

Supporting Information

Synthesis and reactivity of a bis-strained alkyne derived from 1,1'-biphenyl-2,2',6,6'-tetrol.

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S1. ^1H and ^{13}C NMR spectra for synthesised compounds.

S1.1 Literature compounds

S1.1.1. 2,2',6,6'-Tetramethoxy-1,1'-biphenyl 5.

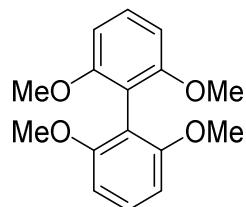


Figure S1.1.1

^1H NMR spectrum (400 MHz, CDCl_3)

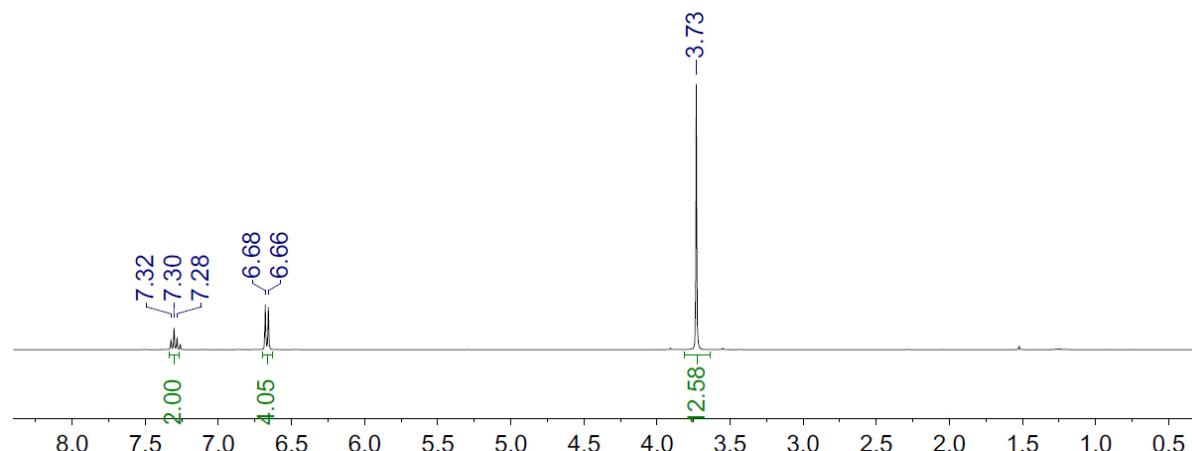
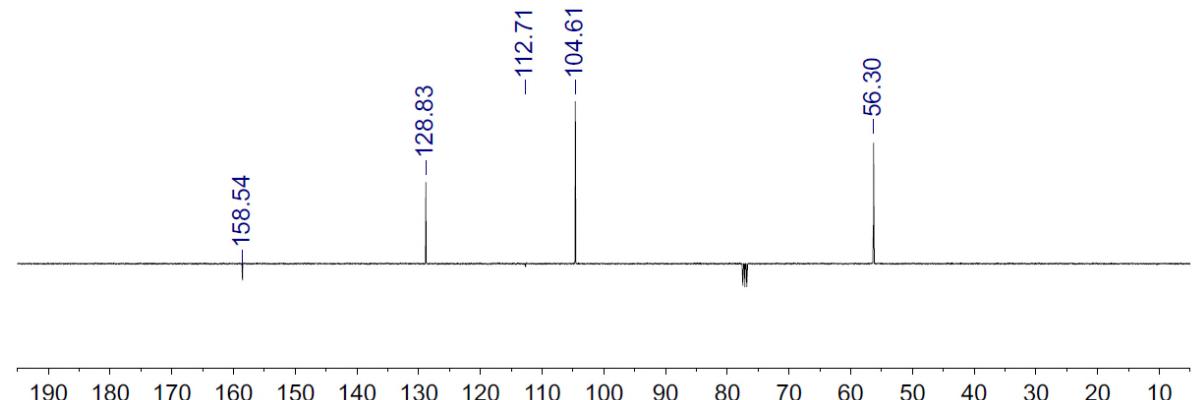


Figure S1.1.2

^{13}C NMR spectrum (101 MHz, CDCl_3)



S1.1.2. [1,1'-Biphenyl]-2,2',6,6'-tetrol 4.

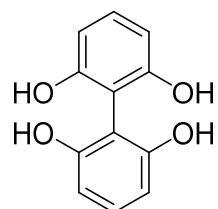


Figure S1.1.3

¹H NMR spectrum (500 MHz, (CD₃)₂CO)

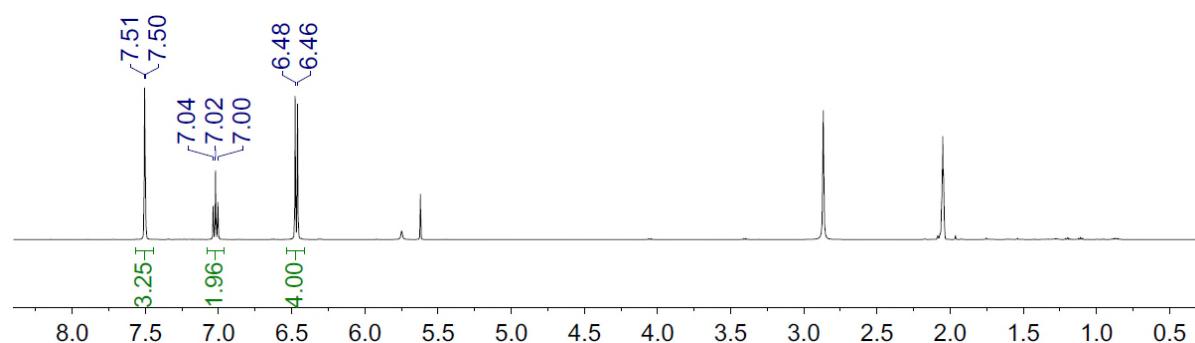
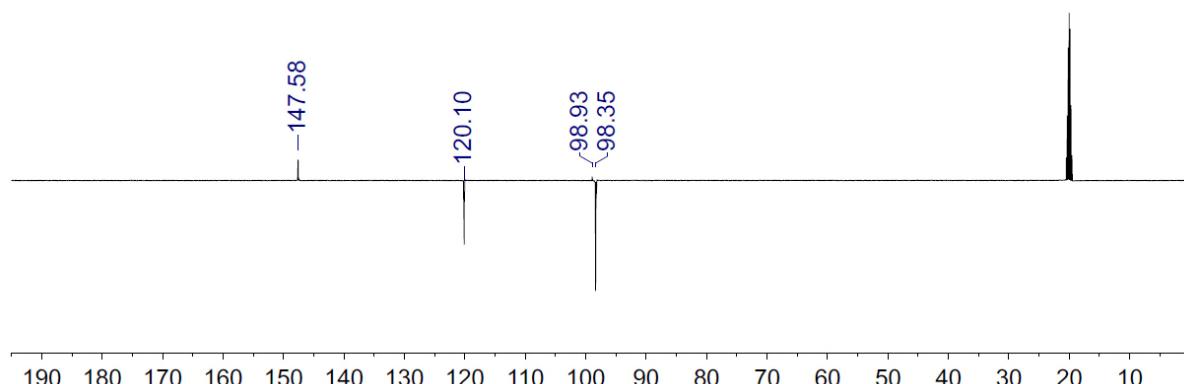


Figure S1.1.4

¹³C NMR spectrum (126 MHz, CDCl₃)



S1.2 Spectra of novel compounds

S1.2.1. bis-Alkyne 3

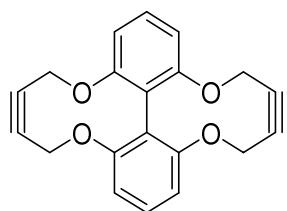


Figure S1.2.1

^1H NMR spectrum (500 MHz, CDCl_3)

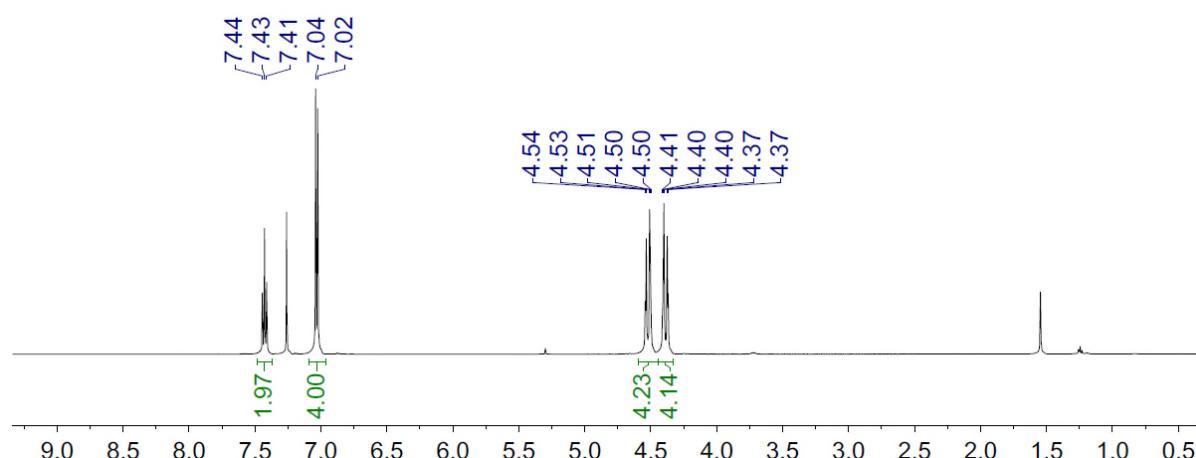
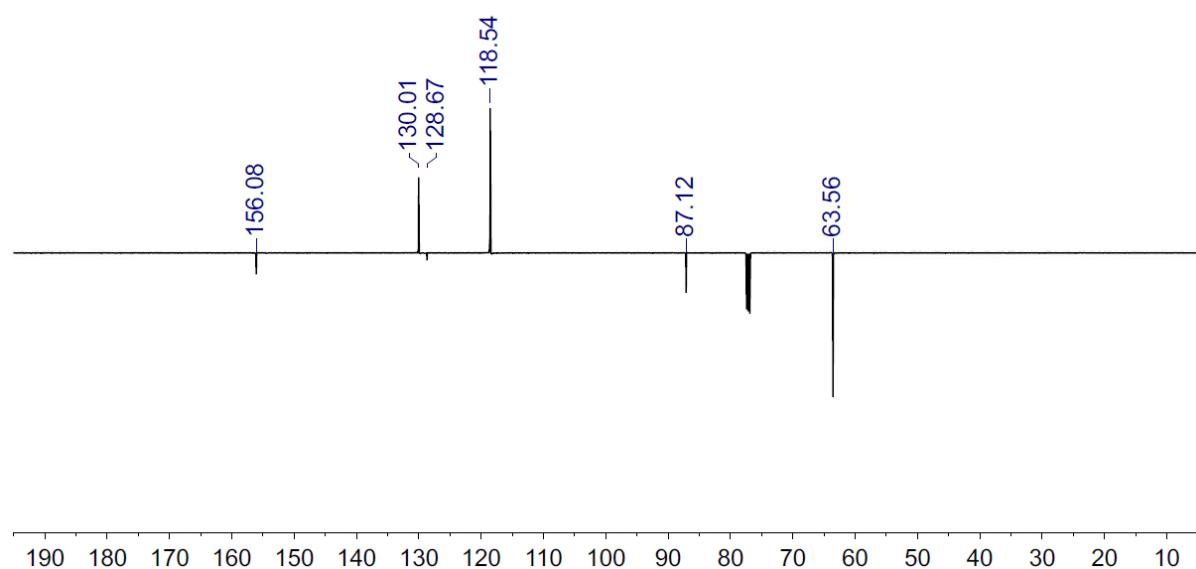


Figure S1.2.2

^{13}C NMR spectrum (126 MHz, CDCl_3)



S1.2.2. bis-Benzyl triazole 7.

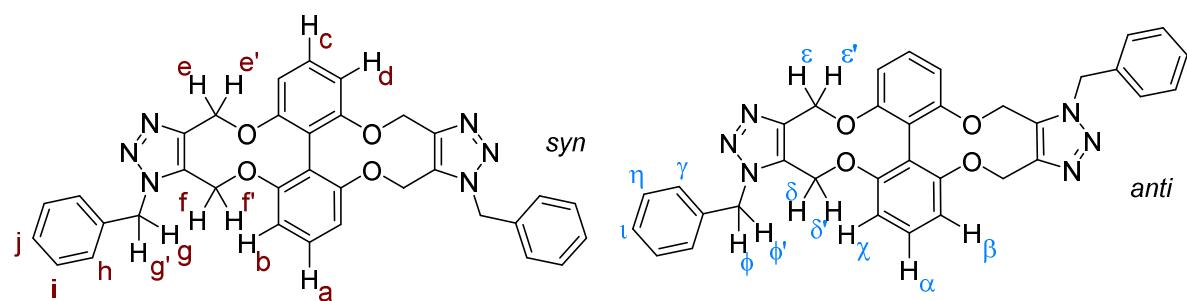


Figure S1.2.3

¹H NMR spectrum (600 MHz, CDCl₃)

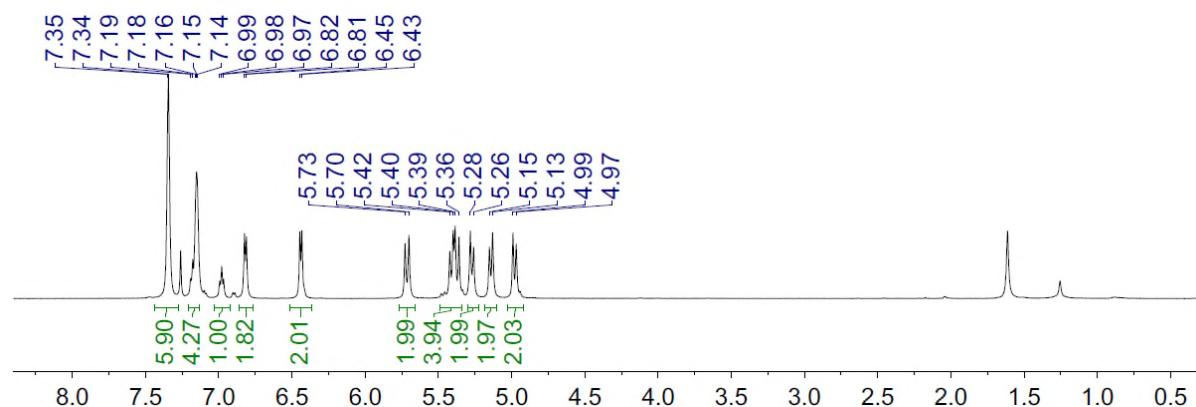


Figure S1.2.4

¹³C NMR spectrum (151 MHz, CDCl₃)

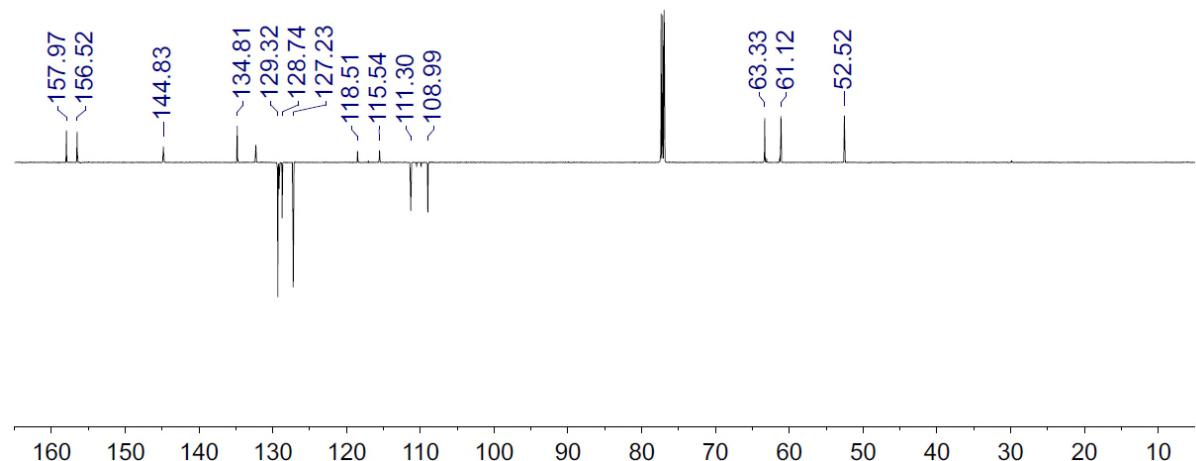


Figure S1.2.5

^1H NMR spectrum (500 MHz, $(\text{CD}_3)_2\text{SO}$)

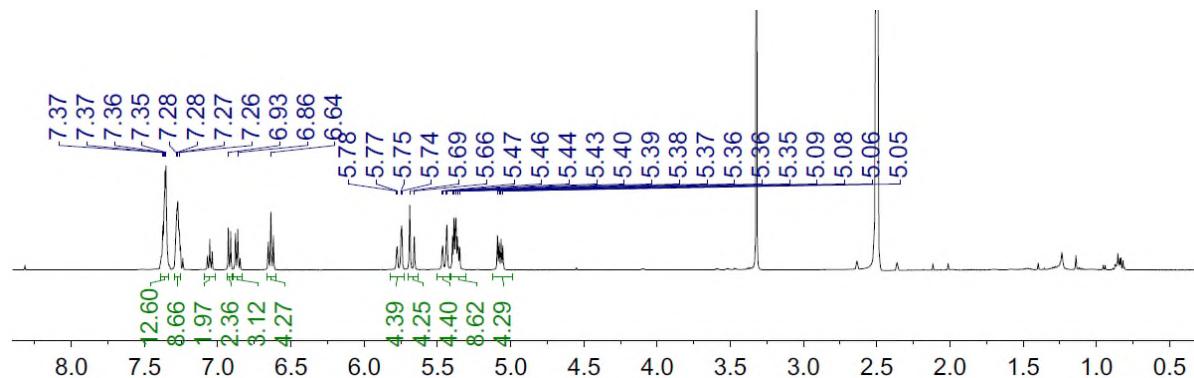


Figure S1.2.6

Truncated ^1H NMR spectrum (500 MHz, $(\text{CD}_3)_2\text{SO}$)

