

First Synthesis of (-)-Altenuene-D₃ suitable as Internal Standard for Isotope Dilution Mass Spectrometry

Michael A. Sebold ^{1*}, Julian Gebauer ², Thomas Sommerfeld ³ and Matthias Koch ³

¹ HPC Standards GmbH, Am Wieseneck 7, D-04451 Borsdorf, Germany; sebold@hpc-standards.com

² AnalytiCon Discovery GmbH, Hermannswerder Haus 17, D-14473 Potsdam, Germany; J.Gebauer@ac-discovery.com

³ Bundesanstalt für Materialforschung und -prüfung, Abteilung Analytische Chemie, Referenzmaterialien, Richard-Willstätter-Strasse 11, D-12489 Berlin-Adlershof, Germany; matthias.koch@bam.de

* Correspondence: sebold@hpc-standards.com; Tel.: +49 (0) 34291 / 33 72 36

Content

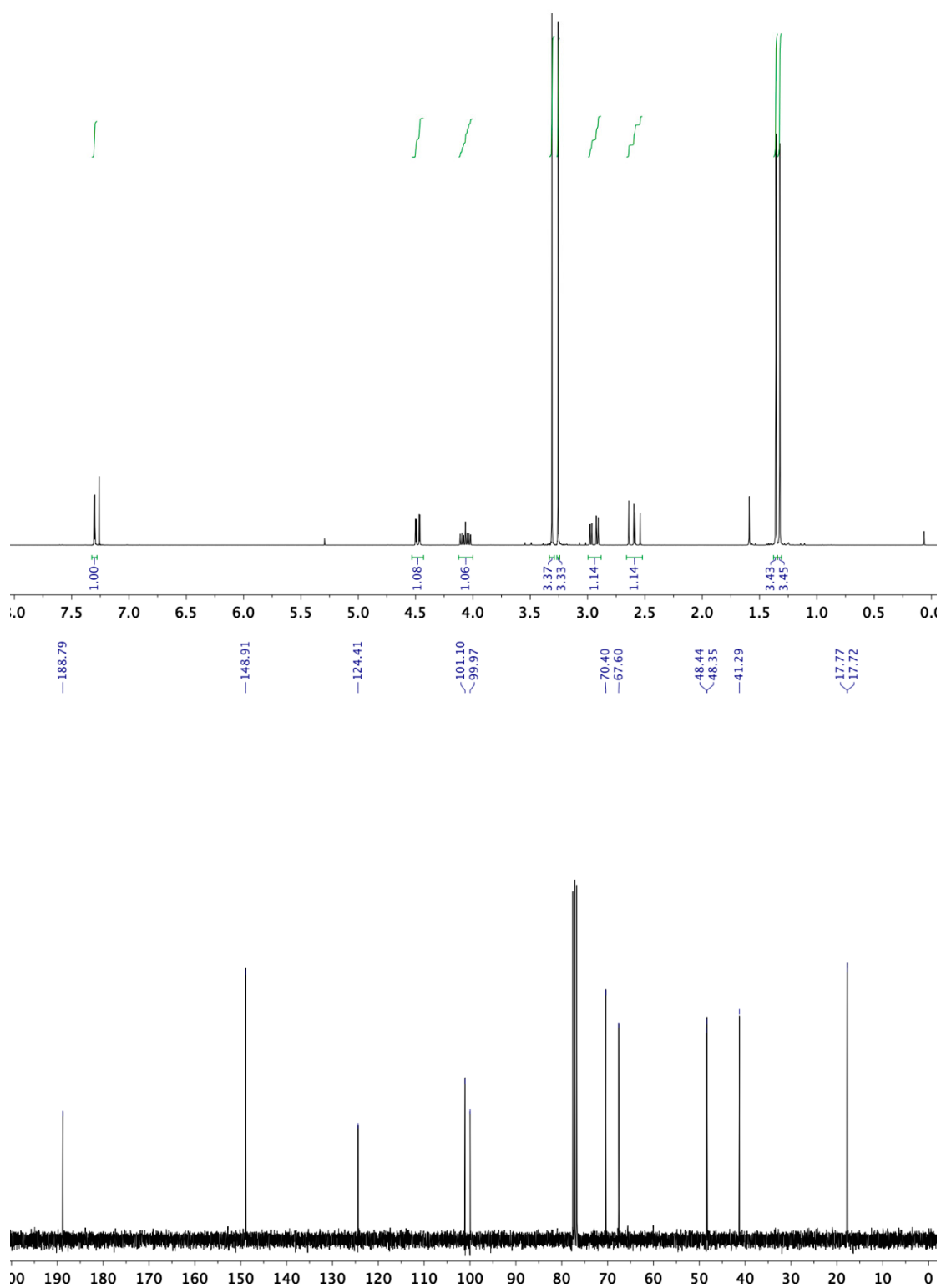
¹H- and ¹³C-NMR spectra of all new synthesized compounds. Additional IR- and UV/Vis-spectra of (-)-Altenuene-D₃ (**1b**) and native (-)-Altenuene (**1a**).

