*J. Braz. Chem. Soc.*, Vol. 25, No. 10, S1-S26, 2014.
Printed in Brazil - ©2014 Sociedade Brasileira de Química
0103 - 5053 $6.00+0.00

# Supplementary Information

## The Semisynthetic Landscape of Aphidicolin: Inspiration Towards Leishmanicidal Compounds

***Gabriela B. Santos,[a] Marília O. Almeida,[a] Iara A. Cardoso,[a] Viviane Manfrim,[a] Fernanda O. Chagas,[a] Juliano S. Toledo,[b] Camila C. Pinzan,[b] Alexandre Suman de Araujo,[c] Angela K. Cruz,[b] Monica T. Pupo[a] and Flavio S. Emery*[a]***

*[a]Departamento de Ciências Farmacêuticas, Faculdade de Ciências Farmacêuticas de Ribeirão Preto and [b]Departamento de Biologia Celular e Molecular e Bioagentes Patogênicos, Faculdade Medicina de Ribeirão Preto, Universidade de São Paulo, 14040-903 Ribeirão Preto-SP, Brazil*

*[c]Departamento de Física, Instituto de Biociências Letras e Ciências Exatas de São José do Rio Preto, Universidade Estadual Paulista Júlio de Mesquita Filho, Rua Cristóvão Colombo, 2265, Jardim Nazareth, 15054-000 São José do Rio Preto-SP, Brazil*

**Table S1.** Aphidicolin derivatives via biotransformation reactions and molecular properties

| Name | MW | ΔMW | XLogP | LogP | HBA | ΔHBA | HBD | ΔHBD | TPSA_NOPS | ΔTPSA | RBC | ΔRBC |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Aphidicolin | 338.48 | – | 1.12 | – | 4 | – | 4 | – | 80.9 | – | 2 | – |
| Ref 11 compound **12** | 380.52 | 42.04 | 2.07 | 0.95 | 5 | 1 | 3 | –1 | 87 | 6.1 | 4 | 2 |
| Ref 11 compound **11** | 380.52 | 42.04 | 2.07 | 0.95 | 5 | 1 | 3 | –1 | 87 | 6.1 | 4 | 2 |
| Ref 11 compound **10** | 366.49 | 28.01 | 1.4 | 0.28 | 5 | 1 | 4 | 0 | 98 | 17.1 | 3 | 1 |
| Ref 11 compound **9** | 418.61 | 80.13 | 5.81 | 4.69 | 4 | 0 | 0 | –4 | 36.9 | –44 | 0 | –2 |
| Ref 11 compound **8** | 418.61 | 80.13 | 5.81 | 4.69 | 4 | 0 | 0 | –4 | 36.9 | –44 | 0 | –2 |
| Ref 11 compound **7** | 338.48 | 0 | 1.12 | 0 | 4 | 0 | 4 | 0 | 80.9 | 0 | 2 | 0 |
| Ref 11 compound **6** | 366.49 | 28.01 | 1.4 | 0.28 | 5 | 1 | 4 | 0 | 98 | 17.1 | 3 | 1 |
| Ref 11 compound **5** | 354.48 | 16 | –0.06 | –1.18 | 5 | 1 | 5 | 1 | 101.1 | 20.2 | 2 | 0 |
| Ref 11 compound **4** | 336.47 | –2.01 | 1.42 | 0.3 | 4 | 0 | 3 | –1 | 77.8 | –3.1 | 2 | 0 |
| Ref 11 compound **3** | 380.52 | 42.04 | 2.07 | 0.95 | 5 | 1 | 3 | –1 | 87 | 6.1 | 4 | 2 |
| Ref 11 compound **2** | 484.62 | 146.14 | 4.72 | 3.6 | 6 | 2 | 2 | –2 | 85.2 | 4.3 | 4 | 2 |
| Ref 11 compound **1** | 442.59 | 104.11 | 3.77 | 2.65 | 5 | 1 | 3 | –1 | 79.1 | –1.8 | 2 | 0 |
| Mean differences | – | 50.55 | – | 1.51 | – | 0.75 | – | –1.16 | – | –1.32 | – | 0.5 |
| Mean | 389 | – | 2.63 | – | 4.75 | – | 2.83 | – | 79.57 | – | 2.5 | – |

*e-mail: flavioemery@fcfrp.usp.br

**Table S2.** Aphidicolin derivatives via semisynthesis and molecular properties

| Name | XLogP | ΔLogP | HBD | ΔHBD | HBA | ΔHBA | MW | ΔMW | TPSA | ΔTPSA | RBC | ΔRBC |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Aphidicolin | 1.12 | – | 4 | – | 4 | – | 338.48 | – | 80.9 | – | 2 | – |
| Ref 7 compound 42 | 4.57 | 3.45 | 0 | –4 | 3 | –1 | 360.53 | 22.05 | 31 | –49.9 | 0 | –2 |
| Ref 7 compound 41 | 5.81 | 4.69 | 0 | –4 | 4 | 0 | 418.61 | 80.13 | 36.9 | –44 | 0 | –2 |
| Ref 7 compound 36 | 5.61 | 4.49 | 0 | –4 | 2 | –2 | 344.53 | 6.05 | 18.5 | –62.4 | 0 | –2 |
| Ref 7 compound 35 | 4.6 | 3.48 | 0 | –4 | 3 | –1 | 346.5 | 8.02 | 35.5 | –45.4 | 0 | –2 |
| Ref 7 compound 34 | 9.09 | 7.97 | 0 | –4 | 0 | –4 | 270.45 | –68.03 | 0 | –80.9 | 0 | –2 |
| Ref 7 compound 32 | 6.09 | 4.97 | 0 | –4 | 1 | –3 | 380.59 | 42.11 | 42.4 | –38.5 | 3 | 1 |
| Ref 7 compound 29 | 3.73 | 2.61 | 1 | –3 | 5 | 1 | 378.5 | 40.02 | 72.8 | –8.1 | 3 | 1 |
| Ref 7 compound 26 | 2.18 | 1.06 | 2 | –2 | 4 | 0 | 322.44 | –16.04 | 66.8 | –14.1 | 1 | –1 |
| Ref 7 compound 21 | 3.22 | 2.1 | 1 | –3 | 4 | 0 | 320.42 | –18.06 | 71.4 | –9.5 | 5 | 3 |
| Ref 7 compound 20 | 5.81 | 4.69 | 0 | –4 | 4 | 0 | 418.61 | 80.13 | 36.9 | –44 | 0 | –2 |
| Ref 7 compound 19 | 1.12 | 0 | 4 | 0 | 4 | 0 | 338.48 | 0 | 80.9 | 0 | 2 | 0 |
| Ref 7 compound 18 | 2.25 | 1.13 | 2 | –2 | 3 | –1 | 306.44 | –32.04 | 57.5 | –23.4 | 1 | –1 |
| Ref 7 compound 17 | 1.12 | 0 | 4 | 0 | 4 | 0 | 338.48 | 0 | 80.9 | 0 | 2 | 0 |
| Ref 7 compound 15 | 9.46 | 8.34 | 0 | –4 | 0 | –4 | 272.47 | –66.01 | 0 | –80.9 | 0 | –2 |
| Ref 7 compound 14 | 4.65 | 3.53 | 0 | –4 | 1 | –3 | 274.44 | –64.04 | 17.1 | –63.8 | 0 | –2 |
| Ref 7 compound 12 | 3.43 | 2.31 | 1 | –3 | 2 | –2 | 290.44 | –48.04 | 37.3 | –43.6 | 1 | –1 |
| Ref 7 compound 9 | 3.12 | 2 | 2 | –2 | 2 | –2 | 292.46 | –46.02 | 40.5 | –40.4 | 1 | –1 |
| Ref 7 compound 8 | 4.16 | 3.04 | 0 | –4 | 5 | 1 | 390.51 | 52.03 | 69.7 | –11.2 | 5 | 3 |
| Ref 7 compound 6 | 2.37 | 1.25 | 2 | –2 | 5 | 1 | 378.5 | 40.02 | 83.8 | 2.9 | 4 | 2 |
| Ref 6 compound 17 | 3.26 | 2.14 | 2 | –2 | 2 | –2 | 304.47 | –34.01 | 40.5 | –40.4 | 1 | –1 |
| Ref 6 compound 15 | 4.64 | 3.52 | 1 | –3 | 5 | 1 | 434.61 | 96.13 | 57.1 | –23.8 | 0 | –2 |
| Ref 6 compound 14 | 4.6 | 3.48 | 0 | –4 | 3 | –1 | 346.5 | 8.02 | 35.5 | –45.4 | 0 | –2 |
| Ref 6 compound 13 | 4.22 | 3.1 | 3 | –1 | 3 | –1 | 444.67 | 106.19 | 86 | 5.1 | 5 | 3 |
| Ref 6 compound 11 | 3.41 | 2.29 | 0 | –4 | 3 | –1 | 318.45 | –20.03 | 35.5 | –45.4 | 0 | –2 |
| Ref 6 compound 8 | 3.36 | 2.24 | 0 | –4 | 2 | –2 | 288.42 | –50.06 | 26.3 | –54.6 | 0 | –2 |
| Ref 8 compound 17 | 4.62 | 3.5 | 0 | –4 | 4 | 0 | 390.56 | 52.08 | 36.9 | –44 | 0 | –2 |
| Ref 8 compound 16 | 2.22 | 1.1 | 2 | –2 | 3 | –1 | 320.47 | –18.01 | 49.7 | –31.2 | 1 | –1 |
| Ref 8 compound 14 | 4.69 | 3.57 | 1 | –3 | 3 | –1 | 362.55 | 24.07 | 38.7 | –42.2 | 0 | –2 |
| Ref 8 compound 11 | 1.95 | 0.83 | 3 | –1 | 3 | –1 | 308.46 | –30.02 | 60.7 | –20.2 | 1 | –1 |
| Ref 8 compound 10 | 1.95 | 0.83 | 3 | –1 | 3 | –1 | 308.46 | –30.02 | 60.7 | –20.2 | 1 | –1 |
| Ref 8 compound 8 | 2.34 | 1.22 | 3 | –1 | 3 | –1 | 322.48 | –16 | 60.7 | –20.2 | 1 | –1 |
| Ref 8 compound 4 | 3.57 | 2.45 | 2 | –2 | 2 | –2 | 306.48 | –32 | 40.5 | –40.4 | 0 | –2 |
| Ref 8 compound 2 | –0.06 | –1.18 | 5 | 1 | 5 | 1 | 354.48 | 16 | 101.1 | 20.2 | 2 | 0 |
| Ref 9 compound 22 | 2.34 | 1.22 | 3 | –1 | 3 | –1 | 322.48 | –16 | 60.7 | –20.2 | 1 | –1 |
| Ref 9 compound 21 | 3.37 | 2.25 | 2 | –2 | 2 | –2 | 292.46 | –46.02 | 40.5 | –40.4 | 1 | –1 |
| Ref 9 compound 20 | 1.12 | 0 | 4 | 0 | 4 | 0 | 338.48 | 0 | 80.9 | 0 | 2 | 0 |
| Ref 9 compound 18 | 3.46 | 2.34 | 2 | –2 | 4 | 0 | 378.55 | 40.07 | 58.9 | –22 | 1 | –1 |
| Ref 9 compound 15 | 4.6 | 3.48 | 0 | –4 | 3 | –1 | 346.5 | 8.02 | 35.5 | –45.4 | 0 | –2 |
| Ref 9 compound 14 | 3.46 | 2.34 | 2 | –2 | 4 | 0 | 378.55 | 40.07 | 58.9 | –22 | 1 | –1 |
| Ref 9 compound 13 | 2.77 | 1.65 | 1 | –3 | 4 | 0 | 306.4 | –32.08 | 71.4 | –9.5 | 4 | 2 |
| Ref 9 compound 12 | 1.65 | 0.53 | 3 | –1 | 5 | 1 | 366.49 | 28.01 | 87 | 6.1 | 3 | 1 |
| Ref 9 compound 10 | 2.66 | 1.54 | 2 | –2 | 3 | –1 | 320.47 | –18.01 | 57.5 | –23.4 | 1 | –1 |
| Ref 9 compound 9 | 2.34 | 1.22 | 3 | –1 | 3 | –1 | 322.48 | –16 | 60.7 | –20.2 | 1 | –1 |
| Ref 9 compound 8 | 1.76 | 0.64 | 2 | –2 | 4 | 0 | 334.45 | –4.03 | 74.6 | –6.3 | 2 | 0 |
| Ref 9 compound 7 | 1.44 | 0.32 | 3 | –1 | 4 | 0 | 336.47 | –2.01 | 77.8 | –3.1 | 2 | 0 |
| Ref 9 compound 3 | 1.27 | 0.15 | 3 | –1 | 5 | 1 | 350.45 | 11.97 | 94.8 | 13.9 | 2 | 0 |
| Ref 9 compound 1 | 3.05 | 1.93 | 3 | –1 | 6 | 2 | 492.67 | 154.19 | 112.4 | 31.5 | 5 | 3 |
| Ref 10 compound 25 | 1.95 | 0.83 | 3 | –1 | 3 | –1 | 320.47 | –18.01 | 60.7 | –20.2 | 2 | 0 |
| Ref 10 compound 23 | 1.12 | 0 | 4 | 0 | 4 | 0 | 338.48 | 0 | 80.9 | 0 | 2 | 0 |
| Ref 10 compound 22 | 2.34 | 1.22 | 3 | –1 | 3 | –1 | 322.48 | –16 | 60.7 | –20.2 | 1 | –1 |
| Ref 10 compound 19 | 1.7 | 0.58 | 3 | –1 | 5 | 1 | 364.48 | 26 | 94.8 | 13.9 | 3 | 1 |
| Ref 10 compound 17 | 1.72 | 0.6 | 3 | –1 | 5 | 1 | 364.48 | 26 | 94.8 | 13.9 | 3 | 1 |