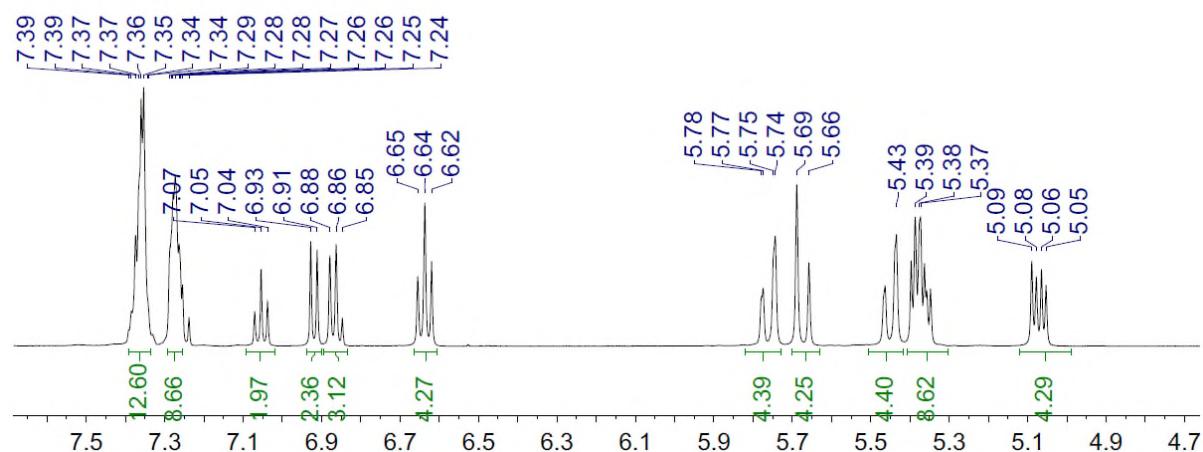
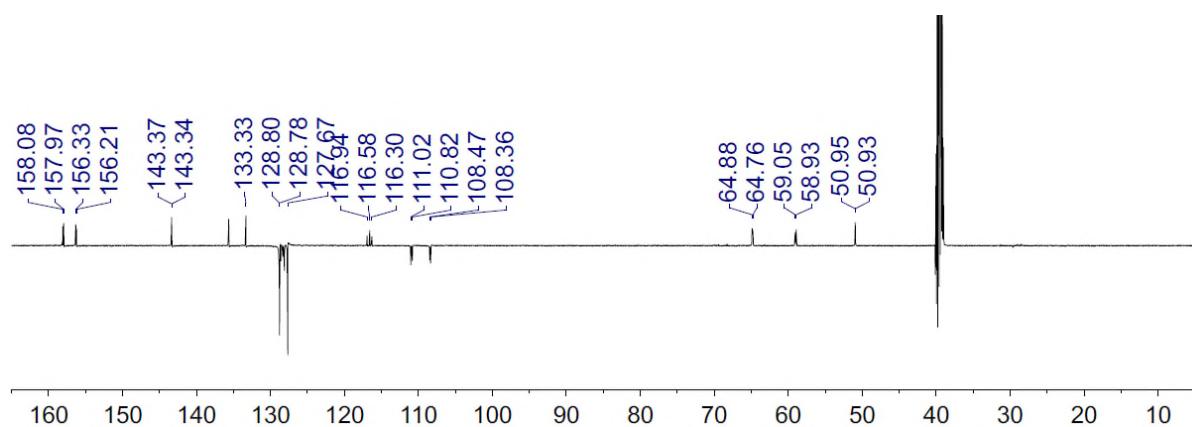


Figure S1.2.7

^{13}C NMR spectrum (126 MHz, $(\text{CD}_3)_2\text{SO}$)



S1.2.3. bis-Octyl trizole 8.

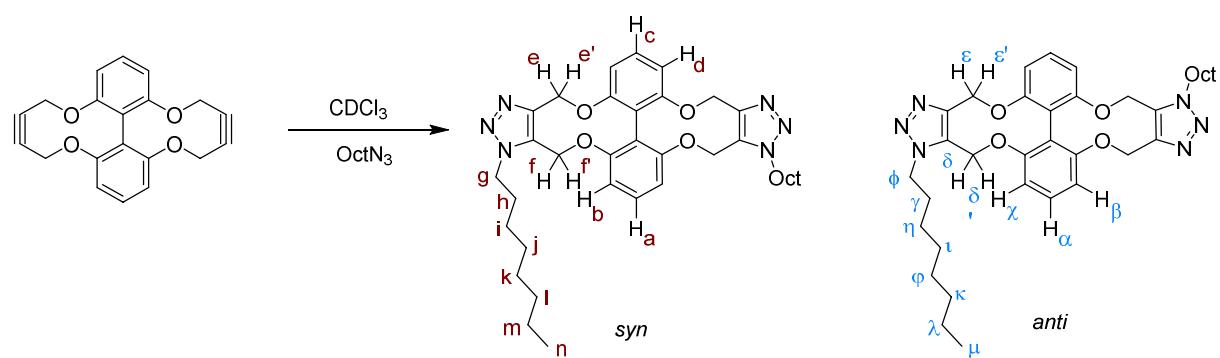


Figure S1.2.8

¹H NMR spectrum (500 MHz, CDCl₃)

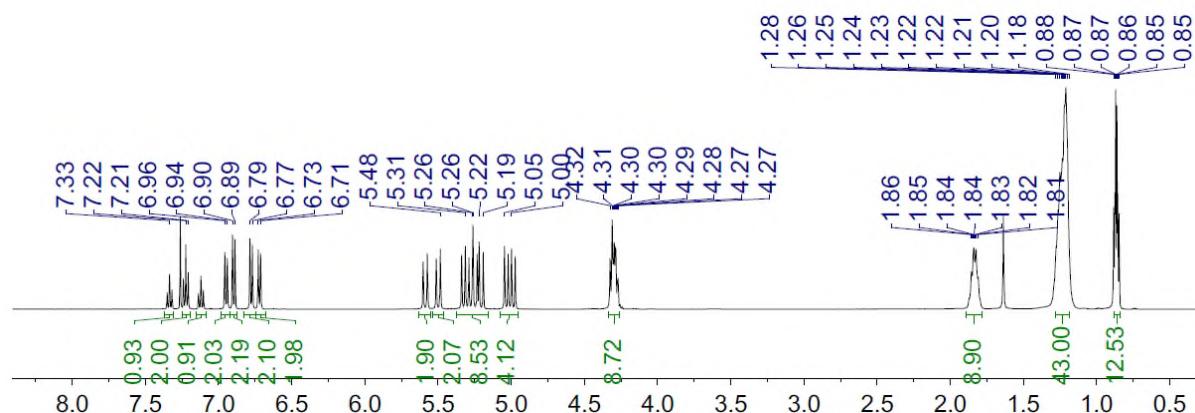


Figure S1.2.9

Truncated ^1H NMR spectrum (500 MHz, CDCl_3)

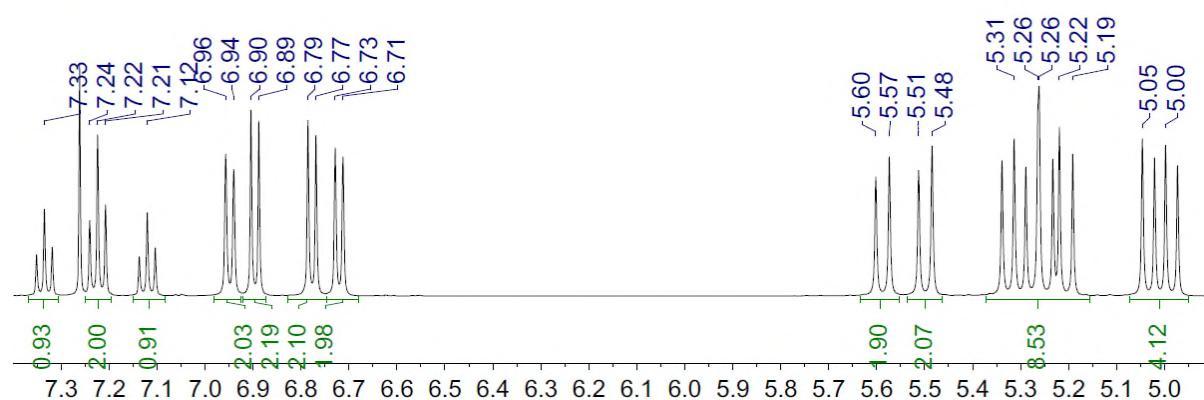
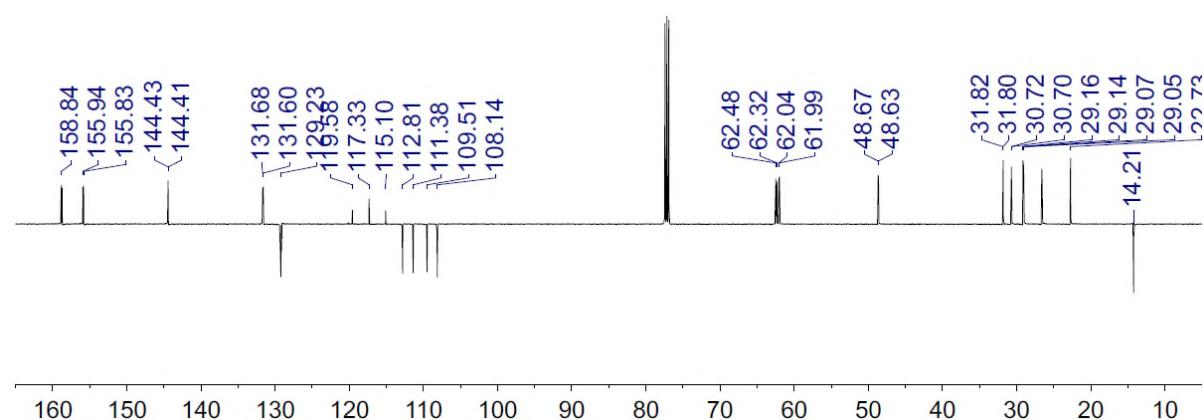


Figure S1.2.10

^{13}C NMR spectrum (126 MHz, CDCl_3)



S2. Cycloaddition reactions of bis-strained alkyne compound 3 followed by NMR spectroscopy.

S2.1 Benzyl Azide

A solution of **3** (15.9 mg, 0.05 mmol) and benzyl azide (13.3 mg, 0.10 mmol) in CDCl_3 (0.5 mL, 1 mM) was prepared with a J. Young's NMR tube. Analysis *in situ* by NMR spectroscopy was used to monitor formation of the desired bis-triazole compound.

Figure S2.1.1 ^1H NMR spectrum (CDCl_3 , 400 MHz) of **3** with 2.0 equivalents of benzyl azide

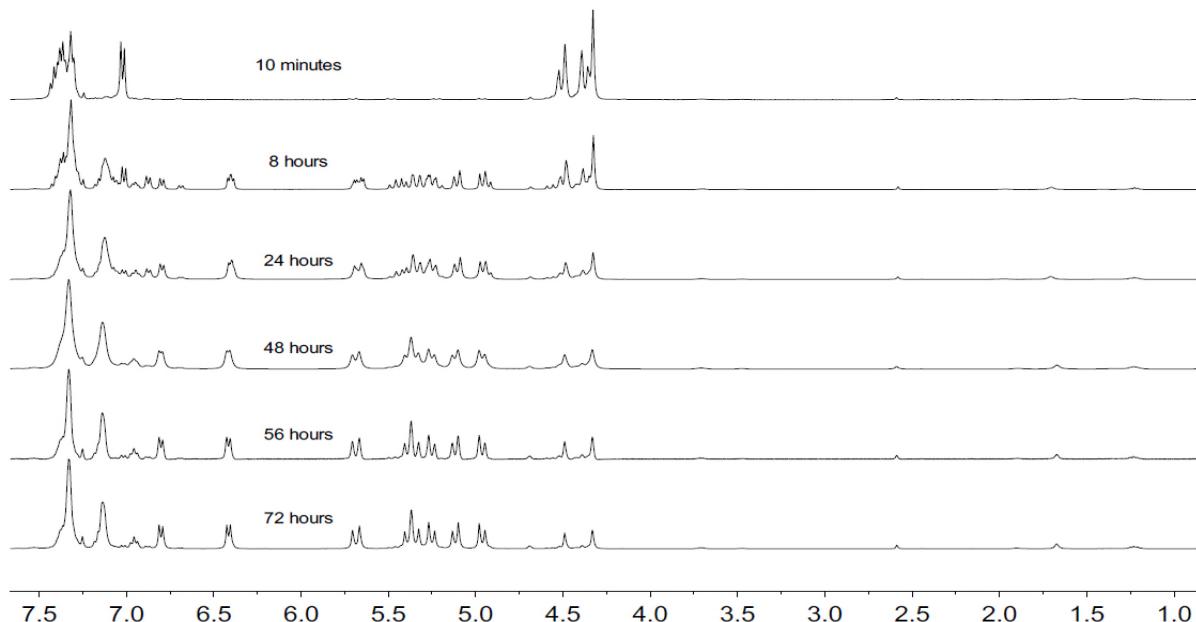


Figure S2.1.2 ^1H NMR truncated spectrum (CDCl_3 , 400 MHz) of **3** with 2.0 equivalents of benzyl azide

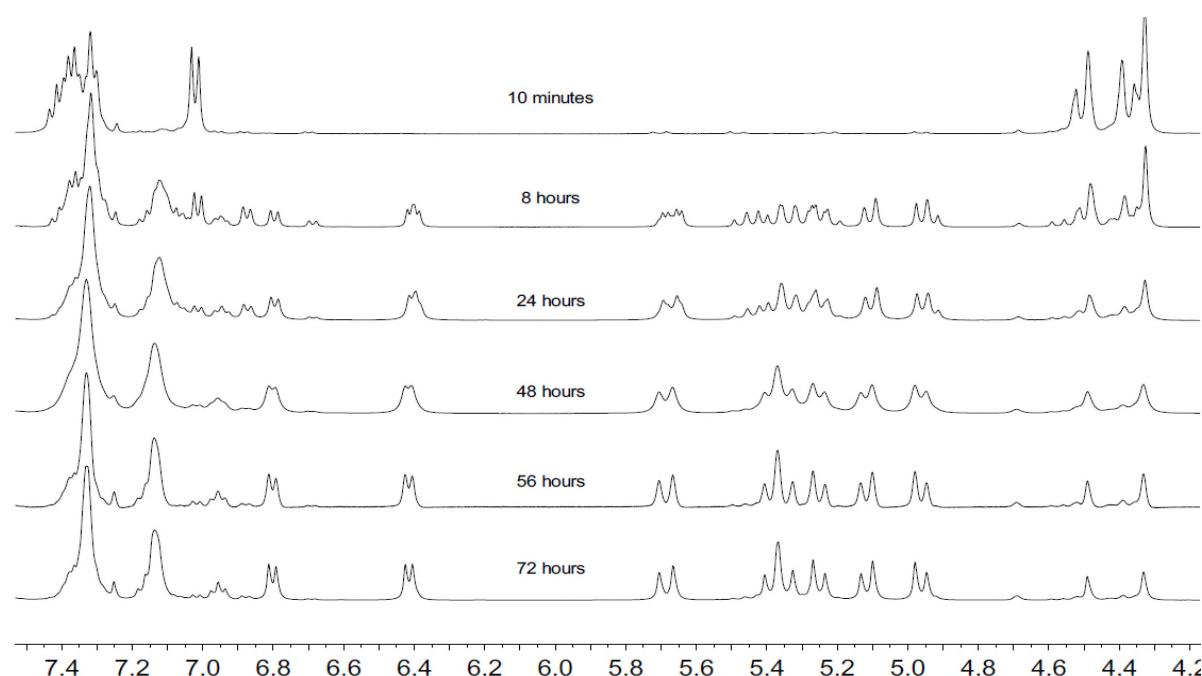
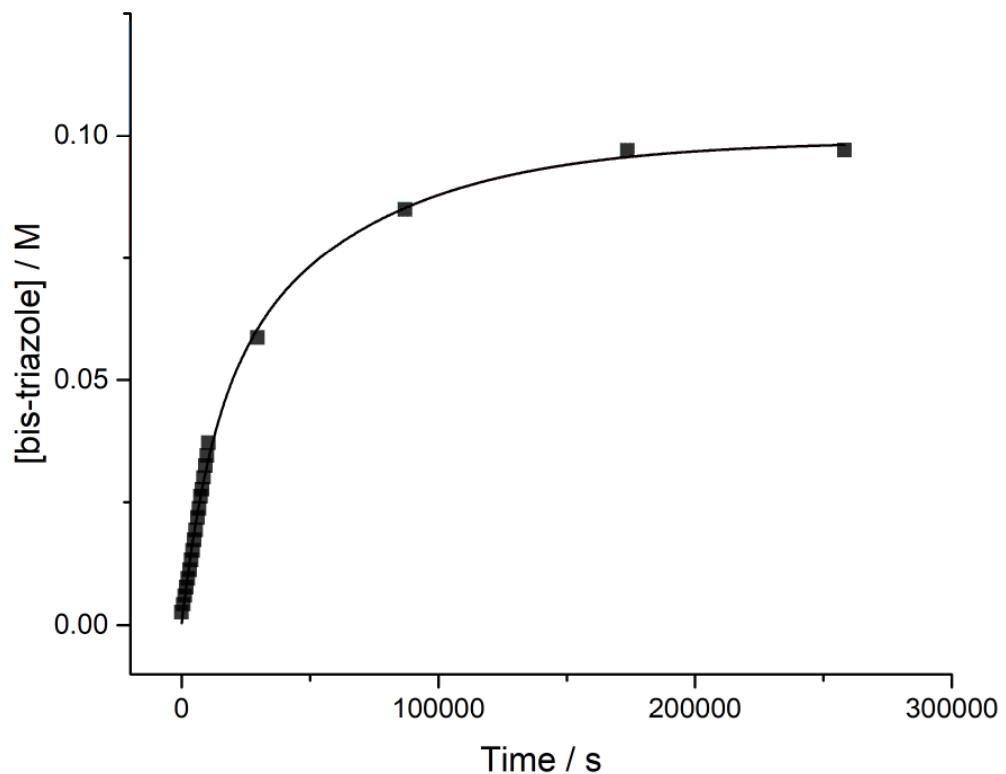


Figure S2.1.3 ^1H NMR plot (400 MHz, CDCl_3 , 0.1 M), of conversion to bis-triazole **7**



S2.2 Octyl Azide

A solution of **3** (15.9 mg, 0.05 mmol) and octyl azide (15.5 mg, 0.10 mmol) in CDCl_3 (0.5 mL, 1 mM) was prepared with a J. Young's NMR tube. Analysis *in situ* by NMR spectroscopy was used to monitor formation of the desired bis-triazole compound.

