Electronic Supplementary Information

Continuous-flow photo-induced decarboxylated annulative access to fused Imidazole derivatives *via* Ruthenium immobilized microreactor

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EXPERIMENTAL SECTION:

1) General Information:

All the reagents, chemicals and common laboratory solvents (LR grade) were purchased from Sigma-Aldrich or Alfa Aesar or TCI chemicals through domestic suppliers and were used as received without any further purification unless otherwise not mentioned. Analytical thin layer chromatography (TLC) was performed with E. Merck silica gel 60 F aluminium plates and visualized under UV 254 nm radiation. NMR spectra were measured with 300 MHZ, 500 MHZ spectrometer at RT in CDCl₃. Chemical shifts are reported in δ units, parts per million (ppm) downfield from TMS. Coupling constants (*J*) are in hertz (Hz) and are unadjusted; therefore, due to limits in resolution, in some cases there are small differences (<1 Hz) in the measured *J* value of the same coupling constant determined from different signals. Splitting patterns are designed as follows: s, singlet; d, doublet; t, triplet; dd, doublet of doublets; m, multiplet; High-resolution mass spectra (HR-MS) were recorded using Q-TOF multimode source.

Silicon wafer (100) (p-type, dopant: boron), AZ 1512 positive photoresist, SU-8negative photoresist were purchased from Semi-Materials Co. Ltd, AZ Electronic Materials, Micro Chem Newton MA, respectively, and curing agent (Sylgard 184) were purchased from Dow Corning (Midland, MI, USA). Allylhydridopolycarbosilane (AHPCS, SMP-10) was provided from Starfire System(USA). PDMS (Sylgard 184) BTES (3-bormopropyltriethoxysilane) and thermal initiator (Dicumyl peroxide) were purchased from Sigma Aldrich, USA. Photoinitiator (Irgacure 369) was purchased from Ciba Specialty Chemicals Inc., Switzerland. Sodium hydroxide and ammonia solution (28.0-30.0%) were purchased from Sigma Aldrich, USA. Flexible white LED strip was purchased from MANILED (Korea) and the light intensity was measured by digital illuminance/light meter (LX1330B). High resolution SEM images were taken by JSM-7800F Prime with Dual EDS, Platinum sputtering, at pressure ranging between 1 and 0.1 Pa, was implemented prior to SEM experiments.

Generally, reactions were run under open atmosphere. Acme's silica gel (230-400 mesh) was used for column chromatography (approximately 20 gr per one gram of crude material). For all compounds, we have determined the ¹H and ¹³C NMR spectrum. For unknown compounds, we have included HRMS data along with ¹H and ¹³C NMR.

2) Experimental procedures:

a) Preparation of phenacyl azides:¹

General experimental procedure for the synthesis of phenacyl azides: All the phenacyl azides were synthesized from corresponding α -bromo ketones and sodium azide using reported procedure.¹

To a stirred solution of sodium azide (0.65g, 10 mmol) in 20 mL of acetone–water (2:1, v/v) or DMSO was added 2-bromo-1-arylethanone (3 mmol) at room temperature. After 2 h of stirring, the mixture was poured onto ice–water (100g) and extracted with ethyl acetate (3×50 mL). The combined organic phases were dried (Na₂SO₄), filtered and evaporated in vacuum to yield corresponding 2-azido-1-arylethanone.

Note: These organic azides are potentially explosive substances and may easily decompose. They should not be heated when concentrating. The azides should be stored in dark and at low temperature in a refrigerator.

Scheme S1.



b) Preparation of α-azidochalcones:²

Phenacyl azide (0.5 mmol), aldehyde (0.5 mmol), piperidinium acetate (0.5 mmol) and MeOH (5 mmol) were taken in a 10 mL round bottom flask and stirred until the reaction was complete (12-24h). Next, the reaction mixture was concentrated under reduced pressure and extracted with EtOAc/water. The organic layer was dried over anhydrous sodium sulphate and concentrated to yield crude product which was sufficiently pure for further reactions. In some cases, additional purification was done by crystallization or column chromatography.

Scheme S2.



Figure S1: Imidazole-containing some medicinally important drugs



c) Preparation of Ru-P4VP complex:

Slightly modified the reported procedure.³ P4VP (Mn, P4VP: 5000 g mol⁻¹) (100 mg,) was dissolved in DMF (5 mL). Then, RuCl₃·2H₂O (5 mg) was added. The solution was stirred over night at room temperature. Once the reaction was completed, then formation of precipitate was observed and then centrifuge the reaction mixture with little amount of THF and 20 ml of hexane. The filtered precipitate was centrifuge for several times. Then filtered the solution and collected the brown red colored compound as Ru-P4VP complex.

d) Decarboxylative annulation of L-proline with α -azidochalconesin batch (3a-3t):

In a 5 mL snap vial equipped with magnetic stirring bar the Ru-P4VP complex (2 mg), L-proline **1** (1 equiv.) and α -azidochalcone **2** (1 equiv.) were dissolved in 2 mL of DMSO (0.20 M) then slowly added the DABCO (3 equiv.) to the reaction mixture. The resulting reaction mixture was irradiated with flexible CFL light for white LED light source at room temperature with cooling by fan. The progress of the reaction was monitored by TLC. After completion, the reaction mixture was transferred to a separating funnel, diluted with ethyl acetate and washed with 15 mL of water. The aqueous layer was washed three times with ethyl acetate. The combined organic layers were dried over Na₂SO₄, filtered and

concentrated in vacuum. Purification of the crude product was achieved by column chromatography using petrol ether/ethyl acetate as an eluent.



