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Supporting Information

for

Oxidative Ring-Opening of 3-Aminoindazoles for the Synthesis

of 2-Aminobenzoates

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1. General information

The 1*H*-indazol-3-amines were purchased from Bide Pharmatech Ltd. Other chemicals were purchased from Adamas Reagent, Ltd, Energy chemical company, J&K Scientific Ltd and so forth. The reagents and solvents were purchased from commercial suppliers and used without further purification. Unless otherwise stated, all experiments were conducted in a sealed tube under air atmosphere. Reactions were monitored by TLC or GC-MS analysis. Flash column chromatography was performed over silica gel (200-300 mesh).

¹H-NMR and ¹³C-NMR spectra were recorded in CDCl₃ on a Bruker Avance III 500 spectrometer (500 MHz ¹H, 126 MHz ¹³C) at room temperature. Chemical shifts were reported in ppm on the scale relative to CDCl₃ (δ = 7.26 for ¹H-NMR, δ = 77.00 for ¹³C-NMR) or DMSO-*d*₆ (δ = 2.50 for ¹H-NMR, δ = 39.60 for ¹³C-NMR) as an internal reference. Coupling constants (*J*) were reported in Hertz (Hz).

The starting materials 1H-indazol-3-amine, 4-chloro-1H-indazol-3amine, 5-nitro-1H-indazol-3-amine, and 6-bromo-1H-indazol-3-amine were purchased from commercial suppliers. Other 1H-indazol-3-amines were synthetized according to methods reported by previous literatures.¹

¹ (a) S. Antonysamy, G. Hirst, F. Park, P. Sprengeler, F. Stappenbeck, P. Steensma, M. Wilson, M. Wong, *Bioorg. Med. Chem. Lett.* 2009, **19**, 279; (b) D. N. Rao, Sk. Rasheed, R. A. Vishwakarm and P. Das. *Chem. Commun.*, 2014, **50**, 12911; (c) Kong, W.; Zhou, Y.; Song, Q. *Adv. Synth. Catal.* 2018, **360**, 1943.

2. General procedure for the synthesis of 2-aminobenzoates 2



In a sealed tube were placed 1 (0.4 mmol, 1 equiv), NBS (0.4 mmol, 1 equiv) and CAN (0.6 mol, 1.5 equiv) in ROH (1.5 mL). The resulting mixture was stirred at room temperature for 15 h. Upon completion of the reaction, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 10:1, v/v) to give the desired product 2. When glycol, ethylene glycol monomethyl ether and ethylene glycol monoethyl ether were used as solvents, the resulting solution was extracted with EtOAc and saturated brine three times.

3. General procedure for the synthesis of 2-aminobenzoates 3



In a sealed tube were placed **1** (0.3 mmol, 1 equiv), NBS (0.45 mmol, 1.5 equiv) and $K_2S_2O_8$ (0.6 mol, 2 equiv) in ROH (1.5 mL). The resulting mixture was stirred at 60 °C for 16 h. Upon completion of the reaction, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 30:1, v/v) to give the desired product **3**.

4. General procedure for the synthesis of 2-aminobenzoates 4



In a sealed tube were placed 1 (0.3 mmol, 1 equiv), DBDMH (0.6 mmol, 2 equiv), H₂O (3 equiv) and $K_2S_2O_8$ (0.9 mmol, 3 equiv) in ROH (2 mL). The resulting mixture was stirred at 60 °C for 24 h. Upon completion of the reaction, ethyl acetate (20 mL) was added to the

mixture, and then washed with saturated brine (15 mL \times 3). The combined water layers were extracted with ethyl acetate (15 mL \times 2). The combined organic layers were dried over anhydrous Na₂SO₄. The solvents were removed via rotary evaporator and the residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 50:1, v/v) to give the desired product **4**.

5. Mechanism Studies



5.1 Control experiments and isotope labeling experiment

When the reaction was carried out with 1*H*-indazole, 3-iodo-1*H*-indazole or 1*H*-indazole-3-carboxylic acid as starting material, no desired product was achieved via N-N bond cleavage. And When the common radical probe 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and 2,6-di-

tert-butyl-4-methylphen-ol (BHT) were added to the reactions under the standard conditions, trace amount or low yield of **2a** was gained. And when 2-aminobenzonitrile was empolyed as starting material to react under the optimal conditions, no corresponding methyl 2-aminobenzoate (**2a**) was detected. The result revealed that 2-aminobenzonitrile might not be the key intermediate of this ring-opening of 3-aminoindazoles. When benzimidamide was submitted to this transformation, benzonitrile was detected as marjor product and no methyl benzoate was observed as well, from which we could speculate that methyl 2-aminobenzoate (**2a**) might not be generated from 2-aminobenzimidamide in this transformation. When substrate **1a** was executed with 6 equivalents H₂O¹⁸ under the standard conditions, 88% of ¹⁸O-labeled product **2a** could be detected by GC-MS , which manifested that the oxygen in the carbonyl group of 2-aminobenzoates should be originated from water.

