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Supplementary Information

Base-Controlled Copper-Catalyzed Cascade Multi-Component Reactions of Cyanamides, Diaryliodonium Triflates and Propargylamine for Rapid Assembly of Polysubstituted 2-aminoimidazoles and 2-iminomidazoles

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1. General Information

All starting materials were purchased from commercial sources and used as received. The base and solvents were obtained from commercial suppliers, the solvents and liquid bases were dried using 4 Å molecular sieves. The copper and palladium catalysts were purchased from Shanghai Aladdin Biochemical Technology Co., Ltd in China. Merck silica gel thin-layer chromatography was used to monitor reaction process. Silica gel preparative TLC plate purchased from Shanxiesser Biotechnology Co., Ltd. in China was used to purify reaction product (Developing solvent: EtOAc/petroleum ether = 1/1-3/1, petroleum ether/EtOAc/ EtOH/Et₃N = 20/1/1/1-10/1/1/1).

NMR spectra were recorded on a Bruker Advance NEO spectrometer at 400 MHz (¹H)) and 100 MHz (¹³C), residual solvent peaks (CDCl₃: δ = 7.26, 77.16) were used as an internal reference. Chemical shifts (δ) were reported in ppm, and coupling constants (J) were given in Hertz (Hz). The multiplicities were reported as: s = singlet, d = doublet, t = triplet, q = quadruplet, sept = septuplet, m = multiplet, bs = broad signal. The isomers of 2-aminoimidazoles were indentified by ¹H-¹H NOESY spectra, and their ratios were quantified by ¹H NMR. High resolution mass spectra (HRMS) were recorded by Shimadzu LCMS-IT-TOF mass spectrometer using ESI-TOF techniques. Fourier transform infrared (FTIR) spectra were performed on a Bruker T27 spectrometer in 4000-400 cm⁻¹ range with KBr pellets.

2. Associated schemes and discussion



Scheme S1. Previous method of synthesis of 2-aminoimidazoles.

To point out 1,3,5-trisubstituted 2-iminoimidazoles (5) was resulted from C-N coupling of 1,5disubstituted 2-aminoimidazoles (4) with diaryliodonium triflates or in-situ generated aryliodides, the control experiments were performed (Scheme S2). The reaction of di(*p*-tolyl)iodonium triflate proceeded rapidly to produce **5a** in high yield (> 90%) under simulative optimal reaction conditions within 2 h (Scheme S2a), but the reaction of *p*-tolyliodide rarely produced **5a** with recovery of most **4a** (Scheme S2b). Additionally, the C-N coupling with di(*p*-tolyl)iodonium triflate rarely took place without copper (Scheme S2a). Phenylation product was hardly detected as adding phenyliodide into the reaction system of *p*-tolylcyanamide, di(*p*-tolyl)iodonium triflate, and propargylamine under the standard reaction conditions (Scheme S2c), confirming the C-N coupling of in-situ generated aryliodide hardly occurred. Therefore, 1,3,5-trisubstituted 2-iminoimidazoles was resulted from the cascade four-component reaction of cyanamides, diaryliodonium triflates, propargylamine, and diaryliodonium triflates via sequential guanidination/hydroamination/C-N coupling with promotion of pyridine. This copper-catalyzed C-N coupling of diaryliodonium triflates with 2aminoimidazoles should be a highly efficient method for the synthesis of N-aryl 2-aminoimidazoles.





The large scale synthesis of 1,5-disubstituted 2-aminoimidazoles (4) and 1,3,5-trisubstituted 2iminoimidazoles (5) was demonstrated to be feasible by the cascade reactions of *p*-tolylcyanamide, di(*p*-tolyl)iodonium triflate, and propargylamine (Scheme S3). The desired products 4a and 5a were obtained in 49% and 5% yields for the K₂CO₃-accelerated cascade reaction on a 5 mmol scale, respectively. The 5a was produced in 40% yield via the pyridine-promoted four-component cascade reaction on a 3.75 mmol scale, accompanying with the formation of 4a in



16% yield. This ratio of 5a/4a (2.5/1) was much lower than that (9.4/1) achieved on a 0.15 mmol, showing the C-N coupling of 4a with di(*p*-tolyl)iodonium triflate dramatically slowed down comparing to guanidination and hydroamination in a large scale reaction.

The effect of counter anions was evaluated using commercially available diphenyliodonium tetrafluoroborate and chloride (Scheme S4a). The four-component cascade reaction of tetrafluoroborate afforded corresponding product **5b** with lower yields comparing the corresponding triflate. While the chloride was employed, no desired product was observed and the intermediate **4b** was rarely generated. Thus, the counter anion imposed great influence on the cascade reaction as the first step guanidination was subjected to the oxidative addition of counter anion to Cu (I).¹



Scheme S4. Effect of counter anion on the four-component cascade reaction (a) and atom-economical reaction of di(*p*-tolyl)iodonium triflate (b).

The atom-economical three-component reaction of diaryliononium triflates with cyanamides and propargylamine was also investigated under the relay catalysis of copper and palladium using K_2CO_3 as base. Brief investigation showed that this reaction failed to afford desired product as the Heck coupling of in-situ generated aryliodide rarely occurred accompanying with multiple side reactions even using different palladium catalysts (Scheme S4b).