Figure S2.2.1 ^1H NMR spectrum (CDCl_3 , 400 MHz) of **3** with 2.0 equivalents of octyl azide

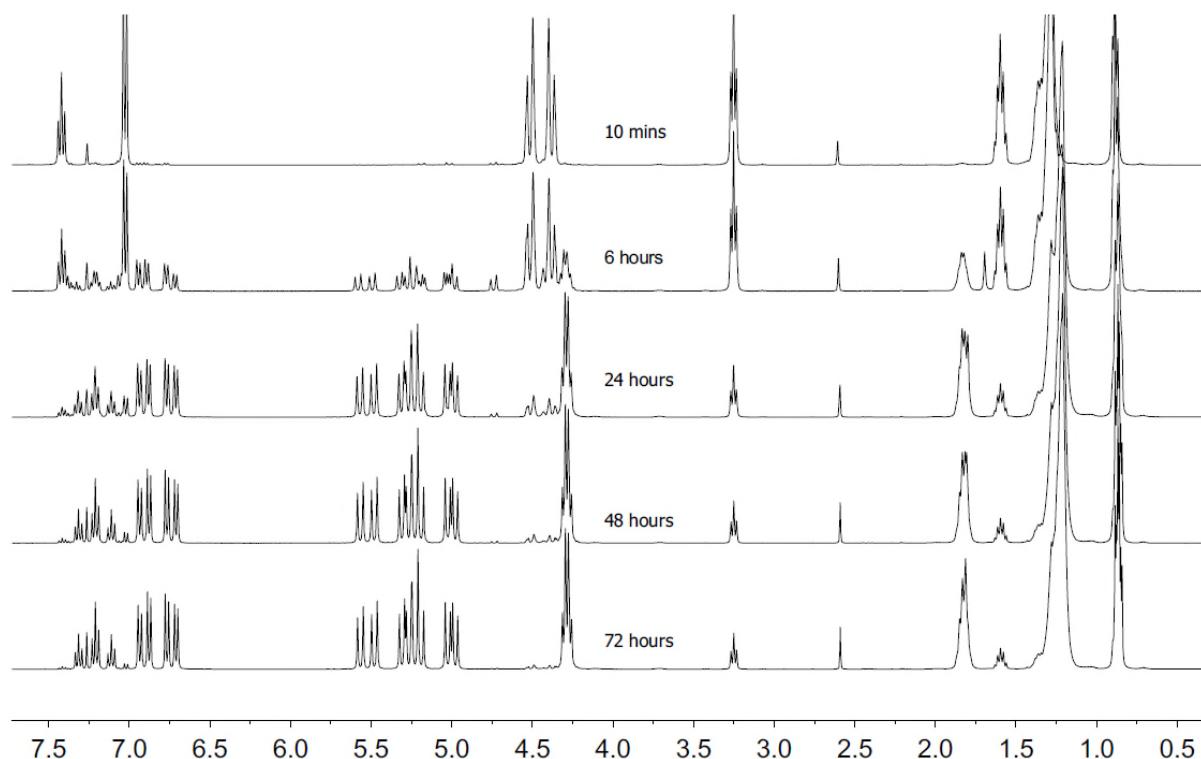


Figure S2.2.2 ^1H NMR spectrum (CDCl_3 , 400 MHz) of **3** with 2.0 equivalents of octyl azide

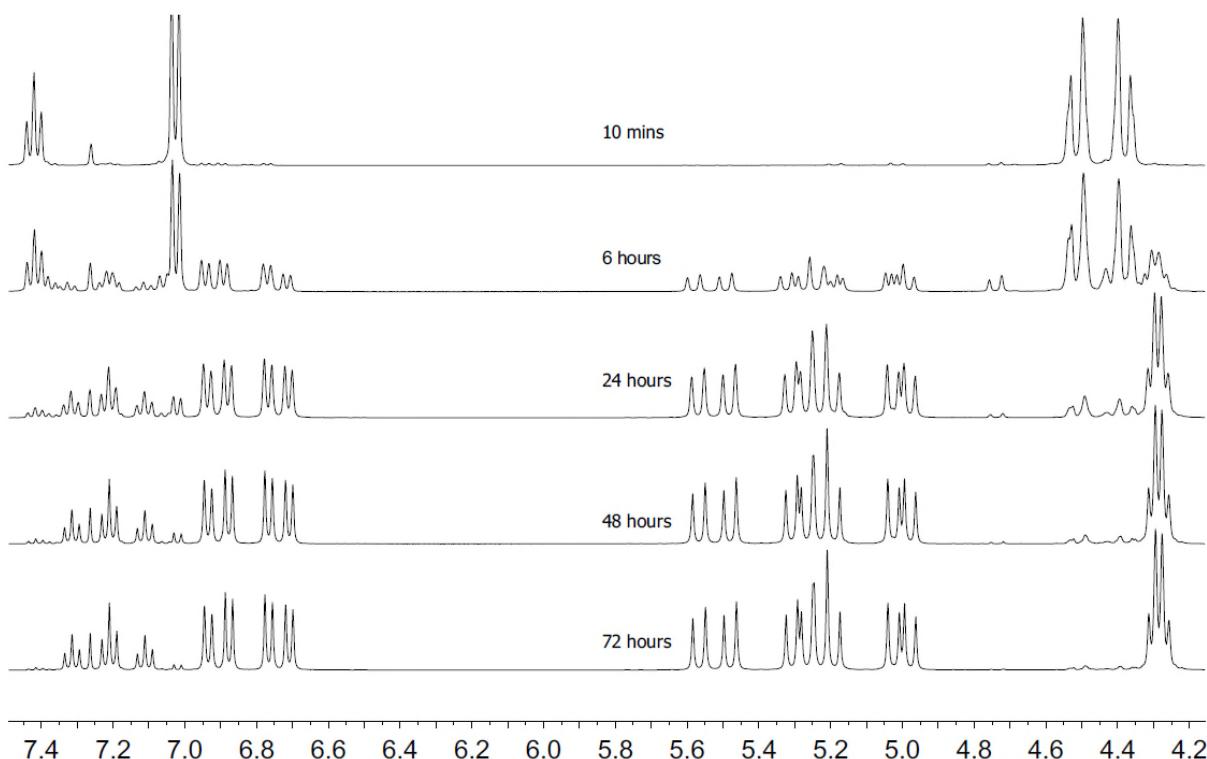
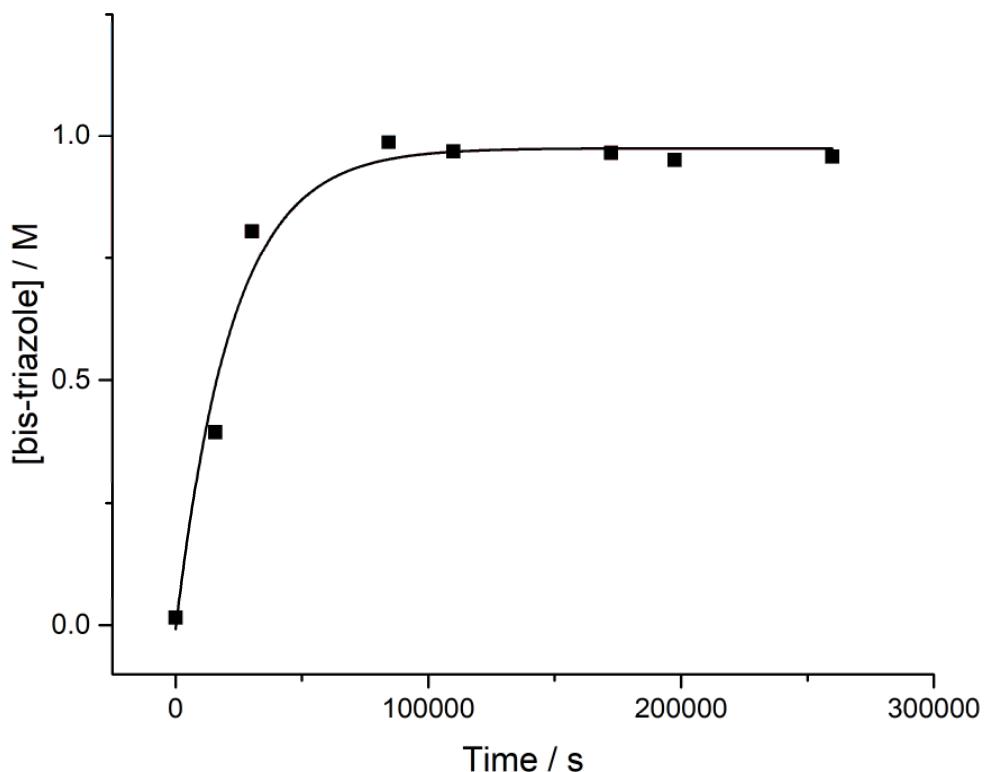


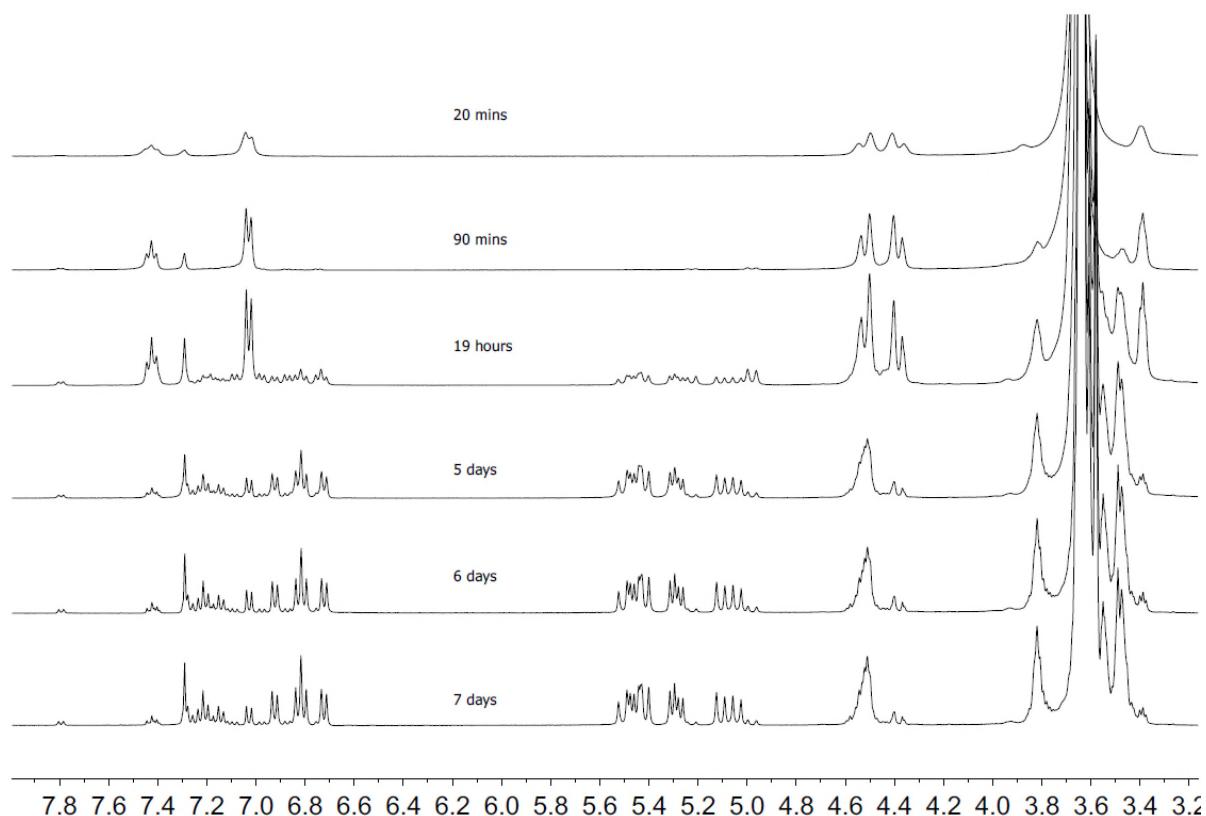
Figure S2.2.3 ^1H NMR plot (400 MHz, CDCl_3 , 0.1 M), of conversion to bis-triazole **8**



S2.3 Polyoxyethylene diazide (MW = 2000) addition

A solution of **3** (5.0 mg, 15.7 μmol) and PEG-2000 polyoxyethylene diazide (MW = 2000) (31.4 mg, 15.7 μmol) in CDCl_3 (0.5 mL, 0.33 mM) was prepared with a J. Young's NMR tube. Analysis *in situ* by NMR spectroscopy indicated formation of a polymeric species. The conversion after 7 days was determined to be 86% by integration of the starting material versus the polymeric product. Due to the heterogeneous nature of this compound, it was not worked up or purified.

Figure S2.3.1 ^1H NMR spectrum (CDCl_3 , 400 MHz) of **3** with 1.0 equivalent of PEG-2000 diazide (MW = 2000)



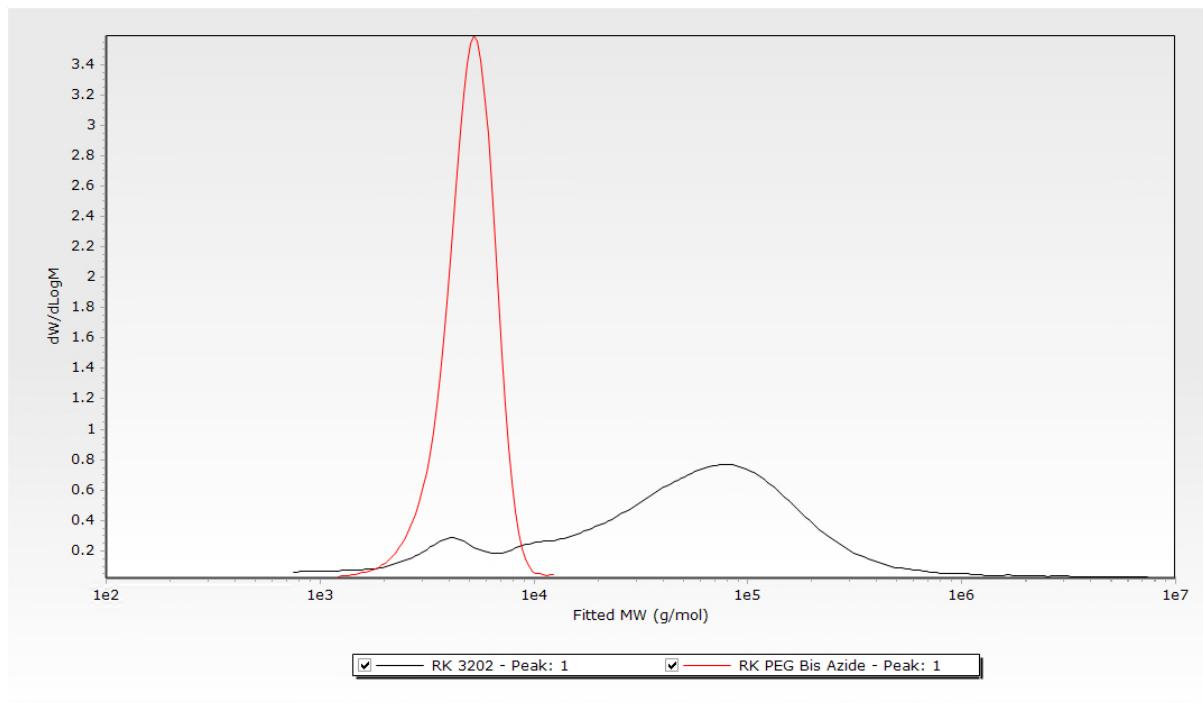
S2.4. GPC results.

The product was analysed by GPC to determine its molecular weight relative to linear standards (molecular weight averages and dispersities presented in table below). When the product was reacted with PEG-2000 diazide, a bimodal distribution was observed in the molecular weight distribution. These were not suitably resolved to analyse independently. The lower molecular weight part of the distribution (black trace – left part) is attributed to unbound reagent, the higher part of the molecular weight distribution (black trace – right hand side) is shifted to higher molecular weight than the product, evidence that an adduct has been formed with the PEG.

Table S2.4.1

MW Averages	Mn (g/mol)	Mw (g/mol)	PDI
Peaks			
PEG-2000 diazide (red trace)	4600	5100	1.10
Product (black trace)	13000	186000	14.25

Figure S2.4.1 GPC trace of PEG-2000 diazide and addition product



The red line is PEG-2000 bis azide.

The black line is the sample generated in the reaction.

GPC was carried out on an Agilent 390LC MDS instrument equipped with differential refractive index (DRI), viscometry (VS) and dual angle light scatter (LS) detectors. The system was equipped with 2 x PLgel Mixed C columns (300 x 7.5 mm) and a PLgel 5 μ m guard column. The eluent was CHCl_3 with 2 % TEA (triethylamine) additive. Samples were run at 1ml/min at 30°C and narrow Poly(methyl methacrylate) standards were used to create a third order calibration between 1,568,000 – 550 gmol-

1. Analyte samples were filtered through a GVHP membrane with 0.22 µm pore size before injection. Respectively, experimental molar mass and dispersity values of synthesized polymers were determined by conventional calibration using Agilent GPC/SEC software.

S3. Single-crystal X-ray crystallographic figures and data.

