

Supplementary Materials: Design, Synthesis and Biological Evaluation of Brain-Targeted Thiamine Disulfide Prodrugs of Ampakine Compound LCX001

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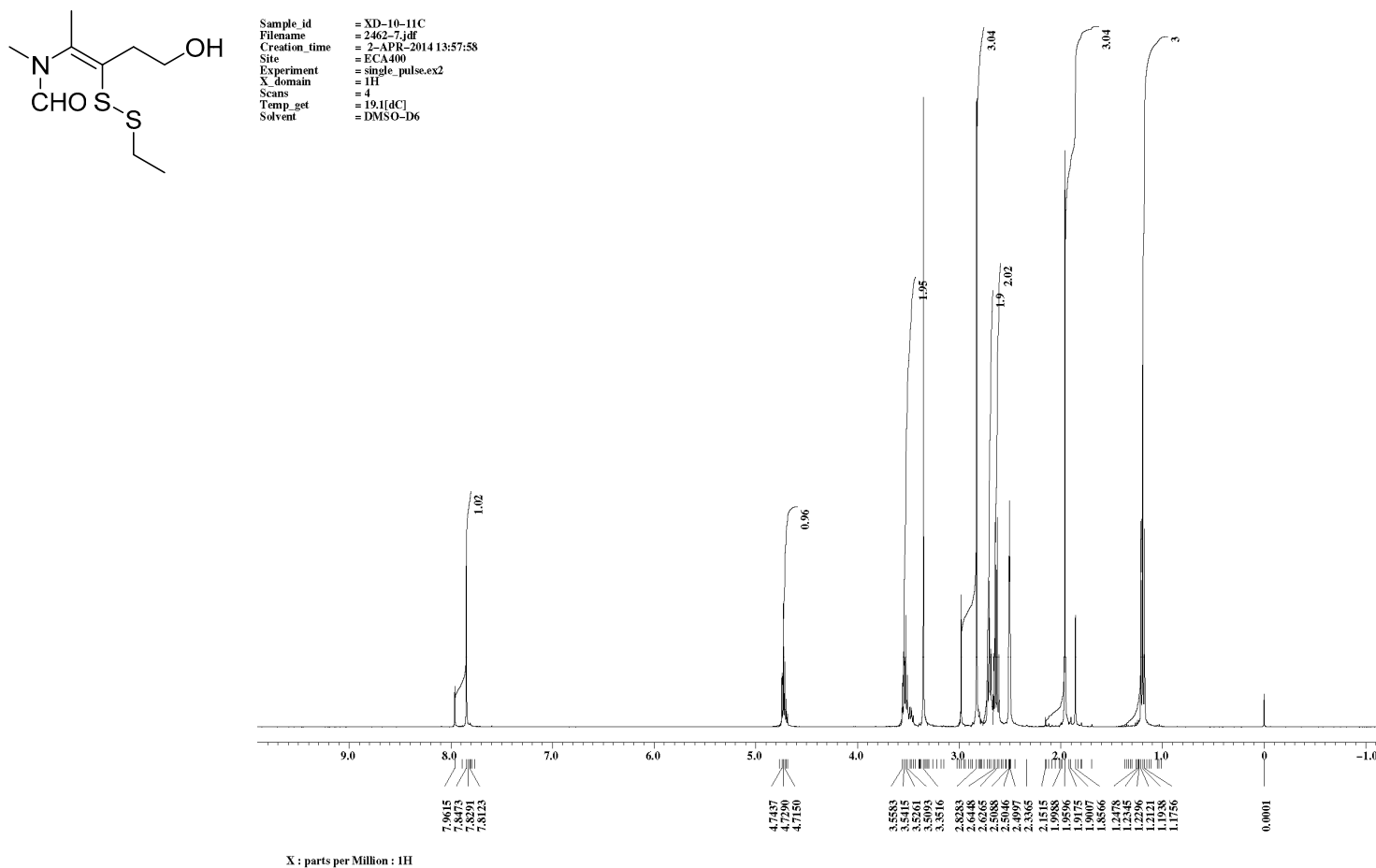


Figure S1. $^1\text{H-NMR}$ spectra of *N*-(3-(ethyl-disulfanyl)-5-hydroxypent-2-en-2-yl)-*N*-methylformamide 5a (CDCl_3 , 400MHz).

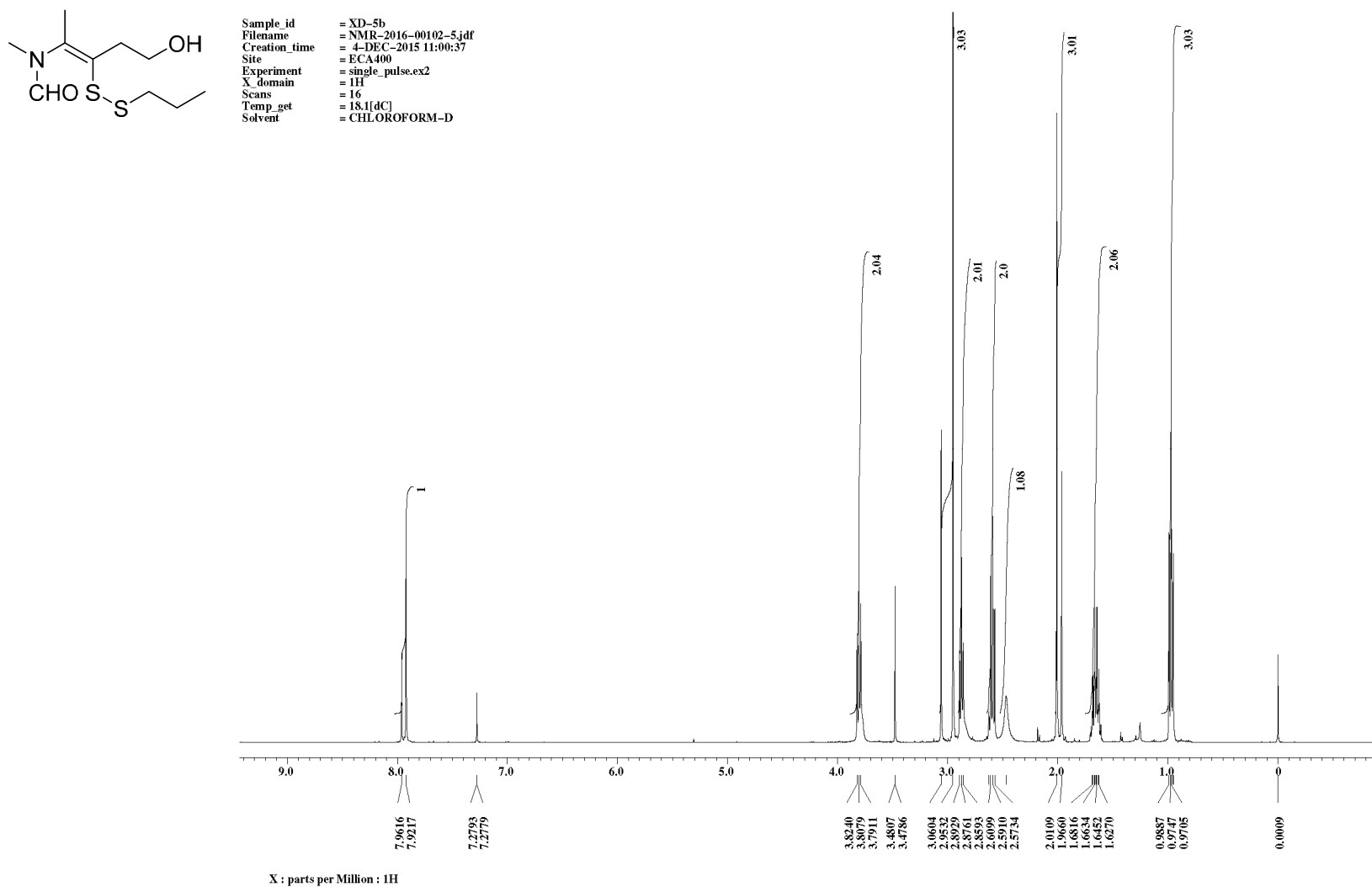
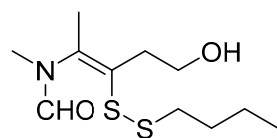


