Supplementary Information

Montmorillonite K-10 supported palladium nanoparticles: A catalyst for the preparation of α-aminoynones employing copper free acyl Sonogashira reaction

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Experimental Section

All chemicals were used as obtained from Sigma Aldrich Company, USA. All the solvents were dried and purified using recommended procedures in the literature whenever necessary. Mass spectra were recorded on a Micromass Q-TOF micromass spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AV NMR 400 MHz and 100 MHz spectrometers, respectively, at the Indian Institute of Science, Bangalore. The RP-HPLC analysis of isomers was carried out by using an Agilent instrument at $\lambda = 254$ nm; flow rate: 0.5 mL/min; column: Phenomenex Lux Amylose-2, pore size-5 μm, diameter × length = 4.6 × 250 mm; method: gradient 0.1% TFA water-acetonitrile; in 10 min. TLC experiments were performed using MERCK TLC aluminum sheets (silica gel 60 F254) and chromatograms were visualized by exposing in an iodine chamber or to a UV-lamp. Column chromatography was performed on silica gel (100–200 mesh) using ethyl acetate and hexane as the eluent.ICP-OES data were obtained from Shiva Analyticals (India) Ltd., Bangalore 562114,India using Perkin Elmer OPTIMA 5300DV.

Procedure for the preparation of MMT K-10/Pd^{0}:

A suspension of montmorillonite K-10 (500 mg) in ethanol (90 mL) was stirred for 30 min along with $PdCl_2$ (2.5mmol). It was then refluxed for 20 min and a solution of $NaBH_4$ (3 mmol) in ethanol (6 mL) was added slowly. The initial brownish solution immediately turned colorless shows the reduction of Pd (II) to Pd (0). It was then allowed to cool to room temperature, and the black precipitate obtained was filtered. After simple washings with water and ethanol, black powder of montmorillonite K-10/Pd^0 was obtained which was dried under vacuum and characterized.

Procedure for the preparation of N$^\alpha$-protected amino ynones:

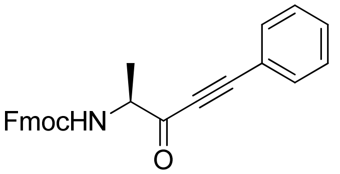
A solution of amino/peptide acid chloride (1 mmol), aryl/alkyl acetylene (1.2 mmol), TEA (3 mmol) was stirred in 1,4-dioxane, 15 mg of MMT K-10/Pd^0 was added and the stirring was continued at room temperature. After the completion of the reaction (as analyzed by TLC), the reaction mixture was filtered, residue was washed with ethanol. Solvent was evaporated under *vacuum*and extracted into ethyl acetate. The organic layer was washed with water, brine and dried over anhydrous sodium sulfate. The solvent was evaporated under *vacuum*. The crude was subjected to column chromatography using n-hexane and ethyl acetate as eluent.

Procedure for deprotection reaction:

A solution of Z-Phe-OH (200 mg) was treated with MMT K-10/Pd^0 (20 mg) in ethanol (5 mL) and the reaction mixture was stirred under hydrogen at room temperature for 30 min. After the completion of the reaction, (as identified by TLC analysis), the product was filtered and evaporated filtrate under reduced pressure. And the product was confirmed by comparing the physical constants with the reported data.

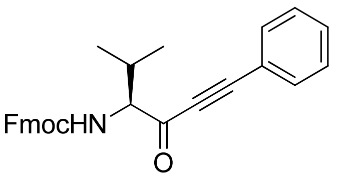
Characterization data

1. [3a]:



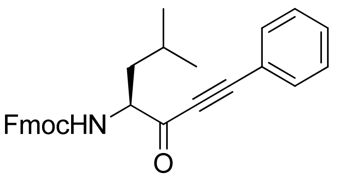
Gummy solid, yield = 88%, $[\alpha]^{25}_D$ = +0.22 (c 1.0, DCM). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 - 7.23 (m, 13H), 5.67 (s, 1H), 4.51 (d, J = 6.4 Hz, 2H), 4.29 - 4.19 (m, 1H), 4.11 (t, J = 6 Hz, 1H), 1.40 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.2, 155.6, 143.5, 141.6, 132.5, 129.1, 128.4, 126.9, 126.1, 125.3, 122.7, 120.4, 95.6, 88.4, 67.3, 64.2, 47.2, 15.7. HRMS: m/z Calculated for $C_{26}H_{21}NNaO_3$ $[M + Na]^+$ 418.1419; found: 418.1423.

2. [3b]:



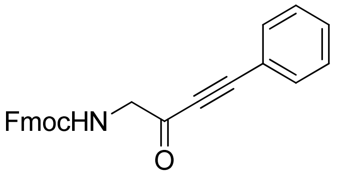
Gummy solid, yield = 79%, $[\alpha]^{25}_D$ = +51 (c 1.0, DCM). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 - 7.22 (m, 13H), 5.65 (s, 1H), 4.49 (d, J = 6.4 Hz, 2H), 4.25 - 4.09 (m, 2H), 2.60 - 2.51 (m, 1H), 0.92 (d, J = 6.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.9, 155.4, 143.5, 141.3, 132.1, 128.9, 128.3, 126.6, 126.2, 125.5, 122.6, 120.3, 95.3, 88.2, 67.2, 64.3, 47.3, 28.6, 19.3. HRMS: m/z Calculated for $C_{28}H_{26}NO_3$ $[M + H]^+$ 424.1913; found: 424.1906.

