

Synthesis and Late-Stage Modification of (-)-Doliculide Derivatives Using Matteson's Homologation approach

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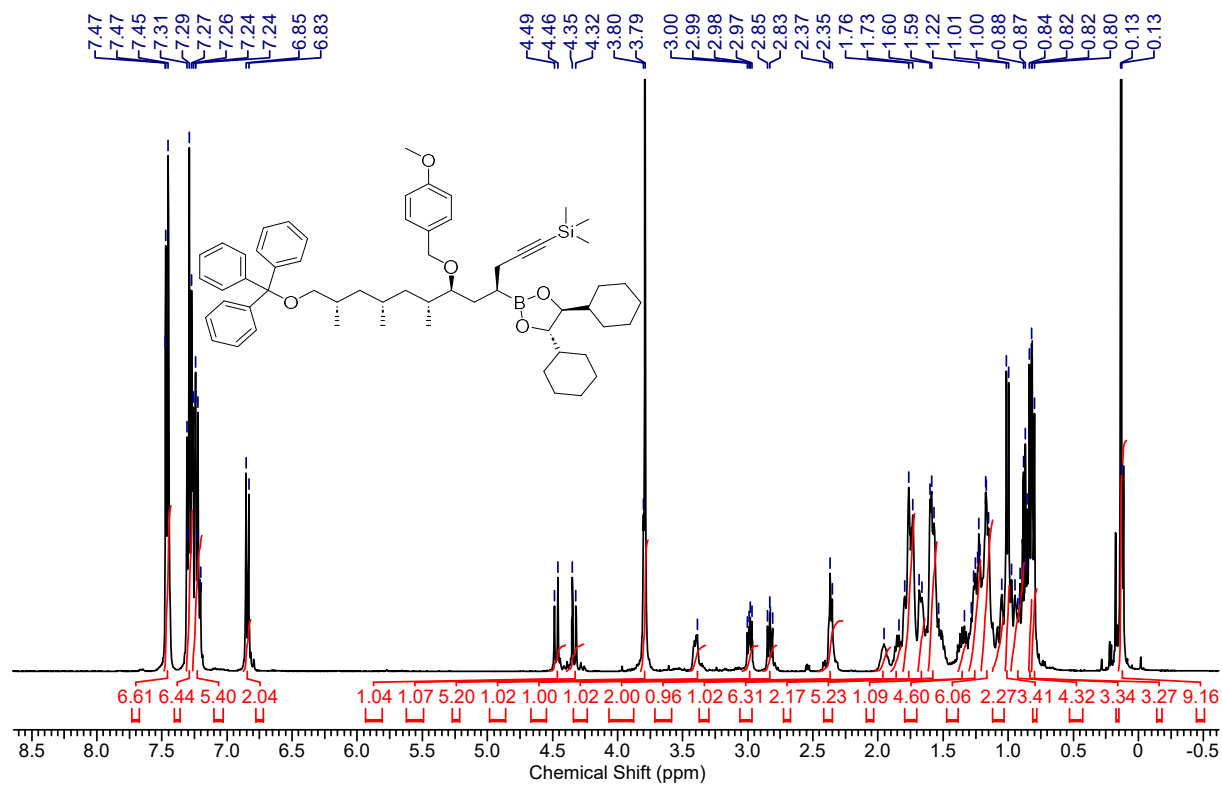
Copies of the NMR spectra

¹ H/ ¹³ C-NMR Compound 2a	S2
¹ H/ ¹³ C-NMR Compound 2b	S3
¹ H/ ¹³ C-NMR Compound 3a	S4
¹ H/ ¹³ C-NMR Compound 3b	S5
¹ H/ ¹³ C-NMR Compound 5a	S6
¹ H/ ¹³ C-NMR Compound 5b	S8
¹ H/ ¹³ C-NMR Compound 5a-1	S10
¹ H/ ¹³ C-NMR Compound 5b-1	S11
¹ H/ ¹³ C-NMR Compound 6a	S12
¹ H/ ¹³ C-NMR Compound 6b	S13
¹ H/ ¹³ C-NMR Compound 7a	S14
¹ H/ ¹³ C-NMR Compound 7b	S15
¹ H/ ¹³ C-NMR Compound 7a-1	S16
¹ H/ ¹³ C-NMR Compound 7b-1	S17
¹ H/ ¹³ C-NMR Compound 8a	S18
¹ H/ ¹³ C-NMR Compound 8b	S19
¹ H/ ¹³ C-NMR Compound 8c	S20
¹ H/ ¹³ C-NMR Compound 9a	S21
¹ H/ ¹³ C-NMR Compound 9b	S22
¹ H/ ¹³ C-NMR Compound 9c	S23
¹ H/ ¹³ C-NMR Compound 9d	S24
¹ H/ ¹³ C-NMR Compound 9e	S25
¹ H/ ¹³ C-NMR Compound 9f	S26
¹ H/ ¹³ C-NMR Compound 9g	S27
¹ H/ ¹³ C-NMR Compound 10a	S28
¹ H/ ¹³ C-NMR Compound 10b	S29
¹ H/ ¹³ C-NMR Compound 10c	S30
¹ H/ ¹³ C-NMR Compound 11a	S31
¹ H/ ¹³ C-NMR Compound 11b	S32
¹ H/ ¹³ C-NMR Compound 11c	S33
¹ H/ ¹³ C-NMR Compound 11d	S34
¹ H/ ¹³ C-NMR Compound 11e	S35
¹ H/ ¹³ C-NMR Compound 11f	S36

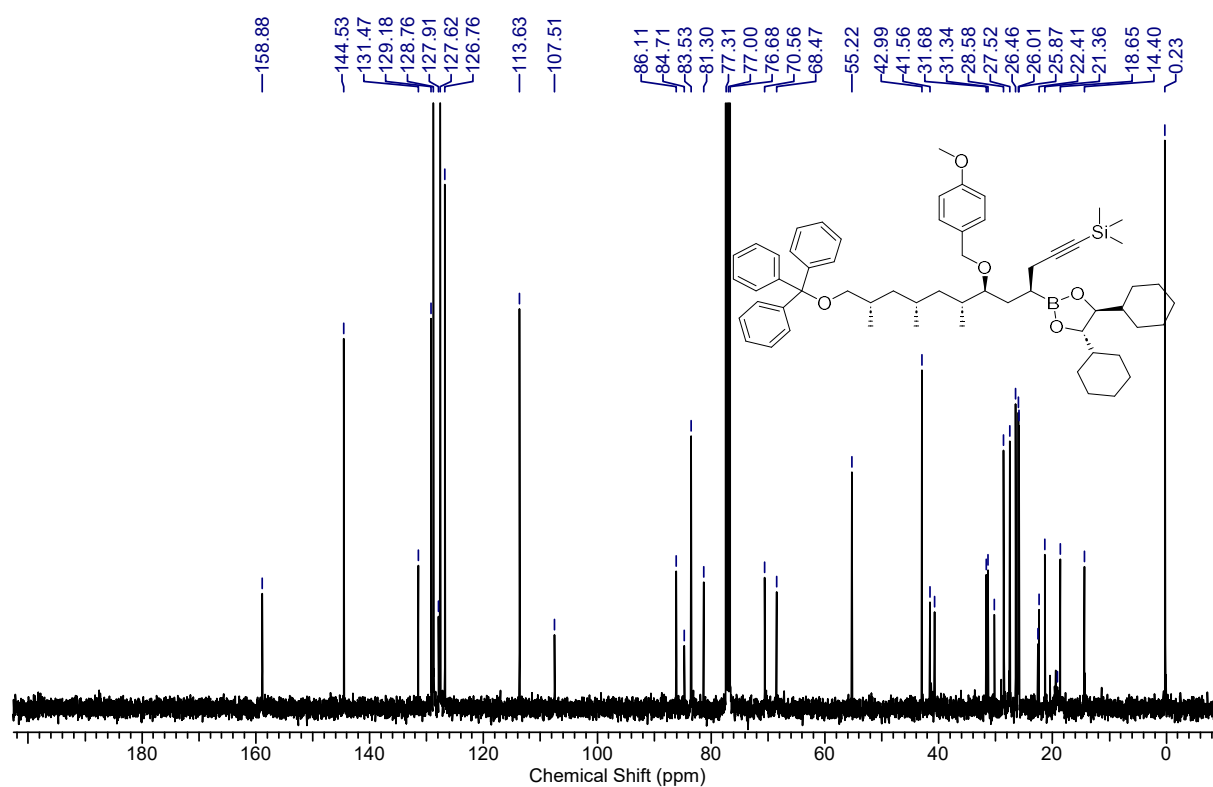
Copies of NMR spectra

{(4*R*,6*S*,7*R*,9*R*,11*S*)-4-[(4*S*,5*S*)-4,5-Dicyclohexyl-1,3,2-dioxaborolan-2-yl]-6-[(4-methoxybenzyl)oxy]-7,9,11-trimethyl-12-(trityloxy)dodec-1-yn-1-yl}trimethylsilane (2a)

¹H-NMR (400 MHz, CDCl₃)

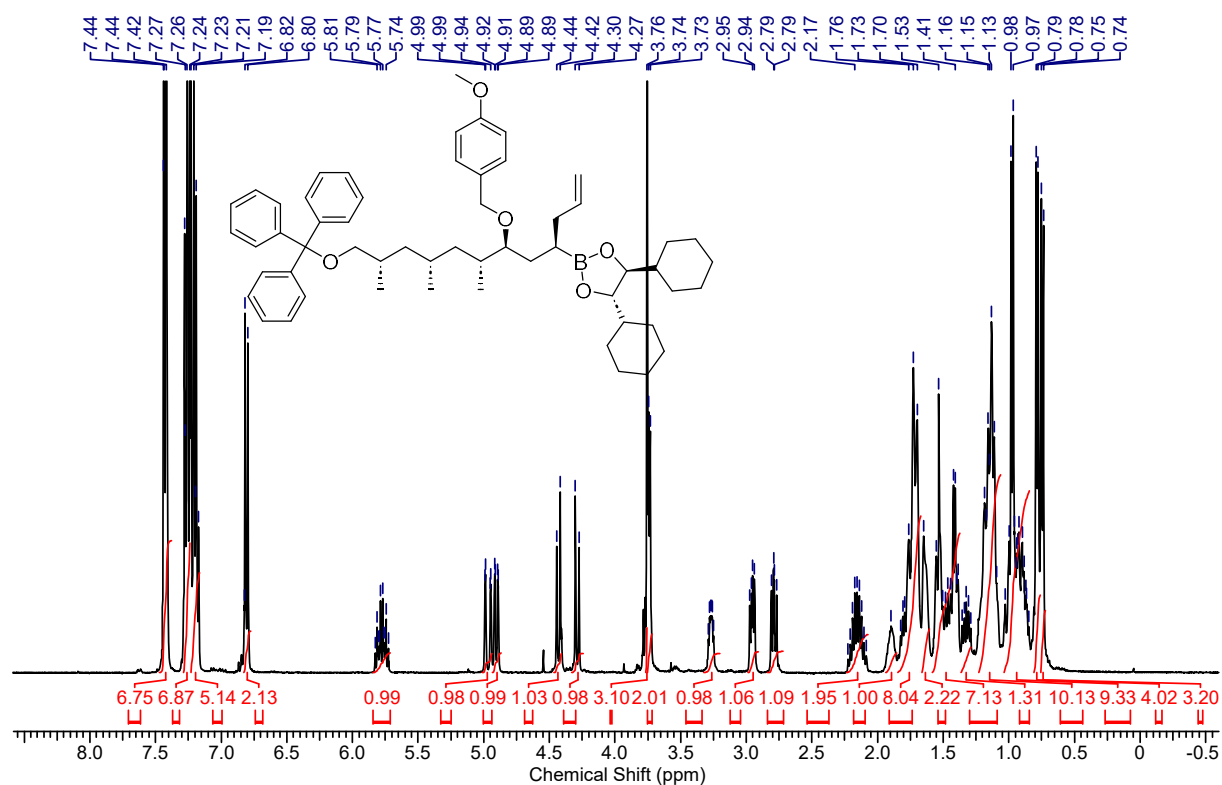


¹³C-NMR (100 MHz, CDCl₃)

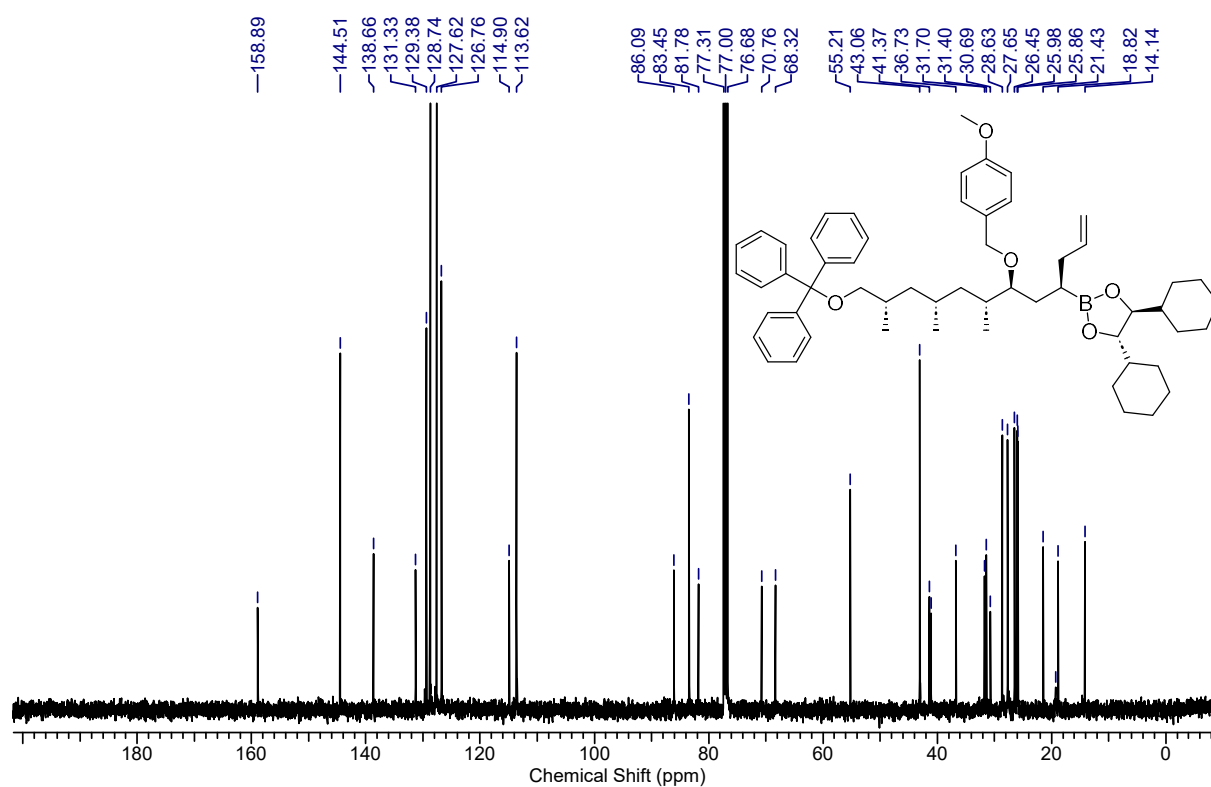


(4*S*,5*S*)-4,5-Dicyclohexyl-2-[(4*R*,6*S*,7*R*,9*R*,11*S*)-6-[(4-methoxybenzyl)oxy]-7,9,11-trimethyl-12-(trityloxy)dodec-1-en-4-yl]-1,3,2-dioxaborolane (2b)

¹H-NMR (400 MHz, CDCl₃)

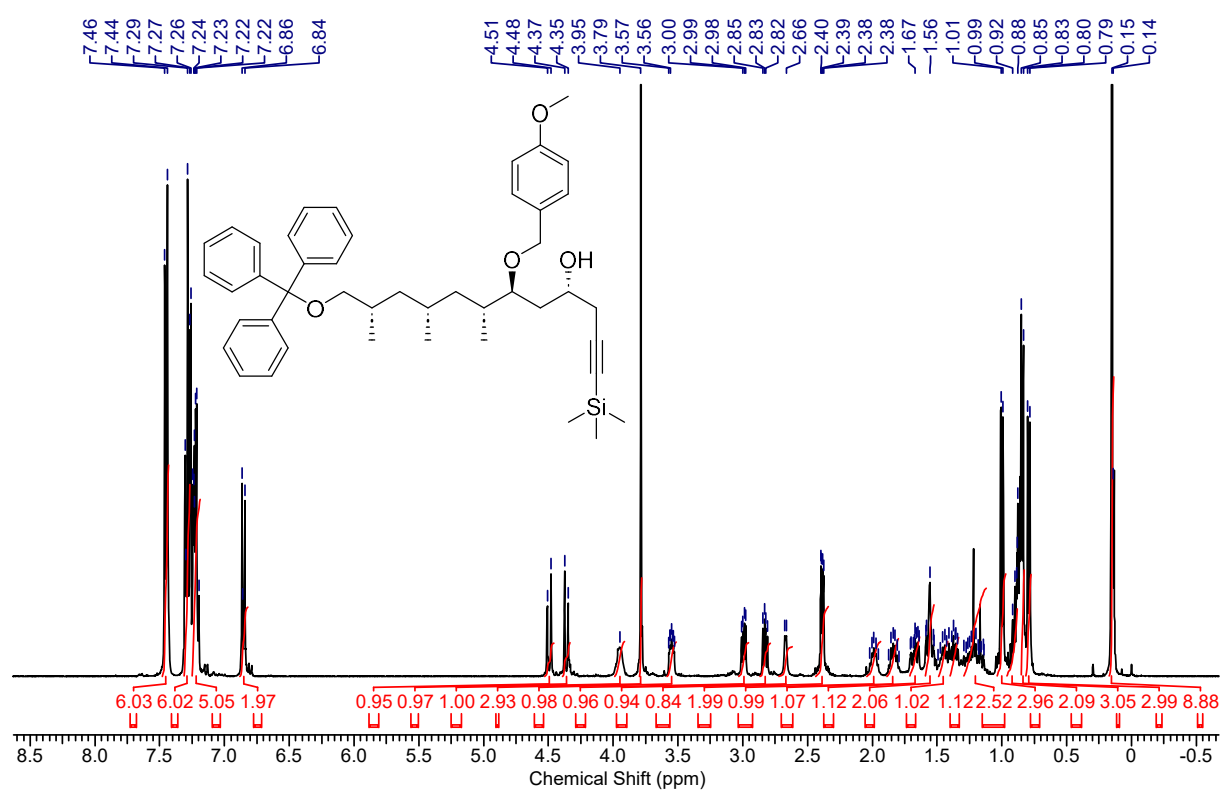


¹³C-NMR (100 MHz, CDCl₃)

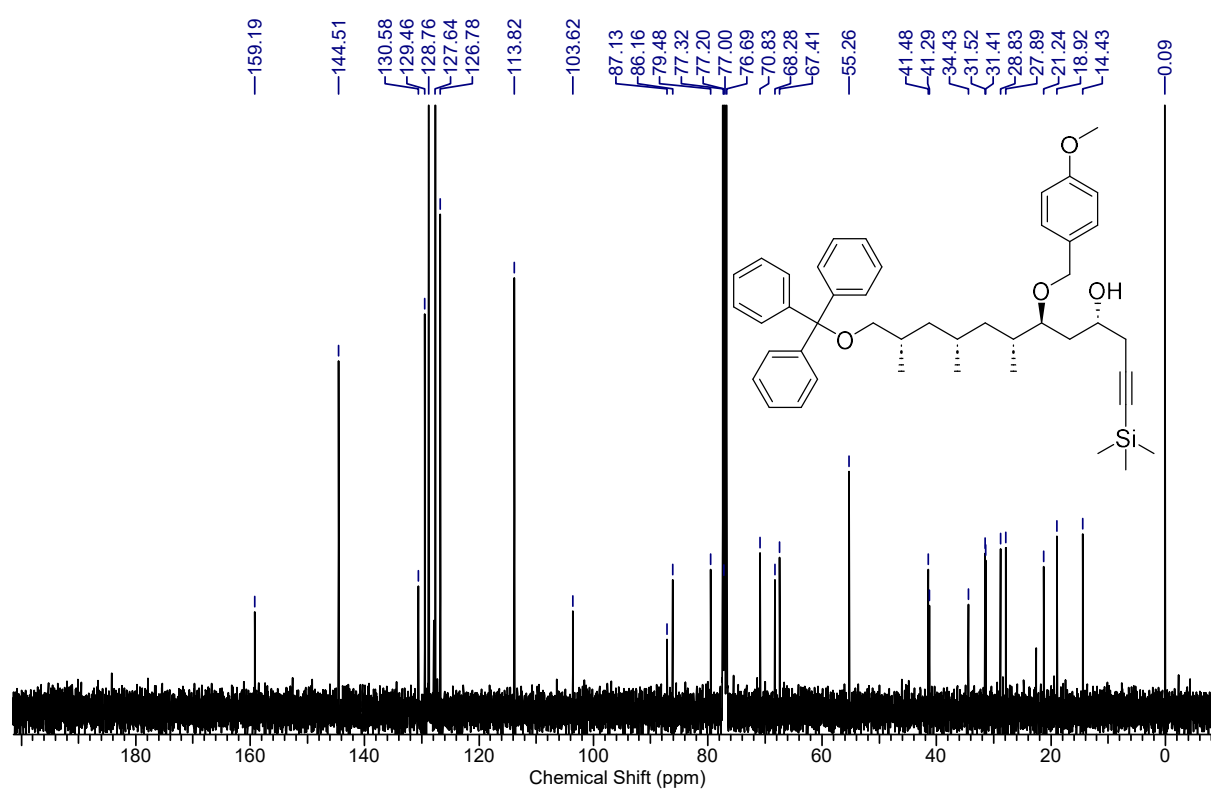


(4*R*,6*S*,7*R*,9*R*,11*S*)-6-[(4-Methoxybenzyl)oxy]-7,9,11-trimethyl-1-(trimethylsilyl)-12-(trityloxy)dodec-1-yn-4-ol (3a)

¹H-NMR (400 MHz, CDCl₃)

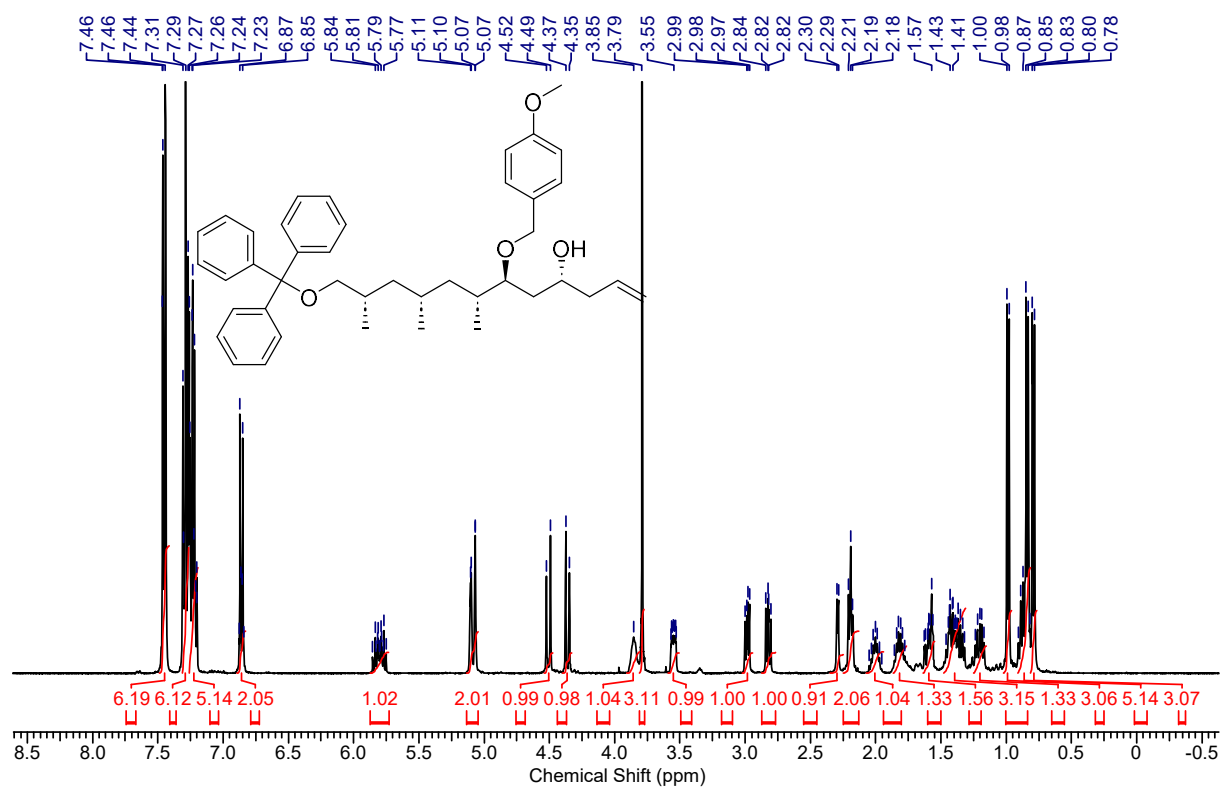


¹³C-NMR (100 MHz, CDCl₃)

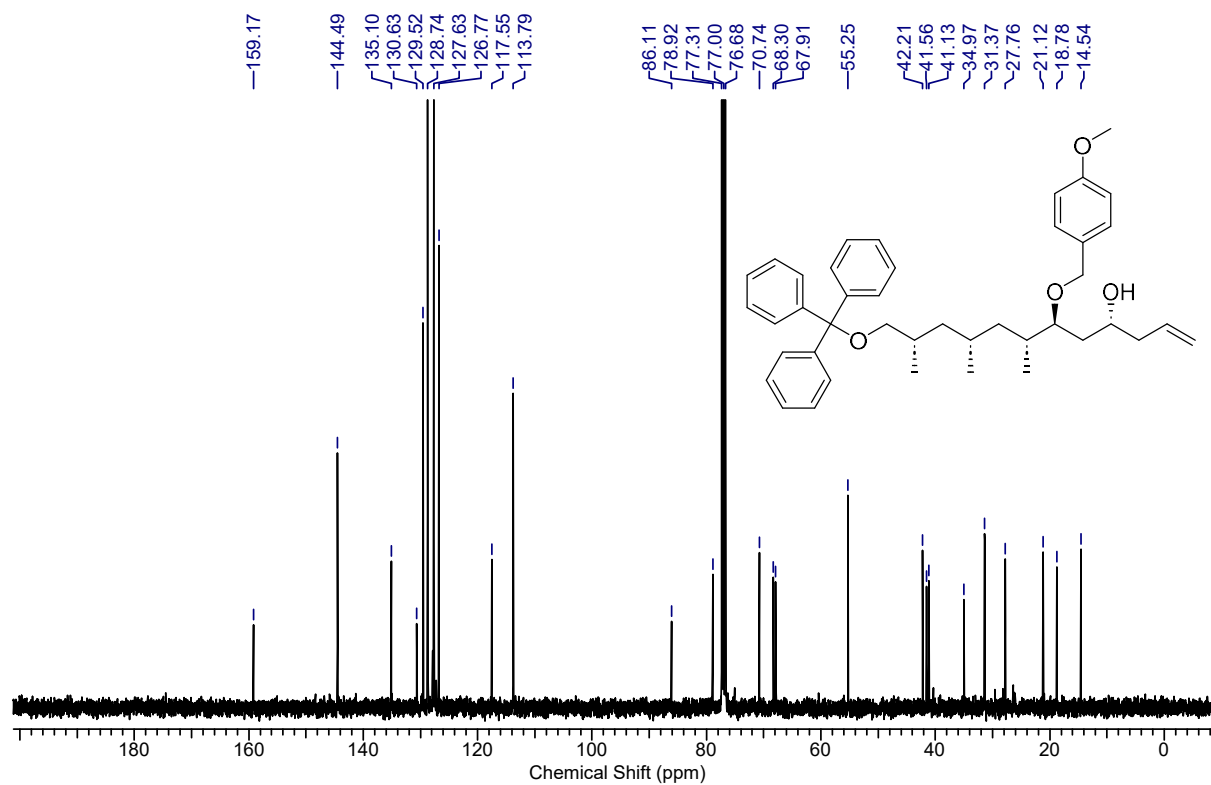


(4*R*,6*S*,7*R*,9*R*,11*S*)-6-[(4-Methoxybenzyl)oxy]-7,9,11-trimethyl-12-(trityloxy)dodec-1-en-4-ol (3b)

¹H-NMR (400 MHz, CDCl₃)

