

Synthesis of Carbo[6]Helicene Derivatives Grafted with Amino or Aminoester Substituents from Enantiopure [6]Helicenyl Boronates

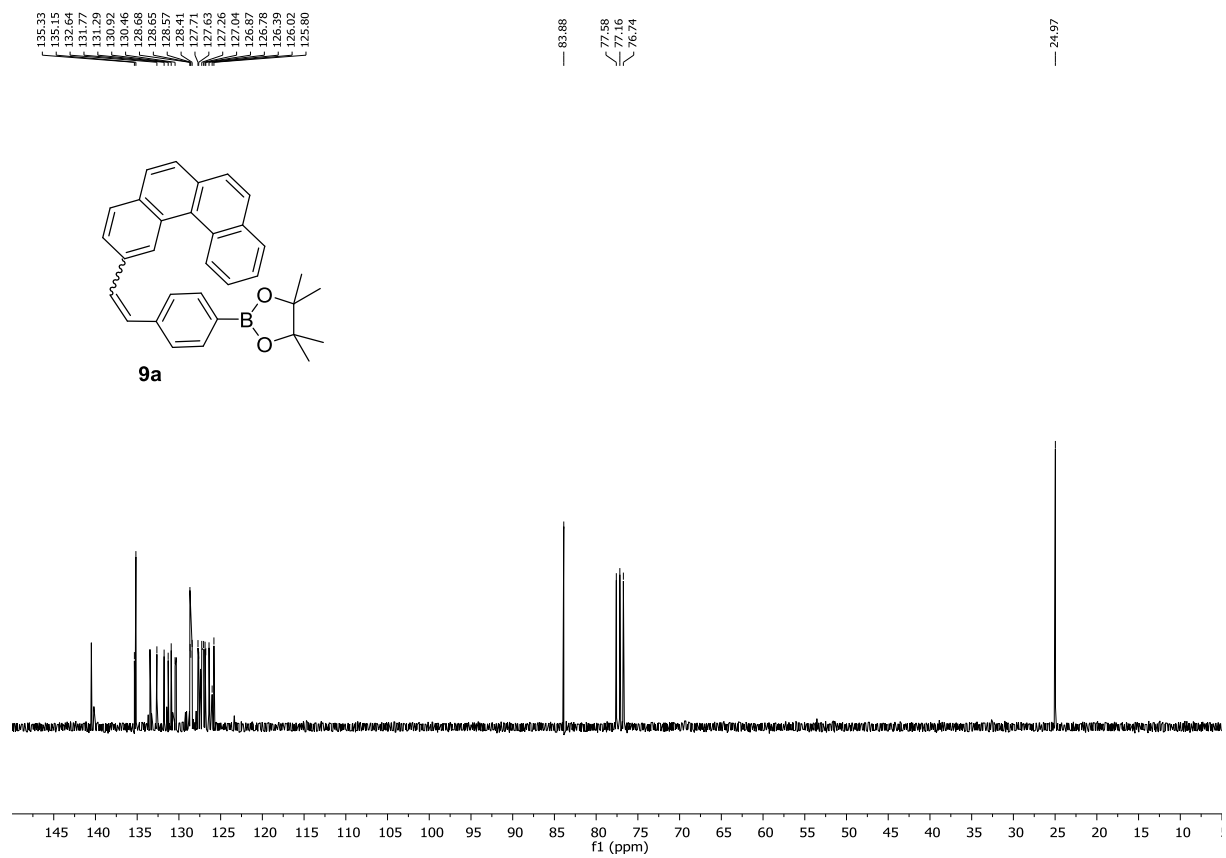
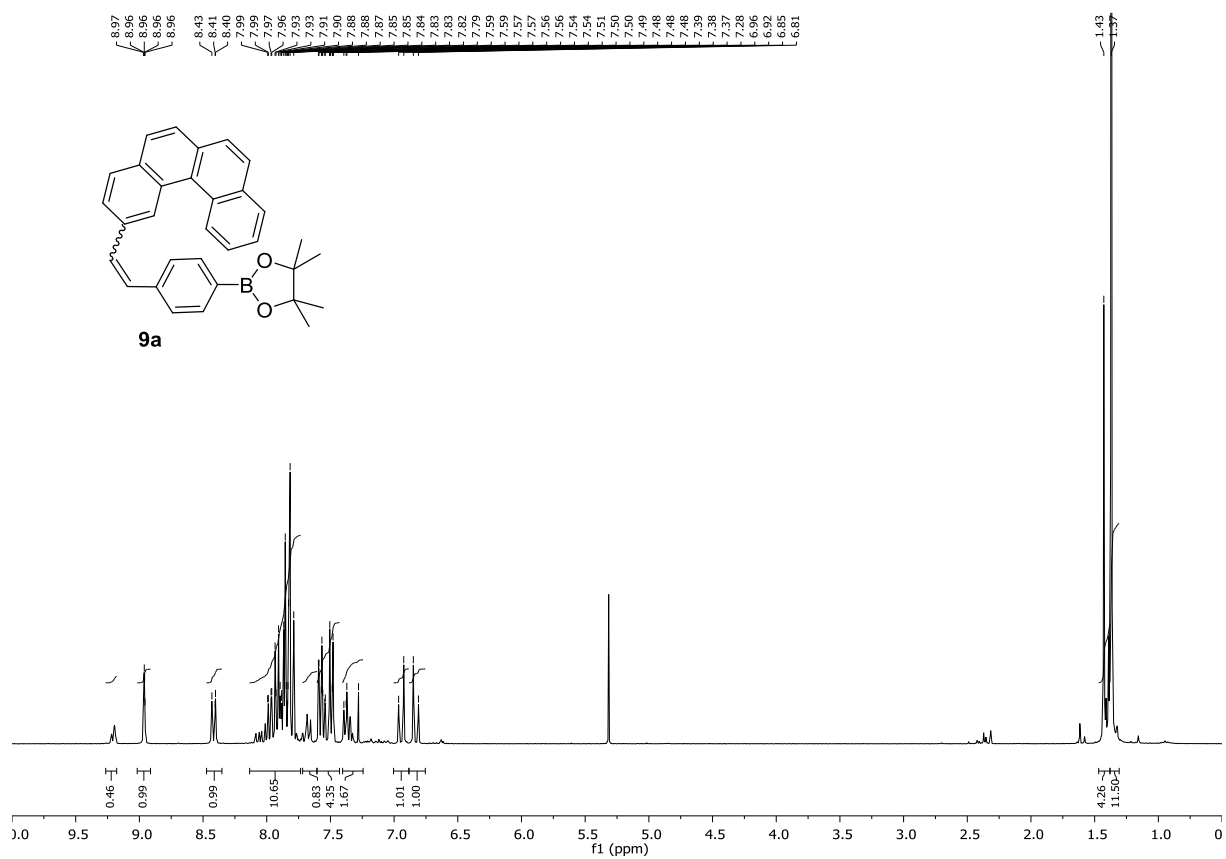
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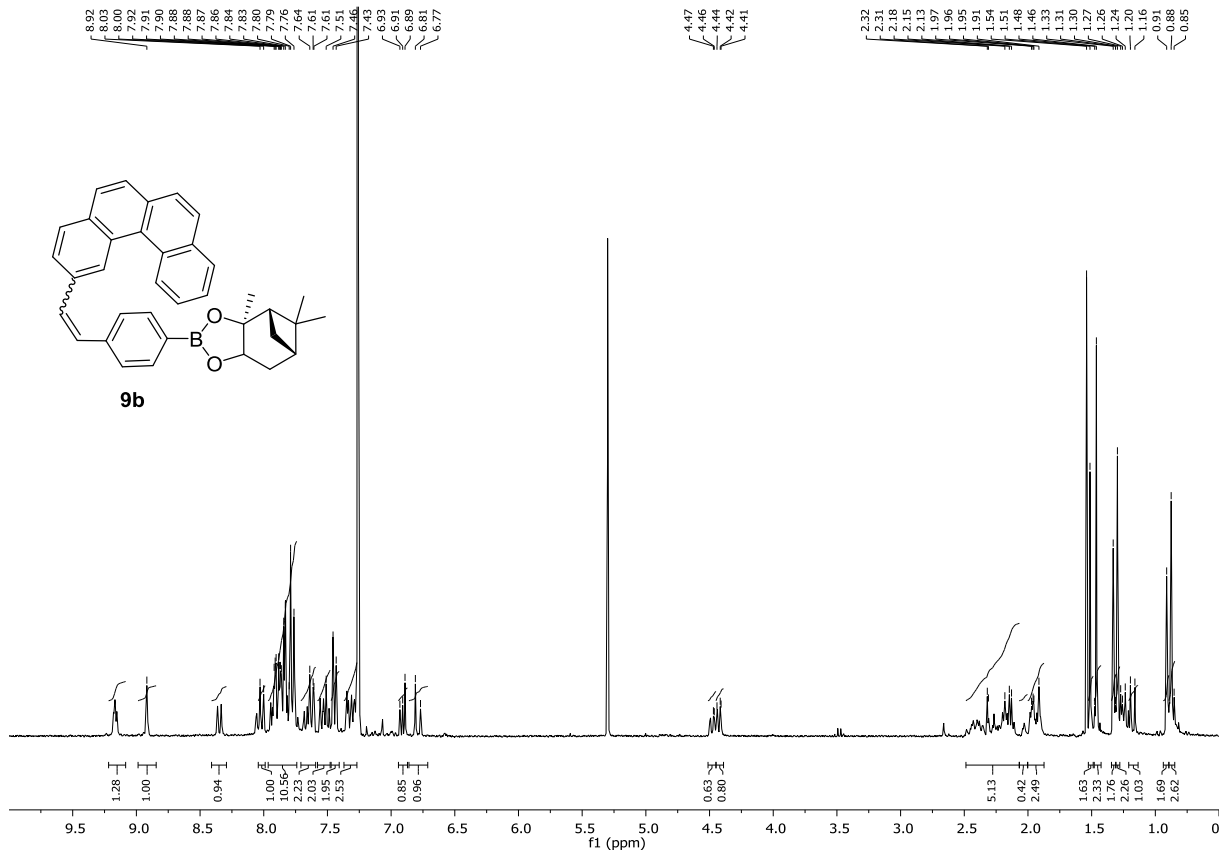
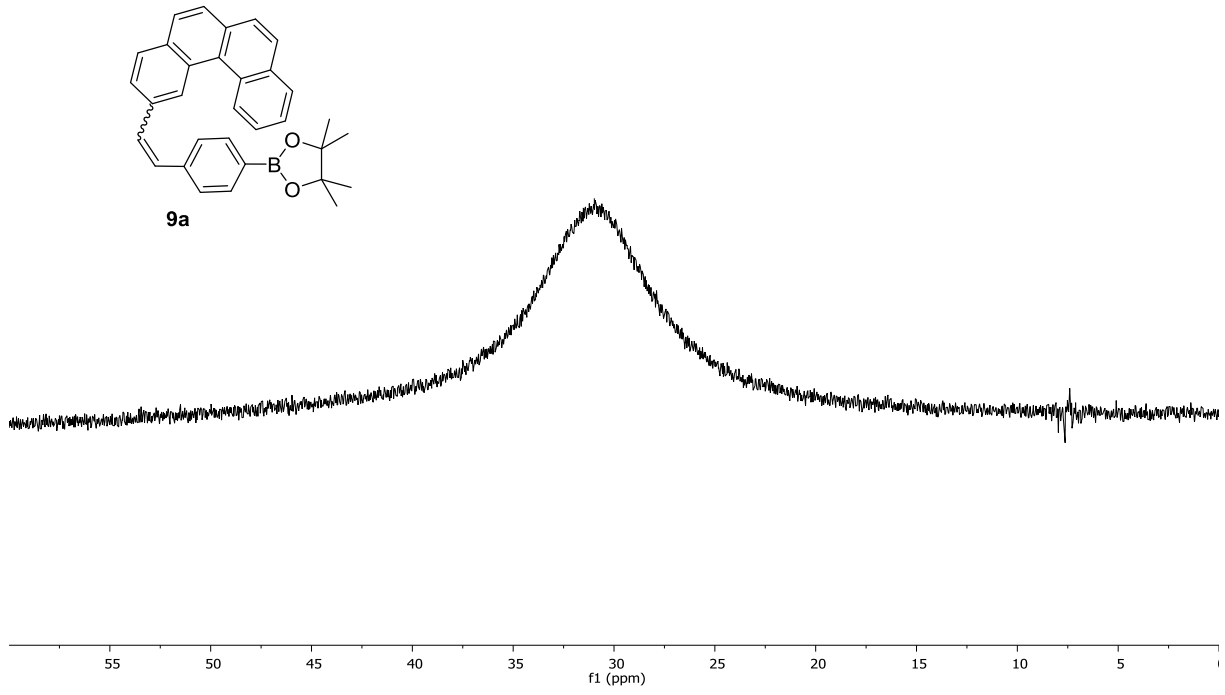
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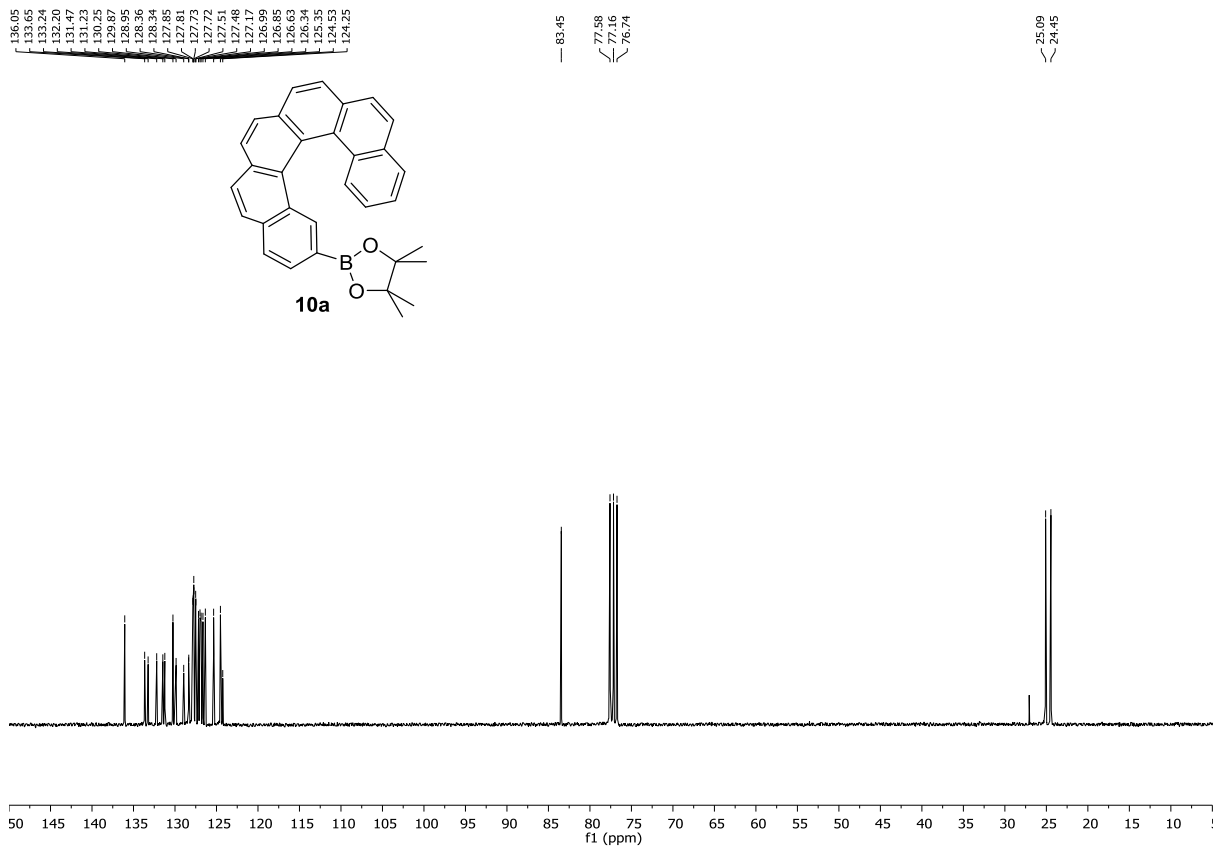
