ELECTRONIC SUPPLEMENTARY INFORMATION

for

NHC-catalysed diastereoselective synthesis of multifunctionalised piperidines via cascade reaction of enals with azalactones

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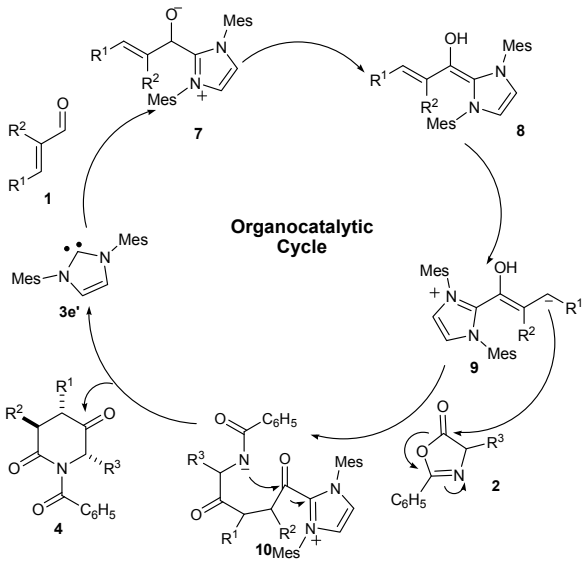
I. General methods

A. General Information: Reagents were obtained from commercial suppliers, and used without further purification unless otherwise specified by a reference. All reactions were performed using oven-dried glassware under a nitrogen atmosphere. Organic solutions were concentrated using a Buchi rotary evaporator. Column chromatography was carried out over silica gel (Merck 100–200 mesh) and TLC was performed using silica gel GF254 (Merck) plates. Melting points were determined by open glass capillary method and are uncorrected. IR spectra in KBr were recorded on a Perkin-Elmer 993 IR spectrophotometer, ^{1}H NMR spectra were recorded on a Bruker AVII 400 spectrometer in $CDCl_3$ using TMS as internal reference with chemical shift value being reported in ppm. All coupling constants (*J*) are reported in Hertz (Hz). ^{13}C NMR spectra were recorded on the same instrument at 100 MHz in $CDCl_3$ and TMS was used as internal reference. Mass (EI) spectra were recorded on a JEOL D-300 mass spectrometer. Elemental analyses were carried out in a Coleman automatic carbon, hydrogen and nitrogen analyzer.

B. General procedure for the synthesis of piperidines 4

A flame-dried round bottom flask was charged with benzimidazolium salt **3e** (0.2 mmol), α,β-unsaturated aldehyde **2** (1 mmol), azalactone **1** (1 mmol) and THF (5 mL) under positive pressure of nitrogen followed by addition of DBU (0.2 mmol) with a syringe. The resulting yellow-orange solution was stirred for 5-6 h at room temperature (Table 2). After completion of the reaction (monitered by TLC), water (5 mL) was added and the mixture was extracted with ethyl acetate (3 x 5 mL). The combined organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The concentrated residue was purified by silica gel chromatography hexane/ethyl acetate (20:1) to afford analytically pure **4**.

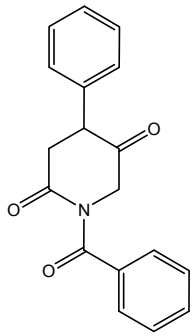
II. A plausible mechanism for the formation of piperidines 4



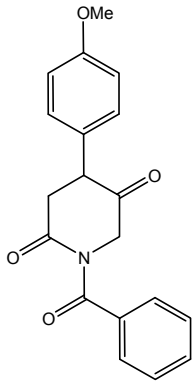
Scheme 2

On the basis of the experimental results a plausible mechanism for the formation of piperidines **4** is depicted in Scheme 2. As might be expected, a zwitterionic structure **7** is formed by the addition of the catalyst imidazolin-2-ylidene **3e** to α,β-unsaturated aldehyde **1**, which gives the Breslow intermediate **8**. The intermediate **8** generates a more reactive homoenolate **9**, which attacks at the electrophilic site of azalactone **2** as a d^3 nucleophile to form intermediate **10**. The intermediate **10** undergoes intramolecular attack of N-atom at the carbonyl unit to afford piperidine **4** and the catalyst to complete the catalytic cycle Scheme 2.