As diaryliodonium could induce radical reaction,² the radical trapper (TEMPO and BHT) were added to the four-component cascade reaction for investigating the reaction mechanism (Scheme S5). The reaction provided decreased yields of desired product (**5a**) with these radical trappers. Moreover, the trapped product of *p*-tolyl radical was detected during the reaction with TEMPO, suggesting radical reaction occurred in the cascade process. It was demonstrated that TEMPO rarely imposed influence on the guanidination in our previous work.¹ Thus, the radical pathway should be mainly involved in the C-N coupling of 2-aminoimidazoles (**4**) with diaryliodonium triflates.



Scheme S5. Radical trap experiments.

References

1. J. Li, H. Wang, Y. Hou, W. Yu, S. Xu, and Y. C. Zhang, Eur. J. Org. Chem., 2016, 2388-2392.

2. S. M. Zeitler, P. Chakma and M. R. Golder, Chem. Sci., 2022, 13, 4131-4138.

3. Preparation of starting materials

A. The general procedures for preparation of cyanamides.

The cyanamides were synthesized through the substitution of cyanogen bromide with amines (J. Li, L. Neuville, Org. Lett., 2013, 15, 6124-6127.). Aromatic cyanamides were prepared in toluene using NaHCO₃ as base, and purified by silica gel column chromatography. Aliphatic cyanamides were prepared in Et_2O using excessive amount of aliphatic amines. The aliphatic cyanamides except benzylcyanamide were obtained by filtration and removal of the solvent in vacuo, and used without further purification. The benzylcyanamide was purified by silica gel column chromatography.

B. The general procedure for preparation of diaryliodonium triflates.

The diaryliodonium triflates were synthesized according to the reported methods in the literature (M. Bielawski, M. Zhu, B. Olofsson, Adv. Synth. Catal., 2007, 349, 2610-2618.). The reaction of arenes, I_2 (or aryliodides) and HOTf was performed in CH_2Cl_2 with *m*-Chloroperbenzoic acid as oxidant, the reaction mixture was concentrated under vacuum and recrystallized in Et₂O to obtain pure diaryliodonium triflates. The reaction mixture was washed by distilled water to remove excessive HOTf before concentration for recrystallization if necessary.

4. The general procedure for the synthesis of 2-aminoimidazoles and 2-iminoimidazoles.

A. The synthesis of 1,5-disubstituted 2-aminoimidazoles (4) through cooper-catalyzed threecomponent cascade reaction of cyanamides, diaryliodonium triflates and propargyl amine.

Cyanamide (0.2 mmol), diaryliodonium triflate (1.5 eq), K_2CO_3 (1.5 eq), 2,2 '- bipyridine (10 mmol%) and CuCl (10 mmol%) were quickly added into a round bottom sidearm flask (25 mL) under nitrogen atmosphere, evacuated and backfilled with nitrogen in balloon for four times. Then,

DMF (1.5 mL) and propargylamine (1.5 eq) were injected into the mixture, and the reaction mixture was stirred at 80 °C for 2 hours under nitrogen atmosphere. The obtained reaction mixture was cooled down to room temperature, quenched with H₂O, and extracted with EtOAc (3×10 mL). The combined EtOAc phase was washed with saturated NaCl solution, dried by anhydrous MgSO₄, and concentrated under reduced pressure to get crude product. The crude product was then purified by silica gel preparative TLC plate using developing solvent (EtOAc/petroleum ether = 1/1-3/1, petroleum ether/EtOAc/ EtOH/Et₃N = 20/1/1/1-10/1/1/1) to get the desired product.

B. The synthesis of 1,3,5-trisubstituted 2-iminoimidazoles (5) through four-component cascade reaction of cyanamides, diaryliodonium triflates, propargyl amine, and diaryliodonium triflates.

Cyanamide (0.2 mmol), diaryliodonium triflate (1.5 eq), 2,2 '- bipyridine (10 mmol%) and CuCl (10 mmol%) were quickly added into a round bottom sidearm flask (25 mL) under nitrogen atmosphere, evacuated and backfilled with nitrogen in balloon for four times. Then, DMF (1.5 mL), pyridine (1.5 eq) and propargylamine (1.5 eq) were injected into the mixture, and the reaction mixture was stirred at 80 °C for 2 hours under nitrogen atmosphere. The obtained reaction mixture was cooled down to room temperature, quenched with H₂O, and extracted with EtOAc (3 × 10 mL). The combined EtOAc phase was washed with saturated NaCl solution, dried by anhydrous MgSO₄, and concentrated under reduced pressure to get crude product. The crude product was purified by silica gel preparative TLC plate using developing solvent (EtOAc/petroleum ether = 1/1-3/1, petroleum ether/EtOAc/ EtOH/Et₃N = 20/1/1/1-10/1/1/1) to get the desired product.

