Electronic Supplementary Material (ESI) for Chemical Communications

Supporting Information

Total syntheses of S_p-(+)- and R_p-(−)-spiniferin-1,

a pair of unusual natural products with planar chirality

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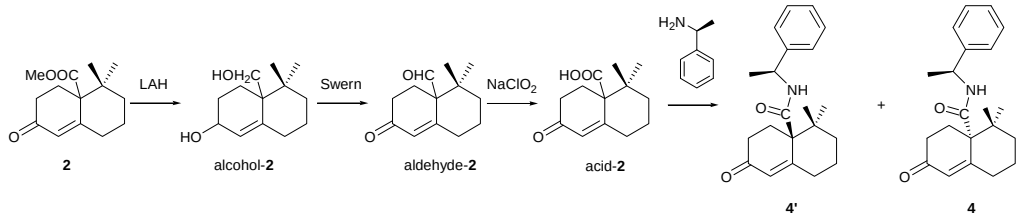
Experimental Section

General experimental information

Unless otherwise noted, all reactions in exclusively organic solvents were performed under an oxygen-free atmosphere of argon with rigid exclusion of moisture from reagents and glassware. Dichloromethane, DMSO, DMF, ^{i}PrOH and Et_3N was distilled from calcium hydride. Tetrahydrofuran was distilled from a blue solution of sodium benzophenone ketyl. 1,4-Dioxane was distilled from $LiAlH_4$. Analytical thin layer chromatography (TLC) was performed using silica gel F254 plates. The developed chromatogram was analyzed by UV lamp (254 nm). Liquid chromatography was performed using a forced flow (flash chromatography) of the indicated solvent system on Silica Gel (200-300 mesh).[1] ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$, unless otherwise noted, on a Varian 300 MHz spectrometer. Chemical shifts in ^{1}H NMR spectra are reported in parts per million (ppm) on the δ scale referenced to the residual peak of $CHCl_3$ at δ 7.26 ppm. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant in hertz (Hz), and integration. Chemical shifts of ^{13}C NMR spectra are reported in ppm referenced to the central peak of $CDCl_3$ (77.16 ppm) on the δ scale. IR spectra were measured on a BIO-RAD-FTS-185 instrument. Optical rotations were measured on a PERKIN ELMER Polarimeter 341. Melting points were recorded on a SGW X-4 type microscope and not corrected. Chiral HPLC analyses were performed on Waters Millennium station with a tunable UV detector at wavelength λ = 254 nm. The single-crystal X-ray diffraction data for compound **5** were collected on a Brucker Smart Apex diffractometer. Data of mass spectra and elemental analysis were provided by Laboratory of Analytical Chemistry at Shanghai Institute of Organic Chemistry. Compound **6**, **7**, **11a** and **11b** were prepared according to the previous procedures.[2]

Compound 4 and 4′



To a stirred solution of compound **2** (0.634 g, 2.68 mmol) in dry THF (12 mL) at room temperature was added $LiAlH_4$ (0.405 g, 10.72 mmol) in portions. After the addition the mixture was stirred at room temperature for 4 hrs, then quenched carefully by the addition of wet Na_2SO_4. The reaction mixture was filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography to give **alcohol-2** (0.53 g, 94%) as a white solid.

Alcohol-2: m.p. 107-108 °C; IR (KBr) ν 3313, 1666 cm^{-1}; ^{1}HNMR: δ = 5.92 (dd, J = 1.8, 4.8Hz, 1H, C**H**=), 4.05 (dd, J = 4.2, 8.7 Hz, 1H, O-C**H**-C=), 3.95 (d, J = 9.9 Hz, 1H, O-C**H**H-), 3.37 (d, J = 10.2Hz, 1H, O-CH**H**-), 2.62 (broad, 2H, 2O**H**), 2.15 (dt, J = 5.4Hz, 13.2Hz, 1H), 2.01-2.07 (m, 1H), 1.48-1.82 (m, 7H), 1.15-1.23 (m, 1H), 0.88 (s, 3H, C**H**$_3$), 0.82 (s, 3H, C**H**$_3$); EIMS: 210 (M), 162 (M-CH_2OH-H_2O), 147 (M-CH_2OH-H_2O-CH_3, 100); Anal. Calcd. for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.31; H, 10.56.

To a stirred solution of $(COCl)_2$ (1.14 mL, 13.06 mmol) in dry CH_2Cl_2 (100 mL) at -78°C was added DMSO (1.82 mL, 25.67 mmol) dropwise. After stirring at -78°C for half an hour a solution of **alcohol-2** (1.14 g, 5.42 mmol) in CH_2Cl_2 (10 mL) was added dropwise at -78°C. The mixture was stirred at this temperature for another 40 mins, then Et_3N (7.52 mL, 54.20 mmol) was added slowly. The reaction became a clear solution and the solution was allowed to stir at room temperature for 1.5 hours. To the reaction solution was added saturated $NaHCO_3$ aqueous solution (50mL) and the organic phase was separated. The aqueous phase was extracted with CH_2Cl_2 (1 × 40mL) and the combined organic phases were washed with water (30mL), brine (30mL), dried over anhydrous $MgSO_4$ and filtered. The filtrate was evaporated *in vacuo* and the residue was purified by column chromatography (silica gel, petroleum:EtOAc 8:1) to yield **aldehyde-2** (1.01 g, 91%) as a colorless oil.

Aldehyde-**2**: R_f = 0.5 (silica gel, Petroleum: EtOAc 3:1); IR (neat) ν 1716, 1676, 1618 cm^{-1}; ^{1}HNMR: δ = 9.90 (s, 1H, -C**H**O), 6.00 (d, J = 1.5 Hz, 1H, C**H**=), 1.42-2.73 (m, 10H), 1.09 (s, 3H, C**H**$_3$),0.94 (s, 3H, C**H**$_3$); EIMS: 206 (M, 42.65), 191 (M-CH_3, 10.87); Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.38; H, 9.00.

Aldehyde-2 (1.66 g, 8.1 mmol) was dissolved in a mixture of ^{t}BuOH (70 mL) and distilled water (42 mL). At 0°C NaH_2PO_4•$2H_2O$ (4.79 g, 30.71 mmol), DMSO (8.55 mL, 0.12 mol) and $NaClO_2$ (1.82 g, 16.18 mmol, 80% purity) were added in turn. The reaction was done after 18 mins by TLC. To the reaction solution was added EtOAc (100 mL) and water (20 mL) and the organic phase was separated. The aqueous phase was extracted with EtOAc (3 × 50 mL) and the combined organic phases were washed with water (20 mL), brine (20 mL), dried over anhydrous $MgSO_4$ and filtered. The filtrate was evaporated *in vacuo* and the residue was purified by column chromatography (silica gel, petroleum:EtOAc 3:1, several drops of HCOOH added) to yield **acid-2** (1.34 g, 75%) as a white solid.

Acid-2: m.p.: 120-122 °C; R_f = 0.2 (silica gel, Petroleum: EtOAc 3:1); IR (KBr) ν_{max} 2970, 1712, 1628, 1600 cm^{-1}; ^{1}HNMR: δ = 5.97 (d, J = 2.1 Hz, 1H, =C**H**), 2.91-3.05 (m, 1H), 2.36-2.54 (m, 4H), 1.92-2.07 (m, 2H), 1.63-1.75 (m, 2H), 1.37 (d, J = 13.5Hz, 1H), 1.07 (s, 3H, C**H**$_3$), 0.97 (s, 3H, C**H**$_3$); EIMS: 222 (M, 28.97), 207 (M-CH_3, 23.38); Anal. Calcd. for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C,70.15; H, 8.19.

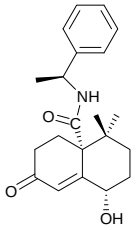
To a stirred solution of DMF (0.48 mL, 6.26 mmol) in dry CH_2Cl_2 (9 mL) at −20 °C was added $(COCl)_2$ (0.22 mL, 2.52 mmol) dropwise. After stirring at −20 °C for 20 mins a solution of **acid-2** (0.46 g, 2.09 mmol) in CH_2Cl_2 (9 mL) was added dropwise at −20 °C. The mixture was stirred at this temperature for another 20 min, then (*S*)-α-methylbenzylamine (1.15 mL, 8.92 mmol) was added slowly. The reaction mixture was stirred at −20 °C for 10 mins then at room temperature for 15 min. To the reaction solution was added EtOAc (50mL) and water (10mL) and the solution was acidified by 5% HCl solution. The organic phase was separated and the aqueous phase was extracted with EtOAc (2 × 30mL). The combined organic phases were washed with 5% $NaHCO_3$ solution (10mL), water (10 mL), brine (10mL), dried over anhydrous $MgSO_4$ and filtered. The filtrate was evaporated *in vacuo* and the residue was purified by column chromatography (silica gel, petroleum:EtOAc 5:1) to **4** (0.26 g, 39%) and **4′** (0.28 g, 41%).

4: as a white solid. m.p.: 149-156 °C; R_f = 0.18 (silica gel, Petroleum: EtOAc 5:1); $[\alpha]_D^{28}$ = −236.6(*c* 0.63, $CHCl_3$); IR (KBr) ν_{max} 3383, 1648, 1611 cm^{-1}; ^{1}HNMR: δ = 7.25-7.40 (m, 5H, C_6**H**$_5$), 6.01 (s, 1H, C**H**=), 5. 89 (d, J = 7.8Hz, 1H, -N**H**-), 5.13 (dt, J = 6.9, 6.9Hz, 1H, PhC**H**), 2.81-2.96 (m, 1H), 2.02-2.55 (m, 5H), 1.65-1.88 (m,

3H), 1.49(d, J = 7.2Hz, 3H, N-C-C**H**$_3$), 1.28-1.34 (m, 1H), 1.08 (s, 3H, C**H**$_3$), 0.91 (s, 3H, C**H**$_3$); EIMS: 325 (M, 18.38); Anal. Calcd. for $C_{21}H_{27}NO_2$: C, 77.50; H, 8.36; N, 4.30. Found: C, 77.41; H, 8.32; N, 4.09.

4′: as a white solid. m.p.: 108-113 °C; R_f = 0.22 (silica gel, Petroleum: EtOAc 5:1); $[\alpha]_D^{28}$ = +163.1(*c* 0.82, $CHCl_3$); IR (KBr) ν_{max} 3371, 1647, 1602 cm^{-1}; ^{1}HNMR: δ = 7.25-7.40(m, 5H, C_6**H**$_5$), 6.00(d, J = 1.8Hz, 1H, C**H**=), 5.87(d, J = 7.2Hz, 1H, -N**H**-), 5.16(dt, J = 6.9, 6.9Hz, 1H, PhC**H**), 2.78-2.93 (m, 1H), 2.04-2.47 (m, 5H), 1.63-1.88 (m, 3H), 1.49(d, J = 7.2Hz, 3H, N-C-C**H**$_3$), 1.28-1.37 (m, 1H), 1.16(s, 3H, C**H**$_3$), 0.94(s, 3H, C**H**$_3$); EIMS: 325 (M, 20.10); Anal. Calcd. for $C_{21}H_{27}NO_2$: C, 77.50; H, 8.36; N, 4.30. Found: C, 77.90; H, 8.65; N, 3.95.

Compound 5



5

To a stirred solution of compound **4** (0.327 g, 1 mmol) in dry ^{i}PrOH (32 mL) at room temperature was added orthoformic acid triisopropyl ester (0.27 mL, 2.58 mmol) and *p*-TsOH•H_2O (38 mg, 0.2 mmol) in turn. The mixture was stirred at 40 °C for 3 hrs. To the reaction solution was added EtOAc (70 mL) and water (20 mL) and the organic phase was separated. The aqueous phase was extracted with EtOAc (3 × 20 mL) and the combined organic phases were washed with brine (20 mL), dried over anhydrous Na_2SO_4 and filtered. The filtrate was evaporated *in vacuo* and the residue was purified by column chromatography (silica gel, petroleum:EtOAc 3:1) to yield **5** (0.299 g, 87%) as a white solid. Crystals suitable for X-ray crystallographic analysis were grown in a mixture of EtOAc and hexane.

5: as a white solid. m.p.: 211-218 °C; $[\alpha]_D^{26}$ = −142.39 (c, 0.36, $CHCl_3$); IR (KBr) ν_{max} 3344, 3240, 3060, 1685, 1633 cm^{-1}; ^{1}HNMR: δ = 8.73 (d, J = 6.6Hz, 1H, -N**H**-), 7.17-7.27 (m, 5H, C_6**H**$_5$), 6.03 (s, 1H, C**H**=), 5.12 (s, 1H, -O**H**), 5.06 (dt, J = 6.9, 7.2Hz, 1H, PhC**H**), 4.34 (s, 1H, -C**H**-O-), 2.48 (dt, J = 13.2, 3.3Hz, 1H), 2.28-2.33 (m, 2H), 2.12 (dt, J = 13.8, 3Hz, 1H), 2.00 (dt, J = 12.6, 4.2Hz, 1H), 1.91 (dt, J = 10.4, 3.3Hz, 1H), 1.82 (dt, J = 10.8, 2.1Hz, 1H), 1.45 (d, J = 7.2Hz, 3H, C**H**$_3$-C-N), 1.24 (d, J = 12.9Hz, 1H), 0.98 (s, 3H, C**H**$_3$), 0.89 (s, 3H, C**H**$_3$); ^{13}CNMR (75 MHz): δ = 200.2, 169.7, 160.1, 143.7, 133.1, 128.7(2C), 127.3, 126.0(2C), 70.9, 56.4, 50.2, 36.1, 35.9, 32.4, 29.8, 28.6, 27.2, 25.4, 22.4; ESIMS: 342 (M+H$^+$); HRMS: 364.1899 (M+Na$^+$).