5.2 ¹H NMR experiments

¹H NMR spectral analysis of the reaction mixture in deuterated DMSO was also carried out at room temperature under air atmosphere for 20 min. As shown in Figure S1b and Figure S1c, a new complex was generated when 3-amino-1*H*-indazole **1a** reacted with NBS or CAN at room temperature. In addition, the H_a and H_b of 3-amino-1*H*-indazole **1a** were missing when **1a** was exposed to CAN in MeOH. The hydrogen at 4.71 ppm in Figure S1c might be the hydroxy of compound **B**. Not surprisingly, when the reaction of **1a**, NBS and CAN proceeded in MeOH at room temperature, the methyl 2-aminobenzoate **2a** was observed.



6. Characterization data for products

methyl 2-aminobenzoate (2a) (CAS Number: 134-20-3)



The reaction was performed following the general procedure **3**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 10:1, v/v) to give the product as a yellow oil (50.1 mg, 83%). IR (KBr, cm⁻¹): 3479, 3369, 1686, 1615. ¹H NMR (500 MHz, DMSO) δ 7.70 (dd, *J* = 8.1, 1.6 Hz,

1H), 7.25 (ddd, J = 8.5, 7.0, 1.6 Hz, 1H), 6.78 (dd, J = 8.4, 1.0 Hz, 1H), 6.64 (brs, 2H), 6.53 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H), 3.78 (s, 3H). ¹³C NMR (126 MHz, DMSO) δ 168.3, 151.8, 134.5, 131.0, 117.0, 115.2, 109.2, 51.8.

ethyl 2-aminobenzoate (2b) (CAS Number: 87-25-2)



The reaction was performed following the general procedure **3**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 10:1, v/v) to give the product as a pink solid (52.8 mg, 80%). IR (KBr, cm⁻¹): 3480, 3371, 1689, 1616. ¹H NMR (500 MHz, DMSO) δ 7.70 (dd, *J* = 8.1, 1.6 Hz,

1H), 7.24 (ddd, J = 8.5, 7.1, 1.6 Hz, 1H), 6.76 (d, J = 8.4 Hz, 1H), 6.63 (brs, 2H), 6.56 – 6.49 (m, 1H), 4.25 (q, J = 7.1 Hz, 2H), 1.30 (t, J = 7.1 Hz, 3H). ¹³C NMR (126 MHz, DMSO) δ 167.9, 151.8, 134.4, 131.0, 117.0, 115.2, 109.4, 60.3, 14.7.

propyl 2-aminobenzoate (2c) (CAS Number: 30954-98-4)



The reaction was performed following the general procedure **3**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 10:1, v/v) to give the product as a yellow oil (60.1 mg, 81%). IR (KBr, cm⁻¹): 3481, 3372, 1694, 1620. ¹H NMR (500 MHz, DMSO) δ 7.70

(dd, J = 8.1, 1.5 Hz, 1H), 7.24 (ddd, J = 8.5, 7.0, 1.7 Hz, 1H), 6.76 (dd, J = 8.4, 0.9 Hz, 1H), 6.62 (brs, 2H), 6.52 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H), 4.15 (t, J = 6.6 Hz, 2H), 1.74 – 1.65 (m, 2H), 0.95 (t, J = 7.4 Hz, 3H). ¹³C NMR (126 MHz, DMSO) δ 167.9, 151.8, 134.4, 131.0, 117.0, 115.2, 109.4, 65.7, 22.1, 10.9.

butyl 2-aminobenzoate (2d) (CAS Number:7756-96-9)



The reaction was performed following the general procedure **3**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 10:1, v/v) to give the product as a yellow oil (59.4 mg, 77%). IR (KBr, cm⁻¹): 3480, 3371, 1686, 1615. ¹H NMR (500

MHz, CDCl₃) δ 7.94 – 7.83 (m, 1H), 7.31 – 7.21 (m, 1H), 6.75 – 6.60 (m, 2H), 5.72 (brs, 2H), 4.28 (t, *J* = 6.6 Hz, 2H), 1.79 – 1.70 (m, 2H), 1.53 – 1.44 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H).¹³C NMR (126 MHz, CDCl₃) δ 168.2, 150.4, 133.9, 131.2, 116.6, 116.2, 111.1, 64.1, 30.8, 19.3, 13.7.

pentyl 2-aminobenzoate (2e) (CAS Number: 30100-15-3)



The reaction was performed following the general procedure **3**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 10:1, v/v) to give the product as a brown oil (57.9 mg, 70%). IR (KBr, cm⁻¹): 3481, 3372, 1686, 1615. ¹H NMR (500 MHz, DMSO) δ 7.73 (dd, *J* = 8.0, 1.5 Hz,