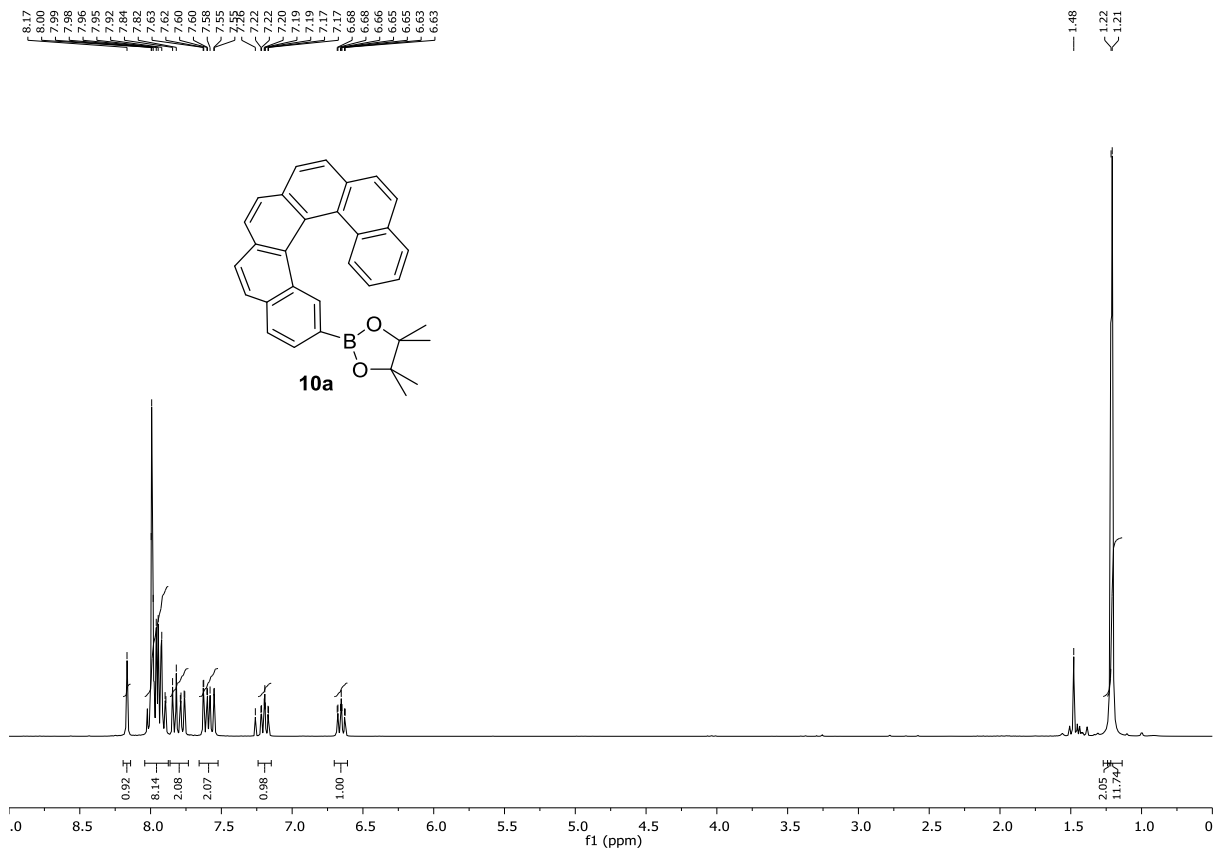
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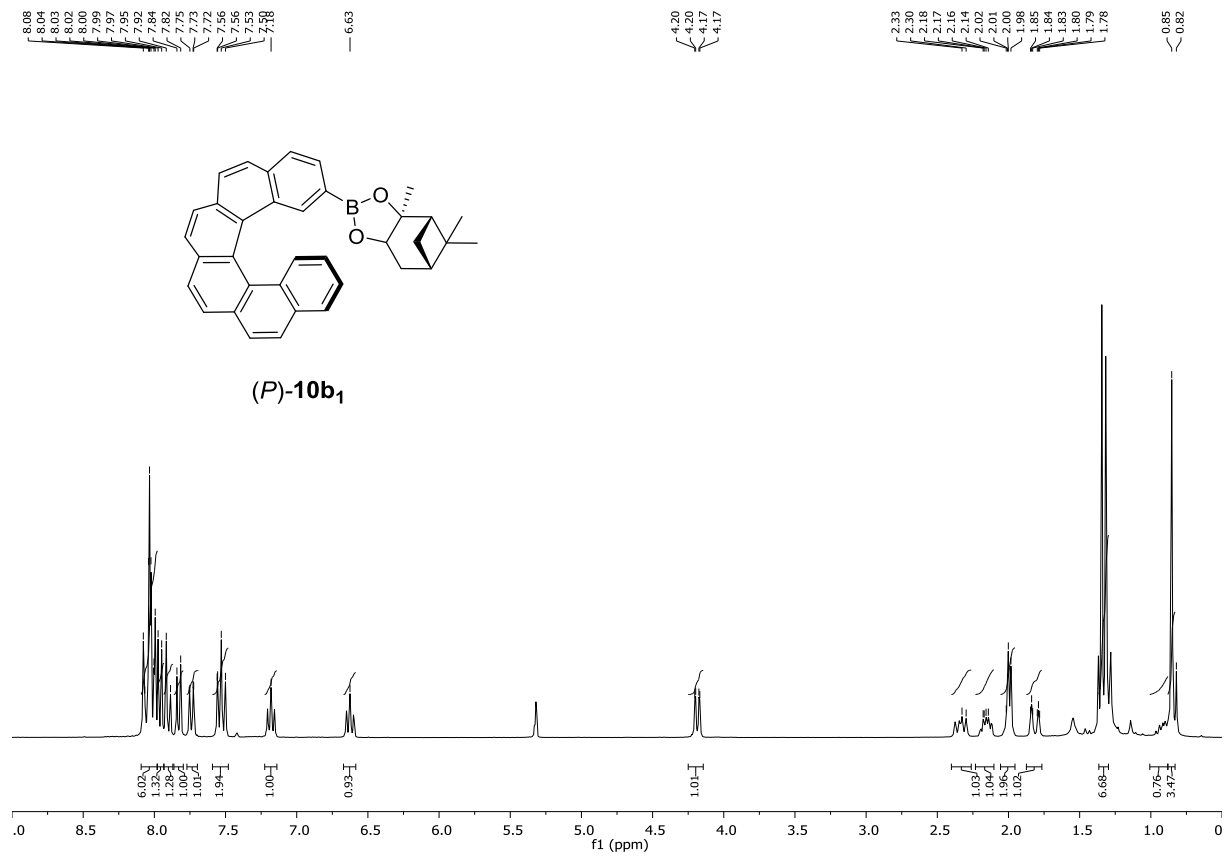
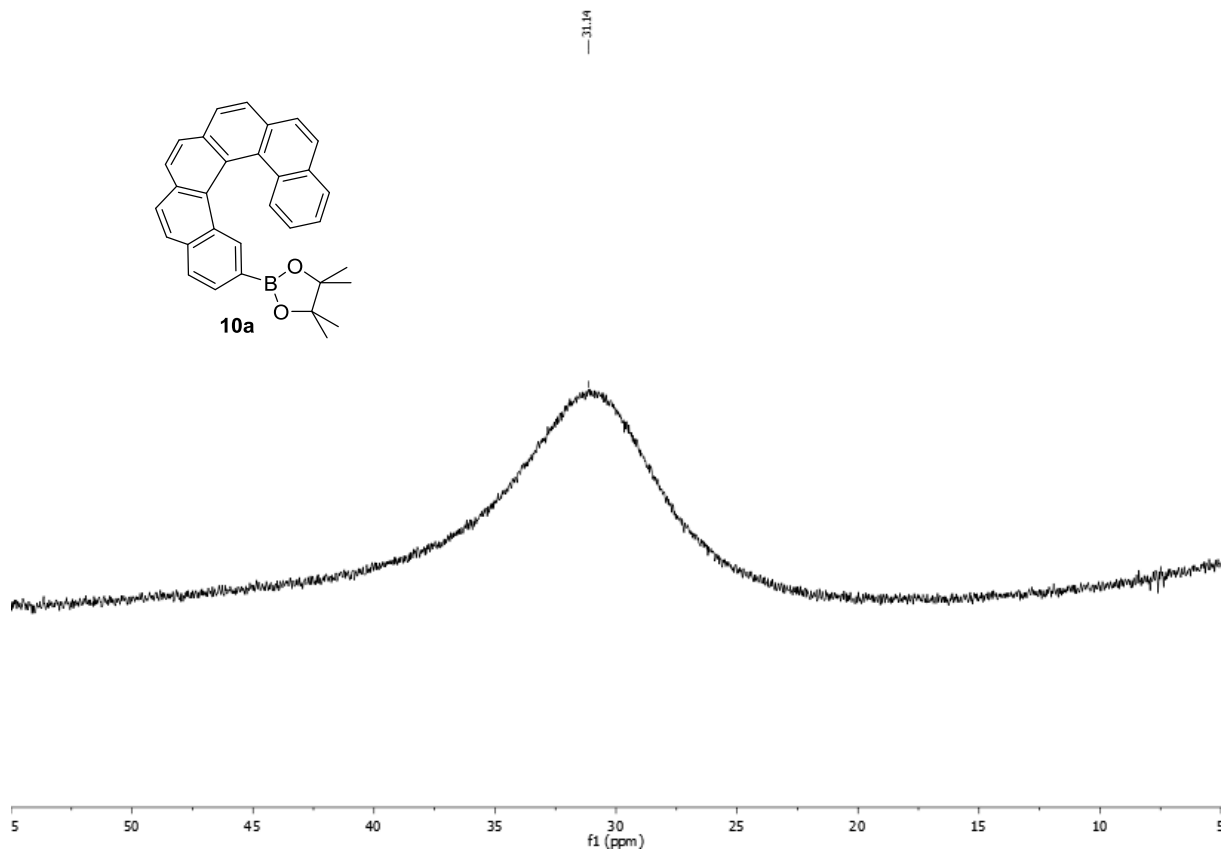
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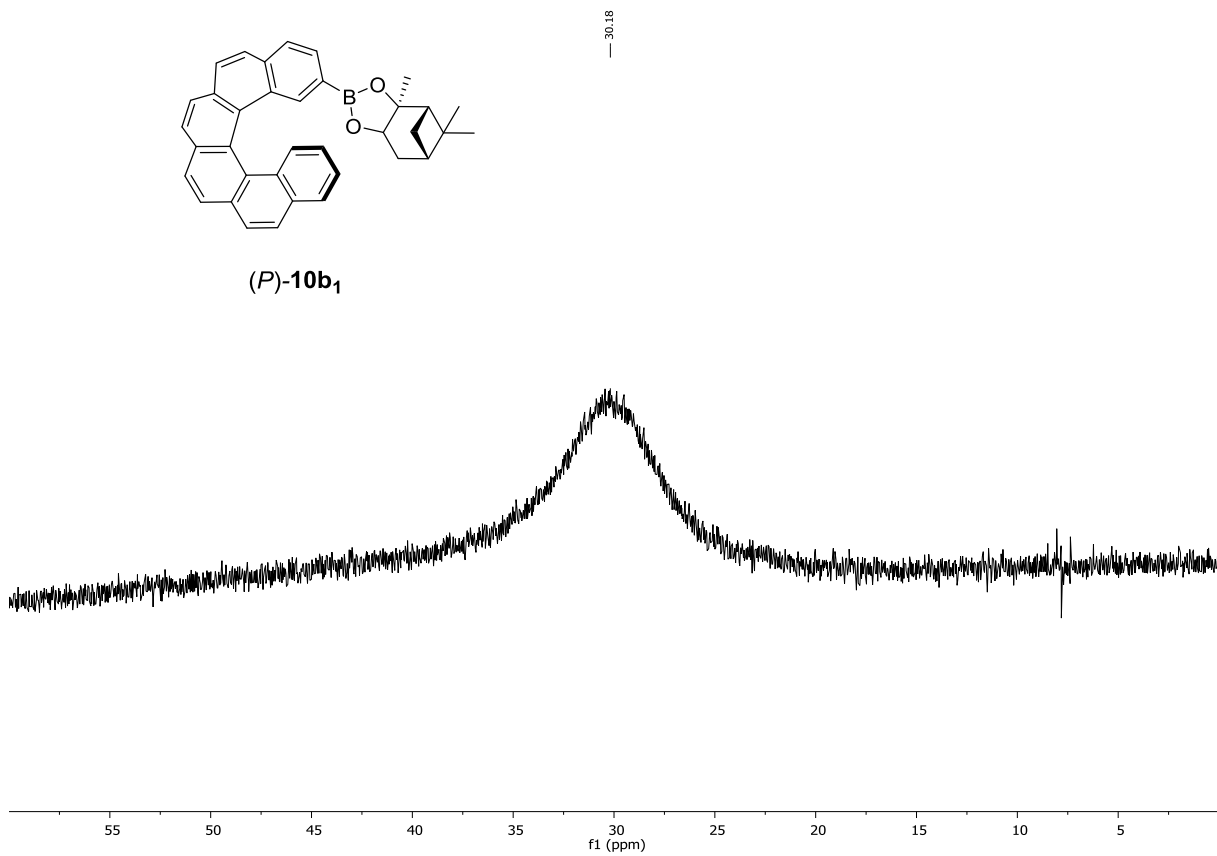
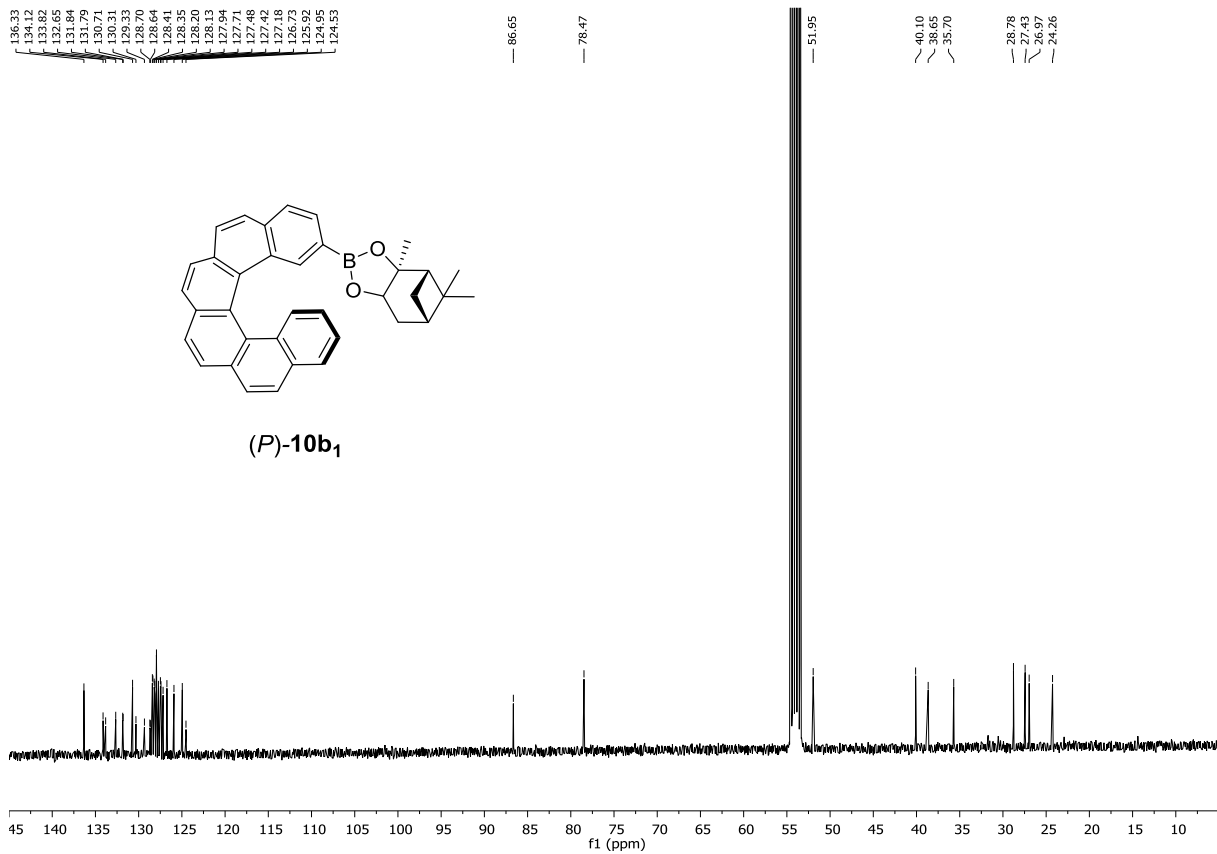
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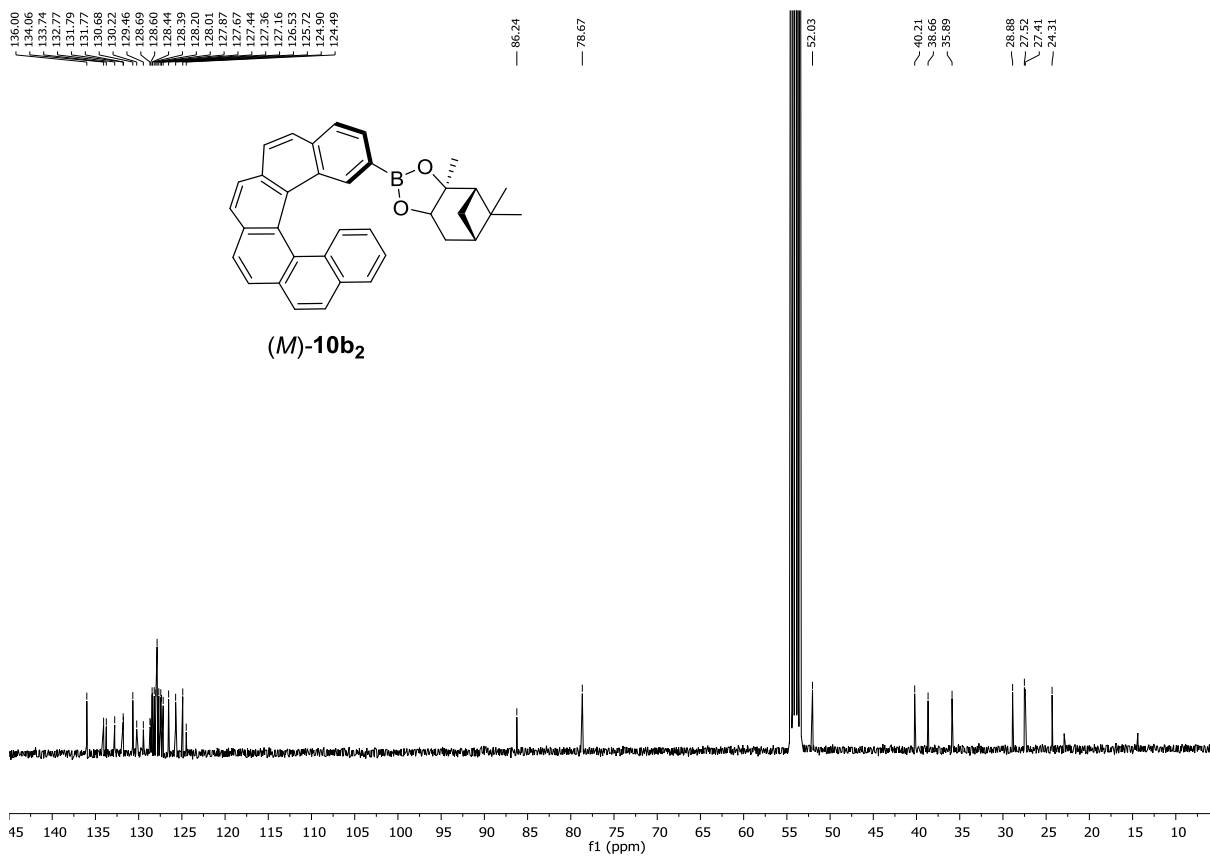
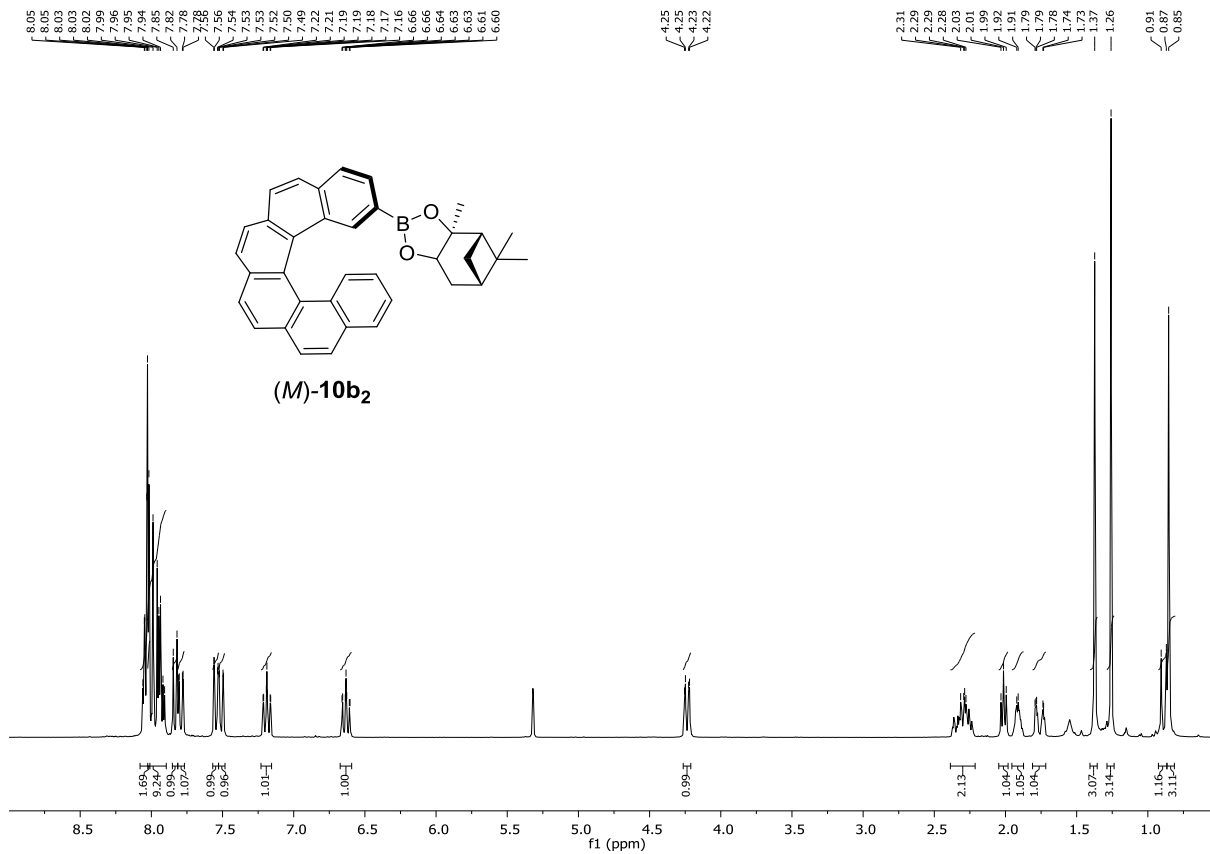