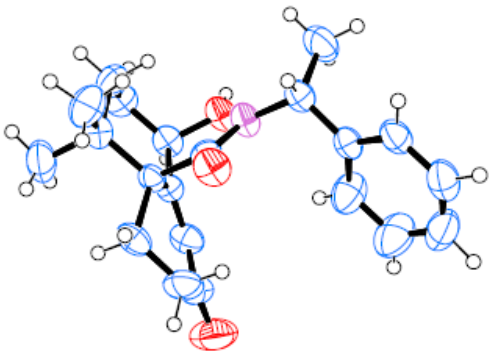
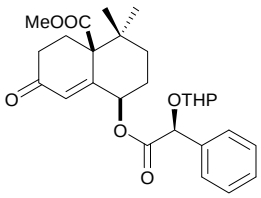


Table 1. Crystal data and structure refinement for **5**

Empirical formula	$C_{21}H_{27}NO_3$
Formula weight	341.44
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 11.4805 (10) Å α = 90 °
	b = 11.8426 (10) Å β = 90 °
	c = 14.1986 (12) Å γ = 90 °
Volume	1930.4 (3) $Å^3$
Z, calculated density	4, 1.171 Mg/m^3
Absorption coefficient	0.078 mm^{-1}
F (000)	732
Theta range for data collection	2.24 to 28.26 °
Limiting indices	−14<=h<=14, −14<=k<=15, −16<=l<=18
Reflections collected/unique	11865 / 4489 [R(int) = = 0.0775]
Completeness to theta = 28.26	96.0%
Absorption correction	Empirical
Max. and min. transmission	1.00000 and 0.75955
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	4489/ 2 /266
Goodness-of-fit on F^2	0.701
Final R indices [I>2sigma(I)]	R1 = 0.0454, wR2 = 0.0734
R indices (all data)	R1 = 0.1130, wR2 = 0.0856
Absolute structure parameter	1.1 (15)
Extinction coefficient	0.0046 (6)
Largest diff. peak and hole	0.209 and −0.103 e. $Å^{-3}$

Compound 8

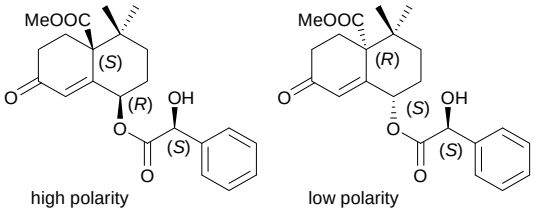


8

To a stirred solution of compound **7** (4.00 g, 15.86 mmol), *O*-tetrahydropyranyl-*S*-mandelic acid (4.97 g, 21 mmol) and 4-dimethylaminopyridine (48 mg, 0.39 mmol) in dry CH_2Cl_2 (76 mL) under ice bath was added *N*,*N*'-dicyclohexylcarbodiimide (4.37 g, 21 mmol) in one portion, and the mixture was stirred at 0^oC for 2.7 hrs and then filtered. The filtrate was concentrated under vacuum and the residue was purified by column chromatography (silica gel, petroleum:EtOAc 8:1) to yield compound **8** (6.36 g, 85%) as a colorless oil.

8: R_f = 0.45 (silica gel, Petroleum: EtOAc 3:1); IR (neat) ν 3065, 3033, 2951, 2875, 1739, 1684, 1635, 1496, 1455, 1392, 1370, 766, 726, 702 cm^{-1}; ^{1}HNMR: δ = 7.31-7.48 (m, 5H, -C_6**H**$_5$), 6.05 (s) and 6.23 (s, 1H, -C**H**=C-), 5.47-5.56 (m, 1H, O=C-C=C-C**H**-), 5.10 (s), 5.13 (s), 5.22 (s) and 5.27 (s, 1H, C_6H_5-C**H**-), 4.53 (s), 4.60 (s), 4.83 (s) and 4.87 (s, 1H, -O-C**H**-O-), 3.64-3.69 (m) and 3.86-3.96 (m, 1H, -O-C**H**H-), 3.44-3.52 (m, 1H, -O-CH**H**-), 3.42 (s), 3.56 (s), 3.71 (s) and 3.74 (s, 3H, -COOC**H**$_3$), 2.52-2.79 (m, 1H), 2.34-2.47 (m, 1H), 2.12-2.31 (m, 2H), 1.92-2.06 (m, 1H), 1.73-1.92 (m, 3H), 1.66-1.73 (m, 1H), 1.42-1.59 (m, 3H), 1.24-1.32 (m, 2H), 1.13 (s), 1.16 (s) and 1.20 (s, 3H, -C**H**$_3$), 0.88 (s) and 0.91 (s, 3H, -C**H**$_3$); EIMS: 251 (M-PhCH(OTHP)CO, 0.27), 235 (M-PhCH(OTHP)COO or PhCH(OTHP)COO, 12.03), 107 (C_7H_7OH, 100), 91 (C_7H_7, 21.55), 85 (THP, 37.35); ESIMS: 488 (M+NH_4^+); HRMS: 493.2196745 (M+Na^+); Anal. Calcd. for $C_{27}H_{34}O_7$: C, 68.92; H, 7.28. Found: C, 68.97; H, 7.44.

Compound 9 and 9′



To a stirred solution of compound **8** (1.95 g, 4.14 mmol) in absolute MeOH (13 mL) was added *p*-TsOH•H_2O (13 mg, 0.068 mmol) in one portion at ambient temperature, and the solution was stirred at ambient temperature for 2.4 hrs. To the reaction solution was added EtOAc (50 mL) and water (20 mL) and the organic phase was separated. The aqueous phase was extracted with EtOAc (3 × 30 mL) and the combined organic phases were washed with water (20 mL), brine (20 mL), dried over anhydrous Na_2SO_4 and filtered. The filtrate was evaporated *in vacuo* and the residue was purified by column chromatography (silica gel, petroleum:EtOAc 5:1) to yield a mixture of compound **9** and **9′** (1.5 g) as a colorless oil. Column chromatography resolution (silica gel, petroleum:EtOAc 5:1 to 4:1) gave compound **9** (0.58 g, 36%), **9′** (0.60 g, 38%) and their mixture (0.17 g, 11%).

9: Slowly solidified as a white solid when standing at room temperature. m.p.: 89-90 °C; R_f = 0.18 (silica gel, Petroleum: EtOAc 3:1); $[\alpha]_D^{24}$ = +132.4 (*c* 0.98, $CHCl_3$); de%: 93.8%; ee%: 83.6%; IR (KBr) ν_{max} 3474, 3034, 30007, 2967, 1741, 1729, 1682, 1638, 1493, 1459, 767, 747cm^{-1}; ^{1}HNMR: δ = 7.32-7.44 (m, 5H, -C_6**H**$_5$), 6.27 (s 1H, -C**H**=C-), 5.46 (s, 1H, O=C-C=C-C**H**-), 5.09 (d, J = 6.0Hz, 1H, C_6H_5-C**H**-), 3.72 (s, 3H, -COOC**H**$_3$), 3.50 (d, J = 5.7Hz, 1H, -O**H**), 2.62-2.73 (m, 1H), 2.40-2.47 (m, 1H), 2.08-2.33 (m, 3H), 1.82-1.96 (m, 1H), 1.54-1.60 (m, 1H), 1.26-1.42 (m, 1H), 1.20 (s, 3H, -C**H**$_3$), 0.91 (s, 3H, -C**H**$_3$); EIMS: 252 (M+1-PhCH(OH)CO, 0.65), 236 (M+1-PhCH(OH)COO, 17.53), 107 ($C_7H_7OH^+$, 100), 91 ($C_7H_7^+$, 15.57); ESIMS: 404 (M+NH_4^+); HRMS: 409.1621597 (M+Na^+); Anal. Calcd. for $C_{22}H_{26}O_6$: C, 68.38; H, 6.78. Found: C, 68.13; H, 6.76.

9′: R_f = 0.22 (silica gel, Petroleum: EtOAc 3:1); $[\alpha]_D^{24}$ = −58.0 (*c* 1.13, $CHCl_3$); de%: 98.5%; ee%: 95.5%; IR (neat) ν_{max} 3488, 3064, 3033, 2955, 2877, 1734, 1683, 1604, 1496, 1455, 1394, 1372, 766, 733, 699 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.30-7.43 (m, 5H, -C_6**H**$_5$), 6.16 (s, 1H, -C**H**=C-), 5.58 (s, 1H, O=C-C=C-C**H**-), 5.19 (d, J = 6.0 Hz, 1H, C_6H_5-C**H**-), 3.64 (d, J = 6.3 Hz, 1H, -O**H**), 3.51 (s, 3H, -COOC**H**$_3$), 2.29-2.64 (m, 4H), 1.93-2.09 (m, 2H), 1.80-1.86 (m, 1H), 1.26-1.32 (m, 1H), 1.13 (s, 3H, -C**H**$_3$), 0.94 (s, 3H, -C**H**$_3$); ESIMS: 404

($M+NH_4^+$); HRMS: 409.1621597 ($M+Na^+$); Anal. Calcd. for $C_{22}H_{26}O_6$: C, 68.38; H, 6.78. Found: C, 68.04; H, 6.89.

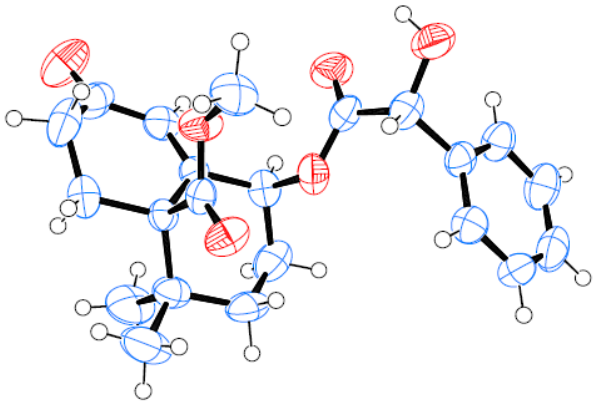
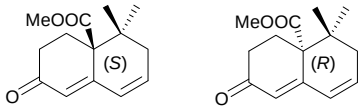


Table 2. Crystal data and structure refinement for **9/9'**

Empirical formula	$C_{22}H_{26}O_6$
Formula weight	386.43
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, Pn
Unit cell dimensions	a = 10.5615 (12) Å α = 90 °
	b = 8.3727 (9) Å β = 108.972 (2) °
	c = 11.8537 (12) Å γ = 90 °
Volume	991.26 (18) $Å^3$
Z, calculated density	2, 1.295 Mg/m^3
Absorption coefficient	0.094 mm^{-1}
F (000)	412
Theta range for data collection	2.25 to 27.00 °
Limiting indices	−13<=h<=13, −10<=k<=8, −11<=l<=15
Reflections collected/unique	5692 / 2159 [R(int) = 0.0680]
Completeness to theta = 27.00	99.4%
Absorption correction	Empirical
Max. and min. transmission	1.00000 and 0.76531
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	2159/ 2 /257
Goodness-of-fit on F^2	0.764
Final R indices [I>2sigma(I)]	R1 = 0.0399, wR2 = 0.0516
R indices (all data)	R1 = 0.0790, wR2 = 0.0581
Absolute structure parameter	10 (10)
Largest diff. peak and hole	0.116 and −0.123 e. $Å^{-3}$

Compound (+)-10 and (-)-10



(+)-10 **(-)-10**

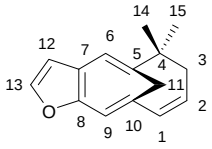
To a stirred solution of compound **9′** (1.76 g, 4.57 mmol) in dry 1,4-dioxane (30 mL) was added Et_3N (0.79 mL, 5.48 mmol) and $Pd(PPh_3)_4$ (0.26 g, 0.23 mmol) in turn at ambient temperature, and the solution was stirred at 75°C for 1.5 hrs. To the reaction solution was added EtOAc (100mL) and water (30mL) and the organic phase was separated. The aqueous phase was extracted with EtOAc (3 × 50mL) and the combined organic phases were washed with water (20mL), brine (20mL), dried over anhydrous Na_2SO_4 and filtered. The filtrate was evaporated in vacuo and the residue was purified by column chromatography (silica gel, petroleum:EtOAc 8:1) to yield compound **(-)-10** (0.84 g, 79%) as a pale yellow oil.

(-)-10: $[\alpha]_D^{24}$ = −213.4 (*c* 1.08, $CHCl_3$); e.e.: 93.0%; ^{1}HNMR: δ = 6.30 (dd, J = 9.9, 2.4Hz, 1H, O=C-C=C-C-C**H**=), 6.20 (ddd, J = 9.9, 6.0, 2.1Hz, 1H, O=C-C=C-C=C**H**-), 5.86 (s, 1H, O=C-C**H**=), 3.68 (s, 3H, -COOC**H**$_3$), 1.9-2.6 (m, 6H), 1.07 (s, 3H, C**H**$_3$), 0.96 (s, 3H, C**H**$_3$).

Compound **9** (1.48 g, 3.83 mmol) was converted into compound **(+)-10** (0.75 g, 84%) as a pale yellow oil.

(+)-10: $[\alpha]_D^{24}$ = +183.1 (*c* 1.15, $CHCl_3$); e.e.: 80.9%. ^{1}H NMR: δ = 6.27-6.34 (m, 1H, O=C-C=C-C-C**H**=), 6.15-6.23 (m, 1H, O=C-C=C-C=C**H**-), 5.86 (s, 1H, O=C-C**H**=), 3.68 (s, 3H, -COOC**H**$_3$), 1.9-2.6 (m, 6H), 1.07 (s, 3H, C**H**$_3$), 0.96 (s, 3H, C**H**$_3$).

(+)-Spiniferin-1



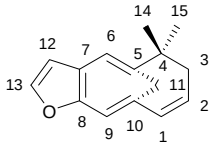
(+)-spiniferin-1

To a solution of **11a** (1.16 g, 3.07 mmol) in THF (12 mL) was added TsOH (58 mg). The solution was refluxed for 40 minutes under oxygen-free atmosphere, then $LiAlH_4$ (408 mg, 10.75 mmol) and additional THF (12 mL) was added directly. After stirring for 1.8 hour at 40°C, the reaction mixture was quenched with wet Na_2SO_4, filtered and washed with THF (3 x 8 mL). The filtrate was concentrated *in vacuo* and the residue was dissolved in THF (12 mL). DBU (1.5 mL, 10.13 mmol) was added in one portion at 0 °C then $CF_3CF_2CF_2CF_2SO_2F$ (3.06 g, 10.13 mmol) was added dropwise at 0 °C. After the addition the reaction mixture was stirred at 0 °C for 5 minutes, then at room temperature for 10 mins. TLC showed the reaction was complete. The reaction mixture was concentrated *in vacuo* and silica gel chromatography of the crude mixture (99:1 petrol ether : ethyl acetate) afforded **(+)-Spiniferin-1** (230 mg, 35% in 3 steps) as a colorless oil, which solidified as a white solid when standing in the freezer.

