Supporting Information

Structural Modifications that Increase Gut Restriction of Bile Acid Derivatives

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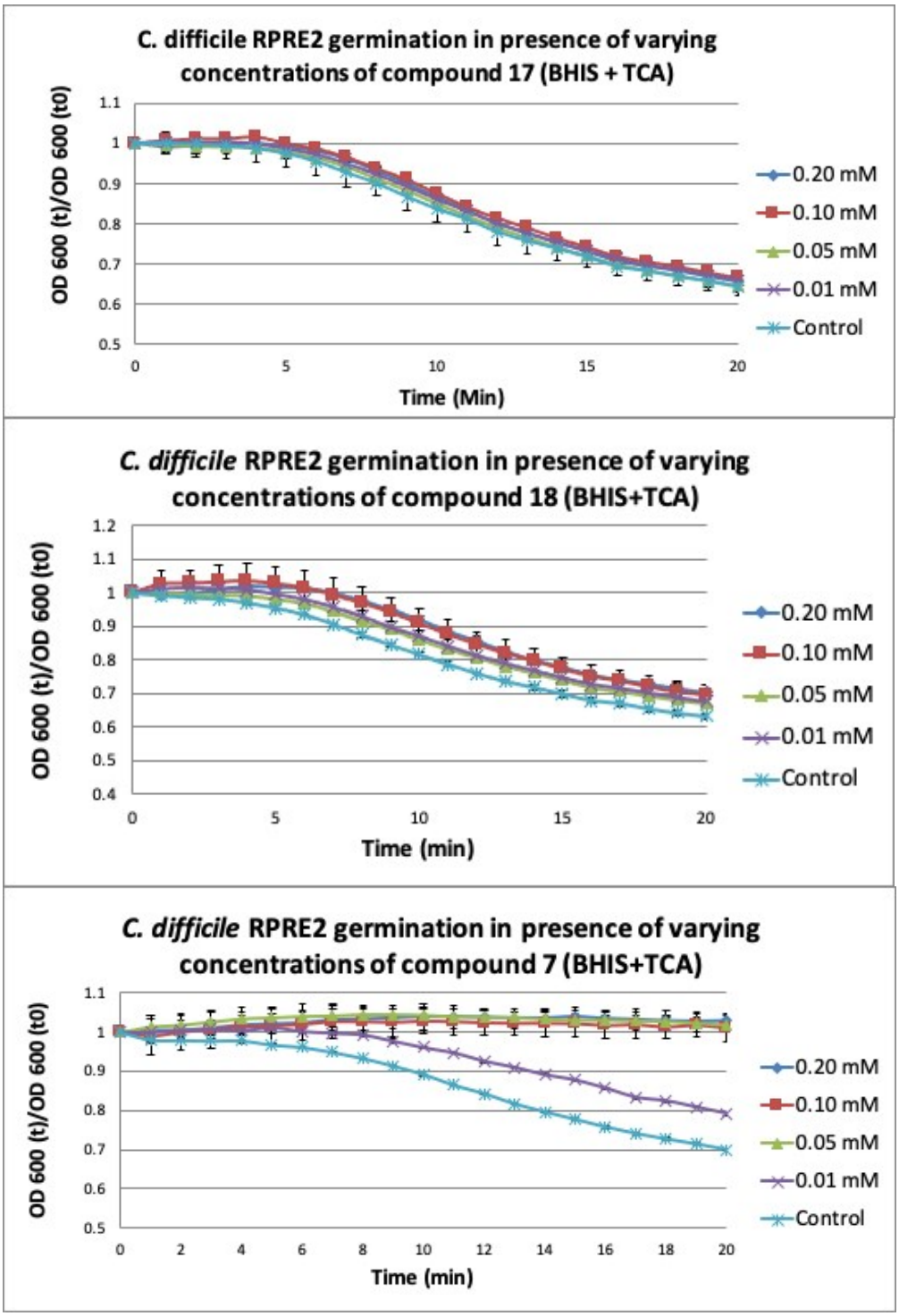


Figure S1. Spores of the RPRE2 strain of *C. difficile* were incubated in BHIS with 2000 μM TCA (which promotes germination). Both compounds **17** and **18** failed to inhibit spore germination at concentrations as high as 200 μM. In contrast, compound **7** completely inhibited spore germination at 50 μM. For experimental conditions, see Stoltz et al. *J. Med. Chem.* **2017**, *60*, 3451-3471.

