Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Synthesis, photophysical and antibacterial, larvicidal studies on triazolophanes with 5-nitroisophthalate functionality at the intraannular position

Sivasamy Selvarani[a], Perumal Rajakumar[a,]* Subramani Nagaraj [b] and Manisha Choudhury[c], Devadasan Velmurugan[c]

[a]*Department of Organic Chemistry,* [b]Centre for Advanced Studies in Botany, [c]*CAS in Crystallography and Biophysics,*

University of Madras, Maraimalai (Guindy) Campus,

Chennai – 600 025, INDIA.

Tel: +91 044 22202810; fax: +91-44-22300488

E-mail: perumalrajakumar@gmail.com

Supporting Information

Content

S-1

GENERAL CONSIDERATIONS:

All the melting points were determined by using Toshniwal melting point apparatus by open capillary tube method and were uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on Bruker 300 MHz spectrometer with 75 MHz for ^{13}C nucleus. The chemical shifts are reported in ppm (δ) with TMS as internal standard and coupling constant (*J*) are expressed in Hz. MALDI-TOF mass spectrum on Voyager-DE PRO mass spectrometer using α-cyano-4-hydroxycinnamic acid (α-CHCA) matrix and EI-MS spectra on JEOL DX-303 mass spectrometer. The FAB-MS spectra were recorded on a JEOL SX 102/DA-6000 mass spectrometer using a *p*-nitrobenzyl alcohol (NBA) matrix. Elemental analyses were performed on a Perkin-Elmer 240B elemental analyzer. Glass plates coated with silica gel-G (ACME) of about 0.25 mm thickness were used for TLC and visualized with iodine. Column chromatography was carried out with silica gel (ACME, 100-200 mesh). The organic extracts of crude products were dried over anhydrous magnesium sulphate or sodium sulphate.

Synthesis of Diprop-2-ynyl 5-nitroisophthalate 27 by Steglich Esterification (« two steps » acylation)

To a solution of propargyl alcohol (1.64 g, 26.7 mmol, 2.2 equiv.) and DMAP (3.0 equiv.) in dry CH_2Cl_2 (100 mL) was added slowly at 0°C the appropriate acyl chloride (3.0 g, 12 mmol, 1.0 equiv.). The solution was purged with nitrogen and stirred at room temperature for 24 h. The reaction was quenched with saturated aqueous sodium bicarbonate solution and the aqueous layer was extracted with CH_2Cl_2 (3 x 100 mL).The combined organic layer was washed with brine (2 x 100 mL), dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue obtained was purified by column chromatography with Hexane: $CHCl_3$ (9:1) as a eluent to afford the precyclophane diyne **27** as white crystalline solid in 78% yield. Mp. 146 ^oC: ^1H NMR: (300 MHz, $CDCl_3$): δ_H 2.60 (t, 2H, *J* = 2.4 Hz); 5.02 (d, 4H, *J* = 2.4 Hz); 9.03 (s, 1H); 9.08 (s, 2H). ^{13}C NMR: (75 MHz, $CDCl_3$): δ_C 53.6, 76.0, 77.4, 128.7, 131.9, 136.1, 148.5, 162.9. (ESI-MS) *m/z* 287 [M^+]. Elemental Anal. Calcd for $C_{14}H_9NO_6$: C, 58.54; H, 3.16, ; N, 4.88%. Found: C, 58.51; H, 3.16; N, 4.84%.

General procedure for synthesis of bisbromides by O-alkylation (Procedure A)

A mixture of 1.0 equiv. of each of E-4-((4-nitrophenyl) diazenyl) benzene-1, 3-diol/Resorcinol/2,7-dihydroxynaphthalene/1,4-dihydroxybenzene and potassium carbonate (3.0 equiv.) in acetone (30 mL) was stirred for 15 minutes for at 60 ^oC. 1, 4-Dibromobutane (4.0 equiv.) was added to the reaction mixture and stirred at 60 ^oC for 7 h. After the completion of the reaction, the solvent was removed under reduced pressure and the residue was extracted with $CHCl_3$ (3 x 100 mL), washed with water (2 x 100

mL), brine (150 mL) and dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue obtained was purified by column chromatography with the indicated eluent to afford the desired bisazide.

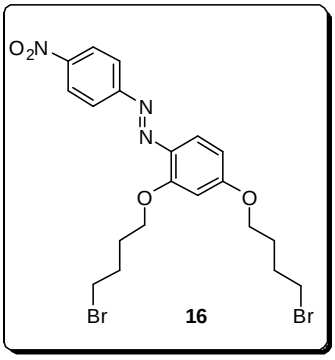
General procedure for the synthesis of bisazide (Procedure B)

The dibromide (1.0 mmol, 1.0 equiv.) was dissolved in a mixture of acetone/water (4:1, 40 mL). NaN_3 (2.2 mmol, 2.2 equiv.) was added to the reaction mixture and then heated to 60 ºC for 12 h. After completion of the reaction, the reaction mixture was cooled to room temperature, acetone was evaporated, to afford the crude product which was dissolved with $CHCl_3$ (3 x 100 mL) and washed with water (100 mL). The combined organic layer was washed with brine solution (2 x 50 mL) and dried with anhydrous sodium sulphate and filtered. The solvent was evaporated under vacuum and the residue was column chromatographed with the indicated eluent to give the desired azide**.**

General procedure for the synthesis of cyclophane by Click reaction (Procedure C)

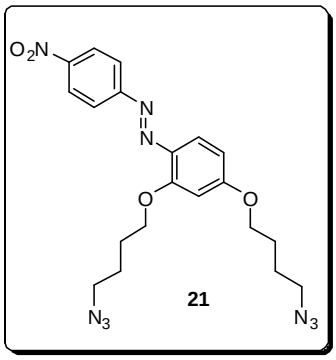
To a solution of alkyne (1 equiv.) and bisazide (1.1 equiv.) in a mixture of THF/ H_2O (3:1, 40 mL) was added sodium ascorbate (10 mol %) and $CuSO_4.5H_2O$ (10 mol %). The reaction mixture was stirred at room temperature for 12 h. After completion of the reaction, the solvent was evaporated to give the crude product which was dissolved in $CHCl_3$ (150 mL) and washed with water (100 mL) and brine (150 mL), dried over anhydrous Na_2SO_4, filtered and concentrated to afforded the desired triazoles, purified by column chromatography (SiO_2) using the eluent as mentioned under each compound.

E-1-(2,4-Bis(4-bromobutoxy)phenyl)-2-(4-nitrophenyl) diazene 16:



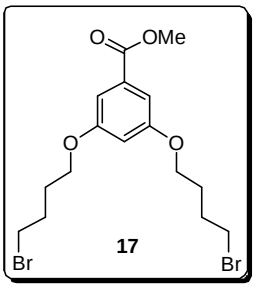
Following the general procedure A, E-1-(2,4-bis(4-bromobutoxy)phenyl)-2-(4-nitrophenyl) diazene **16** was obtained as brick red solid from E-4-((4-nitrophenyl) diazenyl) benzene-1, 3-diol **11** (1.0 g, 3.86 mmol) and 1, 4- dibromobutane **26** (3.4 g, 15.74 mmol). Yield 69%; Mp: 104^{o}C; ^{1}H NMR: (300 MHz, $CDCl_3$): δ_H 1.95-2.2 (m, 8H); 3.51 (t, 2H, *J* = 6.6 Hz); 3.58 (t, 2H, *J* = 6 Hz); 4.09 (t, 2H, *J* = 5.1 Hz); 4.23 (t, 2H, *J* = 5.1 Hz); 6.54 (t, 2H, *J* = 8.4 Hz); 7.79 (d, 1H, *J* = 8.7 Hz); 7.96 (d, 2H, *J* = 8.7 Hz); 8.34 (d, 2H, *J* = 9 Hz). ^{13}C NMR: (75 MHz, $CDCl_3$): δ_C 27.6, 27.7, 29.3, 29.8, 33.2, 33.5, 67.4, 68.7, 100.5, 106.9, 118.3, 123.1, 124.7, 137.1, 147.9, 156.5, 159.3, 164.4. (ESI-MS) *m/z* 527[M^+]. Elemental Anal. Calcd for $C_{20}H_{23}Br_2N_3O_4$:C, 45.39; H, 4.38; N, 7.94%. Found: C, 45.34; H, 4.31; N, 7.86%.

E-1-(2,4-Bis(4-azidobutoxy)phenyl)-2-(4-nitrophenyl) diazene21:



Following the general procedure B, E-1-(2,4-bis(4-azidobutoxy)phenyl)-2-(4-nitrophenyl) diazene **21** was obtained as red solid from (E)-1-(2,4-bis(4-bromobutoxy)phenyl)-2-(4-nitrophenyl) diazene **16** (1.0 g, 1.90 mmol) and sodium azide (0.5 g, 7.59 mmol). Yield 77%; Mp 72^{o}C: ^{1}H NMR: (300 MHz, $CDCl_3$): δ_H 1.72-1.98 (m, 8H); 3.32 (t, 2H, *J* = 3 Hz); 3.36 (t, 2H, *J* = 6.6 Hz); 4.01 (t, 2H, *J* = 5.4 Hz); 4.14 (t, 2H, *J* = 5.7 Hz); 6.46 (d, 2H, *J* = 9 Hz); 7.72 (d, 1H, *J* = 8.7 Hz); 7.86 (d, 2H, *J* = 8.4 Hz); 8.26 (d, 2H, *J* = 8.7 Hz). ^{13}C NMR: (75 MHz, $CDCl_3$): δ_C 27.6, 27.7, 29.3, 29.8, 33.2, 33.5, 64.4, 68.8, 100.5, 106.9, 118.3, 123.1, 124.7, 137.0, 147.9, 156.5, 159.3, 164.4. (ESI-MS) *m/z* 453[M^+]. Elemental Anal. Calcd for $C_{20}H_{23}N_9O_4$: C, 52.97; H, 5.11; N, 27.80%. Found: C, 52.89; H, 5.16; N, 27.71%.

Methyl 3,5-bis(4-bromobutoxy) benzoate 17:

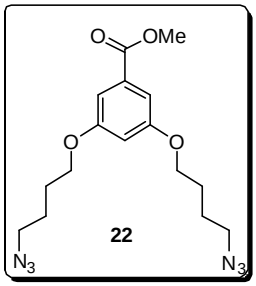


17

Following the general procedure A, methyl 3,5-bis(4-bromobutoxy)benzoate **17** was obtained as colourless viscous liquid from methyl 3,5-dihydroxy benzoate **12** (1.0 g, 5.95 mmol) and 1, 4-dibromobutane **26** (5.14 g, 23.81 mmol). Yield 79%: ^{1}H NMR: (300 MHz, $CDCl_3$): δ_H 1.87-2.01 (m, 8H); 3.40 (t, 4H, *J* = 4.5 Hz); 3.82 (s, 3H); 3.94 (t, 4H, *J* = 5.7 Hz); 6.54 (d, 1H, *J* = 2.1 Hz); 7.09 (s, 2H). ^{13}C NMR: (75 MHz, $CDCl_3$): δ_C 52.8,

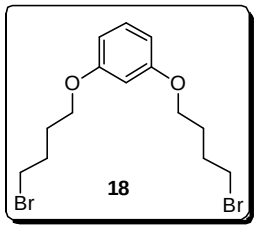
75.4, 76.6, 129.8, 133.5, 164.8. (ESI-MS) *m/z* 436 [M^+]. Elemental Anal. $C_{16}H_{22}Br_2O_4$ Calcd for: C, 43.86; H, 5.06%. Found: C, 43.78; H, 4.95%

Methyl 3,5-bis(4-azidobutoxy)benzoate 22:



Following the general procedure B, methyl 3,5-bis(4-azidobutoxy)benzoate **22** was obtained as colourless viscous liquid from methyl 3,5-bis(4-bromobutoxy)benzoate **17** (1.0 g, 2.30 mmol) and sodium azide (0.60 g, 9.23 mmol). Yield 79 %.^{1}H NMR: (300 MHz, $CDCl_3$): δ_H (300 MHz, $CDCl_3$): δ_H 1.70-1.81 (m, 8H); 3.27 (t, 4H, *J* = 6.6 Hz); 3.81 (s, 3H); 3.92(t, 4H, *J* = 5.7 Hz); 6.54 (t, 1H, *J* = 1.8 Hz); 7.08 (d, 2H, *J* = 2.4 Hz). ^{13}C NMR: (75 MHz, $CDCl_3$): δ_C 25.8, 26.5, 51.2, 67.2, 101.5, 106.8, 129.9, 160.1 (ESI-MS) *m/z* 362 [M^+]. Elemental Anal. Calcd for $C_{16}H_{22}N_6O_4$: C, 53.03; H, 6.12; N, 23.19%. Found: C, 52.93; H, 6.01; S, 23.09%.

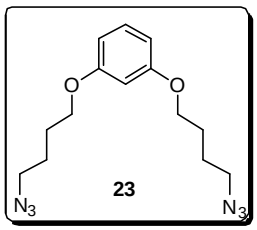
1,3-Bis(4-bromobutoxy)benzene 18:



Following the general procedure A, 1, 3-bis (4-bromobutoxy) benzene **18** was obtained as white solid from resorcinol **13** (1.0 g, 9.09 mmol) and 1,4-dibromobutane **26** (7.85 g,

36.36 mmol).Yield 72%; Mp. 88 ^{o}C: ^{1}H NMR: (300 MHz, $CDCl_3$): δ_H 1.89-1.97 (m, 4H); 2.02-2.11 (m, 4H); 3.49 (t, 4H, *J* = 6.6 Hz); 3.97 (t, 4H, *J* = 6 Hz); 6.64-6.50 (m, 3H); 7.16 (t, 1H, *J* = 8.1 Hz).^{13}C NMR: (75 MHz, $CDCl_3$): δ_C 27.9, 29.5, 33.4, 66.8, 101.5, 106.8, 129.9, 160.1. (ESI-MS) *m/z* 378 [M^+]. Elemental Anal. Calcd for $C_{14}H_{20}Br_2O_2$: C, 44.24; H, 5.30%. Found: C, 44.19; H, 5.39%.

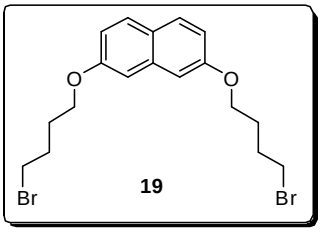
1,3-Bis(4-azidobutoxy)benzene 23:



23

Following the general procedure B, 1, 3-bis (4-azidobutoxy) benzene **23** was obtained as colourless viscous liquid from 1, 3-bis (4-bromobutoxy) benzene **18** (1 g, 2.64 mmol) and sodium azide (0.69 g, 10.58 mmol). Yield 71%. ^{1}H NMR: (300 MHz, $CDCl_3$): δ_H 1.76-1.88 (m, 8H); 3, 36 (t, 4H, *J* = 6.6 Hz); 3.96 (t, 4H, *J* = 5.4 Hz); 6.44-6.50 (m, 3H); 7.16 (t, 1H, *J* = 8.1 Hz). ^{13}C NMR: (75 MHz, $CDCl_3$): δ_C 25.8, 26.5, 51.2, 67.2, 101.5, 106.8, 129.9, 160.1. (ESI-MS) *m/z* 304 [M^+]. Elemental Anal. Calcd for $C_{14}H_{20}N_6O_2$: C, 55.25; H, 6.62; N, 27.61%. Found: C, 55.27; H, 6.55; N, 27.52%.

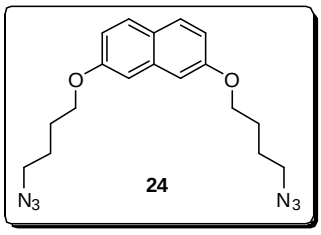
2,7-Bis(4-bromobutoxy)naphthalene 19:



19

Following the general procedure A, 2,7-bis(4-bromobutoxy)naphthalene **19** was obtained as white solid from naphthalene-2,7-diol **14** (1.0 g, 6.25 mmol) and 1,4-dibromobutane **26** (5.40 g, 25 mmol).Yield 78%; Mp. 106-111 ^{o}C: ^{1}H NMR: (300 MHz, $CDCl_3$): δ_H 1.85-2.02 (m, 8H); 3.41 (t, 4H, *J* = 6.3 Hz); 3.98 (t, 4H, *J* = 6 Hz); 6.86-6.93 (m, 4H); 7.55 (d, 2H, *J* = 8.7 Hz). ^{13}C NMR: (75 MHz, $CDCl_3$): δ_C 26.9, 28.5, 32.5, 65.8, 105.0, 115.1, 123.2, 128.1, 134.8, 156.4. (ESI-MS) *m/z* 428 [M^+]. Elemental Anal. Calcd for $C_{18}H_{22}Br_2O_2$: C, 50.26; H, 5.15%. Found: C, 50.18; H, 5.04%.

