

Continuous flow synthesis of 1,4-disubstituted 1,2,3-triazoles *via* consecutive β -azidation of α,β -unsaturated carbonyl compounds and CuAAC reaction.

Giulia Brufani,^{a†} Federica Valentini,^{a†} Gabriele Rossini,^a Luigi Carpisassi,^a Daniela Lanari,^{*b} Luigi Vaccaro^{*a}

^aLaboratory of Green S.O.C. – Dipartimento di Chimica, Biologia e Biotecnologie, Università degli Studi di Perugia, Via Elce di Sotto 8, 06123 – Perugia – Italy;
E-mail: luigi.vaccaro@unipg.it; Web: <http://greensoc.chm.unipg.it/>

^bDipartimento di Scienze Farmaceutiche, Università degli Studi di Perugia, Via del Liceo 1, 06123 – Perugia – Italy;

[†] These authors contributed equally.

e-mail: luigi.vaccaro@unipg.it

daniela.lanari@unipg.it

Table of Contents:

1. General Remarks	ESI-2
2. General Procedures	ESI-3
3. Green metrics calculation	ESI-5
4. E-factor calculation (continuous flow protocol)	ESI-7
5. Characterization Data	ESI-10
6. NMR copies	ESI-30

1. General Remarks

Unless otherwise stated, all chemicals were purchased and used without any further purification. GLC analyses were performed by using Hewlett-Packard HP 5890 SERIES II equipped with a capillary column DB-5MS (30 m, 0.32 mm), a FID detector, and helium as gas carrier. GC-EIMS analyses were carried out by using a Hewlett-Packard HP 6890N Network GC system/5975 mass selective detector equipped with an electron impact ionizer at 70 eV. Melting points were measured on a Büchi 510 apparatus. NMR spectra were recorded on a Bruker DRX-ADVANCE 400 MHz (^1H at 400 MHz, ^{13}C at 100.6 MHz and ^{19}F at 376.4 MHz) in CDCl_3 . Chemical shifts are reported in ppm (δ), coupling constant (J) in hertz and multiplicity are reported as follows: *s* = singlet, *bs* = broad singlet, *d* = doublet, *dd* = double doublet, *td* = double triplet, *t* = triplet, *m* = multiplet. Elemental Analysis (EA) were conducted on Elementar UNICUBE® elemental analyzer. Metal contamination in the final products was measured using MP-AES 4210 instrument.

Pincer-type ligand 3,3-di(1H-imidazol-1-yl)propan-1-ol (**L**),¹ and **POLITAG-F** organocatalyst² were prepared as described in literature.

The aqueous acetonitrile azeotrope consists of 83.7 wt% of acetonitrile and 16.3 wt% of water.

Characterization data, ^1H , ^{13}C and ^{19}F NMR spectra are reported below.

2. General procedures

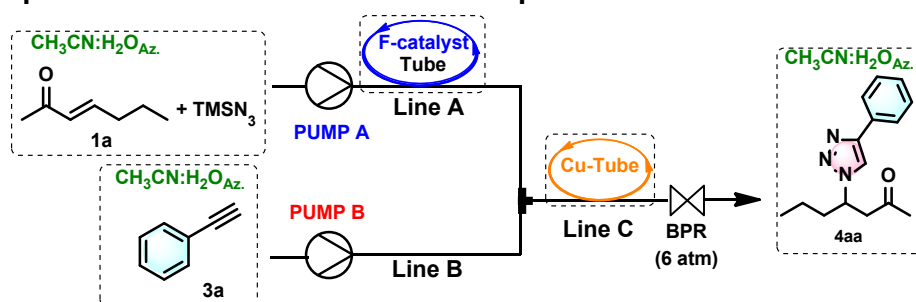
Loading calculation of POLITAG-F.²

Loading of fluoride anions supported on polymer were determined by elemental analysis calculated on the *bis*-imidazolium units (C: 54.31; H: 6.02; N: 3.54; loading F⁻: 1.26 mmol/g).

Continuous flow protocol for the synthesis of triazoles (4)

The mixture of **1** (5 mmol) and trimethylsilylazide (1.02 eq) in azeotrope CH₃CN:H₂O (1 mL, 5 M) was pumped through the PTFE reactor, packed with **POLITAG-F** (2.0 g) and quartz powder, thermostated at 60 °C (0.018 mL/min flow rate measured at the outlet of the first reactor). After a residence time of 3.8 h the resulting azide intermediate **2** formed was mixed, through a T joint, with a 1.2 M solution of terminal alkyne **3** (1.2 eq) in CH₃CN:H₂O azeotrope pumped at 0.1 mL/min. The obtained mixture was passed in a CTFR (10 m, 1/32" ID, 2 mL) heated at 100 °C with a BPR of 10 atm. The reactors were finally washed with 15 mL of aqueous azeotrope. The azeotrope was recovered by distillation affording in pure product **4**.

Table ESI-1. Optimization of the consecutive flow protocol.^a



entry	Conc A (M) ^b	Conc B (M) ^c	mL/min A	mL/min B	TMSN ₃ (eq)	3a (eq)	4aa (%) ^d
1	5	1.0	0.05	0.10	1.05	1.0	-
2	5	1.0	0.10	0.25	1.05	1.0	-
3	5	1.0	0.25	0.25	1.05	1.0	-
4	5	1.0	0.10	0.10	1.05	1.0	<5
5	5	0.1	0.10	0.10	1.05	2.0	<5
6	5	1.2	0.10	0.10	1.05	2.0	<5
7 ^e	5	1.2	0.10	0.10	1.02	1.2	25
8 ^f	5	1.2	0.10	0.10	1.02	1.2	30
9 ^g	5	1.2	0.10	0.10	1.02	1.2	27
10 ^{h,i}	5	1.2	0.10	0.10	1.02	1.2	56
11 ^{h,j}	5	1.2	0.10	0.10	1.02	1.2	70
12 ⁱ	5	1.2	0.10	0.10	1.02	1.2	>99
13 ^{e,i}	5	1.2	0.10	0.10	1.02	1.2	75
14 ^{f,i}	5	1.2	0.10	0.10	1.02	1.2	84
15 ^{g,i}	5	1.2	0.10	0.10	1.02	1.2	82

^aReaction conditions: **1a** (5 mmol), 1st reactor (POLITAG-F, 0.2 g) thermostated at 60 °C; Cu-tube thermostated at 100 °C. BPR (6 atm). ^bReferred to **1a**. ^cReferred to **3a**. ^dDetermined by GC analysis. ^ePS-DABCOF₂ catalyst³ (0.346 g; loading: 7.4 mmol_F/g). ^fIRA900-F catalyst⁴ (0.983 g; loading: 2.6 mmol_F/g). ^gPOLITAG-M-F catalyst² (0.947 g; loading: 2.7 mmol_F/g). ^hCu-tube (5 m). ⁱBPR (10 atm). ^jBPR (17 atm).

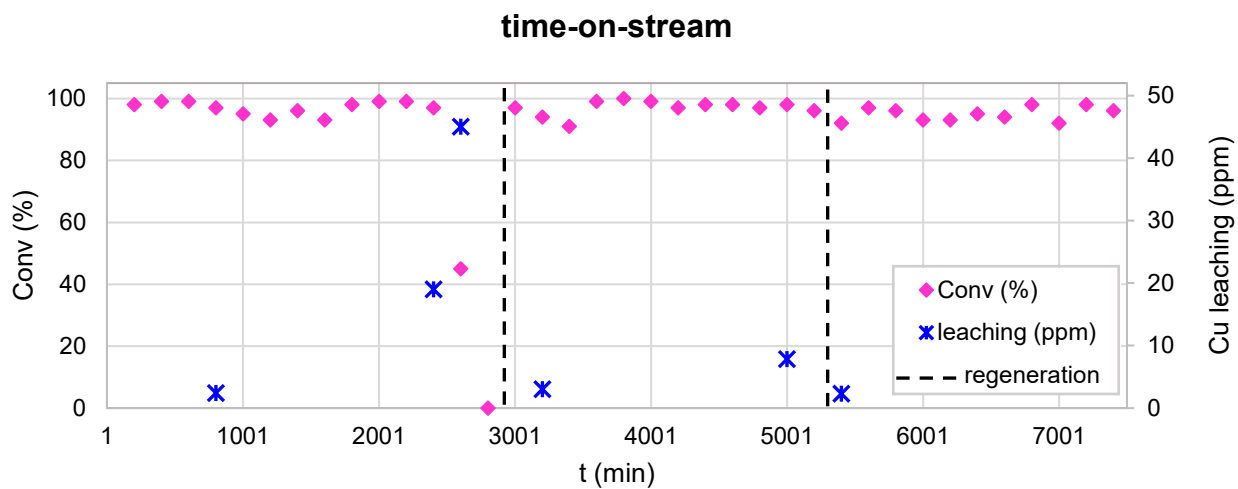


Figure ESI-1. Time on stream of the consecutive flow protocol for the synthesis of 1,4-disubstituted 1,2,3-triazoles.

3. Green Metrics Calculation⁵

Batch	Flow
Reactants: 1a = 112.17 mg (1 mmol) TMSN ₃ = 120.97 (1.05 eq) H ₂ O = 18.01 mg (1 eq) 3a = 102.13 mg (1 eq)	Reactants: 1a = 560.85 mg (5 mmol) TMSN ₃ = 587.57 mg (1.02 eq) H ₂ O = 90.05 mg (1 eq) 3a = 612.78 mg (1.2 eq)
Solvent: CH ₃ CN/H ₂ O _{Az.} = 1 mL	Solvent: CH ₃ CN/H ₂ O _{Az.} = 6 mL
Work-up: CH ₃ CN/H ₂ O _{Az.} = 2 mL	Work-up: CH ₃ CN/H ₂ O _{Az.} = 15 mL
Purification: CH ₃ CN/H ₂ O _{Az.} = 0.5mL	Purification: Not performed
Recovered materials: CH ₃ CN/H ₂ O _{Az.} [solvent+work-up] = 2.67 mL (89 %)	Recovered materials: CH ₃ CN/H ₂ O _{Az.} [solvent+work-up] = 19.74 mL (94 %)
Product: 4aa = 241.9 mg (94 % yield)	Product: 4aa = 1.248 g (97 % yield)
E-factor = 3.25	E-factor = 1.27
AE = 0.741	AE = 0.741
Rxn Yield = 0.940	Rxn Yield = 0.970
1/SF = 0.984	1/SF = 0.939
MRP = 0.343	MRP = 0.654
RME = 0.235	RME = 0.441
VMR = 0.717327917	VMR = 0.773582143

Atom Economy (AE)

$$AE = \frac{MW_{product}}{\sum_j v_j MW_{reactant}}$$

Stoichiometric Factor (SF)

$$SF = 1 + \frac{m_{excess\ reagents}}{m_{stoichiometric\ reagents}}$$

Reaction Mass Efficiency (RME)

$$RME = \frac{1}{1 + E\ factor}$$

Mass Recovery Parameter (MRP)

$$MRP = \frac{RME \cdot SF}{AE \cdot \left(\frac{yield}{100}\right)}$$

References

1. V. Kozell, F. Rahmani, O. Piermatti, D. Lanari, L. Vaccaro, *Mol. Catal.* **2018**, *455*, 188–191
2. F. Ferlin, F. Valentini, G. Brufani, D. Lanari, L. Vaccaro *ACS Sustainable Chem. Eng.* **2021**, *9*, 5740–5749
3. T. Angelini, D. Lanari, R. Maggi, F. Pizzo, G. Sartori, L. Vaccaro, *Adv. Synth. Catal.*, **2012**, *354*, 908-916
4. L. Castrica, F. Fringuelli, L. Gregoli, F. Pizzo, L. Vaccaro, *J. Org. Chem.* **2006**, *71*, 9536–9539
5. J. Andraos, A. Hent, *J. Chem. Educ.* **2015**, *92*, 1820–1830

4. E-factor calculation (continuous flow protocol)

β -Azidation of **1a** and consecutive CuAAC with **3a**:

$$\text{E-factor} = [560.85 \text{ mg (1a)} + 90.05 \text{ mg (H}_2\text{O)} + 587.57 \text{ mg (TMSN}_3\text{)} + 612.78 \text{ mg (3a)} + 980.00 \text{ mg (CH}_3\text{CN/H}_2\text{O}_{\text{Az. not recovered)}}] - 1248.00 \text{ mg (4aa)} / 1248.00 \text{ mg (4aa)} = 1.3$$

β -Azidation of **1b** and consecutive CuAAC with **3a**:

$$\text{E-factor} = [701.10 \text{ mg (1b)} + 90.05 \text{ mg (H}_2\text{O)} + 587.57 \text{ mg (TMSN}_3\text{)} + 612.78 \text{ mg (3a)} + 980.00 \text{ mg (CH}_3\text{CN/H}_2\text{O}_{\text{Az. not recovered)}}] - 1384.12 \text{ mg (4ba)} / 1384.12 \text{ mg (4ba)} = 1.2$$

β -Azidation of **1a** and consecutive CuAAC with **3b**:

$$\text{E-factor} = [560.85 \text{ mg (1a)} + 90.05 \text{ mg (H}_2\text{O)} + 587.57 \text{ mg (TMSN}_3\text{)} + 792.96 \text{ mg (3b)} + 980.00 \text{ mg (CH}_3\text{CN/H}_2\text{O}_{\text{Az. not recovered)}}] - 1408.06 \text{ mg (4ab)} / 1408.06 \text{ mg (4ab)} = 1.1$$

β -Azidation of **1b** and consecutive CuAAC with **3b**:

$$\text{E-factor} = [701.10 \text{ mg (1b)} + 90.05 \text{ mg (H}_2\text{O)} + 587.57 \text{ mg (TMSN}_3\text{)} + 792.96 \text{ mg (3b)} + 980.00 \text{ mg (CH}_3\text{CN/H}_2\text{O}_{\text{Az. not recovered)}}] - 1545.55 \text{ mg (4bb)} / 1545.55 \text{ mg (4bb)} = 1.0$$

β -Azidation of **1a** and consecutive CuAAC with **3c**:

$$\text{E-factor} = [560.85 \text{ mg (1a)} + 90.05 \text{ mg (H}_2\text{O)} + 587.57 \text{ mg (TMSN}_3\text{)} + 1086.18 \text{ mg (3c)} + 980.00 \text{ mg (CH}_3\text{CN/H}_2\text{O}_{\text{Az. not recovered)}}] - 1646.82 \text{ mg (4ac)} / 1646.82 \text{ mg (4ac)} = 1.0$$

β -Azidation of **1b** and consecutive CuAAC with **3c**:

$$\text{E-factor} = [701.10 \text{ mg (1b)} + 90.05 \text{ mg (H}_2\text{O)} + 587.57 \text{ mg (TMSN}_3\text{)} + 1086.18 \text{ mg (3c)} + 980.00 \text{ mg (CH}_3\text{CN/H}_2\text{O}_{\text{Az. not recovered)}}] - 1784.49 \text{ mg (4bc)} / 1784.49 \text{ mg (4bc)} = 0.9$$

β -Azidation of **1a** and consecutive CuAAC with **3d**:

$$\text{E-factor} = [560.85 \text{ mg (1a)} + 90.05 \text{ mg (H}_2\text{O)} + 587.57 \text{ mg (TMSN}_3\text{)} + 1020.78 \text{ mg (3d)} + 980.00 \text{ mg (CH}_3\text{CN/H}_2\text{O}_{\text{Az. not recovered)}}] - 1495.67 \text{ mg (4ad)} / 1495.67 \text{ mg (4ad)} = 1.2$$

β -Azidation of **1b** and consecutive CuAAC with **3d**:

$$\text{E-factor} = [701.10 \text{ mg (1b)} + 90.05 \text{ mg (H}_2\text{O)} + 587.57 \text{ mg (TMSN}_3\text{)} + 1020.78 \text{ mg (3d)} + 980.00 \text{ mg (CH}_3\text{CN/H}_2\text{O}_{\text{Az. not recovered)}}] - 1730.6 \text{ mg (4bd)} / 1730.6 \text{ mg (4bd)} = 1.0$$

β -Azidation of **1a** and consecutive CuAAC with **3e**:

$$\text{E-factor} = [560.85 \text{ mg (1a)} + 90.05 \text{ mg (H}_2\text{O)} + 587.57 \text{ mg (TMSN}_3\text{)} + 696.96 \text{ mg (3e)} + 980.00 \text{ mg (CH}_3\text{CN/H}_2\text{O}_{\text{Az. not recovered)}}] - 1248.59 \text{ mg (4ae)} / 1248.59 \text{ mg (4ae)} = 1.3$$

β -Azidation of **1b** and consecutive CuAAC with **3e**:

E-factor = [701.10 mg (**1b**) + 90.05 mg (H₂O) + 587.57 mg (TMSN₃) + 696.96 mg (**3e**) + 980.00 mg (CH₃CN/H₂O_{Az.} not recovered) – 1481.85 mg (**4be**)] / 1481.85 mg (**4be**) = 1.1

β-Azidation of **1a** and consecutive CuAAC with **3f**:

E-factor = [560.85 mg (**1a**) + 90.05 mg (H₂O) + 587.57 mg (TMSN₃) + 1482.78 mg (**3a**) + 980.00 mg (CH₃CN/H₂O_{Az.} not recovered) – 1908.55 mg (**4af**)] / 1908.55 mg (**4af**) = 0.9

β-Azidation of **1b** and consecutive CuAAC with **3f**:

E-factor = [701.10 mg (**1b**) + 90.05 mg (H₂O) + 587.57 mg (TMSN₃) + 1482.78 mg (**3a**) + 980.00 mg (CH₃CN/H₂O_{Az.} not recovered) – 2021.88 mg (**4bf**)] / 2021.88 mg (**4bf**) = 0.9

β-Azidation of **1a** and consecutive CuAAC with **3g**:

E-factor = [560.85 mg (**1a**) + 90.05 mg (H₂O) + 587.57 mg (TMSN₃) + 648.96 mg (**3g**) + 980.00 mg (CH₃CN/H₂O_{Az.} not recovered) – 1211.69 mg (**4ag**)] / 1211.69 mg (**4ag**) = 1.4

β-Azidation of **1b** and consecutive CuAAC with **3g**:

E-factor = [701.10 mg (**1b**) + 90.05 mg (H₂O) + 587.57 mg (TMSN₃) + 648.96 mg (**3g**) + 980.00 mg (CH₃CN/H₂O_{Az.} not recovered) – 1413.91 mg (**4bg**)] / 1413.91 mg (**4bg**) = 1.1

β-Azidation of **1a** and consecutive CuAAC with **3h**:

E-factor = [560.85 mg (**1a**) + 90.05 mg (H₂O) + 587.57 mg (TMSN₃) + 492.84 mg (**3h**) + 980.00 mg (CH₃CN/H₂O_{Az.} not recovered) – 1101.49 mg (**4ah**)] / 1101.49 mg (**4ah**) = 1.5

β-Azidation of **1b** and consecutive CuAAC with **3h**:

E-factor = [701.10 mg (**1b**) + 90.05 mg (H₂O) + 587.57 mg (TMSN₃) + 492.84 mg (**3h**) + 980.00 mg (CH₃CN/H₂O_{Az.} not recovered) – 1235.13 mg (**4bh**)] / 1235.13 mg (**4bh**) = 1.3

β-Azidation of **1a** and consecutive CuAAC with **3i**:

E-factor = [560.85 mg (**1a**) + 90.05 mg (H₂O) + 587.57 mg (TMSN₃) + 661.20 mg (**3i**) + 980.00 mg (CH₃CN/H₂O_{Az.} not recovered) – 1166.45 mg (**4ai**)] / 1166.45 mg (**4ai**) = 1.5

β-Azidation of **1b** and consecutive CuAAC with **3i**:

E-factor = [701.10 mg (**1b**) + 90.05 mg (H₂O) + 587.57 mg (TMSN₃) + 661.20 mg (**3i**) + 980.00 mg (CH₃CN/H₂O_{Az.} not recovered) – 1290.39 mg (**4ai**)] / 1290.39 mg (**4ai**) = 1.3

β-Azidation of **1a** and consecutive CuAAC with **3j**:

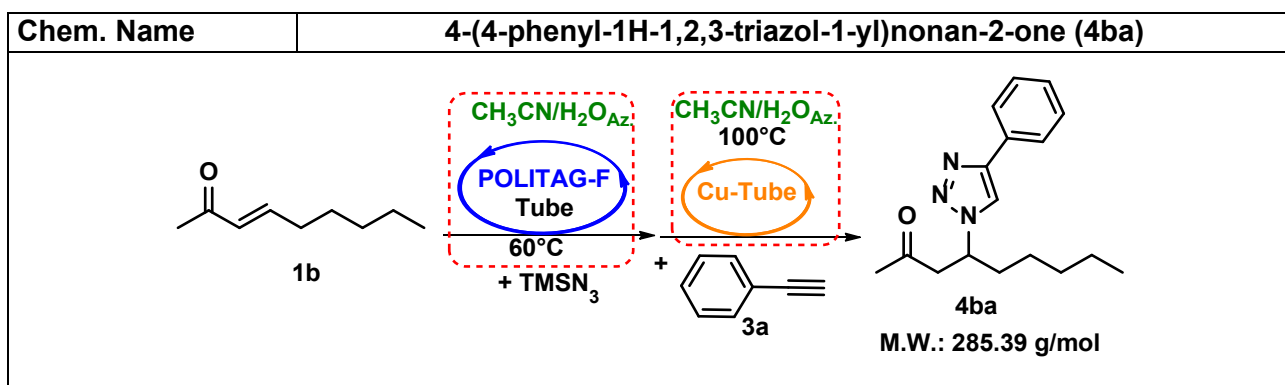
E-factor = [560.85 mg (**1a**) + 90.05 mg (H₂O) + 587.57 mg (TMSN₃) + 649.08 mg (**3j**) + 980.00 mg (CH₃CN/H₂O_{Az.} not recovered) – 1092.83 mg (**4aj**)] / 1092.83 mg (**4aj**) = 1.6

β -Azidation of **1b** and consecutive CuAAC with **3j**:

E-factor = [701.10 mg (**1b**) + 90.05 mg (H₂O) + 587.57 mg (TMSN₃) + 649.08 mg (**3j**) + 980.00 mg (CH₃CN/H₂O_{Az.} not recovered) – 1354.97 mg (**4bj**)] / 1354.97 mg (**4bj**) = 1.2

5. Characterization data

Chem. Name	4-(4-phenyl-1H-1,2,3-triazol-1-yl)heptan-2-one (4aa)				
<p style="text-align: center;">M.W.: 257.34 g/mol</p>					
METHOD:					
<p>The mixture of 1a (5 mmol) and trimethylsilylazide (0.67 mL, 1.02 eq) in azeotrope CH₃CN:H₂O (1 mL, 5 M) was pumped through the PTFE reactor, thermostated at 60 °C, packed with POLITAG-F (2.0 g) and quartz powder (0.018 mL/min flow rate measured at the outlet of the first reactor). After a residence time of 3.8 h the resulting azide intermediate formed was mixed, through a T joint, with a 1.2 M solution of phenylacetylene 3a (1.2 eq) in CH₃CN:H₂O azeotrope continuously pumped at 0.1 mL/min. This mixture was passed in a CTRF heated at 100 °C with a BPR of 10 atm. The azeotrope was recovered by distillation affording in 4aa pure product as white solid (1.248 g, 97 % yield, >98% NMR purity).</p>					
Mol Formula		C ₁₅ H ₁₉ N ₃ O		m. p.	68-71 °C
¹H NMR (400 MHz, DMSO-<i>d</i>₆)	δ Value	No. H	Mult.	j Value/Hz	
	8.65	1	<i>s</i>		
	7.83	2	<i>d</i>	7.6	
	7.44	2	<i>t</i>	7.6	
	7.32	1	<i>t</i>	7.5	
	4.97-4.95	2	<i>m</i>		
	3.32-3.35	1	<i>m</i>		
	3.13	1	<i>dd</i>	17.8-5.4	
	2.09	3	<i>s</i>		
	1.85-1.74	1	<i>m</i>		
	1-17-1.13	1	<i>m</i>		
	1.10-1.05	1	<i>m</i>		
0.83	3	<i>t</i>	7.4		
¹³C NMR (100.6 MHz, DMSO-<i>d</i>₆) δ : 205.4, 145.9, 130.8, 128.9, 127.8, 125.0, 120.7, 56.3, 47.4, 36.9, 29.9, 18.4, 13.3					
GC-EIMS (m/z, %): 257 (M ⁺ , 40); 186 (27); 145 (70); 118 (23); 117 (100); 116 (80); 113 (24); 91 (21); 90 (21); 89 (32).					