Figure S2. $^1\text{H-NMR}$ spectra of *N*-(3-(propyldisulfanyl)-5-hydroxypent-2-en-2-yl)-*N*-methylformamide 5b (CDCl_3 , 400MHz).



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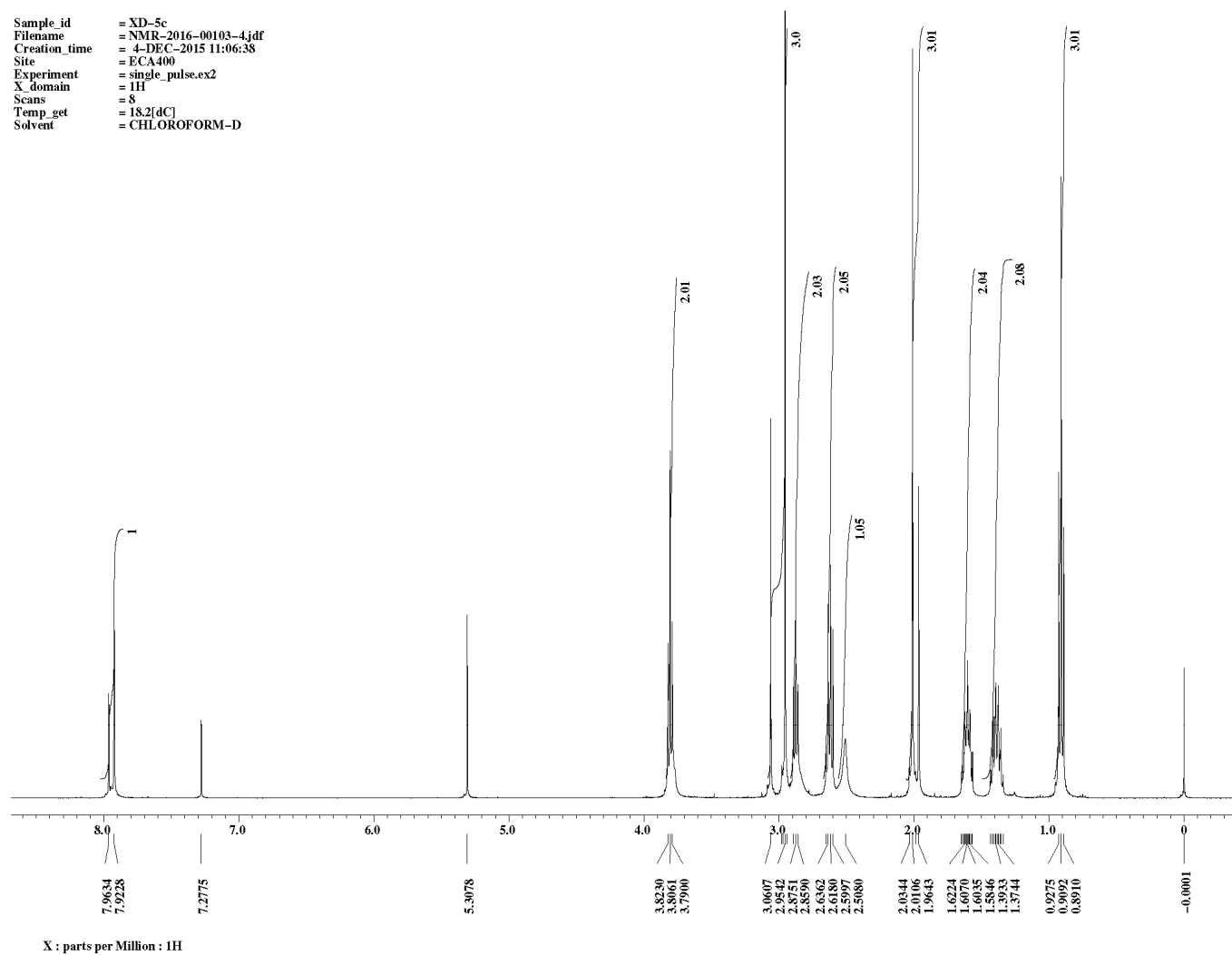


Figure S3. ¹H-NMR spectra of *N*-(3-(butyldisulfanyl)-5-hydroxypent-2-en-2-yl)-*N*-methylformamide 5c (CDCl₃, 400MHz).