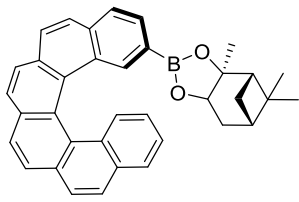




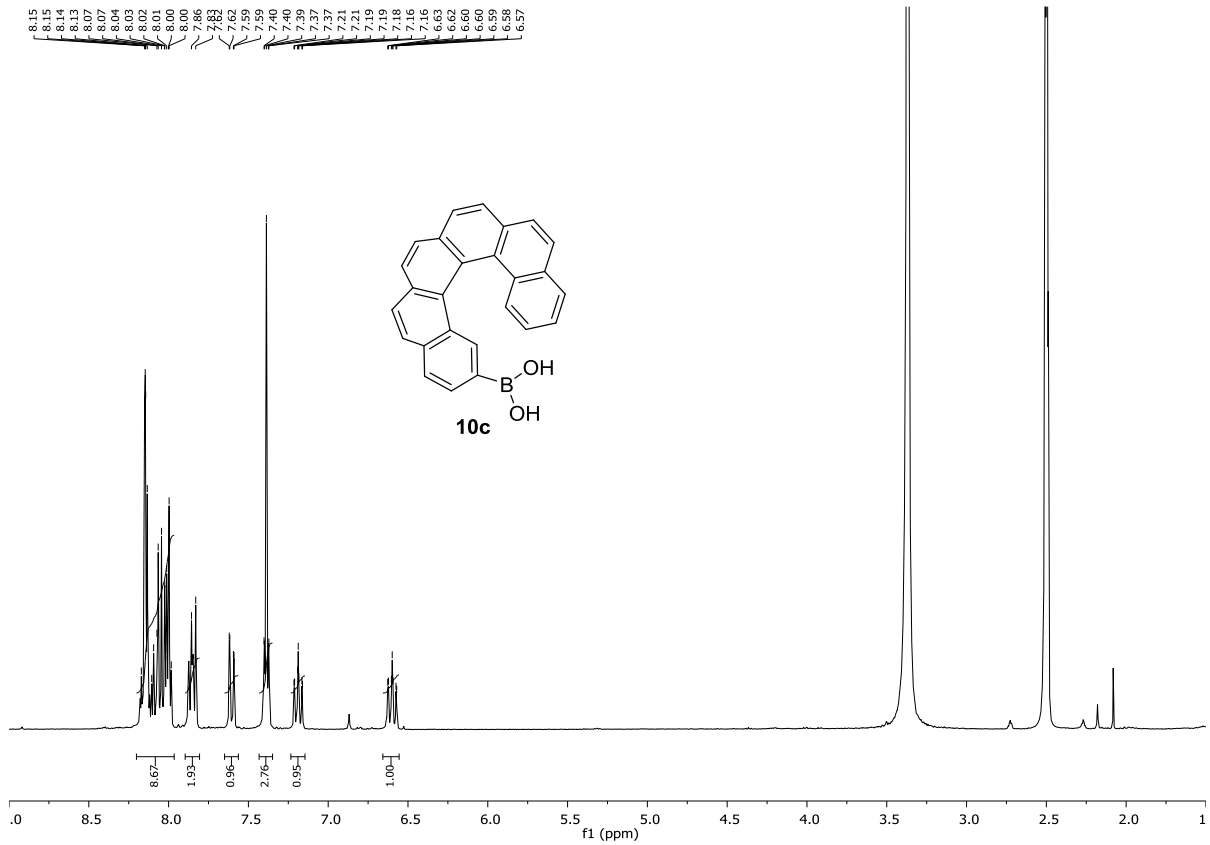
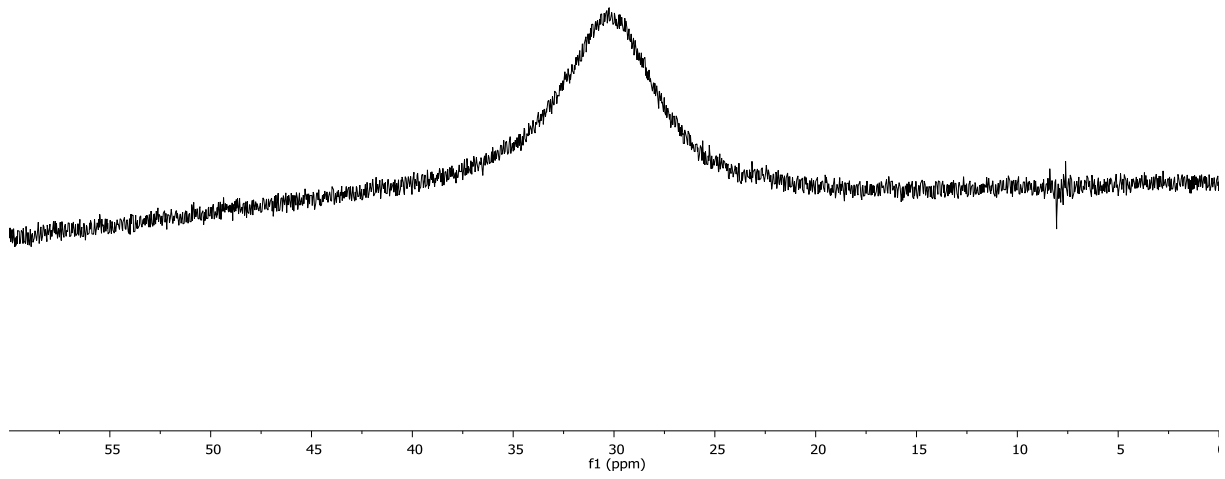