**Table S2.** continuation

| Name | XLogP | ΔLogP | HBD | ΔHBD | HBA | ΔHBA | MW | ΔMW | TPSA | ΔTPSA | RBC | ΔRBC |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ref 10 compound 16 | 1.76 | 0.64 | 2 | –2 | 4 | 0 | 334.45 | –4.03 | 74.6 | –6.3 | 2 | 0 |
| Ref 10 compound 15 | 1.44 | 0.32 | 3 | –1 | 4 | 0 | 336.47 | –2.01 | 77.8 | –3.1 | 2 | 0 |
| Ref 10 compound 4 | 3.97 | 2.85 | 1 | –3 | 7 | 3 | 464.59 | 126.11 | 99.1 | 18.2 | 8 | 6 |
| Ref 10 compound 2 | 2.07 | 0.95 | 3 | –1 | 5 | 1 | 380.52 | 42.04 | 87 | 6.1 | 4 | 2 |
| Ref 7 compound 44 | 5.81 | 4.69 | 0 | –4 | 4 | 0 | 418.61 | 80.13 | 36.9 | –44 | 0 | –2 |
| Ref 7 compound 43 | 4.57 | 3.45 | 0 | –4 | 3 | –1 | 360.53 | 22.05 | 31 | –49.9 | 0 | –2 |
| Ref 7 compound 33 | 4.32 | 3.2 | 0 | –4 | 1 | –3 | 272.42 | –66.06 | 17.1 | –63.8 | 0 | –2 |
| Ref 7 compound 30 | 4.6 | 3.48 | 1 | –3 | 4 | 0 | 364.52 | 26.04 | 55.8 | –25.1 | 3 | 1 |
| Ref 7 compound 27 | 4.53 | 3.41 | 0 | –4 | 4 | 0 | 362.5 | 24.02 | 44.8 | –36.1 | 0 | –2 |
| Ref 7 compound 24 | 4.02 | 2.9 | 0 | –4 | 6 | 2 | 448.59 | 110.11 | 71.1 | –9.8 | 5 | 3 |
| Ref 7 compound 16 | 3.26 | 2.14 | 2 | –2 | 2 | –2 | 304.47 | –34.01 | 40.5 | –40.4 | 1 | –1 |
| Ref 7 compound 11 | 4.38 | 3.26 | 0 | –4 | 3 | –1 | 332.48 | –6 | 43.4 | –37.5 | 3 | 1 |
| Ref 7 compound 10 | 4.07 | 2.95 | 1 | –3 | 3 | –1 | 334.49 | –3.99 | 46.5 | –34.4 | 3 | 1 |
| Ref 7 compound 7 | 1.42 | 0.3 | 3 | –1 | 4 | 0 | 336.47 | –2.01 | 77.8 | –3.1 | 2 | 0 |
| Ref 6 compound 20 | 3.05 | 1.93 | 3 | –1 | 6 | 2 | 492.67 | 154.19 | 112.4 | 31.5 | 5 | 3 |
| Ref 6 compound 10 | 4.65 | 3.53 | 0 | –4 | 1 | –3 | 274.44 | –64.04 | 17.1 | –63.8 | 0 | –2 |
| Ref 6 compound 5 | 3.42 | 2.3 | 0 | –4 | 4 | 0 | 362.5 | 24.02 | 36.9 | –44 | 0 | –2 |
| Ref 6 compound 4 | 6.02 | 4.9 | 0 | –4 | 2 | –2 | 358.56 | 20.08 | 18.5 | –62.4 | 0 | –2 |
| Ref 8 compound 18 | 1.76 | 0.64 | 4 | 0 | 6 | 2 | 431.99 | 93.51 | 113 | 32.1 | 5 | 3 |
| Ref 8 compound 15 | 4.62 | 3.5 | 0 | –4 | 4 | 0 | 390.56 | 52.08 | 36.9 | –44 | 0 | –2 |
| Ref 8 compound 13 | 2.34 | 1.22 | 3 | –1 | 3 | –1 | 322.48 | –16 | 60.7 | –20.2 | 1 | –1 |
| Ref 8 compound 12 | 3.8 | 2.68 | 2 | –2 | 3 | –1 | 334.49 | –3.99 | 57.5 | –23.4 | 2 | 0 |
| Ref 8 compound 9 | 2.27 | 1.15 | 2 | –2 | 3 | –1 | 320.47 | –18.01 | 53 | –27.9 | 1 | –1 |
| Ref 8 compound 7 | 4.3 | 3.18 | 1 | –3 | 7 | 3 | 532.69 | 194.21 | 115.3 | 34.4 | 7 | 5 |
| Ref 8 compound 6 | 2.22 | 1.1 | 2 | –2 | 3 | –1 | 320.47 | –18.01 | 53 | –27.9 | 1 | –1 |
| Ref 8 compound 5 | 4.27 | 3.15 | 2 | –2 | 5 | 1 | 476.67 | 138.19 | 92.2 | 11.3 | 4 | 2 |
| Ref 8 compound 3 | 3.52 | 2.4 | 2 | –2 | 2 | –2 | 306.48 | –32 | 40.5 | –40.4 | 1 | –1 |
| Ref 8 compound 6 | 3.12 | 2 | 2 | –2 | 2 | –2 | 292.46 | –46.02 | 40.5 | –40.4 | 1 | –1 |
| Ref 9 compound 23 | 5.81 | 4.69 | 0 | –4 | 4 | 0 | 418.61 | 80.13 | 36.9 | –44 | 0 | –2 |
| Ref 9 compound 19 | 2.88 | 1.76 | 2 | –2 | 4 | 0 | 350.49 | 12.01 | 66.8 | –14.1 | 2 | 0 |
| Ref 9 compound 17 | 3.78 | 2.66 | 1 | –3 | 4 | 0 | 376.53 | 38.05 | 55.8 | –25.1 | 1 | –1 |
| Ref 9 compound 16 | 5.4 | 4.28 | 1 | –3 | 6 | 2 | 532.73 | 194.25 | 90.4 | 9.5 | 4 | 2 |
| Ref 9 compound 11 | 1.97 | 0.85 | 2 | –2 | 5 | 1 | 364.48 | 26 | 83.8 | 2.9 | 3 | 1 |
| Ref 9 compound 6 | 2.25 | 1.13 | 2 | –2 | 3 | –1 | 306.44 | –32.04 | 57.5 | –23.4 | 1 | –1 |
| Ref 9 compound 5 | 1.25 | 0.13 | 3 | –1 | 5 | 1 | 350.45 | 11.97 | 94.8 | 13.9 | 2 | 0 |
| Ref 9 compound 4 | 1.57 | 0.45 | 2 | –2 | 5 | 1 | 348.43 | 9.95 | 91.7 | 10.8 | 2 | 0 |
| Ref 9 compound 2 | 4.98 | 3.86 | 2 | –2 | 8 | 4 | 646.85 | 308.37 | 144 | 63.1 | 8 | 6 |
| Ref 10 compound 24 | 2 | 0.88 | 3 | –1 | 3 | –1 | 320.47 | –18.01 | 60.7 | –20.2 | 2 | 0 |
| Ref 10 compound 21 | 2.34 | 1.22 | 3 | –1 | 3 | –1 | 322.48 | –16 | 60.7 | –20.2 | 1 | –1 |
| Ref 10 compound 20 | 2.29 | 1.17 | 3 | –1 | 3 | –1 | 322.48 | –16 | 60.7 | –20.2 | 2 | 0 |
| Ref 10 compound 18 | 2.02 | 0.9 | 2 | –2 | 5 | 1 | 362.46 | 23.98 | 91.7 | 10.8 | 3 | 1 |
| Ref 10 compound 14 | 1.42 | 0.3 | 3 | –1 | 4 | 0 | 336.47 | –2.01 | 77.8 | –3.1 | 2 | 0 |
| Ref 10 compound 13 | 2.25 | 1.13 | 2 | –2 | 3 | –1 | 306.44 | –32.04 | 57.5 | –23.4 | 1 | –1 |
| Ref 10 compound 12 | 1.82 | 0.7 | 3 | –1 | 5 | 1 | 394.54 | 56.06 | 87 | 6.1 | 5 | 3 |
| Ref 10 compound 11 | 2.42 | 1.3 | 2 | –2 | 8 | 4 | 514.69 | 176.21 | 95.8 | 14.9 | 14 | 12 |
| Ref 10 compound 10 | 2.42 | 1.3 | 2 | –2 | 8 | 4 | 514.69 | 176.21 | 95.8 | 14.9 | 14 | 12 |
| Ref 10 compound 7 | 3.55 | 2.43 | 3 | –1 | 4 | 0 | 428.6 | 90.12 | 69.9 | –11 | 5 | 3 |
| Ref 10 compound 6 | 4 | 2.88 | 3 | –1 | 4 | 0 | 452.74 | 114.26 | 69.9 | –11 | 4 | 2 |
| Ref 10 compound 5 | 2.63 | 1.51 | 3 | –1 | 5 | 1 | 406.56 | 68.08 | 87 | 6.1 | 5 | 3 |
| Ref 10 compound 3 | 3.02 | 1.9 | 2 | –2 | 6 | 2 | 422.55 | 84.07 | 93.1 | 12.2 | 6 | 4 |
| Mean differences | – | 2.14 | – | –2.2 | – | –0.2 | – | 23.6 | – | –18.6 | – | 0.18 |
| Mean | 3.27 | – | 1.8 | – | 3.81 | – | 364.6 | – | 62.9 | – | 2.28 | – |

**Table S3.** Main crystal data and refinement results for aphidicolin **1**

| | |
|---|---|
| Empirical formula | $C_{20}H_{34}O_4$ |
| Formula weight | 338.47 |
| Temperature / K | 293(2) |
| Wavelength / Å | 0.71073 |
| Crystal system | Orthorhombic |
| Space group | $P2_12_12_1$ |
| | |
| Unit cell dimensions | |
| a / Å | 11.7093(1) |
| b / Å | 11.7636(2) |
| c / Å | 25.5233(5) |
| | |
| Volume / Å$^3$ | 3515.67(10) |
| Z, calculated density / Mg m$^{-3}$ | 8, 1.279 |
| Absorption coefficient / mm$^{-1}$ | 0.087 |
| F(000) | 1488 |
| Crystal size / mm | 0.50 × 0.3 × 0.1 |
| Crystal color/shape | Colorless/rough |
| θ-range for data collection / degree | 2.93 to 27.40 |
| Limiting indices | $-15 \leq h \leq 15$, $-14 \leq k \leq 15$, $-32 \leq l \leq 33$ |
| Reflections collected/unique | 7833/7833 [R(int) = 0.0000] |
| Completeness / % | 98.5 (to θ = 27.40°) |
| Absorption correction | None |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Weights, w | $[\sigma^2(F_o^2) + (0.0518P)^2 + 6.2056P]^{-1}$ $P = (F_o^2 + 2F_c^2) / 3$ |
| Data/restraints/parameters | 7833/0/445 |
| Goodness-of-fit on $F^2$ | 1.086 |
| Final R indices [$I > 2\sigma(I)$] | $R_1 = 0.0728$, $wR_2 = 0.1695$ |
| R indices (all data) | $R_1 = 0.0922$, $wR_2 = 0.1809$ |
| Largest diff. peak and hole | 0.292 and –0.287 e A$^{-3}$ |