Materials and Methods

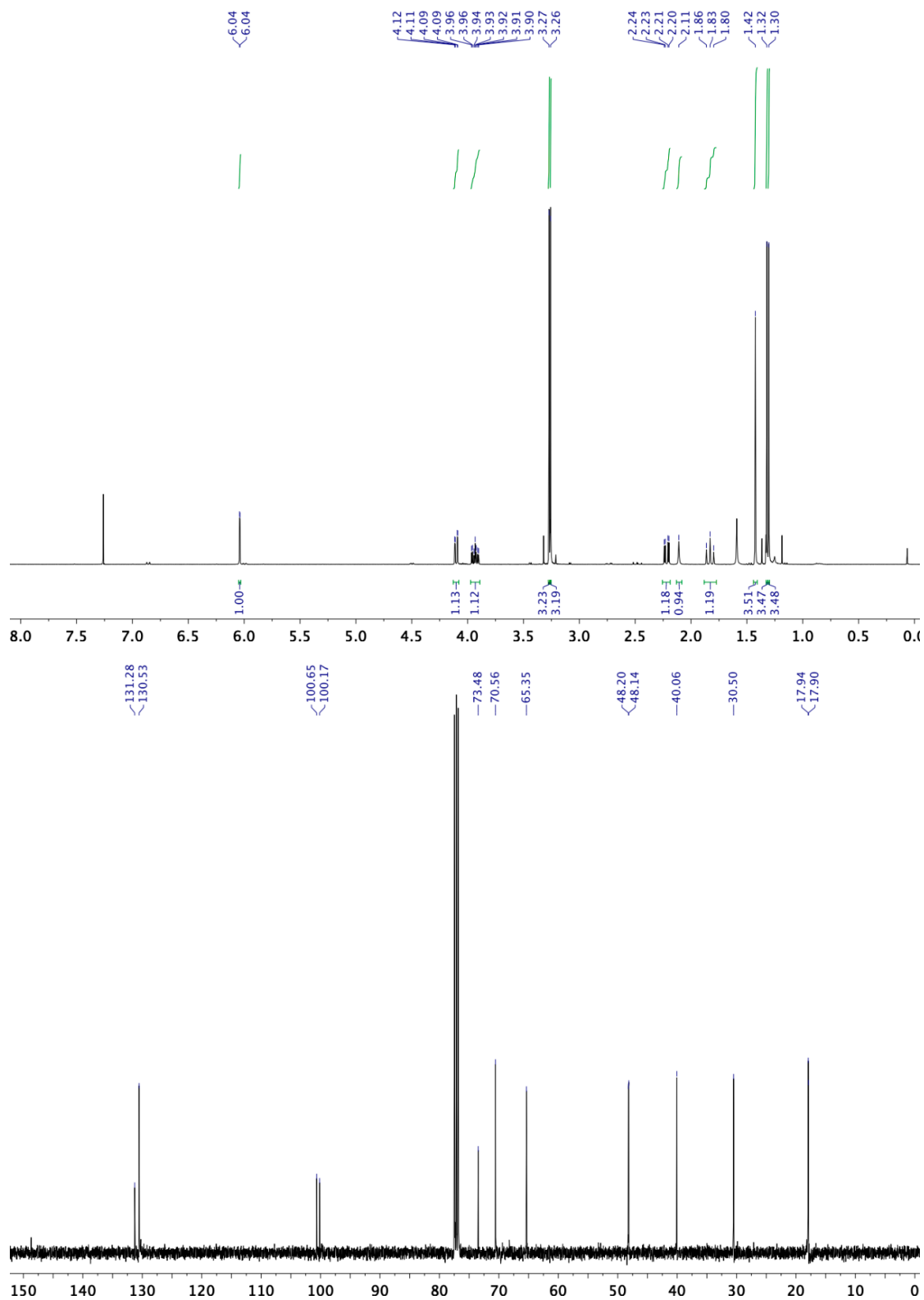
NMR spectra were recorded either on a *Varian Mercury Plus 300* (300.8 MHz), *Varian Mercury Plus 400* (399.95 MHz) or a *Bruker Avance III HD* (400.13 MHz) spectrometer with the compounds being dissolved in deuterated solvents. The spectra were processed and the images created with *MestReNova 10* and *MestReNova 14*. The signals were referenced to the solvent signals (CDCl₃: ¹H-NMR δ = 7.26 ppm, ¹³C-NMR δ = 77.16 ppm; DMSO-D₆: ¹H-NMR δ = 2.50 ppm, ¹³C-NMR δ = 39.52 ppm).

IR spectra were recorded with a *Bruker Tensor 27* FT-IR spectrometre operated by *OPUS v6.5*. UV/Vis spectra were measured with a V-670 UV-Vis/NIR spectrophotometer by *JASCO*. Visualization of both, IR and UV/Vis spectra, was conducted with *Origin 2017*.