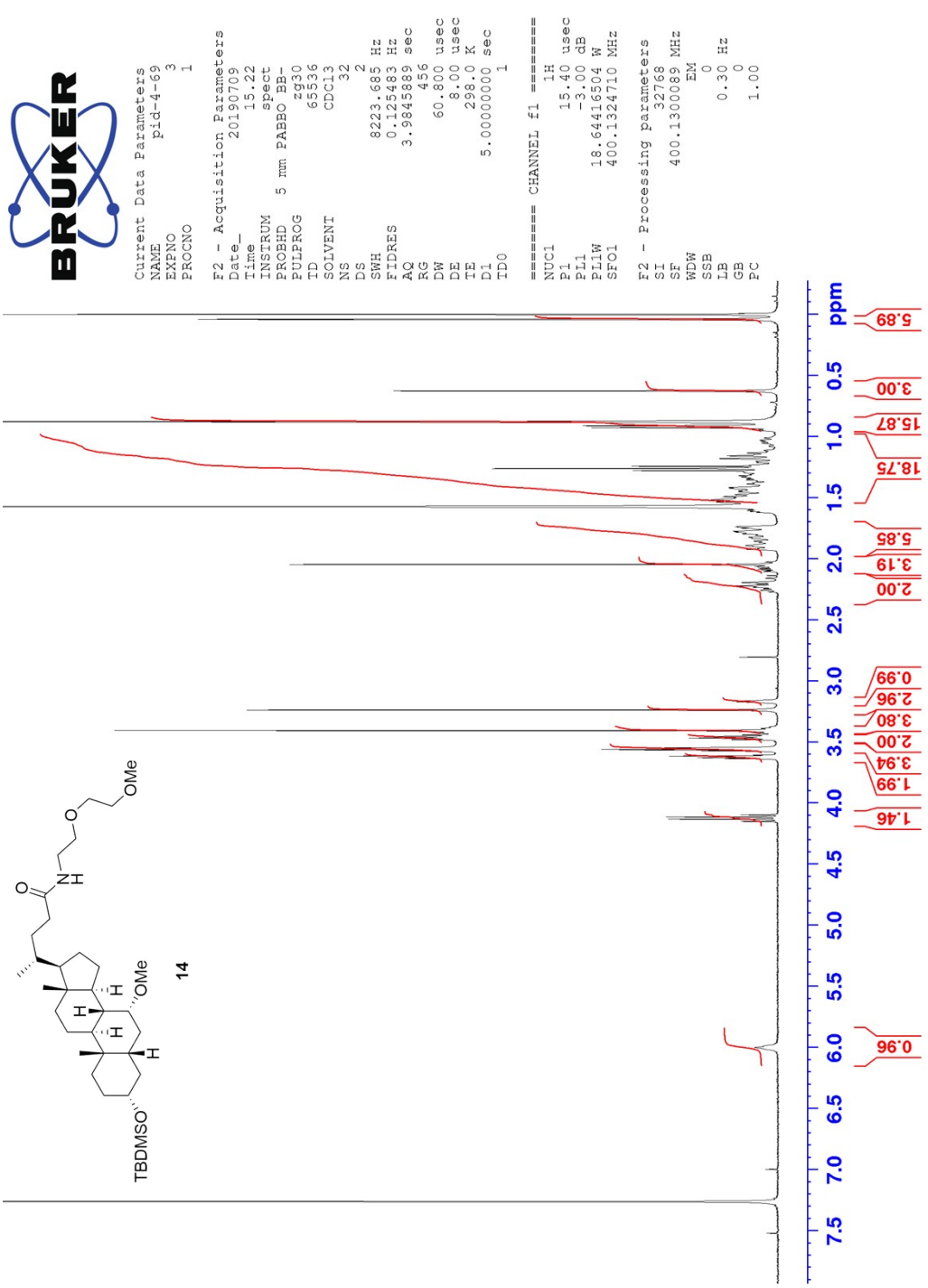


Figure S2. ^{1}H NMR spectrum of **14** (400 MHz, $CDCl_3$).