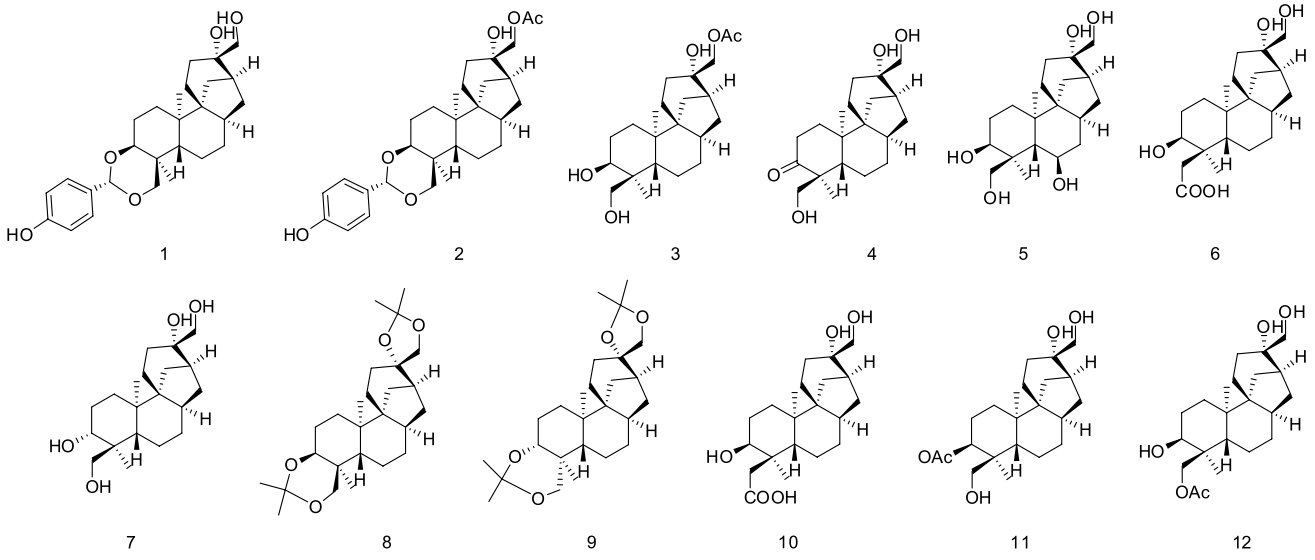


**Figure S1.** Structure of aphidicolin derivatives via biotransformation reactions.

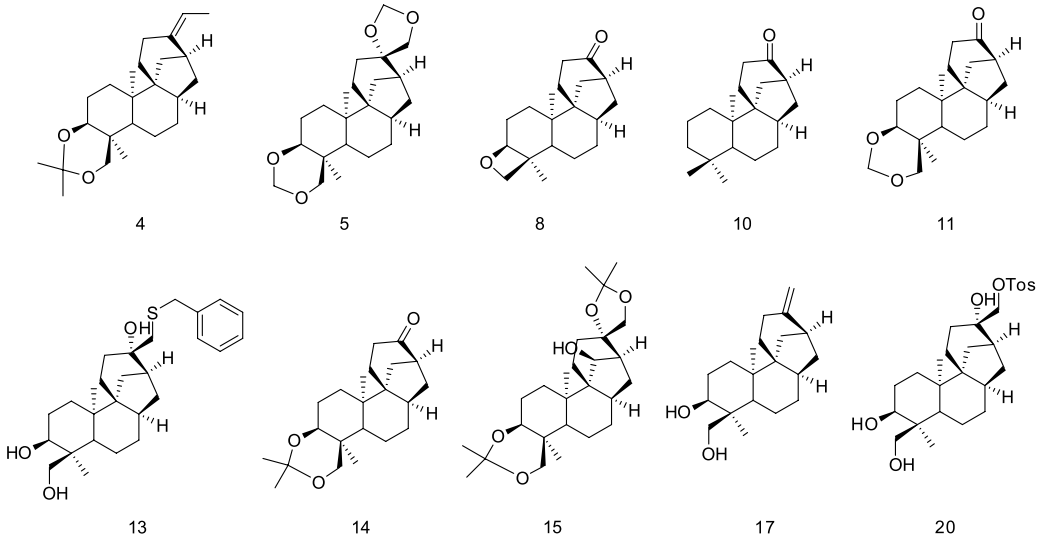


**Figure S2.** Structures of semisynthetic modification of **1** in the literature (reference 6).

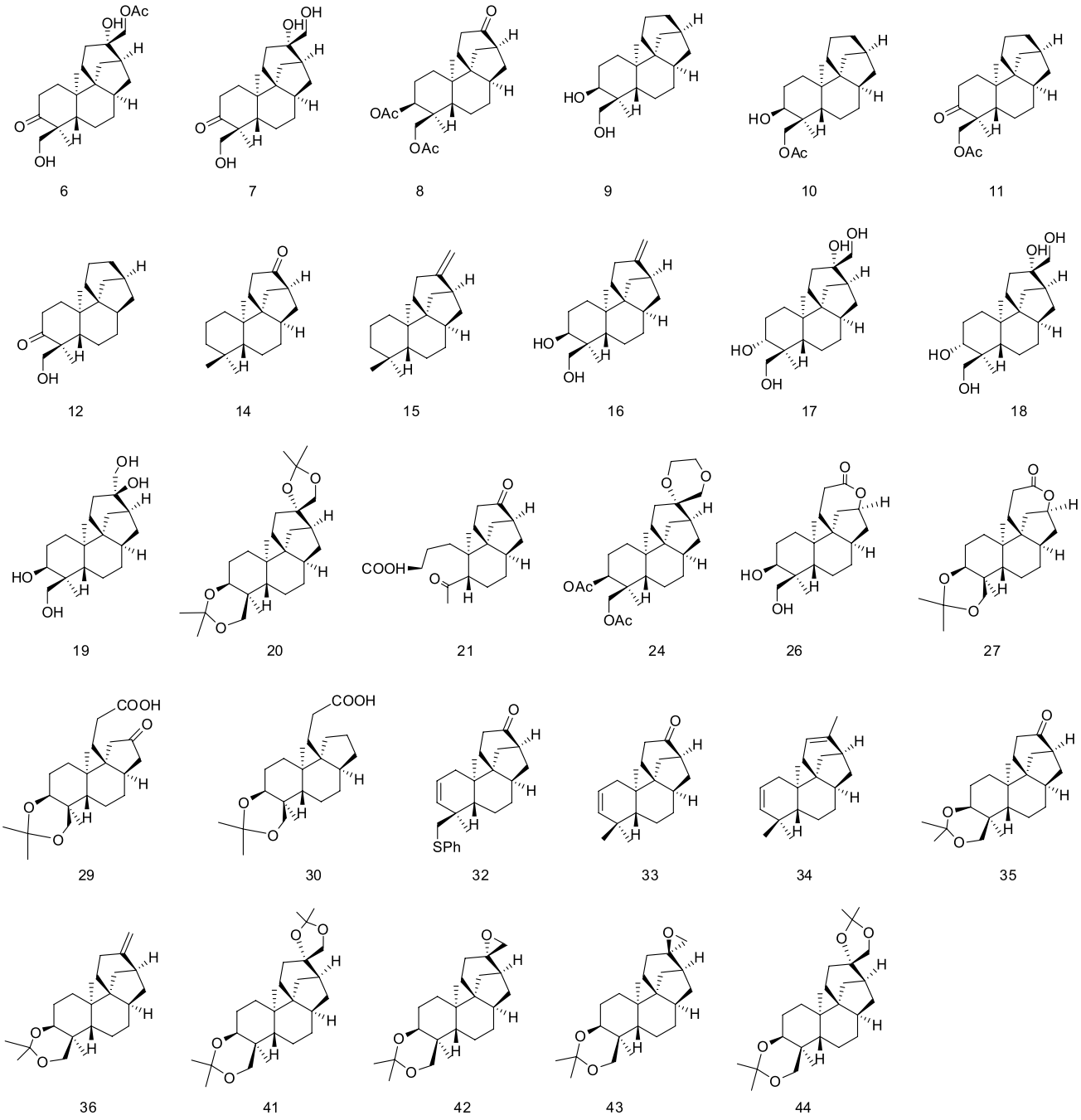


**Figure S3.** Structures of semisynthetic modification of **1** in the literature (reference 7).

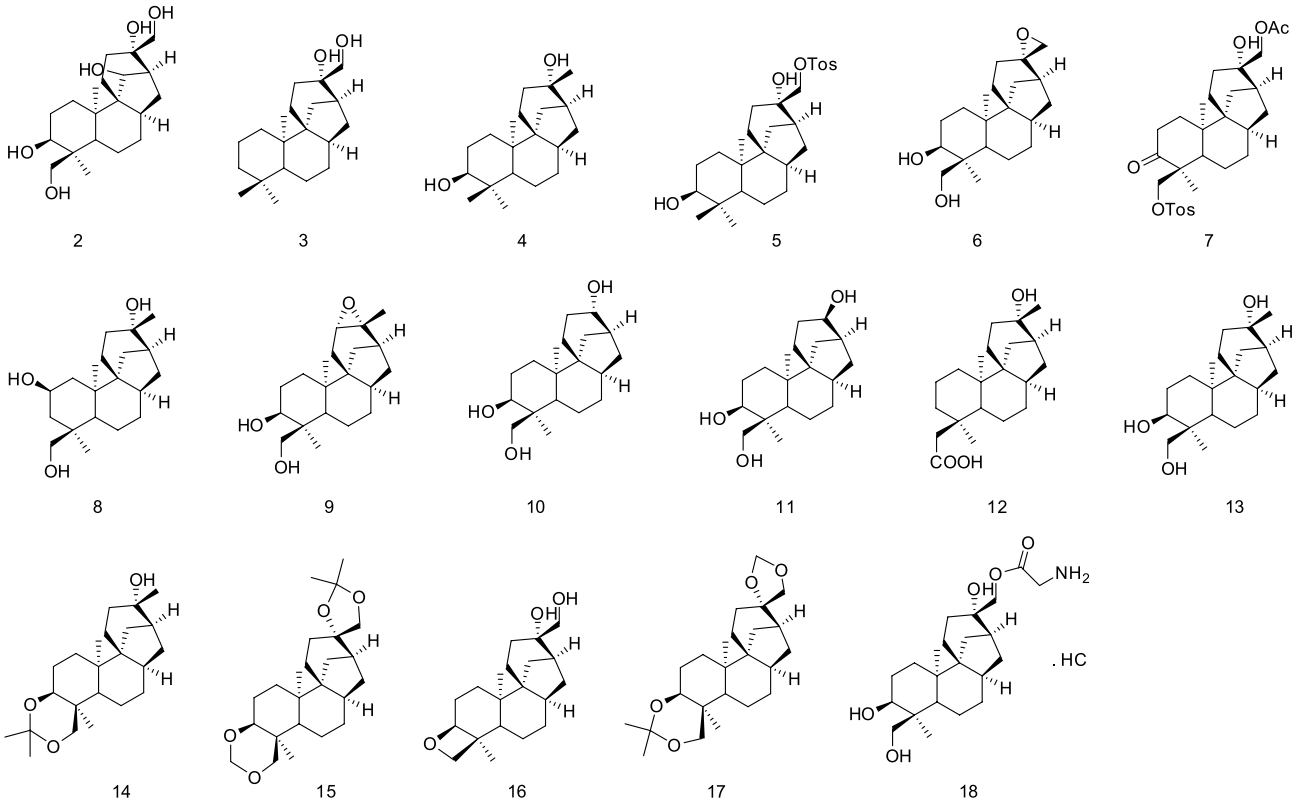


**Figure S4.** Structures of semisynthetic modification of **1** in the literature (reference 8).

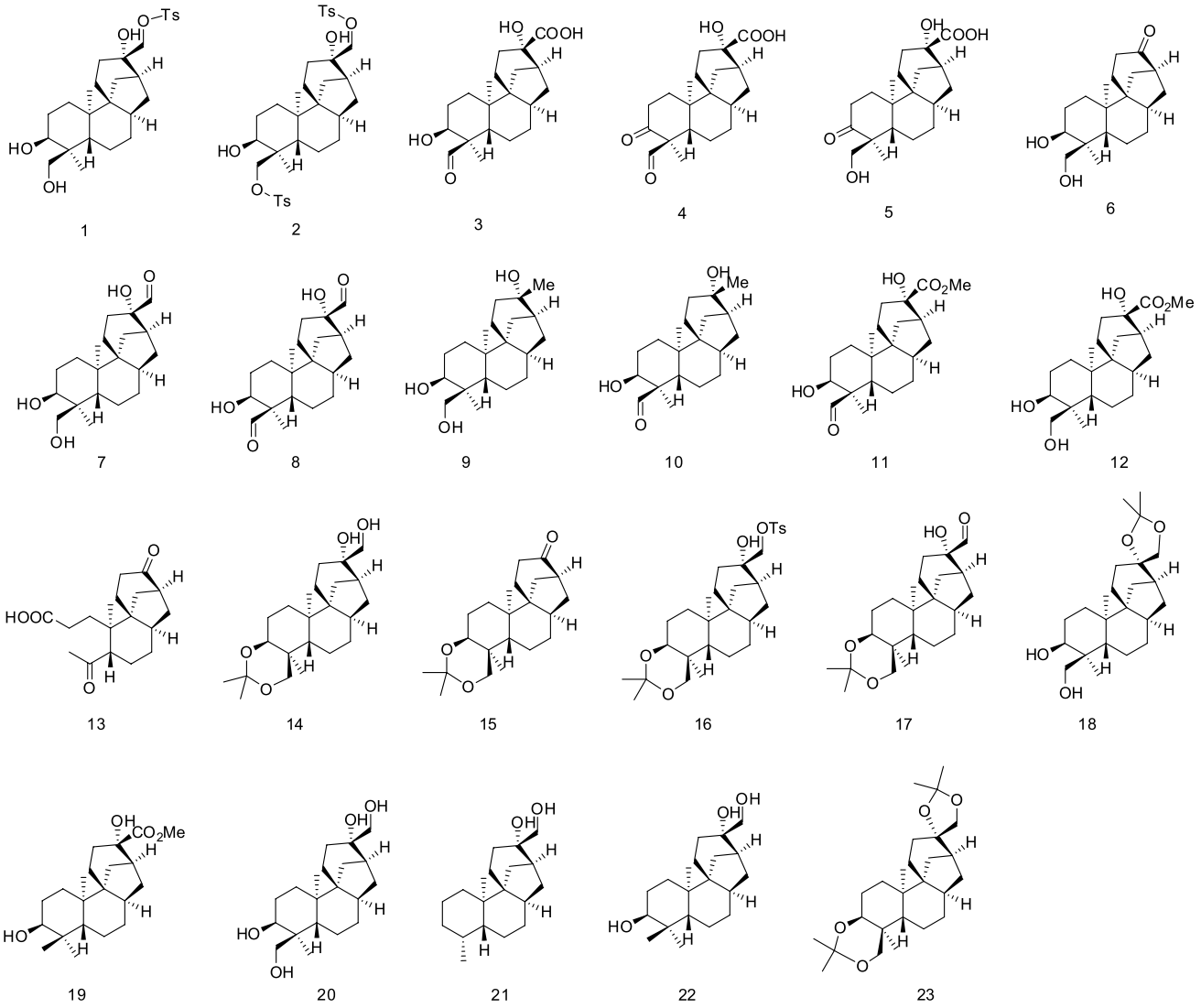


**Figure S5.** Structures of semisynthetic modification of **1** in the literature (reference 9).

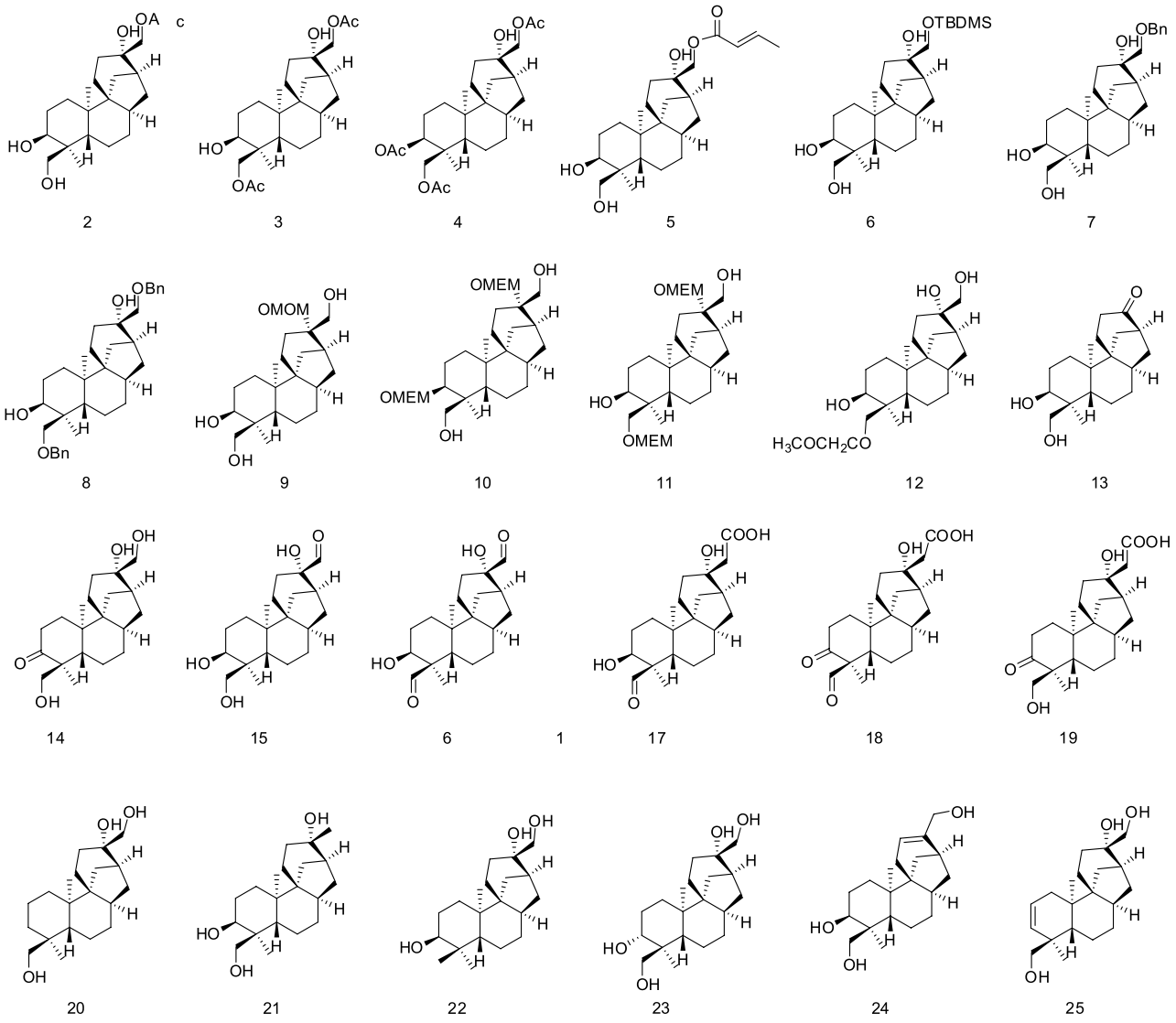


**Figure S6.** Structures of semisynthetic modification of **1** in the literature (reference 10).

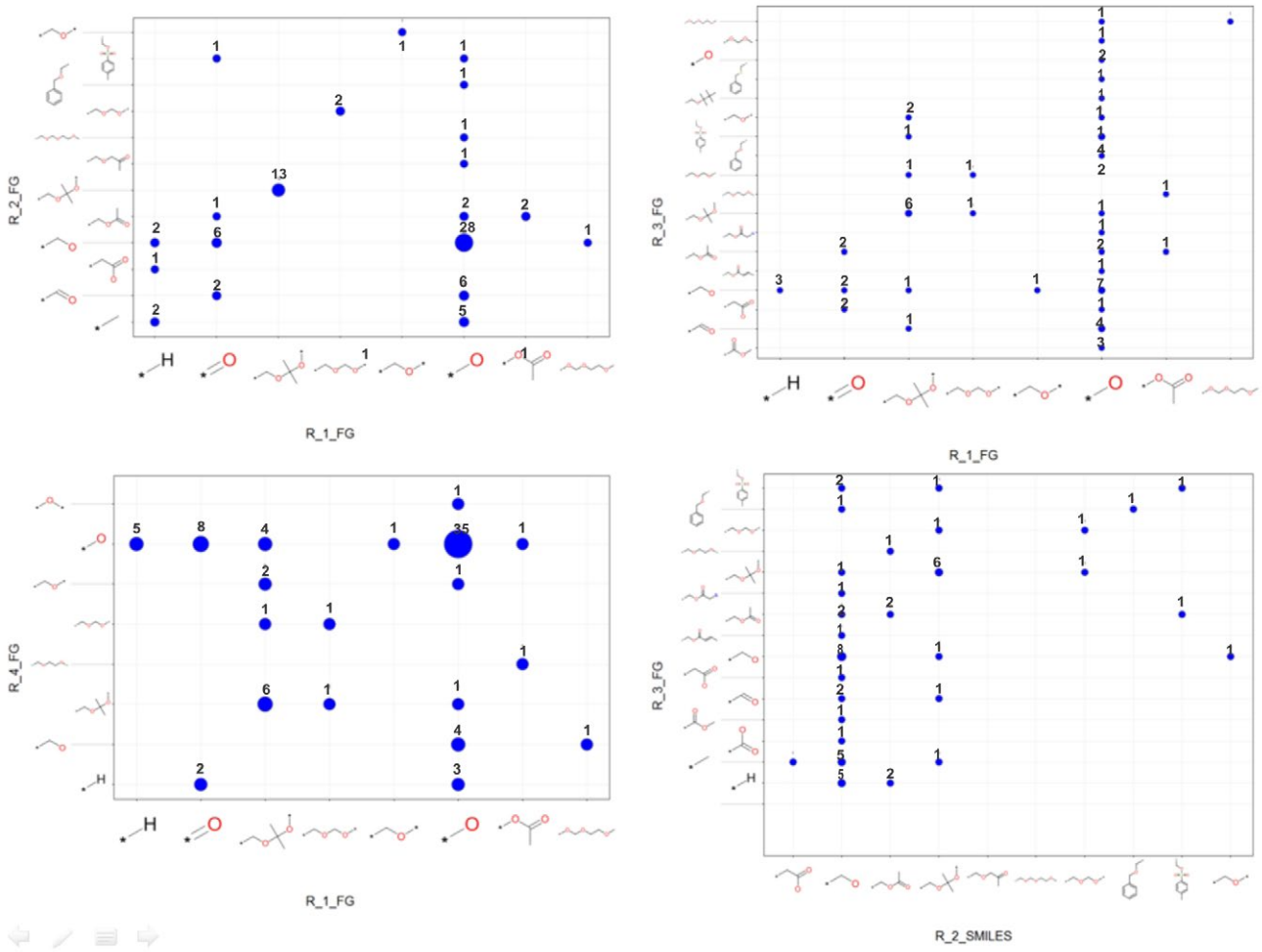


**Figure S7.** Correlation between sites of modification in semisynthetic compounds (each number over the blue dots in the graphs represents the number of examples of the correspondent modification).

