

Selective Synthesis of Multifunctionalized Cyclopent-3-ene-1-carboxamides and

2-Oxabicyclo[2.2.1]heptane derivatives

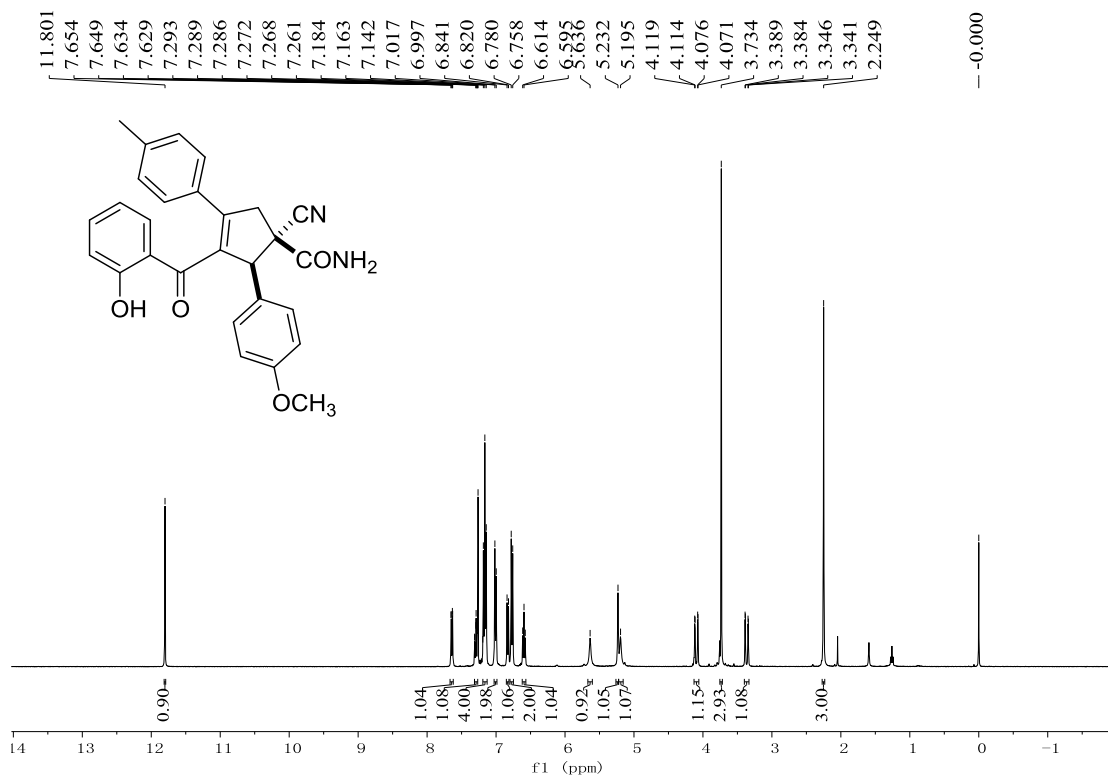
Hui Zheng, Ying Han,* Jing Sun, Chao-Guo Yan*

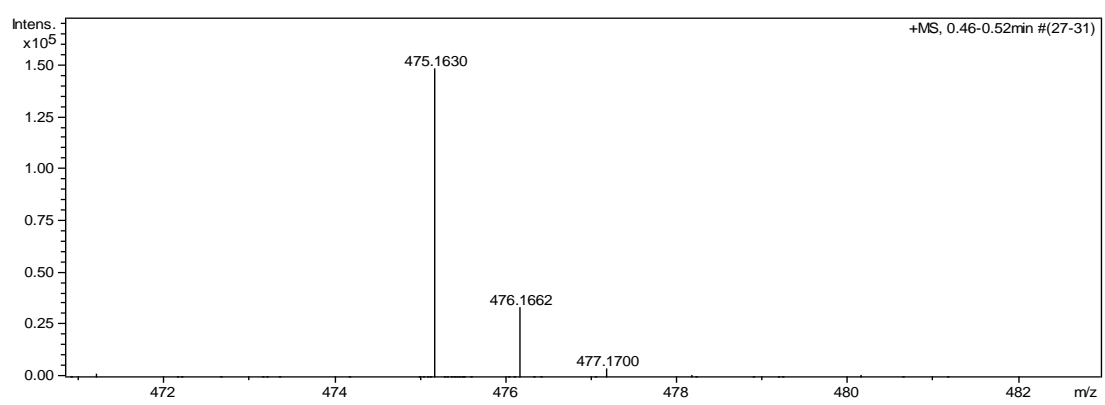
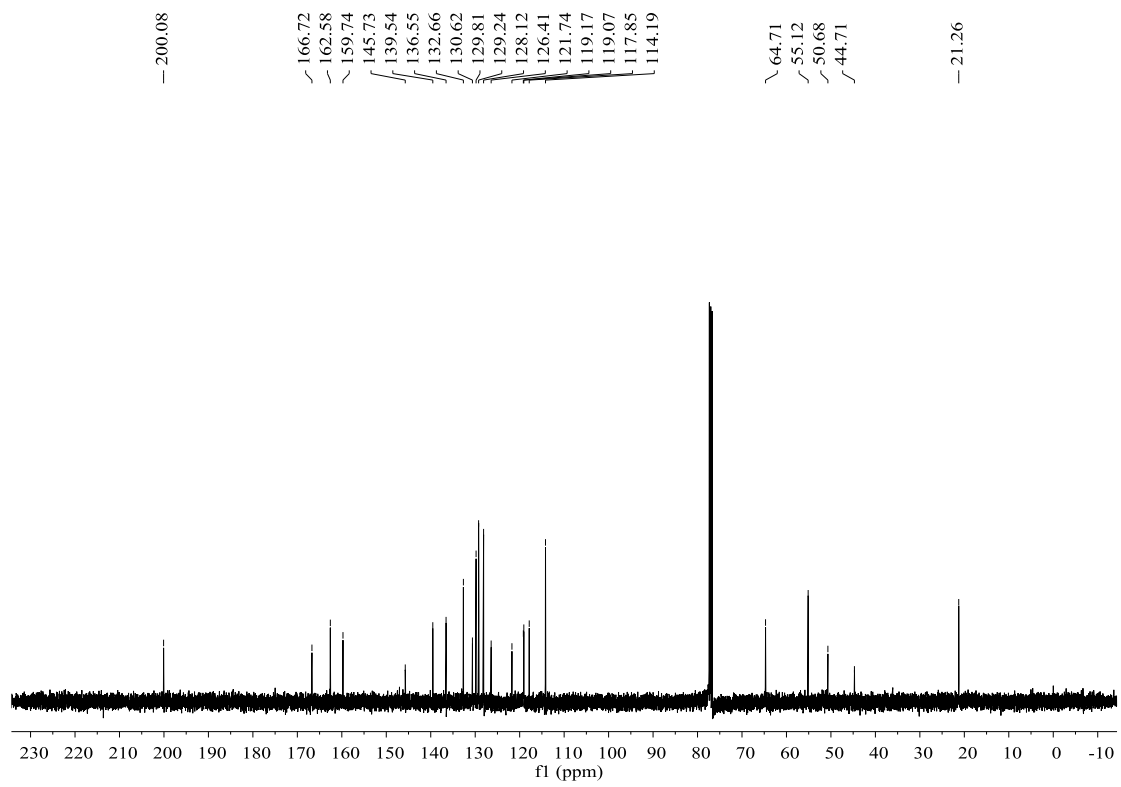
Supporting Information

Characterization data and spectroscopy

2-47

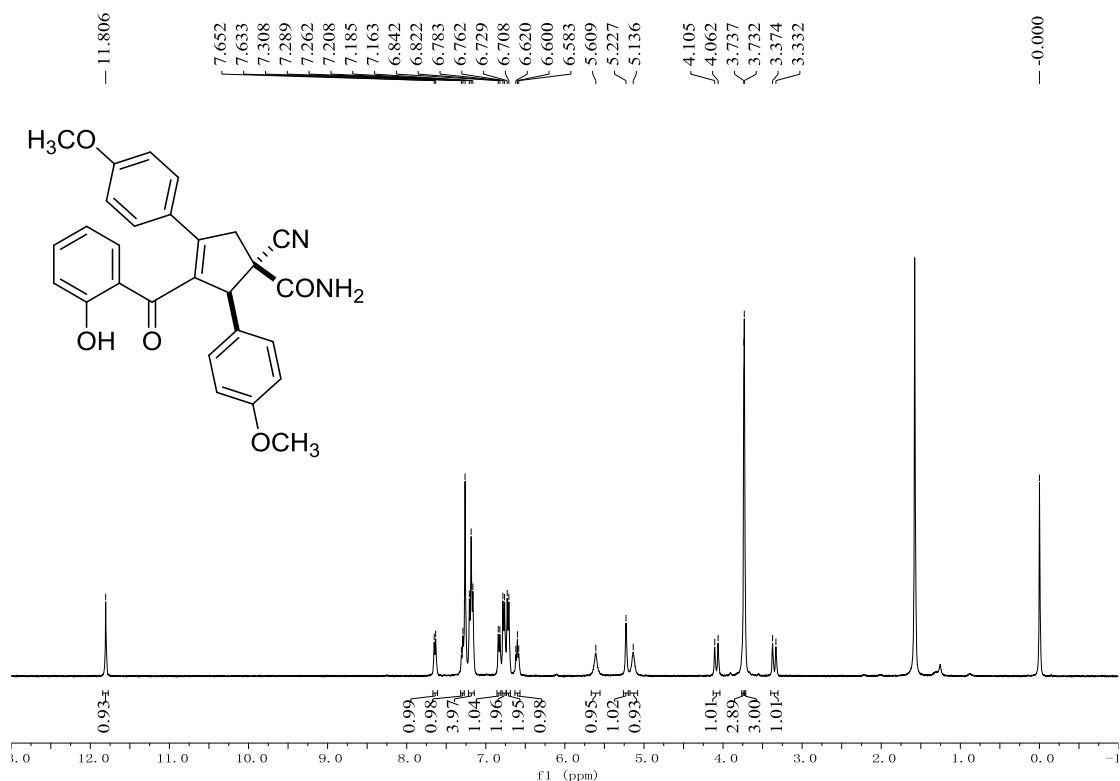
(E)-1-cyano-3-(2-hydroxybenzoyl)-2-(4-methoxyphenyl)-4-(p-tolyl)cyclopent-3-ene-1-carboxamide (3a): pale yellow solid, 85%, m.p. 225-227 °C; ^1H NMR (400 MHz, CDCl_3) δ 11.80 (s, 1H, OH), 7.65-7.63 (m, 1H, ArH), 7.31-7.27 (m, 1H, ArH), 7.19-7.14 (m, 4H, ArH), 7.01 (d, $J = 8.0$ Hz, 2H, ArH), 6.83 (d, $J = 8.4$ Hz, 1H, ArH), 6.77 (d, $J = 8.8$ Hz, 2H, ArH), 6.60 (t, $J = 7.6$ Hz, 1H, ArH), 5.64 (s, 1H, NH_2), 5.23 (s, 1H, CH), 5.20 (s, 1H, NH_2), 4.12-4.07 (m, 1H, CH_2), 3.73 (s, 3H, OCH_3), 3.39-3.34 (m, 1H, CH_2), 2.25 (s, 3H, CH_3). ^{13}C NMR (100 MHz, CDCl_3) δ 200.1, 166.7, 162.6, 159.7, 145.7, 139.5, 136.6, 132.7, 130.6, 129.8, 129.2, 128.1, 126.4, 121.7, 119.2, 119.1, 117.9, 114.2, 64.7, 55.1, 50.7, 44.7, 21.3. MS (m/z): HRMS (ESI) Calcd. for $\text{C}_{28}\text{H}_{24}\text{NaN}_2\text{O}_4$ ($[\text{M}+\text{Na}]^+$): 475.1634, found: 475.1630.

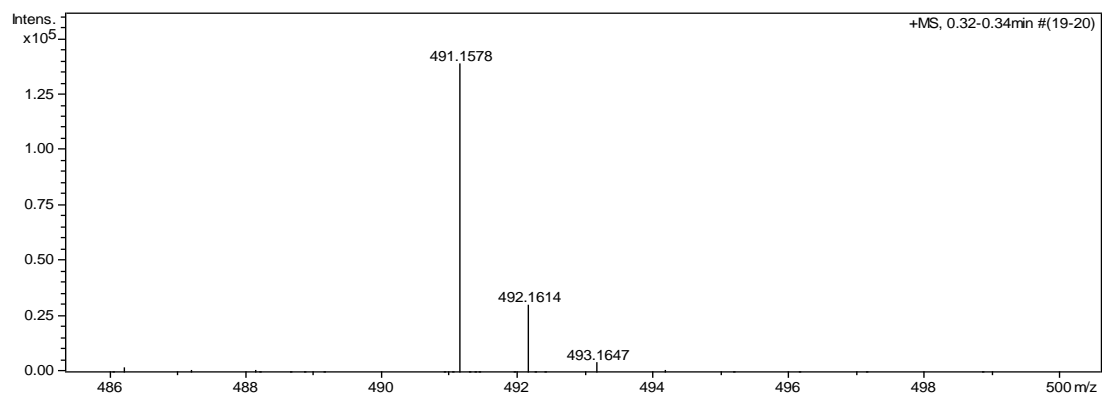
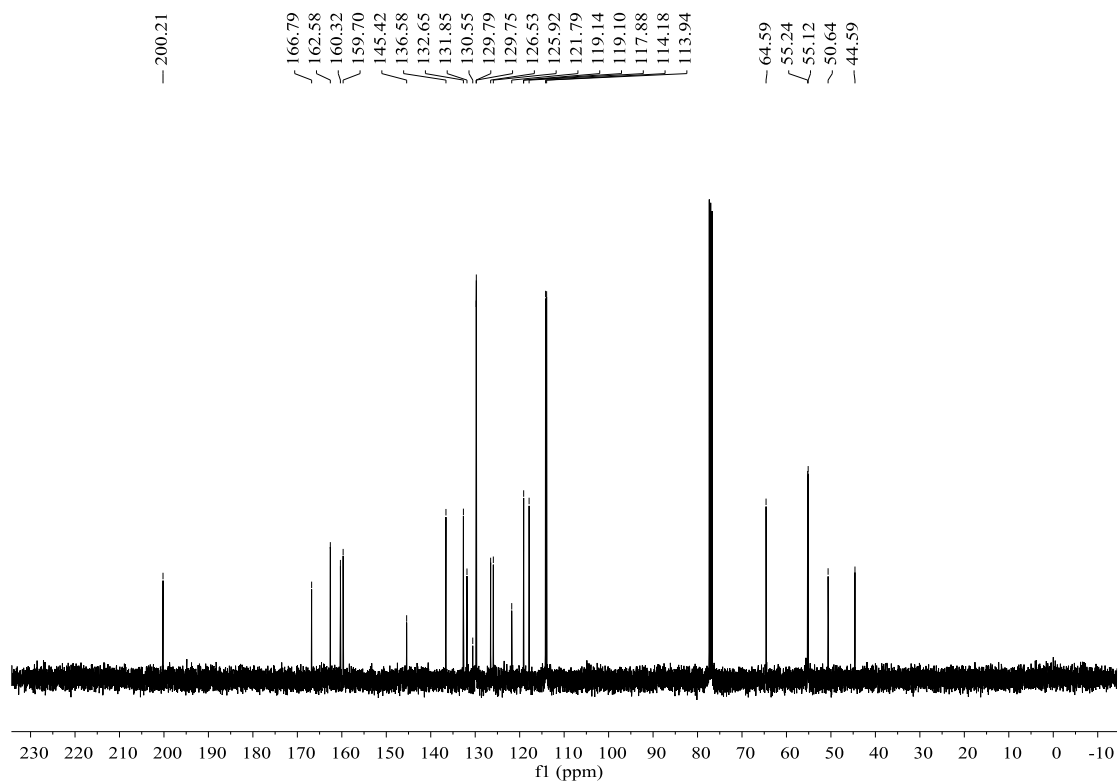




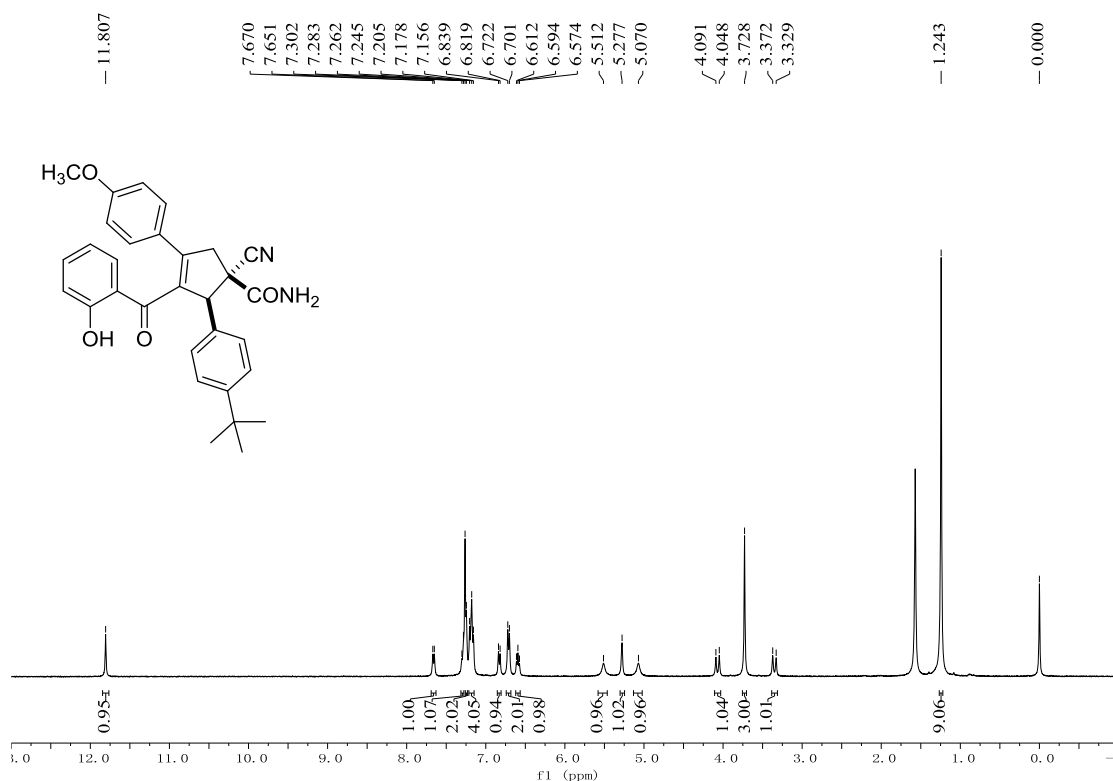
(E)-1-cyano-3-(2-hydroxybenzoyl)-2,4-bis(4-methoxyphenyl)cyclopent-3-ene-1-carboxamide

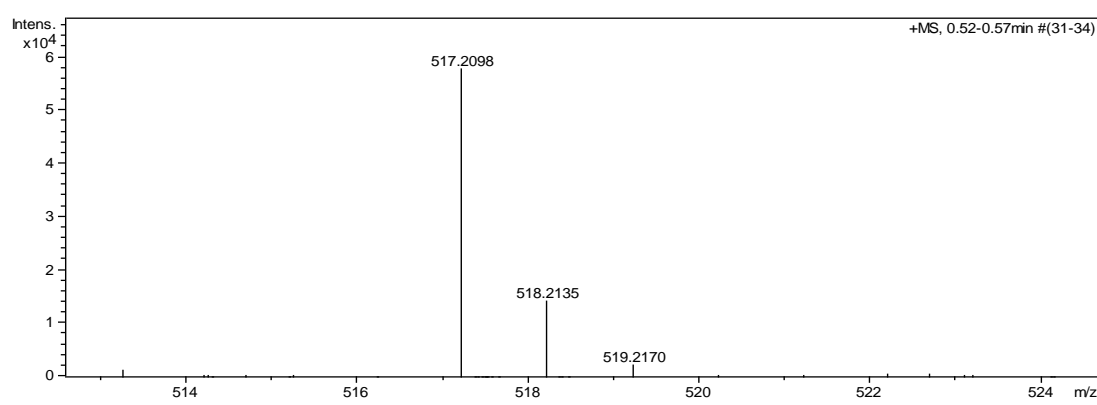
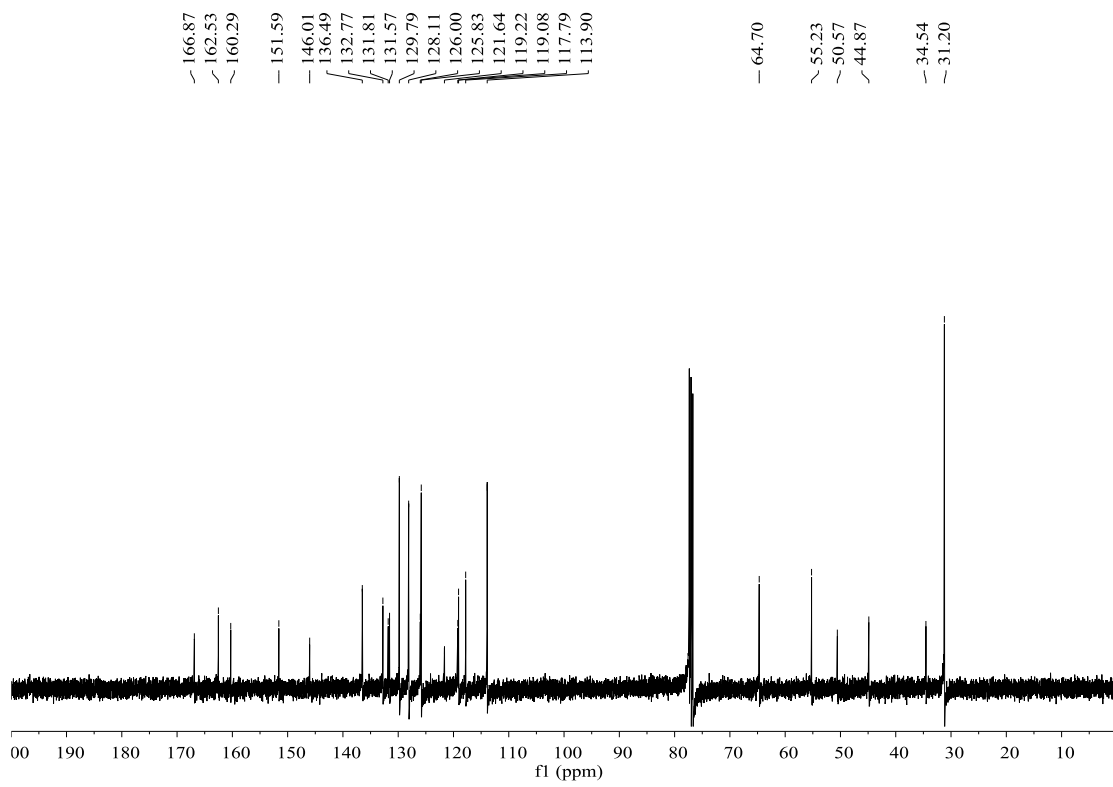
(3b): pale yellow solid, 60%, m.p. 199-201 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.81 (s, 1H, OH), 7.64 (d, *J* = 7.6 Hz, 1H, ArH), 7.31-7.29 (m, 1H, ArH), 7.19 (t, *J* = 9.2 Hz, 4H, ArH), 6.83 (d, *J* = 8.0 Hz, 1H, ArH), 6.77 (d, *J* = 8.4 Hz, 2H, ArH), 6.72 (d, *J* = 8.0 Hz, 2H, ArH), 6.60 (t, *J* = 8.0 Hz, 1H, ArH), 5.61 (s, 1H, NH₂), 5.23 (s, 1H, CH), 5.14 (s, 1H, NH₂), 4.08 (d, *J* = 17.2 Hz, 1H, CH₂), 3.74 (s, 3H, OCH₃), 3.73 (s, 3H, OCH₃), 3.35 (d, *J* = 16.8 Hz, 1H, CH₂). ¹³C NMR (100 MHz, CDCl₃) δ 200.2, 166.8, 162.6, 160.3, 159.7, 145.4, 136.6, 132.7, 131.9, 130.6, 129.8, 129.7, 126.5, 125.9, 121.8, 119.2, 119.1, 117.9, 114.2, 113.9, 64.6, 55.2, 55.1, 50.6, 44.6. MS (*m/z*): HRMS (ESI) Calcd. for C₂₈H₂₄NaN₂O₅ ([M+Na]⁺): 491.1583, found: 491.1578.