1H), 7.30 (ddd, J = 8.5, 7.2, 1.6 Hz, 1H), 6.85 (d, J = 8.3 Hz, 1H), 6.73 – 6.60 (m, 1H), 4.34 (brs, 2H), 4.20 (t, J = 6.5 Hz, 2H), 1.75 – 1.64 (m, 2H), 1.39 – 1.29 (m, 4H), 0.88 (t, J = 7.0 Hz, 3H). ¹³C NMR (126 MHz, DMSO) δ 167.6, 149.5, 134.5, 131.1, 118.0, 116.9, 111.1, 64.5, 28.3, 28.2, 22.3, 14.3.

isobutyl 2-aminobenzoate (2f) (CAS Number: 7779-77-3)



The reaction was performed following the general procedure **3**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 10:1, v/v) to give the product as a white solid (50.9 mg, 66%). IR (KBr, cm⁻¹): 3480, 3371, 1686, 1615. ¹H NMR (500 MHz, CDCl₃) δ 8.73 (brs, 2H), 8.07 (d, *J* = 7.6 Hz, 1H), 7.61 – 7.52 (m, 2H), 7.33

(ddd, J = 8.3, 5.5, 3.0 Hz, 1H), 4.09 (d, J = 6.6 Hz, 2H), 2.07 (dp, J = 13.4, 6.7 Hz, 1H), 1.00 (d, J = 6.7 Hz, 6H). ¹³C NMR (126 MHz, CDCl₃) δ 167.0, 135.9, 134.7, 131.2, 126.7, 124.2, 120.3, 72.0, 27.6, 19.1.

2-methylbutyl 2-aminobenzoate (2g) (CAS Number: 1249533-08-1)



The reaction was performed following the general procedure **3**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 10:1, v/v) to give the product as a colourless oil (57.1 mg, 69%). IR (KBr, cm⁻¹): 3482, 3372, 1686, 1615. ¹H NMR (500 MHz, CDCl₃) δ 7.87 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.29

-7.25 (m, 1H), 6.67 - 6.63 (m, 2H), 5.70 (brs, 2H), 4.16 (dd, *J* = 10.7, 6.0 Hz, 1H), 4.08 (dd, *J* = 10.7, 6.6 Hz, 1H), 1.85 (td, *J* = 13.0, 6.5 Hz, 1H), 1.58 - 1.49 (m, 1H), 1.35 - 1.27 (m, 1H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.96 (t, *J* = 7.5 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 168.2, 150.41 (s), 134.0, 131.1, 116.7, 116.3, 111.1, 68.9, 34.3, 26.2, 16.6, 11.3.

isopropyl 2-aminobenzoate (2h) (CAS Number:18189-02-1)



The reaction was performed following the general procedure **3**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 10:1, v/v) to give the product as a yellow oil (20.7 mg, 29%). IR (KBr, cm⁻¹): 3481, 3372, 1671, 1604. ¹H NMR (500 MHz, CDCl₃) δ 7.90 – 7.83 (m, 1H), 7.25 (ddd, J = 8.6, 7.1, 1.6 Hz, 1H), 6.69 – 6.61 (m,

2H), 5.71 (brs, 2H), 5.22 (hept, J = 6.3 Hz, 1H), 1.36 (d, J = 6.3 Hz, 6H). ¹³C NMR (126 MHz, CDCl₃) δ 167.7, 150.4, 133.8, 131.2, 116.6, 116.2, 111.5, 67.6, 22.0.

2-methoxyethyl 2-aminobenzoate (2j) (CAS Number: 67836-95-7)



The reaction was performed following the general procedure **3**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 5:1, v/v) to give the product as a yellow oil (52.2 mg, 67%). IR (KBr, cm⁻¹): 3475, 3370, 1679, 1619. ¹H NMR (500 MHz,

DMSO) δ 7.70 (dd, J = 8.1, 1.6 Hz, 1H), 7.25 (ddd, J = 8.5, 7.0, 1.6 Hz, 1H), 6.77 (dd, J = 8.4, 0.8 Hz, 1H), 6.62 (brs, 2H), 6.54 (ddd, J = 8.1, 7.0, 1.1 Hz, 1H), 4.35 – 4.31 (m, 2H), 3.64 (dt, J = 4.7, 3.0 Hz, 2H), 3.31 (s, 3H).¹³C NMR (126 MHz, CDCl₃) δ 167.0, 135.9, 134.6, 131.2, 126.7, 124.2, 120.3, 72.0, 27.6, 19.1.

