Three-Component Synthesis of Enaminones via Ketene Cyclization

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Supporting information

1. General methods

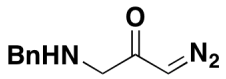
All reactions were performed in oven-dried glassware. Dichloroethane was distilled from CaH_2, and CH_2Cl_2 was dried before use over an activated alumina column. All reagents were used as received. The methods for analysis are as following.

1) All diazoketones and enaminones were UV-active on TLC, and were also detectible with ninhydrine and $KMnO_4$ solutions.
2) ^1H NMR data were recorded at 400 MHz spectrometer and ^{13}C NMR data at 100 MHz. Chemical shifts are shown as ppm values relative to internal $CHCl_3$ (δ 7.26 for ^1H, δ 77.16 for ^{13}C).
3) Melting points are uncorrected.
4) Optical rotation was measured at 23 °C.

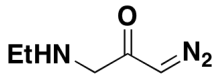
2. General procedure for the preparation of amino diazoketones

Synthesis of amino diazoketones 3a-3g: To a solution of the amine (10 mmol, 4 equiv) in dichloroethane (9 mL), bromo diazoacetone (2.5 mmol) in dichloroethane (1 mL) was added dropwise.[1] The reaction mixture was heated to 50 °C for 3 h, then washed with aq. $NaHCO_3$ and brine, dried over $MgSO_4$ and concentrated *in vacuo*. The crude mixture was subjected to column chromatography ($MeOH/CH_2Cl_2$), affording the amino diazoketones as yellow oils.

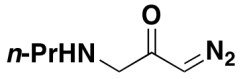
Synthesis of amino diazoketone 3h: Bromo diazoacetone (2.5 mmol) and tryptamine hydrochloride (5 mmol, 2 equiv) were dissolved in MeONa/MeOH (0.5 M, 10mL). The solution was heated at 50 °C for 3 h, concentrated *in vacuo*, and re-dissolved in CH_2Cl_2. This organic solution was washed with aq. $NaHCO_3$ and brine, dried over $MgSO_4$ and again concentrated *in vacuo*. The crude mixture was subjected to column chromatography ($NH_4OH/MeOH/CH_2Cl_2$), affording amino diazoketone **8** as a yellow oil.



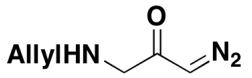
1-(Benzylamino)-3-diazopropan-2-one (3a), Yellow oil (87%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.21 (m, 5H), 5.63 (s, 1H), 3.79 (s, 2H), 3.40 (s, 2H), 1.96 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.8, 139.6, 128.6, 128.3, 127.4, 56.3, 53.7, 53.1; IR (neat, cm^{-1}): 1143, 1343, 1638, 2105; HRMS (ESI) calcd for $C_{10}H_{12}N_3O$ $(M + H)^+$ 190.0980, found 190.0981.



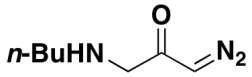
1-Diazo-3-(ethylamino)propan-2-one (3b). Yellow oil (65%);[1]^1H NMR (400 MHz, $CDCl_3$) δ 5.63 (s, 1H), 3.38 (s, 2H), 2.63 (q, *J* = 7.1 Hz, 2H), 1.60 (s, 1H), 1.10 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.2, 57.1, 52.9, 44.3, 15.4; IR (neat, cm^{-1}): 1139, 1352, 1635, 2106, 2968; HRMS (ESI) calcd for $C_5H_{10}N_3O$ $(M + H)^+$ 128.0824, found 128.0817.



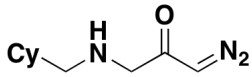
1-Diazo-3-(propylamino)propan-2-one (3c). Yellow oil (63%); ^1H NMR (400 MHz, $CDCl_3$) δ 5.65 (s, 1H), 3.38 (s, 2H), 2.55 (t, *J* = 7.1 Hz, 2H), 1.60 (s, 1H), 1.60 – 1.41 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.4, 57.3, 52.9, 52.0, 23.4, 11.8; IR (neat, cm^{-1}): 1139, 1343, 1637, 2104, 2960; HRMS (ESI) calcd for $C_6H_{12}N_3O$ $(M + H)^+$ 142.0980, found 142.0979.



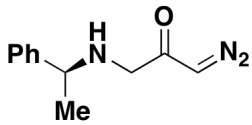
1-(Allylamino)-3-diazopropan-2-one (3d). Yellow oil (72%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.89 (m, 1H), 5.63 (s, 1H), 5.26 – 5.07 (m, 2H), 3.39 (s, 2H), 3.24 (d, *J* = 5.9 Hz, 2H), 1.71 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.0, 136.3, 116.7, 56.2, 53.1, 52.2; IR (neat, cm^{-1}): 923, 1143, 1344, 1638, 2105, 3080; HRMS (ESI) calcd for $C_6H_{10}N_3O$ $(M + H)^+$ 140.0824, found 140.0811.