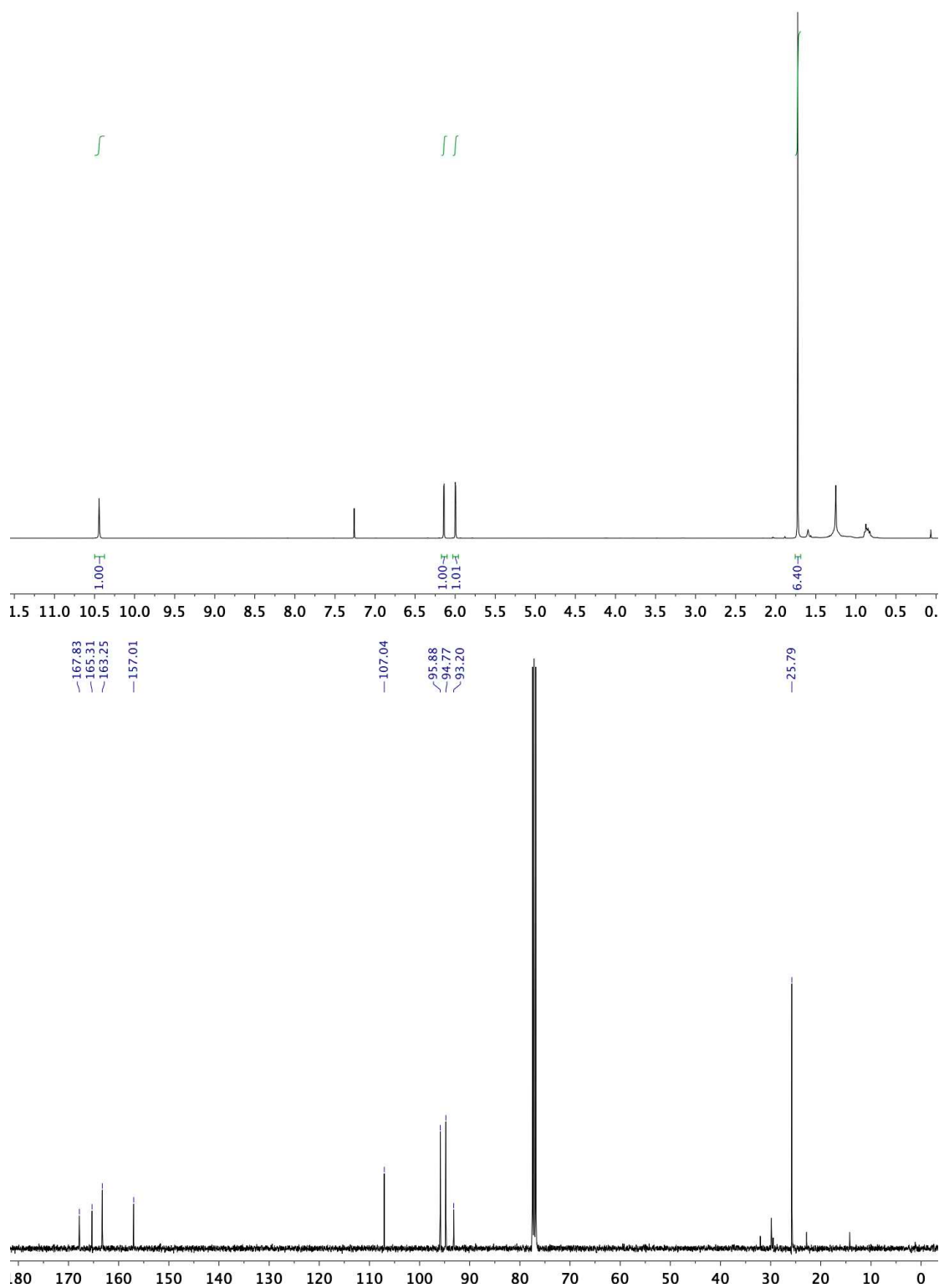
(2*S*,3*S*,4*aR*,8*aR*)-7-bromo-2,3,4*a*,5-tetrahydro-2,3-dimethoxy-2,3-dimethylbenzo[*b*][1,4]dioxin-6(8*aH*)-one (10*b*)