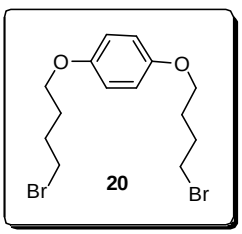
2,7-Bis(4-azidobutoxy)naphthalene 24:



24

Following the general procedure B, 2,7-bis(4-azidobutoxy)naphthalene **24** was obtained as white solid from 2,7-bis(4-bromobutoxy)naphthalene **19** (1.0 g, 2.33 mmol) and Sodium azide (0.61 g, 9.35 mmol). Yield 75 %; Mp.72 ^{o}C: ^{1}H NMR: (300 MHz, $CDCl_3$): δ_H 1.79-2.15 (m, 8H); 3.36 (t, 4H, *J* = 6.9 Hz); 4.06 (t, 4H, *J* = 5.7 Hz); 6.96-7.01(m, 4H); 7.64 (d, 2H, *J* = 8.7 Hz). ^{13}C NMR: (75 MHz, $CDCl_3$): δ_C 25.8, 26.5, 51.2, 67.1, 106.0, 116.3, 124.4, 129.2, 135.9, 157.5. (ESI-MS) *m/z* 354 [M^+]. Elemental Anal. Calcd for $C_{18}H_{22}N_6O_2$: C, 61.00; H, 6.26; N, 23.71%. Found: C, 60.85; H, 6.32; N, 23.64%.

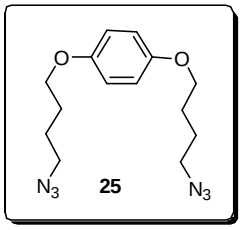
1, 4-Bis (4-bromobutoxy) benzene 20:



20

Following the general procedure A, 1, 4-bis (4-bromobutoxy) benzene **20** was obtained as crystalline white solid from the hydroquinone **15** (1.0 g, 9.09 mmol) and 1,4-dibromobutane **26** (7.85 g, 36.36 mmol).Yield 75%; Mp. 106-112 ^{o}C: ^{1}H NMR: (300 MHz, $CDCl_3$): δ_H 1.88-2.11 (m, 8H); 3.48 (t, 4H, *J* = 6.3 Hz); 3.93 (t, 4H, *J* = 6.3 Hz); 6.80 (t, 4H, *J* = 3.3 Hz). ^{13}C NMR: (75 MHz, $CDCl_3$): δ_C 28.0, 29.5, 33.5, 67.4, 115.4, 153.0. (ESI-MS) *m/z* 378 [M^+]. Elemental Anal. Calcd for $C_{14}H_{20}Br_2O_2$: C, 44.24; H, 5.30%. Found: C, 44.16; H, 5.36%.

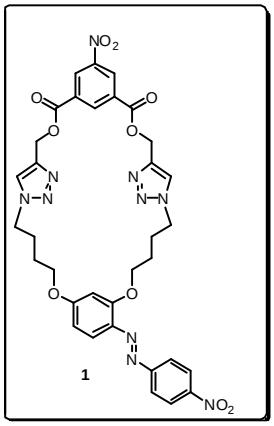
1,4-Bis(4-azidobutoxy)benzene 25:



25

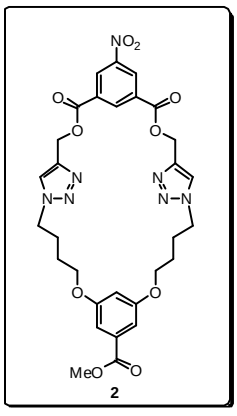
Following the general procedure B, 1,4-bis(4-azidobutoxy)benzene **25** was obtained as colourless oily liquid from 1, 4-bis (4-bromobutoxy) benzene **20** (1.0 g, 2.64 mmol) and sodium azide (0.69 g, 10.58 mmol). Yield 81 %.^{1}H NMR: (300 MHz, $CDCl_3$): δ_H 1.74-1.84 (m, 8H); 3.33 (t, 4H, *J* = 6.3 Hz); 3.90 (t, 4H, *J* = 5.4 Hz); 6.81 (s, 4H). ^{13}C NMR: (75 MHz, $CDCl_3$): δ_C 25.7, 26.6, 51.2, 67.8, 115.3, 153.0. (ESI-MS) *m/z* 304 [M^+]. Elemental Anal. Calcd for $C_{14}H_{20}N_6O_2$: C, 55.25; H, 6.62; N, 27.61%. Found: C, 55.17; H, 6.52; N, 27.54%

Triazolophane 1:



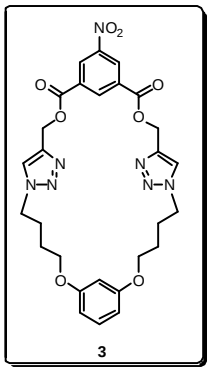
Triazolophane **1** was synthesized as red solid in 32% yield from (E)-1-(2,4-bis(4-azidobutoxy)phenyl)-2-(4-nitrophenyl) diazene **21** (0.35 g, 0.77 mmol, 1.1 equiv.) and diprop-2-ynyl 5-nitroisophthalate **27** (0.2 g, 0.69 mmol, 1 equiv.) by click reaction as per the procedure C, followed by purification from column using a mixture of $CHCl_3$-MeOH (9:2). Mp: 148 ^oC. ^1H NMR : (300 MHz, $CDCl_3$): δ_H 1.85 (s, 4H); 2.10 (s, 4H) ; 4.05 (d, 4H, *J* = 33.9 Hz); 4.43 (s, 4H); 5.49 (s, 4H); 6.44 (s, 2H); 7.66 (s, 2H); 7.86 (s, 3H); 7.28 (d, 2H, *J* = 6.3 Hz); 8.84 (s, 1H); 8.96 (s, 2H). ^{13}C NMR: (75 MHz, $CDCl_3$): δc 24.8, 26.4, 58.1, 66.5, 68.2, 100.6, 105.6, 117.4, 122.1, 123.2, 123.7, 127.7, 131.0, 134.9, 136.2, 141.4, 147.4, 155.3, 158.0, 162.7, 162.9. MS(ES1): m/z 741($M+H^+$). Elemental anal.calcd for $C_{34}H_{32}N_{10}O_{10}$: C, 55.13;H, 4.35 ;N, 18.91%.Found: C, 55.03;H, 4.42 ;N, 18.82%.

Triazolophane 2:



Triazolophane **2** was synthesized as yellow solid in 25% yield from methyl 3,5-bis(4-azidobutoxy)benzoate **22** (0.33 g, 0.82 mmol, 1.1 equiv.) and diprop-2-ynyl 5-nitroisophthalate **27** (0.24 g, 0.83 mmol, 1 equiv.) by click reaction as per the procedure C, followed by purification from column using a mixture of $CHCl_3$-MeOH (9:2). Mp: 189 ^oC. ^1H NMR : (300 MHz, $CDCl_3$): δ_H 1.76-1.82 (m, 4H); 2.00-2.10 (m, 4H) ; 3.82 (s, 3H); 3.96 (t, 4H, *J* = 5.4 Hz); 4.38 (t, 4H, *J* = 7.5 Hz); 5.50 (s, 4H); 6.51 (s, 1H); 7.07 (d, 2H, *J* = 2.1 Hz); 7.65 (s, 2H); 8.87 (s, 1H); 8.98 (s, 2H). ^{13}C NMR: (75 MHz, $CDCl_3$): δc 26.0, 27.7, 50.2, 52.3, 59.1, 67.4, 107.0, 107.9, 124.2, 128.7, 132.1, 132.2, 136.0, 142.2, 148.6, 159.5, 163.6, 166.9. MS(E1): m/z 649 [M^+]. Elemental anal.calcd for $C_{30}H_{31}N_7O_{10}$: C, 55.47 ; H, 4.81 ; N,15.09%.Found: : C, 55.53 ; H, 4.73 ; N,15.18%.

Triazolophane 3:

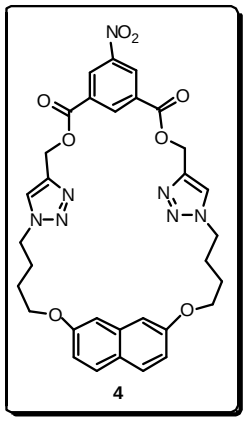


3

Triazolophane **3** was synthesized as white solid in 38% yield from 1, 3-bis (4-azidobutoxy) benzene **23** (0.28 g, 0.92 mmol, 1.1 equiv.) and diprop-2-ynyl 5-nitroisophthalate **27** (0.24 g, 0.83 mmol, 1 equiv.) by click reaction as per the procedure C, followed by purification from column using a mixture of $CHCl_3$-MeOH (9:2). Mp: 197 ^oC. ^1H NMR : (300 MHz, $CDCl_3$): δ_H 1.73-1.75 (m, 4H); 1.97-2.10 (m, 4H);

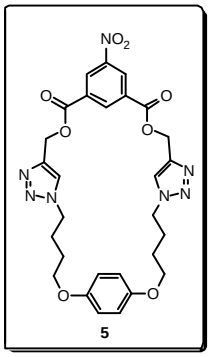
3.90 (t, 4H, *J* = 5.4Hz); 4.38 (t, 4H, *J* = 7.2 Hz); 5.50 (s, 4H); 6.32 (s, 1H); 6.38 (d, 2H, *J* = 8.1 Hz); 7.08 (t, 1H, *J* = 7.5Hz); 7.64 (s, 2H); 8.88 (s, 1H); 8.99 (s, 2H). ^{13}C NMR: (75 MHz, $CDCl_3$): δc 25.8, 27.5, 108.6, 111.7, 115.4, 115.6, 124.3, 132.1, 136.4, 142.2, 152.8, 163.5. MS(E1): m/z 591(M^+). Elemental anal.calcd for $C_{28}H_{29}N_7O_8$: C, 56.85 ; H, 4.94 ; N,16.57%.Found: C,56.78 ;H, 4.89 ;N,16.49%.

Triazolophane 4:



Triazolophane **4** was synthesized as pale yellow solid in 38% yield from 2,7-bis(4-azidobutoxy)naphthalene **24** (0.28 g, 0.92 mmol, 1.1 equiv.) and diprop-2-ynyl 5-nitroisophthalate **27** (0.24 g, 0.86 mmol, 1 equiv.) by click reaction as per the procedure C, followed by purification from column using a mixture of $CHCl_3$-MeOH (9:2). Mp: 253 ^{o}C. ^{1}H NMR : (300 MHz, $CDCl_3$): δ_H 1.89 (t, 4H, *J* = 5.7 Hz); 2.16 (t, 4H, *J* = 6.3 Hz); 4.04 (t, 4H, *J* = 5.1 Hz); 4.48 (t, 4H, *J* = 6.6 Hz); 5.48 (s, 4H); 6.92 (d, 4H, *J* = 9.3 Hz); 7.58 (d, 2H, *J* = 8.4 Hz); 7.73 (s, 2H); 8.86 (s, 1H); 8.94 (s, 2H). ^{13}C NMR: (75 MHz, $CDCl_3$): δc 25.5, 26.7, 49.9, 58.9, 66.7, 106.5, 115.8, 124.1, 124.2, 128.3, 128.9, 131.7, 135.4, 135.6, 142.0, 156.8, 163.4. MS(E1): *m/z* 641[M^+]. Elemental anal.calcd for $C_{32}H_{31}N_7O_8$: C, 59.90; H, 4.87 ; N,15.28%.Found: C, 59.83 ; H, 4.75 ; N,15.17%.

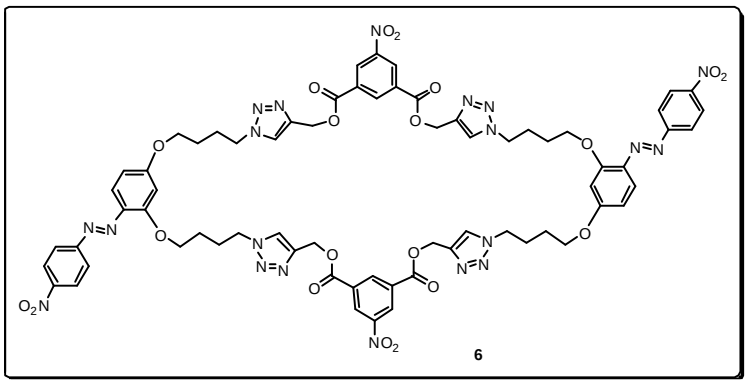
Triazolophane 5:



5

Triazolophane **5** was synthesized as yellow solid in 32% yield from (E)-1-(2,4-bis(4-azidobutoxy)phenyl)-2-(4-nitrophenyl) diazene **25** (0.28 g, 0.92 mmol, 1.1 equiv.) and diprop-2-ynyl 5-nitroisophthalate **27** (0.24 g, 0.86 mmol, 1 equiv.) by click reaction as per the procedure C, followed by purification from column using a mixture of $CHCl_3$-MeOH (9:1). Mp: 238 ^oC. ^1H NMR : (300 MHz, $CDCl_3$): δ_H 1.76-1.85 (m, 4H); 2.03-2.12 (m, 4H) ; 3.93 (t, 4H, *J* = 5.4 Hz); 4.42 (t, 4H, *J* = 7.2 Hz); 5.56 (s, 4H); 6.69 (s, 4H); 7.73 (s, 2H); 8.97 (s, 1H); 9.01(d, 2H, *J* = 14.1 Hz). ^{13}C NMR: (75 MHz, $CDCl_3$): δc 25.9, 27.6, 50.0, 59.3, 67.6, 115.4, 124.4, 128.6, 132.1, 136.2, 142.3, 148.4, 152.8, 163.6. MS(E1): m/z 591 [M^+]. Elemental anal.calcd for $C_{28}H_{29}N_7O_8$: C, 56.85 ; H, 4.94 ; N,16.57%. Found: C, 56.71 ; H, 5.02 ; N,16.66%.

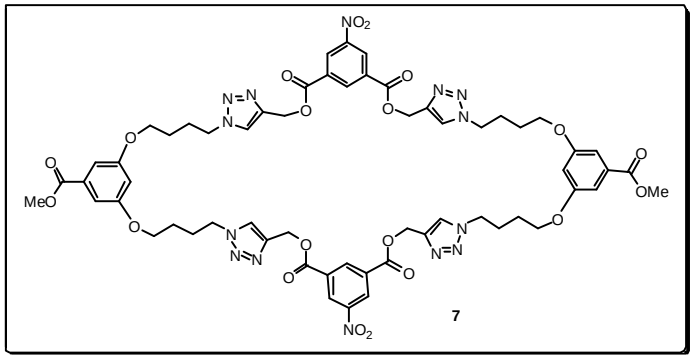
Triazolophane 6:



6

Triazolophane **6** was synthesized as red solid in 30% yield from (E)-1-(2,4-bis(4-azidobutoxy)phenyl)-2-(4-nitrophenyl) diazene **21** (0.35 g, 0.77 mmol, 1.1 equiv.) and diprop-2-ynyl 5-nitroisophthalate **27** (0.2 g, 0.69 mmol, 1 equiv.) by click reaction as per the procedure C, followed by purification from column using a mixture of $CHCl_3$-MeOH (9:2). Mp: 146 ^oC. ^1H NMR : (300 MHz, $CDCl_3$): δ_H 1.91-1.97 (m, 8H); 2.20-2.24 (m, 8H) ; 4.02 (t, 4H, *J* = 3.3 Hz); 4.16 (t, 4H, *J* = 6.6 Hz); 4,52 (d, 4H, *J* = 5.1 Hz); 4.56 (d, 4H, *J* = 7.2 Hz); 5.46 (d, 4H, *J* = 3.3 Hz); 5.53 (d, 4H, *J* = 7.5 Hz); 6.45 (t, 4H, *J* = 11.1 Hz); 7.60 (d, 1H, *J* = 9.6 Hz); 7.69 (d, 1H, *J* = 9 Hz); 7.74 (s, 1H); 7.78 (s, 4H); 7.85 (t, 3H, *J* = 7.8 Hz); 8.14 (d, 2H, *J* = 8.7 Hz); 8.84 (s, 2H); 8.93 (t, 4H, *J* = 21.6 Hz). ^{13}C NMR: (75 MHz, $CDCl_3$): δc 26.0, 27.0, 59.0, 67.4, 68.7, 100.4, 106.9, 118.4, 123.0, 124.5, 124.7, 128.4, 132.1, 135.8, 137.0, 148.0, 148.3, 156.3, 159.0, 163.4, 164.0. MS(E1): m/z 1480 [M^+]. Elemental anal.calcd for $C_{68}H_{64}N_{20}O_{20}$: C, 55.13;H, 4.35 ;N, 18.91%.Found: C, 55.01;H, 4.43 ;N, 18.78%.

