Supporting Information

Efficient route for the construction of polycyclic systems from bioderived HMF

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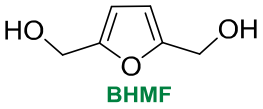
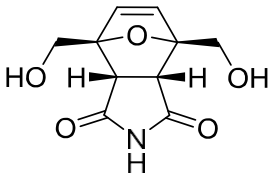
Spectroscopic data and synthetic procedures

2,5-Bis(hydroxymethyl)furan (BHMF), **2** (*lit.* [1])



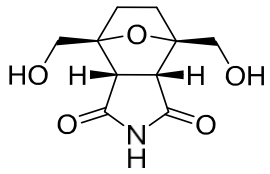
^{1}H NMR (DMSO-d6) δ = 6.19 (s, 2H), 5.17 (t, 2H, *J* = 5.7 Hz), 4.36 (d, 4H, *J* = 5.7 Hz) ppm.

Endo-4,7-bis(hydroxymethyl)-3a,4,7,7a-tetrahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione (endo-4,7-bis(hydroxymethyl)norcantharimid-5-ene), **3**



^{1}H NMR (DMSO-d6) δ = 10.82 (s, 1H), 6.37 (s, 2H), 5.11 (t, 2H, *J* = 5.7 Hz), 3.97 (dd, 2H, *J* = 5.7 Hz, 12.8 Hz), 3.84 (dd, 2H, *J* = 5.7 Hz, 12.8 Hz), 3.44 (s, 2H); ^{13}C NMR (DMSO-d6) δ = 176.9, 136.0, 92.1, 59.8, 48.8 ppm. m/z HRMS (ESI) Calcd. for $C_{10}H_{11}NO_5$ [M+Na]: 248.0529. Found 248.0536.

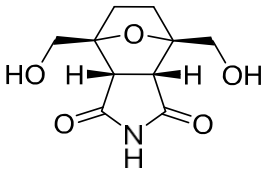
Endo-4,7-bis(hydroxymethyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione (e*ndo-4,7-bis(hydroxymethyl)norcantharimide),* **4** (**method A)**



Endo-4,7-bis(hydroxymethyl)norcantharimid-5-ene (120 mg, 0.53 mmol) was dissolved in water (3 mL), Pd/C 10% was added (15 mg) and reaction mixture was placed under hydrogen atmosphere for 8 h at 24 °C. Catalyst was filtered off and washed thoroughly with water (3 × 3 mL), filtrate was evaporated under reduced pressure. Target compound **4** was obtained as white solid, yield 87% (110 mg).

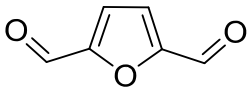
^{1}H NMR (D_2O) δ = 3.76 (s, 4H), 3.46 (s, 2H), 1.61-1.72 (m, 4H); ^{1}H NMR (DMSO-d6) δ = 11.10 (s, 1H), 5.08 (s, 2H), 3.66 (s, 4H), 3.37 (s, 2H), 1.71 (m, 2H), 1.49 (m, 2H); ^{13}C NMR (D_2O) δ = 179.0, 88.8, 60.7, 52.3, 27.0 ppm. m/z HRMS (ESI) Calcd. for $C_{10}H_{13}NO_5$ [M+Na]:
250.0686. Found 250.0696.

Endo-4,7-bis(hydroxymethyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione (endo-4,7-bis(hydroxymethyl)norcantharimide), **4** (**method B**, one-pot two stages)



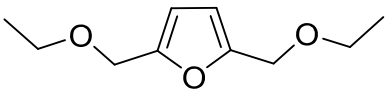
2,5-Bis(hydroxymethyl)furan **2** (1.07 g, 8.4 mmol) was dissolved in water (30 mL), maleimide (1.62 g, 16.8 mmol, 2 eq) was added, solution was stirred for 16 h at 24 °C. Pd/C 10% was added (80 mg) and reaction mixture was placed under hydrogen atmosphere for 12 h at 24 °C. Catalyst was filtered off and washed thoroughly with water (3 × 5 mL), filtrate was evaporated under reduced pressure. Residue was washed with diethyl ether (3 × 5 mL) to remove succinimide. Target compound **4** recrystallized from ethanol and obtained as white solid, yield 75% (1.42 g).

2,5-Diformylfuran (DFF), **5** (lit. [2])



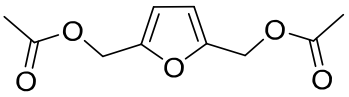
^{1}H NMR ($CDCl_3$) δ = 9.87 (s, 2H), 7.35 (s, 2H); ^{13}C NMR ($CDCl_3$) δ = 181.1, 154.1, 122.5 ppm.

2,5-Bis(ethoxymethyl)furan, **6**



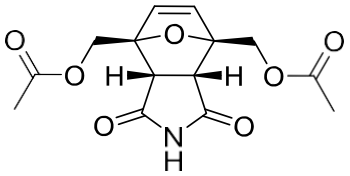
^{1}H NMR ($CDCl_3$) δ = 6.20 (s, 2H), 4.36 (s, 4H), 3.47 (q, 4H, *J* = 7.1 Hz), 1.16 (t, 6H, *J* = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ = 150.9, 109.7, 65.7, 64.7, 15.1 ppm.

2,5-Bis(acetoxymethyl)furan, **7** *(lit. [1])*



^{1}H NMR ($CDCl_3$) δ = 6.32 (s, 2H), 4.98 (s, 4H), 2.03 (s, 6H) ppm.

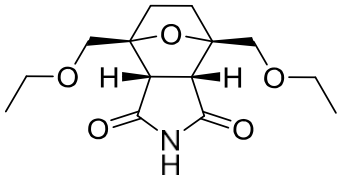
Endo-(1,3-dioxo-2,3,3a,7a-tetrahydro-1H-4,7-epoxyisoindole-4,7-diyl)bis(methylene) diacetate (endo-4,7-bis(acetoxymethyl)norcantharimid-5-ene), ***9a***



2,5-Bis(acetoxymethyl)furan **7** (200 g, 0.94 mmol) was dissolved in ethyl acetate (1.5 mL), maleimide (180 g, 1.8 mmol) was added, reaction was stirred at 24 °C for 24 h. Precipitate was filtered off, washed with ethyl acetate (2 × 1 mL), dryed on filter. Target compound **9a** was obtained as white solid, yield 42% (120 g).

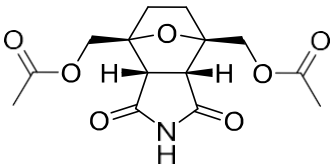
^{1}H NMR (DMSO-d6) δ = 11.03 (s, 1H), 6.51 (s, 2H), 4.67 (d, 2H, *J* = 12.9 Hz), 4.45 (d, 2H, *J* = 12.9 Hz), 3.56 (s, 2H), 2.08 (s, 6H); ^{13}C NMR (DMSO-d6) δ = 175.9, 170.1, 135.7, 89.1, 61.7, 49.5, 20.1 ppm. m/z HRMS (ESI) Calcd. for $C_{14}H_{15}NO_7$ [M+Na]: 332.0741. Found 332.0747.

Endo-4,7-bis(ethoxymethyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione (endo-4,7-bis(ethoxymethyl)norcantharimide), **8**



^{1}H NMR ($CDCl_3$) δ = 8.58 (s, 1H), 3.71 (dd, 4H, *J* = 11.5 Hz), 3.54 (q, 4H, *J* = 7.0 Hz), 3.50 (s, 2H), 1.82 (m, 2H), 1.68 (m, 2H), 1.15 (t, 6H, *J* = 7.0 Hz). ^{13}C NMR ($CDCl_3$) δ = 175.9, 88.2, 68.9, 66.8, 52.3, 27.5, 14.5. m/z HRMS (ESI) Calcd. for $C_{14}H_{21}NO_5$ [M+Na]: 306.1312. Found 306.1319.

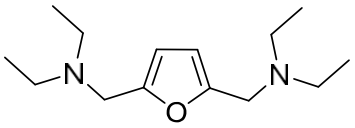
Endo-1,3-dioxohexahydro-1H-4,7-epoxyisoindole-4,7-diyl)bis(methylene) diacetate (endo-4,7-bis(acetoxymethyl)norcantharimide), **9**



Endo-4,7-bis(acetoxymethyl)norcantharimid-5-ene **9a** (100 g, 0.32 mmol) was dissolved in ethanol (2 mL), Pd/C 10% was added (10 mg) and reaction mixture was placed under hydrogen atmosphere for 8 h at 24 °C. Catalyst was filtered off and washed thoroughly with ethanol (3 × 3 mL), filtrate was evaporated under reduced pressure. Target compound **9** was obtained as white solid, yield 91% (91 mg).

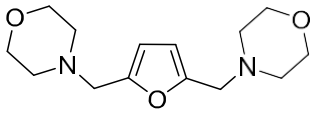
^{1}H NMR (acetone-d6) δ = 10.09 (br.s, 1H), 4.50 (d, 2H, *J* = 12.6 Hz), 4.32 (d, 2H, *J* = 12.6 Hz), 3.56 (s, 2H), 2.09 (s, 6H), 1.84-1.93 (m, 4H); ^{13}C NMR (acetone-d6) δ = 175.7, 169.7, 86.5, 62.9, 53.6, 28.1, 19.8 ppm. m/z HRMS (ESI) Calcd. for $C_{14}H_{17}NO_7$ [M+Na]: 334.0897. Found 334.0900.

2,5-Bis(N,N-diethylaminomethyl)furan, **10**



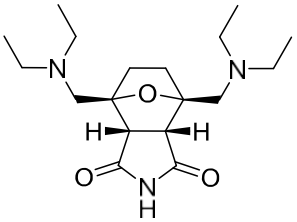
Yield 80%, ^{1}H NMR ($CDCl_3$) δ = 6.10 (s, 2H), 3.67 (s, 4H), 2.52 (q, 8H, *J* = 7.2 Hz), 1.08 (t, 12H, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ = 151.4, 109.1, 48.6, 46.9, 12.0 ppm. m/z HRMS (ESI) Calcd. for $C_{14}H_{26}N_2O$ [M+H]: 239.2118. Found 239.2118.

2,5-Bis(morpholinomethyl)furan, **11**



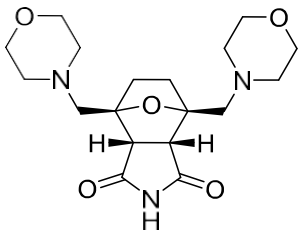
Yield 98%, ^{1}H NMR ($CDCl_3$) δ = 6.13 (s, 2H), 3.70 (m, 8H), 3.51 (s, 4H), 2.45 (m, 8H); ^{13}C NMR ($CDCl_3$) δ = 150.9, 109.7, 66.8, 55.3, 53.2 ppm. m/z HRMS (ESI) Calcd. for $C_{14}H_{22}N_2O_3$ [M+H]: 267.1703. Found 267.1703.

Endo-4,7-bis((diethylamino)methyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione (endo-4,7-bis(diethylamino)norcantharimide), **12**



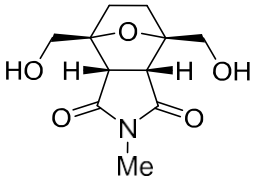
^{1}H NMR (CD_3OD) δ = 3.66 (s, 2H), 2.99 (m, 4H), 2.76-2.89 (m, 8H), 1.76-1.85 (m, 4H), 1.12 (t, 12H, *J* = 7.1 Hz); ^{13}C NMR (CD_3OD) δ = 177.8, 88.6, 54.5, 53.6, 48.4, 29.1, 10.3 ppm. m/z HRMS (ESI) Calcd. for $C_{18}H_{31}N_3O_3$ [M+H]: 338.2438. Found 338.2448.

Endo-4,7-bis(morpholinomethyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione (endo-4,7-bis(morpholinomethyl)norcantharimide), **13**



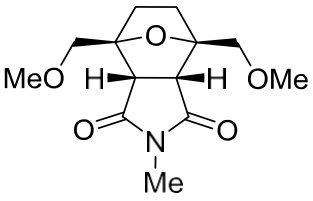
^{1}H NMR (CD_3OD) δ = 3.58-3.65 (m, 10H), 2.72 (m, 4H), 2.48-2.66 (m, 8H), 1.69-1.83 (m, 4H); ^{13}C NMR (CD_3OD) δ = 178.2, 89.1, 66.7, 59.8, 54.6, 53.7, 28.9 ppm. m/z HRMS (ESI) Calcd. for $C_{18}H_{27}N_3O_5$ [M+H]: 366.2023. Found 366.2021.

Endo-4,7-bis(hydroxymethyl)-2-methylhexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione (endo-N-methyl-4,7-bis(hydroxymethyl)norcantharimide), **14**



^{1}H NMR (CD_3OD) δ = 3.88 (s, 4H), 3.54 (s, 2H), 2.95 (s, 3H), 1.80 (m, 2H), 1.55 (m, 2H); ^{13}C NMR (CD_3OD) δ = 176.6, 89.1, 61.5, 51.5, 27.3, 23.5 ppm. m/z HRMS (ESI) Calcd. for $C_{11}H_{15}NO_5$ [M+H]: 242.1023. Found 242.1025.

Endo-4,7-bis(methoxymethyl)-2-methylhexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione (endo-N-methyl-4,7-bis(methoxymethyl)norcantharimide), **15**



^{1}H NMR (CD_3OD) δ = 3.75 (m, 4H), 3.53 (s, 2H), 3.46 (s, 6H), 2.95 (s, 3H), 1.80 (m, 2H), 1.55 (m, 2H); ^{13}C NMR (CD_3OD) δ = 176.3, 88.3, 71.5, 58.4, 51.5, 27.4, 23.5 ppm. m/z HRMS (ESI) Calcd. for $C_{13}H_{19}NO_5$ [M+Na]: 292.1155. Found 292.1155.

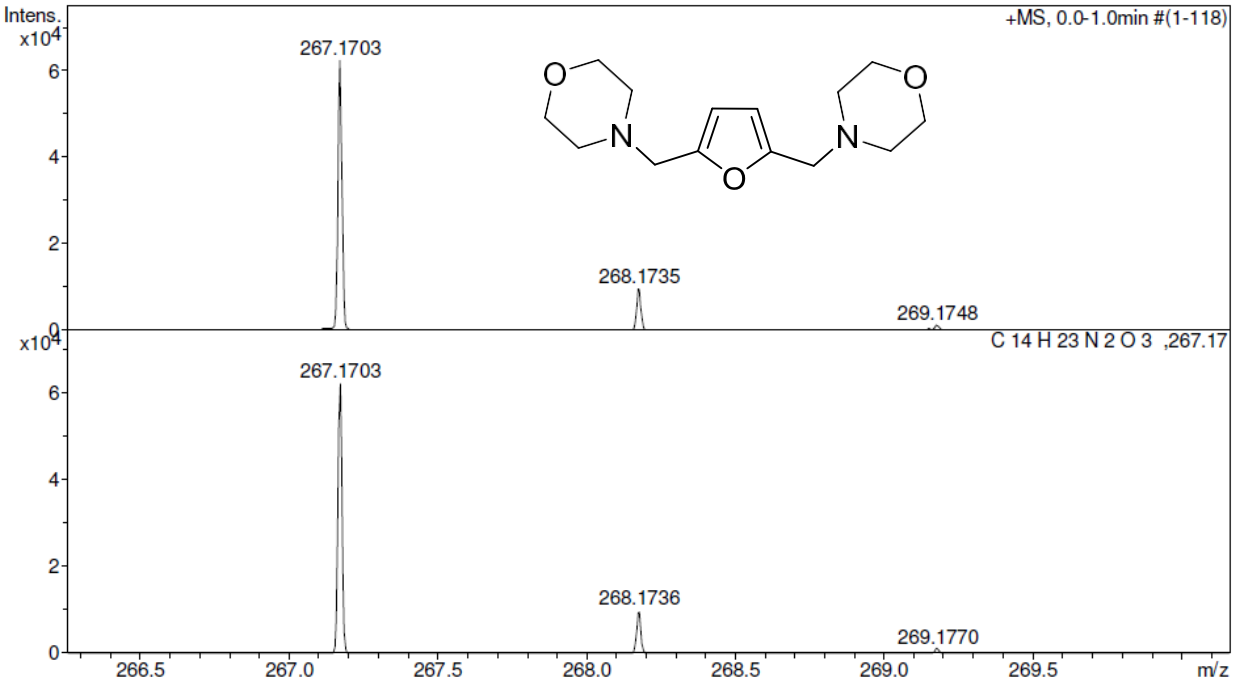


Fig. S1. HRMS (ESI) spectrum of 2,5-bis(morpholinomethyl)furan 11.

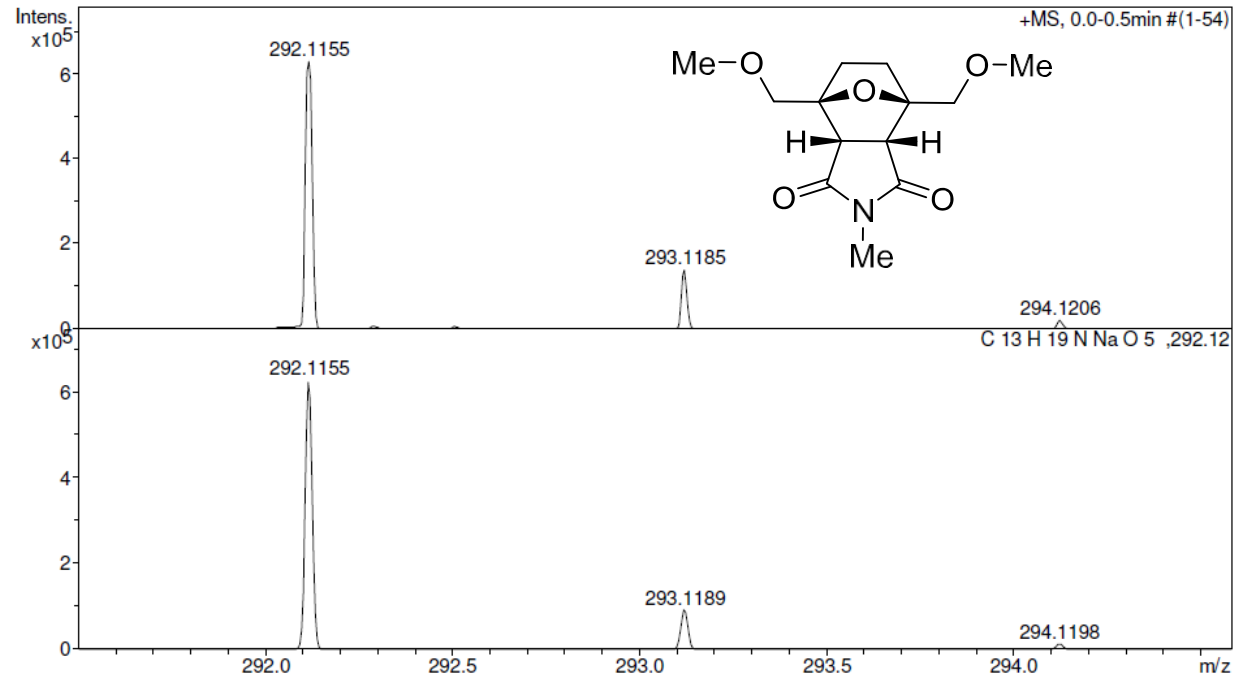


Fig. S2. HRMS (ESI) spectrum of *endo*-4,7-bis(methoxymethyl)-2-methylhexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 15.

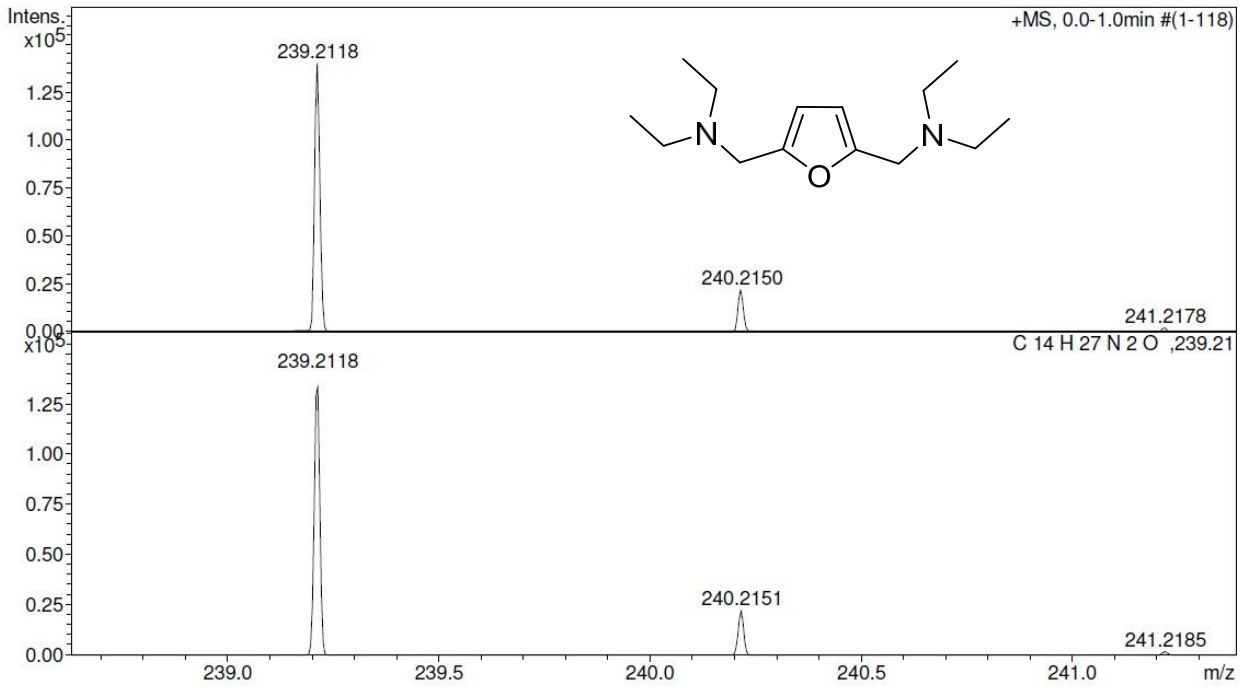


Fig. S3. HRMS (ESI) spectrum of 2,5-bis(diethylaminomethyl)furan 10.

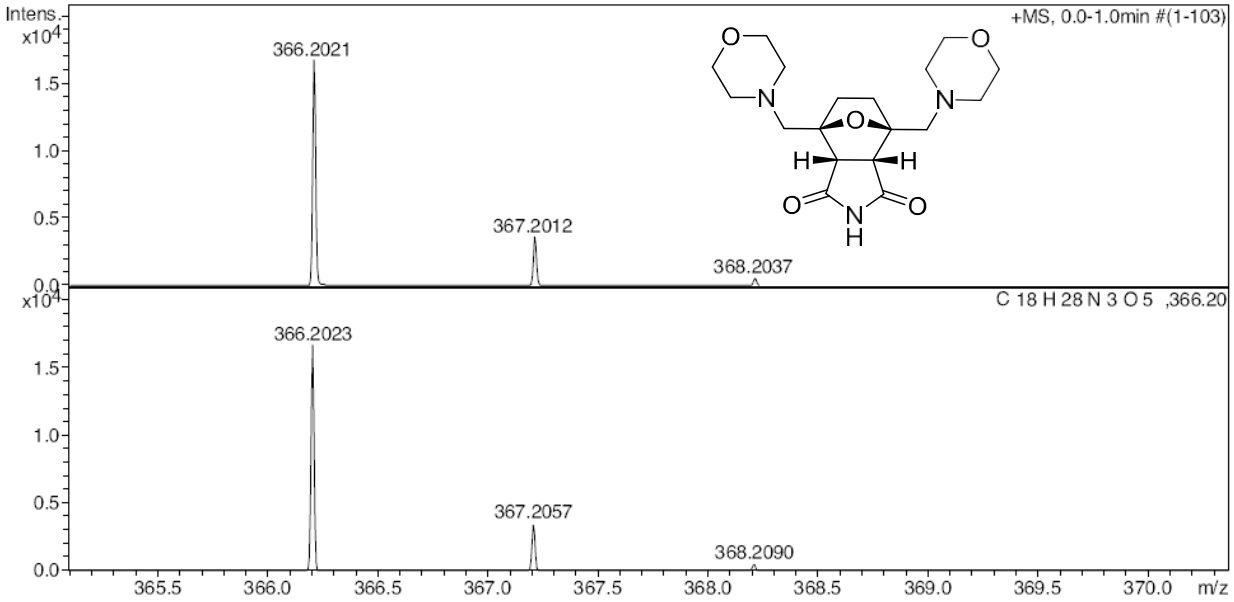


Fig. S4. HRMS (ESI) spectrum of *endo*-4,7-bis(morpholinomethyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 13.

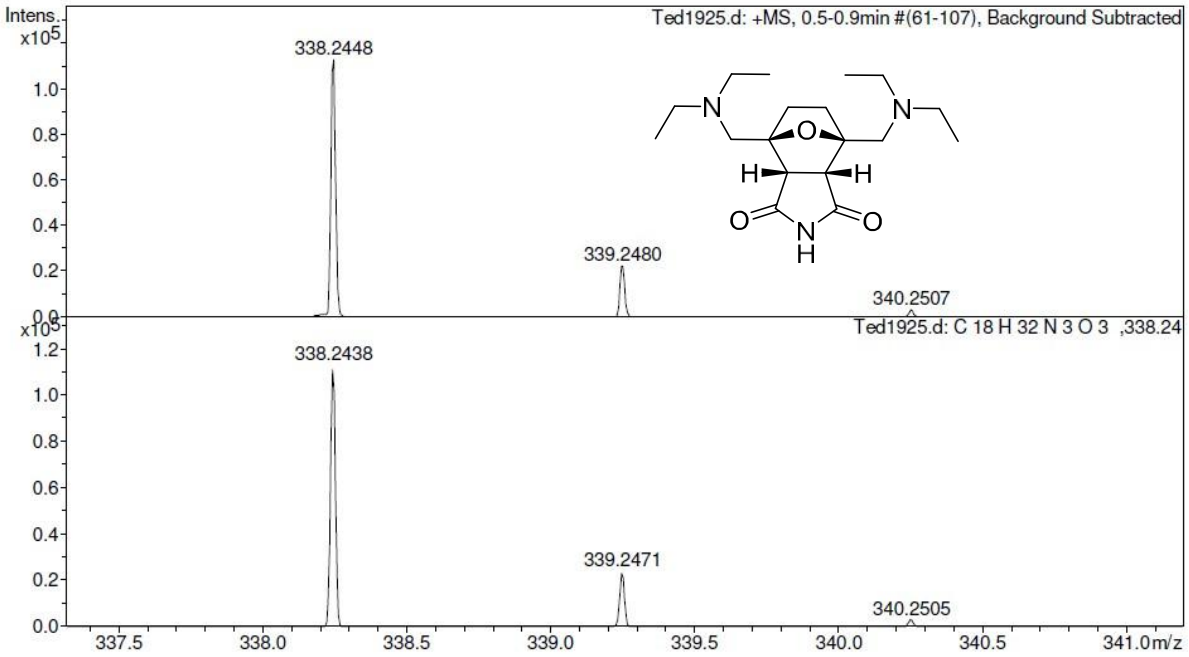


Fig. S5. HRMS (ESI) spectrum of *endo*-4,7-bis((diethylamino)methyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 12.

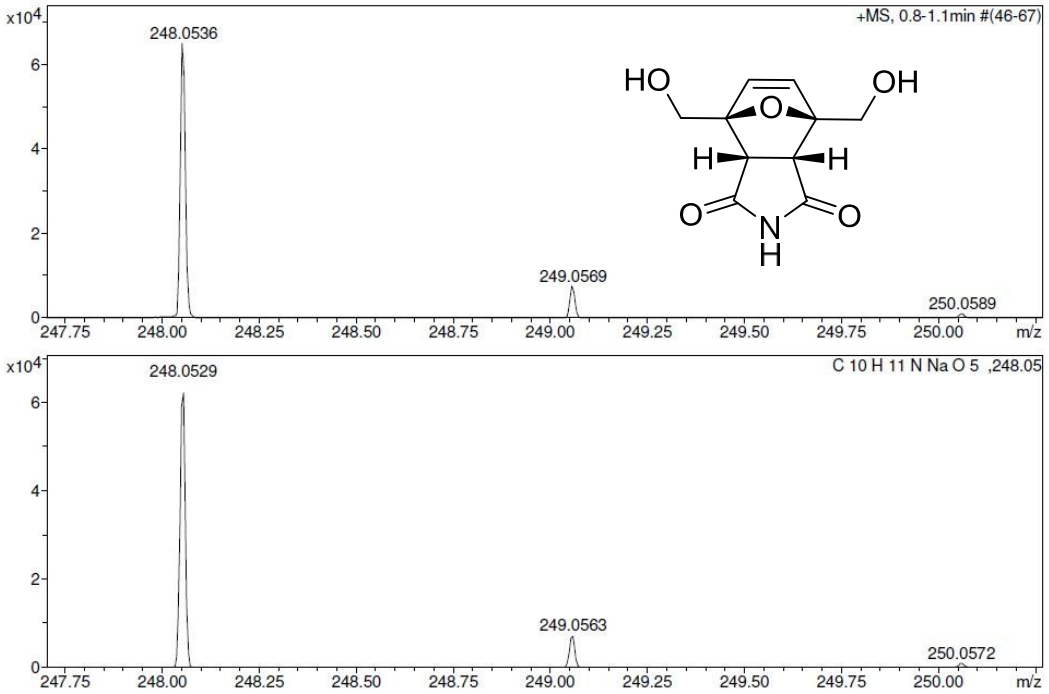


Fig. S6. HRMS (ESI) spectrum of *endo*-4,7-bis(hydroxymethyl)-3a,4,7,7a-tetrahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 3.