Table S1. Screening of catalyst and solvent for visible-light-induced decarboxylative annulation^a

^{*a*}Reaction conditions: All reactions were carried out on 1 equiv. scale of **1** and 1 equiv. of **2a**, 2 mg of Ru-PV4P Complex and 3 equiv. of DABCO and 2 mL of DMSO was used. All the cases apart from product **3a**, ^{*b*}Isolated yields of chromatographically pure products.

e) Reusablity of Ru⁺³-P4VP complex catalyst:

After the reaction, Ru⁺³-P4VP complex catalyst was recovered from the reaction mixture by a simple filtration method then washed with THF and hexane to remove residual products or unreacted substrates, and dried in vacuum. The resulted catalyst was stable up to six cycles without significant loss of catalytic efficiency as shown in **Table S2 and Figure S2**.

Table S2: Recyclability of the catalyst



Figure S2: Reusability graph



ICP-OES analysis:

Reaction was carried out on 1 equiv. scale of 1 and 1 equiv. of 2a, 2 mg of Ru-PV4P Complex and 3 equiv. of DABCO and 2 mL of DMSO in batch condition. After completion, the reaction mixture was centrifuge with little amount of THF and 10 ml of hexane. The filtered precipitate was centrifuge for several times and dry it. Again we have conducted one more fresh experiment with recovered catalyst from the first reaction and after the completion of reaction we have followed the same centrifuge procedure as mentioned in the first reaction. In this manner we have tested three cycles. Then we conducted the ICP-OES analysis for the ruthenium catalyst before the reaction and after the three cycles recovered catalyst. The results were presented in **figure S2a**.

Figure S2a: ICP-OES analysis



Date: 30-12-2019.

Registrion No	118057059
Sample Submitted by	Praveen Kumar Reddy Adiyala
Supervisor	Praveen Kumar Reddy Adiyala
Project Name and Code/Division	HCP-0011/ Catalysis & Fine Chemicals

Results:

S.No	Sample Code	Ru (mg/l)
1	Empty	0.0003
2	Before Reaction	0.0085
3	After Reaction	0.0029

12017

Analyzed by

Scientist-in-charge

(3) Fabrication of Ru⁺³-P4VP immobilized PDMS microreactor:

The following steps has been adopted for the fabrication of Ru⁺³-P4VP immobilized PDMS microreactor:

a) Fabrication of PDMS microreactor: PDMS microreactor (as shown in Figure S3) was fabricated by simple photo-lithography and soft-lithography. The 3 inch size of Si wafer was washed with acetone/ethanol and dried with nitrogen flow. A SU-8 50 (Microchem) negative photoresist was spin coated on Si wafer with 100 μ m thickness. The photoresist Si wafer was soft baked at 75 °C for 10 min followed by 105 °C for 30 min. Then UV (4.5 mW/cm²) was irradiated on the baked Si wafer for 3 min. After UV treatment, the wafer was post baked at 75 °C for 1 min followed by 105 °C for 3 min. Finally, the cured SU-8 was developed with SU-8 developer for 5 min and washed with isopropanol and water and dried with nitrogen flow. The SU-8 pattern was poured with a PDMS (Sylgard 184) and curing agent (10:1, w/w) in a petri dish. The trapped air in the PDMS mixture was removed under vacuum desiccator then thermally cured in an oven at 80 °C for 2 h. The cured PDMS was peeled off and made an inlet/outlet by punching needle to joint tubing.

Figure S3. Top view images of PDMS microchannel with 500 μ m channel width by (a) optical microscope and (b) SEM, (c) cross-sectional SEM image of PDMS channel with 100 um height.



b) Fabrication of solvent-resistant PDMS channel:⁴ The allylhydridopolycarbosilane (AHPCS) was on PDMS channel to improve the solvent resistivity. The prepared PDMS channel and a flat PDMS plate were first treated with O_2 plasma prior to AHPCS resin coating step to strengthen the adhesion between PDMS and AHPCS. The coating AHPCS resin was prepared by mixing with dicumyl peroxide (thermal curing agent) and Irgacure 369 (photocuring agent) (100:1:1, w/w). After spin coating (2000 rpm, 30 sec) to become 8-13 μ m thickness,⁵ excess AHPCS from the PDMS channel was removed gently by a slide glass blade. Then, both PDMS channel and flat PDMS plate were attached together and irradiated with