Triazolophane 7:

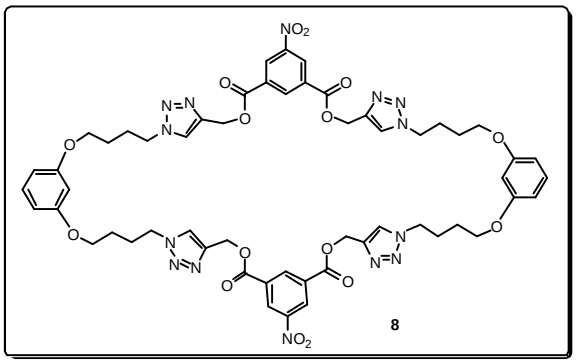


7

Triazolophane **7** was synthesized as pale yellow solid in 28% yield from methyl 3,5-bis(4-azidobutoxy)benzoate **22** (0.33 g, 0.82 mmol, 1.1 equiv.) and diprop-2-ynyl 5-nitroisophthalate **27** (0.24 g, 0.83 mmol, 1 equiv.) by click reaction as per the procedure

C, followed by purification from column using a mixture of $CHCl_3$-MeOH (9:2). Mp: 120 ^oC. ^1H NMR : (300 MHz, $CDCl_3$): δ_H 1.73-1.80 (m, 8H); 2.03-2.10 (m, 8H) ; 3.80 (s, 6H); 3.91 (t, 8H, *J* = 7.2 Hz); 4.41 (t, 8H, *J* = 7.2 Hz); 5.45 (s, 8H); 6.47 (s, 2H); 7.01 (d, 4H, *J* = 2.1 Hz); 7.71 (s, 4H); 8.34 (s, 2H); 8.89 (s, 4H). ^{13}C NMR: (75 MHz, $CDCl_3$): δc 26.2, 28.3, 49.1, 51.3, 58.1, 66.2, 105.5, 106.7, 123.2, 127.5, 131.0, 131.2, 134.9, 141.0, 147.3, 158.7, 162.5, 165.6. MS(E1): m/z 1298(M^+). Elemental anal.calcd for $C_{60}H_{62}N_{14}O_{20}$: C, 55.47 ; H, 4.81 ; N,15.09%.Found: : C, 55.39 ; H, 4.74 ; N,14.97%.

Triazolophane 8:

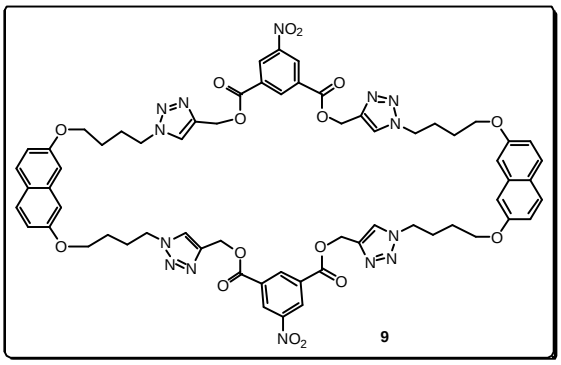


8

Triazolophane **8** was synthesized as white solid in 30% yield from 1, 3-bis (4-azidobutoxy)benzene **23** (0.28 g, 0.92 mmol, 1.1 equiv.) and diprop-2-ynyl 5-nitroisophthalate **27** (0.24 g, 0.83 mmol, 1 equiv.) by click reaction as per the procedure C, followed by purification from column using a mixture of $CHCl_3$-MeOH (9:2). Mp: 164 ^oC. ^1H NMR : (300 MHz, $CDCl_3$): δ_H 1.56 (t, 8H, *J* = 7.8 Hz); 1.73 (t, 8H, *J* = 6.9 Hz); 3.87 (t, 8H, *J* = 5.7 Hz); 4.40 (t, 8H, *J* = 6.9 Hz); 5.48 (d, 8H, *J* = 6.9 Hz); 6.28-6.36 (m, 6H); 7.03 (t, 2H, *J* = 8.4 Hz); 7.69 (s, 4H); 8.85 (s, 2H); 8.93 (d, 4H, *J* = 10.5 Hz). ^{13}C NMR: (75 MHz, $CDCl_3$): δc 26.2, 28.3, 49.1, 58.1, 65.8, 100.5, 105.7, 113.1, 123.2,

127.5, 129.0, 131.2, 134.9, 138.2, 140.9, 147.4, 158.9, 162.6. MS(E1): m/z 1182(M^+). Elemental anal.calcd for $C_{56}H_{58}N_{14}O_{16}$: C, 56.85 ; H, 4.94 ; N,16.57 %. Found: C,59.73 ;H, 5.05 ;N,16.56%.

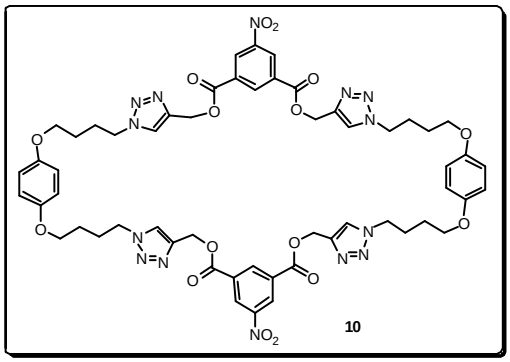
Triazolophane 9:



9

Triazolophane **9** was synthesized as pale yellow solid in 25% yield from 2,7-bis(4-azidobutoxy)naphthalene **24** (0.28 g, 0.92 mmol, 1.1 equiv.) and diprop-2-ynyl 5-nitroisophthalate **27** (0.24 g, 0.86 mmol, 1 equiv.) by click reaction as per the procedure C, followed by purification from column using a mixture of $CHCl_3$-MeOH (9:2) Mp: 142 ^oC. ^1H NMR : (300 MHz, $CDCl_3$): δ_H 1.80 (t, 8H, *J* = 5.5 Hz); 2.11 (t, 8H, *J* = 6.2 Hz); 4.00 (t, 8H, *J* = 5.5 Hz); 4.41 (t, 8H, *J* = 6.3 Hz); 5.47 (s, 8H); 6.93 (d, 8H, *J* = 9.2 Hz); 7.57 (d, 4H, *J* = 8.1 Hz); 7.72 (s, 4H); 8.87 (s, 2H); 8.96 (s, 4H). ^{13}C NMR: (75 MHz, $CDCl_3$): δc 25.5, 26.7, 49.9, 58.9, 66.7, 106.5, 115.8, 124.1, 124.2, 128.3, 128.9, 131.7, 135.4, 135.6, 142.0, 156.8, 163.4. MS(E1): m/z 1282 (M^+). Elemental anal.calcd for $C_{64}H_{62}N_{14}O_{16}$: C, 59.90 ; H, 4.87 ; N,15.28%.Found: C, 59.81 ; H, 4.95 ; N,15.13%.

Triazolophane 10:



10

Triazolophane **10** was synthesized as yellow solid in 33% yield from (E)-1-(2,4-bis(4-azidobutoxy)phenyl)-2-(4-nitrophenyl) diazene **25** (0.28 g, 0.92 mmol, 1.1 equiv.) and diprop-2-ynyl 5-nitroisophthalate **27** (0.24 g, 0.86 mmol, 1 equiv.) by click reaction as per the procedure C, followed by purification from column using a mixture of $CHCl_3$-MeOH (9:2). Mp: 122 ^oC. ^1H NMR : (300 MHz, $CDCl_3$): δ_H 1.80 (s, 8H); 2.04-2.14 (m, 8H) ; 3.92 (t, 8H, *J* = 5.1 Hz); 4.47 (t, 8H, *J* = 7.2 Hz); 5.54 (d, 8H, *J* = 7.5 Hz); 6.75 (d, 8H, *J* = 7.8 Hz); 7.78 (s, 4H); 8.94 (d, 2H, *J* = 4.5 Hz); 9.01 (d, 4H, *J* = 14.1 Hz). ^{13}C NMR: (75 MHz, $CDCl_3$): δc26.3, 27.2, 50.2, 59.1, 67.4, 115.3, 124.3, 128.5, 132.2, 136.0, 141.8, 148.3, 152.9, 163.6. MS(E1): m/z 1182 (M^+). Elemental anal.calcd for $C_{56}H_{58}N_{14}O_{16}$: C, 56.85 ; H, 4.94 ; N,16.57%.Found: C,56.76 ;H, 4.83 ;N,16.61%.

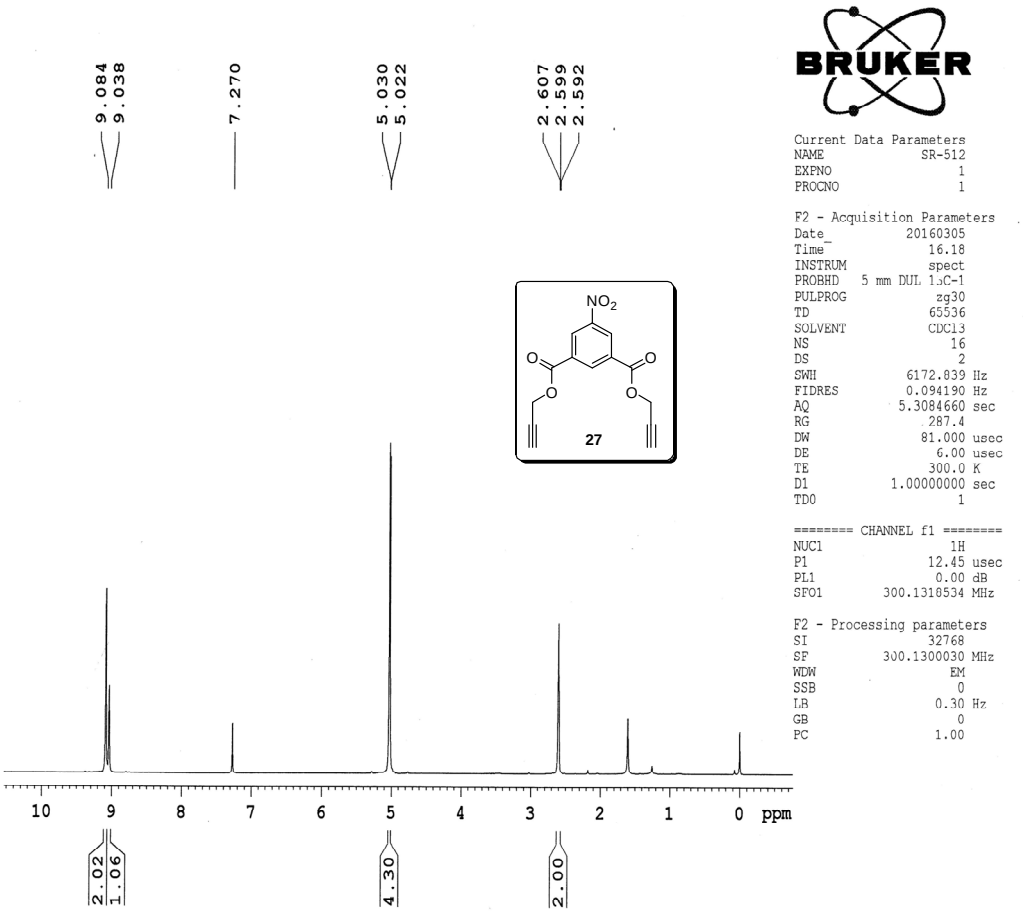


Figure 1: ^{1}H NMR spectrum (300MHz, $CDCl_3$) of diprop-2-ynyl 5-nitroisophthalate 27

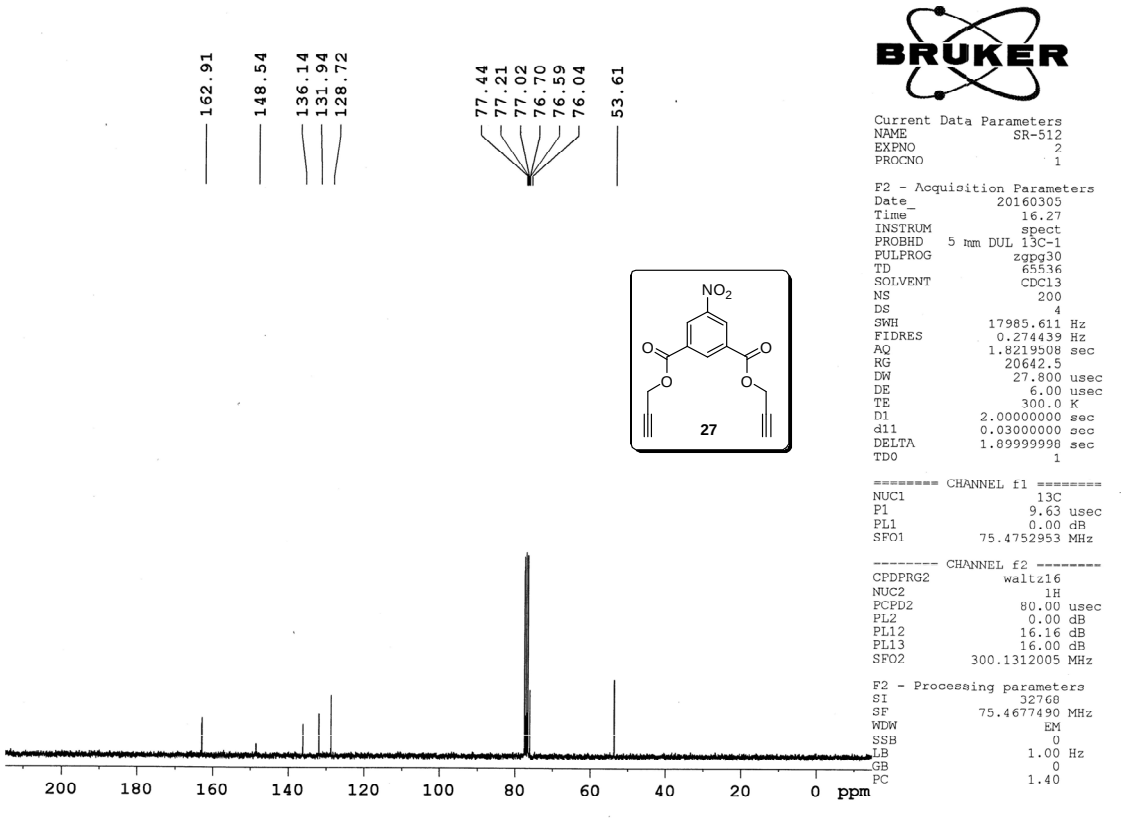


Figure 2: ^{13}C NMR spectrum (75MHz, $CDCl_3$) of diprop-2-ynyl 5-nitroisophthalate 27

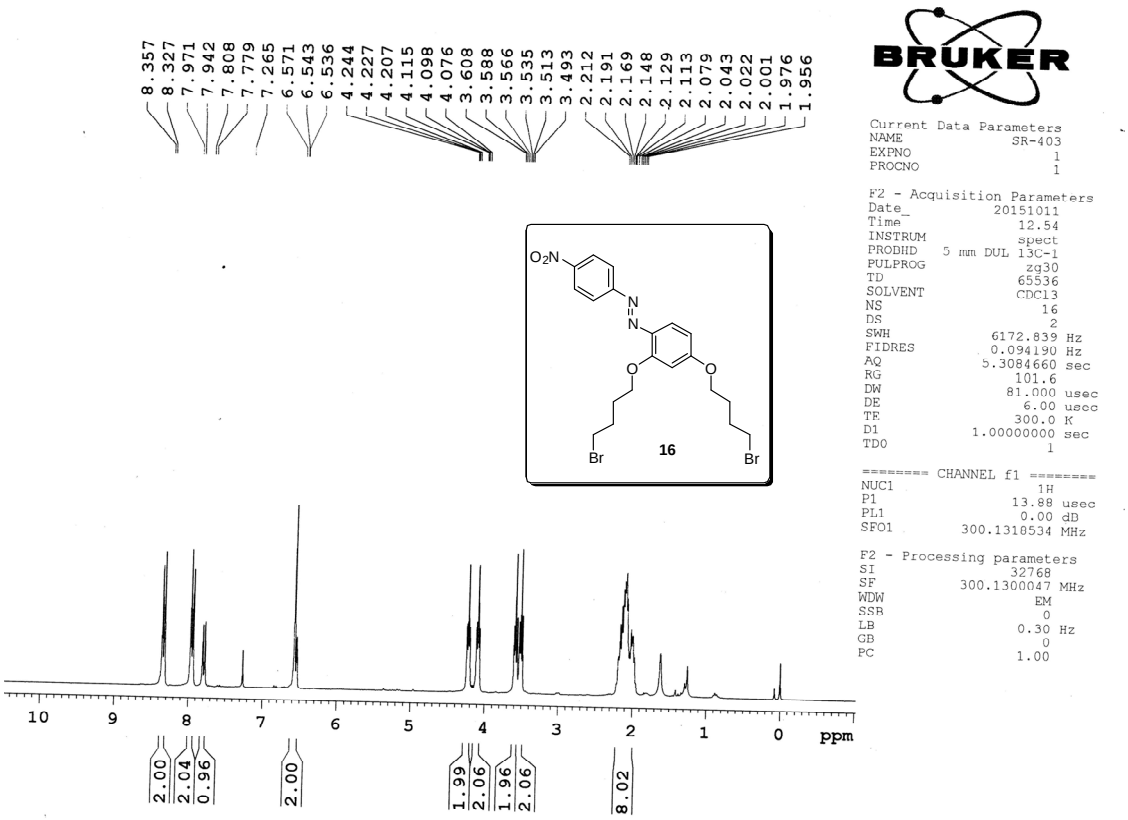


Figure 3: ^{1}H NMR spectrum (300MHz, $CDCl_3$) of (E)-1-(2,4-bis(4-bromobutoxy)phenyl)-2-(4-nitrophenyl)diazene 16

