Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Direct and Highly Diastereoselective Synthesis of 3,4-Epoxy-2-Piperidones. Application to the Total Synthesis and Absolute Configurational Assignment of 3α,4α-Epoxy-5β-Pipermethystine

*Urbano Osorio-Nieto,[a] Laura Y. Vázquez-Amaya,[a] Herbert Höpfl,[b] Leticia Quintero,[a] and Fernando Sartillo-Piscil.[a]**

[a]Centro de Investigación de la Facultad de Ciencias Químicas, Benemérita Universidad Autónoma de Puebla (BUAP). 14 Sur Esq. San Claudio, Col. San Manuel. 72570, Puebla, México.

[b]Centro de Investigaciones Químicas, Instituto de Investigación en Ciencias Básicas y Aplicadas, Universidad Autónoma del Estado de Morelos. Avenida Universidad 1001, Col. Chamilpa. 62209, Cuernavaca, México.

Table of Contents

General considerations: Unless otherwise stated, ^{1}H NMR and ^{13}C NMR spectra were obtained in a 500 MHz spectrometer. All samples were analyzed in $CDCl_3$ with TMS as internal reference using a relative scale in parts per million (ppm) for the chemical shift.

Single-Crystal X-ray Diffraction Analysis.

Single crystals of compounds **13**, (1'*S*,3*R*,4*R*,5*S*)-**20** and (1'*S*,3*S*,4*S*,5*R*)-**20** were grown from solutions in CH_2Cl_2 and hexanes. Single-crystal X-ray diffraction studies were carried out on an Agilent Technologies SuperNova diffractometer equipped with a CCD area detector **(**EosS2) using Cu-Kα radiation (λ = 1.54184 Å). Frames were collected at T = 293 K for **13** and T = 100 K for the remaining compounds. The measured intensities were reduced to F^2 and corrected for absorption using spherical harmonics (CrysAlisPro).[1] Intensities were corrected for Lorentz and polarization effects. Structure solution, refinement, and data output were performed with the OLEX2[2] program package using SHELXT-2014[3] for the structure solution and SHELXL-2008[4] for the refinement. Non-hydrogen atoms were refined anisotropically. All hydrogen atoms were placed in geometrically calculated positions using the riding model. Figures were created with Diamond.[5]

Crystallographic data for the crystal structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications no. 1576887−1576889. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk, http://www.ccdc.cam.ac.uk).

References

(1) Agilent Technologies. *CrysAlisPro*, Version 1.171.37.35. Yarnton, Oxfordshire, United Kindom: 2014.

(2) Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J; Howard, J. A. K.; Puschmann, H. *J. Appl. Cryst.* **2009**, *42*, 339-341.

(3) Sheldrick, G. M. *Acta Cryst.* **2015**, *C71*, 3-8.

(4) Sheldrick, G. M. *Acta Cryst.* **2008**, *A64*, 112-122.

(5) Brandenburg, K. *Diamond*, Crystal Impact GbR, Bonn, Germany, **1997**

Table 1. Selected crystallographic data for compounds **13**, (1'*S*,3*R*,4*R*,5*S*)-**20** and (1'*S*,3*S*,4*S*,5*R*)-**20**.

Crystal data[a]	**13**	(1'*S*,3*R*,4*R*,5*S*)-**20**	(1'*S*,3*S*,4*S*,5*R*)-**20**
Formula	$C_{17}H_{19}NO_5$	$C_{14}H_{17}NO_4$	$C_{14}H_{17}NO_4$
MW (g mol^{-1})	317.33	263.28	263.28
Space group	$P2_1$	$P2_12_12_1$	$P2_12_12_1$
Temp. (K)	292	100	100
a (Å)	9.66134(17)	6.32903(9)	6.38939(11)
b (Å)	5.45597(10)	8.54815(13)	7.59037(13)
c (Å)	14.8724(2)	23.7167(4)	26.8562(5)
α (°)	90.0	90.0	90.0
β (°)	93.7727(16)	90.0	90.0
γ (°)	90.0	90.0	90.0
V (Å^3)	1797.12(8)	1283.11(3)	1302.47(4)
Z	2	4	4
μ (mm^{-1})	0.827	0.829	0.817
ρ_{calcd} (g cm^{-3})	1.347	1.363	1.343
R[b, c]	0.0332	0.0297	0.0304
R_w[d, e]	0.0904	0.0743	0.0785
GOF	1.049	1.025	1.070
CCDC	1576888	1576887	1576889

[a] $\lambda_{MoK\alpha}$ = 0.71073 Å. [b] $F_o > 4\sigma(F_o)$. [c] $R = \Sigma||F_o|-|F_c||/\Sigma|F_o|$. [d] all data.

[e] $R_w = [\Sigma w(F_o^2-F_c^2)^2/\Sigma w(F_o^2)^2]^{½}$.

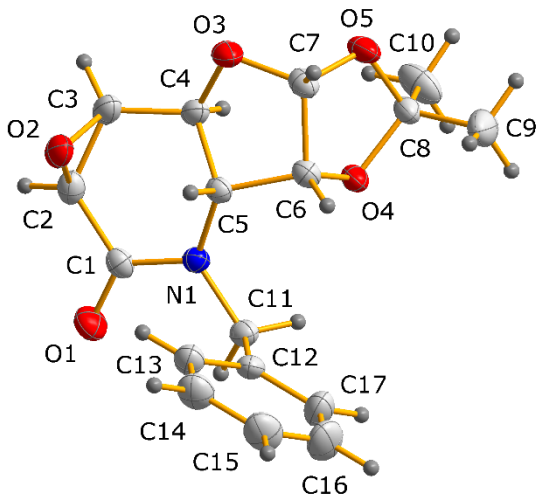


Figure S1. Perspective view of the molecular structure of compound **13**. Ellipsoids are drawn at the 30% probability level.

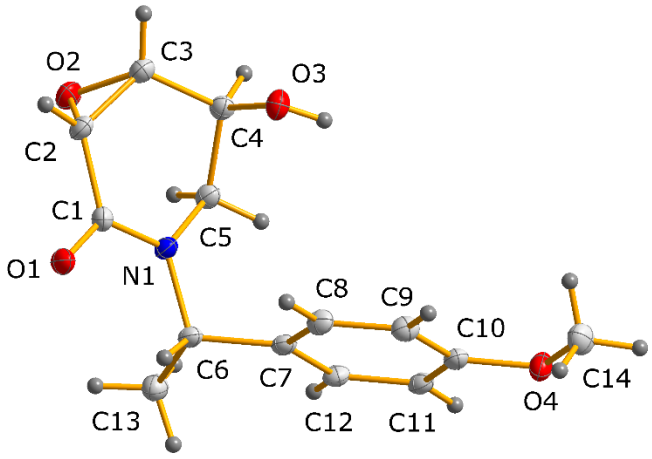


Figure S2. Perspective view of the molecular structure of compound (1'*S*,3*R*,4*R*,5*S*)-**20**. Ellipsoids are drawn at the 50% probability level.

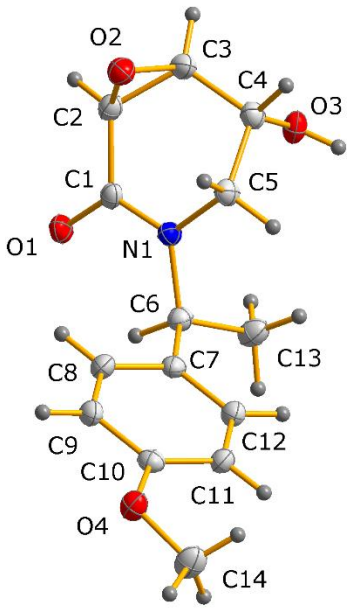
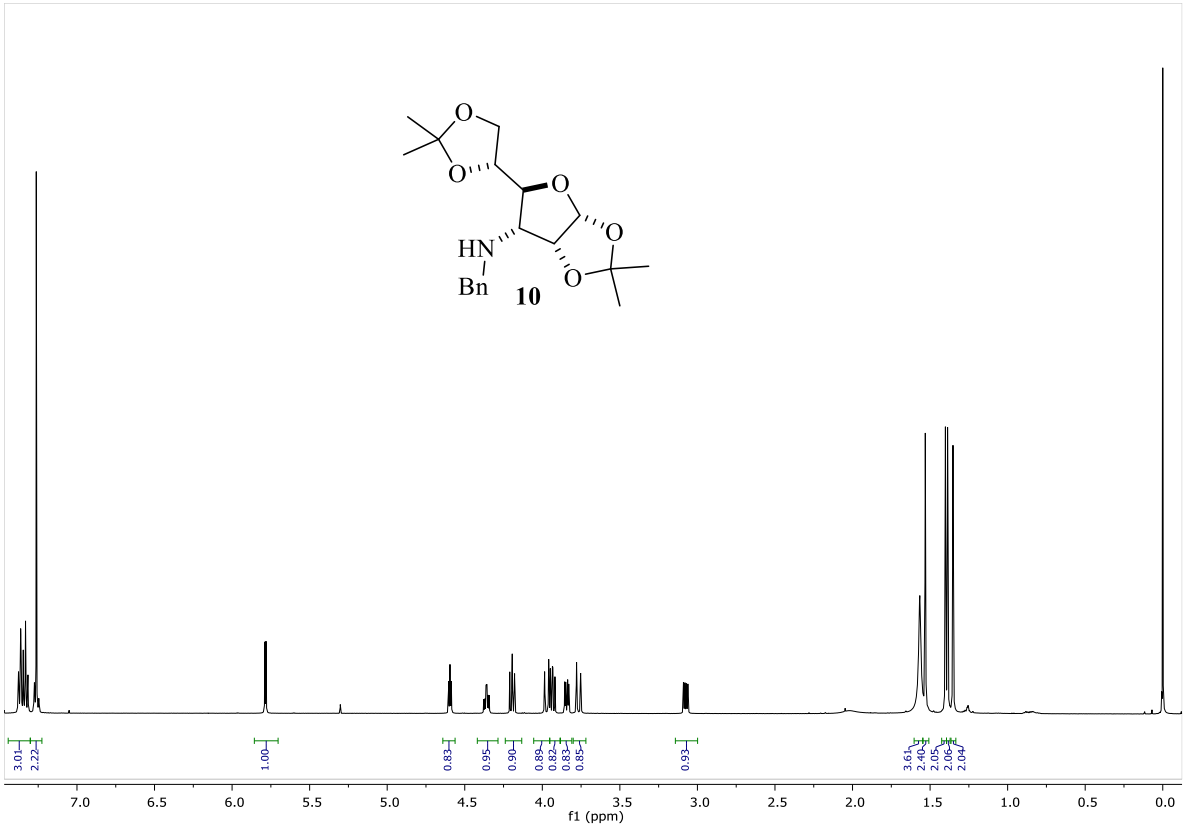
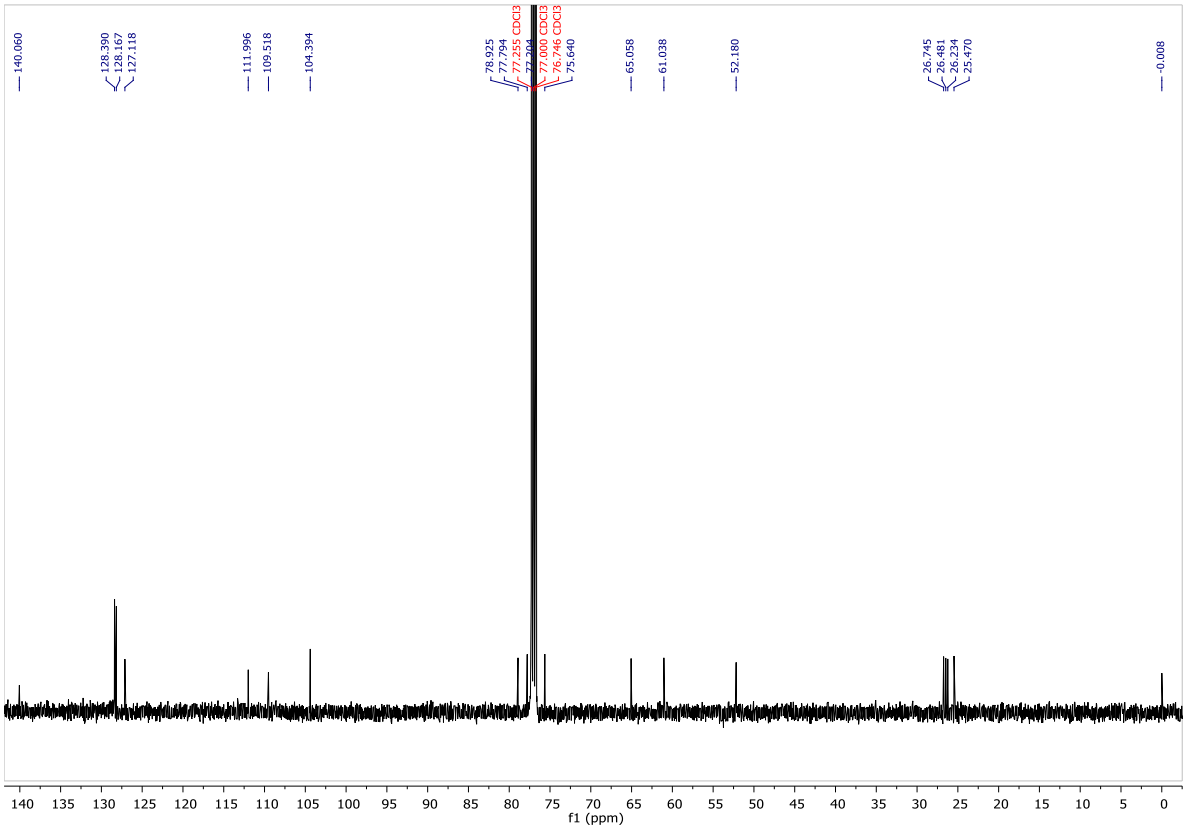