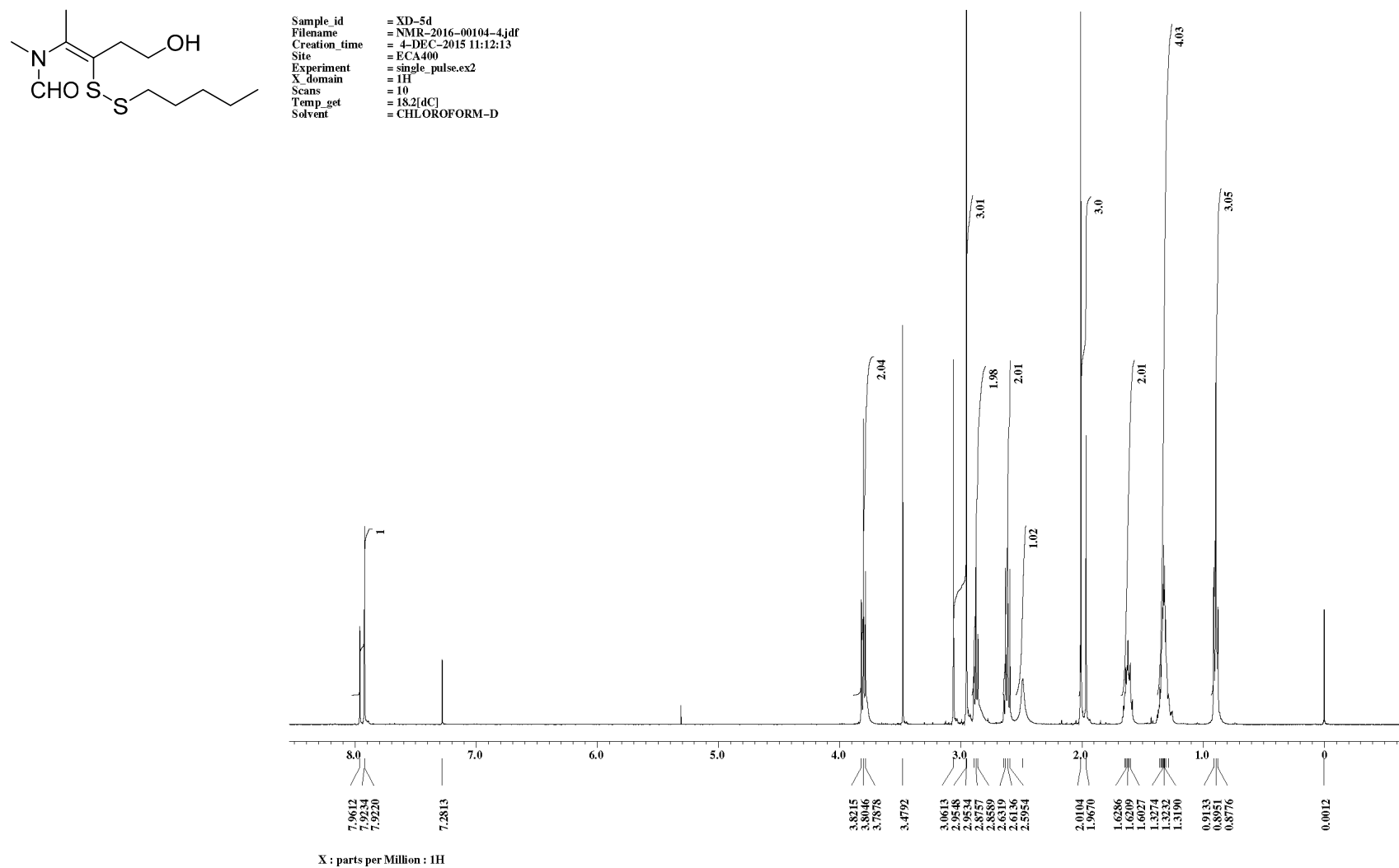
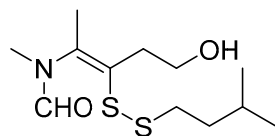


Figure S4. ¹H-NMR spectra of *N*-(3-(amyldisulfanyl)-5-hydroxypent-2-en-2-yl)-*N*-methylformamide 5d (CDCl₃, 400MHz).



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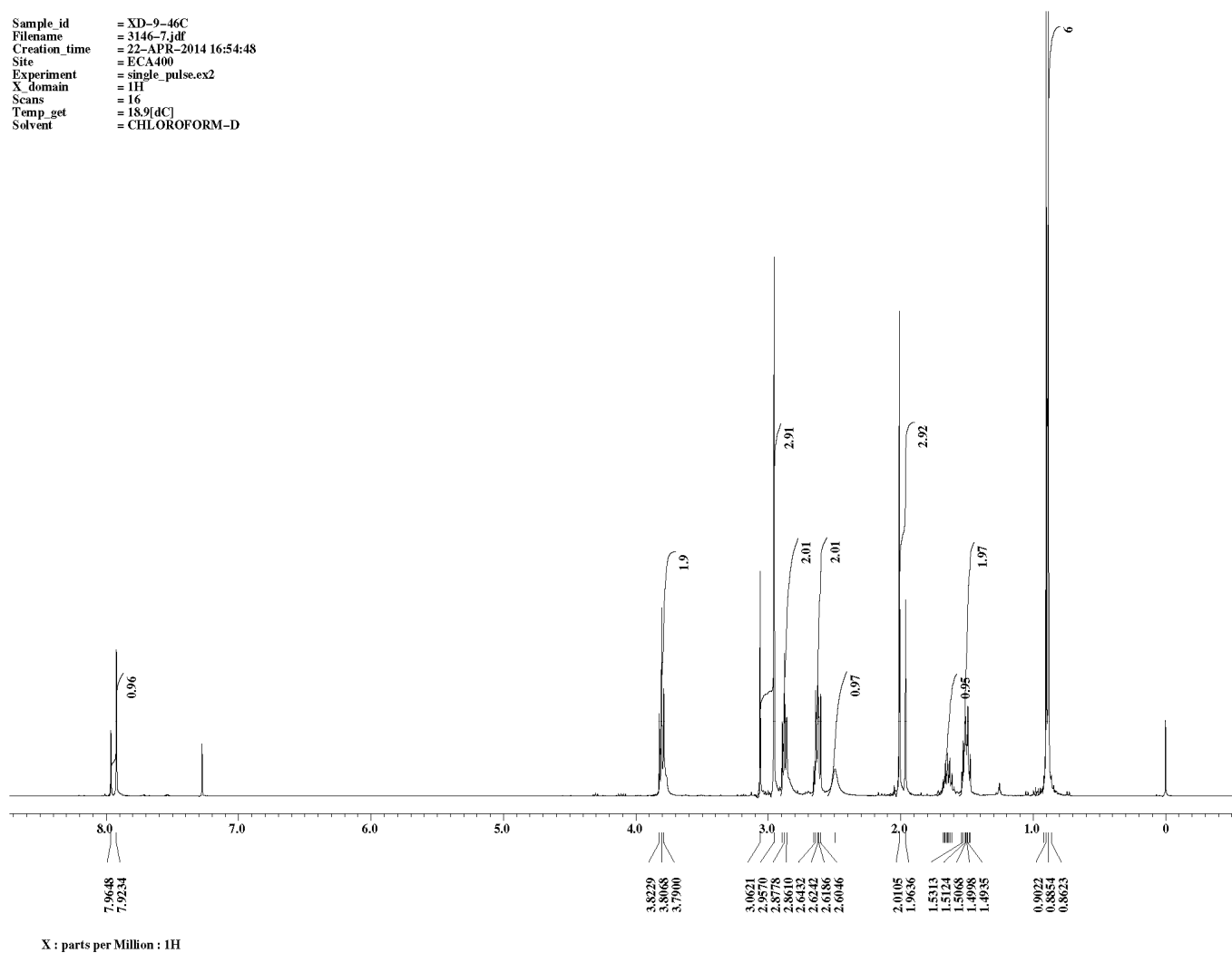
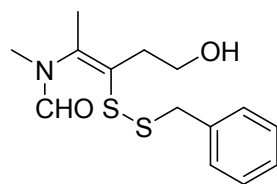


