[bmIm]OH-catalyzed amidation of azides and aldehydes: An efficient route to amides

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(A) Materials and equipment

Reagents were obtained commercially and used as received. Solvents were purified and dried by standard methods. Substrates 1 were prepared according the literature methods.1 [bmIm]OH was prepared according to our previous reported method.2 All title products were characterized by Infrared (IR), MS, 1H NMR, 13C NMR and High Resolution mass spectrometer (HRMS). 1H NMR spectra were recorded on 400 MHz in CDCl₃, and 13C NMR spectra were recorded on 100 MHz in CDCl₃ using tetramethylsilane (TMS) as an internal standard. Chemical shift values (δ) are given in ppm. Coupling constants (J) were measured in Hz. Mass spectra were obtained with ionization voltages of 70 eV. HRMS spectra were obtained by ESI on a TOF mass. 200-300 mesh silica gel was used for column chromatography.

(B) Experimental procedure

Typical Experimental Procedure for the Synthesis of compounds 3:

To a Schlenk tube were added aryl azides 1 (0.3 mmol), aldehydes 2 (0.36 mmol), [bmIm]OH (10% mmol), DMSO (2 mL). Then the tube was charged with argon, and was stirred at 30 °C for about 5 h, then 10 mL saturated NH₄Cl was added. The reaction mixture was stirred at 25 °C for about 0.5 h. The reaction mixture was extracted with 40 mL ethyl acetate. The extract was washed with brine, dried (Na₂SO₄) and concentrated in vacuum, and the resulting residue was purified by silica gel column chromatography (hexane/ethyl acetate) to afford the desired products 3.

Experimental Procedure for the Synthesis of compounds 4:

To a Schlenk tube were added aryl azides 1 (0.3 mmol), aldehydes 2 (0.36 mmol), [bmIm]OH (4 mmol). Then the tube was charged with argon, and was stirred at 25 °C for about 5 h. After the reaction was finished, the reaction mixture was extracted with 8 mL CDCl₃ to give the crude 1,2,3-triazolines 4.

(C) Analytical data

N-Phenylcyclohexanecarboxamide (3aa):

1H NMR (400 MHz, CDCl₃) δ: 7.53 (d, J = 7.6 Hz, 2H), 7.32-7.21 (m, 3H), 7.10 (t, J = 7.4 Hz, 1H), 2.25 (t, J = 11.0 Hz, 1H), 1.96 (d, J = 12.4 Hz, 2H), 1.84 (d, J = 10.4 Hz, 2H), 1.71 (s, 1H), 1.58 (q, J = 11.2 Hz, 2H), 1.35-1.22 (m. 3H); 13C NMR (100 MHz, CDCl₃) δ: 174.3, 138.0, 128.9, 124.0, 2
119.7, 46.6, 29.6, 25.6; LRMS (EI 70 ev) m/z (%): 203 (M⁺, 100); HRMS m/z (ESI) calcd for C_{13}H_{18}NO (M+H)⁺ 204.1362, found 204.1368.

![Structure 3ab](image)

**N-p-Tolylenecyclohexanecarboxamide (3ab):**

$^1$H NMR (400 MHz, CDCl₃) δ: 7.41 (d, $J = 7.6$ Hz, 2H), 7.15 (s, 1H), 7.11 (d, $J = 8.0$ Hz, 2H), 2.33-2.17 (m, 4H), 1.96 (d, $J = 12.0$ Hz, 2H), 1.84 (d, $J = 11.2$ Hz, 2H), 1.71 (s, 1H), 1.54-1.48 (m, 2H), 1.31-1.21 (m, 3H); $^{13}$C NMR (100 MHz, CDCl₃) δ: 174.2, 135.4, 133.6, 129.4, 119.7, 46.5, 29.6, 25.7, 20.8; LRMS (EI 70 ev) m/z (%): 217 (M⁺, 100); HRMS m/z (ESI) calcd for C_{14}H_{20}NO (M+H)⁺ 218.1514, found 218.1519.

