A General and Efficient Approach to 2*H*-Indazoles and 1*H*-Pyrazoles Through Copper-catalyzed Intramolecular N-N Bond Formation under Mild Conditions

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Support Information 1

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General Information.

^{1}H NMR and ^{13}C NMR spectra were recorded at ambient temperature using 600 MHz, 400 MHz or 300 MHz spectrometers. The data are reported as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. High resolution mass spectra were were obtained by peak matching. Analytical thin layer chromatography was performed on 0.25 mm extra hard silica gel plates with UV254 fluorescent indicator. Liquid chromatography was performed using forced flow (flash chromatography) of the indicated solvent system on 100-200 Å (40 – 60 μm) mesh silica gel (SiO_2). All reactions were carried out under an atmosphere of argon in glassware, which had been oven-dried. Unless otherwise noted, all reagents were commercially obtained from Aladdin, Alfa-Asea and Beijing Ouhe company and used directly without further purification. CH_2Cl_2, MeCN, THF, Methanol, EtOH, Toluene, 1,4-Dioxane were dried according to the procedure described in the fifth edition of <Purafication of Laboratory Chemicals > by W.L.F. Armarego & C.L.L. Chai.[1] Metal salts were stored in a dry box filled with silica gel.

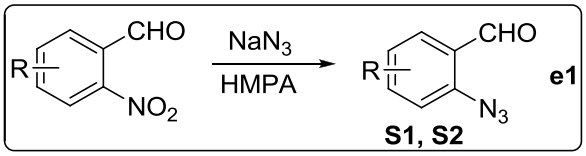
Experimental Procedure

I Preparation of 2-Azidobenzaldehyde and 2-Azidobenzketone

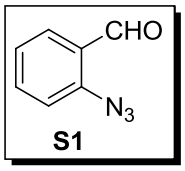
Procedure A:

Nucleophilic Aromatic Substitution of 2-Nitrobenzaldehyde with Sodium Azide

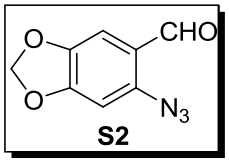
The requisite *ortho*-azidobenzaldehydes could be synthesized from the corresponding commercially available *ortho*-nitrobenzaldehydes with sodium azide in HMPA following the procedure reported by Spagnolo and coworkers (eq. **e1**).[2] Yields were not optimized.



To a stirring solution of 2-nitrobenzaldehyde (1.0 equiv) in HMPA was added sodium azide (2.0 equiv). The reaction mixture was stirred at ambident temperature and monitored by TLC. Once the starting material had disappeared, the mixture was diluted with ice-cold water and extracted with diethyl ether (×2). The ether layer was washed with water(×2), brine (×1). The organic layer was dried over Na_2SO_4, filtered and concentrated to give the crude product, which was further puried by column chromatography to give the final analytically pure product.



***ortho*-Azidobenzaldehyde S1.** The general procedure A was followed using 5.1 g of commercially available 2-nitrobenzaldehyde (33 mmol), 4.3 g of sodium azide (66 mmol), and 15 mL of HMPA. Purification by column chromatography with hexanes:EtOAc/30:1 afforded the final analytically pure **S1** as a slightly yellow solid (4.0 g, 83%). For the characterizeation (^{1}H NMR and ^{13}C NMR) of **S1** see: Tom G. Driver*, *J. Am. Chem. Soc*. **2011**, *133*, 4702.[3]

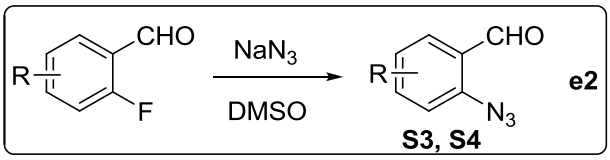


***ortho*-Azidobenzaldehyde S2.** The general procedure A was followed using 5.1 g of commercially available 6-nitropiperonal (10 mmol), 1.3 g of sodium azide (20 mmol), and 10.0 mL of HMPA. Purification by column chromatography with hexanes:EtOAc/20:1 afforded the final analytically pure **S2** as a yellow powder (1.4 g, 70%). For the characterizeation (^{1}H NMR and ^{13}C NMR) of **S2** see: Tom G. Driver*, *J. Am. Chem. Soc*. **2011**, *133*, 4702.[3]

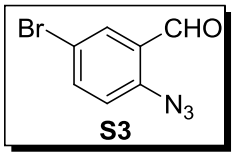
Procedure B:

Nucleophilic Aromatic Substitution of 2-Fluorobenzaldehyde with Sodium Azide

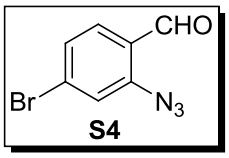
The requisite *ortho*-azidobenzaldehydes could be synthesized from the corresponding commercially available *ortho*-fluorobenzaldehydes with sodium azide in DMSO following the procedure reported by C. A. Main and coworkers (eq. **e2**).[4] Yields were not optimized.



Sodium azide (2.0 equiv) was added to a stirring solution of *ortho*-fluorobenzaldehydes (1.0 equiv) in DMSO under argon. The reaction mixture was stirred at 50 ℃ for 5-6 h and then poured into ice-cold water and acidified with drops of concentrated HCl. It was then extracted with DCM(×2), washed with water(×2), brine(×1). The organic layer was dried over Na_2SO_4, filtered and concentrated to give the crude product, which was further puried by column chromatography with hexanes/EtOAc to give the final analytically pure product.



***ortho*-Azidobenzaldehyde S3.** The general procedure B was followed using 9.94 g of commercially available 5-bromo-2-fluorobenzaldehyde (49.0 mmol), 6.37 g of sodium azide (98.0 mmol), and 25 mL of DMSO. Purification by column chromatography with hexanes:EtOAc/50:1 afforded the final analytically pure **S3** as a slightly yellow solid (9.08 g. 82%).

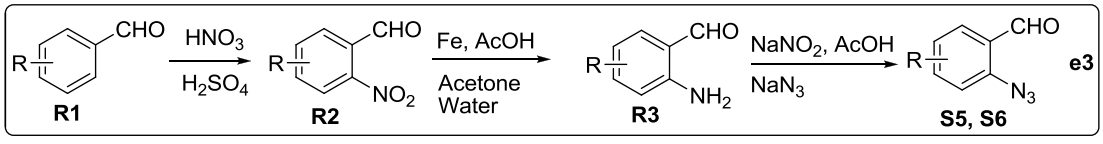


***ortho*-Azidobenzaldehyde S4.** The general procedure B was followed using 1.02 g of commercially available 4-bromo-2-fluorobenzaldehyde (5.0 mmol), 650 mg of sodium azide (10.0 mmol), and 7.0 mL of DMSO. Purification by column chromatography with hexanes:EtOAc/60:1 afforded the final analytically pure **S4** as an white solid (791 mg, 70%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 10.26 (s, 1H), 7.72 (d, *J* = 8.25 Hz, 1H), 7.40 (d, *J* = 1.38 Hz, 1H), 7.35 (d, *J* = 8.25 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 187.5 (CH), 144.0 (C), 130.2 (CH), 128.5 (CH), 125.8 (C), 122.2 (CH); MS (ESI): m / z calculated for C_7H_5BrNO $(M - N_2 + H)^+$: 197.96, found: 197.73.

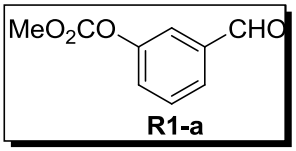
Procedure C:

Nitrification of Aromatic Aldehydes, Followed with Reduction and Diazotization, further Substitution with Sodium Azide

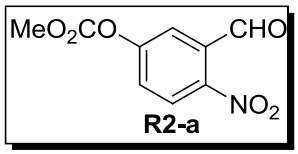
General synthetic route to *ortho*-azidobenzaldehyde from substituted aromatic aldehyde (eq. **e3**)



Preparation of R1-a



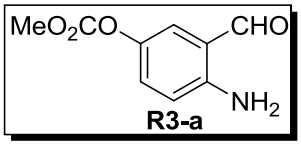
R1-a was prepared following the procedure reported by Cava and co-workers.[5] A simple procedure was below: To a ice-cold solution of commercially available 3-hydrobenzaldehyde (1.22 g, 10.0 mmol, 1.0 equiv) in 10.0 mL pyridine was dropwised methyl chloroformate (1.5 mL, 20.0 mmol, 2.0 equiv) over a period of 10min. The resulting mixture was stirred at 0 ℃ for 0.5 h, then warmed to ambient temperature to stir for 0.5 h. The solvent was evaporated and diluted with water, extracted with diethyl ether (×2). The ether layer was washed with 5%NaOH solution (×1) , water (×1) and brine (×1). The organic layer was dried over Na_2SO_4, filtered and concentrated to afford the crude product. Further purification with hexanes:EtOAc/8:1 afforded the analytically pure product **R1-a** as an white solid(1.57 g, 87%).



R2-a

Preparation of R2-a

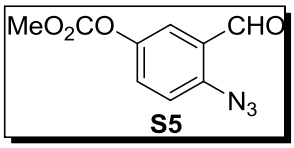
R2-a was prepared following the procedure reported by Cava and co-workers.[5] A simple procedure was below: To a ice-cold solution of **R1-a** (1.57 g, 7.0 mmol, 1.0 equiv) in concentrated sulfuric acid (7.0 mL) was dropwised a solution of fuming nitric acid (0.88 mL, 21.0 mmol, 3.0 equiv) in 3.0 mL of concentrated acid. The resulting mixture was stirred at 0℃ for 1h. Water was added slowly and the mixture was extracted with dichloromethane (×2), the organic layer was washed with saturated Na_2CO_3 solution (×2) and brine (×1). The organic layer was dried over Na_2SO_4, filtered and concentrated to afford the crude product. Further purification with hexanes:EtOAc/7:1 afforded the analytically pure product **R2-a** as an white solid (1.01 g, 64%).



R3-a

Preparation of R3-a

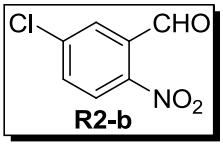
Follow the procedure reported by Tom. G. Driver and coworkers.[6] The detailed procedure was below: To a solution of 800mg of **R2-a** (3.5 mmol) in 3.0 mL of acetone was added 3.0 mL of glacial acetic acid, 3.0 mL of water and 2.3 g of iron powder (21.0mmol, 6.0 equiv). The mixture was heated to reflux. After 8 h, the reaction mixture was cooled and filtered through a pad of Celite. The filtrate was concentrate ed in vacuo. The residue was diluted with water and extracted with dichloromethane (×2). The DCM layer was washed with brine (×1), filtered and concentrated to afford the crude product, which was puried by column chromatography with hexanes:EtOAc/10:1 to afford **R3-a** as a slightly yellow solid(198 mg, 30%).



S5

***ortho*-Azidobenzaldehyde S5.** The general procedure D was followed using 198 mg of **R3-a** (1.04 mmol), 108 mg of sodium nitrite (1.56 mmol), and 102 mg of sodium azide (1.56 mmol) in 3.0 mL of H_2O and 3.0mL of AcOH. Purification by column chromatography with hexanes:EtOAc/30:1 afforded the final analytically pure **S5** as an white solid (196 mg, 85%). ^1H NMR ($CDCl_3$, 300 MHz): δ (ppm) 10.23 (s, 1H), 7.61 (d, J = 2.76 Hz, 1H), 7.37 (dd, J = 2.73 Hz,

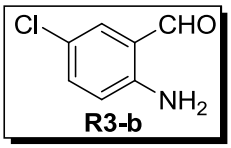
8.58 Hz, 1H), 7.22 (d, *J* = 8.91 Hz, 1H), 3.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 187.5 (CH), 154.0 (C), 148.1 (C), 140.6 (C), 128.3 (CH), 127.7 (C), 121.2 (CH), 120.4 (CH), 55.8 (CH_3); MS (ESI): m / z calculated for $C_9H_8NO_4$ $(M - N_2 + H)^+$: 194.05, found: 193.87



R2-b

Preparation of R2-b

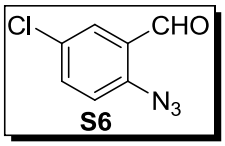
R2-b was prepared following the procedure reported by L. C. Clark. Jr and coworkers.[7] Detailed procedure was below: To a cold solution of KNO_3 (1.21 g, 12 mmol, 1.2 equiv) in 8.0 mL of concentrated H_2SO_4 was dropwised commercially available 3-chlorobenzaldehyde (1.13 mL, 10 mmol, 1.0 equiv).The resulting mixture was stirred at 0 ℃ overnight. Then the mixture was poured into ice-cooled water, and extracted with dichloromethane (×2), the organic layer was washed with brine (×1), dried over Na_2SO_4, filtered and concentrated to afford the crude product, which was further puried by column chromatography with hexanes:EtOAc/20:1 to afford the product **R2-b** as an white solid (1.6 g, 86%).



R3-b

Preparation of R3-b

R3-b was prepared following the procedure of the preparation of **R3-a** using 1.52 g of **R2-b** (8.19 mmol), 3.0 mL of AcOH, 3.0 mL of water, and 20.0 mL of acetone, and 2.75 g of iron powder (49.2 mmol). Purification by column chromatography with hexanes:EtOAc/10:1 afforded the product R3-b as a yellow solid (714 mg, 56%).



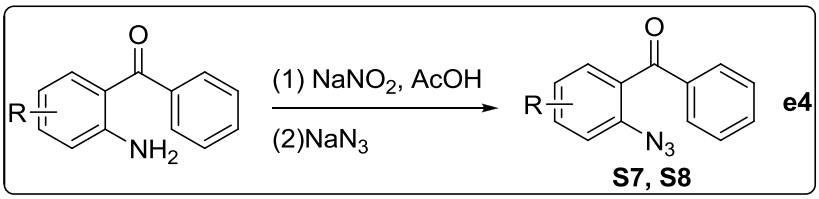
S6

***ortho*-Azidobenzaldehyde S6.** The general procedure D was followed using 714 mg of **R3-b** (4.6 mmol), 476 mg of sodium nitrite (6.9 mmol), and 449 mg of sodium azide (6.9 mmol) in 3.0 mL of H_2O and 3.0 mL of AcOH. Purification by column chromatography with hexanes:EtOAc/20:1 afforded the final analytically pure **S6** as a slightly yellow solid (668 mg, 80%).

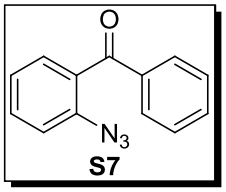
Procedure D:

Diazotization and Further Substitution with Sodium Azide

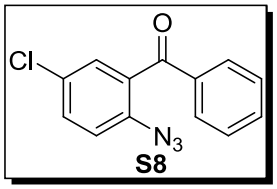
Unless otherwise noted, the requisite azides were prepared in one step from substituted 2-aminobenzophenones following the procedure reported by Driver. T. G. and co-workers (eq. **e4**)[6,8]. The yields were not optimized.