S3.1 Bis-strained alkyne 3 CCDC 1881599

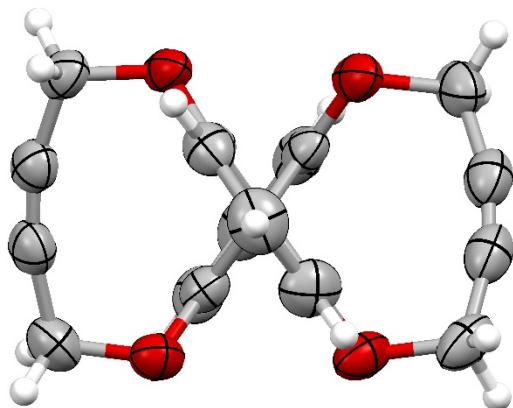


Figure S3.1.1: Single crystal X-ray structure of **3** (ellipsoids are plotted at the 50% probability level)

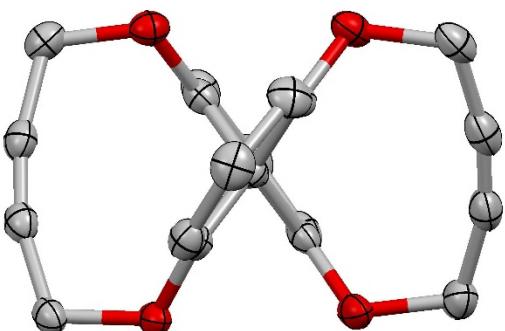


Figure S3.1.2: Single crystal X-ray structure of **3** (ellipsoids are plotted at the 50% probability level;
hydrogen atoms omitted for clarity)

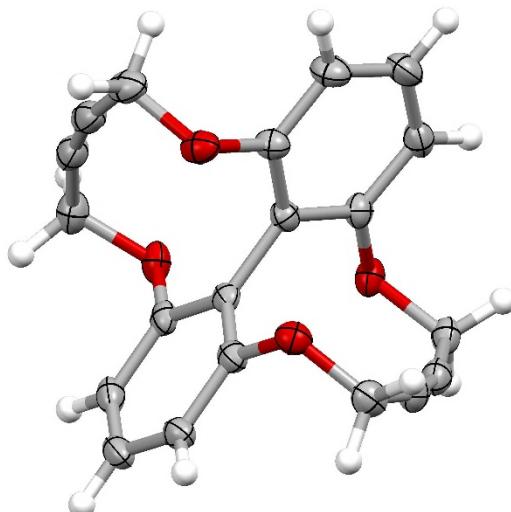


Figure S3.1.3: Single crystal X-ray structure of **3** (ellipsoids are plotted at the 50% probability level)

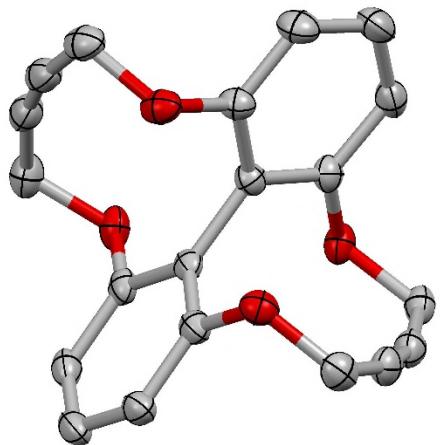


Figure S3.1.4: Single crystal X-ray structure of **3** (ellipsoids are plotted at the 50% probability level; hydrogen atoms omitted for clarity)

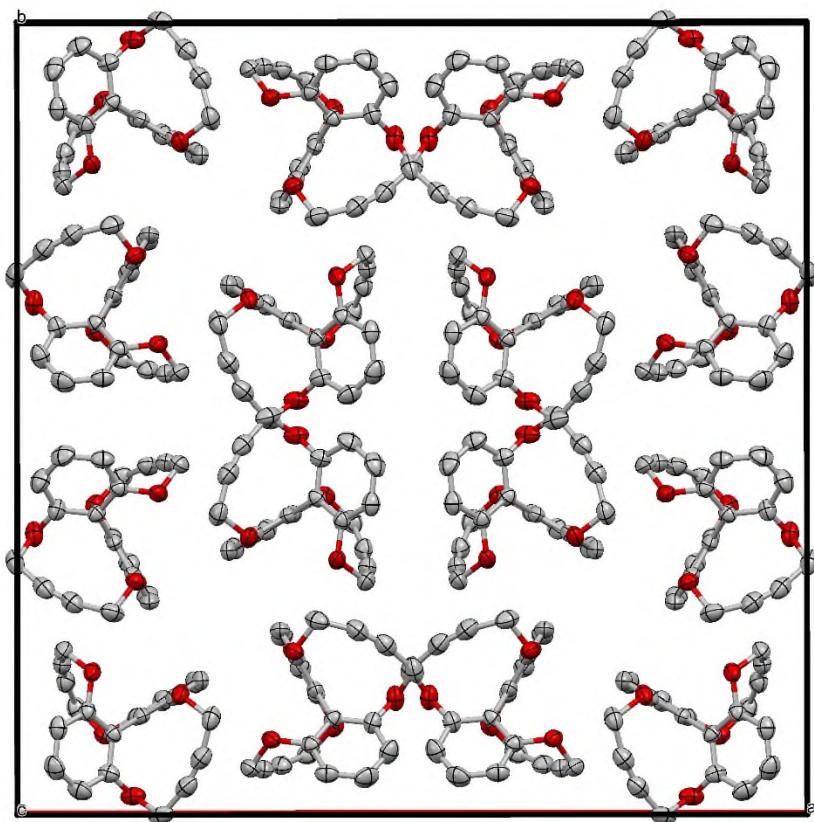


Figure S3.1.5: Unit cell of **3** (ellipsoids are plotted at the 50% probability level; hydrogen atoms omitted for clarity)

CCDC 1881599 contains the supplementary crystallographic data for this paper. These can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Single crystals of **3** were grown from vapour diffusion of *n*-hexane into a chloroform solution of the compound over several days. A suitable crystal was selected and mounted on a glass fibre with Fromblin oil and placed on a Rigaku Oxford Diffraction SuperNova diffractometer with a duel source (Cu at zero) equipped with an AtlasS2 CCD area detector. at 150(2) K. The structure was solved using Olex2¹ and the ShelXT² structure solution program using Direct Methods and refined with the ShelXL³ refinement package using Least Squares refinement.

The asymmetric unit contains one crystallographically distinct molecule, with Z = 16.. The alkyne group displays significant deviation from linearity, the C14-C15-C16 and C15-C16-C17 bond angles are 166.8(2)^o and 164.1(2)^o and the C20-C21-C22 and C21-C22-C23 are 163.9(2)^o and 166.3(2)^o respectively. This is accompanied by a large biphenyl torsion angle (C5-C6-C7-C8) of 69.8(3)^o.

Table S3.1.1: single-crystal X-ray data for compound **3**

Compound Reference	Compound 3
Chemical Formula	C ₂₀ H ₁₄ O ₄
Formula Mass	318.33
Crystal system	tetragonal
<i>a</i> / Å	27.5013(2)
<i>b</i> / Å	27.5013(2)
<i>c</i> / Å	8.0044(1)
α / °	90
β / °	90
γ / °	90
Unit cell volume/ Å	6053.9(1)
Temperature/ K	150(2) K
Space group	<i>I</i> 4 ₁ <i>bw</i> -2 ₁ <i>c</i>
Crystal size/ mm	0.06 × 0.07 × 0.35
Radiation	Cu K\α
Goodness-of-fit on F ²	1.0482
No. of formula units per unit cell, Z	16
No. of reflections measured	19642
No. of independent reflections	3041
Final R ₁ vaules ($I > 2\sigma(I)$)	0.0517
Final <i>wR</i> (F ²) values ($I > 2\sigma(I)$)	0.1388
Final <i>R</i> ₁ values (all data)	0.0524
Final <i>wR</i> (F ²) (all data)	0.1400

- Dolomanov, O.V., Bourhis, L.J., Gildea, R.J., Howard, J.A.K. & Puschmann, H. (2009), *J. Appl. Cryst.* 42, 339-341.
- Sheldrick, G.M. (2015). *Acta Cryst. A*71, 3-8.
- Sheldrick, G.M. (2015). *Acta Cryst. C*71, 3-8

S3.2 Bis-benzyl triazole *anti*-7 CCDC 1881560.

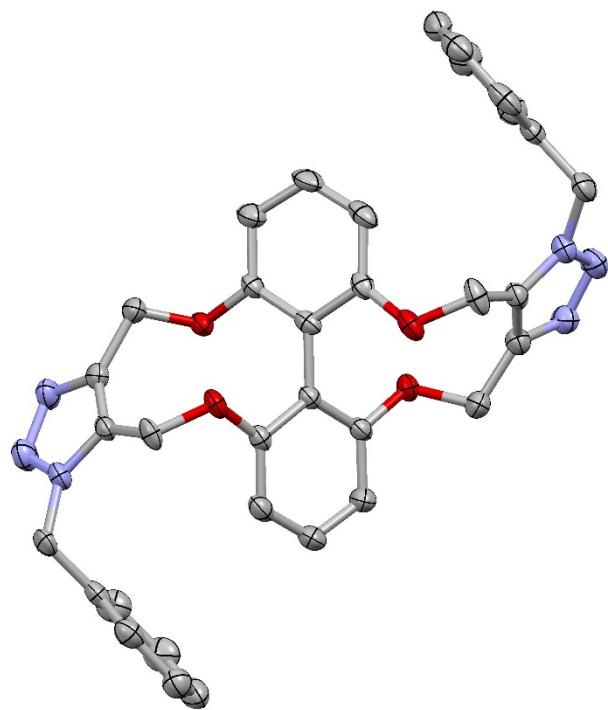


Figure S3.2.1: Single crystal X-ray structure of *anti*-7 (ellipsoids are plotted at the 50% probability level, solvent and H-atoms are omitted for clarity)

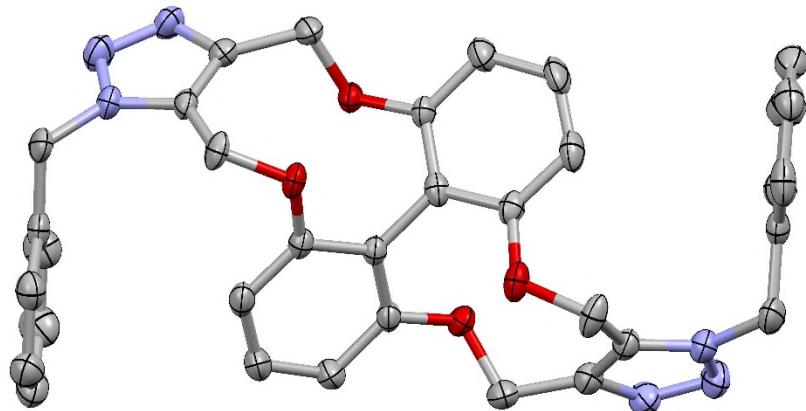


Figure S3.2.2: Single crystal x-ray structure of *anti*-7 (ellipsoids are plotted at the 50% probability level, solvent and H-atoms are omitted for clarity)

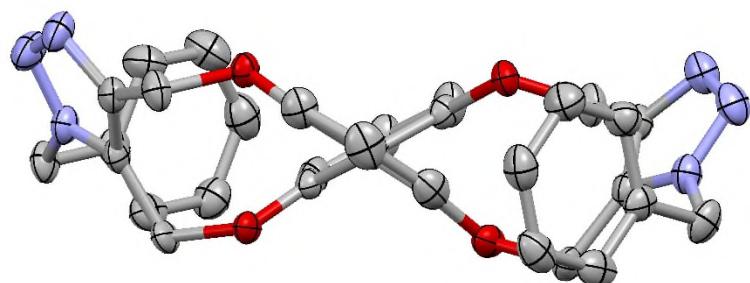


Figure S3.2.3: Single crystal X-ray structure of **anti-7** (ellipsoids are plotted at the 50% probability level, solvent and H-atoms are omitted for clarity)

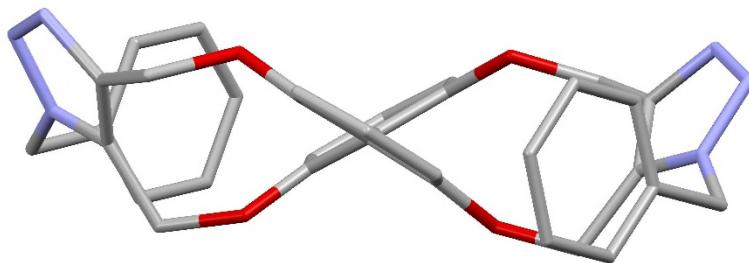


Figure S3.2.4: Single crystal X-ray structure of **anti-7** (solvent and H-atoms are omitted for clarity)

CCDC 1881560 contains the supplementary crystallographic data for this paper. These can be obtained free of charge from the Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Single crystals of **anti-7** were grown from vapour diffusion of *n*-hexane into a chloroform solution of the compound over several days. A suitable crystal was selected and mounted on a glass fibre with Fromblin oil and placed on a glass fibre with Fomblin oil and placed on a Rigaku Oxford Diffraction SuperNova diffractometer with a duel source (Cu at zero) equipped with an AtlasS2 CCD area detector. The structure was solved using Olex2¹ and the ShelXT² structure solution program using Direct Methods and refined with the ShelXL³ refinement package using Least Squares refinement.

The asymmetric unit contains one crystallographically distinct molecule, with Z = 4. The bis-triazole product also exhibits a large biphenyl torsion angle (C5-C6-C7-C8) of 60.6°.

Table S3.2.1: single-crystal X-ray data for compound **anti-7**

Compound Reference	Compound anti-7
Chemical Formula	C ₃₇ H ₃₁ C ₁₉ N ₆ O ₄
Formula Mass	942.73
Crystal system	monoclinic
a/ Å	10.5961(2)
b/ Å	25.9364(5)
c/ Å	15.8162(3)
α/ °	90
β/ °	108.823(2)
γ/ °	90
Unit cell volume/ Å	4114.22(14)
Temperature/ K	150(2)K
Space group	-P 2ybc
Crystal size/ mm	0.05 × 0.08 × 0.22
Radiation	CuK\λ
Goodness-of-fit on F ²	1.021
No. of formula units per unit cell, Z	4
No. of reflections measured	32987
No. of independent reflections	8223

Final R_1 values ($I > 2\sigma(I)$)	0.0921
Final $wR(F^2)$ values ($I > 2\sigma(I)$)	0.2509
Final R_1 values (all data)	0.1069
Final $wR(F^2)$ (all data)	0.2681

1. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J., Howard, J.A.K. & Puschmann, H. (2009), *J. Appl. Cryst.* **42**, 339-341.
2. Sheldrick, G.M. (2015). *Acta Cryst. A* **71**, 3-8.
3. Sheldrick, G.M. (2015). *Acta Cryst. C* **71**, 3-8

S4. Peptide stapling.

S4.1 Peptide synthesis.

Peptide synthesis was carried out on solid-phase using Fmoc-protecting group strategy on a CEM LibertyBlue Automated Microwave Peptide Synthesizer using Rink Amide MBHA LL resin (0.33 mmol/g) (Merck Millipore). Fmoc-protected amino acids were made up as a solution of 0.2 M in DMF to give 5 equivalents relative to resin. Oxyma Pure was made up as a 1 M solution in DMF to give 5 equivalents relative to resin and *N,N'*-Diisopropylcarbodiimide as a 1 M solution in DMF to give 10 equivalents relative to the resin. All amino acid couplings were single coupled and heated to 90 °C for two mins, except for Fmoc-Arg(Pbf)-OH which was double coupled and heated to 75 °C for 300 seconds for each coupling. Fmoc deprotection was carried out using 20 % (v/v) piperidine in DMF and heated at 90 °C for 60 seconds.

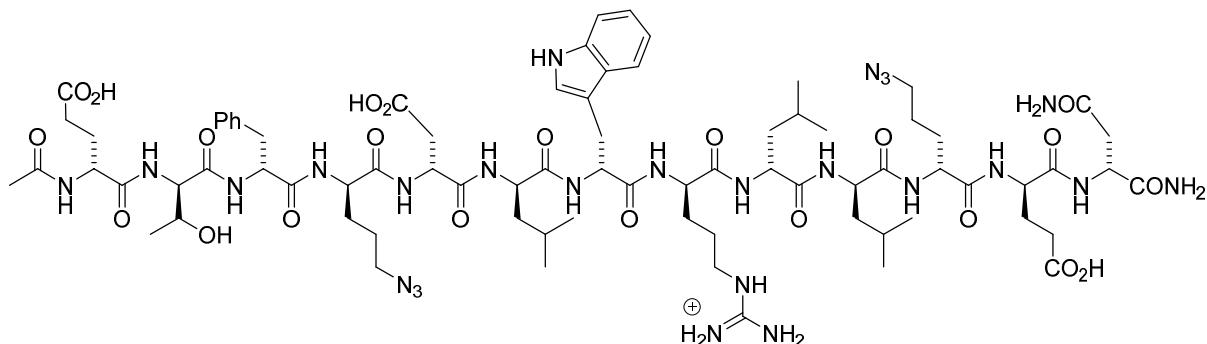
The peptide was cleaved from the resin using a cleavage cocktail of TFA/TIPS/H₂O (95:2.5:2.5) for 3 hours at room temperature. The resin was filtered, the filtrate collected and the TFA blown off with a steady stream of nitrogen. The peptide was precipitated and washed three times in cold diethyl ether, then spun down to a pellet before the diethyl ether was removed and the peptide dried under a steady stream of nitrogen.

Peptide purification was carried out using a semi-preparative HPLC on an Agilent 1260 Infinity using a Supelcosil ABZ+PLUS column (250 mm × 21.2 mm, 5 µm) eluting with a linear gradient system (solvent A: 0.1% (v/v) TFA in water, solvent B: 0.05% (v/v) TFA in acetonitrile) over 20 minutes at a flow rate of 20 mL/min. Analytical HPLC was run on an Agilent 1260 Infinity using a Supelcosil ABZ+PLUS column (150 mm × 4.6 mm, 3 µm) eluting with a linear gradient system (solvent A: 0.05% (v/v) TFA in water, solvent B: 0.05% (v/v) TFA in acetonitrile) over 15 minutes at a flow rate of 1 mL/min. HPLC was monitored by UV absorbance at 220 and 254 nm.

S4.2 Peptide stapling:

Purified peptide (5.5 mg, 3.13 µmol, 1 eq.) was dissolved in ^tBuOH/H₂O (5 mL, 1:1, v/v), followed by the addition of the linker (**3**, 1.1 mg, 3.44 µmol, 1.1 eq.) dissolved in ^tBuOH/H₂O (0.5 mL, 1:1, v/v). The resulting solution was stirred at room temperature for 72h.

After 24h at room temperature, some stapled product was observed. It co-elutes with the LCMS peak of the starting material (below).