![Structure 3ac](image)

**N-(4-Methoxyphenyl)cyclohexanecarboxamide (3ac):**

$^1$H NMR (400 MHz, CDCl₃) δ: 7.43 (d, $J = 8.4$ Hz, 2H), 7.03 (s, 1H), 6.83 (d, $J = 8.0$ Hz, 2H), 3.81 (s, 1H), 2.22 (d, $J = 13.0$ Hz, 1H), 1.97 (d, $J = 16.8$ Hz, 2H), 1.85 (d, $J = 11.2$ Hz, 2H), 1.72 (s, 1H), 1.59-1.48 (m, 2H), 1.33-1.19 (m, 3H); $^{13}$C NMR (100 MHz, CDCl₃) δ: 174.4, 156.8, 131.3, 121.8, 115.0, 55.7, 46.4, 29.2, 25.4; LRMS (EI 70 ev) m/z (%): 233 (M⁺, 100); HRMS m/z (ESI) calcd for C_{14}H_{20}NO₂ (M+H)⁺ 234.1468, found 234.1471.

![Structure 3ad](image)

**N-(4-Fluorophenyl)cyclohexanecarboxamide (3ad):**

$^1$H NMR (400 MHz, CDCl₃) δ: 7.49 (dd, $J = 4.8$ Hz, $J = 5.2$ Hz, 2H), 7.21 (s, 1H), 7.01 (t, $J = 8.6$ Hz, 2H), 2.24 (d, $J = 11.6$ Hz, 1H), 1.96 (d, $J = 12.4$ Hz, 2H), 1.84 (d, $J = 10.4$ Hz, 2H), 1.71 (s, 1H), 1.63-1.48 (m, 2H), 1.34-1.22 (m, 3H); $^{13}$C NMR (100 MHz, CDCl₃) δ: 174.3, 160.4 (d, $J = 240$ Hz), 134, 121.6 (d, $J = 10$ Hz), 115.7 (d, $J = 20$ Hz), 46.4, 29.7, 25.7; LRMS (EI 70 ev) m/z (%): 221 (M⁺, 100); HRMS m/z (ESI) calcd for C_{13}H_{17}FNO (M+H)⁺ 222.1268, found 222.1276.
N-(4-chlorophenyl)cyclohexanecarboxamide (3ae):

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.49 (d, $J = 8.0$ Hz, 2H), 7.34 (t, $J = 8.4$ Hz, 3H), 2.24 (t, $J = 11.2$ Hz, 1H), 1.95 (d, $J = 12.8$ Hz, 2H), 1.84 (d, $J = 10.8$ Hz, 2H), 1.71 (s, 1H), 1.57 (d, $J = 12.4$ Hz, $J = 12.0$ Hz, 2H), 1.34-1.92 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 174.4, 136.6, 129.1, 128.9, 120.9, 46.5, 29.6, 25.6; LRMS (EI 70 ev) m/z (%): 237 (M$^+$, 67); HRMS m/z (ESI) calcd for C$_{13}$H$_{17}$ClNO (M+H)$^+$ 238.0973, found 238.0979.

N-(4-Nitrophenyl)cyclohexanecarboxamide (3af):

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 8.21 (d, $J = 8.4$ Hz, 2H), 7.78 (d, $J = 8.8$ Hz, 2H), 7.55 (brs, 1H), 2.31 (t, $J = 13.8$ Hz, 1H), 2.02 (d, $J = 10.0$ Hz, 2H), 1.93 (d, $J = 11.2$ Hz, 2H), 1.84-1.71 (m, 1H), 1.57 (dd, $J = 8.0$ Hz, $J = 8.8$ Hz, 2H), 1.35-1.27 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 174.8, 144.0, 143.1, 125.0, 119.1, 46.6, 29.3, 25.4; LRMS (EI 70 ev) m/z (%): 248 (M$^+$, 100); HRMS m/z (ESI) calcd for C$_{13}$H$_{17}$N$_2$O$_3$ (M+H)$^+$ 249.1146, found 249.1150.

N-(4-(Trifluoromethyl)phenyl)cyclohexanecarboxamide (3ag):

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 8.11 (d, $J = 7.6$ Hz, 2H), 7.78 (d, $J = 8.0$ Hz, 2H), 7.49 (s, 1H), 2.33 (t, $J = 13.2$ Hz, 1H), 2.00 (d, $J = 10.4$ Hz, 2H), 1.81 (d, $J = 12.0$ Hz, 2H), 1.64 (s, 1H), 1.52-1.43 (m, 2H), 1.31-1.24 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 175.0, 148.4, 128.9, 126.7 (q, $J = 3.7$ Hz), 126.2, 123.5, 120.9, 120.4 (q, $J = 32.4$ Hz), 114.1, 46.2, 28.9, 25.8; LRMS (EI 70 ev) m/z (%): 271 (M$^+$, 100); HRMS m/z (ESI) calcd for C$_{14}$H$_{17}$F$_3$NO (M+H)$^+$ 272.1236, found 272.1245.
N-(2-Chlorophenyl)cyclohexanecarboxamide (3ah):

