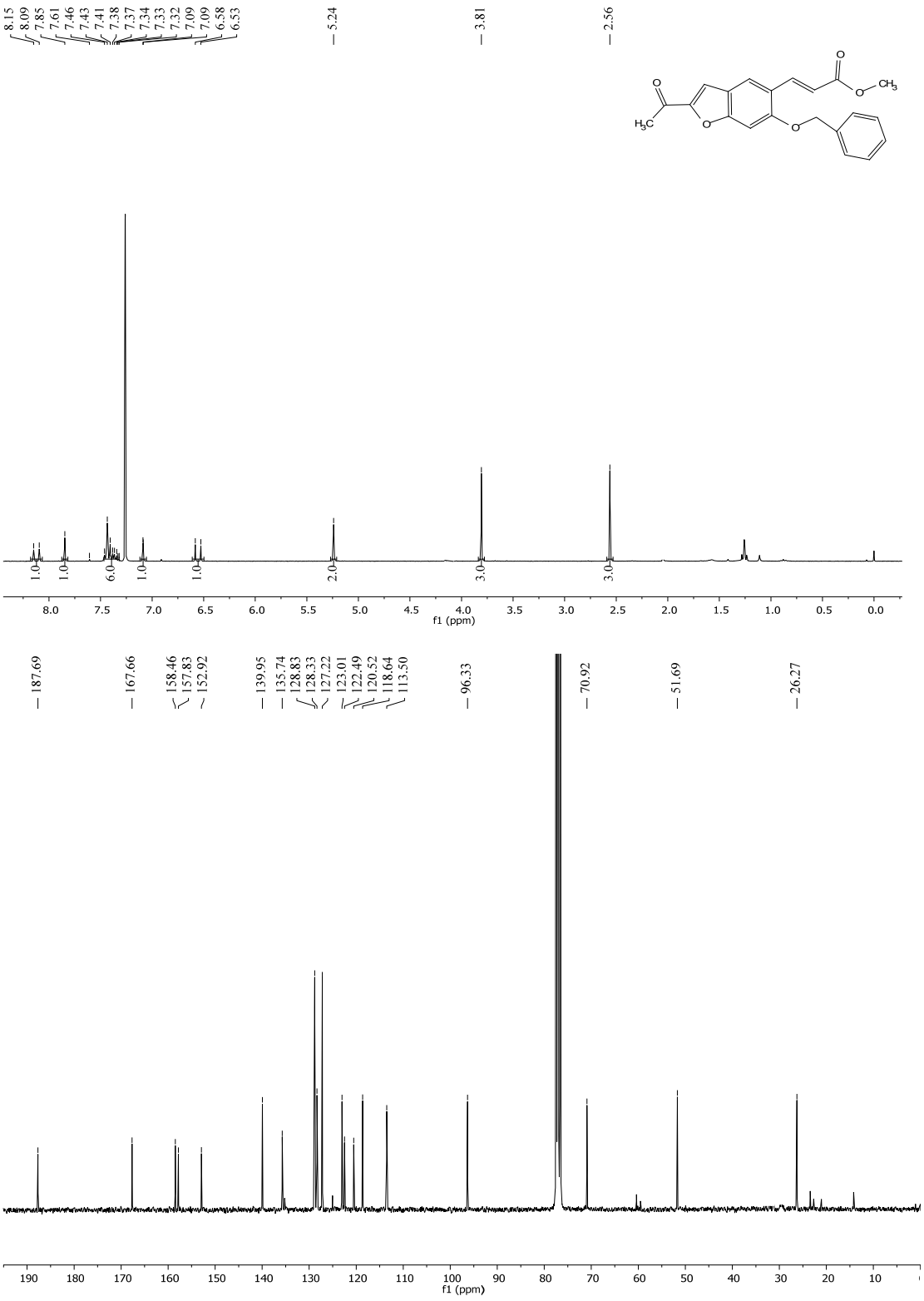


Figure S19. 400 MHz ^{1}H (top) and 101 MHz ^{13}C (bottom) NMR spectra of **20** in $CDCl_3$.

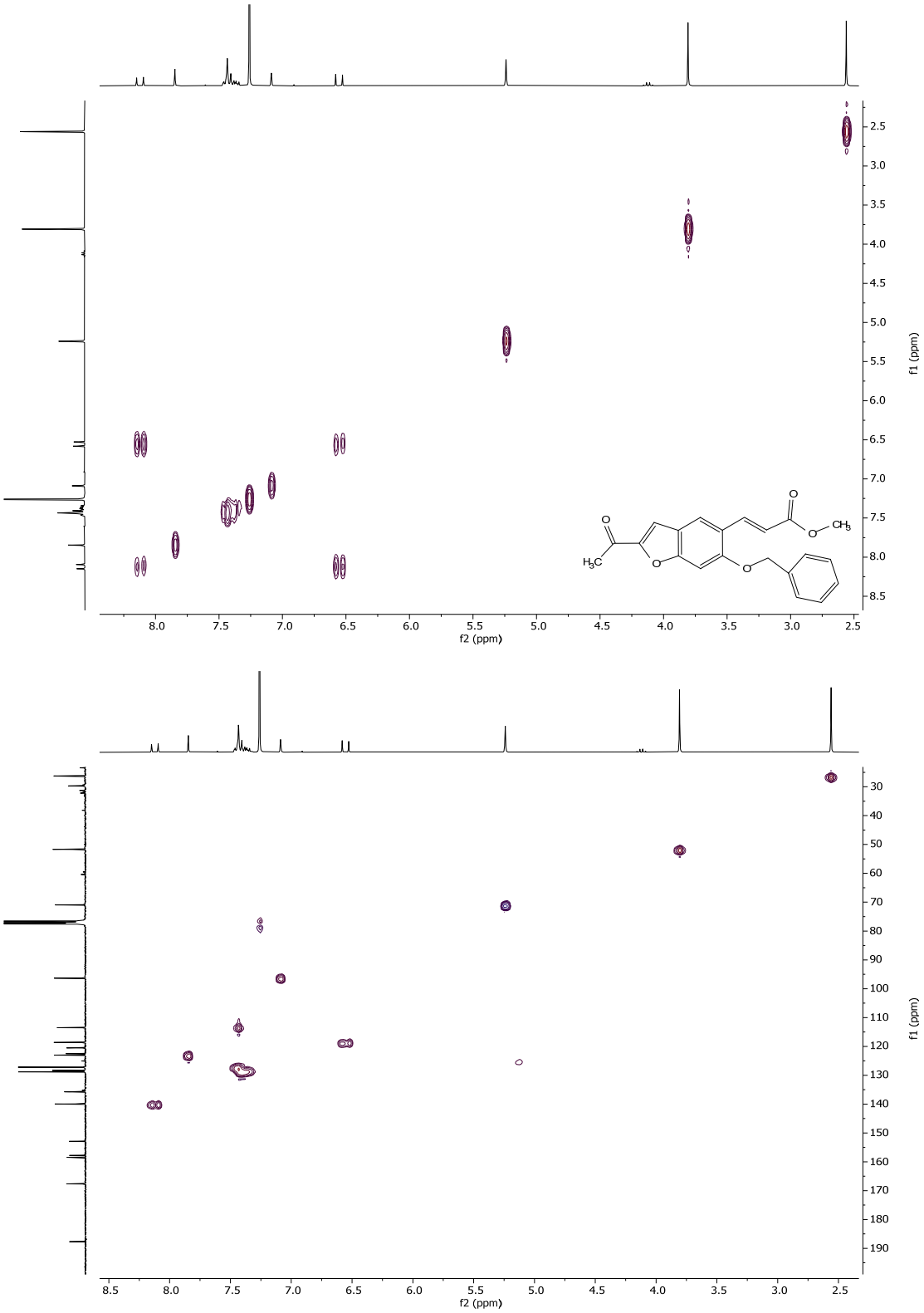


Figure S20. COSY (top) and HSQC (bottom) spectra of compound **20** in $CDCl_3$.

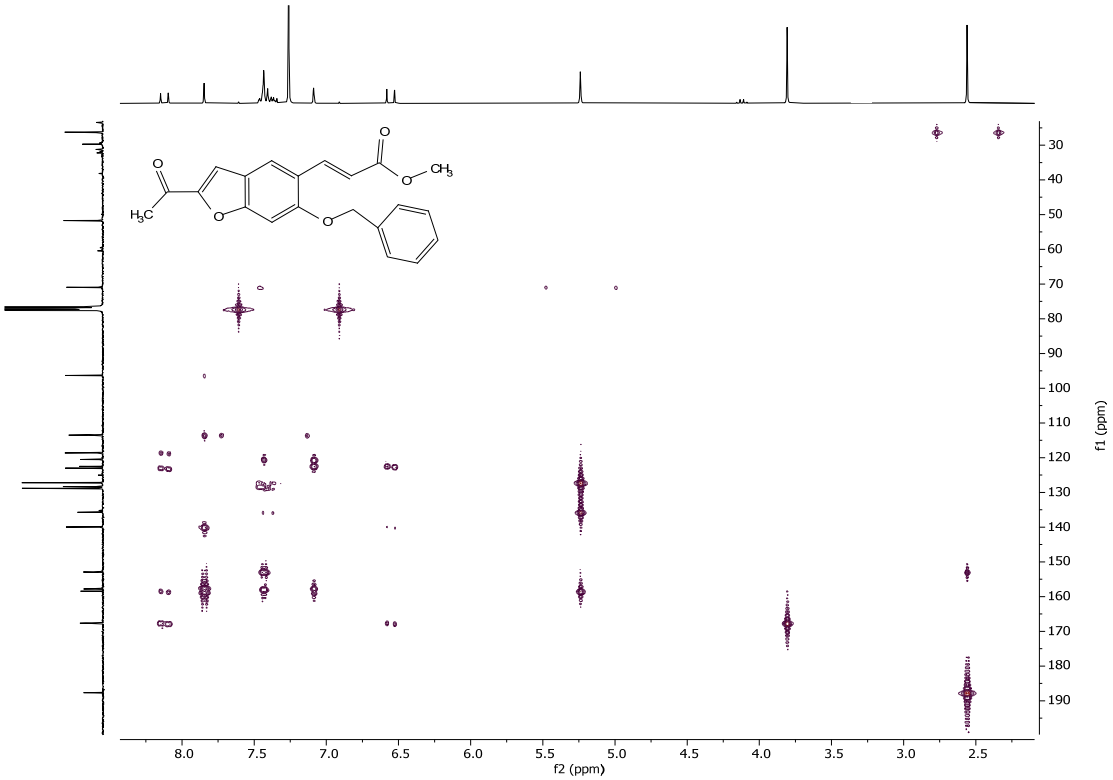


Figure S21. HMBC spectrum of compound **20** in $CDCl_3$.

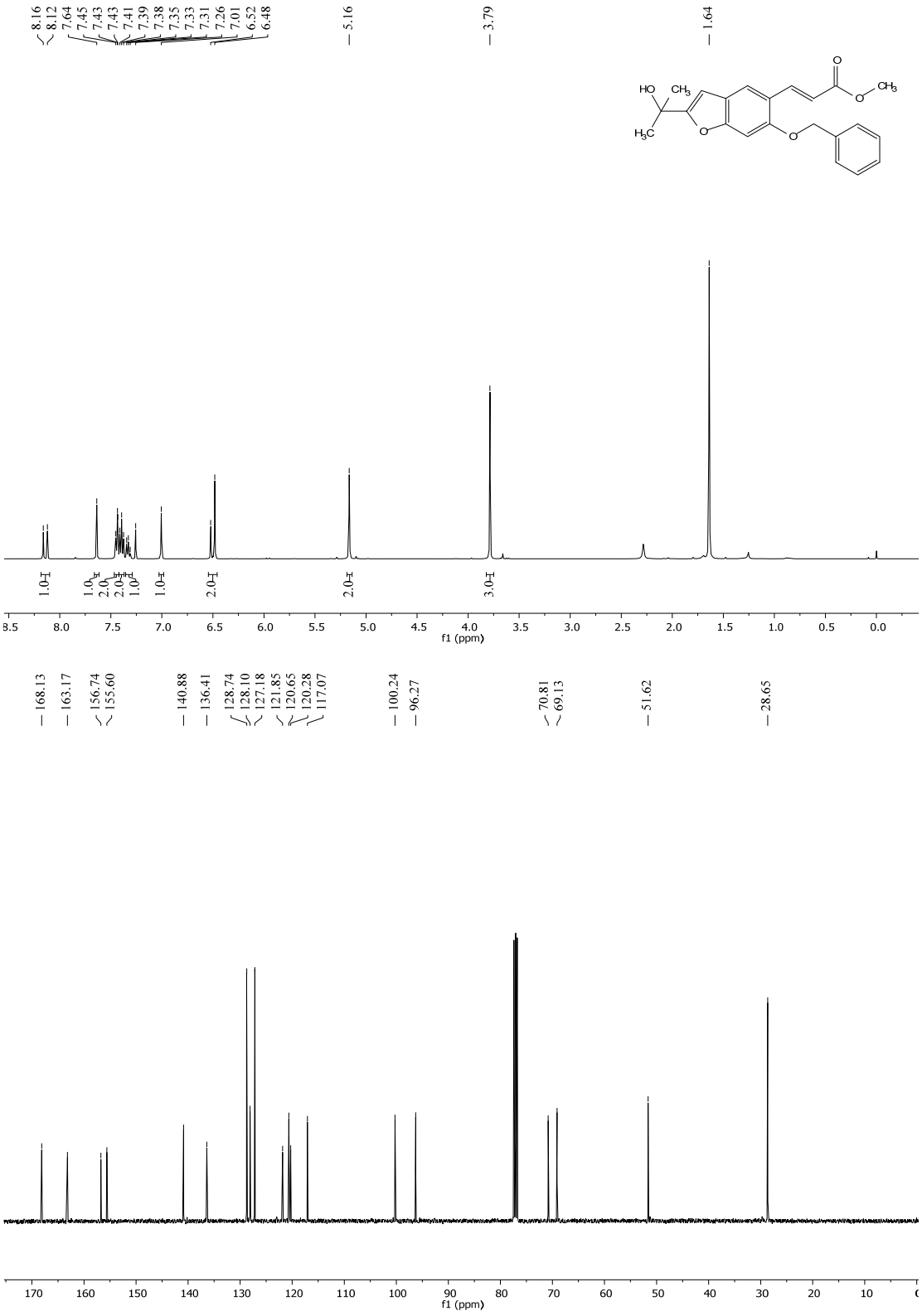


Figure S22. 400 MHz ^{1}H (top) and 101 MHz ^{13}C (bottom) NMR spectra of **21** in $CDCl_3$.