$C_{79}H_{107}N_{25}O_{22}$ 1,757 (1756.95) as the cation, 1756.4 shows on MS ES- and 1758.4 on ES+
dialkyne is $C_{20}H_{14}O_4$ (318).

Stapled adduct is 2075 (2075.28), 2074.8 shows up on MS ES- and 2076.8 on MS+.

Ac-Glu(E)-Thr(T)-Phe(F)-Orn(N3)-Asp(D)-Leu(L)-Trp(W)-Arg(R)-Leu(L)-Leu(L)-Orn(N3)-Glu(E)-Asp(N)-NH2

Starting material peptide MW: 1756.95. Stapled peptide MW: 2075.28.

Figure S4.2.1

Openlynx Report - Naomi Robertson
 Sample: 1 Vial:2:46 Page 1
 File:Naomi Robertson46-1 Date:16-Nov-2017
 Description: Method:C:\MassLynx\Fast_Acidic_Peptide.olp
 ID:nsr32_136_+MeOH
 Time:11:31:16

Printed: Thu Nov 16 11:38:15 2017

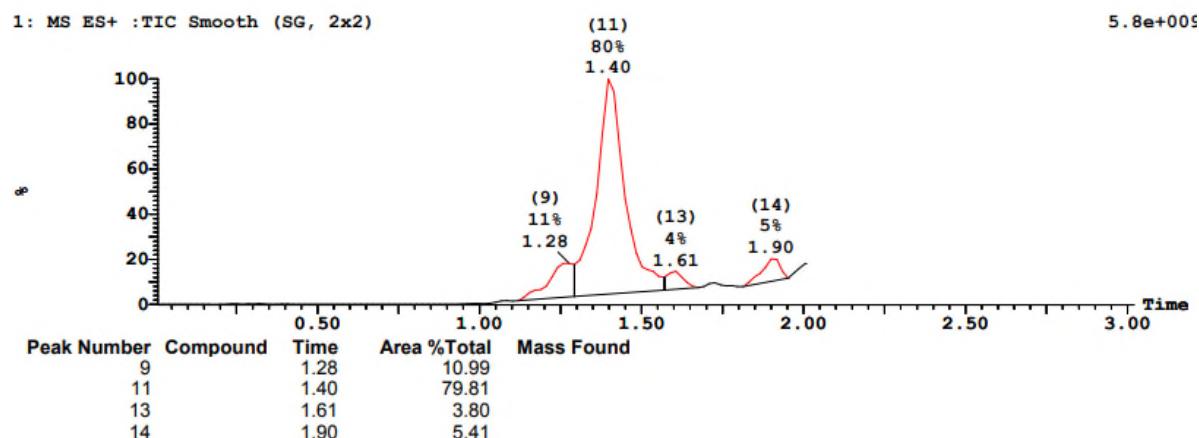
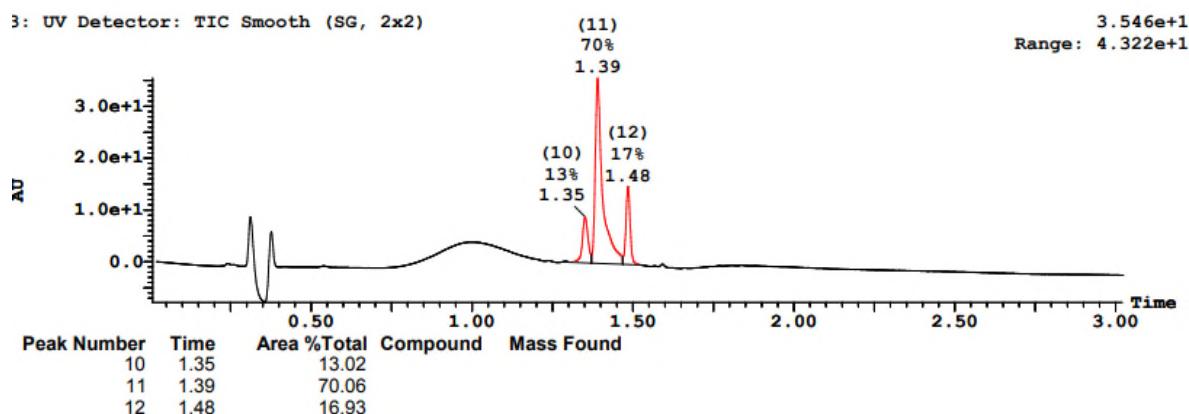


Figure S4.2.1



Initial test after 24h at rt which show minimal peptide stapling:

Figure S4.2.3

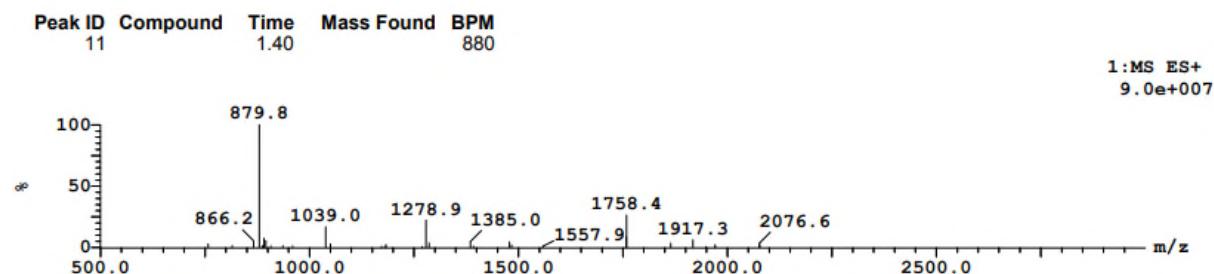
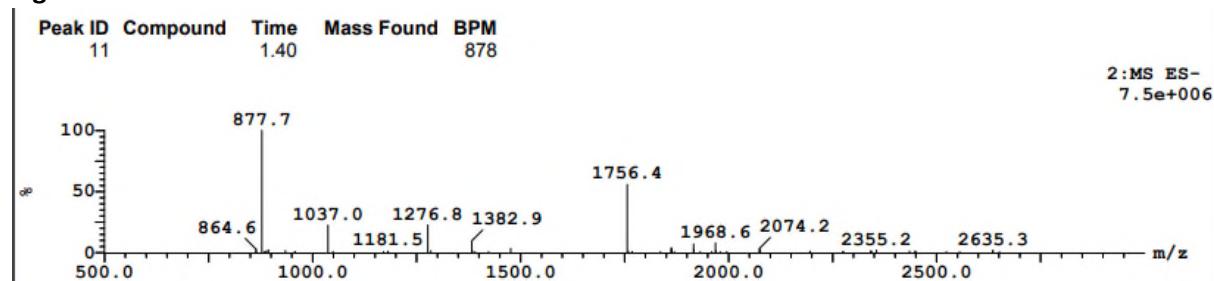


Figure S4.2.4



The reaction was left over a weekend, after which it appears to contain more of the stapled peptide, but a significant amount of the linear starting material is still visible:

Figure S4.2.5

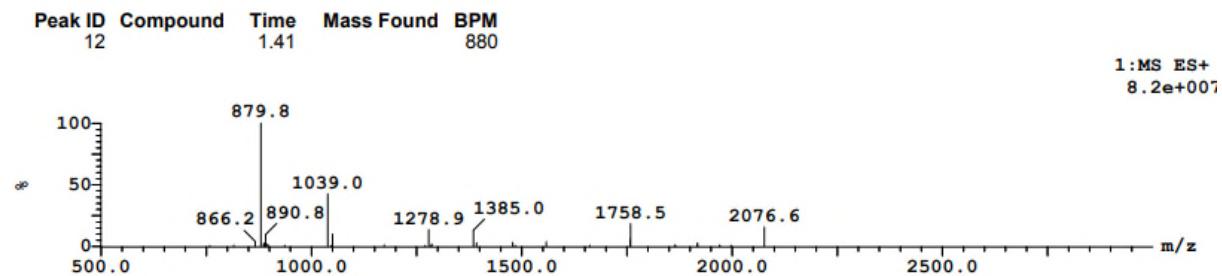
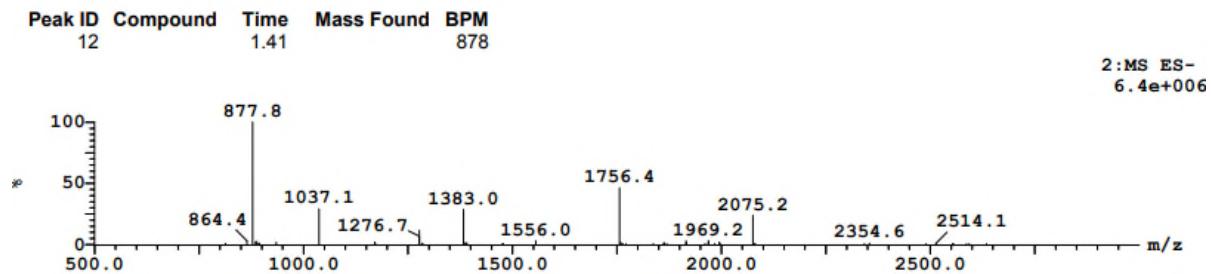


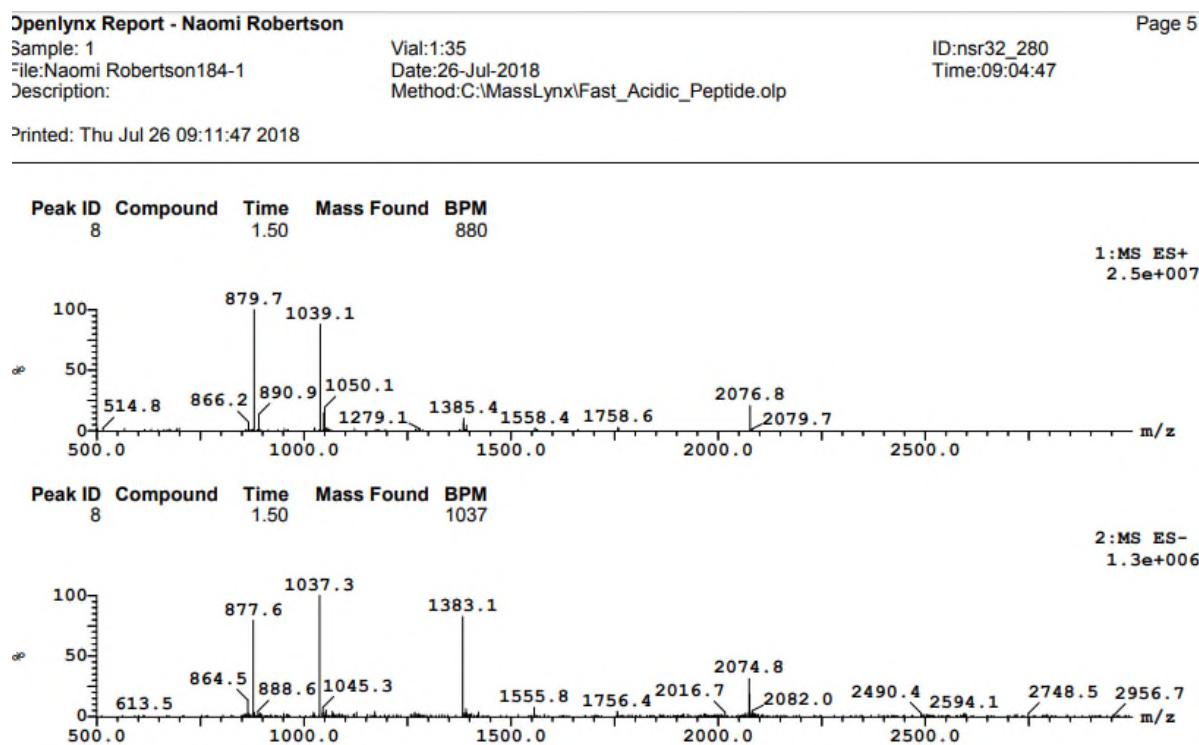
Figure S4.2.6



The reaction was carried out at 24h at rt, followed by 24h at 37 °C, but the reaction did not reach completion. At 48h, another 1.5 eq. of linker was added, while still keeping reaction stirring at 37 °C,

for 72h. Maintaining the temperature at 37 °C gave better results however conversion to the stapled peptide was incomplete and some starting material was still observed after 72 hours:

Figure S4.2.7



S4.3 Infrared spectra.

The IR spectrum of the stapled peptide revealed the disappearance of the azide stretch at 2097 cm⁻¹.

Figure 4.3.1 Unclicked reaction IR:

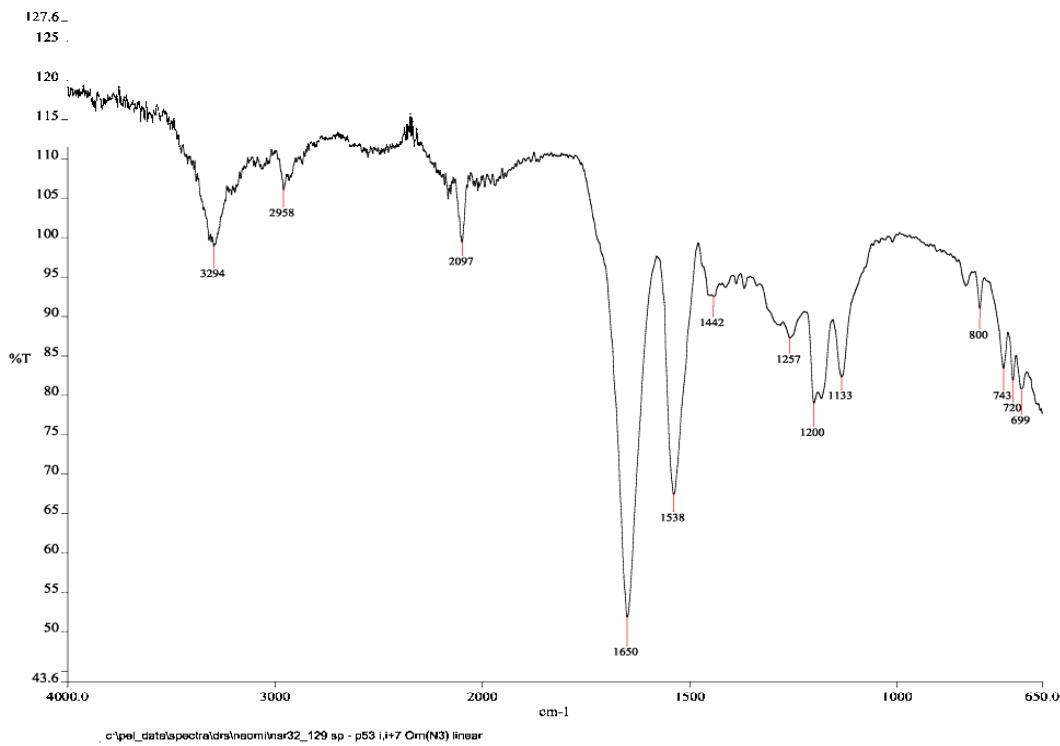
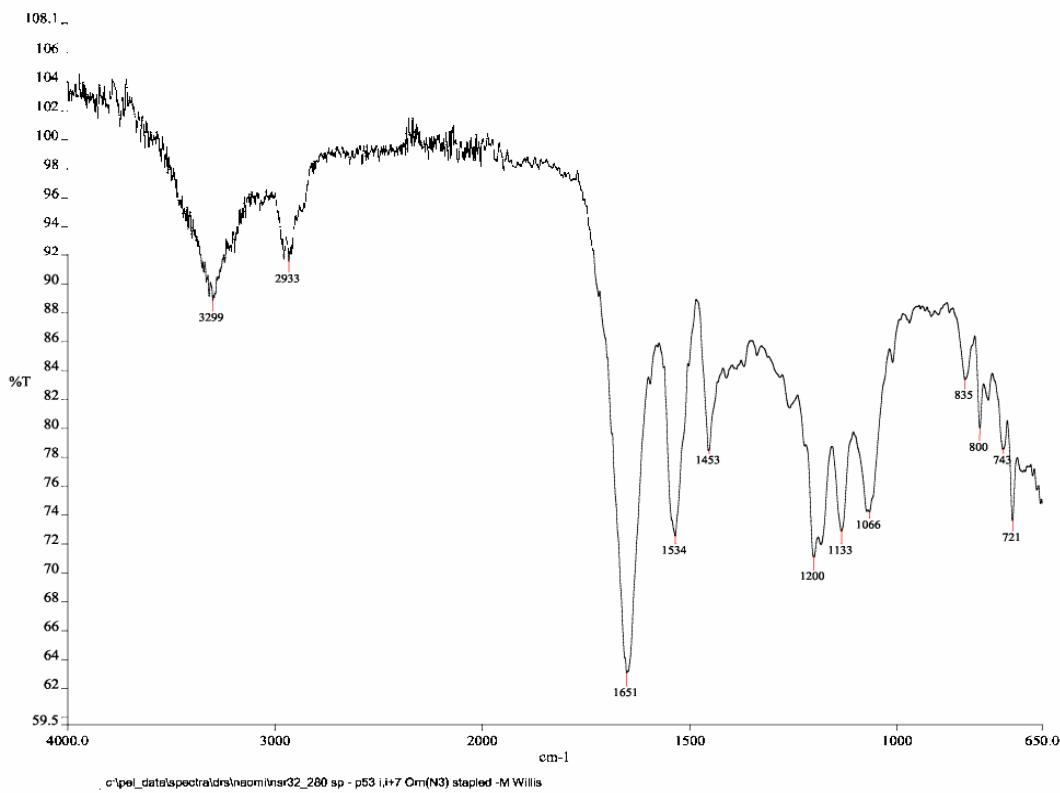


Figure 4.3.2 Clicked reaction IR:



S4.4. Peptide characterisation for synthesized peptides. Analytical reverse-phase HPLC using the following gradients: ^a5-95% MeCN/H₂O (0.05% TFA) 15 min gradient and ^b20-60% MeCN/H₂O (0.05%

TFA) 15 min gradient. The observation of two product peaks for the stapled product indicates that two regioisomers may have formed.