(+)-Spiniferin-1: m.p.: 65-75 °C; $[\alpha]_D^{28}$ = +375.0 (*c* 1.01, $CHCl_3$); e.e.: 80.6%; IR (neat) ν_{max} 3112, 3013, 1604, 1467, 1268, 1087, 811 746 cm^{-1}; ^{1}HNMR: δ = 7.28 (d, J = 2.1Hz, 1H, 13-H), 6.52 (d, J = 1.8Hz, 1H, 12-H), 6.33 (s, 1H, 6-H or 9-H), 6.30 (s, 1H, 9-H or 6-H), 6.22 (dd, J = 3.3, 11.4Hz, 1H, 1-H), 5.32 (ddd, J = 3.9, 9.0, 12.6Hz,

1H, 2-H), 3.56 (d, J = 10.8Hz, 1H, 11-H), 2.77 (dt, J = 16.2, 3.3Hz, 1H, 3-H), 1.98 (dd, J = 9.0, 16.5Hz, 1H, 3-H), 1.33 (s, 3H, 15-H), 0.72 (s, 3H, 14-H), 0.68 (d, J = 11.1Hz, 1H, 11-H); ^{13}CNMR (75MHz): δ = 153.3 (s, 8-C), 141.3 (s, 13-C), 131.9 (s, 10-C), 130.4 (s, 1-C), 127.6 (s, 5-C), 125.3 (s, 2-C), 118.8 (s, 7-C), 112.6 (s, 9-C), 110.1 (s, 12-C), 109.5 (s, 6-C), 44.4 (s, 3-C), 39.8 (s, 4-C), 34.2 (s, 11-C), 30.9 (s, 15-C), 28.4 (s, 14-C); EIMS: 212 (M, 100); Anal. Calcd. for $C_{15}H_{16}O$: C, 84.87; H, 7.60. Found: C, 85.02; H, 7.77.

(-)-Spiniferin-1:



(-)-spiniferin-1

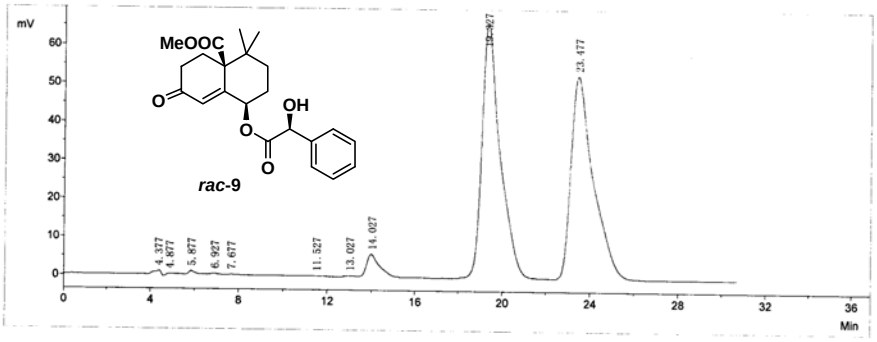
11b (0.375 g, 1 mmol) was converted into **(-)-Spiniferin-1** (0.065 g, 31%) as a colorless oil via three steps, which solidified as a white solid when standing in the freezer.

(-)-Spiniferin-1: m.p.: 71-76 °C; $[\alpha]_D^{28}$ = −432.0 (*c* 1.06, $CHCl_3$); e.e.: 90.8%; IR (neat) ν_{max} 3112, 3014, 1604, 1467, 1268, 1087, 811 746 cm^{-1}; ^{1}HNMR: δ = 7.28 (d, J = 2.1Hz, 1H, 13-H), 6.52 (d, J = 2.1Hz, 1H, 12-H), 6.33 (s, 1H, 6-H or 9-H), 6.30 (s, 1H, 9-H or 6-H), 6.23 (m, 1H, 1-H), 5.32 (ddd, J = 3.9, 9.0, 12.3Hz, 1H, 2-H), 3.56 (d, J = 10.5Hz, 1H, 11-H), 2.78 (dt, J = 3.6, 16.5Hz, 1H, 3-H), 1.97 (dd, J = 9.0, 16.8Hz, 1H, 3-H), 1.34 (s, 3H, 15-H), 0.73 (s, 3H, 14-H), 0.68 (d, J = 10.5Hz, 1H, 11-H); ^{13}CNMR (75MHz): δ = 153.3 (s, 8-C), 141.3 (s, 13-C), 131.9 (s, 10-C), 130.4 (s, 1-C), 127.6 (s, 5-C), 125.3 (s, 2-C), 118.8 (s, 7-C), 112.6 (s, 9-C), 110.1 (s, 12-C), 109.5 (s, 6-C), 44.4 (s, 3-C), 39.8 (s, 4-C), 34.2 (s, 11-C), 30.9 (s, 15-C), 28.4 (s, 14-C); EIMS: 212 (M, 43.14); Anal. Calcd. for $C_{15}H_{16}O$: C, 84.87; H, 7.60. Found: C, 84.46; H, 7.61.

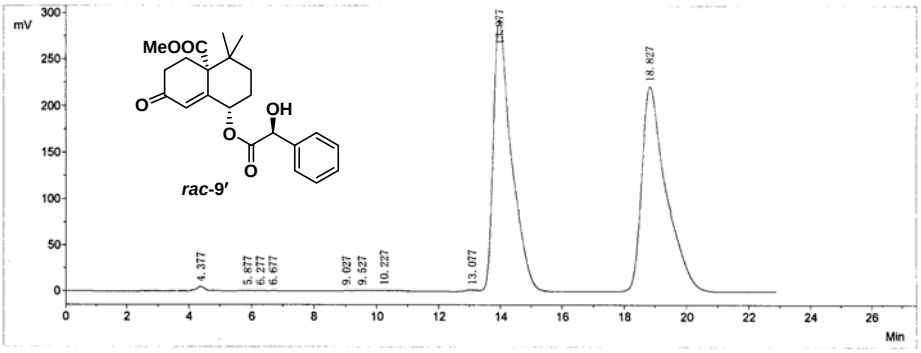
Chiral HPLC data

1.Compound 9 and 9′

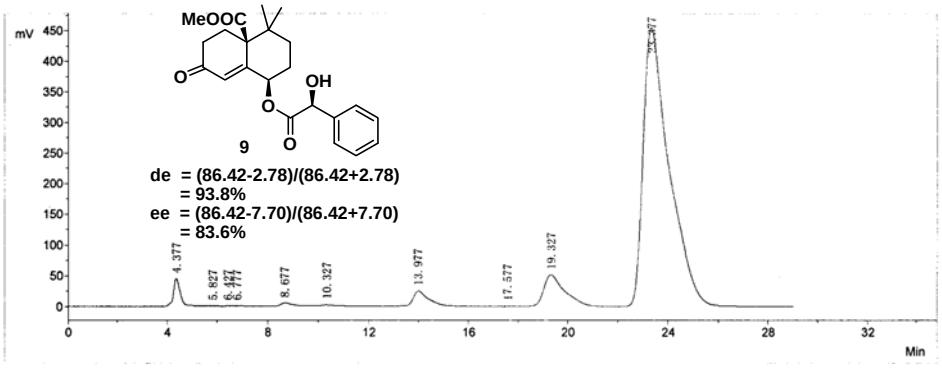
HPLC analysis of 9 and 9′: column: Chiral AD; mobile phase: hexane / *iso*-propanol = 80 / 20; flow rate: 0.80 mL / min; detection: UV 214 nm; *t* for **9**: 23.5 min; *t* for *ent*-**9**: 19.3 min; *t* for **9′**: 14.0 min; *t* for *ent*-**9′**: 18.8 min.



序号	峰号	组份名	保留时间	峰高	峰面积	面积百分比(%)
1	1		4.377	1143.9	25596.0	0.3257
2	2		4.877	400.3	8149.0	0.1037
3	3		5.877	769.9	13516.5	0.1720
4	4		6.927	245.0	5714.6	0.0727
5	5		7.677	131.6	2773.8	0.0353
6	6		11.527	60.0	5195.3	0.0661
7	7		13.027	256.7	7125.1	0.0907
8	8		14.027	5802.5	240101.6	3.0551
9	9		19.327	66217.8	3841101.2	48.8749
10	10		23.477	52578.4	3709768.7	47.2038
合计:				127606.0	7859041.8	100.0000

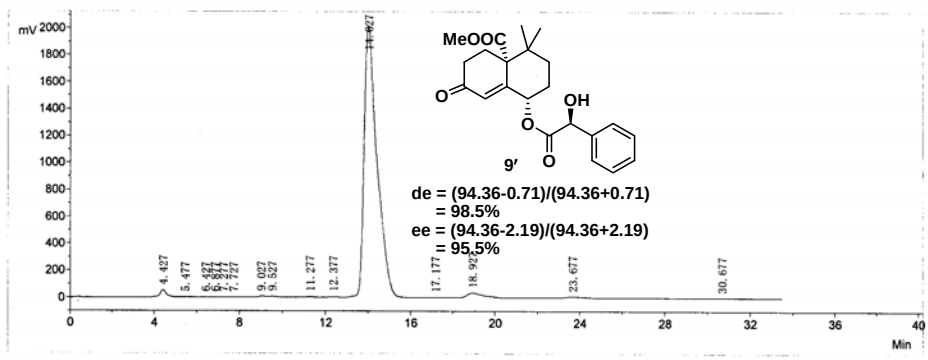


序号	峰号	组份名	保留时间	峰高	峰面积	面积百分比(%)
1	1		4.377	4625.4	100562.2	0.4148
2	2		5.877	750.0	20394.0	0.0841
3	3		6.277	461.9	9613.9	0.0397
4	4		6.677	427.2	11867.4	0.0489
5	5		9.027	344.8	7214.0	0.0298
6	6		9.527	711.2	17599.9	0.0726
7	7		10.227	685.3	42992.2	0.1773
8	8		13.077	1553.5	34584.0	0.1426
9	9		13.977	292710.9	11937763.9	49.2363
10	10		18.827	220547.3	12063286.6	49.7540
合计:				522817.5	24245878.1	100.0000



序号	峰号	组份名	保留时间	峰高	峰面积	面积百分比(%)
1	1		4.377	44783.8	896478.8	2.3852
2	2		5.827	351.2	5657.7	0.0151
3	3		6.427	264.3	3710.8	0.0099
4	4		6.777	521.1	13690.6	0.0364
5	5		8.677	4955.4	161858.9	0.4307
6	6		10.327	1929.9	77368.7	0.2059
7	7		13.977	24374.0	1045274.5	2.7811
8	8		17.577	168.4	5034.2	0.0134
9	9		19.327	50846.6	2895709.1	7.7045
10	10		23.377	454030.6	32479997.9	86.4180
合计:				582225.4	37584781.2	100.0000

The estimated ee of (+)-**10** prepared from **9** is calculated to be 78.4% (0.938×0.836).

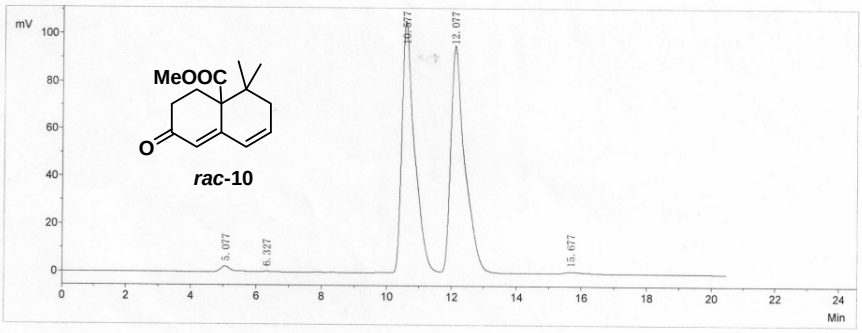


序号	峰号	组份名	保留时间	峰高	峰面积	面积百分比(%)
1	1		4.427	54180.7	1181078.3	1.3081
2	2		5.477	2136.6	88059.9	0.0975
3	3		6.427	1672.8	34889.5	0.0386
4	4		6.877	1102.0	26640.3	0.0295
5	5		7.277	1104.2	23153.8	0.0256
6	6		7.727	1123.1	35386.9	0.0392
7	7		9.027	10227.6	257083.4	0.2847
8	8		9.527	8327.3	293316.9	0.3249
9	9		11.277	5593.1	198689.4	0.2201
10	10		12.377	6305.6	216186.1	0.2394
11	11		14.027	2016941.7	85200656.6	94.3653
12	12		17.177	1007.4	43438.3	0.0481
13	13		18.927	35931.4	1978879.9	2.1917
14	14		23.677	8933.9	638273.3	0.7069
15	15		30.677	878.4	72408.7	0.0802
合计:				2155465.7	90288141.3	100.0000

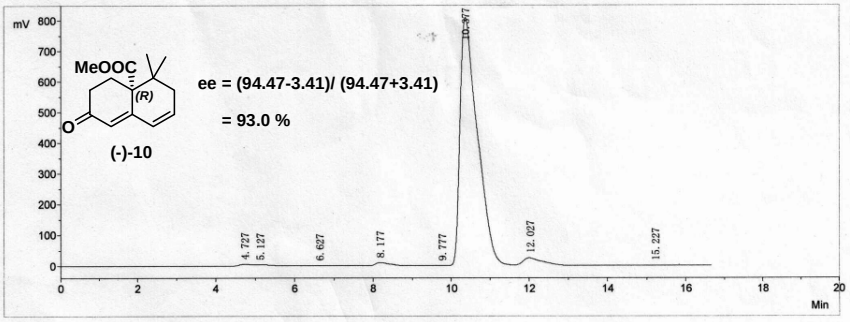
The estimated ee of (-)-**10** prepared from **9′** is calculated to be 94.1% (0.985×0.955).

2. Compound 10

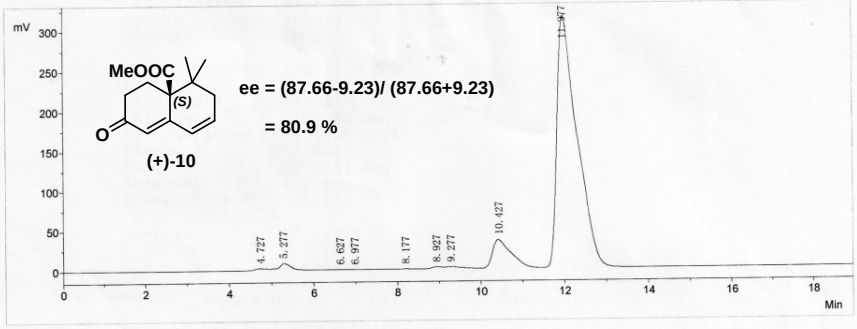
HPLC analysis of 10: column: Chiralpak AD; mobile phase: hexane / *iso*-propanol = 90 / 10; flow rate: 0.80 mL / min; detection: UV 230 nm; *t* for (-)-**10**: 10.6 min; *t* for (+)-**10**: 12.1 min.