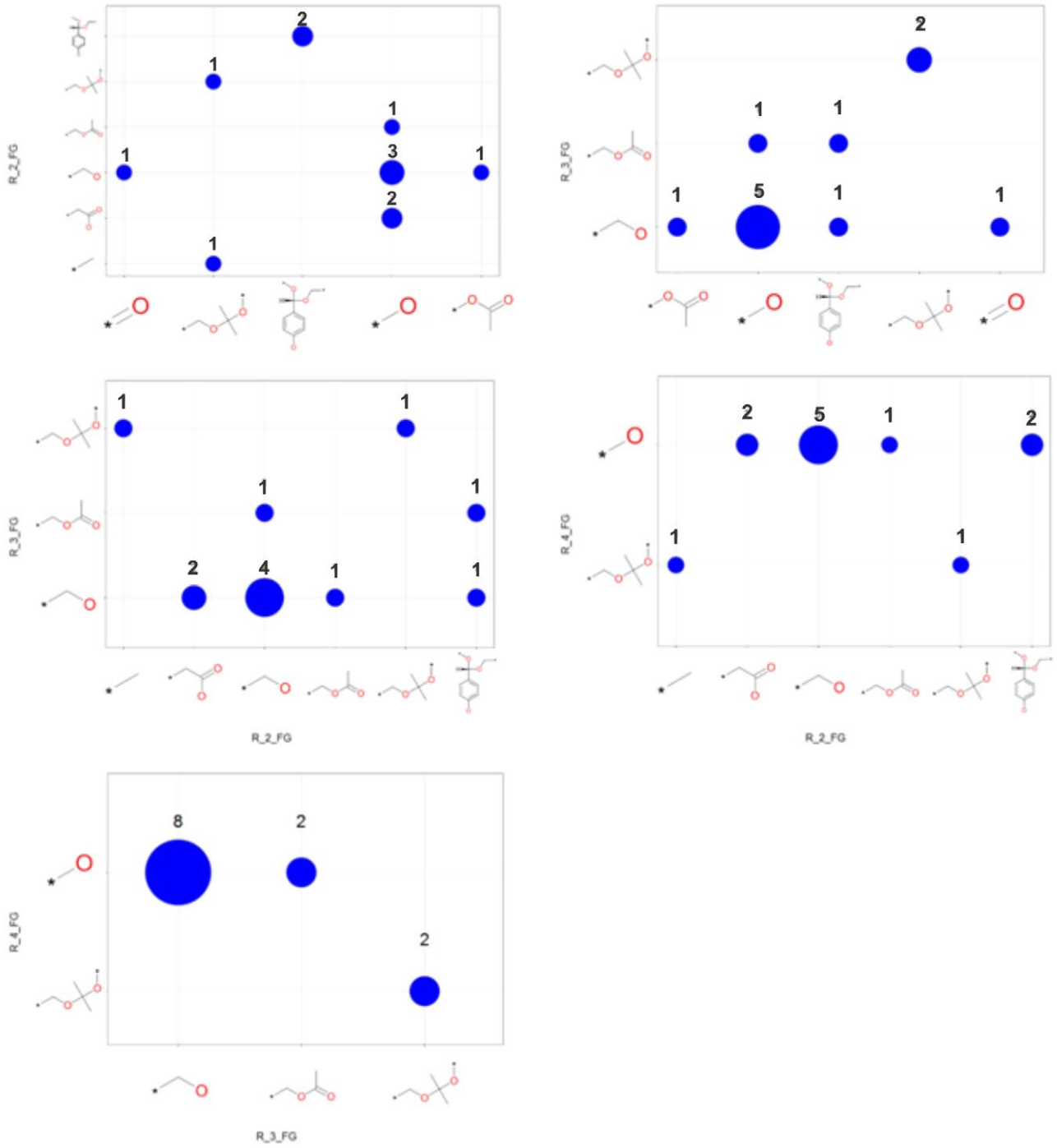


**Figure S8.** Correlation between site modifications in biotransformation compounds (each number over the blue dots in the graphs represents the number of examples of the correspondent modification).

