Electronic Supplementary Information

Ni-catalyzed regio- and diastereoselective *syn*-alkynylamination of unactivated alkenes with alkylamine sources

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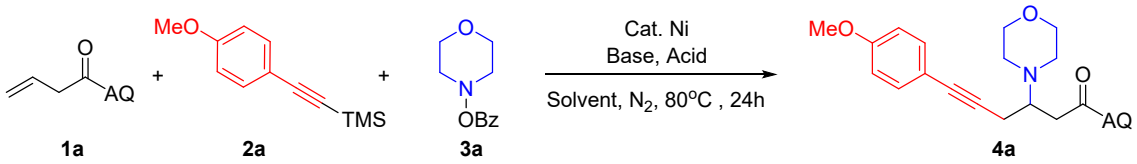
General Information

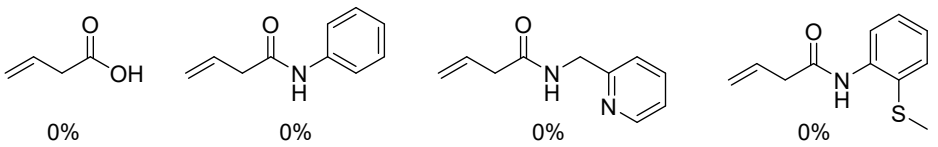
All reactions were performed under air atmosphere in a 25 mL sealed tube. The materials, solvents and alkynylsilanes **2** were purchased from common commercial sources and used without additional purification, if there is no special version. Starting materials **1**[1-9] and **3**[10-14] were synthesized according to literature procedures. ^{1}H NMR spectra were recorded at 400 MHz using TMS as internal standard, ^{13}C NMR spectra was recorded at 100 MHz using TMS as internal standard. The multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), multiplet (m), and and triplet (t). Mass spectroscopy data of the products were collected on an HRMS-TOF instrument.

Optimization of Reaction Conditions[a]



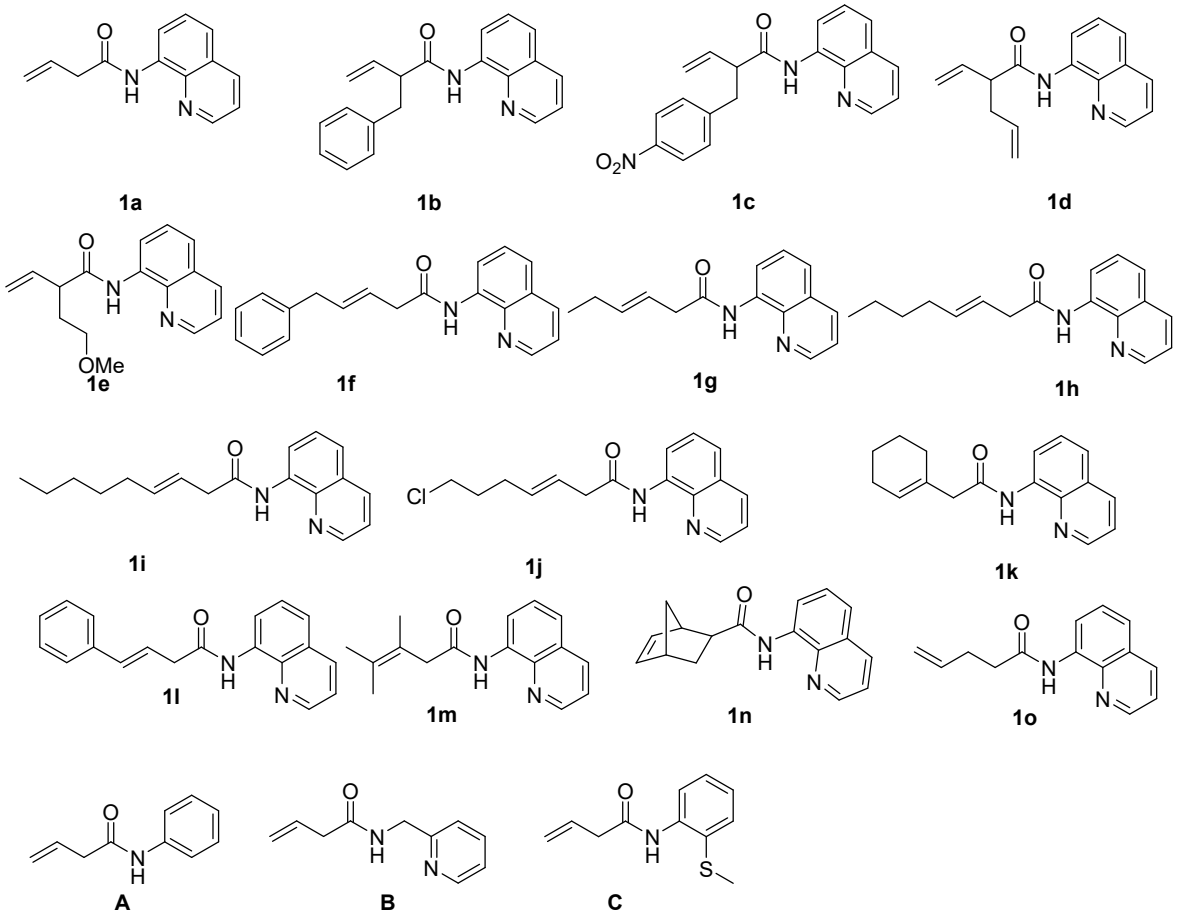
1a **2a** **3a** **4a**

Entry	Cat. Ni	Base	Acid	Solvent	Yield (%)[b]
1	$NiCl_2$	CsF	PhCOOH	DMSO	30
2	$NiCl_2$	CsF	PhCOOH	DMF	42
3	$NiCl_2$	CsF	PhCOOH	THF	10
4	$NiCl_2$	CsF	PhCOOH	DCE	0
5	$NiCl_2$	CsF	PhCOOH	CH_3CN	10
7	$NiCl_2$	CsF	PhCOOH	Toluene	0
8	$NiCl_2$	CsF	PhCOOH	TFE	trace
9	$NiBr_2$	CsF	PhCOOH	DMF	55
10	NiI_2	CsF	PhCOOH	DMF	45
11	$Ni(OTf)_2$	CsF	PhCOOH	DMF	39
12	$(Cy_3P)_2NiCl_2$	CsF	PhCOOH	DMF	43
13	$NiBr_2$·glyme	CsF	PhCOOH	DMF	50
14	$Ni(OAc)_2$	CsF	PhCOOH	DMF	46
15	$Pd(OAc)_2$	CsF	PhCOOH	DMF	0
16	$Cu(OAc)_2$	CsF	PhCOOH	DMF	0
17	$Co(OAc)_2$	CsF	PhCOOH	DMF	0
18	$NiBr_2$	CsF	HOAc	DMF	0
19	**$NiBr_2$**	**CsF**	**1-AdCOOH**	**DMF**	**80**
20	$NiBr_2$	CsF	MesCOOH	DMF	0
21	$NiBr_2$	CsF	*o*-PhPhCOOH	DMF	51
22	$NiBr_2$	KF	1-AdCOOH	DMF	21
23	$NiBr_2$	NaF	1-AdCOOH	DMF	20
24	$NiBr_2$	KOH	1-AdCOOH	DMF	30
25	$NiBr_2$	NaOH	1-AdCOOH	DMF	25
26	$NiBr_2$	K_2CO_3	1-AdCOOH	DMF	20
27	$NiBr_2$	Cs_2CO_3	1-AdCOOH	DMF	20
28	-	CsF	1-AdCOOH	DMF	0
29	$NiBr_2$	-	1-AdCOOH	DMF	0
30	$NiBr_2$	CsF	-	DMF	28
31[c]	$NiBr_2$	CsF	1-AdCOOH	DMF	73
32[d]	$NiBr_2$	CsF	1-AdCOOH	DMF	60
33[e]	$NiBr_2$	CsF	1-AdCOOH	DMF	70
34[f]	$NiBr_2$	CsF	1-AdCOOH	DMF	10



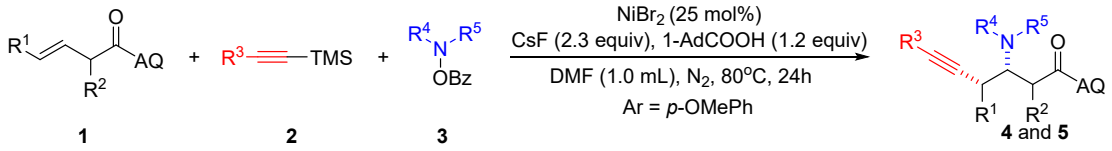
[a]Reactions were carried out by using **1a** (0.1 mmol), **2a** (0.25 mmol), **2a** (0.18 mmol), $NiBr_2$ (0.025 mmol), 1-AdCOOH (0.12 mmol), CsF (0.25 mmol), and DMF (1.0 mL) under N_2 atmosphere at 80 ℃ for 24 h. [b]Isolated yield. [c]60 ℃. [d]100 ℃. [e]CsF (0.15 mmol). [f] air atmosphere.

Typical Procedure for the Synthesis of Starting Materials 1



Note: alkene substrates **1a**[1], **1b-e**[2], **1f-g**[3], **1h**[4], **1i**[6], **1j**[4], **1k**[7], **1l-m**[5], **1o**[5], **1n**[1], **A**[8], **B-C**[9], were known compounds and prepared according to the corresponding literature methods.

Typical Procedure for Ni-catalyzed Regio- and Diastereoselective Alkynylamination of Unactivated Alkenes with Alkylamine Sources

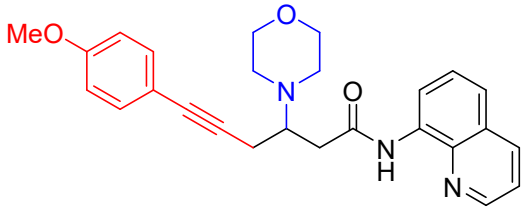


1 **2** **3**

A 25 mL thick wall pressure sealed tube was charged with **1** (0.1 mmol), **2** (0.25 mmol), **3** (0.18 mmol), $NiBr_2$ (5.5 mg, 0.025 mmol), 1-AdCOOH (21.6 mg, 0.12 mmol), CsF (38.0 mg, 0.25 mmol) and DMF (1.0 mL). The vial was evacuated and filled with N_2 atmosphere for five times, and stirred at 80 °C on an oil bath for 24 h. The mixture was then cooled to room temperature, diluted with EtOAc, filtered through a celite pad, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/PE (1:10 ~ 1:2, v/v), to give the corresponding product **4** and **5**.

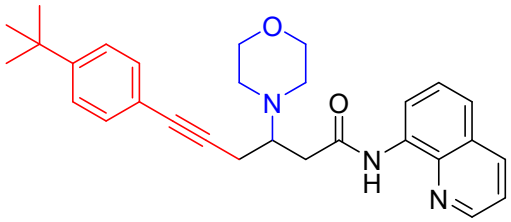
Analytical Data for Products

6-(4-methoxyphenyl)-3-morpholino-*N*-(quinolin-8-yl)hex-5-ynamide (4a)



Rf 0.48 (PE/EtOAc = 2/1). M. p. 102.8-103.7 °C. 80%, 34.3 mg. Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.35 (s, 1H), 8.78-8.73 (m, 2H), 8.08 (dd, J_1 = 2.0 Hz; J_2 = 8.4 Hz, 1H), 7.48-7.44 (m, 2H), 7.37 (dd, J_1 = 4.0 Hz; J_2 = 8.0 Hz, 1H), 7.24 (d, J = 7.2 Hz, 2H), 6.72 (d, J = 8.4 Hz, 2H), 3.98-3.94 (m, 2H), 3.88-3.84 (m, 2H), 3.72 (s, 3H), 3.35 (s, 1H), 2.90-2.84 (m, 4H), 2.76-2.69 (m, 3H), 2.50-2.44 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 159.4, 147.9, 139.0, 136.3, 132.9, 128.1, 127.4, 124.5, 123.9, 121.6, 121.4, 117.7, 113.9, 85.2, 83.2, 66.7, 60.9, 55.2, 48.9, 31.4, 30.2. IR (neat): 3347, 2953, 2923, 2854, 1626, 1523, 1485, 1457, 1430, 1384, 1360, 1325, 1273, 1256, 1208, 1182, 1113, 1083, 1002, 968, 887, 804, 791, 753, 668, 645, 604, 557 cm^{-1}. HRMS (EI-TOF) calcd for $C_{26}H_{27}N_3O_3$ (M^+): 429.2052, found: 429.2053.

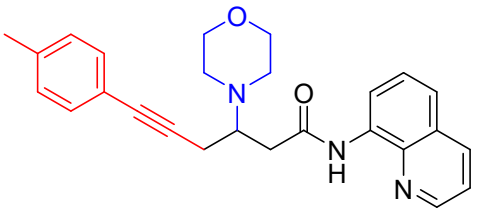
6-(4-(tert-butyl)phenyl)-3-morpholino-*N*-(quinolin-8-yl)hex-5-ynamide (4b)



Rf = 0.54 (PE/EA = 2/1). 67%, 30.5 mg. Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.40 (s, 1H), 8.85-8.76 (m, 2H), 8.16 (d, J = 8.4 Hz, 1H), 7.56-7.50 (m, 2H), 7.45 (dd, J_1 = 4.4 Hz; J_2 = 8.4 Hz, 1H), 7.41 (s, 1H), 7.31 (d, J = 8.4 Hz, 3H), 4.04-3.95 (m, 4H), 3.46-3.45 (m, 1H), 3.12-2.80 (m, 7H), 2.59 (t, J = 7.6 Hz, 1H), 1.41 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 151.1, 147.9, 136.3, 131.3, 128.5, 127.4, 125.2, 124.5, 123.9, 121.6, 121.4, 119.2, 117.6, 85.9, 83.6, 66.9, 60.9, 49.0, 34.9, 31.9, 30.3,

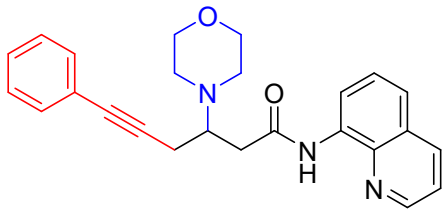
29.3. IR (neat): 3350, 2953, 2921, 2846, 1676, 1528, 1485, 1458, 1423, 1386, 1366, 1400, 1258, 1208, 1182, 1113, 1075, 965, 891, 833, 791, 746, 667, 646, 605, 533 cm^{-1}. HRMS (EI-TOF) calcd for $C_{29}H_{33}N_3O_2$ (M^+): 455.2573, found: 455.2573.

3-morpholino-*N*-(quinolin-8-yl)-6-(p-tolyl)hex-5-ynamide (4c)



Rf 0.32 (PE/EA = 5/1). M. p. 100.3-101.1 °C. 79%, 32.7 mg. Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.48 (s, 1H), 8.86-8.81 (m, 2H), 8.16 (d, J = 8.4 Hz, 1H), 7.55-7.50 (m, 2H), 7.45 (dd, J_1 = 4.0 Hz; J_2 = 8.4 Hz, 1H), 7.29 (d, J = 8.8 Hz, 2H), 7.08 (d, J = 7.6 Hz, 2H), 4.05-4.02 (m, 2H), 3.95-3.91 (m, 2H), 3.45-3.41 (m, 1H), 2.98-2.90 (m, 4H), 2.83-2.75 (m, 2H), 2.56-2.51 (m, 1H), 2.33 (s, 3H), 2.05-2.01 (m, 1H).^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 147.9, 136.3, 131.4, 128.9, 128.5, 127.4, 127.1, 124.5, 123.9, 121.6, 121.4, 119.2, 117.7, 86.0, 83.4, 66.8, 60.9, 48.9, 31.4, 30.2, 21.3. IR (neat): 3347, 2958, 2923, 2850, 1677, 1542, 1486, 1463, 1423, 1385, 1361, 1323, 1268, 1207, 1182, 1121, 1078, 968, 894, 834, 789, 756, 678, 646, 605, 551 cm^{-1}. HRMS(EI-TOF) calcd for $C_{26}H_{27}N_3O_2$ (M^+): 413.2103, found: 413.2106.

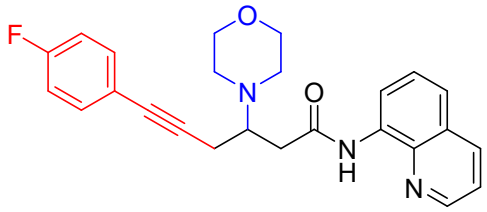
3-morpholino-6-phenyl-*N*-(quinolin-8-yl)hex-5-ynamide (4d)



Rf 0.50 (PE/EtOAc = 2/1). M. p. 111.1-112.0 °C. 66%, 26.4 mg. Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.43 (s, 1H), 8.86-8.80 (m, 2H), 8.16 (d, J = 8.0 Hz, 1H), 7.56-7.50 (m, 2H), 7.45 (dd, J_1 = 4.0 Hz; J_2 = 8.0 Hz, 1H), 7.41-7.38 (m, 2H), 7.28-7.26 (m, 3H), 4.05-4.01 (m, 2H), 3.94-3.91 (m, 2H), 3.50-3.41 (m, 2H), 2.99-2.89 (m,

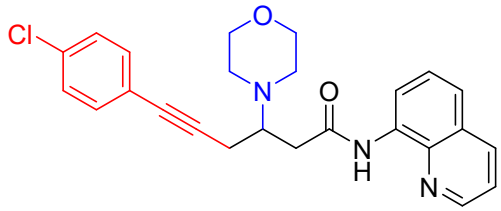
3H), 2.86-2.73 (m, 3H), 2.59-2.52 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 147.0, 136.3, 131.5, 128.5, 128.2, 127.8, 127.4, 124.5, 123.9, 121.6, 121.4, 119.2, 117.7, 86.9, 83.4, 66.8, 60.8, 48.9, 31.4, 29.7. IR (neat): 3350, 2960, 2924, 2850, 1662, 1523, 1479, 1468, 1421, 1361, 1323, 1251, 1206, 1182, 1095, 961, 891, 791, 754, 664, 646, 604, 541 cm^{-1}. HRMS (EI-TOF) calcd for $C_{25}H_{25}N_3O_2$ (M^+): 399.1947, found: 399.1948.

6-(4-fluoropheyl)-3-morpholino-*N*-(quinolin-8-yl)hex-5-ynamide (4e)



Rf 0.52 (PE/EA = 1/2). M. p. 120.7-121.3 °C. 37%, 15.2 mg. Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.04 (s, 1H), 8.83-8.74 (m, 2H), 8.18-8.15 (m, 1H), 7.54-7.52 (m, 2H), 7.46 (dd, J_1 = 4.0 Hz; J_2 = 8.4 Hz, 1H), 7.35 (d, J = 8,8 Hz, 2H), 7.00-6.92 (m, 2H), 4.08-3.93 (m, 2H), 3.68-3.64 (m, 1H), 3.17-2.74 (m, 7H), 2.64-2.58 (m, 1H), 2.35-2.21 (m, 1H), 2.04-1.96 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.5, 162.3 (d, $J_{C\text{-}F}$ = 247.4 Hz), 147.1, 138.6, 136.4, 133.5 (d, $J_{C\text{-}F}$ = 15.2 Hz), 127.4, 124.5, 123.9, 121.7 (d, $J_{C\text{-}F}$ = 46.2 Hz), 119.2, 116.9, 115.5, 115.3, 85.2, 82.2, 67.5, 60.9, 49.1, 30.3, 27.5. ^{19}F NMR (375 MHz, $CDCl_3$) δ -113.33 (m). IR (neat): 3347, 2957, 2923, 2849, 1673, 1552, 1495, 1463, 1433, 1409, 1369, 1322, 1257, 1208, 1182, 1120, 1079, 964, 893, 821, 793, 775, 642, 624, 604, 553 cm^{-1}. HRMS (EI-TOF) calcd for $C_{25}H_{24}FN_3O_2$ (M^+): 417.1853, found: 417.1857.

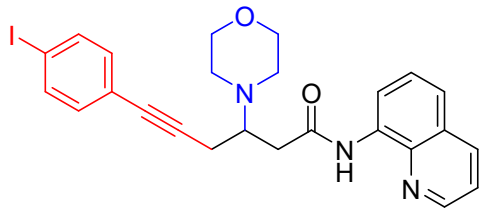
6-(4-chlorophenyl)-3-morpholino-*N*-(quinolin-8-yl)hex-5-ynamide (4f)



Rf 0.51 (PE/EA = 2/1). M. p. 123.5-124.3 °C. 43%, 18.8 mg. Yellow solid; ^{1}H NMR

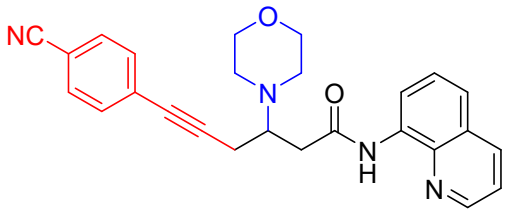
($CDCl_3$, 400 MHz) δ 11.30 (s, 1H), 8.78-8.73 (m, 2H), 8.09 (d, J = 8.4 Hz, 1H), 7.49-7.43 (m, 2H), 7.38 (dd, J_1 = 4.0 Hz; J_2 = 8.4 Hz, 1H), 7.22 (d, J = 8.4 Hz, 2H), 7.16-7.14 (m, 2H) 4.00-3.93 (m, 2H), 3.87-3.83 (m, 2H), 3.37-3.33 (m, 1H), 2.90-2.84 (m, 3H), 2.81-2.71 (m, 2H), 2.68-2.64 (m, 2H), 2.47 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 147.9, 139.0, 136.3, 135.3, 133.9, 132.8, 128.5, 127.4, 127.1, 124.5, 121.6, 121.4, 117.6, 88.0, 82.3, 66.8, 60.8, 48.9, 31.4, 30.2. IR (neat): 3348, 2957, 2921, 2851, 1673, 1608, 1521, 1483, 1421, 1360, 1312, 1289, 1243, 1228, 1184, 1163, 1123, 1080, 1008, 912, 891, 823, 791, 721, 691, 645, 604, 537 cm^{-1}. HRMS (EI-TOF) calcd for $C_{25}H_{24}ClN_3O_2$ (M^+): 433.1557, found: 433.1560.

3-hydroxy-4-(4-methoxyphenyl)-*N*-phenylbutanamid (4g)



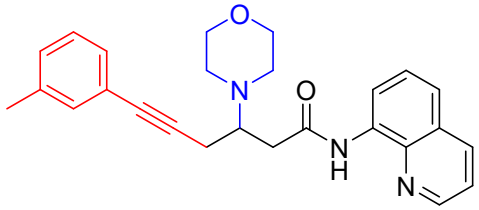
Rf 0.52 (PE/EA = 2/1). M. p. 125.1-126.0 °C. 39%, 20.5 mg. Yellow solid; ^1H NMR ($CDCl_3$, 400 MHz) δ 11.31 (s, 1H), 8.77-8.73 (m, 2H), 8.09 (d, J = 8.4 Hz, 1H), 7.51 (d, J = 8.0 Hz, 2H), 7.47-7.43 (m, 2H), 7.39 (dd, J_1 = 4.0 Hz; J_2 = 8.4 Hz, 1H), 7.20 (d, J = 8.0 Hz, 2H), 4.00-3.93 (m, 2H), 3.87-3.83 (m, 2H), 3.42-3.33 (m, 1H), 2.90-2.83 (m, 3H), 2.80-2.70 (m, 2H), 2.67-2.64 (m, 2H), 2.49-2.43 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 147.9, 147.1, 137.3, 136.3, 133.1, 127.4, 124.5, 124.0, 121.6, 121.5, 119.1, 117.7, 93.5, 88.5, 82.5, 66.8, 60.7, 48.9, 31.4, 29.7. IR (neat): 3350, 2953, 2923, 2850, 1673, 1608, 1501, 1483, 1421, 1350, 1323, 1291, 1228, 1184, 1157, 1123, 1056, 1007, 917, 890, 823, 789, 690, 645, 605, 551, 501 cm^{-1}. HRMS (EI-TOF) calcd for $C_{25}H_{24}IN_3O_2$ (M^+): 525.0913, found: 525.0919.

6-(4-cyanophenyl)-3-morpholino-*N*-(quinolin-8-yl)hex-5-ynamide (4h)



Rf 0.43 (PE/EA = 2/1). M. p. 113.1-113.9 °C. 96%, 40.9 mg. Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.27 (s, 1H), 8.77-8.73 (m, 2H), 8.10 (d, J = 8.0 Hz, 1H), 7.47-7.44 (m, 5H), 7.39 (dd, J_1 = 4.0 Hz; J_2 = 8.0 Hz, 1H), 7.05 (dd, J_1 = 2.4 Hz; J_2 = 8.8 Hz, 1H), 3.98-3.94 (m, 2H), 3.88-3.84 (m, 2H), 2.89-2.85 (m, 3H), 2.81-2.75 (m, 2H), 2.68-2.64 (m, 2H), 2.51 (dd, J_1 = 8.0 Hz; J_2 = 16.4 Hz, 1H), 1.99-1.94 (m, 1H). IR (neat): 3350, 2957, 2923, 2853, 2227, 1667, 1604, 1523, 1486, 1461, 1422, 1362, 1312, 1291, 1248, 1208, 1184, 1109, 1080, 1005, 962, 894, 823, 789, 757, 690, 645, 604, 551 cm^{-1}. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.2, 148.0, 147.1, 138.9, 136.4, 132.1, 131.9, 127.4, 124.5, 124.0, 121.8, 121.5, 119.1, 117.6, 92.0, 82.0, 66.8, 58.5, 48.9, 31.4, 29.7. HRMS (EI-TOF) calcd for $C_{26}H_{24}N_4O_2$ (M^+): 424.1899, found: 424.1899.

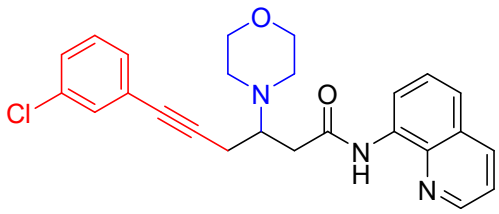
3-morpholino-*N*-(quinolin-8-yl)-6-(m-tolyl)hex-5-ynamide (4i)



Rf = 0.46 (PE/EA = 2/1). M. p. 102.2-103.0 °C. 68%, 28.1 mg. Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.06 (s, 1H), 8.79-8.75 (m, 2H), 8.17 (d, J = 8.4 Hz, 1H), 7.54-7.52 (m, 2H), 7.46 (dd, J_1 = 4.0 Hz; J_2 = 8.0 Hz, 1H), 7.41 (s, 2H), 7.20-7.17 (m, 1H), 6.99 (s, 1H), 3.84-3.62 (m, 4H), 3.47-3.41 (m, 1H), 3.03-2.57 (m, 4H), 2.61-2.57 (m, 1H), 2.35-2.29 (m, 4H), 2.21 (dd, J_1 = 8.0 Hz; J_2 = 16.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 147.1, 138.5, 136.3, 132.3, 129.9, 128.9, 128.5, 127.4, 127.1, 124.5, 123.9, 121.9, 119.2, 116.9, 114.0, 85.1, 83.5, 66.9, 64.5, 51.0, 31.9, 27.6, 22.6. IR (neat): 3348, 2957, 2923, 2851, 1678, 1523, 1485, 1457, 1423, 1386, 1361,

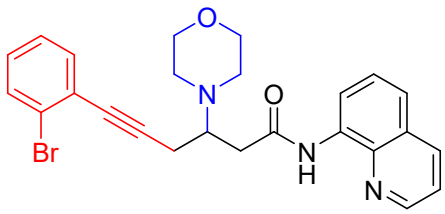
1323, 1258, 1208, 1182, 1125, 1083, 968, 891, 823, 799, 756, 668, 646, 604, 547 cm^{-1}. HRMS (EI-TOF) calcd for $C_{26}H_{27}N_3O_2$ (M^+): 413.2103, found: 413.2103.

6-(3-chlorophenyl)-3-morpholino-*N*-(quinolin-8-yl)hex-5-ynamide (4j)



Rf 0.53 (PE/EA = 2/1). M. p. 122.1-123.0 °C. 43%, 18.6 mg. Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.34 (s, 1H), 8.78-8.74 (m, 2H), 8.09 (d, J = 7.6 Hz, 1H), 7.48-7.45 (m, 2H), 7.40-7.37 (m, 1H), 7.28 (s, 1H), 7.17-7.11 (m, 3H) 3.98-3.94 (m, 2H), 3.88-3.84 (m, 2H), 3.36-3.35 (m, 1H), 2.91-2.84 (m, 3H), 2.81-2.73 (m, 2H), 2.67-2.66 (m, 2H), 2.48 (dd, J_1 = 8.0 Hz J_2 = 16.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 148.0, 136.3, 135.3, 131.4, 129.7, 129.4, 128.6, 128.2, 127.4, 124.5, 124.0, 121.7, 121.5, 119.1, 117.7, 88.3, 82.1, 66.8, 60.7, 48.9, 31.4, 29.7. HRMS (EI-TOF) calcd for $C_{25}H_{24}ClN_3O_2$ (M^+): 433.1557, found: 433.1558.

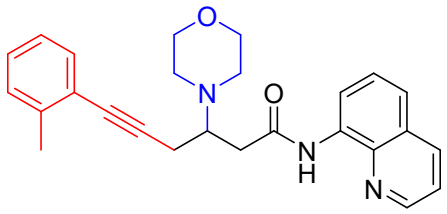
6-(3-bromophenyl)-3-morpholino-*N*-(quinolin-8-yl)hex-5-ynamide (4k)



Rf = 0.57 (PE/EA = 2/1). M. p. 123.9-124.8 °C. 31%, 14.8 mg. Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.38 (s, 1H), 8.85-8.79 (m, 2H), 8.16 (dd, J_1 = 1.6 Hz; J_2 = 8.4 Hz, 1H), 7.56-7.53 (m, 2H), 7.47-7.44 (m, 1H), 7.42-7.40 (m, 1H), 7.22 (t, J = 7.6Hz, 1H), 7.15-7.12 (m, 2H), 4.07-4.02 (m, 2H), 3.95-3.90 (m, 2H), 3.53-3.44 (m, 1H), 3.06-2.97 (m, 4H), 2.87-2.74 (m, 3H), 2.27-2.20 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.1, 147.9, 138.6, 136.3, 133.4, 132.3, 129.4, 129.0, 128.3, 126.9, 124.4, 123.9, 121.6, 119.1, 117.6, 91.8, 81.4, 66.9, 60.7, 49.1, 31.4, 29.7. HRMS (EI-TOF)

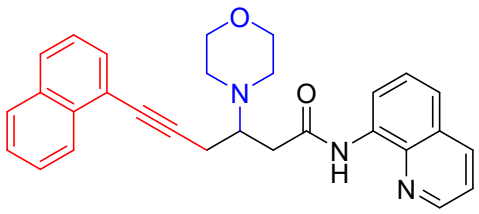
calcd for $C_{25}H_{24}BrN_3O_2$ (M^+): 477.1052, found: 477.1052.

3-morpholino-*N*-(quinolin-8-yl)-6-(o-tolyl)hex-5-ynamide (4l)



Rf 0.39 (PE/EA = 2/1). M. p. 101.5-102.3 °C. 86%, 35.5 mg. Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.46 (s, 1H), 8.87-8.80 (m, 2H), 8.16 (d, J = 8.0 Hz, 1H), 7.55-7.53 (m, 2H), 7.45 (dd, J_1 = 4.0 Hz; J_2 = 8.0 Hz, 1H), 7.38-7.36 (m, 1H), 7.17 (d, J = 3.2 Hz, 2H), 7.12-7.09 (m, 1H), 4.07-4.03 (m, 2H), 3.96-3.92 (m, 2H), 3.46-3.41 (m, 1H), 3.01-2.97 (m, 3H), 2.92-2.84 (m, 2H), 2.77-2.74 (m, 2H), 2.62 (dd, J_1 = 7.6 Hz; J_2 = 16.8 Hz, 1H), 2.43 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.5, 147.9, 140.0, 136.3, 135.4, 132.0, 129.4, 127.9, 127.4, 125.5, 124.5, 124.0, 121.6, 121.5, 119.2, 117.7, 90.7, 82.3, 66.8, 60.9, 48.9, 31.4, 29.7, 19.3. IR (neat): 3350, 2956, 2920, 2851, 1673, 1522, 1485, 1457, 1423, 1383, 1361, 1323, 1259, 1208, 1182, 1113, 1078, 963, 894, 824, 791, 755, 668, 646, 604, 563 cm^{-1}. HRMS(EI-TOF) calcd for $C_{26}H_{27}N_3O_2$ (M^+): 413.2103, found: 413.2105.

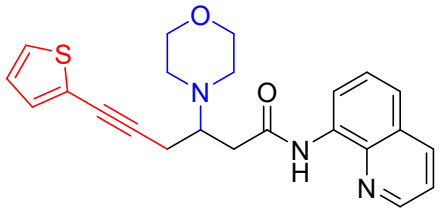
3-morpholino-6-(naphthalen-1-yl)-*N*-(quinolin-8-yl)hex-5-ynamide (4m)



Rf 0.47 (PE/EA = 2/1). M. p. 132.2-133.1 °C. 72%, 32.3 mg. Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.33 (s, 1H), 8.77 (dd, J_1 = 1.6 Hz; J_2 = 7.2 Hz, 1H), 8.71 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.24 (d, J = 8.0 Hz, 1H), 8.07 (dd, J_1 = 1.2 Hz; J_2 = 8.0 Hz, 1H), 7.75-7.69 (m, 2H), 7.55 (d, J = 6.8 Hz, 1H), 7.47-7.43 (m, 3H), 7.36 (dd, J_1 = 4.0 Hz; J_2 = 8.0 Hz, 1H), 7.30-7.28 (m, 1H), 7.06 (dd, J_1 = 1.6 Hz; J_2 = 8.8 Hz, 1H),

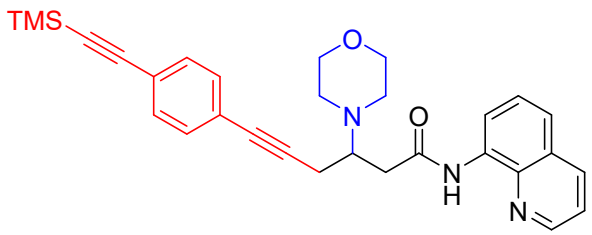
4.01-3.95 (m, 2H), 3.90-3.85 (m, 2H), 3.48-3.44 (m, 1H), 2.97-2.88 (m, 5H), 2.75-2.69 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 147.9, 147.1, 139.0, 136.3, 135.3, 130.3, 128.3, 128.2, 127.4, 126.7, 126.3, 126.2, 125.2, 124.5, 124.0, 121.6, 121.4, 119.2, 117.7, 91.7, 81.5, 66.8, 60.9, 49.0, 31.4, 29.7. IR (neat): 3350, 2961, 2923, 2854, 1667, 1523, 1501, 1481, 1468, 1421, 1395, 1366, 1323, 1251, 1210, 1192, 1096, 961, 891, 789, 754, 664, 647, 605, 533 cm^{-1}. HRMS (EI-TOF) calcd for $C_{29}H_{27}N_3O_2$ (M^+): 449.2103, found: 449.2105.

3-morpholino-*N*-(quinolin-8-yl)-6-(thiophen-2-yl)hex-5-ynamide (4n)



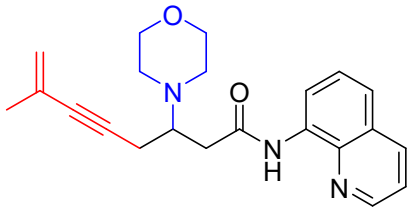
Rf 0.47 (PE/EA = 2/1). M. p. 103.3-103.8 °C. 51%, 20.7 mg. Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.38 (s, 1H), 8.78-8.73 (m, 2H), 8.09 (dd, J_1 = 1.2 Hz; J_2 = 8.4 Hz, 1H), 7.47-7.45 (m, 2H), 7.38 (dd, J_1 = 4.0 Hz; J_2 = 8.4 Hz, 1H), 7.16-7.14 (m, 1H), 7.07-7.04 (m, 1H), 6.99 (d, J = 4.8 Hz, 1H), 4.00-3.98 (m, 2H), 3.88-3.83 (m, 2H), 3.37-3.32 (m, 1H), 2.91-2.86 (m, 3H), 2.83-2.81 (m, 1H), 2.76-2.70 (m, 1H), 2.67-2.63 (m, 2H), 2.44 (dd, J_1 = 8.0 Hz; J_2 = 16.4 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 147.9, 136.3, 135.4, 129.9, 128.1, 127.4, 125.1, 124.5, 124.0, 121.6, 121.4, 119.1, 117.7, 86.4, 78.4, 66.8, 60.8, 48.8, 31.4, 29.7. IR (neat): 3350, 2959, 2921, 2850, 1673, 1596, 1525, 1464, 1453, 1384, 1366, 1323, 1259, 1103, 1067, 1012, 950, 817, 791, 756, 665, 625, 563 cm^{-1}. HRMS (EI-TOF) calcd for $C_{23}H_{23}N_3O_2S$ (M^+): 405.1511, found: 405.1515.

3-morpholino-*N*-(quinolin-8-yl)-6-(4-((trimethylsilyl)ethynyl)phenyl)hex-5-ynamide (4o)



Rf 0.47 (PE/EA = 2/1). M. p. 112.2-113.1 °C. 68%, 33.7 mg. Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.41 (s, 1H), 8.86-8.81 (m, 2H), 8.17 (dd, J_1 = 1.2 Hz; J_2 = 8.4 Hz, 1H), 7.55 (d, J = 8.8 Hz, 4H), 7.47 (dd, J_1 = 4.0 Hz; J_2 = 8.4 Hz, 1H), 7.14 (dd, J_1 = 2.4 Hz; J_2 = 8.4 Hz, 2H), 4.10-4.02 (m, 2H), 3.95-3.92 (m, 2H), 2.99-2.95 (m, 3H), 2.89-2.81 (m, 2H), 2.76-2.73 (m, 2H), 2.62-2.56 (m, 1H), 2.06-1.97 (m, 1H), 0.09 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 147.1, 138.4, 136.3, 131.9, 131.4, 129.9, 128.6, 127.1, 124.5, 124.0, 119.1, 117.7, 89.1, 83.3, 82.9, 78.6, 66.9, 60.8, 58.3, 31.4, 29.7, 0.99. IR (neat): 3349, 2958, 2921, 2851, 1672, 1630, 1523, 1486, 1486, 1458, 1442, 1384, 1361, 1323, 1259, 1207, 1171, 1160, 1112, 1077, 1018, 963, 893, 825, 791, 758, 695, 646, 604, 547, 513 cm^{-1}. HRMS (EI-TOF) calcd for $C_{30}H_{33}N_3O_2Si$ (M^+): 495.2342, found: 495.2346.

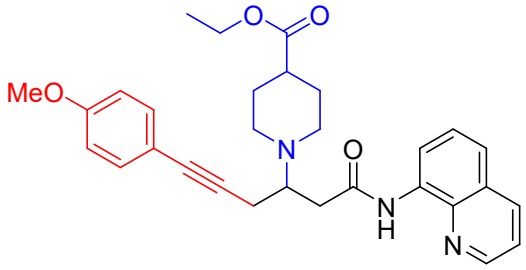
7-methyl-3-morpholino-*N*-(quinolin-8-yl)oct-7-en-5-ynamide (4p)



Rf 0.72 (PE/EA = 2/1). M. p. 92.1-92.9 °C. 36%, 13.2 mg. Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.39 (s, 1H), 8.79-8.75 (m, 2H), 8.09 (dd, J_1 = 1.2 Hz; J_2 = 8.4 Hz, 1H), 7.48-7.45 (m, 2H), 7.39 (dd, J_1 = 4.0 Hz; J_2 = 8.0 Hz, 1H), 5.15-5.09 (m, 2H), 4.01-3.94 (m, 2H), 3.87-3.83 (m, 2H), 3.31-3.24 (m, 1H), 2.87-2.63 (m, 7H), 2.54-2.50 (m, 1H), 1.79 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 147.9, 147.1, 138.5, 136.3, 127.4, 124.5, 124.0, 121.6, 121.4, 119.2, 117.7, 89.1, 84.5, 66.7, 60.8, 48.8, 31.4, 29.7, 22.6. IR (neat): 3347, 2956, 2920, 2851, 1680, 1524, 1467, 1401, 1323, 1257, 1226, 1102, 1002, 951, 891, 778, 754, 646, 614, 572 cm^{-1}. HRMS (EI-

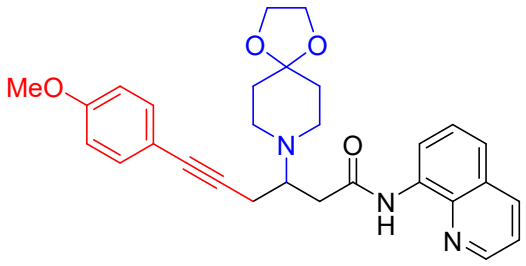
TOF) calcd for $C_{22}H_{25}N_3O_2$ (M^+): 363.1947, found: 363.1948.

ethyl-1-(6-(4-methoxyphenyl)-1-oxo-1-(quinolin-8-ylamino)hex-5-yn-3-yl)piperidine-4-carboxylate (4r)



Rf 0.53 (PE/EA = 2/1). M. p. 118.8-119.7 °C. 70%, 35.1 mg. Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.53 (s, 1H), 8.86-8.85 (m, 1H), 8.78 (d, J = 7.6 Hz, 1H), 8.06 (d, J = 8.4 Hz, 1H), 7.47-7.43 (m, 2H), 7.37 (dd, J_1 = 4.4 Hz; J_2 = 8.4 Hz, 1H), 7.26 (t, J = 8.8 Hz, 2H), 6.74-6.72 (m, 2H), 4.11 (dd, J_1 = 7.2 Hz; J_2 = 14.4 Hz, 2H), 3.72 (s, 3H), 3.41-3.36 (m, 2H), 3.15 (d, J = 14.8 Hz, 1H), 2.94-2.85 (m, 2H), 2.79-2.65 (m, 3H), 2.42-2.28 (m, 3H), 2.00-1.89 (m, 3H), 0.81 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.3, 170.9, 159.3, 148.3, 139.2, 136.1, 132.9, 127.2, 124.5, 124.0, 121.6, 121.5, 119.1, 117.8, 113.9, 85.5, 83.0, 61.0, 60.3, 58.5, 55.3, 41.9, 31.4, 29.7, 28.2, 14.3. IR (neat): 3351, 2963, 2920, 2845, 1682, 1606, 1524, 1487, 1461, 1421, 1389, 1364, 1320, 1261, 1107, 1079, 1033, 1012, 991, 894, 861, 791, 738, 679, 646, 604, 554 cm^{-1}. HRMS (EI-TOF) calcd for $C_{30}H_{33}N_3O$ (M^+): 499.2471, found: 499.2471.

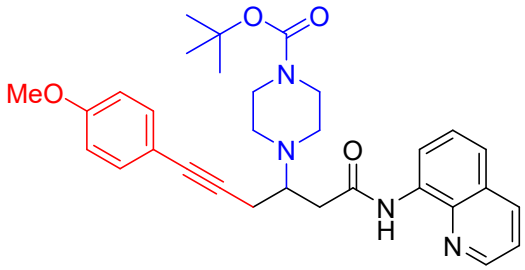
6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)-3-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)hex-5-ynamide (4s)



Rf 0.48 (PE/EtOAc = 2/1). M. p. 112.3-113.1 °C. 72%, 34.8 mg. Yellow solid; ^{1}H

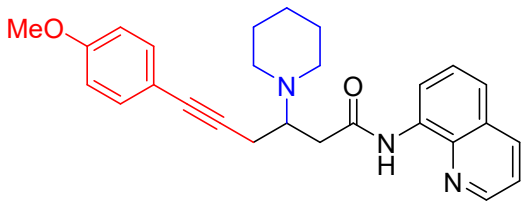
NMR ($CDCl_3$, 400 MHz) δ 11.79 (s, 1H), 8.85-8.84 (m, 1H), 8.78 (d, J = 7.2 Hz, 1H), 8.06 (d, J = 8.0 Hz, 1H), 7.47-7.43 (m, 2H), 7.39-7.36 (m, 1H), 7.26 (d, J = 7.2 Hz, 2H), 6.73 (d, J = 8.8 Hz, 2H), 3.95 (s, 4H), 3.72 (s, 3H), 3.37-3.29 (m, 2H), 3.00-2.96 (m, 2H), 2.86-2.78 (m, 2H), 2.69-2.65 (m, 2H), 2.40-2.36 (m, 1H), 2.09-1.96 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.9, 159.3, 148.2, 139.2, 136.1, 132.9, 127.3, 124.5, 124.0, 121.53, 121.48, 119.1, 117.9, 113.9, 107.8, 85.5, 83.0, 64.3, 60.7, 55.2, 38.6, 34.6, 31.4, 29.7. IR (neat): 3351, 2954, 2921, 2850, 1626, 1523, 1495, 1437, 1431, 1384, 1360, 1324, 1271, 1246, 1218, 1182, 1127, 1113, 1083, 1059, 1062, 1008, 995, 891, 803, 791, 753, 664, 645, 604, 557 cm^{-1}. HRMS (EI-TOF) calcd for $C_{29}H_{31}N_3O_4$ (M^+): 485.2315, found: 485.2318.