3. [3c]:



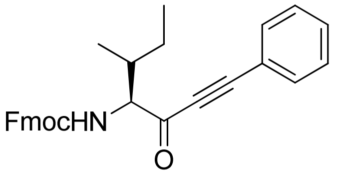
Gummy solid, yield = 84%, $[\alpha]^{25}_D$ = -13.46 (c 1.0, DCM). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 - 7.22 (m, 13H), 5.63 (s, 1H), 4.52 (d, J = 6.4 Hz, 2H), 4.28 - 4.12 (m, 2H), 1.97 - 1.78 (m, 2H), 1.53 - 1.39 (m, 1H), 0.91 (d, J = 6.4 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.1, 155.6, 144.3, 141.4, 132.5, 129.1, 128.5, 126.8, 126.4, 125.4, 122.6, 120.5, 95.1, 88.2, 67.5, 64.9, 47.4, 38.9, 24.5, 22.8. HRMS: m/z Calculated for $C_{29}H_{27}NNaO_3$ $[M + Na]^+$ 460.1889; found: 460.1890.

4. [3d]:



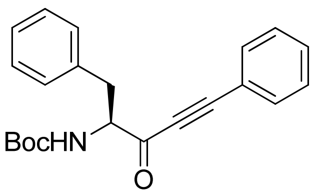
Oil, yield = 85%, $[\alpha]^{25}_{D}$ = +22.11 (c 1.0, DCM).^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 - 7.21 (m, 13H), 5.62 (s, 1H), 4.51 (d, J = 6.4 Hz, 2H), 4.17 (t, J = 6.4 Hz, 1H), 4.05 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.8, 155.7, 144.1, 141.0, 132.1, 128.9, 128.3, 126.5, 126.1, 125.2, 122.4, 120.3, 95.2, 88.3, 67.2, 54.9, 47.1. HRMS: m/z Calculated for$C_{25}H_{19}NNaO_3$ $[M + Na]^{+}$404.1263; found: 404.1270.

5. [3e]:



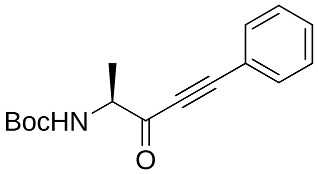
Gum, yield = 83%, $[\alpha]^{25}_{D}$ = +48.17 (c 1.0, DCM).^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 - 7.24 (m, 13H), 5.62 (s, 1H), 4.52 (d, J = 6.4 Hz, 2H), 4.25 - 4.08 (m, 2H), 2.02 (m, 1H), 1.52 (m, 2H), 0.92 (t, J = 6.4 Hz, 3H), 1.18 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.2, 155.5, 144.4, 141.1, 132.3, 128.9, 128.4, 126.7, 125.1, 122.4, 120.2, 95.3, 88.1, 67.2, 64.3, 47.3, 34.3, 24.9, 15.2, 11.3.HRMS: m/z Calculated for$C_{29}H_{27}NNaO_3$ $[M + Na]^{+}$460.1889; found: 460.1895.

6. [3f]:



White solid, yield = 82%, mp = 91-95 °C, $[\alpha]^{25}_{D}$ = +3.07 (c 1.0, DCM).^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 - 7.22 (m, 10H), 5.45 (s, 1H), 4.42 (m, 1H), 3.19 - 2.99 (m, 2H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.3, 155.3, 135.9, 132.8, 131.2, 128.5, 128.2, 127.8, 126.9, 124.2, 94.6, 88.2, 79.9, 64.5, 35.6, 28.5. HRMS: m/z Calculated for$C_{22}H_{23}NNaO_3$ $[M + Na]^{+}$372.1576; found: 372.1581.

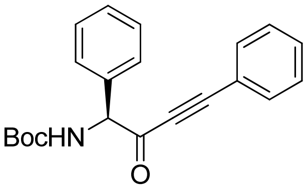
7. [3g]:



White solid, yield = 80%, mp = 64 - 66 °C, $[\alpha]^{25}_{D}$ = +0.006° (c 1.0, DCM).^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 - 7.39 (m, 5H), 5.43 (s, 1H), 4.43 (m, 1H), 1.52 (d, J = 6 Hz, 3H), 1.4 (s, 9H). ^{13}C NMR

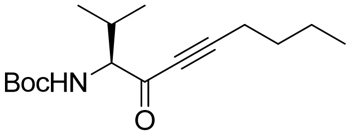
(100 MHz, CDCl$_3$): δ 183.1, 155.2, 132.5, 128.9, 128.5, 122.9, 94.5, 88.3, 79.7, 64.3, 28.4, 15.9. HRMS: m/z Calculated forC$_{16}$H$_{19}$NNaO$_3$ [M + Na]$^+$296.1263; found: 296.1262.

8. [3h]:



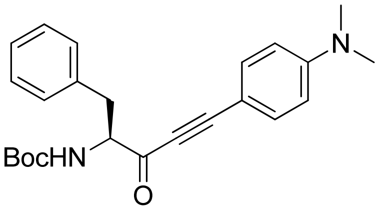
Oil, yield = 79%, [α]$^{25}_D$ = +53.1 (c 1.0, DCM).^{1}H NMR (400 MHz, CDCl$_3$): δ 7.56 - 7.35 (m, 5H), 5.41 (s, 1H), 4.42 (t, J = 7.2 Hz, 1H), 2.61 - 2.52 (m, 1H), 0.91 (d, J = 6.8 Hz, 6H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 183.5, 155.7, 132.6, 128.7, 128.1, 122.6, 94.6, 88.4, 79.7, 64.6, 28.8, 28.2, 19.4. HRMS: m/z Calculated forC$_{21}$H$_{21}$NNaO$_3$ [M + Na]$^+$358.1419; found: 358.1420.