UV light (4.5 mWcm⁻²) for 30 min followed by baking at 120 °C for 2 h. The tubing was connected to inlet and outlet with help of epoxy adhesive.

c) Immobilization of Ru catalyst-P4VP (Mn, P4VP: 5000 g mol⁻¹) over the PDMS channel:⁶ To get – OH functional group on the channel, the AHPCS surface was hydrolyzed by flowing 5% NaOH solution to the channel for 3 h then washed with water and ethanol. The channel was dried with nitrogen flow connected with Schlenk line. To get -Br functional group on the channel, a 10% (3-bromopropyl) trimethoxysilane (Br-PTMS, Sigma-aldrich) solution in anhydrous acetonitrile was infused to the channel at 60 °C for 3 h by the syringe pump. The channel was washed with anhydrous acetonitrile and dried by nitrogen flow. After surface modification to -Br surface, the P4VP polymer was immobilized by quaternization reaction between Br functionalized surface and terminal pyridine of P4VP. A 1.0 w% P4VP solution in anhydrous DMF was infused to the channel at room temperature for 3 h. The unreacted polymer was washed with fresh DMF. Finally, to immobilize Ru³⁺ metal ion over the P4VP block, a RuCl₃ solution (0.1 wt %) in DMF was infused to the channel at room temperature for 1 h. (Figure S4), The channel was washed with fresh DMF to remove unbounded metal ions The images of PDMS microreactor before and after the immobilization of catalyst as shown in Figure S5. The distribution of the metal ions throughout the channel surface was analysed by energy-dispersive X-ray spectroscopy (EDX). SEM images and EDX mapping images are depicted in the Figure S6. The amount of Ru⁺³ ions immobilized into channel was determined by comparing the induced coupled plasma-mass spectroscopy (ICP-MS) of initial and final concentration of Ru⁺³ solution infused.

Figure S4: Immobilization of Ru⁺³ catalyst using poly(4-vinylpyridine) over AHPCS-coated PDMS microreactor



Immobilization of Ru catalyst using poly(4-vinyl pyridine) over PDMS microchannel

Micro reactor dimension (length 1meter, , width 500 μ m, height 100 μ m)

Figure S5. Images of (a) bare PDMS microreactor and (b) Ru immobilized AHPCS coated PDMS microreactor.





Figure S6. (a) HR-SEM image of PDMS microchannel with 500 mm width, EDS mapping images of (b) Si K, (c) Ru K, (d) Cl K element in the selected area.



4) Visible-light-induced continuous-flow synthesis of fused imidazoles in Ruthenium immobilized PDMS microreactor:

In an oven-dried glass vial Ru-P4VP complex (2 mg), L-proline **1** (1 equiv.) and α -azidochalcone **2** (1 equiv.) were dissolved in 2 mL of DMSO (0.20 M) then slowly added DABCO (3 equiv.) to the reaction mixture. The solutions were transferred into 5 mL NORM-JECT plastic syringes and introduced into the ruthenium immobilized PDMS micro reactor through a syringe pump (as shown in **FigureS7** and **SchemeS3**). The flow rate was set to 20μ Lmin⁻¹, thus resulting in 2 min of residence time. After reaching steady state, a product sample was collected at the end of PDMS reactor in a vial. The volume collected was measured and the sample was then diluted with water and extracted with ethyl acetate (x 3). The organic layer was washed with brine, dried with Na₂SO₄ and evaporated under reduced pressure. The resulting crude compound was absorbed on silica gel and purified via column chromatography (EtOAc/Hexane). The isolated compound was analysed by NMR.

Figure S7. Experimental set-up of photocatalysed continuous-flow reaction through ruthenium immobilized PDMS micro reactor under light source.



Scheme S3: Scheme of continuous-flow decarboxylative annulation of L-proline with α -azidochalcones in a Ru⁺³ immobilized PDMS micro reactor



5) Additional experiments to support the mechanism:

Scheme S4: Visible-Light and Ru-P4VP complex mediated decomposition of α -azidochalcone 2 to 2*H*-azirine 4



Scheme S5: Radical Trapping Experiment.



Scheme S6: Formation of 2*H*-azirine 4



Scheme S6a: Control experiments in oxygen and nitrogen atmosphere:



Fluorescence quenching studies:

The absorbance intensities were recorded on a UV-visible absorption spectrophotometer. To know the quenching phenomenon of ruthenium catalyst, we have performed the UV-visible absorption spectra in DMSO with 1X 10⁻⁵ M. The samples were prepared by mixing Ru-P4VP complex (1 mg) and different amount of DABCO in DMSO (total volume = 1 mL) in a light path quartz fluorescence cuvette. For each quenching experiment, 1 mL of 1 stock solution was titrated to Ru-P4VP complex (1 mg). Then the absorbance intensities were presented shown in **Figure a in S8**.

