Electronic Supplementary Material (ESI) for RSC Advances

Synthesis of Carbohydrate Fused Chiral Macrocyclic Benzolactones through Sonogashira Reaction

Altaf Hussain,[1,2] Mallikharjuna Rao L,[1,2] Deepak K. Sharma,[1,2] Anil K. Tripathi,[2] Baldev Singh,[2] Debaraj Mukherjee*[1,2]

[1]Academy of Scientific & Innovative Research (AcSIR, India). [2]CSIR-IIIM (Indian Institute of Integrative Medicine, Canal Road, Jammu (J & K, India) 180001.

E-mail: *dmukherjee@iiim.ac.in*

Supporting information

Section A: General information

Unless otherwise stated, materials were obtained from commercial suppliers and were used without further purification. All reactions were performed under nitrogen atmosphere unless stated otherwise. TLC was performed on pre-coated silica plates (F254, 0.25 mm thickness); compounds were visualized by charring with Cerric Ammonium Sulphate-H_2SO_4 System or UV light. ^1H and ^{13}C NMR spectra were recorded on 400 MHz and 125 MHz spectrometers respectively. Chemical shifts (δ) are quoted in ppm and are referenced to TMS as internal standard. Optical rotations were measured using Perkin-Elmer 241 Polarimeter. Solvents used were mainly of LR grade and for reactions dry solvents were used purchased from Sigma Aldrich.

Section B: General procedure for cyclization using intramolecular Sonogashira reaction

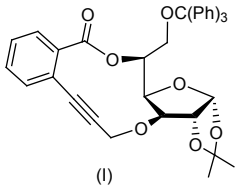
The substrate containing alkynyl group and aryl halide moiety (100 mg) was dissolved in dry THF (3.0 mL). Heterogeneous Pd-catalyst **R** (reported in our previous paper reference 29) containing basic support (100 mg) and co-catalyst CuI (5 mol%) were added to the above solution and the reaction mixture were allowed to stir for several hours at room temperature under nitrogen environment. After ascertaining completion of the reaction by TLC, the catalyst was filtered and the solvent was evaporated under vacuum. The reaction mixture was extracted with ethyl acetate, dried over anhydrous Na_2SO_4 and the product was purified by column chromatography on silica gel using petroleum ether–ethyl acetate as the eluent to obtain the pure product (81-90%).

Section C: Experimental procedures

1. Preparation of compound **2**: prepared by phase transfer method from diacetone glucose and propargyl bromide in 80% yield.[1]
2. Preparation of compound **3a, 3b** & **3c**: selective cleavage of 5,6-isopropylidene unit of compound **2** gave a diol which on tritylation gave **3a** (65% yield),[2] on silylation gave **3c** (81% yield)[2] and on tosylation gave **3b** (85% yield).[1]
3. Preparation of compound to give **4a, 4b** & **4c**: compounds **3a, 3b** & **3c** were subjected to EDC coupling to give **4a, 4b** & **4c** respectively. The substrate **3a** (1.0 g) was dissolved in DCM (5 mL) followed by the addition of 2-bromobenzoic acid (1.2 equiv., 0.48 g), EDC (1.5 equiv., 0.58 g) and DMAP (1.1 equiv., 0.27 g). The reaction mixture was allowed to stir for 3 hours at room temperature. The formation of product was confirmed by TLC. The product was extracted with DCM and dried over sodium sulfate. Solvent was removed under reduced pressure to leave behind a syrupy liquid. Chromatography on silica gel with petroleum ether-ethyl acetate as the eluent yielded product (**4a**) as a syrupy liquid (80% yield). Exactly similar procedure was followed to synthesize **4b** & **4c** from **3b** & **3c** respectively.
4. Preparation of compound **5**: EDC coupling of compound **3a**, as described above for the preparation of **4a, 4b** & **4c**, followed by de-tritylation gave the compound **5** in 60% yield.[2]

5. Preparation of compound **6a, 6b** & **6c**: the compound **5** was subjected to benzylation/methylation to give **6a, 6b** & **6c** in 85% yields according to literature methods.[1]
6. Preparation of compound **7**: the compound **3a** was subjected to benzylation to give **7** in 80% yield.[2]
7. Preparation of compound **8**: de-tritylation of the compound **7**[2] followed EDC coupling of the product so obtained as described for **4a, 4b** & **4c** gave **8** in 70% yield over two steps.
8. Preparation of compound **9**: the compound **9** was obtained by selective cleavage of 5,6-isopropylidene unit of intermediate **2** followed by cleavage of the resulting diol using silica supported $NaIO_4$ and reduction of aldehyde so obtained with $NaBH_4$.[2]
9. Preparation of compound **9'**: The compound **9'** was obtained from diacetone allose following a similar set of reactions as that for **9**.[2]
10. Preparation of compound **10** & **10'**: EDC coupling of **9** and **9'** gave **10** & **10'** respectively (80% yield) as described above for **4a/4b/4c**.
11. Preparation of compound **11**: prepared by the benzylation of diacetone glucose.[2]
12. Preparation of compound **12**: selective cleavage of 5,6-isopropylidene unit of compound **11** gave a diol which on tritylation gave **12** (65% yield).[2]
13. Preparation of compound **13**: prepared by phase transfer method from compound **12** and propargyl bromide in 80% yield.[1]
14. Preparation of compound **14**: de-tritylation of the compound **13**[2] followed EDC coupling of the product so obtained as described for the preparation of **4a, 4b** & **4c** gave **14** in 70% yield over two steps.
15. Preparation of compound **16** & **17**: the intermediate compounds (**16** & **17**) were obtained by doing a sequence reactions described in literature.[3]
16. Preparation of compound **18**: EDC coupling of compound **17** (500 mg) with 2-bromobenzoic acid (1.2 equiv.) using EDC (1.1 equiv.) and DMAP (1.1 e quiv.) in DCM (5 mL) gave the scaffold **18** in 80% yield.

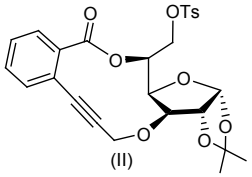
Section D: ^{1}H NMR and ^{13}C NMR data of compounds



(I)

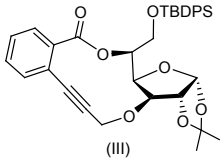
Preparation & spectral analysis of compound (I): Prepared by the general procedure for Sonogashira reaction by using **4a** (100 mg, 0.15 mmol) to yield the desired product **I** as semisolid (76.8 mg, 85 %); Rf (45% EtOAc/hexane) 0.55;); $[\alpha]^{25}_{D}$ –1.15 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2985, 2931, 2211, 1733, 1585 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.65 (dd, *J* = 7.3, 1.9 Hz, 1H), 7.43 (dd, *J* = 8.1, 1.4 Hz, 5H), 7.37 – 7.28 (m, 2H), 7.26 (d, *J* = 1.9 Hz, 2H), 7.24 – 7.15 (m, 8H), 5.88 (d, *J* = 3.6 Hz, 1H), 5.55 (ddd, *J* = 9.0, 4.9, 1.9 Hz, 1H), 4.74 (dd, *J* = 9.1, 2.9 Hz, 1H), 4.60 (d, *J* = 8.6 Hz, 1H), 4.20 (d, *J* = 16.6 Hz, 1H), 4.12 (dd, *J* = 9.7, 6.7 Hz, 2H), 3.54 (dd, *J* = 10.5, 1.9 Hz, 1H), 3.43 (dd, *J* = 10.6, 5.0 Hz, 1H),

1.55 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 144.5, 144.5, 144.5, 134.6, 134.6, 132.4, 131.2, 129.2, 129.2, 129.2, 129.2, 129.2, 129.2, 128.5, 128. 5, 128. 5, 128. 5, 128. 5, 128. 5, 128.4, 127.6, 127.2, 127.2, 127.2, 112.5, 106.02, 84.5, 83.2, 82.2, 79.5, 76.2, 73.9, 70.0, 63.9, 55.6, 26.3, 26.3; ESI MS (m/z): 602 [M^+]; Anal. Calcd for $C_{38}H_{34}O_7$: C, 75.73; H, 5.69. Found C, 75.71; H, 5.61



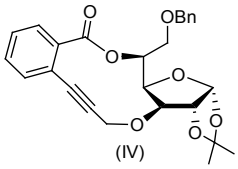
(II)

Preparation & spectral analysis of compound (II): Prepared by the general procedure for Sonogashira reaction by using **4b** (100 mg, 0.17 mmol) to yield the desired product **II** as semisolid (69.9 mg, 81 %); Rf (50% EtOAc/hexane) 0.4); $[\alpha]^{25}_D$ –1.11 (*c* 1.0, $CHCl_3$); IR (CHCl3) 2980, 2937, 2210, 1735, 1585 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 7.0, 2.5 Hz, 1H), 7.74 (d, *J* = 8.3 Hz, 2H), 7.65 (dd, *J* = 7.1, 2.2 Hz, 1H), 7.40 – 7.31 (m, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 5.85 (d, *J* = 3.6 Hz, 1H), 5.42 (ddd, *J* = 8.1, 4.6, 2.1 Hz, 1H), 4.55 – 4.48 (m, 2H), 4.35 – 4.29 (m, 1H), 4.19 (d, *J* = 16.5 Hz, 1H), 4.13 (d, *J* = 16.5 Hz, 1H), 4.05 (dd, *J* = 8.2, 2.8 Hz, 1H), 3.85 (dd, *J* = 14.9, 6.9 Hz, 1H), 2.38 (s, 3H), 1.50 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.3, 144.5, 134.3, 132.9, 132.5, 132.1, 129.9, 129.9, 128.2, 127.9, 127.9, 127.4, 121.9, 112.3, 105.1, 98.2, 81.6, 81.1, 74.1, 70.6, 68.6, 68.2, 58.1, 26.8, 26.4, 21.1; ESI MS (m/z): 514 [M^+]; Anal. Calcd for $C_{26}H_{26}O_9S$: C, 60.69; H, 5.09. Found C, 60.63; H, 4.97



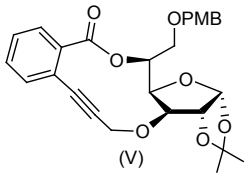
(III)

Preparation & spectral analysis of compound (III): Prepared by the general procedure for Sonogashira reaction by using **4c** (100 mg, 0.15 mmol) to yield the desired product **III** as semisolid (76.6 mg, 87 %); Rf (40% EtOAc/hexane) 0.50; $[\alpha]^{25}_D$ –1.17 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2980, 2934, 2214, 1731, 1589 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 7.1, 1.8 Hz, 1H), 7.56 – 7.50 (m, 5H), 7.47 – 7.36 (m, 8H), 5.60 (d, *J* = 3.5 Hz, 1H), 4.77 (dt, *J* = 8.5, 5.3 Hz, 1H), 4.44 (t, *J* = 8.9 Hz, 1H), 4.32 (dd, *J* = 12.3, 5.3 Hz, 1H), 4.20 (t, *J* = 3.7 Hz, 1H), 4.16 (d, *J* = 12.5 Hz, 1H), 4.06 (dd, *J* = 12.5, 7.2 Hz, 2H), 3.75 (dd, *J* = 9.3, 3.9 Hz, 1H), 1.41 (s, 6H), 1.09 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 134.6, 134.6, 134.6, 134.6, 134.6, 134.6, 133.4, 133.4, 132.4, 131.2, 131.1, 131.1, 131.1, 131.1, 130.3, 130.3, 128.4, 127.6, 112.5, 106.0, 83.2, 82.2, 79.5, 76.2, 74.0, 70.1, 63.3, 55.6, 26.8, 26.8, 26.8, 26.3, 26.3, 19.7; ESI MS (m/z): 598 [M^+]; Anal. Calcd for $C_{35}H_{38}O_7Si$: C, 70.21; H, 6.40. Found C, 60.63; H, 4.97



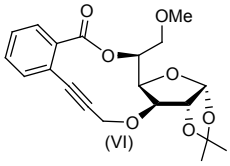
(IV)