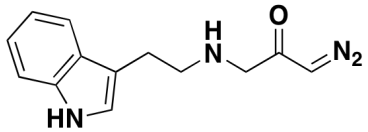
1-(Butylamino)-3-diazopropan-2-one (3e). Yellow oil (80%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.64 (s, 1H), 3.38 (s, 2H), 2.58 (t, *J* = 7.1 Hz, 2H), 1.78 (s, 1H), 1.46 (m, 2H), 1.35 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.3, 57.3, 52.9, 49.9, 32.3, 20.5, 14.1; IR (neat, cm^{-1}): 927, 1141, 1344, 1639, 2105, 2930; HRMS (ESI) calcd for $C_7H_{14}N_3O$ $(M + H)^+$ 156.1137, found 156.1132.



1-((Cyclohexylmethyl)amino)-3-diazopropan-2-one (3f). Yellow oil (81%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.67 (s, 1H), 3.36 (s, 2H), 2.41 (d, *J* = 6.6 Hz, 2H), 1.78 – 1.55 (m, 6H), 1.41 (m, 1H), 1.29 – 1.08 (m, 3H), 0.98 – 0.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.7, 57.5, 56.9, 52.9, 38.3, 31.5, 26.8, 26.2; IR (neat, cm^{-1}): 1140, 1340, 1638, 2102, 2923; HRMS (ESI) calcd for $C_{10}H_{18}N_3O$ $(M + H)^+$ 196.1450, found 196.1450.



(*S*)-1-Diazo-3-((1-phenylethyl)amino)propan-2-one (3g). Yellow oil (93%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.20 (m, 5H), 5.49 (s, 1H), 3.75 (q, *J* = 6.6 Hz, 1H), 3.25 (s, 2H), 1.90 (s, 1H), 1.37 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.7, 144.8, 128.7, 127.4, 126.8, 58.2, 55.1, 53.2, 24.4; IR (neat, cm^{-1}): 1143, 1349, 1638, 2104, 2967; $[\alpha]_D$= −82.4 (*c* = 1.09 in $CHCl_3$); HRMS (ESI) calcd for $C_{11}H_{14}N_3O$ $(M + H)^+$ 204.1137, found 204.1132.



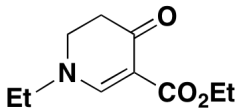
1-((2-(1*H*-Indol-3-yl)ethyl)amino)-3-diazopropan-2-one (3h). Yellow oil (73%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.30 – 7.08 (m, 2H), 7.04 (s, 1H), 5.60 (s, 1H), 3.39 (s, 2H), 3.27 – 2.91 (m, 4H), 1.72 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.4, 136.5, 127.5, 122.2, 122.1, 119.4, 118.9, 113.7, 111.3, 57.2, 53.0, 50.0, 26.0; IR (neat, cm^{-1}): 1147, 1342, 1634, 2105, 2918; HRMS (ESI) calcd for $C_{13}H_{15}N_4O$ $(M + H)^+$ 243.1246, found 243.1239.

3. General procedure for the preparation of enaminones.[2]

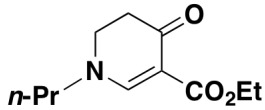
The amino diazoketone (0.20 mmol) was reacted with an alkyne (0.24 mmol, 1.2 equiv) in ethanol (1 mL) at ambient temperature overnight.[3,4] Upon evaporation, the reaction mixture was treated

with the Ag catalyst (0.04 mmol, 20 mmol%) in CH_2Cl_2 (1 mL) at ambient temperature overnight, during which the flask was covered with aluminum foil to exclude light. This mixture was then washed with aq. $NaHCO_3$ and brine, dried over $MgSO_4$ and concentrated *in vacuo*. The crude mixture was subjected to column chromatography ($MeOH/CH_2Cl_2$), affording a desired enaminone.

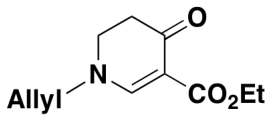
$PhCO_2Ag$ was used as a catalyst for the Wolff rearrangement in all cases except for the synthesis of enaminone **2c**, **4c**, **5c**, **5e** and **8a-c**, where Ag_2O was used instead.