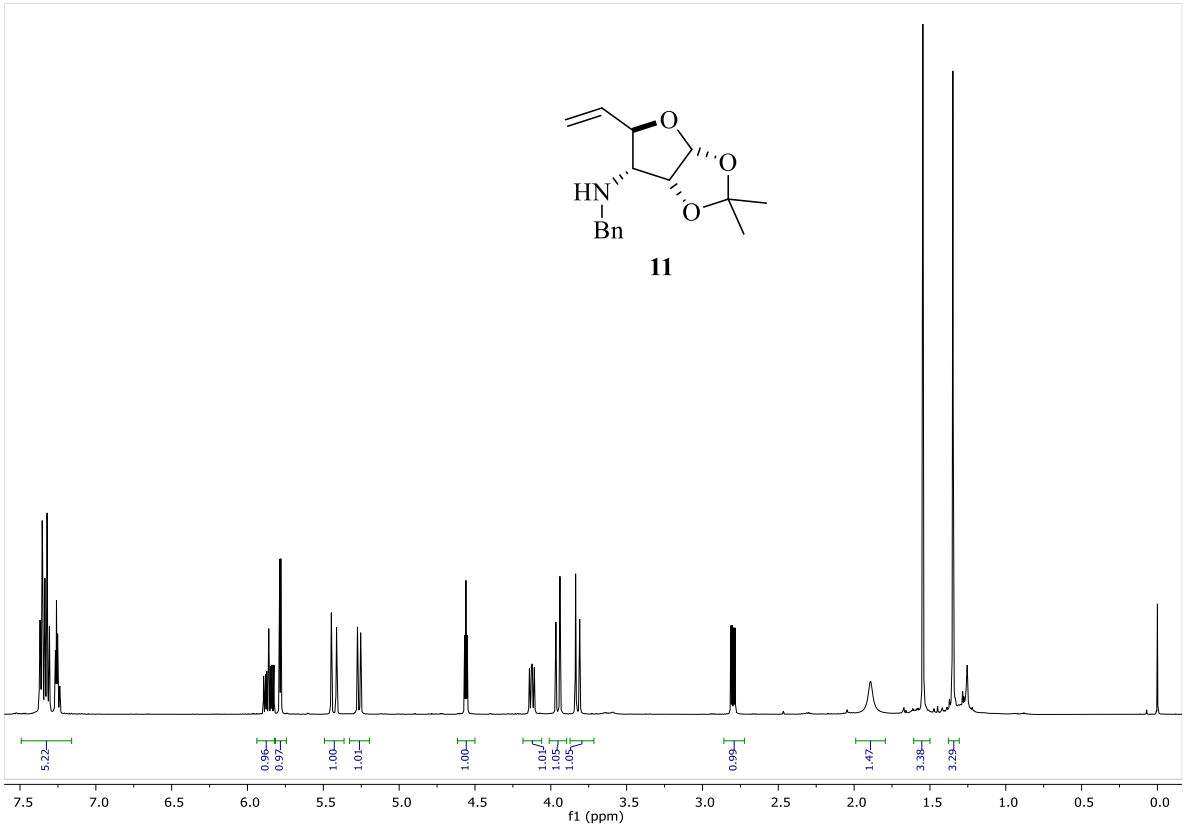
Figure S3. Perspective view of the molecular structure of compound (1'*S*,3*S*,4*S*,5*R*)-**20**. Ellipsoids are drawn at the 50% probability level.

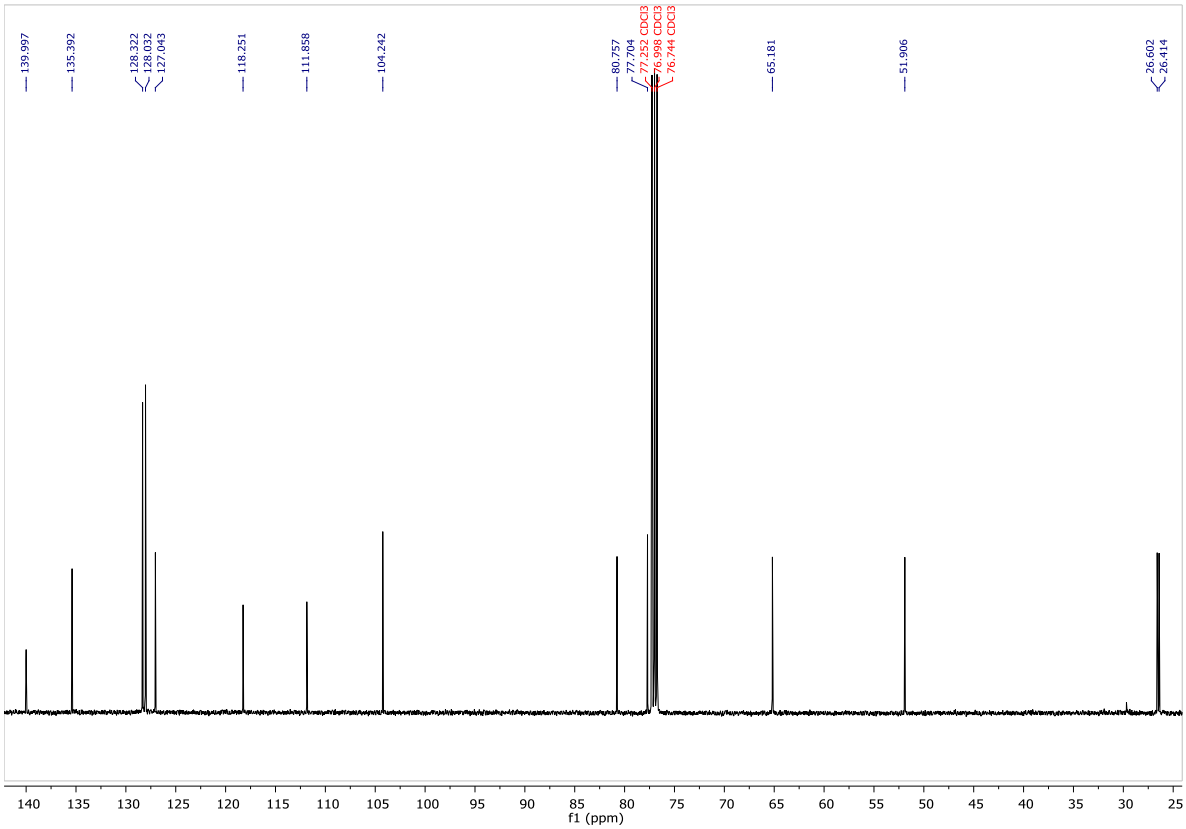
^{1}H and ^{13}C NMR spectra of compound **10**



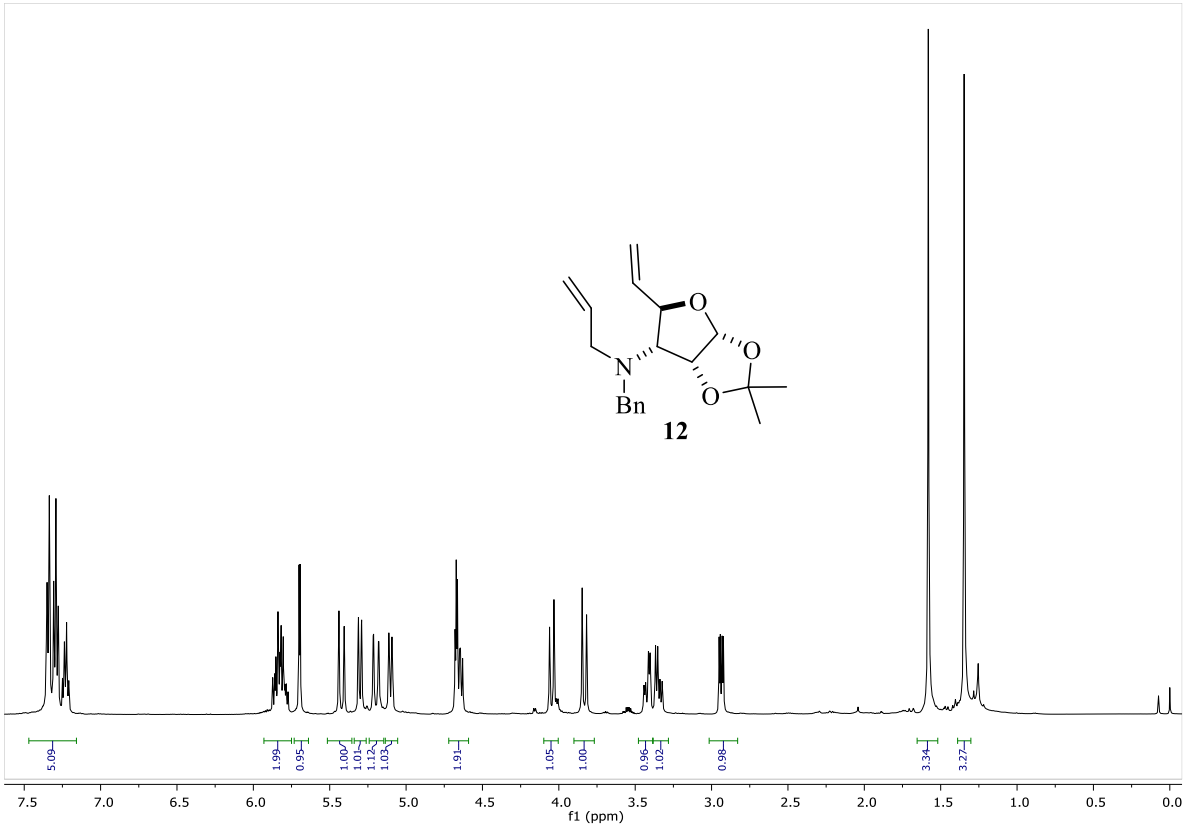


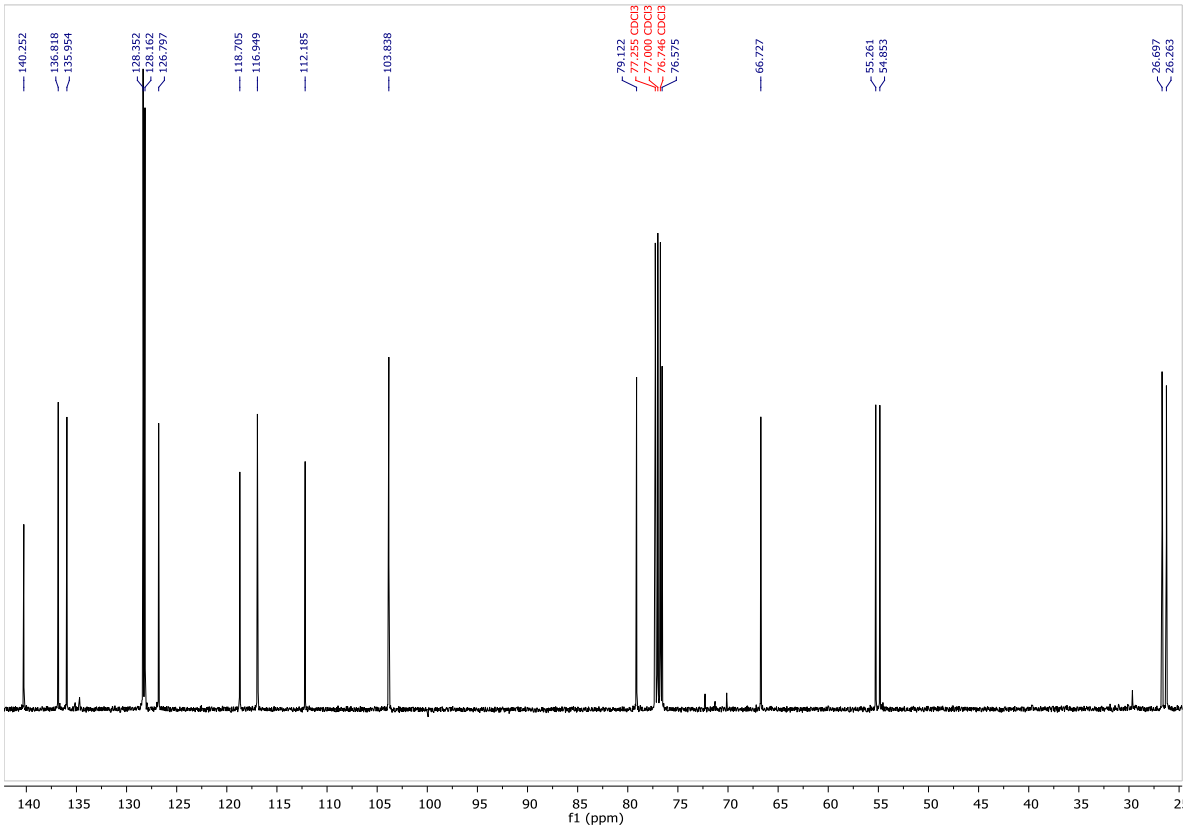
^{1}H and ^{13}C NMR spectra of compound **11**



