Supplemental Information for

Synthesis and evaluation of carbagalactosyl 1,2 aziridines and epoxides as potential glycosidase inhibitors

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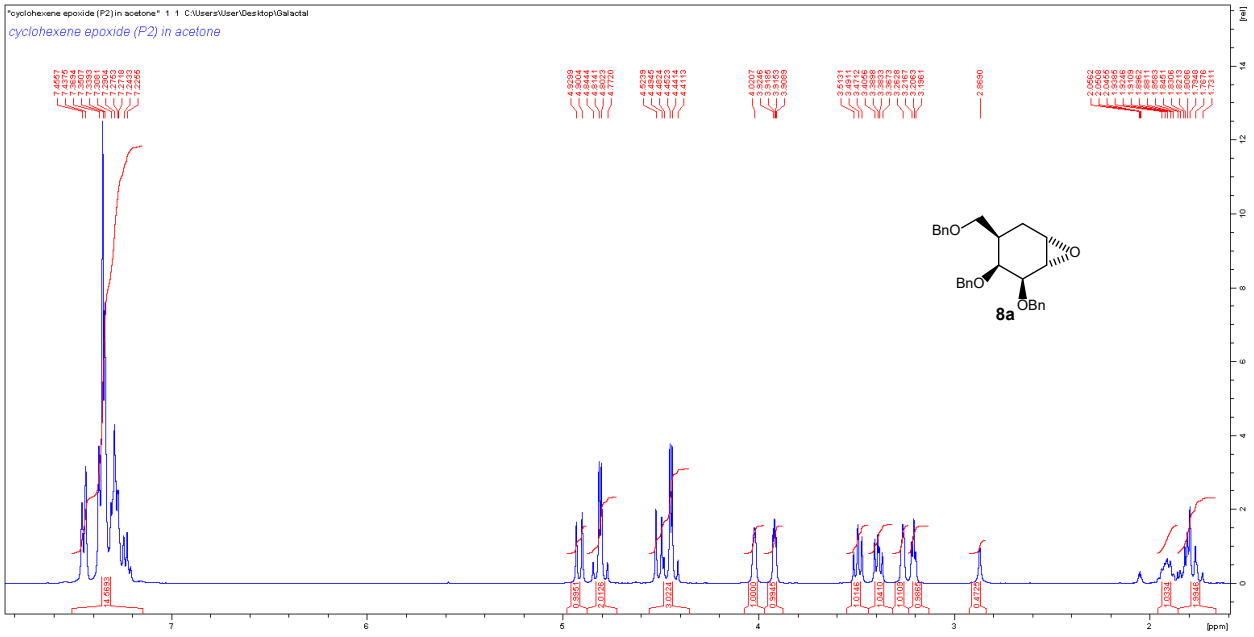


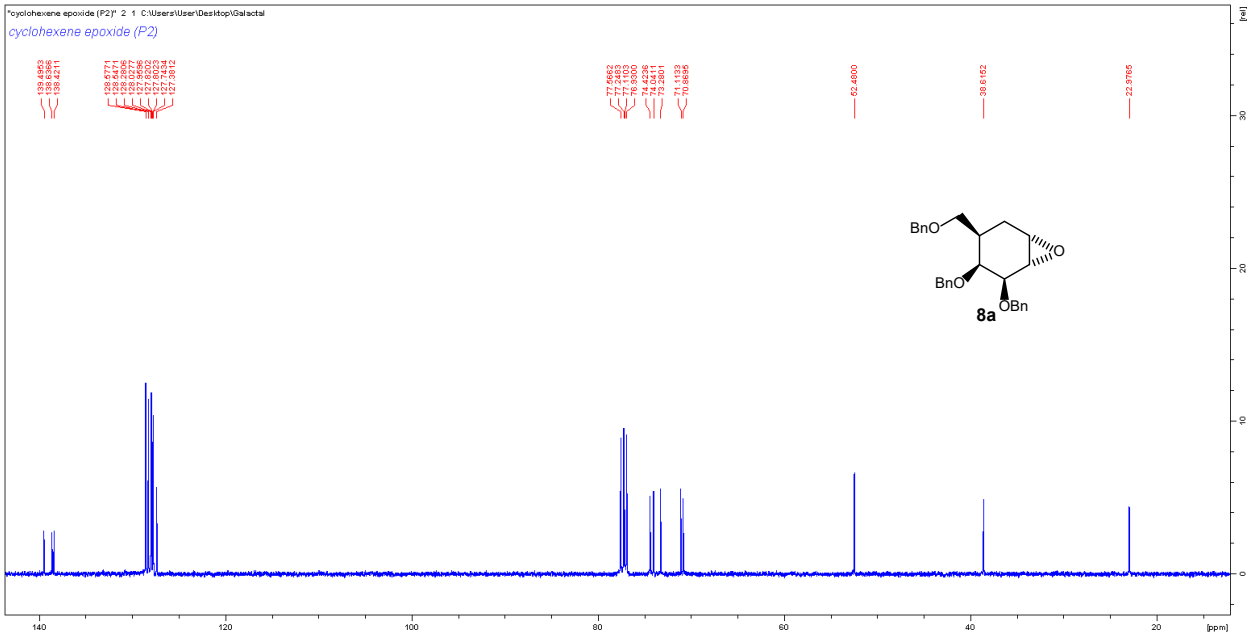
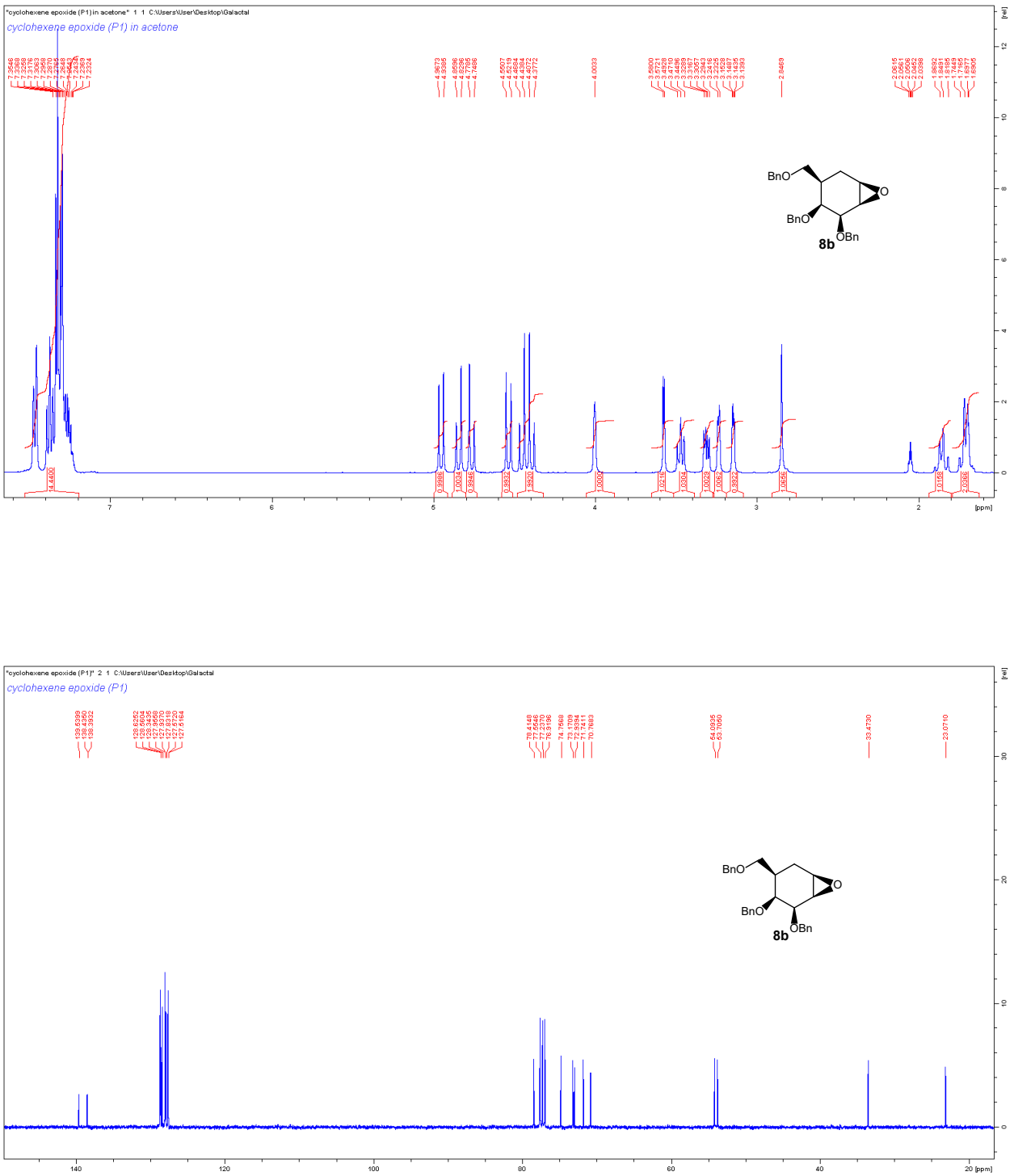


Figure S1 ^{1}H and ^{13}C NMR of (8a).



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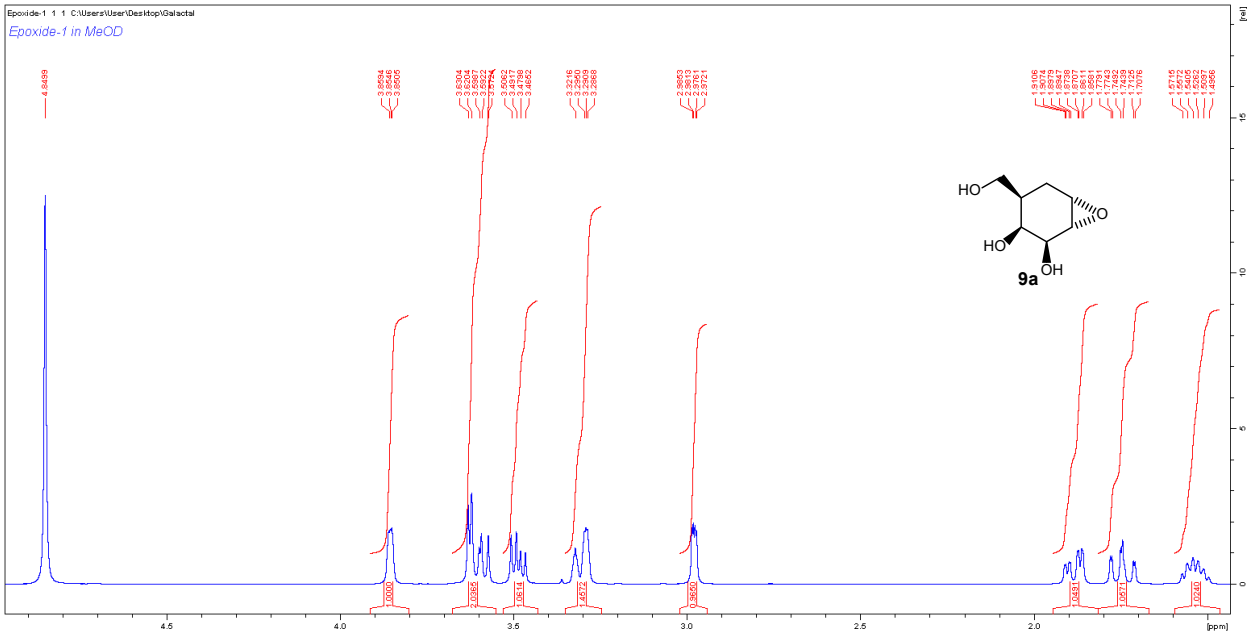