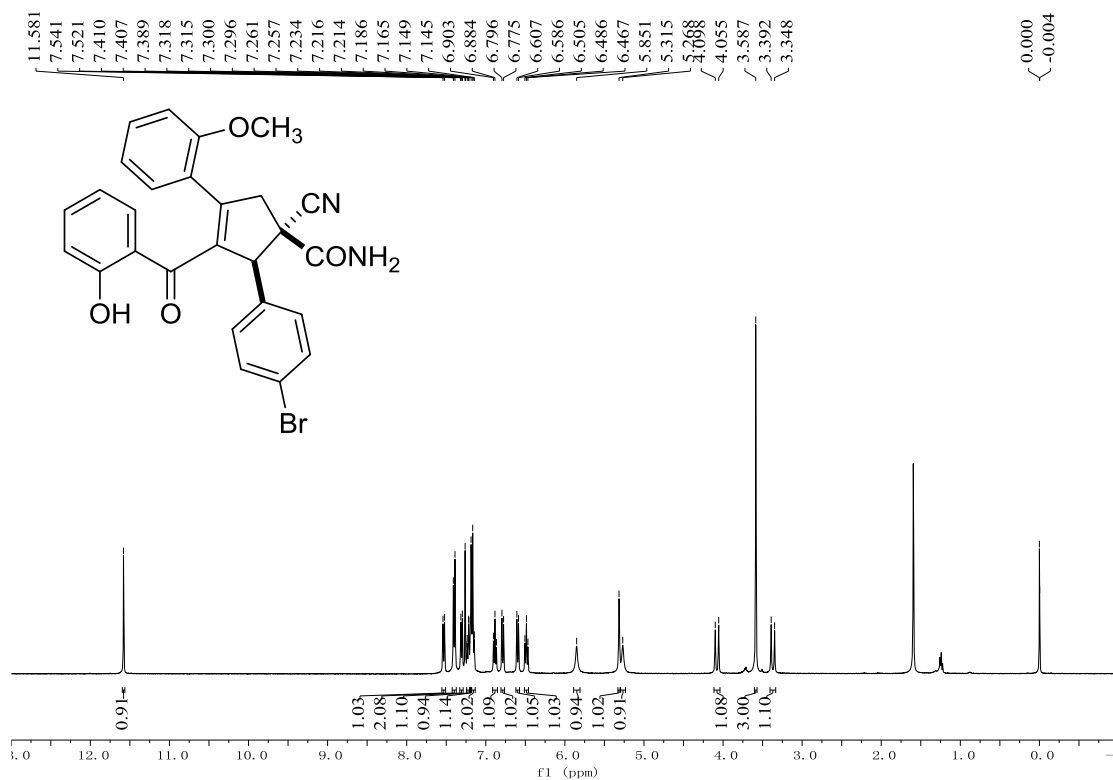


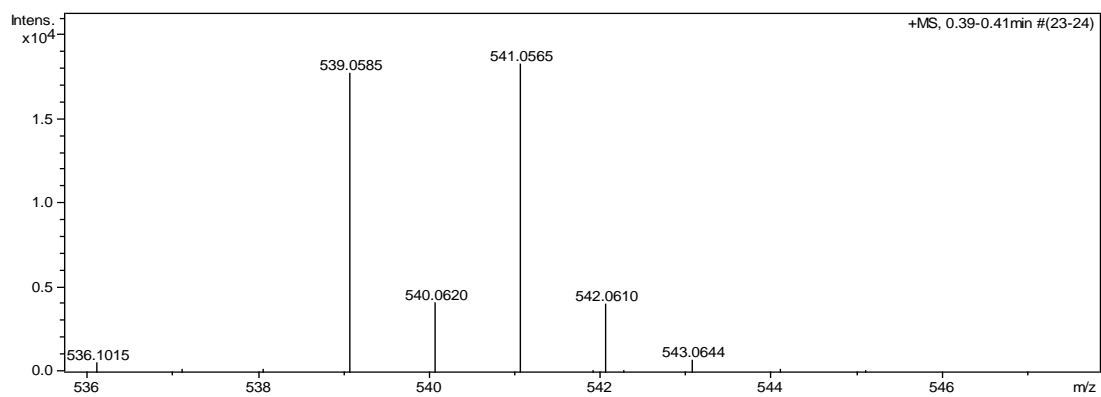
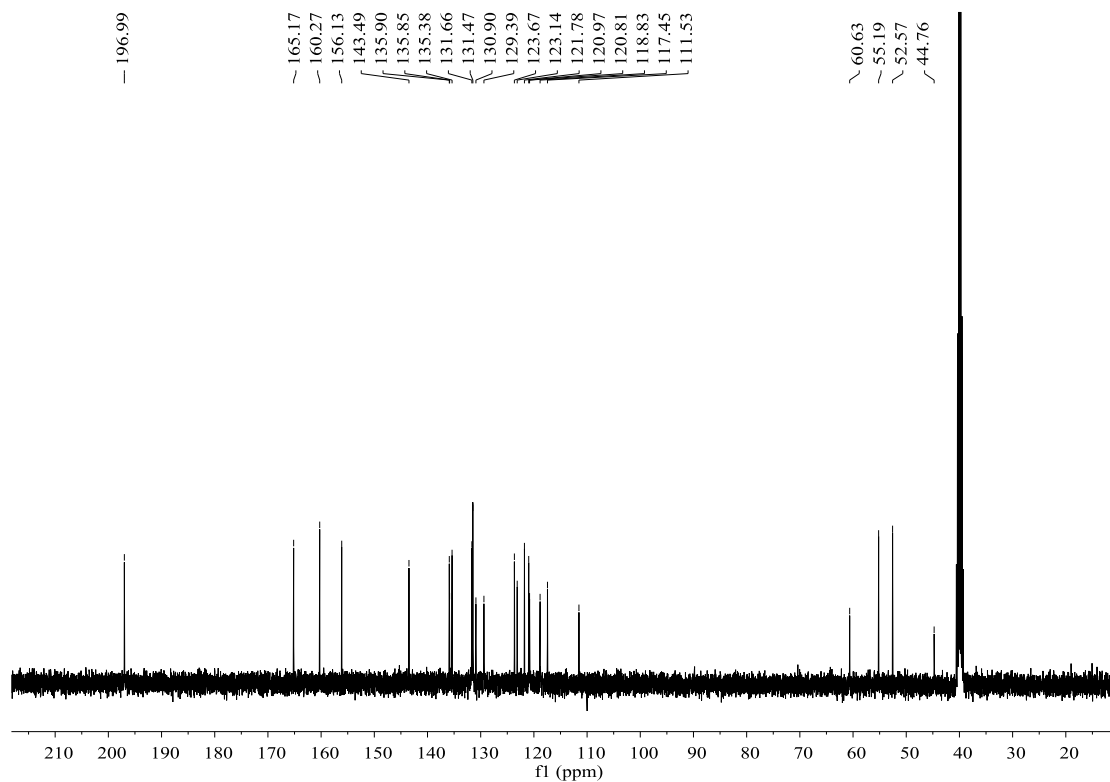
(E)-2-(4-(*tert*-butyl)phenyl)-1-cyano-3-(2-hydroxybenzoyl)-4-(4-methoxyphenyl)cyclopent-3-ene-1-carboxamide (3c): pale yellow solid, 78%, m.p. 200-201 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.81 (s, 1H, OH), 7.66 (d, *J* = 7.6 Hz, 1H, ArH), 7.30-7.28 (m, 1H, ArH), 7.26-7.25 (m, 2H, ArH), 7.21-7.16 (m, 4H, ArH), 6.83 (d, *J* = 8.0 Hz, 1H, ArH), 6.71 (d, *J* = 8.4 Hz, 2H, ArH), 6.59 (t, *J* = 8.0 Hz, 1H, ArH), 5.51 (s, 1H, NH₂), 5.28 (s, 1H, CH), 5.07 (s, 1H, NH₂), 4.07 (d, *J* = 17.2 Hz, 1H, CH₂), 3.73 (s, 3H, OCH₃), 3.35 (d, *J* = 17.2 Hz, 1H, CH₂), 1.24 (s, 9H, (CH₃)₃). ¹³C NMR (100 MHz, CDCl₃) δ 200.1, 166.9, 162.5, 160.3, 151.6, 146.0, 136.5, 132.8, 131.8, 131.6, 129.8, 128.1, 126.0, 125.8, 121.6, 119.2, 119.1, 117.8, 113.9, 64.7, 55.2, 50.6, 44.9, 34.5, 31.2. MS (*m/z*): HRMS (ESI) Calcd. for C₃₁H₃₀NaN₂O₄ ([M+Na]⁺): 517.2103, found: 517.2098.



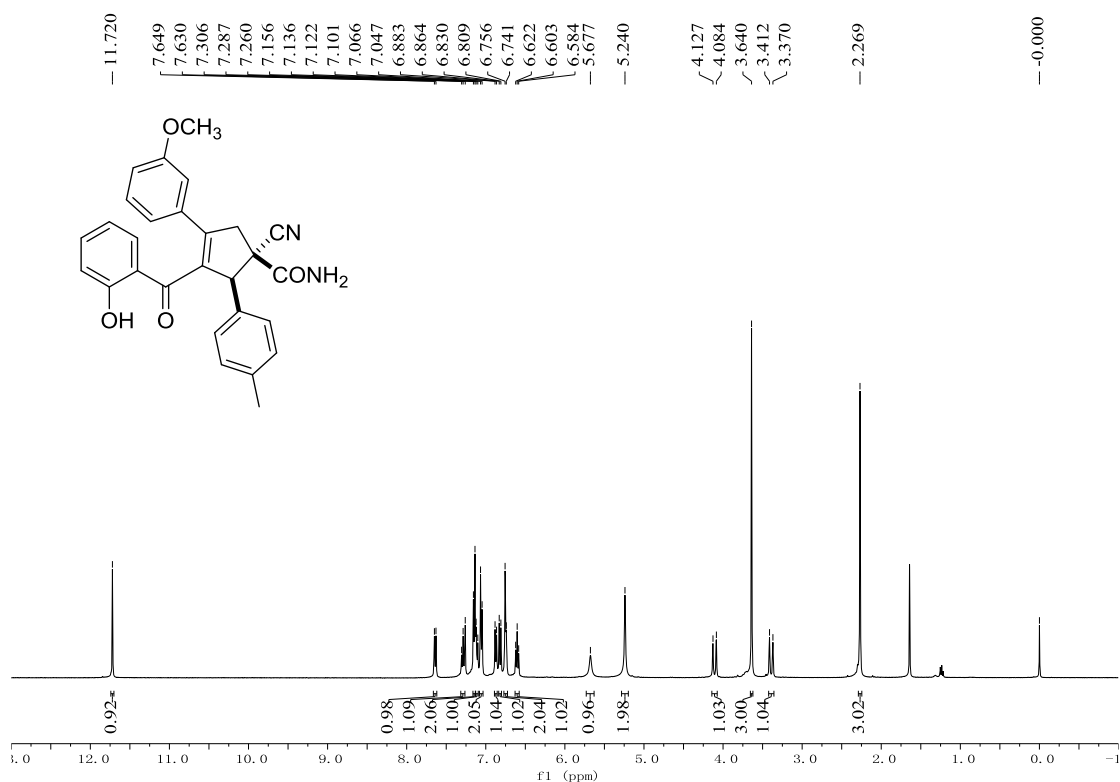


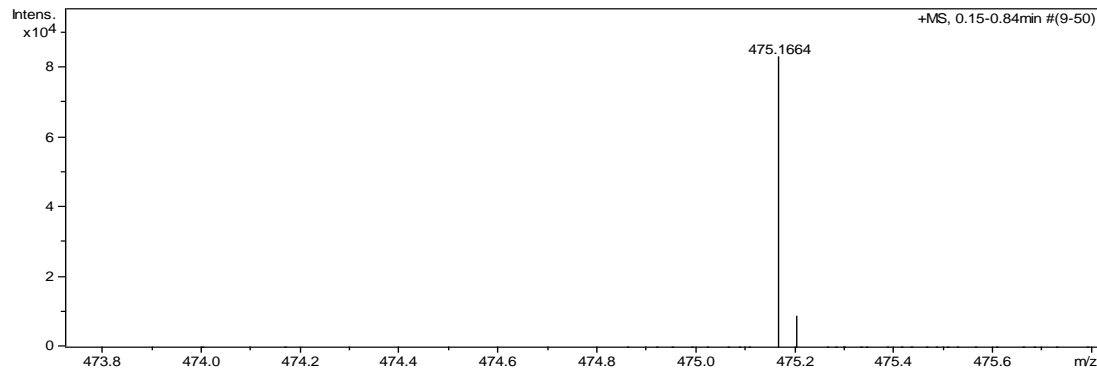
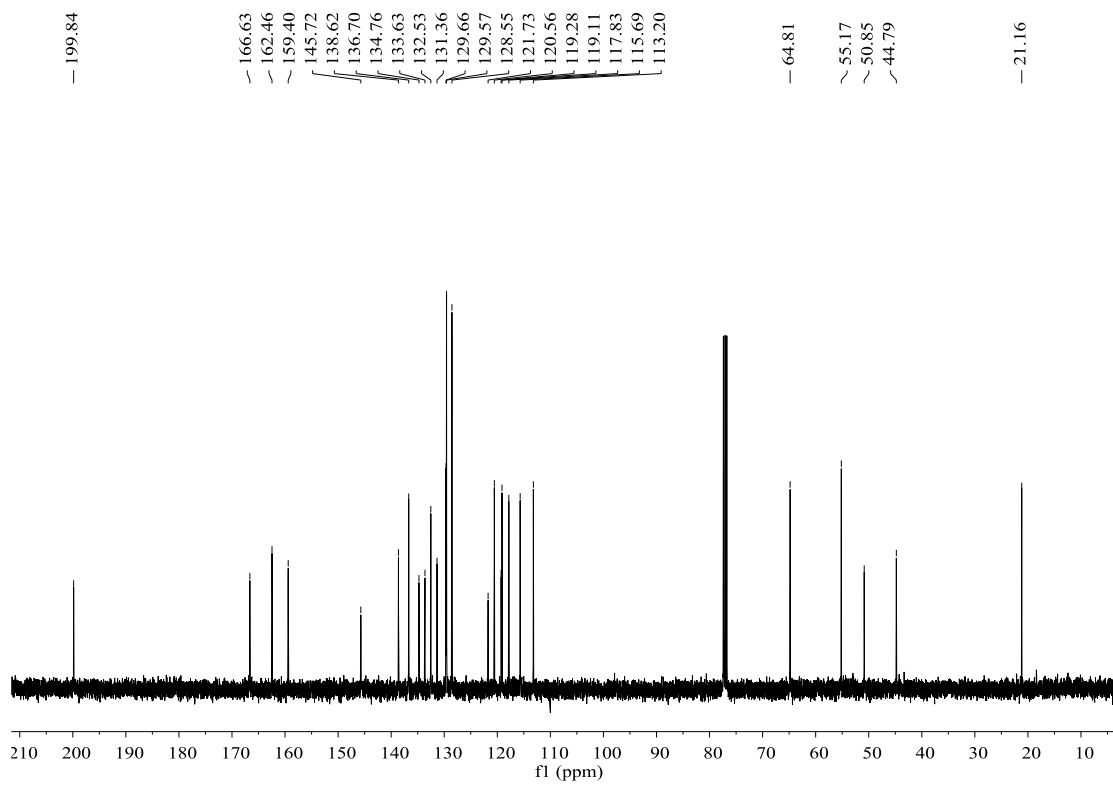
(E)-2-(4-bromophenyl)-1-cyano-3-(2-hydroxybenzoyl)-4-(2-methoxyphenyl)cyclopent-3-ene-1-carboxamide (3d): pale yellow solid, 80%, m.p. 226-227 °C; ^1H NMR (400 MHz, CDCl_3) δ 11.58 (s, 1H, OH), 7.53 (d, $J = 8.0$ Hz, 1H, ArH), 7.41-7.39 (m, 2H, ArH), 7.32-7.30 (m, 1H, ArH), 7.24-7.21 (m, 1H, ArH), 7.19 (s, 1H, ArH), 7.17-7.15 (m, 2H, ArH), 6.88 (t, $J = 7.6$ Hz, 1H, ArH), 6.79 (d, $J = 8.4$ Hz, 1H, ArH), 6.60 (d, $J = 8.4$ Hz, 1H, ArH), 6.49 (t, $J = 7.6$ Hz, 1H, ArH), 5.85 (s, 1H, NH_2), 5.32 (s, 1H, CH), 5.27 (s, 1H, NH_2), 4.08 (d, $J = 17.2$ Hz, 1H, CH_2), 3.59 (s, 3H, OCH_3), 3.37 (d, $J = 17.2$ Hz, 1H, CH_2). ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ 197.0, 165.2, 160.3, 156.1, 143.5, 135.9, 135.8, 135.4, 131.7, 131.5, 130.9, 129.4, 123.7, 123.1, 121.8, 121.0, 120.8, 118.8, 117.5, 111.5, 60.6, 55.2, 52.6, 44.8. MS (m/z): HRMS (ESI) Calcd. for $\text{C}_{27}\text{H}_{21}\text{BrNaN}_2\text{O}_4$ ($[\text{M}+\text{Na}]^+$): 539.0582, found: 539.0585.





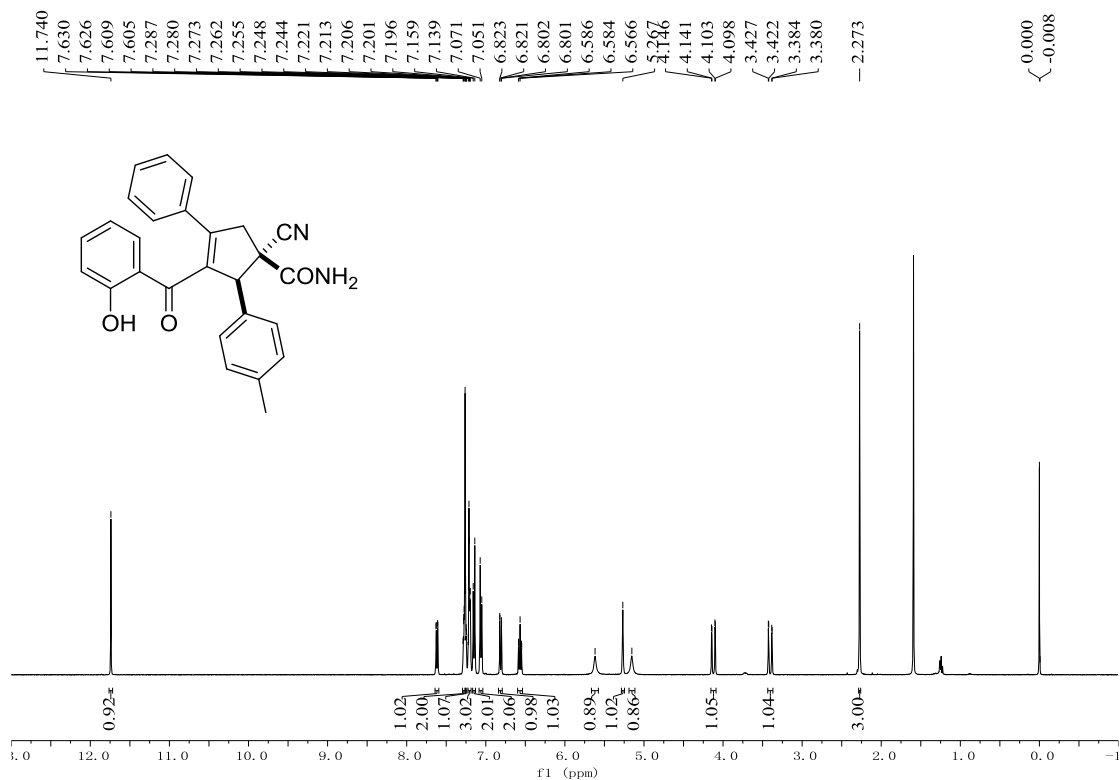
(E)-1-cyano-3-(2-hydroxybenzoyl)-4-(3-methoxyphenyl)-2-(p-tolyl)cyclopent-3-ene-1-carboxamide (3e): pale yellow solid, 56%, m.p. 168-170 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.72 (s, 1H, OH), 7.64 (d, *J* = 7.6 Hz, 1H, ArH), 7.31-7.29 (m, 1H, ArH), 7.16-7.14 (m, 2H, ArH), 7.12-7.10 (m, 1H, ArH), 7.06 (d, *J* = 7.6 Hz, 2H, ArH), 6.87 (d, *J* = 7.6 Hz, 1H, ArH), 6.82 (d, *J* = 8.4 Hz, 1H, ArH), 6.76-6.74 (m, 2H, ArH), 6.60 (t, *J* = 7.6 Hz, 1H, ArH), 5.68 (s, 1H, NH₂), 5.24 (s, 2H, CH, NH₂), 4.10 (d, *J* = 17.2 Hz, 1H, CH₂), 3.64 (s, 3H, OCH₃), 3.39 (d, *J* = 16.8 Hz, 1H, CH₂), 2.27 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 199.8, 166.6, 162.5, 159.4, 145.7, 138.6, 136.7, 134.8, 133.6, 132.5, 131.4, 129.7, 129.6, 128.6, 121.7, 120.6, 119.3, 119.1, 117.8, 115.7, 113.2, 64.8, 55.2, 50.9, 44.8, 21.2. MS (*m/z*): HRMS (ESI) Calcd. for C₂₈H₂₄NaN₂O₄ ([M+Na]⁺): 475.1634, found: 475.1664.

