Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Orthogonal dual-click diyne for CuAAC and/or SPAAC couplings

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Supporting Information

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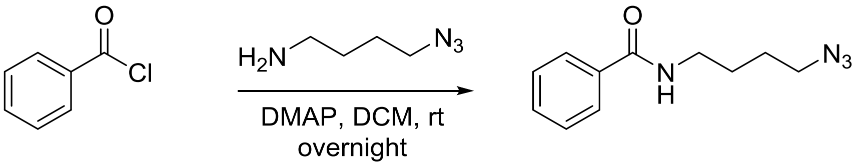
1. General Information

^1H-NMR and ^{13}C-NMR spectra were recorded on a 400 or 600 MHz spectrometer using $CDCl_3$ as the deuterated solvent. The chemical shifts (δ) are reported in parts per million (ppm) relative to the residual $CHCl_3$ peak (7.26 ppm for ^1H-NMR and 77.0 for ^{13}C-NMR). The coupling constants (*J*) are reported in Hertz (Hz). Mass spectra were recorded using electrospray ionization (ESI). Yields refer to isolated material judged to be ≥ 95% pure by ^1H NMR spectroscopy following silica gel chromatography. All chemicals were used as received unless otherwise stated. The purifications were performed by flash chromatography using silica gel with 40-63 micron particle size.

2. Synthesis of N-(4-azidobutyl)benzamide



10

***N*-(4-azidobutyl)benzamide (10):** To a solution of benzoyl chloride (0.610 ml, 5.26 mmol, 1.2 equiv) in DCM (0.63 M) under nitrogen was added N,N-dimethylpyridin-4-amine (0.803g, 6.57 mmol, 1.5 equiv). 4-azidobutan-1-amine[1] (0.500g, 4.38 mmol, 1 equiv) was then added to the reaction and left to run at room temp overnight. After completion, the reaction was quenched with H_2O (7 ml). The mixture was then extracted with DCM (3 x 7 ml). The DCM layers were collected, washed with saturated Na_2CO_3, washed with brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica (10% EtOAc/hexanes) to give 0.434g (45%) as a yellowish oil.

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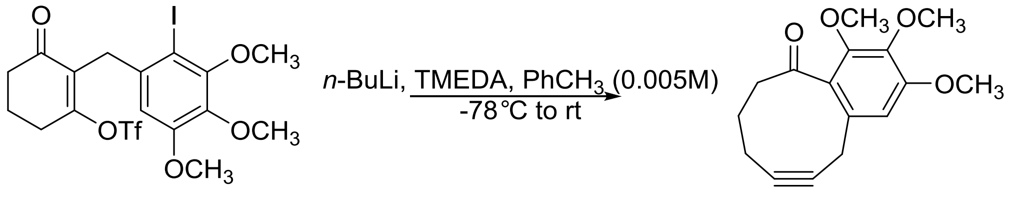
[1] R. Srinivasan, L.Tan, H.Wu, P.Yang, K.Kalesh, and S. Yao, *Org. Biomol. Chem.,* 2009, **7**, 1821-1828

3. General procedure of benzocyclononyne (BONO)

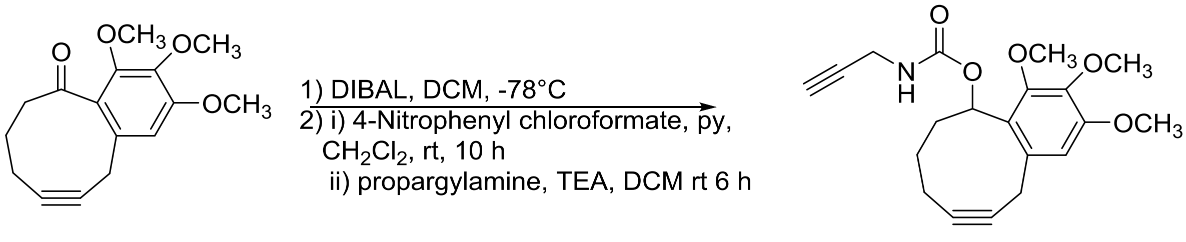


3

4

Benzocyclononyne ketone (4): To a solution of 2-(2-iodo-3,4,5-trimethoxybenzyl)-3-oxocyclohex-1-en-1-yl trifluoromethanesulfonate[2] (1.81g, 3.29 mmol, 1 equiv) in toluene (0.005M) under nitrogen was added TMEDA (0.492 ml, 3.29 mmol, 1 equiv). The reaction mixture was cooled to -78°C and was added *n*-BuLi (3.95 ml, 1.6M in hexanes, 3.95 mmol, 1.2 equiv) dropwise. The reaction remain stirring for 30 min at -78°C. After 30 min, the reaction was allowed to warm up to room temp and was left to stir 3h and 30 min. After completion, the mixture was quenched with water. The mixture was extracted with EtOAc three times, washed with brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica (15% EtOAc/hexanes) to give 0.469g (52%) benzocyclononyne **4** as light yellowish solid. NMR product agrees with known spectra in the literature[2].

4. Synthesis of BONO *N*-propargyl carbamate (1)



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1

Benzocyclononyne alcohol: To a solution of **4** (0.100g, 0.365 mmol, 1 equiv) in DCM (18. 2 ml, 0.02 M) under nitrogen at -78°C was added DIBAL dropwise (1.10 ml, 1 M in toluene, 1.10 mmol, 3 equiv). After 90 min at -78°C, the reaction mixture was quenched with by addition of 2 M NaOH (2.8 ml, 5.5 mmol, 5 equiv) at -78°C. The reaction was allowed to reach room temperature which was then added $MgSO_4$. After additional stirring for 15 min, the reaction mixture was filtered and concentrated under reduce pressure. The residue was purified by flash chromatography on silica

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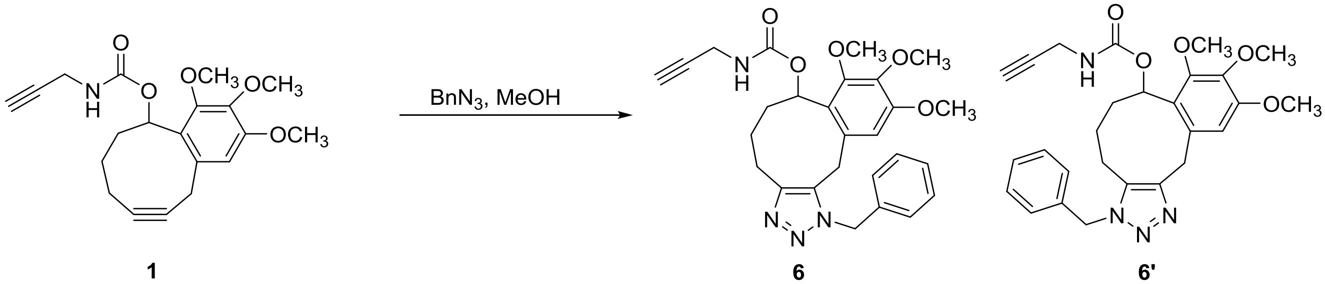
[2] J. Tummatorn, P. Batsomboon, R. J. Clark, I. V. Alabugin, G. B. Dudley, *J. Org. Chem.* 2012, ***77***, 2093-2097

(10% EtOAc/hexanes) to provide 0.087g (87%) of benzocyclononyne alcohol as a white solid. NMR product agrees with known spectra in the literature[3].

Benzocyclononyne carbamate (1): To a solution of benzocyclononyne alcohol (0.050g, 0.182 mmol, 1 equiv) in CH_2Cl_2 (1.82 ml, 0.1M) under nitrogen at 0°C was added pyridine (0.032 ml, 0.400 mmol, 2.2 equiv). 4-nitrophenyl chloroformate (0.055g, 0.273 mmol, 1.5 equiv) was then added to the cooled solution and left stirring at 0°C for 10 min. The reaction was allowed to reach room temp and left stirring for 10h (monitored by TLC).

Propargylamine (0.047 ml, 0.728 mmol, 4 equiv) was added to CH_2Cl_2 (3.64 ml, 0.1M) under nitrogen in a separate vessel. The reaction mixture was cooled to 0°C which was followed by the addition of trimethylamine (0.076 ml, 0.546 mmol, 3 equiv). The solution of the carbonated protected benzocyclononyne was then added dropwise to the cooled solution. After 10 min at 0°C, the reaction was permitted to reach ambient temperature and left stirring for 6h (monitored by TLC). After completion, the solution was quenched with a saturated solution of Na_2CO_3. The organic layer was washed four more times with saturated Na_2CO_3, washed with brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica (0 to 10% EtOAc/hexanes) to give 0.049g (76%) of **1** as a white solid.

5. General procedure of triazoles (Table 1)



Triazole (6&6') (entry 1): To solution of benzocyclononyne carbamate **1** (0.011g, 0.030 mmol, 1equiv) in MeOH (0.03 M) under nitrogen was added benzyl azide (0.004g, 0.033mmol, 1.1 equiv). The reaction left to run at room temp for 48 h. Crude ^1H NMR revealed the triazole formed on the strain cycloalkyne. Product was not further purified.

Triazole (6&6') (entry 2): To solution of benzocyclononyne carbamate **1** (0.0106g, 0.030 mmol, 1 equiv) in MeOH (0.03 M) under nitrogen was added benzyl azide (0.004g, 0.033 mmol, 1.1

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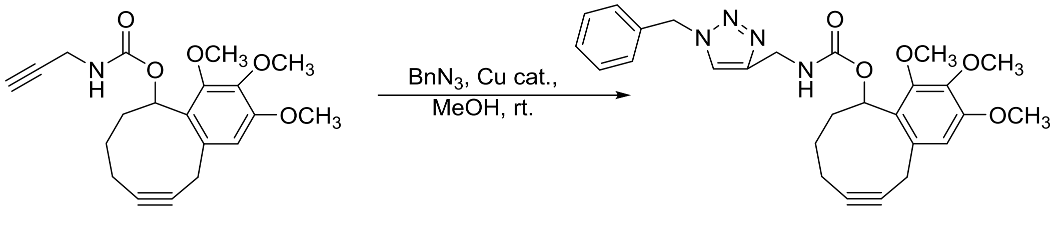
[3] J. Tummatorn, P. Batsomboon, R. J. Clark, I. V. Alabugin, G. B. Dudley, *J. Org. Chem.* 2012, ***77***, 2093-2097

equiv). The reaction was heated to 40°C went to completion in 16 h showed by TLC. The reaction was then concentrated under vaccuum to give an oil residue. The residue was purified by flash chromatography on silica (100% $CHCl_3$ to 0.5% MeOH/$CHCl_3$) to give 0.010g (70%) of **6 & 6'** as a light yellow oil.

Triazole (6&6') (entry 8): To solution of benzocyclononyne carbamate **1** (0.010g, 0.028 mmol, 1 equiv) in MeOH (0.2 M) under nitrogen was added benzyl azide (0.019g, 0.14 mmol, 5 equiv). The reaction was heated to 40°C and went to completion in 60 min showed by TLC. The reaction was then concentrated under vacuum to give an oil residue. The residue was purified by flash chromatography on silica (100% $CHCl_3$ to 0.5% MeOH/$CHCl_3$) to give 12.1 mg (88%) of **6 & 6'** as a light yellow oil.