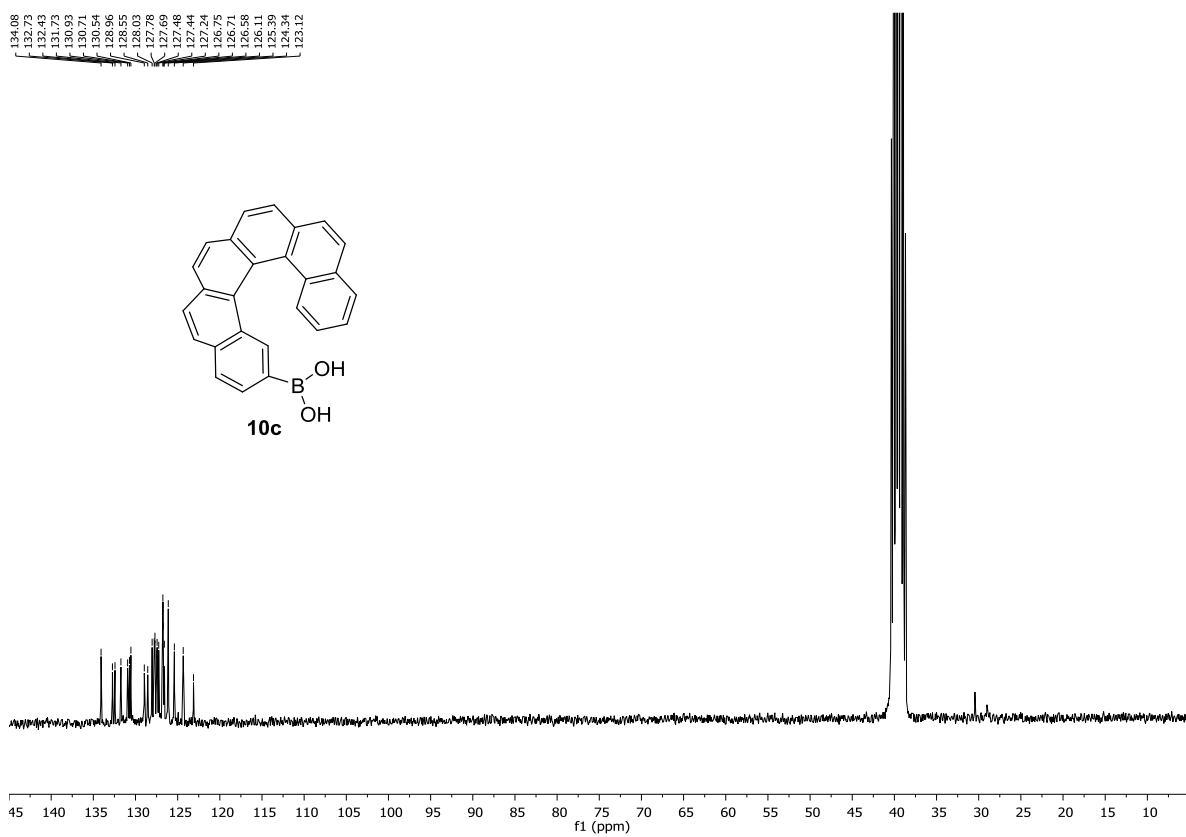
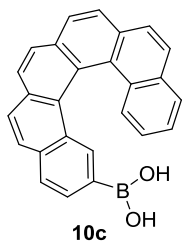




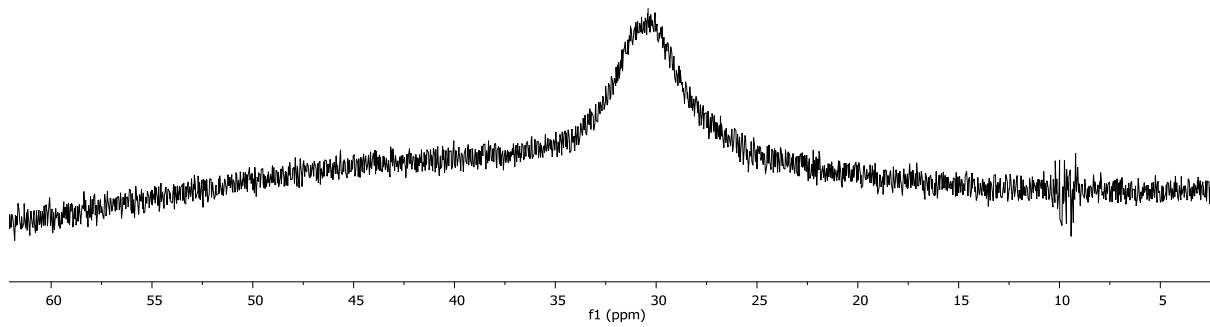
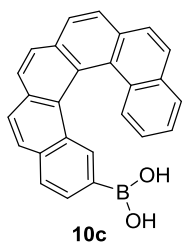
(M)-10b₂

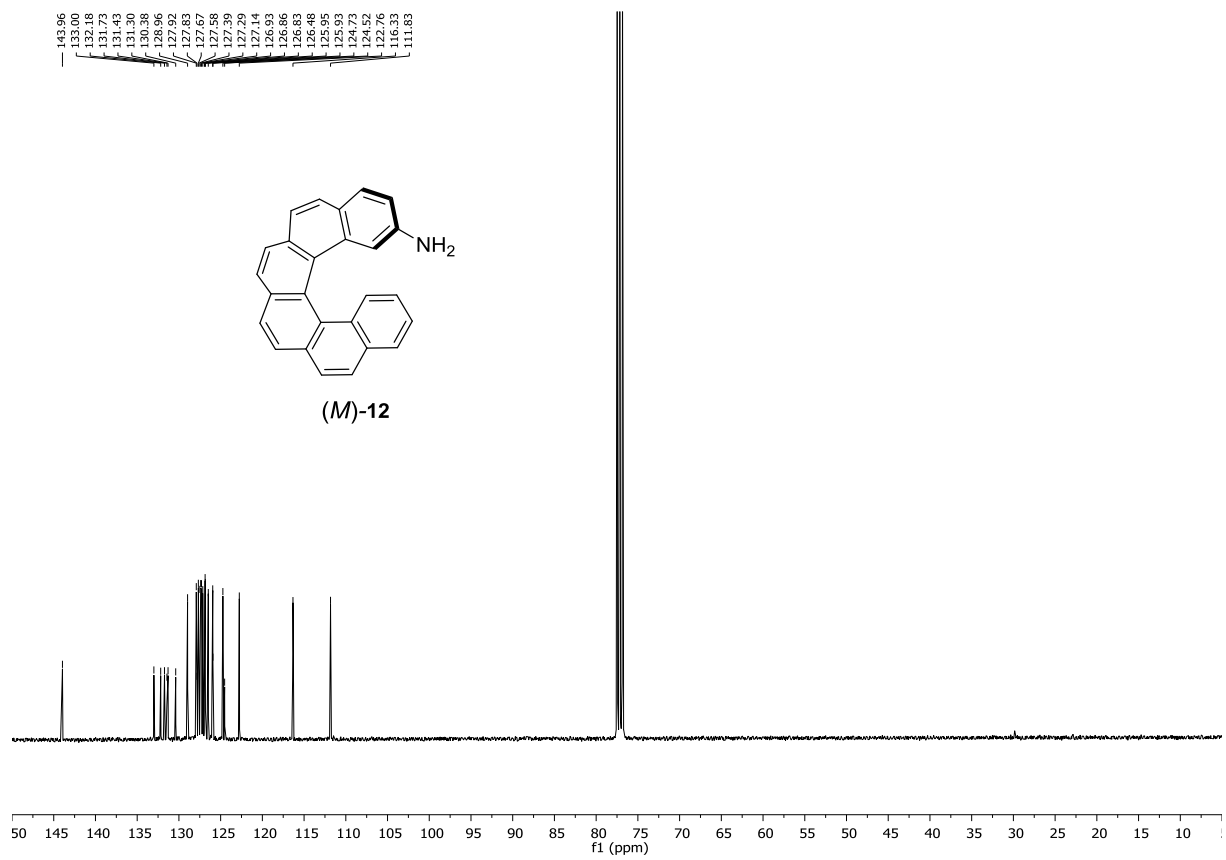
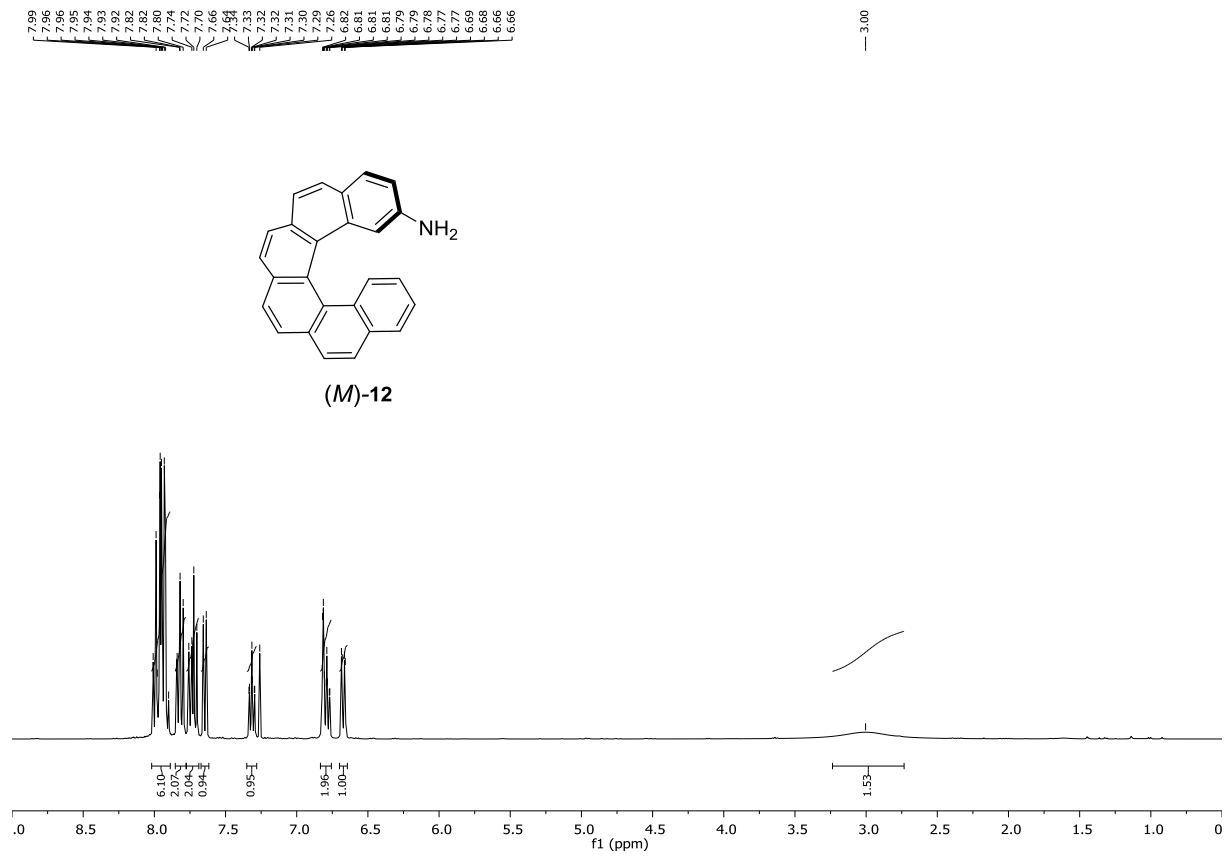