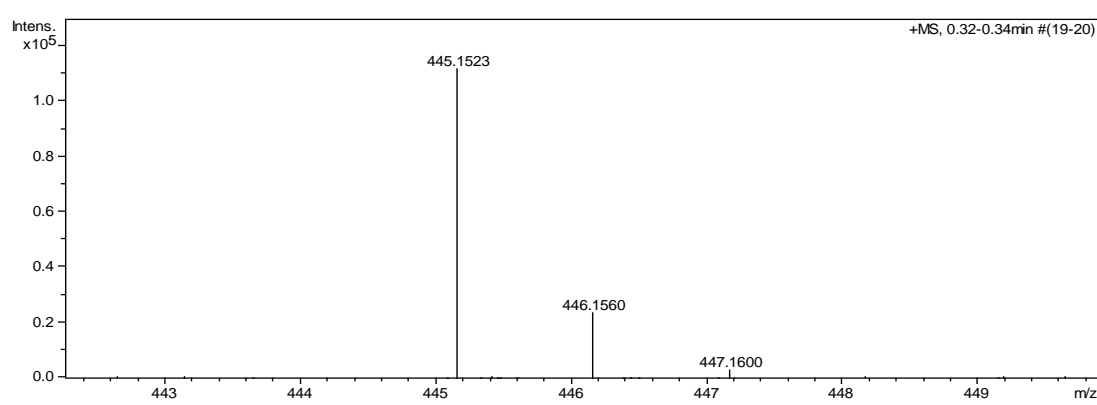
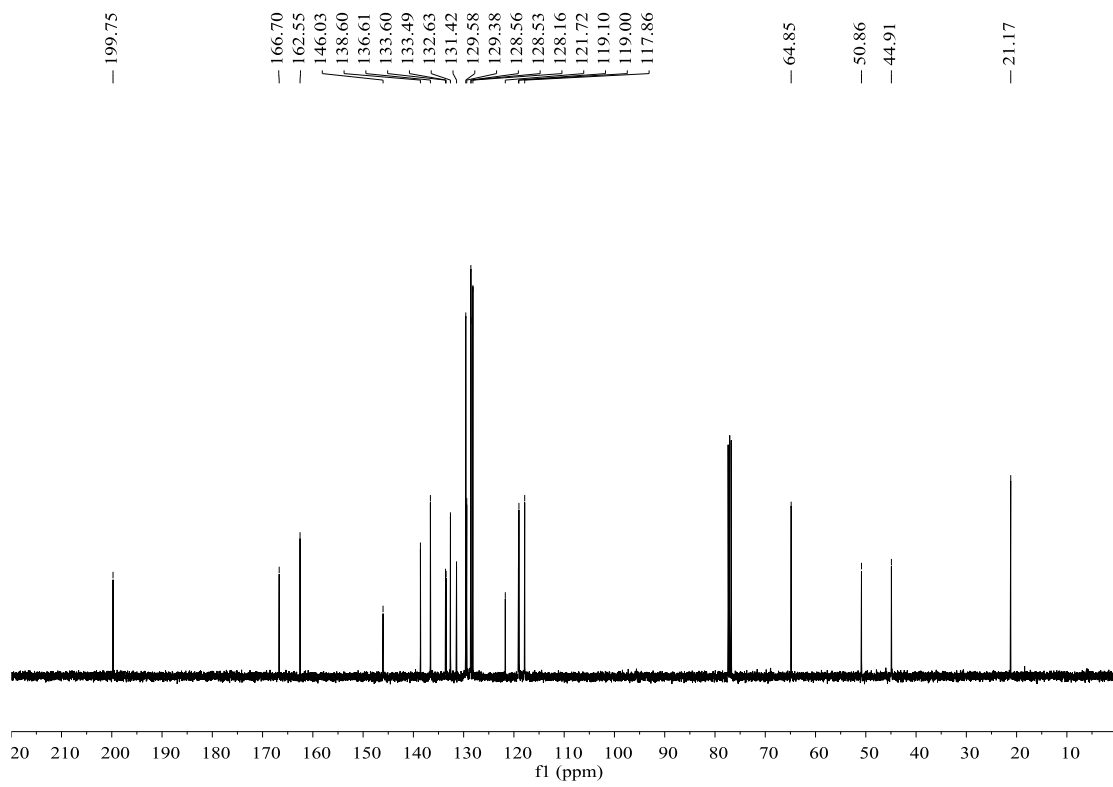




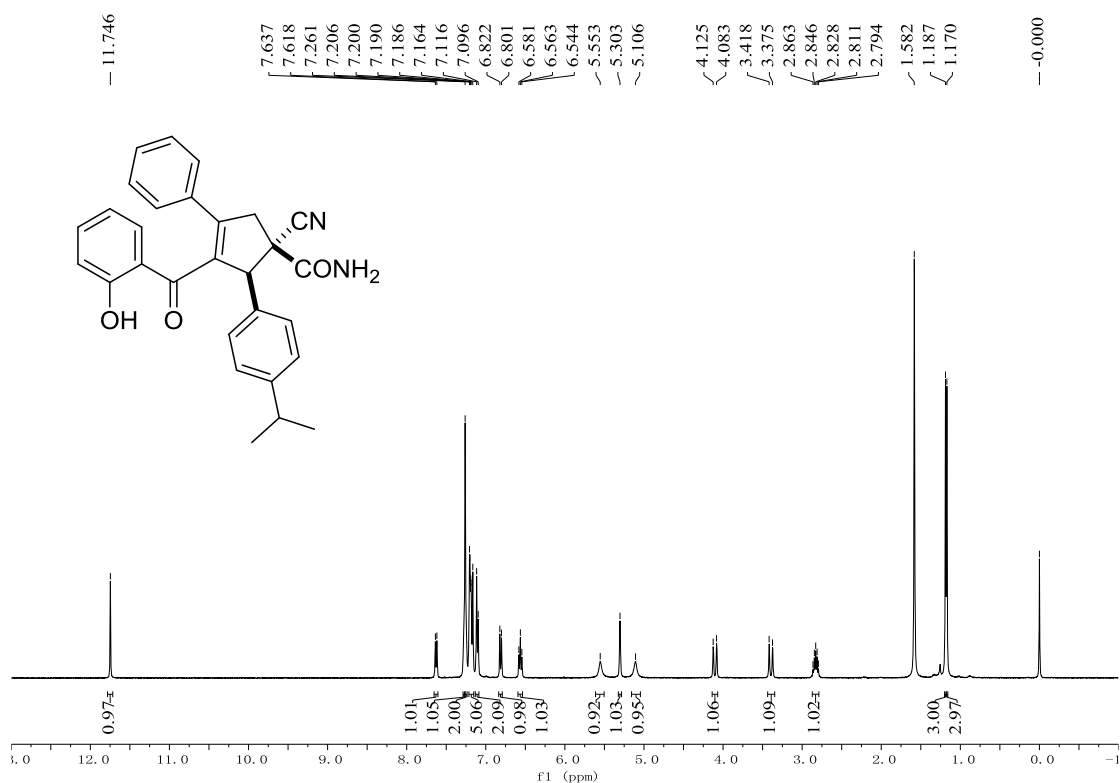
(E)-1-cyano-3-(2-hydroxybenzoyl)-4-phenyl-2-(p-tolyl)cyclopent-3-ene-1-carboxamide (3f):

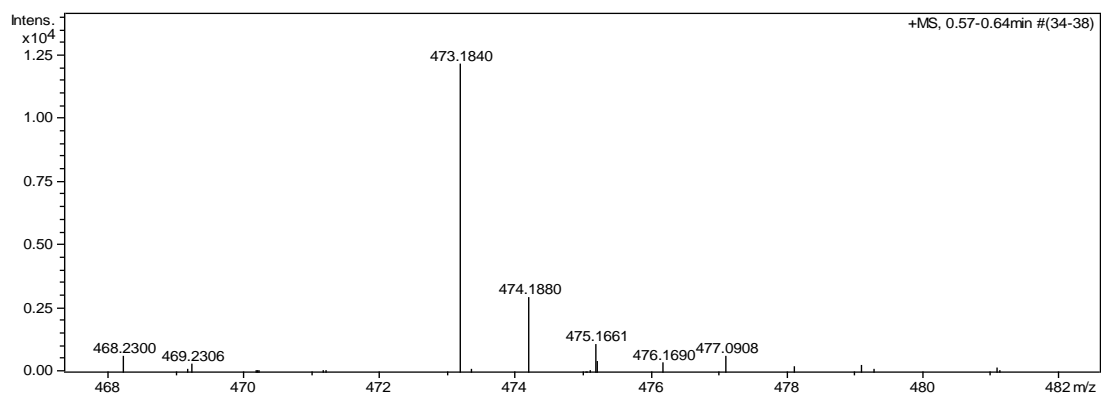
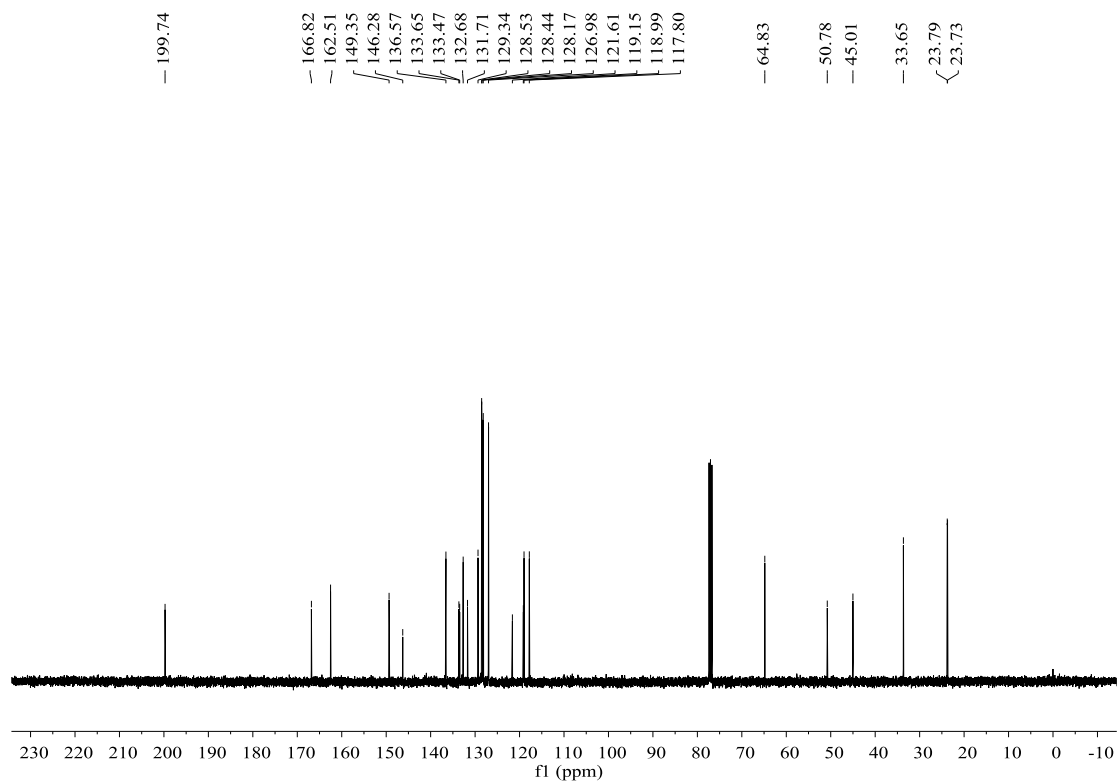
pale yellow solid, 86%, m.p. 201-203 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.74 (s, 1H, OH), 7.63-7.61 (m, 1H, ArH), 7.29-7.27 (m, 2H, ArH), 7.26-7.24 (m, 1H, ArH), 7.22-7.20 (m, 3H, ArH), 7.15 (d, *J* = 8.0 Hz, 2H, ArH), 7.06 (d, *J* = 8.0 Hz, 2H, ArH), 6.82-6.80 (m, 1H, ArH), 6.59-6.55 (m, 1H, ArH), 5.62 (s, 1H, NH₂), 5.27 (s, 1H, CH), 5.15 (s, 1H, NH₂), 4.15-4.10 (m, 1H, CH₂), 3.43-3.38 (m, 1H, CH₂), 2.27 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 199.8, 166.7, 162.6, 146.0, 138.6, 136.6, 133.6, 133.5, 132.6, 131.4, 129.6, 129.4, 128.6, 128.5, 128.2, 121.7, 119.1, 119.0, 117.9, 64.9, 50.9, 44.9, 21.2. MS (*m/z*): HRMS (ESI) Calcd. for C₂₇H₂₂NaN₂O₃ ([M+Na]⁺): 445.1528, found: 445.1523.





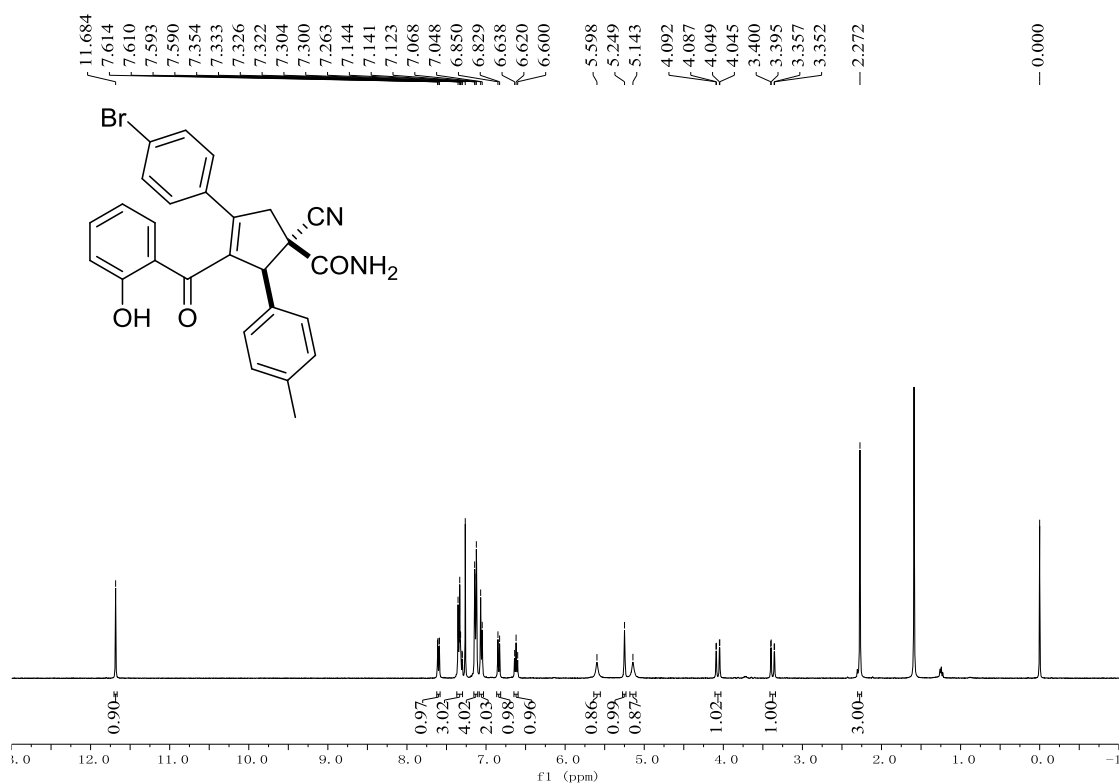
(E)-1-cyano-3-(2-hydroxybenzoyl)-2-(4-isopropylphenyl)-4-phenylcyclopent-3-ene-1-carboxamide (3g): pale yellow solid, 85%, m.p. 177-179 °C; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 11.75 (s, 1H, OH), 7.63 (d, $J = 7.6$ Hz, 1H, ArH), 7.26 (s, 3H, ArH), 7.21-7.16 (m, 4H, ArH), 7.11 (d, $J = 8.0$ Hz, 2H, ArH), 6.81 (d, $J = 8.4$ Hz, 1H, ArH), 6.56 (t, $J = 7.6$ Hz, 1H, ArH), 5.55 (s, 1H, NH_2), 5.30 (s, 1H, CH), 5.11 (s, 1H, NH_2), 4.10 (d, $J = 16.8$ Hz, 1H, CH_2), 3.40 (d, $J = 17.2$ Hz, 1H, CH_2), 2.86-2.79 (m, 1H, CH), 1.19 (s, 3H, CH_3), 1.17 (s, 3H, CH_3). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 199.7, 166.8, 162.5, 149.4, 146.3, 136.6, 133.7, 133.5, 132.7, 131.7, 129.3, 128.5, 128.4, 128.2, 127.0, 121.6, 119.2, 119.0, 117.8, 64.8, 50.8, 45.0, 33.7, 23.8, 23.7. MS (m/z): HRMS (ESI) Calcd. for $\text{C}_{29}\text{H}_{26}\text{NaN}_2\text{O}_3$ ($[\text{M}+\text{Na}]^+$): 473.1841, found: 473.1840.

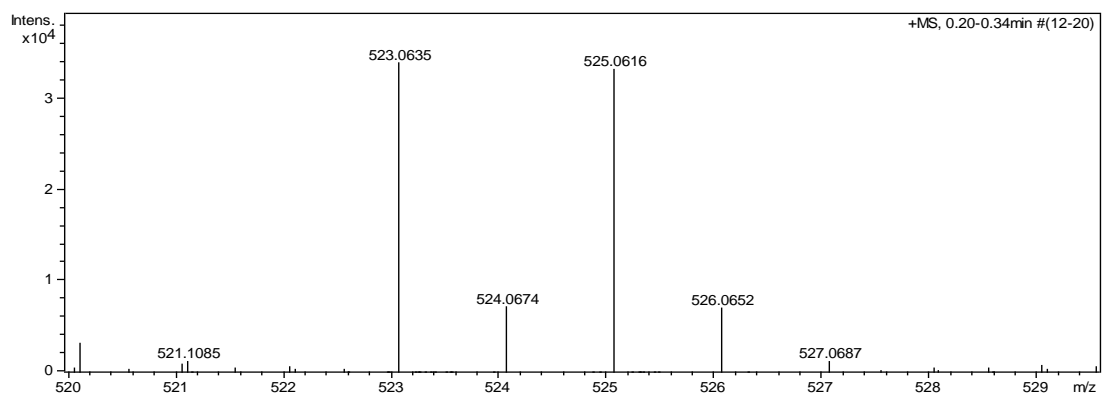
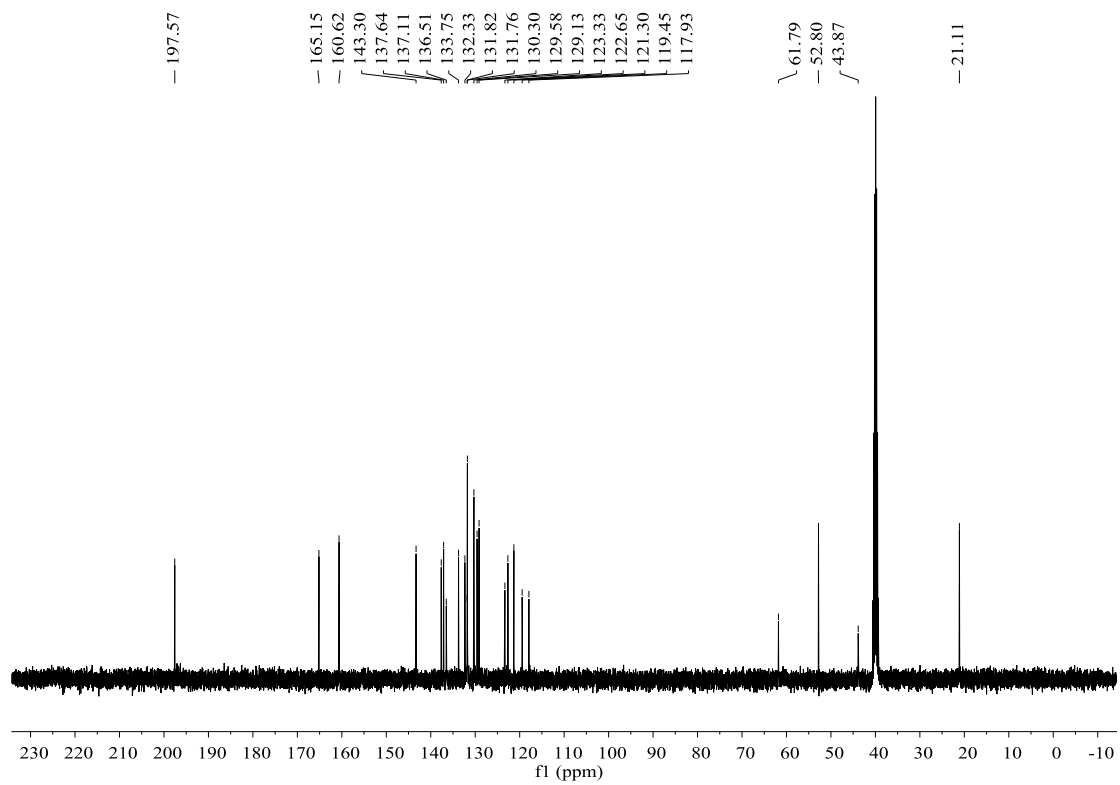




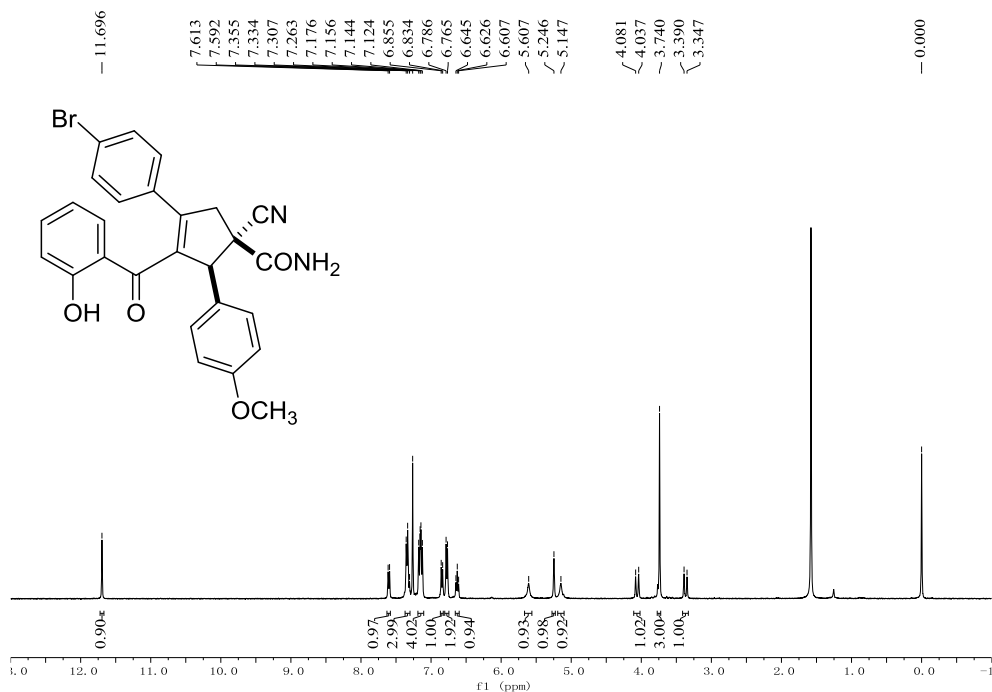
(E)-4-(4-bromophenyl)-1-cyano-3-(2-hydroxybenzoyl)-2-(p-tolyl)cyclopent-3-ene-1-

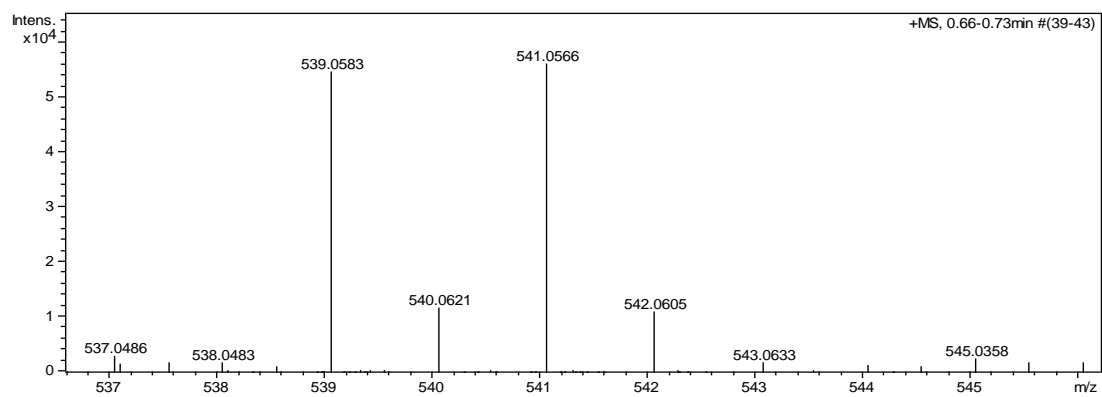
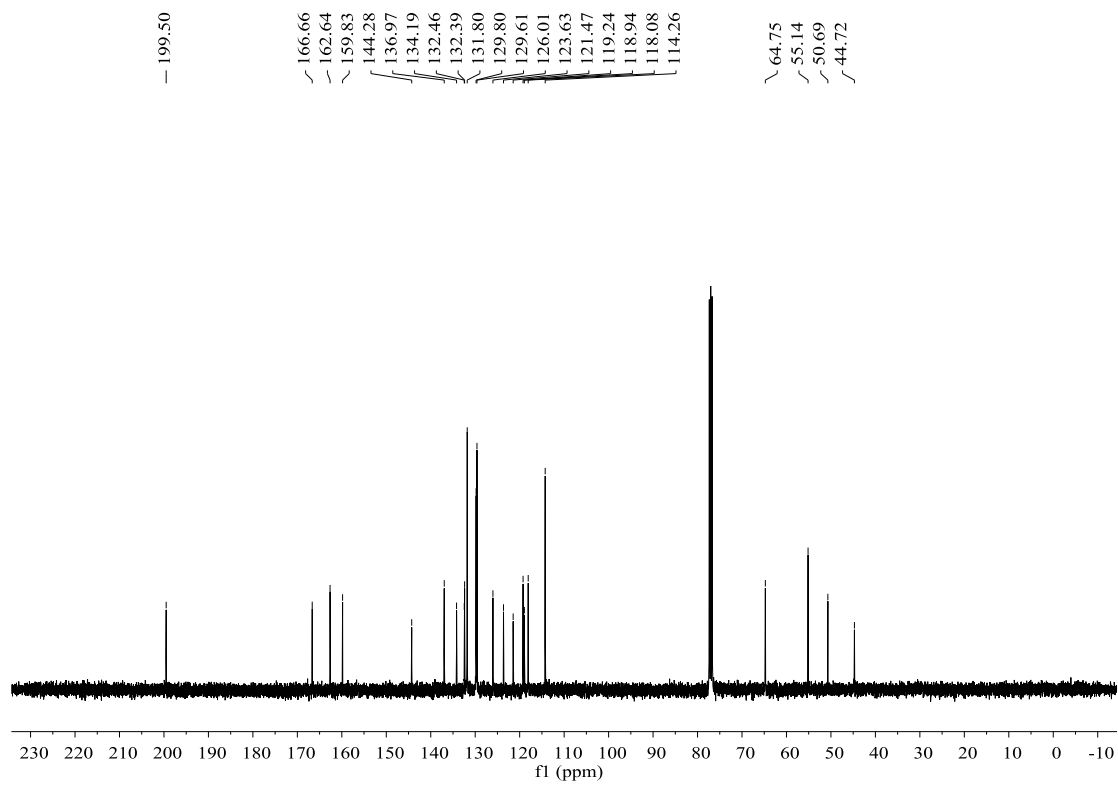
carboxamide (3h): pale yellow solid, 75%, m.p. 206-208 °C; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 11.68 (s, 1H, OH), 7.61-7.59 (m, 1H, ArH), 7.35-7.30 (m, 3H, ArH), 7.14-7.12 (m, 4H, ArH), 7.06 (d, $J = 8.0$ Hz, 2H, ArH), 6.84 (d, $J = 8.4$ Hz, 1H, ArH), 6.62 (t, $J = 8.0$ Hz, 1H, ArH), 5.60 (s, 1H, NH_2), 5.25 (s, 1H, CH), 5.14 (s, 1H, NH_2), 4.09-4.05 (m, 1H, CH_2), 3.40-3.35 (m, 1H, CH_2), 2.27 (s, 3H, CH_3). $^{13}\text{C NMR}$ (100 MHz, $\text{DMSO-}d_6$) δ 197.6, 165.2, 160.6, 143.3, 137.6, 137.1, 136.5, 133.8, 132.3, 131.8, 131.7, 130.3, 129.6, 129.1, 123.3, 122.7, 121.3, 119.5, 117.9, 61.8, 52.8, 43.9, 21.1. MS (m/z): HRMS (ESI) Calcd. for $\text{C}_{27}\text{H}_{21}\text{BrNaN}_2\text{O}_3$ ($[\text{M}+\text{Na}]^+$): 523.0633, found: 523.0635.



