Synergistic catalysis: Highly diastereoselective benzoazole addition to Morita-Baylis-Hillman carbonates

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Supporting information

General: The general reaction is:

\begin{align*}
\text{R}_1 \text{R}_2 \text{N}^\text{O} \quad + \quad \text{R}_1 \text{R}_2 \text{O}^\text{Boc} \quad \text{COOMe} \\
\quad \text{Toluene, rt, 14h} \\
\quad \text{AgOAc 10 mol\%} \\
\quad \text{DABCO 10 mol\%} \\
\quad \text{R}_1 \text{R}_2 \text{N}^\text{O} \quad \text{COOMe} \\
\end{align*}

The benzoxazoles(1) were synthesized and analysed following the procedure from the article: “Diastereo- and Enantioselective Pd(II)-Catalyzed Additions of 2-Alkylazaarenes to N-Boc Imines and Nitroalkenes” (\textit{J. Am. Chem. Soc.} 2012, 134, 18193−18196).

The MBH-carbonates(2) were synthesized and analysed following the procedure from the article “Construction of adjacent quaternary and tertiary stereocenters via an organocatalytic allylic alkylation of Morita-Baylis-Hillman carbonates” (\textit{Adv. Synth. Catal.} 2007, 349, 281 – 286).

Thin layer chromatography (TLC) was performed on Merck TLC Silicagel 60 F\textsubscript{254}. Product spots were visualized by UV-light at 254nm, and developed with potassium permanganate. Column chromatography was effected using silica gel (Geduran Si60, 40-63μm). Infra-red spectra were recorded on a Nicolet 280 FT-IR. 1H-NMR, 13C-NMR, 19F-NMR were recorded with Bruker AV300, Bruker DPX400. High resolution mass spectra were recorded using a MaXis (Bruker Daltonics, Bremen, Germany) mass spectrometer equipped with a Time of Flight (TOF) analyser.
Final compounds corresponding to the Scheme 2: Study of MBH-carbonates reaction with benzoxazole.

(**+)methyl 2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)-3-phenylpentanoate (3a’)

To a solution of 2-ethyl-6-nitrobenzo[d]oxazole (1 equiv, 19 mg, 0.1 mmol) in anhydrous toluene (0.1 mol/L) was added methyl 2-(((tert-butoxycarbonyl)oxy)(phenyl)methyl)acrylate (2a) (2 equiv, 58 mg, 0.2 mmol), Pd(OAc)₂ (10 mol%, 2 mg, 0.01 mmol), 1,4-diaza-bicyclo[2.2.2]octane (10 mol%, 1 mg, 0.01 mmol). The reaction was stirred for 14 hours at room temperature. The conversion was checked by NMR. D.r. is 2:1. The reaction mixture was purified by column chromatography (10:1 Hexane/EtOAc) to obtain 18 mg of desired product as oil. The product yield is 50%.

1H-NMR (CDCl₃, 300 MHz): Diastereomer 1: 8.35 (d, J = 2.0 Hz, 1H), 8.22 (dd, J = 8.8 Hz, J = 2.1 Hz, 1H), 7.69 (d, J = 8.8 Hz, 1H), 7.31-7.20 (m, 5H), 6.10 (s, 1H), 5.77 (s, 1H), 4.36 (d, J = 11.9 Hz, 1H), 3.8 (m, 1H), 3.54 (s, 3H), 1.20 (d, J = 6.9 Hz, 3H). Diastereomer 2: 8.2 (d, J = 2.0 Hz, 1H), 8.12 (dd, J = 8.8 Hz, J = 2.1 Hz, 1H), 7.56 (d, J = 8.8 Hz, 1H), 7.16-6.93 (m, 5H), 6.38 (s, 1H), 5.84 (s, 1H), 4.34 (d, J = 11.2 Hz, 1H), 4.00 (m, 1H), 3.66 (s, 3H), 1.45 (d, J = 6.9 Hz, 3H).

(**+)methyl 2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)-3-(p-tolyl)pentanoate (3a)

To a solution of 2-ethyl-6-nitrobenzo[d]oxazole (1 equiv, 19 mg, 0.1 mmol) in anhydrous toluene (0.1 mol/L) was added methyl 2-(((tert-butoxycarbonyl)oxy)(p-tolyl)methyl)acrylate (2b) (4 equiv, 120 mg, 0.4 mmol), silver acetate (10 mol%, 2 mg, 0.01 mmol), 1,4-diaza-bicyclo[2.2.2]octane (10 mol%, 1 mg, 0.01 mmol). The reaction was stirred for 14 hours at 0°C. The conversion was checked by NMR. The reaction mixture was purified by column chromatography (7:1 Hexane/EtOAc) to obtain 34 mg of desired product as oil. The product yield is 92%. HR-MS (m/z) for C₂₀H₁₉N₂O₅ calculated [M+H]⁺ 367.1288, measured [M+H]⁺ 367.1280. IR (cm⁻¹): 2985, 1720, 1620, 1524, 1343, 1150. ¹H-NMR (CDCl₃, 300 MHz): 8.41 (d, J = 2.2 Hz, 1H), 8.29 (dd, J = 2.2 Hz, J = 8.8 Hz), 7.76 (d, 1H, J = 8.8 Hz), 7.40-7.25 (m, 5H, phenyl), 6.19 (s, 1H), 5.86 (d, 1H, J = 0.7 Hz), 4.45 (d, 1H, J = 11.7 Hz), 3.90 (m, 1H), 3.61 (s, 3H), 2.27 (s, 3H), 1.19 (d, 3H, J = 6.6 Hz).