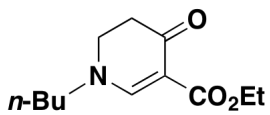
Ethyl 1-Ethyl-4-oxo-1,4,5,6-tetrahydropyridine-3-carboxylate (2b). White solid (85%); mp: 45.8-47.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.60 – 3.41 (t, *J* = 7.5 Hz, 2H), 3.49 – 3.43 (q, *J* = 7.3 Hz, 2H), 2.59 – 2.50 (t, *J* = 7.8 Hz, 2H), 1.32 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.5, 165.6, 158.9, 100.5, 60.0, 52.1, 46.2, 36.1, 14.7, 14.0; IR (neat, cm^{-1}): 1053, 1159, 1246, 1303, 1335, 1398, 1605, 1714, 2978; HRMS (ESI) calcd for $C_{10}H_{16}N_1O_3$ $(M + H)^+$ 198.1130, found 198.1124.



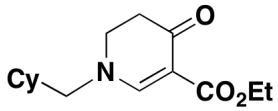
Ethyl 4-Oxo-1-propyl-1,4,5,6-tetrahydropyridine-3-carboxylate (2c). Off-white solid (88%); mp: 55.8-57.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.59 – 3.48 (t, *J* = 7.5 Hz, 2H), 3.36 (t, *J* = 7.1 Hz, 2H), 2.60 – 2.47 (t, *J* = 7.5 Hz, 2H), 1.76 – 1.66 (m, 2H), 1.31 (t, *J* = 7.1 Hz, 3H), 0.97 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.5, 165.6, 159.5, 100.3, 60.0, 59.1, 46.5, 36.1, 21.7, 14.7, 11.0; IR (neat, cm^{-1}): 1054, 1157, 1240, 1301, 1333, 1384, 1459, 1602, 1658, 1719, 2966; HRMS (ESI) calcd for $C_{11}H_{18}N_1O_3$ $(M + H)^+$ 212.1287, found 212.1290.



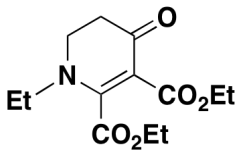
Ethyl 1-Allyl-4-oxo-1,4,5,6-tetrahydropyridine-3-carboxylate (2d). Yellow oil (76%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 5.84 (dq, *J* = 10.8, 6.0 Hz, 1H), 5.36 (m, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.98 (d, *J* = 6.0 Hz, 2H), 3.53 (t, *J* = 7.7 Hz, 2H), 2.54 (t, *J* = 7.7 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.5, 165.5, 159.4, 131.3, 120.7, 100.9, 60.00, 59.58, 46.4, 36.1, 14.7; IR (neat, cm^{-1}): 1053, 1152, 1241, 1303, 1338, 1397, 1602, 1645, 1715, 2978; HRMS (ESI) calcd for $C_{11}H_{16}N_1O_3$ $(M + H)^+$ 210.1130, found 210.1130.



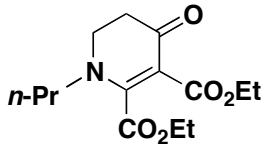
Ethyl 1-Butyl-4-oxo-1,4,5,6-tetrahydropyridine-3-carboxylate (2e). Clear oil (78%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.59 – 3.48 (t, *J* = 7.8 Hz, 2H), 3.39 (t, *J* = 7.2 Hz, 2H), 2.60 – 2.48 (t, *J* = 7.8 Hz, 2H), 1.71 – 1.57 (m, 2H), 1.42 – 1.29 (m, 5H), 0.98 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.4, 165.7, 159.5, 100.4, 60.0, 57.2, 46.6, 36.2, 30.5, 20.0, 14.7, 13.7; IR (neat, cm^{-1}): 1054, 1158, 1245, 1302, 1335, 1395, 1462, 1603, 1659, 1714, 2960; HRMS (ESI) calcd for $C_{12}H_{20}N_1O_3$ $(M + H)^+$ 226.1443, found 226.1432.



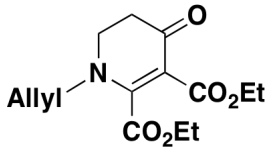
Ethyl 1-(Cyclohexylmethyl)-4-oxo-1,4,5,6-tetrahydropyridine-3-carboxylate (2f). Off-white solid (88%); mp: 65.1-66.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.61 – 3.48 (t, *J* = 7.6 Hz, 2H), 3.20 (d, *J* = 6.9 Hz, 2H), 2.61 – 2.47 (t, *J* = 7.6 Hz, 2H), 1.83 – 1.61 (m, 7H), 1.36 – 1.11 (m, 5H), 0.94 (q, *J* = 11.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.4, 165.67, 159.8, 100.1, 64.0, 60.0, 47.2, 36.8, 36.1, 30.6, 26.3, 25.7, 14.7; IR (neat, cm^{-1}): 1055, 1158, 1249, 1306, 1331, 1403, 1451, 1603, 1709, 2927; HRMS (ESI) calcd for $C_{15}H_{24}N_1O_3$ $(M + H)^+$ 266.1756, found 266.1766.



