

Supplementary Materials

Stereospecific synthesis of *bis*-homoconduritol-A via bicyclic *bis*-epoxide ring opening

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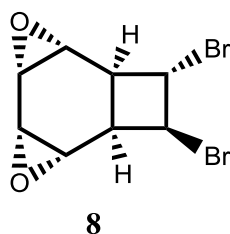
EXPERIMENTAL SECTION

General Information

A capillary melting apparatus (Electrothermal) was used to determine melting points without further correction. IR spectra were obtained from KBr (solution in 0.1 mm cells) or film with a Shimadzu spectrophotometer. The ^1H NMR and ^{13}C NMR spectra were recorded on 400 (100) MHz Bruker spectrometer (Avance III) and are reported in δ units with SiMe_4 as internal standard. When necessary, 2D correlation experiments (COSY) have been used to define the structures. TLC was performed on E. Merck Silica Gel 60 F₂₅₄ plate (0.2 mm). Flash-column chromatography was performed on Merck silica gel (60 mesh). All organic extracts were dried with MgSO_4 , filtered, and concentrated on a rotary evaporator. All solvents have been distilled prior to their use in the syntheses. HRMS were recorded by LC-MS TOF electrospray ionization technique (6230, Agilent) and elemental analyses were performed using Elementar Vario Micro Cube.

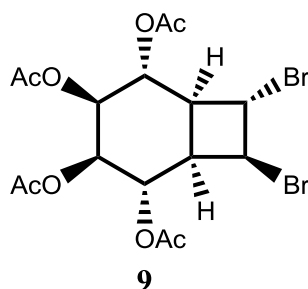
3,4-Dibromo-7,8-dioxatricyclo[4.2.2.0^{2,5}]dec-9-ene (7)

Endoperoxide **7** was synthesized from cyclooctatetraene (COT) according to literature protocols. The ^1H - and ^{13}C -NMR spectra data of the compound were found to be in agreement with previous reports [1].



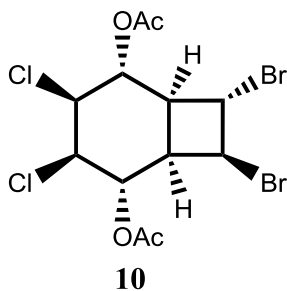
9,10-Dibromo-3,6 dioxatetracyclo [6.2.0.0^{2,4}.0^{5,7}] decane (8)

A solution of 1.65 g (5.57 mmol) endoperoxide **7** in 50.0 mL of CHCl_3 was heated for 48h at 75°C. Evaporation of the solvent carefully gave the crude product. Recrystallization from CHCl_3 / hexane afforded the pure *bis*-epoxide **8** as white crystals (1.56 g, 95%, mp133–134°C). IR (KBr, cm^{-1}): 3487, 3002, 1419, 1268, 1160, 945, 862, 746, 663, 631, 559. ^1H -NMR (400 MHz, CDCl_3): δ =4.72 (t, 1H, J =8.4 Hz, H_{10}), 4.23 (td, 1H, J =8.4, 0.8 Hz, H_9), 3.59 (bd, 2H, J =1.6 Hz, H_4 and H_5), 3.32 (bd, 1H, J =3.2 Hz, H_2), 3.19 (dd, 1H, J =3.2, 1.6 Hz, H_7), 3.18 (bt, 1H, J =9.2 Hz, H_8), 3.10 (td, 1H, J =9.2, 1.6 Hz, H_1); ^{13}C -NMR (100 MHz, CDCl_3): δ =49.0 (C), 48.50 (C), 48.49 (C), 47.7 (C), 47.5 (C), 47.1 (C), 40.4 (bridgehead-C), 34.0 (bridgehead-C); Anal. calcd. for $\text{C}_8\text{H}_8\text{Br}_2\text{O}_2$: C, 32.47; H, 2.72; found: C, 32.57; H, 2.83.



7,8-Dibromobicyclo[4.2.0]octane-2,3,4,5-tetraol tetraacetate (**9**)

