Supporting Information

Rapid and halide compatible synthesis of 2-N-substituted indazolone derivatives via photochemical cyclization in aqueous media

Hui-Jun Nie\textsuperscript{a}, An-Di Guo\textsuperscript{b}, Hai-Xia Lin\textsuperscript{a}, Xiao-Hua Chen\textsuperscript{*b}

\textsuperscript{a} Department of Chemistry, Innovative Drug Research Center, college of sciences Shanghai University, Shanghai, 200444, China.

\textsuperscript{b} Chinese Academy of Sciences Key Laboratory of Receptor Research, and Synthetic Organic & Medicinal Chemistry Laboratory, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, 201203, China.

E-mail: xhchen@simm.ac.cn
Table of contents:

1. General information........................................................................................................................................S3

2. Experimental procedures, characterization data and supplementary figures........S4

3. $^1$H, $^{13}$C NMR and $^{19}$F NMR spectra..................................................................................................S17
1. General information

Unless otherwise stated, all starting materials, catalysts, and solvents were commercially available and were used as purchased without any pretreatment. Analytical TLC was performed using pre-coated plates (HSGF254) and visualized with UV light or an I$_2$ chamber. Flash column chromatography was performed using the indicated solvent system on Sinopharm Chemical Reagent silica gel (200–300 mesh). $^1$H NMR spectra and proton decoupled $^{13}$C NMR spectra were obtained on a 400 MHz Bruker, 500 MHz Bruker NMR spectrometer. $^1$H and $^{13}$C chemical shifts (δ) are reported in parts per million (ppm) relative to residual solvent peaks. Multiplicities are given as s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). Coupling constants (J) are given in Hz. For HRMS analysis, samples were analyzed by flow-injection analysis into a Agilent G6520 Q-TOF. LCMS analysis was carried out using a Waters UPLC-MS (ESI), UPLC: Waters HPLC H-CLASS, MS: Waters SQ Detector 2. Photochemical reactions were carried out in Shanghai Heqi glassware B-002601 40×25mm flat bottom flask. Light sources used were a ZF-7A 16W 365nm UV source. Melting points were determined on a SGWX-4 melting point apparatus.
2. Experimental procedures and compound characterization data

General Procedure (Ⅰ) for the preparation of Substituted (2-Nitrophenyl)methanols.[1]

To a solution of the substituted 2-nitrobenzoic acid in dried THF was added drop wise a 2M solution of borane dimethylsulfide complex (1.3 equiv - 5equiv). The resulting solution was then reflux over for 3 h. After allowed to room temperature, 3M aqueous solution of hydrochloric acid was added drop wise into this reaction system until effervescence was no longer observed. The resulting mixture was then extracted with (3 × 30 mL) of ethyl acetate. The combined organic phases were washed with a saturated aqueous solution of Na₂CO₃ followed by brine. The resulting organic phase was dried over Na₂SO₄ and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by chromatograph on silica gel with petroleum ether/ethyl acetate as the eluent to afford the desired products.

(4-methoxy-2-nitrophenyl)methanol (14a)[1]: The general procedure (I) was followed using 2 g of 4-methoxy-2-nitrobenzoic acid (10.14 mmol) in 40 mL THF and 6.6 mL of BH₃-Me₂S (13.19 mmol, 1.3 equiv). Intermediate 14a was obtained as yellow solid (1.75 g, 94%). ¹H NMR (400 MHz, DMSO) δ 7.70 (d, J = 8.7 Hz, 1H), 7.54 (d, J = 2.6 Hz, 1H), 7.34 (dd, J = 8.6, 2.6 Hz, 1H), 5.45 (t, J = 5.5 Hz, 1H), 4.72 (d, J = 5.5 Hz, 2H), 3.84 (s, 3H). The ¹H NMR data are good in agreement with the literature date.[1]

(5-bromo-2-nitrophenyl)methanol (14b)[2]: The general procedure (I) was followed using 2 g of 5-bromo-2-nitrobenzoic acid (8.13 mmol) in 40 mL THF and 5.3 mL of BH₃-Me₂S (10.57 mmol, 1.3 equiv), intermediate 14b as obtained as yellow solid (1.21 g, 64%). ¹H NMR (400 MHz, DMSO) δ 8.06 – 7.96 (m, 2H), 7.75 (dd, J = 8.7, 2.2 Hz, 1H), 7.34 (dd, J = 8.6, 2.6 Hz, 1H), 5.45 (t, J = 5.5 Hz, 1H), 4.72 (d, J = 5.5 Hz, 2H), 3.84 (s, 3H). The ¹H NMR data are good in agreement with the literature data.[2]

(2-nitro-5-(trifluoromethyl)phenyl)methanol (14c)[3]: The general procedure (I) was followed using 2 g of 2-nitro-5-(trifluoromethyl) benzoic acid (8.51 mmol) in 40 mL THF and 5.5 mL of BH₃-Me₂S (10.06 mmol, 1.3 equiv). Intermediate 14c as obtained as yellow solid (1.73 g, 92%). ¹H NMR (400 MHz, DMSO) δ 8.36 (s, 1H), 8.16 (d, J = 8.2 Hz, 1H), 8.07 (d, J = 8.2 Hz, 1H), 5.77 (t, J = 5.5 Hz, 1H), 4.90 (d, J = 5.5 Hz, 2H).

(3-chloro-2-nitrophenyl)methanol (14d)[4]: The general procedure (I) was followed using 4g of 3-chloro-2-nitrobenzoic acid (19.85 mmol) in 60 mL THF and 12.9 mL of BH₃-Me₂S (25.80 mmol, 1.3 equiv). Intermediate 14d as obtained as yellow solid (3.36 g, 90%). ¹H NMR (400 MHz, CDCl₃) δ 7.51 (dt, J = 8.3, 4.2 Hz,
(5-fluoro-2-nitrophenyl)methanol (14e): The general procedure (I) was followed using 2 g of 5-fluoro-2-nitrobenzoic acid (10.80 mmol) in 40 mL THF and 7.02 mL of BH₃·Me₂S (14.04 mmol, 1.3 equiv), intermediate 14e as obtained as yellow solid (1.73 g, 92%) as obtained as yellow solid (1.7 g, 92%).

