Electronic Supplementary Material (ESI) for ChemComm.

Supplementary Information

Azide-Alkyne Cycloadditions in a Vortex Fluidic Device: Enhanced "On Water" Effects and Catalysis in Flow

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Table of contents

General considerations.

All NMR experiments were performed on a 600 MHz Bruker advance spectrometers using $CDCl_3$ as the solvent, as specified. Spectra were acquired using a relaxation delay time of 4 seconds. All chemical shifts are presented in ppm and referenced to the solvent. All solvents and reagents were used as received from commercial suppliers, except for benzyl azide derivates which were synthesized from the corresponding benzyl halide by a bimolecular nucleophilic substitution reaction (S_N2), employing NaN_3 and DMF as the nucleophile and solvent respectively. Trifluoromethyl-α,β-ynones was synthesized according to known procedures.[1] All triazole products are known compounds and have been reported in the literature (see page S8-S9 for references).

The vortex fluidic device (VFD) is modular in nature, thus this device can have many configurations. Unless otherwise specified, throughout this report the following specifications were used. The tube used was a borosilicate glass, 19 cm long with a 20 mm or 10 mm outer diameter (OD), as specified. “Confined mode” refers to the mode of operation where a finite amount of reagent is reacted within the tube, “continuous flow” refers to mode of operation where reagents are delivered via a 2 mm outer diameter stainless steel or copper jet feed (as specified) to the base of the rotating tube, with the reaction mixture collected after exiting the tube. Liquid reagents were delivered using syringe pumps, with a borosilicate glass syringe and plunger, and stainless steel 17 G needles. The rotating tube was always operated at a 45° tilt angle (θ).

Catalyst-free azide-alkyne cycloadditions

General procedures for batch reactions and VFD confined mode reactions:

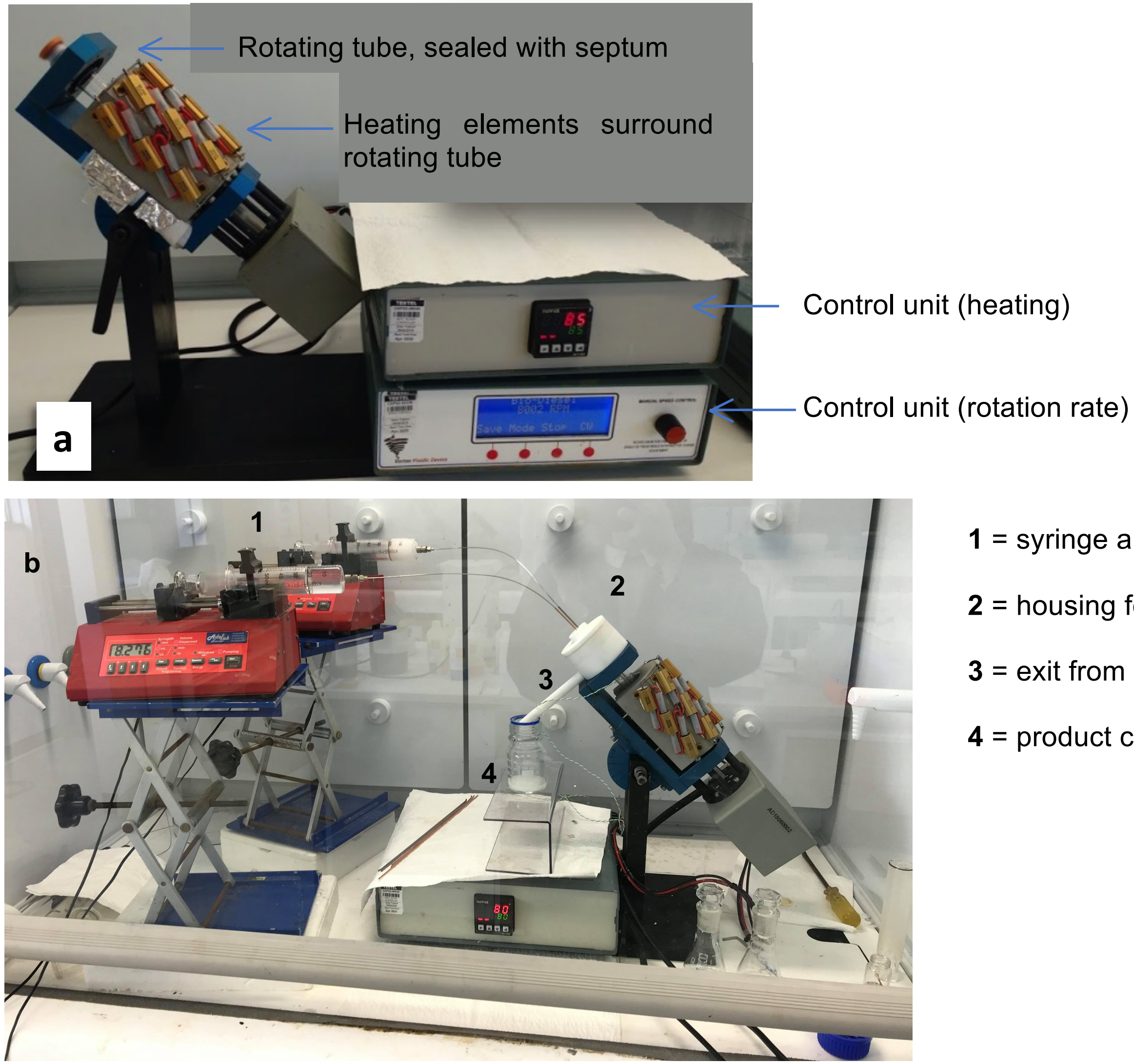
(a) – Batch procedure for catalyst-free reaction of benzyl azide and trifluoromethyl-α,β-ynones at 80 °C

Benzyl azide (0.25 mmol), alkyne (0.3 mmol) and 0.5 mL of solvent (water or acetonitrile) were added sequentially in a 20 mm outer diameter VFD reaction tube. The tube was sealed with a rubber stopper and stirred with a magnetic stirrer bar for 1h at 80 °C using an oil bath. After this time, the organic material was extracted with $CDCl_3$ and analyzed by ^1H NMR spectroscopy using 1,3,5-trimethoxy benzene as internal standard to assess mass balance.

(b) – VFD Confined mode procedure for the catalyst-free reaction of benzyl azide and trifluoromethyl-α,β-ynones at 80 °C

The cycloaddition reaction was carried out using the confined mode of operation of the VFD. Benzyl azide (0.25 mmol), alkyne (0.3 mmol) and 0.5 mL of solvent (water or acetonitrile) were added sequentially in a 20 mm O.D reaction tube. The tube was sealed with a rubber stopper and the VFD was operated between 3k-9k rpm for 1h at 80 °C, with the tube set at 45° tilt angle. The organic material was extracted with $CDCl_3$ and analyzed by ^1H NMR spectroscopy using 1,3,5-trimethoxy benzene as internal standard to assess mass balance. These experiments were performed in triplicate and the average yield of the three runs is reported. The average ratio of the triazole regioisomers is also reported.

Figure S1. Vortex Fluidic Device operating in (a) confined mode and (b) continuous mode at 80°C.

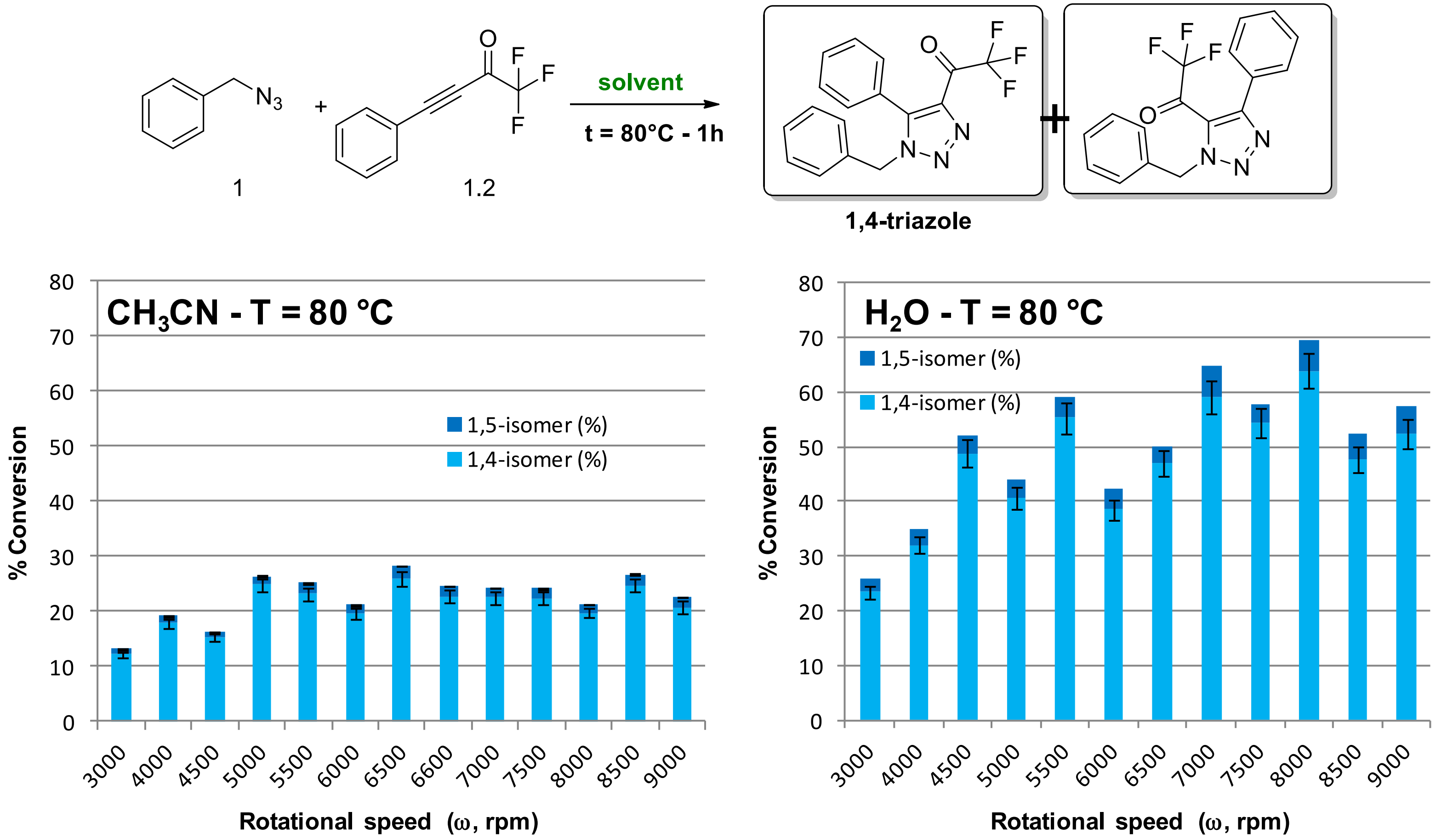


1 = syringe and syringe pump to deliver reagents to VFD

2 = housing for delivery of reagents to rotating VFD tube

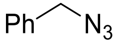
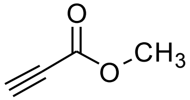
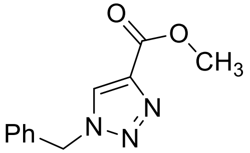
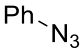
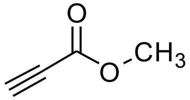
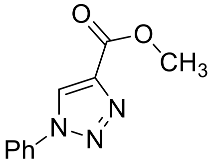
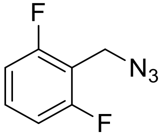
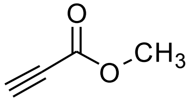
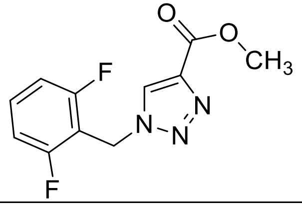
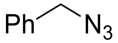
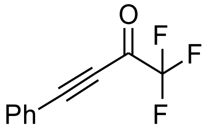
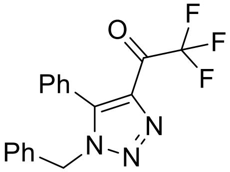
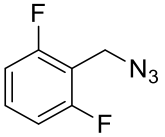
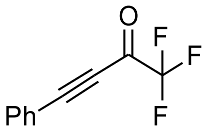
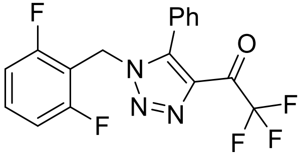
3 = exit from rotating VFD tube

4 = product collection vessel



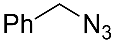
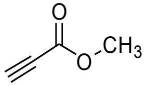
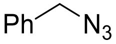
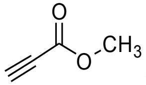
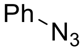
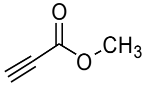
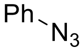
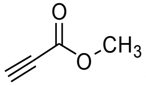
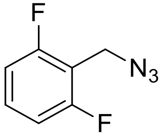
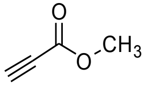
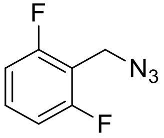
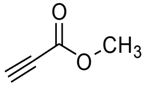
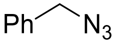
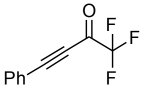
Scheme 1. Effect of rotational speed (ω) and solvent in the confined mode of operation of the VFD with the tube inclined at 45°, at 80 °C, for the reaction between benzyl azide (0.25 mmol) and trifluoromethyl-α,β-ynones (0.3 mmol).

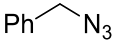
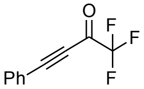
Table S1. Comparative synthesis of 1,2,3-triazoles under catalyst-free conditions in confined mode VFD and in batch at 80 °C.[a]

Entry	Azide	Alkyne	Product (1,4-isomer)	% Conversion[b]		1,4-/1,5-isomer	
				Batch	VFD (8k rpm)	Batch	VFD
1				50	91 ± 2	5.0	5.6
2				14	82 ± 1	4.5	7
3				41	86 ± 3	5.6	6.1
4				27	70 ± 4	7.9	11.1
5				31	42 ± 2	7.0	7.4

[a] Reaction conditions: azide (1 equiv, 0.25 mmol), alkyne (1.2 equiv, 0.3 mmol) in 0.5 mL H_2O at 80 °C for 1h in batch or in VFD following the procedure A. [b] Conversion was calculated by using ^1H NMR spectroscopy with the use of 1,3,5-trimethoxy benzene as internal standard.

Table S2. Comparison of VFD and reported synthesis of 1,2,3-triazoles.

t (h)	T (°C)	Azide	Alkyne (equiv.)	% Conversion[b]	1,4/1,5 isomer	Condition	Reference
1	80		 (1.2)	91	5.6	water - VFD (8k rpm)	This work
0.5	140		 (2)	99	2.5	NMP - 400bar	Hessel [d]
1	80		 (1.2)	82	7	water - VFD (8k rpm)	This work
0.5	140		 (2)	99	3.5	NMP - 400bar	Hessel [d]
1	80		 (1.2)	86	6.1	water - VFD (8k rpm)	This work
24	90		 (2)	84	6.3	NMP - 1800bar (autoclave)	Hessel [d]
1	80		 (1.2)	70	11.1	water - VFD (8k rpm)	This work

7	80		 (1)	58	10.1	DMSO	Nenajdenk[c]

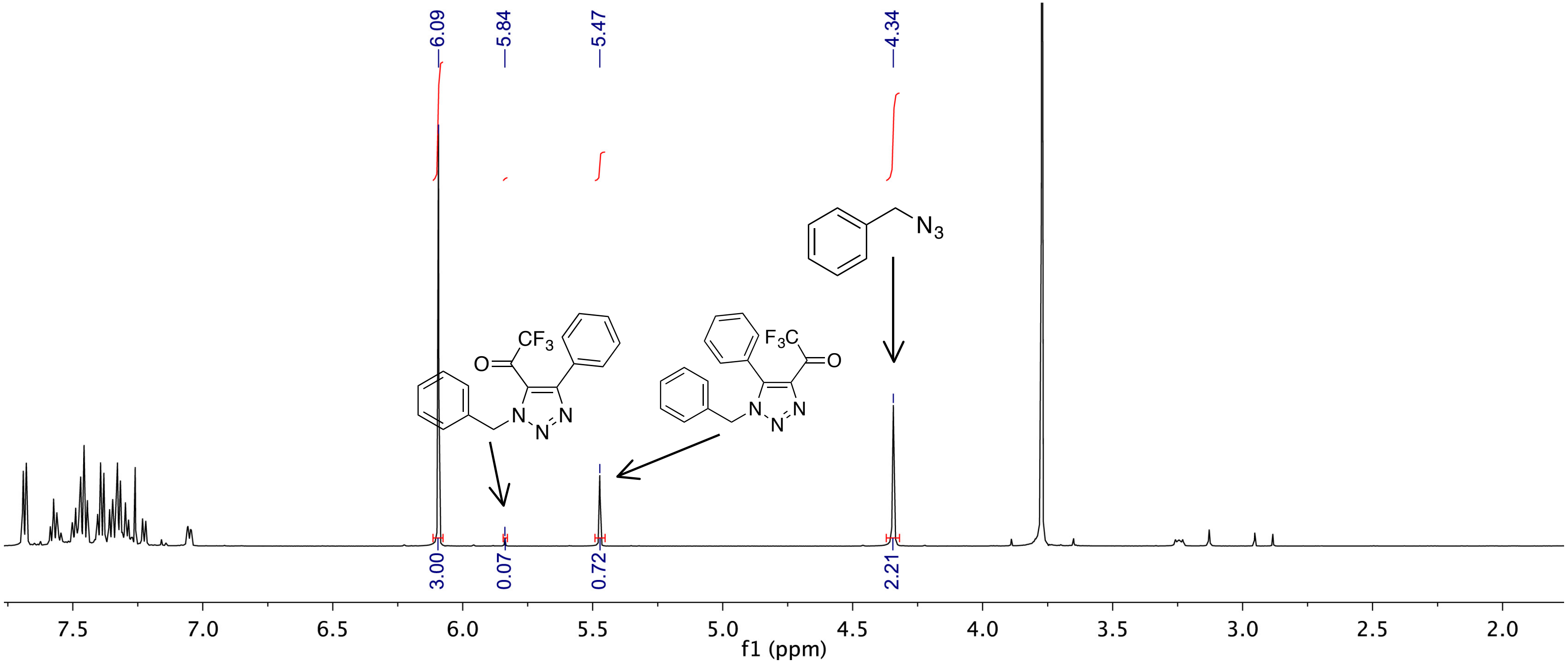
[a] Reaction conditions of this work: azide (1 equiv, 0.25 mmol), alkyne (ene) (1.2 equiv, 0.3 mmol) in 0.5mL H_2O in Batch or in VFD under confined mode. [b] Conversion was calculated by using ^{1}H NMR spectroscopy with the use of 1,3,5-trimethoxy benzene as internal standard. [c] *Mendeleev Commun.*, **2018**, *28*, 17 [d] *ChemSusChem* **2015**, *8*, 504.

Control (neat): VFD Confined mode procedure for the catalyst-free reaction of benzyl azide and trifluoromethyl-α,β-ynones at 80 °C

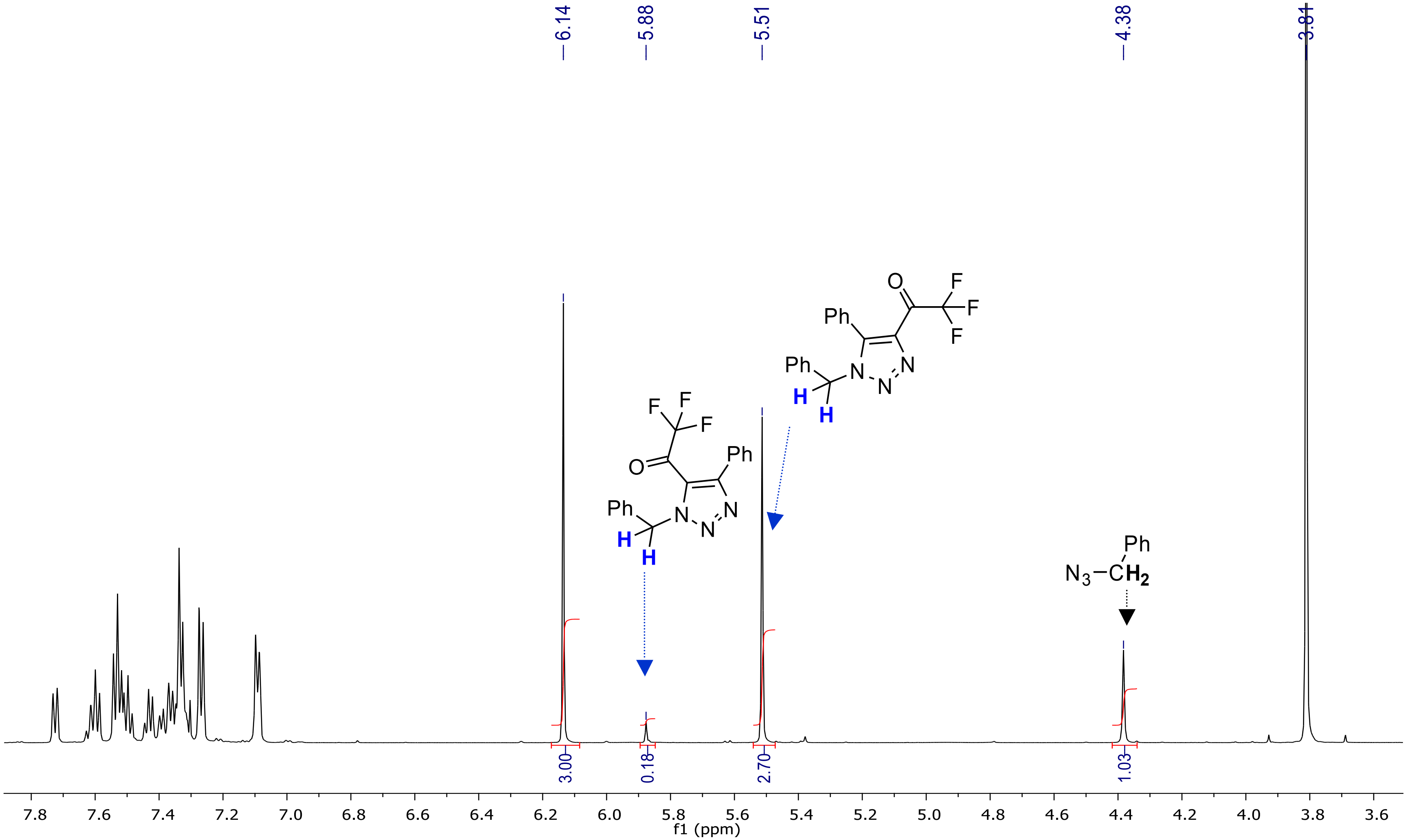
The cycloaddition reaction was carried out using the confined mode of operation of the VFD. Benzyl azide (0.25 mmol), alkyne (0.3 mmol) were added sequentially in a 20 mm O.D reaction tube. The tube was sealed with a rubber stopper and the VFD was operated at 8k rpm for 1h at 80° C, with the tube set at 45° tilt angle. The organic material was analyzed by ^{1}H NMR spectroscopy (in $CDCl_3$) using 1,3,5-trimethoxy benzene as internal standard to assess mass balance. These experiments were performed in triplicate and the average yield of the three runs is reported. The average ratio of the triazole regioisomers is also reported. **Replicate 1:** 26% conversion, **1,4-/1,5-isomer:** 10.3; **Replicate 2:** 21% conversion, **1,4-/1,5-isomer:** 10.6;