9. [3i]:



Oil, yield = 78%, [α]$^{25}_D$ = +62 (c 1.0, DCM).^{1}H NMR (400 MHz, CDCl$_3$): δ 5.42 (s, 1H), 4.41 (d, J = 6.0 Hz, 1H), 2.60 - 2.51 (m, 1H), 2.41 (t, J = 6.2 Hz, 2H), 1.46 - 1.40 (m, 11H), 1.31 (m, 2H), 0.92 - 0.88 (m, 9H). ^{13}C NMR (100 MHz, CDCl$_3$): δ182.5, 155.6, 95.3, 79.6, 79.3, 74.9, 31.0, 29.1, 28.6, 21.4, 19.2, 18.1, 13.2. HRMS: m/z Calculated forC$_{16}$H$_{28}$NO$_3$ [M + H]$^+$282.2069; found: 282.2068.

10. [3j]:



White solid, yield = 80%, mp = 131 - 133 °C, [α]$^{25}_D$ = -101 (c 1.0, DCM).^{1}H NMR (400 MHz, CDCl$_3$): δ7.45 - 7.27 (m, 7H), 6.74 (d, J = 8.0 Hz, 2H), 5.42 (s, 1H), 4.65 - 4.57 (m, 1H), 3.32-3.15 (m, 2H), 3.10 (s, 6H), 1.42 (s, 9H).^{13}C NMR (100 MHz, CDCl$_3$): δ183.1, 155.5, 149.1, 136.9, 131.8, 128.9, 127.6, 126.2, 112.6, 109.5, 94.1, 88.3, 79.8, 63.9, 40.3, 35.4, 28.6. HRMS: m/z Calculated forC$_{24}$H$_{29}$N$_2$O$_3$ [M + H]$^+$393.2178; found: 393.2179.

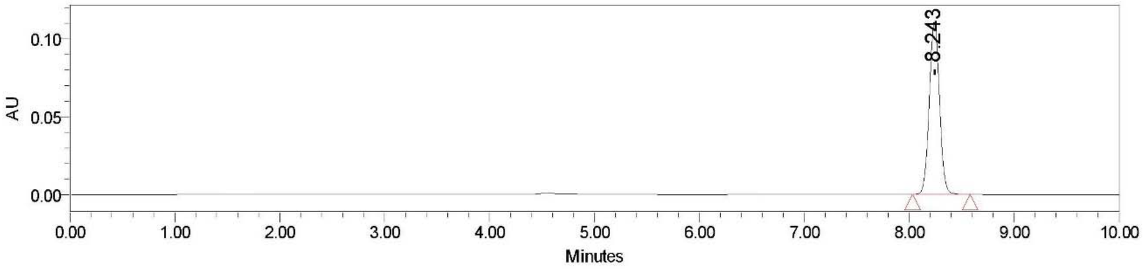
Recycling efficacy of MMT K-10/Pd^0

Substrate	Yield and duration			
	Fresh catalyst (15 mg)	Catalyst recovered after I cycle (14 mg)	Catalyst recovered after II cycle (14 mg)	Catalyst recovered after III cycle (13 mg)
[3a]	88 %, 60 min	88 %, 60 min	86 %, 65 min	83%, 70 min
H-Phe-OH	100%, 30 min	100 %, 30 min	98 %, 35 min	95 %, 40 min

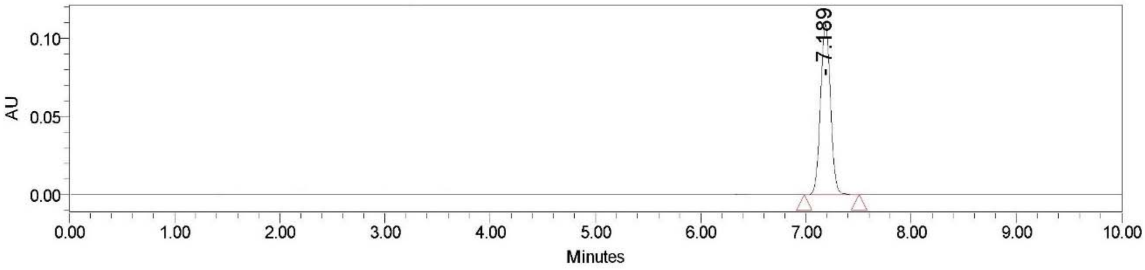
Physical data for the products listed in the table 3 of the Manuscript

Entry	Product	Melting point (°C)	
		Reported	Obtained
1.	H-Phe-OH	270-275	271 - 275
2.	H-Val-OH	295 - 300	294 - 299
3.	H-Phe-Ala-OMe	GUM	GUM
4.	Ala-Asp-Ser-Gly-OH	190 -194	190 - 193
5.	H-Glu-OH	205	204 - 206
6.	Boc-Thr-OMe	GUM	GUM