Preparation & spectral analysis of compound (IV): Prepared by the general procedure for Sonogashira reaction by using **6a** (100 mg, 0.19 mmol) to yield the desired product **IV** as semisolid (74.6 mg, 88%); Rf (45% EtOAc/hexane) 0.53; $[\alpha]^{25}_{D}$ –1.10 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2980, 2934, 2211, 1733, 1590 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.3 Hz, 1H), 7.54 (d, *J* = 7.4 Hz, 1H), 7.42 – 7.33 (m, 2H), 7.25 (d, *J* = 7.6 Hz, 5H), 5.60 (d, *J* = 3.8 Hz, 1H), 4.97 (td, *J* = 8.2, 3.8 Hz, 1H), 4.65 (s, 2H), 4.44 (dd, *J* = 8.8, 3.8 Hz, 1H), 4.21 – 4.18 (m, 1H), 4.16 (d, *J* = 12.5 Hz, 1H), 4.06 (d, *J* = 12.5 Hz, 1H), 3.90 (dd, *J* = 12.5, 8.2 Hz, 1H), 3.77 – 3.73 (m, 1H), 3.65 (dd, *J* = 12.5, 6.2 Hz, 1H), 1.51 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 138.9, 134.6, 134.6, 132.5, 132.4, 131.2, 131.2, 129.0, 129.0, 128.4, 128.4, 127.6, 112.5, 106.0, 83.2, 82.2, 79.5, 76.2, 74.8, 73.7, 70.1, 68.8, 55.6, 26.3, 26.3; ESI MS (m/z): 450 [M^+]; Anal. Calcd for $C_{26}H_{26}O_7$: C, 69.32; H, 5.82. Found C, 69.24; H, 5.73



(V)

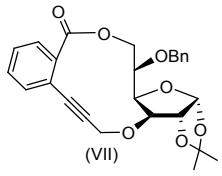
Preparation & spectral analysis of compound (V): Prepared by the typical procedure for Sonogashira reaction by using **6b** (100 mg, 0.18 mmol) to yield the desired product **V** as semisolid (71.1 mg, 83 %); Rf (45% EtOAc/hexane) 0.56; $[\alpha]^{25}_{D}$ –1.10 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2981, 2937, 2214, 1732, 1585 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.3 Hz, 1H), 7.54 (d, *J* = 7.4 Hz, 1H), 7.42 – 7.33 (m, 2H), 7.25 (d, *J* = 7.6 Hz, 2H), 6.89 (d, *J* = 7.6 Hz, 2H), 5.60 (d, *J* = 3.8 Hz, 1H), 4.97 (td, *J* = 8.2, 3.8 Hz, 1H), 4.64 (s, 2H), 4.44 (dd, *J* = 8.8, 3.8 Hz, 1H), 4.21 – 4.13 (m, 2H), 4.06 (d, *J* = 12.5 Hz, 1H), 3.90 (dd, *J* = 12.5, 8.2 Hz, 1H), 3.81 (s, 3H), 3.77 – 3.73 (m, 1H), 3.69 – 3.61 (m, 1H), 1.51 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 159.1, 134.6, 134.6, 132.5, 132.4, 131.2, 129.0, 129.0, 128.4, 127.6, 113.5, 113.5, 112.5, 106.0, 83.2, 82.2, 79.5, 76.2, 74.8, 73.7, 70.1, 68.8, 56.0, 55.6, 26.3, 26.3; ESI MS (m/z): 480 [M^+]; Anal. Calcd for $C_{27}H_{28}O_8$: C, 67.49; H, 5.87. Found C, 67.41; H, 5.79



(VI)

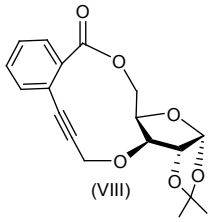
Preparation & spectral analysis of compound (VI): Prepared by the typical procedure for Sonogashira reaction by using **6c** (100 mg, 0.22 mmol) to yield the desired product V**I** as semisolid (65.8 mg, 80 %); Rf (40% EtOAc/hexane) 0.52; $[\alpha]^{25}_{D}$ –1.18 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2980, 2935, 2211, 1733, 1589 cm^{-1}; ^1H NMR (400 MHz, $CHCl_3$) δ 7.74 – 7.69 (m, 1H), 7.50 (d, *J* = 7.3 Hz, 1H), 7.43 – 7.35 (m, 2H), 5.60 (d, *J* = 3.5 Hz, 1H), 4.96 (d, *J* = 6.1 Hz, 1H), 4.44 (dd, *J* = 8.9, 4.2 Hz, 1H), 4.23 – 4.13 (m, 2H), 4.06 (d, *J* = 12.5 Hz, 1H), 3.90 (dd, *J* = 12.5, 6.2 Hz, 1H), 3.78 – 3.72 (m, 1H), 3.65 (dd, *J* = 12.5, 6.2 Hz, 1H), 3.35 (s, 3H), 1.51 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (125 MHz, $CHCl_3$) δ 170.1, 134.6, 134.6, 132.4, 131.2, 128.4, 127.6, 112.5,

106.0, 83.2, 82.2, 79.5, 76.2, 75.4, 71.9, 70.1, 58.7, 55.6, 26.3, 26.3; ESI MS (m/z): 374 [M^+]; Anal. Calcd for $C_{20}H_{22}O_7$: C, 64.16; H, 5.92. Found C, 64.09; H, 5.85

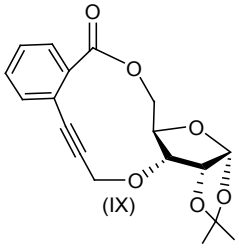


(VII)

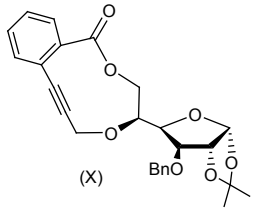
Preparation & spectral analysis of compound (VII): Prepared by the typical procedure for Sonogashira reaction by using **8** (100 mg, 0.19 mmol) to yield the desired product **VII** as semisolid (76.1 mg, 89 %); Rf (45% EtOAc/hexane) 0.54; $[\alpha]^{25}_D$ –1.13 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2981, 2938, 2210, 1735, 1586 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.5 Hz, 1H), 7.56 (d, *J* = 8.9 Hz, 1H), 7.38 – 7.20 (m, 7H), 5.60 (d, *J* = 5.6 Hz, 1H), 4.67 (s, 2H), 4.49 (dd, *J* = 12.4, 2.7 Hz, 1H), 4.24 (dd, *J* = 12.9, 3.2 Hz, 1H), 4.21 – 4.17 (m, 1H), 4.14 (d, *J* = 12.3 Hz, 1H), 4.09 (d, *J* = 12.3 Hz, 1H), 4.05 (t, *J* = 1.6 Hz, 1H), 3.99 (t, *J* = 3.5 Hz, 1H), 3.75 (d, *J* = 8.4 Hz, 1H), 1.51 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.3, 137.9, 134.2, 134.2, 132.3, 130.8, 128.5, 128.3, 128.3, 128.2, 28.2, 127.9, 127.5, 112.5, 106.0, 83.22, 82.2, 81.6, 78.2, 76.2, 73.5, 72.1, 72.1, 64.9, 55.6, 26.3, 26.3; ESI MS (m/z): 450 [M^+]; Anal. Calcd for $C_{26}H_{26}O_7$: C, 69.32; H, 5.82. Found C, 69.29; H, 5.78


(VIII)

Preparation & spectral analysis of compound (VIII): Prepared by the typical procedure for Sonogashira reaction by using **10** (100 mg, 0.24 mmol) to yield the desired product **VIII** as semisolid (72.3 mg, 90%); Rf (45% EtOAc/hexane) 0.50; $[\alpha]^{25}_D$ –1.3 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2985, 2938, 2210, 1733, 1588 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 7.4, 2.0 Hz, 1H), 7.66 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.44 – 7.27 (m, 2H), 5.96 (d, *J* = 3.7 Hz, 1H), 4.63 (d, *J* = 3.7 Hz, 1H), 4.62 – 4.58 (m, 1H), 4.56 (dd, *J* = 7.0, 3.6 Hz, 1H), 4.50 (dd, *J* = 10.1, 6.0 Hz, 1H), 4.35 (d, *J* = 16.5 Hz, 1H), 4.30 (d, *J* = 16.5 Hz, 1H), 4.18 (d, *J* = 2.9 Hz, 1H), 1.51 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.7, 134.4, 132.7, 131.7, 131.6, 127.2, 121.9, 112.1, 105.2, 81.9, 81.7, 76.8, 74.8, 70.9, 62.9, 57.9, 26.8, 26.3; ESI MS (m/z): 330 [M^+]; Anal. Calcd for $C_{18}H_{18}O_6$: C, 65.45; H, 5.49. Found C, 65.35; H, 5.38

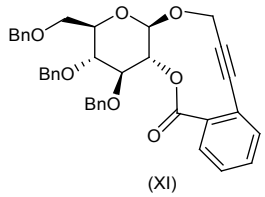

(IX)

Preparation & spectral analysis of compound (IX): Prepared by the typical procedure for Sonogashira reaction by using **10'** (100 mg, 0.24 mmol) to yield the desired product **IX** as semisolid (64.9 mg, 82%). Rf (45% EtOAc/hexane) 0.49; $[\alpha]^{25}_{D}$ +0.19 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2985, 2938, 2210, 1732, 1588 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 7.3, 2.1 Hz, 1H), 7.66 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.41 – 7.28 (m, 2H), 5.96 (d, *J* = 3.7 Hz, 1H), 4.63 (d, *J* = 3.6 Hz, 1H), 4.60 (dd, *J* = 9.1, 4.5 Hz, 1H), 4.57 (dd, *J* = 7.0, 3.6 Hz, 1H), 4.50 (dd, *J* = 10.1, 6.0 Hz, 1H), 4.35 (d, *J* = 16.6 Hz, 1H), 4.30 (d, *J* = 16.5 Hz, 1H), 4.18 (d, *J* = 2.9 Hz, 1H), 1.51 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.3, 134.2, 134.2, 132.3, 130.8, 128.5, 127.5, 112.5, 104.3, 83.3, 81.1, 79.7, 76.2, 71.5, 64.4, 55.6, 26.3, 26.3; ESI MS (m/z): 330 [M^+]; Anal. Calcd for $C_{18}H_{18}O_6$: C, 65.45; H, 5.49. Found C, 65.41; H, 5.39



(X)

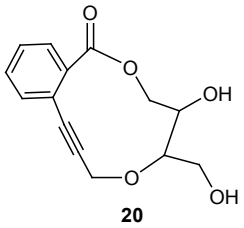
Preparation & spectral analysis of compound (X): Prepared by the typical procedure for Sonogashira reaction by using **14** (100 mg, 0.18 mmol) to yield the desired product **X** as semisolid (68.9 mg, 85%); Rf (45% EtOAc/hexane) 0.48; $[\alpha]^{25}_{D}$ –1.12 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2982, 2935, 2211, 1733, 1588 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 7.3, 1.6 Hz, 1H), 7.53 (dd, *J* = 7.3, 1.6 Hz, 1H), 7.45 – 7.35 (m, 2H), 7.31 – 7.19 (m, 5H), 5.38 (d, *J* = 3.7 Hz, 1H), 4.70 – 4.63 (m, 3H), 4.49 (dd, *J* = 12.4, 4.6 Hz, 1H), 4.24 (dd, *J* = 12.4, 4.5 Hz, 1H), 4.20 (t, *J* = 3.7 Hz, 1H), 4.16 (d, *J* = 12.5 Hz, 1H), 4.08 – 4.02 (m, 2H), 3.99 (dd, *J* = 8.6, 4.4 Hz, 1H), 1.51 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.3, 137.9, 134.2, 134.2, 132.3, 130.8, 128.5, 128.3, 128.3, 128.2, 128.2, 127.9, 127.5, 112.5, 106.0, 83.2, 82.2, 81.6, 78.2, 76.2, 73.0, 70.5, 64.9, 54.9, 26.3, 26.3; ESI MS (m/z): 450 [M^+]; Anal. Calcd for $C_{26}H_{26}O_7$: C, 69.32; H, 5.82. Found C, 69.23; H, 5.78



(XI)

Preparation & spectral analysis of compound (XI): Prepared by the typical procedure for Sonogashira reaction by using **18** (100 mg, 0.15 mmol) to yield the desired product **XI** as semisolid (75.6 mg, 86%); Rf (40% EtOAc/hexane) 0.57; $[\alpha]^{25}_{D}$ +1.18 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2984, 2934, 2212, 1733, 1585 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (dd, *J* = 7.0, 2.3 Hz, 1H), 7.60 (dd, *J* = 6.9, 2.0 Hz, 1H), 7.31 – 7.15 (m, 17H), 5.31 (d, *J* = 6.8 Hz, 1H), 5.15 (dd, *J* = 10.1, 3.7 Hz, 1H), 4.83 – 4.70 (m, 4H), 4.62 (s, 1H), 4.54 (d, *J* = 7.4 Hz, 1H), 4.51 (d, *J* = 8.6 Hz, 1H), 4.30 (s, 1H), 4.14 – 4.08 (m, 1H), 3.86 (dd, *J* = 11.2, 2.2 Hz, 1H), 3.82 – 3.74 (m, 2H), 3.69 (d, *J* = 9.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.5, 138.3, 138.1, 138.0, 134.2,