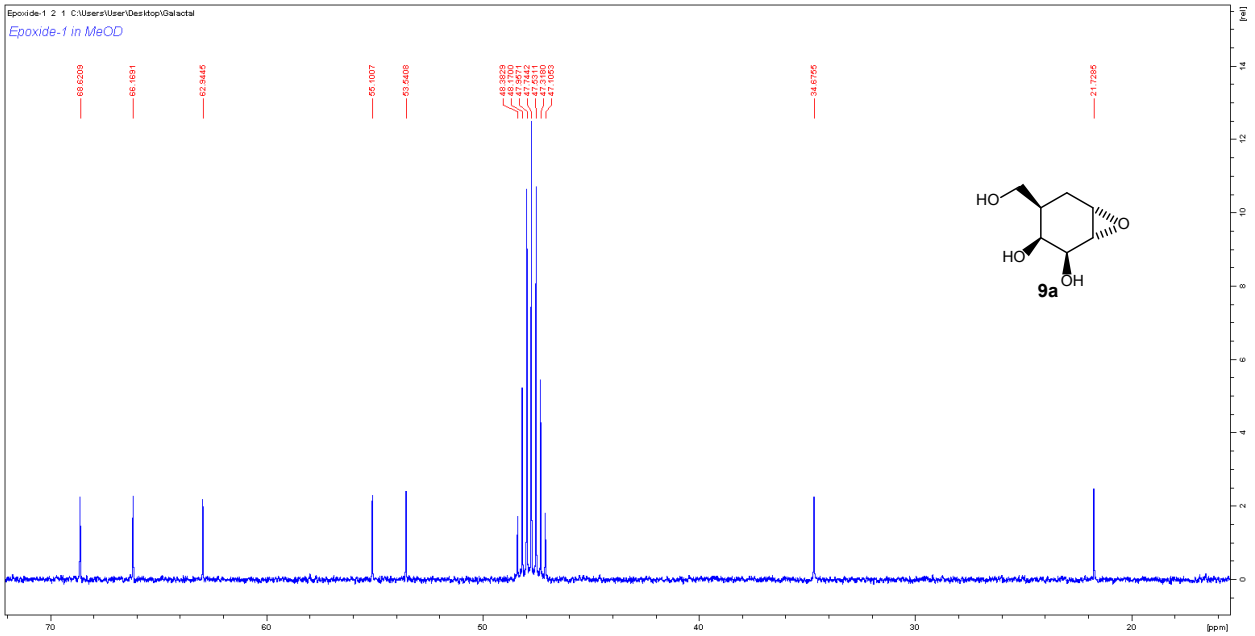

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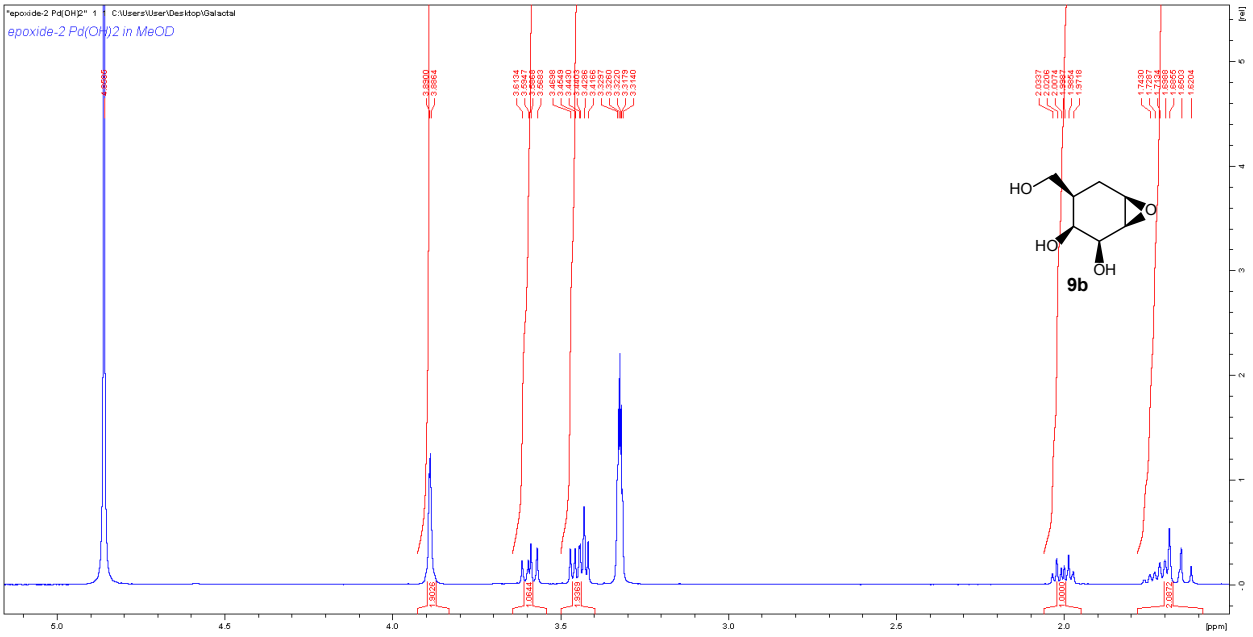

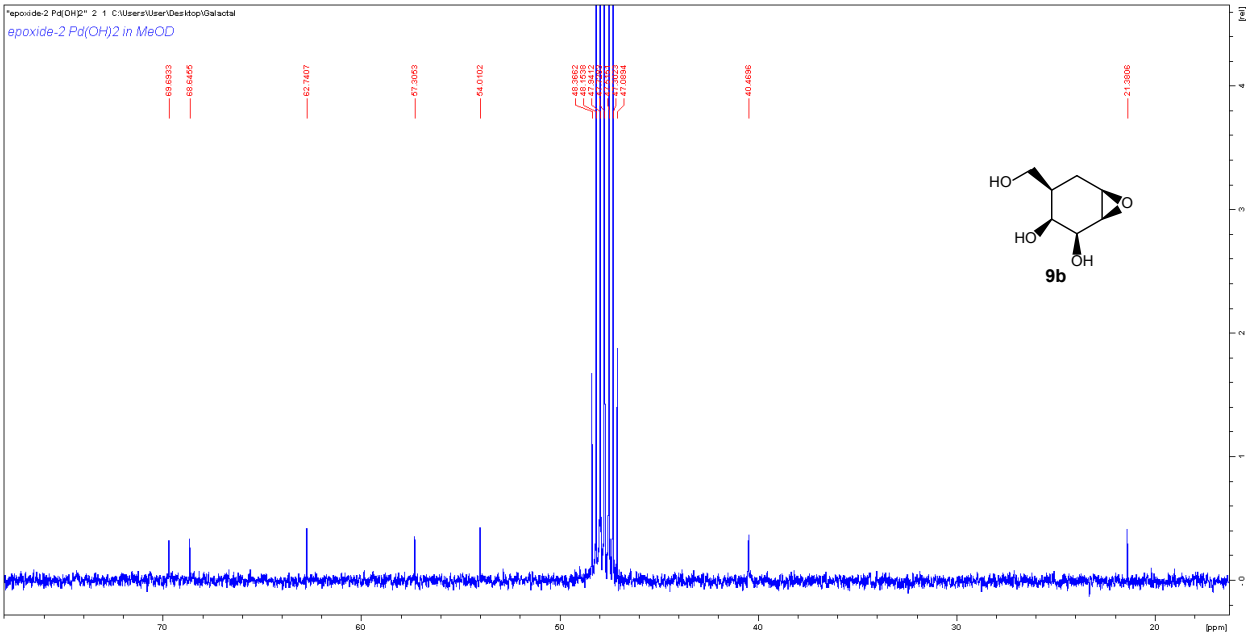

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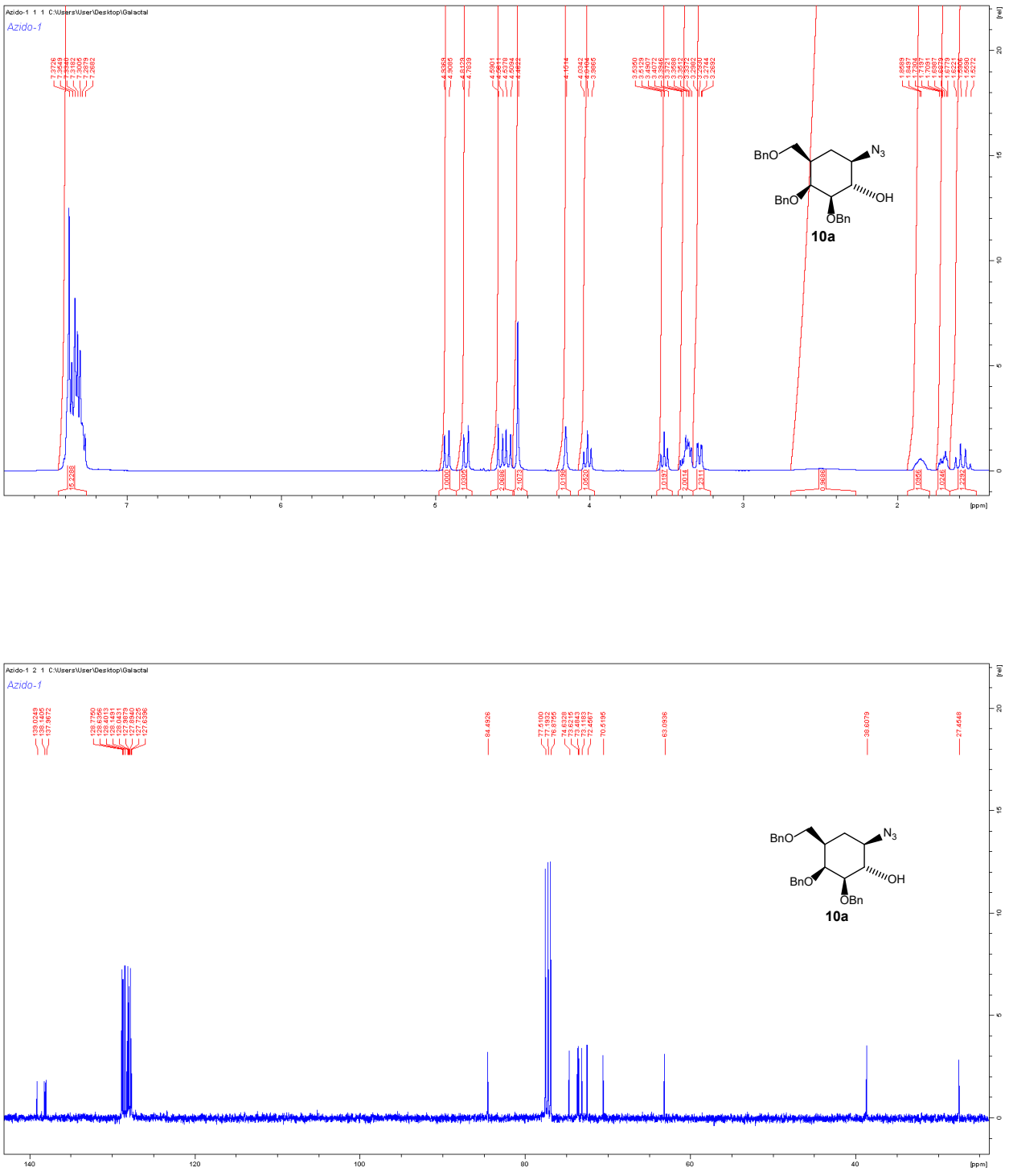


Figure S5 ^{1}H and ^{13}C NMR of (10a).