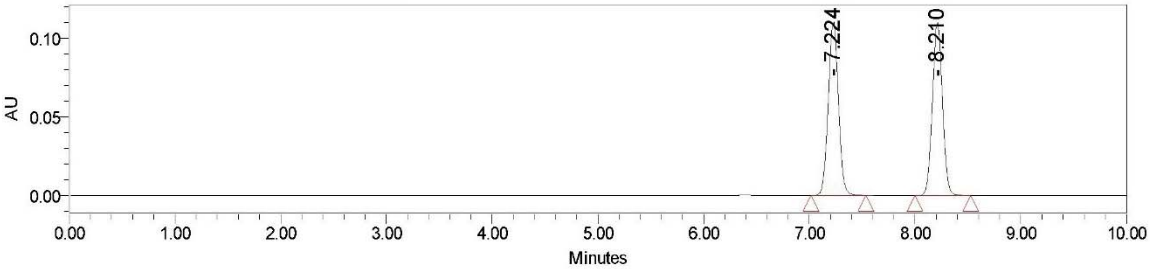
Spectral data



RP-HPLC of compound 3a



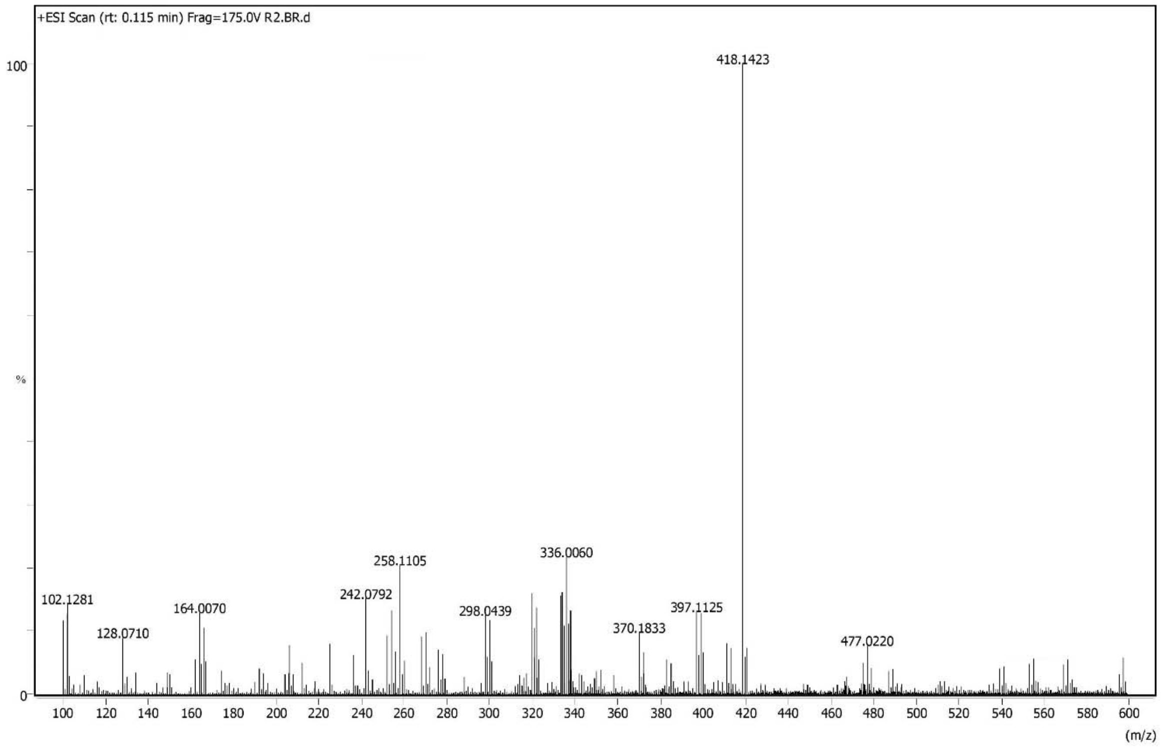
RP-HPLC of compound 3a*



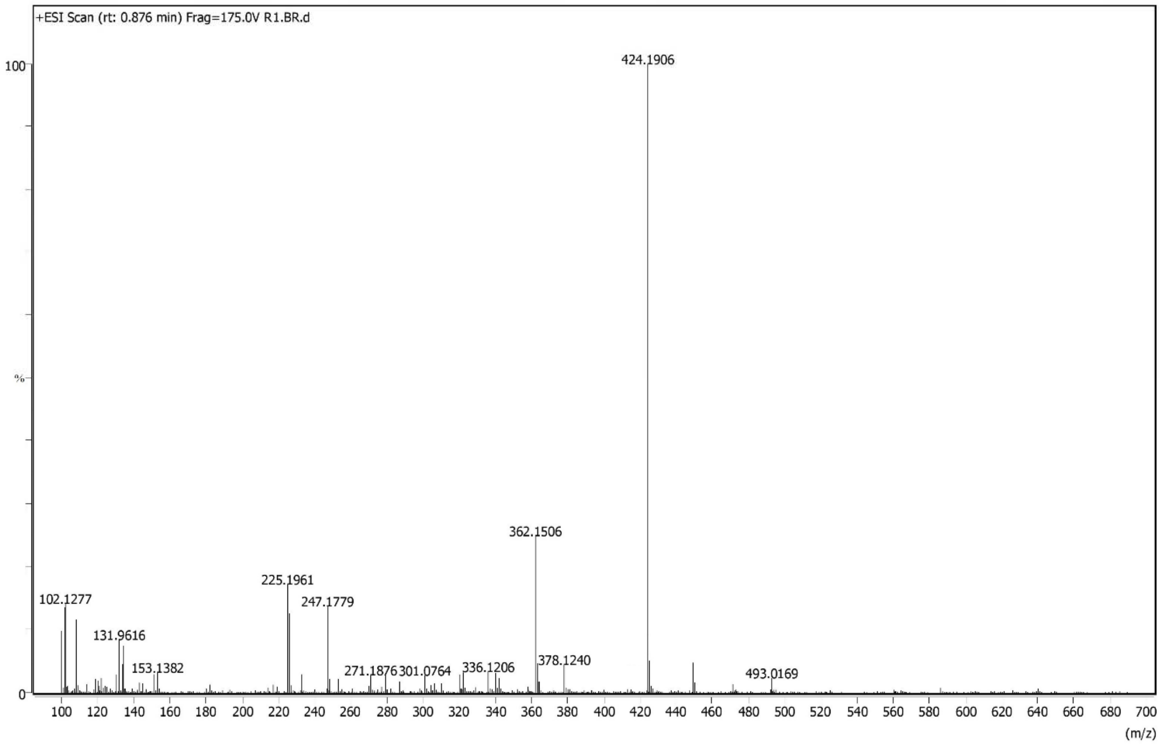
RP HPLC of mixture of compounds 3a and 3a*

Phenomenex Lux, Amylose-2, Pore size: 5.0 µm; diameter x length = 4.6 x 250 mm;