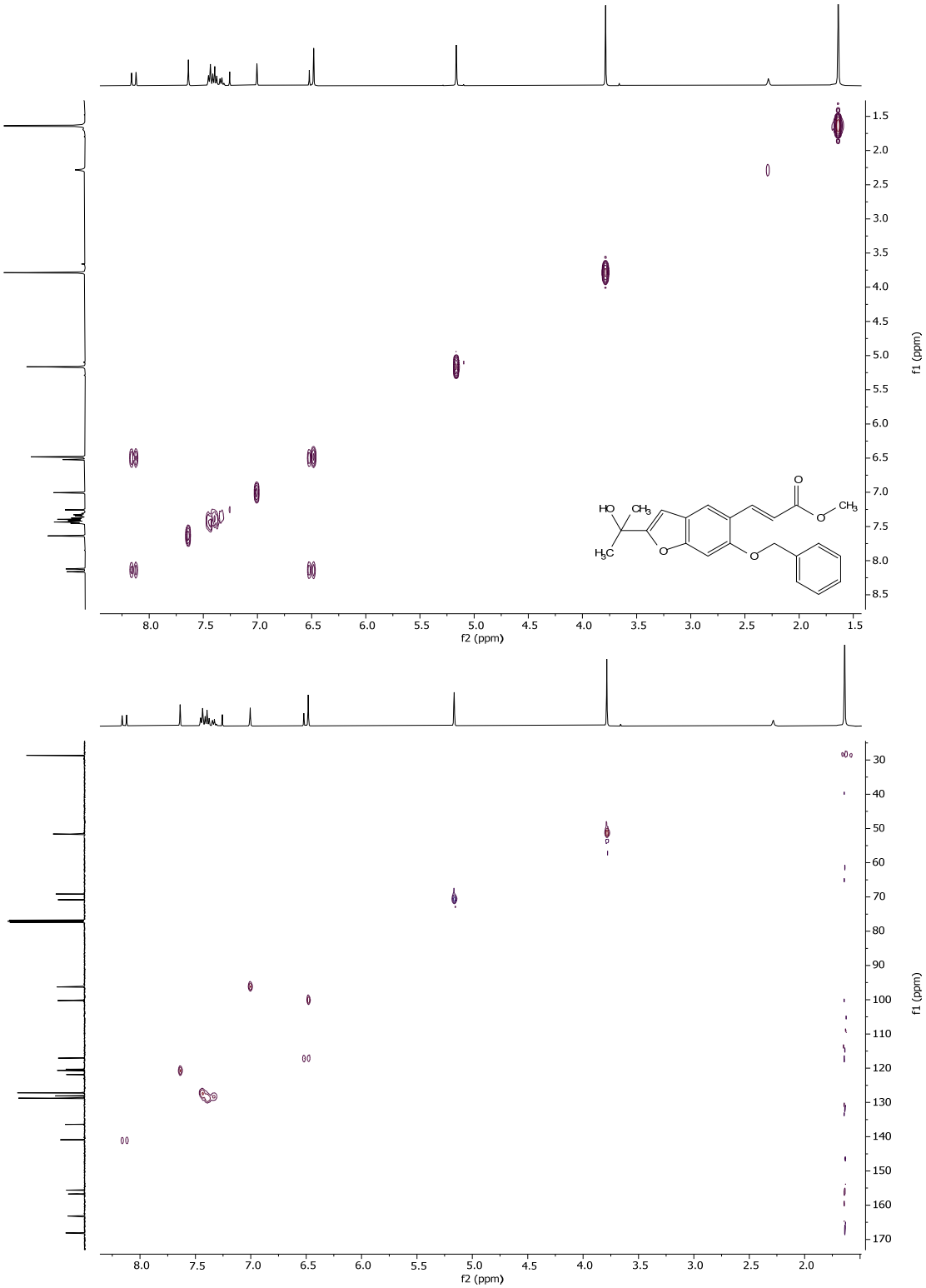


Figure S23. COSY (top) and HSQC (bottom) spectra of compound **21** in $CDCl_3$.

Figure S24. HMBC spectrum of compound **21** in $CDCl_3$.

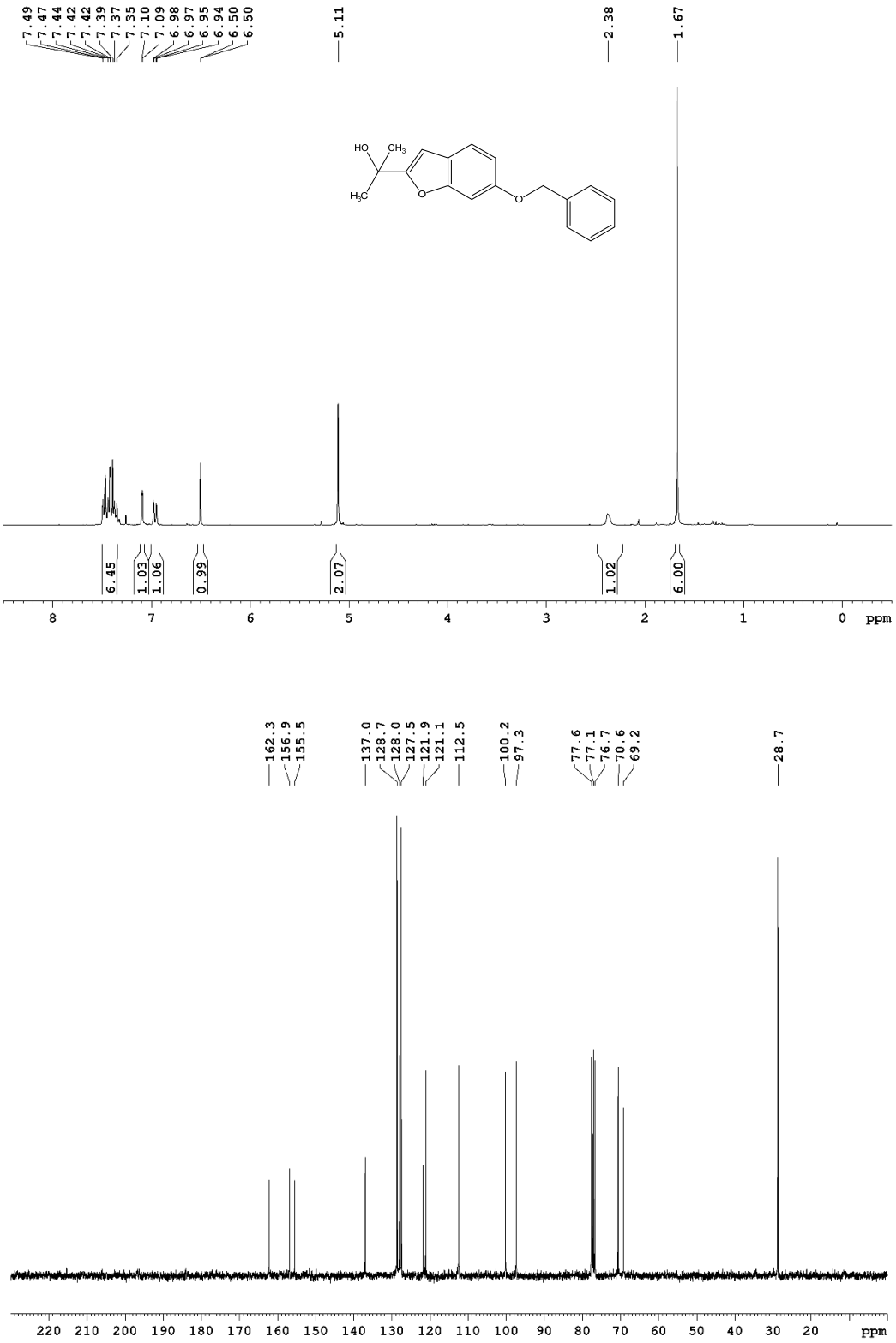


Figure S25. 300 MHz ^{1}H (top) and 75 MHz ^{13}C (bottom) NMR spectra of **23** in $CDCl_3$.

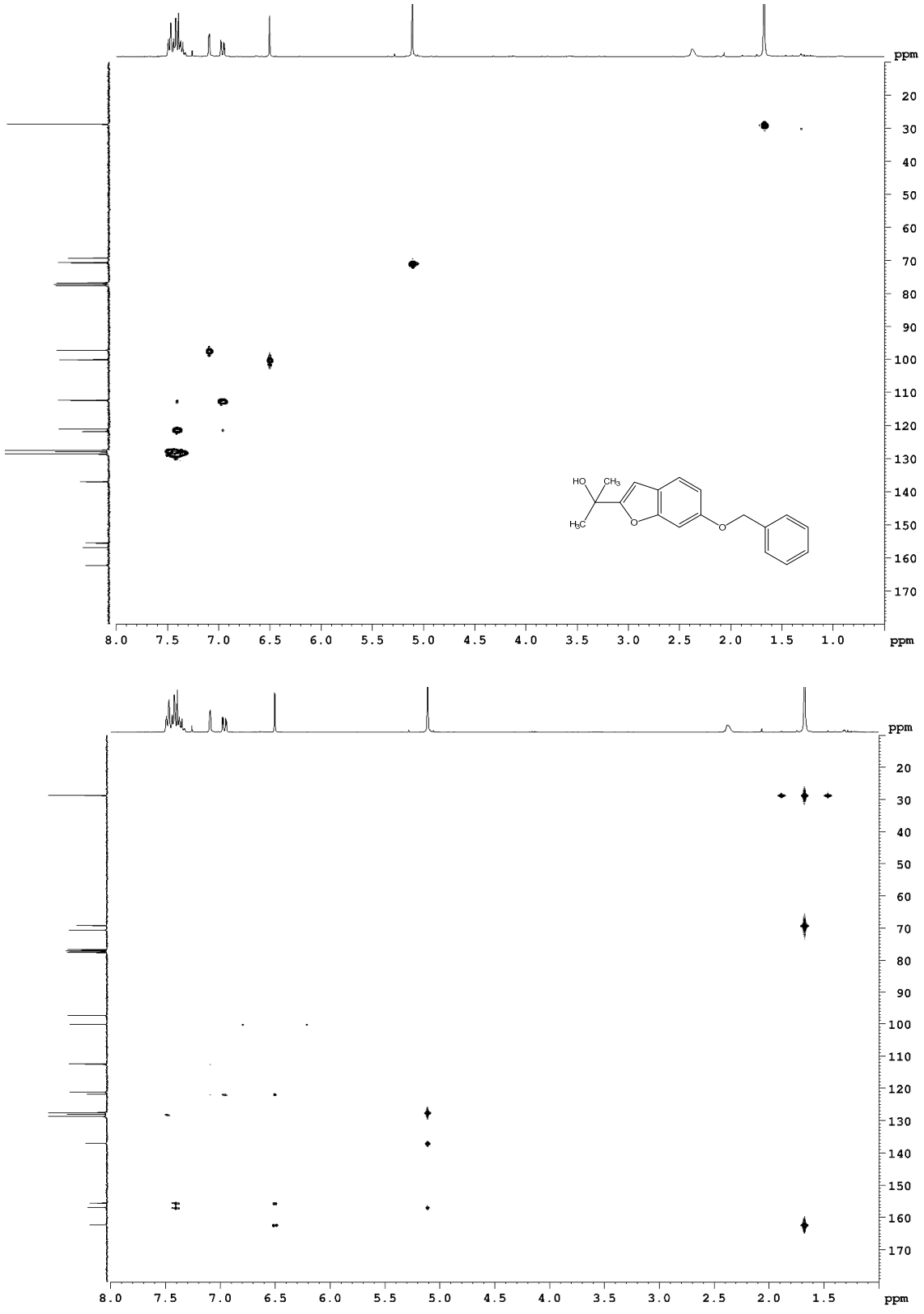


Figure S26. HSQC (top) and HMBC (bottom) spectra of compound **23** in $CDCl_3$.