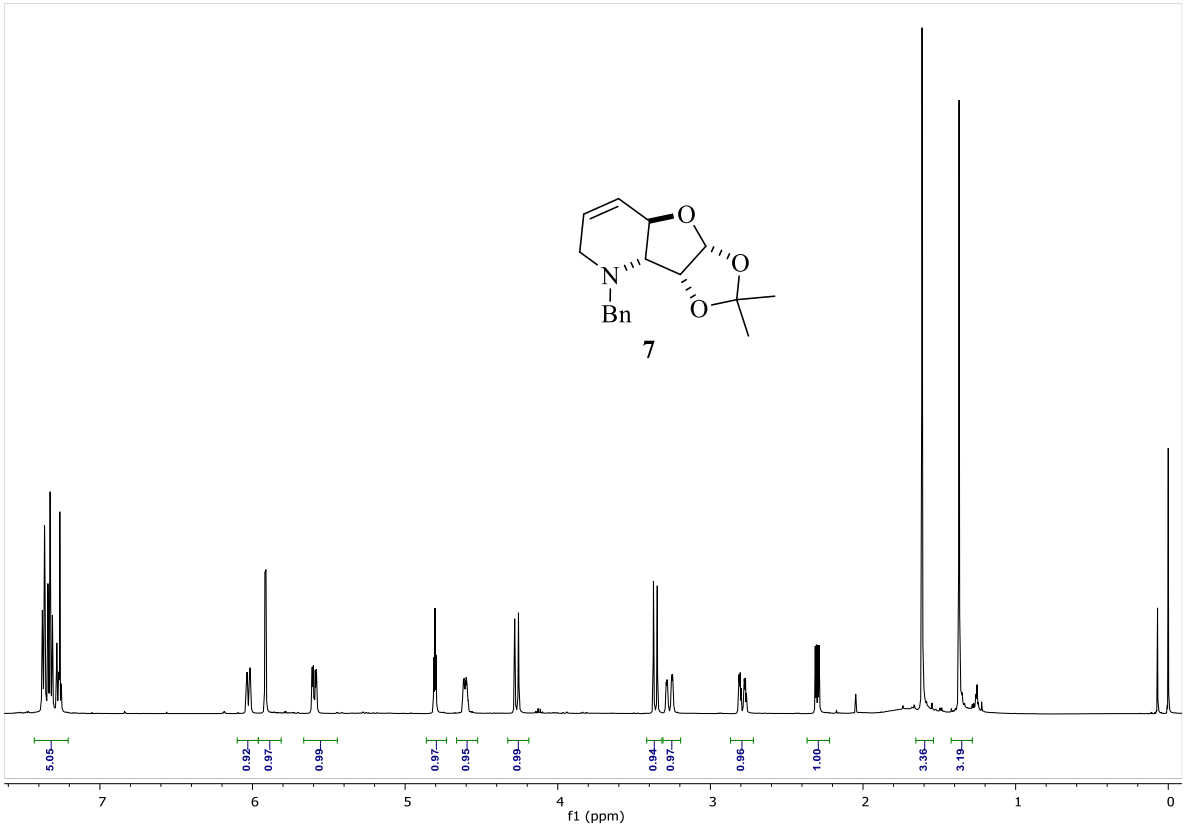


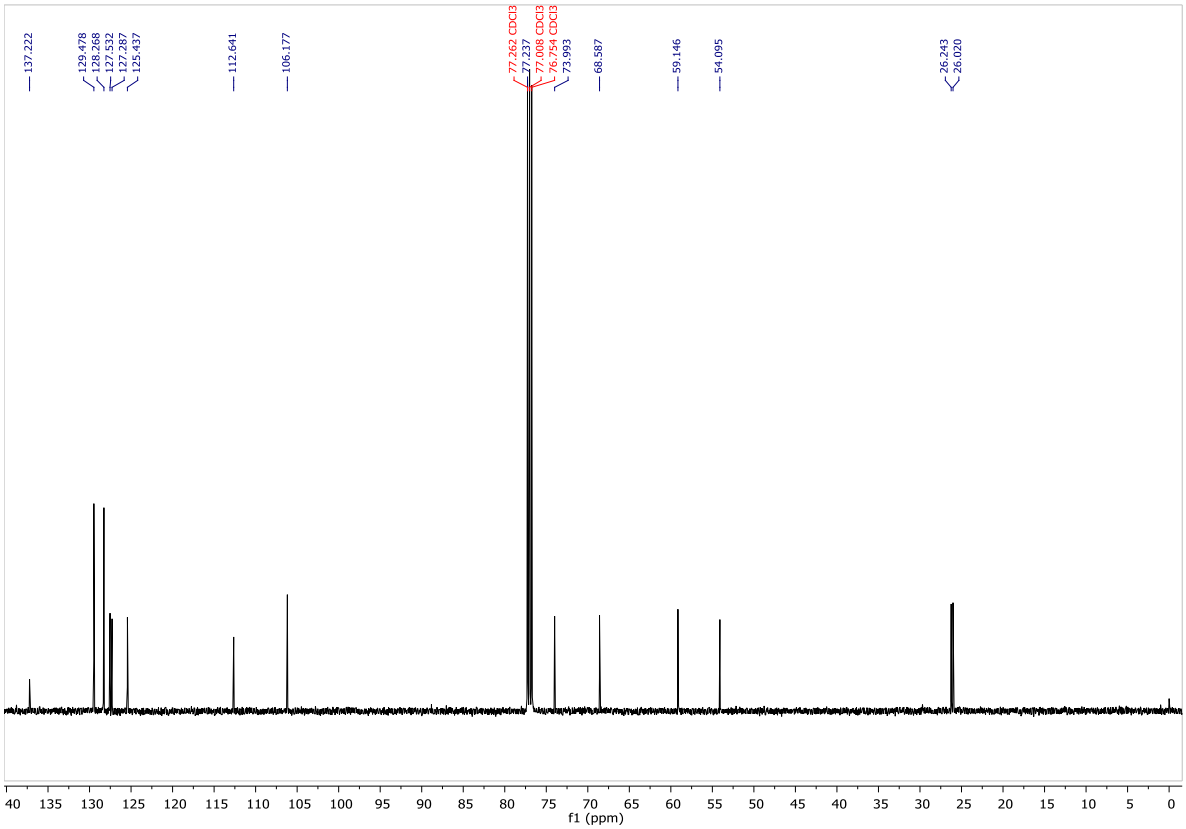
^{1}H and ^{13}C NMR spectra of compound **12**



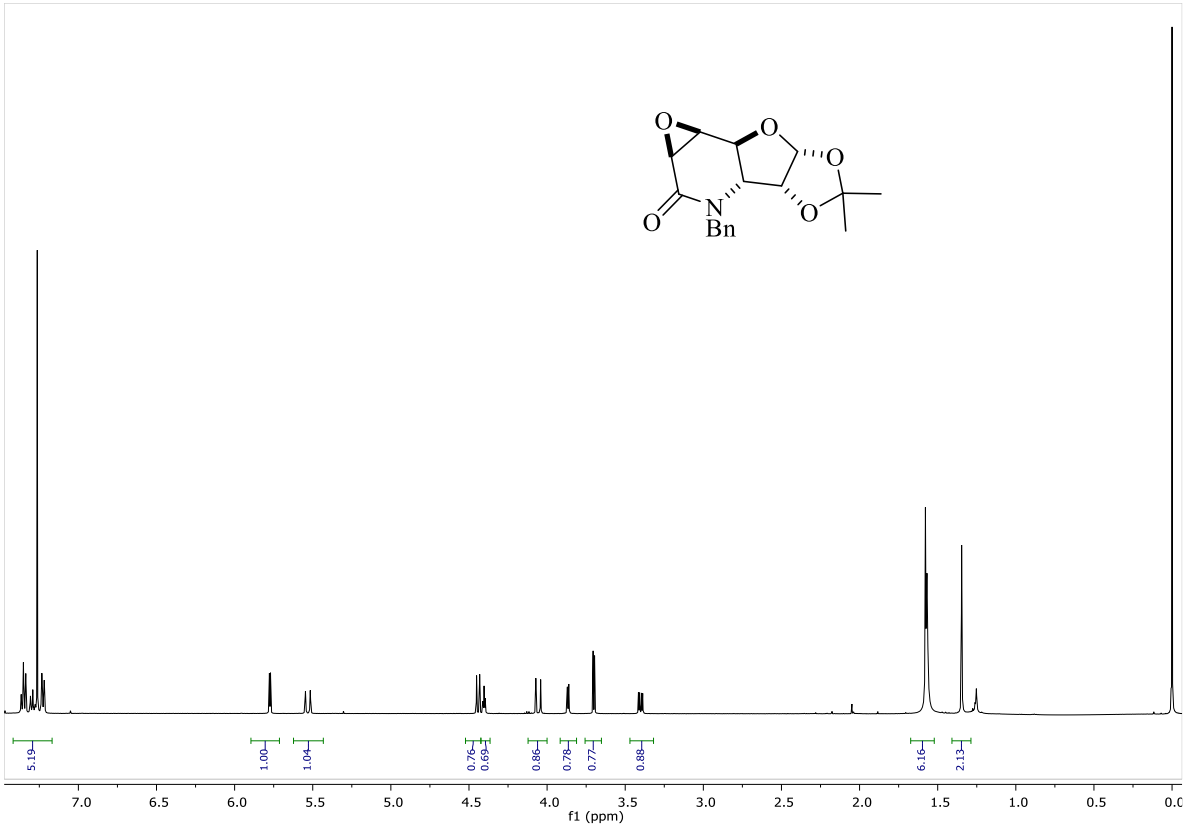


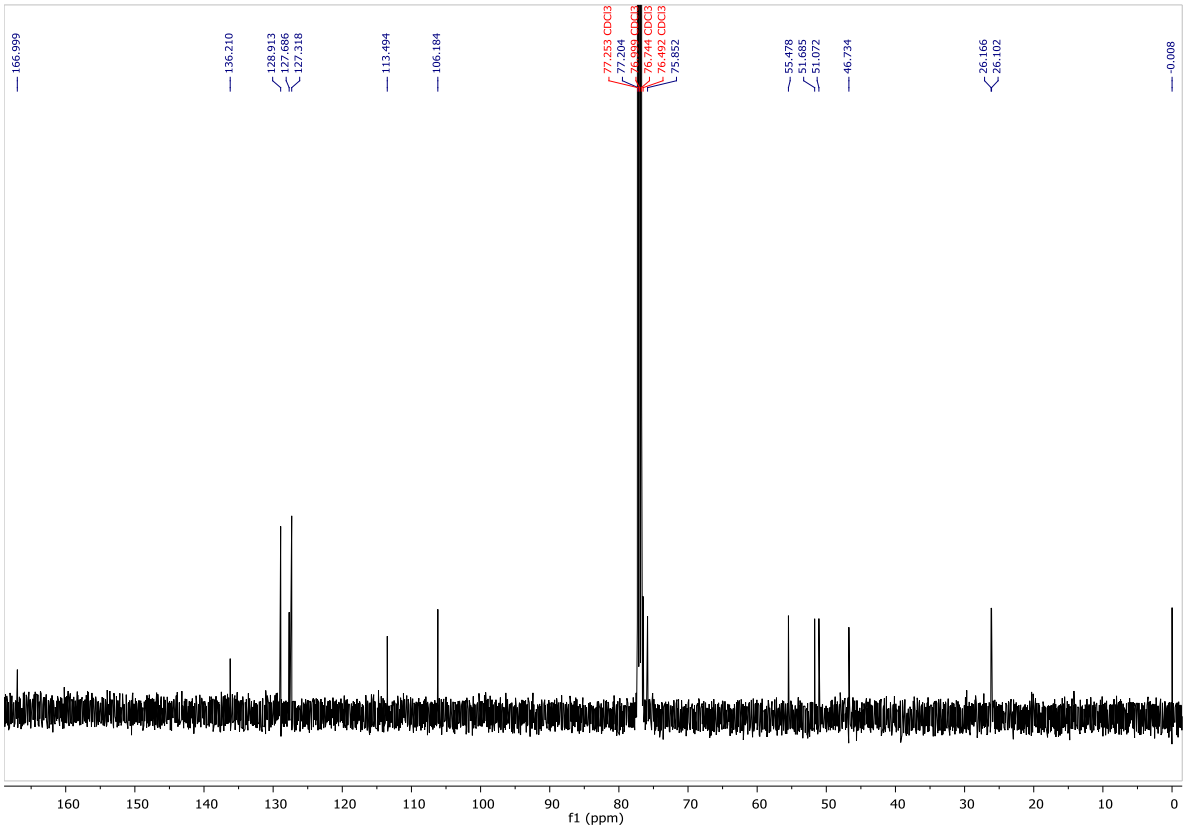
^{1}H and ^{13}C NMR spectra of compound **7**