To a cold solution of substituted 2-aminobenzophenone (10.0 mmol, 1.0 equiv) in 10 mL of acetic acid and 10 mL of water was added sodium nitrite (1.04 g, 15.0 mmol, 1.5 equiv). After stirring for 1 hour, sodium azide (0.975 g, 15.0 mmol, 1.5 equiv) was added slowly into the stirring mixture, and the mixture was allowed to warm to ambient temperature. After an additional hour of stirring, the resulting mixture was neutralized with a saturated aqueous solution of Na_2CO_3 and extracted with dichloromethane (×2). The resulting organic phase was dried over Na_2SO_4, filtered and concentrated to give the crude product. Purification by column chromatography afforded the final analytically pure product.



***ortho*-Azidoketone S7.** The general procedure D was followed using 1.97 g of commercially available 2-aminobenzophenone (10.0 mmol), 1.04 g of sodium nitrite (15.0 mmol), and 0.975 g of sodium azide (15.0 mmol) in 10.0 mL of H_2O and 10.0 mL of AcOH. Purification by column chromatography with hexanes:EtOAc/70:1 afforded the final analytically pure **S7** as a yellow oil (1.81g, 81%). For the characterizeation (^{1}H NMR) of **S7** see: Tom G. Driver*, *Org Lett*, **2010**, *12*, 2884-2887.

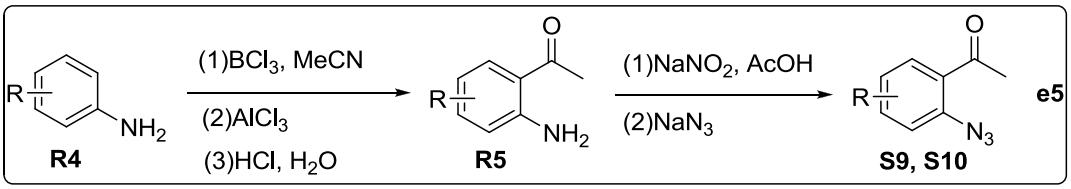


***ortho*-Azidoketone S8.** The general procedure D was followed using 2.32 g of commercially available 2-amino-5-chlorobenzophenone (10.0 mmol), 1.04 g of sodium nitrite (15.0 mmol), and 0.975 g of sodium azide (15.0 mmol) in 10.0 mL of H_2O and 10.0 mL of AcOH. Purification by column chromatography with hexanes:EtOAc/70:1 afforded the final analytically pure **S8** as a yellow oil (2.44 g, 95%). For the characterizeation (^{1}H NMR) of **S8** see: Tom G. Driver*, *Org Lett*, **2010**, *12*, 2884-2887.

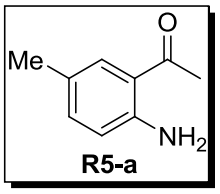
Procedure E:

Acetylation of the *para*-substituted Aromatic Aniline, then Diazotization and Further Substitution with Sodium Azide

General synthetic route to *ortho*-azidoacetophenone from substituted aromatic aniline (eq. **e5**)

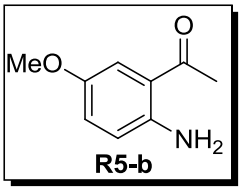


The synthesis of R5 followed the procedure reported by J. Nilsson and coworkers (**e5**).[9] The yields were not optimized. Detailed procedures were below: To a cold solution of *para*-substituted aniline **R4** (3.0 mmol, 1.0 equiv) in 5.0mL of toluene was added 3.3 mL of a 1M solution of boron trichloride (3.3 mmol, 1.1 equiv) in heptane. To the mixture was added $AlCl_3$ (480 mg, 3.6 mmol, 1.2 equiv) and acetonitrile (1.25 mL, 24.0 mmol, 8.0 equiv) and the mixture was heated to reflux for 2 h under argon. The reaction mixture was cooled to room temperature and 4.0 mL of an aqueous solution of 1M hydrochloric acid was added. The mixture was heated to 80℃ to stir for 0.5 h and then was poured into ice water. Then aqueous 5M solution of sodium hydroxide was added to attain pH > 13 and the mixture was extracted with EtOAc (×2). The combined organic layers were washed with brine (×1) and dried over Na_2SO_4, filtered and concentrated. Purification by column chromatography with hexanes:EtOAc afforded the final product **R5**.



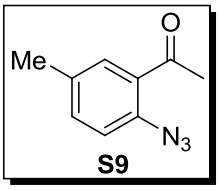
Preparation of R5-a

The general procedure E was followed using 321 mg of commercially available 4-methylanline (3.0 mmol), 1.25 mL of acetonitrile (24.0 mmol), 3.3 mL of 1M solution of boron trichloride (3.3 mmol), 480 mg of $AlCl_3$ (3.6 mmol), and 5.0mL of toluene. Purification by column chromatography with hexanes:EtOAc/10:1 afforded the final analytically pure **R5-a** as a yellow oil (215 mg, 48%).



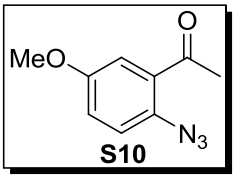
Preparation of R5-b

The general procedure E was followed using 369 mg of commercially available 4-methoxylanline (3.0 mmol), 1.25 mL of acetonitrile (24.0 mmol), 3.3mL of 1M solution of boron trichloride (3.3 mmol), 480 mg of $AlCl_3$ (3.6 mmol), and 5.0 mL of toluene. Purification by column chromatography with hexanes:EtOAc/10:1 afforded the final analytically pure **R5-a** as a yellow oil (149 mg, 30%).



S9

***ortho*-Azidoketone S9.** The general procedure followed the procedure D using 149 mg of **R5-a** (1.0 mmol), 104 mg of sodium nitrite (1.5 mmol), and 98mg of sodium azide (1.5 mmol) in 2.0 mL of H_2O and 2.0 mL of AcOH. Purification by column chromatography with hexanes:EtOAc/20:1 afforded the final analytically pure **S9** as a yellow oil (142 mg, 81%).



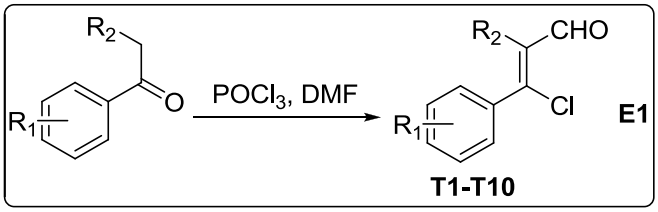
S10

***ortho*-Azidoketone S10.** The general procedure followed the procedure D using 165 mg of **R5-b** (1.0 mmol), 104 mg of sodium nitrite (1.5 mmol), and 98 mg of sodium azide (1.5 mmol) in 2.0 mL of H_2O and 2.0 mL of AcOH. Purification by column chromatography with hexanes:EtOAc/20:1 afforded the final analytically pure **S10** as a yellow oil (156 mg, 81%).

II Preparation of 3-Chloro-2-Alkenals

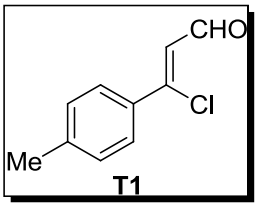
A. General Procedure for the Preparation 3-Chloro-2-Alkenals

Unless otherwise noted, 3-chloro-2-alkenals were synthesized from the corresponding arylketone following the procedure reported by R.Romagnoli and co-workers (eq. **E1**).[10] Yields were not optimized.

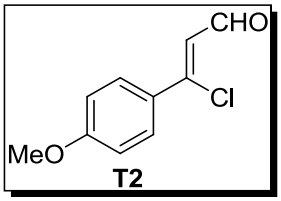


A flame-dried round bottom flask containing a stir bar and DMF (7.0 mL) was cooled to 0 ℃ and $POCl_3$ (3.0 mL, 32.0 mmol, 4.0 equiv) was added dropwise while stirring. The mixture was warmed to ambient temperature to stir for 30 minutes, then cooled to 0 ℃ before the slow addition of the appropriate acetophenone derivative (8.0 mmol, 1.0 equiv). The reaction mixture was stirred for 1h at 0 ℃, then heat to 65 ℃ to stir for 5h, then cooled to ambient temperature and finally poured in a ice-cold saturated $NaHCO_3$ solution. Once neutralized, the mixture was extracted with dichloromethane and washed with water (×2) and brine (×1). The organic phase was dried over Na_2SO_4, filtered, and concentrated to afford the crude product. Further purification by column chromatography with hexanes/EtOAc afforded the final analytically pure product.

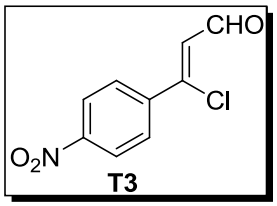
B. 3-Chloro-2-alkenal synthesis



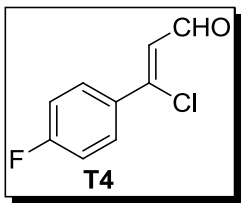
Chloroalkenal T1. The general procedure was followed using 1.07 mL of 4-methylacetophenone (8.0 mmol)，3.0 mL of $POCl_3$ (32.0 mmol), and 7.0 ml of DMF. Purification by column chromatography with Hexanes:EtOAc/20:1 afforded **T1** as a slightly yellow oil (1.04 g, 72%). For the characterizeation (^{1}H NMR) of **T1** see: Ali, M. M.; Okuro, K.; Hattori, A.; Nomura, M. *J. Chem. Soc., Perkin Trans. 1* **1989**, *73*.



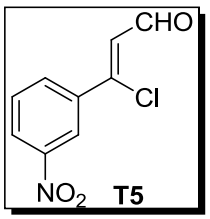
Chloroalkenal T2. The general procedure was followed using 1.2 g of 4-methoxylacetophenone (8.0 mmol)，3.0 mL of $POCl_3$ (32.0 mmol), and 7.0 ml of DMF. Purification by column chromatography with Hexanes:EtOAc/10:1 afforded **T2** as a yellow oil (1.1 g, 70%). For the characterizeation (^{1}H NMR) of **T2** see: R. Romagnoli et al. *Bioorg. Med. Chem*. **2008**. *16*. 5367–5376.



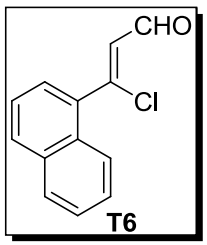
Chloroalkenal T3. The general procedure was followed using 0.83 g of 4-nitroacetophenone (5.0 mmol)，1.86 mL of $POCl_3$ (20.0 mmol), and 5.0 ml of DMF. Purification by column chromatography with Hexanes:EtOAc/10:1 afforded **T3** as a yellow solid (0.67 g, 63%). For the characterizeation (^{1}H NMR) of **T3** see: Rappoport, Z.; Gazit, A. *J. Org. Chem*. **1986**, *51*, 4112.



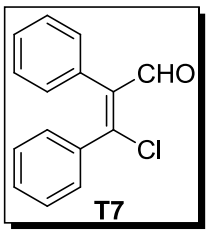
Chloroalkenal T4. The general procedure was followed using 0.97 mL of 4-fluoroacetophenone (8.0 mmol)，3.0 mL of $POCl_3$ (32.0 mmol), and 7.0 ml of DMF. Purification by column chromatography with Hexanes:EtOAc/20:1-15:1 afforded **T4** as a slightly yellow solid (0.75 g, 51%). For the characterizeation (^{1}H NMR) of **T4** see: R. Romagnoli et al. *Bioorg. Med. Chem*. **2008**. *16*. 5367–5376.



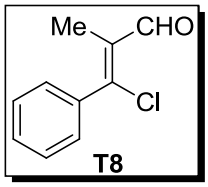
Chloroalkenal T5. The general procedure was followed using 0.5 g of 3-nitroacetophenone (3.0 mmol)，1.1 mL of $POCl_3$ (12.0 mmol), and 3.0 ml of DMF. Purification by column chromatography with Hexanes:EtOAc/15:1 afforded **T5** as a slightly yellow solid (0.33 g, 52%). For the characterizeation (^{1}H NMR) of **T5** see: R. Romagnoli et al. *Bioorg. Med. Chem*. **2008**. *16*. 5367–5376.



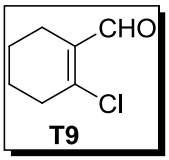
Chloroalkenal T6. The general procedure was followed using 0.6 ml of 1-acetylnaphthalene (4.0 mmol)，1.5 mL of $POCl_3$ (16.0 mmol), and 3.0 ml of DMF. Purification by column chromatography with Hexanes:EtOAc/30:1 afforded **T6** as a yellow oil (0.61 g, 70%). For the characterizeation (^{1}H NMR) of **T6** see: A.L. LaFrate et al. *Bioorg. Med. Chem*. **2008**. *16*. 10075-10084.



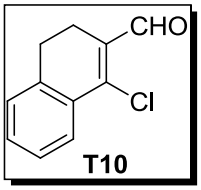
Chloroalkenal T7. The general procedure was followed using 0.6 g of phenylacetophenone (3.0 mmol), 1.1 mL of $POCl_3$ (12.0 mmol), and 3.0 ml of DMF. Purification by column chromatography with Hexanes:EtOAc/20:1 afforded **T7** as an white solid (0.66 g, 90%). For the characterizeation (^{1}H NMR) of **T7** see: M. Scholz et al. *European Journal of Medicinal Chemistry* **2008**. *43*. 1152-1159.



Chloroalkenal T8. The general procedure was followed using 0.53 mL of ethyl phenyl ketone (4.0 mmol), 1.5 mL of $POCl_3$ (16.0 mmol), and 3.5 ml of DMF. Purification by column chromatography with Hexanes:EtOAc/20:1 afforded **T8** as a slightly yellow oil (0.6 g, 83%). For the characterizeation (^{1}H NMR) of **T8** see: G. Fronza, C. Fuganti, S. Serra et al. *Eur. J. Org. Chem.* **2009**, 6160-6171.



Chloroalkenal T9. The general procedure was followed using 1.04 mL of cyclohexanone (10.0 mmol), 1.9 mL of $POCl_3$ (20.0 mmol), and 4.0 ml of DMF. Purification by column chromatography with Hexanes:EtOAc/15:1 afforded **T9** as a clear colorless oil (1.2 g, 80%). (**Caution**: the reaction should be carried at room temperature for the product is volatile.) For the characterizeation (^{1}H NMR) of **T9** see: Tom G. Driver*, *Org Lett*, **2010**. *12*. 2884-2887.

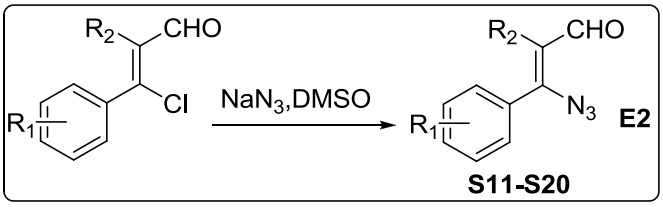


Chloroalkenal T10. The general procedure was followed using 1.33 mL of α-tetralone(10.0 mmol), 1.9 mL of $POCl_3$ (20.0 mmol), and 4.0 ml of DMF. Purification by column chromatography with Hexanes:EtOAc/20:1 afforded **T10** as a slightly yellow oil (1.4 g, 73%). (**Caution**: the reaction should be carried at room temperature for the product is volatile.) For the characterizeation (^{1}H NMR) of **T10** see: Tom G. Driver*, *Org Lett*, **2010**, *12*, 2884-2887.