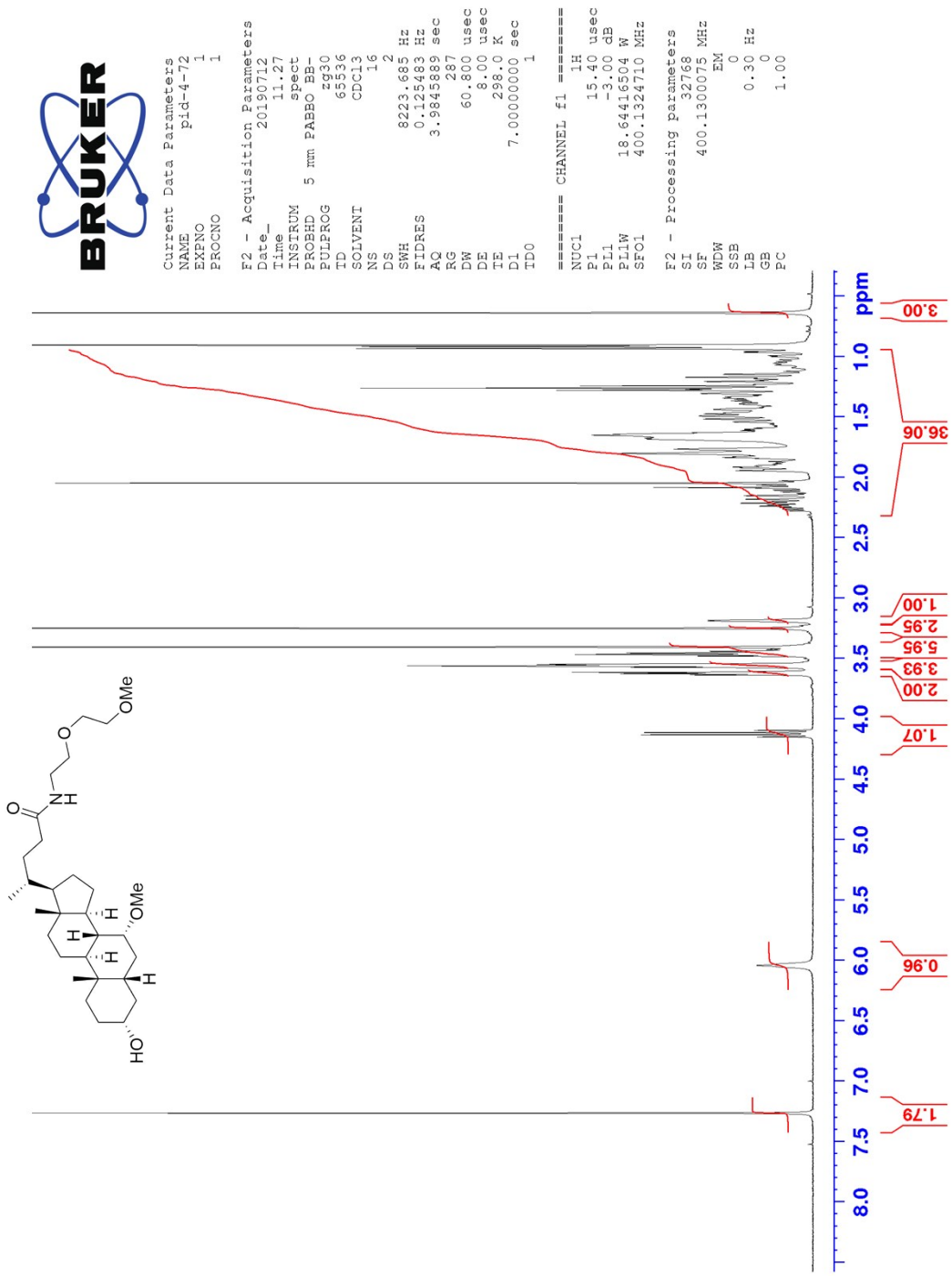


Figure S3. ^{1}H NMR spectrum of **15** (400 MHz, $CDCl_3$).

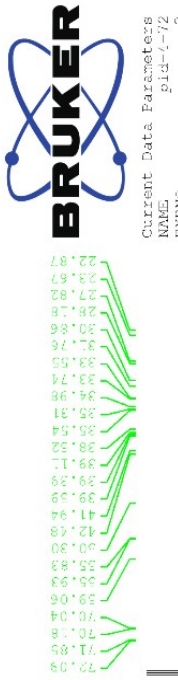
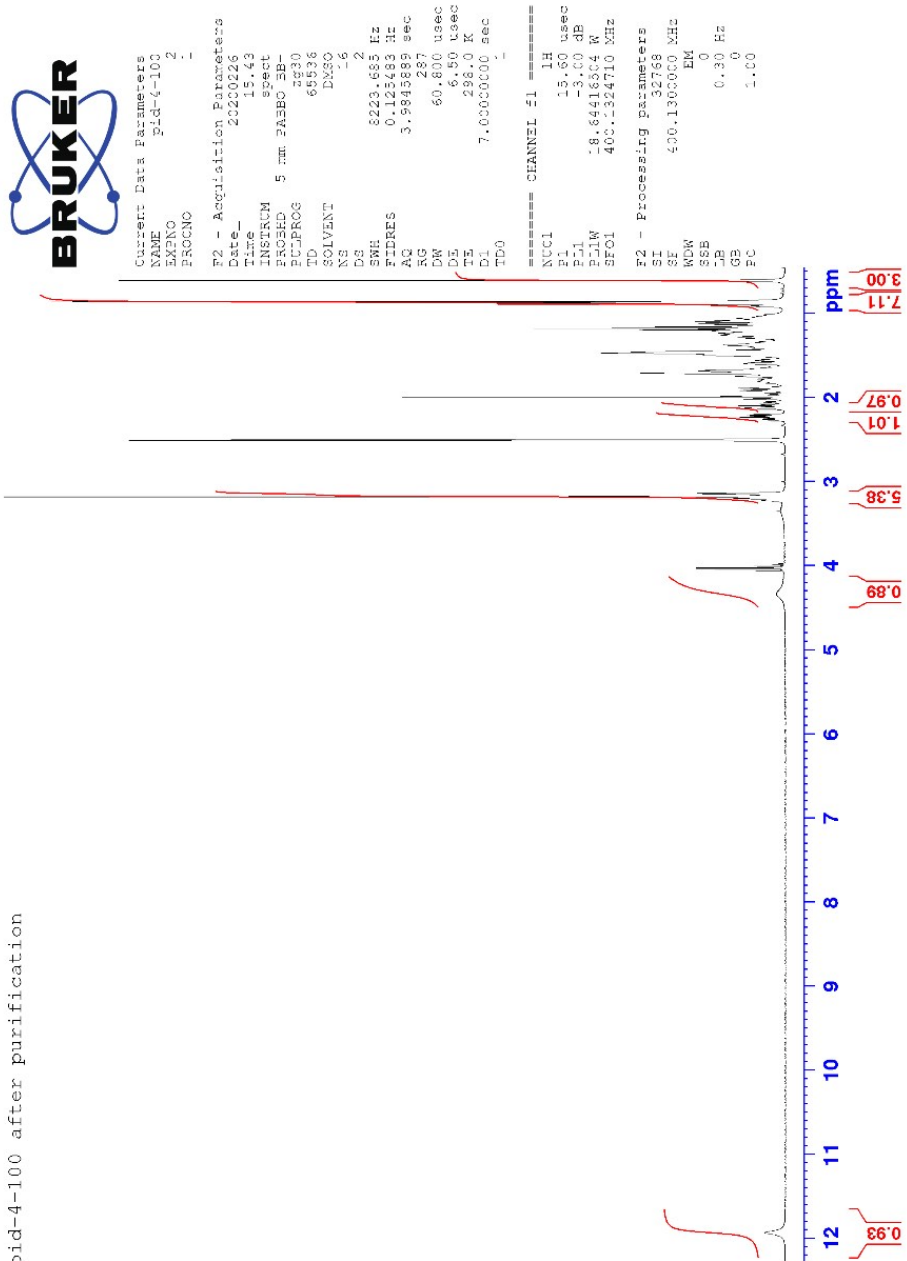