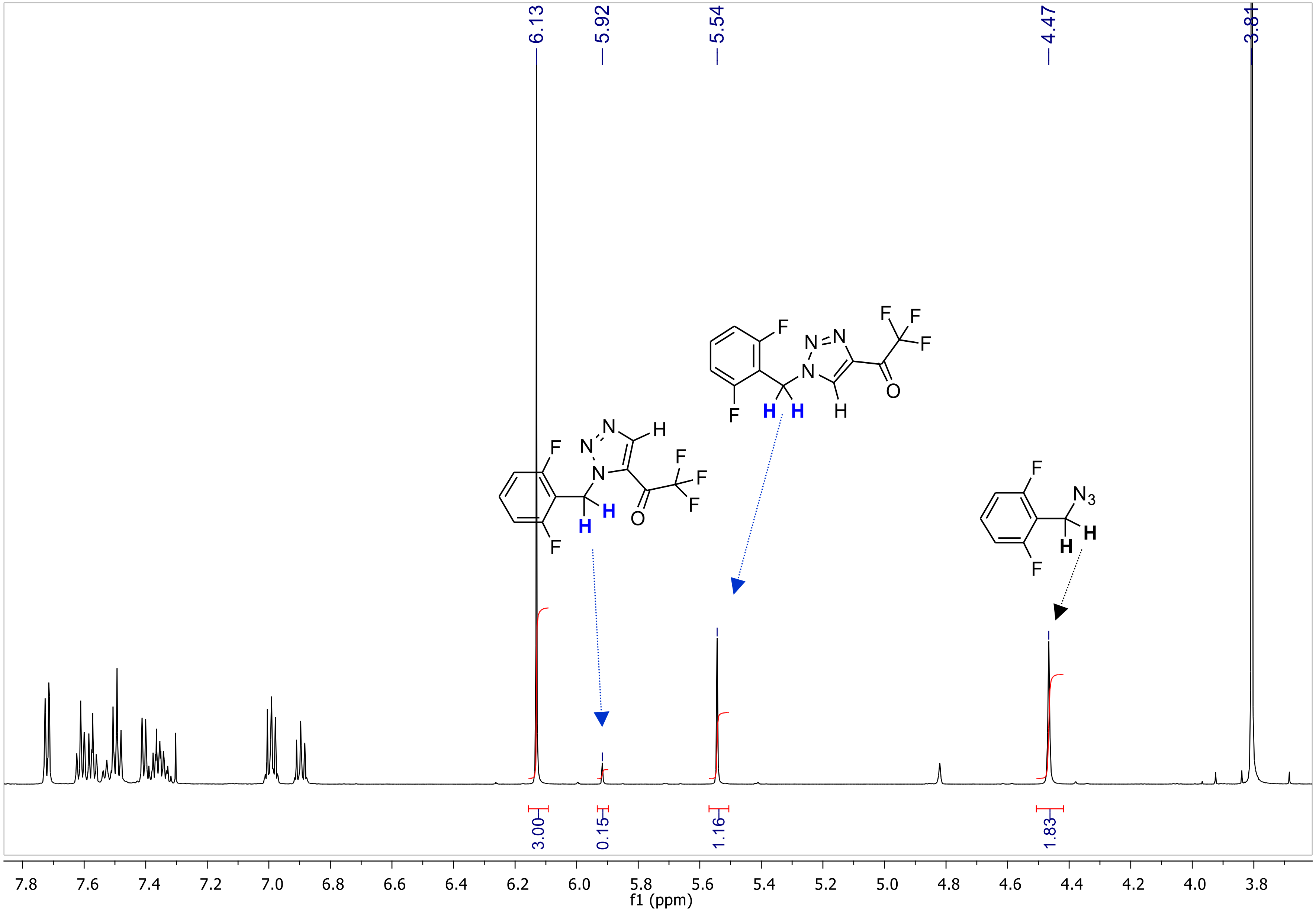
Replicate 3: 23% conversion, **1,4-/1,5-isomer:** 10.2

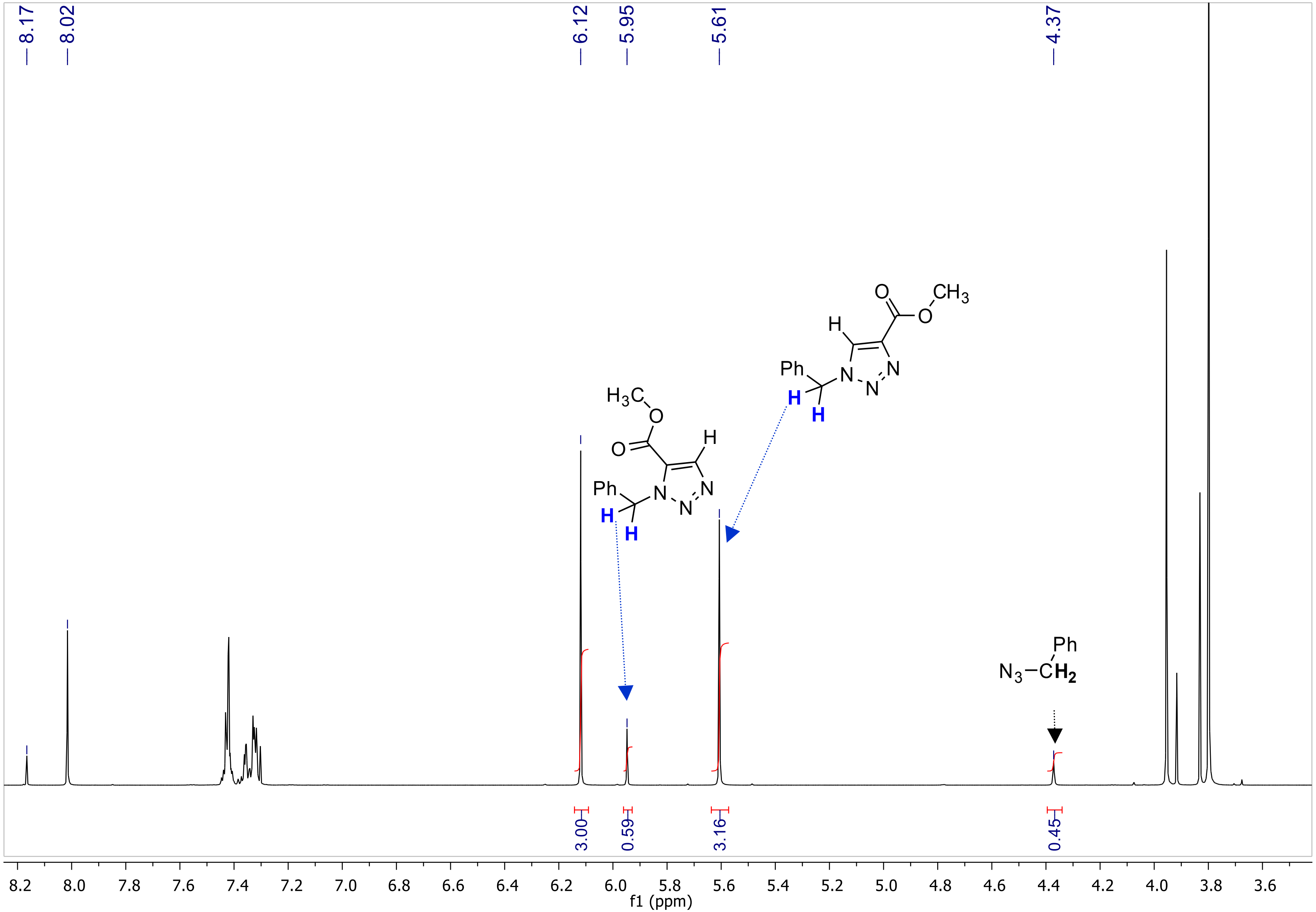
Average conversion: 23%; Average 1,4-/1,5-isomer ratio: 10.4

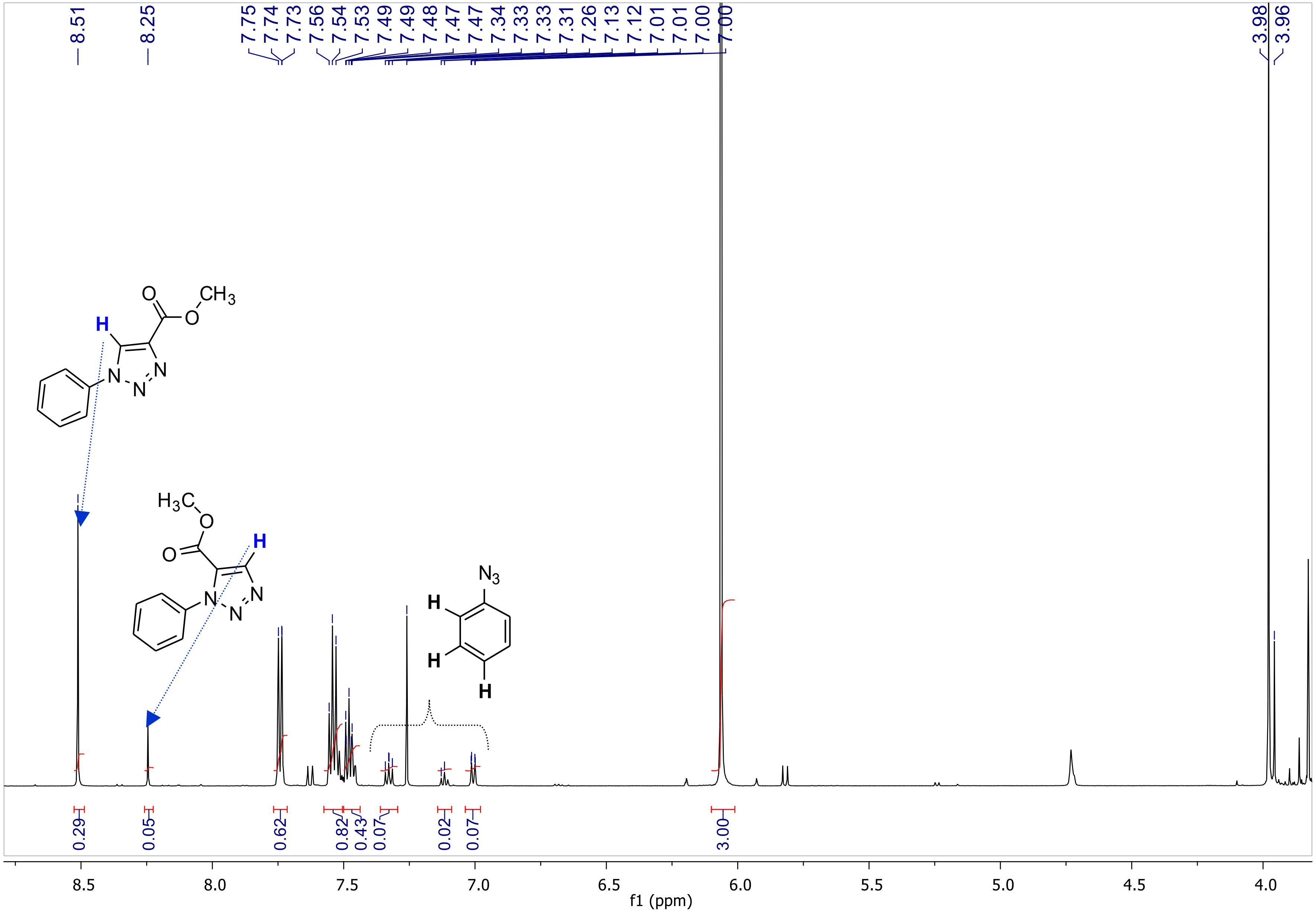


Representative ^{1}H-NMR spectra from Table S1:
Reaction conditions: azide (1 equiv, 0.25 mmol), alkyne (1.2 equiv, 0.3 mmol) in 0.5 mL H_2O at 80 °C for 1h in VFD




6.13
5.92
5.54
4.47
3.81
3.00
0.15
1.16
1.83
F
N
H
O
N3
7.8
7.6
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
f1 (ppm)


8.17
8.02
6.12
5.95
5.61
4.37
H$_3$C
O
O
H
Ph
N
N
N
H
H
O
CH$_3$
O
H
Ph
N
N
N
H
H
Ph
N$_3$–CH$_2$
3.00
0.59
3.16
0.45
8.2
8.0
7.8
7.6
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
f1 (ppm)


8.51
8.25
7.75
7.74
7.73
7.56
7.54
7.53
7.49
7.49
7.48
7.47
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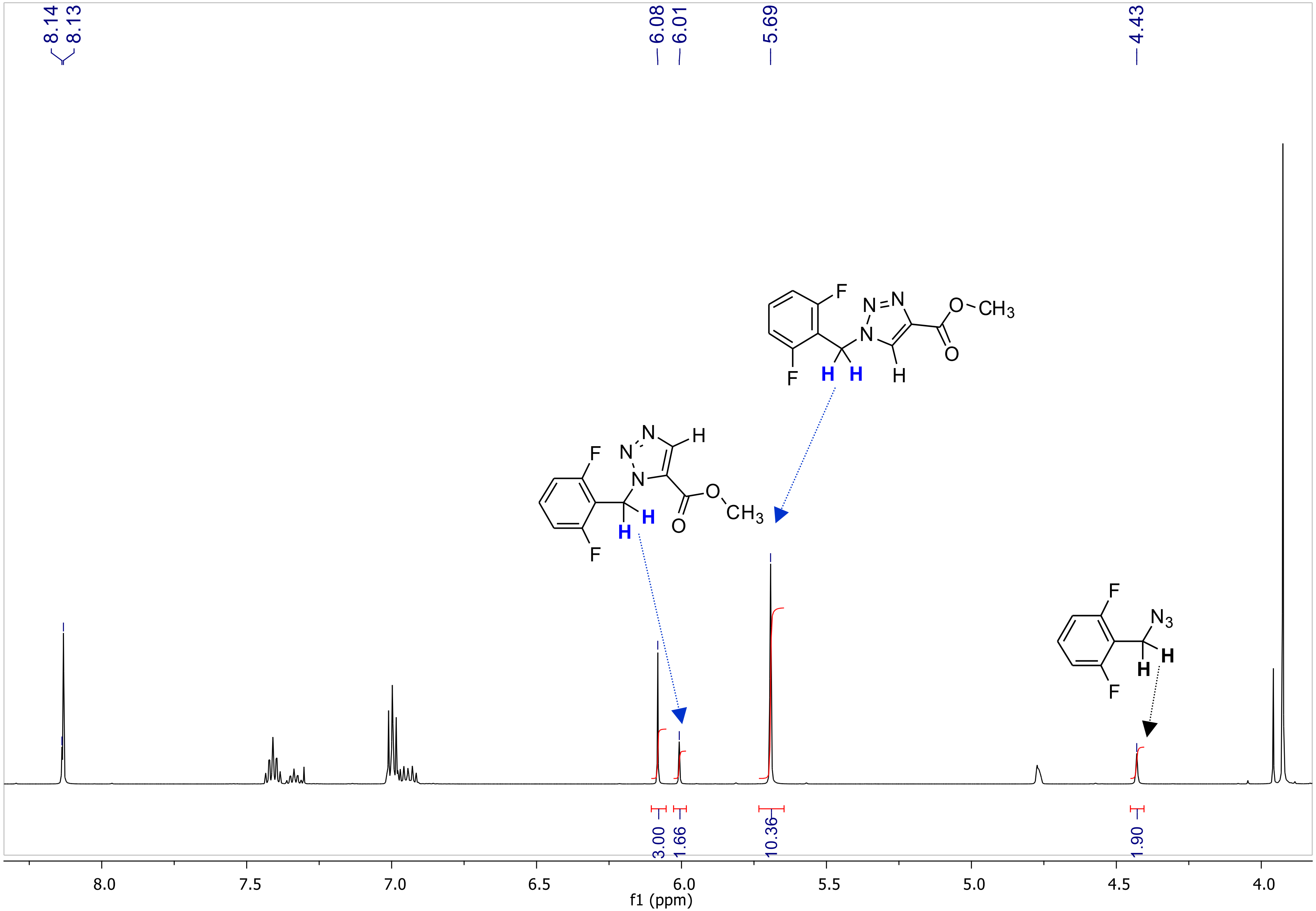
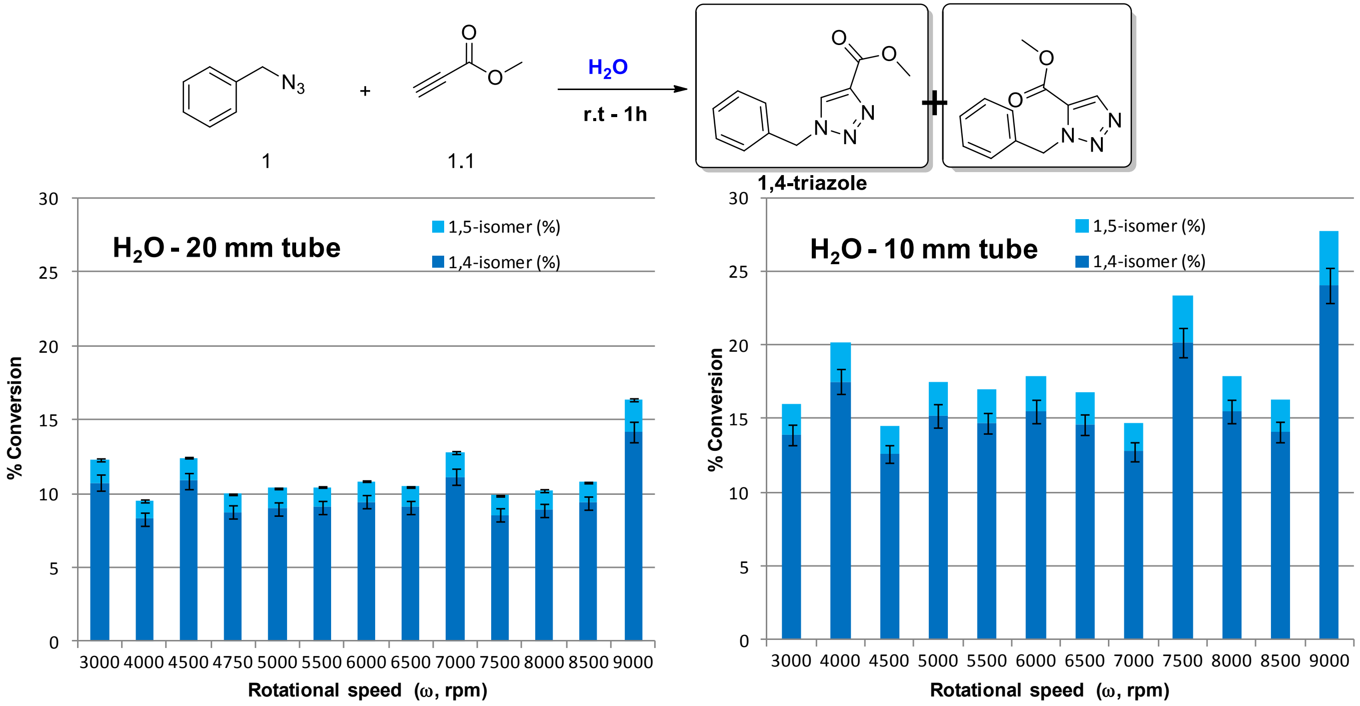
7.34
7.33
7.33
7.31
7.26
7.13
7.12
7.01
7.01
7.00
7.00
3.98
3.96
H
O
CH3
N
N
N
H3C
O
O
H
N
N
N
N3
H
H
H
0.29
0.05
0.62
0.82
0.43
0.07
0.02
0.07
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
f1 (ppm)


8.14
8.13
6.08
6.01
5.69
4.43
F
N
N
N
H
F
O
CH3
H
H
H
H
H
F
N
N
N
O
O
CH3
F
H
F
N3
H
H
F
3.00
1.66
10.36
1.90
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
f1 (ppm)

(c) - Catalyst-free reaction of benzyl azide and methyl propiolate in the confined mode operation of the VFD at room temperature

The cycloaddition reaction was carried out using the confined mode of operation of the VFD. Benzyl azide (0.25 mmol), alkyne (0.3 mmol) and 0.5 mL of solvent (water or acetonitrile) were added sequentially in a 20 mm O.D or 10 mm O.D tube, as specified. The tube was sealed with a rubber stopper and the VFD was operated between 3k-9k rpm for 1h, with the tube set at 45° tilt angle. The organic material was extracted with $CDCl_3$ and analyzed by ^1H NMR spectroscopy using 1,3,5-trimethoxy benzene as internal standard to assess mass balance. These experiments were performed in triplicate.



Scheme 2. Assessment of the effect of rotational speed (ω) and tube diameter in the confined mode of operation of the VFD with the tube inclined at 45° for the reaction of benzyl azide (0.25 mmol) and methyl propiolate (0.3 mmol).

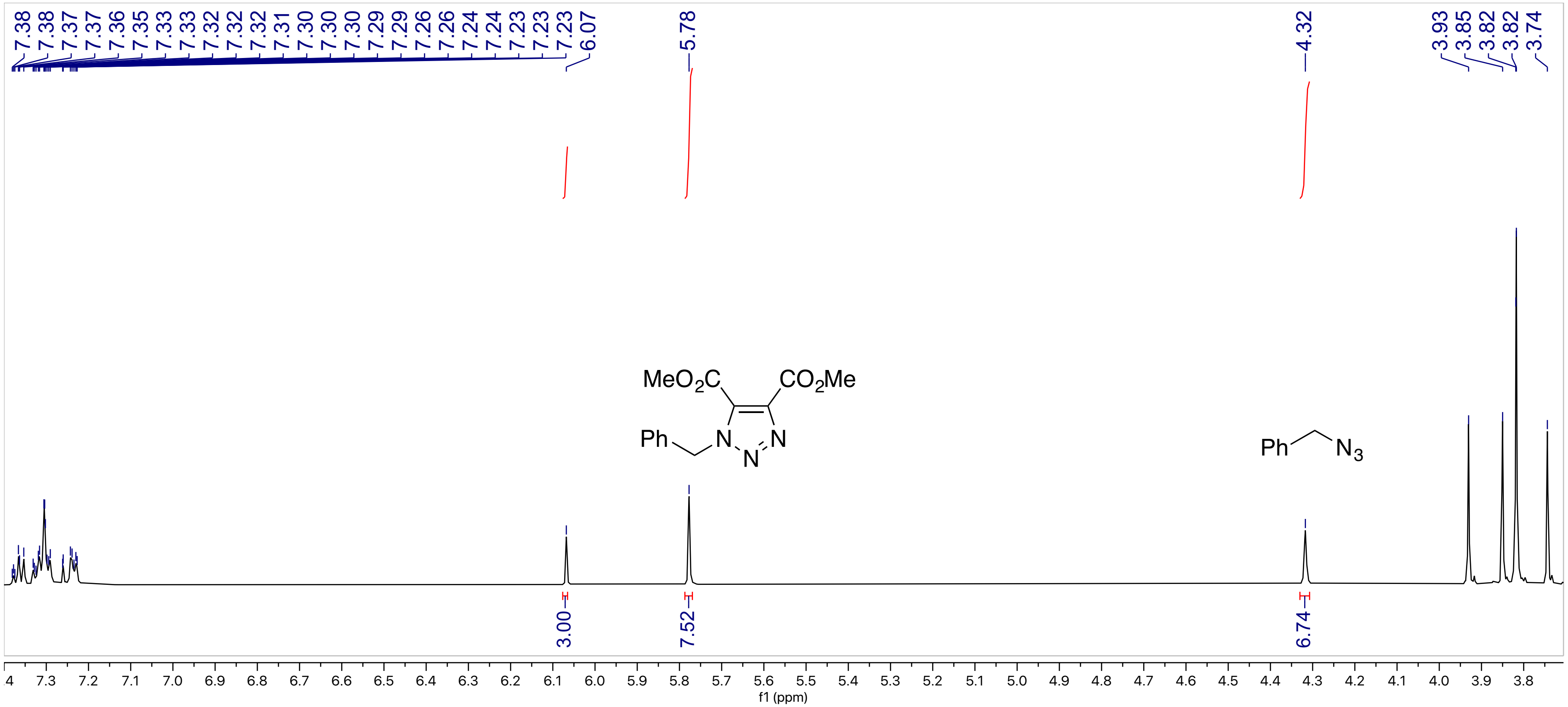
Table S3. Improving the synthesis of 1,2,3-triazoles on water at r.t. under catalyst-free conditions in confined mode VFD. Reaction shown for reaction of benzyl azide and methyl propiolate.[a]

Entry	Alkyne (equiv.)	Time (h)	Condition	Conversion (%)
1	1.2	1	batch	<5
2	1.2	1	VFD (9k rpm)	28
3	2	1	VFD (9k rpm)	43
4	2	2.5	VFD (9k rpm)	49

Preparative scale azide-alkyne cycloadditions in confined mode VFD, including *in-situ* generation of azide (bottom 4 entries in Table 1)

Batch procedure for the catalyst-free reaction of benzyl azide and dimethyl acetylenedicarboxylate at room temperature

Benzyl azide (1.5 mmol), dimethyl acetylenedicarboxylate (1.8 mmol) and 5 mL of water were added sequentially in a 20 mm O.D reaction tube. The tube was sealed with a rubber stopper and stirred with a magnetic stirrer bar for 2h at room temperature. After this time, the organic material was extracted $CDCl_3$ and analyzed by ^1H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard to assess mass balance. Conversion to the product was 53%.