The absorbance intensities were recorded on a UV-visible absorption spectrophotometer. To know the quenching phenomenon of ruthenium catalyst, we have performed the UV-visible absorption spectra in DMSO with 1X 10⁻⁵ M. The samples were prepared by mixing Ru-P4VP complex (1 mg) and different amount of α -azidochalcone **2a** in DMSO (total volume = 1 mL) in a light path quartz fluorescence cuvette. For each quenching experiment, 1 mL of 1 stock solution was titrated to Ru-P4VP complex (1 mg). Then the absorbance intensities were presented shown in **Figure b in S8**.

The absorbance intensities were recorded on a UV-visible absorption spectrophotometer. To know the quenching phenomenon of ruthenium catalyst, we have performed the UV-visible absorption spectra in DMSO with 1X 10⁻⁵ M. The samples were prepared by mixing Ru-P4VP complex (1 mg) and different amount of L-proline **1** in DMSO (total volume = 1 mL) in a light path quartz fluorescence cuvette. For each quenching experiment, 1 mL of 1 stock solution was titrated to Ru-P4VP complex (1 mg). Then the absorbance intensities were presented shown in **Figure c in S8**.

These results reveals that L-proline was found to be viable quencher to Ru. But oxygen is the good quencher when compared to L-proline.



Figure S8: Quenching study: Fluorescence quenching of Ruthenium in presence of different amounts of DABCO, α -azidochalcone and L-proline respectively.

6) Spectral data of all compounds:

(2-(4-chlorophenyl)-2*H*-azirin-3-yl)(4-methoxyphenyl)methanone (4m)



¹**H NMR** (500 MHz, CDCl₃) δ 8.22 – 8.18 (m, 2H), 7.24 – 7.20 (m, 2H), 7.07 – 7.03 (m, 2H), 6.98 – 6.95 (m, 2H), 3.85 (s, 3H), 3.37 (s, 1H). ¹³**C NMR** (126 MHz, CDCl₃) δ 180.15, 165.62, 164.86, 137.55, 133.53, 132.12, 128.53, 127.66, 127.57, 114.59, 55.68, 36.69.

(4-methoxyphenyl)(2-(4-nitrophenyl)-6,7-dihydro-5*H*-pyrrolo[1,2-a]imidazol-3-yl)methanone 3a:



3a: 60% ethyl acetate in petroleum ether to afford the product as a light yellow solid, ¹HNMR (500 MHz, **CDCl₃**): δ 2.54-2.62 (m, 2H), 2.85 (t, 2H, *J* = 7.5, 7.5 Hz), 2.61 (s, 3H), 4.26 (t, 2H, *J* = 7.2, 7.2 Hz), 6.68 (d, 2H, *J* = 8.8 Hz), 7.51 (d, 2H, *J* = 8.8 Hz), 7.60 (d, 1H, *J* = 8.8 Hz), 7.99 (d, 2H, *J* = 8.8 Hz). ¹³C NMR (151 MHz, CDCl₃): δ 185.40, 162.57, 157.35, 136.00, 132.59, 132.47, 132.27, 131.44, 130.30, 129.19, 126.81, 123.61, 112.87, 55.07, 46.44, 25.99, 23.46. HRMS (ESI, Orbitrap) m/z calcd for C₂₀H₁₇N₃O₄[M]⁺ is 363.1219 and found 363.1220.

(2-(4-nitrophenyl)-6,7-dihydro-5*H*-pyrrolo[1,2-a]imidazol-3-yl)(phenyl)methanone 3b:



3b:60% ethyl acetate in petroleum ether to afford the product as a white solid, ¹HNMR (600 MHz, CDCl₃): δ 2.69-2.75 (m, 2H), 3.03 (t, 2H, J = 7.7, 7.7 Hz), 4.34 (t, 2H, J = 7.2, 7.2 Hz), 7.17 (t, J = 7.8, 2H), 7.35-7.39 (m, 1H), 7.41 (d, 2H, J = 8.8 Hz), 7.55-7.57 (m, 2H), 7.92 (d, 2H, J = 8.8 Hz). ¹³C NMR (151 MHz, CDCl₃): δ 186.55, 157.79, 149.95, 146.89, 140.73, 137.28, 132.72, 129.84, 129.32, 128.37, 125.48, 122.73, 46.51, 26.00, 23.49. HRMS (ESI, Orbitrap) m/z calcd for C₁₉H₁₅N₃O₃ [M]⁺ is 333.1113 and found 333.1109.