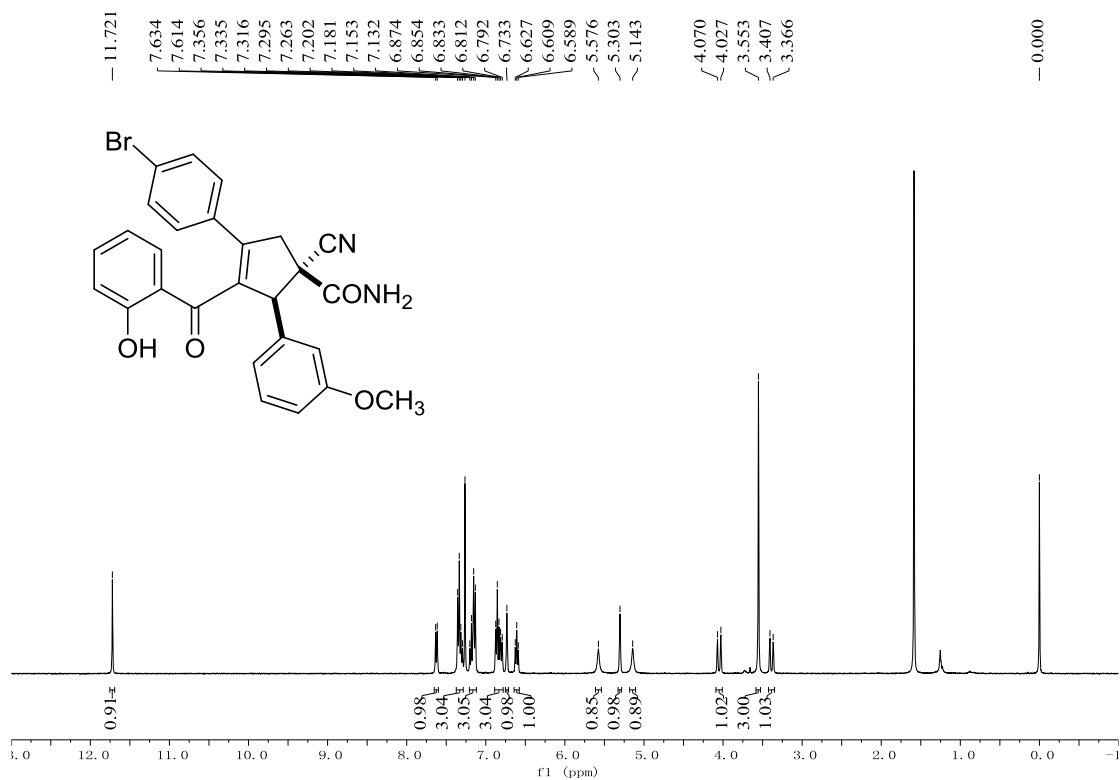


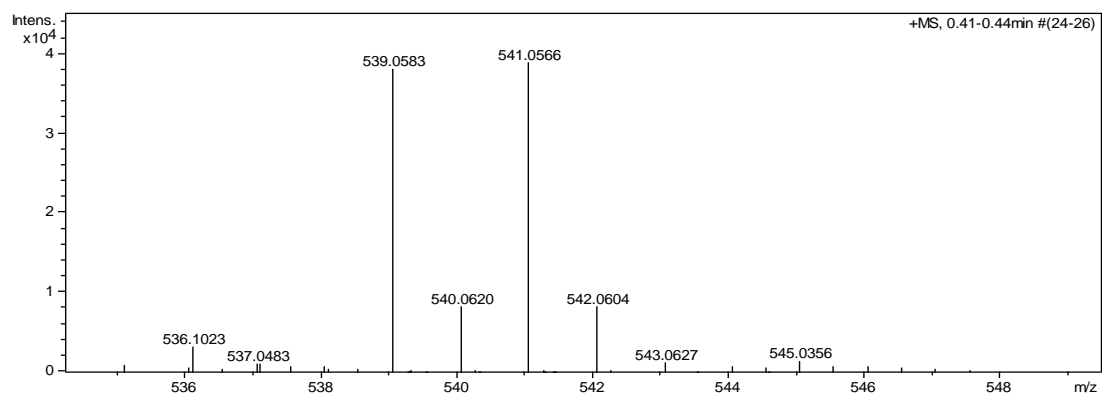
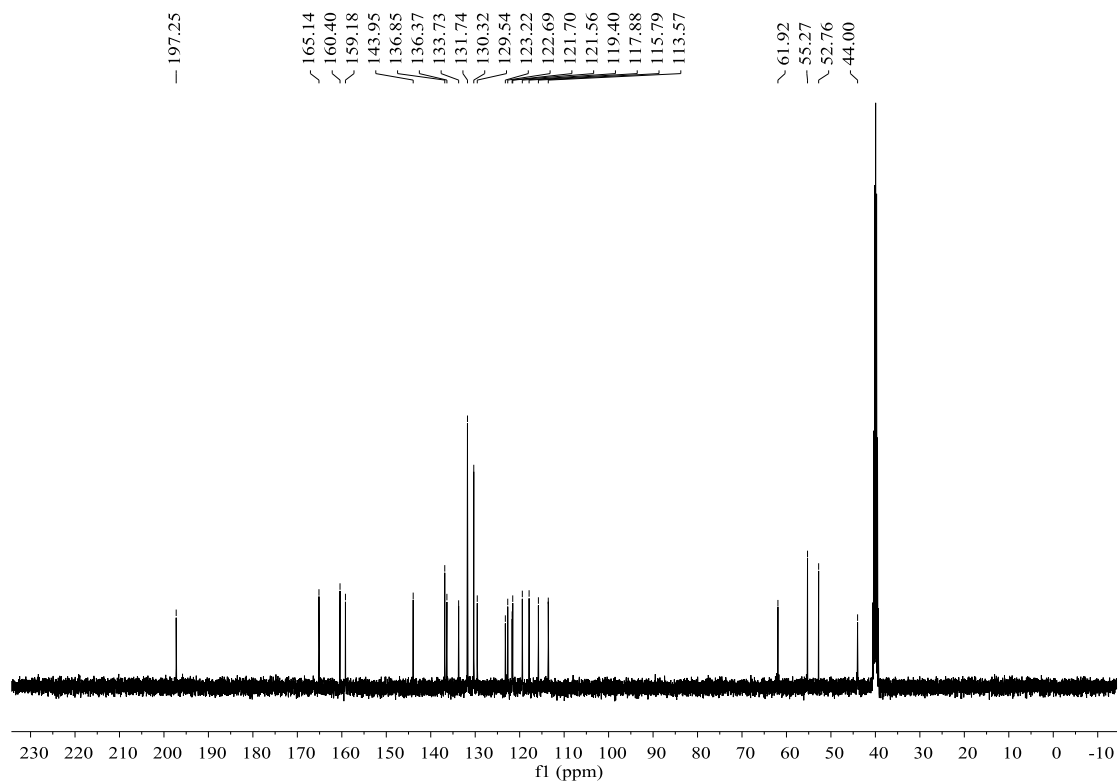
(E)-4-(4-bromophenyl)-1-cyano-3-(2-hydroxybenzoyl)-2-(4-methoxyphenyl)cyclopent-3-ene-1-carboxamide (3i): pale yellow solid, 62%, m.p. 178-180 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.70 (s, 1H, OH), 7.60 (d, *J* = 8.4 Hz, 1H, ArH), 7.36-7.31 (m, 3H, ArH), 7.18-7.12 (m, 4H, ArH), 6.84 (d, *J* = 8.4 Hz, 1H, ArH), 6.78 (d, *J* = 8.4 Hz, 2H, ArH), 6.63 (t, *J* = 7.6 Hz, 1H, ArH), 5.61 (s, 1H, NH₂), 5.25 (s, 1H, CH), 5.15 (s, 1H, NH₂), 4.06 (d, *J* = 17.6 Hz, 1H, CH₂), 3.74 (s, 3H, OCH₃), 3.37 (d, *J* = 17.2 Hz, 1H, CH₂). ¹³C NMR (100 MHz, CDCl₃) δ 199.5, 166.7, 162.6, 159.8, 144.3, 137.0, 134.2, 132.5, 132.4, 131.8, 129.8, 129.6, 126.0, 123.6, 121.5, 119.2, 118.9, 118.1, 114.3, 64.8, 55.1, 50.7, 44.7. MS (*m/z*): HRMS (ESI) Calcd. for C₂₇H₂₁BrNaN₂O₄ ([M+Na]⁺): 539.0582, found: 539.0583.



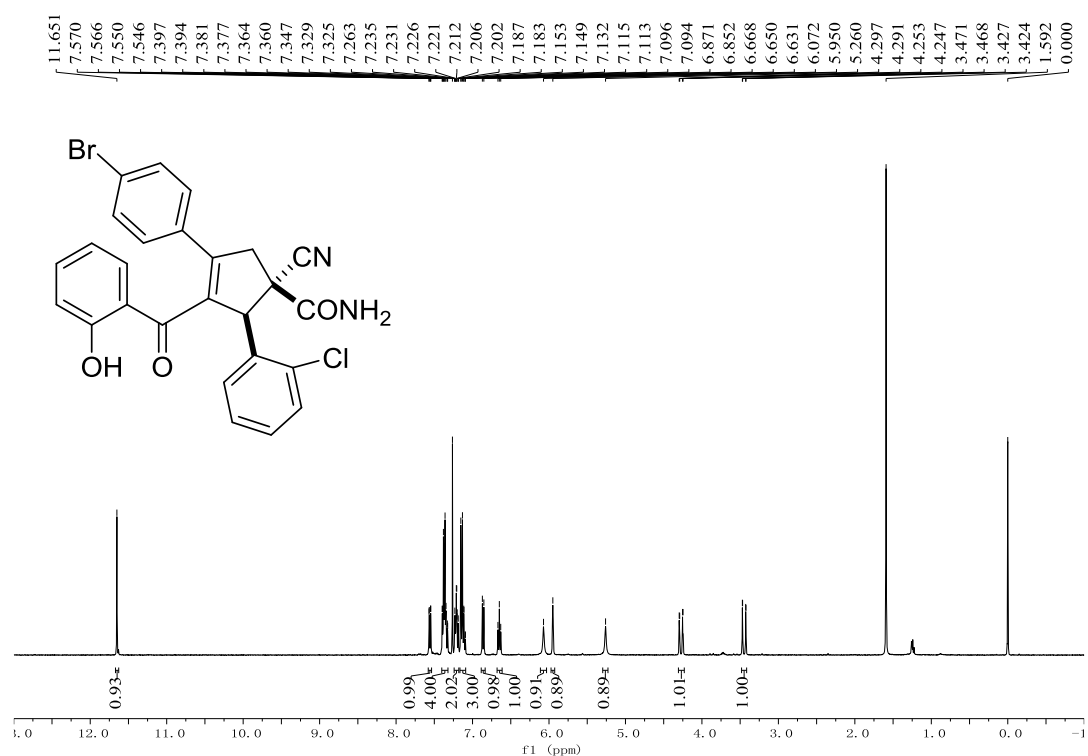


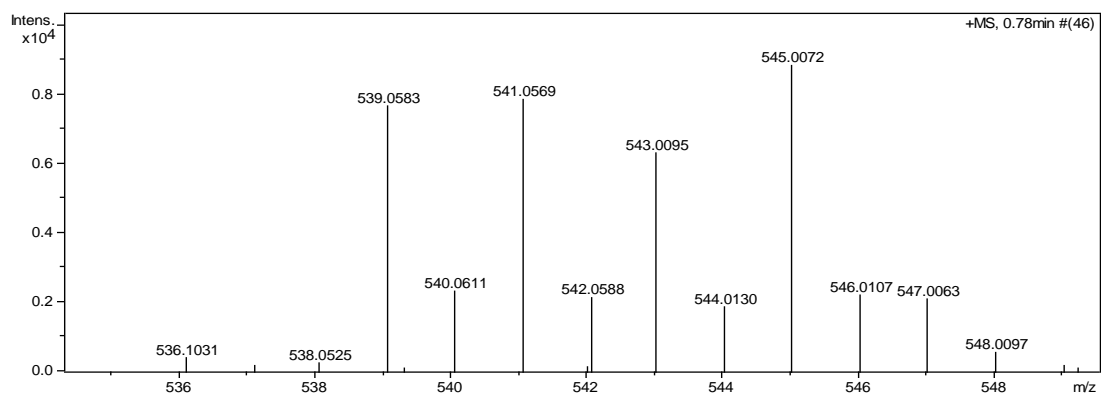
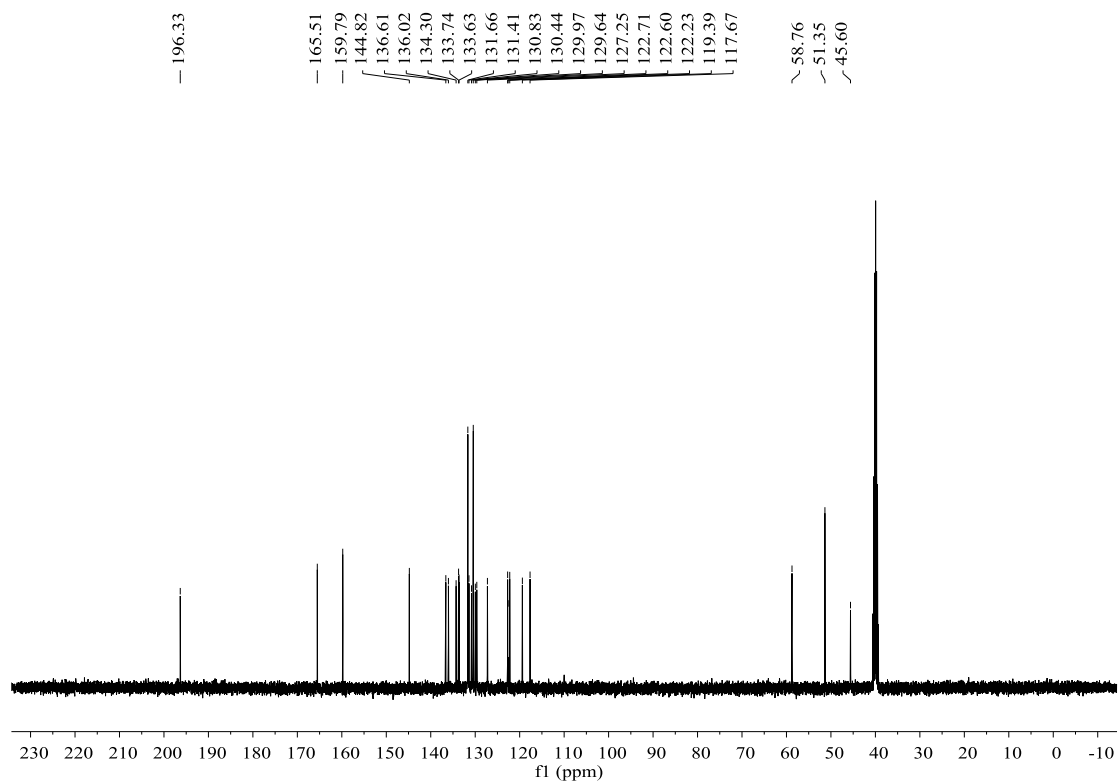
(E)-4-(4-bromophenyl)-1-cyano-3-(2-hydroxybenzoyl)-2-(3-methoxyphenyl)cyclopent-3-ene-1-carboxamide (3j): pale yellow solid, 72%, m.p. 236-238 °C; ^1H NMR (400 MHz, CDCl_3) δ 11.72 (s, 1H, OH), 7.62 (d, $J = 8.0$ Hz, 1H, ArH), 7.36-7.30 (m, 3H, ArH), 7.20-7.13 (m, 3H, ArH), 6.87-6.79 (m, 3H, ArH), 6.73 (s, 1H, ArH), 6.61 (t, $J = 8.0$ Hz, 1H, ArH), 5.58 (s, 1H, NH_2), 5.30 (s, 1H, CH), 5.14 (s, 1H, NH_2), 4.05 (d, $J = 17.2$ Hz, 1H, CH_2), 3.55 (s, 3H, OCH_3), 3.39 (d, $J = 16.4$ Hz, 1H, CH_2). ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ 197.3, 165.1, 160.4, 159.2, 144.0, 136.9, 136.4, 133.7, 131.7, 130.3, 129.5, 123.2, 122.7, 121.7, 121.6, 119.4, 117.9, 115.8, 113.6, 61.9, 55.3, 52.8, 44.0. MS (m/z): HRMS (ESI) Calcd. for $\text{C}_{27}\text{H}_{21}\text{BrNaN}_2\text{O}_4$ ($[\text{M}+\text{Na}]^+$): 539.0582, found: 539.0583.