VFD confined mode procedure for the catalyst-free reaction of benzyl azide and dimethyl acetylenedicarboxylate at room temperature (>300 mg scale)

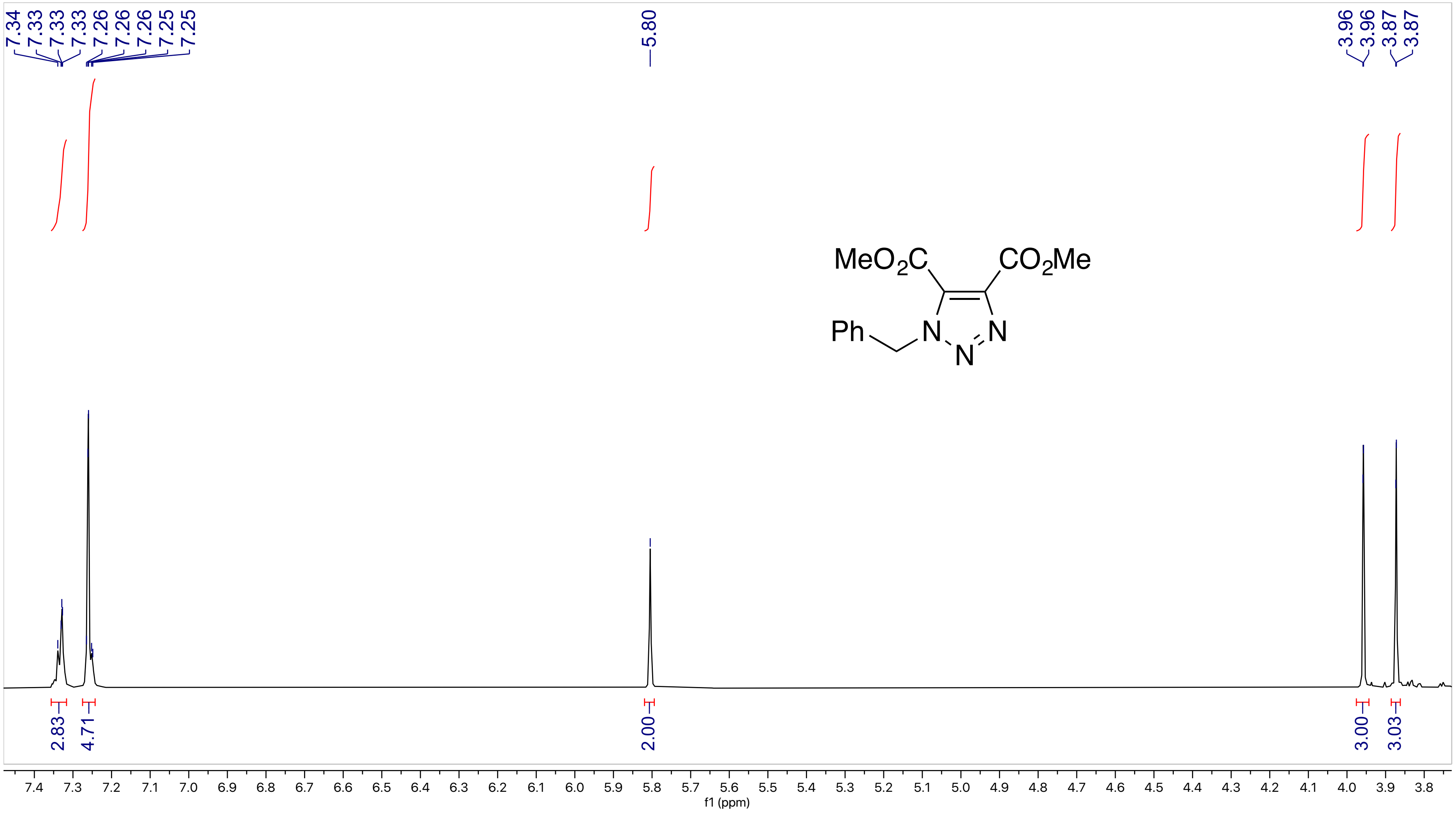
The cycloaddition reaction was carried out using the confined mode of operation of the VFD. Benzyl azide (1.5 mmol), dimethyl acetylenedicarboxylate (1.8 mmol) and 5 mL of water were added sequentially in a 20 mm O.D reaction tube. The tube was sealed with a rubber stopper and the VFD was operated at 8k rpm for 2h at room temperature, with the tube set at 45° tilt angle. After this time, the organic material was extracted with dichloromethane (2 x 15 mL), dried with anhydrous sodium sulfate and solvent removed under reduced pressure. The product was obtained as a wax (87%, 359 mg).

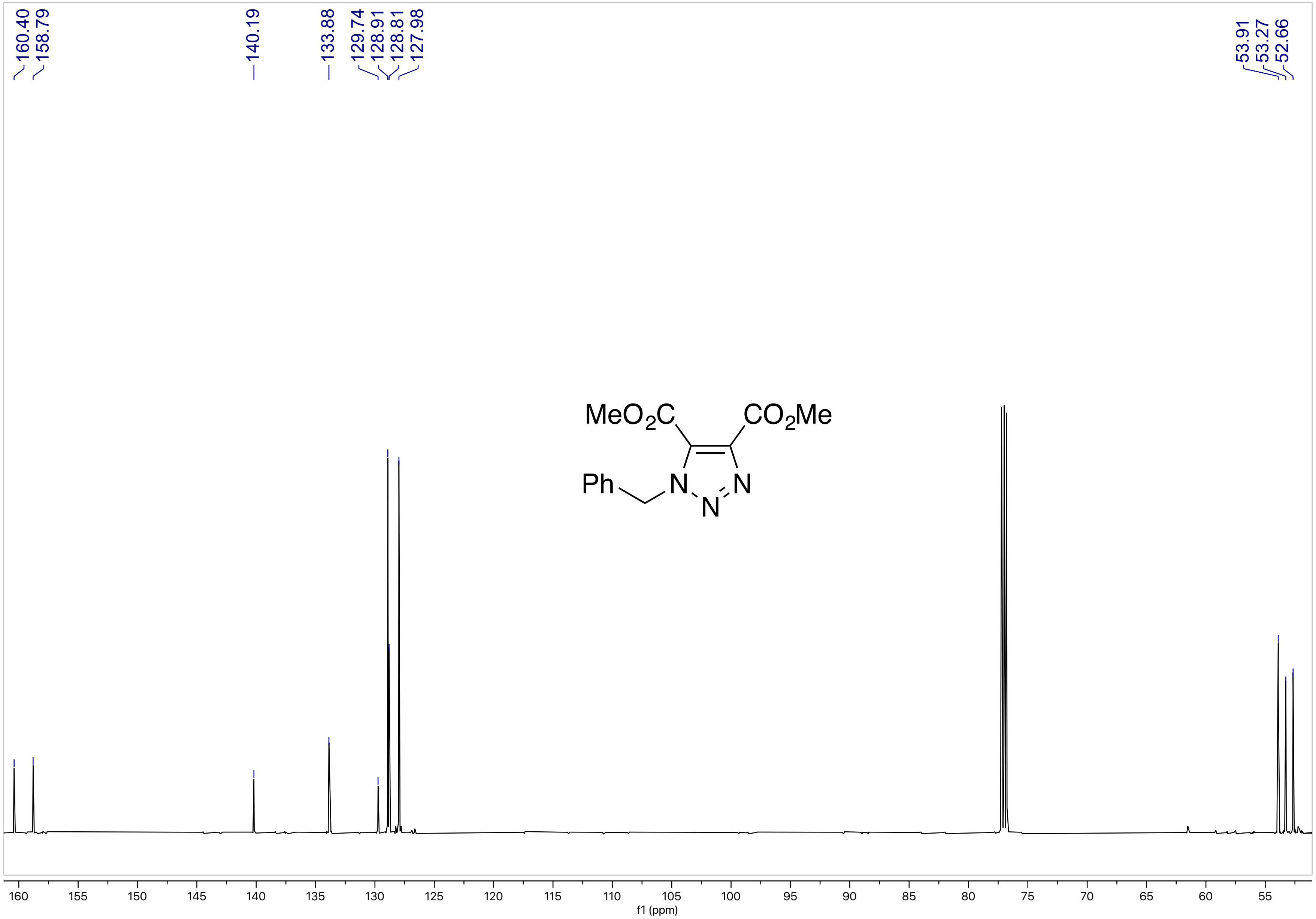
VFD confined mode procedure for the *in-situ* generation of benzyl azide its reaction with dimethyl acetylenedicarboxylate at room temperature (>300 mg scale)

The *in-situ* generation of benzyl azide and its reaction with dimethyl acetylenedicarboxylate was carried out using the confined mode operation of the VFD. Benzyl bromide (1.6 mmol), sodium azide (1.7 mmol), and 5 mL of water were added sequentially in a 20 mm O.D reaction tube. The tube was sealed with a rubber stopper and the VFD was operated at 8k rpm for 3.5h at room temperature, with the tube set at 45° tilt angle. After this time, dimethyl acetylenedicarboxylate (1.8 mmol) was added to the reaction tube and the tube was again sealed with a rubber stopper and the VFD was operated at 8k rpm for 2.5h at room temperature, with the tube set at 45° tilt angle. After this time, the organic material was extracted with dichloromethane (2 x 15 mL), dried with anhydrous sodium sulfate and solvent removed under reduced pressure. The product was obtained as a wax (82%, 366 mg).

Representative NMR data for the isolated products are shown on the next page:

^{1}H NMR (600 MHz, CDCl$_3$): δ = 7.34-7.33 (m, 3 H), 7.26-7.25 (m, 2 H), 5.80 (s, 2 H), 3.96 (s, 3 H), 3.87 (s, 3 H) ppm; ^{13}C NMR (600 MHz, CDCl$_3$): δ = 160.5, 158.8, 140.2, 133.9, 129.7, 128.9, 128.8, 127.9, 53.9, 53.3, 52.7 ppm.




160.40
158.79
140.19
133.88
129.74
128.91
128.81
127.98
53.91
53.27
52.66
MeO2C
CO2Me
Ph
N
N
N
160
155
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
f1 (ppm)

VFD confined mode procedure for the catalyst-free reaction of benzyl azide and di-*tert*-butyl acetylenedicarboxylate at 80 °C (> 300 mg scale)

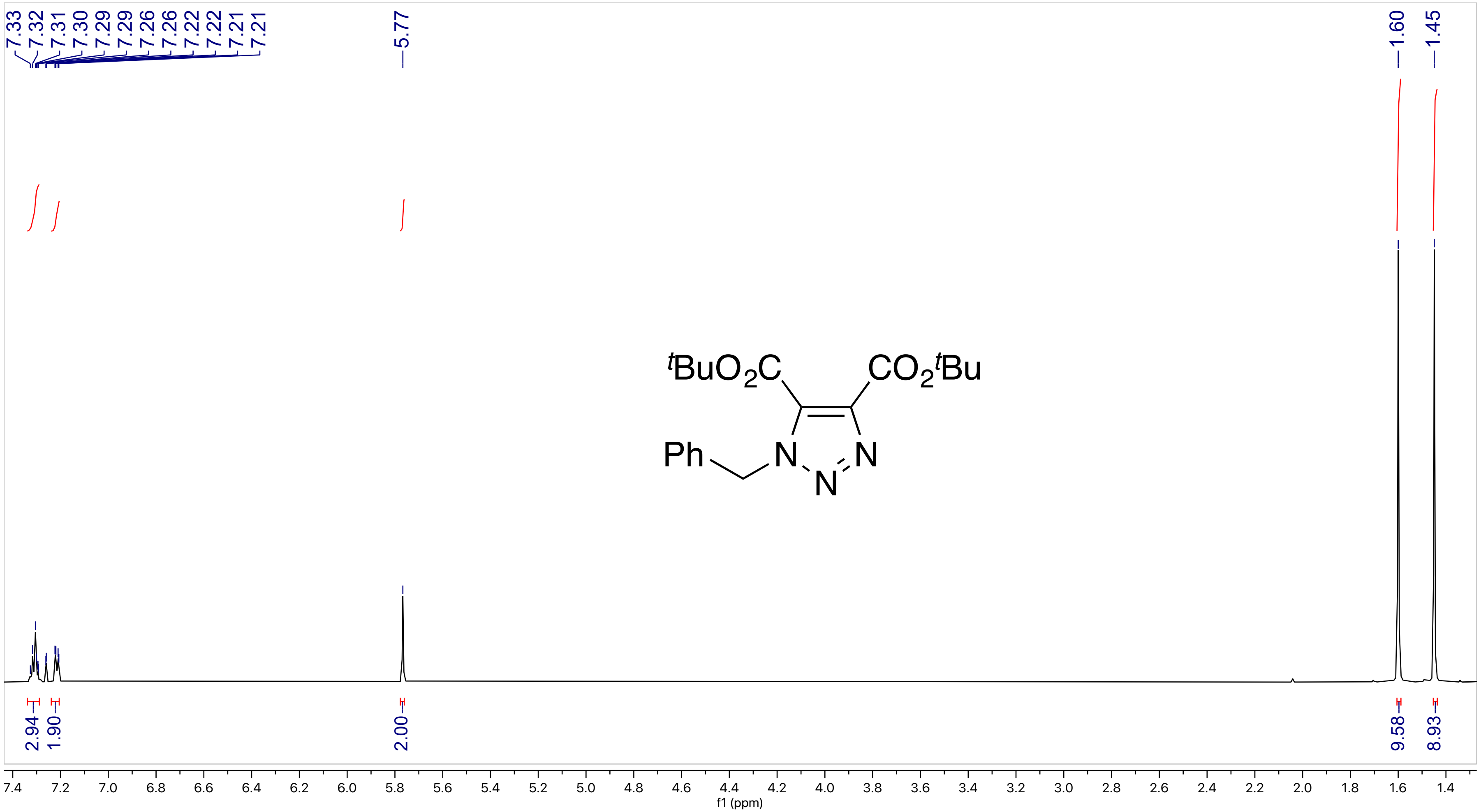
The cycloaddition reaction was carried out using the confined mode of operation of the VFD. Benzyl azide (1.5 mmol), di-*tert*-butyl acetylenedicarboxylate (1.8 mmol) and 5 mL of water were added sequentially in a 20 mm O.D reaction tube. The tube was sealed with a rubber stopper and the VFD was operated at 8k rpm for 1h at 80 °C, with the tube set at 45° tilt angle. After this time, the organic material was extracted with dichloromethane (2 x 15 mL), dried with anhydrous sodium sulfate and solvent removed under reduced pressure. The crude product was purified by column chromatography to remove excess alkyne (25% EtOAc in hexanes, Rf 0.47) and obtained as a white solid (90%, 485 mg).

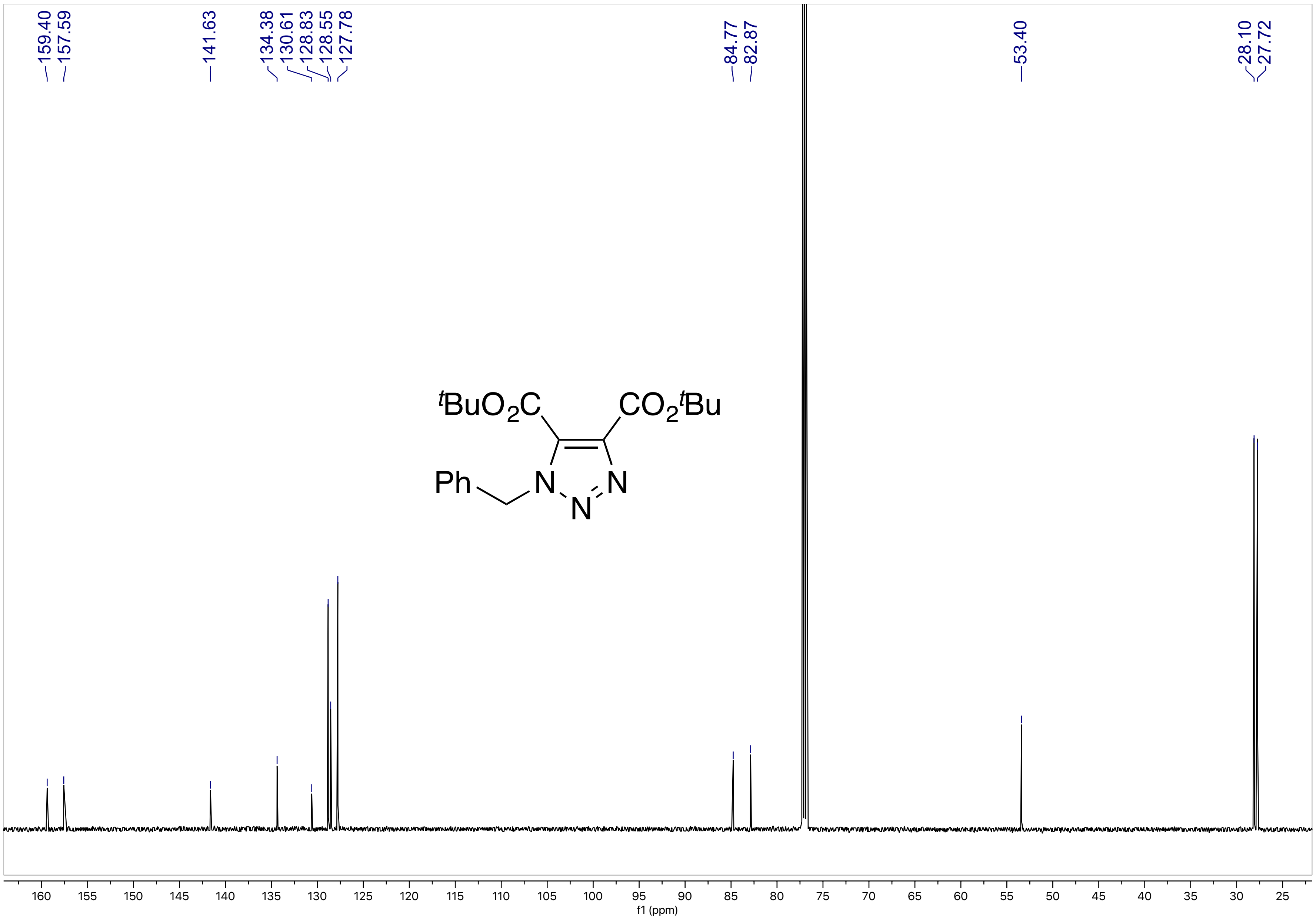
VFD confined mode procedure for the *in-situ* generation of benzyl azide its reaction with di-*tert*-butyl acetylenedicarboxylate at 80 °C (>300 mg scale)

The *in-situ* generation of benzyl azide and its reaction with di-*tert*-butyl acetylenedicarboxylate was carried out using the confined mode operation of the VFD. Benzyl bromide (1.6 mmol), sodium azide (1.7 mmol), and 5 mL of water were added sequentially in a 20 mm O.D reaction tube. The tube was sealed with a rubber stopper and the VFD was operated at 8k rpm for 3.5h at room temperature, with the tube set at 45° tilt angle. After this time, di-*tert*-butyl acetylenedicarboxylate (1.8 mmol) was added to the reaction tube and the tube was again sealed with a rubber stopper and the VFD was operated at 8k rpm for 1h at 80 °C, with the tube set at 45° tilt angle. After this time, the organic material was extracted with dichloromethane (2 x 15 mL), dried with anhydrous sodium sulfate and solvent removed under reduced pressure. The crude product was purified by column chromatography to remove excess alkyne (25% EtOAc in hexanes, Rf 0.47) and obtained as a white solid (83%, 476 mg).

Representative NMR and characterization data for the isolated products are shown on the next page:

^{1}H NMR (600 MHz, CDCl$_3$): δ = 7.33-7.29 (m, 3 H), 7.22-7.21 (m, 2 H), 5.77 (s, 2 H), 1.60 (s, 9 H), 1.45 (s, 9 H) ppm; ^{13}C NMR (600 MHz, CDCl$_3$): δ = 159.4, 157.6, 141.6, 134.4, 130.6, 128.8, 128.6, 127.8, 84.8, 82.9, 53.4, 28.1, 27.7 ppm; HRMS (ESI): [M+Na$^+$] found 382.1762. $C_{19}H_{25}N_3O_4Na^+$ requires 382.1743. m.p: 88-90 °C.

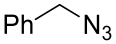
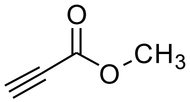
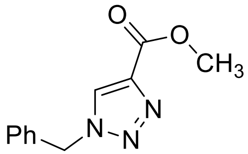
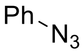
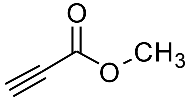
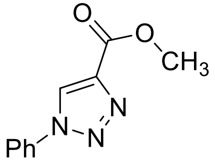


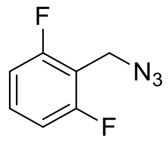
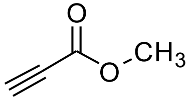
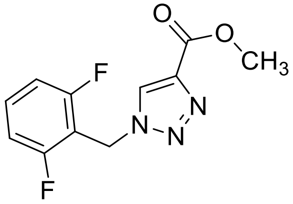

159.40
157.59
141.63
134.38
130.61
128.83
128.55
127.78
84.77
82.87
53.40
28.10
27.72
tBuO2C
CO2tBu
Ph
N
N
N
160
155
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
f1 (ppm)

(d) – “Catalyst-free” azide-alkyne cycloaddition in the continuous mode operation of the VFD at 80 °C and copper leaching from steel jet feed

Two syringe pumps were used to pump the liquid reagents through the continuous flow set up. A solution of benzyl azide (10 mL, 0.025 M, in H_2O:CH_3CN 70:30) was transferred into 1 of the 2 syringes. This syringe was set to deliver contents at 0.05 mL min^{-1}. The other syringe contained methyl propiolate (10 mL, 0.034 M, in H_2O:CH_3CN 80:20) and was set to deliver contents at 0.05 mL min^{-1}. This resulted in a total flow rate of 0.1 mL min^{-1}, which relates to 11.7 minutes residence time (time for the liquid delivered to the base of the rotating tube to leave the top).[2] The solutions were injected *via* syringe pump into the base of the VFD tube, using two stainless steel jet feeds. The tube was rotated at 8k rpm at 80 °C with a 45° tilt angle. The total reaction time was 3.3 hours, over which time the collection vessel was changed every 70 min giving 3 fractions of reaction product. The organic material was extracted from these fractions with $CDCl_3$ and analyzed each by ^{1}H NMR. Conversions for the reactions examined are tabulated on the next page.