4-(3-(4-chlorobenzoyl)-6,7-dihydro-5H-pyrrolo[1,2-a]imidazol-2-yl)benzonitrile 3c :



3c: 65% ethyl acetate in petroleum ether to afford the product as a white solid, ¹HNMR (500 MHz, **CDCl₃**): δ 2.68-2.75 (m, 2H), 3.02 (t, 2H, J = 7.2, 7.2 Hz), 4.32 (t, 2H, J = 7.2, 7.2 Hz), 7.16 (d, 2H, J = 8.5 Hz), 7.36 (d, 2H, J = 8.5 Hz), 7.41 (m, 2H), 7.50 (d, 2H, J = 8.6 Hz). ¹³C NMR (151 MHz, CDCl₃): δ 185.19, 158.34, 139.24, 138.70, 135.70, 131.60, 130.89, 129.83, 128.51, 125.20, 118.60, 111.32, 46.55, 26.06, 23.34. HRMS (ESI, Orbitrap) m/z calcd for C₂₀H₁₄ClN₃O [M]⁺ is 347.0825 and found 347.0825.

(4-chlorophenyl)(2-(4-nitrophenyl)-6,7-dihydro-5*H*-pyrrolo[1,2-a]imidazol-3-yl)methanone 3d :



3d: 50% ethyl acetate in petroleum ether to afford the product as a yellow solid, ¹HNMR (500 MHz, **CDCl₃**): δ 2.69-2.76 (m, 2H), 3.03 (t, 2H, J = 7.7, 7.7 Hz), 4.32 (t, 2H, J = 7.2, 7.2 Hz), 7.17 (d, 2H, J = 8.6 Hz), 7.44 (d, 2H, J = 8.9 Hz), 7.53 (d, 2H, J = 8.6 Hz), 7.98 (d, 2H, J = 8.9 Hz). ¹³C NMR (151 MHz, **CDCl₃**): δ 185.19, 158.35, 150.00, 146.98, 140.58, 139.37, 135.69, 130.89, 129.93, 128.59, 125.42,

123.10, 46.53, 25.98, 23.50.HRMS (ESI, Orbitrap) m/z calcd for $C_{19}H_{14}ClN_3O_3$ [M]⁺ is 367.0724 and found 367.0727.

(4-methoxyphenyl)(2-(2-nitrophenyl)-6,7-dihydro-5*H*-pyrrolo[1,2-a]imidazol-3-yl)methanone 3e:



3e: 60% ethyl acetate in petroleum ether to afford the product as a yellowish semi solid, ¹HNMR (500 MHz, CDCl₃): δ 2.58-2.65 (m, 2H), 2.88 (t, 2H, J = 7.6, 7.6 Hz), 3.64 (s, 3H), 4.28 (t, 2H, J = 7.2, 7.2 Hz), 6.51 (d, 2H, J = 8.7 Hz), 6.89 (d, 1H, J = 7.5 Hz), 7.11 (t, 1H, J = 7.4, 7.6), 7.19 (t,1H, J = 6.9, 7.4), 7.58 (d, 2H, J = 8.7 Hz), 7.67 (d, 1H, J = 7.9 Hz). ¹³C NMR (151 MHz, CDCl₃): δ 184.74, 162.80, 157.79, 148.77, 147.95, 133.30, 131.49, 131.43, 130.27, 129.86, 128.38, 125.57, 123.81, 113.02, 55.24, 46.34, 25.88, 23.33. HRMS (ESI, Orbitrap) m/z calcd for C₂₀H₁₇N₃O₄ [M]⁺ is 363.1219 and found 363.1220.

4-(3-(4-methoxybenzoyl)-6,7-dihydro-5*H*-pyrrolo[1,2-a]imidazol-2-yl)benzonitrile 3f:



3f:60% ethyl acetate in petroleum ether to afford the product as a light red solid, ¹HNMR (500 MHz, **CDCl₃**): δ 2.66-2.73 (m, 2H), 3.02 (t, 2H, *J* = 7.5, 7.8 Hz), 3.78 (s, 3H), 4.28 (t, 2H, *J* = 7.2, 7.2 Hz), 6.67 (d, 2H, *J* = 8.9 Hz), 7.38-7.43 (m, 4H), 7.57 (d, 2H, *J* = 8.9 Hz). ¹³C NMR (151 MHz, CDCl₃): δ 185.33, 163.48, 157.57, 149.23, 138.99, 131.97, 131.52, 129.81, 129.63, 125.48, 118.79, 113.45, 110.73, 55.42, 46.23, 25.95, 23.44. HRMS (ESI, Orbitrap) m/z calcd for C₂₁H₁₇N₃O₂ [M]⁺ is 343.1321 and found 343.1320.