¹³C-NMR (CDCl₃, 75 MHz): 174.2, 166.4, 149.7, 146.5, 145.0, 141.6, 139.3, 128.7, 128.6, 127.4, 124.9, 120.4, 119.6, 119.4, 107.2, 106.9, 52.0, 50.7, 38.2, 18.4.

(**+)methyl 2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)-3-(p-tolyl)pentanoate (3b)

To a solution of 2-ethyl-6-nitrobenzo[d]oxazole (1 equiv, 19 mg, 0.1 mmol) in anhydrous toluene (0.1 mol/L) was added methyl 2-(((tert-butoxycarbonyl)oxy)(p-tolyl)methyl)acrylate (2b) (4 equiv, 122 mg, 0.4 mmol), silver acetate (10 mol%, 2 mg, 0.01 mmol), 1,4-diaza-bicyclo[2.2.2]octane (10 mol%, 1 mg, 0.01 mmol). The reaction was stirred for 14 hours. The conversion was checked by NMR. The reaction mixture was purified by column chromatography (5:1 Hexane/EtOAc) to obtain 43 mg of the desired product as oil. The product yield is 90%. MS (ESI+) m/z: 381.1 [M+H]+. IR (cm⁻¹): 2985, 2950, 1720, 1626, 1524, 1343, 1149. ¹H-NMR (CDCl₃, 300 MHz): 8.33 (d, 1H, J = 2.2 Hz), 8.20 (dd, 1H, J = 2.2 Hz, J = 8.8 Hz), 7.68 (d, 1H, J = 8.8 Hz), 7.16 (d, 2H, J = 8.1 Hz), 7.08 (d, 2H, J = 8.1 Hz), 6.08 (s, 1H), 5.74 (s, 1H), 4.32 (d, 1H, J = 12.1 Hz), 3.79 (m, 1H), 3.53 (s, 3H), 2.27 (s, 3H), 1.19 (d, 3H, J = 6.9 Hz). ¹³C-NMR (CDCl₃, 75 MHz):
(±)methyl 3-(4-bromophenyl)-2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)pentanoate (3c)

To a solution of 2-ethyl-6-nitrobenzo[d]oxazole (1 equiv, 100 mg, 0.52 mmol) in anhydrous toluene (0.1 mol/L) was added methyl 2-((4-bromophenyl)((tert-butoxycarbonyl)oxy)methyl)acrylate (2c) (4 equiv, 768 mg, 2.08 mmol), silver acetate (10 mol%, 12 mg, 0.052 mmol), 1,4-diazabicyclo[2.2.2]octane (10 mol%, 6 mg, 0.052 mmol). The reaction was stirred for 14 hours at room temperature. The conversion was checked by NMR. The reaction mixture was purified by column chromatography (5:1 Hexane/EtOAc) to obtain 188 mg of the desired product as oil. The product yield is 80%. HR-MS (m/z) for C₂₀H₁₈BrN₂O₅ calculated [M+H]+ 445.0394, measured [M+H]+ 445.0386. IR (cm⁻¹): 2989, 2951, 1717, 1624, 1524, 1342, 1148. ¹H-NMR (CDCl₃, 300 MHz): 8.33 (d, 1H, J=2.2 Hz), 8.21 (dd, 1H, J=2.2 Hz, J=8.8 Hz), 7.68 (d, 1H, J=7.7 Hz), 7.40 (d, 2H, J=8.4 Hz), 7.16 (d, 2H, J=8.4 Hz), 6.77 (s, 1H), 5.76 (d, 1H, J=0.7 Hz), 4.33 (d, 1H, J=11.7 Hz), 3.79 (m, 1H), 3.54 (s, 3H), 1.19 (d, 3H, J=6.9 Hz).

13C-NMR (CDCl₃, 75 MHz): 173.8, 166.2, 149.6, 146.4, 145.1, 141.1, 138.4, 131.9, 130.3, 125.2, 120.3, 119.7, 107.2, 52.1, 50.2, 37.9, 18.3.