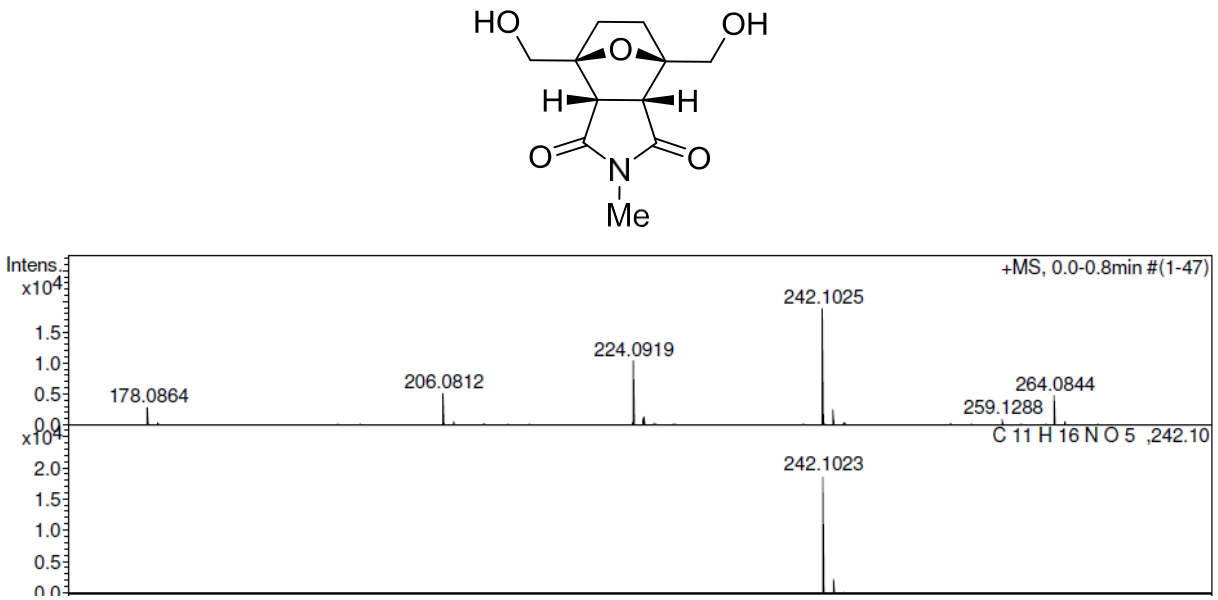


Fig. S7. HRMS (ESI) spectrum of *endo*-4,7-bis(hydroxymethyl)-2-methylhexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 14.

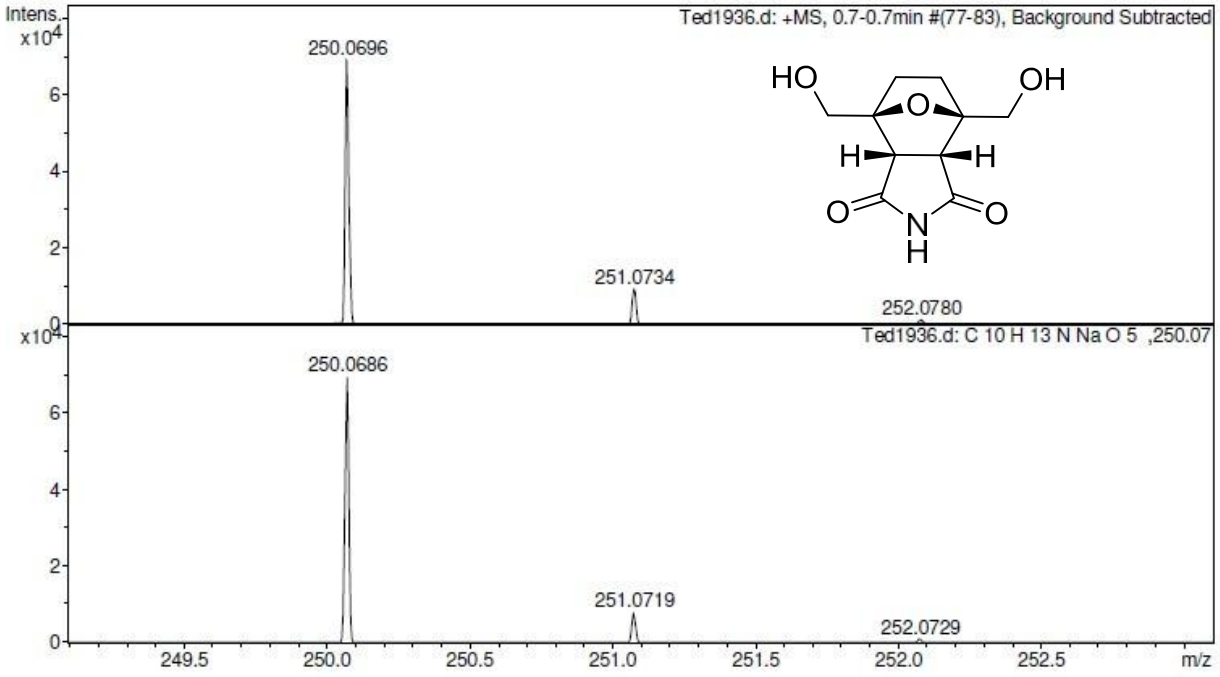


Fig. S8. HRMS (ESI) spectrum of *endo*-4,7-bis(hydroxymethyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 4.

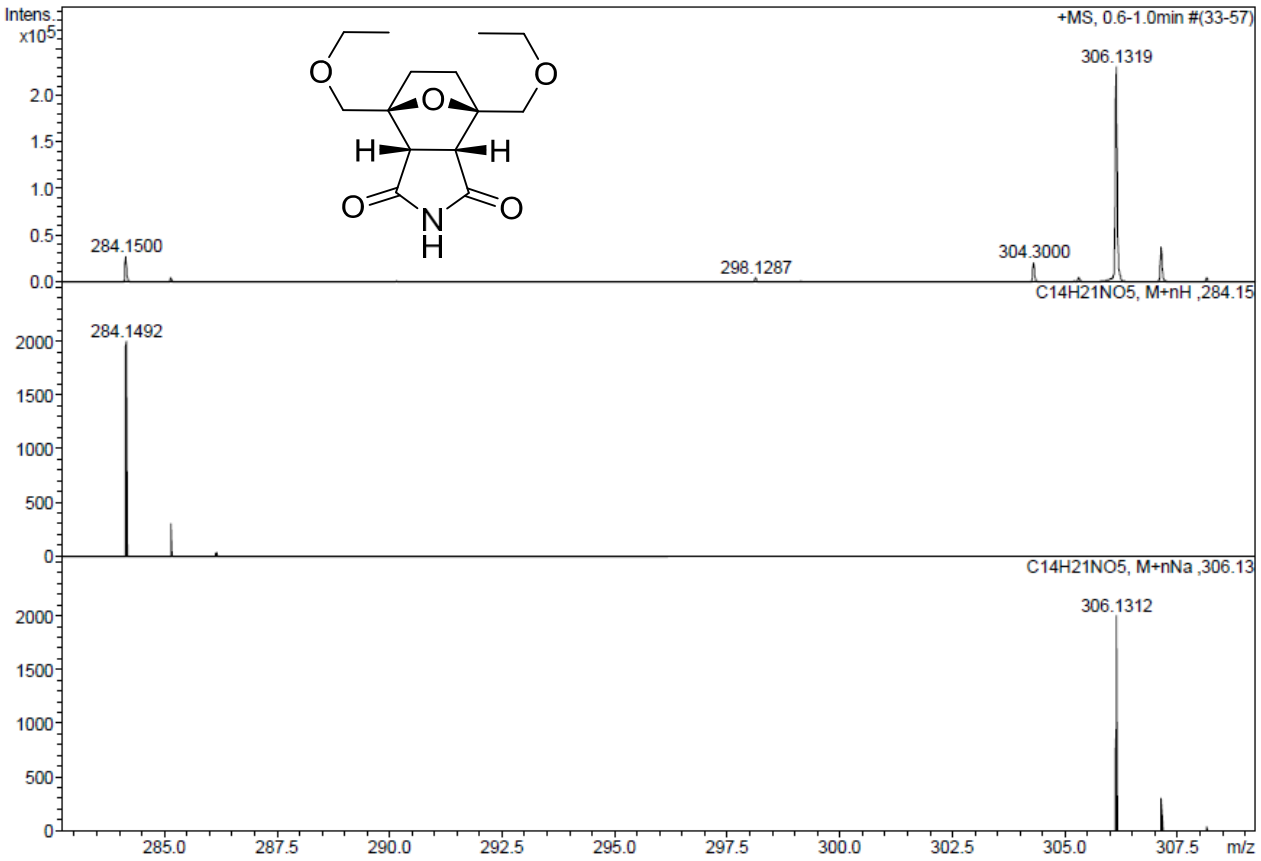


Fig. S9. HRMS (ESI) spectrum of *endo*-4,7-bis(ethoxymethyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 8, ([M+Na] = 306.1312).

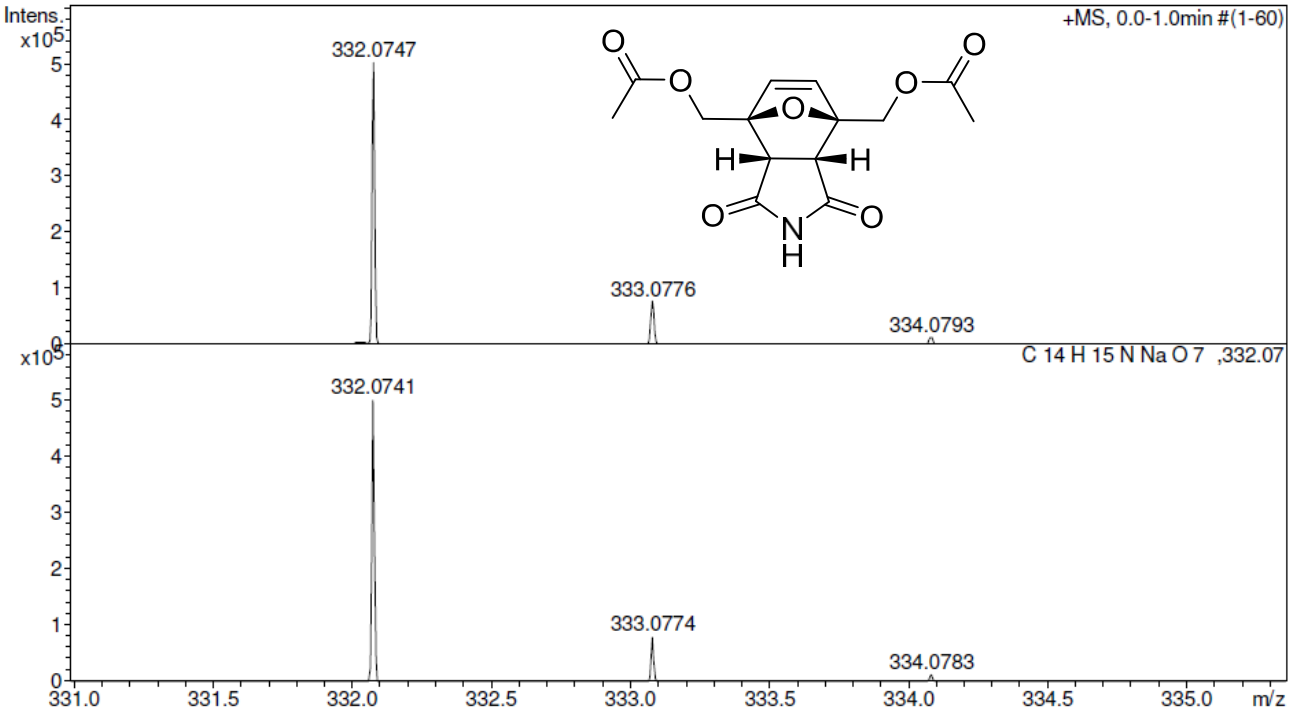


Fig. S10. HRMS (ESI) spectrum of *endo*-(1,3-dioxo-2,3,3a,7a-tetrahydro-1H-4,7-epoxyisoindole-4,7-diyl)bis(methylene) diacetate 9a, ([M+Na] = 332.0741).

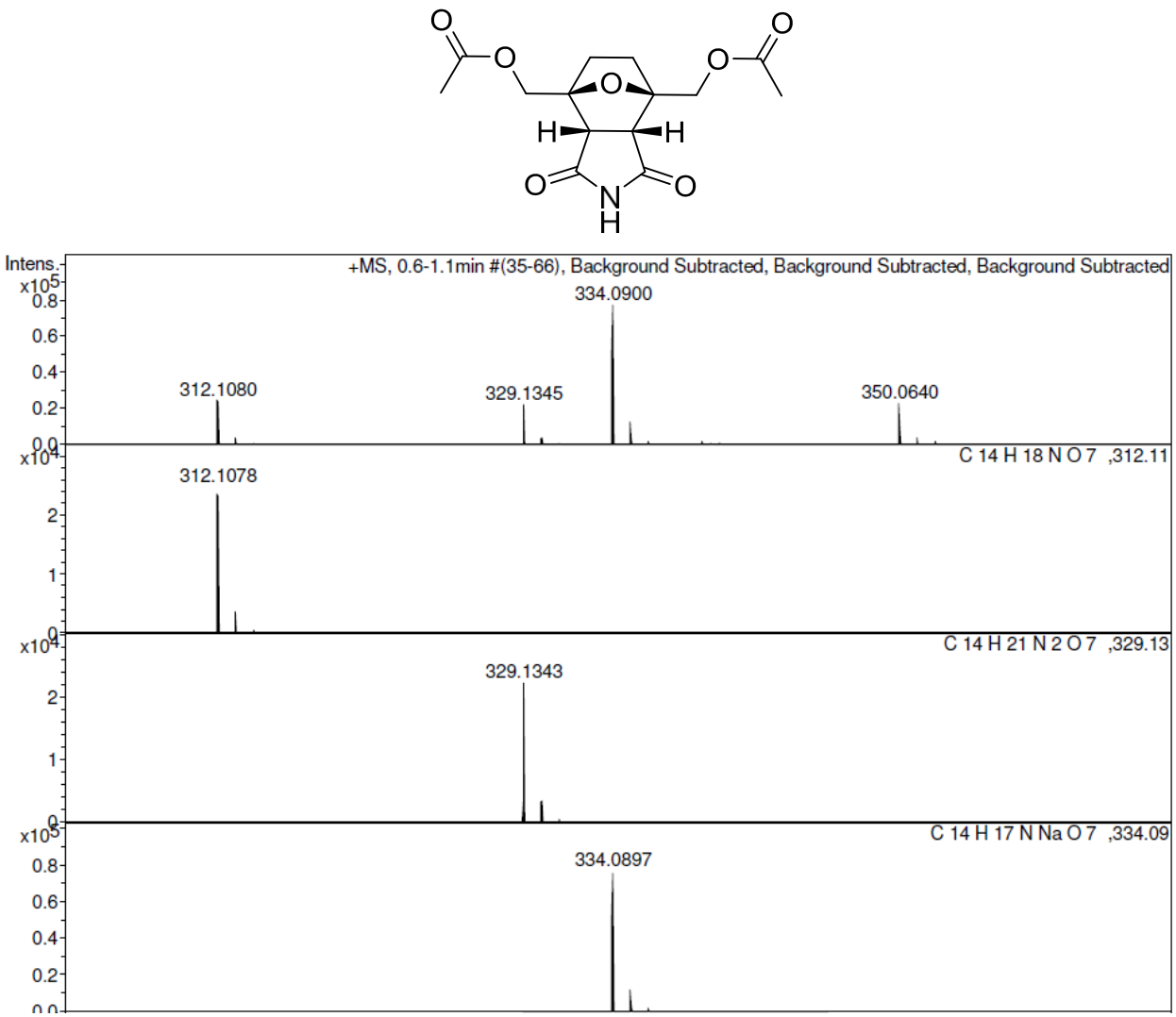


Fig. S11. HRMS (ESI) spectrum of *endo*-(1,3-dioxohexahydro-1H-4,7-epoxyisoindole-4,7-diyl)bis(methylene) diacetate 9, ([M+Na] = 334.0897).

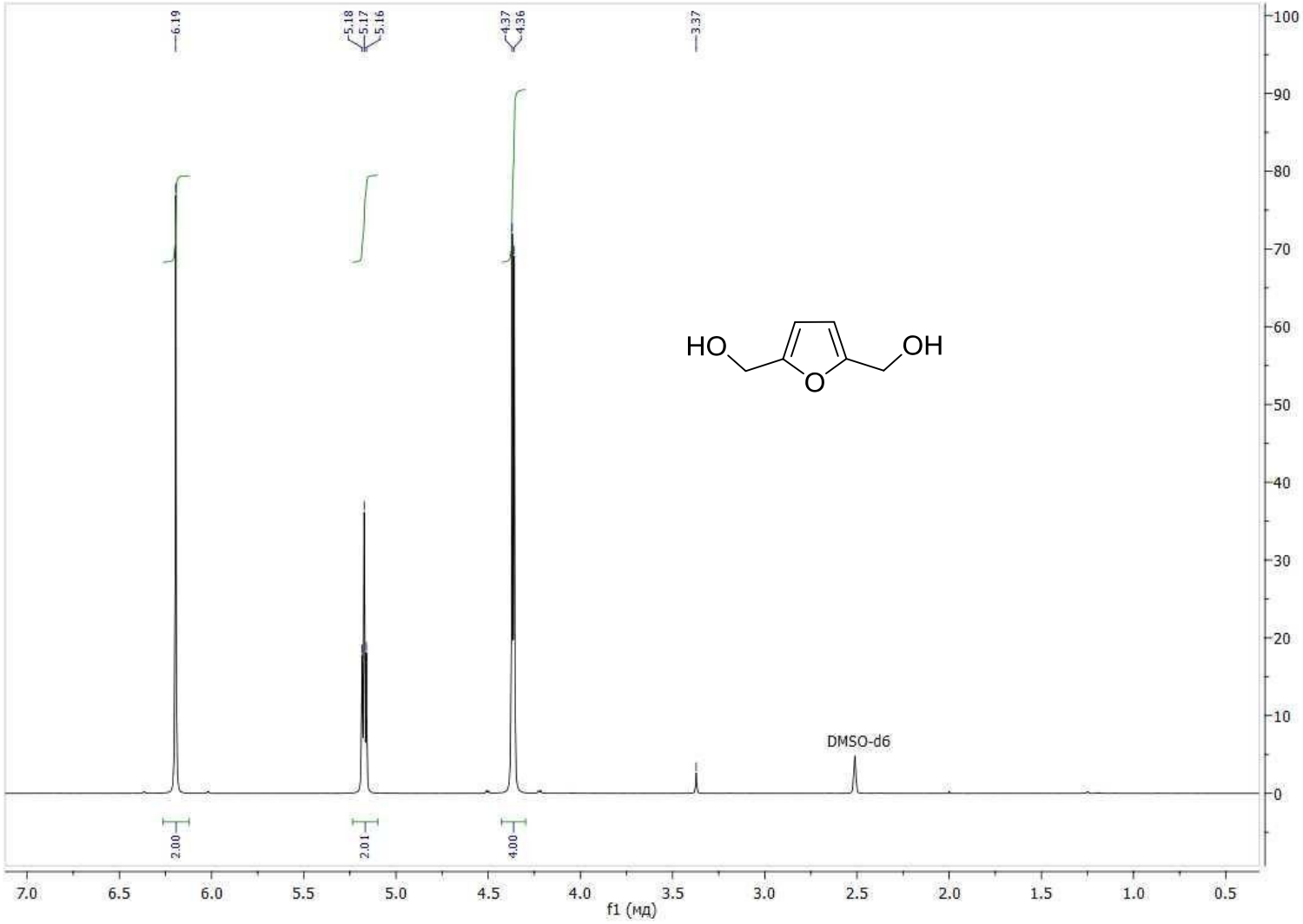


Fig. S12. ^{1}H NMR spectrum of 2,5-bis(hydroxymethyl)furan 2, BHMF (DMSO-d6, 298 K, 500 MHz).

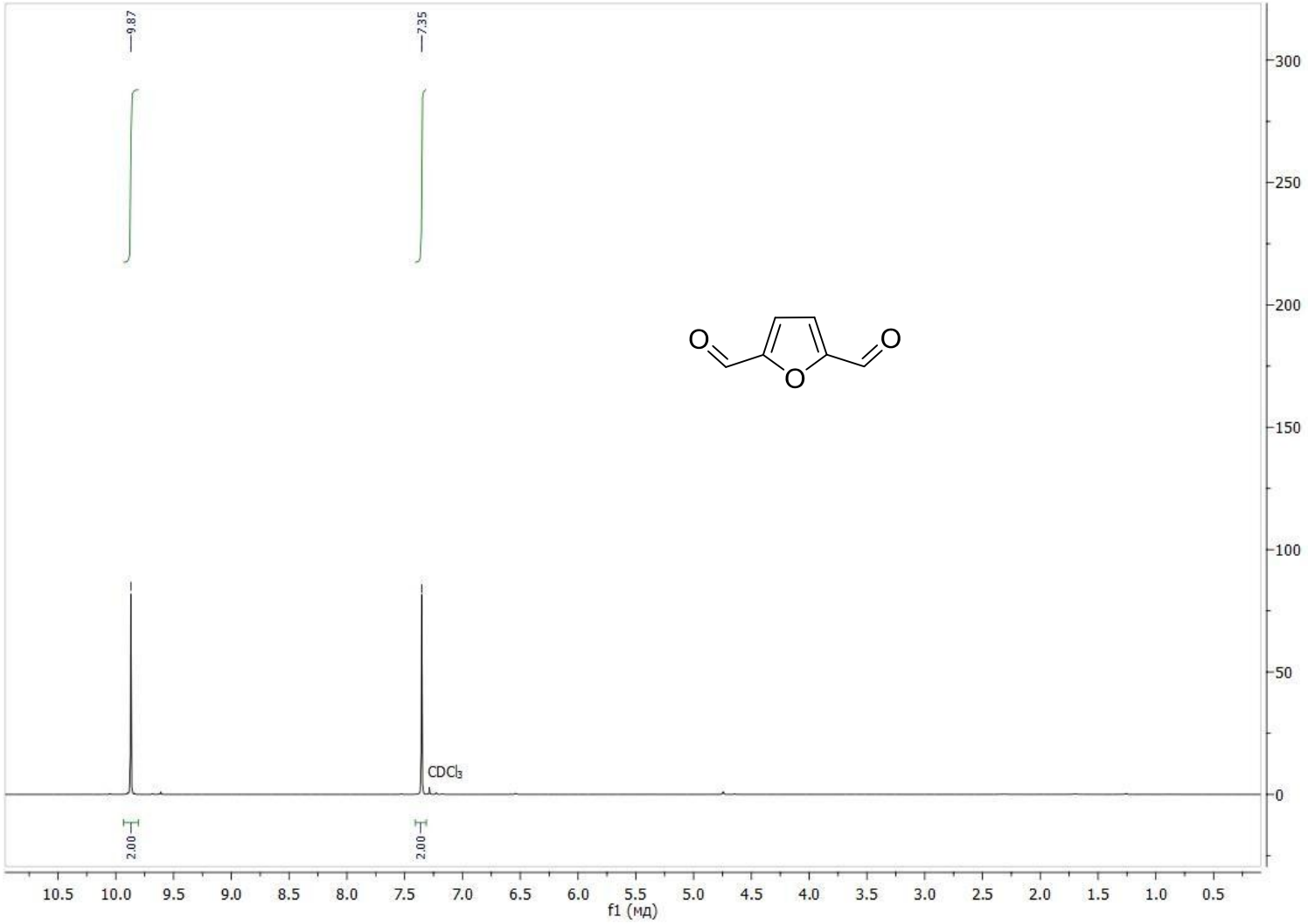


Fig. S13. ^{1}H NMR spectrum of 2,5-diformylfuran 5, DFF ($CDCl_3$, 298 K, 500 MHz).

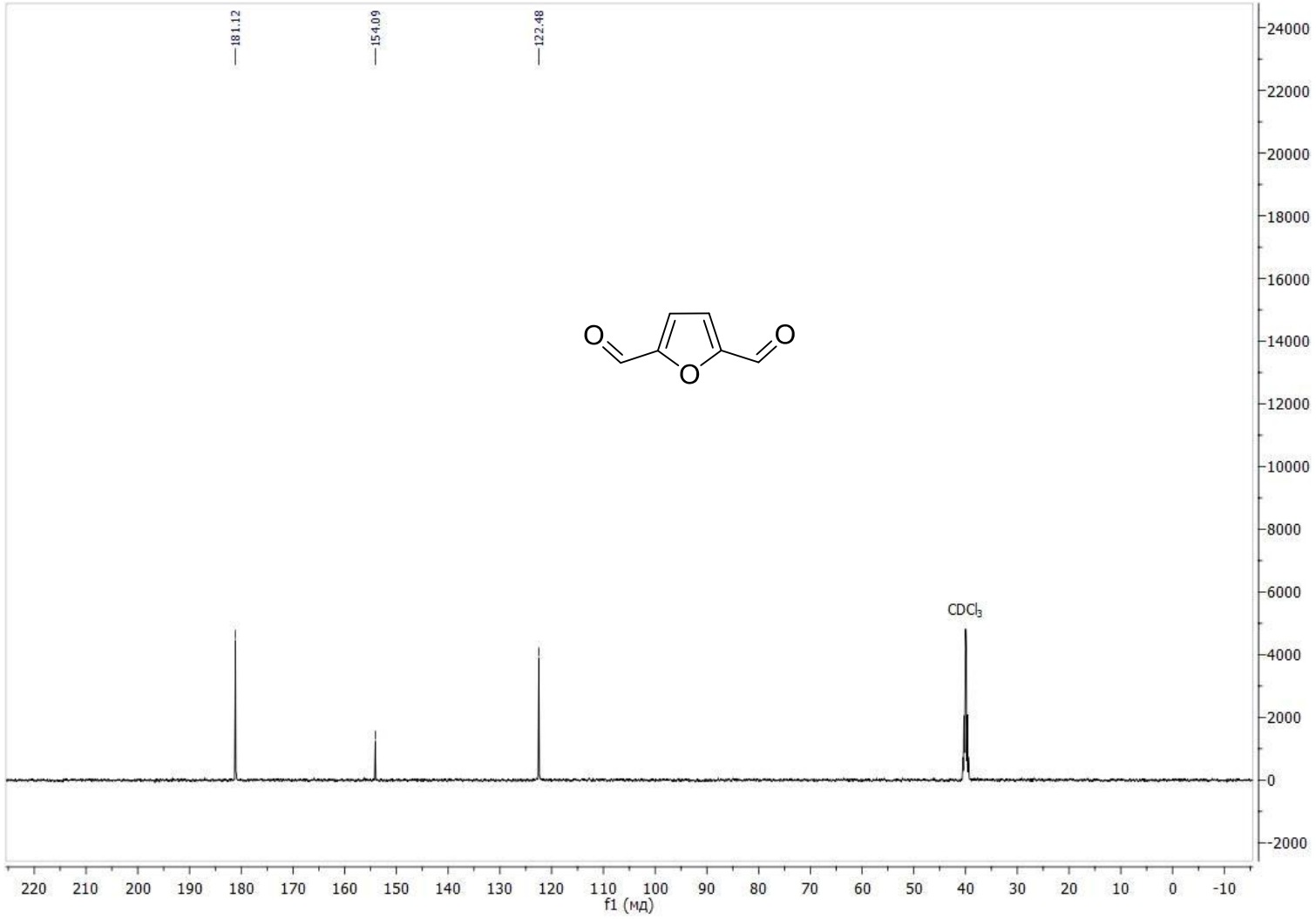


Fig. S14. ^{13}C NMR spectrum of 2,5-diformylfuran 5, DFF (DMSO-d6, 298 K, 125 MHz).

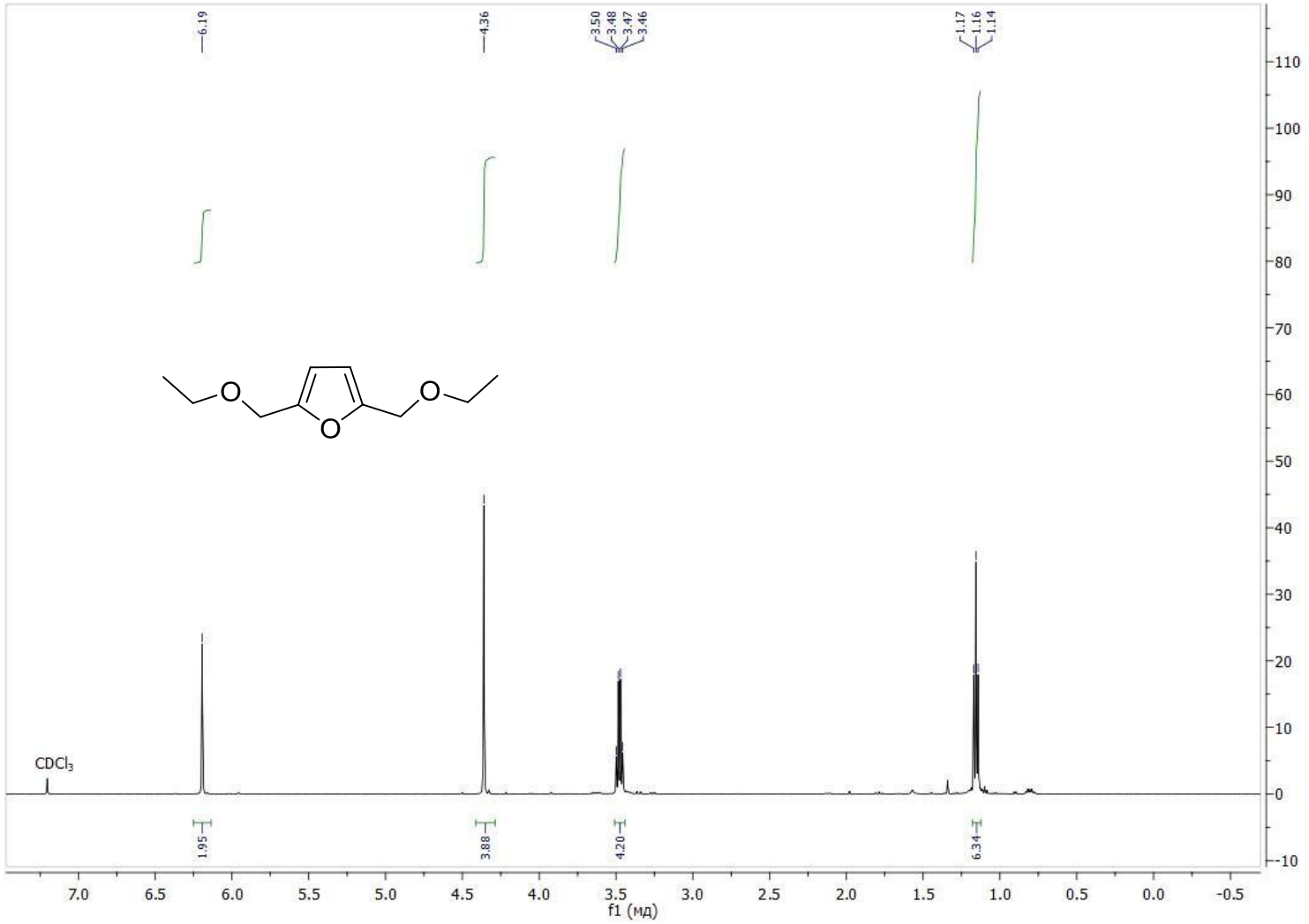


Fig. S15. ^{1}H NMR spectrum of 2,5-bis(ethoxymethyl)furan 6 ($CDCl_3$, 298 K, 500 MHz).

