

Supporting Information's

Exploring the Anti-diabetic Potential of *Bis*-Schiff Bases of Ibuprofen: Insight into the *In Vitro*, Molecular Docking and Density Functional Theory Analysis

Muhammad Ayaz^a, Aftab Alam^b, Zainab^c, Ahmed A. Elhenawy^{d,e}, Imtiaz Ahmad^f, Sajjad Ur Rahman^a, Liaqat Ali^g, Abdul Latif^a, Mumtaz Ali^{a*}, Manzoor Ahmad^{a*}

^aDepartment of Chemistry, University of Malakand, P.O. Box 18800, Dir Lower, Khyber Pakhtunkhwa, Pakistan

^bDepartment of Chemistry, Rawalpindi Women University, Rawalpindi, Pakistan

^cCollege of Chemistry and Materials Science, Hebei Normal University, Shijiazhuang, China

^dChemistry Department, Faculty of Science, Al-Azhar University, Nasr City 11884, Cairo, Egypt

^eChemistry Department, Faculty of Science, Al-Baha University, Al-Bahah 65731, Saudi Arabia

^fPrograma de Pós-Graduação em Bioquímica e Bioprospecção, Universidade Federal de Pelotas, Campus Universitário Capão do Leão S/N, Pelotas, RS CEP 96010-900, Brazil

^gDepartment of Chemistry, University of Mianwali, Mianwali, 42200 Pakistan

Correspondence to: manzoorahmad@uom.edu.pk; mumtazali@uom.edu.pk;

Spectral Interpretation of the Synthesized Products (4-15)

2-(4-isobutylphenyl)-N'-4-(2-(2-4-nitrobenzylidene)hydrazinyl)-2-oxoethoxy)benzylidene)propanehydrazide (4)

Off white Amorphous Solid: Yield: 90%, 118 mg; M.P: 185-187 °C; ¹H-NMR (600 MHz, CDCl₃): δ 9.41 (br.s, 2H, 2-NH), 8.47 (s, 2H, 2-N=CH-), 8.24 (d, *J* = 9.0 Hz, 2H, Ar-H), 7.80-7.73 (m, 4H, Ar-H), 7.27 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.14-7.12 (m, 2H, Ar-H), 7.06 (d, *J* = 7.8 Hz, 2H, Ar-H), 4.68 (s, 2H, -CH₂), 4.64-4.62 (m, 1H, -CH), 2.39 (d, *J* = 7.2 Hz, 2H -CH₂), 1.80-1.75 (m, 1H, -CH), 1.53 (d, *J* = 7.2 Hz, 3H, -CH₃), 0.84-0.82 (m, 6H, 2-CH₃). ¹³C-NMR (150 MHz, CDCl₃): δ 176.9 (C=O), 170.2 (C=O), 148.4 (Ar-C-NO₂), 141.3 (Ar-C), 140.4 (2-N=CH), 140.0 (Ar-C), 139.8 (Ar-C), 138.1 (Ar-C), 130.0 (2Ar-CH), 129.6 (2Ar-CH), 128.0 (2Ar-CH), 127.6 (2Ar-CH), 127.0 (Ar-C), 124.1 (2Ar-CH), 123.9 (2Ar-CH), 69.0 (-CH₂), 45.0 (-CH₂), 41.6 (-CH), 30.1 (-CH), 22.4 (2-CH₃), 18.4 (-CH₃). HRMS (ESI⁺): 545.2675 [M+Na]⁺ calcd for C₂₉H₃₁N₅NaO₅: 545.2724.

2-(4-isobutylphenyl)-N'-4-(2-(3-nitrobenzylidene)hydrazinyl)-2-oxoethoxy)benzylidene)propanehydrazide (5)

Brownish Amorphous Solid: Yield: 88%, 116 mg; M.P: 163-165 °C; ¹H-NMR (600 MHz, CDCl₃): δ 9.41 (br.s, 2H, 2-NH), 8.46 (s, 2H, 2-N=CH-), 8.21-8.17 (m, 2H, Ar-H), 7.87 (d, *J* = 7.2 Hz, 2H, Ar-H), 7.73 (br.s, 1H, Ar-H), 7.54 (t, *J* = 7.8 Hz, 1H, Ar-H), 7.30 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.16-7.13 (m, 1H, Ar-H), 7.10 (d, *J* = 7.8 Hz, 3H, Ar-H), 4.68 (s, 2H, -CH₂), 4.63-4.59 (m, 1H, -CH), 2.38 (d, *J* = 7.2 Hz, 2H -CH₂), 1.83-1.75 (m, 1H, -CH), 1.53 (d, *J* = 7.2 Hz, 3H, -CH₃), 0.86-0.84 (m, 6H, 2-CH₃). ¹³C-NMR (150 MHz, CDCl₃): δ 176.8 (C=O), 170.2 (C=O), 148.7 (Ar-C-NO₂), 140.4 (Ar-C), 140.3 (2-N=CH), 137.4 (Ar-C), 134.6 (2Ar-C), 132.6 (Ar-CH), 129.8 (Ar-CH), 129.6 (2Ar-CH), 129.4 (2Ar-CH), 128.6 (Ar-C), 127.4 (2Ar-CH), 127.0 (2Ar-CH), 124.3 (Ar-CH), 121.6 (Ar-CH), 69.0 (-CH₂), 45.0 (-CH₂), 41.8 (-CH), 30.1 (-CH), 22.3 (2-CH₃), 18.5 (-CH₃). HRMS (ESI⁺): 551.2729 [M+Na]⁺ calcd for C₂₉H₃₁NaN₅O₅: 551.2736.

N'-(4-(2-(2-(4-fluorobenzylidene)hydrazinyl)-2-oxoethoxy)benzylidene)-2-(4-isobutylphenyl)propanehydrazide (6)

Off white Amorphous Solid: Yield: 92%, 119 mg; M.P: 185-187 °C; ¹H-NMR (600 MHz, CDCl₃): δ 9.41 (br.s, 2H, 2-NH), 8.84 (s, 2H, 2-N=CH), 7.59-7.57 (m, 4H, Ar-H), 7.29 (d, *J* = 7.8 Hz, 4H, Ar-H), 7.23-7.14 (m, 4H, Ar-H), 4.65-4.62 (m, 2H, -CH₂), 3.69-3.62 (m, 1H, -CH), 2.39 (d, *J* = 6.6 Hz, 2H, -CH₂), 1.83-1.76 (m, 1H, -CH), 1.52 (d, *J* = 7.2 Hz, 3H, -CH₃), 0.88-

0.85 (m, 6H, 2-CH₃). ¹³C-NMR (150 MHz, CDCl₃): δ 176.3 (C=O), 171.7 (C=O), 162.4 (Ar-C-F), 147.3 (Ar-C), 141.7 (2-N=CH), 140.2 (Ar-C), 138.4 (Ar-C), 130.0 (Ar-C), 129.2 (4Ar-CH), 128.9 (2Ar-CH), 127.5 (2Ar-CH), 127.2 (2Ar-CH), 127.0 (Ar-C), 115.7 (2Ar-CH), 69.0 (-CH₂), 45.0 (-CH₂), 41.4 (-CH), 30.1 (-CH), 22.4 (2-CH₃), 18.3 (-CH₃). HRMS (ESI⁺): 520.2724 [M+NH₄]⁺ calcd for C₂₉H₃₅FN₅O₃: 520.3336.

***N'*-(4-(2-(2-(4-bromo-2-fluorobenzylidene)hydrazinyl)-2-oxoethoxy)benzylidene)-2-(4-isobutylphenyl)propanehydrazide (7)**

Orange Amorphous Solid: Yield: 92%, 133 mg; M.P: 162-164 °C; ¹H-NMR (600 MHz, CDCl₃): δ 8.89 (s, 2H, 2-NH), 8.46 (br.s, 1H, -N=CH), 8.12 (br.s, 1H, -N=CH), 7.89 (br.s, 1H, Ar-H), 7.78 (s, 1H, Ar-H), 7.71 (t, *J* = 7.8 Hz, 1H, Ar-H), 7.32 (d, *J* = 8.4 Hz, 1H, Ar-H), 7.26-7.19 (m, 4H, Ar-H), 7.13 (d, *J* = 8.4 Hz, 1H, Ar-H), 7.05 (d, *J* = 7.8 Hz, 2H, Ar-H), 4.61-4.57 (m, 2H, -CH₂), 3.65-3.61 (m, 1H, -CH), 2.39 (d, *J* = 7.2 Hz, 2H -CH₂), 1.80-1.76 (m, 1H, -CH), 1.51 (d, *J* = 7.2 Hz, 3H, -CH₃), 0.86-0.82 (m, 6H, 2-CH₃). ¹³C-NMR (150 MHz, CDCl₃): δ 176.3 (C=O), 170.6 (C=O), 161.6 (Ar-C-F), 159.9 (Ar-C), 140.3 (-N=CH), 139.4 (Ar-C), 135.1 (-N=CH, Ar-C), 130.0 (Ar-CH), 129.6 (2Ar-CH), 129.3 (2Ar-CH), 128.2 (Ar-C-Br), 128.0 (2Ar-CH), 127.4 (2Ar-CH), 127.3 (Ar-C), 127.0 (Ar-CH), 120.8 (Ar-C), 119.6 (Ar-CH), 69.0 (-CH₂), 45.0 (-CH₂), 41.6 (-CH), 30.1 (-CH), 22.4 (2-CH₃), 18.5 (-CH₃). HRMS (ESI⁺): 598.1829 [M+NH₄]⁺ calcd for C₂₉H₃₄BrFN₅O₃: 599.3258.

***N'*-(4-(2-(2-(2,4-dichlorobenzylidene)hydrazinyl)-2-oxoethoxy)benzylidene)-2-(4-isobutylphenyl)propanehydrazide (8)**

Off white Amorphous Solid: Yield: 80%, 110 mg; M.P: 168-169 °C; ¹H-NMR (600 MHz, CDCl₃): δ 9.00 (s, 2H, 2-NH), 8.55 (s, 1H, -N=CH-), 8.29 (s, 1H, -N=CH-), 7.97 (s, 1H, Ar-H), 7.82 (d, *J* = 9.0 Hz, 1H, Ar-H), 7.36 (s, 1H, Ar-H), 7.31 (br.s, 1H, Ar-H), 7.26-7.19 (m, 4H, Ar-H), 7.13 (d, *J* = 7.8 Hz, 1H, Ar-H), 7.05 (d, *J* = 8.4 Hz, 2H, Ar-H), 4.60-4.56 (m, 2H, -CH₂), 3.64-3.62 (m, 1H, -CH), 2.39 (d, *J* = 7.2 Hz, 2H -CH₂), 1.82-1.76 (m, 1H, -CH), 1.51 (d, *J* = 7.2 Hz, 3H, -CH₃), 0.84 (d, *J* = 6.6 Hz, 6H, 2-CH₃). ¹³C-NMR (150 MHz, CDCl₃): δ 176.2 (C=O), 170.6 (C=O), 142.6 (-N=CH), 141.3 (Ar-C), 140.3 (Ar-C), 138.4 (-N=CH), 137.3 (Ar-C), 130.5 (Ar-C-Cl), 130.3 (Ar-C), 130.2 (2Ar-CH), 129.9 (Ar-CH), 129.7 (Ar-CH), 129.3 (2Ar-CH), 128.6 (Ar-C-Cl), 128.0 (Ar-C), 127.8 (2Ar-CH), 127.6 (2Ar-CH), 127.4 (Ar-CH), 69.0 (-CH₂), 45.0 (-CH₂), 41.6 (-CH), 30.1 (-CH), 22.4 (2-CH₃), 18.5 (-CH₃). HRMS (ESI⁺): 522.5970 [M+H]⁺ calcd for C₂₉H₃₀Cl₂N₄O₃: 522.5982.

***N'*-4-(2-(2-(2-hydroxy-3-methoxybenzylidene)hydrazinyl)-2-oxoethoxy)benzylidene)-2-(4-isobutylphenyl)propanehydrazide (9)**

Pale Yellow Amorphous Solid: Yield: 90%, 119 mg; M.P: 171-172 °C; ¹H-NMR (600 MHz, CDCl₃): δ 10.79 (br.s, 1H, -OH), 9.90 (s, 1H, -NH), 9.35 (s, 1H, -NH), 8.32 (s, 2H, 2-N=CH-), 7.28 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.22 (d, *J* = 8.4 Hz, 1H, Ar-H), 7.13 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.05 (d, *J* = 7.8 Hz, 2H, Ar-H), 6.91-6.90 (m, 1H, Ar-H), 6.84-6.83 (m, 2H, Ar-H), 6.78 (d, *J* = 7.2 Hz, 1H, Ar-H), 4.36-4.33 (m, 2H, -CH₂), 3.90 (s, 3H, -OCH₃), 3.65-3.61 (m, 1H, -CH), 2.38 (d, *J* = 7.2 Hz, 2H -CH₂), 1.85-1.76 (m, 1H, -CH), 1.50 (d, *J* = 7.2 Hz, 3H, -CH₃), 0.84 (d, *J* = 6.6 Hz, 6H, 2-CH₃). ¹³C-NMR (150 MHz, CDCl₃): δ 175.6 (C=O), 170.3 (C=O), 148.2 (Ar-C-OH), 147.1 (Ar-C-OCH₃), 150.7 (-N=CH), 146.3 (-N=CH), 141.3 (Ar-C), 140.6 (Ar-C), 137.2 (Ar-C), 129.9 (2Ar-CH), 129.5 (2Ar-CH), 127.4 (2Ar-CH), 127.3 (2Ar-CH), 124.5 (Ar-C), 122.3 (Ar-CH), 119.5 (Ar-CH), 119.1 (Ar-C), 113.6 (Ar-CH), 69.0 (-CH₂), 56.2 (-OCH₃), 45.0 (-CH₂), 41.8 (-CH), 30.1 (-CH), 22.4 (2-CH₃), 18.4 (-CH₃). HRMS (ESI⁺): 530.3537 [M+H]⁺ calcd for C₃₀H₃₄N₄O₅: 530.3541.

***N'*-4-(2-(2-(2-hydroxy-4-methoxybenzylidene)hydrazinyl)-2-oxoethoxy)benzylidene)-2-(4-isobutylphenyl)propanehydrazide (10)**

Brownish Amorphous Solid: Yield: 88%, 116 mg; M.P: 169-171 °C; ¹H-NMR (600 MHz, CDCl₃): δ 11.08 (br.s, 1H, -OH), 9.90 (s, 1H, -NH), 9.36 (s, 1H, -NH), 8.37 (br.s, 1H, -N=CH), 8.31 (br.s, 1H, -N=CH), 7.83 (s, 1H, Ar-H), 7.27 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.16-7.08 (m, 4H, Ar-H), 7.05 (d, *J* = 7.8 Hz, 2H, Ar-H), 6.95-6.94 (m, 2H, Ar-H), 4.68 (s, 2H, -CH₂), 4.36-4.32 (m, 1H, -CH), 3.90 (s, 3H, -OCH₃), 2.37 (d, *J* = 7.2 Hz, 2H -CH₂), 1.83-1.75 (m, 1H, -CH), 1.50 (d, *J* = 6.6 Hz, 3H, -CH₃), 0.83 (d, *J* = 6.6 Hz, 6H, 2-CH₃). ¹³C-NMR (150 MHz, CDCl₃): δ 175.6 (C=O), 164.8 (C=O), 150.7 (Ar-C-OH), 149.7 (Ar-C-OCH₃), 148.3 (Ar-C), 146.2 (-N=CH), 141.3 (Ar-C), 140.6 (-N=CH), 137.3 (Ar-C), 129.9 (Ar-CH), 129.6 (Ar-CH), 129.5 (2Ar-CH), 127.3 (2Ar-CH), 127.0 (Ar-C), 124.5 (Ar-CH), 124.1 (Ar-CH), 122.3 (Ar-CH), 119.0 (Ar-C), 117.9 (Ar-CH), 115.2 (Ar-CH), 69.0 (-CH₂), 56.2 (-OCH₃), 45.0 (-CH₂), 41.8 (-CH), 30.1 (-CH), 22.4 (2-CH₃), 19.0 (-CH₃). HRMS (ESI⁺): 530.0492 [M+H]⁺ calcd for C₃₀H₃₄N₄O₅: 530.0505.