序号	峰号	组份名	保留时间	峰高	峰面积	面积百分比(%)
1	1		5.077	2361.8	52600.2	0.8992
2	2		6.327	268.3	6337.2	0.1083
3	3		10.577	104842.5	2871849.8	49.0925
4	4		12.077	94921.8	2886354.3	49.3404
5	5		15.677	813.9	32736.3	0.5596
合计:				203208.2	5849877.9	100.0000



序号	峰号	组份名	保留时间	峰高	峰面积	面积百分比(%)
1	1		4.727	5684.4	114290.9	0.4321
2	2		5.127	3749.6	141949.0	0.5366
3	3		6.627	558.2	11437.1	0.0432
4	4		8.177	10619.8	262857.5	0.9937
5	5		9.777	977.5	18130.5	0.0685
6	6		10.377	807770.9	24990248.0	94.4710
7	7		12.027	24925.4	901311.3	3.1072
8	8		15.227	287.0	12594.4	0.0476
合计:				854572.7	26452818.8	100.0000

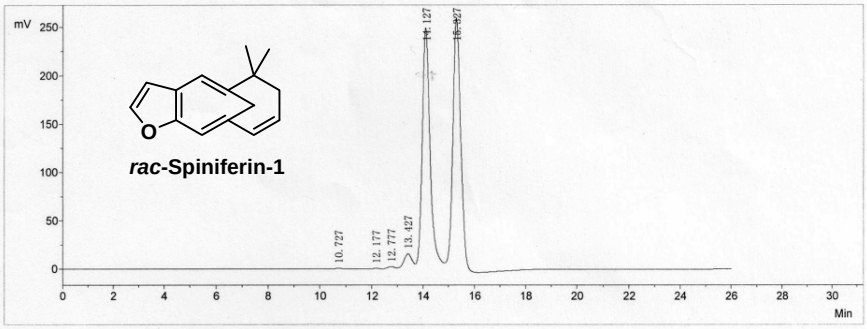


序号	峰号	组份名	保留时间	峰高	峰面积	面积百分比(%)
1	1		4.727	2482.2	50397.1	0.4232
2	2		5.277	8508.9	178871.0	1.5020
3	3		6.627	282.6	4599.0	0.0386
4	4		6.977	360.9	8665.0	0.0728
5	5		8.177	453.9	10527.9	0.0884
6	6		8.927	2665.2	47806.6	0.4014
7	7		9.277	2669.2	68900.4	0.5786
8	8		10.427	35741.8	1099732.7	9.2348
9	9		11.977	313491.1	10439052.9	87.6601
合计:				366655.8	11908552.7	100.0000

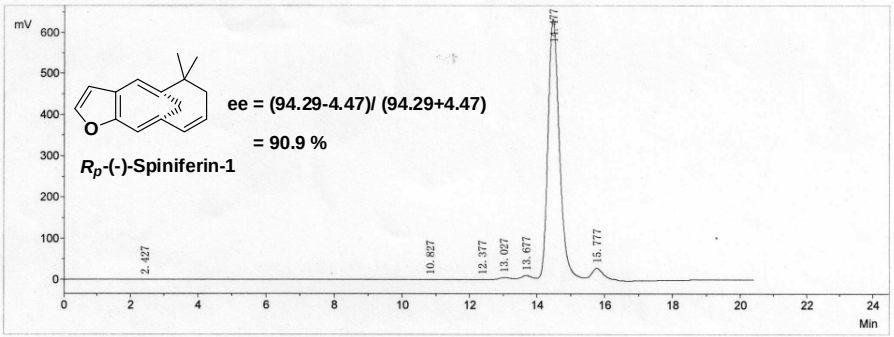
The ee of (+)-**10** and (-)-**10** (80.9% and 93.0% respectively) are nearly consistent with the calculated ee of 78.4% and 94.1% based on the optical purity of **9** and **9′**, indicating no further racemization in $Pd(PPh_3)_4$-catalyzed β-H elimination reaction.

3. Spiniferin-1

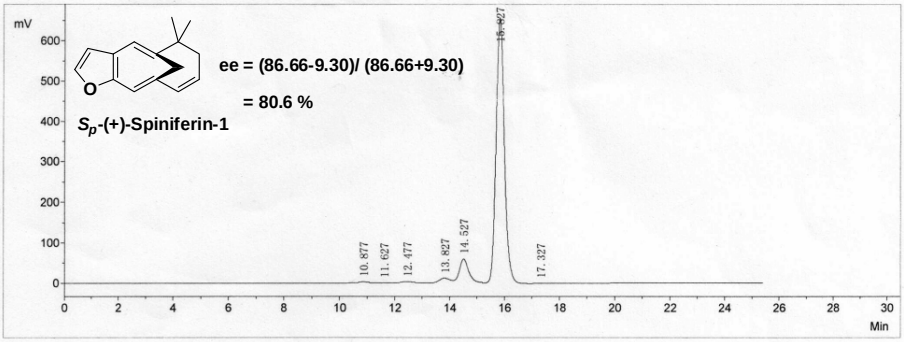
HPLC analysis of Spiniferin-1: column: Nucleocel Delta S; mobile phase: hexane / *iso*-propanol = 100 / 1; flow rate: 0.30 mL / min; detection: UV 254 nm; *t* for p*R*-(-)-enantiomer: 14.1 min; *t* for p*S*-(+)-enantiomer: 15.3 min.



序号	峰号	组份名	保留时间	峰高	峰面积	面积百分比(%)
1	1		10.727	546.3	19085.3	0.1677
2	2		12.177	581.8	20271.5	0.1781
3	3		12.777	2364.9	50095.1	0.4402
4	4		13.427	15695.5	343004.3	3.0140
5	5		14.127	245056.7	5350970.1	47.0191
6	6		15.327	257684.0	5596979.8	49.1808
合计:				521929.2	11380406.1	100.0000



序号	峰号	组份名	保留时间	峰高	峰面积	面积百分比(%)
1	1		2.427	111.4	6679.2	0.0419
2	2		10.827	209.8	5992.3	0.0376
3	3		12.377	128.2	3353.4	0.0210
4	4		13.027	5168.2	112442.3	0.7050
5	5		13.677	9707.2	227307.6	1.4251
6	6		14.477	630353.7	14880157.2	93.2922
7	7		15.777	28514.1	714117.9	4.4772
合计:				674192.6	15950050.0	100.0000

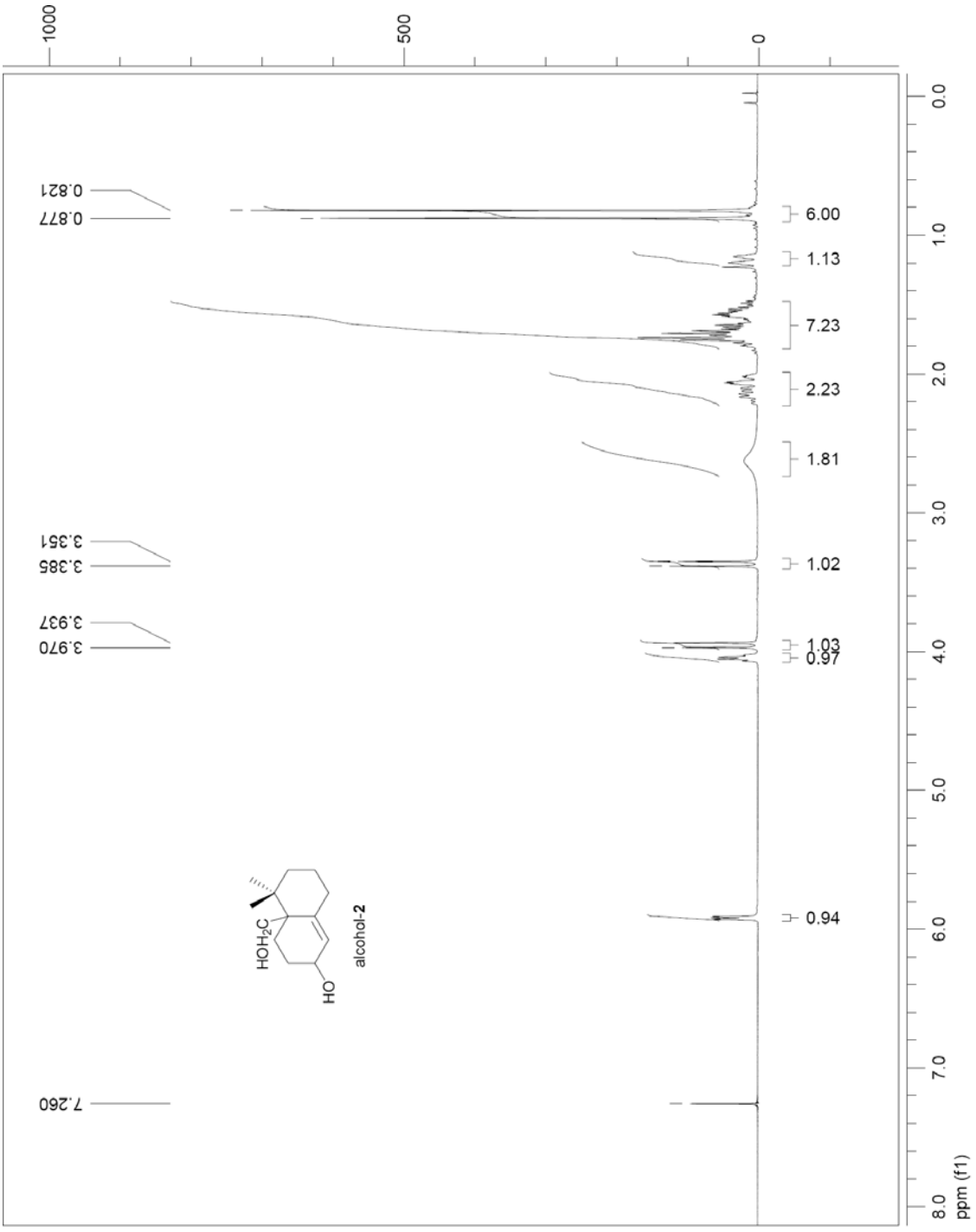


序号	峰号	组份名	保留时间	峰高	峰面积	面积百分比(%)
1	1		10.877	3037.9	87466.1	0.5498
2	2		11.627	1426.2	42180.3	0.2651
3	3		12.477	3988.1	145006.0	0.9114
4	4		13.827	12387.7	358265.7	2.2519
5	5		14.527	60476.5	1479316.1	9.2983
6	6		15.827	656894.5	13786906.7	86.6581
7	7		17.327	382.7	10396.5	0.0653
合计:				738593.6	15909537.4	100.0000

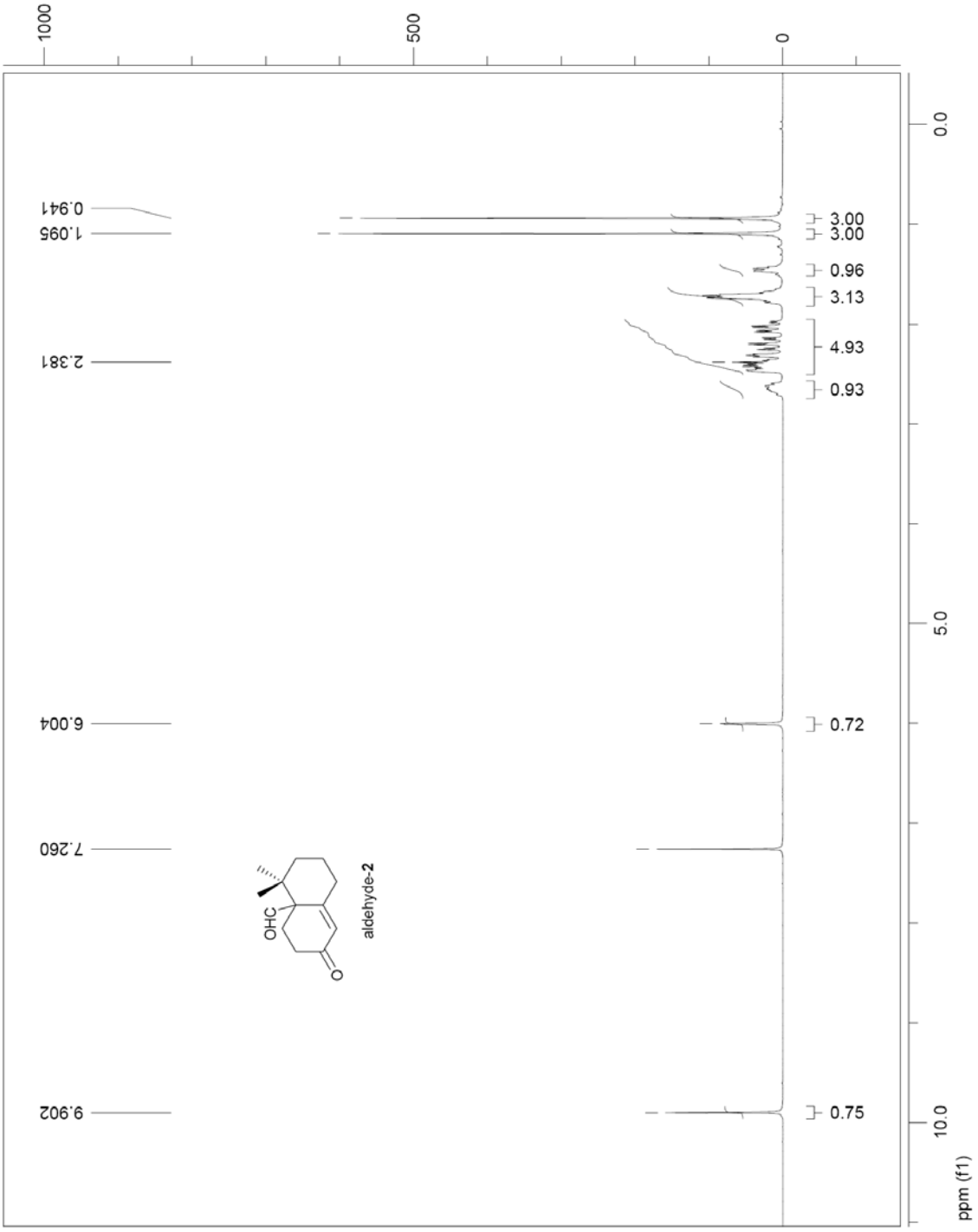
The ee of (+)-spiniferin-1 and (-)-spiniferin-1 (80.6% and 90.9% respectively) are nearly consistent with the ee of (+)-**10** and (-)-**10** (80.9% and 93.0% respectively), indicating no racemization in the last four steps to prepare final products.