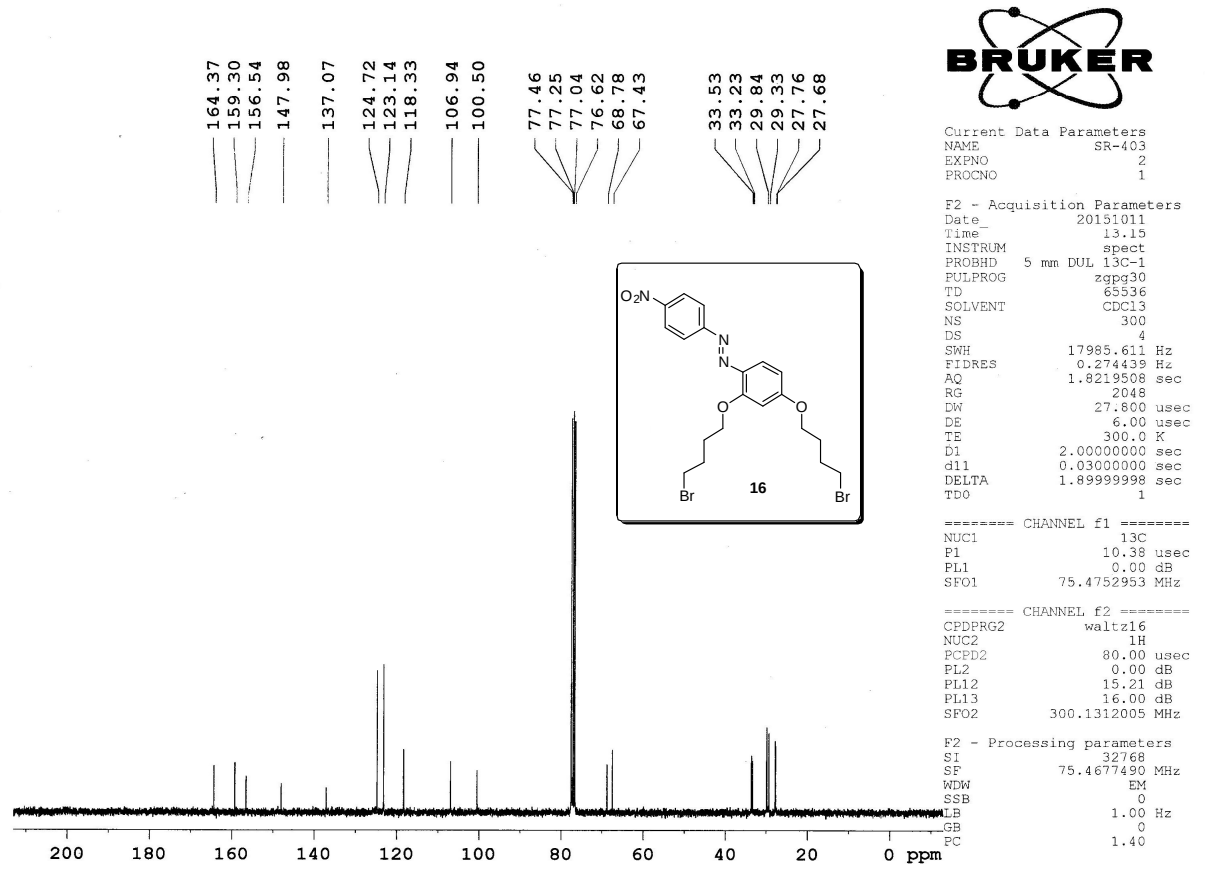


Figure 4: ^{13}C NMR spectrum (75MHz, $CDCl_3$) of (E)-1-(2,4-bis(4-bromobutoxy)phenyl)-2-(4-nitrophenyl)diazene 16

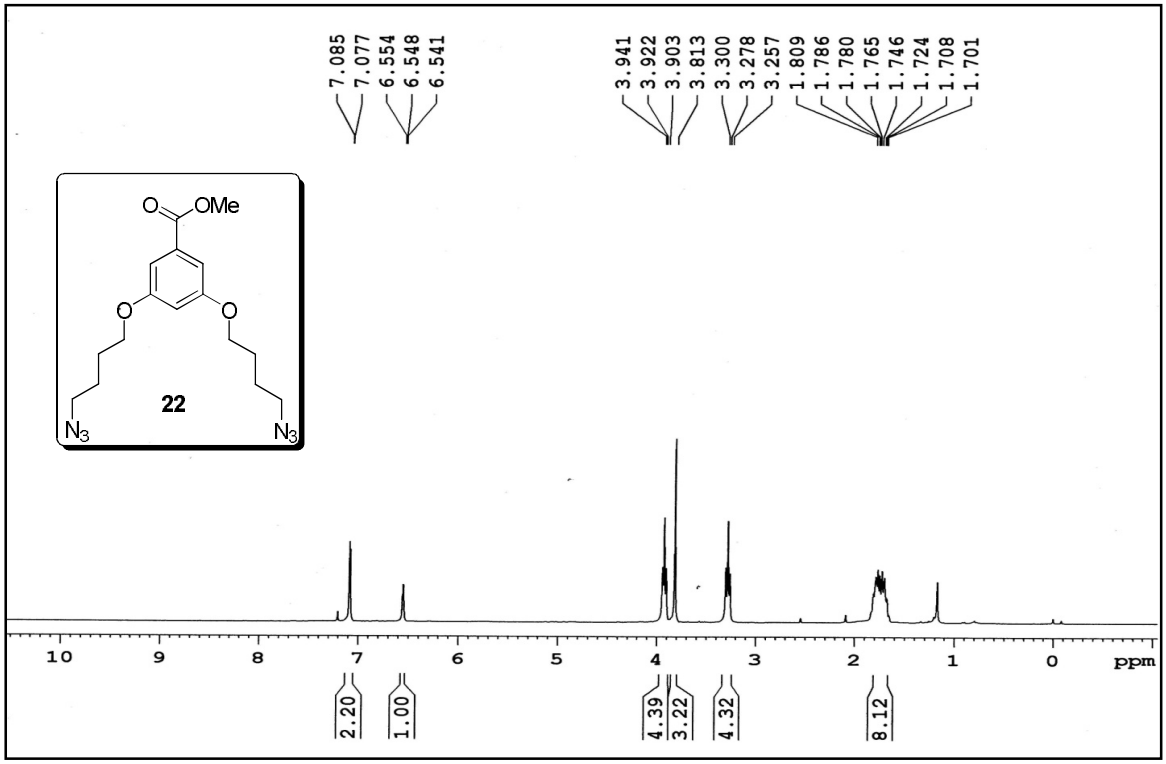


Figure 5: ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of Methyl 3,5-bis(4-azidobutoxy)benzoate 22

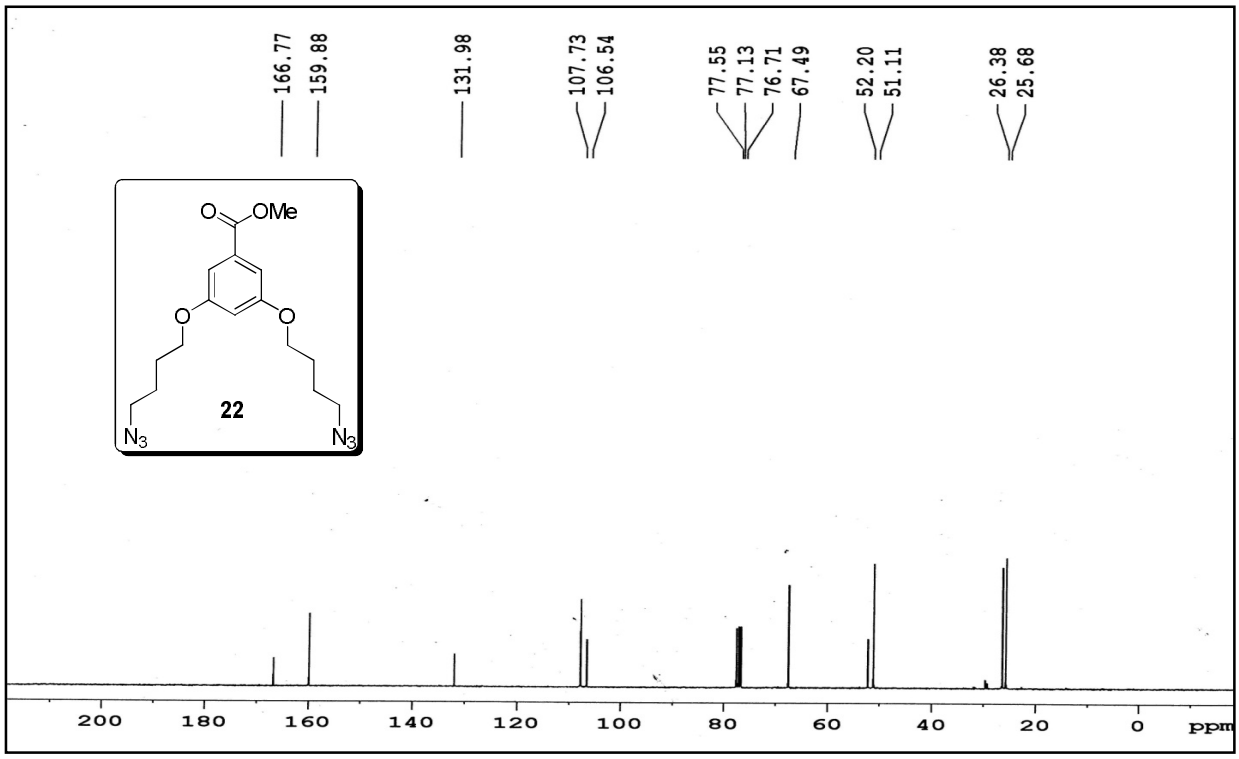


Figure 6: ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of Methyl 3, 5-bis(4-azidobutoxy)benzoate 22

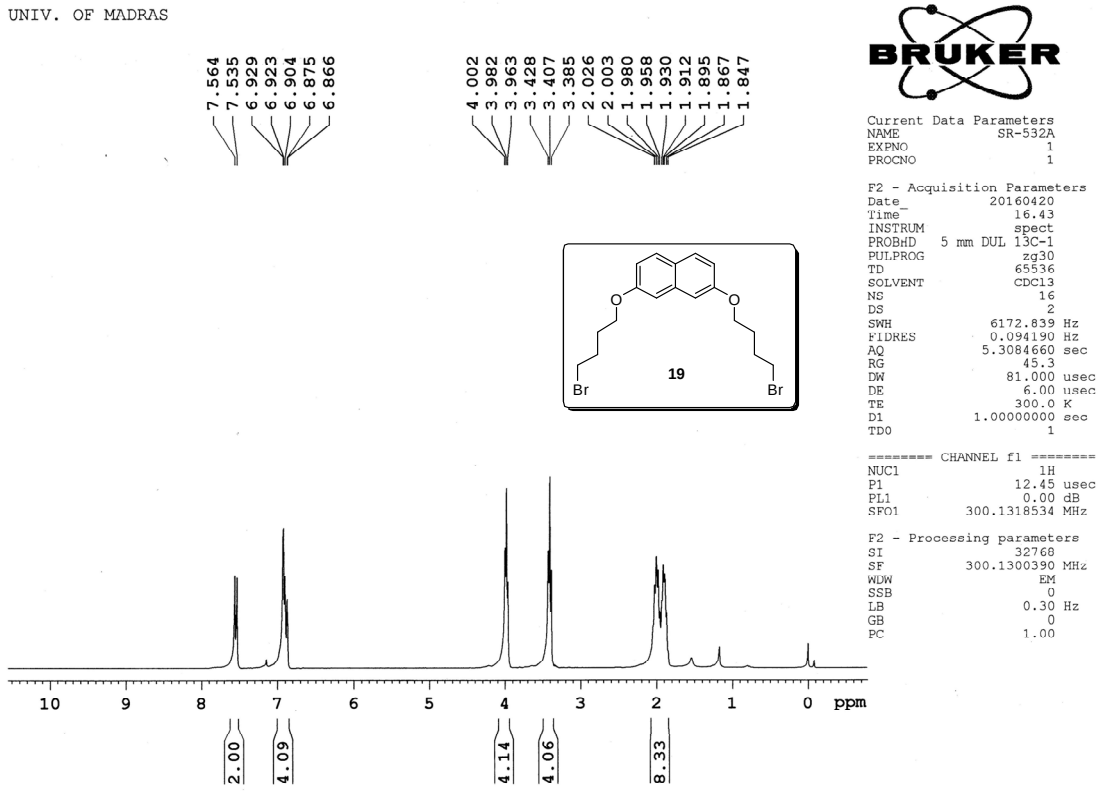


Figure 7:^{1}H NMR spectrum (300MHz, $CDCl_3$) of 2,7-bis(4-bromobutoxy)naphthalene 19

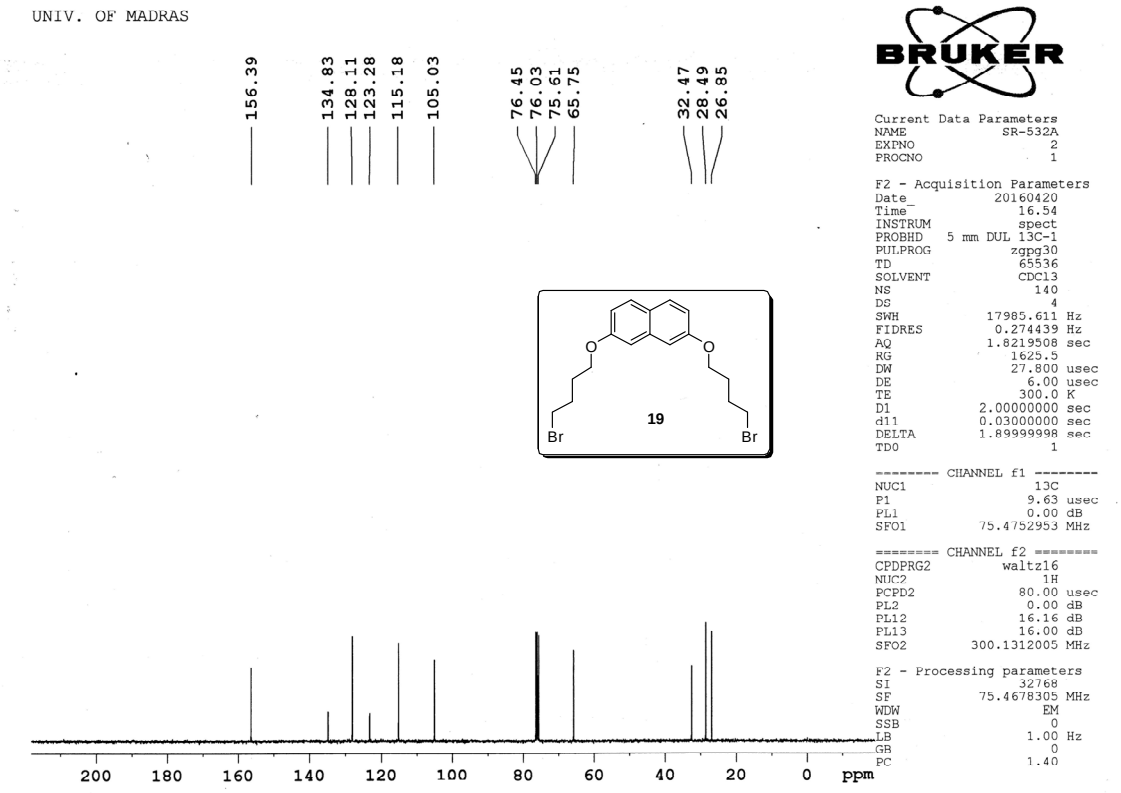


Figure 8: ^{13}C NMR spectrum (75MHz, $CDCl_3$) of 2,7-bis(4-bromobutoxy)naphthalene 19