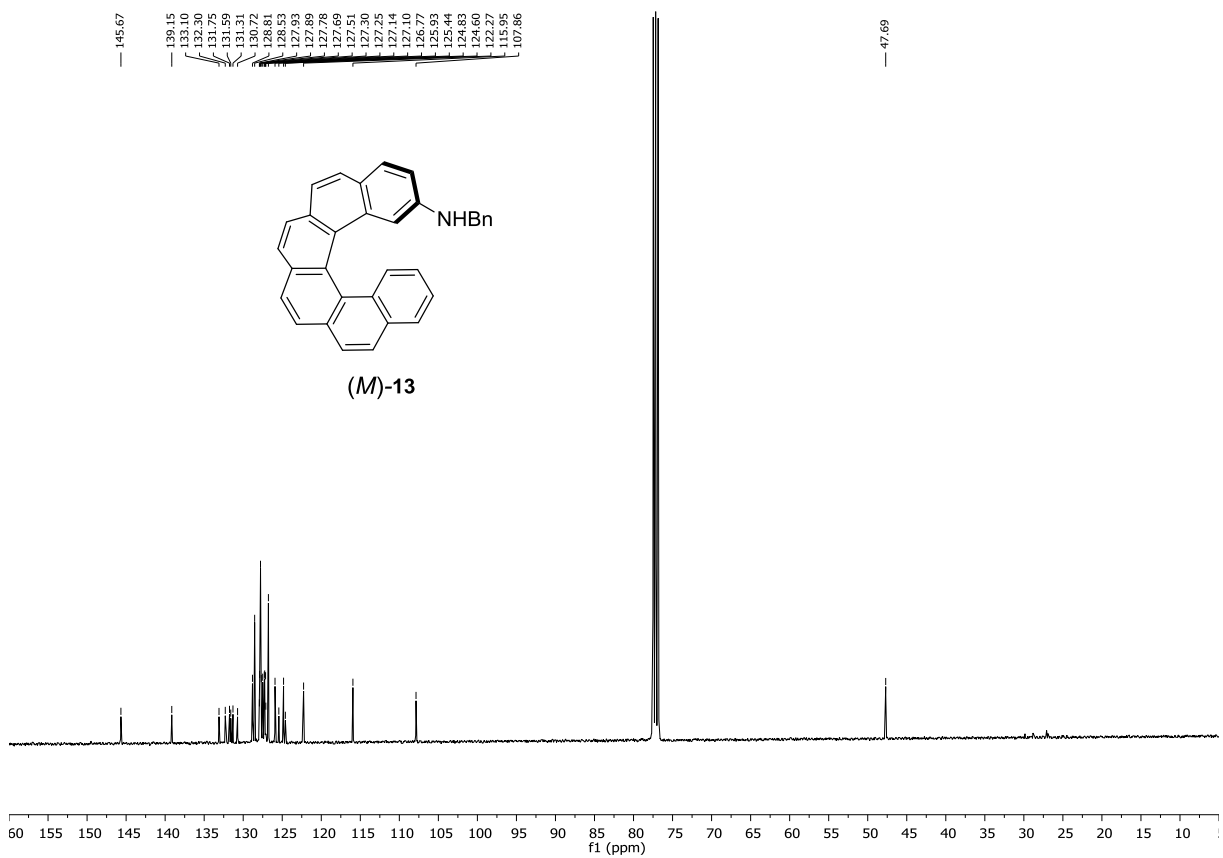
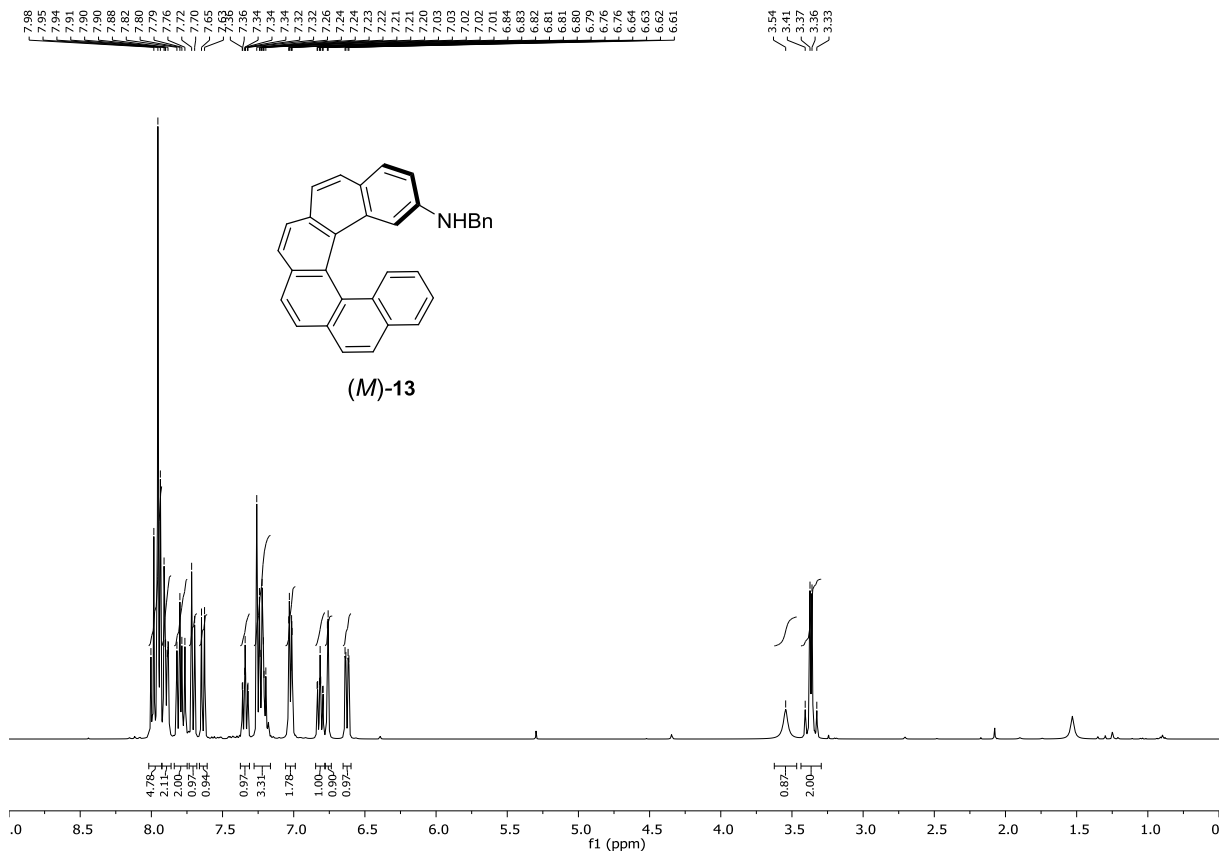
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128.03
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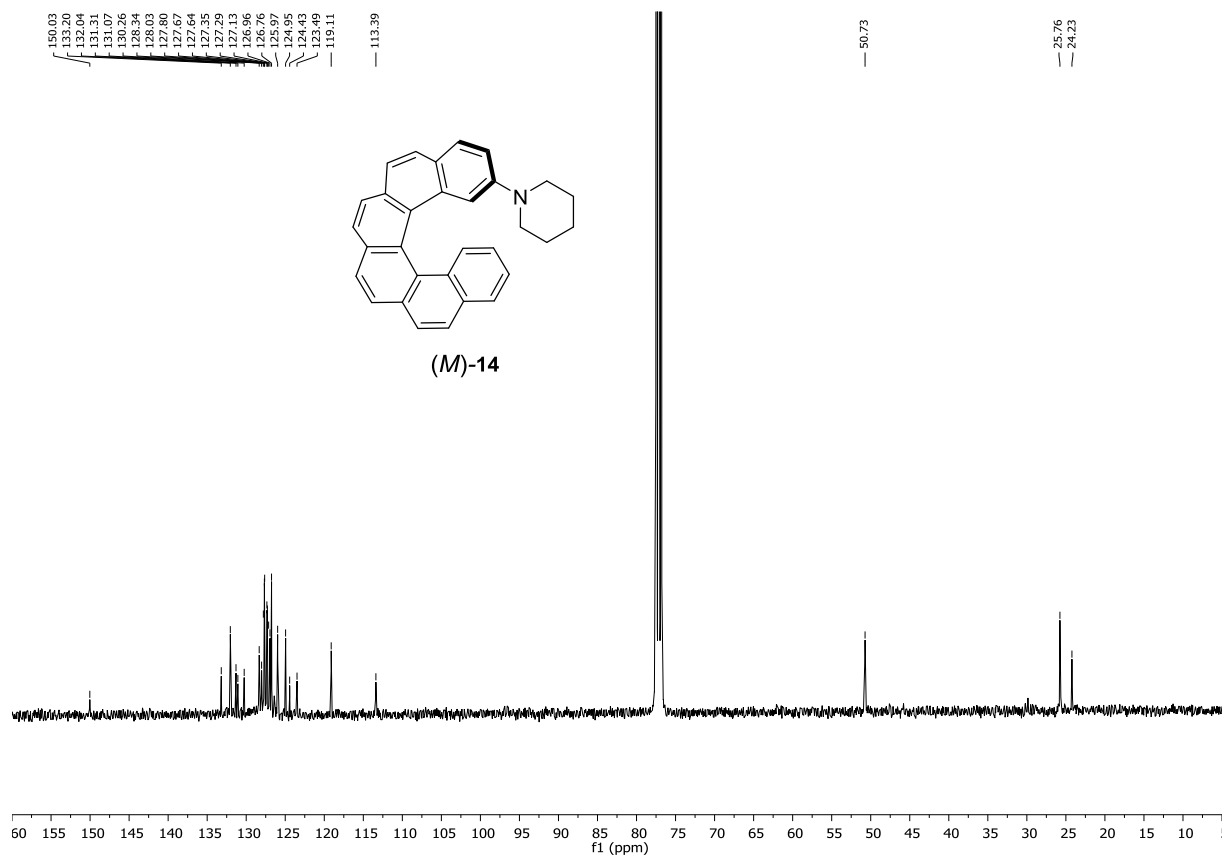
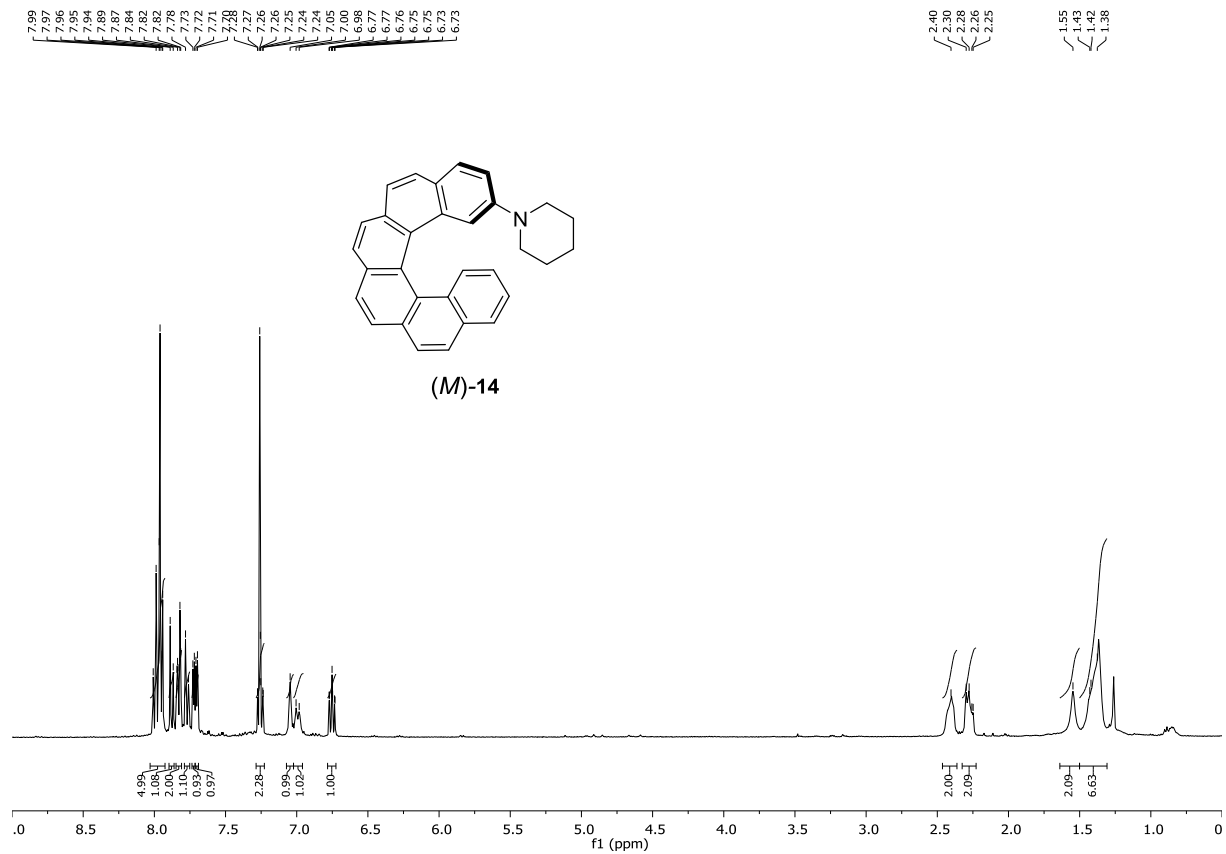