(±)methyl 3-(4-fluorophenyl)-2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)pentanoate (3d)

To a solution of 2-ethyl-6-nitrobenzo[d]oxazole (1 equiv, 19 mg, 0.1 mmol) in anhydrous toluene (0.1 mol/L) was added methyl 2-(((tert-butoxycarbonyl)oxy)(4-fluorophenyl)methyl)acrylate (2d) (4 equiv, 124 mg, 0.4 mmol), silver acetate (10 mol%, 2 mg, 0.01 mmol), 1,4-diazabicyclo[2.2.2]octane (10 mol%, 1 mg, 0.01 mmol). The reaction was stirred for 14 hours at room temperature. The conversion was checked by NMR. The reaction mixture was purified by column chromatography (5:1 Hexane/EtOAc) to obtain 32 mg of the desired product as oil. The product yield is 82%. HR-MS (m/z) for C₂₀H₁₈FN₂O₅ calculated [M+H]+ 385.1194, measured [M+H]+ 385.1200. IR (cm⁻¹): 2946, 1724, 1625, 1527, 1341, 1151. ¹H-NMR (CDCl₃, 300 MHz): 8.34 (d, 1H, J=2.2 Hz), 8.21 (dd, 1H, J=2.2 Hz, J=8.8 Hz), 7.68 (d, 1H, J=8.8 Hz), 7.40 (d, 2H, J=8.4 Hz), 7.16 (d, 2H, J=8.4 Hz), 6.77 (s, 1H), 5.76 (d, 1H, J=0.7 Hz), 4.33 (d, 1H, J=11.7 Hz), 3.79 (m, 1H), 3.54 (s, 3H), 1.19 (d, 3H, J=6.9 Hz). ¹³C-NMR (CDCl₃, 75 MHz): 173.8, 166.2, 149.6, 146.4, 145.1, 141.1, 138.4, 131.9, 130.3, 125.2, 121.33, 120.5, 119.7, 107.2, 52.1, 50.2, 37.9, 18.3.

19F-NMR (CDCl₃, 300 MHz): -115.2 ppm.

(±)methyl 2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)-3-(4-nitrophenyl)pentanoate (3e)

To a solution of 2-ethyl-6-nitrobenzo[d]oxazole (1 equiv, 19 mg, 0.1 mmol) in anhydrous toluene (0.1 mol/L) was added methyl 2-(((tertbutoxycarbonyl)oxy)(4-nitrophenyl)methyl)acrylate (2e) (4 equiv, 135 mg, 0.4 mmol), silver acetate (10 mol%, 2 mg, 0.01 mmol), 1,4-diazabicyclo[2.2.2]octane (10 mol%, 1 mg, 0.01 mmol). The reaction was stirred for 14 hours. The conversion was checked by NMR. The reaction mixture was purified by column chromatography (5:1 Hexane/EtOAc) to obtain 41 mg of the desired product as white solid (melting point T = 136 °C). The product yield is 99%. HR-MS (m/z) for C₂₀H₁₈N₃O₇ calculated [M+H]+ 412.1139, measured [M+H]+ 412.1146. IR(cm⁻¹): 2986, 2950, 1719, 1604, 1520,
H-NMR (CDCl$_3$, 300 MHz): 8.35 (d, 1H, J=1.9 Hz), 8.23 (dd, 1H, J=2.3 Hz, J=8.7 Hz), 8.16 (d, 2H, J=9.0 Hz), 7.70 (d, 1H, J=8.7 Hz), 7.49 (d, 2H, J=8.7 Hz), 6.19 (s, 1H), 5.85 (d, 1H, J=1.1 Hz), 4.50 (d, 1H, J=11.7 Hz), 3.92-3.80 (m, 1H), 3.56 (s, 3H), 1.21 (d, 3H, J=7.2 Hz).

C-NMR (CDCl$_3$, 75 MHz): 173.1, 165.9, 149.6, 147.3, 147.0, 146.2, 140.4, 129.6, 126.2, 124.0, 120.6, 119.8, 107.2, 52.2, 37.7, 18.3.

(±)methyl 3-(3-bromophenyl)-2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)pentanoate (3f)

To a solution of 2-ethyl-6-nitrobenzo[d]oxazole (1 equiv, 19 mg, 0.1 mmol) in anhydrous toluene (0.1 mol/L) was added methyl 2-(((tert-butoxycarbonyl)oxy)(3-bromophenyl)methyl)acrylate (2f) (4 equiv, 148 mg, 0.4 mmol), silver acetate (10 mol%, 2 mg, 0.01 mmol), 1,4-diaza-bicyclo[2.2.2]octane (10 mol%, 1 mg, 0.01 mmol). The reaction was stirred for 14 hours at room temperature. The conversion was checked by NMR. The reaction mixture was purified by column chromatography (7:1 Hexane/EtOAc) to obtain 43 mg of the desired product as oil. The product yield is 97%. HR-MS (m/z) for C$_{20}$H$_{18}$BrN$_2$O$_5$ calculated [M+H]$^+$ 445.0394, measured [M+H]$^+$ 445.0397. IR (cm$^{-1}$): 2985, 2950, 1718, 1618, 1527, 1343, 1150.

H-NMR (CDCl$_3$, 300 MHz): 8.34 (d, 1H, J=2.2 Hz), 8.21 (dd, 1H, J=2.2 Hz, J=8.8 Hz), 7.68 (d, 1H, J=8.8 Hz), 7.45-7.10 (m, 4H), 6.14 (s, 1H), 5.78 (s, 1H), 4.33 (d, 1H, J=11.7 Hz), 3.85-3.70 (m, 1H), 3.54 (s, 3H), 1.20 (d, 3H, J=6.9 Hz).