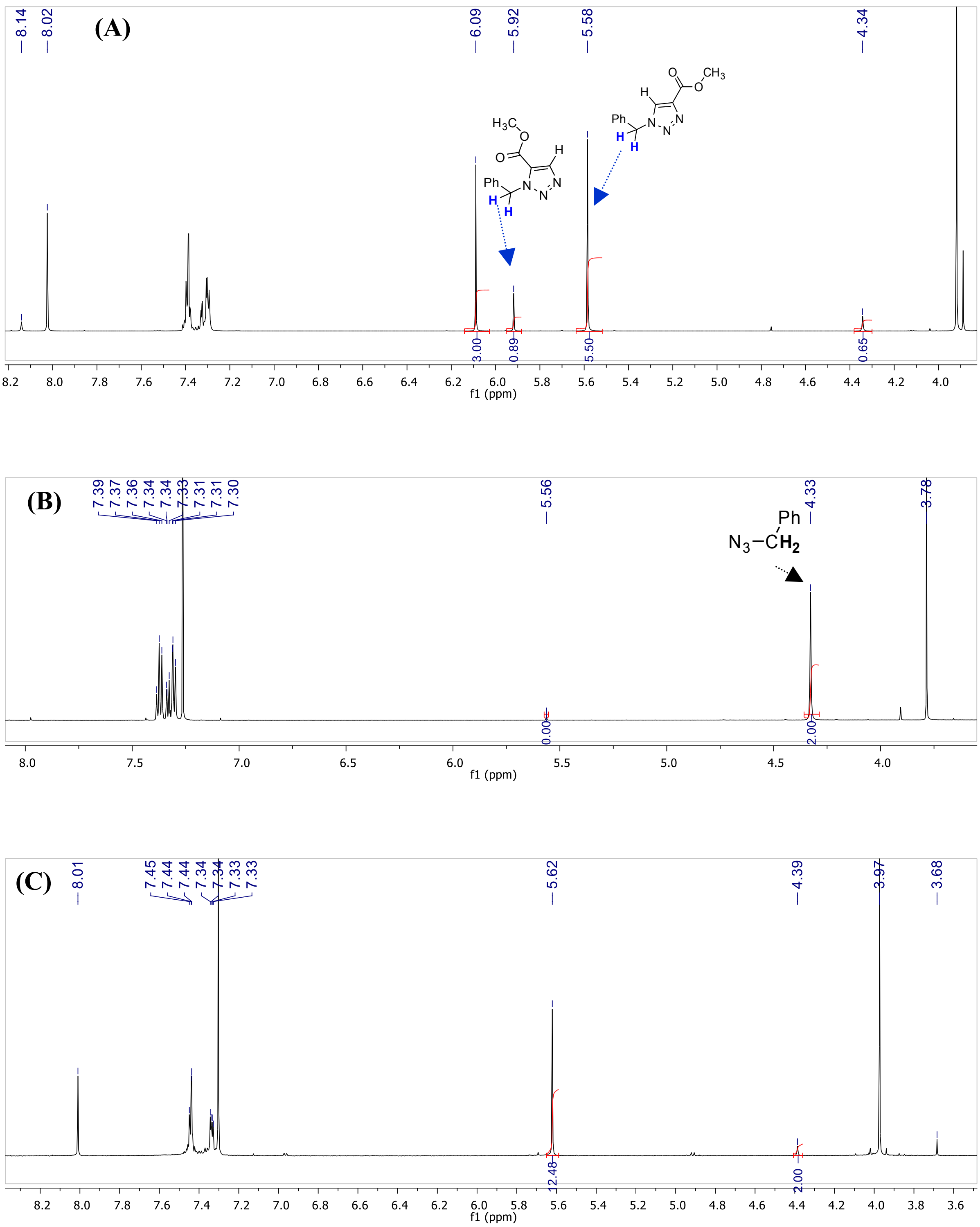
Table S4. Regioselective synthesis of 1,2,3-triazoles in continuous mode operation of the VFD.

Entry	**Azide**	**Alkyne**	**Product (1,4-isomer)**	**Conversion (%)**	**1,4-isomer (%)**
1				>99	100
2				>99	100

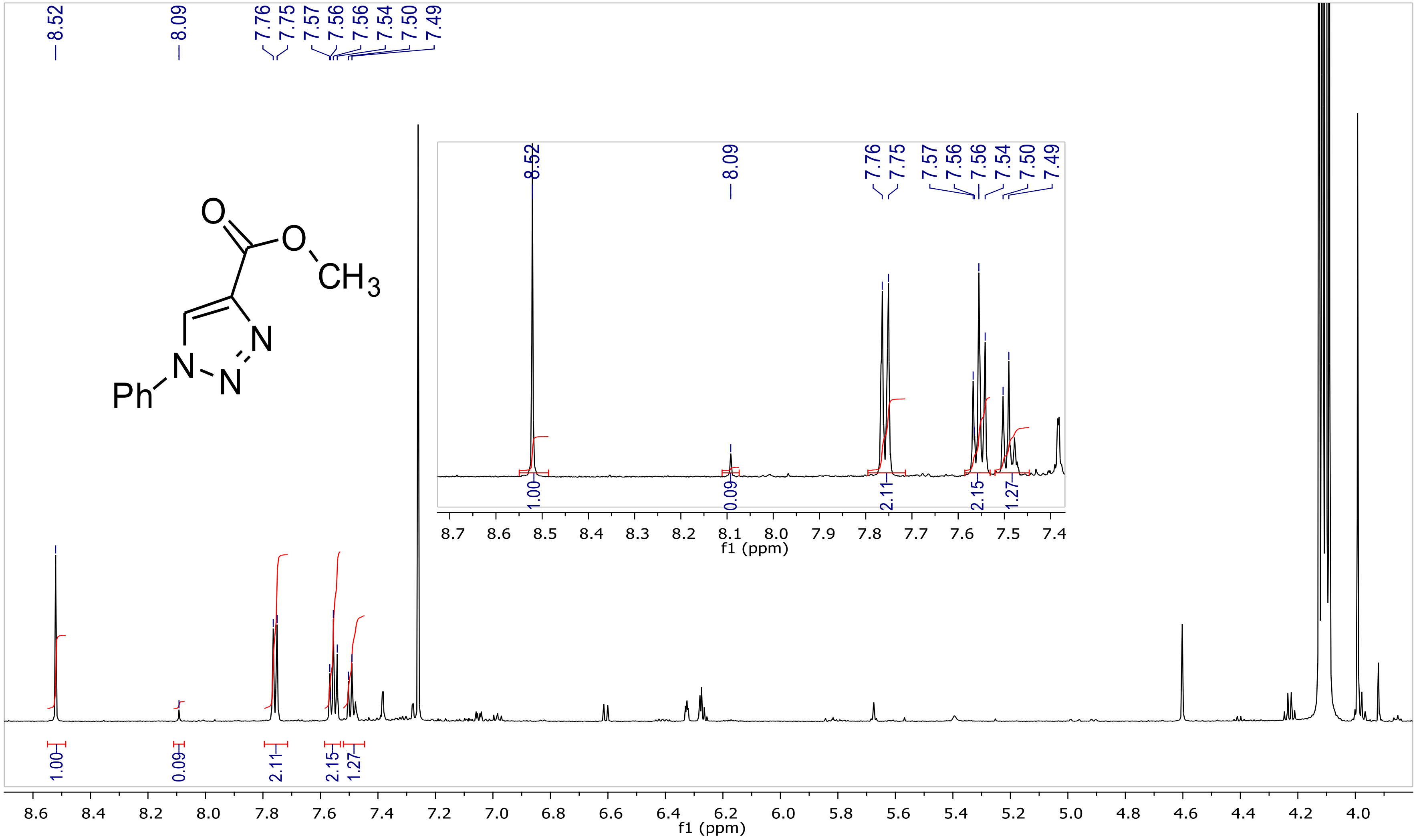
3				97	100

[a] Reaction conditions: azide (1 equiv, 0.25 mmol), alkyne (2 equiv, 0.5 mmol) in 10 mL H_2O:CH_3CN (70:30) at 80 °C following the procedure C. [b] Determined by ^{1}H-NMR peak integration relative to benzyl azide. Only the 1,4-isomer was detected. The copper concentration in undiluted product solution was 0.009 ppm (ICP-MS). LOQ- Limit of Quantification 0.005 ppm

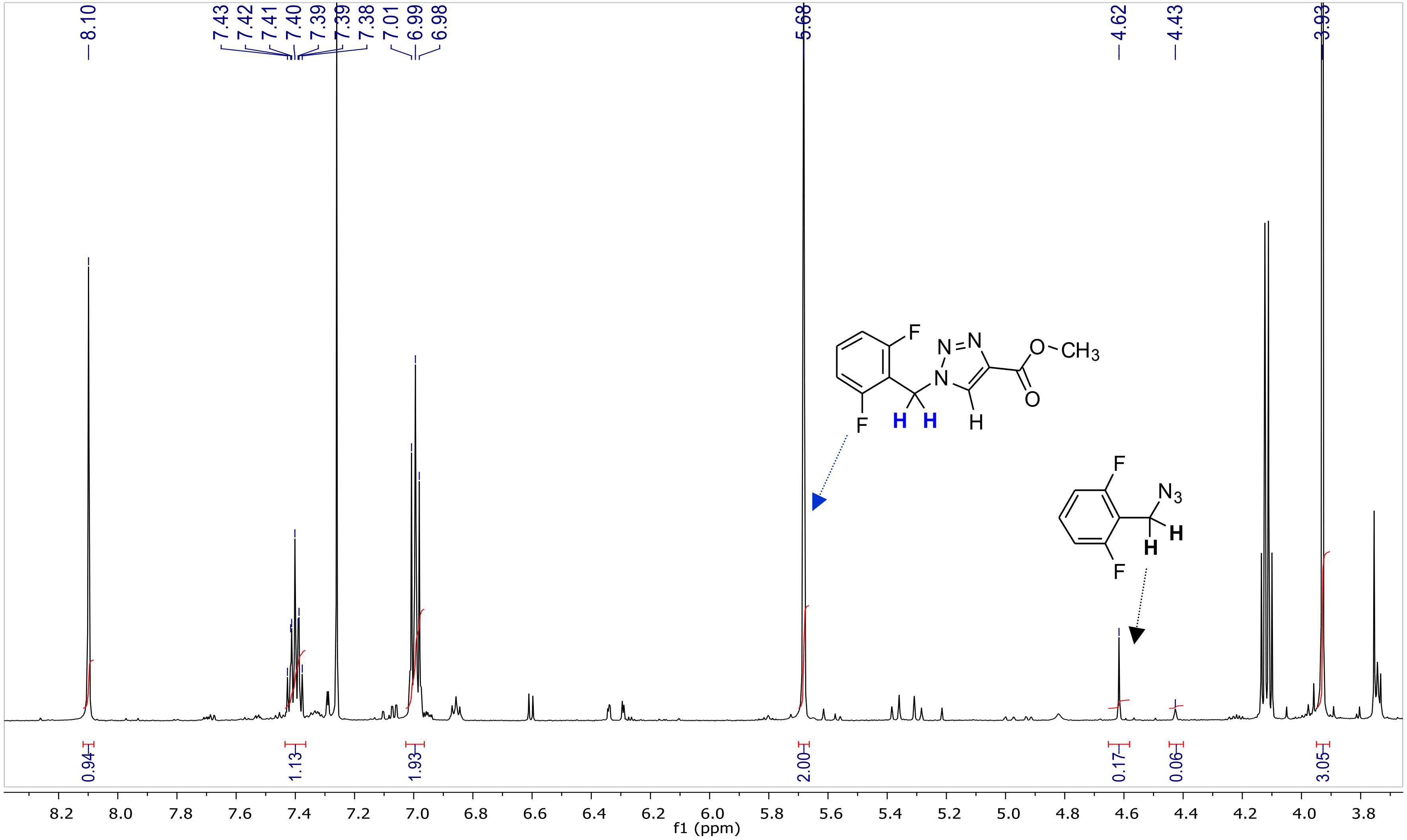
Figure S2. Representative ^{1}H NMR spectra from free-catalyst benzyl azide and methyl propiolate cycloaddition in the VFD. A) In confined mode at T = 80 °C, B) Continuous flow at r.t and C) Continuous flow at T = 80 °C.



^{1}H-NMR spectra of crude 1,4-isomer product for phenyl azide and methyl propiolate reaction in continuous mode operation of the VFD at 80 °C



^{1}**H-NMR spectra of crude 1,4-isomer product for 2,6-difluoro-benzyl azide and methyl propiolate reaction in continuous mode operation of the VFD at 80 °C**



Copper-catalyzed azide-alkyne cycloadditions (CuAAC)

(e) – Copper Catalysed azide-alkyne cycloaddition in confined mode operation of the VFD at room temperature

The cycloaddition reaction was carried out using the confined mode of operation of the VFD. Benzyl azide (0.25 mmol), $CuSO_4 \bullet 5H_2O$ (3 mol % or 0.06 mol %, as been specified), ascorbic acid (30 mol %), alkyne (0.3 mmol), and 0.5 mL of solvent (water:acetonitrile) were added sequentially in a 20 mm O.D tube. The tube was sealed with a rubber stopper and the VFD was operated between 9k rpm for 1h at r.t, with the tube set at 45° tilt angle. The organic material was extracted from these fractions with $CDCl_3$ and analyzed by ^1H NMR spectroscopy using 1,3,5-trimethoxy benzene as internal standard to assess mass balance.

(f) – Copper leaching experiment in VFD continuous mode using a copper jet feed

A solvent mixture, an alkyne solution (0.03 M) or an azide solution (0.02 M), as specified, was injected *via* syringe pump (set at 0.05 mL min^{-1} or as specified) into a copper jet feed (diameter = 1.28 mm, volume = 0.39 mL, surface area = 12.1 cm^2), while the VFD tube was operating at 9k rpm with a 45° tilt angle. 3 fractions (3 mL each) were collected. The soluble copper species content were analyzed using a Perkin-Elmer NexION ICP-MS.

Table S5. Copper concentration in undiluted outflow solution detected using ICP-MS.

Entry	Condition[a]	[Cu] (ppm)[b]	Averange [Cu] (ppm)
1	H_2O	0.078	0.075
		0.072	
		0.076	
2	$H_2O:CH_3CN$ (80:20)	8.9	7.33
		6	
		7.1	
3	$H_2O:CH_3CN$ (20:80)	2.49	2.74
		2.5	
		2.23	
4	$H_2O:CH_3CN$ (80:20) : alkyne (0.03M)	3.5	3.33
		3.6	
		2.9	
5	$H_2O:CH_3CN$ (80:20) : azide (0.02M)	5.1	5.23
		4.6	
		6.0	

[a] The solution was injected *via* syringe pump set at 0.05 mL min^{-1}. [b] LOQ- Limit of Quantification 0.02 ppm

(g) – Copper-catalyzed azide-alkyne cycloaddition in continuous mode operation of the VFD at room temperature

Two syringe pumps were used to pump the liquid reagents through the continuous flow set up. A solution of benzyl azide (10 mL, 0.025 M, in H_2O:CH_3CN 70:30) was transferred into 1 of the 2 syringes. This syringe was set to deliver contents at 0.05 mL min^{-1}. The other syringe contained methyl propiolate (10 mL, 0.034 M, in H_2O:CH_3CN 80:20) and was set to deliver contents at 0.05 mL min^{-1} using a copper jet feed (diameter = 1.28 mm, volume = 0.39 mL, surface area = 12.1 cm^2). This resulted in a total flow rate of 0.1 mL min^{-1}, which relates to 11.7 minutes residence time (time for the liquid delivered to the base of the rotating tube to leave the top). The solutions were injected *via* syringe pump into the base of the VFD tube, operating at 9k rpm with a 45° tilt angle (Figure S3). The total reaction time was 3.3 hours, over which time the collection vessel was changed every 70 min giving 3 fractions of reaction product. The organic material was extracted from these fractions with $CDCl_3$ and analyzed each by ^{1}H-NMR.

Table S6. Optimization of flow rate in the CuAAC reaction in continuous mode operation of the VFD following procedure F.

Total Flow Rate (mL min^{-1})	Residence Time (min)	% Conversion[a]	[Cu] (ppm)[b]
0.2	5.6	16	3.33
0.1	11.7	23	3.97

[a] Determined by ^{1}H-NMR peak integration relative to benzyl azide. Only 1,4-isomer was detected. [b] Determined using ICP-MS following procedure E. LOQ- Limit of Quantification 0.02 ppm

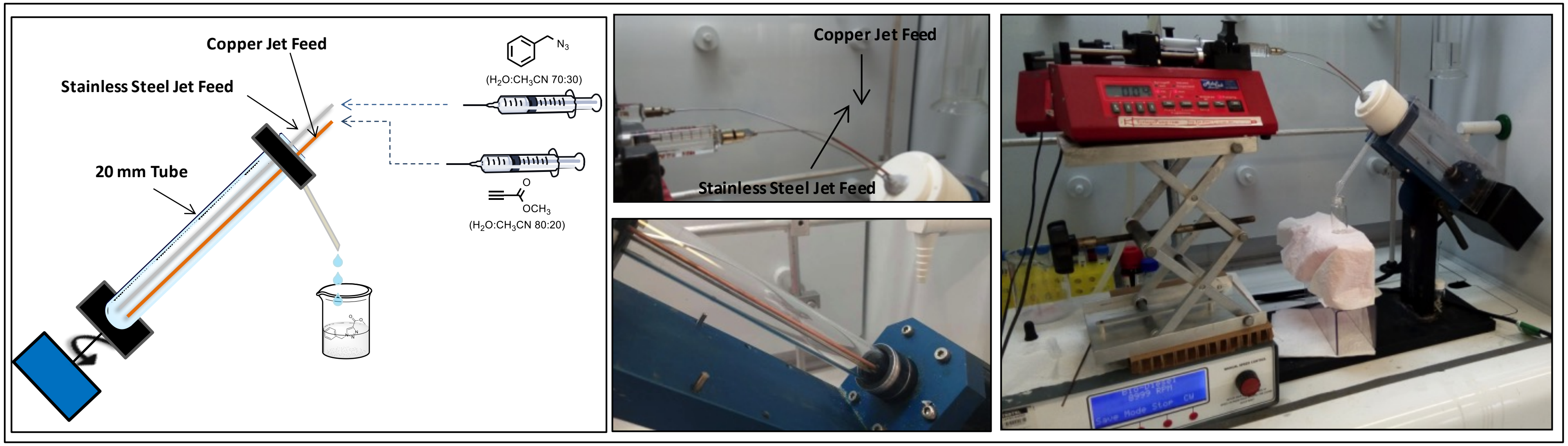
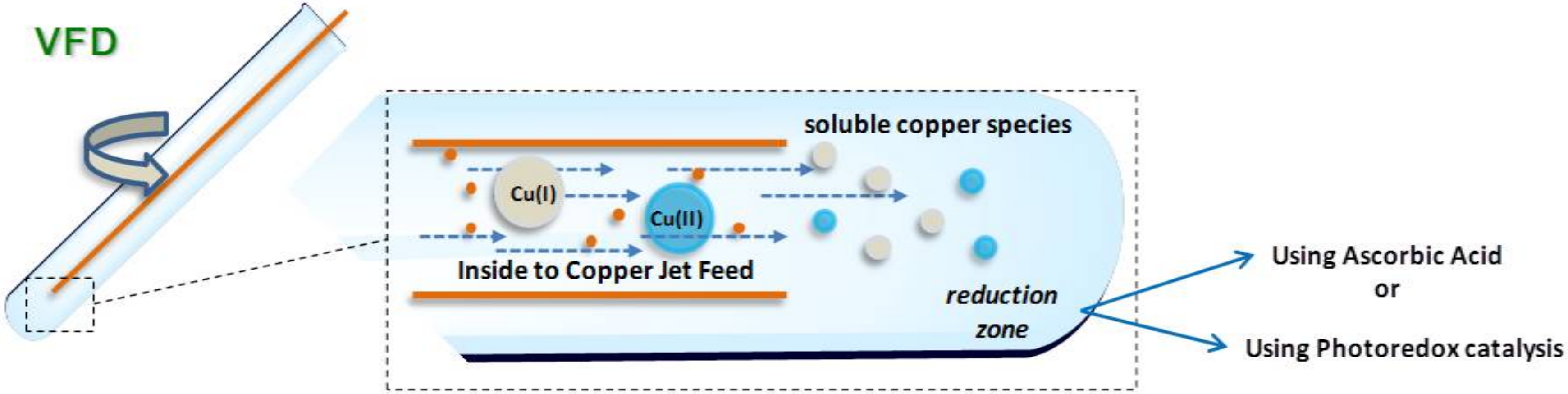


Figure S3. (A) Schematic of continuous flow CuAAC in the VFD at room temperature. (B) Photograph of the VFD operating in continuous mode.

(h) – Copper-catalyzed azide-alkyne cycloaddition using ascorbic acid as a reducing agent in continuous mode operation of the VFD at room temperature.

Two syringe pumps were used to pump the liquid reagents through the continuous flow set up. A solution of benzyl azide (10 mL, 0.025 M, in H_2O:CH_3CN 70:30) together with ascorbic acid (10 mol %) were transferred into 1 of the 2 syringes. This syringe was set to deliver contents at 0.05 mL min^{-1}. The other syringe contained methyl propiolate (10 mL, 0.034 M, in H_2O:CH_3CN 80:20) and was set to deliver contents at 0.05 mL min^{-1} using a copper jet feed (diameter = 1.28 mm, volume = 0.39 mL, surface area = 12.1 cm^2). This resulted in a total flow rate of 0.1 mL min^{-1}, which relates to 11.7 minutes residence time (time for the liquid delivered to the base of the rotating tube to leave the top). The solutions were injected *via* syringe pump into the base of the VFD tube, operating at 9k rpm with a 45° tilt angle

(Scheme 2). The total reaction time was 3.3 hours, over which time the collection vessel was changed every 70 min giving 3 fractions of reaction product. The organic material was extracted from these fractions with $CDCl_3$ and analyzed each by ^{1}H-NMR.



Scheme S3. Schematic representation of copper jet feed and chemistry in reactor tube of VFD.

Table S7. Optimization of flow rate and ascorbic acid (mol%) in the CuAAC following procedure G.

Total Flow rate (mL min^{-1})	Residence Time (min)	Ascorbic Acid (mol %)	% Conversion[a]	[Cu] (ppm)[b]
0.5	2.3	30	<5	4.41
0.2	5.6	30	37.7	3.97
0.1	**11.7**	**30**	**>99**	4.72
0.1	11.7	15	68.4	3.33

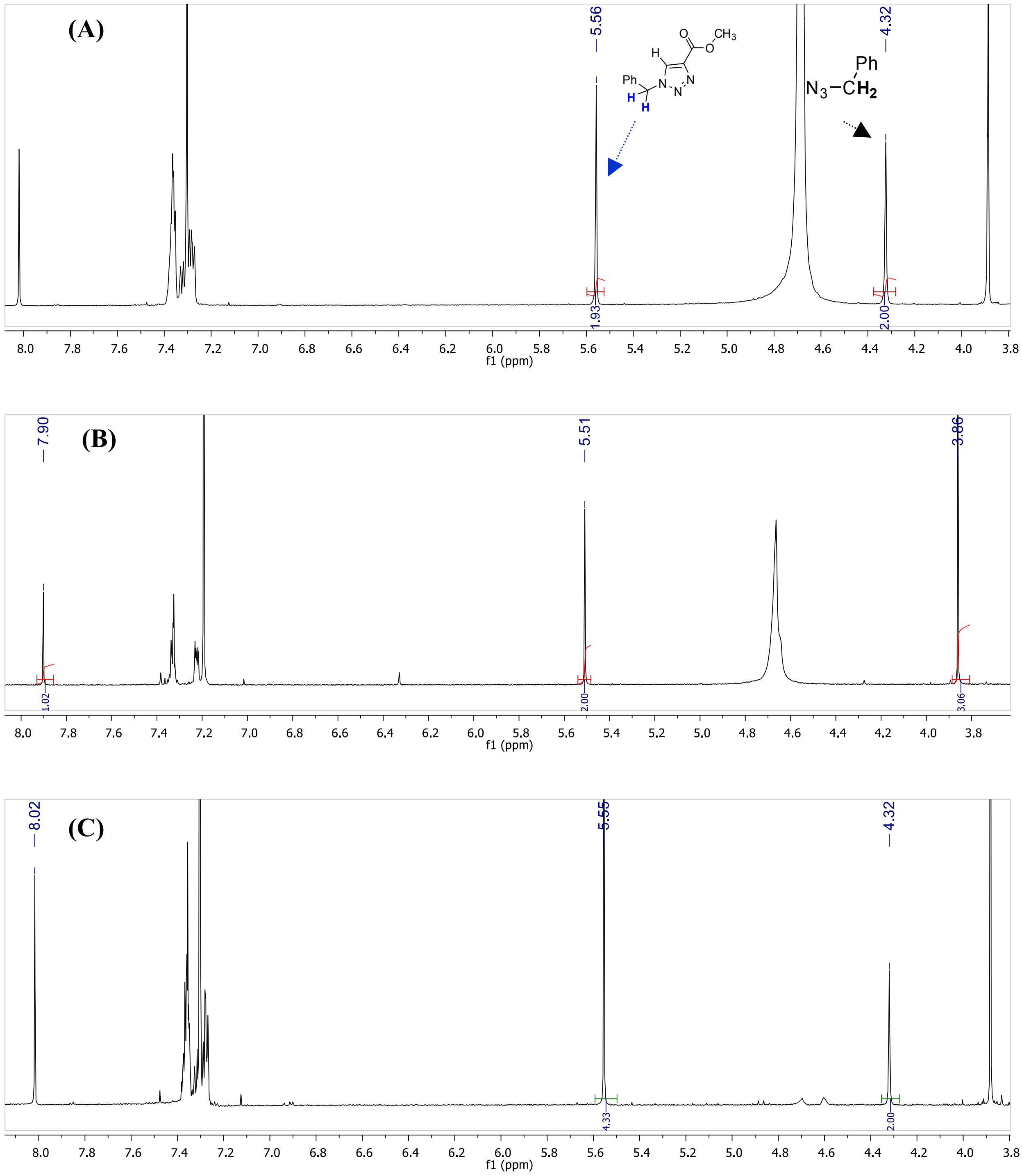
[a] Determined by ^{1}H-NMR peak integration relative to benzyl azide. Only the 1,4-isomer was detected. [b] Determined using ICP-MS following procedure E. LOQ- Limit of Quantification 0.005 ppm

Table S8. Summary the CuAAC using the continuous mode operation of the VFD.