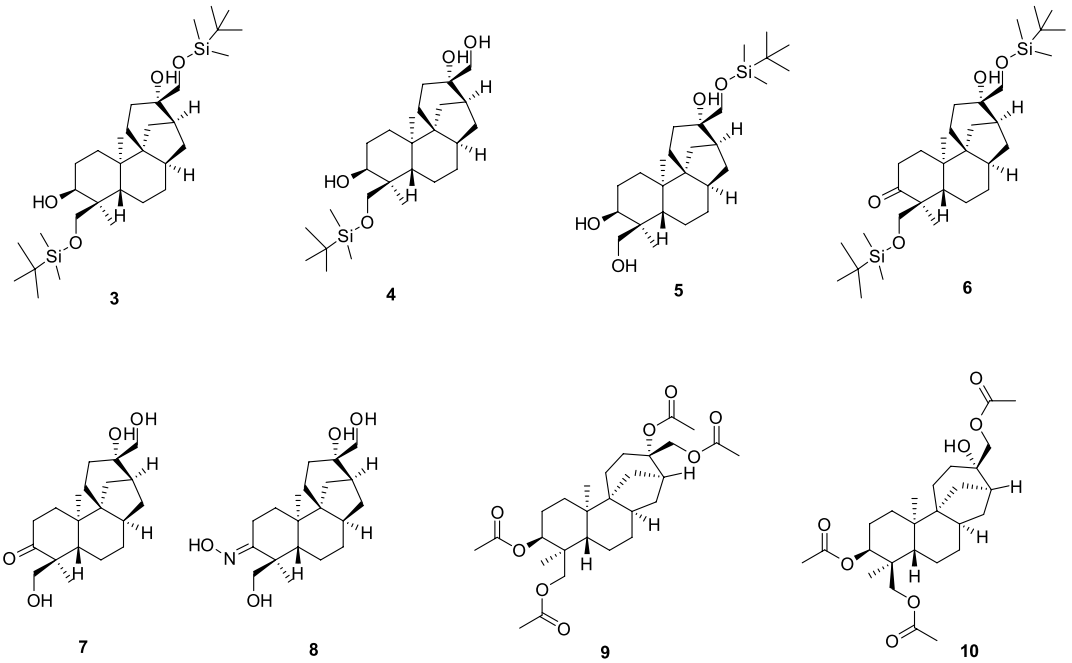


**Figure S9.** Structure of the semisynthetic compounds **3**-**10**.

## Spectroscopic data of semisynthetic compounds **3**-**10**

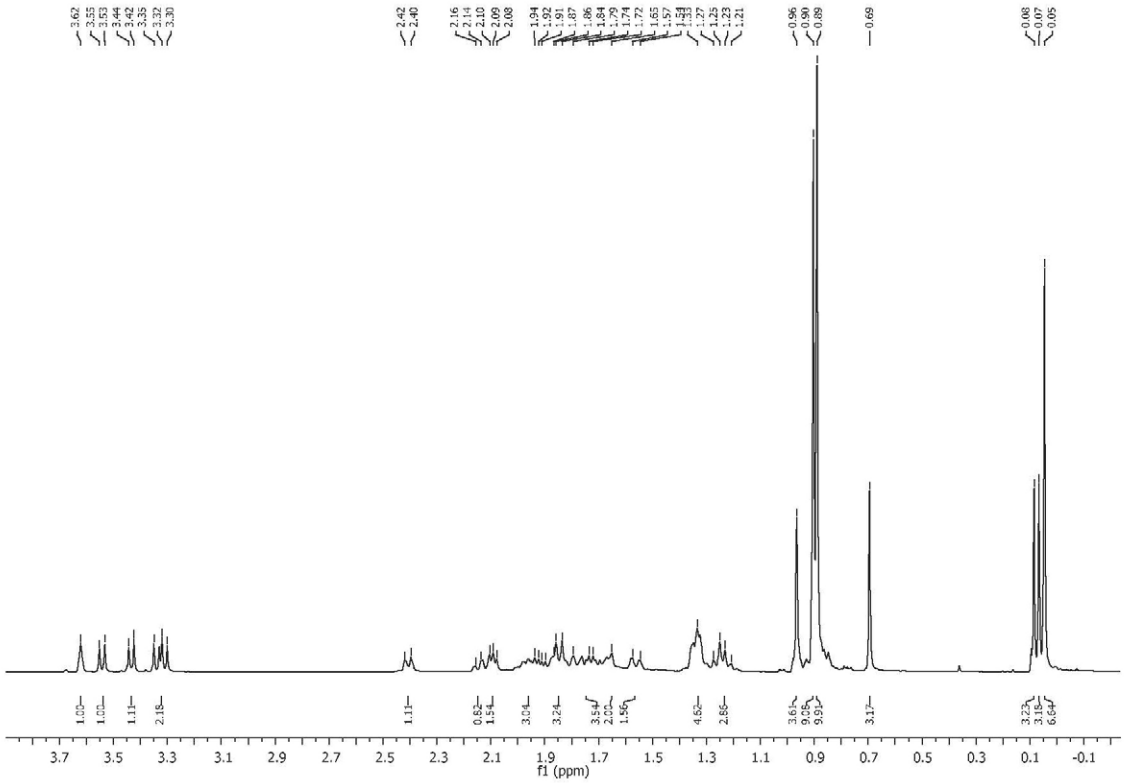


**Figure S10.** $^{1}$H NMR spectrum (500 MHz, $CDCl_3$) – compound **3**.

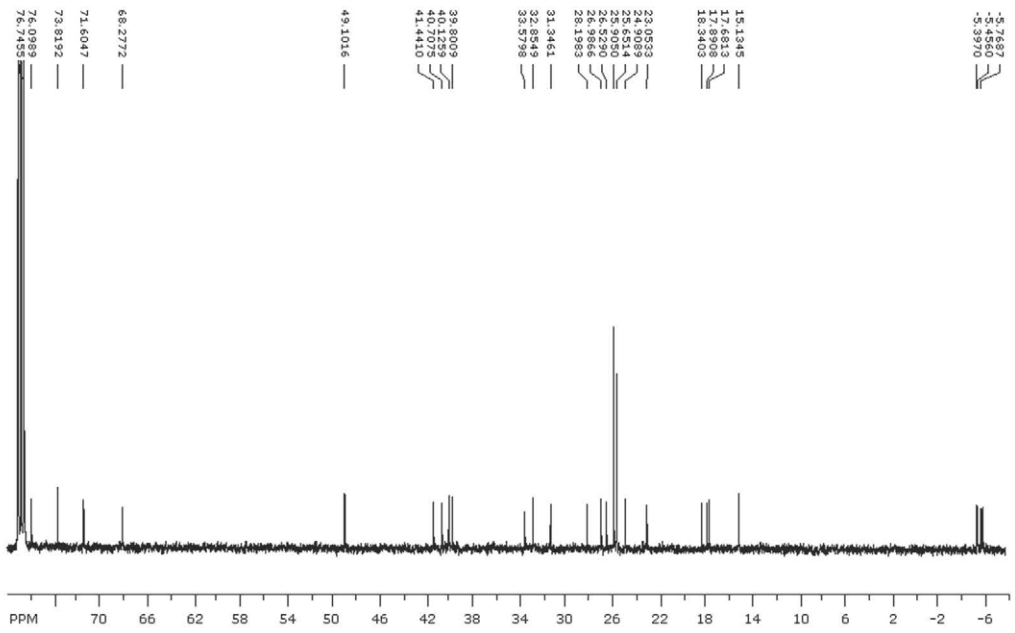


**Figure S11.** $^{13}C$ NMR spectrum (125 MHz, $CDCl_3$) – compound **3**.

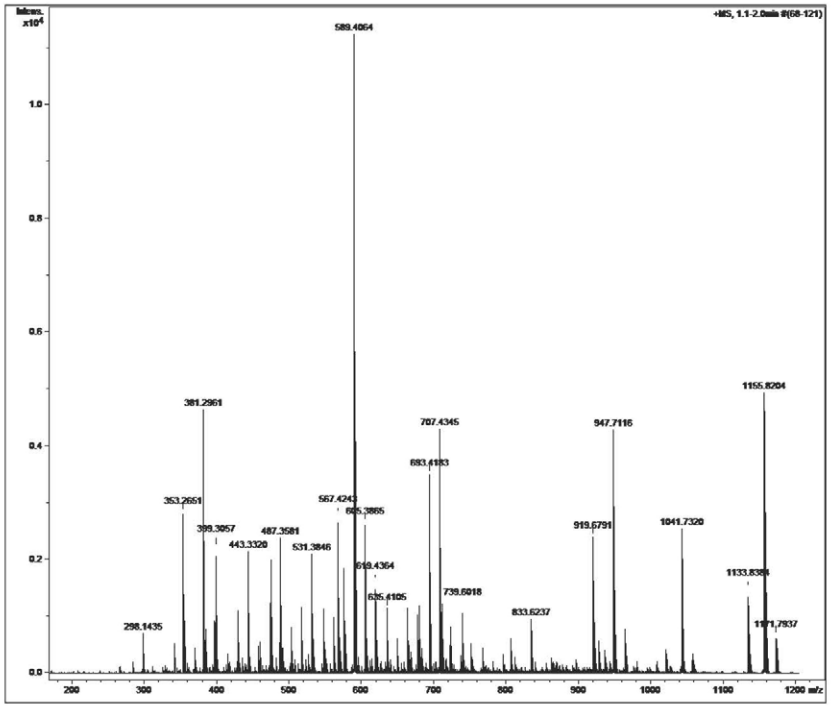


**Figure S12.** HRMS-ESI – compound **3**.

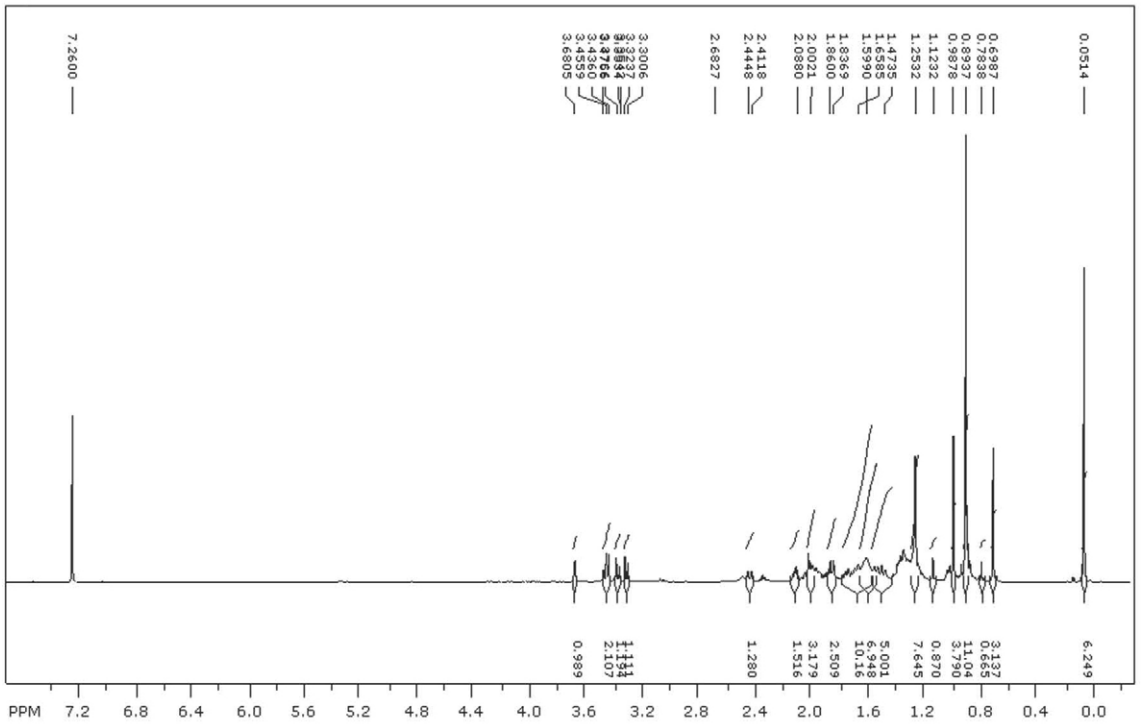


**Figure S13.** $^1$H NMR spectrum (500 MHz, $CDCl_3$) – compound **4**.

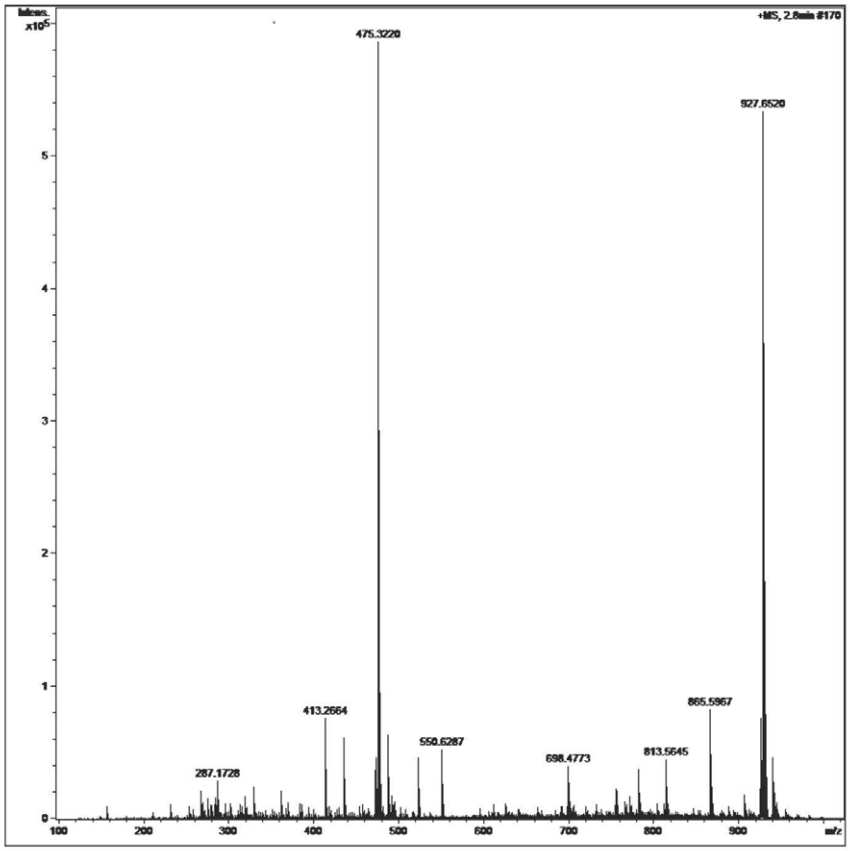


**Figure S14.** HRMS-ESI – compound **4**.

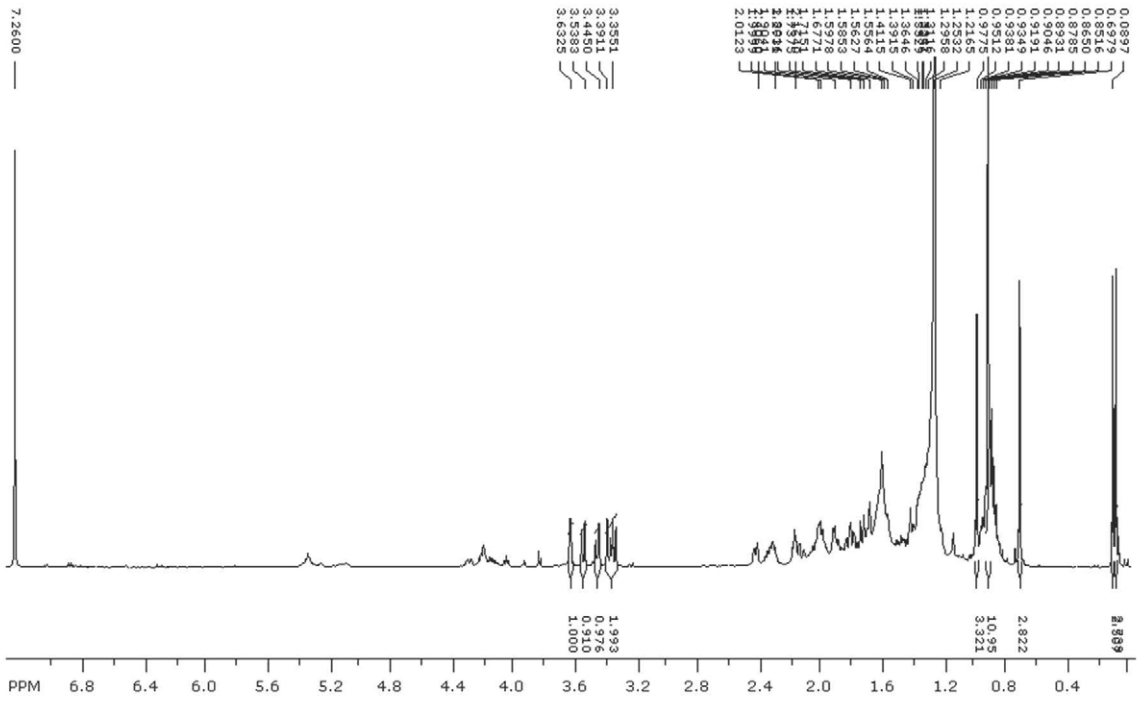


**Figure S15.** $^1$H NMR spectrum (500 MHz, $CDCl_3$) – compound **5**.

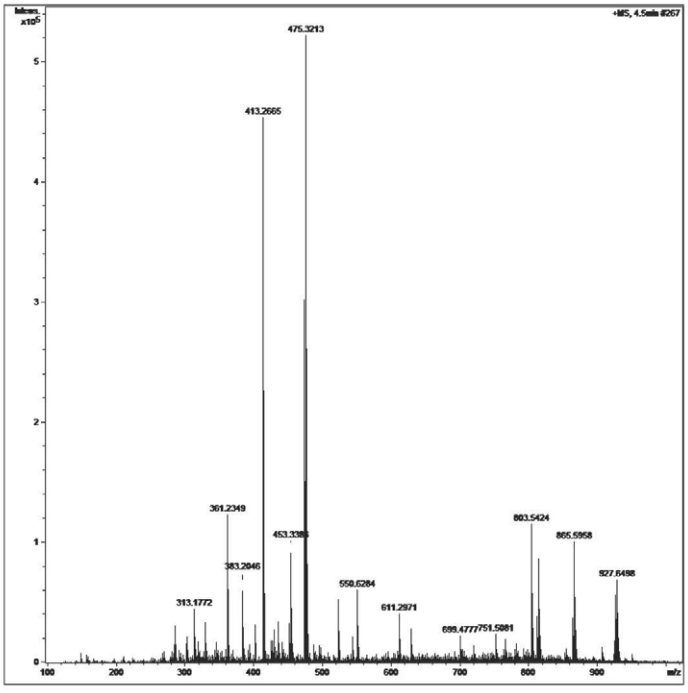


**Figure S16.** HRMS-ESI – compound **5**.

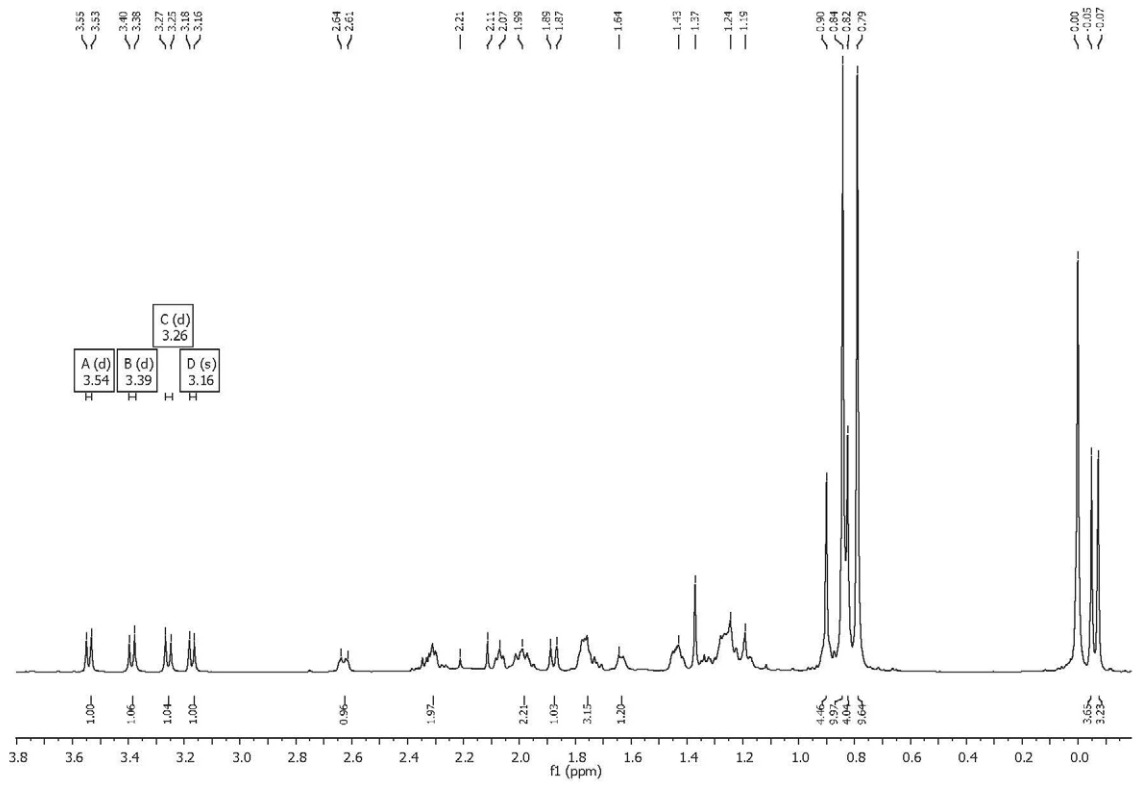


**Figure S17.** $^{1}$H NMR spectrum (500 MHz, $CDCl_3$) – compound **6**.

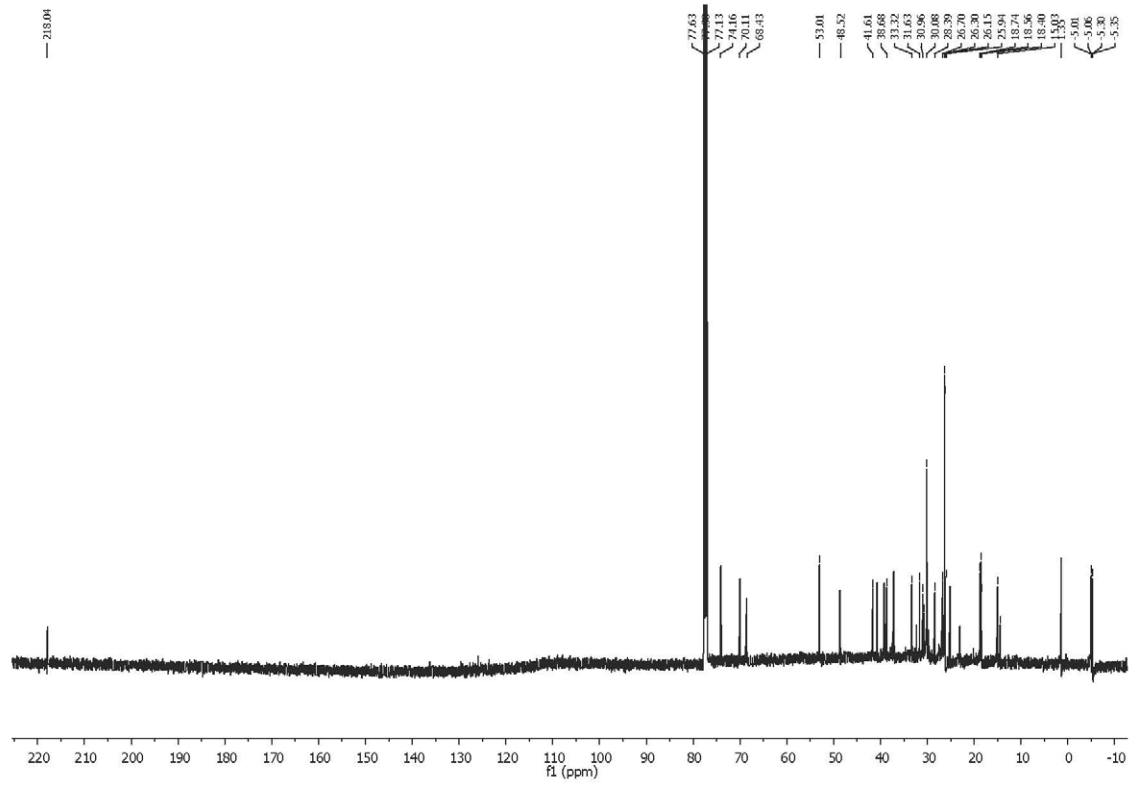