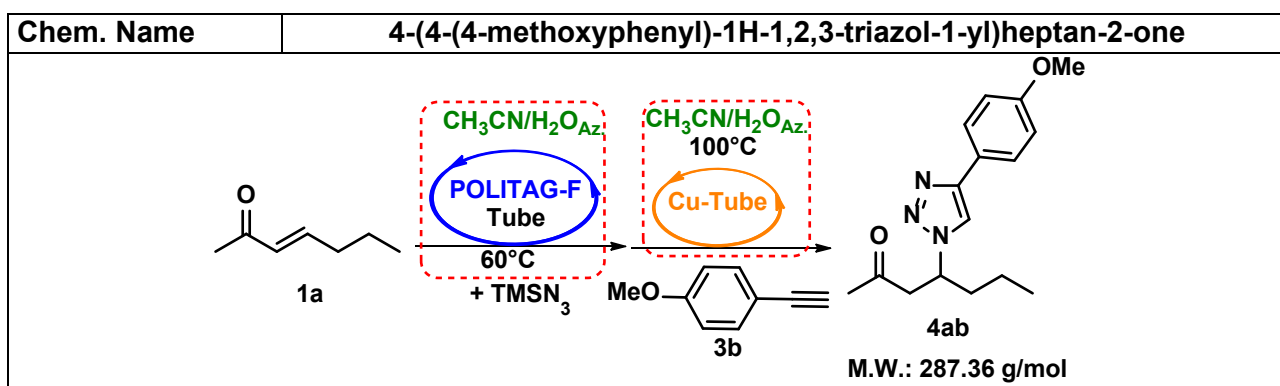
METHOD:

The mixture of **1b** (5 mmol) and trimethylsilylazide (0.67 mL, 1.02 eq) in azeotrope CH₃CN:H₂O (1 mL, 5 M) was pumped through the PTFE reactor, thermostated at 60 °C, packed with **POLITAG-F** (2.0 g) and quartz powder (0.018 mL/min flow rate measured at the outlet of the first reactor). After a residence time of 3.8 h the resulting azide intermediate formed was mixed, through a T joint, with a 1.2 M solution of phenylacetylene **3a** (1.2 eq) in CH₃CN:H₂O azeotrope continuously pumped at 0.1 mL/min. This mixture was passed in a CTFR heated at 100 °C with a BPR of 10 atm. The azeotrope was recovered by distillation affording in **4ba** pure product as white solid (1.384 g, 97 % yield).

Mol Formula		C ₁₇ H ₂₃ N ₃ O		m. p.	64-67 °C
¹H NMR (400 MHz, CDCl₃)	δ Value	No. H	Mult.	j Value/Hz	
	7.83	2	<i>d</i>	7.5	
	7.79	1	<i>s</i>		
	7.41	2	<i>t</i>	7.4	
	7.33-7.30	1	<i>m</i>		
	4.96-4.89	1	<i>m</i>		
	3.42	1	<i>dd</i>	18.4-8.6	
	2.95	1	<i>dd</i>	18.0-4.4	
	2.12	3	<i>s</i>		
	2.09-2.04	1	<i>m</i>		
	1.88-1.82	1	<i>m</i>		
	1.30-1.20	5	<i>m</i>		
1.13-1.11	1	<i>m</i>			
0.86-0.84	3	<i>m</i>			

¹³C NMR (100.6 MHz, CDCl₃) δ : 205.4, 147.0, 130.8, 128.9, 128.2, 125.8, 120.7, 57.3, 48.4, 35.3, 31.3, 30.6, 25.7, 22.5, 14.1

GC-EIMS (m/z, %): 285 (M⁺, 43); 242 (28); 186 (36); 144 (22), 123 (27); 118 (100); 116 (76); 102 (28); 91 (19); 90 (22); 43 (89).



METHOD:

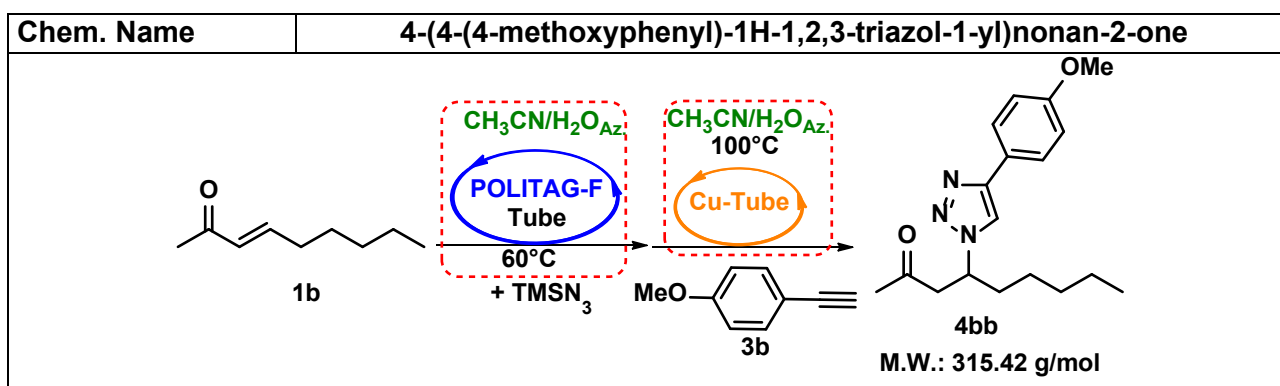
The mixture of **1a** (5 mmol) and trimethylsilylazide (0.67 mL, 1.02 eq) in azeotrope CH₃CN:H₂O (1 mL, 5 M) was pumped through the PTFE reactor, thermostated at 60 °C, packed with **POLITAG-F** (2.0 g) and quartz powder (0.018 mL/min flow rate measured at the outlet of the first reactor). After a residence time of 3.8 h the resulting azide intermediate formed was mixed, through a T joint, with a 1.2 M solution of 1-ethynyl-4-methoxybenzene **3b** (1.2 eq) in CH₃CN:H₂O azeotrope continuously pumped at 0.1 mL/min. This mixture was passed in a CTRF heated at 100 °C with a BPR of 10 atm.

The azeotrope was recovered by distillation affording in **4ba** pure product as white solid (1.408 g, 98 % yield).

Mol Formula		C ₁₆ H ₂₁ N ₃ O ₂		m. p.	104-107 °C
¹H NMR (400 MHz, DMSO-<i>d</i>₆)	δ Value	No. H	Mult.	j Value/Hz	
	8.52	1	s		
	7.75	2	d	8.7	
	7.70	2	d	8.7	
	4.97-4.90	1	m		
	3.78	3	s		
	3.27	1	dd	17.9-8.3	
	3.12	1	dd	17.7-5.3	
	2.08	3	s		
	1.87-1.71	2	m		
	1.18-1.09	1	m		
	1.08-1.01	1	m		
	1.83	3	t	7.3	

¹³C NMR (100.6 MHz, DMSO-*d*₆) δ : 205.5, 158.9, 145.9, 126.4, 123.5, 119.7, 114.3, 56.2, 55.1, 47.4, 36.9, 30.0, 18.4, 13.3

GC-EIMS (m/z, %): 287 (M⁺,75); 244 (97); 216 (98); 202 (25); 189 (33); 188 (28); 175 (22); 174 (20); 173 (27); 158 (23); 147 (100); 146 (78); 133 (32); 132 (80); 121 (23); 119 (23); 117 (20); 89 (22).

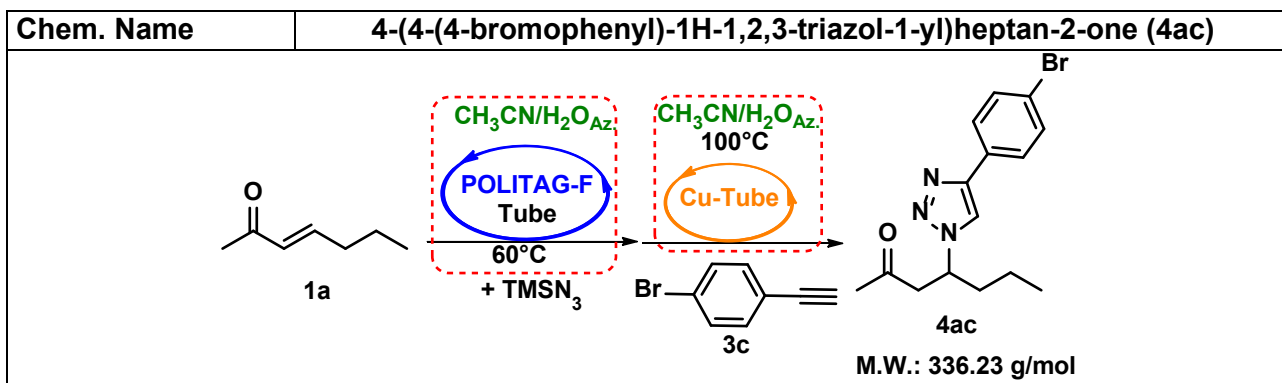


METHOD:

The mixture of **1b** (5 mmol) and trimethylsilylazide (0.67 mL, 1.02 eq) in azeotrope CH₃CN:H₂O (1 mL, 5 M) was pumped through the PTFE reactor, thermostated at 60 °C, packed with **POLITAG-F** (2.0 g) and quartz powder (0.018 mL/min flow rate measured at the outlet of the first reactor). After a residence time of 3.8 h the resulting azide intermediate formed was mixed, through a T joint, with a 1.2 M solution of 1-ethynyl-4-methoxybenzene **3b** (1.2 eq) in CH₃CN:H₂O azeotrope continuously pumped at 0.1 mL/min. This mixture was passed in a CTRF heated at 100 °C with a BPR of 10 atm.

The azeotrope was recovered by distillation affording in **4ba** pure product as white solid (1.546 g, 98 % yield, 95% NMR purity).

Mol Formula		C ₁₈ H ₂₅ N ₃ O ₂		m. p.	99-103 °C
¹H NMR (400 MHz, CDCl₃)	δ Value	No. H	Mult.	j Value/Hz	
	7.75	2	<i>d</i>	8.6	
	7.70	1	<i>s</i>		
	6.95	2	<i>d</i>	8.7	
	4.94-4.88	1	<i>m</i>		
	3.84	3	<i>s</i>		
	3.41	1	<i>dd</i>	17.9-8.3	
	2.94	1	<i>dd</i>	17.8-4.7	
	2.12	3	<i>s</i>		
	2.08-2.01	1	<i>m</i>		
	1.88-1.80	1	<i>m</i>		
	1.27-1.20	5	<i>m</i>		
1.17-1.04	1	<i>m</i>			
0.84	3	<i>t</i>	6.3		
¹³C NMR (100.6 MHz, CDCl₃) δ: 205.5; 159.7; 146.9; 127.1; 123.5; 119.9; 114.3; 57.3; 55.5; 48.4; 35.3; 31.3; 30.6; 25.7; 22.5; 14.1.					
GC-EIMS (m/z, %): 315 (M ⁺ , 72); 272 (67); 244 (33); 231 (20); 230 (23); 229 (33); 216 (51); 207 (27); 189 (23); 188 (48); 176 (25); 175 (100); 174 (29); 160 (37); 159 (20); 148 (28); 147 (90); 146 (42); 133 (48); 132 (94); 125 (28); 121 (23); 119 (23); 104 (27); 97 (29); 89 (20); 83 (21); 77 (25); 69 (27); 68 (24); 55 (47).					



METHOD:

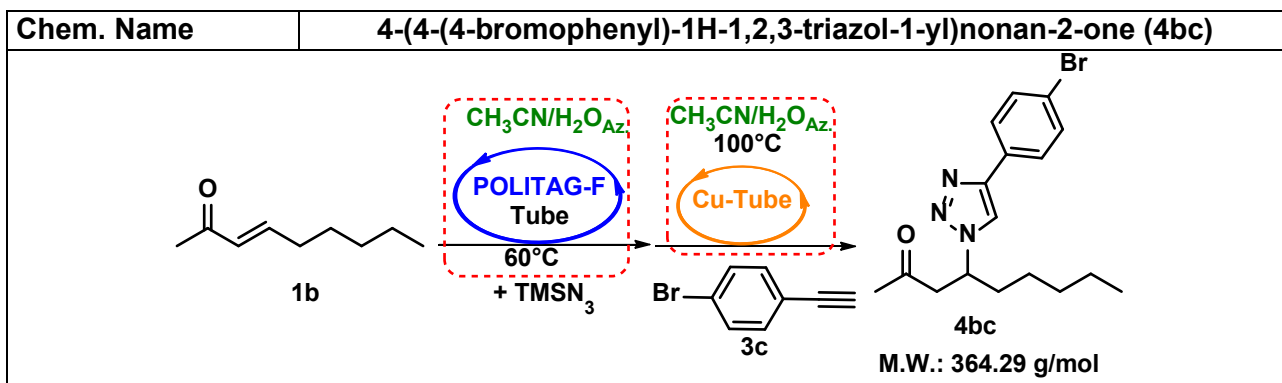
The mixture of **1a** (5 mmol) and trimethylsilylazide (0.67 mL, 1.02 eq) in azeotrope CH₃CN:H₂O (1 mL, 5 M) was pumped through the PTFE reactor, thermostated at 60 °C, packed with **POLITAG-F** (2.0 g) and quartz powder (0.018 mL/min flow rate measured at the outlet of the first reactor). After a residence time of 3.8 h the resulting azide intermediate formed was mixed, through a T joint, with a 1.2 M solution of 1-bromo-4-ethynylbenzene **3c** (1.2 eq) in CH₃CN:H₂O azeotrope continuously pumped at 0.1 mL/min. This mixture was passed in a CTRF heated at 100 °C with a BPR of 10 atm.

The azeotrope was recovered by distillation affording in **4ac** pure product as white solid (1.648 g, 98 % yield).

Mol Formula		C₁₅H₁₈BrN₃O		m. p.	118-122 °C
¹H NMR (400 MHz, CDCl₃)	δ Value	No. H	Mult.	j Value/Hz	
	7.80	1	<i>s</i>		
	7.70	2	<i>d</i>	8.4	
	7.53	2	<i>d</i>	8.4	
	4.97-4.90	1	<i>m</i>		
	3.43	1	<i>dd</i>	18.0-8.6	
	2.95	1	<i>dd</i>	18.0-4.7	
	2.12	3	<i>s</i>		
	2.09-2.02	1	<i>m</i>		
	1.87-1.78	1	<i>m</i>		
	1.31-1.10	2	<i>m</i>		
0.90	3	<i>t</i>	7.3		

¹³C NMR (100.6 MHz, CDCl₃) δ : 205.3; 146.0; 132.1; 129.8; 127.3; 122.0; 120.9; 57.1; 48.3; 37.3; 30.5; 19.3; 13.6

GC-EIMS (m/z, %): 336 (M⁺, <1); 335 (71); 294 (41); 292 (37); 266 (54); 264 (53); 237 (20); 224 (21); 223 (25); 197 (94); 196 (99); 195 (100); 194 (85); 182 (31); 180 (26); 169 (38); 167 (27); 143 (27); 116 (40); 115 (44); 114 (25); 113 (52); 102 (20); 101 (36); 89 (37); 88 (26).



METHOD:

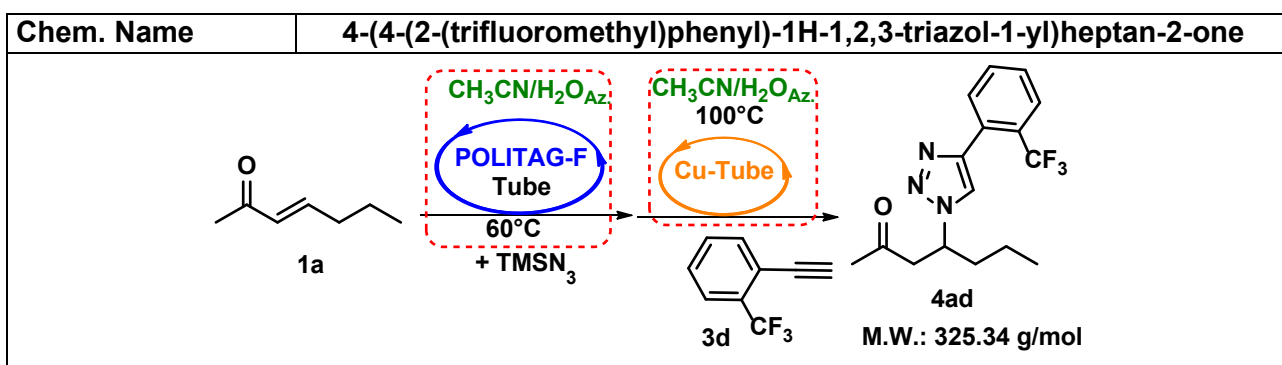
The mixture of **1b** (5 mmol) and trimethylsilylazide (0.67 mL, 1.02 eq) in azeotrope CH₃CN:H₂O (1 mL, 5 M) was pumped through the PTFE reactor, thermostated at 60 °C, packed with **POLITAG-F** (2.0 g) and quartz powder (0.018 mL/min flow rate measured at the outlet of the first reactor). After a residence time of 3.8 h the resulting azide intermediate formed was mixed, through a T joint, with a 1.2 M solution of 1-bromo-4-ethynylbenzene **3c** (1.2 eq) in CH₃CN:H₂O azeotrope continuously pumped at 0.1 mL/min. This mixture was passed in a CTRF heated at 100 °C with a BPR of 10 atm.

The azeotrope was recovered by distillation affording in **4bc** pure product as white solid (1.784 g, 98 % yield, 96% NMR purity).

Mol Formula		C ₁₇ H ₂₂ BrN ₃ O		m. p.	118-122 °C
¹H NMR (400 MHz, CDCl₃)	δ Value	No. H	Mult.	j Value/Hz	
	7.80	1	<i>s</i>		
	7.70	2	<i>d</i>	8.1	
	7.53	2	<i>d</i>	8.2	
	4.95-4.88	1	<i>m</i>		
	3.41	1	<i>dd</i>	18.4-8.6	
	2.95	1	<i>dd</i>	18.1-4.3	
	2.12	3	<i>s</i>		
	2.08-2.03	1	<i>m</i>		
	1.87-1.81	1	<i>m</i>		
	1.29-1.17	5	<i>m</i>		
	1.15-1.10	1	<i>m</i>		
0.85-0.83	3	<i>m</i>			

¹³C NMR (100.6 MHz, CD) δ: 205.3; 146.0; 132.0; 129.8; 127.3; 122.0; 120.8; 57.4; 48.3; 35.2; 31.3; 30.5; 25.7; 22.5; 14.0

GC-EIMS (m/z, %): 366 (M+2, 25); 365 (M+1, 58); 364 (M⁺, < 1); 363 (75); 322 (33); 320 (63); 291 (27); 281 (30); 278 (24); 266 (42); 264 (54); 239 (26); 238 (56); 237 (26); 236 (31); 226 (20); 225 (57); 224 (21); 223 (58); 221 (25); 209 (21); 208 (20); 207 (40); 198 (26); 197 (64); 196 (100); 195 (85); 194 (56); 182 (27); 181 (24); 180 (29); 171 (20); 169 (47); 168 (24); 166 (23); 143 (22); 128 (25); 123 (77); 117 (20); 116 (35); 115 (41); 114 (21); 101 (25); 88 (25); 81 (23); 55 (25)



METHOD:

The mixture of **1a** (5 mmol) and trimethylsilylazide (0.67 mL, 1.02 eq) in azeotrope CH₃CN:H₂O (1 mL, 5 M) was pumped through the PTFE reactor, thermostated at 60 °C, packed with **POLITAG-F** (2.0 g) and quartz powder (0.018 mL/min flow rate measured at the outlet of the first reactor). After a residence time of 3.8 h the resulting azide intermediate formed was mixed, through a T joint, with a 1.2 M solution of 1-ethynyl-2-(trifluoromethyl)benzene **3d** (1.2 eq) in CH₃CN:H₂O azeotrope pumped at 0.1 mL/min. This mixture was passed in a CTRF heated at 100 °C with a BPR of 10 atm.

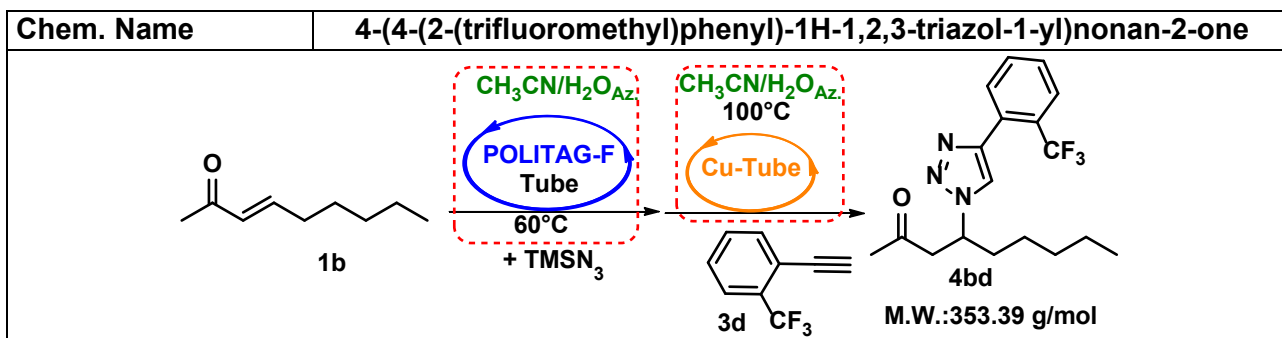
The azeotrope was recovered by distillation affording in **4ad** pure product as oil (1.496 g, 92 % yield).

Mol Formula		C ₁₆ H ₁₈ F ₃ N ₃ O		m. p.	Oil
¹H NMR (400 MHz, CDCl₃)	δ Value	No. H	Mult.	j Value/Hz	
	7.94	1	<i>d</i>	7.8	
	7.78	1	<i>s</i>		
	7.74	1	<i>d</i>	7.9	
	7.61	1	<i>t</i>	7.4	
	7.46	1	<i>t</i>	7.9	
	4.99-4.92	1	<i>m</i>		
	3.43	1	<i>dd</i>	17.9-8.2	
	2.98	1	<i>dd</i>	17.9-4.9	
	2.13	3	<i>s</i>		
	2.08-2.03	1	<i>m</i>		
	1.87-1.78	1	<i>m</i>		
	1.26-1.10	2	<i>m</i>		
0.90	3	<i>t</i>	7.3		

¹³C NMR (100.6 MHz, CD) δ : 205.1; 143.5; 132.0; 131.7; 129.7; 128.2; 127.4 (*q*, J_{C-F}= 30.3); 126.1(*q*, J_{C-F}= 5.6); 124.2 (*q*, J_{C-F}= 273.3), 123.8 (*q*, J_{C-F}= 5.6); 57.0; 48.2; 37.2; 30.4; 19.0; 13.4

¹⁹F NMR (100.6 MHz, CD) δ: -58.74

GC-EIMS (m/z, %): 325 (M⁺, 50); 282 (40); 255 (27); 254 (62); 240 (27); 194 (27); 185 (69); 184 (94); 172 (20); 169 (45); 166 (40); 165 (100); 164 (72); 151 (54); 134 (31); 113 (62).



METHOD:

The mixture of **1b** (5 mmol) and trimethylsilylazide (0.67 mL, 1.02 eq) in azeotrope CH₃CN:H₂O (1 mL, 5 M) was pumped through the PTFE reactor, thermostated at 60 °C, packed with **POLITAG-F** (2.0 g) and quartz powder (0.018 mL/min flow rate measured at the outlet of the first reactor). After a residence time of 3.8 h the resulting azide intermediate formed was mixed, through a T joint, with a 1.2 M solution of 1-ethynyl-2-(trifluoromethyl)benzene **3d** (1.2 eq) in CH₃CN:H₂O azeotrope pumped at 0.1 mL/min. This mixture was passed in a CTRF heated at 100 °C with a BPR of 10 atm.

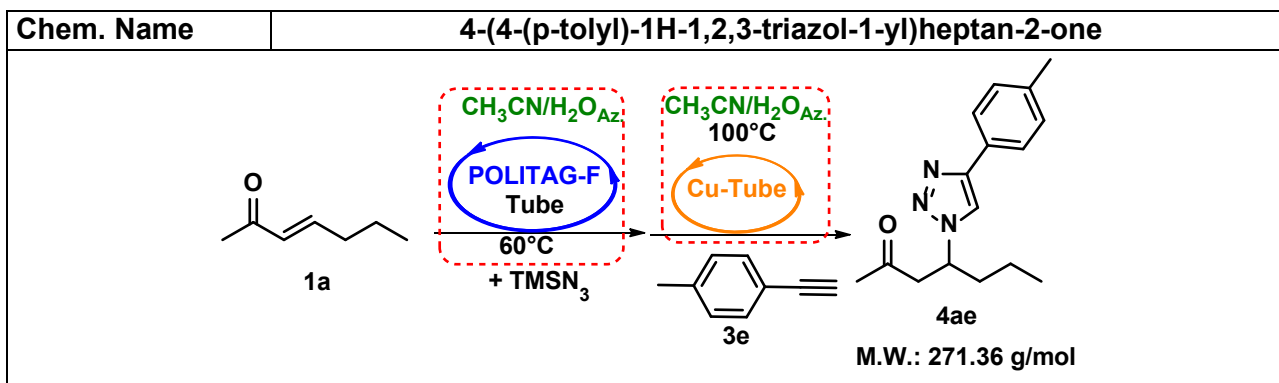
The azeotrope was recovered by distillation affording in **4bd** pure product as oil (1.730 g, 98 % yield).