C-NMR (CDCl$_3$, 75 MHz): 173.7, 166.2, 149.6, 146.4, 145.1, 141.7, 140.9, 131.5, 130.6, 130.3, 127.5, 125.5, 122.8, 120.5, 119.7, 107.2, 50.3, 38.0, 18.4.

(±)methyl 3-(4-chlorophenyl)-2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)pentanoate (3g)

To a solution of 2-ethyl-6-nitrobenzo[d]oxazole (1 equiv, 19 mg, 0.1 mmol) in anhydrous toluene (0.1 mol/L) was added methyl 2-(((tert-butoxycarbonyl)oxy)(4-chlorophenyl)methyl)acrylate (2g) (4 equiv, 148 mg, 0.4 mmol), silver acetate (10 mol%, 2 mg, 0.01 mmol), 1,4-diaza-bicyclo[2.2.2]octane (10 mol%, 1 mg, 0.01 mmol). The reaction was stirred for 14 hours at room temperature. The conversion was checked by NMR. The reaction mixture was purified by column chromatography (7:1 Hexane/EtOAc) to obtain 32 mg of the desired product as oil. The product yield is 80%. HR-MS (m/z) for C$_{20}$H$_{18}$ClN$_2$O$_5$ calculated [M+H]$^+$ 401.0899, measured [M+H]$^+$ 401.0902. IR (cm$^{-1}$): 2989, 2950, 1718, 1618, 1527, 1343, 1150. H-NMR (CDCl$_3$, 300 MHz): 8.34 (d, 1H, J=2.2 Hz), 8.21 (dd, 1H, J=2.2 Hz, J=8.8 Hz), 7.68 (d, 1H, J=8.8 Hz), 7.45-7.10 (m, 4H), 6.14 (s, 1H), 5.78 (s, 1H), 4.33 (d, 1H, J=11.7 Hz), 3.85-3.70 (m, 1H), 3.55 (s, 3H), 1.20 (d, 3H, J=6.9 Hz). C-NMR (CDCl$_3$, 75 MHz): 173.7, 166.2, 149.6, 146.4, 145.1, 141.7, 140.9, 131.5, 130.6, 130.3, 127.5, 125.5, 122.8, 120.5, 119.7, 107.2, 50.3, 38.0, 18.4.

(±)methyl 3-(2-bromophenyl)-2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)pentanoate (3i)

To a solution of 2-ethyl-6-nitrobenzo[d]oxazole (1 equiv, 19 mg, 0.1 mmol) in anhydrous toluene (0.1 mol/L) was added methyl 2-(((tert-butoxycarbonyl)oxy)(2-bromophenyl)methyl)acrylate (2i) (4 equiv, 148 mg, 0.4 mmol), silver acetate (10 mol%, 2 mg, 0.01 mmol), 1,4-diaza-bicyclo[2.2.2]octane (10 mol%, 1 mg, 0.01 mmol). The reaction was stirred for 14 hours at room temperature. The conversion was checked by NMR. The reaction mixture was purified by column chromatography (5:1 Hexane/EtOAc) to obtain 26 mg of the desired product as
white solid (melting point T = 138°C). The product yield is 60%. HR-MS (m/z) for C_{20}H_{18}BrN_{2}O_{5} calculated [M+H]^+ 445.0394, measured [M+H]^+ 445.0397. IR(cm⁻¹): 2983, 2950, 1720, 1625, 1523, 1346, 1153. ^1H-NMR (CDCl₃, 300 MHz): 8.38-8.33 (d, J = 1.8 Hz, 1H), 8.25-8.19 (dd, J = 2.2 Hz, J = 8.8 Hz, 1H), 7.71 (d, J = 8.8 Hz, 1H), 7.59-7.54 (dd, J = 1.1 Hz, J = 7.7 Hz, 1H), 7.34-7.21 (m, 2H), 7.10-7.03 (ddd, J = 2.2 Hz, J = 6.6 Hz, J = 8.8 Hz, 1H), 5.80 (d, J = 0.7 Hz, 1H), 5.00 (d, J = 11.7 Hz, 1H), 3.92-3.75 (m, 1H), 3.53 (s, 3H), 1.26 (d, J = 6.9 Hz, 3H). ^13C-NMR (CDCl₃, 75 MHz): 173.7, 166.3, 149.7, 146.4, 140.4, 138.5, 133.5, 128.8, 127.8, 126.6, 120.5, 119.7, 107.3, 52.0, 48.9, 38.7, 17.3.

Final compounds corresponding to the Scheme 3: Study of benzoxazole reactivity with MBH-carbonate.