2-ethoxyethyl 2-aminobenzoate (2k) (CAS Number: 91247-62-0)



The reaction was performed following the general procedure **3**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 5:1, v/v) to give the product as a yellow oil (50.1 mg, 60%). IR (KBr, cm⁻¹): 3483, 3370, 1679, 1615. ¹H NMR (500

MHz, DMSO) δ 7.69 (dd, J = 8.1, 1.6 Hz, 1H), 7.25 (ddd, J = 8.5, 5.7, 1.7 Hz, 1H), 6.76 (dd, J = 8.3, 1.0 Hz, 1H), 6.53 (ddd, J = 8.1, 7.0, 1.1 Hz, 1H), 4.31 (dd, J = 5.4, 4.2 Hz, 2H), 3.69 – 3.66 (m, 2H), 3.48 (t, J = 7.0 Hz, 2H), 1.11 (t, J = 7.0 Hz, 3H). ¹³C NMR (126 MHz, DMSO) δ 167.8, 151.8, 134.5, 131.1, 117.0, 115.2, 109.3, 68.2, 66.1, 63.7, 15.6.

d₃-methyl 2-aminobenzoate (21) (CAS Number: 1394230-52-4)



The reaction was performed following the general procedure **3**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 10:1, v/v) to give the product as a white solid (41.8 mg, 68%). IR (KBr, cm⁻¹): 3479, 3370, 1688, 1629.¹H NMR (500 MHz, DMSO) δ 7.74 (dd, *J* = 8.0, 1.5 Hz,

1H), 7.32 (ddd, J = 8.5, 7.2, 1.6 Hz, 1H), 6.89 (d, J = 8.3 Hz, 1H), 6.69 (dd, J = 11.1, 3.9 Hz, 1H), 6.21 (brs, 2H). ¹³C NMR (126 MHz, DMSO) δ 167.9, 148.8, 134.6, 131.2, 118.3, 117.4, 111.5.

methyl 2-amino-5-fluorobenzoate (2m) (CAS Number: 319-24-4)



The reaction was performed following the general procedure 3. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 30:1, v/v) to give the product as a colourless oil (48.6 mg, 72%). IR (KBr, cm⁻¹): 3481, 3373, 1694, 1624.¹H NMR (500 MHz, CDCl₃) δ 7.52 (dd, *J* = 9.7, 3.1 Hz, 1H), 7.01 (ddd, *J* = 9.0, 7.8, 3.1 Hz, 1H), 6.60 (dd, *J* = 9.0, 4.6

Hz, 1H), 5.45 (brs, 2H), 3.86 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 167.6 , 153.8 (d, J = 235.6 Hz), 146.9, 122.0 (d, J = 22.7 Hz), 117.75 (d, J = 7.1 Hz), 116.0 (d, J = 22.7 Hz), 110.5 (d, J = 6.8 Hz), 51.7. ¹⁹F NMR (471 MHz, CDCl₃) δ -128.4.

propyl 2-amino-6-chlorobenzoate (2n) (CAS Number: 1343900-84-4)



The reaction was performed following the general procedure **3**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 30:1, v/v) to give the product as a yellow solid (58.7 mg, 69%). IR (KBr, cm⁻¹): 3476, 3367, 1692, 1611. ¹H NMR (500 MHz, DMSO) δ 7.11 (t, *J* = 8.1 Hz, 1H), 6.70 (dd, *J* = 8.3,

0.9 Hz, 1H), 6.61 (dd, J = 7.8, 0.9 Hz, 1H), 5.73 (brs, 2H), 4.23 (t, J = 6.6 Hz, 2H), 1.74 – 1.65 (m, 2H), 0.95 (t, J = 7.4 Hz, 3H).¹³C NMR (126 MHz, DMSO) δ 166.7, 149.2, 132.1, 131.8, 117.0 115.50, 114.9, 67.0, 21.9, 10.9

ethyl 2-amino-4-bromobenzoate (20) (CAS Number: 135484-83-2)



The reaction was performed following the general procedure **3**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 30:1, v/v) to give the product as a yellow oil (64.4 mg, 66%). IR (KBr, cm⁻¹): 3469, 3365, 1689, 1618. ¹H NMR (500 MHz, DMSO) δ 7.61 (d, *J* = 8.6 Hz, 1H), 7.01 (d, *J* = 2.0 Hz, 1H), 6.82 (brs,

2H), 6.68 (dd, J = 8.6, 2.0 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 1.29 (t, J = 7.1 Hz, 3H).¹³C NMR (126 MHz, DMSO) δ 167.3, 152.7, 133.0 128.1, 118.8, 118.0, 108.7, 60.6, 14.6.

methyl 4-amino-[1,1'-biphenyl]-3-carboxylate (2p) (CAS Number:

243989-52-8)



The reaction was performed following the general procedure **3**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 30:1, v/v) to give the product as a white solid (72.5 mg, 80%). IR (KBr, cm⁻¹): 3477, 3368, 1686, 1615. ¹H NMR (500 MHz, DMSO) δ 8.00 (d, J =