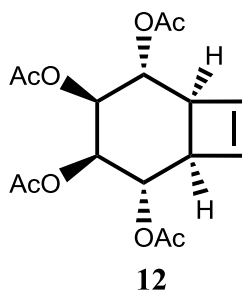
To a slurry of *bis*-epoxide **8** (1.2 g, 4.05 mmol) in 10 mL of water was added H₂SO₄ (1.0 mL), and the resulting mixture was stirred at 80 °C for 24 h. For neutralization of acid, NaHCO₃ (2.50 g) was added in ice-bath. After evaporation of water, the residue was treated with MeOH and the solid was filtered. MeOH was evaporated, and the residue, without any purification, was treated with CH₂Cl₂ (20.0 mL) and CH₃COCl (10.0 mL). The resulting mixture was stirred at room temperature for 24 h. The volatiles were evaporated in *vacuo*. The crude product was chromatographed on a silica gel column eluting with CHCl₃/hexane (2:1) gave 7,8-dibromobicyclo[4.2.0]octane-2,3,4,5-tetraol tetraacetate **9** (1.78 g, 88%) which was crystallized from methylene chloride/hexane: colorless crystals. Mp 115–117°C. IR (KBr, cm⁻¹): 3285, 1736, 1433, 1368, 1211, 1128, 1034, 930, 848, 808, 765; ¹H-NMR (400 MHz, CDCl₃): δ=5.81 (dd, 1H, *J*=10.4, 8.6 Hz, H₅), 5.40 (bs, 1H, H₃), 5.15 (dd, 1H, *J*=10.4, 2.4 Hz, H₄), 4.98 (bd, 1H, *J*=2.4 Hz, H₂), 4.62 (t, 1H, *J*=9.6 Hz, H₈), 4.48 (t, 1H, *J*=8.4 Hz, H₇), 3.13 (q, 1H, *J*=8.4 Hz, H₆), 2.83 (t, 1H, *J*=9.6 Hz, H₁), 2.24 (s, 3H, COCH₃), 2.13 (s, 3H, COCH₃), 2.04 (s, 3H, COCH₃), 2.02 (s, 3H, COCH₃); ¹³C-NMR (100 MHz, CDCl₃): δ=170.2 (C=O), 168.90 (C=O), 168.87 (C=O), 168.85 (C=O), 70.0 (C–O), 69.9 (C–O), 67.6 (C–O), 66.9 (C–O), 47.4 (C–Br), 47.2 (C–Br), 46.3 (bridgehead–C), 43.3 (bridgehead–C), 20.92 (COCH₃), 20.89 (COCH₃), 20.85 (COCH₃), 20.7 (COCH₃); HRMS: *m/z* calculated for C₁₆H₂₀⁷⁹Br⁷⁹BrNaO₈ [M+Na]⁺, 520.9423; found: 520.9416.



7,8-Dibromo-3,4-dichlorobicyclo[4.2.0]octane-2,5-diyl diacetate (**10**)

To a solution of *bis*-epoxide **8** (0.41 g, 1.38 mmol) in CH₂Cl₂ (10 mL) was added AcCl (5

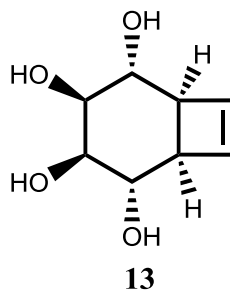
mL) and the resulting solution was added dropwise conc. H₂SO₄ (0.1 mL) and then the mixture were stirred vigorously under nitrogen at room temperature (started at 0 °C) for 20 h (monitored by TLC). The excess of unreacted AcCl and solvent was evaporated (60 °C, 20 mm Hg). The residue was dissolved in CH₂Cl₂. The residue was purified by thin-layer chromatography using a mixture of hexane and ethylacetate (7:3). After the solvent was removed, the remaining residue was filtered through a short silica gel column to obtain 7,8-dibromo-3,4-dichlorobicyclo[4.2.0]octan-2,5-diyl diacetate **10** (56 mg, 89%); (colorless liquid). IR (KBr, cm⁻¹): 3005, 2973, 1752, 1366, 1217, 1047, 1027, 794; ¹H-NMR (400 MHz, CDCl₃): δ=5.86 (t, 1H, *J*=9.2 Hz, H₅), 5.23 (bs, 1H, H₃), 4.96 (t, 1H, *J*=9.2 Hz, H₄), 4.41 (bs, 1H, H₂), 4.42 (t, 1H, *J*=8.0 Hz, H₈), 4.31 (dd, 1H, *J*=10.8, 2.4 Hz, H₇), 3.13 (q, 1H, *J*=8.4 Hz, H₆), 2.83 (t, 1H, *J*=9.6 Hz, H₁), 2.11 (s, 3H, COCH₃), 2.10 (s, 3H, COCH₃); ¹³C-NMR (100 MHz, CDCl₃): δ=168.9 (2x C=O), 70.1 (C–O), 68.6 (C–O), 61.7 (C–Cl), 58.4 (C–Cl), 48.0 (C–Br), 46.8 (C–Br), 46.6 (bridgehead–C), 44.5 (bridgehead–C), 21.2 (COCH₃), 21.1 (COCH₃). HRMS: *m/z* calculated for C₁₂H₁₄⁷⁹Br₂³⁵Cl₂NaO₄ [M+Na]⁺, 472.8518; found: 472.8509.