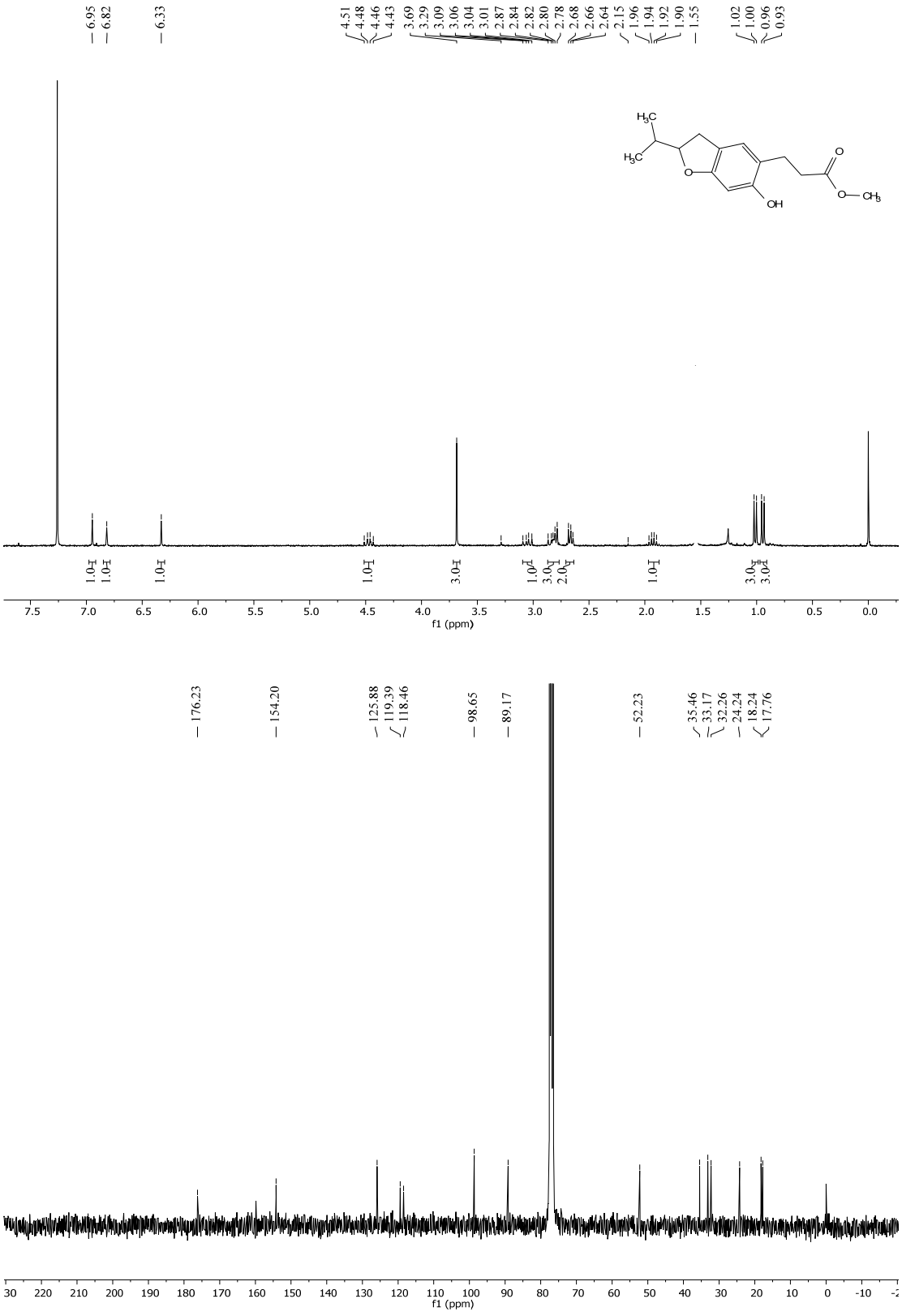


Figure S27. 300 MHz ^{1}H (top) and 75 MHz ^{13}C (bottom) NMR spectra of **29** in $CDCl_3$.

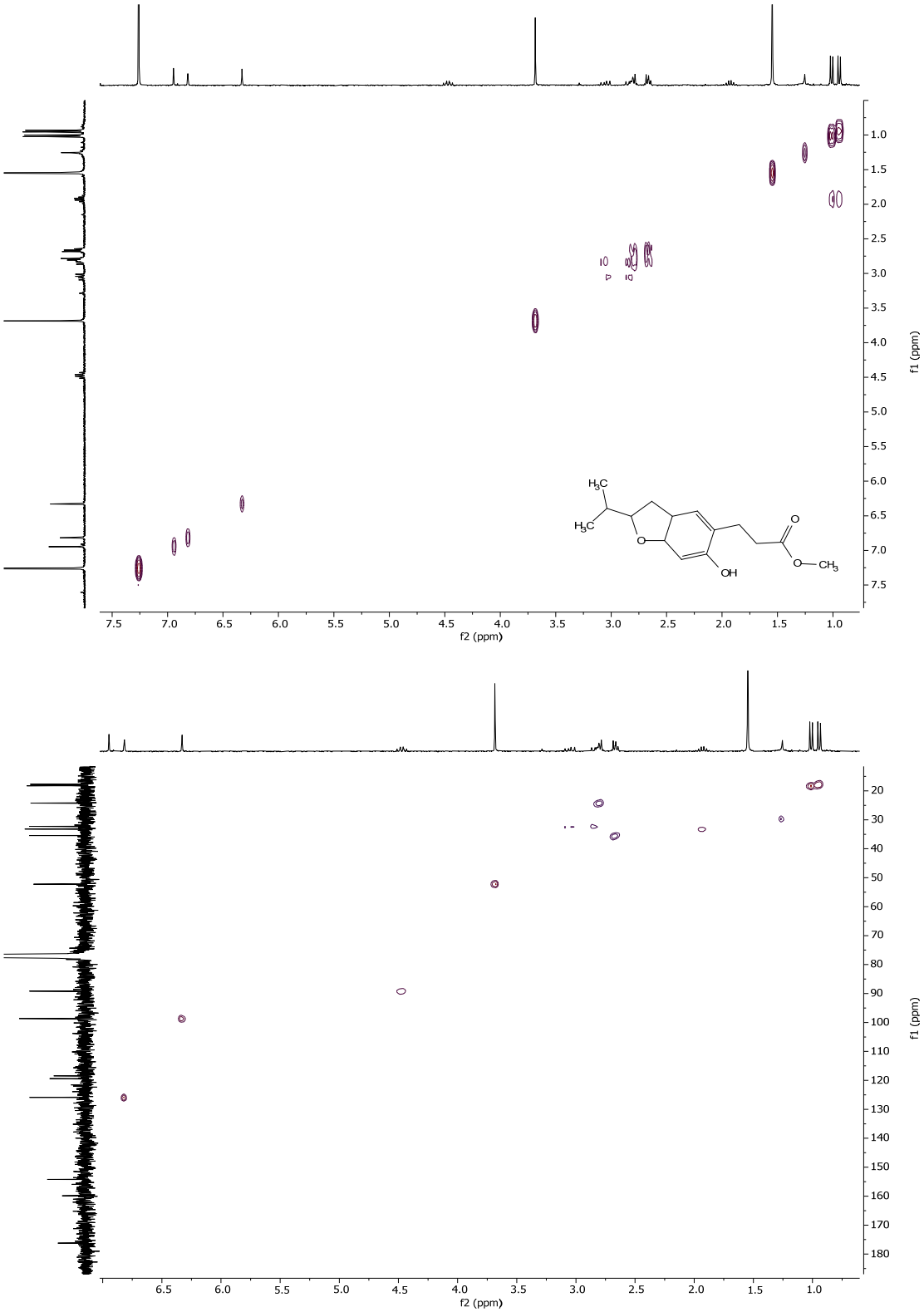


Figure S28. COSY (top) and HSQC (bottom) spectra of compound **29** in $CDCl_3$.

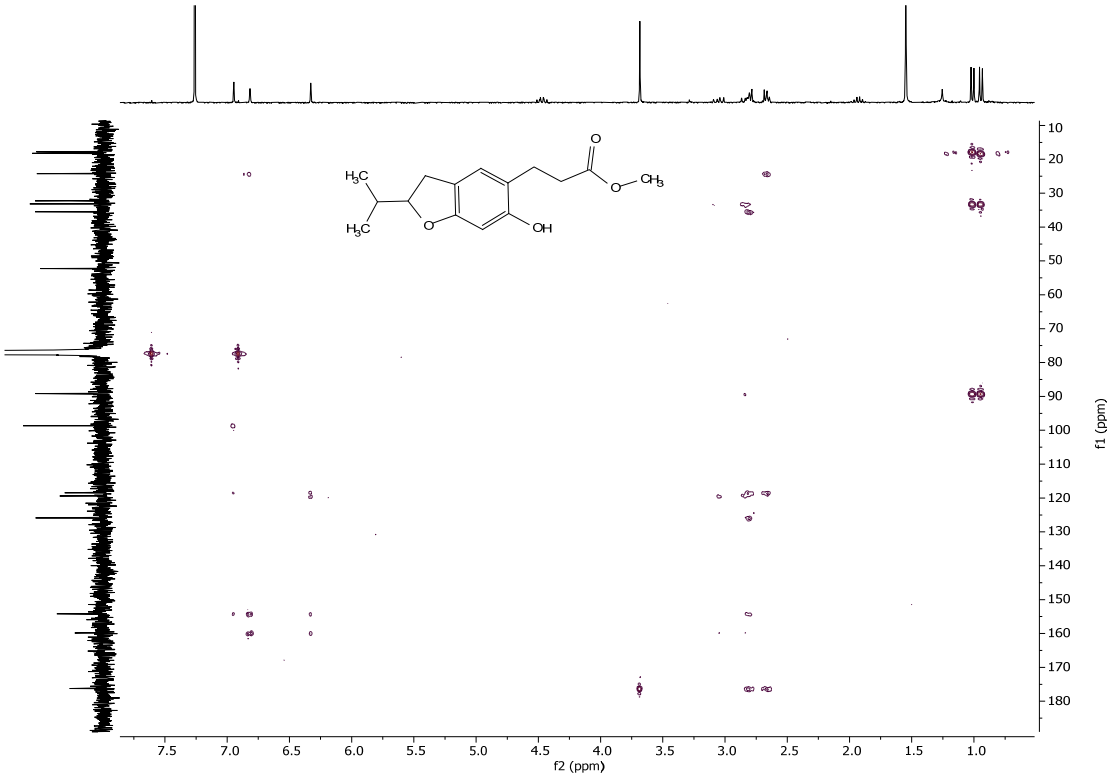


Figure S29. HMBC spectrum of compound **29** in $CDCl_3$.