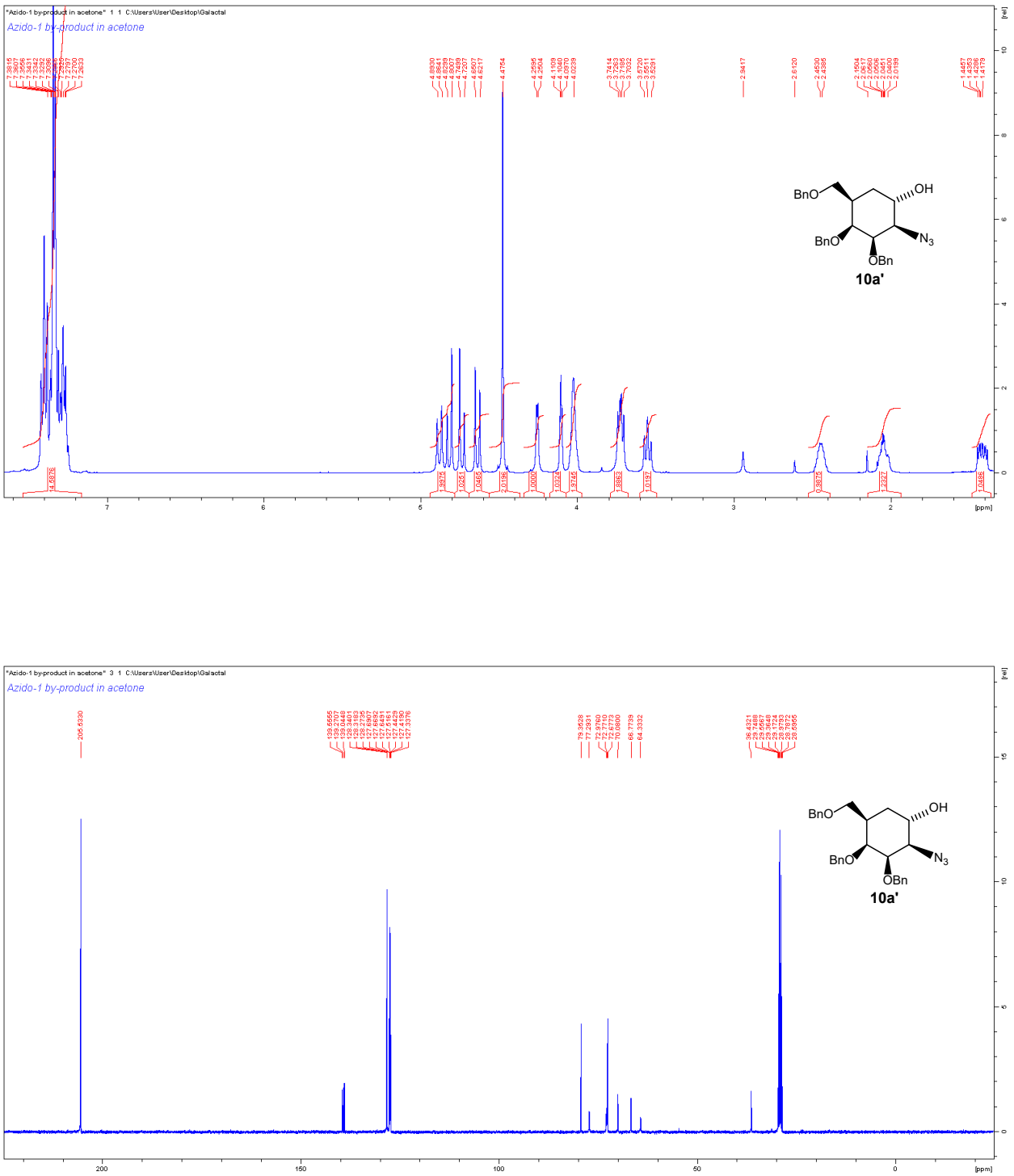
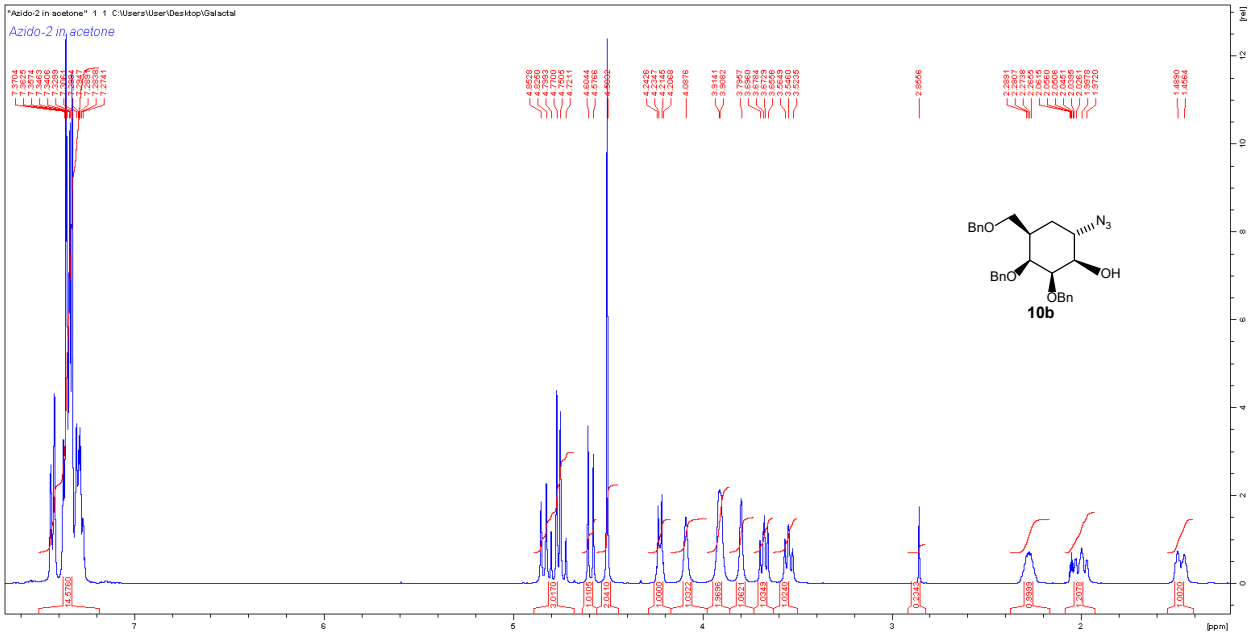


Figure S6 ^{1}H and ^{13}C NMR of (10a').



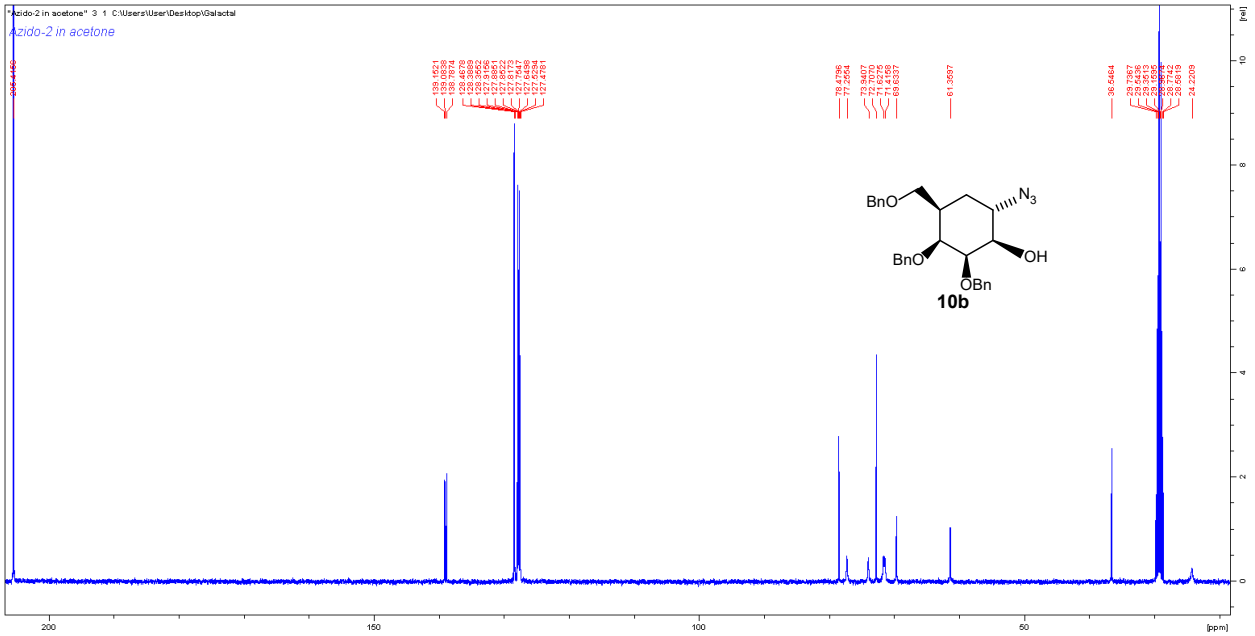


Figure S7 ^{1}H and ^{13}C NMR of (10b).