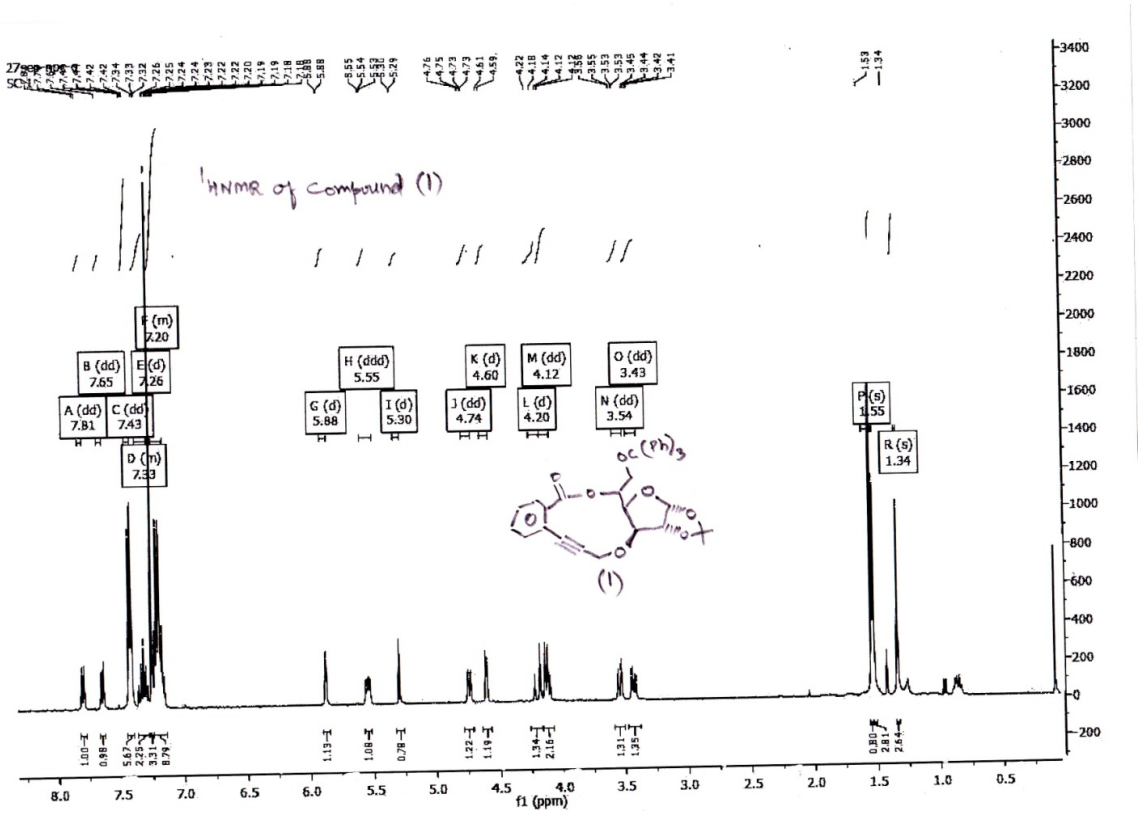
132.6, 132.0, 131.2, 128.4, 128.4, 128.3, 128.3, 127.9, 127.9, 127.9, 127.9, 127.8, 127.8. 127.8, 127.7, 127.7, 127.6, 127.6, 127.2, 121.7, 95.4, 79.9, 77.9, 75.5, 75.2, 74.7, 73.9, 73.6, 71.3, 70.6, 68.3, 55.6; ESI MS (m/z): 590 [M^+]; Anal. Calcd for $C_{37}H_{34}O_7$: C, 75.24; H, 5.80. Found C, 75.19; H, 5.75.

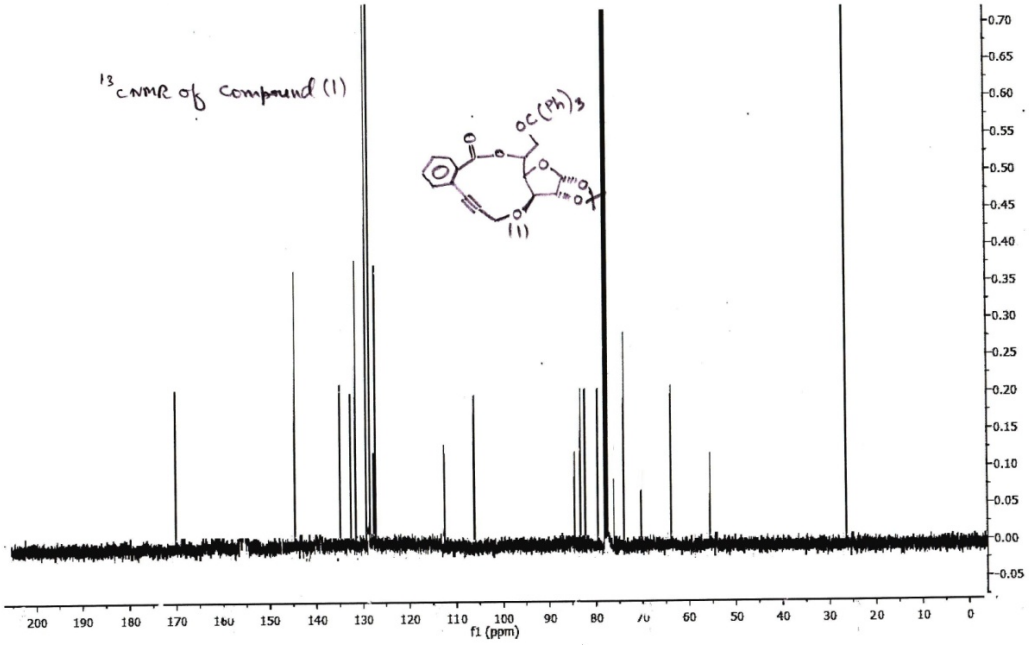


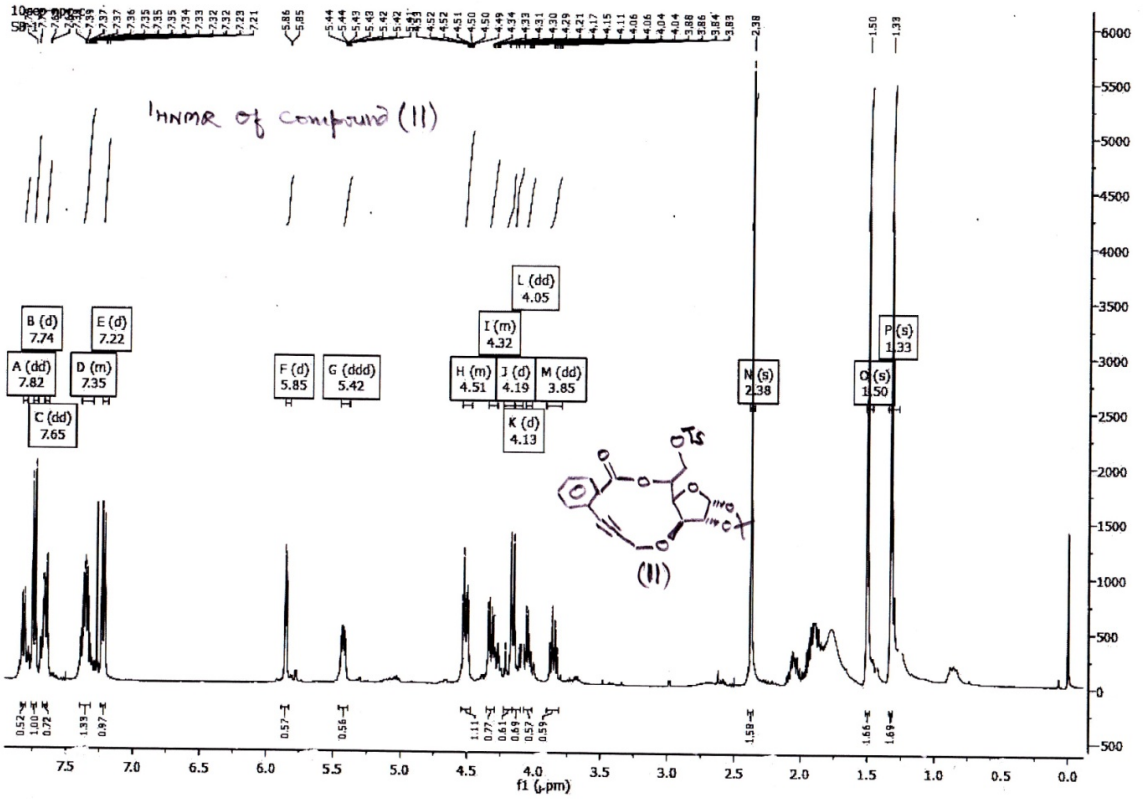
20

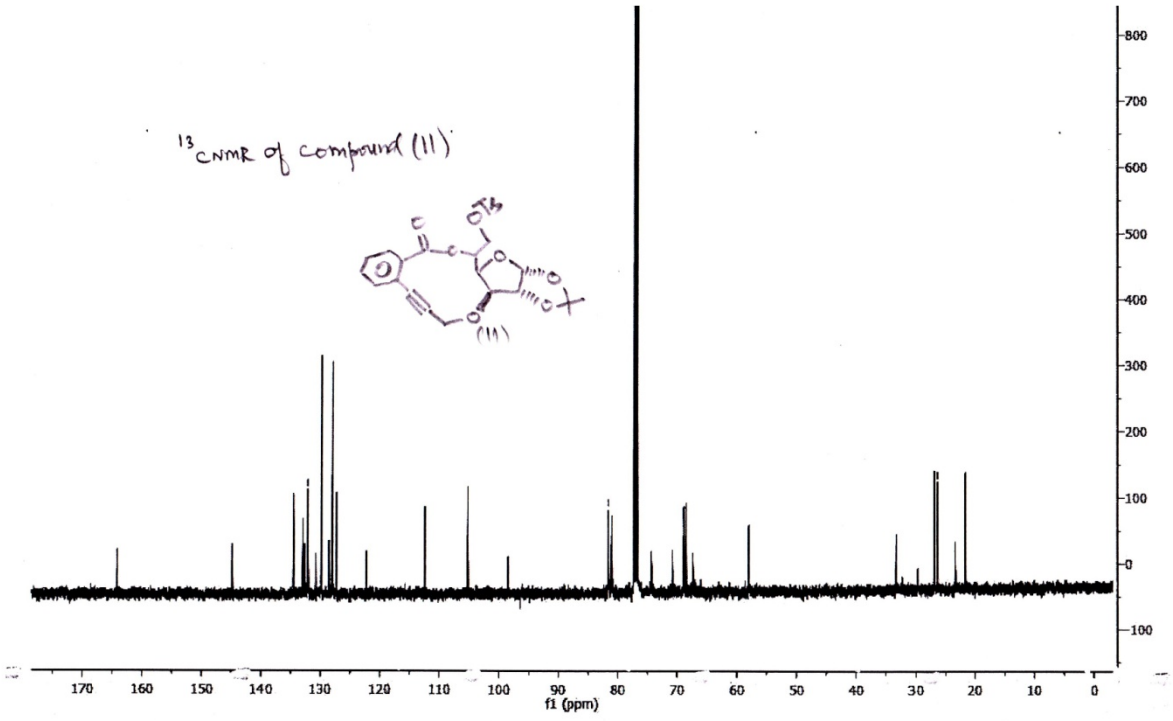
Preparation & spectral analysis of compound (20): Preparation of compound **20**: TFA-water (2 mL, 3:1) was added to the compound **VIII** (500 mg), and the reaction mixture was stirred for 3 h at 0^o C. TFA was coevaporated with toluene to furnish a thick liquid. To an ice-cooled solution of hemiacetal in acetone- water (10 mL, 5:1) was added sodium metaperiodate (1.5 equiv.). After the reaction was stirred at 30^o C for 1.5 h, ethylene glycol (1 mL) was added, the reaction mixture was concentrated, and the residue was extracted with dichloromethane (2 x 50 mL) . The crude di-aldehyde (**19**) so obtained was directly subjected to reduction by using $NaBH_4$ (1.2 equiv.) in MeOH (10 mL,) at 0^o C for 30 min and quenched by addition of saturated NH_4Cl. The reaction mixture was extracted with ethyl acetate (1 x 30 mL). Usual workup and purification by column chromatography (n-hexane/ ethyl acetate = 35/65) gave the product **20** as a thick liquid (68% yield); Rf (80% EtOAc/hexane) 0.55; $[\alpha]^{25}_D$ +4.18 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3200-3300 (br), 2985, 2212, 1733, 1589 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.53 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.41 (dt, *J* = 7.5, 1.6 Hz, 1H), 7.34 (dt, *J* = 7.5, 1.5 Hz, 1H), 4.75 (dd, *J* = 11.7, 6.0 Hz, 1H), 4.61 – 4.35 (m, 2H), 4.37 (d, *J* = 12.5 Hz, 1H), 4.20 (d, *J* = 12.5 Hz, 1H), 3.77 (d, *J* = 12.5 Hz, 1H), 3.52 (d, *J* = 14.0 Hz, 1H), 3.20 (d, *J* = 9.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.2, 134.3, 134.2, 132.3, 130.8, 128.7, 127.4, 81.5, 78.8, 76.2, 70.3, 66.4, 62.3, 54.9; ESI MS (m/z): 262 [M^+]; Anal. Calcd for $C_{14}H_{14}O_5$: C, 64.12; H, 5.38. Found C, 64.01; H, 5.33.