2.3 Hz, 1H), 7.61 (dd, J = 8.7, 2.4 Hz, 1H), 7.57 – 7.52 (m, 2H), 7.42 – 7.36 (m, 2H), 7.32 – 7.22 (m, 1H), 6.91 (d, J = 8.7 Hz, 1H), 6.80 (brs, 2H), 3.83 (s, 3H). ¹³C NMR (126 MHz, DMSO) δ 168.3, 151.2, 140.1, 132.9, 129.3, 128.7, 127.2, 126.7, 125.9, 117.8, 109.5, 52.0.

methyl 2-amino-5-(benzo[d][1,3]dioxol-5-yl)benzoate (2q)



The reaction was performed following the general procedure **3**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 20:1, v/v) to give the product as a white solid (76.9 mg, 71%). IR (KBr, cm⁻¹): 3431, 3325, 1683, 1611. ¹H NMR (500 MHz, CDCl₃) δ 8.03 (d, *J* = 2.3 Hz,

1H), 7.45 (dd, J = 8.5, 2.3 Hz, 1H), 7.05 – 6.96 (m, 2H), 6.85 (d, J = 8.0 Hz, 1H), 6.71

(d, J = 8.5 Hz, 1H), 5.97 (s, 2H), 5.76 (s, 2H), 3.89 (s, 3H).¹³C NMR (126 MHz, CDCl₃) δ 168.5, 149.4, 148.0, 146.4, 134.9, 132.6, 129.2, 129.1, 119.5, 117.1, 110.8, 108.5, 106.9, 101.0, 51.6. HRMS (ESI, m/z) calcd for C₁₅H₁₄NO₄ [M+H]⁺:272.0917; found: 272.0918.

methylbenzoate (2r) (CAS Number: 18595-16-9)



The reaction was performed following the general procedure **3**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 30:1, v/v) to give the product as a white solid (55.4 mg, 84%). IR (KBr, cm⁻¹): 3474, 3369, 1687, 1618. ¹H NMR (500 MHz, CDCl₃) δ 7.66 (s, 1H),

7.09 (d, *J* = 5.9 Hz, 1H), 6.59 (d, *J* = 6.8 Hz, 1H), 5.41 (brs, 2H), 3.86 (s, 3H), 2.23 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 168.6, 148.3, 135.2, 130.8, 125.4, 116.9, 110.7, 51.5, 20.3.

methyl 2-amino-5-(trifluoromethyl)benzoate (2s) (CAS Number:

117324-58-0)



The reaction was performed following the general procedure **3**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 20:1, v/v) to give the product as a colourless oil (63.9 mg, 73%). IR (KBr, cm⁻¹): 3470, 3366, 1695, 1626. ¹H NMR (500 MHz, CDCl₃) δ 8.13 (s, 1H), 7.44 (dd, *J* = 8.7, 2.0 Hz, 1H), 6.69 (d, *J* = 8.7 Hz, 1H),

6.09 (s, 2H), 3.89 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 167.7, 152.6, 130.4 (q, *J* = 3.3 Hz), 129.1 (q, *J* = 4.1 Hz), 124.3 (q, *J* = 271.0 Hz), 118.1 (q, *J* = 33.3 Hz), 116.6, 109.8, 51.8. ¹⁹F NMR (471 MHz, CDCl₃) δ -61.6.

ethyl 2-amino-5-nitrobenzoate (2t) (CAS Number: 32203-24-0)



The reaction was performed following the general procedure **3**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 15:1, v/v) to give the product as a yellow solid (42.0 mg, 50%). IR (KBr, cm⁻¹): 3446, 3342, 1693, 1623. ¹H NMR (500 MHz, DMSO) δ 8.55 (d, *J* = 2.8 Hz, 1H), 8.05 (dd, *J* = 9.3,

2.8 Hz, 1H), 7.82 (brs, 2H), 6.87 (d, J = 9.3 Hz, 1H), 4.30 (q, J = 7.1 Hz, 2H), 1.33 (t, J = 7.1 Hz, 3H). ¹³C NMR (126 MHz, DMSO) δ 166.4, 156.3, 135.6, 129.2, 128.6, 117.2, 108.1, 61.3, 14.5.

1-methyl 4-((1S,2R,4S)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl) 2-

aminoterephthalate (2u)



The reaction was performed following the general procedure **3**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 15:1, v/v) to give the product as a white solid (84.7 mg, 64%). IR (KBr, cm⁻¹): 3466, 3360, 1703, 1635. ¹H NMR (500 MHz, CDCl₃) δ 7.90 (d, *J* = 8.3 Hz, 1H), 7.35 (d, *J* = 1.5 Hz, 1H),