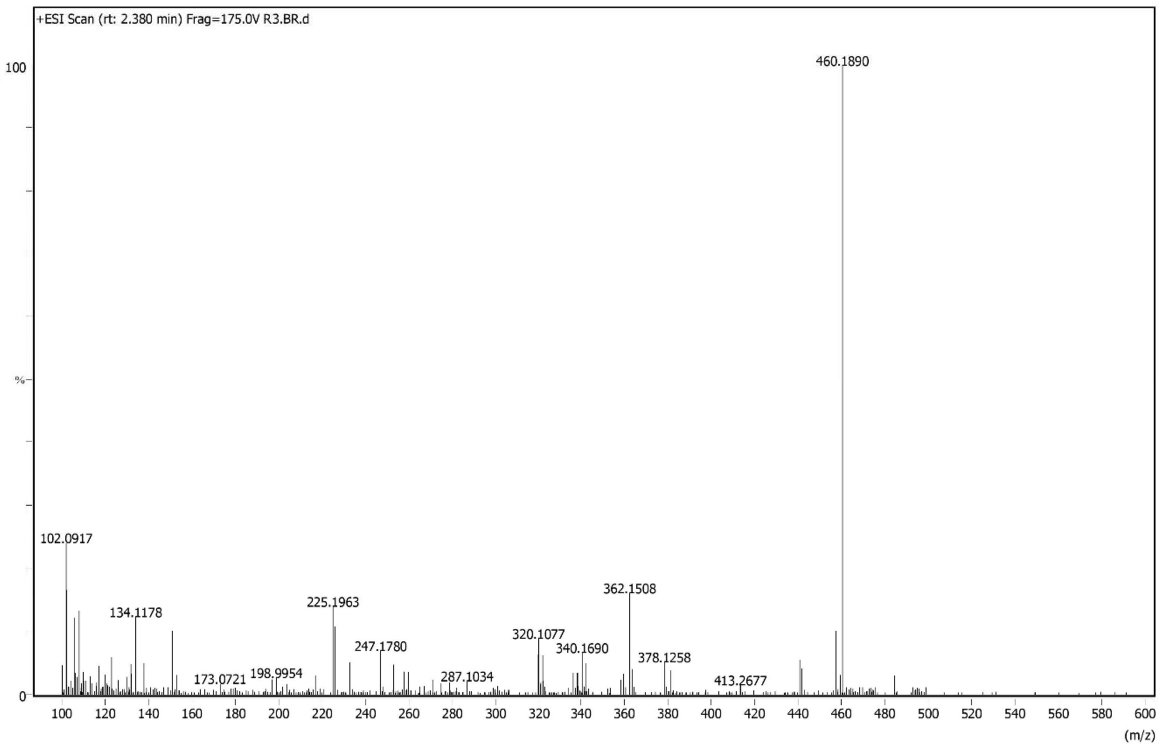
Method: gradient 0.1% TFA Water - Acetonitrile, (0-100%) in 10 min; λ=254 nm.



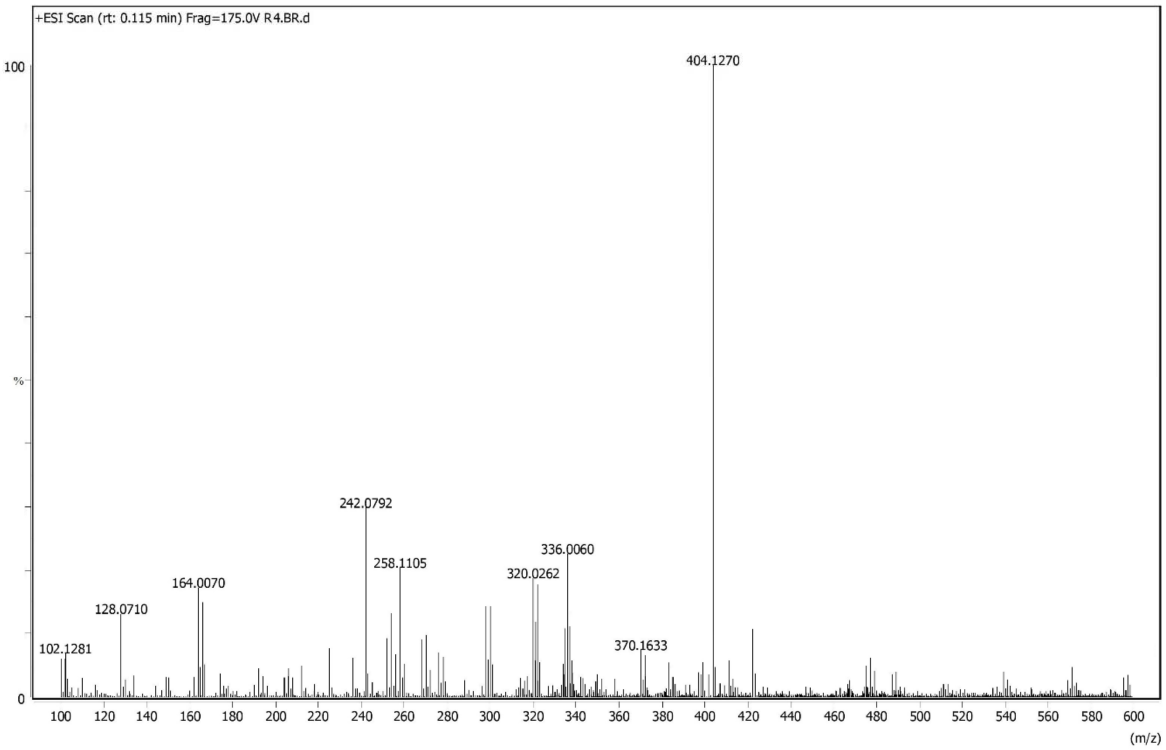
HRMS of compound [3a]