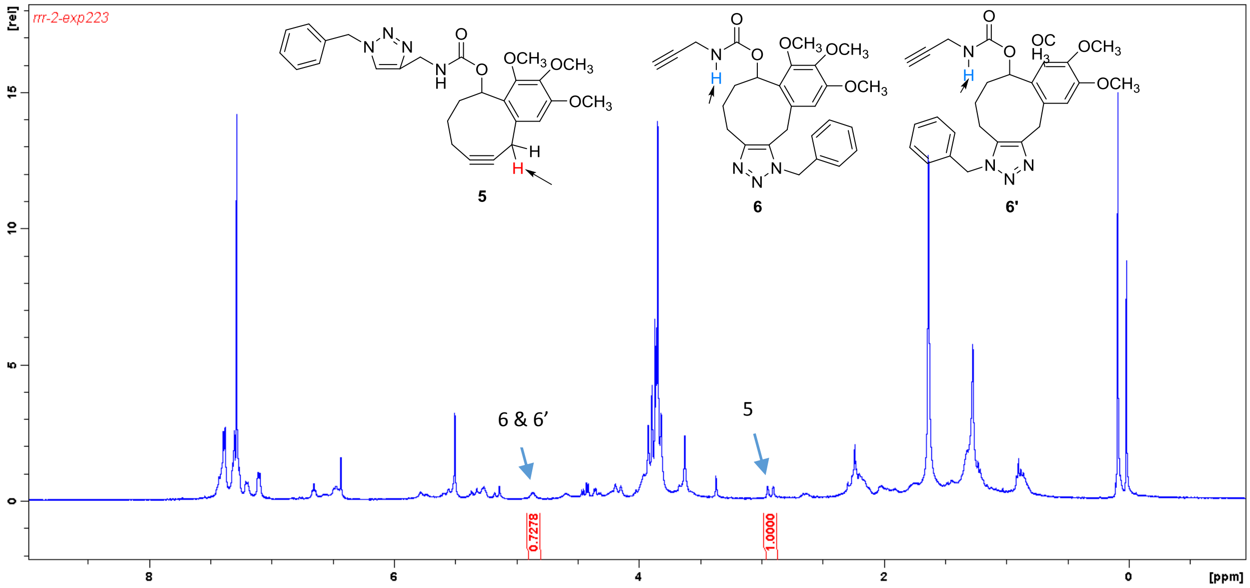
1 **5**

Triazole (5) (entry 3): To a solution of benzocyclononyne carbamate **1** (0.006g, 0.016 mmol, 1 equiv) in MeOH (0.016 M) was added benzyl azide (0.002g, 0.016 mmol, 1 equiv) followed by the addition of the combined solution of 0.25 M $CuSO_4$ (0.32 ml, 0.08 mmol, 5 equiv) and 0.5 M sodium ascorbate (0.224 ml, 0.112 mmol, 7 equiv). The reaction showed completion after 30 min by TLC. The reaction was diluted with DCM and then quenched with a saturated solution of NH_4OH. The organic layer was washed one more time with NH_4OH. The organic layer was collected and dried with sodium sulfate, and concentrated under vacuum to give an oil residue. The residue was purified by flash chromatography on silica (100% $CHCl_3$ to 0.5% MeOH/$CHCl_3$) to give 6.8 mg of **5** (87%) as a colorless oil.

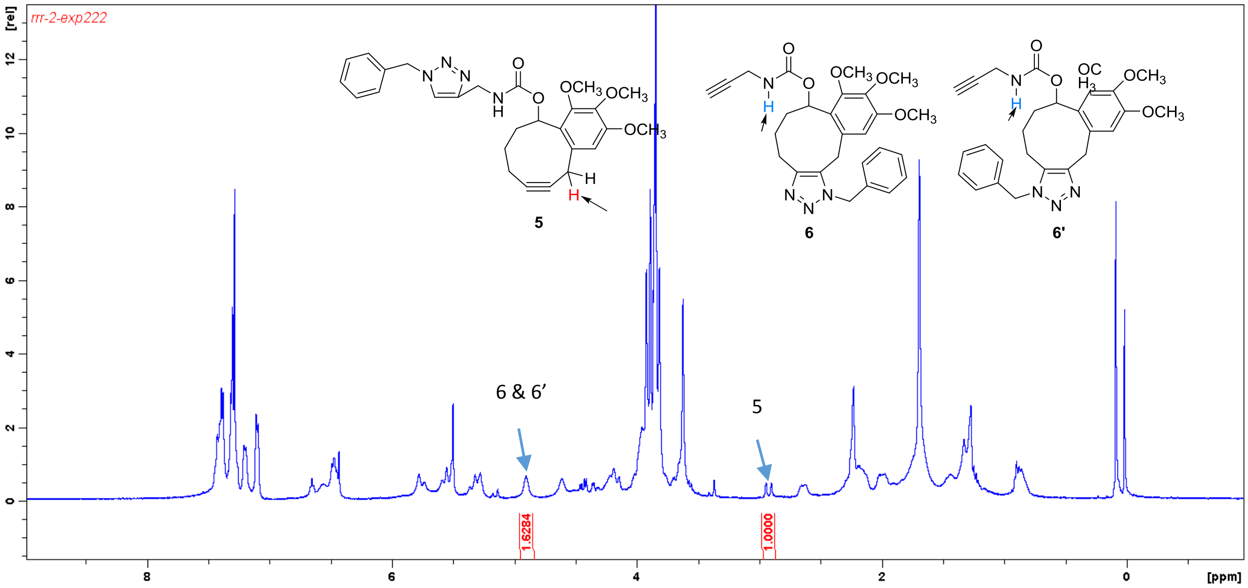
Triazole (5) (entry 4): To a solution of benzocyclononyne carbamate (0.005 g, 0.014 mmol, 1 equiv) in MeOH (0.009 M) was added benzyl azide (0.002 g, 0.015 mmol, 1.1 equiv) followed by the addition of the combined solution of 0.25 M $CuSO_4$ (0.084 ml, 0.021 mmol, 1.5 equiv) and 0.5 M sodium ascorbate (0.059 ml, 0.029 mmol, 2.1 equiv). The reaction showed completion after 45 min by TLC. The reaction was diluted with DCM and then quenched with a saturated solution of NH_4OH. The organic layer was washed one more time with NH_4OH. The organic layer was collected and dried with sodium sulfate, and concentrated under vacuum to give an oil residue.

The residue was purified by flash chromatography on silica (100% $CHCl_3$ to 0.5% MeOH/$CHCl_3$) to give 4.4 mg **5** (65%) as a colorless oil.

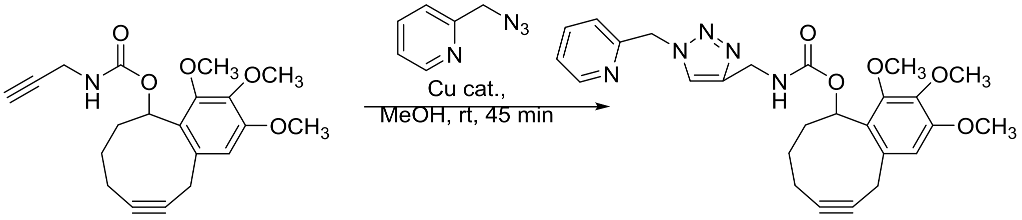
Triazole (5 and 6&6') (entry 5): To a solution of benzocyclononyne carbamate **1** (6.9 mg, 0.019 mmol, 1 equiv) in MeOH (0.024 M) was added benzyl azide (0.003 g, 0.021 mmol, 1.1 equiv) followed by the addition of the combined solution of 0.25 M $CuSO_4$ (0.076 ml, 0.019 mmol, 1 equiv) and 0.5 M sodium ascorbate (0.054 ml, 0.027 mmol, 1.4 equiv). The reaction showed completion after 45 min by TLC. The reaction was diluted with DCM and then quenched with a saturated solution of NH_4OH. The organic layer was washed one more time with NH_4OH. The organic layer was collected and dried with sodium sulfate, and concentrated under vacuum to give an oil residue. The residue was purified by flash chromatography on silica (100% $CHCl_3$ to 0.5% MeOH/$CHCl_3$) to give products 4.6 mg (50%) **5** and **6 & 6'** in a 1:0.7 ratio favoring **5** as a light yellow oil.



Triazole (5 and 6&6') (entry 6): To a solution of benzocyclononyne carbamate **1** (0.010g, 0.027 mmol, 1 equiv) in MeOH (0.054 M) was added benzyl azide (0.04g, 0.03 mmol, 1.1 equiv) followed by the addition of the combined solution of 0.25 M $CuSO_4$ (0.056 ml, 0.014 mmol, 0.5 equiv) and 0.5 M sodium ascorbate (0.136 ml, 0.068 mmol, 2.5 equiv). The reaction showed completion after 24 h by TLC. The reaction was diluted with DCM and then quenched with a saturated solution of NH_4OH. The organic layer was washed one more time with NH_4OH. The organic layer was collected and dried with sodium sulfate, and concentrated under vacuum to give an oil residue. The residue was purified by flash chromatography on silica (100% $CHCl_3$ to 0.5% MeOH/$CHCl_3$) to give 6.6 mg (50%) **5** and **6 & 6'** in a 1:1.6 ratio favoring **6 & 6'** as a light yellow oil.



Triazole (5) (entry 7): To a solution of benzocyclononyne carbamate **1** (0.007g, 0.02 mmol, 1 equiv) and TBTA (0.011g, 0.02 mmol, 1 equiv) in MeOH (0.024 M) was added benzyl azide (0.003g, 0.022 mmol, 1.1 equiv) followed by the addition of the combined solution of 0.25 M $CuSO_4$ (0.08 ml, 0.02 mmol, 1 equiv) and 0.5 M sodium ascorbate (0.056 ml, 0.028 mmol, 1.4 equiv). The reaction showed completion after 45 min by TLC. The reaction was diluted with DCM and then quenched with a saturated solution of NH_4OH. The organic layer was washed one more time with NH_4OH. The organic layer was collected and dried with sodium sulfate, and concentrated under vacuum to give an oil residue. The residue was purified by flash chromatography on silica (100% $CHCl_3$ to 0.5% MeOH/$CHCl_3$) to give 8.2 mg (84%) of **5** as a colorless oil.



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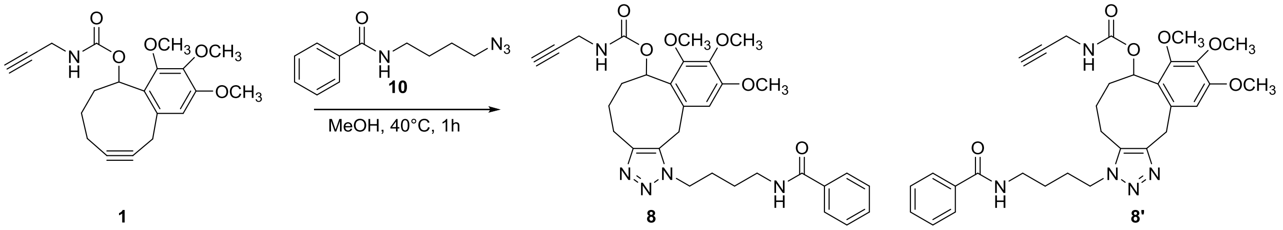
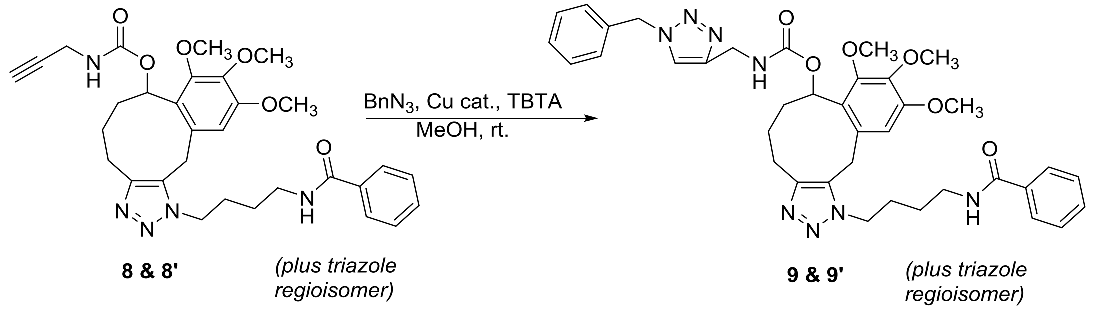
7

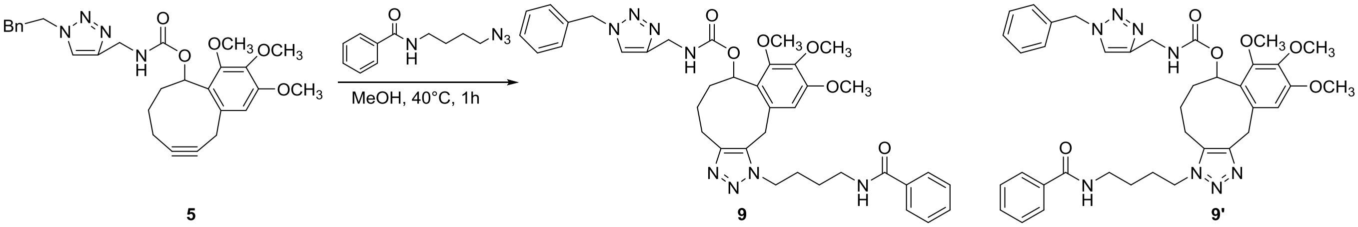
Triazole (7): To a solution of benzocyclononyne carbamate **1** (6.8 mg, 0.019 mmol, 1 equiv) in MeOH (0.024 M) was added picolyl azide (0.003g, 0.021mmol, 1.1 equiv) followed by the addition of the combined solution of 0.25 M $CuSO_4$ (0.076 ml, 0.019 mmol, 1 equiv) and 0.5 M sodium ascorbate (0.054 ml, 0.027 mmol, 1.4 equiv). The reaction showed completion after 24 h by TLC. The reaction was diluted with DCM and then quenched with a saturated solution of NH_4OH. The organic layer was washed one more time with NH_4OH. The organic layer was collected and dried with sodium sulfate, and concentrated under vacuum to give an oil residue. The residue was purified by flash chromatography on silica (100% $CHCl_3$ to 0.5% MeOH/$CHCl_3$) to give 7.3 mg (79%) of **7** as a colorless oil.