Figure S5. ¹H-NMR spectra of *N*-(3-(isoamyldisulfanyl)-5-hydroxypent-2-en-2-yl)-*N*-methylformamide 5e (CDCl₃, 400MHz).



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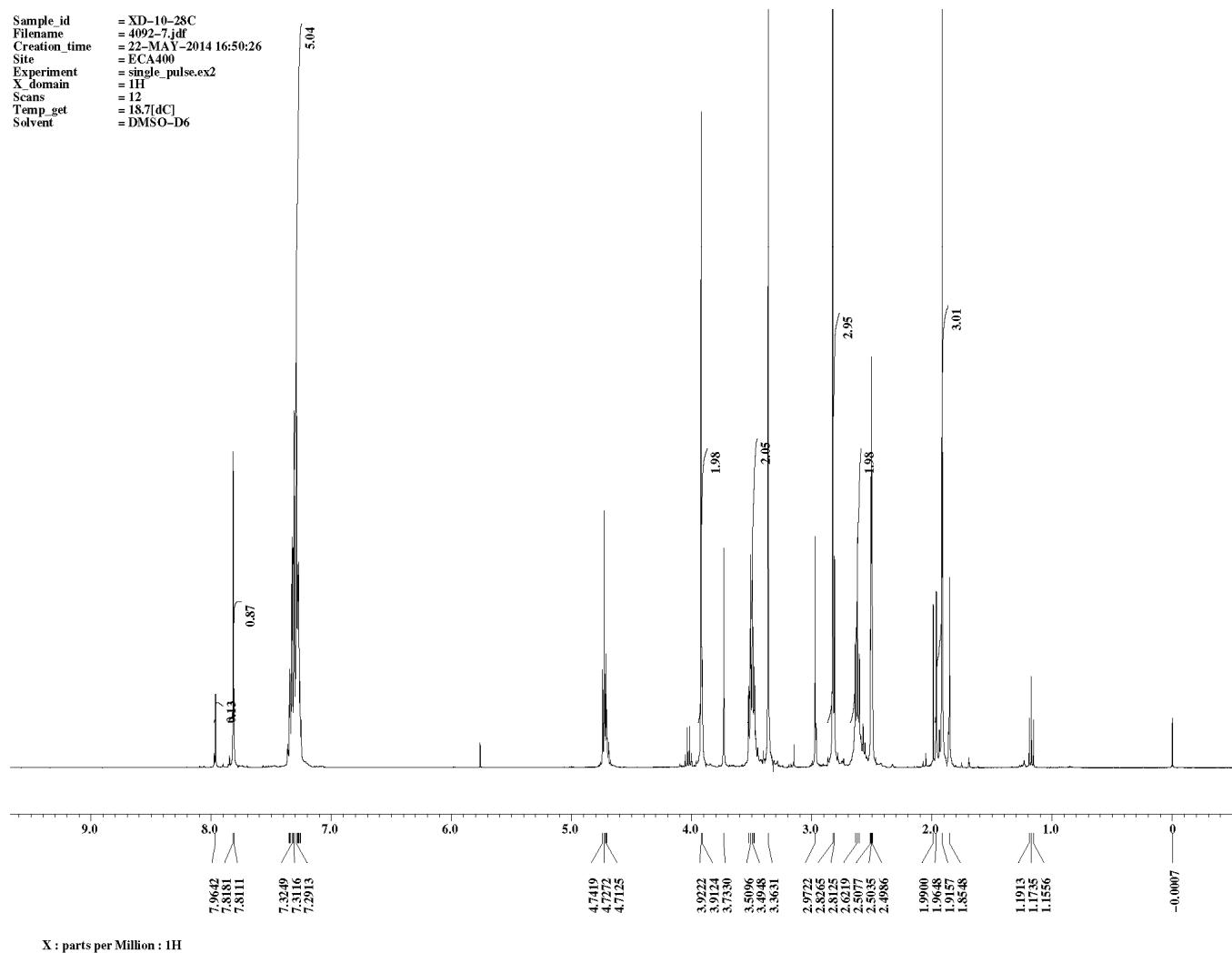


Figure S6. ¹H-NMR spectra of *N*-(3-(benzylsulfanyl)-5-hydroxypent-2-en-2-yl)-*N*-methylformamide 5f (DMSO-*d*₆, 400MHz).