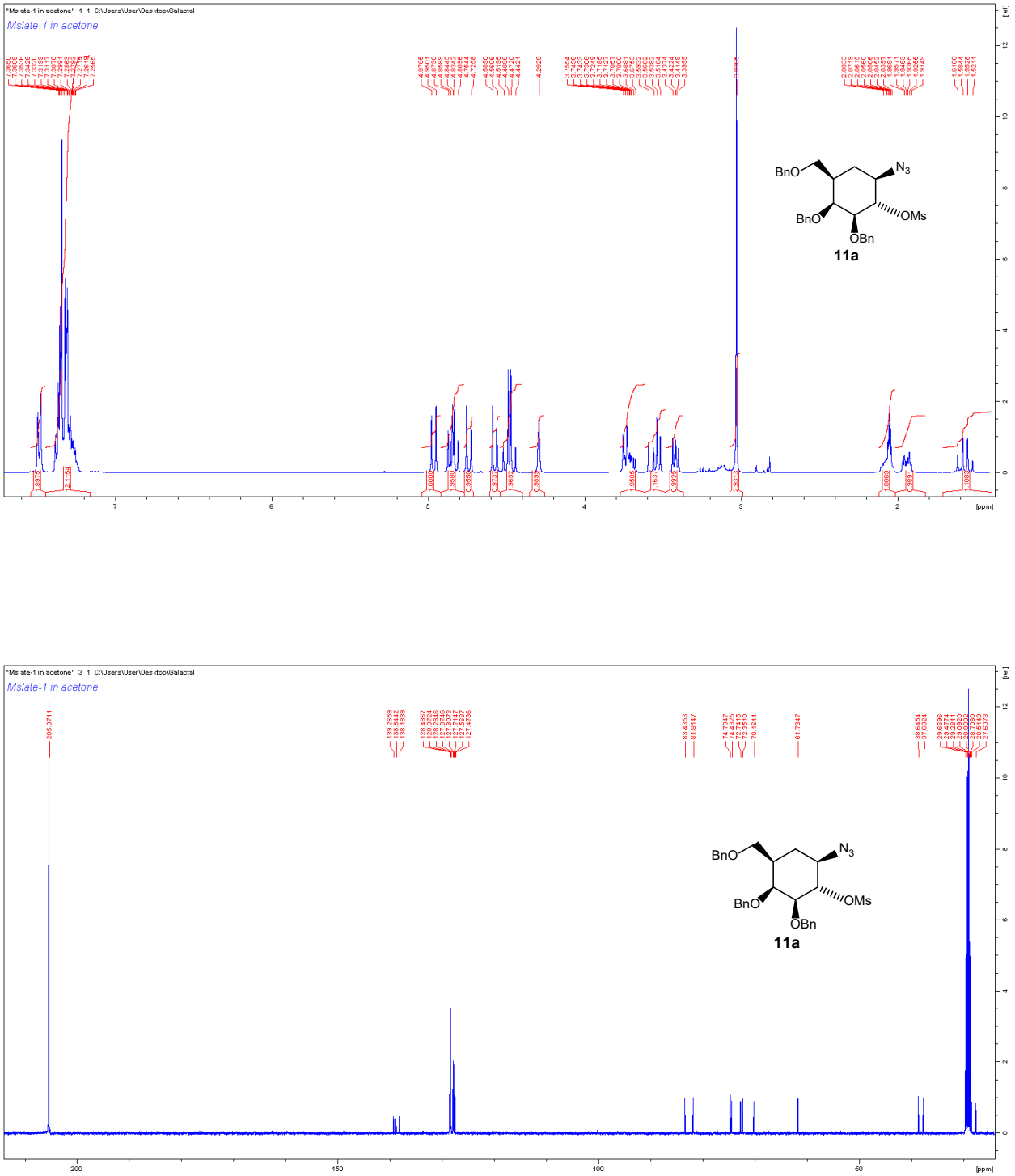


Figure S8 ^{1}H and ^{13}C NMR of (11a).

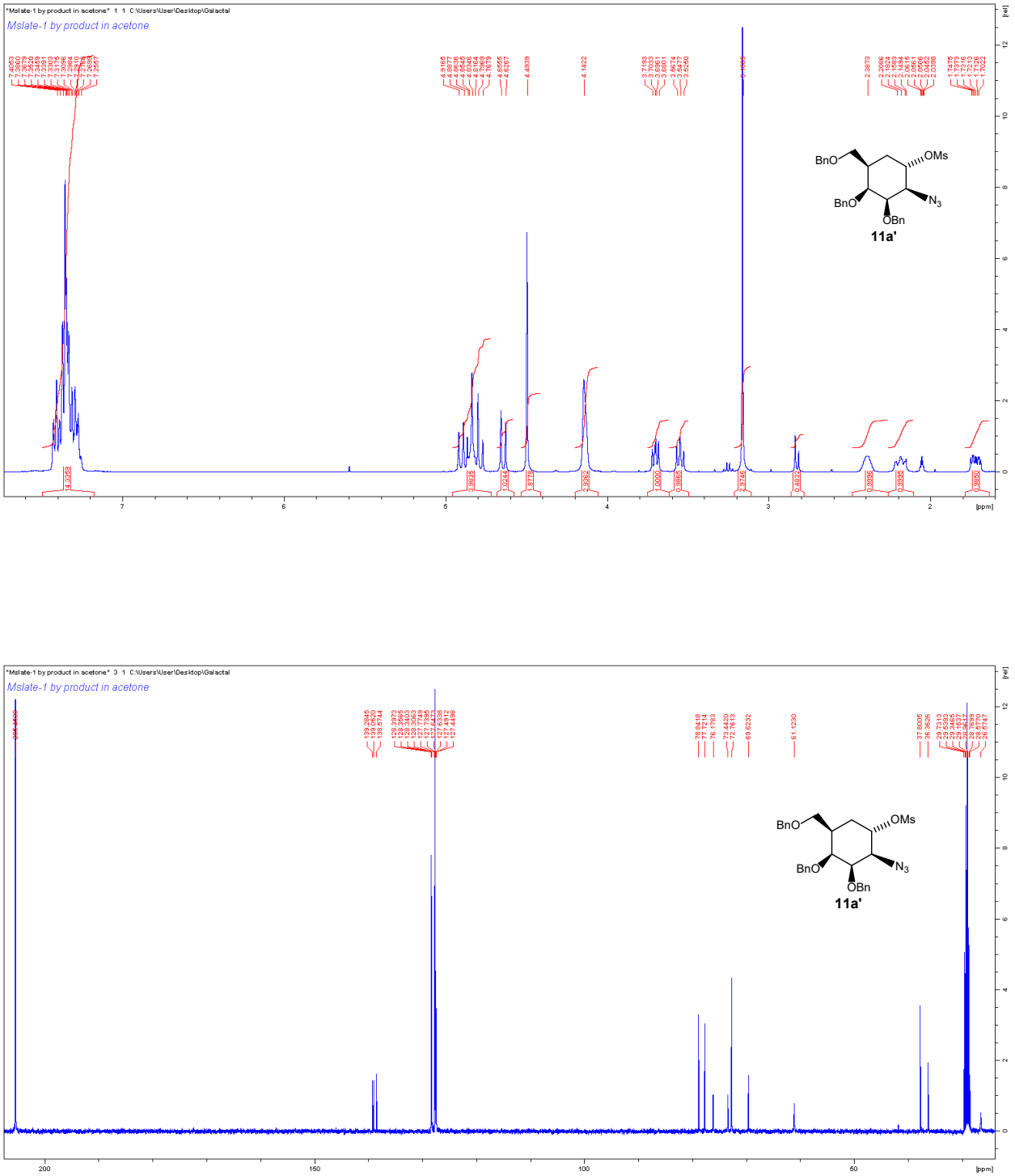


Figure S9 ^{1}H and ^{13}C NMR of (11a').

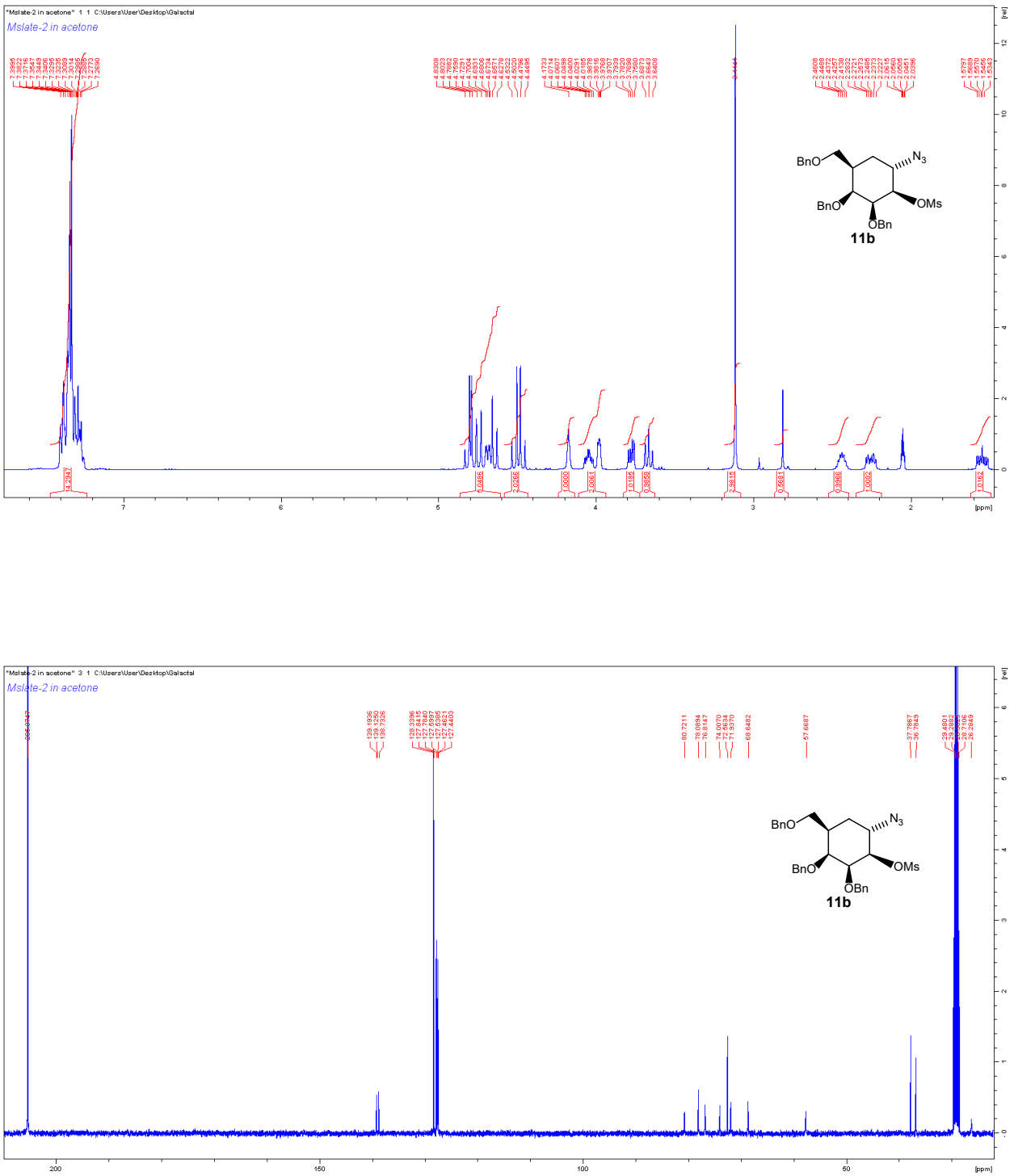
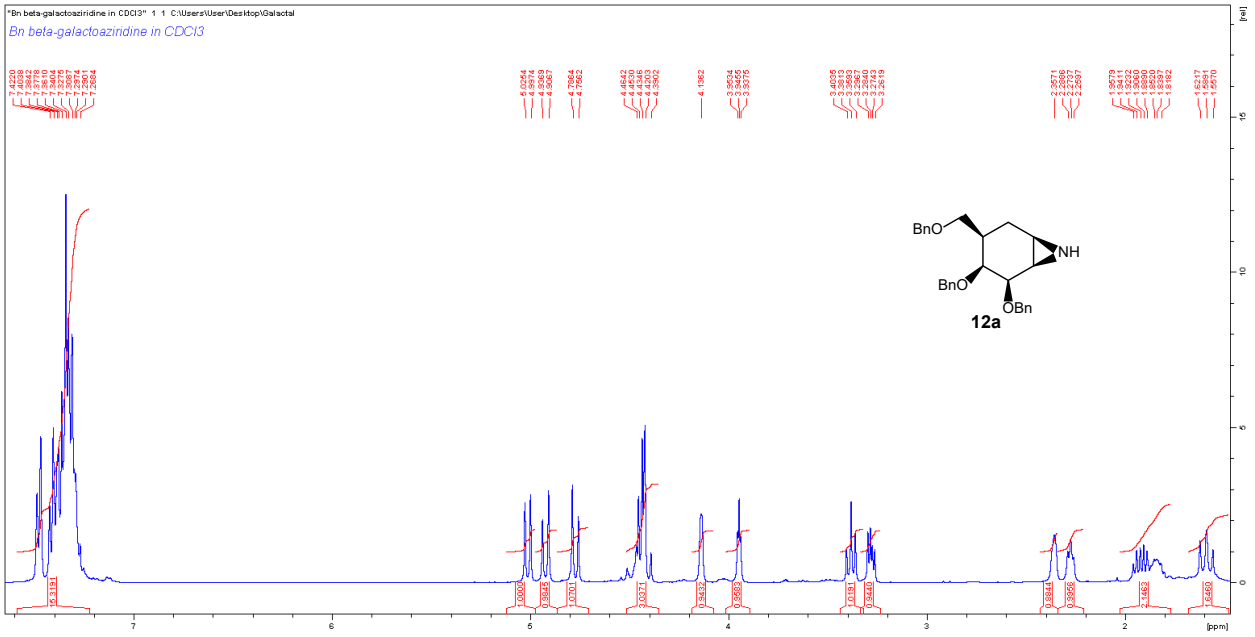