Triazole (8 & 8'): To solution of benzocyclononyne carbamate **1** (7.8 mg, 0.022 mmol, 1 equiv) in MeOH (0.2 M) under nitrogen was added *N*-(4-azidobutyl)benzamide **10** (0.024g, 0.11 mmol, 5 equiv). The reaction was heated to 40°C and went to completion in 60 min showed by TLC. The reaction was then concentrated under vacuum to give an oil residue. The residue was purified by flash chromatography on silica (100% $CHCl_3$ to 2.5% MeOH/$CHCl_3$) to give 10.8 mg (86%) of **8 and 8'** as a white solid.

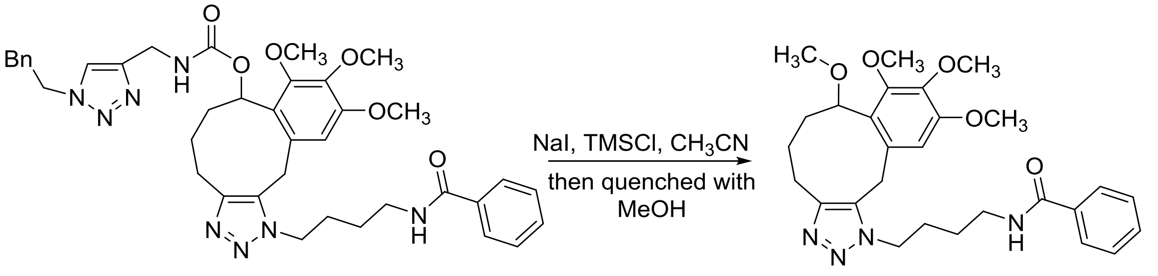


Bis-triazole (9 & 9') : To a solution of triazole **8 & 8'** (0.016g, 0.027 mmol, 1 equiv) and TBTA (0.022g, 0.041 mmol, 1.5 equiv) in MeOH (0.024 M) was added benzyl azide (0.006g, 0.041 mmol, 1.5 equiv) followed by the addition of the combined solution of 0.25 M $CuSO_4$ (0.164 ml, 0.041 mmol, 1.5 equiv) and 0.5 M sodium ascorbate (0.07 ml, 0.057 mmol, 2.1 equiv). The reaction showed completion after 45 min by TLC. The reaction was diluted with DCM and then quenched with a saturated solution of NH_4OH. The organic layer was washed one more time with NH_4OH. The organic layer was collected and dried with sodium sulfate, and concentrated under vacuum to give an oil residue. The residue was purified by flash chromatography on silica (100% $CHCl_3$ to 2.5% MeOH/$CHCl_3$) to give 13.4 mg (70%) of **9 and 9'** as a white solid.



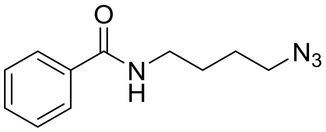
Bis-triazole (9 & 9'): To a solution of triazole (0.018g, 0.037 mmol, 1 equiv) in MeOH (0.2 M) under nitrogen was added *N*-(4-azidobutyl)benzamide **10** (0.041g, 0.187 mmol, 5 equiv). The reaction was heated to 40°C and went to completion in 60 min showed by TLC. The reaction was then concentrated under reduced pressure to give an oil residue. The residue was purified by flash chromatography on silica (100% $CHCl_3$ to 2.5% MeOH/$CHCl_3$) to give 24.8 mg (92%) of **9 and 9'** as a white solid.

6. General procedure for cleavage of tethered triazole of the Bis-triazole

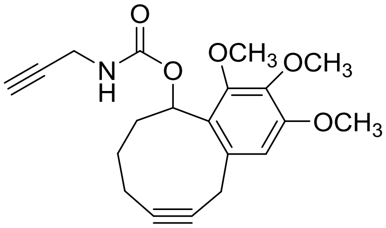


N-(4-(7,8,9,10-tetramethoxy-5,6,7,12-tetrahydrobenzo[4,5]cyclonona[1,2-d][1,2,3]triazol-3(4H)-yl)butyl)benzamide (11): To a solution of TMS-Cl (0.005 ml, 0.042 mmol, 4 equiv) in CH_3CN (0.1 M) was added NaI (0.006 g, 0.042 mmol, 4 equiv). The mixture was then transported into a vial containing the bis-triazole (0.006g, 0.009 mmol, 1 equiv). The reaction was left to stir at room temperature overnight. The reaction was then quenched with MeOH (0.2 ml) and stirred for 5 min. The reaction was diluted with water (3 ml) and extracted with DCM (3 x 3 ml). The organic layers were then collected, dried with sodium sulfate and concentrated under reduced pressure to give an oil residue. The residue was purified by flash chromatography on silica (100% $CHCl_3$ to 2.5% MeOH/$CHCl_3$) to give 2.3 mg (50%) of triazole regioisomers **11** as a light yellowish oil.

7. Characterization data of all compounds

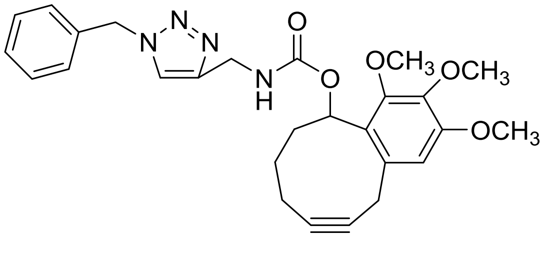


N-(4-azidobutyl)benzamide
Mass = 0.434g; Yield = 45%
Yellowish oil
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 7.69 Hz, 2H), 7.54-7.40 (m, 3H), 6.20 (broad s, 1H), 3.51 (q, *J* = 6.59, 2H), 3.56 (t, *J* = 6.04, 2H), 1.71 (m, 4H) ppm;
^{13}C NMR (600 MHz, $CDCl_3$): δ 167.7, 134.6, 131.5, 130.1, 128.6, 128.4, 126.8, 51.1, 39.4, 27.0, 26.3 ppm;
HRMS (ESI+) calcd for $C_{11}H_{14}N_4ONa$ $(M+Na)^+$ 241.1065 found 241.1068



1

Compound 1
Mass = 49.5 mg; Yield = 76%
White solid
Melting point = 113°C
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.70 (t, *J* = 5.87 Hz, 1H), 6.41 (s, 1H), 4.85 (broad s, 1H), 4.18 (dt, *J* = 17.57, 2.56 Hz, 1H), 4.02-3.80 (m, 12H (CH_3 singlets, 3.89, 3.83, 3.81)), 2.90 (d, *J* = 17.89 Hz, 1H), 2.35-2.08 (m, 5H (CH, t, *J* = 2.56 Hz)), 1.98-1.87 (m, 1H), 1.82-1.71 (m, 1H) ppm;
^{13}C NMR (600 MHz, $CDCl_3$): δ 156.2, 154.1, 152.2, 141.6, 135.9, 126.6, 108.1, 91.7, 91.0, 79.80, 75.0, 71.5, 61.0, 60.6, 55.8, 35.7, 30.7, 27.0, 26.3, 20.0 ppm;
HRMS (ESI+) calcd for $C_{20}H_{23}NO_5Na$ $(M+Na)^+$ 380.1474 found 380.1470



5

Compound 5

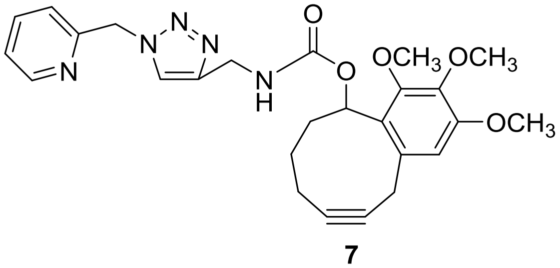
Mass = 16.9 mg; Yield = 87%

Colorless oil

^{1}H NMR (600 MHz, CDCl$_3$): δ 7.38-7.32 (m, 4H), 7.27-7.21 (m, 2H), 6.63 (t, 1H), 6.41 (s, 1H), 5.47 (s, 2H), 5.25 (t, 1H), 4.41 (dd, *J* = 15.36, 6.04 Hz, 1H), 4.31 (dd, *J* = 15.3, 5.44 Hz, 1H), 4.14 (d, *J* = 17.75 Hz, 1H), 3.85-3.80 (m, 9H), 2.90 (d, *J* = 17.75 Hz, 1H), 2.30-2.09 (m, 4H), 1.93-1.86 (m, 1H), 1.78-1.71 (m, 1H) ppm;

^{13}C NMR (600 MHz, CDCl$_3$): δ 156.6, 154.1, 152.2, 145.5, 141.6, 135.7, 134.5, 129.1, 128.7, 128.0, 126.8, 121.7, 108.0, 91.7, 90.9, 74.7, 61.0, 60.6, 55.8, 54.1, 36.4, 35.7, 27.0, 26.3, 19.9 ppm;

HRMS (ESI+) calcd for $C_{27}H_{31}N_4O_5$ $(M+H)^+$ 491.2294 found 491.2287



7

Compound 7

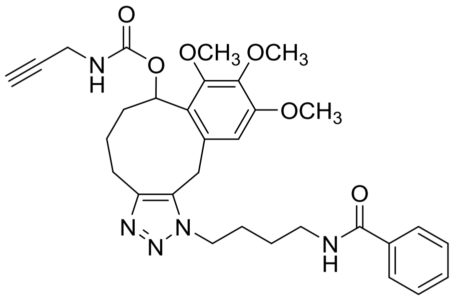
Mass = 7.9 mg; Yield = 79%

Colorless oil

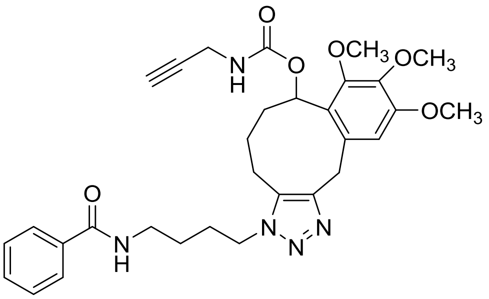
^{1}H NMR (600 MHz, CDCl$_3$): δ 8.58 (s, 1H), 7.68 (t, *J* = 7.86 Hz, 1H), 7.60 (s, 1H), 7.26 (s, 1H CDCl$_3$ excluded), 7.16 (d, *J* = 7.26 Hz, 1H), 6.64 (s, 1H), 6.41 (s, 1H), 5.61 (s, 1H), 5.26 (broad s, 1H), 4.45 (dd, *J* = 15.12, 5.44 Hz, 1H), 4.35 (m, 1H), 4.15 (d, *J* = 18.14 Hz, 1H), 3.89-3.76 (m, 9H), 2.90 (d, *J* = 17.54 Hz, 1H), 2.31-2.09 (m, 4H), 1.95-1.86 (m, 1H), 1.79-1.69 (m, 1H) ppm;

^{13}C NMR (600 MHz, CDCl$_3$): δ 156.7, 154.3, 154.1, 149.8, 145.5, 141.6, 137.3, 135.7, 126.8, 123.4, 122.4, 122.3, 108.0, 91.7, 90.90, 74.7, 61.0, 60.6, 55.8, 55.6, 36.4, 35.7, 27.0, 26.3, 19.9 ppm;

HRMS (ESI+) calcd for $C_{26}H_{30}N_5O_5$ $(M+H)^+$ 492.2246 found 492.2245



8



8'