C. The procedure for investigating copper and palladium relay catalyzed atom-economical three-component cascade reaction of diaryliononium triflates, cyanamides and propargylamine.

p-Tolylcyanamide (0.2 mmol), di(*p*-tolyl)iodonium triflate (1.5 eq), K_2CO_3 (3 eq), 2,2 'bipyridine (10 mmol%), CuCl (10 mmol%), and palladium catalyst (5 or 10 mmol%) were quickly added into a round bottom sidearm flask (25 mL) under nitrogen atmosphere, evacuated and backfilled with nitrogen in balloon for four times. Then, DMF (or toluene) (1.5 mL) and propargylamine (1.5 eq) were injected into the mixture, and stirred at 80 °C for 2 (6) hours under nitrogen atmosphere. The reaction was monitored by silica gel thin-layer chromatography.

Analytical data of 2-aminoimidazoles and 2-iminoimidazoles:



^{CH₃ 4a} 4a was prepared according to the general procedure **3A**, colorless waxy solid, 60% yield (33 mg) + 7% yield of **5a** (5 mg).

¹**H NMR** (400 MHz, CDCl₃): δ (ppm) 7.30 (d, *J* = 8.0 Hz, 2H), 7.16 (q, *J* = 8.0 Hz, 4 H), 7.01 (d, *J* = 4.0 Hz, 2 H), 6.61 (s, 1 H), 5.63 (br, 1 H), 2.42 (s, 3 H), 2.23 (s, 3 H), 1.97 (s, 3 H).

¹³**C NMR** (100 MHz, CDCl₃): δ (ppm) 144.12, 139.06, 138.68, 132.10, 130.57, 129.90, 129.33, 127.53, 123.90, 121.63, 116.48, 21.08, 20.48, 10.06.

IR: 3410.35 cm⁻¹, 2924.42 cm⁻¹, 2854.77 cm⁻¹, 1606.01 cm⁻¹, 1455.11 cm⁻¹, 1248.15 cm⁻¹, 817.11 cm⁻¹, 742.12 cm⁻¹, 506.26 cm⁻¹.

HRMS m/z (ES⁺): calcd for C₁₈H₂₀N₃ ([M+H]⁺): 278.1652, found 278.1651.



4b was prepared according to the general procedure **3A**, slightly yellow waxy solid, 60% yield (30 mg).

¹**H NMR** (400 MHz, CDCl₃): δ (ppm) 7.40-7.45 (m, 3 H), 7.11-7.22 (m, 6 H), 6.79 (*t*, *J* = 8.0 Hz, 1 H), 6.59 (s, 1 H), 5.62 (br, 1 H), 1.93 (s, 3 H).

¹³**C NMR** (100 MHz, CDCl₃): δ (ppm) 143.59, 141.31, 134.88, 130.00, 129.00, 128.92, 127.78, 124.16, 122.12, 120.63, 116.27, 10.16.

IR: 3305.98 cm⁻¹, 2923.28 cm⁻¹, 2852.86 cm⁻¹, 1672.75 cm⁻¹, 1459.93 cm⁻¹, 1162.26 cm⁻¹, 1031.33 cm⁻¹, 750.56 cm⁻¹, 694.35 cm⁻¹, 498.70 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{16}H_{16}N_3$ ([M+H]⁺) 250.1339, found 250.1340.



4c was prepared according to the general procedure 3A, colorless waxy solid, 44%

yield (36 mg).

¹**H** NMR (400 MHz, CDCl₃): δ (ppm) 7.65 (d, *J* = 8.0 Hz, 2 H), 7.28 (d, *J* = 12.0 Hz, 2 H), 7.10-7.16 (m, 4 H),

6.65 (s, 1 H), 2.00 (s, 3 H).

¹³**C NMR** (100 MHz, CDCl₃): δ (ppm) 142.99, 140.48, 133.75, 133.33, 131.79, 129.33, 124.56, 123.26, 122.47, 117.92, 112.86, 10.20.

IR: 3424.11 cm⁻¹, 2921.02 cm⁻¹, 2851.45 cm⁻¹, 1661.04 cm⁻¹, 1541.84 cm⁻¹, 1487.60 cm⁻¹, 1383.73 cm⁻¹, 1253.88 cm⁻¹, 1071.15 cm⁻¹, 820.78 cm⁻¹, 554.62 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{16}H_{14}Br_2N_3$ ([M+H]⁺) 407.9529, found 407.9526.



³ 4d Was prepared according to the general procedure **3A**, colorless waxy solid, 58%

yield (42 mg).

¹**H NMR** (400 MHz, CDCl₃): δ (ppm) 7.51 (d, *J* = 8.0 Hz, 2 H), 7.18-7.22 (m, 6 H), 6.63 (s, 1 H), 2.00 (s, 3 H), 1.37 (s, 9 H), 1.26 (s, 9 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 152.10, 144.40, 143.77, 138.39, 132.05, 127.24, 126.87, 125.68, 124.05, 121.25, 116.83, 34.77, 34.01, 31.38, 31.23, 10.24.

IR: 3251.91 cm⁻¹, 2960.54 cm⁻¹, 2867.79 cm⁻¹, 1668.18 cm⁻¹, 1598.53 cm⁻¹, 1516.44 cm⁻¹, 1265.01 cm⁻¹, 1112.91 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{24}H_{32}N_3([M+H]^+)$ 362.2591, found 362.2588.