***N'*-4-(2-(2-(3-hydroxy-4-methoxybenzylidene)hydrazinyl)-2-oxoethoxy)benzylidene)-2-(4-isobutylphenyl)propanehydrazide (11)**

White Amorphous Solid: Yield: 78%, 103 mg; M.P: 110-113 °C; ¹H-NMR (600 MHz, CDCl₃): δ 9.81 (s, 2H, 2-NH), 8.87 (s, 1H, -N=CH), 7.54 (s, 1H, -N=CH), 7.41 (s, 2H, Ar-H), 7.30-7.29 (m, 3H, Ar-H), 7.15-7.07 (m, 2H, Ar-H), 7.04 (d, *J* = 7.8 Hz, 3H, Ar-H), 6.94 (d, *J* = 8.4 Hz, 1H, Ar-H), 6.82 (d, *J* = 8.4 Hz, 1H, Ar-H), 4.77 (br.s, 2H, -CH₂), 4.68-4.65 (m, 1H, -CH), 3.90 (s, 3H, -OCH₃), 2.38 (d, *J* = 7.2 Hz, 2H -CH₂), 1.82-1.75 (m, 1H, -CH), 1.50 (d, *J* = 7.2 Hz, 3H, -CH₃), 0.83 (d, *J* = 6.0 Hz, 6H, 2-CH₃). ¹³C-NMR (150 MHz, CDCl₃): δ 176.4 (C=O), 171.7 (C=O), 152.1 (Ar-C-OCH₃), 148.3 (Ar-C-OH), 146.1 (Ar-C), 145.9 (-N=CH), 143.0 (-N=CH), 140.1 (Ar-C), 138.4 (Ar-C), 130.4 (Ar-C), 129.8 (Ar-CH), 129.6 (Ar-CH), 129.2 (2Ar-CH), 127.6 (2Ar-CH), 127.5 (Ar-CH), 127.0 (Ar-CH), 126.6 (Ar-C), 120.7 (Ar-CH), 114.1 (Ar-CH), 112.0 (Ar-CH), 69.0 (-CH₂), 56.0 (-OCH₃), 45.0 (-CH₂), 41.1 (-CH), 30.1 (-CH), 22.4 (2-CH₃), 18.2 (-CH₃). HRMS (ESI⁺): 531.2607 [M+H]⁺ calcd for C₃₀H₃₅N₄O₅: 531.2659.

***N'*-(4-(2-(2-(2-hydroxybenzylidene)hydrazinyl)-2-oxoethoxy)benzylidene)-2-(4-isobutylphenyl)propanehydrazide (12)**

Off white Amorphous Solid: Yield: 80%, 109 mg; M.P: 154-155 °C; ¹H-NMR (600 MHz, CDCl₃): δ 10.98 (s, 1H, -OH), 9.93 (br.s, 1H, -NH), 9.87 (s, 1H, -NH), 8.42 (br.s, 1H, -N=CH), 8.22 (br.s, 1H, -N=CH), 7.79 (s, 1H, Ar-H), 7.54-7.48 (m, 2H, Ar-H), 7.36-7.20 (m, 4H, Ar-H), 7.15-7.12 (m, 4H, Ar-H), 6.93-6.86 (m, 1H, Ar-H), 4.30-4.27 (m, 2H, -CH₂), 3.64 (br.s, 1H, -CH), 2.38 (d, *J* = 6.6 Hz, 2H -CH₂), 1.84-1.76 (m, 1H, -CH), 1.50 (d, *J* = 7.2 Hz, 3H, -CH₃), 0.83 (d, *J* = 7.2 Hz, 6H, 2-CH₃). ¹³C-NMR (150 MHz, CDCl₃): δ 175.3 (C=O), 164.7 (C=O), 161.6 (Ar-C), 158.5 (Ar-C-OH), 146.9 (-N=CH), 140.6 (Ar-C), 137.5 (Ar-C), 137.0 (-N=CH), 133.7 (Ar-CH), 130.0 (2Ar-CH), 129.6 (2Ar-CH), 127.4 (2Ar-CH), 127.1 (3Ar-CH), 120.7 (Ar-C), 119.8 (Ar-CH), 119.3 (Ar-C), 117.6 (Ar-CH), 69.0 (-CH₂), 45.0 (-CH₂), 42.2 (-CH), 30.1 (-CH), 22.4 (2-CH₃), 18.4 (-CH₃). HRMS (ESI⁺): 520.2801 [M+NH₄]⁺ calcd for C₃₁H₄₀N₅O₅: 520.3327.

2-(4-isobutylphenyl)-*N'*-(4-(2-oxo-2-(2-(3,4,5-trimethoxybenzylidene)hydrazinyl)ethoxy)benzylidene)propanehydrazide (13)

Gray Amorphous Solid: Yield: 92%, 132 mg; M.P: 195-196 °C; ¹H-NMR (600 MHz, CDCl₃): δ 9.41 (br.s, 2H, 2-NH), 8.77 (s, 1H, -N=CH), 8.30 (br.s, 1H, -N=CH-), 7.95 (br.s, 1H, Ar-H), 7.52 (s, 1H, Ar-H), 7.28 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.14-7.08 (m, 2H, Ar-H), 7.04 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.82 (s, 2H, Ar-H), 4.72 (br.s, 2H, -CH₂), 4.62-4.59 (m, 1H, -CH), 3.89 (s, 6H, -OCH₃), 3.83 (s, 3H, -OCH₃), 2.39 (d, *J* = 7.2 Hz, 2H -CH₂), 1.84-1.76 (m, 1H, -CH), 1.51 (d, *J* = 7.2 Hz, 3H, -CH₃), 0.89-0.84 (m, 6H, 2-CH₃). ¹³C-NMR (150 MHz, CDCl₃): δ 176.1 (C=O), 171.7

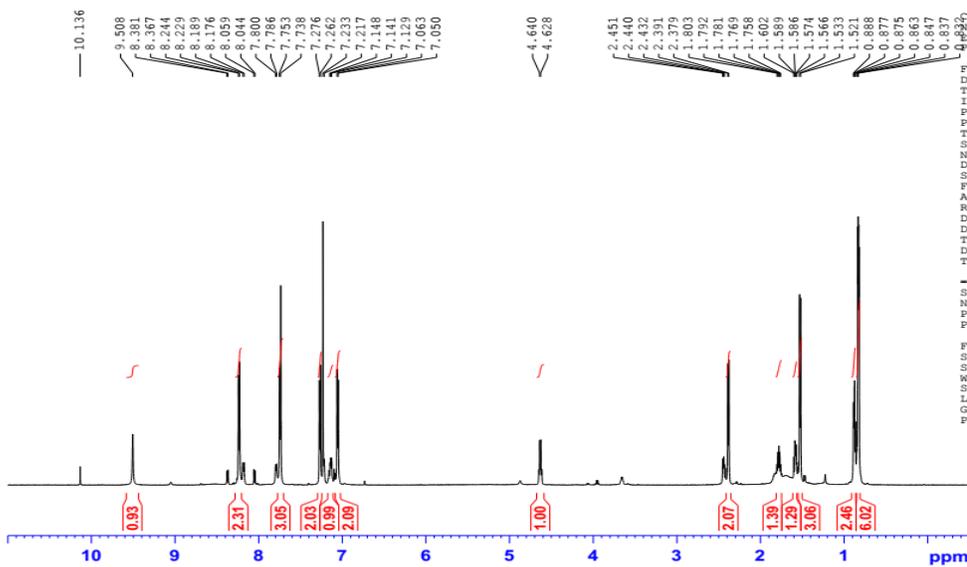
(C=O), 153.5 (2Ar-C-OCH₃), 142.5 (2-N=CH), 141.1 (Ar-C), 140.2 (Ar-C-OCH₃), 139.8 (Ar-C), 138.7 (Ar-C), 129.9 (2Ar-CH), 129.2 (2Ar-CH), 127.4 (2Ar-CH), 127.0 (2Ar-CH), 128.6 (Ar-C), 128.0 (Ar-C), 104.1 (2Ar-CH), 69.0 (-CH₂), 61.0 (-OCH₃), 56.2 (2-OCH₃), 45.0 (-CH₂), 41.8 (-CH), 30.2 (-CH), 22.4 (2-CH₃), 18.4 (-CH₃). HRMS (ESI⁺): 593.3078 [M+NH₄]⁺ calcd for C₃₂H₄₂N₅O₆: 593.3086.

***N'*-(4-(2-(2-(2,4-dimethoxybenzylidene)hydrazinyl)-2-oxoethoxy)benzylidene)-2-(4-isobutylphenyl)propanehydrazide (14)**

Ash white Amorphous Solid: Yield: 88%, 117 mg; M.P: 156-158 °C; ¹H-NMR (600 MHz, CDCl₃): δ 9.90 (s, 1H, -NH), 9.35 (s, 1H, -NH), 8.40 (s, 1H, -N=CH-), 7.92 (s, 1H, -N=CH-), 7.78 (d, *J* = 8.4 Hz, 1H, Ar-H), 7.30 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.11 (d, *J* = 8.4 Hz, 1H, Ar-H), 7.04 (d, *J* = 7.8 Hz, 3H, Ar-H), 6.53-6.52 (m, 2H, Ar-H), 6.40-6.38 (m, 2H, Ar-H), 4.77 (br.s, 2H, -CH₂), 4.67-4.64 (m, 1H, -CH), 3.82 (s, 3H, -OCH₃), 3.78 (s, 3H, -OCH₃), 2.39 (d, *J* = 7.2 Hz, 2H -CH₂), 1.82-1.78 (m, 1H, -CH), 1.50 (d, *J* = 7.2 Hz, 3H, -CH₃), 0.88-0.84 (m, 6H, 2-CH₃). ¹³C-NMR (150 MHz, CDCl₃): δ 175.9 (C=O), 171.7 (C=O), 162.6 (Ar-C-OCH₃), 159.2 (Ar-C-OCH₃), 141.1 (Ar-C), 140.1 (-N=CH), 139.0 (-N=CH, Ar-C), 138.7 (Ar-C), 133.0 (Ar-C), 130.8 (Ar-C), 129.6 (2Ar-CH), 129.2 (2Ar-CH), 127.6 (2Ar-CH), 127.3 (2Ar-CH), 115.3 (Ar-C), 105.8 (Ar-CH), 98.0 (Ar-CH), 69.0 (-CH₂), 55.5 (2-OCH₃), 45.0 (-CH₂), 41.3 (-CH), 30.1 (-CH), 22.4 (2-CH₃), 18.3 (-CH₃). HRMS (ESI⁺): 545.2764 [M+H]⁺ calcd for C₃₁H₃₇N₄O₅: 545.2724.

***N'*-(4-(2-(2-(3,5-dibromo-4-hydroxybenzylidene)hydrazinyl)-2-oxoethoxy)benzylidene)-2-(4-isobutylphenyl)propanehydrazide (15)**

Brownish Amorphous Solid: Yield: 92%, 151 mg; M.P: 138-140 °C; ¹H-NMR (600 MHz, CDCl₃): δ 9.54 (s, 1H, -OH), 9.27 (br.s, 2H, 2-NH), 7.97 (s, 2H, 2-N=CH), 7.72 (br.s, 1H, Ar-H), 7.65 (s, 2H, Ar-H), 7.51 (s, 1H, Ar-H), 7.26 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.23-7.21 (m, 1H, Ar-H), 7.14-7.09 (m, 1H, Ar-H), 7.06 (d, *J* = 7.8 Hz, 2H, Ar-H), 4.59-4.56 (m, 2H, -CH₂), 3.64 (br.s, 1H, -CH), 2.39 (d, *J* = 7.2 Hz, 2H -CH₂), 1.59-1.55 (m, 1H, -CH), 1.50 (d, *J* = 7.2 Hz, 3H, -CH₃), 0.83 (d, *J* = 6.6 Hz, 6H, 2-CH₃). ¹³C-NMR (150 MHz, CDCl₃): δ 176.8 (C=O), 170.6 (C=O), 150.6 (Ar-C-OH), 144.5 (Ar-C), 141.3 (Ar-C), 140.3 (-N=CH), 139.9 (-N=CH), 137.3 (Ar-C), 131.0 (Ar-C), 130.5 (2Ar-CH), 129.9 (2Ar-CH), 129.6 (2Ar-CH), 129.3 (2Ar-CH), 127.4 (2Ar-CH), 127.0 (Ar-C), 110.3 (2Ar-C), 69.0 (-CH₂), 45.0 (-CH₂), 41.5 (-CH), 30.2 (-CH), 22.4 (2-CH₃), 18.4 (-CH₃). HRMS (ESI⁺): 657.4634 [M+H]⁺ calcd for C₂₉H₃₀Br₂N₄O₄: 657.4650.

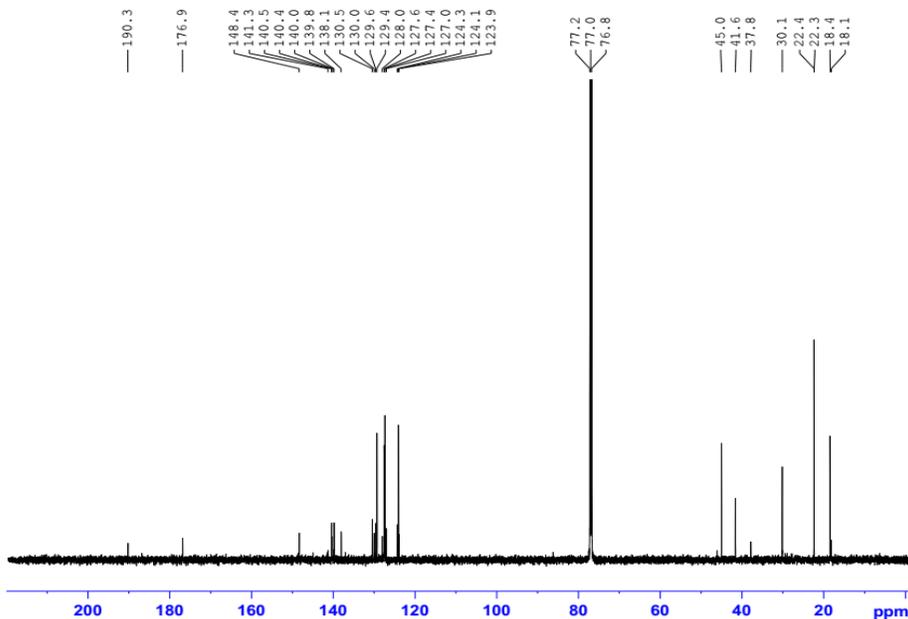


Current Data Parameters
 Name 24-Aug-2022_Dr. Ajmal
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20220824
 Time_ 13.38
 INSTRUM spect
 PROBHD 5 mm PABBO BB/
 PULPROG zg30
 TD 65536
 SOLVENT CDCl3
 NS 16
 DS 2
 SWH 12019.230 Hz
 FIDRES 0.183399 Hz
 AQ 2.7262976 sec
 RG 95.76
 DW 41.600 usec
 DE 6.50 usec
 TE 298.1 K
 D1 1.00000000 sec
 TDO 1

----- CHANNEL f1 -----
 SFO1 600.1537062 MHz
 NUC1 1H
 P1 10.90 usec
 PLW1 22.60000038 W

F2 - Processing parameters
 SI 65536
 SF 600.1500266 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00



Current Data Parameters
 Name 24-Aug-2022_Dr. Ajmal
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20220825
 Time_ 0.29
 INSTRUM spect
 PROBHD 5 mm PABBO BB/
 PULPROG zgpg30
 TD 32768
 SOLVENT CDCl3
 NS 2048
 DS 4
 SWH 36057.681 Hz
 FIDRES 1.100393 Hz
 AQ 0.4543829 sec
 RG 195.2
 DW 13.867 usec
 DE 6.50 usec
 TE 298.2 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TDO 1

