Supporting Information

Amino and Hydroxy-Functionalized 11-Azaartemisinins and Their Derivatives

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1. Experimental Details and Characterization Data.

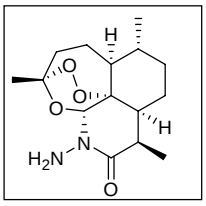
Experimental

General. All glass apparatus were oven dried prior to use. Melting points were taken in open capillaries on Complab melting point apparatus and are presented uncorrected. Infrared spectra were recorded on a Perkin-Elmer FT-IR RXI spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded using Bruker Supercon Magnet DPX-200 or DRX-300 spectrometers (operating at 200 MHz and 300 MHz respectively for 1H; 50 MHz and 75 MHz respectively for ^{13}C) using $CDCl_3$ as solvent. Tetramethylsilane (δ 0.00 ppm) served as an internal standard in ^{1}H NMR and $CDCl_3$ (δ 77.0 ppm) in ^{13}C NMR. Chemical shifts are reported in parts per million. Splitting patterns are described as singlet (s), doublet (d), triplet (t), quintet (quin), multiplet (m), and broad (br). Fast atom bombardment mass spectra (FAB-MS) were obtained on a JEOL SX-102/DA-6000 mass spectrometer using argon/xenon (6 kV, 10 mA) as the FAB gas. Glycerol or *m*-nitrobenzyl alcohol was used as matrix. Electrospray mass spectra (ES-MS) were recorded on a Micromass Quattro II triple quadruple mass spectrometer. High-resolution electron impact mass spectra (EI-HRMS) were obtained on JEOL MS route 600H instrument. Elemental analyses were performed on Vario EL-III C H N S analyzer (Germany), and values were within (0.4% of the calculated values). Column chromatography was performed over Merck silica gel (particle size: 60-120 Mesh) procured from Qualigens (India). All chemicals and reagents were obtained from Aldrich (Milwaukee, WI), Lancaster (England), or Spectrochem (India) and were used without further purification. Nomenclature and Log *p* values of the compounds were assigned using Chem Draw Ultra 7.0 software.

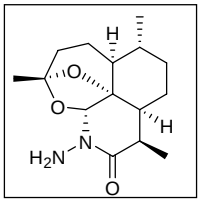
Preparation of N-amino-11-azaartemisnin (9). To a stirred solution of $N_2H_4.H_2O$ (21.28 mL, 425.53 mmol, 20 equiv) in a mixture of $CHCl_3$:MeOH (30:70, 120 mL) at 0 ^{o}C, was added artemisinin **1** (6.0 g, 21.28 mmol) dissolved in $CHCl_3$ (30 mL) gradually over five min. and the reaction mixture was allowed to stir for 1 h at the same temperature. The reaction mixture was diluted with water (300 mL) and extracted with $CHCl_3$ (3 × 100 mL). To the combined organic layer, 2,6-di-*t*-butylphenol (400 mg) and 20% H_2SO_4 (40 mL) and silica gel (40 g) was added and stirred for 12 h at rt. The

reaction mixture was filtered and silica gel was washed with $CHCl_3$ (2 × 100 mL). The combined organic layer was washed with water (2 × 100 mL), dried over anhyd. Na_2SO_4, concentrated under reduced pressure at rt and purified by column chromatography over silica gel using 50% EtOAc/Hexane as eluant to furnish pure N-amino-11-azaartemisinin **9** (4.4 g, 70% yield) as white solid, mp 122-125 ^oC.

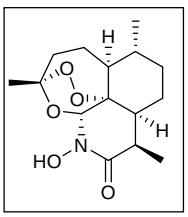
Compounds **11** and **12** were prepared by the above procedure by replacing hydrazine with hydroxylamine and 2-amino ethanol**,** respectively.



N-amino-11-azaartemisinin (9). Yield 70%, white solid, mp 122-125 ^oC; FT-IR (KBr cm^{-1}) 1653, 3315; ^1H NMR (300 MHz, $CDCl_3$) δ 0.86-1.00 (m, 2H), 0.94 (d, 3H, J = 6.2 Hz), 1.10 (d, 3H, J = 7.3 Hz), 1.29-1.44 (m, 3H), 1.33 (s, 3H), 1.59-1.75 (m, 3H), 1.92-2.03 (m, 2H), 2.36 (m, 1H), 3.24-3.33 (m, 1H), 4.63 (brs, 2H, NH_2), 5.26 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.64 (CH_3), 19.80 (CH_3), 22.77 (CH_2), 25.06 (CH_2), 25.51 (CH_3), 32.85 (CH), 33.65 (CH_2), 36.56 (CH_2), 37.38 (CH), 46.01 (CH), 51.35 (CH), 80.66 (C), 80.99 (CH), 104.92 (C), 169.68 (C); ESI-MS (*m/z*) 297 $[M+H]^+$; EI-HRMS Calcd. for $C_{15}H_{24}N_2O_4$ $[M]^+$: 296.1736. Found: 296.1742; Anal. Calcd. for $C_{15}H_{24}N_2O_4$: C, 60.79%, H, 8.16%, N, 9.45%. Found: C, 60.92%, H, 8.65%, N, 9.75%.

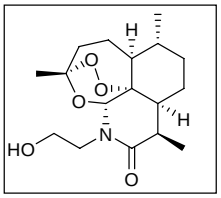


N-amino-10-azadeoxyartemisinin (10). Yield 69%, white solid, mp 147-150 ^oC; FT-IR (KBr cm^{-1}) 1655, 3454; ^1H NMR (300 MHz, $CDCl_3$) δ 0.85-1.08 (m, 2H), 0.93 (d, 3H, J = 5.7 Hz), 1.16 (d, 3H, J = 7.3 Hz), 1.24-1.37 (m, 3H), 1.44 (s, 3H), 1.58-2.00 (m, 6H), 3.03-3.12 (m, 1H), 4.43 (brs, 2H, NH_2), 5.23 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.54 (CH_3), 18.70 (CH_3), 22.29 (CH_2), 23.01 (CH_2), 24.45 (CH_3), 33.25 (CH), 33.66 (CH_2), 34.78 (CH_2), 35.31 (CH), 43.01 (CH), 45.90 (CH), 82.87 (C), 88.06 (CH), 107.74 (C), 170.56 (C); ESI-MS (*m/z*) 281 $[M+H]^+$; EI-HRMS Calcd. for $C_{15}H_{24}N_2O_3$ $[M]^+$: 280.1787. Found: 280.1785; Anal. Calcd. for $C_{15}H_{24}N_2O_3$: C, 64.26%, H, 8.63%, N, 9.99%. Found: C, 64.35%, H, 8.93%, N, 9.88%.



N-hydroxy-11-azaartemisinin (**11)**. Yield 45%, white solid, mp 165-167 °C; IR (KBr, cm^{-1}) 1649, 3418; ^1H NMR (300 MHz, $CDCl_3$) δ 0.89-

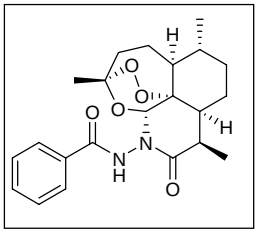
1.02 (m, 2H), 0.97 (d, 3H, J = 5.9 Hz), 1.10 (d, 3H, J = 7.3 Hz), 1.31-1.52 (m, 3H), 1.43 (s, 3H), 1.63-1.77(m, 3H), 1.94-2.07 (m, 2H), 2.35-2.46 (m, 1H), 3.35-3.44 (m, 1H), 5.40 (s, 1H), 8.81 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.11 (CH_3), 19.88 (CH_3), 22.94 (CH_2), 25.18 (CH_2), 25.47 (CH_3), 32.98 (CH), 33.75 (CH_2), 36.70 (CH_2), 37.52 (CH), 46.64 (CH), 51.49 (CH), 81.22 (CH), 81.52 (C), 105.27 (C), 170.08 (C); ESIMS (m/z) 298 $[M+H]^+$; Anal. Calcd for $C_{15}H_{23}NO_5$: C, 60.59%, H, 7.80%, N, 4.71%; found: C, 60.64%, H, 7.89%, N, 4.53%; HRMS [ESI] Calcd for $C_{15}H_{24}NO_5$ $[M+H]^+$: 298.1654; found: 298.1631.



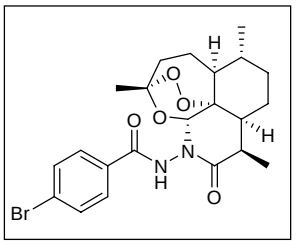
N-ethanol-11-azaartemisinin (**12)**. Yield 52%, white solid, mp 145-147 ^{o}C; IR (KBr, cm^{-1}) 1629, 3395; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91-1.04 (m, 2H), 0.98 (d, 3H, J = 5.8 Hz), 1.13 (d, 3H, J = 7.3 Hz), 1.27-1.46 (m, 3H), 1.36 (s, 3H), 1.65-1.80 (m, 3H), 1.99-2.03 (m, 2H), 2.35-2.45 (m, 1H), 3.27-3.36 (m, 1H), 3.48-3.58 (m, 2H), 3.78-3.81 (m, 3H), 5.27 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.91 (CH_3), 19.86 (CH_3), 22.94 (CH_2), 25.18 (CH_2), 25.52 (CH_3), 33.33 (CH), 33.78 (CH_2), 36.77 (CH_2), 37.65 (CH), 45.88 (CH), 46.30 (CH_2), 51.46 (CH), 62.60 (CH_2), 79.58 (CH), 80.29 (C), 105.10 (C), 174.03 (C); ESIMS (m/z) 326 $[M+H]^+$; Anal. Calcd for $C_{17}H_{27}NO_5$: C, 62.75%, H, 8.36%, N, 4.30%; found: C, 62.32%, H, 8.32%, N, 4.55%; HRMS [ESI] Calcd for $C_{17}H_{28}NO_5$: 326.1967 $[M+H]^+$: found: 326.1960.

General procedure for preparation of amide derivatives (13a-d) of N-amino-11-azaartemisnin (9): Preparation of compound (13a): To a stirred solution of compound **9** (500 mg, 1.689 mmol) and Et_3N (1.17 mL, 11.57 mmol, 5 equiv) in dry benzene (5 mL) at 0 $^{\circ}$C, was added benzoyl chloride (0.97 mL, 6.96 mmol, 5 equiv) dissolved in dry benzene (5 mL) and the reaction mixture was allowed to stir at same temperature for 2 h. The reaction mixture was quenched with water (10 mL) and extracted with ether (3 × 25 mL). The combined organic layer was washed with saturated $NaHCO_3$ (3 × 10 mL), dried over anhyd Na_2SO_4 and concentrated under reduced pressure at rt. Purification by column chromatography over silica gel using 20% EtOAc/Hexane as eluant furnished compound **13a** (628 mg, 93% yield) as a white solid, mp 218-200 ^{o}C.

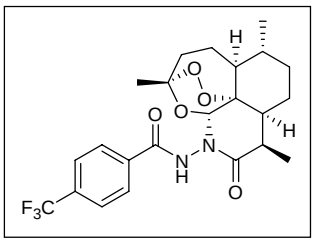
Compounds **13b-d,** were prepared by the above procedure by replacing benzoyl chloride with *p*-bromobenzoyl chloride, *p*-trifluoromethylbenzoyl chloride and 4-phenylbenzoyl chloride**,** respectively.



13a Yield 93%, white solid, mp 218-220 ^{o}C; FT-IR (KBr cm^{-1}) 1654, 1701, 3246; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (d, 3H, J = 6.3 Hz), 1.05-1.09 (m, 1H), 1.22 (d, 3H, J = 7.3 Hz), 1.32-1.52 (m, 3H), 1.47 (s, 3H), 1.70-2.05 (m, 6H), 2.39-2.50 (m, 1H), 3.44-3.48 (m 1H), 5.62 (s, 1H), 7.24-7.77 (m, 5H, Ar), 9.33 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.73 (CH_3), 19.88 (CH_3), 22.74 (CH_2), 25.26 (CH_2), 25.49 (CH_3), 33.71 (CH), 34.05 (CH_2), 36.72 (CH_2), 37.58 (CH), 46.28 (CH), 51.51 (CH), 80.25 (C), 81.29 (CH), 105.19 (C), 127.68 (2 × CH), 128.50 (2 × CH), 131.66 (C), 132.04 (CH), 165.94 (C), 172.51 (C); ESI-MS (*m/z*) 401 $[M+H]^+$; Anal. Calcd. for $C_{22}H_{28}N_2O_5$: C, 65.98%, H, 7.05%, N, 7.00%. Found: C, 66.06%, H, 7.39%, N, 7.01%.

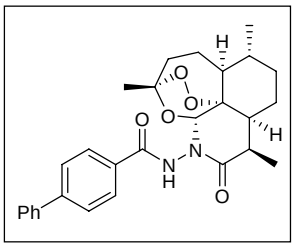


13b. Yield 60%, white solid, mp 230-232 ^{o}C; FT-IR (KBr cm^{-1}) 1692, 1727, 3450; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.97-1.01 (m, 1H), 0.98 (d, 3H, J = 6.0 Hz), 1.21 (d, 3H, J = 7.3 Hz), 1.39-2.04 (m, 8H), 1.48 (s, 3H), 2.39-2.49 (m, 1H), 3.42-3.46 (m, 1H), 5.59 (s, 1H), 7.38 (d, 2H, Ar, J = 8.4 Hz), 7.62 (d, 2H, Ar, J = 8.4 Hz), 9.87 (brs, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.79 (CH_3), 19.90 (CH_3), 22.87 (CH_2), 25.29 (CH_2), 25.47 (CH_3), 33.71 (CH), 34.07 (CH_2), 36.70 (CH_2), 37.64 (CH), 46.14 (CH), 51.48 (CH), 80.03 (C), 81.26 (CH), 105.24 (C), 127.09 (C), 129.27 (2 × CH), 130.22 (C), 131.68 (2 × CH), 164.66 (C), 172.99 (C); ESI-MS (*m/z*) 479 $[M+H]^+$; Anal. Calcd. for $C_{22}H_{27}N_2O_5Br$: C, 55.12%, H, 5.68%, N, 5.84%. Found: C, 54.80%, H, 6.06%, N, 5.80%.



13c.Yield 85%, white solid, mp 217-220 ^{o}C; FT-IR (KBr cm^{-1}) 1653, 1702, 3422, ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.99 (d, 3H, J = 6.1 Hz), 1.03-1.12 (1H), 1.23 (d, 3H, J = 7.3 Hz), 1.37-2.05 (m, 9H), 1.50 (s, 3H), 2.40-2.49 (m, 1H), 3.42-3.5 (m, 1H), 5.60 (s, 1H), 7.93 (d, 2H, Ar, J = 8.2 Hz), 7.84 (d, 2H, Ar, J = 8.2 Hz), 10.35 (brs, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.83 (CH_3),

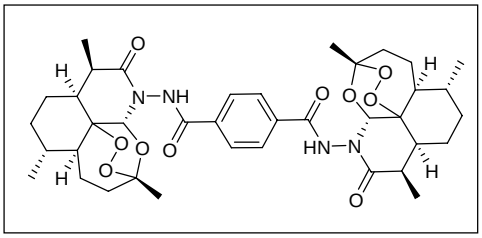
19.90 (CH_3), 22.95 (CH_2), 25.28 (CH_2), 25.40 (CH_3), 33.71 (CH), 34.05 (CH_2), 36.64 (CH_2), 37.66 (CH), 46.02 (CH), 51.42 (CH), 79.87 (C), 81.23 (CH), 105.29 (C), 125.48 (q, C, $J_{C\text{-}F}$ = 3.8 Hz), 128.09 (4 × CH), 133.14 (C), 134.34 (CH), 163.81 (C), 173.26 (C); ESI-MS (*m/z*) 469 $[M+H]^+$; EI-HRMS Calcd. for $C_{23}H_{27}N_2O_5F_3$ $[M]^+$: 468.1872. Found: 468.1843.



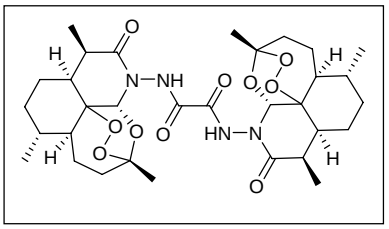
13d. Yield 93%, white solid, mp 205-207 ^oC; FT-IR (KBr cm^{-1}) 1614, 1675, 3396; ^1H NMR (300 MHz, $CDCl_3$) δ 0.99 (d, 3H, J = 6.1 Hz)), 1.07-1.11 (m, 1H), 1.25 (d, 3H, J = 7.3 Hz), 1.38-2.06 (m, 7H), 1.51 (s, 3H), 1.76-2.06 (m, 2H), 2.41-2.51 (m, 1H), 3.47-3.50 (m, 1H), 5.66 (s, 1H), 7.37-7.88 (m, 9H, Ar), 9.59 (brs, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.81 (CH_3), 19.91 (CH_3), 22.85 (CH_2), 25.29 (CH_2), 25.55 (CH_3), 33.74 (CH), 34.09 (CH_2), 36.74 (CH_2), 37.61 (CH), 46.26 (CH), 51.52 (CH), 80.22 (CH), 81.32 (C), 105.20 (C), 127.03 (2 × CH), 127.30 (2 × CH), 128.07 (CH), 128.20 (2 × CH), 128.98 (CH), 130.23 (C), 140.16 (C), 144.55 (C), 165.56 (C), 172.78 (C); ESI-MS (*m/z*) 477 $[M+H]^+$; EI-HRMS Calcd. for $C_{28}H_{32}N_2O_5$ $[M]^+$: 476.2311; Found: 476.2310 Anal. Calcd. for $C_{28}H_{32}N_2O_5$: C, 70.57%, H, 6.77%, N, 5.88%. Found: C, 70.89%, H, 7.00%, N, 6.15%.

General procedure for preparation of dimers (13e and 13f) of N-amino-11-azaartemisnin (9): Preparation of compound (13e): To a stirred solution of compound **9** (500 mg, 1.68 mmol) and Et_3N (1.17 mL, 11.57 mmol, 5 equiv) in dry benzene (5 mL) at 0 ^oC, was added acid chloride of terepthalic acid (0.17mL, 0.844 mmol, 0.5 equiv) dissolved in dry benzene (5 mL) and the reaction mixture was allowed to stir at same temperature for 2 h. The reaction mixture was quenched with water (10 mL) and extracted with ether (3 × 25 mL). The combined organic layer was washed with saturated $NaHCO_3$ (3 × 10 mL), dried over anhyd Na_2SO_4 and concentrated under reduced pressure at rt. Purification by column chromatography over silica gel using 20% EtOAc/Hexane as eluant furnished compound **13e** (240 mg, 20% yield) as a white solid, mp 230-233 ^oC.

Compound **13f** was prepared by the above procedure by replacing terepthoyl chloride with oxalyl chloride.



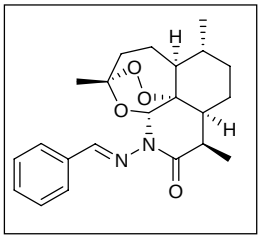
13e. Yield 20% white solid, mp 230-233 ^{o}C; FT-IR (KBr cm^{-1}) 1486, 1658, 3260, 3431; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90-1.06 (m, 4H), 0.98 (d, 6H, J = 6.0 Hz), 1.23 (d, 6H, J = 7.3 Hz), 1.39-2.04 (m, 16H), 1.55 (s, 6H), 2.41-2.49 (m, 2H), 3.44 (m, 2H), 5.66 (s, 2H), 7.81 (s, 4H, Ar), 10.33 (brs, 2H, 2NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.97 (2 × CH_3), 19.94 (2 × CH_3), 22.88 (2 × CH_2), 25.33 (2 × CH_2), 25.60 (2 × CH_3), 33.60 (2 × CH), 34.16 (2 ×CH_2), 36.73 (2 × CH_2), 37.59 (2 × CH), 46.12 (2 × CH), 51.54 (2 × CH), 79.92 (2 × CH), 81.37 (2 × C), 105.26 (2 × C), 128.03 (4 × CH), 134.06 (2 × C), 163.85 (2 × C), 173.31 (C); ESI-MS (*m/z*) 723 $[M+H]^+$; Anal. Calcd. for $C_{38}H_{50}N_4O_{10}$: C, 63.14%, H, 6.97%, N, 7.75%. Found: C, 63.04%, H, 6.56%, N, 8.00%.



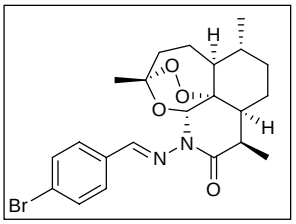
13f. Yield 34%, white solid, mp 245-247 ^{o}C; FT-IR (KBr cm^{-1}) 1488, 1691, 1721, 3415; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89-1.09 (m, 4H), 1.00 (d, 6H, J = 5.6 Hz), 1.19 (d, 6H, J = 7.1 Hz), 1.36-1.52 (m, 7H), 1.40 (s, 6H), 1.69-1.88 (m, 7H), 2.0-2.06 (m, 4H), 2.39-2.49 (m, 2H), 3.40-3.49 (m, 2H), 5.45 (s, 2H), 8.81 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.46 (2 × CH_3), 19.86 (2 × CH_3), 22.63 (2 × CH_2), 25.19 (2 × CH_2), 25.56 (2 × CH_3), 33.82 (2 × CH), 33.91 (2 ×CH_2), 36.69 (2 × CH_2), 37.63 (2 × CH), 46.41 (2 × CH), 51.42 (2 × CH), 80.72 (2 × CH), 80.99 (2 × C), 105.36 (2 × C), 157 (2 × C), 170.78 (2 × C); ESI-MS (*m/z*) 647 $[M+H]^+$; Anal. Calcd. for $C_{32}H_{46}N_4O_{10}$: C, 59.43%, H, 7.17%, N, 8.66%. Found: C, 59.56%, H, 7.35%, N, 8.78%.

General procedure for preparation of imine derivatives (14a-d) of N-amino-11-azaartemisnin (9): Preparation of compound (14a). To a stirred solution of **9** (500 mg, 1.68 mmol) in dry benzene (5 mL) at rt was added benzaldehyde (687 mL, 6.48 mmol, 2 equiv) and amberlyst-15 (50 mg) and the reaction mixture was allowed to stir for 2 h. The reaction mixture was filtered and residue was washed with ether (2 × 50 mL). The combined organic layer was concentrated under reduced pressure at rt and purified by column chromatography over silica gel using 5% EtOAc/Hexane as eluant to furnish compound **14a** (610 mg, 94% yield) as white solid, mp 178-181 ^{o}C.

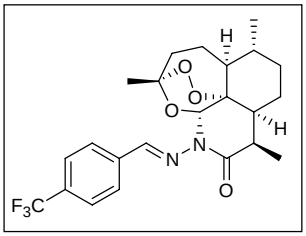
Compounds **14b-d** were prepared by the above procedure by replacing benzaldehyde with *p*-bromobenzaldehyde, *p*-trifluoromethylbenzaldehyde and 4-phenylbenzaldehyde**,** respectively.



14a. Yield 94%**,** white solid, mp 178-181 ^{o}C; FT-IR (KBr cm^{-1}) 1662, 1603; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (d, 3H, J = 6.3 Hz), 1.09-1.16 (m, 2H), 1.20 (d, 3H, J = 7.2 Hz), 1.34 (s, 3H), 1.41-2.07 (m, 8H), 2.45 (m, 1H), 3.50-3.59 (m, 1H), 5.77 (s, 1H), 7.39-7.83 (m, 5H, Ar), 8.61 (s, 1H, imine H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.67 (CH_3), 19.99 (CH_3), 23.02 (CH_2), 25.23 (CH_2), 25.66 (CH_3), 33.91 (CH_2), 34.36 (CH), 36.74 (CH_2), 37.59 (CH), 46.59 (CH), 51.72 (CH), 81.24 (C), 81.80 (CH), 105.20 (C), 128.48 (2 × CH), 128.78 (2 × CH), 131.30 (C), 133.96 (C), 164.67 (CH), 169.12 (C); ESI-MS (*m/z*) 385 $[M+H]^+$; EI-HRMS Calcd. for $C_{22}H_{28}N_2O_4$ $[M]^+$: 384.2049. Found: 384.2024; Anal. Calcd. for $C_{22}H_{28}N_2O_4$: C, 68.73%, H, 7.34%, N, 7.29%. Found: C, 68.80%, H, 7.16%, N, 7.25%.