Bicyclo[4.2.0]oct-7-ene-2,3,4,5-tetraacetate (**12**)

Zinc dust (1.3 g, 20.0 mmol) and a trace of iodine were added to a stirred solution of dibromotetraacetate **9** (1.0 g, 1.99 mmol) in anhydrous diethyl ether (50 mL) and acetic acid (AcOH) (3 mL, 99%). The mixture was refluxed for 4 h and stirred further for 24 h at room temperature (monitored by TLC). It was then filtered and the residue washed with diethyl ether. The organic phase was washed once with saturated aqueous NaHCO₃ and then with brine and dried over Na₂SO₄. Evaporation of the solvent (50 °C, 20 mmHg) and chromatography of residue on a silica gel column (15 g) eluting with hexane/ethylacetate (8:1) gave tetraacetate **12** (0.58 g, 85%). Colorless oily; IR (KBr, cm⁻¹): 3061, 2930, 2861, 1753, 1676, 1600, 1446, 1376, 1238, 1046, 966; ¹H-NMR (400 MHz, CDCl₃): δ=6.15 (s, 2H, C=CH), 5.28 (dd, 2H, *J* = 6.8, 3.4 Hz), 5.14 (m, 2H), 3.08 (dd, 2H, *J* = 3.4, 1.1 Hz, –CH), 2.08

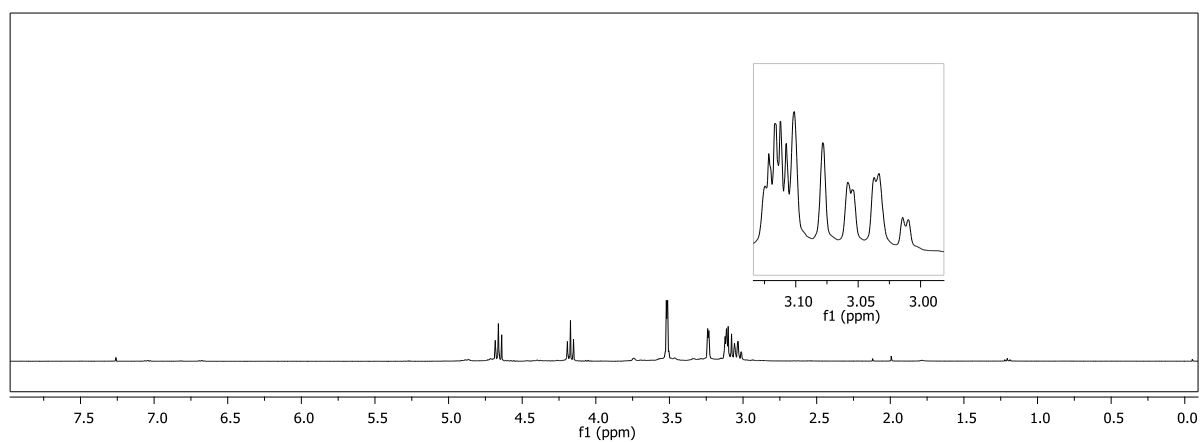
(s, 6H, $-\text{CH}_3$), 2.04 (s, 6H, $-\text{CH}_3$). ^{13}C -NMR (100 MHz, CDCl_3): δ =172.0 (2x C=O), 171.8 (2x C=O), 140.2 (2x C=C), 72.7 (C-O), 72.3 (C-O), 48.4 (2x bridgehead-C), 23.0 (COCH_3), 22.8 (COCH_3).



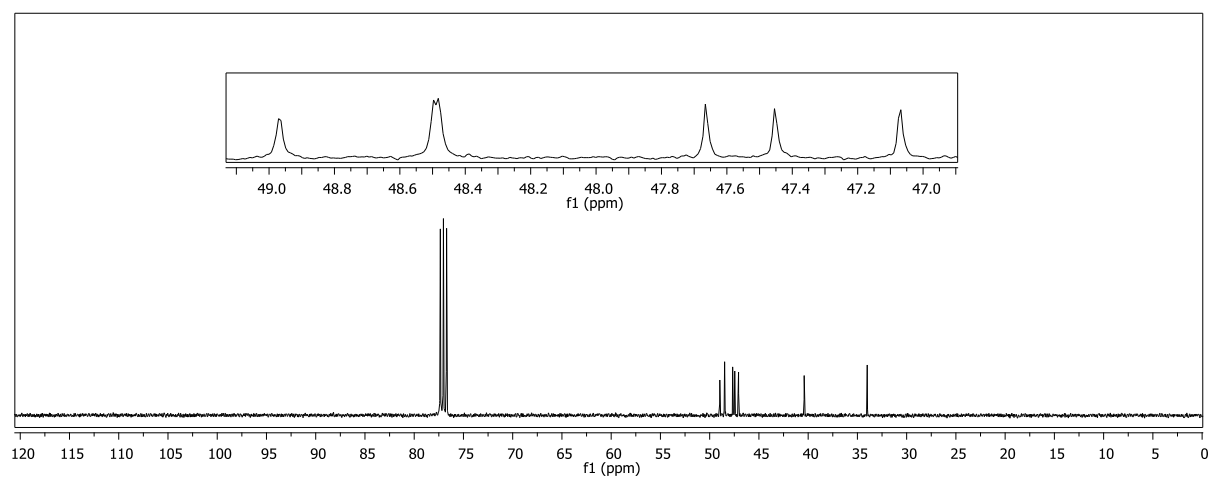
Bicyclo[4.2.0]oct-7-ene-2,3,4,5-tetraol (13)