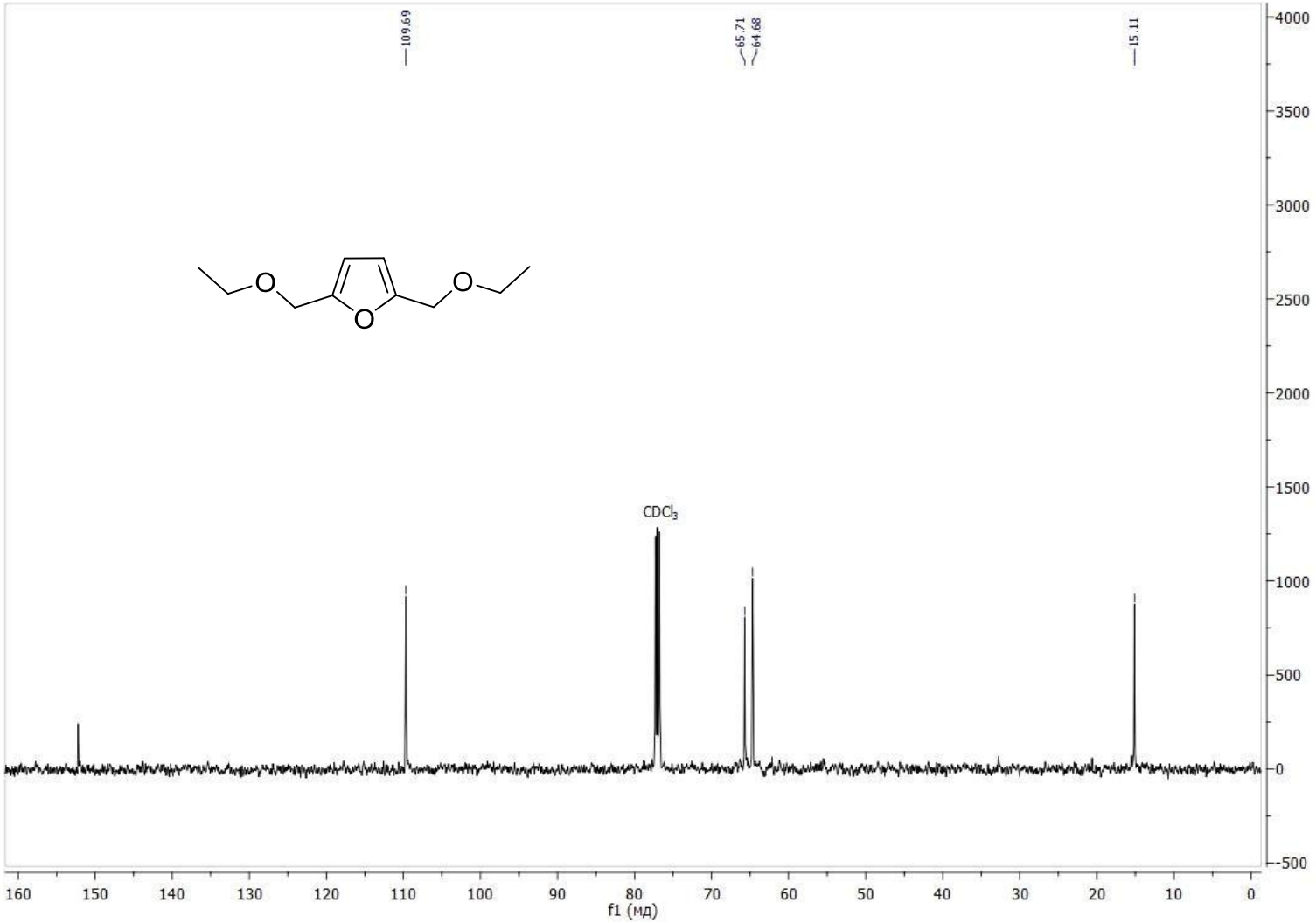


Fig. S16. ^{13}C NMR spectrum of 2,5-bis(ethoxymethyl)furan 6 ($CDCl_3$, 298 K, 125 MHz).

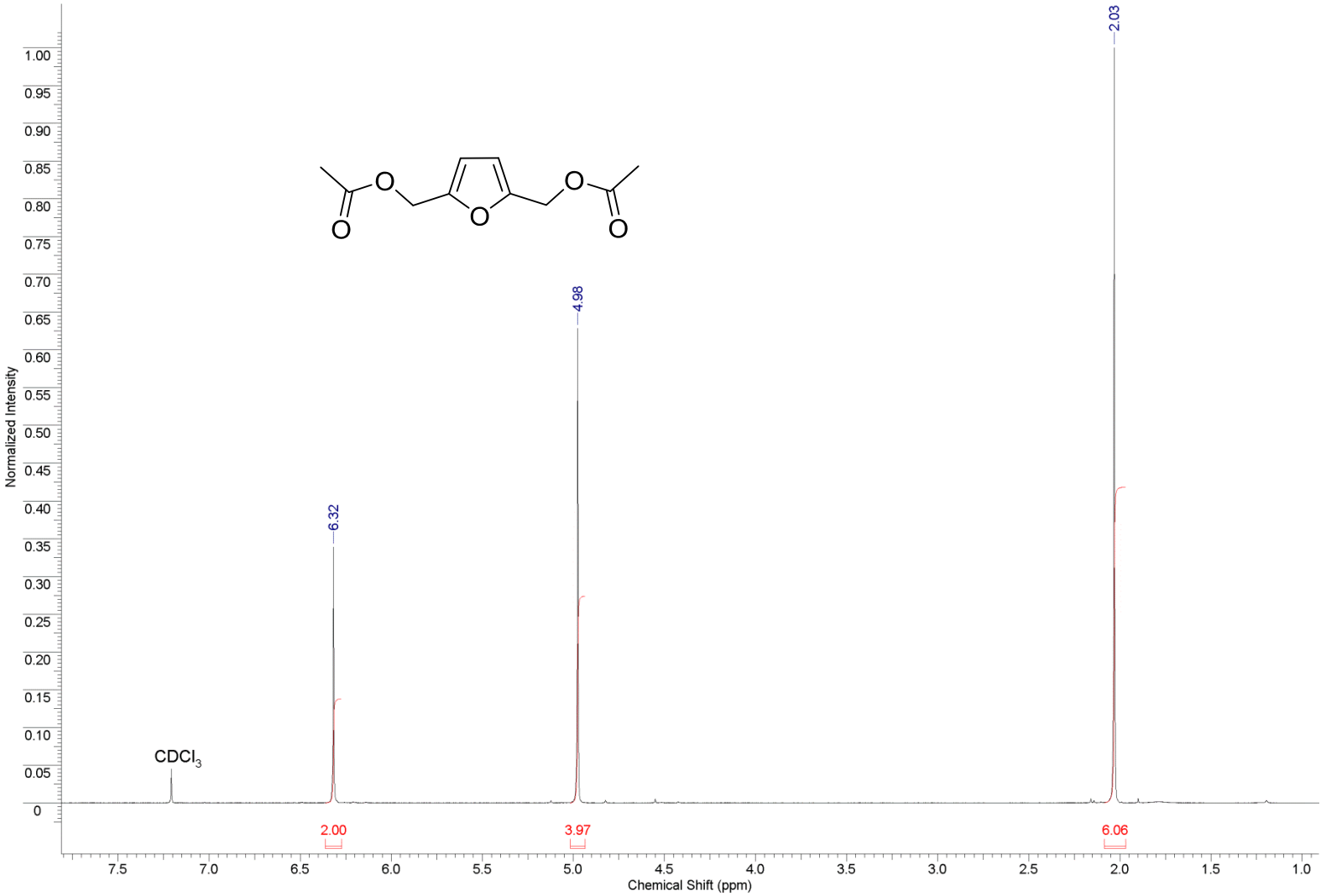


Fig. S17. ^{1}H NMR spectrum of 2,5-bis(acetoxymethyl)furan 7 ($CDCl_3$, 298 K, 500 MHz).

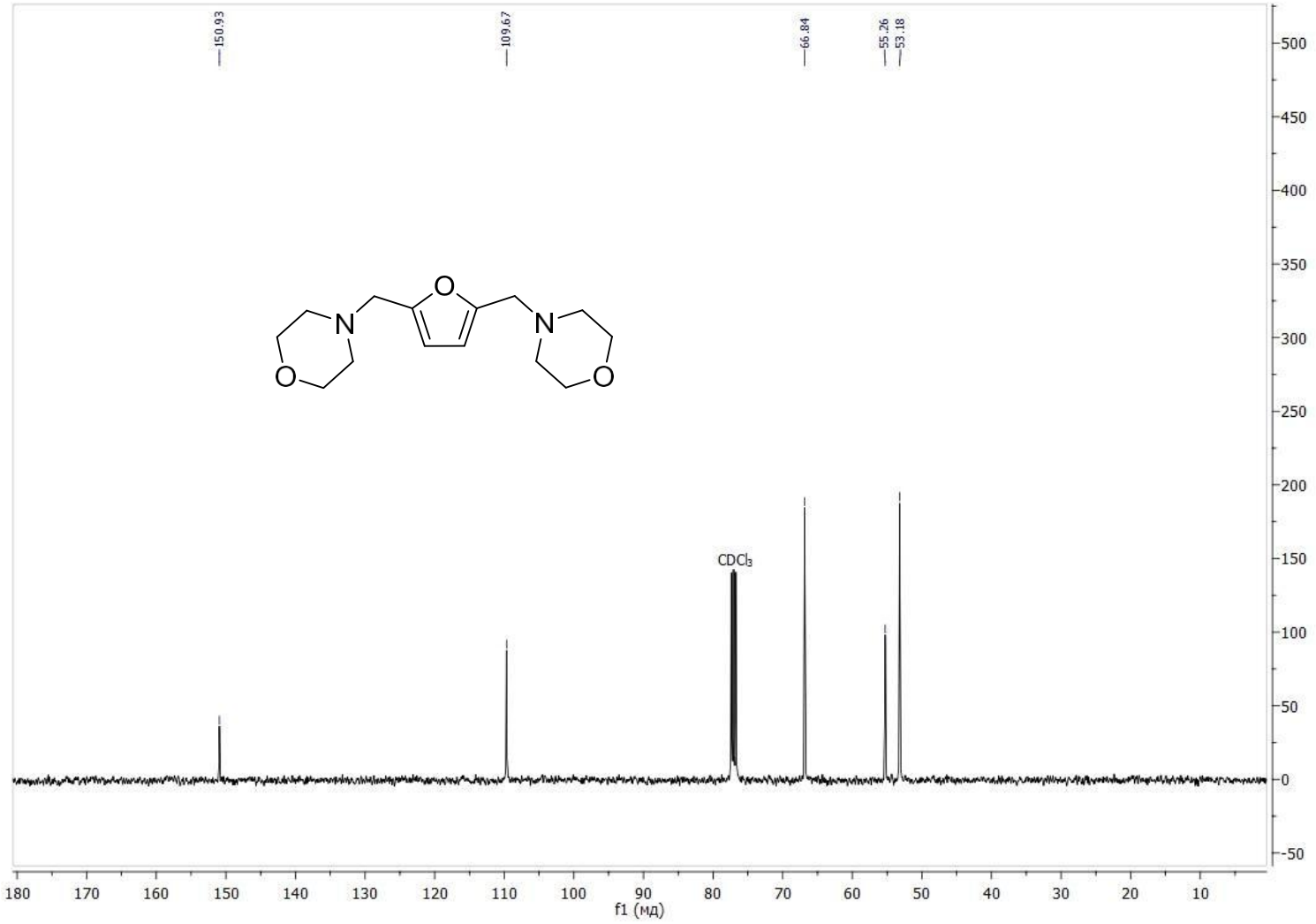


Fig. S18. ^{13}C NMR spectrum of 2,5-bis(morpholinomethyl)furan 11 ($CDCl_3$, 298 K, 125 MHz).

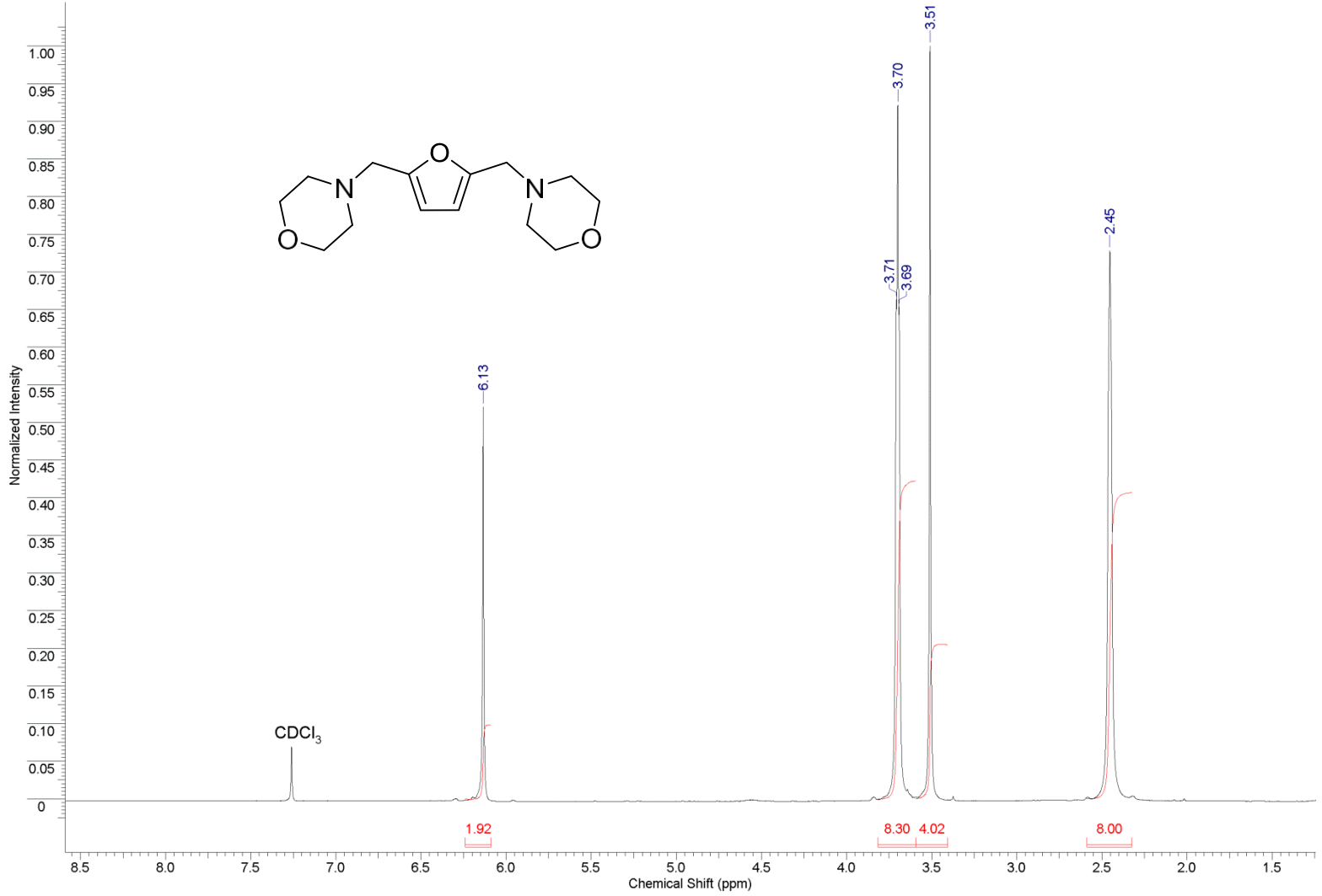


Fig. S19. ^{1}H NMR spectrum of 2,5-bis(morpholinomethyl)furan 11 ($CDCl_3$, 298 K, 500 MHz).

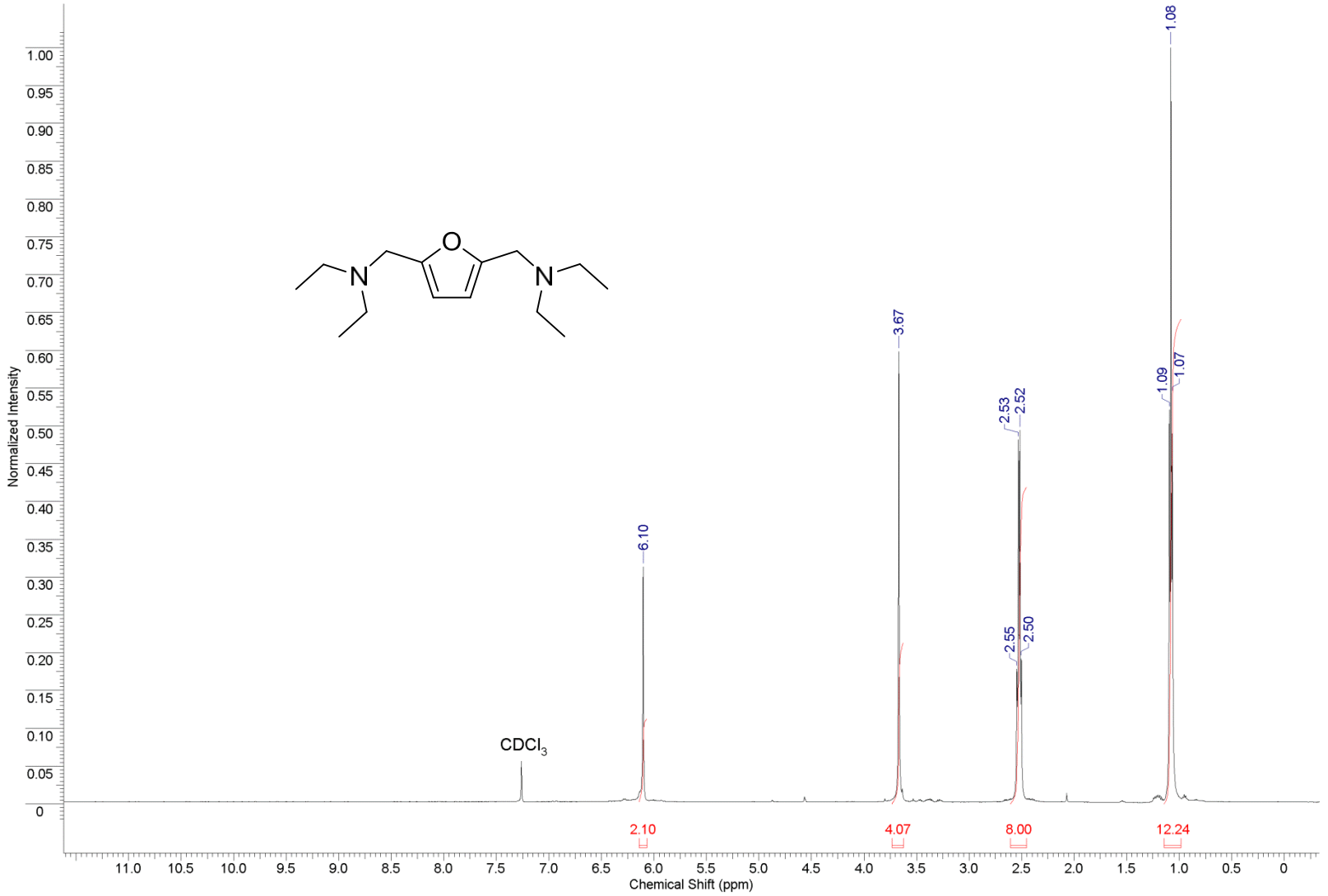


Fig. S20. ^{1}H NMR spectrum of 2,5-bis(diethylaminomethyl)furan 10 ($CDCl_3$, 298 K, 500 MHz).

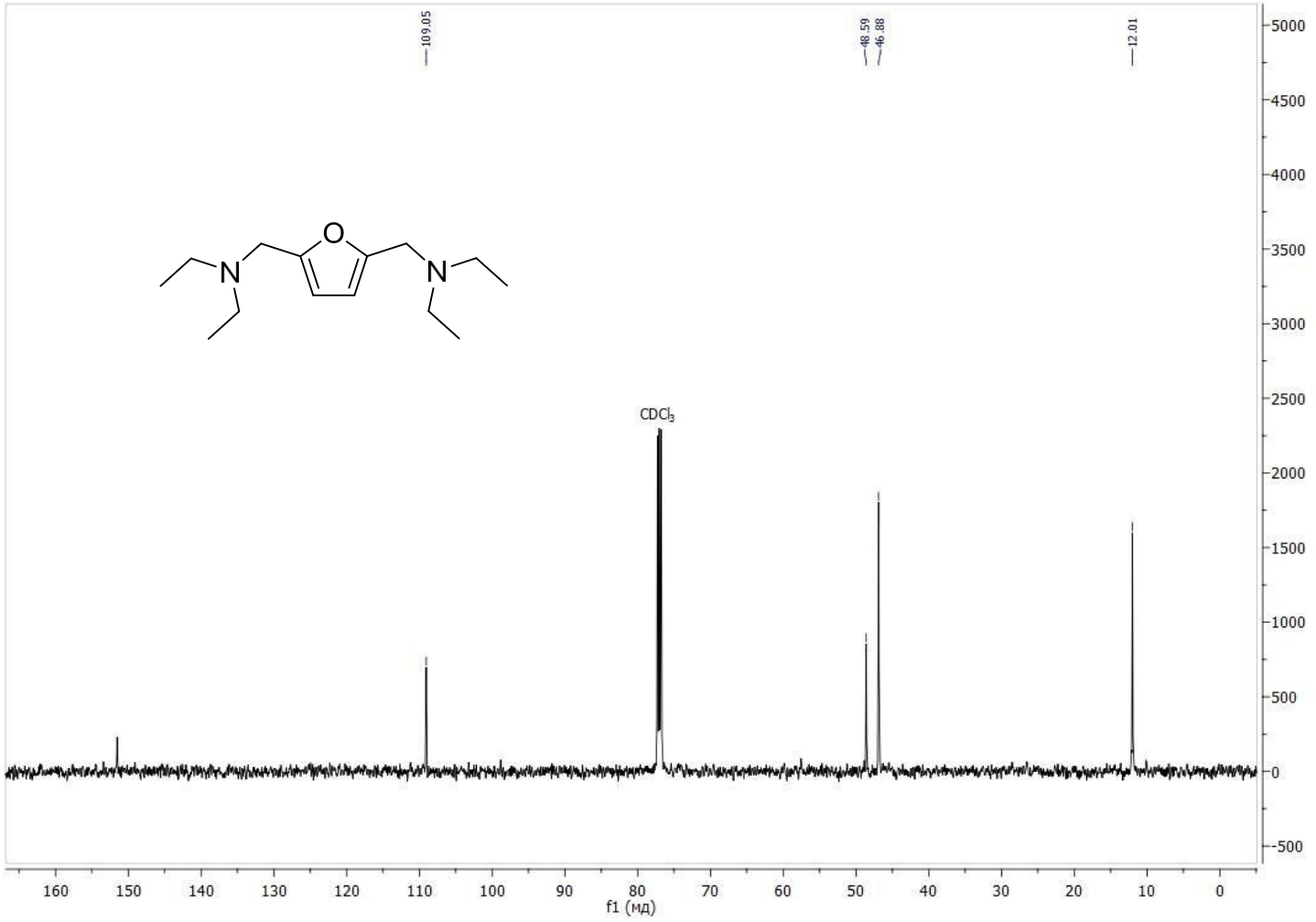


Fig. S21. ^{13}C NMR spectrum of 2,5-bis(diethylaminomethyl)furan 10 ($CDCl_3$, 298 K, 125 MHz).

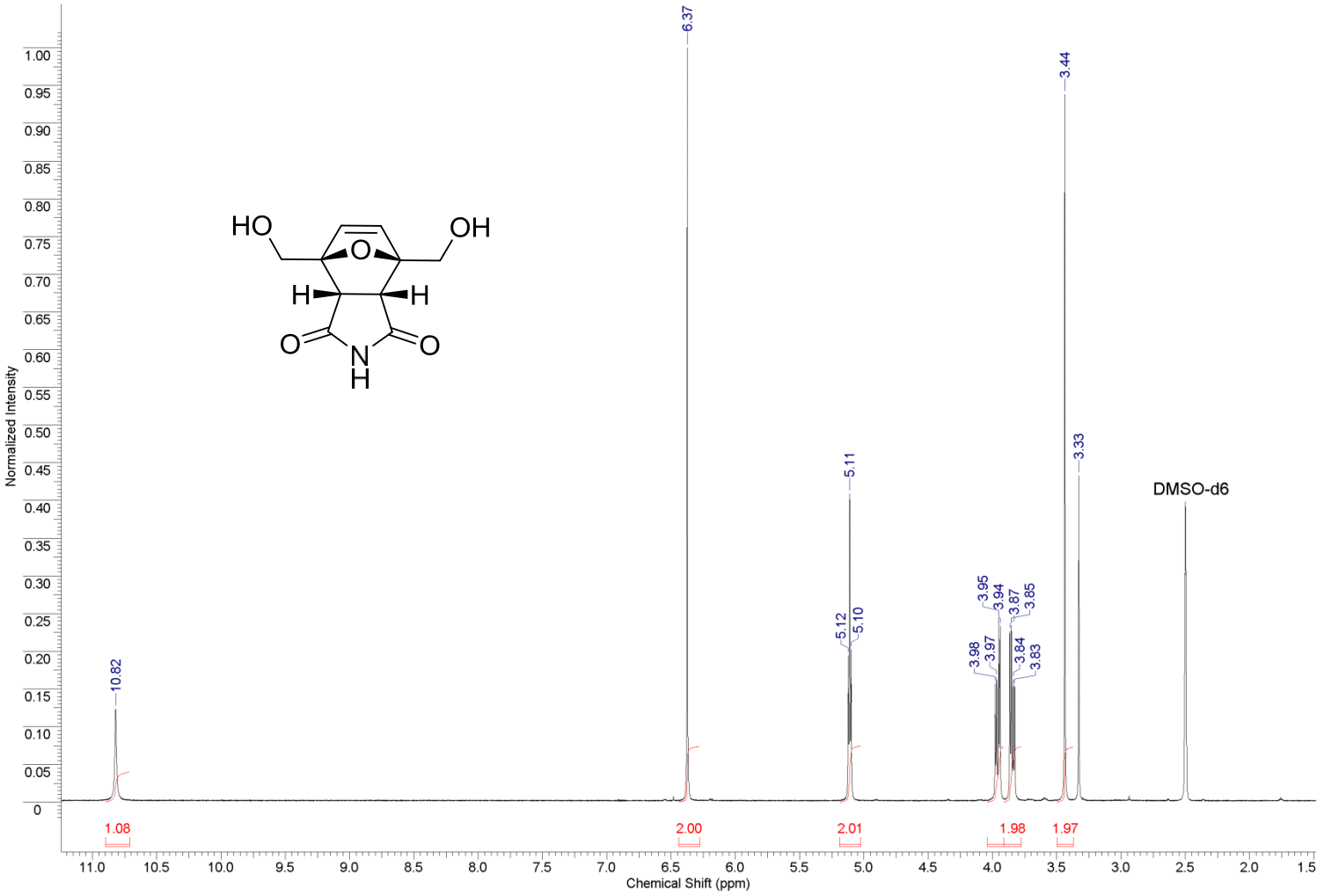


Fig. S22. ^{1}H NMR spectrum of *endo*-4,7-bis(hydroxymethyl)-3a,4,7,7a-tetrahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 3 (DMSO-d6, 298 K, 500 MHz).