**Figure S18.** $^{13}$C NMR spectrum (125 MHz, $CDCl_3$) – compound **6**.

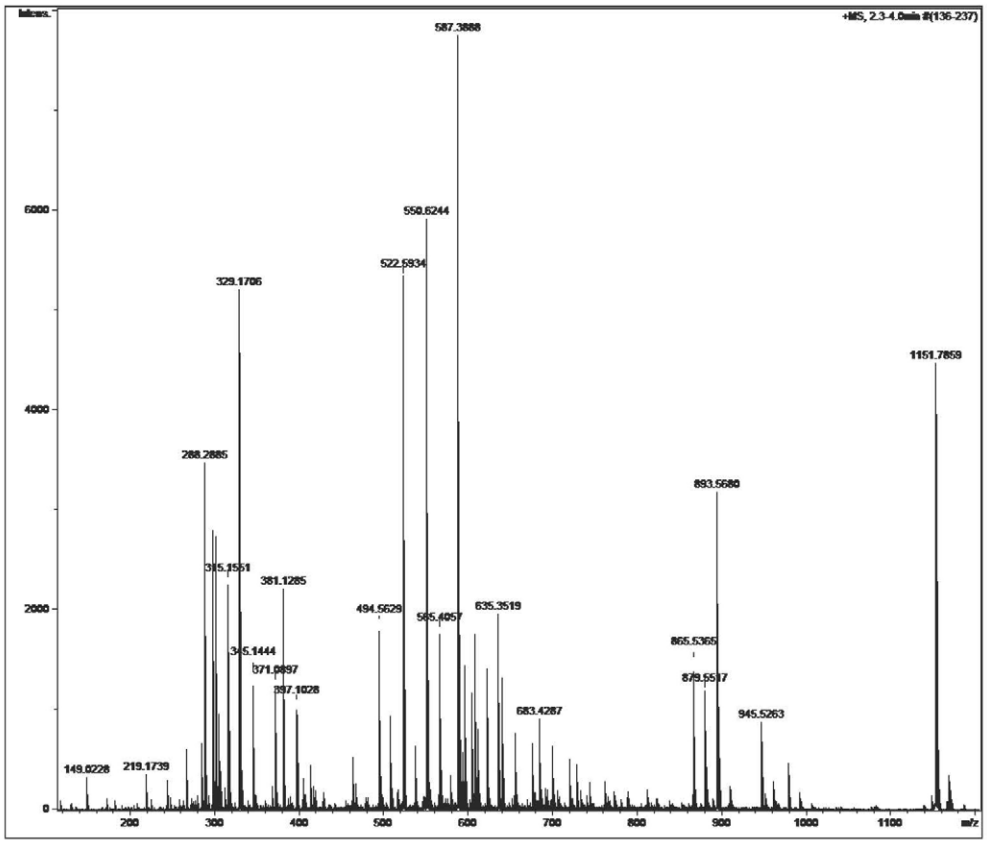


**Figure S19.** HRMS-ESI – compound **6**.

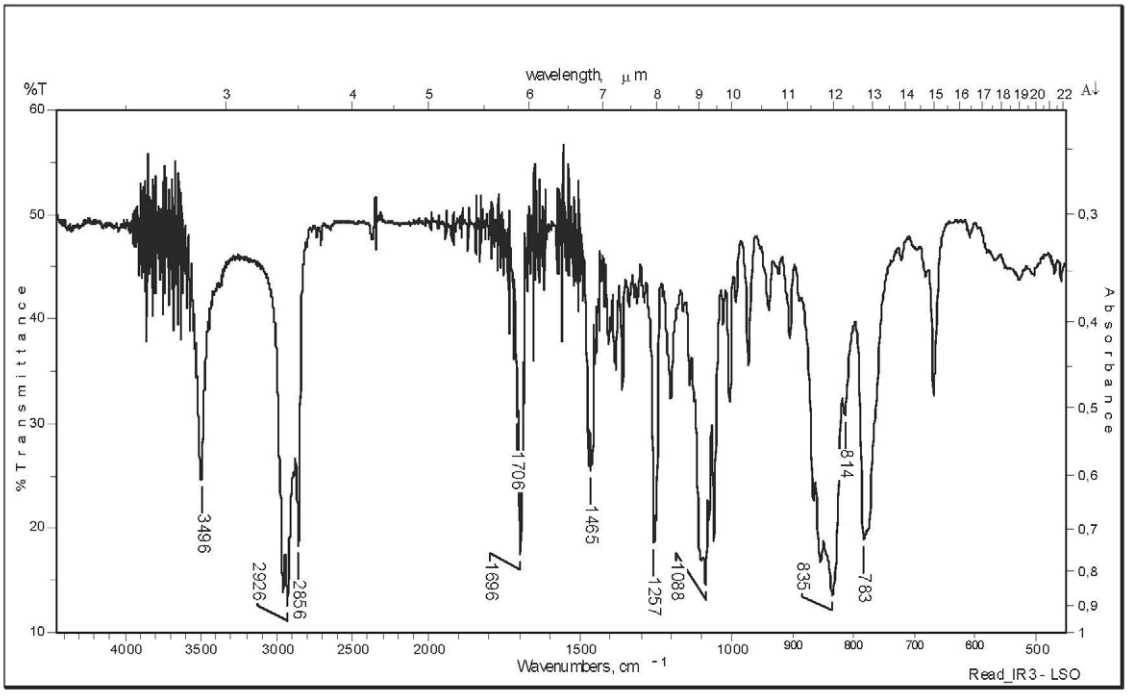


**Figure S20.** Infrared spectrum (KBr) – compound **6**.

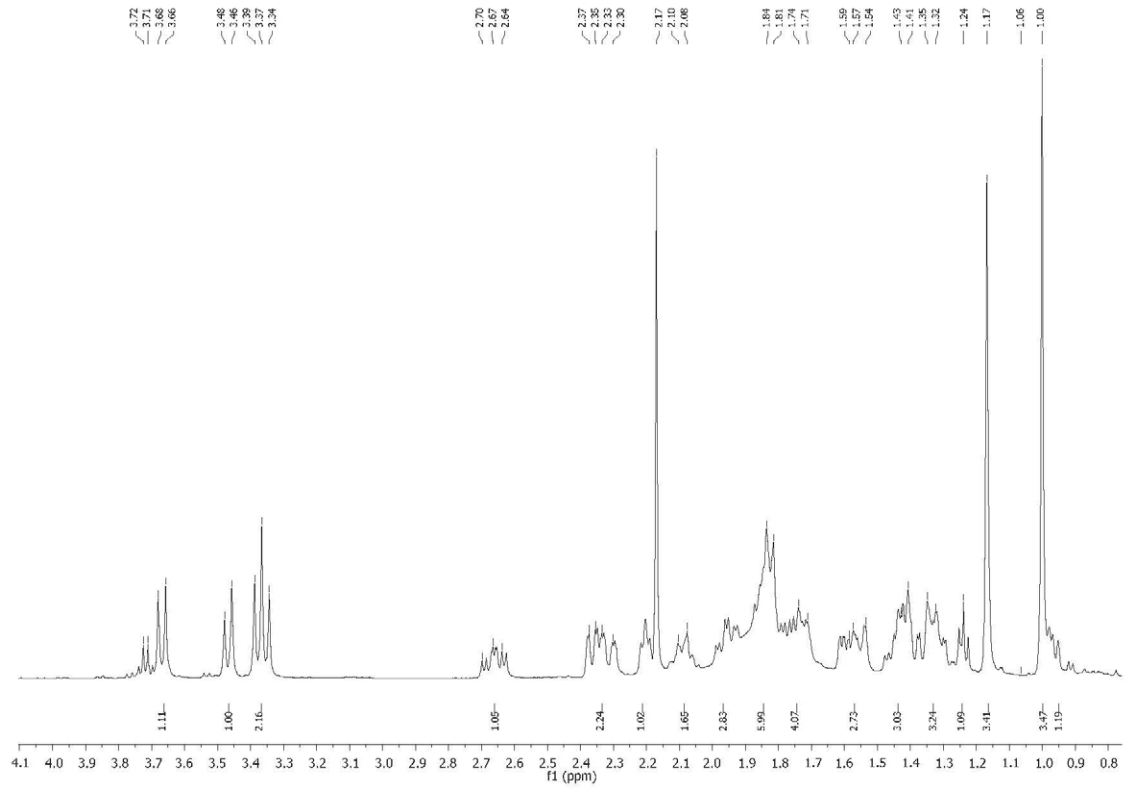


**Figure S21.** $^{1}$H NMR spectrum (500 MHz, $CD_3OD$) – compound **7**.

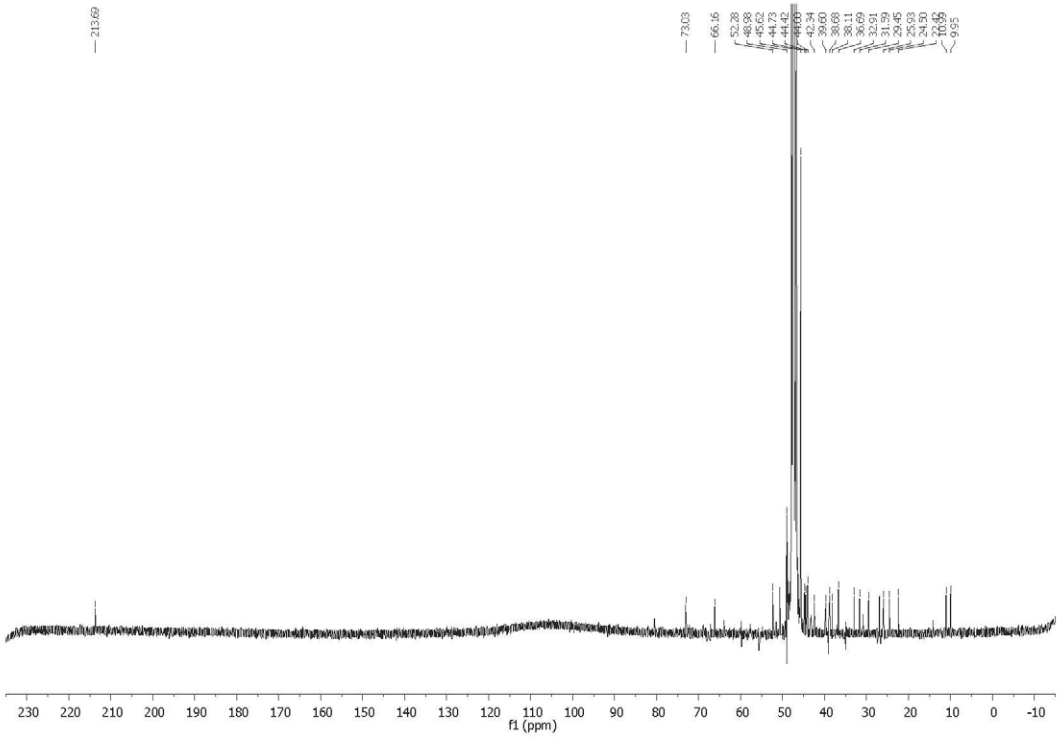


**Figure S22.** $^{13}$C NMR spectrum (125MHz, $CD_3OD$) – compound **7**.

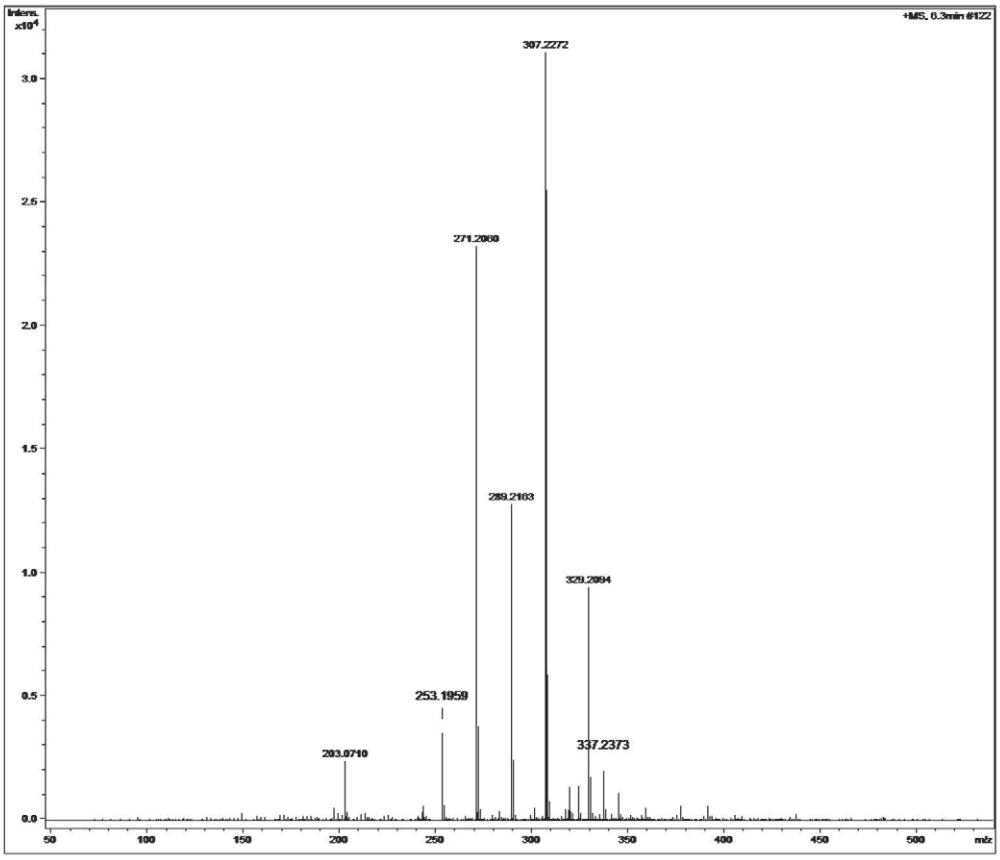


**Figure S23.** HRMS-ESI – compound **7**.

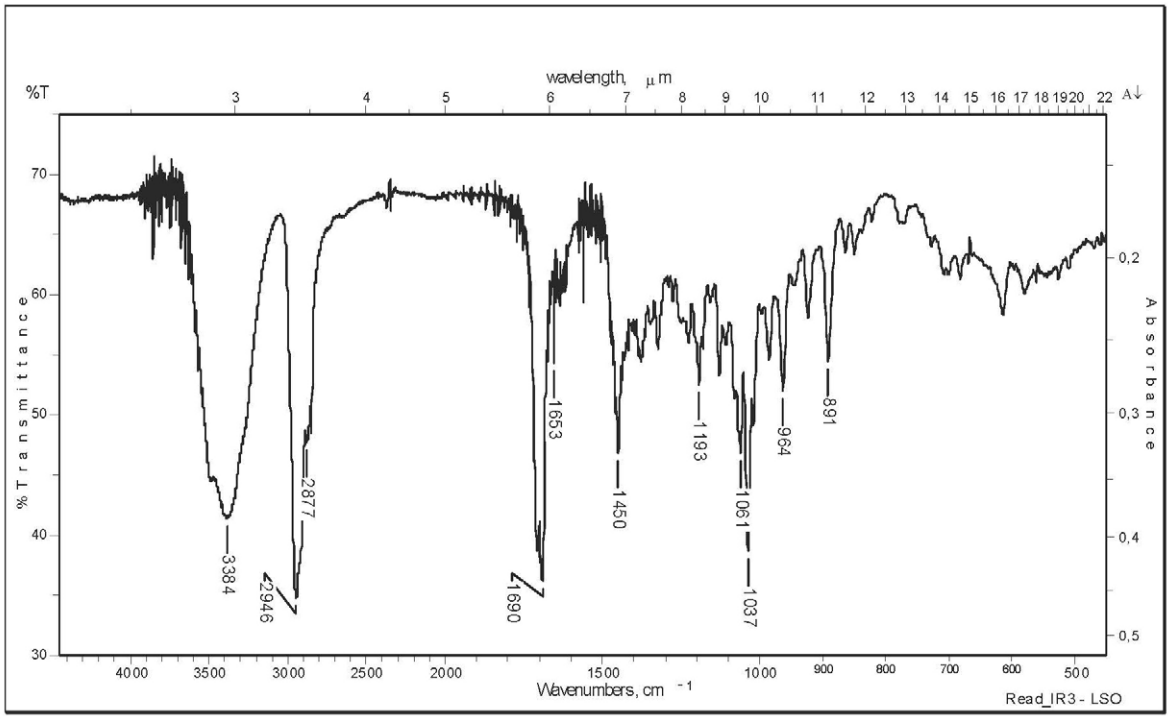


**Figure S24.** Infrared spectrum (KBr) – compound **7**.

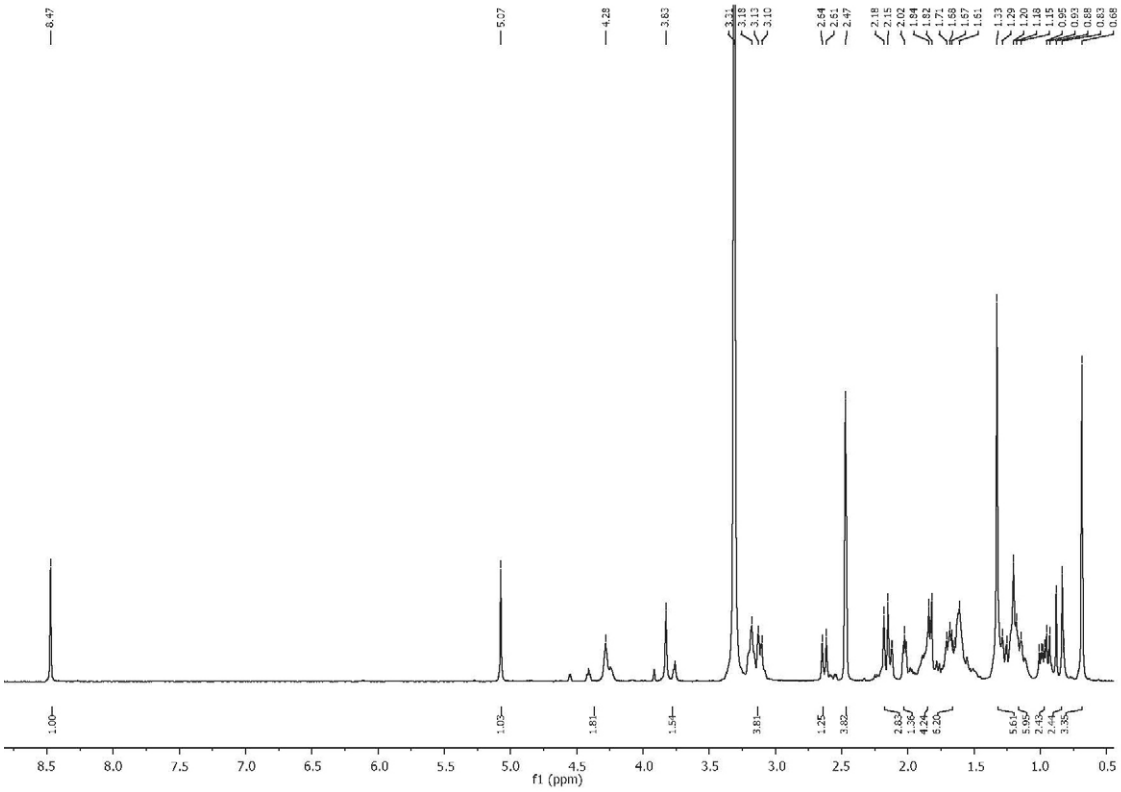


**Figure S25.** $^{1}$H NMR spectrum (500 MHz, $CD_3OD$) – compound **8**.

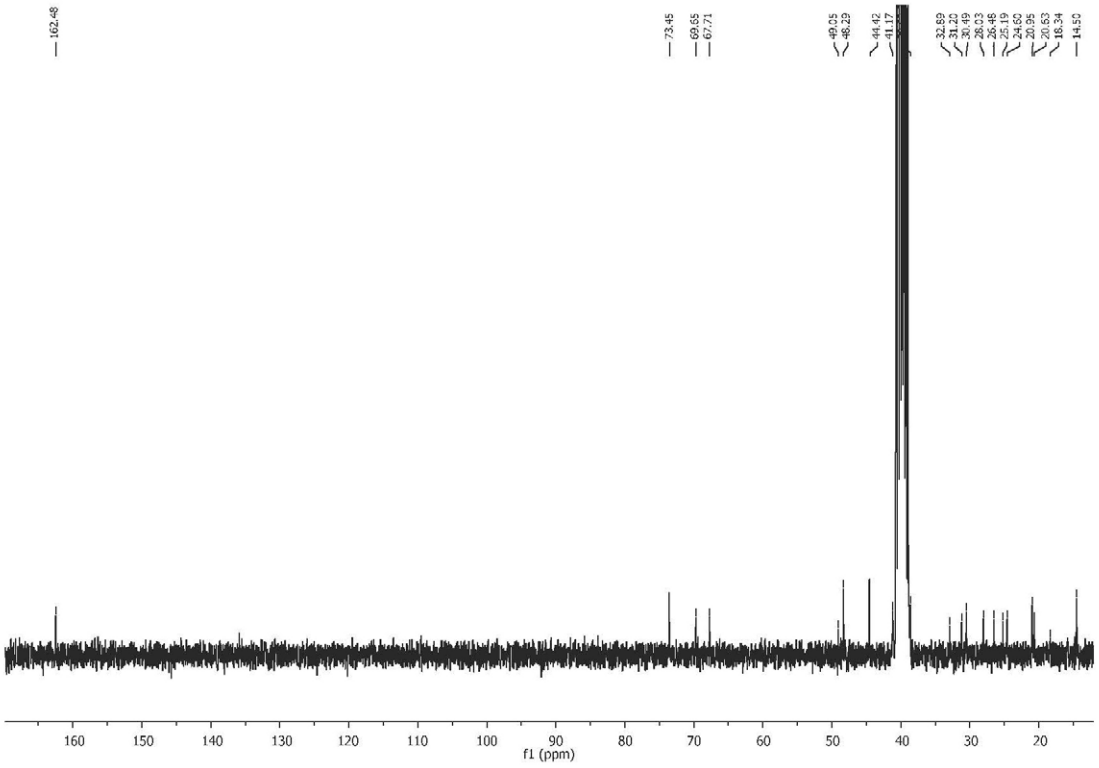


**Figure S26.** $^{13}$C NMR spectrum (125 MHz, $CD_3OD$) – compound **8**.

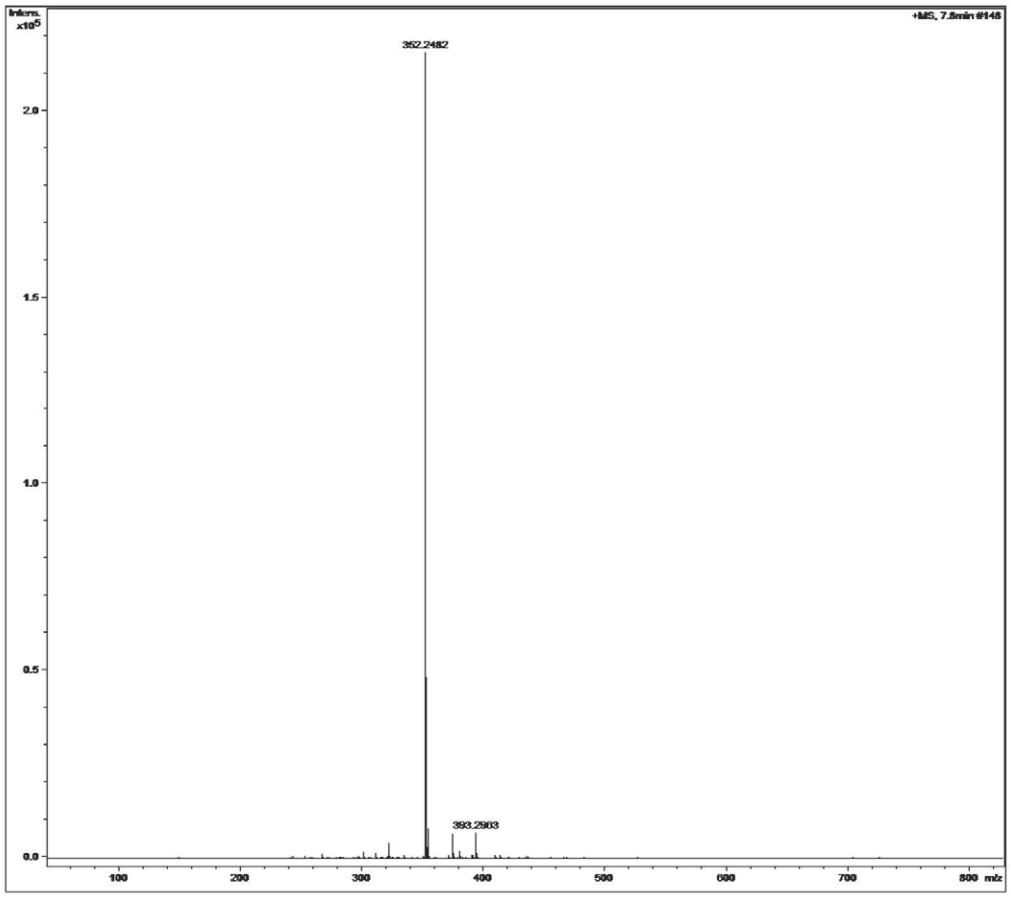


**Figure S27.** HRMS-ESI – compound **8**.

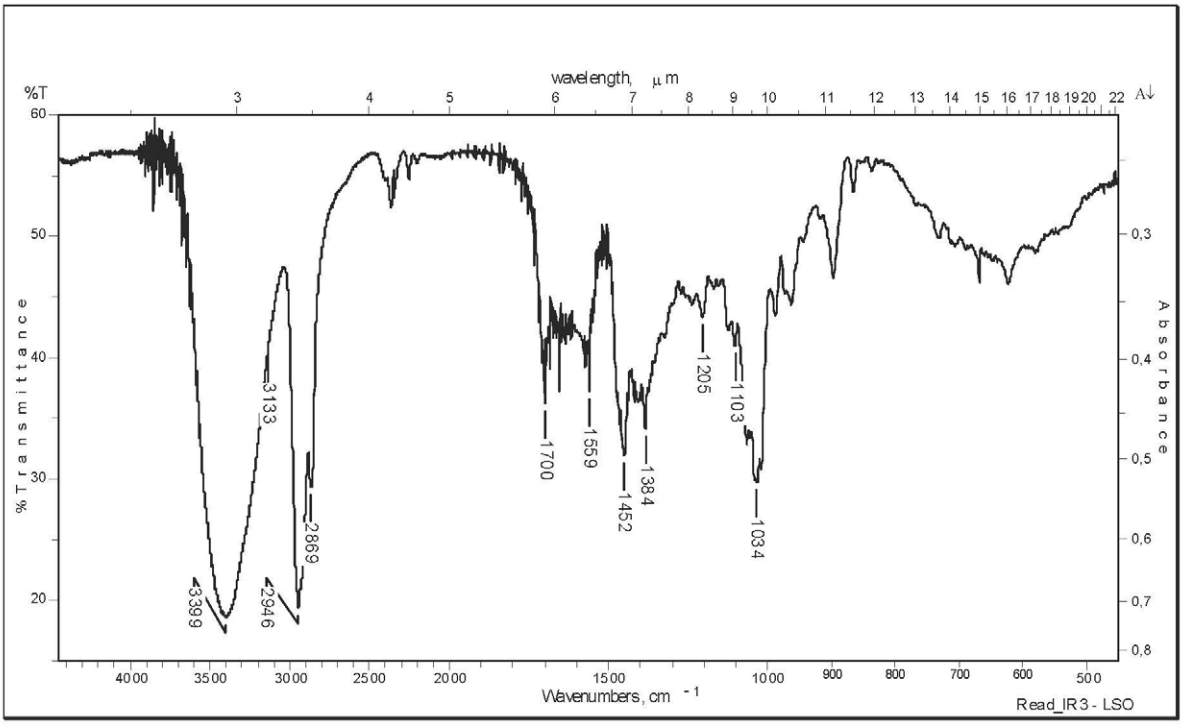