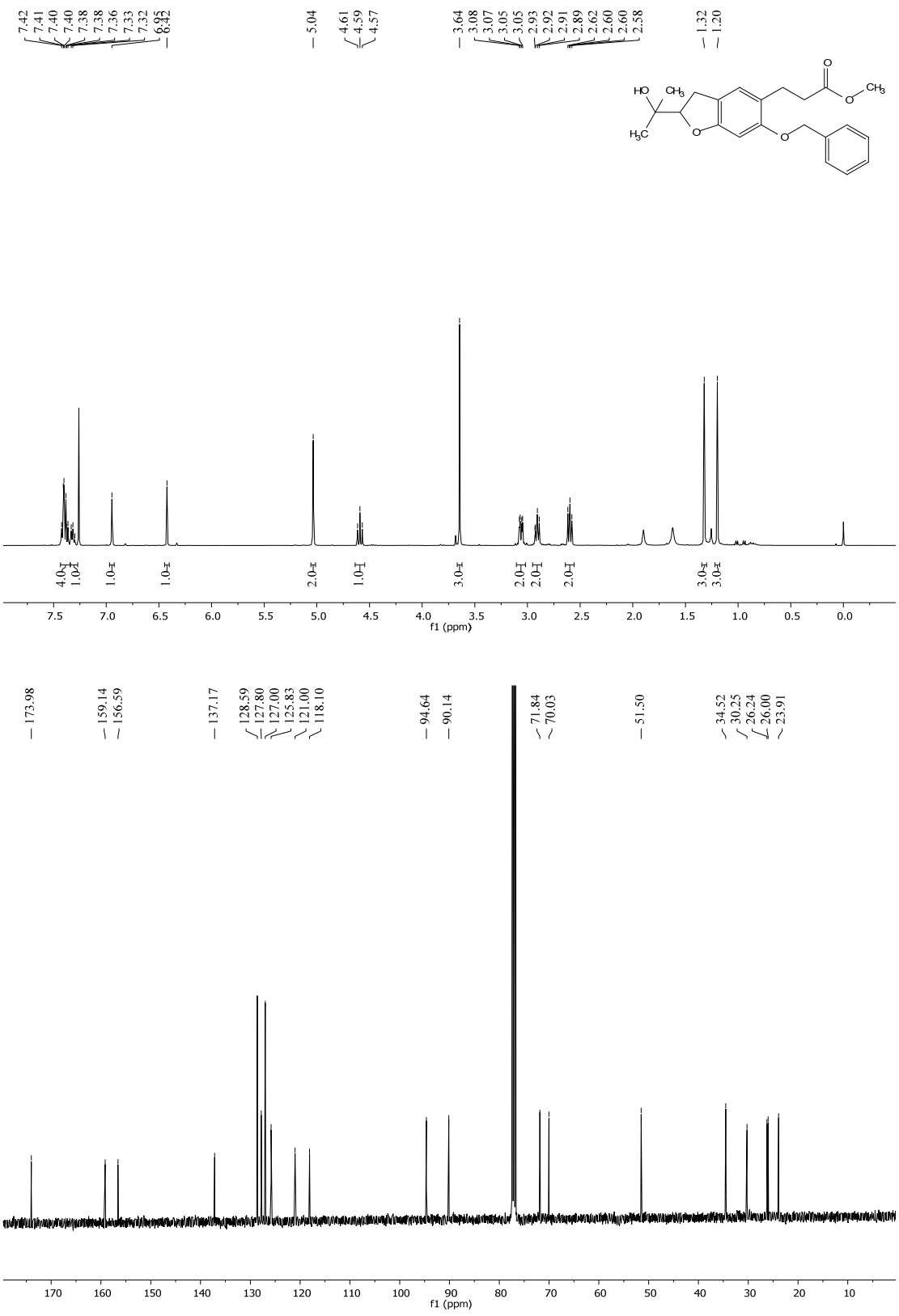


Figure S30. 400 MHz ^{1}H (top) and 101 MHz ^{13}C (bottom) NMR spectra of **30** in $CDCl_3$.

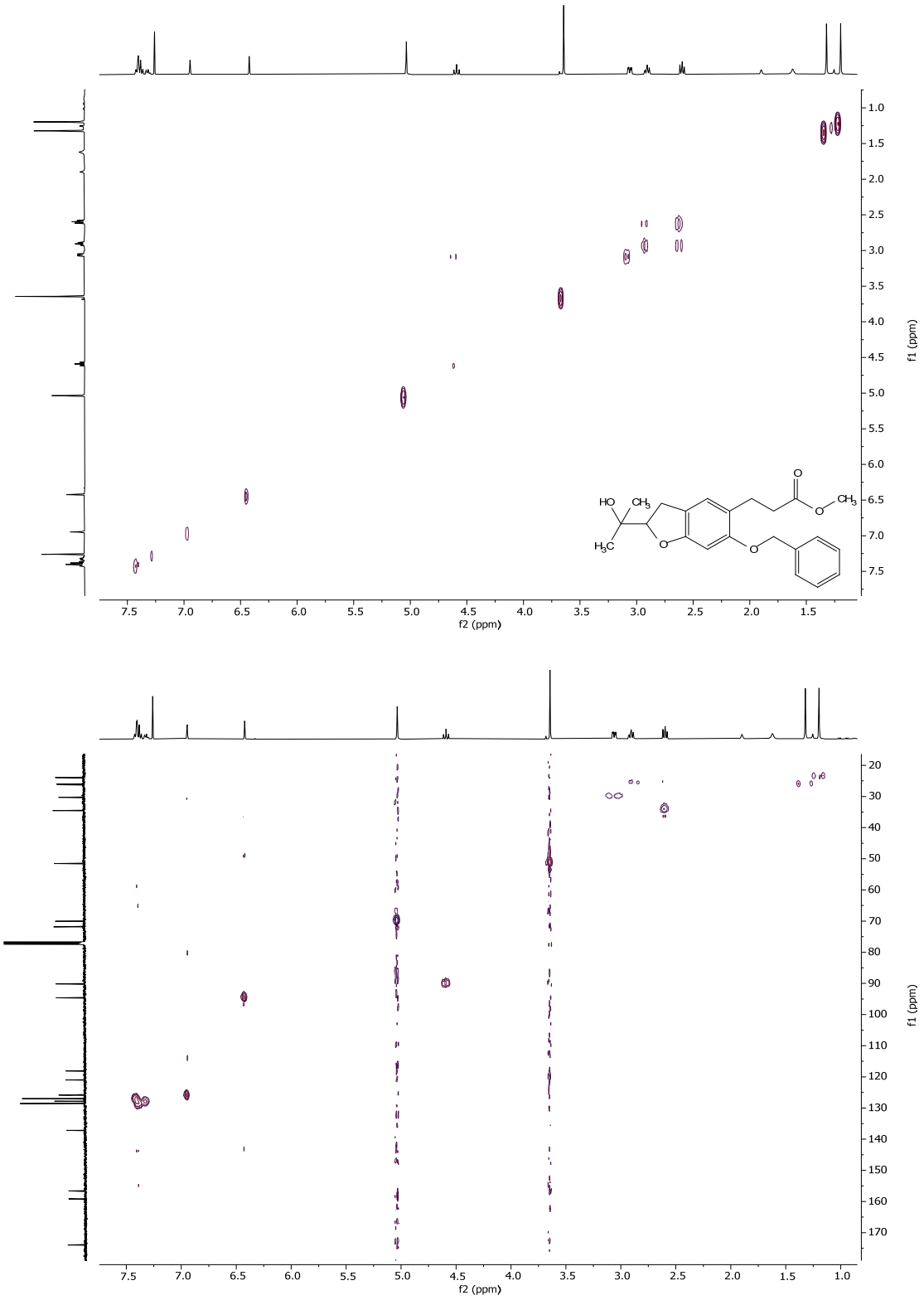


Figure S31. COSY (top) and HSQC (bottom) spectra of compound **30** in $CDCl_3$.

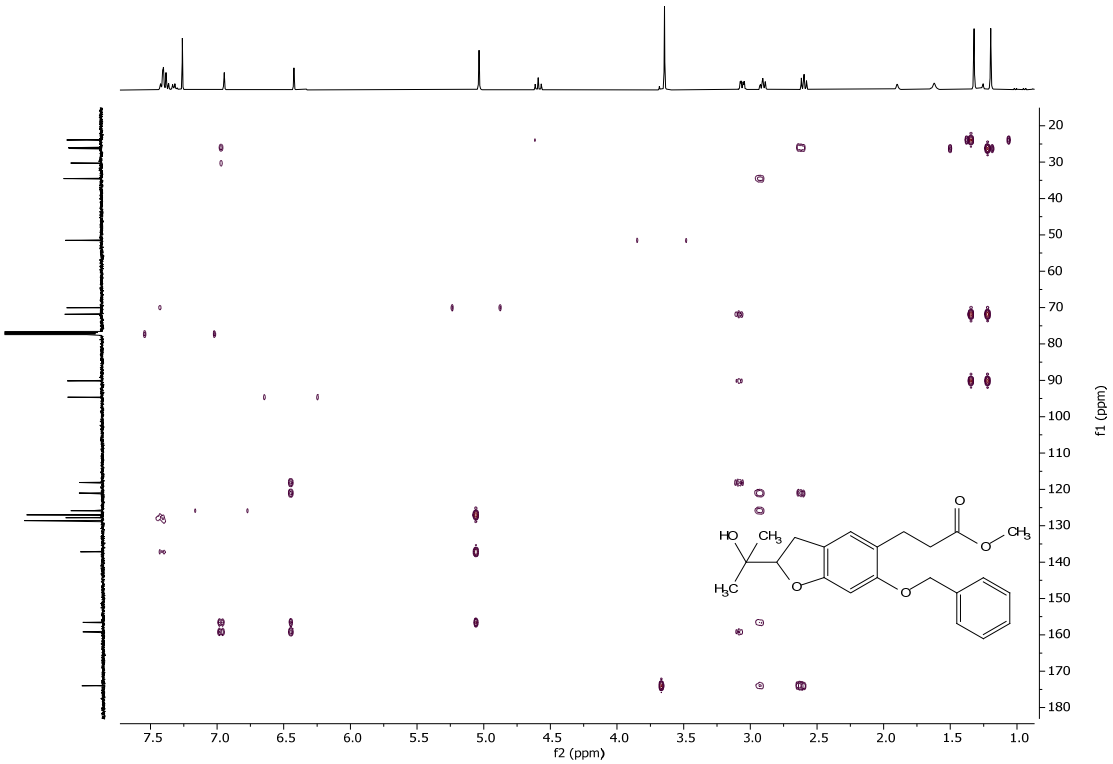


Figure S32. HMBC spectrum of compound **30** in $CDCl_3$.

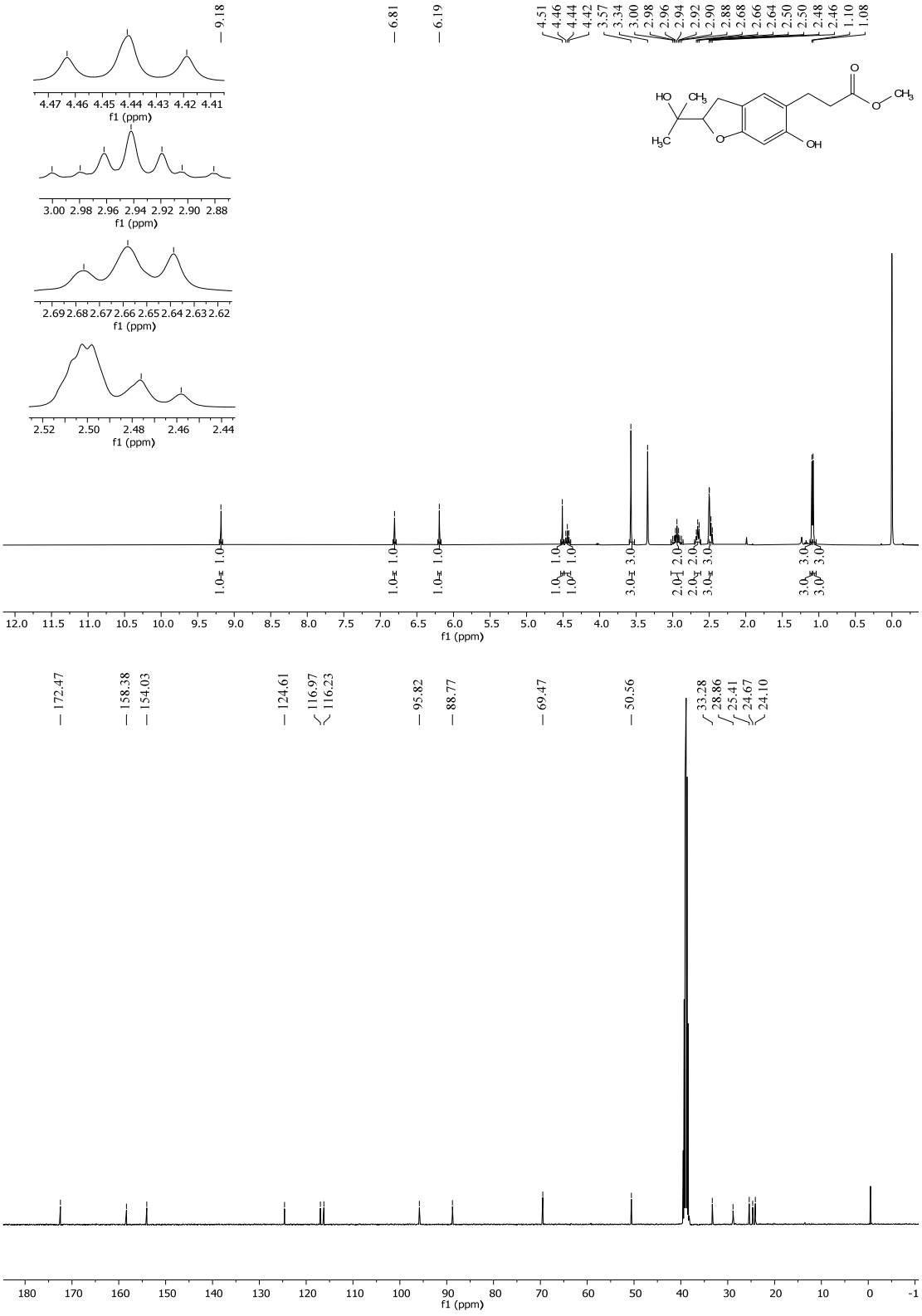


Figure S33. 400 MHz ^{1}H (top) and 101 MHz ^{13}C (bottom) NMR spectra of **1** in $CDCl_3$.