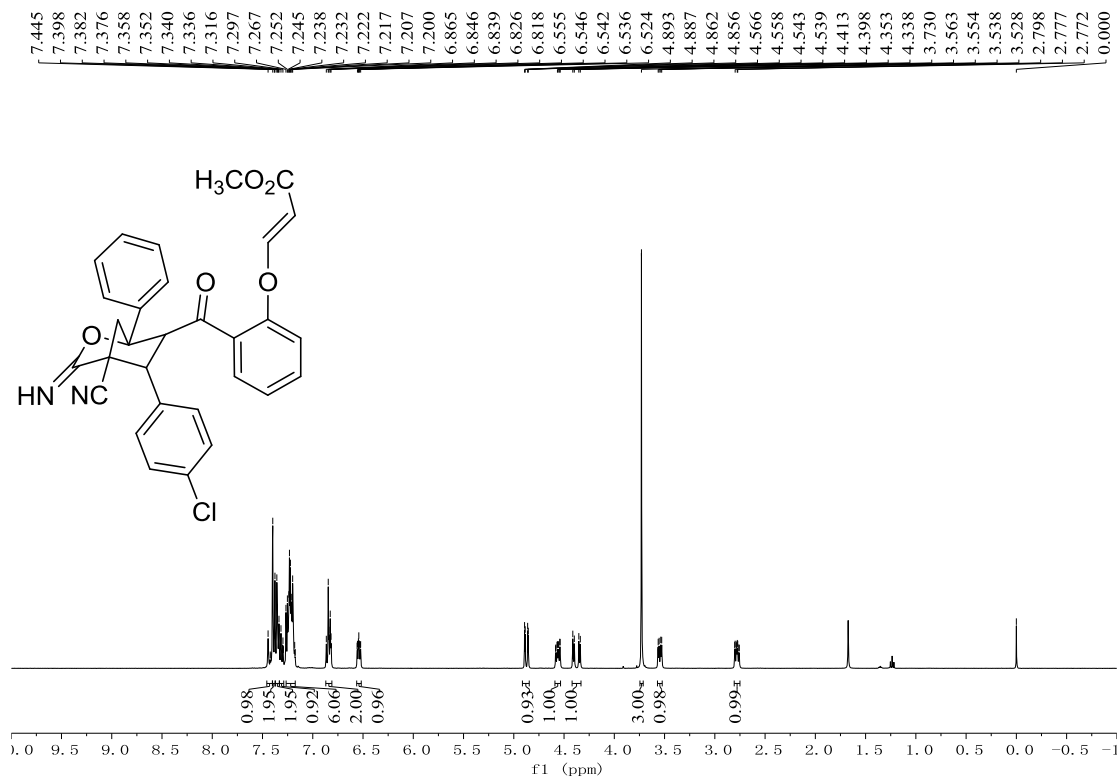


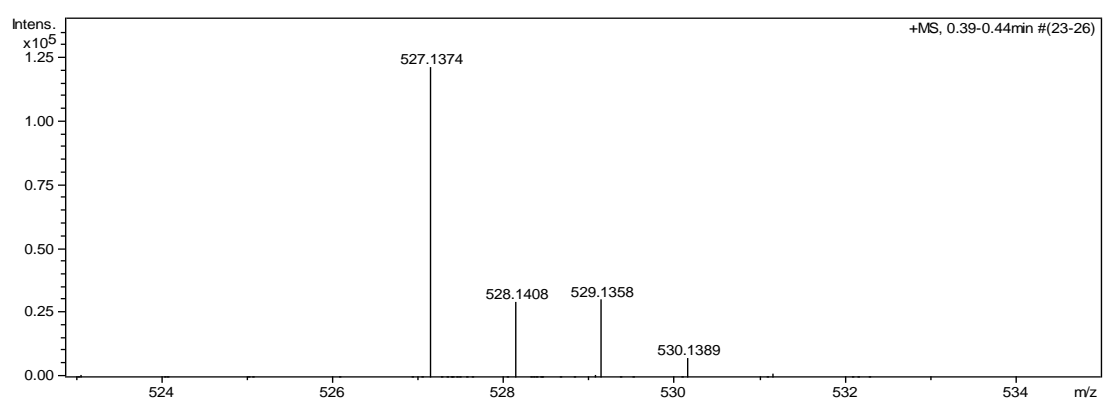
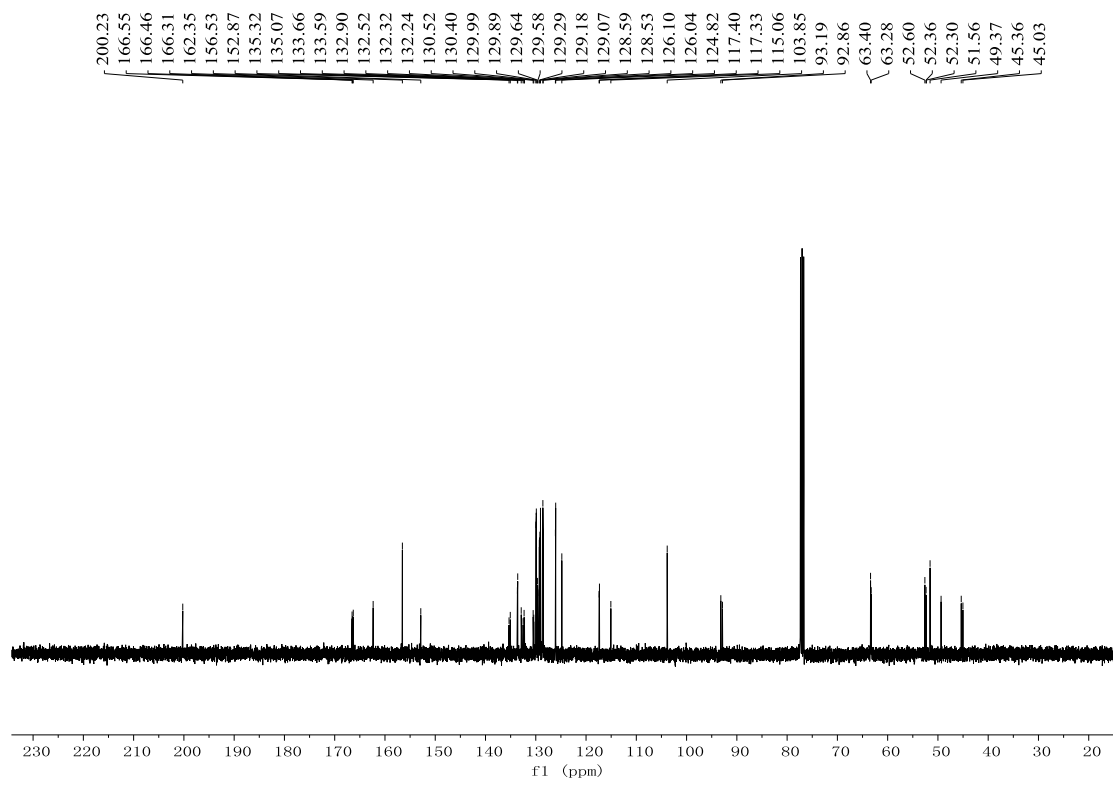
(E)-4-(4-bromophenyl)-2-(2-chlorophenyl)-1-cyano-3-(2-hydroxybenzoyl)cyclopent-3-ene-1-carboxamide (3k): pale yellow solid, 74%, m.p. 238-240 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.65 (s, 1H, OH), 7.57-7.55 (m, 1H, ArH), 7.40-7.33 (m, 4H, ArH), 7.24-7.18 (m, 2H, ArH), 7.15-7.09 (m, 3H, ArH), 6.86 (d, *J* = 7.6 Hz, 1H, ArH), 6.65 (t, *J* = 7.6 Hz, 1H, ArH), 6.07 (s, 1H, NH₂), 5.95 (s, 1H, CH), 5.26 (s, 1H, NH₂), 4.30-4.25 (m, 1H, CH₂), 3.47-3.42 (m, 1H, CH₂). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 196.3, 165.5, 159.8, 144.8, 136.6, 136.0, 134.3, 133.7, 133.6, 131.7, 131.4, 130.8, 130.4, 130.0, 129.6, 127.3, 122.7, 122.6, 122.2, 119.4, 117.7, 58.8, 51.4, 45.6. MS (*m/z*): HRMS (ESI) Calcd. for C₂₆H₁₈ClBrNaN₂O₃ ([M+Na]⁺): 543.0087, found: 543.0095.



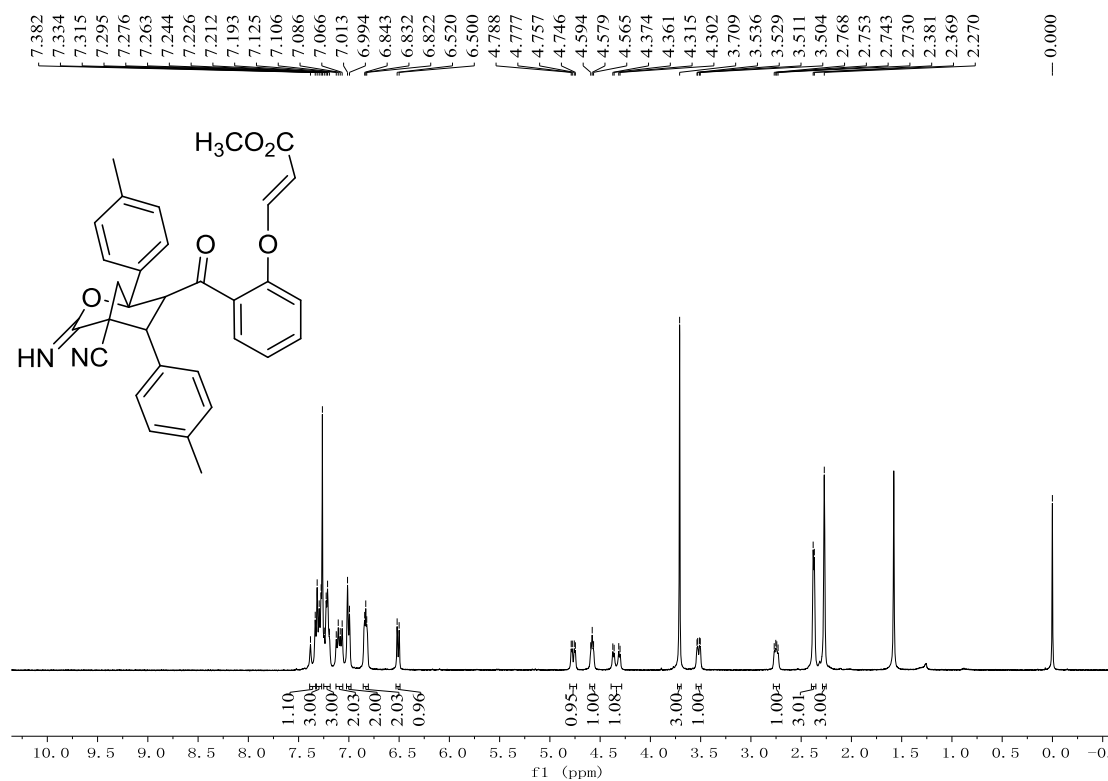


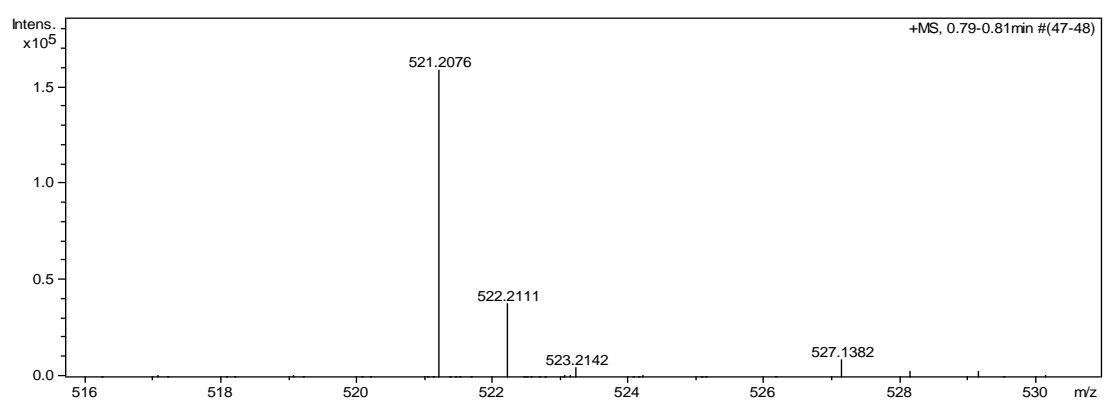
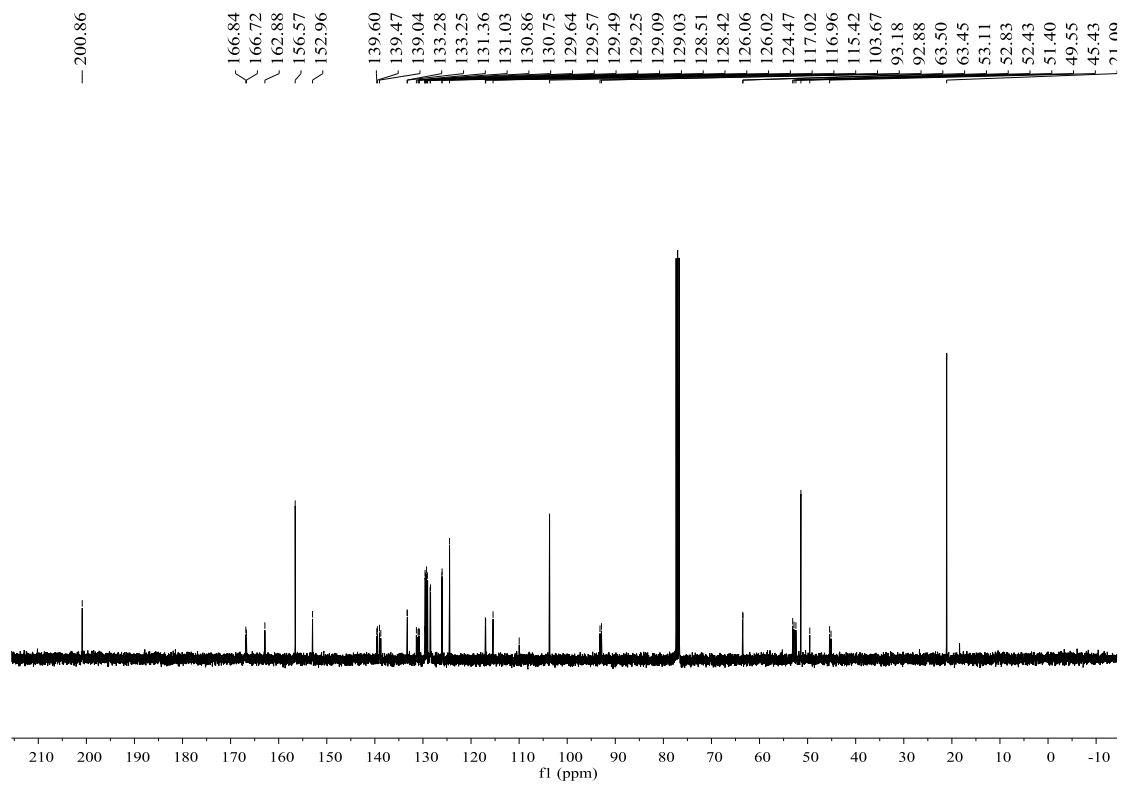
Methyl **(*E*)-3-(2-(*rel*-(1*S*,4*S*,5*R*)-5-(4-chlorophenyl)-4-cyano-3-imino-1-phenyl-2-oxabicyclo[2.2.1]heptane-6-carbonyl)phenoxy)acrylate (5a)**: pale yellow solid, 85%, m.p. 179-181 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.45 (s, 1H, ArH), 7.40-7.38 (m, 2H, ArH), 7.36-7.34 (m, 2H, ArH), 7.32-7.29 (m, 1H, ArH), 7.25-7.18 (m, 6H, ArH), 6.87-6.82 (m, 2H, CH), 6.56-6.52 (m, 1H, ArH), 4.89-4.86 (m, 1H, CH), 4.59-4.54 (m, 1H, NH), 4.41-4.34 (m, 1H, CH), 3.73 (s, 3H, OCH₃), 3.56-3.53 (m, 1H, CH₂), 2.80-2.76 (m, 1H, CH₂). ¹³C NMR (100 MHz, CDCl₃) δ 200.2, 166.6, 166.5, 166.3, 162.4, 156.5, 152.9, 135.3, 135.1, 133.7, 133.6, 132.9, 132.5, 132.3, 132.2, 130.5, 130.4, 130.0, 129.9, 129.6, 129.5, 129.3, 129.2, 129.1, 128.6, 128.5, 126.1, 126.0, 124.8, 117.4, 117.3, 115.1, 103.9, 93.2, 92.9, 63.4, 63.3, 52.6, 52.4, 52.3, 51.6, 49.4, 45.4, 45.0. MS (*m/z*): HRMS (ESI) Calcd. for C₃₀H₂₄ClN₂O₅ ([M+H]⁺): 527.1374, found: 527.1374.



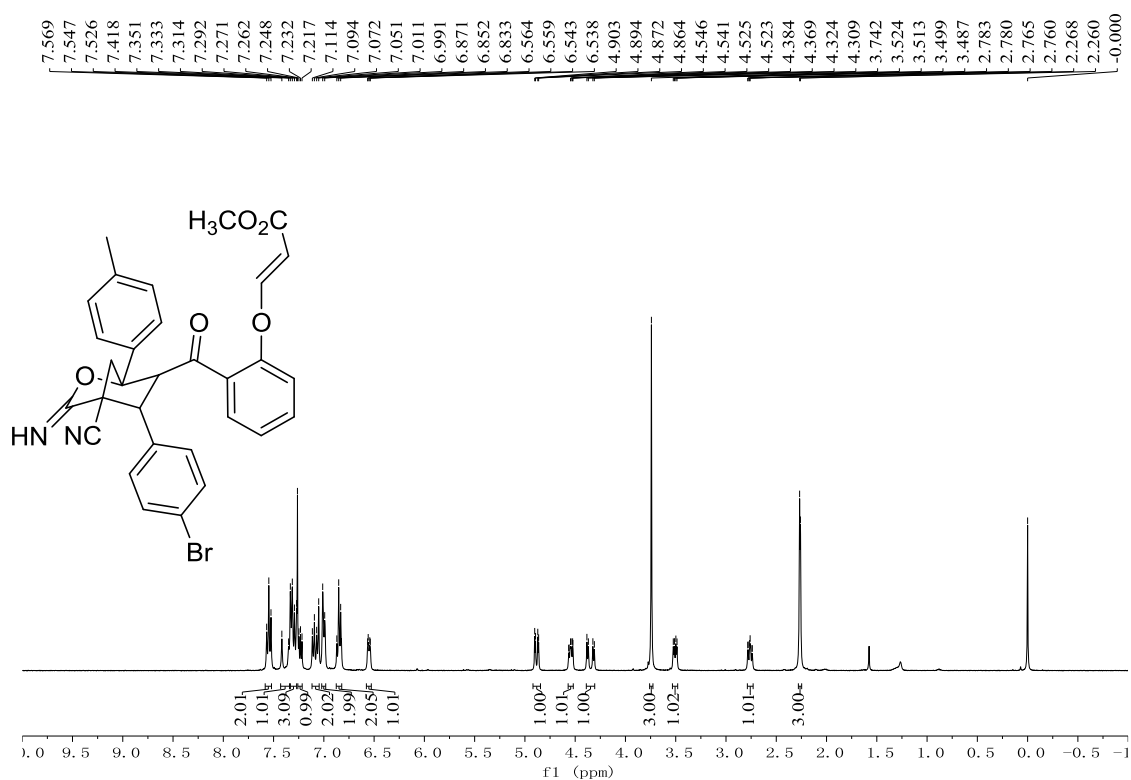


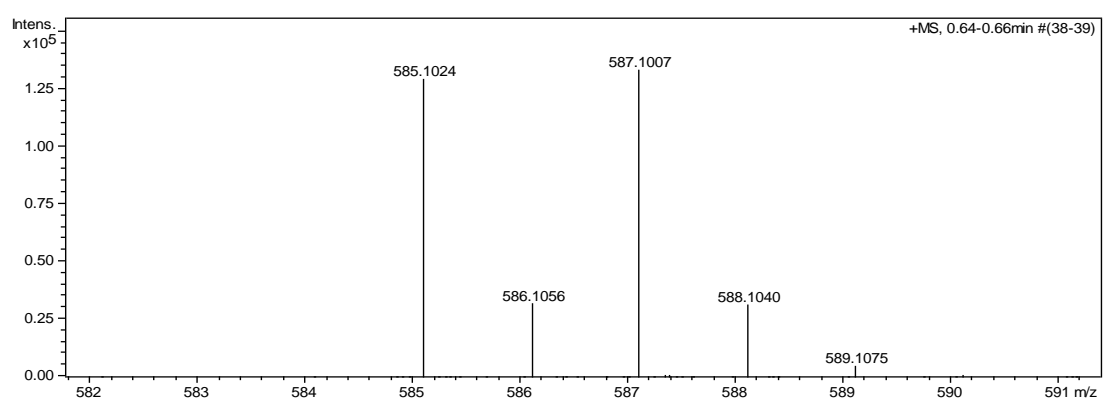
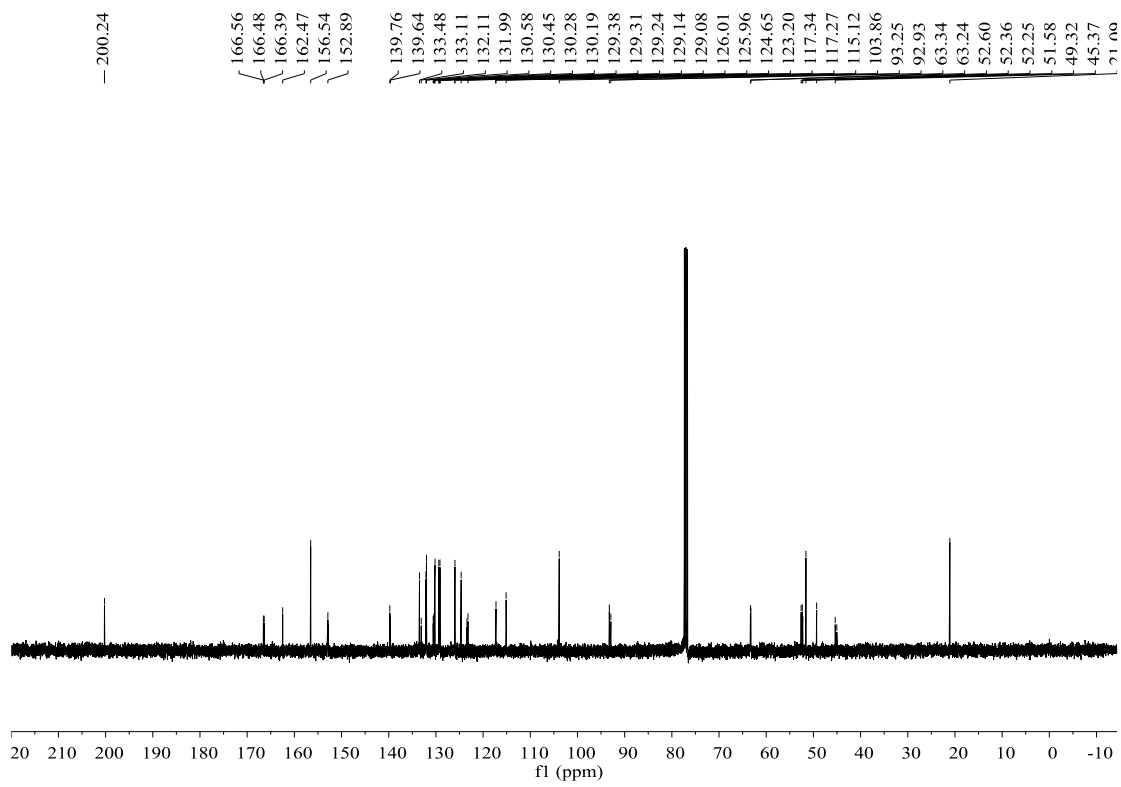
Methyl (*E*)-3-(2-(*rel*-(1*S*,4*S*,5*R*)-4-cyano-3-imino-1,5-di-*p*-tolyl-2-oxabicyclo[2.2.1]heptane-6-carbonyl)phenoxy)acrylate (5b**):** white solid, 90%, m.p. 149-151 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.38-7.33 (m, 1H, ArH), 7.32-7.28 (m, 3H, ArH), 7.24-7.19 (m, 3H, ArH), 7.13-7.07 (m, 2H, ArH), 7.00 (d, *J* = 7.6 Hz, 2H, ArH), 6.84-6.82 (m, 2H, CH), 6.51 (d, *J* = 8.0 Hz, 1H, ArH), 4.79-4.75 (m, 1H, CH), 4.58 (t, *J* = 6.0 Hz, 1H, NH), 4.37-4.30 (m, 1H, CH), 3.71 (s, 3H, OCH₃), 3.54-3.50 (m, 1H, CH₂), 2.77-2.73 (m, 1H, CH₂), 2.37 (d, *J* = 4.8 Hz, 3H, CH₃), 2.27 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 200.9, 166.8, 166.7, 162.9, 156.6, 153.0, 139.6, 139.5, 139.0, 138.8, 133.3, 133.2, 131.4, 131.0, 130.9, 130.8, 129.6, 129.5, 129.4, 129.3, 129.1, 129.0, 128.5, 128.4, 126.1, 126.0, 124.5, 117.0, 116.9, 115.4, 110.0, 103.7, 93.2, 92.9, 63.5, 63.4, 53.1, 52.8, 52.4, 51.4, 49.6, 45.4, 45.1, 21.1. MS (*m/z*): HRMS (ESI) Calcd. for C₃₂H₂₉N₂O₅ ([M+H]⁺): 521.2076, found: 521.2076.