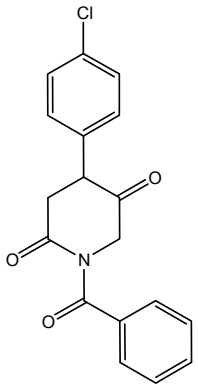
III. Spectroscopic and analytical data for compounds 4



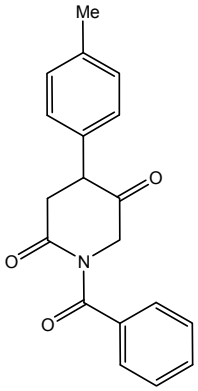
Compound **4a:** Yellowish oil, yield 86%. IR (KBr) υ_{max} 3099, 3050, 1720, 1605, 1584, 1476, 1450, 741, 695 cm^{-1}. ^{1}H NMR (400 MHz; $CDCl_3$) δ = 2.84-2.88 (m, 2H), 3.87 (dd, *J* = 11.2, 4.2 Hz, 1H), 5.54 (d, *J* = 10.4 Hz, 1H), 5.58 (d, *J* = 10.4 Hz, 1H), 7.06-7.28 (m, 10H). ^{13}C NMR (400 MHz; $CDCl_3$) δ = 31.6, 51.2, 52.9, 125.1, 126.0, 127.2, 128.4, 129.2, 132.2, 134.1, 135.3, 171.9, 173.4, 207.2. EIMS (m/e): 293 (M^+). Anal. Calcd. for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78; Found: C, 73.40; H, 5.52; N, 4.96.



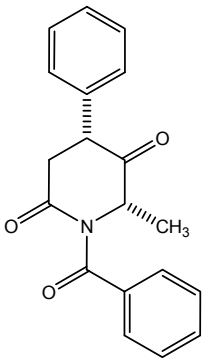
Compound **4b:** Yellowish oil, yield 80%. IR (KBr) υ_{max} 3100, 3052, 2810, 1724, 1601, 1586, 1472, 1452, 745, 690 cm^{-1}. ^{1}H NMR (400 MHz; $CDCl_3$) δ = 2.86-2.89 (m, 2H), 3.85 (s, 3H), 3.90 (dd, *J* = 11.3, 4.3 Hz, 1H), 5.55 (d, *J* = 10.6 Hz, 1H), 5.59 (d, *J* = 10.6 Hz, 1H), 7.10-7.35 (m, 5H), 7.66-7.68 (m, 2H), 8.01-8.03 (m, 2H). ^{13}C NMR (400 MHz; $CDCl_3$) δ = 31.1, 50.4, 51.9, 54.8, 114.9, 126.2, 127.4, 128.6, 130.2, 132.5, 134.0, 158.3, 172.9, 174.3, 206.8. EIMS (m/e): 323 (M^+). Anal. Calcd. for $C_{19}H_{17}NO_4$: C, 70.58; H, 5.30; N, 4.33; Found: C, 70.79; H, 5.05; N, 4.64.



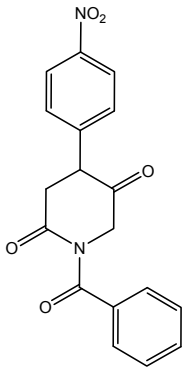
Compound **4c:** Yellowish oil, yield 83%. IR (KBr) υ_{max} 3095, 3054, 1725, 1604, 1581, 1480, 1452, 742, 698 cm^{-1}. ^{1}H NMR (400 MHz; $CDCl_3$) δ = 2.87-2.91 (m, 2H), 3.89 (dd, *J* = 11.2, 4.4 Hz, 1H), 5.55 (d, *J* = 10.5 Hz, 1H), 5.58 (d, *J* = 10.5 Hz, 1H), 7.08-7.31 (m, 5H), 7.65-7.70 (m, 2H), 8.10-8.17 (m, 2H). ^{13}C NMR (400 MHz; $CDCl_3$) δ = 31.9, 51.2, 52.4, 126.7, 127.9, 129.2, 130.4, 131.7, 132.7, 133.5, 134.9, 172.7, 173.9, 207.1. EIMS (m/e): 327, 329 (M^+, M^++2). Anal. Calcd. for $C_{18}H_{14}ClNO_3$: C, 65.96; H, 4.31; N, 4.27; Found: C, 65.59; H, 4.51; N, 4.08.