Figure S4. ^{13}C NMR spectrum of **15** (100 MHz, $CDCl_3$).



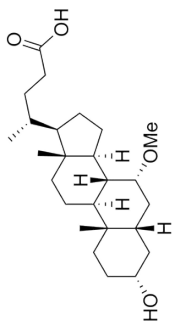


Figure S5. ^{1}H NMR spectrum of **16** (400 MHz, DMSO-d_6).

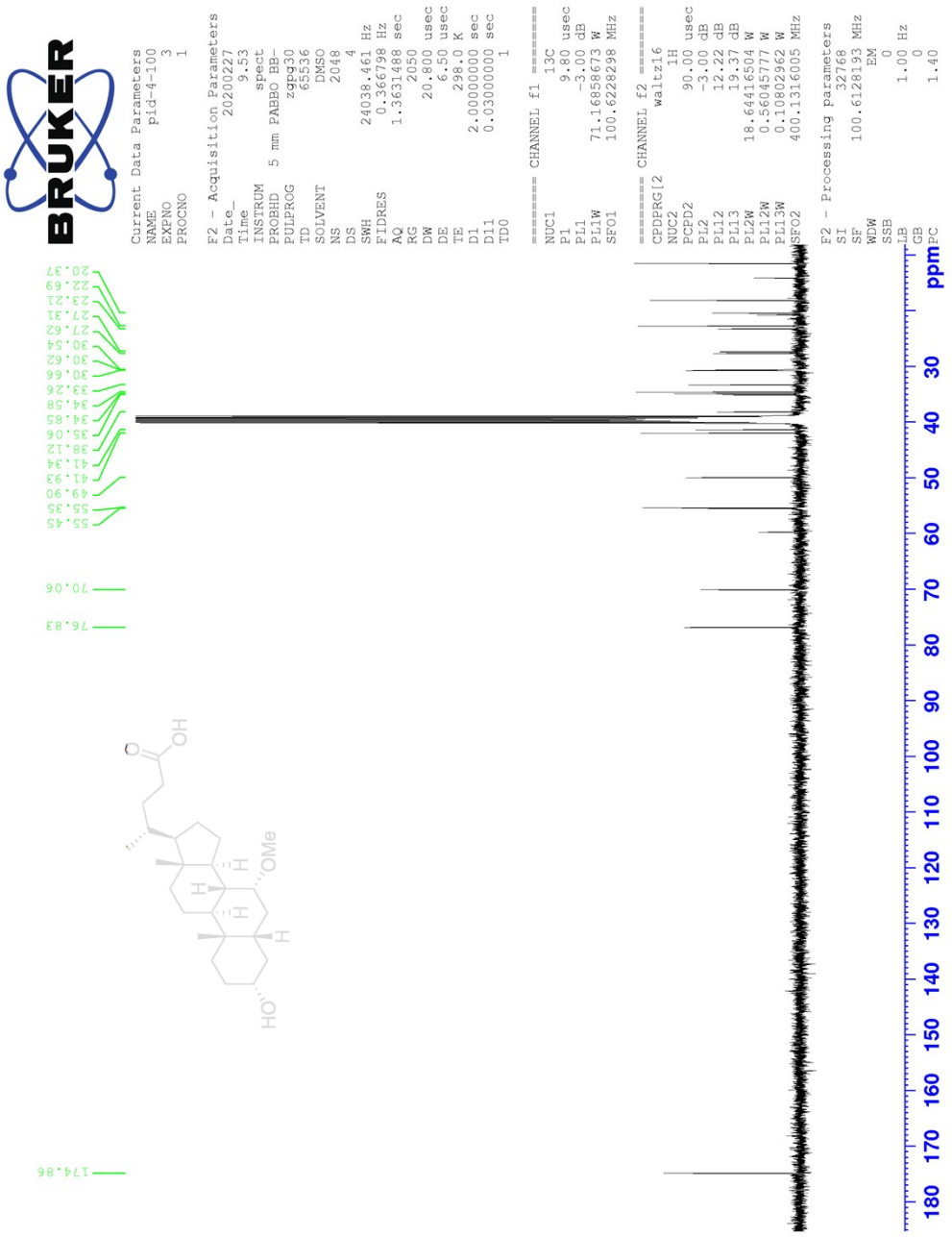


Figure S6. ^{13}C NMR spectrum of **16** (100 MHz, DMSO-d_6).