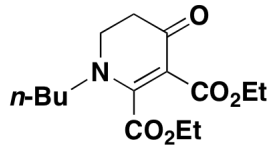
Diethyl 1-Ethyl-4-oxo-1,4,5,6-tetrahydropyridine-2,3-dicarboxylate (4b). Yellow oil (90%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.41 (q, *J* = 7.2 Hz, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.63 (t, *J* = 7.5 Hz, 2H), 3.39 (q, *J* = 7.1 Hz, 2H), 2.55 (t, *J* = 7.5 Hz, 2H), 1.38 (t, *J* = 7.2 Hz, 3H), 1.30 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.9, 165.5, 163.6, 160.4, 100.3, 62.8, 60.6, 49.4, 47.5, 35.8, 14.5, 13.99, 13.96; IR (neat, cm^{-1}): 1050, 1157, 1256, 1379, 1449, 1555, 1666, 1740, 2982; HRMS (ESI) calcd for $C_{13}H_{20}N_1O_5$ $(M + H)^+$ 270.1341, found 270.1330.



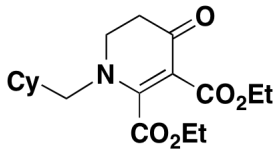
Diethyl 4-Oxo-1-propyl-1,4,5,6-tetrahydropyridine-2,3-dicarboxylate (4c). Clear oil (81%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.39 (q, *J* = 7.2 Hz, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.67 – 3.57 (t, *J* = 7.4 Hz, 2H), 3.31 – 3.22 (t, *J* = 7.6 Hz, 2H), 2.59 – 2.48 (t, *J* = 7.4 Hz, 2H), 1.77 – 1.65 (m, 2H), 1.37 (t, *J* = 7.2 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 0.93 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.9, 165.5, 163.6, 160.6, 100.3, 62.8, 60.5, 55.9, 47.9, 35.8, 22.0, 14.5, 14.0, 11.06; IR (neat, cm^{-1}): 1023, 1071, 1175, 1254, 1299, 1378, 1448, 1552, 1668, 1740, 2978; HRMS (ESI) calcd for $C_{14}H_{22}N_1O_5$ $(M + H)^+$ 284.1498, found 284.1496.



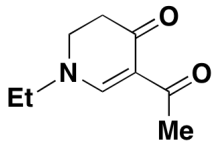
Diethyl 1-Allyl-4-oxo-1,4,5,6-tetrahydropyridine-2,3-dicarboxylate (4d). Yellow oil (quant.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 (ddt, *J* = 16.5, 10.4, 6.1 Hz, 1H), 5.38 – 5.29 (m, 2H), 4.39 (q, *J* = 7.2 Hz, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.90 (d, *J* = 6.1 Hz, 2H), 3.63 – 3.55 (t, *J* = 7.5 Hz, 2H), 2.58 – 2.51 (t, *J* = 7.5 Hz, 2H), 1.37 (t, *J* = 7.2 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.0, 165.4, 163.6, 160.3, 131.2, 120.7, 100.2, 62.9, 60.7, 56.5, 47.6, 35.8, 14.5, 14.0; IR (neat, cm^{-1}): 1025, 1074, 1176, 1255, 1378, 1448, 1551, 1669, 1740, 2981; HRMS (ESI) calcd for $C_{14}H_{20}N_1O_5$ $(M + H)^+$ 282.1341, found 282.1349.



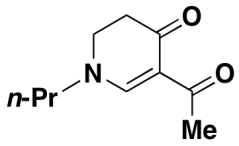
Diethyl 1-Butyl-4-oxo-1,4,5,6-tetrahydropyridine-2,3-dicarboxylate (4e). Clear oil (93%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.40 (q, *J* = 7.2 Hz, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.68 – 3.58 (t, *J* = 7.5 Hz, 2H), 3.36 – 3.26 (t, *J* = 7.7 Hz, 2H), 2.58 – 2.49 (t, *J* = 7.5 Hz, 2H), 1.68 (m, 2H), 1.41 – 1.27 (m, 8H), 0.95 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.9, 165.5, 163.6, 160.5, 100.4, 62.8, 60.6, 54.2, 48.0, 35.8, 30.8, 20.0, 14.5, 14.0, 13.8; IR (neat, cm^{-1}): 1025, 1072, 1175, 1254, 1378, 1459, 1554, 1668, 1741, 2961; HRMS (ESI) calcd for $C_{15}H_{24}N_1O_5$ $(M + H)^+$ 298.1654, found 298.1646.