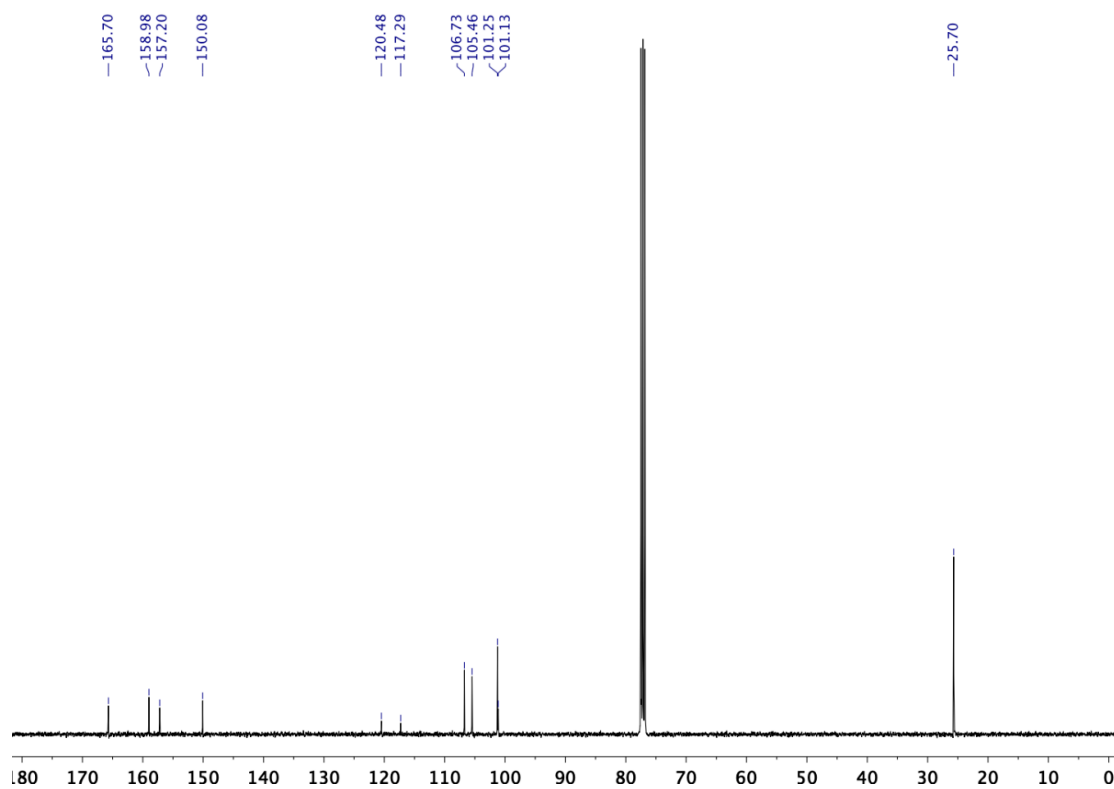
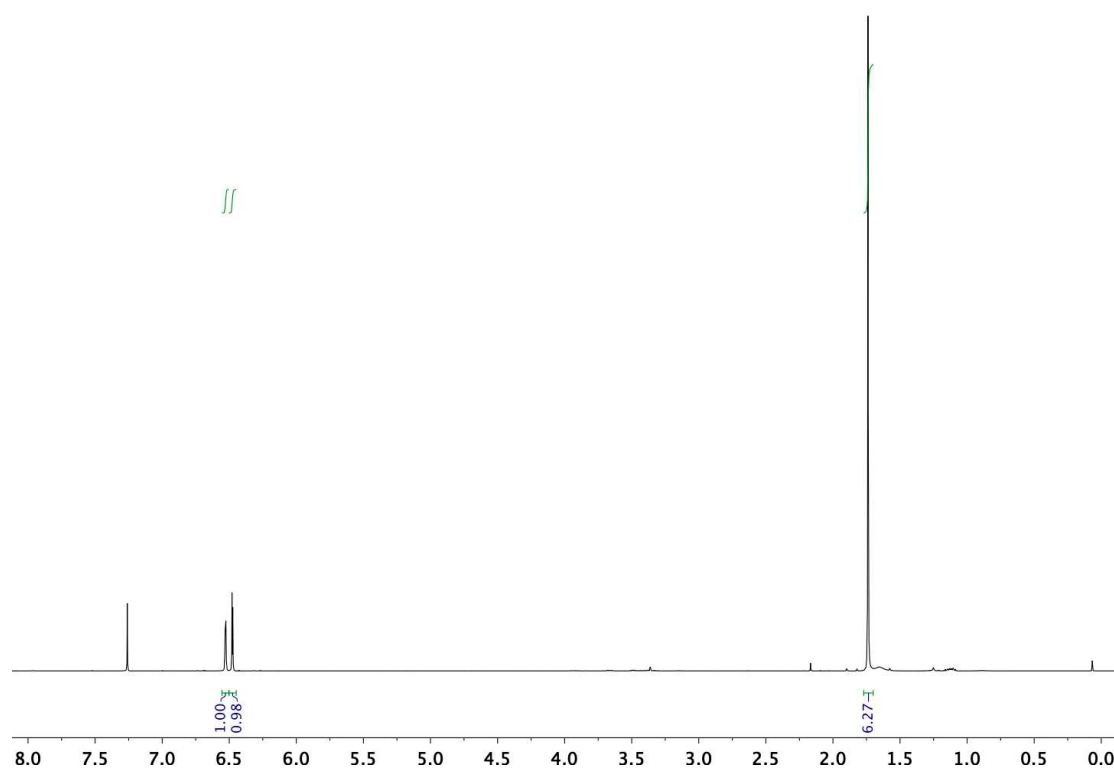
(2*S*,3*S*,4*a**R*,6*R*,8*a**R*)-7-bromo-2,3,4*a*,5,6,8*a*-hexahydro-2,3-dimethoxy-2,3,6-trimethylbenzo[*b*]-[1,4]dioxin-6-ol (5*b*)