Mol Formula		C ₁₈ H ₂₂ F ₃ N ₃ O		m. p.	Oil
¹H NMR (400 MHz, CDCl₃)	δ Value	No. H	Mult.	j Value/Hz	
	7.91	1	<i>d</i>	7.8	
	7.77	1	<i>s</i>		
	7.71	1	<i>d</i>	7.7	
	7.59	1	<i>t</i>	7.5	
	7.44	1	<i>t</i>	7.7	
	4.95-4.90	1	<i>m</i>		
	3.40	1	<i>dd</i>	18.0-8.4	
	2.96	1	<i>dd</i>	18.1-4.7	
	2.10	3	<i>s</i>		
	2.07-2.04	1	<i>m</i>		
	1.88-1.82	1	<i>m</i>		
	1.25-1.20	5	<i>m</i>		
	1.11-1.08	1	<i>m</i>		
0.84-0.80	3	<i>m</i>			

¹³C NMR (100.6 MHz, CD) δ: 205.2; 143.5; 132.0, 131.8, 129.7, 127.7 (*q*, J_{C-F}= 30.3), 128.3, 126.3 (*q*, J_{C-F}= 272.9), 126.2, 124.0, 57.4, 48.3, 35.3, 31.2, 30.5, 25.5, 22.4, 13.9

¹⁹F NMR (100.6 MHz, CD) δ: -58.73

GC-EIMS (m/z, %): 353 (M⁺, < 1); 325 (38); 282 (41); 255 (26); 254 (62); 240 (29); 214 (21); 213 (29); 194 (34); 185 (69); 184 (91); 172 (20); 169 (40); 167 (20); 166 (42); 165 (100); 164 (72); 151 (55); 138 (20); 134 (34); 113 (74); 55 (22).



METHOD:

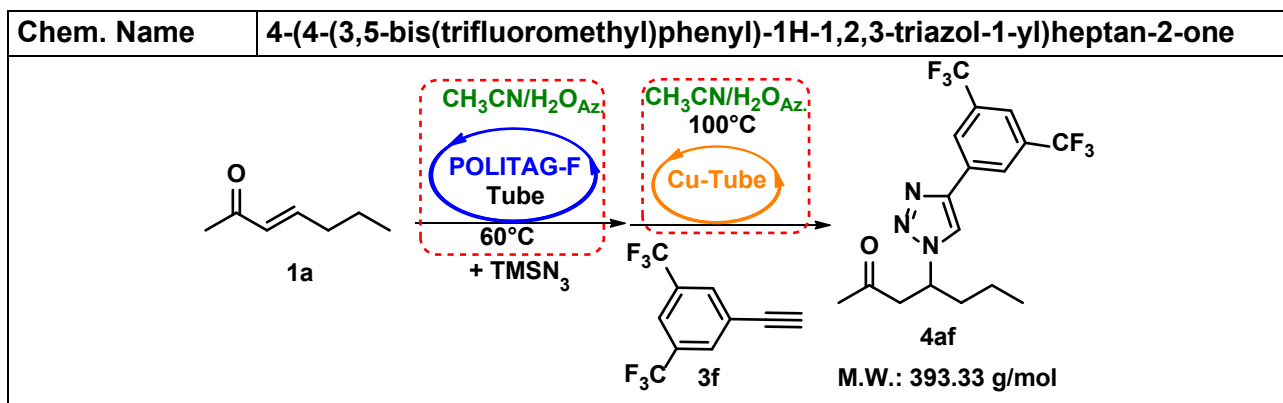
The mixture of **1a** (5 mmol) and trimethylsilylazide (0.67 mL, 1.02 eq) in azeotrope CH₃CN:H₂O (1 mL, 5 M) was pumped through the PTFE reactor, thermostated at 60 °C, packed with **POLITAG-F** (2.0 g) and quartz powder (0.018 mL/min flow rate measured at the outlet of the first reactor). After a residence time of 3.8 h the resulting azide intermediate formed was mixed, through a T joint, with a 1.2 M solution of 1-ethynyl-4-methylbenzene **3e** (1.2 eq) in CH₃CN:H₂O azeotrope pumped at 0.1 mL/min. This mixture was passed in a CTFR heated at 100 °C with a BPR of 10 atm. The azeotrope was recovered by distillation affording in **4ae** pure product as white solid (1.249 g, 92 % yield, 95% NMR purity)

Mol Formula		C ₁₆ H ₂₁ N ₃ O		m. p.	129-131 °C
¹H NMR (400 MHz, CDCl₃)	δ Value	No. H	Mult.	j Value/Hz	
	7.75	1	<i>s</i>		
	7.71	1	<i>d</i>	7.4	
	7.22	2	<i>d</i>	7.5	
	4.95-4.93	1	<i>m</i>		
	3.42	1	<i>dd</i>	18.0-8.5	
	2.94	1	<i>dd</i>	18.1-4.1	
	2.37	3	<i>s</i>		
	2.12	3	<i>s</i>		
	2.07-2.01	1	<i>m</i>		
	1.84-1.79	1	<i>m</i>		
	1.25-1.18	2	<i>m</i>		
0.90	3	<i>t</i>	7.2		

¹³C NMR (100.6 MHz, CDCl₃) δ: 205.4; 147.1; 138.0; 129.6; 128.0; 125.7; 120.3; 57.0; 48.4; 37.3; 30.6; 21.4; 19.3; 13.6

GC-EIMS (m/z, %): 271 (M⁺, 52); 228 (28); 200 (39); 131 (100); 130 (55); 115 (31); 103 (25).

Chem. Name		4-(4-(p-tolyl)-1H-1,2,3-triazol-1-yl)nonan-2-one			
METHOD:					
<p>The mixture of 1b (5 mmol) and trimethylsilylazide (0.67 mL, 1.02 eq) in azeotrope CH₃CN:H₂O (1 mL, 5 M) was pumped through the PTFE reactor, thermostated at 60 °C, packed with POLITAG-F (2.0 g) and quartz powder (0.018 mL/min flow rate measured at the outlet of the first reactor). After a residence time of 3.8 h the resulting azide intermediate formed was mixed, through a T joint, with a 1.2 M solution of 1-ethynyl-4-methylbenzene 3e (1.2 eq) in CH₃CN:H₂O azeotrope pumped at 0.1 mL/min. This mixture was passed in a CTRF heated at 100 °C with a BPR of 10 atm. The azeotrope was recovered by distillation affording in 4be pure product as white solid (1.482 g, 99 % yield)</p>					
Mol Formula		C ₁₈ H ₂₅ N ₃ O		m. p.	90-93 °C
¹H NMR (400 MHz, CDCl₃)	δ Value	No. H	Mult.	j Value/Hz	
	7.75	1	<i>s</i>		
	7.71	2	<i>d</i>	8.0	
	7.22	2	<i>d</i>	7.8	
	4.95-4.88	1	<i>m</i>		
	3.42	1	<i>dd</i>	17.9-8.5	
	2.95	1	<i>dd</i>	17.9-4.6	
	2.37	3	<i>s</i>		
	2.12	3	<i>s</i>		
	2.08-2.04	1	<i>m</i>		
	1.89-1.80	1	<i>m</i>		
	1.26-1.20	5	<i>m</i>		
1.16-1.11	1	<i>m</i>			
0.86-0.84	3	<i>m</i>			
¹³C NMR (100.6 MHz, CDCl₃) δ: 205.4; 147.1; 138.0; 129.6; 128.0; 125.7; 120.3; 57.3; 48.4; 35.3; 31.3; 30.6; 25.7; 22.5; 21.4; 14.1.					
GC-EIMS (m/z, %): 299 (M ⁺ , 47); 256 (36); 200 (32); 131 (100); 130 (48); 115 (28).					



METHOD:

The mixture of **1a** (5 mmol) and trimethylsilylazide (0.67 mL, 1.02 eq) in azeotrope CH₃CN:H₂O (1 mL, 5 M) was pumped through the PTFE reactor, thermostated at 60 °C, packed with **POLITAG-F** (2.0 g) and quartz powder (0.018 mL/min flow rate measured at the outlet of the first reactor). After a residence time of 3.8 h the resulting azide intermediate formed was mixed, through a T joint, with a 1.2 M solution of 1-ethynyl-3,5-bis(trifluoromethyl)benzene **3f** (1.2 eq) in CH₃CN:H₂O azeotrope pumped at 0.1 mL/min. This mixture was passed in a CTRF heated at 100 °C with a BPR of 10 atm.

The azeotrope was recovered by distillation affording in **4af** pure product as white solid (1.908 g, 97 % yield)

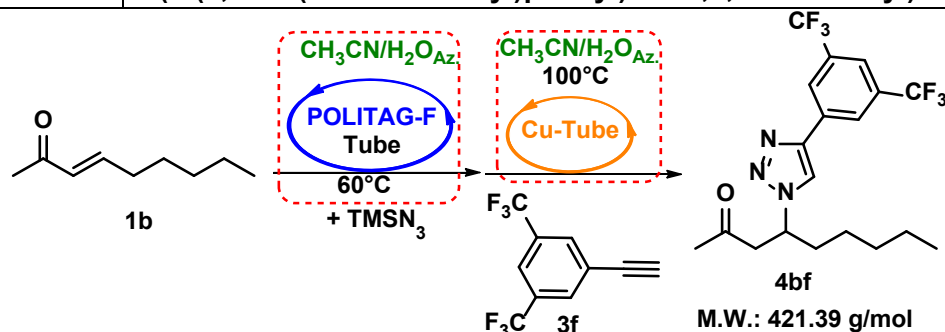
Mol Formula		C₁₇H₁₇F₆N₃O		m. p.	80-82 °C
¹H NMR (400 MHz, CDCl₃)	δ Value	No. H	Mult.	j Value/Hz	
	8.27	2	<i>s</i>		
	7.98	1	<i>s</i>		
	7.80	1	<i>s</i>		
	5.00-4.95	1	<i>m</i>		
	3.46	1	<i>dd</i>	18.4-9.1	
	2.97	1	<i>dd</i>	18.3-4.2	
	2.13	3	<i>s</i>		
	2.12-2.06	1	<i>m</i>		
	1.89-1.80	1	<i>m</i>		
	1.30-1.18	2	<i>m</i>		
0.91	3	<i>t</i>	7.5		

¹³C NMR (100.6 MHz, CDCl₃) δ: 205.2; 144.3; 133.0; 132.3 (*q*, J_{C-F}= 33.4), 125.7, 123.4 (*q*, J_{C-F}= 272.9), 122.0; 121.5 (*q*, J_{C-F}= 3.8); 57.4; 48.2; 37.1; 30.4; 19.3; 13.5.

¹⁹F NMR (100.6 MHz, CD) δ: -63.04

GC-EIMS (m/z, %): 394 (M+1, 21); 393 (M⁺, 83); 374 (87); 350 (76); 323 (22); 322 (88); 308 (40); 295 (24); 294 (31); 282 (30); 253 (51); 252 (100); 233 (20); 169 (21); 113 (22).

Chem. Name 4-(4-(3,5-bis(trifluoromethyl)phenyl)-1H-1,2,3-triazol-1-yl)nonan-2-one



METHOD:

The mixture of **1b** (5 mmol) and trimethylsilylazide (0.67 mL, 1.02 eq) in azeotrope CH₃CN:H₂O (1 mL, 5 M) was pumped through the PTFE reactor, thermostated at 60 °C, packed with **POLITAG-F** (2.0 g) and quartz powder (0.018 mL/min flow rate measured at the outlet of the first reactor). After a residence time of 3.8 h the resulting azide intermediate formed was mixed, through a T joint, with a 1.2 M solution of 1-ethynyl-3,5-bis(trifluoromethyl)benzene **3f** (1.2 eq) in CH₃CN:H₂O azeotrope pumped at 0.1 mL/min. This mixture was passed in a CTFR heated at 100 °C with a BPR of 10 atm. The azeotrope was recovered by distillation affording in **4bf** pure product as white solid (2.021 g, 96 % yield).

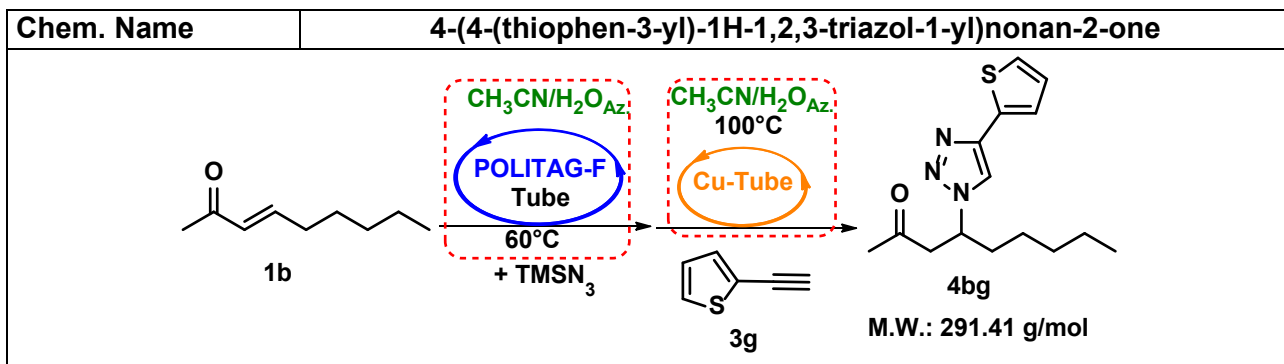
Mol Formula		C ₁₉ H ₂₁ F ₆ N ₃ O		m. p.	95-97 °C
¹H NMR (400 MHz, CDCl₃)	δ Value	No. H	Mult.	j Value/Hz	
	8.28	2	s		
	7.98	1	s		
	7.81	1	s		
	5.01-4.90	1	m		
	3.45	1	dd	18.6-8.8	
	2.97	1	dd	18.2-4.1	
	2.18-2.03	4	m		
	1.94-1.82	1	m		
	1.38-1.19	5	m		
	1.18-1.03	1	m		
0.89-0.79	3	m			

¹³C NMR (100.6 MHz, CDCl₃) δ: 205.2; 144.3; 133.0, 132.3 (q, J_{C-F}= 33.5), 125.7, 123.4 (q, J_{C-F}= 272.9) 122.0, 121.5 (q, J_{C-F}= 3.8), 57.7, 48.3, 35.1, 31.3, 30.4, 25.7, 22.5, 14.0.

¹⁹F NMR (100.6 MHz, CD) δ: -63.00

GC-EIMS (m/z, %): 422 (M+1, 24); 421 (M⁺, 13); 402 (59); 401 (47); 392 (50); 378 (71); 365 (30); 364 (52); 349 (56); 336 (37); 333 (23); 324 (22); 322 (66); 321 (33); 308 (54); 307 (43); 306 (41); 294 (44); 293 (21); 292 (31); 282 (56); 281 (37); 280 (79); 279 (38); 264 (20); 254 (32); 253 (54); 252 (89); 240 (45); 238 (24); 234 (32); 233 (32); 225 (29); 202 (24); 170 (26); 169 (40); 168 (100); 123 (31).

Chem. Name	4-(4-(thiophen-3-yl)-1H-1,2,3-triazol-1-yl)heptan-2-one				
METHOD:					
<p>The mixture of 1a (5 mmol) and trimethylsilylazide (0.67 mL, 1.02 eq) in azeotrope CH₃CN:H₂O (1 mL, 5 M) was pumped through the PTFE reactor, thermostated at 60 °C, packed with POLITAG-F (2.0 g) and quartz powder (0.018 mL/min flow rate measured at the outlet of the first reactor). After a residence time of 3.8 h the resulting azide intermediate formed was mixed, through a T joint, with a 1.2 M solution of 3-ethynylthiophene 3g (1.2 eq) in CH₃CN:H₂O azeotrope pumped at 0.1 mL/min. This mixture was passed in a CTFR heated at 100 °C with a BPR of 10 atm. The azeotrope was recovered by distillation affording in 4ag pure product as white solid (1.212 g, 92 % yield)</p>					
Mol Formula		C ₁₃ H ₁₇ N ₃ OS		m. p.	87-89 °C
¹H NMR (400 MHz, CDCl ₃)	δ Value	No. H	Mult.	j Value/Hz	
	7.69	1	<i>s</i>		
	7.67-7.65	1	<i>m</i>		
	7.45	1	<i>d</i>	4.8	
	7.38	1	<i>d</i>	4.9	
	4.96-4.89	1	<i>m</i>		
	3.42	1	<i>dd</i>	17.9-8.6	
	2.94	1	<i>dd</i>	18.0-4.6	
	2.12	3	<i>s</i>		
	2.09-2.02	1	<i>m</i>		
	1.87-1.76	1	<i>m</i>		
	1.30-1.10	2	<i>m</i>		
0.90	3	<i>t</i>	7.1		
¹³C NMR (100.6 MHz, CD) δ: 205.4; 143.3; 132.0; 126.4; 125.9; 121.1; 120.5; 57.0; 48.4; 37.3; 30.6; 19.3; 13.6.					
GC-EIMS (m/z, %): 263 (M ⁺ , 96); 220 (51); 192 (60); 150 (20); 149 (20); 124 (21); 123 (100); 122 (79); 113 (21); 108 (21); 97 (21); 95 (22).					



METHOD:

The mixture of **1b** (5 mmol) and trimethylsilylazide (0.67 mL, 1.02 eq) in azeotrope CH₃CN:H₂O (1 mL, 5 M) was pumped through the PTFE reactor, thermostated at 60 °C, packed with **POLITAG-F** (2.0 g) and quartz powder (0.018 mL/min flow rate measured at the outlet of the first reactor). After a residence time of 3.8 h the resulting azide intermediate formed was mixed, through a T joint, with a 1.2 M solution of 3-ethynylthiophene **3g** (1.2 eq) in CH₃CN:H₂O azeotrope pumped at 0.1 mL/min. This mixture was passed in a CTFR heated at 100 °C with a BPR of 10 atm.

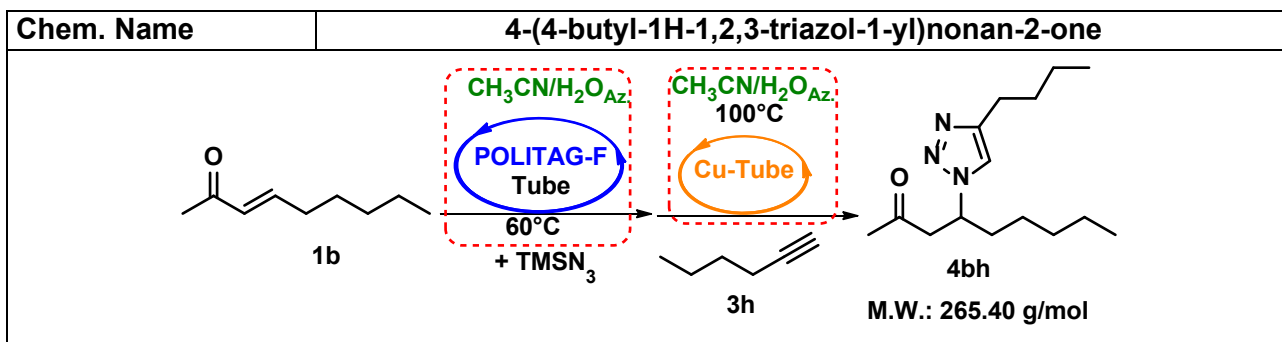
The azeotrope was recovered by distillation affording in **4bg** pure product as white solid (1.411 g, 97 % yield, 95% NMR purity).

Mol Formula		C₁₅H₂₁N₃OS		m. p.	60-62 °C
¹H NMR (400 MHz, CDCl₃)	δ Value	No. H	Mult.	j Value/Hz	
	7.70	1	<i>s</i>		
	7.64	1	<i>s</i>		
	7.43	1	<i>d</i>	4.8	
	7.34	1	<i>d</i>	4.8	
	4.91-4.86	1	<i>m</i>		
	3.36	1	<i>dd</i>	17.9-8.5	
	2.91	1	<i>dd</i>	17.9-4.6	
	2.08	3	<i>s</i>		
	2.03-1.99	1	<i>m</i>		
	1.83-1.77	1	<i>m</i>		
	1.23-1.12	5	<i>m</i>		
	1.09-1.07	1	<i>m</i>		
0.81-0.79	3	<i>m</i>			

¹³C NMR (100.6 MHz, CDCl₃) δ: 205.4, 143.2, 132.0, 126.3, 125.9, 121.0, 120.5, 57.2, 48.4, 35.2, 31.3, 30.5, 25.6, 22.5, 14.0.

GC-EIMS (m/z, %): 291 (M⁺, 52); 248 (46); 192 (65); 165 (26); 164 (23); 152 (25); 151 (85); 150 (21); 149 (20); 125 (31); 124 (24); 123 (100); 122 (66); 109 (23); 108 (20); 97 (44); 96 (28); 95 (32); 81 (23); 69 (22); 55 (31).

Chem. Name		4-(4-butyl-1H-1,2,3-triazol-1-yl)heptan-2-one			
METHOD:					
<p>The mixture of 1a (5 mmol) and trimethylsilylazide (0.67 mL, 1.02 eq) in azeotrope CH₃CN:H₂O (1 mL, 5 M) was pumped through the PTFE reactor, thermostated at 60 °C, packed with POLITAG-F (2.0 g) and quartz powder (0.018 mL/min flow rate measured at the outlet of the first reactor). After a residence time of 3.8 h the resulting azide intermediate formed was mixed, through a T joint, with a 1.2 M solution of hex-1-yne 3h (1.2 eq) in CH₃CN:H₂O azeotrope pumped at 0.1 mL/min. This mixture was passed in a CTRF heated at 100 °C with a BPR of 10 atm.</p> <p>The azeotrope was recovered by distillation affording in 4ah pure product as oil (1.101 g, 93 % yield, 95% NMR purity)</p>					
Mol Formula		C ₁₃ H ₂₃ N ₃ O		m. p.	Oil
¹H NMR (400 MHz, CDCl₃)	δ Value	No. H	Mult.	j Value/Hz	
	7.26	1	<i>s</i>		
	4.86-4.79	1	<i>m</i>		
	3.33	1	<i>dd</i>	17.8-8.3	
	2.88	1	<i>dd</i>	17.7-4.9	
	2.66	2	<i>t</i>	7.7	
	2.08	3	<i>s</i>		
	2.00-0.91	1	<i>m</i>		
	1.79-1.70	1	<i>m</i>		
	1.61	2	<i>t</i>	7.7	
	1.37-1.31	2	<i>m</i>		
	1.19-1.05	2	<i>m</i>		
0.92-0.84	6	<i>m</i>			
¹³C NMR (100.6 MHz, CDCl₃) δ : 205.4; 147.7; 121.5; 56.7; 48.4; 37.4; 31.6; 30.5; 25.4, 22.4, 19.2, 13.9, 13.6.					
GC-EIMS (m/z, %): 238 (M ⁺ , 46); 224 (24); 210 (39); 180 (29); 168 (28); 154 (23); 141 (36); 140 (28); 126 (28); 124 (23); 123 (61); 115 (23); 113 (28); 98 (100); 97 (27); 83 (53); 81 (25); 75 (27); 73 (72); 59 (25); 55 (32).					



METHOD:

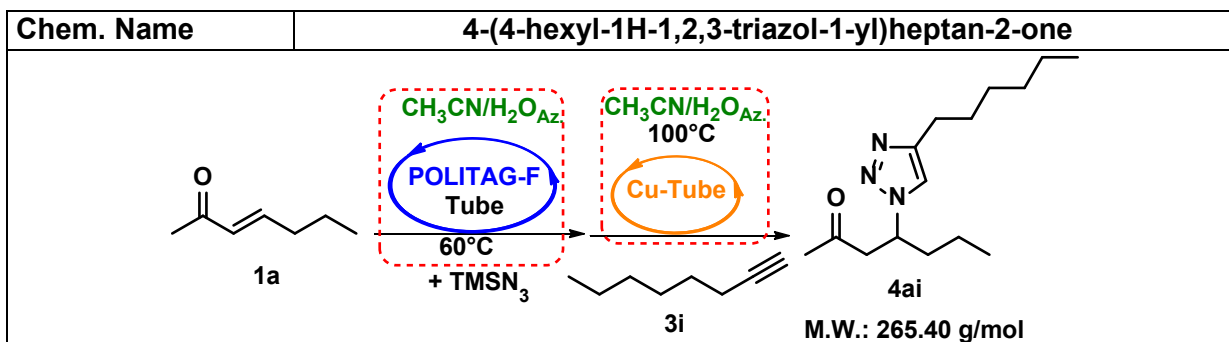
The mixture of **1b** (5 mmol) and trimethylsilylazide (0.67 mL, 1.02 eq) in azeotrope CH₃CN:H₂O (1 mL, 5 M) was pumped through the PTFE reactor, thermostated at 60 °C, packed with **POLITAG-F** (2.0 g) and quartz powder (0.018 mL/min flow rate measured at the outlet of the first reactor). After a residence time of 3.8 h the resulting azide intermediate formed was mixed, through a T joint, with a 1.2 M solution of hex-1-yne **3h** (1.2 eq) in CH₃CN:H₂O azeotrope pumped at 0.1 mL/min. This mixture was passed in a CTRF heated at 100 °C with a BPR of 10 atm.

The azeotrope was recovered by distillation affording in **4bh** pure product as oil (1.235 g, 93 % yield).