**Figure S28.** Infrared spectrum (KBr) – compound **8**.

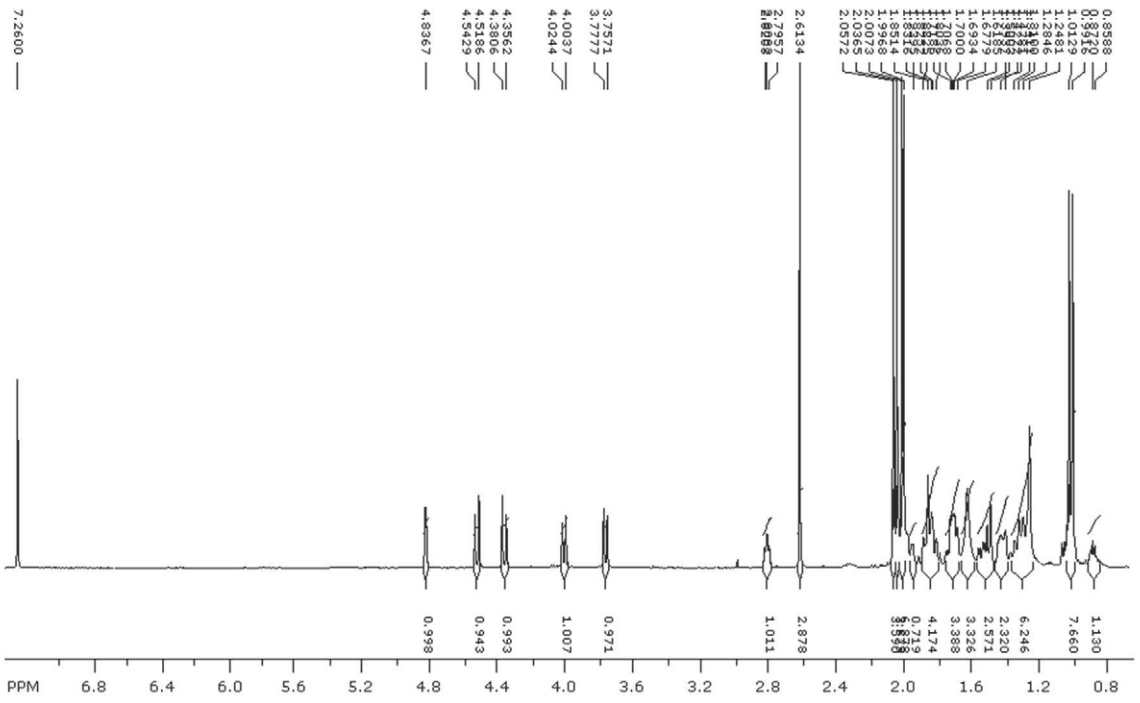


**Figure S29.** $^{1}$H NMR spectrum (500 MHz, $CDCl_3$) – compound **9**.

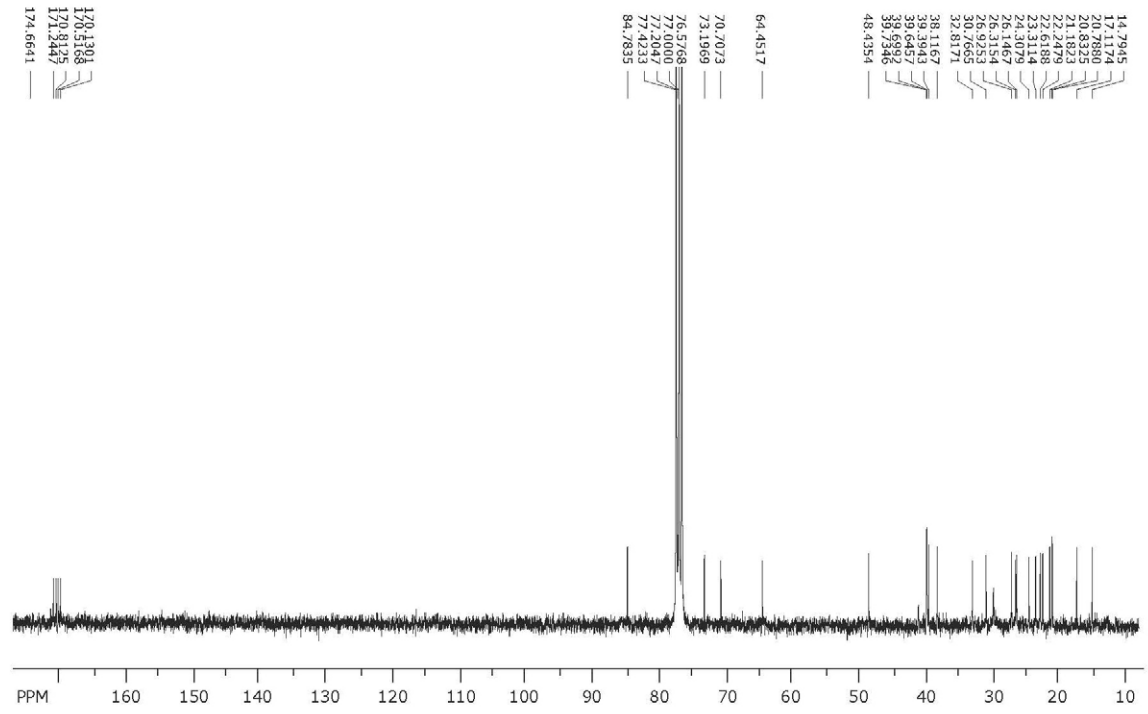


**Figure S30.** $^{13}$C NMR spectrum (125 MHz, $CDCl_3$) – compound **9**.

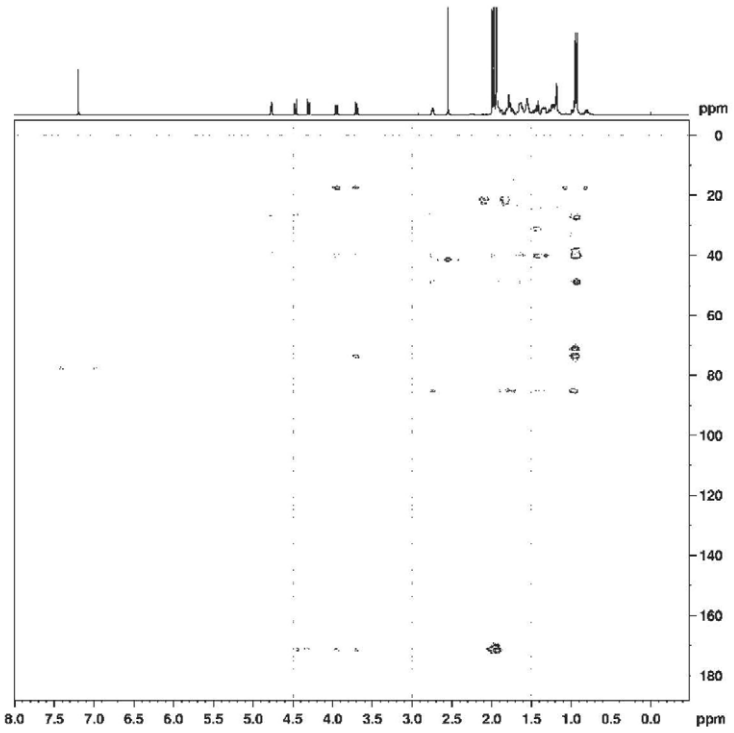


**Figure S31.** HMBC spectrum (500 MHz, $CD_3OD$) – compound **9**.

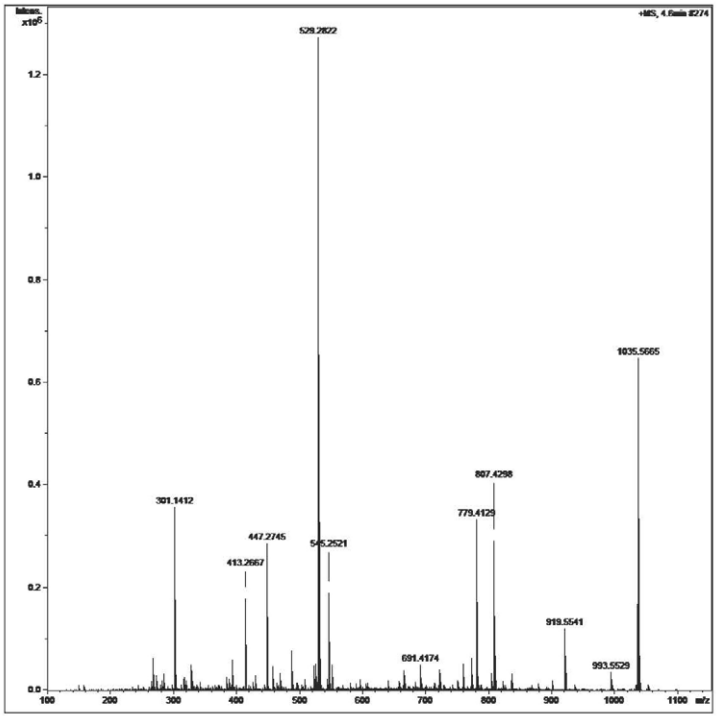


**Figure S32.** HRMS-ESI – compound **9**.

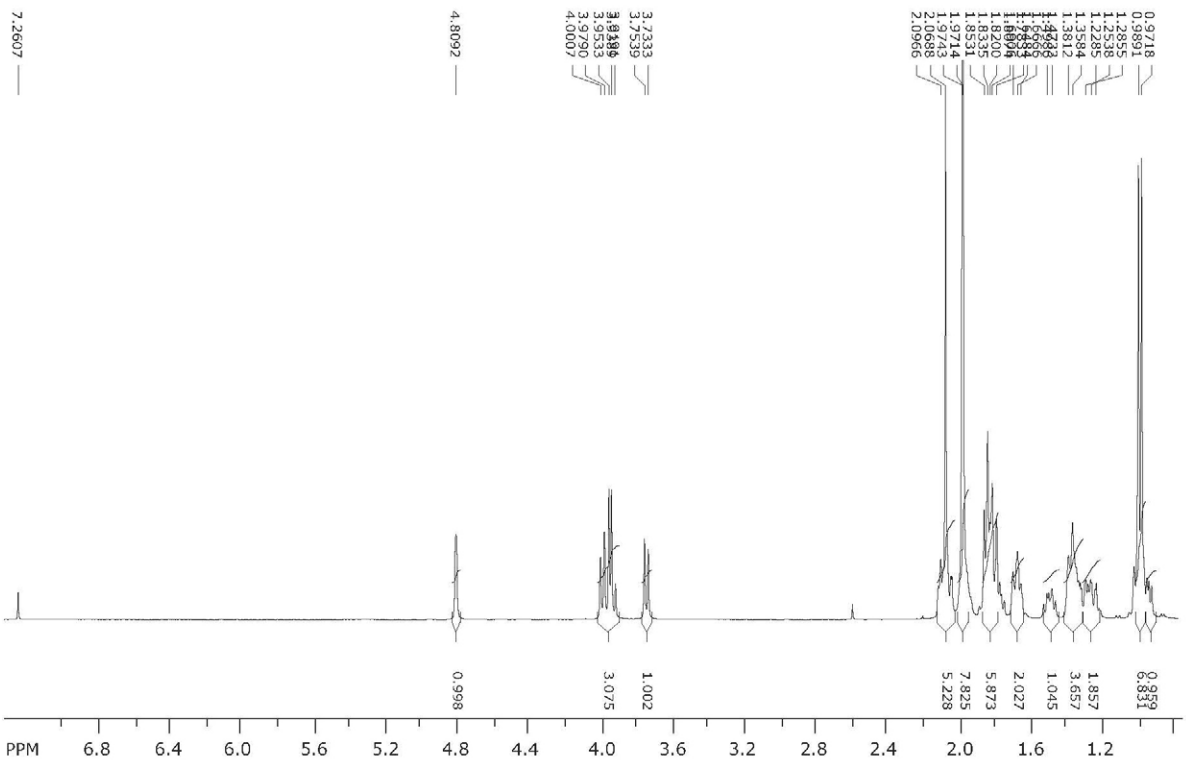


**Figure S33**. $^{1}H$ NMR spectrum (500 MHz, $CDCl_3$) – compound **10**.

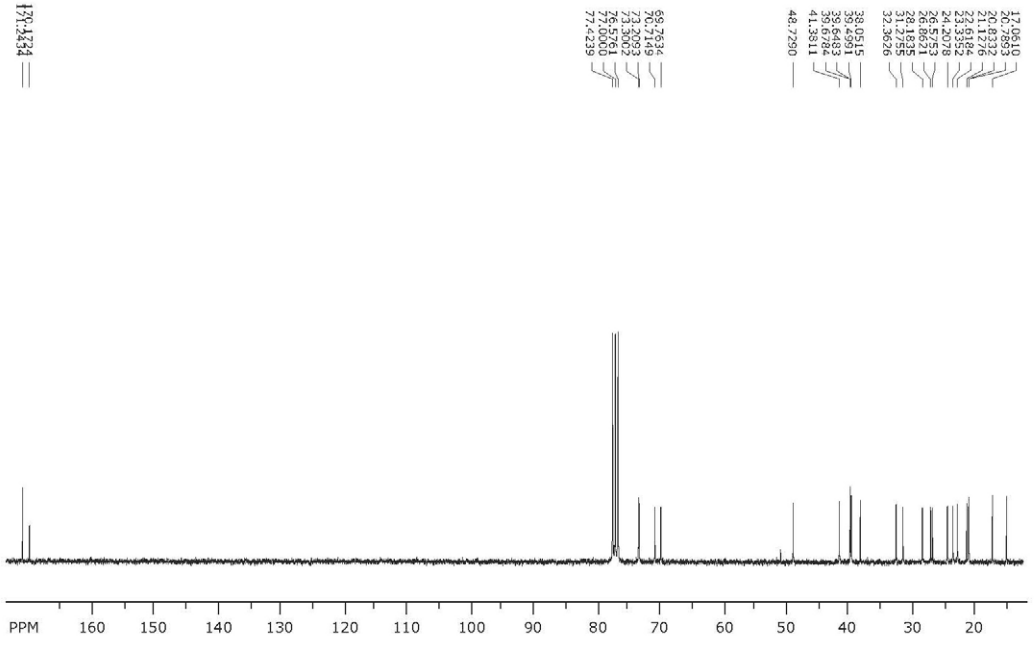


**Figure S34.** $^{13}C$ NMR spectrum (125 MHz, $CDCl_3$)– compound **10**.

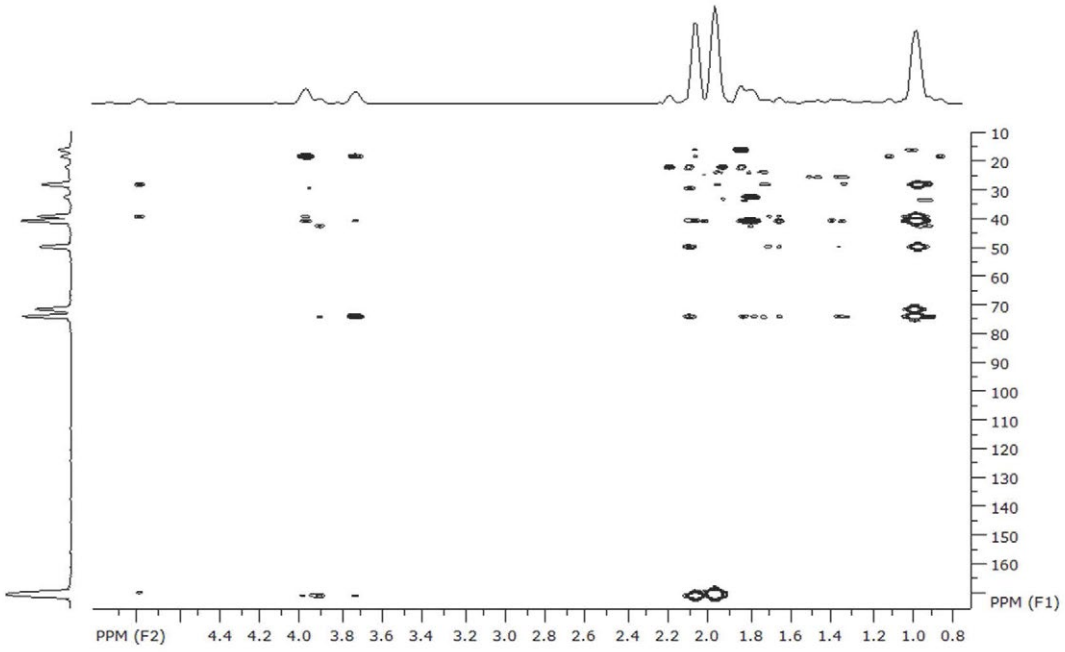


**Figure S35.** HMBC spectrum (500 MHz, $CD_3OD$) – compound **10**.

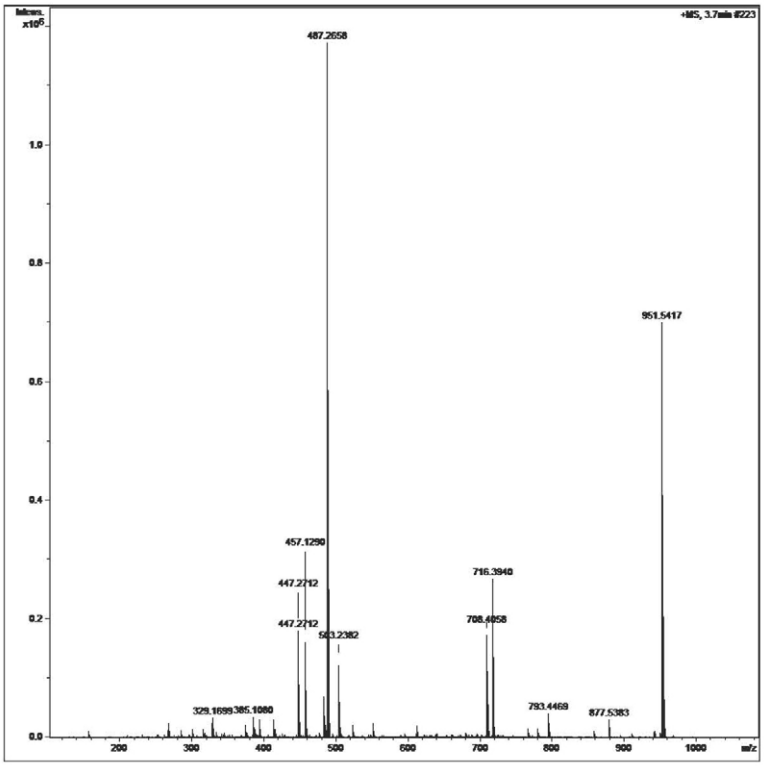


**Figure S36.** HRMS-ESI – compound **10**.

## References


1. Enraf-Nonius; *Collect*; *Program for Crystal Structure Refinement;* Nonius B.V., Delft, The Netherlands, 1997.
2. Otwinowski, Z.; Minor, W. In *Methods in Enzymology*, vol. 276; Carter Jr., S. W.; Sweet, R. M., eds; Academic Press: New York, 1997, pp. 307.