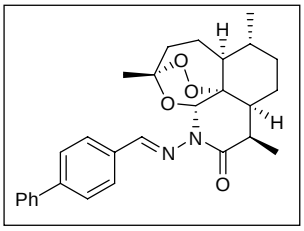


14b. Yield 96%, white solid, mp 176-178 ^{o}C; FT-IR (KBr cm^{-1}) 1659; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (d, 3H, J = 6.3 Hz), 1.09 (m, 2H), 1.19 (d, 3H, J = 7.2 Hz), 1.33 (s, 3H), 1.41-2.06 (m, 8H), 2.45 (m, 1H), 3.49-3.58 (m, 1H), 5.76 (s, 1H), 7.55 (d, 2H, Ar, J = 8.5 Hz), 7.67 (d, 2H, Ar, J = 8.5 Hz), 8.60 (s, 1H, imine H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.64 (CH_3), 19.96 (CH_3), 23.00 (CH_2), 25.21 (CH_2), 25.64 (CH_3), 33.86 (CH_2), 34.42 (CH), 36.70 (CH_2), 37.60 (CH), 46.52 (CH), 51.67 (CH), 81.18 (C), 81.92 (CH), 105.23 (C), 125.63 (C), 129.76 (2 × CH), 132.04 (2 × CH), 133.01 (C), 162.36 (CH), 169.24 (C); ESI-MS (*m/z*) 463 $[M]^+$, 465 $[M+2H]^+$; EI-HRMS Calcd. for $C_{22}H_{27}N_2O_4Br$ $[M]^+$: 462.1154. Found: 462.1152; Anal. Calcd. for $C_{22}H_{27}N_2O_4Br$: C, 56.88%, H, 6.28%, N, 6.02%. Found: C, 57.02%, H, 6.28%, N, 6.08%.



14c. Yield 82%, white solid, mp 170-173 ^{o}C; FT-IR (KBr cm^{-1}), 1672, ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (d, 3H, J = 6.2 Hz), 1.09-1.13 (m, 2H), 1.21 (d, 3H, J = 7.2 Hz), 1.33 (s, 3H), 1.41-

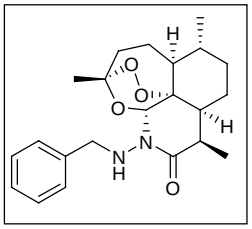
2.06 (m, 8H), 2.40-2.51 (m, 1H), 3.51-3.59 (m, 1H), 5.79 (s, 1H), 7.67 (d, 2H, Ar, J = 8.1 Hz), 8.74 (d, 2H, Ar, J = 8.1 Hz), 8.74 (s, 1H, imine H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.62 (CH_3), 19.92 (CH_3), 22.99 (CH_2), 25.19 (CH_2), 25.60 (CH_3), 33.83 (CH_2), 34.51 (CH), 36.67 (CH_2), 37.59 (CH), 46.46 (CH), 51.64 (CH), 81.15 (C), 82.05 (CH), 105.27 (C), 125.71 (q, C, $J_{C\text{-}F}$ = 4.0 Hz, CF_3), 128.45 (4 × CH), 137.56 (2 × C), 160.75 (CH), 169.38 (C); ESI-MS (*m/z*) 453 $[M+H]^+$; EI-HRMS Calcd. for $C_{23}H_{27}N_2O_4F_3$ $[M]^+$: 452.1923. Found: 452.1922.



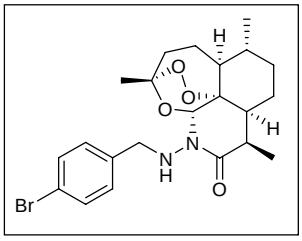
14d. Yield 94%, white solid, mp 118-120 ^{o}C; FT-IR (KBr cm^{-1}) 1601, 1687; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85-1.13 (m, 2H), 1.05 (d, 3H, J = 6.3 Hz), 1.22 (d, 3H, J = 7.3 Hz), 1.35 (s, 3H), 1.42-1.81 (m, 6H), 2.02-2.08 (m, 2H), 2.41-2.52 (m, 1H), 3.52-3.60 (m, 1H), 5.80 (s, 1H), 7.36-7.91 (m, 9H, Ar), 8.66 (s, 1H, imine H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.67 (CH_3), 19.97 (CH_3), 23.01 (CH_2), 25.22 (CH_2), 25.66 (CH_3), 33.90 (CH_2), 34.38 (CH), 36.73 (CH_2), 37.58 (CH), 46.58 (CH), 51.72 (CH), 81.23 (C), 81.81 (CH), 105.20 (C), 127.33 (2 × CH), 127.46 (2 × CH), 127.99 (CH), 128.91 (2 × CH), 129.05 (2 × CH), 132.92 (C), 140.55 (C), 143.99 (C), 164.10 (CH), 169.14 (C); ESI-MS (*m/z*) 461 $[M+H]^+$; Anal. Calcd. for $C_{28}H_{32}N_2O_4$: C, 73.02%, H, 7.00%, N, 6.08%. Found: C, 72.95%, H, 6.91%, N, 6.00%.

General procedure for preparation of amine derivatives of N-amino-11-azaartemisnin (9): Preparation of compound (15a): To a stirred solution of compound **14a** (500 mg, 1.30 mmol) in dry benzene (15 mL) at 0 ^{o}C was added $NaBH_4$ (247 mg, 6.50 mmol, 5 equiv) and the reaction mixture was allowed to stir at same temperature for 4 h. The reaction mixture was quenched with glacial AcOH (3 mL), neutralized with saturated $NaHCO_3$ (10 mL), and extracted with ether (3 × 25 mL). The combined organic layer was concentrated under reduced pressure at rt and purified by column chromatography over silica gel using 5% EtOAc/Hexane as eluant to furnish compound **15a** (336 mg, 67% yield) as oil.

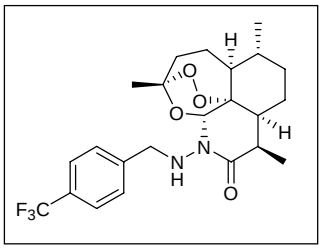
Compounds **15b-d** were prepared by the above procedure from imines **14b-d.**



15a. Yield 67%, oil; FT-IR (neat cm^{-1}) 1659; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.77-1.00 (m, 2H), 0.99 (d, 3H, J = 5.7 Hz), 1.17 (d, 3H, J = 7.3 Hz), 1.27-2.11 (m, 9H), 1.49 (s, 3H), 3.43-3.47 (m, 1H), 4.04 (d, 1H, J = 10.9 Hz, Benzylic H), 4.15 (d, 1H, J = 10.9 Hz, Benzylic H) 5.28 (brs, 1H, NH), 5.36 (s, 1H), 7.28-7.49 (m, 5H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.59 (CH_3), 19.93 (CH_3), 22.88 (CH_2), 25.12 (CH_2), 25.71 (CH_3), 33.59 (CH), 33.78 (CH_2), 36.95 (CH_2), 37.48 (CH), 46.63 (CH), 51.61 (CH), 56.81 (CH_2), 81.11 (C), 82.50 (CH), 105.13 (C), 127.76 (C), 128.67 (2 × CH), 129.43 (2 × CH), 137.69 (C), 172.18 (C); ESI-MS (*m/z*) 387 $[M+H]^+$, 409 $[M+Na]^+$; Anal. Calcd. for $C_{22}H_{30}N_2O_4$: C, 68.37%, H, 7.82%, N, 7.25%. Found: C, 68.59%, H 7.96%, N 7.24%.

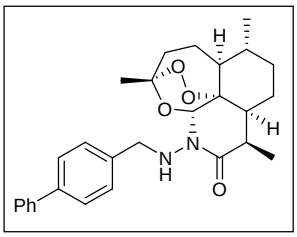


15b. Yield 72%, white solid, mp 152-154 ^{o}C; FT-IR (KBr cm^{-1}) 1650; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.81-1.81 (m, 2H), 1.00 (d, 3H, J = 5.8 Hz), 1.16 (d, 3H, J = 7.2 Hz), 1.32-2.12 (m, 8H), 1.47 (s, 3H), 2.46 (m, 1H), 3.42-3.98 (m, 1H), 4.00 (d, 1H, J = 11.1 Hz, Benzylic H), 4.15 (d, 1H, J = 11.1 Hz, Benzylic H) 5.24 (brs, 1H, NH), 5.35 (s, 1H), 7.36 (d, 2H, Ar, J = 8.3 Hz), 7.47 (d, 2H, Ar, J = 8.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.59 (CH_3), 19.96 (CH_3), 22.93 (CH_2), 25.13 (CH_2), 25.73 (CH_3), 33.61 (CH), 33.76 (CH_2), 36.93 (CH_2), 37.54 (CH), 46.63 (CH), 51.59 (CH), 56.12 (CH_2), 81.14 (C), 82.58 (CH), 105.18 (C), 121.76 (C), 131.15 (2 × CH), 131.79 (2 × CH), 136.72 (C), 172.32 (C); ESI-MS (*m/z*) 465 $[M]^+$, 467 $[M+2H]^+$; Anal. Calcd. for $C_{22}H_{29}N_2O_4Br$: C, 56.78%, H, 6.28%, N, 6.02%. Found: C, 56.66%, H, 6.54%, N, 6.10%.



15c. Yield 68%, white solid, mp 137-140 ^{o}C; FT-IR (KBr cm^{-1}) 1660; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.80-1.03 (m, 2H), 1.00 (d, 3H, J = 5.7 Hz), 1.16 (d, 3H, J = 7.2 Hz), 1.32-2.11 (m, 8H), 1.46 (s, 3H), 2.41-2.51 (m, 1H), 3.40-3.49 (m, 1H), 4.06-4.25 (m, 2H, Benzylic Hs), 5.29 (brs, 1H, NH), 5.35 (s, 1H), 7.59 (s, 4H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.55 (CH_3), 19.90 (CH_3), 22.93 (CH_2), 25.13 (CH_2), 25.69 (CH_3), 33.62 (CH), 33.75 (CH_2), 36.92 (CH_2), 37.54 (CH), 46.63 (CH), 51.59 (CH), 56.17 (CH_2), 81.13 (C), 82.64 (CH), 105.18 (C), 125.58 (q, C,

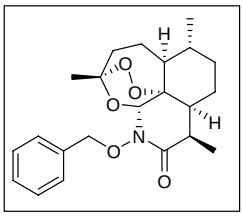
$J_{C\text{-}F}$ = 3.8 Hz, CF_3), 129.63 (4 × CH), 141.83 (C), 141.85 (C), 172.42 (C); ESI-MS (*m/z*) 455 $[M+H]^+$; EI-HRMS Calcd. for $C_{23}H_{29}N_2O_4F_3$ $[M]^+$: 454.2079. Found: 454.2078.



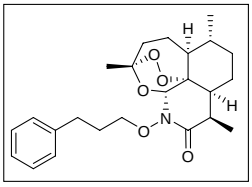
15d. Yield 62%, white solid, mp 68-70 ^oC; FT-IR (KBr cm^{-1}) 1652; ^1H NMR (300 MHz, $CDCl_3$) δ 0.82-1.04 (m, 2H), 1.00 (d, 3H, *J* = 5.8 Hz), 1.19 (d, 3H, *J* = 7.3 Hz), 1.28-1.75 (m, 6H), 1.51 (s, 3H), 1.99-2.14 (m, 2H), 2.42-2.53 (m, 1H), 3.47 (dq, 1H, *J* = 7.2 and 4.5 Hz), 4.12 (d, 1H, *J* = 11.1 Hz, Benzylic H), 4.21 (d, 1H, *J* = 11.1 Hz, Benzylic H), 5.32 (d, 1H, NH), 5.38 (s, 1H), 7.33-7.62 (m, 9H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.61 (CH_3), 19.94 (CH_3), 22.89 (CH_2), 25.13 (CH_2), 25.73 (CH_3), 33.61 (CH), 33.77 (CH_2), 36.94 (CH_2), 37.49 (CH), 46.61 (CH), 51.60 (CH), 56.41 (CH_2), 81.12 (C), 82.51 (CH), 105.14 (C), 127.27 (2 × CH), 127.43 (3 × CH), 128.91 (2 × CH), 129.87 (2 × CH), 136.77 (C), 140.71 (C), 141.14 (C), 172.22 (C); ESI-MS (*m/z*) 463 $[M+H]^+$; EI-HRMS Calcd. for $C_{28}H_{34}N_2O_4$ $[M]^+$: 462.2519. Found: 462.2511; Anal. Calcd. for $C_{28}H_{34}N_2O_4$: C, 72.70%, H, 7.41%, N, 6.06%. Found: C, 72.99%, H, 7.02%, N, 5.95%.

General procedure for preparation of ether derivatives of N-hydroxy-11-azaartemisnin (11): Preparation of compound 16a: To a stirred slurry of NaH (60% dispersion in mineral oil, 0.323 g, 13.45 mmol, 10 equiv), in dry THF (10 mL) at 0 ^oC, N-hydroxy-11-azaartemisnin **11** (0.4 g, 1.34 mmol) dissolved in dry THF (10 mL) was added and the reaction mixture was stirred at 0 ^oC for 2h. To this reaction mixture benzyl bromide (0.96 mL, 8.08 mmol, 6 equvi) was added and further stirred at rt for 12 h. The reaction mixture was quenched with water (10 mL) and extracted with ether (3 × 10 mL). The organic layer was dried over anhyd Na_2SO_4, concentrated under reduced pressure at rt and purified by column chromatography over silica gel (60-120 mesh) using EtOAc/Hexane (5:95) as eluant to furnish compound **16a** (0.375 g, 72% yield) as a white solid, mp 120-122 ^oC.

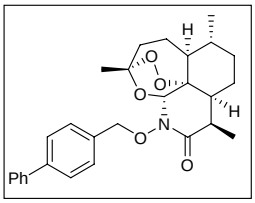
Compounds **16b-d** were prepared by the above procedure by replacing benzyl bromide with (3-Bromo-propyl)-benzene, 4-phenylbenzyl bromide and *o*-fluorobenzyl bromide**,** respectively.



16a. Yield 72%, white solid, mp 120-122 ^{o}C; IR (KBr, cm^{-1}) 1731; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.86-1.02 (m, 2H), 0.98 (d, 3H, J = 5.4 Hz), 1.15 (d, 3H, J = 7.2 Hz), 1.33-1.57 (m, 3H), 1.50 (s, 3H), 1.64-1.79 (m, 3H), 1.98-2.11 (m, 2H), 2.42-2.52 (m, 1H), 3.42-3.51 (m, 1H), 5.01 (d, 1H, J = 9.1 Hz), 5.20 (d, 1H, J = 9.1 Hz), 5.46 (s, 1H), 7.32-7.39 (m, 3H, Ar), 7.53-7.56 (m, 2H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.00 (CH_3), 19.87 (CH_3), 22.86 (CH_2), 25.06 (CH_2), 25.67 (CH_3), 33.69 (CH_2), 34.07 (CH), 36.77 (CH_2), 37.48 (CH), 46.82 (CH), 51.48 (CH), 79.13 (CH_2), 81.90 (C), 82.65 (CH), 105.05 (C), 128.53 (2 × CH), 128.67 (CH), 129.68 (2 × CH), 135.63 (C), 171.27 (C); ESIMS (m/z) 388 $[M+H]^+$; EI-HRMS Calcd. for $C_{22}H_{30}NO_5$ $[M+H]^+$: 388.2124; Found: 388.2116; Anal. Calcd for $C_{22}H_{29}NO_5$: C, 68.20%, H, 7.54%, N, 3.61%; found: C, 67.84%, H, 7.52%, N, 3.31%;

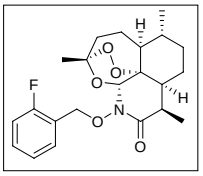


16b. Yield 60%, oil; IR (Neat, cm^{-1}) 1729; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.89-0.91 (m, 2H), 0.98 (d, 3H, J = 5.5 Hz), 1.10 (d, 3H, J = 7.1Hz), 1.17-1.24 (m, 1H), 1.29 (s, 3H), 1.45-2.03 (m, 9H), 2.32-2.46 (m, 1H), 2.75 (t, 2H, J = 7.3 Hz), 3.56-3.41 (m, 1H), 3.99-4.20 (m, 2H), 5.37 (s, 1H), 7.12-7.24 (m, 5H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.98 (CH_3), 19.86 (CH_3), 22.90 (CH_2), 25.04 (CH_2), 25.45 (CH_3), 30.13 (CH_2), 32.36 (CH_2), 33.71 (CH_2), 34.00 (CH), 36.75 (CH_2), 37.50 (CH), 46.87 (CH), 51.47 (CH), 76.24 (CH_2), 81.83 (C), 82.67 (CH), 104.96 (C), 125.88 (CH), 128.42 (2 × CH), 128.63 (2 × CH), 142.03 (C), 171.43 (C); ESIMS (m/z) 416 $[M+H]^+$; Anal. Calcd for $C_{24}H_{33}NO_5$: C, 69.37%, H, 8.00%, N, 3.37%; found: C, 68.94%, H, 7.80%, N, 3.16%.



16c. Yield 74%, white solid, mp 65-66 ^{o}C; IR (KBr, cm^{-1}) 1728; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89-1.01 (m, 2H), 1.00 (d, 3H, J = 5.3 Hz), 1.16 (d, 3H, J = 7.2 Hz), 1.33-1.42 (m, 3H), 1.51 (s, 3H), 1.64-1.80 (m, 3H), 1.98-2.12 (m, 2H), 2.42-2.53 (m, 1H), 3.44-3.52 (m, 1H), 5.04 (d, 1H, J = 9.1 Hz), 5.24 (d, 1H, J = 9.1 Hz), 5.47 (s, 1H), 7.31-7.66 (m, 3H, Ar), 7.57-7.64 (m, 6H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.06 (CH_3), 19.92 (CH_3), 22.93 (CH_2), 25.13 (CH_2), 25.75 (CH_3), 33.76 (CH_2), 34.15 (CH), 36.84 (CH_2), 37.55 (CH), 46.91 (CH), 51.55 (CH), 78.89 (CH_2), 81.98 (C), 82.75 (CH), 105.14 (C), 127.35

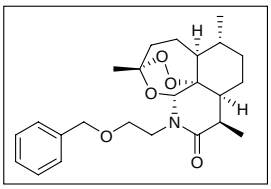
(2 × CH), 127.40 (2 × CH), 127.52 (CH), 128.94 (2 × CH), 130.19 (2 × CH), 134.73 (C), 141.13 (C), 141.69 (C), 171.39 (C); ESIMS (m/z) 464 $[M+H]^+$; Anal. Calcd for $C_{28}H_{33}NO_5$: C, 72.55%, H, 7.18%, N, 3.02%; found: C, 72.48%, H, 7.34%, N, 2.81%; HRMS [ESI] Calcd for $C_{24}H_{34}NO_5$: 464.2359 $[M+H]^+$; found: 464.2361.



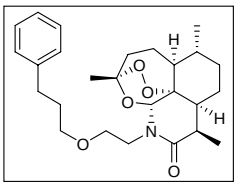
16d. Yield 65%, oil; IR (Neat, cm^{-1}) 1720; ^1H NMR (300 MHz, $CDCl_3$) δ 0.88-1.00 (m, 2H), 0.96 (d, 3H, J = 5.2 Hz), 1.13 (d, 3H, J = 7.2 Hz), 1.18-1.42 (m, 3H), 1.47 (s, 3H), 1.67-1.78 (m, 3H), 1.95-2.09 (m, 2H), 2.39-2.49 (m, 1H), 3.43-3.47 (m, 1H), 5.18 (s, 2H), 5.46 (s, 1H), 5.44 (s, 1H), 7.03 (t, 1H, Ar, J = 9.01 Hz), 7.13 (t, 1H, Ar, J = 7.44 Hz), 7.26-7.34 (m, 1H, Ar), 7.63-7.68 (m, 1H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 11.74 (CH_3), 19.60 (CH_3), 22.66 (CH_2), 24.81 (CH_2), 25.32 (CH_3), 33.47 (CH_2), 33.87 (CH), 36.55 (CH_2), 37.23 (CH), 46.58 (CH), 51.25 (CH), 71.43 (CH_2, $J_{C\text{-}F}$ = 3.9 Hz), 81.65 (C), 82.45 (CH), 104.85 (C), 115.18 (CH, $J_{C\text{-}F}$ = 21.3 Hz), 122.66 (C, $J_{C\text{-}F}$ = 15.1 Hz), 124.04 (CH, $J_{C\text{-}F}$ = 3.7 Hz), 130.22 (CH, $J_{C\text{-}F}$ = 8.2 Hz), 131.91 (CH, $J_{C\text{-}F}$ = 3.7 Hz), 160.97 (C, $J_{C\text{-}F}$ = 248.1 Hz), 171.15 (C); ESIMS (m/z) 406 $[M+H]^+$; HRMS [ESI] Calcd for $C_{22}H_{29}NO_5F$: 406.2030 $[M+H]^+$; found: 406.2020.

General procedure for preparation of ether derivatives of N-ethanol-11-azaartemisnin (12): Preparation of compound 17a: To a stirred slurry of NaH (60% dispersion in mineral oil, 0.295 g, 12.29 mmol, 10 equiv), in dry THF (10 mL) at 0 ^oC, N-ethanol-11-azaartemisnin **12** (0.4 g, 1.23 mmol) dissolved in dry THF (10 mL) was added and the reaction mixture was stirred at 0 ^oC for 2h. To this reaction mixture benzyl bromide (0.88 mL, 7.38 mmol, 6 equiv) was added and further stirred at rt for 12 h. The reaction mixture was quenched with water (10 mL) and extracted with ether (3 × 10 mL). The organic layer was dried over anhyd Na_2SO_4, concentrated under reduced pressure at rt and purified by column chromatography over silica gel (60-120 mesh) using EtOAc/Hexane (5:95) as eluant to furnish compound **17a** (0.342 g, 67% yield) as oil.

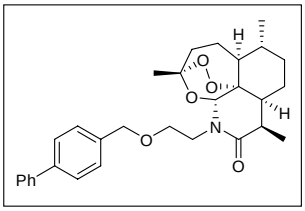
Compounds **17b-d** were prepared by the above procedure by replacing benzyl bromide with (3-Bromo-propyl)-benzene, 4-phenyl benzyl bromide and *o*-fluorobenzyl bromide**,** respectively.



17a. Yield 67%, oil; IR (Neat, cm^{-1}) 1635; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85-0.95 (m, 2H), 0.89 (d, 3H, J = 5.8 Hz), 1.13 (d, 3H, J = 7.2 Hz), 1.24-1.42 (m, 3H), 1.33 (s, 3H), 1.50-1.68 (m, 3H), 1.90-2.01 (m, 2H), 2.33-2.44 (m, 1H), 3.26-3.32 (m, 1H), 3.63-3.73 (m, 2H), 3.82-3.89 (m, 2H), 4.44 (d, 1H, J = 11.3 Hz), 4.52 (d, 1H, J = 11.3 Hz), 5.46 (s, 1H), 7.31 (s, 5H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.04 (CH_3), 19.79 (CH_3), 22.59 (CH_2), 25.23 (CH_2), 25.58 (CH_3), 33.21 (CH), 33.85 (CH_2), 36.81 (CH_2), 37.37 (CH), 40.92 (CH_2), 45.94 (CH), 51.44 (CH), 69.00 (CH_2), 73.30 (CH_2), 79.53 (CH), 80.31 (C), 104.75 (C), 127.76 (CH), 128.02 (2 × CH), 128.41 (2 × CH), 138.44 (C), 171.97 (C); ESIMS (m/z) 416 $[M+H]^+$; Anal. Calcd for $C_{24}H_{33}NO_5$: C, 69.37%, H, 8.00%, N, 3.37%; found: C, 68.97%, H, 8.28%, N, 3.11%; HRMS Calcd for $C_{24}H_{33}NO_5$: 415.2359; found: 415.2386.

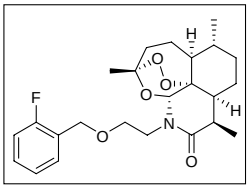


17b. Yield 64%, oil IR (Neat, cm^{-1}) 1641; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87-1.07 (m, 2H), 0.95 (d, 3H, J = 6.1 Hz), 1.14 (d, 3H, J = 7.3 Hz), 1.26-1.32 (m, 1H), 1.37 (s, 3H), 1.39-1.51 (m, 2H), 1.61-1.69 (m, 2H), 1.75-1.90 (m, 3H), 1.95-2.03 (m, 2H), 2.36-2.46 (m, 1H), 2.67 (t, 2H, J = 8.2 Hz), 3.25-3.34 (m, 1H), 3.42-3.48 (m, 2H), 3.53-3.86 (m, 4H), 5.51 (s, 1H), 7.15-7.20 (m, 3H, Ar), 7.25-7.30 (m, 2H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.99 (CH_3), 19.77 (CH_3), 22.61 (CH_2), 25.23 (CH_2), 25.51 (CH_3), 33.61 (CH_2), 32.49 (CH_2), 33.13 (CH), 33.79 (CH_2), 36.72 (CH_2), 37.64 (CH), 40.95 (CH_2), 45.83 (CH), 51.39 (CH), 69.08 (CH_2), 70.33 (CH_2), 79.39 (CH), 80.19 (C), 104.67 (C), 125.85 (CH), 128.35 (2 × CH), 128.39 (2 × CH), 141.93 (C), 171.80 (C); ESIMS (m/z) 444 $[M+H]^+$; Anal. Calcd for $C_{26}H_{37}NO_5$: C, 70.40%, H, 8.41%, N, 3.16%; found: C, 70.54%, H, 8.67%, N, 3.24%;



17c. Yield 71%, oil; IR (Neat, cm^{-1}) 1640; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85 (d, 3H, J = 5.8 Hz), 0.92-1.01 (m, 2H), 1.13 (d, 3H, J = 7.3 Hz), 1.19-1.28 (m, 2H), 1.33 (s, 3H), 1.37-1.69 (m, 4H), 1.88-2.00 (m, 2H), 2.32-2.42 (m, 1H), 3.24-3.32 (m, 1H), 3.68-3.73 (m, 2H), 3.83-3.92 (m, 2H), 4.48 (d, 1H, J = 11.3 Hz), 4.55 (d, 1H, J = 11.3 Hz), 5.47 (s, 1H), 7.31-7.45 (m, 5H, Ar), 7.53-7.58 (m, 4H, Ar); ^{13}C NMR (50 MHz,

$CDCl_3$) δ 13.03 (CH_3), 19.81 (CH_3), 22.56 (CH_2), 25.20 (CH_2), 25.55 (CH_3), 33.19 (CH), 33.83 (CH_2), 36.77 (CH_2), 37.37 (CH), 40.93 (CH_2), 45.90 (CH), 51.39 (CH), 68.99 (CH_2), 72.95 (CH_2), 79.53 (CH), 80.27 (C), 104.72 (C), 127.13 (4 × CH), 127.43 (CH), 128.48 (2 × CH), 128.91 (2 × CH), 137.45 (C), 140.71 (C), 140.93 (C), 171.95 (C); ESIMS (m/z) 492 $[M+H]^+$; Anal. Calcd for $C_{30}H_{37}NO_5$: C, 73.29%, H, 7.59%, N, 2.85%; found: C, 73.14%, H, 7.71%, N, 2.92%; HRMS Calcd for $C_{30}H_{37}NO_5$: 491.2672; found: 491.2714.