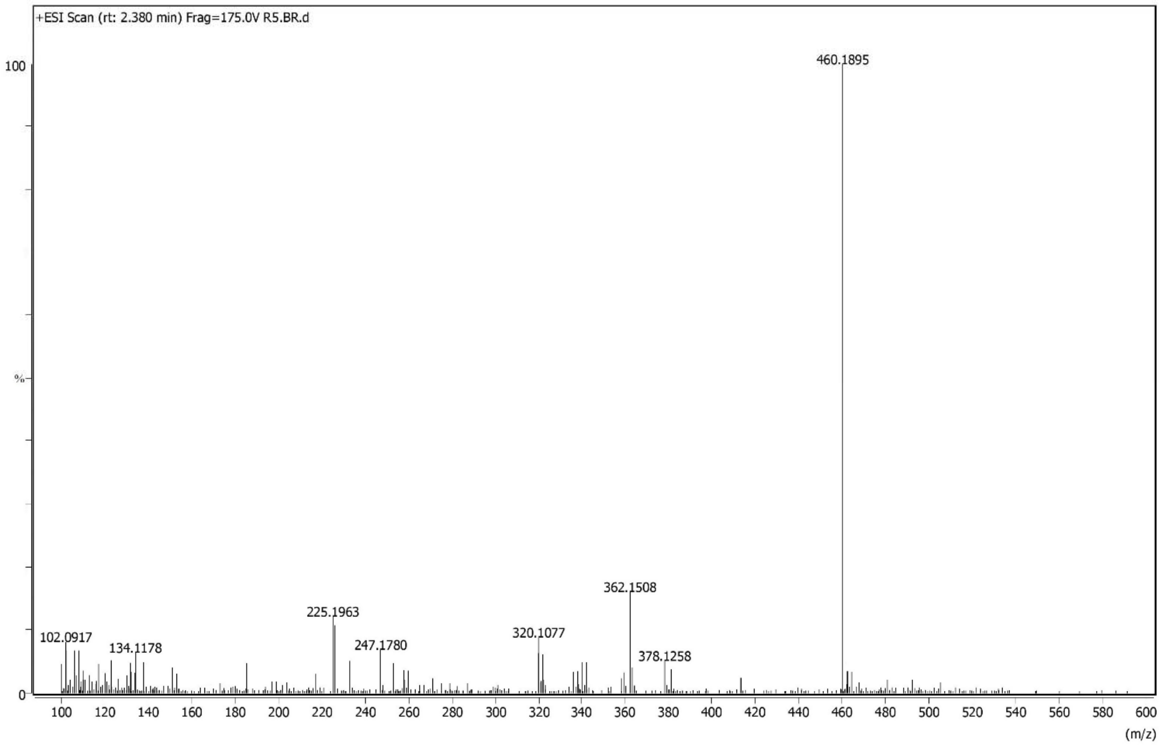
HRMS of compound [3b]



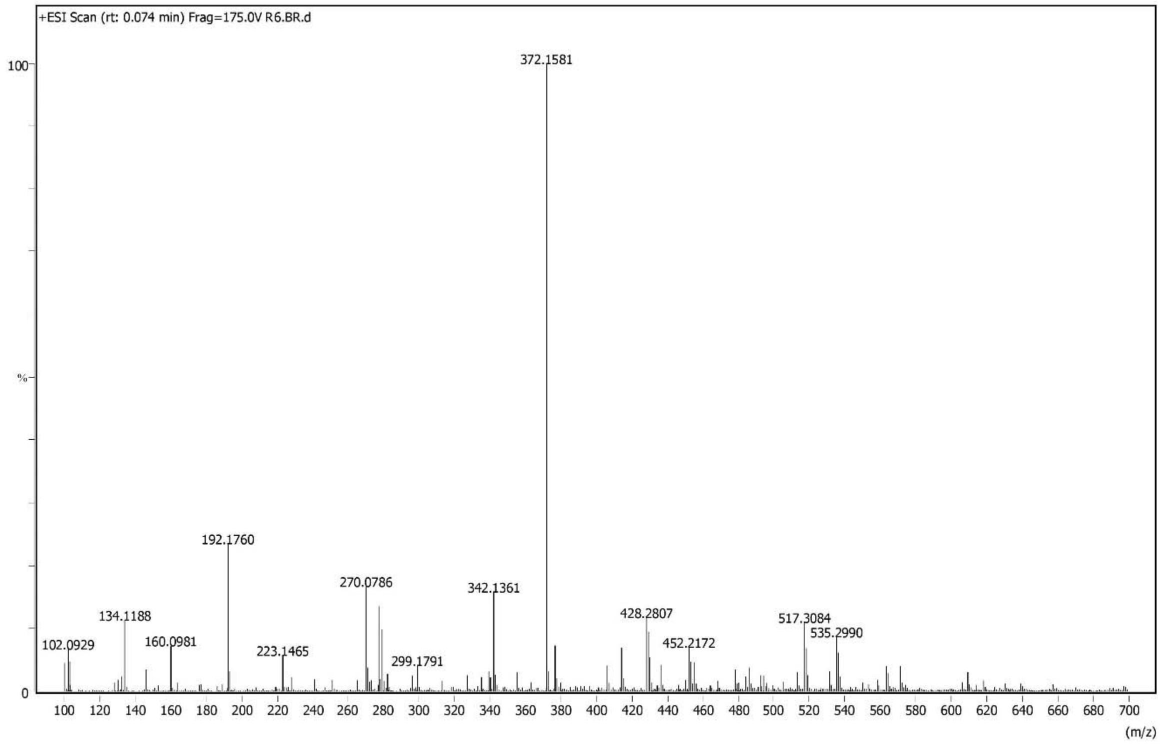
HRMS of compound [3c]