^{1}H and ^{13}C NMR spectra of compound **13**





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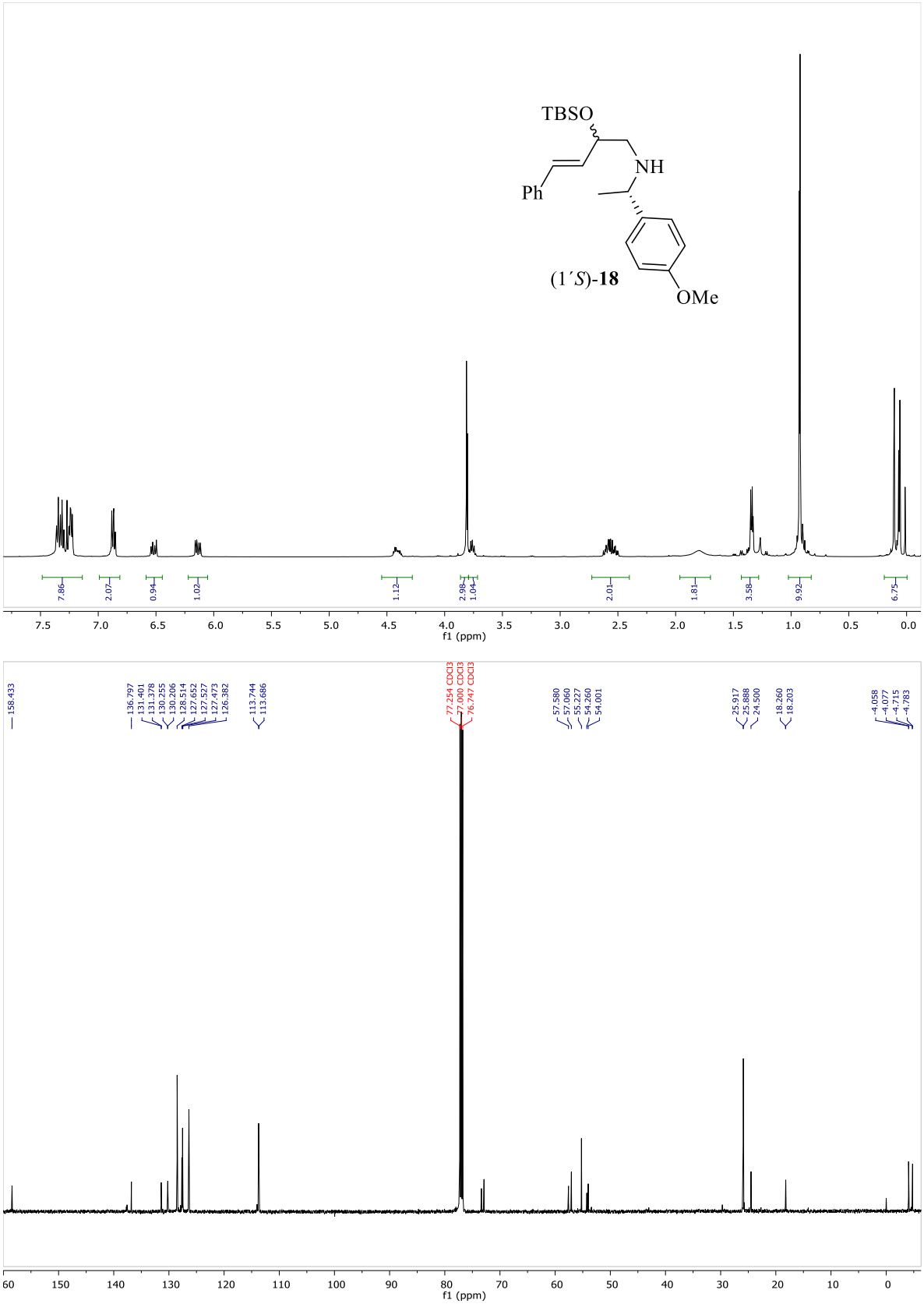
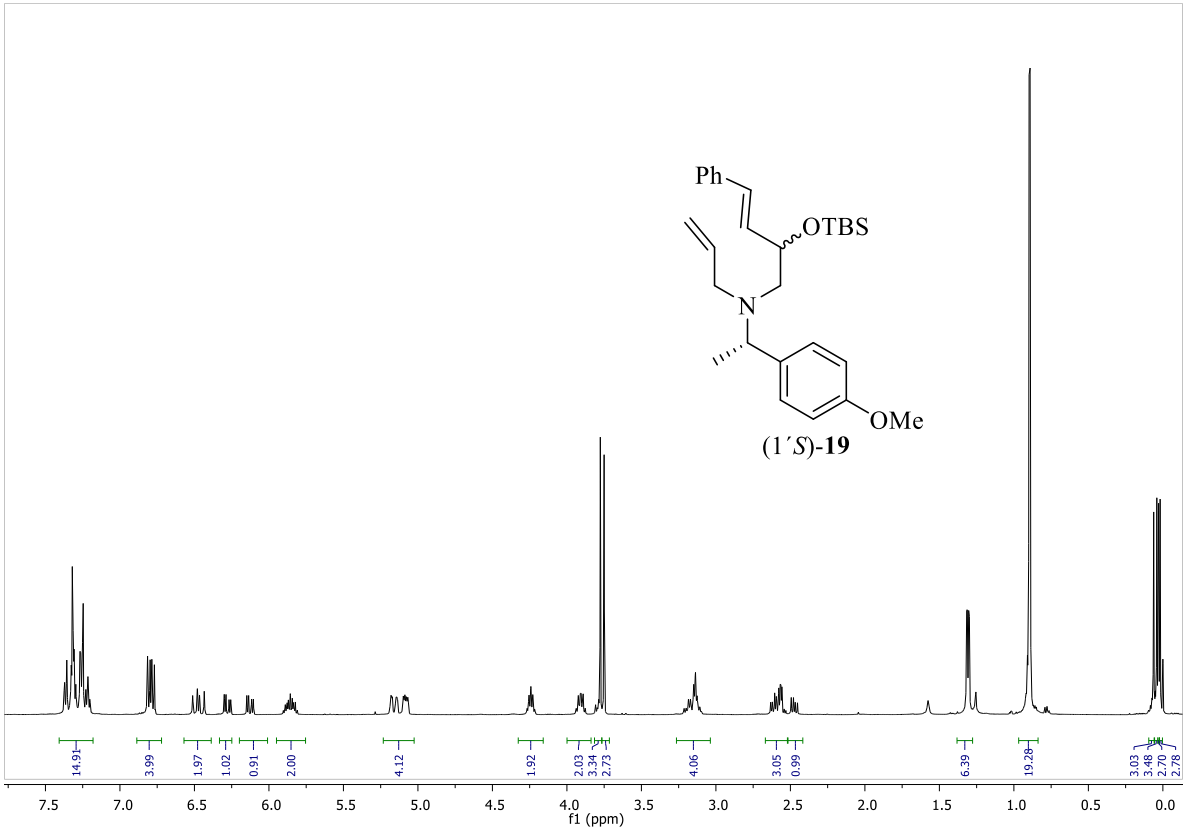
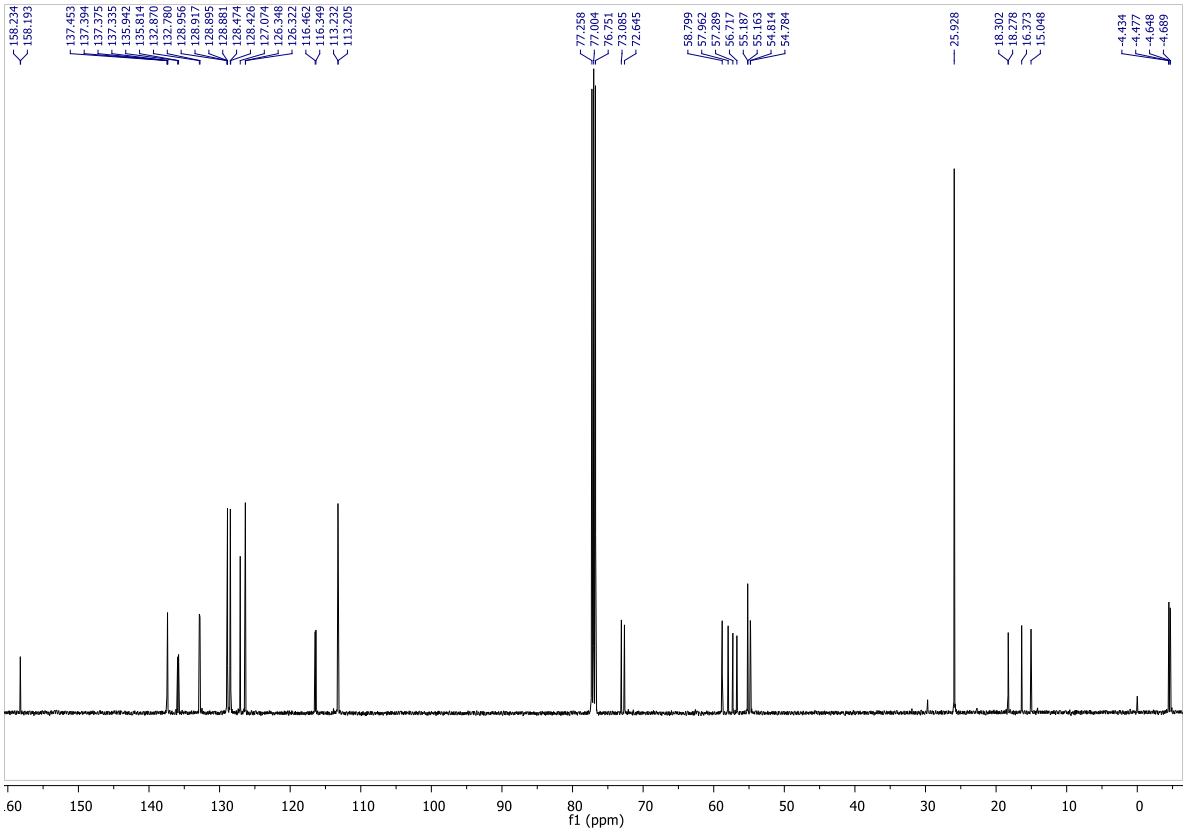
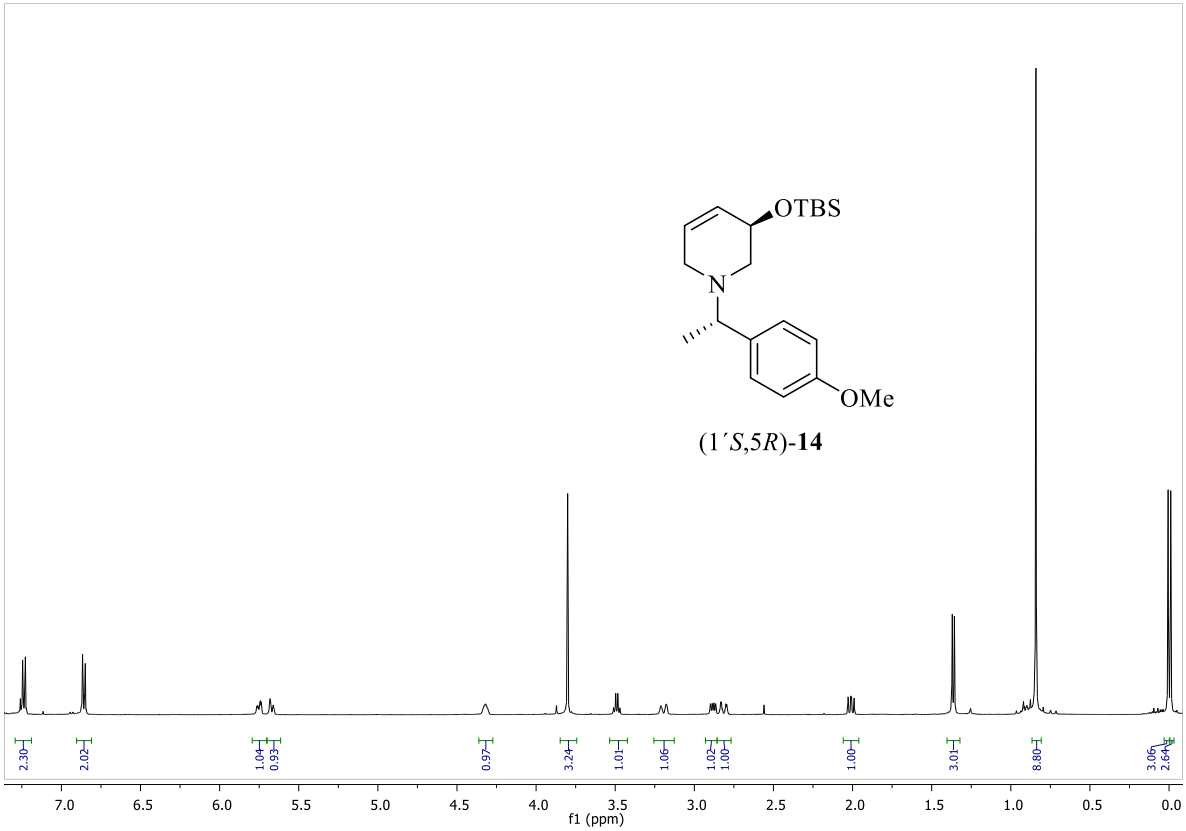


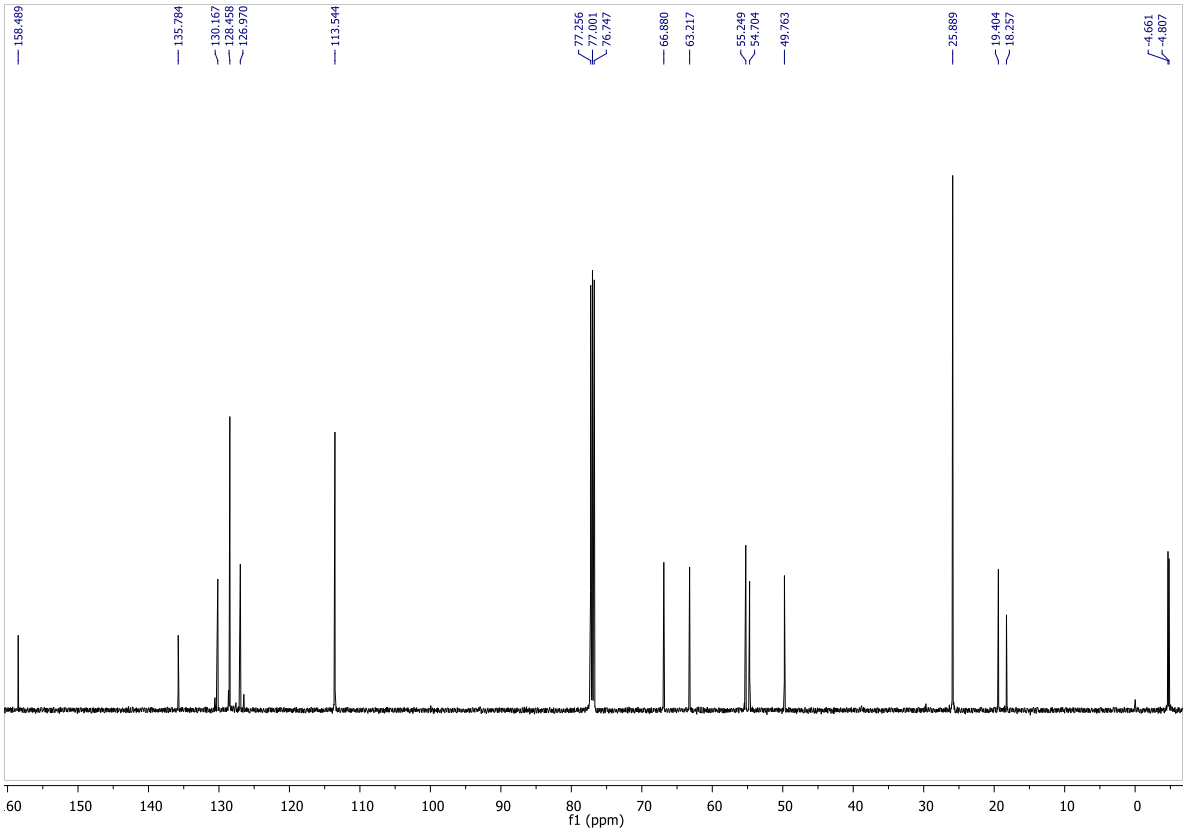
^{1}H and ^{13}C NMR spectra of compound (1´*S*)-**19**