III Preparation of 3-Azido-2-Alkenals

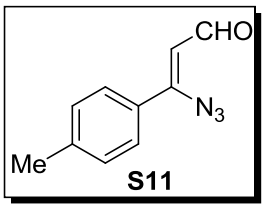
A. General Procedure for the Preparation 3-Azido-2-Alkenals

Unless otherwise noted, 3-azido-2-alkenals were synthesized from the corresponding substituted 3-chloro-2-alkenals using nucleophilic substitution with sodium azide following the procedure reported by Tom. G. Driver* and co-workers (eq. **E2**).[8] Yields were not optimized.

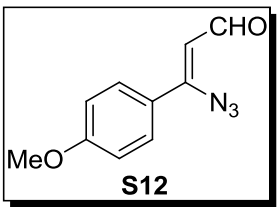


To a solution of 3-chloro-2-propenal (2.0 mmol, 1.0 equiv) in 3.0mL of DMSO was added NaN_3 (2.4 mmol, 1.2 equiv). The mixture was stirred at ambient temperature with aluminum foil wrapped to avoid light and was monitored by TLC. Once the starting material disappeared, the reaction mixture was diluted with water (30.0 mL) and extracted with dichloromethane(10 mL×2). The DCM layer was washed with water (10 mL×2), brine (20 mL×1). The organic layer was dried over Na_2SO_4, filtered and concentrated to afford the crude product. Rapid purification by column chromatography with hexanes/EtOAc/(1%v)Et_3N to afford the final analytically pure product. (**Caution:** these azides are unstable to silica gel and volatile when open to air).

B. 3-Azido-2-Alkenal Synthesis

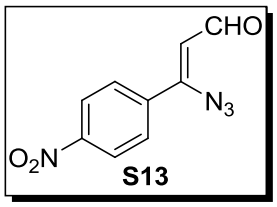


Azidoaldehyde S11. The general procedure was followed using 90 mg of chloroalkenal **T1** (0.50 mmol), 39 mg of NaN_3 (0.6 mmol) and 2.0 mL of DMSO. Purification by column chromatography with hexanes:EtOAc/15:1(1%v Et_3N) to give **S11** as a yellow oil (65 mg, 69%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 8.89 (d, *J* = 6.69 Hz, 1H), 7.75 (d, *J* = 7.23 Hz, 2H), 7.38 (d, *J* = 7.89 Hz, 2H), 2.79 (d, *J* = 6.69 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 200.3 (CH), 159.0 (C), 145.8 (C), 130.7 (CH), 130.4 (CH), 119.9 (C), 39.0 (CH), 22.1 (CH_3); MS (ESI): m / z calculated for $C_{10}H_{10}NO$ $(M - N_2 + H)^+$: 160.08, found: 159.96.

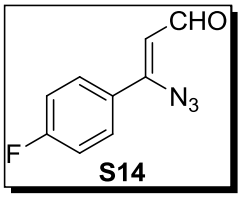


Azidoaldehyde S12. The general procedure was followed using 396 mg of chloroalkenal **T2** (2.0 mmol), 157 mg of NaN_3 (2.4 mmol) and 4.0 mL of DMSO. Purification by column chromatography with hexanes:EtOAc/10:1(1%v Et_3N) to give **S12** as a slightly yellow oil (172 mg, 42%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 8.91 (d, *J* = 6.51 Hz, 1H), 7.85 (m, 2H), 7.38 (m, 2H), 3.92 (s, 1H), 2.82 (d, *J* = 6.87 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 200.6 (CH),

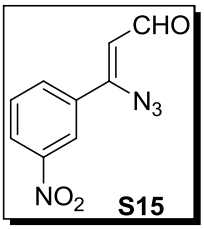
164.6 (C), 158.0 (C), 132.8 (CH), 115.2 (CH), 114.9 (C), 55.8 (CH_3), 39.1 (CH); MS (ESI): m / z calculated for $C_{10}H_{10}NO_2$ $(M - N_2 + H)^+$: 176.07, found: 175.95.



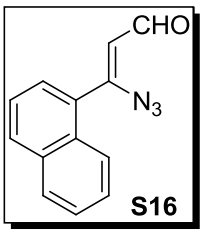
Azidoaldehyde S13. The general procedure was followed using 155 mg of chloroalkenal **T3** (0.73 mmol), 57 mg of NaN_3 (0.88 mmol) and 3.0 mL of DMSO. Purification by column chromatography with hexanes:EtOAc/10:1(1%v Et_3N) to give **S13** as a slightly yellow oil (122 mg, 76%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 9.10 (d, *J* = 5.82 Hz, 1H), 8.47 (m, 2H), 8.14 (m, 2H), 3.05 (d, *J* = 5.82 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 198.8 (CH), 159.2 (C), 151.1 (C), 131.6 (CH), 128.0 (C), 124.8 (CH), 39.2 (CH); MS (ESI): m / z calculated for $C_9H_7N_2O_3$ $(M - N_2 + H)^+$: 191.05, found: 190.88.



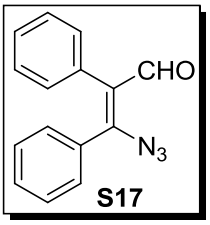
Azidoaldehyde S14. The general procedure was followed using 370 mg of chloroalkenal **T4** (2.0 mmol), 57 mg of NaN_3 (2.4 mmol) and 3.5 mL of DMSO. Purification by column chromatography with hexanes:EtOAc/10:1(1%v Et_3N) to give **S14** as a slightly yellow oil (180 mg, 47%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 8.98 (d, *J* = 6.18 Hz, 1H), 7.95 (m, 2H), 7.33 (m, 2H), 2.90 (d, *J* = 6.18 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 199.9 (CH), 166.4 (d, J_{CF} = 256.0Hz, C), 158.5 (C), 133.2 (d, J_{CF} = 10.0 Hz, CH), 119.1 (C), 117.3 (d, J_{CF} = 22.9 Hz, CH), 39.1 (CH); MS (ESI): m / z calculated for C_9H_7FNO $(M - N_2 + H)^+$: 164.05, found: 163.97.



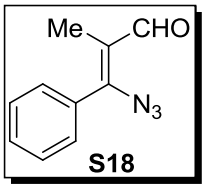
Azidoaldehyde S15. The general procedure was followed using 106 mg of chloroalkenal **T5** (0.5 mmol), 39 mg of NaN_3 (0.6 mmol) and 2.5 mL of DMSO. Purification by column chromatography with hexanes:EtOAc/10:1(1%v Et_3N) to give **S15** as a dark yellow oil (45 mg, 41%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 9.12 (d, *J* = 5.82 Hz, 1H), 8.75 (s, 1H), 8.56 (q, 1H), 8.30 (q, 1H), 7.90 (t, 1H), 3.06 (d, *J* = 5.85 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 198.9 (CH), 159.0 (C), 148.8 (C), 135.7 (CH), 131.1 (CH), 128.7 (CH), 125.3 (CH), 124.5 (C), 39.1 (CH); MS (ESI): m / z calculated for $C_9H_7N_2O_3$ $(M - N_2 + H)^+$: 191.05, found: 190.88.



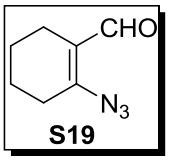
Azidoaldehyde S16. The general procedure was followed using 190 mg of chloroalkenal **T6** (0.88 mmol), 69 mg of NaN_3 (1.06 mmol) and 3.5 mL of DMSO. Purification by column chromatography with hexanes:EtOAc/7:1(1%v Et_3N) to give **S16** as a yellow oil (47 mg, 24%). The Z/E mixture was directly used in the next reaction without confirmed by NMR for each isomer. MS (ESI): m / z calculated for $C_{13}H_{10}NO$ $(M - N_2 + H)^+$: 196.08, found: 195.93.



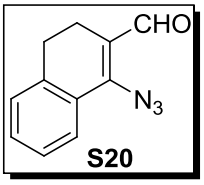
Azidoaldehyde S17. The general procedure was followed using 140 mg of chloroalkenal **T7** (0.58 mmol), 46 mg of NaN_3 (0.70 mmol) and 2.0 mL of DMSO. Purification by column chromatography with hexanes:EtOAc/10:1(1%v Et_3N) to give **S17** as a yellow oil (76 mg, 53%). The Z/E mixture was directly used in the next reaction without confirmed by NMR for each isomer; MS (ESI): m / z calculated for $C_{15}H_{12}NO$ $(M - N_2 + H)^+$: 222.09, found: 222.09.



Azidoaldehyde S18. The general procedure was followed using 240 mg of chloroalkenal **T8** (1.33 mmol), 104 mg of NaN_3 (1.60 mmol) and 2.5 mL of DMSO. Purification by column chromatography with hexanes:EtOAc/10:1(1%v Et_3N) to give **S18** as a yellow oil (227 mg, 91%). The Z/E mixture was directly used in the next reaction without confirmed by NMR for each isomer. MS (ESI): m / z calculated for $C_{10}H_{10}NO$ $(M - N_2 + H)^+$: 160.08, found: 160.01.



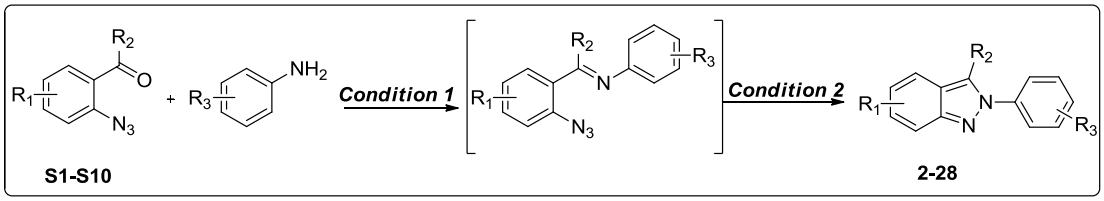
Azidoaldehyde S19. The general procedure was followed using 289 mg of chloroalkenal **T9** (2.0 mmol), 156 mg of NaN_3 (2.4 mmol) and 3.0 mL of DMSO. Purification by column chromatography with hexanes:EtOAc/10:1(1%v Et_3N) to give **S19** as a yellow oil (212 mg, 70%). For the characterizeation (^1H NMR, ^{13}C NMR and MS) of **S19** see: Tom G. Driver*, *Org Lett*, **2010**, *12* , 2884-2887.



Azidoaldehyde S20. The general procedure was followed using 221 mg of chloroalkenal **T10** (1.15 mmol), 90 mg of NaN_3 (1.38 mmol) and 3.0 mL of DMSO. Purification by column chromatography with hexanes:EtOAc/25:1(1%v Et_3N) to give **S20** as a yellow oil (110 mg, 48%). For the characterizeation (^{1}H NMR, ^{13}C NMR) of **S20** see: Tom G. Driver*, *Org Lett*, **2010**, *12*, 2884-2887. MS (ESI): m / z calculated for $C_{11}H_{12}NO_2$ $(M - N_2 + H + H_2O)^+$: 190.22, found: 190.02.

IV. CuI-Catalyzed Synthesis of Indazoles from Aryl Azides

A. General synthetic route to Indazoles from aryl azides(two step procedure)



B. Typical procedure for the preparation of 2-azidoarylimines(*condition 1*)

Procedure a. (AcOH, EtOH/MeOH)[11]

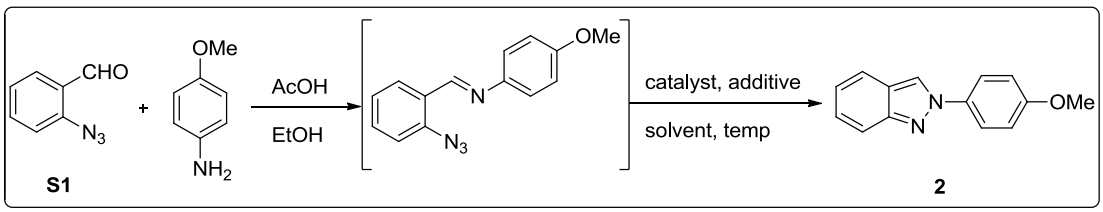
To a solution of ortho-azidobenazldehyde (1.2 equiv) in 1.0 mL anhydrous EtOH was added anline (1.0 equiv) and dropwised AcOH (0.1-0.3 equiv). The resulting mixture was stirred at ambient temperature for 2-8 h. Once the starting materials disappeared mostly on TLC, the solution was evaporated to give the crude product, which was further dried in vaccum.

Procedure b. ($TiCl_4$, Et_3N)[12]

To a 0 ℃ solution of ortho-azidobenzketone (1.0 equiv) in 2.0 mL anhydrous DCM was added aniline (1.0 equiv), $TiCl_4$ (0.6 equiv), Et_3N(3.0 equiv). The resulting mixture was stirred at 0 ℃ for 0.5 h-1 h. When the starting materials appeared, a cooled saturated solution of $NaHCO_3$ was added to quench the reaction and filter to remove the solid TiO_2. The solution was extracted with DCM (×2), the DCM layer was washed with water (×1), brine (×1). The organic layer was dried over Na_2SO_4, filtered and evaporated to give the crude product, which was further dried in vaccum.

(Caution: Product of step1 schiff base was unstable to untreated silica gel. So after optimization, the yield of two step procedure was higher than separated two procedures)

C. General procedure for the optimization of the reaction *condition 2*.



To a diluted solution of the crude product of step1 in 1.0 mL solvent was added crushed 4Å molecular sieves (100 wt %), catalyst (0.1-1.0 equiv), additive (0.1-1.0 equiv). After 4 h, the heterogenous mixture was filtered through SiO_2. The filtrate was concentrated in vacuo and diluted in equal 1.0 mL dichloromethane, each added equal *ortho*-hydroxyacetophenone (as internal standard). Compare the area of peak of indazole **2** and *ortho*-hydroxyacetophenone to give the relative values. Once getting one actual yield, we afforded other yields.

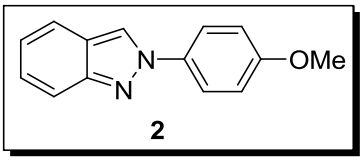
D. Optimized two step typical procedure[6]

Step1: The generation of Schiff base followed the general procedure **a** or **b.** The solution was concentrated in vacuo once more to afford crude *or*tho-azidoarylimine .

Step2: To the unpurified product Schiff base, 1.0-2.0 mL of THF or 1,4-dioxane, crushed 4Å molecular sieves (100 wt%), CuI (0.1 equiv) and TMEDA (0.5 equiv) or Et_3N (1.0 equiv) was added. The resulting mixture was stirred at room temperature for 4 h or 40 ℃ for 2 h. The reaction mixture was cooled to room temperature, and the heterogenous mixture was filtered through SiO_2. The filtrate was concentrated in vacuo. Purification by column chromatography provided the

indazoles (**2-28**).