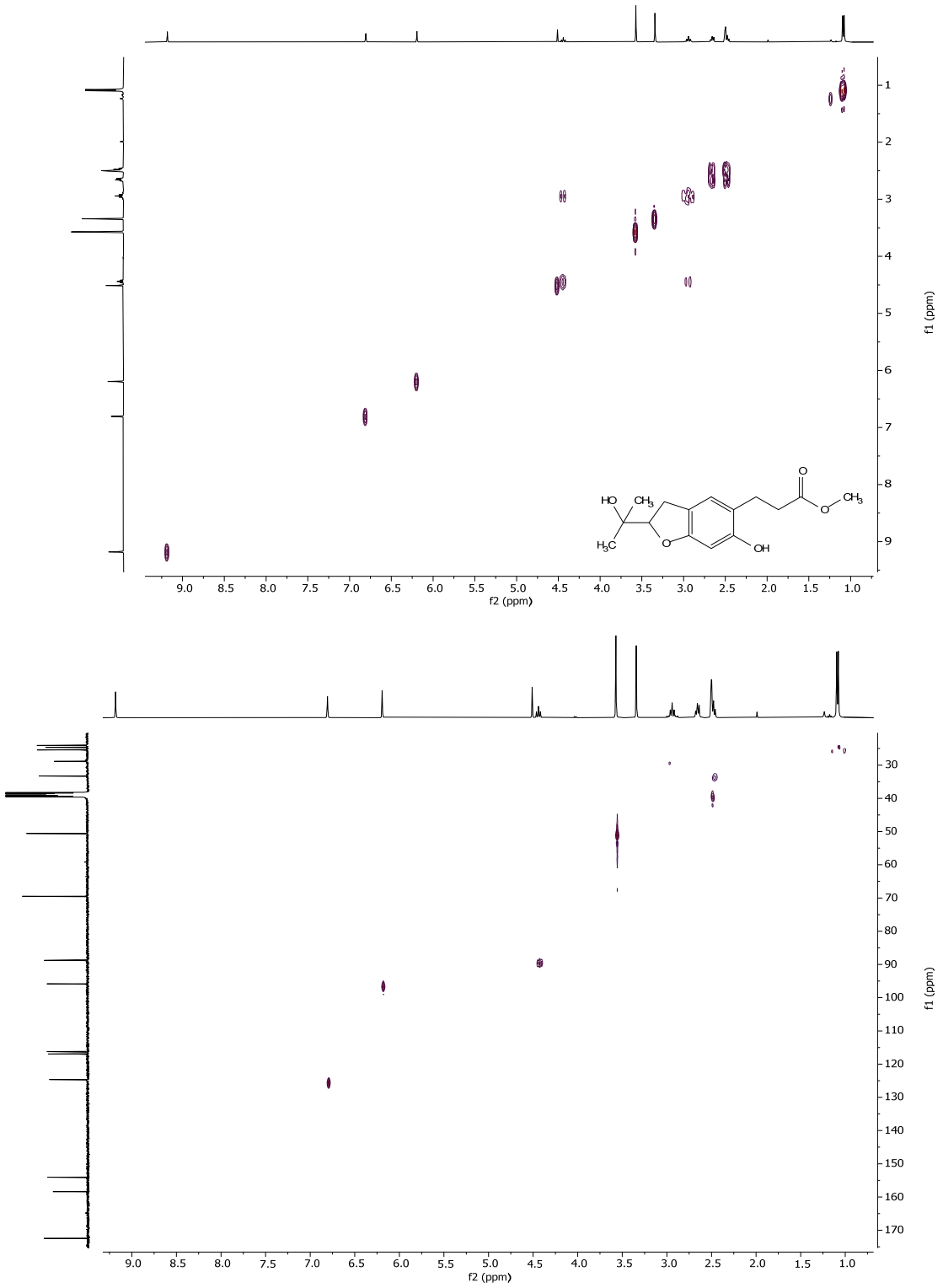


Figure S34. COSY (top) and HSQC (bottom) spectra of compound **1** in $CDCl_3$.

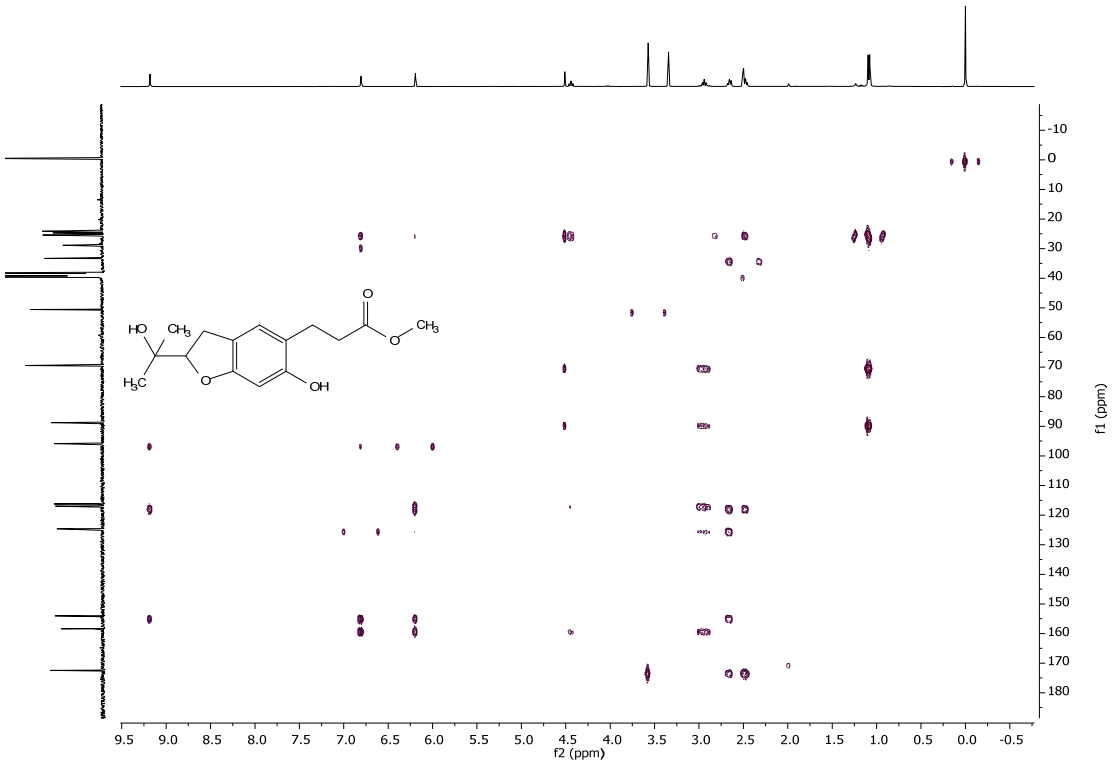


Figure S35. HMBC spectrum of compound **1** in $CDCl_3$.

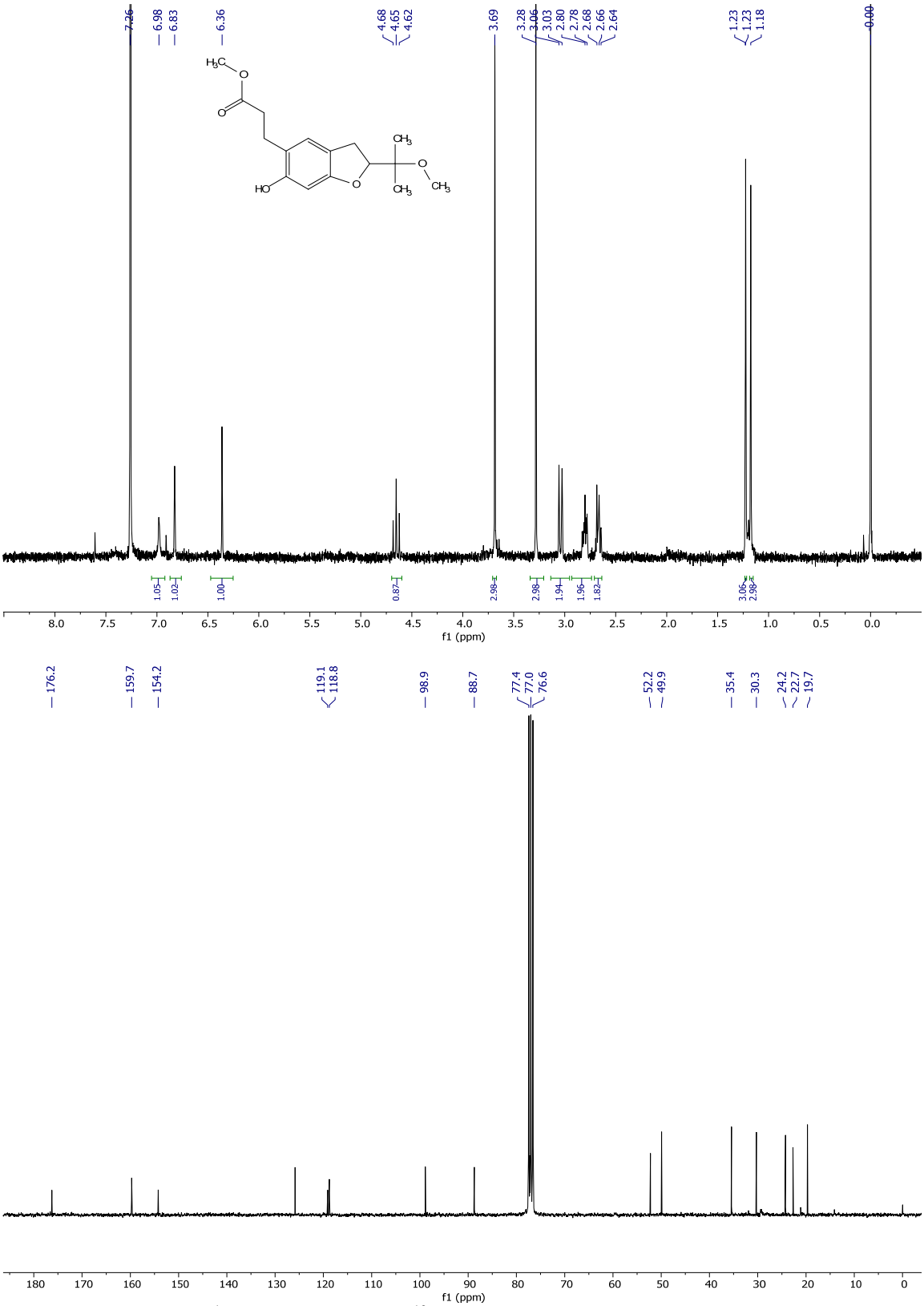


Figure S36. 300 MHz ^{1}H (top) and 75 MHz ^{13}C (bottom) NMR spectra of **31** in $CDCl_3$.