The tetraacetate **12** (0.161 g, 0.05 mmol) was dissolved in 30.0 mL of absolute MeOH. The mixture was stirred for 4 h while NH_3 gas was being passed through the solution, (monitored by TLC and IR) at room temperature. Evaporation of MeOH and formed acetamide gave tetraol (*bis*-homoconduritol-A) **13** (0.152 g, 95%) as colorless viscous oil. IR (KBr, cm^{-1}): 3435, 2921, 1650, 1432, 1066, 746; ^1H -NMR (400 MHz, CD_3OD): δ =6.30 (s, 2H, C=CH), 3.70 (br s, 4H, CH-O), 2.80 (m, 2H, CH); ^{13}C -NMR (100 MHz, CD_3OD): δ =140.7 (2x C=C), 74.7 (2x C-O), 74.4 (2x C-O), 48.4 (2x bridgehead-C); Anal. calcd. for $\text{C}_8\text{H}_{12}\text{O}_4$: C, 55.81; H, 7.02; found: C, 55.58; H, 7.00.

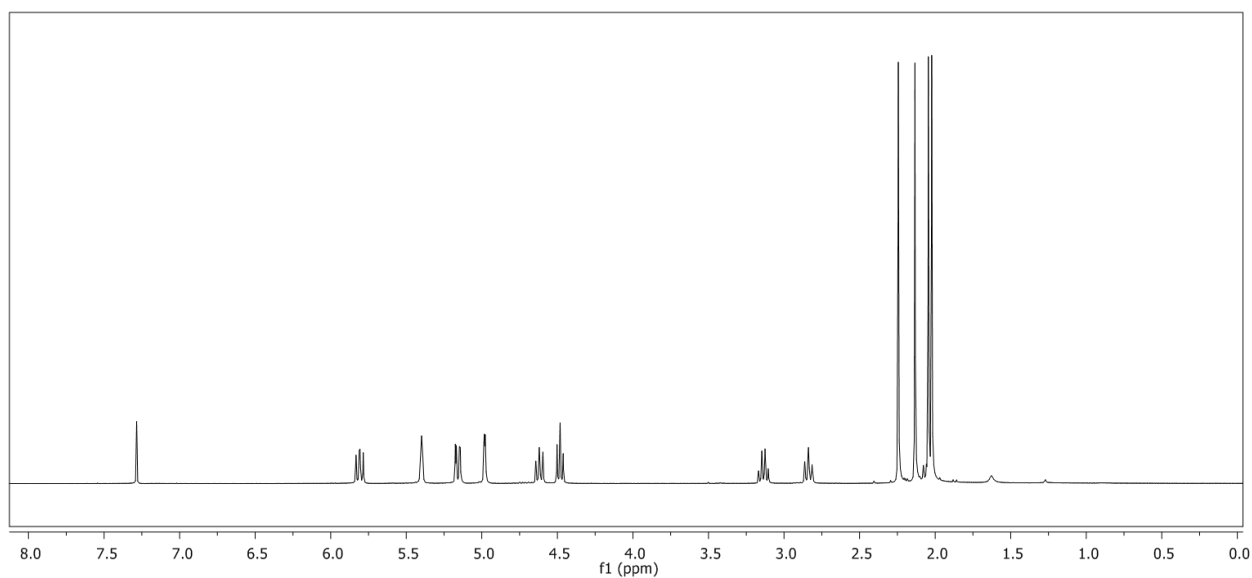
NMR spectra of the compounds 8, 9, 10, 14 and 15
2D NMR spectra of the compounds 9