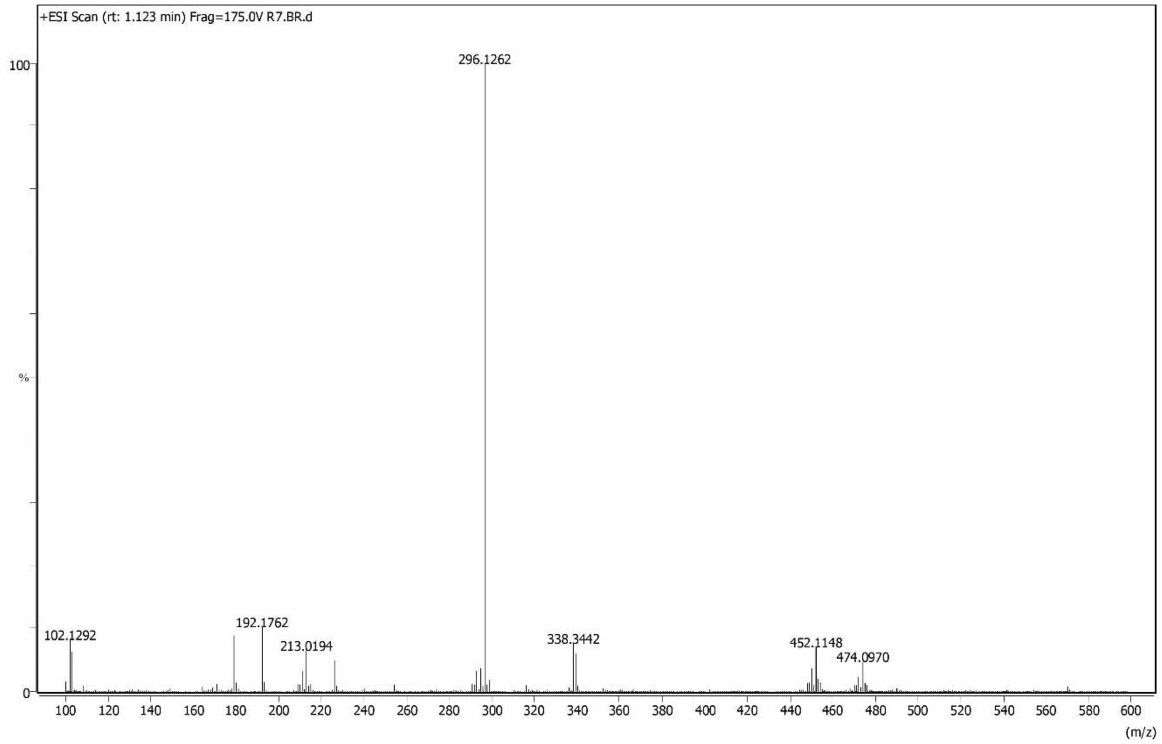
HRMS of compound [3d]



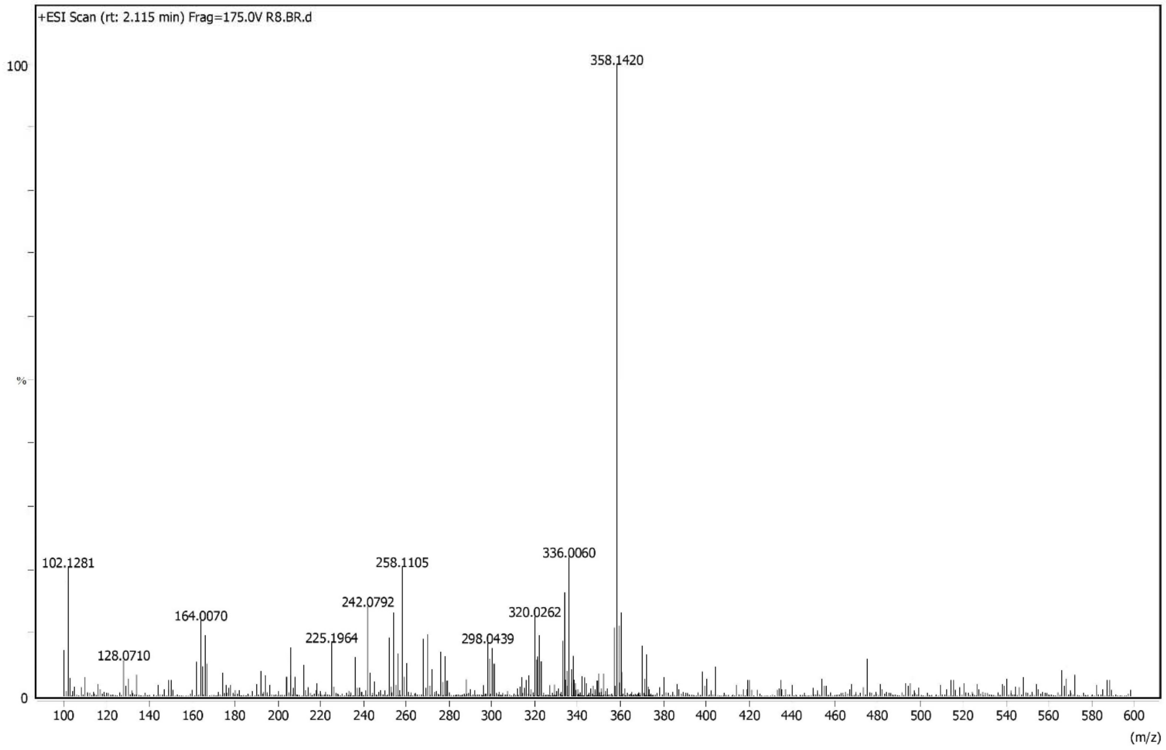
HRMS of compound [3e]