4-(6-(4-methoxyphenyl)-1-oxo-1-(quinolin-8-ylamino)hex-5-yn-3-yl)piperazine-1-carboxylate (4t)



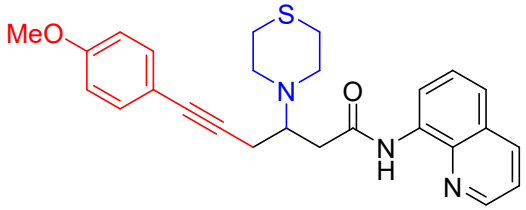
Rf 0.57 (PE/EA = 2/1). M. p. 122.3-123.1 °C.75%, 39.6 mg. Yellow solid; ^1H NMR ($CDCl_3$, 400 MHz) δ 11.35 (s, 1H), 8.77 (d, J = 6.8 Hz, 1H), 8.66-8.65 (m, 1H), 8.07 (d, J = 8.4 Hz, 1H), 7.48-7.44 (m, 2H), 7.37-7.34 (m, 1H), 7.29-7.23 (m, 2H), 6.72 (dd, J_1 = 1.6 Hz; J_2 = 8.4 Hz, 2H), 3.72-3.68 (m, 5H), 3.591-3.586 (m, 2H), 3.41-3.37 (m, 1H), 2.90-2.80 (m, 4H), 2.70-2.60 (m, 3H), 2.41 (dd, J_1 = 7.6 Hz J_2 = 16.4 Hz, 1H), 1.41 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.5, 154.9, 147.9, 139.0, 136.3, 132.9, 127.4, 124.5, 124.0, 121.6, 121.5, 119.1, 117.7, 113.9, 85.2, 83.2, 79.7, 60.8, 55.3, 48.3, 38.7, 31.4, 29.7, 28.5. IR (neat): 3351, 2960, 2922, 2847, 1682, 1606, 1523, 1486, 1461, 1422, 1389, 1364, 1323 1288, 1244, 1169, 1119, 1079, 1030, 1004, 963, 894, 863, 826, 791, 758, 696, 644, 605, 535 cm^{-1}. HRMS (EI-TOF) calcd for $C_{31}H_{36}N_4O_4$ (M^+): 528.2737, found: 528.2738.

6-(4-methoxyphenyl)-3-(piperidin-1-yl)-*N*-(quinolin-8-yl)hex-5-ynamide (4u)



Rf 0.43 (PE/EA = 2/1).M. p. 101.1-102.0 °C. 97%, 41.7 mg. Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.61 (s, 1H), 8.79-8.71 (m, 2H), 8.07 (t, J = 8.4 Hz, 1H), 7.47-7.42 (m, 2H), 7.35 (dd, J_1 = 4.0 Hz; J_2 = 8.4 Hz, 1H), 7.29-7.24 (m, 2H), 6.73-6.71 (m, 2H), 3.71 (s, 3H), 3.40-3.31 (m, 1H), 2.87-2.68 (m, 4H), 2.53 (d, J = 8.0 Hz, 2H), 2.38 (dd, J_1 = 8.4 Hz J_2 = 16.8 Hz, 1H), 1.97-1.73 (m, 5H), 1.49 (t, J = 5.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.1, 159.2, 147.8, 136.1, 132.9, 127.4, 124.5, 124.0, 121.5, 121.3, 119.1, 117.9, 116.7, 113.8, 85.9, 82.8, 61.3, 55.2, 49.6, 38.4, 31.4, 29.7, 25.7. IR (neat): 3347, 2953, 2924, 2850, 1647, 1533, 1456, 1431, 1380, 1360, 1324, 1278, 1246, 1201, 1182, 1122, 1083, 1030, 962, 885, 804, 789, 743, 665, 646, 604, 561 cm^{-1}. HRMS (EI-TOF) calcd for $C_{27}H_{29}N_3O_2$ (M^+):427.2260, found: 427.2266.

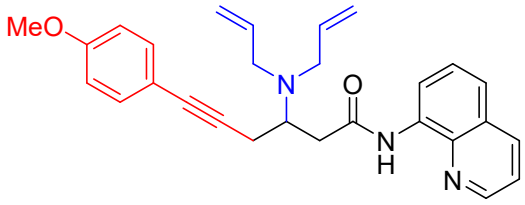
6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)-3-thiomorpholinohex-5-ynamide (4v)



Rf 0.75 (PE/EA = 2/1). M. p. 112.5-113.2 °C. 73%, 32.7 mg. Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.45 (s, 1H), 8.88-8.87 (m, 1H), 8.77 (d, J = 7.2 Hz, 1H), 8.09 (d, J = 8.4 Hz, 1H), 7.47-7.44 (m, 2H), 7.39 (dd, J_1 = 4.4 Hz J_2 = 8.4 Hz, 1H), 7.28-7.25 (m, 2H), 6.74-6.72 (m, 2H), 3.72 (s, 3H), 3.41-3.32 (m, 2H), 3.33-3.19 (m, 2H), 3.04-2.99 (m, 2H), 2.91-2.86 (m, 2H), 2.79-2.67 (m, 2H), 2.57-2.42 (m, 1H), 2.40 (dd, J_1 = 4.4 Hz J_2 = 16.4 Hz, 1H), 1.97-1.88 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 159.4, 147.9, 136.3, 132.9, 127.4, 124.5, 124.0, 121.6, 119.1, 117.8, 113.9, 113.7, 85.2, 83.1, 62.5, 58.4, 55.3, 31.4, 29.7, 27.6. IR (neat): 3350, 2956, 2922, 2852,

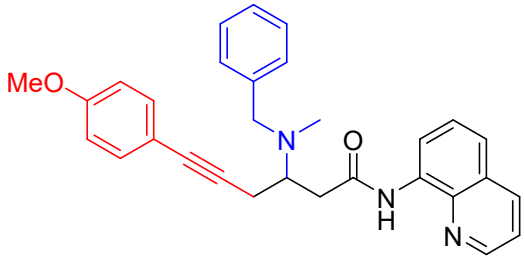
1737, 1674, 1604, 1524, 1508, 1485, 1461, 1423, 1385, 1362, 1312, 1289, 1246, 1208, 1182, 1079, 1029, 962, 893, 824, 790, 762, 696, 645, 603, 560 cm^{-1}. HRMS (EI-TOF) calcd for $C_{26}H_{27}N_3O_2S$ (M^+): 445.1824, found: 445.1825.

3-(diallylamino)-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (4w)



Rf = 0.64 (PE/EA = 2/1). 92%, 40.4 mg. Yellow oil. ^1H NMR ($CDCl_3$, 400 MHz) δ 9.89 (s, 1H), 8.80-8.76 (m, 2H), 8.16 (d, *J* = 8.4 Hz, 1H), 7.54-7.48 (m, 2H), 7.45-7.42 (m, 1H), 7.35 (d, *J* = 8.4 Hz, 2H), 6.81 (d, *J* = 8.8 Hz, 2H), 6.22-6.17 (m, 1H), 5.98-5.92 (m, 1H), 5.30-5.18 (m, 2H), 4.11-4.09 (m, 2H), 3.80 (s, 3H), 2.79-2.76 (m, 2H), 2.59-2.56 (m, 2H), 2.15-2.08 (m, 1H), 1.71-1.55 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.2, 148.1, 136.4, 134.5, 134.2, 133.0, 131.5, 128.6, 127.4, 126.9, 124.5, 123.9, 121.5, 119.1, 116.7, 113.8, 87.3, 81.4, 61.9, 55.2, 54.3, 31.9, 29.3. IR (neat): 3350, 2952, 2924, 2850, 1675, 1663, 1624, 1523, 1484, 1459, 1438, 1380, 1367, 1324, 1273, 1258, 1201, 1182, 1113, 1084, 1030, 991, 884, 804, 791, 754, 664, 645, 605, 539 cm^{-1}. HRMS (EI-TOF) calcd for $C_{28}H_{29}N_3O_2$(M^+): 439.2260, found: 439.2261.

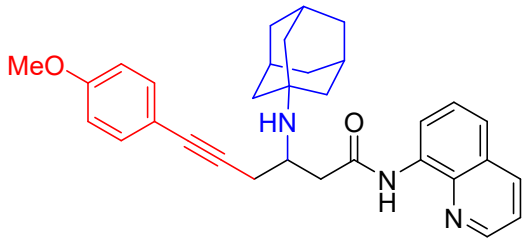
3-(benzyl(methyl)amino)-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (4x)



Rf = 0.50 (PE/EA = 2/1). 33%, 15.2 mg. Yellow oil. ^1H NMR ($CDCl_3$, 400 MHz) δ 9.89 (s, 1H), 8.80-8.76 (m, 2H), 8.16 (d, *J* = 8.0 Hz, 1H), 7.54-7.49 (m, 4H), 7.44 (dd, J_1 = 4.0 Hz; J_2 = 8.0 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 4H), 7.13 (d, *J* = 8.8 Hz, 1H), 6.80

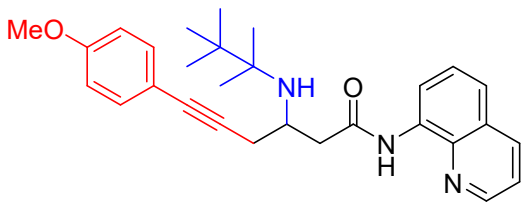
(d, J = 8.8 Hz, 2H), 3.80 (s, 3H), 2.79-2.775 (m, 1H), 2.59-2.56 (m, 1H), 2.13-2.08 (m, 1H), 1.67-1.59 (m, 4H), 1.43 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.1, 159.2, 148.1, 138.6, 138.4, 136.3, 133.0, 128.8, 128.0, 127.4, 126.9, 124.5, 123.9, 121.5, 121.4, 119.1, 116.4, 113.8, 87.3, 81.4, 64.6, 56.6, 55.2, 36.8, 31.9, 29.3. IR (neat): 3347, 2956, 2924, 2853, 1682, 1604, 1576, 1523, 1508, 1485, 1462, 1424, 1386, 1362, 1324, 1288, 1244, 1208, 1171, 1080, 1028, 964, 894, 825, 790, 756, 697, 646, 604, 531 cm^{-1}. HRMS (EI-TOF) calcd for $C_{30}H_{29}N_3O_2$(M^+): 463.2260, found: 463.2263.

3-((adamantan-1-yl)amino)-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (4y)



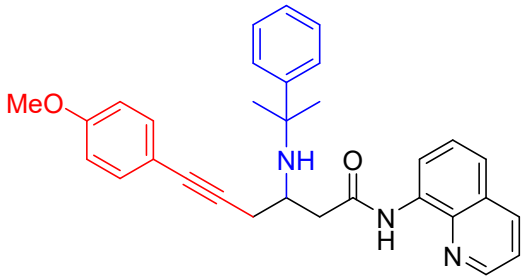
Rf 0.32 (PE/EA = 2/1). M. p. 132.1-133.0 °C.73%, 36.1 mg. Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.28 (s, 1H), 8.84-8.78 (m, 2H), 8.14 (d, J = 8.4 Hz, 1H), 7.55-7.50 (m, 2H), 7.44 (dd, J_1 = 4.0 Hz J_2 = 8.8 Hz, 1H), 7.36-7.34 (m, 2H), 6.82-6.80 (m, 2H), 3.80 (s, 3H), 3.63-3.60 (m, 1H), 3.12 (s, 1H), 2.80-2.68 (m, 4H), 2.13-1.98 (m, 5H), 1.89-1.78 (m, 5H), 1.67-1.58 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.9, 159.3, 148.0, 136.2, 133.0, 128.1, 127.4, 124.5, 124.0, 121.4, 121.3, 119.1, 117.1, 113.9, 85.0, 83.3, 55.3, 51.8, 47.0, 43.4, 36.6, 31.4, 30.2, 29.7. IR (neat): 3351, 2902, 2847, 1673, 1605, 1522, 1508, 1485, 1462, 1423, 1383, 1323, 1289, 1244, 1170, 1138, 1089, 1080, 1030, 962, 894, 825, 790, 755, 689, 641, 600, 534 cm^{-1}. HRMS (EI-TOF) calcd for $C_{32}H_{35}N_3O_2$ (M^+): 493.2729, found: 493.2729.

6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)-3-((2,4,4-trimethylpentan-2-yl)amino)hex-5-ynamide (4z)



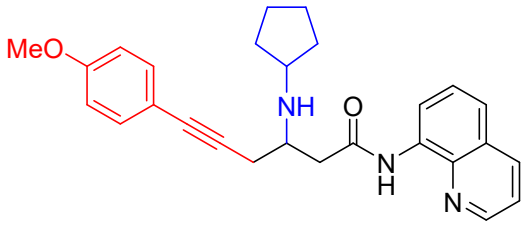
Rf 0.21 (PE/EA = 2/1). M. p. 106.1-106.7 °C. 70%, 33.2 mg. Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.92 (s, 1H), 8.82-8.77 (m, 2H), 8.14 (d, J = 8.4 Hz, 1H), 7.55-7.50 (m, 2H), 7.43 (dd, J_1 = 4.0 Hz J_2 = 8.0 Hz, 1H), 7.35 (d, J = 8.4 Hz, 2H), 6.81 (d, J = 8.4 Hz, 2H), 5.29 (s, 1H), 3.80 (s, 3H), 3.56-3.52 (m, 1H), 2.82-2.70 (m, 3H), 1.97 (d, J = 6.8 Hz, 1H), 1.25 (d, J = 5.6 Hz, 6H), 1.01 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.8, 159.3, 148.0, 138.8, 136.4, 136.2, 135.1, 133.0, 128.1, 127.4, 121.4, 121.3 117.0, 113.8, 85.1, 83.3, 55.8, 55.3, 48.5, 45.5, 31.9, 29.7, 28.5, 28.1. IR (neat): 3347, 2953, 2922, 2852, 1675, 1604, 1574, 1523, 1508, 1485, 1462, 1423, 1383, 1365, 1323, 1289, 1245, 1170, 1132, 1104, 1030, 825, 791, 756, 698, 641, 604, 534 cm^{-1}. HRMS (EI-TOF) calcd for $C_{30}H_{37}N_3O_2$ (M^+): 471.2886, found: 471.2888.

6-(4-methoxyphenyl)-3-((2-phenylpropan-2-yl)amino)-*N*-(quinolin-8-yl)hex-5-ynamide (4aa)



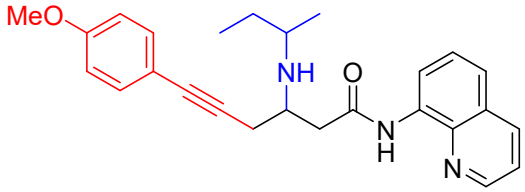
Rf 0.40 (PE/EA = 2/1). M. p. 116.6-117.3 °C. 60%, 28.9 mg. Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.10 (s, 1H), 8.82-8.78 (m, 2H), 8.16 (d, J = 8.0 Hz, 1H), 7.61 (d, J = 8.0 Hz, 2H), 7.53-7.49 (m, 2H), 7.44 (dd, J_1 = 4.0 Hz; J_2 = 8.0 Hz, 1H), 7.34-7.27 (m, 4H), 7.22-7.19 (m, 1H), 6.80 (d, J = 8.8 Hz, 2H), 5.29 (s, 1H), 3.80 (s, 3H), 3.30-3.27 (m, 1H), 2.62-2.32 (m, 4H), 1.66 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.7, 159.3, 148.0, 138.9, 136.2, 135.2, 133.0, 128.3, 128.2, 128.1, 127.4, 127.1, 126.7, 126.2, 121.4, 121.3, 117.0, 113.8, 85.0, 83.2, 56.1, 55.3, 49.5, 30.2, 29.7, 26.9. IR (neat): 3337, 2961, 2924, 2851, 1672, 1604, 1574, 1522, 1508, 1485, 1462, 1442, 1423, 1382, 1323, 1289, 1244, 1170, 1105, 1029, 825, 791, 764, 700, 535 cm^{-1}. HRMS (EI-TOF) calcd for $C_{31}H_{31}N_3O_2$ (M^+): 477.2416, found: 477.2416.

3-(cyclopentylamino)-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (4ab)



Rf 0.39 (PE/EA = 2/1). 67%, 28.6 mg. Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.95 (s, 1H), 8.79 (dd, J_1 = 8.0 Hz; J_2 = 12.0 Hz, 2H), 8.21 (d, J = 8.0 Hz, 1H), 7.58-7.51 (m, 2H), 7.48 (dd, J_1 = 3.6 Hz; J_2 = 8.0 Hz, 1H), 7.13 (dd, J_1 = 2.0 Hz; J_2 = 8.4 Hz, 2H), 6.80 (d, J = 8.4 Hz, 2H), 3.80 (s, 3H), 2.79 (t, J = 7.2 Hz, 2H), 2.61-2.56 (m, 2H), 2.13-2.01 (m, 2H), 1.70-1.48 (m, 8H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.3, 159.2, 147.7, 147.1, 139.2, 138.6, 133.0, 127.6, 124.7, 124.4, 123.9, 121.5, 119.2, 113.8, 87.4, 81.4, 64.6, 55.2, 39.0, 36.8, 34.9, 31.9, 22.6. IR (neat): 3351, 2932, 2846, 1662, 1604, 1525, 1508, 1484, 1457, 1423, 1385, 1301, 1244, 1138, 1103, 1080, 1012, 943, 895, 824, 791, 756, 664, 645, 604, 537 cm^{-1}. HRMS (EI-TOF) calcd for $C_{27}H_{29}N_3O_2$ (M^+): 427.2260, found: 427.2266.

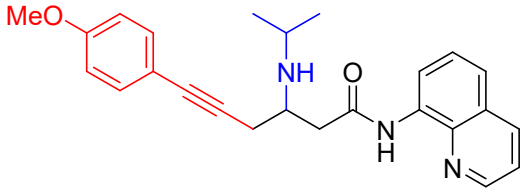
3-(*sec*-butylamino)-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (4ac)



Rf 0.39 (PE/EA = 2/1). 67%, 27.8 mg. Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.90 (s, 1H), 8.86-8.76 (m, 2H), 8.17 (dd, J_1 = 6.4 Hz; J_2 = 8.0 Hz, 1H), 7.75 (d, J = 7.2 Hz, 2H), 7.56-7.43 (m, 3H), 7.36-7.26 (m, 1H), 6.80 (d, J = 11.2 Hz, 1H), 5.30 (s, 1H), 4.17-4.12 (m, 1H), 3.80 (s, 3H), 2.80-2.76 (m, 1H), 2.58 (t, J = 6.8 Hz, 1H), 2.11 (t, J = 6.8 Hz, 1H), 2.05-2.01 (m, 1H), 1.98-1.96 (m, 1H), 1.63-1.55 (m, 5H), 0.97 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.2, 159.2, 148.0, 136.5, 133.0, 131.2, 128.5, 126.8, 124.5, 123.9, 121.5, 121.4, 119.1, 113.8, 87.4, 81.4, 64.6, 55.2, 47.1, 36.8, 31.4, 30.2, 20.5, 10.3. IR (neat): 3347, 2961, 2925, 2847, 1665, 1624, 1574, 1528, 1507, 1485, 1463, 1412, 1381, 1368, 1323, 1289, 1245, 1171, 1135, 1114, 1017, 835, 791, 754, 691, 645, 604, 537 cm^{-1}. HRMS (EI-TOF) calcd for $C_{26}H_{29}N_3O_2$

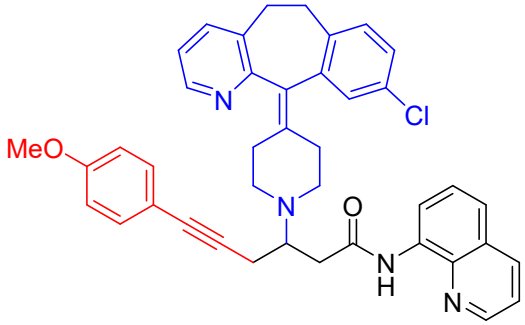
(M^+): 415.2260, found: 415.2265.

3-(isopropylamino)-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (4ad)



Rf 0.39 (PE/EA = 2/1). 67%, 27.8 mg. Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.90 (s, 1H), 8.80-8.76 (m, 2H), 8.18-8.15 (m, 1H), 7.56-7.49 (m, 2H), 7.45 (dd, J_1 = 4.4 Hz; J_2 = 8.4 Hz, 1H), 7.13 (dd, J_1 = 2.0 Hz; J_2 = 8.4 Hz, 2H), 6.80 (d, J = 8.4 Hz, 2H), 3.80 (s, 3H), 2.78 (t, J = 7.2 Hz, 1H), 2.61-2.56 (m, 2H), 2.13-2.07 (m, 1H), 2.05-1.98 (m, 2H), 1.42 (d, J = 4.8 Hz, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.2, 159.2, 148.1, 147.1, 139.3, 138.6, 136.3, 133.0, 127.4, 124.5, 124.0, 121.5, 119.1, 113.8, 87.3, 81.4, 64.6, 55.2, 38.9, 34.8, 31.9, 24.6. IR (neat): 3351, 2950, 2947, 2851, 1675, 1604, 1574, 1523, 1508, 1485, 1462, 1423, 1383, 1365, 1323, 1289, 1245, 1170, 1132, 1104, 1030, 825, 791, 756, 698, 641, 604, 534 cm^{-1}. HRMS (EI-TOF) calcd for $C_{25}H_{27}N_3O_2$ (M^+): 401.2103, found: 401.2108.

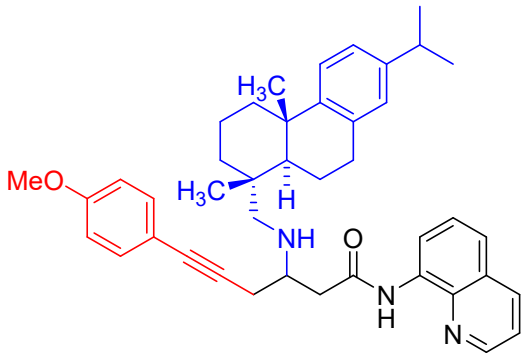
3-(4-(9-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)piperidin-1-yl)-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (4ae)



Rf 0.16 (PE/EA = 2/1). M. p. 143.3-144.1 °C. 56%, 36.5 mg. Brown solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.65 (s, 1H), 8.85-8.81 (m, 2H), 8.45-8.43 (m, 1H), 8.17-8.15 (m, 1H), 8.02 (s, 1H), 7.56-7.52 (m, 2H), 7.46 (dd, J_1 = 4.0 Hz; J_2 = 8.0 Hz, 2H), 7.30 (d, J = 8.8 Hz, 2H), 7.16 (s, 1H), 7.14-7.10 (m, 2H), 6.79 (d, J = 8.4 Hz, 2H), 3.79 (s, 3H), 3.49-3.38 (m, 3H), 3.15-3.12 (m, 1H), 2.88-2.81 (m, 8H), 2.67-2.65 (m, 1H),

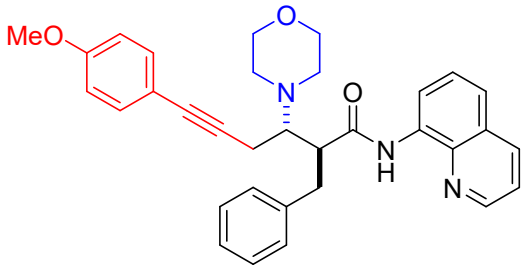
2.58-2.43 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.8, 162.6, 159.3, 148.1, 147.9, 146.5, 139.4, 137.4, 137.3, 136.2, 135.5, 132.9, 132.7, 131.0, 130.9, 129.1, 129.0, 128.1, 127.4, 126.1, 122.2, 121.6, 121.5, 121.4, 117.8, 115.7, 113.8, 85.6, 83.0, 60.7, 55.3, 51.3, 38.8, 36.5, 31.9, 31.4, 28.0. IR (neat): 3347, 2902, 2923, 2847, 1672, 1625, 1604, 1574, 1522, 1518, 1484, 1462, 1442, 1403, 1383, 1323, 1289, 1225, 1173, 1105, 1021, 953, 825, 791, 764, 700, 645, 604, 560 cm^{-1}. HRMS (EI-TOF) calcd for $C_{41}H_{37}ClN_4O_2$ (M^+): 652.2605, found: 652.26059.

3-((((1R,4aS,10aR)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl)methyl)amino)-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (4af)



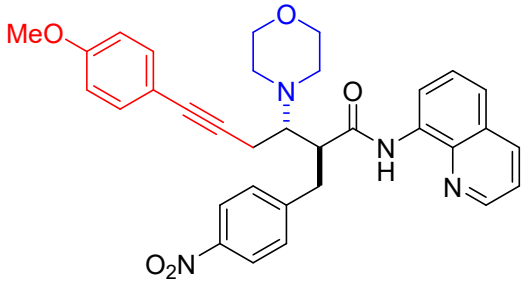
Rf 0.32 (PE/EA = 5/1). M. p. 133.6-134.3 °C. 50%, 31.4 mg. Brown solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.89 (s, 1H), 8.80-8.76 (m, 2H), 8.16 (d, J = 8.0 Hz, 1H), 7.56-7.52 (m, 2H), 7.45 (dd, J_1 = 4.4 Hz; J_2 = 8.0 Hz, 1H), 7.36 (d, J = 8.8 Hz, 2H), 7.27 (s, 1H), 7.05-7.00 (m, 1H), 6.95-6.90 (m, 1H), 6.81 (d, J = 8.8 Hz, 2H), 5.30 (s, 1H), 3.90-3.85 (m, 2H), 3.80 (s, 3H), 3.77-3.66 (m, 2H), 2.80-2.76 (m, 2H), 2.58 (t, J = 6.8 Hz, 1H), 2.12 (t, J = 7.2 Hz, 1H), 2.05-1.96 (m, 2H), 1.67-1.56 (m, 3H), 1.42-1.40 (m, 2H), 1.33 (s, 2H), 1.29-1.22 (m, 14H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.2, 159.1, 148.1, 138.3, 136.4, 134.5, 133.0, 132.3, 131.9, 130.4, 130.1, 128.0, 127.4, 127.3, 126.8, 121.7, 121.6, 121.4, 116.6, 113.8, 87.3, 81.4, 55.5, 55.3, 42.3, 36.8, 31.9, 31.4, 30.3, 30.2, 29.7, 29.5, 29.3, 29.2, 24.5, 23.9, 22.7, 19.0, 14.1. IR (neat): 3351, 2947, 2934, 2845, 1673, 1604, 1588, 1563, 1508, 1483, 1462, 1423, 1380, 1375, 1356, 1320, 1291, 1244, 1151, 1104, 1029, 1001, 803, 791, 753, 664, 645, 604, 557 cm^{-1}. HRMS (EI-TOF) calcd for $C_{42}H_{49}N_3O_2$ (M^+): 627.3825, found: 627.3825.

2-benzyl-6-(4-methoxyphenyl)-3-morpholino-*N*-(quinolin-8-yl)hex-5-ynamide (5a)



Rf 0.39 (PE/EA = 2/1). M. p. 121.1-122.0 °C. 63%, 32.6 mg. Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.68 (s, 1H), 8.72 (d, J = 7.2 Hz, 1H), 8.67 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.10 (dd, J_1 = 1.6 Hz; J_2 = 8.0 Hz, 1H), 7.53-7.37 (m, 5H), 7.31 (d, J = 7.6 Hz, 2H), 7.18 (t, J = 7.6 Hz, 2H), 7.09 (d, J = 7.2 Hz, 1H), 6.88 (d, J = 8.4 Hz, 2H), 3.83 (s, 3H), 3.52-3.41 (m, 4H), 3.23-3.19 (m, 2H), 3.15 (d, J = 6.4 Hz, 2H), 2.98-2.94 (m, 2H), 2.88-2.85 (m, 1H), 2.80-2.78 (m, 1H), 2.65-2.62 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.6, 159.4, 148.0, 139.7, 138.4, 136.2, 134.5, 132.9, 129.0, 128.4, 127.9, 127.4, 126.2, 121.4, 121.3, 116.7, 115.9, 114.0, 85.9, 83.2, 67.4, 64.9, 55.3, 53.7, 50.1, 35.6, 29.7. IR (neat): 3347, 2957, 2901, 2847, 1674, 1623, 1597, 1520, 1480, 1451, 1428, 1383, 1358, 1321, 1259, 1121, 1077, 1002, 954, 874, 791, 756, 665, 604, 561 cm^{-1}. HRMS (EI-TOF) calcd for $C_{33}H_{33}N_3O_3$ (M^+): 519.2522, found: 519.2527.

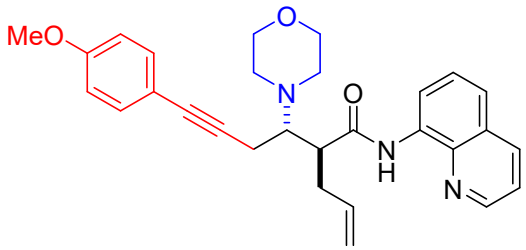
(2S,3S)-6-(4-methoxyphenyl)-3-morpholino-2-(4-nitrobenzyl)-*N*-(quinolin-8-yl)hex-5-ynamide (5b)



Rf 0.37 (PE/EA = 2/1). M. p. 125.3-126.0 °C. 75%, 42.3 mg. Brown solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.48 (s, 1H), 8.61-8.82 (m, 2H), 8.17 (d, J = 8.0 Hz, 1H), 7.68 (d, J_2 = 7.2 Hz, 1H), 7.54-7.52 (m, 2H), 7.47-7.44 (m, 1H), 7.36-7.27 (m, 3H), 7.13 (d, J = 8.4 Hz, 1H), 6.80 (d, J = 8.4 Hz, 2H), 6.68 (d, J = 6.8Hz, 1H), 4.09-4.04 (m, 2H),

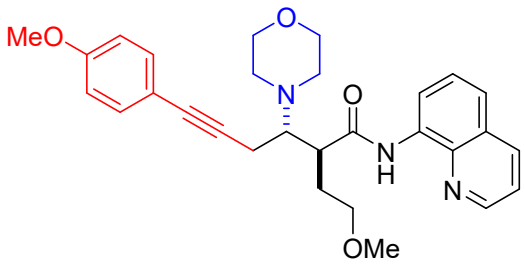
3.95-3.91 (m, 2H), 3.80 (s, 3H), 3.46-3.38 (m, 1H), 2.97-2.83 (m, 4H), 2.79-2.72 (m, 3H), 2.60-2.50 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.5, 162.6, 147.9, 147.1, 138.6, 136.3, 132.9, 128.2, 127.4, 124.7, 124.5, 123.9, 123.5, 121.6, 121.4, 119.1, 117.7, 113.9, 85.2, 83.1, 66.8, 60.9, 55.3, 48.9, 38.5, 34.9, 29.3. IR (neat): 3349, 2955, 2922, 2852, 1671, 1596, 1520, 1508, 1487, 1461, 1423, 1383, 1362, 1343, 1323, 1289, 1245, 1209, 1172, 1157, 1113, 1080, 1030, 1010, 964, 933, 825, 790, 757, 698, 644, 604, 563 cm^{-1}. HRMS (EI-TOF) calcd for $C_{33}H_{32}N_4O_5$ (M^+): 564.2373, found: 564.2375.

2-allyl-6-(4-methoxyphenyl)-3-morpholino-*N*-(quinolin-8-yl)hex-5-ynamide (5c)



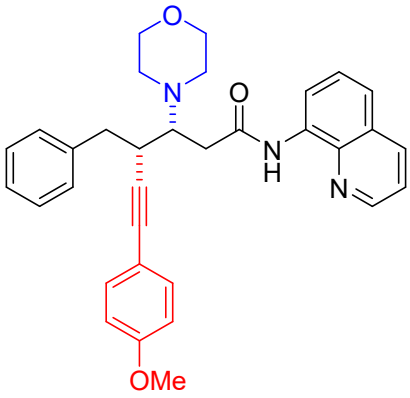
Rf 0.58 (PE/EA = 2/1). M. p. 112.5-113.3 °C. 90%, 42.2 mg. Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.03 (s, 1H), 8.74-8.68 (m, 2H), 8.08 (d, J = 8.0 Hz, 1H), 7.49-7.44 (m, 2H), 7.36 (dd, J_1 = 4.4 Hz; J_2 = 8.4 Hz, 1H), 7.30 (d, J = 8.4 Hz, 2H), 6.78 (d, J = 8.8 Hz, 2H), 5.87-5.80 (m, 1H), 5.12 (d, J = 17.2 Hz, 1H), 4.95 (d, J = 10.4 Hz, 1H), 3.74 (s, 3H), 3.49-3.34 (m, 6H), 3.12-3.07 (m, 1H), 2.98-2.87 (m, 3H), 2.62-2.52 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.7, 159.4, 148.1, 138.6, 136.3, 135.5, 132.8, 127.5, 124.5, 124.0, 121.5, 121.4, 119.1, 117.1, 116.8, 114.0, 85.8, 83.0, 67.3, 64.6, 58.4, 55.3, 50.0, 29.7, 28.2. IR (neat): 3351, 2954, 2854, 1674, 1620, 1547, 1510, 1475, 1451, 1427, 1381, 1358, 1321, 1122, 1053, 1027, 992, 954, 909, 874, 791, 698, 664, 604, 557 cm^{-1}. HRMS (EI-TOF) calcd for $C_{29}H_{31}N_3O_3$ (M^+): 469.2365, found: 469.2366.

2-(2-methoxyethyl)-6-(4-methoxyphenyl)-3-morpholino-*N*-(quinolin-8-yl)hex-5-ynamide (5d)



Rf 0.37 (PE/EA = 2/1). M. p. 125.6-126.5 °C. 72%, 35.1 mg. Yellow solid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.99 (s, 1H), 8.82-8.78 (m, 2H), 8.18 (d, J = 8.0 Hz, 1H), 7.55-7.53 (m, 2H), 7.46 (dd, J_1 = 4.0 Hz; J_2 = 8.4 Hz, 1H), 7.13 (dd, J_1 = 2.4 Hz; J_2 = 8.4 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 3.82 (s, 3H), 3.81-3.77 (m, 2H), 3.56-3.41 (m, 4H), 3.29 (s, 3H), 3.21-3.12 (m, 1H), 3.02-2.99 (m, 2H), 2.88-2.81 (m, 1H), 2.73-2.67 (m, 2H), 2.07-2.01 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.1, 159.3, 148.1, 147.1, 138.6, 136.3, 132.8, 128.5, 127.4, 124.5, 123.9, 121.5, 119.1, 113.9, 87.4, 85.9, 70.5, 67.3, 65.4, 58.7, 55.3, 49.9, 34.9, 27.7, 27.1. IR (neat): 3347, 2954, 2923, 2848, 1670, 1625, 1542, 1473, 1454, 1429, 1383, 1368, 1327, 1259, 1112, 1030, 1002, 954, 874, 791, 756, 665, 604, 560 cm^{-1}. HRMS (EI-TOF) calcd for $C_{29}H_{33}N_3O_4$ (M^+): 487.2471, found: 487.2475.

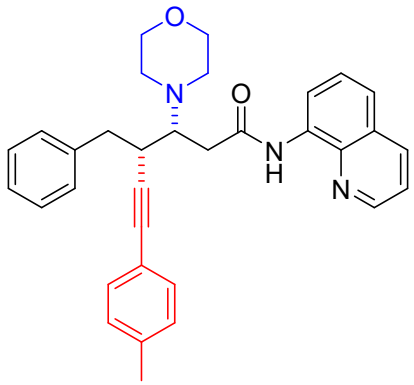
4-benzyl-6-(4-methoxyphenyl)-3-morpholino-*N*-(quinolin-8-yl)hex-5-ynamide (5e)



Rf 0.57 (PE/EA = 2/1). 74%, 38.3 mg. Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.24 (s, 1H), 8.70 (d, J = 6.8 Hz, 1H), 8.54 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.06 (d, J = 8.0 Hz, 1H), 7.47-7.43 (m, 3H), 7.33 (dd, J_1 = 4.0 Hz; J_2 = 8.0 Hz, 1H), 7.25-7.19 (m, 4H), 7.07-7.04 (m, 2H), 6.76 (d, J = 9.2 Hz, 2H), 3.74 (s, 3H), 3.37 (dd, J_1 = 7.2 Hz; J_2 = 14.4 Hz, 2H), 3.16-3.13 (m, 1H), 3.09-3.00 (m, 5H), 2.96-2.89 (m, 2H), 2.87

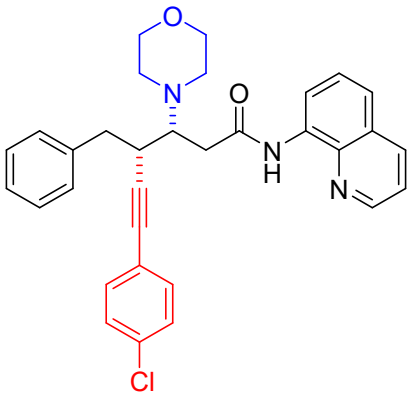
(d, J = 3.2 Hz, 1H), 2.80 (d, J = 3.2 Hz, 1H), 2.60-2.57 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.5, 159.4, 148.1, 147.1, 139.7, 138.5, 136.3, 132.9, 129.3, 128.2, 127.4, 126.2, 124.5, 124.0, 121.5, 119.2, 116.7, 113.9, 89.3, 85.3, 67.4, 62.5, 55.3, 50.2, 38.7, 29.7. IR (neat): 3351, 2957, 2923, 2847, 1657, 1573, 1524, 1484, 1453, 1403, 1380, 1361, 1320, 1259, 1112, 1025, 1012, 950, 896, 791, 756, 664, 605, 565 cm^{-1}. HRMS (EI-TOF) calcd for $C_{33}H_{33}N_3O_3$ (M^+): 519.2522, found: 519.2525.

4-benzyl-3-morpholino-*N*-(quinolin-8-yl)-6-(*p*-tolyl)hex-5-ynamide (5f)



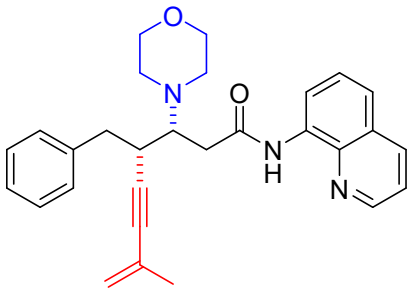
Rf 0.65 (PE/EA = 2/1). 63%, 31.7 mg. Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.33 (s, 1H), 8.78 (dd, J_1 = 1.6 Hz J_2 = 6.8 Hz, 1H),), 8.61 (dd, J_1 = 1.6 Hz; J_2 = 4.4 Hz, 1H), 8.13 (dd, J_1 = 1.6 Hz; J_2 = 8.4 Hz, 1H), 7.55-7.49 (m, 2H), 7.40 (dd, J_1 = 4.4 Hz; J_2 = 8.0 Hz, 1H), 7.33-7.25 (m, 6H), 7.19 (t, J = 7.2 Hz, 1H), 7.12 (d, J = 8.0 Hz, 2H), 3.81 (t, J = 4.4 Hz, 4H), 3.24-3.21 (m, 1H), 3.18-2.97 (m, 7H), 2.69-2.64 (m, 2H), 2.36 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 148.1, 139.7, 138.5, 137.9, 136.3, 134.6, 131.4, 129.3, 129.0, 128.2, 128.0, 127.4, 126.3, 121.7, 121.6, 120.6, 116.8, 90.1, 85.6, 67.4, 62.4, 50.2, 38.7, 29.7, 27.9, 21.4. IR (neat): 3347, 2957, 2901, 2847, 1674, 1623, 1597, 1520, 1480, 1451, 1428, 1383, 1375, 1358, 1321, 1259, 1121, 1077, 1002, 954, 874, 791, 756, 665, 604, 561 cm^{-1}. HRMS (EI-TOF) calcd for $C_{33}H_{33}N_3O_2$ (M^+): 503.2573, found: 503.2577.

4-benzyl-6-(4-chlorophenyl)-3-morpholino-*N*-(quinolin-8-yl)hex-5-ynamide (5g)



Rf 0.65 (PE/EA = 1/2). 39%, 20.4 mg. Brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.30 (s, 1H), 8.78 (dd, J_1 = 1.6 Hz; J_2 = 6.8 Hz, 1H), 8.62-8.61 (m, 1H), 8.15 (dd, J_1 = 1.2 Hz; J_2 = 8.0 Hz, 1H), 7.54-7.53 (m, 2H), 7.43 (dd, J_1 = 4.0 Hz; J_2 = 8.4 Hz, 2H), 7.34-7.28 (m, 6H), 7.22-7.18 (m, 2H), 3.81 (t, J = 4.4 Hz, 4H), 3.25 (dd, J_1 = 6.8 Hz; J_2 = 12.0 Hz, 1H), 3.17-2.97 (m, 7H), 2.69-2.64 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 148.0, 139.5, 138.4, 136.4, 134.6, 133.9, 132.7, 129.3, 128.5, 128.2, 128.0, 127.4, 127.1, 126.4, 121.7, 121.6, 116.7, 91.9, 84.5, 67.4, 62.4, 50.2, 38.5, 29.7. IR (neat): 3348, 2957, 2921, 2851, 1673, 1608, 1521, 1483, 1453, 1421, 1403, 1383, 1361, 1289, 1243, 1227, 1184, 1163, 1123, 1080, 1008, 912, 891, 823, 791, 721, 691, 645, 604, 537 cm^{-1}.HRMS (EI-TOF) calcd for $C_{32}H_{30}ClN_3O_2$ (M^+): 523.2027, found: 523.2028.

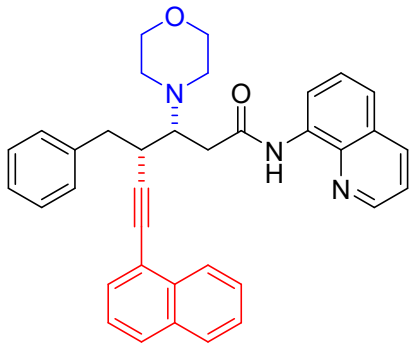
4-benzyl-7-methyl-3-morpholino-*N*-(quinolin-8-yl)oct-7-en-5-ynamide (5h)



Rf 0.67 (PE/EA = 2/1). 34%, 15.4 mg. Brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.28 (s, 1H), 8.78-8.76 (m, 2H), 8.16 (dd, J_1 = 1.2 Hz; J_2 = 8.4 Hz, 1H), 7.56-7.52 (m, 2H), 7.45 (dd, J_1 = 4.4 Hz; J_2 = 8.0 Hz, 1H), 7.27 (d, J = 5.2 Hz, 4H), 7.22-7.18 (m, 1H), 5.21 (d, J = 21.2 Hz, 2H), 3.82-3.79 (m, 4H), 3.21-3.17 (m, 1H), 3.07-2.91

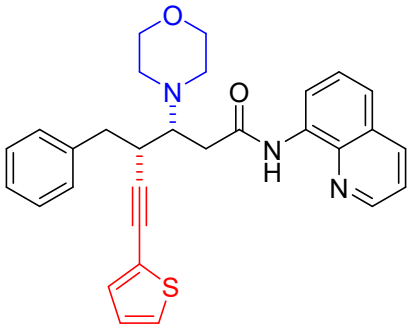
(m, 7H), 2.67-2.62 (m, 2H), 11.89 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 148.1, 139.6, 138.5, 136.3, 134.7, 129.3, 128.4, 128.2, 128.0, 127.4, 126.2, 121.6, 121.5, 120.7, 116.7, 89.9, 86.7, 67.4, 62.3, 50.2, 38.6, 29.7, 23.5. IR (neat): 3351, 2957, 2923, 2854, 1673, 1648, 1521, 1485, 1447, 1421, 1381, 1365, 1289, 1227, 1154, 1132, 1112, 1026, 1012, 912, 891, 823, 791, 721, 689, 646, 604, 577 cm^{-1}. HRMS (EI-TOF) calcd for $C_{29}H_{31}N_3O_2$ (M^+): 453.2416, found: 453.2417.