1H NMR (400 MHz, DMSO) δ 8.20 (dd, J = 9.0, 5.2 Hz, 1H), 7.59 (d, J = 10.1 Hz, 1H), 7.36 (dd, J = 11.0, 5.5 Hz, 1H), 5.71 (t, J = 5.5 Hz, 1H), 4.84 (d, J = 5.5 Hz, 2H).

(2-fluoro-6-nitrophenyl)methanol (14f): The general procedure (I) was followed using 2 g of 2-fluoro-6-nitrobenzoic acid (10.80 mmol) in 40 mL THF and 7.02 mL of BH₃·Me₂S (14.04 mmol, 1.3 equiv), intermediate 14f as obtained as yellow solid (1.38 g, 75%).

1H NMR (400 MHz, DMSO) δ 7.78–7.70 (m, 1H), 7.63–7.53 (m, 2H), 5.41 (t, J = 5.6 Hz, 1H), 4.70 (d, J = 5.6 Hz, 2H).

(4-fluoro-2-nitrophenyl)methanol (14g): The general procedure (I) was followed using 2 g of 4-fluoro-2-nitrobenzoic acid (10.80 mmol) in 40 mL THF and 7.02 mL of BH₃·Me₂S (14.04 mmol, 1.3 equiv), intermediate 14g as obtained as yellow solid (1.79 g, 97%).

1H NMR (400 MHz, DMSO) δ 7.97–7.88 (m, 1H), 7.85 (dd, J = 8.6, 6.0 Hz, 1H), 7.70–7.60 (m, 1H), 5.59 (t, J = 5.5 Hz, 1H), 4.78 (d, J = 5.5 Hz, 2H).

(2-nitro-1, 4-phenylene)dimethanol (14h): The general procedure (I) was followed using 4g of 2-nitroterephthalic acid (18.95 mmol) in 47 mL of BH₃·Me₂S (94.75 mmol, 5 equiv), intermediate 14h was obtained as white solid (3.5 g, 100%).

1H NMR (400 MHz, DMSO) δ 7.97 (s, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 5.50 (t, J = 5.5 Hz, 1H), 5.46 (t, J = 5.7 Hz, 1H), 4.80 (d, J = 5.3 Hz, 2H), 4.59 (d, J = 5.4 Hz, 2H).

(4-nitro-1,3-phenylene)dimethanol (14i): The general procedure (I) was followed using 1g of 4-nitroisophthalic acid (4.74 mol) in 11.85 mL of BH₃·Me₂S (23.70 mmol, 5 equiv), intermediate 14i was obtained as white solid (0.88 g, 88%).

1H NMR (400 MHz, DMSO) δ 7.99 (s, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 7.3 Hz, 1H), 5.55–5.46 (m, 2H), 4.81 (d, J = 3.8 Hz, 2H), 4.60 (d, J = 2.6 Hz, 2H).
General Procedure (Ⅱ) for 14j and 14k

(4-iodo-2-nitrophenyl)methanol (14j): To a suspension of 4-amino-2-nitrozoic (960 mg, 5.27 mmol) in water (40 ml) was added Concentrated hydrochloric acid (1.3 mL) and cooled to 0°C. A solution of NaNO₂ (437 mg, 6.65 mmol) in water (2 mL) was added. After stirring for 10 min, a solution of KI (1.05 g, 12.65 mmol) in water (2 mL) was added. The reaction mixture was stirred at room temperature for 3 hr. And excess iodine was destroyed with saturated NaHSO₃ solution. The mixture was extracted with ethyl acetate and the organic phase was washed with saturated sodium chloride solution and dried over Na₂SO₄ and filtered. The filtrate was concentrated under reduced pressure to give crude product [9]. The crude product was dissolved in 20 mL dried THF followed by dropping 1 M borane tetrahydrofuran complex (15.9 mL, 15.9 mmol), the reaction mixture was stirred at room temperature over night. An 3 M aqueous solution of hydrochloric acid was added drop wise into this reaction system until effervescence was no longer observed. The resulting mixture was then extracted with (3 × 30 mL) of ethyl acetate. The combined organic phases were washed with a saturated aqueous solution of Na₂CO₃ followed by brine. The resulting organic phase was dried over Na₂SO₄ and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by chromatography on silica gel with petroleum ether/ethyl acetate as the eluent to afford 14j as a yellow solid (305 mg, two steps 21%). ¹H NMR (500 MHz, DMSO) δ 8.32 (d, J = 1.7 Hz, 1H), 8.12 (dd, J = 8.2, 1.7 Hz, 1H), 7.59 (d, J = 8.2 Hz, 1H), 5.61 (t, J = 5.5 Hz, 1H), 4.74 (d, J = 5.6 Hz, 2H).

(5-iodo-2-nitrophenyl)methanol (14k): Prepared according to the procedure for the preparation of 14j. Intermediate 14k was obtained as yellow solid (576 mg, two steps 39%). ¹H NMR (400 MHz, DMSO) δ 8.18 (d, J = 0.8 Hz, 1H), 7.92 (dd, J = 8.5, 1.6 Hz, 1H), 7.82 (d, J = 8.5 Hz, 1H), 5.66 (t, J = 5.1 Hz, 1H), 4.80 (d, J = 4.0 Hz, 2H).

Procedure for synthesis of 14l

A solution of 4-(bromomethyl)-3-nitrobenzoic acid (2 g, 7.69 mmol) and Na₂CO₃ (4.07 g, 38.43 mmol) in water/acetone (1:1 v/v, 60 mL) was heated at reflux temperature. After 5 h, the acetone was evaporated. The resulting aqueous solution was washed with ether (40 mL), acidified with 6 M HCl and extracted with EtOAc (3 × 40 mL). The combined organic layers were washed with water (40 mL), dried over Na₂SO₄ and concentrated in vacuo to yield 1.51 g (100%) of 4-(hydroxymethyl)-3-nitrobenzoic acid as a yellow solid [11]. ¹H NMR (400 MHz, DMSO) δ 13.58
(s, 1H), 8.48 (d, J = 1.6 Hz, 1H), 8.28 (dd, J = 8.1, 1.6 Hz, 1H), 7.99 (d, J = 8.1 Hz, 1H), 5.73 (s, 1H), 4.89 (s, 2H).