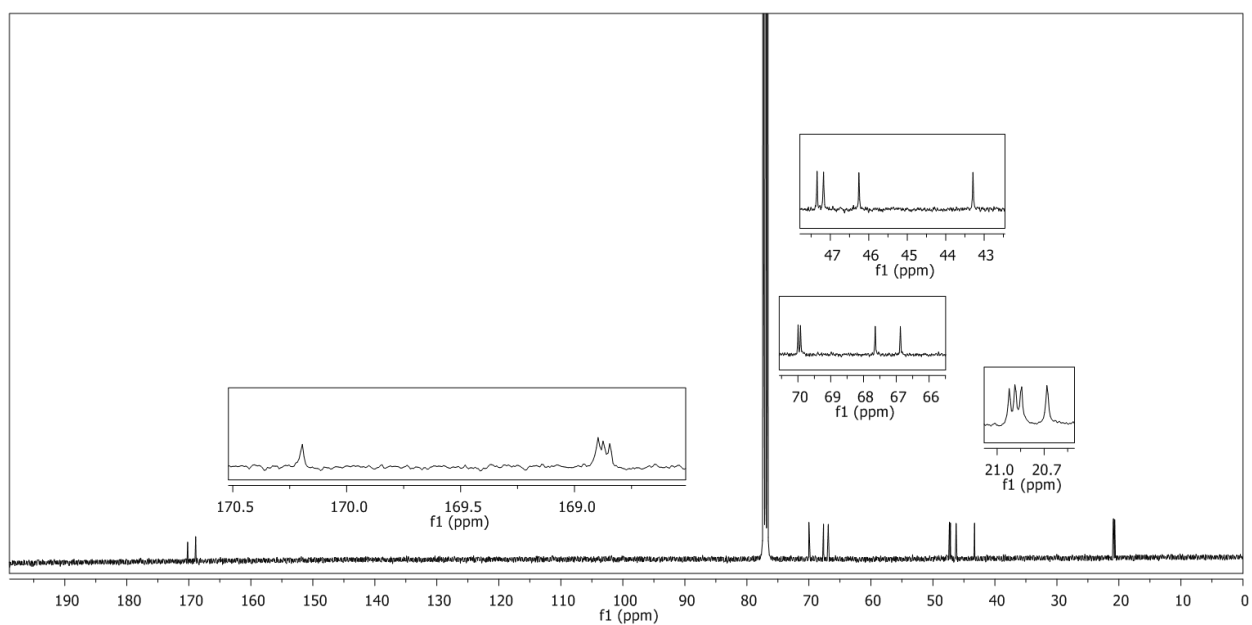
400 MHz ^1H -NMR spectra of compound **8** (CDCl_3)



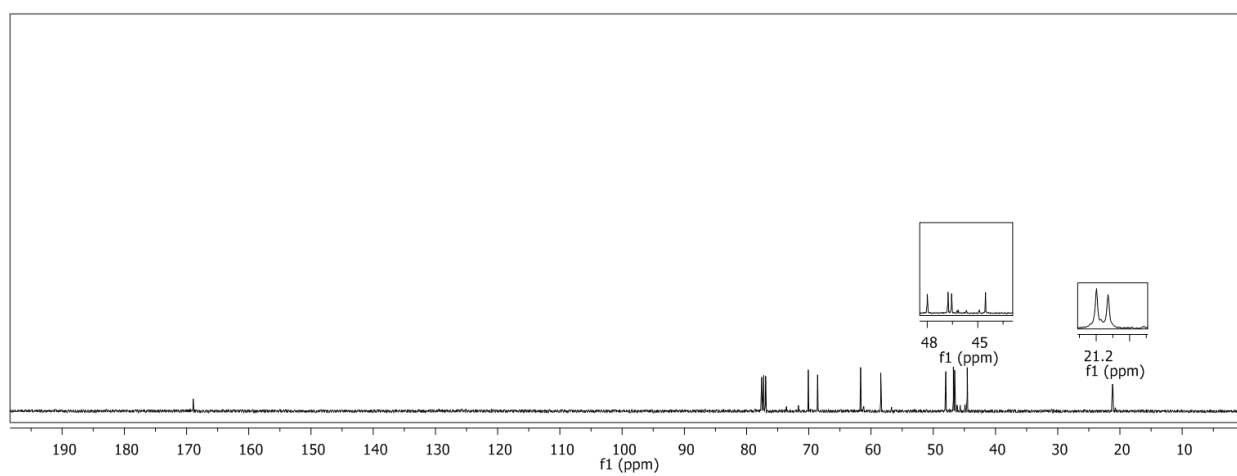
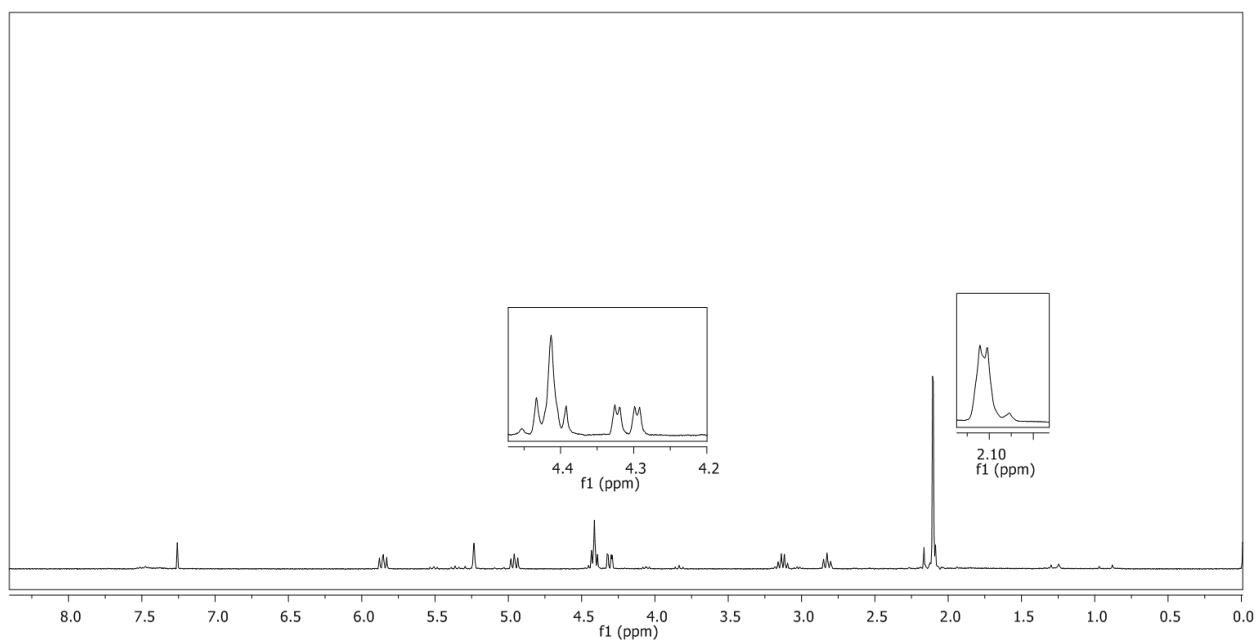
100 MHz ^{13}C -NMR spectra of compound **8** (CDCl_3)