3. Sheldrick, G.; *SHELXS-97*; University of Göttingen, Germany, 1997.
4. Macrae, C. F.; Bruno, I. J.; Chisholm, J. A.; Edgington, P. R.; McCabe, P.; Pidcock, E.; Rodriguez-Monge, L.; Taylor, R.; van de Streek, J.; Wood, P. A.; *J. Appl. Crystallogr.* **2008**, *41*, 466.
5. Humphrey, W.; Dalke, A.; Schulten, K.; *J. Mol. Graphics* **1996**, *14*, 33.
6. Brundret, K. M.; Dalziel, W.; Hesp, B.; Jarvis, J. A. J.; *J. Chem. Soc., Chem. Commun.* **1972**, *18*, 1027.
7. Dalziel, W.; Hesp, B.; Stevenson. K. M.; Jarvis, J. A. J.; *J. Chem. Soc., Perkin Trans. 1* **1973**, 2841.
8. Kayser, O.; Kiderlen, A. F.; Bertels, S.; Siems, K.; *Antimicrob. Agents Chemother.* **2001**, *45*, 288.
9. Gordon, J. F.; Hanson, J. R.; Jarvis, A. G. ; Ratcliffe, A. H. ; *J. Chem. Soc., Perkin Trans. 1* **1992**, 3019.
10. Hiranuma, S.; Shimizu, T.; Yoshioka, H.; Ono, K.; Nakane, H.; Takahashi, T.; *Chem. Pharm. Bull.* **1987**, *35*, 1641.
11. Ipsen, J.; Fuska, J.; Foskova, A.; Rosazza, J. P.; *J. Org. Chem.* **1982**, *47*, 3278.