4-benzyl-3-morpholino-6-(naphthalen-1-yl)-*N*-(quinolin-8-yl)hex-5-ynamide (5i)



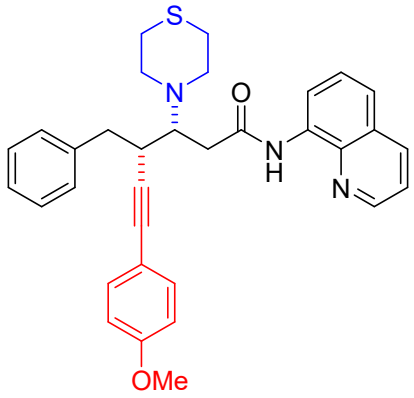
Rf 0.63 (PE/EA = 2/1). 44%, 23.7 mg. Brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.35 (s, 1H), 8.80 (d, J = 7.2 Hz, 1H), 8.41-8.40 (m, 1H), 8.07 (dd, J_1 = 8.4 Hz J_2 = 20.4 Hz, 2H), 7.81 (t, J = 8.4 Hz, 2H), 7.66 (d, J = 6.8 Hz, 1H), 7.53-7.37 (m, 7H), 7.34-7.29 (m, 3H), 7.25-7.21 (m, 1H), 3.83 (t, J = 4.4 Hz, 4H), 3.42-3.35 (m, 2H), 3.22-2.14 (m, 4H), 3.10-3.07 (m, 2H), 2.75-2.71 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 148.0, 139.7, 138.5, 136.2, 134.6, 133.4, 133.2, 130.2, 129.4, 128.6, 128.5, 128.3, 128.2, 128.1, 128.0, 127.3, 126.6, 126.4, 126.3, 125.2, 121.6, 121.5, 116.7, 95.7, 83.7, 67.4, 62.7, 50.3, 38.8, 29.7. IR (neat): 3351, 2967, 2921, 2854, 1667, 1523, 1501, 1481, 1468, 1456, 1421, 1405, 1395, 1366, 1323, 1251, 1210, 1192, 1096, 961, 891, 795, 754, 691, 647, 604, 563 cm^{-1}. HRMS (EI-TOF) calcd for $C_{36}H_{33}N_3O_2$ (M^+): 539.2573, found: 539.2574.

4-benzyl-3-morpholino-*N*-(quinolin-8-yl)-6-(thiophen-2-yl)hex-5-ynamide (5j)



Rf 0.63 (PE/EA = 2/1). 51%, 25.2 mg. Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.31 (s, 1H), 8.79-8.77 (m, 1H), 8.63 (dd, J_1 = 1.6 Hz; J_2 = 4.0 Hz, 1H), 8.14 (dd, J_1 = 1.2 Hz; J_2 = 8.0 Hz, 1H), 7.55-7.49 (m, 2H), 7.43-7.39 (m, 3H), 7.32-7.26 (m, 4H), 7.21-7.18 (m, 1H), 7.10 (d, J = 5.2 Hz, 1H), 3.81 (t, J = 4.4 Hz, 4H), 3.24-3.02 (m, 6H), 2.98 (d, J = 7.2 Hz, 2H), 2.67-2.64 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 148.1, 139.6, 138.5, 136.3, 134.6, 129.9, 129.3, 128.6, 128.4, 128.2, 128.0, 127.9, 127.4, 126.3, 125.1, 121.6, 116.7, 90.4, 80.6, 67.4, 62.3, 50.2, 38.6, 29.7. IR (neat): 3344, 2959, 2921, 2850, 1674, 1596, 1520, 1484, 1453, 1423, 1384, 1358, 1323, 1259, 1112, 1066, 1007, 955, 824, 788, 756, 697, 625, 578 cm^{-1}. HRMS (EI-TOF) calcd for $C_{30}H_{29}N_3O_2S$ (M^+): 495.1980, found: 495.1983.

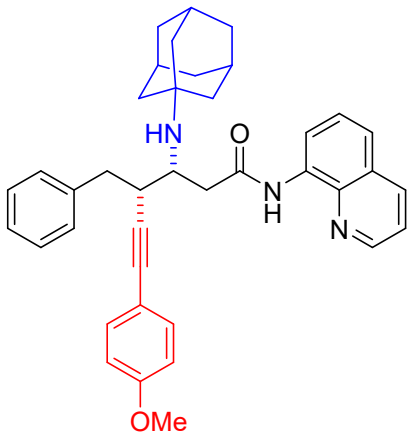
4-benzyl-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)-3-thiomorpholinohex-5-ynamide (5k)



Rf 0.68 (PE/EA = 2/1). 53%, 28.3 mg. Brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.42 (s, 1H), 8.80-8.77 (m, 1H), 8.69-8.68 (m, 1H), 8.15 (d, J = 8.4 Hz, 1H), 7.53-7.49 (m, 2H), 7.42 (dd, J_1 = 4.4 Hz; J_2 = 8.0 Hz, 1H), 7.36-7.26 (m, 6H), 7.21 (d, J = 6.4 Hz, 1H), 6.84 (d, J = 8.4 Hz, 2H), 3.82 (s, 3H), 3.37-3.34 (m, 2H), 3.25-3.22 (m,

2H), 3.13-2.93 (m, 5H), 2.80 (s, 4H), 2.63-2.59 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.5, 159.3, 148.1, 139.6, 138.5, 136.3, 134.7, 132.8, 130.1, 129.7, 129.3, 128.2, 127.4, 126.3, 121.6, 116.8, 113.9, 112.9, 89.2, 85.3, 64.3, 55.3, 52.4, 39.0, 29.7, 28.4. IR (neat): 3350, 2954, 2923, 2852, 1737, 1674, 1604, 1521, 1508, 1484, 1453, 1423, 1385, 1358, 1305, 1291, 1246, 1208, 1175, 1079, 1017, 963, 896, 854, 791, 762, 696, 646, 604, 560 cm^{-1}. HRMS (EI-TOF) calcd for $C_{33}H_{33}N_3O_2S$ (M^+): 535.2293, found: 535.2299.

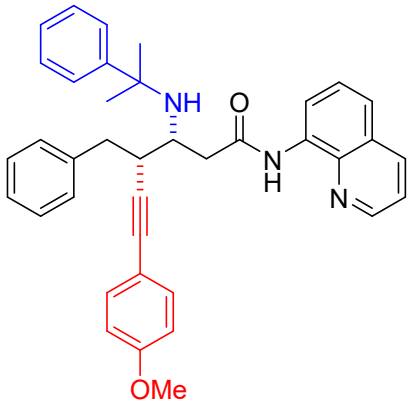
3-((adamantan-1-yl)amino)-4-benzyl-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (5l)



Rf 0.32 (PE/EA = 2/1). 61%, 35.6 mg. Brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.17 (s, 1H), 8.81 (d, J = 7.2 Hz, 1H), 8.74 (dd, J_1 = 1.6 Hz; J_2 = 4.8 Hz, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.52-7.46 (m, 4H), 7.43-7.40 (m, 2H), 7.32 (d, J = 7.2 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H), 6.74 (d, J = 8.4 Hz, 2H), 3.78 (s, 3H), 3.59 (d, J = 5.2 Hz, 1H), 3.17 (s, 1H), 3.13 (dd, J_1 = 4.4 Hz; J_2 = 12.8 Hz, 1H), 3.07-3.00 (m, 2H), 2.84-2.70 (m, 2H), 1.94 (s, 3H), 1.87-1.81 (m, 6H), 1.72 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.7, 159.2, 148.0, 140.0, 138.9, 136.1, 135.3, 132.9, 129.4, 128.4, 128.1, 127.4, 126.7, 126.1, 121.4, 121.3, 116.9, 113.7, 88.8, 84.9, 55.3, 51.4, 51.0, 43.8, 37.9, 36.7, 36.5, 29.7, 29.6. IR (neat): 3351, 2924, 2845, 1667, 1605, 1575, 1508, 1483, 1450, 1423, 1381, 1323, 1293, 1244, 1105, 1138, 1089, 1080, 1031, 964, 894, 845, 795, 755, 669, 645, 601, 535 cm^{-1}. HRMS (EI-TOF) calcd for $C_{39}H_{41}N_3O_2$ (M^+): 583.3199,

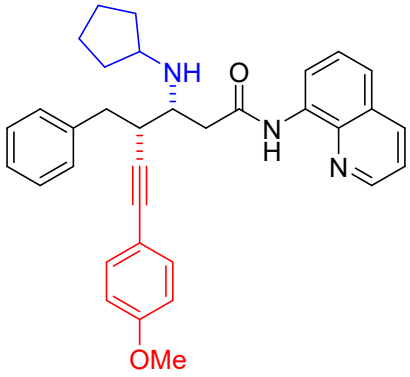
found: 583.3203.

4-benzyl-6-(4-methoxyphenyl)-3-((2-phenylpropan-2-yl)amino)-*N*-(quinolin-8-yl)hex-5-ynamide (5m)



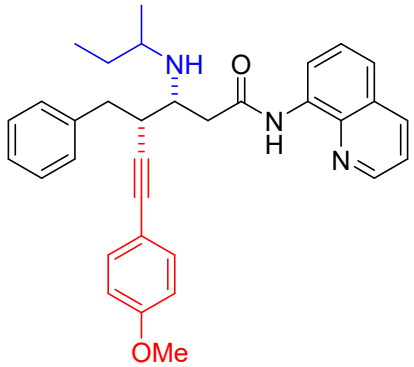
Rf 0.67 (PE/EA = 2/1). 83%, 46.8 mg. Brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.04 (s, 1H), 8.81-8.76 (m, 2H), 8.14 (d, J = 7.2 Hz, 1H), 7.66 (d, J = 7.6 Hz, 2H), 7.51 (t, J = 7.6 Hz, 2H), 7.42 (dd, J_1 = 4.0 Hz; J_2 = 8.4 Hz, 1H), 7.25-7.14 (m, 10H), 6.75 (d, J = 8.8 Hz, 2H), 3.78 (s, 3H), 3.10 (dd, J_1 = 4.0 Hz; J_2 = 12.8 Hz, 1H), 2.91-2.87 (m, 1H), 2.71-2.57 (m, 3H), 2.40 (dd, J_1 = 5.2 Hz; J_2 = 14.8 Hz, 1H), 1.67 (d, J = 15.6 Hz, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.7, 159.2, 148.0, 139.8, 138.8, 136.2, 135.2, 132.8, 129.4, 129.0, 128.9, 128.2, 128.1, 128.0, 127.4, 126.7, 126.3, 126.1, 121.5, 121.3, 116.8, 113.7, 88.8, 84.9, 55.7, 55.3, 53.4, 37.4, 30.3, 29.1. IR (neat): 3350, 2965, 2905, 2827, 1652, 1604, 1574, 1508, 1485, 1473, 1442, 1423, 1383, 1321, 1289, 1244, 1165, 1105, 1030, 845, 791, 754, 708, 537 cm^{-1}. HRMS (EI-TOF) calcd for $C_{38}H_{37}N_3O_2$ (M^+): 567.2886, found: 567.2888.

4-benzyl-3-(cyclopentylamino)-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (5n)



Rf 0.68 (PE/EA = 2/1). 60%, 31.1 mg. Brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.93 (s, 1H), 8.80-8.74 (m, 2H), 8.18 (d, J = 8.4 Hz, 1H), 7.56-7.49 (m, 2H), 7.45 (dd, J_1 = 4.0 Hz J_2 = 8.4 Hz, 1H), 7.35-7.31 (m, 5H), 7.23-7.19 (m, 1H), 7.14-7.07 (m, 1H), 6.78 (d, J = 8.8 Hz, 2H), 5.30 (s, 1H), 3.80 (s, 3H), 2.99-2.75 (m, 4H), 2.20-2.14 (m, 1H), 2.05-2.01 (m, 1H), 1.95-1.92 (m, 1H), 1.66-1.49 (m, 8H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.4, 159.2, 147.8, 139.3, 136.7, 132.9, 129.4, 128.2, 127.6, 126.3, 124.5, 124.0, 123.5, 121.5, 121.4, 119.1, 116.9, 113.8, 90.1, 83.5, 64.6, 55.3, 41.7, 38.9, 36.0, 34.0, 31.9, 22.7. IR (neat): 3351, 2954, 2843, 1675, 1624, 1525, 1508, 1457, 1423, 1402, 1383, 1301, 1254, 1131, 1104, 1080, 1011, 943, 893, 824, 791, 756, 664, 646, 605, 537 cm^{-1}. HRMS (EI-TOF) calcd for $C_{34}H_{35}N_3O_2$ (M^+): 517.2729, found: 517.2732.

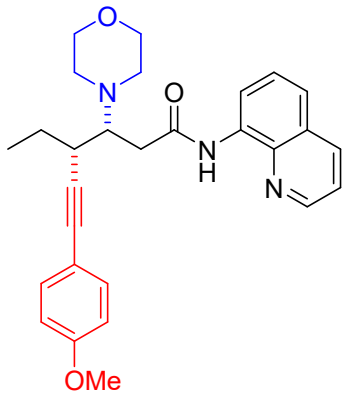
4-benzyl-3-(sec-butylamino)-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (5o)



Rf 0.68 (PE/EA = 1/2). 70%, 35.4 mg. Brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.89 (s, 1H), 8.78-8.74 (m, 2H), 8.15 (d, J = 8.0 Hz, 1H), 8.75 (d, J = 7.2 Hz, 2H), 7.55-7.47 (m, 2H), 7.44-7.41 (m, 2H), 7.32-7.28 (m, 4H), 7.14-7.07 (m, 1H), 6.79 (d, J =

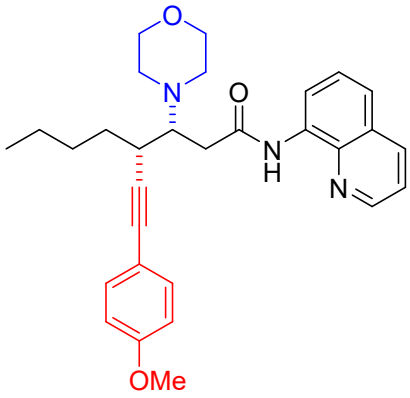
8.8 Hz, 1H), 4.16-4.08 (m, 1H), 3.80 (s, 3H), 3.67 (d, *J* = 15.6 Hz, 1H), 2.98-2.85 (m, 4H), 2.61-2.57 (m, 1H), 2.05-1.95 (m, 2H), 1.73-1.71 (m, 1H), 1.59 (d, *J* = 7.6 Hz, 3H), 0.97 (t, *J* = 8.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.3, 159.2, 148.0, 136.3, 132.9, 131.2, 129.4, 128.5, 128.2, 127.4, 126.8, 124.5, 123.9, 121.5, 121.3, 119.2, 116.5, 113.8, 90.1, 83.5, 64.5, 55.2, 47.1, 38.9, 34.9, 34.0, 31.9, 22.6, 10.4. IR (neat): 3351, 2953, 2923, 2847, 1675, 1624, 1574, 1528, 1507, 1483, 1463, 1383, 1368, 1324, 1289, 1250, 1162, 1117, 1012, 865, 791, 754, 691, 645, 604, 576 cm^{-1}. HRMS (EI-TOF) calcd for $C_{33}H_{35}N_3O_2$ (M^+): 505.2729, found: 505.2733.

4-ethyl-6-(4-methoxyphenyl)-3-morpholino-*N*-(quinolin-8-yl)hex-5-ynamide (5p)



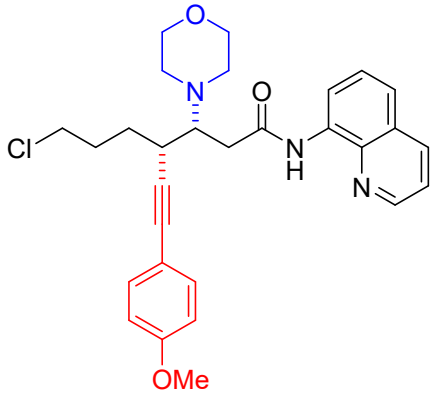
Rf 0.47 (PE/EA = 2/1). 84%, 38.4 mg. Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.50 (s, 1H), 8.82 (d, *J* = 7.2 Hz, 1H), 8.68-8.67 (m, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 7.56-7.50 (m, 2H), 7.44-7.36 (m, 3H), 6.84 (d, *J* = 8.4 Hz, 2H), 3.82 (s, 3H), 3.79 (s, 4H), 3.32 (d, *J* = 4.4 Hz, 1H), 3.05-3.02 (m, 2H), 2.93 (d, *J* = 4.4 Hz, 2H), 2.80 (d, *J* = 5.2 Hz, 3H), 1.75 (t, *J* = 7.2 Hz, 2H), 1.08 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.9, 159.3, 148.1, 138.6, 136.3, 134.8, 132.9, 128.0, 127.4, 124.5, 124.0, 121.6, 116.8, 113.9, 89.7, 84.4, 67.4, 63.5, 55.3, 50.2, 30.2, 29.7, 25.7, 12.3. IR (neat): 3347, 2954, 2923, 2854, 1626, 1527, 1457, 1380, 1361, 1321, 1275, 1256, 1208, 1165, 1112, 1067, 1012, 961, 886, 804, 791, 754, 667, 645, 605, 557 cm^{-1}.HRMS (EI-TOF) calcd for $C_{28}H_{31}N_3O_3$ (M^+): 457.2365, found: 457.2366.

4-((4-methoxyphenyl)ethynyl)-3-morpholino-*N*-(quinolin-8-yl)octanamide (5q)



Rf 0.49 (PE/EA = 2/1). 94%, 45.6 mg. Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.51 (s, 1H), 8.82 (d, *J* = 6.8 Hz, 1H), 8.68 (d, *J* = 2.4 Hz, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 7.55-7.53 (m, 2H), 7.45-7.36 (m, 3H), 6.84 (d, *J* = 8.8 Hz, 2H), 3.82 (s, 3H), 3.79 (s, 4H), 3.31-3.29 (m, 1H), 3.04-3.02 (m, 2H), 2.93 (t, *J* = 3,2 Hz, 2H), 2.86-2.79 (m, 3H), 1.70 (d, *J* = 5.6 Hz, 2H), 1.60-1.57 (m, 2H), 1.42 (d, *J* = 4.0 Hz, 2H), 0.92 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.0, 159.2, 148.1, 138.6, 136.3, 132.9, 128.0, 127.4, 124.5, 124.0, 121.6, 119.1, 116.9, 113.9, 90.0, 84.2, 67.4, 63.7, 55.3, 50.2, 31.4, 30.2, 30.0, 29.7, 22.6, 14.1. IR (neat): 3351, 2947, 2928, 2824, 1616, 1513, 1485, 1457, 1430, 1384, 1361, 1320, 1273, 1256, 1207, 1153, 1127, 1021, 1001, 950, 895, 807, 789, 754, 664, 645, 604, 573 cm^{-1}. HRMS (EI-TOF) calcd for $C_{30}H_{35}N_3O_3$ (M^+): 485.2678, found: 485.2679.

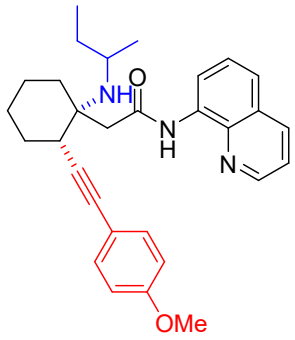
7-chloro-4-((4-methoxyphenyl)ethynyl)-3-morpholino-*N*-(quinolin-8-yl)heptanamide (5r)



Rf 0.42 (PE/EA = 2/1). 55%, 27.5 mg. Yellow oil; ^{1}H NMR (d_6-DMSO, 400 MHz) δ 10.43 (s, 1H), 8.82-8.79 (m, 1H), 8.67-8.65 (m, 1H), 8.16 (d, *J* = 8.0 Hz, 1H), 7.55-

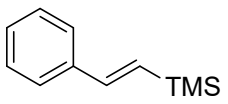
7.51 (m, 2H), 7.45-7.36 (m, 3H), 6.86-6.83 (m, 2H), 4.41-4.36 (m, 1H), 4.12-4.09 (m, 1H), 3.83 (s, 3H), 3.78-3.74 (m, 4H), 3.64-3.58 (m, 1H), 3.36-3.29 (m, 1H), 3.06-3.03 (m, 2H), 2.95 (t, J = 6.4 Hz, 2H), 2.77-2.73 (m, 2H), 1.73-1.58 (m, 4H). ^{13}C NMR (d_6-DMSO, 100 MHz) δ 170.7, 148.1, 138.5, 136.3, 132.9, 129.6, 128.3, 127.4, 124.5, 124.0, 121.6, 119.1, 116.8, 113.9, 93.5, 84.8, 67.4, 63.5, 55.3, 50.3, 38.9, 31.4, 30.2, 27.9, 27.1. IR (neat): 3350, 2953, 2921, 2854, 1626, 1523, 1485, 1457, 1438, 1380, 1373, 1312, 1274, 1209, 1132, 1105, 1087, 1002, 966, 815, 791, 745, 665, 645, 604, 553 cm^{-1}. HRMS (EI-TOF) calcd for $C_{29}H_{32}ClN_3O_3$ (M^+): 505.2132, found: 505.2137.

2-((1R,2S)-1-(sec-butylamino)-2-((4-methoxyphenyl)ethynyl)cyclohexyl)-*N*-(quinolin-8-yl)acetamide (5s)

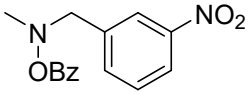


Rf 0.56 (PE/EA = 2/1). 63%, 21.7 mg. Brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.37 (s, 1H), 8.79 (d, J = 2.4 Hz, 2H), 8.20 (dd, J_1 = 0.8 Hz; J_2 = 4.0 Hz, 1H), 7.56-7.53 (m, 2H), 7.47 (dd, J_1 = 2.4 Hz; J_2 = 4.0 Hz, 1H), 7.35 (d, J = 8.4 Hz, 2H), 6.77 (d, J = 8.4 Hz, 2H), 3.79 (s, 3H), 3.20 (d, J = 14.4 Hz, 1H), 2.76-2.73 (m, 2H), 2.05-1.99 (m, 2H), 1.91-1.87 (m, 2H), 1.78-1.74 (m, 2H), 1.63-1.55 (m, 6H), 1.35 (d, J = 15.6 Hz, 3H), 0.88 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 147.8, 136.9, 133.1, 128.0, 127.6, 127.3, 125.7, 125.5, 124.5, 121.8, 121.4, 113.7, 88.2, 84.4, 71.7, 55.2, 48.7, 40.6, 35.7, 31.4, 29.7, 28.7, 24.5, 22.7, 21.4, 14.1. IR (neat): 3351, 2954, 2927, 2847, 1662, 1605, 1573, 1507, 1479, 1381, 1356, 1304, 1285, 1250, 1123, 1117, 1002, 956, 873, 784, 754, 691, 648, 604, 576 cm^{-1}. HRMS (EI-TOF) calcd for $C_{30}H_{35}N_3O_2$ (M^+): 469.2729, found: 469.2729.

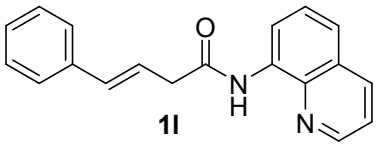
Unsuccessful substrates



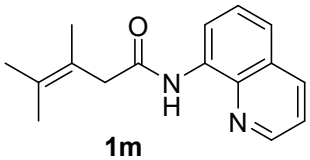
2r



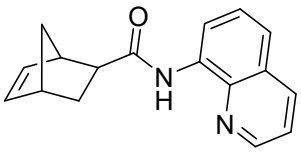
3r



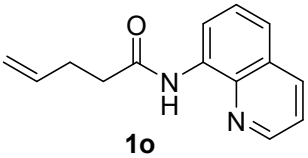
1l



1m

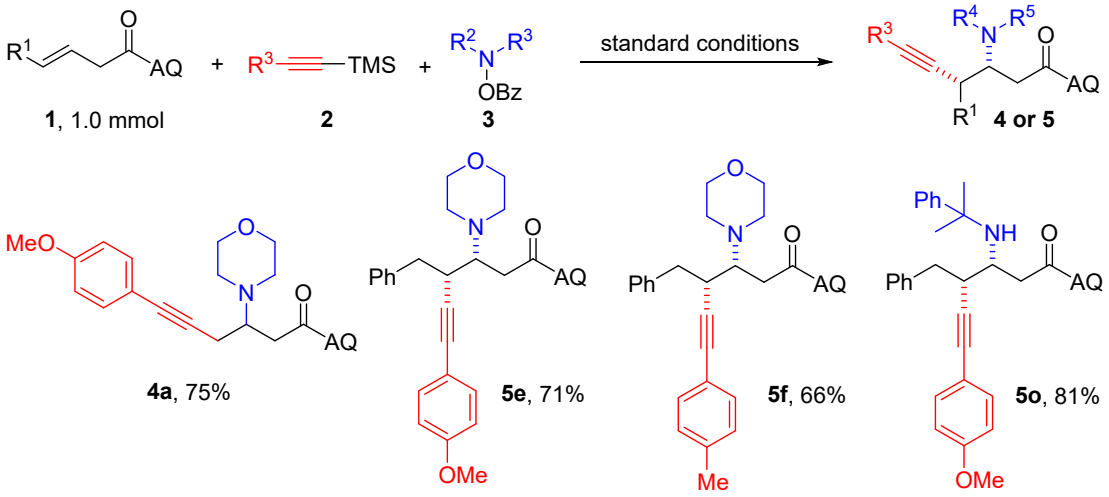


1n



1o

Large-scale synthesis



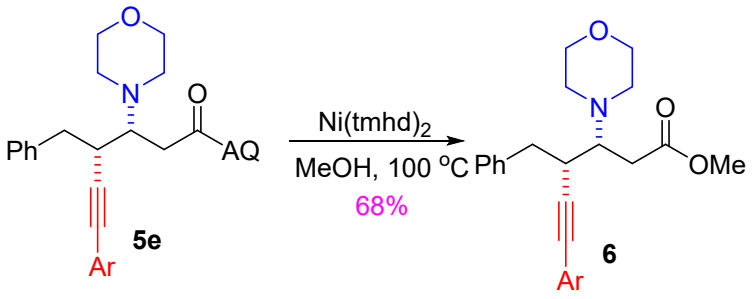
A 25 mL thick wall pressure sealed tube was charged with **1a** (1.0 mmol), **2a** (2.5 mmol), **3a** (1.8 mmol), $NiBr_2$ (55 mg, 0.25 mmol), 1-AdCOOH (216 mg, 1.2 mmol), CsF (380 mg, 2.5 mmol) and DMF (5.0 mL), then stirred at 90 °C on an oil bath for 24 h. The mixture was then cooled to room temperature, diluted with EtOAc, filtered through a celite pad, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/PE (1:10 ~ 1:2, v/v), to give the corresponding product **4a** (75%).

A 25 mL thick wall pressure sealed tube was charged with **1e** (1.0 mmol), **2a** (2.5 mmol), **3a** (1.8 mmol), $NiBr_2$ (55 mg, 0.25 mmol), 1-AdCOOH (216 mg, 1.2 mmol), CsF (380 mg, 2.5 mmol) and DMF (5.0 mL), then stirred at 90 °C on an oil bath for 24 h. The mixture was then cooled to room temperature, diluted with EtOAc, filtered through a celite pad, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/PE (1:10 ~ 1:2, v/v), to give the corresponding product **5e** (71%).

A 25 mL thick wall pressure sealed tube was charged with **1e** (1.0 mmol), **2c** (2.5 mmol), **3a** (1.8 mmol), $NiBr_2$ (55 mg, 0.25 mmol), 1-AdCOOH (216 mg, 1.2 mmol), CsF (380 mg, 2.5 mmol) and DMF (5.0 mL), then stirred at 90 °C on an oil bath for 24 h. The mixture was then cooled to room temperature, diluted with EtOAc, filtered through a celite pad, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/PE (1:10 ~ 1:2, v/v), to give the corresponding product **5f** (66%).

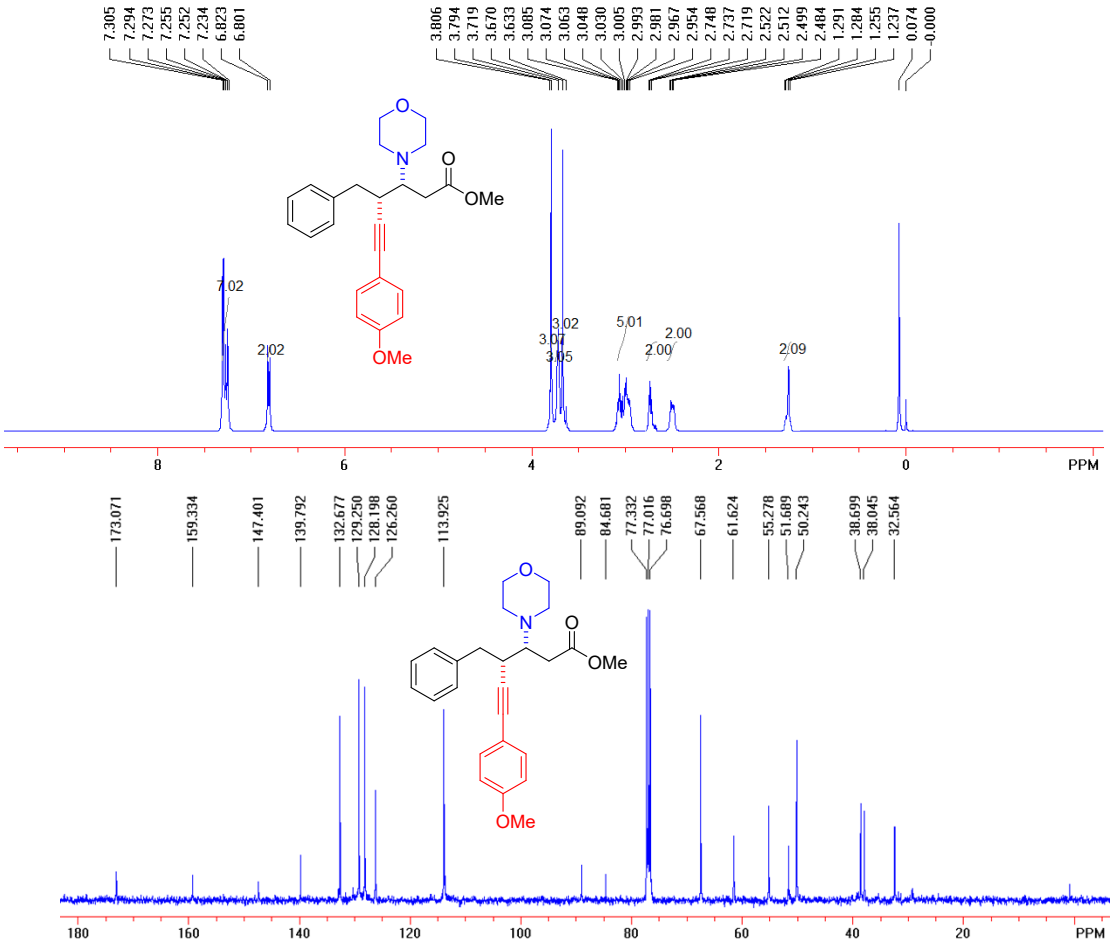
A 25 mL thick wall pressure sealed tube was charged with **1e** (1.0 mmol), **2a** (2.5 mmol), 3m (1.8 mmol), $NiBr_2$ (77 mg, 0.35 mmol), 1-AdCOOH (216 mg, 1.2 mmol), CsF (380 mg, 2.5 mmol) and DMF (5.0 mL), then stirred at 110 °C on an oil bath for 24 h. The mixture was then cooled to room temperature, diluted with EtOAc, filtered through a celite pad, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/PE (1:10 ~ 1:2, v/v), to give the corresponding product **5o** (81%).

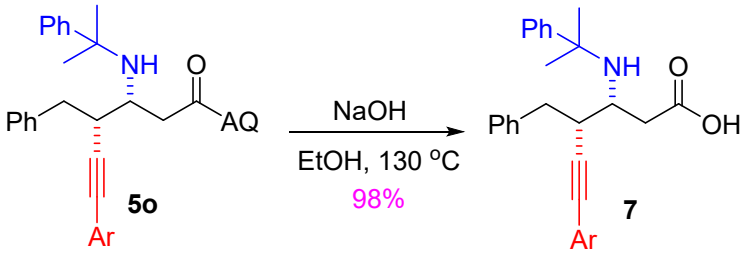
Product deprotection and diversification



The deprotection was accomplished by adapting a literature procedure.[3] Compound **5e** (67.47 mg, 0.13 mmol) and nickel(II) bis(2,2,6,6-tetramethyl3,5-heptanedionate) (18.0 mg, 20 mol%) were stirred in methanol (1.0 mL) at 100 °C under an nitrogen-atmosphere for 2 d. The crude mixture was filtered through a short plug of silica and concentrated under reduced vacuum. The residue was chromatographed through silica gel eluting with ethyl acetate/hexanes (1:5) to give the **methyl-4-benzyl-6-(4-methoxyphenyl)-3-morpholinohex-5-ynoate 6** as a pale yellow oil (27.70 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.25 (m, 7H), 6.81 (d, *J* = 8.8 Hz, 2H), 3.79 (s, 3H), 3.72 (s, 3H), 3.67 (s, 3H), 3.09-2.95 (m, 5H), 2.75-2.72 (m, 2H), 2.52-2.48 (m, 2H), 1.29-1.24 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 159.3, 147.4, 139.8, 132.7, 129.3, 128.2, 126.3, 113.9, 89.1, 84.7, 67.6, 61.6, 55.3, 51.7, 50.2, 38.7, 38.0, 32.6. IR (neat): 3351, 2954, 2911, 2845, 1744, 1673, 1634, 1529, 1483, 1384, 1363, 1310, 1289, 1250, 1162, 1117, 1012, 865, 791, 691, 646, 604,

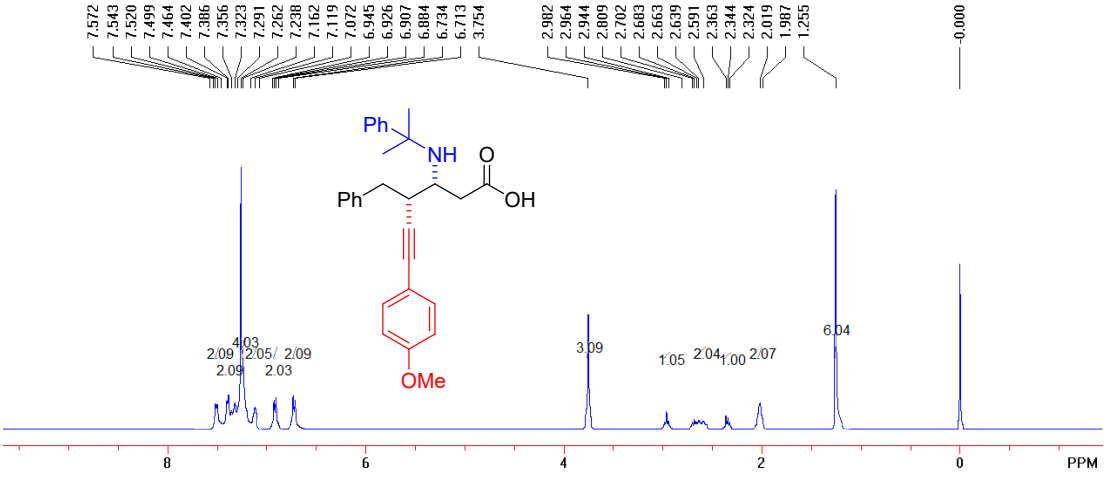
535 cm^{-1}. HRMS (EI-TOF) calcd for $C_{26}H_{29}NO_4$ (M^+): 407.2097, found: 407.2099.

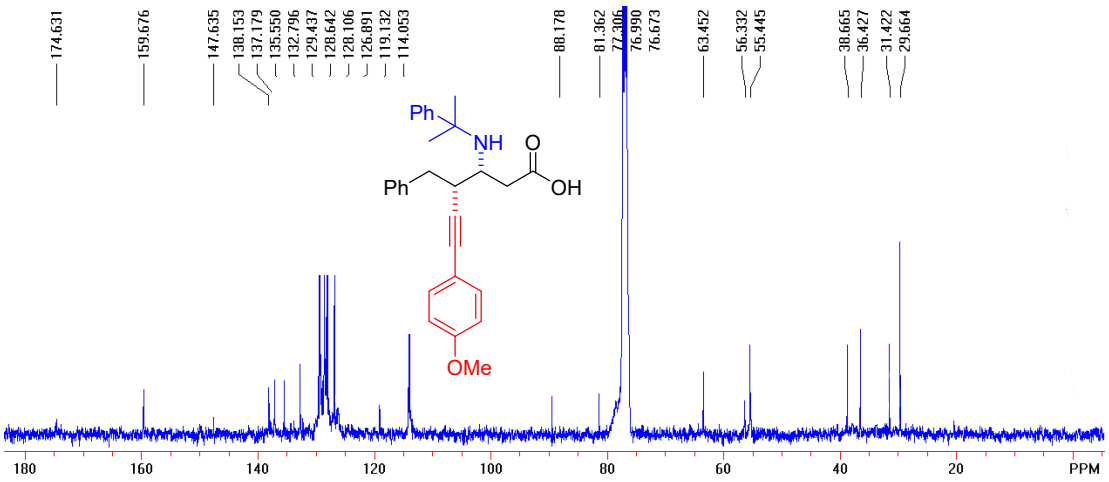


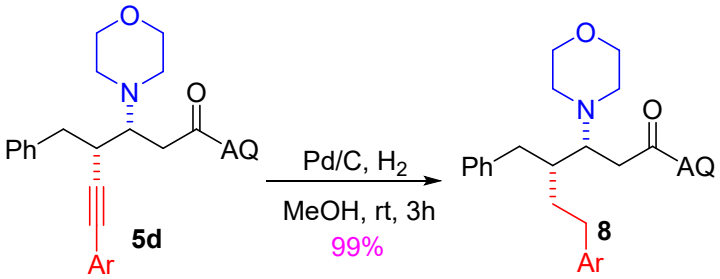


Removal of the 8-aminoquinoline directing group was carried out by adapting a literature procedure. To a flame-dried 48-mL sealed vessel was added the product **5o** (0.25 mmol), NaOH (3.75 mmol, 15 equiv), and 11 mL of EtOH. The resulting mixture was stirred at 130 °C for 24 h. After this time, the reaction mixture was allowed to cool to room temperature, diluted by addition of EtOAc (50 mL) and

washed with HCl (2 × 30 mL). The aqueous layers were combined and extracted with EtOAc (2 × 30 mL). The organic layers were combined, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/PE (1:5 ~ 1:2, v/v), to give the product **4-benzyl-6-(4-methoxyphenyl)-3-((2-phenylpropan-2-yl)amino)hex-5-ynoic acid 7** as a pale yellow oil (72.72 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 6.0 Hz, 2H), 7.26-7.24 (m, 4H), 7.12 (s, 2H), 6.92 (d, *J* = 7.6 Hz, 2H), 6.72 (d, *J* = 8.0 Hz, 2H), 3.78 (s, 3H), 2.96-2.68 (m, 1H), 2.64-2.56 (m, 2H), 2.36-2.33 (m, 1H), 2.05-1.98 (m, 2H), 1.26 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 159.7, 147.6, 138.2, 137.2, 135.6, 132.8, 129.4, 128.6, 128.1, 126.9, 119.1, 114.1, 88.2, 81.4, 63.5, 56.3, 55.4, 38.7, 36.4, 31.4, 29.7. IR (neat): 3537, 3347, 2953, 2923, 2847, 1676, 1574, 1537, 1462, 1383, 1368, 1289, 1250, 1162, 1105, 1037, 901, 865, 789, 754, 691, 646, 566 cm^{-1}. HRMS (EI-TOF) calcd for $C_{29}H_{31}NO_3$ (M^+): 441.2304, found: 441.2306.

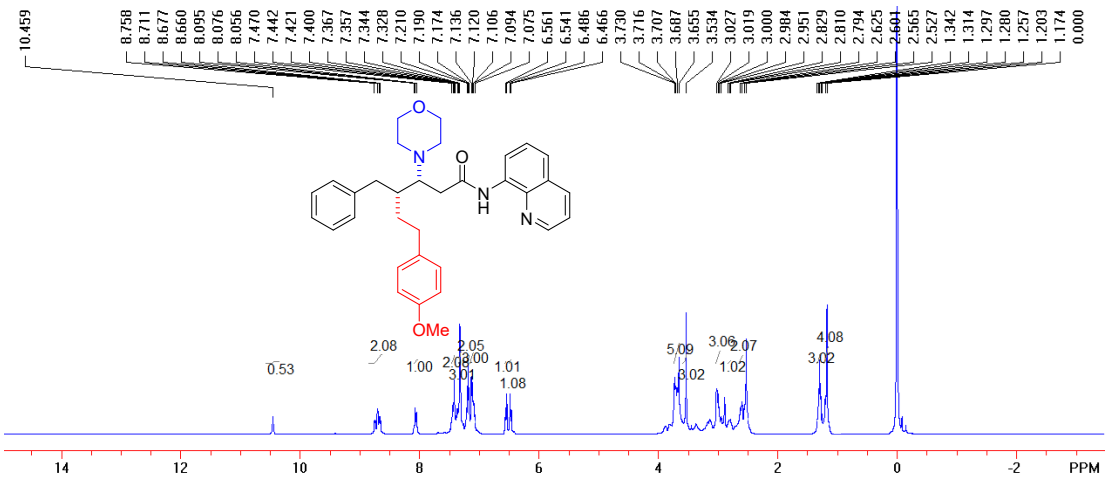


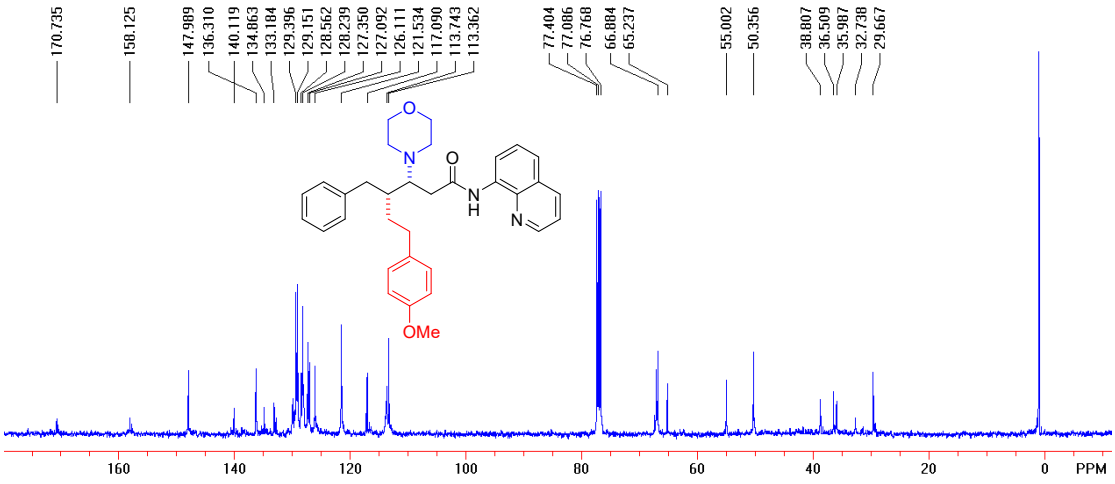


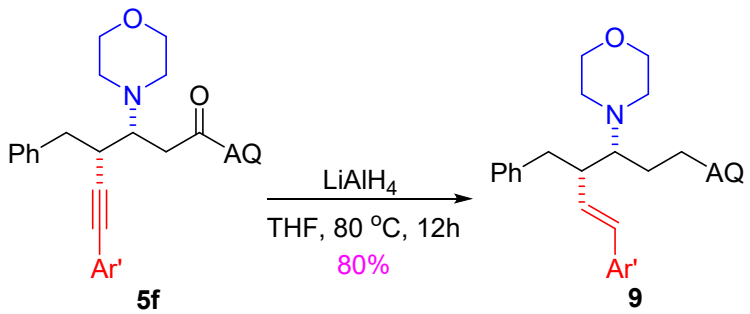


Compound **5e** (51.9 mg, 0.10 mmol) was dissolved in MeOH (2 mL) under argon atmosphere. 5% Pd/C (10 mg, 0.005 mmol) were added. The reaction mixture was then stirred for 3 h under hydrogen atmosphere (balloon). The reaction mixture was filtered through a pad of celite and concentrated under reduced pressure. The residue was chromatographed through silica gel eluting with ethyl acetate/hexanes to give **4-benzyl-6-(4-methoxyphenyl)-3-morpholino-*N*-(quinolin-8-yl)hexanamide 8** as pale yellow oil (51.80 mg, 99%). Rf = 0.64 (PE/EA =2 /1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.46 (s, 1H), 8.76-8.66 (m, 2H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.47-7.40 (m, 2H), 7.37-7.33 (m, 3H), 7.21-7.19 (m, 2H), 7.14-7.08 (m, 3H), 6.55 (d, *J* = 8.0 Hz, 1H), 6.48 (d, *J* = 8.0 Hz, 1H), 3.73-3.66 (m, 5H), 3.53 (s, 3H), 3.03-2.95 (m, 3H), 2.89-2.79 (m, 1H), 2.63-2.53 (m, 2H), 1.34-1.28 (m, 3H), 1.26-1.17 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 158.1, 148.0, 140.1, 136.3, 134.9, 133.2, 129.4, 129.2, 128.6, 128.2, 127.4, 127.1, 126.1, 121.5, 117.1, 113.7, 113.4, 66.9, 65.2, 55.0, 50.4, 38.8, 36.5, 36.0, 32.7, 29.7. IR (neat): 3347, 2954, 2920, 2845, 1657, 1573, 1524, 1484, 1453, 1381, 1357, 1323, 1259, 1123, 1017, 1002, 950, 896, 791, 665, 605,

537 cm^{-1}. HRMS (EI-TOF) calcd for $C_{33}H_{37}N_3O_3$ (M^+): 523.2835, found: 523.2836.