To a solution of 4-(hydroxymethyl)-3-nitrobenzoic acid (1.51 g, 7.69 mmol), Propylamine (948 ul, 11.53 mmol) and HATU (3.22 g, 8.46 mmol) in dry DMF (25 mL) was added N,N-diisopropyl-ethyamine (3.81 mL, 23.07 mmol). The reaction mixture was stirred at room temperature overnight. The reaction system was quenched with water (40 mL) and extracted with EtOAc (2 × 60 mL). The combined organic layers were washed with brine (3 × 40 mL). The resulting organic phase was dried over Na₂SO₄ and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by chromatography on silica gel with dichloromethane/methanol as the eluent to afford 14l as a yellow solid (1.26 g, 69%).

**General Procedure (II) for indazolone synthesis:**

A 40×25mm flat bottom flask was charge with a stir bar, o-nitrobenzyl alcohol (0.75 mmol), amine (0.3 mmol), 1-Butanol (4.5 mL), water (1.5 mL). The reaction mixture was placed under a UV lamp for 3h. The solution was concentrated by rotary evaporation and purified by chromatography on silica gel with dichloromethane/methanol as the eluent to afford the desired products.

2-heptyl-3-oxo-N-propyl-2, 3-dihydro-1H-indazole-6-carboxamide (13). Following general procedure (II) : the substrate 13 was obtained as a yellow solid (78 mg, 82%). Mp: 145-147°C. ¹H NMR (400 MHz, DMSO) δ 8.76 (t, J = 5.4 Hz, 1H), 8.50 (d, J = 1.7 Hz, 1H), 8.22 (dd, J = 8.1, 1.7 Hz, 1H), 7.92 (d, J = 8.1 Hz, 1H), 5.65 (t, J = 5.5 Hz, 1H), 4.87 (d, J = 5.5 Hz, 2H), 3.25 (dd, J = 12.9, 6.9 Hz, 2H), 1.61 – 1.49 (m, 2H), 0.90 (t, J = 7.4 Hz, 3H).

**2-(4-hydroxybutyl)-1, 2-dihydro-3H-indazol-3-one (2) [12].** Following general procedure (II) : the substrate 2 was obtained as a yellow oil (42mg, 68%). ¹H NMR (500 MHz, DMSO) δ 10.18 (s, 1H), 7.62 (d, J = 7.8 Hz, 1H), 7.49 (t, J = 7.2 Hz, 1H), 7.25 (d, J = 8.2 Hz, 1H), 7.09 (t, J = 7.4 Hz, 1H), 3.79 (t, J = 7.0 Hz, 2H), 3.40 (t, J = 6.5 Hz, 2H), 1.71 (dt, J = 14.9, 7.3 Hz, 2H), 1.43-1.36 (m, 2H). ¹³C NMR (101 MHz, DMSO) δ 160.73, 146.04, 131.36, 123.10, 120.97, 117.57, 112.26, 60.41, 43.29, 41.28, 31.30, 28.34, 27.91, 26.16, 22.49, 22.17, 14.06, 11.61. HRMS (ESI-ion trap): m/z [M-H] Calcd for C₁₁H₁₃N₃O₂: 205.0983; found : 205.098.
2-butyl-1,2-dihydro-3H-indazol-3-one (1)[13]. Following general procedure (III) : the substrate 1 was obtained as a yellow oil (54 mg , 95%). 1H NMR (400 MHz , DMSO) δ 10.28 (s, 1H), 7.63 (d, J = 7.8 Hz, 1H), 7.50 – 7.44 (m, 1H), 7.25 (d, J = 8.2 Hz, 1H), 7.07 (t, J = 7.5 Hz, 1H), 3.79 (t, J = 7.0 Hz, 2H), 1.73 – 1.60 (m, 2H), 1.25 (dq, J = 14.7, 7.4 Hz, 2H), 0.87 (t, J = 7.4 Hz, 3H). 13C NMR (101 MHz, DMSO) δ 160.70, 146.06, 131.29, 124.63, 124.26 (q, J = 13.1, 6.7 Hz, 1H), 124.37, 123.06, 120.91, 117.57, 112.24, 42.87, 30.01, 19.47, 13.62. HRMS (ESI-ion trap): m/z [M-H] Calcd for C11H12N2O:189.1033 ; found : 189.1037.

2-cyclopentyl-3-oxo-N-propyl-2, 3-dihydro-1H-indazole-6-carboxamide (16a). Following general procedure (III) : the substrate 16a was obtained as a yellow solid ( 66 mg , 77%). Mp: 90-92°C. 1H NMR (400 MHz, DMSO) δ 10.14 (s, 1H), 8.58 (t, J = 5.5 Hz, 1H), 7.71 – 7.64 (m, 2H), 7.53 (d, J = 9.0 Hz, 1H), 4.85 – 4.76 (m, 1H), 4.85 – 4.76 (m, 1H), 3.23 (dd, J = 13.1, 6.7 Hz, 2H), 2.01 – 1.89 (m, 2H), 1.85-1.72 (m, 4H), 1.66-1.49 (m, 4H), 0.89 (t, J = 7.4 Hz, 3H). 13C NMR (101 MHz, DMSO) δ 165.98, 160.49, 146.03, 137.78, 122.94, 119.86, 119.51, 111.62, 54.41, 41.29, 29.99, 24.37, 22.48, 11.61. HRMS (ESI-ion trap): m/z [M-H] Calcd for C19H20N2O: 286.1561; found: 286.1564