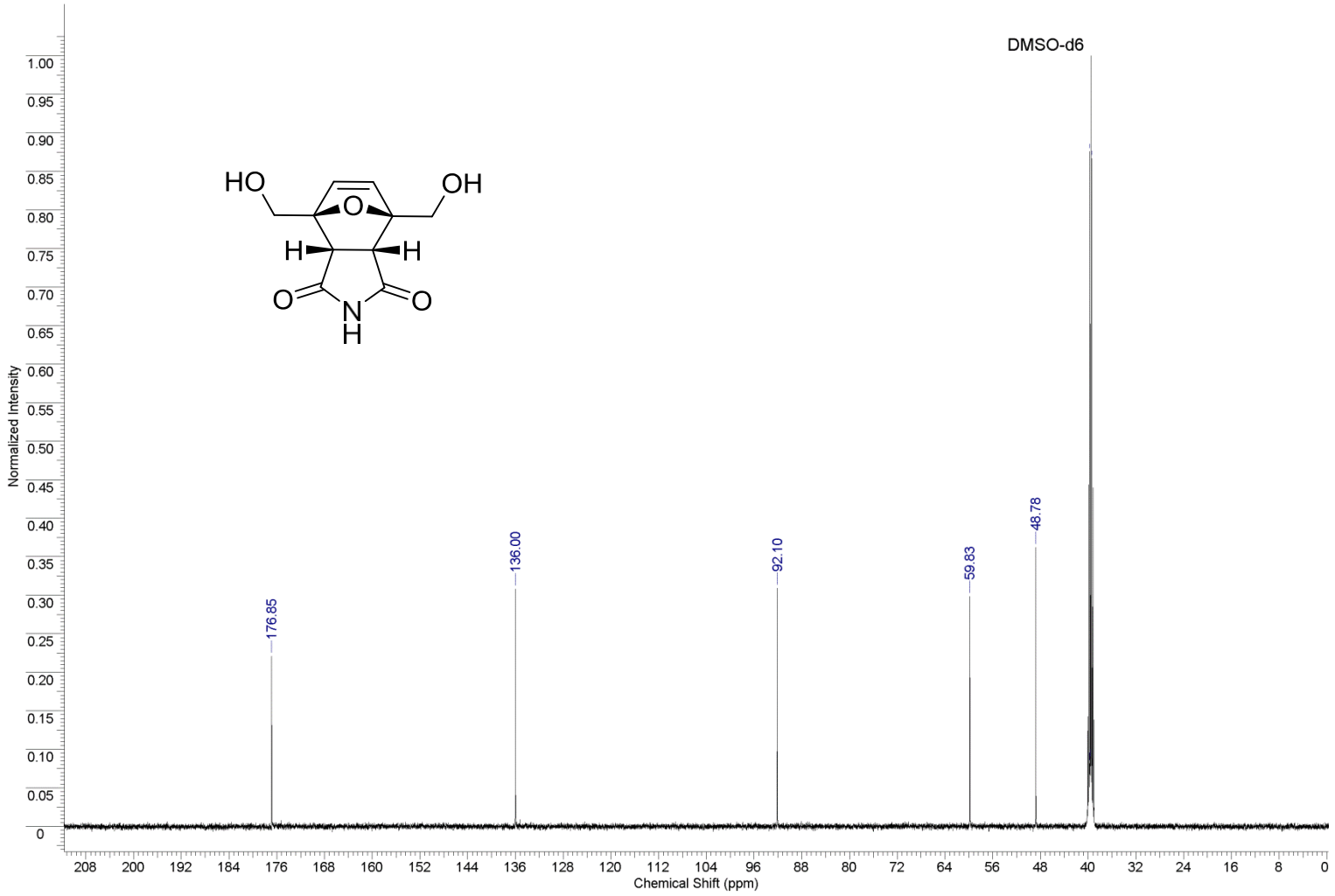


Fig. S23. ^{13}C NMR spectrum of *endo*-4,7-bis(hydroxymethyl)-3a,4,7,7a-tetrahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 3 (DMSO-d6, 298 K, 125 MHz).

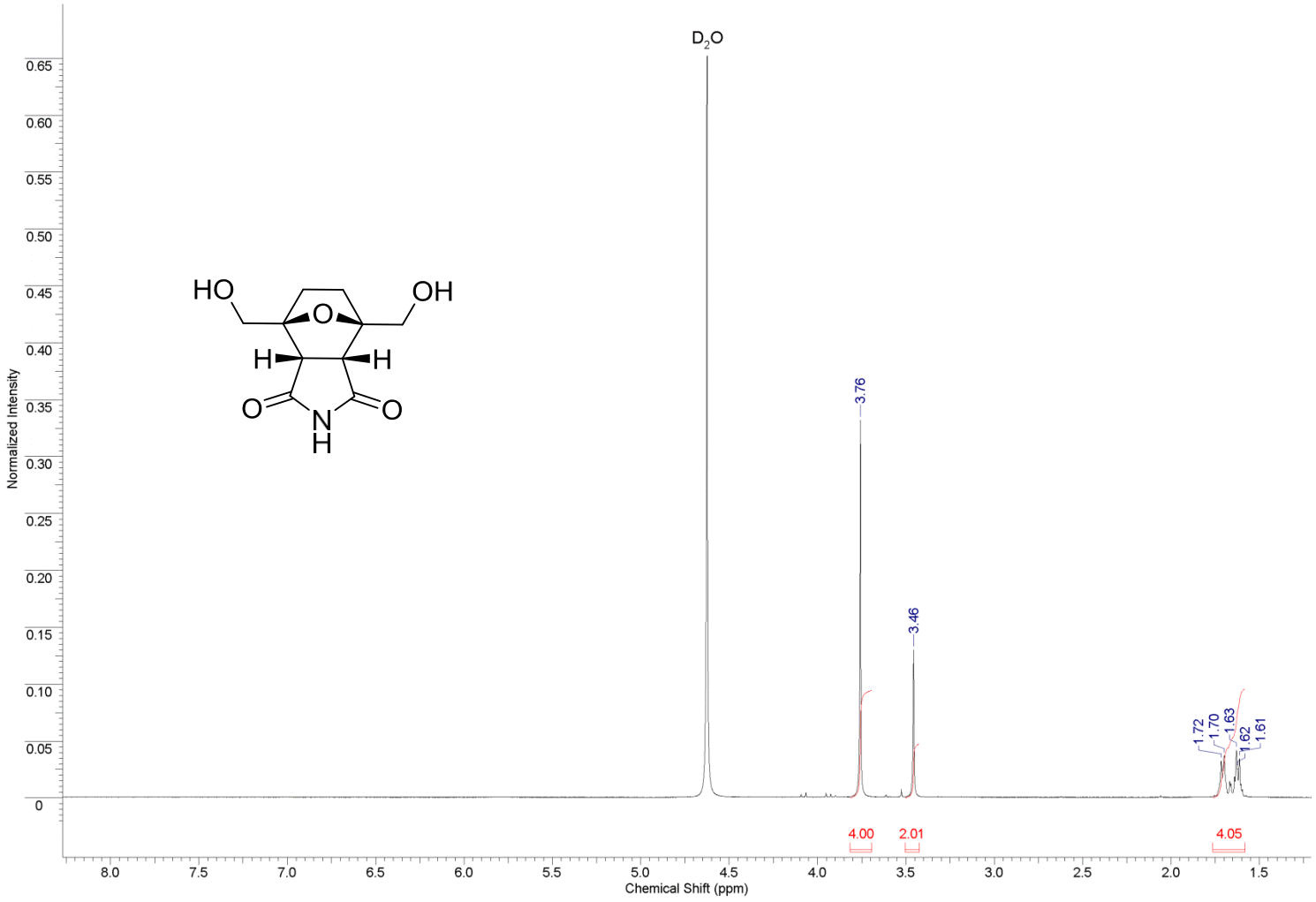


Fig. S24. ^{1}H NMR spectrum of *endo*-4,7-bis(hydroxymethyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 4 (D_2O, 298 K, 500 MHz).

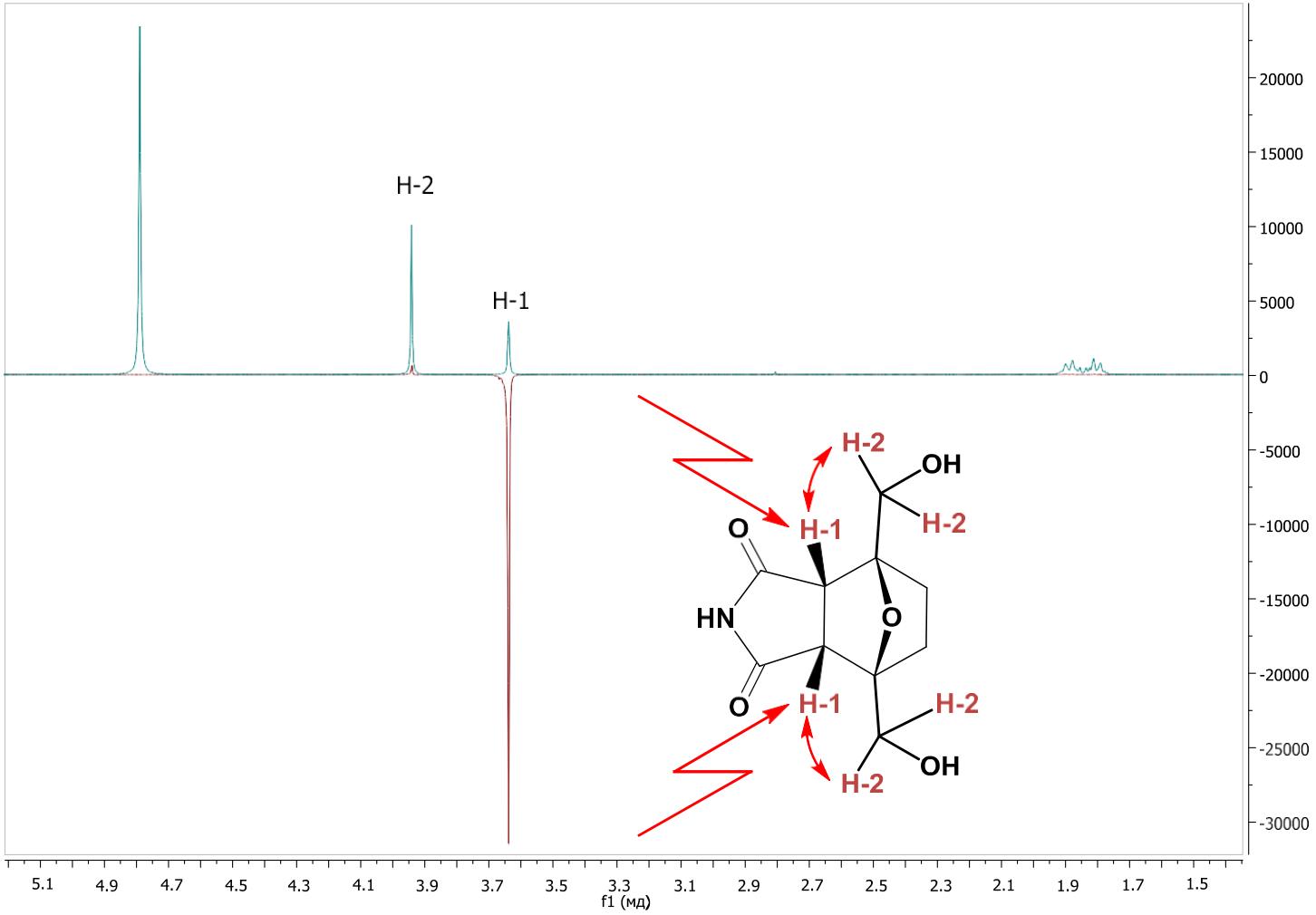


Fig. S25. NOE NMR spectrum of *endo*-4,7-bis(hydroxymethyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 4 (D_2O, 298 K, 500 MHz).

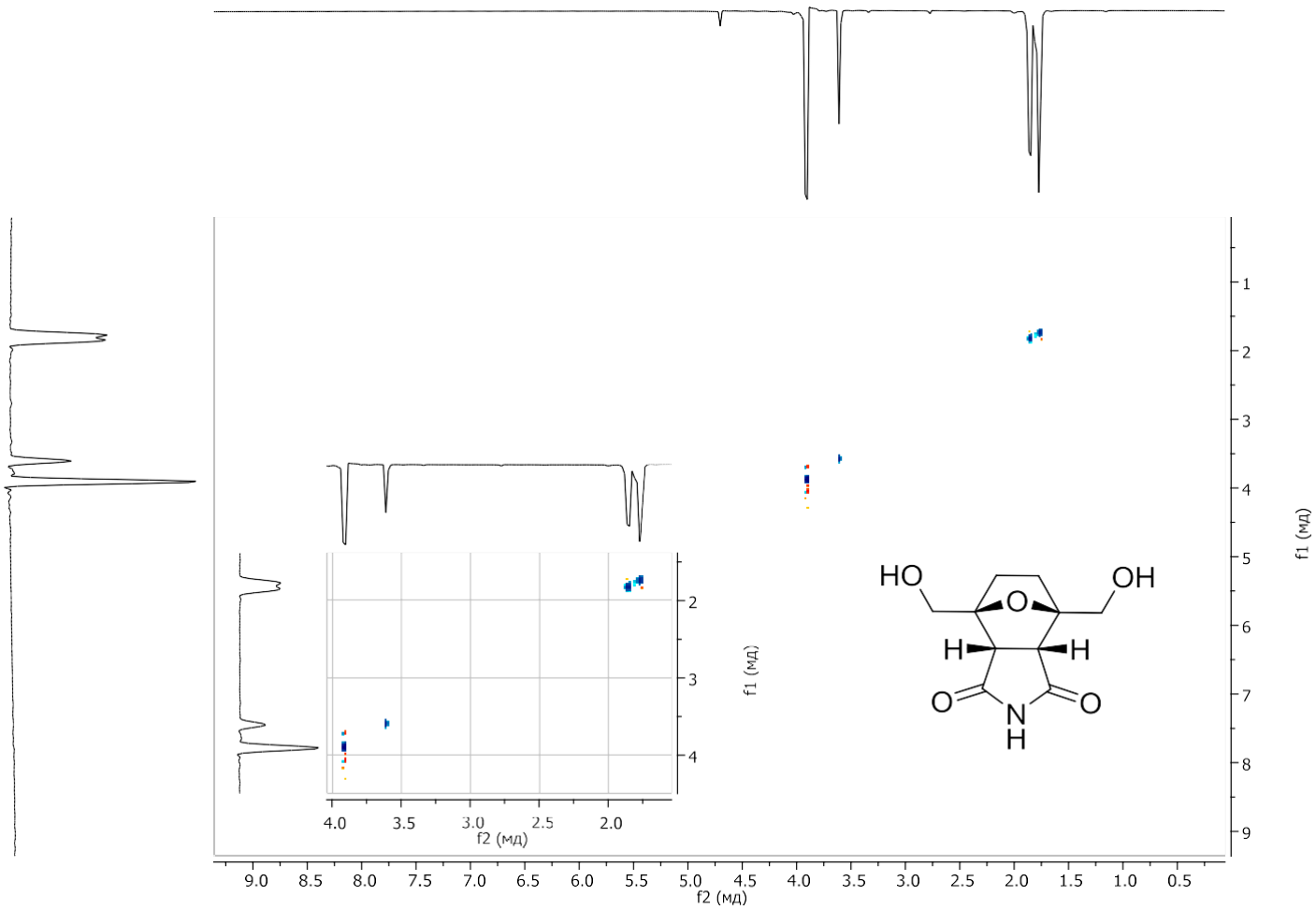


Fig. S26. ^{1}H-^{1}H NOESY NMR spectrum of *endo*-4,7-bis(hydroxymethyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 4 (D_2O, 298 K, 500 MHz).

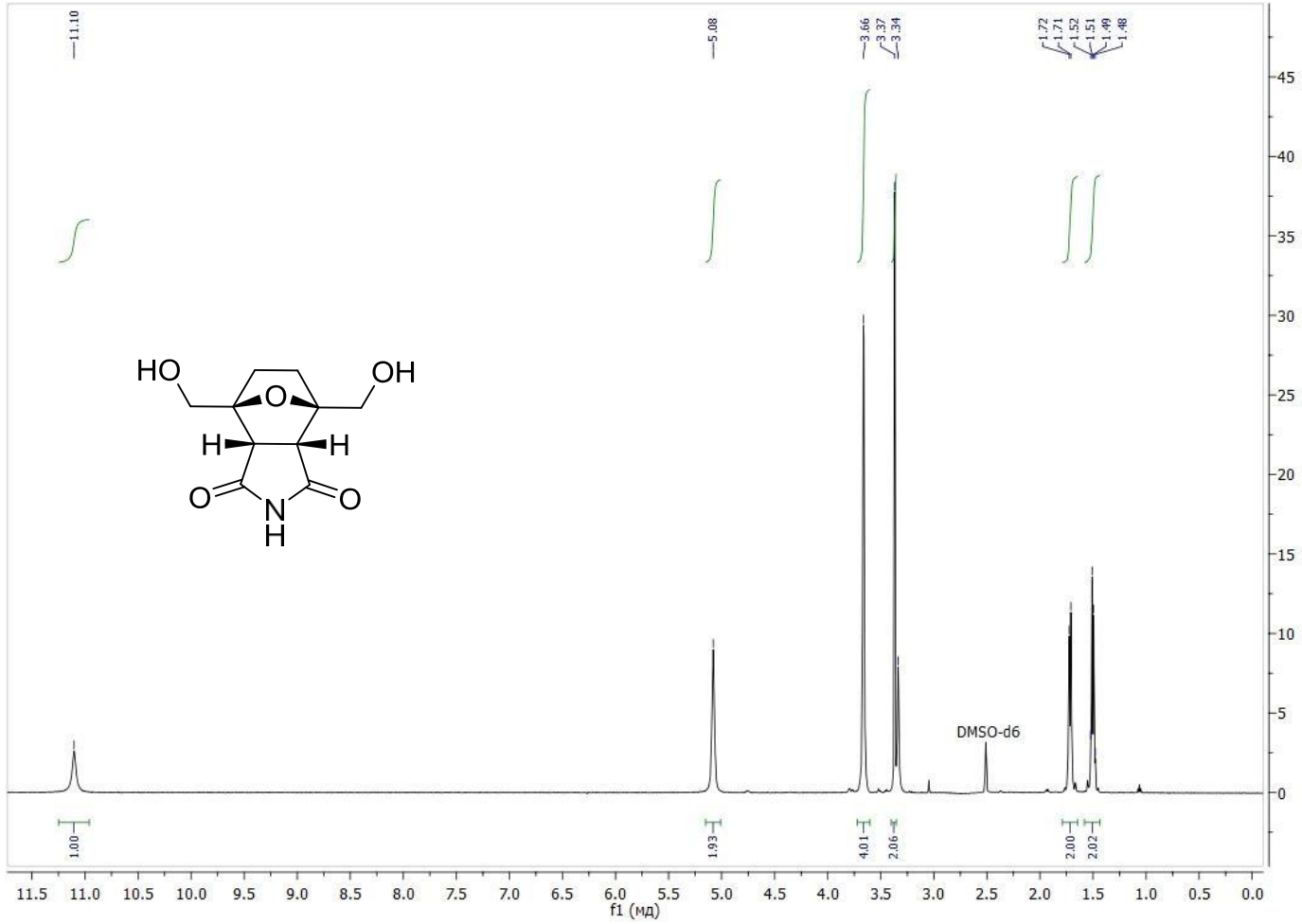


Fig. S27. ^{1}H NMR spectrum of *endo*-4,7-bis(hydroxymethyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 4 (DMSO-d6, 298 K, 500 MHz).

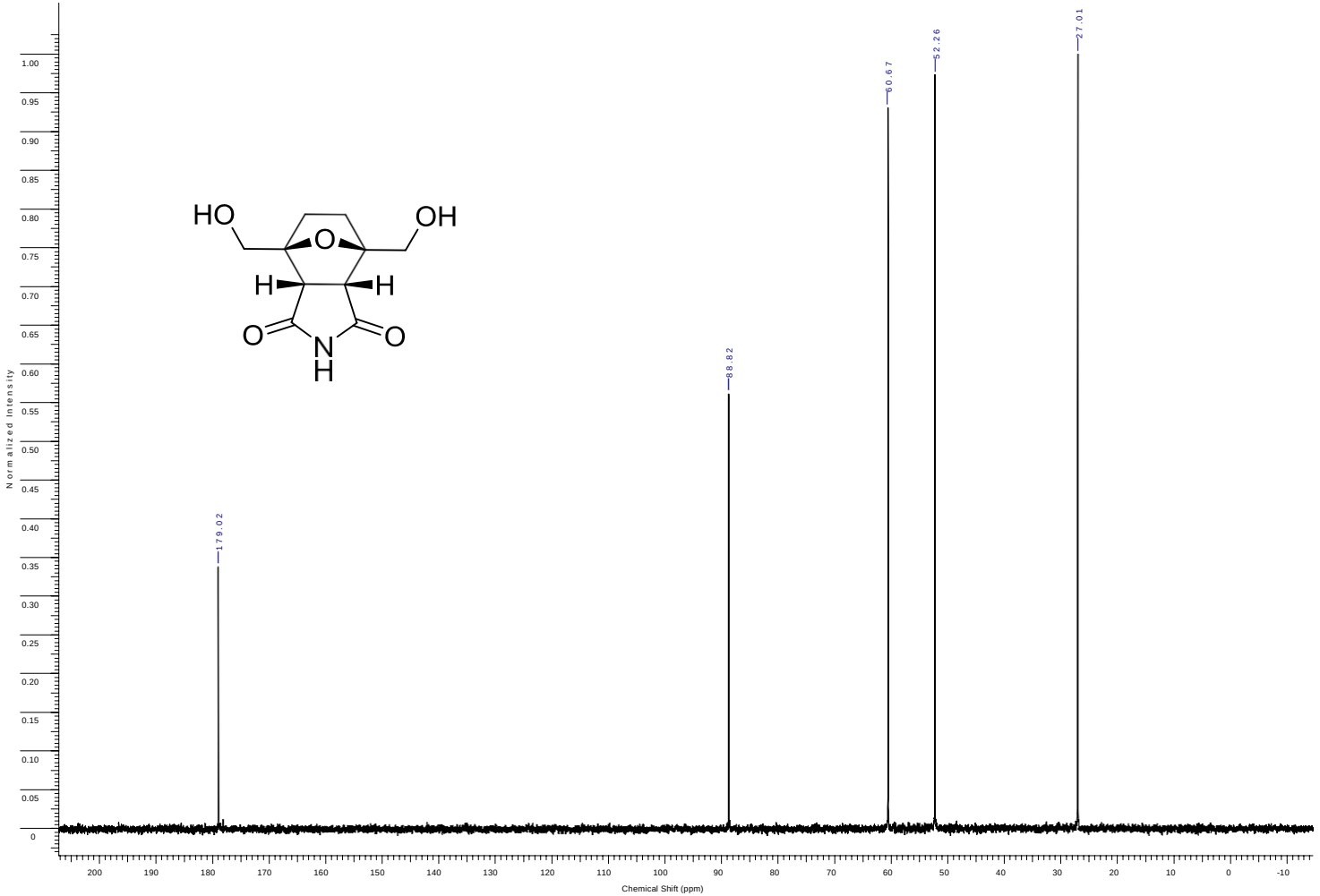


Fig. S28. ^{13}C NMR spectrum of *endo*-4,7-bis(hydroxymethyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 4 (D_2O, 298 K, 125 MHz).

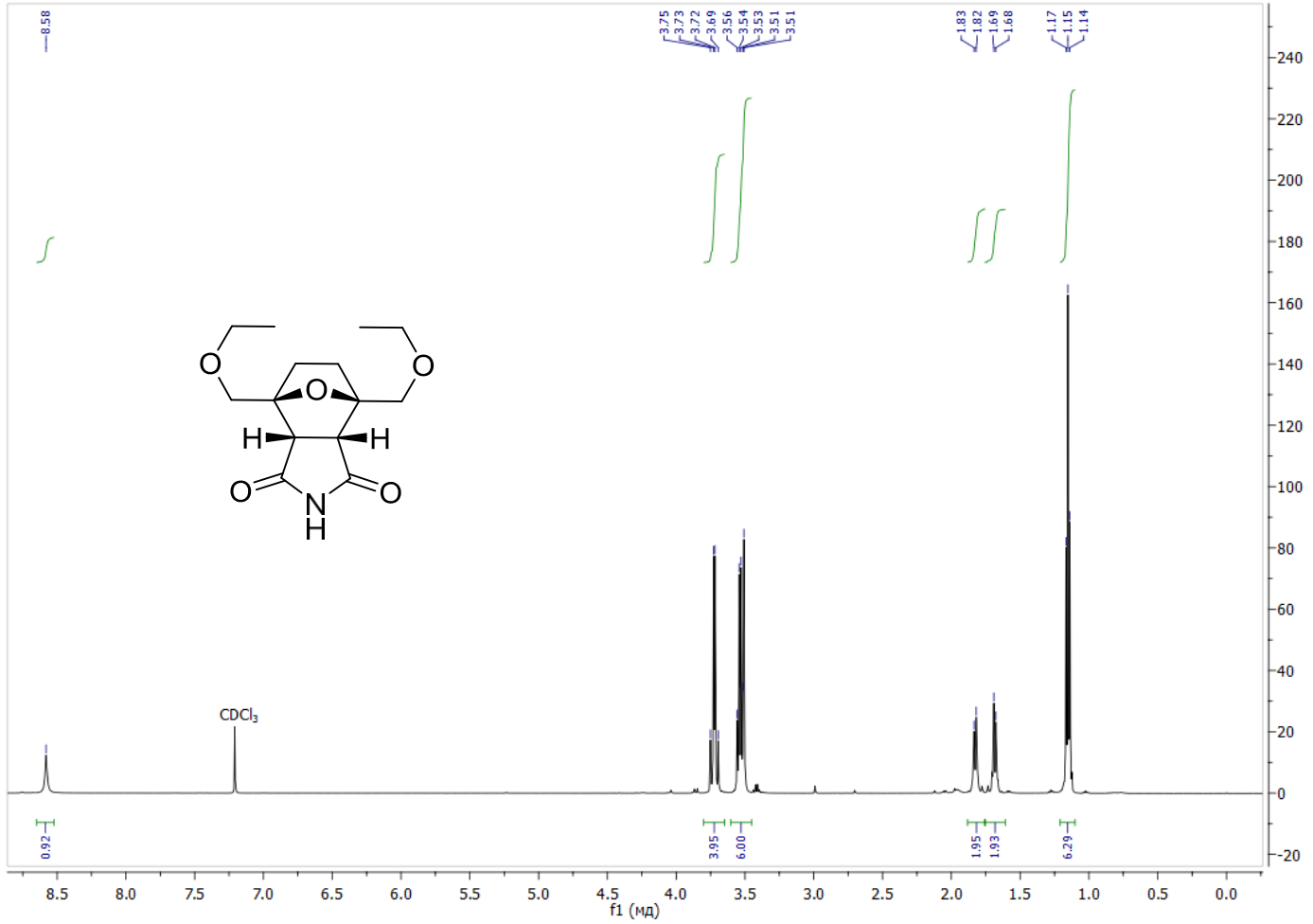


Fig. S29. ^{1}H NMR spectrum of *endo*-4,7-bis(ethoxymethyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 8 ($CDCl_3$, 298 K, 500 MHz).

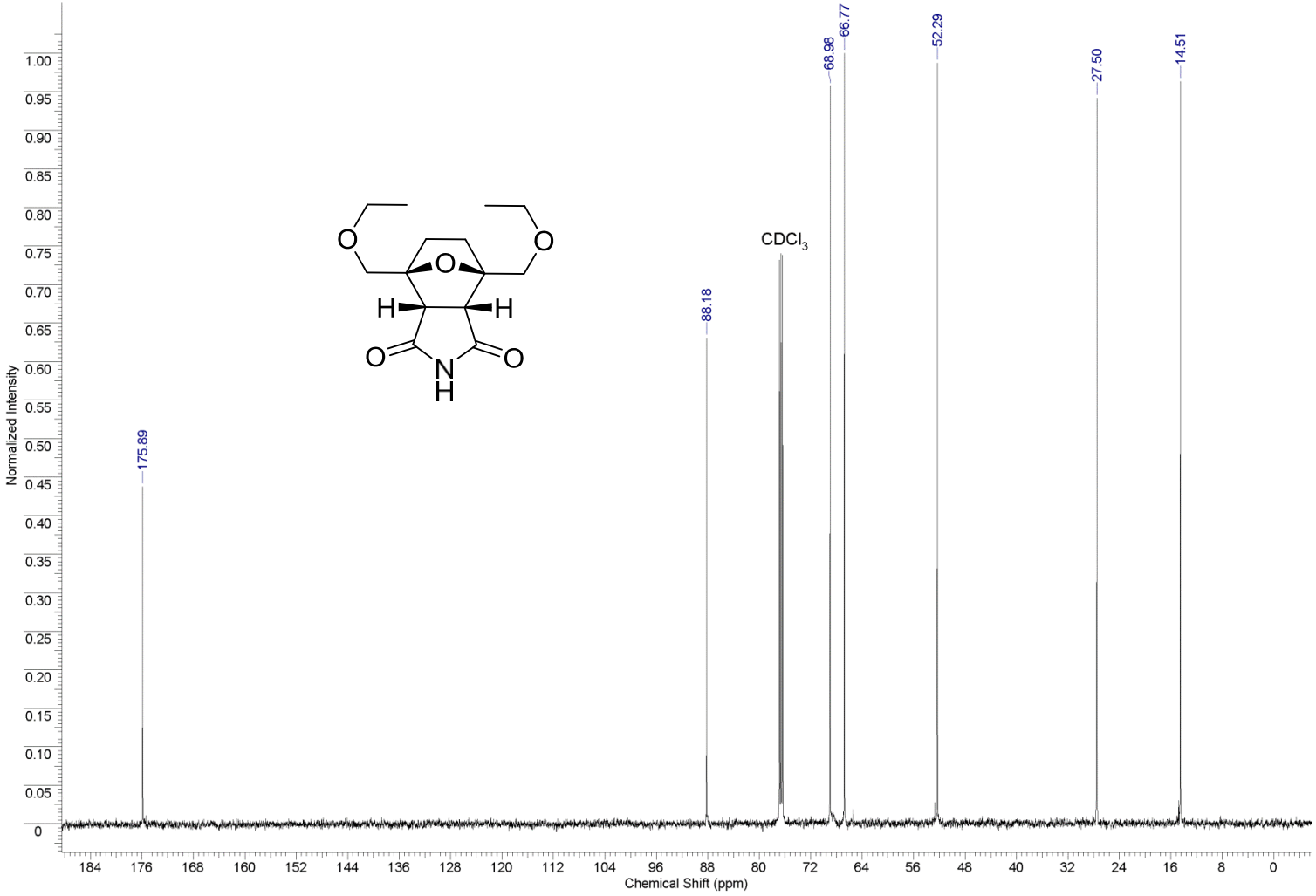


Fig. S30. ^{13}C NMR spectrum of *endo*-4,7-bis(ethoxymethyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 8 ($CDCl_3$, 298 K, 125 MHz).