(±)-methyl 4-(5-chloro-6-nitrobenzo[d]oxazol-2-yl)-3-(4-chlorophenyl)-2-methylenepentanoate (3l)

To a solution of 5-chloro-2-ethyl-6-nitrobenzo[d]oxazole (1 equiv, 23 mg, 0.1 mmol) in anhydrous toluene (0.1 mol/L) was added methyl 2-(((tert-butoxycarbonyl)oxy)(4-chlorophenyl)methyl)acrylate (2g) (4 equiv, 135 mg, 0.4 mmol), silver acetate (10 mol%, 2 mg, 0.01 mmol), 1,4-diazabicyclo[2.2.2]octane (10 mol%, 1 mg, 0.01 mmol). The reaction was stirred for 14 hours at room temperature. The conversion was checked by NMR. The reaction mixture was purified by column chromatography (5:1 Hexane/EtOAc) to obtain 47 mg of the desired product as white solid (melting point T = 138 °C). The product yield is 95%. HR-MS (m/z) for C_{20}H_{17}Cl_{2}N_{2}O_{5} calculated [M+H]^+ 435.0509, measured [M+H]^+ 445.0509. IR(cm⁻¹): 2993, 2951, 1720, 1627, 1151. ^1H-NMR (CDCl₃, 400 MHz): 8.00 (s, 1H), 7.74 (s, 1H), 7.3-7.1 (m, 4H), 6.11 (s, 1H), 5.74 (s, 1H), 4.31 (d, J = 11.6 Hz, 1H), 3.80-3.70 (m, 1H), 3.55 (s, 3H), 1.18 (d, J = 6.9 Hz, 3H). ^13C-NMR (CDCl₃, 100 MHz): 174.4, 166.2, 147.9, 144.8, 141.1, 137.7, 133.3, 130.0, 129.0, 125.2, 122.3, 108.6, 52.1, 50.2, 37.9, 18.3.

(±)-methyl 3-(4-chlorophenyl)-2-methylene-4-(oxazolo[4,5-b]pyridin-2-yl)pentanoate(3m)

To a solution of 2-ethyloxazolo[4,5-b]pyridine (1equiv, 15 mg, 0.1 mmol) in anhydrous toluene (0.1 mol/L) was added methyl 2-(((tert-butoxycarbonyl)oxy)(4-chlorophenyl)methyl)acrylate (2g) (4 equiv, 135 mg, 0.4 mmol), silver acetate (10 mol%, 2 mg, 0.01 mmol), 1,4-diazabicyclo[2.2.2]octane (10 mol%, 1 mg, 0.01 mmol). The reaction was stirred for 14 hours at room temperature. The conversion was checked by NMR. The reaction mixture was purified by column chromatography (4:1 Hexane/EtOAc) to obtain 23 mg of the desired product as oil. The product yield is 65%. HR-MS (m/z) for C_{19}H_{18}Cl_{2}N_{2}O_{3} calculated [M+H]^+ 357.1000, measured [M+H]^+ 357.1004. IR (cm⁻¹): 2986, 2947, 1720, 1624, 1151. ^1H-NMR (CDCl₃, 400 MHz): 8.57-8.53 (dd, J = 1.5 Hz, J = 4.9 Hz, 1H), 7.83-7.78 (dd, J = 1.5 Hz, J = 8.1 Hz, 1H), 7.37-7.25 (m, 5H), 6.21 (s, 1H), 5.92 (d, J = 1.0 Hz, 1H), 4.45 (d, J = 11.7 Hz, 1H), 3.92-3.82 (m, 1H), 3.63 (s, 3H), 1.27 (d, J = 6.9 Hz, 3H). ^13C-NMR (CDCl₃, 100 MHz): 174.4, 166.2, 147.9, 144.8, 141.1, 137.7, 133.3, 130.0, 129.0, 125.4, 119.8, 118.2, 52.0, 50.0, 37.9, 18.3.
(±)methyl 3-(4-chlorophenyl)-2-methylene-4-(5-nitrobenzo[d]oxazol-2-yl)pentanoate (3n)

To a solution of 2-ethyl-5-nitrobenzo[d]oxazole (1equiv, 20 mg, 0.1 mmol) in anhydrous toluene (0.1 mol/L) was added methyl 2-(((tert-butoxycarbonyl)oxy)(4-chlorophenyl)methyl)acrylate (2g) (4 equiv, 135 mg, 0.4 mmol), silver acetate (10 mol%, 2 mg, 0.01 mmol), 1,4-diazabicyclo[2.2.2]octane (10 mol%, 1 mg, 0.01 mmol). The reaction was stirred for 14 hours at room temperature. The conversion was checked by NMR. The reaction mixture was purified by column chromatography (4:1 Hexane/EtOAc) to obtain 38 mg of the desired product as oil. The product yield is 90%. HR-MS (m/z) for C_{20}H_{18}ClN_{2}O_{5} calculated [M+H]^+ 401.0899, measured [M+H]^+ 401.0889. IR (cm⁻¹): 2986, 2954, 1720, 1617, 1528, 1346, 1151. 1H-NMR (CDCl₃, 300 MHz): 8.52-8.47 (d, J = 2.2 Hz, 1H), 8.25-8.19 (dd, J = 2.2 Hz, J = 8.8 Hz, 1H), 7.55-7.49 (d, J = 9.2 Hz, 1H), 7.30-7.19 (m, 4H), 6.11 (s, 1H), 5.77 (s, 1H), 4.33 (d, J = 12.1 Hz, 1H), 3.83-3.69 (m, 1H), 3.54 (s, 3H), 1.19 (d, J = 7.0 Hz, 3H).