17d. Yield 62%, oil; IR (Neat, cm^{-1}) 1632; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.88-0.96 (m, 2H), 0.99 (d, 3H, J = 5.7 Hz), 1.11 (d, 3H, J = 7.4 Hz), 1.19-1.26 (m, 2H), 1.32 (s, 3H), 1.37-1.68 (m, 4H), 1.88-2.01 (m, 2H), 2.29-2.45 (m, 1H), 3.19-3.32 (m, 1H), 3.62-3.75 (m, 2H), 3.83-3.92 (m, 2H), 4.49 (d, 1H, J = 11.7 Hz), 4.57 (d, 1H, J = 11.7 Hz), 5.44 (s, 1H), 6.96-7.13 (m, 2H, Ar), 7.24-7.40 (m, 2H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.87 (CH_3), 19.62 (CH_3), 22.40 (CH_2), 25.05 (CH_2), 25.37 (CH_3), 33.06 (CH), 33.75 (CH_2), 36.64 (CH_2), 37.23 (CH), 40.77 (CH_2), 45.76 (CH), 51.29 (CH), 66.52 (CH_2, $J_{C\text{-}F}$ = 3.7 Hz), 69.09 (CH_2), 79.32 (CH), 80.12 (C), 104.58 (C), 115.16 (CH, $J_{C\text{-}F}$ = 21.5 Hz), 123.92 (CH, $J_{C\text{-}F}$ = 3.6 Hz), 125.31 (C, $J_{C\text{-}F}$=14.8 Hz), 129.45 (CH, $J_{C\text{-}F}$ = 8.1 Hz), 130.34 (CH, $J_{C\text{-}F}$ = 4.5 Hz), 160.74 (C, $J_{C\text{-}F}$ = 247.3 Hz), 171.85 (C); ESIMS (m/z) 434 $[M+H]^+$; EI-HRMS Calcd. for $C_{24}H_{33}NO_5F$, $[M+H]^+$: 434.2343. Found: 434.2328.

2. Purity/Characterization Table showing degree of purity for compounds 9, 10, 11, 12, 13a, 13b, 13d, 13e, 13f, 14a, 14b, 14d, 15a, 15b, 15d, 16a, 16b, 16c, 17a, 17b and 17c.

Compound	Molecular Formula	Calculated			Found		
		C%	H%	N%	C%	H%	N%
9	$C_{15}H_{24}N_2O_4$	60.79	8.16	9.45	60.92	8.65	9.75
10	$C_{15}H_{24}N_2O_3$	64.26	8.63	9.99	64.35	8.93	9.88
11	$C_{15}H_{23}NO_5$	60.59	7.80	4.71	60.64	7.89	4.53
12	$C_{17}H_{27}NO_5$	62.75	8.36	4.30	62.32	8.32	4.55
13a	$C_{22}H_{28}N_2O_5$	65.98	7.05	7.00	66.06	7.39	7.01
13b	$C_{22}H_{27}BrN_2O_5$	55.12	5.68	5.84	54.80	6.06	5.80
13d	$C_{28}H_{32}N_2O_5$	70.57	6.77	5.88	70.89	7.00	6.15
13e	$C_{38}H_{50}N_4O_{10}$	63.14	6.97	7.75	63.04	6.56	8.00
13f	$C_{32}H_{46}N_4O_{10}$	59.43	7.17	8.66	59.56	7.35	8.78
14a	$C_{22}H_{28}N_2O_4$	68.73	7.34	7.29	68.80	7.16	7.25
14b	$C_{22}H_{27}BrN_2O_4$	57.03	5.87	6.05	57.02	6.28	6.08
14d	$C_{28}H_{32}N_2O_4$	73.02	7.00	6.08	72.95	6.91	6.00
15a	$C_{22}H_{30}N_2O_4$	68.37	7.82	7.25	68.59	7.96	7.24
15b	$C_{22}H_{29}BrN_2O_4$	56.78	6.28	6.02	56.66	6.54	6.10
15d	$C_{28}H_{34}N_2O_4$	72.70	7.41	6.06	72.99	7.02	5.95
16a	$C_{22}H_{29}NO_5$	68.20	7.54	3.61	67.84	7.52	3.31
16b	$C_{24}H_{33}NO_5$	69.37	8.00	3.37	68.94	7.80	3.16
16c	$C_{28}H_{33}NO_5$	72.55	7.18	3.02	72.48	7.34	2.81
17a	$C_{24}H_{33}NO_5$	69.37	8.00	3.37	68.97	8.28	3.11
17b	$C_{26}H_{37}NO_5$	70.40	8.41	3.16	70.54	8.67	3.24
17c	$C_{30}H_{37}NO_5$	73.29	7.59	2.85	73.14	7.71	2.92

3. HRMS for Compounds 9, 10, 11, 12, 13c, 13d, 14a, 14b, 14c, 15c, 15d, 16a, 16c, 16d, 17a, 17c and 17d.

Compound	Molecular Formula	Calculated Mass	Found Mass
9	$C_{15}H_{24}N_2O_4$	**296.1736 $[M]^+$**	**296.1742**
10	$C_{15}H_{24}N_2O_3$	**280.1785 $[M]^+$**	**280.1787**
11	$C_{15}H_{24}NO_5$	**298.1654 $[M+H]^+$**	**298.1631**
12	$C_{17}H_{28}NO_5$	**326.1967 $[M+H]^+$**	**326.1960**
13c	$C_{23}H_{27}F_3N_2O_5$	**468.1872 $[M]^+$**	**468.1843**
13d	$C_{28}H_{32}N_2O_5$	**476.2311 $[M]^+$**	**476.2310**
14a	$C_{22}H_{28}N_2O_4$	**384.2049 $[M]^+$**	**384.2024**
14b	$C_{22}H_{27}BrN_2O_4$	**462.1154 $[M]^+$**	**462.1152**
14c	$C_{23}H_{27}F_3N_2O_4$	**452.1923 $[M]^+$**	**452.1922**
15c	$C_{23}H_{29}F_3N_2O_4$	**545.2079 $[M]^+$**	**454.2078**
15d	$C_{28}H_{34}N_2O_4$	**462.2519 $[M]^+$**	**462.2511**
16a	$C_{22}H_{30}NO_5$	**388.2124 $[M+H]^+$**	**388.2116**
16c	$C_{28}H_{34}NO_5$	**464.2359 $[M+H]^+$**	**464.2361**
16d	$C_{22}H_{29}NO_5F$	**406.2030 $[M+H]^+$**	**406.2020**
17a	$C_{24}H_{33}NO_5$	**415.2359 $[M]^+$**	**415.2386**
17c	$C_{30}H_{37}NO_5$	**491.2672 $[M]^+$**	**491.2714**
17d	$C_{24}H_{33}NO_5F$	**434.2343 $[M+H]^+$**	**434.2328**

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4. ^{1}H NMR and ^{13}C NMR spectra of compounds 9, 10, 11, 12, 13a, 13b, 13c, 13d, 13e, 13f, 14a, 14b, 14c, 14d, 15a, 15b, 15c, 15d, 16a, 16b, 16c,16d, 17a, 17b, 17c and 17d.