Reaction Vessel	Additive	[Cu] (ppm)[c]	time (min)	T (°C)	% Conversion
Confined mode[a]	$CuSO_4\bullet 5H_2O$ (3 %)/ Asc. Acid (30%)	968.7	60	80	98.4
Confined mode[a]	$CuSO_4\bullet 5H_2O$ (0.06 %)/ Asc. Acid	26.5	60		76
Continuous mode[b]	**stainless steel jet feed**	**0.009**	**11.7**		**>99**
Confined mode[a]	$CuSO_4\bullet 5H_2O$ (3 %) / Asc. Acid (30%)	968.7	60	r.t.	10.6
Confined mode[a]	$CuSO_4\bullet 5H_2O$ (0.06 %)/ Asc. Acid	26.5	60		7.2
Continuous mode[b]	**copper jet feed / Asc. Acid (30%)**	**4.72**	**11.7**		**>99**

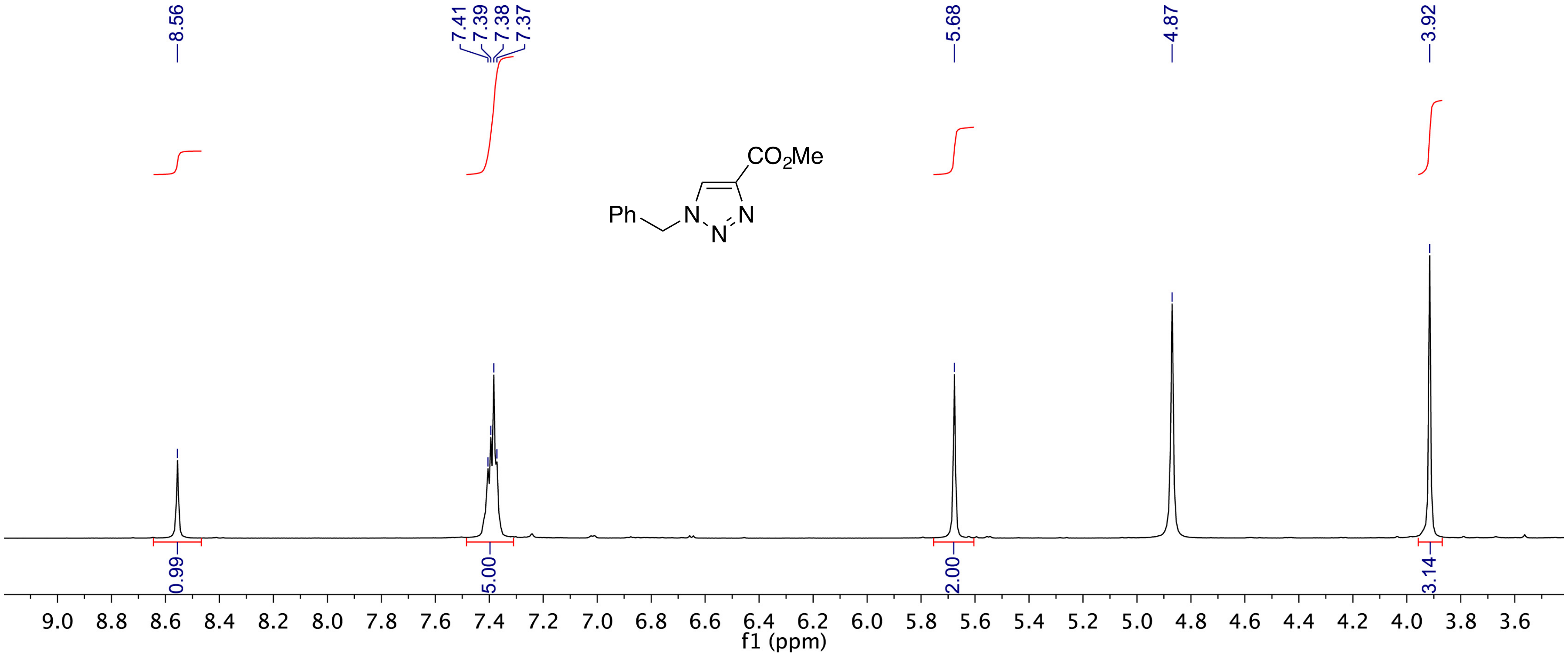
[a] Following procedure D. [b] flow rate = 0.05 mL min^{-1}. [c] Determined using ICP-MS following procedure E. LOQ- Limit of Quantification 0.005

Figure S4. Representative ^{1}H NMR spectra from CuAAC in continuous flow mode operation of the VFD. A) 30 mol % Ascorbic Acid – 0.5 mL min^{-1}, B) 30 mol % Ascorbic Acid – 0.1 mL min^{-1} and C) 15 mol % Ascorbic Acid – 0.1 mL min^{-1}



Copper-catalyzed azide-alkyne cycloaddition using ascorbic acid as a reducing agent in continuous mode operation of the VFD at 80 °C (gram-scale)

Two syringe pumps were used to pump the liquid reagents through the continuous flow set up. A solution of benzyl azide (30 mL, 0.25 M, in H_2O:CH_3CN 70:30) together with ascorbic acid (30 mol %) were transferred into 1 of the 2 syringes. This syringe was set to deliver contents at 0.5 mL min^{-1}. The other syringe contained methyl propiolate (30 mL, 0.34 M, in H_2O:CH_3CN 80:20) and was set to deliver contents at 0.5 mL min^{-1} using a copper jet feed (diameter = 1.28 mm, volume = 0.39 mL, surface area = 12.1 cm^2). This resulted in a total flow rate of 1 mL min^{-1}. The solutions were injected *via* syringe pump into the base of the VFD tube, operating at 9k rpm with a 45° tilt angle. The total reaction time was 1 hour, over which time the reaction product was collected in a single flask. After the solvent was removed under reduced pressure, ^1H NMR (CD_3OD) of the collected product revealed full consumption of the azide and alkyne and conversion to the triazole:



Preparative scale copper-catalyzed azide-alkyne cycloadditions in VFD (continuous mode) using ascorbic acid as reducing agent (From entries in Table 3 in the main text)

Copper-catalyzed azide-alkyne cycloaddition with benzyl azide and methyl propiolate using ascorbic acid as a reducing agent in continuous mode operation of the VFD at room temperature (>200 mg scale)

Two syringe pumps were used to pump the liquid reagents through the continuous flow set up. A solution of benzyl azide (6 mL, 0.25 M, in H_2O:CH_3CN 20:80) together with ascorbic acid (30 mol %) were transferred into 1 of the 2 syringes. This syringe was set to deliver contents at 0.5 mL min^{-1}. The other syringe contained methyl propiolate (6 mL, 0.34 M, in H_2O:CH_3CN 20:80) and was set to deliver contents at 0.5 mL min^{-1} using a copper jet feed (diameter = 1.28 mm, volume = 0.39 mL, surface area = 12.1 cm^2). This resulted in a total flow rate of 1 mL min^{-1}. The solutions were injected via syringe pump into the base of the VFD tube, operating at 9k rpm with a 45° tilt angle. The total reaction time was 12 minutes, over which time the reaction product was collected in a single flask. After this time, the system was flushed with 4 mL H_2O:CH_3CN 20:80 in each syringe and this was collected in the same flask. Next, the solvent was removed under reduced pressure and the crude product was recrystallised from water to obtain the product as clear, colourless crystals (80%, 260 mg).

Copper-catalyzed azide-alkyne cycloaddition with benzyl azide and ethyl propiolate using ascorbic acid as a reducing agent in continuous mode operation of the VFD at room temperature (>200 mg scale)

Two syringe pumps were used to pump the liquid reagents through the continuous flow set up. A solution of benzyl azide (6 mL, 0.25 M, in H_2O:CH_3CN 20:80) together with ascorbic acid (30 mol %) were transferred into 1 of the 2 syringes. This syringe was set to deliver contents at 0.5 mL min^{-1}. The other syringe contained ethyl propiolate (6 mL, 0.34 M, in H_2O:CH_3CN 20:80) and was set to deliver contents at 0.5 mL min^{-1} using a copper jet feed (diameter = 1.28 mm, volume = 0.39 mL, surface area = 12.1 cm^2). This resulted in a total flow rate of 1 mL min^{-1}. The solutions were injected via syringe pump into the base of the VFD tube, operating at 9k rpm with a 45° tilt angle. The total reaction time was 12 minutes, over which time the reaction product was collected in a single flask. After this time, the system was flushed with 4 mL H_2O:CH_3CN 20:80 in each syringe and this was collected in the same flask. Next, the solvent was removed under reduced pressure and the crude product was recrystallised from water to obtain the product as a white solid (82%, 284 mg).

Copper-catalyzed azide-alkyne cycloaddition with benzyl azide and 4-ethynylanisole using ascorbic acid as a reducing agent in continuous mode operation of the VFD at room temperature (>200 mg scale)

Two syringe pumps were used to pump the liquid reagents through the continuous flow set up. A solution of benzyl azide (6 mL, 0.25 M, in H_2O:CH_3CN 20:80) together with ascorbic acid (30 mol %) were transferred into 1 of the 2 syringes. This syringe was set to deliver contents at 0.5 mL min^{-1}. The other syringe contained 4-ethynylanisole (6 mL, 0.34 M, in H_2O:CH_3CN 20:80) and was set to deliver contents at 0.5 mL min^{-1} using a copper jet feed (diameter = 1.28 mm, volume = 0.39 mL, surface area = 12.1 cm^2). This resulted in a total flow rate of 1 mL min^{-1}. The solutions were injected via syringe pump into the base of the VFD tube, operating at 9k rpm with a 45° tilt angle. The total reaction time was 12 minutes, over which time the reaction product was collected in a single flask. After this time, the system was flushed with 4 mL H_2O:CH_3CN 20:80 in each syringe and this was collected in the same flask. Next, the solvent was removed under reduced pressure and the crude product was recrystallised from water to obtain the product as a white solid (90%, 358 mg).

Copper-catalyzed azide-alkyne cycloaddition with 3-methoxybenzyl azide and 4-ethynylanisole using ascorbic acid as a reducing agent in continuous mode operation of the VFD at room temperature (>200 mg scale)

3-methoxybenzyl azide was synthesised from 3-methoxybenzyl chloride (6.39 mmol), sodium azide (6.15 mmol) in CH_3CN (20 mL) by stirring for 18 hours at room temperature. A solution of 3-methoxybenzyl azide (6 mL, 0.25 M, in H_2O:CH_3CN 20:80) together with ascorbic acid (30 mol %) were transferred into 1 of the 2 syringes. This syringe was set to deliver contents at 0.5 mL min^{-1}. The other syringe contained 4-ethynylanisole (6 mL, 0.34 M, in H_2O:CH_3CN 20:80) and was set to deliver contents at 0.5 mL min^{-1} using a copper jet feed (diameter = 1.28 mm, volume = 0.39 mL, surface area = 12.1 cm^2). This resulted in a total flow rate of 1 mL min^{-1}. The solutions were injected via syringe pump into the base of the VFD tube, operating at 9k rpm with a 45° tilt angle. The total reaction time was 12 minutes, over which time the reaction product was collected in a single flask. After this time, the system was flushed with 4 mL H_2O:CH_3CN 20:80 in each syringe and this was collected in the same flask. Next, the solvent was removed under reduced pressure and the product was extracted from DCM (2 x 15 mL), dried with anhydrous sodium sulfate, filtered and solvent removed under reduced pressure. The product was obtained as a wax (93%, 412 mg).

Copper-catalyzed azide-alkyne cycloaddition with 3-methoxybenzyl azide and propargyl alcohol using ascorbic acid as a reducing agent in continuous mode operation of the VFD at room temperature (>200 mg scale)

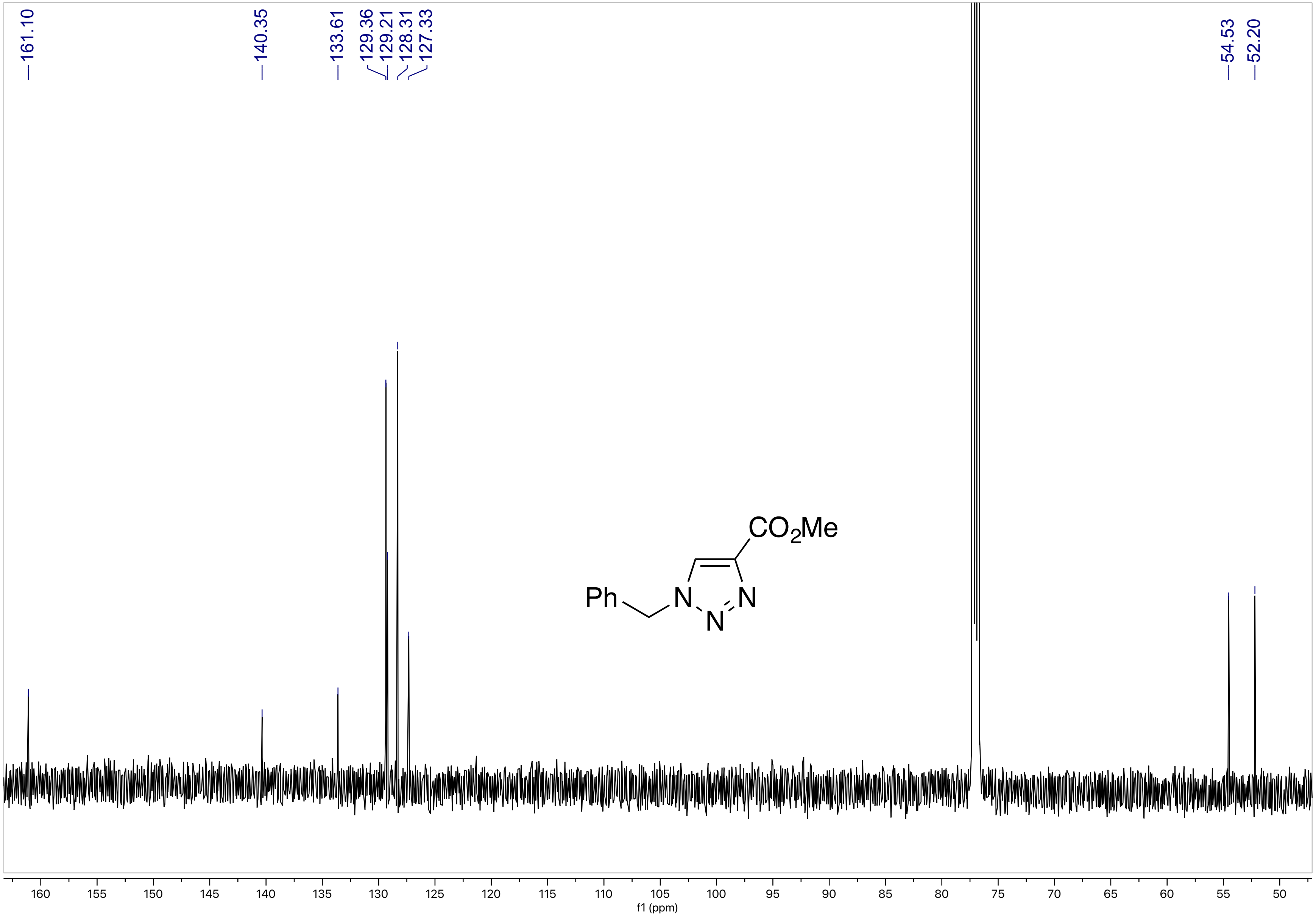
3-methoxybenzyl azide was synthesised from 3-methoxybenzyl chloride (6.39 mmol), sodium azide (6.15 mmol) in CH_3CN (20 mL) by stirring for 18 hours at room temperature. A solution of 3-methoxybenzyl azide (6 mL, 0.25 M, in H_2O:CH_3CN 20:80) together with ascorbic acid (30 mol %) were transferred into 1 of the 2 syringes. This syringe was set to deliver contents at 0.5 mL min^{-1}. The other syringe contained propargyl alcohol (6 mL, 0.34 M, in H_2O:CH_3CN 20:80) and was set to deliver contents at 0.5 mL min^{-1} using a copper jet feed (diameter = 1.28 mm, volume = 0.39 mL, surface area = 12.1 cm^2). This resulted in a total flow rate of 1 mL min^{-1}. The solutions were injected via syringe pump into the base of the VFD tube, operating at 9k rpm with a 45° tilt angle. The total reaction time was 12 minutes, over which time the reaction product was collected in a single flask. After this time, the system was flushed with 4 mL H_2O:CH_3CN 20:80 in each syringe and this was collected in the same flask. Next, the solvent was removed under reduced pressure and the product was extracted from DCM (2 x 15 mL), dried with anhydrous sodium sulfate, filtered and solvent removed under reduced pressure. The product was obtained as pale-yellow oil without the need for further purification (82%, 270 mg).

Copper-catalyzed azide-alkyne cycloaddition with 3-methoxybenzyl azide and 3-ethynylanisole using ascorbic acid as a reducing agent in continuous mode operation of the VFD at room temperature (>200 mg scale)

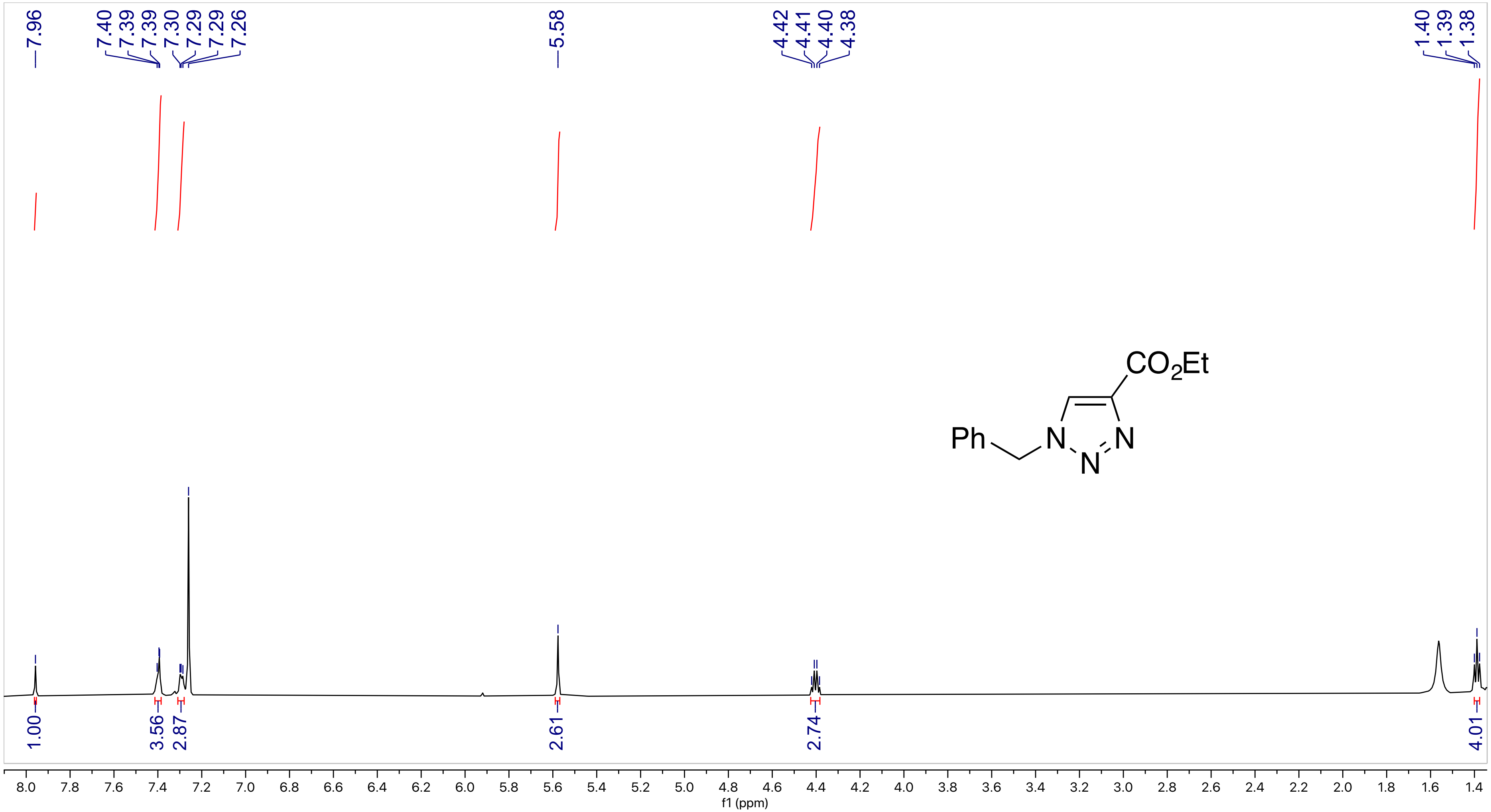
3-methoxybenzyl azide was synthesised from 3-methoxybenzyl chloride (6.39 mmol), sodium azide (6.15 mmol) in CH_3CN (20 mL) by stirring for 18 hours at room temperature. A solution of 3-methoxybenzyl azide (6 mL, 0.25 M, in H_2O:CH_3CN 20:80) together with ascorbic acid (30 mol %) were transferred into 1 of the 2 syringes. This syringe was set to deliver contents at 0.5 mL min^{-1}. The other syringe contained 3-ethynylanisole (6 mL, 0.34 M, in H_2O:CH_3CN 20:80) and was set to deliver contents at 0.5 mL min^{-1} using a copper jet feed (diameter = 1.28 mm, volume = 0.39 mL, surface area = 12.1 cm^2). This resulted in a total flow rate of 1 mL min^{-1}. The solutions were injected via syringe pump into the base of the VFD tube, operating at 9k rpm with a 45° tilt angle. The total reaction time was 12 minutes, over which time the reaction product was collected in a single flask. After this time, the system was flushed with 4 mL H_2O:CH_3CN 20:80 in each syringe and this was collected in the same flask. Next, the solvent was removed under reduced pressure and the product was extracted from DCM (2 x 15 mL), dried with anhydrous sodium sulfate, filtered and solvent removed under reduced pressure. The crude product was purified by column chromatography to remove excess alkyne (50% EtOAc in hexanes, Rf 0.45) and obtained as a pale-yellow oil (73%, 326 mg). HRMS $[M + Na]^+$ calculated = 318.1213, observed = 318.1214

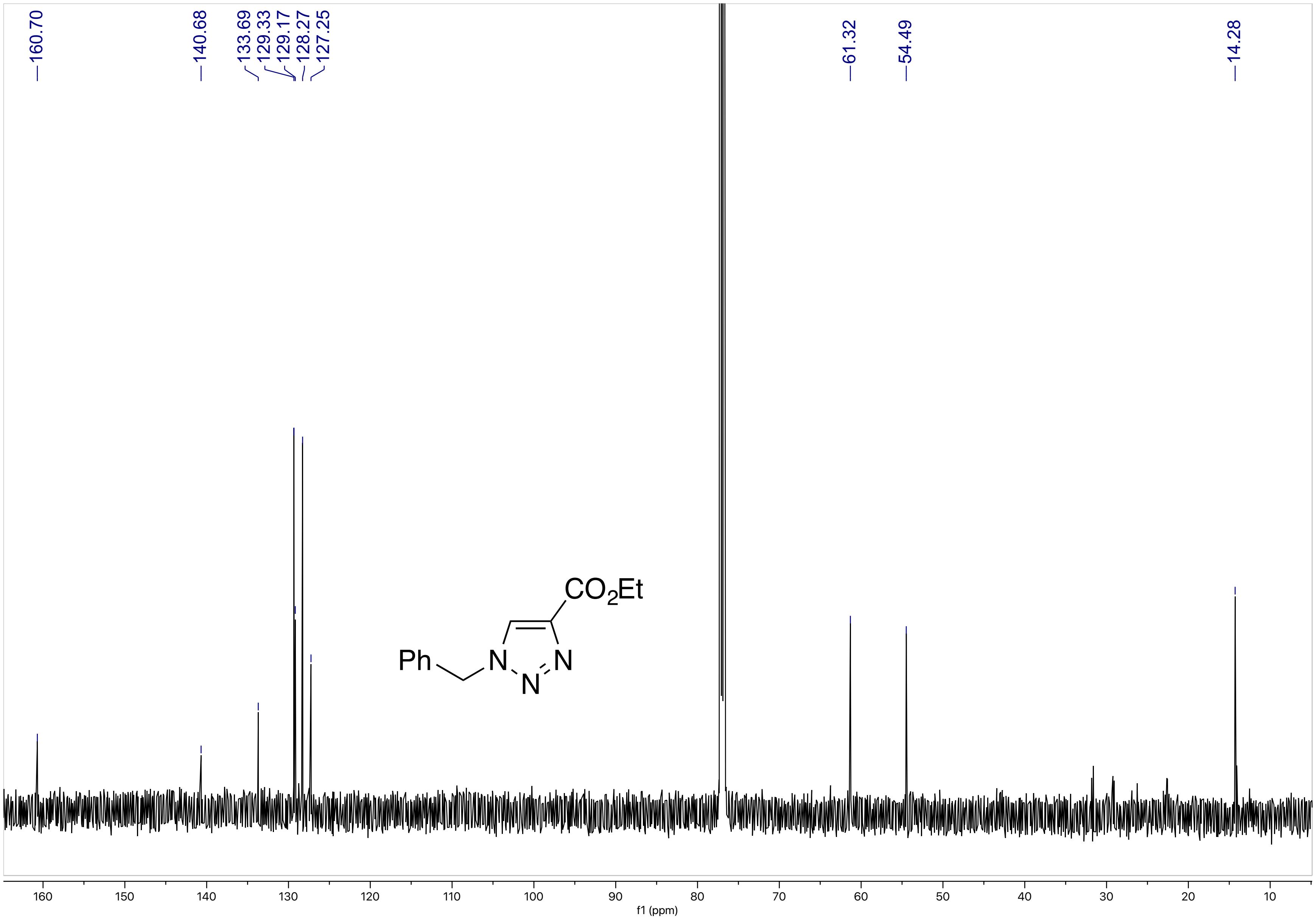
NMR and characterization data for preparative scale copper-catalyzed azide-alkyne cycloadditions in VFD (continuous mode) using ascorbic acid as reducing agent (isolated compounds from Table 3 in main text)

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.97 (s, 1 H), 7.41-7.39 (m, 3 H), 7.30-7.29 (m, 2 H), 5.58 (s, 2 H), 3.93 (s, 3 H) ppm; ^{13}C NMR (600 MHz, $CDCl_3$): δ = 161.1, 140.4, 133.6, 129.4, 129.2, 128.3, 127.3, 54.5, 52.2 ppm.