Mol Formula		C ₁₅ H ₂₇ N ₃ O		m. p.	Oil
¹ H NMR (400 MHz, CDCl ₃)	δ Value	No. H	Mult.	j Value/Hz	
	7.26	1	<i>s</i>		
	4.85-4.78	1	<i>m</i>		
	3.31	1	<i>dd</i>	17.7-8.2	
	2.87	1	<i>dd</i>	17.7-4.7	
	2.62	2	<i>t</i>	7.7	
	2.06	3	<i>s</i>		
	2.05-1.90	1	<i>m</i>		
	1.77-1.69	1	<i>m</i>		
	1.62-1.57	2	<i>m</i>		
	1.34-1.20	6	<i>m</i>		
	1.12-1.02	2	<i>m</i>		
0.86-0.81	6	<i>m</i>			

¹³C NMR (100.6 MHz, CD) δ: 205.4; 147.7; 121.4; 56.6; 48.3; 37.3; 31.6; 30.4; 29.4; 28.9; 25.7; 22.6; 19.2; 14.1; 13.5.

GC-EIMS (m/z, %): 265 (M⁺, 59); 222 (27); 208 (25); 194 (100); 180 (53); 167 (51); 166 (39); 152 (91); 136 (26); 124 (44); 113 (32); 110 (30); 97 (29); 96 (39); 95 (29); 94 (24); 83 (25); 82 (54); 80 (32); 67 (24); 55 (45); 54 (26).



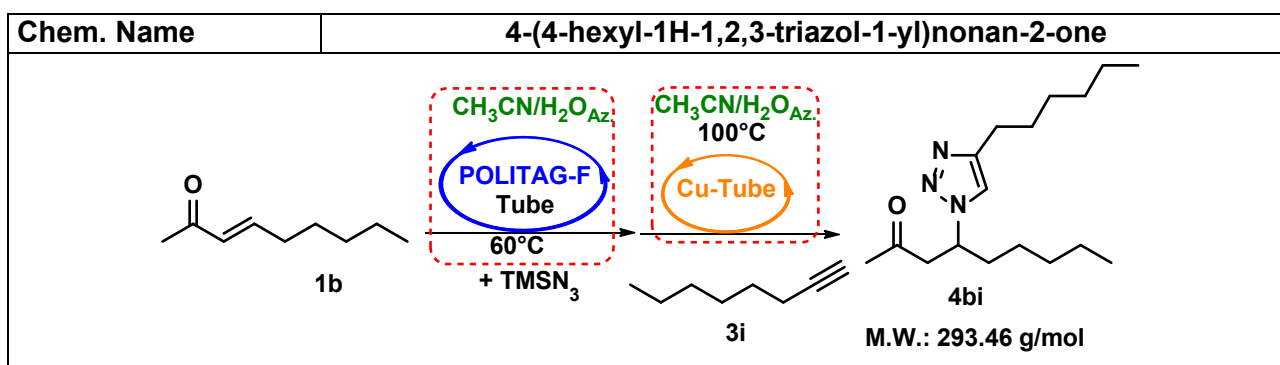
METHOD:

The mixture of **1a** (5 mmol) and trimethylsilylazide (0.67 mL, 1.02 eq) in azeotrope CH₃CN:H₂O (1 mL, 5 M) was pumped through the PTFE reactor, thermostated at 60 °C, packed with **POLITAG-F** (2.0 g) and quartz powder (0.018 mL/min flow rate measured at the outlet of the first reactor). After a residence time of 3.8 h the resulting azide intermediate formed was mixed, through a T joint, with a 1.2 M solution of oct-1-yne **3i** (1.2 eq) in CH₃CN:H₂O azeotrope pumped at 0.1 mL/min. This mixture was passed in a CTFR heated at 100 °C with a BPR of 10 atm. The azeotrope was recovered by distillation affording in **4ai** pure product as oil (1.166 g, 88 % yield, 97% NMR purity).

Mol Formula		C ₁₅ H ₂₇ N ₃ O		m. p.	Oil
¹ H NMR (400 MHz, CDCl ₃)	δ Value	No. H	Mult.	j Value/Hz	
	7.26	1	<i>s</i>		
	4.86-4.79	1	<i>m</i>		
	3.32	1	<i>dd</i>	17.9-8.3	
	2.88	1	<i>dd</i>	18.1-4.7	
	2.66-2.63	2	<i>m</i>		
	2.07	3	<i>s</i>		
	1.99-1.91	1	<i>m</i>		
	1.78-1.70	1	<i>m</i>		
	1.65-1.58	2	<i>m</i>		
	1.30-1.21	6	<i>m</i>		
	1.18-1.07	2	<i>m</i>		
0.87-0.83	6	<i>m</i>			

¹³C NMR (100.6 MHz, CDCl₃) δ: 205.4, 128.8, 121.5, 56.6, 48.4, 37.4, 31.6, 30.5, 29.4, 29.0, 25.7, 22.6, 19.2, 14.1, 13.5.

GC-EIMS (m/z, %): 265 (M⁺, 58); 222 (25); 208 (25); 195 (81); 180 (55); 166 (39), 152 (94); 136 (29); 124 (43); 113 (30); 110 (27); 97 (26); 96 (37); 95 (26); 94 (22); 83 (21); 82 (50); 80 (31); 67 (21); 55 (39); 54 (22).



METHOD:

The mixture of **1b** (5 mmol) and trimethylsilylazide (0.67 mL, 1.02 eq) in azeotrope CH₃CN:H₂O (1 mL, 5 M) was pumped through the PTFE reactor, thermostated at 60 °C, packed with **POLITAG-F** (2.0 g) and quartz powder (0.018 mL/min flow rate measured at the outlet of the first reactor). After a residence time of 3.8 h the resulting azide intermediate formed was mixed, through a T joint, with a 1.2 M solution of oct-1-yne **3i** (1.2 eq) in CH₃CN:H₂O azeotrope pumped at 0.1 mL/min. This mixture was passed in a CTRF heated at 100 °C with a BPR of 10 atm.

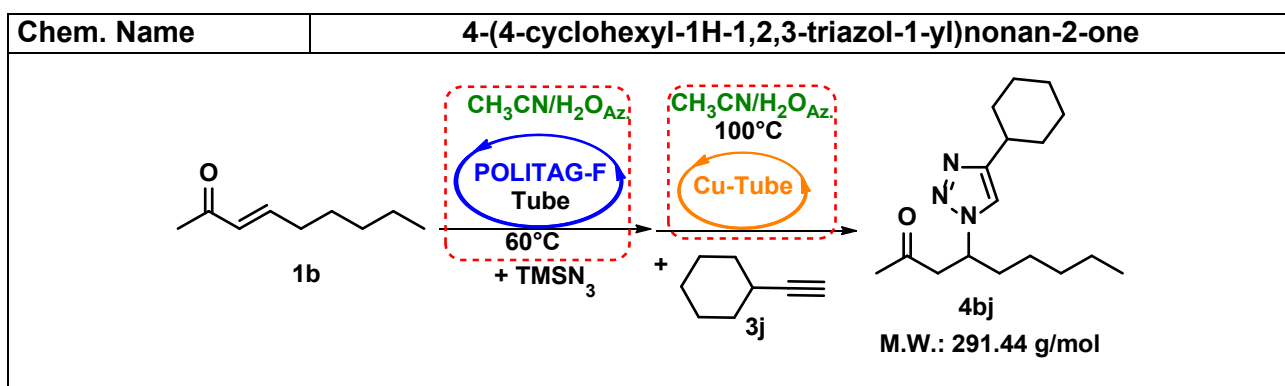
The azeotrope was recovered by distillation affording in **4bi** pure product as oil (1.290 g, 88 % yield, 95% NMR purity).

Mol Formula		C ₁₇ H ₃₁ N ₃ O		m. p.	Oil
¹H NMR (400 MHz, CDCl ₃)	δ Value	No. H	Mult.	j Value/Hz	
	7.29	1	<i>s</i>		
	4.86-4.82	1	<i>m</i>		
	3.36	1	<i>dd</i>	18.1-8.4	
	2.92	1	<i>dd</i>	18.1-4.6	
	2.70-2.67	3	<i>m</i>		
	2.11	3	<i>s</i>		
	2.03-1.97	1	<i>m</i>		
	1.84-1.80	1	<i>m</i>		
	1.67-1.63	2	<i>m</i>		
	1.39-1.30	7	<i>m</i>		
	1.27-1.23	5	<i>m</i>		
0.88-0.84	6	<i>m</i>			

¹³C NMR (100.6 MHz, CD) δ: 205.5, 147.7, 121.5, 56.9, 48.4, 35.3, 31.6, 31.2, 30.5, 29.4, 29.0, 25.7, 25.6, 22.6, 22.5, 14.1, 14.0

GC-EIMS (m/z, %): 293 (M⁺, 57); 250 (37); 236 (59); 223 (67); 222 (100); 208 (52); 194 (55); 168 (20); 166 (25); 152 (76); 124 (29); 123 (50); 110 (20); 97 (28); 96 (27); 83 (47); 82 (46); 81 (35); 80 (27); 71 (22); 67 (24); 55 (58); 54 (25).

Chem. Name	4-(4-cyclohexyl-1H-1,2,3-triazol-1-yl)heptan-2-one				
Lit. Ref.					
<p style="text-align: center;">M.W.: 263.39 g/mol</p>					
METHOD:					
<p>The mixture of 1a (5 mmol) and trimethylsilylazide (0.67 mL, 1.02 eq) in azeotrope CH₃CN:H₂O (1 mL, 5 M) was pumped through the PTFE reactor, thermostated at 60 °C, packed with POLITAG-F (2.0 g) and quartz powder (0.018 mL/min flow rate measured at the outlet of the first reactor). After a residence time of 3.8 h the resulting azide intermediate formed was mixed, through a T joint, with a 1.2 M solution of ethynylcyclohexane 3j (1.2 eq) in CH₃CN:H₂O azeotrope pumped at 0.1 mL/min. This mixture was passed in a CTRF heated at 100 °C with a BPR of 10 atm.</p> <p>The azeotrope was recovered by distillation affording in 4aj pure product as white solid (1.093 g, 83 % yield, 98% NMR purity).</p>					
Mol Formula		C ₁₅ H ₂₅ N ₃ O		m. p.	59-61 °C
¹H NMR (400 MHz, CDCl ₃)	δ Value	No. H	Mult.	j Value/Hz	
	7.24	1	<i>s</i>		
	4.86-4.81	1	<i>m</i>		
	3.35	1	<i>dd</i>	18.0-8.1	
	2.90	1	<i>dd</i>	17.8-4.9	
	2.72-2.65	1	<i>m</i>		
	2.10	3	<i>s</i>		
	2.08-2.05	2	<i>m</i>		
	2.04-1.93	1	<i>m</i>		
	1.83-1.79	3	<i>m</i>		
	1.79-1.69	1	<i>m</i>		
	1.40-1.35	4	<i>m</i>		
	1.22-1.16	2	<i>m</i>		
1.15-1.09	1	<i>m</i>			
0.89-0.84	3	<i>m</i>			
¹³C NMR (100.6 MHz, CD) δ: 205.3; 153.0; 120.1; 56.7; 48.5; 37.5; 35.4; 33.1; 26.3; 26.2; 19.3; 13.6					
GC-EIMS (m/z, %): 263 (M ⁺ , 72); 207 (30); 192 (100); 178 (77); 164 (21); 150 (79); 148 (22); 134 (29); 122 (36); 113 (34); 106 (23); 95 (24); 94 (23); 67 (24); 55 (22).					



METHOD:

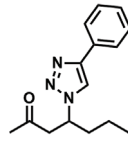
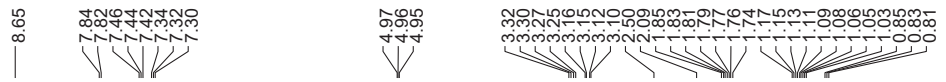
The mixture of **1b** (5 mmol) and trimethylsilylazide (0.67 mL, 1.02 eq) in azeotrope CH₃CN:H₂O (1 mL, 5 M) was pumped through the PTFE reactor, thermostated at 60 °C, packed with **POLITAG-F** (2.0 g) and quartz powder (0.018 mL/min flow rate measured at the outlet of the first reactor). After a residence time of 3.8 h the resulting azide intermediate formed was mixed, through a T joint, with a 1.2 M solution of ethynylcyclohexane **3j** (1.2 eq) in CH₃CN:H₂O azeotrope pumped at 0.1 mL/min. This mixture was passed in a CTRF heated at 100 °C with a BPR of 10 atm. The azeotrope was recovered by distillation affording in **4b_j** pure product as white solid (1.355 g, 93 % yield, 95% NMR purity).

Mol Formula		C ₁₇ H ₂₉ N ₃ O		m. p.	Oil
¹H NMR (400 MHz, CDCl₃)	δ Value	No. H	Mult.	j Value/Hz	
	7.28	1	<i>s</i>		
	4.87-4.80	1	<i>m</i>		
	1.36	1	<i>dd</i>	18.4-8.2	
	2.92	1	<i>dd</i>	17.8-4.8	
	2.76-7.72	1	<i>m</i>		
	2.11	3	<i>s</i>		
	2.06-2.02	2	<i>m</i>		
	2.01-1.94	1	<i>m</i>		
	1.83-1.80	3	<i>m</i>		
	1.74-1.71	1	<i>m</i>		
	1.42-1.37	4	<i>m</i>		
	1.22-1.17	6	<i>m</i>		
	1.08-1.05	1	<i>m</i>		
0.85-0.82	3	<i>m</i>			

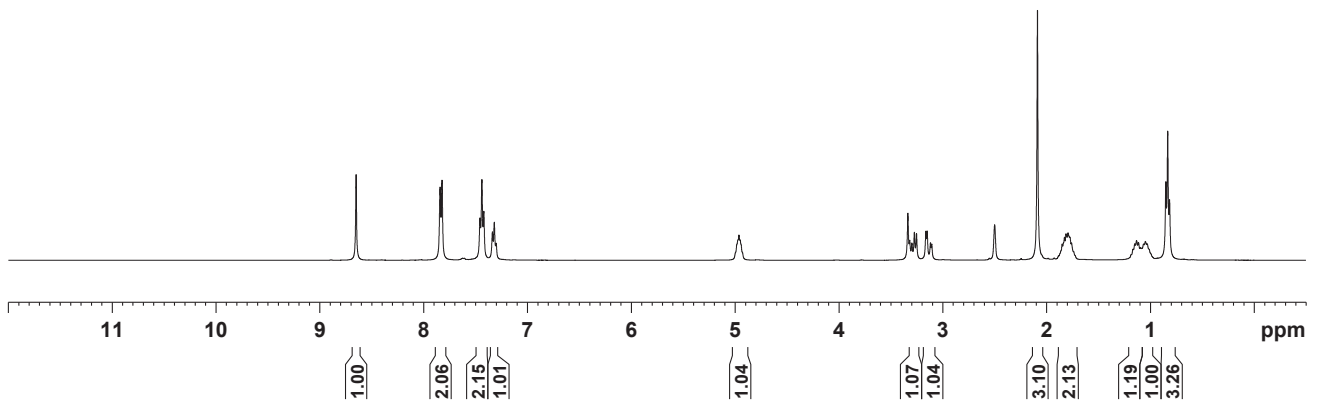
¹³C NMR (100.6 MHz, CDCl₃) δ: 205.6, 153.0, 120.1, 56.9, 48.4, 35.3, 35.1, 31.2, 30.5, 26.2, 26.2, 25.6, 22.5, 14.0

GC-EIMS (m/z, %): 285 (43); 242 (28); 186 (36); 144 (22); 116 (76); 102 (28); 90 (22); 89 (43).

6. NMR copies



4-(4-phenyl-1H-1,2,3-triazol-1-yl)heptan-2-one
4aa



205.42

145.93

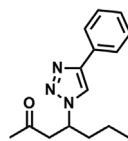
130.84, 129.96, 127.09, 125.01, 120.65

56.27

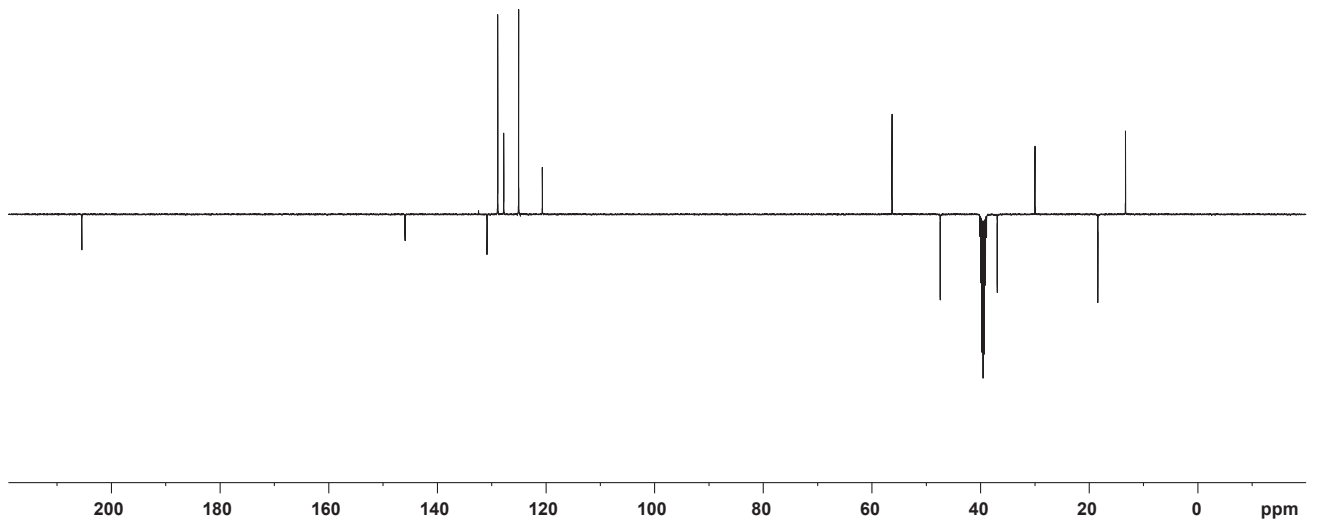
47.41, 40.14, 39.93, 39.72, 39.51, 39.30, 39.10, 38.89, 36.91, 29.95

18.39

13.29



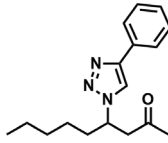
4-(4-phenyl-1H-1,2,3-triazol-1-yl)heptan-2-one
4aa



7.84
7.82
7.79
7.43
7.41
7.39
7.33
7.31
7.20

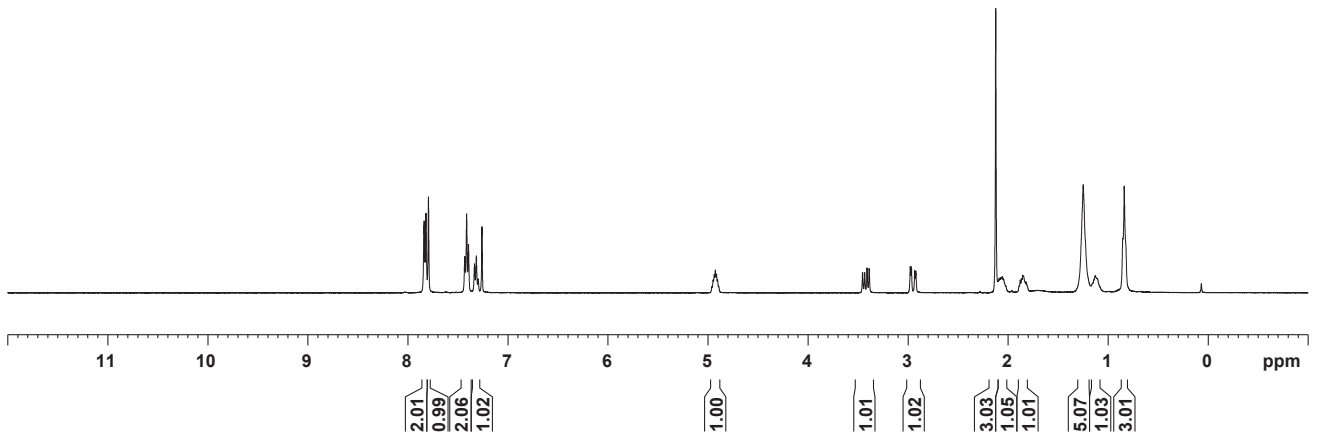
4.96
4.95
4.93
4.91
4.90
4.89

4.5
3.43
3.41
3.39
3.38
3.37
3.35
3.34
3.33
3.32
3.31
3.30
3.29
3.28
3.27
3.26
3.25
3.24
3.23
3.22
3.21
3.20
3.19
3.18
3.17
3.16
3.15
3.14
3.13
3.12
3.11
3.10
3.09
3.08
3.07
3.06
3.05
3.04
3.03
3.02
3.01
3.00
2.99
2.98
2.97
2.96
2.95
2.94
2.93
2.92
2.91
2.90
2.89
2.88
2.87
2.86
2.85
2.84
2.83
2.82
2.81
2.80
2.79
2.78
2.77
2.76
2.75
2.74
2.73
2.72
2.71
2.70
2.69
2.68
2.67
2.66
2.65
2.64
2.63
2.62
2.61
2.60
2.59
2.58
2.57
2.56
2.55
2.54
2.53
2.52
2.51
2.50
2.49
2.48
2.47
2.46
2.45
2.44
2.43
2.42
2.41
2.40
2.39
2.38
2.37
2.36
2.35
2.34
2.33
2.32
2.31
2.30
2.29
2.28
2.27
2.26
2.25
2.24
2.23
2.22
2.21
2.20
2.19
2.18
2.17
2.16
2.15
2.14
2.13
2.12
2.11
2.10
2.09
2.08
2.07
2.06
2.05
2.04
2.03
2.02
2.01
2.00
1.99
1.98
1.97
1.96
1.95
1.94
1.93
1.92
1.91
1.90
1.89
1.88
1.87
1.86
1.85
1.84
1.83
1.82
1.81
1.80
1.79
1.78
1.77
1.76
1.75
1.74
1.73
1.72
1.71
1.70
1.69
1.68
1.67
1.66
1.65
1.64
1.63
1.62
1.61
1.60
1.59
1.58
1.57
1.56
1.55
1.54
1.53
1.52
1.51
1.50
1.49
1.48
1.47
1.46
1.45
1.44
1.43
1.42
1.41
1.40
1.39
1.38
1.37
1.36
1.35
1.34
1.33
1.32
1.31
1.30
1.29
1.28
1.27
1.26
1.25
1.24
1.23
1.22
1.21
1.20
1.19
1.18
1.17
1.16
1.15
1.14
1.13
1.12
1.11
1.10
1.09
1.08
1.07
1.06
1.05
1.04
1.03
1.02
1.01
1.00
0.99
0.98
0.97
0.96
0.95
0.94
0.93
0.92
0.91
0.90
0.89
0.88
0.87
0.86
0.85
0.84