 CH_3 **4e** and **4e'** were prepared according to the general procedure **3A**, slightly yellow waxy solid, 65% yield (38 mg, 4e/4e' = 1/2).

¹**H NMR** (400 MHz, CDCl₃): δ (ppm) 7.31 (d, *J* = 8.0 Hz, 0.67 H), 7.15-7.23 (m, 4.08 H), 7.00-7.03 (m, 2.84 H), 6.78 (d, *J* = 8.0 Hz, 0.76 H), 6.60-6.62 (d, *J* = 8.0 Hz, 1.00 H), 5.78 (br, 1.00 H), 3.86 (s, 2.00 H), 3.74 (s, 1.00 H), 2.43 (s, 1.00 H), 2.25 (s, 2.00 H), 1.97 (s, 3.00 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 159.81, 154.24, 144.84, 144.41, 139.10, 138.63, 134.50, 132.15, 130.61, 130.04, 129.39, 129.08, 127.60, 127.25, 124.16, 123.87, 121.41, 121.27, 118.70, 116.59, 115.13, 114.24, 55.50,

21.14, 20.54, 10.11, 10.09.

IR: 3419.55 cm⁻¹, 2924.37, 2853.75 cm⁻¹, 1668.43 cm⁻¹, 1513.06 cm⁻¹, 1247.72 cm⁻¹, 1107.53 cm⁻¹, 1037.53 cm⁻¹, 831.88 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{18}H_{20}N_3O$ ([M+H]⁺) 294.1601, found 294.1585.



4f and 4f' were prepared according to the general procedure

3A, colorless waxy solid, 68% yield (44 mg, 4f/4f' = 1/1).

¹H NMR (400 MHz, CDCl₃): δ (ppm) 7.32 (d, *J* = 8.0 Hz, 1.89 H), 7.15-7.20 (m, 3.90 H), 7.02 (d, *J* = 8.0 Hz, 1.94 H), 6.63 (s, 0.93 H), 2.68 (t, *J* = 8.0 Hz, 0.98 H), 2.51 (t, *J* = 8.0 Hz, 1.05 H), 2.43 (s, 1.58 H), 2.25 (s, 1.55 H), 1.99 (s, 3.00 H), 1.62 (m, 1.17 H), 1.43 (m, 1.05 H), 1.30 (m, 2.49 H), 0.96 (t, *J* = 8.0 Hz, 1.48 H), 0.89 (t, *J* = 8.0 Hz, 1.68 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 144.30, 144.05, 139.12, 138.81, 138.66, 135.34, 132.32, 132.21, 130.62, 130.12, 129.92, 129.41, 128.82, 127.63, 127.58, 124.03, 121.66, 121.62, 116.73, 116.69, 35.26, 34.81, 33.79, 33.36, 22.36, 22.20, 21.16, 20.56, 13.91, 10.19, 10.16.

IR: 3424.02 cm⁻¹, 2925.44 cm⁻¹, 2855.81 cm⁻¹, 1598.12 cm⁻¹, 1515.52 cm⁻¹, 1379.54 cm⁻¹, 1245.99 cm⁻¹, 1115.43 cm⁻¹, 818.83 cm⁻¹, 506.69 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{21}H_{26}N_3$ ([M+H]⁺) 320.2121, found 320.2121.



waxy solid, 56% yield (31 mg, 4g/4g' > 10/1) was obtained for 4g.

¹**H NMR** (400 MHz, CDCl₃): δ (ppm) 7.34-7.41 (m, 3.11 H), 7.19-7.22 (m, 3.03 H), 7.02 (d, *J* = 8.0 Hz, 2.01 H), 6.67 (s, 0.95 H), 5.57 (br, 0.94 H), 2.25 (s, 3.00 H), 2.05 (s, 2.98 H), 1.90 (s, 2.97 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 144.08, 138.33, 137.26, 133.48, 131.58, 130.28, 129.74, 129.39, 128.93, 127.47, 123.44, 121.53, 116.88, 20.55, 17.20, 9.78.

IR: 3290.41 cm⁻¹, 2923.45 cm⁻¹, 2854.61 cm⁻¹, 1668.28 cm⁻¹, 1549.50 cm⁻¹, 1378.11 cm⁻¹, 1246.57 cm⁻¹, 1117.01 cm⁻¹, 1042.06 cm⁻¹, 809.08 cm⁻¹, 504.09 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{17}H_{18}N_3([M+H]^+)$ 278.1652, found 278.1651.



 CH_3 4h CH_3 4h' 4h and 4h' were prepared according to the general procedure 3A, colorless waxy solid, 57% yield (32 mg, 4h/4h' = 1.4/1).