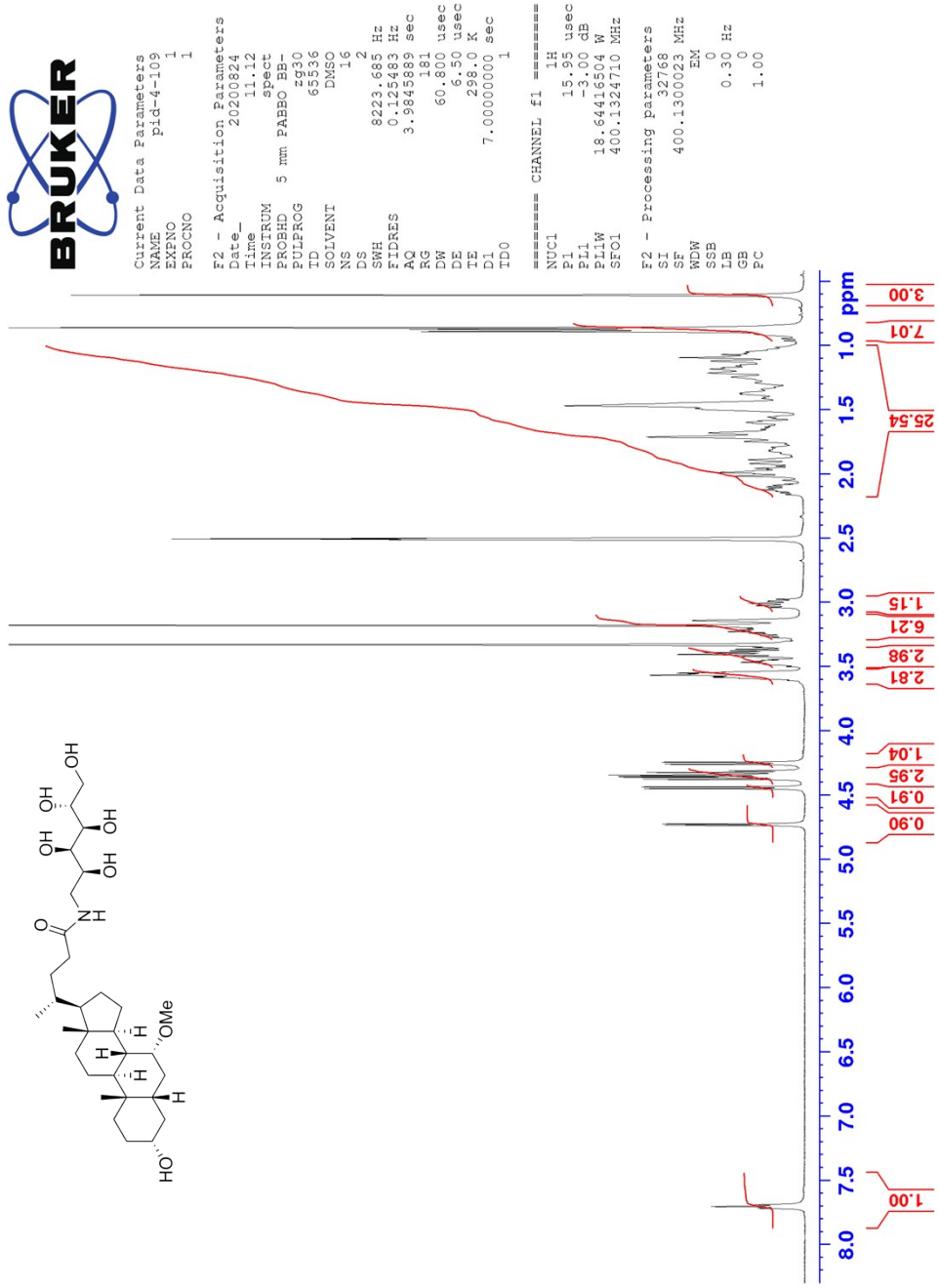


Figure S7. ^{1}H NMR spectrum of **17** (400 MHz, DMSO-d_6).