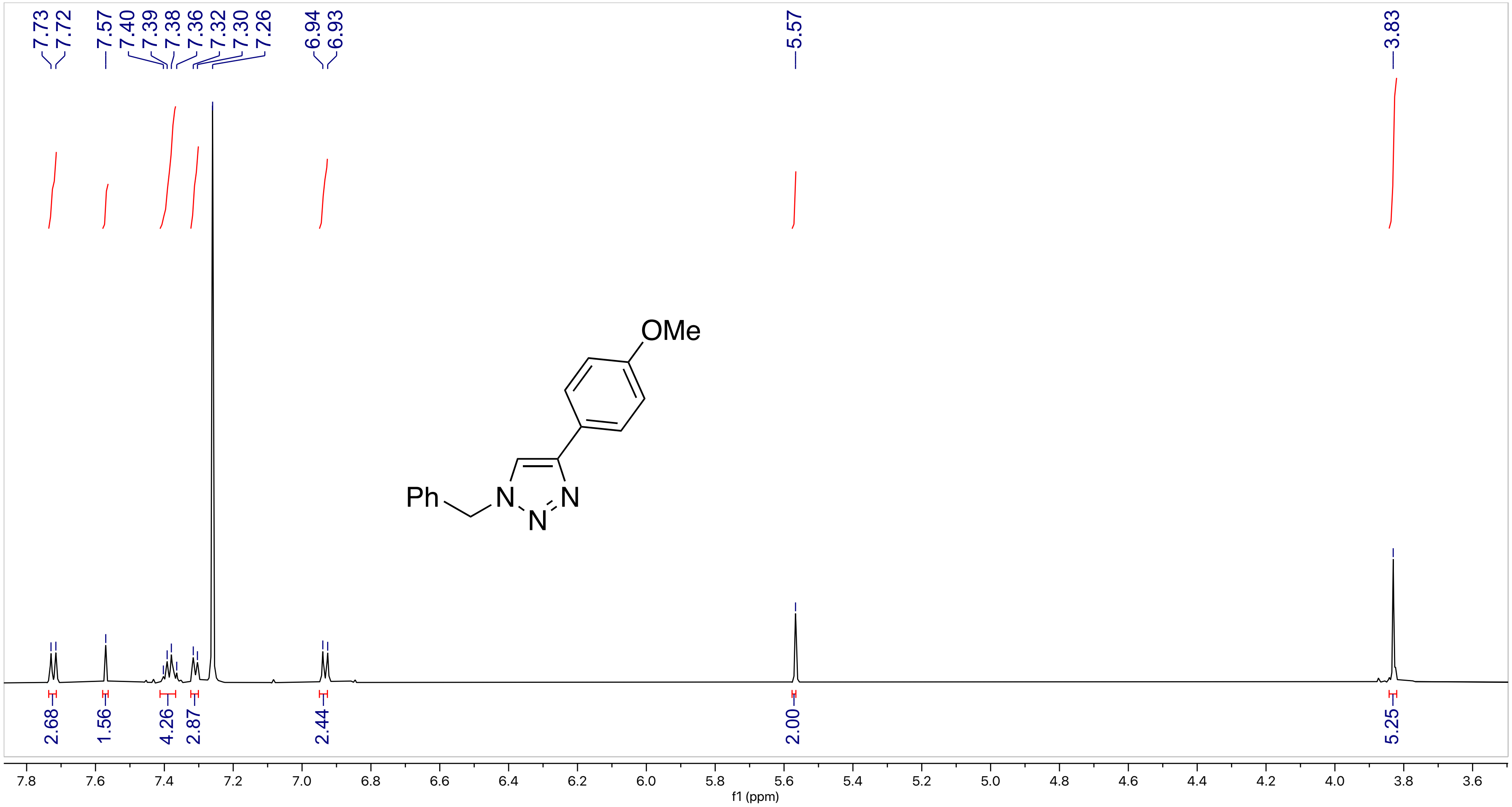

161.10
140.35
133.61
129.36
129.21
128.31
127.33
54.53
52.20
CO2Me
Ph
N
N
N
160
155
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
f1 (ppm)

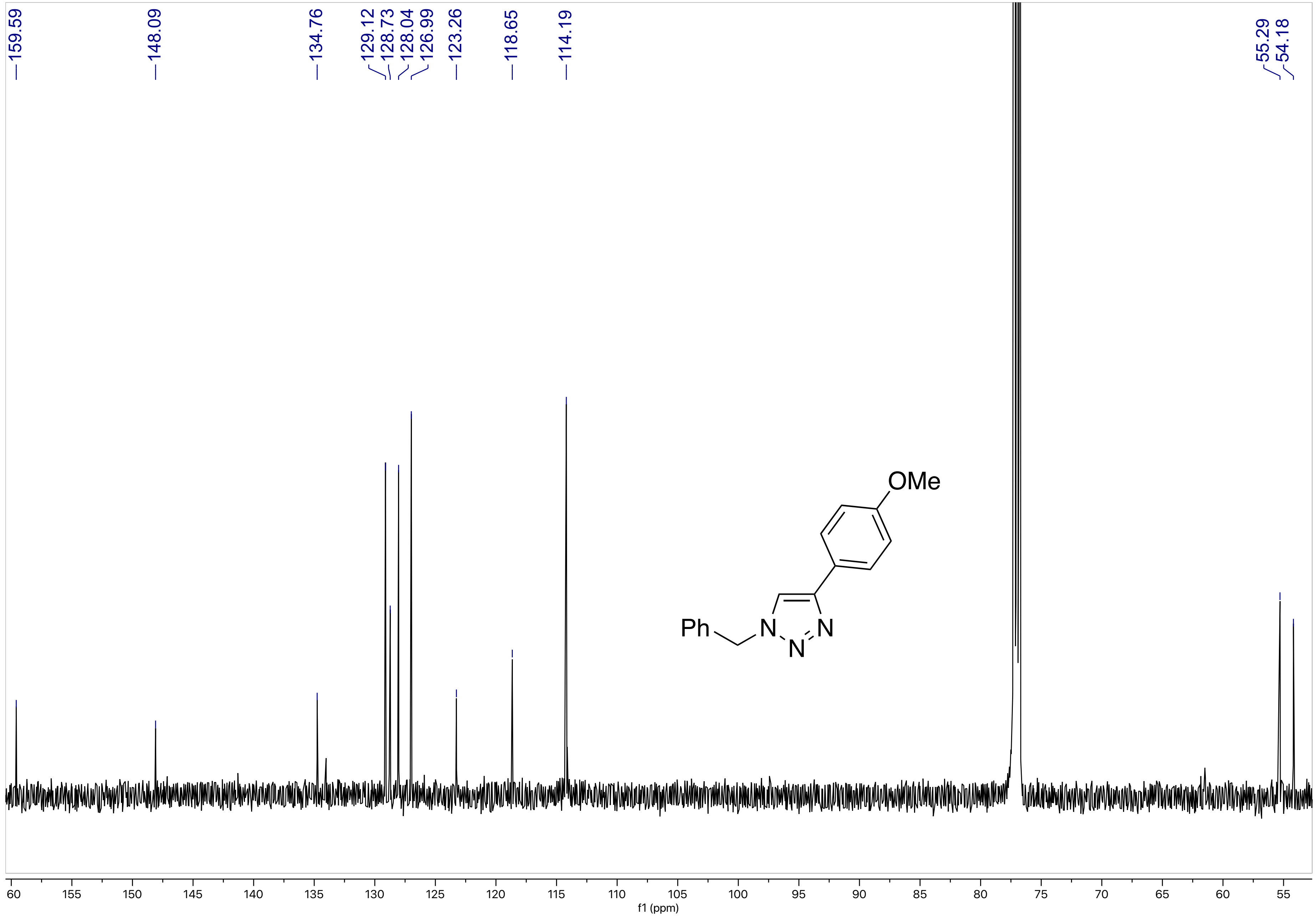
^{1}H NMR (600 MHz, CDCl$_3$): δ = 7.96 (s, 1 H), 7.40-7.39 (m, 3 H), 7.30-7.29 (m, 2 H), 5.58 (s, 2 H), 4.41 (q, 2 H, J = 7.1 Hz), 1.39, (t, 3 H, J = 6.7 Hz) ppm; ^{13}C NMR (600 MHz, CDCl$_3$): δ = 160.7, 140.7, 133.7, 129.3, 129.2, 128.3, 127.3, 61.3, 54.5, 14.3 ppm.



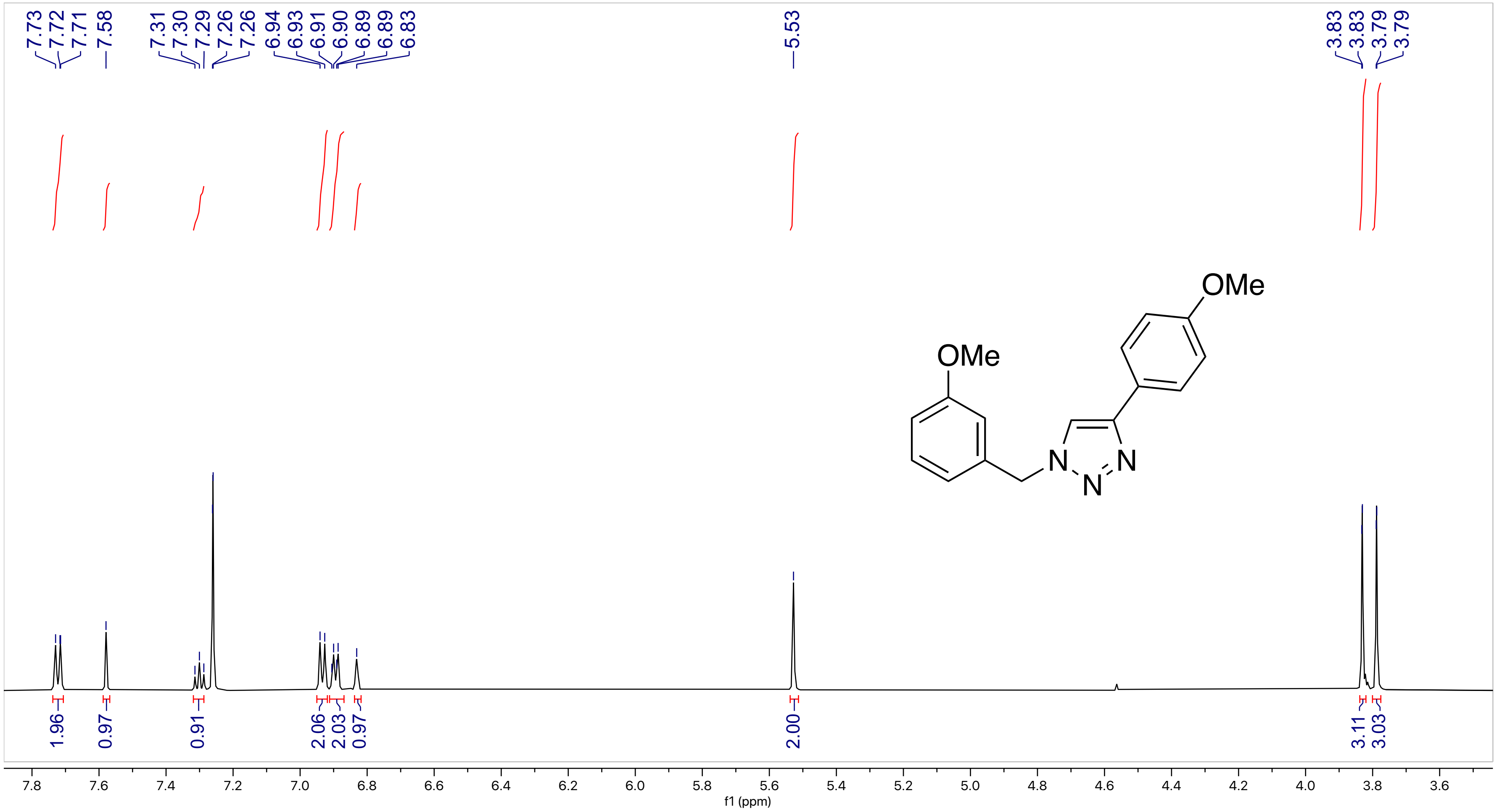

160.70
140.68
133.69
129.33
129.17
128.27
127.25
61.32
54.49
14.28
CO2Et
Ph
N
N
N
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

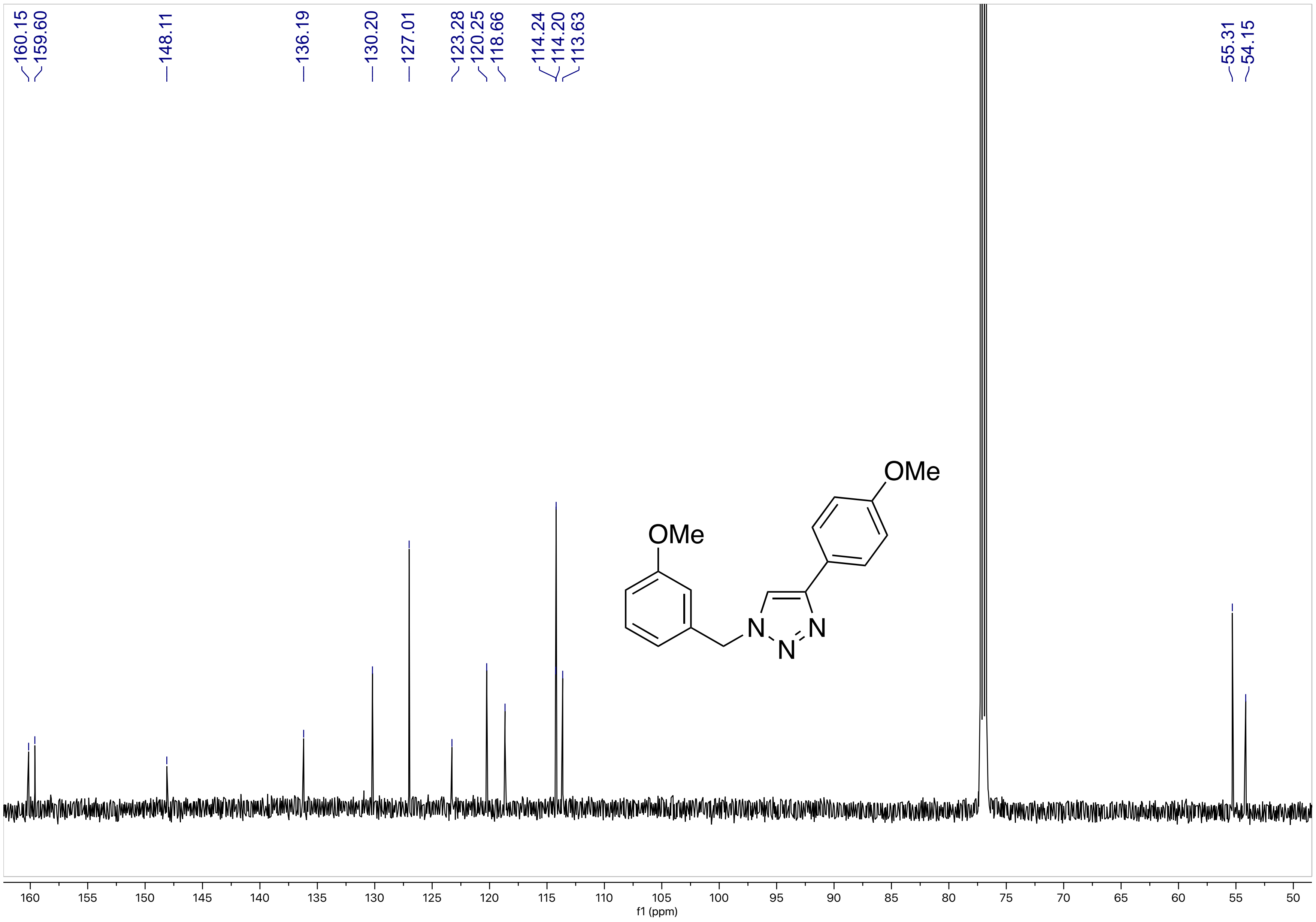
^{1}H NMR (600 MHz, CDCl$_3$): δ = 7.73 (d, 2 H, J = 8.5 Hz), 7.57 (s, 1 H), 7.40-7.36 (m, 3 H), 7.32-7.30 (m, 2 H), 6.94 (d, 2 H, J = 8.5), 5.57 (s, 2 H), 3.83 (s, 3 H) ppm; ^{13}C NMR (600 MHz, CDCl$_3$): δ = 155.6, 148.1, 134.8, 129.1, 128.7, 128.0, 126.9, 123.3, 118.7, 114.2, 55.3, 54.2 ppm.



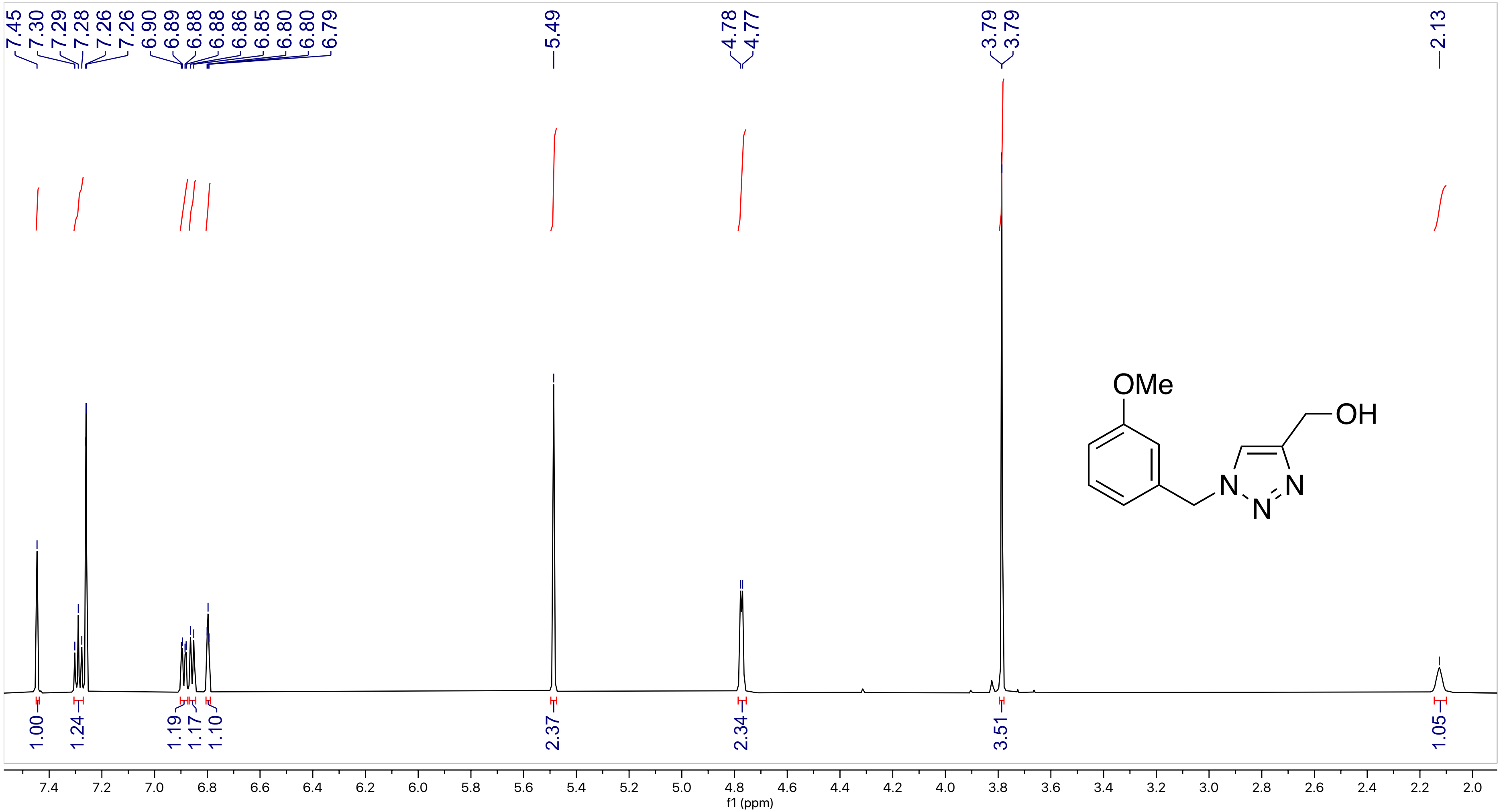

159.59
148.09
134.76
129.12
128.73
128.04
126.99
123.26
118.65
114.19
55.29
54.18
OMe
Ph
N
N
N
60
155
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
f1 (ppm)