7.26 (dd, J = 8.3, 1.6 Hz, 1H), 5.85 (s, 2H), 5.13 – 5.04 (m, 1H), 3.89 (s, 3H), 2.51 – 2.41 (m, 1H), 2.14 – 2.05 (m, 1H), 1.81 (dd, J = 12.1, 3.7 Hz, 1H), 1.73 (t, J = 4.5 Hz, 1H), 1.46 – 1.36 (m, 1H), 1.34 – 1.26 (m, 1H), 1.10 (dd, J = 13.8, 3.5 Hz, 1H), 0.96 (s, 3H), 0.90 (d, J = 3.7 Hz, 6H).¹³C NMR (126 MHz, CDCl₃) δ 168.0, 166.2, 150.1, 135.5, 131.4, 117.8, 116.5, 113.6, 80.9, 51.8, 49.1, 47.9, 44.9, 36.8, 28.0, 27.4, 19.7, 18.9, 13.6. HRMS (ESI, m/z) calcd for C₁₉H₂₆NO₄ [M+H]⁺: 332.1856; found: 332.1859.

methyl 2-amino-5-(thiophen-2-yl)benzoate (2v) (CAS Number:

926254-39-9)



The reaction was performed following the general procedure **3**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 25:1, v/v) to give the product as a white solid (56.8 mg, 61%). IR (KBr, cm⁻¹): 3432, 3331, 1701, 1632. ¹H NMR (500

MHz, DMSO) δ 7.93 (d, J = 2.3 Hz, 1H), 7.60 (dd, J = 8.7, 2.3 Hz, 1H), 7.38 (dd, J = 5.1, 1.1 Hz, 1H), 7.28 (dd, J = 3.6, 1.1 Hz, 1H), 7.06 (dd, J = 5.1, 3.6 Hz, 1H), 6.86 (d, J = 8.7 Hz, 1H), 6.83 (brs, 2H), 3.83 (s, 3H). ¹³C NMR (126 MHz, DMSO) δ 167.0, 151.2, 143.9, 132.0, 128.8, 127.6, 124.0, 121.9, 121.4, 117.9, 109.2, 52.1.

methyl 2-amino-5-bromobenzoate (3a) (CAS Number: 52727-57-8)



The reaction was performed following the general procedure **4**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 25:1, v/v) to give the product as a brown solid (48.5 mg, 70%). IR (KBr, cm⁻¹): 3476, 3362, 1698, 1626. ¹H NMR (500 MHz, DMSO) δ 7.77

(d, *J* = 2.4 Hz, 1H), 7.37 (dd, *J* = 8.9, 2.5 Hz, 1H), 6.80 (brs, 2H), 6.77 (d, *J* = 8.9 Hz, 1H), 3.79 (s, 3H). ¹³C NMR (126 MHz, DMSO) δ 167.1, 150.8, 136.9, 132.7, 119.4, 110.6, 105.2, 52.2.

ethyl 2-amino-5-bromobenzoate (3b) (CAS Number: 63243-76-5)



The reaction was performed following the general procedure **4**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 30:1, v/v) to give the product as a yellow solid (48.8 mg, 67%). IR (KBr, cm⁻¹): 3467, 3356, 1689, 1612. ¹H NMR (500

MHz, DMSO) δ 7.77 (d, J = 2.5 Hz, 1H), 7.37 (dd, J = 8.9, 2.5 Hz, 1H), 6.80 (brs, 2H), 6.76 (d, J = 8.9 Hz, 1H), 4.26 (q, J = 7.1 Hz, 2H), 1.30 (t, J = 7.1 Hz, 3H). ¹³C NMR (126 MHz, DMSO) δ 166.7, 150.0, 136.8, 132.7, 119.4, 110.8, 105.2, 60.8, 14.6.

methyl 2-amino-3-bromo-5-fluorobenzoate (3c) (CAS Number:

864293-46-9)



The reaction was performed following the general procedure **4**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 50:1, v/v) to give the product as a pale yellow oil (43.5 mg, 59%). IR (KBr, cm⁻¹): 3480, 3359, 1698, 1620. ¹H NMR (500 MHz, CDCl₃) δ 7.57 (dd, *J* = 9.3, 3.0 Hz, 1H), 7.38 (dd, *J* = 7.4, 3.0 Hz, 1H), 6.15

(brs, 2H), 3.88 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 167.1, 152.5 (d, J = 238.1 Hz), 144.4, 125.2 (d, J = 25.2 Hz), 116.2 (d, J = 23.9 Hz), 111.0 (d, J = 7.0 Hz), 110.2 (d, J = 9.3 Hz), 52.1.

ethyl 2-amino-3-bromo-5-nitrobenzoate (3d) (CAS Number: 101621-

28-7)



The reaction was performed following the general procedure **4**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 20:1, v/v) to give the product as a yellow solid (36.2 mg, 42%). IR (KBr, cm⁻¹): 3449, 3337, 1696, 1621. ¹H NMR (500 MHz, CDCl₃) δ 8.82 (d, *J* = 2.7 Hz, 1H), 8.11 (dd, *J* = 9.2, 2.7 Hz, 1H), 6.66 (d, *J*