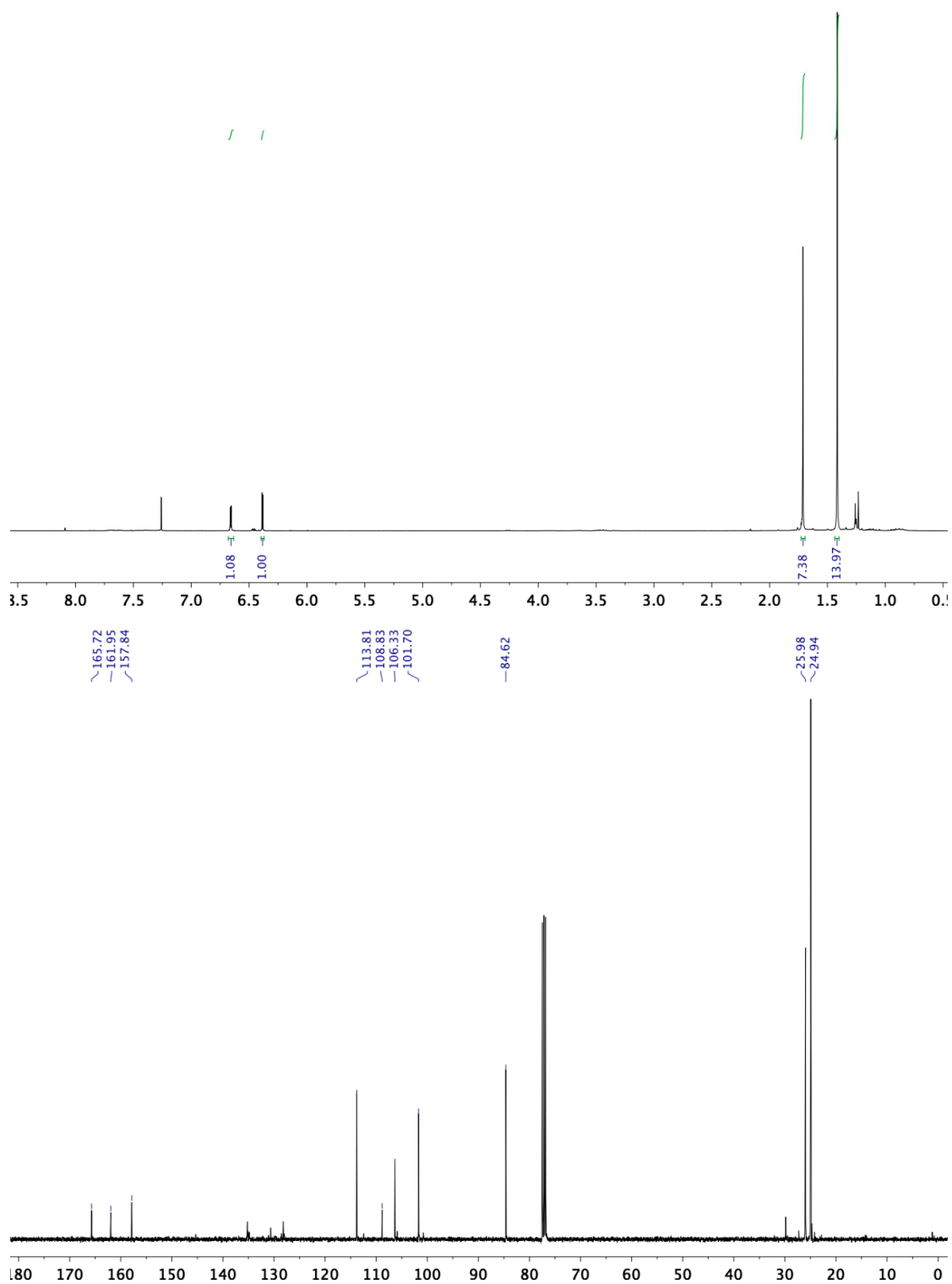
5-hydroxy-7-methoxy-2,2-dimethyl-4H-benzo[d][1,3]dioxin-4-one-D₃ (7)