----- CHANNEL f1 -----
 SFO1 150.929276 MHz
 NUC1 13C
 P1 11.60 usec
 PLW1 83.00000000 W

----- CHANNEL f2 -----
 SFO2 600.1524006 MHz
 NUC2 1H
 CPDPRG2 waltz16
 PCPD2 70.00 usec
 PLW2 22.60000038 W
 PLW12 0.52806002 W
 PLW13 0.25874999 W

F2 - Processing parameters
 SI 32768
 SF 150.9078399 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

Sample Name	Position	Vial 36	Instrument Name	Instrument 1
User Name	Inj Vol	10	InjPosition	
Sample Type	IRM Calibration Status	Success	Data Filename	
ACQ Method	Comment		Acquired Time	08-Oct-22 3:03:11 PM

Sample
DMSO POS.m

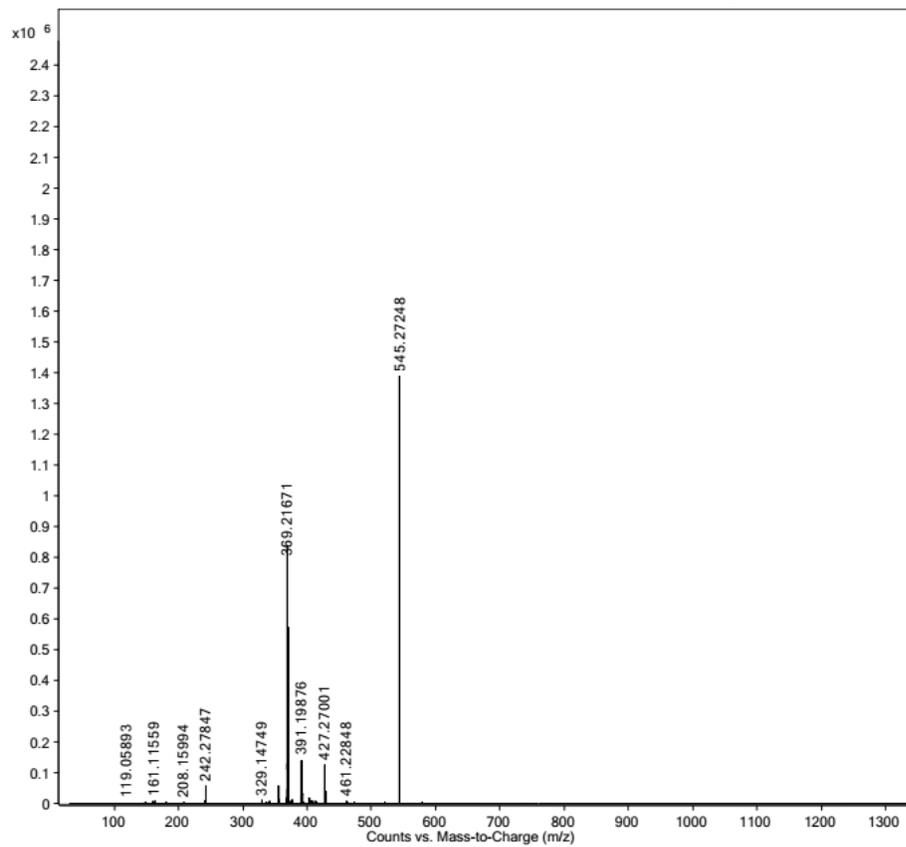
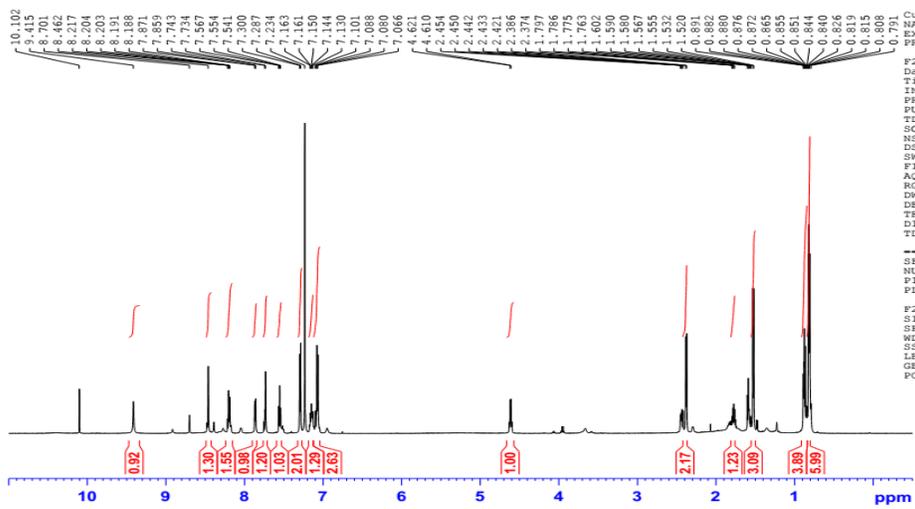


Figure-S1: ^1H -, ^{13}C -NMR and HR-ESI-MS spectrum of compound 4



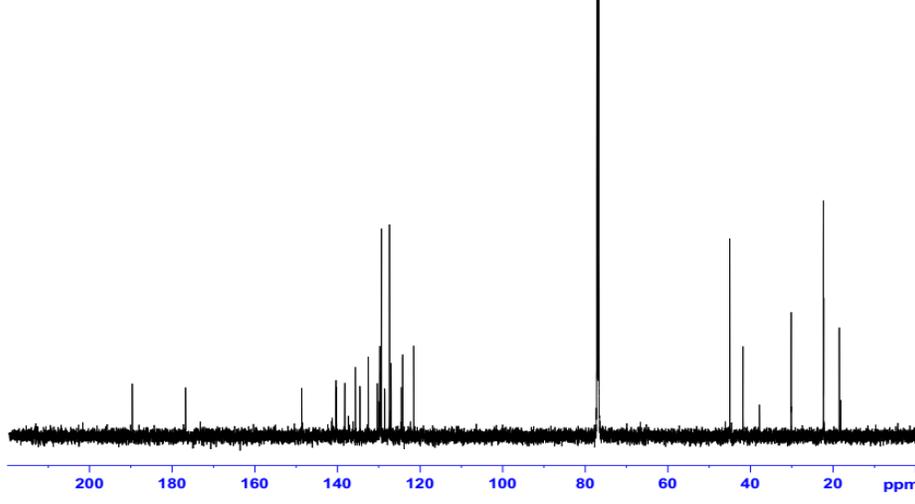
Current Data Parameters
 NAME 24-Aug-2022_Dr. Ajmal
 EXPNO 2
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20220824
 Time 13.42
 INSTRUM spect
 PROBHD 5 mm PABBO BB/
 PULPROG zg30
 TD 65536
 SOLVENT CDCl3
 NS 16
 DS 2
 SWH 12019.230 Hz
 FIDRES 0.183399 Hz
 AQ 2.7262976 sec
 RG 95.76
 DW 41.600 usec
 DE 6.50 usec
 TE 298.1 K
 D1 1.00000000 sec
 TDO

----- CHANNEL f1 -----
 SFO1 600.1537062 MHz
 NUC1 1H
 P1 10.90 usec
 PLW1 22.60000038 W

F2 - Processing parameters
 SI 65536
 SF 600.1500266 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

189.7
176.8
148.7
140.4
140.3
137.4
135.7
134.6
132.6
130.0
129.8
129.7
129.6
129.4
128.6
127.3
127.1
124.5
124.3
121.6
77.2
77.0
76.8
45.0
41.8
37.8
30.2
30.1
22.3
22.3
18.5
18.1



Current Data Parameters
 NAME 24-Aug-2022_Dr. Ajmal
 EXPNO 2
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20220825
 Time 3.51
 INSTRUM spect
 PROBHD 5 mm PABBO BB/
 PULPROG zgpg30
 TD 65768
 SOLVENT CDCl3
 NS 2048
 DS 4
 SWH 36057.691 Hz
 FIDRES 1.100393 Hz
 AQ 0.4543828 sec
 RG 195.2
 DW 13.867 usec
 DE 6.50 usec
 TE 298.1 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TDO 1

----- CHANNEL f1 -----
 SFO1 150.9229276 MHz
 NUC1 13C
 P1 11.60 usec
 PLW1 83.00000000 W

----- CHANNEL f2 -----
 SFO2 600.1524006 MHz
 NUC2 1H
 CHOPRG2 waltz16
 PCPD2 70.00 usec
 PLW2 22.60000038 W
 PLW12 0.52800002 W
 PLW13 0.25874999 W

F2 - Processing parameters
 SI 32768
 SF 150.9078399 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

Sample Name
User Name
Sample Type
ACQ Method

Sample
DMSO POS.m

Position Vial 34
Inj Vol 10
IRM Calibration Status Success
Comment

Instrument Name Instrument 1
InjPosition
Data Filename
Acquired Time 08-Oct-22 2:51:47 PM

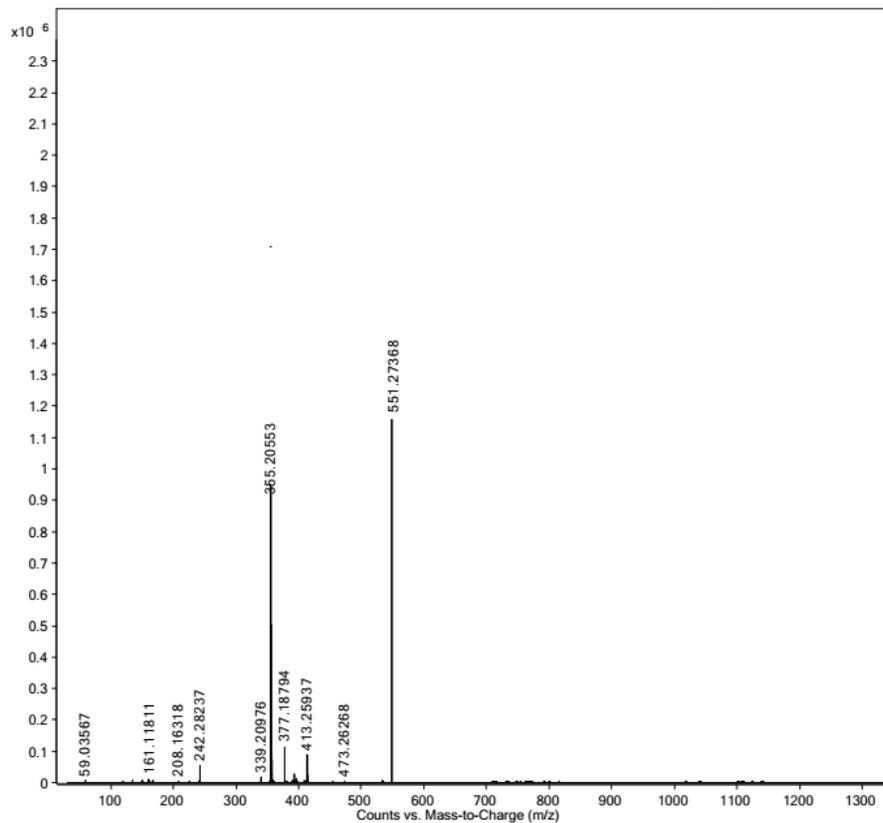
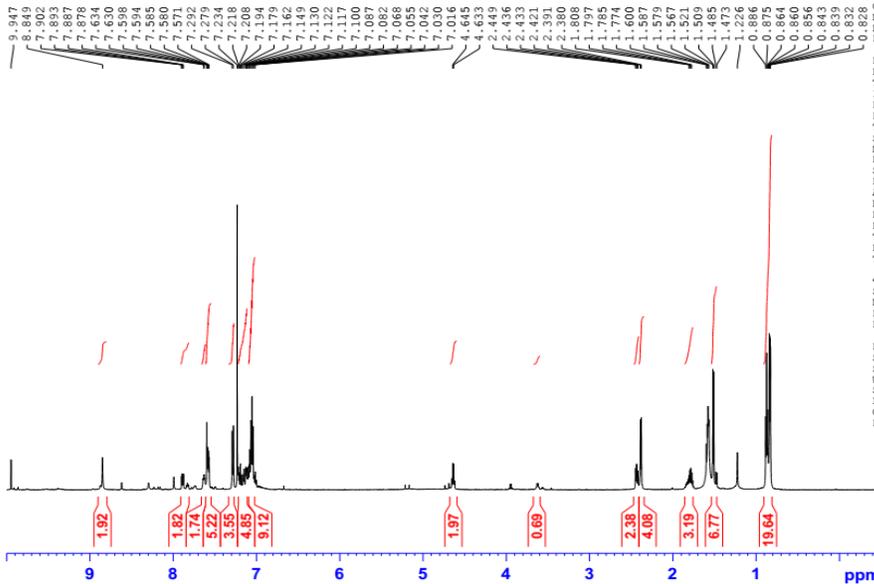


Figure-S2: ¹H-, ¹³C-NMR and HR-ESI-MS spectrum of compound 5

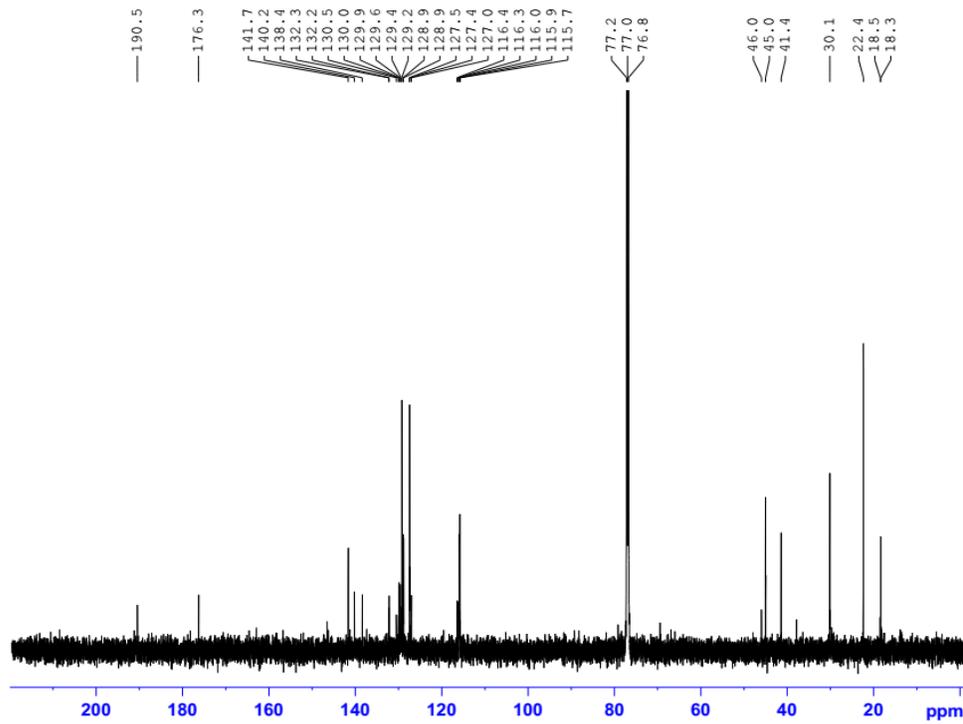


Current Data Parameters
 NAME 24-Aug-2022_Dr. Ajmal
 EXPNO 17
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20220825
 Time 13.34
 INSTRUM spect
 PROBHD 5 mm PABBO BB/
 PULPROG zg30
 TD 65536
 SOLVENT cdcl3
 NS 16
 DS 2
 SWH 12019.230 Hz
 FIDRES 0.183399 Hz
 AQ 2.7262976 sec
 RG 109.89
 DW 41.600 usec
 DE 6.50 usec
 TE 298.1 K
 D1 1.00000000 sec
 TDO 1