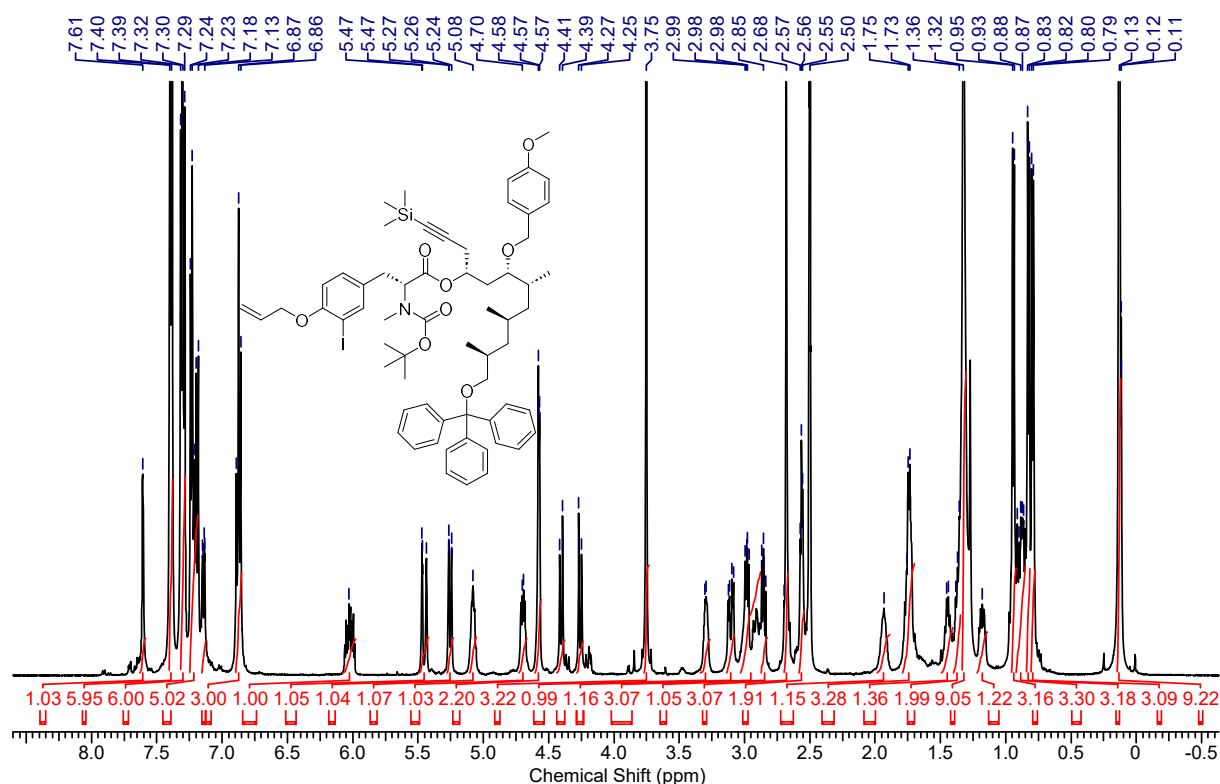


¹³C-NMR (100 MHz, CDCl₃)

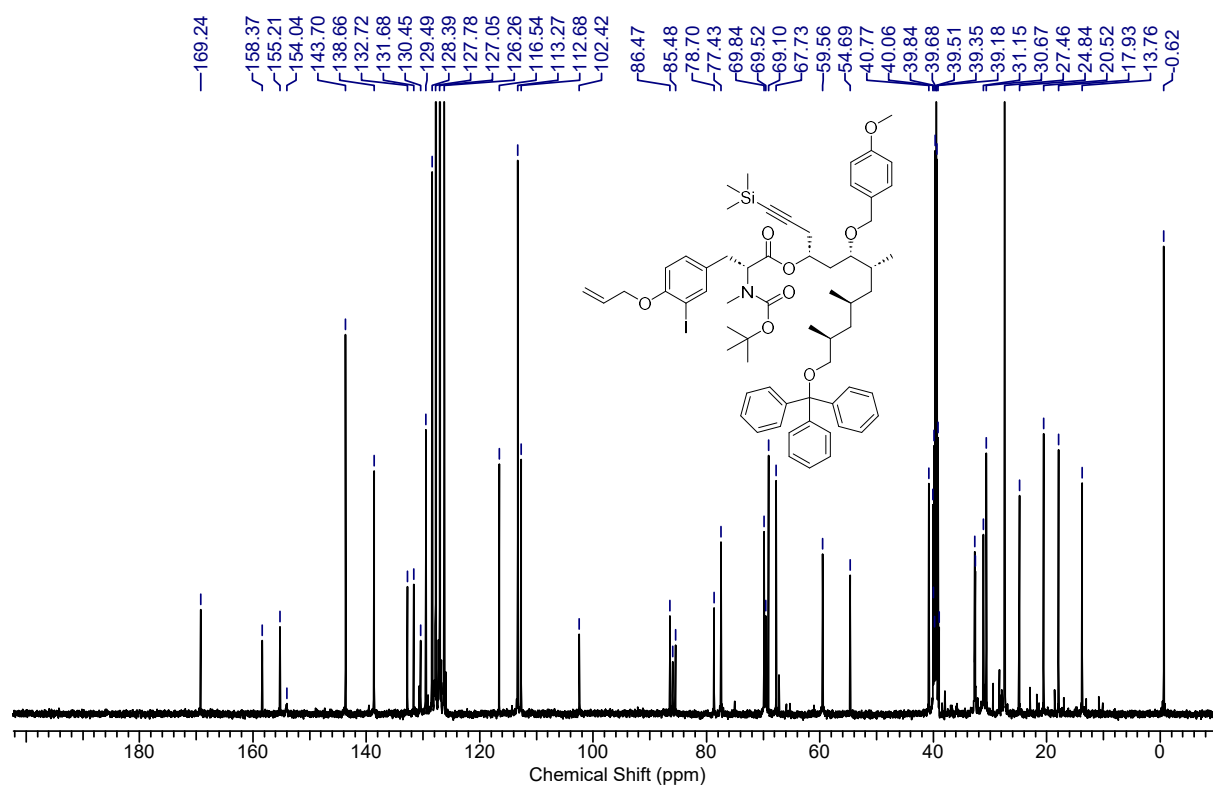


(4*R*,6*S*,7*R*,9*R*,11*S*)-6-[(4-Methoxybenzyl)oxy]-7,9,11-trimethyl-1-(trimethylsilyl)-12-(trityloxy)dodec-1-yn-4-yl (*R*)-3-[4-(allyloxy)-3-iodophenyl]-2-[(*tert*-butoxycarbonyl)(methyl)amino]propanoate (5a)

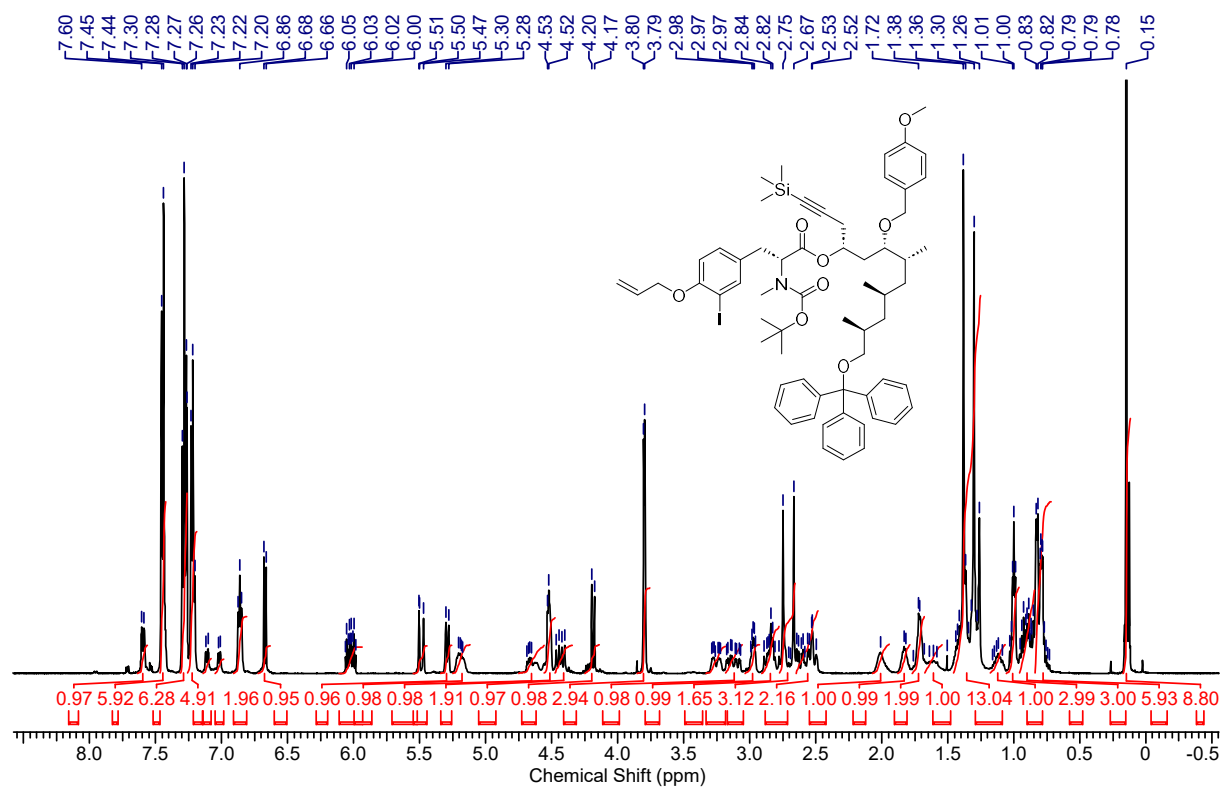
¹H-NMR (500 MHz, 373 K, DMSO-D₆)



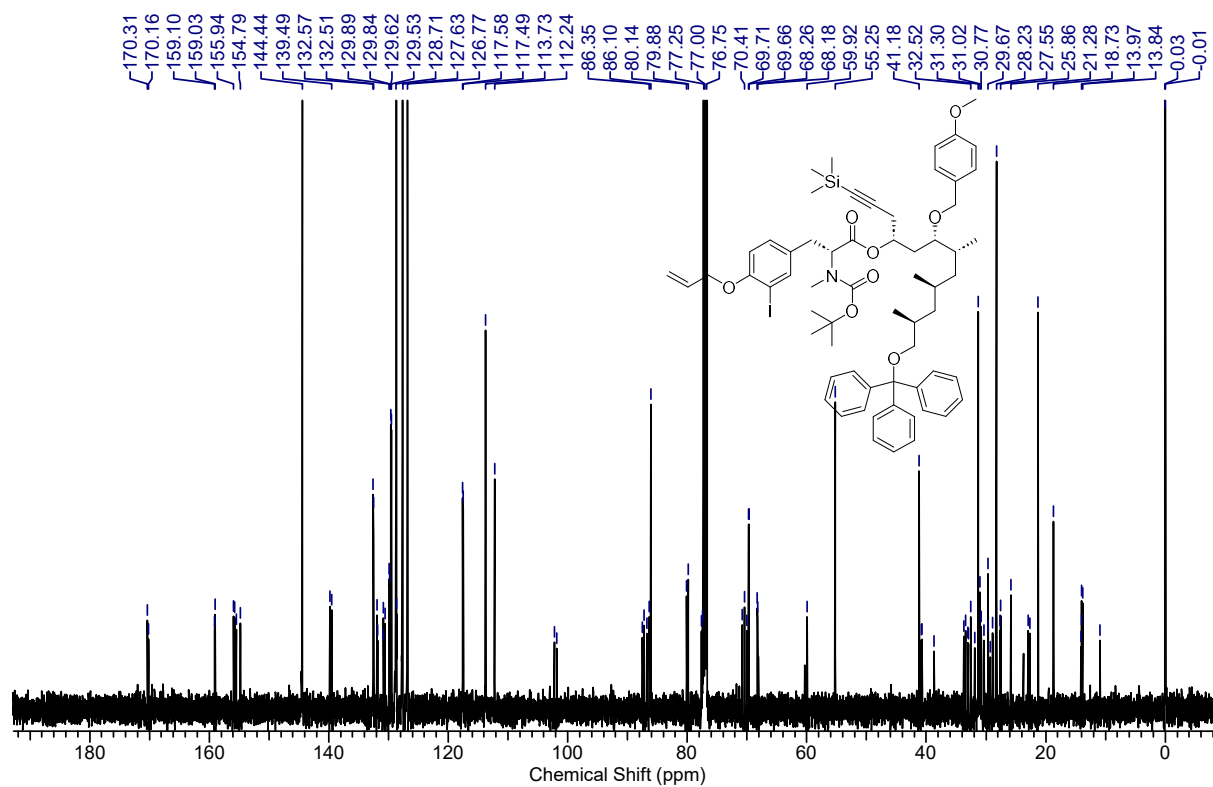
¹³C-NMR (125 MHz, 373 K, DMSO-D₆)



¹H-NMR (500 MHz, CDCl₃)

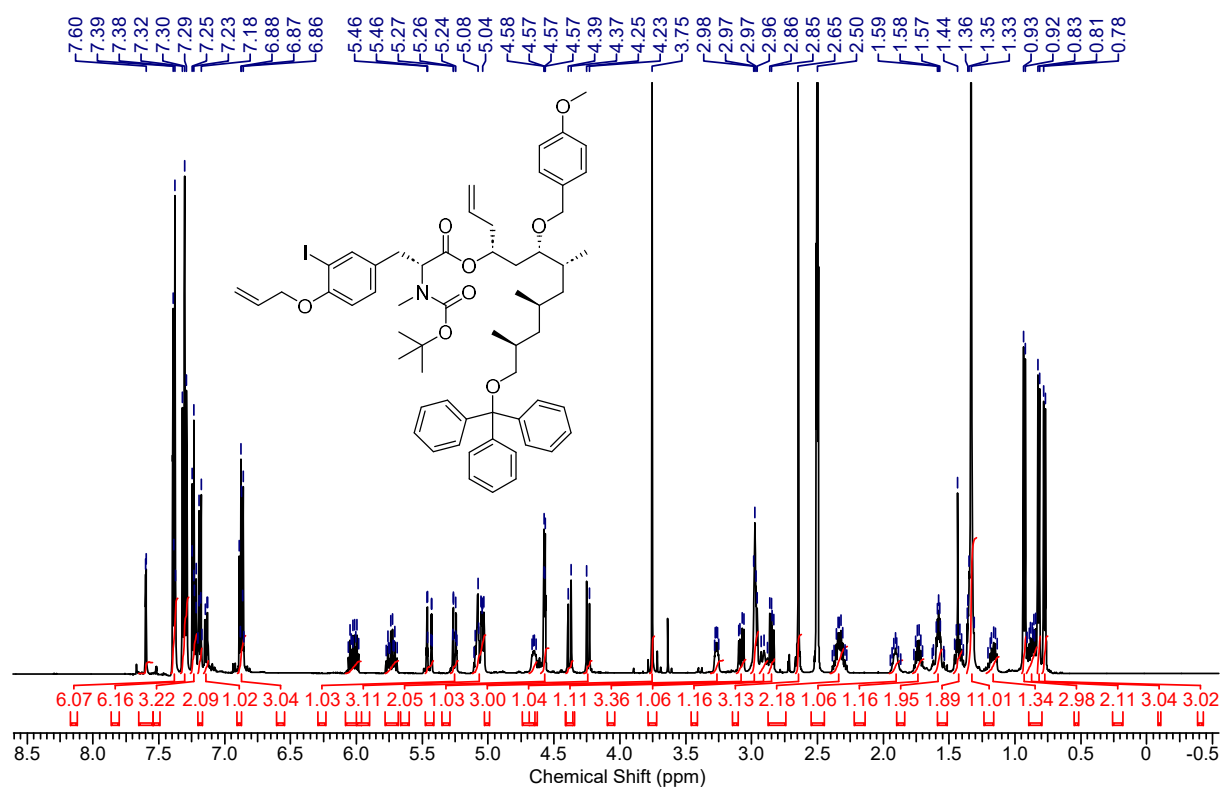


¹³C-NMR (125 MHz, CDCl₃)

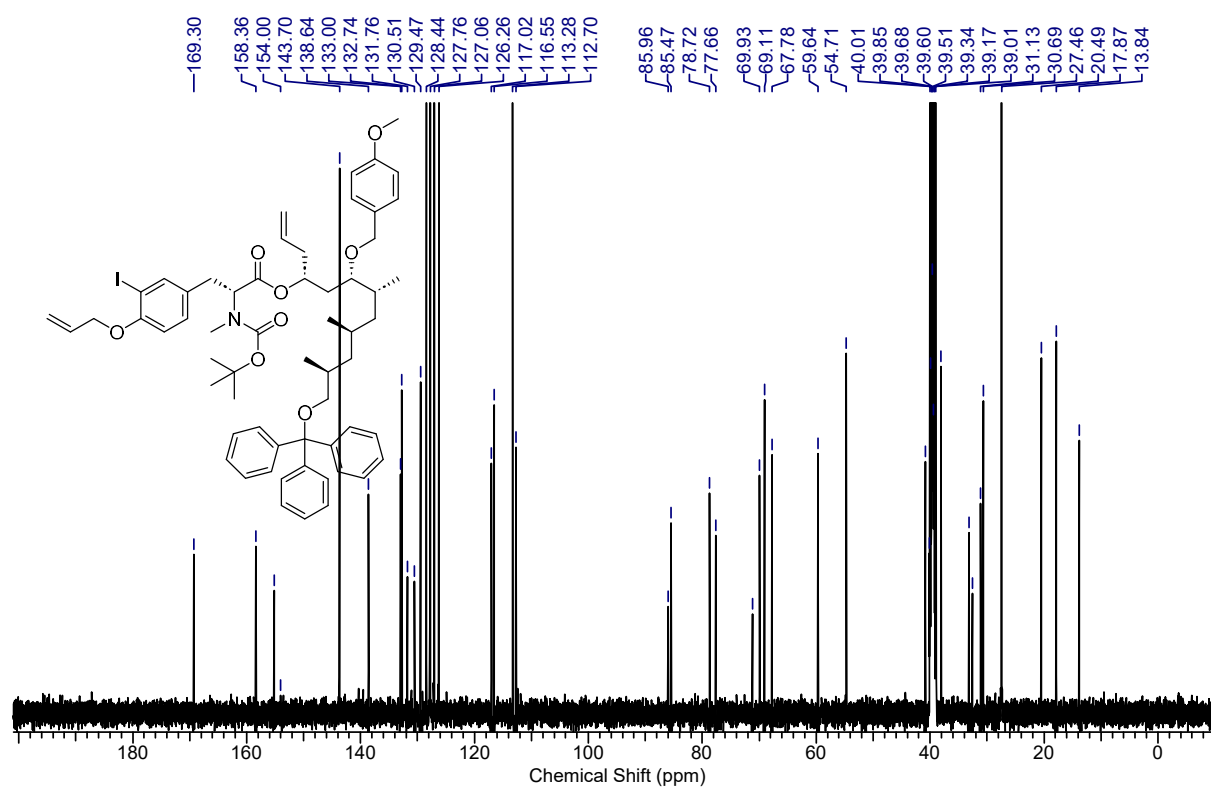


(4*R*,6*S*,7*R*,9*R*,11*S*)-6-[[4-Methoxybenzyl]oxy]-7,9,11-trimethyl-12-(trityloxy)dodec-1-en-4-yl (R)-3-[4-(allyloxy)-3-iodophenyl]-2-[(*tert*-butoxycarbonyl)(methyl)amino]propanoate (5b)

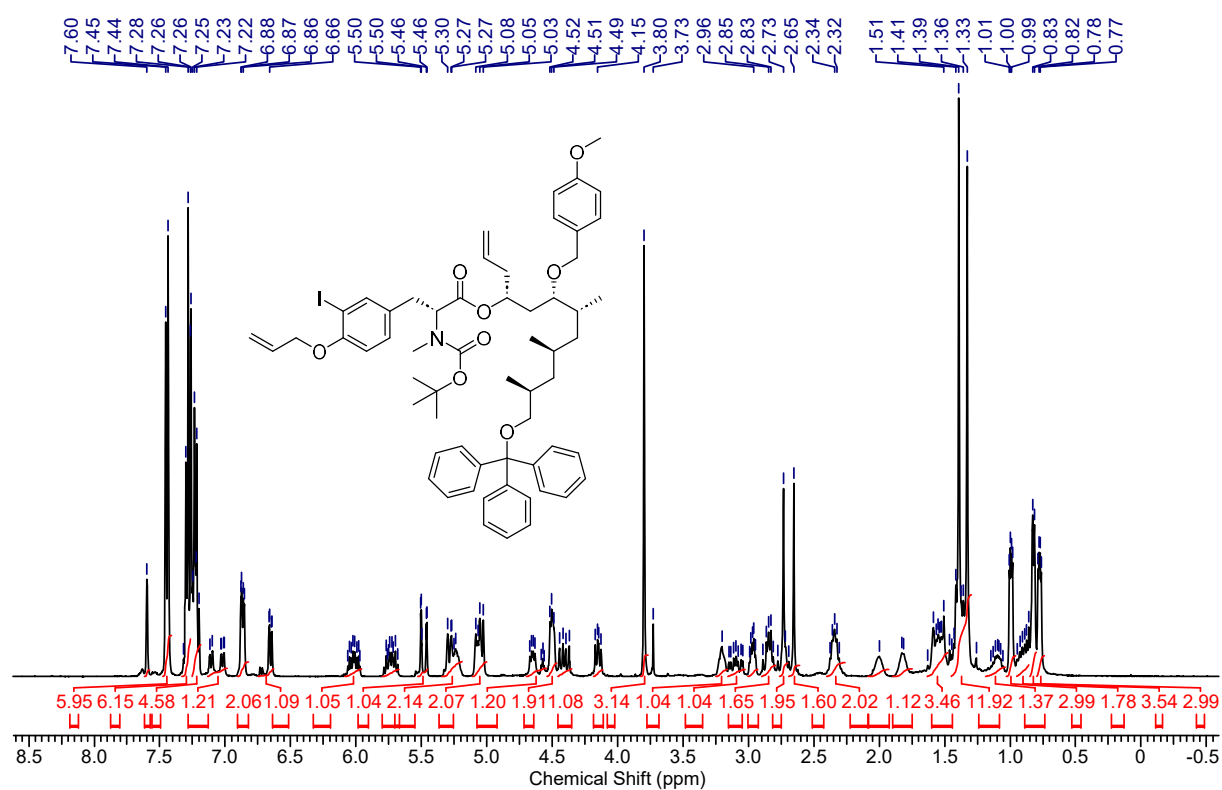
¹H-NMR (500 MHz, 373 K, DMSO-D₆)



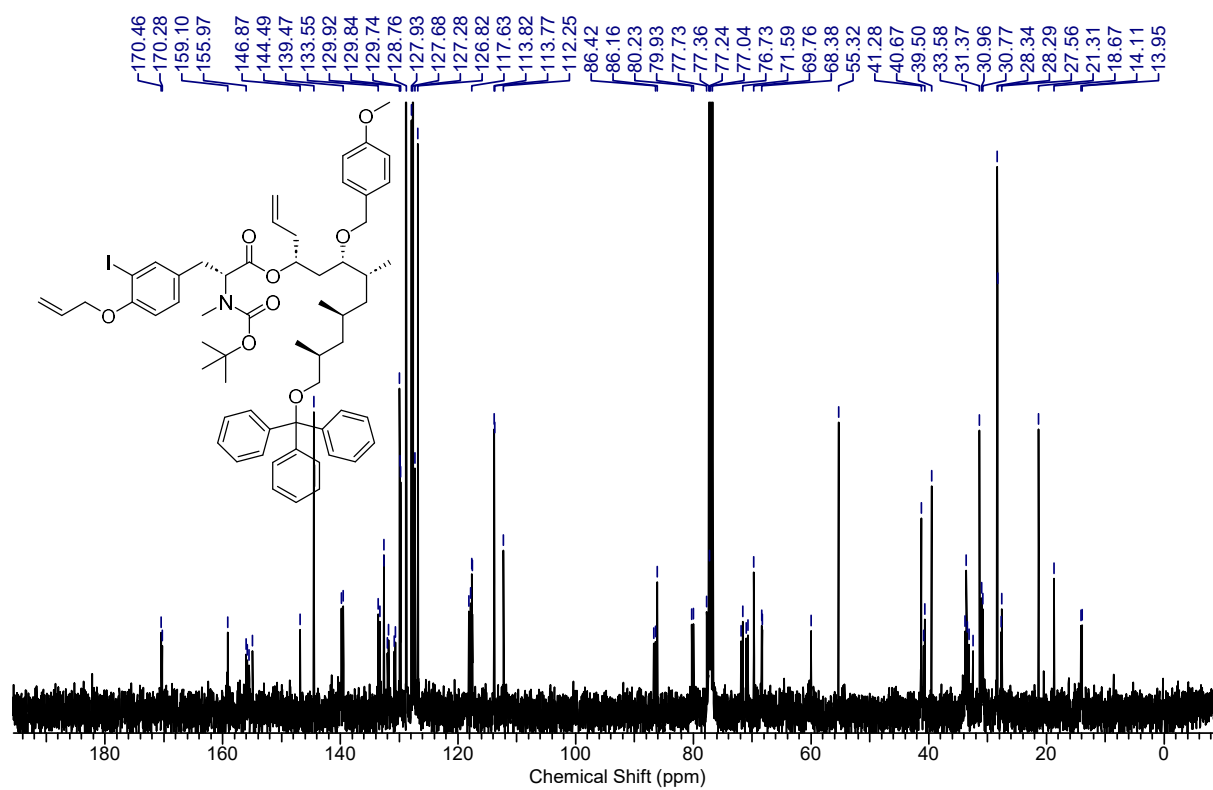
¹³C-NMR (125 MHz, 373 K, DMSO-D₆)



¹H-NMR (400 MHz, CDCl₃)

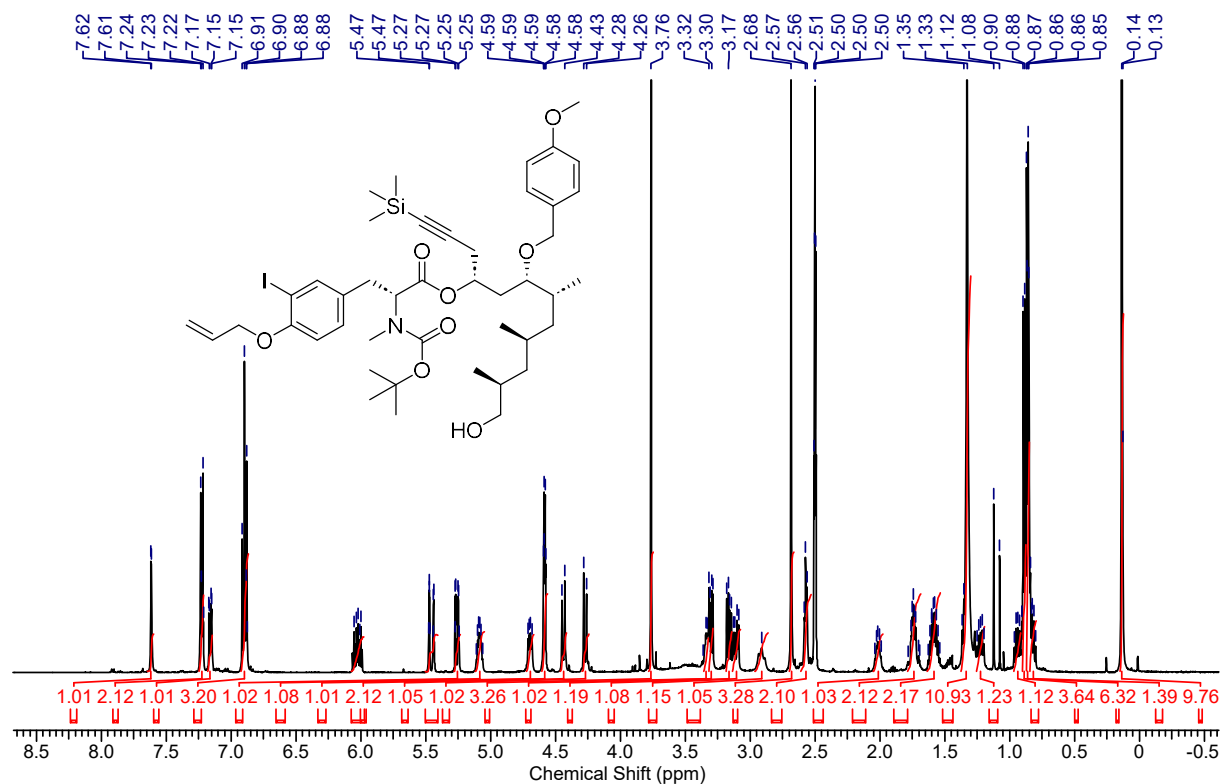


¹³C-NMR (100 MHz, CDCl₃)