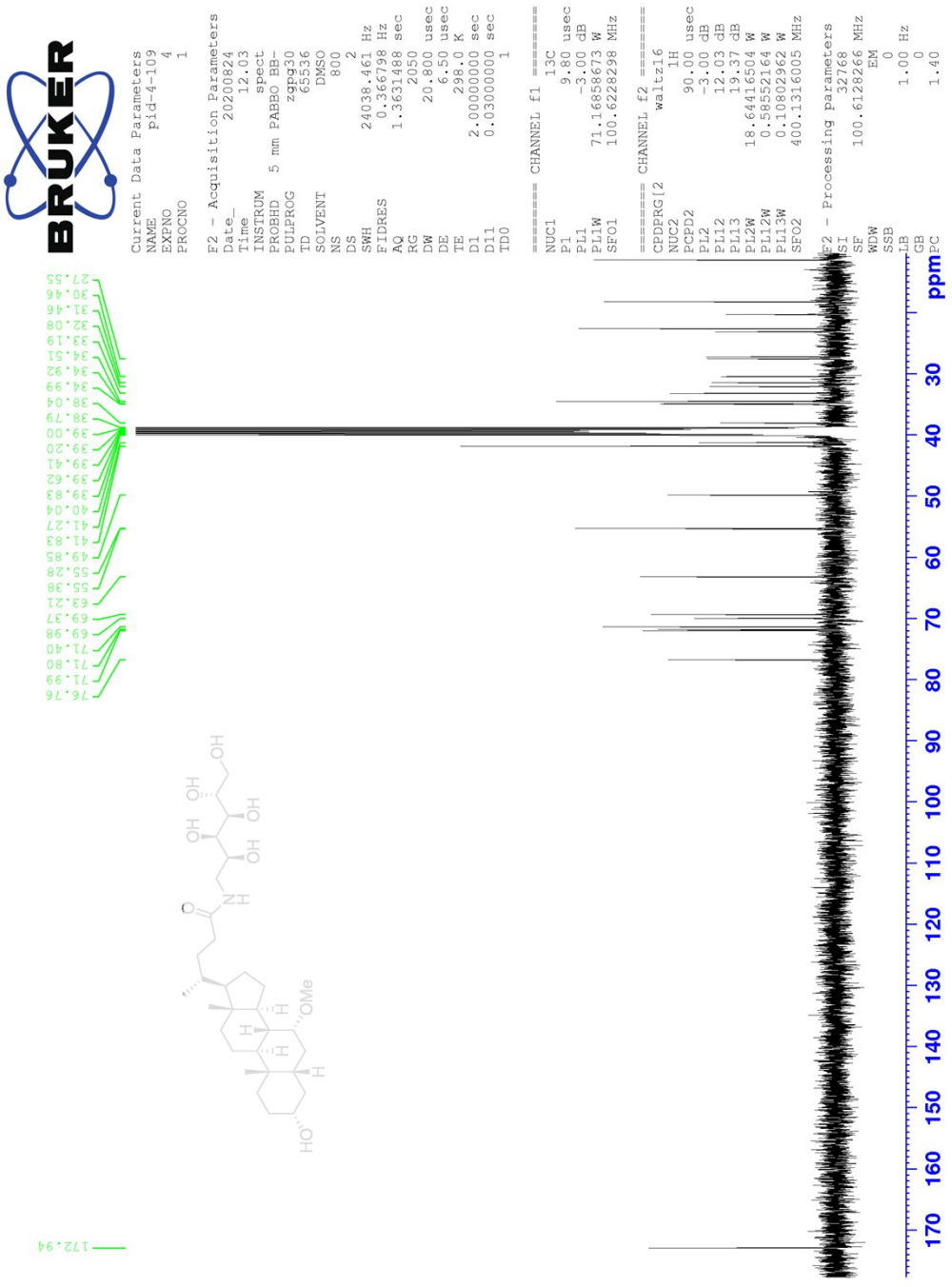


Figure S8. ^{13}C NMR spectrum of **17** (100 MHz, DMSO-d_6).