Table 4.4.1

Peptide	Calculated MW [M+H] ⁺ (Da)	Found MW [M+H] ⁺ (Da)	R _t (min)
Ac-ETFOrn(N ₃)DLWRLLOrn(N ₃)EN-NH ₂	1756.8	1758.4	10.43 ^a 10.08 ^b
stapled ⁽¹⁷⁻²⁹⁾ p53 peptide	2075.0	2076.8	9.90 ^a 9.32 ^b

Figure 4.4.1 HPLC trace for unstapled ⁽¹⁷⁻²⁹⁾p53 peptide 5-95% B over 15 mins.

DAD1 A, Sig=220,4 Ref=off (NAOMI\NAOMI 2018-11-23 11-10-54\0002NAOMI.D)

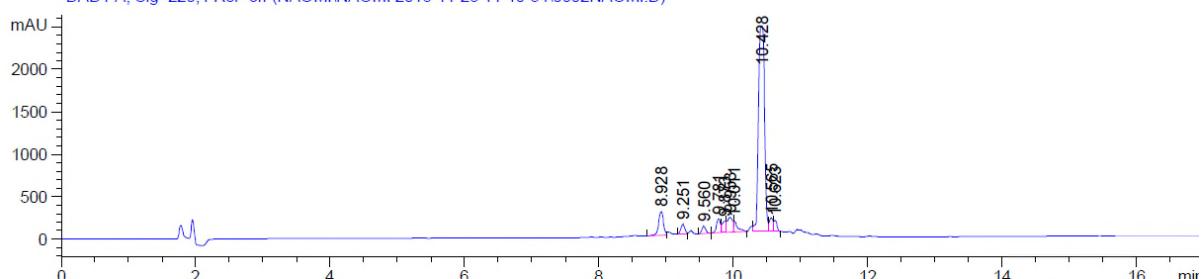


Figure 4.4.2 HPLC trace for unstapled ⁽¹⁷⁻²⁹⁾p53 peptide 20-60% B over 15 mins.

DAD1 B, Sig=220,4 Ref=off (NAOMI\NAOMI 2018-11-23 11-59-37\0004NAOMI.D)

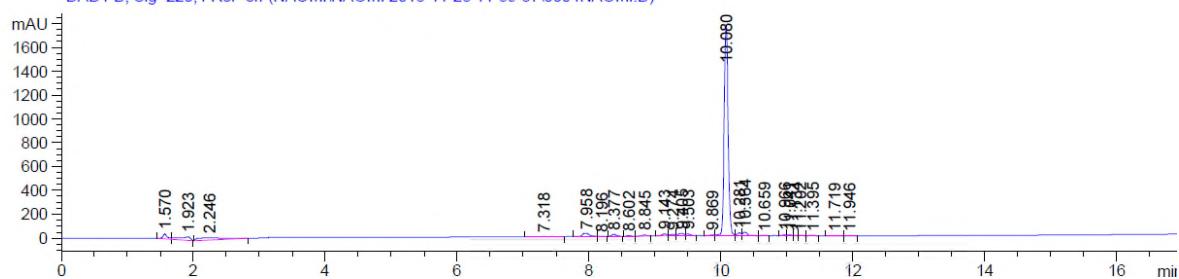


Figure 4.4.3 HPLC trace for stapled ⁽¹⁷⁻²⁹⁾p53 peptide 5-95% B over 15 mins.

DAD1 A, Sig=220,4 Ref=off (NAOMI\NAOMI 2018-11-23 11-35-14\0003NAOMI.D)

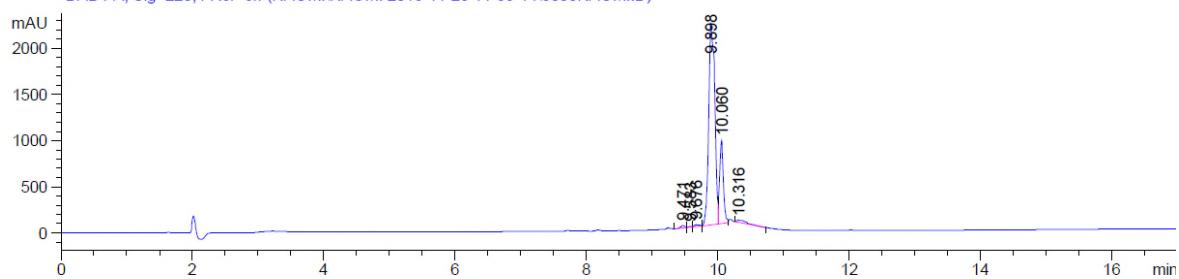
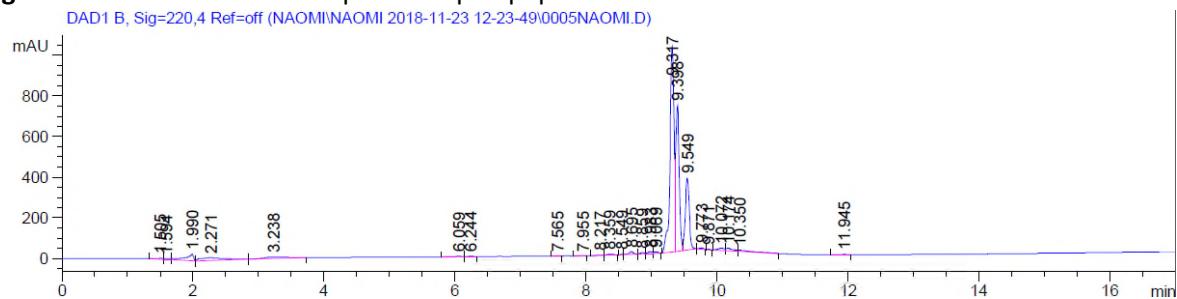


Figure 4.4.4 HPLC trace for stapled ⁽¹⁷⁻²⁹⁾p53 peptide 20-60% B over 15 mins.



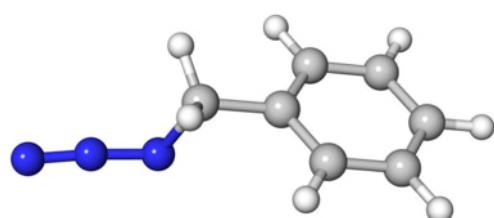
S5. Computational data

All calculations were performed with Gaussian 09 Rev D.01¹ using the B3LYP density functional and the 6-31G(d) basis set within the conductor-like polarizable continuum solvation model (CPCM)²⁻³ for methanol, using the default integration grid. Vibrational frequencies were computed for all optimized structures to verify that they were either minima (zero imaginary frequencies) or transition states (a single imaginary frequency). The strain-promoted click reaction of **3** with benzyl azide was modelled at 298.15 K at 1 atm in methanol. Previous computational studies with similar methods provided results in accordance with the experiment.⁴⁻⁶

S5.1 Cartesian coordinates and energies of all stationary points. Absolute energies depicted in hartrees.

S5.1.1 Reactants

Table S5.1.1.1 Benzyl azide



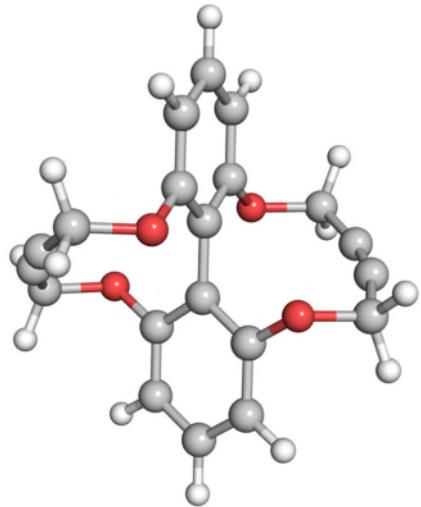
<i>E</i>	<i>H</i>	<i>G</i>
-435.149488	-435.007608	-435.053196

	X	Y	Z
6	-4.335439	-2.308814	-0.943689
6	-5.432894	-1.447235	-1.012201
6	-5.409576	-0.242669	-0.306121
6	-4.292322	0.098233	0.458711
6	-3.189530	-0.762883	0.534175
6	-3.221659	-1.972459	-0.171490
1	-4.345494	-3.248226	-1.489678

1	-6.298716	-1.711941	-1.612751
1	-6.256045	0.436704	-0.355366
1	-4.276970	1.041594	0.999344
1	-2.376642	-2.651758	-0.115020
6	-2.023411	-0.387090	1.434796
1	-2.016433	0.685843	1.627390
1	-2.114364	-0.895037	2.399597
7	-0.694042	-0.765129	0.931194
7	-0.280319	-2.017284	1.193706
7	0.950666	-2.118957	0.790031
6	0.302043	-0.015791	0.343532
6	1.381232	-0.925737	0.274627
6	2.814455	-0.927850	-0.147798
6	3.724621	0.131363	0.134275
6	3.104629	1.330533	0.577322
6	2.165191	2.097289	0.677778
6	0.852213	2.482724	0.283321
6	-0.005827	1.391922	-0.048390
6	-1.206301	1.685604	-0.705813
1	-1.852100	0.875610	-1.026094
6	0.448160	3.801077	0.048136
1	1.114709	4.613154	0.320360
6	3.333705	-2.096605	-0.719379
1	2.657912	-2.915421	-0.940947
6	5.093514	-0.011773	-0.128349
1	5.763597	0.810952	0.100494
6	5.581388	-1.191286	-0.688391
1	6.642584	-1.295298	-0.894036
6	4.697731	-2.227935	-0.992854
1	5.066998	-3.145518	-1.441643
6	-0.778282	4.064040	-0.564323
1	-1.081177	5.090261	-0.749338
6	-1.592014	3.005670	-0.963562

1	-2.531757	3.196700	-1.472700
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Table S5.1.1.2 Compound 3



<i>E</i>	<i>H</i>	<i>G</i>
-1071.251626	-1070.940670	-1071.005881

	X	Y	Z
6	-0.705907	1.483699	0.974075
6	-0.001042	0.748318	-0.000185
6	0.702628	1.484618	-0.974609
6	-0.702769	2.880167	0.981934
1	-1.248798	3.406615	1.758878
6	-0.003507	3.578397	-0.000673
1	-0.004518	4.664419	-0.000847
6	0.697005	2.881083	-0.983006
1	1.242104	3.408196	-1.760160
6	0.000628	-0.748380	-0.000054
6	0.705603	-1.483199	0.974523
6	-0.702523	-1.485135	-0.974487
6	0.702932	-2.879666	0.982800
6	-0.696461	-2.881576	-0.982480
6	0.004094	-3.578360	0.000238

1	1.248947	-3.405800	1.759975
1	-1.241211	-3.409172	-1.759539
1	0.005404	-4.664384	0.000362
8	1.397824	0.809403	-1.966872
8	1.399120	-0.806492	1.966901
8	-1.399720	0.807773	1.966809
8	-1.397637	-0.810371	-1.967185
6	-2.840601	0.839897	1.835028
1	-3.218206	0.279957	2.694604
1	-3.209599	1.870789	1.910109
6	-3.221903	0.230229	0.558578
6	-2.838453	-0.845125	-1.834949
1	-3.205646	-1.876616	-1.910536
1	-3.217359	-0.285290	-2.694020
6	-3.220345	-0.236879	-0.558057
6	2.838632	0.844905	-1.834653
1	3.217846	0.285895	-2.694117
1	3.205235	1.876652	-1.909515
6	2.840037	-0.839472	1.835453
1	3.217806	-0.279556	2.694963
1	3.208466	-1.870534	1.910775
6	3.220769	0.236105	-0.558060
6	3.221655	-0.230236	0.558891

S5.1.2 Associated states

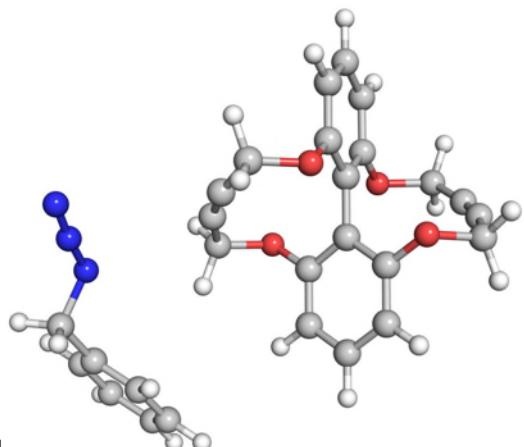


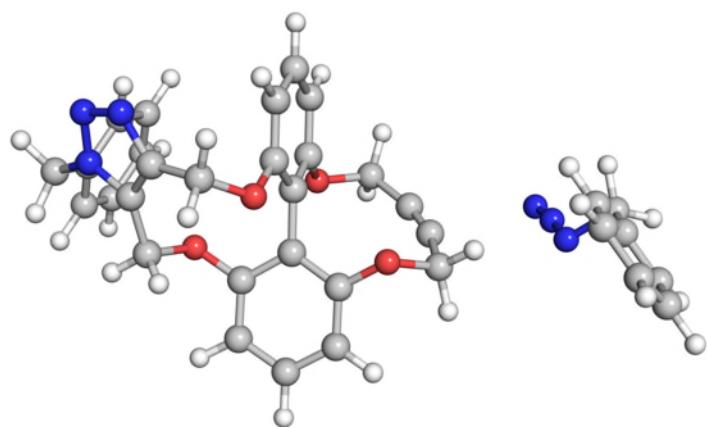
Table S5.1.2.1 A1

<i>E</i>	<i>H</i>	<i>G</i>
-1506.402942	-1505.948065	-1506.046089

	X	Y	Z
6	-2.402562	1.816383	-0.356467
6	-2.380179	0.571920	0.290605
6	-2.865683	0.555918	1.627797
6	-2.875756	2.976687	0.264374
1	-2.877053	3.904956	-0.295152
6	-3.333392	2.919797	1.572836
1	-3.700211	3.815200	2.066230
6	-3.327253	1.700472	2.260157
1	-3.679911	1.636545	3.284671
6	-1.873036	-0.656973	-0.392076
6	-2.614481	-1.294487	-1.416234
6	-0.643890	-1.234508	-0.048635
6	-2.139603	-2.435709	-2.054320
6	-0.166628	-2.395083	-0.676373
6	-0.911724	-2.993483	-1.681183
1	-2.741587	-2.880572	-2.843193
1	0.788036	-2.800046	-0.353933
1	-0.550370	-3.888575	-2.178188
8	-2.872211	-0.633967	2.344230
8	-3.832427	-0.784246	-1.829137
8	-1.964972	1.921934	-1.680662
8	0.123150	-0.667853	0.961883
6	-0.709025	2.605598	-1.829159
1	-0.529144	2.630937	-2.907386
1	-0.796479	3.645600	-1.478343
6	0.352133	1.894176	-1.107799
6	1.308199	0.029143	0.531173
1	2.008979	-0.668011	0.045795

1	1.783511	0.386131	1.448703
6	0.947859	1.129919	-0.359889
6	-4.185929	-1.231415	2.538518
1	-4.001373	-2.136206	3.123969
1	-4.832427	-0.567286	3.127243
6	-4.984893	-1.537112	-1.401861
1	-5.843405	-1.001508	-1.817780
1	-4.966320	-2.547068	-1.838084
6	-4.768639	-1.527004	1.236257
6	-5.037121	-1.592127	0.057318
6	6.093537	-1.928653	1.680762
6	5.610961	-2.894675	0.801998
6	5.090988	-2.508136	-0.440986
6	5.058339	-1.162597	-0.791517
6	5.541696	-0.177686	0.090281
6	6.056945	-0.571703	1.323458
1	6.502219	-2.218647	2.644835
1	5.639560	-3.946139	1.074114
1	4.720425	-3.261111	-1.130274
1	4.662431	-0.858711	-1.758292
1	6.437985	0.177601	2.017275
6	5.463398	1.270441	-0.330104
1	6.267341	1.846592	0.133862
1	5.565313	1.365619	-1.416705
7	4.144860	1.814472	0.102137
7	3.884703	2.926349	-0.400656
7	3.497377	3.931054	-0.794833

Table S5.1.2.2 A2: *syn*-attack second cycloaddition



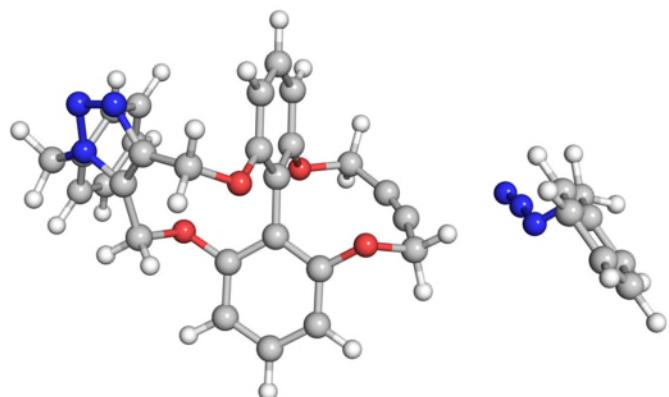
<i>E</i>	<i>H</i>	<i>G</i>
-1941.669481	-1941.067138	-1941.185703

	X	Y	Z
6	0.950558	-1.441585	-1.129952
6	0.587200	-0.305623	-0.381193
6	0.516707	0.926685	-1.055842
6	1.124401	-1.378757	-2.514119
1	1.384833	-2.268832	-3.076144
6	0.982652	-0.152386	-3.164305
1	1.124627	-0.095283	-4.239662
6	0.698269	1.002994	-2.441142
1	0.648284	1.967866	-2.935970
6	0.381077	-0.444962	1.094323
6	-0.874979	-0.728360	1.666260
6	1.486751	-0.387546	1.962155
6	-1.029419	-0.846080	3.051705
6	1.342382	-0.494951	3.346764
6	0.075728	-0.712105	3.888753
1	-2.008940	-1.072262	3.461671
1	2.218415	-0.417951	3.983273