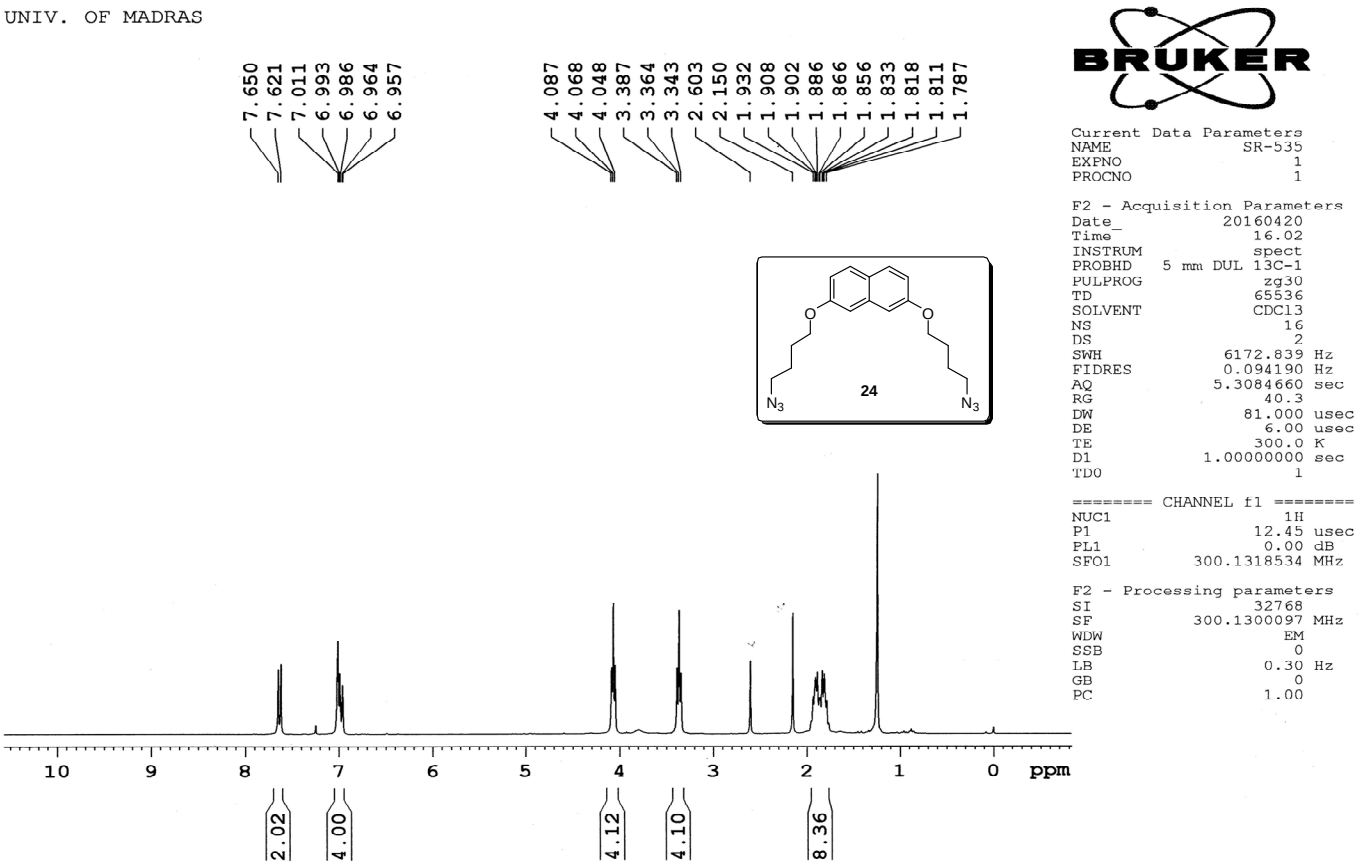


Figure 9: ^{1}H NMR spectrum (300MHz, $CDCl_3$) of 2,7-bis(4-azidobutoxy)naphthalene 24

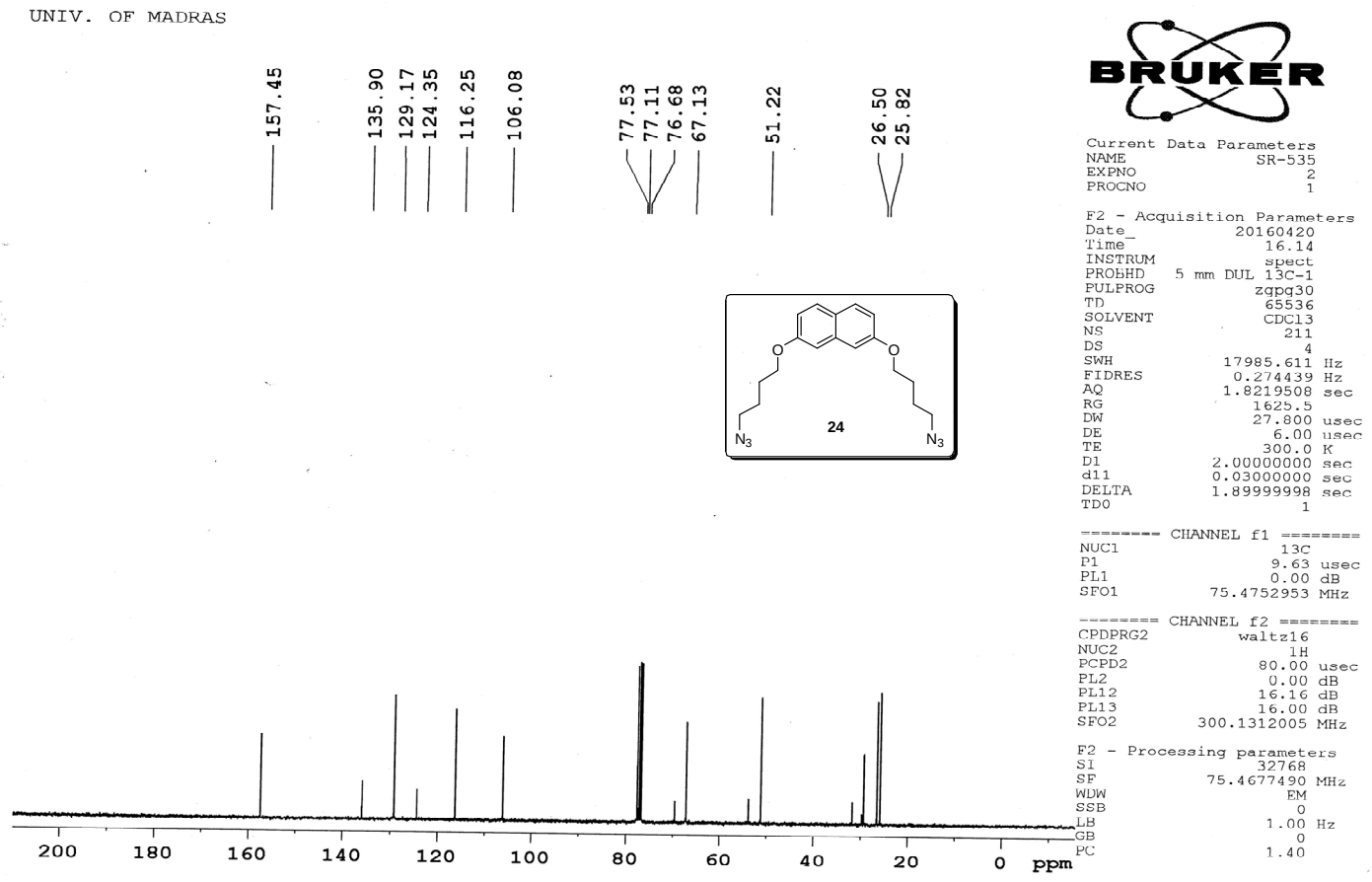


Figure 10: ^{13}C NMR spectrum (75MHz, $CDCl_3$) of 2,7-bis(4-azidobutoxy)naphthalene 24

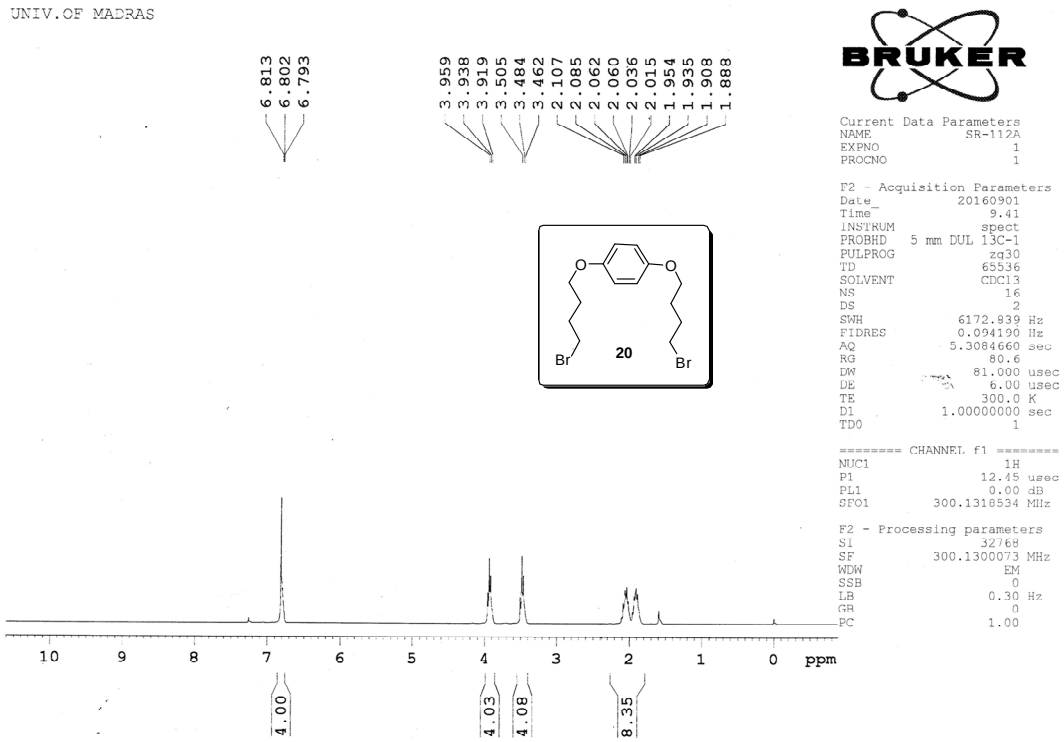


Figure 11: ^{1}H NMR spectrum (300MHz, $CDCl_3$) of 1, 4-bis (4-bromobutoxy) benzene 20

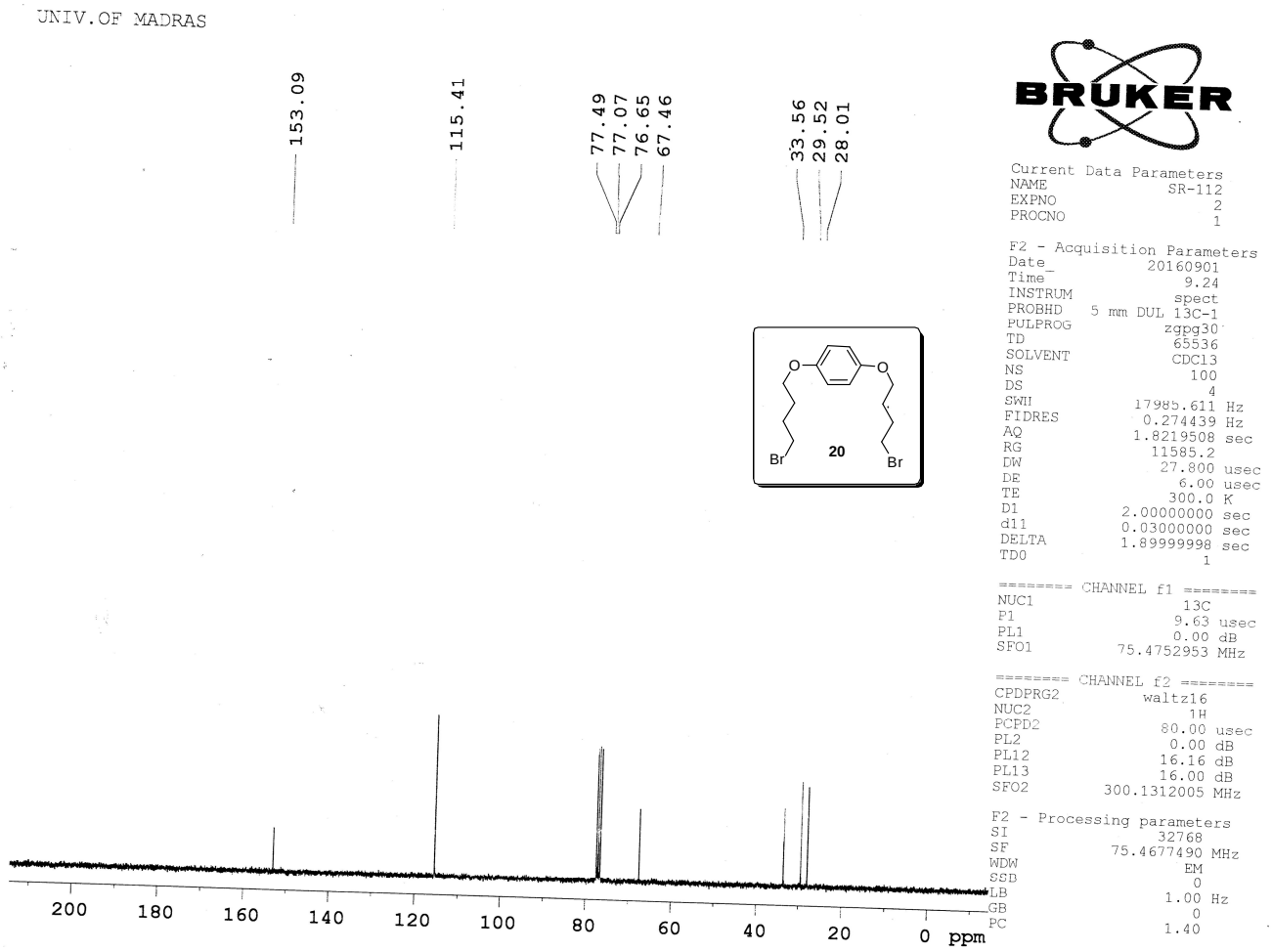


Figure 12: ^{13}C NMR spectrum (75MHz, $CDCl_3$) of 1, 4-bis (4-bromobutoxy) benzene 20

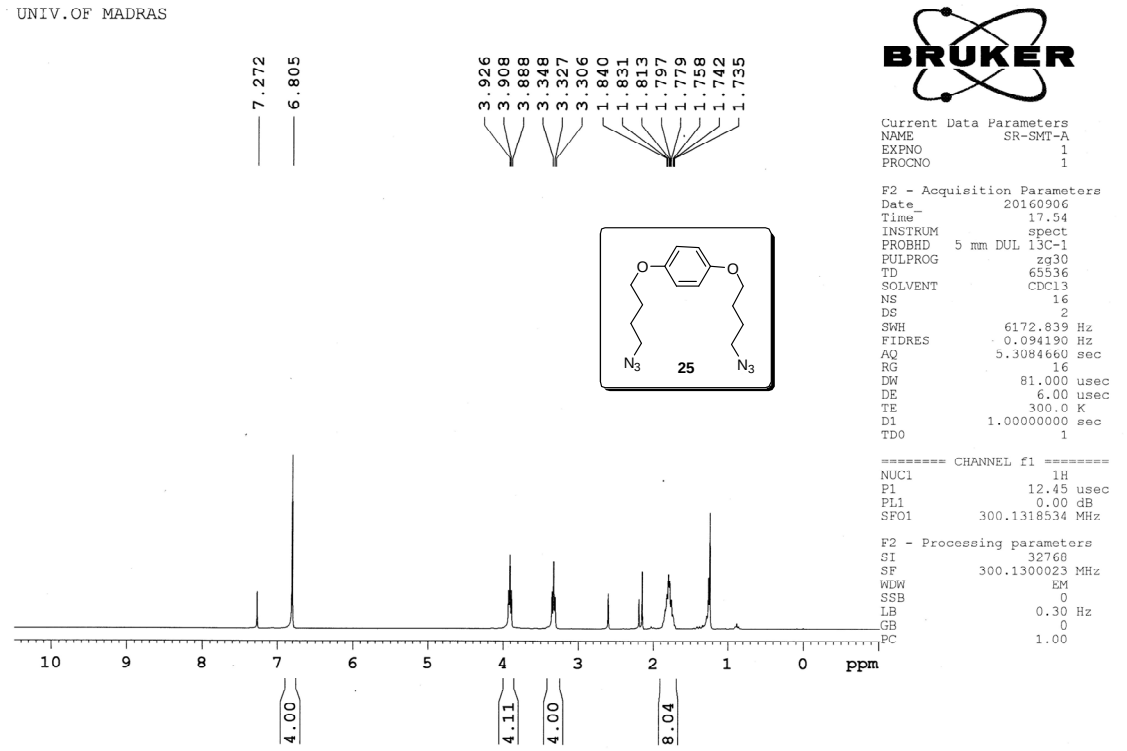


Figure 13: ^{1}H NMR spectrum (300MHz, $CDCl_3$) of 1,4-bis(4-azidobutoxy)benzene 25