----- CHANNEL f1 -----
 SF01 600.1537062 MHz
 NUC1 1H
 P1 10.90 usec
 PLW1 22.60000038 W

F2 - Processing parameters
 SI 65536
 SF 600.1500266 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00



Current Data Parameters
 NAME 24-Aug-2022_Dr. Ajmal
 EXPNO 69
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20220826
 Time 5.06
 INSTRUM spect
 PROBHD 5 mm PABBO BB/
 PULPROG zgpg30
 TD 32768
 SOLVENT CDCl3
 NS 2048
 DS 4
 SWH 36057.691 Hz
 FIDRES 1.100393 Hz
 AQ 0.4543829 sec
 RG 195.2
 DW 13.867 usec
 DE 6.50 usec
 TE 298.8 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TDO 1

----- CHANNEL f1 -----
 SF01 150.9229276 MHz
 NUC1 13C
 P1 11.00 usec
 PLW1 83.00000000 W

----- CHANNEL f2 -----
 SF02 600.1524006 MHz
 NUC2 1H
 CPOPRG[2] waltz16
 PCPD2 70.00 usec
 PLW2 22.60000038 W
 PLW12 0.52805002 W
 PLW13 0.25874999 W

F2 - Processing parameters
 SI 32768
 SF 150.9078399 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

Sample Name	WA-S-17	Position	Vial 47	Instrument Name	Instrument 1
User Name		Inj Vol	10	InjPosition	
Sample Type	Sample	IRM Calibration Status	Success	Data Filename	WA-S-17.d
ACQ Method	DMSO POS.m	Comment		Acquired Time	08-Oct-22 4:06:46 PM

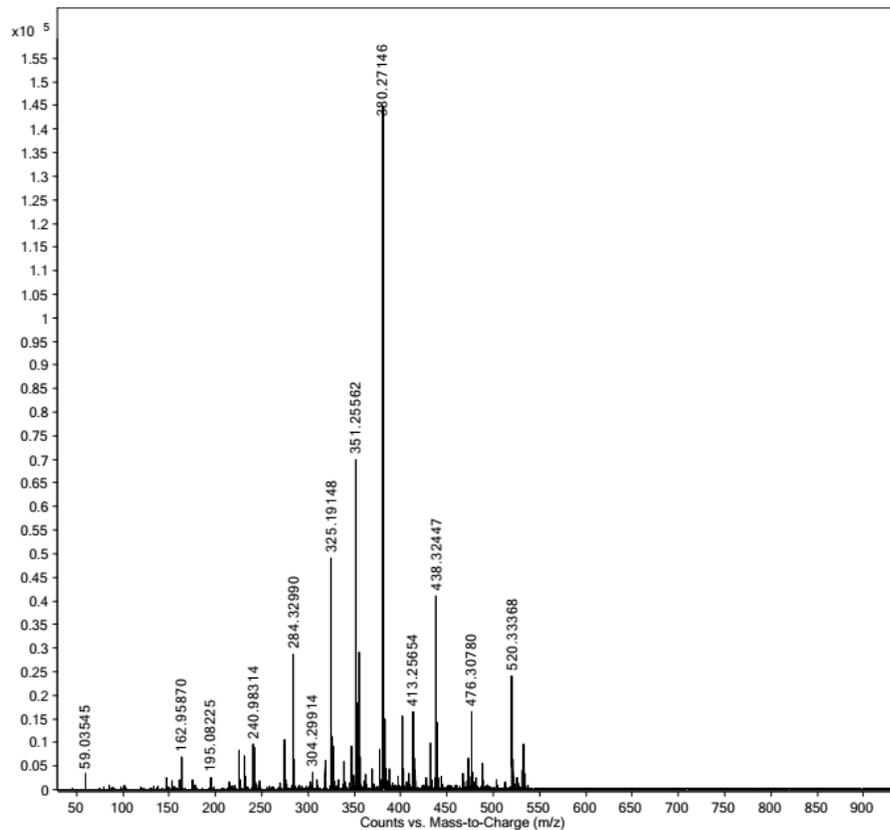
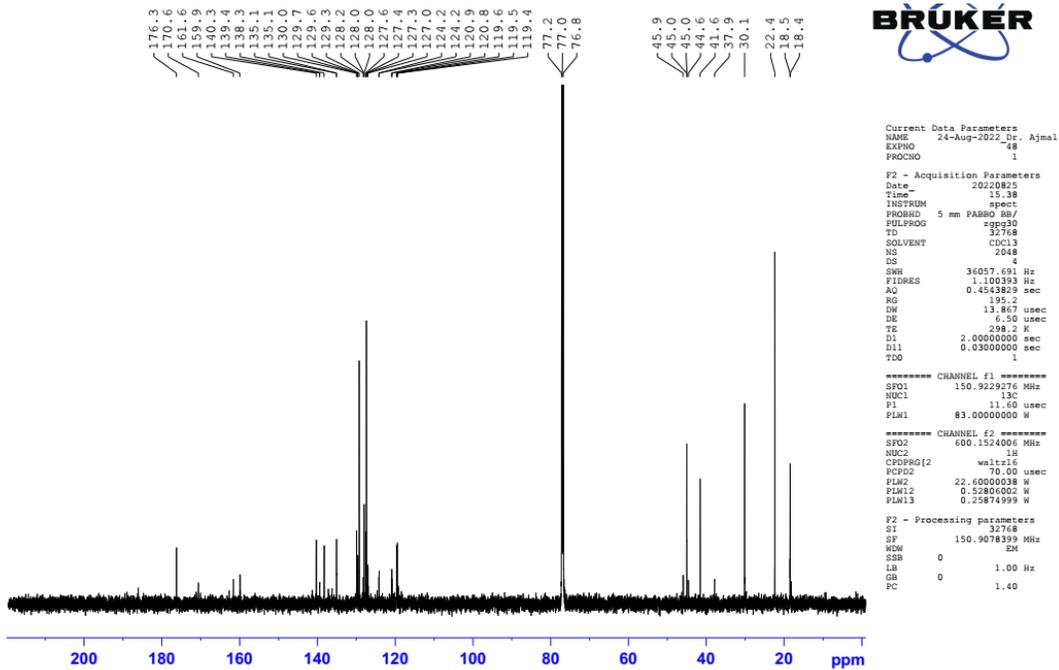
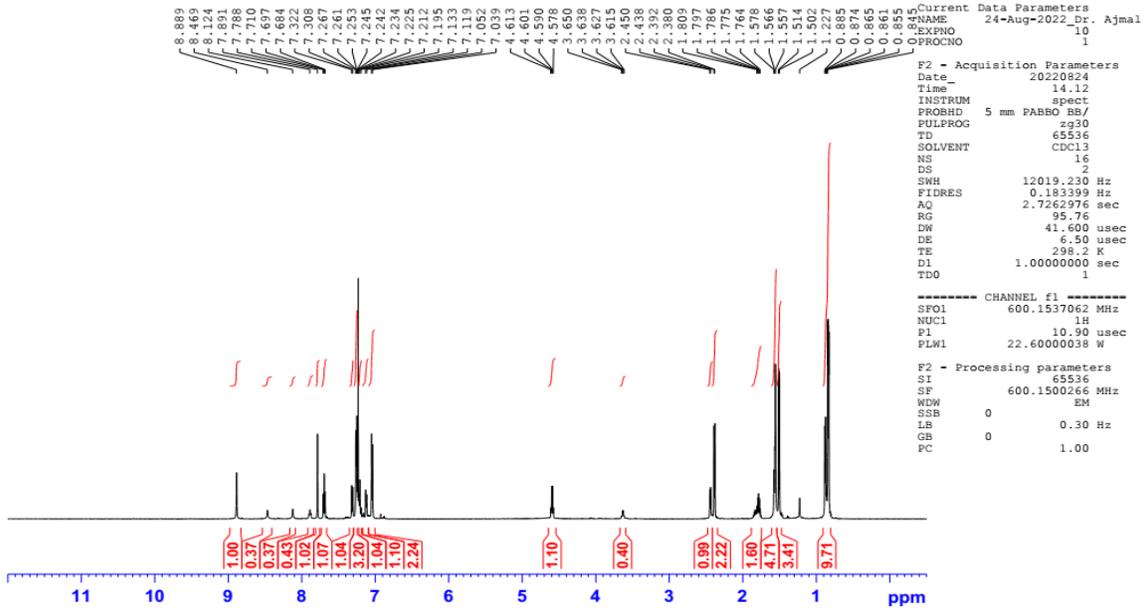


Figure-S3: ¹H-, ¹³C-NMR and HR-ESI-MS spectrum of compound 6



Sample Name	WA-S-5	Position	Vial 35	Instrument Name	Instrument 1
User Name		Inj Vol	10	InjPosition	
Sample Type	Sample	IRM Calibration Status	Success	Data Filename	WA-S-5.d
ACQ Method	DMSO POS.m	Comment		Acquired Time	08-Oct-22 2:57:30 PM

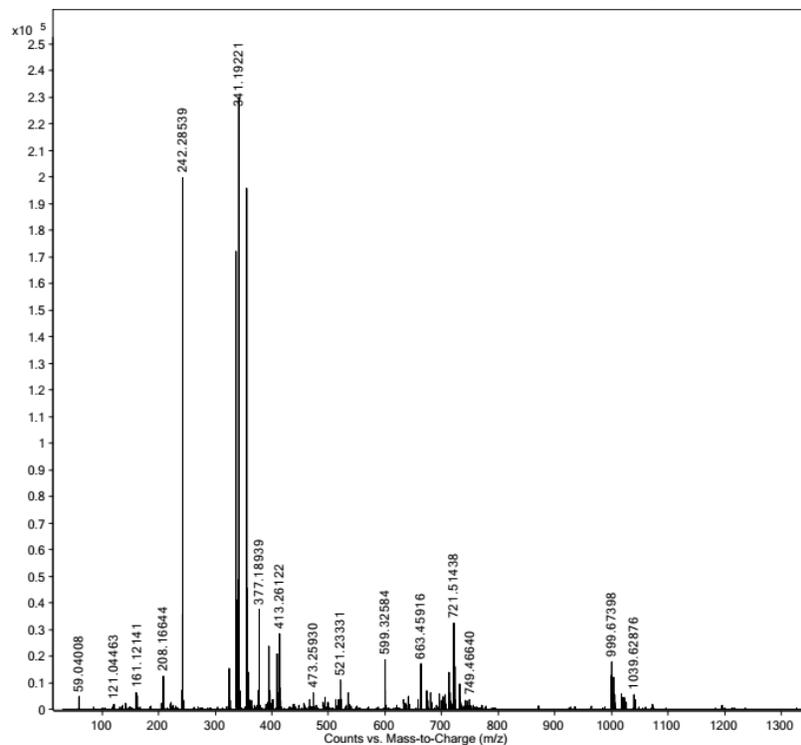
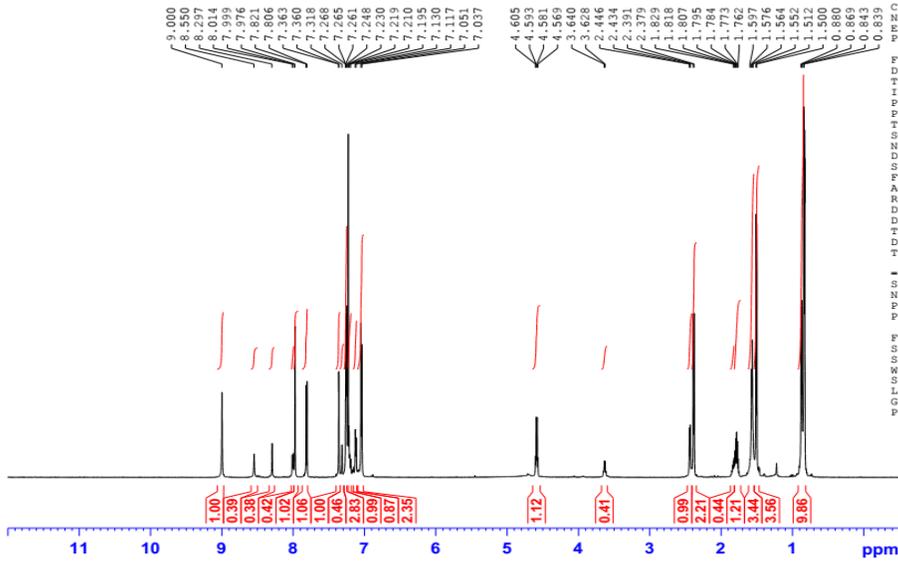


Figure-S4: ^1H -, ^{13}C -NMR and HR-ESI-MS spectrum of compound 7

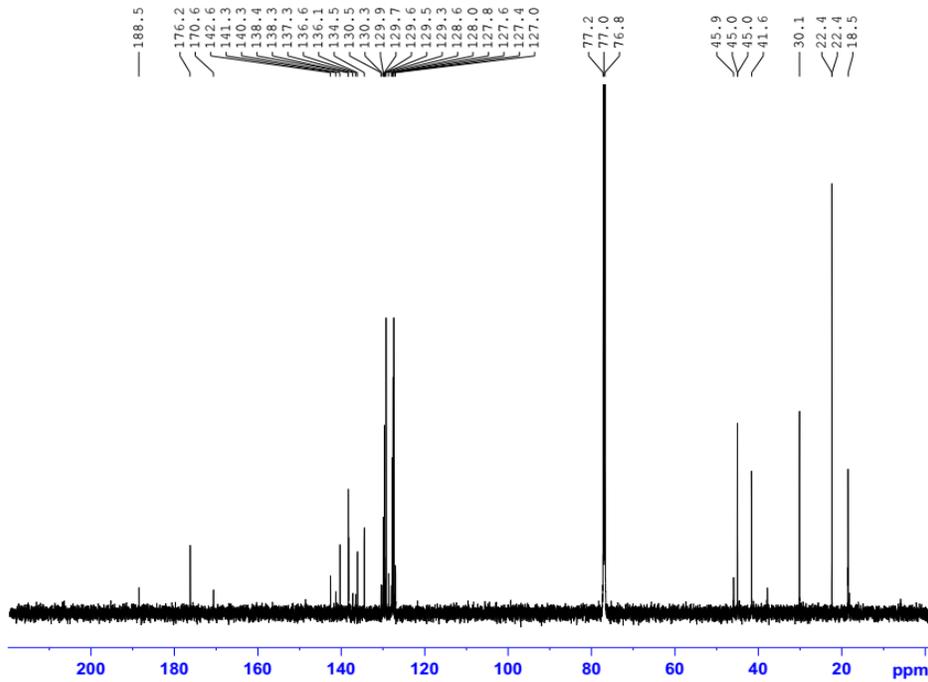


Current Data Parameters
 NAME 24-Aug-2022_Dr. Ajmal
 EXPNO 8
 PROCNO 1

F2 - Acquisition Parameters
 Date 20220824
 Time 14.05
 INSTRUM spect
 PROBHD 5 mm PABBO BBI
 PULPROG zg30
 TD 65536
 SOLVENT CDCl3
 NS 16
 DS 2
 SWH 12019.230 Hz
 FIDRES 0.183399 Hz
 AQ 2.7262976 sec
 RG 95.76
 DW 41.600 usec
 DE 6.50 usec
 TE 298.1 K
 D1 1.00000000 sec
 TDO 1

----- CHANNEL f1 -----
 SFO1 600.1537062 MHz
 NUC1 1H
 P1 10.90 usec
 PLW1 22.60000038 W

F2 - Processing parameters
 SI 65536
 SF 600.1500266 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00



Current Data Parameters
 NAME 24-Aug-2022_Dr. Ajmal
 EXPNO 42
 PROCNO 1

F2 - Acquisition Parameters
 Date 20220826
 Time 12.47
 INSTRUM spect
 PROBHD 5 mm PABBO BBI
 PULPROG zgpg30
 TD 32768
 SOLVENT CDCl3
 NS 2048
 DS 4
 SWH 36057.691 Hz
 FIDRES 1.100393 Hz
 AQ 0.4543829 sec
 RG 195.2
 DW 13.867 usec
 DE 6.50 usec
 TE 298.2 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TDO 1