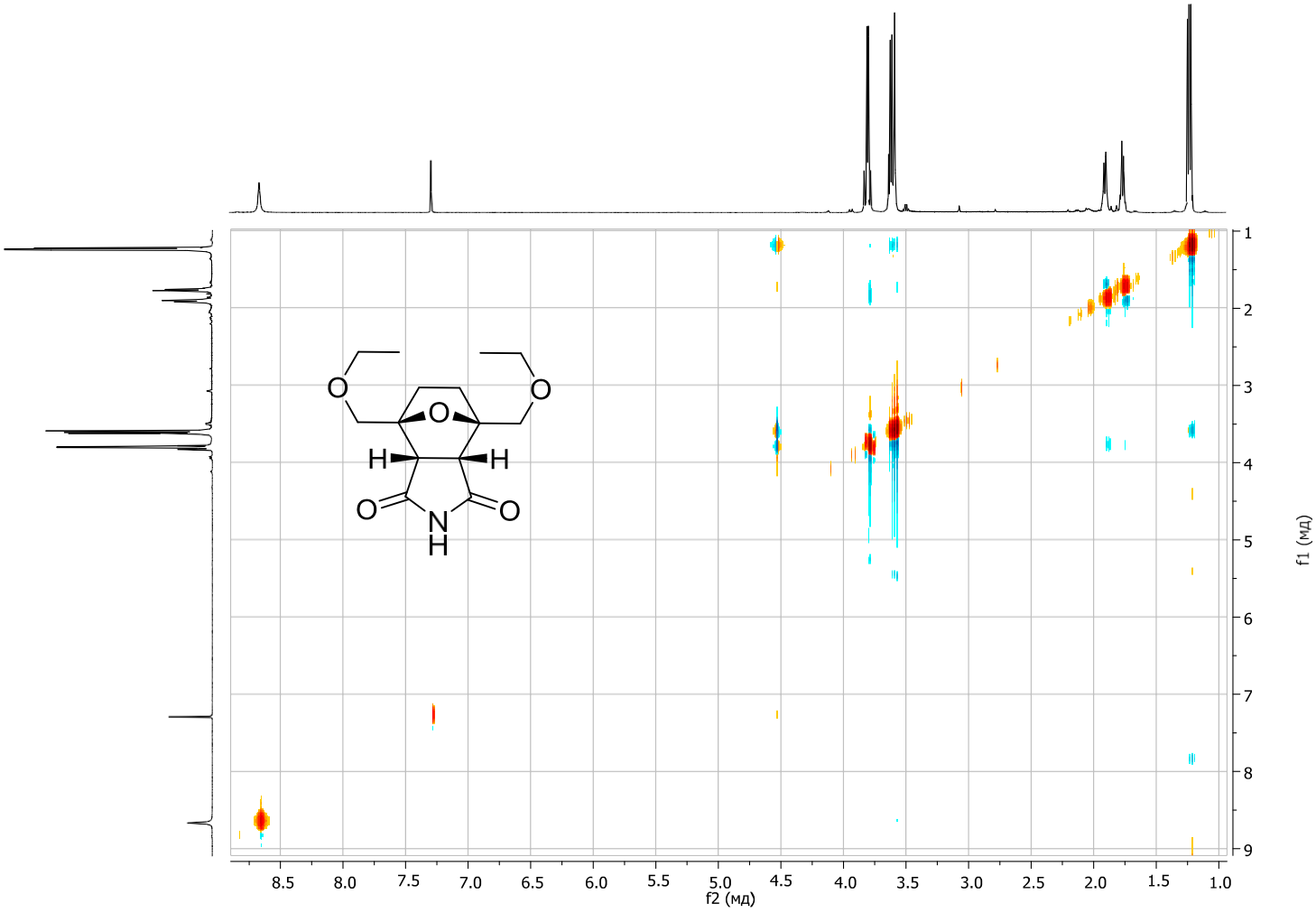


Fig. S31. ^{1}H-^{1}H NOESY NMR spectrum of *endo*-4,7-bis(ethoxymethyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 8 ($CDCl_3$, 298 K, 500 MHz).

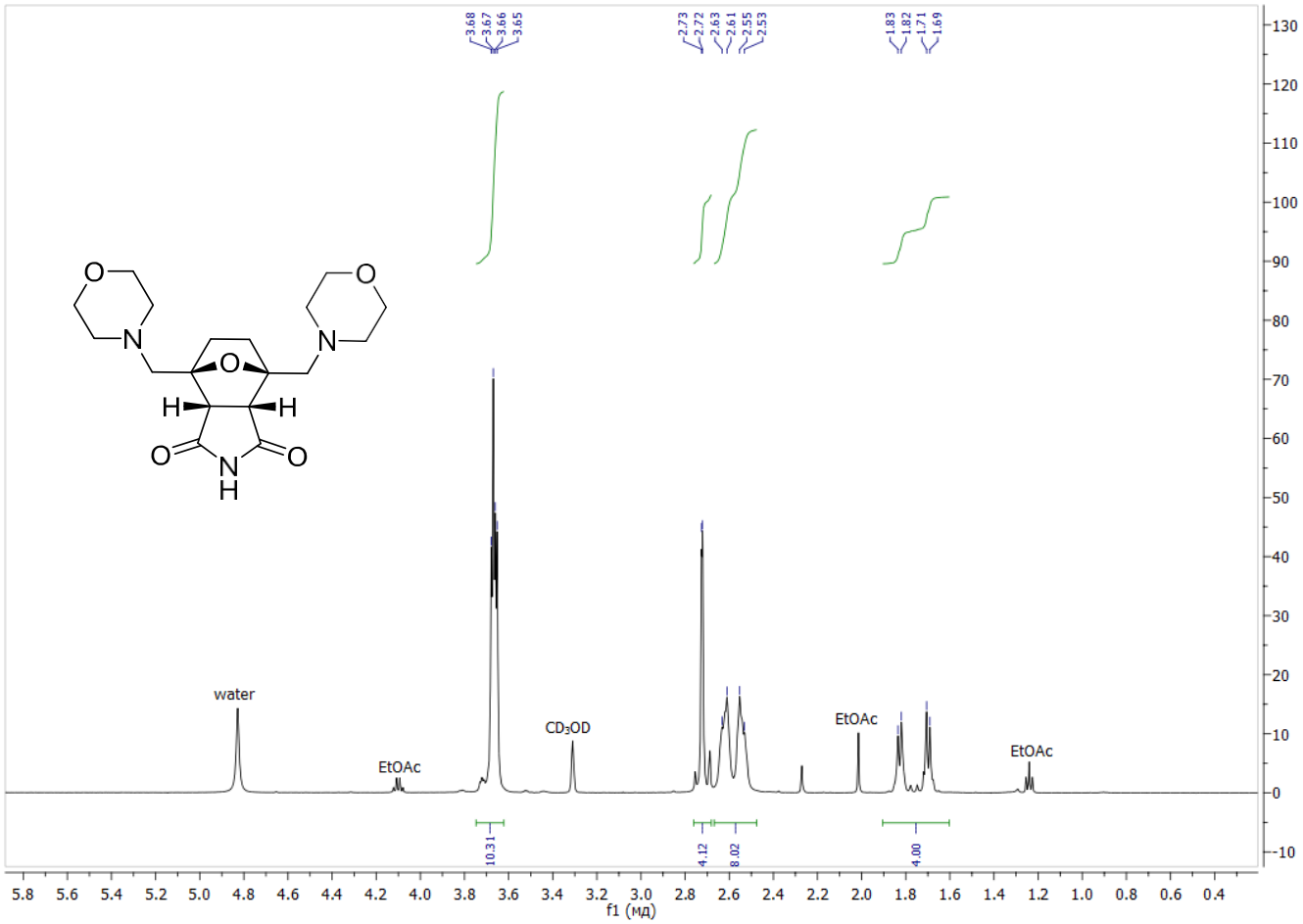


Fig. S32. ^{1}H NMR spectrum of *endo*-4,7-bis(morpholinomethyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 13 (CD_3OD, 298 K, 500 MHz).

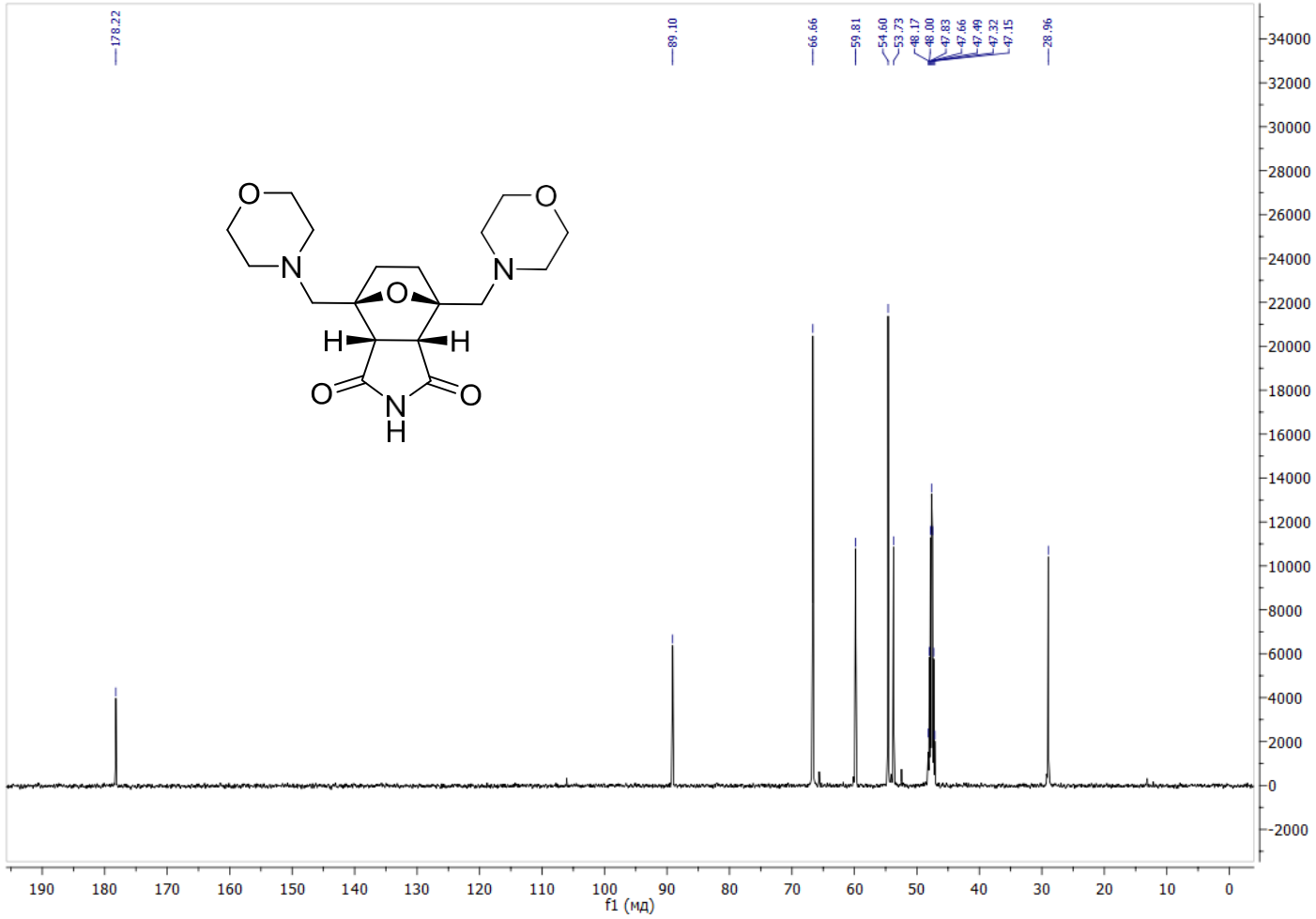


Fig. S33. ^{13}C NMR spectrum of *endo*-4,7-bis(morpholinomethyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 13 (CD_3OD, 298 K, 125 MHz).

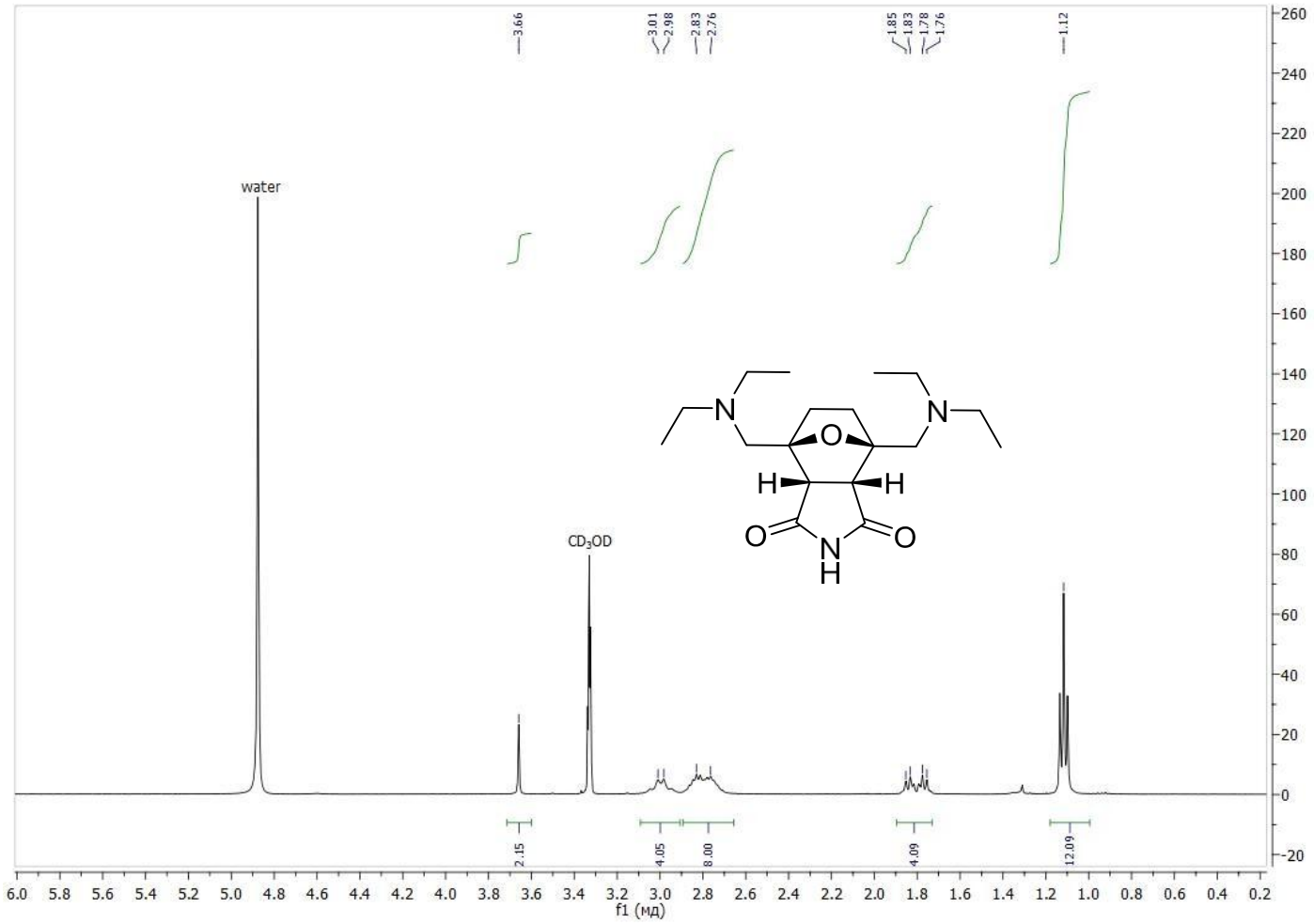


Fig. S34. ^{1}H NMR spectrum of *endo*-4,7-bis((diethylamino)methyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 12 (CD_3OD, 298 K, 500 MHz).

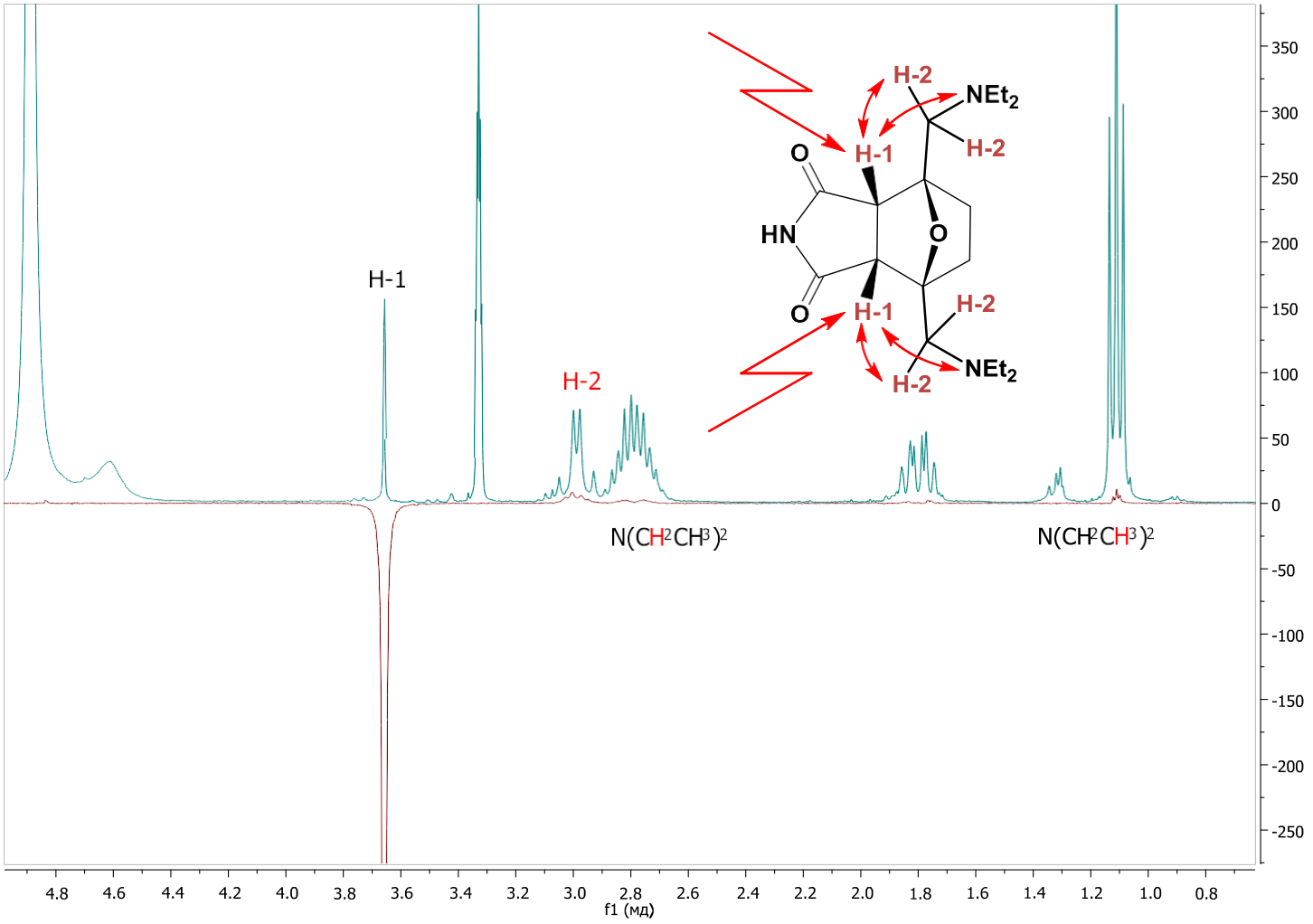


Fig. S35. NOE NMR spectrum of *endo*-4,7-bis((diethylamino)methyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 12 (CD_3OD, 298 K, 500 MHz).

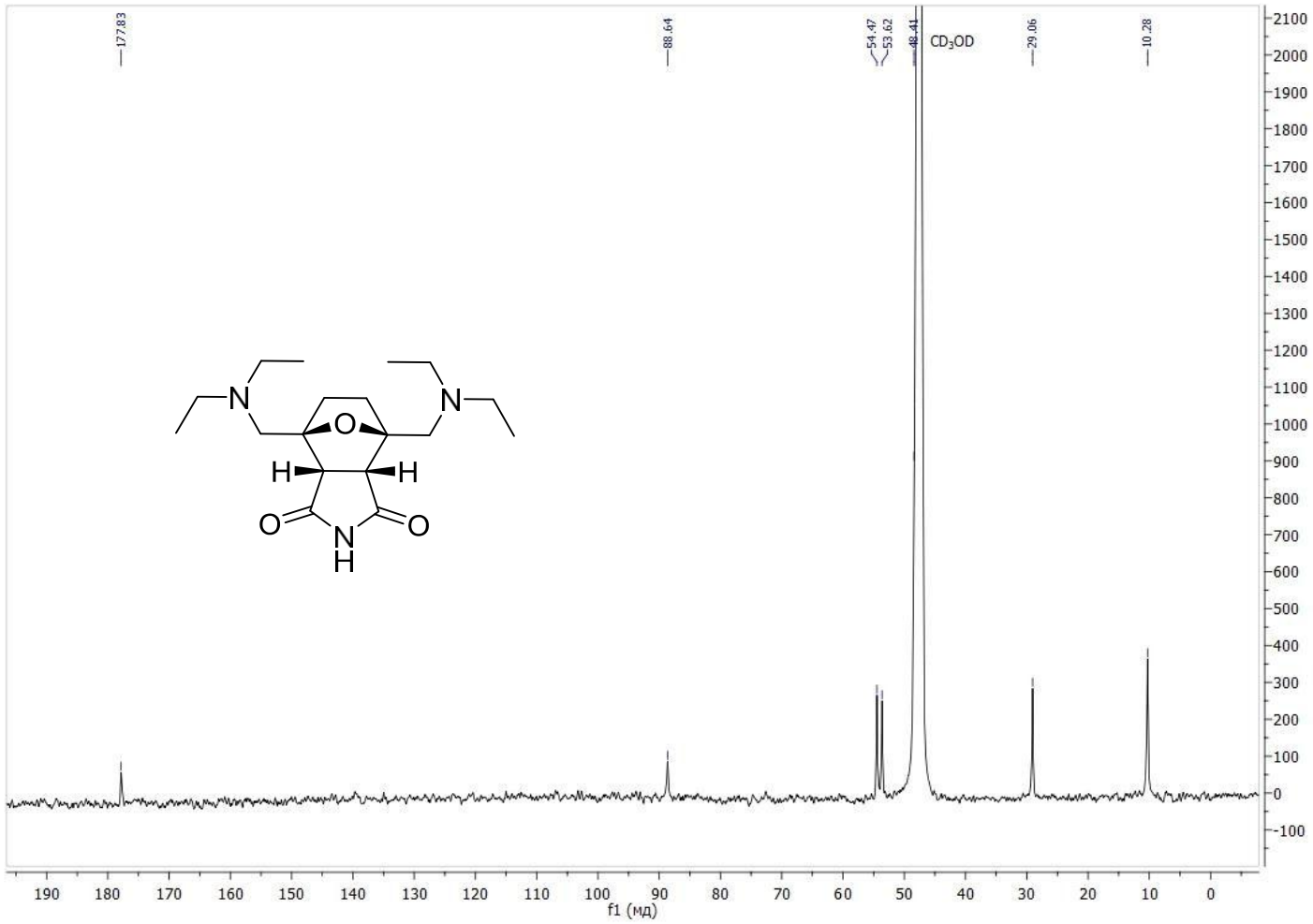


Fig. S36. ^{13}C NMR spectrum of *endo*-4,7-bis((diethylamino)methyl)hexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 12 (CD_3OD, 298 K, 125 MHz).

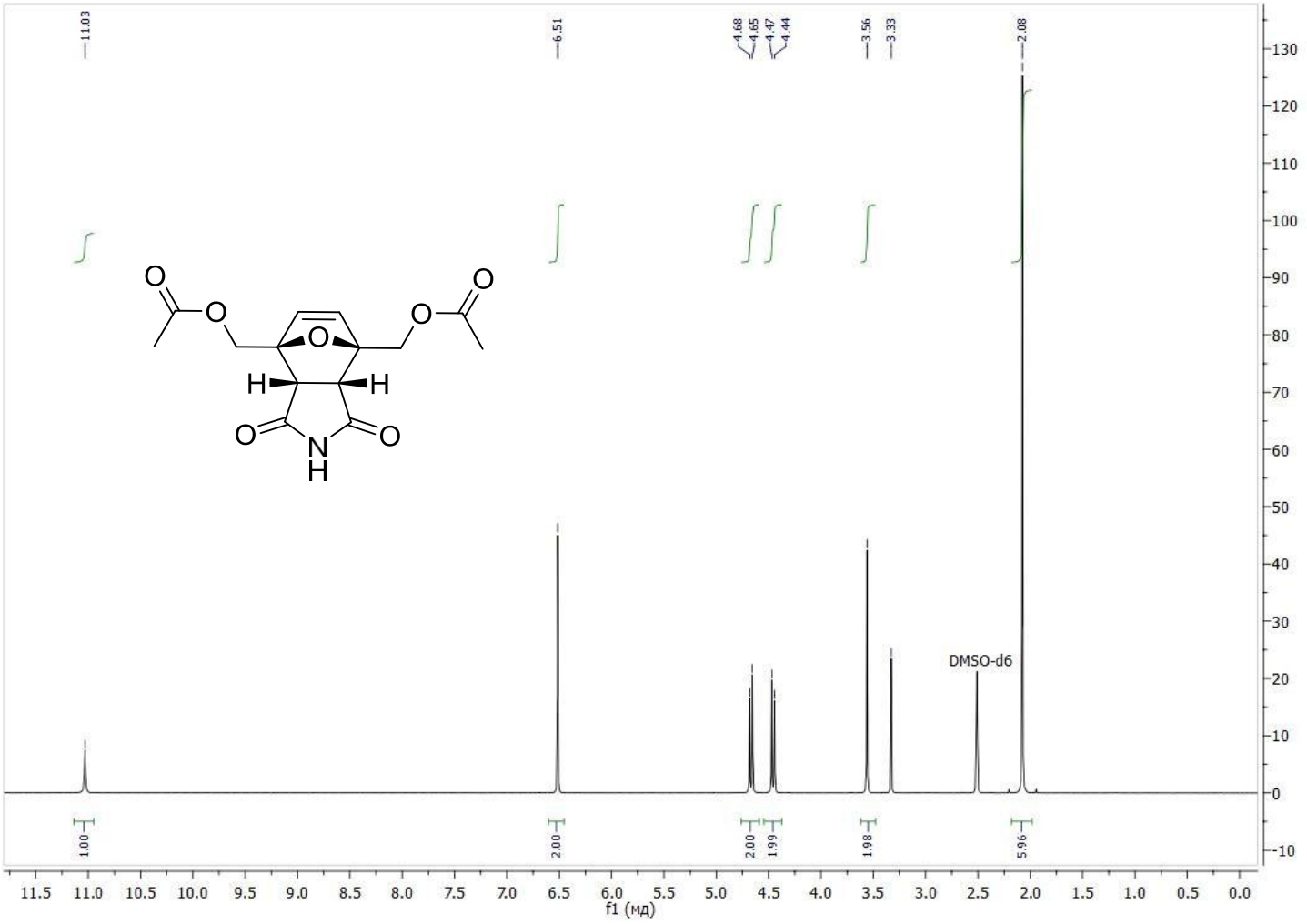


Fig. S37. ^{1}H NMR spectrum of *endo*-(1,3-dioxo-2,3,3a,7a-tetrahydro-1H-4,7-epoxyisoindole-4,7-diyl)bis(methylene) diacetate 9a (DMSO-d6, 298 K, 500 MHz).

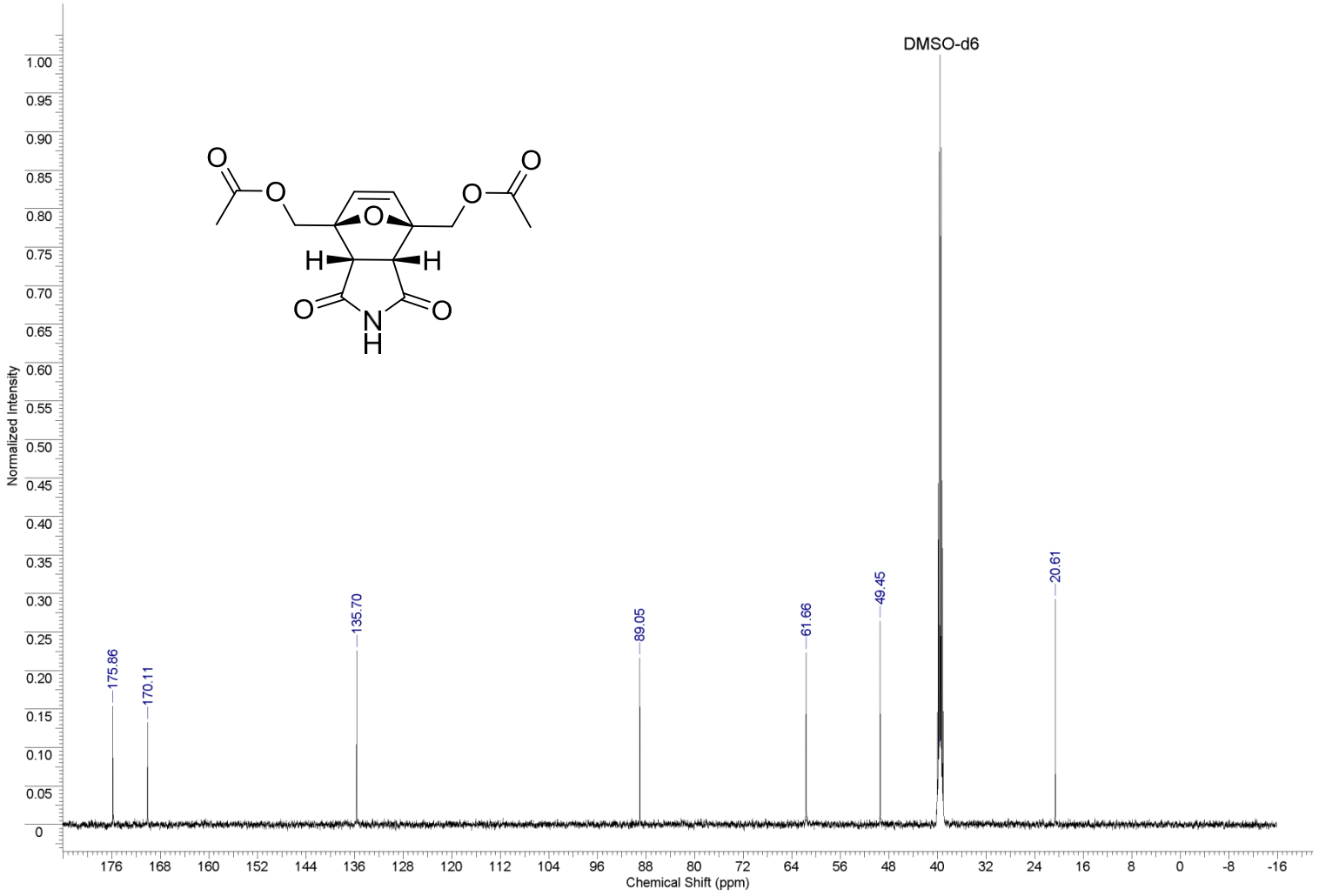


Fig. S38. ^{13}C NMR spectrum of *endo*-(1,3-dioxo-2,3,3a,7a-tetrahydro-1H-4,7-epoxyisoindole-4,7-diyl)bis(methylene) diacetate 9a (DMSO-d6, 298 K, 125 MHz).