Compound 8

Mass = 10.8 mg; Yield = 86%

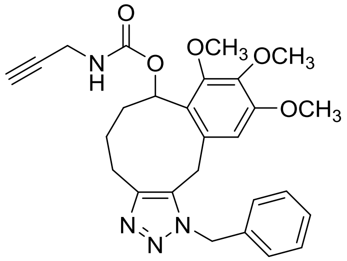
White solid

Melting point = 78°C

^{1}H NMR (400 MHz, CDCl$_3$): δ 7.68 (t, *J* = 7.06 Hz, 4H), 7.58-7.37 (m, 7H), 6.76-6.68 (m, 1H), 6.64-6.44 (m, 4H), 6.36-6.27 (broad s, 1H), 5.66-5.55 (broad s, 1H), 5.11-5.01 (m, 1H), 4.59-4.27 (m, 4H), 4.19 (t, *J* = 7.06 Hz), 4.04-3.65 (m, 24H), 3.59-3.42 (m, 4H), 2.62-2.51 (broad m, 1H), 2.21 (t, *J* = 2.52 Hz, 1H), 2.19-1.43 (m, 18H) ppm;

^{13}C NMR (600 MHz, CDCl$_3$): δ 167.7, 155.2, 153.7, 152.2, 134.2, 133.0, 131.5, 131.4, 129.9, 128.5, 128.5, 128.3, 126.9, 126.9, 110.7, 79.6, 71.5, 71.3, 61.5, 60.8, 60.8, 55.8, 47.3, 47.2, 39.2, 39.1, 30.7, 30.6, 29.3, 29.1, 27.6, 27.1, 26.5, 26.5, 24.0 21.8, 18.8 ppm;

HRMS (ESI+) calcd for $C_{31}H_{37}N_5O_6$ $(M+Na)^+$ 598.2641 found 598.2645



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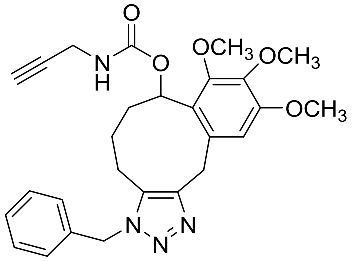


6'

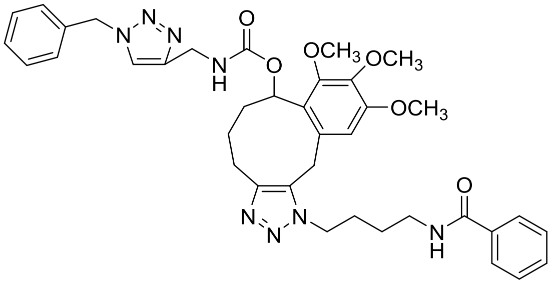
Compound 6

Mass = 13 mg; Yield = 88%

Light yellow oil

^{1}H NMR (600 MHz, CDCl$_3$): δ 7.43-7.32 (m, 3H), 7.31-7.24 (m, 5H), 7.20-7.13 (broad m, 2H), 7.10-7.05 (m, 2H), 6.58-6.41 (m, 3H), 5.79-5.68 (m, 2H), 5.58-5.45 (m, 2H), 5.32-5.21 (broad singlet, 1H), 4.95 (broad singlet, 1H), 4.68-4.41 (m, 2H), 4.17 (d, *J* = 14.98 Hz, 2H), 4.00-3.72 (m,

21H), 3.65-3.55 (m, 4H), 2.66-2.56 (m, 1H), 2.25-2.17 (m, 2H), 2.15-2.07 (broad singlet, 1H), 2.00-1.91 (broad singlet, 1H), 1.84-1.55 (m, 6H), 1.48-1.19 (m, 3H), 0.83 (broad singlet, 1H) ppm;
^{13}C NMR (600 MHz, CDCl$_3$): δ 153.7, 152.2, 145.4, 135.5, 135.4, 129.7, 129.0, 128.9, 128.3, 127.1, 127.0, 110.2, 79.6,79.6. 71.6, 71.6, 69.6, 61.4, 60.8, 55.8, 55.7, 52.3, 51.8, 30.7, 29.4, 28.9, 24.1, 23.1, 22.1, 19.1 ppm;
HRMS (ESI+) calcd for $C_{27}H_{31}N_4O_5$ $(M+H)^+$ 491.2294 found 491.2292



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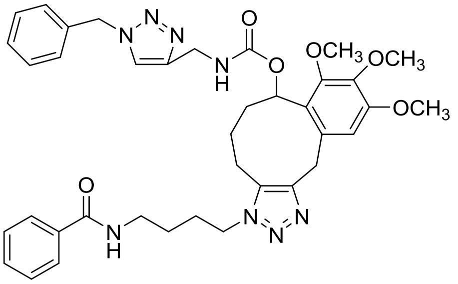
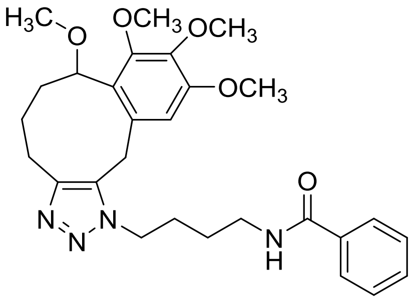


9'

Compound 9
Mass = 24.8 mg; Yield = 92%
White solid
Melting point = 88°C-92°C
^{1}H NMR (600 MHz, CDCl$_3$): δ 7.81-7.72 (m, 4H), 7.50-7.30 (m, 13H), 7.25-7.18 (m, 3H), 6.66 (m, 1H), 6.58-6.43 (m, 4H), 6.30 (s, 1H), 5.72 (broad singlet, 1H), 5.50-5.39 (m, 5H), 4.52-4.26 (m, 7H), 4.18 (t, *J* = 6.96 Hz, 2H), 3.93-3.69 (m, 18H), 3.56-3.49 (m, 2H), 3.46 (q, *J* = 6.66 Hz, 2H), 2.60-2.51 (m, 1H), 2.12-1.45 (m, 22H), 1.32-1.18 (broad singlet, 4H) ppm;
^{13}C NMR (600 MHz, CDCl$_3$): δ 167.9, 167.6, 155.6, 153.6, 152.2, 145.4, 141.6, 134.4, 134.3, 132.8, 131.4, 129.9, 129.0, 128.7, 128.5, 128.0, 126.9, 121.8, 110.8, 69.1, 61.4, 60.8, 55.8, 54.1, 53.4, 47.4, 47.1, 39.1, 39.1, 36.4, 29.6, 29.3, 29.0, 27.6, 27.2, 26.5, 26.5, 24.0, 21.8, 18.8 ppm;
HRMS (ESI+) calcd for $C_{38}H_{44}N_8O_6Na$ (M+Na) 731.3281 found 731.3285



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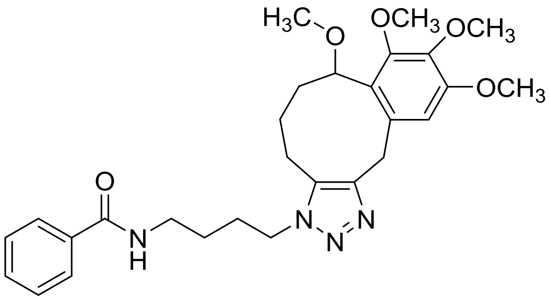


11'

N-(4-(7,8,9,10-tetramethoxy-5,6,7,12-tetrahydrobenzo[4,5]cyclonona[1,2-d][1,2,3]triazol-3(4H)-yl)butyl)benzamide (11)