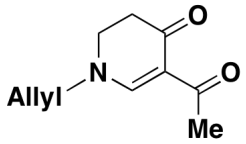
Diethyl 1-(Cyclohexylmethyl)-4-oxo-1,4,5,6-tetrahydropyridine-2,3-dicarboxylate (4f). Yellow oil (86%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.38 (q, *J* = 7.2 Hz, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.68 – 3.57 (t, *J* = 7.4 Hz, 2H), 3.16 (d, *J* = 6.9 Hz, 2H), 2.57 – 2.48 (t, *J* = 7.4 Hz, 2H), 1.81 – 1.66 (m, 6H), 1.37 (t, *J* = 7.2 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.27 – 1.11 (m, 3H), 0.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.0, 165.6, 163.5, 160.7, 100.6, 62.8, 60.6, 60.2, 48.6, 37.5, 35.8, 30.9, 26.2, 25.8, 14.5, 14.0; IR (neat, cm^{-1}): 1154, 1246, 1378, 1449, 1547, 1668, 1740, 2927; HRMS (ESI) calcd for $C_{18}H_{28}N_1O_5$ $(M + H)^+$ 338.1967, found 338.1970.



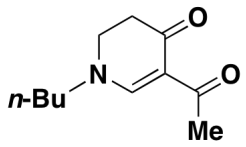
5-Acetyl-1-ethyl-2,3-dihydropyridin-4(1*H*)-one (5b). White solid (94%); mp: 55.0-57.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 3.61 – 3.55 (t, *J* = 7.7 Hz, 2H), 3.49 (q, *J* = 7.3 Hz, 2H), 2.59 – 2.52 (t, *J* = 7.7 Hz, 2H), 2.49 (s, 3H), 1.34 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.3, 188.0, 158.7, 110.0, 52.3, 46.5, 36.0, 30.6, 13.9; IR (neat, cm^{-1}): 1150, 1248, 1324, 1360, 1388, 1586, 1634, 2975; HRMS (ESI) calcd for $C_9H_{14}N_1O_2$ $(M + H)^+$ 168.1025, found 168.1021.



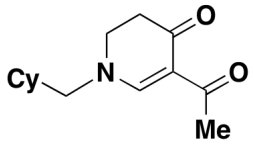
5-Acetyl-1-propyl-2,3-dihydropyridin-4(1*H*)-one (5c). White solid (84%); mp: 81.3-83.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 3.62 – 3.51 (t, *J* = 7.7 Hz, 2H), 3.40 (t, *J* = 7.1 Hz, 2H), 2.58 – 2.52 (t, *J* = 7.7 Hz, 2H), 2.50 (s, 3H), 1.79 – 1.66 (m, 2H), 0.97 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.3, 188.0, 159.3, 109.8, 59.2, 46.8, 36.0, 30.6, 21.7, 11.0; IR (neat, cm^{-1}): 1150, 1246, 1325, 1394, 1595, 1626, 2965; HRMS (ESI) calcd for $C_{10}H_{16}N_1O_2$ $(M + H)^+$ 182.1181, found 182.1174.



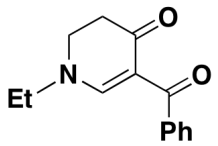
5-Acetyl-1-allyl-2,3-dihydropyridin-4(1*H*)-one (5d). White solid (90%); mp: 42.5-44.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 5.84 (ddt, *J* = 16.4, 10.2, 6.1 Hz, 1H), 5.43 – 5.30 (m, 2H), 4.01 (d, *J* = 6.1 Hz, 2H), 3.55 (t, *J* = 7.7 Hz, 2H), 2.58 – 2.52 (t, *J* = 7.7 Hz, 2H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.3, 188.1, 159.2, 131.0, 121.0, 110.3, 59.8, 46.6, 36.0, 30.6; IR (neat, cm^{-1}): 1148, 1237, 1323, 1361, 1388, 1583, 1635, 2922; HRMS (ESI) calcd for $C_{10}H_{14}N_1O_2$ $(M + H)^+$ 180.1025, found 180.1022.



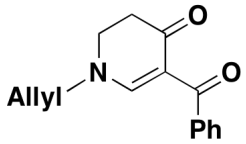
5-Acetyl-1-butyl-2,3-dihydropyridin-4(1*H*)-one (5e). Off-white solid (81%); mp: 60.4-62.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 3.56 (t, *J* = 7.7 Hz, 2H), 3.42 (t, *J* = 7.2 Hz, 2H), 2.54 (t, *J* = 7.7 Hz, 2H), 2.49 (s, 3H), 1.75 – 1.53 (m, 2H), 1.36 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.2, 188.0, 159.2, 109.8, 57.4, 46.8, 36.0, 30.6, 30.4, 19.8, 13.7; IR (neat, cm^{-1}): 1153, 1328, 1359, 1395, 1595, 1623, 2958; HRMS (ESI) calcd for $C_{11}H_{18}N_1O_2$ $(M + H)^+$ 196.1338, found 196.1331.