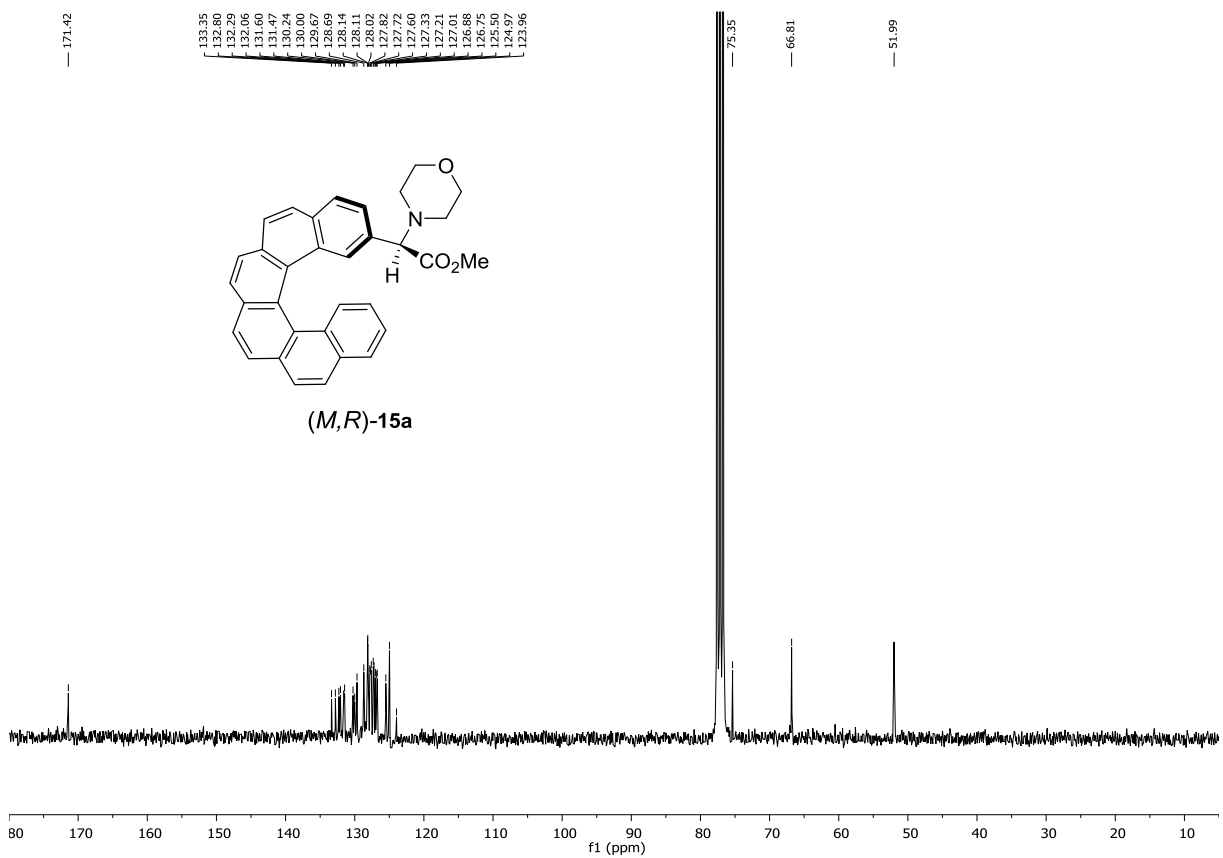
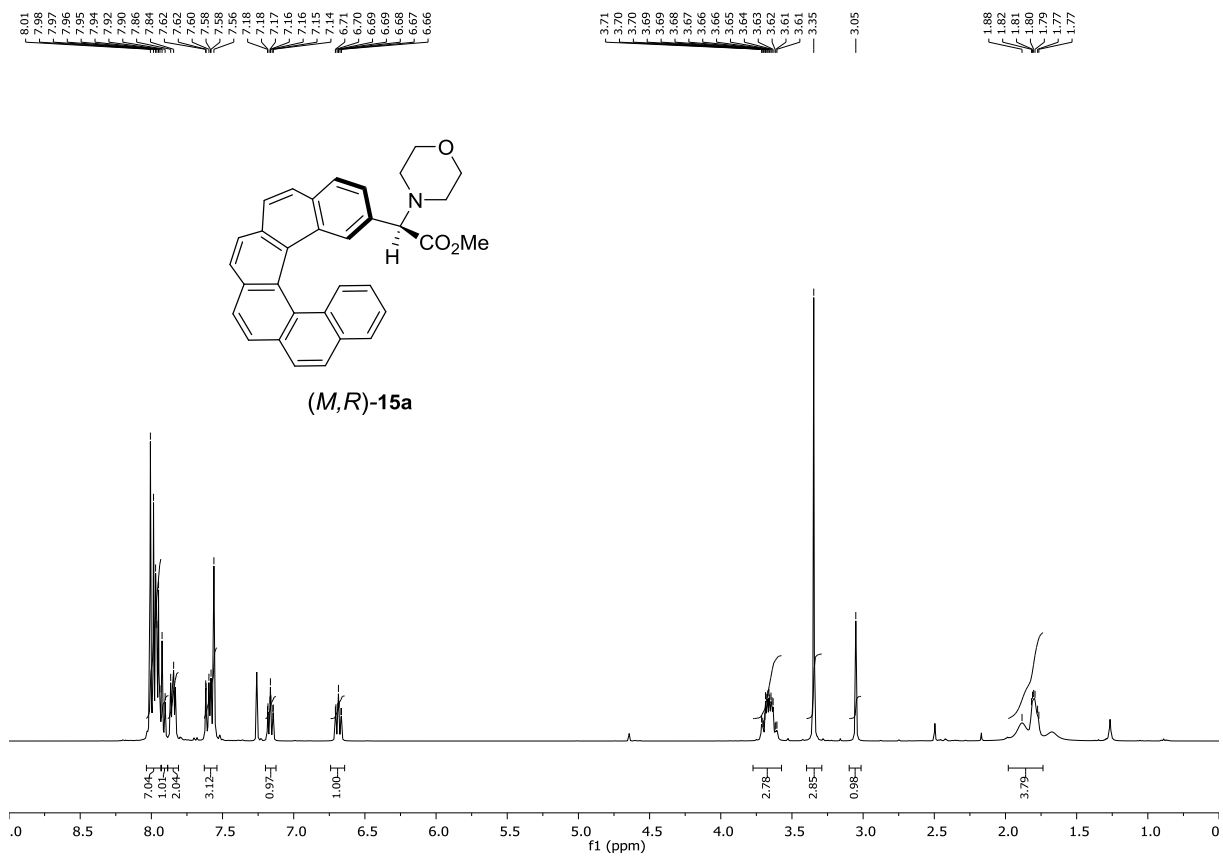
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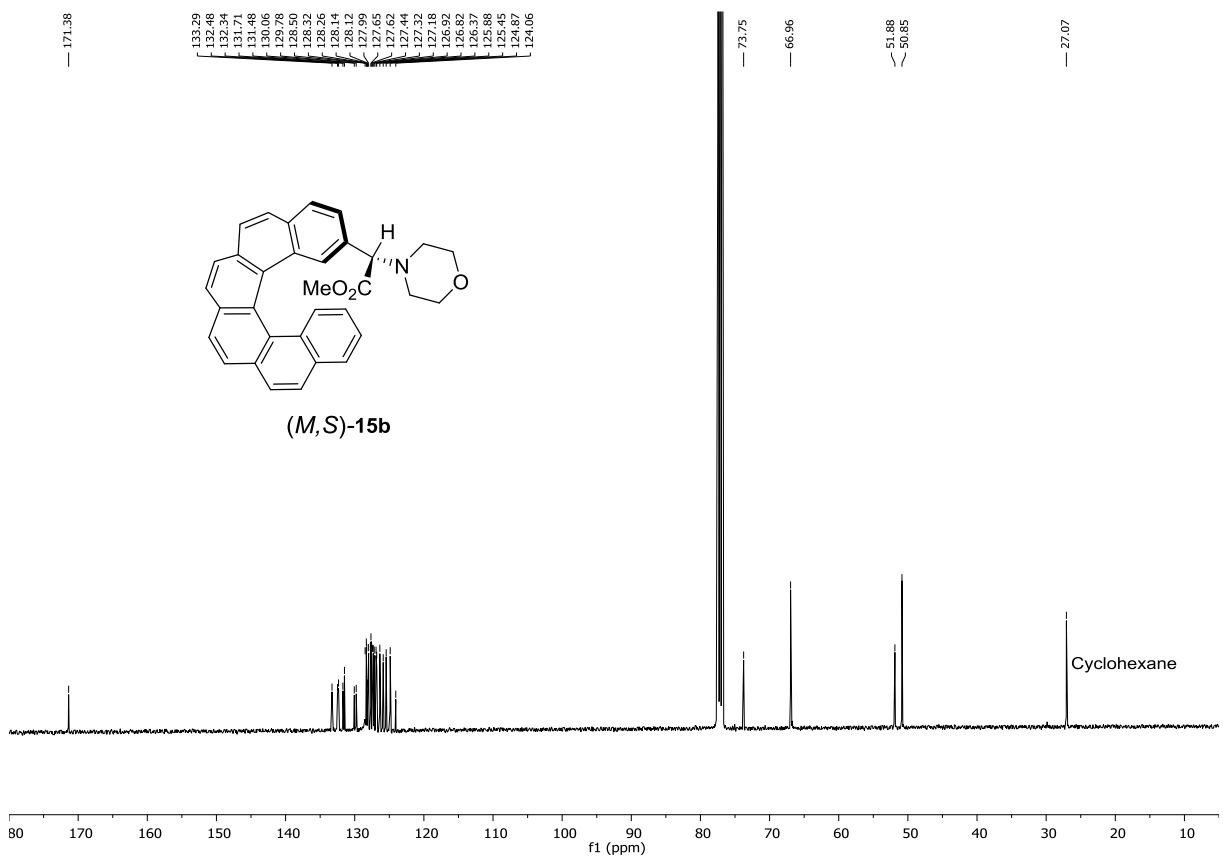
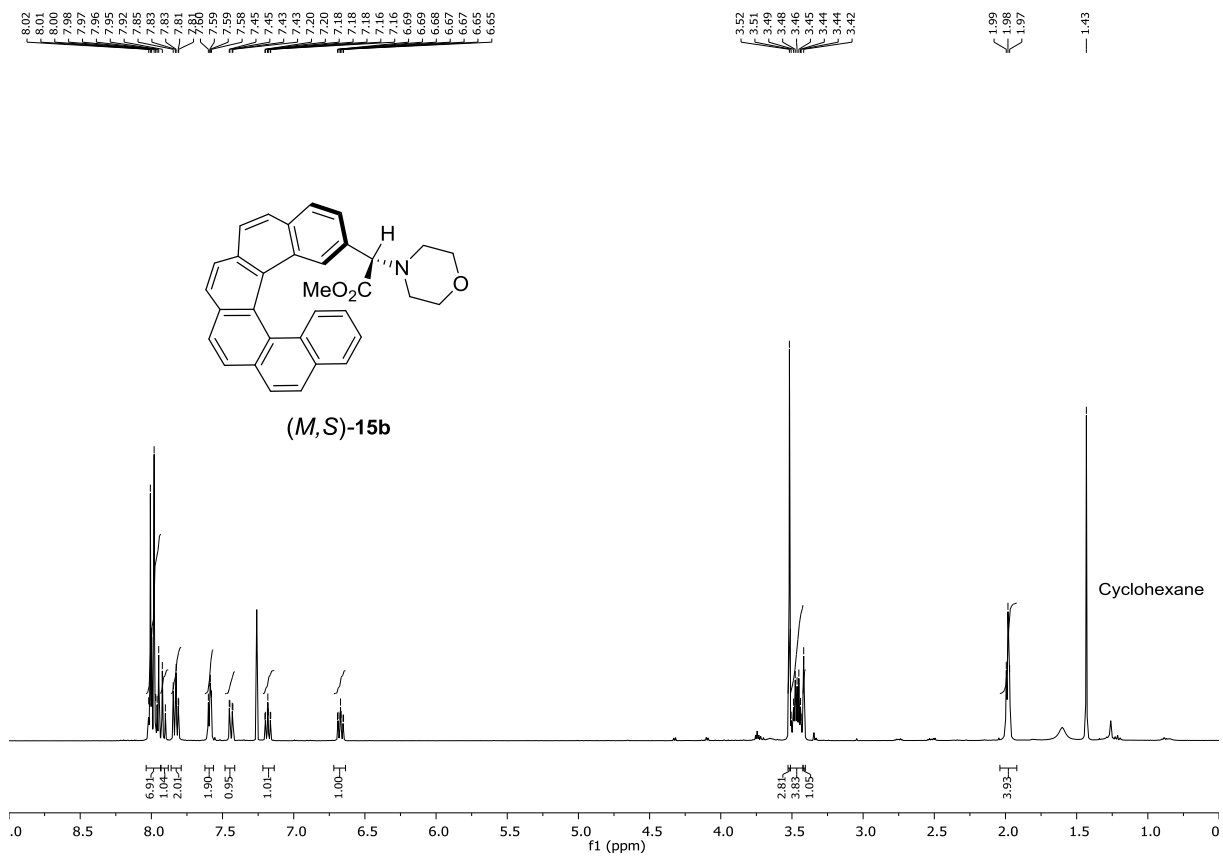








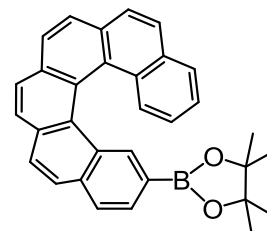




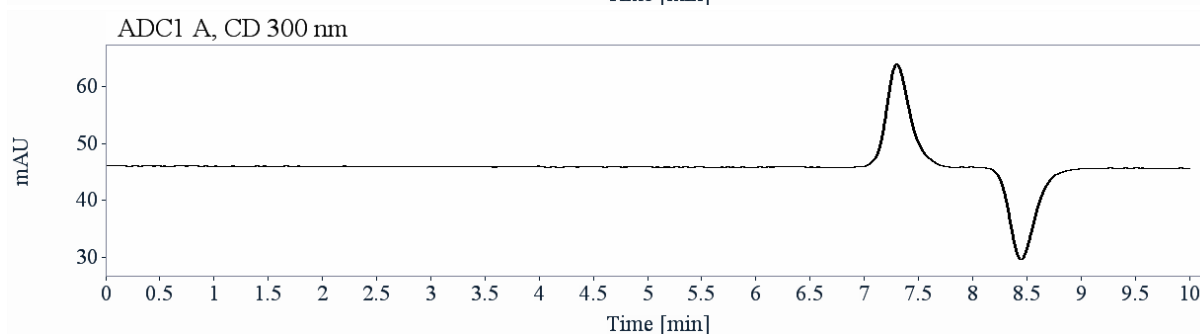
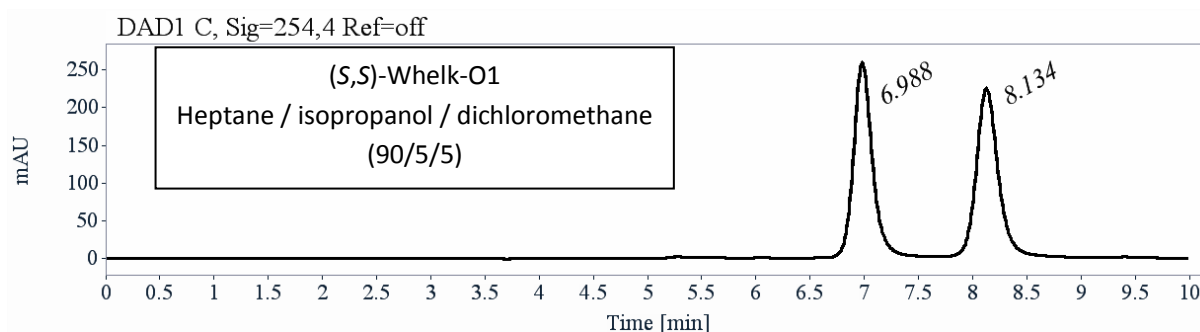
HPLC separations

Analytical chiral HPLC separation for compound (10a)

The sample is dissolved in chloroform, injected on the chiral column, and detected with an UV detector at 254 nm and circular dichroism detector at 300 nm. The flow-rate is 1 mL/min.