Mass = 2.5 mg; Yield = 50%

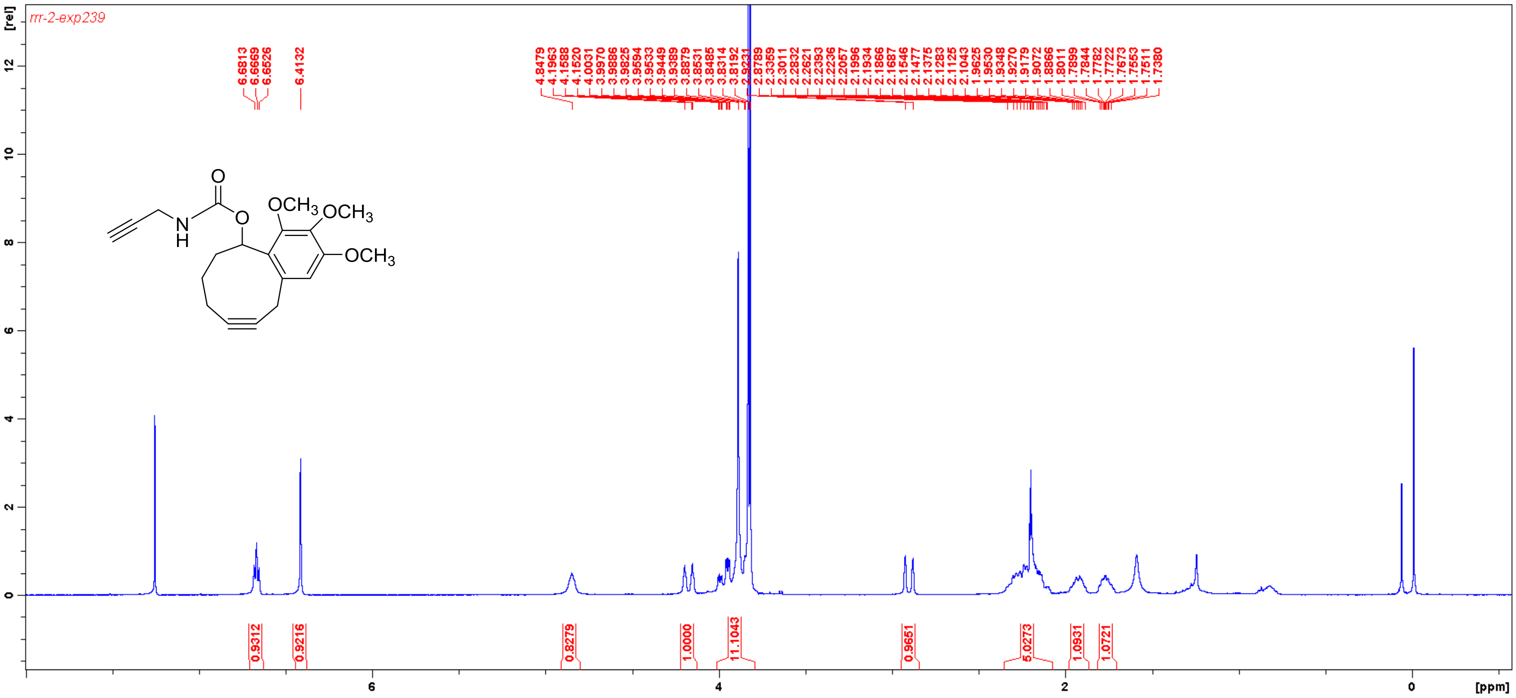
Light yellowish oil

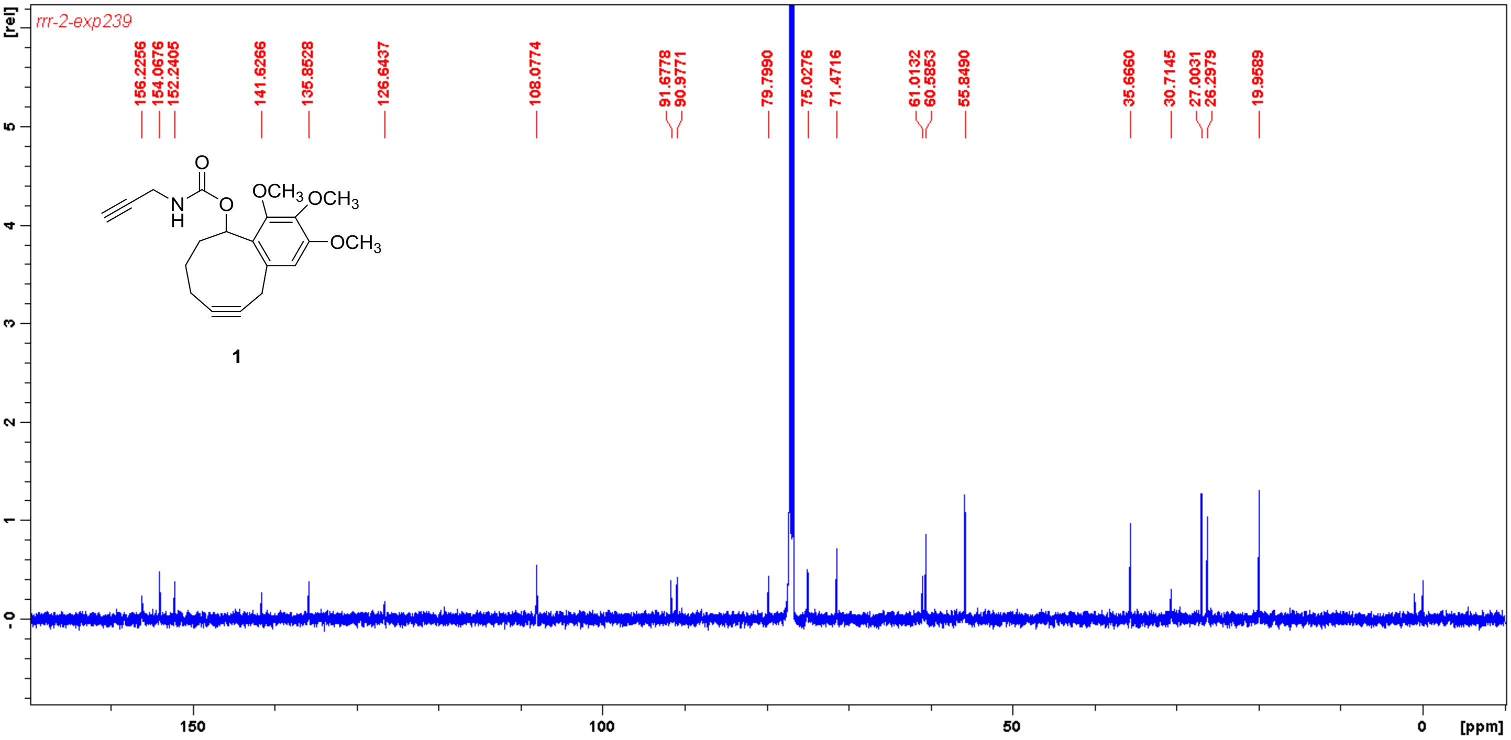
^{1}H NMR (600 MHz, CDCl$_3$): δ 7.78 (dd, *J* = 15.59, 6.99 Hz, 2H), 7.50 (t, *J* = 7.53, 1H), 7.43 (t, *J* = 7.53 Hz, 2H), 6.55-6.43 (m, 1H), 6.38 (m, 1H), 6.32 (s, 1H), 5.03-4.96 (m, 1H), 4.61 (d, *J* = 16.13 Hz, 1H), 4.49-4.42 (m, 1H), 4.40-4.33 (m, 1H), 4.20 (t, *J* = 6.99 Hz, 1H), 3.94-3.69 (m, 10H), 3.60-3.52 (m, 1H), 3.47 (q, *J* = 6.45 Hz, 1H), 3.27-3.19 (2 broad singlets, 3H), 2.62-2.56 (m, 1H), 2.11-2.04 (m, 2H), 1.93-1.82 (m, 2H), 1.79-1.69 (m, 2H), 1.67-1.61 (m, 2H), 1.56-1.23 (m, 6H)

^{13}C NMR (?, CDCl$_3$): δ 167.6, 153.2, 134.4, 131.5, 130.0, 128.6, 126.9, 126.9, 111.0, 74.9, 61.2, 60.9, 60.8, 56.0, 55.9, 55.8, 47.4, 47.0, 39.3, 39.3, 31.2, 30.0, 29.7, 28.5, 27.8, 27.3, 26.6,, 26.5, 24.3, 22.1, 19.2