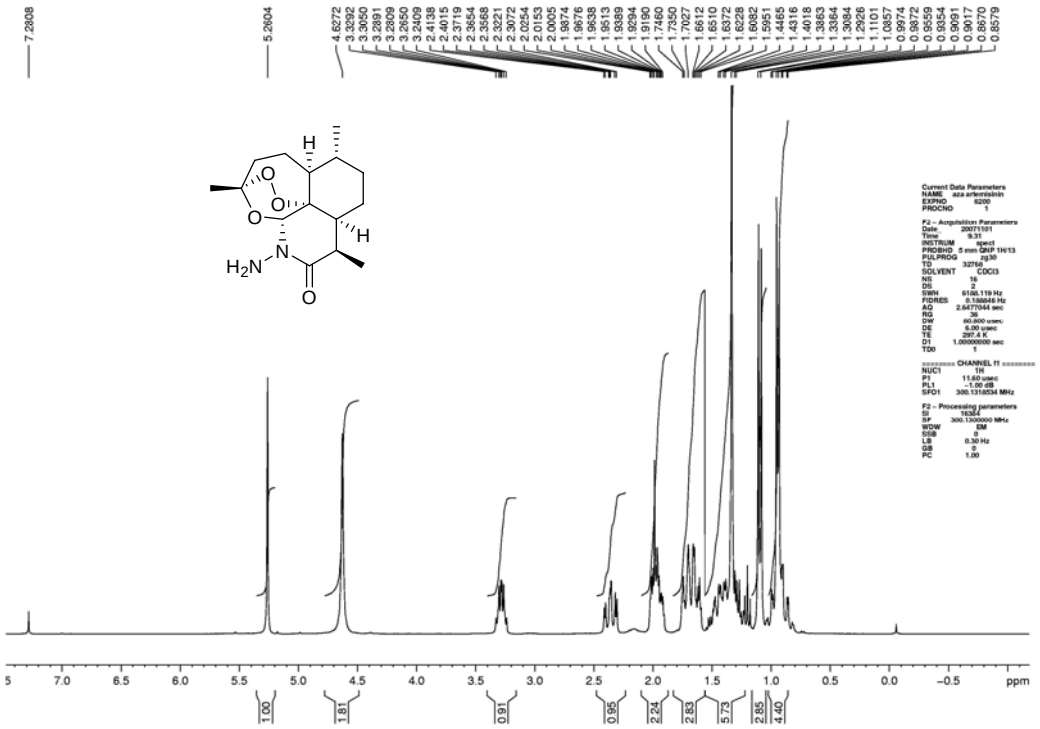

Fig 1: ^{1}H NMR Spectra of **9.**

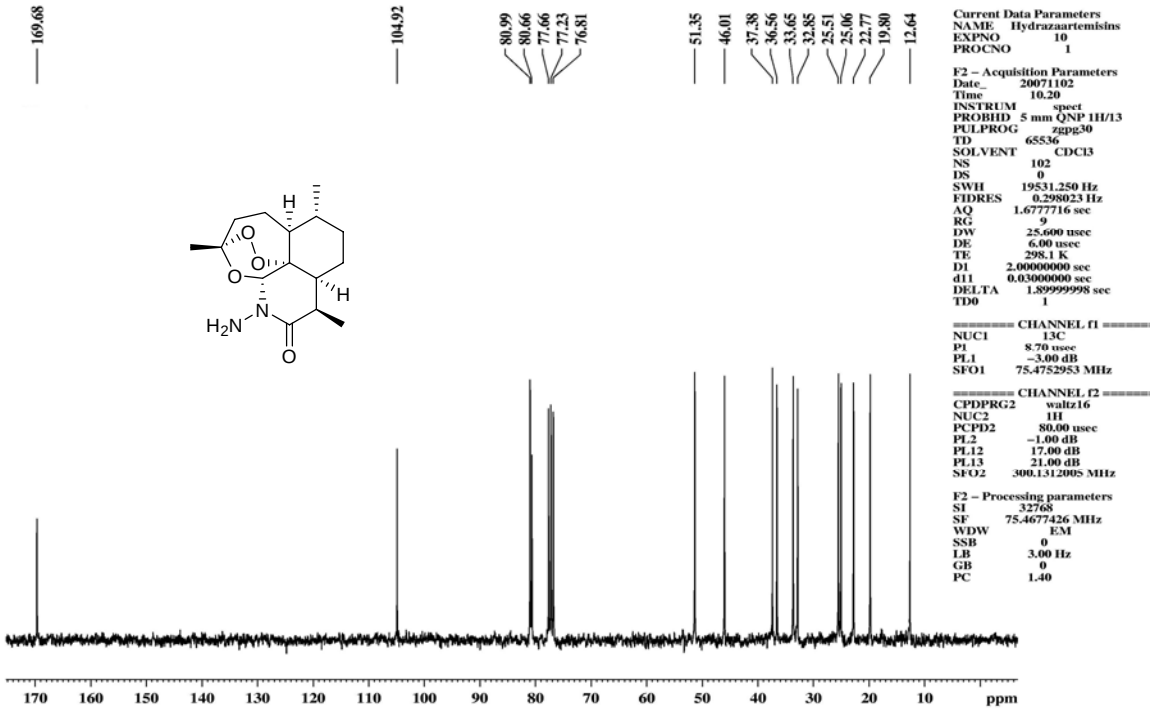

Fig 2: ^{13}C NMR Spectra of **9.**

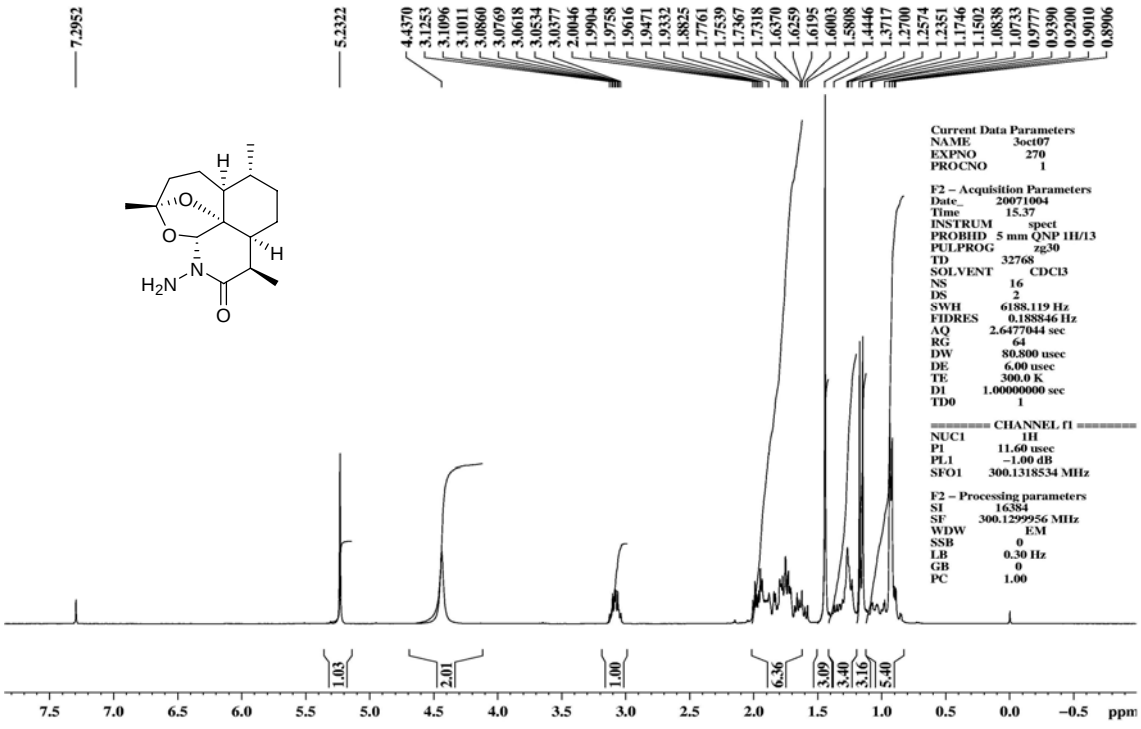

Fig 3: ^{1}H NMR Spectra of **10.**

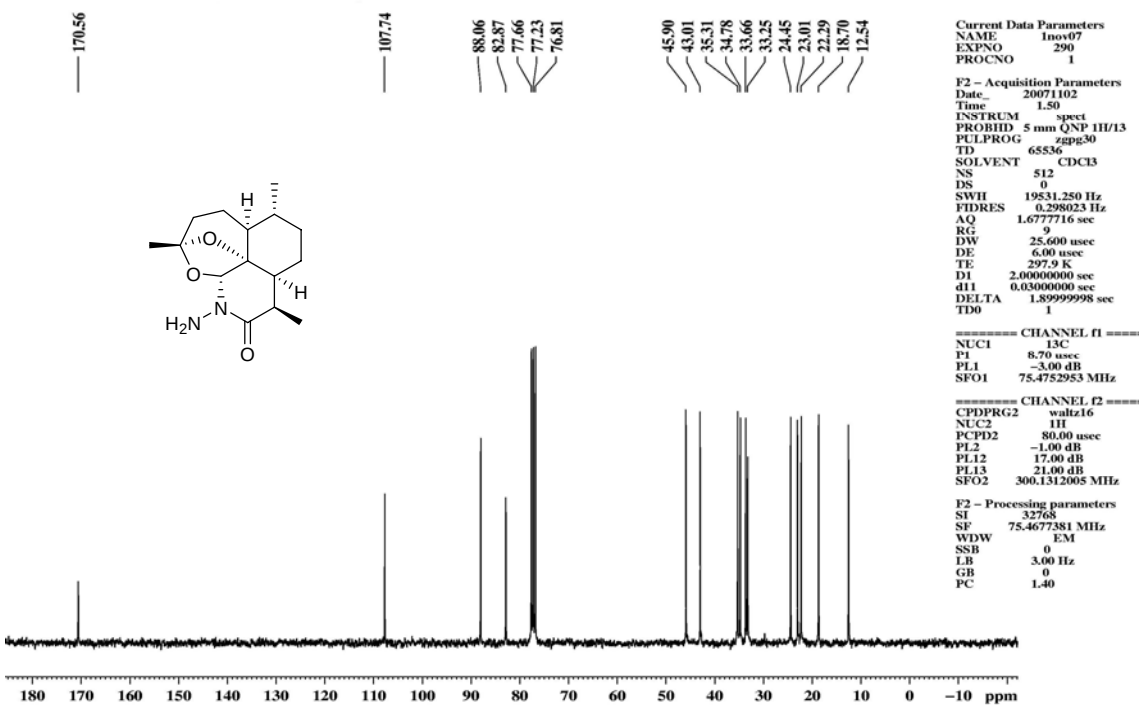

Fig 4: ^{13}C NMR Spectra of **10.**

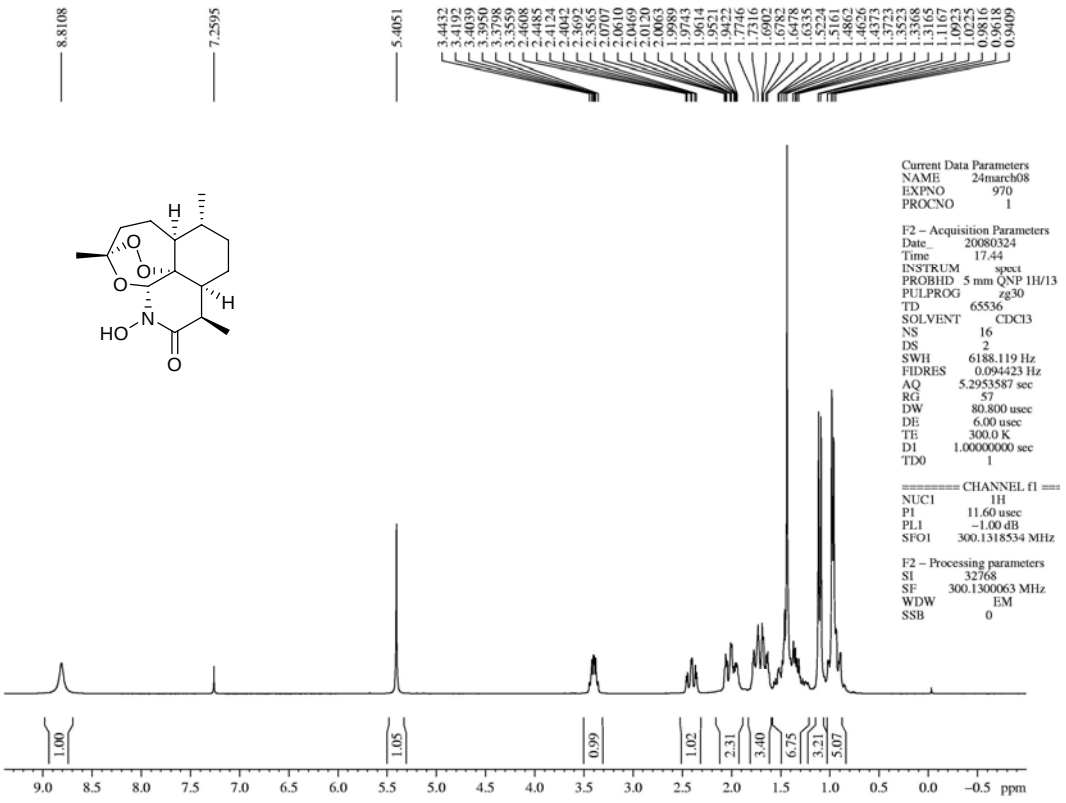

Fig 5: ^{1}H NMR Spectra of **11.**

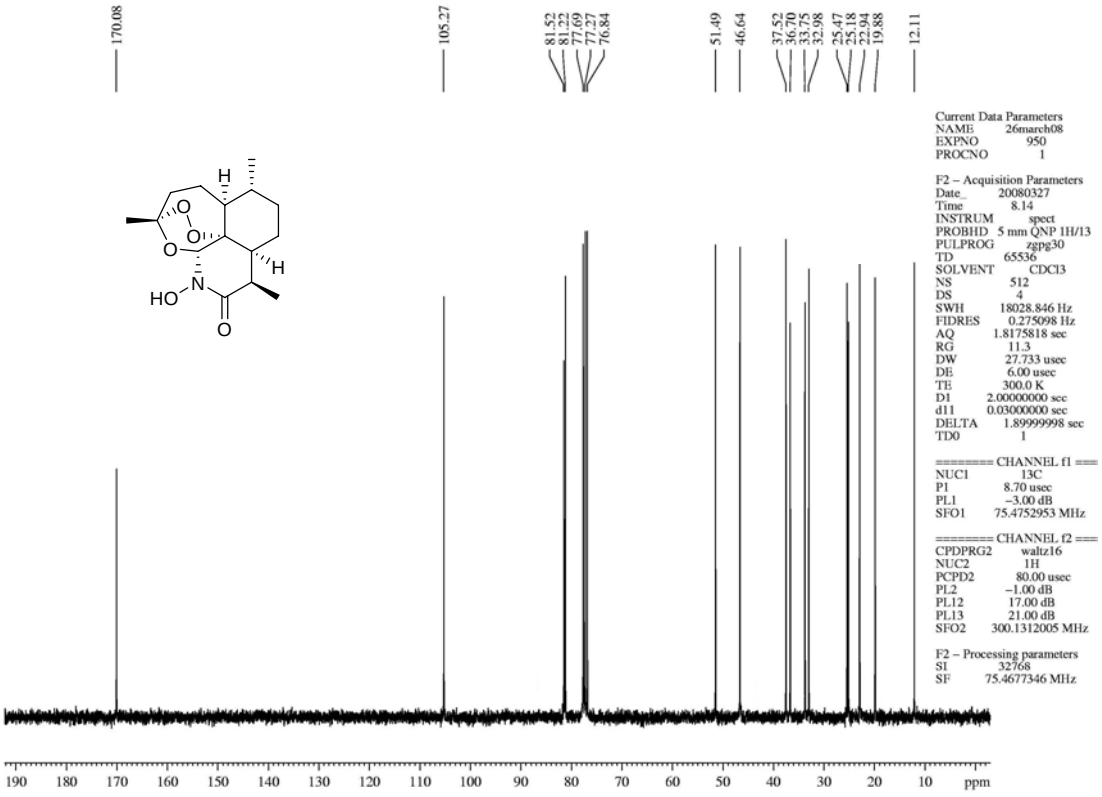

Fig 6: ^{13}C NMR Spectra of **11.**

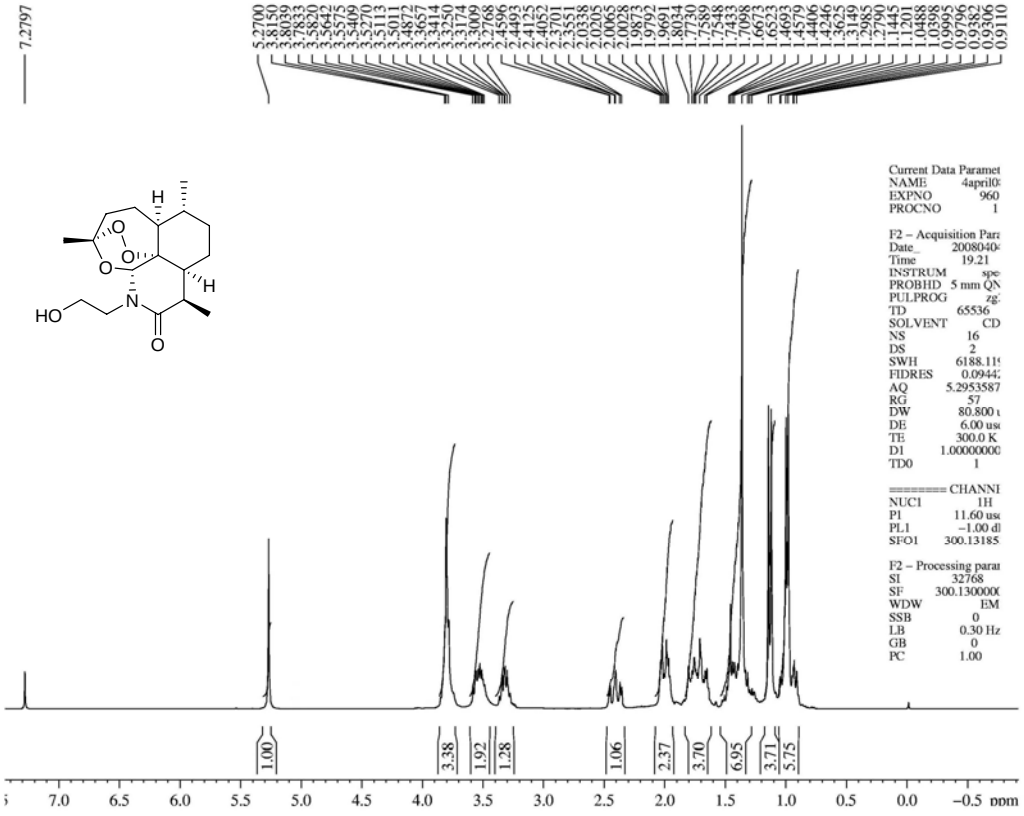

Fig 7: ^{1}H NMR Spectra of **12.**

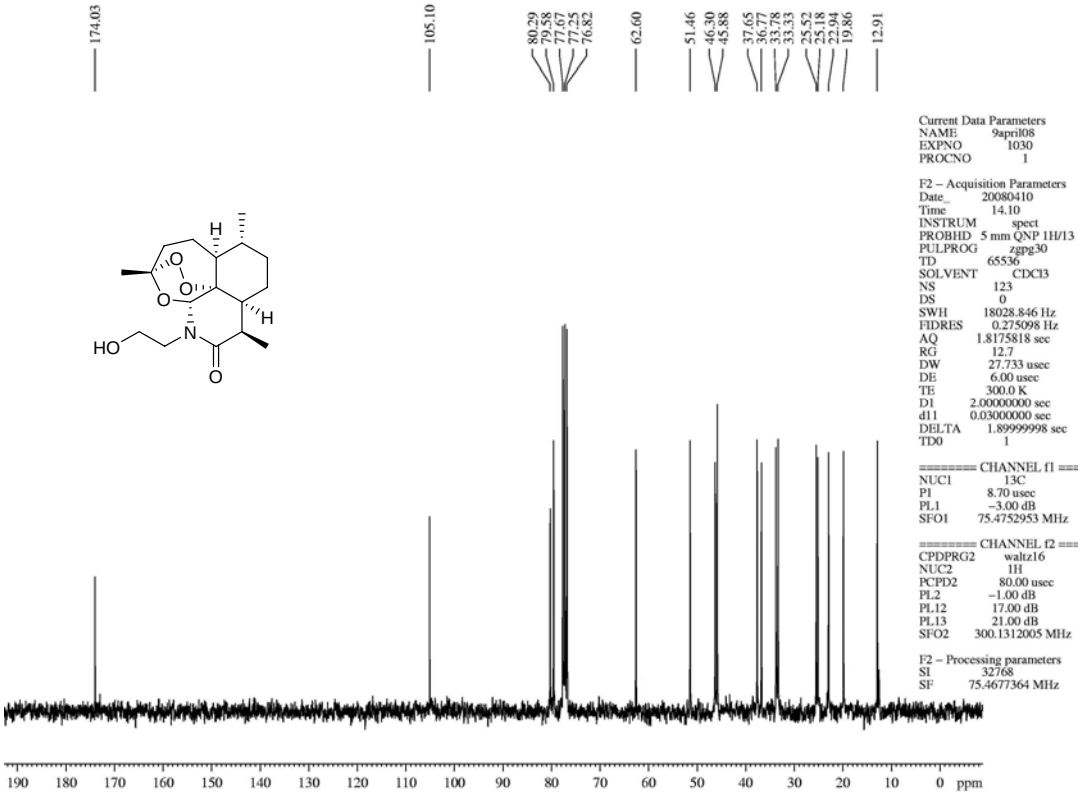

Fig 8: ^{13}C NMR Spectra of **12.**

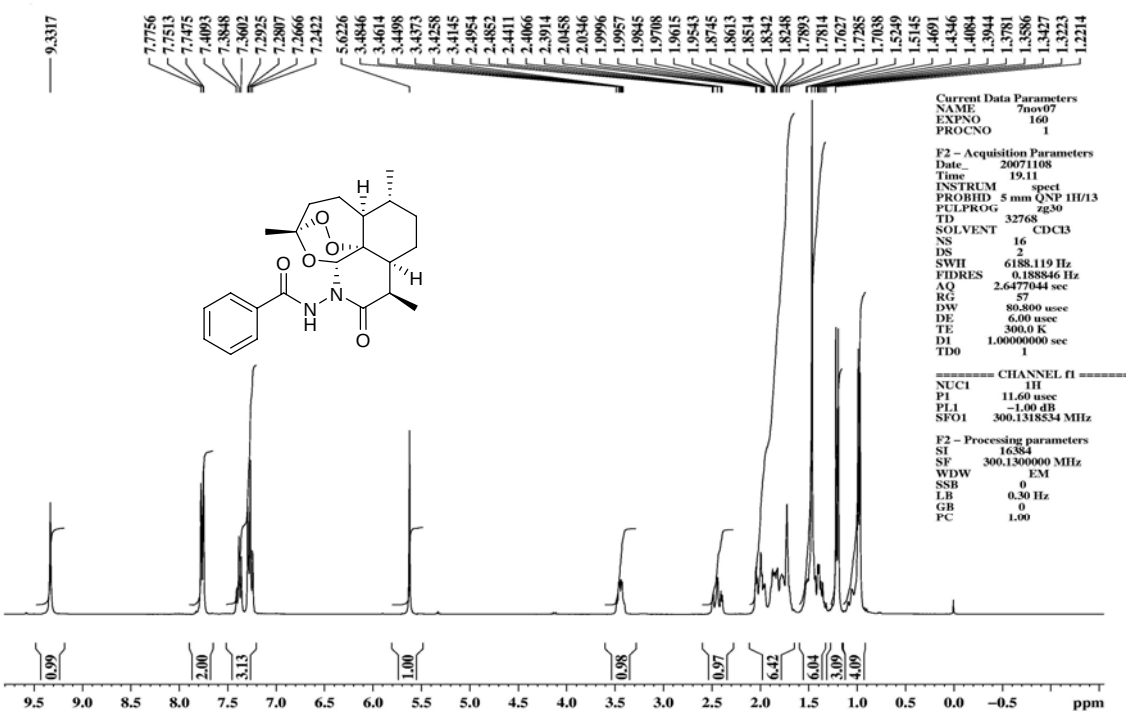

Fig 9: ^{1}H NMR Spectra of **13a.**

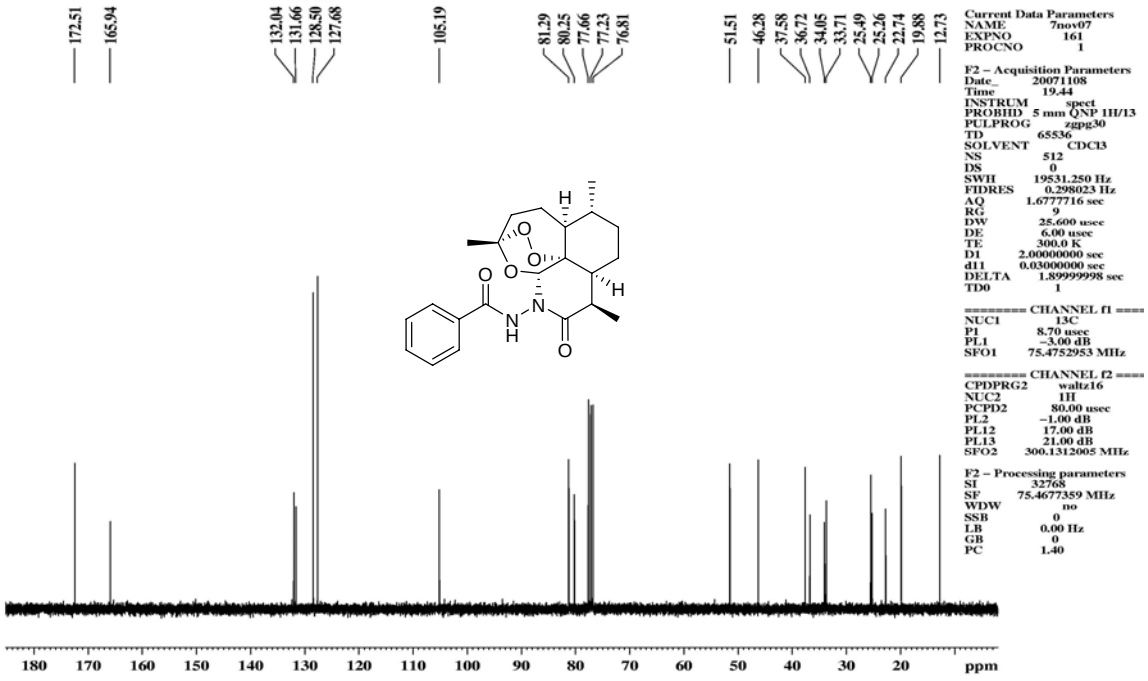

Fig 10: ^{13}C NMR Spectra of **13a.**

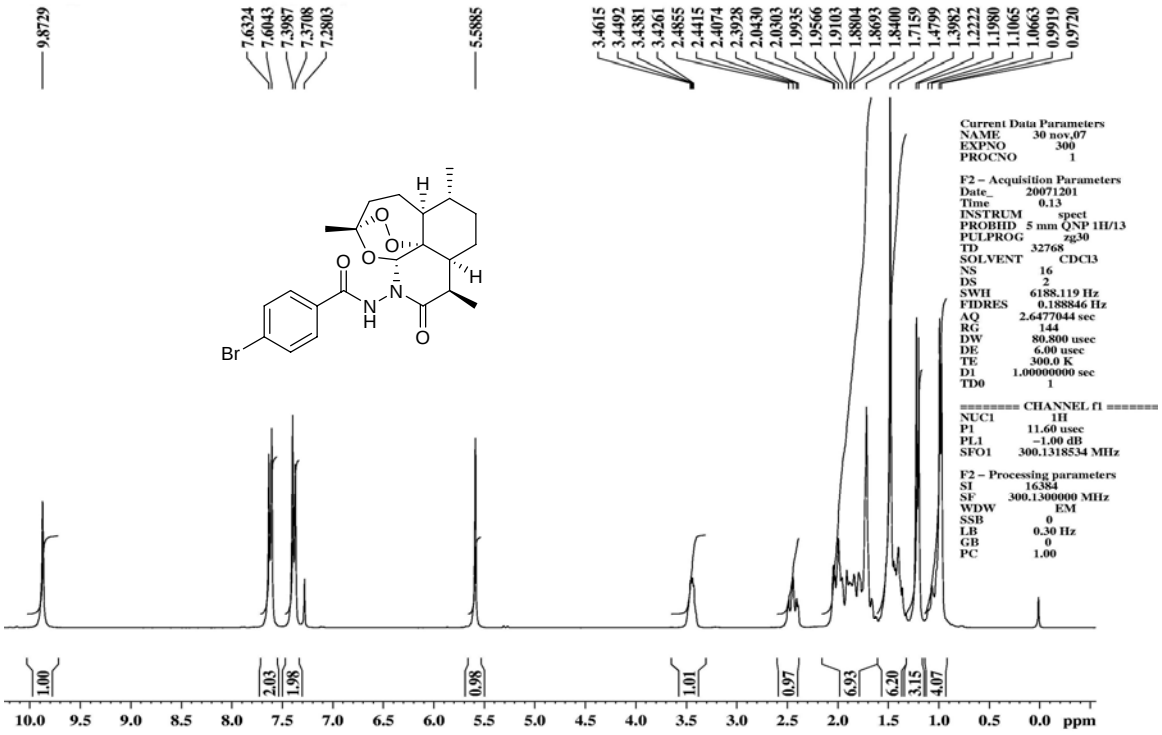