----- CHANNEL f1 -----
 SFO1 150.9229276 MHz
 NUC1 13C
 P1 11.60 usec
 PLW1 83.00000000 W

----- CHANNEL f2 -----
 SFO2 600.1524006 MHz
 NUC2 1H
 CPDPRG[2] waltz16
 PCPD2 70.00 usec
 PLW2 22.60000038 W
 PLW12 0.52806002 W
 PLW13 0.25874999 W

F2 - Processing parameters
 SI 32768
 SF 150.9078399 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

Sample Name		Position	Vial 23	Instrument Name	Instrument 1
User Name		Inj Vol	10	InjPosition	
Sample Type	Sample	IRM Calibration Status	Success	Data Filename	
ACQ Method	POSITIVE ION METHOD MS.m	Comment		Acquired Time	13-Oct-22 2:52:37 PM

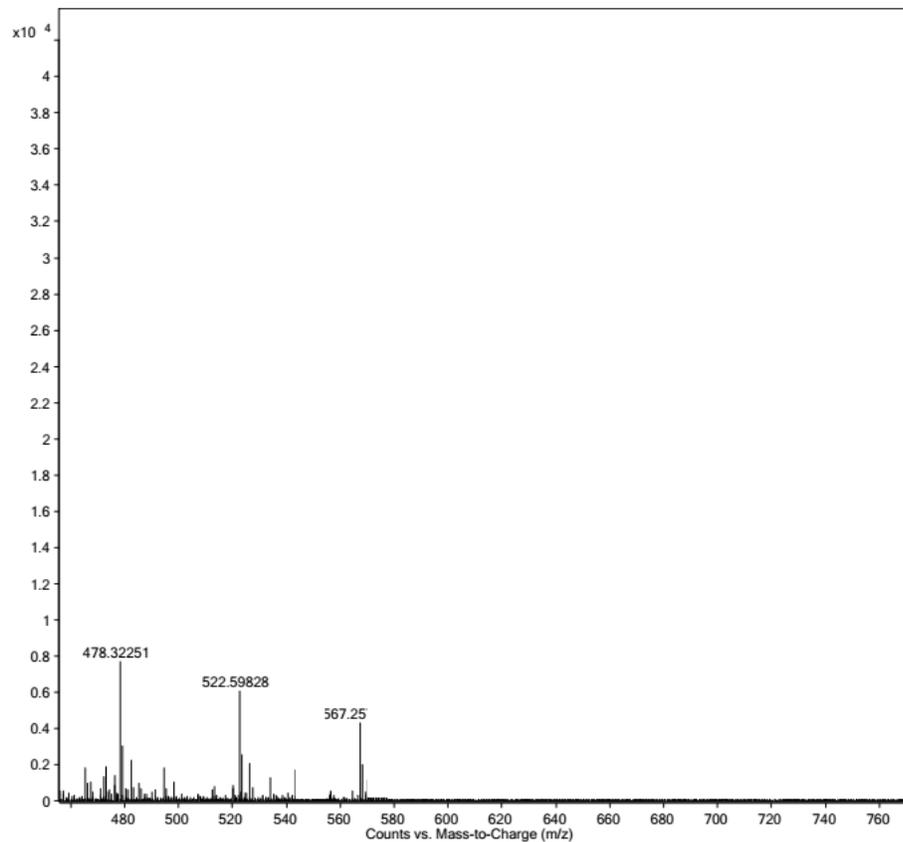
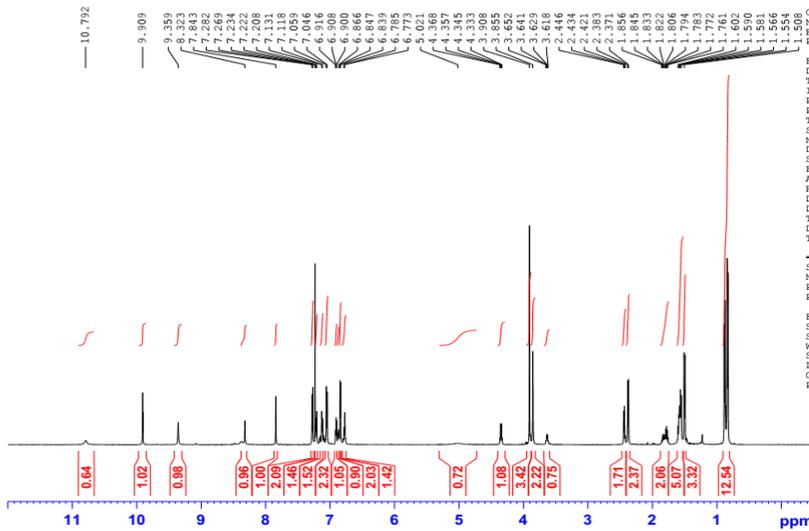


Figure-S5: ^1H -, ^{13}C -NMR and HR-ESI-MS spectrum of compound **8**

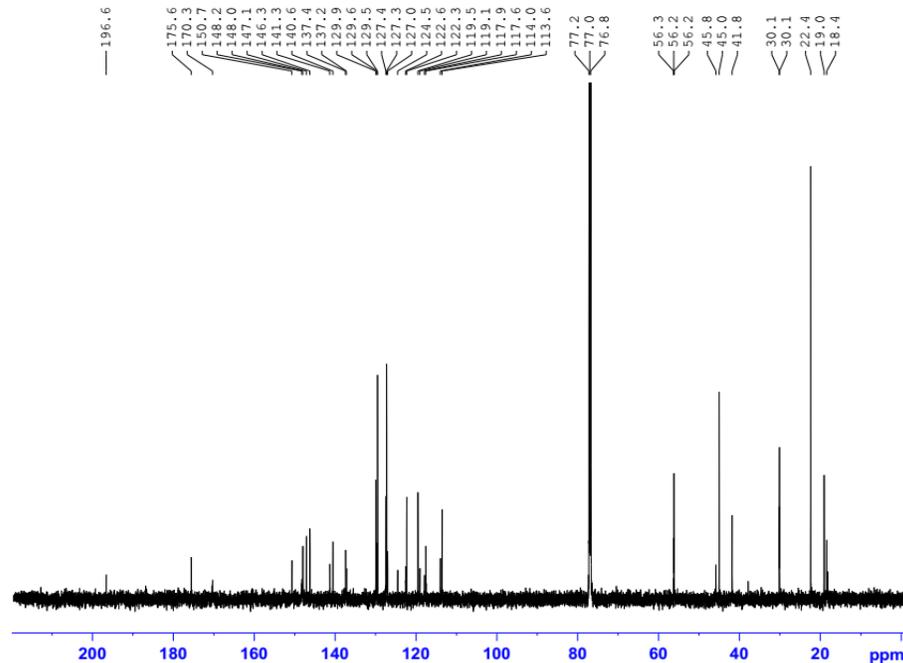


Current Data Parameters
 NAME 24-Aug-2022_Dr. Ajmal
 EXPNO 4
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20220824
 Time 13:49
 INSTRUM spect
 PROBHD 5 mm PABBO BB/
 PULPROG zg30
 TD 65536
 SOLVENT cdc13
 NS 16
 DS 2
 SWH 12019.230 Hz
 FIDRES 0.183399 Hz
 AQ 2.7262976 sec
 RG 86.85
 DW 41.600 usec
 DE 6.50 usec
 TE 298.1 K
 D1 1.00000000 sec
 TDO

CHANNEL f1
 SF01 600.1537062 MHz
 NUCL1 1H
 P1 10.90 usec
 PLW1 22.60000038 W

F2 - Processing parameters
 SI 65536
 SF 600.1500066 MHz
 WDM EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00



Current Data Parameters
 NAME 24-Aug-2022_Dr. Ajmal
 EXPNO 30
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20220825
 Time 5:31
 INSTRUM spect
 PROBHD 5 mm PABBO BB/
 PULPROG zgpg30
 TD 32768
 SOLVENT cdc13
 NS 2048
 DS 4
 SWH 36057.691 Hz
 FIDRES 1.100393 Hz
 AQ 0.4543829 sec
 RG 195.2
 DW 13.867 usec
 DE 6.50 usec
 TE 298.9 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TDO 1

CHANNEL f1
 SF01 150.9229276 MHz
 NUCL1 13C
 P1 11.60 usec
 PLW1 83.00000000 W

CHANNEL f2
 SF02 600.1524006 MHz
 NUCL2 1H
 CPDPRG2 waltz16
 PCPD2 70.00 usec
 PLW2 22.60000038 W
 PLW12 0.52806002 W
 PLW13 0.25874999 W

F2 - Processing parameters
 SI 32768
 SF 150.9078399 MHz
 WDM EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

Sample Name
User Name
Sample Type
ACQ Method

Sample
POSITIONAL ION METHOD MS.m

Position Vial 81
Inj Vol 10
IRM Calibration Status Success
Comment

Instrument Name Instrument 1
InjPosition
Data Filename
Acquired Time 05-Sep-22 12:05:24 PM

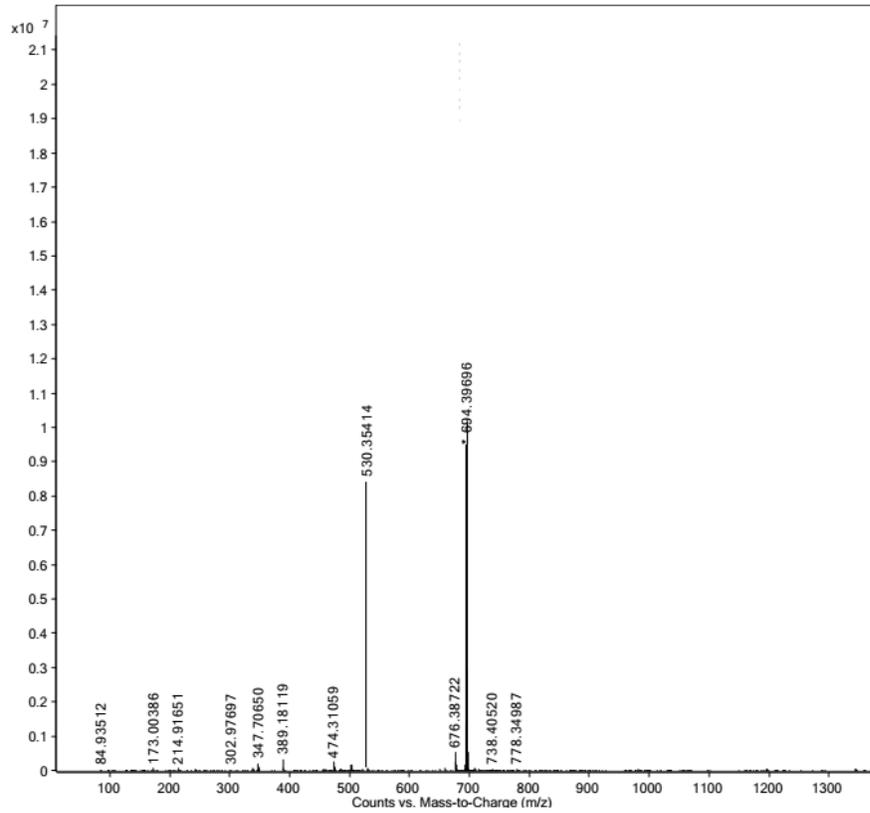
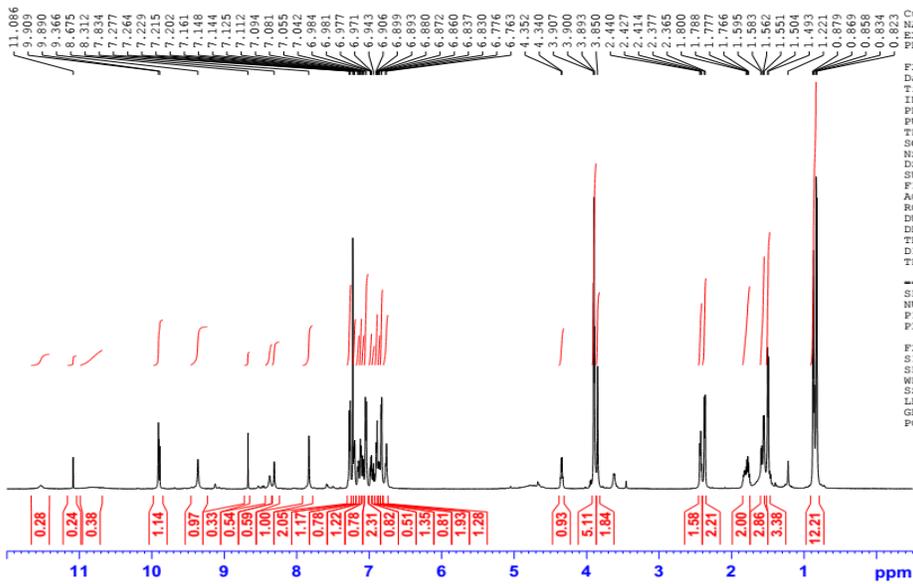


Figure-S6: ¹H-, ¹³C-NMR and HR-ESI-MS spectrum of compound 9

BRUKER



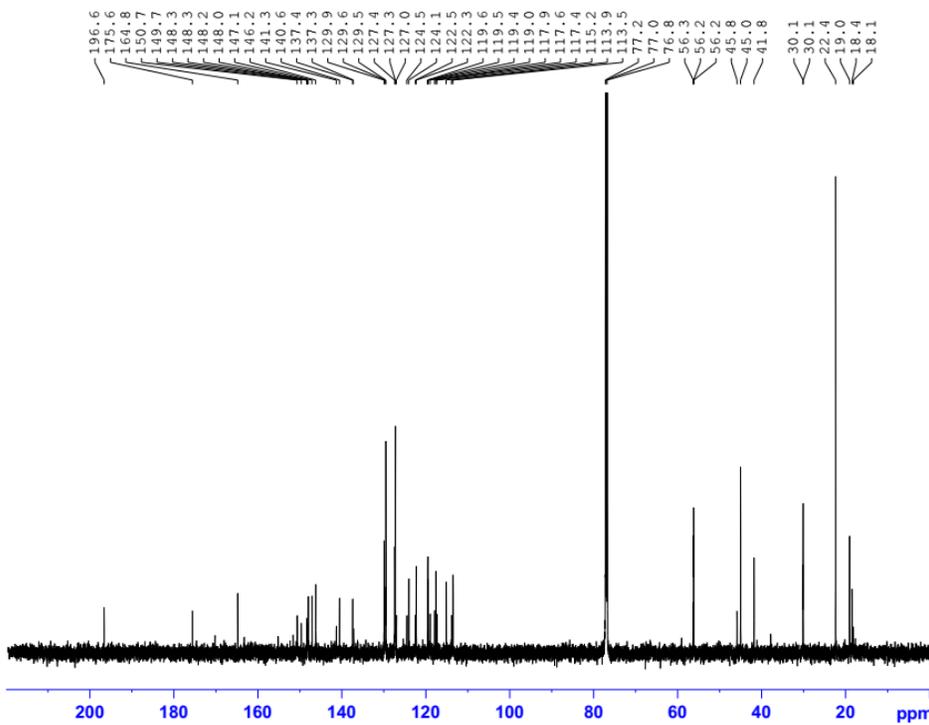
Current Data Parameters
 NAME 24-Aug-2022 Dr. Ajmal
 EXPNO 13
 PROCNO 1

F2 - Acquisition Parameters
 Date 20220824
 Time 15.25
 INSTRUM spect
 PROBHD 5 mm PABBO BB/
 PULPROG zg30
 TD 65536
 SOLVENT CDC13
 NS 16
 DS 2
 SWH 12019.230 Hz
 FIDRES 0.183399 Hz
 AQ 2.7262976 sec
 RG 76.79
 DW 41.600 usec
 DE 6.50 usec
 TE 298.1 K
 D1 1.00000000 sec
 TDO 1