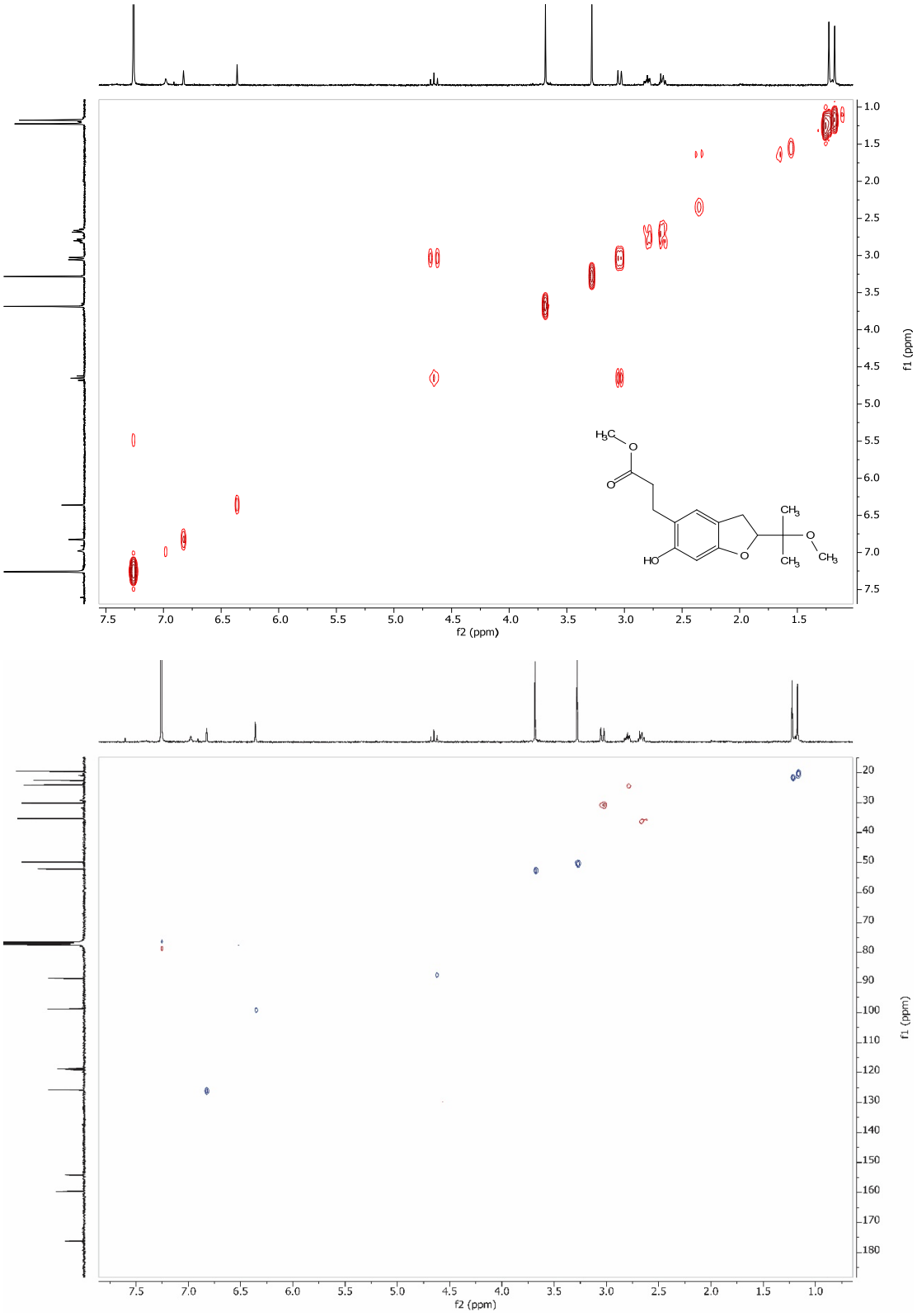


Figure S37. COSY (top) and HSQC (bottom) spectra of compound **31** in $CDCl_3$.

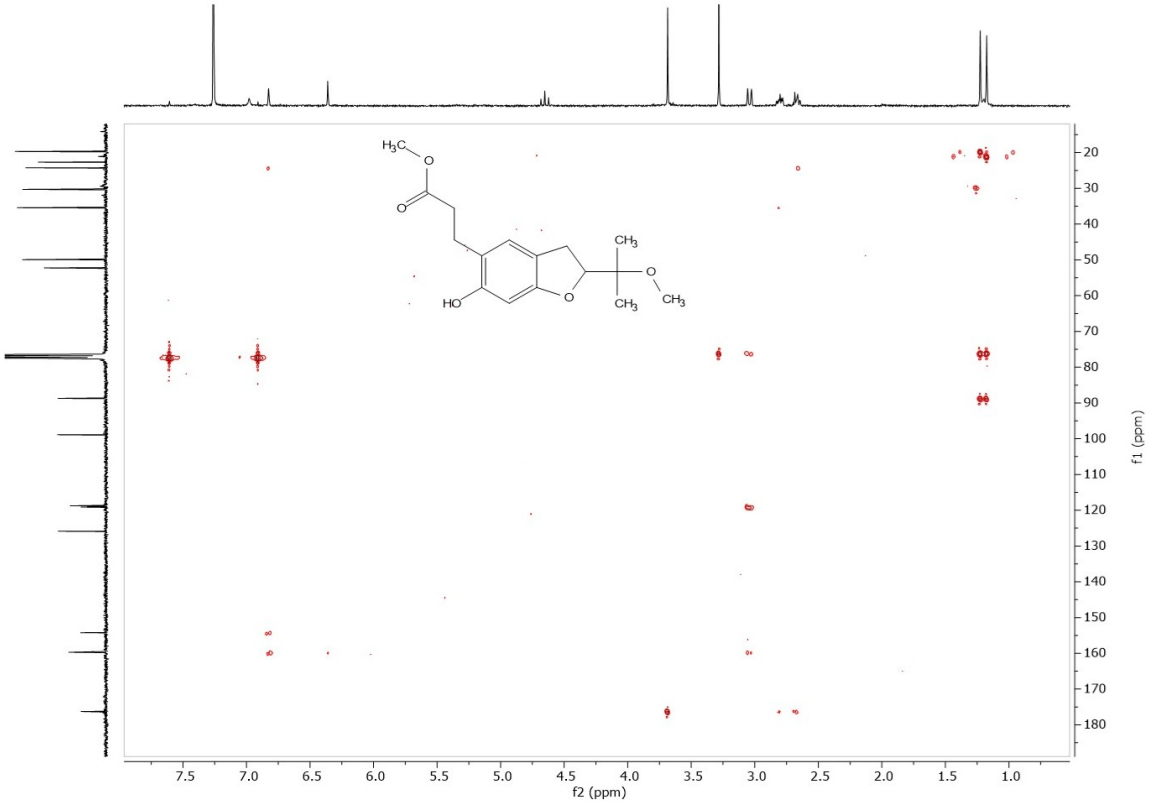


Figure S38. HMBC spectrum of compound **31** in $CDCl_3$.

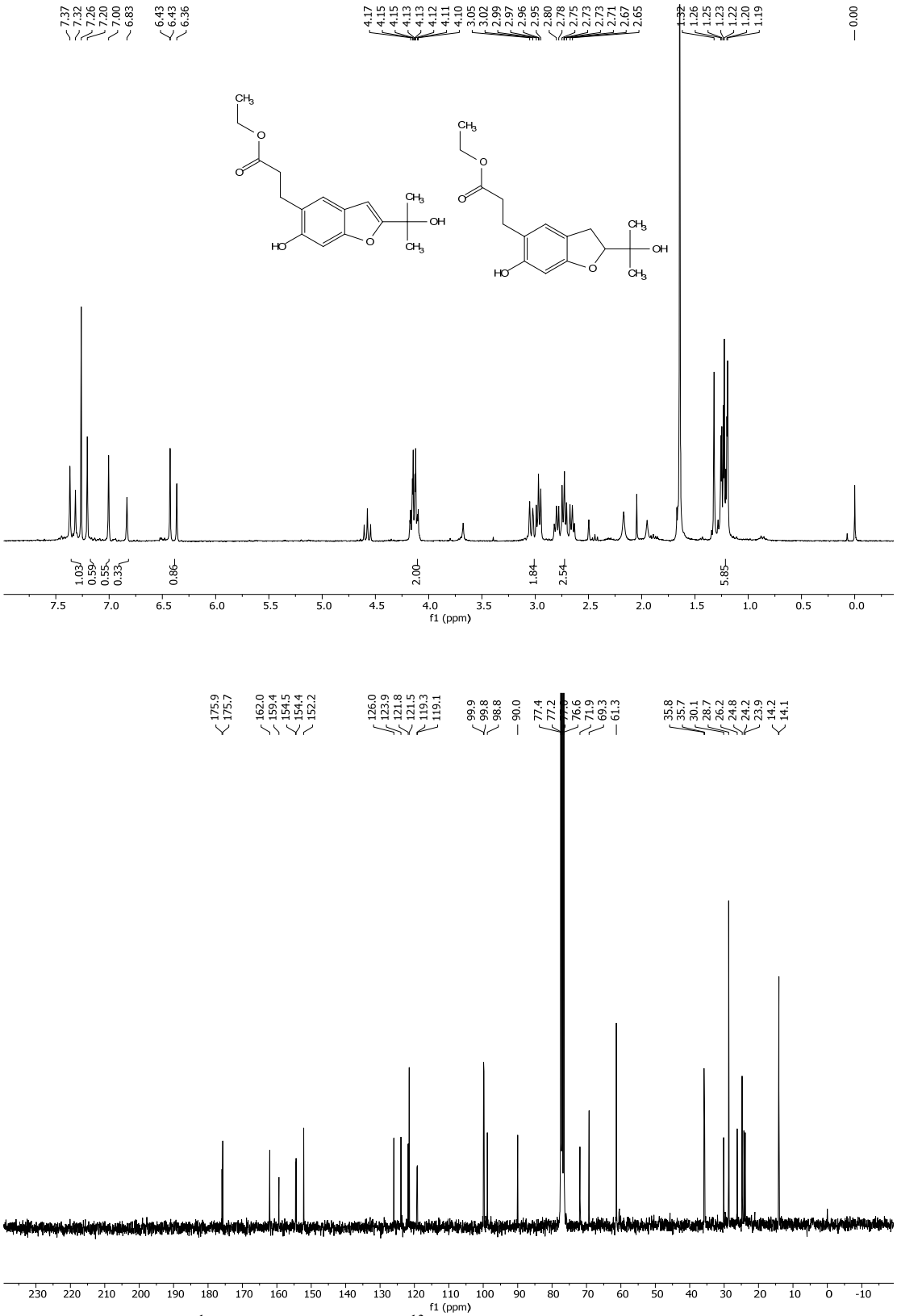


Figure S39. 400 MHz ^{1}H (top) and 101 MHz ^{13}C (bottom) NMR spectra of **32a,b** in $CDCl_3$.

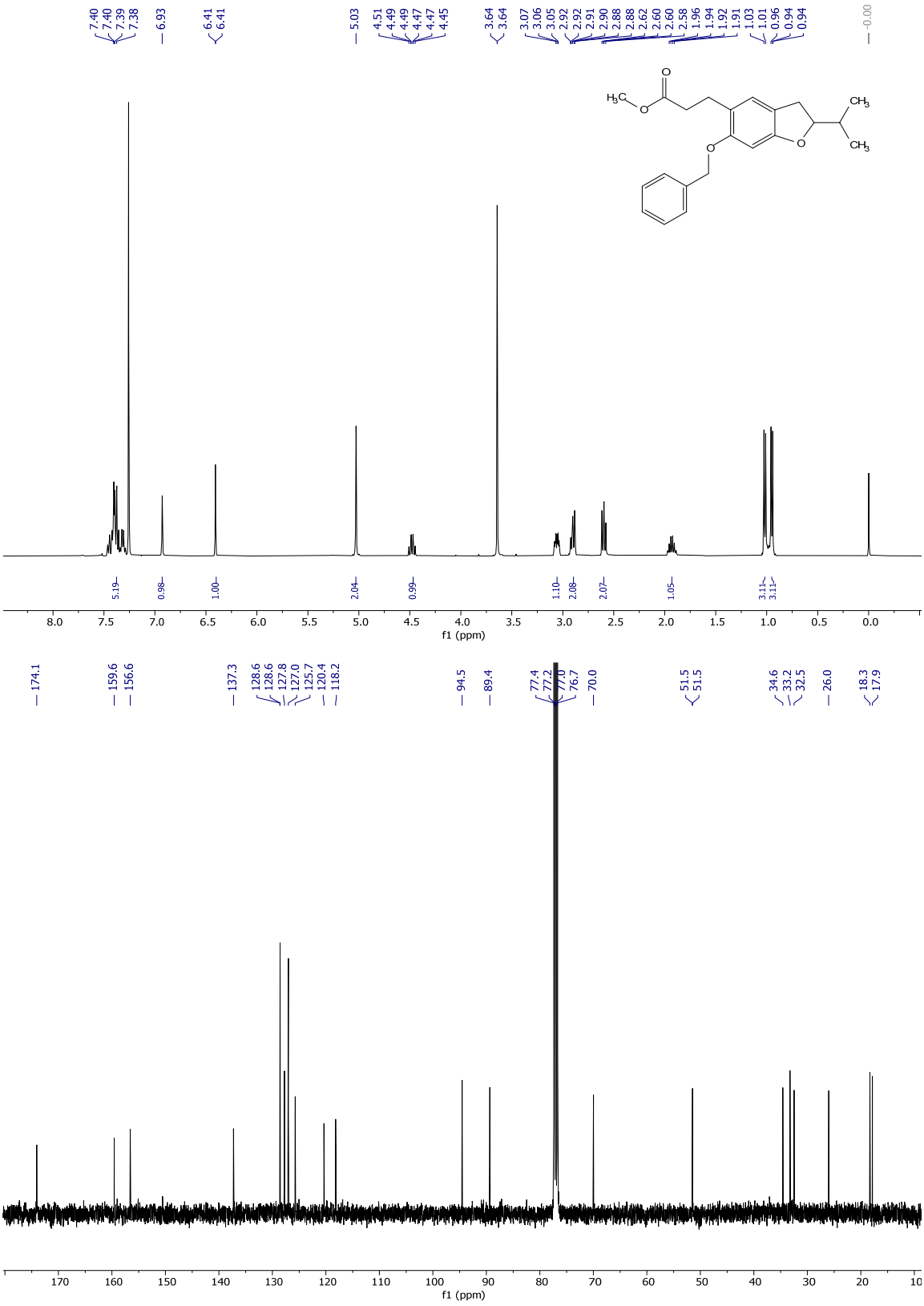


Figure S40. 300 MHz ^{1}H (top) and 75 MHz ^{13}C (bottom) NMR spectra of **34** in $CDCl_3$.