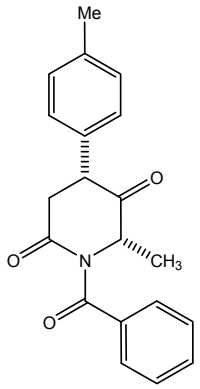
Compound **4d:** Yellowish oil, yield 79%. IR (KBr) υ_{max} 3098, 3051, 1715, 1601, 1583, 1485, 1450, 741, 695 cm^{-1}. ^{1}H NMR (400 MHz; $CDCl_3$) δ = 2.40 (s, 3H), 2.81-2.86 (m, 2H), 3.85 (dd, *J* = 11.4, 4.5 Hz, 1H), 5.52 (d, *J* = 10.7 Hz, 1H), 5.57 (d, *J* = 10.7 Hz, 1H), 7.01-7.06 (m, 2H), 7.10-7.32 (m, 5H), 7.46-7.53 (m, 2H). ^{13}C NMR (400 MHz; $CDCl_3$) δ = 24.7, 32.6, 50.5, 52.9, 126.5, 127.9, 129.1, 130.4, 131.8, 132.7, 134.1, 136.5, 172.1, 173.3, 207.7. EIMS (m/e): 307 (M^+). Anal. Calcd. for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.56; Found: C, 74.54; H, 5.76; N, 4.26.



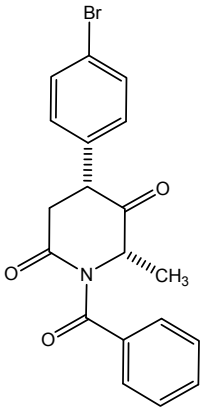
Compound **4e:** Yellowish oil, yield 77%. IR (KBr) υ_{max} 3099, 3056, 2855, 1719, 1605, 1582, 1481, 1455, 749, 699 cm^{-1}. ^{1}H NMR (400 MHz; $CDCl_3$) δ = 1.35 (d, J = 6.4 Hz, 3H), 2.81-2.87 (m, 2H), 3.87 (dd, J = 11.3, 4.3 Hz, 1H), 5.60 (q, J = 6.4 Hz, 1H), 7.05-7.35 (m, 10H). ^{13}C NMR (400 MHz; $CDCl_3$) δ = 13.6, 32.9, 48.1, 54.6, 126.6, 127.5, 128.8, 129.9, 131.1, 132.8, 134.2, 135.7, 171.6, 172.7, 208.0. EIMS (m/e): 307 (M^+). Anal. Calcd. for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.56; Found: C, 74.62; H, 5.76; N, 4.27.



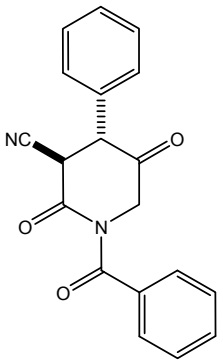
Compound **4f:** Yellowish oil, yield 88%. IR (KBr) υ_{max} 3100, 3054, 1721, 1608, 1585, 1453, 741, 690 cm^{-1}. ^{1}H NMR (400 MHz; $CDCl_3$) δ = 2.86-2.90 (m, 2H), 3.90 (dd, J = 11.2, 4.2 Hz, 1H), 5.55 (d, J = 10.5 Hz, 1H), 5.59 (d, J = 10.5 Hz, 1H), 7.10-7.32 (m, 5H), 7.66-7.69 (m, 2H), 8.15-8.19 (m, 2H). ^{13}C NMR (400 MHz; $CDCl_3$) δ = 31.4, 51.8, 53.2, 121.7, 127.5, 128.7, 130.4, 131.9, 134.4, 141.1, 146.6, 172.9, 174.1, 207.4. EIMS (m/e): 338 (M^+). Anal. Calcd. for $C_{18}H_{14}N_2O_5$: C, 63.90; H, 4.17; N, 8.28; Found: C, 63.59; H, 4.53; N, 8.52.