Fig 11: ^{1}H NMR Spectra of **13b.**

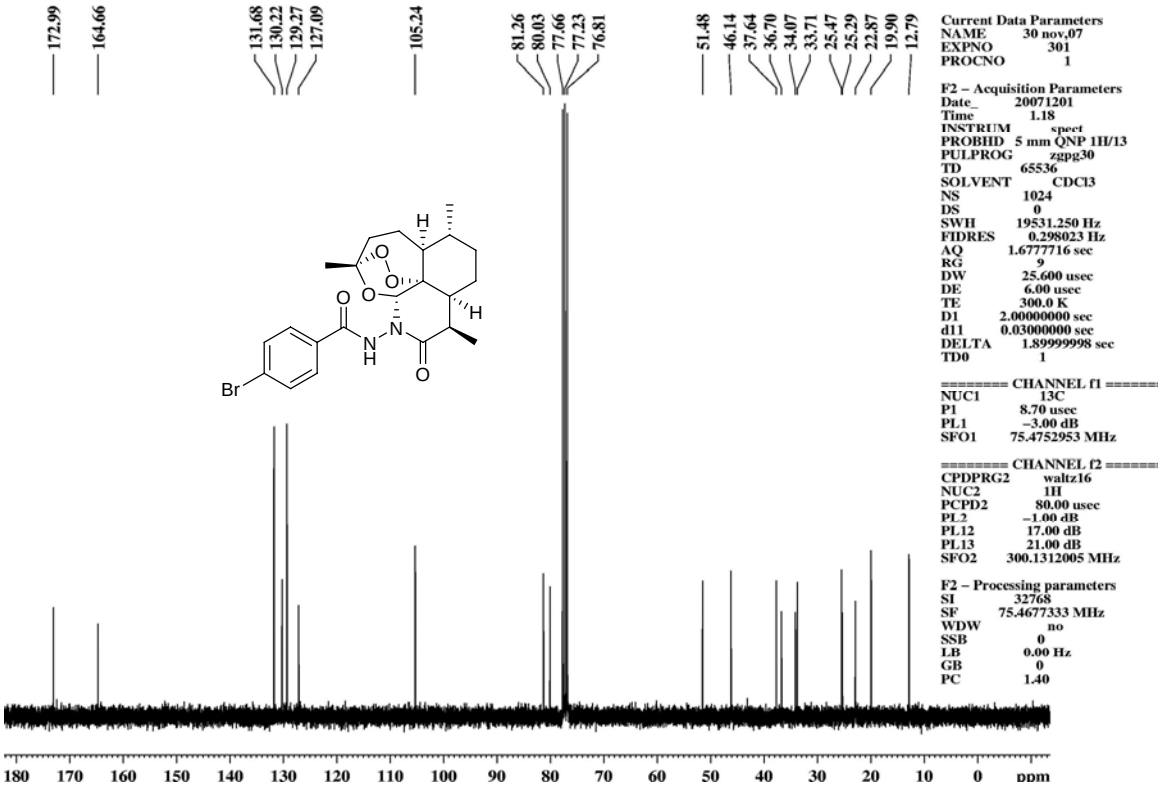

Fig 12: ^{13}C NMR Spectra of **13b.**

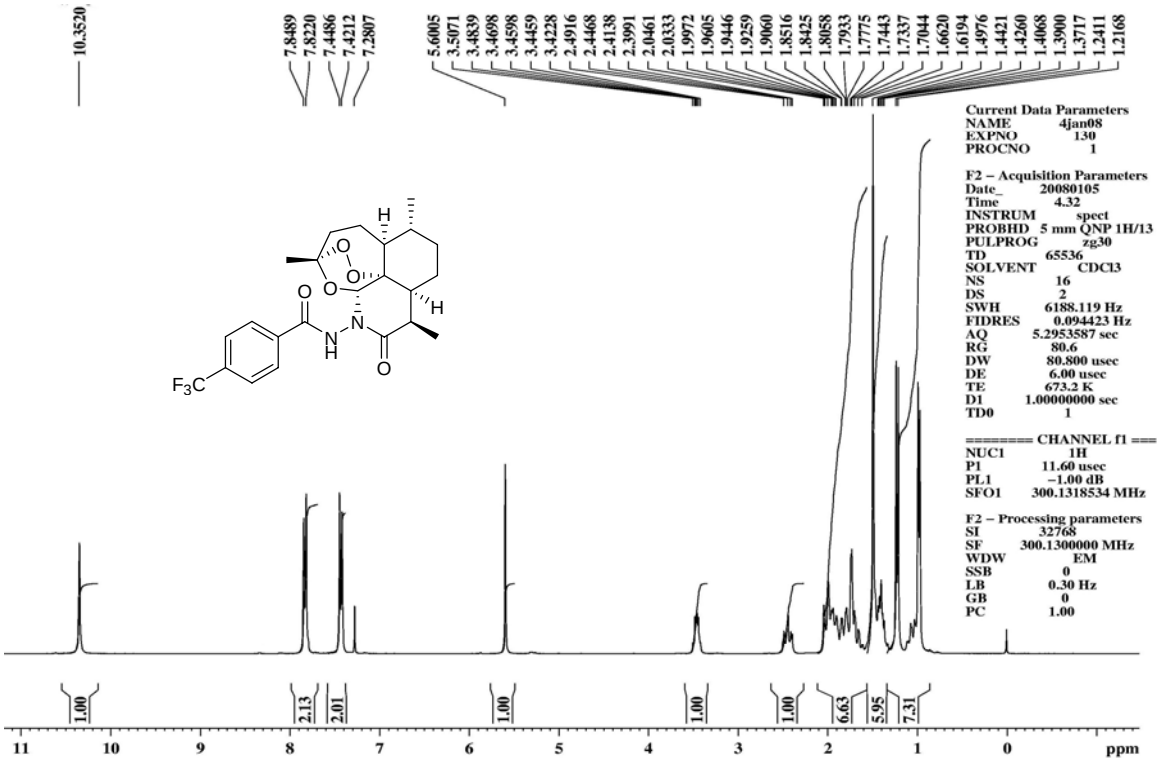

Fig 13: ^{1}H NMR Spectra of **13c.**

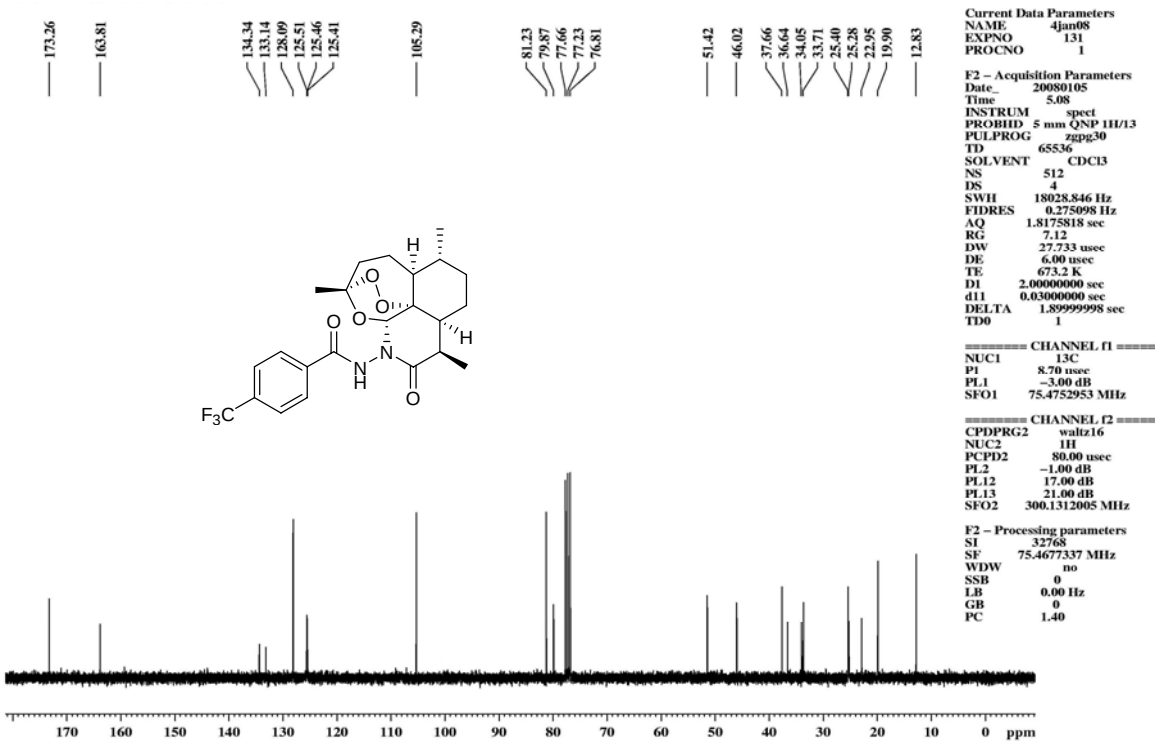

Fig 14: ^{13}C NMR Spectra of **13c.**

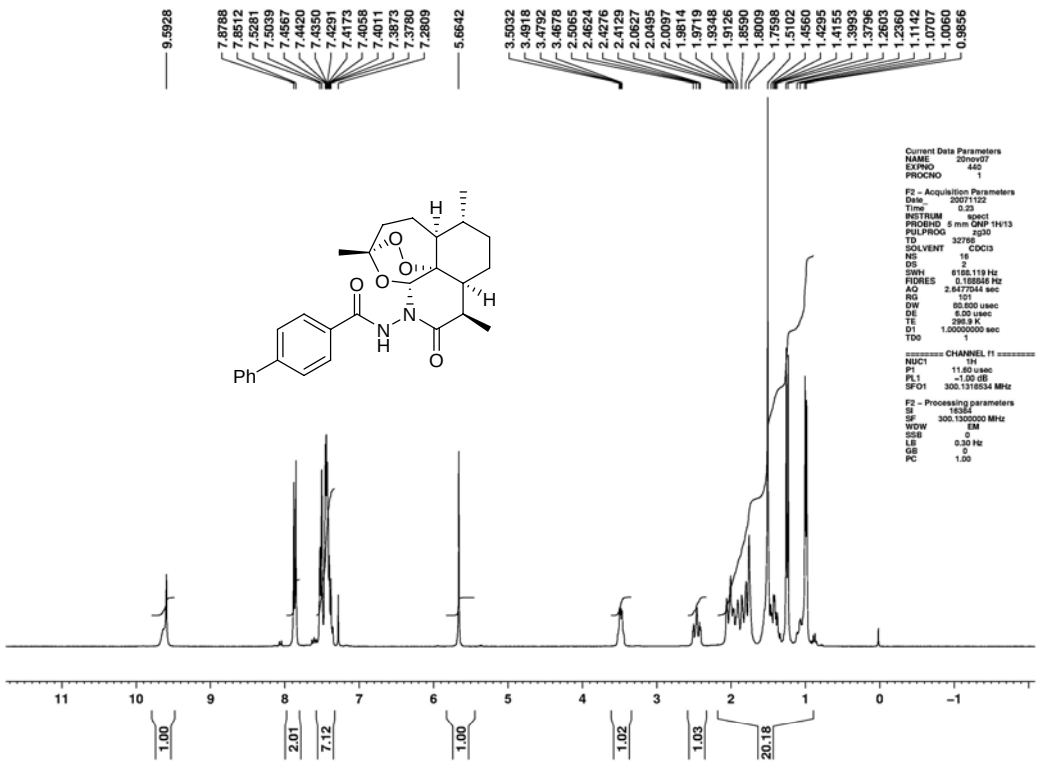

Fig 15: ^{1}H NMR Spectra of **13d.**

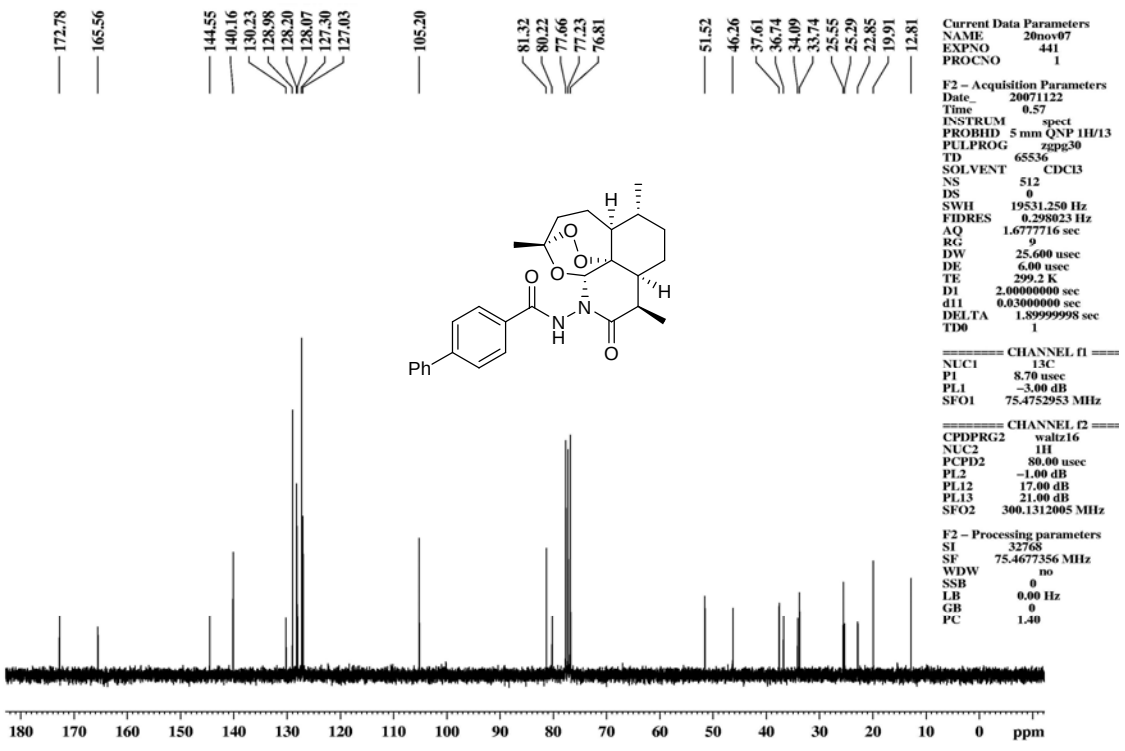

Fig 16: ^{13}C NMR Spectra of **13d.**

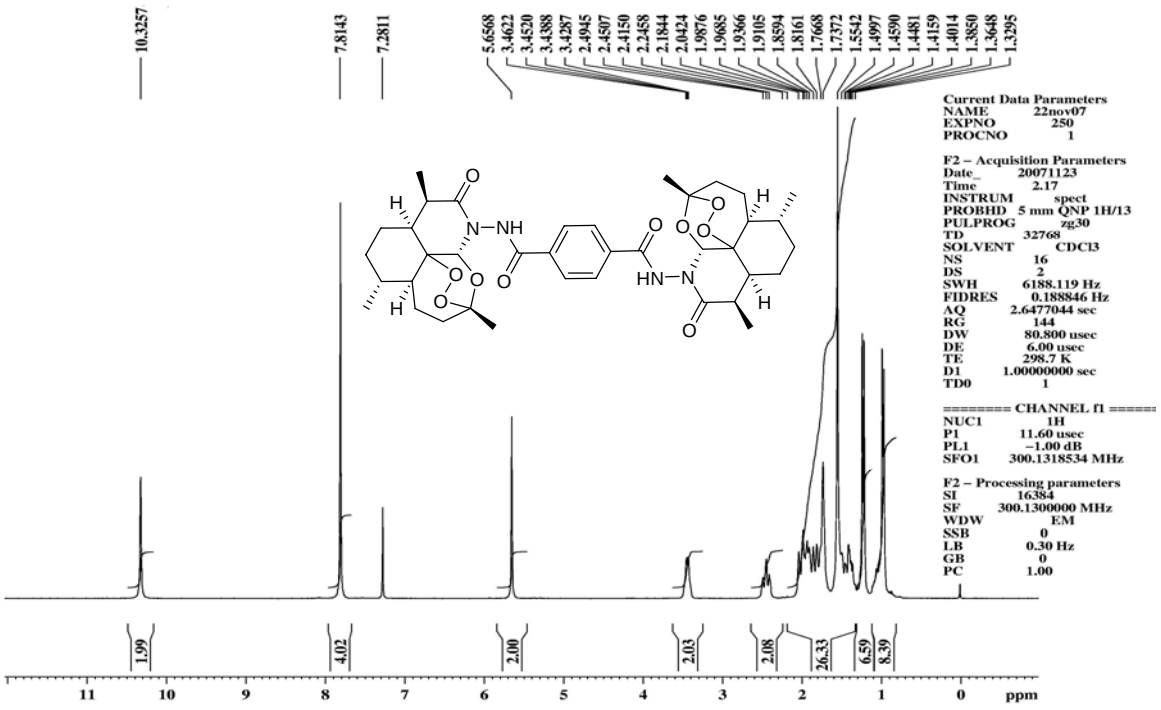

Fig 17: ^{1}H NMR Spectra of **13e.**

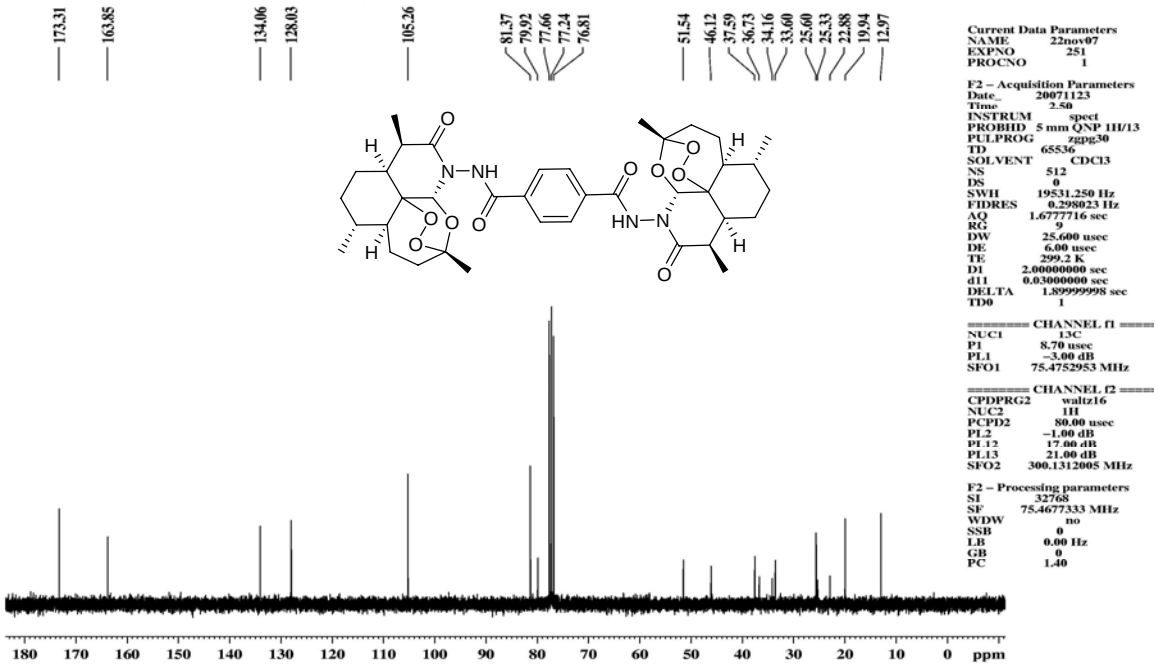

Fig 18: ^{13}C NMR Spectra of **13e.**

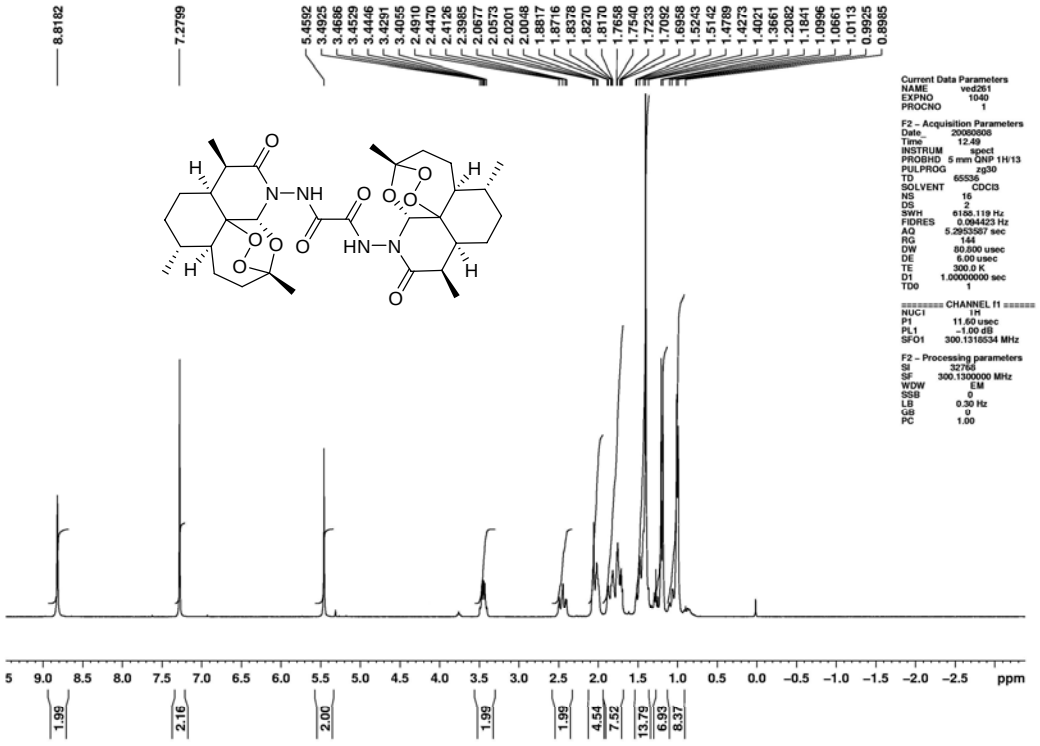

Fig 19: ^{1}H NMR Spectra of **13f.**

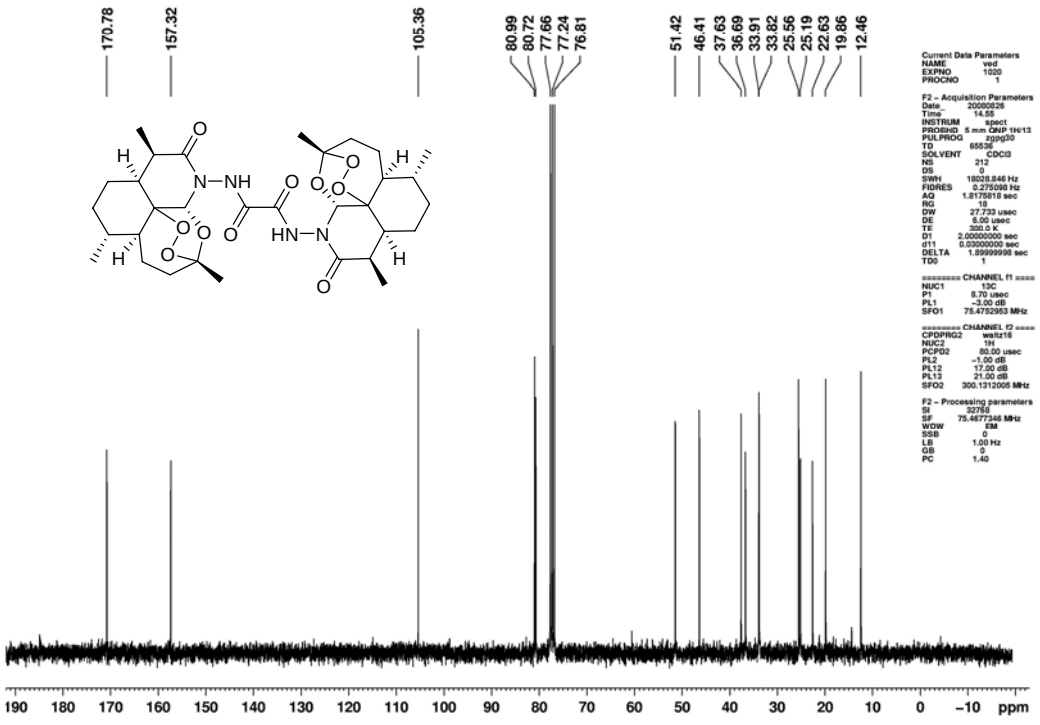

Fig 20: ^{13}C NMR Spectra of **13f.**

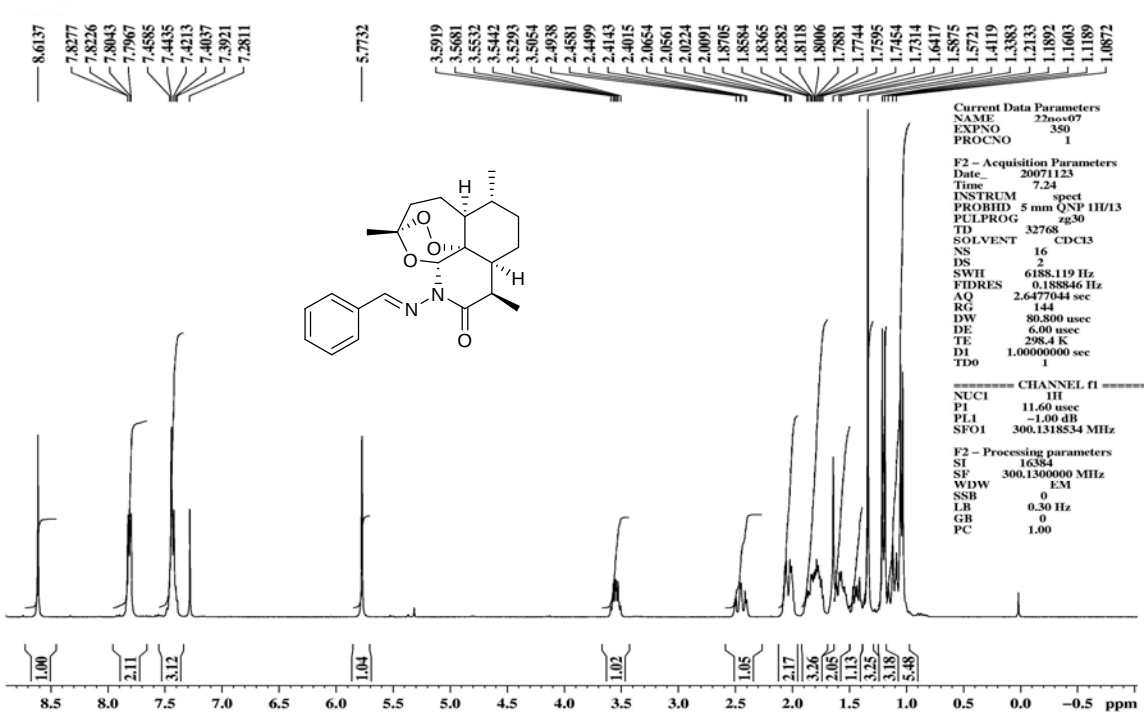

Fig 21: ^{1}H NMR Spectra of **14a.**