= 9.2 Hz, 1H), 4.37 (q, J = 7.1 Hz, 2H), 1.41 (t, J = 7.1 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 166.8, 154.8, 137.2, 129.1, 128.8, 116.2, 109.5, 61.3, 14.3.

methyl 2-amino-3,5-dibromobenzoate (4a) (CAS Number: 606-00-8)



The reaction was performed following the general procedure **5**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 30:1, v/v) to give the product as a white solid (53.5 mg, 58%). IR (KBr, cm⁻¹): 3472, 3373, 1686, 1615. ¹H NMR (500 MHz, CDCl₃) δ 7.95

(d, J = 2.3 Hz, 1H), 7.66 (d, J = 2.3 Hz, 1H), 3.88 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 166.9, 146.5, 139.0, 133.0, 112.5, 111.0, 106.4, 52.1.

2-hydroxyethyl 2-amino-3,5-dibromobenzoate (4b) (CAS Number:

1870467-80-3)



The reaction was performed following the general procedure **5**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 4:1, v/v) to give the product as a yellow solid (46.6 mg, 46%). IR (KBr, cm⁻¹): 3290, 1697, 1626. ¹H NMR (500 MHz, CDCl₃) δ 7.98 (d, *J* = 2.3 Hz, 1H), 7.68 (d, *J* =

2.3 Hz, 1H), 4.43 (dd, J = 5.5, 3.8 Hz, 2H), 3.97 – 3.94 (m, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 166.7, 146.7, 139.3, 132.9, 112.2, 111.2, 106.5, 66.7, 61.2.

2-methoxyethyl 2-amino-3,5-dibromobenzoate (4c) (CAS Number:

1343073-63-1)



The reaction was performed following the general procedure **5**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 5:1, v/v) to give the product as a yellow oil (52.8 mg, 50%). IR (KBr, cm⁻¹): 3479, 3369, 1697, 1626. ¹H NMR (500 MHz, DMSO) δ 7.88 (d, J = 2.4 Hz, 1H),

7.85 (d, J = 2.4 Hz, 1H), 6.82 (brs, 2H), 4.39 – 4.36 (m, 2H), 3.67 – 3.65 (m, 2H), 3.31 (s, 3H). ¹³C NMR (126 MHz, DMSO) δ 165.8, 147.1, 139.0, 132.4, 111.9, 110.9, 105.1, 69.7, 64.1, 58.2.

2-ethoxyethyl 2-amino-3,5-dibromobenzoate (4d) (CAS Number:

1283501-98-3)



The reaction was performed following the general procedure **4**. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 5:1, v/v) to give the product as a brown oil (45.0 mg, 41%). IR (KBr, cm⁻¹): 3476, 3367, 1697, 1623. ¹H NMR (500 MHz, DMSO) δ 7.76 (d, J = 2.5 Hz, 1H),

7.39 (dd, J = 8.9, 2.5 Hz, 1H), 6.77 (d, J = 8.9 Hz, 1H), 4.33 (dd, J = 5.5, 4.0 Hz, 2H), 3.71 – 3.65 (m, 2H), 3.50 (dd, J = 14.0, 7.0 Hz, 3H), 1.12 (t, J = 7.0 Hz, 3H). ¹³C NMR (126 MHz, DMSO) δ 166.6, 150.9, 137.0, 132.7, 119.4, 1107, 105.2, 68.1, 66.0, 64.0, 15.5.

methyl 2-amino-5-iodobenzoate (5a) (CAS Number: 77317-55-6)



The reaction was performed following the general procedure **4** by using NIS as iodine source. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 30:1, v/v) to give the product as a brown solid (43.2 mg, 52%). IR (KBr, cm⁻¹): 3471, 3366, 1698, 1631. ¹H

NMR (500 MHz, CDCl₃) δ 8.13 (d, J = 2.2 Hz, 1H), 7.46 (dd, J = 8.7, 2.2 Hz, 1H), 6.45 (d, J = 8.7 Hz, 1H), 5.75 (brs, 2H), 3.86 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ = 167.3, 149.8, 142.2, 139.4, 118.7, 112.8, 75.8, 51.7.

ethyl 2-amino-5-iodobenzoate (5b) (CAS Number: 268568-11-2)



The reaction was performed following the general procedure **4** by using NIS as iodine source. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 30:1, v/v) to give the product as a brown solid (42.7 mg, 49%). IR (KBr, cm⁻¹): 3464, 3358,

1681, 1611. ¹H NMR (500 MHz, CDCl₃) δ 8.14 (d, J = 2.2 Hz, 1H), 7.47 (dd, J = 8.7, 2.2 Hz, 1H), 6.45 (d, J = 8.7 Hz, 1H), 5.77 (brs, 2H), 4.35 – 4.30 (m, 2H), 1.38 (t, J = 7.1 Hz, 3H).¹³C NMR (126 MHz, CDCl₃) δ 166.9, 149.8, 142.1, 139.4, 118.7, 113.1, 75.9, 60.7, 14.3.