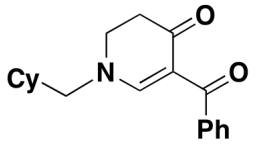
5-Acetyl-1-(cyclohexylmethyl)-2,3-dihydropyridin-4(1*H*)-one (5f). Off-white solid (92%); mp: 124.8-126.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 3.61 – 3.51 (t, *J* = 7.7 Hz, 2H), 3.23 (d, *J* = 6.9 Hz, 2H), 2.57 – 2.51 (t, *J* = 7.7 Hz, 2H), 2.49 (s, 3H), 1.82 – 1.63 (m, 6H), 1.32 – 1.10 (m, 3H), 0.94 (q, *J* = 12.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.3, 188.4, 159.6, 109.7, 64.1, 47.5, 36.7, 36.0, 30.6 (overlap of two non-equivalent carbons), 26.2, 25.7; IR (neat, cm^{-1}): 1152, 1249, 1324, 1362, 1388, 1451, 1584, 1634, 2925; HRMS (ESI) calcd for $C_{14}H_{22}N_1O_2$ $(M + H)^+$ 236.1651, found 236.1653.



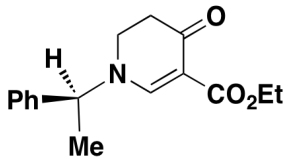
5-Benzoyl-1-ethyl-2,3-dihydropyridin-4(1*H*)-one (6b). Off-white solid (81%); mp: 89.5-91.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.67 – 7.59 (m, 2H), 7.48 – 7.41 (m, 1H), 7.37 (t, *J* = 7.4 Hz, 2H), 3.69 – 3.61 (t, *J* = 7.7 Hz, 2H), 3.53 (q, *J* = 7.2 Hz, 2H), 2.64 – 2.53 (t, *J* = 7.7 Hz, 2H), 1.37 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.6, 186.7, 159.1, 140.5, 131.3, 129.0, 127.7, 110.1, 52.2, 46.4, 35.9, 14.0; IR (neat, cm^{-1}): 1191, 1252, 1325, 1384, 1447, 1587, 1623, 2975; HRMS (ESI) calcd for $C_{14}H_{16}N_1O_2$ $(M + H)^+$ 230.1181, found 230.1179.



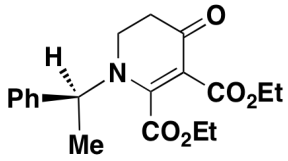
1-Allyl-5-benzoyl-2,3-dihydropyridin-4(1*H*)-one (6c). Off-white solid (63%); mp: 88.1-89.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.63 (m, 2H), 7.49 – 7.42 (m, 1H), 7.37 (m, 2H), 5.89 (ddt, *J* = 16.4, 10.2, 6.1 Hz, 1H), 5.40 (m, 2H), 4.03 (d, *J* = 6.1 Hz, 2H), 3.62 (t, *J* = 7.7 Hz, 2H), 2.60 (t, *J* = 7.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.7, 186.9, 159.6, 140.3, 131.4, 131.1, 129.0, 127.7, 121.0, 110.5, 59.8, 46.6, 35.8; IR (neat, cm^{-1}): 1190, 1239, 1323, 1385, 1585, 1623, 2923; HRMS (ESI) calcd for $C_{15}H_{16}N_1O_2$ $(M + H)^+$ 242.1181, found 242.1173.



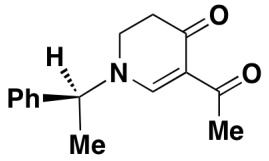
5-Benzoyl-1-(cyclohexylmethyl)-2,3-dihydropyridin-4(1*H*)-one (6d). Off-white solid (88%); mp: 152.4-154.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.69 – 7.59 (m, 2H), 7.48 – 7.41 (m, 1H), 7.40 – 7.33 (m, 2H), 3.62 (t, *J* = 7.6 Hz, 2H), 3.26 (d, *J* = 6.9 Hz, 2H), 2.63 – 2.52 (t, *J* = 7.6 Hz, 2H), 1.86 – 1.64 (m, 6H), 1.35 – 1.12 (m, 3H), 1.04 – 0.89 (m, 2H);^{1} ^{3}C NMR (100 MHz, $CDCl_3$) δ 192.6, 186.8, 160.1, 140.5, 131.3, 129.0, 127.7, 109.7, 64.1, 47.5, 36.8, 35.9, 30.7, 26.3, 25.7; IR (neat, cm^{-1}): 1191, 1254, 1322, 1385, 1449, 1584, 1622, 2925; HRMS (ESI) calcd for $C_{19}H_{24}N_1O_2$ $(M + H)^+$ 298.1807, found 298.1804.