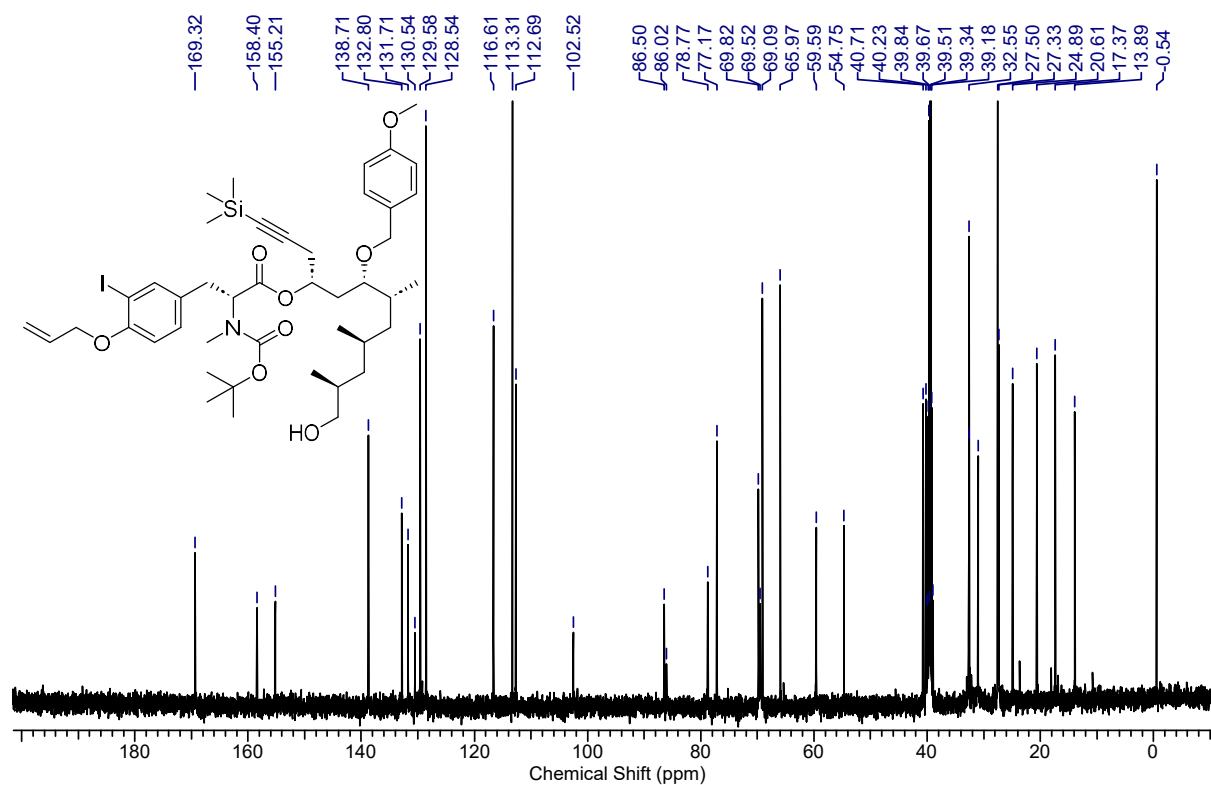


(4*R*,6*S*,7*R*,9*R*,11*S*)-12-Hydroxy-6-[(4-methoxybenzyl)oxy]-7,9,11-trimethyl-1-(trimethylsilyl)dodec-1-yn-4-yl (*R*)-3-[4-(allyloxy)-3-iodophenyl]-2-[(*tert*-butoxycarbonyl)(methyl)amino]propanoate (5a-1)

¹H-NMR (500 MHz, 373 K, DMSO-D₆)

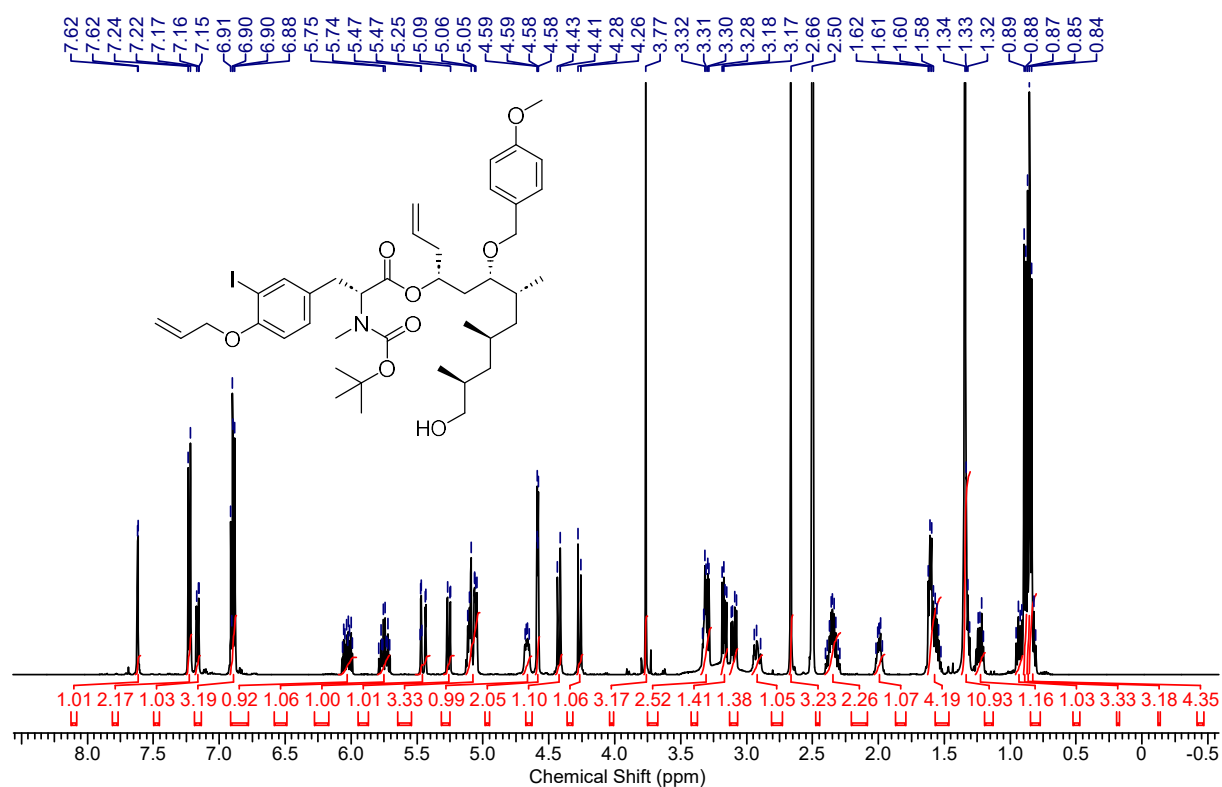


¹³C-NMR (125 MHz, 373 K, DMSO-D₆)

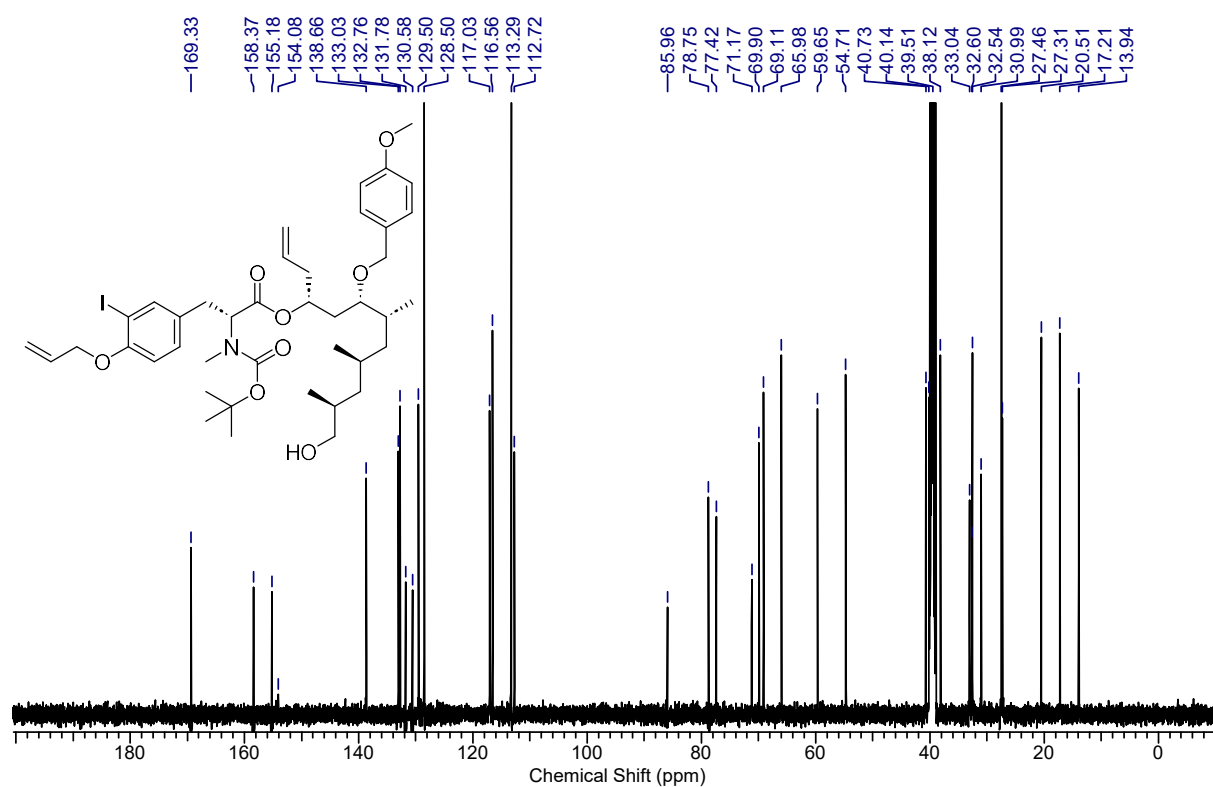


(4*R*,6*S*,7*R*,9*R*,11*S*)-12-Hydroxy-6-[(4-methoxybenzyl)oxy]-7,9,11-trimethyldodec-1-en-4-yl (R)-3-[4-(allyloxy)-3-iodophenyl]-2-[(*tert*-butoxycarbonyl)(methyl)amino]propanoate (5b-1)

¹H-NMR (500 MHz, 373 K, DMSO-D₆)

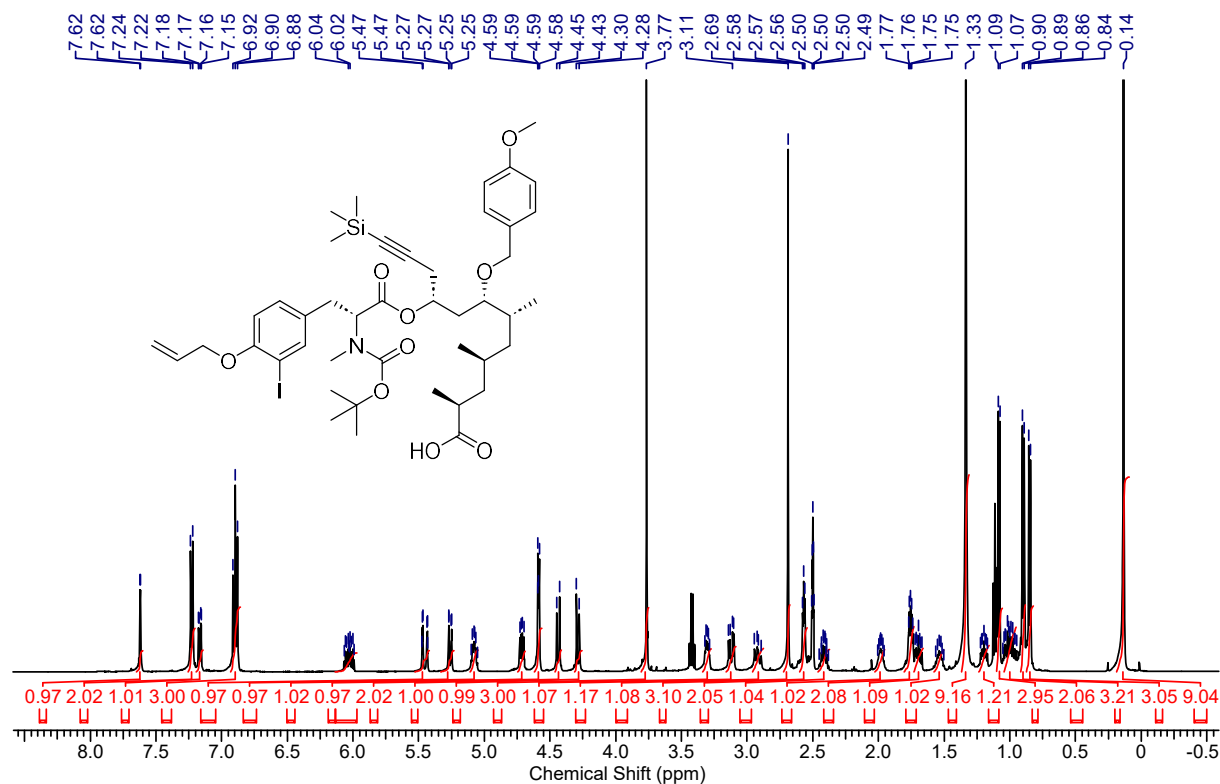


¹³C-NMR (125 MHz, 373 K, DMSO-D₆)

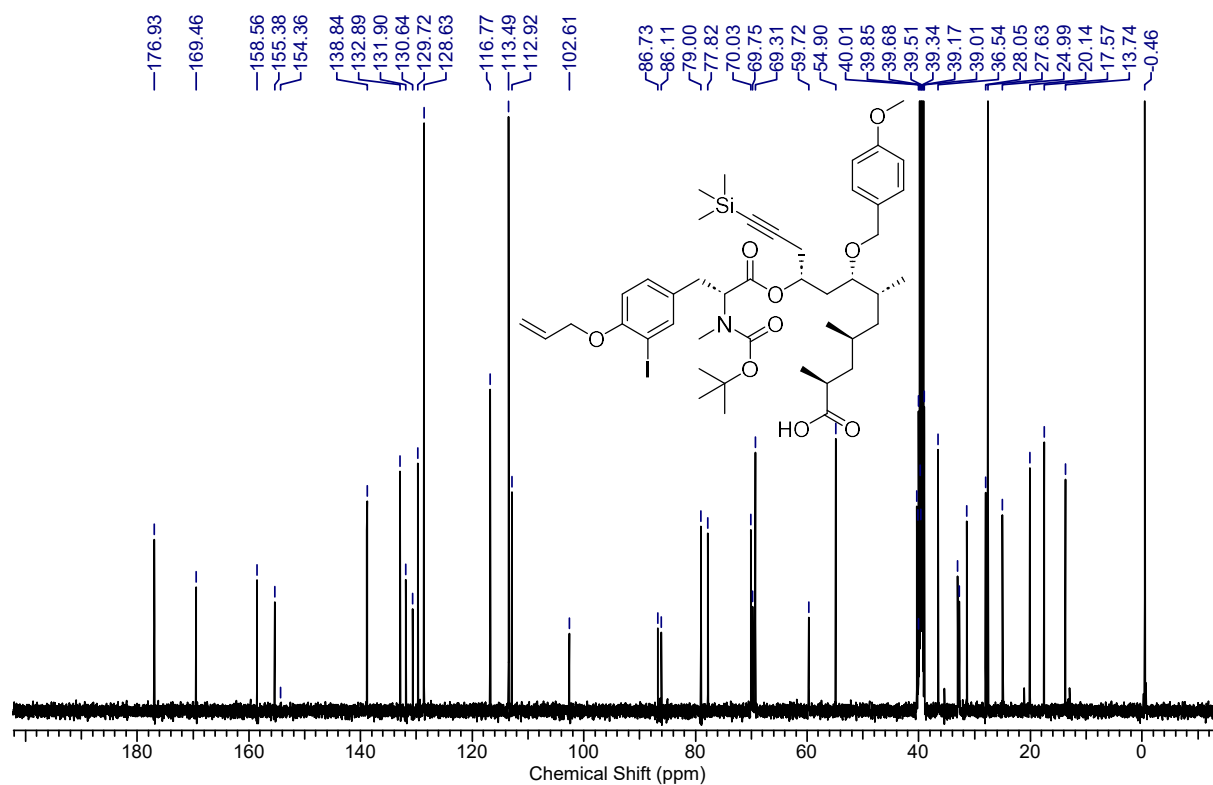


(2*S*,4*S*,6*R*,7*S*,9*R*)-9-((*R*)-3-[4-(Allyloxy)-3-iodophenyl]-2-[(*tert*-butoxycarbonyl)(methyl)amino]propanoyl)oxy)-7-[(4-methoxybenzyl)oxy]-2,4,6-trimethyl-12-(trimethylsilyl)dodec-11-ynoic acid (6a)

¹H-NMR (500 MHz, 373 K, DMSO-D₆)

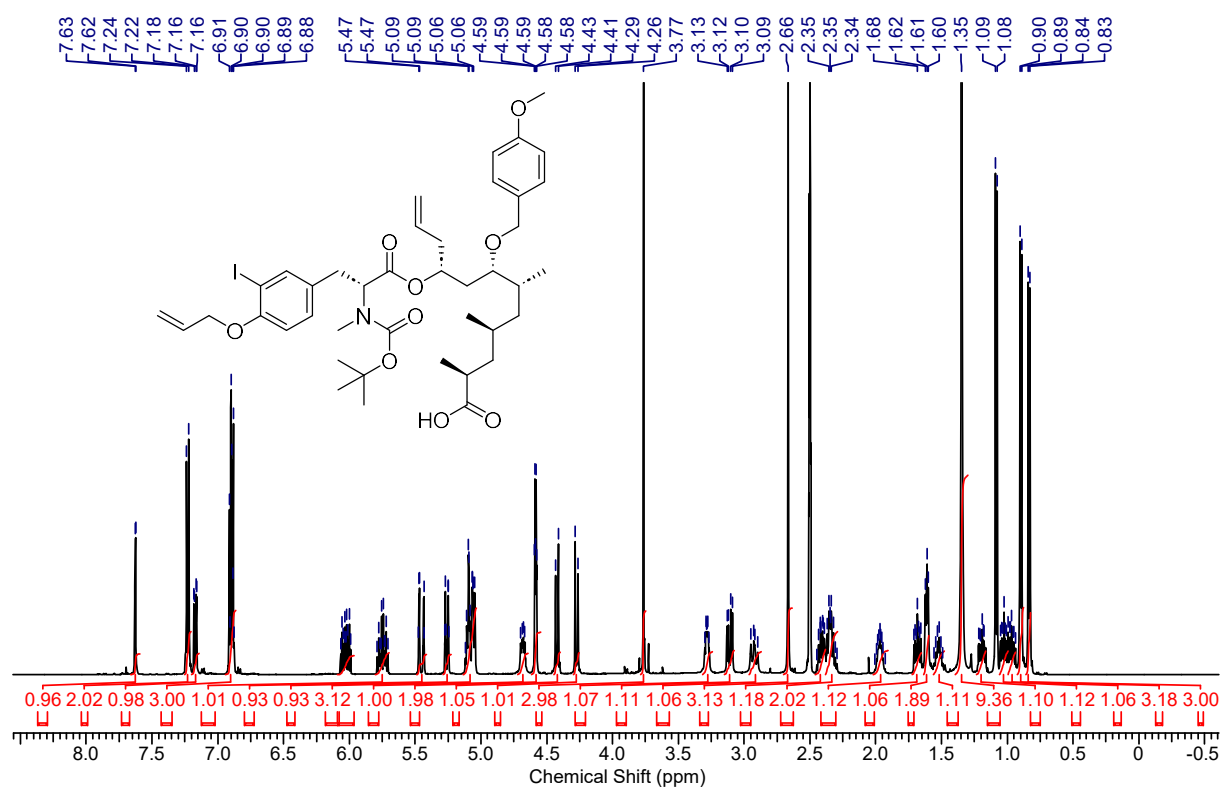


¹³C-NMR (125 MHz, 373 K, DMSO-D₆)

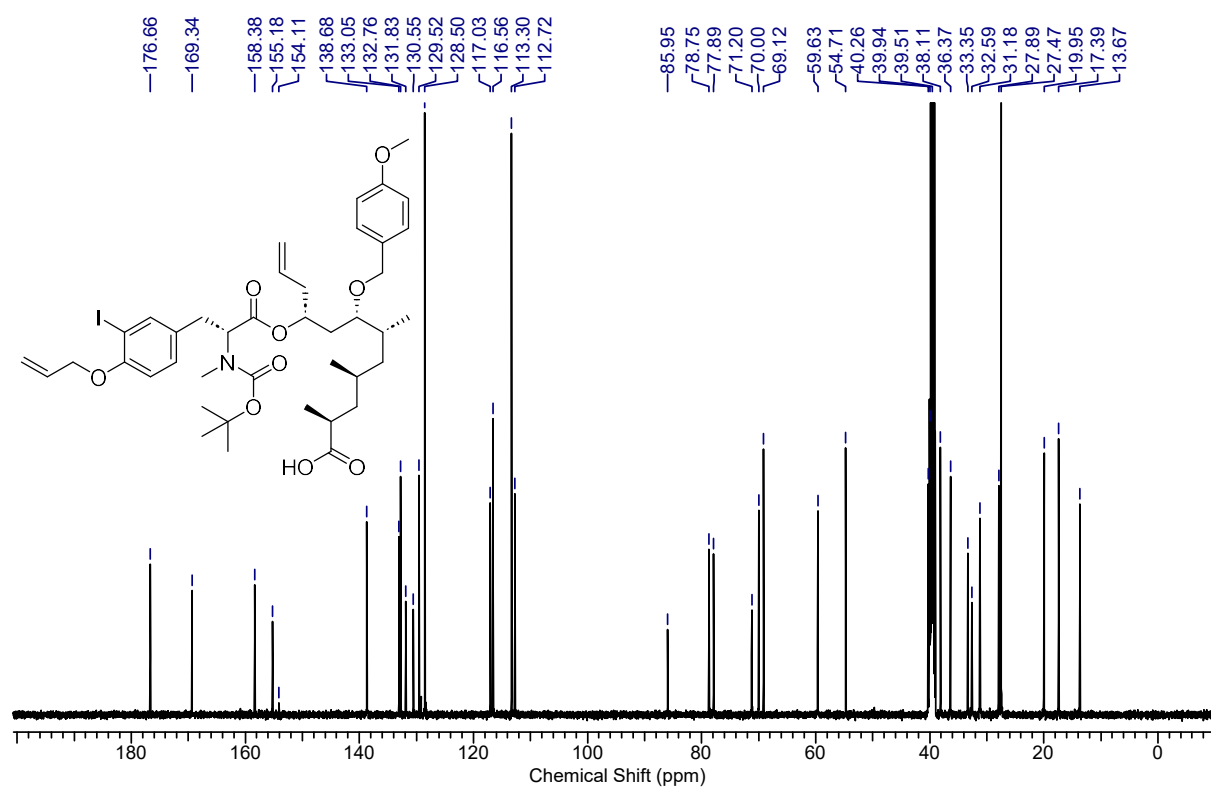


(2*S*,4*S*,6*R*,7*S*,9*R*)-9-({(*R*)-3-[4-(Allyloxy)-3-iodophenyl]-2-[(*tert*-butoxycarbonyl)(methyl)amino]-propanoyl}oxy)-7-[(4-methoxybenzyl)oxy]-2,4,6-trimethyldodec-11-enoic acid (6b)

¹H-NMR (500 MHz, 373 K, DMSO-D₆)

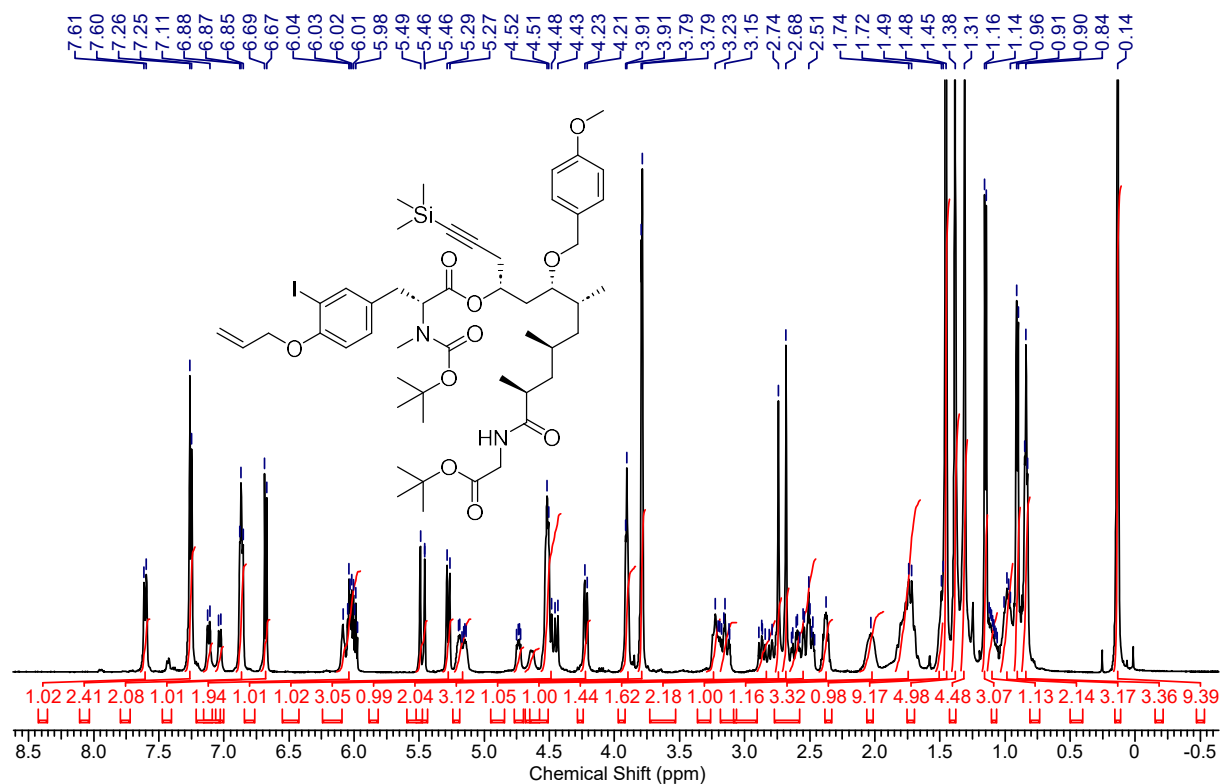


¹³C-NMR (125 MHz, 373 K, DMSO-D₆)

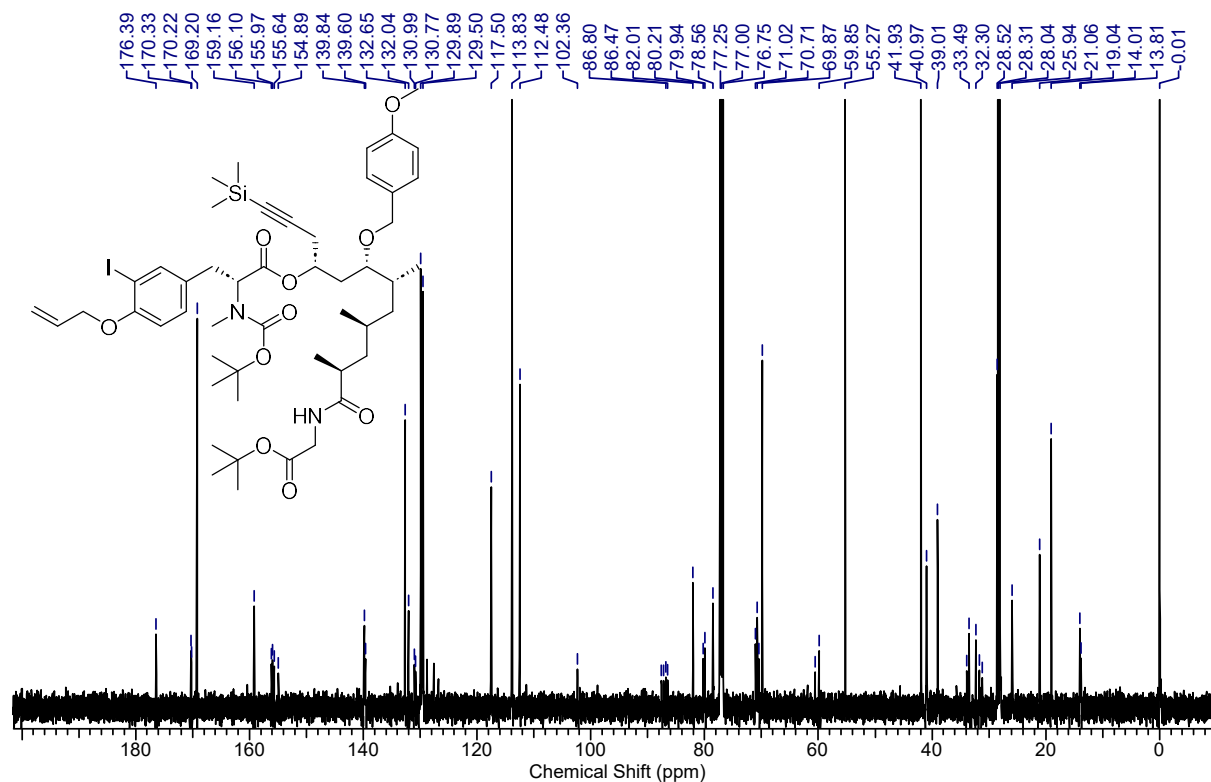


(4*R*,6*S*,7*R*,9*S*,11*S*)-12-[[2-(*tert*-Butoxy)-2-oxoethyl]amino]-6-[(4-methoxybenzyl)oxy]-7,9,11-trimethyl-12-oxo-1-(trimethylsilyl)dodec-1-yn-4-yl (*R*)-3-[4-(allyloxy)-3-iodophenyl]-2-[(*tert*-butoxy-carbonyl)(methyl)amino]propanoate (7a)