3-cyclopentyl-6-(trifluoromethyl)-1, 2-dihydro-3H-indazol-3-one (16b). Following general procedure (III) : the substrate 16b was obtained as a brown solid (51 mg , 63%). Mp: 156-158°C. 1H NMR (400 MHz, DMSO) δ 10.53 (s, 1H), 7.84 (d, J = 8.2 Hz, 1H), 7.59 (s, 1H), 7.37 (d, J = 7.8 Hz, 1H), 4.88 – 4.78 (m, 1H), 2.04 – 1.90 (m, 2H), 1.88-1.72 (m, 4H), 1.71-1.55 (m, 2H). 13C NMR (126 MHz, DMSO) δ 159.65, 145.21, 131.53 (q, J = 31.6 Hz), 124.63, 124.26 (q, J = 272.7 Hz),120.34, 117.08 (d, J = 2.9Hz), 109.78 (d, J = 4.2 Hz), 54.49, 30.05, 24.39. HRMS (ESI-ion trap): m/z [M-H] Calcd for C19H19F2N2O: 269.0907 ; found: 269.0908.

2-cyclopentyl-5-(hydroxymethyl)-1, 2-dihydro-3H-indazol-3-one (16c). Following general procedure (III) : the substrate 16c was obtained as a yellow solid (50 mg , 71%). Mp: 134-136°C. 1H NMR (400 MHz, DMSO) δ 9.81 (s, 1H), 7.55 (s, 1H), 7.46 (dd, J = 8.4, 1.3 Hz, 1H), 7.21 (d, J = 8.4 Hz, 1H), 5.19 (t, J = 5.7 Hz, 1H), 4.84 – 4.73 (m, 1H), 4.52 (d, J = 5.5 Hz, 2H), 1.98 – 1.85 (m, 2H), 1.83 – 1.71 (m, 4H), 1.67 – 1.52 (m, 2H). 13C NMR (101 MHz, DMSO) δ 161.44, 146.01, 135.75, 130.72, 120.58, 117.87, 112.37, 62.93, 54.28, 29.94, 24.44. HRMS (ESI-ion trap): m/z [M-H] Calcd for C13H14N2O: 231.1139; found: 231.1142.

2-heptyl-6-methoxy-1, 2-dihydro-3H-indazol-3-one (16d). Following general procedure (III) : the substrate 16d was obtained as a yellow solid (44 mg , 56%). Mp: 61-63°C. 1H NMR (400 MHz, DMSO) δ 10.08 (s, 1H),
7.49 (d, J = 8.5 Hz, 1H), 6.72 – 6.60 (m, 2H), 3.80 (s, 3H), 3.70 (t, J = 7.0 Hz, 2H), 1.68 – 1.58 (m, 2H), 1.31 – 1.17 (m, 8H), 0.83 (t, J = 6.9 Hz, 3H). 13C NMR (101 MHz, DMSO) δ 162.64, 160.98, 148.01, 124.17, 110.99, 110.91, 94.58, 55.68, 43.30, 31.37, 28.44, 27.95, 26.24, 22.23, 14.12. HRMS (ESI-ion trap): m/z [M-H]⁻ Calcd for C13H21N2O2: 261.1609; found: 261.1611.

2-heptyl-1,2-dihydro-3H-indazol-3-one(16e) Following general procedure (III) : the substrate 16e was obtained as a yellow solid (56 mg, 80%). 1H NMR (400 MHz, DMSO) δ 10.34 (s, 1H), 7.62 (d, J = 7.8 Hz, 1H), 7.52 – 7.41 (m, 1H), 7.24 (d, J = 8.2 Hz, 1H), 7.07 (t, J = 7.4 Hz, 1H), 3.77 (t, J = 7.0 Hz, 2H), 1.74 – 1.59 (m, 2H), 1.28-1.17 (m, 8H). 0.82 (t, J = 6.8 Hz, 3H). 13C NMR (101 MHz, DMSO) δ 160.63, 146.03, 131.26, 123.06, 120.87, 117.55, 112.15, 31.36, 28.43, 27.98, 26.24, 22.23, 14.09. LCMS: [M+H]⁺ 233.21.

3-oxo-2-(3-phenylpropyl)-N-propyl-2,3-dihydro-1H-indazole-6-carboxamide (16f). Following general procedure (III) : the substrate 16f was obtained as a yellow solid (77 mg, 76%). Mp: 153-155°C. 1H NMR (400 MHz, DMSO) δ 10.47 (s, 1H), 8.60 (t, J = 5.5 Hz, 1H), 7.70 (d, J = 8.2 Hz, 2H), 7.54 (d, J = 9.1 Hz, 1H), 7.28 (t, J = 7.4 Hz, 2H), 7.23 (d, J = 7.0 Hz, 2H), 7.18 (t, J = 7.1 Hz, 1H), 3.84 (t, J = 7.0 Hz, 2H), 3.23 (dd, J = 13.1, 6.6 Hz, 2H), 2.59 (t, J = 7.7 Hz, 2H), 2.05 – 1.93 (m, 2H), 1.60 – 1.49 (m, 2H), 0.89 (t, J = 7.4 Hz, 3H). 13C NMR (101 MHz, DMSO) δ 166.01, 160.20, 145.58, 141.40, 137.79, 128.54, 126.08, 123.09, 119.83, 119.17, 111.35, 43.13, 41.32, 32.38, 29.79, 22.53, 11.66. HRMS (ESI-ion trap): m/z [M-H]⁻ Calcd for C33H23N3O2: 336.1718; found: 336.1725.

3-(tert-butyl)-3-oxo-N-propyl-2,3-dihydro-1H-indazole-6-carboxamide (16g) Following general procedure (III) : the substrate 16g was obtained as a yellow solid (45 mg, 55%). Mp: 179-181°C. 1H NMR (400 MHz, DMSO) δ 9.85 (s, 1H), 8.57 (t, J = 5.5 Hz, 1H), 7.67 (s, 1H), 7.63 (d, J = 8.1 Hz, 1H), 7.52 (dd, J = 8.2, 1.1 Hz, 1H), 3.23 (dd, J = 13.1, 6.7 Hz, 2H), 1.60 – 1.49 (m, 11H), 0.89 (t, J = 7.4 Hz, 3H). 13C NMR (101 MHz, DMSO) δ 166.02, 161.93, 146.05, 137.76, 122.76, 121.04, 119.79, 111.79, 57.86, 41.30, 27.37, 22.50, 11.64. HRMS (ESI-ion trap): m/z [M-H]⁻ Calcd for C33H23N3O2: 274.1569; found: 274.1569.