¹**H** NMR (400 MHz, CDCl₃): δ (ppm) 7.40 (t, *J* = 8.0 Hz, 0.44 H), 7.27-7.32 (m, 1.56 H), 7.10-7.20 (m, 2.02 H), 7.01-7.08 (m, 3.45 H), 6.63-6.70 (m, 1.55 H), 5.75 (br, 0.89 H), 2.43 (s, 1.74 H), 2.41 (s, 1.25 H), 2.28 (s, 1.73 H), 2.25 (s, 1.26 H), 1.99 (s, 3.00 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 144.21, 143.81, 141.16, 140.22, 139.16, 138.77, 138.54, 134.77, 132.15, 130.62, 130.22, 129.81, 129.76, 129.40, 128.79, 128.39, 127.57, 124.80, 124.14, 123.91, 121.68, 121.57, 121.49, 116.95, 116.85, 113.56, 21.49, 21.26, 21.15, 20.55, 10.15.

IR: 3243.58 cm⁻¹, 2923.20 cm⁻¹, 2859.12 cm⁻¹, 1670.69 cm⁻¹, 1549.80 cm⁻¹, 1250.77 cm⁻¹, 1044.07 cm⁻¹, 818.52 cm⁻¹, 508.85 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{18}H_{20}N_3$ ([M+H]⁺) 278.1652, found 278.1649.



 CH₃ 4i
 4i and 4i' were prepared according to the general procedure 3A, slightly yellow waxy solid, 49% yield (30 mg, 4i/4i' < 1/10) was obtained for 4i'.</td>

¹**H** NMR (400 MHz, CDCl₃): δ (ppm) 7.24 (d, *J* = 8.0 Hz, 2.06 H), 7.00-7.02 (m, 4.15 H), 6.70 (s, 0.97 H), 5.76 (br, 0.93 H), 2.35 (s, 3.07 H), 2.24 (s, 3.06 H), 1.98 (s, 6.04 H), 1.86 (s, 3.00 H).

¹³**C NMR** (100 MHz, CDCl₃): δ (ppm) 143.72, 139.51, 138.00, 137.11, 130.54, 129.60, 129.49, 129.36, 122.63, 21.09, 20.58, 17.47, 9.49.

IR: 3417.60 cm⁻¹, 2922.95 cm⁻¹, 2855.32 cm⁻¹, 1598.89 cm⁻¹, 1549.68 cm⁻¹, 1375.99 cm⁻¹, 1244.52 cm⁻¹, 1041.54 cm⁻¹, 809.88 cm⁻¹, 503.07 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{20}H_{24}N_3$ ([M+H]⁺) 306.1965, found 306.1957.



4j and **4j**' were prepared according to the general procedure **3A**, colorless

waxy solid, 55% yield (32 mg, 4j/4j' < 1/10) was obtained for 4j'.

¹**H** NMR (400 MHz, CDCl₃): δ (ppm) 7.24 (d, *J* = 8.0 Hz, 1.86 H), 7.20 (s, 1.01 H), 7.15 (d, *J* = 8.0 Hz, 1.14 H), 7.09 (d, *J* = 8.0 Hz, 1.19 H), 7.03 (d, *J* = 8.0 Hz, 2.13 H), 6.65 (s, 1.02 H), 2.41 (s, 3.01 H), 2.25 (s, 3.08 H), 2.00 (s, 3.13 H), 1.90 (s, 3.00 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 139.79, 138.50, 136.90, 132.28, 130.80, 130.04, 129.41, 128.67, 128.17, 121.73, 116.58, 21.15, 20.56, 17.13.

IR: 3418.57 cm⁻¹, 2923.39 cm⁻¹, 2855.63 cm⁻¹, 1598.61 cm⁻¹, 1549.77 cm⁻¹, 1378.20 cm⁻¹, 1242.30 cm⁻¹, 1041.51 cm⁻¹, 815.38 cm⁻¹, 504.21 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{19}H_{22}N_3([M+H]^+)$ 292.1808, found 292.1808.



 CH_3 4k and 4k' were prepared according to the general procedure 3A, slightly yellow waxy solid, 59% yield (34 mg, 4k/4k' = 2.5/1).

¹**H NMR** (400 MHz, CDCl₃): δ (ppm) .7.44-7.69 (m, 2.71 H), 7.20-7.32 (m, 2.32 H), 7.94-7.13 (m, 3.45 H), 6.17 (br, 0.73 H), 5.88 (br, 0.27 H), 2.41 (s, 2.16 H), 2.21 (s, 0.87 H), 1.98-1.99 (m, 3.00 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 143.98, 142.29, 139.38, 139.07, 136.22, 132.29, 132.14, 131.74, 131.10, 130.77, 130.64, 130.39, 129.56, 129.39, 127.37, 124.99, 124.14, 123.62, 123.05, 122.03, 120.10, 118.90, 118.67, 117.32, 116.73, 113.90, 112.49, 21.08, 20.45, 10.26, 10.03.

IR: 3337.70 cm⁻¹, 2923.62 cm⁻¹, 2859.06 cm⁻¹, 2230.28 cm⁻¹, 1665.12 cm⁻¹, 1443.43 cm⁻¹, 1150.49 cm⁻¹, 1044.28 cm⁻¹, 791.31 cm⁻¹, 687.16 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{18}H_{17}N_4([M+H]^+)$ 289.1448, found 289.1448.