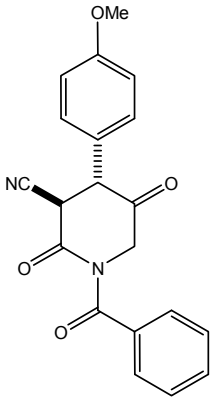
Compound **4g:** Yellowish oil, yield 76%. IR (KBr) υ_{max} 3095, 3050, 2850, 1725, 1606, 1581, 1455, 742, 697 cm^{-1}. ^{1}H NMR (400 MHz; $CDCl_3$) δ = 1.32 (d, *J* = 6.8 Hz, 3H), 2.41 (s, 3H,, 2.82-2.87 (m, 2H), 3.84 (dd, *J* = 11.3, 4.3 Hz, 1H), 5.55 (q, *J* = 6.8 Hz, 1H), 7.02-7.06 (m, 2H), 7.10-7.30 (m, 5H), 7.42-7.51 (m, 2H). ^{13}C NMR (400 MHz; $CDCl_3$) δ = 13.4, 24.1, 32.7, 48.7, 56.2, 126.5, 127.8, 128.9, 130.2, 131.8, 132.7, 134.1, 136.5, 172.2, 173.1, 208.2. EIMS (m/e): 321 (M^+). Anal. Calcd. for $C_{20}H_{19}NO_3$: C, 74.75; H, 5.96; N, 4.36; Found: C, 74.97; H, 5.60; N, 4.63.



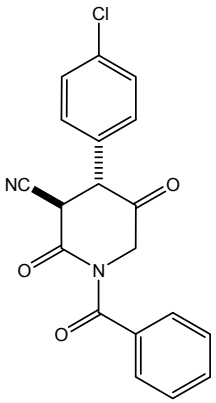
Compound **4h:** Yellowish oil, yield 78%. IR (KBr) υ_{max} 3098, 3052, 2852, 1724, 1609, 1584, 1453, 744, 693 cm^{-1}. ^{1}H NMR (400 MHz; $CDCl_3$) δ = 1.39 (d, *J* = 6.9 Hz, 3H), 2.87-2.90 (m, 2H), 3.89 (dd, *J* = 11.4, 4.4 Hz, 1H), 5.56 (q, *J* = 6.9 Hz, 1H), 7.09-7.29 (m, 5H), 7.35-7.42 (m, 2H), 7.63-7.65 (m, 2H). ^{13}C NMR (400 MHz; $CDCl_3$) δ = 12.8, 32.4, 48.1, 54.8, 121.2, 126.5, 127.9, 129.4, 131.2, 132.4, 133.7, 134.9, 172.1, 173.6, 208.5. EIMS (m/e): 385, 387 (M^+, M^++2). Anal. Calcd. for $C_{19}H_{16}BrNO_3$: C, 59.08; H, 4.18; N, 3.63; Found: C, 58.88; H, 4.52; N, 3.86.



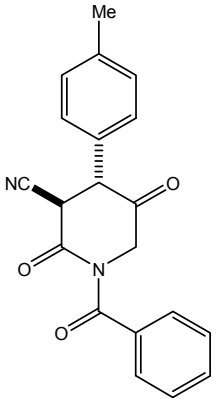
Compound **4i:** Yellowish oil, yield 89%. IR (KBr) υ_{max} 3092, 3055, 2240, 1723, 1608, 1582, 1451, 747, 699 cm^{-1}. ^{1}H NMR (400 MHz; $CDCl_3$) δ = 3.90 (d, J = 11.3 Hz, 1H), 4.57 (d, J = 11.3 Hz, 1H), 5.61 (d, J = 10.5 Hz, 1H), 5.64 (d, J = 10.5 Hz, 1H), 7.08-7.37 (m, 10H). ^{13}C NMR (400 MHz; $CDCl_3$) δ = 32.1, 47.9, 56.7, 16.7, 126.7, 127.5, 128.8, 129.9, 131.2, 132.2, 134.5, 135.8, 164.4, 171.9, 207.2. EIMS (m/e): 318 (M^+). Anal. Calcd. for $C_{19}H_{14}N_2O_3$: C, 71.69; H, 4.43; N, 8.80; Found: C, 71.40; H, 4.11; N, 8.37.