^{1}H and ^{13}C NMR spectra of compound (1'*S*,5*R*)-**14**





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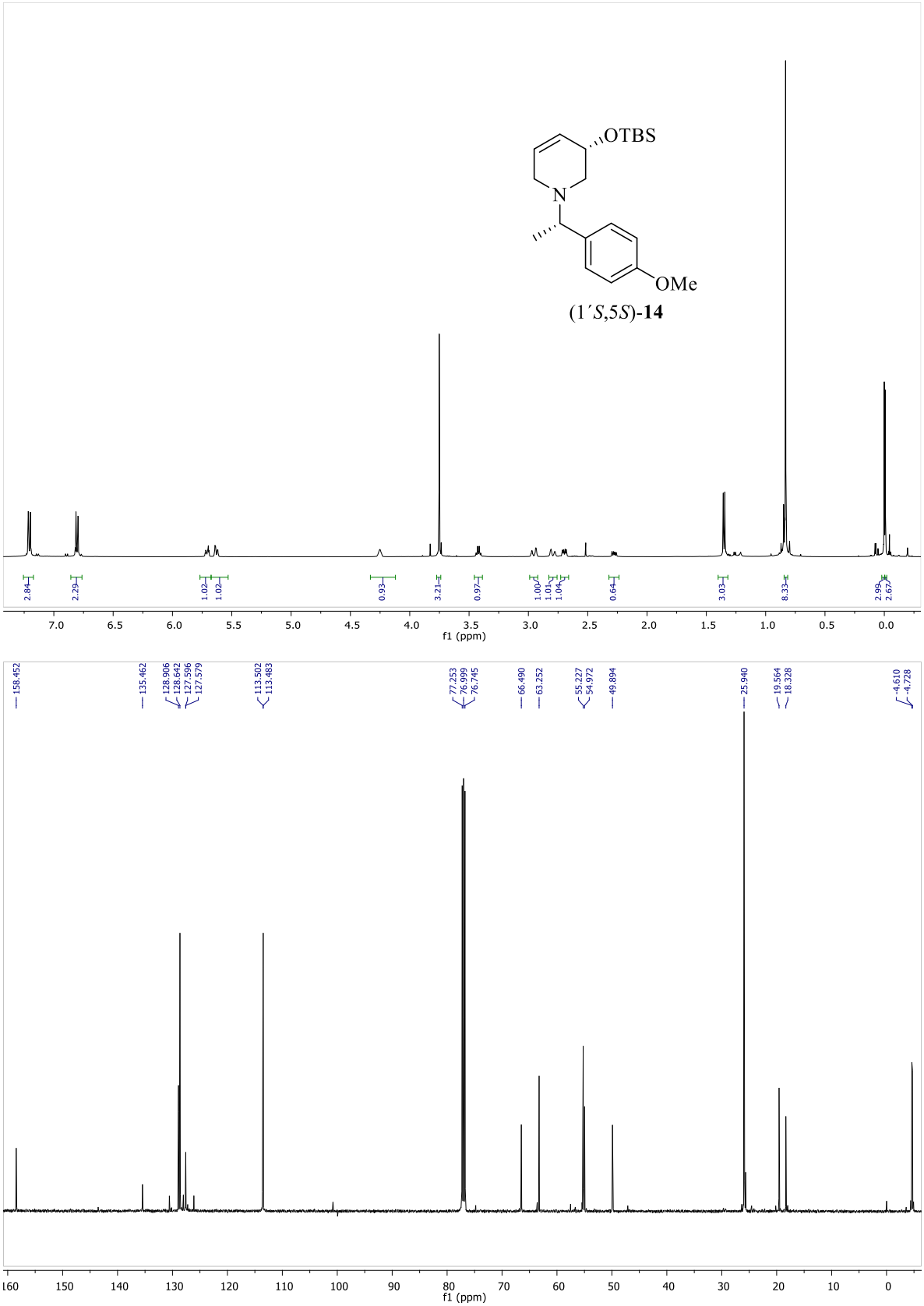
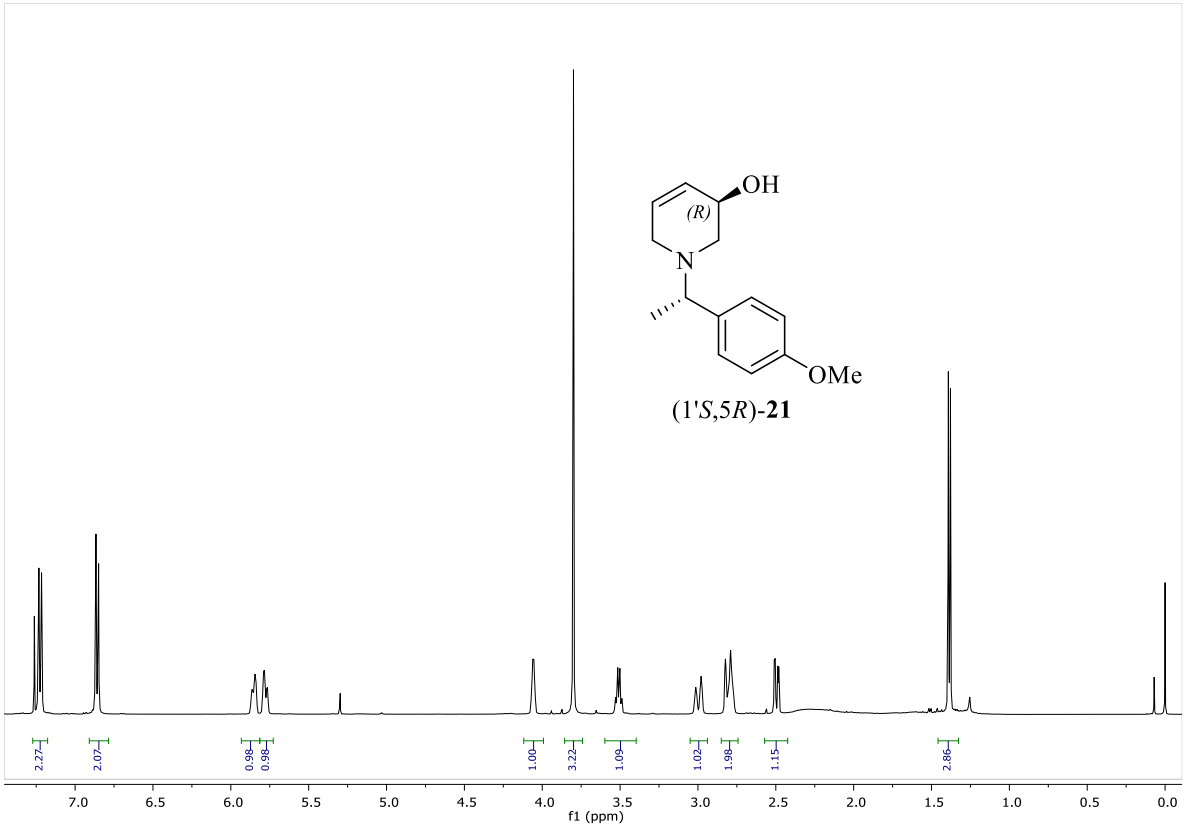
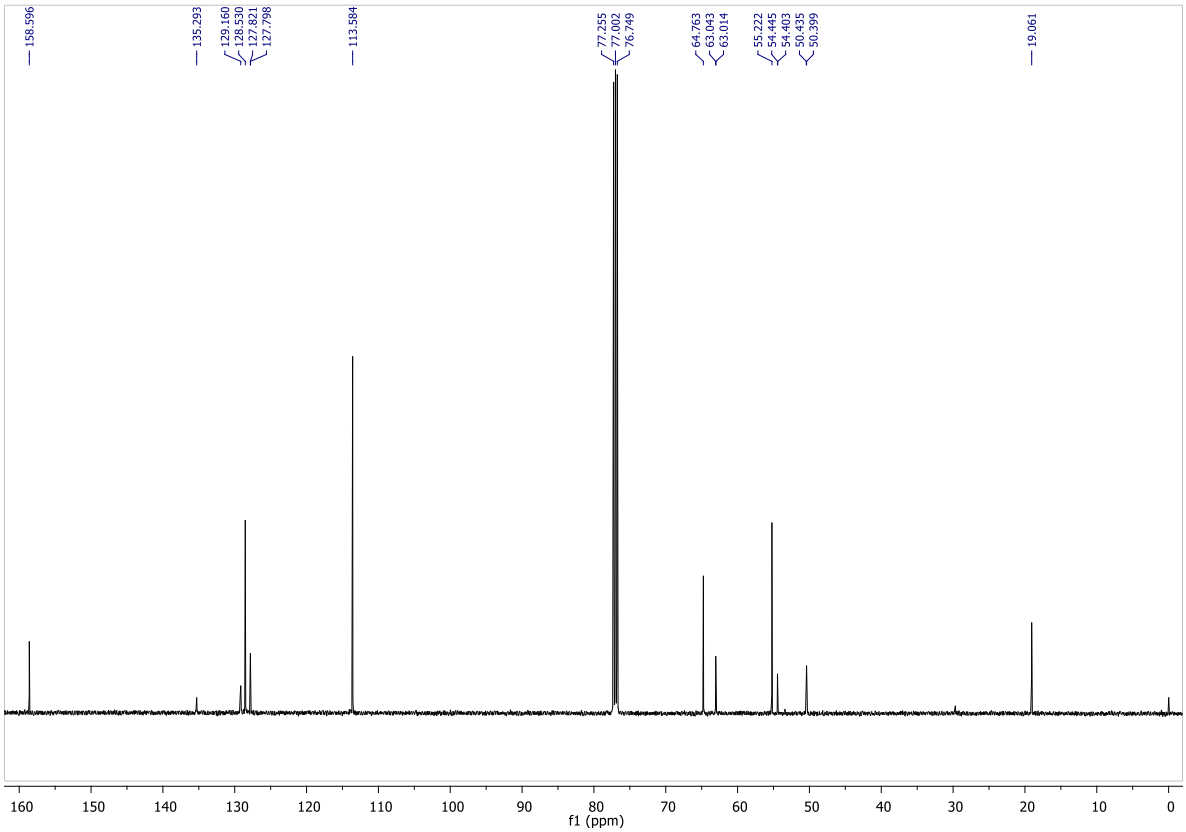
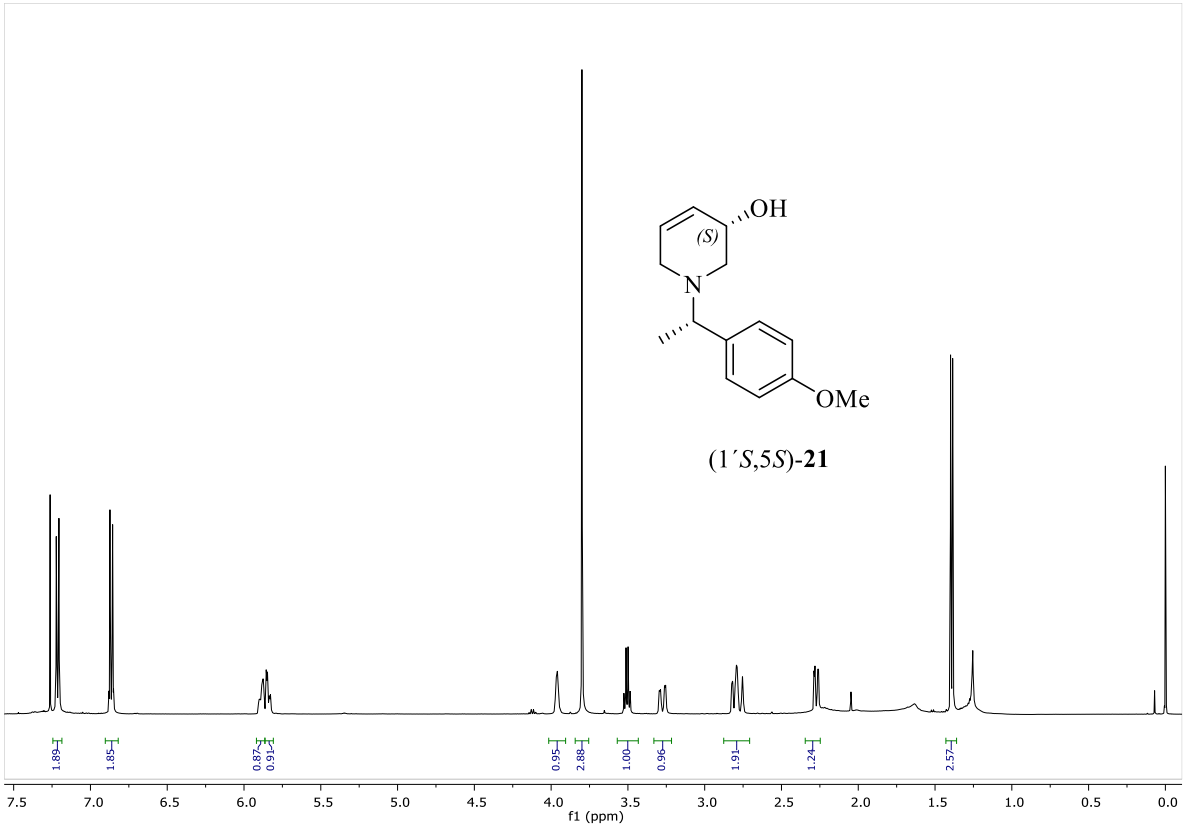