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 8.41 (d, $J = 8.4$ Hz, 1H), 7.76 (s, 1H), 7.37 (d, $J = 8.0$ Hz, 1H), 7.28 (t, $J = 8.0$ Hz, 1H), 7.04 (t, $J = 7.6$ Hz, 1H), 2.35 (t, $J = 11.6$ Hz, 1H), 2.03 (d, $J = 11.2$ Hz, 2H), 1.87 (d, $J = 12.0$ Hz, 2H), 1.74 (d, $J = 11.2$ Hz, 1H), 1.59 (q, $J = 12.0$ Hz, 2H), 1.47-1.36 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 174.2, 134.5, 128.7, 127.5, 124.3, 122.5, 121.4, 46.4, 29.5, 25.53, 25.50; LRMS (EI 70 ev) m/z (%): 237 (M$^+$, 63); HRMS m/z (ESI) calcd for C$_{13}$H$_{17}$ClNO (M+H)$^+$ 238.0973, found 238.0981.

N-(3-Chlorophenyl)cyclohexanecarboxamide (3ai):

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.51 (s, 1H), 7.42 (dd, $J = 4.0$ Hz, $J = 4.4$ Hz, 2H), 7.28 (t, $J = 2.4$ Hz, 2H), 2.28 (t, $J = 10.0$ Hz, 1H), 1.96 (d, $J = 12.8$ Hz, 2H), 1.84 (d, $J = 12.4$ Hz, 2H), 1.74 (d, $J = 7.6$ Hz, 1H), 1.54-1.49 (m, 2H), 1.32-1.23 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 174.8, 134.5, 128.7, 127.5, 124.3, 122.5, 121.4, 46.4, 29.5, 25.3; LRMS (EI 70 ev) m/z (%): 237 (M$^+$, 63); HRMS m/z (ESI) calcd for C$_{13}$H$_{17}$ClNO (M+H)$^+$ 238.0973, found 238.0977.

N-(3,4-Difluorophenyl)cyclohexanecarboxamide (3aj):

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.49 (dd, $J = 0.8$ Hz, $J = 2.4$ Hz, 1H), 7.41-7.38 (m, 1H), 7.27-7.22 (m, 2H), 2.31 (t, $J = 13.2$ Hz, 1H), 2.00 (d, $J = 13.0$ Hz, 2H), 1.86 (d, $J = 9.6$ Hz, 2H), 1.72 (d, $J = 3.2$ Hz, 1H), 1.57-1.51 (m, 2H), 1.34-1.24 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 174.8, 151.8, 151.7, 149.4, 149.3, 144.8, 144.7, 143.5, 143.4, 142.4, 142.3, 117.56, 117.55, 117.38, 117.37, 110.32, 110.29, 110.27, 110.24, 103.9, 103.7, 46.9, 29.7, 25.5; LRMS (EI 70 ev) m/z (%): 239 (M$^+$, 100); HRMS m/z (ESI) calcd for C$_{13}$H$_{16}$F$_2$NO (M+H)$^+$ 240.1174, found 240.1181.
N-(Pyridin-3-yl)cyclohexanecarboxamide (3ak):

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 8.59 (s, 1H), 8.29 (s, 1H), 8.13 (d, $J = 6.4$ Hz, 1H), 7.77 (s, 1H), 7.29 (d, $J = 4.8$ Hz, 1H), 2.33-2.26 (m, 1H), 1.97 (d, $J = 12.8$ Hz, 2H), 1.87 (d, $J = 10.4$ Hz, 2H), 1.73 (d, $J = 12.4$ Hz, 1H), 1.57-1.50 (m, 2H), 1.34-1.24 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 175.0, 144.4, 140.7, 136.1, 126.3, 123.7, 46.7, 29.6, 25.66, 25.62; LRMS (EI 70 ev) m/z (%): 204 (M$^+$, 100); HRMS m/z (ESI) calcd for C$_{12}$H$_{17}$N$_2$O (M+H)$^+$ 205.1247, found 205.1255.