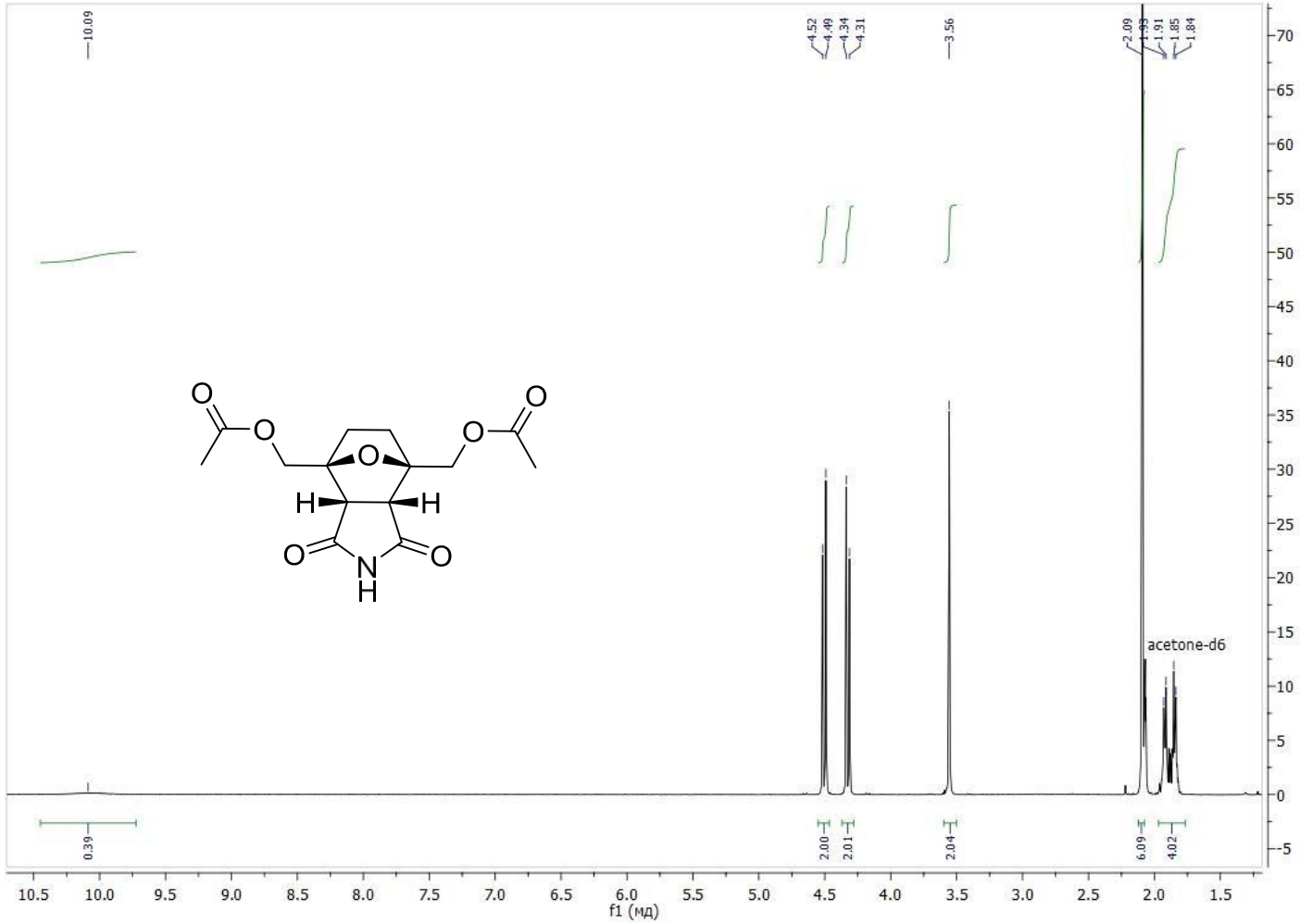


Fig. S39. ^{1}H NMR spectrum of *endo*-(1,3-dioxohexahydro-1H-4,7-epoxyisoindole-4,7-diyl)bis(methylene) diacetate 9 (acetone-d6, 298 K, 500 MHz).

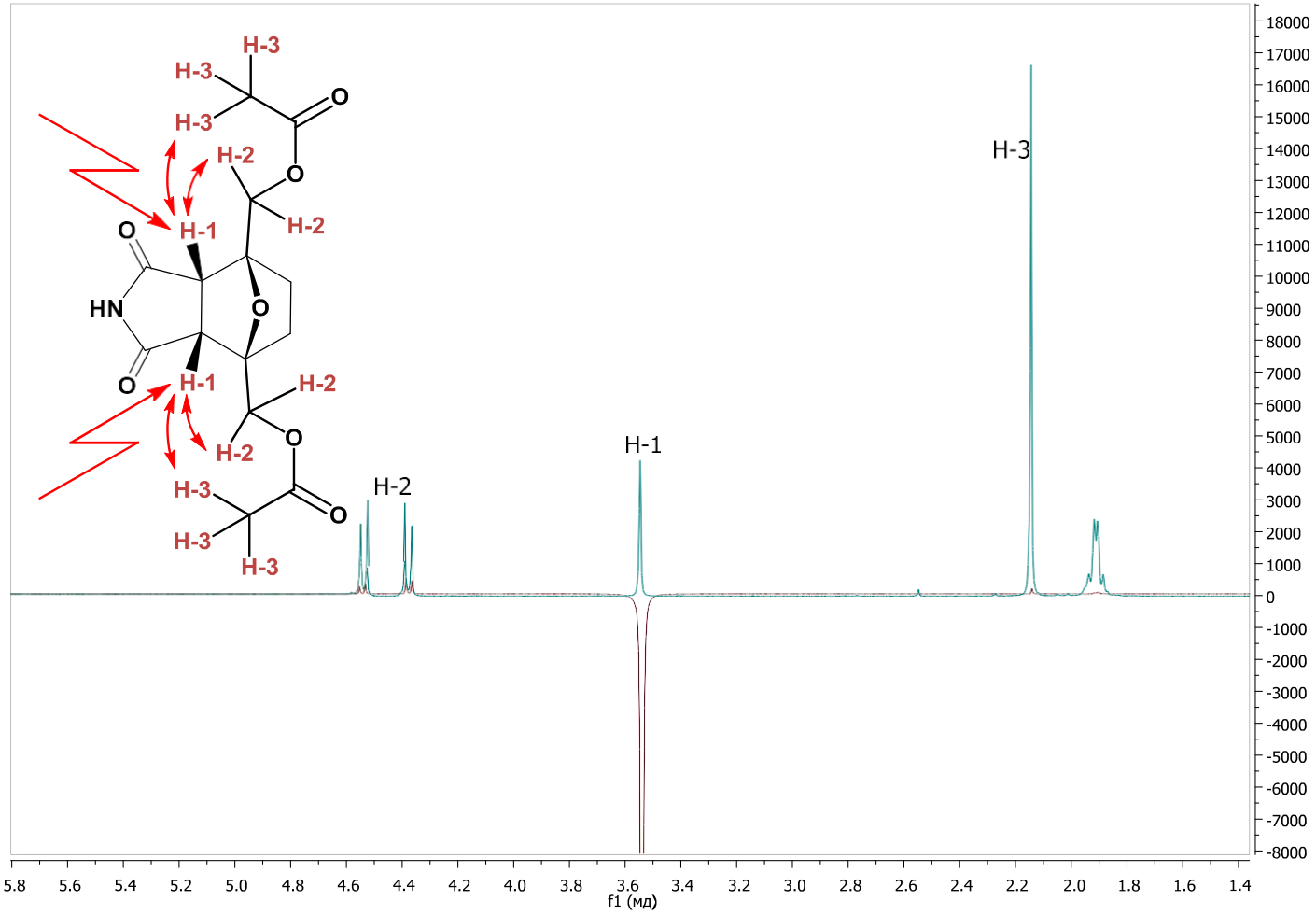


Fig. S40. NOE NMR spectrum of *endo*-(1,3-dioxohexahydro-1H-4, 7-epoxyisoindole-4,7-diyl)bis(methylene) diacetate 9 ($CDCl_3$, 298 K, 500 MHz).

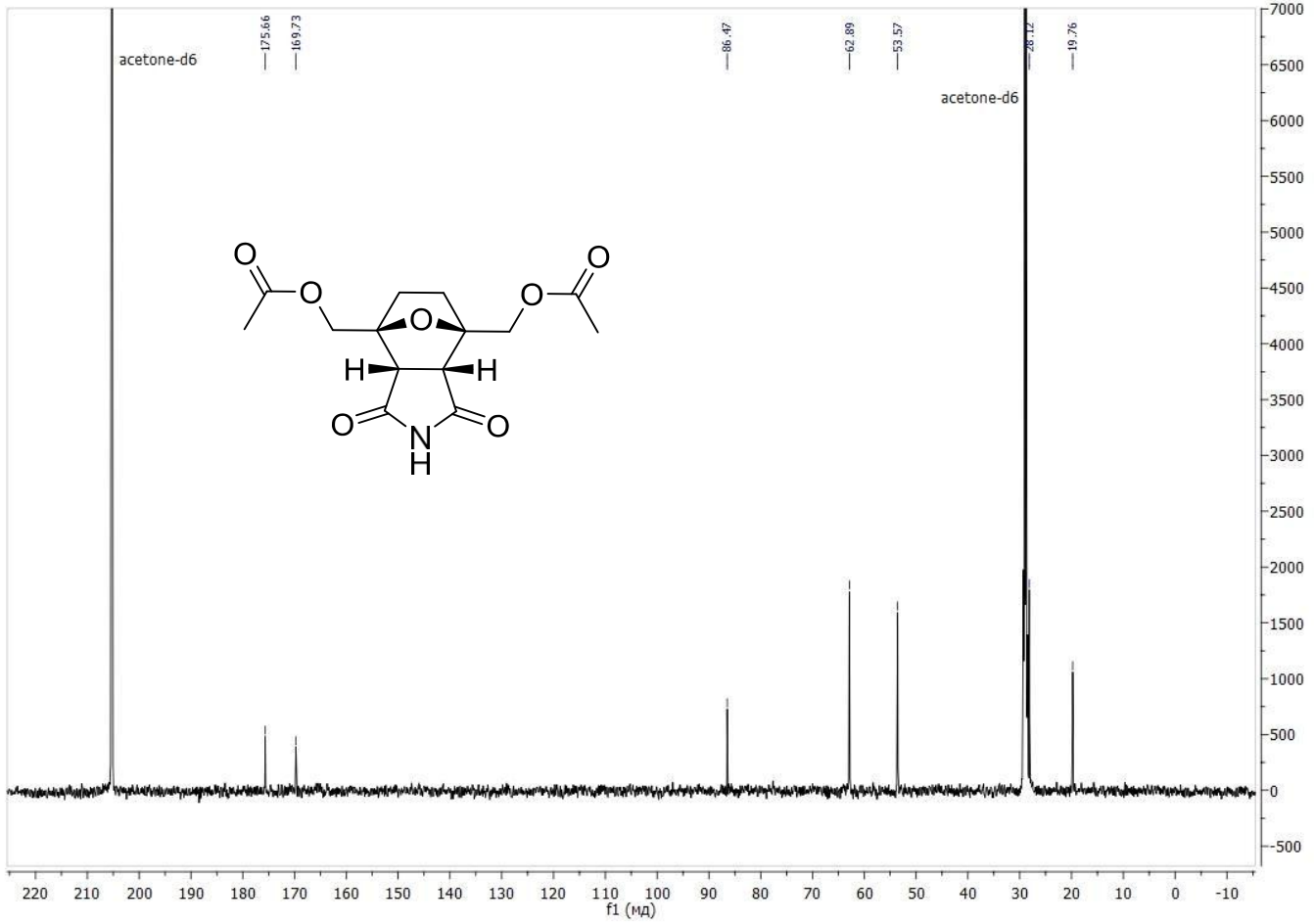


Fig. S41. ^{13}C NMR spectrum of *endo*-(1,3-dioxohexahydro-1H-4,7-epoxyisoindole-4,7-diyl)bis(methylene) diacetate 9 (acetone-d6, 298 K, 125 MHz).

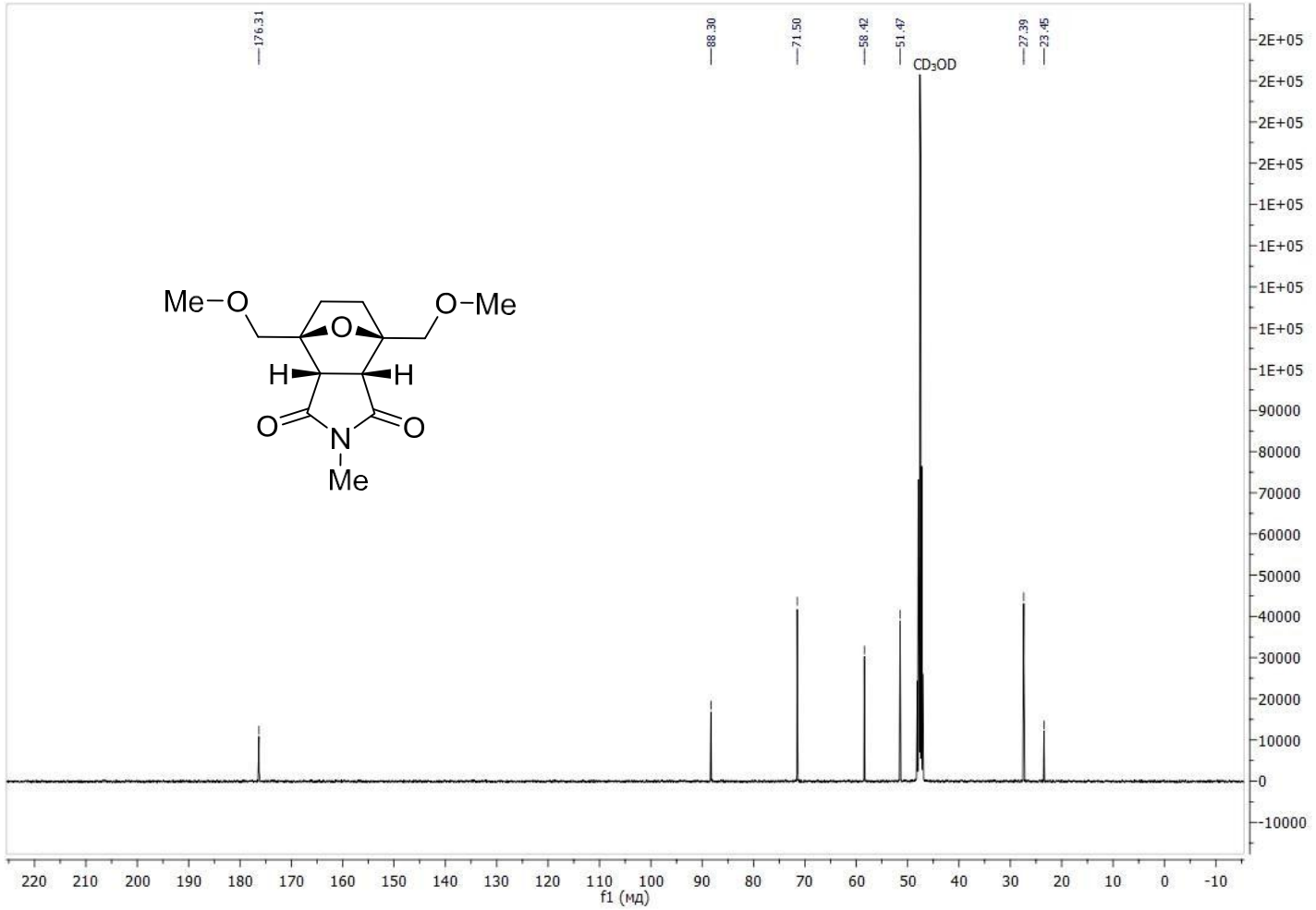


Fig. S42. ^{13}C NMR spectrum of *endo*-4,7-bis(methoxymethyl)-2-methylhexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 15 (CD_3OD, 298 K, 125 MHz).

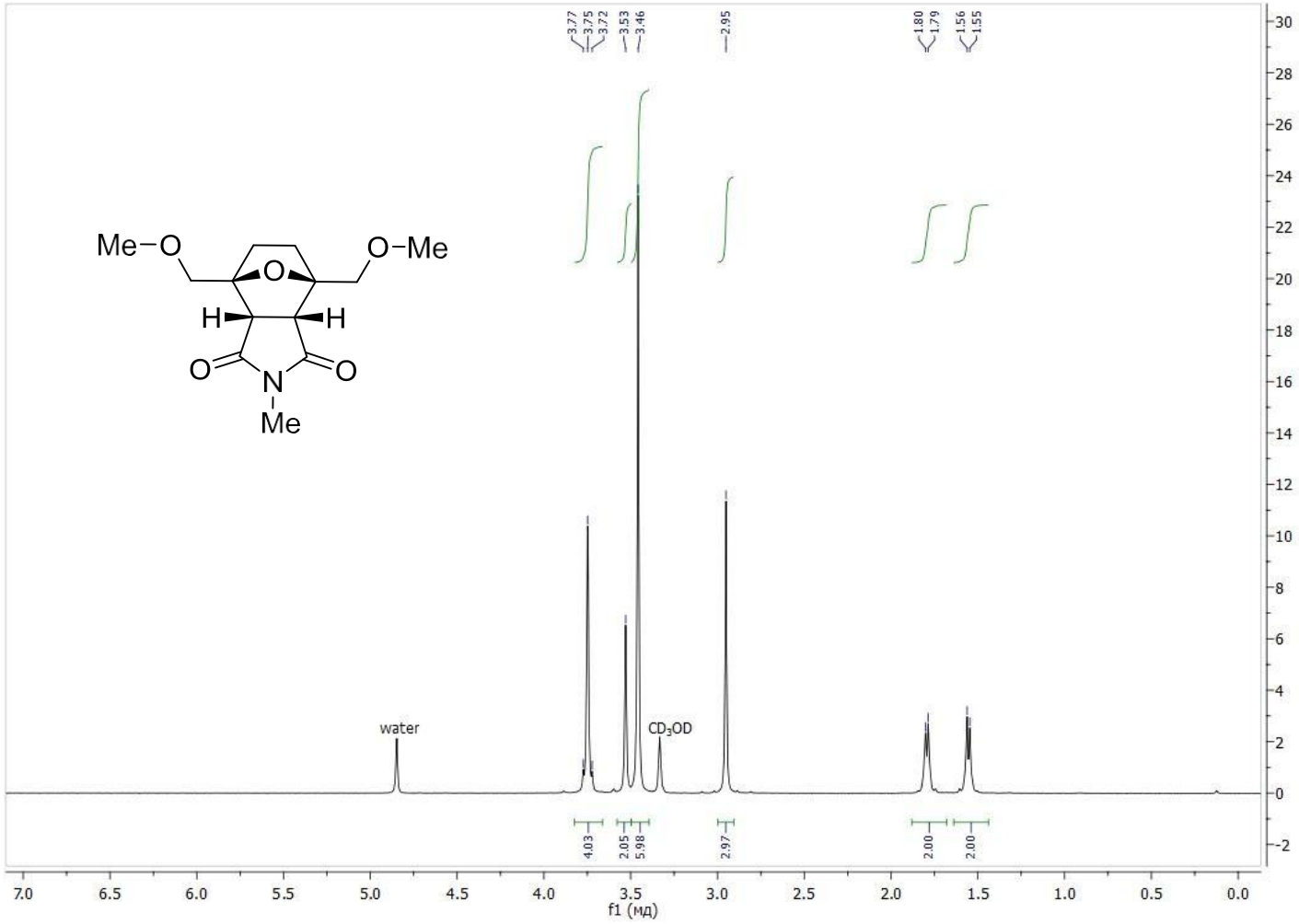


Fig. S43. ^{1}H NMR spectrum of *endo*-4,7-bis(methoxymethyl)-2-methylhexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 15 (CD_3OD, 298 K, 500 MHz).

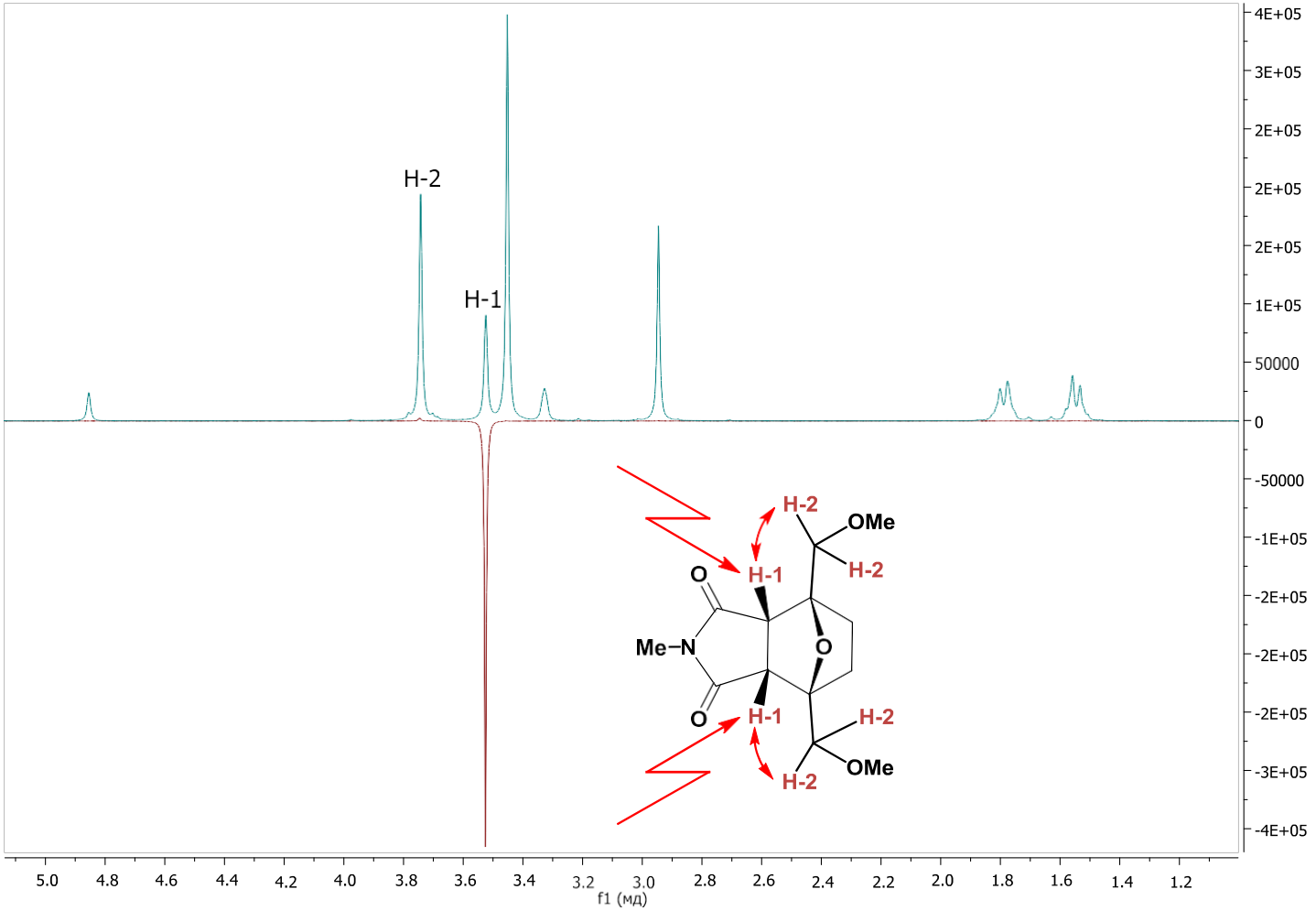


Fig. S44. NOE NMR spectrum of *endo*-4,7-bis(methoxymethyl)-2-methylhexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 15 (CD_3OD, 298 K, 500 MHz).

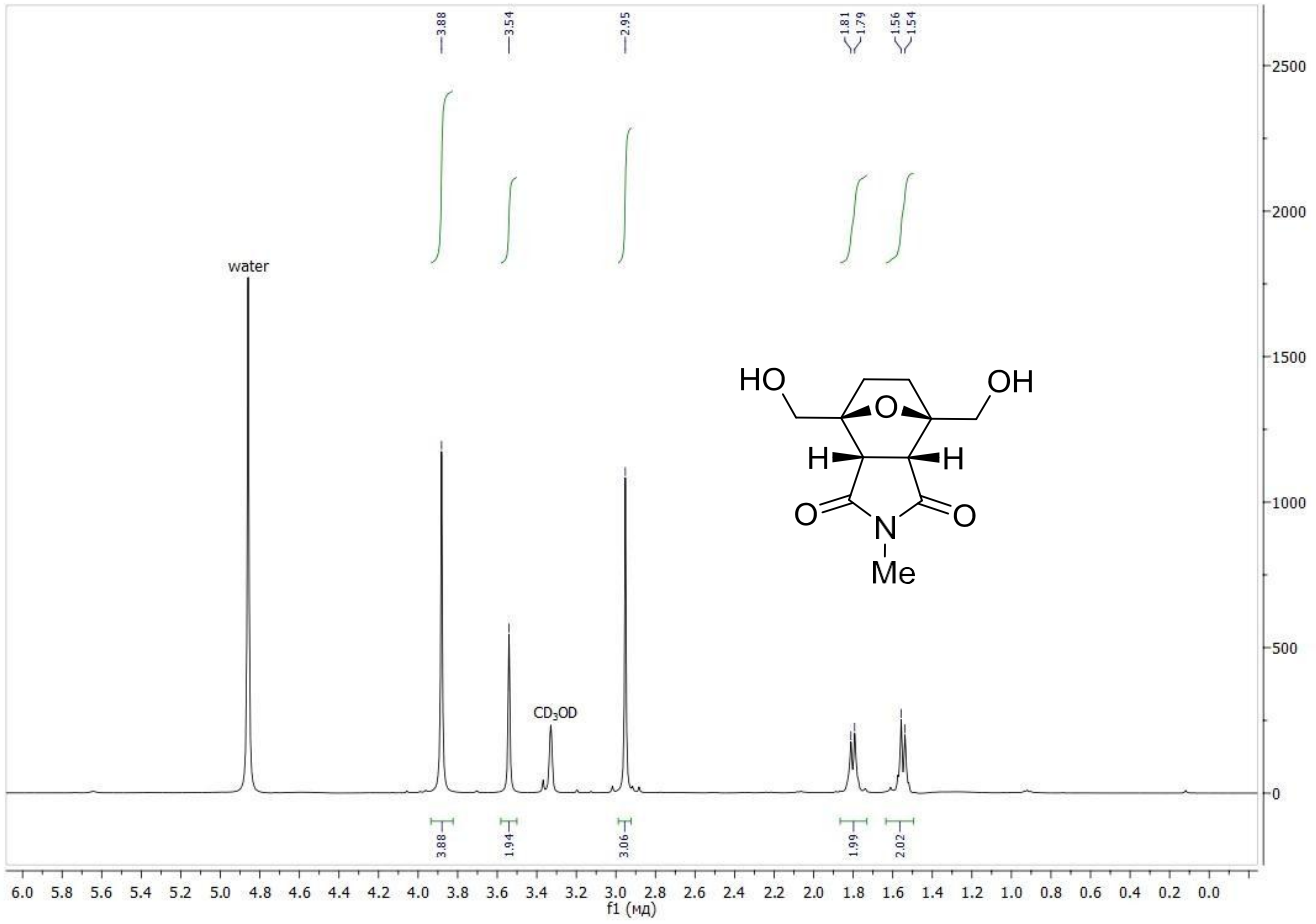


Fig. S45. ^{1}H NMR spectrum of *endo*-4,7-bis(hydroxymethyl)-2-methylhexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 14 (CD_3OD, 298 K, 500 MHz).