HRMS (ESI+) calcd for $C_{28}H_{38}N_3O_5Na$ (M+Na) 531.2583 found 531.2576

8. Copies of ^{1}H-NMR and ^{13}C-NMR spectra of compounds





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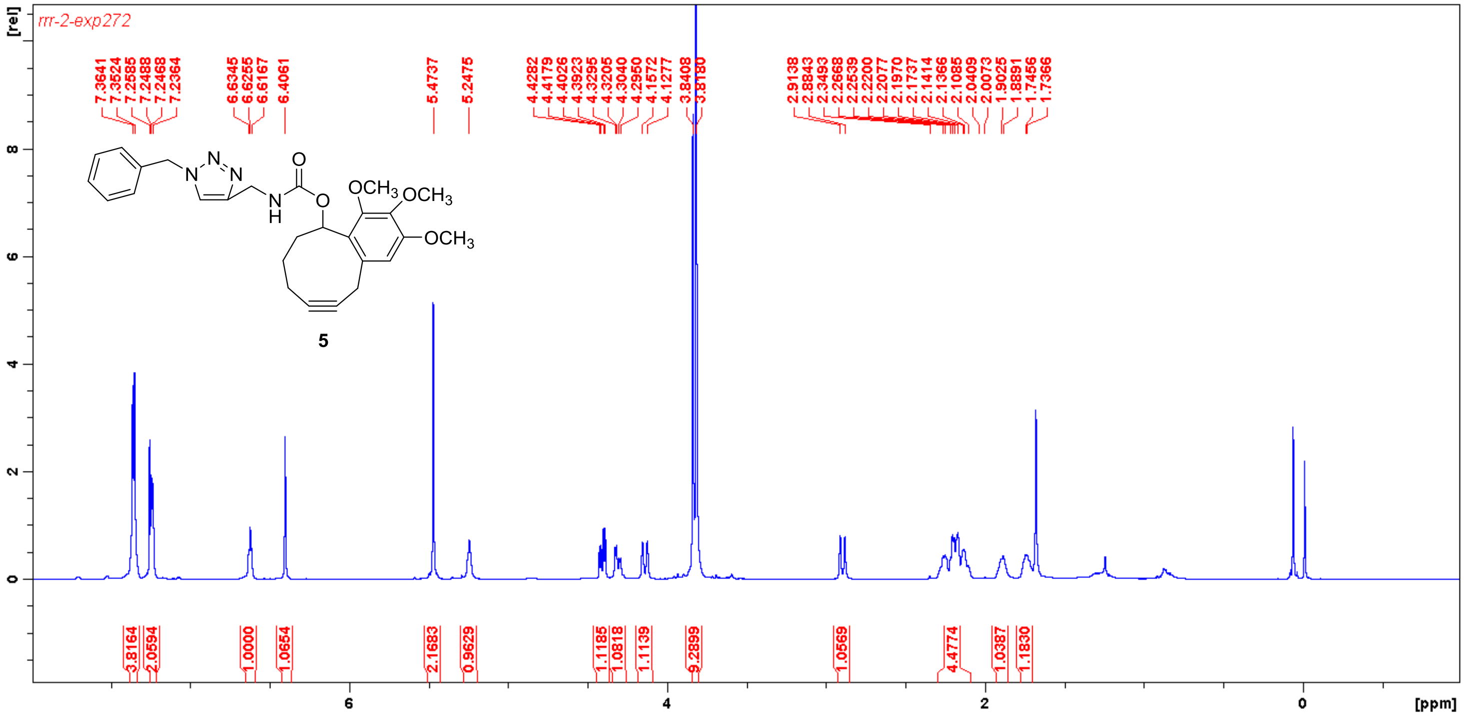
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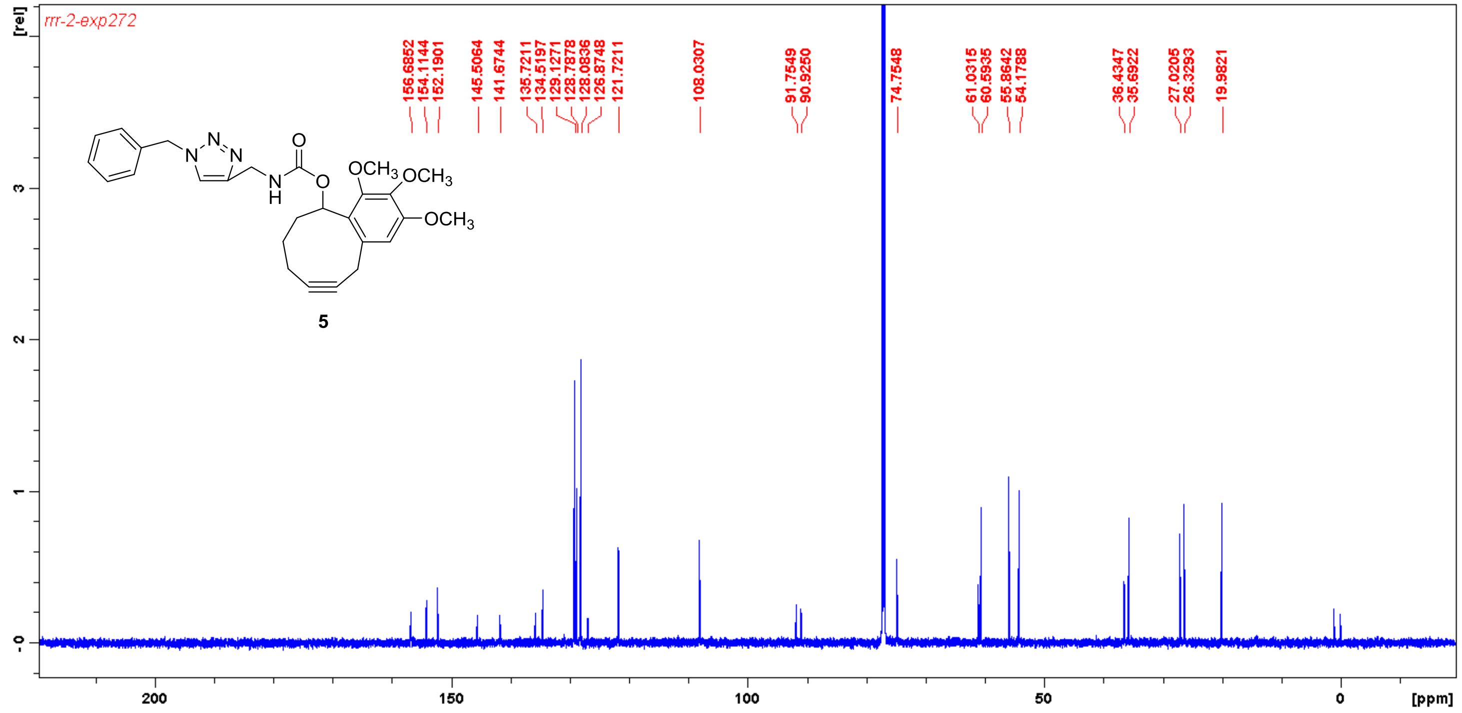
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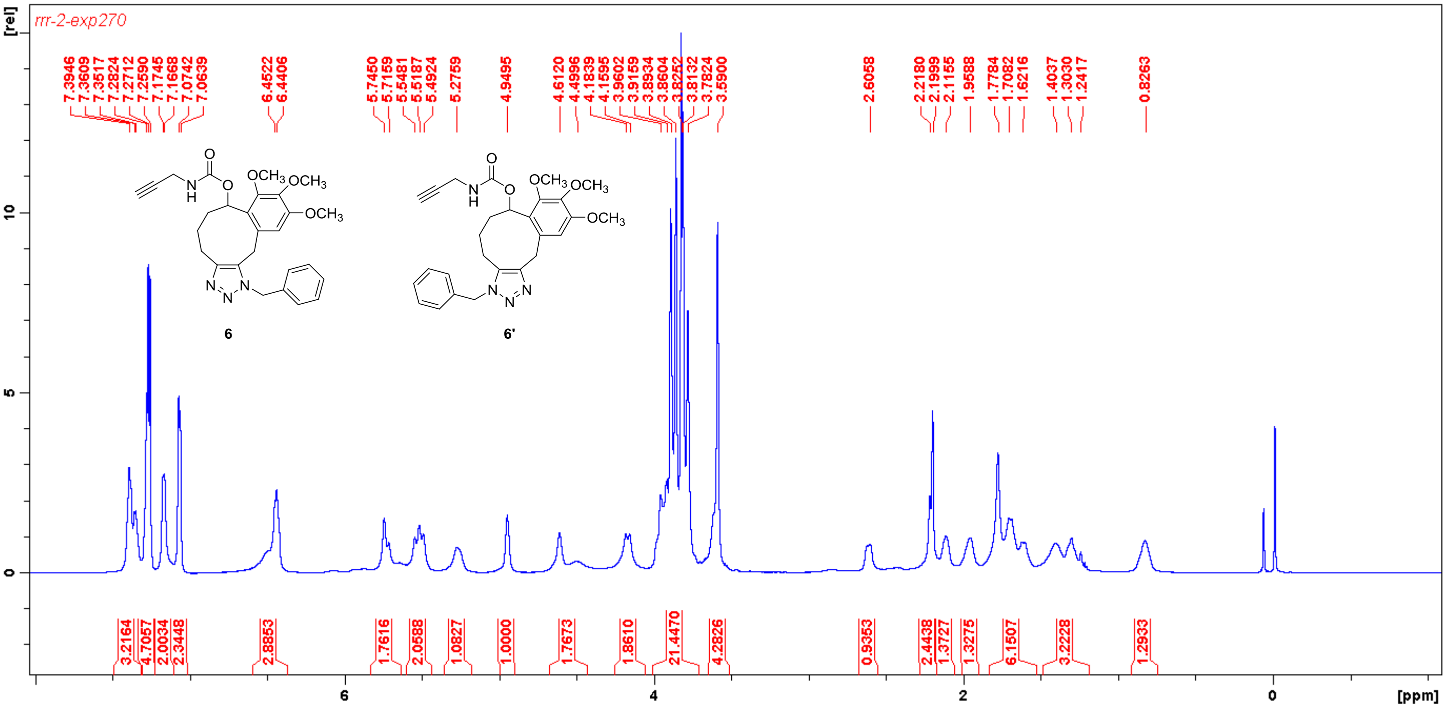
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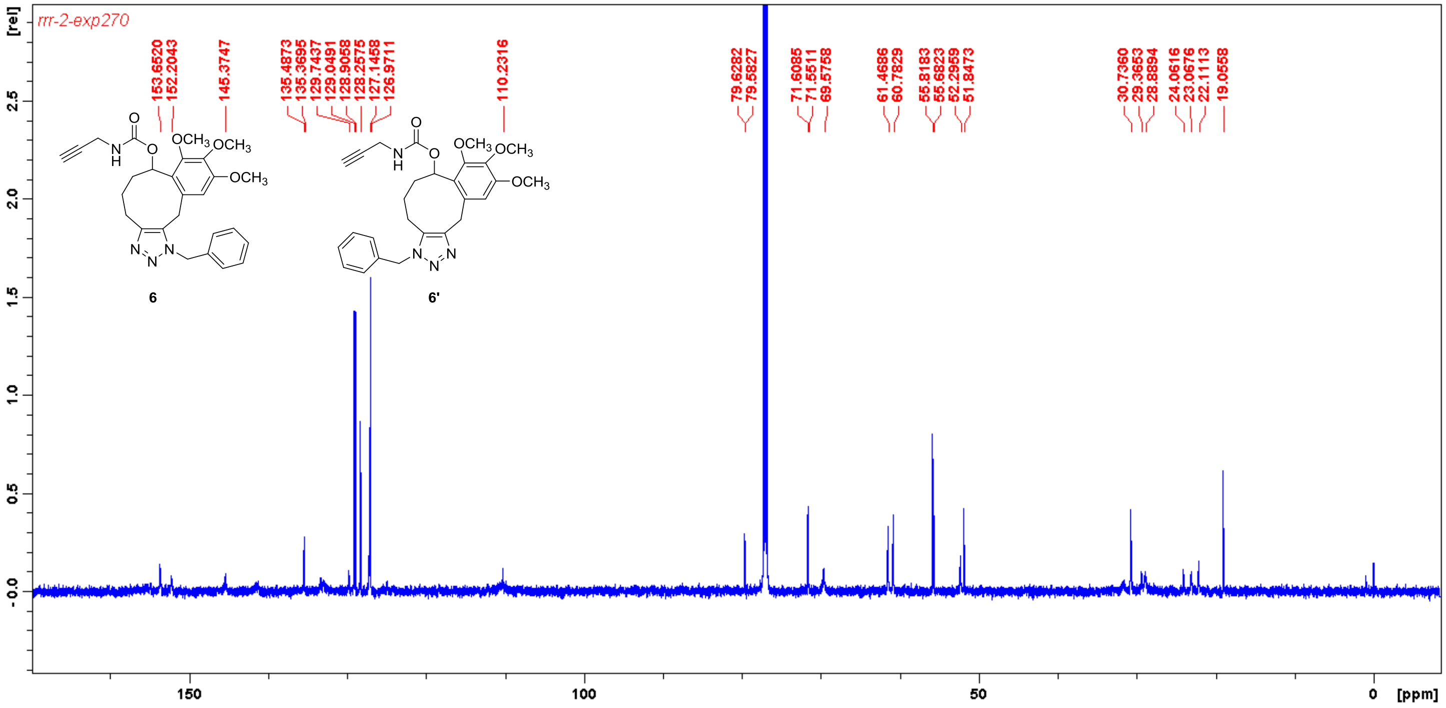
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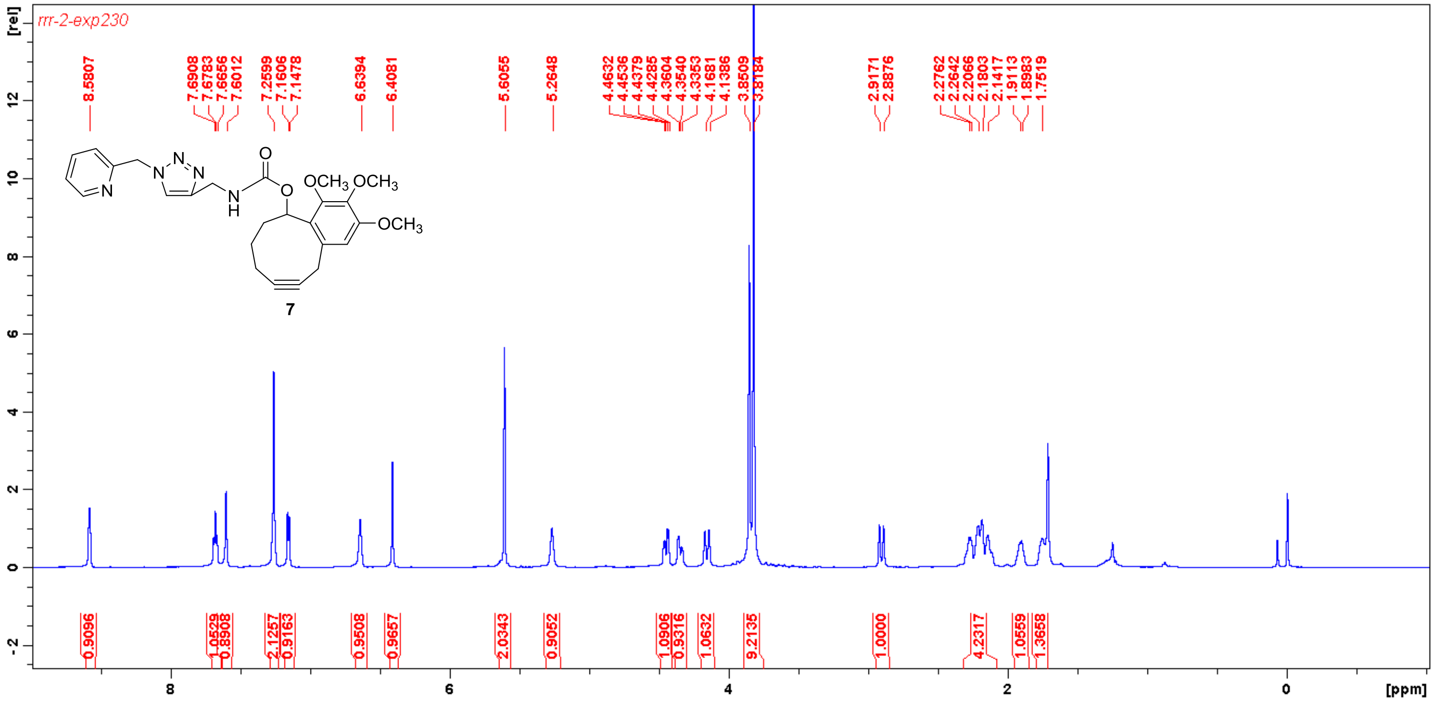