13C-NMR (CDCl₃, 75 MHz): 172.1, 166.3, 154.1, 145.2, 141.5, 141.2, 137.9, 133.2, 130.0, 128.9, 125.2, 120.9, 116.2, 110.7, 52.1, 50.1, 37.8, 18.3.

(±)methyl 3-(4-chlorophenyl)-2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)heptanoate (3o)

To a solution of 2-butyl-6-nitrobenzo[d]oxazole (1equiv, 22 mg, 0.1 mmol) in anhydrous toluene (0.1 mol/L) was added methyl 2-(((tert-butoxycarbonyl)oxy)(4-chlorophenyl)methyl)acrylate (2g) (4equiv, 135 mg, 0.4 mmol), silver acetate (10 mol%, 2 mg, 0.01 mmol), 1,4-diazabicyclo[2.2.2]octane (10 mol%, 1 mg, 0.01 mmol). The reaction was stirred for 14 hours at room temperature. The conversion was checked by NMR. The reaction mixture was purified by column chromatography (5:1 Hexane/EtOAc) to obtain 41 mg of the desired product as oil. The product yield is 92%. HR-MS (m/z) for C_{22}H_{22}ClN_{2}O_{5} calculated [M+H]^+ 429.1212, measured [M+H]^+ 429.1208. IR (cm⁻¹): 2958, 2872, 1720, 1624, 1528, 1346, 1147. 1H-NMR (CDCl₃, 300 MHz): 8.34 (d, J = 1.8 Hz, 1H), 8.21 (dd, J = 2.2 Hz, J = 8.8 Hz, 1H), 7.68 (d, J = 8.8 Hz, 1H), 7.29-7.20 (m, 4H), 6.06 (s, 1H), 5.77 (s, 1H), 4.36 (d, J = 12.1 Hz, 1H), 3.74-3.61 (m, 1H), 3.53 (s, 3H), 1.70-1.59 (m, 1H), 1.47-1.35 (m, 1H), 1.10-1.00 (m, 2H), 0.69 (t, J = 7.0 Hz, 3H). 13C-NMR (CDCl₃, 75 MHz): 173.1, 166.3, 154.1, 145.2, 141.5, 141.2, 137.9, 133.2, 130.0, 128.9, 125.2, 120.9, 116.2, 110.7, 52.1, 49.5, 43.5, 34.6, 20.4, 13.6.

(±)methyl 4-chloro-3-(4-chlorophenyl)-2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)butanoate (3p)

To a solution of 2-(chloromethyl)-6-nitrobenzo[d]oxazole (1equiv, 21 mg, 0.1 mmol) in anhydrous toluene (0.1 mol/L) was added methyl 2-(((tert-butoxycarbonyl)oxy)(4-chlorophenyl)methyl)acrylate (2g) (4 equiv, 135 mg, 0.4 mmol), silver acetate (10 mol%, 2 mg, 0.01 mmol), 1,4-diazabicyclo[2.2.2]octane (10 mol%, 1 mg, 0.01 mmol). The reaction was stirred for 14 hours at room temperature. The conversion was checked by NMR. The reaction mixture was purified by column chromatography (5:1 Hexane/EtOAc to obtain 41 mg of the desired product as oil. The product yield is 92 %. HR-MS (m/z) for C_{22}H_{22}ClN_{2}O_{5} calculated [M+H]^+ 429.1212, measured [M+H]^+ 429.1208. IR (cm⁻¹): 2958, 2872, 1720, 1624, 1528, 1346, 1147. 1H-NMR (CDCl₃, 300 MHz): 8.34 (d, J = 1.8 Hz, 1H), 8.21 (dd, J = 2.2 Hz, J = 8.8 Hz, 1H), 7.68 (d, J = 8.8 Hz, 1H), 7.29-7.20 (m, 4H), 6.06 (s, 1H), 5.77 (s, 1H), 4.36 (d, J = 12.1 Hz, 1H), 3.74-3.61 (m, 1H), 3.53 (s, 3H), 1.70-1.59 (m, 1H), 1.47-1.35 (m, 1H), 1.10-1.00 (m, 2H), 0.69 (t, J = 7.0 Hz, 3H). 13C-NMR (CDCl₃, 75 MHz): 173.1, 166.3, 154.1, 145.2, 141.5, 141.2, 137.9, 133.2, 130.0, 128.9, 125.2, 120.9, 116.2, 110.7, 52.1, 49.5, 43.5, 34.6, 20.4, 13.6.
{\pm} \text{methyl 3-(4-chlorophenyl)-2-methylene-4-(3-nitropyridin-4-yl)butanoate (3q)}

To a solution of 4-methyl-3-nitropyridine (1 equiv, 14 mg, 0.1 mmol) in anhydrous toluene (0.1 mol/L) was added methyl 2-(((tert-butoxycarbonyl)oxy)(4-chlorophenyl)methyl)acrylate (2g) (4 equiv, 135 mg, 0.4 mmol), silver acetate (10 mol%, 2 mg, 0.01 mmol), 1,4-diazabicyclo[2.2.2]octane (10 mol%, 1 mg, 0.01 mmol). The reaction was stirred for 14 hours at room temperature. The conversion was checked by NMR. The reaction mixture was purified by column chromatography (7:1 Hexane/EtOAc) to obtain 6 mg of the desired product as oil. The product yield is 17%. MS (ESI+) \text{m/z}: 347.0 [M+H].