Column	Mobile Phase	t1	k1	t2	k2	α	Rs
(<i>S,S</i>)-Whelk-O1	Heptane / 2-PrOH / dichloromethane (90/5/5)	6.99 (P)	1.37	8.13(-)	1.76	1.28	3.47

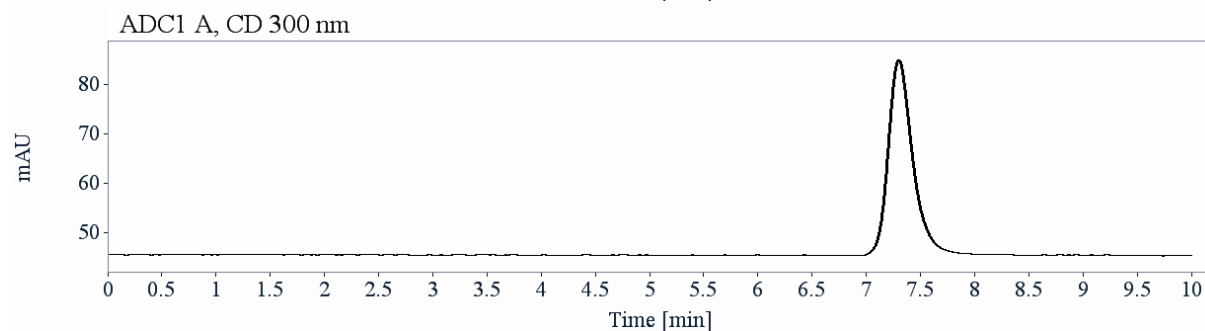
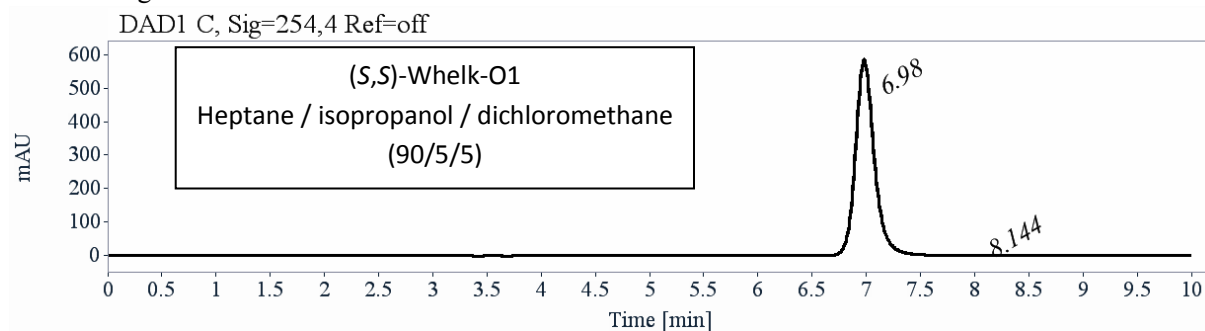


RT [min]	Area	Area%	Capacity Factor	Enantioselectivity	Resolution (USP)
6.99	3088	49.80	1.37		
8.13	3113	50.20	1.76	1.28	3.47
Sum	6201	100.00			

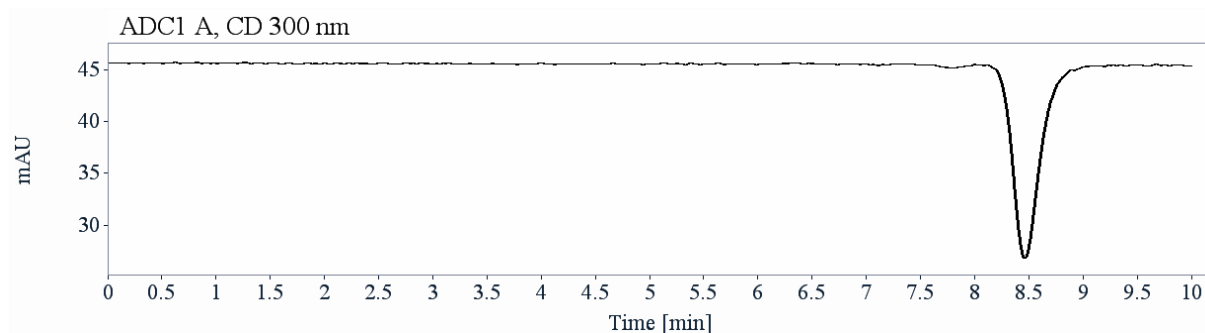
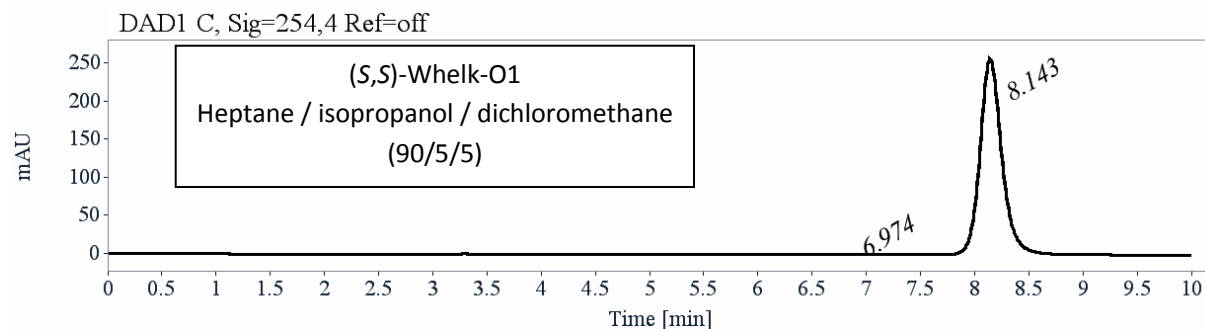
Semi-preparative separation for compound 10a:

- Sample preparation: About 340 mg of compound **10a** are dissolved in 20 mL of a mixture hexane / isopropanol / dichloromethane (65/5/30).
- Chromatographic conditions: (*S,S*)-Whelk-O1 (250 x 10 mm), hexane / isopropanol / dichloromethane (90/5/5) as mobile phase, flow-rate = 5 mL/min, UV detection at 350 nm.
- Injections: 57 times 350 μ L, every 4.5 minutes.
- First fraction: 165 mg of the first eluted (*P*) enantiomer with ee > 99.6 %
- Second fraction: 165 mg of the second eluted (*M*) enantiomer with ee > 99.4 %

• Chromatograms of the collected fractions:



RT [min]	Area	Area%
6.98	6994	99.81
8.14	13	0.19
Sum	7007	100.00

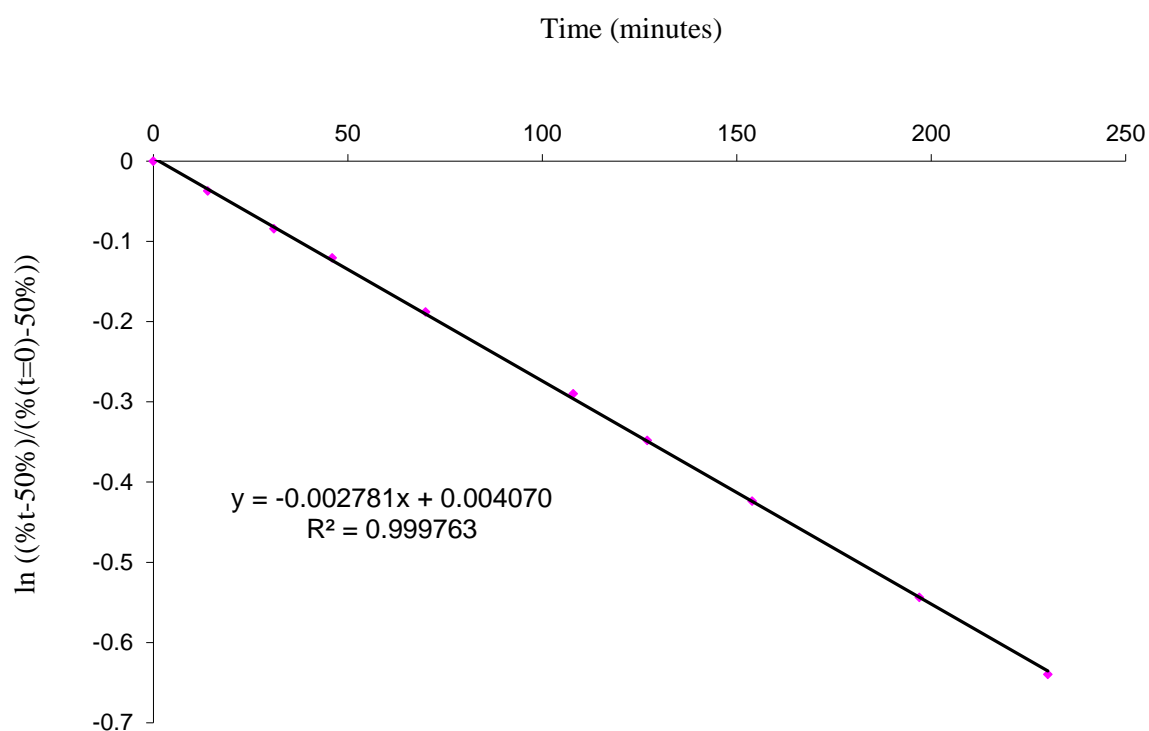


RT [min]	Area	Area%
6.97	11	0.30
8.14	3617	99.70
Sum	3628	100.00

Kinetic of enantiomerization in 1,2-dichlorobenzene

About 1 mg of (*M*)-**10a** is heated in about 15 mL of 1,2-dichlorobenzene at 182 °C. 5 μ L are taken and then injected on (*S,S*)-Whelk-O1 (90:5:5 heptane / isopropanol / dichloromethane, 1 mL/min, UV 300 nm). The percentage decrease (*M*)-**10a** is monitored.

Time (min)	% second eluted enantiomer	$\ln ((\%t-50\%)/(\%t=0)-50\%))$
0	99.32	0.00000
14	97.52	-0.03718
31	95.33	-0.08436
46	93.72	-0.12052
70	90.87	-0.18793
108	86.9	-0.29012
127	84.82	-0.34814
154	82.28	-0.42388
197	78.63	-0.54387
230	76.01	-0.63985



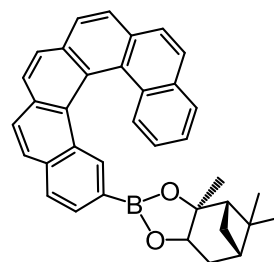
$$k_{\text{enantiomerisation}} = 2.3171\text{E-}05 \text{ s}^{-1} \text{ (182}^\circ\text{C, 1,2-dichlorobenzene)}$$

$$\Delta G^\ddagger = 153.5 \text{ kJ/mol (182}^\circ\text{C, 1,2-dichlorobenzene)}$$

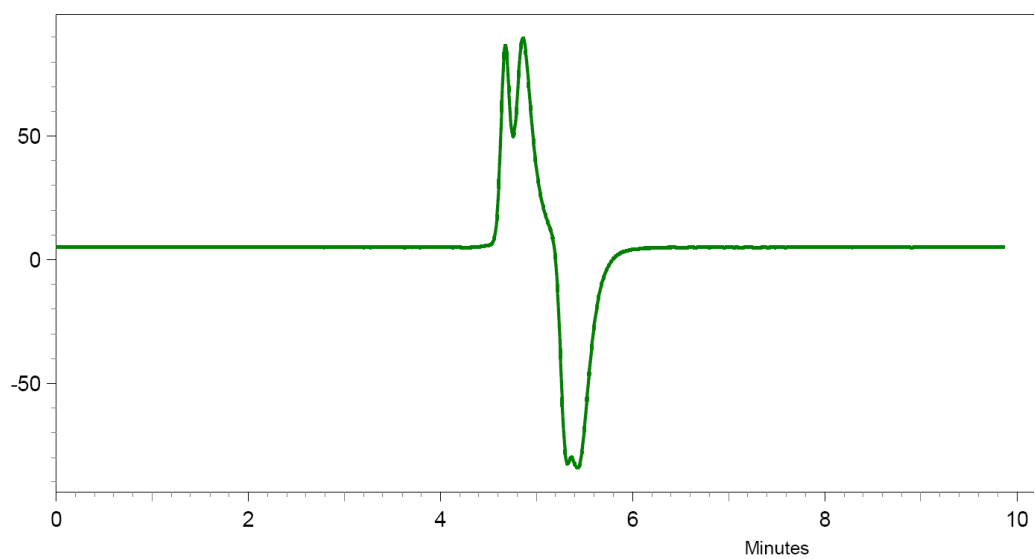
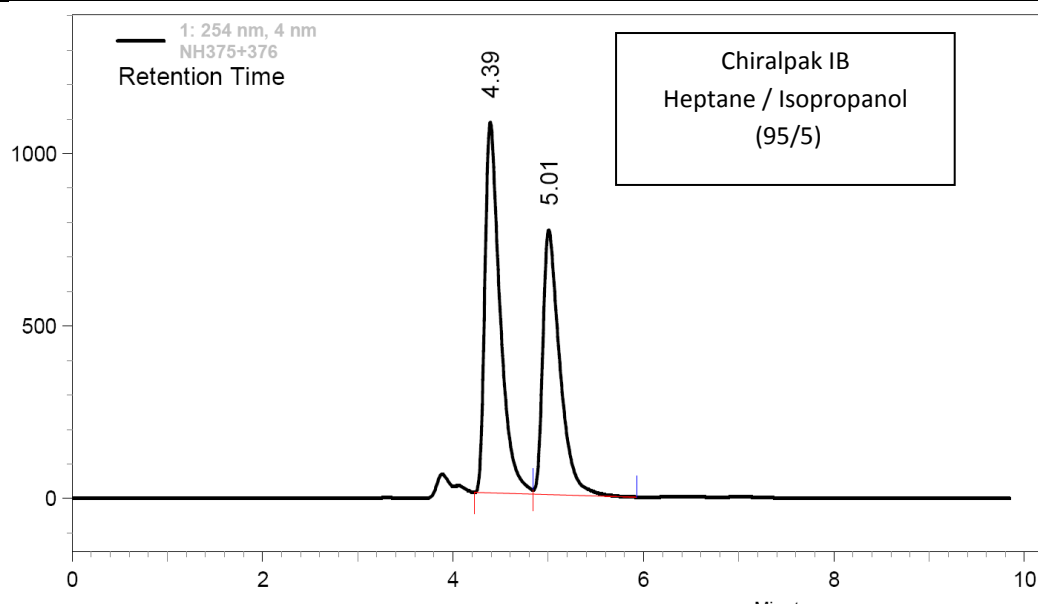
$$t_{1/2} = 4.2 \text{ hours (182}^\circ\text{C, 1,2-dichlorobenzene)}$$

Analytical HPLC separation for diastereomers (10b₁) and (10b₂) over chiral stationary phase

The sample is dissolved in chloroform, injected on the chiral column, and detected with an UV detector at 254 nm and circular dichroism detector at 254 nm. The flow-rate is 1 ml/min.