4-(4-phenyl-1H-1,2,3-triazol-1-yl)nonan-2-one

4ba



205.37

147.04

130.79
128.92
128.18
125.78
120.67

77.47
77.16
76.84

57.30

48.41

35.25

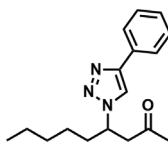
31.30

30.56

25.69

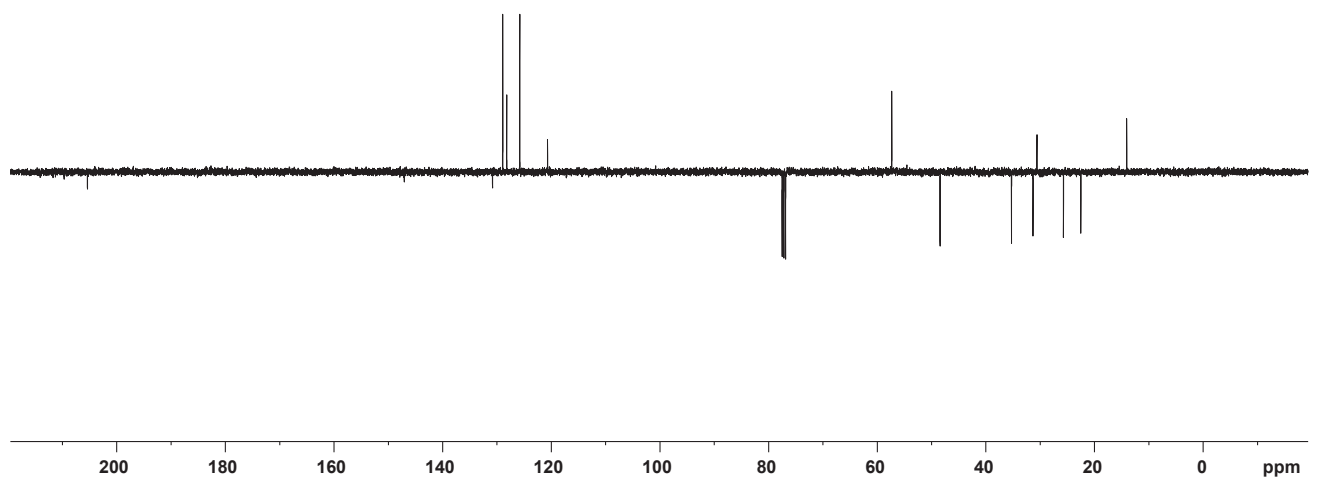
22.49

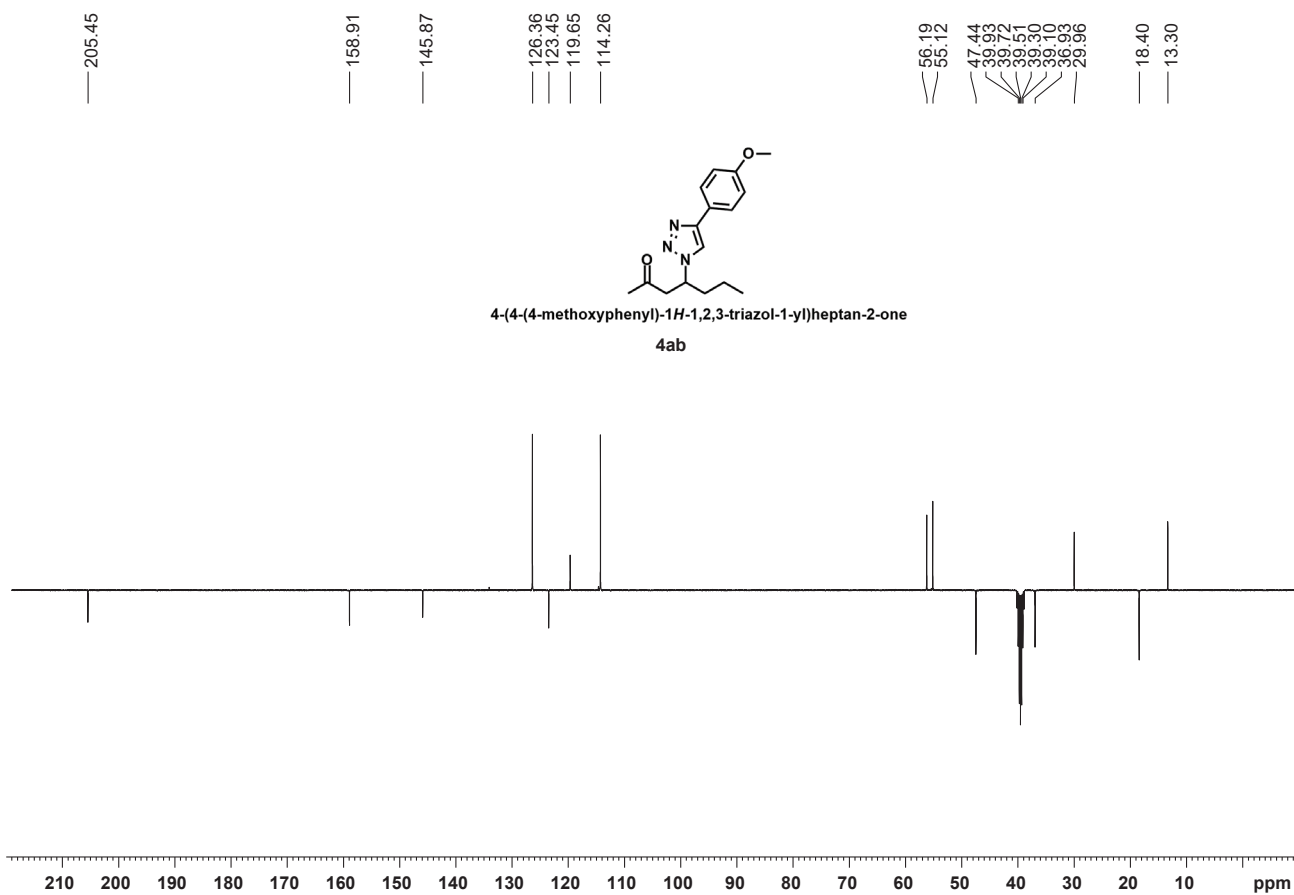
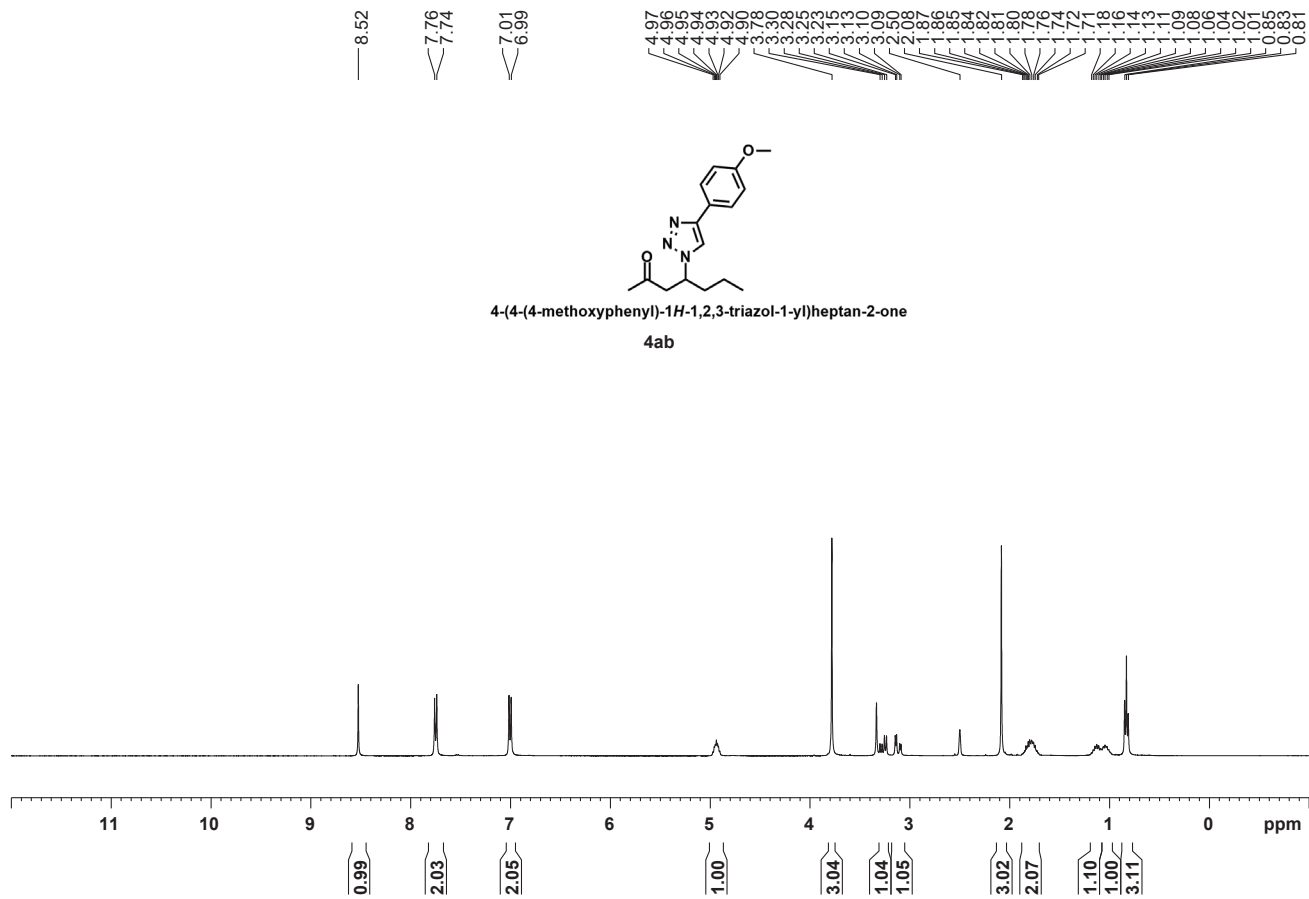
14.05



4-(4-phenyl-1H-1,2,3-triazol-1-yl)nonan-2-one

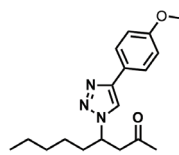
4ba





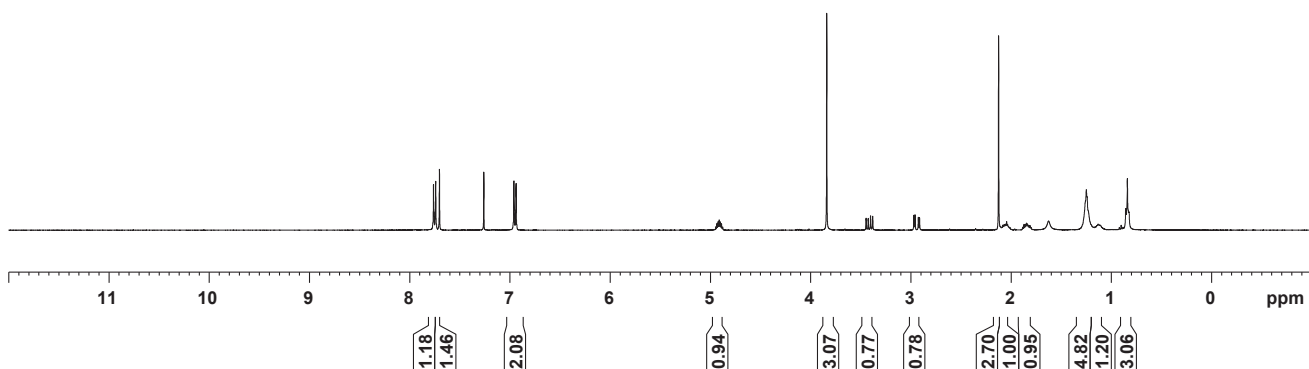
7.76
7.74
7.70
7.26
6.96
6.94

4.95
4.93
4.91
4.90
4.88
4.84
4.74
4.72
4.70
4.68
4.66
4.64
4.62
4.60
4.58
4.56
4.54
4.52
4.50
4.48
4.46
4.44
4.42
4.40
4.38
4.36
4.34
4.32
4.30
4.28
4.26
4.24
4.22
4.20
4.18
4.16
4.14
4.12
4.10
4.08
4.06
4.04
4.02
4.00
3.98
3.96
3.94
3.92
3.90
3.88
3.86
3.84
3.82
3.80
3.78
3.76
3.74
3.72
3.70
3.68
3.66
3.64
3.62
3.60
3.58
3.56
3.54
3.52
3.50
3.48
3.46
3.44
3.42
3.40
3.38
3.36
3.34
3.32
3.30
3.28
3.26
3.24
3.22
3.20
3.18
3.16
3.14
3.12
3.10
3.08
3.06
3.04
3.02
3.00
2.98
2.96
2.94
2.92
2.90
2.88
2.86
2.84
2.82
2.80
2.78
2.76
2.74
2.72
2.70
2.68
2.66
2.64
2.62
2.60
2.58
2.56
2.54
2.52
2.50
2.48
2.46
2.44
2.42
2.40
2.38
2.36
2.34
2.32
2.30
2.28
2.26
2.24
2.22
2.20
2.18
2.16
2.14
2.12
2.10
2.08
2.06
2.04
2.02
2.00
1.98
1.96
1.94
1.92
1.90
1.88
1.86
1.84
1.82
1.80
1.78
1.76
1.74
1.72
1.70
1.68
1.66
1.64
1.62
1.60
1.58
1.56
1.54
1.52
1.50
1.48
1.46
1.44
1.42
1.40
1.38
1.36
1.34
1.32
1.30
1.28
1.26
1.24
1.22
1.20
1.18
1.16
1.14
1.12
1.10
1.08
1.06
1.04
1.02
1.00
0.98
0.96
0.94
0.92
0.90
0.88
0.86
0.84
0.82
0.80
0.78
0.76
0.74
0.72
0.70
0.68
0.66
0.64
0.62
0.60
0.58
0.56
0.54
0.52
0.50
0.48
0.46
0.44
0.42
0.40
0.38
0.36
0.34
0.32
0.30
0.28
0.26
0.24
0.22
0.20
0.18
0.16
0.14
0.12
0.10
0.08
0.06
0.04
0.02
0.00



4-(4-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl)nonan-2-one

4bb



205.45

159.66

146.93

127.10

123.53

119.85

114.34

77.48

77.06

76.84

57.25

55.46

48.43

35.28

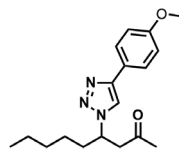
31.32

30.59

25.70

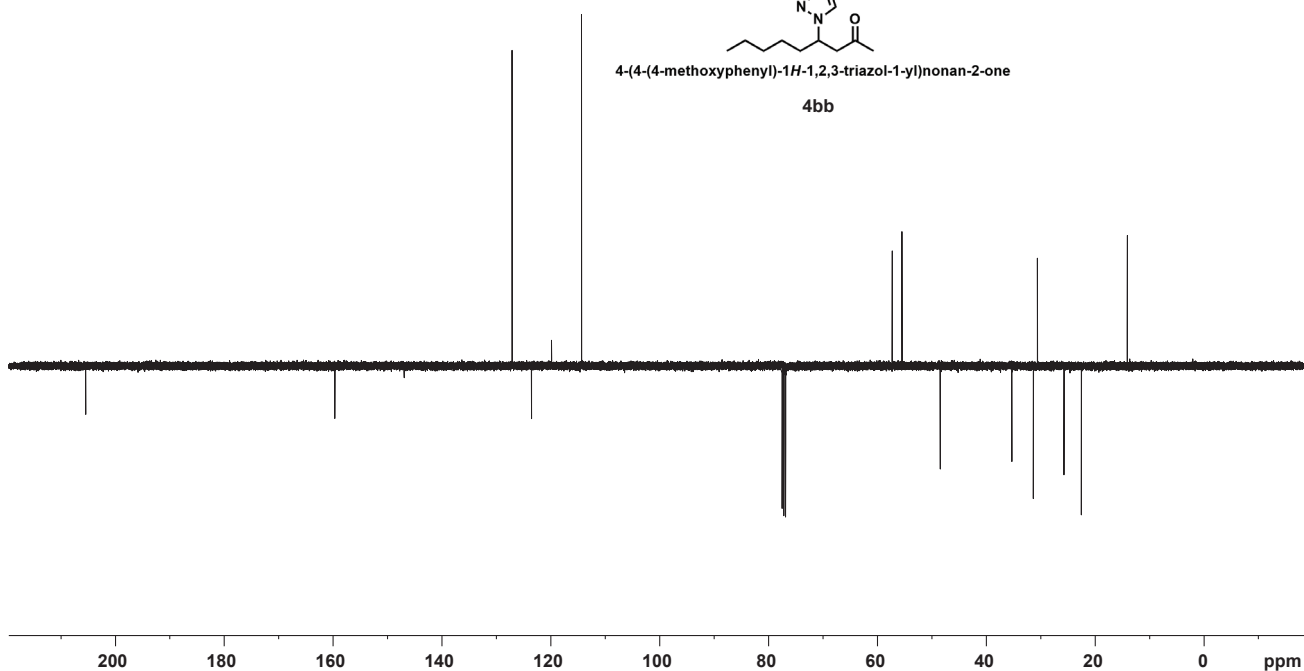
22.50

14.06



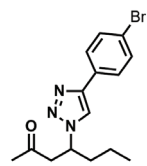
4-(4-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl)nonan-2-one

4bb



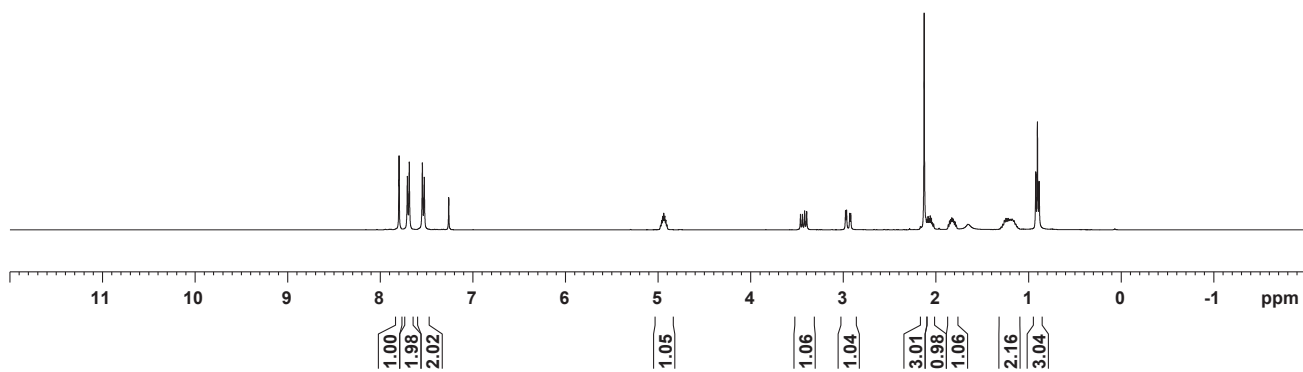
7.80
7.71
7.69
7.54
7.52
7.26

4.07
4.06
4.04
4.04
4.03
4.02
3.90
3.44
3.39
3.37
3.36
3.33
3.32
3.22
3.09
3.09
3.06
3.06
3.04
3.02
3.02
1.86
1.85
1.84
1.83
1.81
1.80
1.79
1.78
2.29
2.28
2.26
2.24
2.23
2.22
2.21
2.20
1.19
1.18
1.15
1.14
1.12
0.92
0.90
0.88



4-(4-(4-bromophenyl)-1H-1,2,3-triazol-1-yl)heptan-2-one

4ac



205.30

145.99

132.05
129.76
127.31
122.02
120.87

77.46
77.15
76.83

57.11

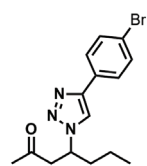
48.31

37.26

30.52

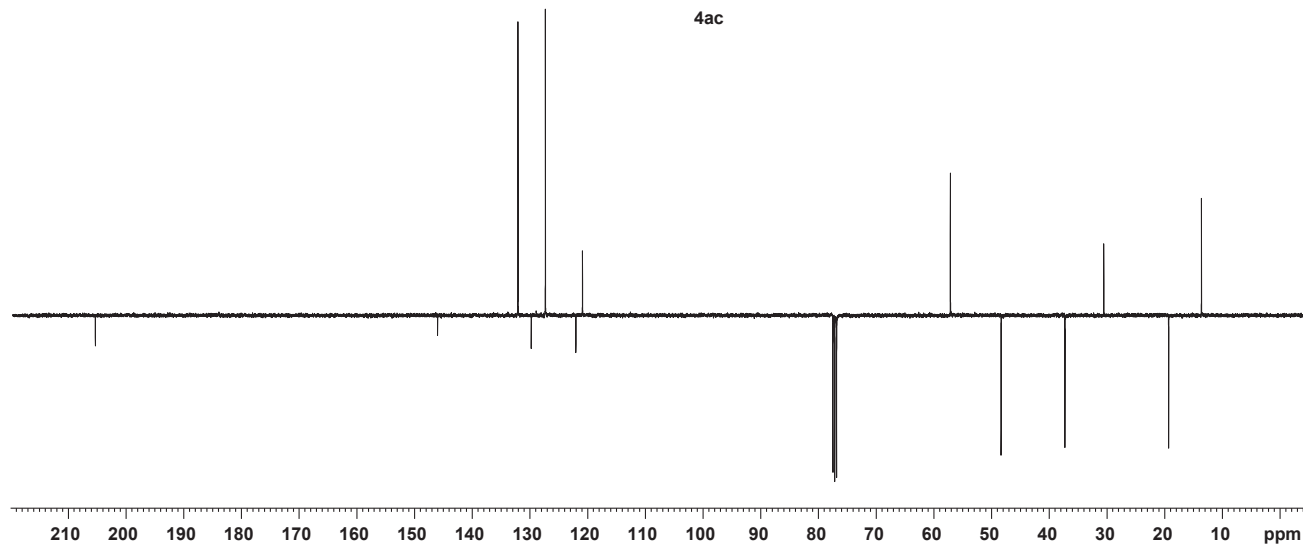
19.28

13.59



4-(4-(4-bromophenyl)-1H-1,2,3-triazol-1-yl)heptan-2-one

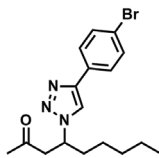
4ac



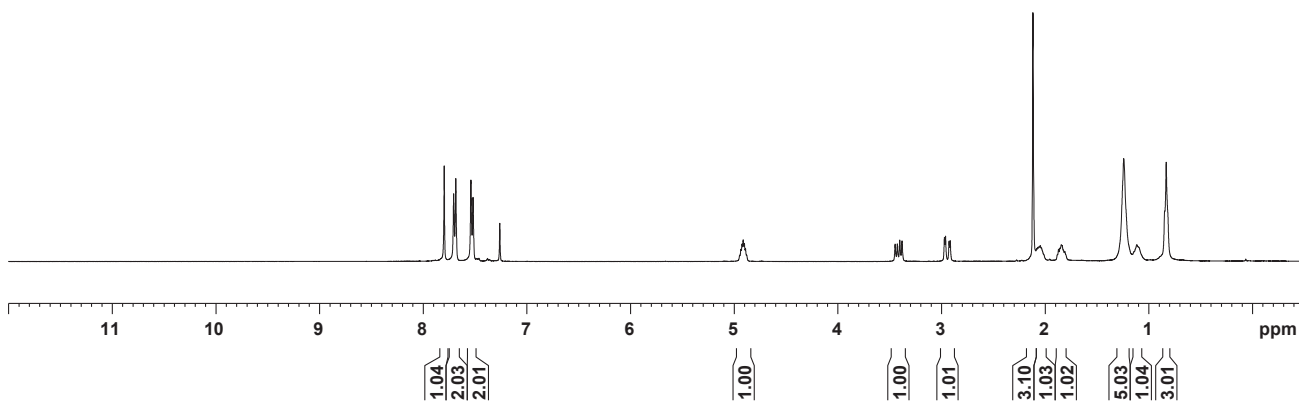
7.80
7.71
7.68
7.64
7.52
7.26

4.95
4.93
4.91
4.90
4.89
4.88

3.45
3.42
3.40
3.38
3.37
3.36
3.35
3.33
3.32
3.31
3.29
3.27
3.06
3.05
3.03
2.87
2.86
2.84
2.81
2.71
0.83



4-(4-(4-bromophenyl)-1H-1,2,3-triazol-1-yl)nonan-2-one
4bc



— 205.29

— 145.97
— 132.04
— 129.77
— 127.30
— 121.99
— 120.84

— 77.48
— 77.16
— 76.84

— 57.36

— 48.31

— 35.18

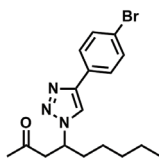
— 31.27

— 30.50

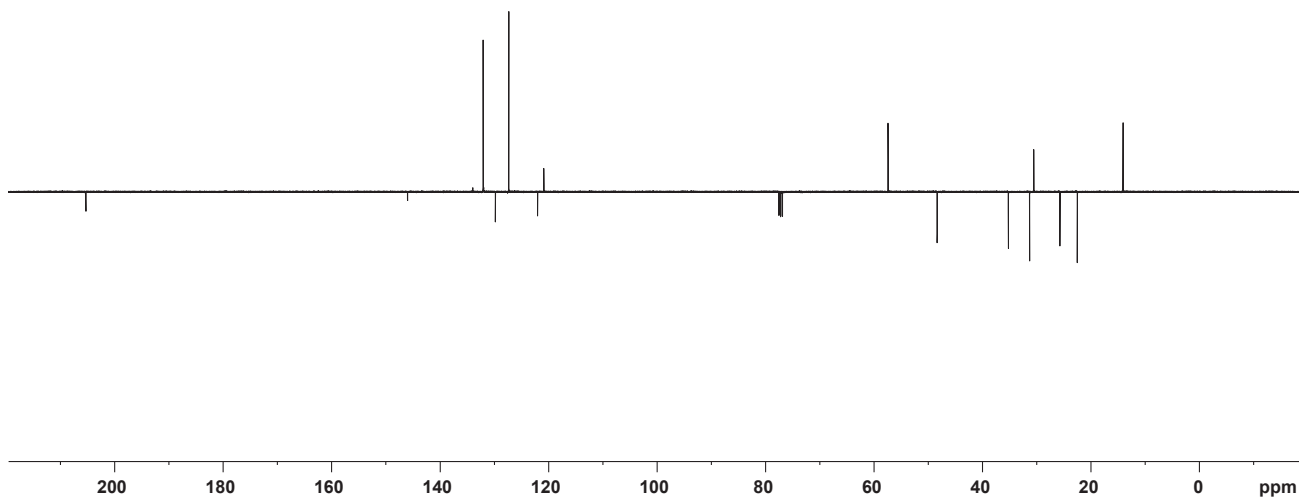
— 25.67

— 22.46

— 14.03



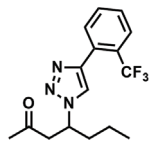
4-(4-(4-bromophenyl)-1H-1,2,3-triazol-1-yl)nonan-2-one
4bc