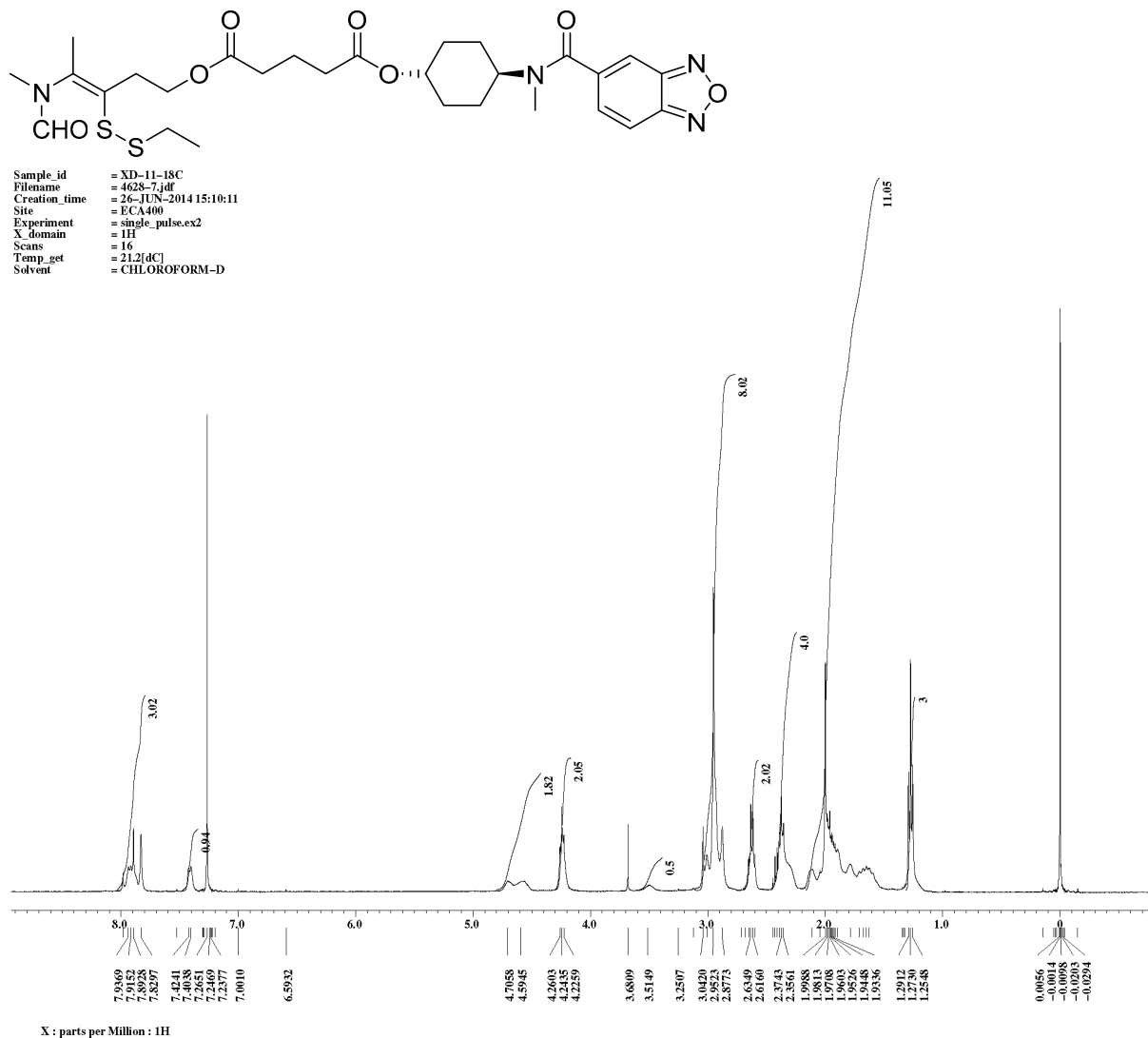


Figure S7. ¹H-NMR spectra of S-3-(ethylsulfanyl)-4-(N-methylformamido)pent-3-en-1-yl((1R,4R)-4-(N-methylbenzo[c][1,2,5]oxadiazole-5-carboxamido)cyclohexyl) glutarate (**7a**) (CDCl₃, 400MHz).