Figure S10 ^{1}H and ^{13}C NMR of (11b).



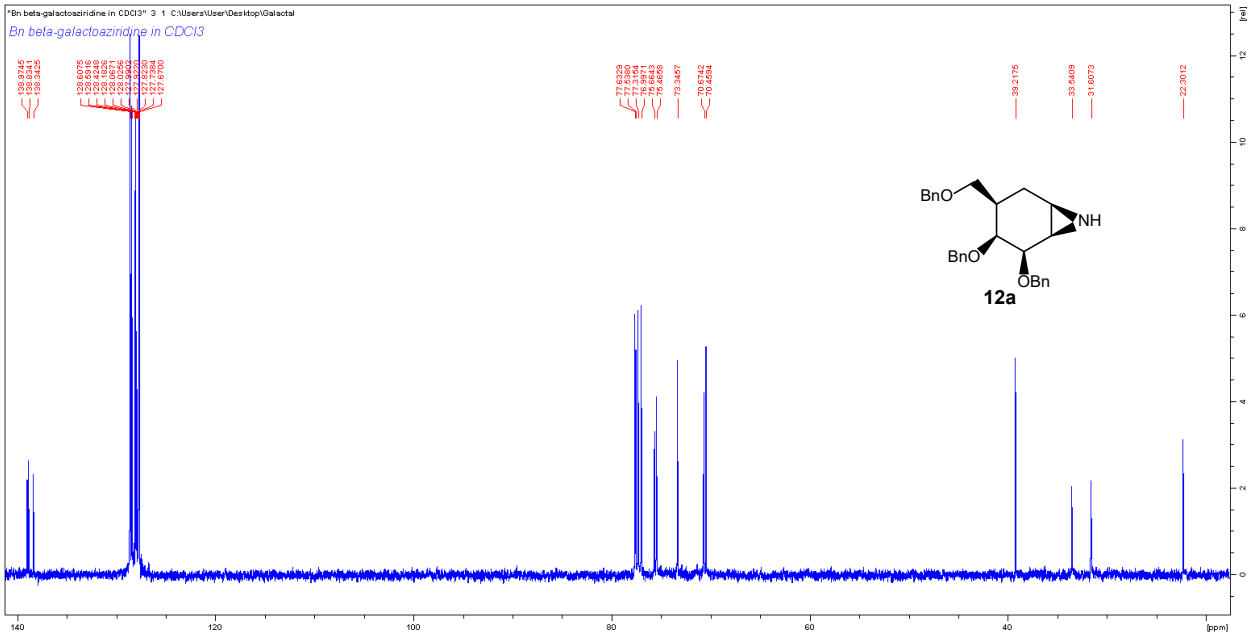
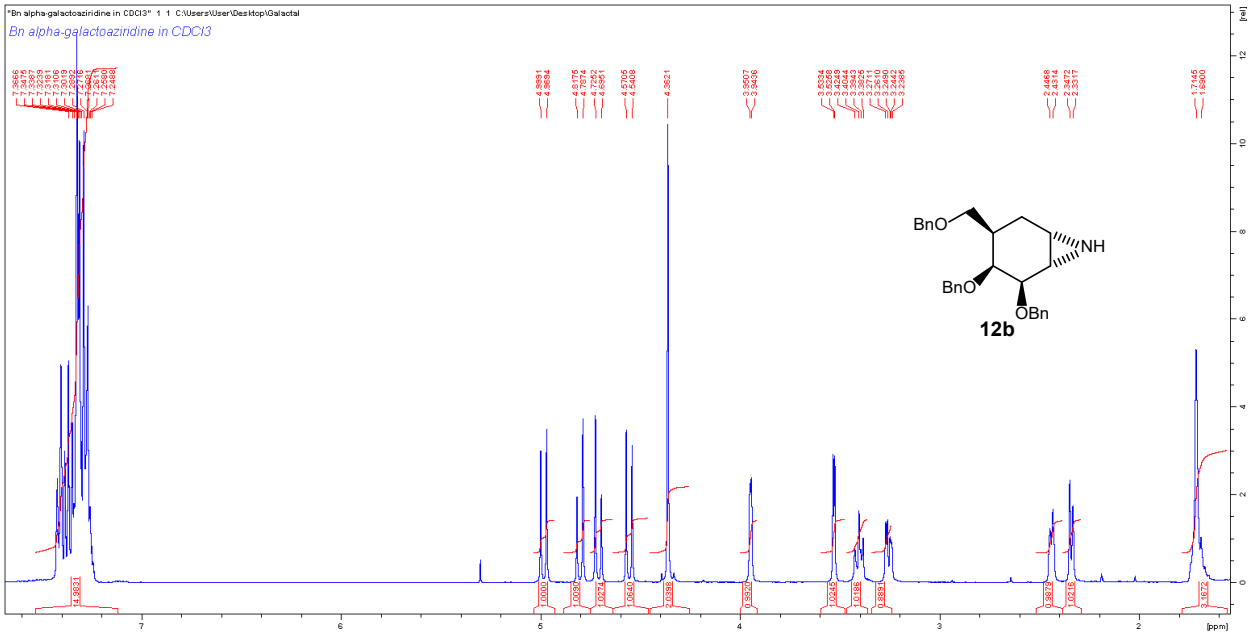


Figure S11 ^{1}H and ^{13}C NMR of (12a).



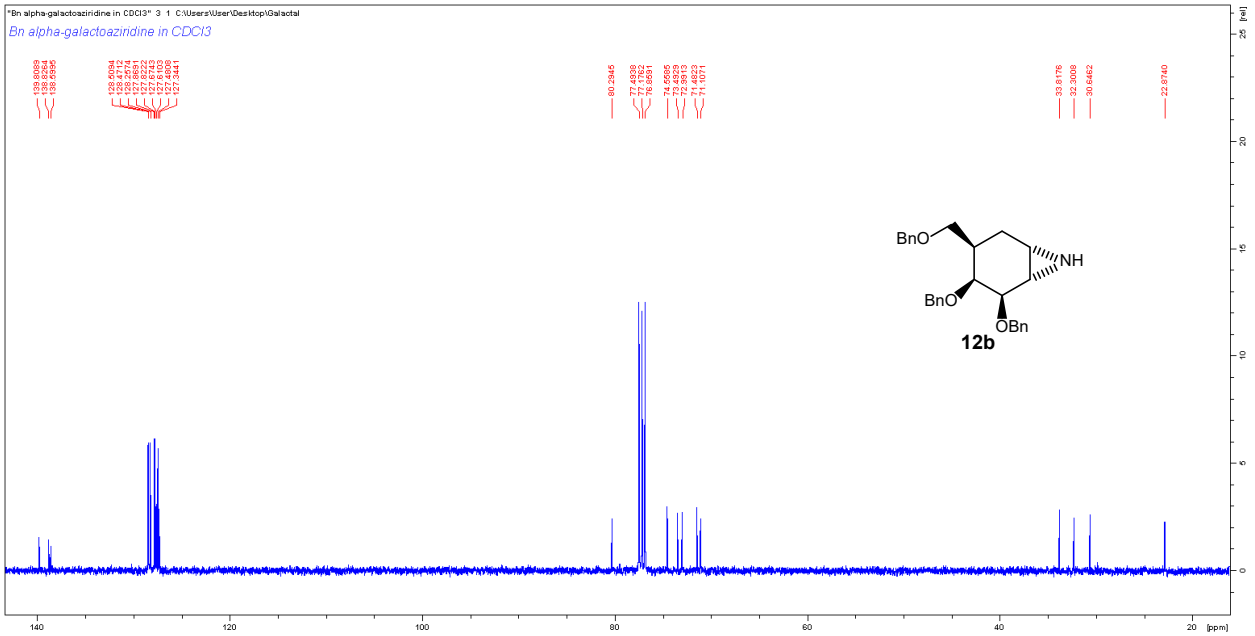


Figure S12 ^{1}H and ^{13}C NMR of (12b).