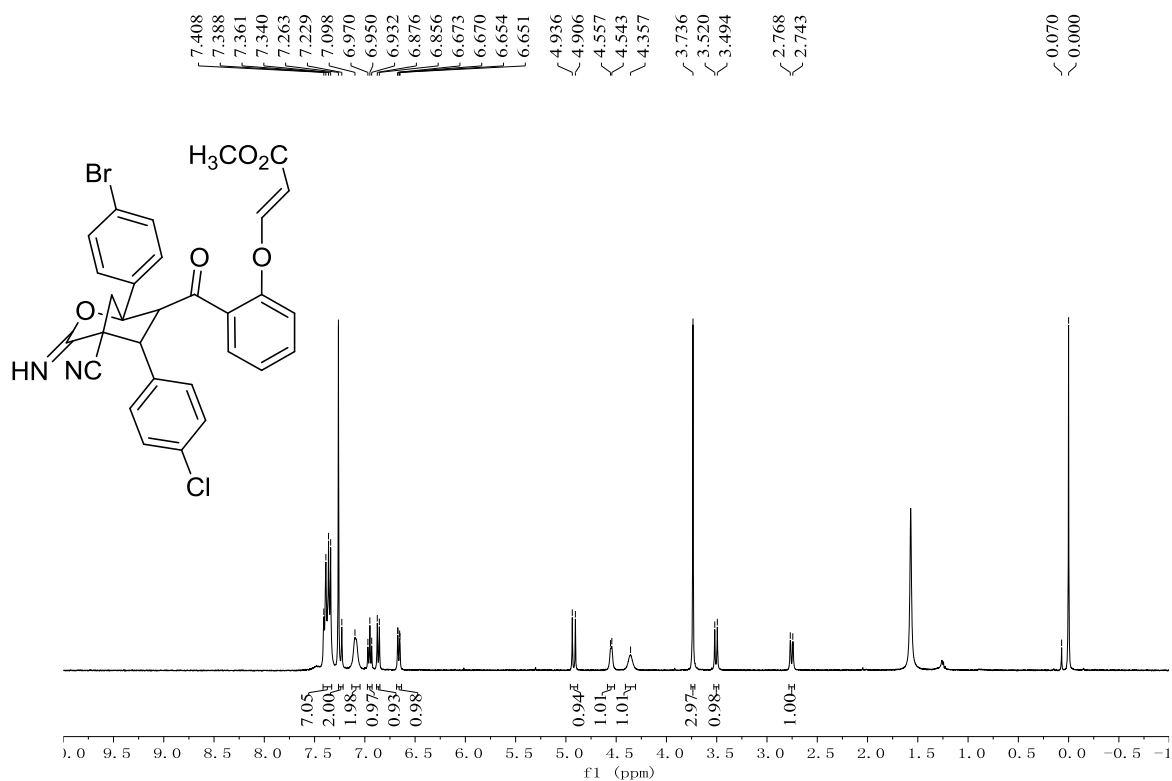


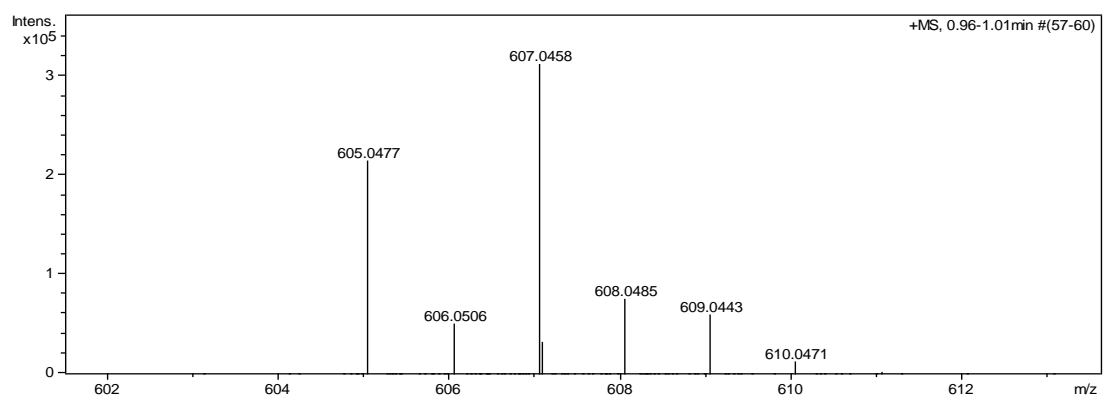
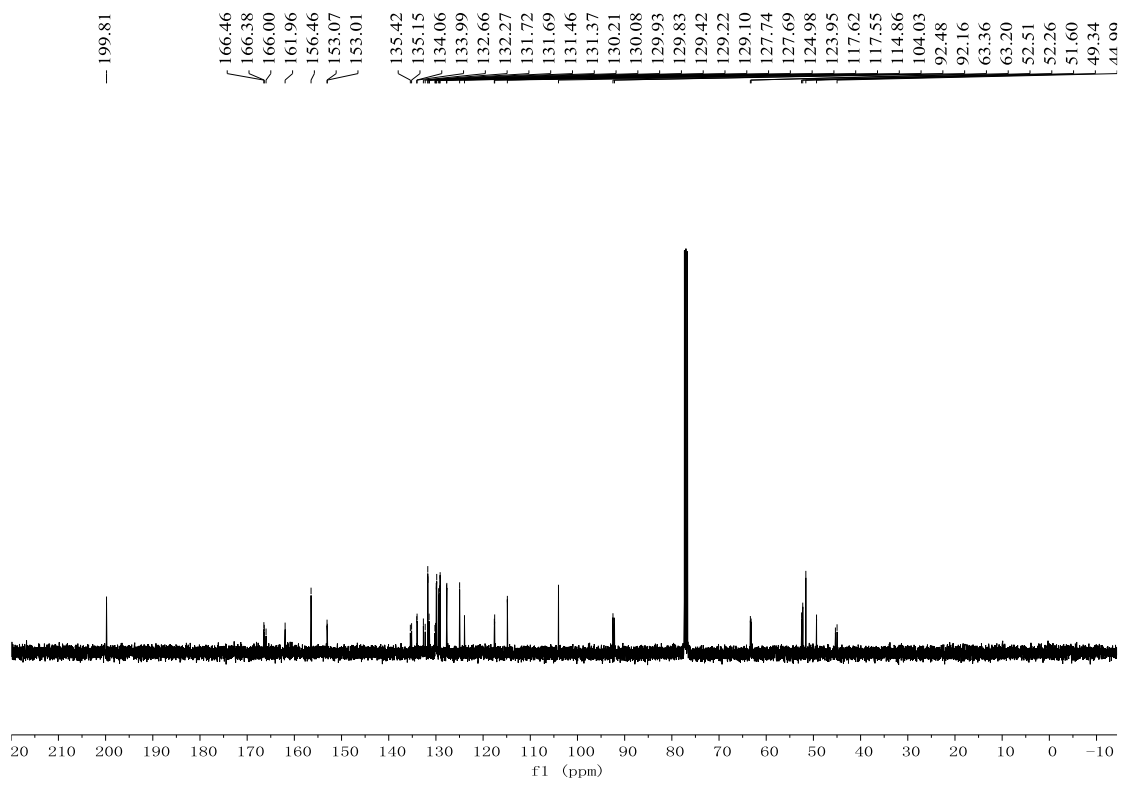
Methyl *(E)*-3-(2-(*rel*-(1*S*,4*S*,5*R*)-5-(4-bromophenyl)-4-cyano-3-imino-1-(*p*-tolyl)-2-oxabicyclo[2.2.1]heptane-6-carbonyl)phenoxy)acrylate (**5c**): white solid, 92%, m.p. 169-171 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.55 (t, *J* = 8.4 Hz, 2H, ArH), 7.42-7.35 (m, 1H, ArH), 7.33-7.27 (m, 3H, ArH), 7.25-7.22 (m, 1H, ArH), 7.11-7.05 (m, 2H, ArH), 7.00 (d, *J* = 8.0 Hz, 2H, ArH), 6.87-6.83 (m, 2H, CH), 6.56-6.54 (m, 1H, ArH), 4.90-4.86 (m, 1H, CH), 4.56-4.52 (m, 1H, NH), 4.38-4.31 (m, 1H, CH), 3.74 (s, 3H, OCH₃), 3.52-3.49 (m, 1H, CH₂), 2.78-2.74 (m, 1H, CH₂), 2.26 (d, *J* = 3.2 Hz, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 200.2, 166.6, 166.5, 166.4, 162.5, 156.5, 152.9, 139.8, 139.6, 133.5, 133.1, 132.1, 132.0, 130.6, 130.5, 130.3, 130.2, 129.4, 129.3, 129.2, 129.1, 129.0, 126.0, 125.9, 124.7, 123.4, 123.2, 117.3, 117.2, 115.1, 103.9, 93.3, 92.9, 63.3, 63.2, 52.6, 52.4, 52.3, 51.6, 49.3, 45.4, 45.0, 21.1. MS (*m/z*): HRMS (ESI) Calcd. for C₃₁H₂₆BrN₂O₅ ([M+H]⁺): 585.1025, found: 585.1024.



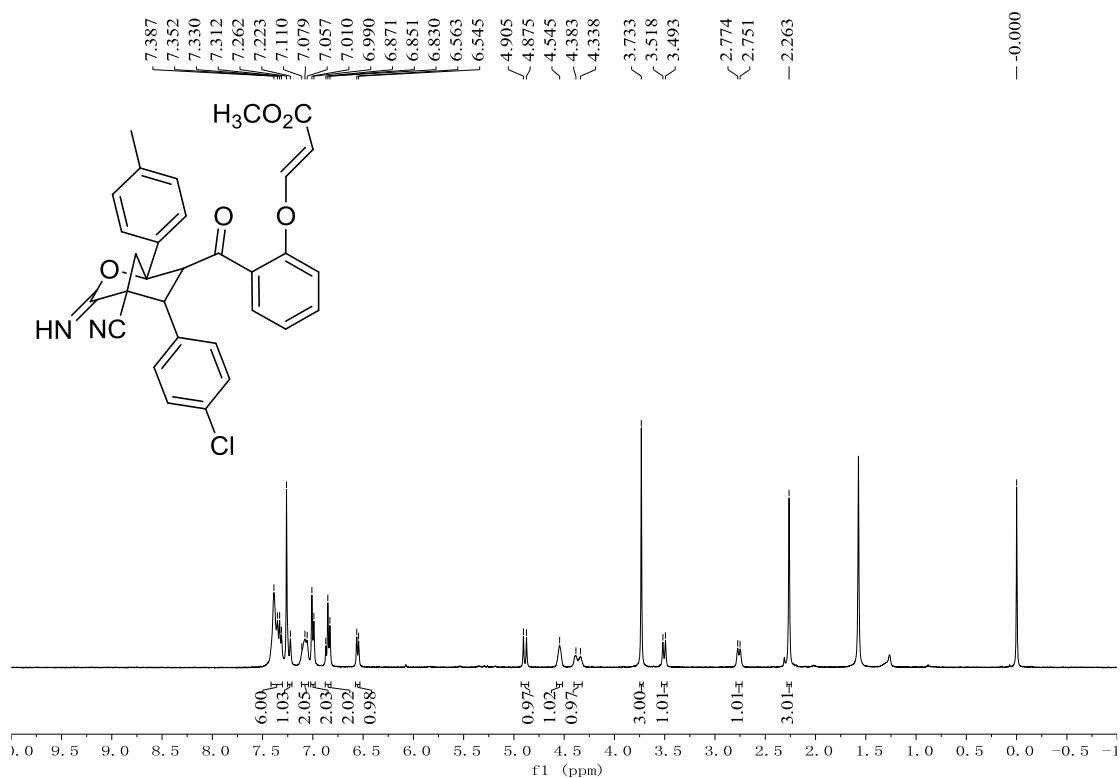


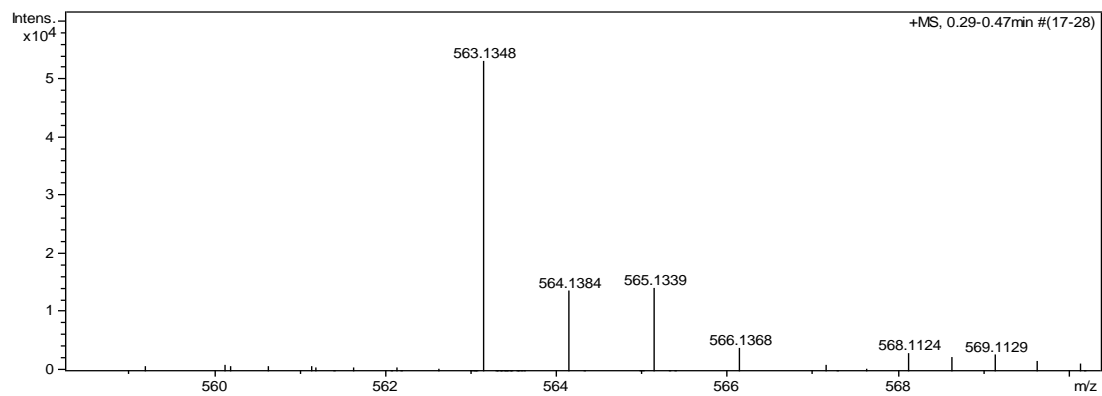
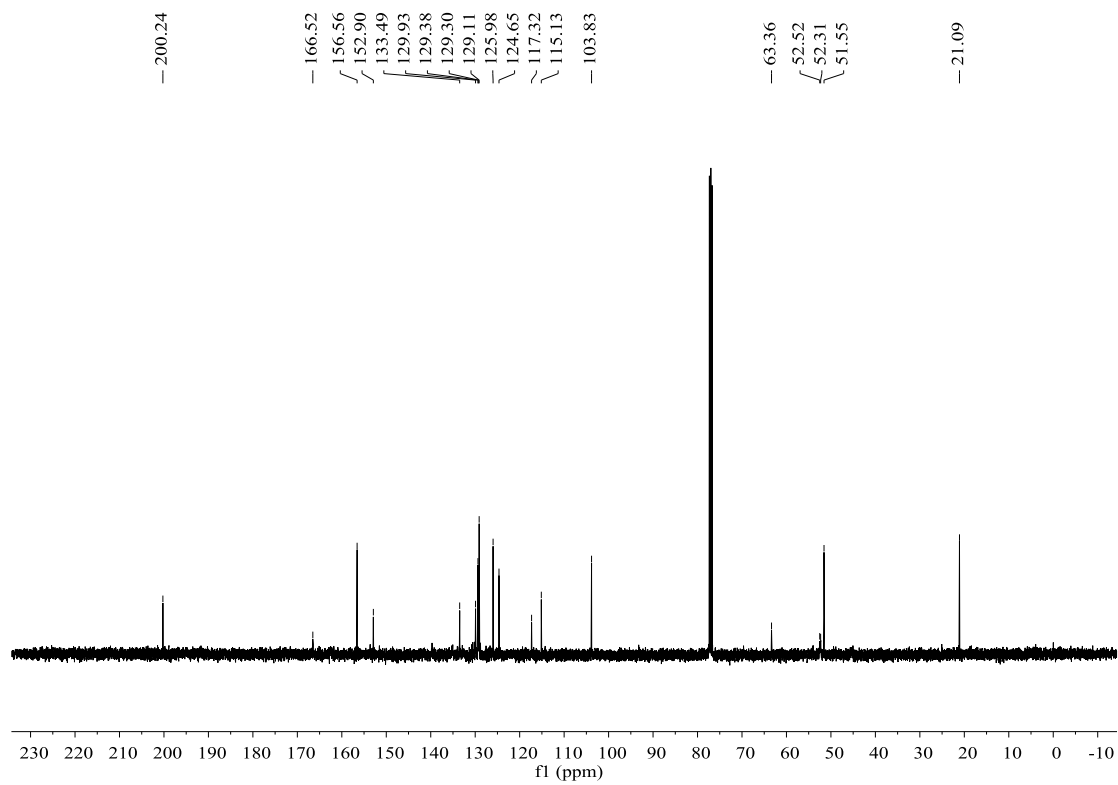
Methyl (E)-3-(2-(*rel*-(1*S*,4*S*,5*R*)-1-(4-bromophenyl)-5-(4-chlorophenyl)-4-cyano-3-imino-2-oxabicyclo[2.2.1]heptane-6-carbonyl)phenoxy)acrylate (5d): white solid, 68%, m.p. 168-170 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.41-7.34 (m, 7H, ArH), 7.25-7.23 (m, 2H, ArH), 7.10 (s, 2H, ArH), 6.95 (t, *J* = 8.0 Hz, 1H, CH), 6.87 (d, *J* = 8.0 Hz, 1H, CH), 6.67-6.65 (m, 1H, ArH), 4.92 (d, *J* = 12.0 Hz, 1H, CH), 4.55 (d, *J* = 5.6 Hz, 1H, CH), 4.36 (s, 1H, NH), 3.74 (s, 3H, OCH₃), 3.51 (d, *J* = 10.4 Hz, 1H, CH₂), 2.75 (d, *J* = 10.0 Hz, 1H, CH₂). ¹³C NMR (100 MHz, CDCl₃) δ 199.8, 166.5, 166.4, 166.0, 162.0, 156.5, 153.1, 153.0, 135.4, 135.2, 134.1, 134.0, 132.7, 132.3, 131.7, 131.6, 131.5, 131.4, 130.2, 130.1, 129.9, 129.8, 129.4, 129.2, 129.1, 127.7, 127.6, 125.0, 124.0, 117.6, 117.6, 114.9, 104.0, 92.5, 92.2, 63.4, 63.2, 52.5, 52.3, 51.6, 49.3, 45.3, 45.0. MS (*m/z*): HRMS (ESI) Calcd. for C₃₀H₂₃BrClN₂O₅ ([M+H]⁺): 605.0479, found: 605.0477.



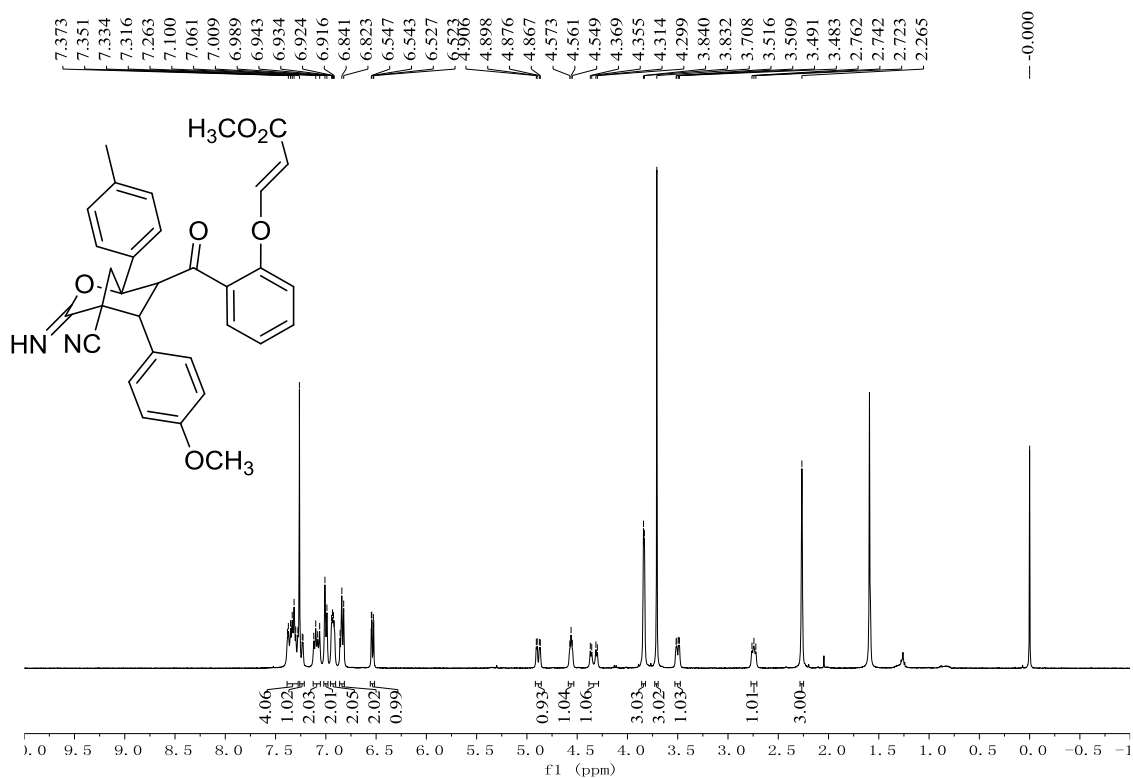


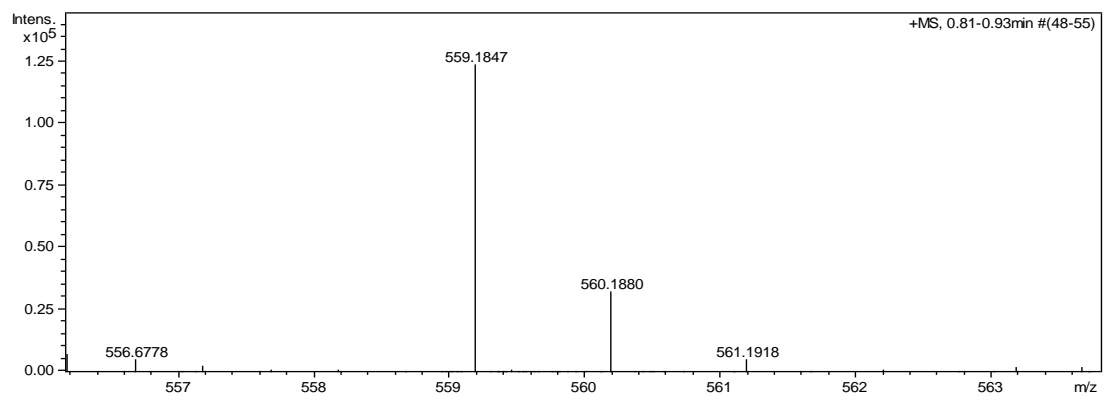
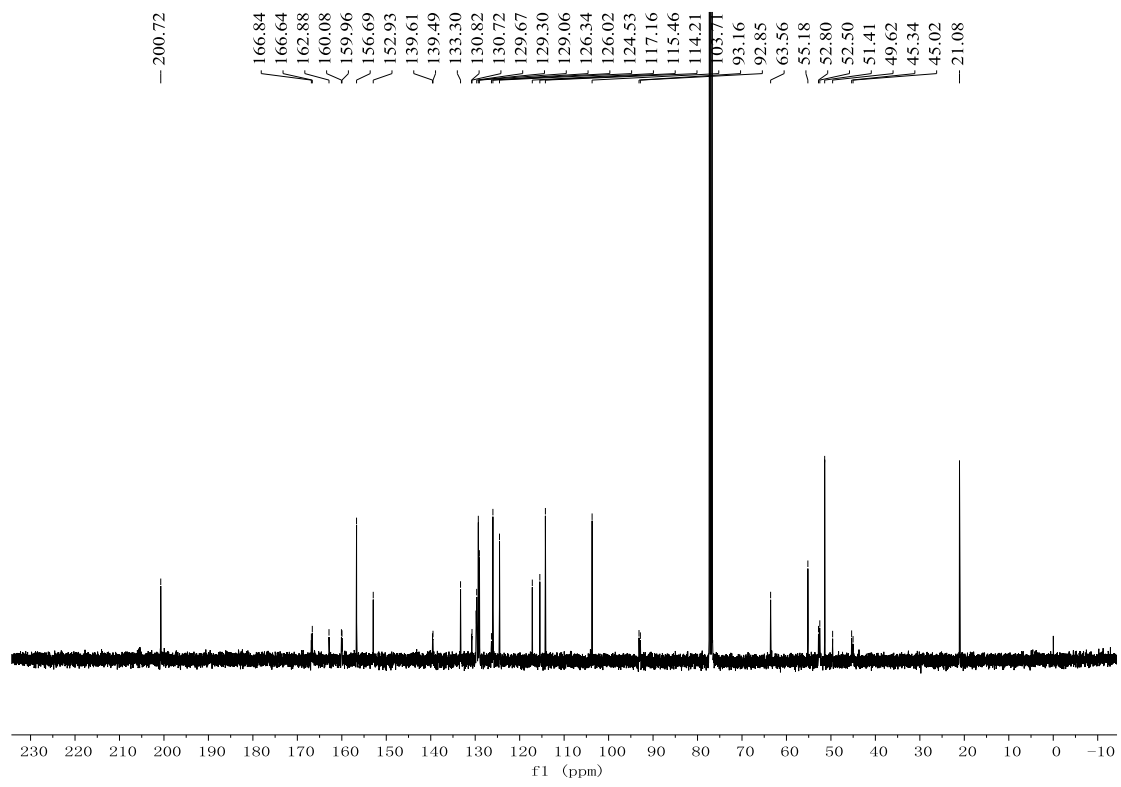
Methyl (E)-3-(2-(rel-(1S,4S,5R)-5-(4-chlorophenyl)-4-cyano-3-imino-1-(p-tolyl)-2-oxabicyclo[2.2.1]heptane-6-carbonyl)phenoxy)acrylate (5e): white solid, 87%, m.p. 152-154 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.39-7.31 (m, 6H, ArH), 7.25-7.22 (m, 1H, ArH), 7.11-7.06 (m, 2H, ArH), 7.00 (t, *J* = 8.0 Hz, 2H, ArH), 6.87-6.83 (m, 2H, CH), 6.55 (d, *J* = 7.2 Hz, 1H, ArH), 4.89 (d, *J* = 12.0 Hz, 1H, CH), 4.55 (s, 1H, NH), 4.36 (d, *J* = 18.0 Hz, 1H, CH), 3.73 (s, 3H, OCH₃), 3.50 (d, *J* = 10.0 Hz, 1H, CH₂), 2.76 (d, *J* = 9.2 Hz, 1H, CH₂), 2.26 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 200.2, 166.5, 156.6, 152.9, 133.5, 129.9, 129.4, 129.3, 129.1, 126.0, 124.7, 117.3, 115.1, 103.8, 63.4, 52.5, 52.3, 51.6, 21.1. MS (*m/z*): HRMS (ESI) Calcd. for C₃₁H₂₅ClNaN₂O₅ ([M+Na]⁺): 563.1350, found: 563.1348.