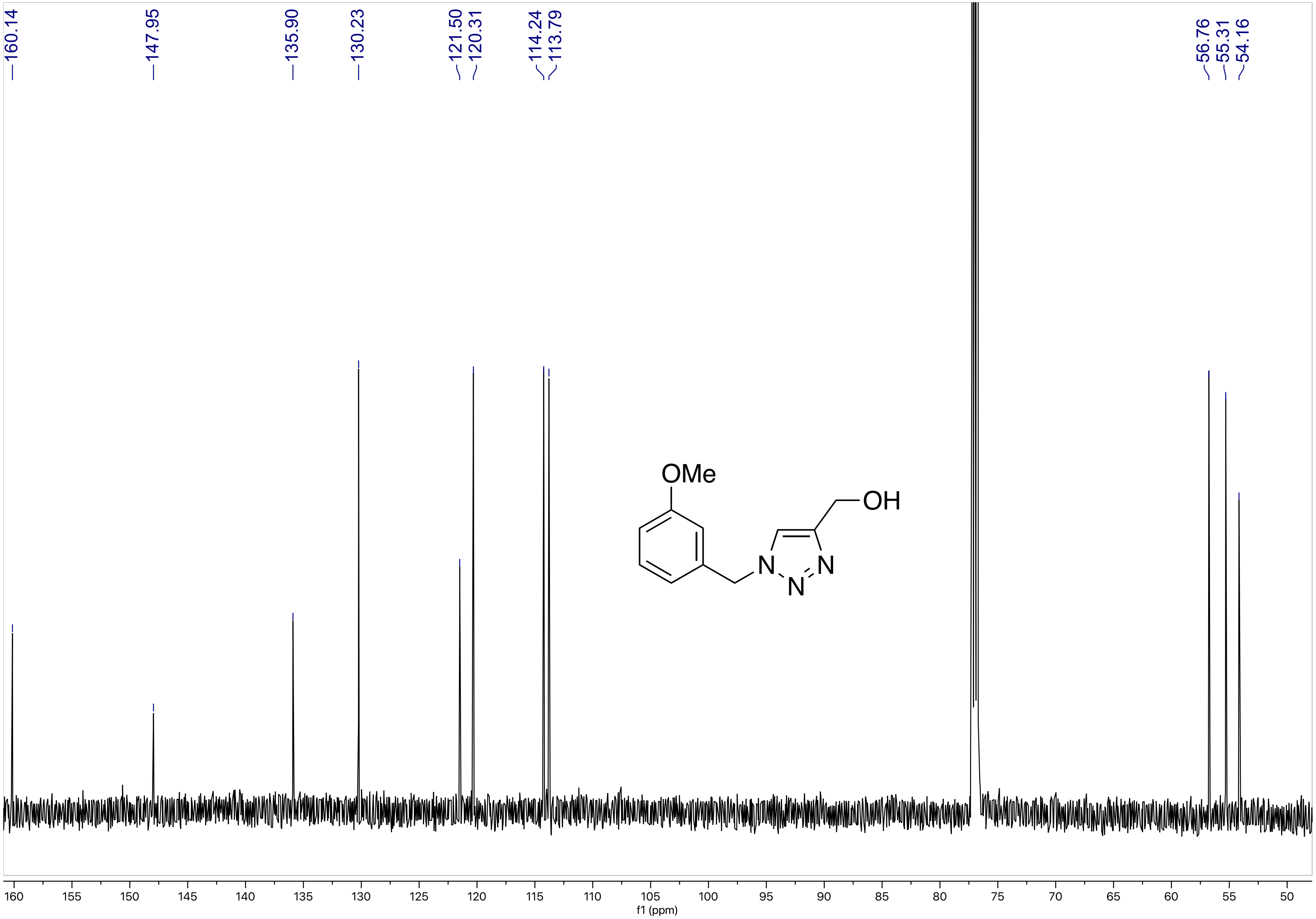
^{1}H NMR (600 MHz, CDCl$_3$): δ = 7.73 (d, 2 H, J = 8.4 Hz), 7.58 (s, 1 H), 7.31 (t, 1 H, J = 7.46 Hz), 6.94 (d, 2 H, J = 8.42 Hz), 6.91 (2 H, J = 8.06 Hz), 6.83 (s, 1 H), 5.53 (s, 2 H), 3.83 (s, 3 H), 3.79 (s, 3 H) ppm; ^{13}C NMR (600 MHz, CDCl$_3$): δ = 160.2, 159.6, 148.1, 136.2, 130.2, 127.0, 123.3, 120.3, 118.7, 114.2, 114.2, 113.6, 55.3, 54.2 ppm. HRMS (ESI): [M+Na$^+$] found 318.1215. C$_{17}$H$_{17}$N$_3$O$_2$Na$^+$ requires 318.1213.



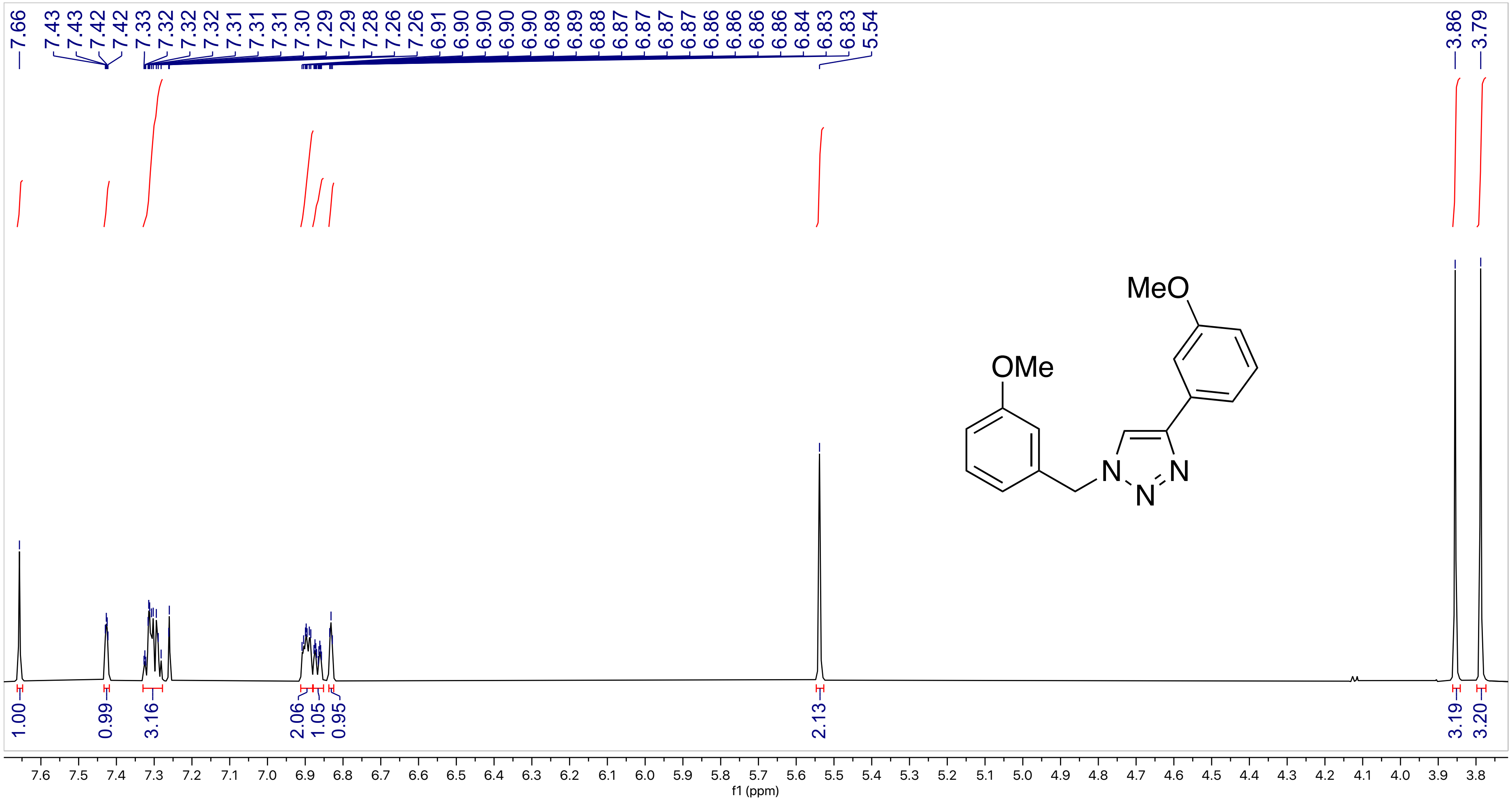

160.15
159.60
148.11
136.19
130.20
127.01
123.28
120.25
118.66
114.24
114.20
113.63
55.31
54.15
OMe
OMe
N
N
N
160
155
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
f1 (ppm)

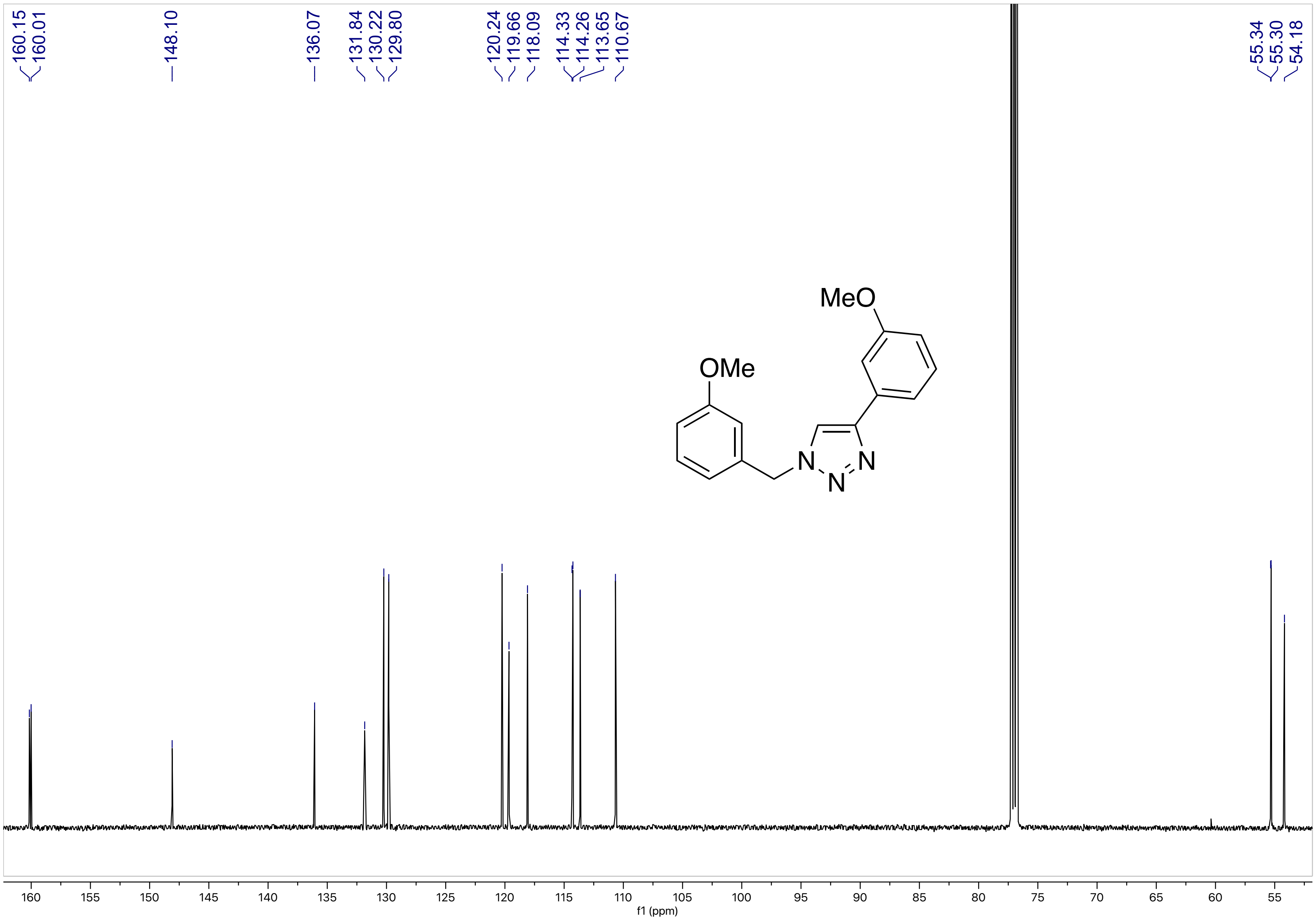
^{1}H NMR (600 MHz, CDCl$_3$): δ = 7.45 (s, 1 H), 7.30 (t, 1 H, J = 7.89 Hz), 6.90 (m, 1 H), 6.86 (d, 1 H, J = 7.50 Hz), 5.49 (s, 2 H), 4.78 (m, 2 H), 3.79 (s, 3 H), 3.79 (s, 3 H), 2.13 (s, 1H) ppm; ^{13}C NMR (600 MHz, CDCl$_3$): δ = 160.1, 147.9, 135.9, 130.2, 121.5, 120.3, 114.2, 113.8, 56.76, 55.3, 54.2 ppm. HRMS (ESI): [M+Na$^+$] found 242.0893. C$_{11}$H$_{13}$N$_3$O$_2$Na$^+$ requires 242.0900.




160.14
147.95
135.90
130.23
121.50
120.31
114.24
113.79
56.76
55.31
54.16
OMe
OH
N
N
N
160
155
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
f1 (ppm)

^{1}H NMR (600 MHz, CDCl$_3$): δ = 7.66 (s, 1H), 7.43 (br, 1 H), 7.32 (m, 3 H), 6.91 (m, 2 H), 6.87 (m, 1 H), 6.84 (s, 1 H), 5.54 (s, 2 H), 3.86 (s, 3 H), 3.79 (s, 3 H) ppm; ^{13}C NMR (600 MHz, CDCl$_3$): δ = 160.2, 160.0, 148.1, 136.1, 131.8, 130.2, 129.8, 120.2, 119.7, 118.1, 114.3, 114.3, 113.7, 110.7, 55.34, 55.3, 54.2 ppm. HRMS (ESI): [M+Na$^+$] found 318.1214. $C_{17}H_{17}N_3O_2Na^+$ requires 318.1213.




160.15
160.01
148.10
136.07
131.84
130.22
129.80
120.24
119.66
118.09
114.33
114.26
113.65
110.67
55.34
55.30
54.18
MeO
OMe
N
N
N
160
155
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
f1 (ppm)

(i) – Photochemical promoted CuAAC reaction in continuous mode operation of the VFD at room temperature

Two syringe pumps were used to pump the liquid reagents through the continuous flow set up. A solution of benzyl azide (10 mL, 0.025 M, in H_2O:CH_3CN 70:30) together of 75 µL eosin Y (5 mM) (0.15 mol %) were transferred into 1 of the 2 syringes. This syringe was set to deliver contents at 0.05 mL min^{-1}. The other syringe contained methyl propiolate (10 mL, 0.034 M, in H_2O:CH_3CN 80:20) and was set to deliver contents at 0.05 mL min^{-1} using a copper jet feed (diameter = 1.28 mm, volume = 0.39 mL, surface area = 12.1 cm^2). This resulted in a total flow rate of 0.1 mL min^{-1}, which relates to 11.7 minutes residence time (time for the liquid delivered to the base of the rotating tube to leave the top). The solutions were injected *via* syringe pump into the base of the VFD tube, operating at 9k rpm with a 45° tilt angle and were irradiated with green-LED device (supporting 10 high power LEDs, 525 nm, 3W_GREEN, LEDsales) (Fig. S5 on the next page) and stirred under an atmosphere of air. The total reaction time was 3.3 hours, over which time the collection vessel was changed every 70 min giving 3 fractions of reaction product. The organic material was extracted from these fractions with $CDCl_3$ and analyzed each by ^{1}H-NMR.

Table S9. Optimization of flow rate and eosin (mol %) in the photochemical promoted CuAAC reaction following procedure H.

Flow rate (mL min^{-1})	**Eosin (mol %)**	**% Conversion[a]**	**[Cu] (ppm)[b]**
0.2	0.3	68	
0.1	0.3	>99	5.29
0.1	0.15	>99	
0.1	0.07	96.6	
0.1	-	21	
0.1	0.07[c]	33	

[a] Determined by ^{1}H-NMR peak integration relative to benzyl azide. Only the 1,4-isomer was detected. [b] Detected using ICP-MS following procedure E under exposure of green LEDs. LOQ-Limit of Quantification 0.02 ppm. [c] Without green LEDs irradiation.

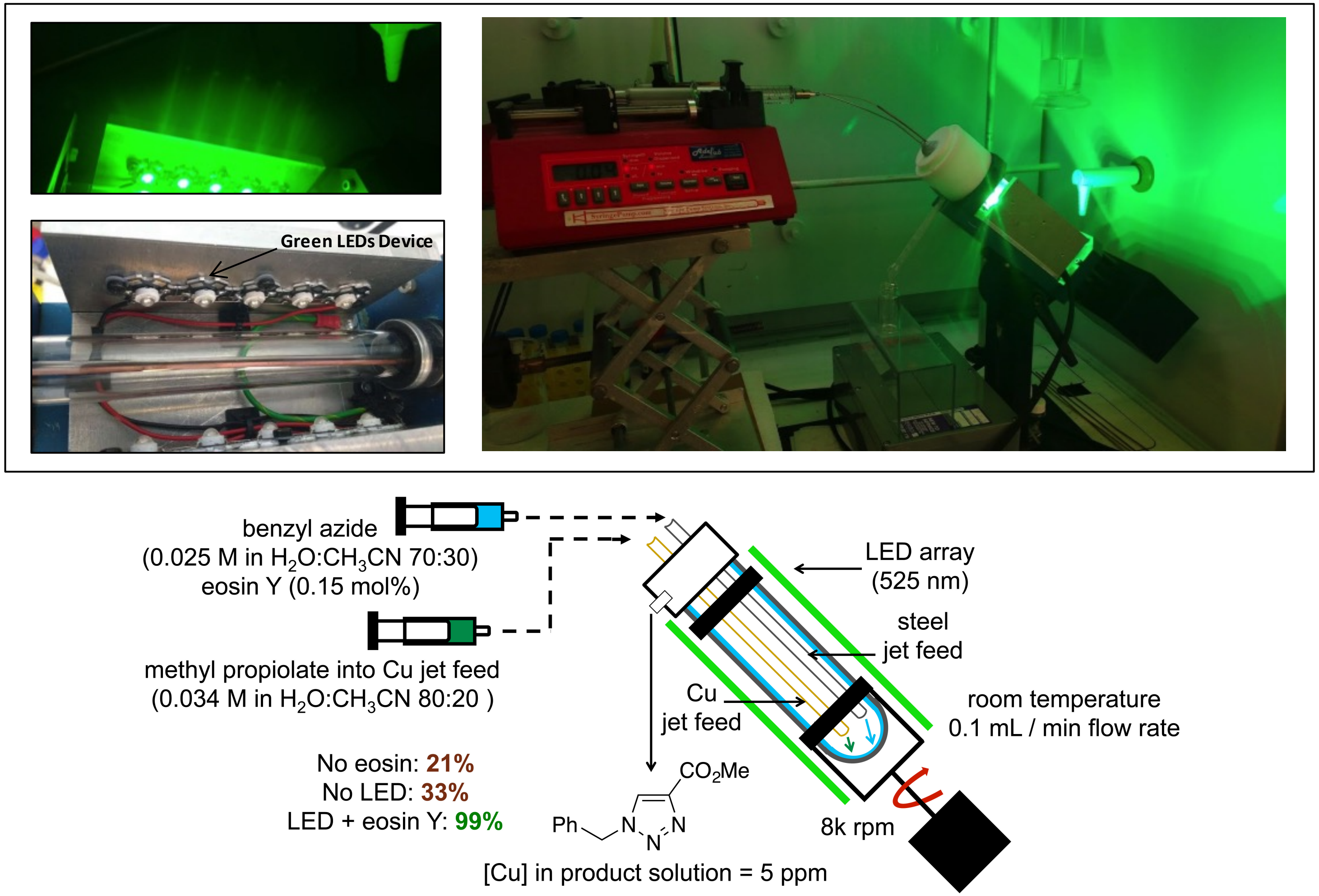
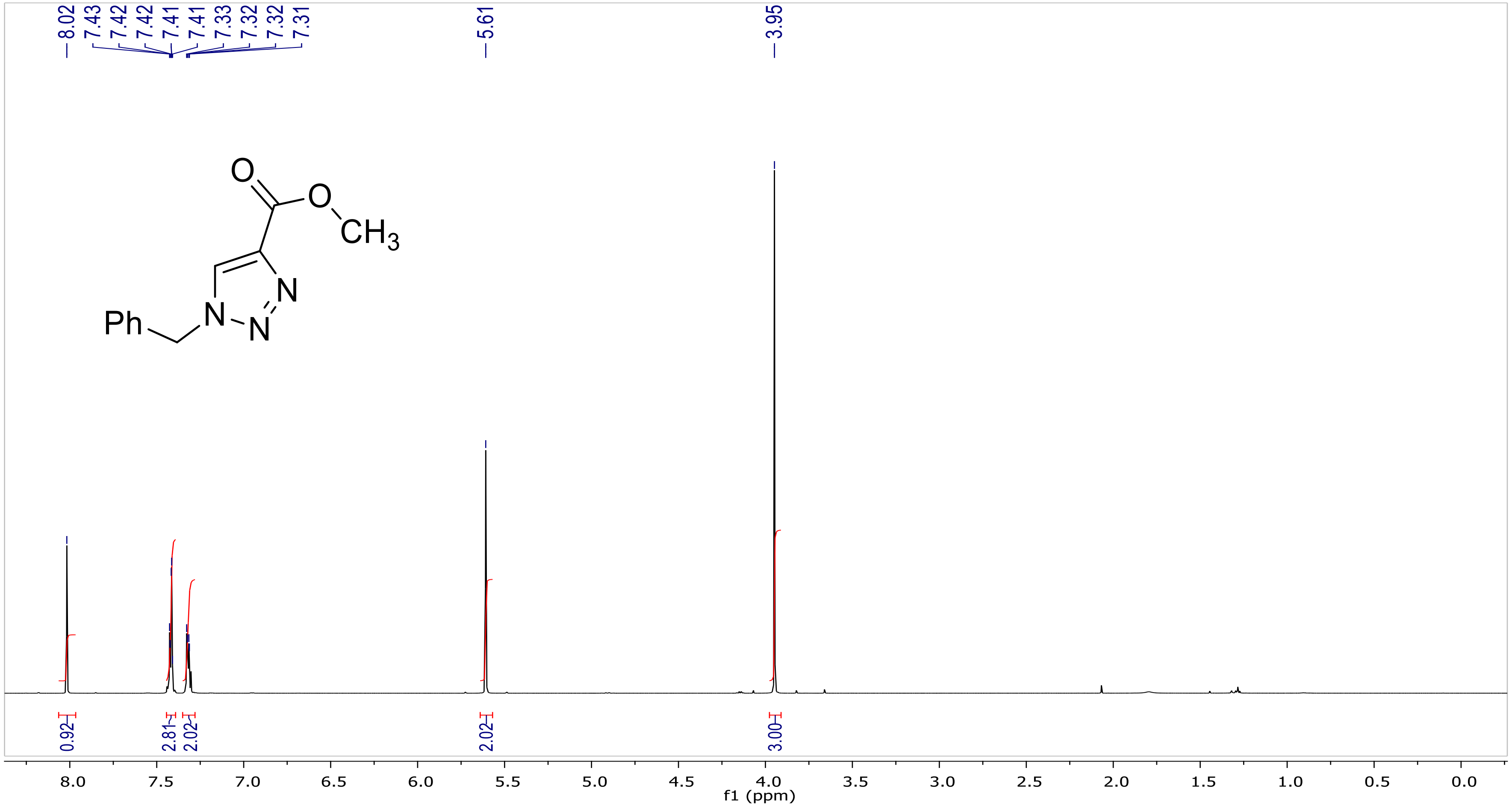
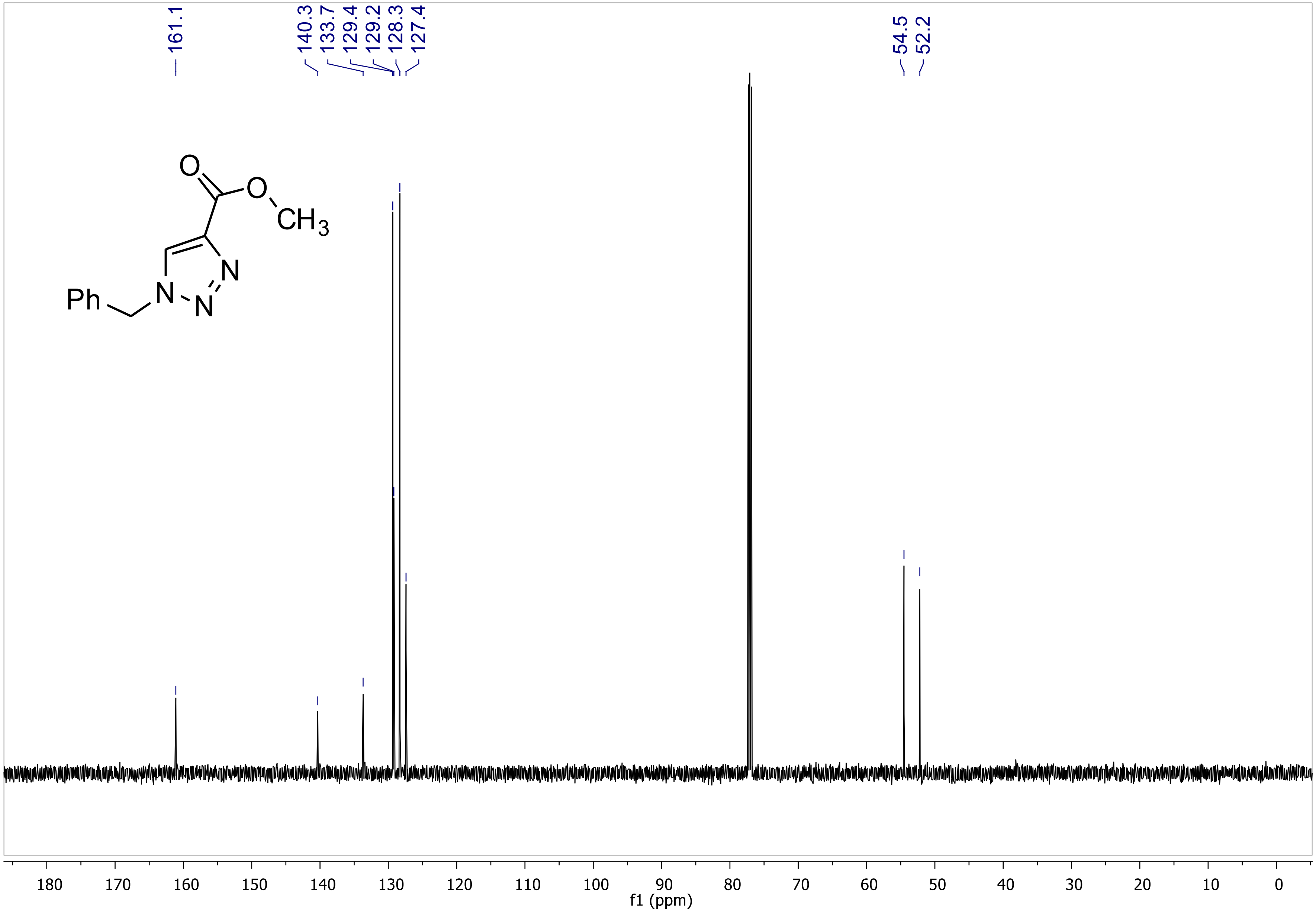


Figure S5. Photograph and schematic of the VFD operating in continuous mode using green LEDs. An LED array (525 nm) and eosin Y were used to photochemically reduce leached copper to the active Cu(I) catalyst, enabling a straightforward continuous production of the product triazole with quantitative conversion.