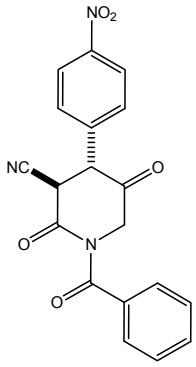
Compound **4j:** Yellowish oil, yield 84%. IR (KBr) υ_{max} 3099, 3054, 2815, 2235, 1725, 1602, 1581, 1454, 745, 695 cm^{-1}. ^{1}H NMR (400 MHz; $CDCl_3$) δ =3.83 (s, 3H), 3.92 (d, J = 11.2 Hz, 1H), 4.55 (d, J = 11.2, 1H), 5.60 (d, J = 10.4, 1H), 5.64 (d, J = 10.4 Hz, 1H), 7.05-7.32 (m, 5H), 7.45-7.57 (m, 2H), 7.63-7.79 (m, 2H). ^{13}C NMR (400 MHz; $CDCl_3$) δ = 32.6, 48.1, 51.2, 55.9, 114.2, 117.6, 126.9, 127.8, 129.4, 131.4, 132.7, 134.2, 159.2, 166.0, 172.7, 207.1. EIMS (m/e): 348 (M^+). Anal. Calcd. for $C_{20}H_{16}N_2O_4$: C, 68.96; H, 4.63; N, 8.04; Found: C, 69.18; H, 4.43; N, 8.37.



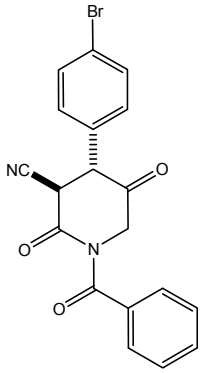
Compound **4k:** Yellowish oil, yield 87%. IR (KBr) υ_{max} 3100, 3059, 2238, 1725, 1604, 1581, 1452, 742, 693 cm^{-1}. ^{1}H NMR (400 MHz; $CDCl_3$) δ = 3.95 (d, J = 11.4 Hz, 1H), 4.58 (d, J = 11.4 Hz, 1H), 5.59 (d, J = 10.3 Hz, 1H), 5.63 (d, J = 10.3 Hz, 1H), 7.10-7.31 (m, 5H), 7.48-7.60 (m, 2H), 8.10-8.15 (m, 2H). ^{13}C NMR (400 MHz; $CDCl_3$) δ = 31.9, 48.6, 51.7, 16.4, 127.1, 128.4, 129.6, 130.9, 132.8, 133.9, 135.0, 136.2, 165.9, 172.1, 207.5. EIMS (m/e): 352, 354 (M^+, M^++2). Anal. Calcd. for $C_{19}H_{13}ClN_2O_3$: C, 64.69; H, 3.71; N, 7.94; Found: C, 64.86; H, 3.96; N, 7.71.



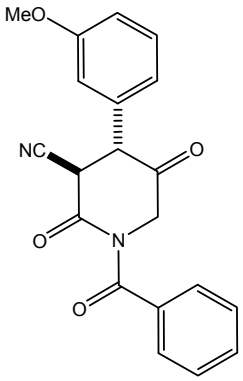
Compound **4l:** Yellowish oil, yield 88%. IR (KBr) υ_{max} 3091, 3052, 2240, 1721, 1605, 1584, 1451, 746, 699 cm^{-1}. ^{1}H NMR (400 MHz; $CDCl_3$) δ = 2.44 (s, 3H), 3.87 (d, J = 11.2 Hz, 1H), 4.55 (d, J = 11.2 Hz, 1H), 5.51 (d, J = 10.5 Hz, 1H), 5.63 (d, J = 10.5 Hz, 1H), 7.03-7.06 (m, 2H), 7.09-7.29 (m, 5H), 7.32-7.39 (m, 2H). ^{13}C NMR (400 MHz; $CDCl_3$) δ = 24.1, 32.4, 48.9, 51.2, 116.3, 127.2, 128.9, 130.1, 131.5, 132.8, 133.9, 135.2, 136.8, 165.7, 172.4, 207.9. EIMS (m/e): 332 (M^+). Anal. Calcd. for $C_{20}H_{16}N_2O_3$: C, 72.28; H, 4.85; N, 8.43; Found: C, 71.92; H, 5.03; N, 8.22.