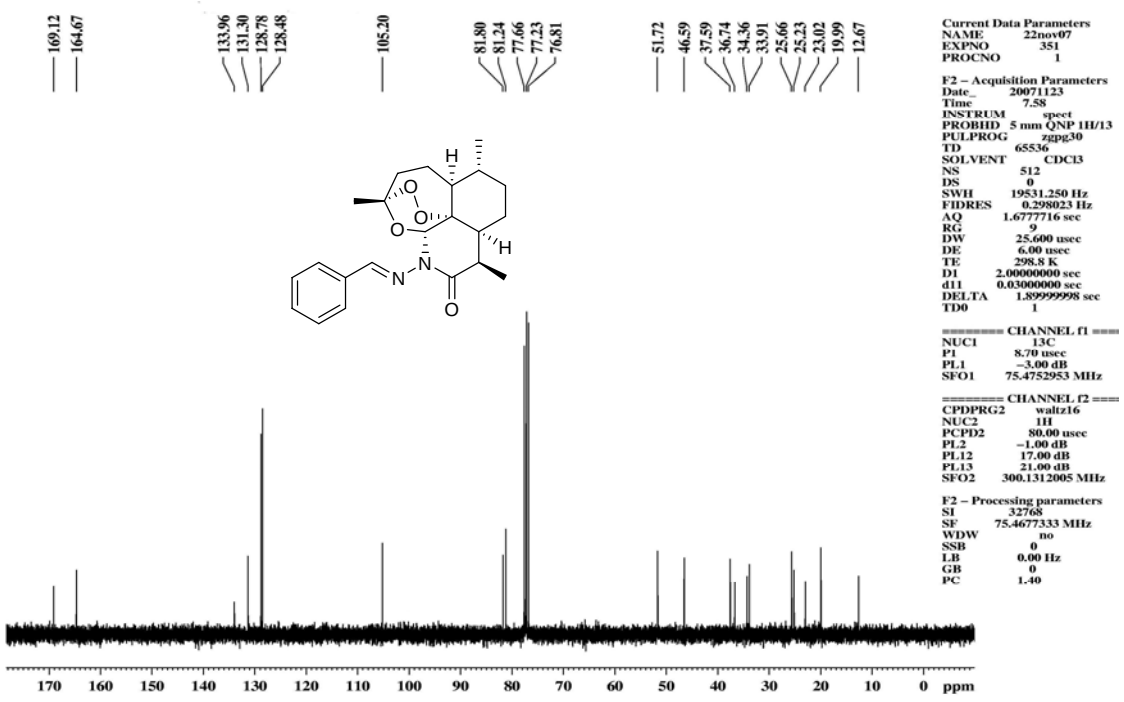

Fig 22: ^{13}C NMR Spectra of **14a.**

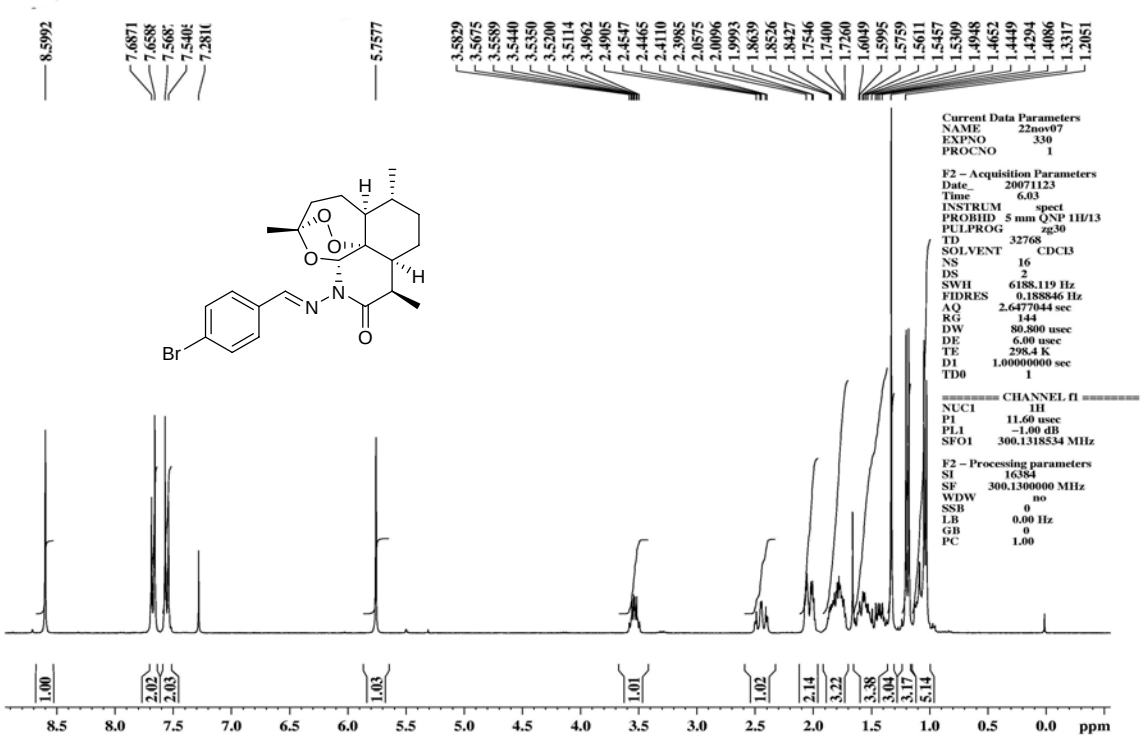

Fig 23: ^{1}H NMR Spectra of **14b.**

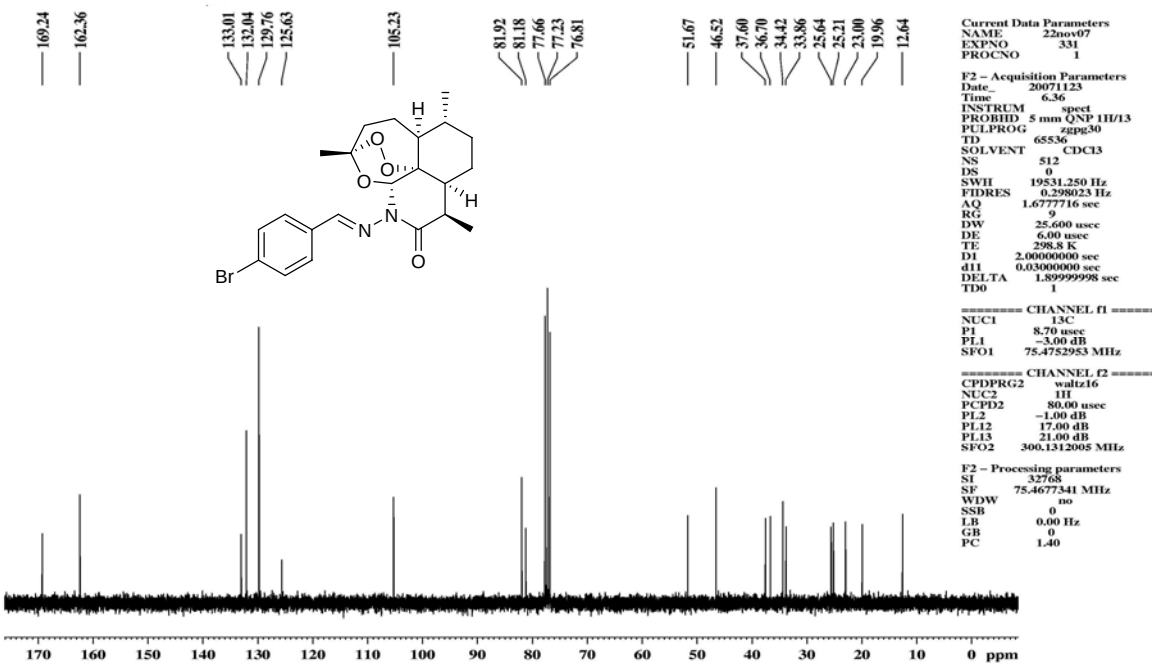

Fig 24: ^{13}C NMR Spectra of **14b.**

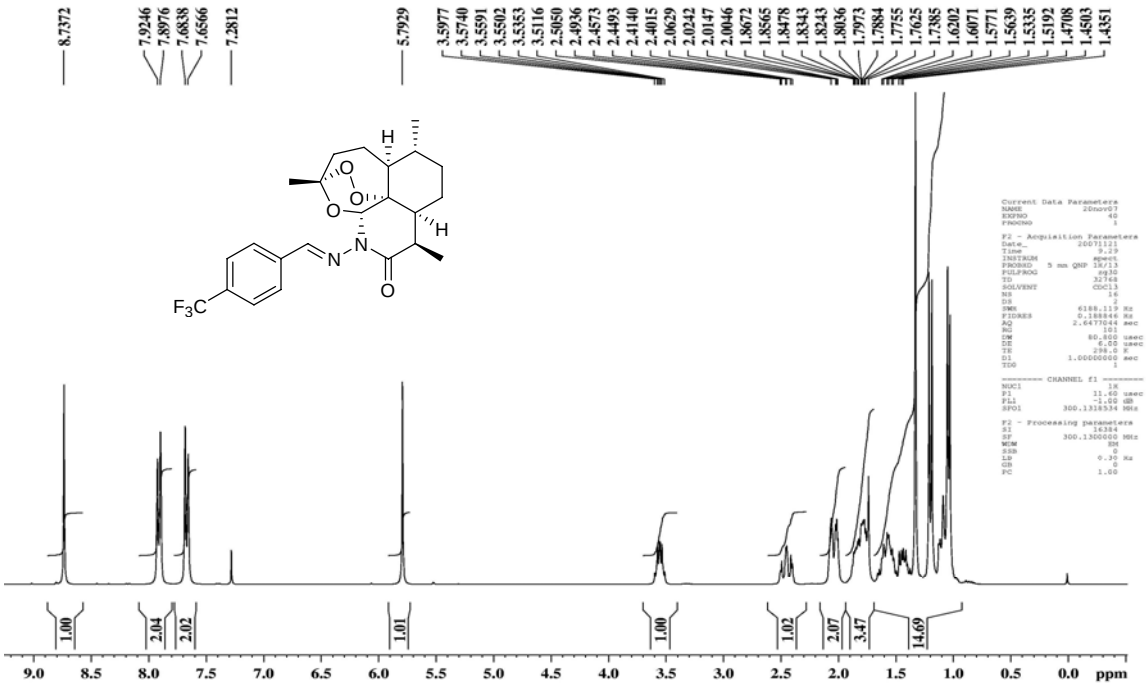

Fig 25: ^{1}H NMR Spectra of **14c.**

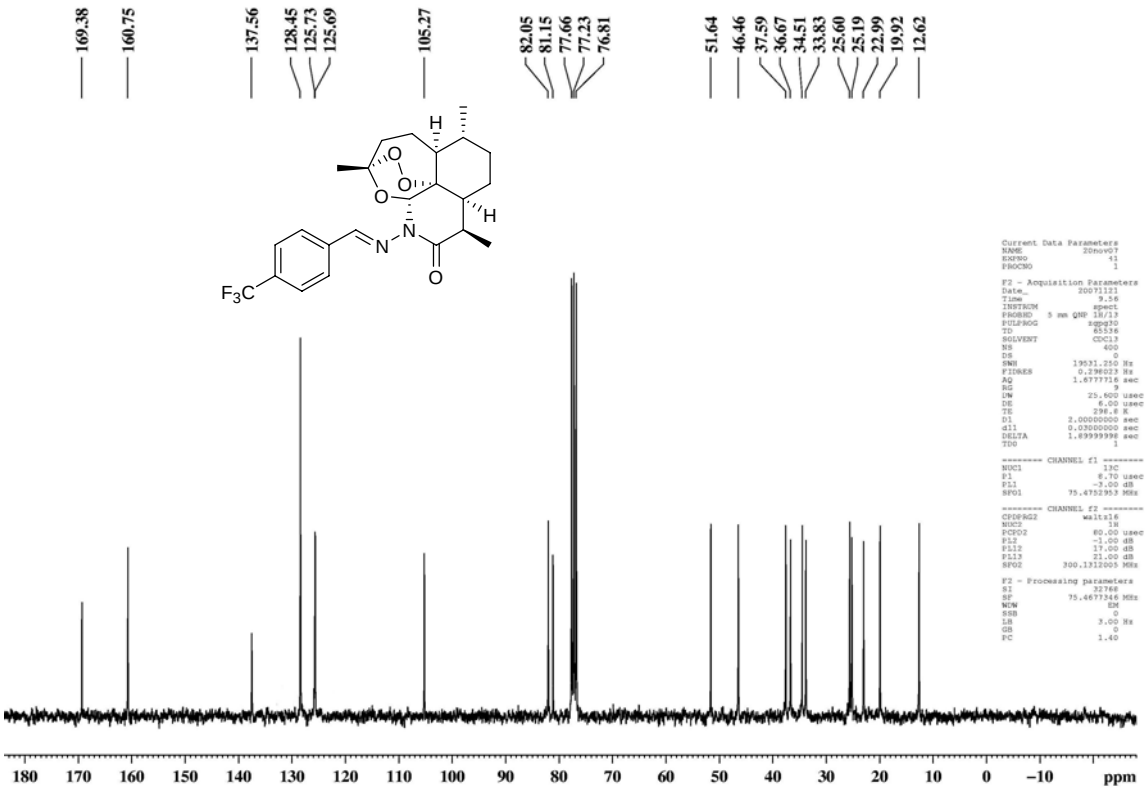

Fig 26: ^{13}C NMR Spectra of **14c.**

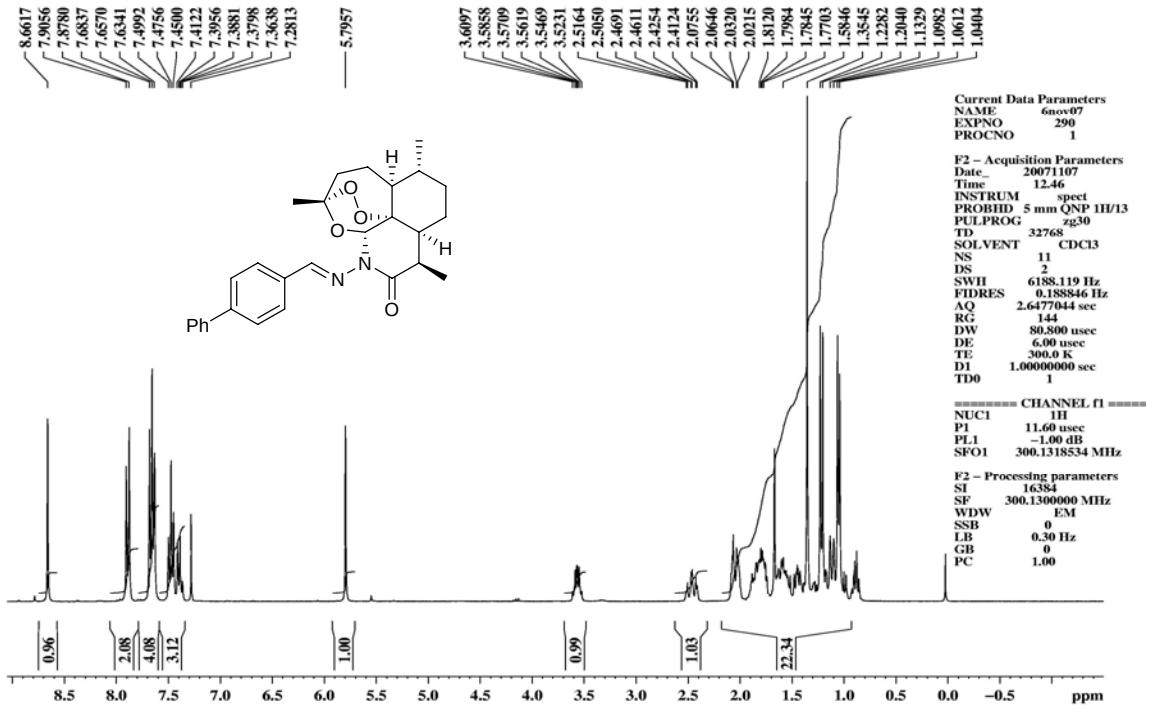

Fig 27: ^{1}H NMR Spectra of **14d.**

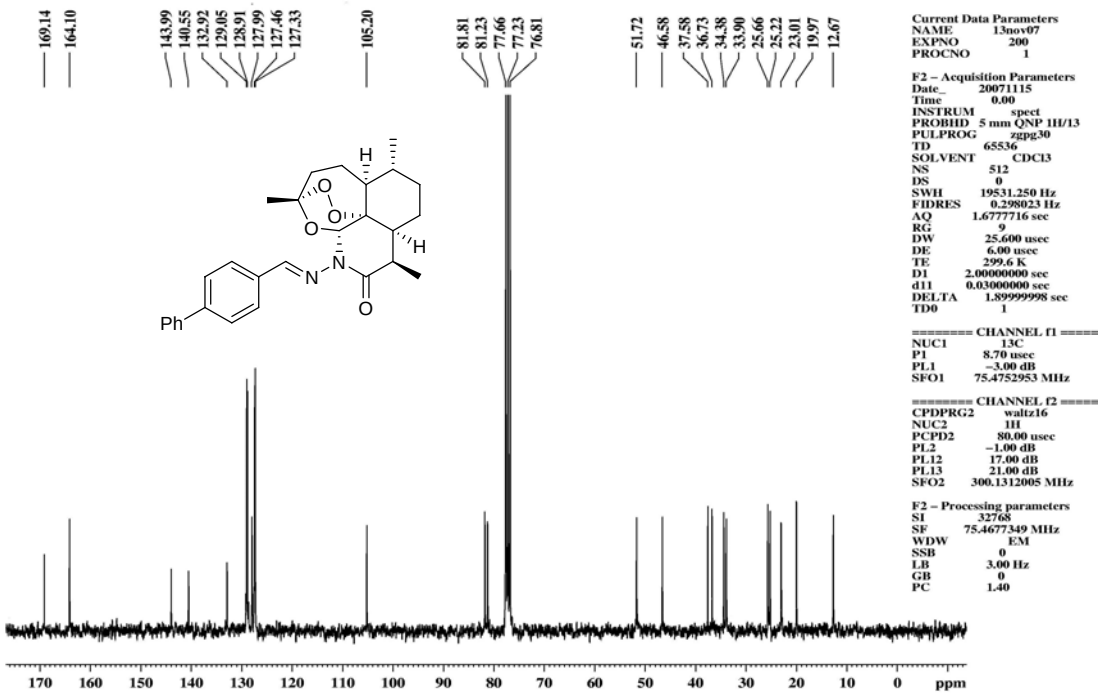

Fig 28: ^{13}C NMR Spectra of **14d.**

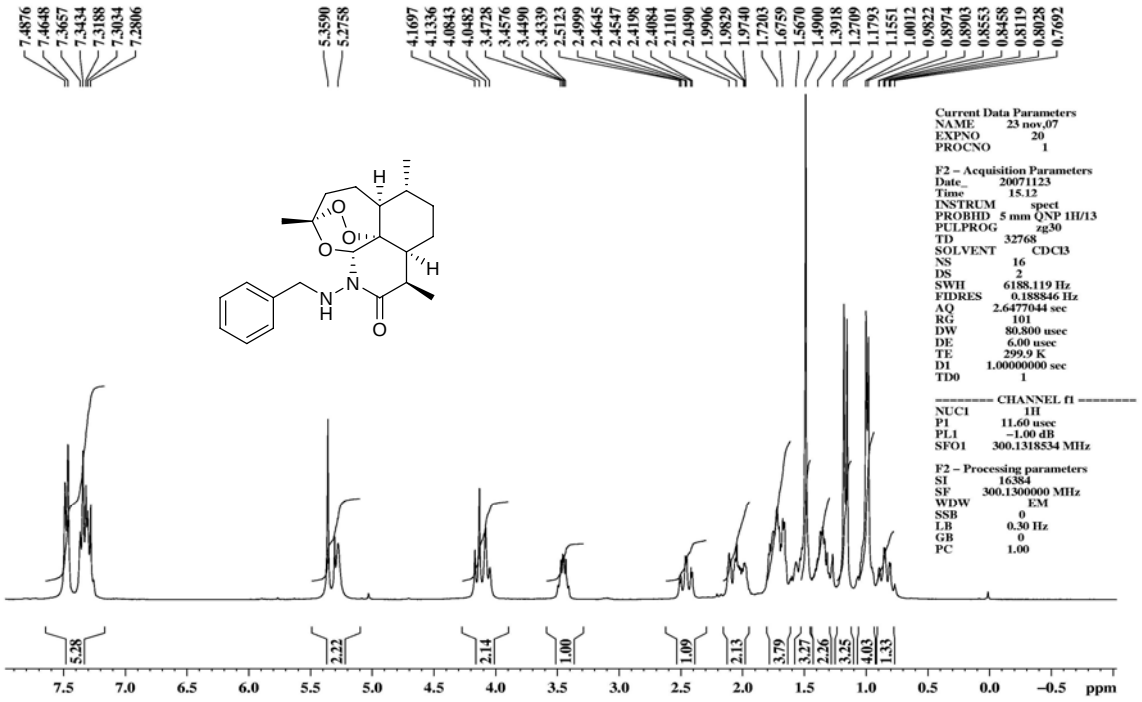

Fig 29: ^{1}H NMR Spectra of **15a.**

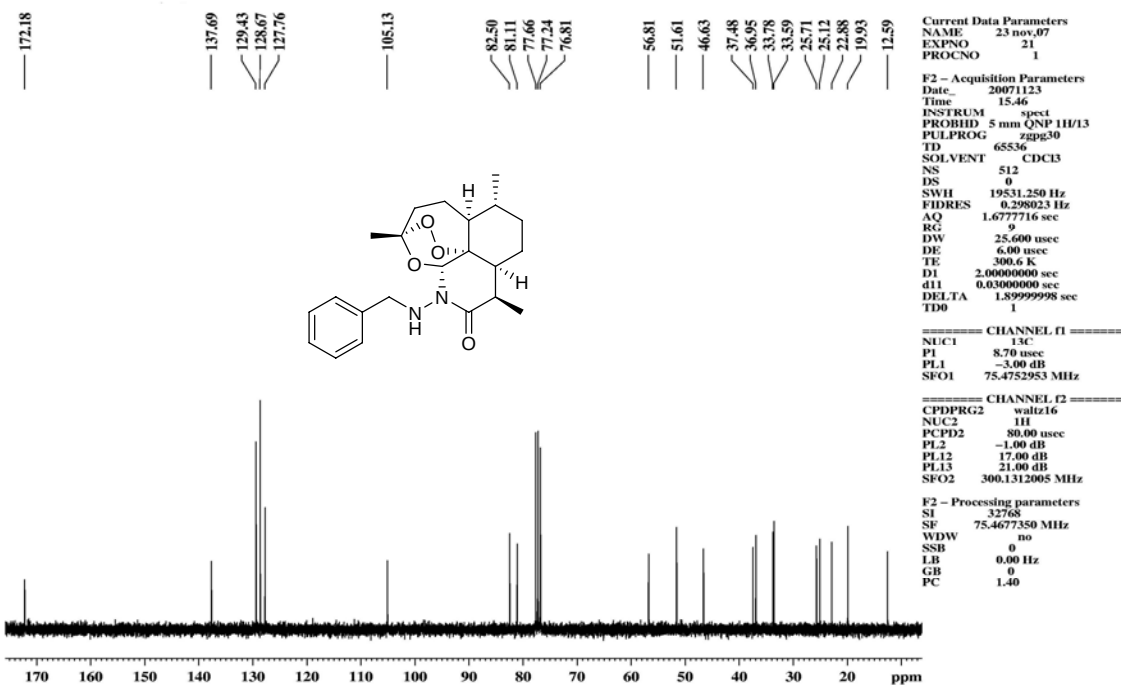

Fig 30: ^{13}C NMR Spectra of **15a.**

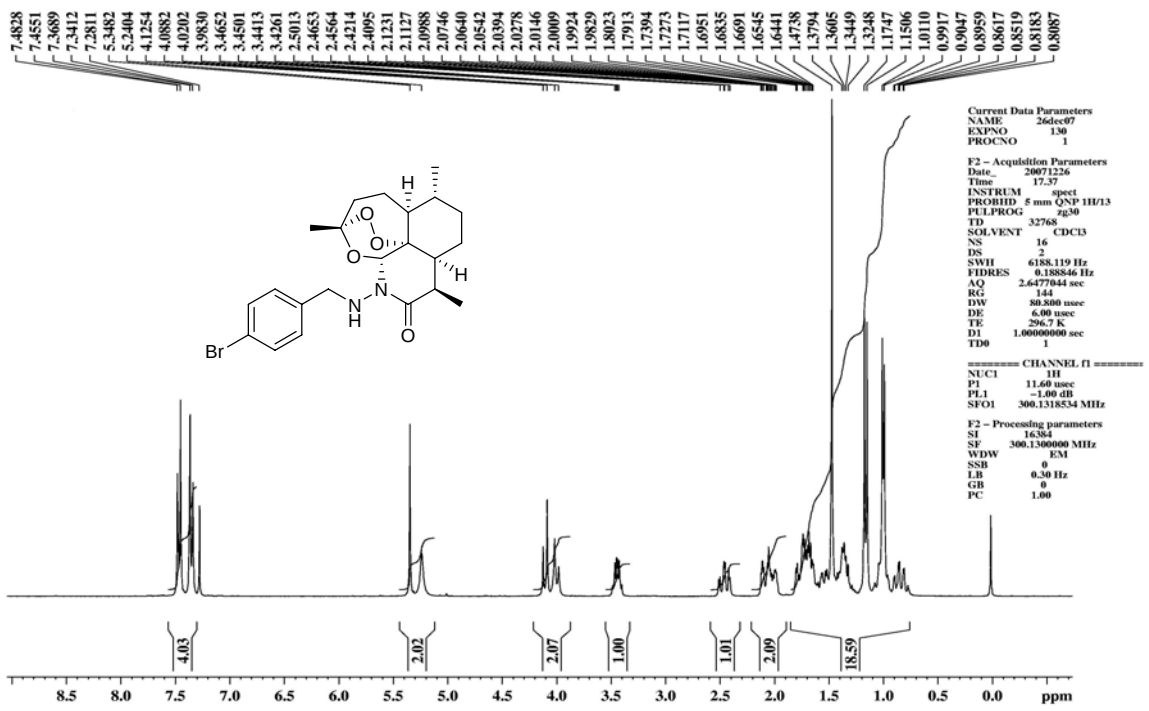

Fig 31: ^{1}H NMR Spectra of **15b.**

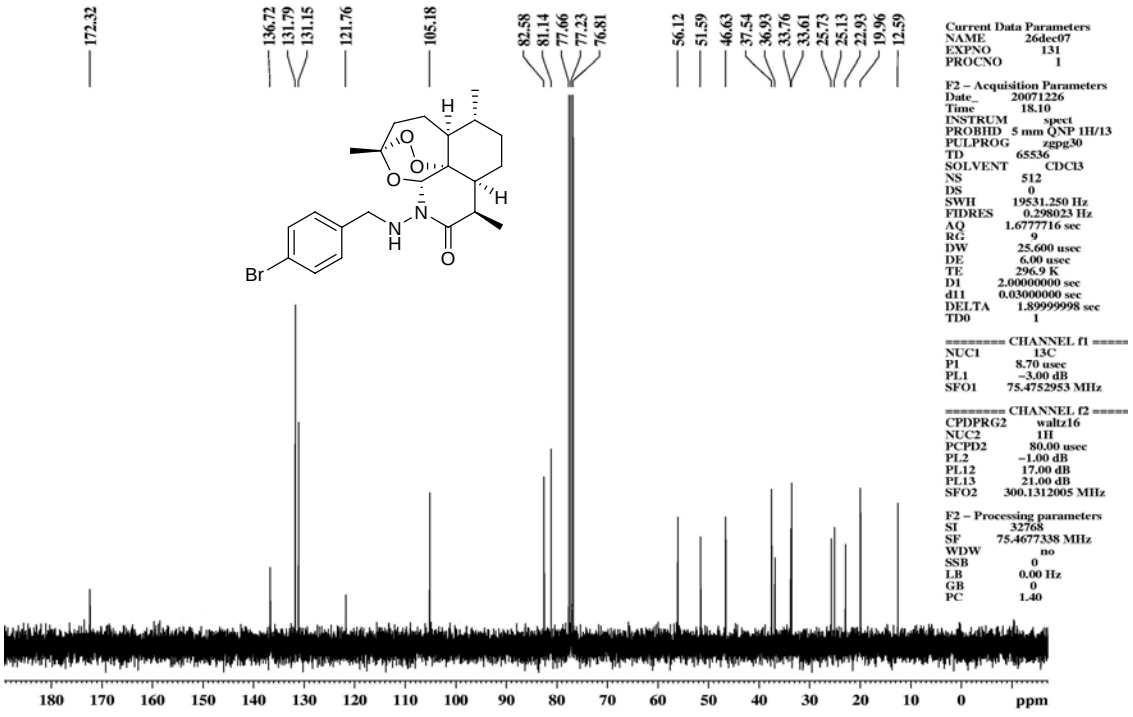