¹H-NMR (500 MHz, CDCl₃)

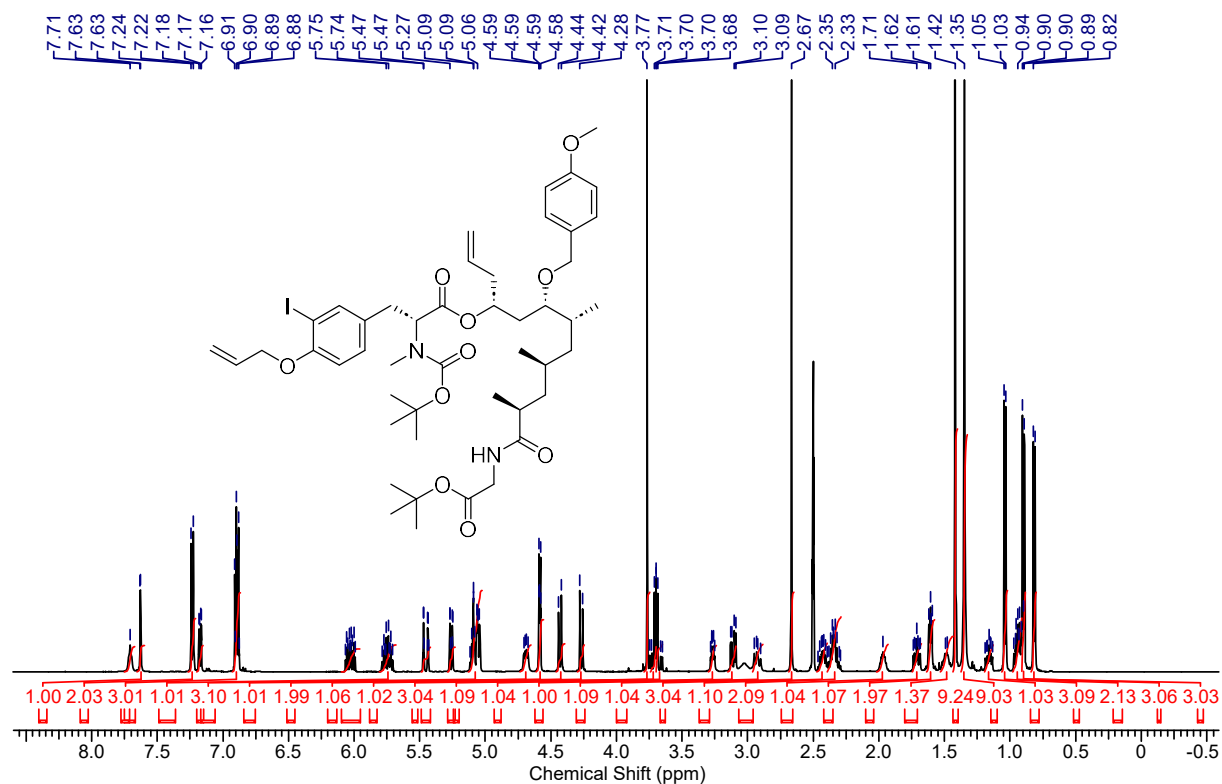


¹³C-NMR (125 MHz, CDCl₃)

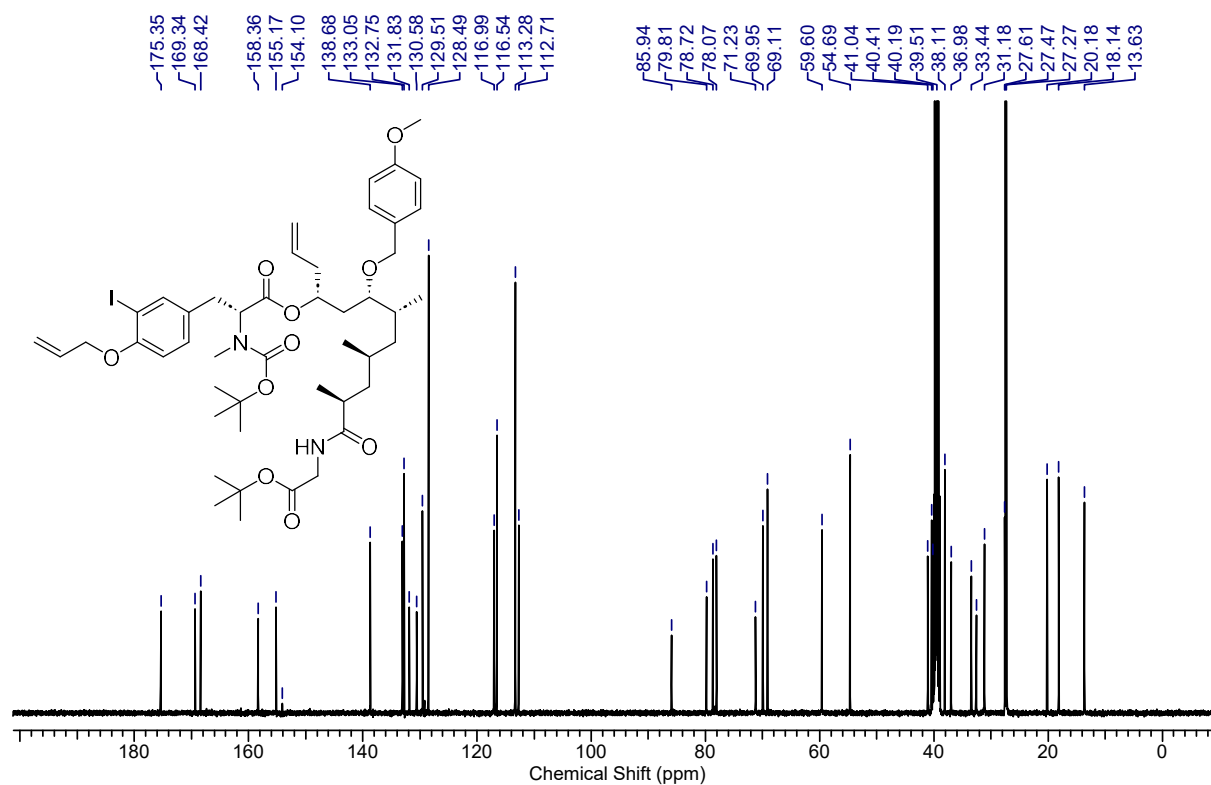


(4*R*,6*S*,7*R*,9*S*,11*S*)-12-[[2-(*tert*-Butoxy)-2-oxoethyl]amino]-6-[(4-methoxybenzyl)oxy]-7,9,11-trimethyl-12-oxododec-1-en-4-yl (R)-3-[4-(allyloxy)-3-iodophenyl]-2-[(*tert*-butoxycarbonyl)(methyl)amino]propanoate (7b)

¹H-NMR (500 MHz, 373 K, DMSO-D₆)

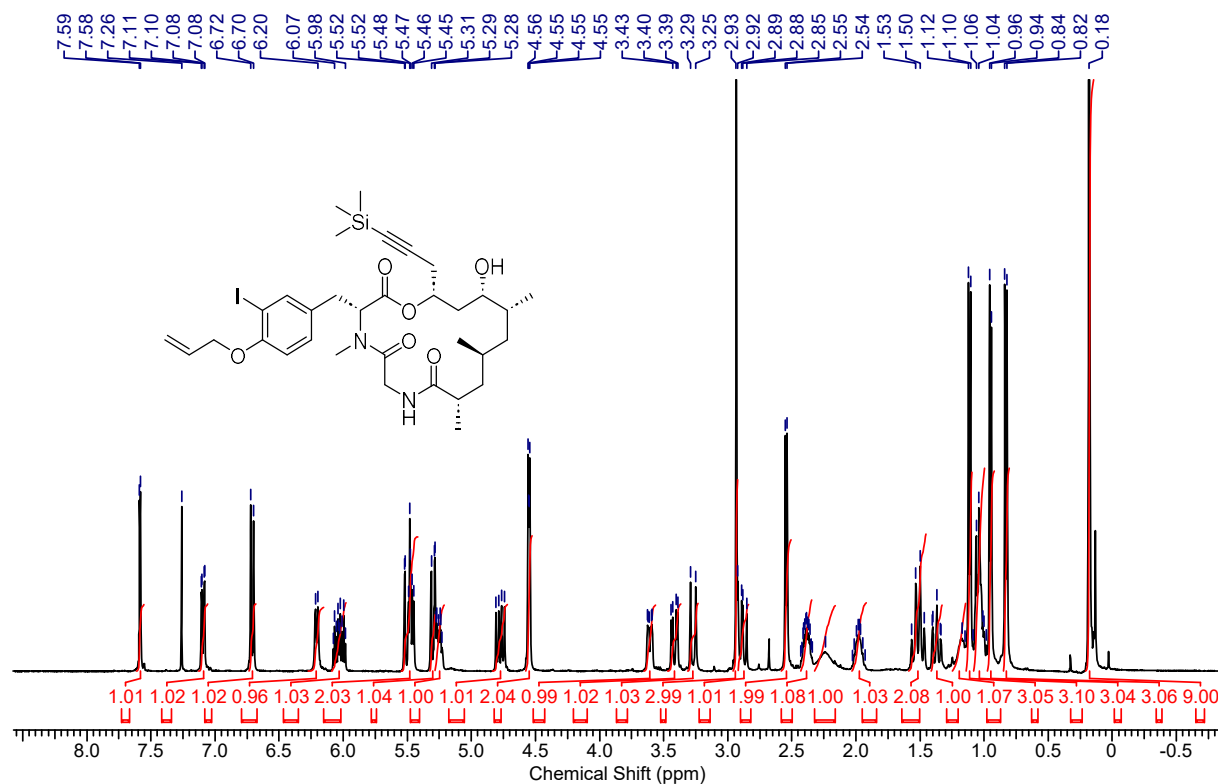


¹³C-NMR (125 MHz, 373 K, DMSO-D₆)

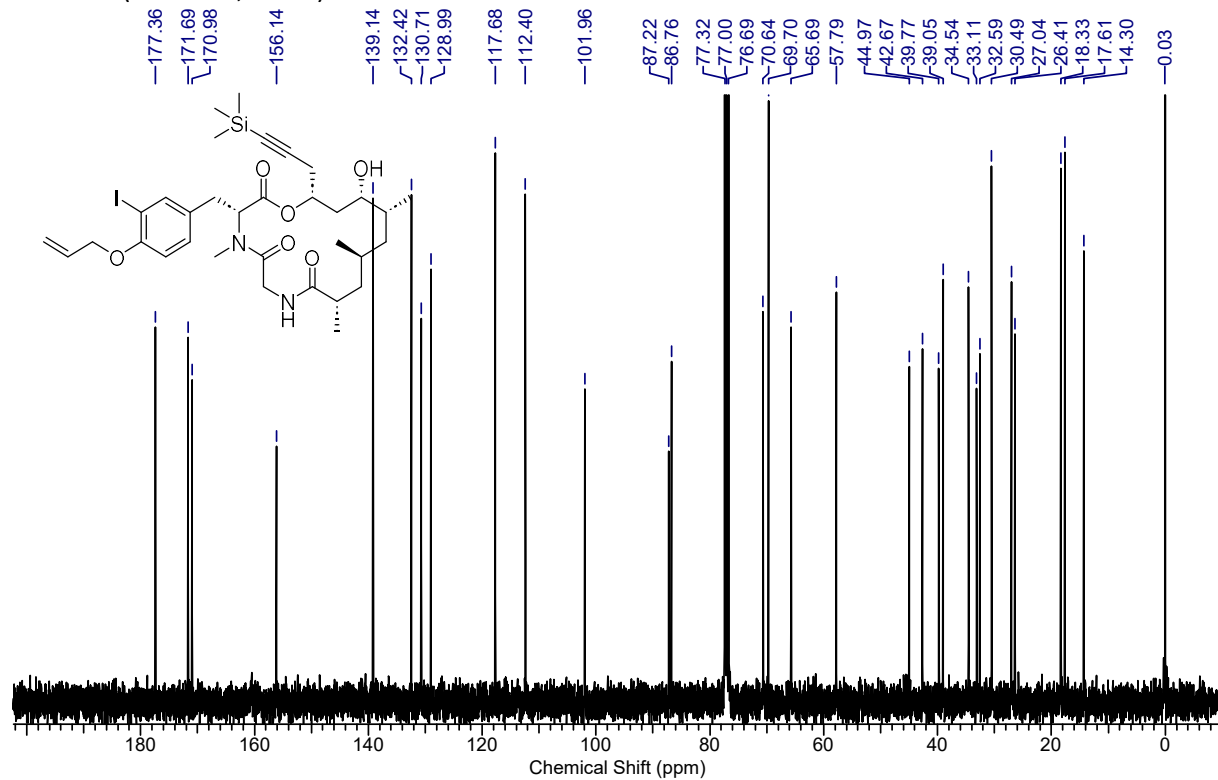


(3*R*,9*S*,11*S*,13*R*,14*S*,16*R*)-3-[4-(Allyloxy)-3-iodobenzyl]-14-hydroxy-4,9,11,13-tetramethyl-16-[3-(trimethylsilyl)prop-2-yn-1-yl]-1-oxa-4,7-diazacyclohexadecane-2,5,8-trione (7a-1)

¹H-NMR (400 MHz, CDCl₃)

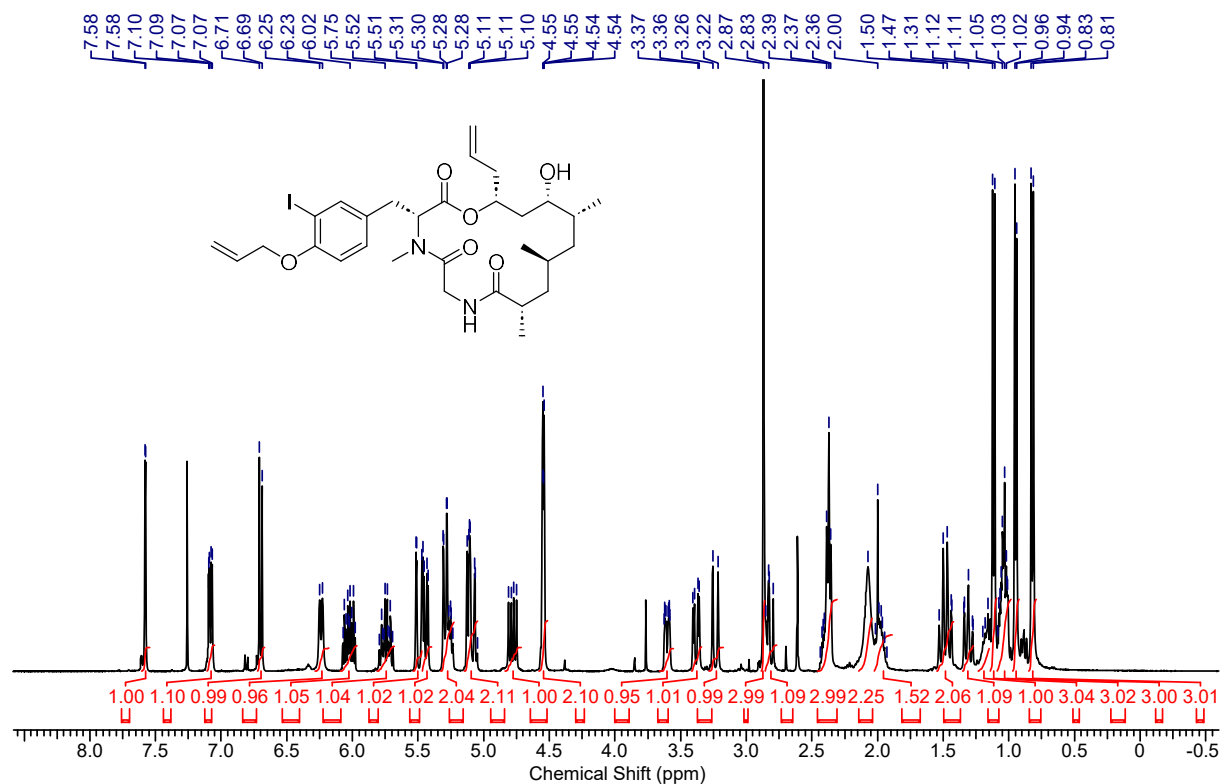


¹³C-NMR (100 MHz, CDCl₃)

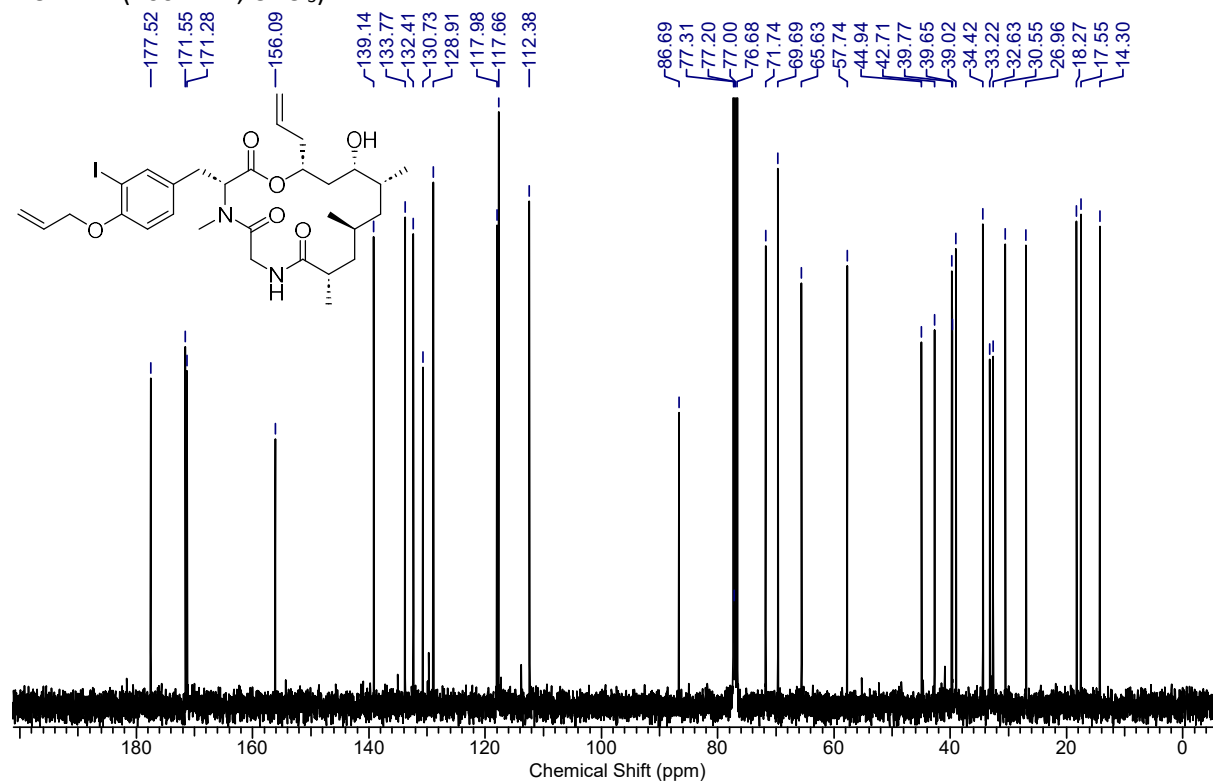


(3*R*,9*S*,11*S*,13*R*,14*S*,16*R*)-16-allyl-3-[4-(allyloxy)-3-iodobenzyl]-14-hydroxy-4,9,11,13-tetramethyl-1-oxa-4,7-diazacyclohexadecane-2,5,8-trione (7b-1)

¹H-NMR (400 MHz, CDCl₃)

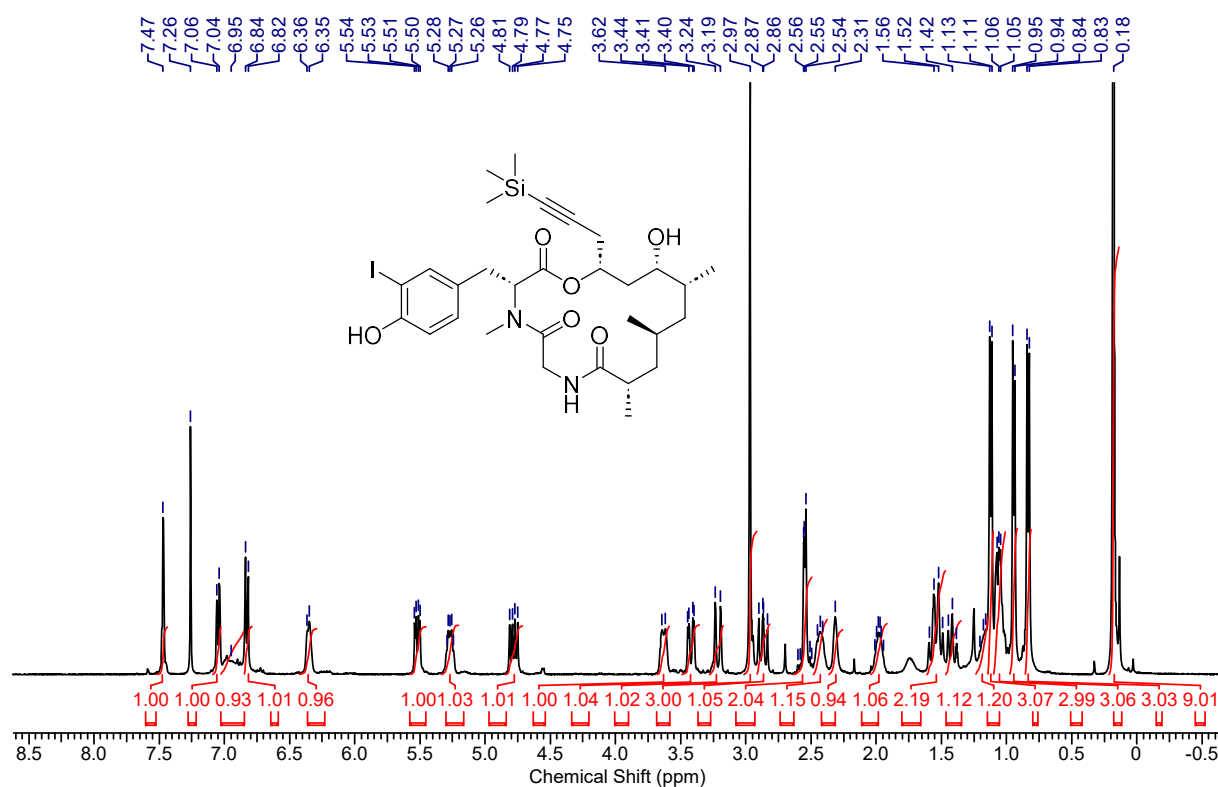


¹³C-NMR (100 MHz, CDCl₃)

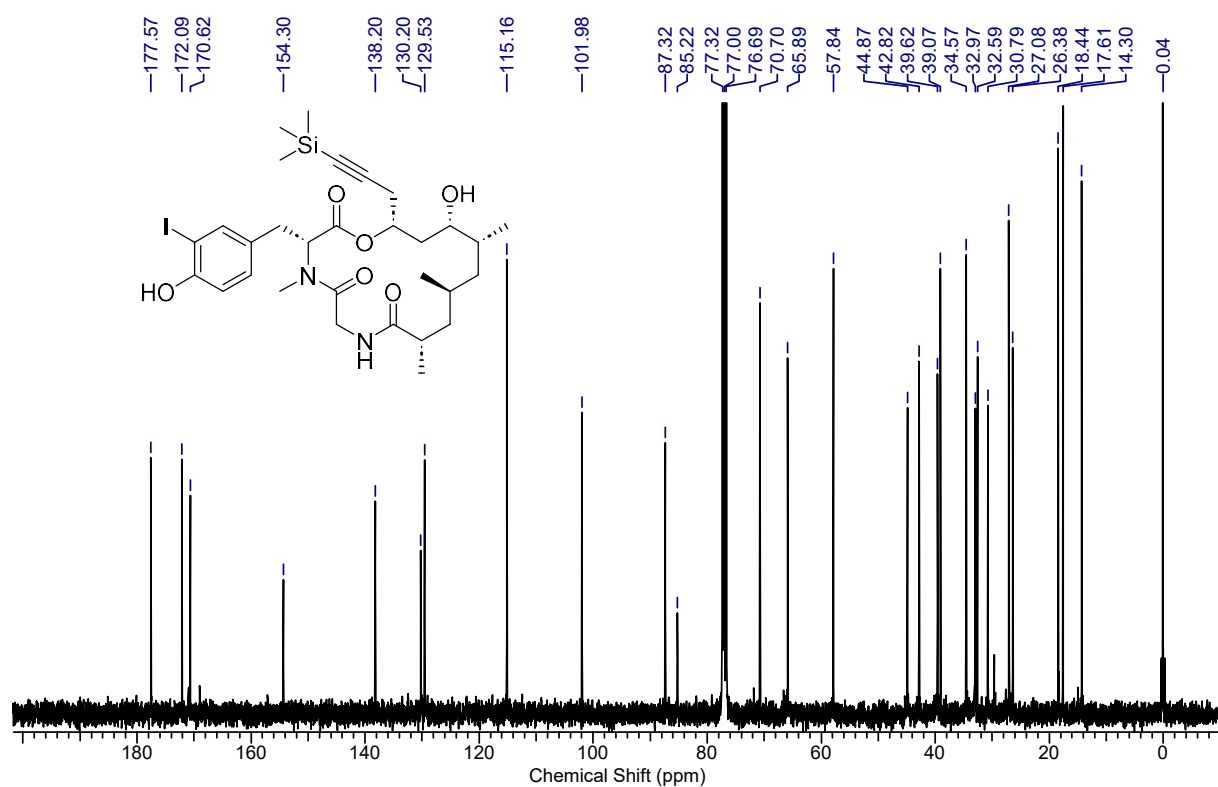


(3*R*,9*S*,11*S*,13*R*,14*S*,16*R*)-14-Hydroxy-3-(4-hydroxy-3-iodobenzyl)-4,9,11,13-tetramethyl-16-[3-(trimethylsilyl)prop-2-yn-1-yl]-1-oxa-4,7-diazacyclohexadecane-2,5,8-trione (8a)

¹H-NMR (400 MHz, CDCl₃)