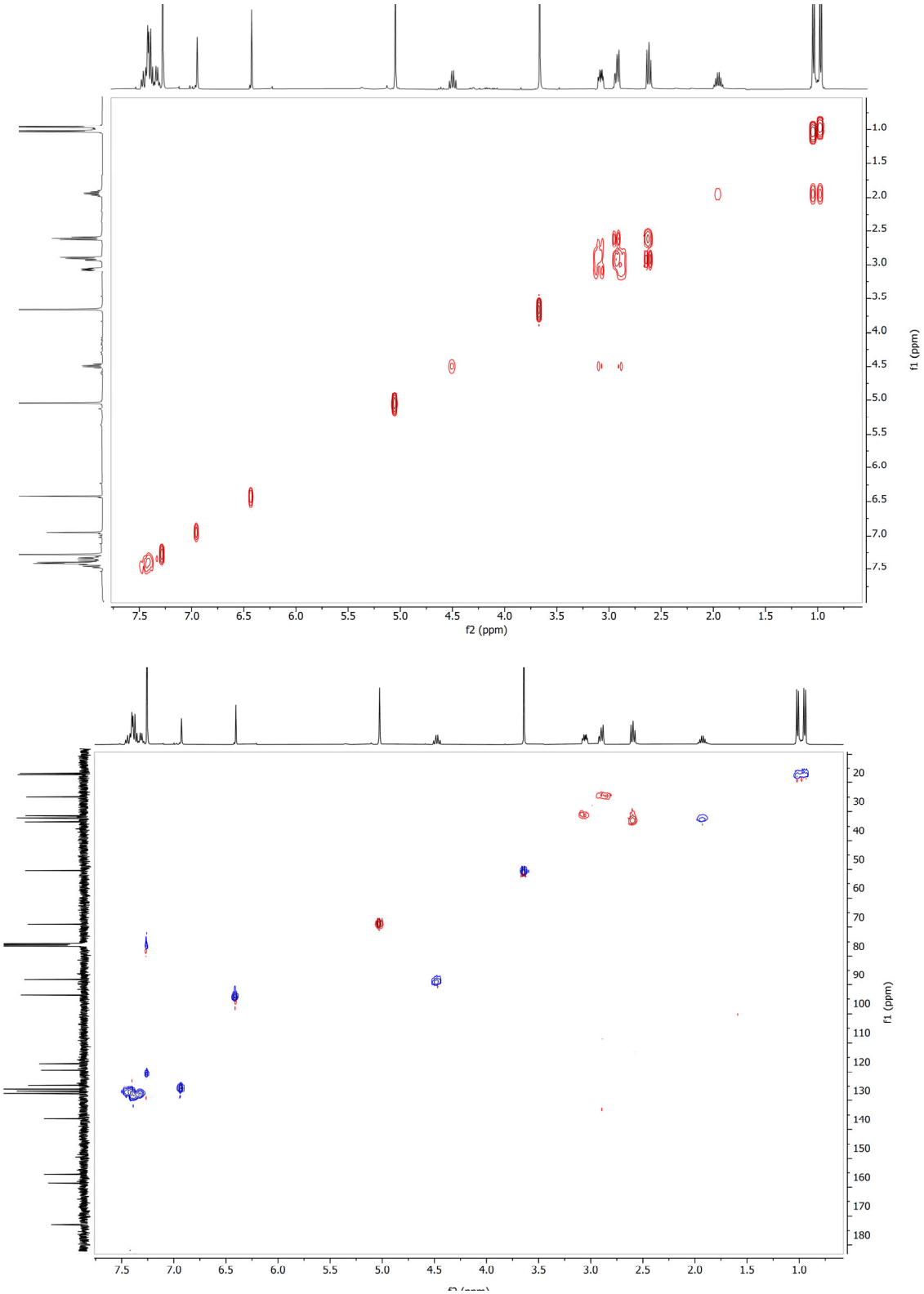


Figure S41. COSY (top) and HSQC (bottom) spectra of compound **34** in $CDCl_3$.

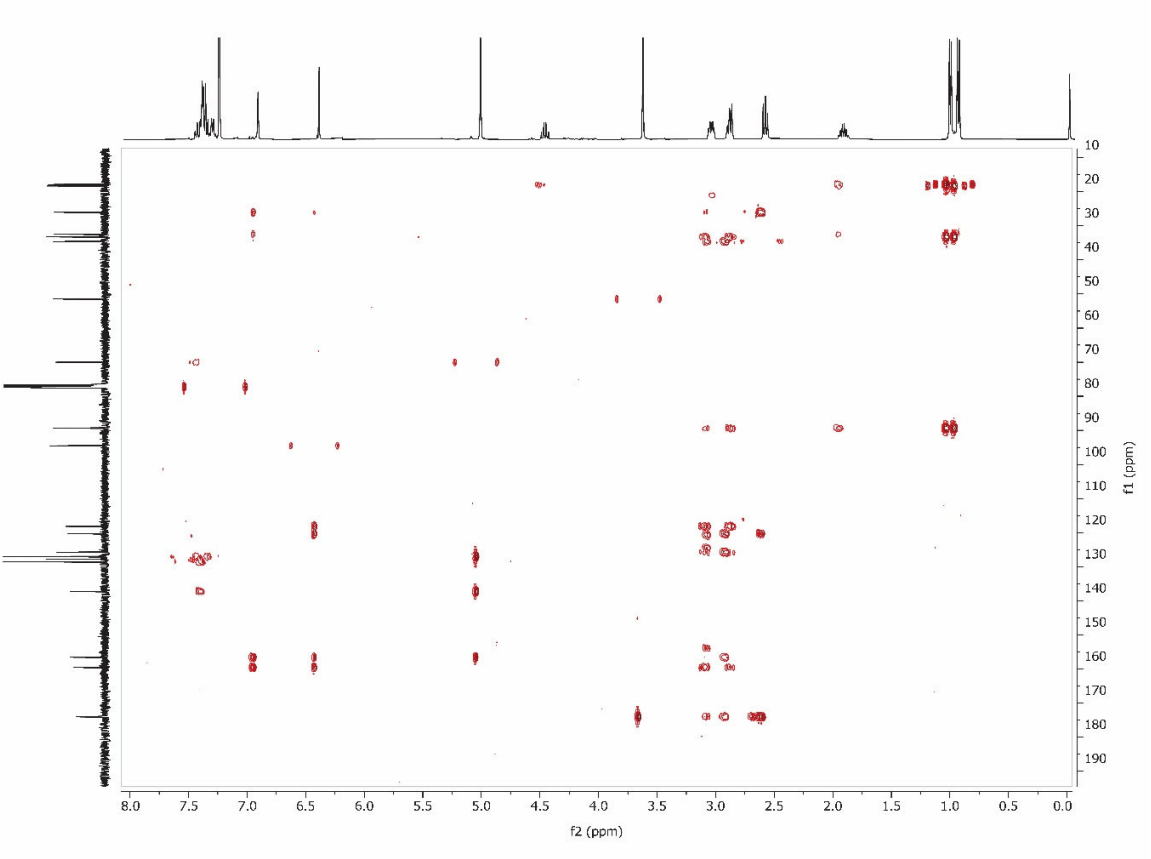
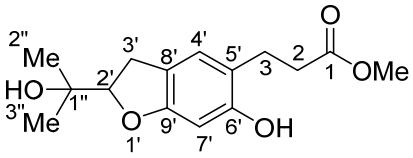


Figure S42. HMBC spectrum of compound **34** in $CDCl_3$.

Table S1. Comparison of ^{1}H and ^{13}C NMR spectra of the natural and synthetic products.



Position N°	^{1}H NMR (DMSO-d_6, 400 MHz)		^{13}C NMR (DMSO-d_6, 101 MHz)		$\Delta\delta_C$ (ppm)
	Natural product	Synthetic	Natural product	Synthetic	
1	-	-	173.1	173.0	0.1
2	2.47 (t, 2H)[a,b]	2.47 (t, *J*= 8.4, 2H)[a]	33.9	33.8	0.1
3	2.66 (m, 2H)	2.66 (t, *J*= 8.4, 2H)	25.3	25.2	0.1
2’	4.44 (t, *J*= 8.3, 1H)	4.44 (t, *J*= 8.7, 1H)	89.4	89.3	0.1
3’	2.94 (t, *J*= 8.3, 2H)	2.94 (t, *J*= 8.7, 2H)	29.5	29.4	0.1
4’	6.80 (s, 1H)	6.81 (s, 1H)	125.2	125.1	0.1
5’	-	-	117.6	117.5	0.1
6’	-	-	154.6	154.5	0.1
7’	6.19 (s, 1H)	6.19 (s, 1H)	96.5	96.3	0.2
8’	-	-	159.0	159.0	0.0
9’	-	-	116.9	116.7	0.2
1”	-	-	70.1	70.0	0.1
2”	1.10 (s, 3H)	1.10 (s, 3H)	26.0	26.0	0.0
3”	1.08 (s, 3H)	1.08 (s, 3H)	24.7	24.6	0.1
1”-OH	4,52[b] (s, 1H)	4.51 (bs, 1H, $w_{½}$= 2.6)	-	-	-
6’-OH	9.18 (s, 1H)	9.18 (s, 1H)	-	-	-
OMe	3.57 (s, 3H)	3.57 (s, 3H)	51.1	51.1	0.0

[a] Overlapped signal.
[b] Data taken from the spectrum shown in the supplementary material.

Table S2. Crystal data and structure refinement for compound **27**.

Empirical formula	C17 H13 I O3	
Formula weight	392.17	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 17.2784(6) Å	α = 90°
	b = 7.6648(3) Å	β = 105.1900(10)°
	c = 12.0994(4) Å	γ = 90°
Volume	1546.41(10) Å3	
Z	4	
Density (calculated)	1.684 Mg/m3	
Absorption coefficient	2.077 mm-1	
F(000)	768	
Crystal size	0.377 x 0.283 x 0.072 mm3	
Theta range for data collection	2.443 to 26.491°	
Reflections collected	36185	
Independent reflections	3184 [R(int) = 0.0607]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Refinement method	Full-matrix least-squares on F2	
Data / restraints / parameters	3184 / 0 / 191	
Goodness-of-fit on F2	1.074	
Final R indices [I>2sigma(I)]	R1 = 0.0448, wR2 = 0.0935	
R indices (all data)	R1 = 0.0717, wR2 = 0.1154	

Table S3. Bond lengths [Å] for compound **27**.

C(2)-C(3)	1.343(7)
C(2)-O(1)	1.391(6)
C(2)-C(19)	1.461(7)
C(3)-C(4)	1.424(7)
C(3)-H(3)	0.9300
O(1)-C(9)	1.372(6)
C(4)-C(9)	1.385(6)
C(4)-C(5)	1.398(7)
C(5)-C(6)	1.374(7)
C(5)-H(5)	0.9300
C(6)-C(7)	1.418(6)
C(6)-I(18)	2.098(5)
C(7)-O(10)	1.362(6)
C(7)-C(8)	1.379(7)
C(8)-C(9)	1.375(7)
C(8)-H(8)	0.9300
O(10)-C(11)	1.428(6)
C(11)-C(12)	1.498(7)
C(11)-H(11A)	0.9700
C(11)-H(11B)	0.9700
C(12)-C(17)	1.380(7)
C(12)-C(13)	1.388(7)
C(13)-C(14)	1.373(8)
C(13)-H(13)	0.9300
C(14)-C(15)	1.367(8)
C(14)-H(14)	0.9300
C(15)-C(16)	1.379(8)
C(15)-H(15)	0.9300
C(16)-C(17)	1.384(8)
C(16)-H(16)	0.9300
C(17)-H(17)	0.9300
C(19)-O(20)	1.211(6)
C(19)-C(21)	1.501(8)
C(21)-H(21A)	0.9600
C(21)-H(21B)	0.9600
C(21)-H(21C)	0.9600

Table S4. Bond angles [°] for compound **27**.