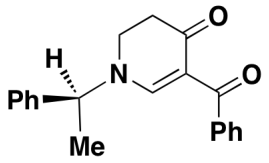
(*S*)-Ethyl 4-Oxo-1-(1-phenylethyl)-1,4,5,6-tetrahydropyridine-3-carboxylate (7a). Yellow oil (86%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), 7.45 – 7.33 (m, 3H), 7.30 – 7.26 (m, 2H), 4.71 (q, *J* = 7.0 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 3.48 – 3.36 (m, 1H), 3.35 – 3.26 (m, 1H), 2.43 (m, 2H), 1.72 (d, *J* = 7.0 Hz, 3H), 1.34 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.7, 165.9, 157.3, 138.8, 129.4, 128.9, 126.5, 100.8, 64.6, 60.1, 44.6, 36.2, 19.2, 14.7; IR (neat, cm^{-1}): 1052, 1140, 1245, 1297, 1394, 1456, 1595, 1659, 1717, 2978; $[\alpha]_D$= −17 (*c* = 0.99 in $CHCl_3$); HRMS (ESI) calcd for $C_{16}H_{20}N_1O_3$ $(M + H)^+$ 274.1443, found 274.1435.



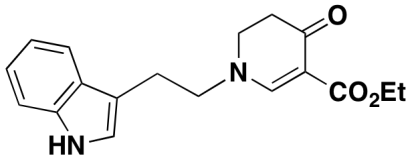
(*S*)-Diethyl 4-Oxo-1-(1-phenylethyl)-1,4,5,6-tetrahydropyridine-2,3-dicarboxylate (7b). Yellow oil (67%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.31 (m, 5H), 4.94 (q, *J* = 6.8 Hz, 1H), 4.54 – 4.41 (m, 2H), 4.32 – 4.20 (m, 2H), 3.40 (ddd, *J* = 13.6, 10.4, 5.8 Hz, 1H), 3.16 (ddd, *J* = 13.5, 7.5, 5.9 Hz, 1H), 2.40 – 2.21 (m, 2H), 1.70 (d, *J* = 6.9 Hz, 3H), 1.40 (t, *J* = 7.2 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.2, 165.7, 164.1, 160.2, 137.5, 129.2, 128.9, 127.3, 100.4, 63.0, 60.6, 60.0, 42.1, 35.8, 16.5, 14.5, 14.1; IR (neat, cm^{-1}): 1026, 1142, 1255, 1299, 1374, 1453, 1538, 1668, 1738, 2982; $[\alpha]_D$= −26 (*c* = 0.97 in $CHCl_3$); HRMS (ESI) calcd for $C_{19}H_{24}N_1O_5$ $(M + H)^+$ 346.1654, found 346.1642.



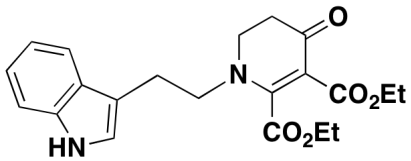
(*S*)-5-Acetyl-1-(1-Phenylethyl)-2,3-dihydropyridin-4(1*H*)-one (7c). Yellow oil (75%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 7.46 – 7.32 (m, 3H), 7.30 – 7.26 (m, 2H), 4.74 (q, *J* = 7.0 Hz, 1H), 3.51 – 3.37 (m, 1H), 3.37 – 3.24 (m, 1H), 2.52 (s, 3H), 2.43 (m, 2H), 1.72 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 188.3, 157.0, 138.6, 129.4, 128.9, 126.6, 110.2, 65.0, 44.8, 36.0, 30.7, 19.2; IR (neat, cm^{-1}): 1051, 1141, 1248, 1292, 1574, 1635, 2978; $[\alpha]_D$= −19 (*c* = 0.95 in $CHCl_3$); HRMS (ESI) calcd for $C_{15}H_{18}N_1O_2$ $(M + H)^+$ 244.1338, found 244.1338.



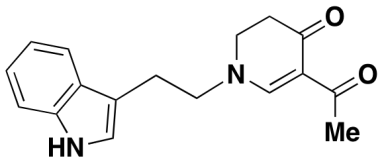
(*S*)-5-Benzoyl-1-(1-phenylethyl)-2,3-dihydropyridin-4(1*H*)-one (7d). Yellow oil (81%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 7.69 – 7.61 (m, 2H), 7.46 – 7.30 (m, 8H), 4.77 (q, *J* = 7.0 Hz, 1H), 3.55 – 3.45 (m, 1H), 3.45 – 3.35 (m, 1H), 2.48 (m, 2H), 1.75 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.8, 187.1, 157.5, 140.4, 138.7, 131.4, 129.4, 129.0, 129.0, 127.7, 126.6, 110.3, 64.9, 44.8, 35.9, 19.2; IR (neat, cm^{-1}): 1080, 1186, 1252, 1296, 1345, 1378, 1455, 1581, 1622, 2980; $[\alpha]_D$= −13 (*c* = 0.98 in $CHCl_3$); HRMS (ESI) calcd for $C_{20}H_{20}N_1O_2$ $(M + H)^+$ 306.1494, found 306.1479.