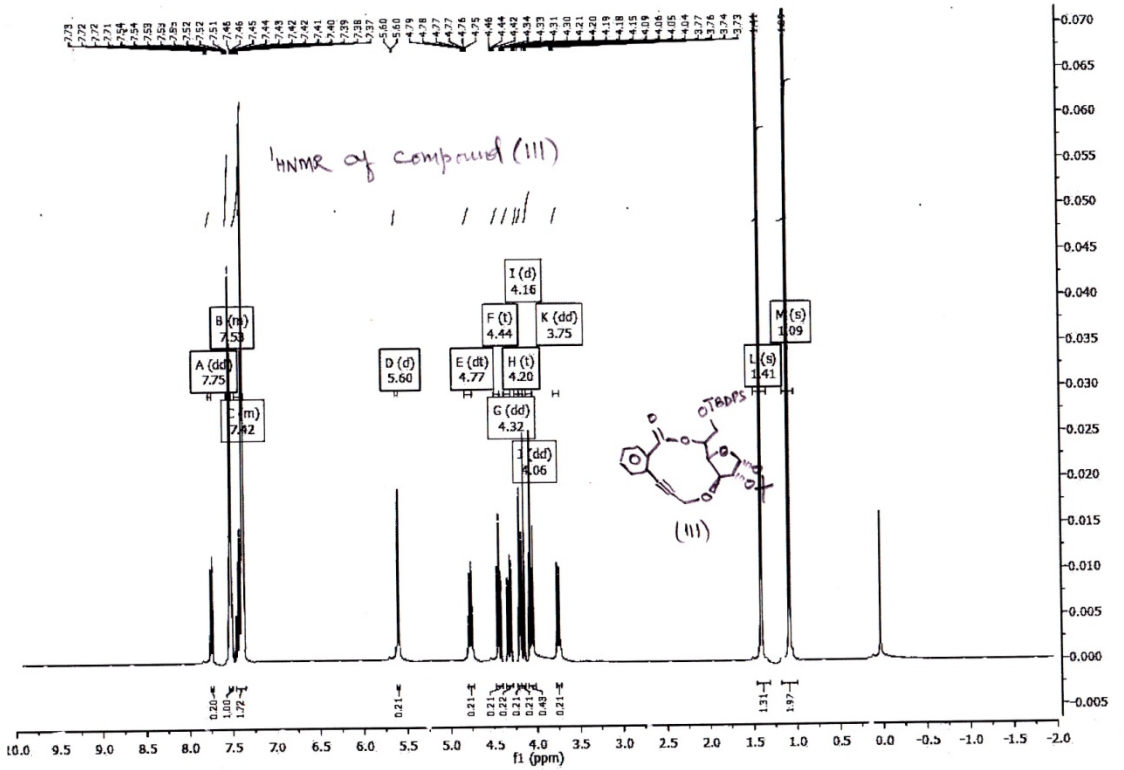
Section E: Copies of ^{1}H NMR and ^{13}C NMR of compounds 1 to XI

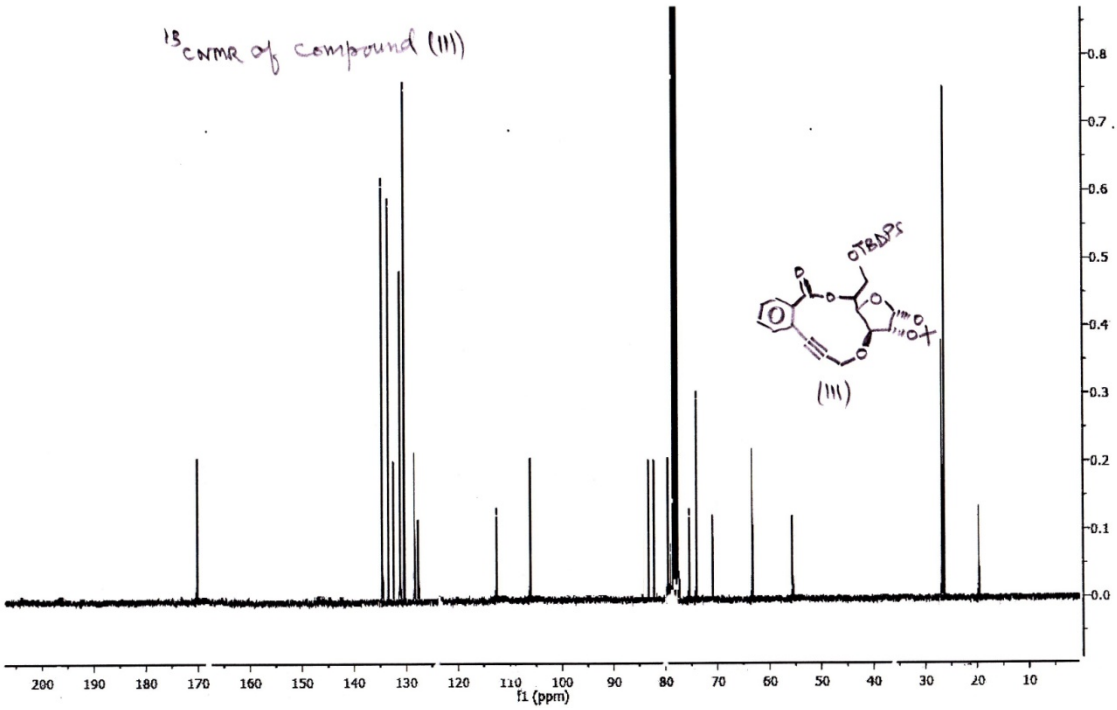


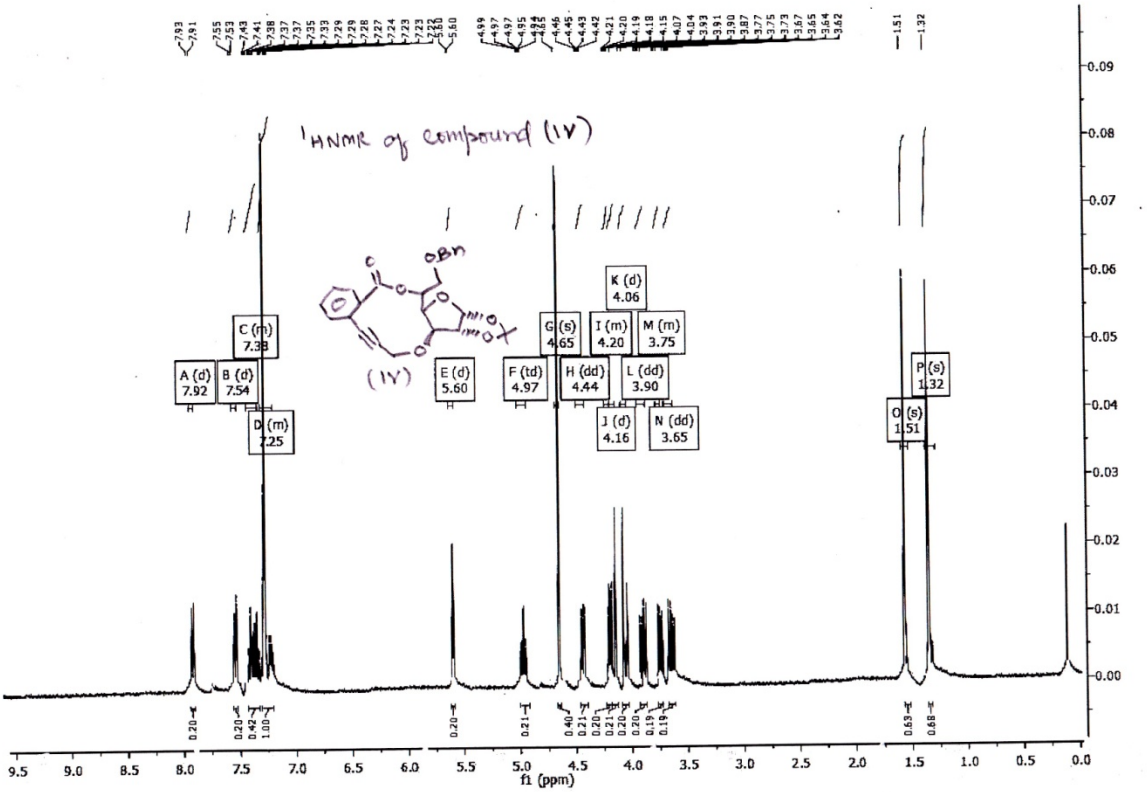


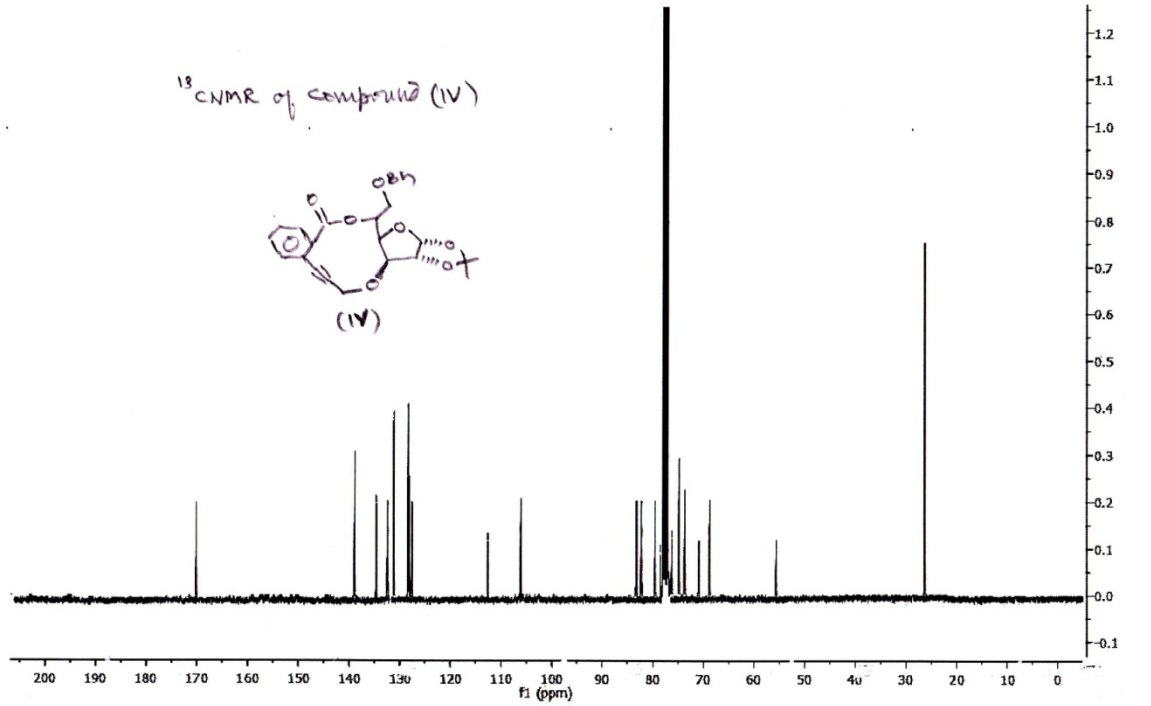

1HNMR of compound (11)
B (d) 7.74
E (d) 7.22
A (dd) 7.82
D (m) 7.35
C (dd) 7.65
F (d) 5.85
G (ddd) 5.42
L (dd) 4.05
I (m) 4.32
H (m) 4.51
J (d) 4.19
M (dd) 3.85
K (d) 4.13
N (s) 2.38
P (s) 1.33
O (s) 1.50
OTs
(11)
f1 (ppm)