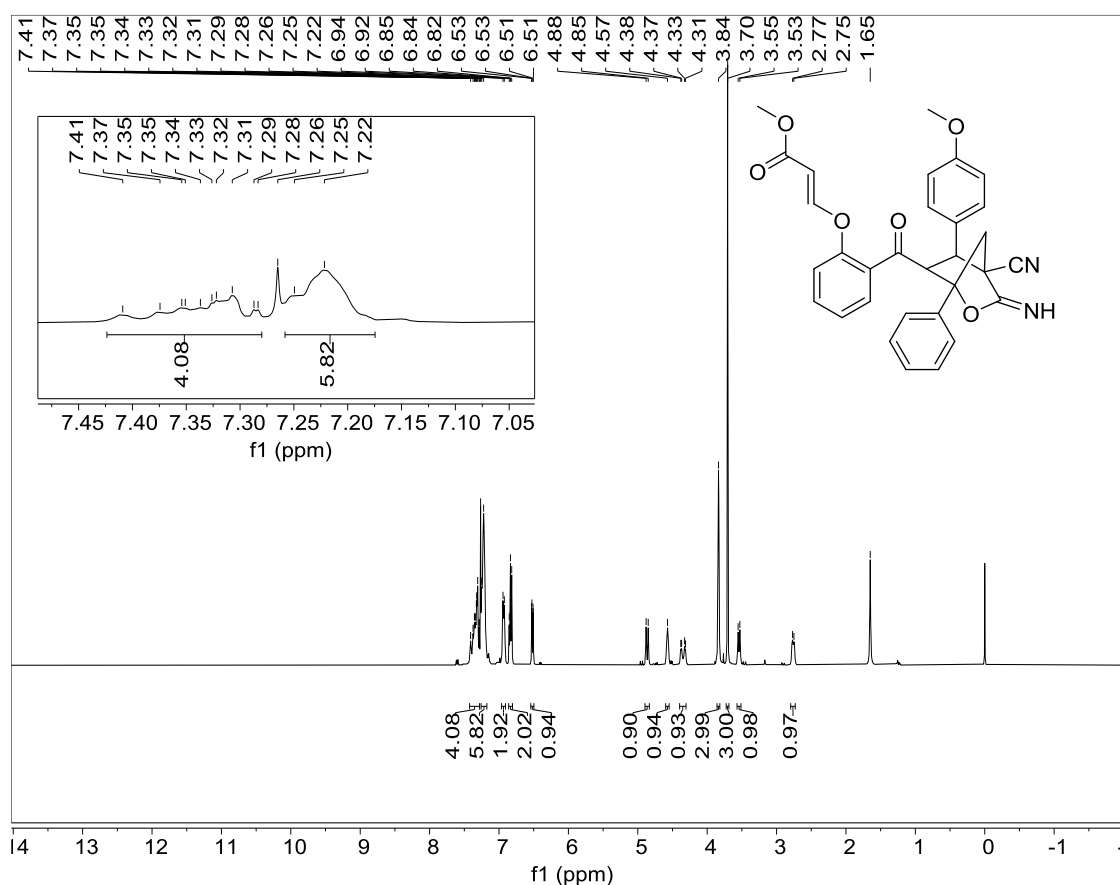


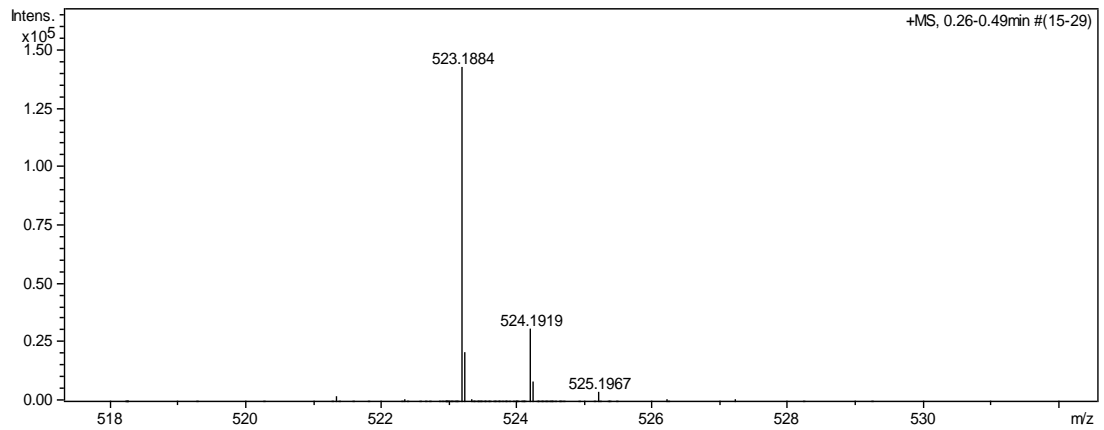
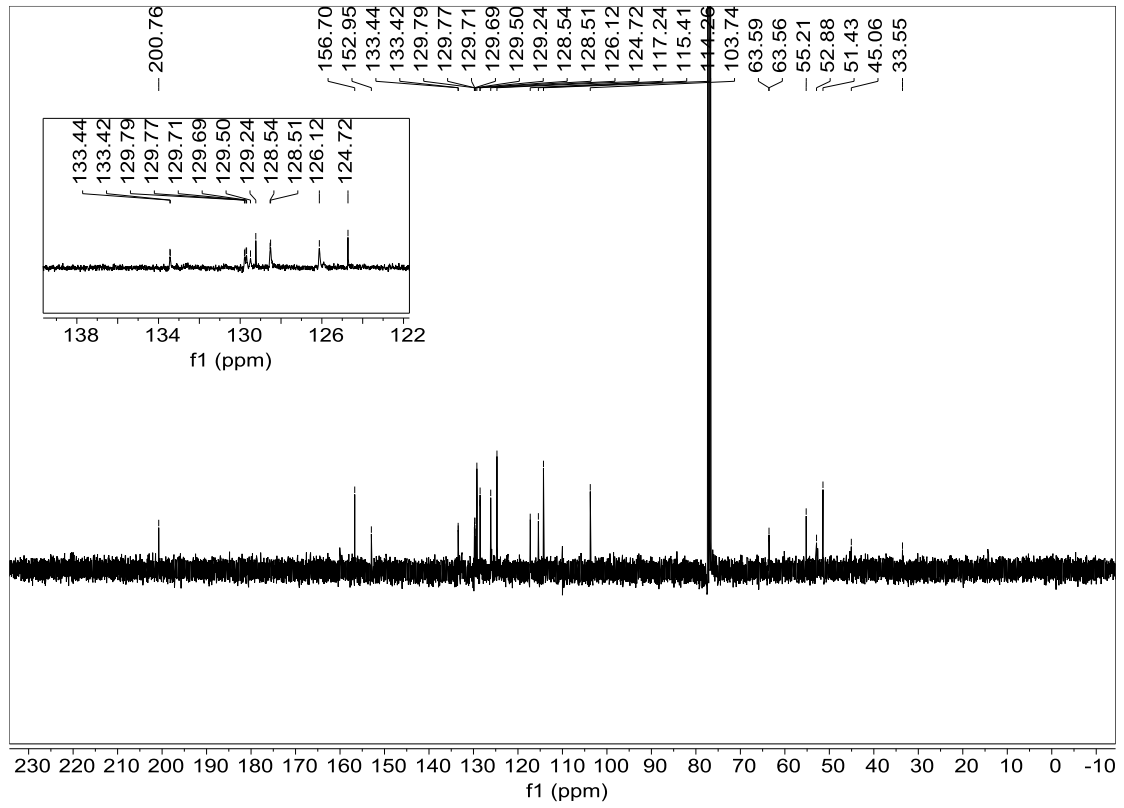
Methyl (E)-3-(2-(rel-(1S,4S,5R)-4-cyano-3-imino-5-(4-methoxyphenyl)-1-(p-tolyl)-2-oxabicyclo[2.2.1]heptane-6-carbonyl)phenoxy)acrylate (5f): white solid, 88%, m.p. 167-169 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.38-7.28 (m, 4H, ArH), 7.25-7.23 (m, 1H, ArH), 7.12-7.06 (m, 2H, ArH), 7.00 (t, *J* = 8.0 Hz, 2H, ArH), 6.94-6.92 (m, 2H, ArH), 6.86-6.82 (m, 2H, CH), 6.55-6.52 (m, 1H, ArH), 4.91-4.87 (m, 1H, CH), 4.56 (t, *J* = 4.8 Hz, 1H, NH), 4.37-4.30 (m, 1H, CH), 3.83 (d, *J* = 3.2 Hz, 3H, OCH₃), 3.71 (s, 3H, OCH₃), 3.52-3.48 (m, 1H, CH₂), 2.76-2.72 (m, 1H, CH₂), 2.27 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 200.7, 166.8, 166.6, 162.9, 160.1, 160.0, 156.7, 152.9, 139.6, 139.5, 133.3, 130.8, 130.7, 129.7, 129.3, 129.1, 126.3, 126.0, 124.5, 117.2, 115.5, 114.2, 103.7, 93.2, 92.9, 63.6, 55.2, 52.8, 52.5, 51.4, 49.6, 45.3, 45.0, 21.1. MS (*m/z*): HRMS (ESI) Calcd. for C₃₂H₂₈NaN₂O₆ ([M+Na]⁺): 559.1845, found: 559.1847.



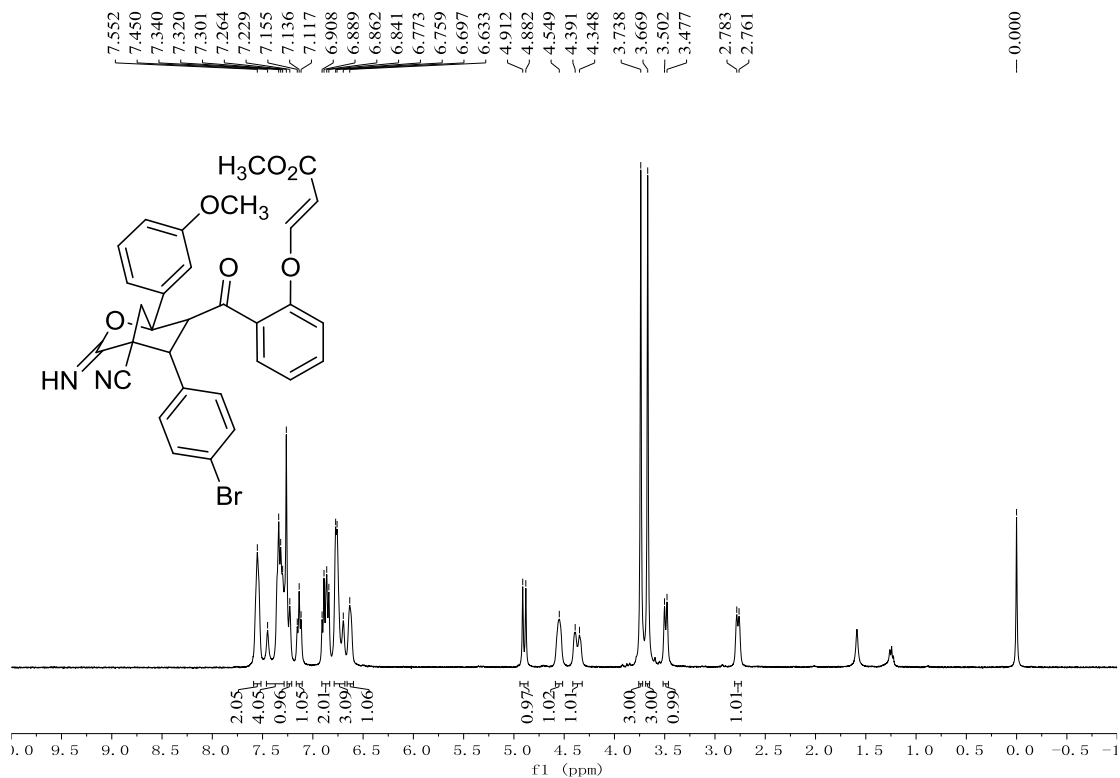


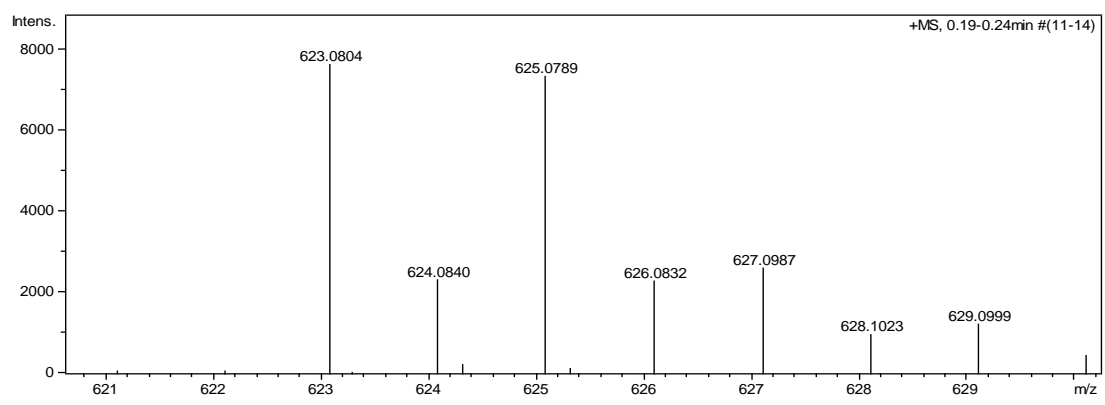
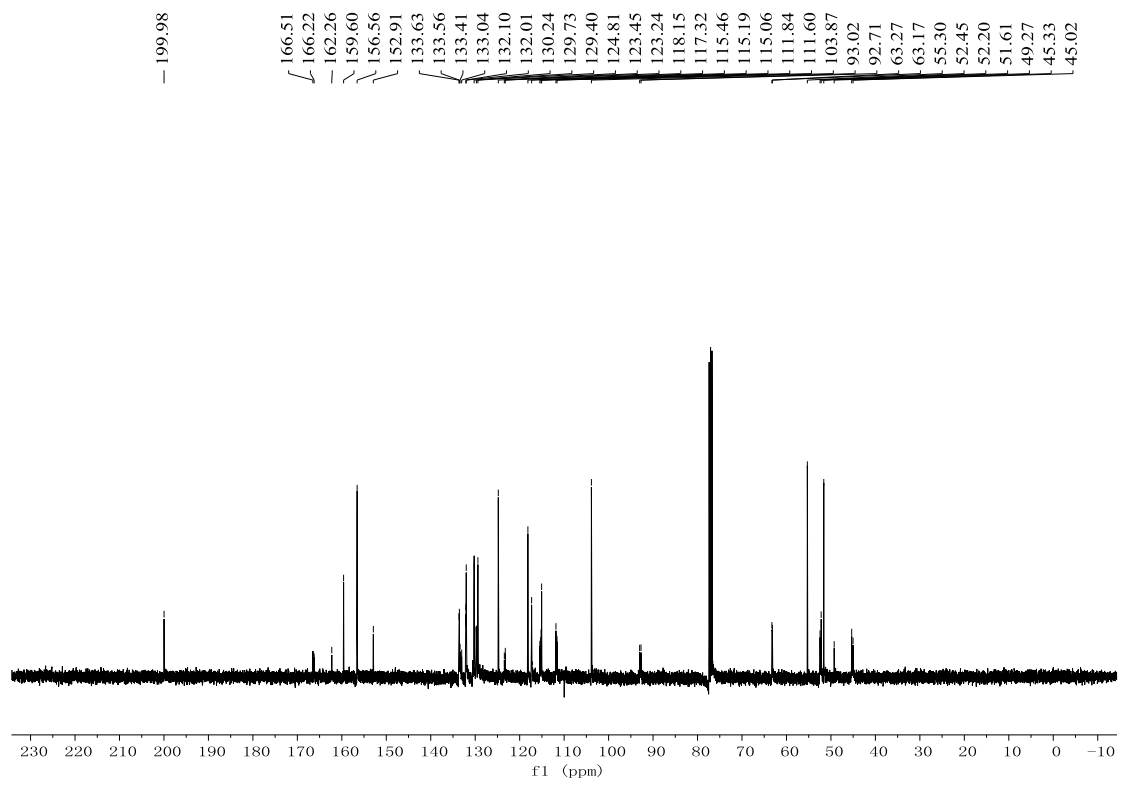
Methyl (E)-3-(2-(rel-(1R,4R,5S,6S)-4-cyano-3-imino-5-(4-methoxyphenyl)-1-phenyl-2-oxabicyclo[2.2.1]heptane-6-carbonyl)phenoxy)acrylate (5g): White solid, 78%; ^1H NMR (400 MHz, CDCl_3) δ : 7.41-7.28 (m, 4H, ArH), 7.25-7.22 (m, 6H, ArH), 6.93 (d, $J = 7.6$ Hz, 2H, ArH), 6.84 (d, $J = 6.1$ Hz, 1H, ArH), 6.82 (s, $J = 7.2$ Hz, 1H, ArH), 6.52 (dd, $J_1 = 1.6$ Hz, $J_2 = 8.0$ Hz, 1H, ArH), 4.87 (d, $J = 12$ Hz, 1H, CH), 4.57 (s, 1H, NH), 4.34 (dd, $J_1 = 5.2$ Hz, $J_2 = 18.0$ Hz, 1H, CH), 3.84 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3), 3.54 (d, $J = 10.0$ Hz, 1H, CH_2), 2.76 (d, $J = 8.0$ Hz, 1H, CH_2); ^{13}C NMR (400 MHz, CDCl_3) δ : 200.7, 156.6, 152.9, 133.4, 133.4, 129.7, 129.7, 129.6, 129.6, 129.4, 129.2, 128.5, 128.4, 126.1, 124.7, 117.2, 115.3, 114.2, 103.7, 63.5, 63.5, 55.2, 52.8, 51.4, 45.0, 33.5; IR (KBr) ν : 3675, 3386, 3285, 3064, 3002, 2933, 2863, 2302, 2245, 2032, 1912, 1722, 1675, 1473, 1232, 1115, 1045, 996, 882, 746 cm^{-1} ; HRMS (ESI) Calcd. for $\text{C}_{31}\text{H}_{26}\text{N}_2\text{O}_6$ ($[\text{M}+\text{H}]^+$): 523.1864, Found: 523.1884.





Methyl (*E*)-3-(2-(*rel*-(1*S*,4*S*,5*R*)-5-(4-bromophenyl)-4-cyano-3-imino-1-(3-methoxyphenyl)-2-oxabicyclo[2.2.1]heptane-6-carbonyl)phenoxy)acrylate (5h**):** white solid, 90%, m.p. 190-192 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.55 (s, 2H, ArH), 7.45-7.30 (m, 4H, ArH), 7.25-7.23 (m, 1H, ArH), 7.14 (t, *J* = 7.6 Hz, 1H, ArH), 6.91-6.84 (m, 2H, CH), 6.77-6.70 (m, 3H, ArH), 6.63 (s, 1H, ArH), 4.90 (d, *J* = 12.0 Hz, 1H, CH), 4.55 (s, 1H, NH), 4.37 (d, *J* = 17.2 Hz, 1H, CH), 3.74 (s, 3H, OCH₃), 3.67 (s, 3H, OCH₃), 3.49 (d, *J* = 10.0 Hz, 1H, CH₂), 2.77 (d, *J* = 8.8 Hz, 1H, CH₂). ¹³C NMR (100 MHz, CDCl₃) δ 200.0, 166.5, 166.2, 162.3, 159.6, 156.6, 152.9, 133.6, 133.5, 133.4, 133.0, 132.1, 132.0, 130.2, 129.7, 129.4, 124.8, 123.5, 123.2, 118.2, 117.3, 115.5, 115.2, 115.1, 111.8, 111.6, 103.9, 93.0, 92.7, 63.3, 63.2, 55.3, 52.5, 52.2, 51.6, 49.3, 45.3, 45.0. MS (*m/z*): HRMS (ESI) Calcd. for C₃₁H₂₅BrNaN₂O₆ ([M+Na]⁺): 623.0794, found: 623.0804.

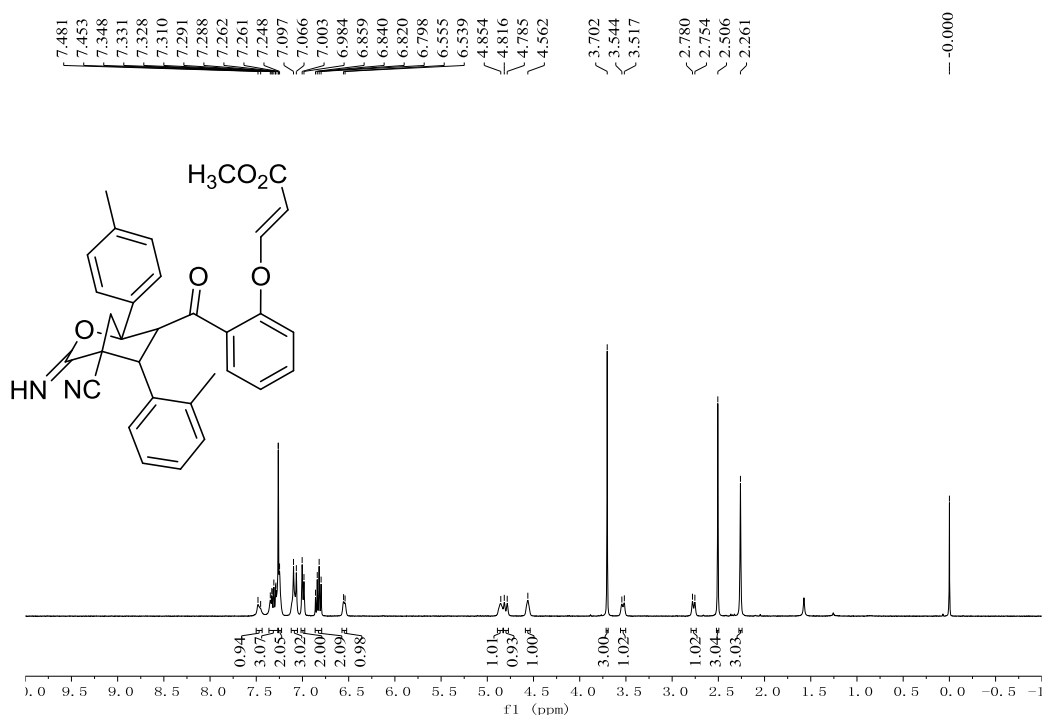


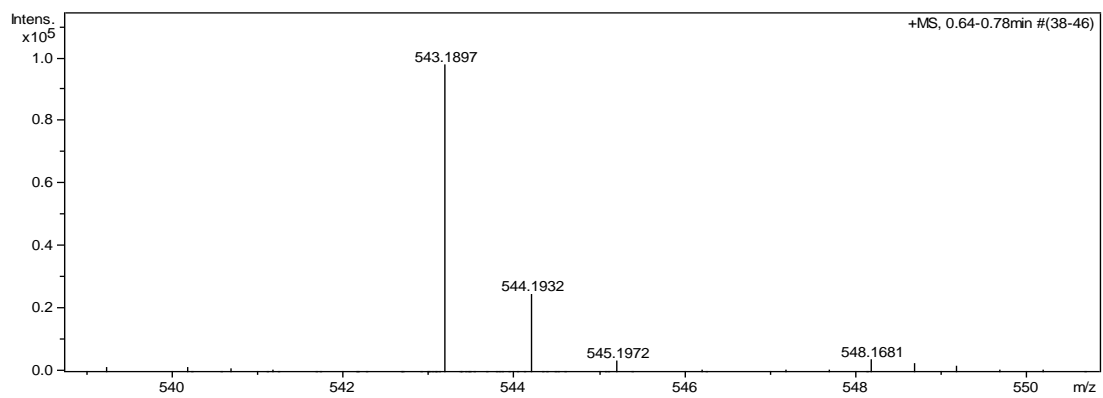
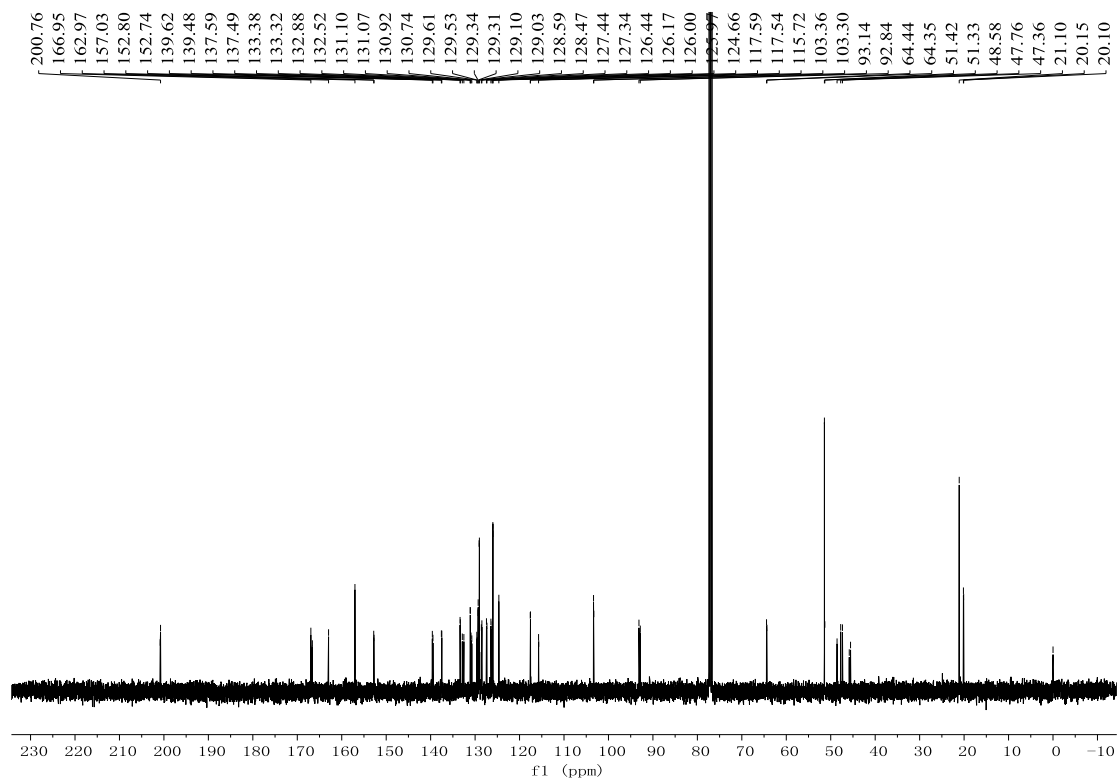