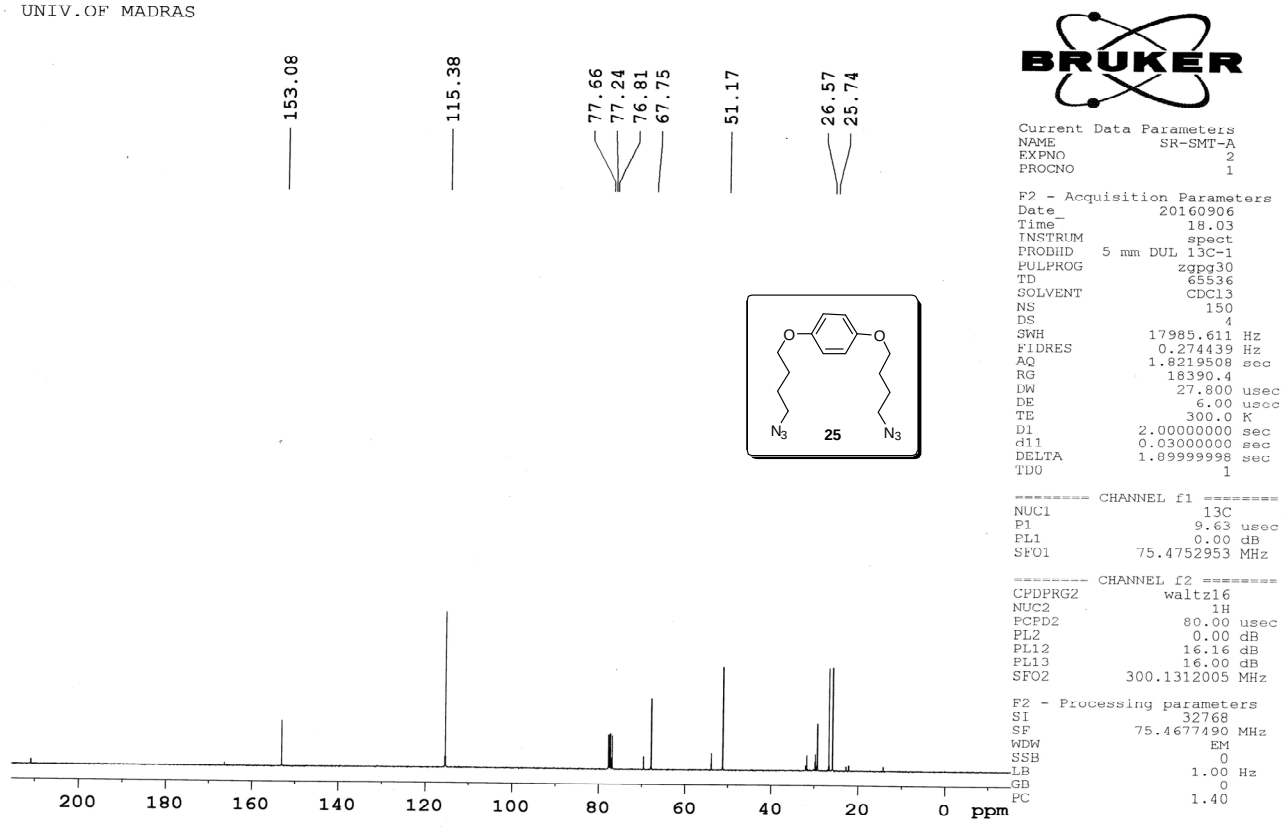


Figure 14: ^{13}C NMR spectrum (75MHz, $CDCl_3$) of 1,4-bis(4-azidobutoxy)benzene 25

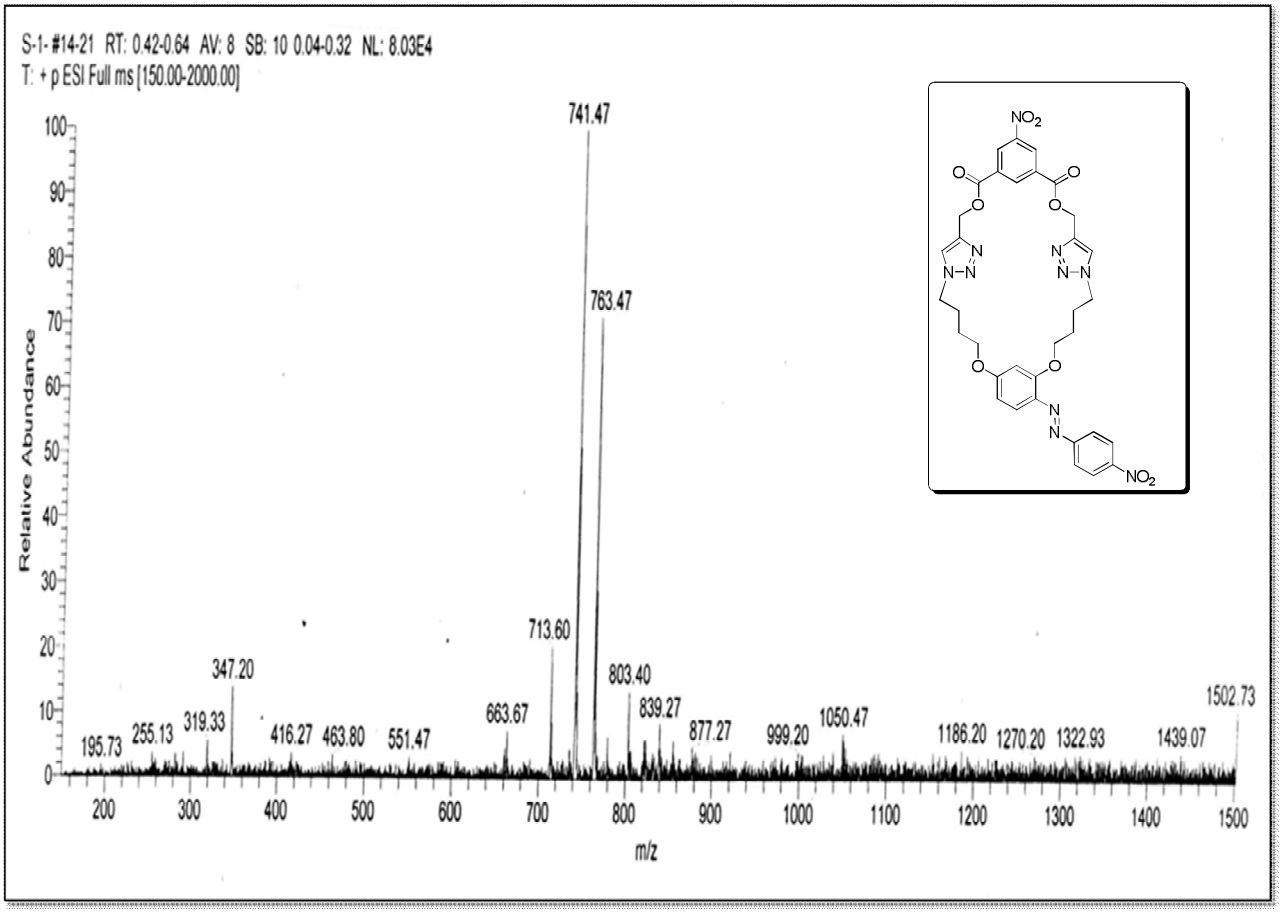


Figure 15: ESI mass spectrum of Triazolophane 1

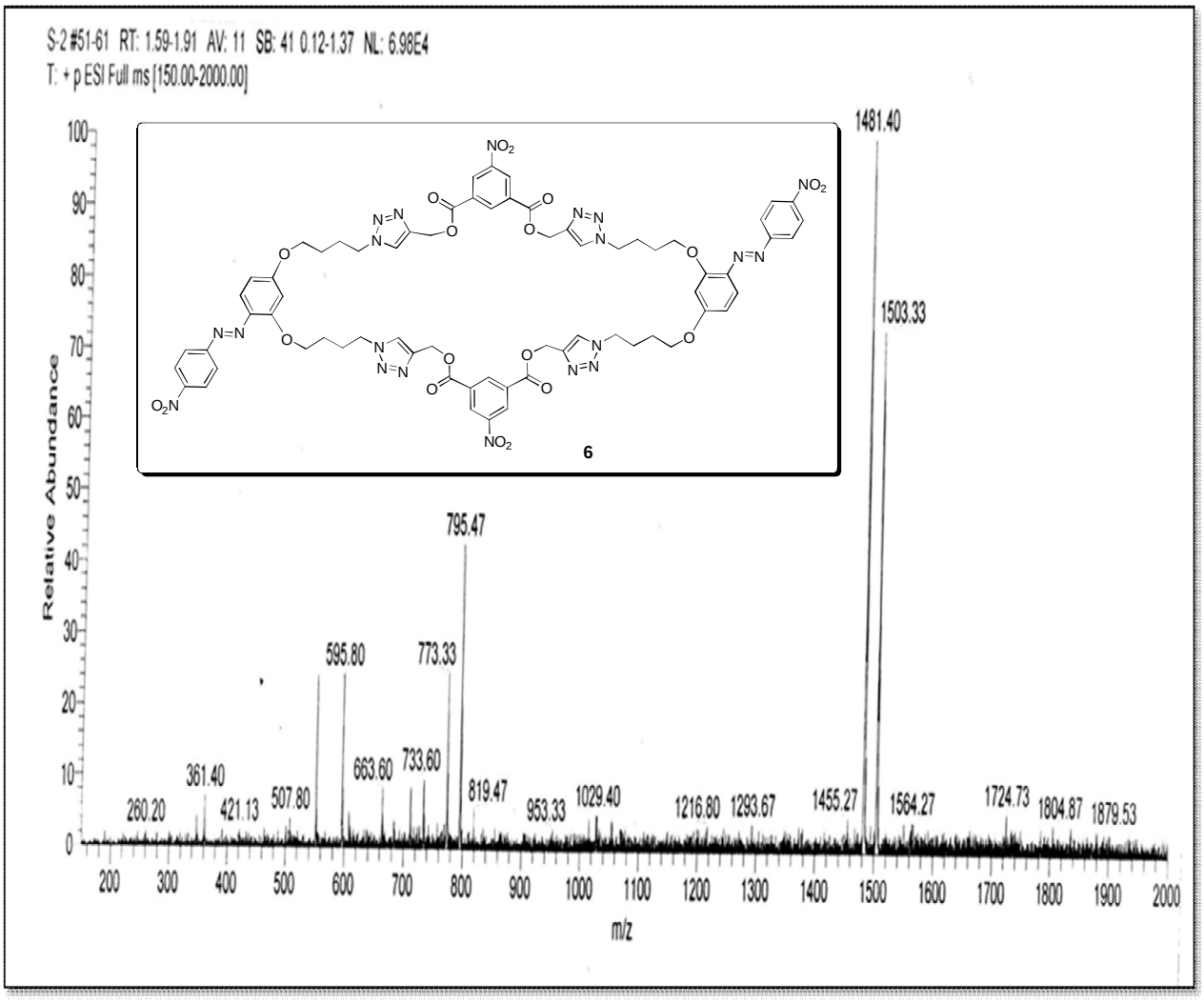


Figure 16: ESI mass spectrum of Triazolophane 6

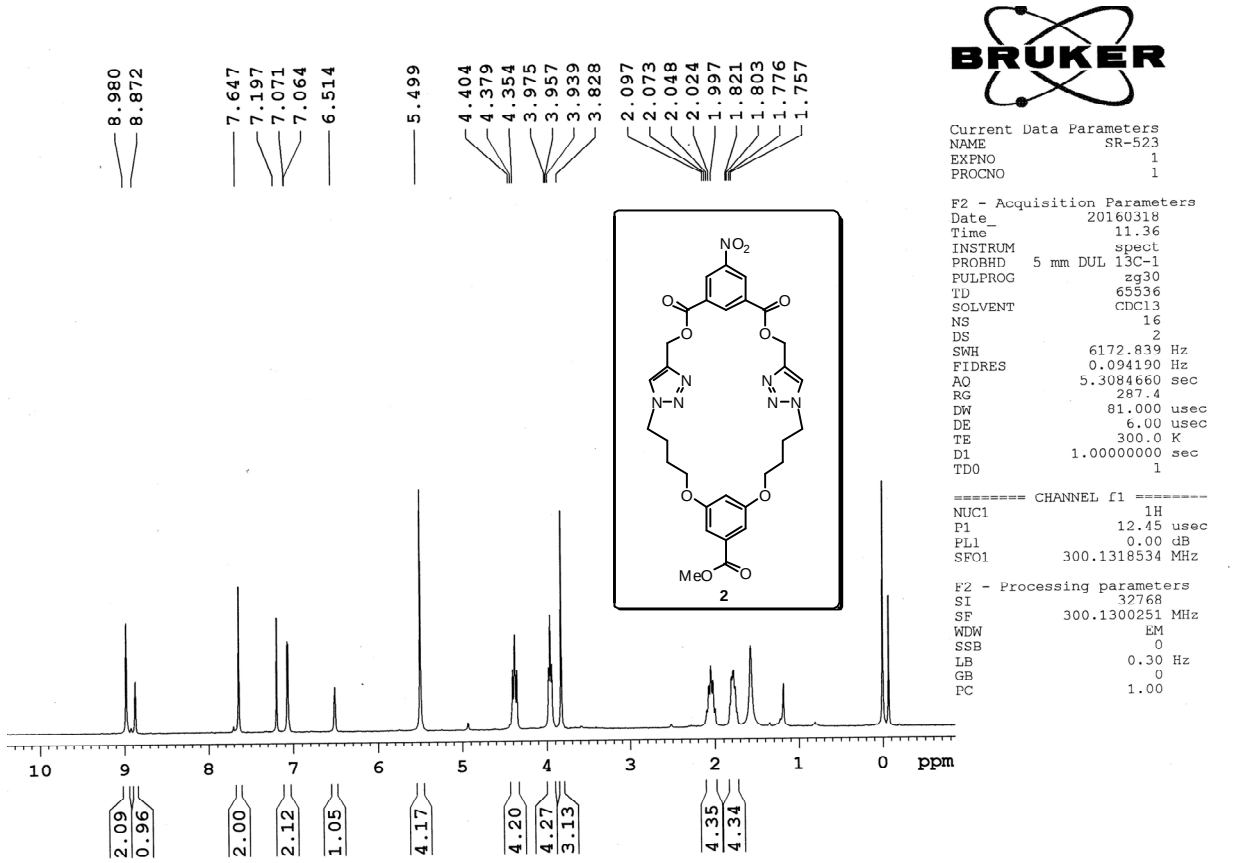


Figure 17: ^{1}H NMR spectrum (300MHz, $CDCl_3$) of Triazolophane 2

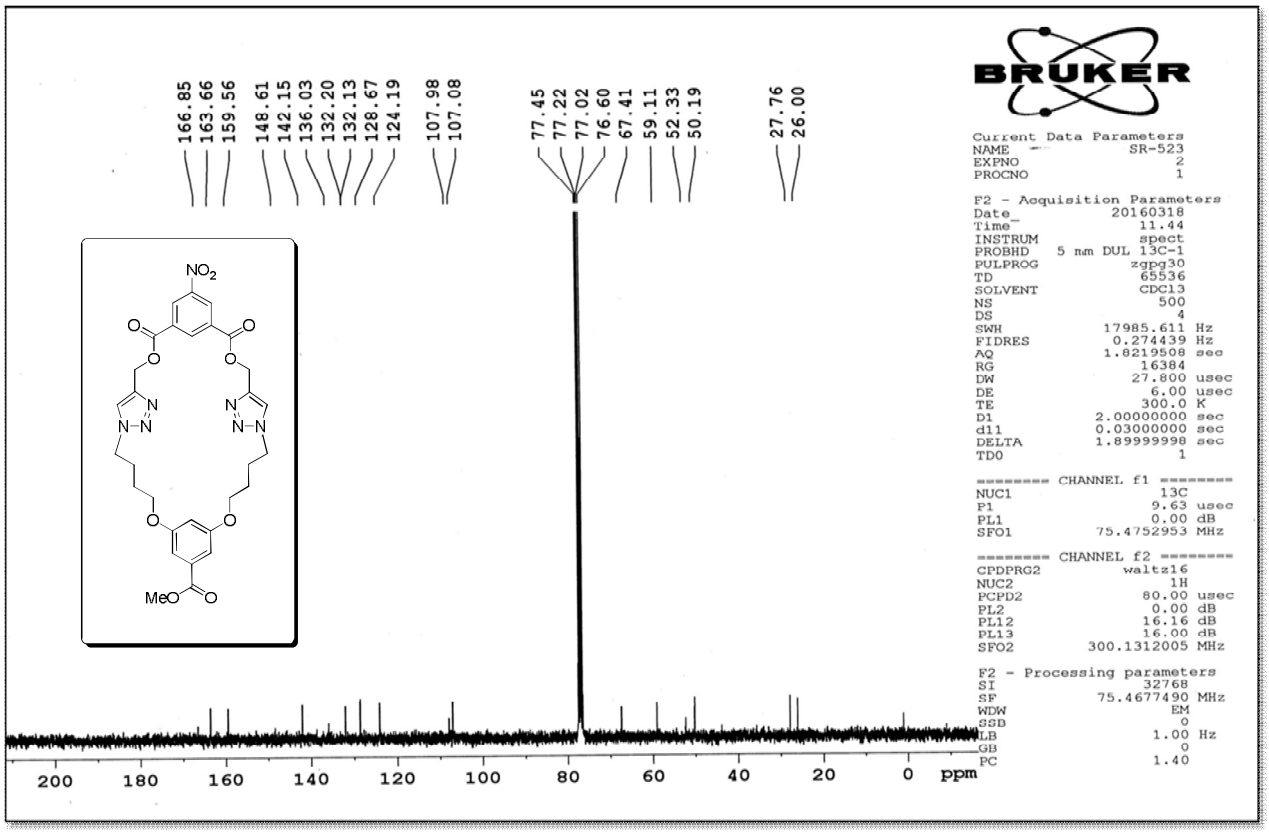


Figure 18: ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of Triazolophane 2