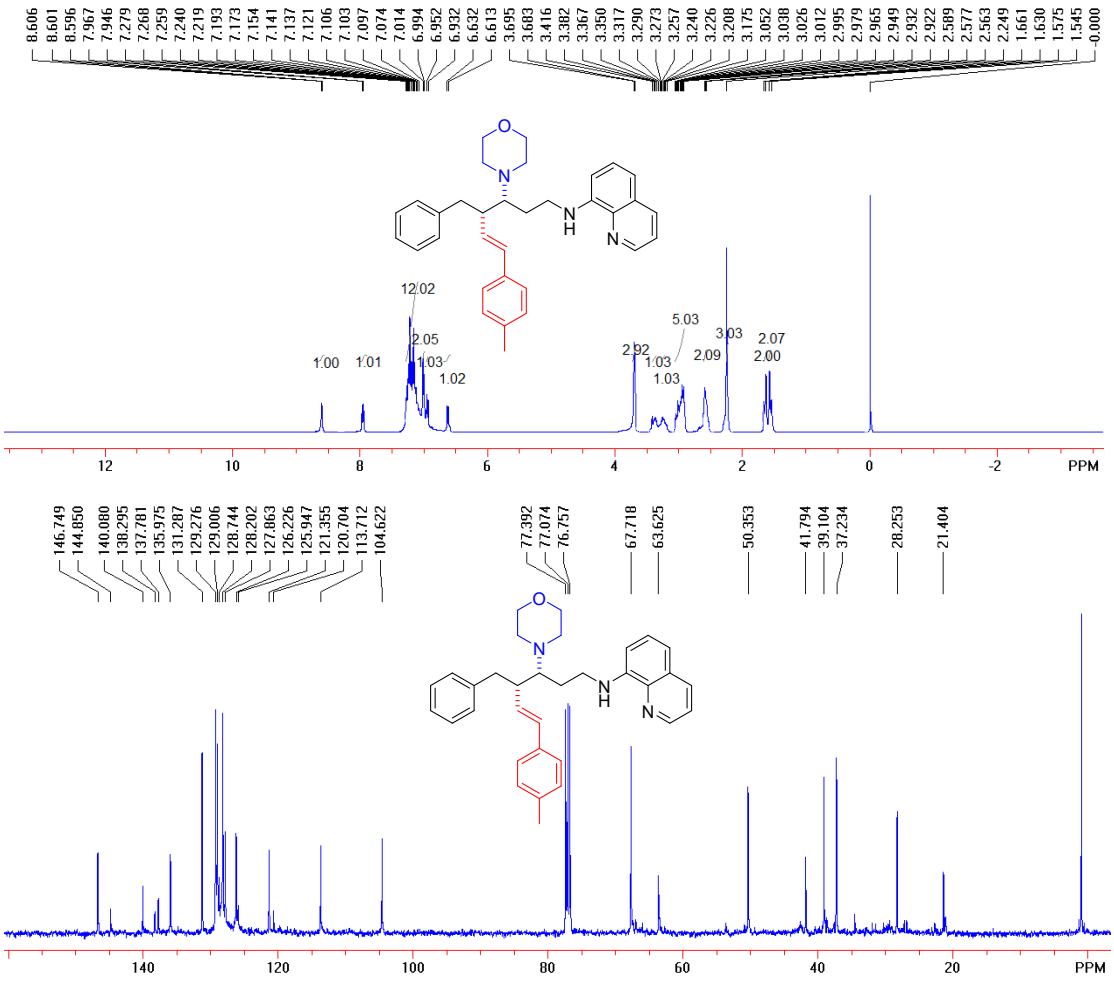




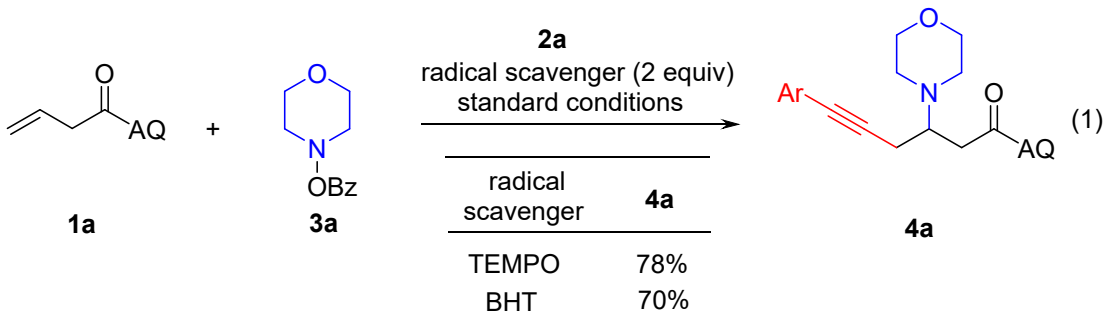
5f **9**

A suspension of $LiAlH_4$ (22.8 mg, 0.6 mmol) in THF (0.5 mL) was mixed slowly to a mixture of **5f** (50.3 mg, 0.1 mmol). The resulting mixture was stirred under reflux condition. The reaction mixture was stirred at 80°C for 5 h, filtered through a pad of celite, and diluted with EtOAc. This organic solution was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was chromatographed through silica gel eluting with ethyl EA/PE = (1:30~1:2, v/v) to

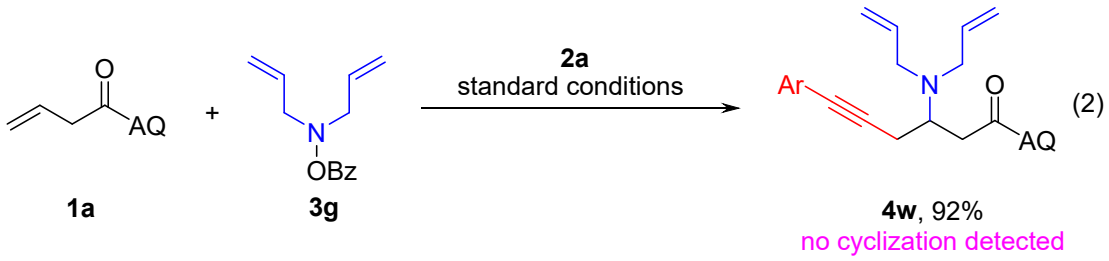
give ***N*-(4-benzyl-3-morpholino-6-(p-tolyl)hex-5-en-1-yl)quinolin-8-amine 9** as light yellow oil (39.28 mg, 80%). Rf = 0.54 (PE/EA =2 /1), Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60-8.59 (m, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.27-7.12 (m, 12H), 7.00 (d, *J* = 8.0 Hz, 2H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.62 (d, *J* = 7.6 Hz, 1H), 5.18 (s, 1H), 3.69-3.66 (m, 3H), 3.41-3.35 (m, 1H), 3.27-3.20 (m, 1H), 3.05-2.92 (m, 5H), 2.58-2.56 (m, 1H), 2.24 (s, 3H), 1.64 (d, *J* = 12.0 Hz, 2H), 1.56 (d, *J* = 12.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.7, 144.9, 140.1, 138.3, 137.8, 136.0, 131.3, 129.3, 129.0, 128.7, 128.2, 127.9, 126.2, 125.9, 121.4, 120.7, 113.7, 104.6, 67.7, 63.6, 50.4, 41.8, 39.1, 37.2, 28.3, 21.4. IR (neat): 3251, 2957, 2921, 2843, 1673, 1573, 1524, 1484, 1456, 1395, 1384, 1361, 1321, 1259, 11232, 1060, 1013, 976, 894, 789, 665, 604, 573 cm^{-1}. HRMS (EI-TOF) calcd for $C_{33}H_{37}N_3O$ (M^+): 491.2937, found: 491.2938.



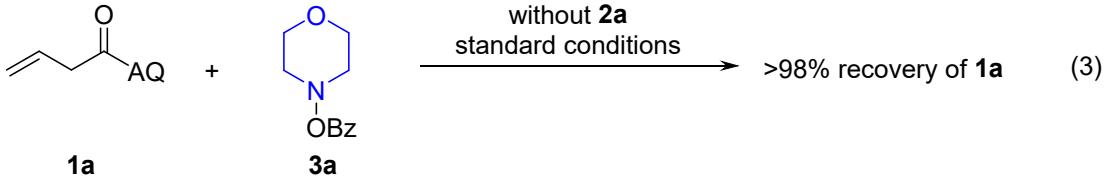
Preliminary Mechanistic Investigations



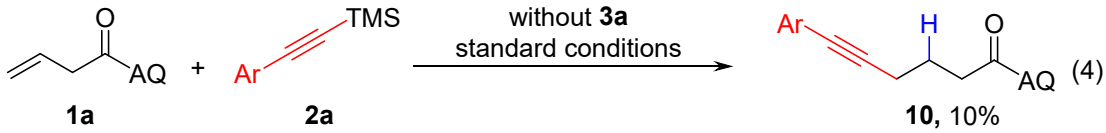
A 25 mL thick wall pressure sealed tube was charged with **1a** (0.1 mmol), **2a** (0.25 mmol), **3a** (0.18 mmol), $NiBr_2$ (5.5 mg, 0.025 mmol), 1-AdCOOH (21.6 mg, 0.12 mmol), CsF (38.0 mg, 0.25 mmol), radical scavenger (0.2 mmol), and DMF (1.0 mL), then stirred at 80 °C on an oil bath for 24 h. The mixture was then cooled to room temperature, diluted with EtOAc, filtered through a celite pad, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/PE (1:10 ~ 1:2, v/v), to give the corresponding product **4a** (78% and 66%). This result indicates that the reaction likely did not involve a radical process.



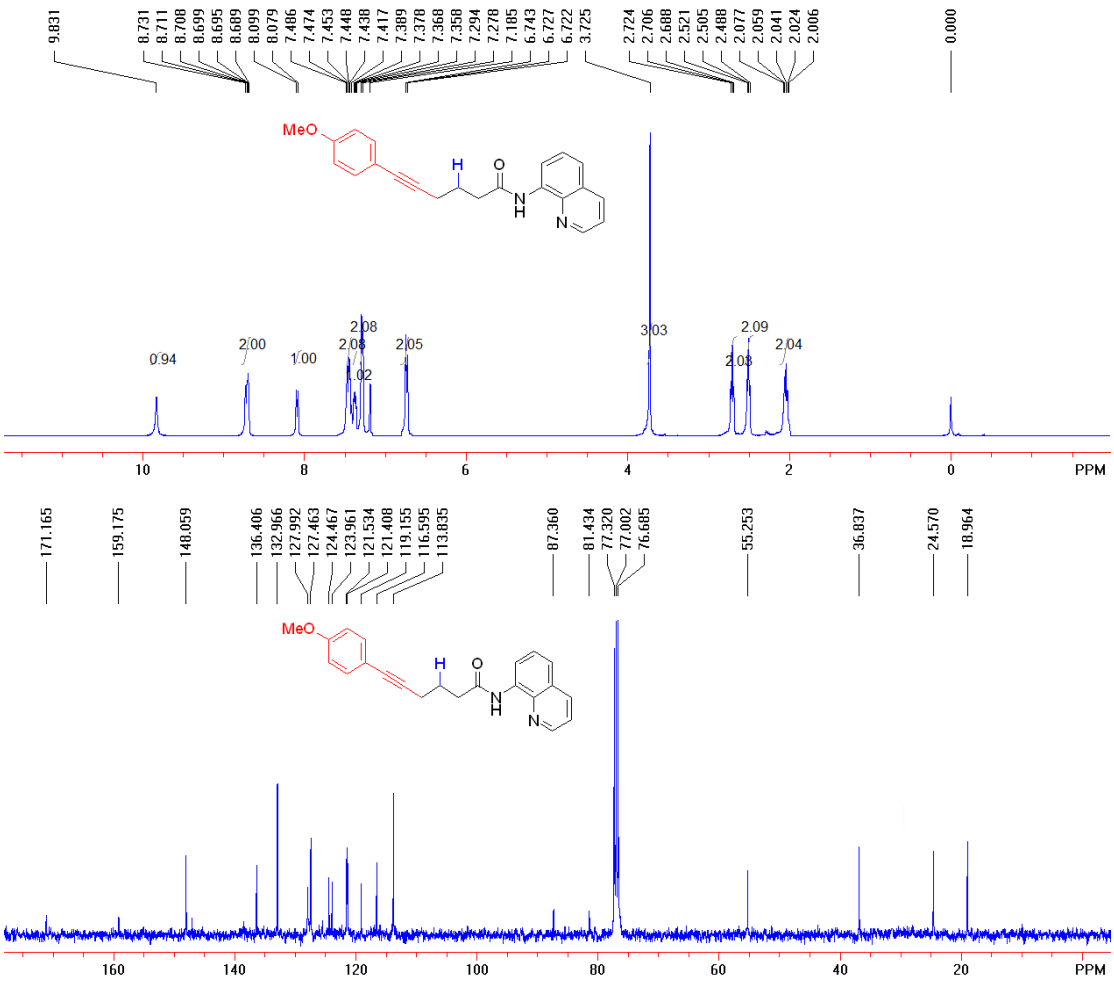
A 25 mL thick wall pressure sealed tube was charged with **1a** (0.1 mmol), **2a** (0.25 mmol), **3g** (0.18 mmol), $NiBr_2$ (5.5 mg, 0.025 mmol), 1-AdCOOH (21.6 mg, 0.12 mmol), CsF (38.0 mg, 0.25 mmol), and DMF (1.0 mL), then stirred at 80 °C on an oil bath for 24 h. The mixture was then cooled to room temperature, diluted with EtOAc, filtered through a celite pad, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/PE (1:10 ~ 1:2, v/v), to give the corresponding product **4w** (92%).

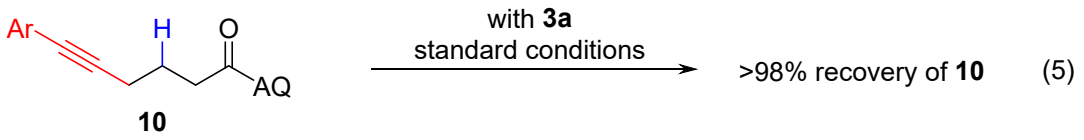


A 25 mL thick wall pressure sealed tube was charged with **1a** (0.1 mmol), **3a** (0.18 mmol), $NiBr_2$ (5.5 mg, 0.025 mmol), 1-AdCOOH (21.6 mg, 0.12 mmol), CsF (38.0 mg, 0.25 mmol), and DMF (1.0 mL), then stirred at 80 °C on an oil bath for 24 h. The mixture was then cooled to room temperature, diluted with EtOAc, filtered through a celite pad, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/PE (1:10, v/v), to give the starting material **1a** (>98%).



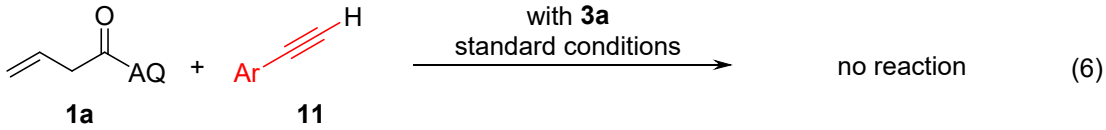
A 25 mL thick wall pressure sealed tube was charged with **1a** (0.1 mmol), **2a** (0.25 mmol), $NiBr_2$ (5.5 mg, 0.025 mmol), 1-AdCOOH (21.6 mg, 0.12 mmol), CsF (38.0 mg, 0.25 mmol), and DMF (1.0 mL), then stirred at 80 °C on an oil bath for 24 h. The mixture was then cooled to room temperature, diluted with EtOAc, filtered through a celite pad, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/PE (1:10, v/v), to give the hydroalkynylation product **6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (10)**. Rf = 0.27 (PE/EA = 5/1). 70%, 23.6 mg. Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.83 (s, 1H), 8.73-8.69 (m, 2H), 8.09 (d, J = 8.0 Hz, 1H), 7.49-7.42 (m, 2H), 7.37 (dd, J_1 = 4.4 Hz; J_2 = 8.4 Hz, 1H), 7.29 (d, J = 6.4 Hz, 2H), 6.74-6.72 (m, 2H), 3.73 (s, 3H), 2.71 (t, J = 7.2 Hz, 2H), 2.51 (t, J = 6.4 Hz, 2H), 2.08-2.01 (m,2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.2, 159.2, 148.1, 136.4, 133.0, 128.0, 127.5, 124.5, 124.0, 121.5, 121.4, 119.2, 116.6, 113.8, 87.4, 81.4, 55.3, 36.8, 24.6, 19.0. HRMS (EI-TOF) calcd for $C_{22}H_{20}N_2O_2$ (M^+): 344.1525, found: 344.1525.



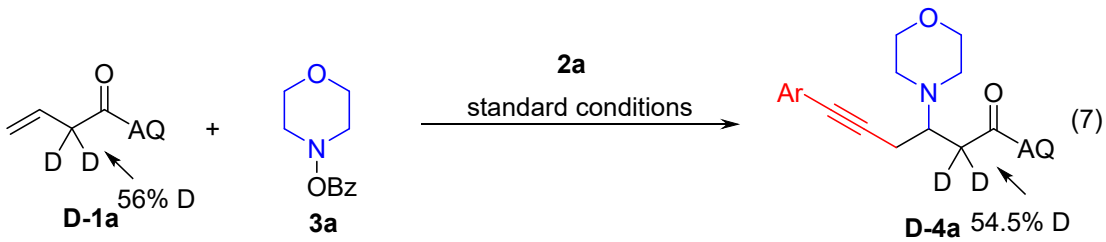


10 (5)

A 25 mL thick wall pressure sealed tube was charged with **10** (0.1 mmol), **3a** (0.18 mmol), $NiBr_2$ (5.5 mg, 0.025 mmol), 1-AdCOOH (21.6 mg, 0.12 mmol), CsF (38.0 mg, 0.25 mmol), and DMF (1.0 mL), then stirred at 80 °C on an oil bath for 24 h. The mixture was then cooled to room temperature, diluted with EtOAc, filtered through a celite pad, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/PE (1:10, v/v), to give the starting material **14** (>98%).

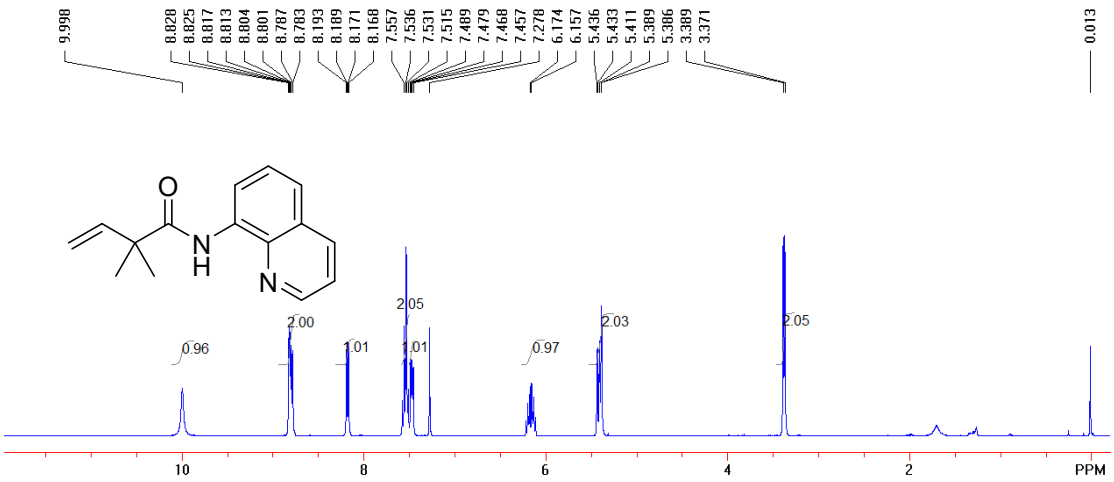


A 25 mL thick wall pressure sealed tube was charged with **1a** (0.1 mmol), **11** (0.25 mmol), **3a** (0.18 mmol), $NiBr_2$ (5.5 mg, 0.025 mmol), 1-AdCOOH (21.6 mg, 0.12 mmol), CsF (38.0 mg, 0.25 mmol), and DMF (1.0 mL), then stirred at 80 °C on an oil bath for 24 h. The mixture was then cooled to room temperature, diluted with EtOAc, filtered through a celite pad, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/PE (1:10, v/v), to give desired product **4a** (not detected).



A 25 mL thick wall pressure sealed tube was charged with **D-1a** (0.1 mmol), **2a** (0.25 mmol), **3a** (0.18 mmol), $NiBr_2$ (5.5 mg, 0.025 mmol), 1-AdCOOH (21.6 mg, 0.12 mmol), CsF (38.0 mg, 0.25 mmol), and DMF (1.0 mL), then stirred at 80 °C on an oil bath for 24 h. The mixture was then cooled to room temperature, diluted with EtOAc, filtered through a celite pad, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, eluting with EtOAc/PE (1:10, v/v), to give desired product **D-4a** (70%).

1a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H
N
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8
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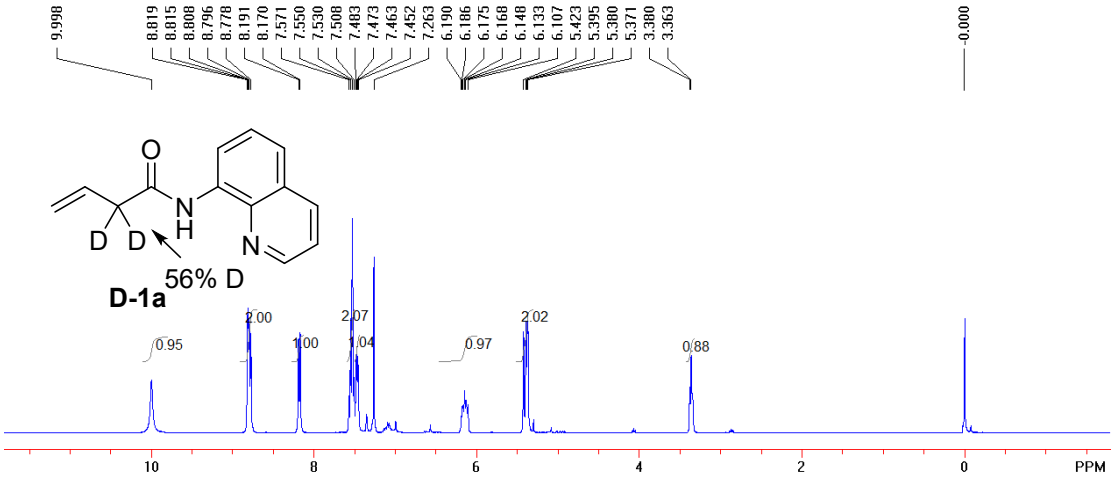
4
2
PPM

D-1a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D
D
N
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D-1a
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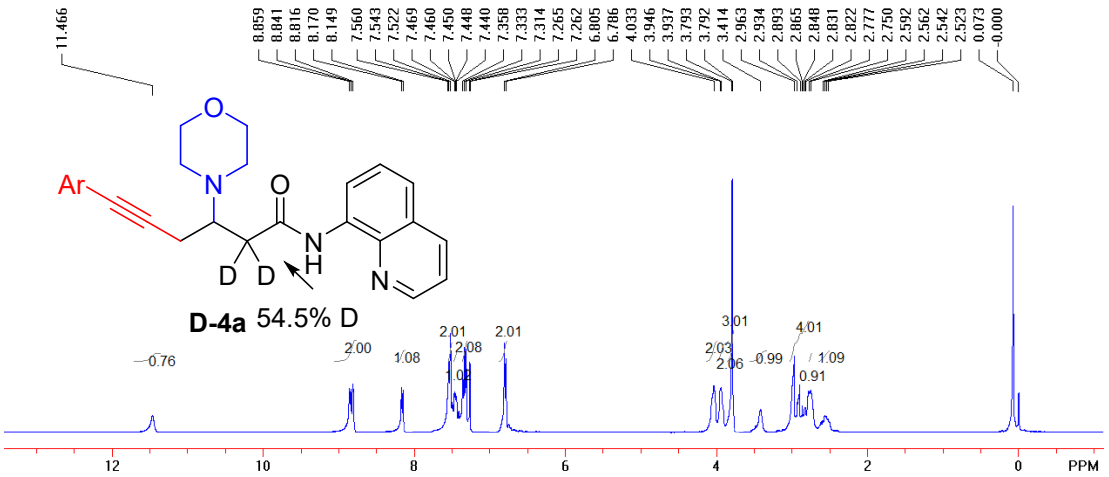
PPM

D-4a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3.937
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N
Ar
O
N
H
D
D
N
D-4a 54.5% D
0.76
2.00
1.08
2.01
2.08
2.01
3.01
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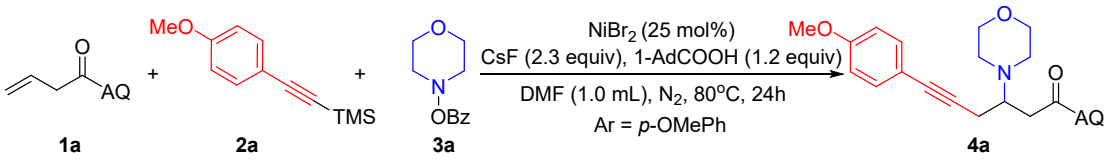
PPM

Kinetic Experiments



1a **2a** **3a** **4a**

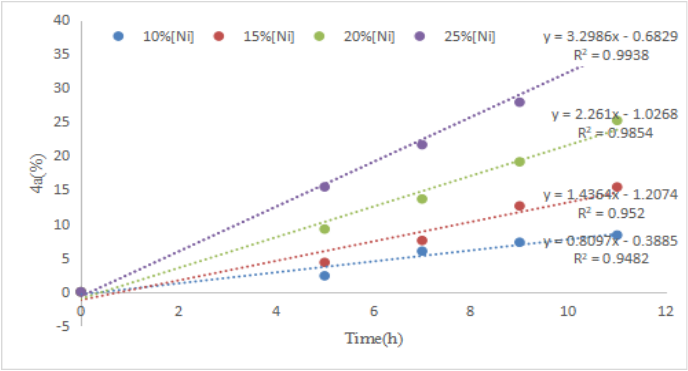
General Kinetics Experimental Procedure: a 25 mL thick wall pressure sealed tube was charged with **1a** (0.1 mmol), **2a** (0.25 mmol), **3a** (0.18 mmol), $NiBr_2$ (5.5 mg, 0.025 mmol), 1-AdCOOH (21.6 mg, 0.12 mmol), CsF (38.0 mg, 0.25 mmol), DMF (1.0 mL) and dodecane (1.0 equiv) as internal standard, then stirred at 80 °C on an oil bath for 24 h. The reaction progress was monitored by removing aliquots (~10 μL) from the reaction mixture via syringe under N_2. Each aliquot was quenched by EA (4.0 mL) in an 8.0 mL tube. The mixture was filtered with a filter head into 2.0 mL GC vial and analyzed by gas chromatography.

Kinetic Plots for Different Concentrations of [Ni] Catalyst

The molar concentration of product **4a** in different concentrations of [Ni] at different time intervals.

Time(h)	10%[Ni]	15%[Ni]	20%[Ni]	25%[Ni]
0	0	0	0	0
5	2.348445	4.32276	9.225489	15.43775
7	5.982676	7.546691	13.65482	21.64274
9	7.289271	12.63488	19.12554	27.89552
11	8.34695	15.42236	25.21365	37.16528

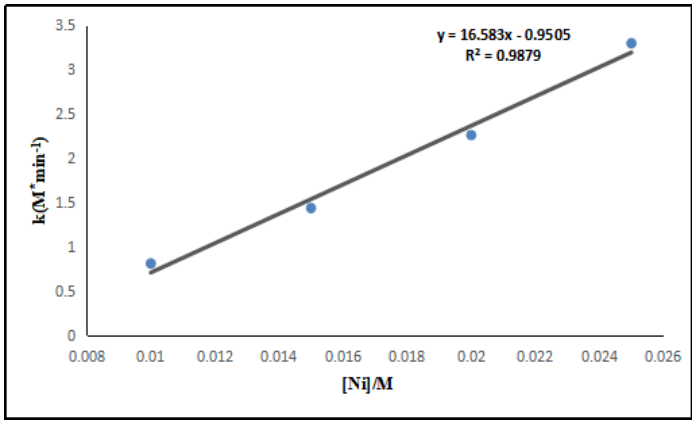
Time-course for the product **4a** in different concentrations of [Ni]



The k value of product **4a** in different concentrations of [Ni]

[Ni]/M	k(M*min^{-1})
0.01	0.8097
0.015	1.4364
0.02	2.261
0.025	3.2986

The reaction rate course in different concentrations of [Ni]

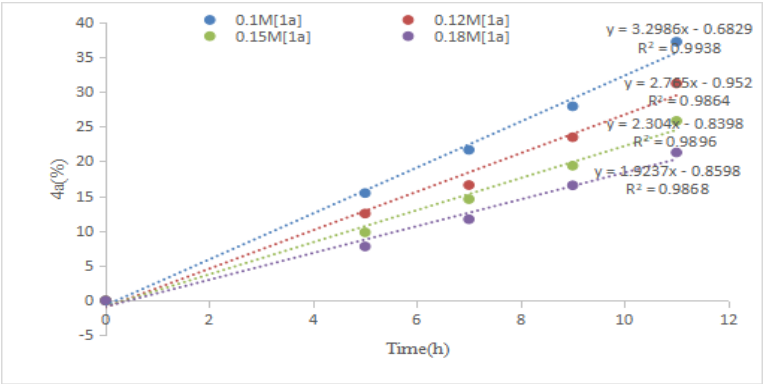


Kinetic Plots for Different Concentrations of alkene 1a

The molar concentration of product **4a** in different concentrations of alkene **1a** at different time intervals.

Time(h)	0.1M[**1a**]	0.12M[**1a**]	0.15M[**1a**]	0.18M[**1a**]
0	0	0	0	0
5	15.43775	12.49779	9.79825	7.76985
7	21.64274	16.58642	14.56528	11.67895
9	27.89552	23.45521	19.36752	16.54779
11	37.16528	31.17995	25.79668	21.26457

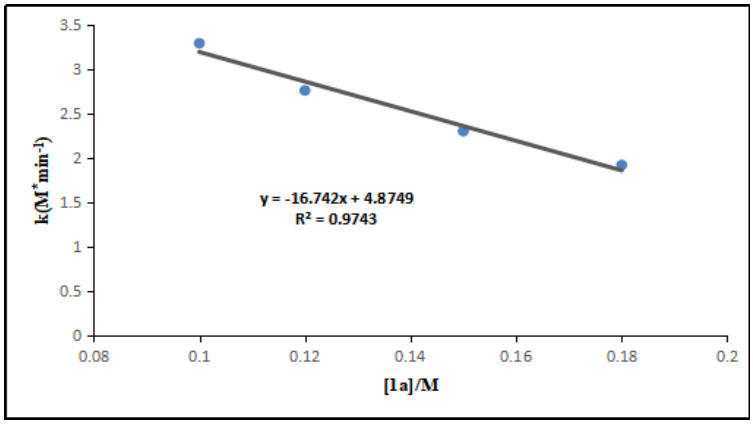
Time-course for the product **4a** in different concentrations of alkene **1a**



The k value of product **4a** in different concentrations of alkene **1a**

[**1a**]/M	k(M*min^{-1})
0.1	3.2986
0.12	2.765
0.15	2.304
0.18	1.9237

The reaction rate course in different concentrations of alkene **1a**

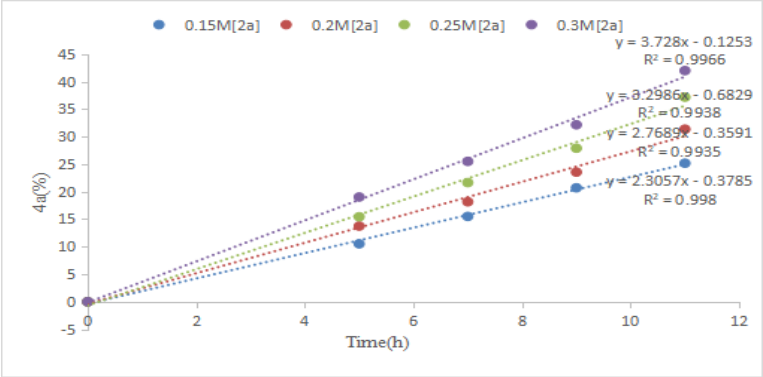


Kinetic Plots for Different Concentrations of alkynylsilane 2a

The molar concentration of product **4a** in different concentrations of alkynylsilane **2a** at different time intervals.

Time (h)	0.15M[**2a**]	0.2M[**2a**]	0.25M[**2a**]	0.3M[**2a**]
0	0	0	0	0
5	10.52269	13.74022	15.43775	19.02583
7	15.49754	18.15772	21.64274	25.49871
9	20.70025	23.55278	27.89552	32.14915
11	25.16899	31.35876	37.16528	41.99661

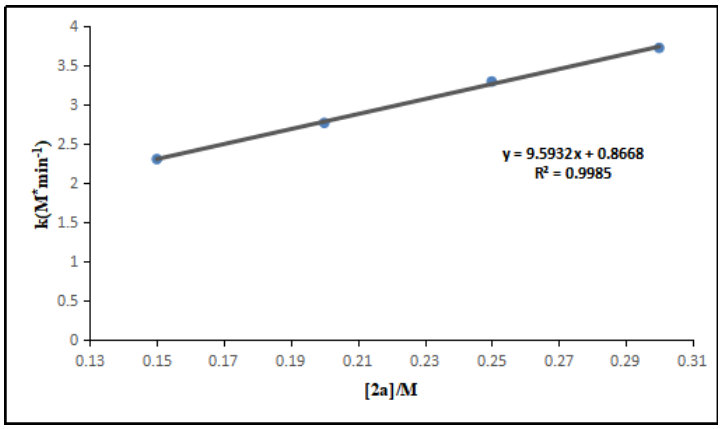
Time-course for the product **4a** in different concentrations of alkynylsilane **2a**



The k value of product **4a** in different concentrations of alkynylsilane **2a**

[**2a**]/M	k(M*min^{-1})
0.15	2.3057
0.2	2.7689
0.25	3.2986
0.3	3.728

The reaction rate course in different concentrations of alkynylsilane **2a**

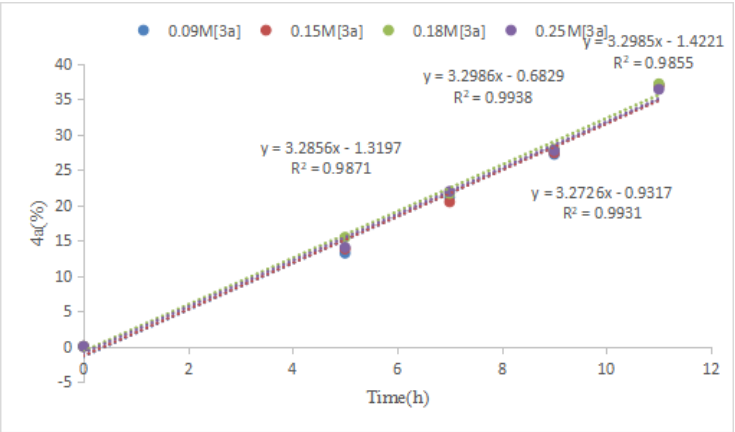


Kinetic Plots for Different Concentrations of N-O electrophiles 3a

The molar concentration of product **4a** in different concentrations of N-O electrophiles **3a** at different time intervals.

Time(h)	0.09M[**3a**]	0.15M[**3a**]	0.18M[**3a**]	0.25M[**3a**]
0	0	0	0	0
5	13.19891	13.79152	15.43775	14.01679
7	21.10619	20.45161	21.64274	21.93882
9	27.1787	27.39782	27.89552	27.71756
11	36.95682	36.89933	37.16528	36.39241

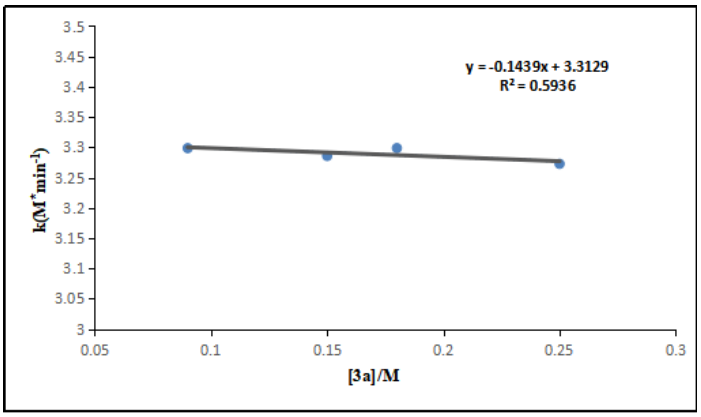
Time-course for the product **4a** in different concentrations of N-O electrophiles **3a**



The k value of product **4a** in different concentrations of N-O electrophiles **3a**

[**3a**]/M	k(M*min^{-1})
0.09	3.2985
0.15	3.2856
0.18	3.2986
0.25	3.2726

The reaction rate course in different concentrations of N-O electrophiles **3a**



checkCIF/PLATON report

Structure factors have been supplied for datablock(s) 1

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: 1

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Bond precision:   C-C = 0.0023 A          Wavelength=0.71073

Cell:             a=11.3578(7)     b=8.4335(5)        c=29.2356(17)
                  alpha=90         beta=95.409(2)     gamma=90
Temperature:      103 K

                 Calculated                Reported
Volume           2787.9(3)                 2787.9(3)
Space group      P 21/n                    P 1 21/n 1
Hall group       -P 2yn                    -P 2yn
Moiety formula   C33 H32 N3 O3             C33 H32 N3 O3
Sum formula      C33 H32 N3 O3             C33 H32 N3 O3
Mr               518.62                    518.61
Dx,g cm-3        1.236                     1.236
Z                4                         4
Mu (mm-1)        0.080                     0.080
F000             1100.0                    1100.0
F000'            1100.45
h,k,lmax         14,10,37                  14,10,37
Nref             6173                      6154
Tmin,Tmax        0.989,0.990               0.631,0.746
Tmin'            0.989

Correction method= # Reported T Limits: Tmin=0.631 Tmax=0.746
AbsCorr = MULTI-SCAN

Data completeness= 0.997           Theta(max)= 27.136

R(reflections)= 0.0458( 4901)                    wR2(reflections)=
                                                 0.1256( 6154)
S = 1.044                Npar= 353
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The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

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DIFMX02_ALERT_1_C  The maximum difference density is > 0.1*ZMAX*0.75
          The relevant atom site should be identified.
PLAT094_ALERT_2_C Ratio of Maximum / Minimum Residual Density ....       3.41 Report
PLAT097_ALERT_2_C Large Reported Max.  (Positive) Residual Density       0.75 eA-3
PLAT220_ALERT_2_C NonSolvent   Resd 1  C   Ueq(max)/Ueq(min) Range        3.4 Ratio
PLAT911_ALERT_3_C Missing FCF Refl Between Thmin & STh/L=    0.600          4 Report
               1  0 15,   6  0 24,  -6  5 25,  -8  2 29,
PLAT975_ALERT_2_C Check Calcd Resid. Dens.  0.90Ang From N3      .       0.75 eA-3
```

Alert level G

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PLAT371_ALERT_2_G Long   C(sp2)-C(sp1) Bond  C8       - C14      .       1.44 Ang.
PLAT398_ALERT_2_G Deviating  C-O-C   Angle From 120 for O2       .      109.6 Degree
PLAT793_ALERT_4_G Model has Chirality at C1          (Centro SpGr)          S Verify
PLAT793_ALERT_4_G Model has Chirality at C6          (Centro SpGr)          S Verify
PLAT910_ALERT_3_G Missing # of FCF Reflection(s) Below Theta(Min).          3 Note
              -1  0  1,   1  0  1,   0  0  2,
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L=  0.600         12 Note
PLAT941_ALERT_3_G Average HKL Measurement Multiplicity ...........        3.9 Low
PLAT969_ALERT_5_G The 'Henn et al.' R-Factor-gap value ...........      2.256 Note
            Predicted wR2: Based on SigI**2  5.57 or SHELX Weight 12.04
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.          8 Info
PLAT992_ALERT_5_G Repd & Actual _reflns_number_gt Values Differ by          2 Check
```

```
   0 ALERT level A = Most likely a serious problem - resolve or explain
   0 ALERT level B = A potentially serious problem, consider carefully
   6 ALERT level C = Check. Ensure it is not caused by an omission or oversight
  10 ALERT level G = General information/check it is not something unexpected

   1 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
   7 ALERT type 2 Indicator that the structure model may be wrong or deficient
   3 ALERT type 3 Indicator that the structure quality may be low
   3 ALERT type 4 Improvement, methodology, query or suggestion
   2 ALERT type 5 Informative message, check
```

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

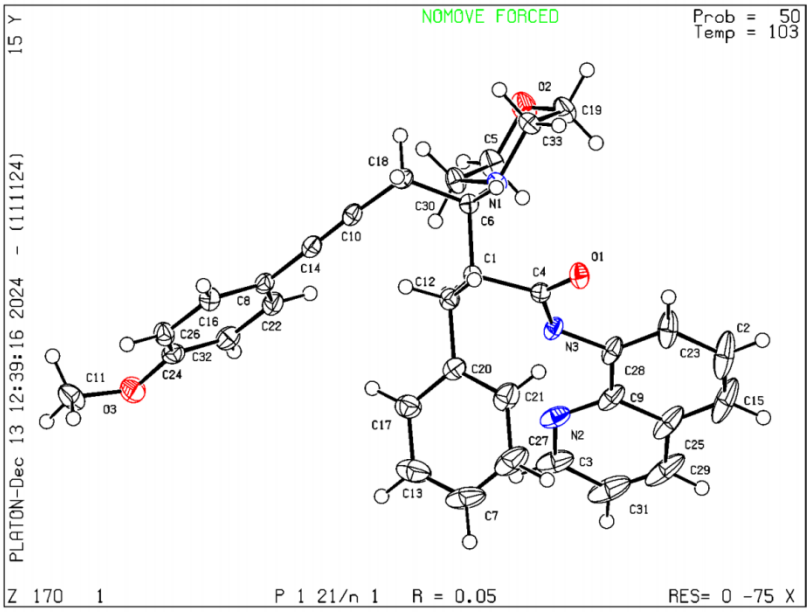
A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 11/11/2024; check.def file version of 11/11/2024

Datablock 1 - ellipsoid plot



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Hydrocarbofunctionalization of Unactivated Alkenes with Diverse C–H Nucleophiles, *J. Am. Chem. Soc.,* 2016, **138**, 14705.