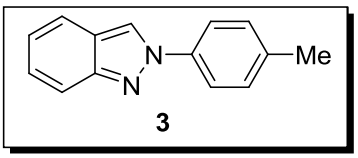
E. Indazole synthesis from aryl azidos S1-S10 (two step procedure)



2

2-(4-methoxyphenyl)-2H-indazole (2)

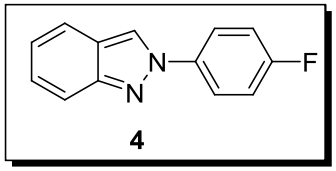
The typical procedure was followed using 40 mg of 2-azidobenazldehyde **S1** (0.272 mmol, 1.1 equiv), 31 mg of 4-methoxyaniline (0.247 mmol, 1.0 equiv), 4 µL of AcOH (0.074 mmol, 0.3 equiv), 1.5 mL of MeOH. 4.7 mg of CuI (0.0247 mmol, 0.1 equiv), 18.5 µL of TMEDA (0.124 mmol, 0.5 equiv), crushed 4Å molecular sieves and 1.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1-10:1 afforded **2** as an white solid (52 mg, 94%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.30 (s, 1H), 7.79 (d, *J* = 8.80Hz, 2H), 7.78 (d, *J* = 8.56 Hz, 1H), 7.69 (d, *J* = 8.36 Hz, 1H), 7.31 (t, *J* = 7.12 Hz, 1H), 7.10 (t, *J* = 7.60 Hz, 1H), 7.01 (d, *J* = 8.76 Hz, 2H), 3.85 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 159.3 (C), 149.7 (C), 134.4 (C), 126.7 (CH), 122.8 (C), 122.4 (CH), 122.3 (CH), 120.4 (CH), 117.9 (CH), 114.7 (CH), 55.7 (CH_3); MS (ESI): m / z calculated for $C_{14}H_{13}N_2O$ $(M + H)^+$: 225.10, found: 224.96.



3

2-p-tolyl-2H-indazole (3)

The typical procedure was followed using 40 mg of 2-azidobenazldehyde **S1** (0.272 mmol, 1.1 equiv), 27 mg of 4-methylaniline (0.247 mmol, 1.0 equiv), 4 µL of AcOH (0.074 mmol, 0.3 equiv), 2.0 mL of MeOH. 4.7 mg of CuI (0.0247 mmol, 0.1 equiv), 18.5 µL of TMEDA (0.124 mmol, 0.5 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1-10:1 afforded **3** as an white solid (50 mg, 97%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.34 (s, 1H), 7.78 (d, *J* = 8.48 Hz, 1H), 7.76 (d, *J* =8.16 Hz, 2H), 7.68 (d, *J* = 8.44 Hz, 1H), 7.31 (t, *J* = 6.48 Hz, 1H), 7.30 (d, *J* =8.36 Hz, 2H), 7.09 (t, *J* =7.48 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 149.8 (C), 138.4 (C), 138.0 (C), 130.2 (CH), 126.8 (CH), 122.8 (C), 122.4 (CH), 120.9 (CH), 120.5 (CH), 120.4 (CH), 118.0 (CH), 21.2 (CH_3); MS (ESI): m / z calculated for $C_{14}H_{13}N_2$ $(M + H)^+$: 209.10, found: 209.04.

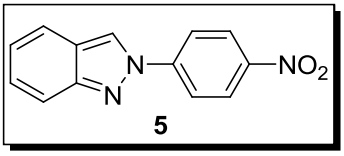


4

2-(4-fluorophenyl)-2H-indazole (4)

The typical procedure was followed using 40 mg of 2-azidobenazldehyde **S1** (0.272 mmol, 1.1 equiv), 24 µL of 4-fluoroaniline (0.247 mmol, 1.0 equiv), 4 µL of AcOH (0.074 mmol, 0.3 equiv), 1.5 mL of MeOH. 4.7 mg of CuI (0.0247 mmol, 0.1 equiv), 18.5 µL of TMEDA (0.124 mmol, 0.5 equiv), crushed 4Å molecular sieves and 1.5 mL of THF was used in the next step. Purification by

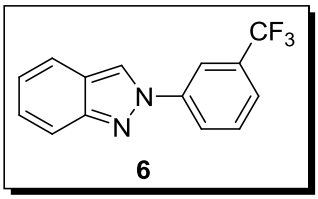
column chromatography with hexanes:EtOAc/20:1-10:1 afforded **4** as an white solid (49 mg, 94%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.32 (s, 1H), 7.87-7.84 (m, 2H), 7.77 (d, *J* = 8.80 Hz, 1H), 7.69 (d, *J* = 8.48 Hz, 1H), 7.32 (t, *J* = 6.84 Hz, 1H), 7.22-7.18 (m, 2H), 7.11 (t, *J* = 7.64 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 162.1 (d, J_{CF} = 245.9 Hz, C), 149.9 (C), 136.9 (C), 127.1 (CH), 122.9 (C), 122.8 (CH), 122.7 (d, J_{CF} = 4.3 Hz, CH), 120.5 (d, J_{CF} = 7.2 Hz CH), 118.0 (CH), 116.7 (CH), 116.4 (CH); MS (ESI): m / z calculated for $C_{13}H_{10}FN_2$ $(M + H)^+$: 213.08, found: 212.99.



5

2-(4-nitrophenyl)-2H-indazole (5)

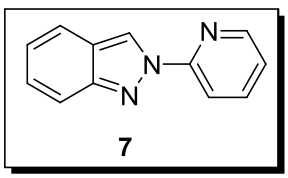
The typical procedure was followed using 60 mg of 2-azidobenazldehyde **S1** (0.408 mmol, 1.1 equiv), 51 mg of 4-nitroaniline (0.37 mmol, 1.0 equiv), 25 µL of $TiCl_4$ (0.222 mmol, 0.6 equiv), 155 µL of Et_3N (1.11 mmol, 3.0 equiv) and 2.0 mL of DCM. 7.0 mg of CuI (0.037 mmol, 0.1 equiv), 28 µL of TMEDA (0.185 mmol, 0.5 equiv), crushed 4Å molecular sieves and 1.5 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1-10:1 afforded **5** as a slightly yellow solid (23 mg, 26%). ^{1}H NMR ($CDCl_3$, 300MHz): δ (ppm) 8.45 (s, 1H), 8.36-8.33 (m, 2H), 8.09-8.06 (m, 2H), 7.70 (d, *J* =8.82Hz, 1H), 7.64 (d, *J* =8.52Hz, 1H), 7.30 (t, *J* =6.60Hz, 1H), 7.08 (t, *J* =6.63Hz, 1H);^{13}C NMR ($CDCl_3$, 150MHz): δ (ppm) 169.0, 164.2, 161.7, 141.1, 137.6, 135.4, 135.0, 131.8, 131.6, 128.5; MS (ESI): m / z calculated for $C_{13}H_{10}N_3O_2$ $(M + H)^+$: 240.07, found: 239.97.



6

2-(3-(trifluoromethyl)phenyl)-2H-indazole (6)

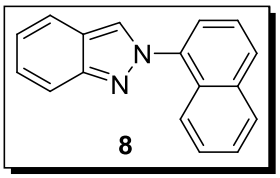
The typical procedure was followed using 40 mg of 2-azidobenazldehyde **S1** (0.272 mmol, 1.1 equiv), 31 µL of *m*-trifluoromethylaniline (0.247 mmol, 1.0 equiv), 4.0 µL of AcOH (0.074 mmol, 0.3 equiv), 1.5 mL of MeOH. 4.7 mg of CuI (0.0247 mmol, 0.1 equiv), 18.5 µL of TMEDA (0.124 mmol, 0.5 equiv), crushed 4Å molecular sieves and 1.5 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1-10:1 afforded **6** as an white solid (55 mg, 85%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.46 (s, 1H), 8.22 (s, 1H), 8.13-8.11 (m, 1H), 7.79 (d, *J* = 8.84 Hz, 1H), 7.71 (d, *J* = 8.52 Hz, 1H), 7.66 (d, *J* = 4.64 Hz, 2H), 7.35 (t, *J* = 7.00 Hz, 1H), 7.13 (t, *J* = 8.00 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) 150.2, 140.9, 132.3 (q, J_{CF} = 33.0Hz, C), 130.3, 127.5, 124.4, 123.7, 123.7 (q, J_{CF} = 271.0Hz. C), 123.1, 120.6, 120.4, 118.1, 117.9; MS (ESI): m / z calculated for $C_{14}H_{10}F_3N_2$ $(M + H)^+$: 263.07, found: 263.00.



7

2-(pyridin-2-yl)-2H-indazole (7)

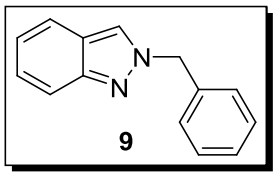
The typical procedure was followed using 40 mg of 2-azidobenazldehyde **S1** (0.272 mmol, 1.1 equiv), 23 mg of 2-aminopyridine (0.247 mmol, 1.0 equiv), 4.0 µL of AcOH (0.074 mmol, 0.3 equiv), 1.5 mL of MeOH. 4.7 mg of CuI (0.0247 mmol, 0.1 equiv), 18.5 µL of TMEDA (0.124 mmol, 0.5 equiv), crushed 4Å molecular sieves and 1.5 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1-10:1 afforded **7** as an white solid (39 mg, 81%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 9.11 (s, 1H), 8.51 (d, *J* = 4.12 Hz, 1H), 8.29 (d, *J* = 8.24 Hz, 1H), 7.89 (t, *J* =7.80 Hz, 1H), 7.76-7.71 (m, 2H), 7.34-7.28 (m, 2H), 7.09 (t, *J* = 8.12 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) 152.0, 150.4, 148.4, 138.9, 127.7, 122.9, 122.8, 122.5, 121.3, 120.7, 118.2, 114.2; MS (ESI): m / z calculated for $C_{12}H_{10}N_3$ $(M + H)^+$: 196.08, found: 195.97.



8

2-(naphthalen-1-yl)-2H-indazole (8)

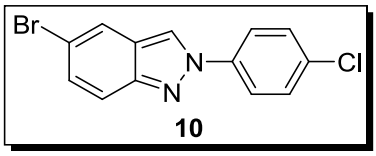
The typical procedure was followed using 40 mg of 2-azidobenazldehyde **S1** (0.272 mmol, 1.1 equiv), 36 mg of 1-naphthylamine (0.247 mmol, 1.0 equiv), 4.0 µL of AcOH (0.074 mmol, 0.3 equiv), 1.5 mL of MeOH. 4.7 mg of CuI (0.0247 mmol, 0.1 equiv), 18.5 µL of TMEDA (0.124 mmol, 0.5 equiv), crushed 4Å molecular sieves and 1.5 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/10:1 afforded **8** as an white solid (56 mg, 93%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.26 (s, 1H), 7.97-7.91 (m, 2H), 7.85 (dd, *J* = 0.72, 8.80 Hz, 1H), 7.77-7.72 (m, 2H), 7.63 (d, *J* = 7.20 Hz, 1H), 7.56-7.45 (m, 3H), 7.37 (t, *J* = 7.20 Hz, 1H), 7.16 (t, *J* = 7.88 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) 149.8, 137.8, 134.3, 129.8, 129.2, 128.3, 127.8, 127.0, 126.8, 125.7, 125.1, 124.0, 123.2, 122.5, 122.2, 120.6, 118.1; MS (ESI): m / z calculated for $C_{17}H_{13}N_2$ $(M + H)^+$: 245.10, found: 244.98.



9

2-benzyl-2H-indazole (9)

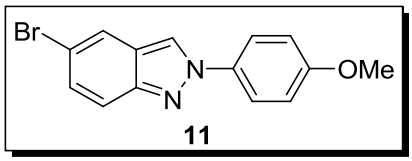
The typical procedure was followed using 40 mg of 2-azidobenazldehyde **S1** (0.272 mmol, 1.1 equiv), 27.0 µL of benzylamine (0.247 mmol, 1.0 equiv), 4.0 µL of AcOH (0.074 mmol, 0.3 equiv), 3.0 mL of MeOH. 4.7 mg of CuI (0.0247 mmol, 0.1 equiv), 18.5 µL of TMEDA (0.124 mmol, 0.5 equiv), crushed 4Å molecular sieves and 1.5 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/15:1 afforded **9** as an white solid (48 mg, 93%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.85 (s, 1H), 7.73 (dd, *J* = 0.80, 8.76 Hz, 1H), 7.60 (d, *J* = 8.44 Hz, 1H), 7.35-7.23 (m, 6H), 7.06 (t, *J* = 7.92 Hz, 1H), 5.57 (s, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) 149.1, 135.9, 129.1, 128.5, 128.1, 126.1, 123.0, 122.3, 121.9, 120.3, 117.7, 57.6; MS (ESI): m / z calculated for $C_{14}H_{13}N_2$ $(M + H)^+$: 209.10, found: 209.06.



10

5-bromo-2-(4-chlorophenyl)-2H-indazole (10)

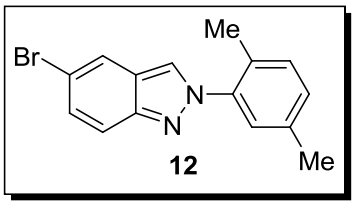
The typical procedure was followed using 40 mg of 2-azido-5-bromobenazldehyde **S3** (0.177 mmol, 1.1 equiv), 21 mg of 4-chloroanline (0.161 mmol, 1.0 equiv), 3.0 µL of AcOH (0.048 mmol, 0.3 equiv), 2.0 mL of MeOH. 3.0 mg of CuI (0.016 mmol, 0.1 equiv), 12.0 µL of TMEDA (0.08 mmol, 0.5 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **10** as an white solid (45 mg, 91%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.32 (d, *J* = 0.84 Hz, 1H), 7.86-7.83 (m, 3H), 7.65 (d, *J* =9.20 Hz, 1H), 7.50 (d, *J* =8.92 Hz, 2H), 7.38 (dd, *J* =1.56, 9.16 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) 148.3, 138.8, 134.0, 130.9, 129.9, 124.1, 122.5, 122.1, 119.8, 116.3; MS (ESI): m / z calculated for $C_{13}H_9BrClN_2$ $(M + H)^+$: 306.96, found: 306.90.



11

5-bromo-2-(4-methoxyphenyl)-2H-indazole (11)

The typical procedure was followed using 40 mg of 2-azido-5-bromobenazldehyde **S3** (0.177 mmol, 1.1 equiv), 20 mg of 4-methoxyanline (0.161 mmol, 1.0 equiv), 3.0 µL of AcOH (0.048 mmol, 0.3 equiv), 2.0 mL of MeOH. 3.0 mg of CuI (0.016 mmol, 0.1 equiv), 12.0 µL of TMEDA (0.08 mmol, 0.5 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1-10:1 afforded **11** as an white solid (46 mg, 94%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.26 (s, 1H), 7.86 (d, *J* = 1.08 Hz, 1H), 7.78 (d, *J* = 9.00 Hz, 2H), 7.66 (d, *J* = 9.20 Hz, 1H), 7.36 (dd, *J* = 1.68, 9.16 Hz, 1H), 7.03 (d, *J* = 9.00 Hz, 2H), 3.87 (s, 3H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) 159.6, 148.0, 133.8, 130.2, 123.9, 122.5, 119.8, 119.6, 115.8, 114.8,55.7; MS (ESI): m / z calculated for $C_{14}H_{12}BrN_2O$ $(M + H)^+$: 303.01, found: 302.94

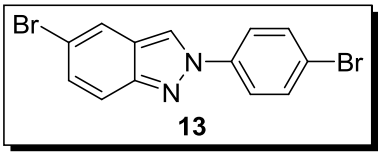


12

5-bromo-2-(2,5-dimethylphenyl)-2H-indazole (12)

The typical procedure was followed using 40 mg of 2-azido-5-bromobenazldehyde **S3** (0.177 mmol, 1.1 equiv), 20.0 µL of 2,5-dimethylaniline (0.161 mmol, 1.0 equiv), 3.0 µL of AcOH (0.048 mmol, 0.3 equiv), 2.0 mL of EtOH. 3.0 mg of CuI (0.016 mmol, 0.1 equiv), 24.0 µL of TMEDA (0.161 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **12** as a yellow liquid (45 mg, 93%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.03 (s, 1H), 7.90 (s, 1H), 7.67 (d, *J* = 9.16 Hz, 1H), 7.38 (dd, *J* = 1.52, 9.16 Hz, 1H), 7.24-7.20 (m, 3H), 2.38 (s, 3H), 2.18 (s, 3H);

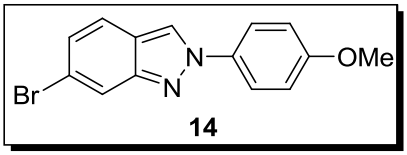
^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) 147.7, 139.9, 136.7, 131.2, 130.5, 130.2, 130.1, 127.1, 123.9, 123.2, 122.5, 119.8, 115.6, 20.8, 17.5; MS (ESI): m / z calculated for $C_{15}H_{14}BrN_2$ $(M + H)^+$: 301.03, found: 300.95.