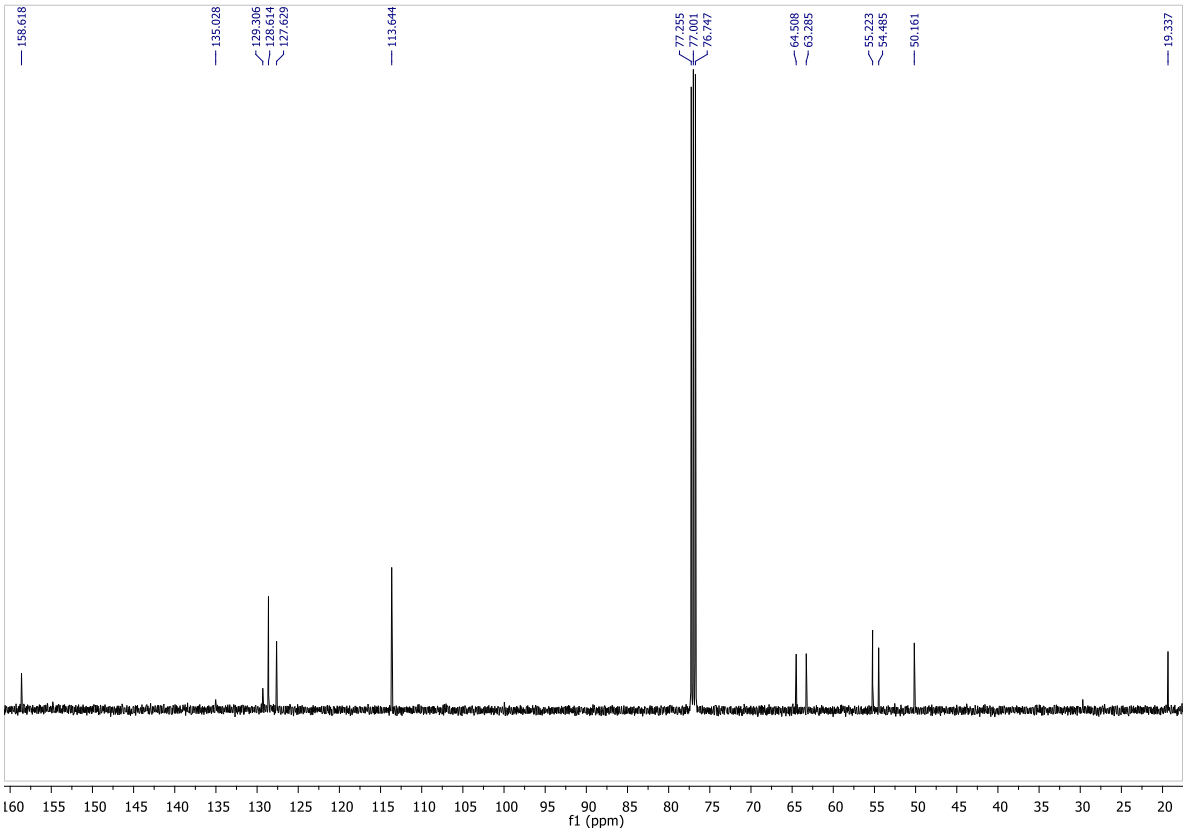
^{1}H and ^{13}C NMR spectra of compound (1'*S*,5*R*)-**21**



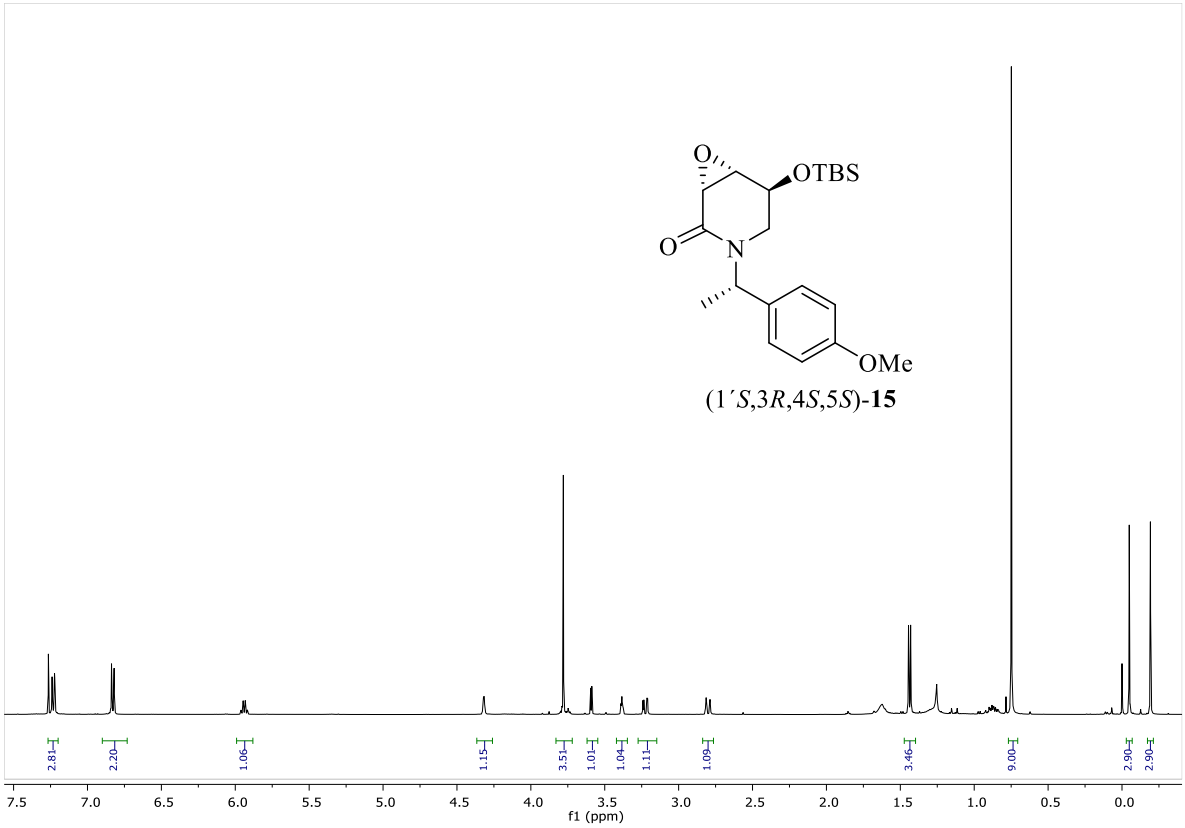


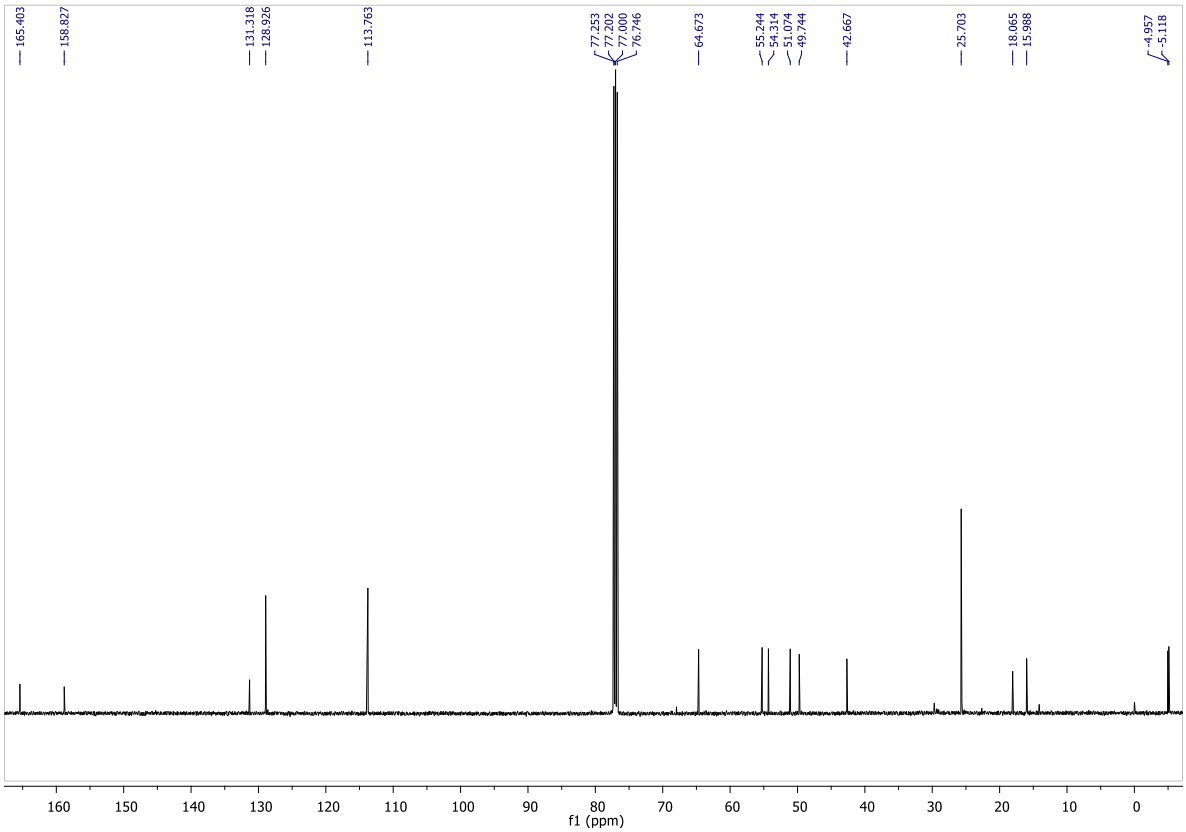
^{1}H and ^{13}C NMR spectra of compound (1'*S*,5*S*)-**21**