C(3)-C(2)-O(1)	111.1(4)
C(3)-C(2)-C(19)	133.7(5)
O(1)-C(2)-C(19)	115.2(4)
C(2)-C(3)-C(4)	107.2(4)
C(2)-C(3)-H(3)	126.4
C(4)-C(3)-H(3)	126.4
C(9)-O(1)-C(2)	105.5(4)
C(9)-C(4)-C(5)	118.1(5)
C(9)-C(4)-C(3)	105.8(4)
C(5)-C(4)-C(3)	136.1(5)
C(6)-C(5)-C(4)	118.3(4)
C(6)-C(5)-H(5)	120.8
C(4)-C(5)-H(5)	120.8
C(5)-C(6)-C(7)	121.9(5)
C(5)-C(6)-I(18)	119.7(4)
C(7)-C(6)-I(18)	118.4(4)
O(10)-C(7)-C(8)	124.2(4)
O(10)-C(7)-C(6)	115.7(4)
C(8)-C(7)-C(6)	120.1(4)
C(9)-C(8)-C(7)	116.4(4)
C(9)-C(8)-H(8)	121.8
C(7)-C(8)-H(8)	121.8
O(1)-C(9)-C(8)	124.4(4)
O(1)-C(9)-C(4)	110.4(4)
C(8)-C(9)-C(4)	125.1(5)
C(7)-O(10)-C(11)	117.4(4)
O(10)-C(11)-C(12)	109.4(4)
O(10)-C(11)-H(11A)	109.8
C(12)-C(11)-H(11A)	109.8
O(10)-C(11)-H(11B)	109.8
C(12)-C(11)-H(11B)	109.8
H(11A)-C(11)-H(11B)	108.2
C(17)-C(12)-C(13)	118.4(5)
C(17)-C(12)-C(11)	122.1(4)
C(13)-C(12)-C(11)	119.5(5)
C(14)-C(13)-C(12)	121.2(5)
C(14)-C(13)-H(13)	119.4
C(12)-C(13)-H(13)	119.4
C(15)-C(14)-C(13)	120.0(5)
C(15)-C(14)-H(14)	120.0
C(13)-C(14)-H(14)	120.0
C(14)-C(15)-C(16)	119.8(5)
C(14)-C(15)-H(15)	120.1

C(16)-C(15)-H(15)	120.1
C(15)-C(16)-C(17)	120.3(6)
C(15)-C(16)-H(16)	119.9
C(17)-C(16)-H(16)	119.9
C(12)-C(17)-C(16)	120.3(5)
C(12)-C(17)-H(17)	119.8
C(16)-C(17)-H(17)	119.8
O(20)-C(19)-C(2)	121.9(5)
O(20)-C(19)-C(21)	120.8(5)
C(2)-C(19)-C(21)	117.3(5)
C(19)-C(21)-H(21A)	109.5
C(19)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
C(19)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table S5. Torsion angles [°] for compound **27**.

O(1)-C(2)-C(3)-C(4)	0.1(6)
C(19)-C(2)-C(3)-C(4)	-177.9(6)
C(3)-C(2)-O(1)-C(9)	0.5(6)
C(19)-C(2)-O(1)-C(9)	178.9(4)
C(2)-C(3)-C(4)-C(9)	-0.6(6)
C(2)-C(3)-C(4)-C(5)	179.1(6)
C(9)-C(4)-C(5)-C(6)	0.7(7)
C(3)-C(4)-C(5)-C(6)	-179.0(6)
C(4)-C(5)-C(6)-C(7)	-2.2(8)
C(4)-C(5)-C(6)-I(18)	178.8(4)
C(5)-C(6)-C(7)-O(10)	-177.3(5)
I(18)-C(6)-C(7)-O(10)	1.7(6)
C(5)-C(6)-C(7)-C(8)	2.6(8)
I(18)-C(6)-C(7)-C(8)	-178.3(4)
O(10)-C(7)-C(8)-C(9)	178.5(5)
C(6)-C(7)-C(8)-C(9)	-1.4(7)
C(2)-O(1)-C(9)-C(8)	179.8(5)
C(2)-O(1)-C(9)-C(4)	-0.9(5)
C(7)-C(8)-C(9)-O(1)	179.0(5)
C(7)-C(8)-C(9)-C(4)	-0.1(8)
C(5)-C(4)-C(9)-O(1)	-178.8(4)
C(3)-C(4)-C(9)-O(1)	1.0(6)
C(5)-C(4)-C(9)-C(8)	0.4(8)
C(3)-C(4)-C(9)-C(8)	-179.8(5)
C(8)-C(7)-O(10)-C(11)	-7.1(7)
C(6)-C(7)-O(10)-C(11)	172.8(4)
C(7)-O(10)-C(11)-C(12)	-166.2(4)
O(10)-C(11)-C(12)-C(17)	26.7(7)
O(10)-C(11)-C(12)-C(13)	-156.9(5)
C(17)-C(12)-C(13)-C(14)	0.7(8)
C(11)-C(12)-C(13)-C(14)	-175.8(5)
C(12)-C(13)-C(14)-C(15)	-0.5(9)
C(13)-C(14)-C(15)-C(16)	0.8(10)
C(14)-C(15)-C(16)-C(17)	-1.2(10)
C(13)-C(12)-C(17)-C(16)	-1.2(8)
C(11)-C(12)-C(17)-C(16)	175.2(5)
C(15)-C(16)-C(17)-C(12)	1.5(10)
C(3)-C(2)-C(19)-O(20)	178.6(6)
O(1)-C(2)-C(19)-O(20)	0.6(8)
C(3)-C(2)-C(19)-C(21)	-0.9(9)
O(1)-C(2)-C(19)-C(21)	-178.9(5)

Symmetry transformations used to generate equivalent atoms:

Table S6. Hydrogen bonds for compound **27** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(5)-H(5)...O(1)#1	0.93	2.64	3.489(6)	152.3
C(8)-H(8)...O(20)#2	0.93	2.59	3.226(6)	126.0
C(11)-H(11B)...O(20)#2	0.97	2.64	3.560(7)	157.7

Symmetry transformations used to generate equivalent atoms:
#1 x,-y+1/2,z+1/2 #2 -x+1,y+1/2,-z+1/2

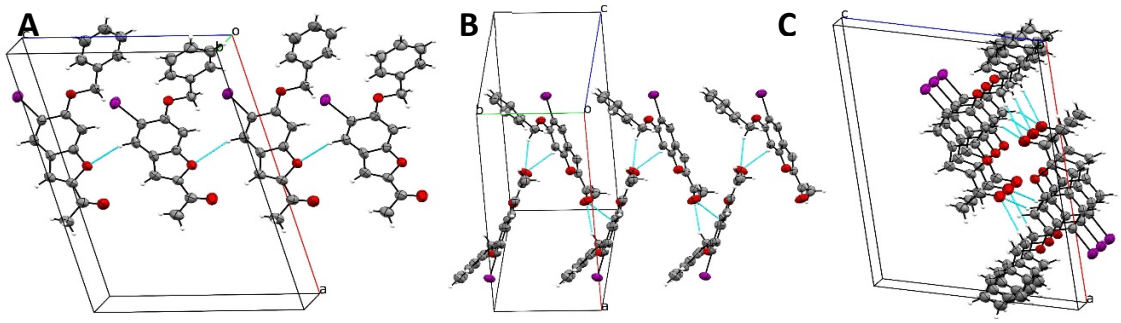


Figure S35. Supramolecular structure of compound **27**. A) The 1D chain extends via C5−H5···O1 bonds (x, -y+1/2, z+1/2) running along the c-axis. The hydrogen bonds are shown with cyan lines. B) The interactions C8-H8 ···O20 and C11-H11B ···O20 (-x+1, y+1/2, -z+1/2) generate a zigzag chain along the b-axis. C) The previous interaction in the view direction [1 0 1].

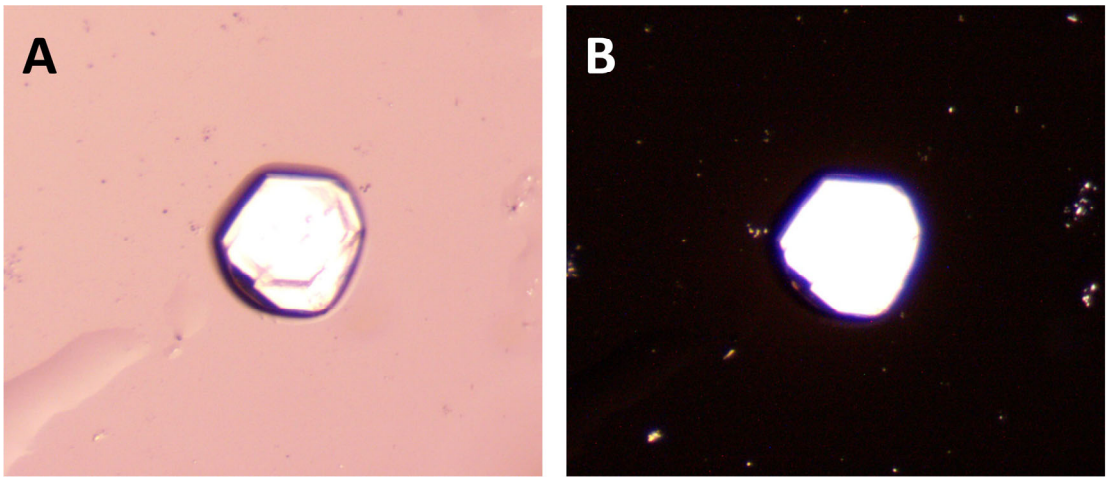


Figure S36. View of a crystal of compound **27** at 5 × magnification under white (A) and polarized (B) light.

checkCIF/PLATON report

Structure factors have been supplied for datablock(s) NLC_047_A_2_0ma_a

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: NLC_047_A_2_0ma_a

```
Bond precision:   C-C = 0.0075 A          Wavelength=0.71073

Cell:             a=17.2784(6)     b=7.6648(3)          c=12.0994(4)
                  alpha=90         beta=105.190(1)      gamma=90
Temperature:      298 K
```

	Calculated	Reported
Volume	1546.41(10)	1546.41(10)
Space group	P 21/c	P 21/c
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C17 H13 I O3	C17 H13 I O3
Sum formula	C17 H13 I O3	C17 H13 I O3
Mr	392.17	392.17
Dx,g cm-3	1.684	1.684
Z	4	4
Mu (mm-1)	2.077	2.077
F000	768.0	768.0
F000'	766.43	
h,k,lmax	21,9,15	21,9,15
Nref	3198	3184
Tmin,Tmax	0.499,0.861	0.499,0.861
Tmin'	0.452	

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Correction method= # Reported T Limits: Tmin=0.499 Tmax=0.861
AbsCorr = MULTI-SCAN
```

Data completeness= 0.996 Theta(max)= 26.491

R(reflections)= 0.0448(2330) wR2(reflections)= 0.1154(3184)

S = 1.074 Npar= 191

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

```
PLAT905_ALERT_3_C Negative K value in the Analysis of Variance ...     -2.905 Report
PLAT911_ALERT_3_C Missing FCF Refl Between Thmin & STh/L=    0.600          2 Report
                  0  1  1,   1  0  2,
```

Alert level G

```
PLAT066_ALERT_1_G Predicted and Reported Tmin&Tmax Range Identical          ? Check
PLAT083_ALERT_2_G SHELXL Second Parameter in WGHT  Unusually Large       6.56 Why ?
PLAT398_ALERT_2_G Deviating  C-O-C   Angle From 120 for O1       .      105.5 Degree
PLAT480_ALERT_4_G Long H...A H-Bond Reported H5       ..O1       .       2.64 Ang.
PLAT480_ALERT_4_G Long H...A H-Bond Reported H11B     ..O20      .       2.64 Ang.
PLAT883_ALERT_1_G Absent Datum for _atom_sites_solution_primary ..     Please Do !
PLAT910_ALERT_3_G Missing FCF Reflection(s) Below Theta(Min)[Deg]=       2.44 Note
                  1  0  0,
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L=  0.600         12 Note
PLAT965_ALERT_2_G The SHELXL WEIGHT Optimisation has not Converged     Please Check
PLAT969_ALERT_5_G The 'Henn et al.' R-Factor-gap value ...........      4.174 Note
              Predicted wR2: Based on SigI**2  2.76 or SHELX Weight 10.74
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.          1 Info
```

```
   0 ALERT level A = Most likely a serious problem - resolve or explain
   0 ALERT level B = A potentially serious problem, consider carefully
   2 ALERT level C = Check. Ensure it is not caused by an omission or oversight
  11 ALERT level G = General information/check it is not something unexpected

   2 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
   4 ALERT type 2 Indicator that the structure model may be wrong or deficient
   3 ALERT type 3 Indicator that the structure quality may be low
   3 ALERT type 4 Improvement, methodology, query or suggestion
   1 ALERT type 5 Informative message, check
```

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

PLATON version of 26/09/2025; check.def file version of 20/09/2025

duplicate check

No duplication found

Datablock NLC_047_A_2_0ma_a - ellipsoid plot