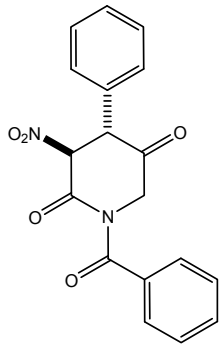
Compound **4m:** Yellowish oil, yield 92%. IR (KBr) υ_{max} 3090, 3049, 2245, 1721, 1602, 1585, 1456, 748, 697 cm^{-1}. ^{1}H NMR (400 MHz; $CDCl_3$) δ = 3.96 (d, J = 11.4 Hz, 1H), 4.60 (d, J = 11.4 Hz, 1H), 5.60 (d, J = 10.4 Hz, 1H), 5.65 (d, J = 10.4 Hz, 1H), 7.12-7.32 (m, 5H), 7.66-7.69 (m, 2H), 8.14-8.18 (m, 2H). ^{13}C NMR (400 MHz; $CDCl_3$) δ = 32.1, 48.8, 51.6, 116.1, 121.5, 126.9, 127.7, 129.9, 132.5, 134.2, 140.8, 145.9, 165.6, 171.7, 206.8. EIMS (m/e): 363 (M^+). Anal. Calcd. for $C_{19}H_{13}N_3O_5$: C, 62.81; H, 3.61; N, 11.57; Found: C, 62.48; H, 3.35; N, 11.94.



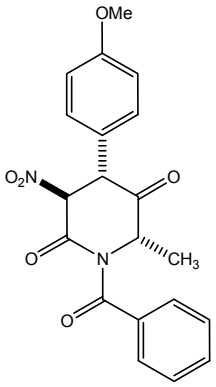
Compound **4n:** Yellowish oil, yield 90%. IR (KBr) υ_{max} 3095, 3050, 2247, 1720, 1604, 1584, 1458, 743, 695 cm^{-1}. ^{1}H NMR (400 MHz; $CDCl_3$) δ = 3.94 (d, J = 11.3 Hz, 1H), 4.60 (d, J = 11.3 Hz, 1H), 5.61 (d, J = 10.5 Hz, 1H), 5.64 (d, J = 10.5 Hz, 1H), 7.10-7.31 (m, 5H), 7.36-7.45 (m, 2H), 7.71-7.87 (m, 2H). ^{13}C NMR (400 MHz; $CDCl_3$) δ = 32.7, 48.5, 51.9, 116.9, 121.5, 126.4, 127.9, 128.4, 131.2, 132.6, 133.8, 134.9, 165.8, 172.7, 207.2. EIMS (m/e): 396, 398 (M^+, M^++2). Anal. Calcd. for $C_{19}H_{13}BrN_2O_3$: C, 57.45; H, 3.30; N, 7.05; Found: C, 57.68; H, 3.62; N, 6.86.



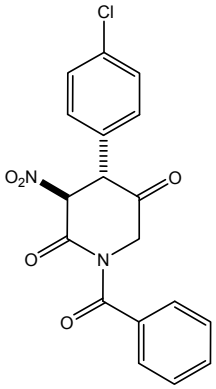
Compound **4o:** Yellowish oil, yield 81%. IR (KBr) υ_{max} 3096, 3055, 2820, 2238, 1723, 1604, 1583, 1452, 745, 698 cm^{-1}. ^{1}H NMR (400 MHz; $CDCl_3$) δ = 3.81 (s, 3H), 3.91 (d, *J* = 11.4 Hz, 1H), 4.56 (d, *J* = 11.4 Hz, 1H), 5.60 (d, *J* = 10.3 Hz, 1H), 6.65 (d, *J* = 10.3 Hz, 1H), 6.85-6.95 (m, 3H), 7.10-7.28 (m, 5H), 7.32-7.44 (m, 1H). ^{13}C NMR (400 MHz; $CDCl_3$) δ = 32.9, 48.2, 51.6, 55.2, 112.3, 113.7, 117.1, 121.2, 126.5, 127.9, 129.2, 131.2, 132.8, 134.6, 159.7, 164.9, 172.7, 207.1. EIMS (m/e): 348 (M^+). Anal. Calcd. for $C_{20}H_{16}N_2O_4$: C, 68.96; H, 4.63; N, 8.04; Found: C, 69.31; H, 4.26; N, 8.34.