1	-0.045322	-0.802585	4.964258
8	0.376999	2.092261	-0.319573
8	-1.948093	-1.007891	0.836009
8	1.121367	-2.604997	-0.410606
8	2.742488	-0.222471	1.406302
6	2.260940	-3.424305	-0.733993
1	2.253040	-4.194876	0.042097
1	2.137292	-3.922229	-1.702077
6	3.554623	-2.664581	-0.749121
6	3.626893	-1.360666	1.539681
1	3.098466	-2.181849	2.030689
1	4.467170	-1.071864	2.177664
6	4.110695	-1.814437	0.198316
6	-0.818876	2.868251	-0.554781
1	-0.673236	3.796683	0.003635
1	-0.918414	3.122589	-1.617002
6	-3.071897	-0.100945	0.898017
1	-3.855719	-0.566046	0.295274
1	-3.444209	-0.007923	1.925434
6	-1.963065	2.094614	-0.071248
6	-2.640401	1.188509	0.358717
6	4.988558	2.866582	-1.175959
6	5.142808	3.683120	-0.051259
6	5.658137	3.145796	1.129180
6	6.013700	1.795531	1.186712
6	5.863924	0.974691	0.064041
6	5.350173	1.520848	-1.120037
1	4.588790	3.279180	-2.098147
1	4.861397	4.731513	-0.096428
1	5.778868	3.772684	2.008263
1	6.411603	1.380546	2.109706
1	5.231739	0.889899	-1.997180
6	6.295579	-0.478822	0.121593

1	7.169356	-0.658844	-0.510293
1	6.561512	-0.766696	1.141694
7	5.277677	-1.410972	-0.375425
7	5.439701	-1.973425	-1.590141
7	4.392797	-2.726414	-1.819540
6	-6.733262	-2.327203	-0.990993
6	-7.706454	-2.678069	-0.051799
6	-8.423816	-1.679084	0.611201
6	-8.166908	-0.334484	0.336461
6	-7.192126	0.026675	-0.601860
6	-6.478600	-0.981433	-1.263576
1	-6.176577	-3.099469	-1.514606
1	-7.907928	-3.724773	0.158865
1	-9.185288	-1.946105	1.338798
1	-8.728959	0.440998	0.851418
1	-5.726392	-0.711197	-2.001060
6	-6.901807	1.479882	-0.883622
1	-6.544938	1.611439	-1.911326
1	-7.805233	2.087108	-0.754741
7	-5.854100	1.966711	0.071928
7	-5.401775	3.087103	-0.170197
7	-4.899616	4.106467	-0.295141

Table S5.1.2.3 A3: *anti*-attack second cycloaddition



<i>E</i>	<i>H</i>	<i>G</i>
-1941.669467	-1941.067064	-1941.186268

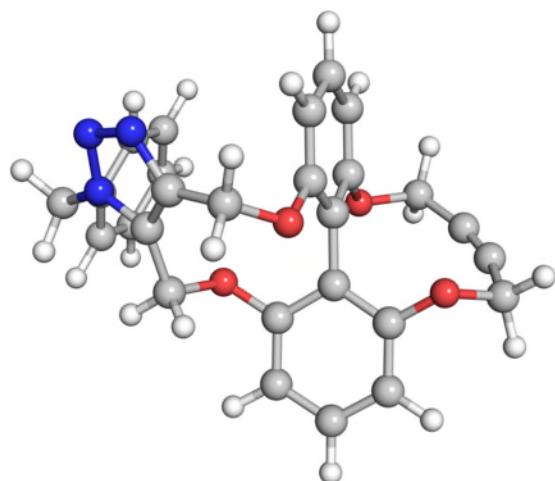
	X	Y	Z
6	1.912943	-1.814367	-1.377619
6	0.890068	-1.395385	-0.505009
6	-0.080721	-0.512411	-1.012063
6	1.910235	-1.461544	-2.728748
1	2.697537	-1.808719	-3.388597
6	0.896203	-0.636449	-3.216287
1	0.893207	-0.351507	-4.264435
6	-0.088100	-0.145890	-2.362445
1	-0.842796	0.544791	-2.725338
6	0.931868	-1.832911	0.925561
6	0.291574	-2.999465	1.388423
6	1.710958	-1.114959	1.851185
6	0.347091	-3.369096	2.736625
6	1.765774	-1.469854	3.200348
6	1.068710	-2.594457	3.641667
1	-0.150271	-4.277900	3.061344
1	2.357929	-0.872564	3.886742
1	1.110037	-2.881901	4.688191
8	-0.972921	0.086514	-0.137267
8	-0.304435	-3.852004	0.473298
8	2.904581	-2.586944	-0.812160
8	2.439894	-0.034201	1.388365
6	4.265946	-2.300212	-1.185715
1	4.855235	-2.942729	-0.525426
1	4.472661	-2.602094	-2.218532
6	4.631294	-0.853672	-1.026954

6	3.876338	-0.211255	1.413498
1	4.115102	-1.221902	1.754012
1	4.299578	0.495148	2.133589
6	4.461571	0.002868	0.053358
6	-2.373044	-0.211181	-0.334187
1	-2.911680	0.458409	0.340809
1	-2.686893	0.019001	-1.358651
6	-1.730420	-4.047510	0.600459
1	-1.973536	-4.850322	-0.100527
1	-1.990501	-4.387769	1.610166
6	-2.580204	-1.622877	-0.009833
6	-2.392471	-2.786828	0.263229
6	1.728517	4.102784	-0.842250
6	1.224748	4.581898	0.371136
6	1.944034	4.376541	1.549268
6	3.160986	3.690177	1.515481
6	3.670506	3.209926	0.304642
6	2.946284	3.423961	-0.876195
1	1.173764	4.261071	-1.762939
1	0.276665	5.111928	0.395996
1	1.558824	4.744223	2.496262
1	3.716414	3.529591	2.436328
1	3.336175	3.053901	-1.820979
6	5.010365	2.497630	0.268850
1	5.748843	3.069021	-0.299430
1	5.405074	2.358288	1.278039
7	4.956592	1.189512	-0.394895
7	5.407143	1.078604	-1.660738
7	5.203597	-0.156937	-2.046010
6	-5.191811	2.760233	1.663567
6	-5.326292	3.862726	0.814997
6	-5.934029	3.708305	-0.433130
6	-6.402914	2.454639	-0.832076

6	-6.271125	1.344518	0.010608
6	-5.662446	1.508621	1.262312
1	-4.726364	2.875788	2.638504
1	-4.963270	4.837947	1.127595
1	-6.045512	4.562696	-1.095016
1	-6.877573	2.337271	-1.803311
1	-5.562435	0.653517	1.926722
6	-6.759348	-0.013956	-0.427920
1	-7.126347	-0.589710	0.429127
1	-7.577625	0.083904	-1.150390
7	-5.631146	-0.756782	-1.078717
7	-5.816847	-1.964372	-1.239769
7	-5.867584	-3.089961	-1.433649

S5.1.3 Products: triazole

Table S5.1.3.1 P1



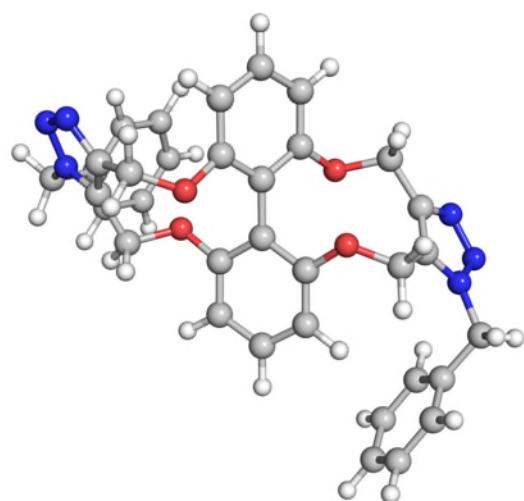
E	H	G
-1506.518375	-1506.059827	-1506.146314

	X	Y	Z
6	-0.895307	1.350584	1.340823
6	-1.343925	0.182359	0.694651

6	-1.259148	-1.029335	1.403844
6	-0.485718	1.335109	2.675685
1	-0.160123	2.248578	3.160785
6	-0.476289	0.126427	3.372728
1	-0.150964	0.106805	4.408849
6	-0.843009	-1.057990	2.739415
1	-0.776817	-2.008233	3.259918
6	-1.795589	0.267819	-0.729742
6	-3.137723	0.485489	-1.098618
6	-0.842547	0.222577	-1.763653
6	-3.517786	0.548323	-2.443597
6	-1.211696	0.275723	-3.109020
6	-2.557167	0.425740	-3.444571
1	-4.558984	0.724360	-2.695788
1	-0.447070	0.209664	-3.876790
1	-2.853367	0.473748	-4.488365
8	-1.483088	-2.221425	0.732775
8	-4.074919	0.757721	-0.114605
8	-0.889638	2.494938	0.573190
8	0.491355	0.124973	-1.412245
6	0.248329	3.369475	0.689333
1	0.076072	4.120946	-0.086412
1	0.264637	3.884093	1.656541
6	1.559203	2.664163	0.499563
6	1.295439	1.285609	-1.730685
1	0.659517	2.069696	-2.149608
1	2.026278	1.002513	-2.493670
6	1.981169	1.803629	-0.506062
6	-2.593712	-3.023871	1.189171
1	-2.508997	-3.968717	0.645944
1	-2.509236	-3.238655	2.261296
6	-5.160596	-0.184259	0.027413
1	-5.854345	0.280329	0.732960

1	-5.686223	-0.324178	-0.924935
6	-3.828113	-2.303242	0.874420
6	-4.603649	-1.440643	0.530190
6	3.330052	-2.763506	0.928101
6	3.312413	-3.639467	-0.161764
6	3.568712	-3.153883	-1.444856
6	3.837667	-1.796289	-1.638403
6	3.859432	-0.915999	-0.551557
6	3.605070	-1.409907	0.735095
1	3.131696	-3.135638	1.929412
1	3.098944	-4.693853	-0.009839
1	3.554456	-3.827271	-2.297316
1	4.033853	-1.421610	-2.640104
1	3.619634	-0.732067	1.584586
6	4.199209	0.547736	-0.765211
1	5.166080	0.799390	-0.321363
1	4.253964	0.783822	-1.830800
7	3.246274	1.466180	-0.132109
7	3.589262	2.076006	1.020432
7	2.564892	2.795297	1.406767

Table S5.1.3.2 P2: *syn*-attack second cycloaddition



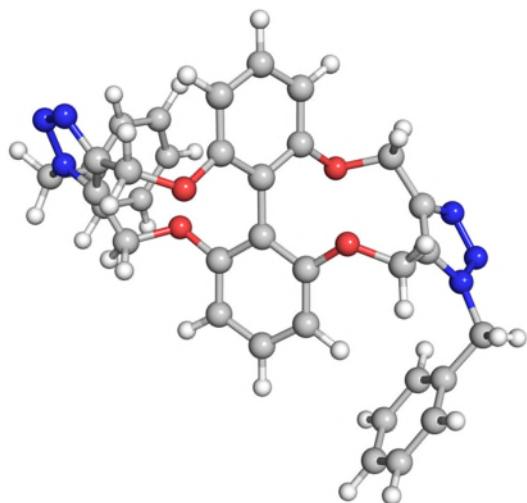
<i>E</i>	<i>H</i>	<i>G</i>
-1941.797151	-1941.190677	-1941.294556

	X	Y	Z
6	1.647547	2.146454	-1.119622
6	0.584174	1.614322	-0.362964
6	0.225473	2.269823	0.827486
6	2.337331	3.285159	-0.690261
1	3.158243	3.689357	-1.270516
6	1.950495	3.914724	0.493546
1	2.485098	4.800505	0.824765
6	0.895338	3.420043	1.257595
1	0.609830	3.898788	2.188663
6	-0.136096	0.386040	-0.796273
6	-1.516534	0.404494	-1.082135
6	0.545156	-0.837653	-0.919846
6	-2.184061	-0.755589	-1.485881
6	-0.107575	-2.002185	-1.334725
6	-1.470802	-1.948411	-1.614552
1	-3.242977	-0.745540	-1.713068
1	0.439798	-2.936580	-1.407033
1	-1.994020	-2.847104	-1.927712
8	-0.775313	1.693684	1.569551
8	-2.117080	1.643458	-1.014651
8	1.895561	1.519114	-2.317871
8	1.870416	-0.850956	-0.549075
6	3.217721	1.549885	-2.872135
1	3.088466	1.122029	-3.870737
1	3.593422	2.570464	-2.998078
6	4.189436	0.746732	-2.060415
6	2.816807	-1.404756	-1.482563
1	2.369848	-1.450290	-2.480169
1	3.082868	-2.422667	-1.181389

6	4.017411	-0.513048	-1.506621
6	-1.845686	2.550037	2.016139
1	-1.709828	2.795030	3.075115
1	-1.828957	3.480148	1.438754
6	-3.515931	1.747090	-0.755146
1	-3.762506	2.779901	-1.020903
1	-4.103973	1.097023	-1.409146
6	-3.152670	1.842123	1.851057
6	-3.838670	1.499379	0.693401
6	4.292454	-0.984844	3.362641
6	3.724990	-2.192893	3.779950
6	3.764122	-3.304359	2.936863
6	4.365266	-3.207600	1.678963
6	4.937292	-2.002532	1.257518
6	4.898305	-0.890712	2.110061
1	4.265246	-0.116211	4.014696
1	3.254127	-2.264937	4.756399
1	3.322942	-4.245734	3.252263
1	4.390773	-4.075086	1.023830
1	5.340472	0.049301	1.789915
6	5.624510	-1.918613	-0.092773
1	6.705823	-1.800622	0.017758
1	5.449380	-2.825659	-0.676914
7	5.203500	-0.760584	-0.889106
7	6.057890	0.270822	-1.055740
7	5.439347	1.187983	-1.760642
6	-5.907597	-2.525564	-2.094523
6	-5.376742	-3.550198	-1.309260
6	-5.075550	-3.309227	0.035242
6	-5.303392	-2.050538	0.590363
6	-5.832198	-1.016119	-0.193876
6	-6.132700	-1.262691	-1.538408
1	-6.144327	-2.703929	-3.139647

1	-5.199874	-4.531816	-1.739803
1	-4.664416	-4.103616	0.651880
1	-5.068183	-1.866497	1.635377
1	-6.547412	-0.467900	-2.153828
6	-6.113441	0.346361	0.411970
1	-6.418586	1.061540	-0.356007
1	-6.919465	0.290617	1.148512
7	-4.975164	0.909445	1.148884
7	-4.993496	0.879713	2.502223
7	-3.887158	1.434948	2.922738

Table S5.1.3.3 P3: anti-attack second cycloaddition



<i>E</i>	<i>H</i>	<i>G</i>
-1941.797594	-1941.191180	-1941.297264

	X	Y	Z
6	-1.622009	-1.386681	1.894657
6	-0.581203	-1.109678	0.985042
6	0.434175	-0.228250	1.393920
6	-1.646240	-0.796254	3.162621
1	-2.448714	-1.009271	3.858915

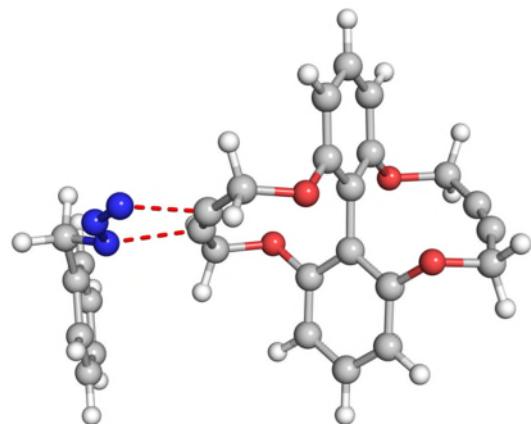
6	-0.614452	0.064423	3.539085
1	-0.633138	0.519214	4.525375
6	0.431313	0.353905	2.664887
1	1.220141	1.043292	2.948418
6	-0.558629	-1.720982	-0.372677
6	0.483482	-2.584181	-0.768358
6	-1.574759	-1.444721	-1.303262
6	0.507829	-3.142961	-2.050566
6	-1.571610	-2.010956	-2.581372
6	-0.524743	-2.855989	-2.944201
1	1.310512	-3.805157	-2.352879
1	-2.361062	-1.767524	-3.285212
1	-0.505890	-3.293242	-3.938384
8	1.397695	0.088651	0.462572
8	1.406969	-2.884459	0.204875
8	-2.544683	-2.316025	1.476084
8	-2.539373	-0.538406	-0.922767
6	-3.888789	-2.249891	1.972198
1	-4.347140	-3.169708	1.597005
1	-3.931875	-2.283068	3.065772
6	-4.616234	-1.038222	1.471955
6	-3.915555	-0.945563	-1.047218
1	-3.972154	-2.033529	-1.147021
1	-4.354919	-0.498524	-1.944327
6	-4.642052	-0.515519	0.187500
6	2.774772	-0.086495	0.849104
1	3.215970	0.880983	1.107474
1	2.833274	-0.731752	1.730586
6	2.751316	-3.212704	-0.173694
1	3.209818	-3.540545	0.763909
1	2.793997	-4.054035	-0.872880
6	3.500171	-0.726539	-0.291714
6	3.478208	-2.035169	-0.750329

6	-3.012184	4.120560	-0.385410
6	-2.678953	4.344734	-1.724975
6	-3.359894	3.659541	-2.732146
6	-4.368181	2.750040	-2.401387
6	-4.707554	2.523652	-1.063320
6	-4.022491	3.217440	-0.056316
1	-2.486158	4.651603	0.403110
1	-1.892091	5.049106	-1.980053
1	-3.105542	3.826141	-3.775162
1	-4.894651	2.217342	-3.189707
1	-4.280620	3.046723	0.985706
6	-5.831883	1.566403	-0.713284
1	-6.682619	2.095676	-0.276066
1	-6.190639	1.042494	-1.602625
7	-5.453330	0.570548	0.295828
7	-5.907871	0.708278	1.559157
7	-5.394081	-0.264355	2.273652
7	4.246888	-2.118722	-1.867877
7	4.748163	-0.935070	-2.130219
7	4.291622	-0.081610	-1.189963
6	4.706618	1.324996	-1.233220
1	3.818755	1.948538	-1.103536
1	5.073768	1.477594	-2.251541
6	5.769715	1.673093	-0.207313
6	5.601316	2.781426	0.629983
6	6.943261	0.912874	-0.109428
6	6.592170	3.129119	1.552423
1	4.695468	3.378869	0.558960
6	7.929558	1.256194	0.814683
1	7.081524	0.051116	-0.757289
6	7.756667	2.366067	1.647808
1	6.449280	3.991920	2.196973
1	8.834801	0.659300	0.883489

1	8.526352	2.632587	2.366760
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S5.1.4 Transition states