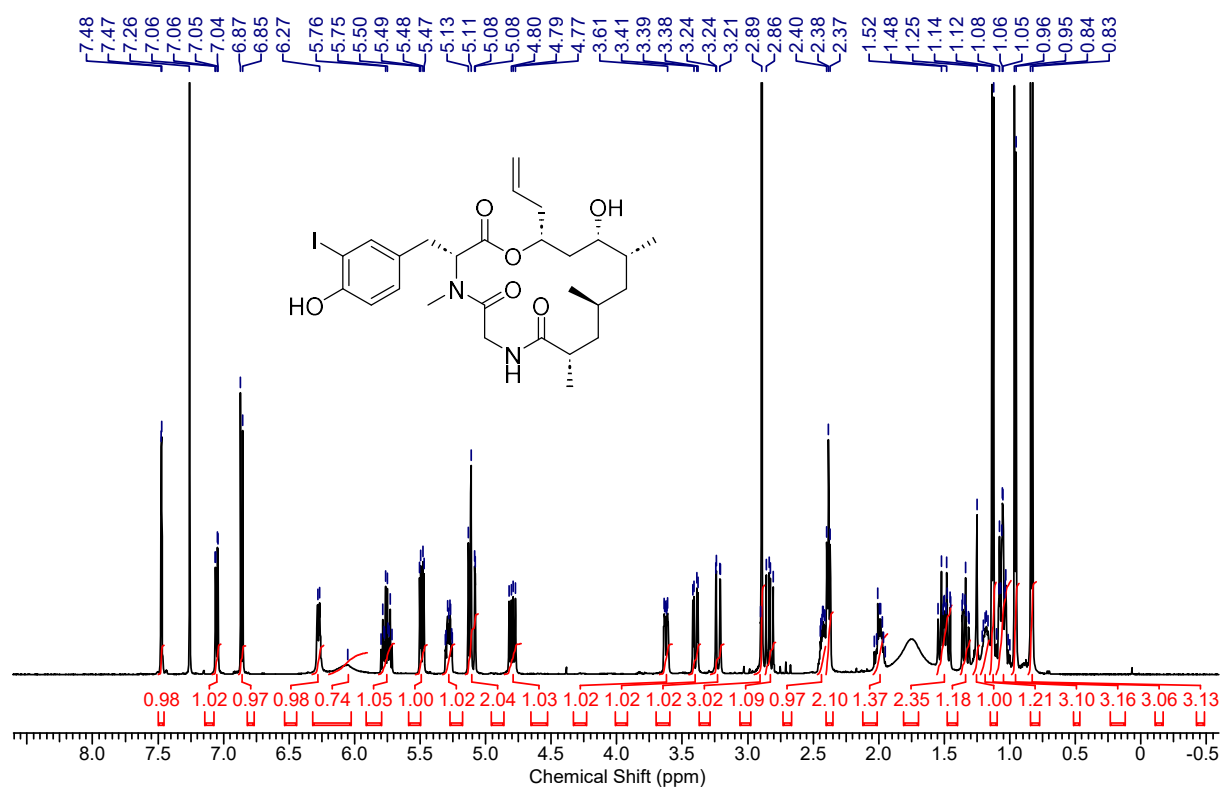


¹³C-NMR (100 MHz, CDCl₃)

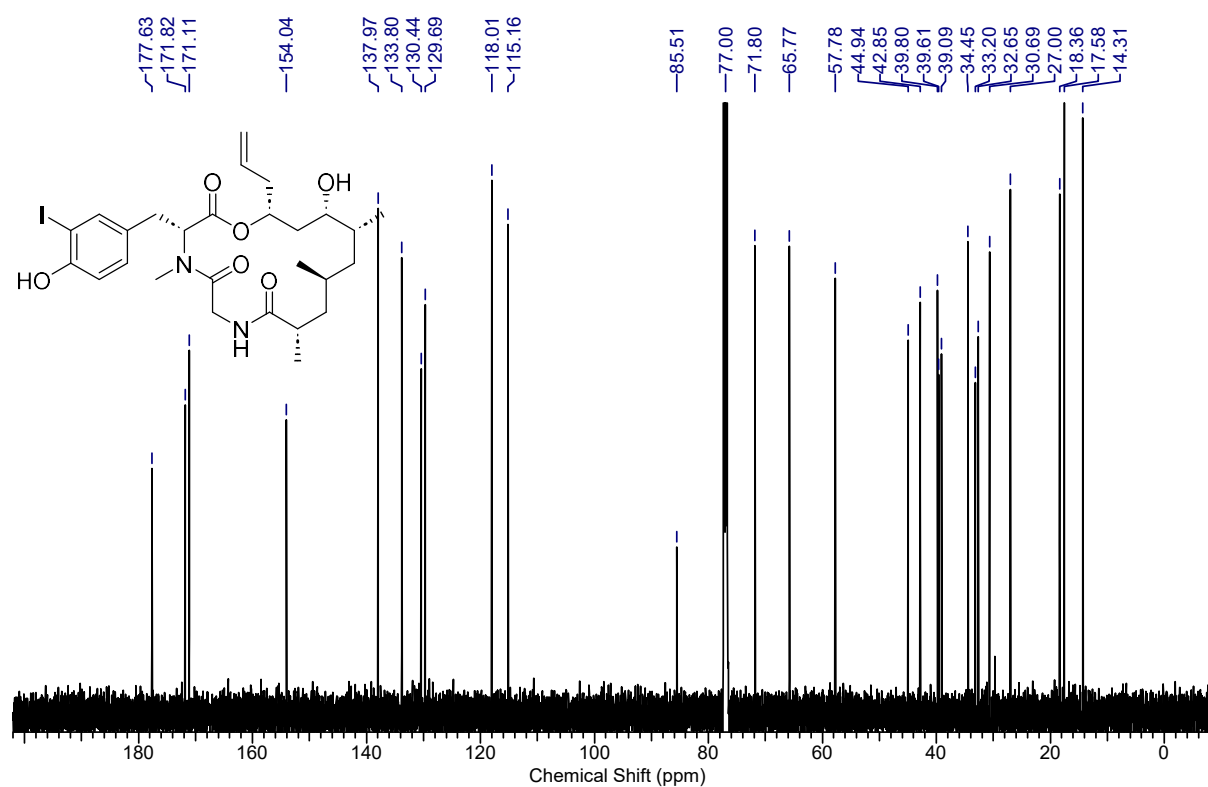


(3*R*,9*S*,11*S*,13*R*,14*S*,16*R*)-16-Allyl-14-hydroxy-3-(4-hydroxy-3-iodobenzyl)-4,9,11,13-tetramethyl-1-oxa-4,7-diazacyclohexadecane-2,5,8-trione (8b)

¹H-NMR (500 MHz, CDCl₃)

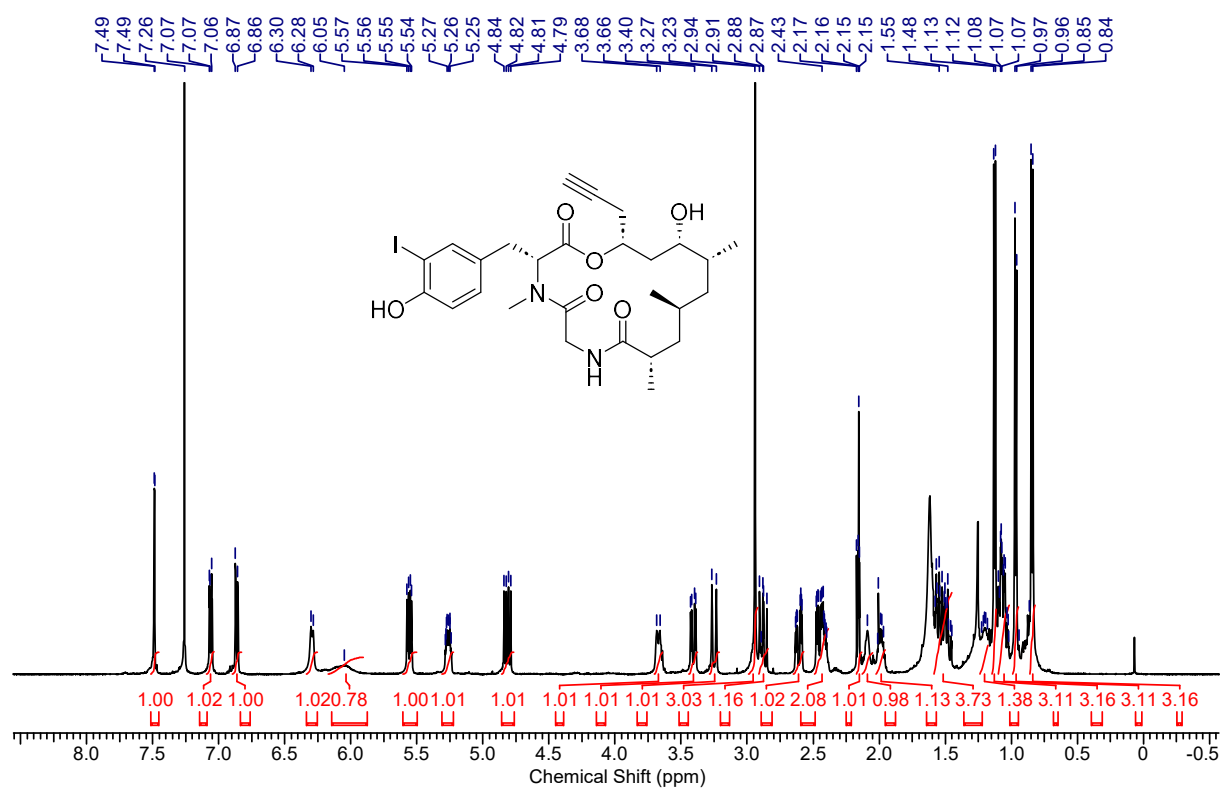


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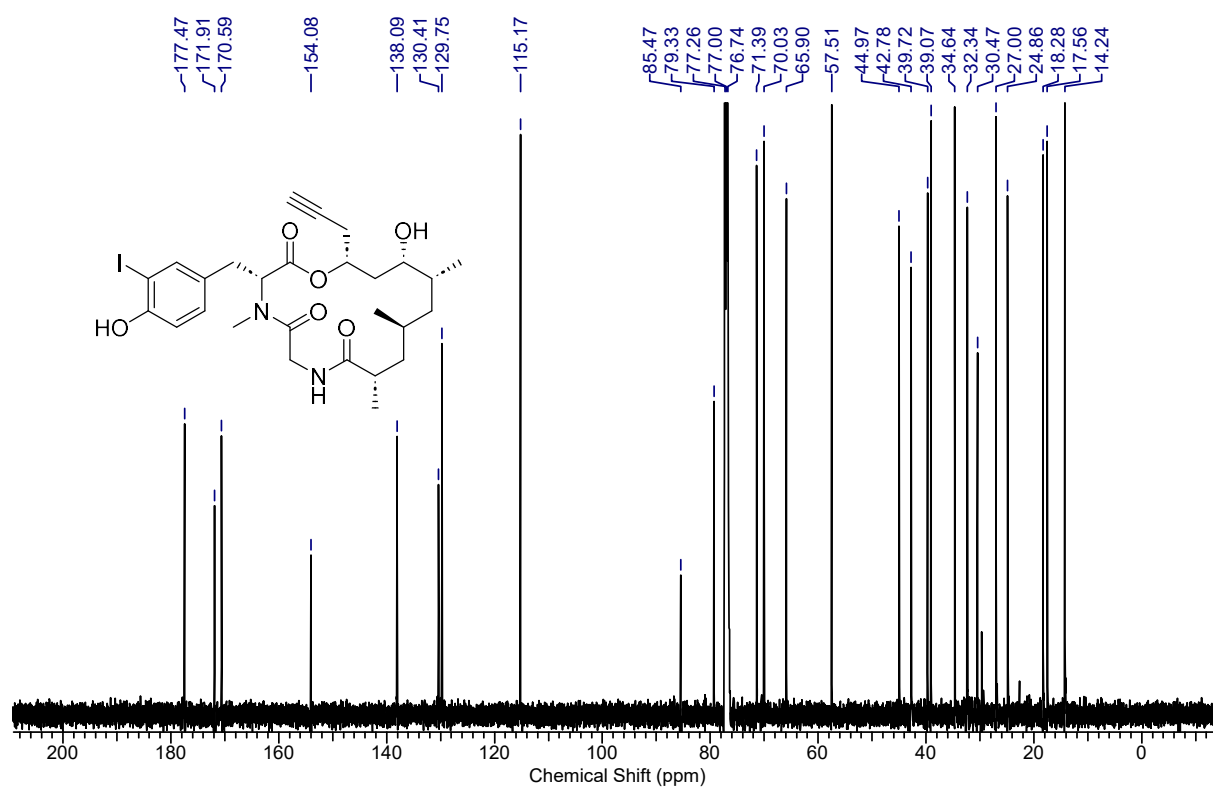


(3*R*,9*S*,11*S*,13*R*,14*S*,16*R*)-14-Hydroxy-3-(4-hydroxy-3-iodobenzyl)-4,9,11,13-tetramethyl-16-(prop-2-yn-1-yl)-1-oxa-4,7-diazacyclohexadecane-2,5,8-trione (8c)

¹H-NMR (500 MHz, CDCl₃)

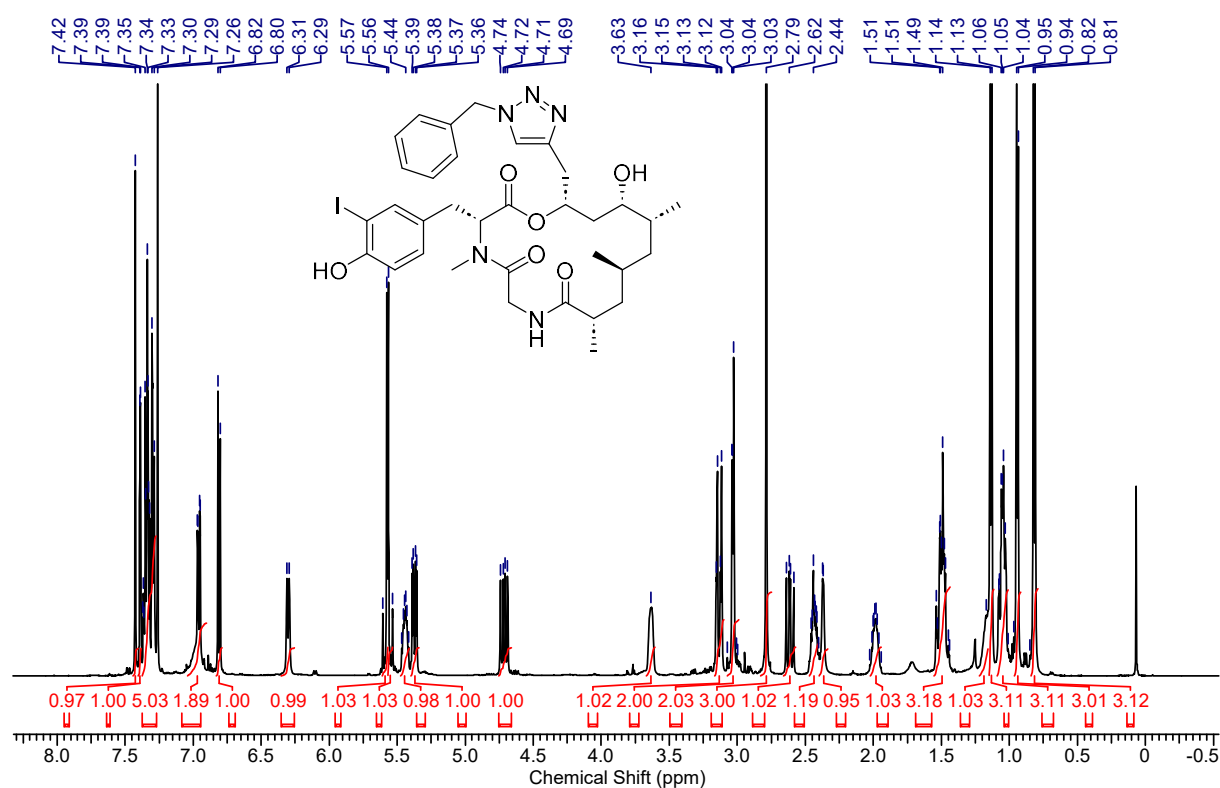


¹³C-NMR (125 MHz, CDCl₃)

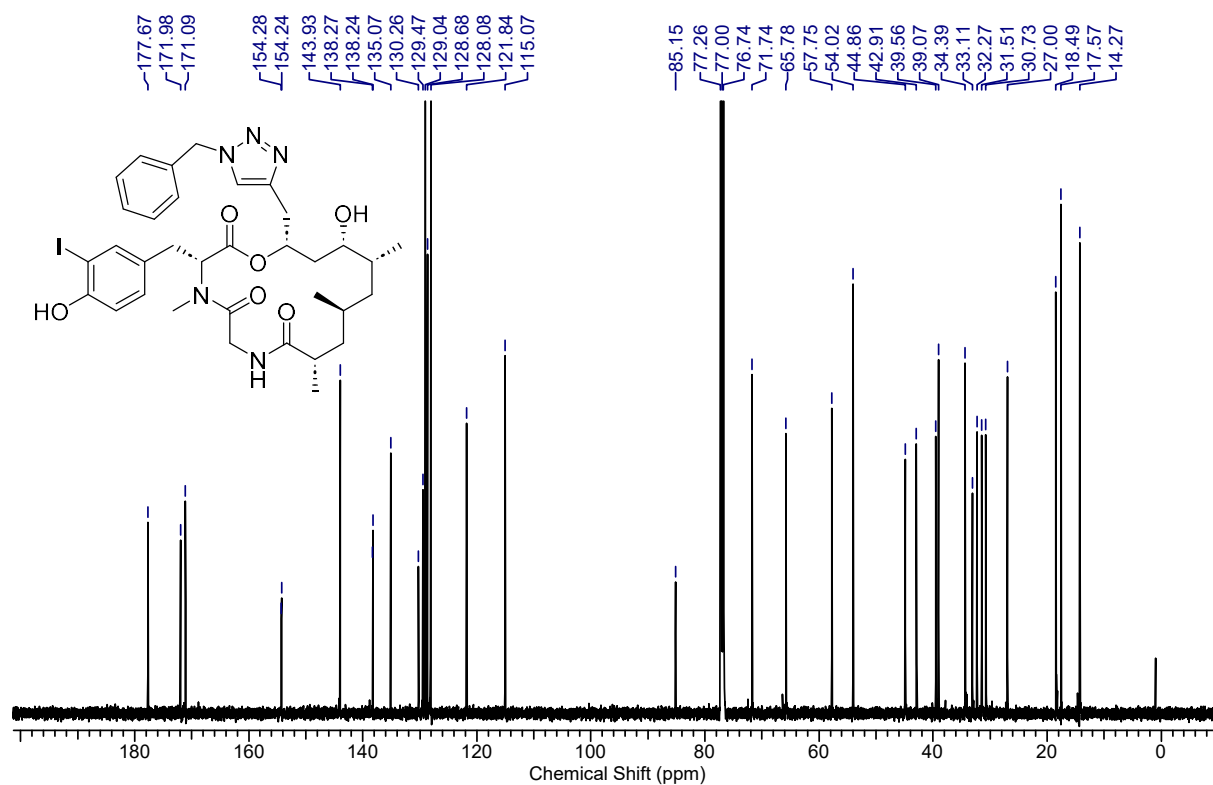


(3*R*,9*S*,11*S*,13*R*,14*S*,16*R*)-16-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methyl]-14-hydroxy-3-(4-hydroxy-3-iodobenzyl)-4,9,11,13-tetramethyl-1-oxa-4,7-diazacyclohexadecane-2,5,8-trione (9a)

¹H-NMR (500 MHz, CDCl₃)

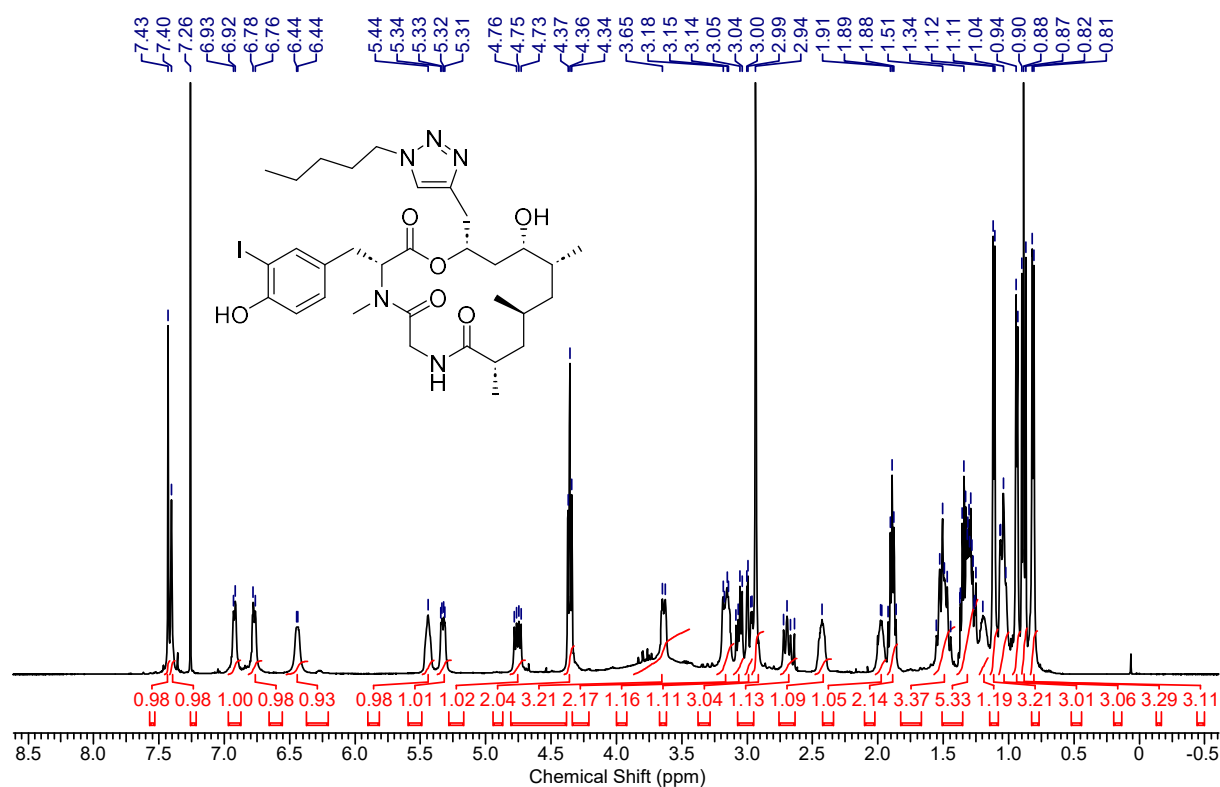


¹³C-NMR (125 MHz, CDCl₃)

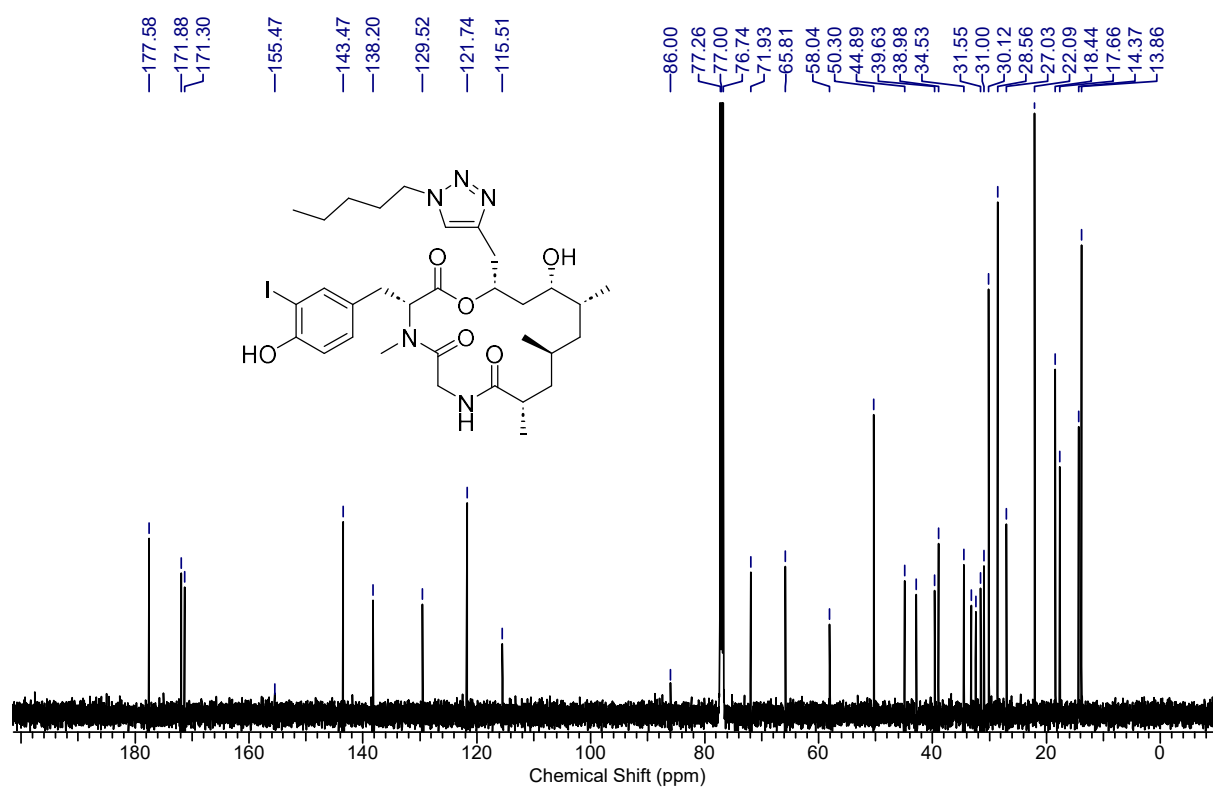


(3*R*,9*S*,11*S*,13*R*,14*S*,16*R*)-14-hydroxy-3-(4-hydroxy-3-iodobenzyl)-4,9,11,13-tetramethyl-16-((1-pentyl-1*H*-1,2,3-triazol-4-yl)methyl)-1-oxa-4,7-diazacyclohexadecane-2,5,8-trione (9b)

¹H-NMR (500 MHz, CDCl₃)

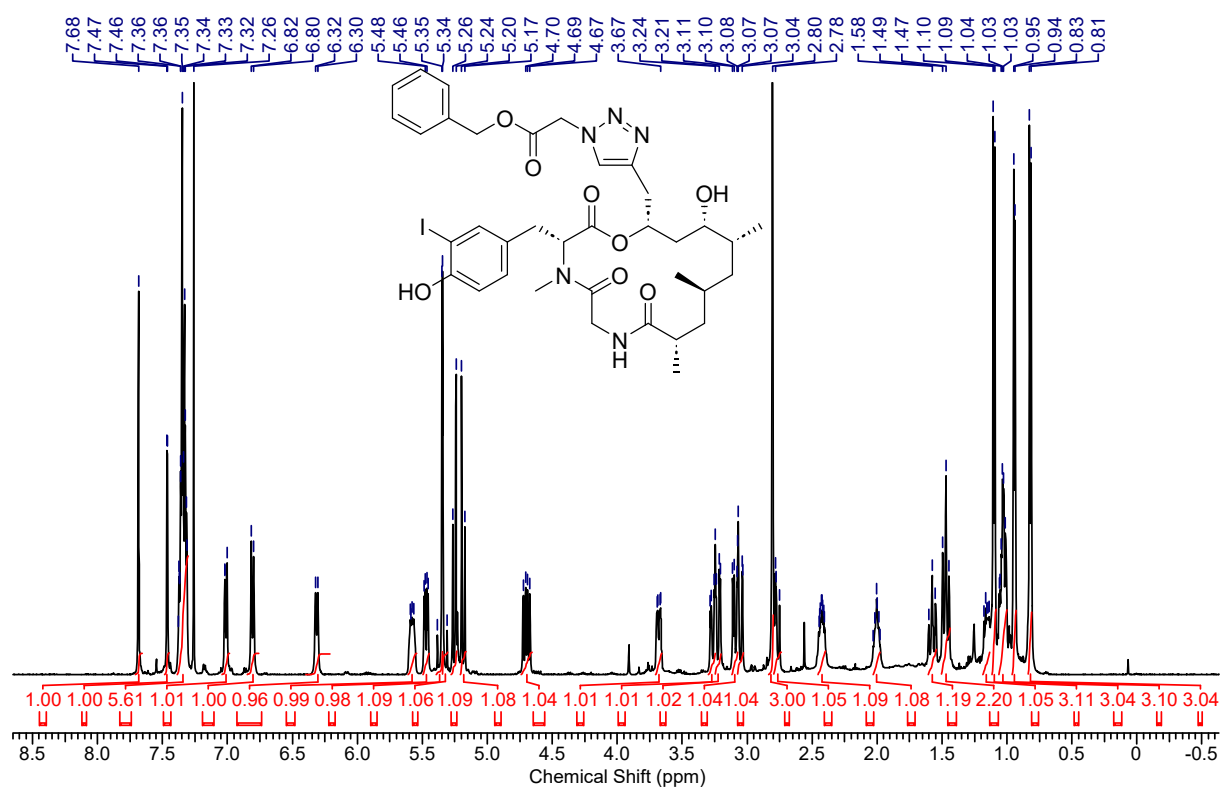


¹³C-NMR (125 MHz, CDCl₃)