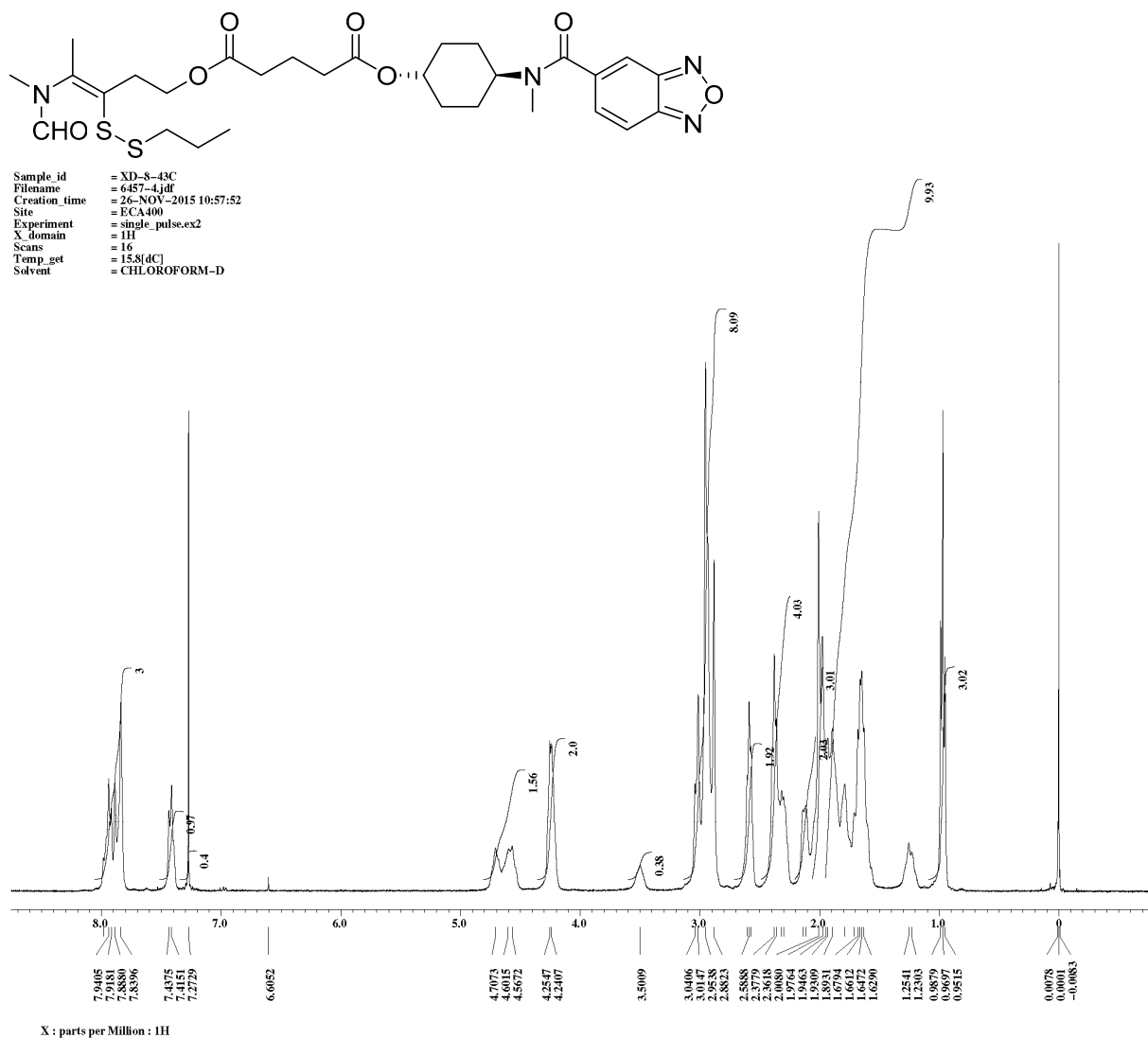


Figure S8. $^1\text{H-NMR}$ spectra of *S*-3-(propyl disulfanyl)-4-(*N*-methylformamido)pent-3-en-1-yl((1*R*,4*R*)-4-(*N*-methylbenzo[*c*][1,2,5]oxadiazol-5-carboxamido)cyclohexyl) glutarate (**7b**) (CDCl_3 , 400MHz).

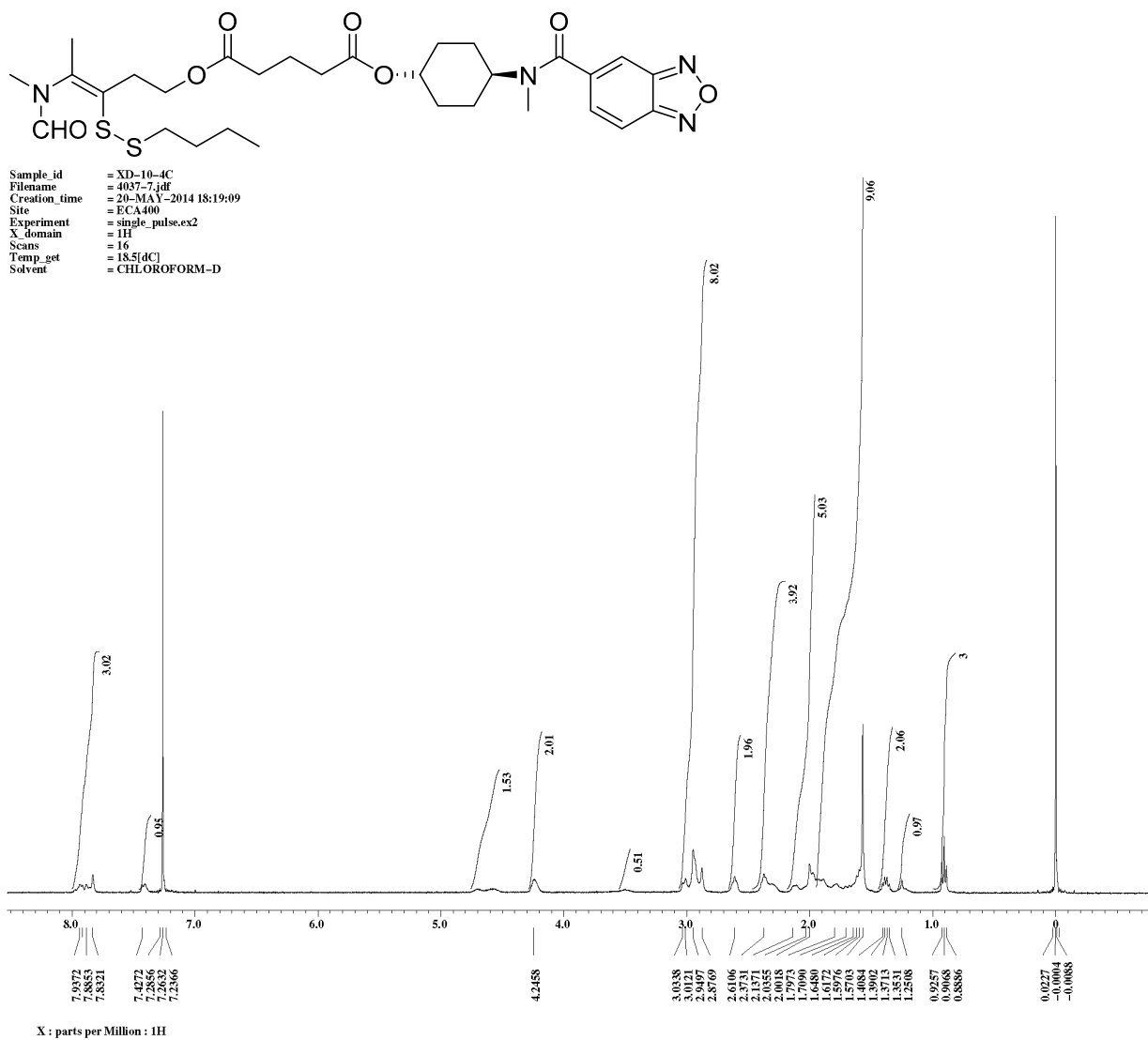


Figure S9. $^1\text{H-NMR}$ spectra of *S*-3-(butyldisulfanyl)-4-(*N*-methylformamido)pent-3-en-1-yl((1*R*,4*R*)-4-(*N*-methylbenzo[*c*][1,2,5]oxadiazole-5-carboxamido)cyclohexyl) glutarate (**7b**) (CDCl₃, 400MHz).