NMR spectra

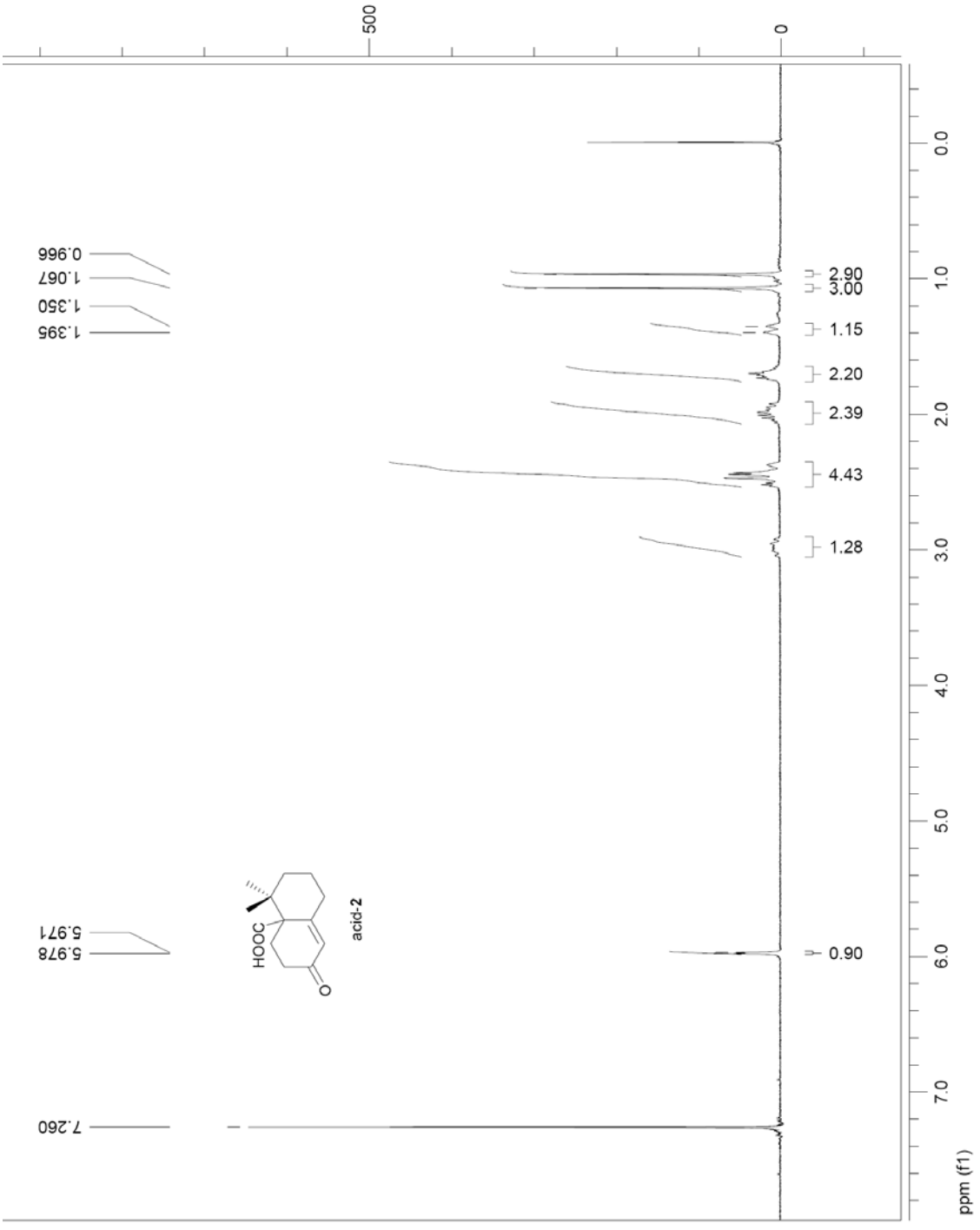
1. Alcohol-**2**



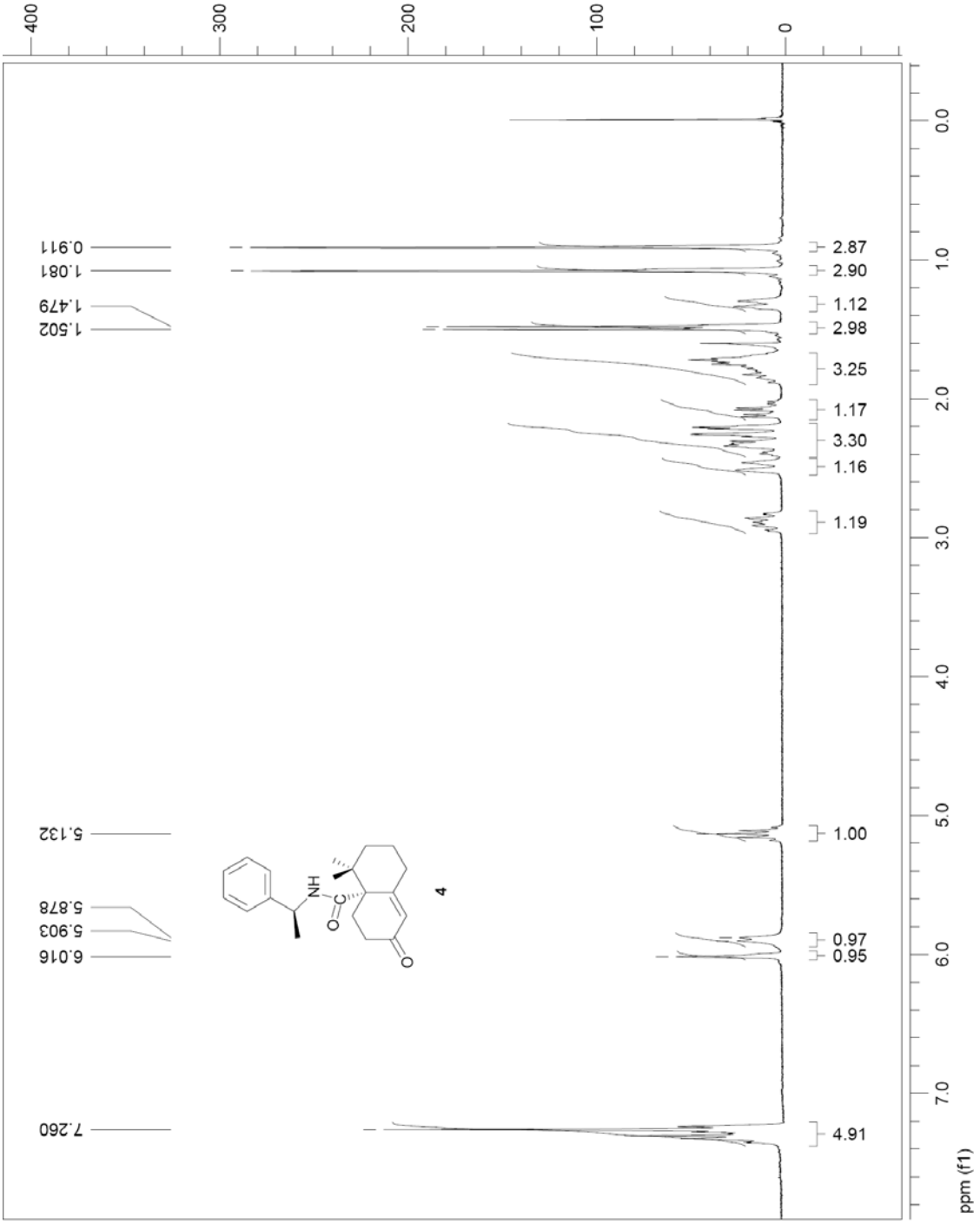
2. Aldehyde-**2**


1000
500
0
0.941
1.095
2.381
6.004
7.260
9.902
3.00
3.00
0.96
3.13
4.93
0.93
0.72
0.75
0.0
5.0
10.0
ppm (f1)
OHC
O
aldehyde-2

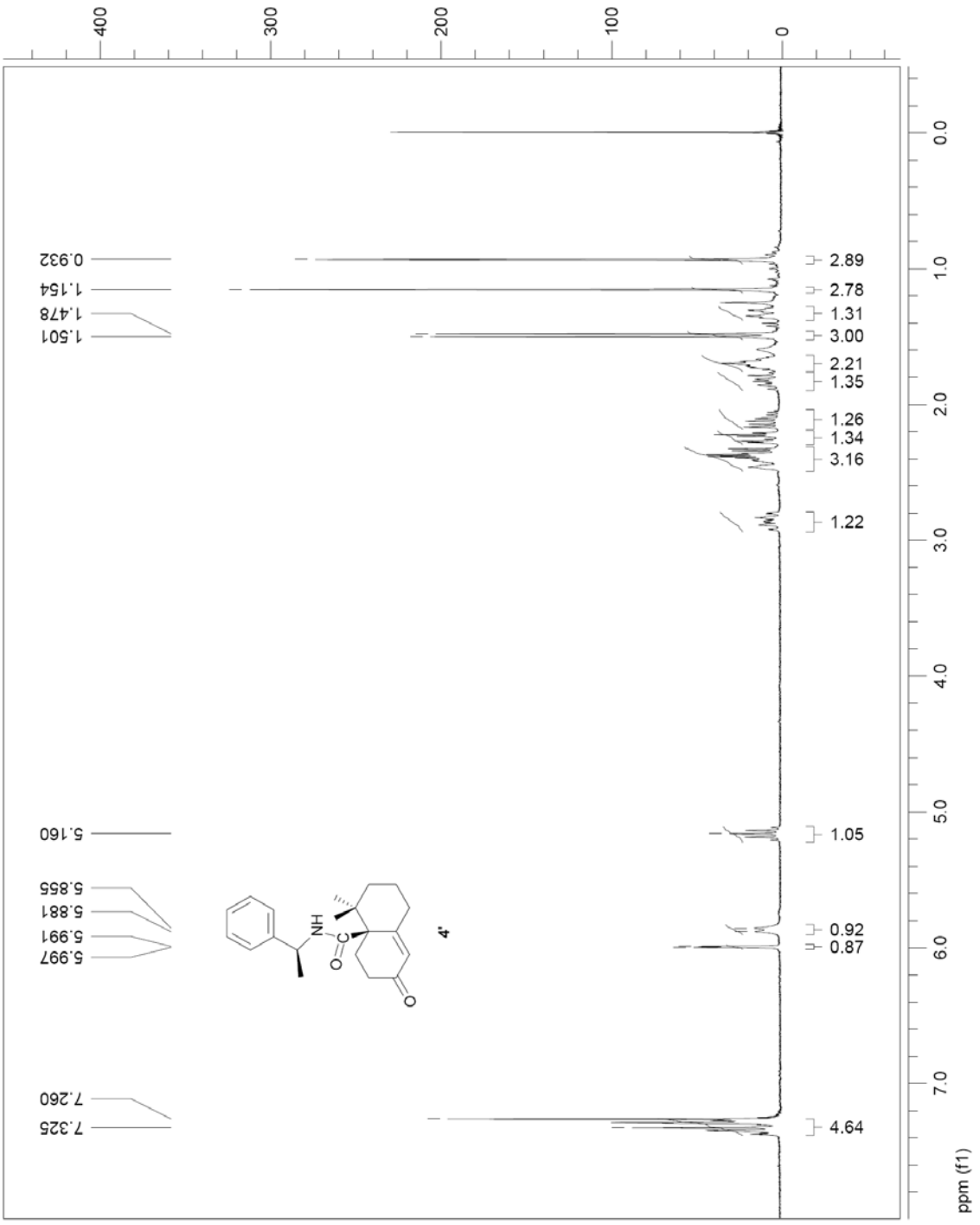
3. Acid-**2**


500
0
0.966
1.067
1.350
1.395
2.90
3.00
1.15
2.20
2.39
4.43
1.28
0.90
5.971
5.978
7.260
HOOC
O
acid-2
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
ppm (f1)