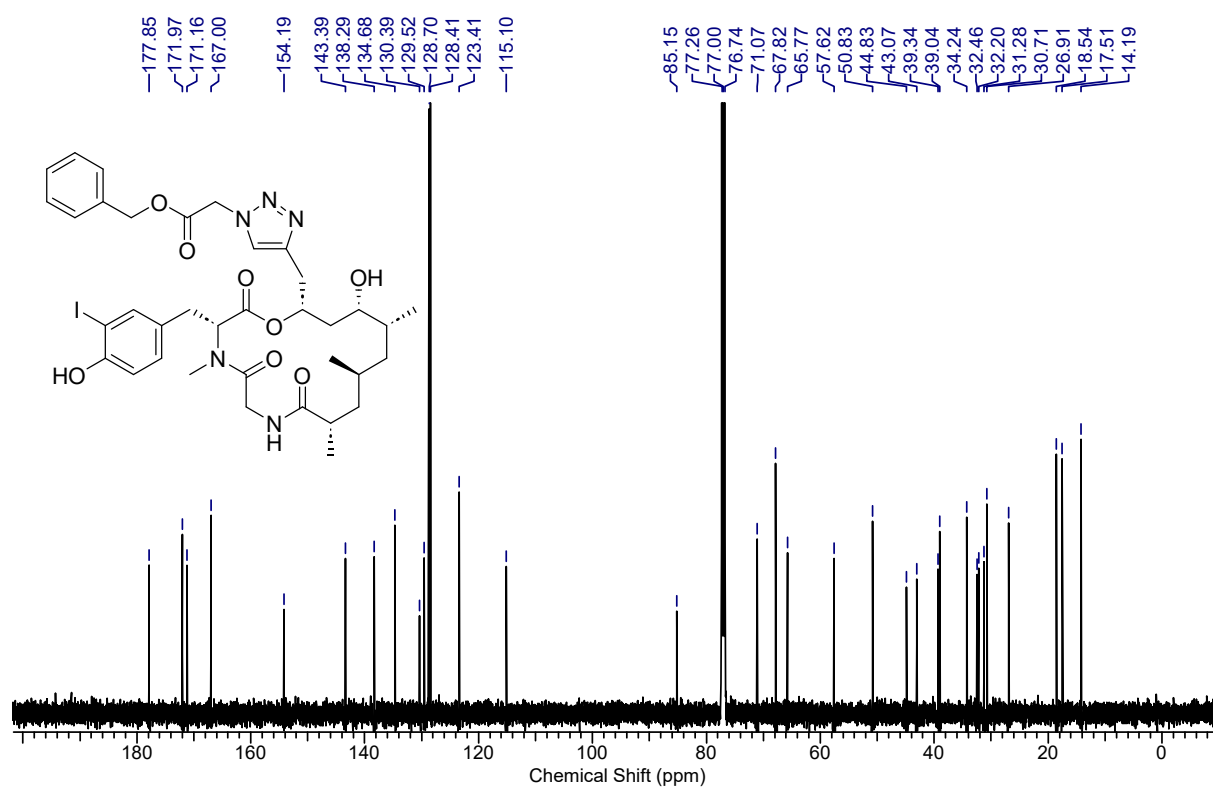


Benzyl 2-(4-[(*(3R,9S,11S,13R,14S,16R)*-14-hydroxy-3-(4-hydroxy-3-iodobenzyl)-4,9,11,13-tetramethyl-2,5,8-trioxo-1-oxa-4,7-diazacyclohexadecan-16-yl)methyl]-1H-1,2,3-triazol-1-yl)acetate (9c)

¹H-NMR (500 MHz, CDCl₃)

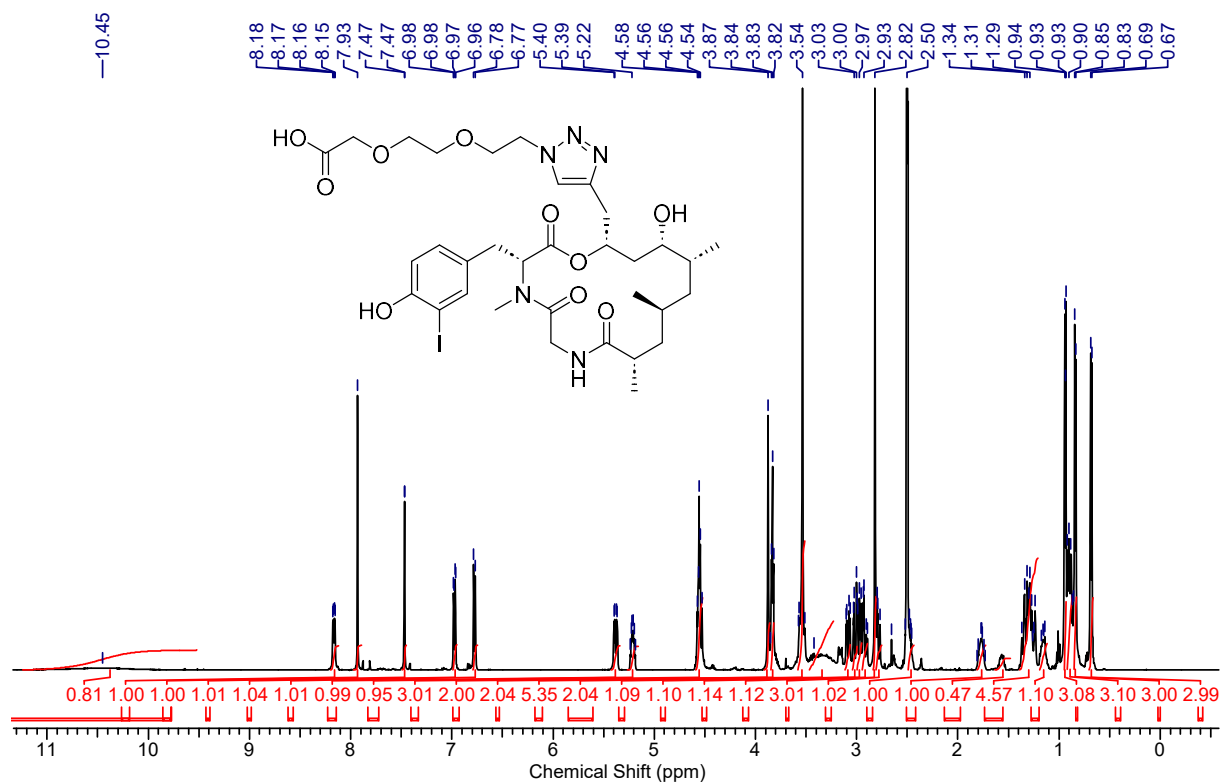


¹³C-NMR (125 MHz, CDCl₃)

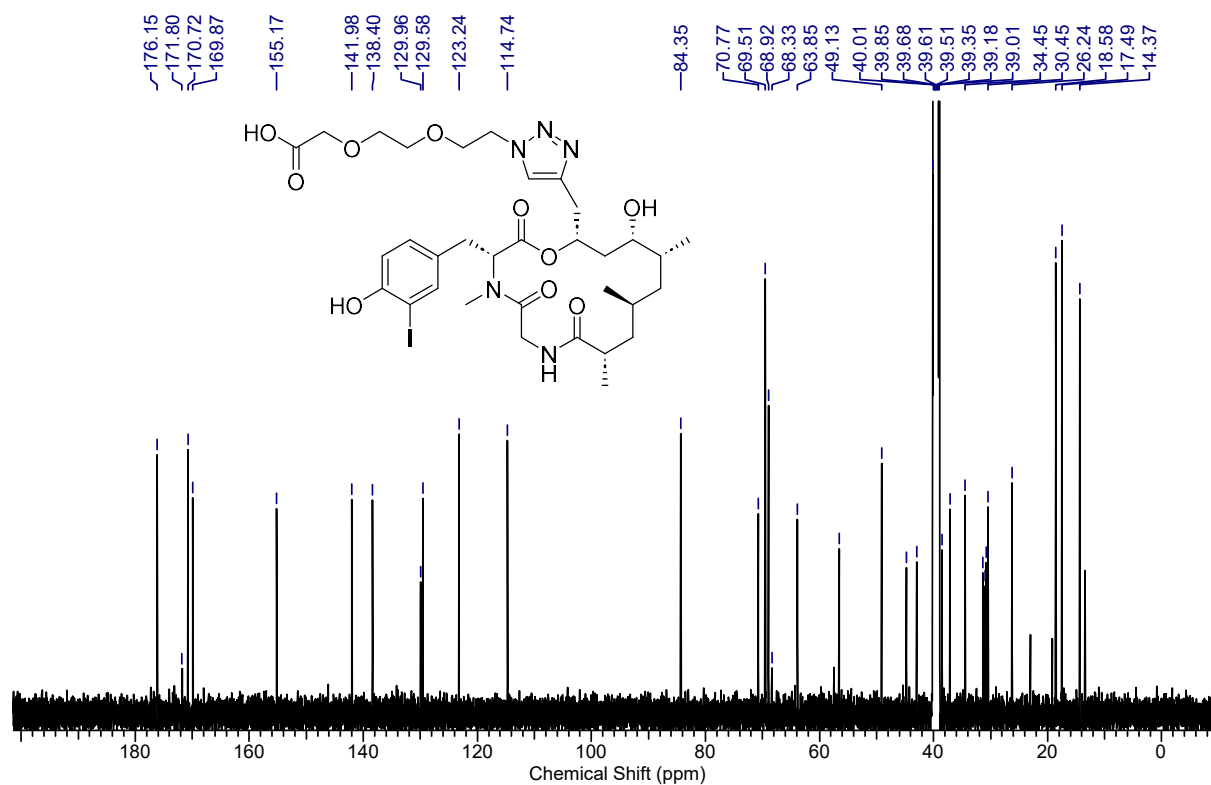


2-{2-[2-(4-[[[(3*R*,9*S*,11*S*,13*R*,14*S*,16*R*)-14-Hydroxy-3-(4-hydroxy-3-iodobenzyl)-4,9,11,13-tetramethyl-2,5,8-trioxo-1-oxa-4,7-diazacyclohexadecan-16-yl]methyl]-1*H*-1,2,3-triazol-1-yl)ethoxy]acetic acid (9d)

¹H-NMR (500 MHz, DMSO-D₆)

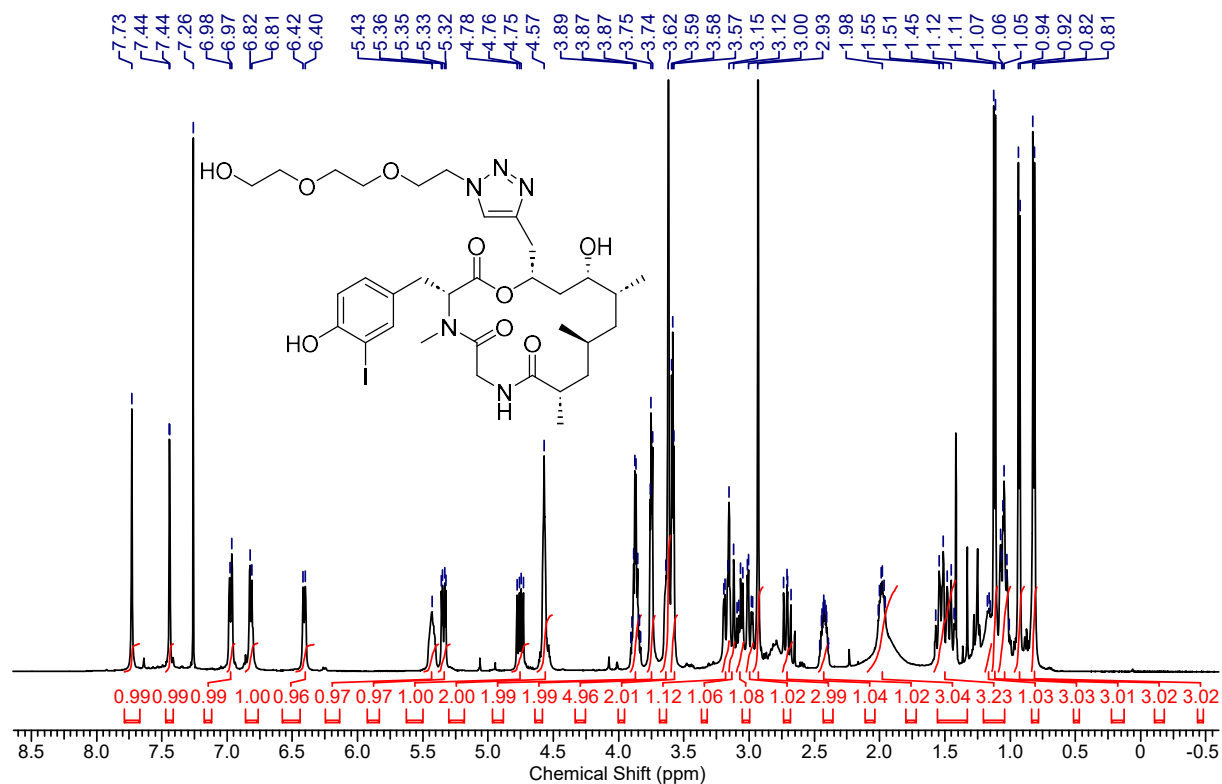


¹³C-NMR (125 MHz, DMSO-D₆)

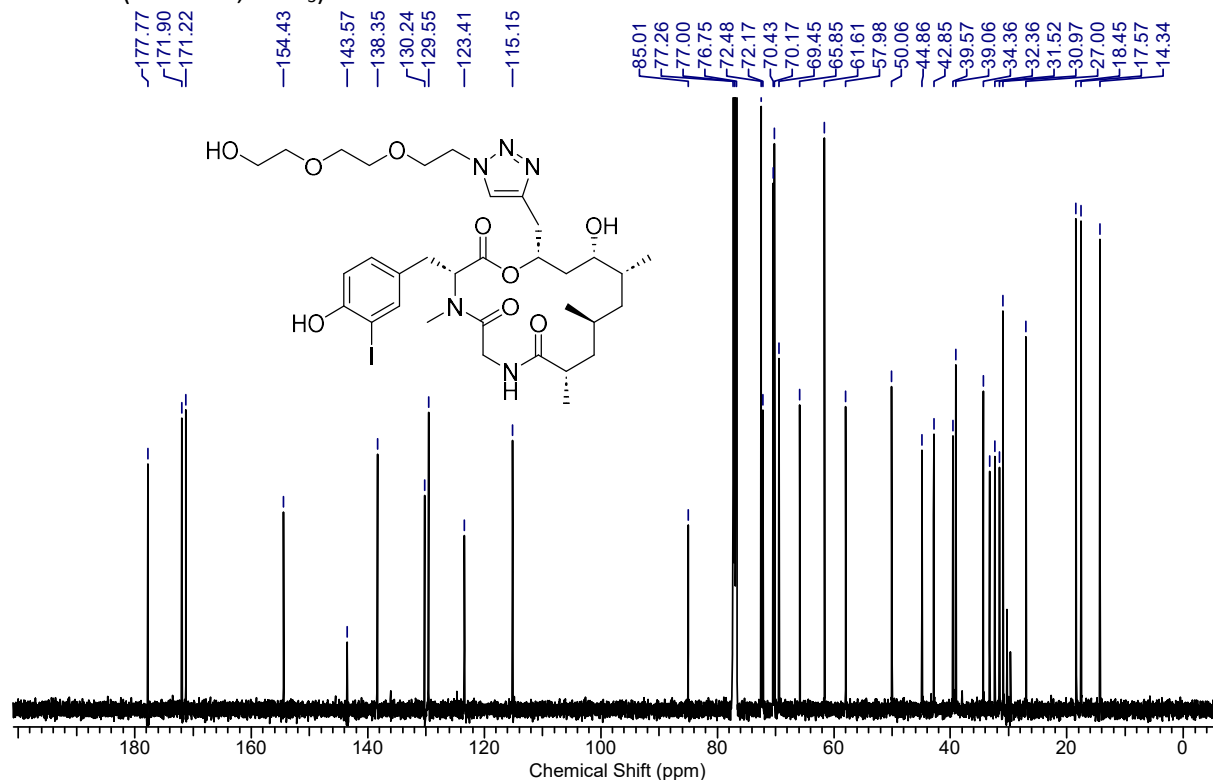


(3*R*,9*S*,11*S*,13*R*,14*S*,16*R*)-14-Hydroxy-3-(4-hydroxy-3-iodobenzyl)-16-((1-(2-(2-(2-hydroxyethoxy)ethoxy)ethoxy)ethyl)-1*H*-1,2,3-triazol-4-yl)methyl)-4,9,11,13-tetramethyl-1-oxa-4,7-diazacyclohexadecane-2,5,8-trione (9e)

¹H-NMR (500 MHz, CDCl₃)

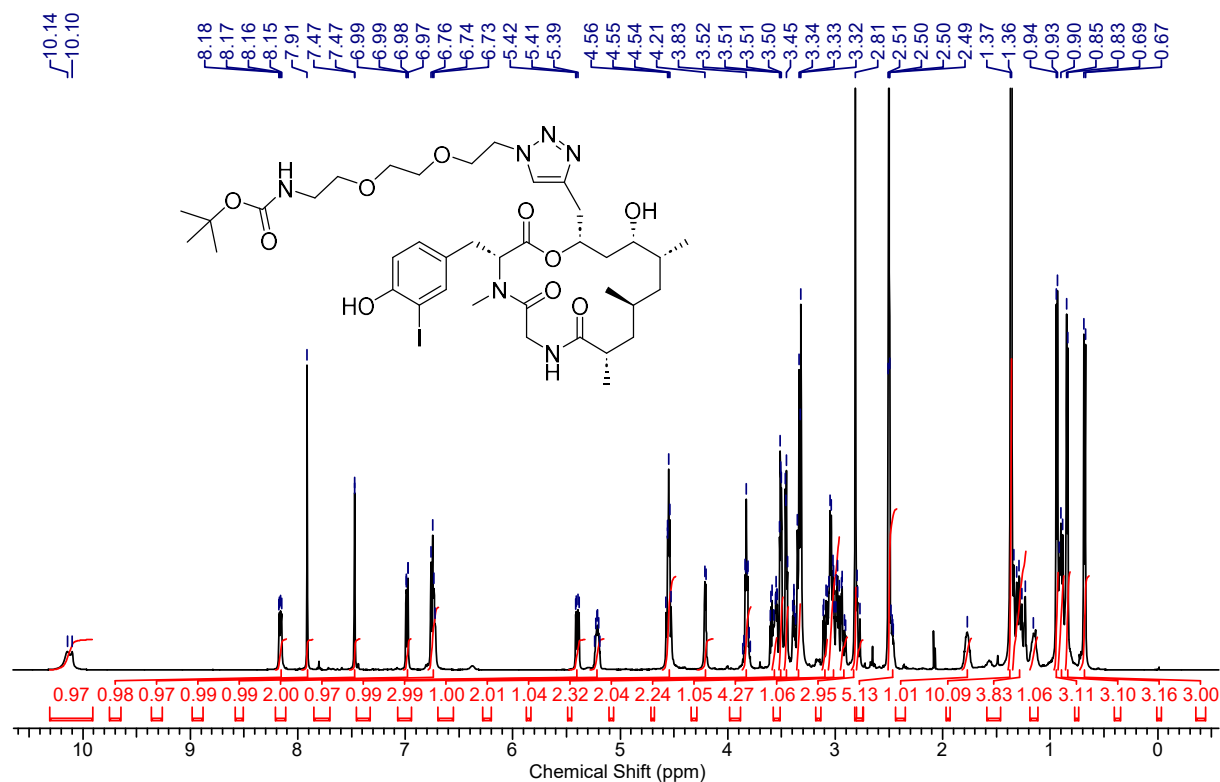


¹³C-NMR (125 MHz, CDCl₃)

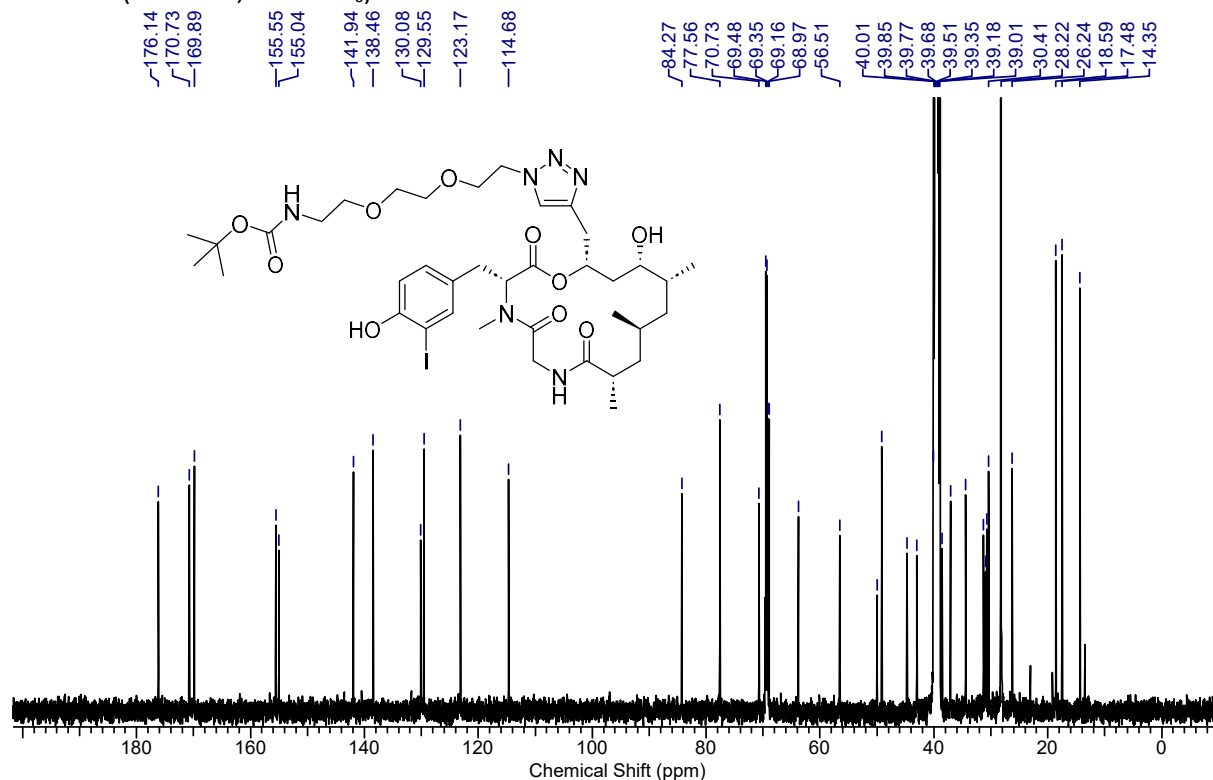


tert-Butyl (2-{2-[2-(4-{[(3*R*,9*S*,11*S*,13*R*,14*S*,16*R*)-14-hydroxy-3-(4-hydroxy-3-iodobenzyl)-4,9,11,13-tetramethyl-2,5,8-trioxo-1-oxa-4,7-diazacyclohexadecan-16-yl]methyl}-1*H*-1,2,3-triazol-1-yl)ethoxy]ethoxy}ethyl)carbamate (9f)

¹H-NMR (500 MHz, DMSO-D₆)

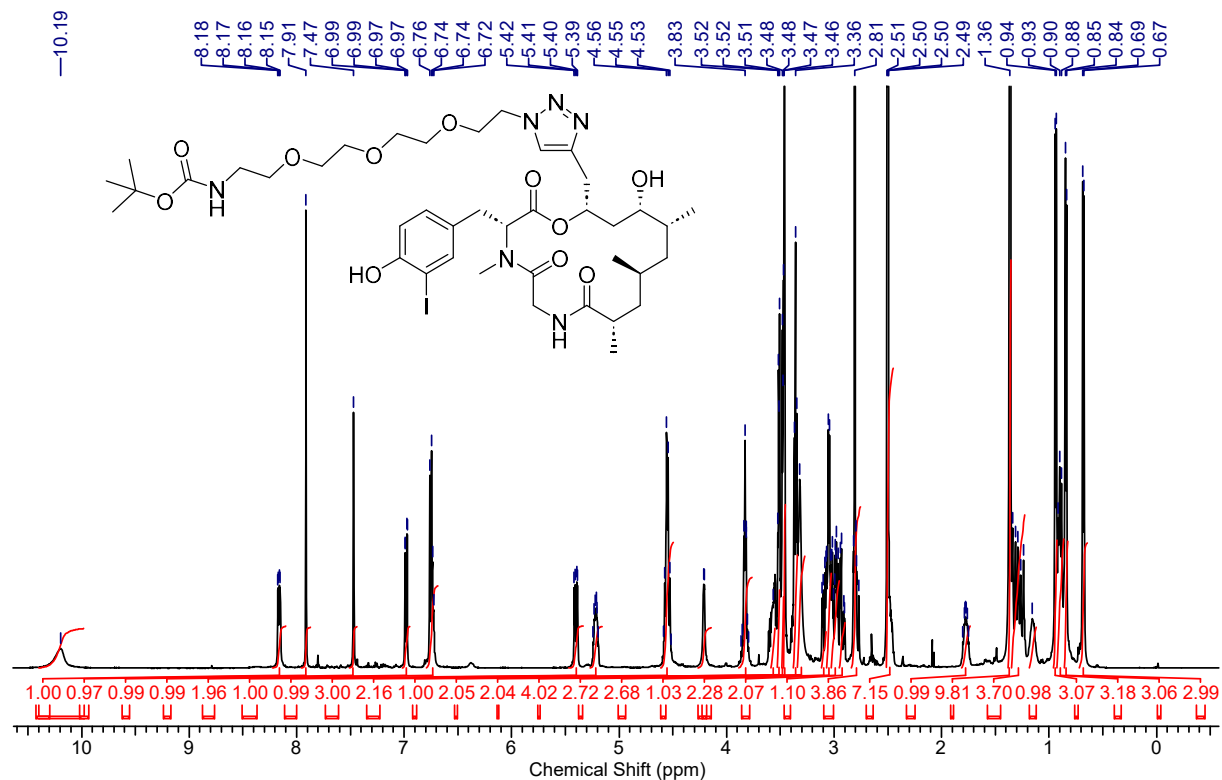


¹³C-NMR (125 MHz, DMSO-D₆)

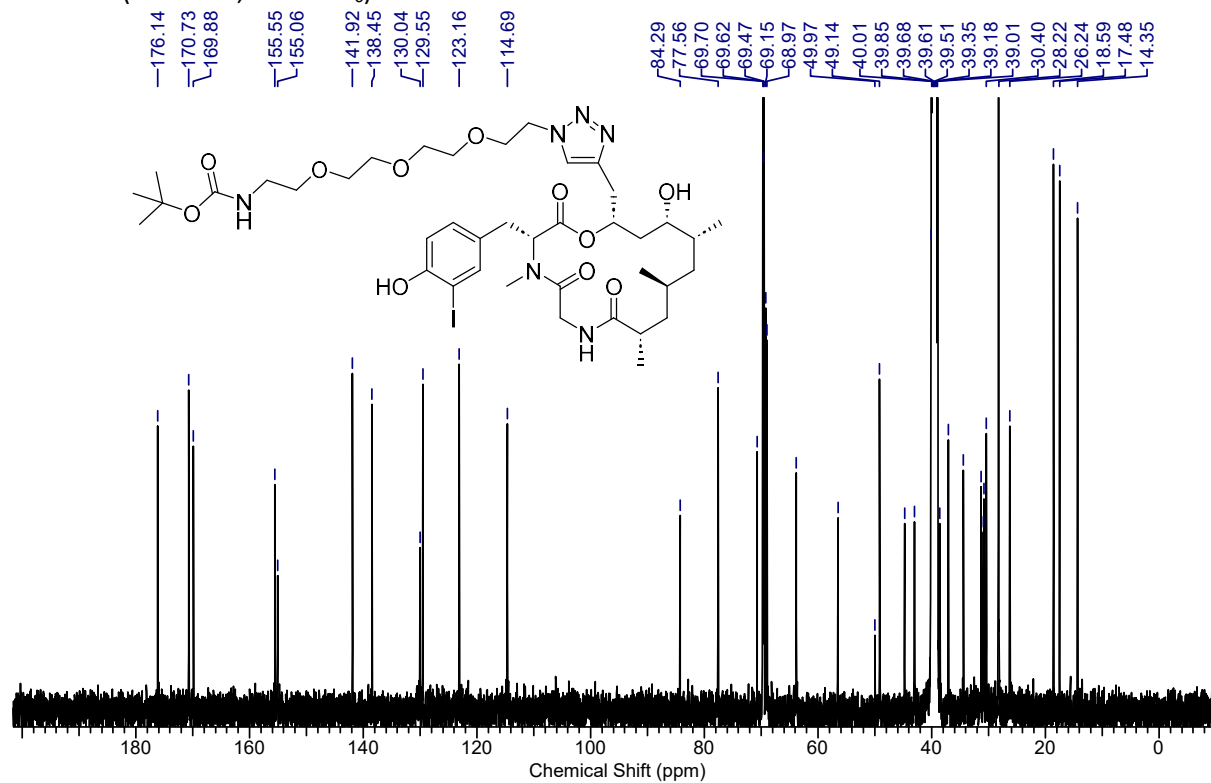


***tert*-Butyl [2-(2-{2-[2-(4-{[(3*R*,9*S*,11*S*,13*R*,14*S*,16*R*)-14-hydroxy-3-(4-hydroxy-3-iodobenzyl)-4,9,11,13-tetramethyl-2,5,8-trioxo-1-oxa-4,7-diazacyclohexadecan-16-yl)methyl}-1*H*-1,2,3-triazol-1-yl)ethoxy]ethoxy}ethoxy)ethyl]carbamate (9g)**