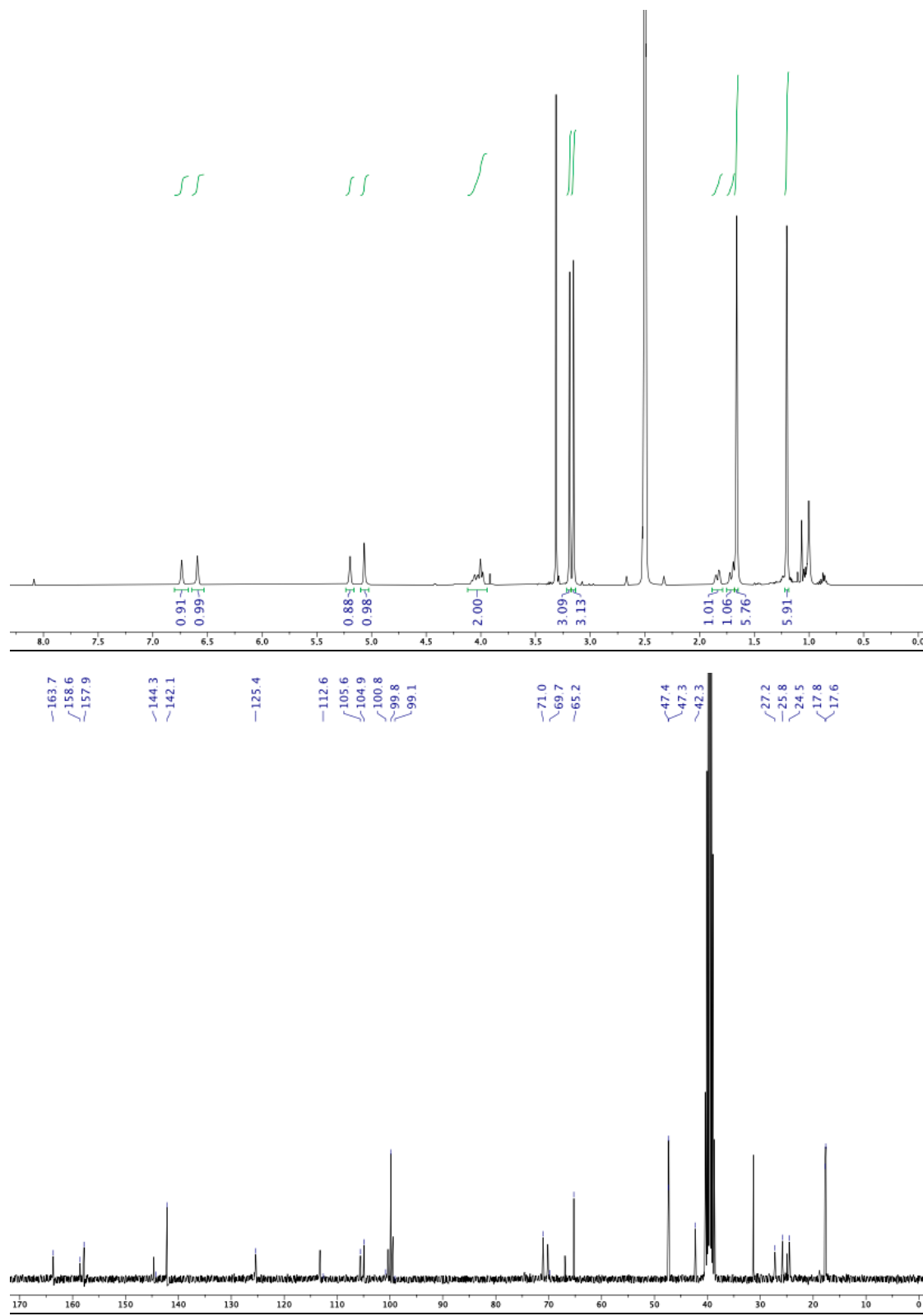
7-methoxy-2,2-dimethyl-4-oxo-4H-benzo[d][1,3]dioxin-5-yl trifluoromethanesulfonate-D₃



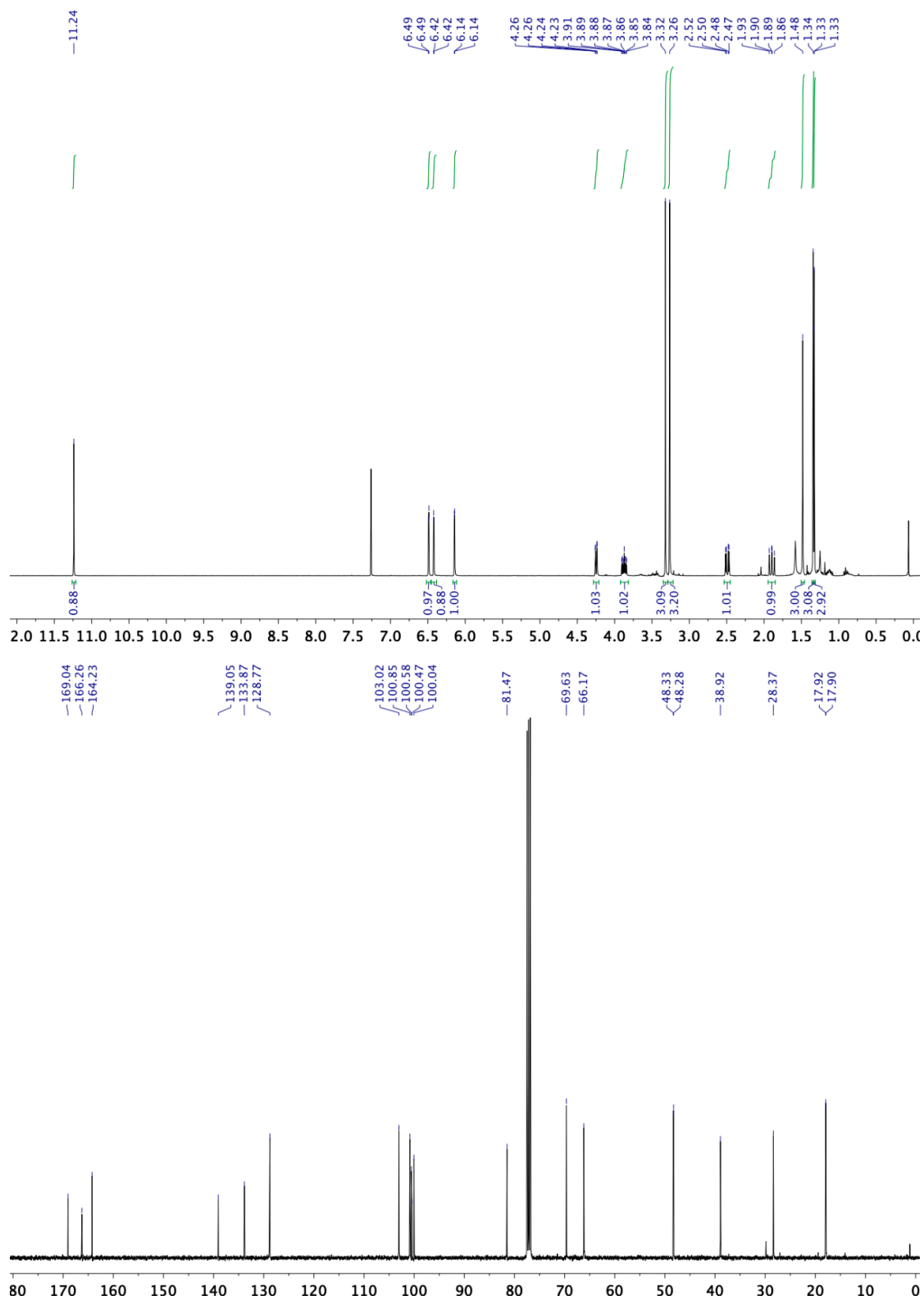
7-methoxy-2,2-dimethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4H-benzo[d][1,3]-dioxin-4-one-
D₃ (4b)