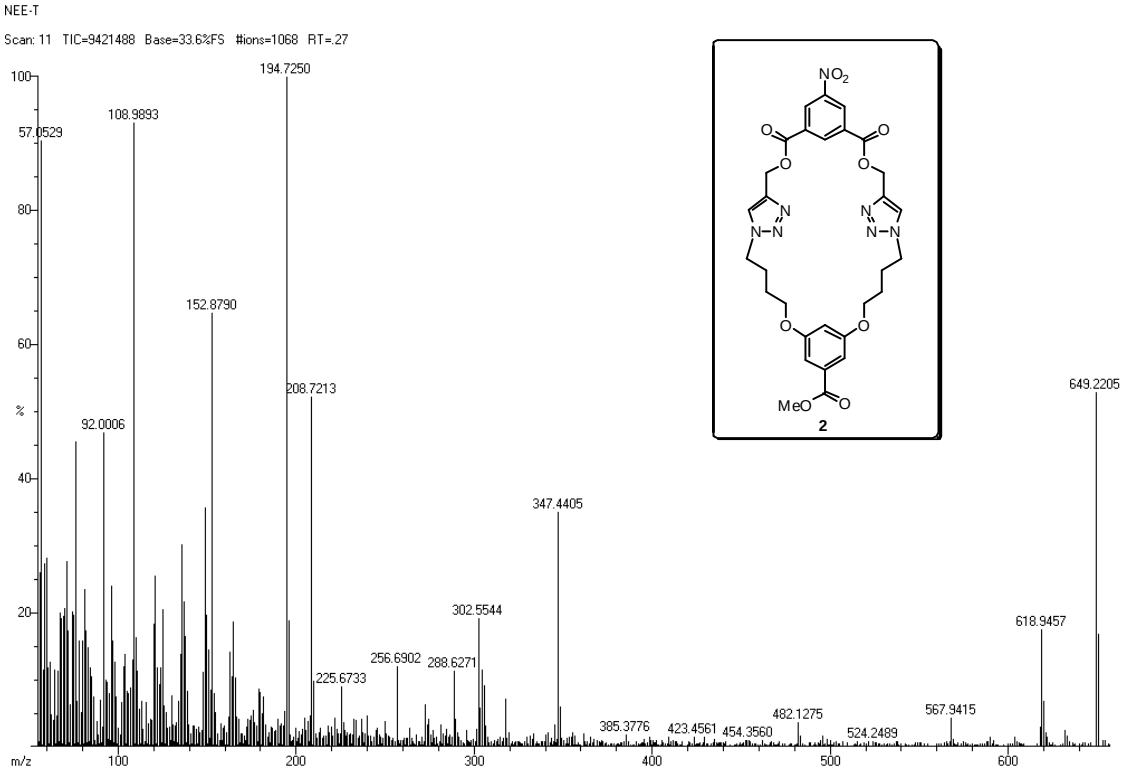


Figure 19: Mass spectrum (EI) of Triazolophane 2

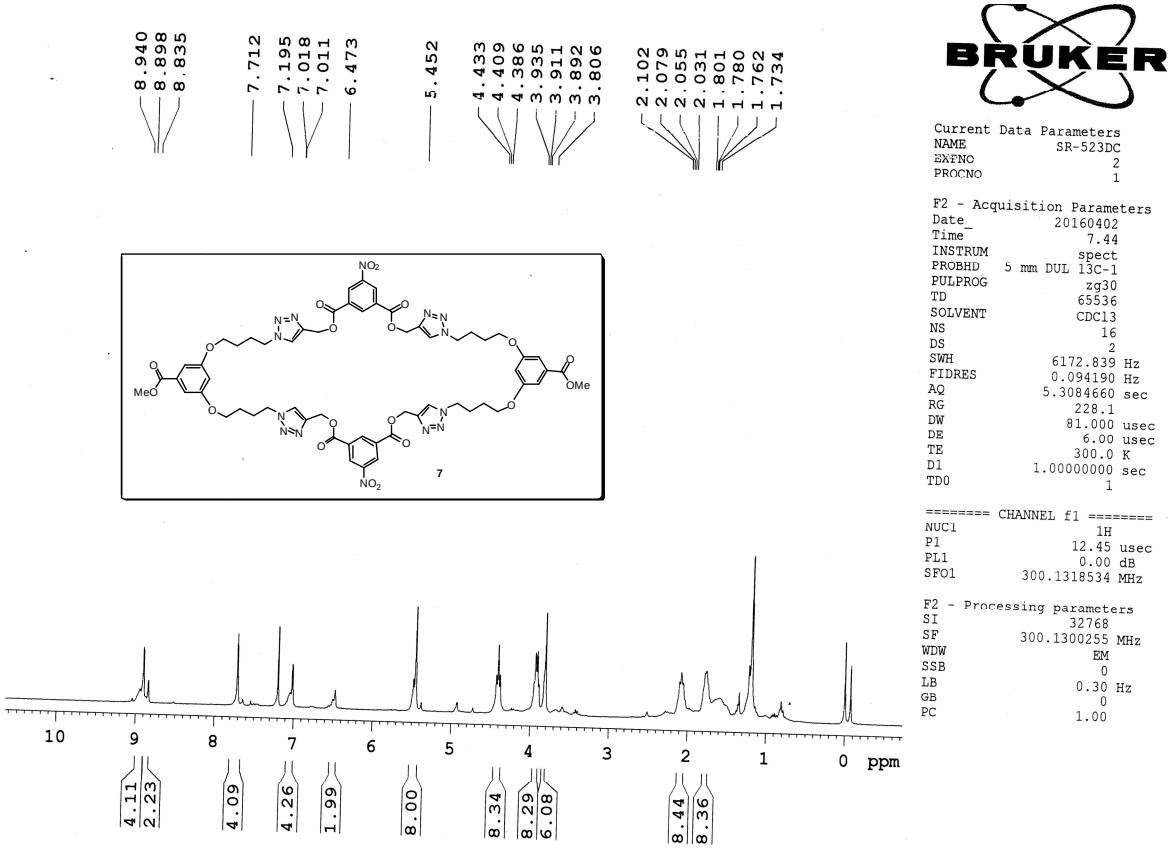


Figure 20: ^{1}H NMR spectrum (300MHz, $CDCl_3$) of Triazolophane 7

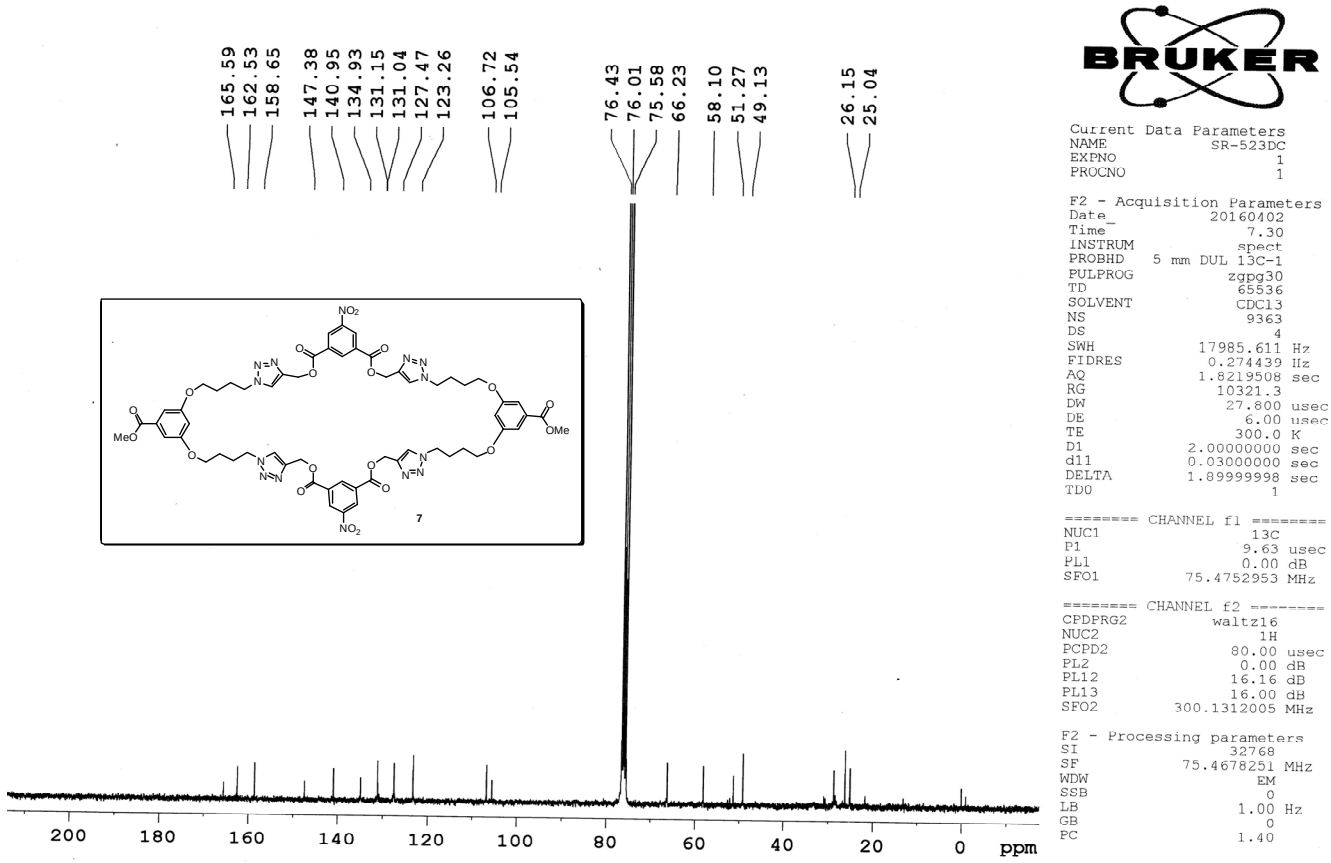


Figure 21: ^{13}C NMR spectrum (75MHz, $CDCl_3$) of Triazolophane 7

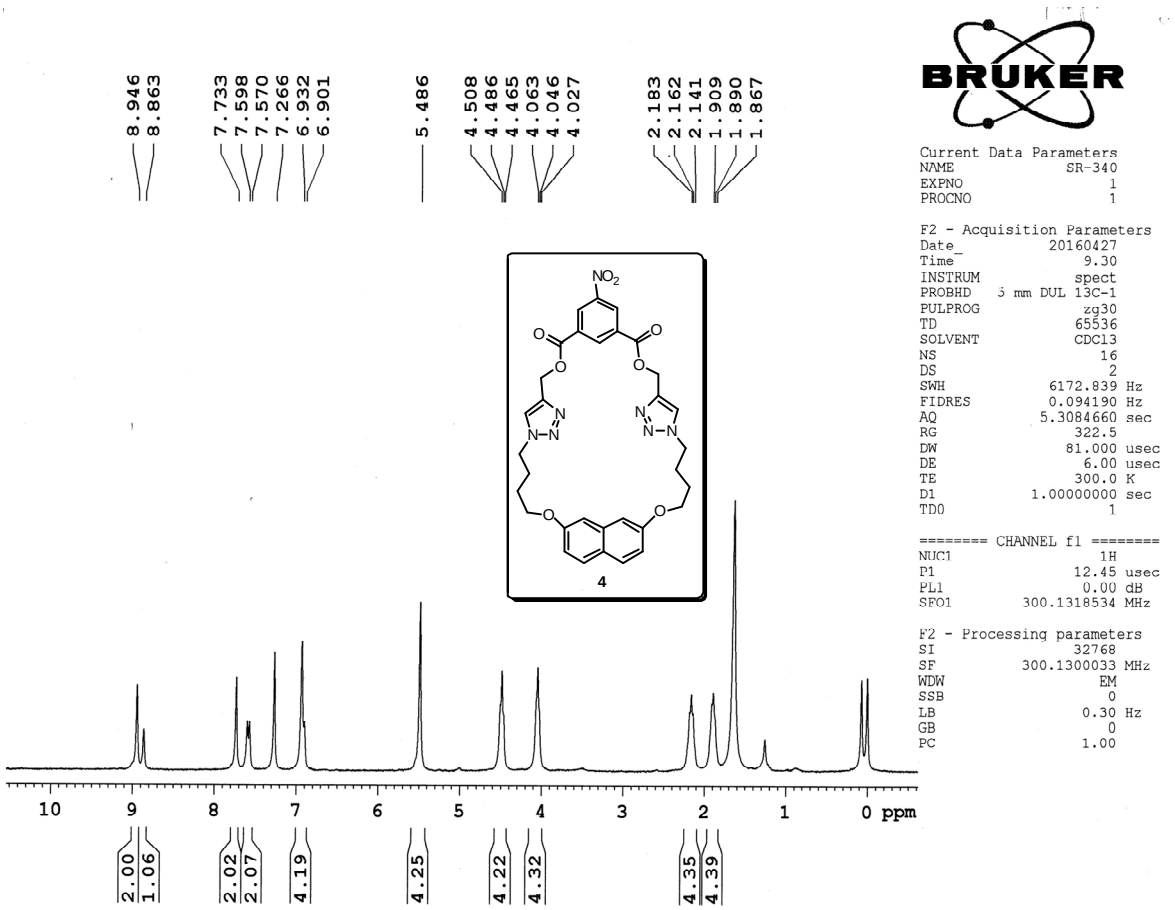


Figure 22: ^{1}H NMR spectrum (300MHz, $CDCl_3$) of Triazolophane 4

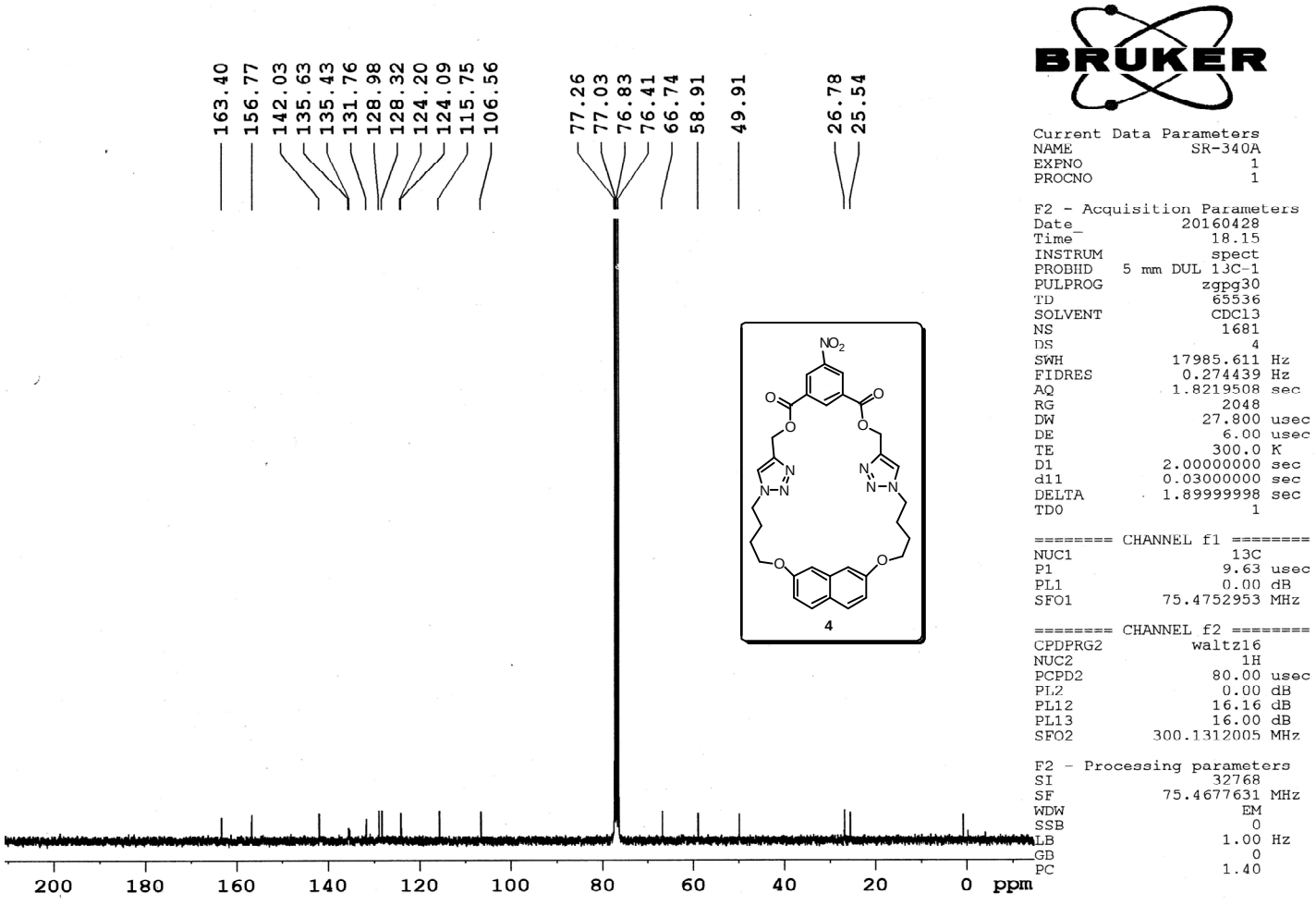


Figure 23: ^{13}C NMR spectrum (75MHz, $CDCl_3$) of Triazolophane 4

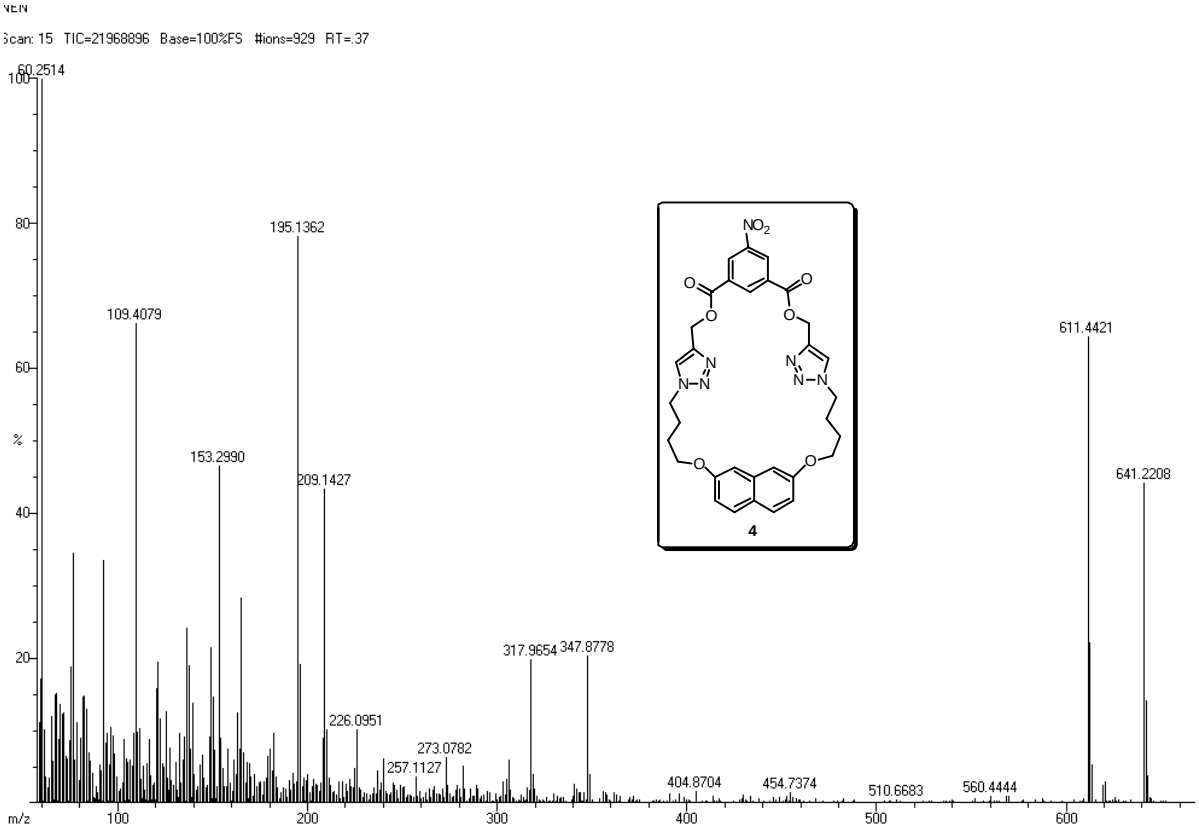


Figure 24: Mass spectrum (EI) of triazolophane 4

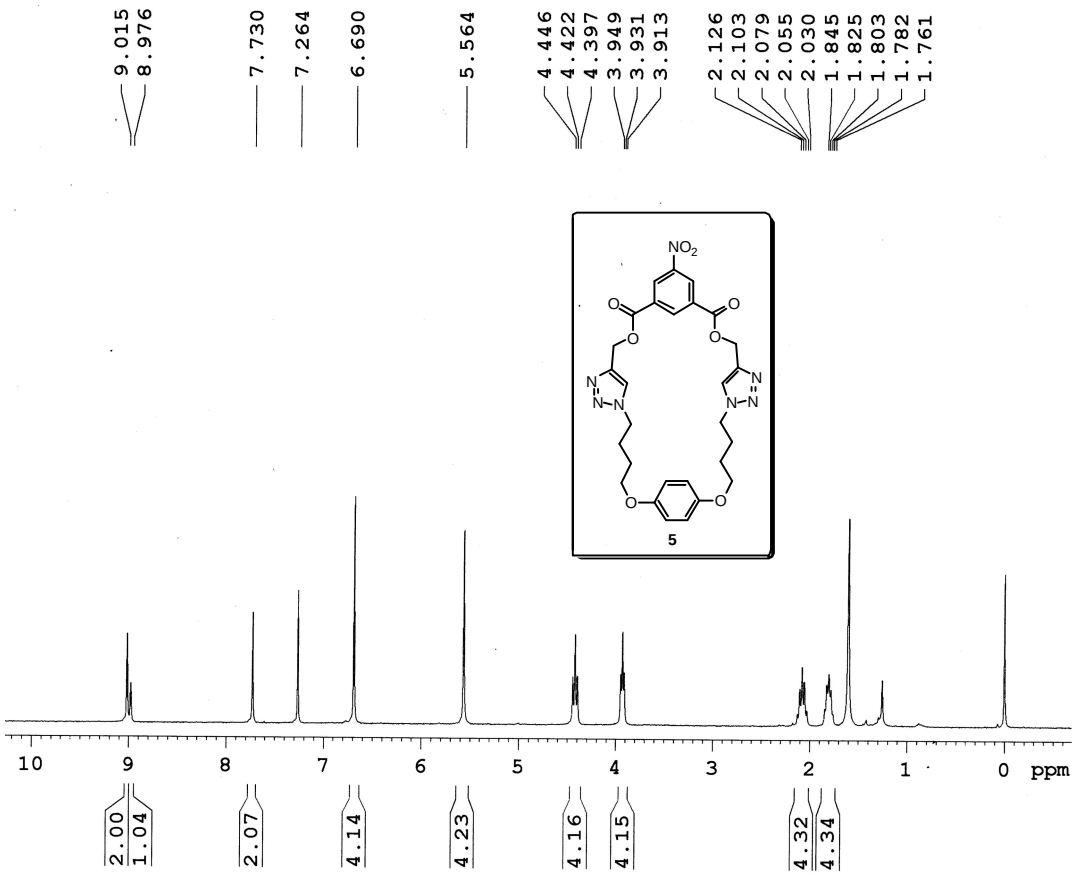


Figure 25: ^{1}H NMR spectrum (300MHz, $CDCl_3$) of Triazolophane 5

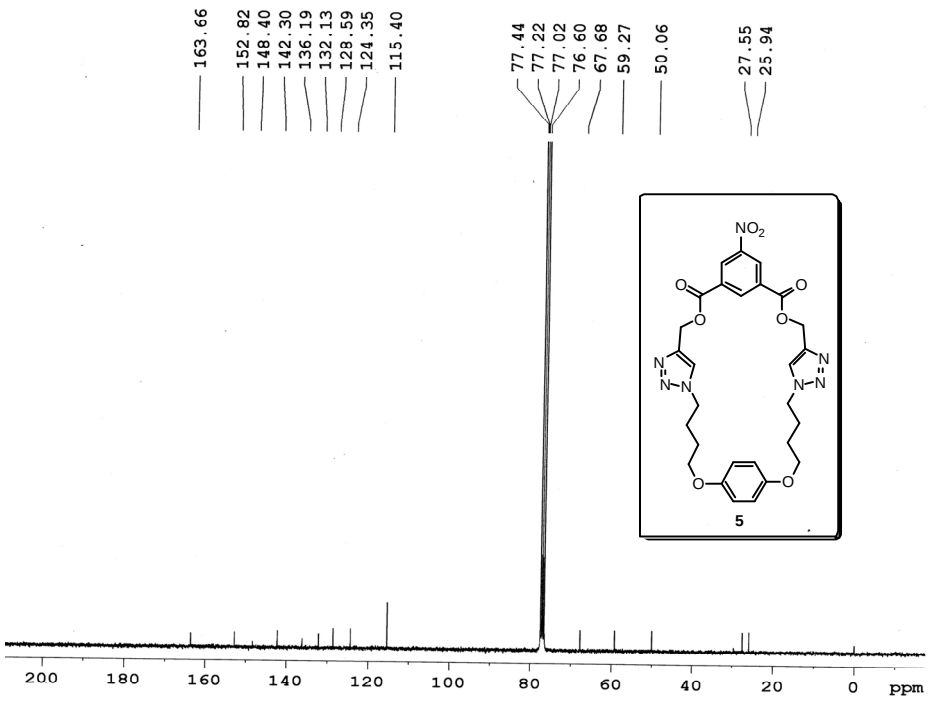


Figure 26: ^{13}C NMR spectrum (75MHz, $CDCl_3$) of Triazolophane 5

Antibacterial Activity

Microorganisms

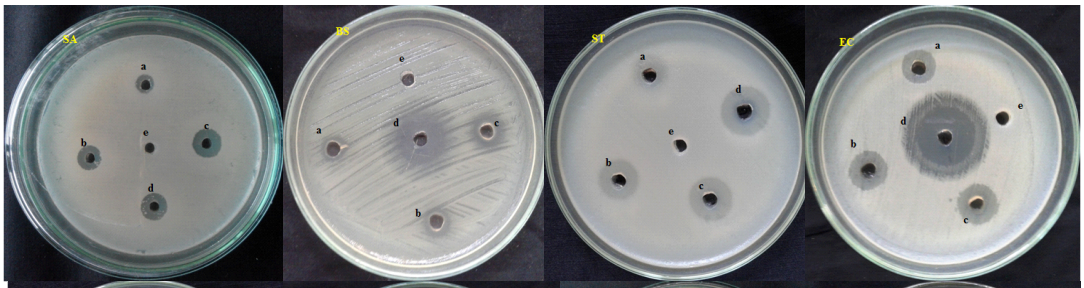
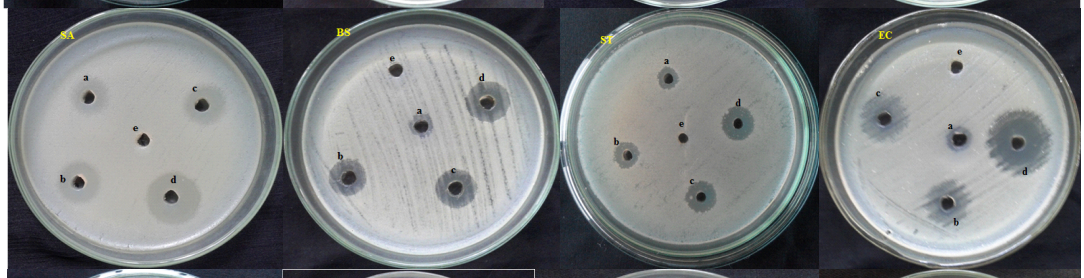
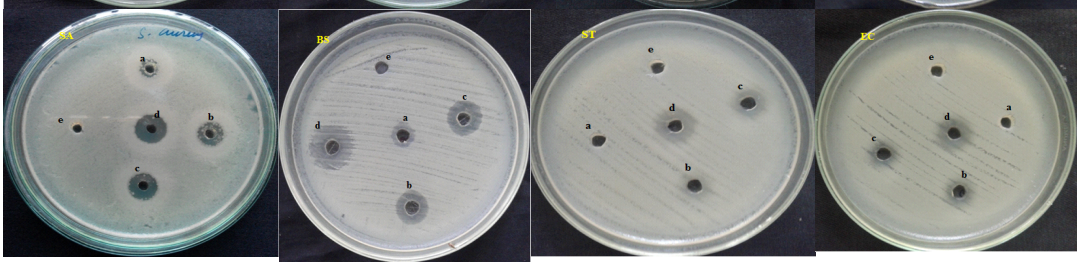
Bacterial microorganisms such as *Staphylococcus aureus, Bacillus subtilis*, *Salmonella typhi and Escherichia coli* were stored in a refrigerator at the microbiology lab, from the Center for Advanced Studies in Botany, University of Madras, Chennai, India under *in vitro* conditions used for antimicrobial activity.