 C_{H_3} **4** C_{H_3} **4** and **4** were prepared according to the general procedure **3**A, slightly yellow waxy solid, 59% yield (37 mg, **4**/**4** = 2/1).

¹**H** NMR (400 MHz, CDCl₃): δ (ppm) 8.01 (d, *J* = 8 Hz, 0.31 H), 7.79-7.85 (m, 1.07 H), 7.48-7.62 (m, 1.02 H), 7.40-7.46 (m, 1.09 H), 7.31-7.34 (m, 2.20 H), 7.15 (d, *J* = 8.0 Hz, 1.39 H), 7.08 (d, *J* = 8.0 Hz, 0.57 H), 6.98 (d, *J* = 8.0 Hz, 0.66 H), 6.65 (d, *J* = 8.0 Hz, 0.93 H), 2.58 (s, 1.00 H), 2.54 (s, 2.17 H), 2.43 (s, 2.09 H), 2.22 (s, 0.94 H), 1.99 (s, 3.00 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 198.38, 196.64, 149.06, 144.02, 143.21, 141.73, 139.37, 139.03, 138.67, 137.61, 136.92, 135.66, 132.20, 131.90, 130.73, 130.24, 129.42, 129.27, 128.52, 127.52, 124.45, 124.12, 122.93, 121.93, 120.65, 120.59, 116.67, 115.47, 26.63, 26.60, 20.50, 10.26, 10.07.

IR: 3261.48 cm⁻¹, 2857.47 cm⁻¹, 1600.38 cm⁻¹, 1550.98 cm⁻¹, 1443.20 cm⁻¹, 1286.62 cm⁻¹, 1176.92 cm⁻¹, 911.21 cm⁻¹, 1042.98 cm⁻¹, 815.56 cm⁻¹, 544.09 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{19}H_{20}N_3O$ ([M+H]⁺) 306.1601, found 306.1600.

$$NHSO_2CH_3$$

 NH
 NH
 $N-$
 CH_3 4m

4m were prepared according to the general procedure 3A, colorless waxy solid, 39%

yield (28 mg).

¹**H NMR** (400 MHz, CDCl₃): δ (ppm) 7.27-7.32 (m, 3.12 H), 7.16 (d, *J* = 8 Hz, 1.96 H), 7.06 (t, *J* = 8 Hz, 1.16 H), 6.78 (d, *J* = 8 Hz, 1.97 H), 6.62 (s, 1.03 H), 2.77 (s, 3.06 H), 2.43 (s, 3.04 H), 1.98 (s, 3.00 H).

¹³**C NMR** (100 MHz, CDCl₃): δ (ppm) 143.07, 139.33, 138.47, 131.87, 130.61, 129.92, 127.45, 125.09, 121.64, 112.39, 111.53, 107.44, 38.66, 21.16, 10.18.

IR: 3256.08 cm⁻¹, 2924.67 cm⁻¹, 2222.35 cm⁻¹, 1549.71 cm⁻¹, 1413.27 cm⁻¹, 1328.72 cm⁻¹, 1112.41 cm⁻¹, 979.11 cm⁻¹, 732.15 cm⁻¹, 518.33 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{18}H_{21}N_4O_2S$ ([M+H]⁺) 357.1380, found 357.1383.



 4m'
 4m'were prepared according to the general procedure 3A, colorless waxy solid, 17%

 yield (12 mg).

¹**H NMR** (400 MHz, d6-DMSO): δ (ppm) 10.00 (s, 1.01 H), 7.82 (s, 0.96 H), 7.49 (t, *J* = 8 Hz, 1.03 H), 7.27 (d, *J* = 8 Hz, 1.15 H), 7.08-7.15 (m, 3.99 H), 6.94 (d, *J* = 8 Hz, 1.96 H), 6.59 (s, 0.97 H), 3.01 (s, 3.08 H), 2.17 (s, 2.83 H), 1.96 (s, 3.00 H).

¹³C NMR (100 MHz, d6-DMSO): δ (ppm) 144.09, 141.17, 139.93, 136.33, 130.88, 129.38, 128.17, 124.33, 123.30, 122.36, 119.87, 118.77, 116.31, 40.60, 40.39, 40.18, 20.67, 10.68, 9.02.

IR: 3343.39 cm⁻¹, 2923.71 cm⁻¹, 1654.49 cm⁻¹, 1480.80 cm⁻¹, 1328.57 cm⁻¹, 1149.08 cm⁻¹, 968.75 cm⁻¹, 807.54 cm⁻¹, 510.16 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{18}H_{21}N_4O_2S$ ([M+H]⁺) 357.1380, found 357.1377.



4n 4n and 4n' were prepared according to the general procedure 3A,

slightly yellow waxy solid, 47% yield (30 mg, 4n/4n' = 1.2/1).