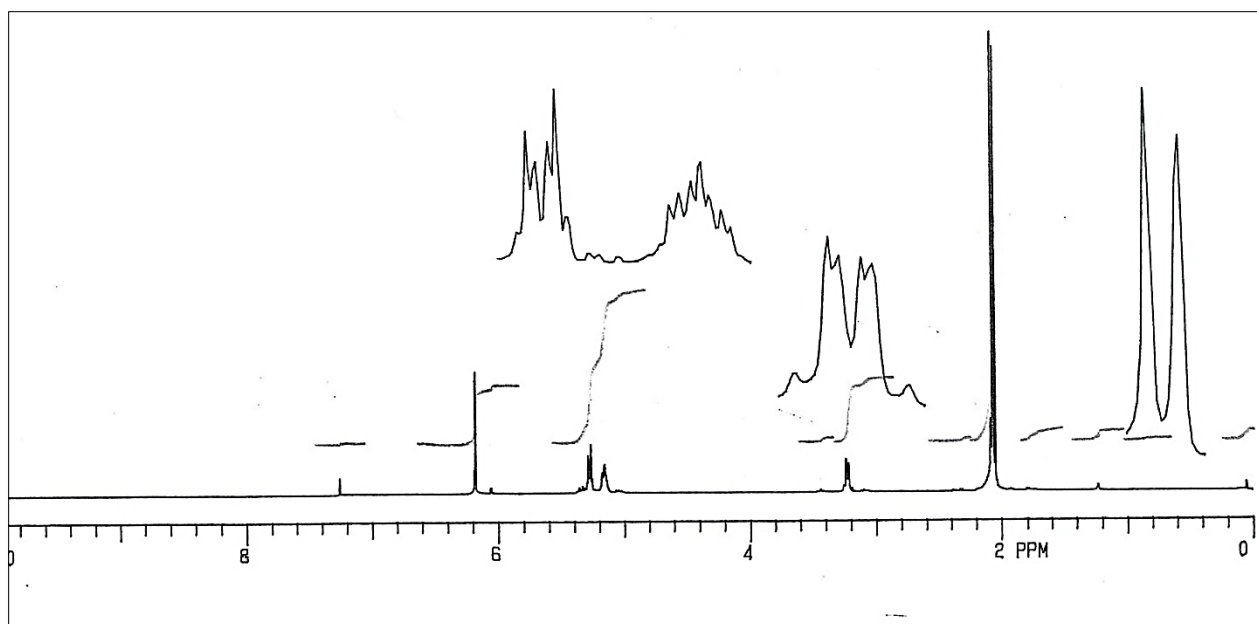


400 MHz ^1H -NMR spectra of compound **9** (CDCl_3)

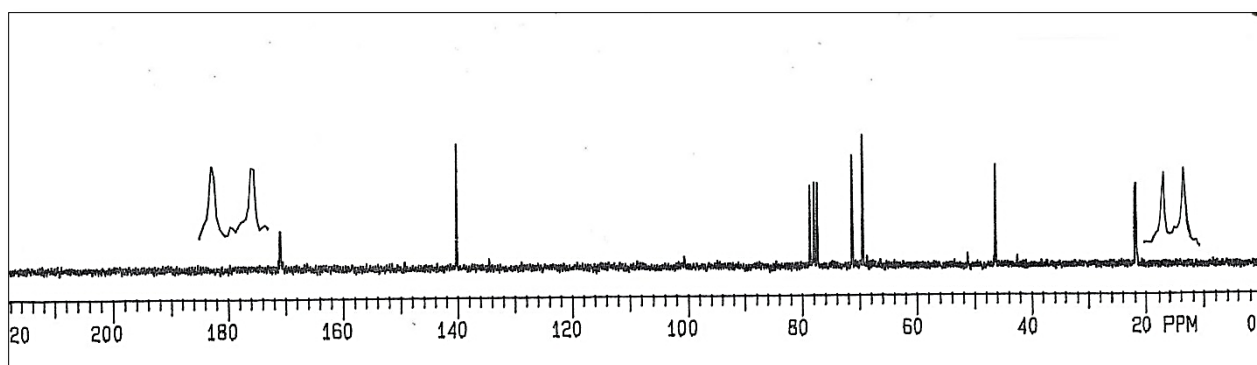


100 MHz ^{13}C -NMR spectra