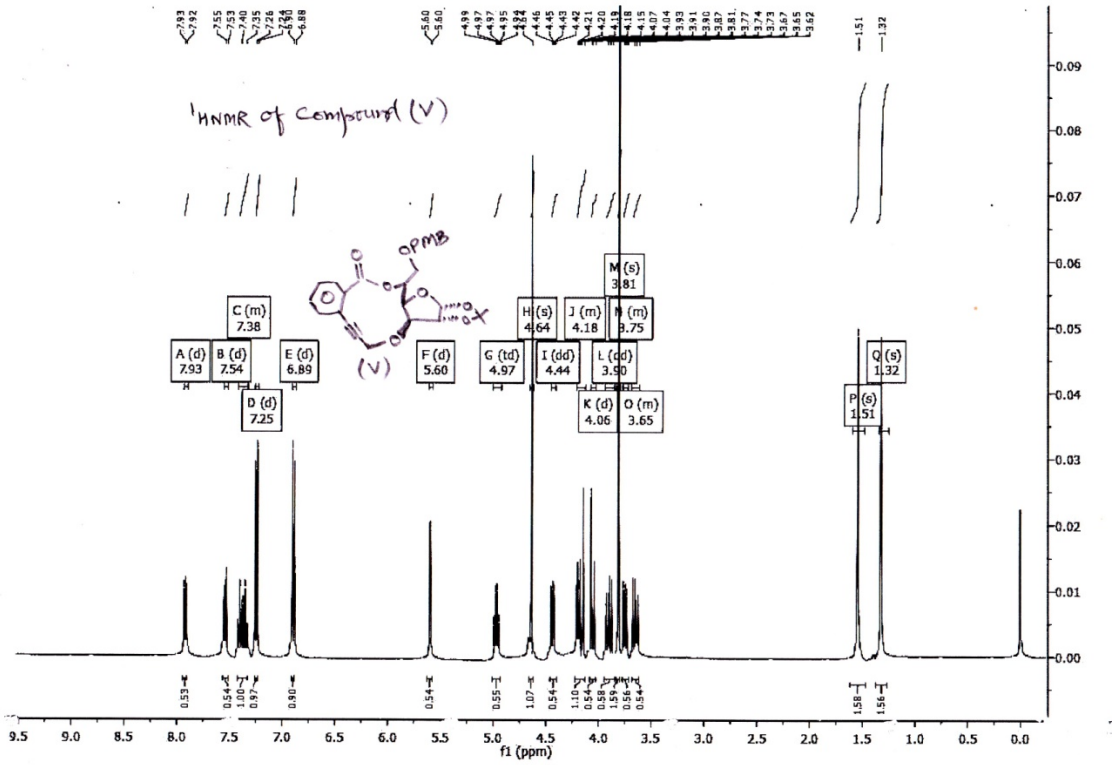

13CNMR of compound (11)
OTs
(11)
f1 (ppm)

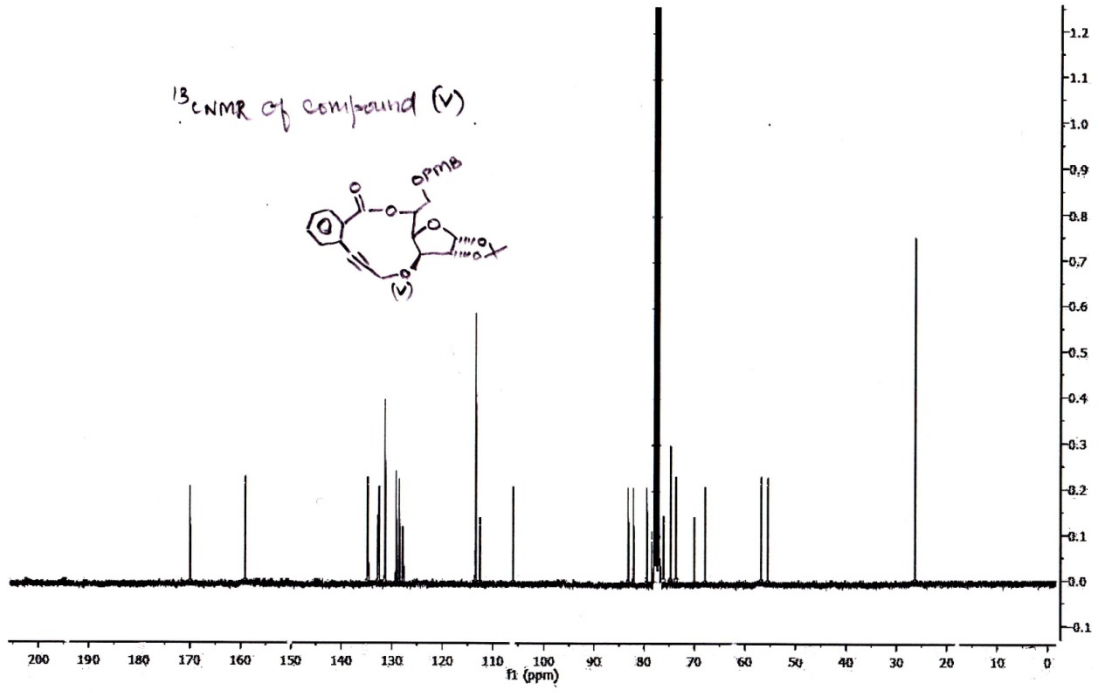

¹HNMR of compound (III)
A (dd) 7.75
B (m) 7.53
C (m) 7.42
D (d) 5.60
E (dt) 4.77
F (t) 4.44
G (dd) 4.32
H (t) 4.20
I (d) 4.16
J (dd) 4.06
K (dd) 3.75
L (s) 1.41
M (s) 1.09
OTBDPS
(III)
f1 (ppm)

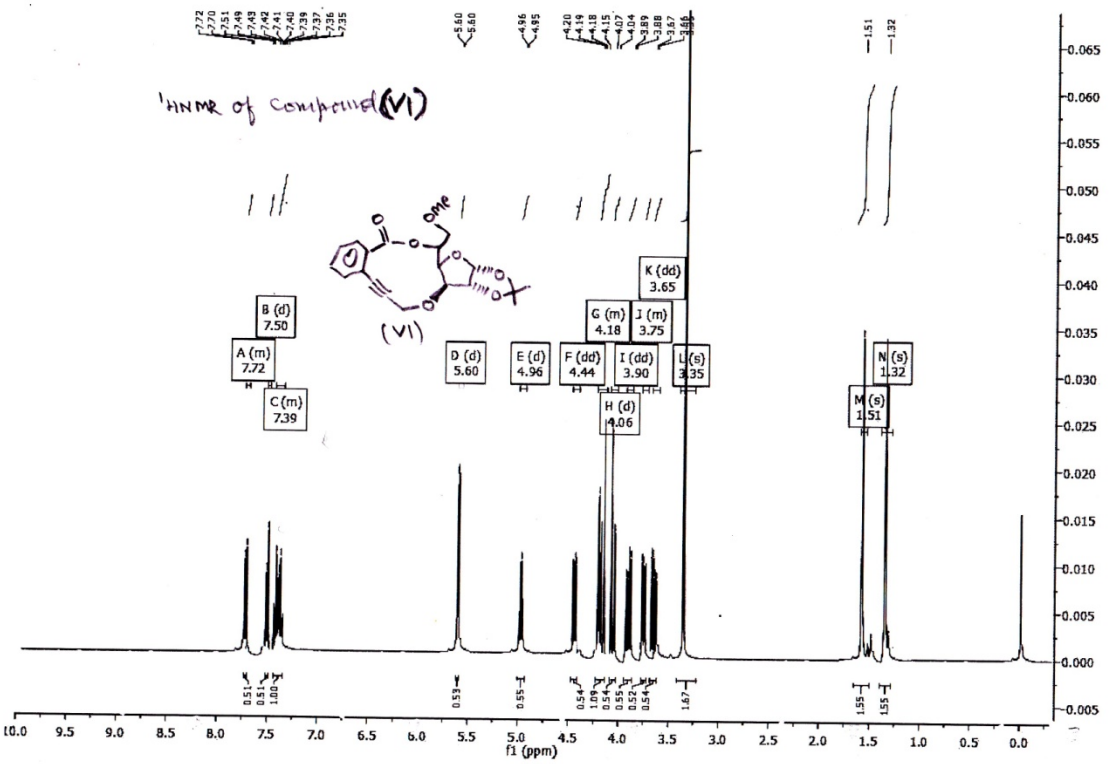

¹³CNMR of compound (III)
OTBDPS
(III)
f1 (ppm)

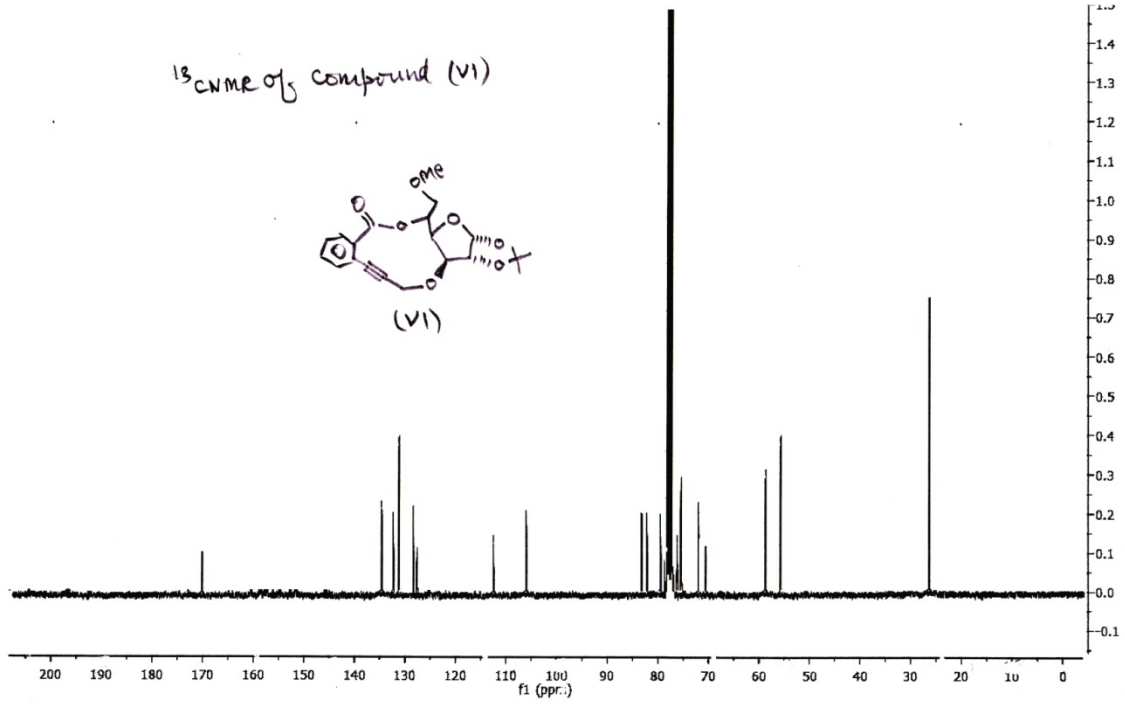

¹HNMR of compound (IV)
A (d) 7.92
B (d) 7.54
C (m) 7.38
D (m) 7.25
E (d) 5.60
F (td) 4.97
G (s) 4.65
H (dd) 4.44
I (m) 4.20
J (d) 4.16
K (d) 4.06
L (dd) 3.90
M (m) 3.75
N (dd) 3.65
O (s) 1.51
P (s) 1.32
(IV)
f1 (ppm)