2-cyclopentyl-6-(hydroxymethyl)-1,2-dihydro-3H-indazol-3-one (16h). Following general procedure (III) : the substrate 16h was obtained as a brown solid ( 49 mg, 70%). Mp: 165-167°C. 1H NMR (400 MHz, DMSO) δ 9.82 (s, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.18 (s, 1H), 7.02 (d, J = 8.0 Hz, 1H), 5.34 (t, J = 5.8 Hz, 1H), 4.82-4.72 (m, 1H), 4.58 (d, J = 5.7 Hz, 2H), 1.95-1.85 (m, 2H), 1.84 – 1.71 (m, 4H), 1.66-1.55 (m, 2H), 13C NMR (101 MHz, DMSO) δ 161.36, 147.07, 146.85, 122.61, 119.73, 116.61, 109.58, 62.96, 54.27, 31.38, 27.37.
24.38. LCMS M+H 233.18. HRMS (ESI-ion trap): m/z [M-H] Calcd for C_{13}H_{15}N_2O_2: 231.1139; found: 231.1138.

2-benzyl-3-oxo-N-propyl-2, 3-dihydro-1H-indazole-6-carboxamide (16i).
Following general procedure (III) : the substrate 16i was obtained as a white solid (54 mg, 58%). Mp: 192-194°C. 1H NMR (400 MHz, DMSO) δ 10.46 (s, 1H), 8.56 (t, J = 5.5 Hz, 1H), 7.74 (d, J = 8.2 Hz, 1H), 7.64 (s, 1H), 7.53 (dd, J = 8.2, 0.9 Hz, 1H), 7.37-7.24 (m, 5H), 5.03 (s, 2H), 3.22 (dd, J = 13.2, 6.6 Hz, 2H), 1.59 – 1.48 (m, 2H), 0.89 (t, J = 7.4 Hz, 3H). 13C NMR (101 MHz, DMSO) δ 165.99, 160.33, 145.60, 138.04, 136.91, 128.76, 127.73, 123.22, 119.82, 118.75, 111.42, 47.05, 41.30, 22.50, 11.64.

2-benzyl-6-(hydroxymethyl)-1, 2-dihydro-3H-indazol-3-one (16j).
Following general procedure (III) : the substrate 16j was obtained as a white solid (42 mg, 55%). Mp: 150-152°C. 1H NMR (400 MHz, DMSO) δ 10.17 (s, 1H), 7.60 (d, J = 8.1 Hz, 1H), 7.34 (t, J = 7.2 Hz, 2H), 7.28 (dd, J = 6.0, 3.9 Hz, 1H), 7.24 (t, J = 5.8 Hz, 2H), 7.15 (s, 1H), 7.04 (d, J = 8.1 Hz, 1H), 5.33 (t, J = 4.2 Hz, 1H), 4.98 (s, 2H), 4.57 (d, J = 4.2 Hz, 2H). 13C NMR (101 MHz, DMSO) δ 161.10, 147.10, 146.65, 137.16, 128.68, 127.67, 127.61, 122.85, 119.71, 115.88, 109.38, 62.95, 46.97.

2-benzyl-5-(hydroxymethyl)-1, 2-dihydro-3H-indazol-3-one (16k).
Following general procedure (III) : the substrate 16k was obtained as a brown oil (33 mg, 43%). 1H NMR (400 MHz, DMSO) δ 10.18 (s, 1H), 7.60 (s, 1H), 7.45 (dd, J = 8.4, 1.2 Hz, 1H), 7.33 (t, J = 7.2 Hz, 2H), 7.28 (d, J = 7.1 Hz, 1H), 7.23 (d, J = 7.0 Hz, 2H), 7.18 (s, 1H), 5.21 (s, 1H), 4.98 (s, 2H), 4.52 (s, 2H). 13C NMR (101 MHz, DMSO) δ 161.19, 145.61, 137.15, 135.70, 130.94, 128.70, 127.74, 127.64, 120.80, 117.15, 112.21, 62.91, 47.00. HRMS (ESI-ion trap): m/z [M-H] Calcd for C_{15}H_{13}N_2O_2: 253.0983; found: 253.0984.

oxo-2-(prop-2-yn-1-yl)-N-propyl-2, 3-dihydro-1H-indazole-6-carboxamide (16l).
Following general procedure (III) : the substrate 16l was obtained as a yellow solid (17 mg, 22%). Mp: 130-132°C. 1H NMR (400 MHz, DMSO) δ 10.50 (s, 1H), 8.62 (t, J = 5.5 Hz, 1H), 7.72 (d, J = 8.5 Hz, 2H), 7.54 (dd, J = 8.2, 1.1 Hz, 1H), 4.63 (d, J = 2.4 Hz, 2H), 3.36 (t, J = 2.4 Hz, 1H), 3.23 (dd, J = 13.1, 6.7 Hz, 2H), 1.61 – 1.48 (m, 2H), 0.89 (t, J = 7.4 Hz, 3H). 13C NMR (101 MHz, DMSO) δ 165.84, 160.74, 146.59, 138.40, 123.28, 119.89, 118.41, 111.70,
78.45, 75.40, 41.33, 33.52, 22.50, 11.65. HRMS (ESI-ion trap): m/z [M-H]⁻ Calcd for C₁₄H₁₄N₃O₂: 256.1092; found: 256.1091.