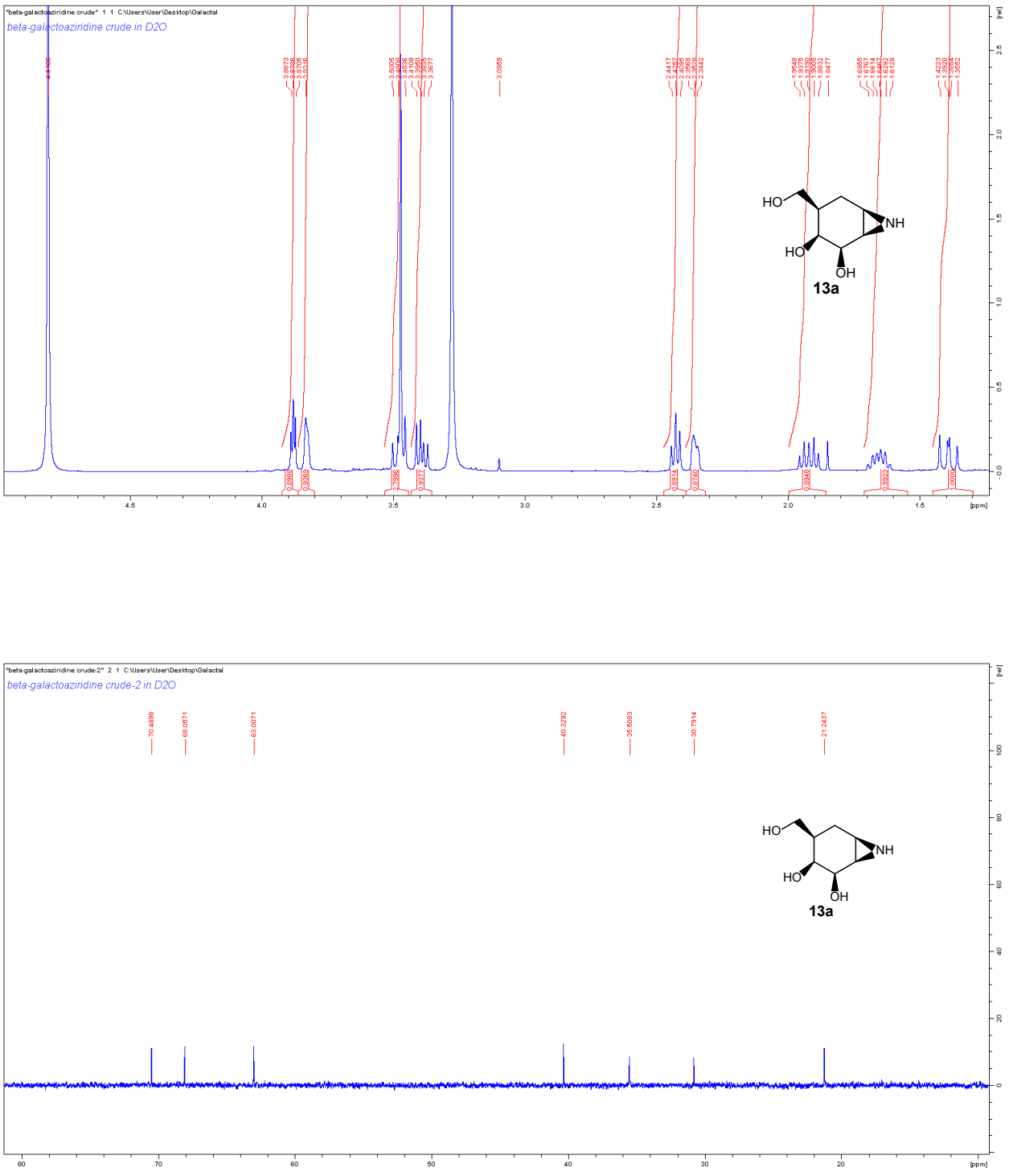


Figure S13 ^{1}H and ^{13}C NMR of (13a).

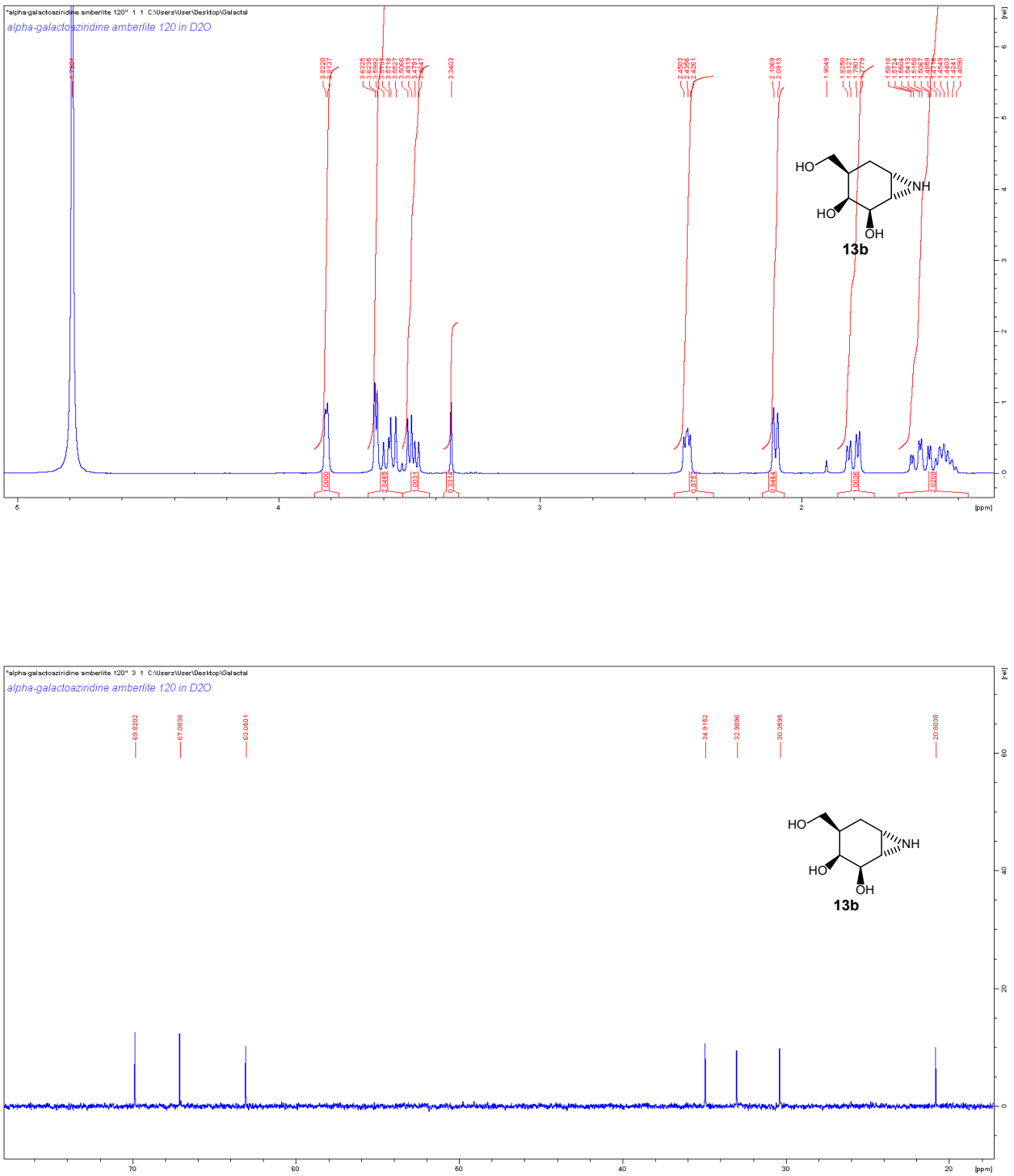


Figure S14 ^{1}H and ^{13}C NMR of (13b).

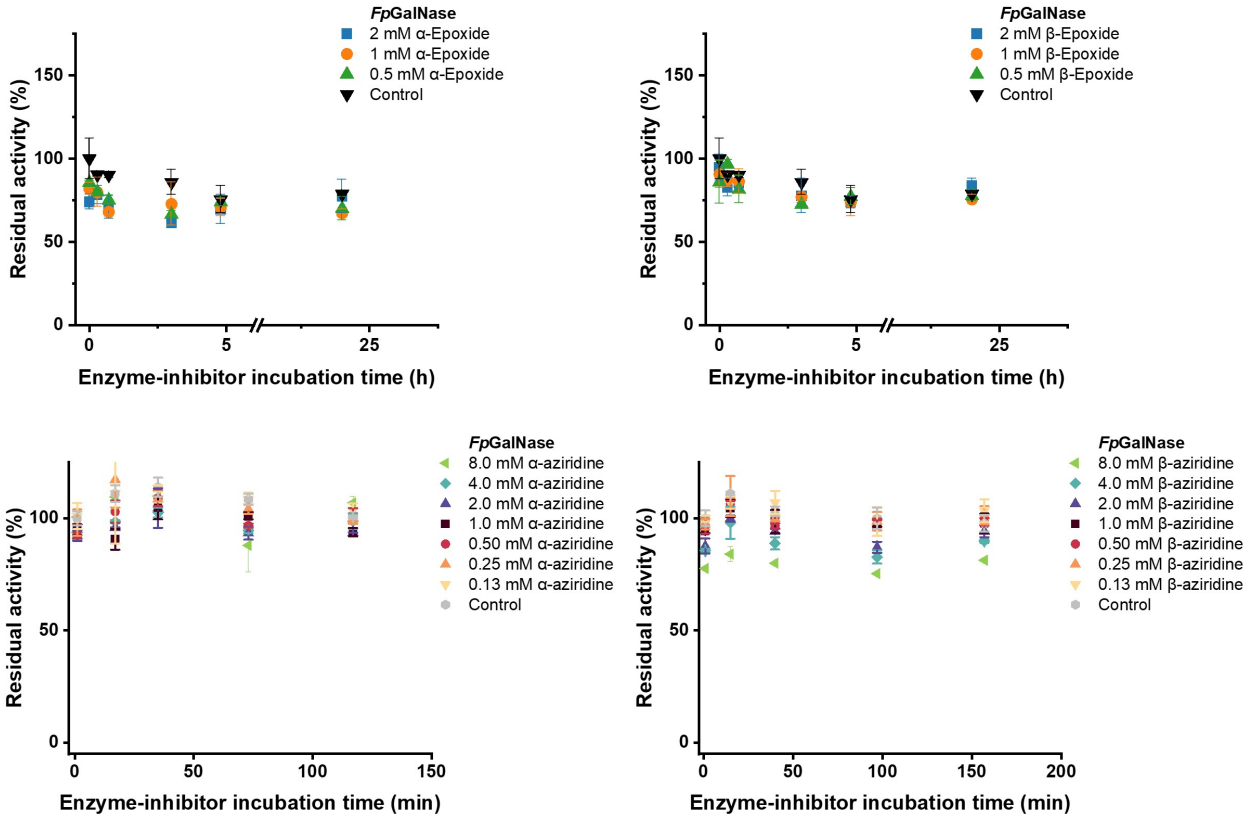


Figure S15 Preliminary inhibitory test of epoxides and aziridines on *Fp*GalNase. During the incubation, the protein concentrations were approximately 0.65 μM for *Fp*GalNase. Activity assay for *Fp*GalNase was performed using 100 μM GalN-α-MU in HEPES buffer (pH 7.4).