¹H-NMR (500 MHz, DMSO-D₆)

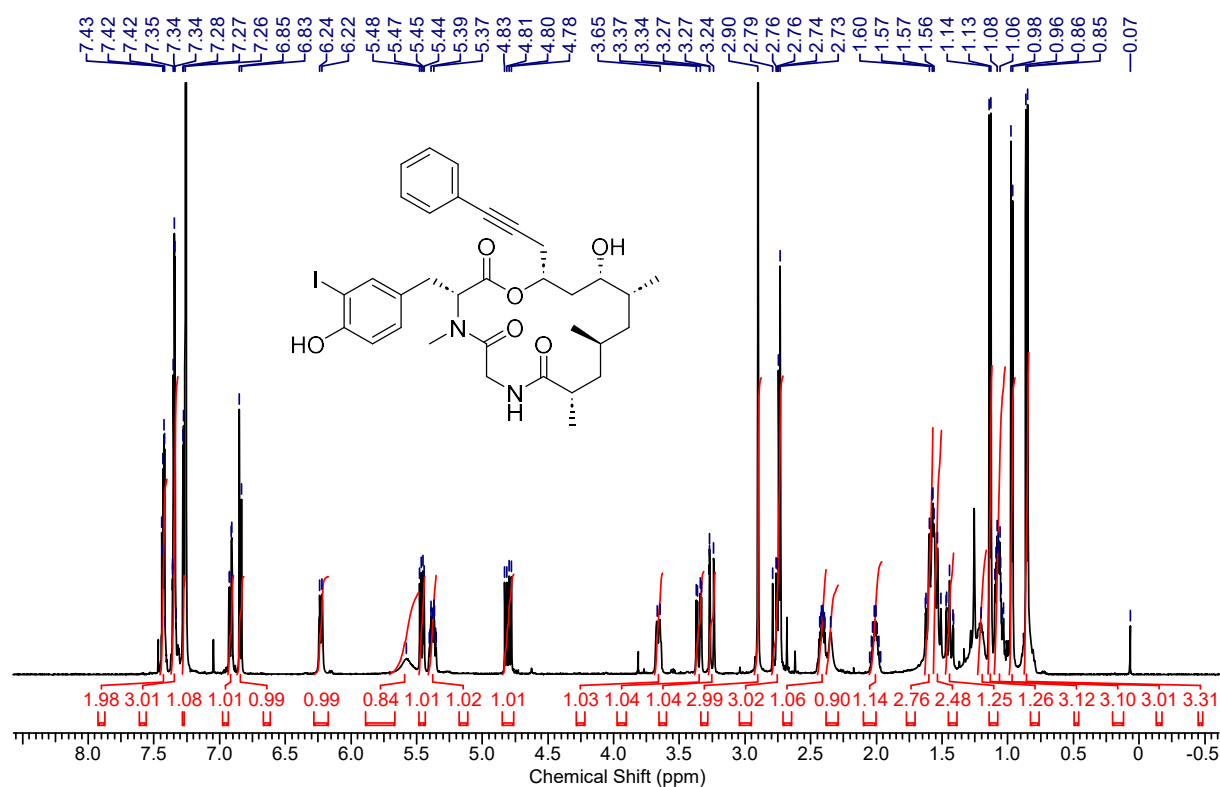


¹³C-NMR (125 MHz, DMSO-D₆)

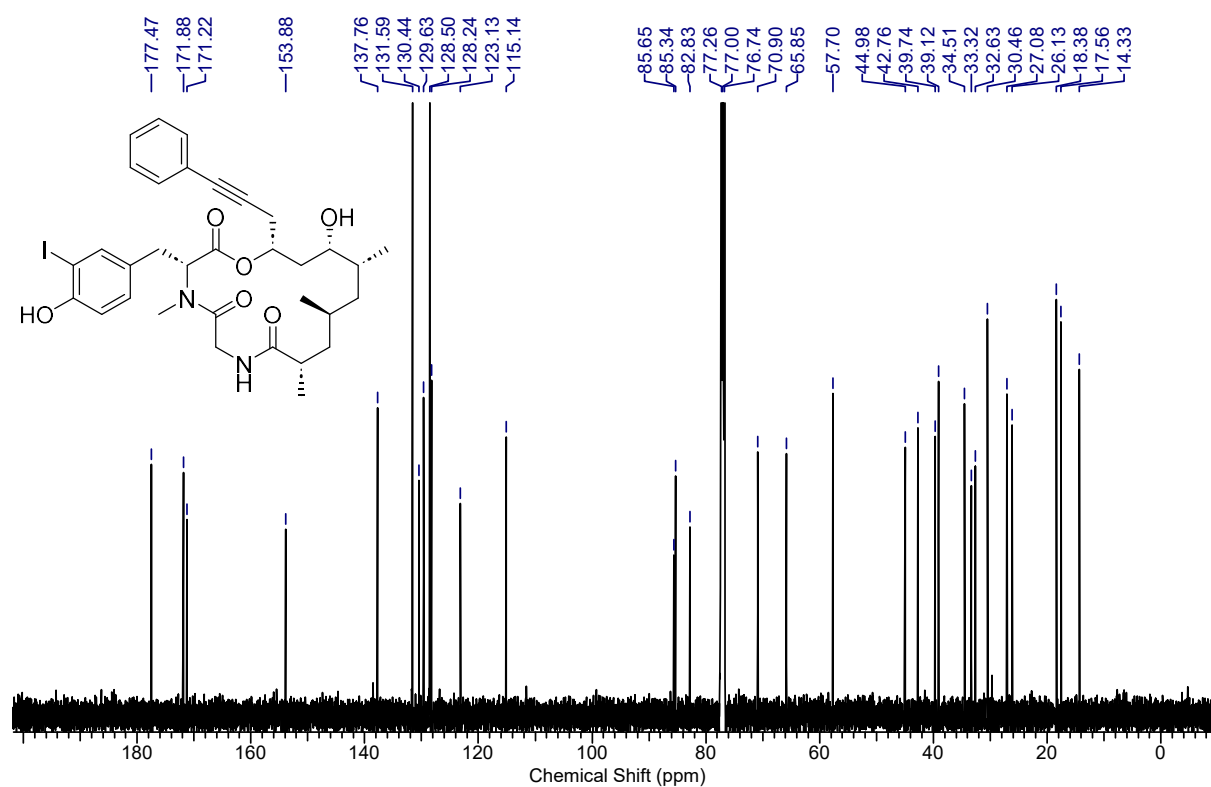


(3*R*,9*S*,11*S*,13*R*,14*S*,16*R*)-14-Hydroxy-3-(4-hydroxy-3-iodobenzyl)-4,9,11,13-tetramethyl-16-(3-phenylprop-2-yn-1-yl)-1-oxa-4,7-diazacyclohexadecane-2,5,8-trione (10a)

¹H-NMR (500 MHz, CDCl₃)

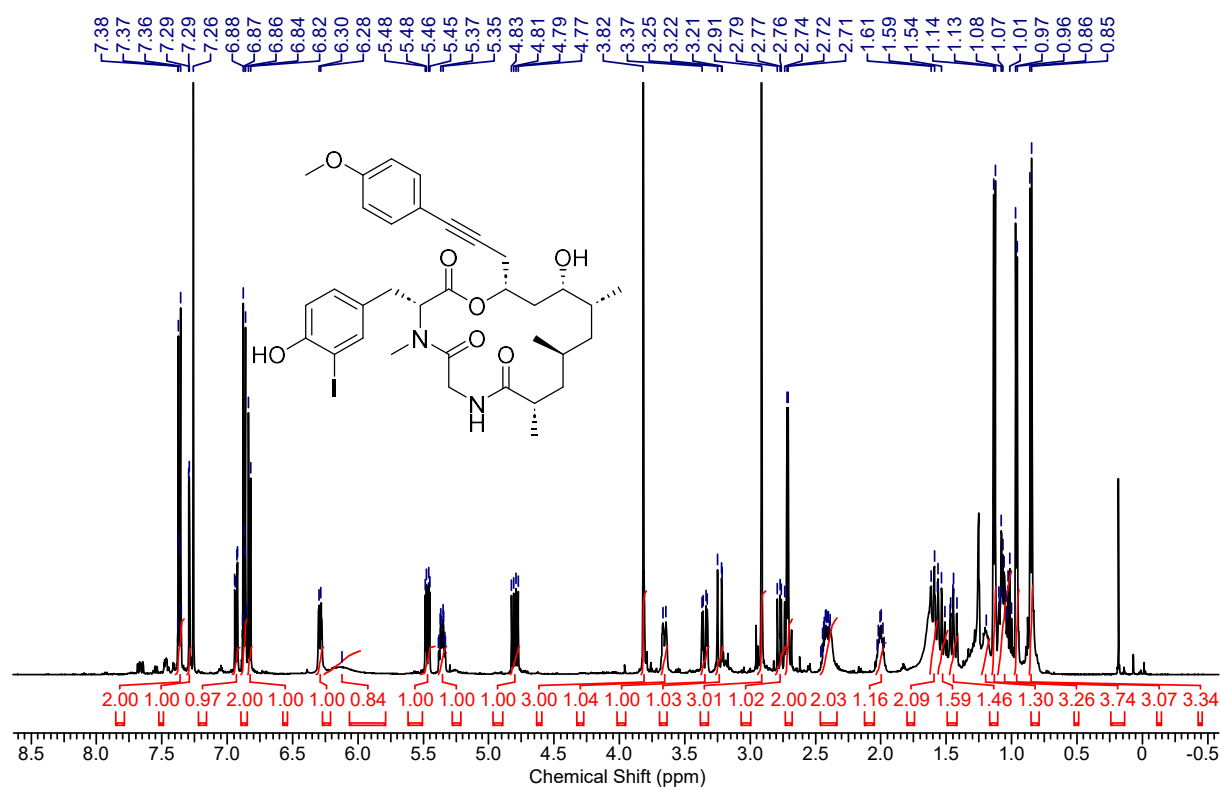


¹³C-NMR (125 MHz, CDCl₃)

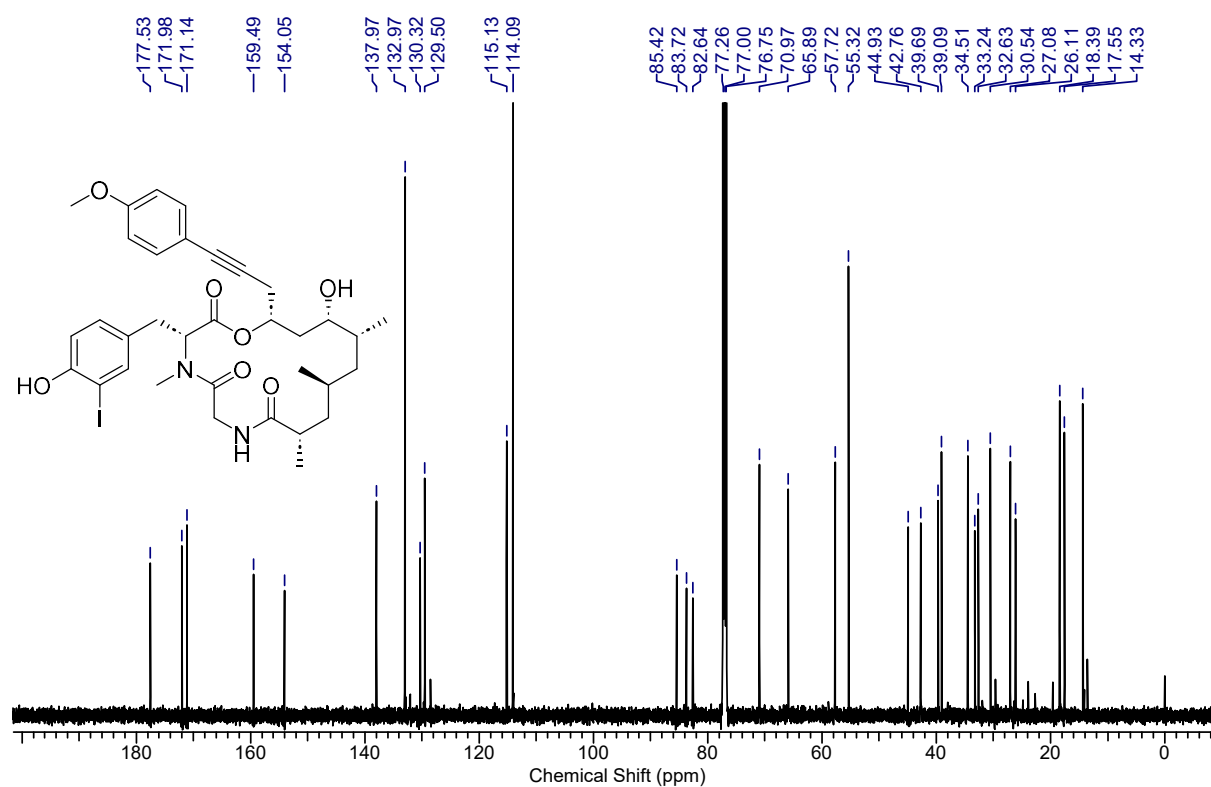


(3*R*,9*S*,11*S*,13*R*,14*S*,16*R*)-14-Hydroxy-3-(4-hydroxy-3-iodobenzyl)-16-[3-(4-methoxyphenyl)prop-2-yn-1-yl]-4,9,11,13-tetramethyl-1-oxa-4,7-diazacyclohexadecane-2,5,8-trione (10b)

¹H-NMR (500 MHz, CDCl₃)

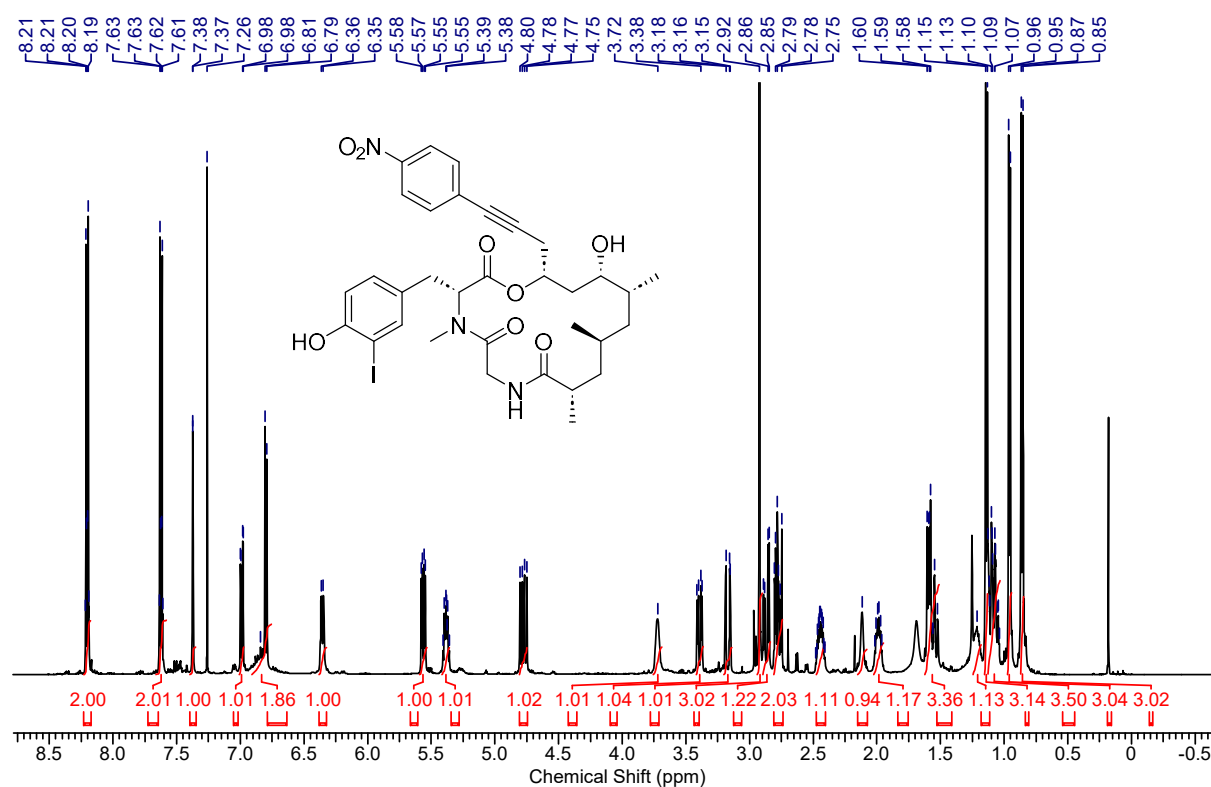


¹³C-NMR (125 MHz, CDCl₃)

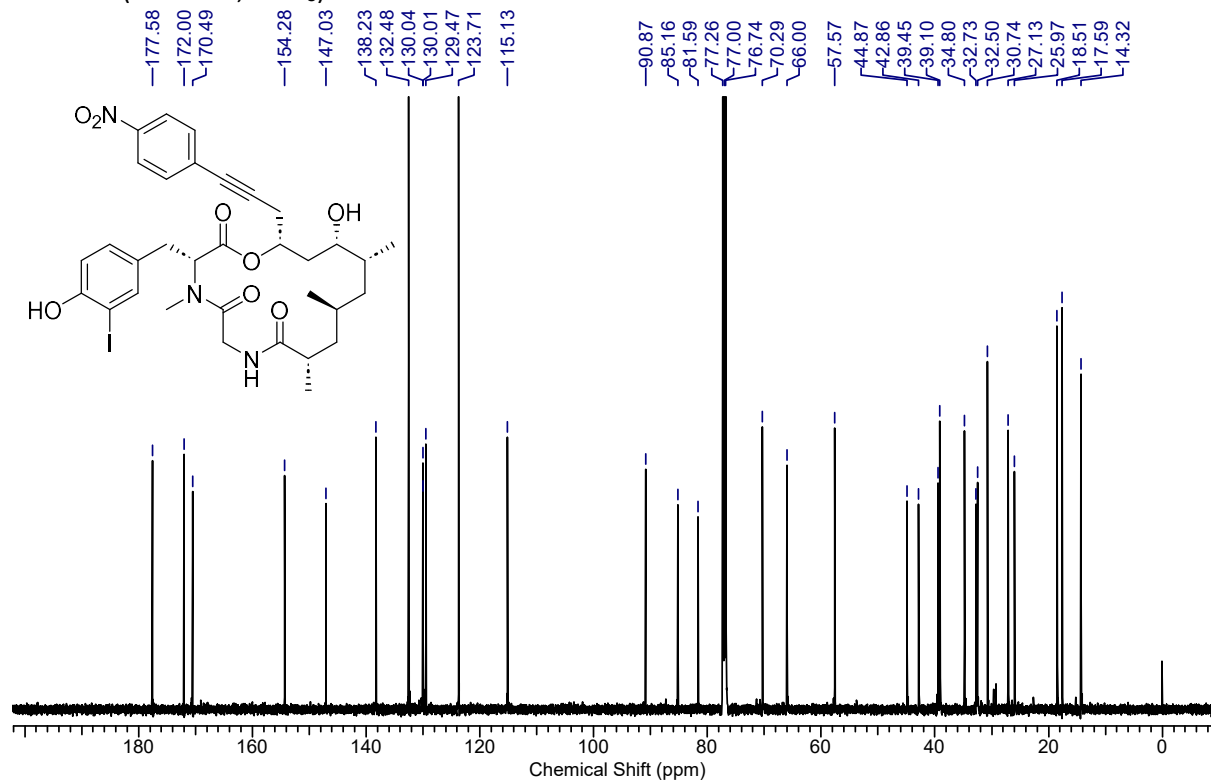


(3*R*,9*S*,11*S*,13*R*,14*S*,16*R*)-14-Hydroxy-3-(4-hydroxy-3-iodobenzyl)-4,9,11,13-tetramethyl-16-[3-(4-nitrophenyl)prop-2-yn-1-yl]-1-oxa-4,7-diazacyclohexadecane-2,5,8-trione (10c)

¹H-NMR (500 MHz, CDCl₃)

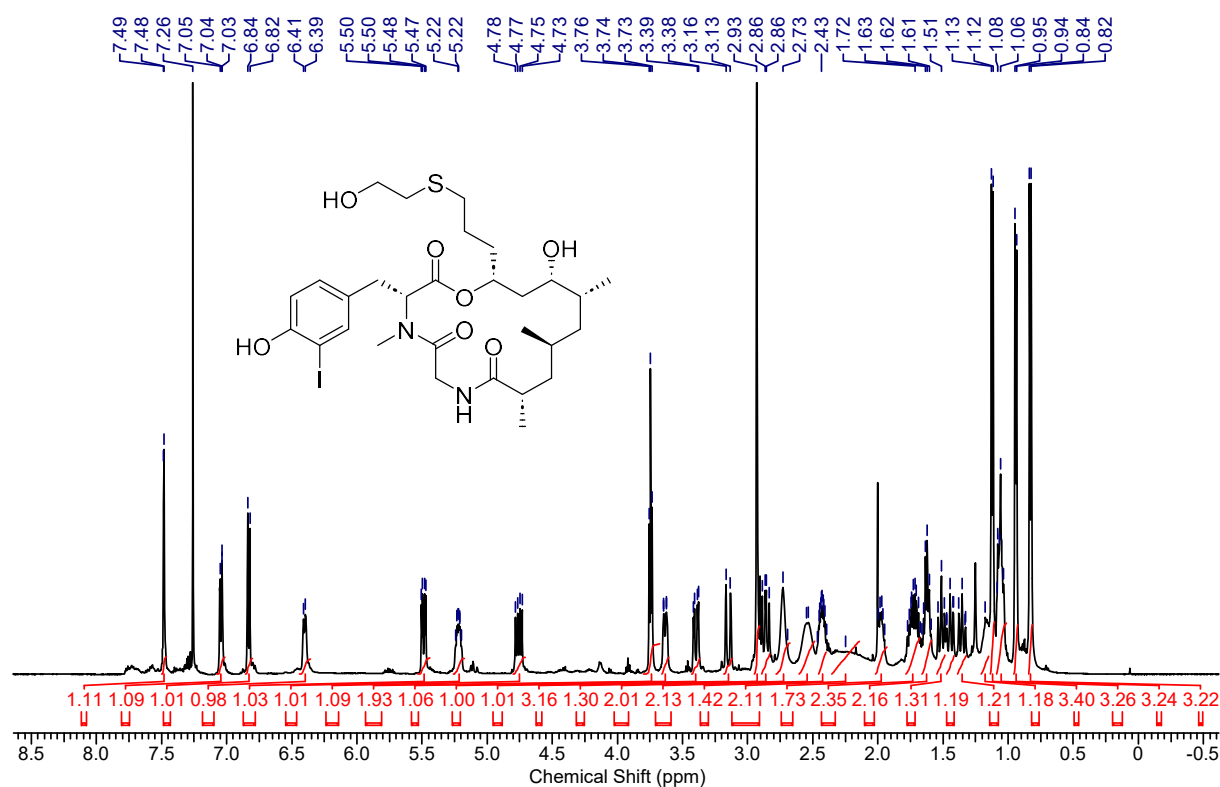


¹³C-NMR (500 MHz, CDCl₃)

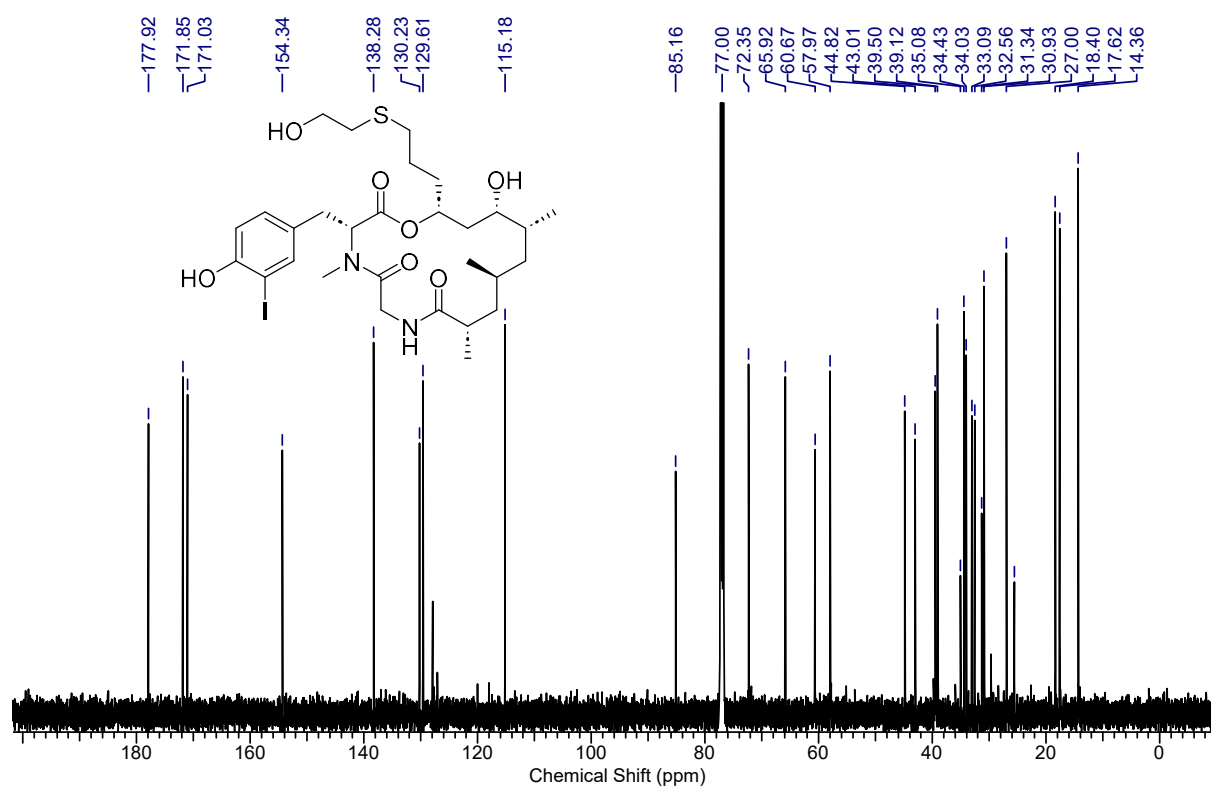


(3*R*,9*S*,11*S*,13*R*,14*S*,16*R*)-14-Hydroxy-3-(4-hydroxy-3-iodobenzyl)-16-{3-[(2-hydroxyethyl)thio]-propyl}-4,9,11,13-tetramethyl-1-oxa-4,7-diazacyclohexadecane-2,5,8-trione (11a)

¹H-NMR (500 MHz, CDCl₃)