7.955
7.775
7.772
7.769
7.691
7.690
7.689
7.686

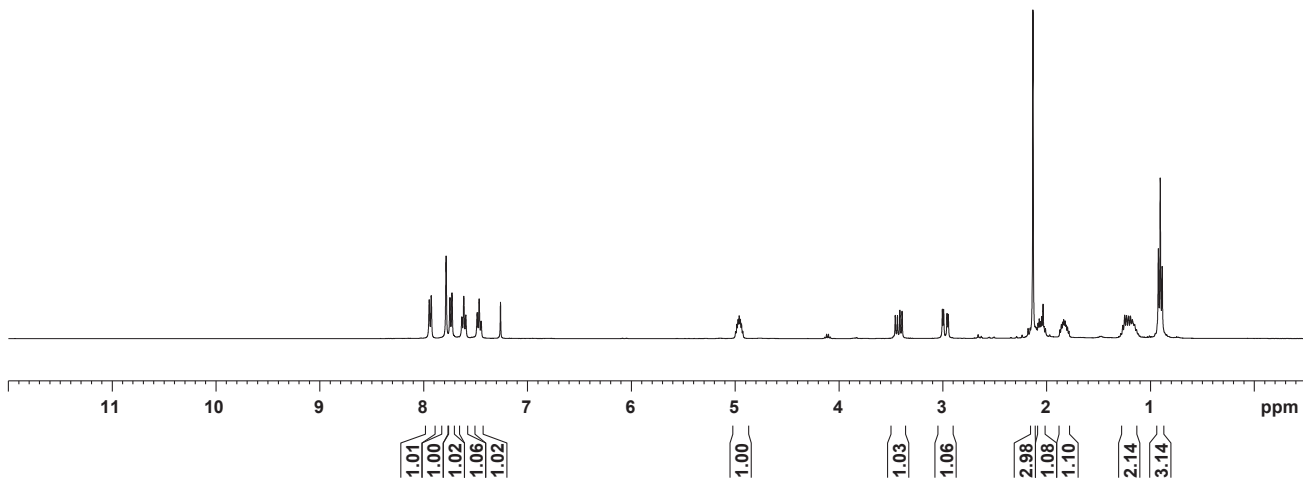
4.998
4.987
4.965
4.955
4.943

4.46
4.44
4.09
4.00
3.99
3.96
3.93
3.92
3.88
3.87
3.86
3.83
3.82
3.81
3.80
3.66
3.65
3.63
3.62
3.61
3.60
3.59
3.58
3.57
3.56
3.55
3.54
3.53
3.52
3.51
3.50
3.49
3.48
3.47
3.46
3.45
3.44
3.43
3.42
3.41
3.40
3.39
3.38
3.37
3.36
3.35
3.34
3.33
3.32
3.31
3.30
3.29
3.28
3.27
3.26
3.25
3.24
3.23
3.22
3.21
3.20
3.19
3.18
3.17
3.16
3.15
3.14
3.13
3.12
3.11
3.10
3.09
3.08
3.07
3.06
3.05
3.04
3.03
3.02
3.01
3.00
2.99
2.98
2.97
2.96
2.95
2.94
2.93
2.92
2.91
2.90
2.89
2.88
2.87
2.86
2.85
2.84
2.83
2.82
2.81
2.80
2.79
2.78
2.77
2.76
2.75
2.74
2.73
2.72
2.71
2.70
2.69
2.68
2.67
2.66
2.65
2.64
2.63
2.62
2.61
2.60
2.59
2.58
2.57
2.56
2.55
2.54
2.53
2.52
2.51
2.50
2.49
2.48
2.47
2.46
2.45
2.44
2.43
2.42
2.41
2.40
2.39
2.38
2.37
2.36
2.35
2.34
2.33
2.32
2.31
2.30
2.29
2.28
2.27
2.26
2.25
2.24
2.23
2.22
2.21
2.20
2.19
2.18
2.17
2.16
2.15
2.14
2.13
2.12
2.11
2.10
2.09
2.08
2.07
2.06
2.05
2.04
2.03
2.02
2.01
2.00
1.99
1.98
1.97
1.96
1.95
1.94
1.93
1.92
1.91
1.90
1.89
1.88
1.87
1.86
1.85
1.84
1.83
1.82
1.81
1.80
1.79
1.78
1.77
1.76
1.75
1.74
1.73
1.72
1.71
1.70
1.69
1.68
1.67
1.66
1.65
1.64
1.63
1.62
1.61
1.60
1.59
1.58
1.57
1.56
1.55
1.54
1.53
1.52
1.51
1.50
1.49
1.48
1.47
1.46
1.45
1.44
1.43
1.42
1.41
1.40
1.39
1.38
1.37
1.36
1.35
1.34
1.33
1.32
1.31
1.30
1.29
1.28
1.27
1.26
1.25
1.24
1.23
1.22
1.21
1.20
1.19
1.18
1.17
1.16
1.15
1.14
1.13
1.12
1.11
1.10
1.09
1.08
1.07
1.06
1.05
1.04
1.03
1.02
1.01
1.00
0.99
0.98
0.97
0.96
0.95
0.94
0.93
0.92
0.91
0.90
0.89
0.88
0.87
0.86
0.85
0.84
0.83
0.82
0.81
0.80
0.79
0.78
0.77
0.76
0.75
0.74
0.73
0.72
0.71
0.70
0.69
0.68
0.67
0.66
0.65
0.64
0.63
0.62
0.61
0.60
0.59
0.58
0.57
0.56
0.55
0.54
0.53
0.52
0.51
0.50
0.49
0.48
0.47
0.46
0.45
0.44
0.43
0.42
0.41
0.40
0.39
0.38
0.37
0.36
0.35
0.34
0.33
0.32
0.31
0.30
0.29
0.28
0.27
0.26
0.25
0.24
0.23
0.22
0.21
0.20
0.19
0.18
0.17
0.16
0.15
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00

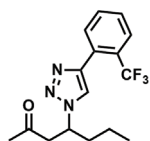


4-(4-(2-(trifluoromethyl)phenyl)-1H-1,2,3-triazol-1-yl)heptan-2-one

4ad

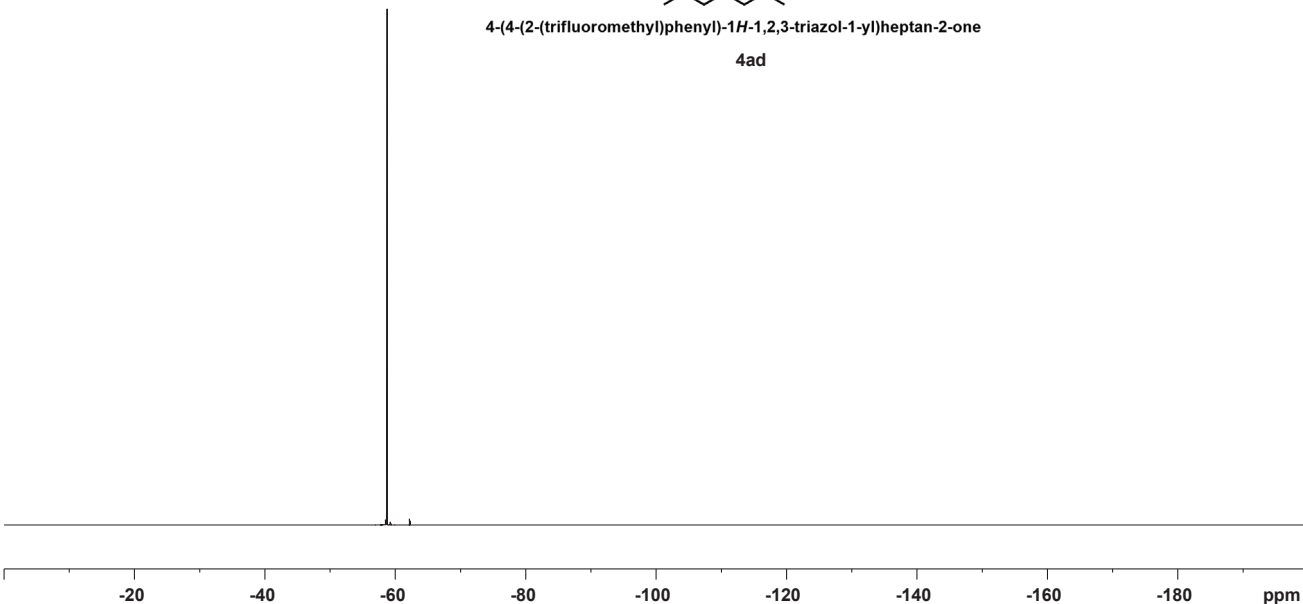


-58.74



4-(4-(2-(trifluoromethyl)phenyl)-1H-1,2,3-triazol-1-yl)heptan-2-one

4ad



— 205.08

143.45
132.00
131.99
131.97
129.70
129.68
129.66
128.24
127.58
126.19
126.14
126.08
126.02
125.53
123.92
123.86
123.81
123.69
122.82

77.48
77.16
76.84

— 57.04

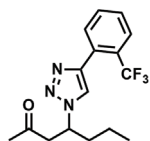
— 48.23

— 37.23

— 30.37

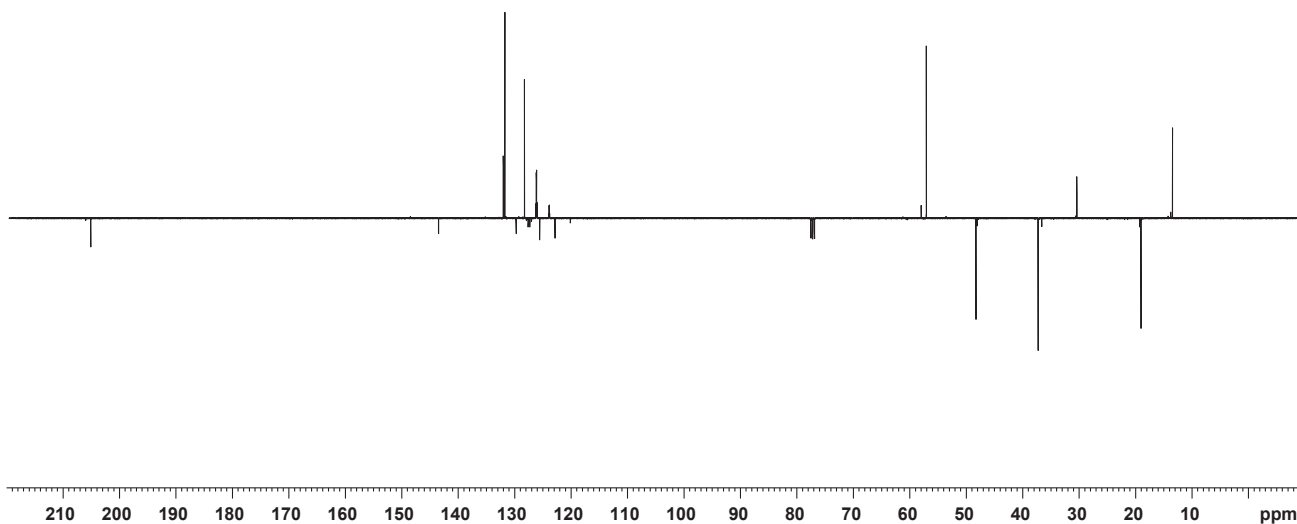
— 19.00

— 13.42



4-(4-(2-(trifluoromethyl)phenyl)-1H-1,2,3-triazol-1-yl)heptan-2-one

4ad



7.92
7.90
7.77
7.72
7.70
7.61
7.59
7.57
7.46
7.44
7.42
7.26

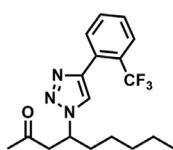
4.95
4.94
4.92
4.91
4.90
4.89

3.43
3.41
3.39
3.37
2.99
2.98
2.94
2.93

2.10
2.01
1.86
1.84

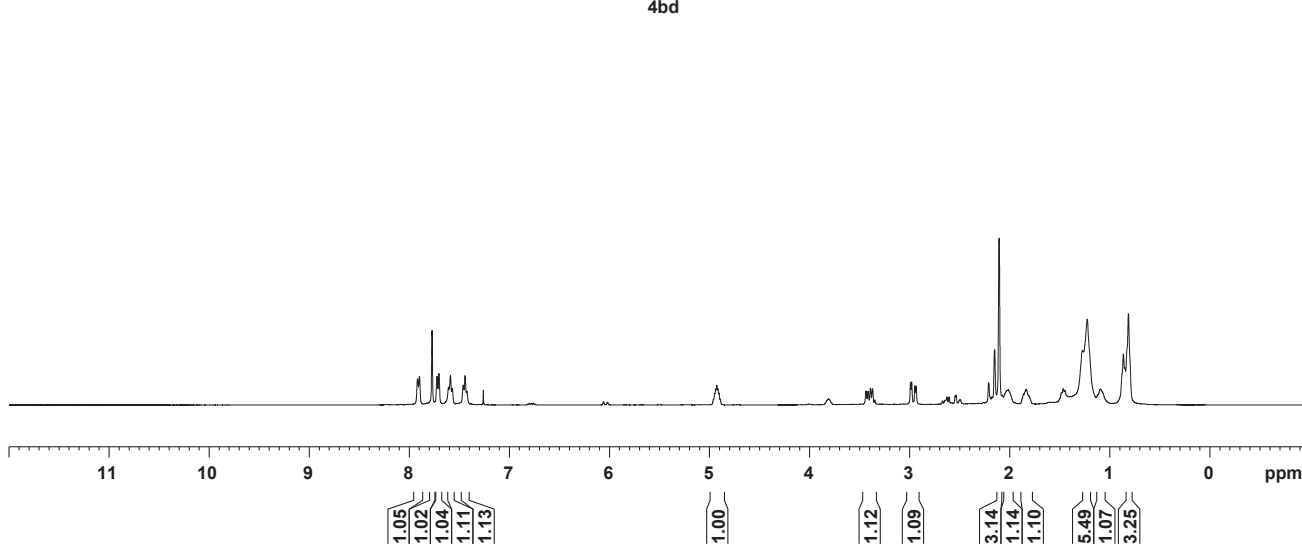
1.22
1.09

— 0.81

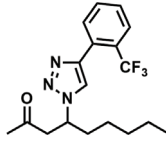


4-(4-(2-(trifluoromethyl)phenyl)-1H-1,2,3-triazol-1-yl)nonan-2-one

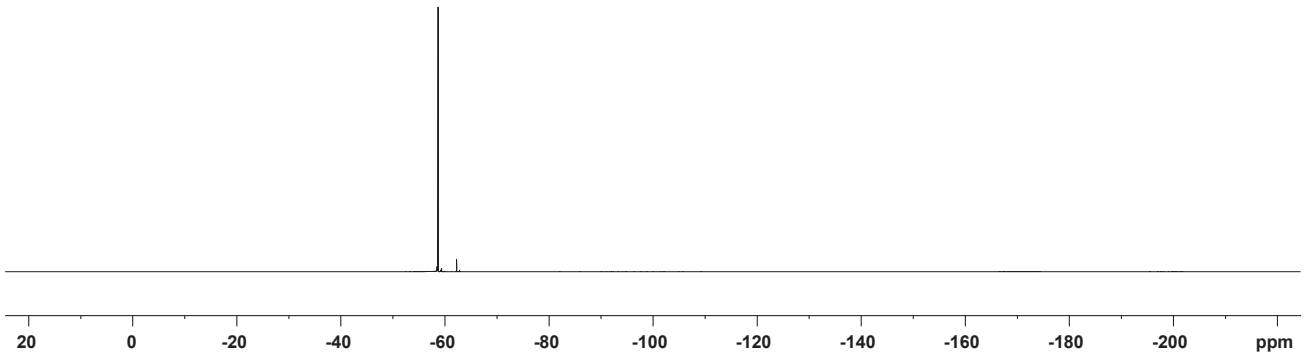
4bd



— 58.73



4-(4-(2-(trifluoromethyl)phenyl)-1H-1,2,3-triazol-1-yl)nonan-2-one
4bd



— 205.19

143.52
132.05
131.79
129.74
128.30
127.39
126.21
126.15
125.59
123.96
122.87

77.48
77.16
76.84

— 57.36

— 48.33

35.25

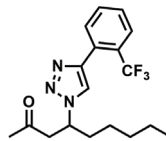
31.17

30.48

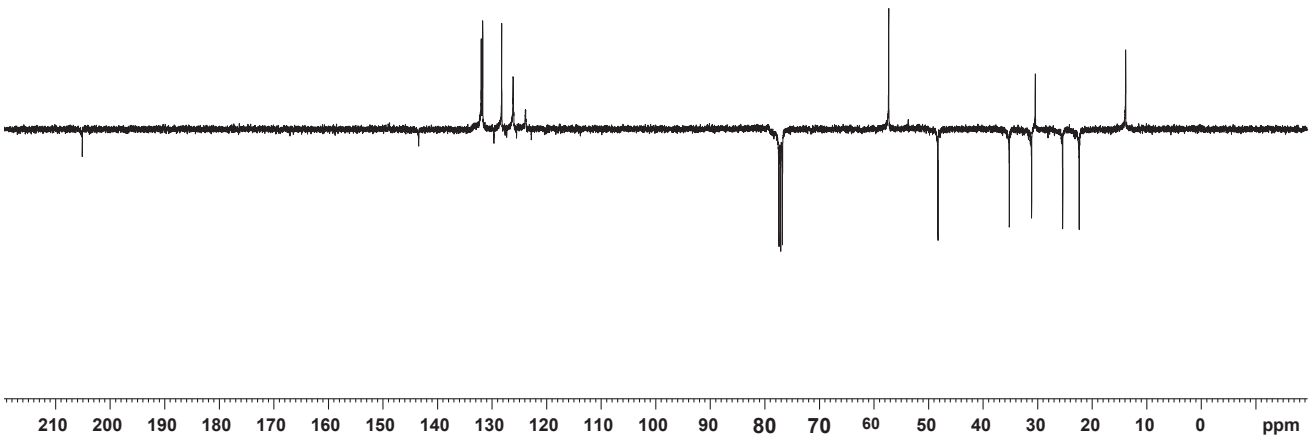
25.48

22.44

— 13.93



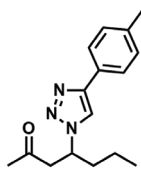
4-(4-(2-(trifluoromethyl)phenyl)-1H-1,2,3-triazol-1-yl)nonan-2-one
4bd



7.75
7.72
7.70
7.26
7.23
7.21

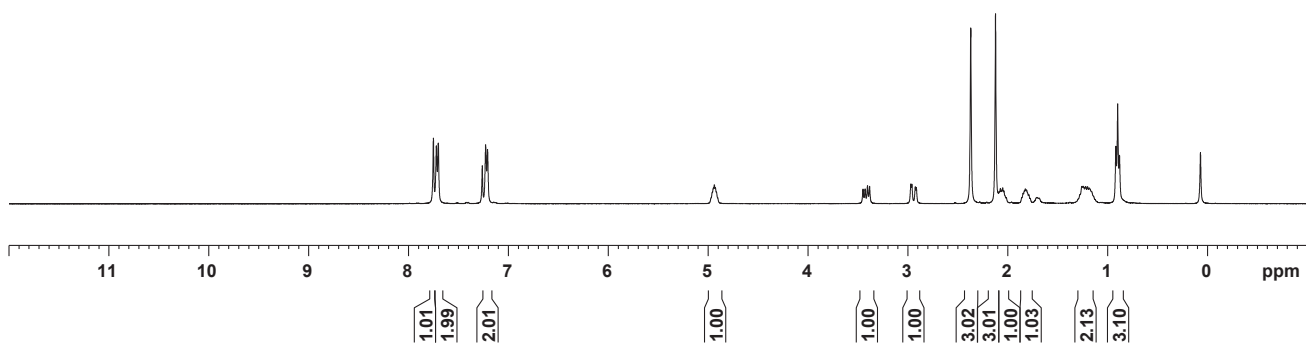
4.95
4.94
4.93

3.45
3.43
3.40
3.38
3.37
3.36
3.35
3.34
3.33
3.32
3.31
3.30
3.29
3.28
3.27
3.26
3.25
3.24
3.23
3.22
3.21
3.20
3.19
3.18
3.17
3.16
3.15
3.14
3.13
3.12
3.11
3.10
3.09
3.08
3.07
3.06
3.05
3.04
3.03
3.02
3.01
3.00
2.99
2.98
2.97
2.96
2.95
2.94
2.93
2.92
2.91
2.90
2.89
2.88
2.87
2.86
2.85
2.84
2.83
2.82
2.81
2.80
2.79
2.78
2.77
2.76
2.75
2.74
2.73
2.72
2.71
2.70
2.69
2.68
2.67
2.66
2.65
2.64
2.63
2.62
2.61
2.60
2.59
2.58
2.57
2.56
2.55
2.54
2.53
2.52
2.51
2.50
2.49
2.48
2.47
2.46
2.45
2.44
2.43
2.42
2.41
2.40
2.39
2.38
2.37
2.36
2.35
2.34
2.33
2.32
2.31
2.30
2.29
2.28
2.27
2.26
2.25
2.24
2.23
2.22
2.21
2.20
2.19
2.18
2.17
2.16
2.15
2.14
2.13
2.12
2.11
2.10
2.09
2.08
2.07
2.06
2.05
2.04
2.03
2.02
2.01
2.00
1.99
1.98
1.97
1.96
1.95
1.94
1.93
1.92
1.91
1.90
1.89
1.88
1.87
1.86
1.85
1.84
1.83
1.82
1.81
1.80
1.79
1.78
1.77
1.76
1.75
1.74
1.73
1.72
1.71
1.70
1.69
1.68
1.67
1.66
1.65
1.64
1.63
1.62
1.61
1.60
1.59
1.58
1.57
1.56
1.55
1.54
1.53
1.52
1.51
1.50
1.49
1.48
1.47
1.46
1.45
1.44
1.43
1.42
1.41
1.40
1.39
1.38
1.37
1.36
1.35
1.34
1.33
1.32
1.31
1.30
1.29
1.28
1.27
1.26
1.25
1.24
1.23
1.22
1.21
1.20
1.19
1.18
1.17
1.16
1.15
1.14
1.13
1.12
1.11
1.10
1.09
1.08
1.07
1.06
1.05
1.04
1.03
1.02
1.01
1.00
0.99
0.98
0.97
0.96
0.95
0.94
0.93
0.92
0.91
0.90
0.89
0.88
0.87
0.86
0.85
0.84
0.83
0.82
0.81
0.80
0.79
0.78
0.77
0.76
0.75
0.74
0.73
0.72
0.71
0.70
0.69
0.68
0.67
0.66
0.65
0.64
0.63
0.62
0.61
0.60
0.59
0.58
0.57
0.56
0.55
0.54
0.53
0.52
0.51
0.50
0.49
0.48
0.47
0.46
0.45
0.44
0.43
0.42
0.41
0.40
0.39
0.38
0.37
0.36
0.35
0.34
0.33
0.32
0.31
0.30
0.29
0.28
0.27
0.26
0.25
0.24
0.23
0.22
0.21
0.20
0.19
0.18
0.17
0.16
0.15
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00



4-(4-(p-tolyl)-1H-1,2,3-triazol-1-yl)heptan-2-one

4ae



— 205.38

— 147.13

— 137.98

— 129.59

— 127.96

— 125.68

— 120.29

— 77.48

— 77.16

— 76.84

— 56.98

— 48.39

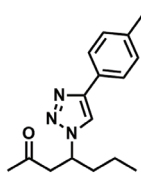
— 37.33

— 30.56

— 21.41

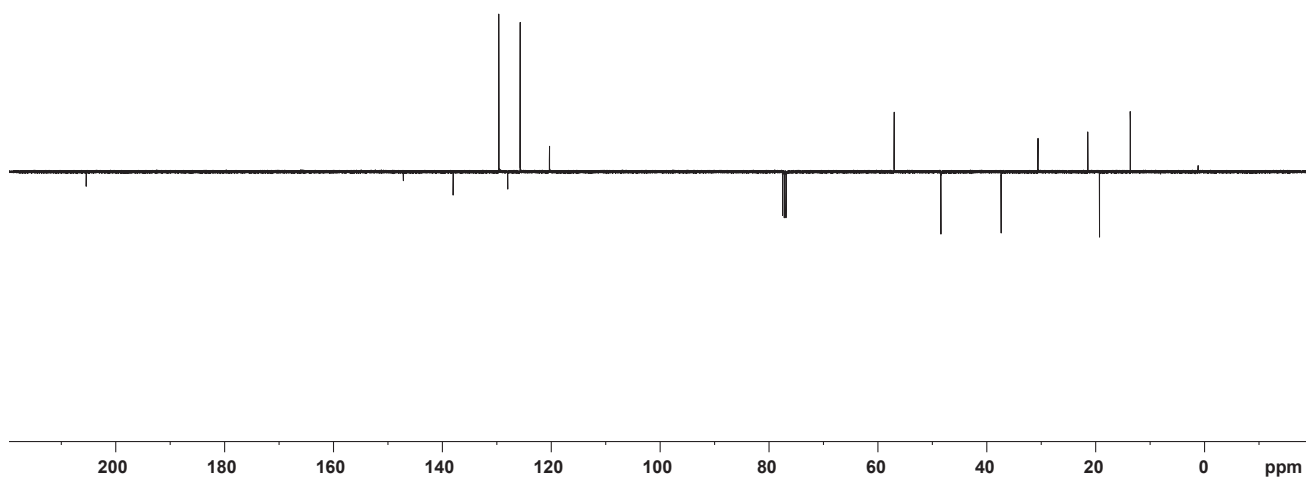
— 19.27

— 13.61



4-(4-(p-tolyl)-1H-1,2,3-triazol-1-yl)heptan-2-one

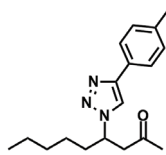
4ae



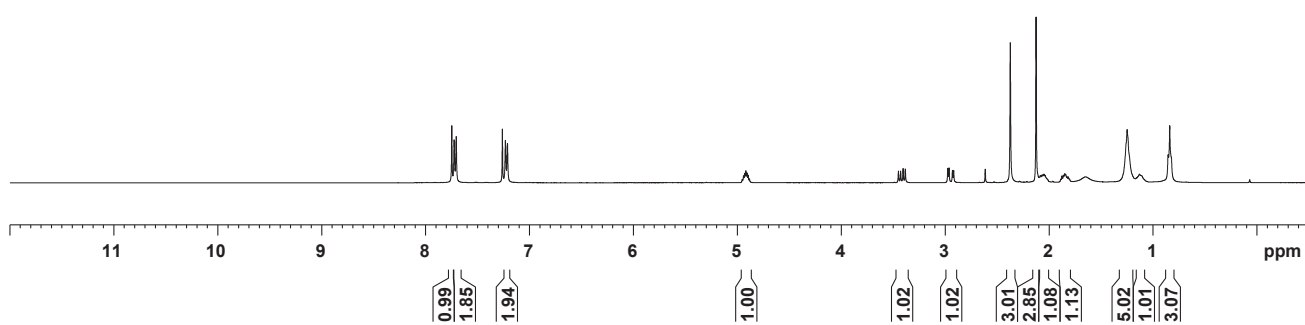
7.75
7.72
7.70
7.26
7.23
7.21

4.05
4.04
4.03
4.02
4.01
4.00

3.45
3.43
3.40
3.38
3.37
3.35
3.33
3.32
3.29
3.28
3.07
3.06
3.05
3.04
2.89
2.87
2.86
2.85
1.84
1.83
1.81
1.75
1.73
1.16
0.85
0.84