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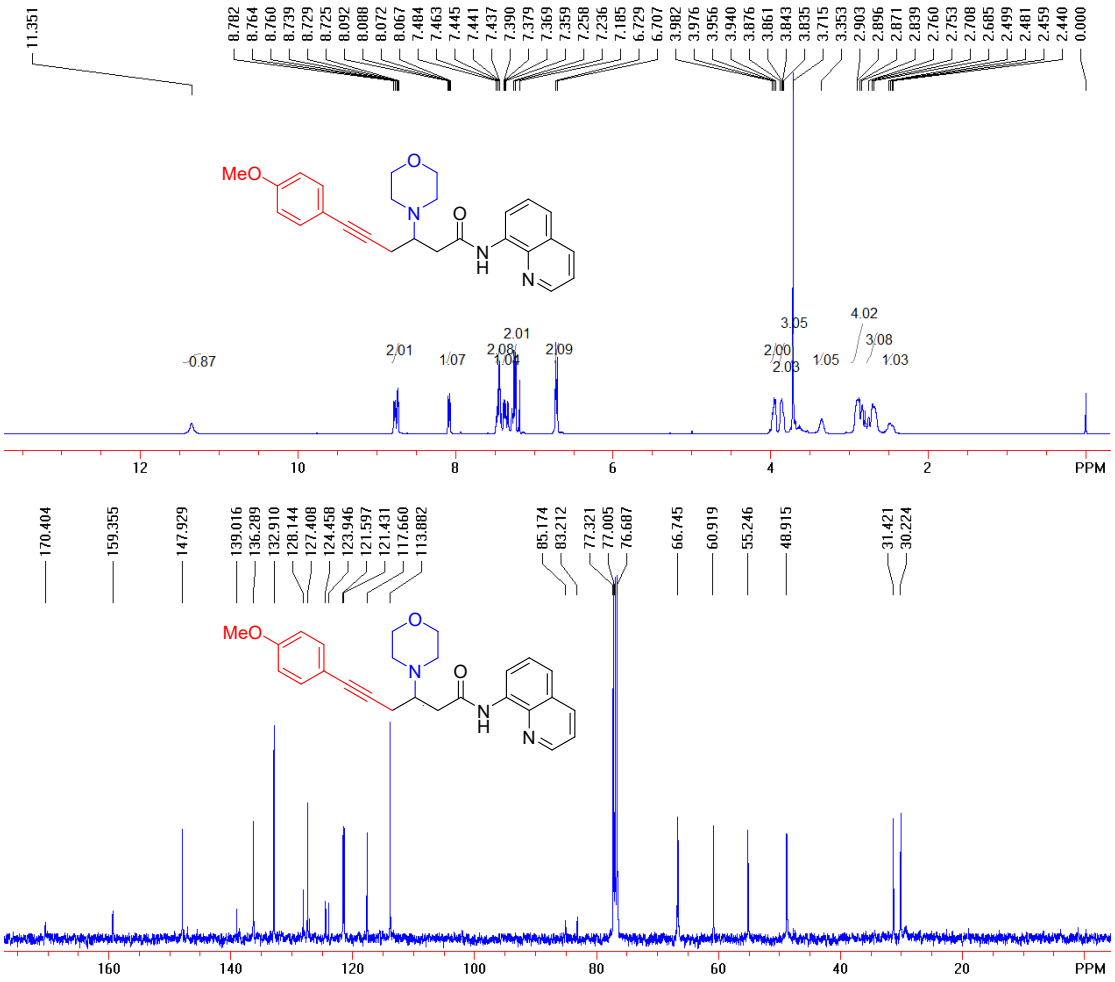
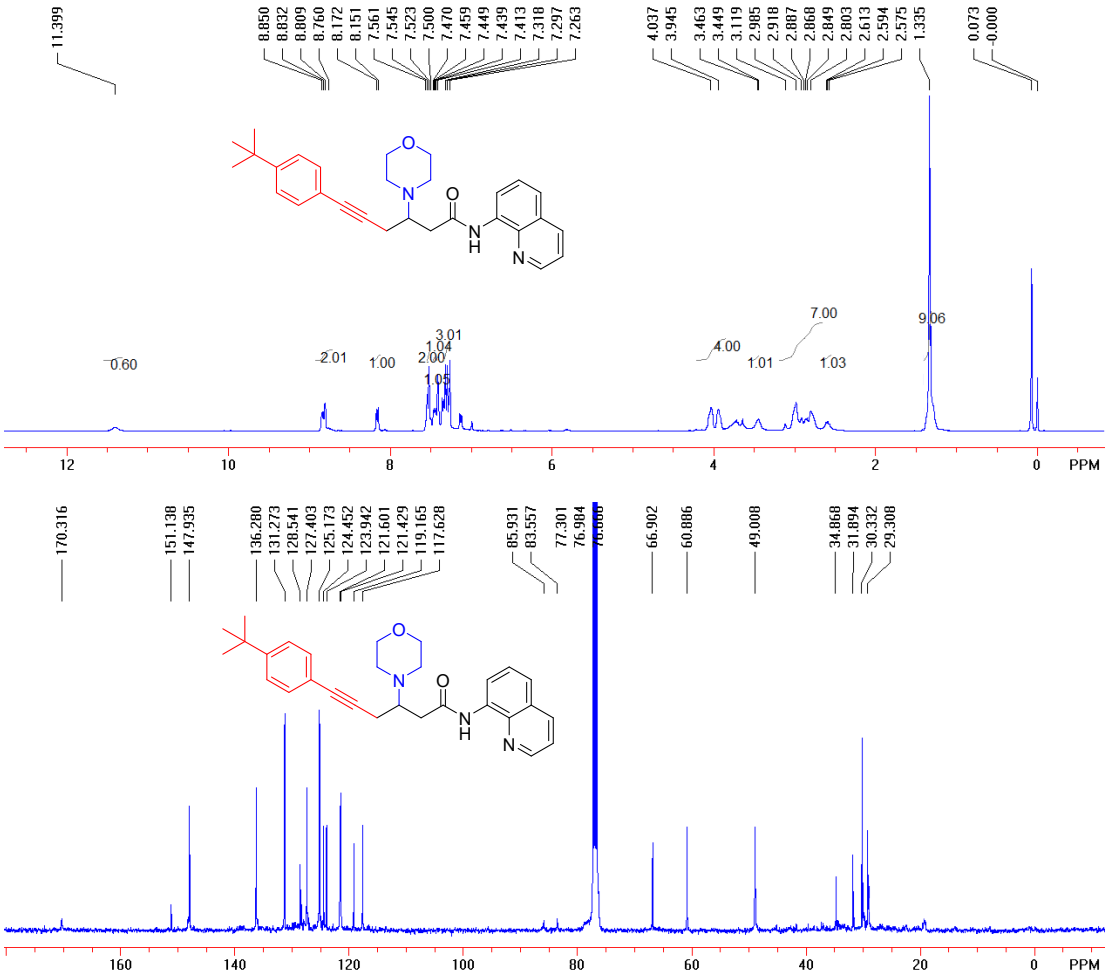
Copies of ^{1}H and ^{13}C NMR Spectra

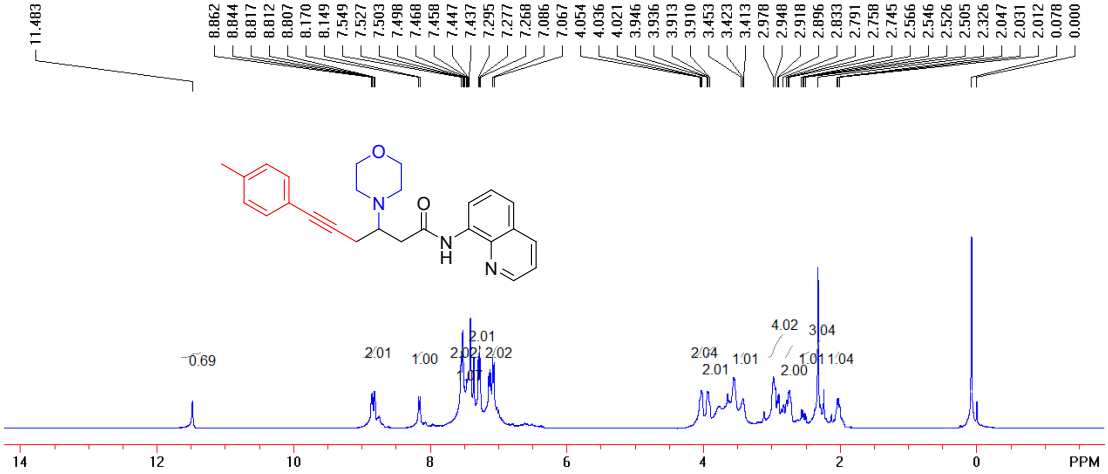
6-(4-methoxyphenyl)-3-morpholino-*N*-(quinolin-8-yl)hex-5-ynamide (4a)

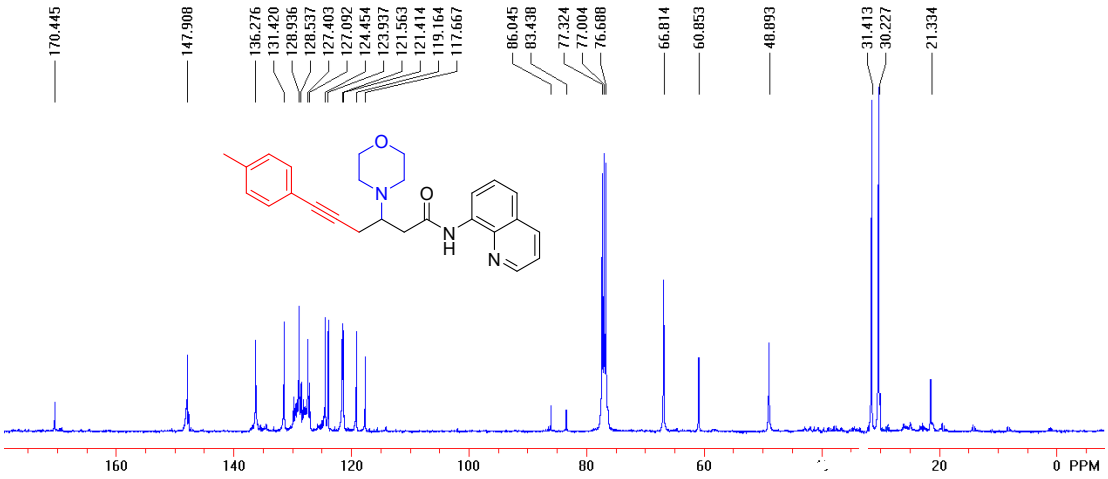


(4-(tert-butyl)phenyl)-3-morpholino-*N*-(quinolin-8-yl)hex-5-ynamide (4b)



3-morpholino-*N*-(quinolin-8-yl)-6-(p-tolyl)hex-5-ynamide (4c)





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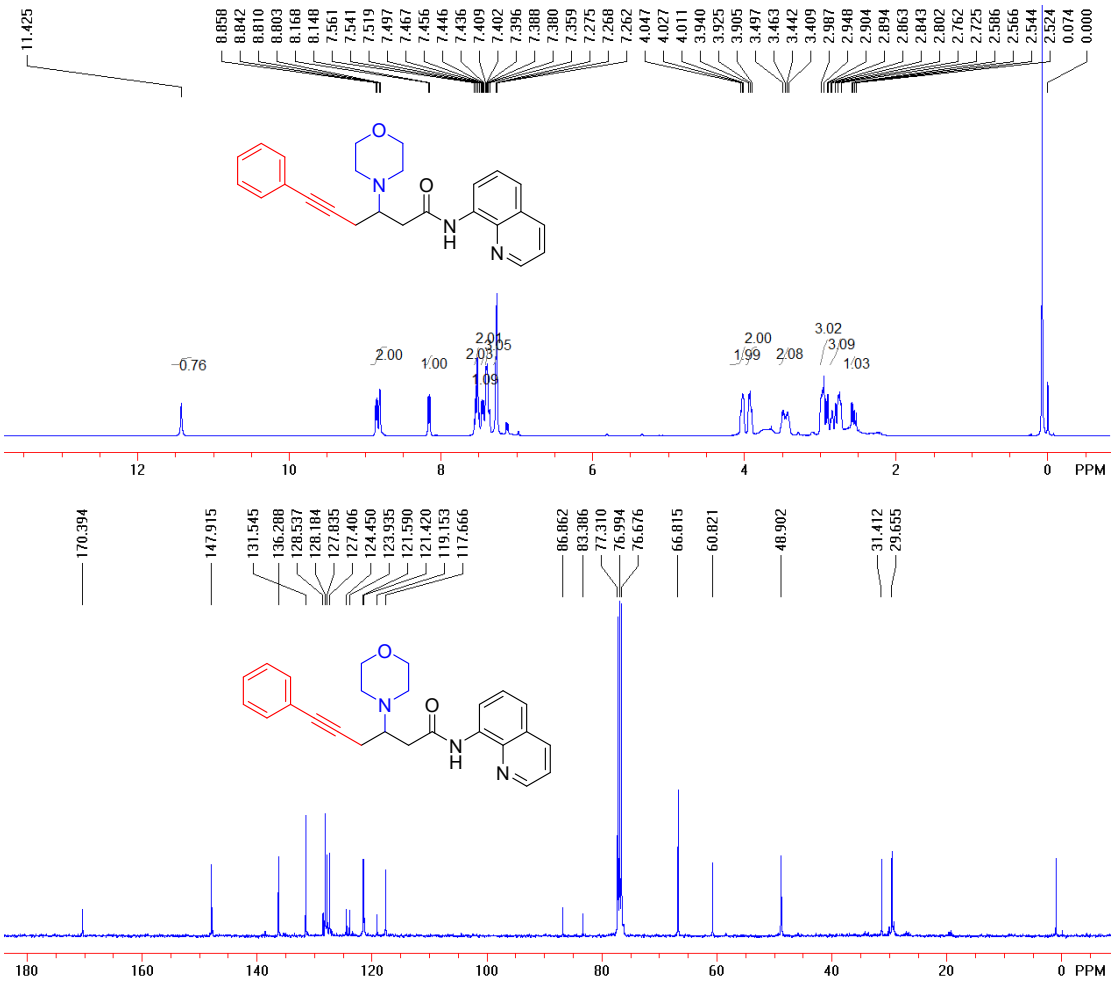

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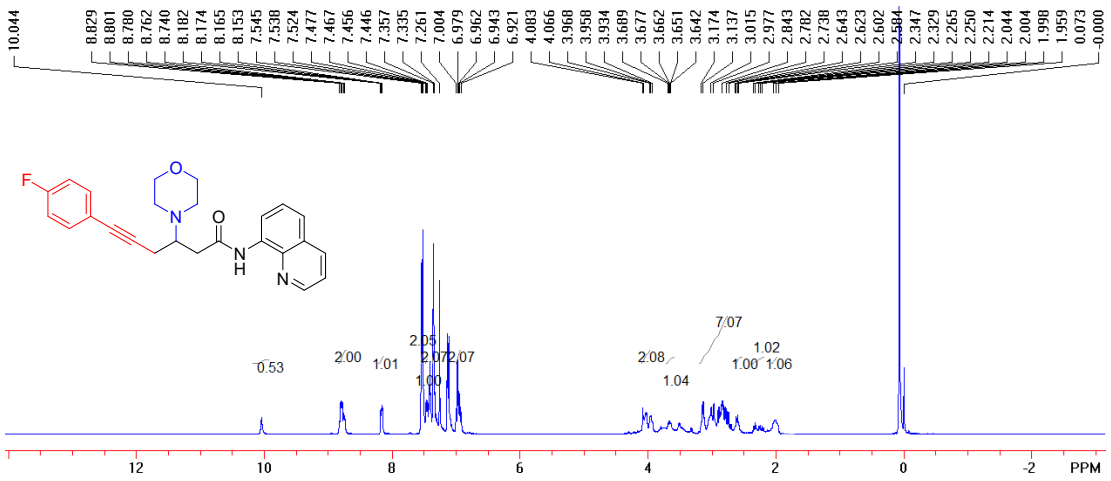

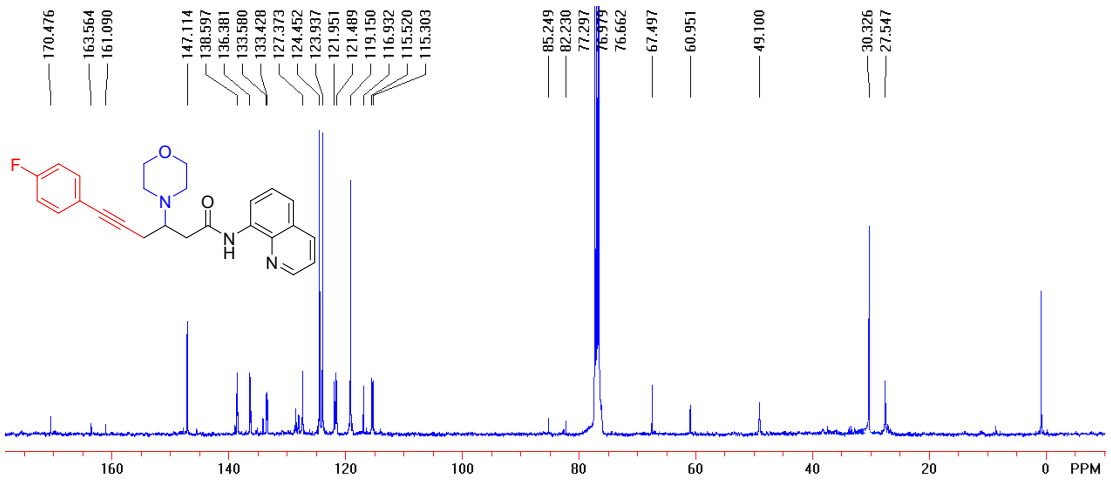

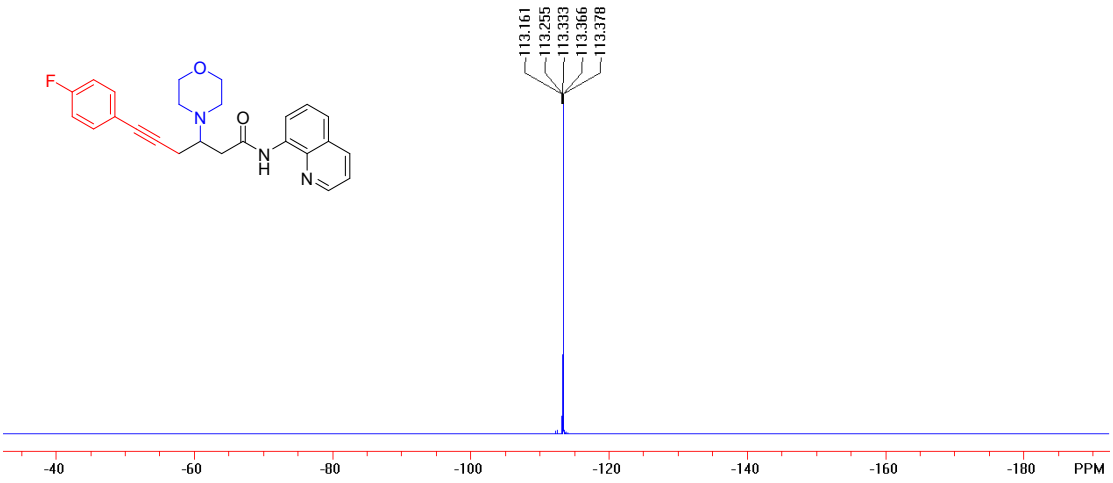

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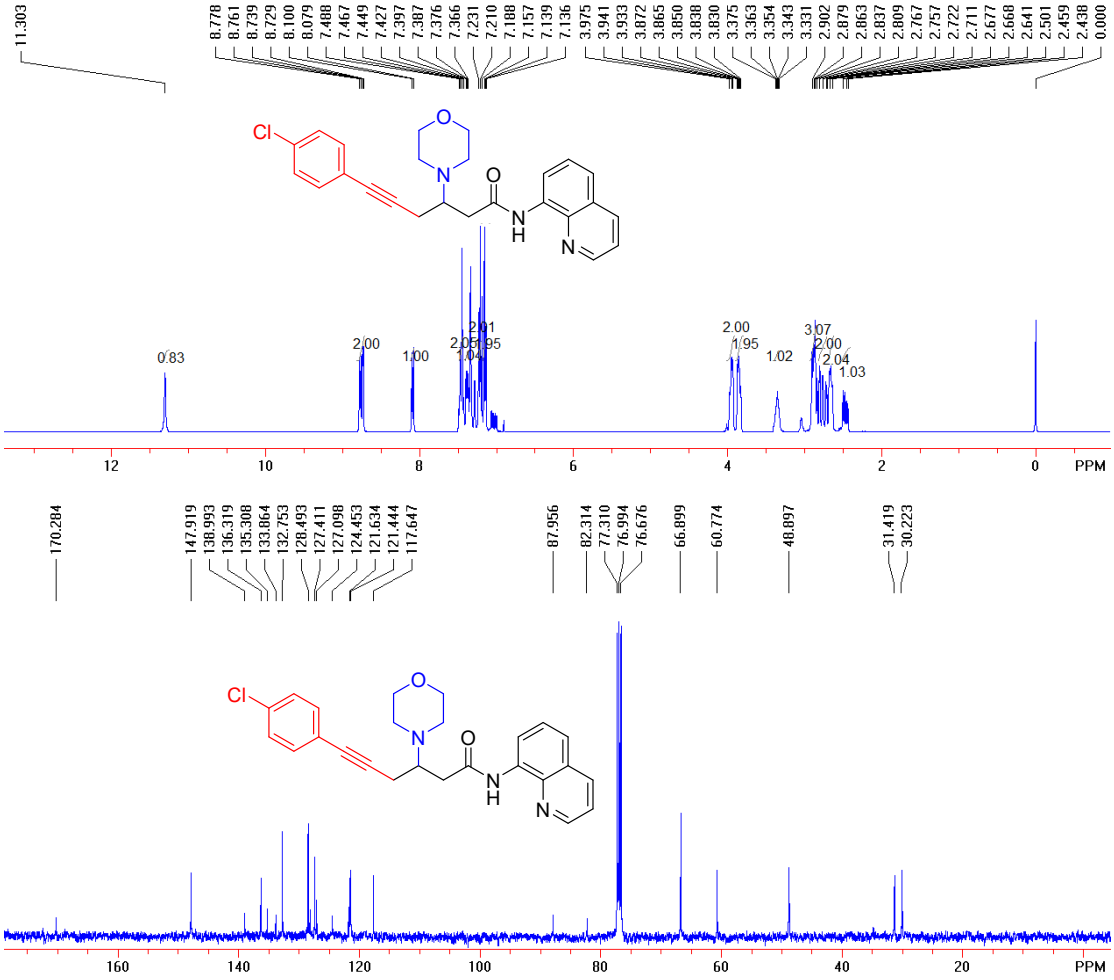

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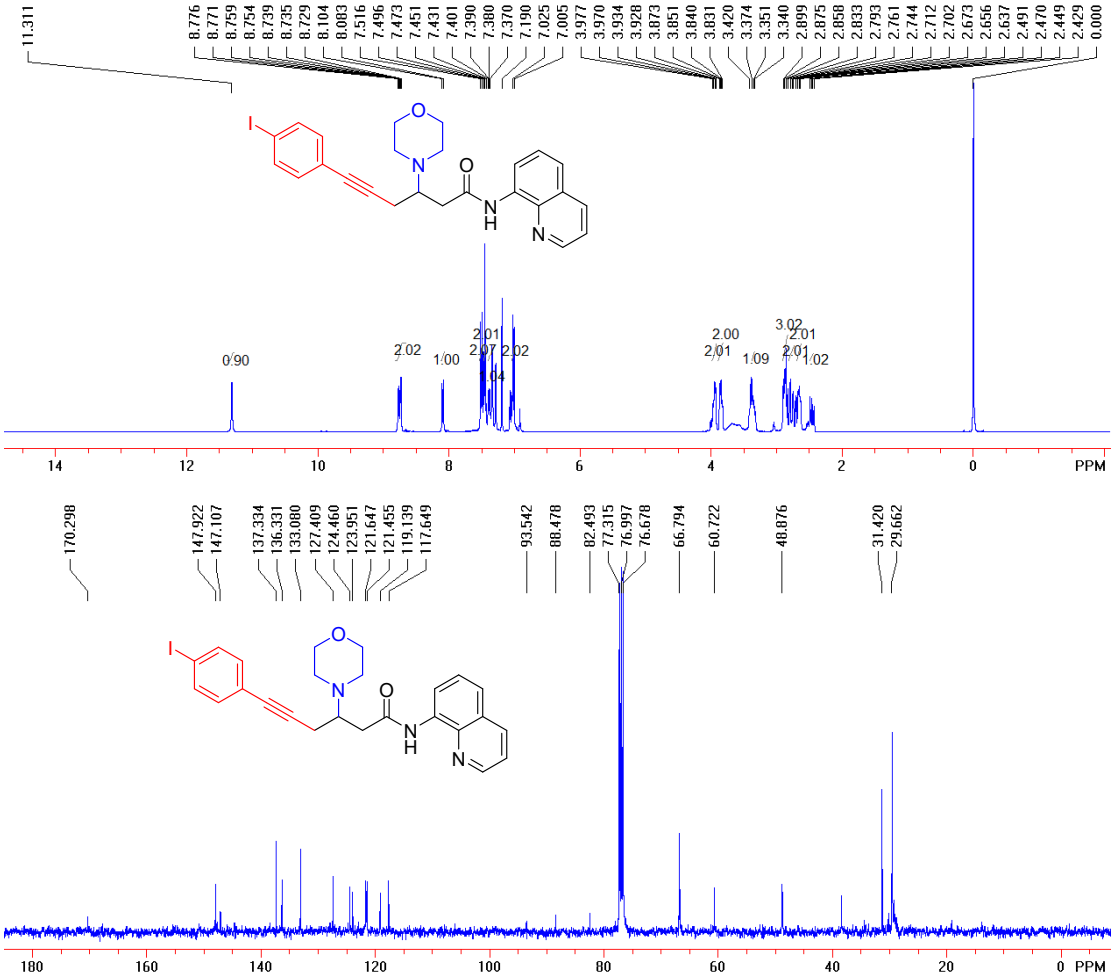

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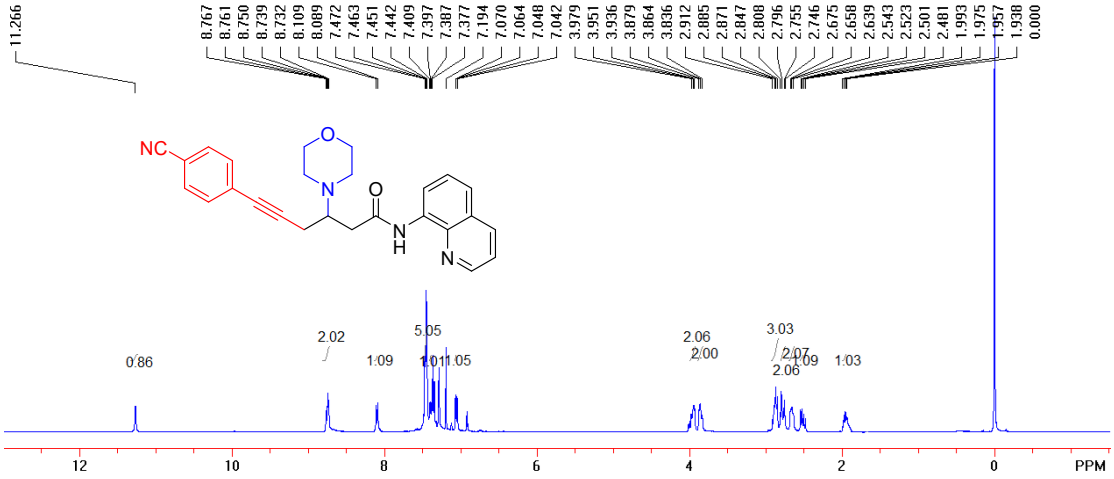

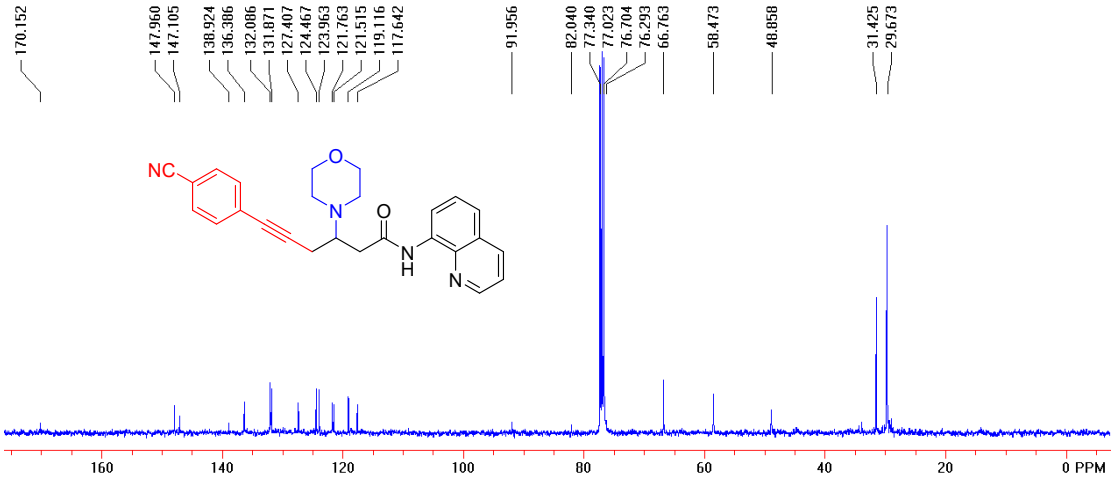

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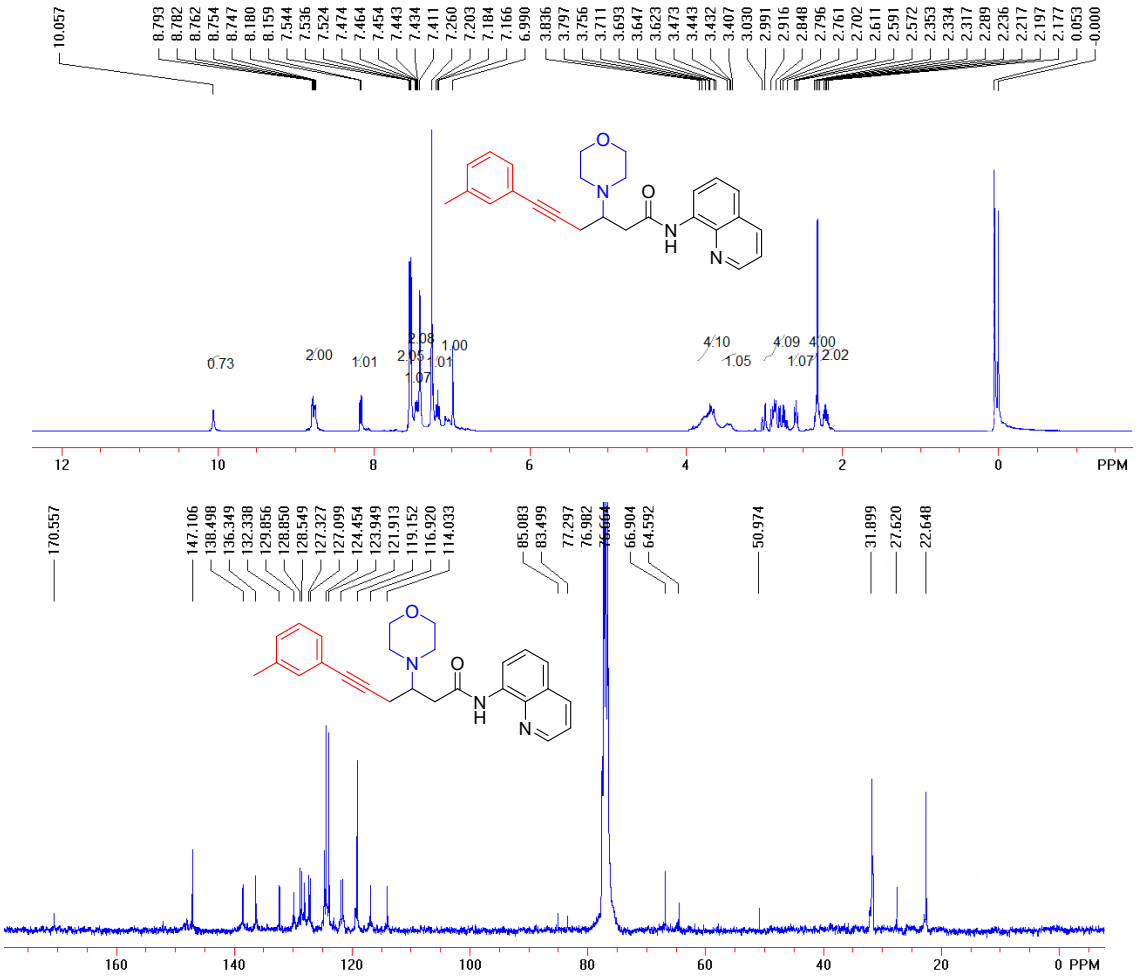

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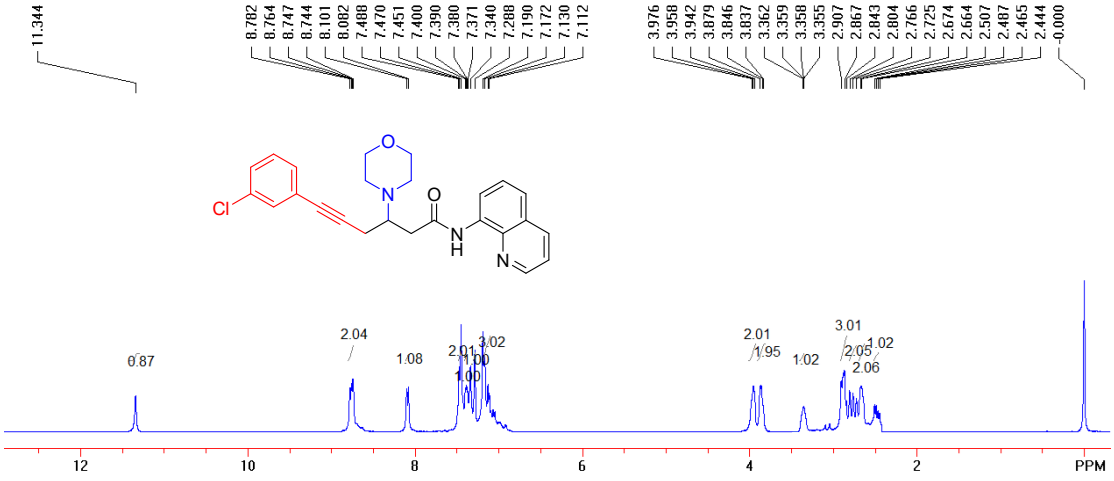

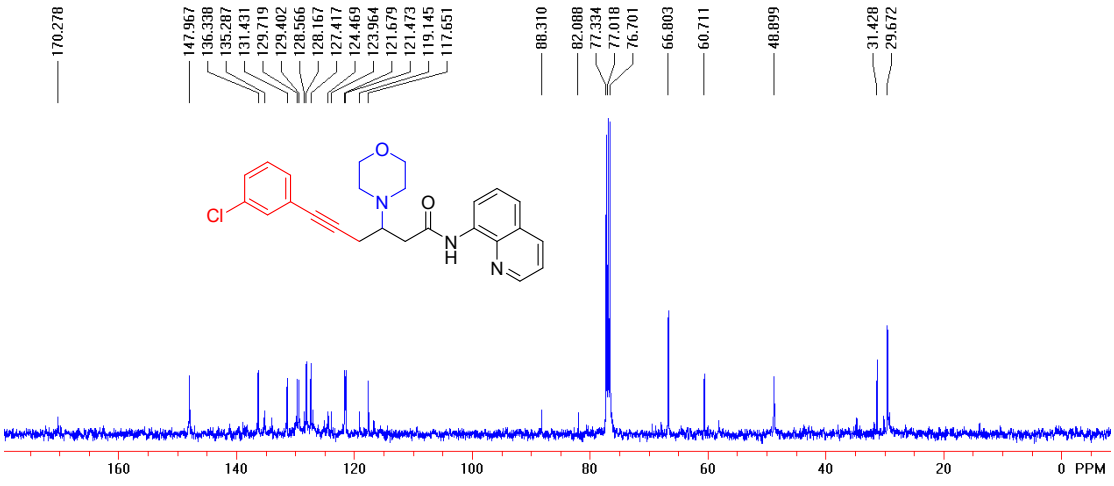

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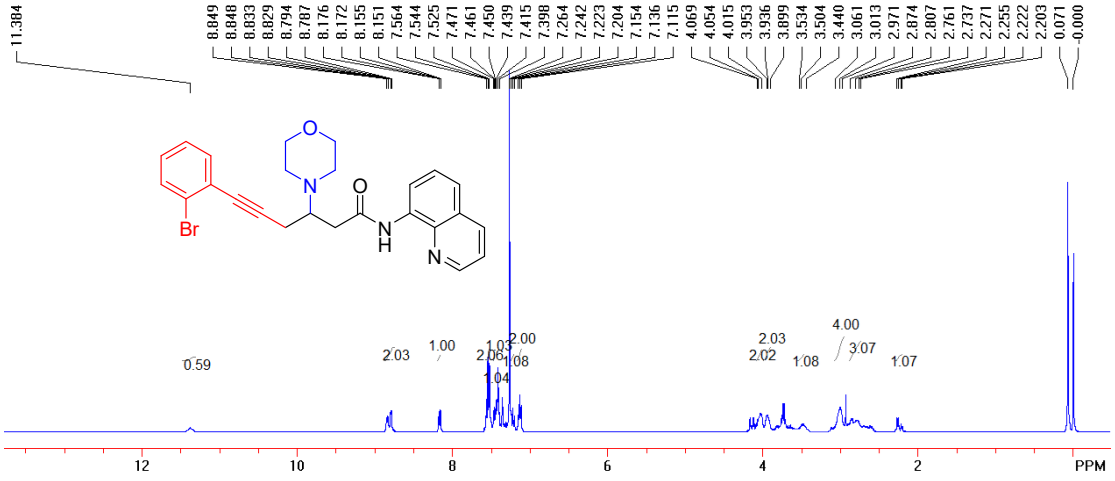

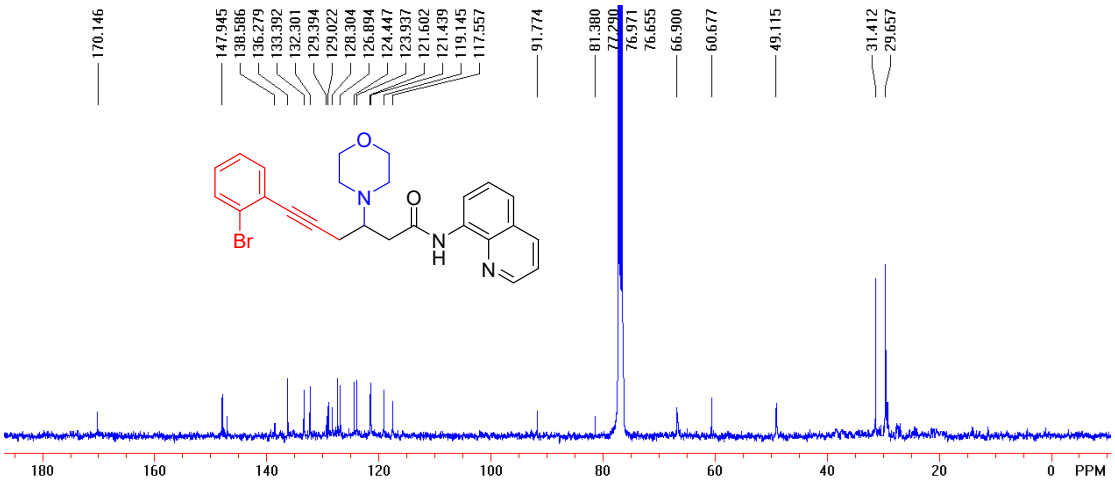

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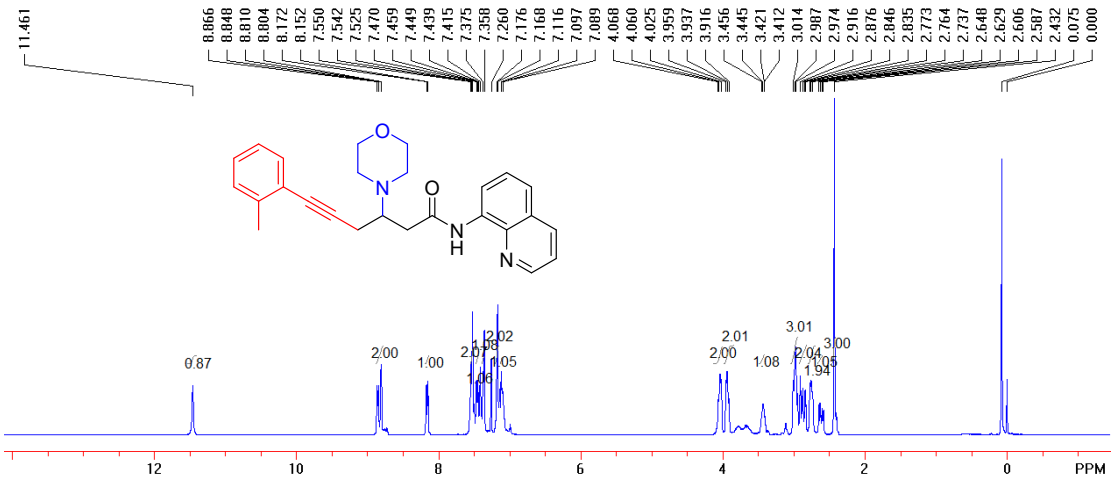

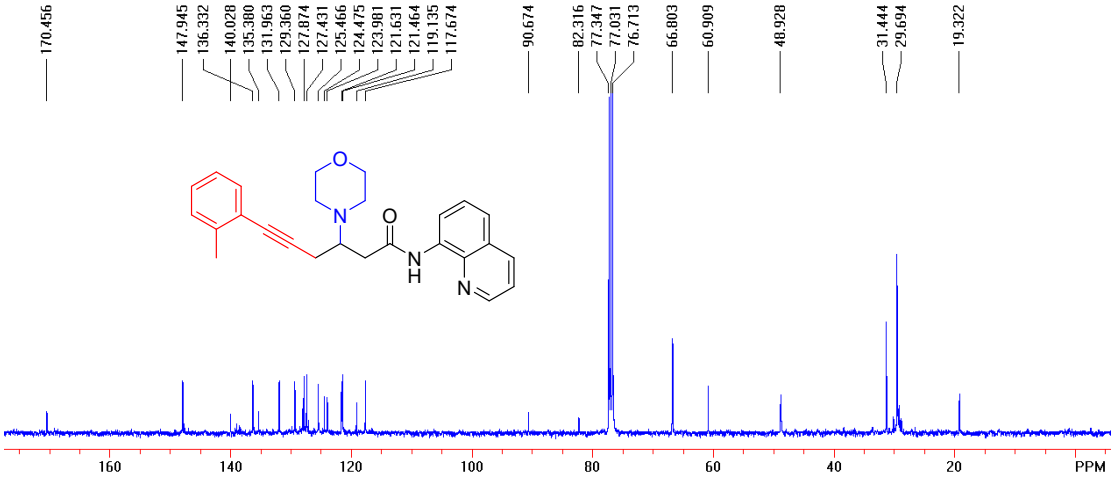

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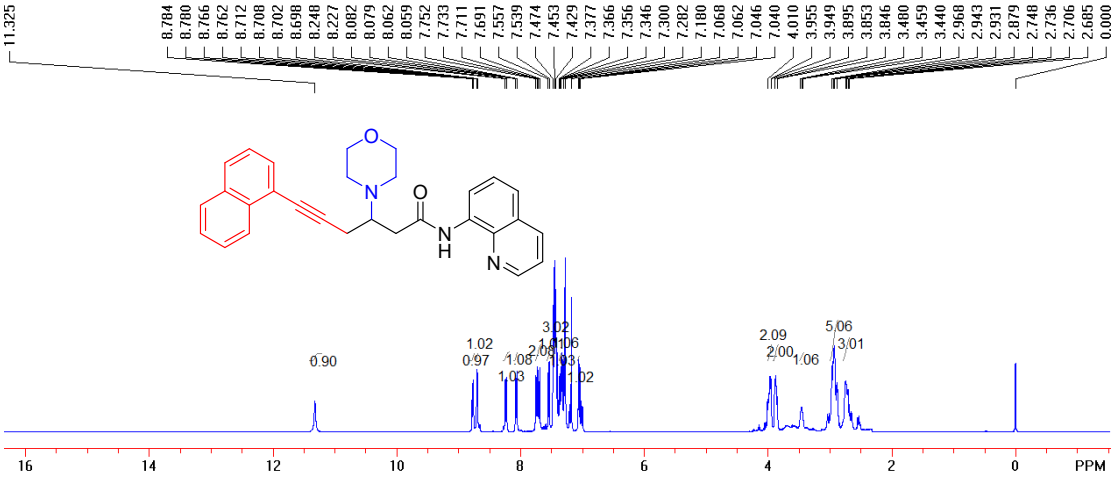