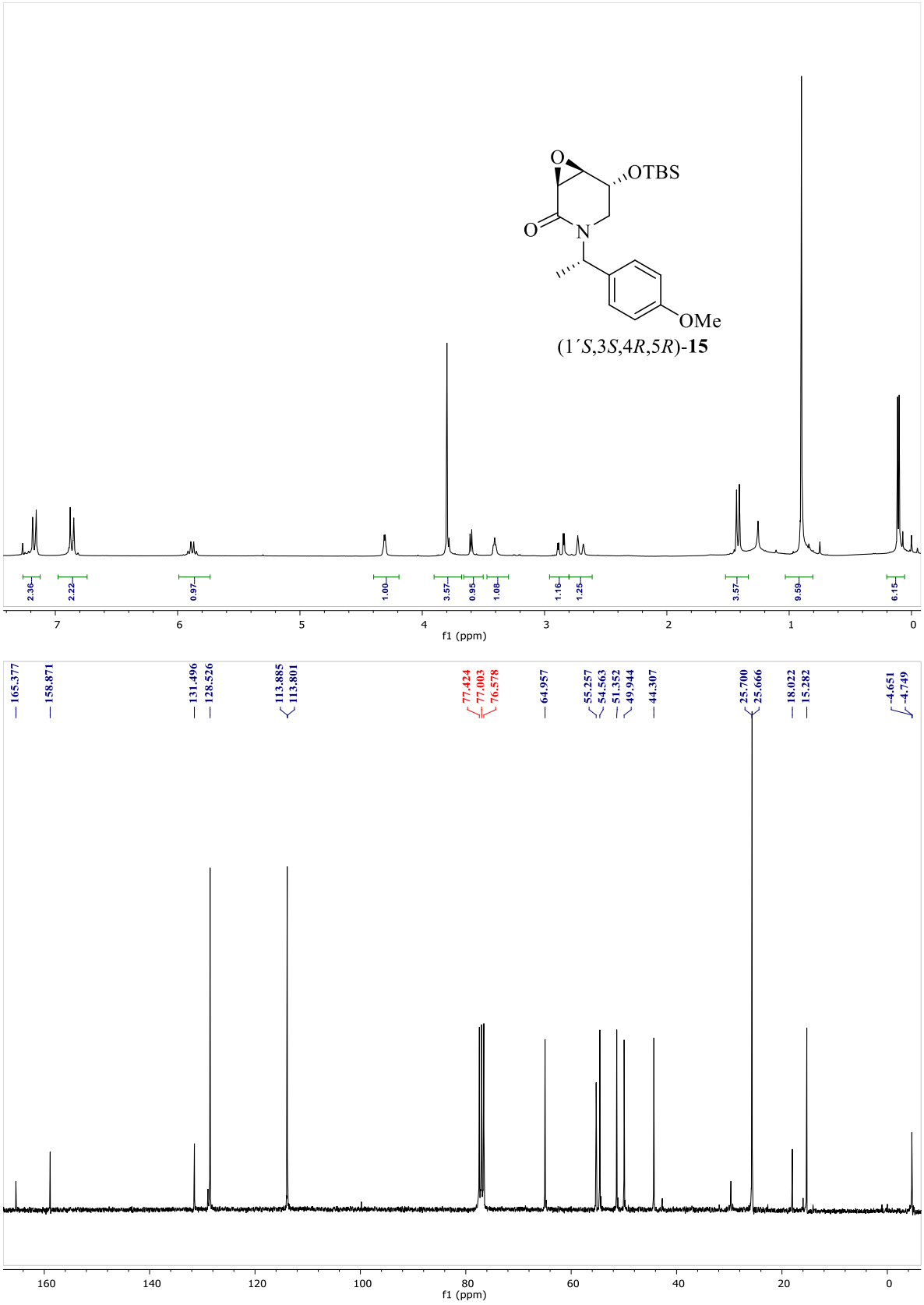


^{1}H and ^{13}C NMR spectra of compound (1'*S*,3*R*,4*S*,5*S*)-**15**

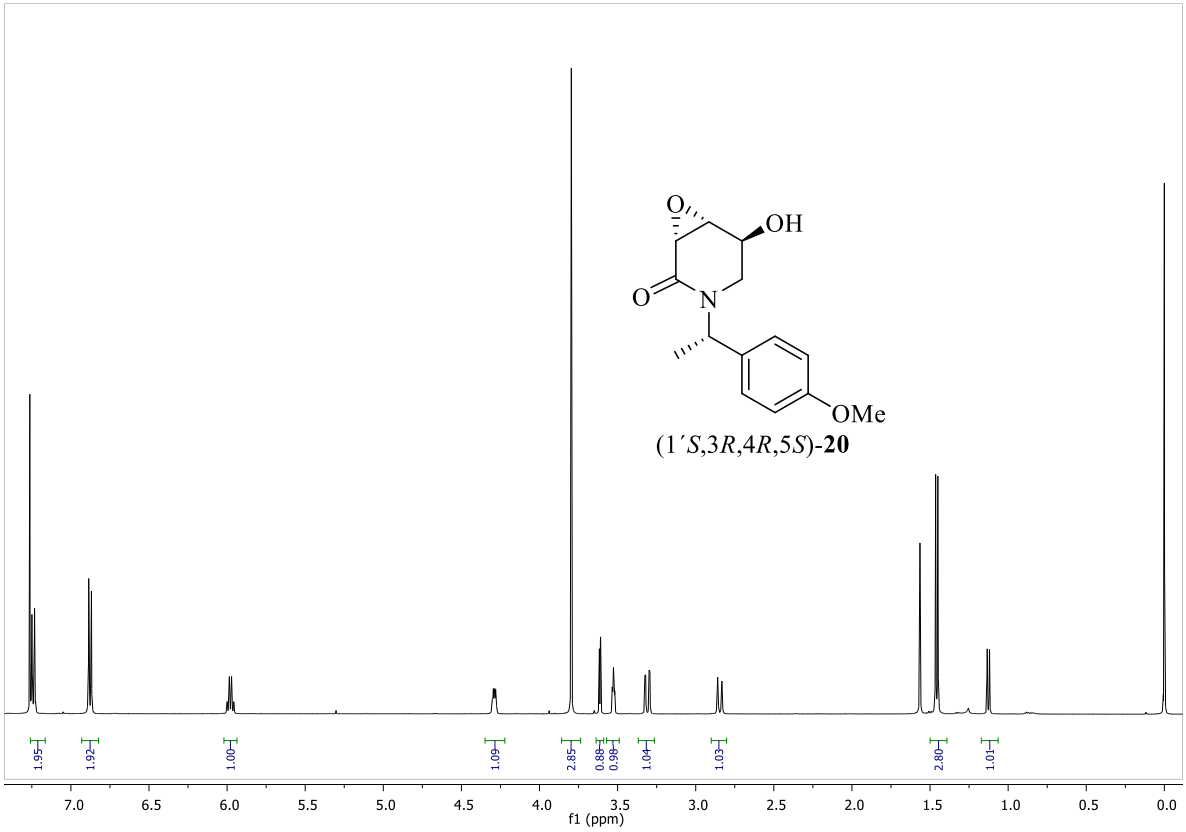


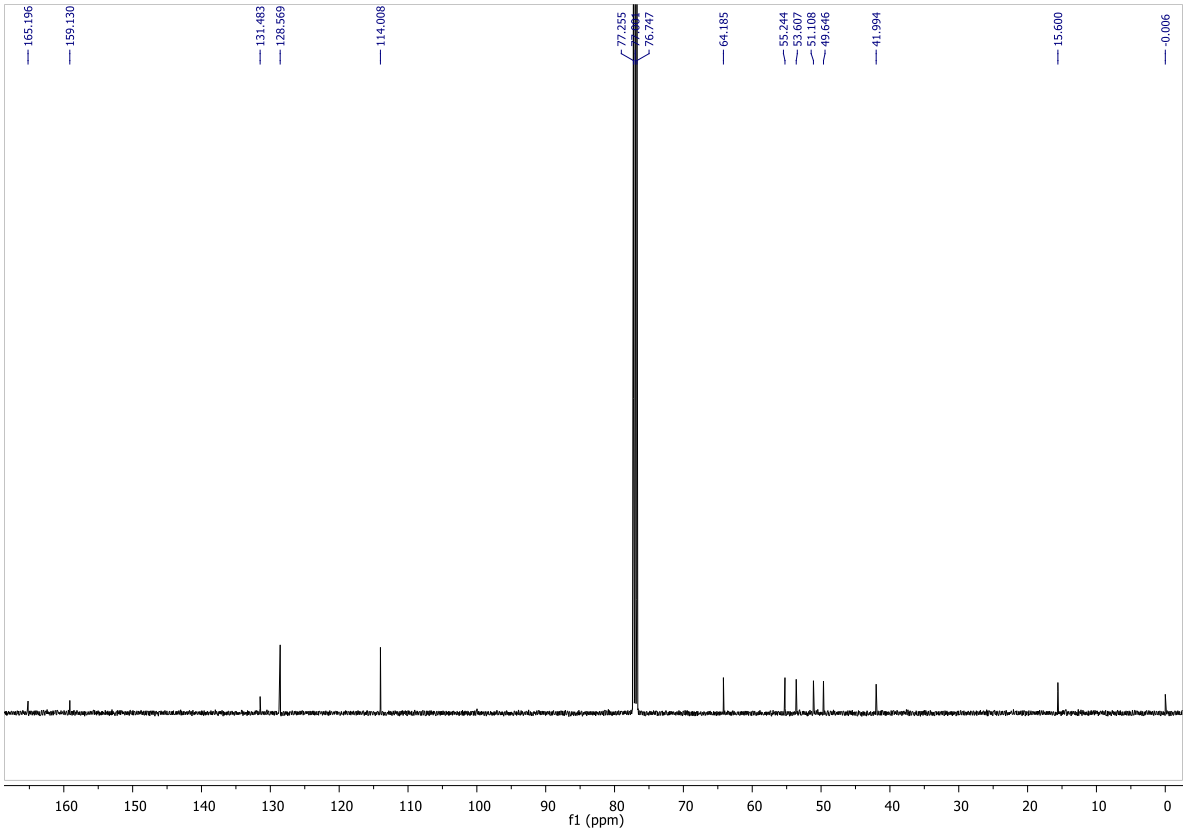


^{1}H and ^{13}C NMR spectra of compound (1'*S*,3*S*,4*R*,5*R*)-**15**



^{1}H and ^{13}C NMR spectra of compound (1'*S*,3*R*,4*R*,5*S*)-**20**





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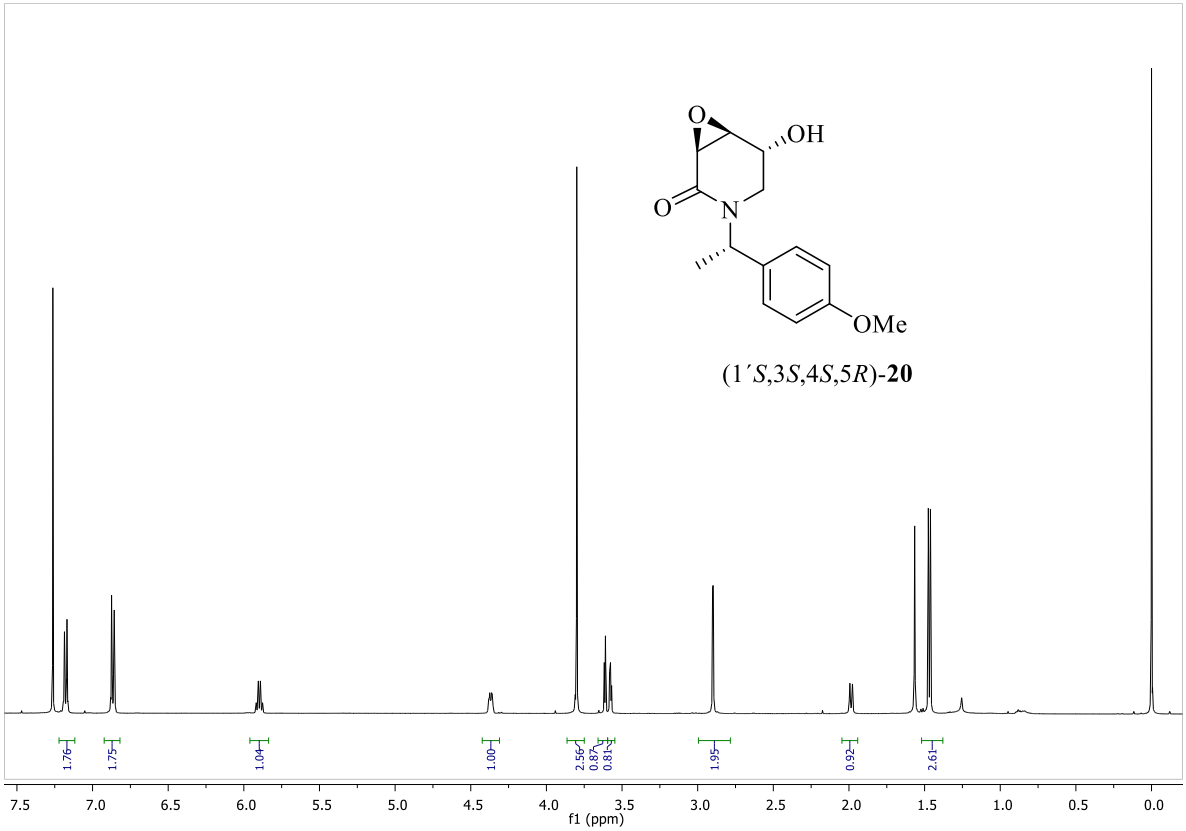

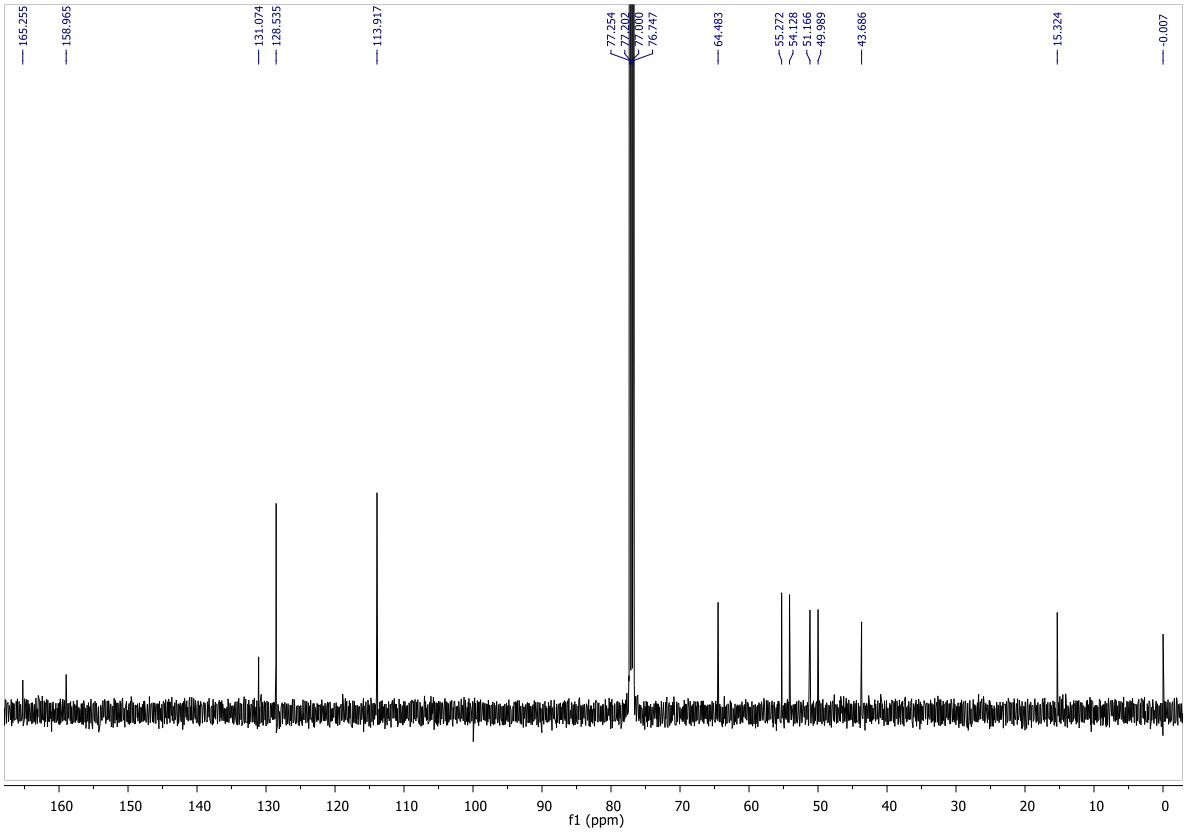

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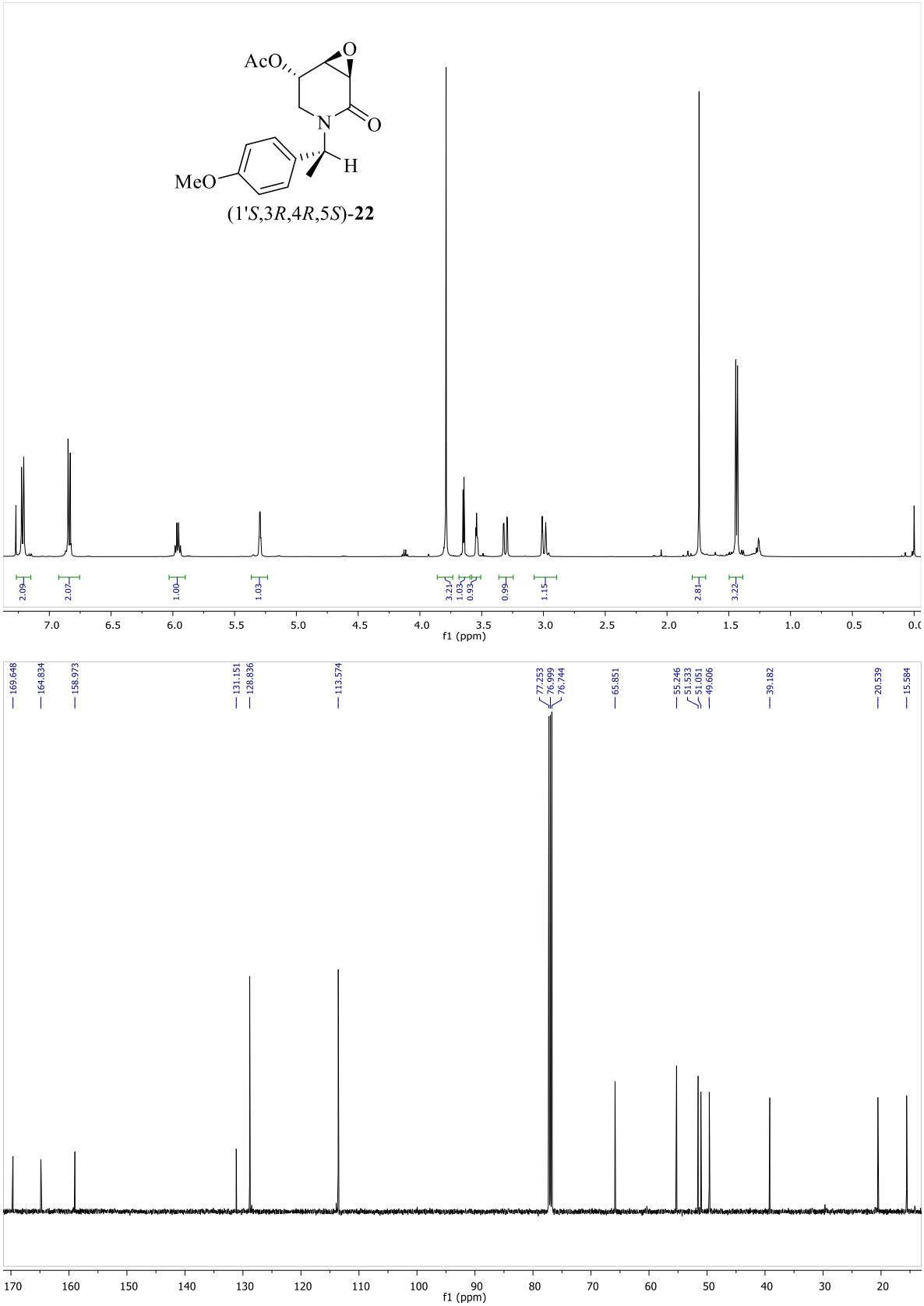