of compound **9** (CDCl_3)

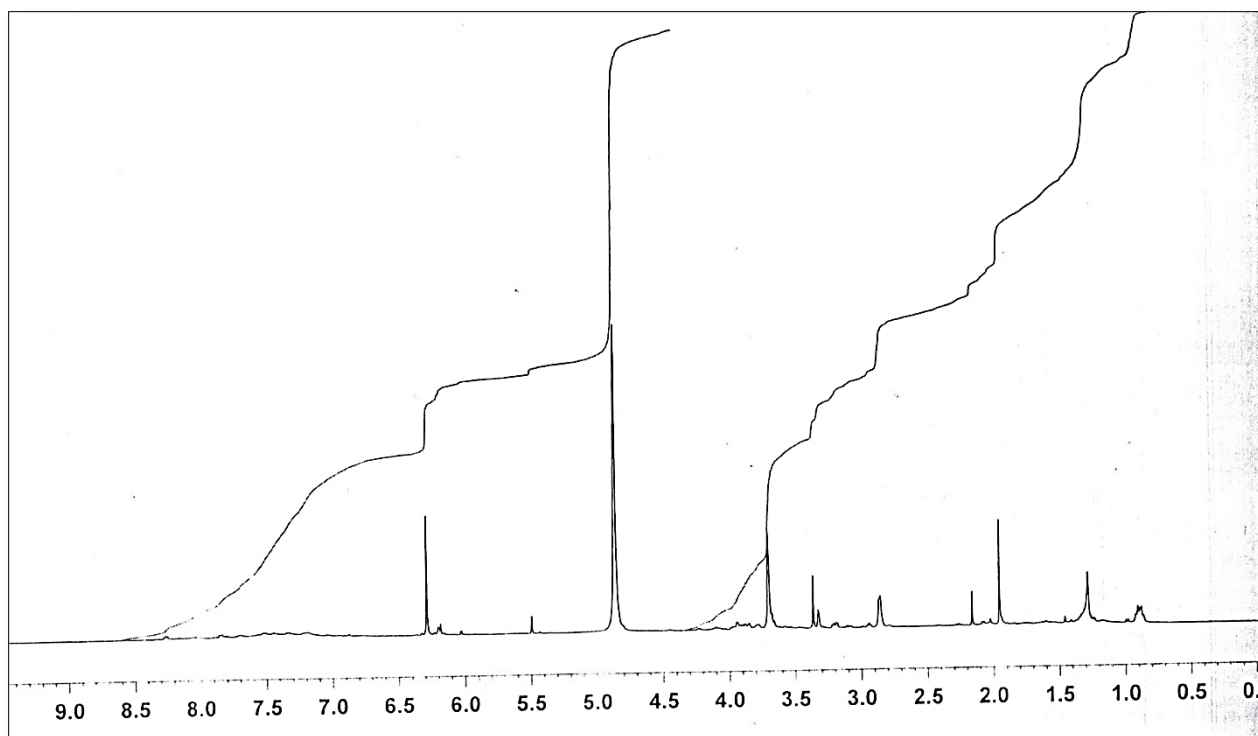




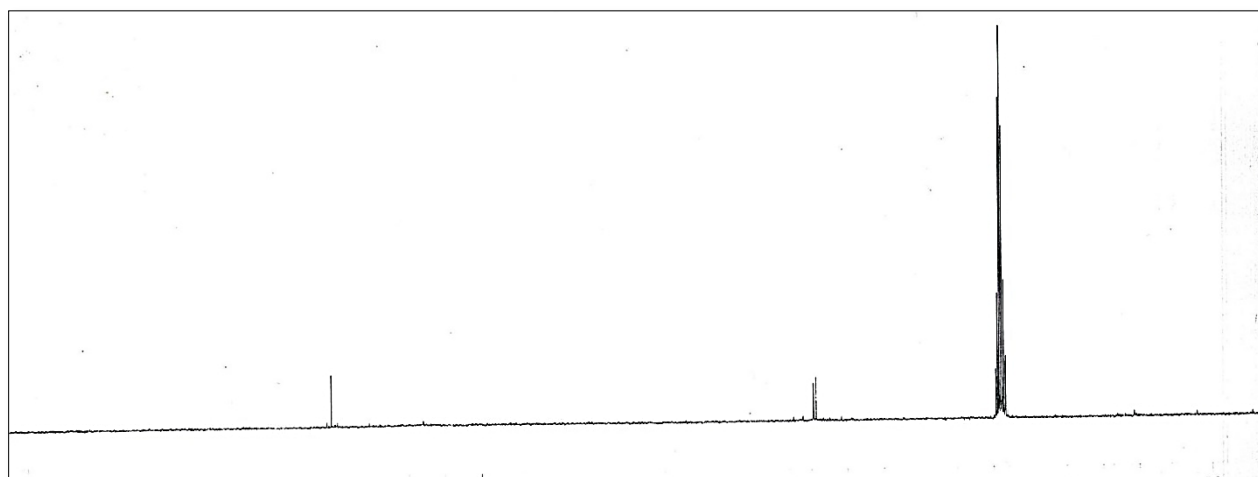
400 MHz ^1H -NMR spectra of compound **12** (CDCl_3)