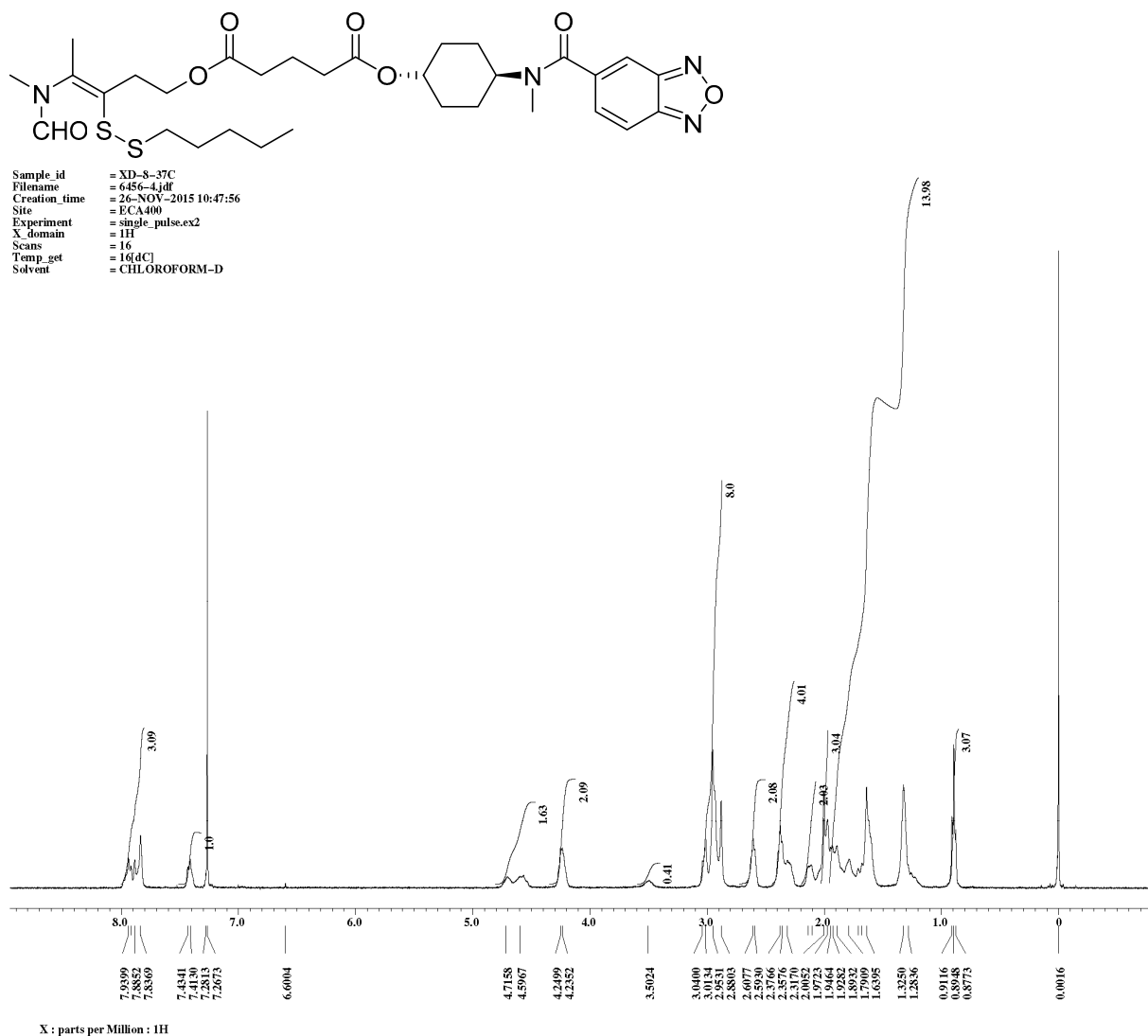


Figure S10. $^1\text{H-NMR}$ spectra of *S*-3-(amyldisulfanyl)-4-(*N*-methylformamido)pent-3-en-1-yl((1*R*,4*R*)-4-(*N*-methylbenzo[*c*][1,2,5]oxadiazole-5-carboxamido)cyclohexyl) glutarate (**7d**) (CDCl_3 , 400MHz).