¹**H** NMR (400 MHz, CDCl₃): δ (ppm) 8.12 (d, *J* = 8 Hz, 0.45 H), 7.95 (s, 0.42 H), 7.81 (d, *J* = 12 Hz, 0.52 H), 7.66 (d, *J* = 4 Hz, 0.50 H), 7.57-7.61 (m, 0.47 H), 7.48-7.54 (m, 1.01 H), 7.27-7.34 (m, 1.57 H), 7.11-7.17 (m, 2.00 H), 7.02 (d, *J* = 4 Hz, 0.94 H), 6.66 (s, 0.97 H), 3.93 (s, 1.39 H), 3.86 (s, 1.61 H), 2.44 (s, 1.61 H), 2.24 (s, 1.44 H), 2.00 (s, 3.00 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 167.08, 165.71, 144.11, 143.20, 141.47, 139.35, 138.72, 135.33, 132.20, 132.11, 131.92, 130.71, 130.58, 130.33, 130.07, 129.94, 129.15, 128.87, 127.52, 124.47, 124.04, 122.27, 121.87, 121.55, 120.47, 117.09, 116.85, 52.47, 52.01, 21.14, 20.53, 10.21, 10.09.

IR: 3244.15 cm⁻¹, 2923.62 cm⁻¹, 1669.71 cm⁻¹, 1551.34 cm⁻¹, 1449.09 cm⁻¹, 1330.18 cm⁻¹, 1226.68 cm⁻¹, 1109.13 cm⁻¹, 810.82 cm⁻¹, 734.18 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{19}H_{20}N_3O_2([M+H]^+)$ 322.1550, found 322.1550.



40 and 40' were prepared according to the general procedure 3A,

slightly yellow waxy solid, 58% yield (36 mg, 40/40' = 1/5). Only ¹H NMR and ¹³C NMR data of 40' was reported here.

¹**H** NMR (400 MHz, CDCl₃): δ (ppm) 7.20 (d, *J* = 8.0 Hz, 2.26 H), 7.10 (d, *J* = 8.0 Hz, 2.07 H), 7.01 (d, *J* = 8.0 Hz, 2.27 H), 6.76 (d, *J* = 8.0 Hz, 1.89 H), 6.59 (s,1.03 H), 3.02 (s, 6.00 H), 2.24 (s, 3 H), 1.96 (s, 3.05 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 150.61, 150.54, 144.68, 144.60, 138.46, 138.39, 130.26, 129.49, 129.41,

128.63, 128.55, 124.57, 122.44, 122.37, 120.39, 120.31, 116.98, 116.90, 112.74, 112.67, 40.32, 20.56, 10.06.

IR: 3431.94 cm⁻¹, 2923.42 cm⁻¹, 2857.42 cm⁻¹, 2217.23 cm⁻¹, 1608.09 cm⁻¹, 1523.81 cm⁻¹, 1354.81 cm⁻¹, 1231.82 cm⁻¹, 817.02 cm⁻¹, 501.70 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{19}H_{23}N_4([M+H]^+)$ 307.1917, found 307.1918.

H₃COCHN



4p were prepared according to the general procedure **3A**, colorless waxy solid, 20%

yield (13 mg).

¹**H NMR** (400 MHz, CDCl₃): δ (ppm) 7.30-7.33 (m, 4.17 H), 7.14-7.16 (m, 4.23 H), 6.58 (s, 1.03 H), 2.43 (s, 3.17 H), 2.07 (s, 3.07 H), 1.98 (s, 3.00 H).

¹³C NMR (100 MHz, d6-DMSO): δ (ppm) 168.50, 144.03, 139.30, 137.65, 131.98, 131.63, 130.70, 127.56, 124.30, 121.42, 121.26, 117.05, 24.17, 21.17, 10.13.

IR: 3098.97 cm⁻¹, 2924.55 cm⁻¹, 1608.44 cm⁻¹, 1515.27 cm⁻¹, 1376.76 cm⁻¹, 1246.07 cm⁻¹, 1039.63 cm⁻¹, 822.71 cm⁻¹, 759.37 cm⁻¹, 515.48 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{19}H_{21}N_4O([M+H]^+)$ 321.1710, found 321.1715.



4p' were prepared according to the general procedure 3A, colorless waxy solid,

48% yield (31 mg).

¹**H NMR** (400 MHz, d6-DMSO): δ (ppm) 10.14 (s, 1.04 H), 7.70 (d, *J* = 8 Hz, 2.03 H), 7.55 (s, 0.93 H), 7.23 (d, *J* = 12 Hz, 2.01 H), 7.10 (d, *J* = 8 Hz, 2.08 H), 6.91 (d, *J* = 8 Hz, 2.03), 6.55 (s, 0.97 H), 2.16 (s, 3.00 H), 2.07 (3.10 H), 1.93 (3.00 H).

¹³C NMR (100 MHz, d6-DMSO): δ (ppm) 168.53, 143.73, 141.15, 139.28, 129.76, 128.84, 128.114, 127.29, 124.18, 121.92, 119.55, 115.51, 40.14, 24.03, 20.19, 10.18.

IR: 3423.22 cm⁻¹, 2857.45 cm⁻¹, 2125.85 cm⁻¹, 2001.46 cm⁻¹, 1542.85 cm⁻¹, 1257.45 cm⁻¹, 1005.54 cm⁻¹, 762.54 cm⁻¹, 625. 06 cm⁻¹.