Table S5.1.4.1 T1



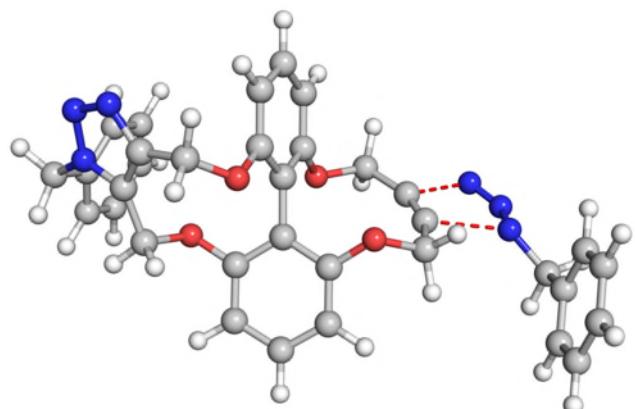
<i>E</i>	<i>H</i>	<i>G</i>
-1506.380698	-1505.927210	-1506.017543

	X	Y	Z
6	-2.103524	1.816635	-0.044365
6	-2.215083	0.492647	0.417092
6	-2.685500	0.301869	1.730610
6	-2.474543	2.903998	0.750590
1	-2.395850	3.911203	0.353151
6	-2.943107	2.682615	2.044383
1	-3.226729	3.524294	2.669438
6	-3.044076	1.383128	2.538756
1	-3.390830	1.196871	3.550660
6	-1.793368	-0.644077	-0.458324
6	-2.579742	-1.106200	-1.531076
6	-0.548762	-1.266177	-0.253637
6	-2.150378	-2.154435	-2.348385
6	-0.117192	-2.325704	-1.055095
6	-0.921897	-2.766331	-2.104389

1	-2.778430	-2.475553	-3.173807
1	0.840089	-2.796292	-0.853350
1	-0.589261	-3.585275	-2.735437
8	-2.747820	-0.980980	2.253919
8	-3.782038	-0.476612	-1.816048
8	-1.648982	2.017377	-1.334705
8	0.233101	-0.823113	0.798565
6	-0.399950	2.717859	-1.461382
1	-0.277044	2.882911	-2.534675
1	-0.457029	3.701907	-0.979856
6	0.745093	1.959217	-0.913784
6	1.491188	-0.224082	0.439437
1	2.098915	-0.919685	-0.150843
1	2.004632	-0.059151	1.389809
6	1.306129	1.041662	-0.297159
6	-4.081260	-1.515369	2.421261
1	-3.941207	-2.494151	2.887509
1	-4.662962	-0.889145	3.109595
6	-4.969344	-1.241419	-1.504734
1	-5.805237	-0.621254	-1.838941
1	-4.986454	-2.176266	-2.079246
6	-4.725738	-1.607531	1.109215
6	-5.005122	-1.499400	-0.063354
6	5.719186	-1.855616	1.848862
6	5.872606	-2.660456	0.719053
6	5.629615	-2.126179	-0.550435
6	5.239586	-0.793861	-0.687380
6	5.081913	0.020733	0.443134
6	5.321582	-0.522761	1.709933
1	5.901633	-2.263520	2.839267
1	6.177291	-3.698044	0.824602
1	5.747207	-2.747501	-1.434158
1	5.050211	-0.381168	-1.674782

1	5.197195	0.099099	2.593328
6	4.689886	1.475680	0.298397
1	4.513496	1.920269	1.285583
1	5.498968	2.042594	-0.177017
7	3.474532	1.605065	-0.531964
7	3.222192	2.695321	-1.099060
7	2.305866	3.273301	-1.550121

Table S5.1.4.2 T2: *syn*-attack second cycloaddition



Imaginary frequency at -347.7 cm^{-1}

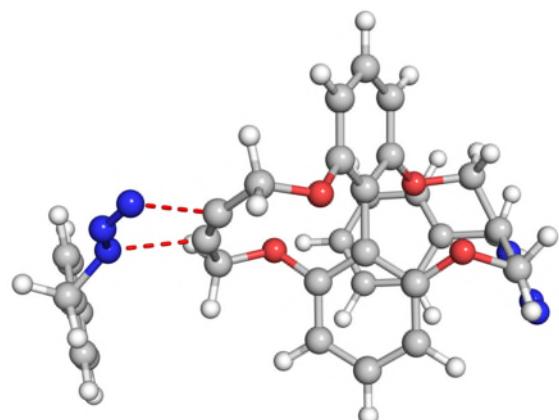
E	H	G
-1941.650392	-1941.049201	-1941.159233

	X	Y	Z
6	1.160327	-1.294933	-1.578167
6	0.557268	-0.324159	-0.756562
6	0.382820	0.968837	-1.278157
6	1.506529	-1.010623	-2.901581
1	1.958048	-1.769201	-3.530805
6	1.273392	0.269340	-3.406373
1	1.546038	0.496660	-4.433020
6	0.726994	1.266242	-2.601944
1	0.604012	2.274269	-2.984213
6	0.174248	-0.667316	0.645497

6	-1.153020	-0.973449	0.999302
6	1.154651	-0.752160	1.649181
6	-1.494471	-1.288439	2.319390
6	0.825667	-1.060720	2.970899
6	-0.505054	-1.318795	3.300259
1	-2.520281	-1.539595	2.569184
1	1.605274	-1.094999	3.725500
1	-0.770099	-1.563837	4.324703
8	-0.018785	1.959400	-0.404569
8	-2.078993	-1.078244	-0.020038
8	1.354262	-2.529632	-0.999098
8	2.463317	-0.495877	1.289696
6	2.554850	-3.249894	-1.326011
1	2.477886	-4.163270	-0.729293
1	2.581872	-3.542848	-2.381163
6	3.799351	-2.479682	-0.998422
6	3.387333	-1.597234	1.441455
1	2.837163	-2.508718	1.689493
1	4.068776	-1.378164	2.268899
6	4.139858	-1.803698	0.165317
6	-1.138739	2.783367	-0.771270
1	-1.067566	3.665845	-0.129981
1	-1.060149	3.122997	-1.810138
6	-3.309885	-0.341355	0.091025
1	-3.992664	-0.808996	-0.622060
1	-3.749225	-0.447392	1.089074
6	-2.406986	2.068601	-0.546040
6	-3.073635	1.071995	-0.244009
6	5.033244	3.061981	-0.271815
6	4.934105	3.686162	0.975580
6	5.243217	2.971757	2.133899
6	5.645785	1.636396	2.045875
6	5.748851	1.007506	0.800682

6	5.441370	1.731277	-0.359436
1	4.794972	3.613249	-1.177265
1	4.616673	4.723070	1.042169
1	5.166771	3.448444	3.107185
1	5.883409	1.083134	2.951273
1	5.520071	1.250245	-1.330939
6	6.230731	-0.428823	0.711547
1	7.214303	-0.488892	0.238054
1	6.314903	-0.874422	1.705655
7	5.366997	-1.283585	-0.110083
7	5.765010	-1.618063	-1.354744
7	4.811545	-2.336718	-1.895464
6	-7.549945	-1.684259	-1.023875
6	-7.779992	-2.427318	0.138511
6	-7.557372	-1.844935	1.387049
6	-7.103395	-0.525702	1.473433
6	-6.876342	0.226212	0.315606
6	-7.104253	-0.365336	-0.935445
1	-7.721454	-2.131634	-1.999158
1	-8.128832	-3.453979	0.069200
1	-7.730518	-2.416136	2.294983
1	-6.926471	-0.077589	2.448234
1	-6.926647	0.210350	-1.840155
6	-6.422451	1.665854	0.417325
1	-7.204757	2.338586	0.045550
1	-6.228231	1.930439	1.463770
7	-5.200282	1.873903	-0.390178
7	-4.821464	3.043637	-0.631325
7	-3.863519	3.663259	-0.888065

Table S5.1.4.3 T3: anti-attack second cycloaddition



Imaginary frequency at -344.1 cm⁻¹

<i>E</i>	<i>H</i>	<i>G</i>
-1941.650362	-1941.049260	-1941.159449

	X	Y	Z
6	-1.585348	-1.596894	1.653955
6	-0.627123	-1.259813	0.679864
6	0.350851	-0.308189	1.014906
6	-1.526223	-1.063198	2.943812
1	-2.260770	-1.339932	3.691507
6	-0.511671	-0.158727	3.260485
1	-0.464619	0.262630	4.260615
6	0.419954	0.234849	2.302947
1	1.169522	0.982513	2.540791
6	-0.703666	-1.864613	-0.683222
6	0.120916	-2.937751	-1.068691
6	-1.657484	-1.406548	-1.608524
6	0.037921	-3.485837	-2.353970
6	-1.747099	-1.942632	-2.894883
6	-0.887285	-2.977582	-3.263599
1	0.669359	-4.325149	-2.627132
1	-2.479931	-1.549376	-3.592504

1	-0.952072	-3.403959	-4.260478
8	1.153819	0.163813	-0.004902
8	0.917596	-3.512817	-0.099319
8	-2.550019	-2.495451	1.255136
8	-2.494920	-0.383853	-1.208871
6	-3.890221	-2.313438	1.741274
1	-4.447266	-3.129636	1.272416
1	-3.954185	-2.447942	2.826539
6	-4.463040	-0.975185	1.379061
6	-3.905402	-0.697033	-1.174470
1	-4.049680	-1.768043	-1.340012
1	-4.408803	-0.159215	-1.983358
6	-4.474092	-0.317653	0.156377
6	2.579792	0.164113	0.185822
1	2.972451	0.852401	-0.566087
1	2.849999	0.559589	1.171047
6	2.318231	-3.686707	-0.376080
1	2.663312	-4.429423	0.348039
1	2.476974	-4.102907	-1.377339
6	3.104709	-1.196990	-0.009287
6	3.043682	-2.414826	-0.213983
6	-2.235326	4.094747	-0.052552
6	-1.932421	4.404408	-1.382224
6	-2.747635	3.924467	-2.408177
6	-3.859519	3.133175	-2.106664
6	-4.168315	2.821756	-0.778381
6	-3.348567	3.310574	0.248033
1	-1.605371	4.466830	0.750670
1	-1.065194	5.015999	-1.615146
1	-2.518100	4.158884	-3.443897
1	-4.489489	2.758174	-2.909778
1	-3.582274	3.072872	1.282656
6	-5.397599	1.993257	-0.454292

1	-6.143107	2.582232	0.086378
1	-5.869749	1.620175	-1.366470
7	-5.113999	0.853268	0.425113
7	-5.481022	0.916865	1.721431
7	-5.080106	-0.188277	2.300831
6	5.578115	3.343039	-1.143444
6	5.370200	4.216068	-0.070699
6	5.445771	3.734970	1.237134
6	5.724902	2.385457	1.471543
6	5.939666	1.506906	0.404146
6	5.864316	1.998346	-0.907238
1	5.521011	3.711344	-2.164160
1	5.148955	5.263657	-0.255495
1	5.281913	4.405376	2.076339
1	5.777011	2.013433	2.491938
1	6.025903	1.321909	-1.742453
6	6.277333	0.055408	0.666213
1	7.302036	-0.161533	0.341035
1	6.217689	-0.160776	1.739738
7	5.350898	-0.825106	-0.078112
7	5.624547	-2.041230	-0.200218
7	5.121499	-3.079976	-0.389463

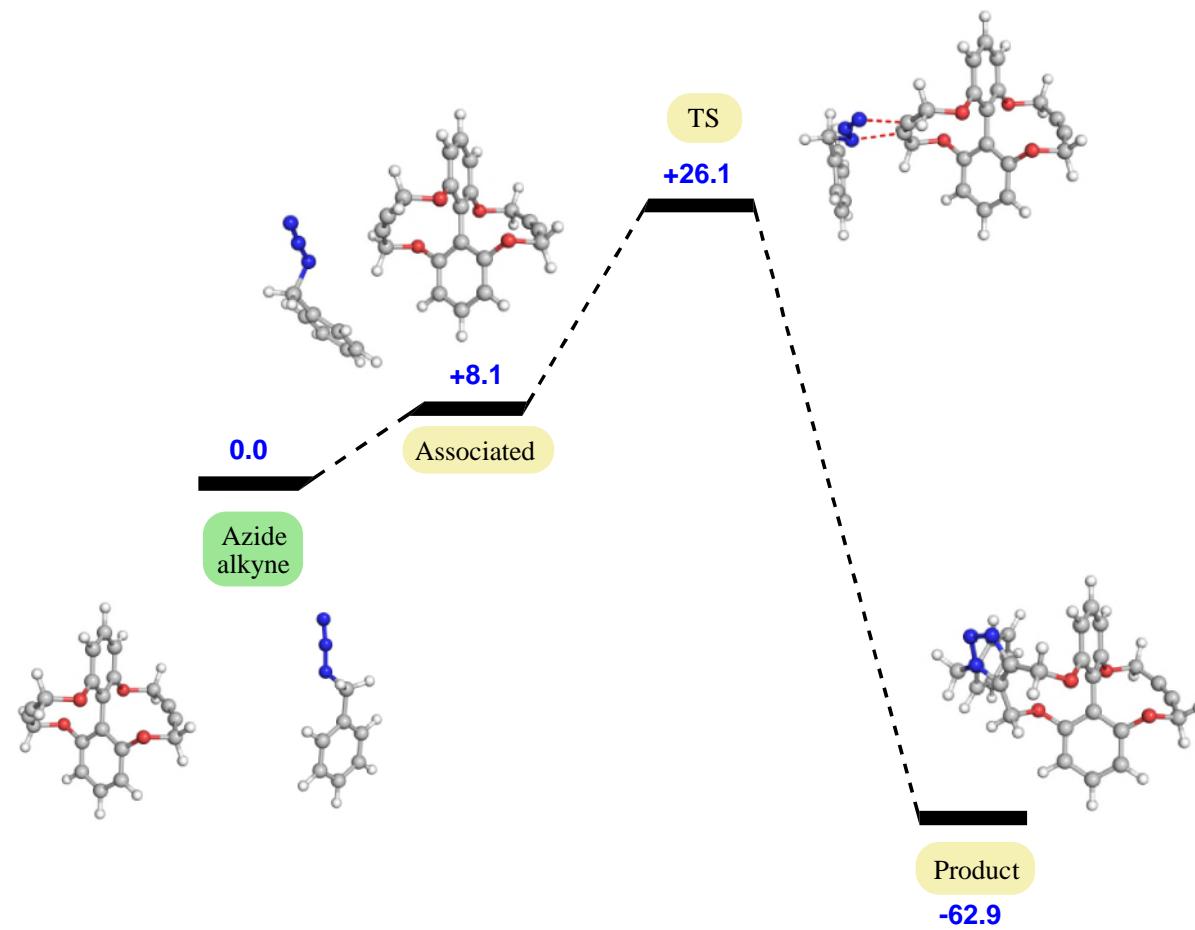


Figure S5.1: Energy level diagram depicting strain-promoted azide-alkyne cycloaddition between dialkyne **3** and benzyl azide (energy values in kcal/mol).

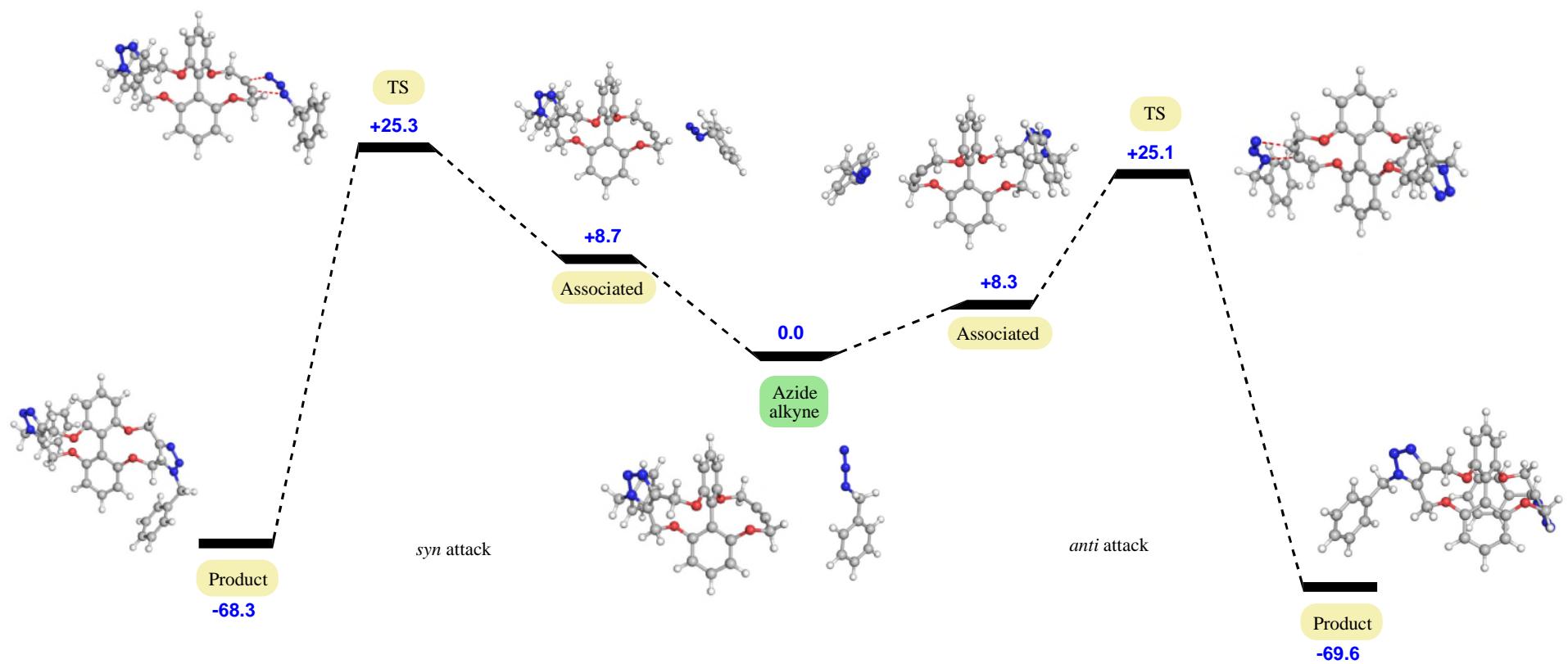


Figure S5.2: Energy level diagram depicting second strain-promoted azide-alkyne cycloaddition (*syn* and *anti*-attack) between dialkyne **3** and benzyl azide (energy values in kcal/mol).

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