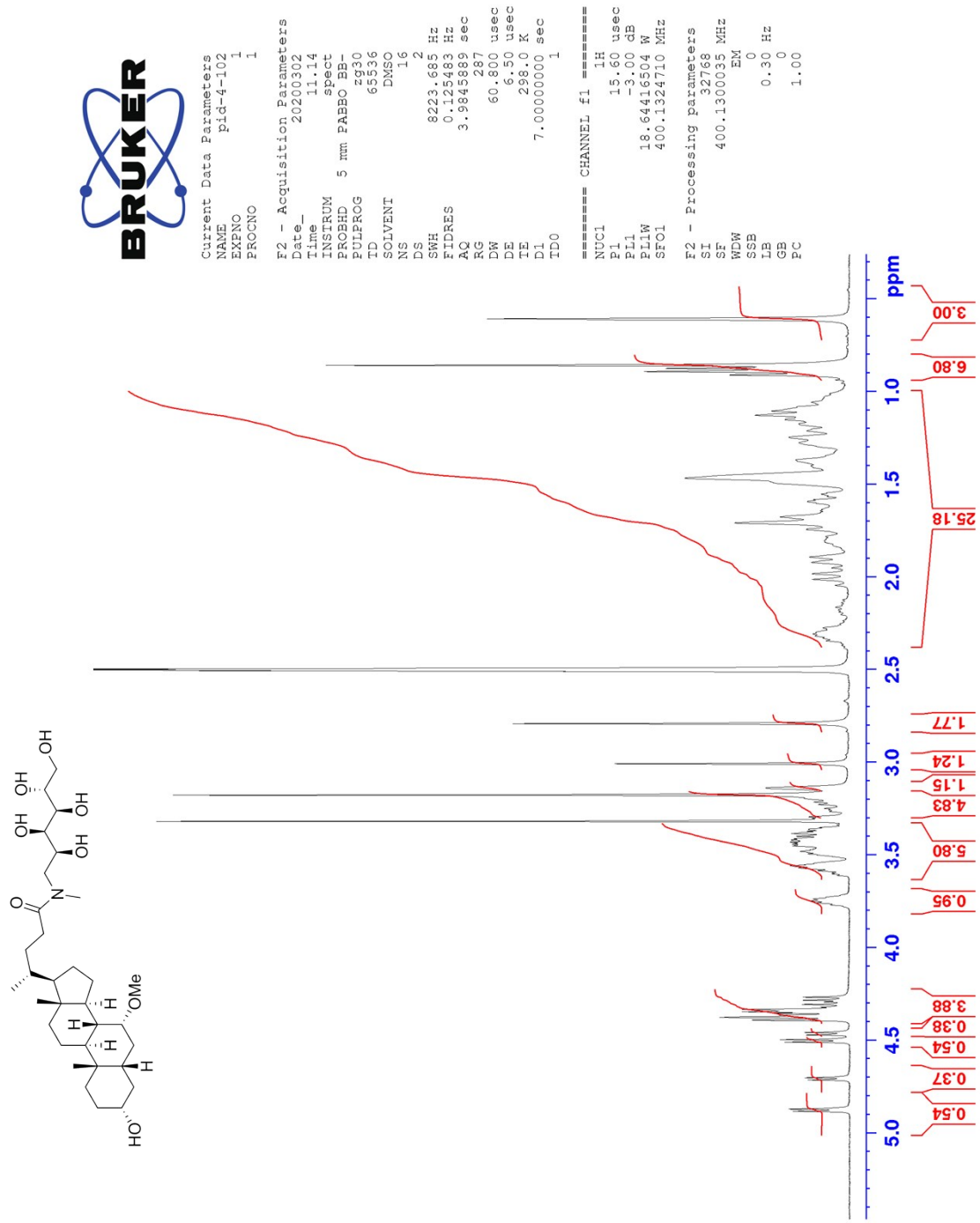


Figure S9. ^{1}H NMR spectrum of **18** (400 MHz, DMSO-d_6).

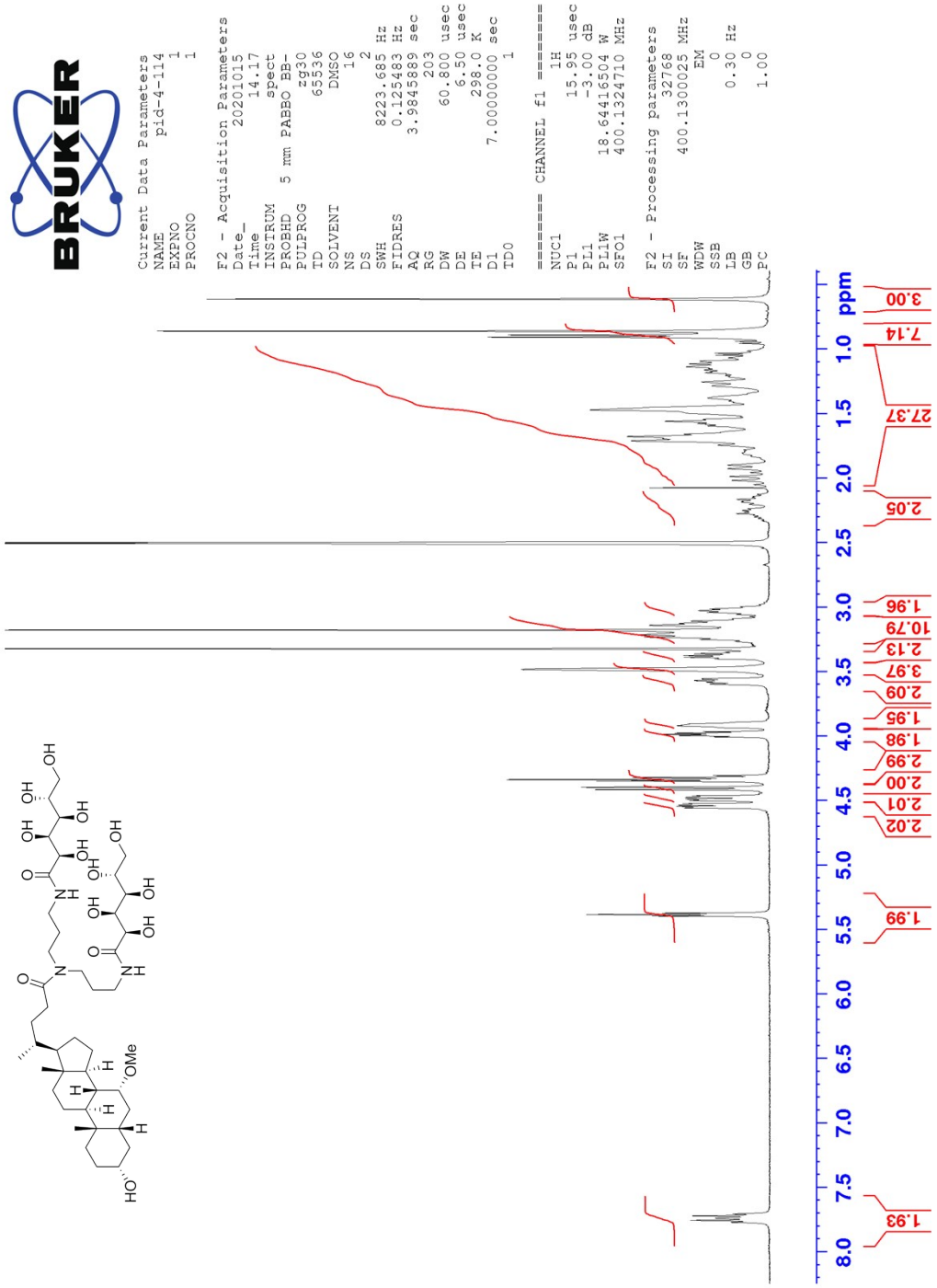


Figure S10. ^{1}H NMR spectrum of **19** (400 MHz, DMSO-d_6).