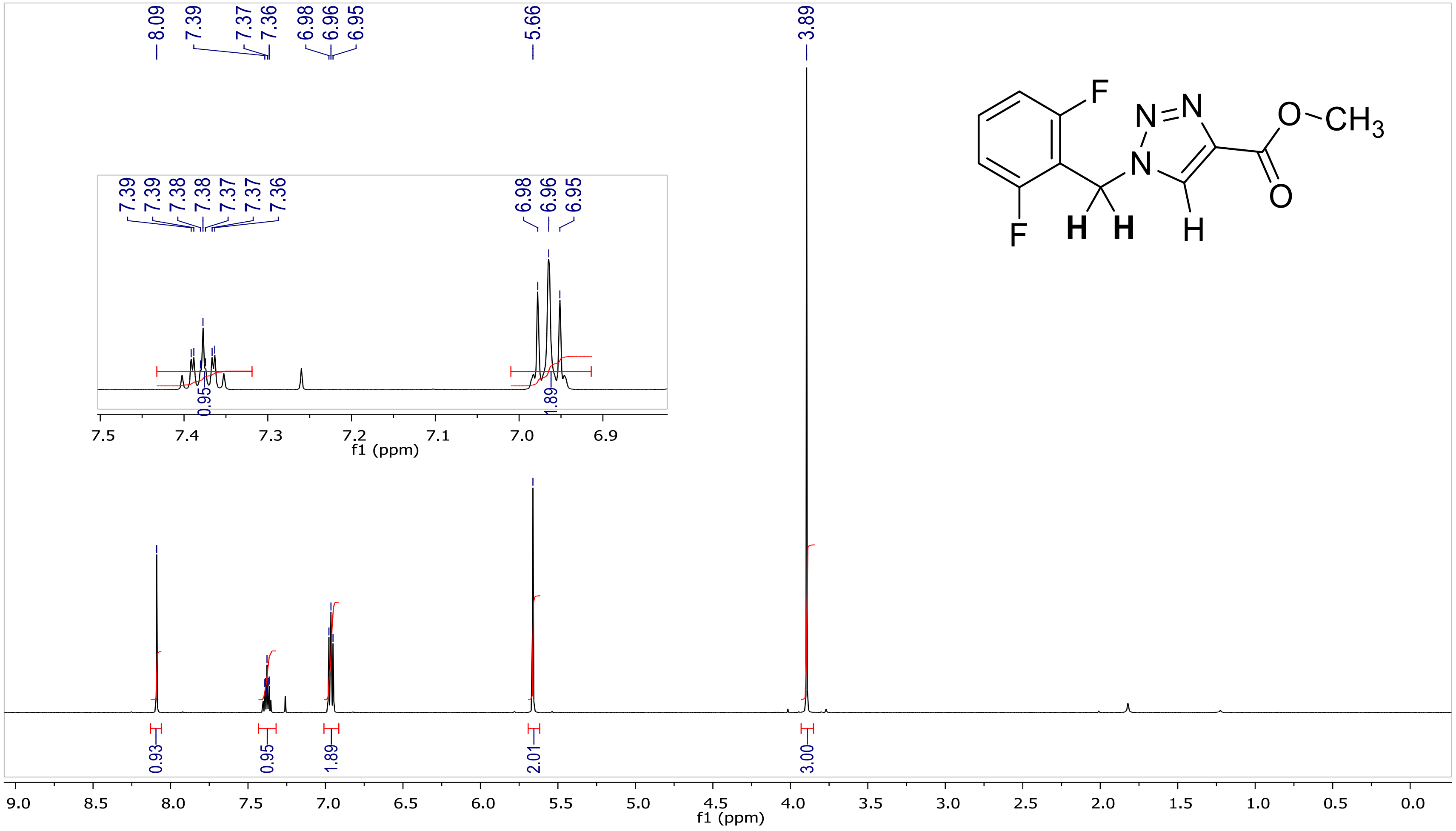
Additional NMR spectra for triazole products (all purified by column chromatography)

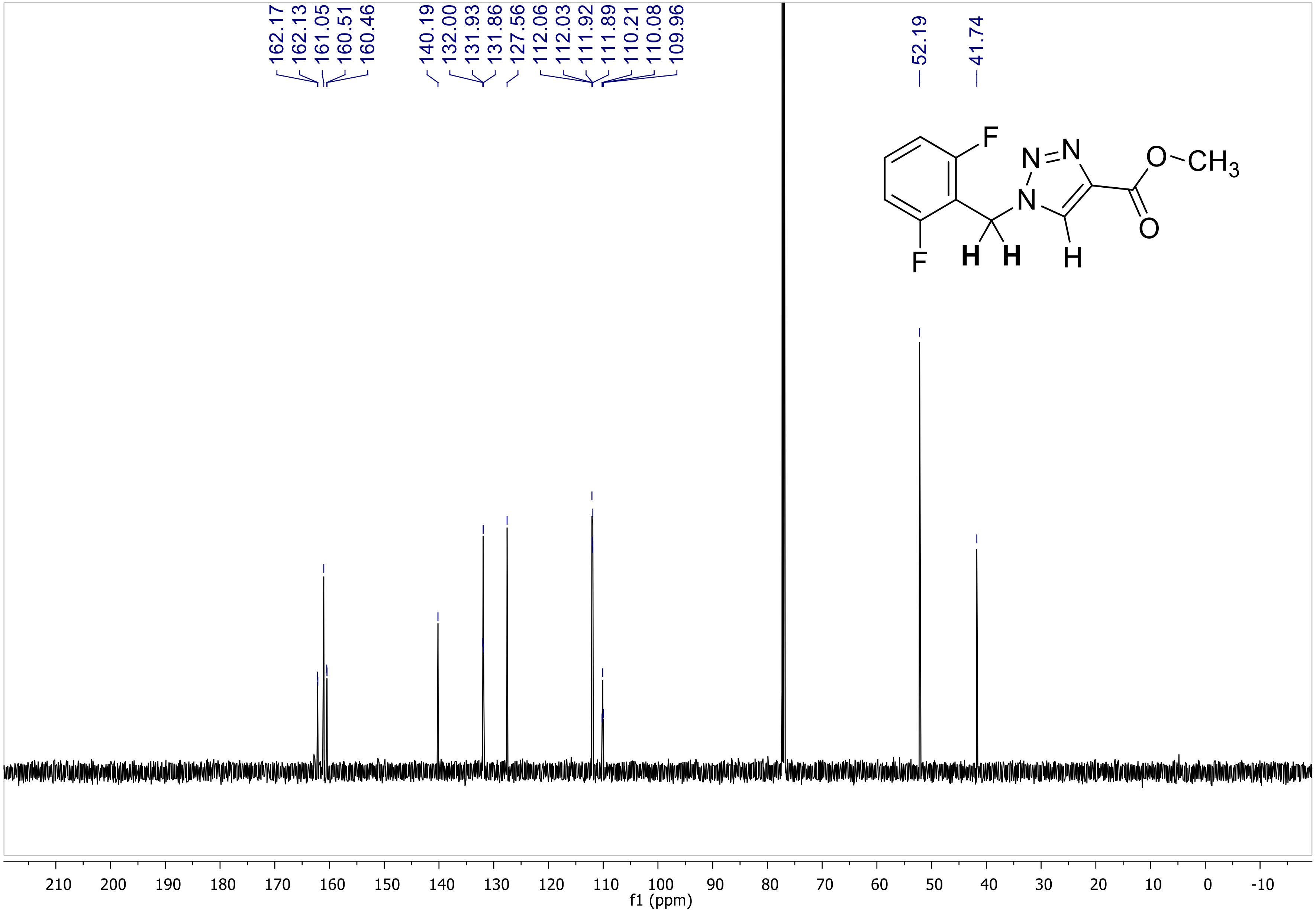
Methyl 1-(benzyl)-1*H*-1,2,3-triazole-4-carboxylate: ^{1}H NMR (600 MHz, $CDCl_3$): δ=8.02 (s, 1 H), 7.43-7.41 (m, 3 H), 7.33-7.31 (m, 2 H), 5.61 (s, 2 H), 3.95 ppm (s, 3 H); ^{13}C (600 MHz, $CDCl_3$): δ= 161.1, 104.3, 133.7, 129.4, 129.2, 128.3, 127.4, 54.5, 52.2 ppm.

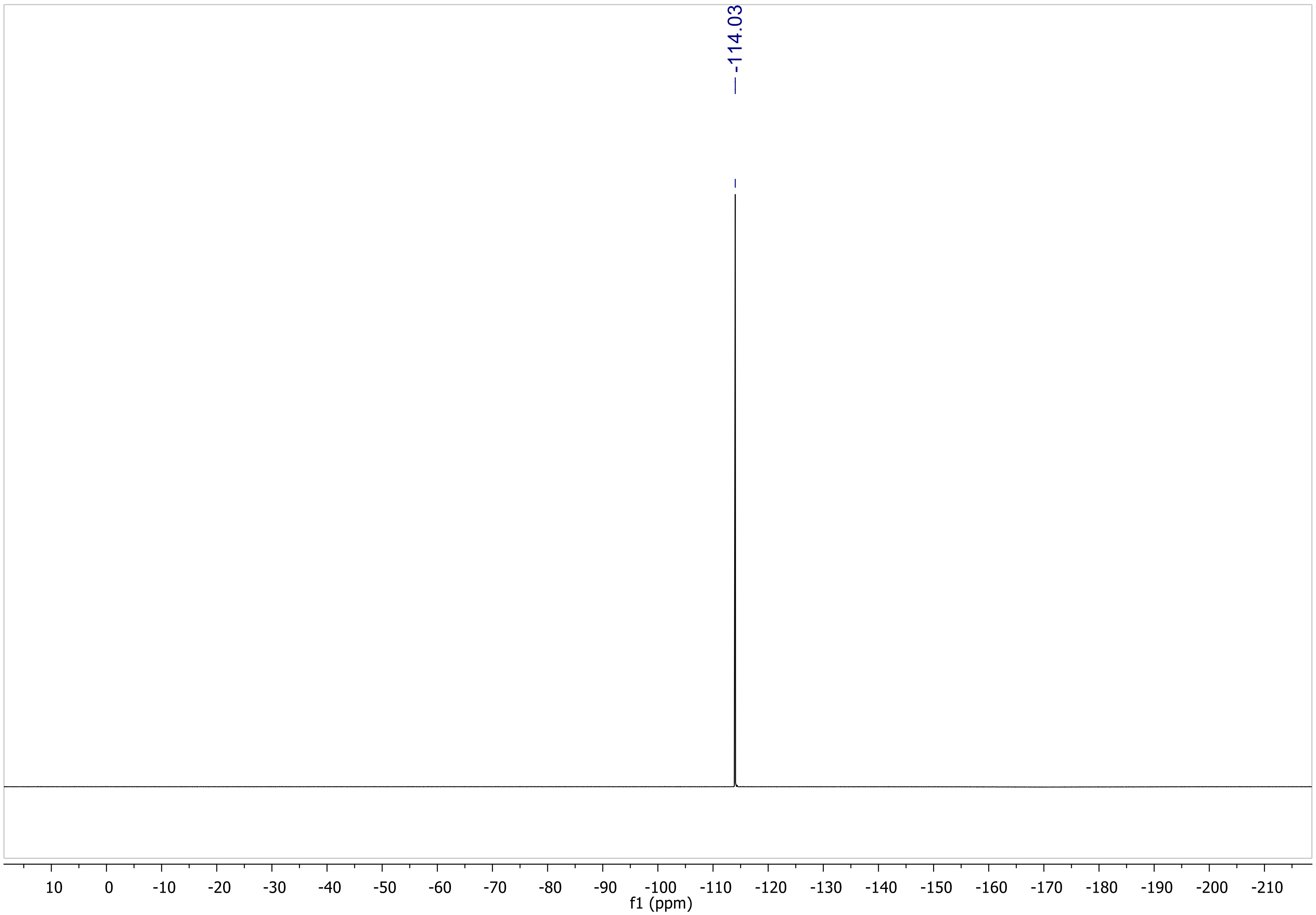



161.1
140.3
133.7
129.4
129.2
128.3
127.4
54.5
52.2
O
O
CH3
N
N
N
Ph
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

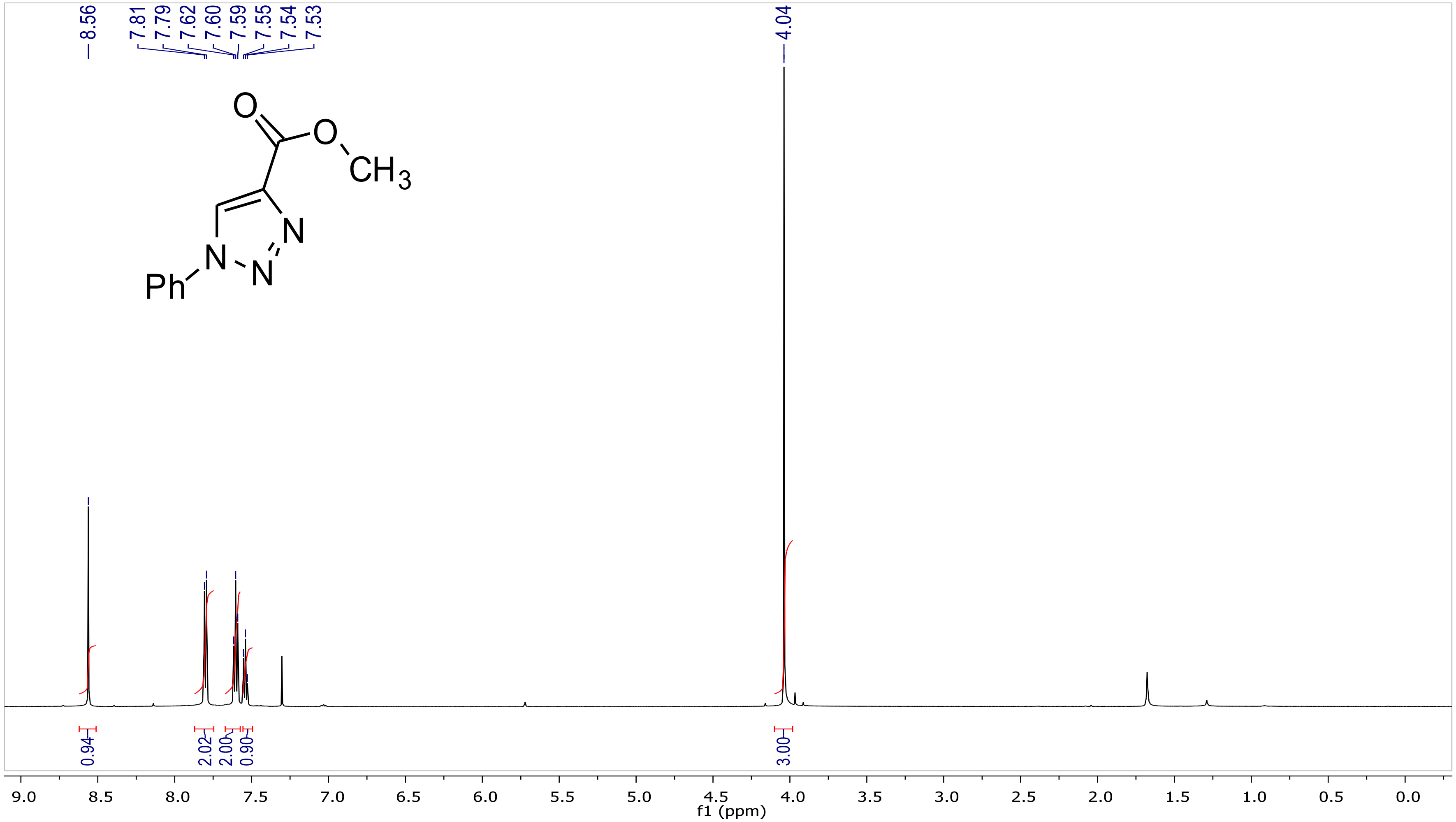
Methyl 1-(2,6-difluorobenzyl)-1H-1,2,3- triazole-4-carboxylate: ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.09 (s, 1H), 7.38 (t, J= 12 Hz, 1H), 7.96 (t, J= 12 Hz, 2H), 5.66 (s, 2H), 3.89 (s, 3H); ^{13}C (600 MHz, CDCl$_3$) δ 162.15 (d, J= 6.7 Hz), 161.05, 160.48 (d, J = 6.8 Hz), 140.19 (s), 131.93 (t, *J* = 10.4 Hz), 127.56 (s), 111.98 (dd, *J* = 20.7, 4.4 Hz), 110.08 (t, *J* = 18.8 Hz), 52.19 (s), 41.74 (s); ^{19}FNMR (600 MHz, CDCl$_3$) δ 114.03 (s, 2F).

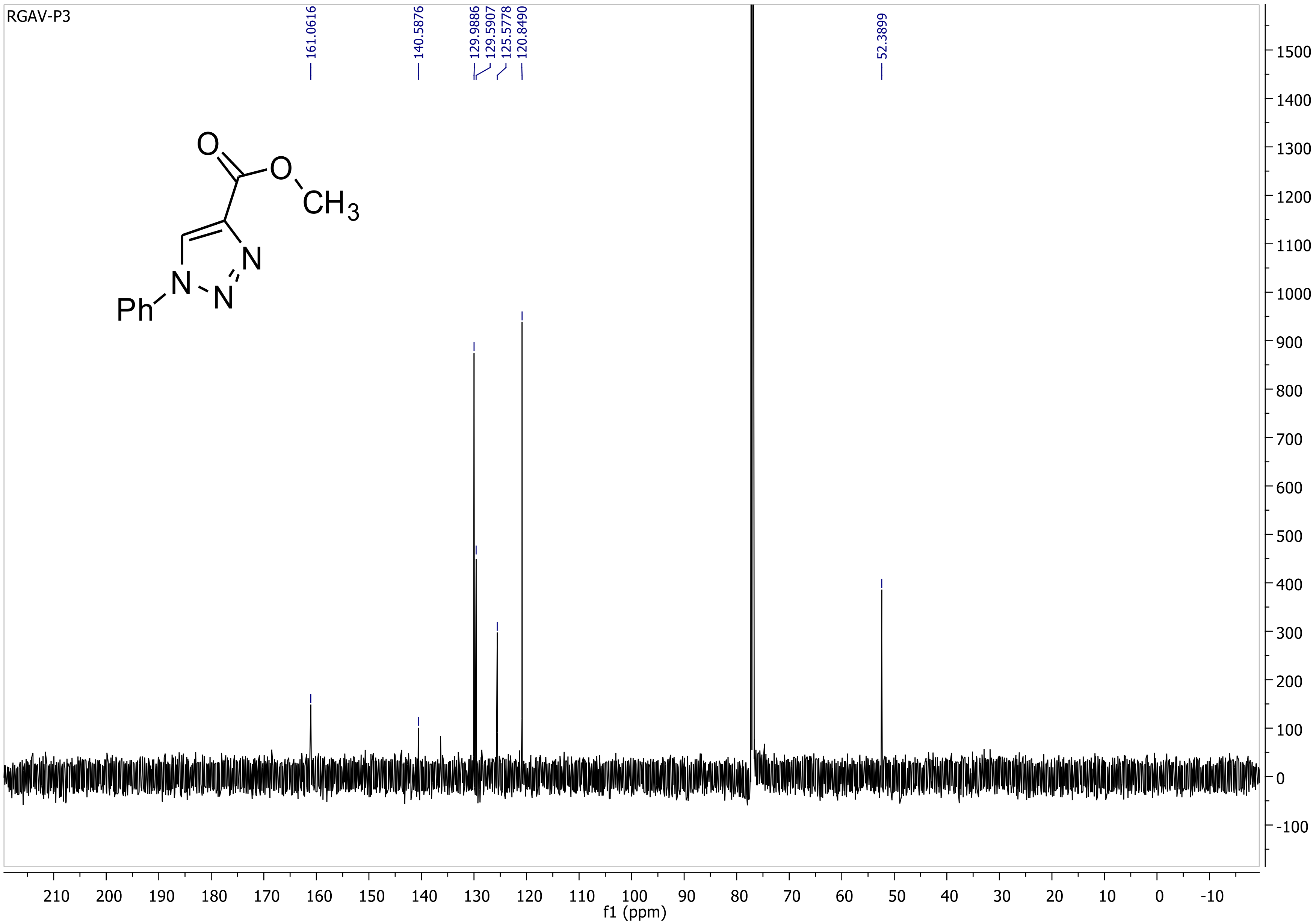



162.17
162.13
161.05
160.51
160.46
140.19
132.00
131.93
131.86
127.56
112.06
112.03
111.92
111.89
110.21
110.08
109.96
52.19
41.74
F
N=N
O
CH3
N
O
H
H
H
F
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


-114.03
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

Methyl 1-Phenyl-1H-1,2,3-triazole-4-carboxylate: ^{1}H NMR (600 MHz, CDCl$_3$): δ = 8.56 (s, 1 H), 7.80 (d, J = 12 Hz, 2 H), 7.60 (t, J = 12 Hz, 2 H), 7.54 (t, J = 6 Hz, 1 H), 4.04 (s, 3 H), ^{13}C NMR (600 MHz, CDCl$_3$): δ = 161.1, 140.6, 138.0, 129.9, 129.6, 127.6, 120.8, 52.3.

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129.9886
129.5907
125.5778
120.8490
52.3899
O
O
CH3
N
N
N
Ph
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

References

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[1] Han, J.; Ran, J-X.;, Che, X-P.; Wang, Z-H.; Wu, F-H. *Tetrahedron*, **2018,** *74*, 6985-6992

[2] Solheim, T. E.; Salvemini, F.; Dalziel, S. B.; Raston, C. L. *Scientific Report*, **2019**, 9, 2817.