4-(4-(p-tolyl)-1H-1,2,3-triazol-1-yl)nonan-2-one
4be

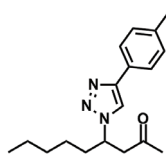


205.42

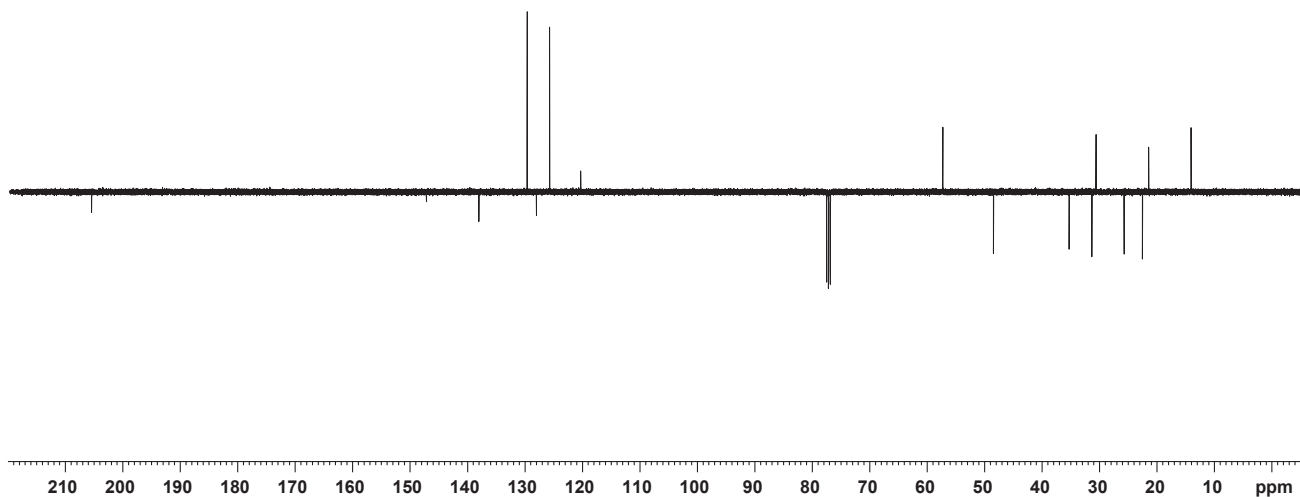
147.13
138.00
129.60
127.07
125.89
120.28

77.47
77.15
76.83

57.26
48.43
35.27
31.31
30.58
25.69
22.50
21.42
14.05

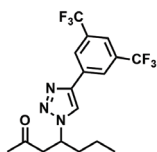


4-(4-(p-tolyl)-1H-1,2,3-triazol-1-yl)nonan-2-one
4be



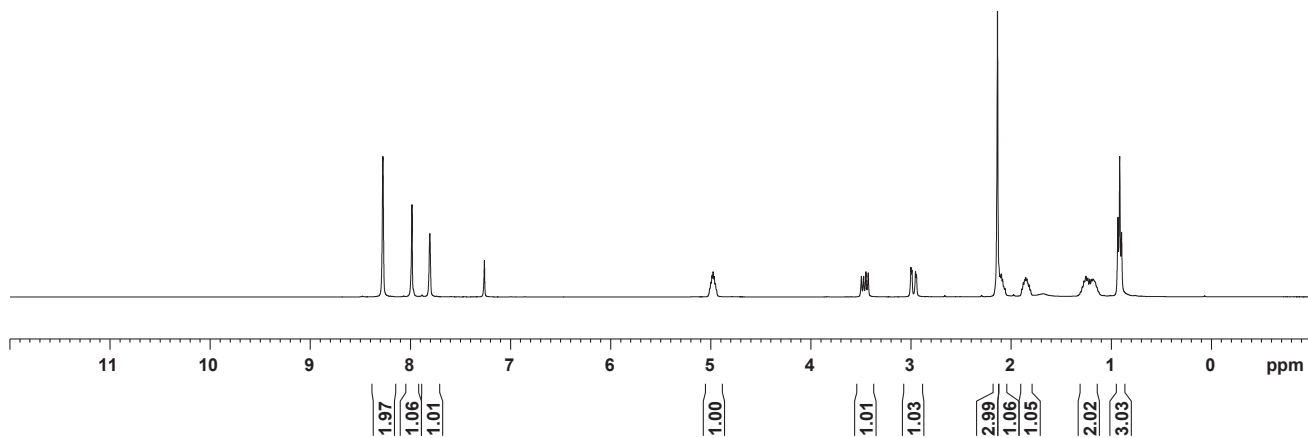
8.27
7.98
7.80
7.26

5.00
4.99
4.97
4.96
4.95
3.49
3.47
3.45
3.43
3.00
2.99
2.95
2.93
2.91
2.88
2.87
2.07
2.06
1.89
1.88
1.86
1.84
1.83
1.82
1.80
1.29
1.27
1.25
1.23
1.19
0.99
0.91
0.89

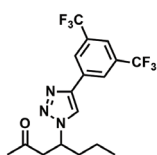


4-(4-(3,5-bis(trifluoromethyl)phenyl)-1H-1,2,3-triazol-1-yl)heptan-2-one

4af

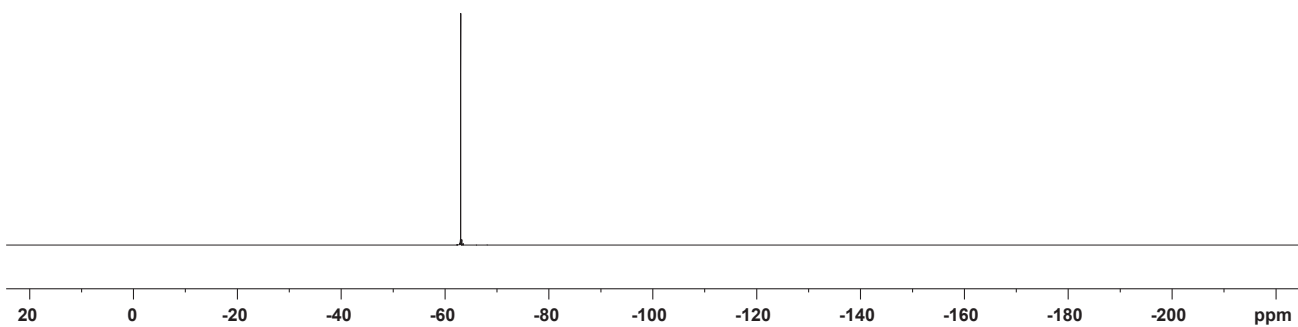


-63.04



4-(4-(3,5-bis(trifluoromethyl)phenyl)-1H-1,2,3-triazol-1-yl)heptan-2-one

4af



— 205.18

144.30
133.00
132.78
132.49
131.78
127.48
125.70
125.69
124.72
122.04
121.52
121.48
121.45
121.41

77.47
77.16
76.84

— 57.40

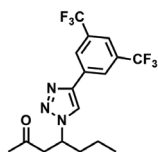
— 48.18

— 37.14

— 30.38

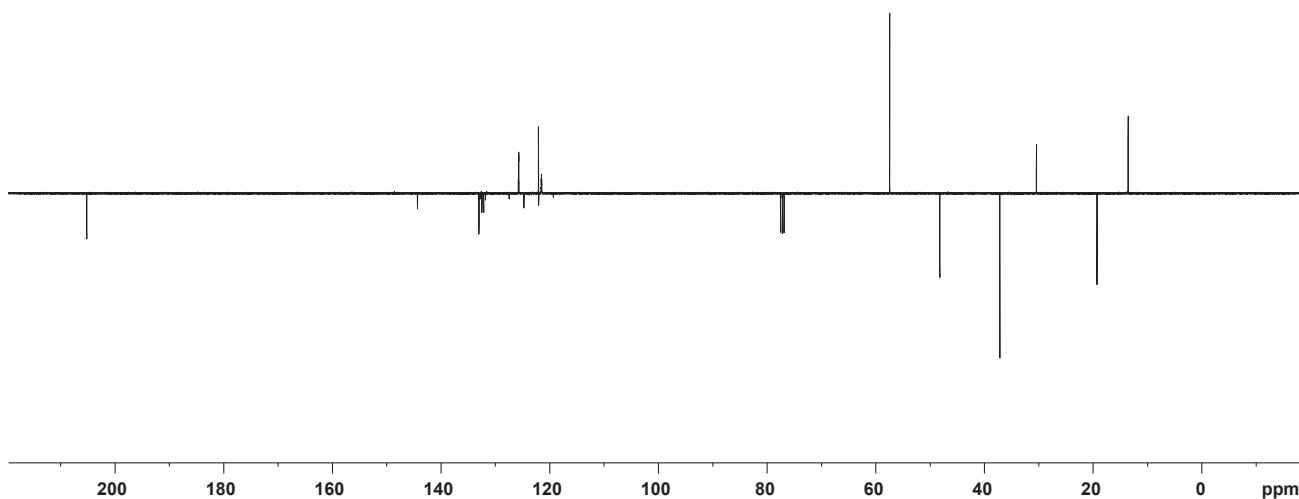
— 19.25

— 13.51



4-(4-(3,5-bis(trifluoromethyl)phenyl)-1H-1,2,3-triazol-1-yl)heptan-2-one

4af



— 8.28

— 7.98

— 7.81

— 7.26

— 4.95

3.49

3.46

3.44

3.42

3.00

2.95

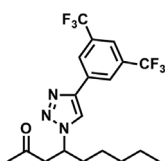
— 2.13

— 1.87

— 1.26

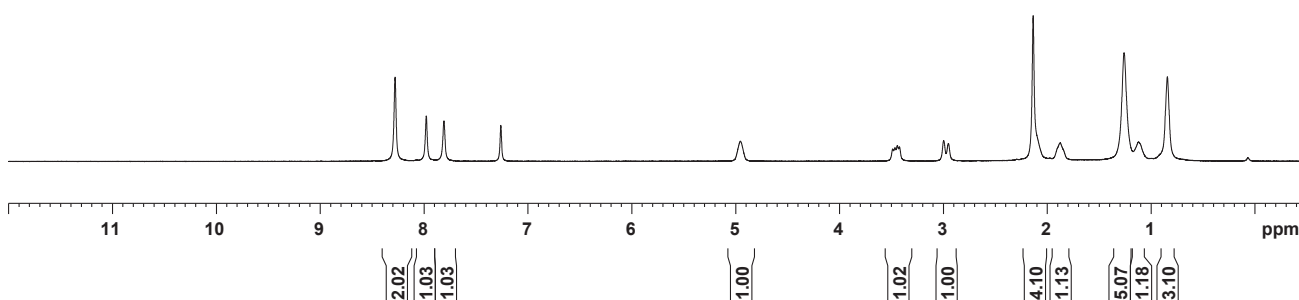
— 1.12

— 0.84

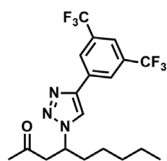


4-(4-(3,5-bis(trifluoromethyl)phenyl)-1H-1,2,3-triazol-1-yl)nonan-2-one

4bf

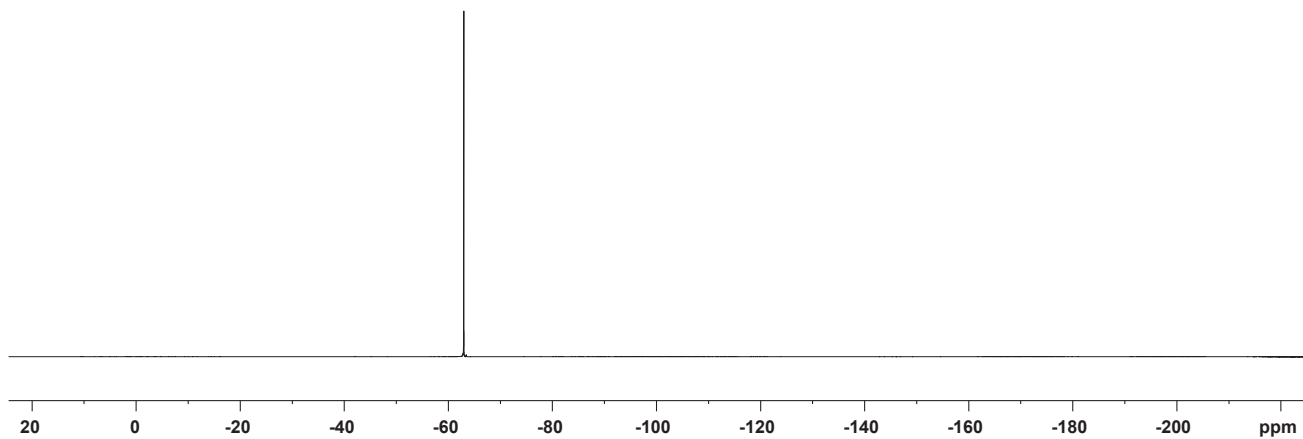


— -63.00



4-(4-(3,5-bis(trifluoromethyl)phenyl)-1H-1,2,3-triazol-1-yl)nonan-2-one

4bf



— 205.22

— 144.34

— 132.99

— 132.50

— 132.17

— 131.94

— 125.71

— 124.96

— 121.59

— 121.51

— 77.48

— 77.16

— 76.84

— 57.70

— 48.27

— 35.11

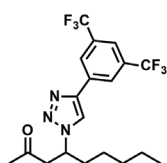
— 31.27

— 30.47

— 25.72

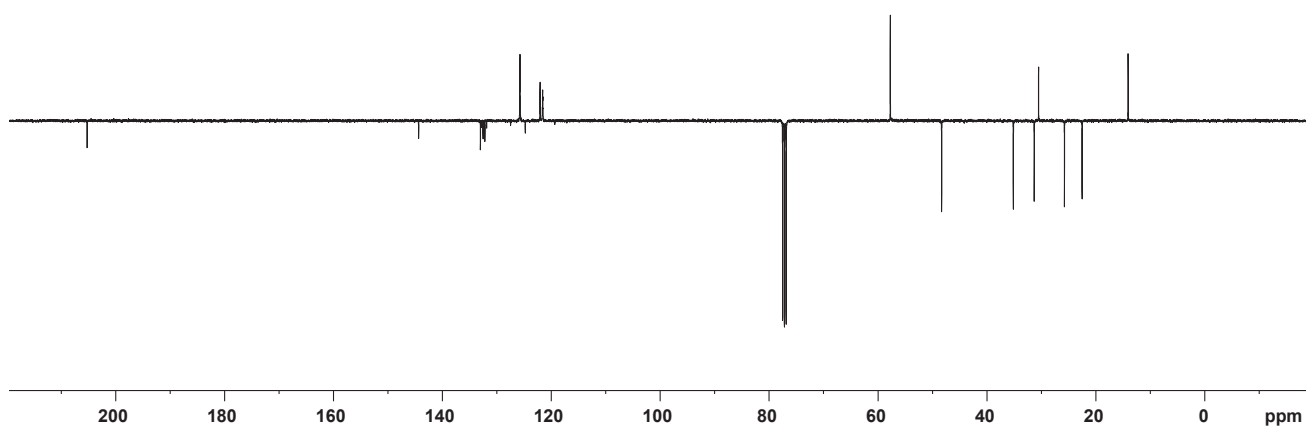
— 22.48

— 14.02



4-(4-(3,5-bis(trifluoromethyl)phenyl)-1H-1,2,3-triazol-1-yl)nonan-2-one

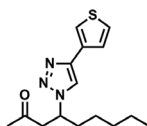
4bf



7.70
7.64
7.43
7.42
7.34
7.26

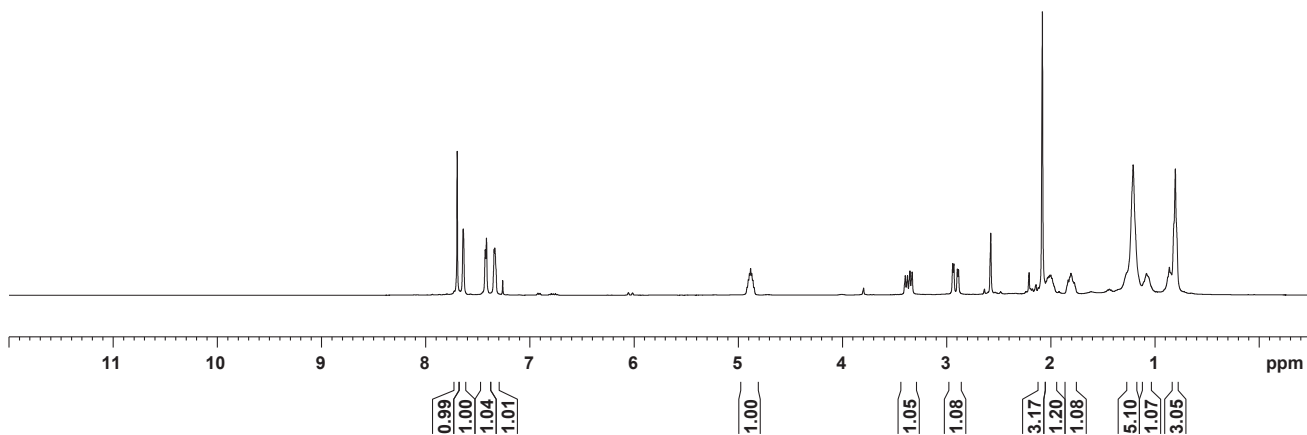
4.91
4.90
4.89
4.88
4.87
4.86

3.39
3.37
3.35
3.33
3.34
2.93
2.88
2.88
2.08
2.03
2.02
2.01
1.83
1.83
1.80
1.77
1.71
1.08
0.80



4-(4-(thiophen-3-yl)-1H-1,2,3-triazol-1-yl)nonan-2-one

4bg



205.35

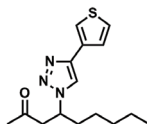
143.23
131.99
126.34
125.91
121.03
120.49

77.47
77.15
76.83

57.24
48.35

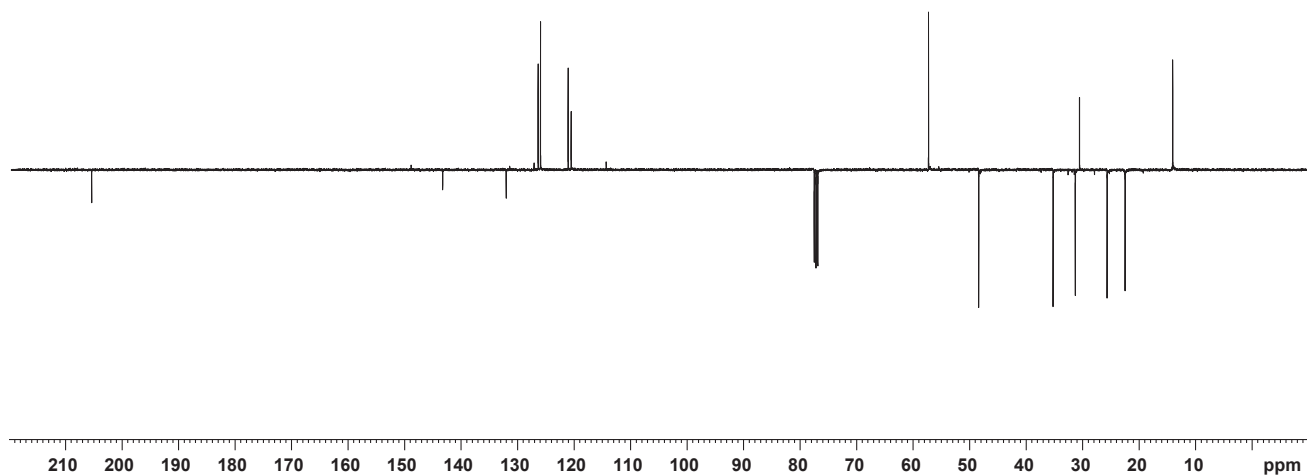
35.19
31.26
30.52
25.64
22.45

14.02

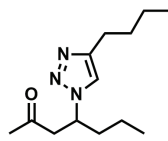


4-(4-(thiophen-3-yl)-1H-1,2,3-triazol-1-yl)nonan-2-one

4bg

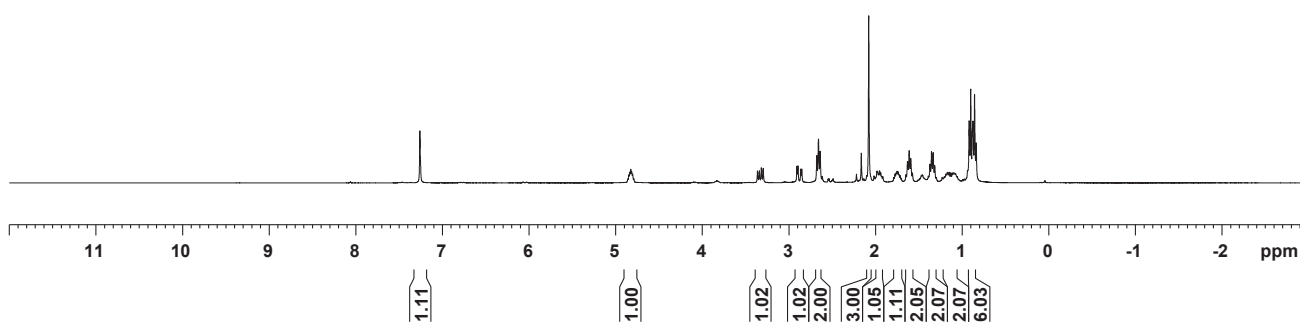


7.26
4.86
4.85
4.83
4.82
4.81
4.79
4.39
3.34
3.30
2.89
2.89
2.88
2.86
2.08
2.08
1.97
1.96
1.95
1.94
1.93
1.91
1.79
1.76
1.75
1.74
1.73
1.71
1.63
1.59
1.39
1.36
1.33
1.17
1.15
1.13
1.11
1.09
1.05
0.92
0.88
0.87
0.84



4-(4-butyl-1H-1,2,3-triazol-1-yl)heptan-2-one

4ah



— 205.50

— 147.71

— 121.48

77.48
77.16
76.84

— 56.66

— 48.42

— 37.40

31.60

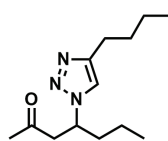
30.52

25.43

22.44

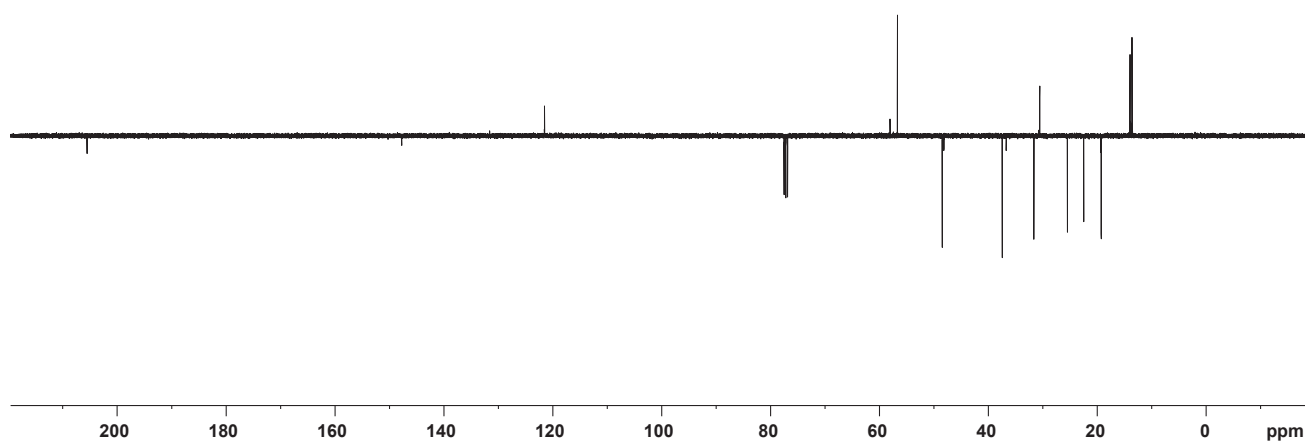
19.23

13.93

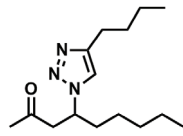


4-(4-butyl-1H-1,2,3-triazol-1-yl)heptan-2-one

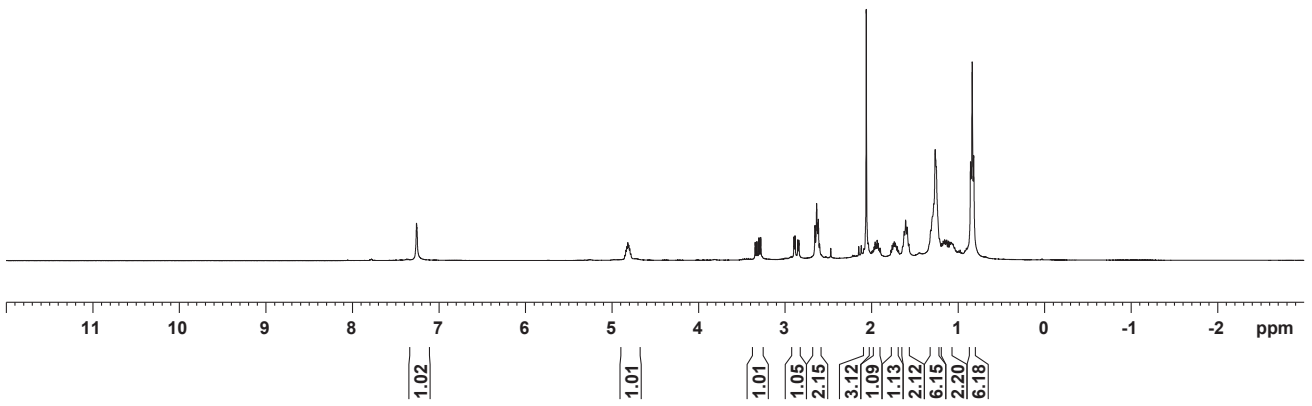
4ah



7.26
4.85
4.44
4.43
4.42
4.40
4.39
4.37
4.34
3.30
3.29
3.08
3.06
3.05
3.04
3.03
3.02
3.01
2.99
2.98
2.97
2.96
2.95
2.94
2.93
2.92
2.91
1.90
1.77
1.76
1.75
1.74
1.72
1.71
1.69
1.68
1.67
1.66
1.65
1.64
1.63
1.62