Methyl

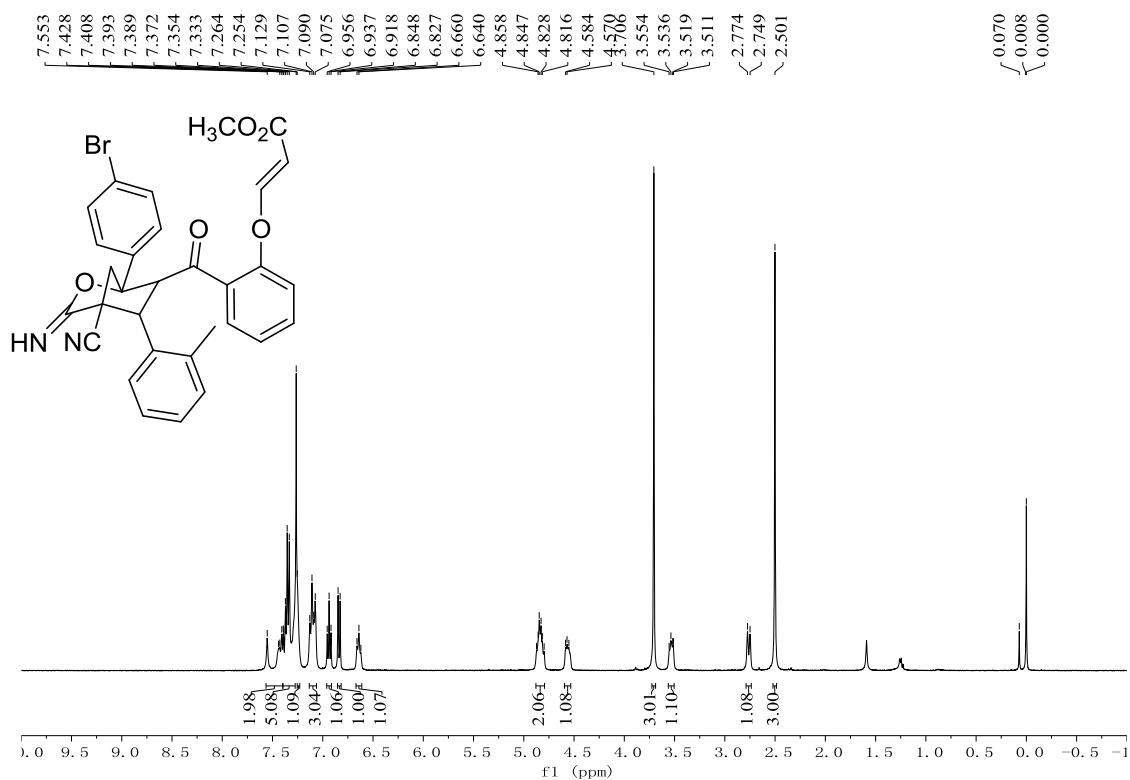
(*E*)-3-(2-(*rel*-(1*S*,4*S*,5*R*)-4-cyano-3-imino-5-(*o*-tolyl)-1-(*p*-tolyl)-2-

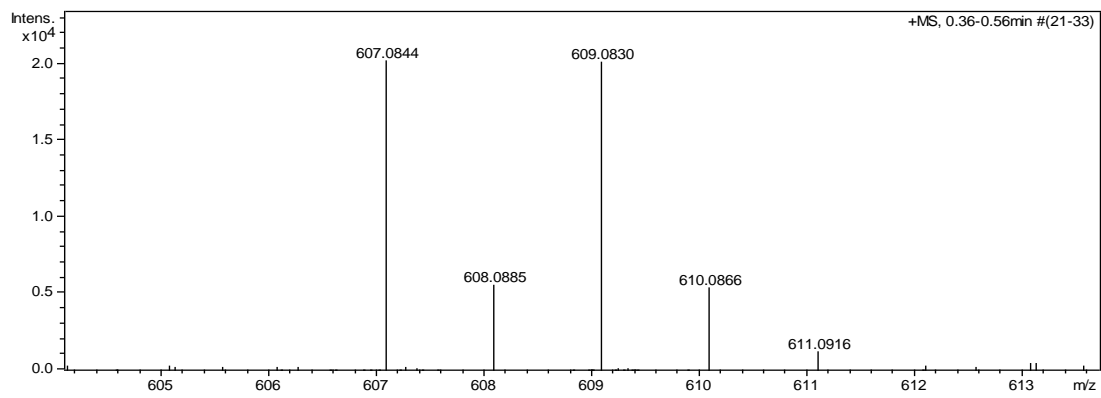
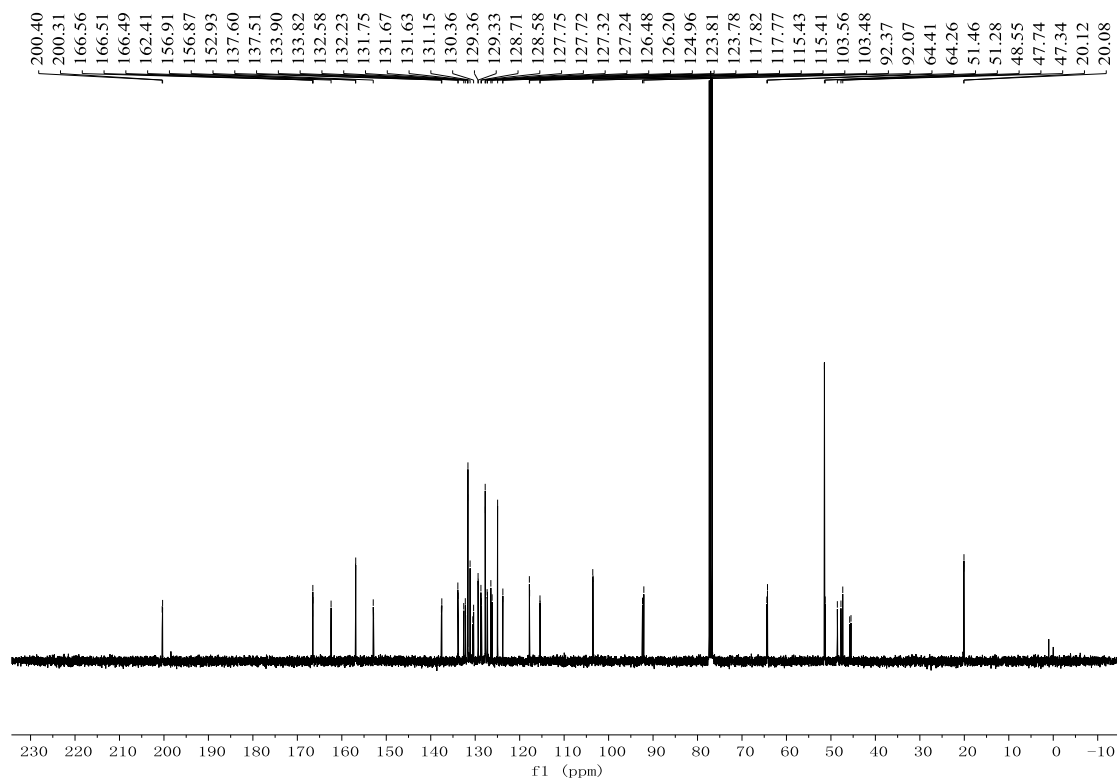
oxabicyclo[2.2.1]heptane-6-carbonyl)phenoxy)acrylate (**5i**): white solid, 70%, m.p. 142-144 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.48-7.45 (m, 1H, ArH), 7.35-7.29 (m, 3H, ArH), 7.26-7.25 (m, 2H, ArH), 7.08 (d, *J* = 12.4 Hz, 3H, ArH), 6.99 (d, *J* = 7.6 Hz, 2H, ArH), 6.86-6.80 (m, 2H, CH), 6.55 (d, *J* = 6.4 Hz, 1H, ArH), 4.85 (s, 1H, CH), 4.81 (d, *J* = 12.4 Hz, 1H, CH), 4.56 (s, 1H, NH), 3.70 (s, 3H, OCH₃), 3.53 (d, *J* = 10.8 Hz, 1H, CH₂), 2.77 (d, *J* = 10.4 Hz, 1H, CH₂), 2.51 (s, 3H, CH₃), 2.26 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 200.8, 200.7, 167.0, 166.7, 166.6, 163.0, 157.0, 152.8, 152.7, 139.6, 139.5, 137.6, 137.5, 133.4, 133.3, 132.9, 132.5, 131.1, 131.0, 130.9, 130.7, 129.6, 129.5, 129.3, 129.2, 129.1, 129.0, 128.6, 128.5, 127.4, 127.3, 126.4, 126.2, 126.0, 125.9, 124.7, 117.6, 117.5, 115.7, 115.6, 103.4, 103.3, 93.1, 92.8, 64.4, 64.3, 51.4, 51.3, 48.6, 47.8, 47.4, 45.8, 45.6, 21.1, 20.2, 20.1. MS (*m/z*): HRMS (ESI) Calcd. for C₃₂H₂₈NaN₂O₅ ([*M*+Na]⁺): 543.1896, found: 543.1897.



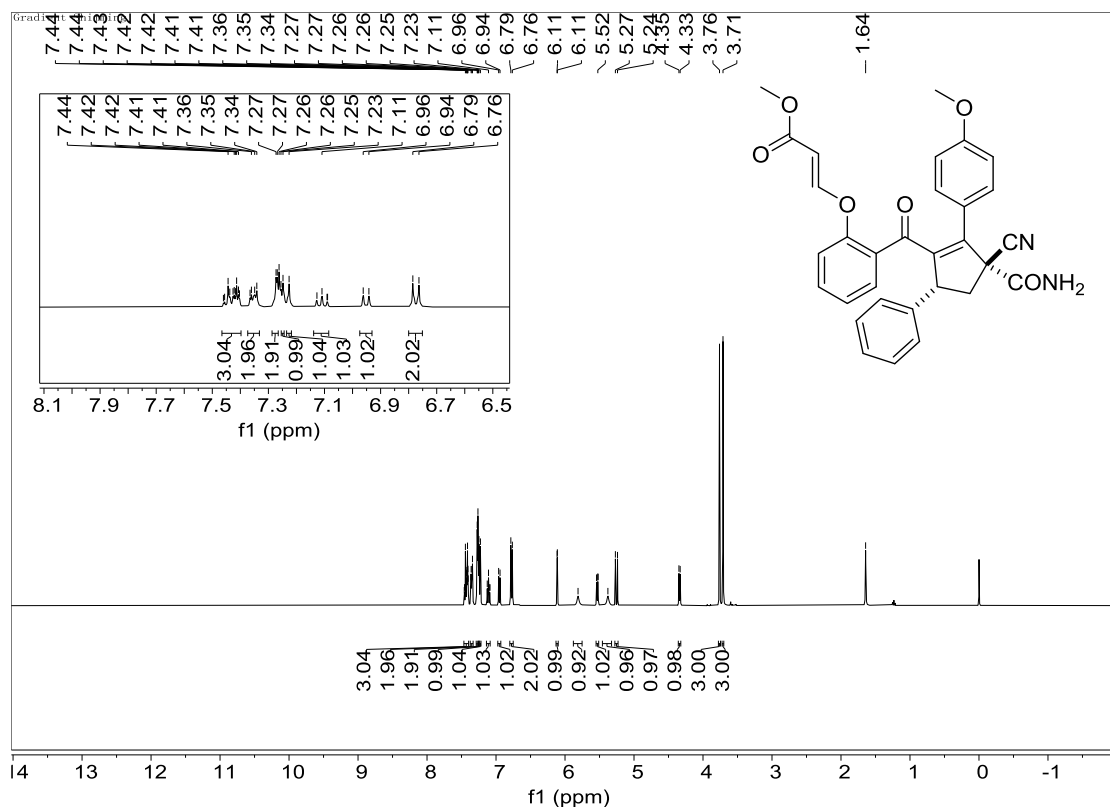


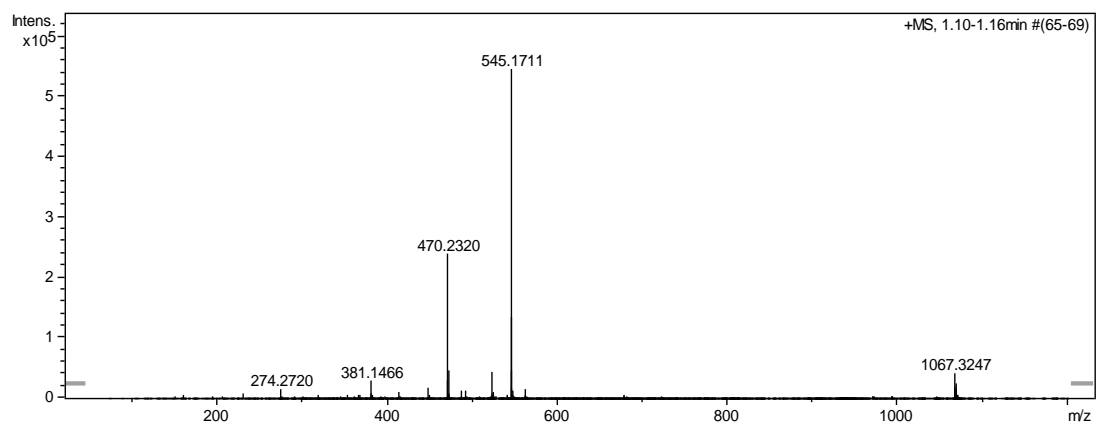
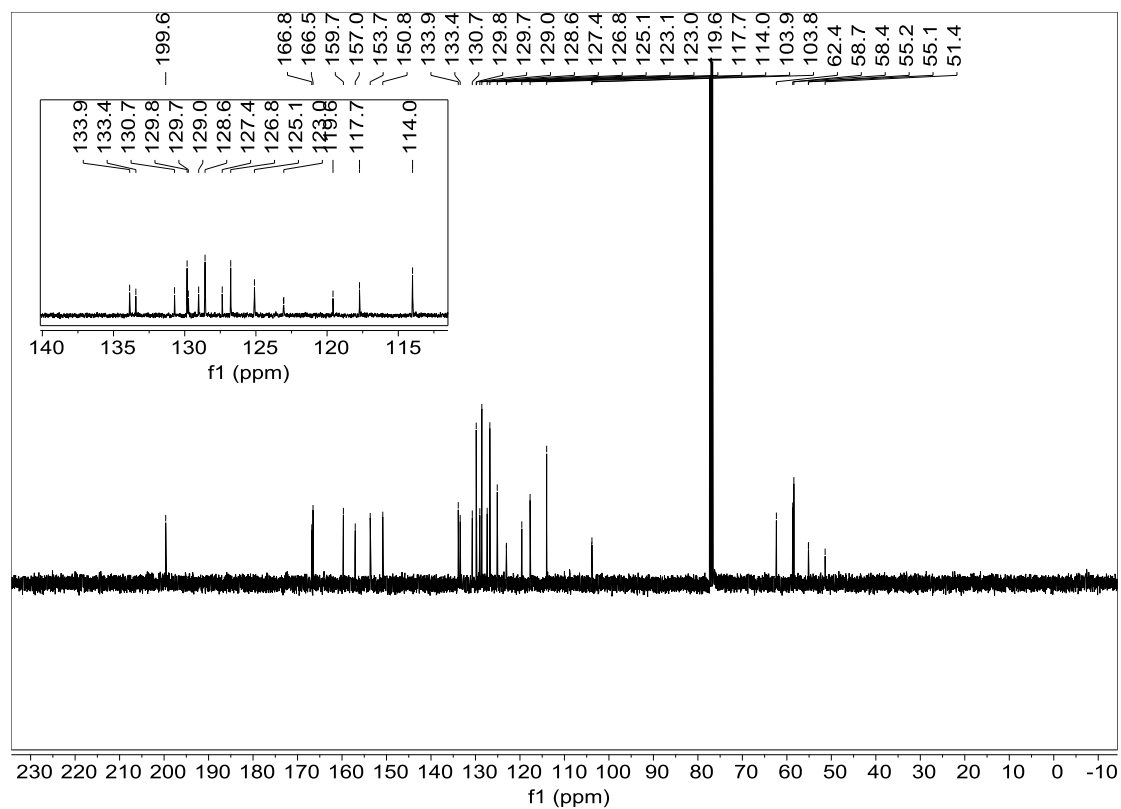
Methyl (*E*)-3-(2-(*rel*-(1*S*,4*S*,5*R*)-1-(4-bromophenyl)-4-cyano-3-imino-5-(*o*-tolyl)-2-oxabicyclo[2.2.1]heptane-6-carbonyl)phenoxy)acrylate (**5j**): white solid, 65%, m.p. 159-161 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.55-7.41 (m, 2H, ArH), 7.39-7.26 (m, 5H, ArH), 7.25 (s, 1H, ArH), 7.13-7.08 (m, 3H, ArH), 6.94 (t, *J* = 7.6 Hz, 1H, ArH), 6.84 (d, *J* = 8.4 Hz, 1H, CH), 6.64 (t, *J* = 7.6 Hz, 1H, CH), 4.87-4.80 (m, 2H, CH), 4.58-4.55 (m, 1H, NH), 3.71 (s, 3H, OCH₃), 3.55-3.51 (m, 1H, CH₂), 2.76 (d, *J* = 10.0 Hz, 1H, CH₂), 2.50 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 200.4, 200.3, 166.6, 166.5, 166.4, 162.4, 156.9, 156.8, 152.9, 152.8, 137.6, 137.5, 133.9, 133.8, 132.6, 132.2, 131.8, 131.7, 131.6, 131.2, 130.5, 130.4, 129.4, 129.3, 128.7, 128.6, 127.8, 127.7, 127.3, 127.2, 126.5, 126.2, 125.0, 123.8, 123.7, 117.8, 117.7, 115.4, 115.3, 103.6, 103.5, 92.4, 92.1, 64.4, 64.3, 51.5, 51.3, 48.6, 47.7, 47.3, 45.8, 45.5, 20.1, 20.0. MS (*m/z*): HRMS (ESI) Calcd. for C₃₁H₂₅BrNaN₂O₅ ([M+Na]⁺): 607.0845, found: 607.0844.





Methyl (*E*)-3-(2-(3-carbamoyl-3-cyano-2-(4-methoxyphenyl)-5-phenylcyclopent-1-ene-1-carbonyl)phenoxy)acrylate (6a): White solid, 95%; ^1H NMR (400 MHz, CDCl_3) δ : 7.46-7.40 (m, 3H, ArH), 7.37-7.34 (m, 2H, ArH), 7.27 (d, $J = 1.6$ Hz, 2H, ArH), 7.26 -7.25 (m, 1H, ArH), 7.23 (s, 1H, ArH), 6.13-7.09 (m, 1H, ArH), 6.95 (d, $J = 8.0$ Hz, 1H, CH), 6.77 (d, $J = 8.4$ Hz, 2H, ArH), 6.11 (d, $J = 1.6$ Hz, 1H, CH), 5.81 (s, 1H, NH_2), 5.53 (dd, $J_1 = 1.2$ Hz, $J_2 = 6.8$ Hz, 1H, CH), 5.38 (s, 1H, NH_2), 5.26 (d, $J = 12.4$ Hz, 1H, CH_2), 4.34 (d, $J = 7.2$ Hz, 1H, CH_2), 3.76 (s, 3H, OCH_3), 3.71 (s, 3H, OCH_3); ^{13}C NMR (400 MHz, CDCl_3) δ : 199.6, 166.7, 166.5, 159.6, 157.0, 153.6, 150.8, 133.8, 133.4, 130.7, 129.8, 129.7, 129.0, 128.5, 127.3, 126.7, 125.0, 123.0, 123.0, 119.5, 117.7, 113.9, 103.8, 103.8, 62.3, 58.6, 58.4, 55.1, 55.1, 51.3; IR (KBr) ν : 3663, 3420, 3230, 3052, 2964, 2835, 2816, 2145, 1916, 1652, 1601, 1463, 1265, 1162, 1045, 965, 936, 852, 725 cm^{-1} ; HRMS (ESI) Calcd. for $\text{C}_{31}\text{H}_{26}\text{N}_2\text{O}_6$ ($[\text{M}+\text{Na}]^+$): 545.1683, Found: 545.1711.





2-(rel-(1R,4R,5S,6S)-4-cyano-3-imino-5-(4-methoxyphenyl)-1-phenyl-2-oxabicyclo[2.2.1]heptane-6-carbonyl)phenyl acetate (7a): White solid, 80%; ^1H NMR (400 MHz, CDCl_3) δ : 7.38-7.37 (m, 3H, ArH), 7.31 (t, $J = 7.6$ Hz, 2H, ArH), 7.23 (s, 4H, ArH), 6.95 (s, 1H, ArH), 6.93 (s, 1H, ArH), 6.89 (t, $J = 8.0$ Hz, 2H, ArH), 6.74 (d, $J = 7.6$ Hz, 1H, CH), 4.45 (d, $J = 2.4$ Hz, 1H, CH), 4.35 (s, 1H, NH), 3.82 (s, 3H, OCH_3), 3.52 (d, $J = 10.0$ Hz, 1H, CH_2), 2.76 (d, $J = 10.4$ Hz, 1H, CH_2), 1.84 (s, 3H, CH_3); ^{13}C NMR (400 MHz, CDCl_3) δ : major 198.8, 169.0, 166.7, 162.7, 160.1, 148.1, 133.1, 132.6, 131.6, 131.4, 129.7, 129.5, 129.0, 128.5, 126.3, 126.0, 125.9, 125.6, 123.2, 115.3, 114.4, 93.2, 62.2, 55.3, 52.6, 52.5, 49.5, 45.2, 20; δ : minor 198.7, 169.0, 160.0, 133.0, 132.5, 129.6, 129.4, 128.9, 128.4, 126.0, 114.4, 92.9, 62.0, 52.3, 45.1; IR (KBr) ν : 3724, 3456, 3243, 3078, 2982, 2823, 2807, 2155, 1910, 1645, 1624, 1450, 1258, 1155, 1040, 955, 862, 752 cm^{-1} ; HRMS (ESI) Calcd. for $\text{C}_{31}\text{H}_{26}\text{N}_2\text{O}_6$ ($[\text{M}+\text{H}]^+$): 481.1758, Found: 481.1761.