(2-(4-chlorophenyl)-6,7-dihydro-5H-pyrrolo[1,2-a]imidazol-3-yl)(phenyl)methanone 3g :



3g: 60% ethyl acetate in petroleum ether to afford the product as a light red semi solid, ¹HNMR (600 MHz, CDCl₃): δ 2.66-2.72 (m, 2H), 3.00 (t, 2H, J = 7.7, 7.8 Hz), 4.32 (t, 2H, J = 7.2, 7.2 Hz), 7.02 (d, 2H, J = 8.5 Hz), 7.14-7.18 (m, 4H), 7.36 (t, 1H, J = 7.4, 7.4 Hz), 7.54 (d, 2H, J = 7.2 Hz). ¹³C NMR (151 MHz, CDCl₃): δ 187.04, 157.84, 137.54, 133.62, 132.87, 132.29, 130.59, 129.47, 128.87, 128.80, 127.98, 127.84, 124.84, 46.73, 25.85, 23.44.HRMS (ESI, Orbitrap) m/z calcd for C₁₉H₁₅ClN₂O [M]⁺ is 322.0873 and found 322.08729.

(2-(4-bromophenyl)-6,7-dihydro-5*H*-pyrrolo[1,2-a]imidazol-3-yl)(4-methoxyphenyl)methanone 3h:



3h: 50% ethyl acetate in petroleum ether to afford the product as a yellowish solid, ¹HNMR (500 MHz, **CDCl**₃): δ 2.57-2.64 (m, 2H), 2.92 (t, 2H, *J* = 7.4, 7.9 Hz), 3.71 (s, 3H), 4.21 (t, 2H, *J* = 7.3, 7.4 Hz), 6.59 (d, 2H, *J* = 8.9 Hz), 7.09 (d, 2H, *J* = 8.54 Hz), 7.16 (d, 1H, *J* = 8.5 Hz), 7.22 (d, 1H, *J* = 8.5 Hz), 7.50 (d, 2H, *J* = 8.8 Hz). ¹³C NMR (151 MHz, CDCl₃): δ 185.61, 163.23, 157.37, 150.69, 133.49, 131.95, 131.84, 130.90, 130.81, 129.98, 128.97, 124.80, 121.71, 113.35, 55.44, 46.27, 25.95, 23.49. HRMS (ESI, Orbitrap) m/z calcd for C₂₀H₁₇BrN₂O₂ [M]⁺ is 396.0473 and found 396.0476.

(2-(2-bromophenyl)-6,7-dihydro-5*H*-pyrrolo[1,2-a]imidazol-3-yl)(4-methoxyphenyl)methanone 3i:



3i: 60% ethyl acetate in petroleum ether to afford the product as a yellowish semi solid, ¹HNMR (600 MHz, CDCl₃): δ 2.59-2.67 (m, 2H), 2.95 (t, 2H, *J* = 7.62, 7.78 Hz), 3.65 (s, 3H), 4.31 (t, 2H, *J* = 7.17, 7.17 Hz), 6.48 (d, 2H, *J* = 8.85 Hz), 6.90-6.93 (dd, 1H, *J* = 7.78, 7.62 Hz), 7.01-7.05 (dd, 1H, *J* = 7.47,

7.62 Hz), 7.14 (q, 1H), 7.29 (q, 1H), 7.44 (d, 2H, J = 8.69 Hz). ¹³C NMR (151 MHz, CDCl₃): δ 185.44, 162.57, 157.29, 150.60, 136.13, 132.59, 132.47, 131.54, 130.30, 129.19, 126.81, 125.98, 123.69, 112.66, 55.26, 46.44, 25.99, 23.53. HRMS (ESI, Orbitrap) m/z calcd for C₂₀H₁₇BrN₂O₂ [M]⁺ is 396.0473 and found 396.0476.

(4-chlorophenyl)(2-(4-chlorophenyl)-6,7-dihydro-5*H*-pyrrolo[1,2-a]imidazol-3-yl)methanone 3k:



3k: 65% ethyl acetate in petroleum ether to afford the product as a white solid, ¹HNMR (500 MHz, **CDCl₃**): δ 2.58-2.66 (m, 2H), 2.93 (t, 2H, *J* = 7.6, 7.8 Hz), 4.24 (t, 2H, *J* = 7.2, 7.2 Hz), 7.01 (d, 2H, *J* = 8.5 Hz), 7.06-7.12 (m, 4H), 7.42 (d, 2H, *J* = 8.5 Hz). ¹³C NMR (151 MHz, CDCl₃): δ 185.33, 158.06, 152.00, 138.67, 135.85, 133.98, 132.68, 130.85, 130.60, 128.26, 128.01, 124.56, 46.50, 25.89, 23.50. HRMS (ESI, Orbitrap) m/z calcd for C₁₉H₁₄Cl₂N₂O [M]⁺ is 356.0483 and found is 356.0483.