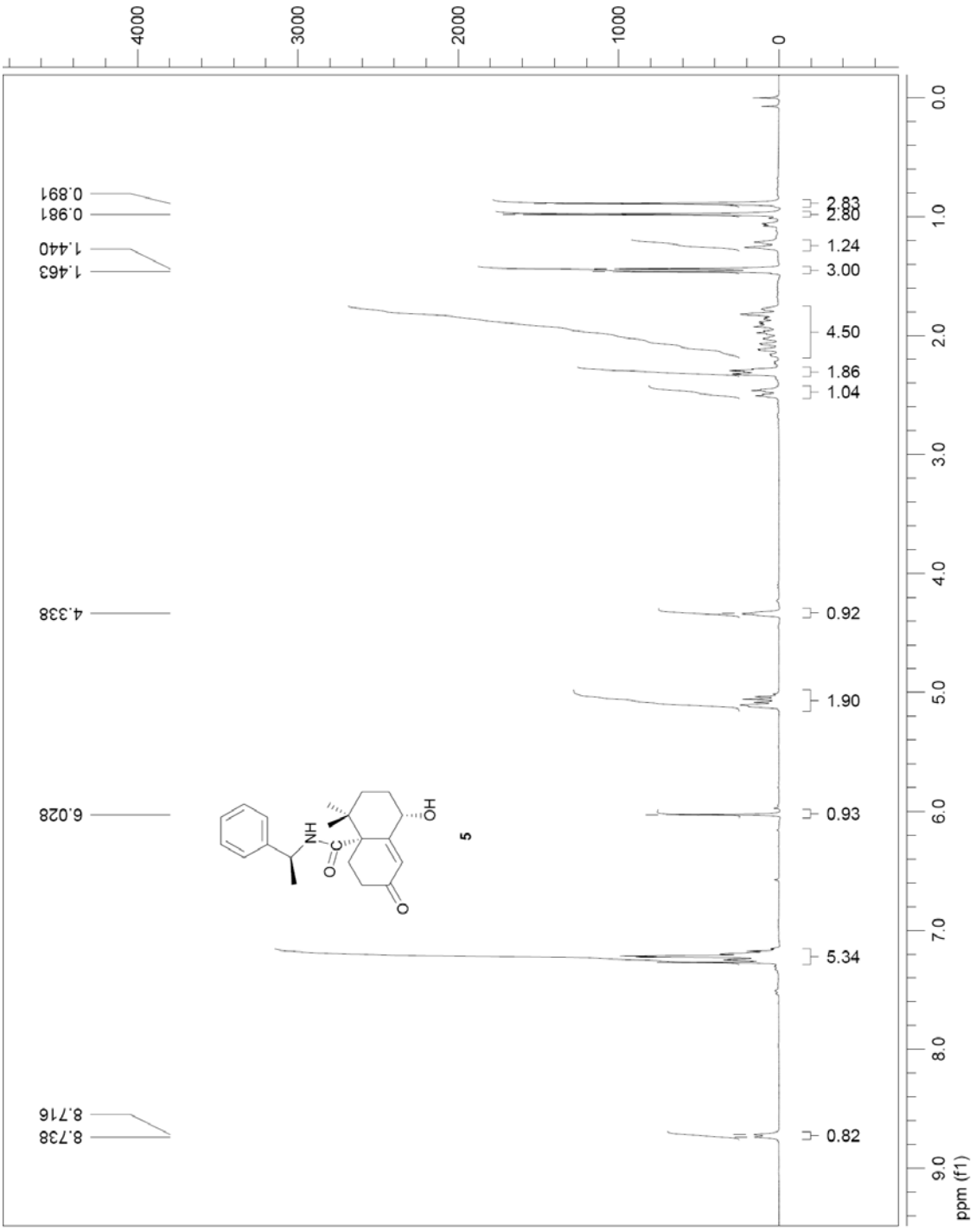
4. **Compound 4**

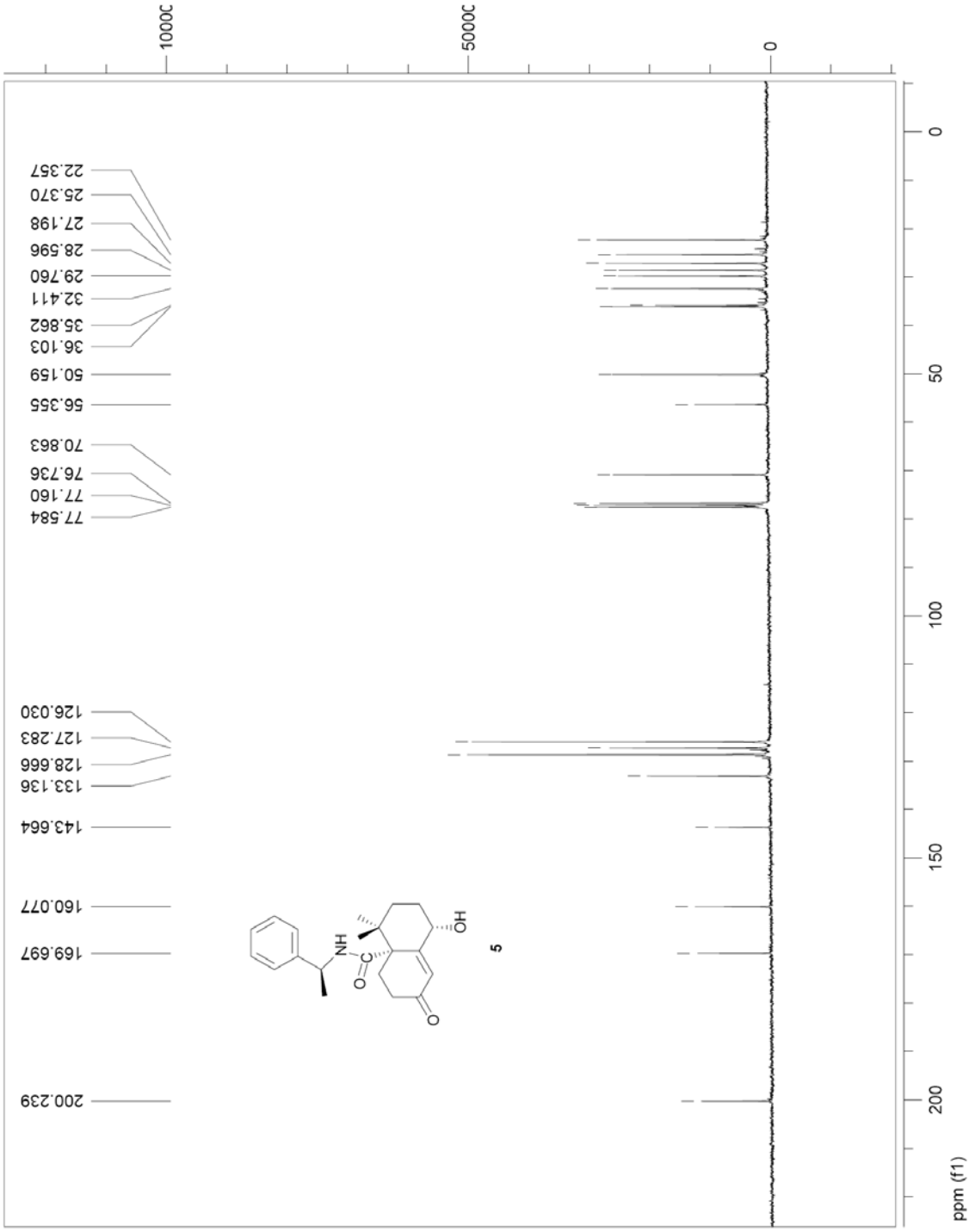

400
300
200
100
0
0.911
1.081
1.479
1.502
5.132
5.878
5.903
6.016
7.260
2.87
2.90
1.12
2.98
3.25
1.17
3.30
1.16
1.19
1.00
0.97
0.95
4.91
NH
O
O
4
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
ppm (f1)

5. **Compound 4′**

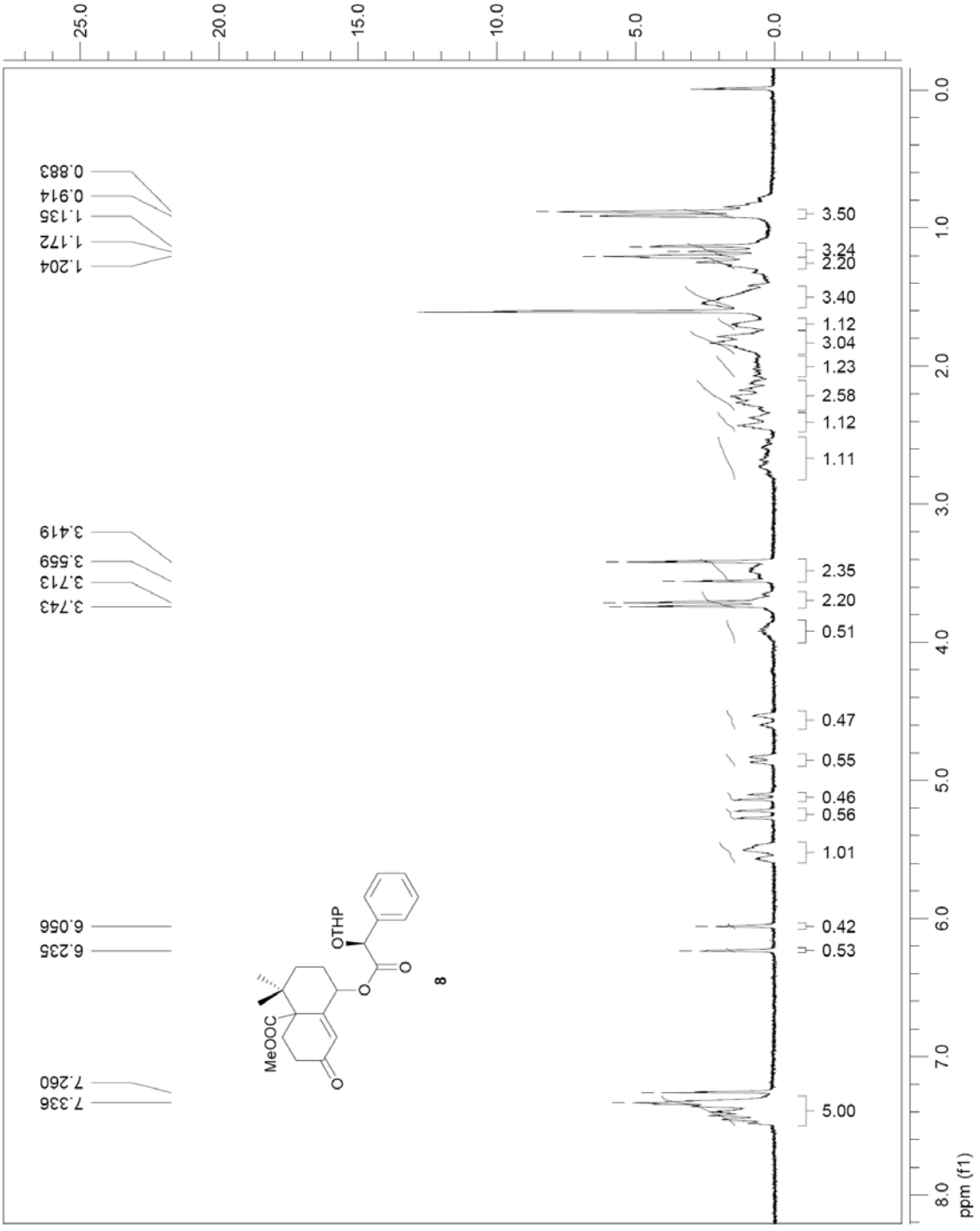

400
300
200
100
0
0.932
1.154
1.478
1.501
5.160
5.855
5.881
5.991
5.997
7.260
7.325
2.89
2.78
1.31
3.00
2.21
1.35
1.26
1.34
3.16
1.22
1.05
0.92
0.87
4.64
NH
O
O
4'
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
ppm (f1)

6. **Compound 5**

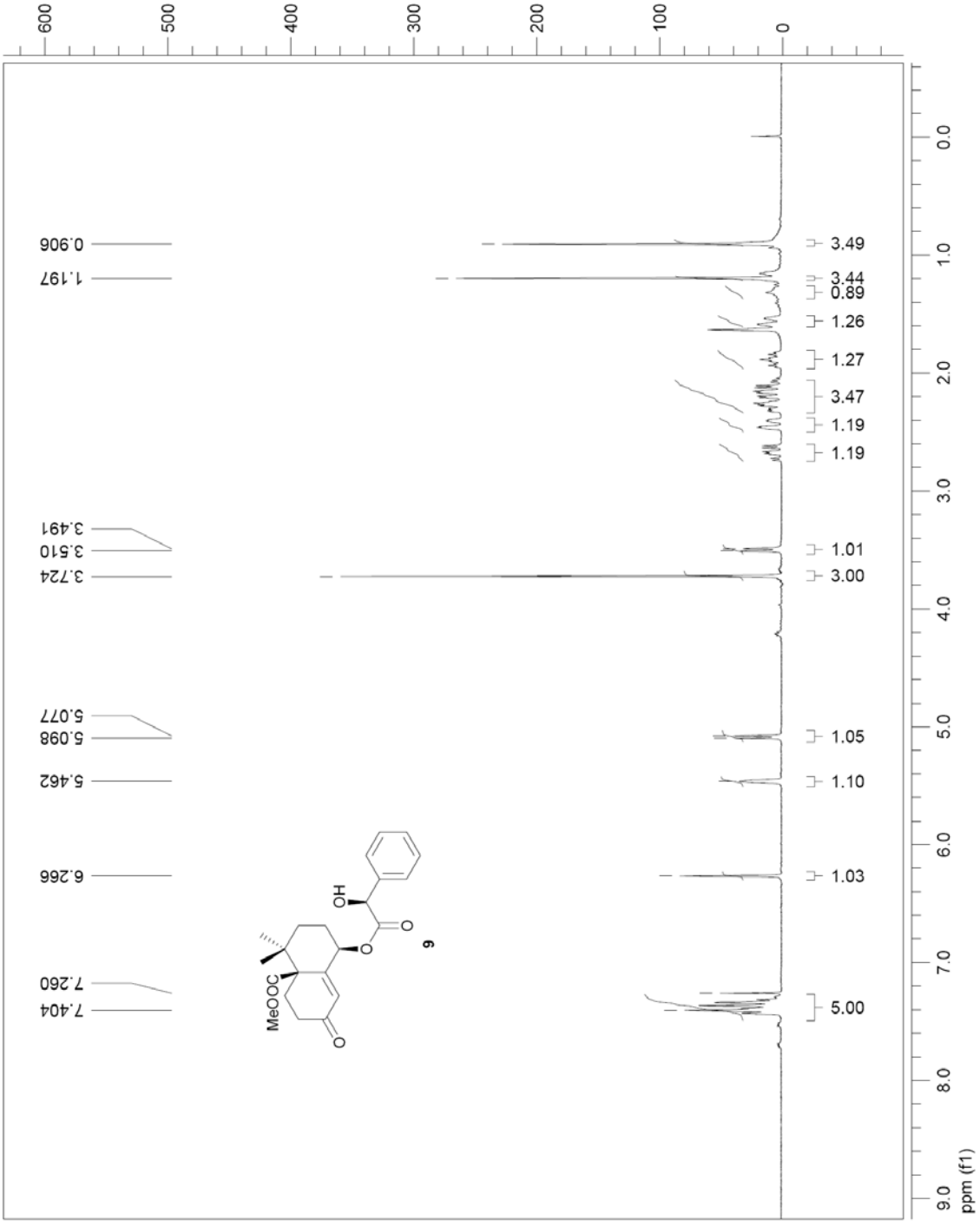

4000
3000
2000
1000
0
0.891
0.981
1.440
1.463
4.338
6.028
8.716
8.738
2.83
2.80
1.24
3.00
4.50
1.86
1.04
0.92
1.90
0.93
5.34
0.82
NH
O
O
OH
5
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
ppm (f1)


10000
5000
0
22.357
25.370
27.198
28.596
29.760
32.411
35.862
36.103
50.159
56.355
70.863
76.736
77.160
77.584
126.030
127.283
128.666
133.136
143.664
160.077
169.697
200.239
NH
O
C
HO
O
5
0
50
100
150
200
ppm (f1)