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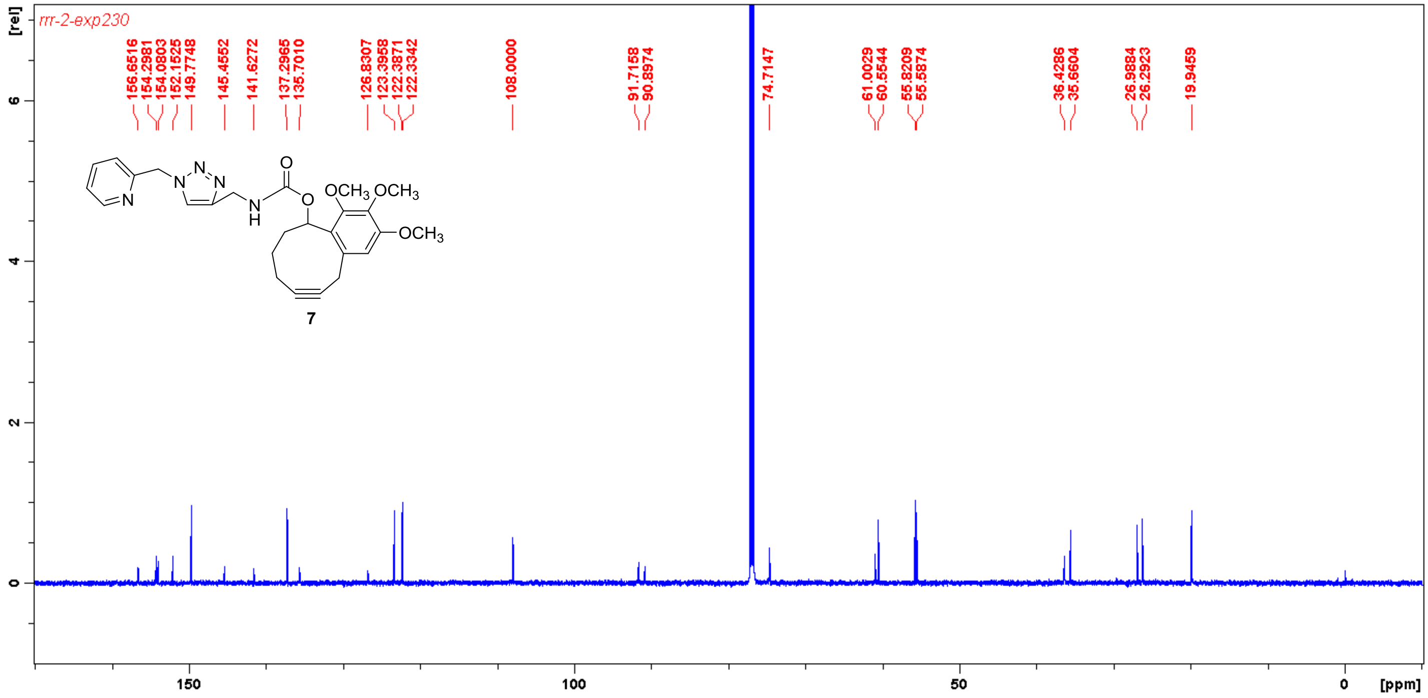
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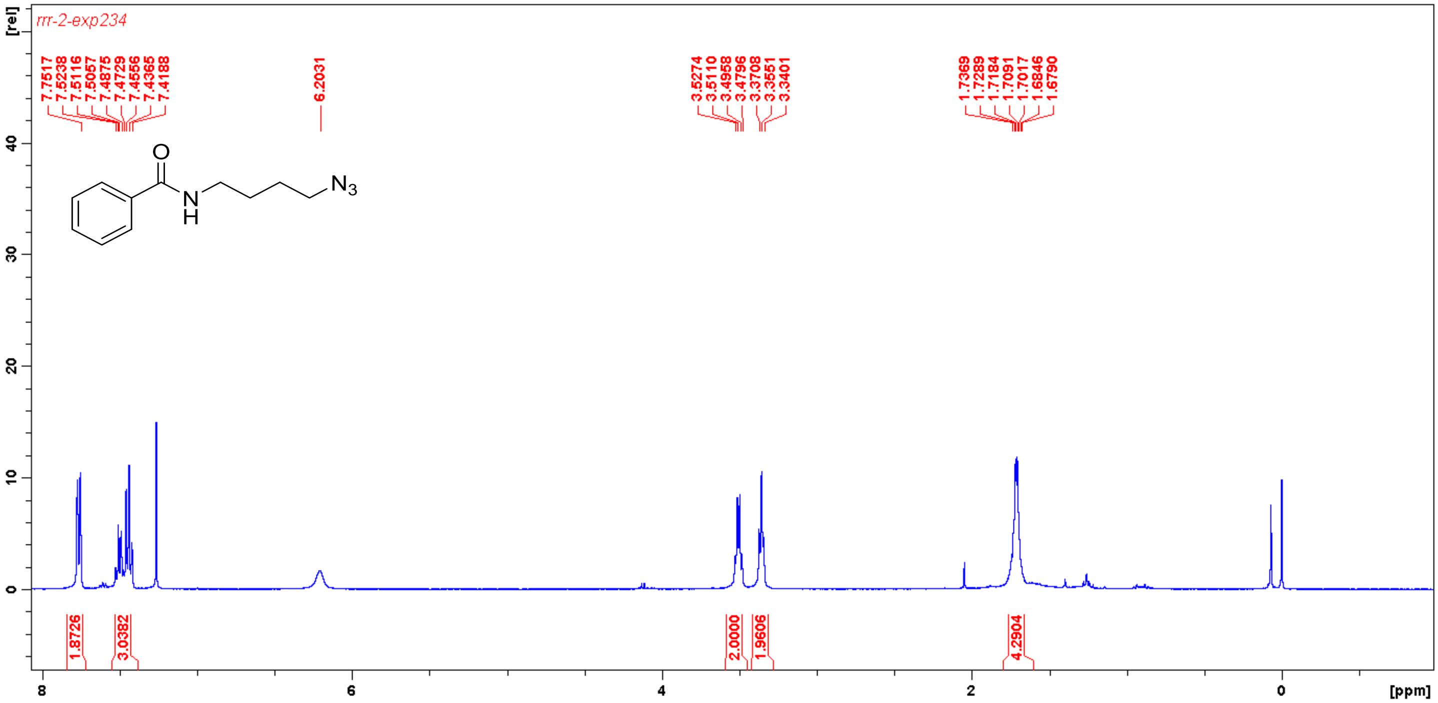
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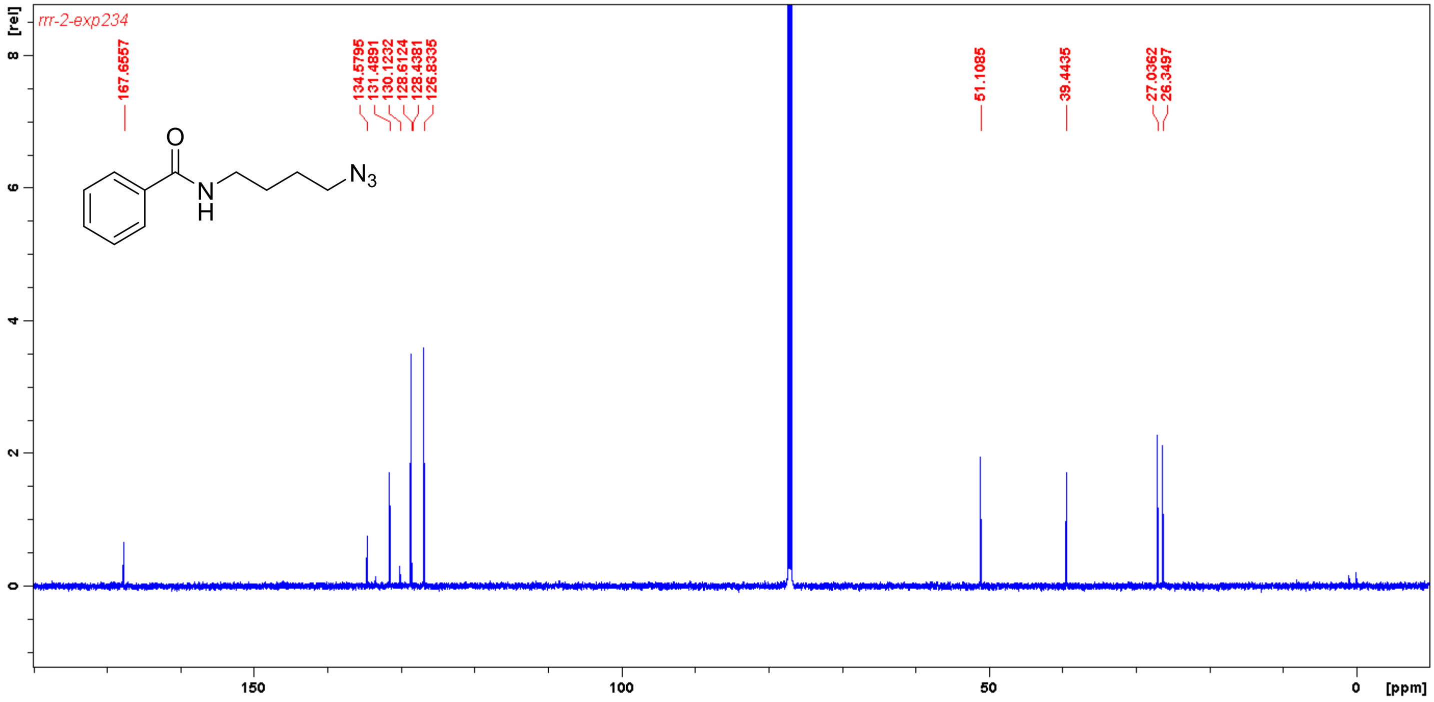
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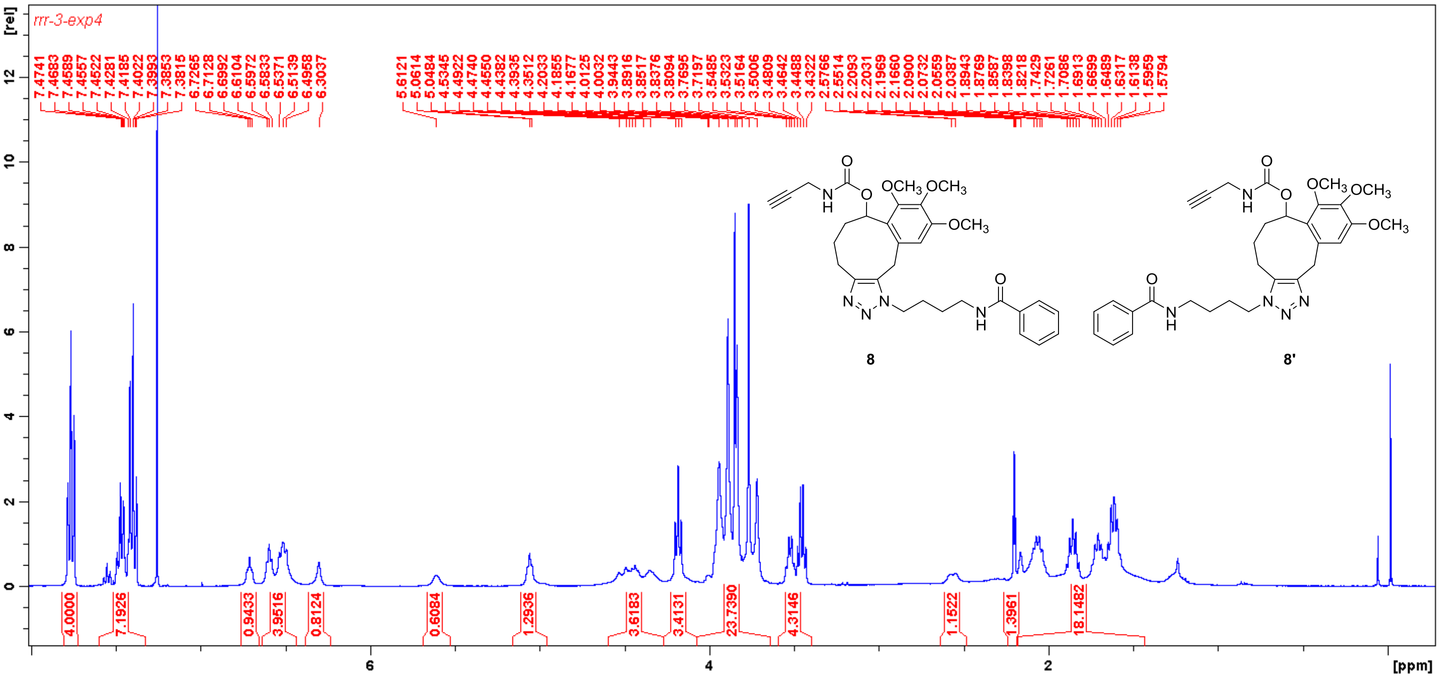
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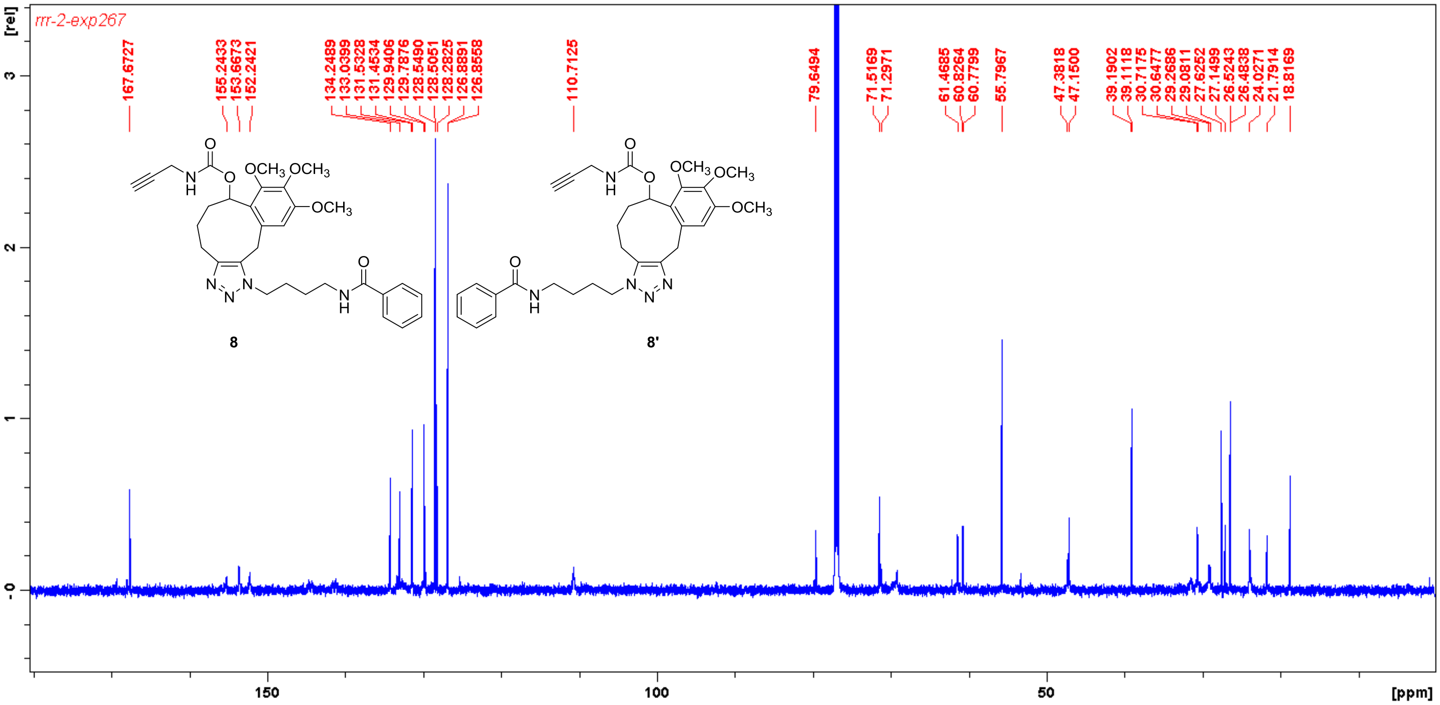
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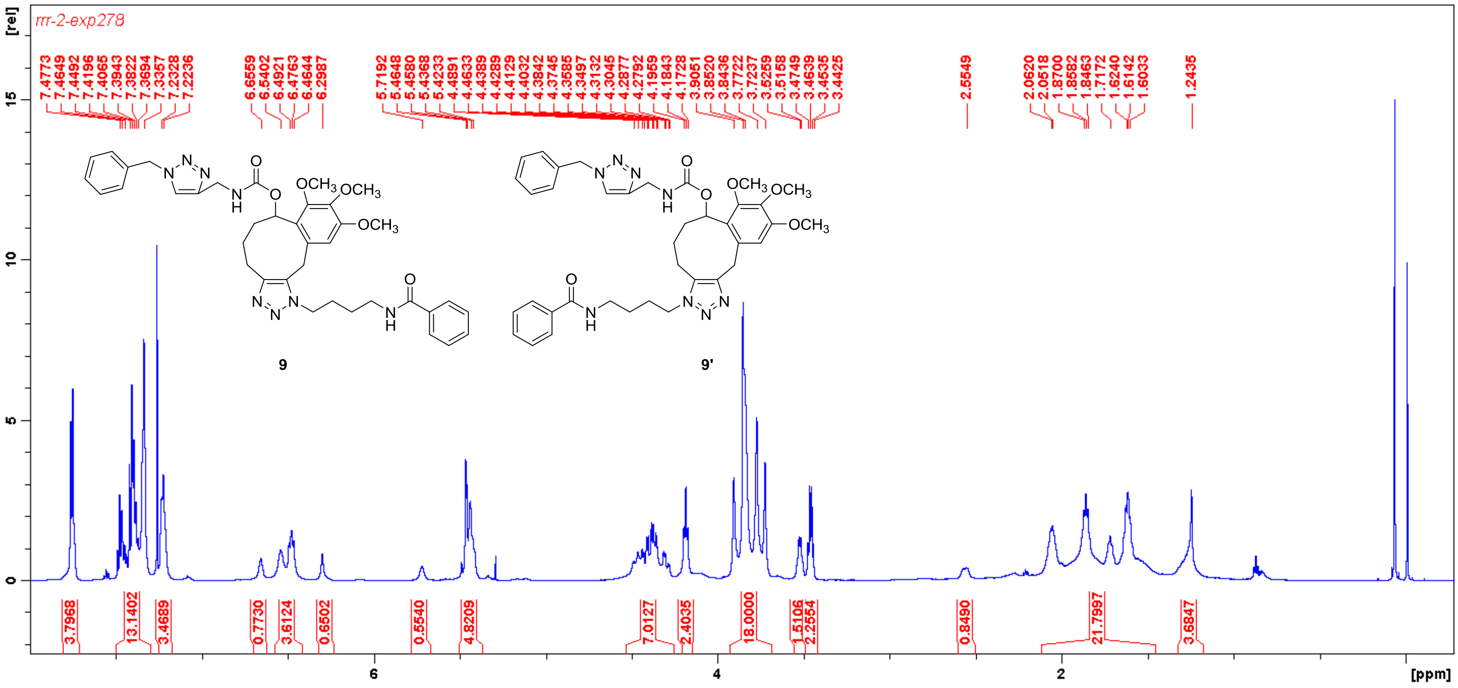