IR (cm\(^{-1}\)): 2951, 1722, 1627, 1522, 1352, 1138.

\(^1\)H-NMR (CDCl\(_3\), 400 MHz): 9.09 (s, 1H), 8.57 (d, \(J = 4.8\) Hz, 1H), 7.23 (d, \(J = 7.8\) Hz, 2H), 7.04 (d, \(J = 7.8\) Hz, 2H), 6.99 (d, \(J = 5.0\) Hz, 1H), 5.73 (s, 1H), 4.24 (t, \(J = 7.6\) Hz, 1H), 3.67 (s, 3H), 3.59-3.37 (dd, \(J = 9.4\) Hz, \(J = 13.6\) Hz, 1H).

\(^{13}\)C-NMR (CDCl\(_3\), 100 MHz): 166.5, 152.7, 145.9, 141.8, 138.6, 133.1, 129.3, 128.8, 125.5, 52.1, 45.9, 36.5.

{\pm} \text{methyl 3-(4-chlorophenyl)-2-methylene-4-(4-nitrobenzo[d]oxazol-2-yl)pentanoate (3r)}

To a solution of 2-ethyl-4-nitrobenzo[d]oxazole (1 equiv, 20 mg, 0.1 mmol) in anhydrous toluene (0.1 mol/L) was added methyl 2-(((tert-butoxycarbonyl)oxy)(4-chlorophenyl)methyl)acrylate (2g) (4 equiv, 135 mg, 0.4 mmol), silver acetate (10 mol%, 2 mg, 0.01 mmol), 1,4-diazabicyclo[2.2.2]octane (10 mol%, 1 mg, 0.01 mmol). The reaction was stirred for 14 hours at room temperature. The conversion was checked by NMR. The reaction mixture was purified by column chromatography (4:1 Hexane/EtOAc) to obtain 30 mg of the desired product as oil. The product yield is 75%. HR-MS (m/z) for C\(_{20}\)H\(_{18}\)ClN\(_2\)O\(_5\) calculated [M+H]\(^+\) 401.0899, measured [M+H]\(^+\) 401.0898. IR (cm\(^{-1}\)): 2990, 2951, 1720, 1624, 1528, 1340, 1147.

\(^1\)H-NMR (CDCl\(_3\), 300 MHz): 8.09 (d, \(J = 8.1\) Hz, 1H), 7.75 (d, \(J = 7.7\) Hz, 1H), 7.39 (t, \(J = 8.1\) Hz, 1H), 7.28-7.17 (m, 4H), 6.11 (s, 1H), 5.87 (s, 1H), 4.38 (d, \(J = 12.1\) Hz, 1H), 3.95-3.82 (m, 1H), 3.55 (s, 3H), 1.20 (d, \(J = 7.0\) Hz, 1H).

\(^{13}\)C-NMR (CDCl\(_3\), 100 MHz): 172.5, 166.3, 152.3, 141.0, 138.1, 135.8, 133.2, 130.0, 128.9, 125.5, 124.2, 120.8, 116.6, 52.1, 49.7, 38.1, 18.4.

{\pm} \text{methyl 3-(4-chlorophenyl)-2-methylene-4-(5-nitropyridin-2-yl)butanoate (3t)}

To a solution of 2-methyl-5-nitropyridine (1 equiv, 14 mg, 0.1 mmol) in anhydrous toluene (0.1 mol/L) was added methyl 2-(((tert-butoxycarbonyl)oxy)(4-chlorophenyl)methyl)acrylate (2g) (4 equiv, 135 mg, 0.4 mmol), silver acetate (10 mol%, 2 mg, 0.01 mmol), 1,4-diazabicyclo[2.2.2]octane (10 mol%, 1 mg, 0.01 mmol). The reaction was stirred for 14 hours at room temperature. The conversion was checked by NMR. The reaction mixture was purified by column chromatography (5:1 Hexane/EtOAc) to obtain 7 mg of the desired product as oil. The product yield is 20%. MS (ESI+) \text{m/z}: 347.0 [M+H].

IR (cm\(^{-1}\)): 2951, 1717, 1631, 1524, 1352, 1145. \(^1\)H-NMR (CDCl\(_3\), 400 MHz): 9.02 (s, 1H), 8.50 (s, 1H), 7.15 (d, \(J = 7.8\) Hz, 2H), 6.96 (d, \(J = 7.8\) Hz, 2H), 6.91 (d, \(J = 4.7\) Hz, 1H), 6.31 (s, 1H), 5.65 (s, 1H), 4.16 (t, \(J = 7.6\) Hz, 1H), 3.60 (s, 3H), 3.53 (dd, \(J = 4.0\) Hz, \(J = 12.0\) Hz, 1H), 3.33 (dd, \(J = 9.3\) Hz, \(J = 9.3\) Hz, 1H).