quinazolin-4(3H)-one (6a) (CAS Number: 491-36-1)



In a dried sealed tube were placed 1H-indazol-3-amine (0.3 mmol, 1 equiv), NBS (0.3 mmol, 1 equiv) and CAN (0.45 mol, 1.5 equiv) in EtOH (1 mL). The resulting mixture was stirred at room temperature for 15 h. Upon completion of the reaction, the solvent was evaporated under reduced pressure to obtain the residue. Then,

NH₄OAc (1.5 mmol) and triethyl orthoformate (2 mL) were added to the residue. The resulting mixture was stirred at reflux for 3 h. Upon completion of the reaction, the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 4:1, v/v) to give the product as a white solid (30.6 mg, 70%). ¹H NMR (500 MHz, DMSO) δ 12.26 (brs, 1H), 8.19 – 8.04 (m, 2H), 7.85 – 7.74 (m, 1H), 7.66 (d, *J* = 8.1 Hz, 1H), 7.52 (dd, *J* = 11.1, 3.9 Hz, 1H). ¹³C NMR (126 MHz, DMSO) δ 161.2, 149.2, 145.8, 134.8, 127.7, 127.2, 126.3, 123.1.

6-bromoquinazolin-4(3H)-one (6b) (CAS Number: 32084-59-6)



In a dried sealed tube were placed 5-bromo-1*H*-indazol-3amine (0.3 mmol, 1 equiv), NBS (0.3 mmol, 1 equiv) and CAN (0.45 mol, 1.5 equiv) in EtOH (1 mL). The resulting mixture was stirred at room temperature for 15 h. Upon completion of the reaction, the solvent was evaporated under reduced

pressure to obtain the residue. Then, NH4OAc (1.5 mmol) and triethyl orthoformate (2

mL) were added to the residue. The resulting mixture was stirred at reflux for 3 h. Upon completion of the reaction, the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatograph (silica gel, petroleum ether:EtOAc = 4:1, v/v) to give the product as a white solid (40.9 mg, 61%). ¹H NMR (500 MHz, DMSO) δ 12.44 (brs, 1H), 8.17 (d, *J* = 2.4 Hz, 1H), 8.13 (s, 1H), 7.93 (dd, *J* = 8.7, 2.4 Hz, 1H), 7.60 (d, *J* = 8.7 Hz, 1H). ¹H NMR (500 MHz, DMSO) δ 12.44 (s, 1H), 8.13 (s, 1H), 7.93 (dd, *J* = 8.7, 2.4 Hz, 1H), 7.60 (d, *J* = 8.7 Hz, 1H).

7. NMR spectroscopic data

methyl 2-aminobenzoate (2a)





ethyl 2-aminobenzoate (2b)





propyl 2-aminobenzoate (2c)





butyl 2-aminobenzoate (2d)



pentyl 2-aminobenzoate (2e)





isobutyl 2-aminobenzoate (2f)







2-methylbutyl 2-aminobenzoate (2g)



isopropyl 2-aminobenzoate (2h)





2-methoxyethyl 2-aminobenzoate (2j)





2-ethoxyethyl 2-aminobenzoate (2k)





d₃-methyl 2-aminobenzoate (21)













propyl 2-amino-6-chlorobenzoate (2n)





ethyl 2-amino-4-bromobenzoate (20)







methyl 4-amino-[1,1'-biphenyl]-3-carboxylate (2p)





methyl 2-amino-5-(benzo[d][1,3]dioxol-5-yl)benzoate (2q)



methyl 2-amino-5-methylbenzoate (2r)





methyl 2-amino-5-(trifluoromethyl)benzoate (2s)







ethyl 2-amino-5-nitrobenzoate (2t)

100 90 f1 (ppm) 40 30

130 120



1-methyl 4-((18,2R,4S)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl) 2aminoterephthalate (2u)





Methyl 2-amino-5-(thiophen-2-yl)benzoate (2v)





methyl 2-amino-5-bromobenzoate (3a)



ethyl 2-amino-5-bromobenzoate (3b)







methyl 2-amino-3-bromo-5-fluorobenzoate (3c)





ethyl 2-amino-3-bromo-5-nitrobenzoate (3d)



methyl 2-amino-3,5-dibromobenzoate (4a)





2-hydroxyethyl 2-amino-3,5-dibromobenzoate (4b)



2-methoxyethyl 2-amino-3,5-dibromobenzoate (4c)

2-ethoxyethyl 2-amino-3,5-dibromobenzoate (4d)

methyl 2-amino-5-iodobenzoate (5a)

ethyl 2-amino-5-iodobenzoate (5b)

quinazolin-4(3H)-one (6a)

6-bromoquinazolin-4(3H)-one (6b)