Fig 32: ^{13}C NMR Spectra of **15b.**

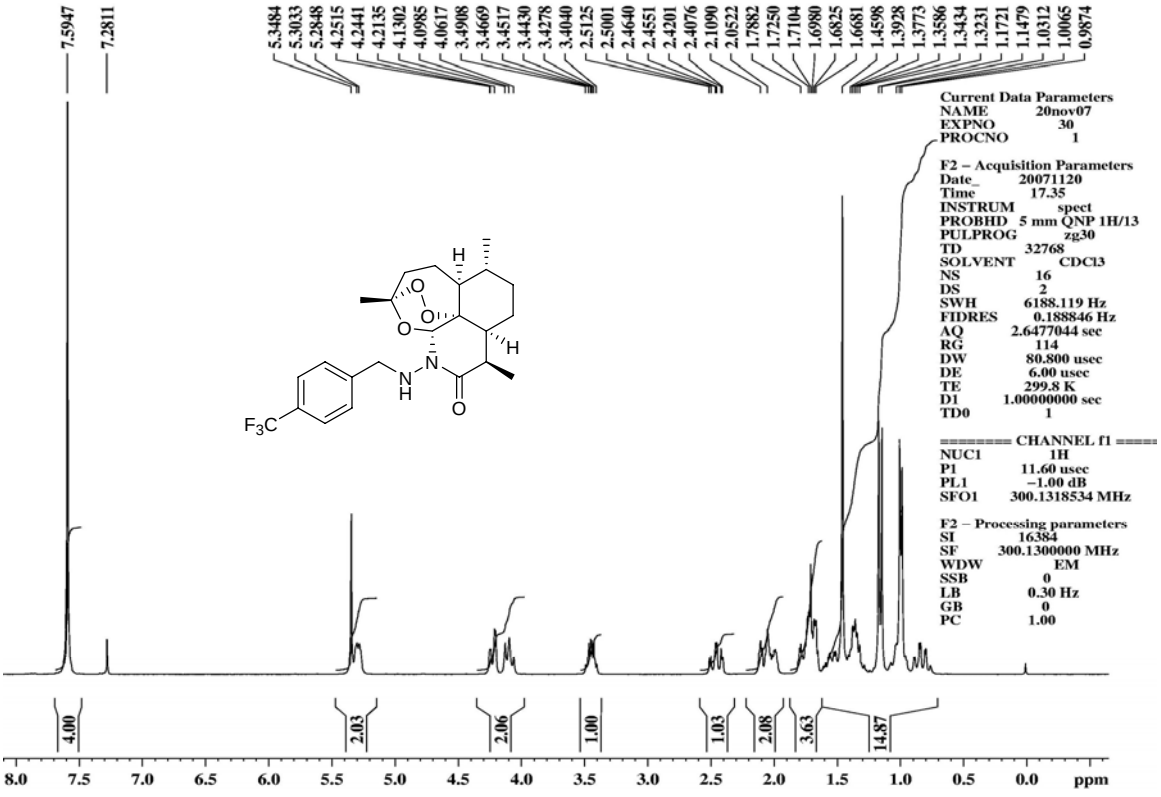

Fig 33: ^{1}H NMR Spectra of **15c.**

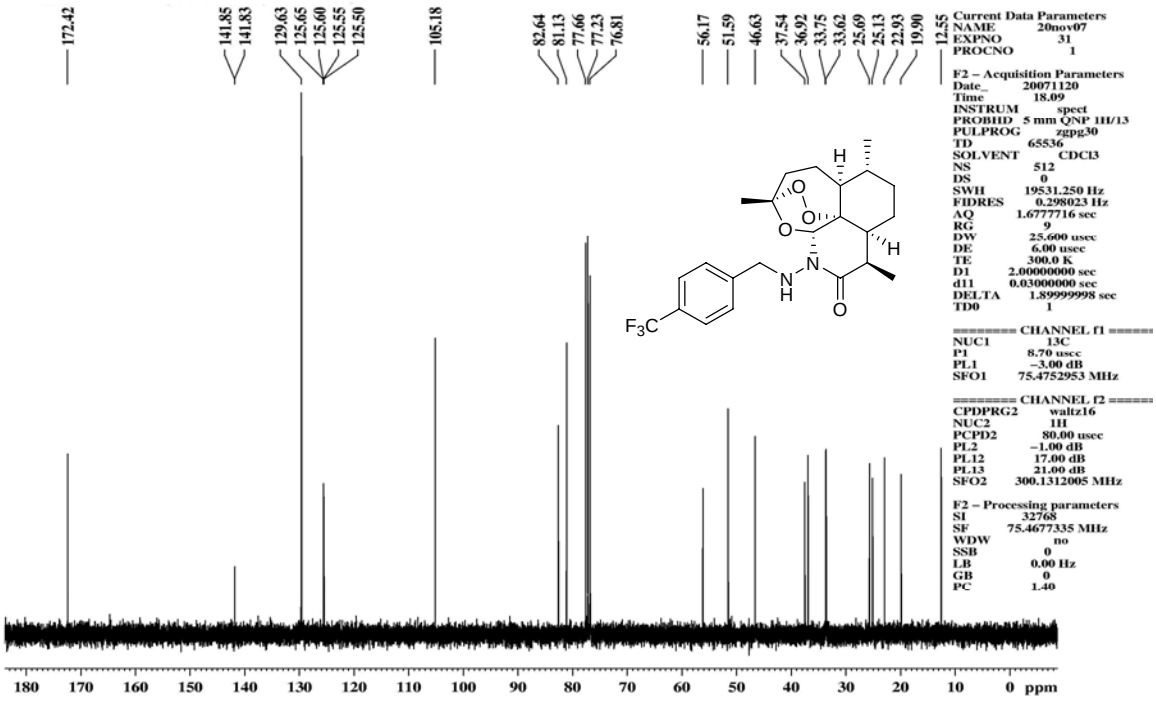

Fig 34: ^{13}C NMR Spectra of **15c.**

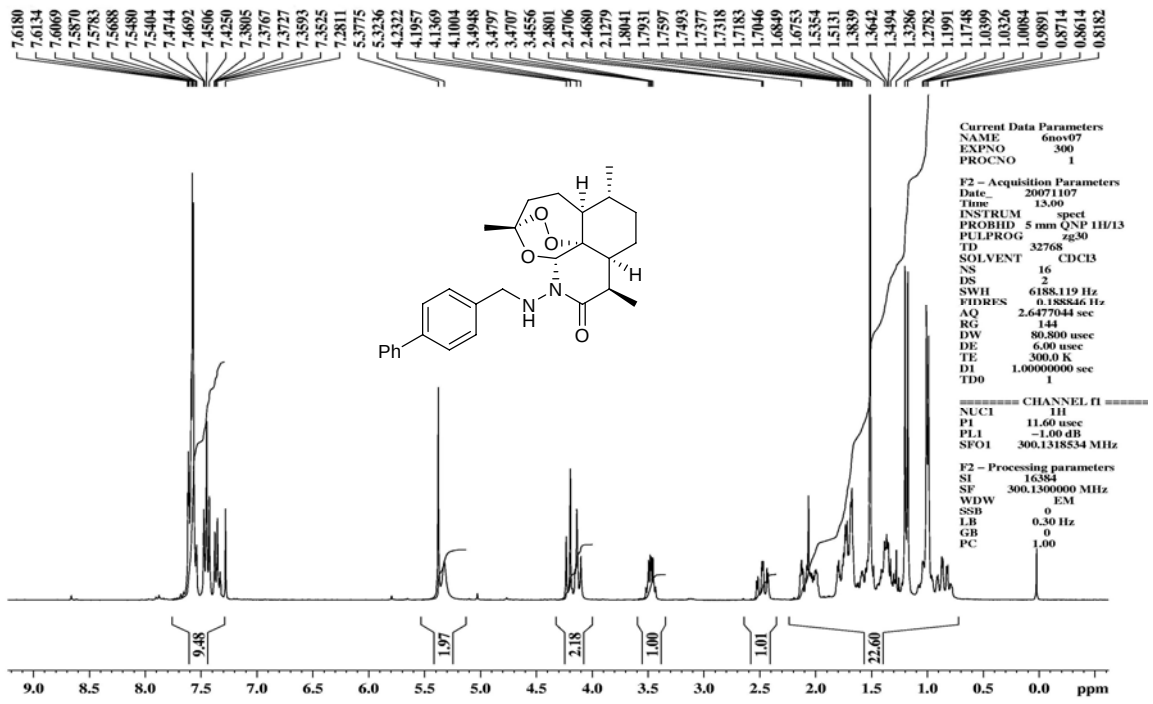

Fig 35: ^{1}H NMR Spectra of **15d.**

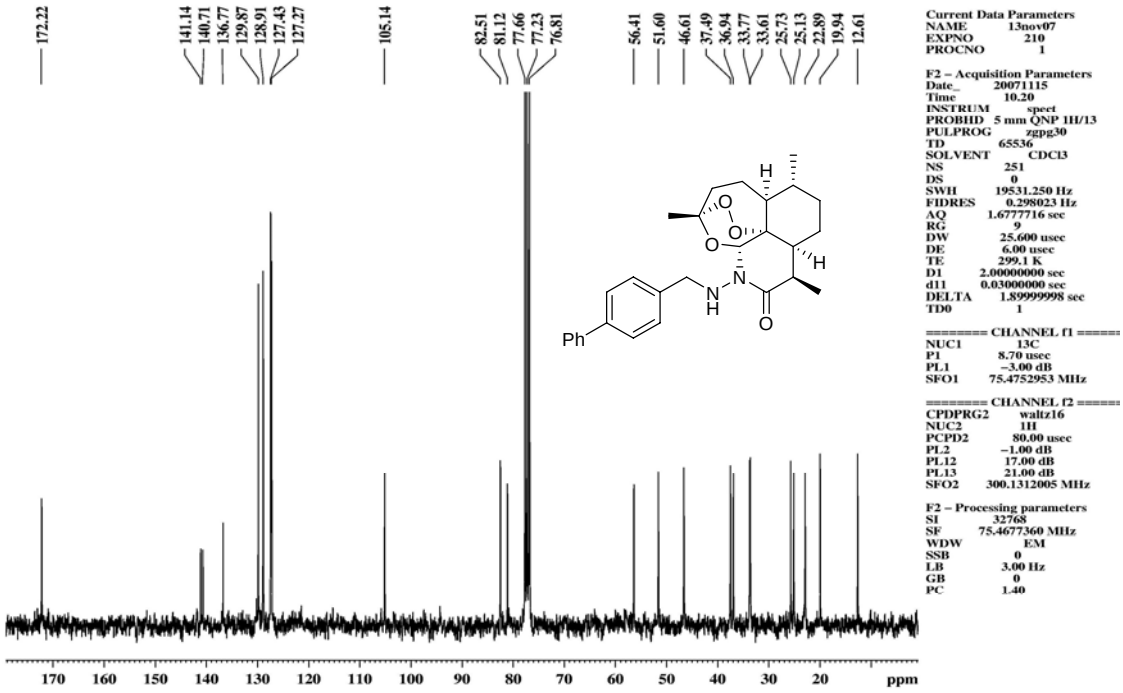

Fig 36: ^{13}C NMR Spectra of **15d.**

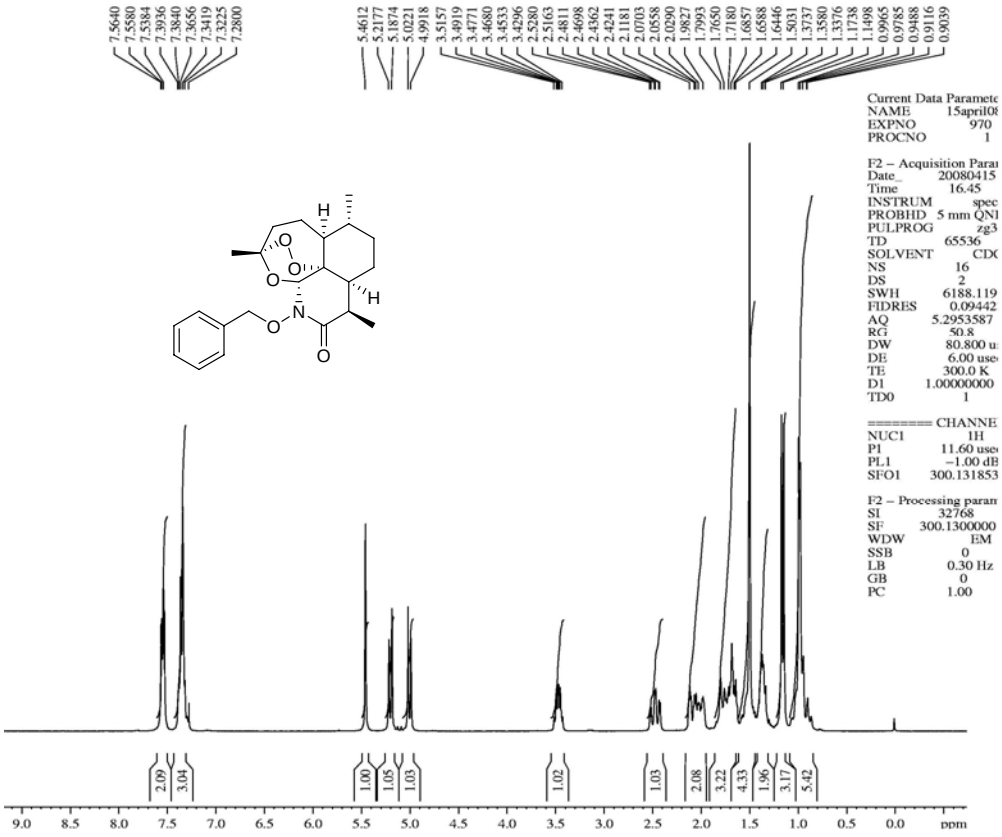

Fig 37: ^{1}H NMR Spectra of **16a.**

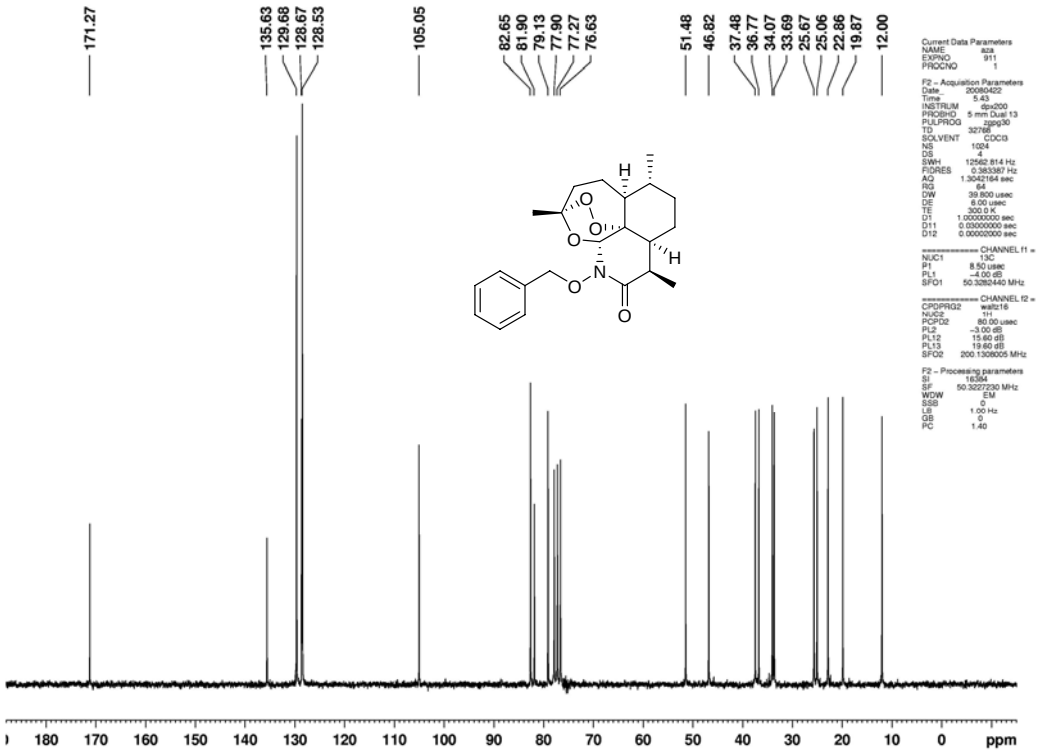

Fig 38: ^{13}C NMR Spectra of **16a.**

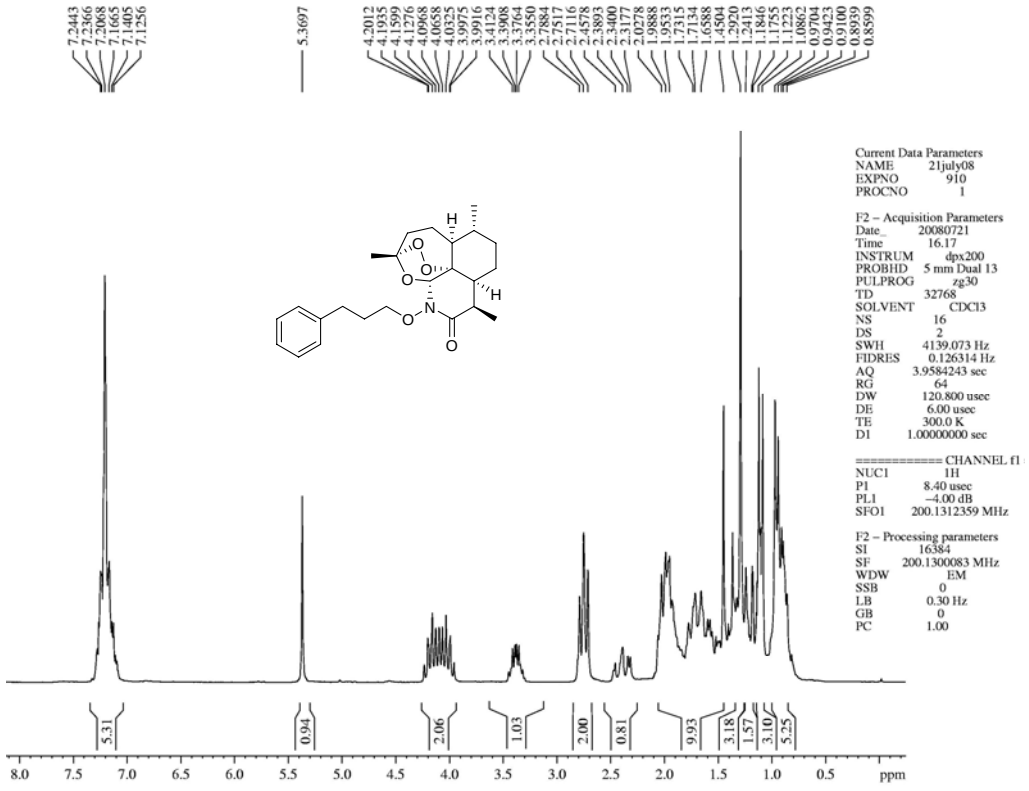

Fig 39: ^{1}H NMR Spectra of **16b.**

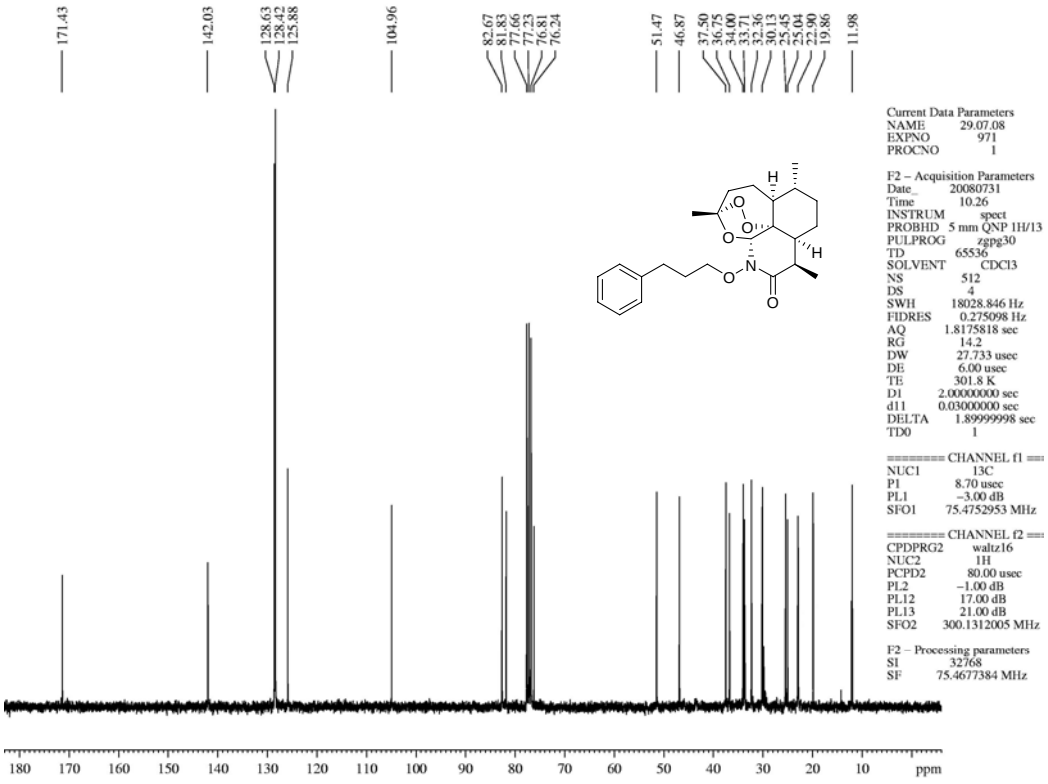

Fig 40: ^{13}C NMR Spectra of **16b.**

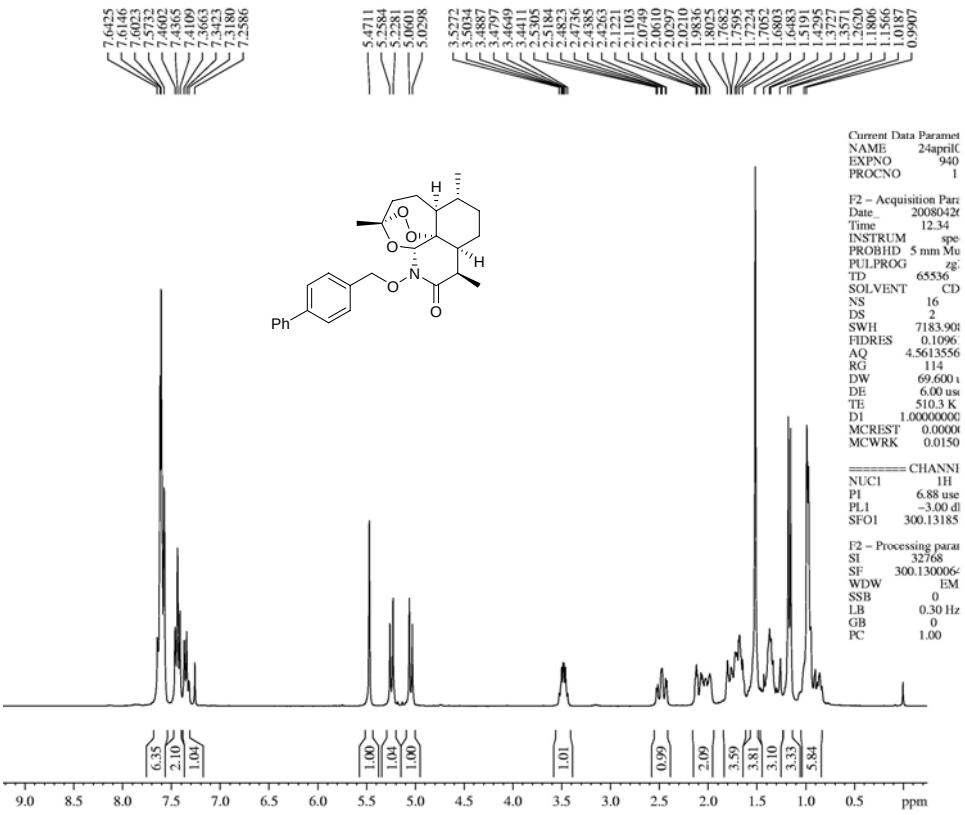

Fig 41: ^{1}H NMR Spectra of **16c.**

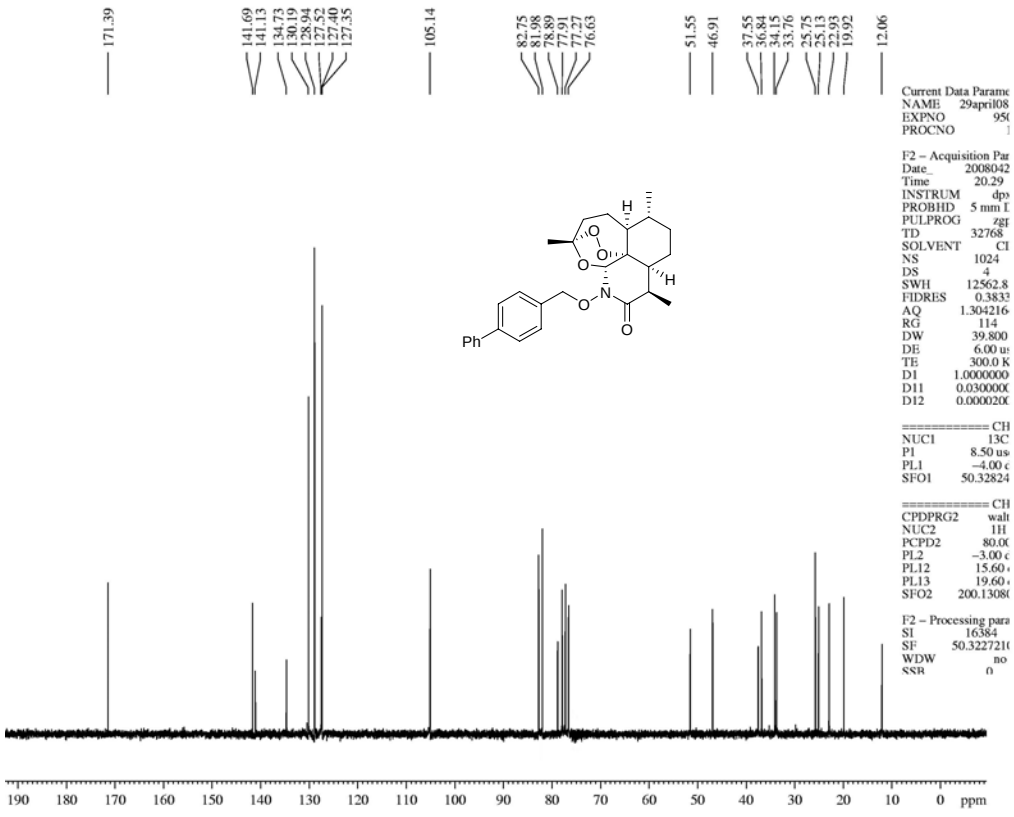