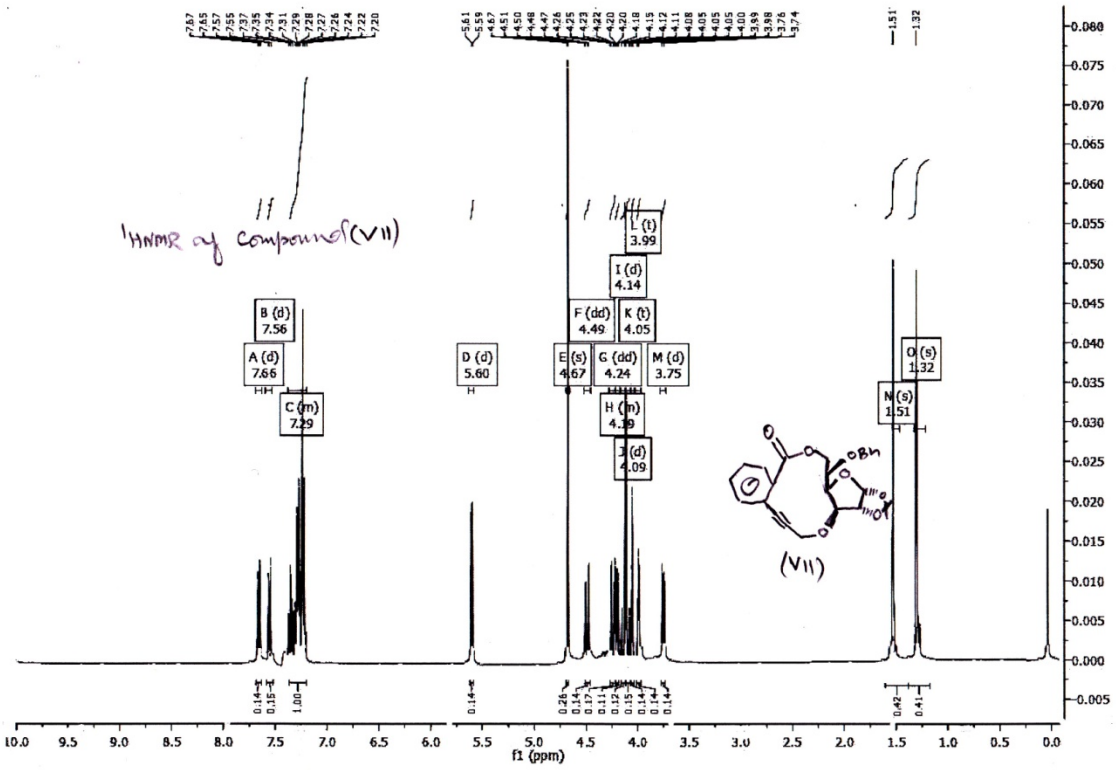

¹³CNMR of compound (IV)
(IV)
f1 (ppm)

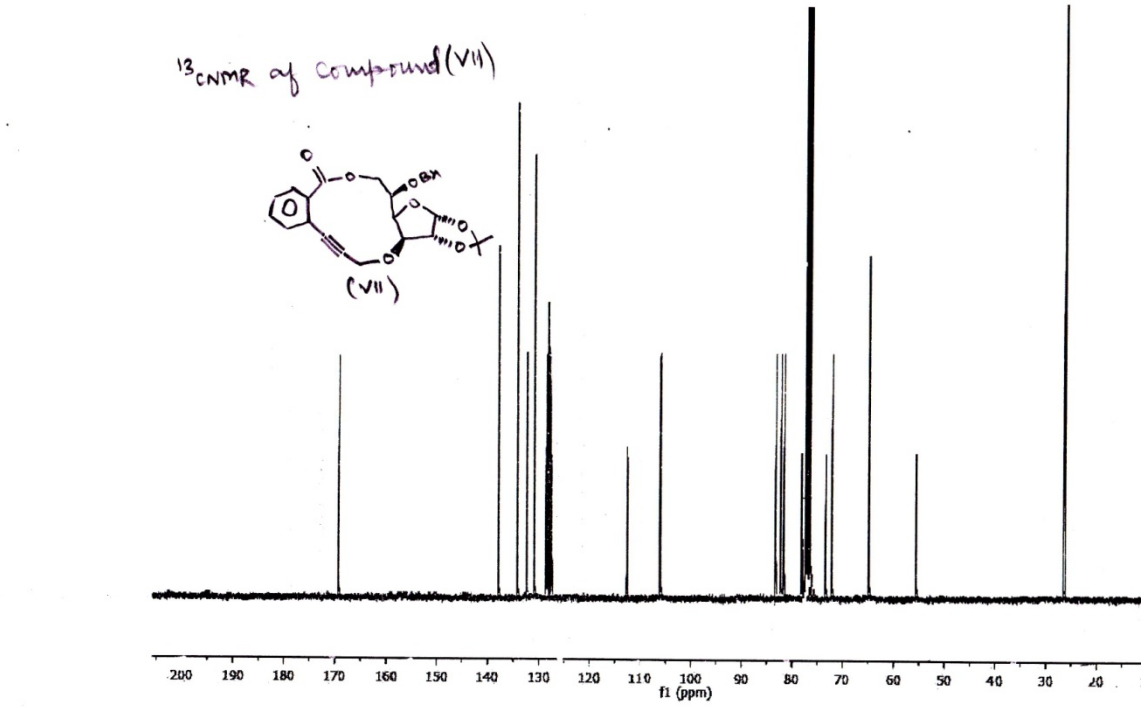

1HNMR of Compound (V)
A (d) 7.93
B (d) 7.54
C (m) 7.38
D (d) 7.25
E (d) 6.89
F (d) 5.60
G (td) 4.97
H (s) 4.64
I (dd) 4.44
J (m) 4.18
K (d) 4.06
L (dd) 3.90
M (s) 3.81
N (m) 3.75
O (m) 3.65
P (s) 1.51
Q (s) 1.32
(V)
f1 (ppm)

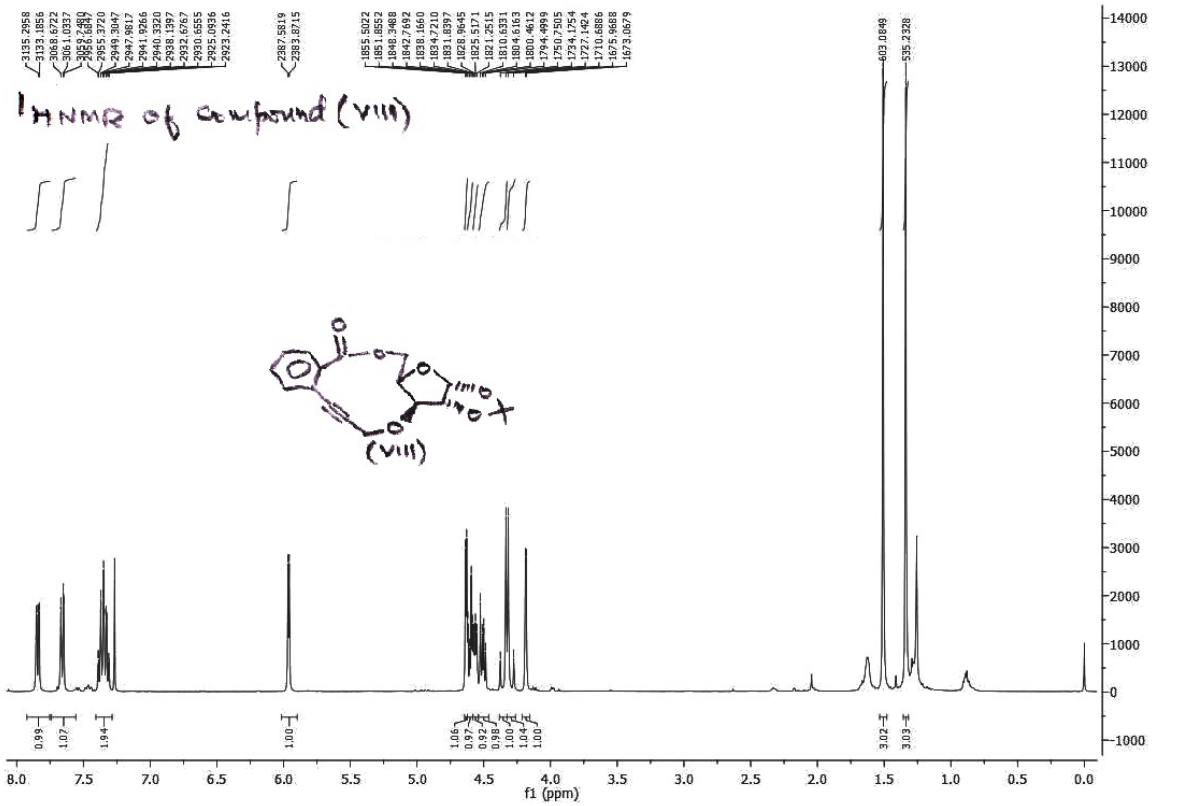

13CNMR of compound (V)
(V)
f1 (ppm)

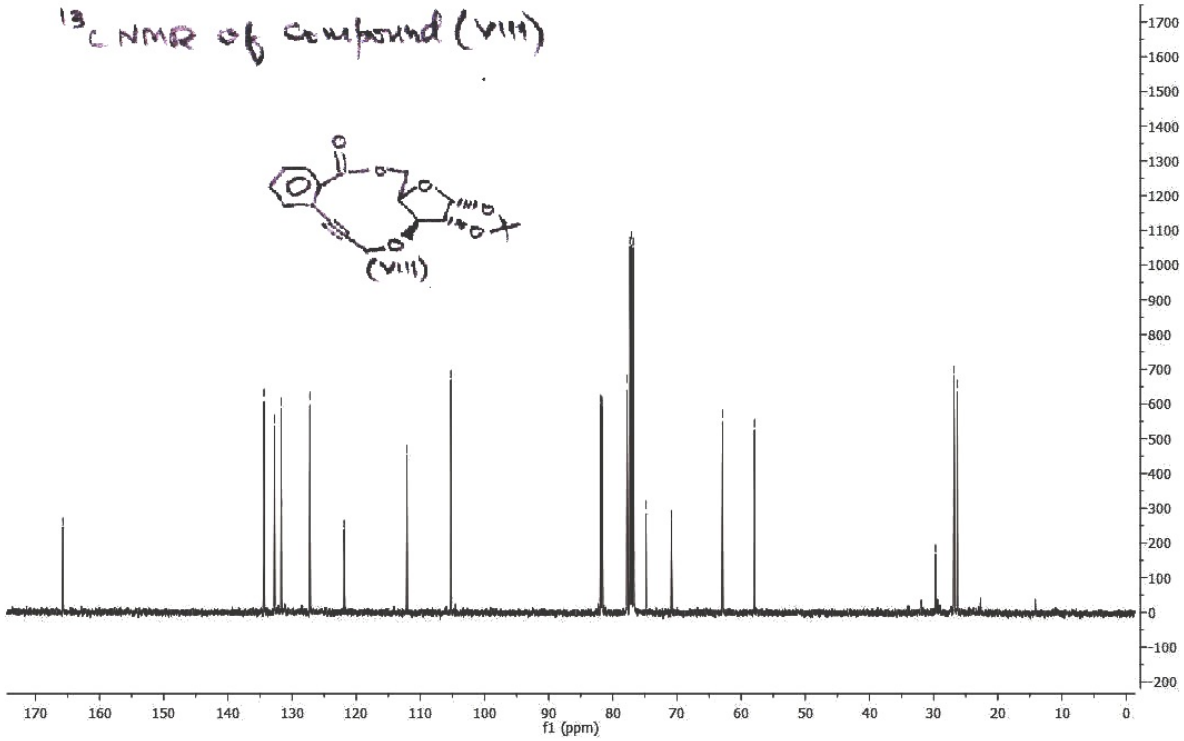

¹HNMR of compound (VI)
OMe
(VI)
A (m) 7.72
B (d) 7.50
C (m) 7.39
D (d) 5.60
E (d) 4.96
F (dd) 4.44
G (m) 4.18
H (d) 4.06
I (dd) 3.90
J (m) 3.75
K (dd) 3.65
L (s) 3.35
M (s) 1.51
N (s) 1.32
f1 (ppm)