Reference and control:

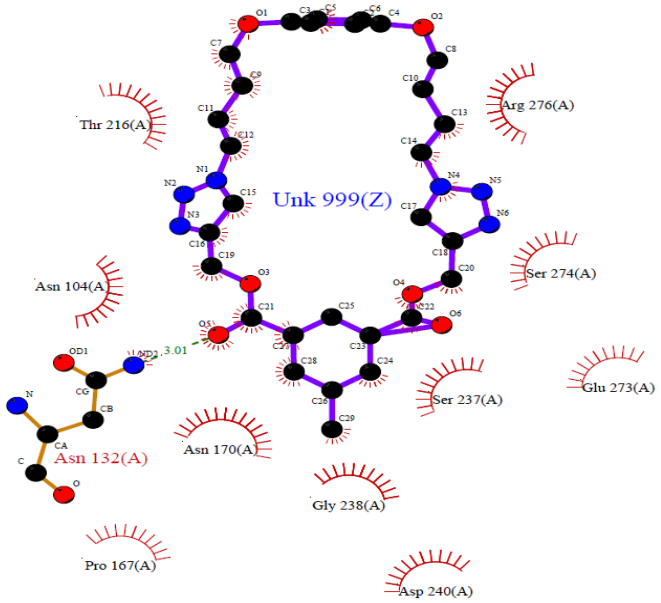
Tetracycline and DMSO was chosen as the standard and reference compound for bacteria.

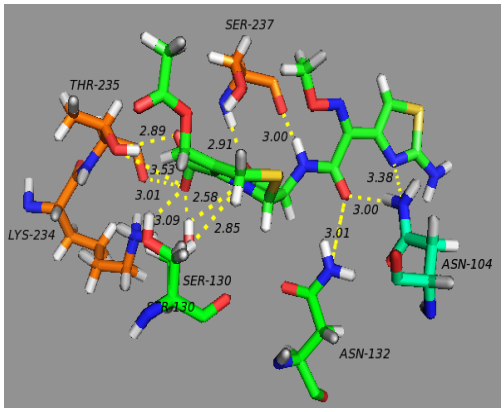
Well diffusion assay:

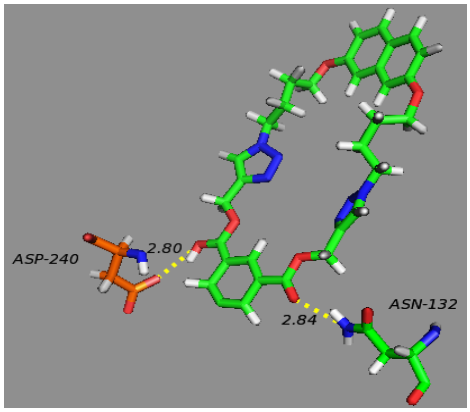
The all bacterial strains were maintained on nutrient agar (NA) consisting of the following (g/L): beef extract 10; yeast extract 20; peptone 10; NaCl 5; agar 15; distilled H_2O 1L; pH 7.2 in slants or petriplates at room temperature (28±2ºC). Effect of the compounds on the growth of human pathogens: the zone of inhibition was determined for compounds 1–10 by well diffusion assay (Riose et al., 1988). The compound at the concentration range of 10–30 µg/ml in 10% DMSO was used in this study with Cefotaxime as reference control. The zone of inhibition value was taken as the lowest concentration of compound that showed prominent inhibition of bacterial growth after 24 h of incubation at 37 ºC.

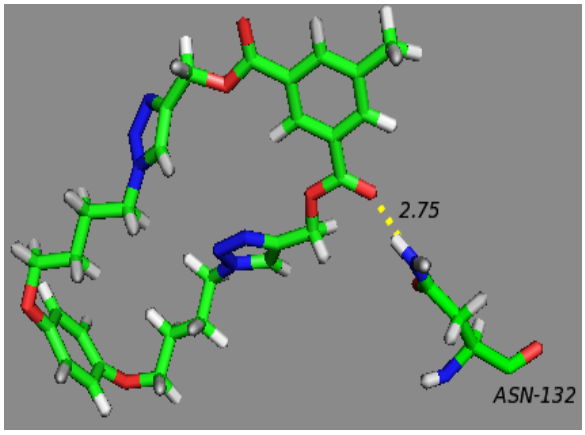
	Staphylococcusaureus	*Bacillus subtilis*	*Salmonella typhi*	*Escherichia coli*
T3				
T5				
T6				

Molecular docking photos









S-7