N-(Benzo[d][1,3]dioxol-5-yl)cyclohexanecarboxamide (3al):

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.79 (d, $J = 8.4$ Hz, 1H), 7.59 (s, 1H), 7.21 (s, 1H), 6.93 (d, $J = 8.4$ Hz, 1H), 3.95 (s, 2H), 2.32-2.24 (m, 1H), 2.04 (d, $J = 10.8$ Hz, 2H), 1.73 (d, $J = 8.4$ Hz, 2H), 1.57 (s, 1H), 1.53-1.48 (m, 2H), 1.38-1.24 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 171.8, 153.6, 148.6, 124.6, 121.6, 112.1, 110.2, 56.1, 46.7, 30.2, 25.8; LRMS (EI 70 ev) m/z (%): 247 (M$^+$, 100); HRMS m/z (ESI) calcd for C$_{14}$H$_{18}$N$_3$O$_3$ (M+H)$^+$ 248.1261, found 248.1269.

N-Benzylcyclohexanecarboxamide (3am):

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.31 (t, $J = 7.0$ Hz, 2H), 7.23 (d, $J = 7.6$ Hz, 3H), 6.16 (s, 1H), 4.38 (d, $J = 5.2$ Hz, 2H), 2.14 (t, $J = 11.8$ Hz, 1H), 1.86 (d, $J = 12.8$ Hz, 2H), 1.77 (d, $J = 9.6$ Hz, 2H), 1.65 (s, 1H), 1.47 (dd, $J = 7.6$ Hz, $J = 12.0$ Hz, 2H), 1.27-1.15 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 176.1, 138.4, 128.4, 127.5, 127.2, 45.3, 43.1, 29.5, 25.5; LRMS (EI 70 ev) m/z (%): 217 (M$^+$, 100); HRMS m/z (ESI) calcd for C$_{14}$H$_{20}$NO (M+H)$^+$ 218.1519, found 218.1523.
N-((Thiophen-2-yl)methyl)cyclohexanecarboxamide (3an):

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.79 (d, $J = 8.4$ Hz, 1H), 7.59 (s, 1H), 6.93 (d, $J = 8.4$ Hz, 1H), 6.23 (s, 1H), 3.95 (s, 2H), 2.22 (d, $J = 12.8$ Hz, 1H), 1.94 (d, $J = 8.4$ Hz, 2H), 1.85 (d, $J = 10.0$ Hz, 2H), 1.73 (s, 1H), 1.55 (d, $J = 7.6$ Hz, $J = 12.4$ Hz, 2H), 1.34-1.23 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 171.7, 146.5, 126.9, 125.8, 125.1, 45.4, 38.2, 29.6, 25.7; LRMS (EI 70 ev) m/z (%): 223 (M$^+$, 100); HRMS m/z (ESI) calcd for C$_{12}$H$_{18}$NOS (M+H)$^+$ 224.1083, found 224.1090.

N-Phenylcyclopentanecarboxamide (3ba):

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.55 (d, $J = 8.0$ Hz, 2H), 7.35 (d, $J = 7.8$ Hz, 2H), 7.14 (s, 1H), 7.11 (d, $J = 7.0$ Hz, 1H), 2.57-2.51 (m, 1H), 1.95-1.89 (m, 4H), 1.78 (t, $J = 3.8$ Hz, 2H), 1.64-1.61 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 174.8, 138.6, 129.7, 124.4, 120.1, 47.2, 30.3, 26.3; LRMS (EI 70 ev) m/z (%): 189 (M$^+$, 100); HRMS m/z (ESI) calcd for C$_{12}$H$_{16}$NO (M+H)$^+$ 190.1205, found 190.1213.

2-Ethyl-N-phenylbutanamide (3ca):

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.56 (d, $J = 7.6$ Hz, 2H), 7.34 (t, $J = 7.4$ Hz, 2H), 7.17 (s, 1H), 7.12 (t, $J = 7.2$ Hz, 1H), 2.02 (d, $J = 4.4$ Hz, 1H), 1.76-1.66 (m, 2H), 1.59-1.53 (m, 2H), 0.97 (t, $J = 7.2$ Hz, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 174.2, 137.8, 128.9, 124.1, 119.7, 52.5, 25.8, 12.1; LRMS (EI 70 ev) m/z (%): 191 (M$^+$, 100); HRMS m/z (ESI) calcd for C$_{12}$H$_{18}$NO (M+H)$^+$ 192.1361, found 192.1356.