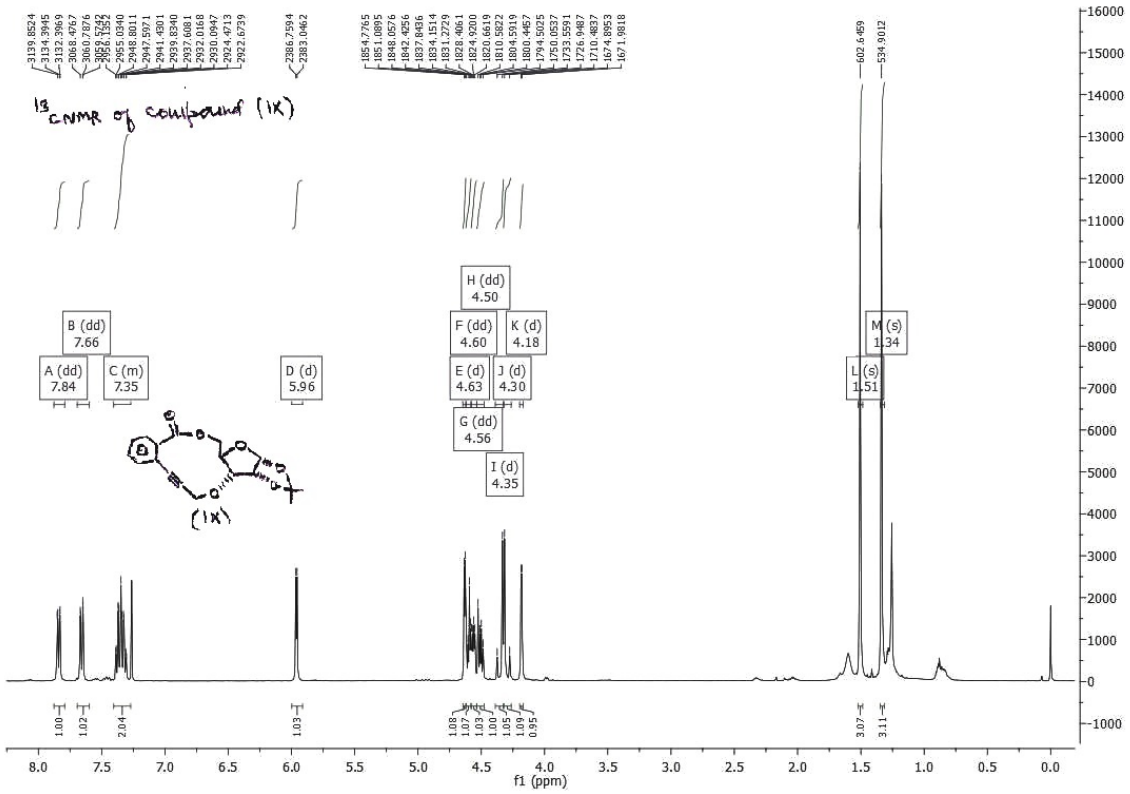

¹³CNMR of compound (VI)
OMe
(VI)
f1 (ppm)

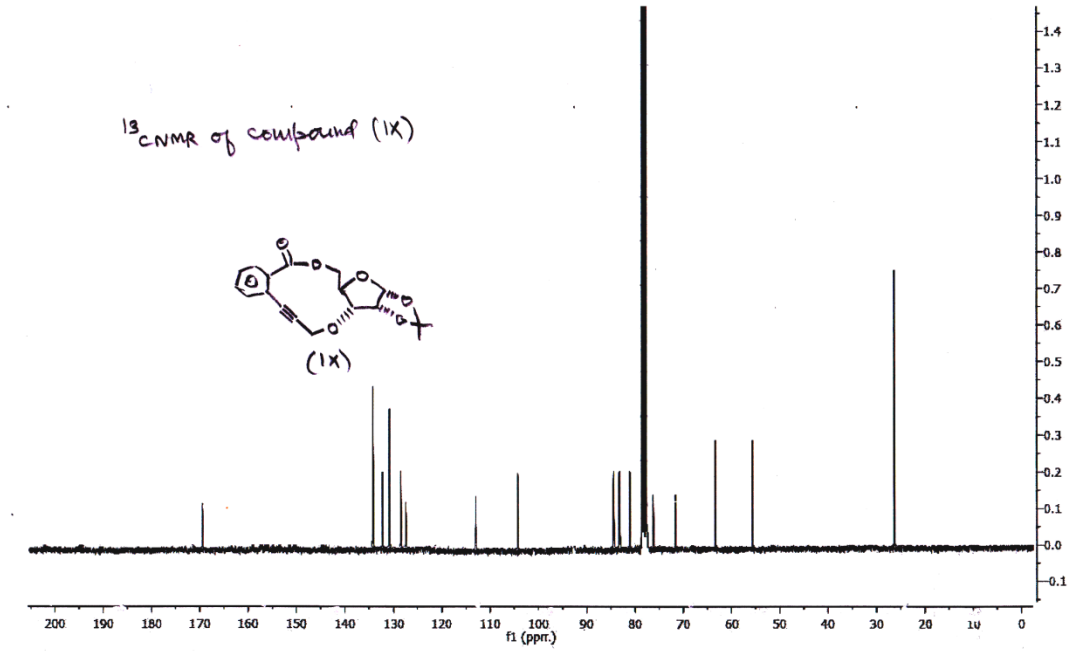

1HNMR of compound(VII)
A (d) 7.66
B (d) 7.56
C (m) 7.29
D (d) 5.60
E (s) 4.67
F (dd) 4.49
G (dd) 4.24
H (m) 4.19
I (d) 4.14
J (d) 4.09
K (t) 4.05
L (t) 3.99
M (d) 3.75
N (s) 1.51
O (s) 1.32
(VII)
f1 (ppm)

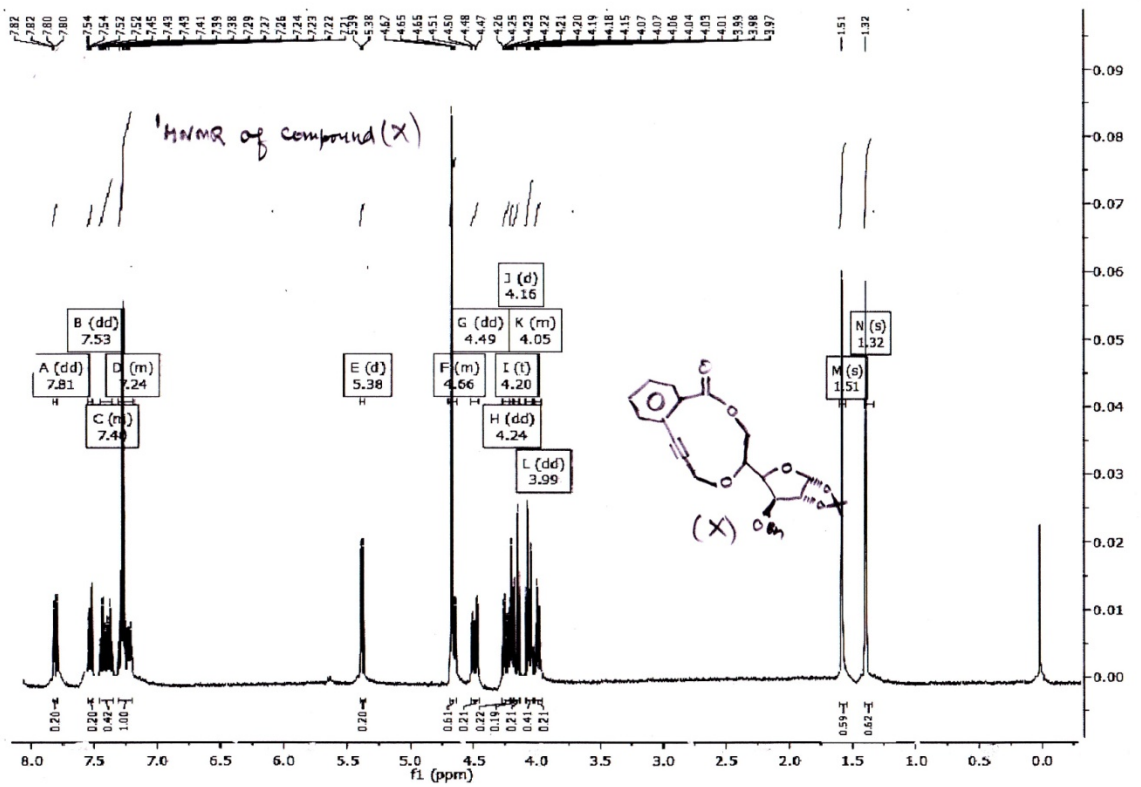

13CNMR of compound(VII)
(VII)
f1 (ppm)

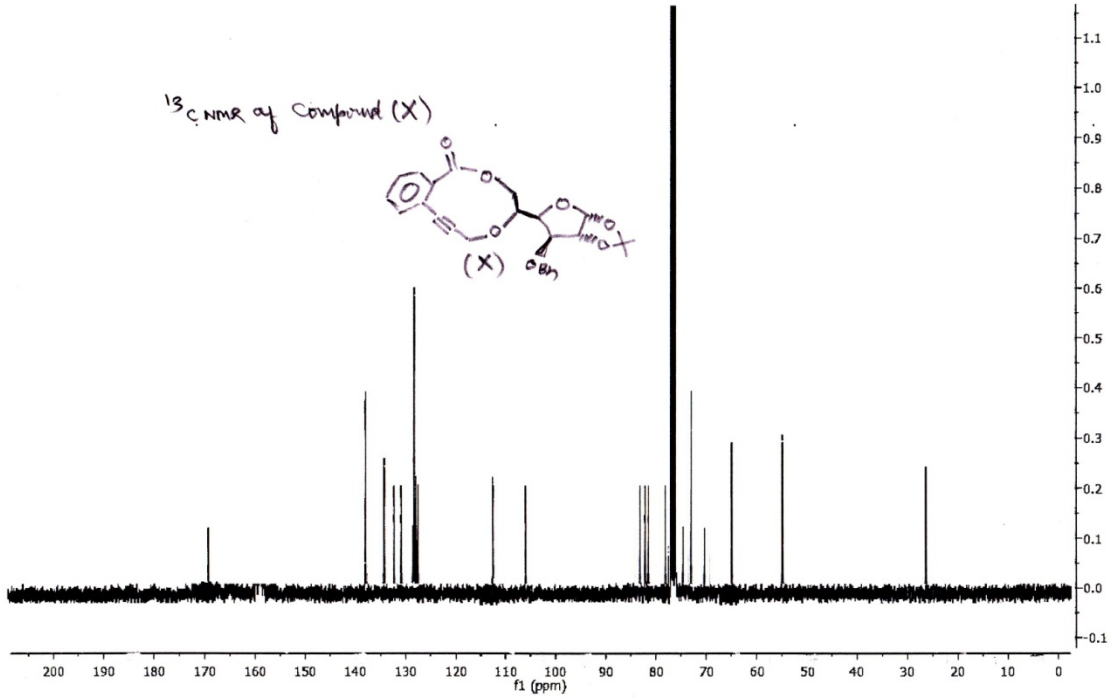

^{1}H NMR of compound (VIII)
(VIII)
f1 (ppm)

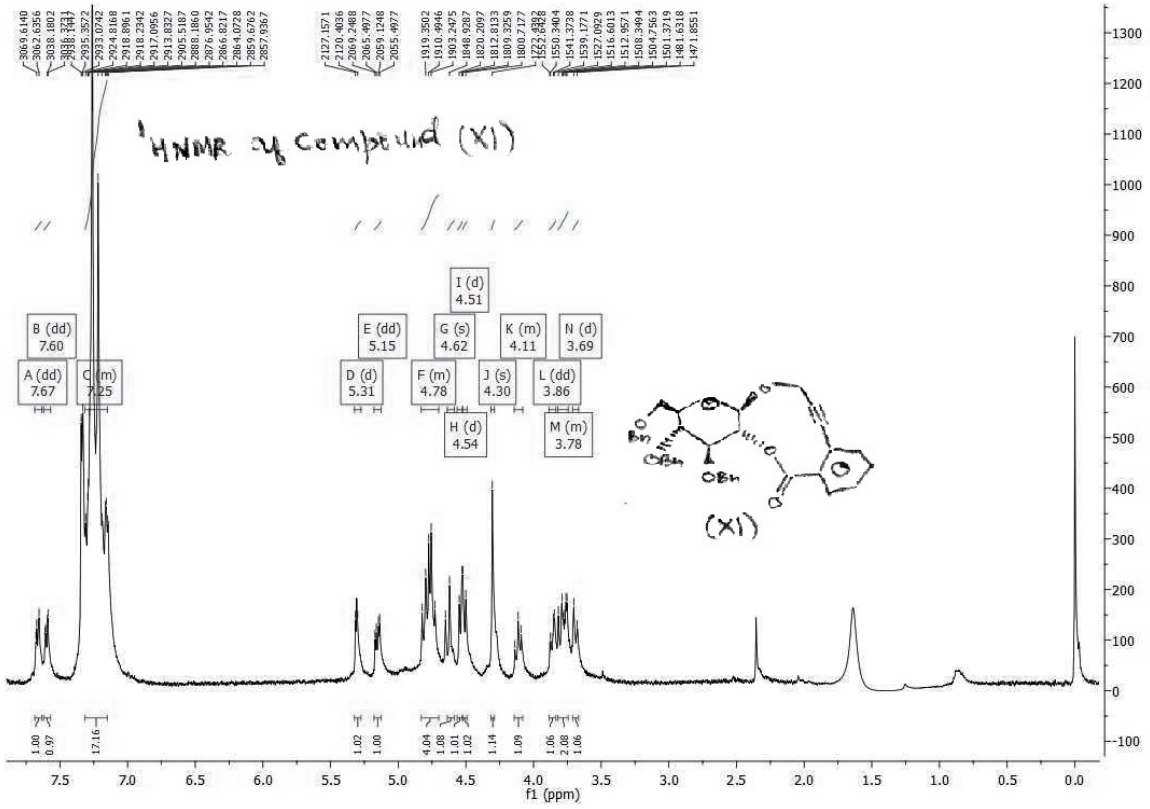

^{13}C NMR of compound (VIII)
(VIII)
f1 (ppm)