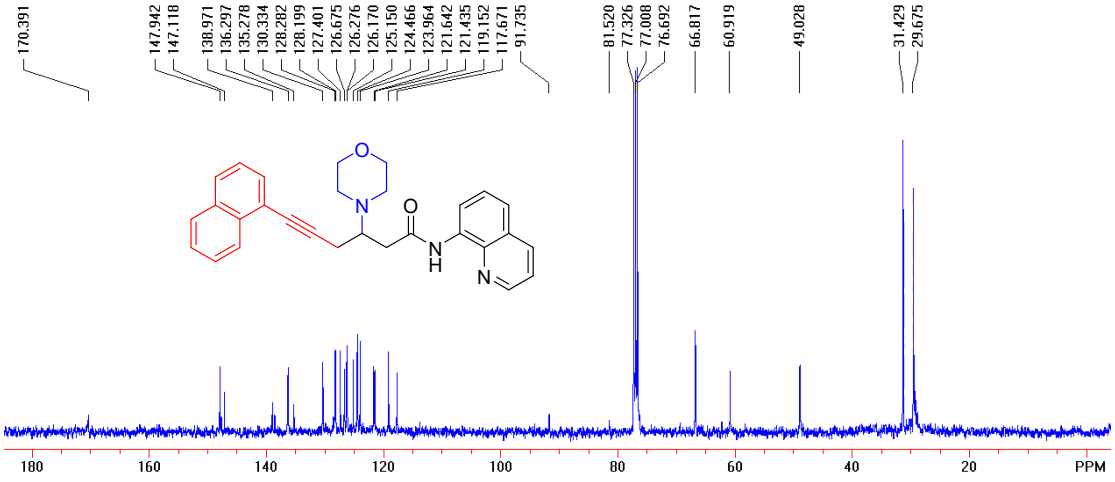

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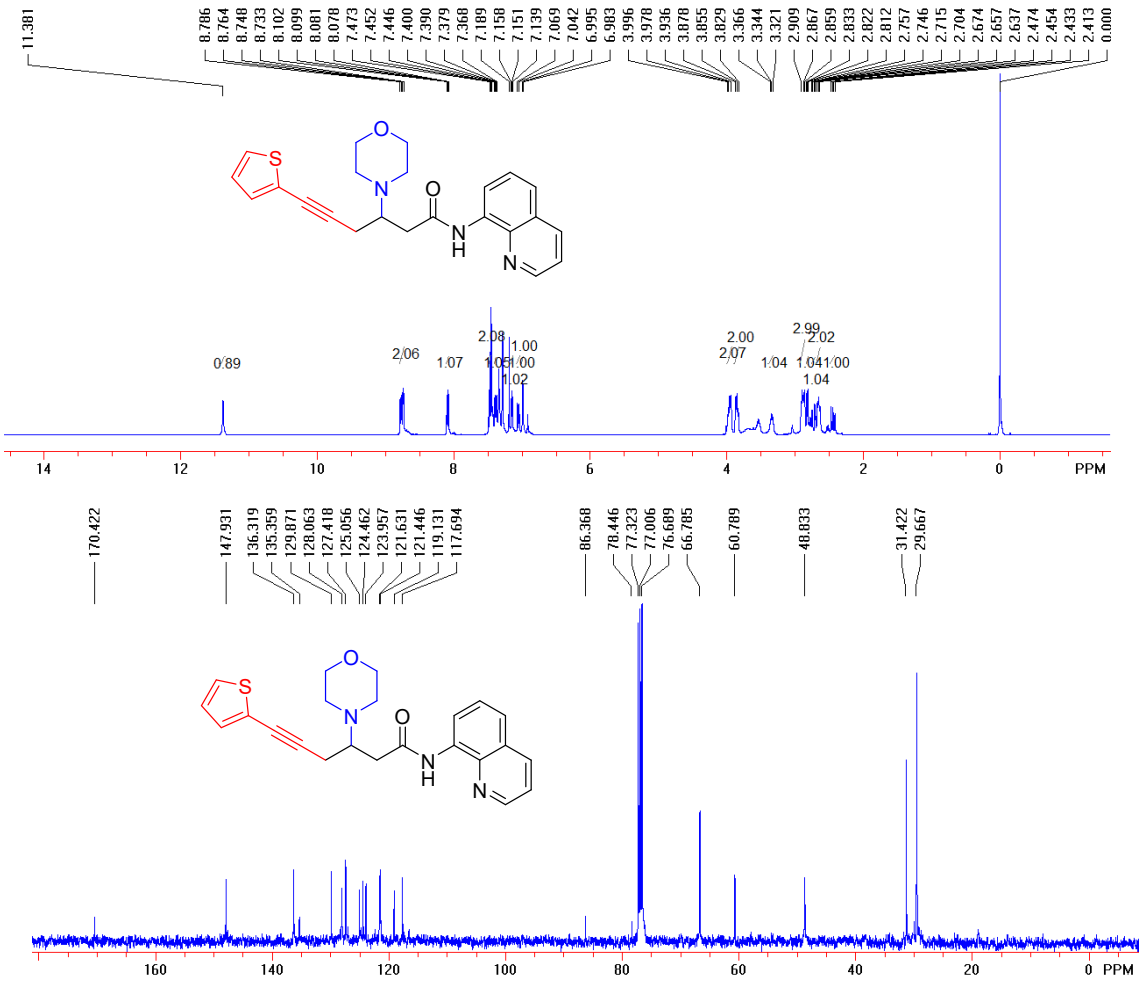
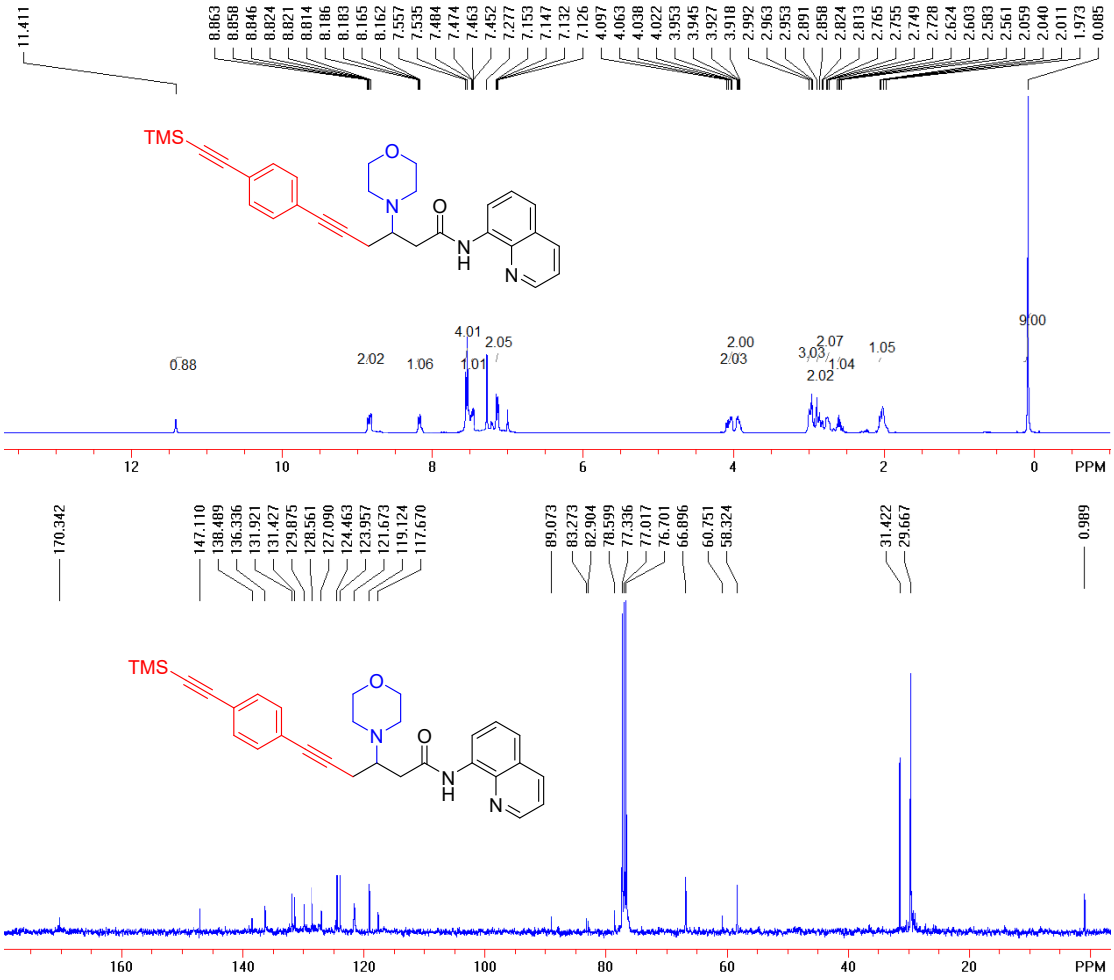
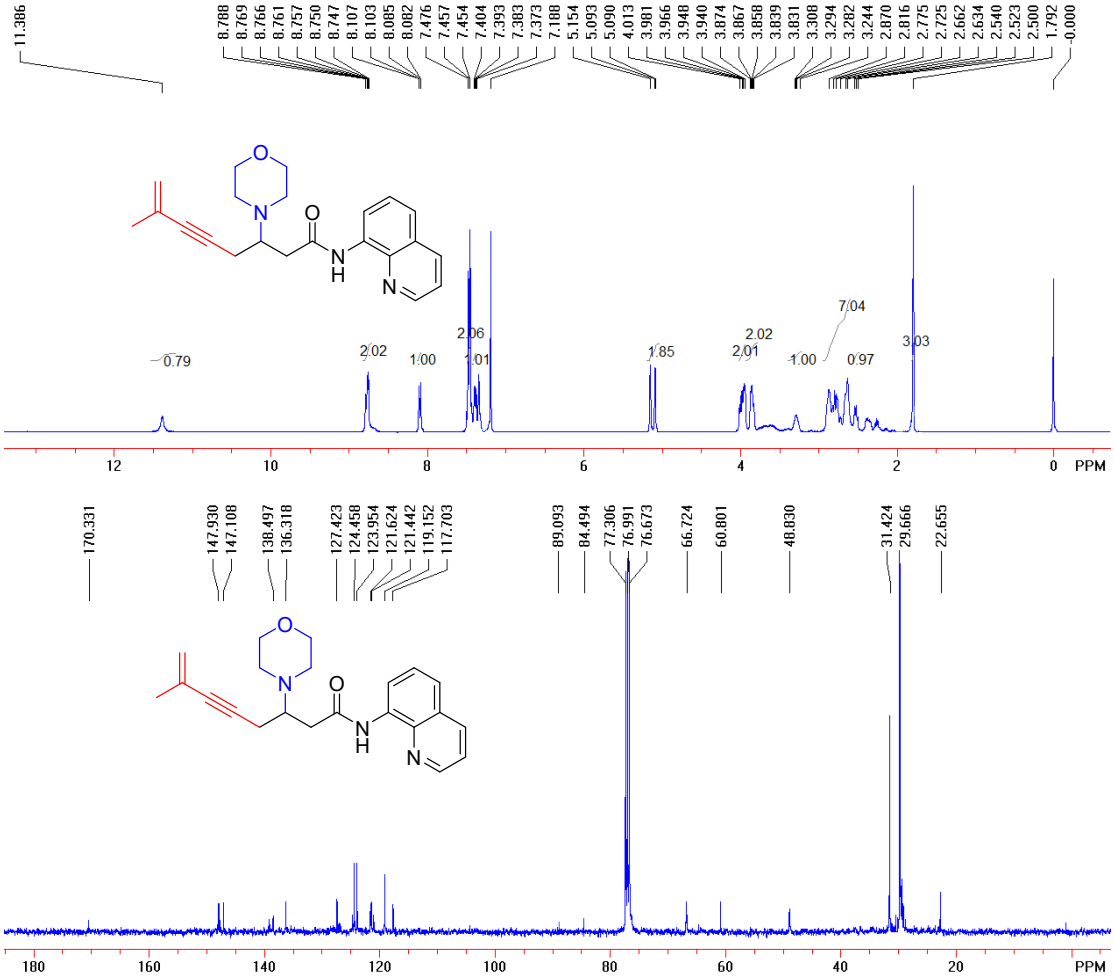


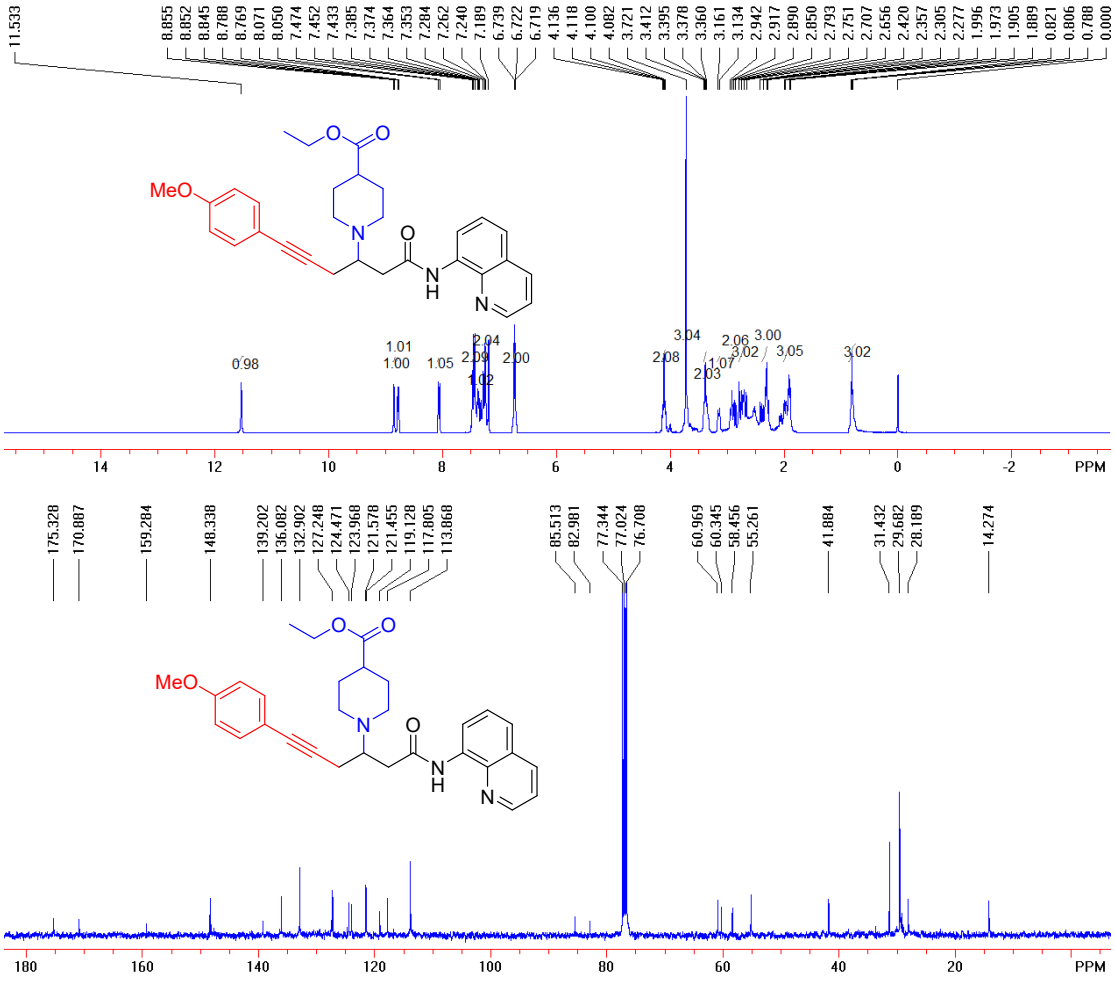
3-morpholino-*N*-(quinolin-8-yl)-6-(4-((trimethylsilyl)ethynyl)phenyl)hex-5-ynamide (4o)



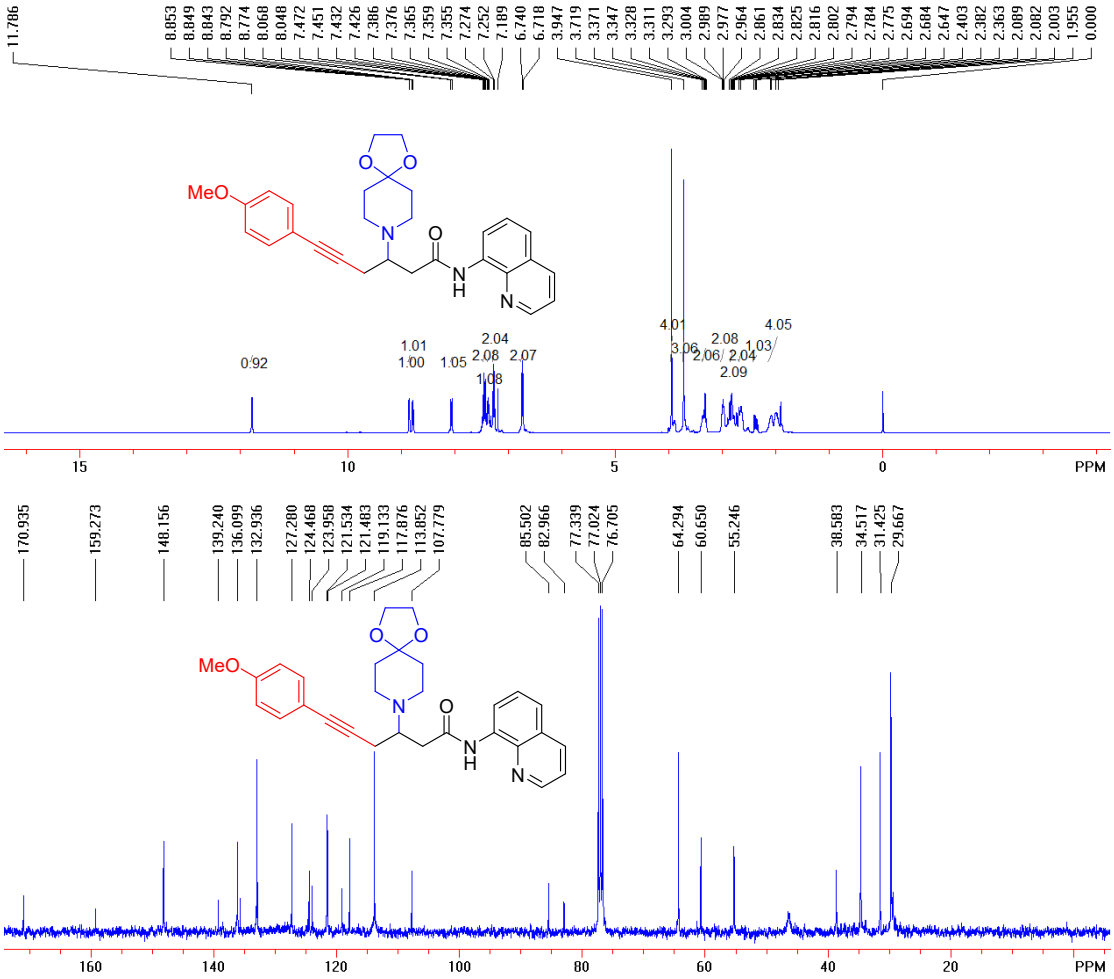
7-methyl-3-morpholino-*N*-(quinolin-8-yl)oct-7-en-5-ynamide (4p)



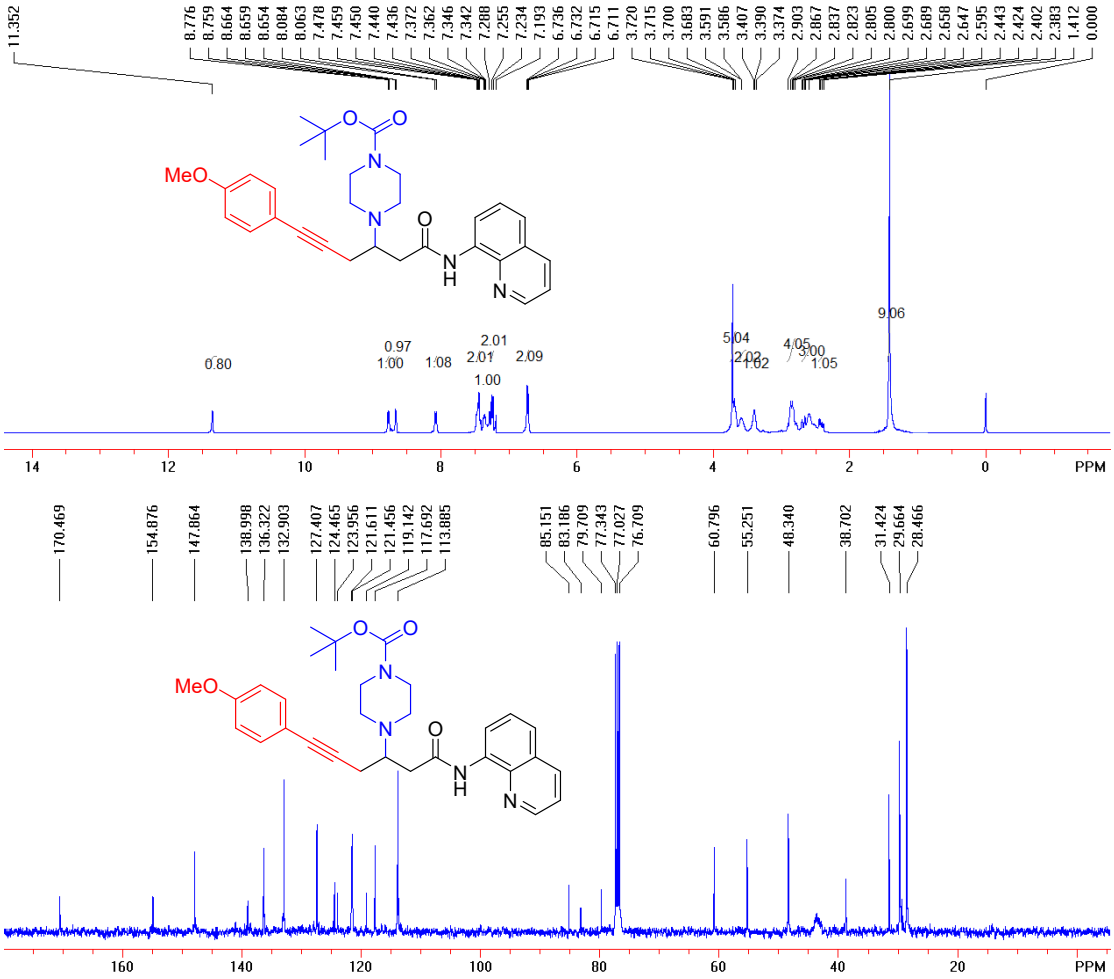
ethyl-1-(6-(4-methoxyphenyl)-1-oxo-1-(quinolin-8-ylamino)hex-5-yn-3-yl)piperidine-4-carboxylate (4r)



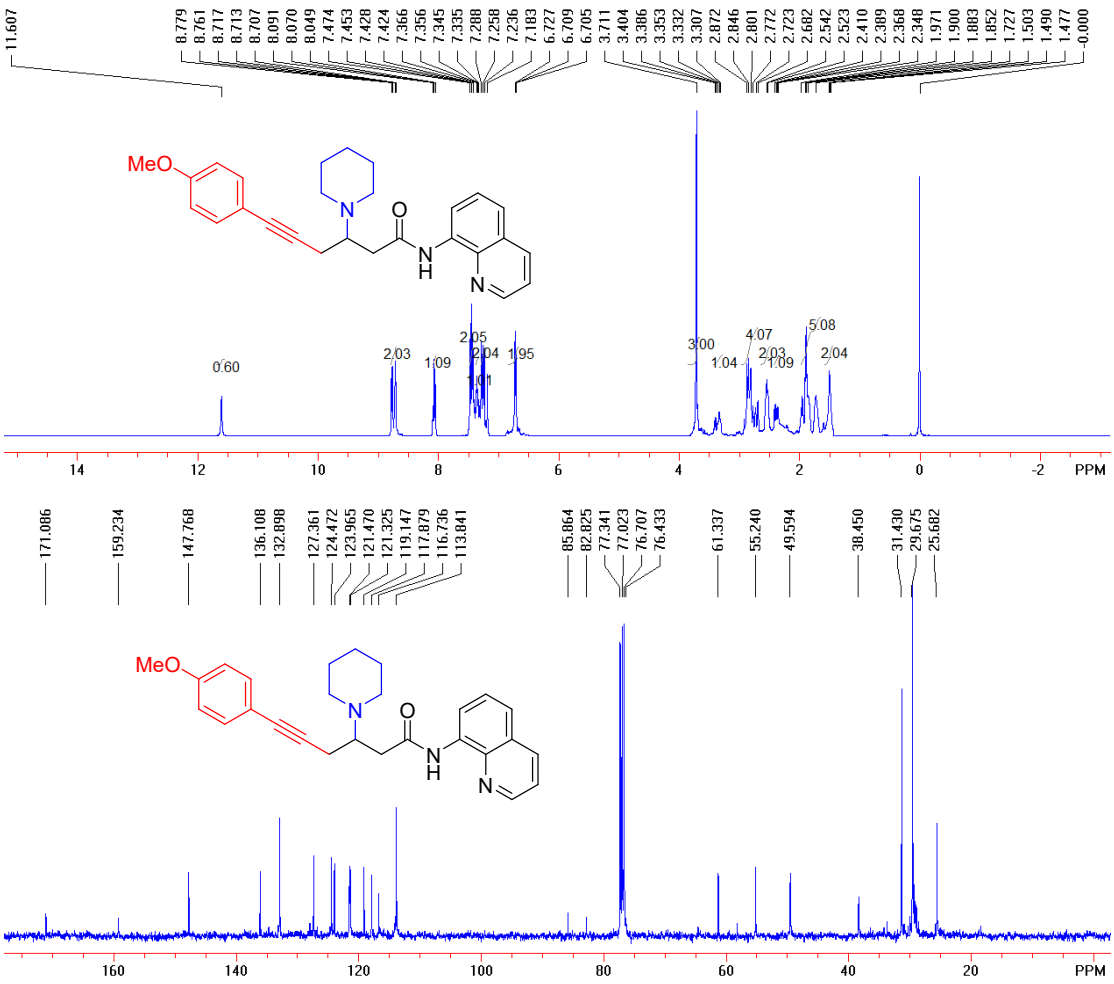
6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)-3-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)hex-5-ynamide (4s)



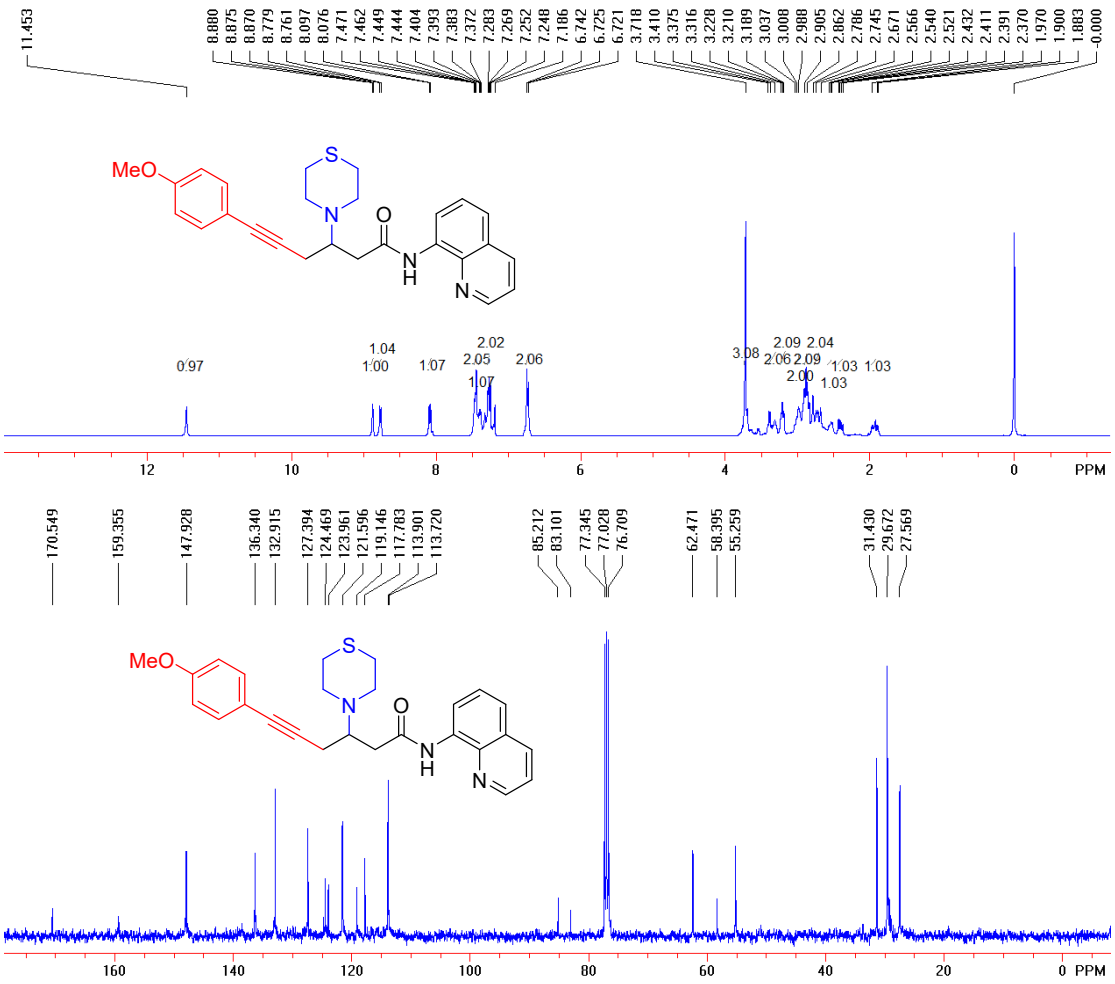
4-(6-(4-methoxyphenyl)-1-oxo-1-(quinolin-8-ylamino)hex-5-yn-3-yl)piperazine-1-carboxylate (4t)



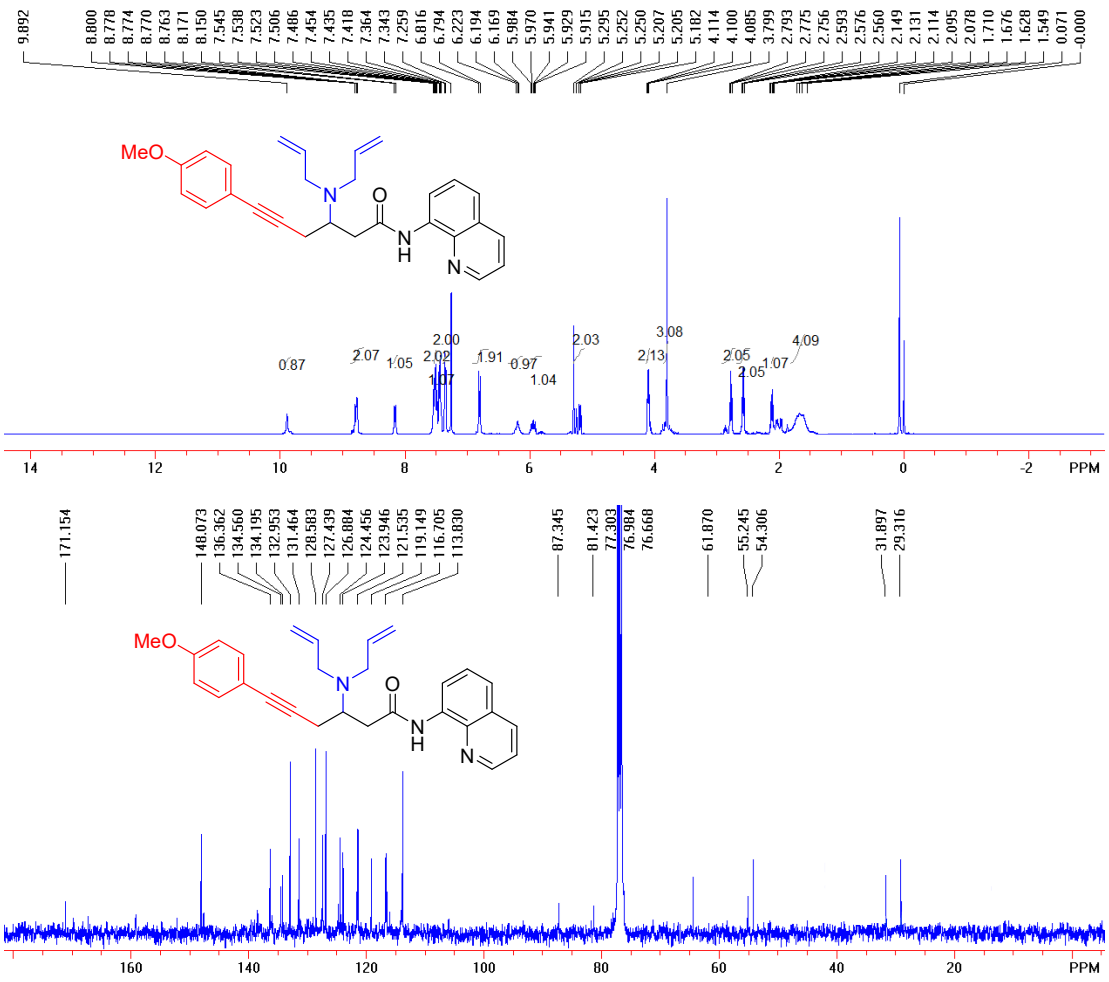
6-(4-methoxyphenyl)-3-(piperidin-1-yl)-*N*-(quinolin-8-yl)hex-5-ynamide (4u)



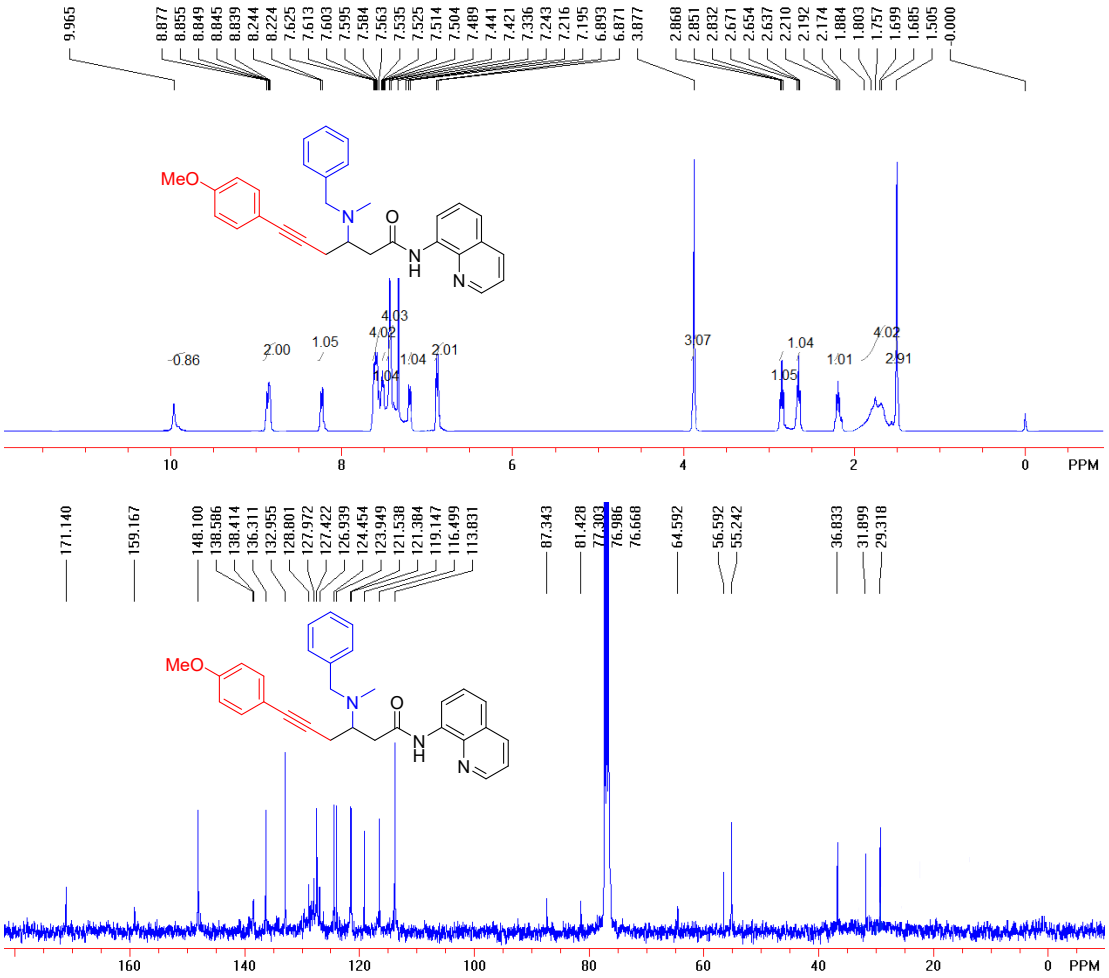
6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)-3-thiomorpholinohex-5-ynamide (4v)



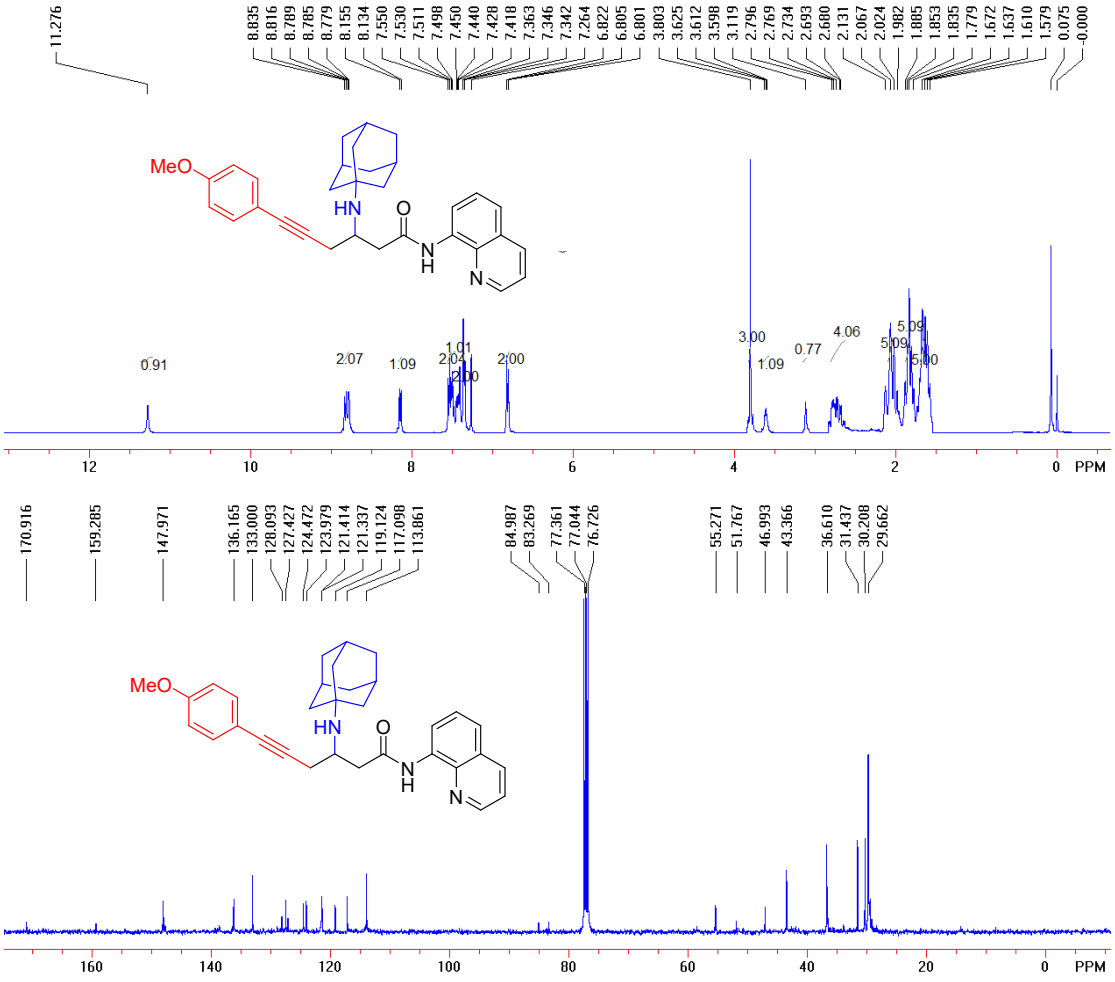
3-(diallylamino)-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (4w)



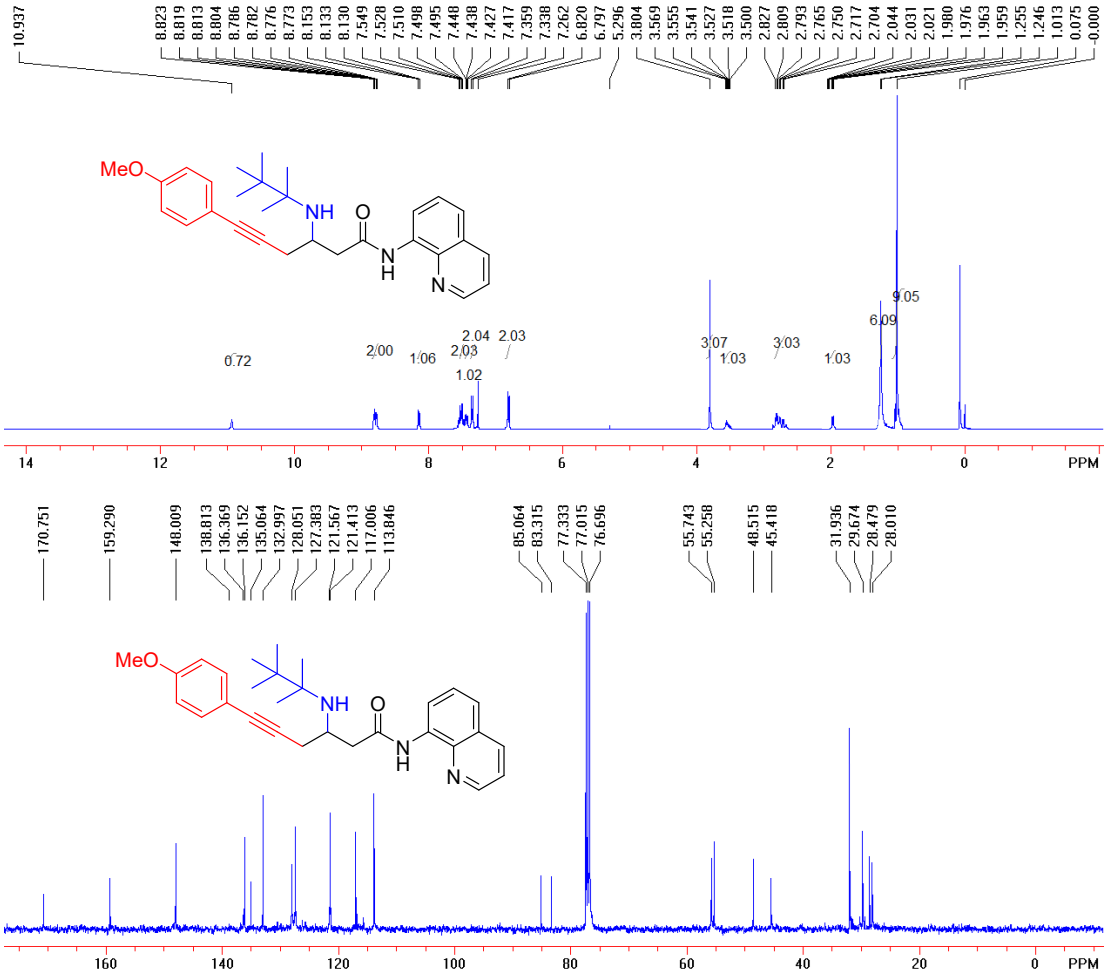
3-(benzyl(methyl)amino)-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (4x)



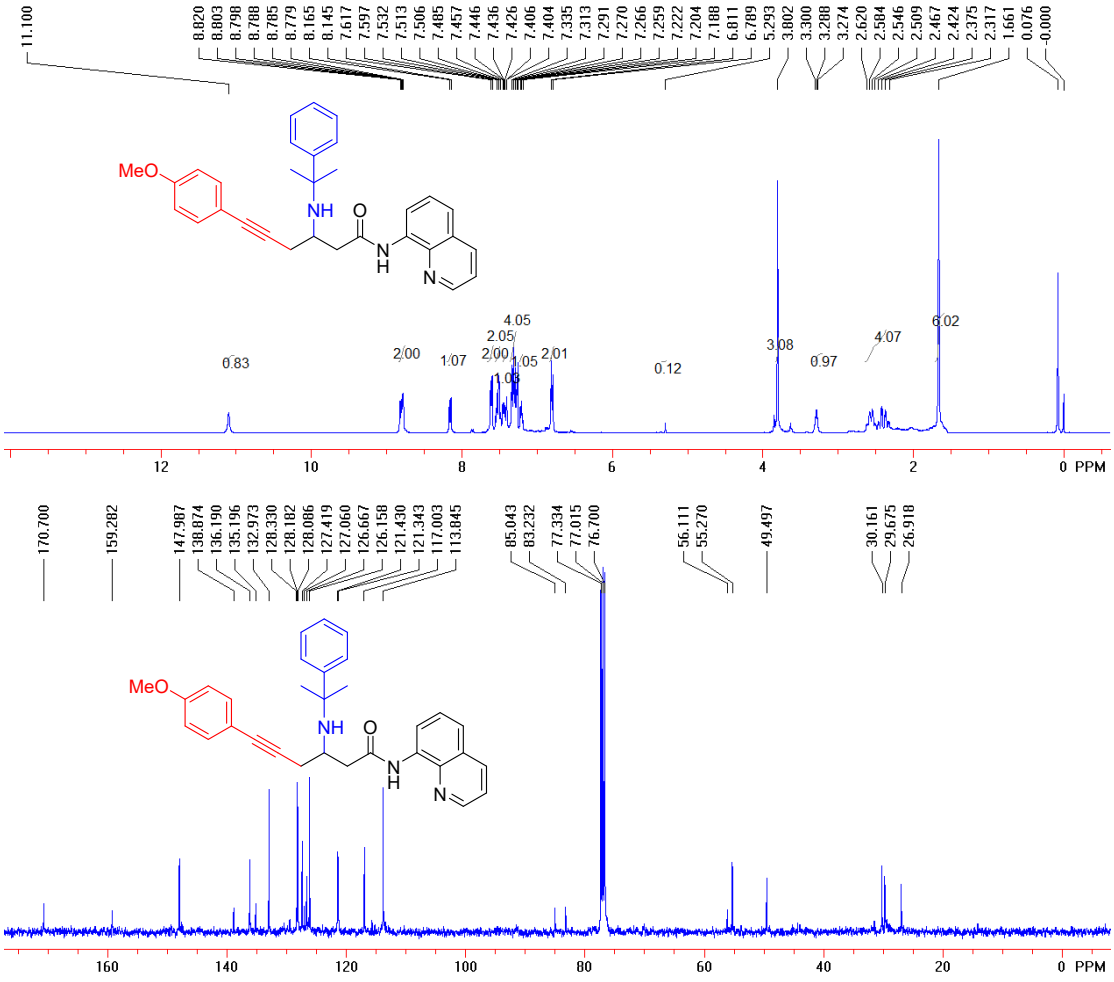
3-((adamantan-1-yl)amino)-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (4y)