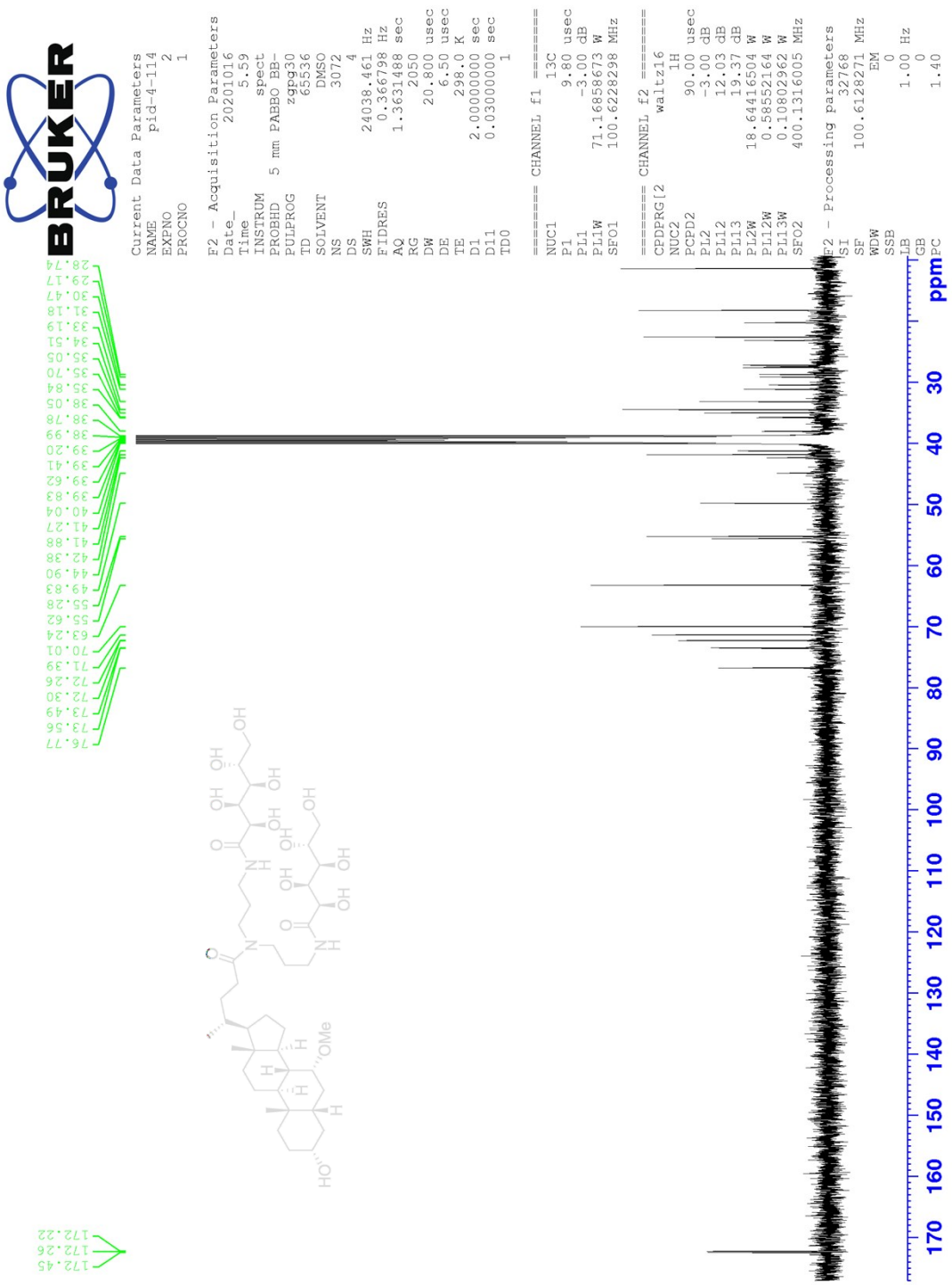
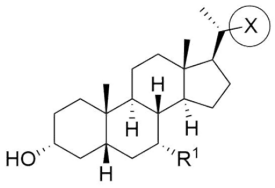
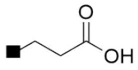
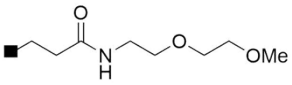
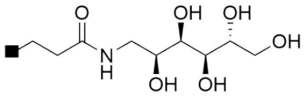
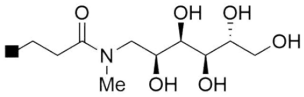
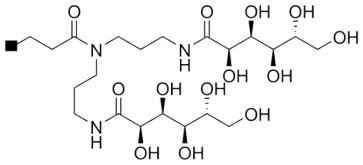
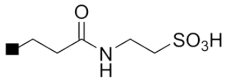


Figure S11. ^{13}C NMR spectrum of **19** (100 MHz, DMSO-d_6).

Table S1: TGR5 Agonist Activity of CDCA Analogs (Individual Experiments)



Compound	R^1	X	EC_{50} (nM)
16	-OMe		74.9, 78.8
15	-OMe		35.0, 64.0
17	-OMe		22.6, 32.8, 44.6
18	-OMe		60.1, 64.6
19	-OMe		597.1, 537.6
TLCA	-H		816.5, 941.6, 1080.5, 1182.8