Fig 42: ^{13}C NMR Spectra of **16c.**

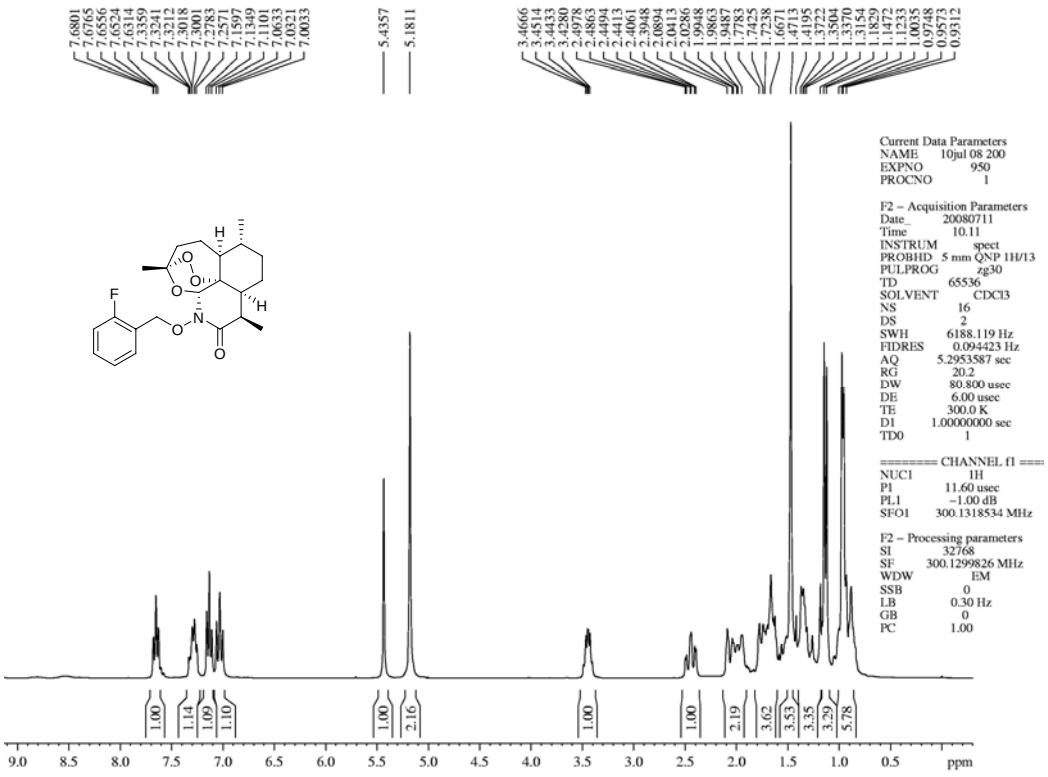

Fig 43: ^{1}H NMR Spectra of **16d.**

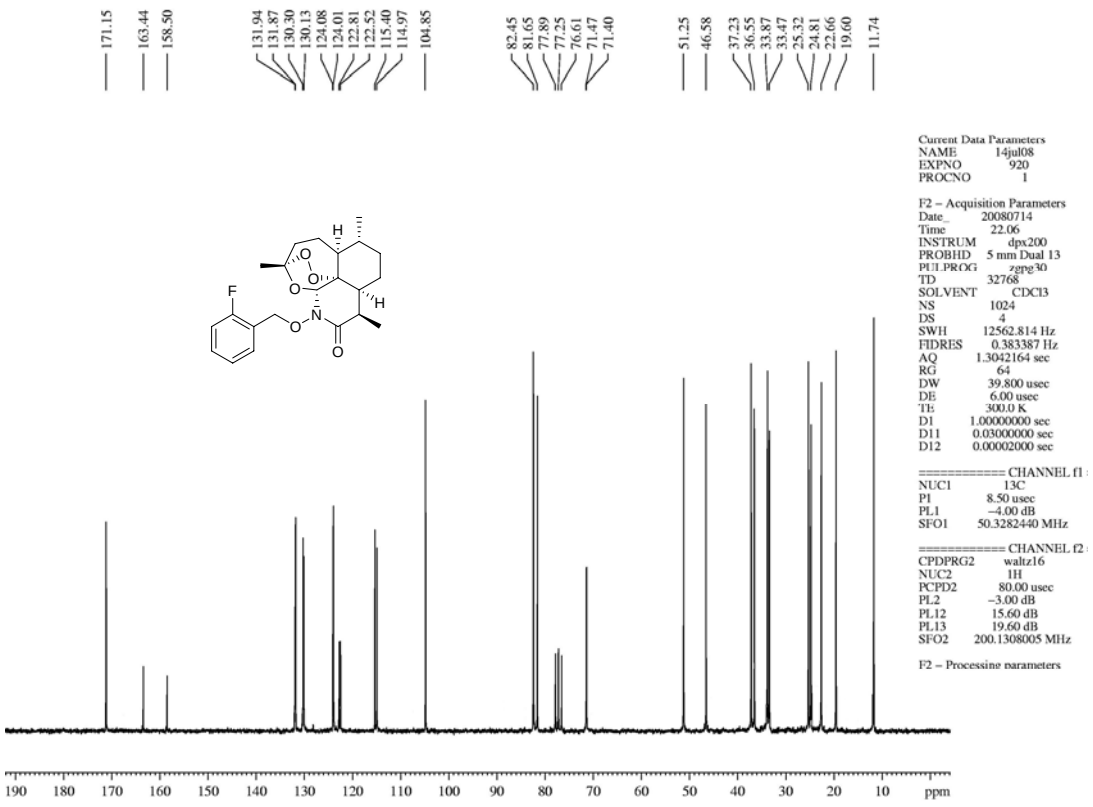

Fig 44: ^{13}C NMR Spectra of **16d.**

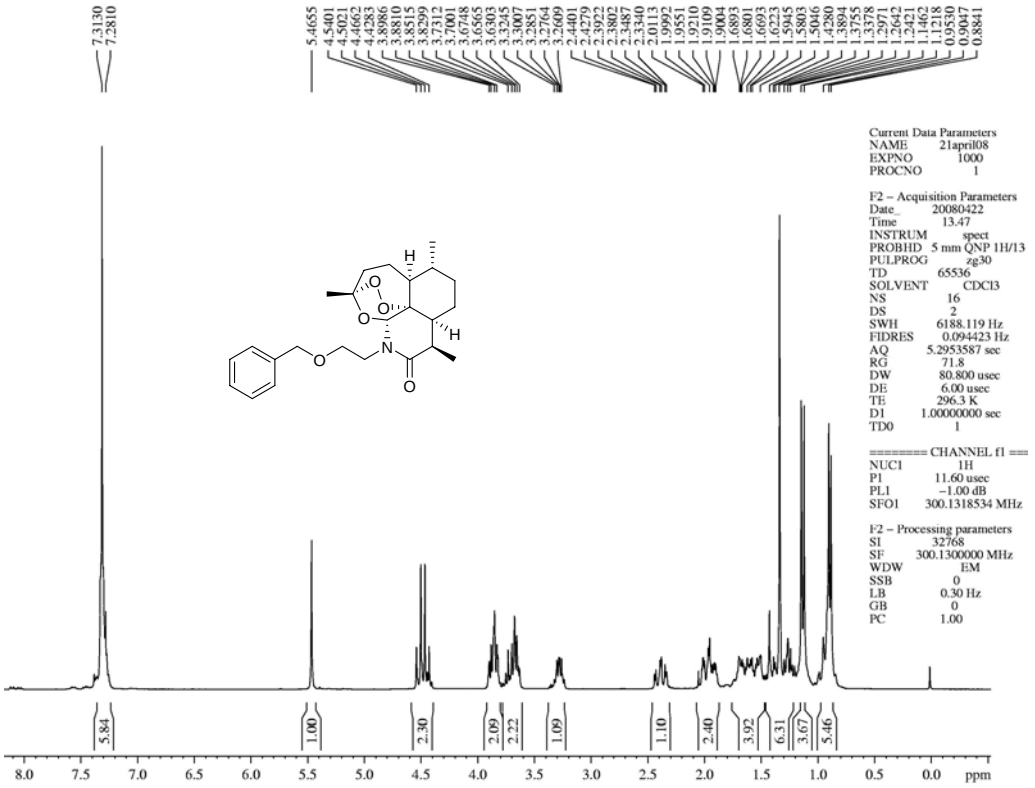

Fig 45: ^{1}H NMR Spectra of **17a.**

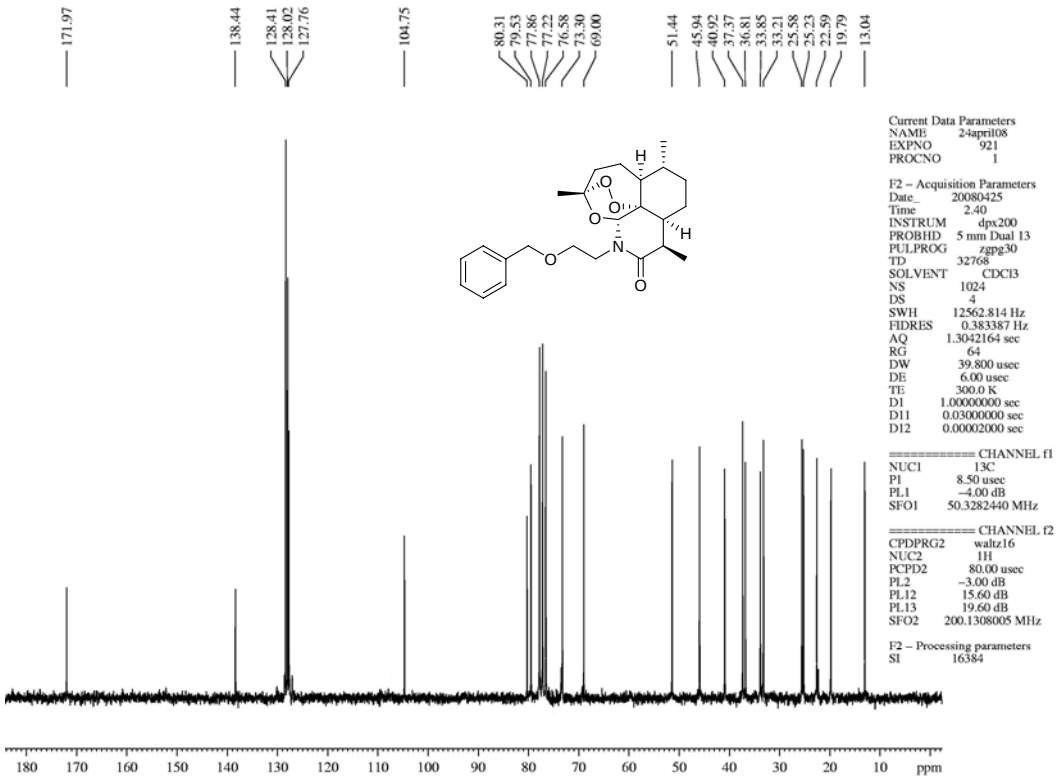

Fig 46: ^{13}C NMR Spectra of **17a.**

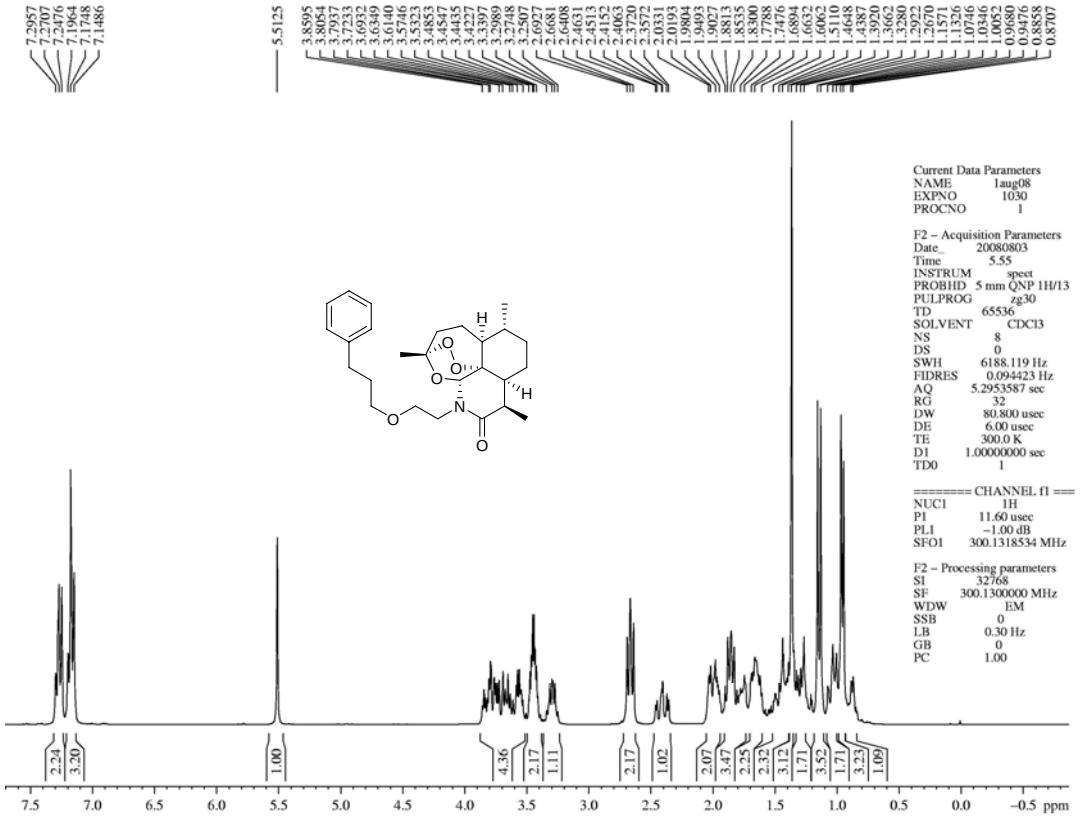

Fig 47: ^{1}H NMR Spectra of **17b.**

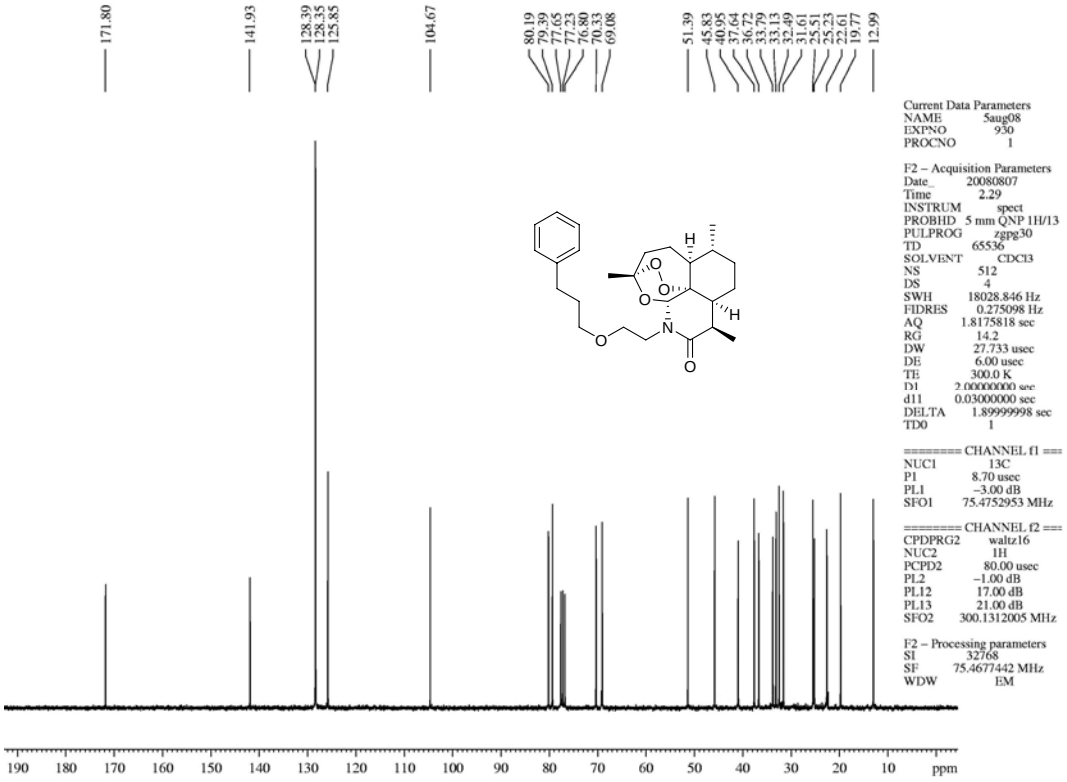

Fig 48: ^{13}C NMR Spectra of **17b.**

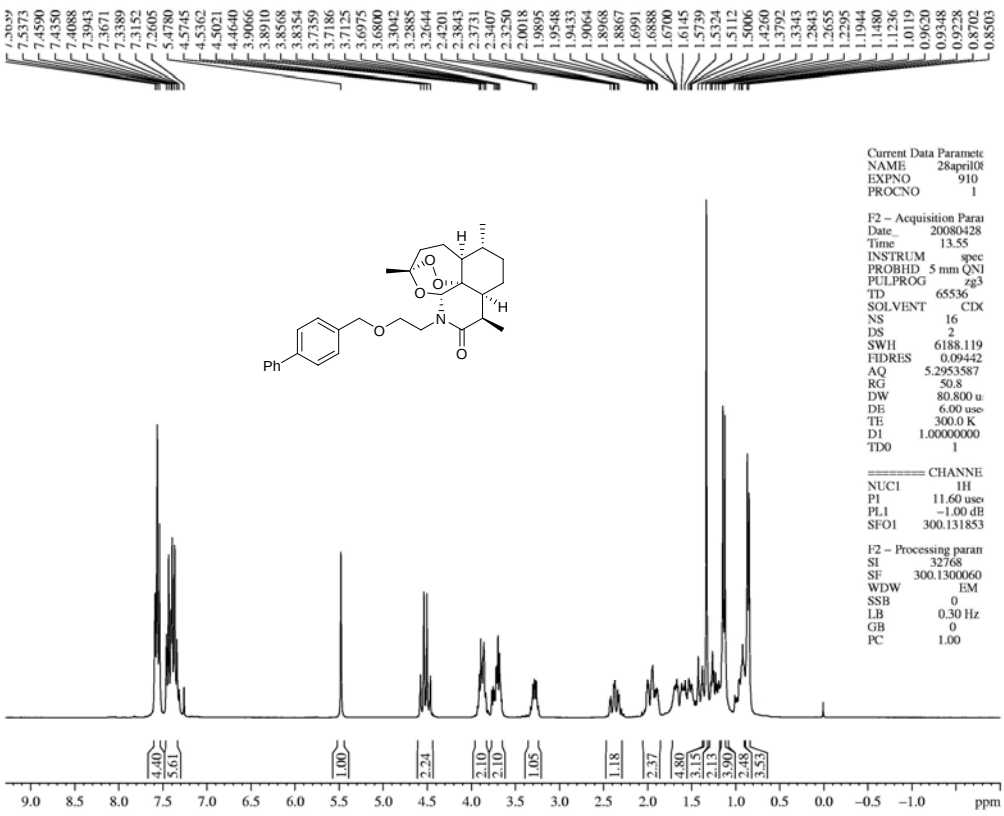

Fig 49: ^{1}H NMR Spectra of **17c.**

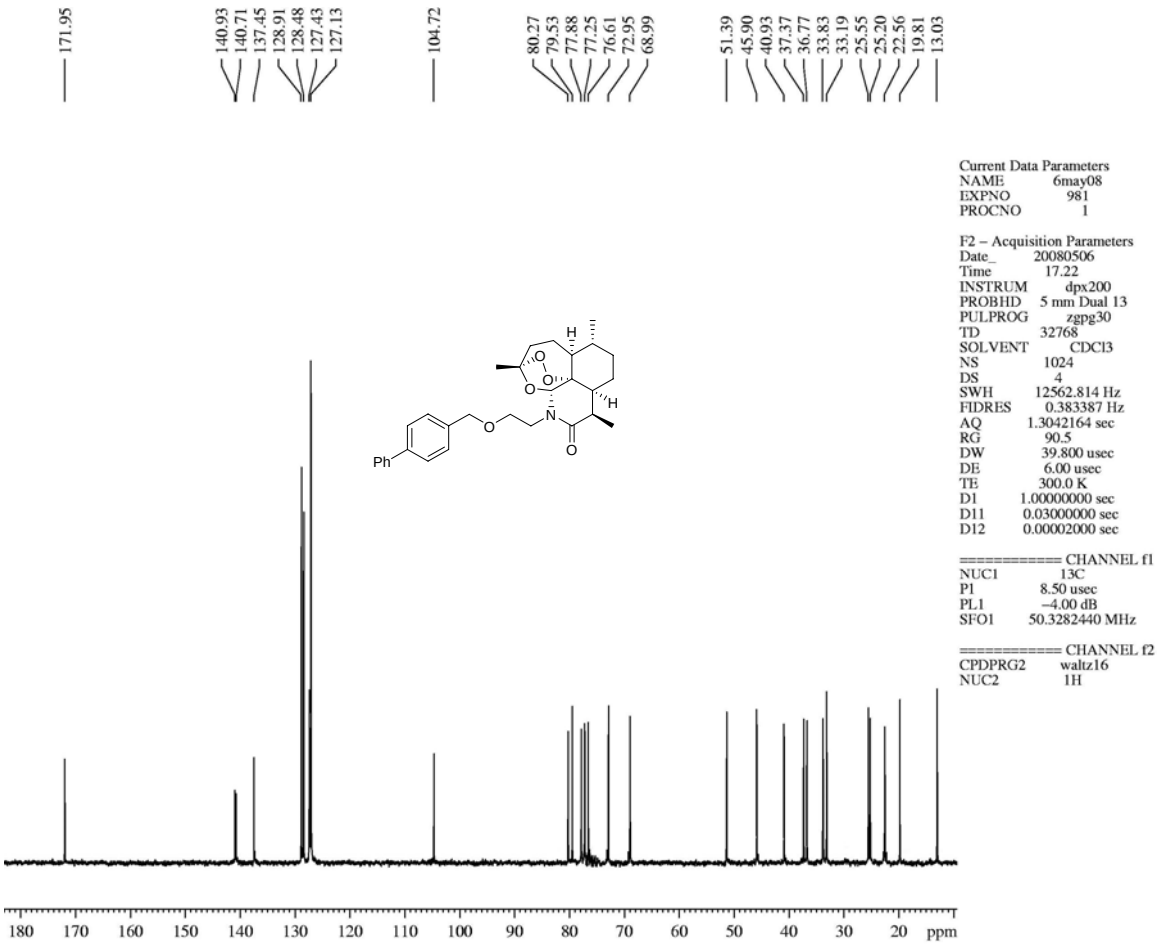

Fig 50: ^{13}C NMR Spectra of **17c.**

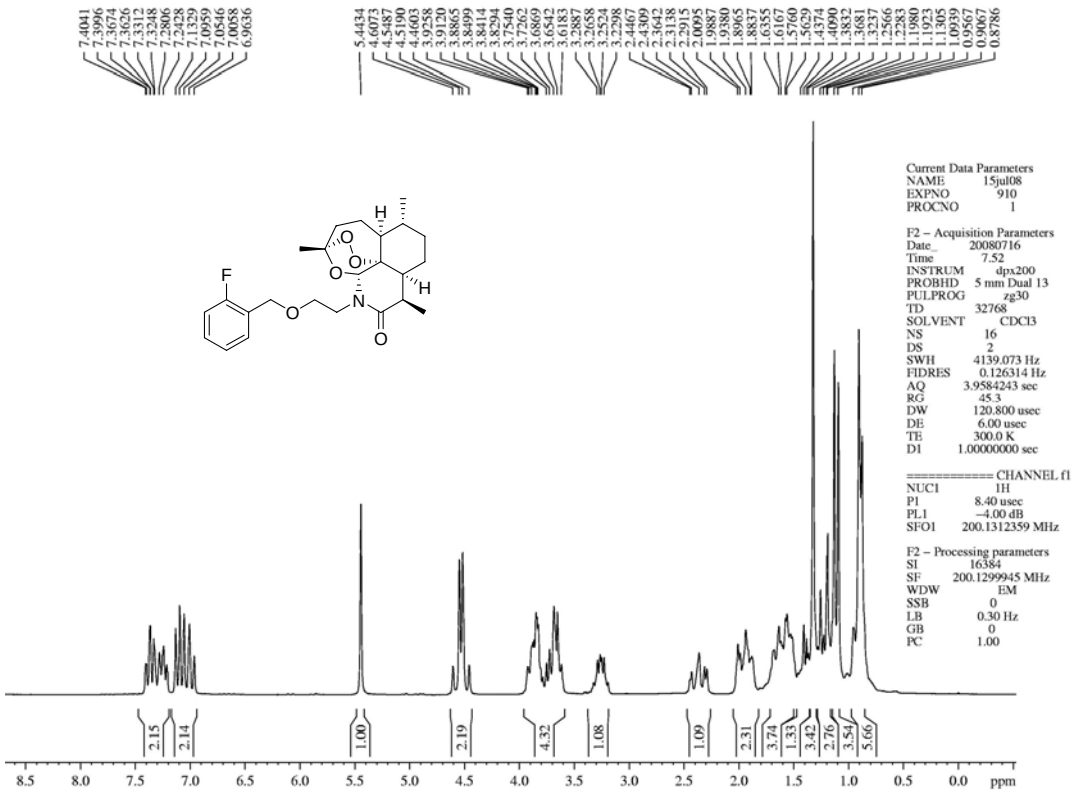

Fig 51: ^{1}H NMR Spectra of **17d.**

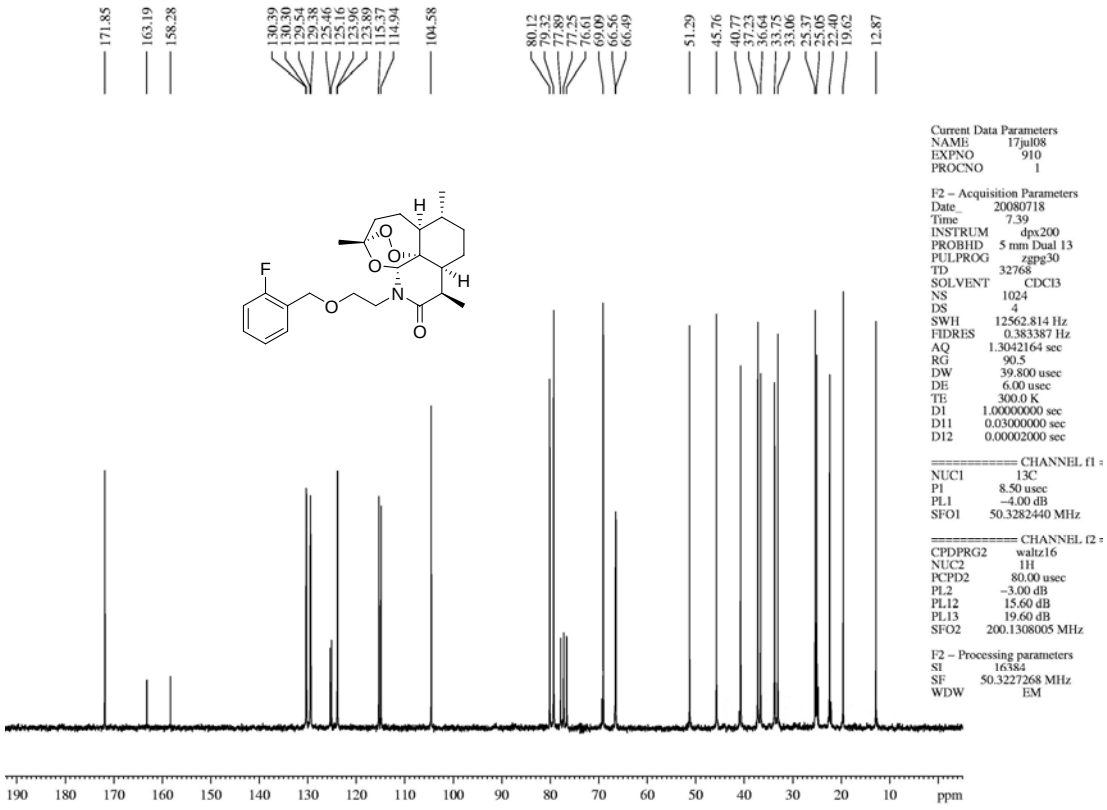

Fig 52: ^{13}C NMR Spectra of **17d.**