2-benzyl-5-chloro-1, 2-dihydro-3H-indazol-3-one (17a). Following general procedure (III): the substrate 17a was obtained as a yellow solid (64 mg, 82%). Mp: 219-221°C. ¹H NMR (400 MHz, DMSO) δ 10.57 (s, 1H), 7.69 (d, J = 2.0 Hz, 1H), 7.52 (dd, J = 8.7, 2.0 Hz, 1H), 7.34 (t, J = 7.1 Hz, 2H), 7.31 – 7.23 (m, 4H), 5.00 (s, 2H). ¹³C NMR (101 MHz, DMSO) δ 159.64, 144.35, 136.78, 131.81, 128.79, 127.82, 125.28, 122.50, 118.20, 114.29, 47.04. LCMS: [M+H]+ M+1 259.10.

2-benzyl-6-bromo-1, 2-dihydro-3H-indazol-3-one (17b). Following general procedure (III): the substrate 17b was obtained as a white solid (71 mg, 78%). Mp: 190-192°C. ¹H NMR (400 MHz, DMSO) δ 10.60 (s, 1H), 7.82 (d, J = 1.8 Hz, 1H), 7.62 (dd, J = 8.7, 1.7 Hz, 1H), 7.34 (t, J = 7.1 Hz, 2H), 7.26 (dt, J = 17.2, 8.0 Hz, 4H), 5.01 (s, 2H). ¹³C NMR (101 MHz, DMSO) δ 159.42, 144.54, 136.78, 134.31, 128.78, 127.80, 125.53, 118.74, 114.62, 112.77, 47.04. HRMS (ESI-ion trap): m/z [M-H]⁻ Calcd for C₁₄H₁₀BrN₂O: 300.9982; found: 300.9987.

2-benzyl-6-chloro-1, 2-dihydro-3H-indazol-3-one (17c). Following general procedure (III): the substrate 17c was obtained as a brown solid (44 mg, 56%). Mp: 185-187°C. ¹H NMR (400 MHz, DMSO) δ 10.60 (s, 1H), 7.69 (d, J = 8.3 Hz, 1H), 7.38 – 7.22 (m, 6H), 7.10 (dd, J = 8.3, 1.4 Hz, 1H), 4.99 (s, 2H). ¹³C NMR (101 MHz, DMSO) δ 159.85, 146.15, 136.63, 136.33, 128.56, 127.59, 124.84, 121.20, 115.58, 111.77, 46.80. LCMS: [M+H]+ M+1 259.13.

6-iodo-2-phenethyl-1, 2-dihydro-3H-indazol-3-one (17d). Following general procedure (III): the substrate 17d was obtained as a brown solid (103 mg, 94%). Mp: 176-178°C. ¹H NMR (500 MHz, DMSO) δ 10.55 (s, 1H), 7.70 (s, 1H), 7.38 (s, 2H), 7.29-7.24 (m, 2H), 7.22-7.16 (m, 3H), 4.00 (t, J = 7.4 Hz, 2H), 2.99 (t, J = 7.4 Hz, 2H). ¹³C NMR (126 MHz, DMSO) δ 159.95, 146.64, 138.43, 129.62, 128.78, 128.58, 126.55, 124.90, 120.71, 116.72, 98.63, 44.55, 33.81. HRMS (ESI-ion trap): m/z [M-H]⁻ Calcd for C₁₆H₁₂IN₃O: 363; found: 362.9997.

6-fluoro-2-phenethyl-1, 2-dihydro-3H-indazol-3-one (17e). Following general procedure (III): the substrate 17e was obtained as a yellow solid (55 mg, 71%). Mp: 179-181°C. ¹H NMR (500 MHz, DMSO) δ 10.62 (s, 1H), 7.65 (dd, J = 8.5, 5.6 Hz, 1H), 7.29-7.16 (m, 5H), 7.14-7.11 (m, 1H), 6.94-6.88 (m, 1H), 4.01 (t, J = 7.4 Hz, 2H), 2.99 (t, J = 7.4 Hz, 2H). ¹³C NMR (126 MHz, DMSO) δ 164.80 (d, J = 245.6 Hz), 160.00, 146.71 (d, J = 13.8 Hz), 138.49, 128.80, 128.60, 126.55, 125.50 (d,
$J = 11.4 \text{ Hz}$), 114.03, 109.61 (d, $J = 25.0 \text{ Hz}$), 98.50 (d, $J = 26.7 \text{ Hz}$), 44.74, 33.85. $^{19}$F NMR (471 MHz, DMSO) $\delta$ -108.61. HRMS (ESI-ion trap): m/z [M-H] Calcd for $C_{15}H_{12}FN_2O$: 255.0939; found: 255.0945.

4-fluoro-2-phenethyl-1, 2-dihydro-3H-indazol-3-one (17f) Following general procedure (III): the substrate 17f was obtained as a yellow solid (52 mg , 68%). Mp: 169-171°C. $^1$H NMR (500 MHz, DMSO) $\delta$ 10.77 (s, 1H), 7.51 – 7.43 (m, 1H), 7.30 – 7.25 (m, 2H), 7.24 – 7.17 (m, 3H), 7.07 (d, $J = 8.2 \text{ Hz}$, 1H), 6.76 (dd, $J = 10.0, 8.0 \text{ Hz}$, 1H), 4.02 – 3.97 (m, 2H), 3.00 (t, $J = 7.4 \text{ Hz}$, 2H). $^{13}$C NMR (126 MHz, DMSO) $\delta$ 159.05, 157.27 (d, $J = 7.1 \text{ Hz}$), 147.62 (d, $J = 8.8 \text{ Hz}$), 128.78, 128.60, 126.57, 112.29,108.27 (d, $J = 4.1 \text{ Hz}$), 105.94 (d, $J = 18.5 \text{ Hz}$), 44.44,33.75. $^{19}$F NMR (471 MHz, DMSO) $\delta$ -119.35. HRMS (ESI-ion trap): m/z [M-H] Calcd for $C_{15}H_{12}FN_2O$: 255.0939; found: 255.0943.