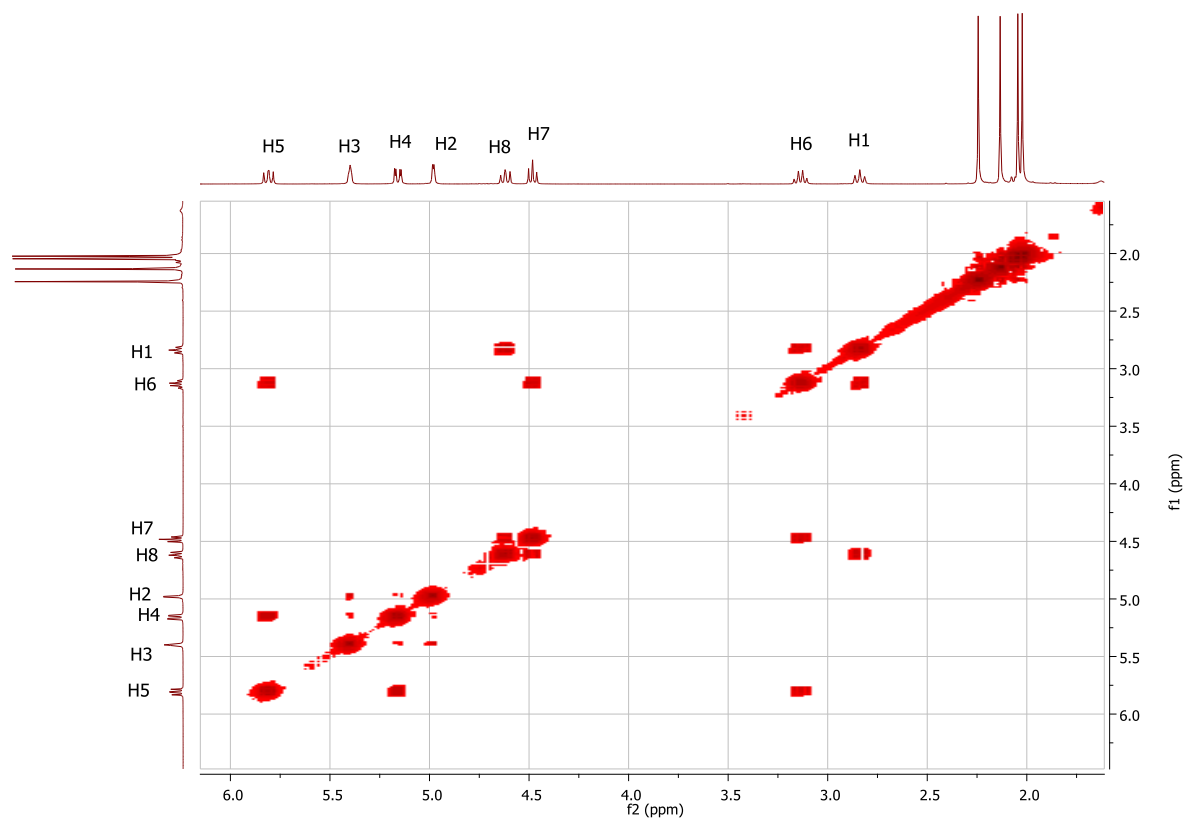
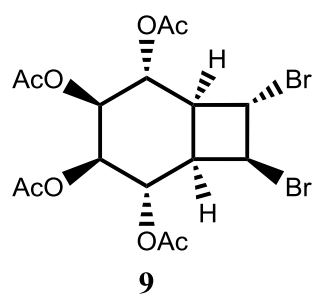
100 MHz ^{13}C -NMR spectra of compound **12** (CDCl_3)



400 MHz ^1H -NMR spectra of compound **13** (CD_3OD)



100 MHz ^{13}C -NMR spectra of compound **13** (CD_3OD)



2D COSY spectrum for compound **9** in CDCl_3 at rt (400 MHz)

References

- [1] Kelebekli, L., Kara, Y., and Balci, M., *Carbohydr. Res.*, 2005, vol. 340, p. 1940.
<https://doi.org/10.1016/j.carres.2005.05.021>