13

5-bromo-2-(4-bromophenyl)-2H-indazole (13)

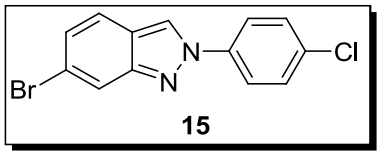
The typical procedure was followed using 40 mg of 2-azido-5-bromobenazldehyde **S3** (0.177 mmol, 1.1 equiv), 28 mg of 4-bromoaniline (0.161 mmol, 1.0 equiv), 3.0 µL of AcOH (0.048 mmol, 0.3 equiv), 2.0 mL of EtOH. 3.0 mg of CuI (0.016 mmol, 0.1 equiv), 24.0 µL of TMEDA (0.161 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **13** as an white solid (55mg, 97%). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) 8.32 (s, 1H), 7.86 (s, 1H), 7.79-7.76 (m, 2H), 7.67-7.64 (m, 3H), 7.39-7.35 (m, 1H);^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) 148.3, 139.3, 132.8, 130.9, 124.1, 122.5, 122.4, 122.0, 119.8, 119.7, 116.4; MS (ESI): m / z calculated for $C_{13}H_9Br_2N_2$ $(M + H)^+$: 350.91, found: 350.75.



14

6-bromo-2-(4-methoxyphenyl)-2H-indazole (14)

The typical procedure was followed using 40 mg of 2-azido-4-bromoaldehyde **S4** (0.177 mmol, 1.1 equiv), 19.8 mg of 4-methoxyaniline (0.161 mmol, 1.0 equiv), 2.9 µL of AcOH (0.048 mmol, 0.3 equiv), 2.0 mL of MeOH. 3.0 mg of CuI (0.016 mmol, 0.1 equiv), 13.0 µL of TMEDA (0.08 mmol, 0.5 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **14** as an white solid (46mg, 94%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.28 (s, 1H), 7.95 (s, 1H), 7.77 (d, *J* = 9.00 Hz, 2H), 7.56 (d, *J* = 8.88 Hz, 1H), 7.18 (d, *J* = 8.84 Hz, 1H), 7.02 (d, *J* = 8.96 Hz, 2H), 3.87 (s, 3H); ^{13}C-NMR ($CDCl_3$, 150 MHz): δ (ppm) 159.6, 150.2, 133.8, 126.1, 122.4, 121.8, 121.3, 120.8, 120.6, 120.2, 114.8, 55.7; MS (ESI): m / z calculated for $C_{14}H_{12}BrN_2O$ $(M + H)^+$: 303.01, found: 302.93.

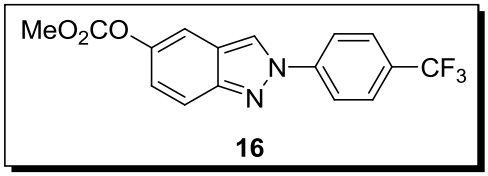


15

6-bromo-2-(4-chlorophenyl)-2H-indazole (15)

The typical procedure was followed using 40 mg of 2-azido-4-bromoaldehyde **S4** (0.177 mmol, 1.1 equiv), 20.5 mg of 4-chloroaniline (0.161 mmol, 1.0 equiv), 2.9 µL of AcOH (0.048 mmol, 0.3 equiv), 2.0 mL of MeOH. 3.0 mg of CuI (0.016 mmol, 0.1 equiv), 13.0 µL of TMEDA (0.08 mmol, 0.5 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **15** as an white solid (44 mg, 89%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.35 (d, *J* = 3.32 Hz, 1H), 7.95 (s, 1H), 7.83 (dd, *J* = 2.48, 8.96 Hz, 2H), 7.57 (dd, *J* = 2.48, 8.92 Hz, 1H), 7.50 (dd, *J* = 2.12, 8.96 Hz, 2H), 7.19 (d, *J* = 8.92

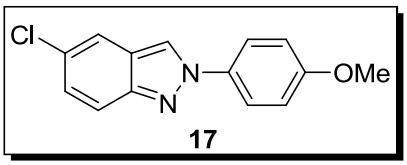
Hz, 1H); ^{13}C-NMR ($CDCl_3$, 150 MHz): δ (ppm) 150.5, 138.7, 134.0, 129.8, 126.6, 122.0, 121.9, 121.4, 121.2, 120.8, 120.3; MS (ESI): m / z calculated for $C_{13}H_9BrClN_2$ $(M + H)^+$: 306.96, found: 307.01.



16

methyl 2-(4-(trifluoromethyl)phenyl)-2H-indazol-5-yl carbonate (16)

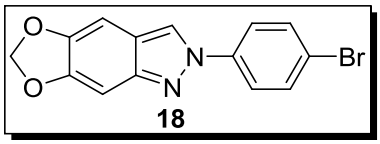
The typical procedure was followed using 19 mg of *ortho*-azidobenzaldehyde **S5** (0.086 mmol, 1.1 equiv), 9.7 µL of 4-trifluoromethylaniline (0.078 mmol, 1.0 equiv), 1.4 µL of AcOH (0.077 mmol, 0.3 equiv), 2.0 mL of EtOH. 1.5 mg of CuI (0.0078 mmol, 0.1 equiv), 12.0 µL of TMEDA (0.078 mmol, 0.5 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **16** as an white solid (19 mg, 73%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.46 (s, 1H), 8.05 (d, J = 8.48 Hz, 2H), 7.81-7.78 (m, 3H), 7.51 (d, J = 2.00 Hz, 1H), 7.16 (dd, J = 1.76, 9.32 Hz, 1H), 3.94 (s, 3H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) 154.6, 148.4, 146.9, 142.8, 129.8 (d, J_{CF} = 36.0 Hz, CH), 127.0 (d, J_{CF} = 3.6 Hz, CH), 123.8 (d, J_{CF} = 270.0 Hz, C), 123.4, 122.4, 121.1, 120.9, 119.7, 55.6; MS (ESI): m / z calculated for $C_{16}H_{12}F_3N_2O_3$ $(M + H)^+$: 337.07, found: 337.13.



17

5-chloro-2-(4-methoxyphenyl)-2H-indazole (17)

The typical procedure was followed using 30 mg of 2-azido-5-chloroaldehyde **S6** (0.165 mmol, 1.1 equiv), 18.5 mg of 4-methoxyaniline (0.15 mmol, 1.0 equiv), 2.6 µL of AcOH (0.045 mmol, 0.3 equiv), 2.0 mL of MeOH. 2.9 mg of CuI (0.015 mmol, 0.1 equiv), 11.0 µL of TMEDA (0.075 mmol, 0.5 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **17** as an white solid (35 mg, 90%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.26 (s, 1H), 7.78 (d, J = 9.00 Hz, 2H), 7.71 (d, J = 9.16 Hz, 1H), 7.67 (d, J = 1.44 Hz, 1H), 7.24 (dd, J = 1.88, 9.28 Hz, 1H), 7.03 (d, J = 9.04 Hz, 2H), 3.88 (s, 3H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) 159.6, 147.9, 133.8, 128.0, 127.9, 123.1, 122.4, 120.0, 119.4, 119.0, 114.8, 55.7; MS (ESI): m / z calculated for $C_{14}H_{12}ClN_2O$ $(M + H)^+$: 259.06, found: 259.18.

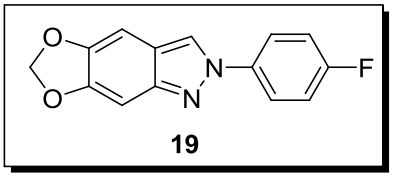


18

2-(4-bromophenyl)-2H-[1,3]dioxolo[4,5-f]indazole (18)

The typical procedure was followed using 40 mg of 6-azidopiperonal **S2** (0.209 mmol, 1.1 equiv), 33 mg of 4-bromoanline (0.19 mmol, 1.0 equiv), 3.3 µL of AcOH (0.057 mmol, 0.3 equiv), 2.0 mL of MeOH. 3.6 mg of CuI (0.019 mmol, 0.1 equiv), 14.2 µL of TMEDA (0.095 mmol, 0.5 equiv), crushed 4Å molecular sieves and 2.0 mL of 1,4-dioxane was used in the next step. Purification by

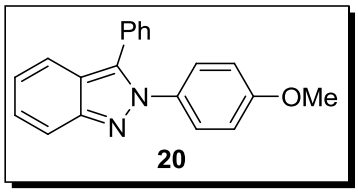
column chromatography with hexanes:EtOAc/20:1 afforded **18** as a slightly yellow solid (54 mg, 90%). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) 8.16 (s, 1H), 7.72 (d, *J* = 8.88 Hz, 2H), 7.61 (d, *J* = 8.88 Hz, 2H), 7.01 (s, 1H), 6.88 (s, 1H), 5.98 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 150.0, 147.7, 132.6, 130.9, 128.9, 121.4, 120.5, 119.5, 118.9, 101.2, 94.8, 94.2. MS (ESI): m / z calculated for $C_{14}H_{10}BrN_2O_2$ $(M + H)^+$: 316.98, found: 316.84.



19

2-(4-fluorophenyl)-2H-[1,3]dioxolo[4,5-f]indazole (19)

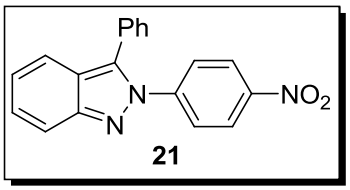
The typical procedure was followed using 40 mg of 6-azidopiperonal **S2** (0.209 mmol, 1.1 equiv), 18.2 µL of 4-fluoroanline (0.19 mmol, 1.0 equiv), 3.3 µL of AcOH (0.057 mmol, 0.3 equiv), 2.0 mL of MeOH. 3.6 mg of CuI (0.019 mmol, 0.1 equiv), 14.2 µL of TMEDA (0.095 mmol, 0.5 equiv), crushed 4Å molecular sieves and 2.0 mL of 1,4-dioxane was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **19** as an white solid (46 mg, 95%). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) 8.11 (s, 1H), 7.79-7.75 (m, 2H), 7.21-7.15 (m, 2H), 7.02 (s, 1H), 6.88 (s, 1H), 5.98 (s, 2H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) 163.2, 160.0, 149.9, 146.9 (d, J_{CF} = 96.1 Hz, C), 137.0, 121.8 (d, J_{CF} = 7.9 Hz, CH), 119.8, 118.7, 116.4 (d, J_{CF} = 22.9 Hz, CH), 101.1, 94.9, 94.2; MS (ESI): m / z calculated for $C_{14}H_{10F}N_2O_2$ $(M + H)^+$: 257.06, found: 256.95.



20

2-(4-methoxyphenyl)-3-phenyl-2H-indazole (20)

The typical procedure was followed using 34 mg of (2-azidophenyl)(phenyl)methanone **S7** (0.152 mmol, 1.1 equiv), 17.0 mg of 4-methoxyaniline (0.138 mmol, 1.0 equiv), 10.0 µL of $TiCl_4$ (0.083 mmol, 0.6 equiv), 58.0 µL of Et_3N (0.414 mmol, 3.0 equiv) and 2.0 mL of DCM. 1.3 mg of CuI (0.007 mmol, 0.1 equiv), 9.6 µL of Et_3N (0.069 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **20** as an white solid (17 mg, 82%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.79 (d, *J* = 8.76 Hz, 1H), 7.71 (d, *J* = 8.52 Hz, 1H), 7.41-7.34 (m, 8H), 7.13 (t, *J* = 7.60 Hz, 1H), 6.89 (d, *J* = 8.92 Hz, 2H) 3.82 (s, 3H); ^{13}C-NMR ($CDCl_3$, 150 MHz): δ (ppm) 159.4, 148.9, 135.4, 133.5, 130.1, 129.8, 128.8, 128.3, 127.3, 126.9, 122.5, 121.7, 120.6, 117.7, 114.2, 55.6; MS (ESI): m / z calculated for $C_{20}H_{17}N_2O$ $(M + H)^+$: 301.13, found: 301.05.

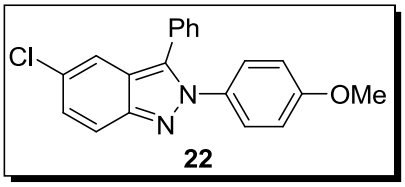


21

2-(4-nitrophenyl)-3-phenyl-2H-indazole (21)

The typical procedure was followed using 76 mg of (2-azidophenyl)(phenyl)methanone **S7** (0.34

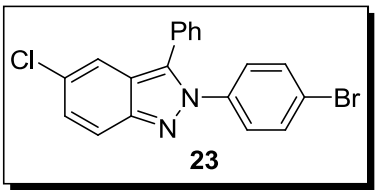
mmol, 1.1 equiv), 43.0 mg of 4-nitroaniline (0.31 mmol, 1.0 equiv), 21.0 µL of $TiCl_4$ (0.186 mmol, 0.6 equiv), 130.0 µL of Et_3N (0.93 mmol, 3.0 equiv) and 2.0 mL of DCM. 6.0 mg of CuI (0.031 mmol, 0.1 equiv), 43.0 µL of Et_3N (0.31 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/10:1 afforded **21** as a white solid (64 mg, 66%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.25 (d, *J* = 8.96 Hz, 2H), 7.79 (d, *J* = 8.84 Hz, 1H), 7.68-7.64 (m, 3H), 7.47-7.45 (m, 3H), 7.42-7.35 (m, 3H), 7.16 (t, *J* = 6.76 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 150 MHz): δ (ppm) 149.8, 146.8, 145.2, 136.1, 129.8, 129.4, 129.3, 129.2, 128.1, 126.3, 124.5, 123.4, 122.5, 120.7, 117.9; MS (ESI): m / z calculated for $C_{19}H_{14}N_3O_2$ $(M + H)^+$: 316.10, found: 315.99.