4-(4-butyl-1H-1,2,3-triazol-1-yl)nonan-2-one
4bh



205.39

147.67

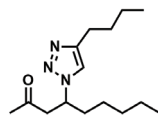
121.42

77.47
77.16
76.84

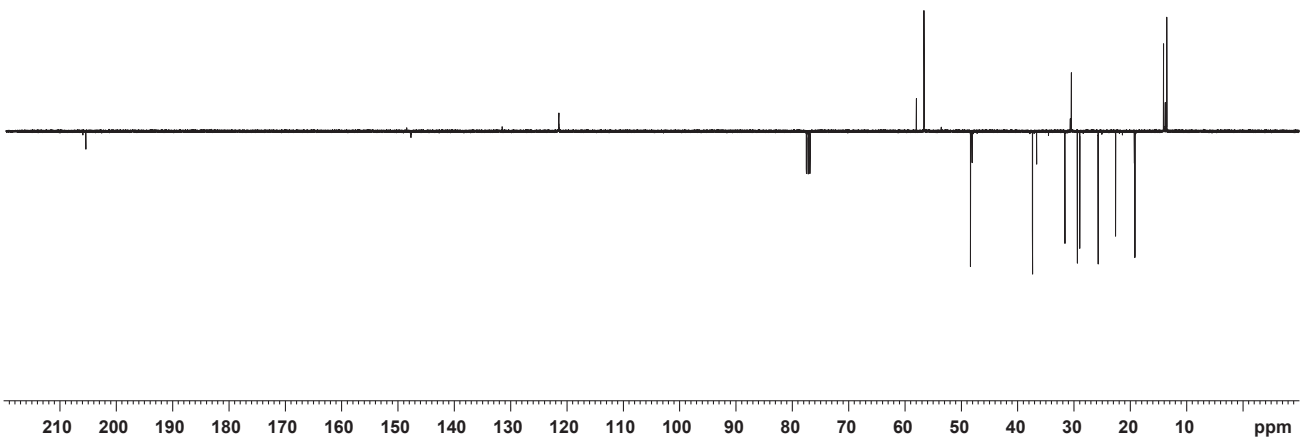
56.59

48.34

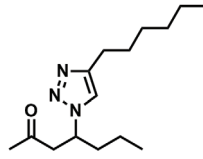
37.33
37.18
30.44
29.21
28.68
28.58
19.75
14.07
13.50



4-(4-butyl-1H-1,2,3-triazol-1-yl)nonan-2-one
4bh

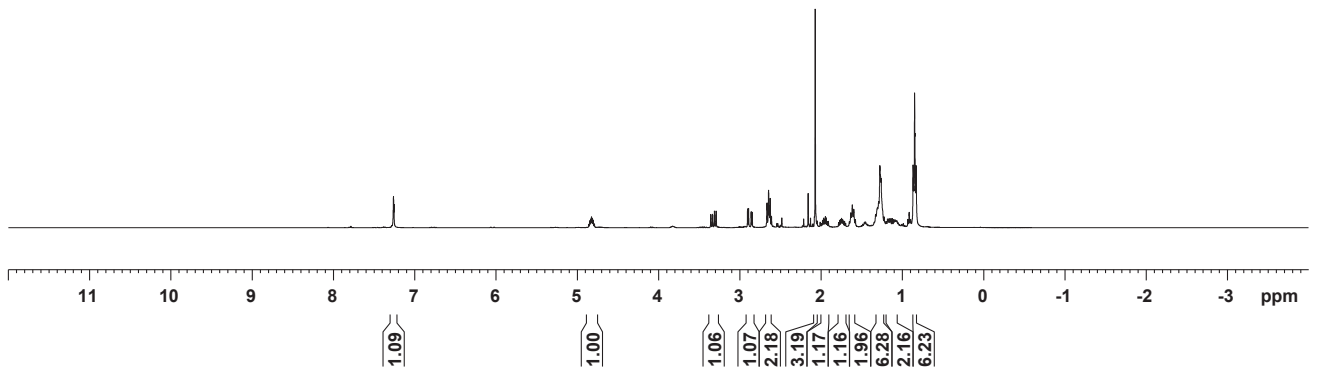


83.61
 77.06
 77.00
 76.94
 44.41
 44.35
 44.29
 44.23
 44.17
 44.11
 44.05
 43.99
 33.31
 33.25
 33.19
 23.00
 22.94
 22.88
 22.82
 22.76
 22.70
 22.64
 22.58
 22.52
 22.46
 22.40
 22.34
 22.28
 22.22
 22.16
 22.10
 22.04
 21.98
 21.92
 21.86
 21.80
 21.74
 21.68
 21.62
 21.56
 21.50
 21.44
 21.38
 21.32
 21.26
 21.20
 21.14
 21.08
 21.02
 20.96
 20.90
 20.84
 20.78
 20.72
 20.66
 20.60
 20.54
 20.48
 20.42
 20.36
 20.30
 20.24
 20.18
 20.12
 20.06
 20.00
 19.94
 19.88
 19.82
 19.76
 19.70
 19.64
 19.58
 19.52
 19.46
 19.40
 19.34
 19.28
 19.22
 19.16
 19.10
 19.04
 18.98
 18.92
 18.86
 18.80
 18.74
 18.68
 18.62
 18.56
 18.50
 18.44
 18.38
 18.32
 18.26
 18.20
 18.14
 18.08
 18.02
 17.96
 17.90
 17.84
 17.78
 17.72
 17.66
 17.60
 17.54
 17.48
 17.42
 17.36
 17.30
 17.24
 17.18
 17.12
 17.06
 17.00
 16.94
 16.88
 16.82
 16.76
 16.70
 16.64
 16.58
 16.52
 16.46
 16.40
 16.34
 16.28
 16.22
 16.16
 16.10
 16.04
 15.98
 15.92
 15.86
 15.80
 15.74
 15.68
 15.62
 15.56
 15.50
 15.44
 15.38
 15.32
 15.26
 15.20
 15.14
 15.08
 15.02
 14.96
 14.90
 14.84
 14.78
 14.72
 14.66
 14.60
 14.54
 14.48
 14.42
 14.36
 14.30
 14.24
 14.18
 14.12
 14.06
 14.00
 13.94
 13.88
 13.82
 13.76
 13.70
 13.64
 13.58
 13.52
 13.46
 13.40
 13.34
 13.28
 13.22
 13.16
 13.10
 13.04
 12.98
 12.92
 12.86
 12.80
 12.74
 12.68
 12.62
 12.56
 12.50
 12.44
 12.38
 12.32
 12.26
 12.20
 12.14
 12.08
 12.02
 11.96
 11.90
 11.84
 11.78
 11.72
 11.66
 11.60
 11.54
 11.48
 11.42
 11.36
 11.30
 11.24
 11.18
 11.12
 11.06
 11.00
 10.94
 10.88
 10.82
 10.76
 10.70
 10.64
 10.58
 10.52
 10.46
 10.40
 10.34
 10.28
 10.22
 10.16
 10.10
 10.04
 9.98
 9.92
 9.86
 9.80
 9.74
 9.68
 9.62
 9.56
 9.50
 9.44
 9.38
 9.32
 9.26
 9.20
 9.14
 9.08
 9.02
 8.96
 8.90
 8.84
 8.78
 8.72
 8.66
 8.60
 8.54
 8.48
 8.42
 8.36
 8.30
 8.24
 8.18
 8.12
 8.06
 8.00
 7.94
 7.88
 7.82
 7.76
 7.70
 7.64
 7.58
 7.52
 7.46
 7.40
 7.34
 7.28
 7.22
 7.16
 7.10
 7.04
 6.98
 6.92
 6.86
 6.80
 6.74
 6.68
 6.62
 6.56
 6.50
 6.44
 6.38
 6.32
 6.26
 6.20
 6.14
 6.08
 6.02
 5.96
 5.90
 5.84
 5.78
 5.72
 5.66
 5.60
 5.54
 5.48
 5.42
 5.36
 5.30
 5.24
 5.18
 5.12
 5.06
 5.00
 4.94
 4.88
 4.82
 4.76
 4.70
 4.64
 4.58
 4.52
 4.46
 4.40
 4.34
 4.28
 4.22
 4.16
 4.10
 4.04
 3.98
 3.92
 3.86
 3.80
 3.74
 3.68
 3.62
 3.56
 3.50
 3.44
 3.38
 3.32
 3.26
 3.20
 3.14
 3.08
 3.02
 2.96
 2.90
 2.84
 2.78
 2.72
 2.66
 2.60
 2.54
 2.48
 2.42
 2.36
 2.30
 2.24
 2.18
 2.12
 2.06
 2.00
 1.94
 1.88
 1.82
 1.76
 1.70
 1.64
 1.58
 1.52
 1.46
 1.40
 1.34
 1.28
 1.22
 1.16
 1.10
 1.04
 1.00
 0.94
 0.88
 0.82
 0.76
 0.70
 0.64
 0.58
 0.52
 0.46
 0.40
 0.34
 0.28
 0.22
 0.16
 0.10
 0.04
 0.00
 -0.04
 -0.08
 -0.12
 -0.16
 -0.20
 -0.24
 -0.28
 -0.32
 -0.36
 -0.40
 -0.44
 -0.48
 -0.52
 -0.56
 -0.60
 -0.64
 -0.68
 -0.72
 -0.76
 -0.80
 -0.84
 -0.88
 -0.92
 -0.96
 -1.00
 -1.04
 -1.08
 -1.12
 -1.16
 -1.20
 -1.24
 -1.28
 -1.32
 -1.36
 -1.40
 -1.44
 -1.48
 -1.52
 -1.56
 -1.60
 -1.64
 -1.68
 -1.72
 -1.76
 -1.80
 -1.84
 -1.88
 -1.92
 -1.96
 -2.00
 -2.04
 -2.08
 -2.12
 -2.16
 -2.20
 -2.24
 -2.28
 -2.32
 -2.36
 -2.40
 -2.44
 -2.48
 -2.52
 -2.56
 -2.60
 -2.64
 -2.68
 -2.72
 -2.76
 -2.80
 -2.84
 -2.88
 -2.92
 -2.96
 -3.00



4-(4-hexyl-1H-1,2,3-triazol-1-yl)heptan-2-one

4ai



205.42

128.84

121.51

77.47
77.16
76.84

56.62

48.37

37.35

31.07

30.49

28.97

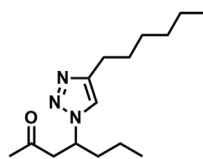
26.72

22.60

19.17

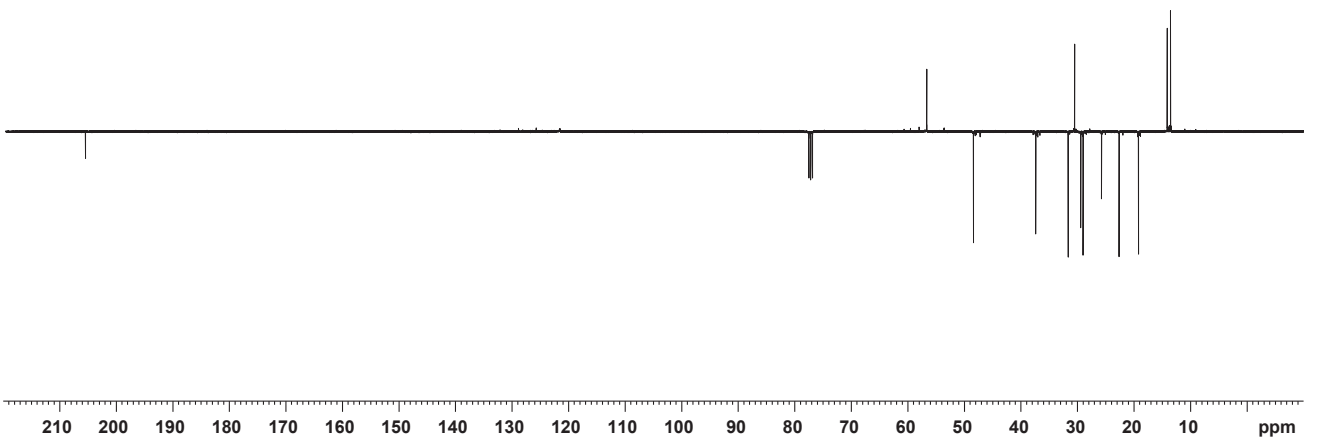
14.10

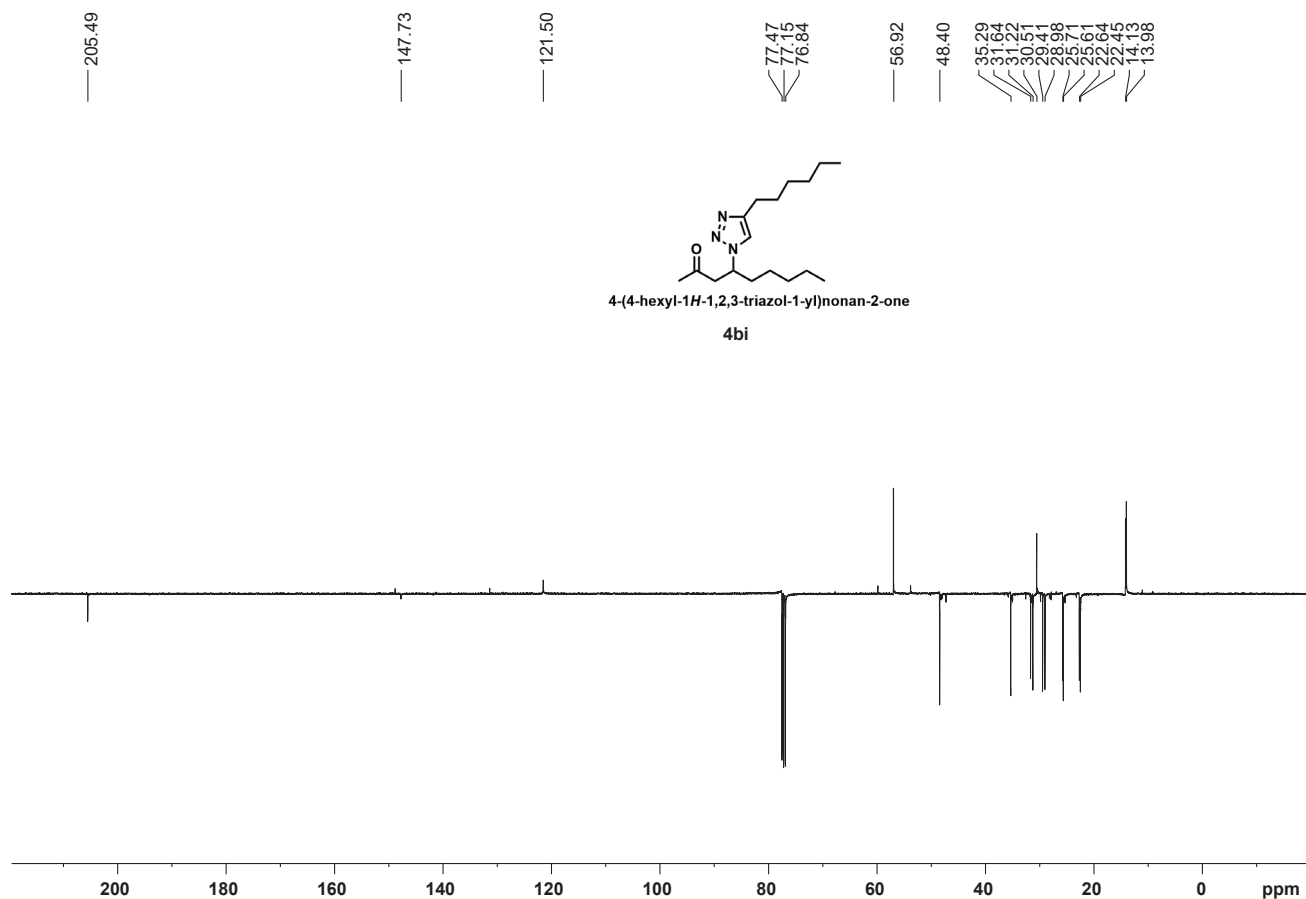
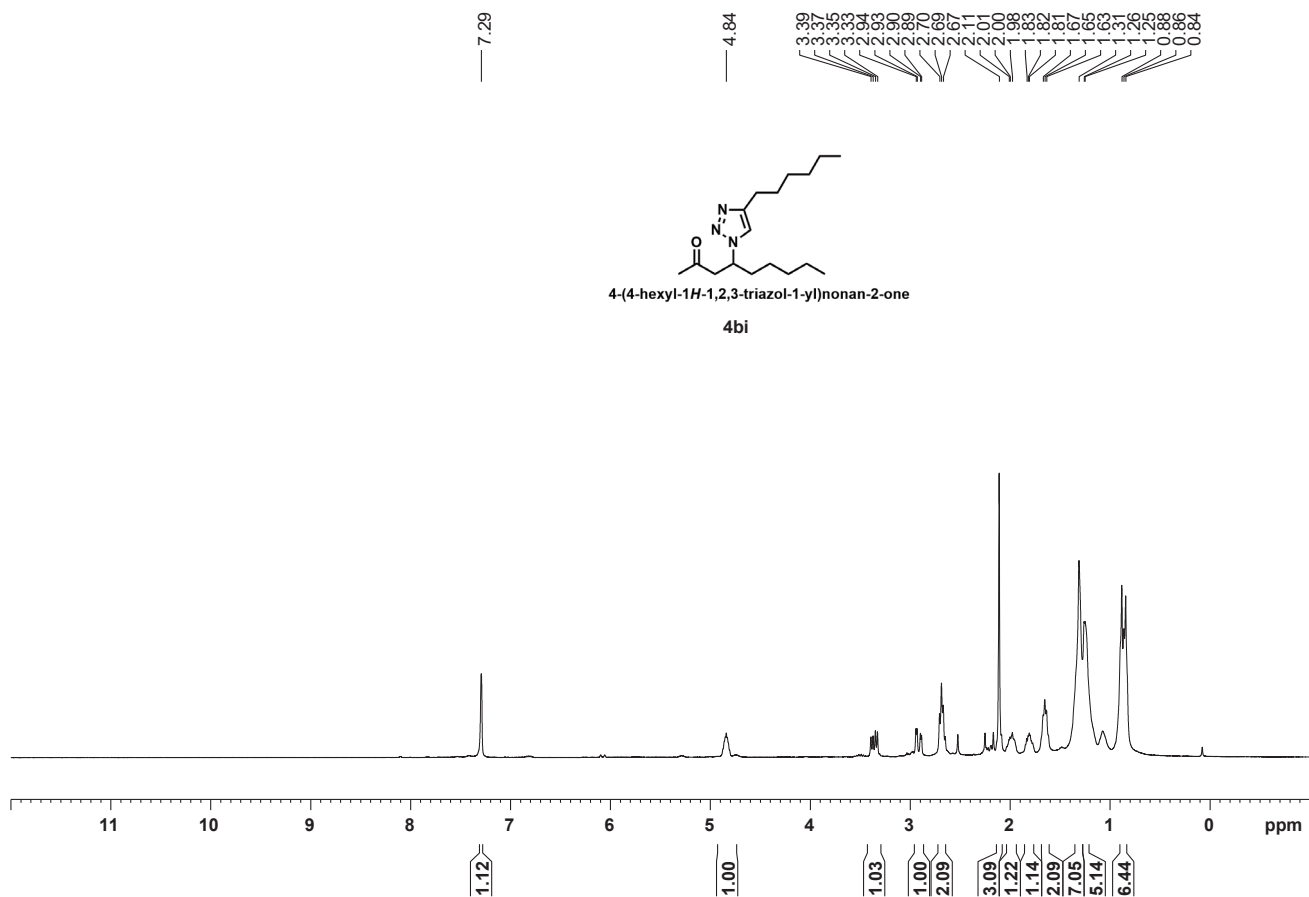
13.52



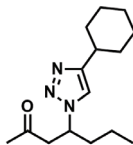
4-(4-hexyl-1H-1,2,3-triazol-1-yl)heptan-2-one

4ai



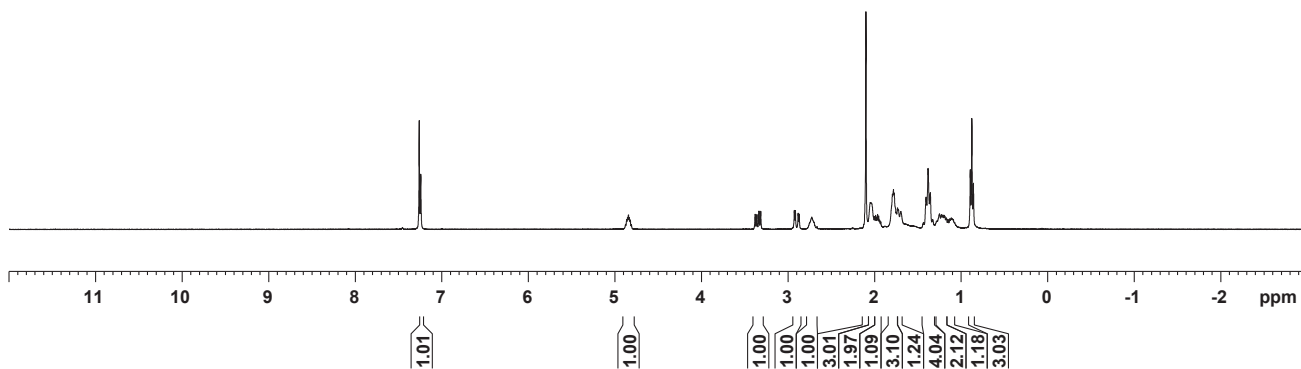


7.26
7.24
4.88
4.86
4.85
4.84
4.83
4.82
4.81
3.98
3.96
3.93
3.92
3.91
3.90
3.89
3.88
3.87
3.86
3.85
3.84
3.83
3.82
3.81
3.80
3.79
3.78
3.77
3.76
3.75
3.74
3.73
3.72
3.71
3.70
3.69
3.68
3.67
3.66
3.65
3.64
3.63
3.62
3.61
3.60
3.59
3.58
3.57
3.56
3.55
3.54
3.53
3.52
3.51
3.50
3.49
3.48
3.47
3.46
3.45
3.44
3.43
3.42
3.41
3.40
3.39
3.38
3.37
3.36
3.35
3.34
3.33
3.32
3.31
3.30
3.29
3.28
3.27
3.26
3.25
3.24
3.23
3.22
3.21
3.20
3.19
3.18
3.17
3.16
3.15
3.14
3.13
3.12
3.11
3.10
3.09
3.08
3.07
3.06
3.05
3.04
3.03
3.02
3.01
3.00
2.99
2.98
2.97
2.96
2.95
2.94
2.93
2.92
2.91
2.90
2.89
2.88
2.87
2.86



4-(4-cyclohexyl-1H-1,2,3-triazol-1-yl)heptan-2-one

4aj



205.56

153.04

120.14

77.48
77.00
76.84

56.72

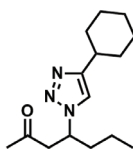
48.45

37.48
35.37
33.13

26.29
26.21

19.29

13.63



4-(4-cyclohexyl-1H-1,2,3-triazol-1-yl)heptan-2-one

4aj