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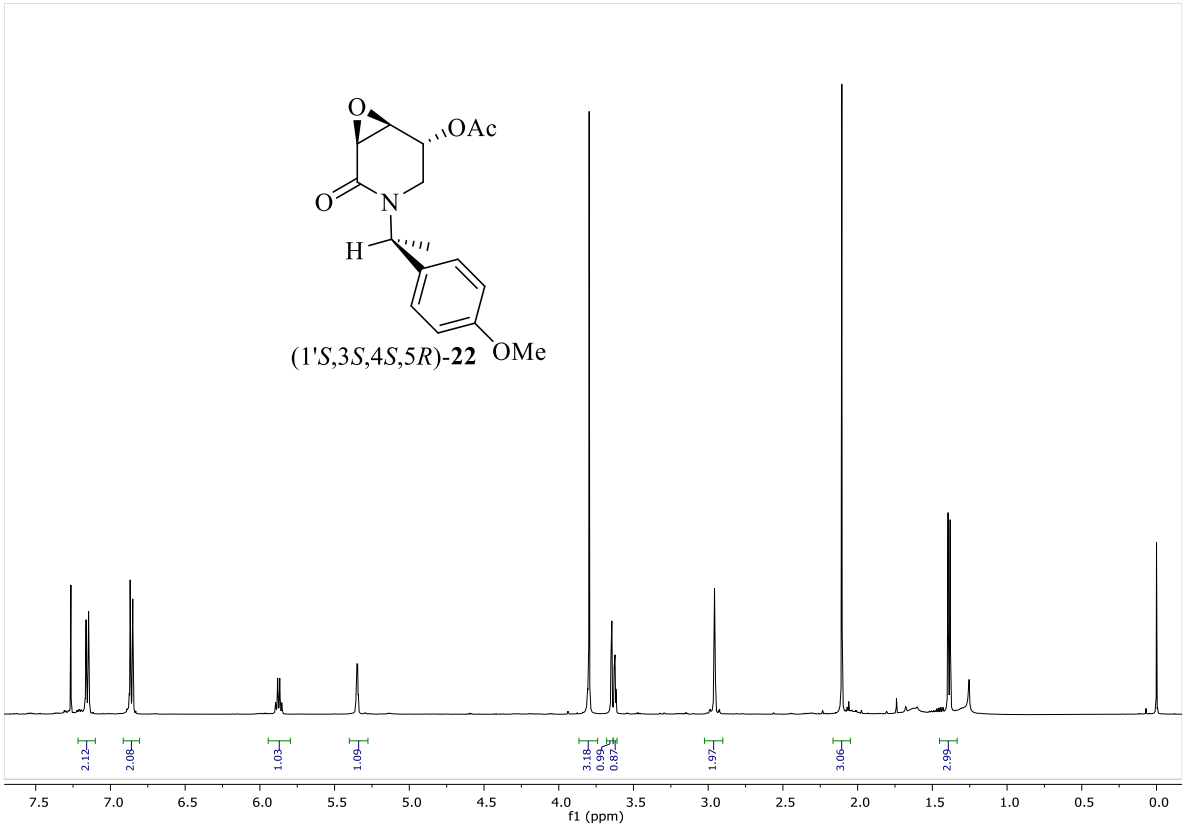

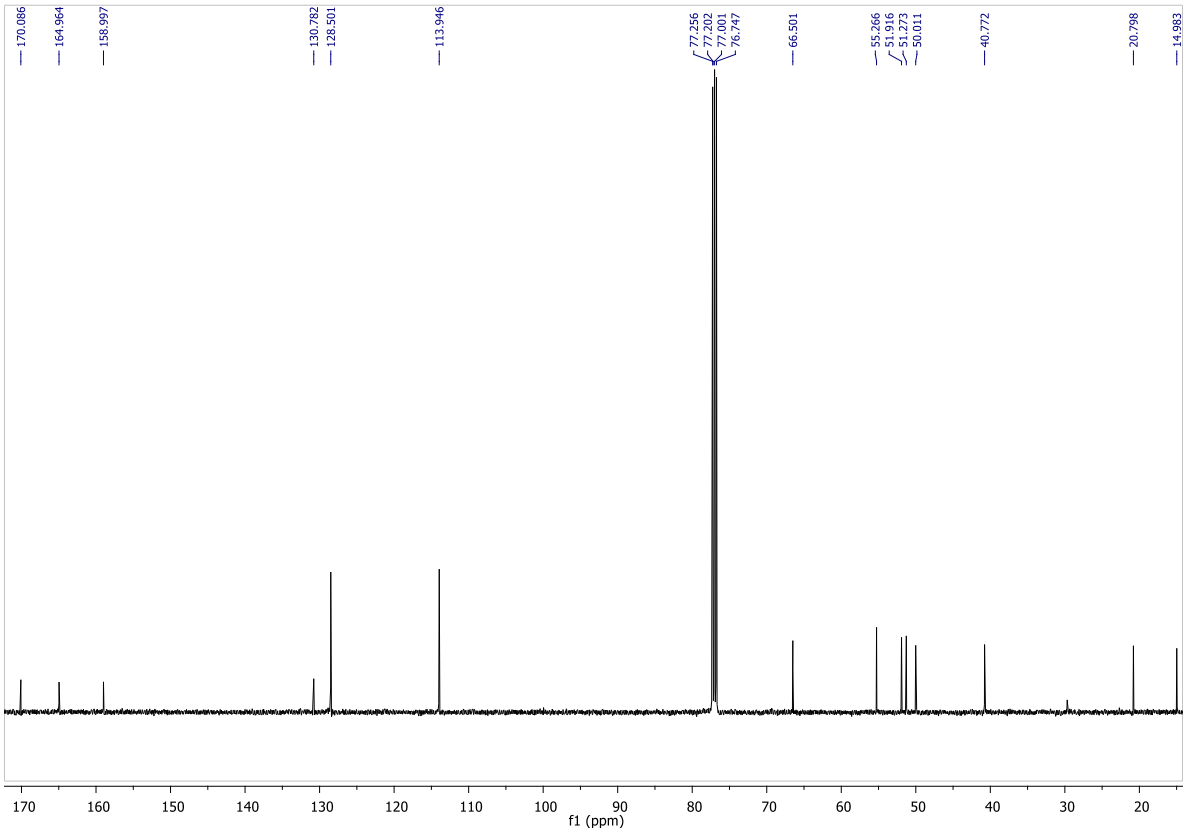

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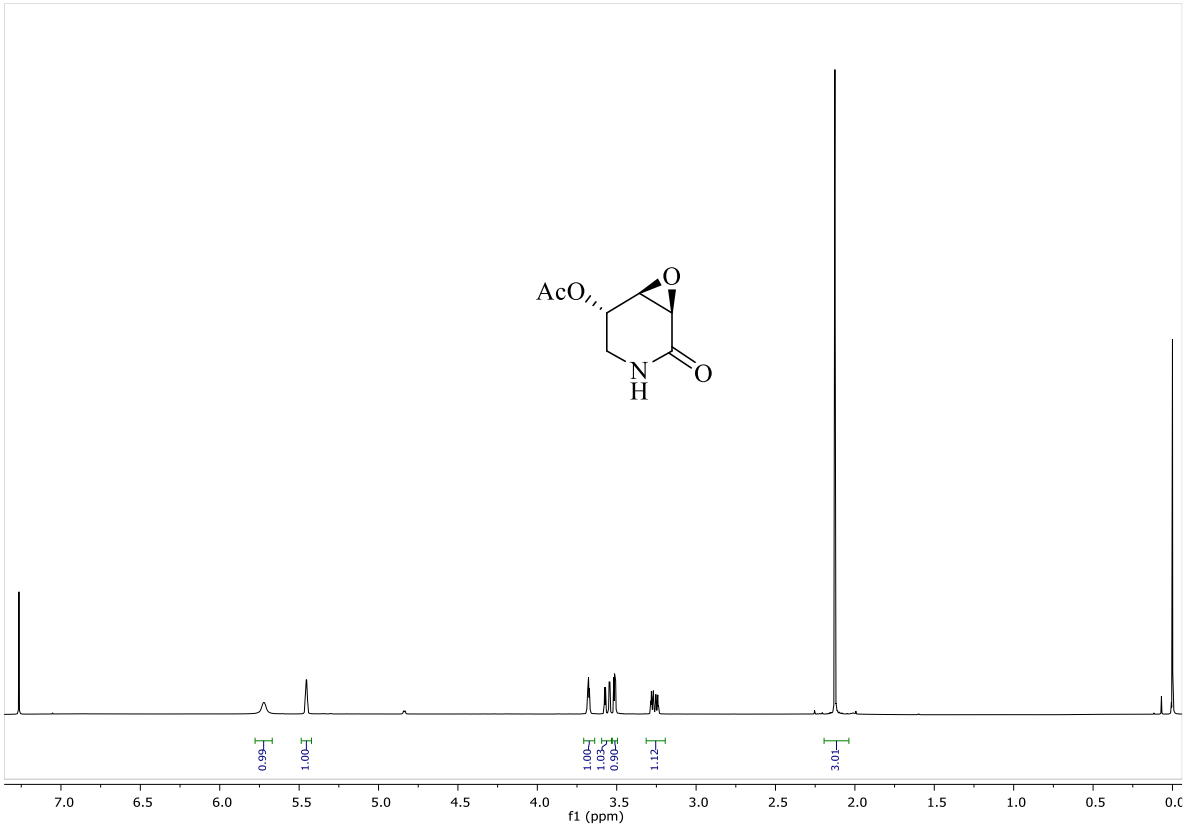

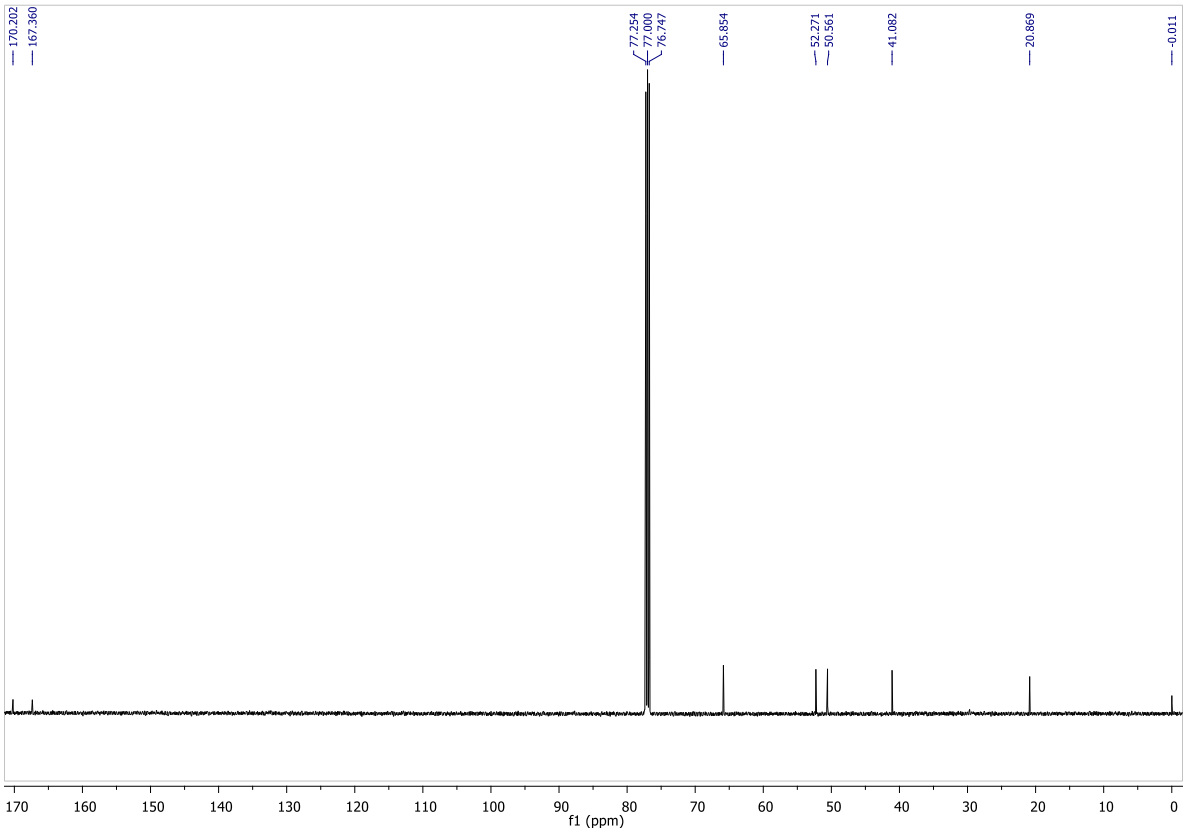

^{1}H and ^{13}C NMR spectra of compound (-)-(3*R*,4*R*,5*S*)-**3** in $(CD_3)_2CO$