7-chloro-2-cyclopentyl-1, 2-dihydro-3H-indazol-3-one (17g) Following general procedure (III): the substrate 17g was obtained as a red solid (29 mg , 41%). Mp: 149-151°C. $^1$H NMR (400 MHz, DMSO) $\delta$ 10.25 (s, 1H), 7.61 (d, $J = 7.7 \text{ Hz}$, 2H), 7.12 (t, $J = 7.7 \text{ Hz}$, 1H), 4.77 (p, $J = 8.1 \text{ Hz}$, 1H), 1.95-1.86 (m, 4H), 1.85 – 1.74 (m, 2H), 1.65 – 1.54 (m, 2H). $^{13}$C NMR (101 MHz, DMSO) $\delta$ 160.79, 143.37, 131.18, 122.43, 122.01, 120.35, 117.28, 55.04, 29.66, 24.30. HRMS (ESI-ion trap): m/z [M-H] Calcd for $C_{16}H_{12}ClN_2O$: 235.0644; found: 235.0648.

5-fluoro-2-phenethyl-1,2-dihydro-3H-indazol-3-one (17h) Following general procedure (III): the substrate 17h was obtained as a yellow solid (53 mg , 69%). Mp: 162-164°C. $^1$H NMR (500 MHz, DMSO) $\delta$ 10.31 (s, 1H), 7.51-7.31 (m, 3H), 7.30 – 7.16 (m, 5H), 4.02 (t, $J = 7.5 \text{ Hz}$, 2H), 3.00 (t, $J = 7.5 \text{ Hz}$, 2H). $^{13}$C NMR (126 MHz, DMSO) $\delta$ 160.16 (d, $J = 3.7 \text{ Hz}$), 157.52 (d, $J = 237.1 \text{ Hz}$), 142.77, 138.47,128.78, 128.59, 126.55,120.03 (d, $J = 25.7 \text{ Hz}$), 118.11 (d, $J = 9.0 \text{ Hz}$), 114.22 (d, $J = 8.5 \text{ Hz}$), 108.11 (d, $J = 23.6 \text{ Hz}$), 44.72, 33.84. $^{19}$F NMR (471 MHz, DMSO) $\delta$ -119.35. HRMS (ESI-ion trap): m/z [M-H] Calcd for $C_{15}H_{12}FN_2O$: 255.0939; found: 255.0941.

5-iodo-2-phenethyl-1, 2-dihydro-3H-indazol-3-one (17i) Following general procedure (III): the substrate 17i was obtained as a yellow solid (75 mg , 69%). Mp: 177-179°C. $^1$H NMR (500 MHz, DMSO) $\delta$ 10.60 (s, 1H), 7.89 (d, $J = 1.3 \text{ Hz}$, 1H), 7.75 (d, $J = 8.5 \text{ Hz}$, 1H), 7.29 – 7.23 (m, 2H), 7.20 (dd, $J = 8.1, 4.4 \text{ Hz}$, 3H), 7.16 (t, $J = 5.5 \text{ Hz}$, 1H), 4.02 (t, $J = 7.4 \text{ Hz}$, 2H), 2.99 (t, $J = 7.4 \text{ Hz}$, 2H). $^{13}$C NMR (126 MHz, DMSO) $\delta$ 158.80, 144.68, 139.42, 138.40, 131.42, 128.77, 128.59, 126.56, 119.76, 114.69, 83.67, 44.58, 33.81. HRMS (ESI-ion trap): m/z [M-H] Calcd for $C_{15}H_{12}I_2N_2O$: 363; found: 363.0003.
5-chloro-2-phenethyl-1, 2-dihydro-3H-indazol-3-one (17j). Following general procedure (Ⅲ): the substrate 17j was obtained as a brown solid (71 mg, 87%). Mp: 158-160°C. 1H NMR (400 MHz, DMSO) δ 10.58 (s, 1H), 7.61 (d, J = 1.8 Hz, 1H), 7.51 (dd, J = 8.7, 2.1 Hz, 1H), 7.33 (dd, J = 8.7 Hz, 1H), 7.30 – 7.24 (m, 2H), 7.23 – 7.16 (m, 3H), 4.03 (t, J = 7.4 Hz, 2H), 3.00 (t, J = 7.4 Hz, 2H). 13C NMR (101 MHz, DMSO) δ 159.12, 143.99, 138.20, 131.39, 128.56, 128.38, 126.36, 124.99, 122.16, 118.34, 113.94, 44.45, 33.61. LCMS: [M+H]+ 273.16

5-chloro-2-heptyl-1, 2-dihydro-3H-indazol-3-one (17k). Following general procedure (Ⅲ): the substrate 17k was obtained as a yellow solid (79 mg, 99%). Mp: 102-105°C. 1H NMR (400 MHz, DMSO) δ 10.48 (s, 1H), 7.63 (d, J = 1.9 Hz, 1H), 7.50 (dd, J = 8.7 Hz, 1H), 3.78 (t, J = 7.0 Hz, 2H), 1.73 – 1.60 (m, 2H), 1.29 – 1.20 (m, 8H), 0.83 (t, J = 6.8 Hz, 3H). 13C NMR (101 MHz, DMSO) δ 159.30, 144.09, 131.41, 125.10, 122.29, 118.52, 114.06, 43.28, 31.27, 28.32, 27.86, 26.13, 22.16, 14.05. HRMS (ESI-ion trap): m/z [M-H] Calcd for C14H18ClN2O: 265.1113; found: 265.112.

2-(tert-butyl)-5-chloro-1, 2-dihydro-3H-indazol-3-one (17l). Following general procedure (Ⅲ): the substrate 17l was obtained as a brown solid (43 mg, 64%). Mp: 178-180°C. 1H NMR (400 MHz, DMSO) δ 9.89 (s, 1H), 7.57 (d, J = 1.9 Hz, 1H), 7.51 (dd, J = 8.7, 2.1 Hz, 1H), 7.27 (d, J = 8.7 Hz, 1H), 1.53 (s, 9H). 13C NMR (101 MHz, DMSO) δ 161.12, 144.76, 131.55, 125.26, 122.02, 118.91, 114.55, 57.91, 27.34. HRMS (ESI-ion trap): m/z [M-H] Calcd for C11H12ClN2O: 223.0644; found: 223.0644.