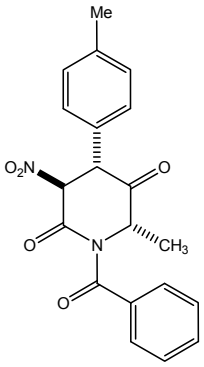
Compound **4p:** Yellowish oil, yield 89%. IR (KBr) υ_{max} 3100, 3054, 1725, 1608, 1589, 1550, 1452, 746, 699 cm^{-1}. ^{1}H NMR (400 MHz; $CDCl_3$) δ = 3.96 (d, *J* = 11.2 Hz, 1H), 5.52 (d, *J* = 11.2 Hz, 1H), 5.59 (d, *J* = 10.5 Hz, 1H), 5.62 (d, *J* = 10.5 Hz, 1H), 7.07-7.35 (m, 10H). ^{13}C NMR (400 MHz; $CDCl_3$) δ = 49.2, 51.4, 89.1, 126.2, 127.4, 128.9, 129.9, 131.2, 132.5, 134.6, 135.8, 172.1, 173.4, 207.6. EIMS (m/e): 338 (M^+). Anal. Calcd. for $C_{18}H_{14}N_2O_5$: C, 63.90; H, 4.17; N, 8.28; Found: C, 63.59; H, 4.46; N, 8.04.



Compound **4q:** Yellowish oil, yield 85%. IR (KBr) υ_{max} 3099, 3060, 2850, 1718, 1606, 1587, 1556, 1452, 741, 699 cm^{-1}. ^1H NMR (400 MHz; $CDCl_3$) δ = 1.37 (d, J = 6.6 Hz, 3H), 3.85 (s, 3H), 3.95 (d, J = 11.3 Hz, 1H), 5.54 (d, J = 11.3 Hz, 1H), 5.60 (q, J = 6.6 Hz, 1H), 7.03-7.31 (m, 5H), 7.42-7.55 (m, 2H), 7.65-7.80 (m, 2H). ^{13}C NMR (400 MHz; $CDCl_3$) δ = 15.4, 49.4, 51.9, 54.7, 89.2, 114.9, 126.9, 128.1, 129.8, 131.7, 133.6, 134.9, 159.4, 172.9, 174.1, 207.4. EIMS (m/e): 382 (M^+). Anal. Calcd. for $C_{20}H_{18}N_2O_6$: C, 62.82; H, 4.74; N, 7.33; Found: C, 62.52; H, 4.96; N, 7.60.



Compound **4r:** Yellowish oil, yield 90%. IR (KBr) υ_{max} 3097, 3052, 2854, 1724, 1603, 1583, 1560, 1454, 746, 695 cm^{-1}. ^1H NMR (400 MHz; $CDCl_3$) δ = 3.97 (d, J = 11.4 Hz, 1H), 5.54 (d, J = 11.4 Hz, 1H), 5.58 (d, J = 10.4 Hz, 1H), 5.62 (d, J = 10.4 Hz, 1H), 7.06-7.27 (m, 5H), 7.65-7.70 (m, 2H), 8.10-8.17 (m, 2H). ^{13}C NMR (400 MHz; $CDCl_3$) δ = 49.1, 51.2, 88.9, 126.5, 27.9, 129.0, 130.6, 131.9, 133.4, 134.9, 135.2, 172.7, 173.9, 207.0. EIMS (m/e): 372, 374 (M^+, M^+ +2). Anal. Calcd. for $C_{18}H_{13}ClN_2O_5$: C, 58.00; H, 3.52; N, 7.52; Found: C, 58.24; H, 3.73; N, 7.22



Compound **4s:** Yellowish oil, yield 86%. IR (KBr) υ_{max} 3092, 3055, 1722, 1604, 1582, 1558, 1455, 742, 696 cm^{-1}. ^{1}H NMR (400 MHz; $CDCl_3$) δ = 1.35 (d, *J* = 6.7 Hz, 3H), 2.42 (s, 3H), 3.93 (d, *J* = 11.3 Hz, 1H), 5.50 (d, *J* = 11.3 Hz, 1H), 5.61 (q, *J* = 6.7 Hz, 1H), 7.02-7.07 (m, 2H), 7.10-7.32 (m, 5H), 7.44-7.57 (m, 2H). ^{13}C NMR (400 MHz; $CDCl_3$) δ = 15.2, 24.3, 49.4, 51.6, 89.2, 126.9, 128.5, 129.8, 130.9, 132.2, 133.4, 134.6, 136.8, 172.1, 173.9, 207.9. EIMS (m/e): 366 (M^+). Anal. Calcd. for $C_{20}H_{18}N_2O_5$: C, 65.57; H, 4.95; N, 7.65; Found: C, 65.82; H, 4.67; N, 7.81.