22

5-chloro-2-(4-methoxyphenyl)-3-phenyl-2H-indazole (22)

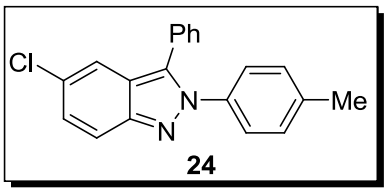
The typical procedure was followed using 67 mg of (2-azido-5-chlorophenyl)(phenyl) methanone **S8** (0.26 mmol, 1.1 equiv), 29 mg of 4-methoxyaniline (0.236 mmol, 1.0 equiv), 16.0 µL of $TiCl_4$ (0.142 mmol, 0.6 equiv), 99.0 µL of Et_3N (0.708 mmol, 3.0 equiv) and 2.0 mL of DCM. 4.5 mg of CuI (0.0236 mmol, 0.1 equiv), 33.0 µL of Et_3N (0.236 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/10:1 afforded **22** as an white solid (54 mg, 67%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.72 (d, *J* = 9.16 Hz, 1H), 7.67 (d, *J* = 1.60 Hz, 1H), 7.42-7.37 (m, 3H), 7.34-7.32 (m, 4H), 7.28 (dd, *J* =1.84, 9.20 Hz, 1H), 6.89 (d, *J* = 8.92 Hz, 2H), 3.83 (s, 3H); ^{13}C-NMR ($CDCl_3$, 150MHz): δ (ppm) 159.6, 147.2, 135.1, 133.1, 129.6, 129.5, 129.0, 128.6, 128.3, 128.1, 127.2, 119.4, 119.3, 114.3, 55.6; MS (ESI): m / z calculated for $C_{20}H_{16}ClN_2O$ $(M + H)^+$: 335.09, found: 334.97.



23

2-(4-bromophenyl)-5-chloro-3-phenyl-2H-indazole (23)

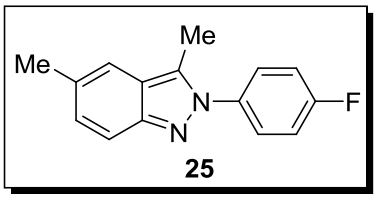
The typical procedure was followed using 40 mg of (2-azido-5-chlorophenyl)(phenyl) methanone **S8** (0.155 mmol, 1.1 equiv), 25 mg of 4-bromoaniline (0.141 mmol, 1.0 equiv), 9.3 µL of $TiCl_4$ (0.085 mmol, 0.6 equiv), 59.0 µL of Et_3N (0.423 mmol, 3.0 equiv) and 2.0 mL of DCM. 2.7 mg of CuI (0.014 mmol, 0.1 equiv), 20.0 µL of Et_3N (0.141 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/10:1 afforded **23** as an white solid (38 mg, 85%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.72 (d, *J* = 9.20 Hz, 1H), 7.66 (s, 1H), 7.52 (d, *J* = 8.60 Hz, 2H), 7.44-7.42 (m, 3H), 7.33-7.28 (m, 5H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) 147.5, 139.0, 135.3, 132.3, 129.7, 129.2, 129.1, 129.0, 128.8, 128.5, 127.3, 122.5, 122.4, 119.4, 119.3; MS (ESI): m / z calculated for $C_{19}H_{13}BrClN_2$ $(M + H)^+$: 382.99, found: 383.06.



24

5-chloro-3-phenyl-2-p-tolyl-2H-indazole (24)

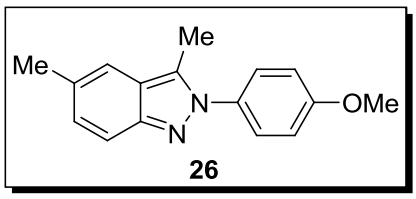
The typical procedure was followed using 40 mg of (2-azido-5-chlorophenyl)(phenyl) methanone **S8** (0.155 mmol, 1.1 equiv), 15 mg of 4-methylaniline (0.141 mmol, 1.0 equiv), 9.3 µL of $TiCl_4$ (0.085 mmol, 0.6 equiv), 59.0 µL of Et_3N (0.423 mmol, 3.0 equiv) and 2.0 mL of DCM. 2.7 mg of CuI (0.014 mmol, 0.1 equiv), 20.0 µL of Et_3N (0.141 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/10:1 afforded **24** as an white solid (38 mg, 84%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.73 (d, *J* = 9.16 Hz, 1H), 7.67 (d, *J* = 1.80 Hz, 1H), 7.42-7.38 (m, 3H), 7.33-7.27 (m, 5H), 7.18 (d, *J* = 8.32 Hz, 2H), 2.38 (s, 3H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) 147.3, 138.6, 137.6, 135.2, 129.74, 129.66, 129.56, 129.0, 128.6, 128.3, 128.1, 125.7, 122.2, 119.4, 119.3, 21.3; MS (ESI): m / z calculated for $C_{20}H_{16}ClN_2$ $(M + H)^+$: 319.09, found: 319.17.



25

2-(4-fluorophenyl)-3,5-dimethyl-2H-indazole (25)

The typical procedure was followed using 47 mg of 1-(2-azido-5-methylphenyl)ethanone **S9** (0.268 mmol, 1.1 equiv), 24.0 µL of 4-fluoroaniline (0.244 mmol, 1.0 equiv), 16.0 µL of $TiCl_4$ (0.146 mmol, 0.6 equiv), 102.0 µL of Et_3N (0.732 mmol, 3.0 equiv) and 2.0 mL of DCM. 4.6 mg of CuI (0.024 mmol, 0.1 equiv), 18.0 µL of Et_3N (0.24 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/10:1 afforded **25** as an white solid (38 mg, 66%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.60 (d, *J* = 8.88 Hz, 1H), 7.55-7.52 (m, 2H), 7.35 (s, 1H), 7.22 (t, *J* = 8.52 Hz, 2H), 7.16 (d, *J* = 8.92 Hz, 1H), 2.59 (s, 3H), 2.44 (s, 3H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) 164.2, 160.9, 147.3, 135.9, 131.5, 130.7, 130.3, 127.7 (d, J_{CF} = 9.3 Hz, CH), 121.8, 117.6 (d, J_{CF} = 77.4 Hz, C), 116.3 (d, J_{CF} = 22.9 Hz, CH), 21.9, 11.1; MS (ESI): m / z calculated for $C_{15}H_{14}FN_2$ $(M + H)^+$: 241.11, found: 241.22.

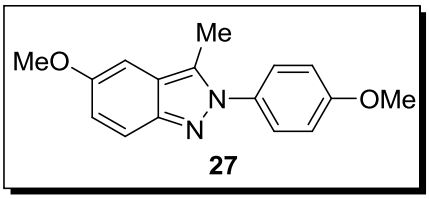


26

2-(4-methoxyphenyl)-3,5-dimethyl-2H-indazole (26)

The typical procedure was followed using 25 mg of 1-(2-azido-5-methylphenyl)ethanone **S9** (0.143 mmol, 1.1 equiv), 16mg of 4-methoxyaniline (0.13 mmol, 1.0 equiv), 8.6 µL of $TiCl_4$ (0.078 mmol, 0.6 equiv), 55µL of Et_3N (0.39 mmol, 3.0 equiv) and 2.0mL of DCM. 2.5mg of CuI (0.013 mmol, 0.1 equiv), 18µL of Et_3N (0.13 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with

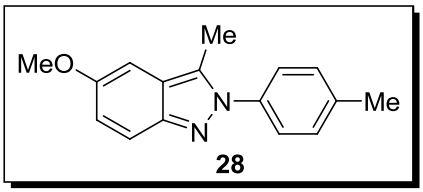
hexanes:EtOAc/10:1 afforded **26** as an white solid (23 mg, 72%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.60 (d, *J* = 8.88 Hz, 1H), 7.46 (d, *J* = 8.88 Hz, 2H), 7.34 (s, 1H), 7.15 (d, *J* = 8.88 Hz, 1H), 7.02 (d, *J* = 8.88 Hz, 2H), 3.88 (s, 3H), 2.57 (s, 3H), 2.44 (s, 3H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) 159.7, 147.5, 133.2, 131.0, 130.1, 129.6, 127.0, 121.7, 118.1, 117.2, 114.3, 55.7, 21.9, 11.1; MS (ESI): m / z calculated for $C_{16}H_{17}N_2O$ $(M + H)^+$: 253.13, found: 253.03.



27

5-methoxy-2-(4-methoxyphenyl)-3-methyl-2H-indazole (27)

The typical procedure was followed using 33 mg of 1-(2-azido-5-methoxyphenyl)ethanone **S10** (0.173 mmol, 1.1 equiv), 19.3 mg of 4-methoxyaniline (0.157 mmol, 1.0 equiv), 11.0 µL of $TiCl_4$ (0.094 mmol, 0.6 equiv), 66.0 µL of Et_3N (0.471 mmol, 3.0 equiv) and 2.0 mL of DCM. 3mg of CuI (0.0157 mmol, 0.1 equiv), 22.0 µL of Et_3N (0.157 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/10:1 afforded **27** as an white solid (35 mg, 83%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.60 (d, *J* = 9.32 Hz, 1H), 7.46-7.44 (m, 2H), 7.03-7.00 (m, 3H), 6.78 (d, *J* = 2.12 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 2.56 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 159.6, 154.6, 145.4, 133.2, 130.7, 126.9, 121.6, 121.1, 119.0, 114.3, 96.2, 55.7, 55.5, 11.1; MS (ESI): m / z calculated for $C_{16}H_{17}N_2O_2$ $(M + H)^+$: 269.12, found: 269.02.



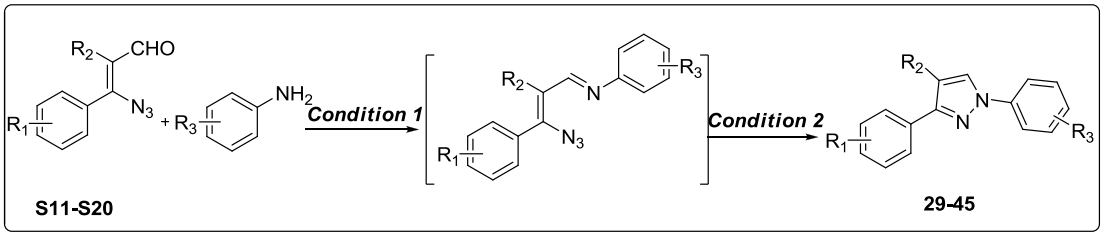
28

5-methoxy-3-methyl-2-p-tolyl-2H-indazole (28)

The typical procedure was followed using 44 mg of 1-(2-azido-5-methoxyphenyl)ethanone **S10** (0.23 mmol, 1.1 equiv), 22.4 mg of 4-methylaniline (0.21 mmol, 1.0 equiv), 14.0 µL of $TiCl_4$ (0.126 mmol, 0.6 equiv), 88.0 µL of Et_3N (0.63 mmol, 3.0 equiv) and 2.0 mL of DCM. 4.0 mg of CuI (0.021 mmol, 0.1 equiv), 29.0 µL of Et_3N (0.21 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/10:1 afforded **28** as an white solid (42 mg,79%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.61 (d, *J* = 9.32 Hz, 1H), 7.42 (d, *J* = 8.28 Hz, 2H), 7.31 (d, *J* = 8.24 Hz, 2H), 7.02 (dd, *J* = 2.32, 9.28 Hz, 1H), 6.78 (d, *J* = 2.12 Hz, 1H), 3.87 (s, 3H), 2.58 (s, 3H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 154.6, 145.5, 138.5, 137.7, 130.6, 129.8, 125.5, 121.7, 121.3, 119.1, 96.2, 55.5, 21.3, 11.2; MS (ESI): m / z calculated for $C_{16}H_{17}N_2O$ $(M + H)^+$: 253.13, found: 253.19.

V. CuI-Catalyzed Synthesis of Pyrazoles from Vinyl Azides

A. General synthetic route to Pyrazoles from vinyl azides.

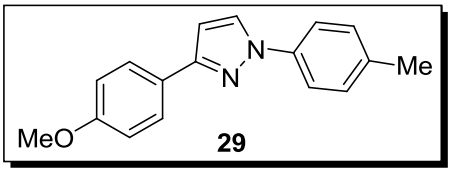


B. Typical procedures for the synthesis of pyrazoles (two step procedure)

Step1: To a solution of vinylazidobenazldehydes **S11-S20** (1.2 equiv) in 1.0 mL anhydrous EtOH or MeOH was added aryl anline (1.0 equiv) and dropwised AcOH (0.1-0.3 equiv). The resulting mixture was stirred at ambient temperature for 2-8 h. Once the starting materials disappeared mostly on TLC, the solution was evaporated to give the crude product, which was further dried in vaccum.

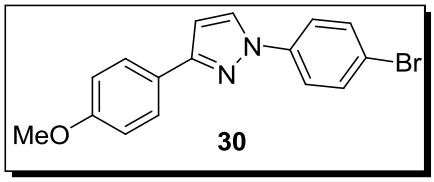
Step2: To the unpurified product Schiff base, 1.0 mL of THF , crushed 4Å molecular sieves (100 wt%), CuI (0.1 equiv) and Et_3N (1.0 equiv) was added. The resulting mixture was stirred at room temperature for 4 h or 40℃ for 2 h. The reaction mixture was cooled to room temperature, and the heterogenous mixture was filtered through SiO_2. The filtrate was concentrated in vacuo. Purification by column chromatography provided the pyrazoles (**29-45**).

C. Pyrazole synthesis from aryl azidos S11-S20.



3-(4-methoxyphenyl)-1-p-tolyl-1H-pyrazole (29)

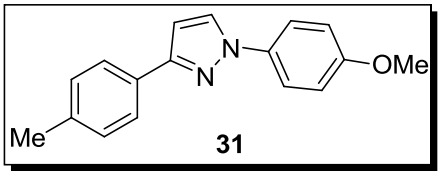
The typical procedure was followed using 35 mg of (Z)-3-azido-3-(4-methoxyphenyl) acrylaldehyde **S12** (0.172 mmol, 1.1 equiv), 16.7 mg of 4-methylaniline (0.156 mmol, 1.0 equiv), 2.9 μL of AcOH (0.0468 mmol, 0.3 equiv), 2.0 mL of MeOH. 3.0 mg of CuI (0.0156 mmol, 0.1 equiv), 22.0 μL of Et_3N (0.156 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **29** as an white solid (34 mg, 83%). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.90-7.84 (m, 3H), 7.65 (d, *J* = 8.40 Hz, 2H), 7.28-7.25 (m, 2H), 6.99-6.96 (m, 2H), 6.70-6.69 (m, 1H), 3.86 (s, 3H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 159.6, 152.5, 138.1, 136.0, 130.0, 127.9, 127.2, 126.1, 118.9, 114.1, 104.4, 55.4, 21.0; MS (ESI): m / z calculated for $C_{17}H_{17}N_2O$ $(M + H)^+$: 265.13, found: 265.04.