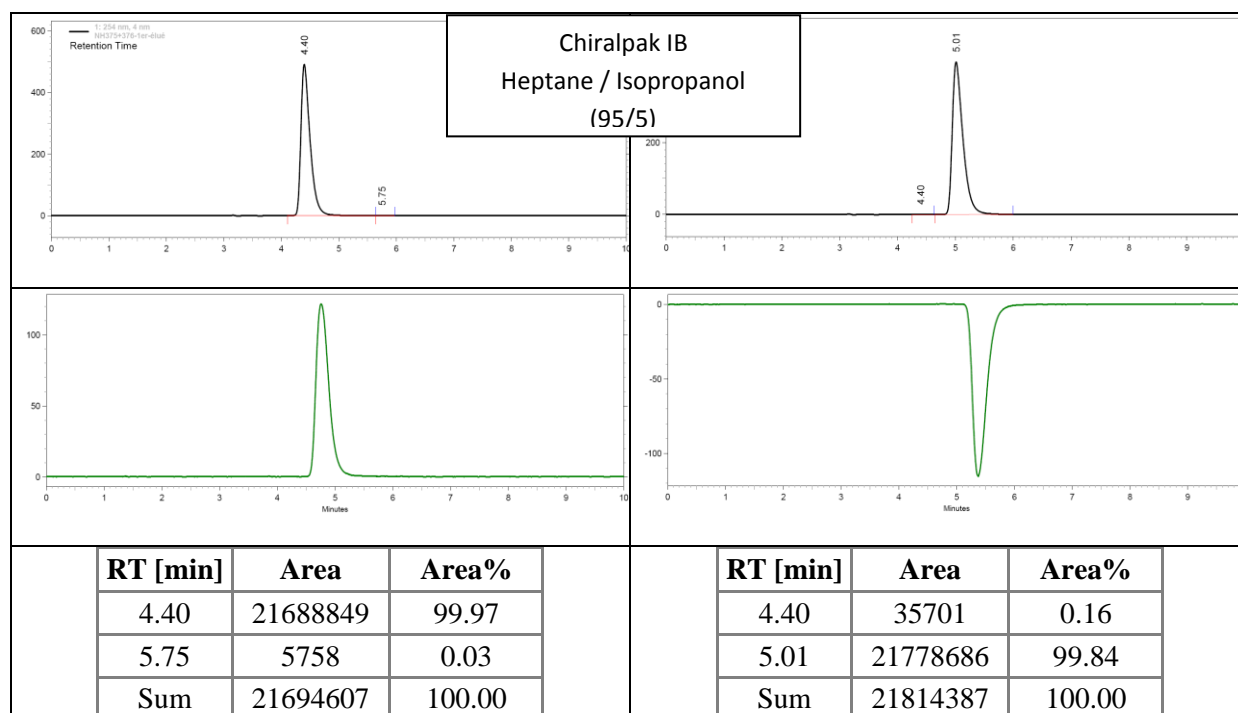


Column	Mobile Phase	t ₁	k ₁	t ₂	k ₂	α	R _s
Chiralpak IB	Heptane / Isopropanol 95/5	4.39 (+)	0.46	5.01(-)	0.67	1.46	2.03



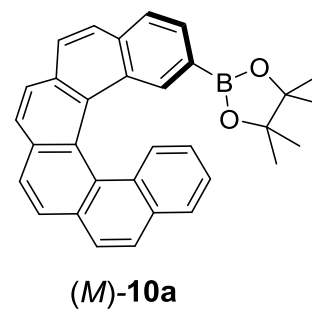
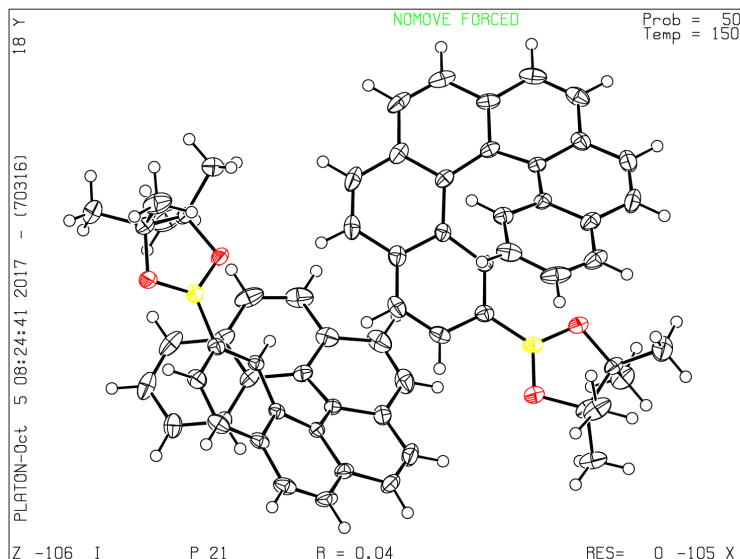
Semi-preparative separation for diastereomers **10b₁** and **10b₂**:

- Sample preparation: About 110 mg of diastereomers **10b₁** and **10b₂** are dissolved in 6 mL of a mixture Hexane / Isopropanol /Chloroform (60/10/30).
- Chromatographic conditions: Chiralpak IB (250 x 10 mm), Hexane / Isopropanol (95/5) as mobile phase, flow-rate = 5 mL/min, UV detection at 254 nm.
- Injections (stacked): 120 times 50 μ L, every 2.7 minutes.
- Collection: the first eluted diastereoisomer is collected between 4.5 and 4.9 minutes and the second between 5.35 and 5.8 minutes.
- First fraction: 52.9 mg of the first eluted ((+, CD254)-enantiomer) with ee > 99.5 %
- Second fraction: 44.3 mg of the second eluted ((-, CD254)-enantiomer) with ee > 99.5 %
- Chromatograms of the collected fractions:

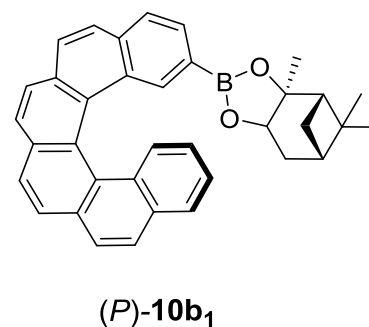
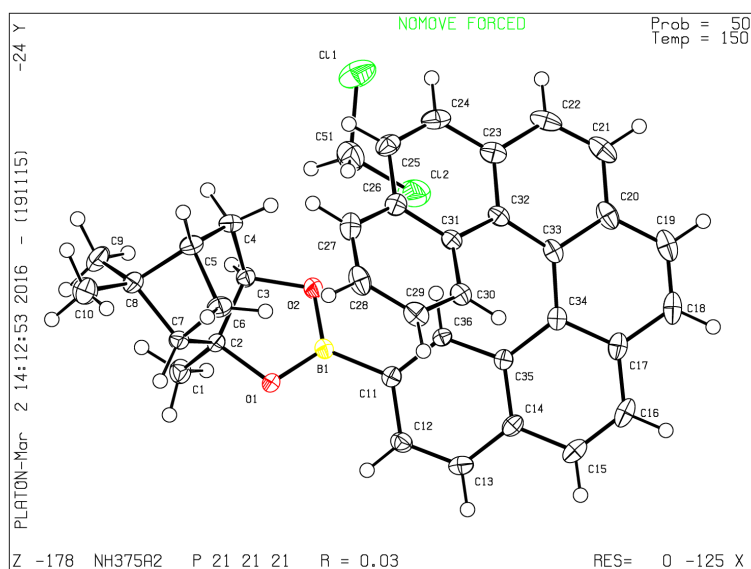


X-ray diffraction data of (*M*)-Pinacol hexahelicen-2-ylboronic ester (10a), (*P*, 1'*S*,2'*S*,3'*R*,5'*S*)-Pinanediol hexahelicen-2-ylboronic ester (10b₁) and (*M,S*)-Methyl-2-(hexahelicen-2-yl)-2-morpholinoacetate (15b)

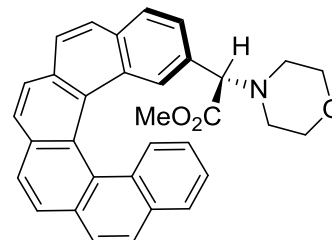
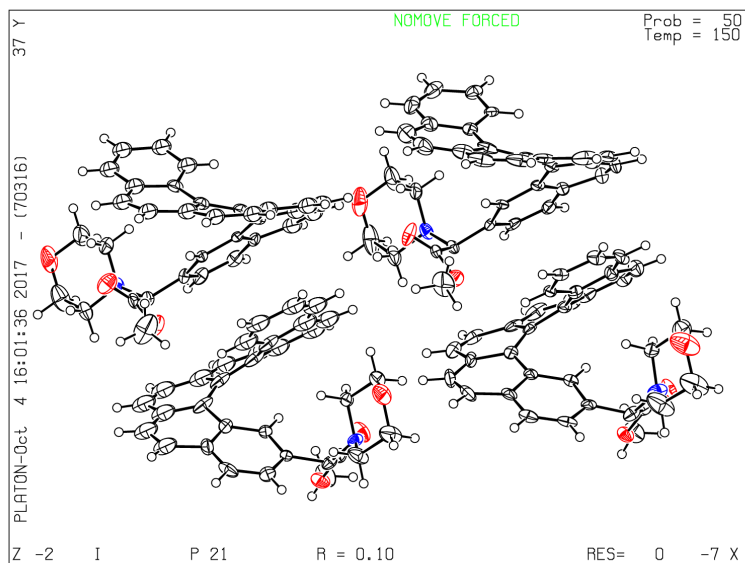
ORTEP diagram of compound (*M*)-10a with ellipsoids at 50% probability



ORTEP diagram of compound (*P*)-10b₁ with ellipsoids at 50% probability



ORTEP diagram of compound (M,S)-15b with ellipsoids at 50% probability



(M,S)-15b

X-ray crystallographic data for compound (M)-10a, (P)-10b₁ and (M,S)-15b

	(M)-10a	(P,1'S,2'S,3'R,5'S)-10b ₁	(M,S)-15b
Empirical Formula	C ₃₂ H ₂₇ B O ₂	C ₃₆ H ₃₁ B O ₂ , CH ₂ Cl ₂	C ₃₃ H ₂₇ N O ₃
CCDC number	CCDC 1579151	CCDC 1573419	CCDC 1579161
Formula Weight	454.34	591.34	485.55
Temperature (K)	150	150(2)	150
Wavelength (Å)	0.71073	1.54178	0.71073
Crystal system	monoclinic	Orthorhombic	monoclinic
Space Group	P 21	P2 ₁ 2 ₁ 2 ₁	P 21
a (Å)	11.1125(4)	12.2364(8)	13.5543(8)
b (Å)	14.1950(5)	14.0290(8)	12.7687(7)
c (Å)	16.2592(5)	17.3796(10)	29.1695(17)
α (°)	90	90	90
β (°)	109.7070(10)	90	100.655(3)
γ (°)	90	90	90
Volume (Å ³)	2414.54(14)	2983.5(3)	4961.3(5)
Z	4	4	8
Color	colourless	colourless	colourless
Calculated density (g.cm ⁻³)	1.250	1.317	1.300
Absorption coefficient (mm ⁻¹)	0.076	2.209	0.083
F(000)	960	1240	2048
Crystal size (mm)	0.460 x 0.320 x 0.240	0.590 x 0.420 x 0.390	0.460 x 0.240 x 0.130
θ range for data collection (°)	3.024 to 27.473	6.807 to 77.388	3.009 to 27.482
Tmin	0.906	0.348	0.877
Tmax	0.982	0.423	0.989
limiting indices	-14≤h≤10 -18≤k≤18 -19≤l≤21	-15≤h≤15 -17≤k≤17 -20≤l≤22	-16≤h≤17 -16≤k≤11 -37≤l≤37
Data completeness	0.993	0.995	0.992
Reflections collected	16267	31829	37718
Reflections unique	9829 [R(int) = 0.0188]	6230 [R(int) = 0.0417]	17795 [R(int) = 0.0467]
Data / restraints / parameters	9829 / 1 / 639	6230 / 0 / 382	17795 / 637 / 1109
Goodness-of-fit	1.020	1.057	1.022
Final R indices [I>2 σ(I)]	R1 = 0.0383, wR2 = 0.0787	R1 = 0.0341, wR2 = 0.0824	R1 = 0.1056, wR2 = 0.2507
R indices (all data)	R1 = 0.0492, wR2 = 0.0841	R1 = 0.0376, wR2 = 0.0846	R1 = 0.1604, wR2 = 0.2904
Largest diff peak and hole (e Å ⁻³)	0.187 and -0.191	0.212 and -0.372	1.020 and -0.670