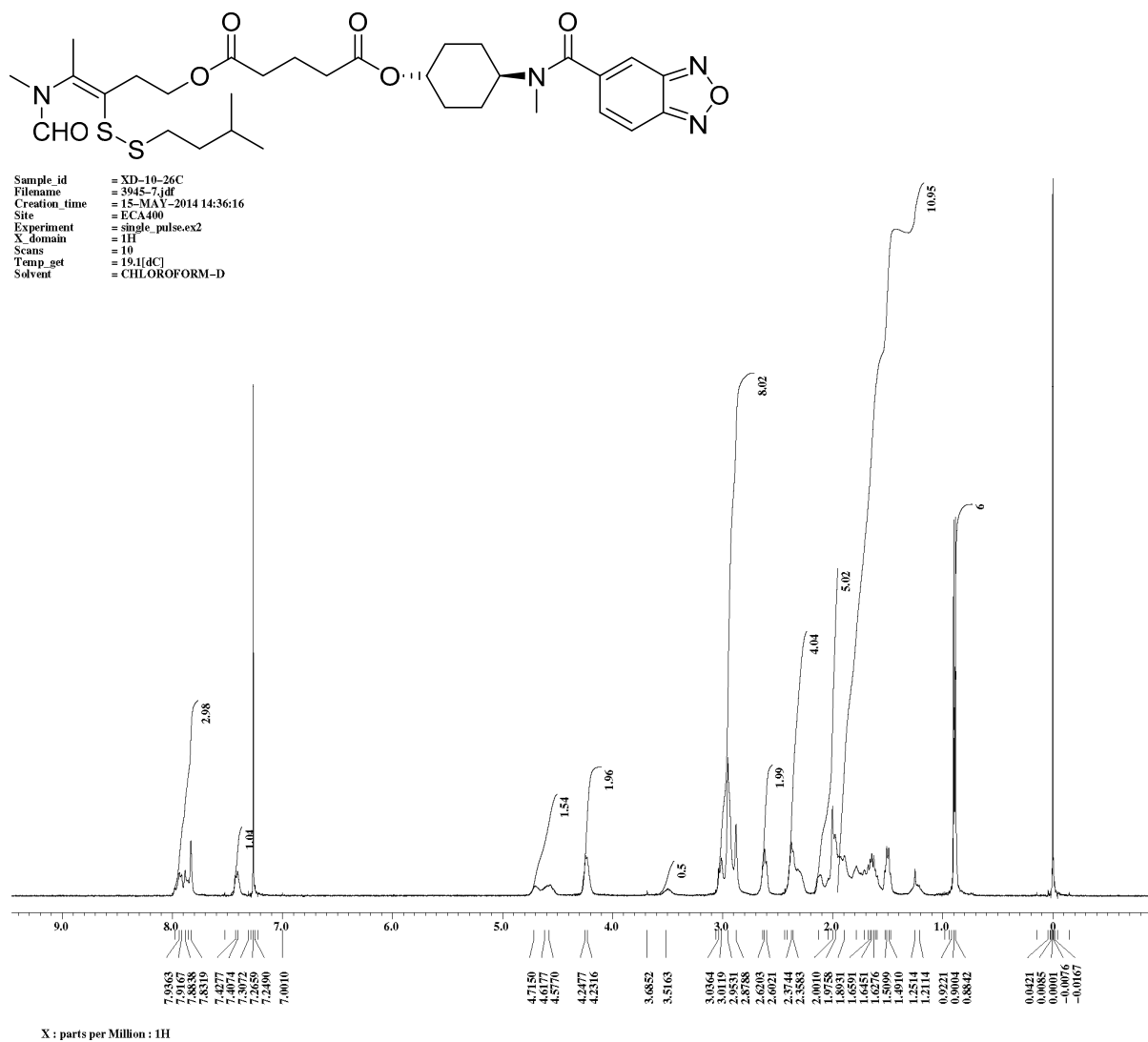


Figure S11. ¹H-NMR spectra of S-3-(isoamyldisulfanyl)-4-(N-methylformamido)pent-3-en-1-yl((1R,4R)-4-(N-methylbenzo[c][1,2,5]oxadiazole-5-carboxamido)cyclohexyl) glutarate (**7d**) (CDCl₃, 400MHz).

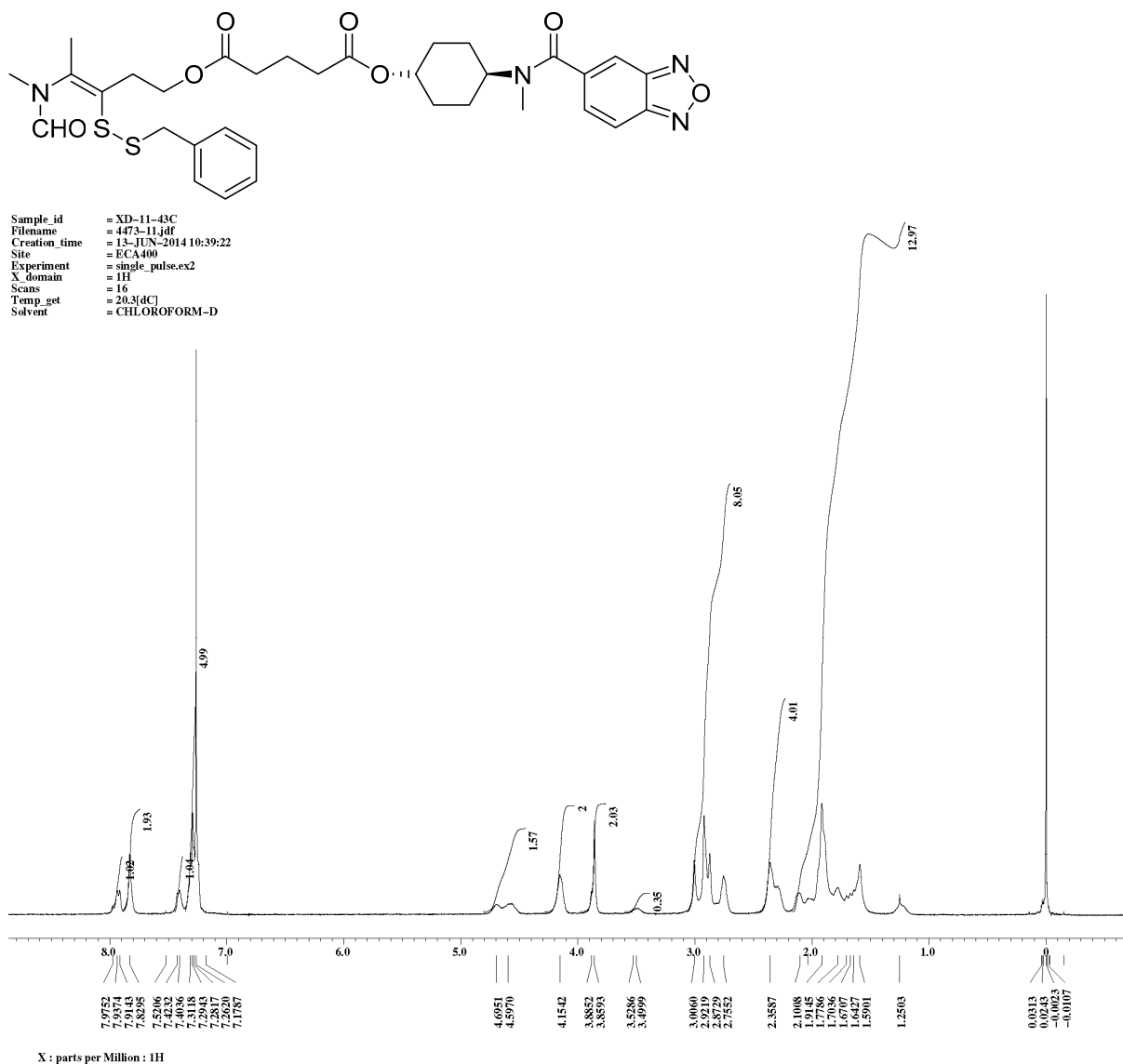


Figure S12. $^1\text{H-NMR}$ spectra of *S*-3-(benzyldisulfanyl)-4-(*N*-methylformamido)pent-3-en-1-yl((1*R*,4*R*)-4-(*N*-methylbenzo[*c*][1,2,5]oxadiazol-5-carboxamido)cyclohexyl) glutarate (**7d**) (CDCl_3 , 400MHz).