----- CHANNEL f1 -----
 SFO1 600.1537062 MHz
 NUC1 1H
 F1 10.90 usec
 PLW1 22.60000038 W

F2 - Processing parameters
 SI 65536
 SF 600.1500266 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

BRUKER



Current Data Parameters
 NAME 24-Aug-2022 Dr. Ajmal
 EXPNO 57
 PROCNO 1

F2 - Acquisition Parameters
 Date 20220825
 Time 19.29
 INSTRUM spect
 PROBHD 5 mm PABBO BB/
 PULPROG zgpg30
 TD 32768
 SOLVENT CDC13
 NS 2048
 DS 4
 SWH 36057.691 Hz
 FIDRES 1.100393 Hz
 AQ 0.4543829 sec
 RG 195.2
 DW 13.867 usec
 DE 6.50 usec
 TE 298.1 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TDO 1

----- CHANNEL f1 -----
 SFO1 150.9229276 MHz
 NUC1 13C
 F1 11.60 usec
 PLW1 83.00000000 W

----- CHANNEL f2 -----
 SFO2 600.1524006 MHz
 NUC2 1H
 CPDPRG2 waltz16
 PCPD2 70.00 usec
 PLW2 22.60000038 W
 PLW3 0.52800002 W
 PLW13 0.25874999 W

F2 - Processing parameters
 SI 32768
 SF 150.9078399 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

Sample Name		Position	Vial 72	Instrument Name	Instrument 1
User Name		Inj Vol	10	InjPosition	
Sample Type	Sample	IRM Calibration Status	Success	Data Filename	
ACQ Method	POSITIVE ION METHOD MS.m	Comment		Acquired Time	05-Sep-22 11:12:20 AM

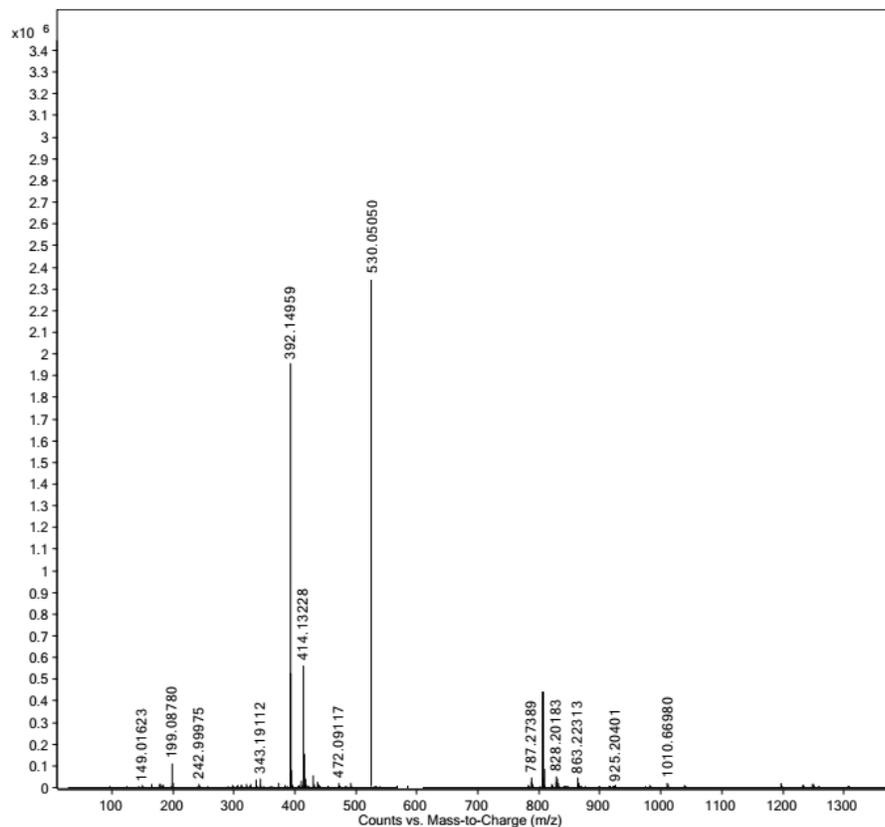
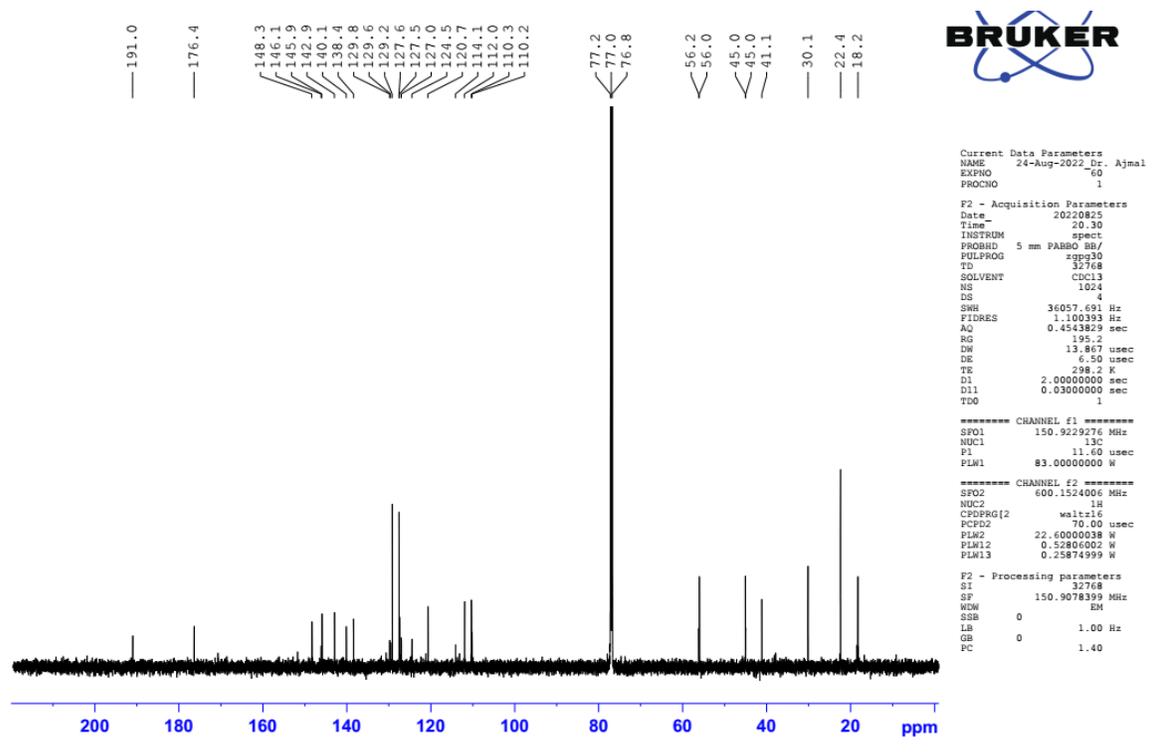
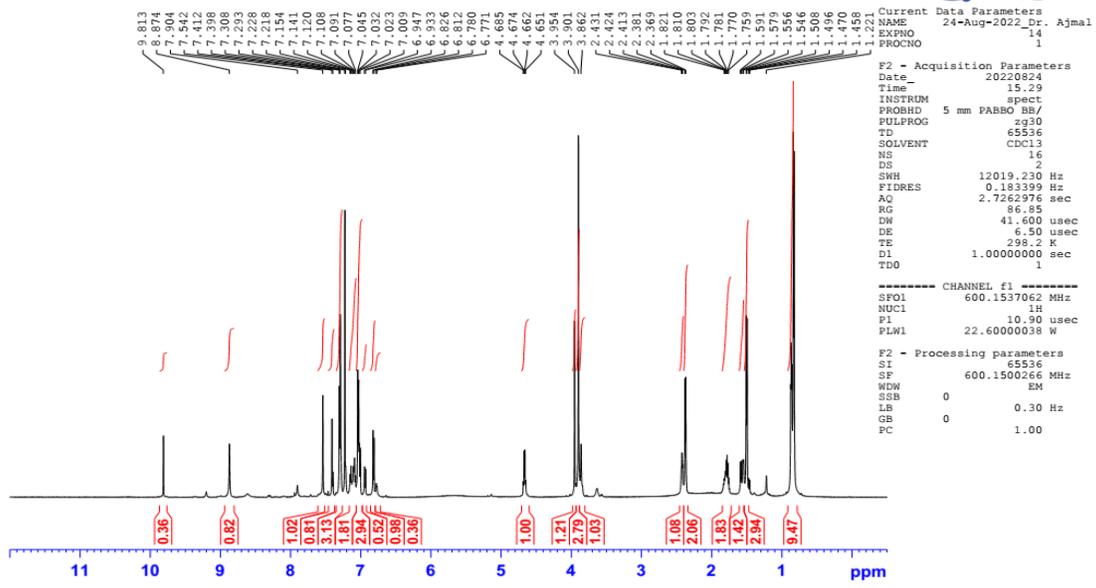


Figure-S7: ¹H-, ¹³C-NMR and HR-ESI-MS spectrum of compound **10**



Sample Name	WA-S-14	Position	Vial 44	Instrument Name	Instrument 1
User Name		Inj Vol	10	InjPosition	
Sample Type	Sample	IRM Calibration Status	Success	Data Filename	WA-S-14.d
ACQ Method	DMSO POS.m	Comment		Acquired Time	08-Oct-22 3:49:22 PM

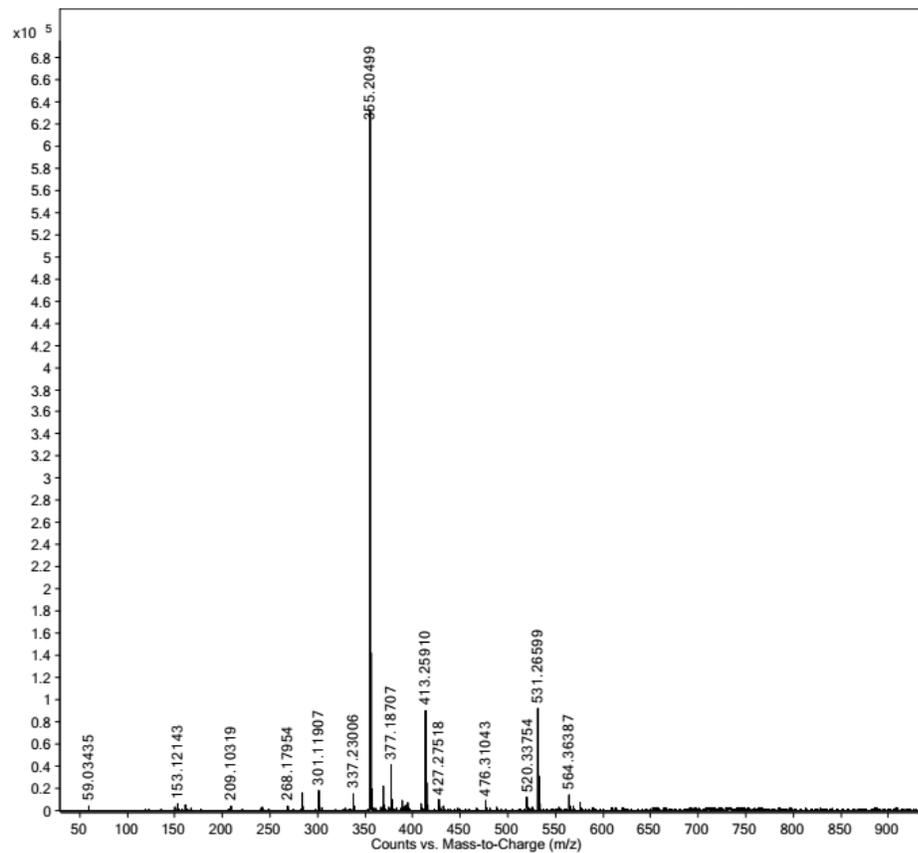
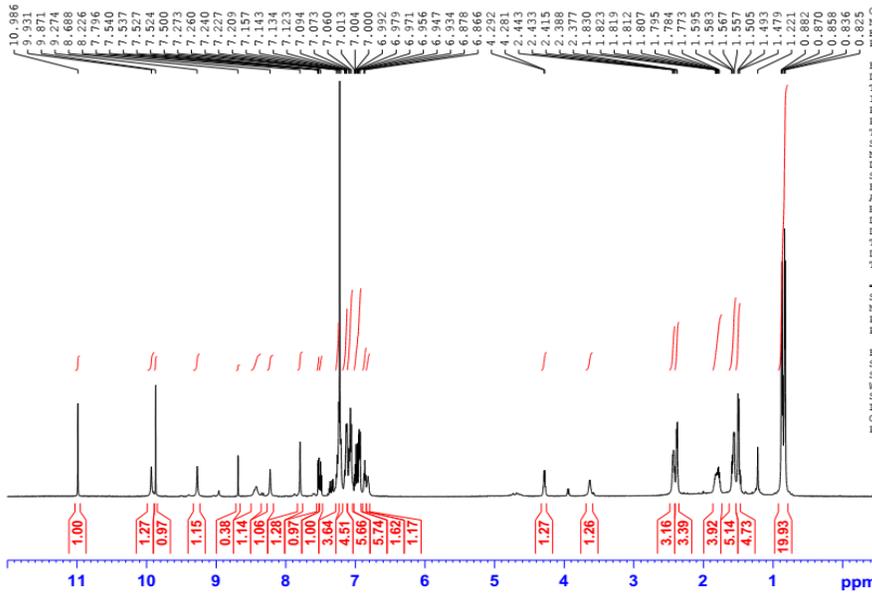


Figure-S8: ¹H-, ¹³C-NMR and HR-ESI-MS spectrum of compound 11

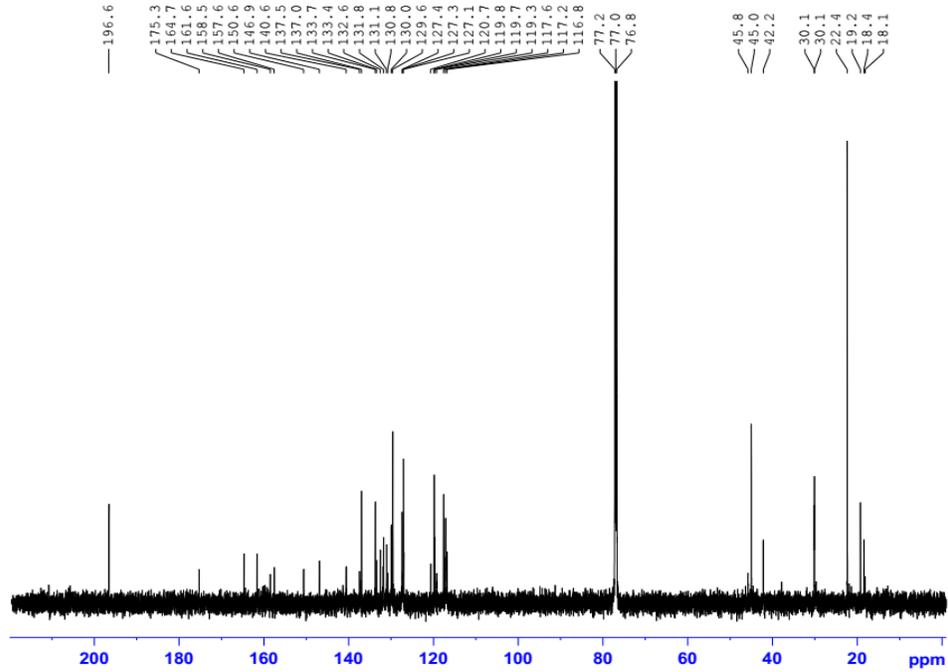


Current Data Parameters
 NAME 24-Aug-2022_Dr. Ajmal
 EXPNO 18
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20220825
 Time 12.29
 INSTRUM spect
 PROBHD 5 mm PABBO BB/
 PULPROG zg30
 TD 65536
 SOLVENT CDC13
 NS 16
 DS 2
 SWH 12019.230 Hz
 FIDRES 0.193399 Hz
 AQ 2.7262976 sec
 RG 86.85
 DW 41.600 usec
 DE 6.50 usec
 TE 298.2 K
 D1 1.00000000 sec
 TDO 1