5-chloro-2-cyclopentyl-1, 2-dihydro-3H-indazol-3-one (17m). Following general procedure (Ⅲ): the substrate 17m was obtained as a gray solid (43 mg, 61%). Mp: 176-178°C. 1H NMR (400 MHz, DMSO) δ 10.20 (s, 1H), 7.62 (d, J = 1.9 Hz, 1H), 7.51 (d, J = 8.6 Hz, 1H), 7.29 (d, J = 8.7 Hz, 1H), 4.84 – 4.73 (m, 1H), 2.00 – 1.88 (m, 2H), 1.85-1.71(m, 4H), 1.67-1.53 (m, 2H). 13C NMR (101 MHz, DMSO) δ 159.75, 144.76, 131.55, 125.26, 122.02, 120.43, 114.55, 57.91, 27.34. HRMS (ESI-ion trap): m/z [M-H] Calcd for C12H12ClN2O: 235.0644; found: 235.065.

5-bromo-2-cyclopentyl-1, 2-dihydro-3H-indazol-3-one (17n). Following general procedure (Ⅲ): the substrate 17n was obtained as a brown solid(61 mg, 72%). Mp: 175-177°C. 1H NMR (400 MHz, DMSO) δ 10.25 (s, 1H), 7.75 (d, J = 1.7 Hz, 1H), 7.62 (dd, J = 8.7, 1.9 Hz, 1H), 7.24 (d, J = 8.7 Hz, 1H), 4.84 – 4.73 (m, 1H), 1.97 – 1.89 (m, 2H), 1.84-1.69 (m, 4H), 1.65-1.54(m, 2H). 13C NMR (126 MHz, DMSO) δ 159.44, 144.85, 134.07,
125.27, 119.43, 114.79, 112.79, 54.41, 30.02, 24.39. HRMS (ESI-ion trap): m/z [M-H] Calcd for C_{12}H_{13}BrN_{2}O: 279.0138; found: 279.0142

**5-chloro-2-(4-ethoxyphenyl)-1, 2-dihydro-3H-indazol-3-one (17o).**

Following general procedure (III): the substrate 17o was obtained as a yellow solid (38 mg, 44%). Mp: 139-141 °C. 1H NMR (400 MHz, DMSO) δ 8.12 (s, 1H), 7.78 (s, 1H), 7.67 (d, J = 8.8 Hz, 2H), 7.59 (d, J = 9.3 Hz, 1H), 7.23 (d, J = 9.1 Hz, 1H), 7.14 (d, J = 8.9 Hz, 2H), 4.13 (q, J = 7.0 Hz, 2H), 1.37 (t, J = 7.0 Hz, 3H). 13C NMR (126 MHz, DMSO) δ 159.89, 128.54, 128.23, 127.63, 126.68, 126.76, 120.25, 115.96, 115.45, 115.20, 110.90, 64.20, 14.92. HRMS (ESI-ion trap): m/z [M-H] Calcd for C_{15}H_{12}ClN_{2}O_{2}: 287.0593; found: 287.0594

**The product yield of indazolones with different methods**

| Method | Yield | Reference |
|--------|-------|-----------|
| This work | 41-99% | |  

Figure S1. The product yield of indazolones with different methods

**Proposed reaction mechanism**

Previous research reported that o-nitrobenzyl alcohol derivatives generated corresponding aryl-nitroso compounds via photoisomerization, upon UV light-activation (for details, please see references, *J. Am. Chem. Soc.* 2004, 126, 4581; *Chem. Rev.*, 2013, 113, 119; *Chem. Commun.*, 2011, 47, 3822).[[14-16]]

The photogenerated intermediate is reactive and not very stable for subsequent isolation. We could detect the aryl-nitroso compound (exact mass 220.08) with UPLC-MS analysis as follows:
This date can support our proposed mechanism that the intermediate aryl-nitroso compound *in situ* generated from o-nitrobenzyl alcohol upon UV light-activation. In the presence of primary amines, the aryl-nitroso compound can rapidly form indazolones via cyclization in suitable reaction conditions, subsequent for dehydration and tautomerization (Ref, *J. Org. Chem.*, 2005, 70, 1060-1062). We have proposed the reaction mechanism combining this date and previous references.[17-18]

**Proposed Reaction Mechanism**

Figure S3. Proposed reaction mechanism
References
1. C. Kong, N. Jana, T. G. Driver, Org. Lett. 2013, 15, 824-827.
2. Tabomedex Biosciences, LLC; McComas, Casey C.; Serrano-Wu, Michael H.; Vacca, Joseph
   P. US2017/190713, 2017, A1
3. A. Laura, et al, J. Org. Chem., 2011, 76, 3484–3497.
4. T. Kataoka, et al, Bioorg. Med. Chem., 2004, 12, 2397-2407.
5. A. Thomas, et al, J. Med. Chem., 2004, 47, 3934–3937.
6. D. C. Laurène, J. Med. Chem., 2018, 61, 18, 8402–8416.
7. Z. Li, et al, J. Med. Chem., 2016, 59, 10577–10585.
8. N. W. Polaske, et al, Org. Lett., 2010, 12, 4944–4947.
9. Hoffmann-La Roche Inc.US5753679, 1998.
10. I. Aujard, et al, Chem.Eur. J., 2006, 12, 6865-6879.
11. A. Eisenführ, et al, Bioorg. Med. Chem., 2003, 11, 235-249.
12. E. Tse, et al, Archiv der Pharmazie, 1996, 329, 35–40.
13. J. S. Zhu, et al, J. Org. Chem. 2018, 83, 15493-15498
14. J. P. Lai, et al, Chem. Commun., 2011, 47, 3822.
15. P. Klan, et al, Chem. Rev., 2013, 113, 119.
16. Y. V. Il'ichev, et al, J. Am. Chem. Soc. 2004, 126, 4581.
17. M. J. Kurth, et al, J. Org. Chem., 2005, 70, 1060.
18. J. S. Zhu, et al, Org. Lett., 2018, 20, 4736.
3. 1H, 13C NMR and 19F NMR spectra
16c

16c