\(^{13}\)C-NMR (CDCl\(_3\), 100 MHz): 166.5, 152.7, 146.0, 141.8, 138.6, 133.1, 129.3, 128.8, 125.5, 52.1, 45.9, 36.5.
(±)-methyl 4-(6-acetoxybenzo[d]oxazol-2-yl)-3-(4-chlorophenyl)-2-methylenepentanoate (3w)

To a solution of methyl 2-ethylbenzo[d]oxazole-6-carboxylate (1 equiv, 21 mg, 0.1 mmol) in anhydrous toluene (0.1 mol/L) was added methyl 2-(((tert-butoxycarbonyl)oxy)(4-chlorophenyl)methyl)acrylate (2g) (4 equiv, 135 mg, 0.4 mmol), silver acetate (10 mol%, 2 mg, 0.01 mmol), 1,4-diaza-bicyclo[2.2.2]octane (10 mol%, 1 mg, 0.01 mmol). The reaction was stirred for 14 hours at room temperature. The conversion was checked by NMR. The reaction mixture was purified by column chromatography (7:1 Hexane/EtOAc) to obtain 24 mg of the desired product as oil. The product yield is 58%. HR-MS (m/z) for C_{22}H_{21}ClNO_{5} calculated [M+H]^+ 414.1103, measured [M+H]^+ 414.1106. IR (cm\(^{-1}\)): 2990, 2950, 1716, 1624, 1147, 1079. \(^1\)H-NMR (CDCl\(_3\), 400 MHz): 8.11 (s, 1H), 7.98 (d, \(J = 8.3\) Hz, 1H), 7.61 (d, \(J = 8.3\) Hz, 1H), 7.27-7.23 (d, \(J = 8.7\) Hz, 2H), 7.23-7.19 (d, \(J = 8.7\) Hz, 2H), 6.10 (s, 1H), 5.77 (s, 1H), 4.33 (d, \(J = 11.7\) Hz, 1H), 3.88 (s, 3H), 3.79-3.69 (m, 1H), 3.53 (s, 3H), 1.17 (d, \(J = 6.9\) Hz, 3H). \(^{13}\)C-NMR (CDCl\(_3\), 100 MHz): 172.0, 166.3, 155.6, 146.3, 142.7, 141.0, 138.2, 133.1, 130.0, 128.9, 125.4, 119.8, 118.2, 52.0, 50.0, 38.0, 18.3.
Final compounds corresponding to the Scheme 2: Study of MBH-carbonates reaction with benzoxazole.

\((\pm)\)methyl 2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)-3-phenylpentanoate(3a')
(±)methyl 2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)-3-phenylpentanoate (3a)
(±)methyl 2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)-3-(p-tolyl)pentanoate (3b)
(±)methyl 3-(4-bromophenyl)-2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)pentanoate(3c)
(+)-methyl 3-(4-fluorophenyl)-2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)pentanoate(3d)
(±)methyl 2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)-3-(4-nitrophenyl)pentanoate(3e)
(±)methyl 3-(3-bromophenyl)-2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)pentanoate(3f)
(±)methyl 3-(4-chlorophenyl)-2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)pentanoate(3g)
(±)methyl 3-(2-bromophenyl)-2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)pentanoate(3i)
Final compounds corresponding to the Scheme 3: Study of benzoxazole reactivity with MBH-carbonate.

(±)methyl 4-(5-chloro-6-nitrobenzo[d]oxazol-2-yl)-3-(4-chlorophenyl)-2-methylenepentanoate(3I)
(±)-methyl 3-(4-chlorophenyl)-2-methylene-4-oxazol[4,5-b]pyridin-2-yl)pentanoate (3m)
(±)-methyl 3-(4-chlorophenyl)-2-methylene-4-(5-nitrobenzo[d]oxazol-2-yl)pentanoate (3n)
(±)-methyl 3-(4-chlorophenyl)-2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)heptanoate(3o)
$^{(+)}$methyl 4-chloro-3-(4-chlorophenyl)-2-methylene-4-(6-nitrobenzo[d]oxazol-2-yl)butanoate (3p)
(±)methyl 3-(4-chlorophenyl)-2-methylene-4-(3-nitropyridin-4-yl)butanoate(3q)
(±)methyl 3-(4-chlorophenyl)-2-methylene-4-(4-nitrobenzo[d]oxazol-2-yl)pentanoate (3r)
(+)-methyl 3-(4-chlorophenyl)-2-methylene-4-(5-nitropyridin-2-yl)butanoate (3t)
(+)-methyl 4-({6-acetoxybenzo[\text{d}]oxazol-2-yl})-3-(4-chlorophenyl)-2-methylenepentanoate(3w)