N,N,2-Diphenylpropanamide (3da):

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.44-7.33 (m, 6H), 7.32-7.27 (m, 1H), 7.25 (d, $J = 4.0$ Hz, 1H), 7.08 (s, 1H), 7.07 (d, $J = 7.6$ Hz, 1H), 3.76 (q, $J = 5.6$ Hz, 1H), 1.48 (d, $J = 7.2$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 172.3, 140.8, 137.9, 129.4, 129.1, 127.8, 127.7, 124.2, 119.6, 48.1, 18.6; LRMS (EI 70 ev) m/z (%): 225 (M$^+$, 100); HRMS m/z (ESI) calcd for C$_{15}$H$_{16}$NO (M+H)$^+$ 226.1293, found 226.1293.
N,3-Diphenylpropanamide (3ea):

$^1$H NMR (400 MHz, CDCl$_3$) δ: 7.46 (d, $J = 8.0$ Hz, 2H), 7.32 (s, 4H), 7.23 (s, 3H), 7.13 (t, $J = 5.6$ Hz, 2H), 3.10 (t, $J = 7.4$ Hz, 2H), 2.70 (t, $J = 7.6$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 170.3, 140.5, 137.6, 128.9, 128.6, 128.3, 126.3, 124.2, 119.8, 39.5, 31.5; LRMS (EI 70 ev) m/z (%): 225 (M$^+$, 100); HRMS m/z (ESI) calcd for C$_{15}$H$_{16}$NO (M+H)$^+$ 226.1293, found 226.1299.

N-Phenylbutyramide (3fa):

$^1$H NMR (400 MHz, CDCl$_3$) δ: 7.53 (t, $J = 10.0$ Hz, 2H), 7.32 (t, $J = 7.4$ Hz, 2H), 7.11 (t, $J = 7.2$ Hz, 1H), 2.34 (t, $J = 7.4$ Hz, 2H), 1.79-1.72 (m, 2H), 1.00 (t, $J = 7.4$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 171.4, 137.9, 128.9, 124.1, 119.7, 39.5, 19.0, 13.7; LRMS (EI 70 ev) m/z (%): 163 (M$^+$, 100); HRMS m/z (ESI) calcd for C$_{10}$H$_{14}$NO (M+H)$^+$ 164.1047, found 164.1041.

1,2,3-triazolines (4):

$^1$H NMR (400 MHz, CDCl$_3$) δ: 7.45 (d, $J = 8.0$ Hz, 2H), 7.31 (t, $J = 7.80$ Hz, 2H), 6.99 (t, $J = 7.6$ Hz, 1H), 5.28 (s, 1H), 4.97 (brs, 1H), 1.86-1.79 (m, 2H), 1.59-1.49 (m, 4H), 1.29-1.19 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 140.6, 129.2, 121.9, 115.8, 82.8, 82.1, 32.0, 27.4, 25.3, 22.9, 22.3.

(D) References

(E) Spectra

$^1$H NMR of pure [bmim][OH]
$^{13}$C NMR of pure [bmim][OH]
$^1$H NMR of [bmim][OH] after 5th cycle of reaction
$^1$H NMR of Compound 3aa
$^{13}$C NMR of Compound 3aa
$^{13}$C NMR of Compound 3ab
$^1$H NMR of Compound 3ac
$^{13}$C NMR of Compound 3ac
$^1$H NMR of Compound 3ad
$^{13}$C NMR of Compound 3ad
$^1$H NMR of Compound 3ae
$^{13}$C NMR of Compound 3ae
$^1$H NMR of Compound 3af
$^{13}$C NMR of Compound 3af
$^1$H NMR of Compound 3ag
$^{13}$C NMR of Compound 3ag
$^1$H NMR of Compound 3ah
$^{13}$C NMR of Compound 3ah
$^1$H NMR of Compound 3ai
$^{13}$C NMR of Compound 3ai
$^1$H NMR of Compound 3aj
$^{13}$C NMR of Compound 3aj
$^1$H NMR of Compound 3ak
$^{13}$C NMR of Compound 3ak
$^1$H NMR of Compound 3a
$^{13}$C NMR of Compound 3a1
$^1$H NMR of Compound 3am
$^{13}$C NMR of Compound 3am
\(^1\)H NMR of Compound 3an
$^{13}$C NMR of Compound 3an
$^{1}$H NMR of Compound 3ab
$^{13}$C NMR of Compound 3ba
$^1$H NMR of Compound 3ca
$^{13}$C NMR of Compound 3ca
$^1$H NMR of Compound 3da
$^{13}$C NMR of Compound 3da
$^1$H NMR of Compound 3ea
$^{13}$C NMR of Compound 3ea
$^1$H NMR of Compound 3fa
$^{13}$C NMR of Compound 3fa
$^1$H NMR of Compound 4
$^{13}$C NMR of Compound 4