Ethyl 1-(2-(1*H*-Indol-3-yl)ethyl)-4-oxo-1,4,5,6-tetrahydropyridine-3-carboxylate (8a). White solid (76%); mp: 157.5-158.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.91 (s, 1H), 7.56 (d, *J* = 7.9 Hz, 1H), 7.41 (d, *J* = 8.1 Hz, 1H), 7.23 (m, 1H), 7.15 (t, *J* = 7.1 Hz, 1H), 7.02 (d, *J* = 2.0 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.72 (t, *J* = 6.7 Hz, 2H), 3.49 (t, *J* = 7.7 Hz, 2H), 3.14 (t, *J* = 6.7 Hz, 2H), 2.48 – 2.38 (t, *J* = 7.6 Hz, 2H), 1.23 (t, *J* = 7.1 Hz, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ 186.7, 165.3, 159.5, 136.6, 126.7, 122.9, 122.7, 120.0, 118.2, 111.9, 110.8, 100.2, 60.0, 57.6, 47.2, 36.1, 25.3, 14.6; IR (neat, cm^{-1}): 1054, 1157, 1243, 1338, 1400, 1457, 1602, 1709, 3286; HRMS (ESI) calcd for $C_{18}H_{21}N_2O_3$ $(M + H)^+$ 313.1552, found 313.1541.



Diethyl 1-(2-(1*H*-Indol-3-yl)ethyl)-4-oxo-1,4,5,6-tetrahydropyridine-2,3-dicarboxylate (8b). Off-white solid (73%); mp: 46.9-48.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.40 (d, *J* = 8.1 Hz, 1H), 7.25 – 7.20 (m, 1H), 7.16 (m, 1H), 7.06 (d, *J* = 2.0 Hz, 1H), 4.30 (q, *J* = 7.2 Hz, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.72 – 3.62 (m, 2H), 3.57 – 3.48 (t, *J* = 7.5 Hz, 2H), 3.16 (t, *J* = 7.3 Hz, 2H), 2.42 – 2.30 (m, 2H), 1.31 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.2, 165.5, 163.7, 160.4, 136.5, 127.0, 122.7, 122.6, 120.0, 118.4, 111.7, 111.3, 100.7, 62.9, 60.6, 54.9, 49.0, 35.7, 25.6, 14.5, 14.0; IR (neat, cm^{-1}): 1028, 1174, 1257, 1378, 1458, 1552, 1658, 1714, 1739, 3306; HRMS (ESI) calcd for $C_{21}H_{25}N_2O_5$ $(M + H)^+$ 385.1763, found 385.1747.



1-(2-(1*H*-Indol-3-yl)ethyl)-5-acetyl-2,3-dihydropyridin-4(1*H*)-one (8c). Off-white solid (61%); mp: 183.7-184.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 8.15 (s, 1H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.23 (t, *J* = 7.6 Hz, 1H), 7.16 (m, 1H), 7.02 (d, *J* = 2.0 Hz, 1H), 3.73 (t, *J* = 7.0 Hz, 2H), 3.50 (t, *J* = 7.7 Hz, 2H), 3.15 (t, *J* = 6.9 Hz, 2H), 2.47 (s, 3H), 2.45 – 2.39 (t, *J* = 7.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.2, 188.1, 159.2, 136.5, 126.8, 122.8, 122.5, 120.0, 118.2, 111.8, 111.0, 109.9, 57.8, 47.5, 36.0, 30.6, 25.4; IR (neat, cm^{-1}): 1151, 1323, 1361, 1583, 1629, 2924, 3282; HRMS (ESI) calcd for $C_{17}H_{19}N_2O_2$ $(M + H)^+$ 283.1447, found 283.1450.

4. References and notes

1. Bromo diazoacetone was synthesized according to the literature: Padwa, A.; Austin, D. J.; Precedo, L.; Zhi, L. *J. Org. Chem,* **1993**, *58*, 1144.

2. Products **2a**, **4a**, **5a** and **6a** have been reported by us: Seki, H.; Georg, G. I. *J. Am. Chem. Soc*. **2010**, *132*, 15512.

3. All amino diazoketones were carried to the next reaction immediately after isolation because they are not stable over a long period of time.

4. 1-Phenylprop-2-yn-1-one used for the synthesis of enaminones **6** was prepared using a reported method: Chassaing, S.; Kueny-Stotz, M.; Isorez, G.; Brouillard, R. *Eur. J. Org. Chem.* **2007**, 2438.