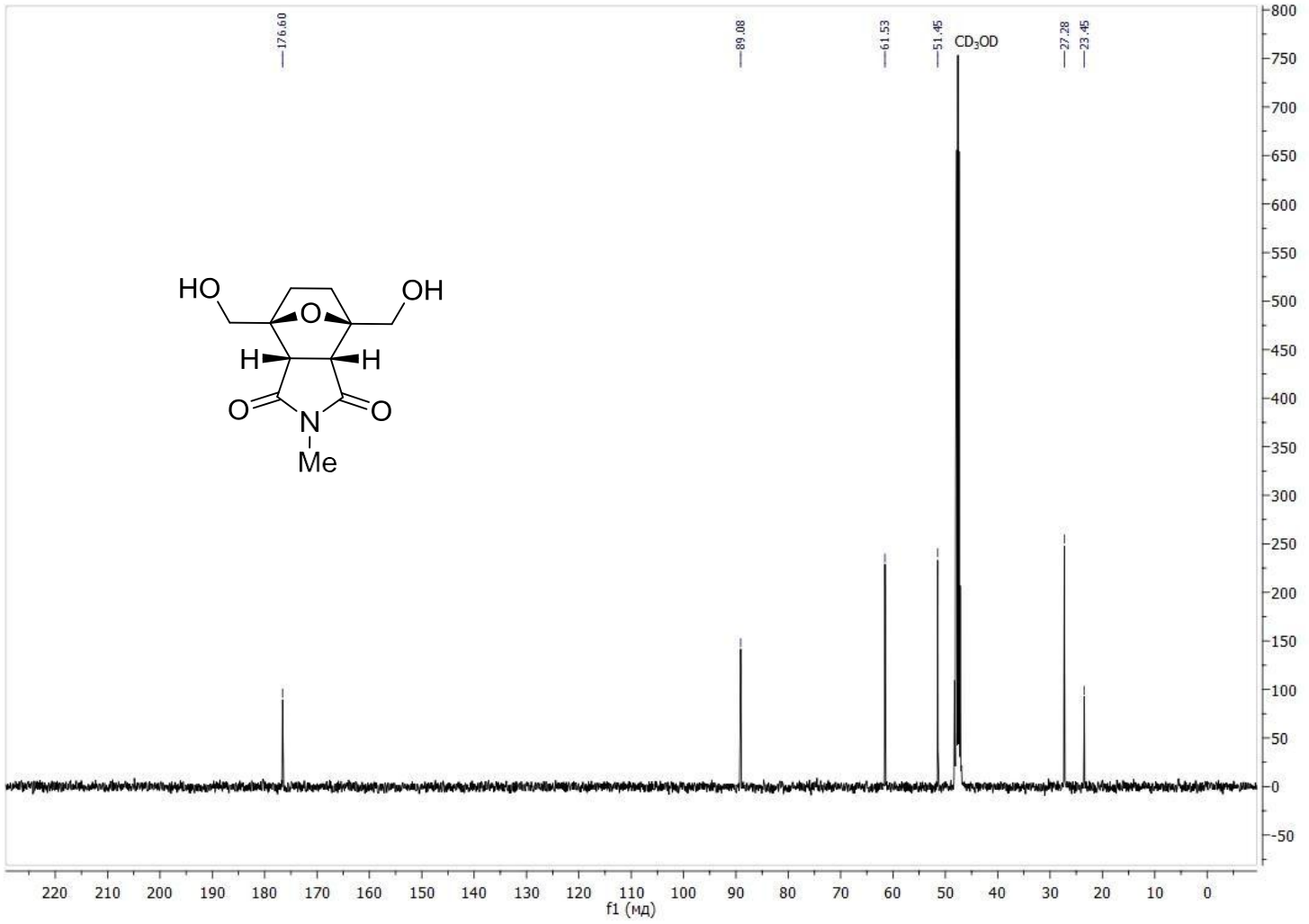


Fig. S46. ^{13}C NMR spectrum of *endo*-4,7-bis(hydroxymethyl)-2-methylhexahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione 14 (CD_3OD, 298 K, 125 MHz).

Fig. S47. X-Ray data of *Endo*-4,7-bis(hydroxymethyl)norcantharimide 4.

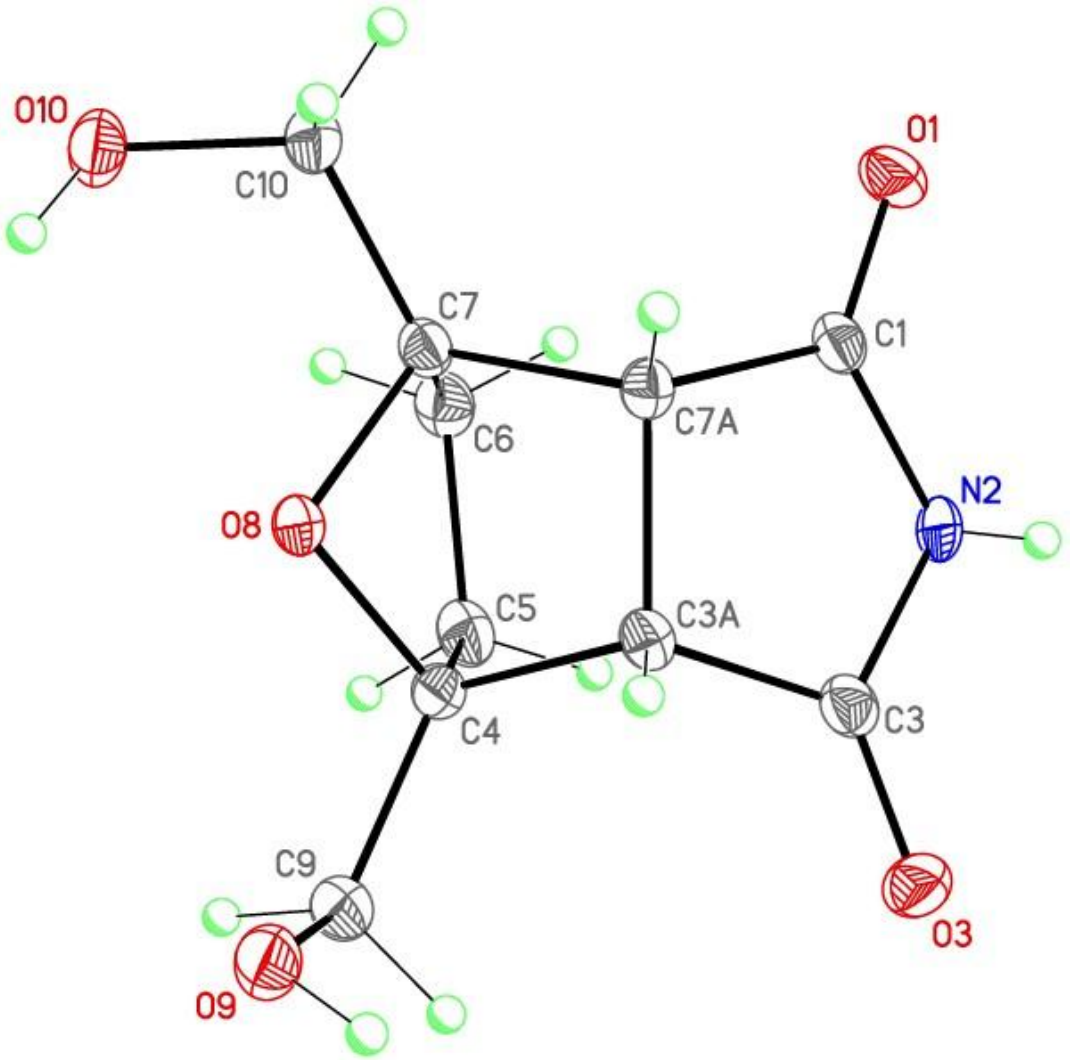


Table S01. Crystal data and structure refinement for *endo*-4,7-bis(hydroxymethyl)norcantharimide.

Empirical formula	C10 H13 N O5	
Formula weight	227.21	
Temperature	100(2) K	
Wavelength	0.96990 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 11.602(2) Å	α = 90 °.
	b = 7.6108(15) Å	β = 95.45(3) °.
	c = 11.152(2) Å	γ = 90 °.
Volume	980.3(3) $Å^3$	
Z	4	
Density (calculated)	1.539 Mg/m^3	
Absorption coefficient	0.269 mm^{-1}	
F(000)	480	

Crystal size	0.07 x 0.05 x 0.01 mm^3
Theta range for data collection	4.431 to 38.358 °.
Index ranges	-14<=h<=12, -8<=k<=9, -13<=l<=13
Reflections collected	5203
Independent reflections	1993 [R(int) = 0.0823]
Completeness to theta = 35.587 °	96.2 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.990 and 0.975
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1993 / 0 / 155
Goodness-of-fit on F^2	0.876
Final R indices [for 1373 rflns with $I>2\sigma(I)$]	R1 = 0.0635, wR2 = 0.1183
R indices (all data)	R1 = 0.0853, wR2 = 0.1342
Extinction coefficient	0.010(1)
Largest diff. peak and hole	0.299 and -0.319 e.$Å^{-3}$

Table S02. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for *endo*-4,7-bis(hydroxymethyl) norcantharimide. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	4570(2)	3873(3)	6506(2)	15(1)
O(1)	5296(1)	5045(2)	6579(1)	21(1)
N(2)	4649(1)	2332(2)	5853(2)	16(1)
C(3)	3720(2)	1214(3)	5891(2)	16(1)
O(3)	3632(1)	-231(2)	5406(1)	22(1)
C(3A)	2854(1)	2085(2)	6629(2)	14(1)
C(4)	1732(1)	2802(3)	5917(2)	14(1)
C(5)	2019(2)	3828(3)	4786(2)	19(1)
C(6)	2493(2)	5600(3)	5337(2)	19(1)
C(7)	2491(1)	5231(3)	6689(2)	14(1)
C(7A)	3443(1)	3811(3)	7101(2)	14(1)
O(8)	1445(1)	4184(2)	6722(1)	16(1)
C(9)	745(2)	1528(3)	5683(2)	19(1)
O(9)	353(1)	858(2)	6764(1)	22(1)
C(10)	2423(2)	6783(3)	7527(2)	18(1)
O(10)	1347(1)	7708(2)	7288(1)	23(1)

Table S03. Bond lengths [Å] and angles [°] for *endo*-4,7-bis(hydroxymethyl) norcantharimide.

C(1)-O(1)	1.224(2)	O(3)-C(3)-C(3A)	127.02(17)
C(1)-N(2)	1.388(3)	N(2)-C(3)-C(3A)	107.97(17)
C(1)-C(7A)	1.523(3)	C(3)-C(3A)-C(7A)	105.22(14)
N(2)-C(3)	1.378(2)	C(3)-C(3A)-C(4)	116.28(16)
N(2)-H(2)	0.83(2)	C(7A)-C(3A)-C(4)	101.30(14)
C(3)-O(3)	1.225(2)	C(3)-C(3A)-H(3A)	111.1
C(3)-C(3A)	1.511(3)	C(7A)-C(3A)-H(3A)	111.1
C(3A)-C(7A)	1.550(3)	C(4)-C(3A)-H(3A)	111.1
C(3A)-C(4)	1.558(2)	O(8)-C(4)-C(9)	111.15(15)
C(3A)-H(3A)	1.0000	O(8)-C(4)-C(5)	102.69(15)
C(4)-O(8)	1.442(2)	C(9)-C(4)-C(5)	113.80(15)
C(4)-C(9)	1.504(2)	O(8)-C(4)-C(3A)	99.76(14)
C(4)-C(5)	1.546(3)	C(9)-C(4)-C(3A)	116.62(16)
C(5)-C(6)	1.560(3)	C(5)-C(4)-C(3A)	111.00(14)
C(5)-H(5A)	0.9900	C(4)-C(5)-C(6)	102.15(16)
C(5)-H(5B)	0.9900	C(4)-C(5)-H(5A)	111.3
C(6)-C(7)	1.534(3)	C(6)-C(5)-H(5A)	111.3
C(6)-H(6A)	0.9900	C(4)-C(5)-H(5B)	111.3
C(6)-H(6B)	0.9900	C(6)-C(5)-H(5B)	111.3
C(7)-O(8)	1.456(2)	H(5A)-C(5)-H(5B)	109.2
C(7)-C(10)	1.513(3)	C(7)-C(6)-C(5)	101.27(16)
C(7)-C(7A)	1.581(2)	C(7)-C(6)-H(6A)	111.5
C(7A)-H(7A)	1.0000	C(5)-C(6)-H(6A)	111.5
C(9)-O(9)	1.423(3)	C(7)-C(6)-H(6B)	111.5
C(9)-H(9A)	0.9900	C(5)-C(6)-H(6B)	111.5
C(9)-H(9B)	0.9900	H(6A)-C(6)-H(6B)	109.3
O(9)-H(9)	0.83(3)	O(8)-C(7)-C(10)	108.61(15)
C(10)-O(10)	1.436(2)	O(8)-C(7)-C(6)	101.79(13)
C(10)-H(10A)	0.9900	C(10)-C(7)-C(6)	117.98(18)
C(10)-H(10B)	0.9900	O(8)-C(7)-C(7A)	100.36(14)
O(10)-H(10)	0.83(2)	C(10)-C(7)-C(7A)	115.46(15)
O(1)-C(1)-N(2)	124.86(18)	C(6)-C(7)-C(7A)	110.16(16)
O(1)-C(1)-C(7A)	127.41(18)	C(1)-C(7A)-C(3A)	104.31(16)
N(2)-C(1)-C(7A)	107.73(15)	C(1)-C(7A)-C(7)	117.21(16)
C(3)-N(2)-C(1)	114.55(17)	C(3A)-C(7A)-C(7)	101.98(12)
C(3)-N(2)-H(2)	120.1(15)	C(1)-C(7A)-H(7A)	110.9
C(1)-N(2)-H(2)	125.3(15)	C(3A)-C(7A)-H(7A)	110.9
O(3)-C(3)-N(2)	125.02(19)	C(7)-C(7A)-H(7A)	110.9

C(4)-O(8)-C(7)	98.10(13)	O(10)-C(10)-C(7)	111.32(14)
O(9)-C(9)-C(4)	112.54(16)	O(10)-C(10)-H(10A)	109.4
O(9)-C(9)-H(9A)	109.1	C(7)-C(10)-H(10A)	109.4
C(4)-C(9)-H(9A)	109.1	O(10)-C(10)-H(10B)	109.4
O(9)-C(9)-H(9B)	109.1	C(7)-C(10)-H(10B)	109.4
C(4)-C(9)-H(9B)	109.1	H(10A)-C(10)-H(10B)	108.0
H(9A)-C(9)-H(9B)	107.8	C(10)-O(10)-H(10)	108.5(16)
C(9)-O(9)-H(9)	112.2(18)		

Table S04. Anisotropic displacement parameters ($Å^2$ x 10^3) for *endo*-4,7-bis(hydroxymethyl) norcantharimide. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	11(1)	19(1)	14(1)	-1(1)	0(1)	1(1)
O(1)	14(1)	22(1)	25(1)	-3(1)	3(1)	-6(1)
N(2)	10(1)	18(1)	21(1)	-3(1)	7(1)	2(1)
C(3)	14(1)	16(1)	19(1)	2(1)	-2(1)	0(1)
O(3)	21(1)	18(1)	27(1)	-5(1)	7(1)	-1(1)
C(3A)	12(1)	15(1)	14(1)	1(1)	2(1)	0(1)
C(4)	13(1)	15(1)	14(1)	-3(1)	2(1)	0(1)
C(5)	15(1)	24(1)	17(1)	0(1)	2(1)	0(1)
C(6)	17(1)	18(1)	23(1)	4(1)	5(1)	-1(1)
C(7)	11(1)	14(1)	18(1)	1(1)	2(1)	-1(1)
C(7A)	12(1)	16(1)	15(1)	-1(1)	3(1)	1(1)
O(8)	12(1)	16(1)	19(1)	-3(1)	5(1)	-1(1)
C(9)	16(1)	17(1)	24(1)	0(1)	4(1)	-1(1)
O(9)	19(1)	16(1)	32(1)	4(1)	10(1)	0(1)
C(10)	14(1)	18(1)	22(1)	-2(1)	4(1)	1(1)
O(10)	17(1)	17(1)	37(1)	1(1)	9(1)	2(1)

Table S05. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for *endo*-4,7-bis(hydroxymethyl) norcantharimide.

Atom	x	y	z	U(iso)
H(2)	5198(16)	2060(30)	5470(20)	19
H(3A)	2666	1314	7309	16
H(5A)	1319	4015	4221	22
H(5B)	2612	3211	4361	22
H(6A)	3284	5847	5117	22
H(6B)	1978	6595	5081	22
H(7A)	3597	3789	7998	17
H(9A)	94	2125	5209	23
H(9B)	997	537	5195	23
H(9)	673(19)	-80(40)	6970(20)	33
H(10A)	2499	6365	8372	22
H(10B)	3073	7595	7426	22
H(10)	814(18)	7060(30)	7470(20)	35

Table S06. Hydrogen bonds for *endo*-4,7-bis(hydroxymethyl) norcantharimide [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(2)-H(2)...O(3)#1	0.83(2)	2.23(2)	3.006(2)	156(2)
O(9)-H(9)...O(10)#2	0.83(3)	1.87(3)	2.701(2)	174(3)
O(10)-H(10)...O(9)#3	0.83(2)	1.90(3)	2.717(2)	167(3)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1, -y, -z+1 #2 x, y-1, z #3 -x, y+1/2, -z+3/2

Table S07. Torsion angles [°] for *endo*-4,7-bis(hydroxymethyl) norcantharimide.

O(1)-C(1)-N(2)-C(3)	-179.24(17)	N(2)-C(3)-C(3A)-C(7A)	-4.1(2)
C(7A)-C(1)-N(2)-C(3)	1.2(2)	O(3)-C(3)-C(3A)-C(4)	-73.1(3)
C(1)-N(2)-C(3)-O(3)	-177.91(18)	N(2)-C(3)-C(3A)-C(4)	107.05(17)
C(1)-N(2)-C(3)-C(3A)	1.9(2)	C(3)-C(3A)-C(4)-O(8)	-153.20(16)
O(3)-C(3)-C(3A)-C(7A)	175.72(19)	C(7A)-C(3A)-C(4)-O(8)	-39.79(17)

C(3)-C(3A)-C(4)-C(9)	87.1(2)
C(7A)-C(3A)-C(4)-C(9)	-159.51(17)
C(3)-C(3A)-C(4)-C(5)	-45.5(2)
C(7A)-C(3A)-C(4)-C(5)	67.96(19)
O(8)-C(4)-C(5)-C(6)	29.75(16)
C(9)-C(4)-C(5)-C(6)	149.99(15)
C(3A)-C(4)-C(5)-C(6)	-76.07(18)
C(4)-C(5)-C(6)-C(7)	4.45(17)
C(5)-C(6)-C(7)-O(8)	-36.99(17)
C(5)-C(6)-C(7)-C(10)	-155.67(15)
C(5)-C(6)-C(7)-C(7A)	68.80(16)
O(1)-C(1)-C(7A)-C(3A)	176.79(17)
N(2)-C(1)-C(7A)-C(3A)	-3.66(19)
O(1)-C(1)-C(7A)-C(7)	65.0(2)
N(2)-C(1)-C(7A)-C(7)	-115.50(17)
C(3)-C(3A)-C(7A)-C(1)	4.62(18)
C(4)-C(3A)-C(7A)-C(1)	-116.87(15)
C(3)-C(3A)-C(7A)-C(7)	127.06(16)
C(4)-C(3A)-C(7A)-C(7)	5.57(18)
O(8)-C(7)-C(7A)-C(1)	143.02(16)
C(10)-C(7)-C(7A)-C(1)	-100.5(2)
C(6)-C(7)-C(7A)-C(1)	36.3(2)
O(8)-C(7)-C(7A)-C(3A)	29.87(18)
C(10)-C(7)-C(7A)-C(3A)	146.37(17)
C(6)-C(7)-C(7A)-C(3A)	-76.89(18)
C(9)-C(4)-O(8)-C(7)	-175.68(14)
C(5)-C(4)-O(8)-C(7)	-53.63(14)
C(3A)-C(4)-O(8)-C(7)	60.67(15)
C(10)-C(7)-O(8)-C(4)	-177.92(15)
C(6)-C(7)-O(8)-C(4)	56.91(16)
C(7A)-C(7)-O(8)-C(4)	-56.41(15)
O(8)-C(4)-C(9)-O(9)	-53.2(2)
C(5)-C(4)-C(9)-O(9)	-168.55(16)
C(3A)-C(4)-C(9)-O(9)	60.2(2)
O(8)-C(7)-C(10)-O(10)	-51.0(2)
C(6)-C(7)-C(10)-O(10)	64.0(2)
C(7A)-C(7)-C(10)-O(10)	-162.74(16)

Fig. S48. X-Ray data of *endo*-N-methyl-4,7-bis(methoxymethyl)-norcantharimide 15.

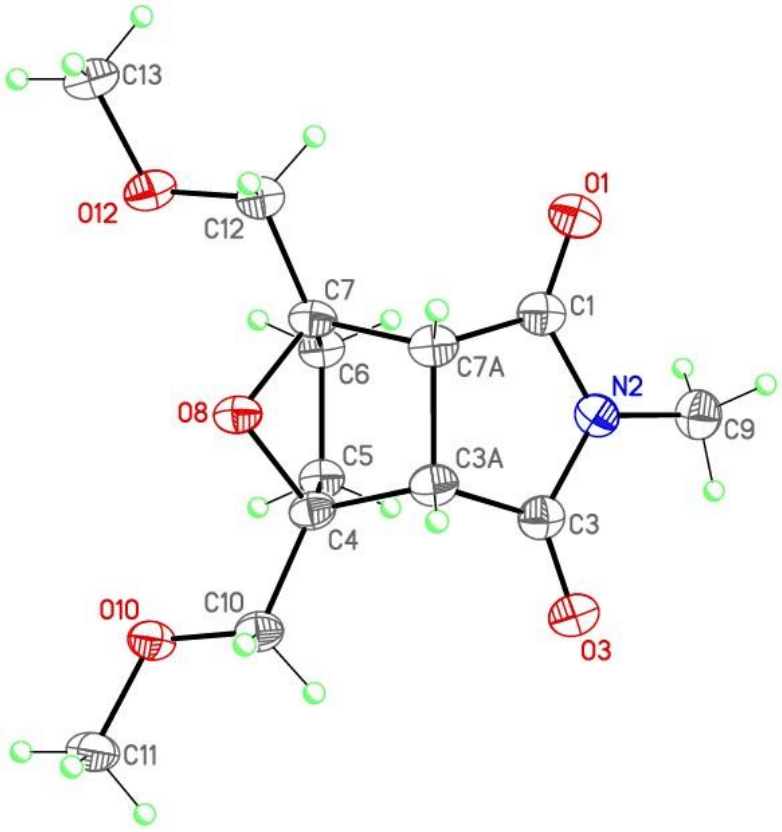


Table S08. Crystal data and structure refinement for *endo*-N-methyl-4,7-bis(methoxymethyl)norcantharimide.

Empirical formula	C13 H19 N O5	
Formula weight	269.29	
Temperature	100(2) K	
Wavelength	0.96990 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 10.389(2) Å	α = 90 °.
	b = 15.957(3) Å	β = 111.16(3) °.
	c = 8.4911(17) Å	γ = 90 °.
Volume	1312.7(5) $Å^3$	
Z	4	
Density (calculated)	1.363 Mg/m^3	
Absorption coefficient	0.223 mm^{-1}	
F(000)	576	
Crystal size	0.20 x 0.05 x 0.05 mm^3	
Theta range for data collection	1.742 to 38.407 °.	

Index ranges	-13<=h<=13, -20<=k<=13, -10<=l<=9
Reflections collected	10961
Independent reflections	2578 [R(int) = 0.0936]
Completeness to theta = 35.587 °	96.3 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.980 and 0.945
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2578 / 0 / 177
Goodness-of-fit on F^2	1.095
Final R indices [for 1924 rflns with I>2σ(I)]	R1 = 0.0878, wR2 = 0.2002
R indices (all data)	R1 = 0.1043, wR2 = 0.2168
Extinction coefficient	0.084(8)
Largest diff. peak and hole	0.319 and -0.316 e.$Å^{-3}$

Table S09. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for *endo*-N-methyl-4,7-bis(methoxymethyl)norcantharimide. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	3742(3)	6300(2)	9709(4)	33(1)
O(1)	4910(2)	6145(1)	10701(2)	39(1)
N(2)	2541(2)	6026(1)	9928(3)	32(1)
C(3)	1339(3)	6278(2)	8614(4)	32(1)
O(3)	168(2)	6108(1)	8530(3)	38(1)
C(3A)	1750(2)	6786(2)	7374(3)	31(1)
C(4)	1455(2)	6378(2)	5601(3)	29(1)
C(5)	1806(2)	5433(2)	5771(3)	30(1)
C(6)	3418(2)	5449(2)	6506(3)	30(1)
C(7)	3705(2)	6403(2)	6630(3)	30(1)
C(7A)	3345(2)	6800(2)	8094(3)	30(1)
O(8)	2585(2)	6728(1)	5175(2)	29(1)
C(9)	2545(3)	5533(2)	11388(4)	40(1)
C(10)	72(2)	6617(2)	4297(3)	31(1)
O(10)	-70(2)	6252(1)	2716(2)	34(1)
C(11)	-1335(3)	6488(2)	1415(4)	40(1)
C(12)	5098(2)	6670(2)	6603(3)	30(1)
O(12)	5261(2)	6332(1)	5130(3)	36(1)
C(13)	6524(3)	6603(2)	4986(4)	37(1)

Table S10. Bond lengths [Å] and angles [°] for *endo*-N-methyl-4,7-bis(methoxymethyl)norcantharimide.

C(1)-O(1)	1.227(3)	C(13)-H(13B)	0.9800
C(1)-N(2)	1.395(3)	C(13)-H(13C)	0.9800
C(1)-C(7A)	1.510(4)	O(1)-C(1)-N(2)	123.7(3)
N(2)-C(3)	1.401(3)	O(1)-C(1)-C(7A)	127.5(2)
N(2)-C(9)	1.468(4)	N(2)-C(1)-C(7A)	108.8(2)
C(3)-O(3)	1.223(3)	C(1)-N(2)-C(3)	112.8(2)
C(3)-C(3A)	1.507(4)	C(1)-N(2)-C(9)	123.4(2)
C(3A)-C(7A)	1.545(3)	C(3)-N(2)-C(9)	123.8(2)
C(3A)-C(4)	1.565(4)	O(3)-C(3)-N(2)	124.4(3)
C(3A)-H(3A)	1.0000	O(3)-C(3)-C(3A)	127.3(2)
C(4)-O(8)	1.459(3)	N(2)-C(3)-C(3A)	108.3(2)
C(4)-C(10)	1.513(3)	C(3)-C(3A)-C(7A)	105.4(2)
C(4)-C(5)	1.546(3)	C(3)-C(3A)-C(4)	116.2(2)
C(5)-C(6)	1.562(3)	C(7A)-C(3A)-C(4)	101.30(19)
C(5)-H(5A)	0.9900	C(3)-C(3A)-H(3A)	111.1
C(5)-H(5B)	0.9900	C(7A)-C(3A)-H(3A)	111.1
C(6)-C(7)	1.547(3)	C(4)-C(3A)-H(3A)	111.1
C(6)-H(6A)	0.9900	O(8)-C(4)-C(10)	111.0(2)
C(6)-H(6B)	0.9900	O(8)-C(4)-C(5)	102.28(18)
C(7)-O(8)	1.453(3)	C(10)-C(4)-C(5)	116.3(2)
C(7)-C(12)	1.516(3)	O(8)-C(4)-C(3A)	100.61(19)
C(7)-C(7A)	1.556(4)	C(10)-C(4)-C(3A)	113.8(2)
C(7A)-H(7A)	1.0000	C(5)-C(4)-C(3A)	111.0(2)
C(9)-H(9A)	0.9800	C(4)-C(5)-C(6)	101.73(17)
C(9)-H(9B)	0.9800	C(4)-C(5)-H(5A)	111.4
C(9)-H(9C)	0.9800	C(6)-C(5)-H(5A)	111.4
C(10)-O(10)	1.421(3)	C(4)-C(5)-H(5B)	111.4
C(10)-H(10A)	0.9900	C(6)-C(5)-H(5B)	111.4
C(10)-H(10B)	0.9900	H(5A)-C(5)-H(5B)	109.3
O(10)-C(11)	1.428(3)	C(7)-C(6)-C(5)	101.34(17)
C(11)-H(11A)	0.9800	C(7)-C(6)-H(6A)	111.5
C(11)-H(11B)	0.9800	C(5)-C(6)-H(6A)	111.5
C(11)-H(11C)	0.9800	C(7)-C(6)-H(6B)	111.5
C(12)-O(12)	1.427(3)	C(5)-C(6)-H(6B)	111.5
C(12)-H(12A)	0.9900	H(6A)-C(6)-H(6B)	109.3
C(12)-H(12B)	0.9900	O(8)-C(7)-C(12)	111.3(2)
O(12)-C(13)	1.428(3)	O(8)-C(7)-C(6)	102.52(19)
C(13)-H(13A)	0.9800	C(12)-C(7)-C(6)	115.9(2)

O(8)-C(7)-C(7A)	100.66(19)	H(10A)-C(10)-H(10B)	108.2
C(12)-C(7)-C(7A)	113.8(2)	C(10)-O(10)-C(11)	112.0(2)
C(6)-C(7)-C(7A)	111.0(2)	O(10)-C(11)-H(11A)	109.5
C(1)-C(7A)-C(3A)	104.7(2)	O(10)-C(11)-H(11B)	109.5
C(1)-C(7A)-C(7)	116.4(2)	H(11A)-C(11)-H(11B)	109.5
C(3A)-C(7A)-C(7)	102.2(2)	O(10)-C(11)-H(11C)	109.5
C(1)-C(7A)-H(7A)	111.0	H(11A)-C(11)-H(11C)	109.5
C(3A)-C(7A)-H(7A)	111.0	H(11B)-C(11)-H(11C)	109.5
C(7)-C(7A)-H(7A)	111.0	O(12)-C(12)-C(7)	108.9(2)
C(7)-O(8)-C(4)	96.99(18)	O(12)-C(12)-H(12A)	109.9
N(2)-C(9)-H(9A)	109.5	C(7)-C(12)-H(12A)	109.9
N(2)-C(9)-H(9B)	109.5	O(12)-C(12)-H(12B)	109.9
H(9A)-C(9)-H(9B)	109.5	C(7)-C(12)-H(12B)	109.9
N(2)-C(9)-H(9C)	109.5	H(12A)-C(12)-H(12B)	108.3
H(9A)-C(9)-H(9C)	109.5	C(12)-O(12)-C(13)	111.4(2)
H(9B)-C(9)-H(9C)	109.5	O(12)-C(13)-H(13A)	109.5
O(10)-C(10)-C(4)	109.6(2)	O(12)-C(13)-H(13B)	109.5
O(10)-C(10)-H(10A)	109.8	H(13A)-C(13)-H(13B)	109.5
C(4)-C(10)-H(10A)	109.8	O(12)-C(13)-H(13C)	109.5
O(10)-C(10)-H(10B)	109.8	H(13A)-C(13)-H(13C)	109.5
C(4)-C(10)-H(10B)	109.8	H(13B)-C(13)-H(13C)	109.5

Table S11. Anisotropic displacement parameters ($Å^2$ x 10^3) for *endo*-N-methyl-4,7-bis(methoxymethyl)norcantharimide. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	31(1)	26(1)	39(2)	-5(1)	11(1)	0(1)
O(1)	33(1)	36(1)	42(1)	1(1)	7(1)	1(1)
N(2)	32(1)	29(1)	32(1)	1(1)	10(1)	1(1)
C(3)	33(1)	26(1)	38(2)	-4(1)	13(1)	2(1)
O(3)	31(1)	40(1)	46(1)	0(1)	16(1)	0(1)
C(3A)	29(1)	25(1)	38(2)	0(1)	12(1)	2(1)
C(4)	25(1)	24(1)	38(2)	1(1)	12(1)	-1(1)
C(5)	28(1)	23(1)	37(2)	-1(1)	11(1)	-1(1)
C(6)	28(1)	23(1)	39(2)	-1(1)	12(1)	1(1)
C(7)	24(1)	26(1)	37(2)	1(1)	7(1)	1(1)
C(7A)	28(1)	21(1)	39(2)	0(1)	11(1)	0(1)
O(8)	23(1)	24(1)	38(1)	3(1)	9(1)	0(1)
C(9)	46(2)	36(2)	40(2)	4(1)	16(1)	2(1)
C(10)	27(1)	26(1)	38(2)	1(1)	11(1)	1(1)
O(10)	27(1)	37(1)	36(1)	-1(1)	7(1)	3(1)
C(11)	26(1)	46(2)	44(2)	4(1)	6(1)	3(1)
C(12)	29(1)	23(1)	38(2)	-4(1)	12(1)	0(1)
O(12)	29(1)	33(1)	49(1)	-5(1)	16(1)	-4(1)
C(13)	27(1)	32(2)	54(2)	0(1)	16(1)	-2(1)

Table S12. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for *endo*-N-methyl-4,7-bis(methoxymethyl)norcantharimide.