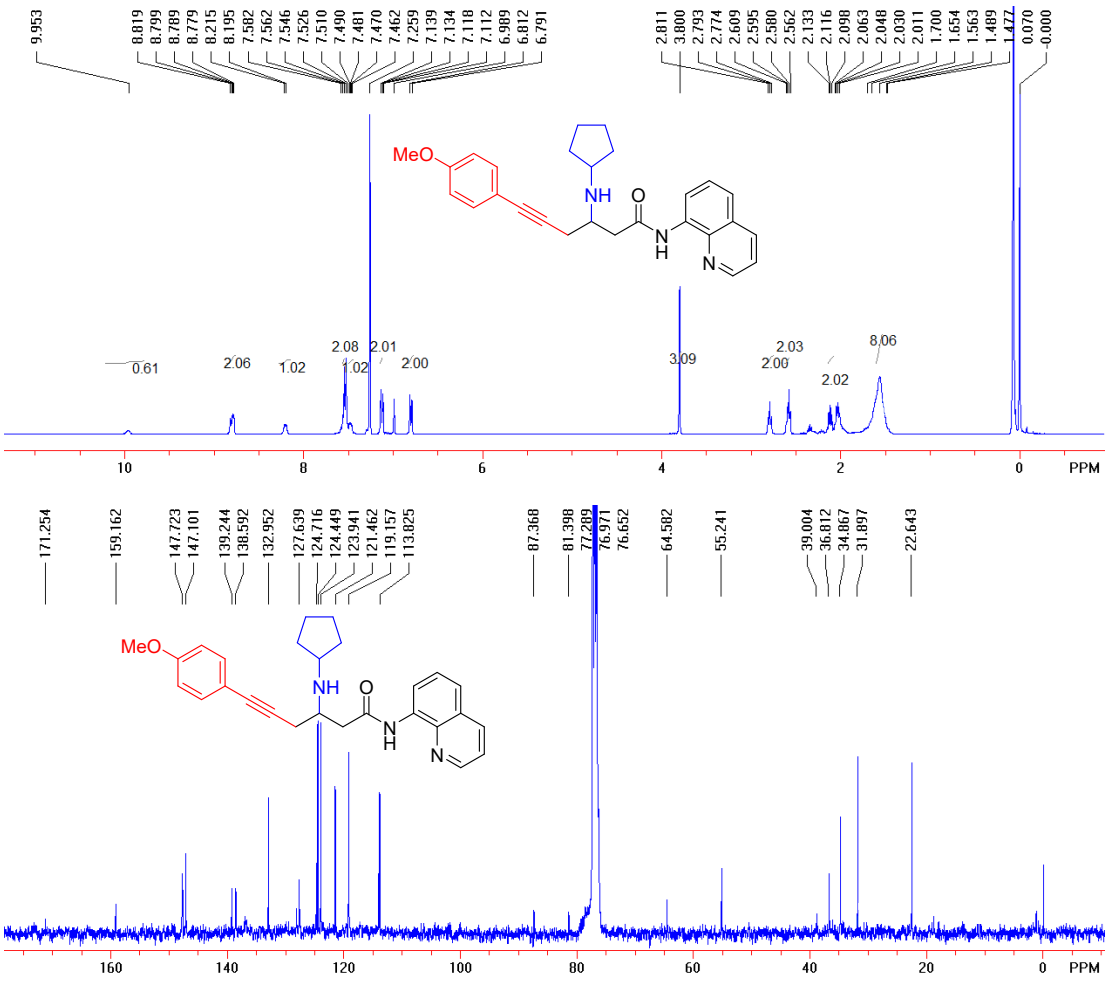
6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)-3-((2,4,4-trimethylpentan-2-yl)amino)hex-5-ynamide (4z)



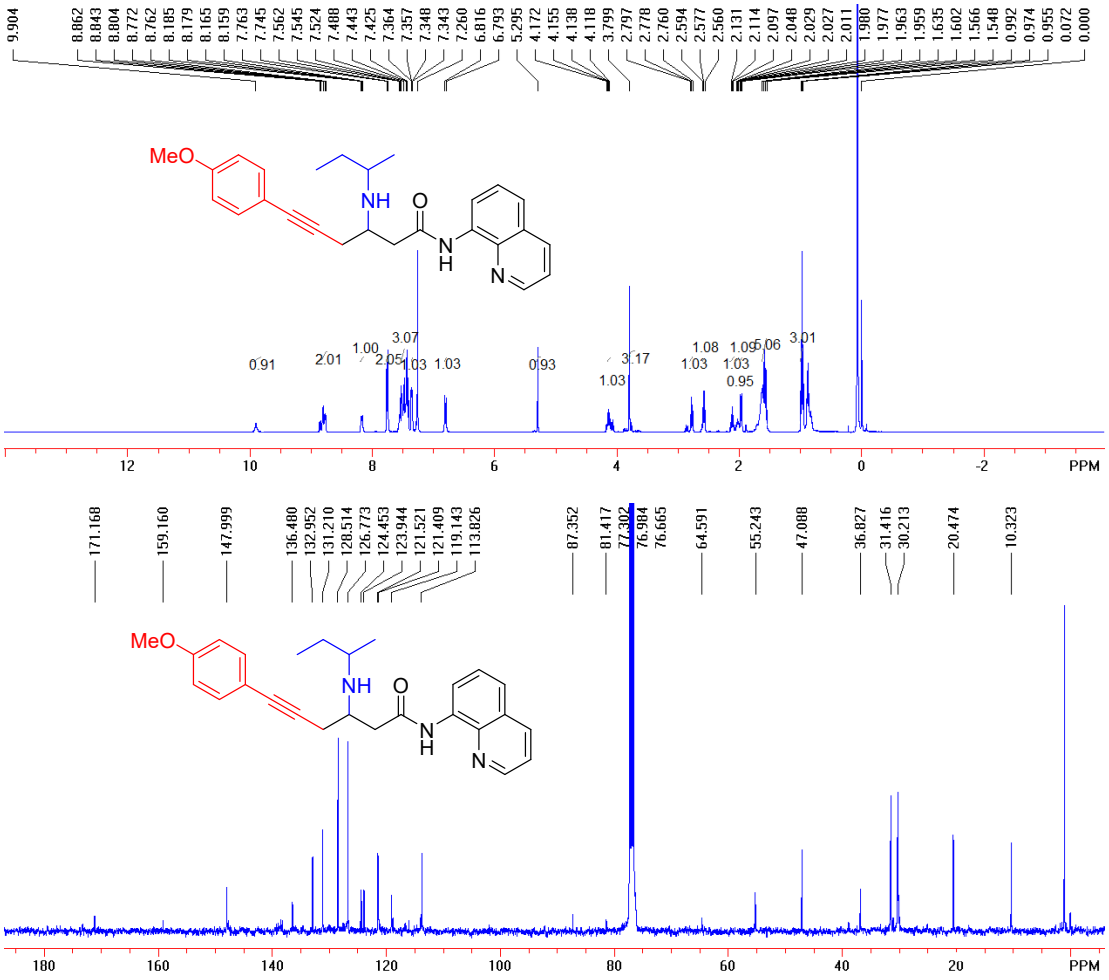
6-(4-methoxyphenyl)-3-((2-phenylpropan-2-yl)amino)-*N*-(quinolin-8-yl)hex-5-ynamide (4aa)



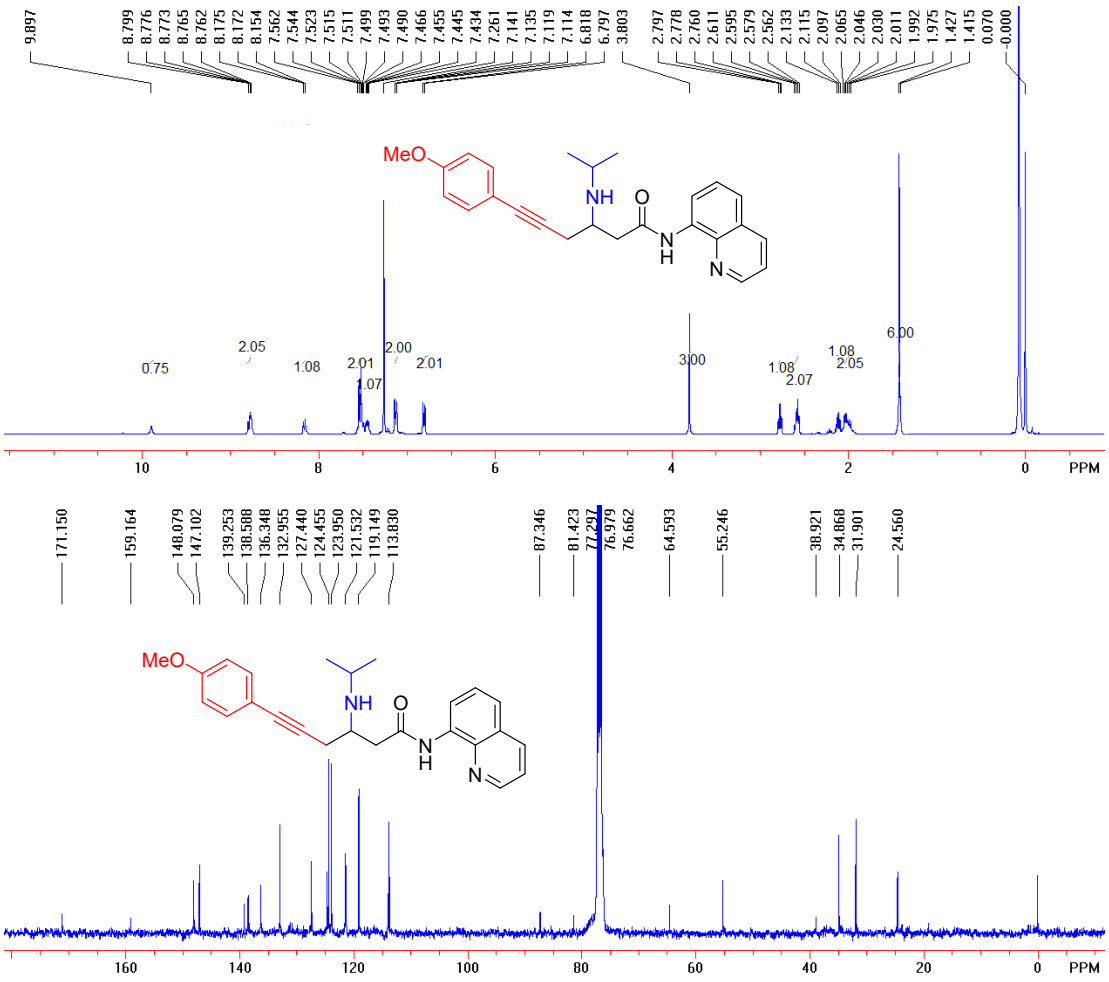
3-(*sec*-butylamino)-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (4ab)



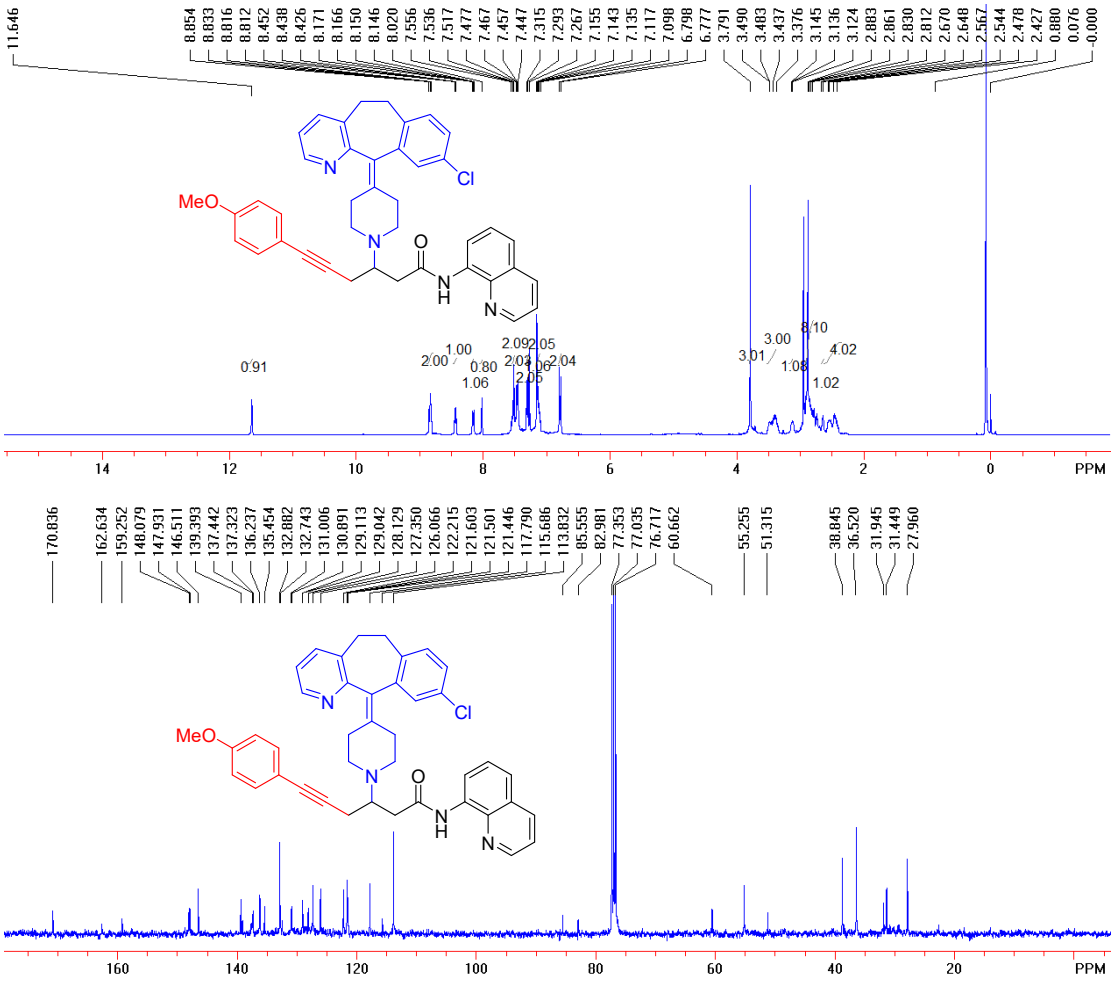
3-(*sec*-butylamino)-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (4ac)



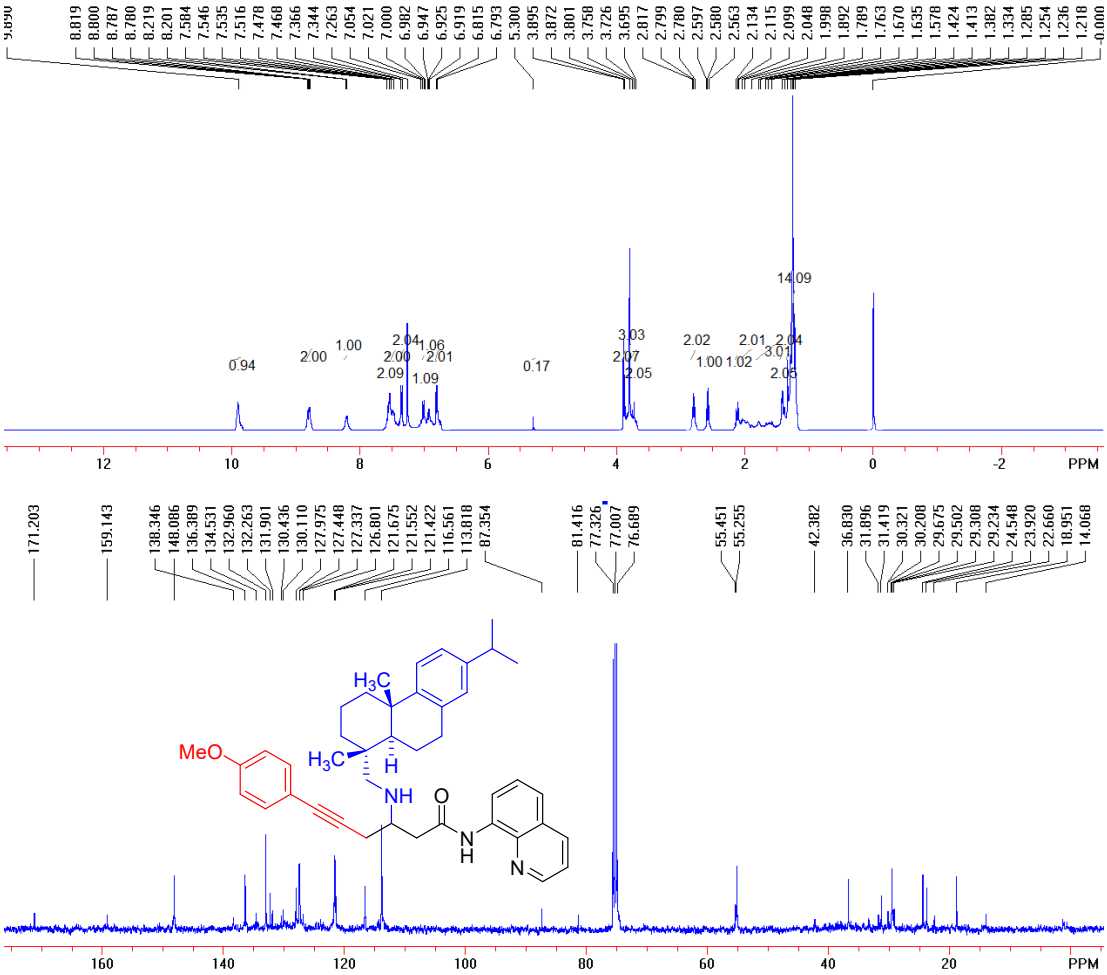
3-(*sec*-butylamino)-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (4ad)



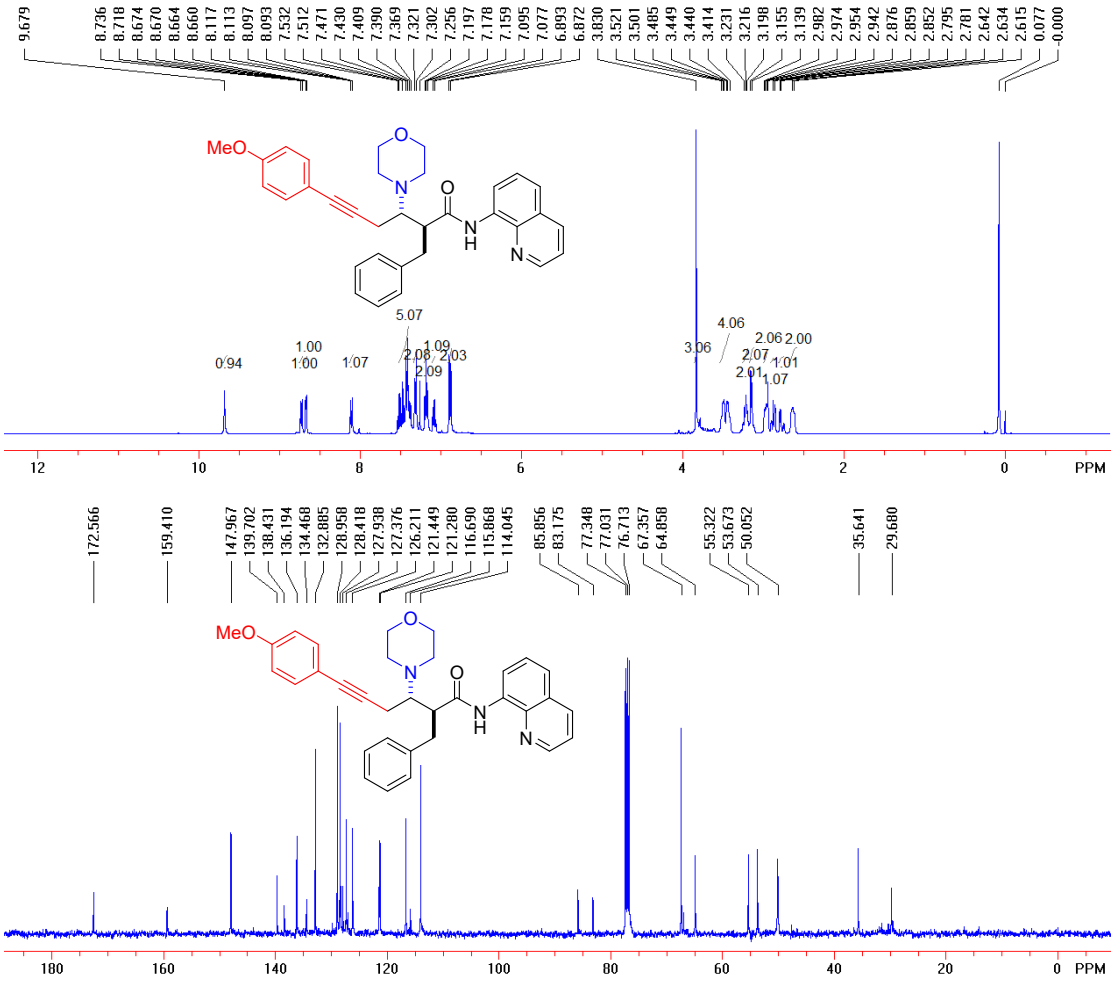
3-(4-(9-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)piperidin-1-yl)-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (4ae)



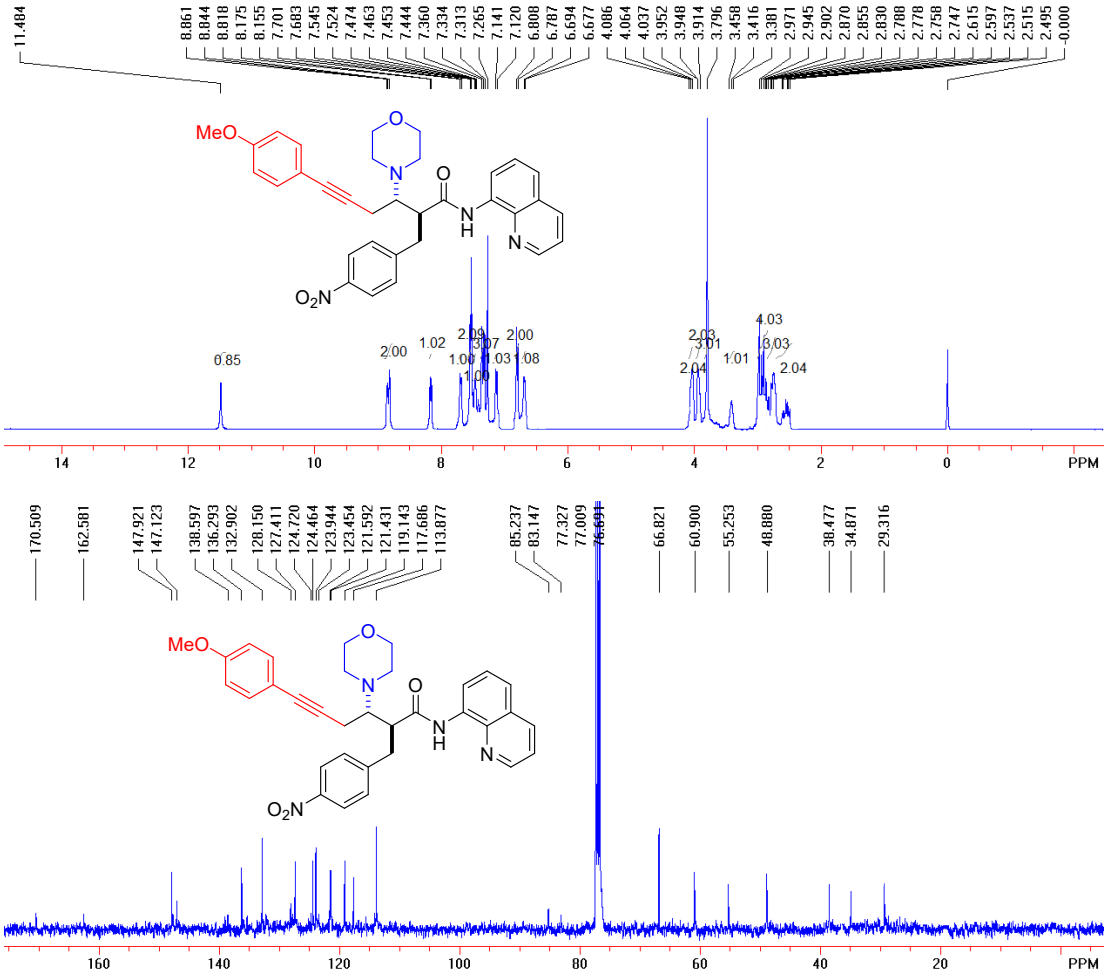
3-((((1R,4aS,10aR)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl)methyl)amino)-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (4af)



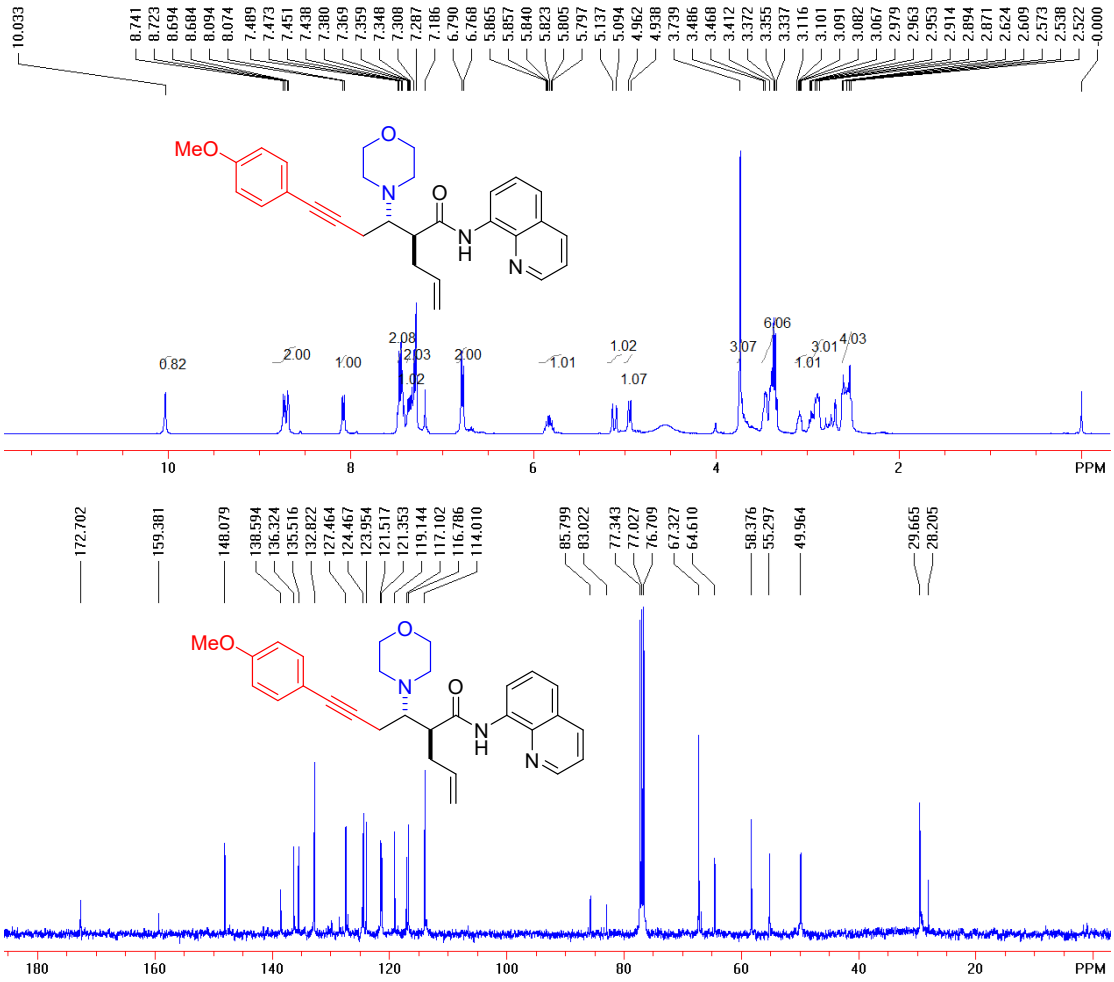
2-benzyl-6-(4-methoxyphenyl)-3-morpholino-*N*-(quinolin-8-yl)hex-5-ynamide (5a)



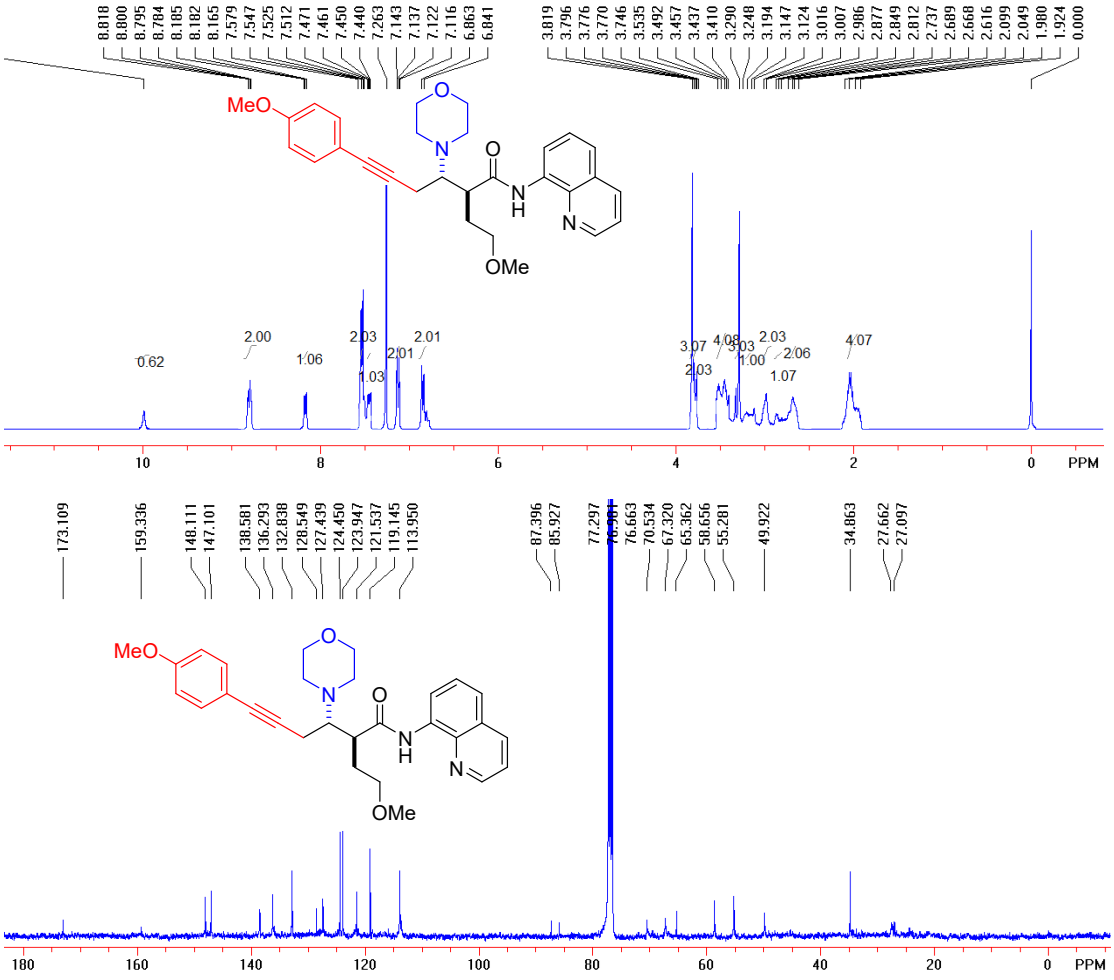
(2S,3S)-6-(4-methoxyphenyl)-3-morpholino-2-(4-nitrobenzyl)-*N*-(quinolin-8-yl)hex-5-ynamide (5b)



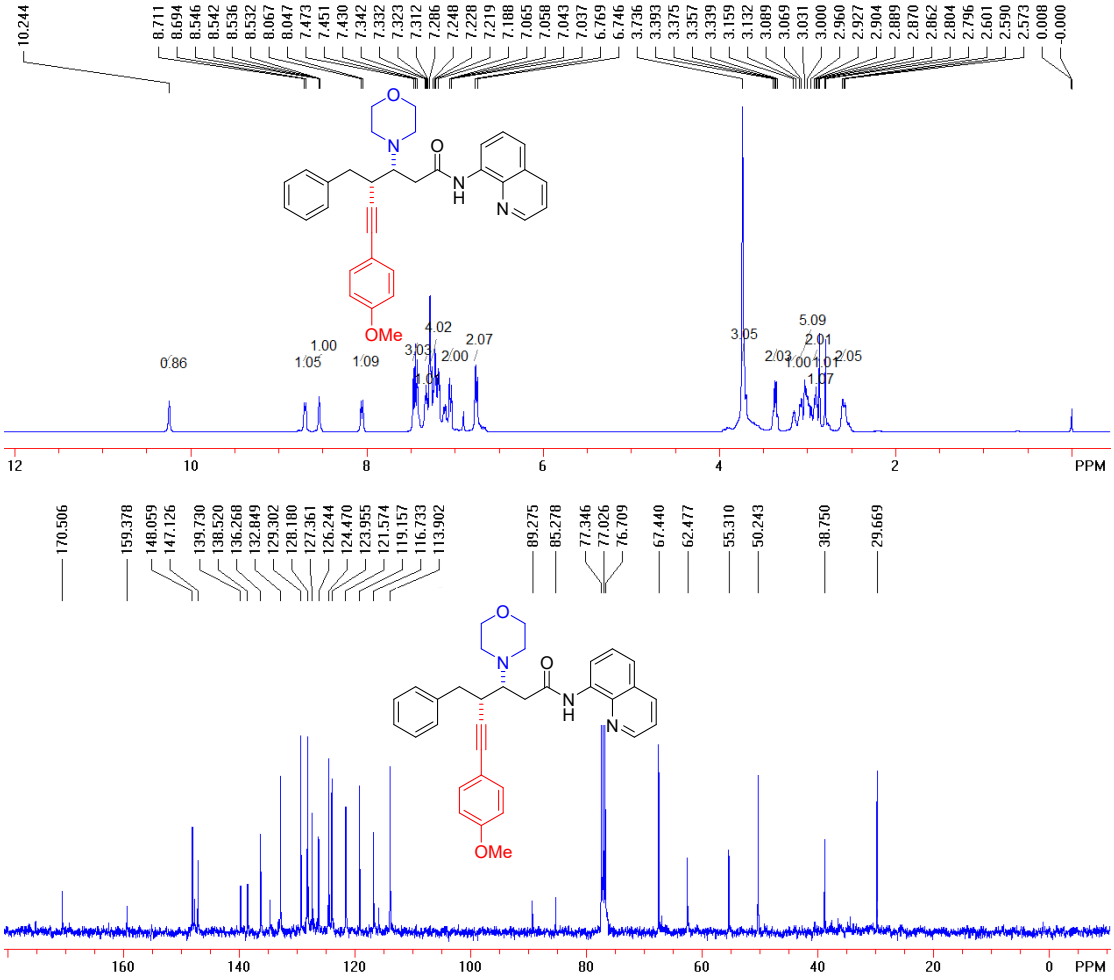
2-allyl-6-(4-methoxyphenyl)-3-morpholino-*N*-(quinolin-8-yl)hex-5-ynamide (5c)



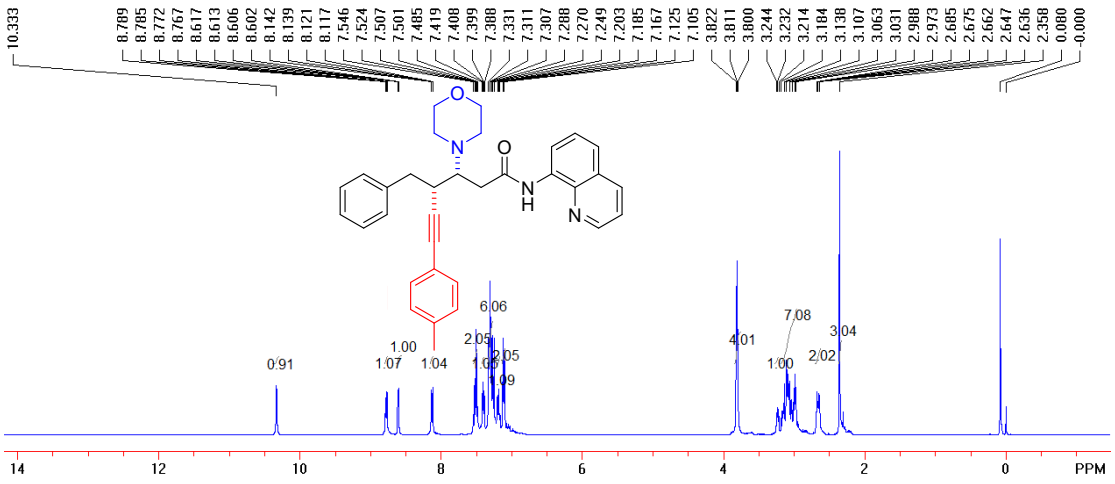
2-(2-methoxyethyl)-6-(4-methoxyphenyl)-3-morpholino-*N*-(quinolin-8-yl)hex-5-ynamide (5d)

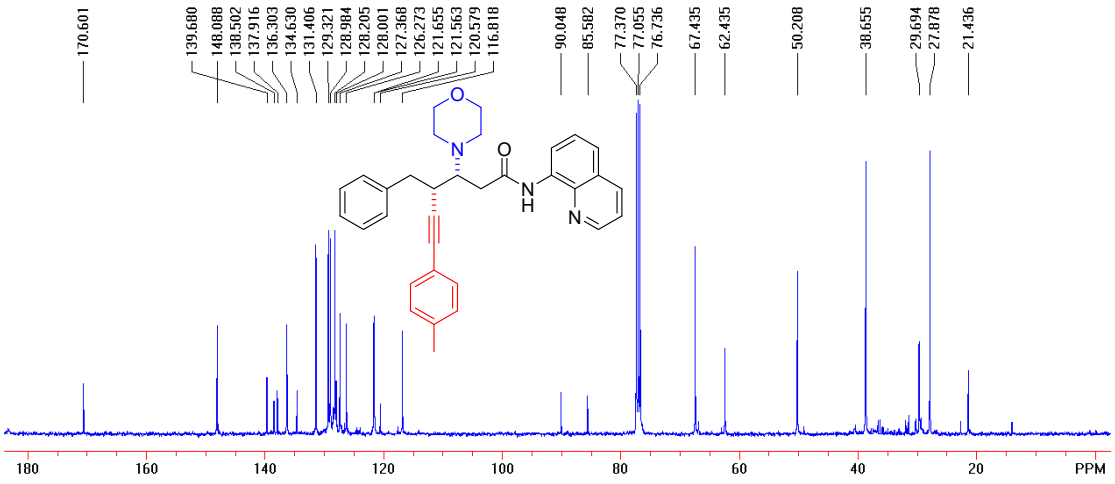


4-benzyl-6-(4-methoxyphenyl)-3-morpholino-*N*-(quinolin-8-yl)hex-5-ynamide (5e)

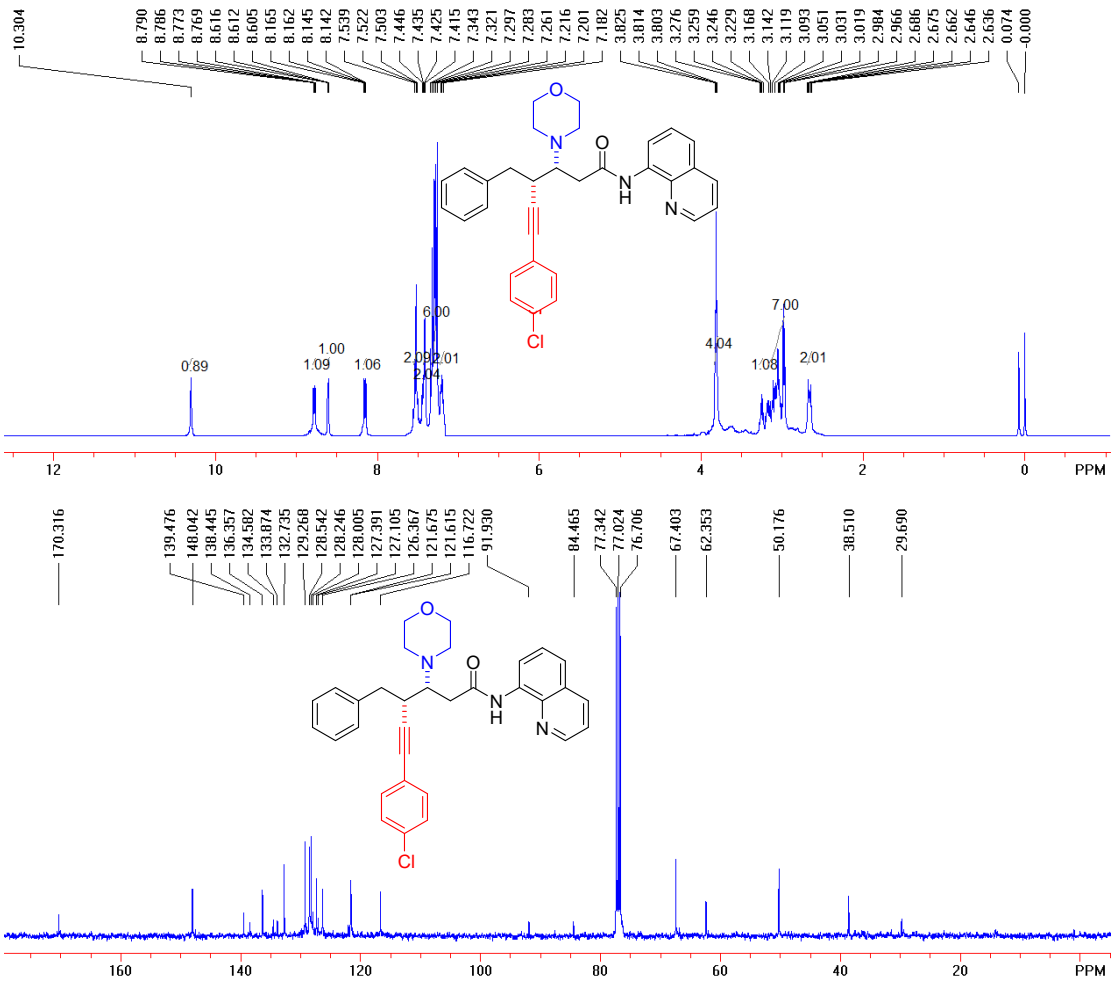


4-benzyl-3-morpholino-*N*-(quinolin-8-yl)-6-(*p*-tolyl)hex-5-ynamide (5f)