----- CHANNEL f1 -----
 SF01 600.1537062 MHz
 NUC1 1H
 P1 10.90 usec
 PLW1 22.60000038 W

F2 - Processing parameters
 SI 65536
 SF 600.1500366 MHz
 WDW EM
 SSB 0 0.30 Hz
 LB 0
 GB 0
 PC 1.00



Current Data Parameters
 NAME 24-Aug-2022_Dr. Ajmal
 EXPNO 72
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20220826
 Time 8.11
 INSTRUM spect
 PROBHD 5 mm PABBO BB/
 PULPROG zgpg30
 TD 32768
 SOLVENT CDC13
 NS 2048
 DS 4
 SWH 36057.691 Hz
 FIDRES 1.100393 Hz
 AQ 0.4543829 sec
 RG 195.2
 DW 13.867 usec
 DE 6.50 usec
 TE 299.3 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TDO 1

----- CHANNEL f1 -----
 SF01 150.9220776 MHz
 NUC1 13C
 P1 11.60 usec
 PLW1 83.00000000 W

----- CHANNEL f2 -----
 SF02 600.1524006 MHz
 NUC2 1H
 CFPDPRG2 wait16
 PCPD2 70.00 usec
 PLW2 22.60000038 W
 PLW12 0.52806002 W
 PLW13 0.25874999 W

F2 - Processing parameters
 SI 32768
 SF 150.9078399 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

Sample Name WA-S-18
User Name
Sample Type Sample
ACQ Method DMSO POS.m

Position Vial 48
Inj Vol 10
IRM Calibration Status Success
Comment

Instrument Name Instrument 1
InjPosition
Data Filename WA-S-18.d
Acquired Time 08-Oct-22 4:12:36 PM

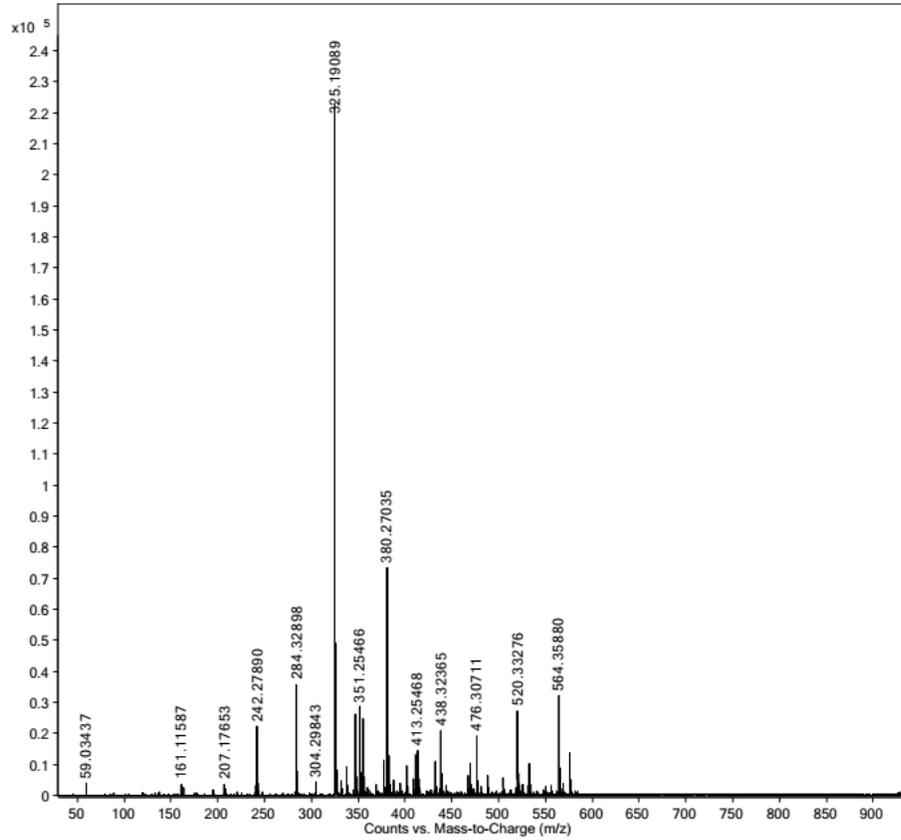
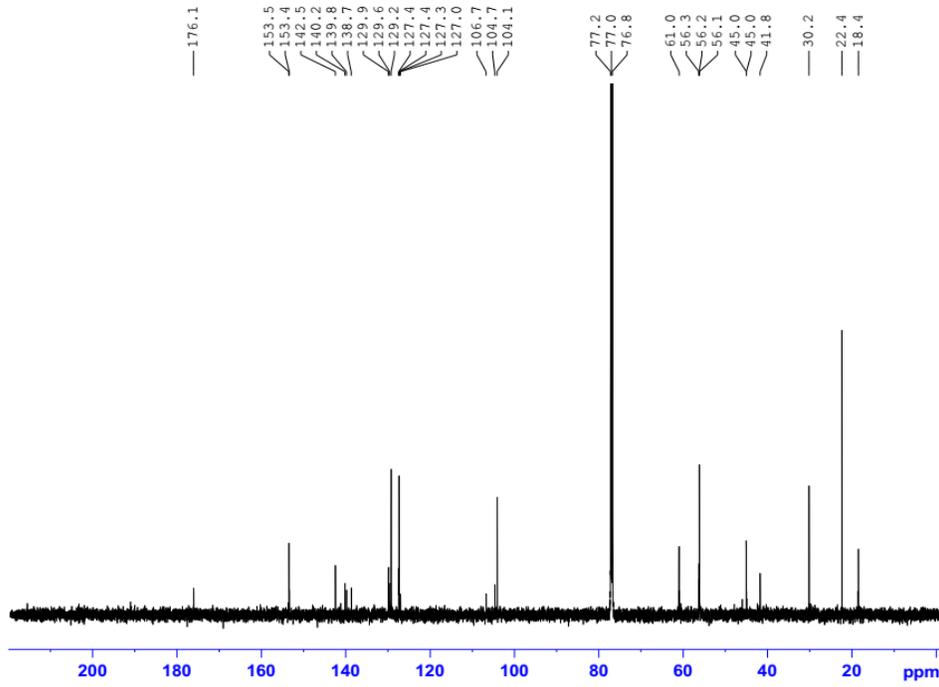
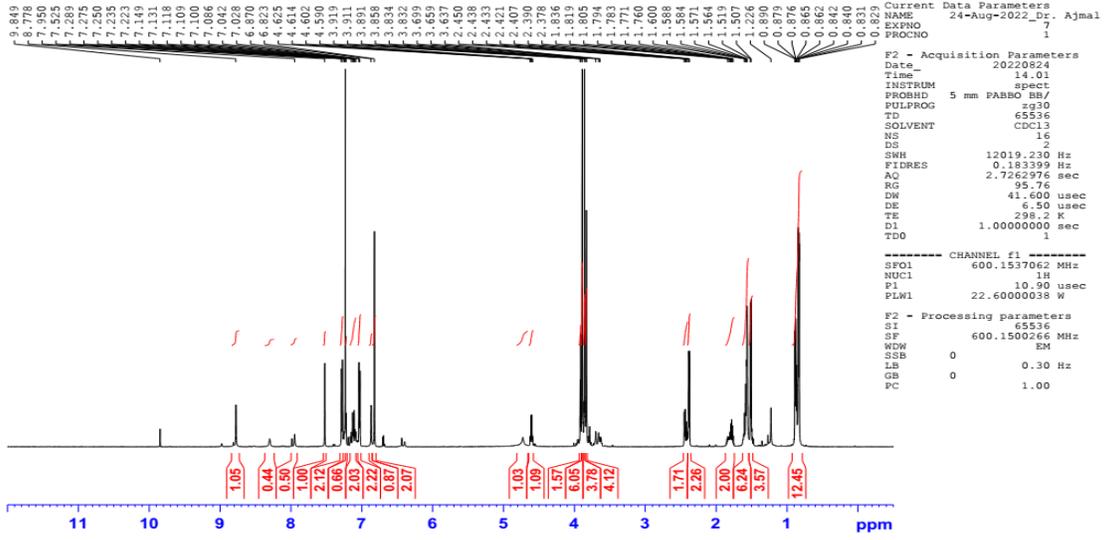


Figure-S9: ¹H-, ¹³C-NMR and HR-ESI-MS spectrum of compound **12**



Current Data Parameters
 NAME 24-Aug-2022_Dr. Ajmal
 EXPNO 39
 PROCNO 1

F2 - Acquisition Parameters
 Date 20220825
 Time 9.14
 INSTRUM spect
 PROBHD 5 mm PABBO BB/
 PULPROG zgpg30
 TD 32768
 SOLVENT CDCl3
 NS 4
 DS 4
 SWH 36057.691 Hz
 FIDRES 1.100393 Hz
 AQ 0.4543829 sec
 RG 195.2
 DW 13.867 usec
 DE 6.50 usec
 TE 298.2 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TDO 1

----- CHANNEL f1 -----
 SFO1 150.9229276 MHz
 NUC1 13C
 P1 11.60 usec
 PLW1 83.00000000 W

----- CHANNEL f2 -----
 SFO2 600.1524006 MHz
 NUC2 1H
 CPDPRG2 waltz16
 PCPD2 70.00 usec
 PLW2 22.60000038 W
 PLW12 0.52806002 W
 PLW13 0.25874999 W

F2 - Processing parameters
 SI 32768
 SF 150.9078399 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

Sample Name		Position	Vial 39	Instrument Name	Instrument 1
User Name		Inj Vol	10	InjPosition	
Sample Type	Sample	IRM Calibration Status	Success	Data Filename	
ACQ Method	DMSO POS.m	Comment		Acquired Time	08-Oct-22 3:20:25 PM

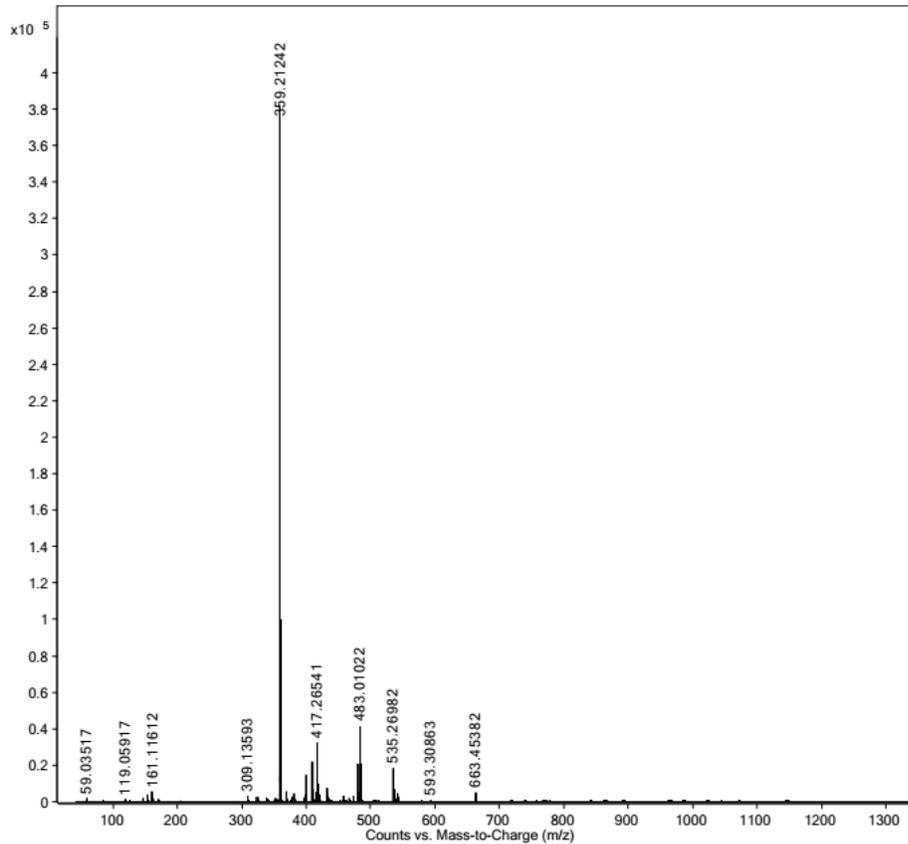
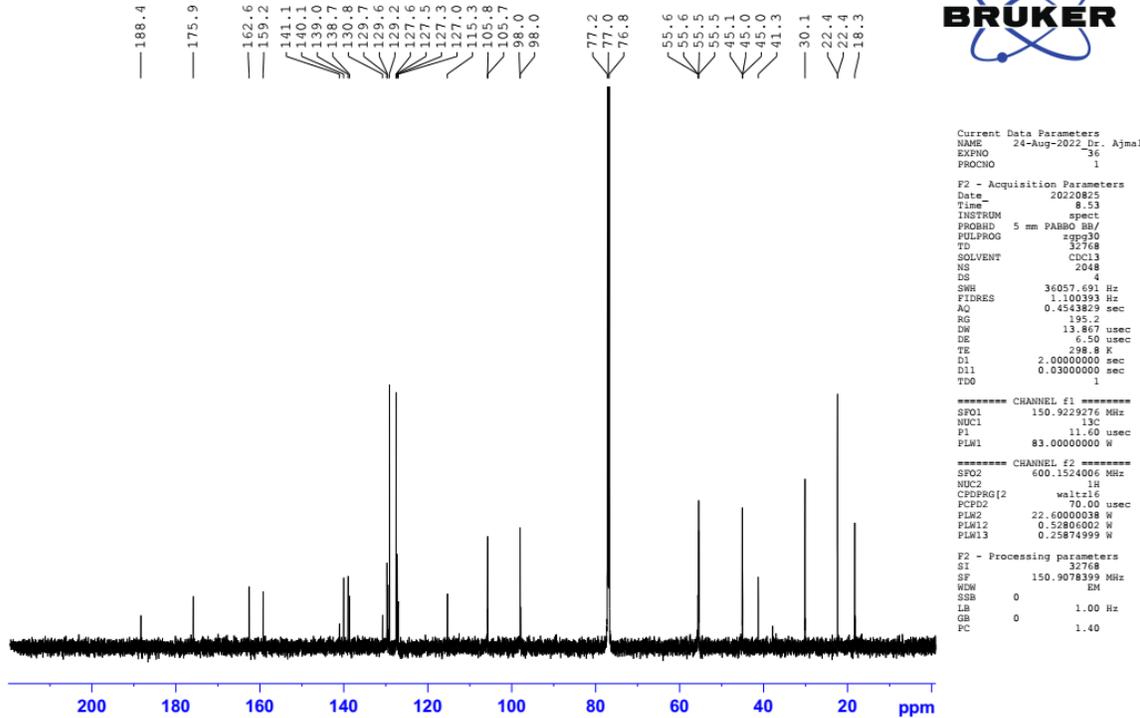
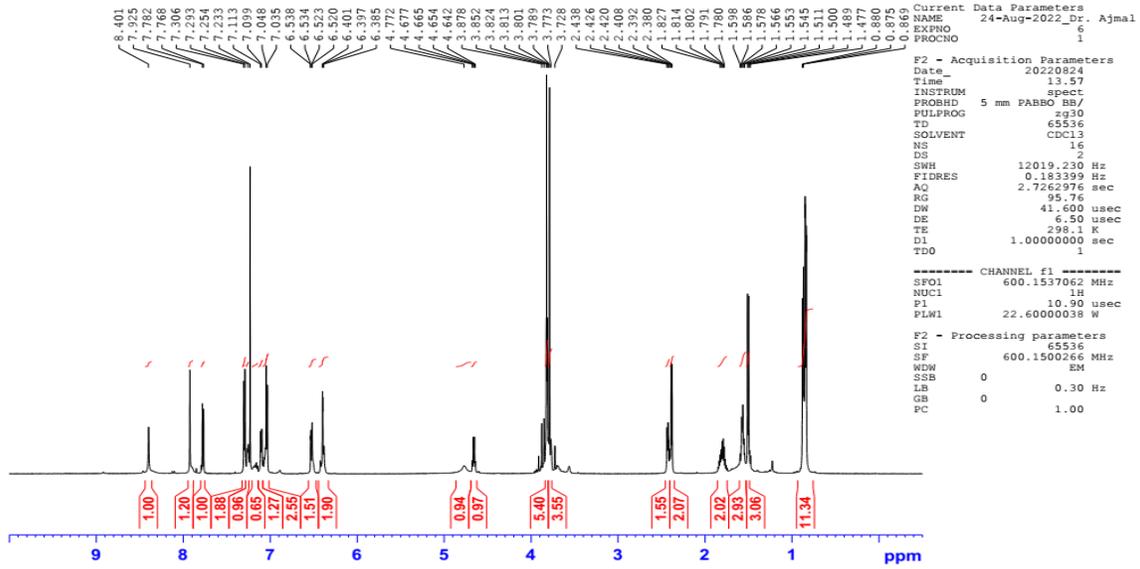