Atom	x	y	z	U(iso)
H(3A)	1364	7366	7260	37
H(5A)	1451	5148	4661	36
H(5B)	1430	5153	6553	36
H(6A)	3789	5178	7629	36
H(6B)	3810	5174	5736	36
H(7A)	3700	7387	8323	36
H(9A)	2892	5879	12409	61
H(9B)	3143	5042	11520	61
H(9C)	1604	5348	11210	61
H(10A)	-679	6417	4661	37
H(10B)	2	7234	4185	37
H(11A)	-1381	6236	343	60
H(11B)	-1377	7100	1305	60
H(11C)	-2114	6289	1705	60
H(12A)	5154	7289	6589	36
H(12B)	5843	6462	7628	36
H(13A)	6594	6374	3949	56
H(13B)	7304	6404	5963	56
H(13C)	6540	7216	4945	56

Table S13. Torsion angles [°] for *endo*-N-methyl-4,7-bis(methoxymethyl)norcantharimide.

O(1)-C(1)-N(2)-C(3)	-179.4(2)	C(6)-C(7)-C(7A)-C(3A)	-72.8(2)
C(7A)-C(1)-N(2)-C(3)	0.6(3)	C(12)-C(7)-O(8)-C(4)	-179.27(19)
O(1)-C(1)-N(2)-C(9)	1.0(4)	C(6)-C(7)-O(8)-C(4)	56.2(2)
C(7A)-C(1)-N(2)-C(9)	-179.0(2)	C(7A)-C(7)-O(8)-C(4)	-58.3(2)
C(1)-N(2)-C(3)-O(3)	179.6(2)	C(10)-C(4)-O(8)-C(7)	179.2(2)
C(9)-N(2)-C(3)-O(3)	-0.8(4)	C(5)-C(4)-O(8)-C(7)	-56.0(2)
C(1)-N(2)-C(3)-C(3A)	-0.8(3)	C(3A)-C(4)-O(8)-C(7)	58.4(2)
C(9)-N(2)-C(3)-C(3A)	178.8(2)	O(8)-C(4)-C(10)-O(10)	64.4(3)
O(3)-C(3)-C(3A)-C(7A)	-179.8(3)	C(5)-C(4)-C(10)-O(10)	-52.0(3)
N(2)-C(3)-C(3A)-C(7A)	0.6(3)	C(3A)-C(4)-C(10)-O(10)	177.0(2)
O(3)-C(3)-C(3A)-C(4)	-68.6(3)	C(4)-C(10)-O(10)-C(11)	-177.4(2)
N(2)-C(3)-C(3A)-C(4)	111.8(2)	O(8)-C(7)-C(12)-O(12)	-61.8(3)
C(3)-C(3A)-C(4)-O(8)	-148.8(2)	C(6)-C(7)-C(12)-O(12)	54.7(3)
C(7A)-C(3A)-C(4)-O(8)	-35.2(2)	C(7A)-C(7)-C(12)-O(12)	-174.7(2)
C(3)-C(3A)-C(4)-C(10)	92.4(3)	C(7)-C(12)-O(12)-C(13)	176.6(2)
C(7A)-C(3A)-C(4)-C(10)	-154.0(2)		
C(3)-C(3A)-C(4)-C(5)	-41.1(3)		
C(7A)-C(3A)-C(4)-C(5)	72.4(2)		
O(8)-C(4)-C(5)-C(6)	34.0(2)		
C(10)-C(4)-C(5)-C(6)	155.2(2)		
C(3A)-C(4)-C(5)-C(6)	-72.6(2)		
C(4)-C(5)-C(6)-C(7)	0.1(3)		
C(5)-C(6)-C(7)-O(8)	-34.3(2)		
C(5)-C(6)-C(7)-C(12)	-155.7(2)		
C(5)-C(6)-C(7)-C(7A)	72.4(2)		
O(1)-C(1)-C(7A)-C(3A)	179.8(3)		
N(2)-C(1)-C(7A)-C(3A)	-0.2(3)		
O(1)-C(1)-C(7A)-C(7)	67.9(3)		
N(2)-C(1)-C(7A)-C(7)	-112.2(2)		
C(3)-C(3A)-C(7A)-C(1)	-0.2(3)		
C(4)-C(3A)-C(7A)-C(1)	-121.7(2)		
C(3)-C(3A)-C(7A)-C(7)	121.6(2)		
C(4)-C(3A)-C(7A)-C(7)	0.1(2)		
O(8)-C(7)-C(7A)-C(1)	148.6(2)		
C(12)-C(7)-C(7A)-C(1)	-92.3(3)		
C(6)-C(7)-C(7A)-C(1)	40.6(3)		
O(8)-C(7)-C(7A)-C(3A)	35.1(2)		
C(12)-C(7)-C(7A)-C(3A)	154.3(2)		

Quantum chemical calculations

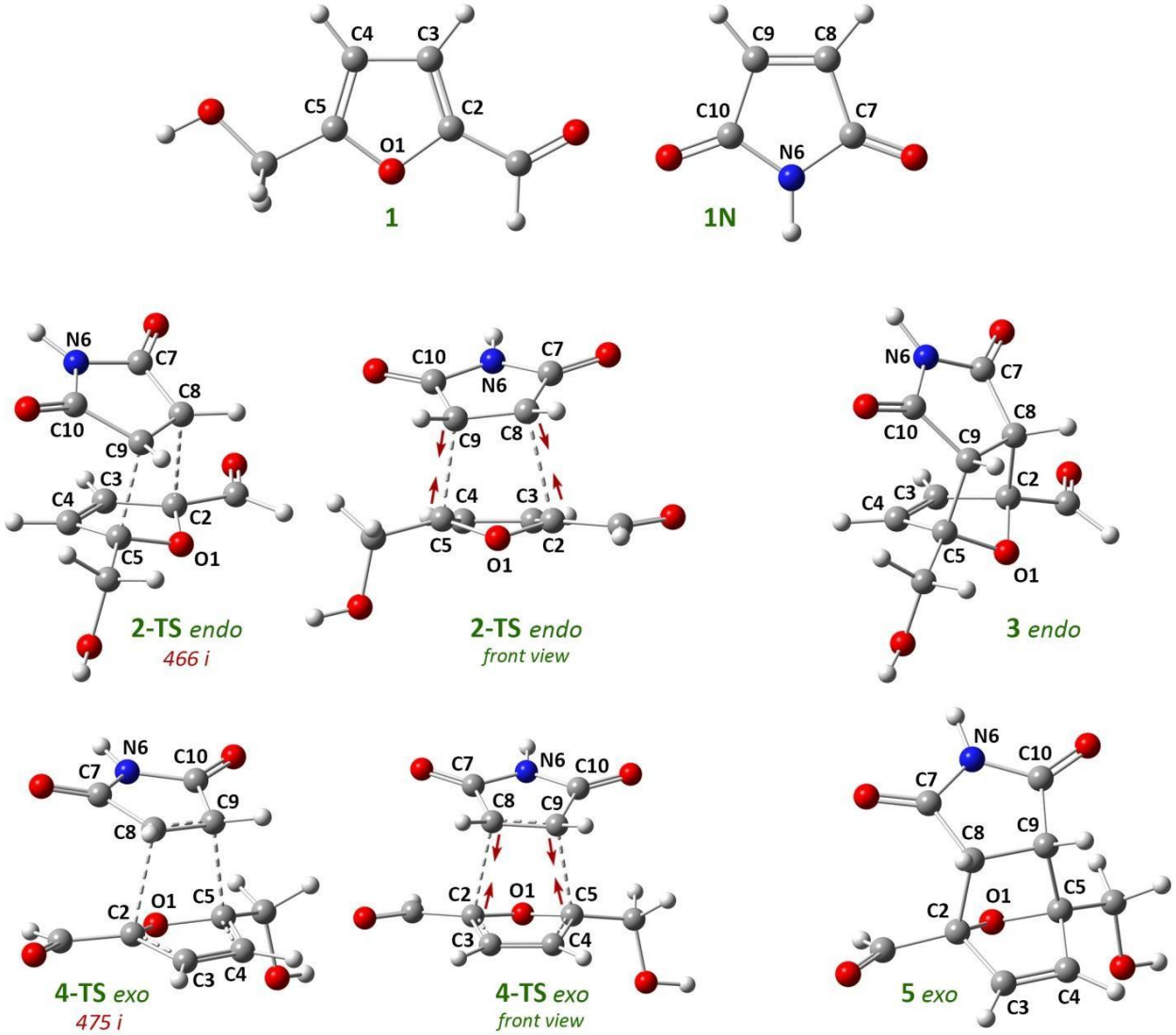


Fig. S49. Optimized molecular structures of the reagents, transition states and products for 5-HMF cycloaddition reaction. The values of imaginary frequencies are shown (cm^{-1}). Vibrations corresponding imaginary frequencies are denoted by red arrows. PBE1PBE/6-311++G(d,p) EmpiricalDispersion=GD3BJ SCRF(SMD,Solvent=Water).

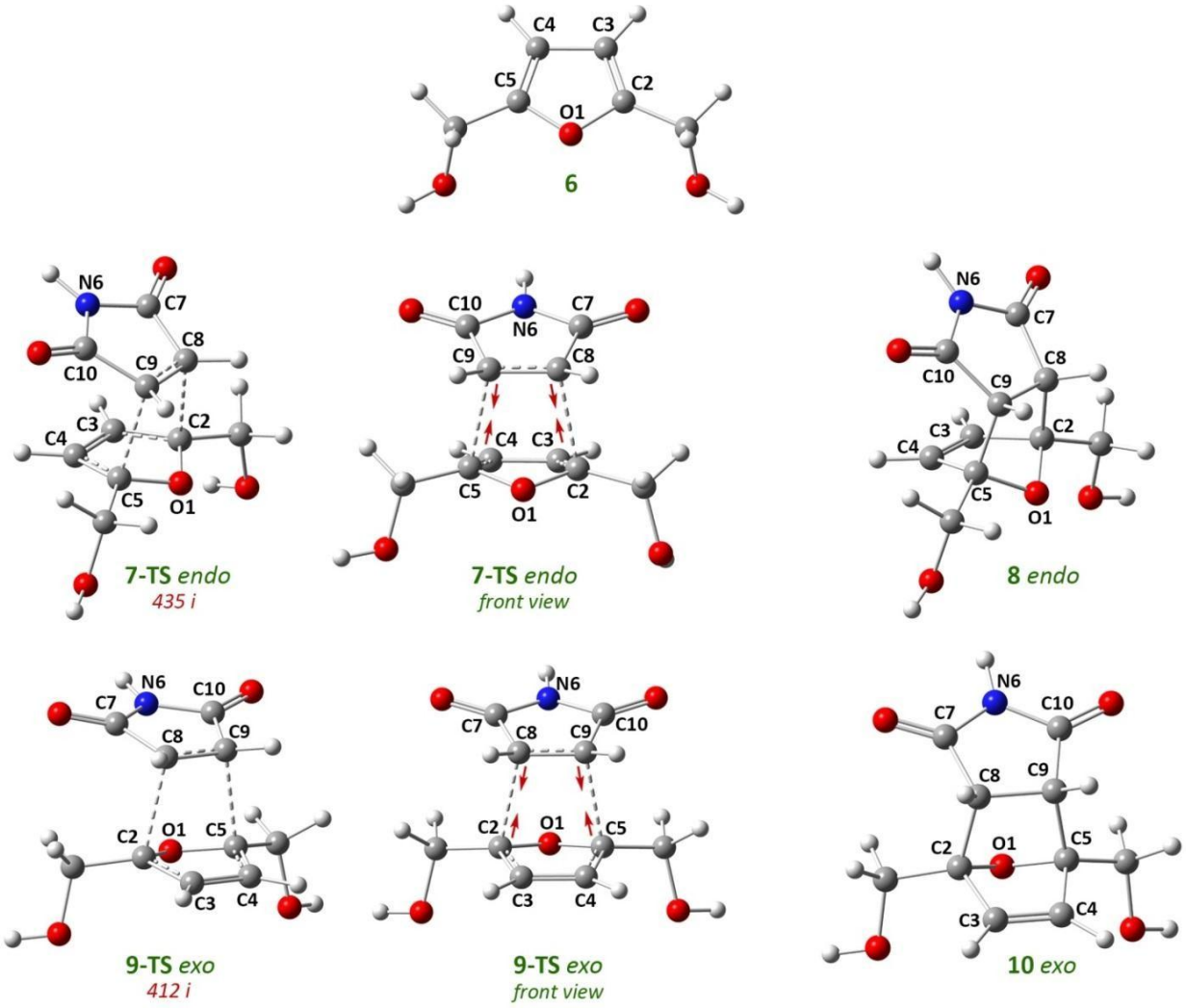


Fig. S50. Optimized molecular structures of the reagents, transition states and products for BHMF cycloaddition reaction. The values of imaginary frequencies are shown (cm^{-1}). Vibrations corresponding imaginary frequencies are denoted by red arrows. PBE1PBE/6-311++G(d,p) EmpiricalDispersion=GD3BJ SCRF(SMD,Solvent=Water).

Table S14. Interatomic distances (Å) for optimized 1-10 molecular structures (see Figs. S43 and S44).

	HMF						BHMF				
distance	**1**	**1N**	**2-TS endo**	**3 endo**	**4-TS exo**	**5 exo**	**6**	**7-TS endo**	**8 endo**	**9-TS exo**	**10 exo**
O1-C2	1.378	–	1.361	1.424	1.363	1.425	1.367	1.369	1.435	1.365	1.434
C2-C3	1.371	–	1.416	1.513	1.422	1.516	1.359	1.417	1.517	1.418	1.518
C3-C4	1.413	–	1.366	1.331	1.363	1.329	1.429	1.370	1.331	1.368	1.329
C4-C5	1.370	–	1.431	1.517	1.429	1.519	1.359	1.417	1.517	1.418	1.518
O1-C5	1.343	–	1.378	1.440	1.370	1.439	1.367	1.372	1.435	1.365	1.434
N6-C7	–	1.380	1.388	1.377	1.383	1.372	–	1.385	1.377	1.383	1.375
C7-C8	–	1.491	1.469	1.507	1.481	1.512	–	1.476	1.505	1.479	1.509
C8-C9	–	1.331	1.406	1.530	1.408	1.536	–	1.403	1.529	1.405	1.538
C9-C10	–	1.491	1.492	1.507	1.489	1.510	–	1.478	1.505	1.479	1.509
N6-C10	–	1.380	1.379	1.377	1.381	1.376	–	1.384	1.377	1.383	1.375

C2-C8	–	–	2.253	1.579	2.195	1.568	–	2.156	1.569	2.178	1.567
C5-C9	–	–	2.014	1.568	2.087	1.570	–	2.137	1.569	2.178	1.567

Computational Details

All molecular structures were optimized by PBE1PBE [3,4] density functional method with 6-311++G(d,p) [5-7] basis set. Geometry optimization was performed in the water medium described by SMD continuum solvation model. [8] Dispersion interaction was taken into account by Grimme D3BJ corrections. [9] For all structures the normal mode analysis was carried out and all transition states are characterized by one imaginary frequency corresponding to cycloaddition reaction. Gaussian 09 program was used for all calculations. [10]

Table S15. XYZ coordinates, total energy and thermodynamic parameters of the optimized 1-10 molecular structures. ***PBE1PBE/6-311++G(d,p) EmpiricalDispersion=GD3BJ SCRF(SMD,Solvent=Water)***

1	**1N**
E = -457.524766 a.u. H = -457.402712 a.u. G = -457.445720 a.u.	E = -359.160064 a.u. H = -359.085396 a.u. G = -359.120390 a.u.
C 0.77490 1.28720 0.01690 C -0.63720 1.24850 0.03090 C 1.20570 -0.01380 0.00580 C -0.98220 -0.07690 0.02750 O 0.11340 -0.85370 0.01110 C 2.49410 -0.63900 -0.01730 O 3.55670 -0.02660 -0.02870 H 2.47380 -1.74230 -0.02490 C -2.28740 -0.77860 0.04530 O -3.31070 0.18560 -0.09700 H 1.41040 2.16090 0.01440 H -1.32000 2.08390 0.04290 H -2.30780 -1.51430 -0.76930 H -2.38610 -1.32920 0.99020 H -4.15320 -0.26650 0.00870	C 0.00000 0.66570 -1.26190 C 0.00000 -0.66570 -1.26190 C 0.00000 1.13530 0.15350 C 0.00000 -1.13530 0.15350 N 0.00000 0.00000 0.93730 O 0.00000 2.27670 0.56160 O 0.00000 -2.27670 0.56160 H 0.00000 1.35180 -2.09770 H 0.00000 -1.35180 -2.09770 H 0.00000 0.00000 1.94890
2-TS endo	**3 endo**
E = -816.672759 a.u. H = -816.475509 a.u. G = -816.531108 a.u.	E = -816.713523 a.u. H = -816.513218 a.u. G = -816.568259 a.u.
C -0.34420 -0.84970 1.38410 C 0.88060 -0.24850 1.32580 C -0.54340 -1.43610 0.11120 C 1.37110 -0.45320 -0.00250 O 0.64280 -1.48470 -0.55450 C -1.62020 -2.29510 -0.37130 O -2.67720 -2.41350 0.21700 H -1.41900 -2.80950 -1.32560 C 2.78290 -0.32350 -0.45650 O 3.57730 -1.25570 0.26120 H -1.07780 -0.81760 2.17640 H 1.35460 0.38030 2.06610 H 2.83110 -0.50870 -1.53460 H 3.10590 0.70510 -0.26170 H 4.48900 -1.14150 -0.02690 C 0.33600 0.94840 -1.01310 C -0.96700 0.42560 -1.08480 C 0.27250 2.12430 -0.09760 C -1.82490 1.20410 -0.18080 N -1.00310 2.14370 0.42600 O 1.14880 2.92550 0.16130 O -3.02040 1.09480 0.02670 H 1.01580 0.98430 -1.85640 H -1.38840 -0.11420 -1.92110 H -1.32020 2.80690 1.12200	C -0.38400 -0.81630 1.35520 C 0.85410 -0.32790 1.34300 C -0.68810 -1.15070 -0.08900 C 1.30070 -0.35330 -0.10670 O 0.59080 -1.50090 -0.60820 C -1.71890 -2.19170 -0.39760 O -2.75050 -2.29010 0.22230 H -1.48260 -2.85050 -1.25200 C 2.76530 -0.39410 -0.41440 O 3.36550 -1.44040 0.32870 H -1.09520 -0.88550 2.16730 H 1.42070 0.10750 2.15560 H 2.89930 -0.54440 -1.49200 H 3.19110 0.57980 -0.14490 H 4.31110 -1.41970 0.15290 C 0.50720 0.77440 -0.85410 C -0.91550 0.21140 -0.85540 C 0.40370 2.08970 -0.12580 C -1.74810 1.23410 -0.12620 N -0.91320 2.26690 0.23640 O 1.29570 2.87540 0.11220 O -2.93600 1.18920 0.11000 H 0.92310 0.92760 -1.85120 H -1.32400 0.02830 -1.85020 H -1.23350 3.07050 0.76670
4-TS exo	**5 exo**
E = -816.670156 a.u. H = -816.472823 a.u. G = -816.528592 a.u.	E = -816.715114 a.u. H = -816.514762 a.u. G = -816.569041 a.u.
C -0.24440 -2.05170 0.99010 C 1.05270 -1.65690 1.12510	C -0.36420 -2.01050 0.97950 C 0.93720 -1.75450 1.06460

C -0.76280 -1.30230 -0.10090 C 1.28470 -0.66690 0.12040 O 0.27550 -0.76430 -0.80030 C -2.02560 -1.46110 -0.82200 O -2.98670 -2.02700 -0.34150 H -2.05230 -1.01230 -1.82860 C 2.60920 -0.21930 -0.38900 O 3.28310 -1.35150 -0.92430 H -0.82590 -2.70400 1.62510 H 1.75870 -1.91860 1.90020 H 2.47110 0.54940 -1.15440 H 3.17020 0.21240 0.44630 H 4.15730 -1.05980 -1.20340 C -1.00050 0.56450 1.02850 C 0.36120 0.90500 1.13660 C -1.60230 1.44510 0.00120 C 0.59110 2.04470 0.20690 N -0.57590 2.21810 -0.51000 O -2.76680 1.52250 -0.34570 O 1.58930 2.72780 0.08400 H -1.62380 0.16290 1.81440 H 0.93620 0.86870 2.05170 H -0.69390 2.90920 -1.24010	C -0.90570 -0.97540 0.01390 C 1.19150 -0.56040 0.16160 O 0.19630 -0.74870 -0.86000 C -2.16030 -1.30180 -0.74090 O -3.12490 -1.79290 -0.20490 H -2.14480 -1.06750 -1.81940 C 2.56700 -0.38300 -0.40900 O 2.97910 -1.61440 -0.97860 H -0.97560 -2.71470 1.52720 H 1.68200 -2.20230 1.70920 H 2.55270 0.41030 -1.16390 H 3.23840 -0.07730 0.40150 H 3.87340 -1.49600 -1.31270 C -0.92390 0.37750 0.80650 C 0.58030 0.65650 0.94340 C -1.45190 1.51420 -0.03950 C 0.78530 1.98490 0.25510 N -0.41450 2.37500 -0.29450 O -2.58800 1.65460 -0.43970 O 1.81190 2.62540 0.18860 H -1.48720 0.30790 1.73610 H 0.96010 0.71080 1.96260 H -0.52410 3.22790 -0.83370
6	**7-TS endo**
E = -458.734558 a.u. H = -458.588508 a.u. G = -458.633044 a.u.	E = -817.890940 a.u. H = -817.669254 a.u. G = -817.726463 a.u.
C 0.71450 1.60990 -0.30710 C -0.71450 1.60990 -0.30700 C 1.10230 0.39870 0.17060 C -1.10230 0.39870 0.17060 O 0.00000 -0.35190 0.47180 C 2.42320 -0.21530 0.41190 H 3.18300 0.56920 0.33520 C -2.42320 -0.21530 0.41190 O -2.65570 -1.24590 -0.55030 H 1.37400 2.40560 -0.62150 H -1.37400 2.40560 -0.62140 H -2.45990 -0.63390 1.42430 H -3.18300 0.56920 0.33520 H -3.44420 -1.72560 -0.27600 H 2.45990 -0.63390 1.42430 O 2.65570 -1.24590 -0.55030 H 3.44430 -1.72560 -0.27600	C -0.60310 0.59390 1.32370 C -0.33990 -0.75110 1.32510 C -1.09180 0.90490 0.03020 C -0.66930 -1.22340 0.03050 O -1.43780 -0.26810 -0.58520 C -1.79030 2.14070 -0.42090 O -3.11080 2.23690 0.09530 H -1.88040 2.13410 -1.50800 C -0.84630 -2.62760 -0.41860 O -1.97100 -3.18840 0.24990 H -0.37120 1.32220 2.08800 H 0.14870 -1.33720 2.09060 H -0.98830 -2.64470 -1.50400 H 0.06790 -3.18010 -0.17640 H -2.03830 -4.10970 -0.02230 H -3.05330 2.33830 1.05140 H -1.18560 3.00470 -0.12660 C 1.03720 -0.50630 -1.03840 C 0.78200 0.87350 -1.03640 C 2.16810 -0.75000 -0.11910 C 1.74730 1.50220 -0.11360 N 2.47880 0.47150 0.45220 O 2.74840 -1.79430 0.12280 O 1.91430 2.68410 0.13530 H 0.87130 -1.17300 -1.87450 H 0.38310 1.44090 -1.86690 H 3.18630 0.60120 1.16400
8 endo	**9-TS exo**
E = -817.937157 a.u. H = -817.712298 a.u.	E = -817.886552 a.u. H = -817.665197 a.u.

G = -817.767830 a.u.	G = -817.722861 a.u.
C -2.42860 -1.25320 -0.43580 O -2.60100 -2.46230 0.28380 H -3.18000 -0.50900 -0.14630 H -2.50810 -1.42080 -1.51650 H -3.50380 -2.76180 0.14080 C -0.66550 -0.52310 1.32460 C 0.66590 -0.52270 1.32460 C -1.07770 -0.68500 -0.12640 C 1.07820 -0.68430 -0.12640 O 0.00050 -1.47610 -0.64810 C 2.42950 -1.25160 -0.43580 O 2.60270 -2.46060 0.28370 H -1.34830 -0.33600 2.14330 H 1.34860 -0.33530 2.14330 H 2.50900 -1.41910 -1.51660 H 3.18040 -0.50690 -0.14640 H 3.50570 -2.75950 0.14080 C 0.76430 0.67310 -0.84760 C -0.76480 0.67260 -0.84770 C 1.15630 1.91680 -0.09530 C -1.15760 1.91610 -0.09550 N -0.00090 2.56220 0.28000 O 2.27630 2.31150 0.15450 O -2.27780 2.31000 0.15450 H 1.21170 0.68080 -1.84280 H -1.21220 0.67990 -1.84280 H -0.00110 3.41950 0.82310	C -0.70240 1.03560 1.09970 C 0.70230 1.03570 1.09970 C -1.14090 1.91640 -0.00460 C 1.14070 1.91660 -0.00460 N -0.00010 2.30410 -0.68410 O -2.26960 2.27780 -0.28990 O 2.26940 2.27810 -0.28990 H -1.33720 0.92820 1.96730 H 1.33710 0.92840 1.96730 H -0.00020 2.89650 -1.50410 C -2.42100 -0.89130 -0.44220 O -2.72430 -2.20810 -0.89430 H -3.16000 -0.55140 0.29100 H -3.56980 -2.16680 -1.35310 H -2.40830 -0.18800 -1.27970 C -0.68410 -1.63820 1.35880 C 0.68430 -1.63820 1.35880 C -1.08540 -0.91420 0.20720 C 1.08540 -0.91410 0.20720 O 0.00000 -0.78860 -0.61170 C 2.42110 -0.89110 -0.44230 O 2.72460 -2.20790 -0.89420 H -1.35600 -1.99150 2.12790 H 1.35630 -1.99140 2.12790 H 2.40820 -0.18780 -1.27980 H 3.16000 -0.55090 0.29090 H 3.57020 -2.16640 -1.35290
10 exo	
E = -817.937438 a.u. H = -817.712525 a.u. G = -817.767451 a.u.	
C -2.42170 -0.83300 -0.42300 O -2.56420 -2.17940 -0.84800 H -3.19340 -0.56680 0.30880 H -3.40430 -2.25160 -1.31120 H -2.50110 -0.14760 -1.27310 C -0.66450 -1.70060 1.26820 C 0.66470 -1.70050 1.26820 C -1.07820 -0.67670 0.22610 C 1.07830 -0.67660 0.22610 O 0.00010 -0.76040 -0.71590 C 2.42180 -0.83270 -0.42300 O 2.56450 -2.17910 -0.84800 H -1.35100 -2.21360 1.92900 H 1.35120 -2.21340 1.92910 H 2.50110 -0.14740 -1.27310 H 3.19350 -0.56650 0.30880 H 3.40460 -2.25130 -1.31110 C -0.76910 0.70830 0.89150 C 0.76900 0.70840 0.89140 C -1.15300 1.88430 0.02700 C 1.15280 1.88440 0.02700 N -0.00020 2.46060 -0.45110 O -2.27200 2.28750 -0.21330 O 2.27170 2.28780 -0.21330 H -1.24210 0.80780 1.86800	

H 1.24210 0.80800 1.86800 H -0.00020 3.27680 -1.05420	

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