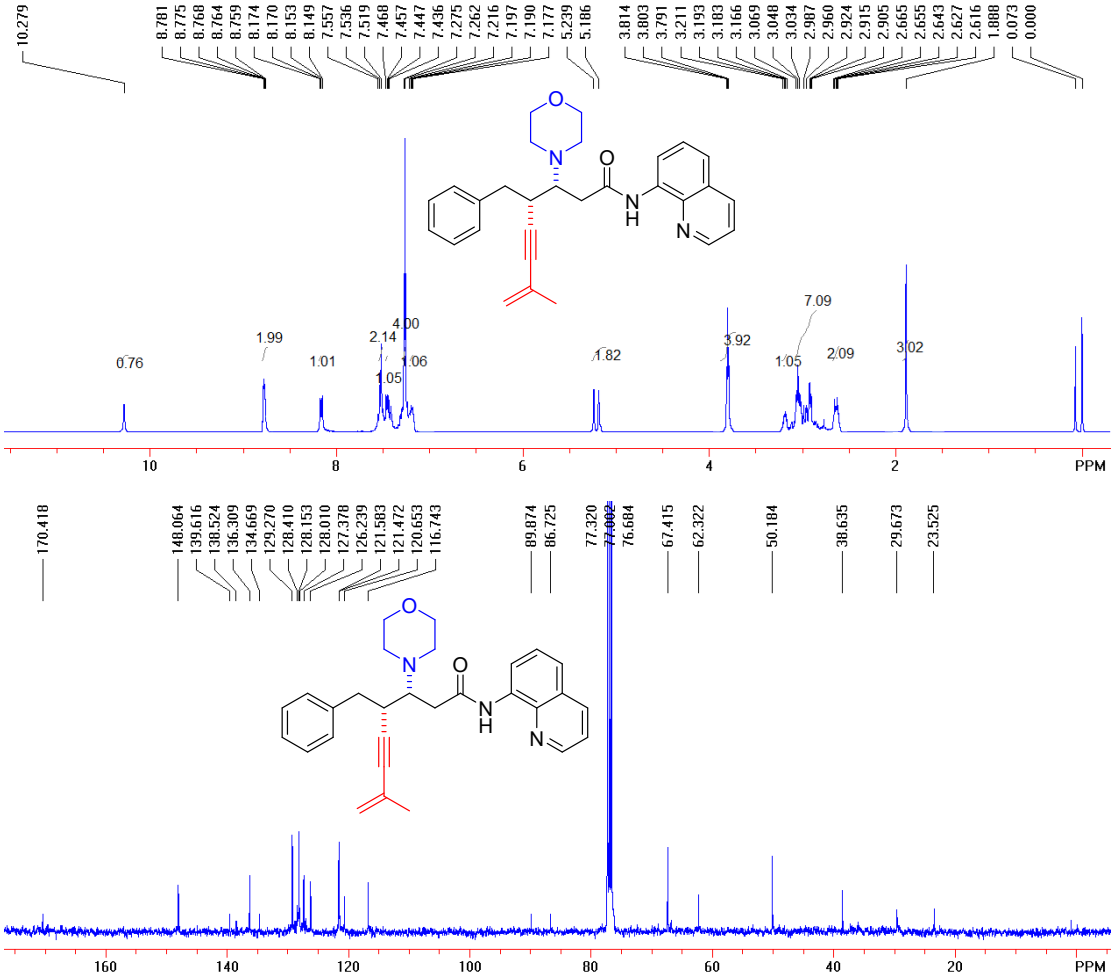




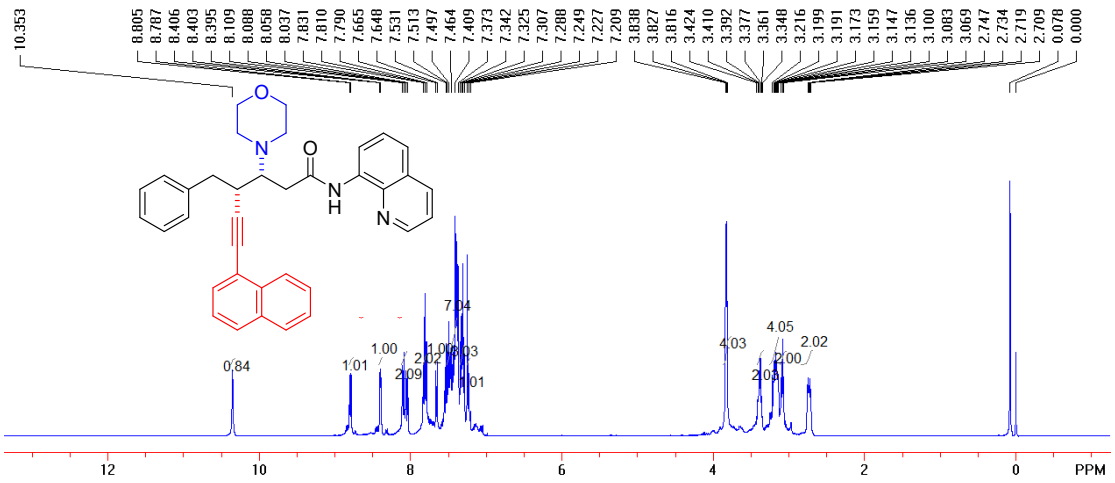
4-benzyl-6-(4-chlorophenyl)-3-morpholino-*N*-(quinolin-8-yl)hex-5-ynamide (5g)

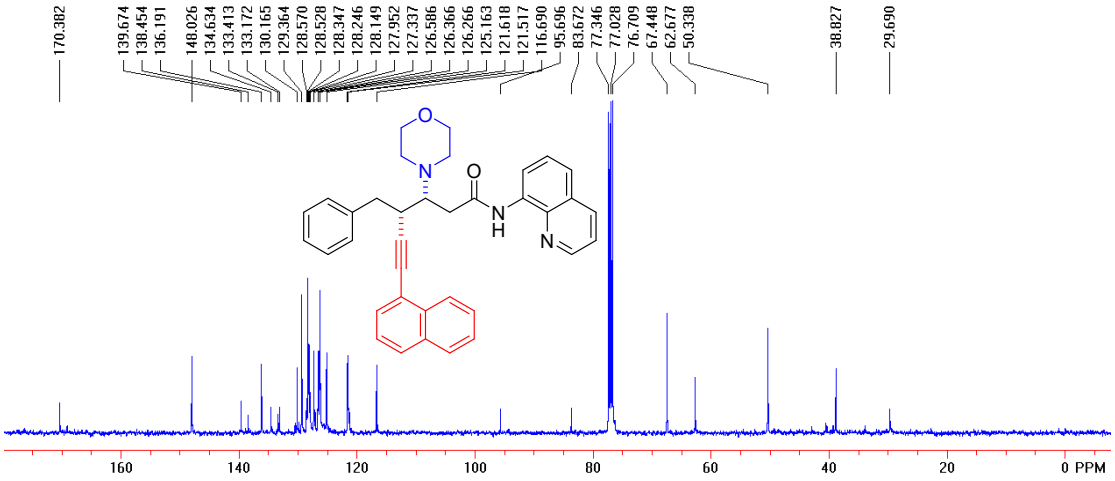


4-benzyl-7-methyl-3-morpholino-*N*-(quinolin-8-yl)oct-7-en-5-ynamide (5h)

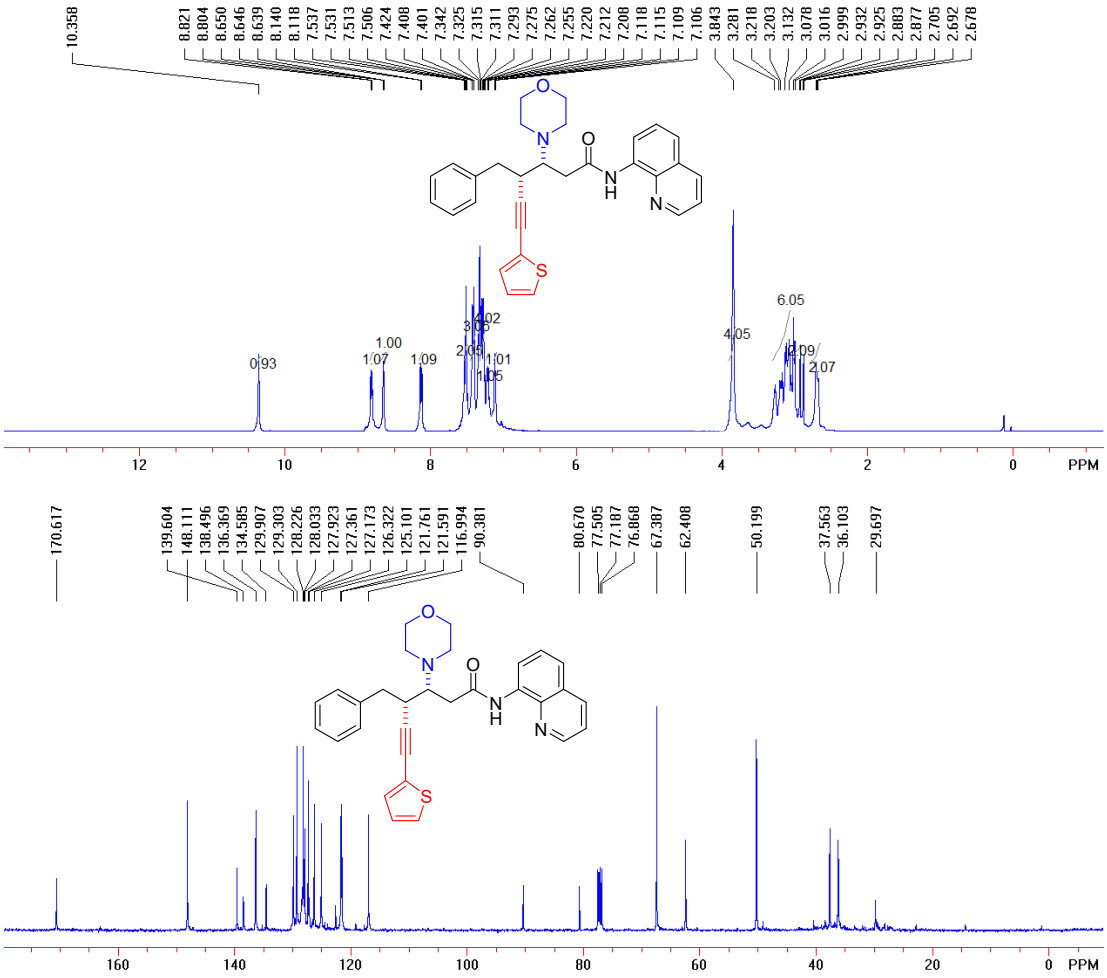


4-benzyl-3-morpholino-6-(naphthalen-1-yl)-*N*-(quinolin-8-yl)hex-5-ynamide (5i)

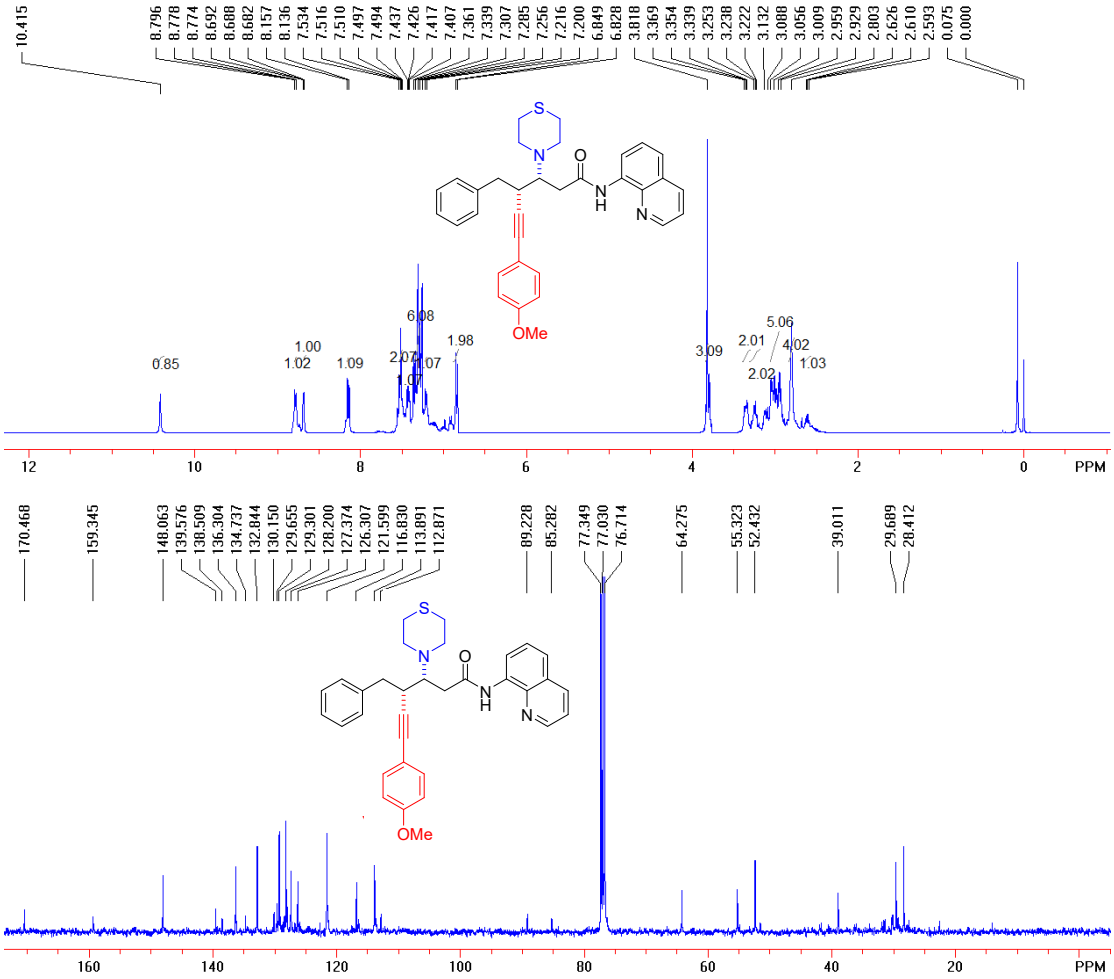




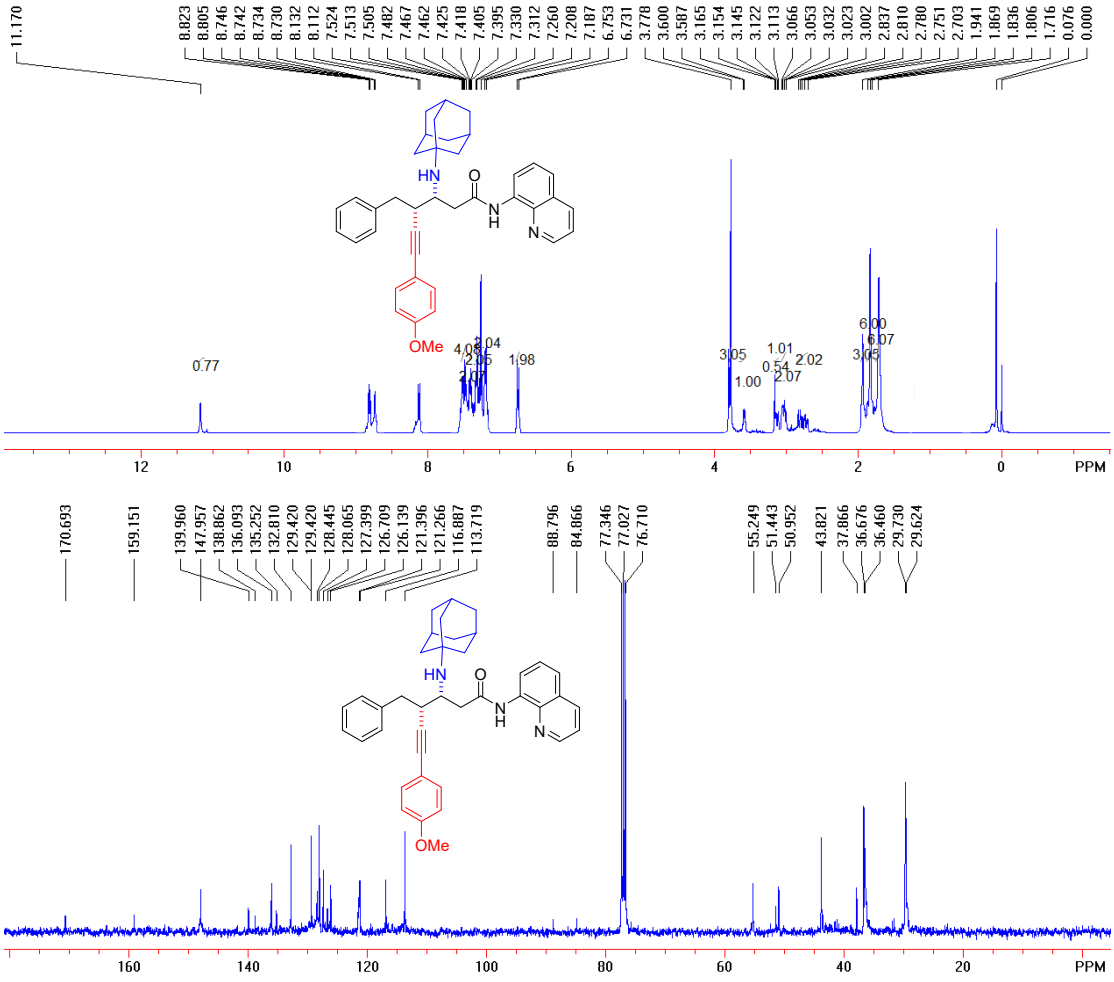
4-benzyl-3-morpholino-*N*-(quinolin-8-yl)-6-(thiophen-2-yl)hex-5-ynamide (5j)



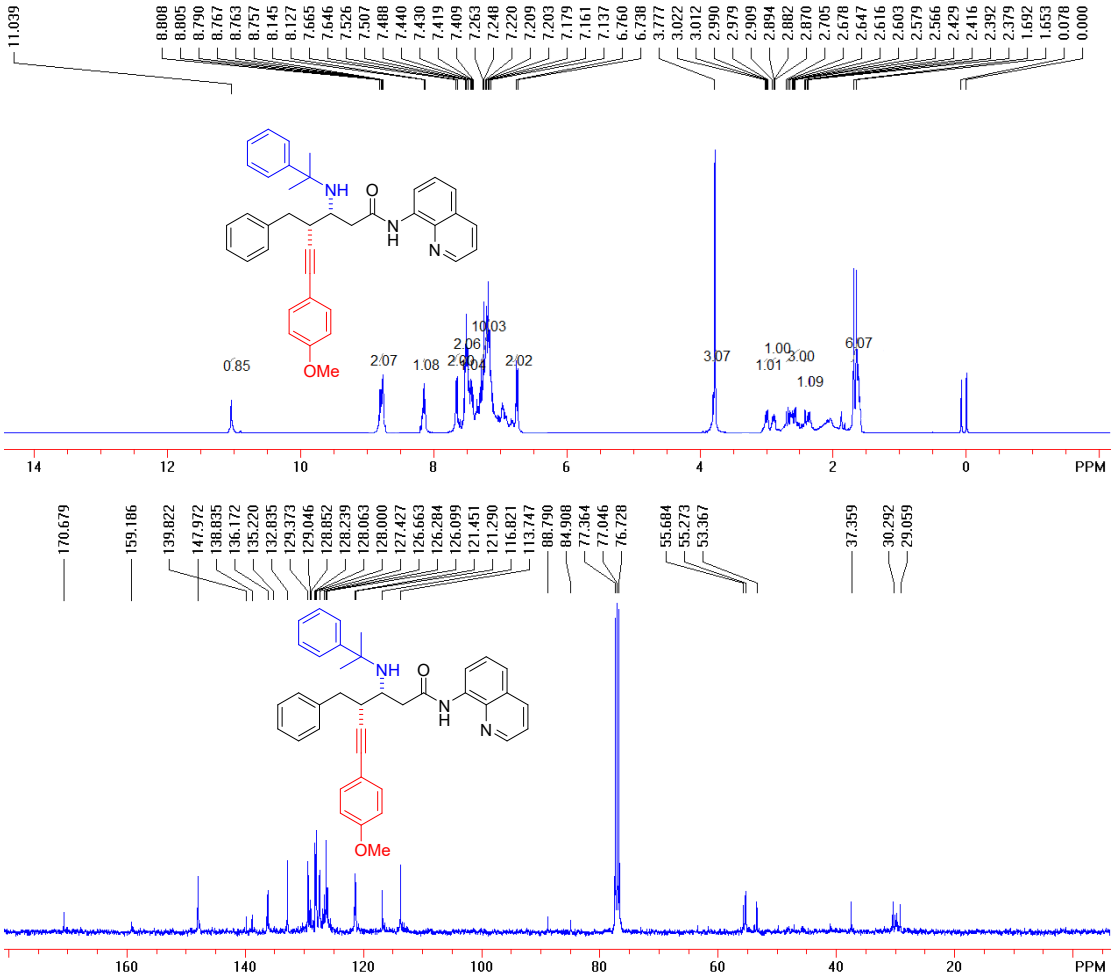
4-benzyl-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)-3-thiomorpholinohex-5-ynamide (5k)



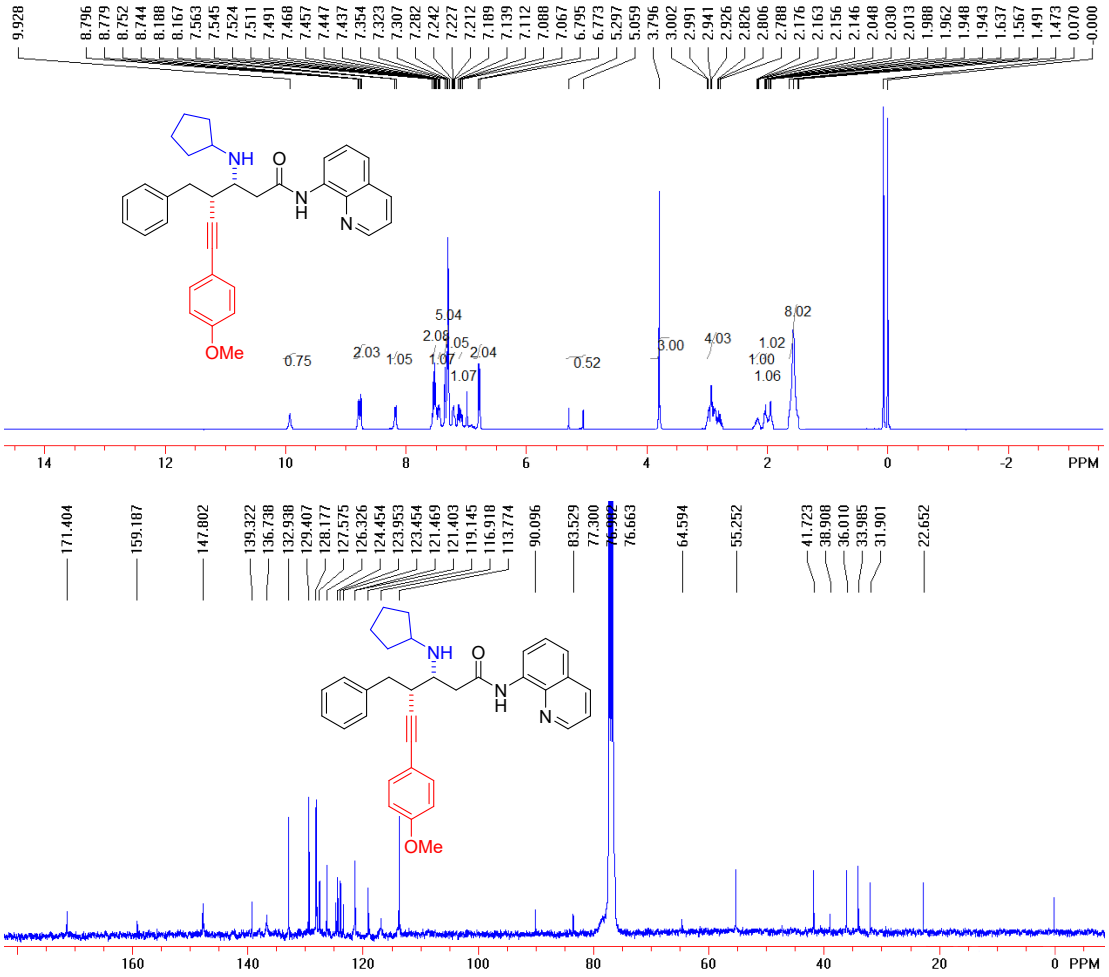
3--adamantan-1-yl)amino)-4-benzyl-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (5l)



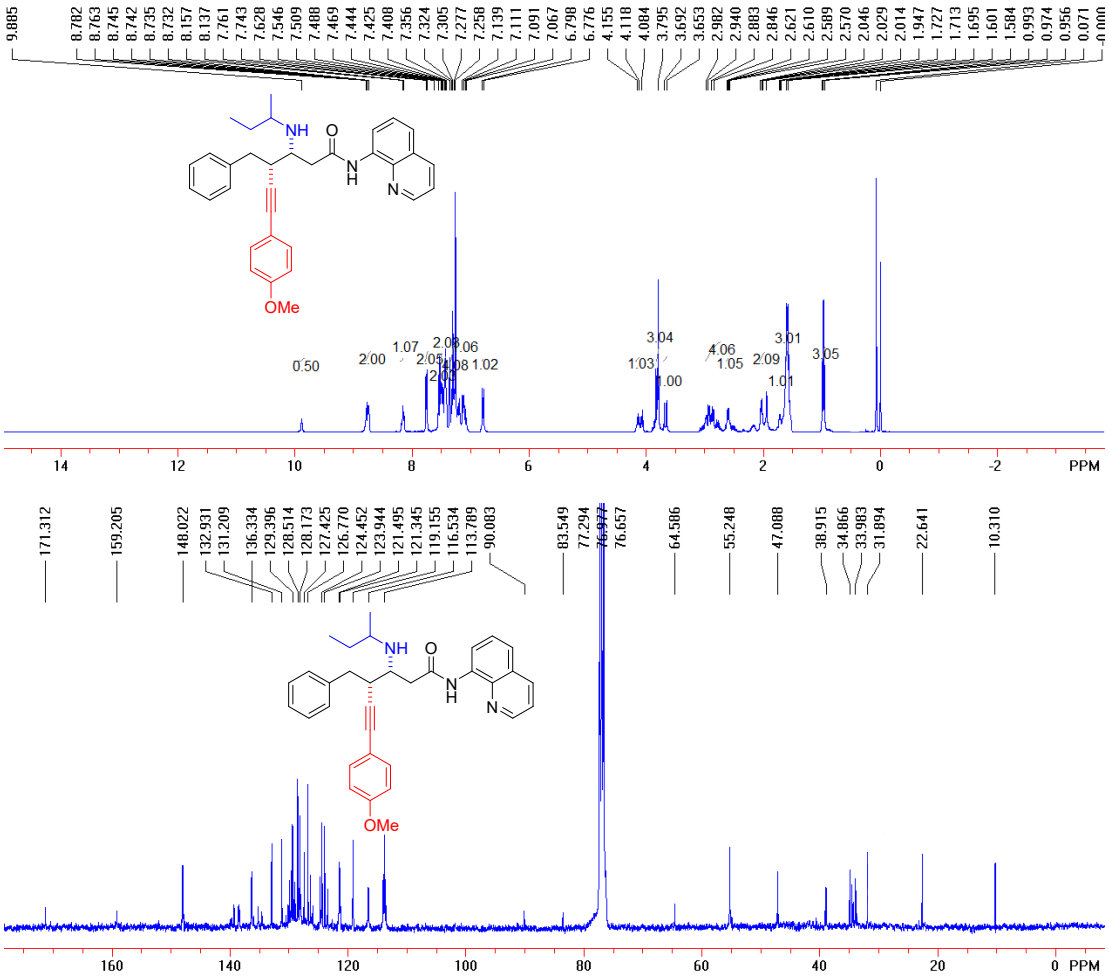
4-benzyl-6-(4-methoxyphenyl)-3-((2-phenylpropan-2-yl)amino)-*N*-(quinolin-8-yl)hex-5-ynamide (5m)



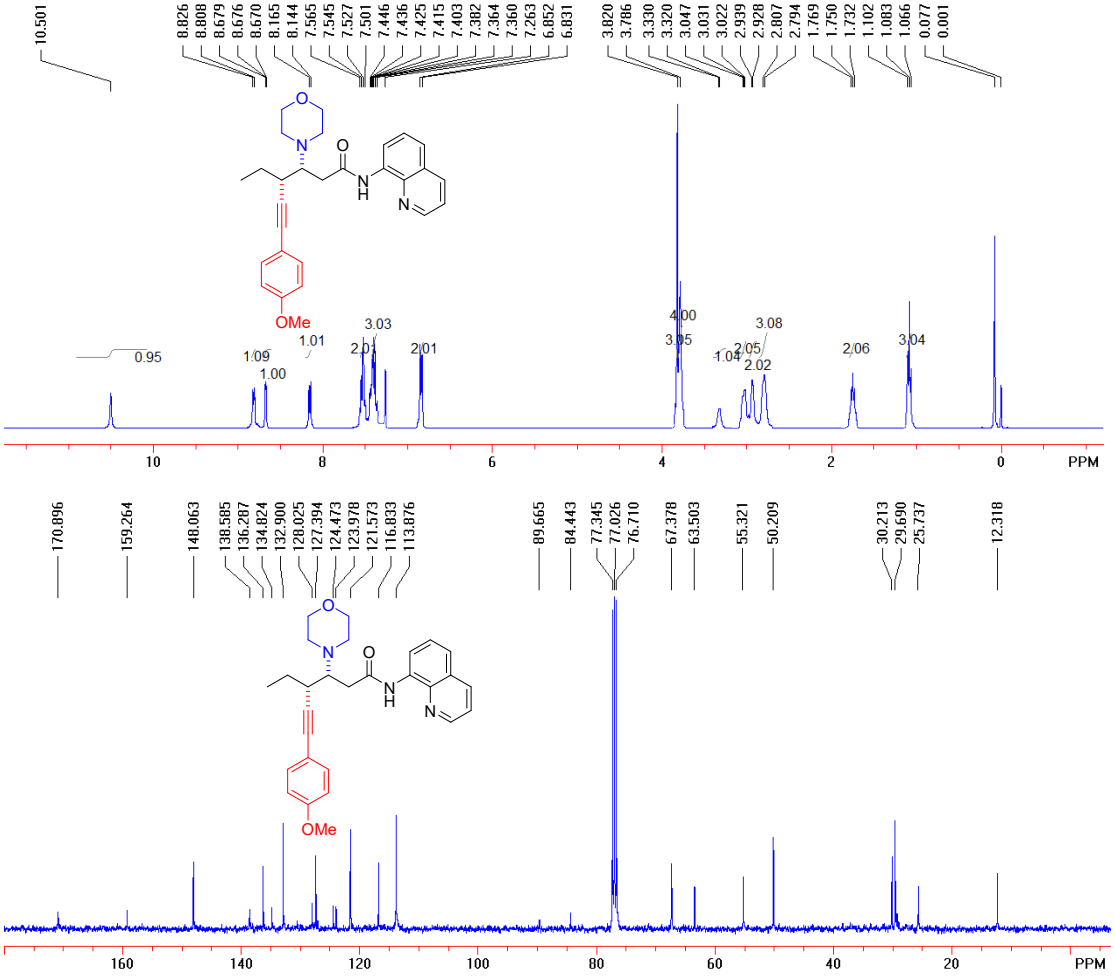
4-benzyl-3-(cyclopentylamino)-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (5n)



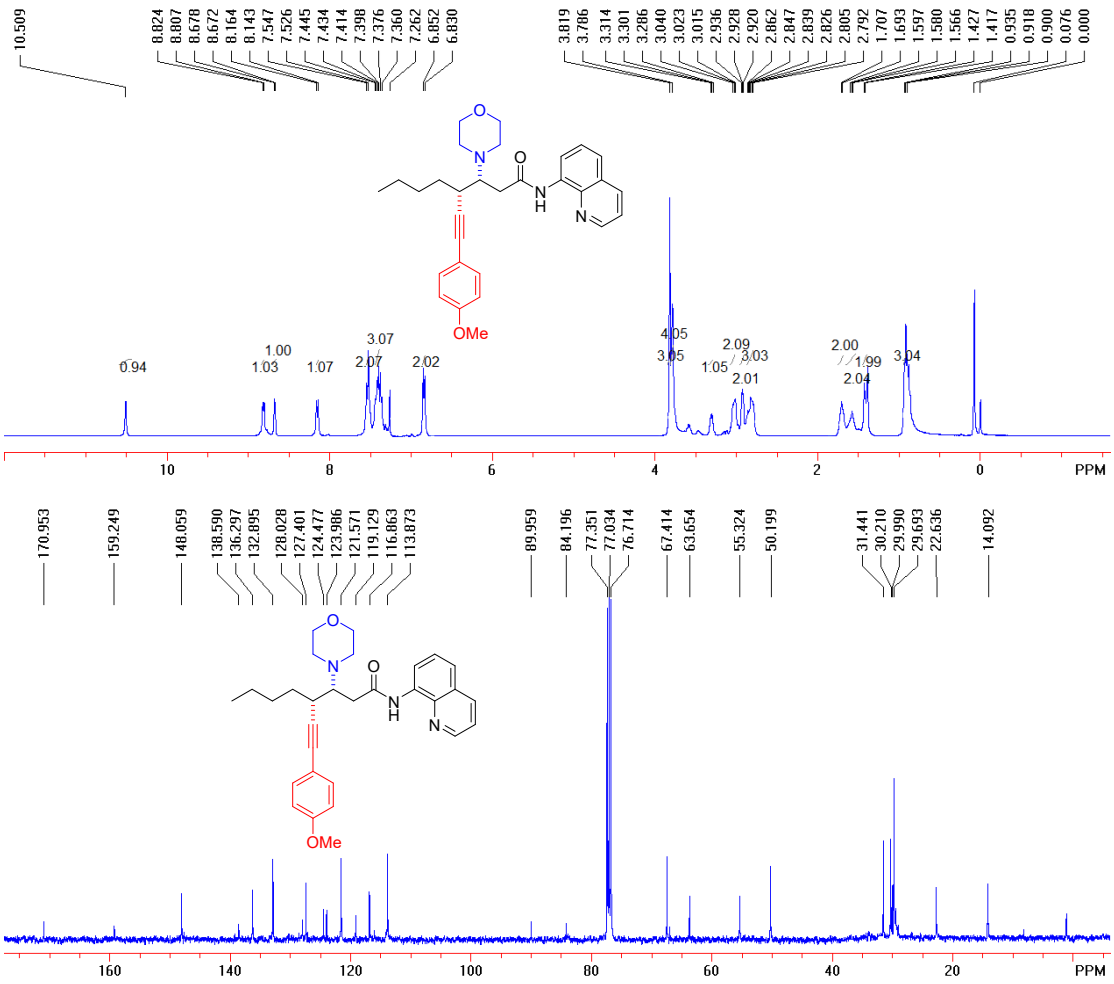
4-benzyl-3-(sec-butylamino)-6-(4-methoxyphenyl)-*N*-(quinolin-8-yl)hex-5-ynamide (5o)



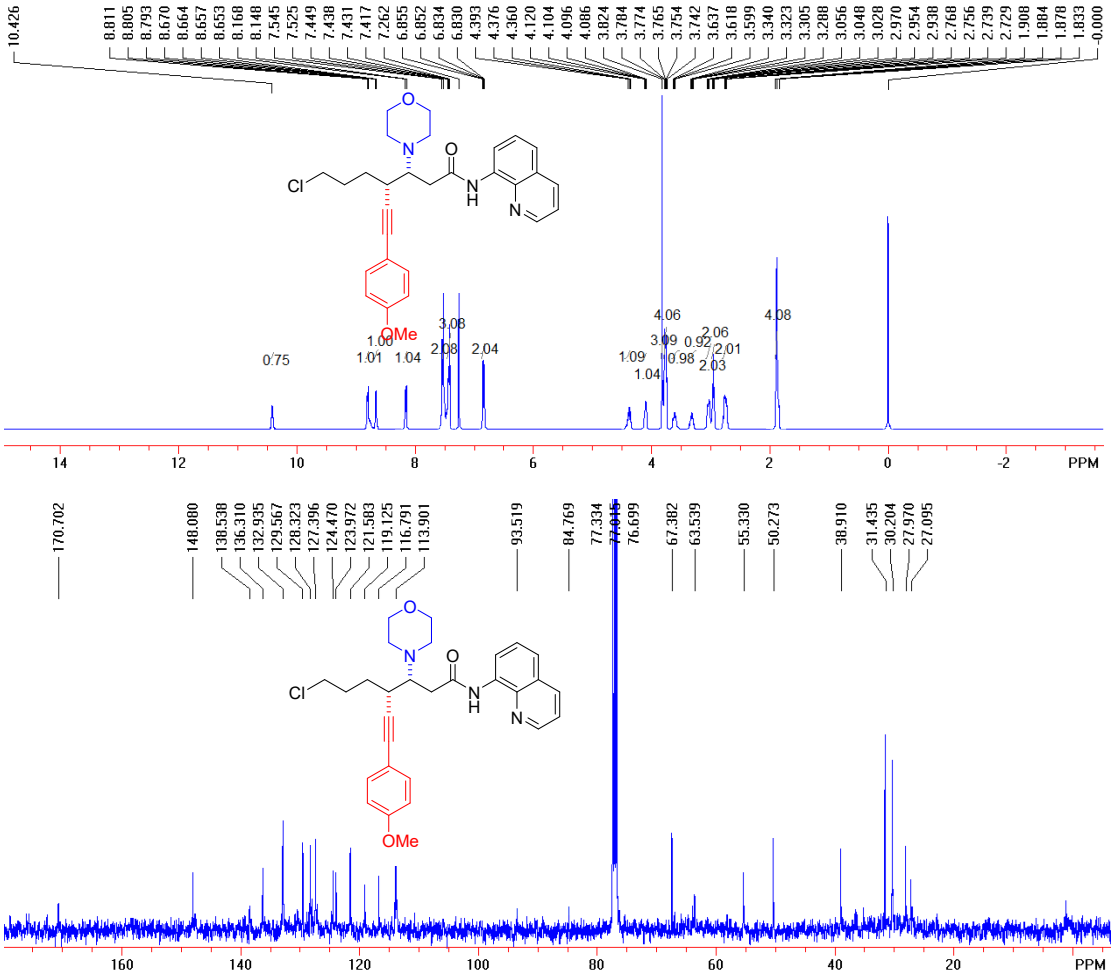
4-ethyl-6-(4-methoxyphenyl)-3-morpholino-*N*-(quinolin-8-yl)hex-5-ynamide (5p)



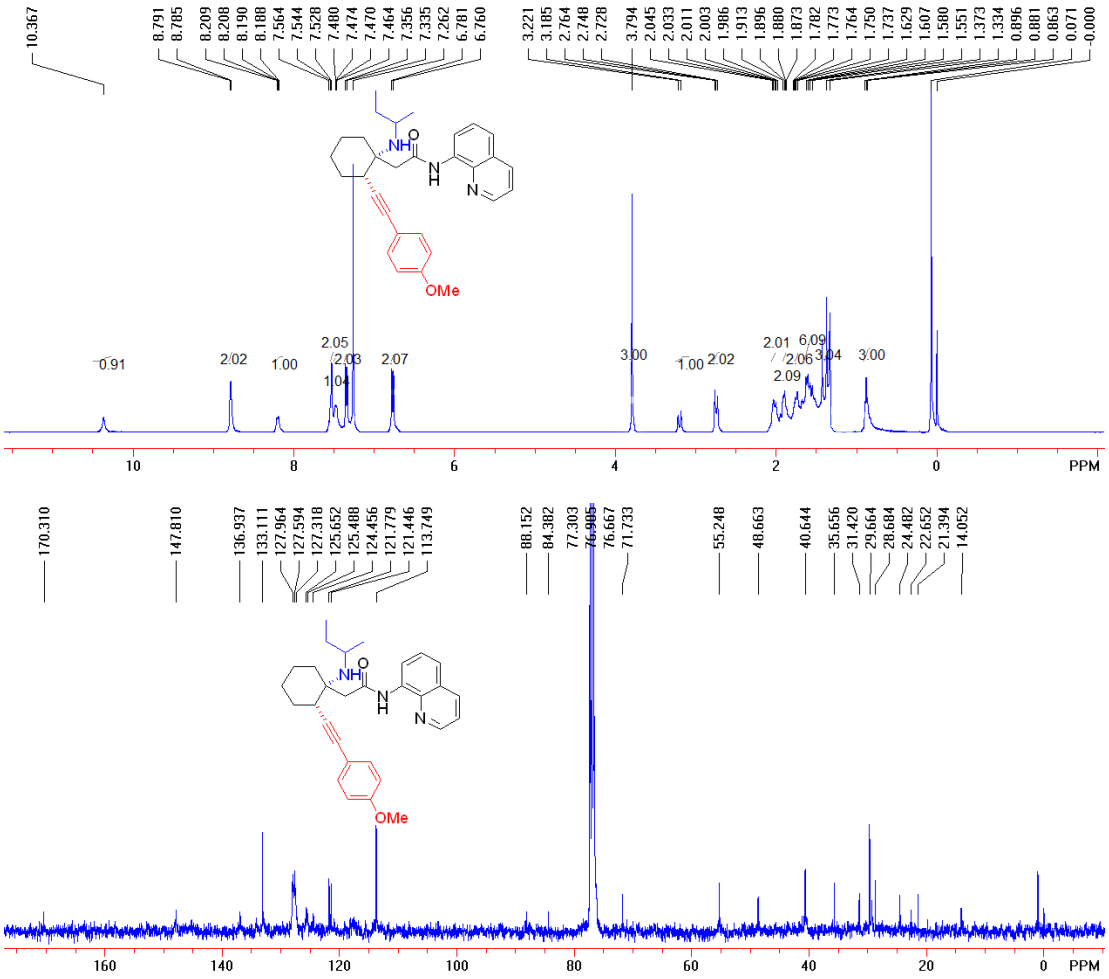
4-((4-methoxyphenyl)ethynyl)-3-morpholino-*N*-(quinolin-8-yl)octanamide (5q)

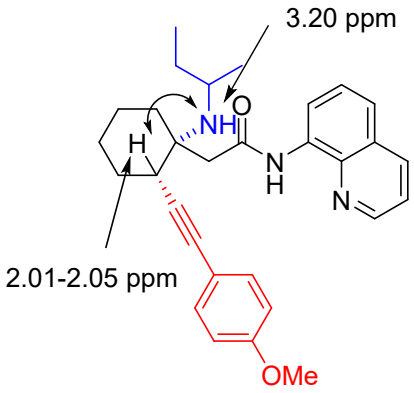


7-chloro-4-((4-methoxyphenyl)ethynyl)-3-morpholino-*N*-(quinolin-8-yl)heptanamide (5r)



2-((1R,2S)-1-(*sec*-butylamino)-2-((4-methoxyphenyl)ethynyl)cyclohexyl)-*N*-(quinolin-8-yl)acetamide (5s)

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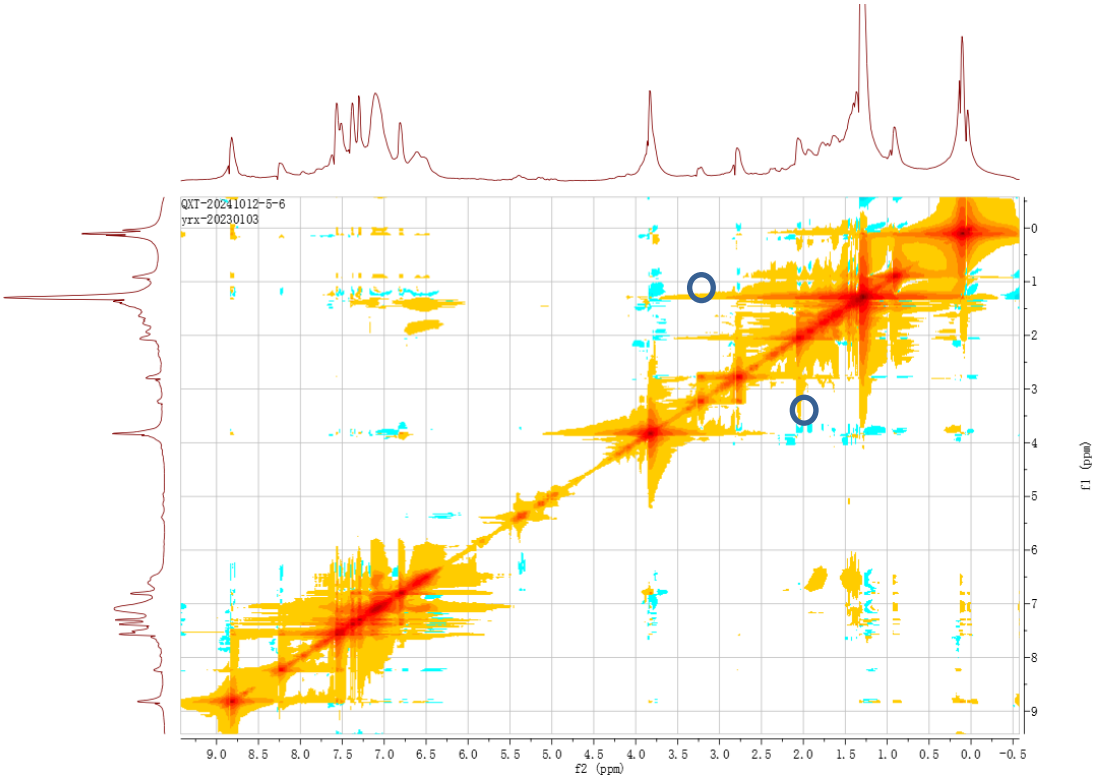
O
H
N
H
N
2.01-2.05 ppm
OMe

no signal


QXT-20241012-5-6
yrx-20230103
f2 (ppm)
f1 (ppm)