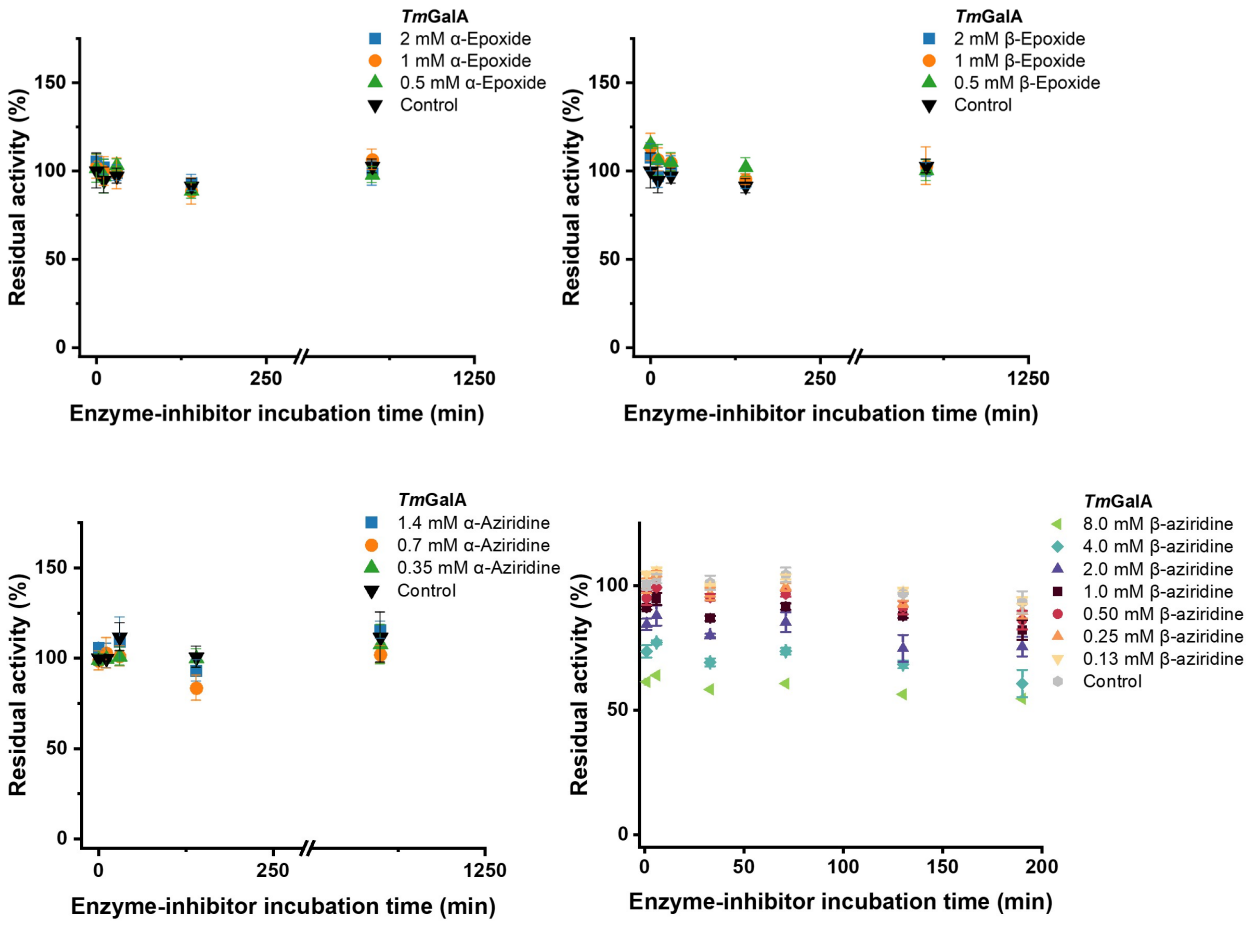


Figure S16 Preliminary inhibitory test of epoxides and aziridines on *Tm*GalA.

During the incubation with the inhibitor, the protein concentrations of *Tm*GalA were 0.2 μM with 0.1 mg/mL BSA. Activity assay was performed using 200 μM Gal-α-*p*NP in Napi buffer (pH 7.4).

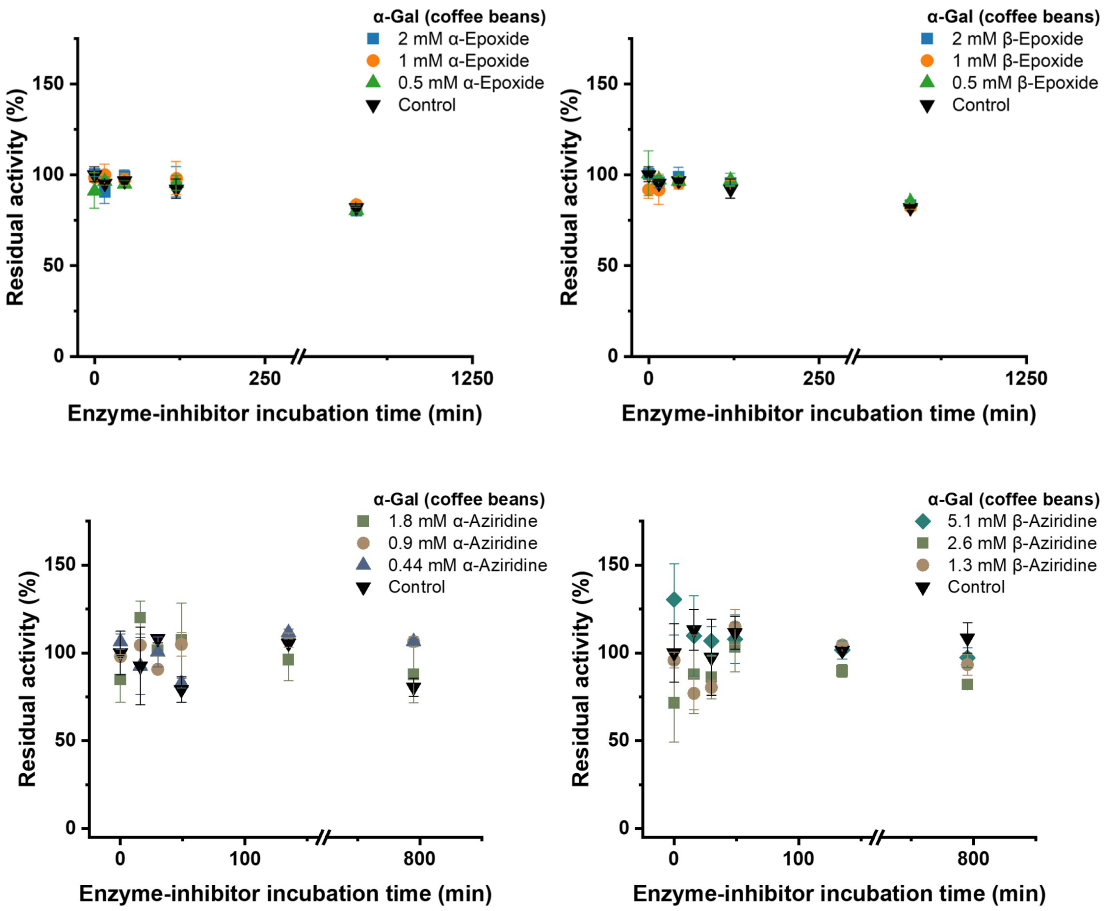


Figure S17 Preliminary inhibitory test of epoxides and aziridines on α-Gal from green coffee beans.

During the incubation with the inhibitor, the protein concentrations were approximately 1 μg/mL for α-Gal from coffee beans (with 0.1 mg/mL BSA). Activity assays for α-Gal from coffee beans was performed using 200 μM Gal-α-pNP in PBS (pH 7.4).

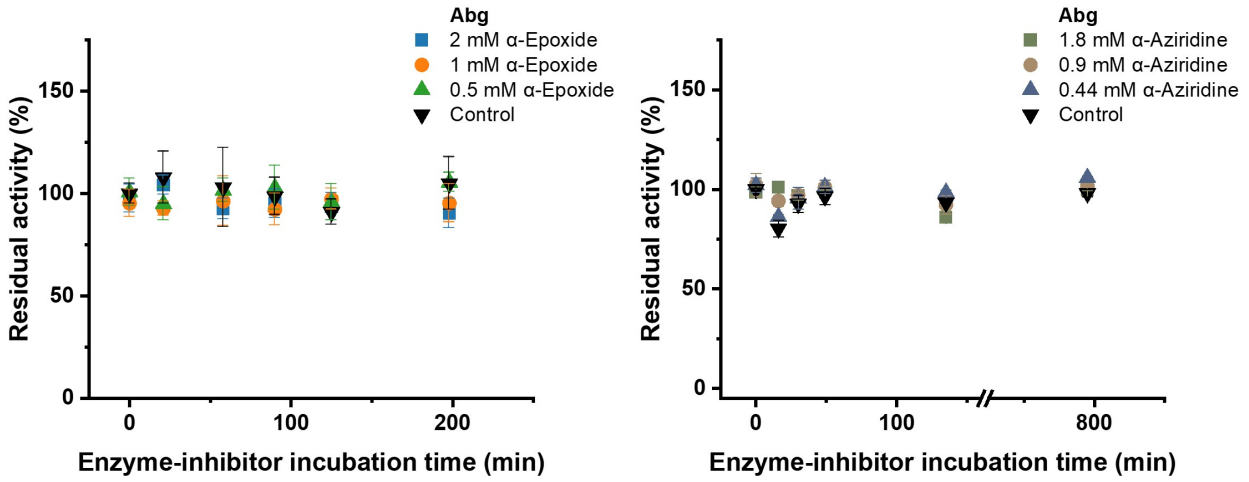


Figure S18. Preliminary inhibitory test of α-epoxide and α-aziridine on Abg.

Residual activities of Abg were measured after incubation with varying concentrations of compounds over different time periods. During the incubation, the protein concentrations were approximately 1.9 nM for Abg (with 0.1 mg/mL BSA). For the activity assay, 100 μM Gal-β-MU was used as the substrate, in PBS (pH 7.4).