(2-(4-bromophenyl)-6,7-dihydro-5*H*-pyrrolo[1,2-a]imidazol-3-yl)(phenyl)methanone 31:



31: 60% ethyl acetate in petroleum ether to afford the product as a red semi solid, ¹HNMR (600 MHz, **CDCl₃**): δ 2.65-2.71 (m, 2H), 2.99 (t, 2H, J = 7.7, 7.9 Hz), 4.31 (t, 2H, J = 7.2, 7.2 Hz), 7.10 (d, 2H, J = 8.5 Hz), 7.14-7.19 (m, 4H), 7.36 (t, 1H, J = 7.4, 7.4 Hz), 7.53 (d, 2H, J = 7.1). ¹³C NMR (151 MHz, **CDCl₃**): δ 186.81, 157.82, 151.88, 137.49, 133.28, 132.27, 130.84, 130.75, 129.43, 127.97, 124.80, 121.86, 46.51, 25.90, 23.48. HRMS (ESI, Orbitrap) m/z calcd for C₁₉H₁₅BrN₂O [M]⁺ is 366.0368 and found 366.0367.

(2-(4-chlorophenyl)-6,7-dihydro-5*H*-pyrrolo[1,2-a]imidazol-3-yl)(4-methoxyphenyl)methanone 3m:



3m:70% ethyl acetate in petroleum ether to afford the product as a red semi solid, ¹HNMR (500 MHz, **CDCl₃**): δ 2.63-2.73 (m, 2H), 2.99 (t, 2H, *J* = 7.6, 7.8 Hz), 3.78 (s, 3H), 4.30 (t, 2H, *J* = 7.2, 7.3 Hz), 6.66 (d, 2H, *J* = 8.5 Hz), 7.08 (d, 2H, *J* = 8.68 Hz), 7.25-7.19 (m, 2H), 7.57 (d, 2H, *J* = 8.5 Hz); ¹³C NMR (151 MHz, CDCl₃): δ 185.63, 163.23, 157.37, 150.73, 133.47, 133.07, 131.97, 130.54, 130.05, 127.97, 124.83, 113.36, 55.43, 46.29, 25.96, 23.51. HRMS (ESI, Orbitrap) m/z calcd for C₂₀H₁₇ClN₂O₂ [M]⁺ is 352.0979 and found 352.0980.

(4-chlorophenyl)(2-(3,4,5-trimethoxyphenyl)-6,7-dihydro-5*H*-pyrrolo[1,2-a]imidazol-3-yl)methanone 3n :



3n: 90% ethyl acetate in petroleum ether to afford the product as a yellowish semi solid, ¹HNMR (500 MHz, CDCl₃): δ 2.66-2.73 (m, 2H), 3.01 (t, 2H, *J* = 7.6, 7.7 Hz), 3.62 (s, 6H), 3.77 (s, 3H), 4.34 (t, 2H, *J* = 7.2, 7.1 Hz), 6.55 (s, 2H), 6.68 (d, 2H, *J* = 8.8 Hz), 7.62 (d, 2H, *J* = 8.54 Hz). ¹³C NMR (151 MHz, CDCl₃): δ 185.32, 157.92, 152.77, 138.57, 138.46, 136.27, 130.87, 128.15, 124.45, 107.17, 61.00, 55.98, 46.67, 25.93, 23.63. HRMS (ESI, Orbitrap) m/z calcd for C₂₂H₂₁ClN₂O₄ [M]⁺ is 412.1190 and found 412.1187.

(2-(3,5-dimethoxyphenyl)-6,7-dihydro-5*H*-pyrrolo[1,2-a]imidazol-3-yl)(4-methoxyphenyl)methanone 30:



30:80% ethyl acetate in petroleum ether to afford the product as a yellowish solid, ¹HNMR (**500** MHz, **CDCl**₃): δ 2.63-2.71 (m, 2H), 3.00 (t, 2H, *J* = 7.3, 8.0 Hz), 3.57 (s, 6H), 3.77 (s, 3H), 4.29 (t, 2H, *J* = 7.1, 7.2 Hz), 6.25 (t, 1H, *J* = 2.3, 2.3 Hz), 6.48 (d, 2H, *J* = 2.2 Hz), 6.68 (d, 2H, *J* = 8.9 Hz), 7.63 (d, 2H, *J* = 8.8 Hz). ¹³C NMR (**151** MHz, CDCl₃): δ 185.67, 163.11, 160.17, 157.12, 151.87, 136.18, 131.92, 130.40, 124.72, 113.23, 107.19, 101.37, 55.39, 55.22, 46.28, 25.92, 23.55. HRMS (ESI, Orbitrap) m/z calcd for C₂₂H₂₂N₂O₄[M]⁺ is 378.1579 and found 378.1580.

(4-chlorophenyl)(2-(3,5-dimethoxyphenyl)-6,7-dihydro-5*H*-pyrrolo[1,2-a]imidazol-3-yl)methanone 3p:



3p:80% ethyl acetate in petroleum ether to afford the product as a red semi solid, ¹HNMR (500 MHz, **CDCl₃**): δ 2.64-2.72 (m, 2H), 3.00 (t, 2H, *J* = 7.7, 7.8 Hz), 3.60 (s, 6H), 4.33 (t, 2H, *J* = 7.2, 7.2 Hz), 6.28 (t, 1H, *J* = 2.3, 2.3 Hz), 6.38 (d, 2H, *J* = 2.2 Hz), 7.14 (d, 2H, *J* = 8.5 Hz), 7.51 (d, 2H, *J* = 8.4 Hz). ¹³C **NMR (151 MHz, CDCl₃):** δ 185.42, 160.25, 157.89, 138.42, 136.26, 135.81, 130.77, 128.08, 124.56, 107.62, 105.27, 101.20, 55.26, 46.57, 25.89, 23.57. HRMS (ESI, Orbitrap) m/z calcd for C₂₁H₁₉ClN₂O₃ [M]⁺ is 382.1084 and found 382.1084.