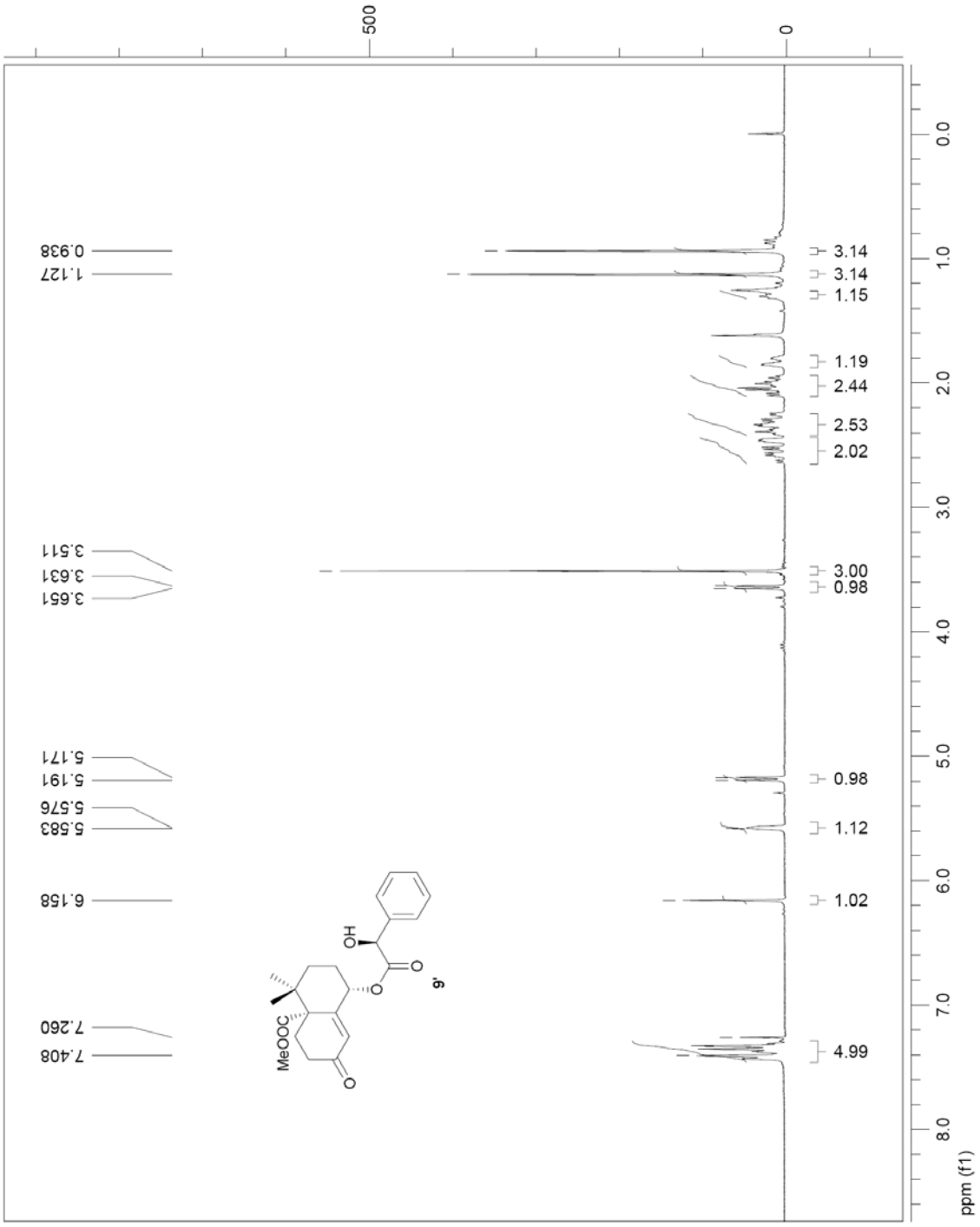
7. **Compound 8**


25.0
20.0
15.0
10.0
5.0
0.0
0.883
0.914
1.135
1.172
1.204
3.419
3.559
3.713
3.743
6.056
6.235
7.260
7.336
3.50
3.24
2.20
3.40
1.12
3.04
1.23
2.58
1.12
1.11
2.35
2.20
0.51
0.47
0.55
0.46
0.56
1.01
0.42
0.53
5.00
OTHP
MeOOC
O
8
ppm (f1)

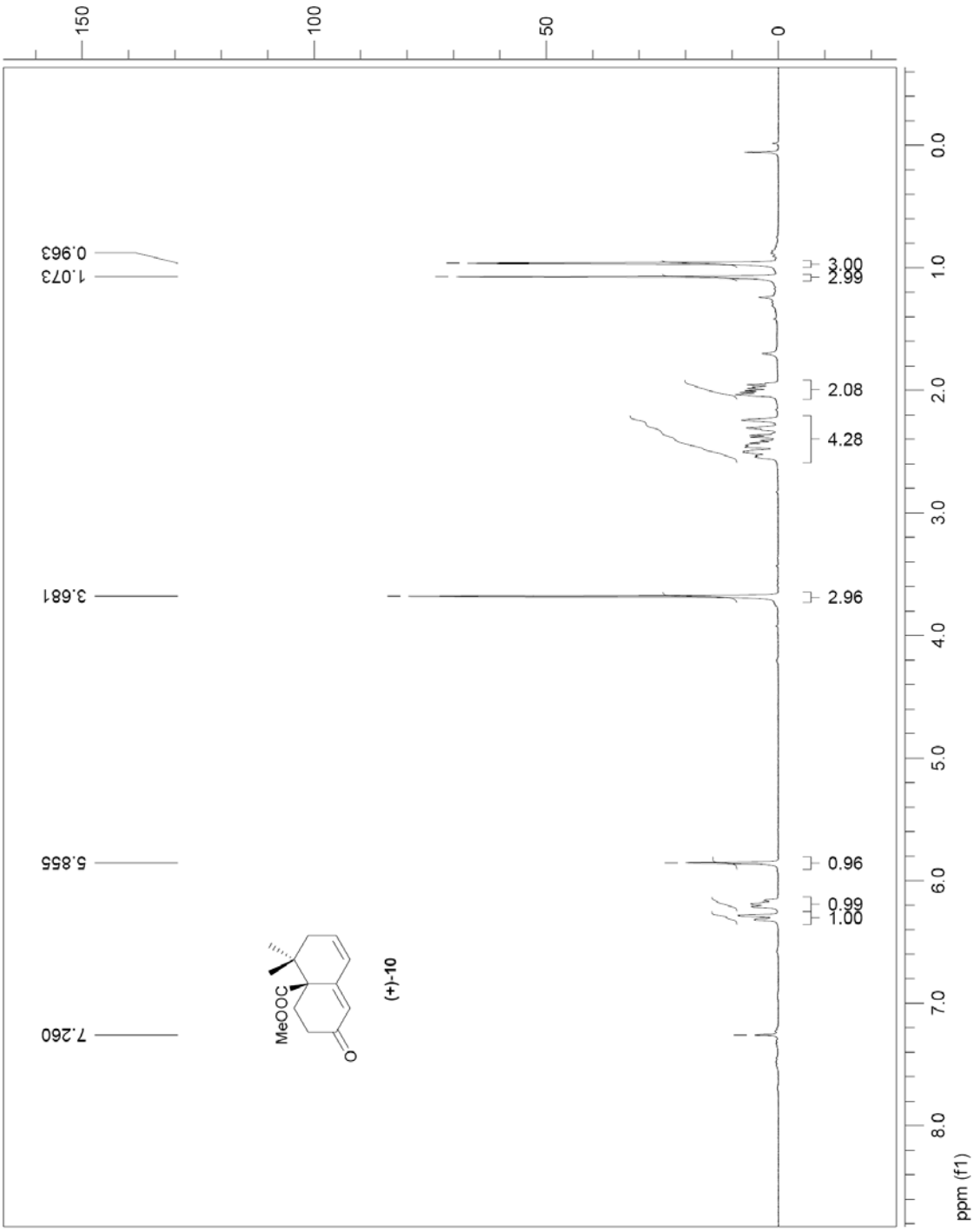
8. Compound 9


0.906
1.197
3.491
3.510
3.724
5.077
5.098
5.462
6.266
7.260
7.404
3.49
3.44
0.89
1.26
1.27
3.47
1.19
1.19
1.01
3.00
1.05
1.10
1.03
5.00
OH
O
O
MeOOC
O
9
ppm (f1)

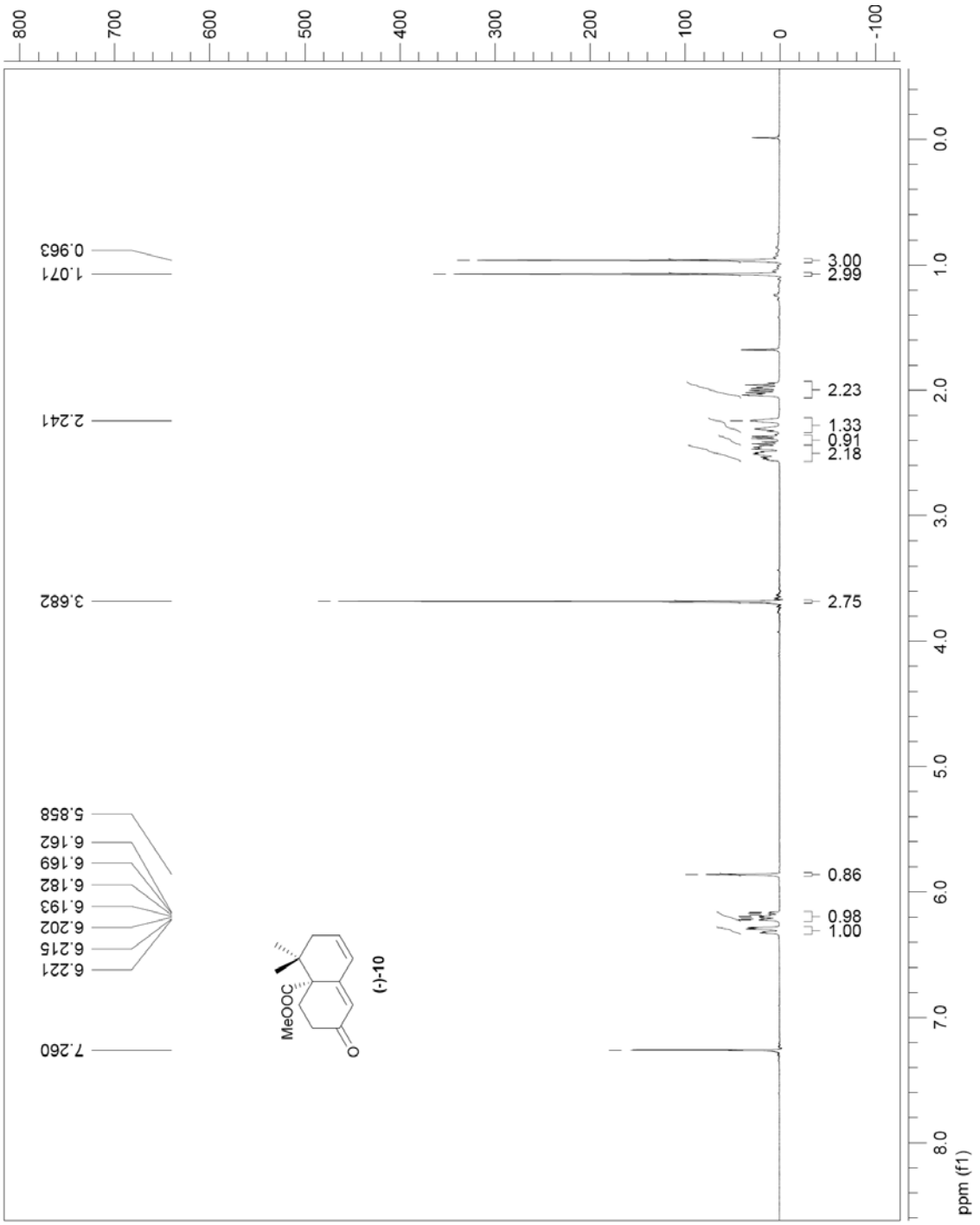
9. Compound 9′


500
0
0.938
1.127
3.511
3.631
3.651
5.171
5.191
5.576
5.583
6.158
7.260
7.408
3.14
3.14
1.15
1.19
2.44
2.53
2.02
3.00
0.98
0.98
1.12
1.02
4.99
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
ppm (f1)
OH
O
O
O
MeOOC
9'