1-(4-bromophenyl)-3-(4-methoxyphenyl)-1H-pyrazole (30)

The typical procedure was followed using 27 mg of (Z)-3-azido-3-(4-methoxyphenyl) acrylaldehyde **S12** (0.137 mmol, 1.1 equiv), 22 mg of 4-bromoaniline (0.125 mmol, 1.0 equiv),

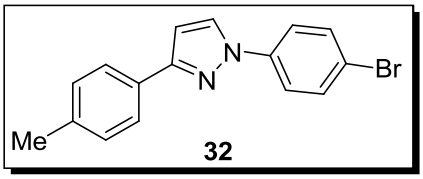
2.3 μL of AcOH (0.0375 mmol, 0.3 equiv), 2.0 mL of MeOH. 2.4 mg of CuI (0.0125 mmol, 0.1 equiv), 17.4 μL of Et_3N (0.125 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **30** as an white solid (33 mg, 80%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.88 (d, *J* = 2.52 Hz, 1H), 7.82 (d, *J* = 8.68 Hz, 2H), 7.64 (d, *J* = 8.84 Hz, 2H), 7.56 (d, *J* = 8.80 Hz, 2H), 6.96 (d, *J* = 8.68 Hz, 2H), 6.70 (d, *J* = 2.48 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 159.8, 153.2, 139.3, 132.5, 127.8, 127.2, 125.7, 120.3, 119.3, 114.2, 105.1, 55.4; MS (ESI): m / z calculated for $C_{16}H_{14}BrN_2O$ $(M + H)^+$: 329.02, found: 329.00.



31

1-(4-methoxyphenyl)-3-p-tolyl-1H-pyrazole (31)

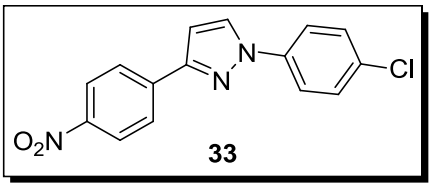
The typical procedure was followed using 62 mg of (Z)-3-azido-3-p-tolylacrylaldehyde **S11** (0.33 mmol, 1.1 equiv), 37 mg of 4-methoxyaniline (0.30 mmol, 1.0 equiv), 5.6 μL of AcOH (0.09 mmol, 0.3 equiv), 2.0 mL of MeOH. 5.7 mg of CuI (0.03 mmol, 0.1 equiv), 42.0 μL of Et_3N (0.30 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **31** as an white solid (56 mg, 46%). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.85-7.80 (m, 3H), 7.67 (d, *J* = 8.94 Hz, 2H), 7.27-7.24 (m, 2H), 7.00 (d, *J* = 8.91 Hz, 2H), 6.72 (d, *J* = 2.34 Hz, 1H), 3.86 (s, 3H), 2.41 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 158.2, 152.7, 137.7, 134.2, 130.6, 129.4, 128.1, 125.8, 120.8, 114.6, 104.5, 55.7, 21.4; MS (ESI): m / z calculated for $C_{17}H_{17}N_2O$ $(M + H)^+$: 265.13, found: 265.06.



32

1-(4-bromophenyl)-3-p-tolyl-1H-pyrazole (32)

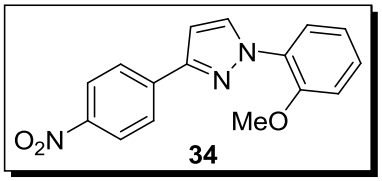
The typical procedure was followed using 67 mg of (Z)-3-azido-3-p-tolylacrylaldehyde **S11** (0.358 mmol, 1.1 equiv), 56 mg of 4-bromoaniline (0.325 mmol, 1.0 equiv), 6.1 μL of AcOH (0.0976 mmol, 0.3 equiv), 2.0 mL of MeOH. 6.2 mg of CuI (0.0325 mmol, 0.1 equiv), 45.0 μL of Et_3N (0.325 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **32** as a slightly yellow solid (35 mg, 34%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.90 (d, *J* = 2.44 Hz, 1H) 7.79 (d, *J* = 8.04 Hz, 2H), 7.65 (d, *J* = 8.84 Hz, 2H), 7.57 (d, *J* = 8.80 Hz, 2H), 7.25-7.23 (m, 3H), 6.75 (d, *J* = 2.44 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 153.4, 139.3, 138.2, 132.5, 130.1, 129.5, 127.8, 125.9, 120.4, 119.4, 105.4, 21.4; MS (ESI): m / z calculated for $C_{16}H_{14}BrN_2$ $(M + H)^+$: 313.03, found: 313.03.



33

1-(4-chlorophenyl)-3-(4-nitrophenyl)-1H-pyrazole (33)

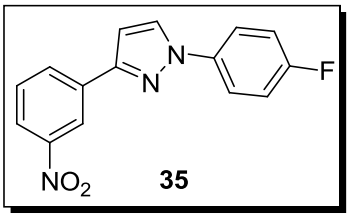
The typical procedure was followed using 43 mg of Z/E mixture of 3-azido-3-(4-nitro phenyl)acrylaldehyde **S13** (0.197 mmol, 1.1 equiv), 23 mg of 4-chloroaniline (0.179 mmol, 1.0 equiv), 3.3 µL of AcOH (0.0537 mmol, 0.3 equiv), 2.0 mL of MeOH. 3.4 mg of CuI (0.0179 mmol, 0.1 equiv), 25.0 µL of Et_3N (0.179 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **33** as a green yellow solid (29 mg, 85%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.29 (d, *J* = 8.80 Hz, 2H), 8.06 (d, *J* = 8.76 Hz, 2H), 7.98 (d, *J* = 2.48 Hz, 1H), 7.73 (d, *J* = 2.20 Hz, 2H), 7.47 (d, *J* = 8.80 Hz, 2H), 6.88 (d, *J* = 2.52 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 159.9, 147.5, 139.2, 138.5, 132.6, 129.8, 128.7, 126.3, 124.2, 120.4, 106.3; MS (ESI): m / z calculated for $C_{15}H_{11}ClN_3O_2$ $(M + H)^+$: 230.05, found: 299.97.



34

1-(2-methoxyphenyl)-3-(4-nitrophenyl)-1H-pyrazole (34)

The typical procedure was followed using 27 mg of Z/E mixture of 3-azido-3-(4-nitro phenyl)acrylaldehyde **S13** (0.124 mmol, 1.1 equiv), 12.7 µL of 2-methoxyaniline (0.113 mmol, 1.0 equiv), 2.1 µL of AcOH (0.0339 mmol, 0.3 equiv), 2.0 mL of MeOH. 2.2 mg of CuI (0.0113 mmol, 0.1 equiv), 7.9 µL of Et_3N (0.0565 mmol, 0.5 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **34** as a yellow solid (9 mg, 42%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.27 (d, *J* = 8.68 Hz, 2H), 8.13 (d, *J* = 2.36 Hz, 1H), 8.06 (d, *J* = 8.72 Hz, 2H), 7.84 (d, *J* = 6.88 Hz, 1H), 7.35 (t, *J* = 8.52 Hz, 1H), 7.13-7.07 (m, 2H), 6.83 (d, *J* = 2.40 Hz, 1H), 3.92 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 151.4, 149.6, 147.2, 139.8, 133.8, 129.4, 128.6, 126.3, 125.3, 124.2, 121.4, 112.4, 104.7, 56.1; MS (ESI): m / z calculated for $C_{16}H_{14}N_3O_3$ $(M + H)^+$: 296.10, found: 295.95.

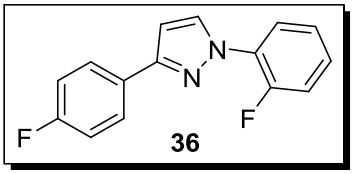


35

1-(4-fluorophenyl)-3-(3-nitrophenyl)-1H-pyrazole (35)

The typical procedure was followed using 49.5 mg of Z/E mixture of 3-azido-3-(3-nitrophenyl) acrylaldehyde **S15** (0.227 mmol, 1.1 equiv), 19.5 µL of 4-fluoroaniline (0.206 mmol, 1.0 equiv), 3.8 µL of AcOH (0.0618 mmol, 0.3 equiv), 2.0 mL of MeOH. 3.9 mg of CuI (0.0206 mmol, 0.1 equiv), 29.0 µL of Et_3N (0.206 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF

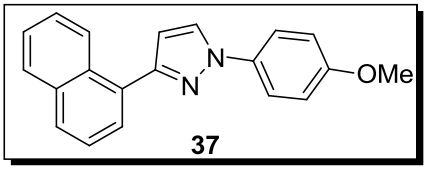
was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **35** as a slightly yellow solid (30 mg, 87%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.72 (s, 1H), 8.23 (d, *J* = 7.74 Hz, 1H), 8.17 (d, *J* = 8.12 Hz, 1H), 7.94 (d, *J* = 2.28 Hz, 1H), 7.76-7.73 (m, 2H), 7.59 (t, *J* = 8.04 Hz, 1H), 7.18 (t, *J* = 8.56 Hz, 2H), 6.85 (d, *J* = 2.24 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 163.0, 159.4, 149.7 (d, J_{CF} = 140.3 Hz, C), 136.3, 134.9, 131.6, 129.7, 128.7, 122.6, 120.9 (d, J_{CF} = 8.3 Hz, CH), 120.6, 116.4 (d, J_{CF} = 23.3 Hz, C), 105.5; MS (ESI): m / z calculated for $C_{15}H_{11}FN_3O_2$ $(M + H)^+$: 284.08, found: 283.94.



36

1-(2-fluorophenyl)-3-(4-fluorophenyl)-1H-pyrazole (36)

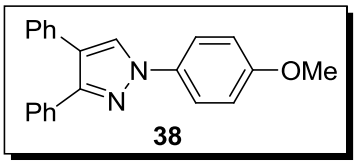
The typical procedure was followed using 47 mg of (Z)-3-azido-3-(4-fluorophenyl) acrylaldehyde **S14** (0.246 mmol, 1.1 equiv), 22.0 µL of 2-fluoroaniline (0.224 mmol, 1.0 equiv), 4.2 µL of AcOH (0.0672 mmol, 0.3 equiv), 2.0 mL of MeOH. 4.3 mg of CuI (0.0224 mmol, 0.1 equiv), 32.0 µL of Et_3N (0.224 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **36** as a dark yellow solid (26 mg, 45%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.04-8.00 (m, 2H), 7.89-7.86 (m, 2H), 7.28-7.20 (m, 3H), 7.11 (t, *J* = 8.68 Hz, 2H), 6.73 (d, *J* = 2.48 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 164.6, 161.3, 155.2, 151.8 (d, J_{CF} = 8.6 Hz, CH), 132.3 (d, J_{CF} = 10.5 Hz, CH), 129.3 (d, J_{CF} = 3.0 Hz, CH), 128.5 (d, J_{CF} = 9.0 Hz, CH), 127.7 (t, J_{CF} = 9.0 Hz, CH), 125.1 (d, J_{CF} = 3.8 Hz, CH), 124.3, 116.9 (d, J_{CF} = 21.0 Hz, C), 115.70 (d, J_{CF} = 21.8 Hz, C), 104.9; MS (ESI): m / z calculated for $C_{15}H_{11}F_2N_2$ $(M + H)^+$: 257.08, found: 256.97.



37

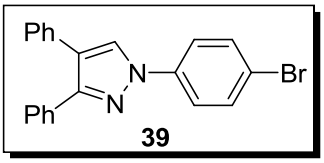
1-(4-methoxyphenyl)-3-(naphthalen-1-yl)-1H-pyrazole (37)

The typical procedure was followed using 49 mg of Z/E mixture of 3-azido-3-(naphthalen-1-yl)acrylaldehyde **S16** (0.22 mmol, 1.1 equiv), 24.6 mg of 4-methoxyaniline (0.2 mmol, 1.0 equiv), 3.7 µL of AcOH (0.06 mmol, 0.3 equiv), 2.0 mL of MeOH. 3.8 mg of CuI (0.02 mmol, 0.1 equiv), 28.0 µL of Et_3N (0.2 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **37** as a slightly yellow oil (25 mg, 44%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.64-8.62 (m, 1H), 7.96 (d, *J* = 2.28 Hz, 1H), 7.90-7.86 (m, 2H), 7.77 (d, *J* = 7.08 Hz, 1H), 7.72 (d, *J* = 8.96 Hz, 2H), 7.55-7.50 (m, 3H), 7.01 (d, *J* = 8.96 Hz, 2H), 6.75 (d, *J* = 2.24 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 158.3, 152.5, 134.1, 131.5, 131.4, 128.6, 128.4, 127.4, 127.3, 126.5, 126.4, 125.9, 125.5, 120.9, 114.6, 108.5, 55.7; MS (ESI): m / z calculated for $C_{20}H_{17}N_2O$ $(M + H)^+$: 301.13, found: 300.98.



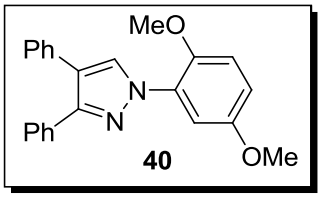
1-(4-methoxyphenyl)-3,4-diphenyl-1H-pyrazole (38)

The typical procedure was followed using 36 mg of Z/E mixture of 3-azido-2,3-diphenyl acrylaldehyde **S17** (0.143 mmol, 1.1 equiv), 16 mg of 4-methoxyaniline (0.13 mmol, 1.0 equiv), 2.4 µL of AcOH (0.039 mmol, 0.3 equiv), 2.0 mL of MeOH. 3.8 mg of CuI (0.013 mmol, 0.1 equiv), 18.0 µL of Et_3N (0.13 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **38** as a yellow solid (29 mg, 91%). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.92 (s, 1H), 7.70 (d, *J* = 9.00 Hz, 2H), 7.62-7.59 (m, 2H), 7.37-7.27 (m, 8H), 7.01 (d, *J* = 9.00 Hz, 2H), 3.85 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 158.4, 150.1, 133.8, 133.5, 133.2, 128.8, 128.7, 128.6, 128.5, 127.9, 127.0, 126.9, 122.6, 120.7, 114.7, 55.7; MS (ESI): m / z calculated for $C_{22}H_{19}N_2O$ $(M + H)^+$: 327.14, found: 327.10.



1-(4-bromophenyl)-3,4-diphenyl-1H-pyrazole (39)

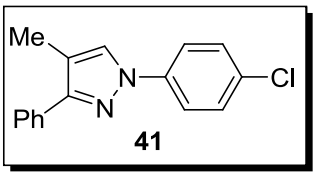
The typical procedure was followed using 36 mg of Z/E mixture of 3-azido-2,3-diphenyl acrylaldehyde **S17** (0.143 mmol, 1.1 equiv), 23 mg of 4-bromoaniline (0.13 mmol, 1.0 equiv), 2.4 µL of AcOH (0.039 mmol, 0.3 equiv), 2.0 mL of MeOH. 3.8 mg of CuI (0.013 mmol, 0.1 equiv), 18.0 µL of Et_3N (0.13 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **39** as a white solid (30 mg, 81%). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.96 (s, 1H), 7.69-7.66 (m, 2H), 7.59-7.56 (m, 4H), 7.34-7.30 (m, 8H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 150.9, 139.0, 133.0, 132.7, 132.6, 128.8, 128.7, 128.6, 128.5, 128.2, 127.3, 126.5, 123.5, 120.3; MS (ESI): m / z calculated for $C_{21}H_{16}BrN_2$ $(M + H)^+$: 375.04, found: 374.91.