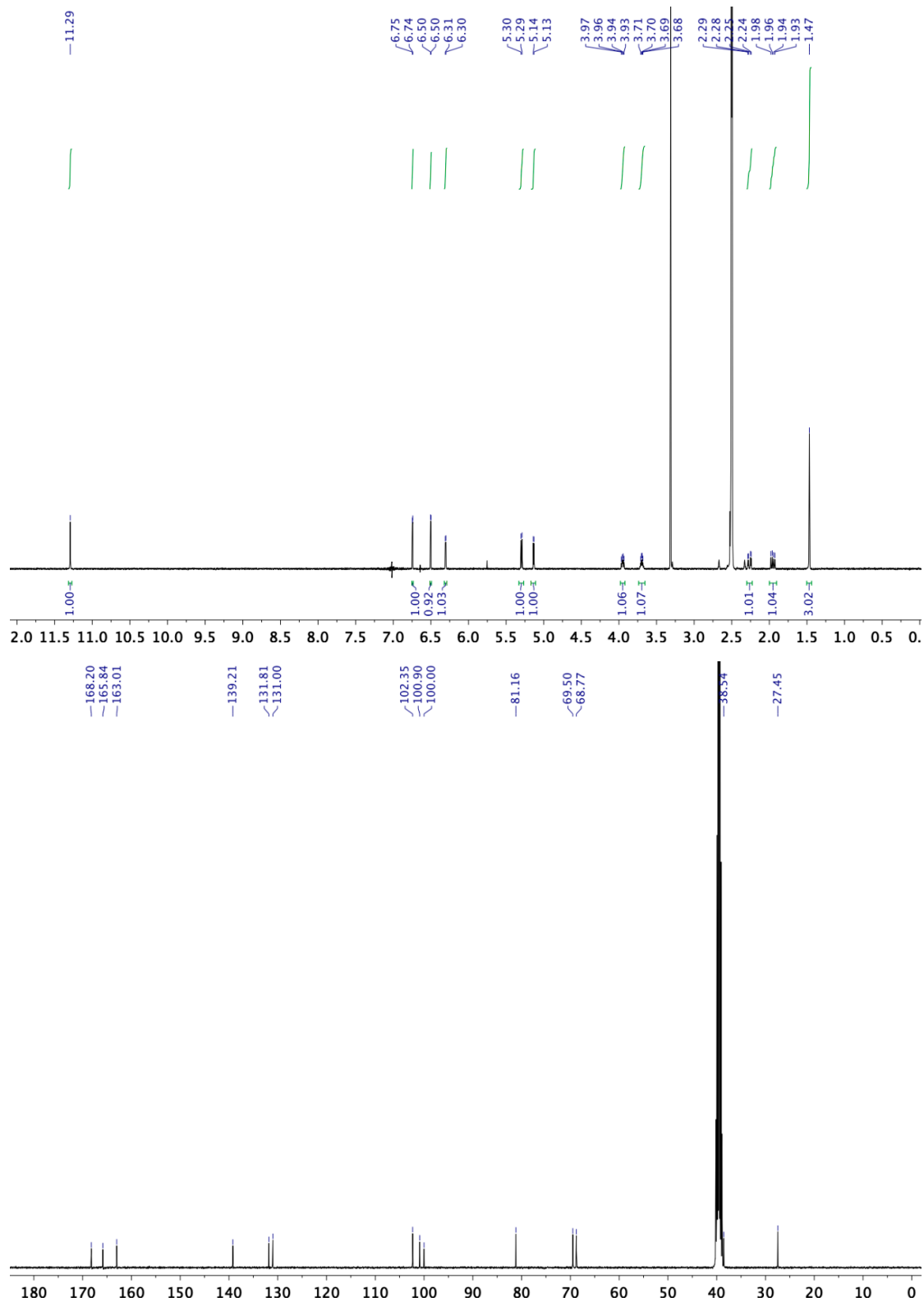
5-((2*S*,3*R*,4*aR*,6*R*,8*aR*)-2,3,4*a*,5,6,8*a*-hexahydro-6-hydroxy-2,3-dimethoxy-2,3,6-trimethylbenzo[*b*][1,4]dioxin-7-yl)-7-methoxy-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one-*D*₃ (**11b**)