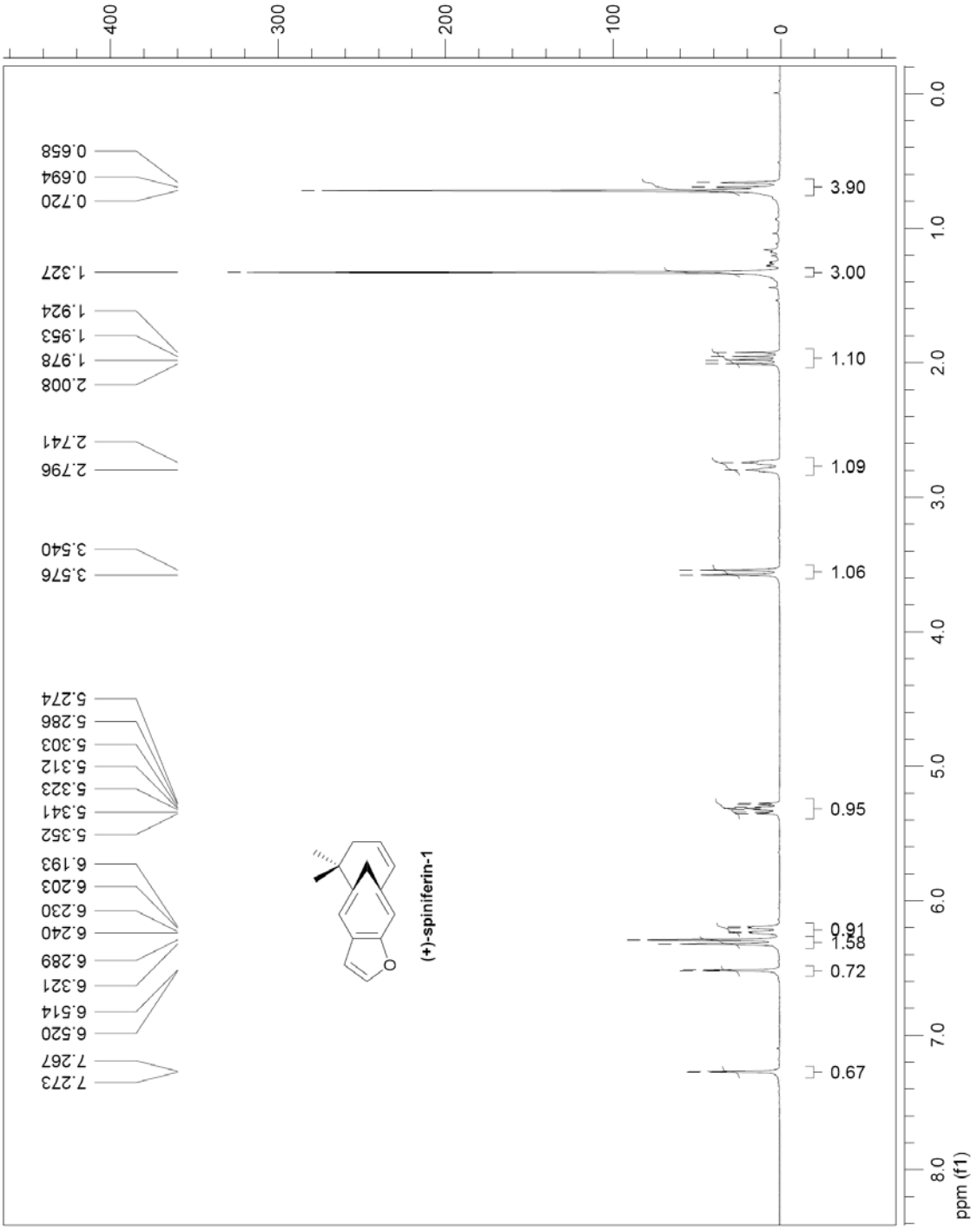
10. Compound (+)-10

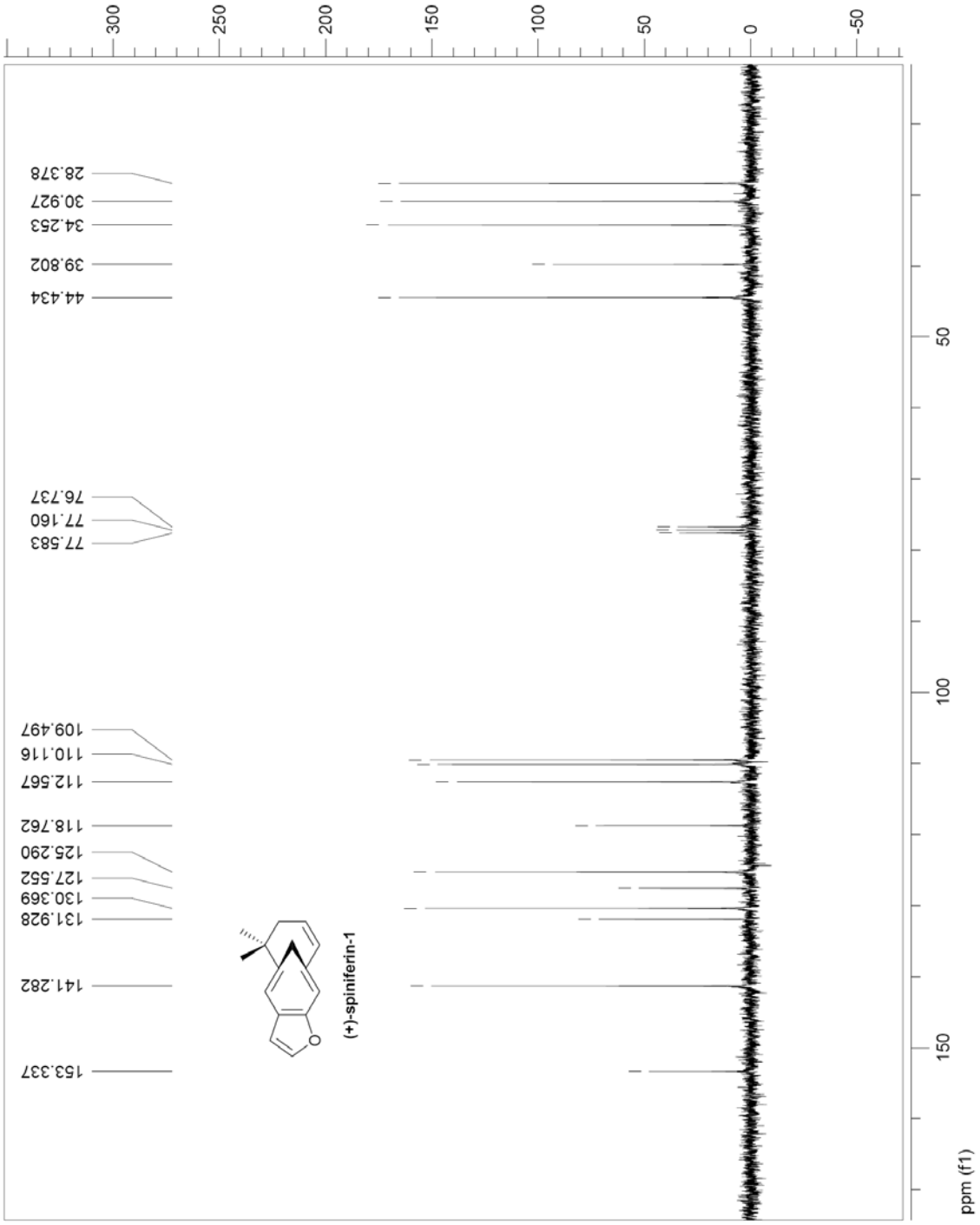


11. Compound (-)-10

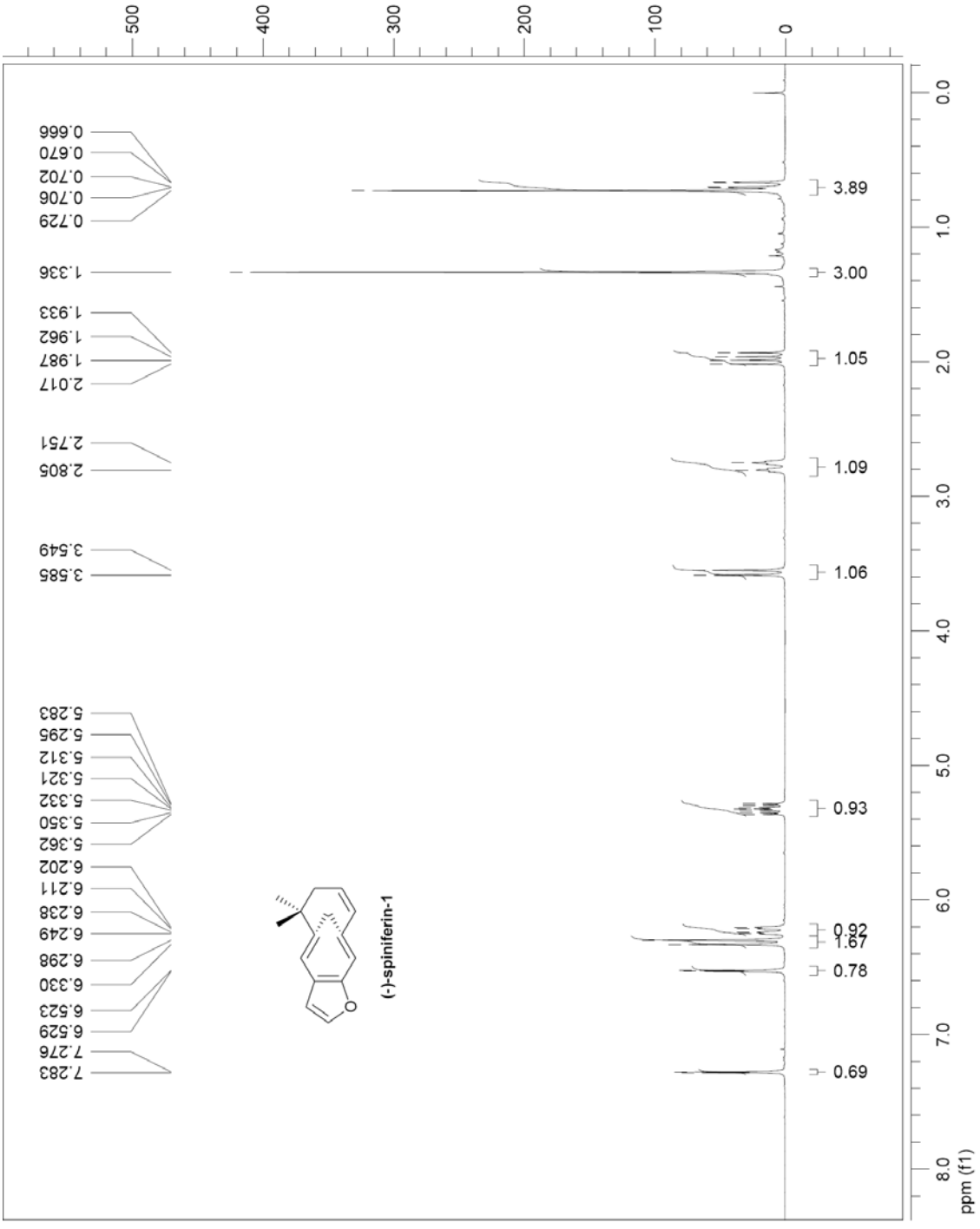


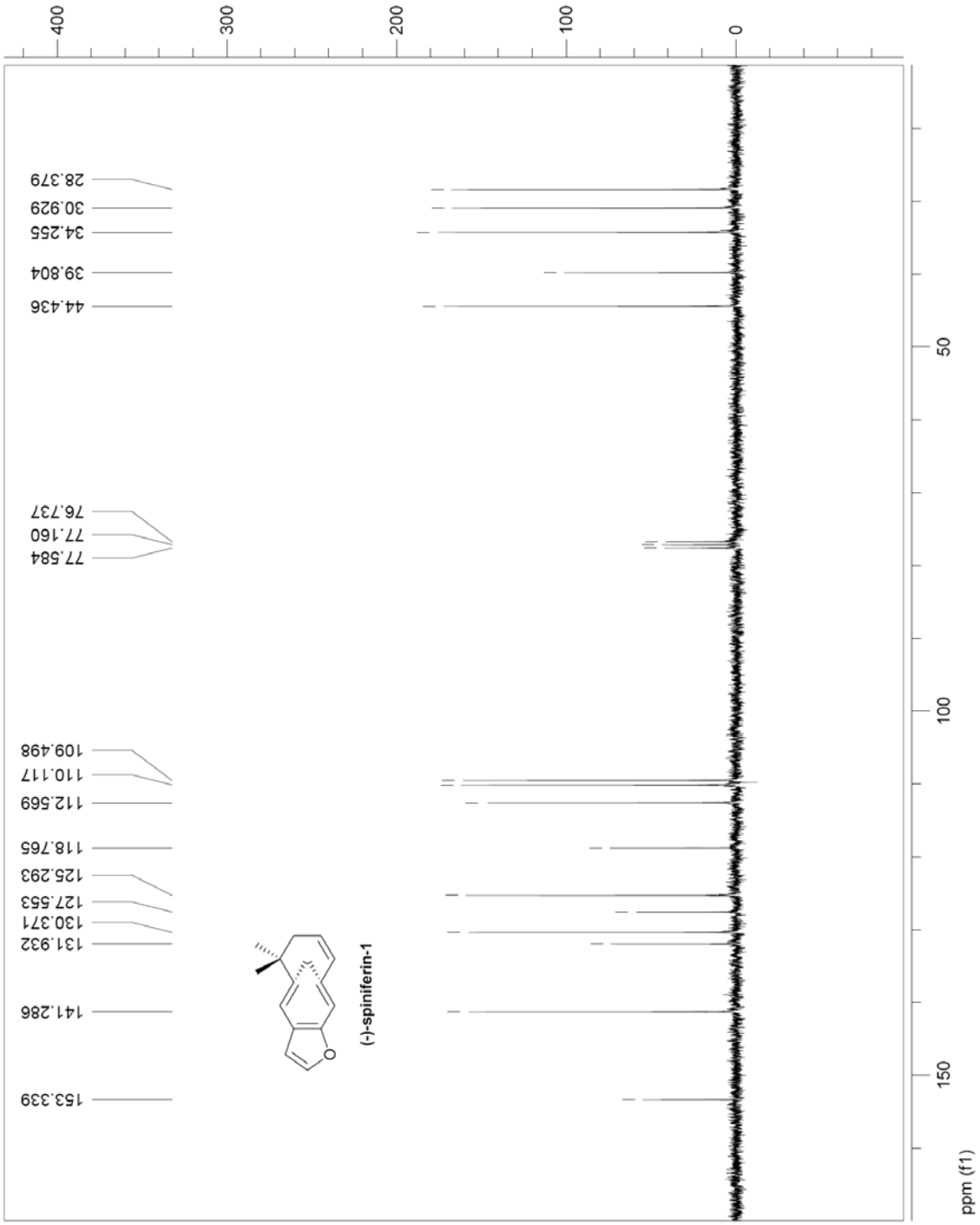
12. (+)-Spiniferin-1




300
250
200
150
100
50
0
-50
28.378
30.927
34.253
39.802
44.434
76.737
77.160
77.583
109.497
110.116
112.567
118.762
125.290
127.552
130.369
131.928
141.282
153.337
(+)-spiniferin-1
50
100
150
ppm (f1)

13. (-)-Spiniferin-1

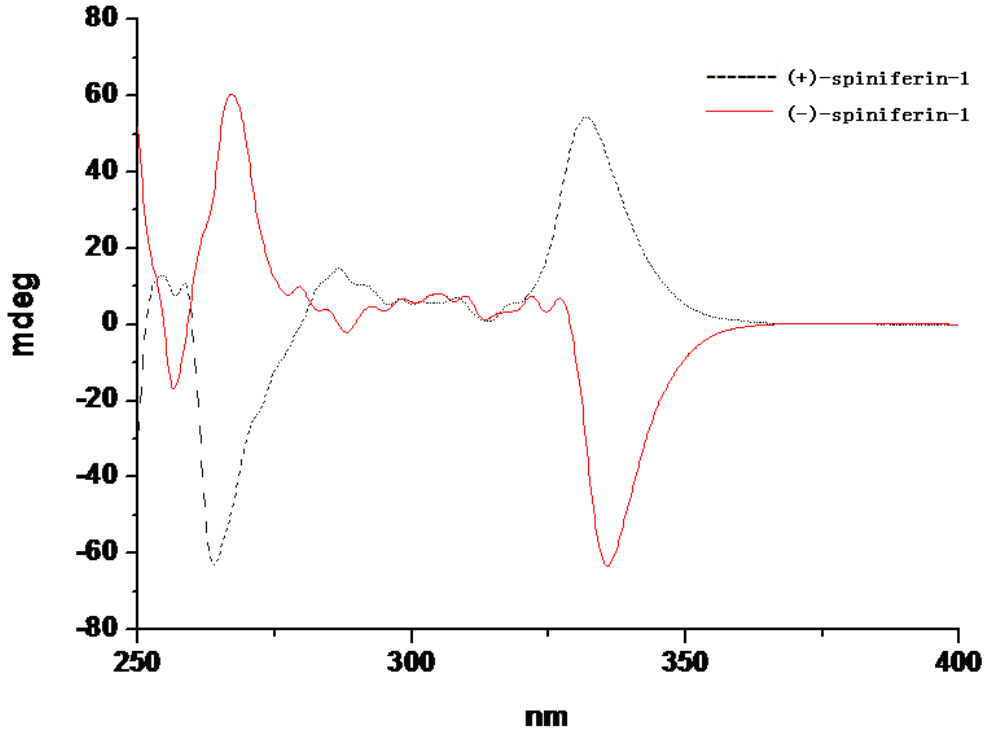



400
300
200
100
0
28.379
30.929
34.255
39.804
44.436
76.737
77.160
77.584
109.498
110.117
112.569
118.765
125.293
127.553
130.371
131.932
141.286
153.339
(-)-spiniferin-1
50
100
150
ppm (f1)

CD Spectra of (+)-spiniferin-1 and (-)-spiniferin-1 in methanol

*Spectrometer / Data system JASCO Corp., J-810, Rev. 1.00

Xunits: nanometers; Yunits: CD[mdeg]



1. W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem.* 1978, **43**, 2923.
2. K. Ding, Y. S. Sun and W. S. Tian, *J. Org. Chem.*, 2011, **76**, 1495.