1-(2,5-dimethoxyphenyl)-3,4-diphenyl-1H-pyrazole (40)

The typical procedure was followed using 36 mg of Z/E mixture of 3-azido-2,3-diphenyl acrylaldehyde **S17** (0.143 mmol, 1.1 equiv), 20 mg of 2,5-dimethoxyaniline (0.13 mmol, 1.0 equiv), 2.4 µL of AcOH (0.039 mmol, 0.3 equiv), 2.0 mL of MeOH. 3.8 mg of CuI (0.013 mmol, 0.1 equiv), 18.0 µL of Et_3N (0.13 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **40** as a yellow solid (30 mg, 66%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.24 (s, 1H), 7.61-7.59 (m, 2H), 7.54 (d, *J* = 3.04 Hz, 1H), 7.37-7.27 (m, 8H), 7.00 (d, *J* = 9.04 Hz, 1H), 6.84

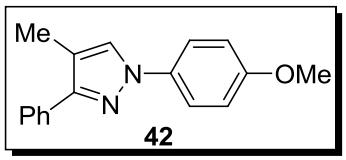
(dd, *J* = 3.08, 9.00 Hz, 1H), 3.86 (s, 3H), 3.83 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 154.2, 149.5, 145.1, 133.4, 131.9, 130.0, 128.9, 128.6, 128.4, 127.9, 126.8, 121.8, 113.9, 113.4, 110.1, 56.8, 56.1; MS (ESI): m / z calculated for $C_{23}H_{21}N_2O_2$ $(M + H)^+$: 357.15, found: 357.09.



41

1-(4-chlorophenyl)-4-methyl-3-phenyl-1H-pyrazole (41)

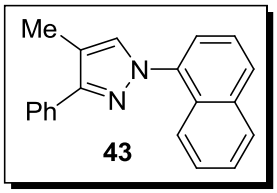
The typical procedure was followed using 60 mg of Z/E mixture of 3-azido-2-methyl-3-phenylacrylaldehyde **S18** (0.319 mmol, 1.1 equiv), 37 mg of 4-chloroaniline (0.290 mmol, 1.0 equiv), 5.4 μL of AcOH (0.087 mmol, 0.3 equiv), 2.0 mL of MeOH. 5.5 mg of CuI (0.029 mmol, 0.1 equiv), 41.0 μL of Et_3N (0.29 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **41** as an white solid (69 mg, 97%). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.80-7.77 (m, 2H) 7.73 (s, 1H), 7.67 (d, *J* = 8.79 Hz, 2H), 7.49-7.37 (m, 5H), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 152.0, 138.7, 133.7, 131.3, 129.5, 128.7, 127.7, 127.0, 129.7, 116.8, 10.4; MS (ESI): m / z calculated for $C_{16}H_{14}ClN_2$ $(M + H)^+$: 269.08, found: 268.94.



42

1-(4-methoxyphenyl)-4-methyl-3-phenyl-1H-pyrazole (42)

The typical procedure was followed using 223 mg of Z/E mixture of 3-azido-2-methyl-3-phenylacrylaldehyde **S18** (1.19 mmol, 1.1 equiv), 133 mg of 4-methoxyaniline (1.08 mmol, 1.0 equiv), 20.0 μL of AcOH (0.324 mmol, 0.3 equiv), 2.0 mL of MeOH. 21.0 mg of CuI (0.108 mmol, 0.1 equiv), 76.0 μL of Et_3N (0.54 mmol, 0.5 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **42** as an white solid (193 mg, 93%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.77 (d, *J* = 7.40 Hz, 2H), 7.61 (s, 1H), 7.59 (d, *J* = 8.92 Hz, 2H), 7.42 (t, *J* = 7.44 Hz, 2H), 7.32 (t, *J* = 7.40 Hz, 1H), 6.91 (d, *J* = 8.96 Hz, 2H), 3.77 (s, 3H), 2.27 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 158.0, 151.2, 134.1, 128.6, 127.7, 127.6, 127.3, 120.4, 115.9, 114.6, 55.6, 10.4; MS (ESI): m / z calculated for $C_{17}H_{17}N_2O$ $(M + H)^+$: 265.13, found: 265.11.

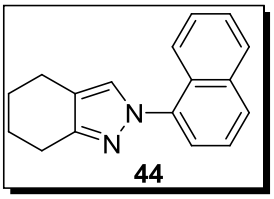


43

4-methyl-1-(naphthalen-1-yl)-3-phenyl-1H-pyrazole (43)

The typical procedure was followed using 206 mg of Z/E mixture of 3-azido-2-methyl-3-phenylacrylaldehyde **S18** (1.10 mmol, 1.1 equiv), 143 mg of 1-naphthylamine (1.00 mmol, 1.0 equiv), 20.0 μL of AcOH (0.30 mmol, 0.3 equiv), 2.0 mL of MeOH. 19.0 mg of CuI (0.10 mmol, 0.1 equiv), 70.0 μL of Et_3N (0.50 mmol, 0.5 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1

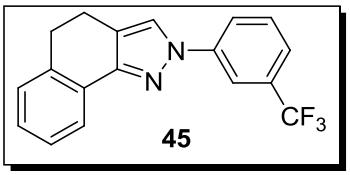
afforded **43** as a dark yellow oil (173 mg, 89%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.02-8.00 (m, 1H), 7.92-7.88 (m, 2H), 7.83 (d, *J* = 7.64 Hz, 2H), 7.63 (s,1H), 7.58 (d, *J* = 7.24 Hz, 1H), 7.54-7.50 (m, 3H), 7.44 (t, *J* = 7.52 Hz, 2H), 7.35 (t, *J* = 7.28 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 151.5, 137.6, 134.6, 134.2, 132.4, 129.2, 128.8, 128.7, 128.3, 127.9, 127.8, 127.3, 126.8, 125.4, 123.8, 123.1, 115.2, 10.5; MS (ESI): m / z calculated for $C_{20}H_{17}N_2$ $(M + H)^+$: 285.13, found: 285.01.



44

2-(naphthalen-1-yl)-4,5,6,7-tetrahydro-2H-indazole (44)

The typical procedure was followed using 39 mg of 2-azidocyclohex-1-enecarbaldehyde **S19** (0.261 mmol, 1.1 equiv), 34 mg of 1-naphthylamine (0.237 mmol, 1.0 equiv), 4.4 µL of AcOH (0.071 mmol, 0.3 equiv), 2.0 mL of MeOH. 4.6 mg of CuI (0.024 mmol, 0.1 equiv), 33.0 µL of Et_3N (0.237 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **44** as a slightly yellow oil (48 mg, 81%). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.99-7.95 (m, 1H), 7.88-7.82 (m, 2H), 7.50-7.46 (m, 5H), 2.83 (t, *J* = 6.00 Hz, 2H), 2.66 (t, *J* = 6.21 Hz, 2H), 1.92-1.80 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 150.9, 137.9, 134.4, 129.1, 128.7, 128.3, 128.1, 127.0, 126.5, 125.2, 123.7, 122.9, 117.1, 23.7, 20.8; MS (ESI): m / z calculated for $C_{17}H_{17}N_2$ $(M + H)^+$: 249.13, found: 249.10.



45

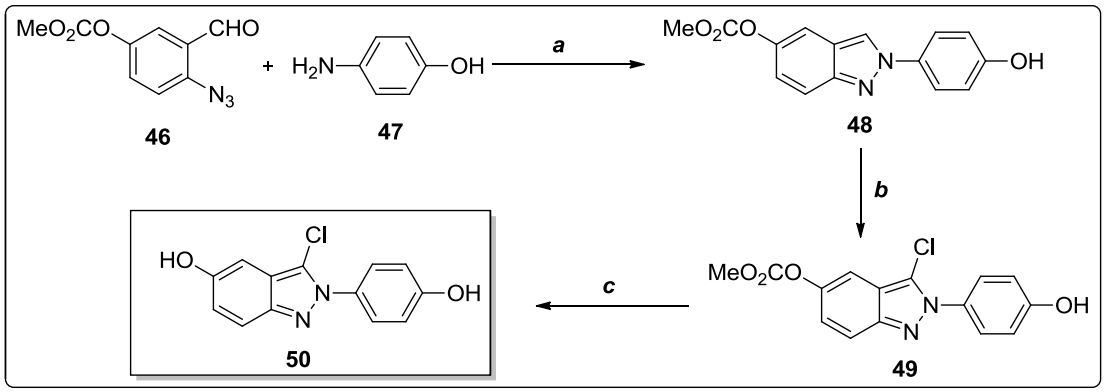
2-(3-(trifluoromethyl)phenyl)-4,5-dihydro-2H-benzo[g]indazole (45)

The typical procedure was followed using 59 mg of 1-chloro-3,4-dihydronaphthalene-2-carbaldehyde **S20** (0.298 mmol, 1.2 equiv), 31.0 µL of 3-(trifluoromethyl)aniline (0.248 mmol, 1.0 equiv), 4.6 µL of AcOH (0.074 mmol, 0.3 equiv), 2.0 mL of MeOH. 4.8 mg of CuI (0.025 mmol, 0.1 equiv), 35.0 µL of Et_3N (0.248 mmol, 1.0 equiv), crushed 4Å molecular sieves and 2.0 mL of THF was used in the next step. Purification by column chromatography with hexanes:EtOAc/20:1 afforded **45** as a slightly yellow solid (68 mg, 88%). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) 8.03-7.98 (m, 2H), 7.92 (d, *J* = 7.86 Hz, 1H), 7.75 (s, 1H), 7.59-7.48 (m, 2H), 7.35-7.29 (m, 1H), 7.27-7.25(m, 2H), 2.99 (m, 2H), 2.86 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 150.55, 140.82, 137.20, 131.9 (q, J_{CF} = 32.4 Hz, CH), 130.1, 129.3, 128.6, 128.3, 127.1, 125.9, 123.3, 122.9, 122.2 (d, J_{CF} = 3.0 Hz, CH), 121.32, 119.73, 115.4, 29.5, 19.3; MS (ESI): m / z calculated for $C_{18}H_{14}F_3N_2$ $(M + H)^+$: 315.10, found: 314.99.

VI. Application: Synthesis of Selective Ligand for Estrogen Receptor β

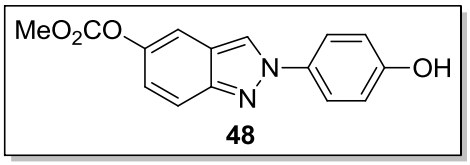
The procedure mainly contains three-step independent reactions from the starting material *o*-azidobenzaldehyde **46 (S5)** (***Condition a, b and c***).

General synthetic route to Selective Ligand for Estrogen Receptor β



Detailed procedures were below:

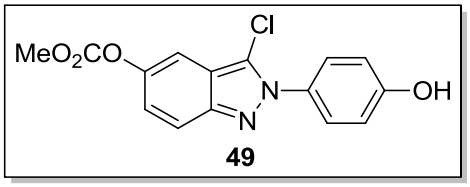
A. Preparation of 48 (Indazole formation: *Condition a*)



Step1: To a solution of ortho-azidobenazldehyde **46** (60 mg, 0.271 mmol, 1.05 equiv) in 2.5 mL anhydrous MeOH was added p-aminophenol **47** (28.2 mg, 0.258 mmol, 1.0 equiv) and dropwised AcOH (4.4 μL , 0.0774 mmol, 0.3 equiv). The resulting mixture was stirred at ambient temperature for 2 h. The solution was evaporated to give the crude product, which was further dried in vaccum.

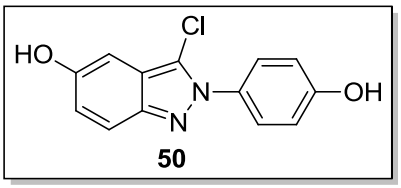
Step2: To the unpurified schiff base, 2.0 mL of THF, crushed 4Å molecular sieves (100 wt%), CuI (4.9 mg, 0.0258 mmol, 0.1 equiv) and TMEDA (19.3 μL, 0.129 mmol, 0.5 equiv) was added. The resulting mixture was heated to 40℃. After 2 h, the reaction mixture was cooled to room temperature, and the heterogenous mixture was filtered through SiO_2. The filtrate was concentrated in vacuo. Purification by column chromatography provided **48** as an white solid (31 mg, 42%). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.25 (s, 1H), 7.77 (d, *J* = 9.32 Hz, 1H), 7.62 (d, *J* = 8.84 Hz, 2H), 7.47 (d, *J* = 2.04 Hz, 1H), 7.12 (dd, *J* = 2.04, 9.28 Hz, 1H), 6.86 (d, *J* = 8.80 Hz, 2H), 5.76 (s, 1H), 3.94 (s, 3H); ^{13}NMR (DMSO-d_6, 75 MHz): δ (ppm) 157.9, 154.6, 147.3, 146.1, 132.6, 122.6, 122.5, 122.2, 122.1, 119.1, 116.5, 111.6, 55.9; MS (ESI): m / z calculated for $C_{15}H_{13}N_2O_4$ $(M + H)^+$: 285.08, found: 285.16.

B. Preparation of 49 (Chlorination: *Condition b*)[13]



To a solution of 31 mg of **48** (0.109 mmol, 1.0 equiv) in 2.0 mL of anhydrous THF was added 15 mg of N-chlorosuccinimide (0.109 mmol, 1.0 equiv). The resulting solution was stirred at 40℃ for 2 h under argon.After cooling to ambient temperature, most of the solvent was removed under vaccum. Saturated NH_4Cl solution was added and extracted with EtOAc (×3). The combined organic layer was dried over Na_2SO_4, filtered and evaporated to give the crude product. Purification by column chromatography afforded **49** as an white solid (30 mg, 85%). ^{1}H-NMR (DMSO-d_6, 300 MHz): δ (ppm) 10.08 (s, 1H), 7.72 (d, J = 9.30 Hz) 7.49-7.46 (m, 3H), 7.22 (dd, J = 2.07, 9.27 Hz, 1H), 6.95 (d, J = 8.73 Hz, 2H), 3.82 (s, 3H); ^{13}C NMR (DMSO-d_6, 75 MHz): δ (ppm) 159.0, 154.4, 146.7, 146.1, 129.9, 127.7, 123.9, 120.0, 119.9, 118.8, 116.2, 109.9, 56.0; MS (ESI): m / z calculated for $C_{15}H_{12}ClN_2O_4$ $(M + H)^+$: 319.04, found: 319.12.

C. Preparation of 50 (Deprotection: *Condition c*)[13]



50

To a 30 mg of **49** (0.094 mmol, 1.0 equiv) in 3.0 mL of THF/H_2O (2:1) was added 37.6 mg of NaOH (0.94 mmol, 10.0 equiv) in 0.5 mL of water. After 0.5 h, 1M HCl was added to make the pH ≈ 4.0. The aqueous layer was extracted with DCM (×3). The combined organic layer was dried over Na_2SO_4, filtered and evaporated to give the crude product. Purification by column chromatography afforded **50** as an white solid (25 mg, 95%). ^{1}H-NMR (DMSO-d_6, 300 MHz): δ (ppm) 9.97 (s, 1H), 9.55 (s, 1H), 7.52 (d, J = 9.21 Hz, 1H), 7.42 (d, J = 8.76 Hz, 2H), 6.97-6.89 (m, 3H), 6.67 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz): δ (ppm) 158.6, 153.4, 144.5, 130.3, 127.5, 127.4, 120.0, 116.3, 116.1, 116.0, 97.6. MS (ESI): m / z calculated for $C_{13}H_9ClN_2O_2$ $(M + H)^+$: 261.04, found:261.08.

VII. References.

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