Figure-S10: ¹H-, ¹³C-NMR and HR-ESI-MS spectrum of compound **13**



Sample Name		Position	Vial 36	Instrument Name	Instrument 1
User Name		Inj Vol	10	InjPosition	
Sample Type	Sample	IRM Calibration Status	Success	Data Filename	
ACQ Method	DMSO POS.m	Comment		Acquired Time	08-Oct-22 3:03:11 PM

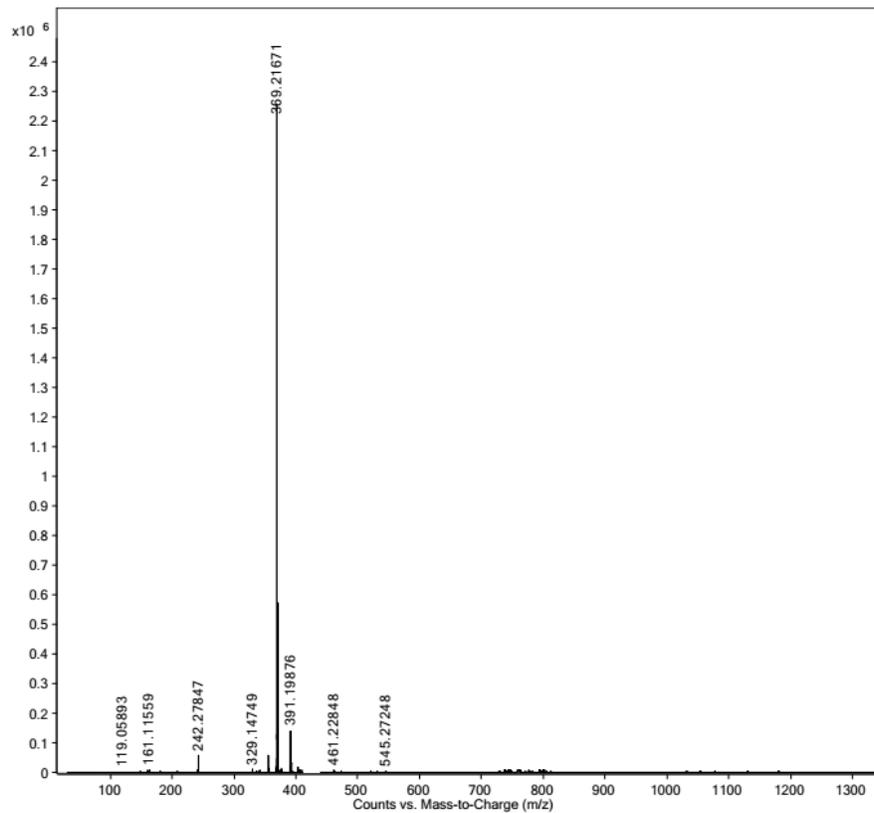
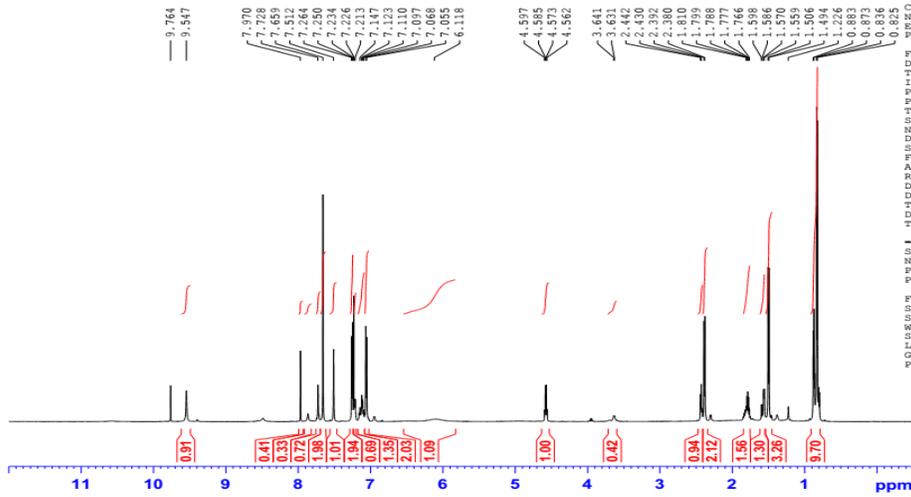


Figure-S11: ¹H-, ¹³C-NMR and HR-ESI-MS spectrum of compound 14

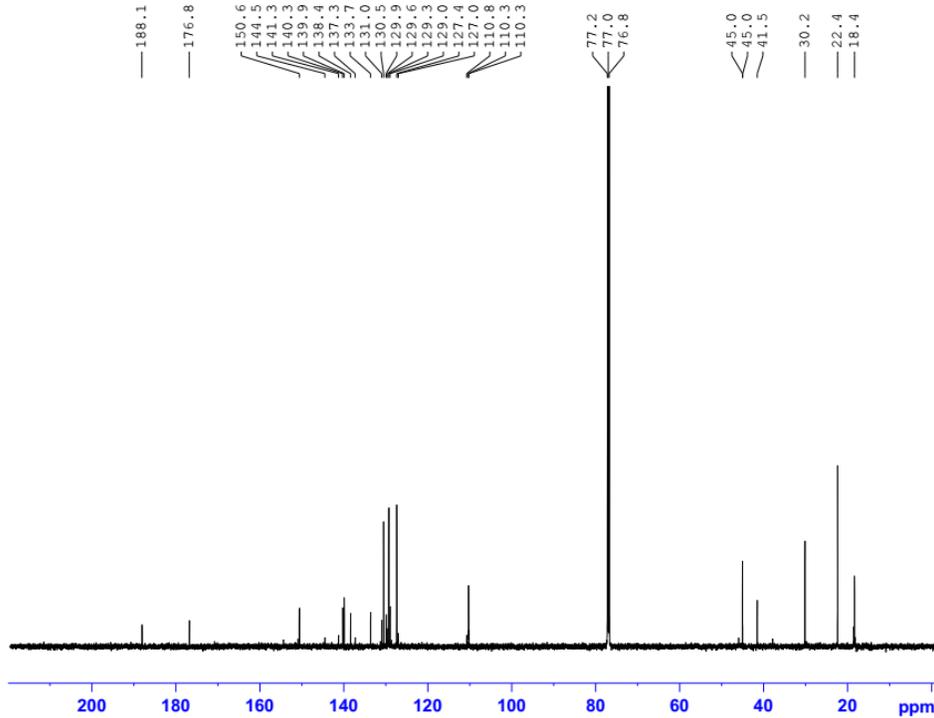


Current Data Parameters
 NAME: 24-Aug-2022_Dr. Ajmal
 EXPNO: 9
 PROCNO: 1

F2 - Acquisition Parameters
 Date_: 20220824
 Time: 14.08
 INSTRUM: spect
 PROBHD: 5 mm PABBO BB/
 PULPROG: zg30
 TD: 65536
 SOLVENT: CDCl3
 NS: 16
 DS: 2
 SWH: 12019.230 Hz
 FIDRES: 0.183399 Hz
 AQ: 2.7262976 sec
 RG: 76.79
 DW: 41.600 usec
 DE: 6.50 usec
 TE: 298.1 K
 D1: 1.00000000 sec
 TDO: 1

----- CHANNEL f1 -----
 SFO1: 600.1537062 MHz
 NUC1: 1H
 P1: 10.90 usec
 PLW1: 22.60000038 W

F2 - Processing parameters
 SI: 65536
 SF: 600.1500266 MHz
 WDW: EM
 SSB: 0
 LB: 0.30 Hz
 GB: 0
 PC: 1.00



Current Data Parameters
 NAME: 24-Aug-2022_Dr. Ajmal
 EXPNO: 45
 PROCNO: 1

F2 - Acquisition Parameters
 Date_: 20220825
 Time: 14.28
 INSTRUM: spect
 PROBHD: 5 mm PABBO BB/
 PULPROG: zgpg30
 TD: 32768
 SOLVENT: CDCl3
 NS: 1024
 DS: 4
 SWH: 36057.691 Hz
 FIDRES: 1.100393 Hz
 AQ: 0.4543829 sec
 RG: 195.2
 DW: 13.867 usec
 DE: 6.50 usec
 TE: 298.2 K
 D1: 2.00000000 sec
 D11: 0.03000000 sec
 TDO: 1

===== CHANNEL f1 =====
 SFO1: 150.9229276 MHz
 NUC1: 13C
 P1: 11.60 usec
 PLW1: 83.00000000 W

===== CHANNEL f2 =====
 SFO2: 600.1524006 MHz
 NUC2: 1H
 CPDPRG[2]: waltz16
 PCPD2: 70.00 usec
 PLW2: 22.60000038 W
 PLW12: 0.52800002 W
 PLW13: 0.25874999 W

F2 - Processing parameters
 SI: 32768
 SF: 150.9078399 MHz
 WDW: EM
 SSB: 0
 LB: 1.00 Hz
 GB: 0
 PC: 1.40

Sample Name
User Name
Sample Type
ACQ Method

Sample
POSITIVE ION METHOD MS.m

Position Vial 36
Inj Vol 10
IRM Calibration Status Success
Comment

Instrument Name Instrument 1
InjPosition
Data Filename
Acquired Time 21-Aug-22 2:00:01 PM

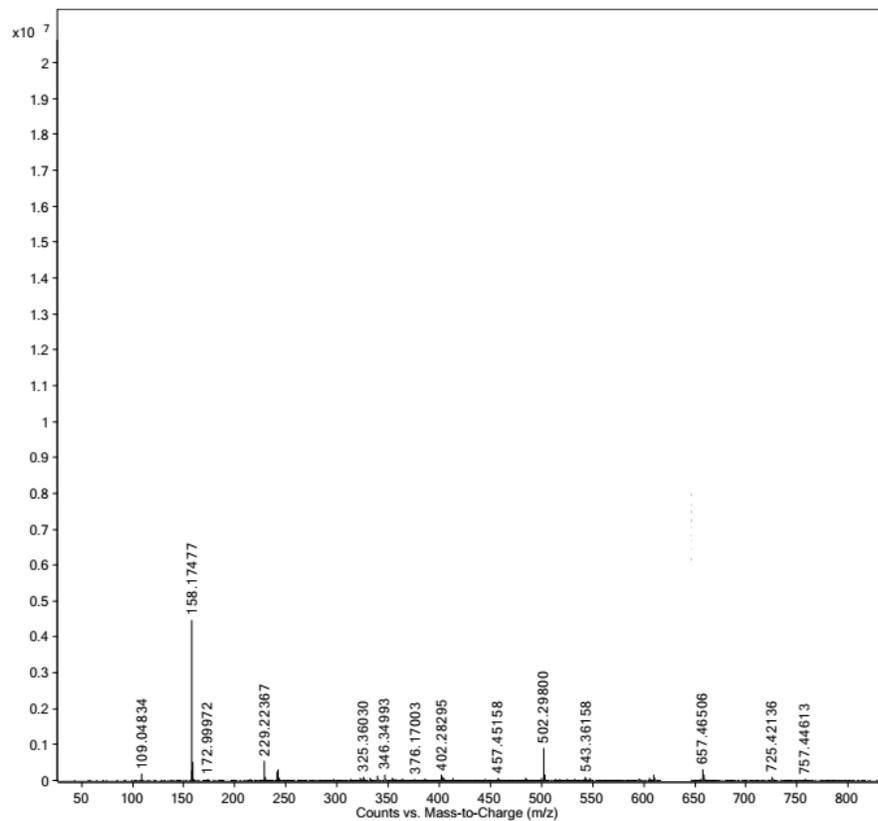


Figure-S12: ¹H-, ¹³C-NMR and HR-ESI-MS spectrum of compound 15

Table S1. Comparative *In Silico* ADMET and Physicochemical Profile of Active Bis-Schiff Base Derivatives (9–14) and Acarbose

Parameter (Category)	13	12	14	10	9	11	Acarbose
Physicochemical Properties							
Molecular Weight (MW)	574.28	544.27	544.27	530.25	530.25	530.25	645.25
cLogP	6.12	6.24	6.59	6.02	5.78	6.06	-2.88
Topological Polar Surface Area (TPSA, Å²)	119.84	110.61	110.61	121.61	121.61	121.61	321.17
Rotatable Bonds (nRot)	16	15	15	14	14	14	9
Solubility & Absorption							
Predicted Solubility (LogS)	-7.54	-7.65	-7.89	-5.90	-5.49	-6.68	-0.73
GI Absorption	High	High	High	High	High	High	Low
Caco-2 Permeability (log Papp, cm/s)	-4.63	-4.65	-4.68	-4.90	-4.86	-4.69	-6.35
P-glycoprotein Inhibitor (Prob.)	0.998	0.997	0.995	0.991	0.992	0.506	0.000
P-glycoprotein Substrate (Prob.)	0.114	0.103	0.054	0.311	0.234	0.569	0.985
Distribution							
Plasma Protein Binding (PPB, %)	104.56	105.51	105.61	102.88	103.32	104.95	23.91
Volume of Distribution (VD_{ss}, L/kg)	0.509	0.970	0.962	0.603	0.461	0.649	0.159

Blood-Brain Barrier Penetration (BBB Prob.)	0.020	0.017	0.015	0.021	0.041	0.008	0.331
Metabolism							
CYP2C9 Inhibitor (Prob.)	0.634	0.647	0.777	0.807	0.870	0.707	0.000
CYP2C19 Inhibitor (Prob.)	0.562	0.539	0.594	0.624	0.662	0.576	0.010
CYP3A4 Inhibitor (Prob.)	0.444	0.373	0.596	0.345	0.290	0.321	0.005
Total Clearance (CL, mL/min/kg)	5.887	5.992	6.183	2.181	2.010	5.569	0.681
Half-Life (T1/2, h)	0.163	0.156	0.103	0.402	0.557	0.202	0.835
Toxicity							
hERG Inhibition (Prob.)	0.075	0.047	0.038	0.051	0.037	0.036	0.199
Drug-Induced Liver Injury (DILI Prob.)	0.973	0.975	0.974	0.968	0.972	0.977	0.977
Ames Mutagenicity (Prob.)	0.573	0.740	0.760	0.867	0.851	0.658	0.117
Carcinogenicity (Prob.)	0.103	0.368	0.414	0.789	0.805	0.416	0.044
Drug-likeness							
Lipinski's Rule of 5 (# Violations)	2 (MW, LogP)	3 (MW, HBD, HBA)					
Pfizer Rule	Accepted						
Synthetic Accessibility (Scale 1-10)	3.07	2.96	3.00	3.05	3.04	3.02	5.63

PAINS Alerts	0	0	0	1	1	0	0
Key Structural Alert	None	None	None	Chelator, PAINS	Chelator, PAINS	None	None