(4-methoxyphenyl)(2-phenyl-6,7-dihydro-5H-pyrrolo[1,2-a]imidazol-3-yl)methanone 3q:



3q:80% ethyl acetate in petroleum ether to afford the product as a purple solid, ¹HNMR (500 MHz, **CDCl₃**): δ 2.60-2.72 (m, 2H), 2.93-3.02 (m, 2H), 3.73 (s, 3H), 4.23-4.33 (m, 2H),6.56-6.67(m,2H),7.06-7.15 (m, 3H),7.23-7.33 (m, 2H),7.53-7.61 (m, 2H). ¹³C NMR (151 MHz, CDCl₃): δ 185.72, 162.86, 157.23, 152.21, 134.44, 131.92, 130.12, 129.32, 127.69, 127.42, 124.62, 113.06, 55.25, 46.18, 25.87, 23.46. HRMS (ESI, Orbitrap) m/z calcd for C₂₀H₁₈N₂O₂ [M]⁺ is 318.1368 and found 318.1367.

(4-methoxyphenyl)(2-(p-tolyl)-6,7-dihydro-5*H*-pyrrolo[1,2-a]imidazol-3-yl)methanone 3r:



3r: 70% ethyl acetate in petroleum ether to afford the product as a white solid, ¹HNMR (500 MHz, **CDCl₃**): δ 2.23 (s, 3H), 2.61-2.69 (m, 2H), 2.98 (t, 2H, *J* = 7.3, 8.0 Hz), 3.74 (s, 3H), 4.28 (t, 2H, *J* = 7.2, 7.2 Hz), 6.62 (d, 2H, *J* = 8.9 Hz), 6.90 (d, 2H, *J* = 7.8 Hz), 7.18 (d, 2H, *J* = 8.9 Hz), 7.59 (d, 2H, *J* = 8.9 Hz). ¹³C NMR (151 MHz, CDCl₃): δ 185.94, 162.89, 157.19, 137.20, 131.98, 131.60, 130.25, 129.23, 128.45, 127.37, 124.52, 112.97, 55.18, 46.22, 25.91, 23.46, 21.11. HRMS (ESI, Orbitrap) m/z calcd for C₂₁H₂₀N₂O₂[M]⁺ is 332.1525 and found 332.1525.

(4-chlorophenyl)(2-(p-tolyl)-6,7-dihydro-5H-pyrrolo[1,2-a]imidazol-3-yl)methanone 3s:



3s: 60% ethyl acetate in petroleum ether to afford the product as a yellow semi solid, ¹HNMR (500 MHz, **CDCl₃**): δ 2.25 (s, 3H), 2.64-2.71 (m, 2H), 2.99 (t, 2H, J = 7.5, 7.9 Hz), 4.32 (t, 2H, J = 7.2, 7.2 Hz), 6.89 (d, 2H, J = 7.8 Hz), 7.07-7.11 (m, 4H), 7.47 (d, 2H, J = 8.5 Hz). ¹³C NMR (151 MHz, CDCl₃): δ 185.57, 157.93, 153.84, 138.11, 137.80, 130.84, 129.33, 129.15, 128.44, 127.97, 127.34, 124.32, 46.45, 25.84, 23.51, 21.09. HRMS (ESI, Orbitrap) m/z calcd for C₂₀H₁₇ClN₂O [M]⁺ is 336.1029 and found 336.1029.

7) Reference:

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8) Copies of ¹H/¹³C NMR Spectra:

¹H NMR spectrum of compound 4m



¹H spectra of compound 3a





¹H spectra of compound 3b







¹H spectra of compound 3c



¹H spectra of compound 3d



100 90 f1 (ppm) ò 150 140

¹H spectra of compound 3e







¹H spectra of compound 3f



13C spectra of compound 3f





13C spectra of compound 3g



¹H spectra of compound 3g

¹H spectra of compound 3h



13C spectra of compound 3h



¹H spectra of compound 3i



13C spectra of compound 3i







13C spectra of compound 3k









¹H spectra of compound 3m



13C spectra of compound 3m



¹H spectra of compound 3n



¹H spectra of compound 30



¹H spectra of compound 3p







¹H spectra of compound 3q



13C spectra of compound 3q



¹H spectra of compound 3r



13C spectra of compound 3r



¹H spectra of compound 3s