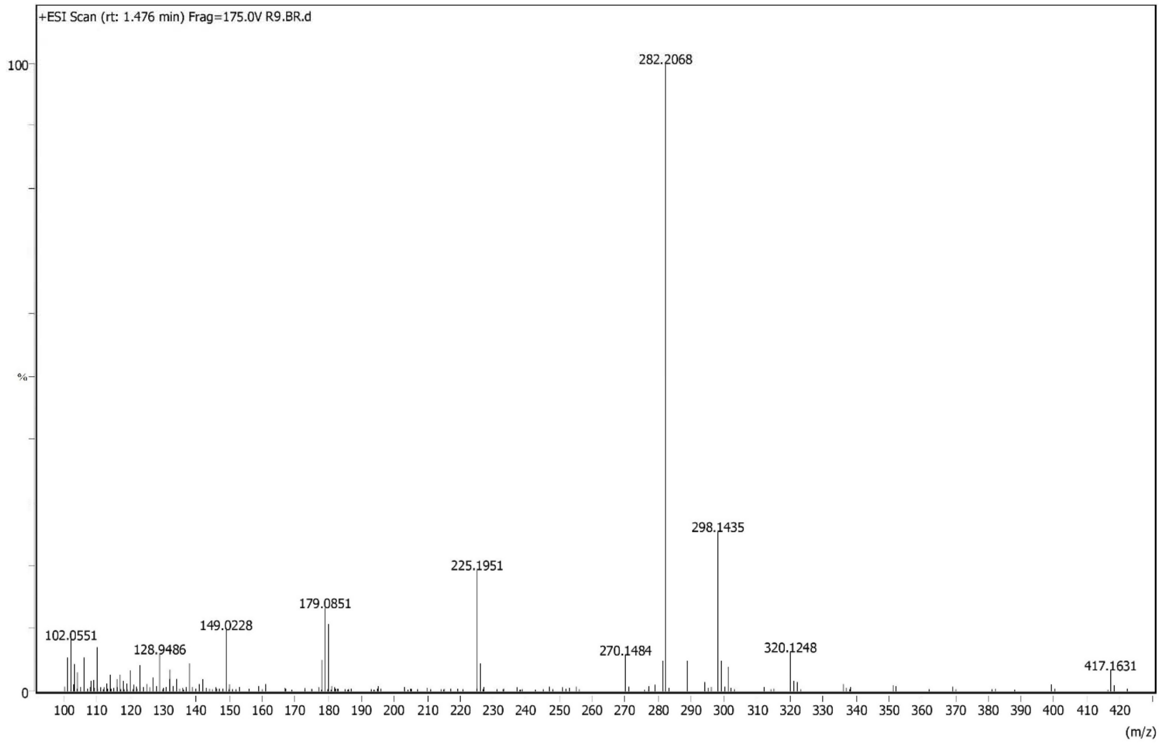
HRMS of compound [3f]



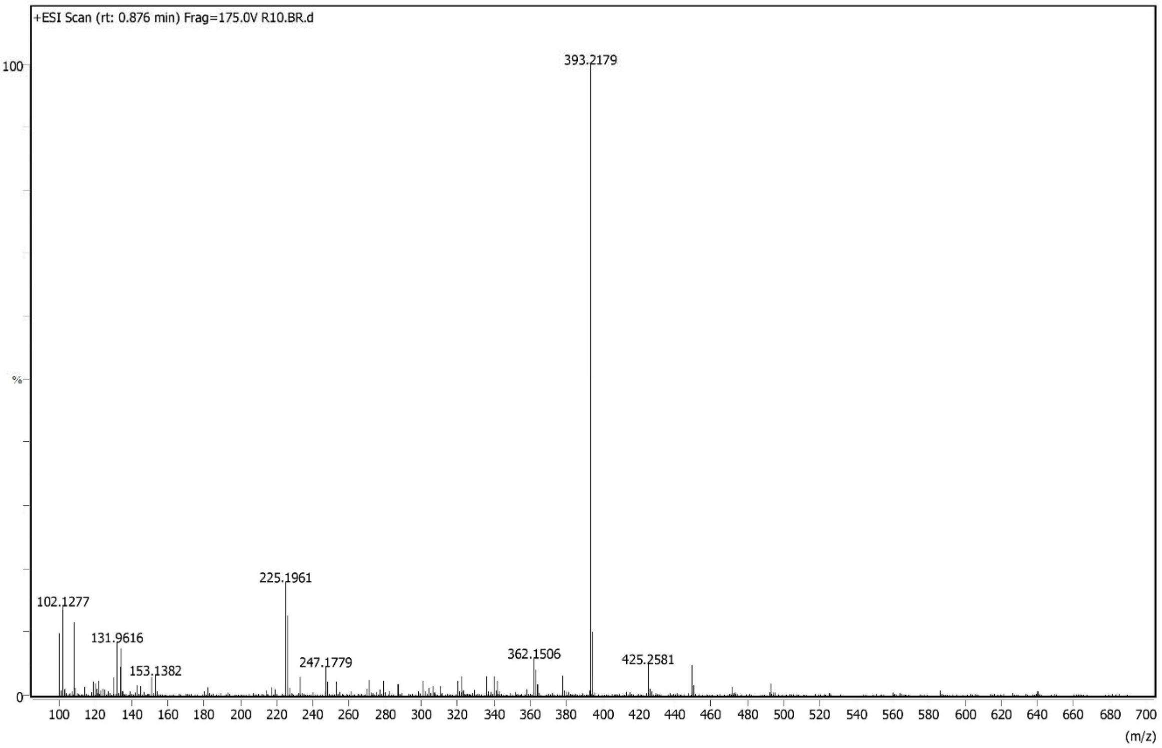
HRMS of compound [3g]



HRMS of compound [3h]



HRMS of compound [3i]



HRMS of compound [3j]