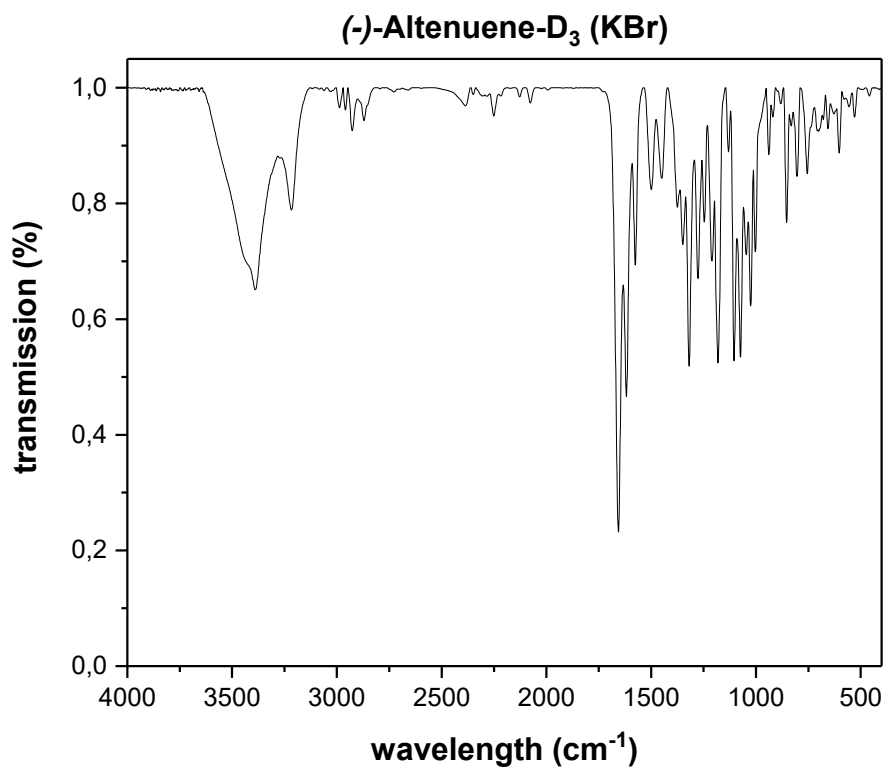
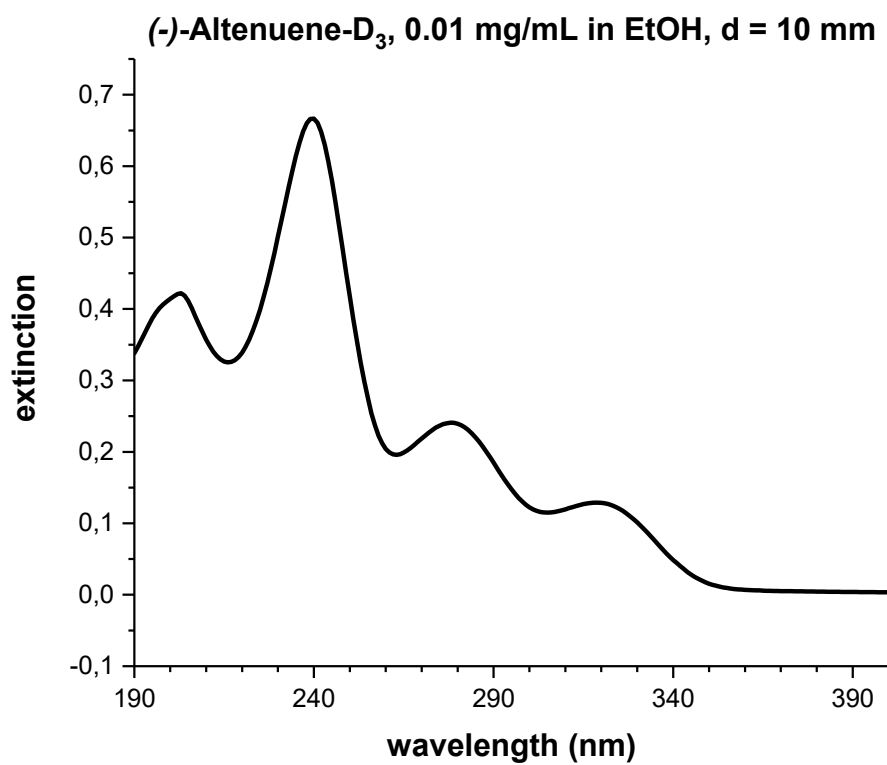


(6aR,7aR,9S,10S,11aR)-4-Hydroxy-2,9,10-trimethoxy-7a,9,10-trimethyl-6a,7,7a,9,10,11a-hexahydro-5H-benzo[c][1,4]dioxino[2,3-g]chromen-5-one-D₃ (12b)



(2R,3R,4aR)-2,3,4a-tetrahydro-2,3,7-trihydroxy-9-methoxy-4a-methylbenzo[c]chromen-6-one-D₃
((-)-*Altenuene-D₃*, **1b**)





(2R,3R,4aR)-2,3,4a-tetrahydro-2,3,7-trihydroxy-9-methoxy-4a-methylbenzo[c]chromen-6-one
((-)-Altenuene, **1a**)