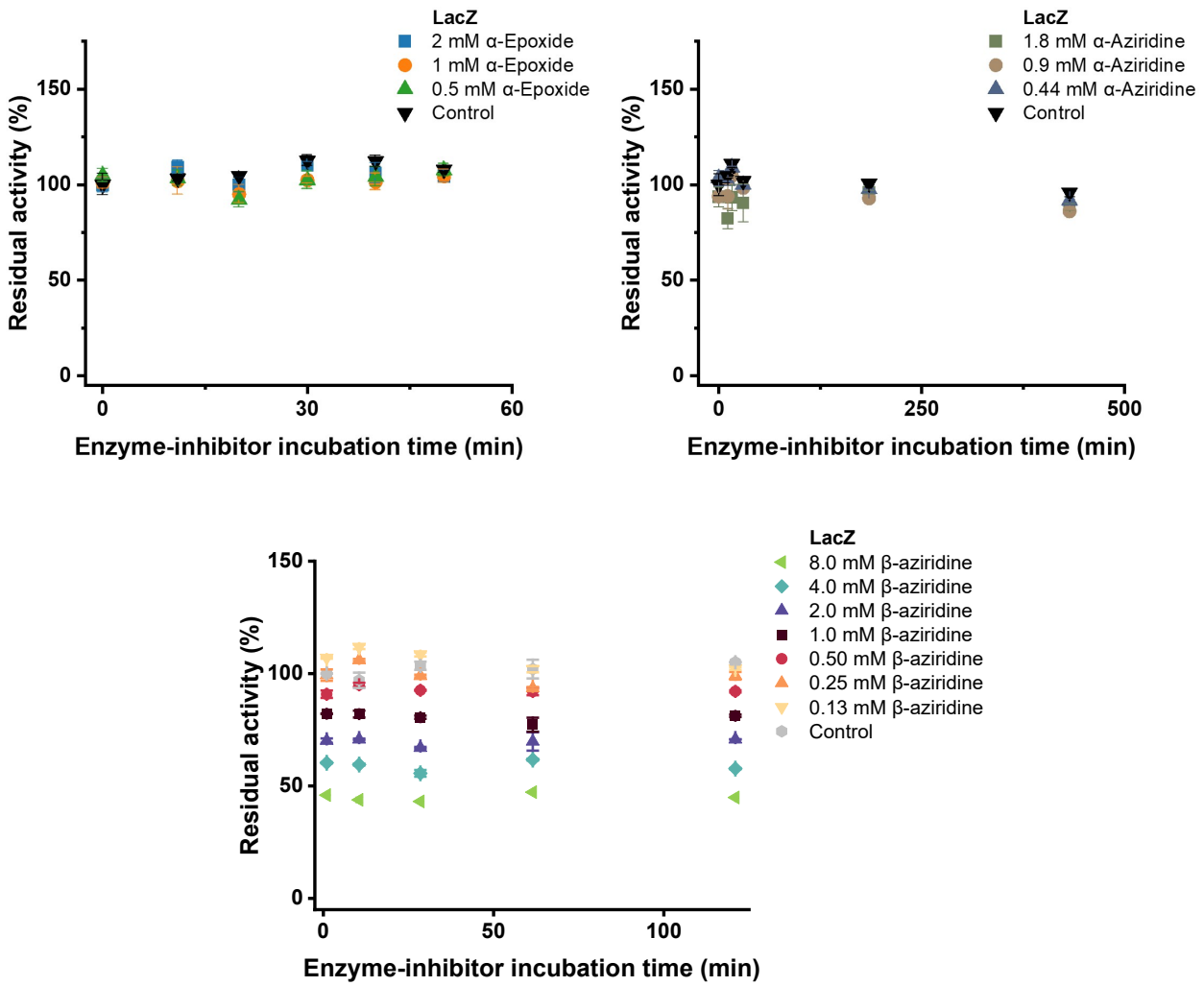


Figure S19. Preliminary inhibitory test of epoxides and aziridines on LacZ.

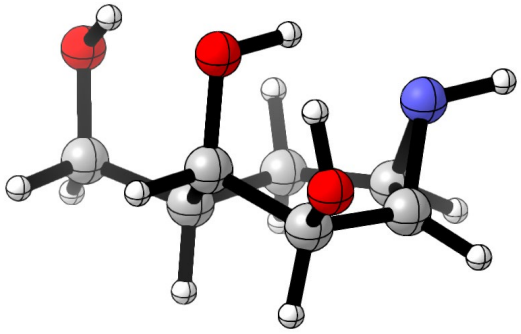
Residual activities of LacZ were measured after incubation with varying concentrations of compounds over different time periods. During the incubation, the protein concentrations were approximately 1.2 nM for LacZ (with 0.1 mg/mL BSA). The activity assay used 100 μM Gal-β-pNP as the substrate, HEPES bufffer (pH 7.4) supplemented with 1 mM Mg^{2+}.

Computational details

The most stable conformations of the "α"- and "β"-1,2-galacto-configured aziridines, in both neutral and protonated forms, were optimized in the gas phase using the M06-2X density functional, and the triple-ζ valence quality def2TZVP basis set of Weigend and Ahlrichs,[1] as implemented in Gaussian 16 (revision C.01).[2] Conformational searches were performed with Macromodel version 11.7[3] and the OPLS3 force field.[4] Additional tests with implicit solvation (IEFPCM, water) showed minimal structural changes compared to the gas-phase geometries.[5]

Figure S20 Cartesian coordinates of computed structures

β-*Galacto* neutral

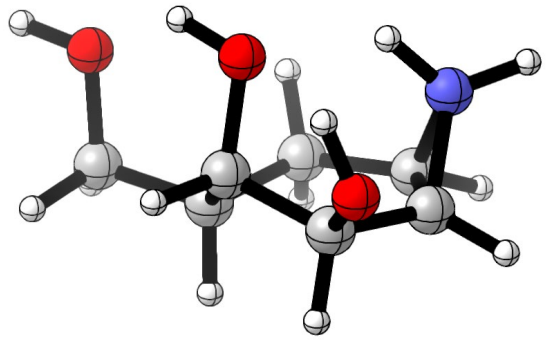


M06-2X/def2TZVP Geometry

C	1.36370	-0.68400	-0.71110
C	1.80140	0.70390	-0.30670
C	0.80000	1.77250	-0.06730
C	-0.68420	1.51810	-0.23480
C	-1.01740	0.14050	-0.82270
C	-0.08670	-0.95750	-0.30470
O	-0.17640	-1.14680	1.10550
C	-2.48590	-0.21720	-0.59650
O	2.22700	-1.66190	-0.17750
N	1.44190	1.09040	1.05980
O	-2.84790	-0.25130	0.76530
H	1.43380	-0.76450	-1.79930
H	2.78590	0.99170	-0.65650
H	1.12960	2.78810	-0.25110

H	-1.17210	1.62310	0.73660
H	-1.10910	2.28580	-0.88370
H	-0.85960	0.17810	-1.90740
H	-0.38200	-1.91410	-0.74370
H	0.25220	-0.37150	1.51580
H	-3.12480	0.53360	-1.06690
H	-2.69640	-1.17980	-1.08050
H	1.90450	-1.86480	0.71000
H	2.15870	1.65740	1.49470
H	-2.18020	-0.77410	1.22900

β-*Galacto* protonated

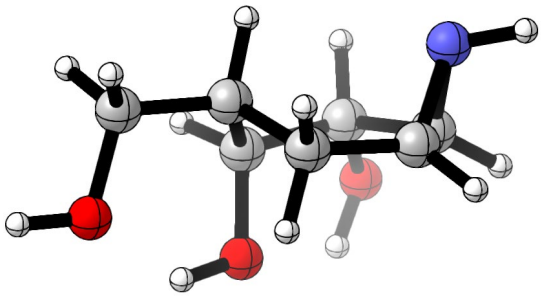


M06-2X/def2TZVP Geometry

C	1.29830	-0.75770	-0.74230
C	1.81490	0.62730	-0.39150
C	0.87860	1.73550	-0.09280
C	-0.62120	1.54100	-0.17920
C	-1.02540	0.21040	-0.82910
C	-0.15640	-0.94030	-0.31950
O	-0.13700	-1.01240	1.10670
C	-2.50640	-0.07560	-0.62400
O	2.14040	-1.72560	-0.18800
N	1.58530	1.03530	1.01760
O	-2.70870	-0.32950	0.76170
H	1.35440	-0.84390	-1.83070
H	2.81250	0.85960	-0.74030
H	1.25170	2.74280	-0.22170

H	-1.05780	1.62170	0.81830
H	-1.02660	2.36620	-0.76420
H	-0.85980	0.28160	-1.90900
H	-0.51230	-1.89120	-0.72810
H	-1.05850	-1.05720	1.41190
H	-3.10260	0.78180	-0.94880
H	-2.79740	-0.94560	-1.21890
H	1.74800	-2.05720	0.63000
H	1.01260	0.36940	1.55360
H	-3.63910	-0.49790	0.93960
H	2.32520	1.51930	1.51290

α-*Galacto* neutral

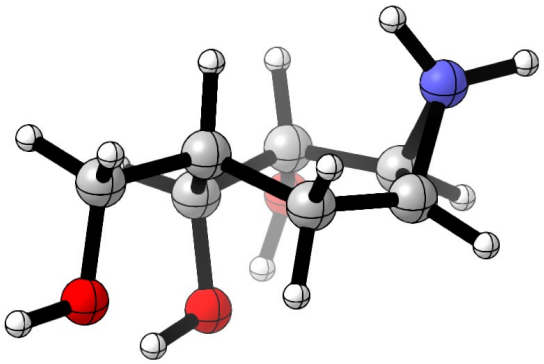


M06-2X/def2TZVP Geometry

C	1.31770	0.81820	0.54470
C	1.89470	-0.38030	-0.19530
C	1.03500	-1.47230	-0.71030
C	-0.46010	-1.42070	-0.52530
C	-0.85300	-0.46890	0.60520
C	-0.20100	0.90030	0.39570
O	-0.43080	1.40660	-0.91030
C	-2.35890	-0.35870	0.75670
O	1.90880	2.01980	0.10670
N	1.81920	-1.66040	0.50660
O	-2.89740	0.25480	-0.41440
H	1.56050	0.70880	1.60430
H	2.80420	-0.15180	-0.73860
H	1.37700	-1.98250	-1.60410

H	-0.92410	-1.09210	-1.45630
H	-0.83620	-2.42370	-0.30460
H	-0.46730	-0.87210	1.54700
H	-0.58280	1.61290	1.13830
H	-1.37720	1.33880	-1.08910
H	-2.79340	-1.35480	0.89180
H	-2.59730	0.24700	1.63730
H	1.41470	2.29920	-0.67490
H	2.64330	-2.22340	0.33390
H	-3.84640	0.36090	-0.31600

β-*Galacto* protonated



M06-2X/def2TZVP Geometry

C	1.26590	0.86950	0.54900
C	1.84230	-0.28300	-0.28370
C	0.99610	-1.39130	-0.76870
C	-0.47360	-1.43270	-0.45310
C	-0.88350	-0.45280	0.65120
C	-0.25120	0.92070	0.39080
O	-0.44380	1.35260	-0.93730
C	-2.40130	-0.35930	0.75550
O	1.86370	2.05930	0.14900
N	1.93420	-1.61960	0.37970
O	-2.87770	0.21630	-0.45010
H	1.52350	0.71030	1.60120
H	2.74260	-0.03350	-0.82980

H	1.32410	-1.92310	-1.65250
H	-0.99260	-1.16180	-1.37340
H	-0.77010	-2.45420	-0.20590
H	-0.53800	-0.80490	1.63210
H	-0.64430	1.65430	1.10320
H	-1.39390	1.36830	-1.12210
H	-2.82830	-1.35560	0.90560
H	-2.66700	0.26440	1.61390
H	1.33810	2.42800	-0.57610
H	2.76580	-2.18130	0.23180
H	-3.83730	0.28260	-0.43380
H	1.53280	-1.71030	1.30870

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