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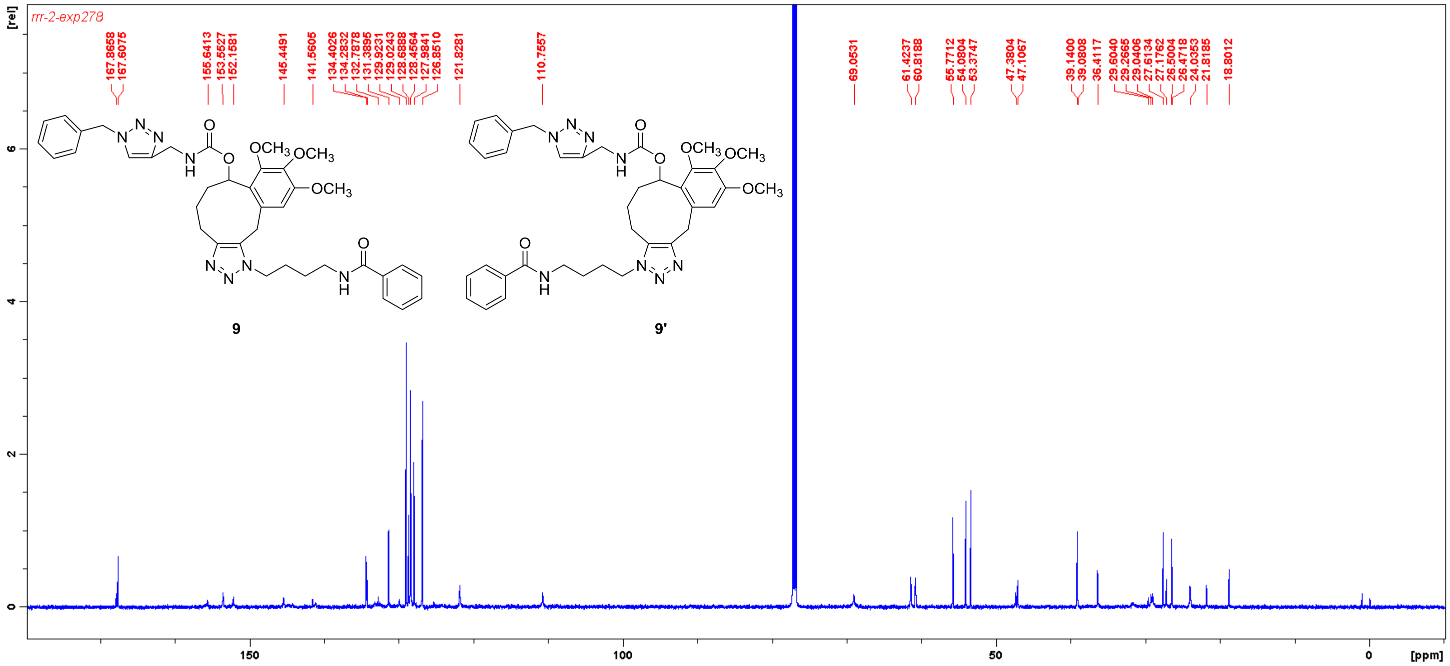
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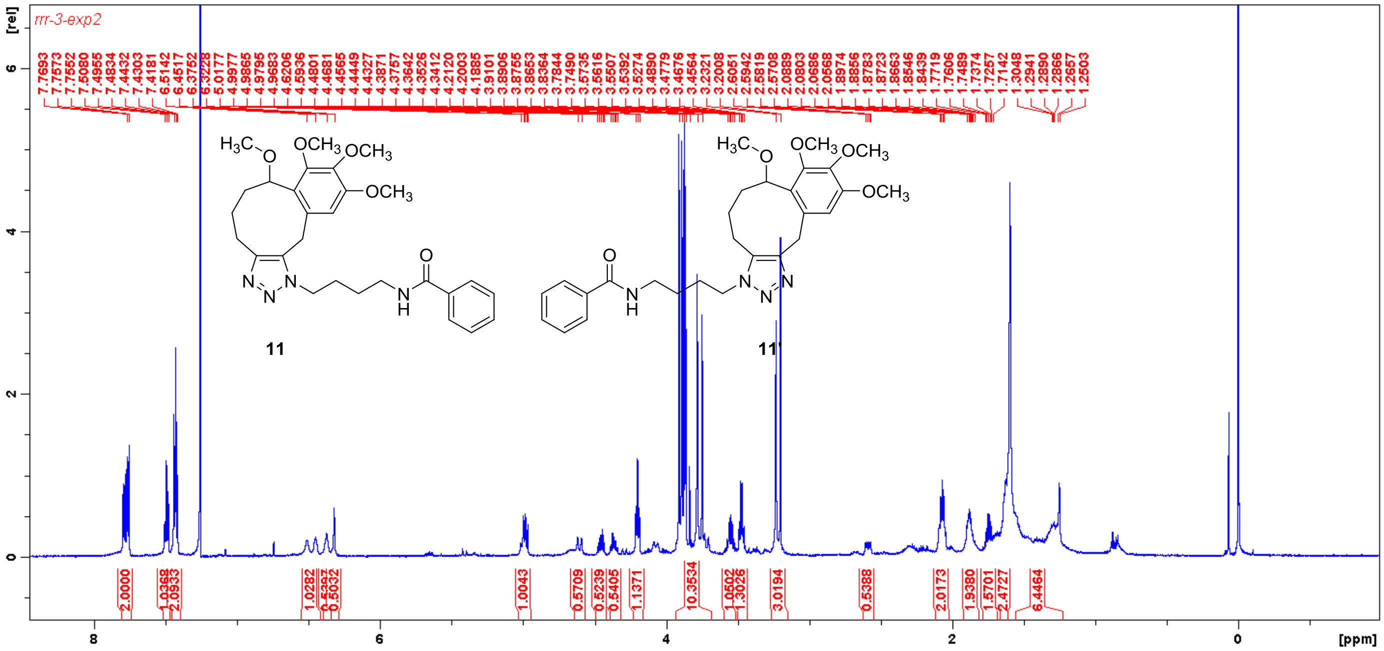
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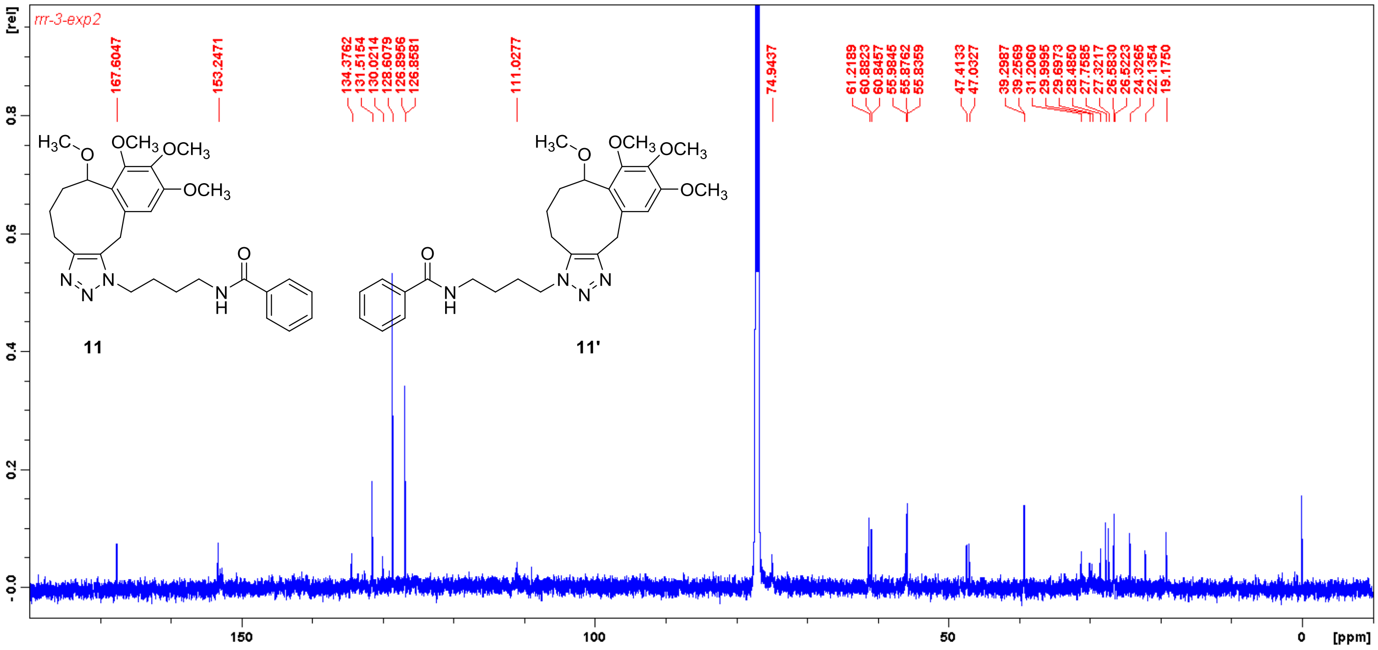
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39.2987
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0.8
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H3C
O
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OCH3
OCH3
N
N
N
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H
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