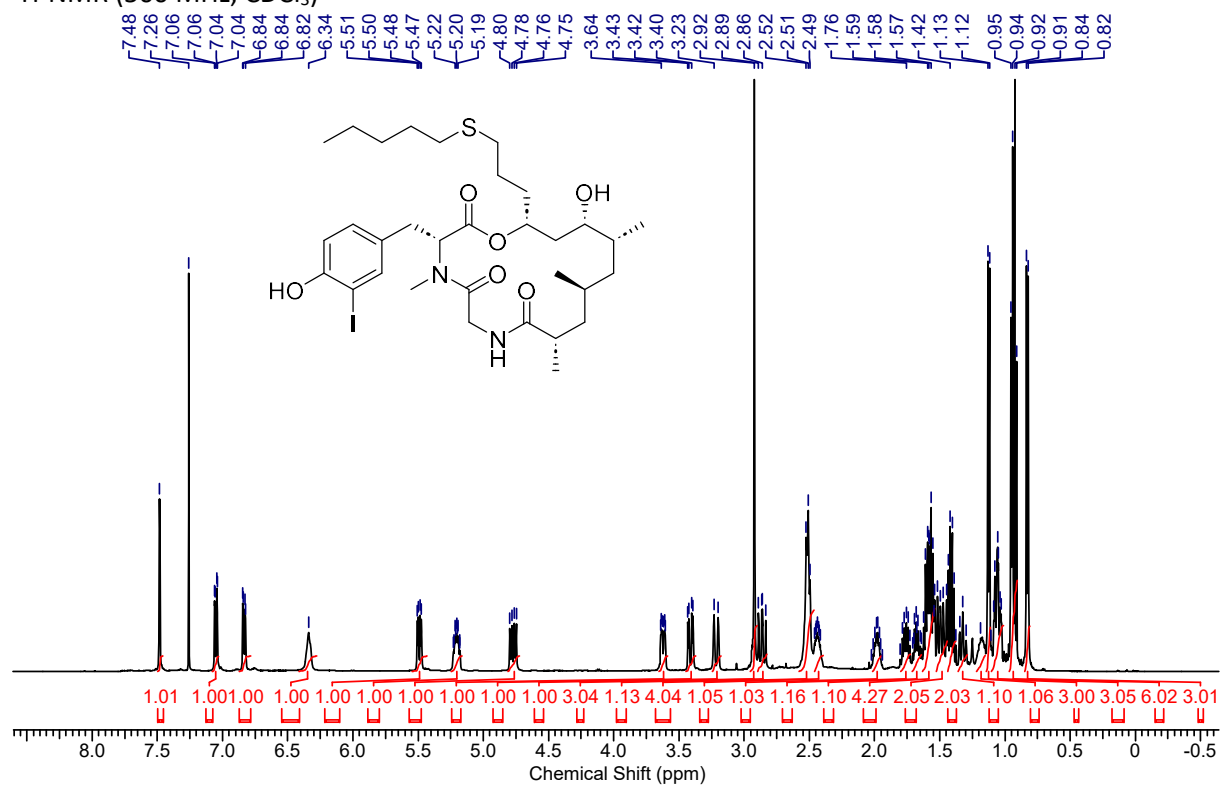


¹³C-NMR (125 MHz, CDCl₃)

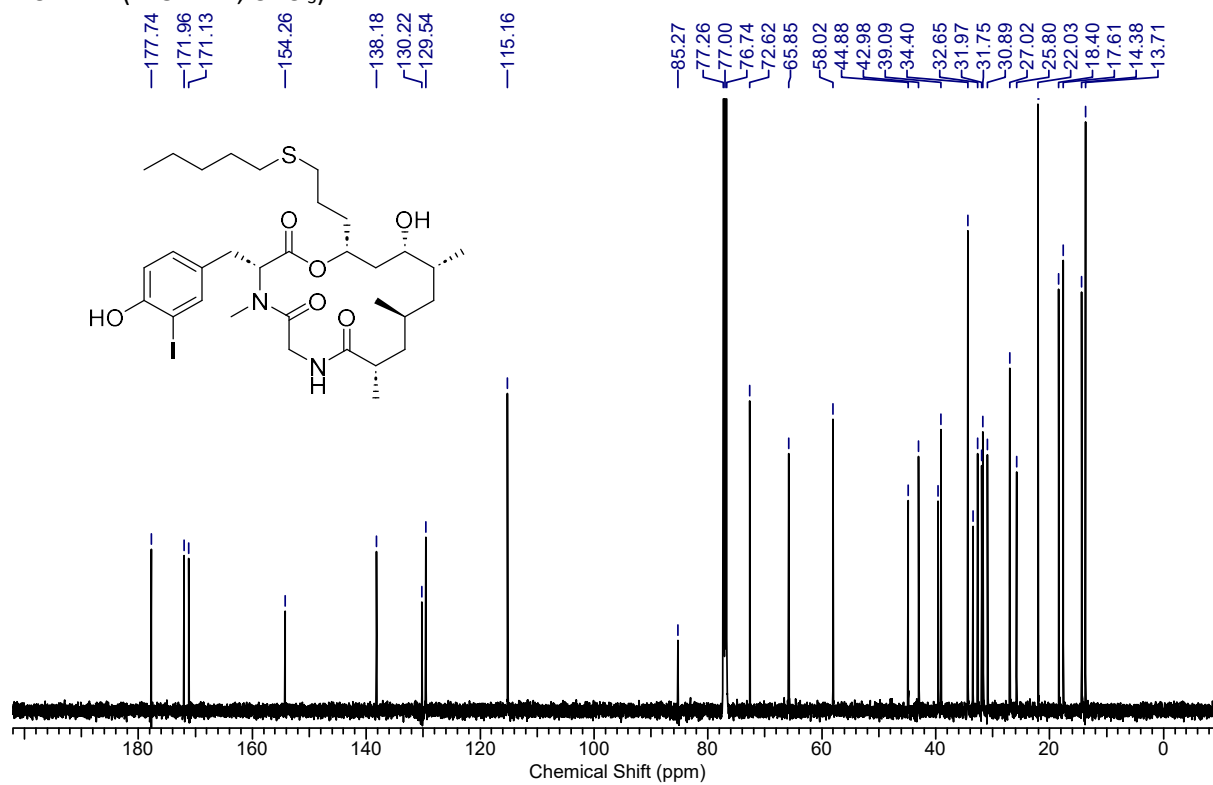


(3*R*,9*S*,11*S*,13*R*,14*S*,16*R*)-14-Hydroxy-3-(4-hydroxy-3-iodobenzyl)-4,9,11,13-tetramethyl-16-[3-(pentylthio)propyl]-1-oxa-4,7-diazacyclohexadecane-2,5,8-trione (11b)

¹H-NMR (500 MHz, CDCl₃)

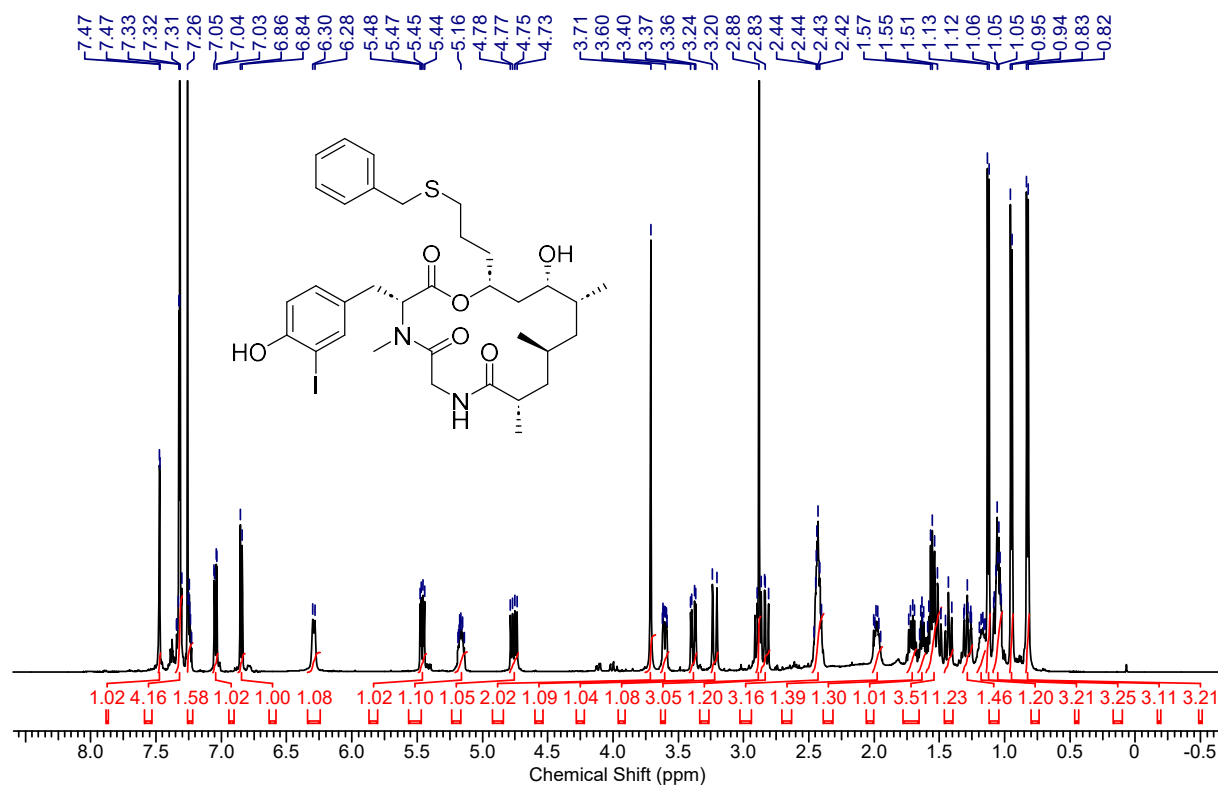


¹³C-NMR (125 MHz, CDCl₃)

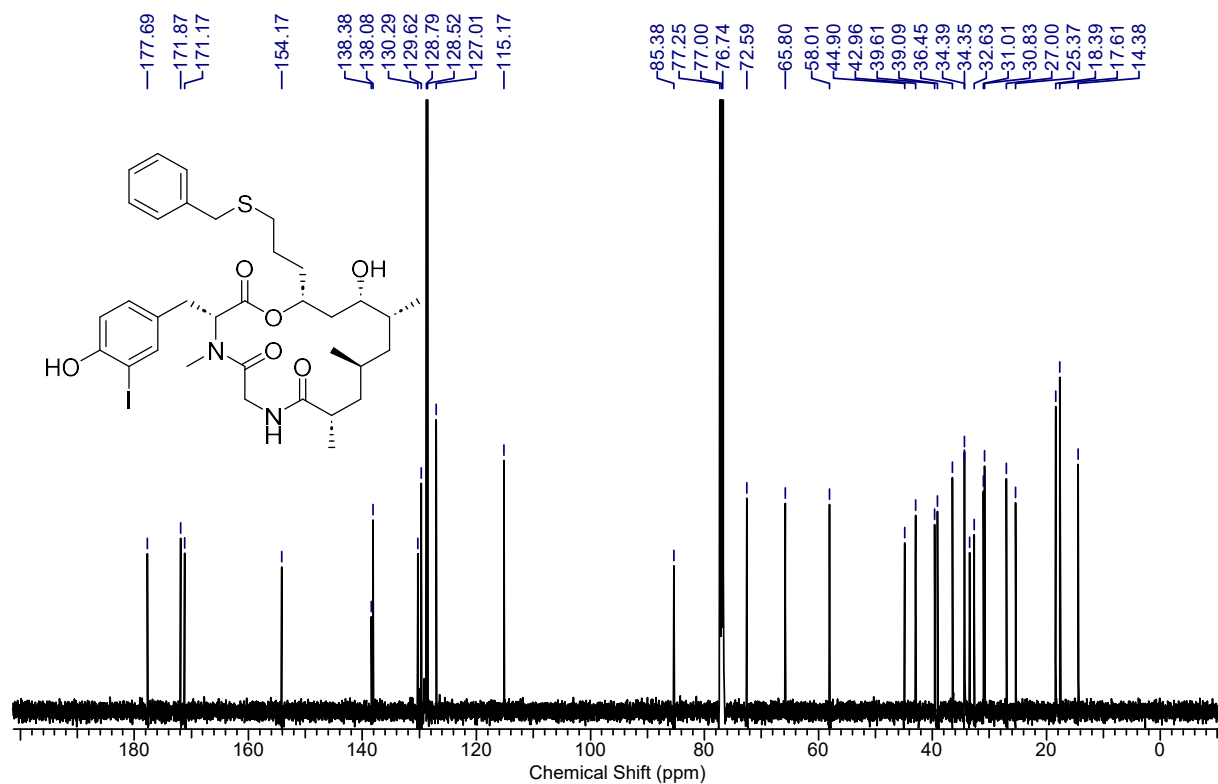


(3*R*,9*S*,11*S*,13*R*,14*S*,16*R*)-16-[3-(Benzylthio)propyl]-14-hydroxy-3-(4-hydroxy-3-iodobenzyl)-4,9,11,13-tetramethyl-1-oxa-4,7-diazacyclohexadecane-2,5,8-trione (11c)

¹H-NMR (500 MHz, CDCl₃)

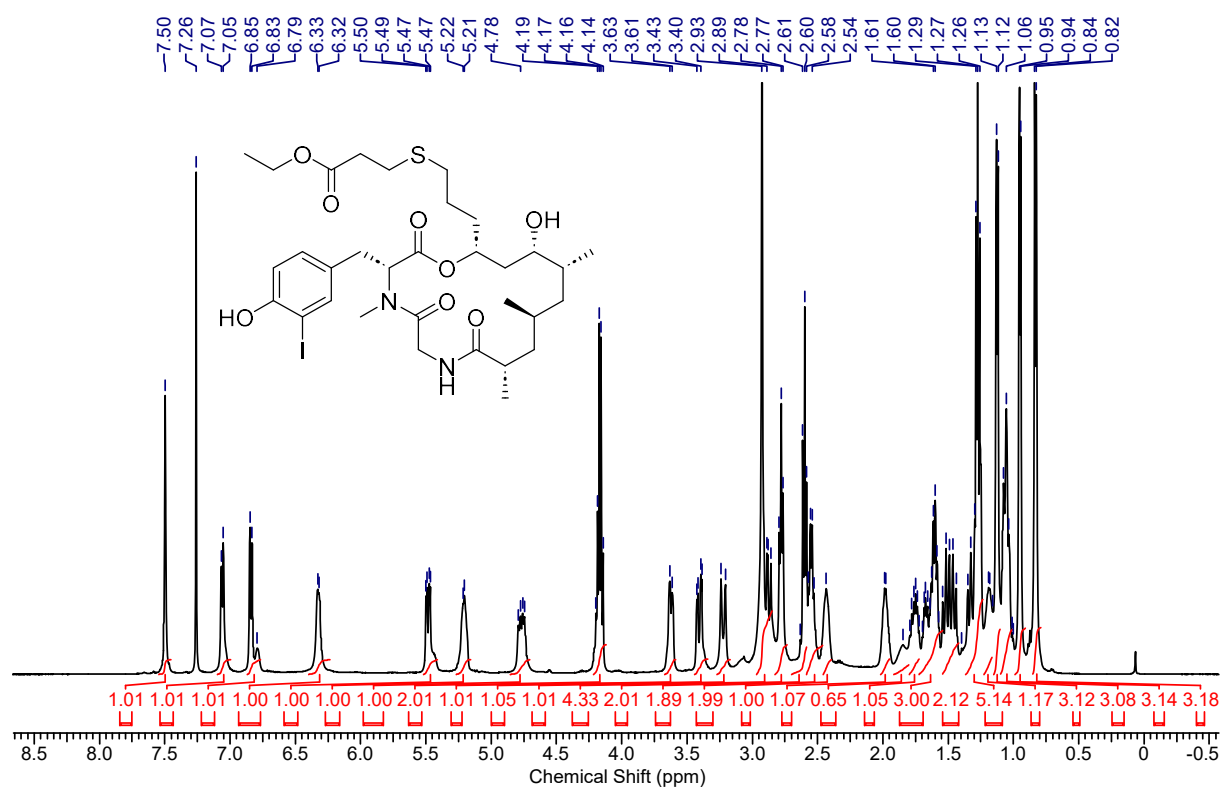


¹³C-NMR (125 MHz, CDCl₃)

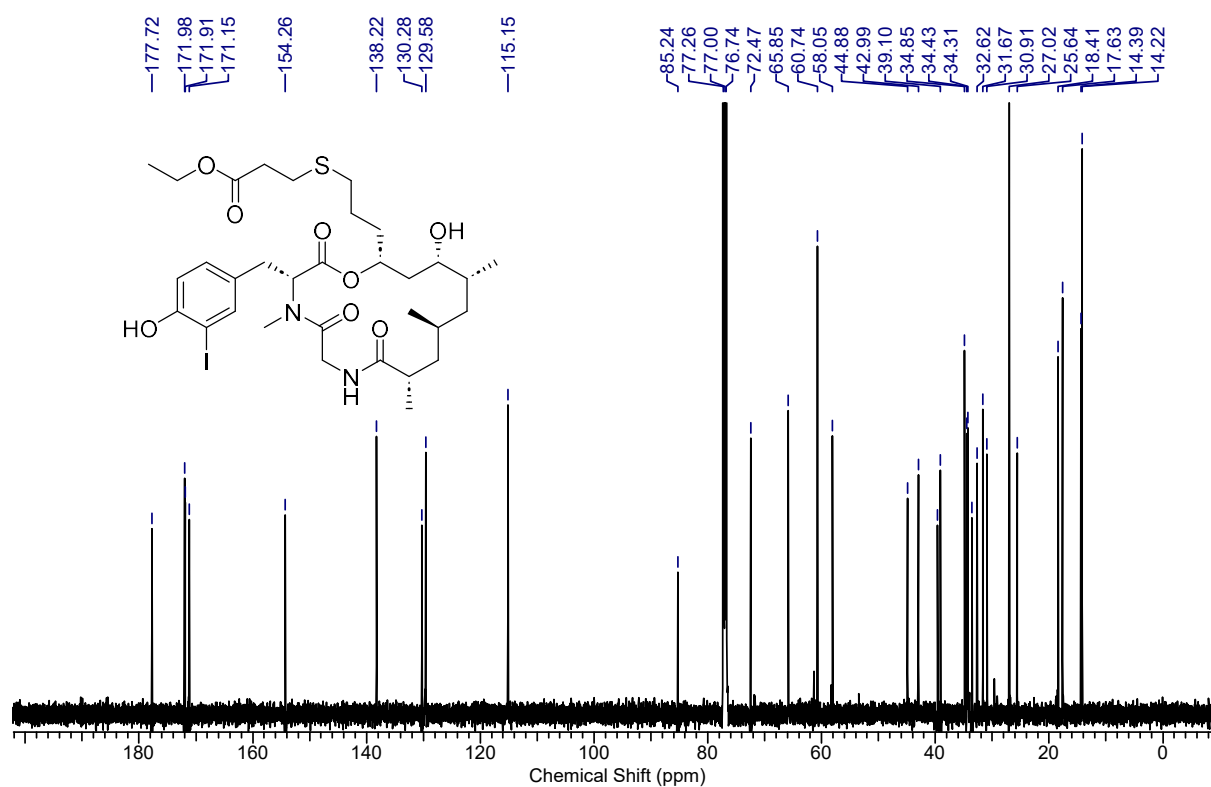


Ethyl 3-({3-[(*3R,9S,11S,13R,14S,16R*)-14-hydroxy-3-(4-hydroxy-3-iodobenzyl)-4,9,11,13-tetramethyl-2,5,8-trioxo-1-oxa-4,7-diazacyclohexadecan-16-yl]propyl}thio)propanoate (11d)

¹H-NMR (500 MHz, CDCl₃)

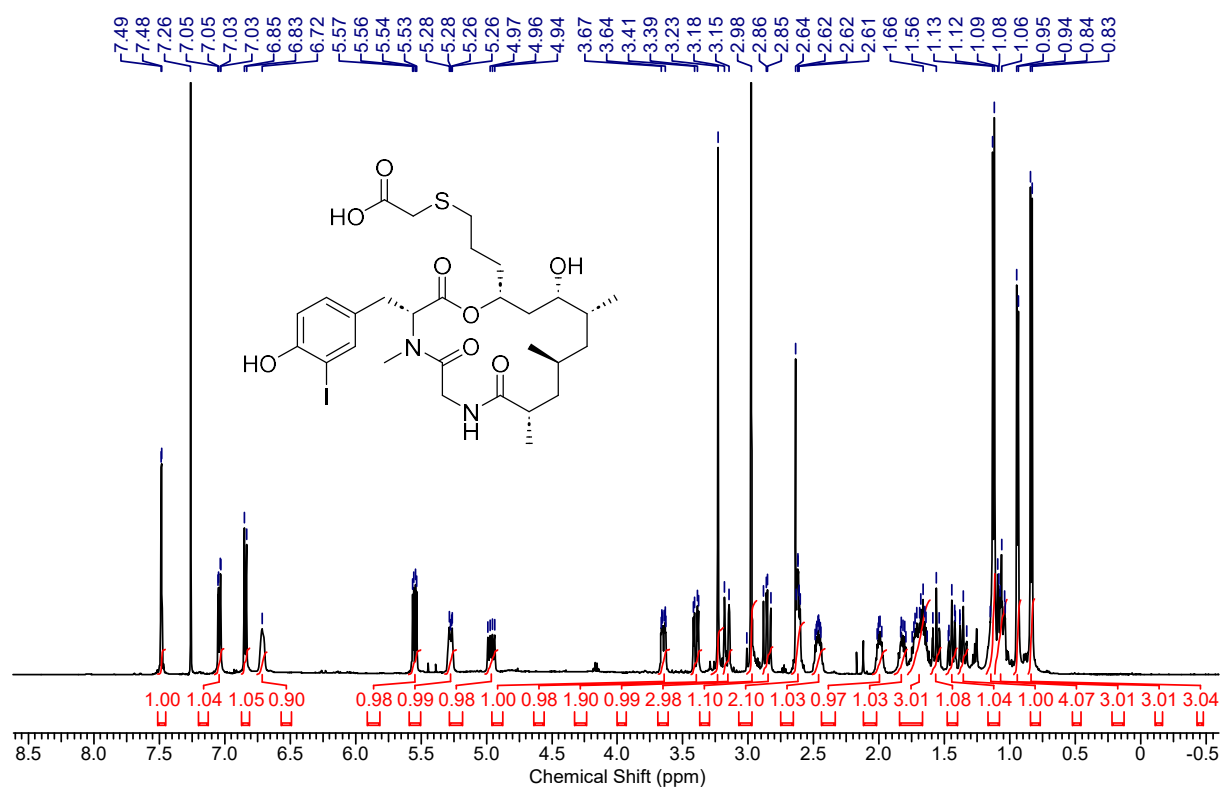


¹³C-NMR (125 MHz, CDCl₃)

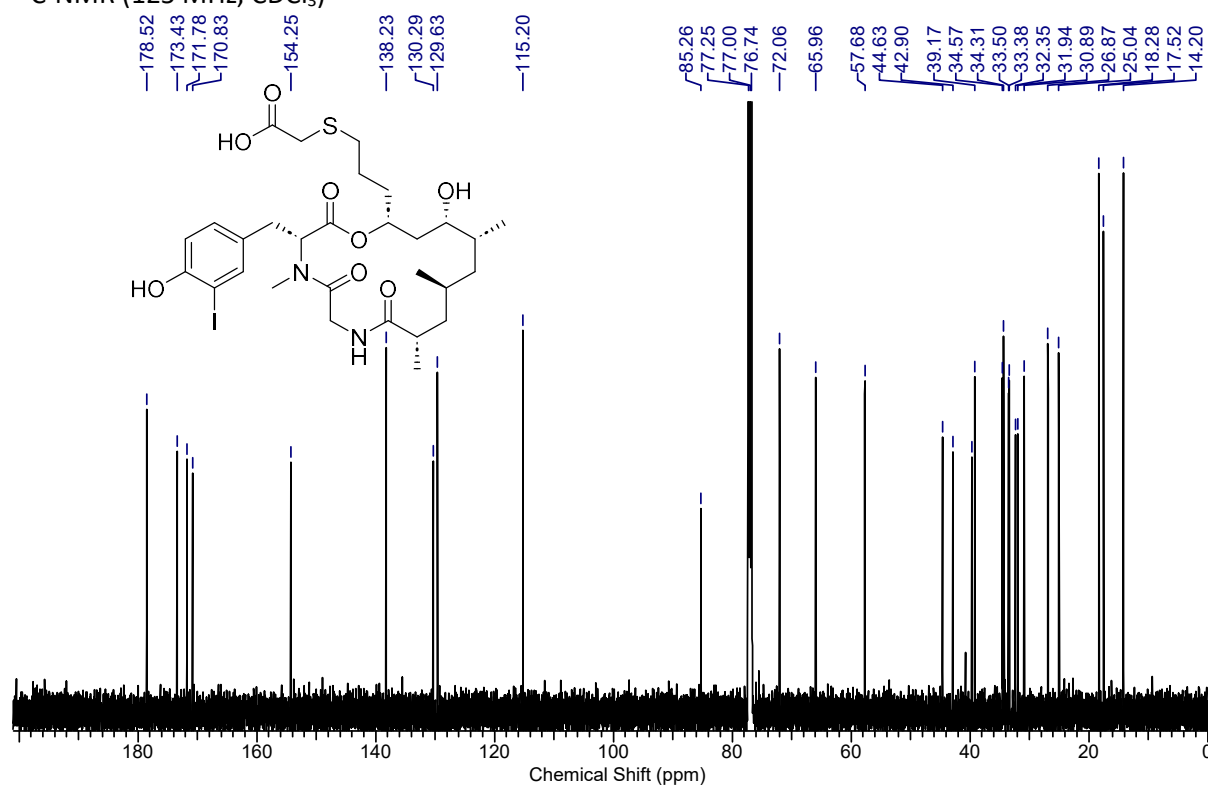


2-({3-[(3*R*,9*S*,11*S*,13*R*,14*S*,16*R*)-14-Hydroxy-3-(4-hydroxy-3-iodobenzyl)-4,9,11,13-tetramethyl-2,5,8-trioxo-1-oxa-4,7-diazacyclohexadecan-16-yl]propyl}thio)acetic acid (11e)

¹H-NMR (500 MHz, CDCl₃)

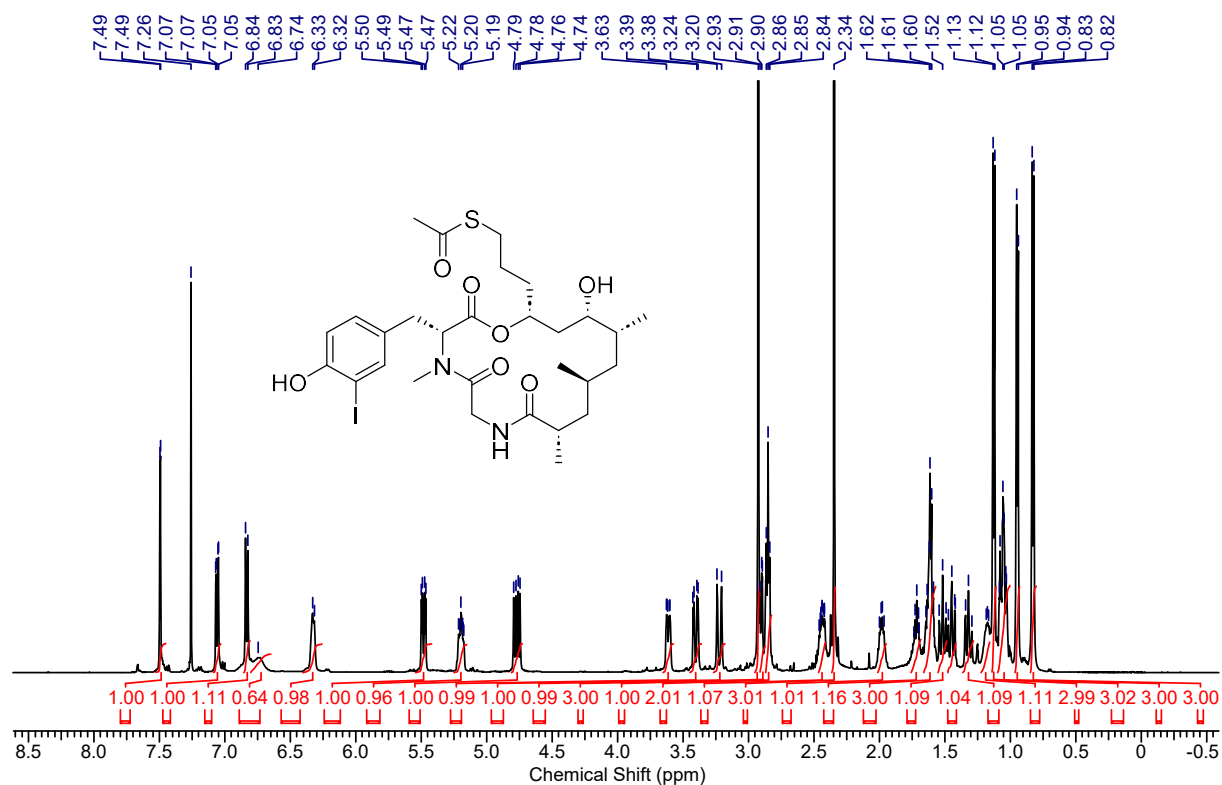


¹³C-NMR (125 MHz, CDCl₃)



S-{3-[(3*R*,9*S*,11*S*,13*R*,14*S*,16*R*)-14-Hydroxy-3-(4-hydroxy-3-iodobenzyl)-4,9,11,13-tetramethyl-2,5,8-trioxo-1-oxa-4,7-diazacyclohexadecan-16-yl]propyl} ethanethioate (11f)

¹H-NMR (500 MHz, CDCl₃)



¹³C-NMR (125 MHz, CDCl₃)