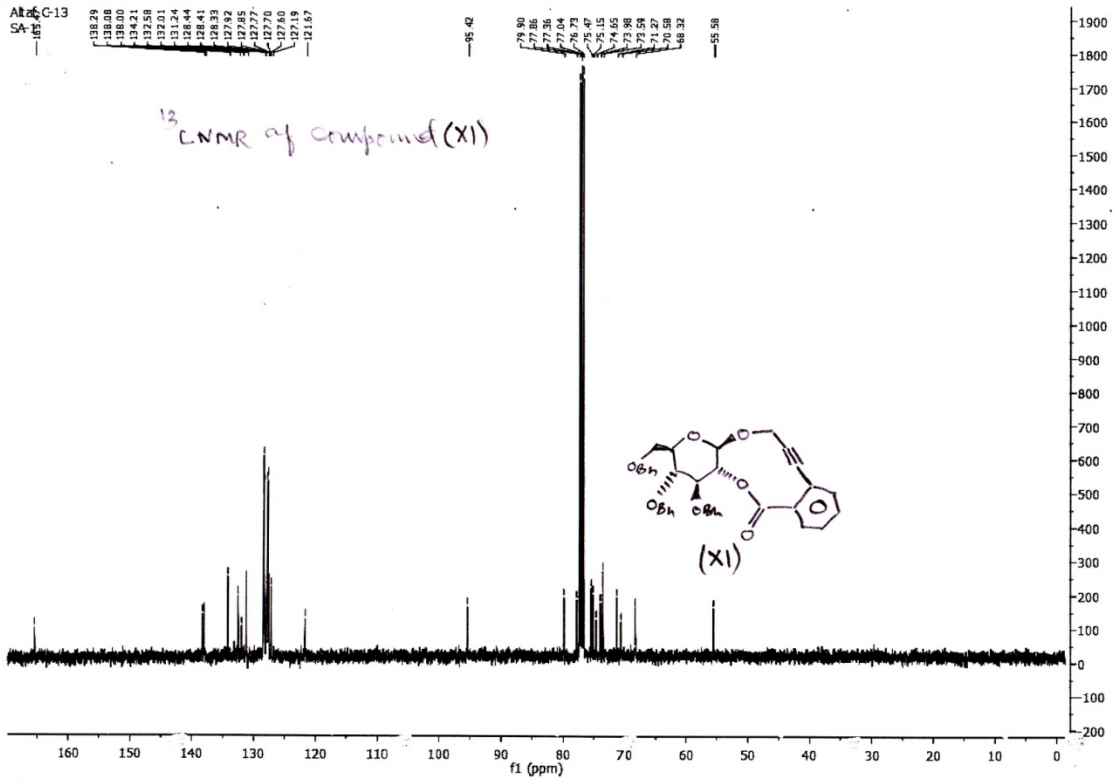

13CNMR of compound (IX)
B (dd) 7.66
A (dd) 7.84
C (m) 7.35
D (d) 5.96
H (dd) 4.50
F (dd) 4.60
K (d) 4.18
E (d) 4.63
J (d) 4.30
G (dd) 4.56
I (d) 4.35
M (s) 1.34
L (s) 1.51
(IX)
f1 (ppm)


13CNMR of compound (IX)
(IX)
f1 (ppm)

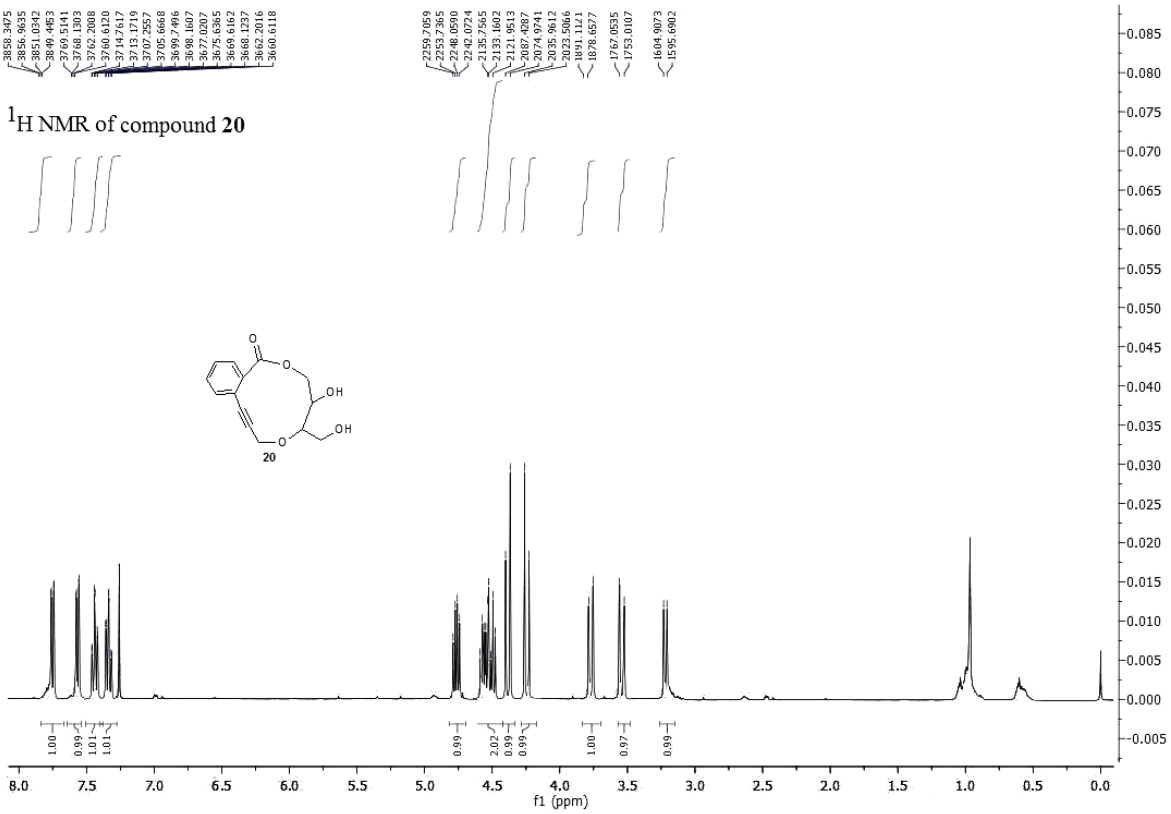

¹H NMR of compound (X)
A (dd) 7.81
B (dd) 7.53
C (m) 7.40
D (m) 7.24
E (d) 5.38
F (m) 4.66
G (dd) 4.49
H (dd) 4.24
I (t) 4.20
J (d) 4.16
K (m) 4.05
L (dd) 3.99
M (s) 1.51
N (s) 1.32
(X)
f1 (ppm)


¹³C NMR of Compound (X)
(X)
f1 (ppm)

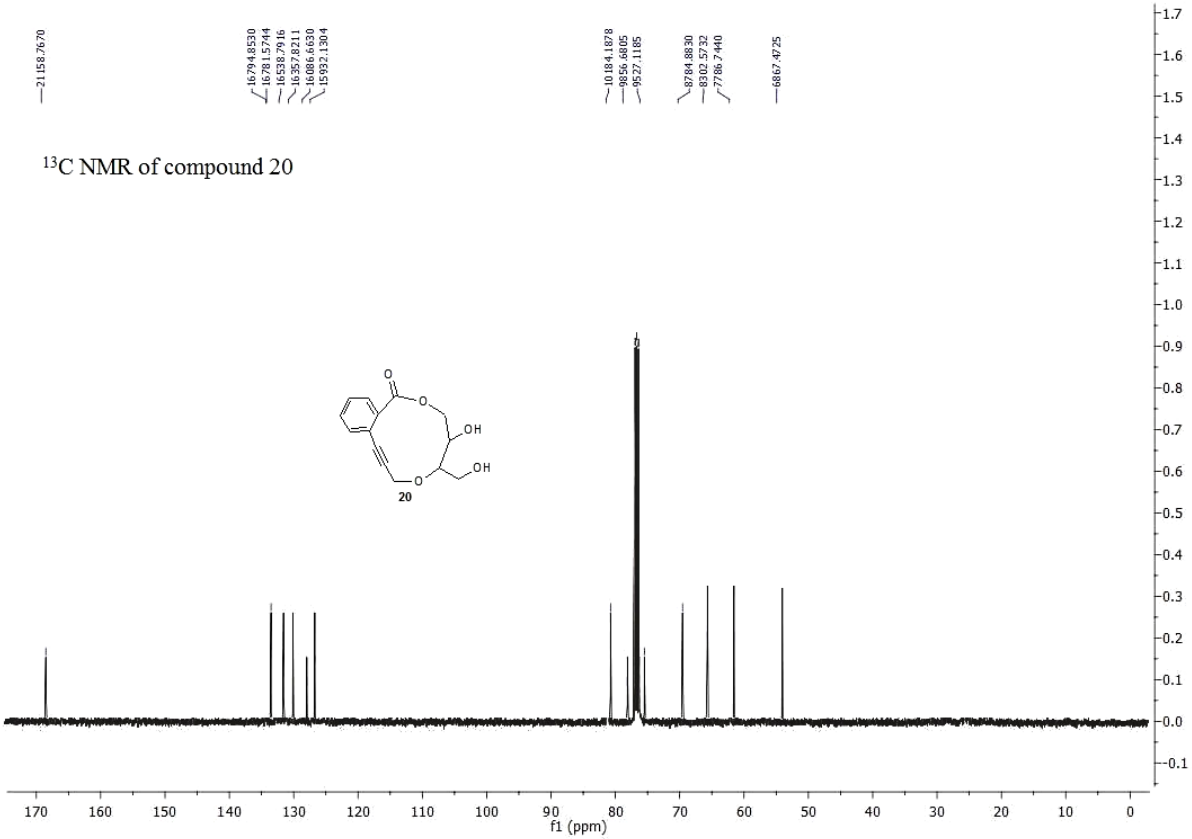

1HNMR of Compound (XI)
B (dd) 7.60
A (dd) 7.67
C (m) 7.25
D (d) 5.31
E (dd) 5.15
F (m) 4.78
G (s) 4.62
H (d) 4.54
I (d) 4.51
J (s) 4.30
K (m) 4.11
L (dd) 3.86
M (m) 3.78
N (d) 3.69
(XI)
f1 (ppm)


13C-NMR of Compound (XI)
(XI)
f1 (ppm)

^{1}H NMR of compound **20**



^{13}C NMR of compound 20



References

1. A. Hussain, S.K. Yousuf, D. Kumar, M. R. Lambu, B. Singh, D. Mukherjee, *Tetrahedron,* **2013**, *69*, 5517–5524.
2. A. Hussain, S.K. Yousuf, D. Kumar, M. R. Lambu, B. Singh, S. Maity, D. Mukherjee, *Adv. Synth. Catal.* **2012**, *354*, 1933–1940.
3. S. Hotha, S. Kashyap, *J. Am. Chem. Soc.* **2006**, *128*, 9620-9621.