HRMS m/z (ES⁺): calcd for C₁₉H₂₁N₄O ([M+H]⁺) 321.1710, found 321.1711.



CH₃⁴⁴ CH₃⁴⁴ 4q and 4q'were prepared according to the general procedure 3A, colorless waxy solid, 36% yield (20 mg, 4q/4q' < 1/10) was obtained for 4q'.

¹**H NMR** (400 MHz, CDCl₃): δ (ppm) 7.22 (d, *J* = 8 Hz, 2.27 H), 7.02-7.04 (m, 4.01 H), 6.76 (d, *J* = 8 Hz, 1.85 H), 6.60 (s, 1.21 H), 2.25 (s, 3.00 H), 1.97 (s, 3. 15 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 147.19, 144.53, 138.65, 129.98, 129.42, 128.97, 124.80, 124.24, 121.12, 116.57, 115.73, 20.57, 10.07.

IR: 3415.13 cm⁻¹, 2923.21 cm⁻¹, 1613.55 cm⁻¹, 1516.74 cm⁻¹, 1382.07 cm⁻¹, 1298.58 cm⁻¹, 1040.08 cm⁻¹, 811.60 cm⁻¹, 529.85 cm⁻¹.

HRMS m/z (ES⁺): calcd for C₁₇H₁₉N₄ ([M+H]⁺) 279.1604, found 279.1594.



 CH_3 ⁴¹ 4r and 4r' were prepared according to the general procedure 3A, colorless waxy solid, 54% yield (34 mg, 4r/4r' < 1/10) was obtained for 4r'.

¹H NMR (400 MHz, CDCl₃): δ (ppm) 7.97-8.03 (m, 2.07 H), 7.40-7.62 (m, 4.34 H), 7.61(m, 1.09 H), 7.16 (d, J = 8.0 Hz, 2.15 H), 6.98 (d, J = 8.0 Hz, 2.10 H), 6.76 (s, 1.02 H), 5.48 (br, 0.96 H), 2.22 (s, 3.05 H), 1.88 (s, 3.00 H).
¹³C NMR (100 MHz, CDCl₃): δ (ppm) 144.98, 138.31, 134.52, 130.06, 129.83, 129.32, 129.19, 129.05, 128.35, 127.43, 126.75, 126.17, 125.78, 124.66, 123.83, 121.50, 120.86, 116.81, 20.52, 9.73.
IR: 3416.66 cm⁻¹, 2922.23 cm⁻¹, 2856.42 cm⁻¹, 1669.80 cm⁻¹, 1550.30 cm⁻¹, 1417.92 cm⁻¹, 1245.05 cm⁻¹, 806.04

cm⁻¹, 776.54 cm⁻¹, 504.17 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{21}H_{20}N_3([M+H]^+)$ 314.1652, found 314.1646.



4s and 4s' were prepared according to the general procedure 3A,

colorless waxy solid, 59% yield (37 mg, 4s/4s' = 1/1).

¹**H NMR** (400 MHz, CDCl₃): δ (ppm) 7.87-8.0 (m, 2.05 H), 7.58-7.78 (m, 3.13 H), 7.16-7.38 (m, 5.00 H), 7.01 (d, *J* = 8.0 Hz, 0.96 H), 6.71(d, *J* = 12.0 Hz, 0.96 H), 5.98 (br, 0.49 H), 5.75 (br, 0.52 H), 2.44 (s, 1.56 H), 2.25 (s, 1.41 H), 2.02-2.03 (m, 3.00 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 144.40, 144.30, 143.64, 143.54, 139.36, 138.88, 138.66, 138.56, 134.55, 133.56, 132.99, 132.17, 130.78, 130.29, 129.51, 128.98, 128.72, 128.11, 127.97, 127.87, 127.67, 127.50, 127.36, 127.30, 126.98, 126.86, 126.76, 126.25, 125.37, 124.46, 124.13, 123.32, 121.93, 118.35, 116.68, 110.75, 21.15, 20.53, 10.24, 10.16.

IR: 3419.18 cm⁻¹, 3053.15 cm⁻¹, 2922.30 cm⁻¹, 1667.46 cm⁻¹, 1551.86 cm⁻¹, 1512.34 cm⁻¹, 1395.91 cm⁻¹, 815.41 cm⁻¹, 749.15 cm⁻¹, 475.63 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{21}H_{20}N_3([M+H]^+)$ 314.1652, found 314.1647.



5a was prepared according to the general procedure 3B, colorless waxy solid, 67% yield (37 mg) + 7% yield of 4a (3 mg).
¹H NMR (400 MHz, CDCl₃): δ (ppm) 7.41 (d, J = 8.0 Hz, 2 H), 7.18 (d, J = 8.0 Hz, 2 H), 7.07 (d, J = 8.0 Hz, 4 H), 6.58 (m, 3 H), 6.45 (t, J = 8.0 Hz, 2 H), 2.17-2.28 (m, 6 H), 2.04 (s, 3 H), 1.95 (d, J = 4.0 Hz, 3 H).
¹³C NMR (100 MHz, CDCl₃): δ (ppm) 144.23, 143.00, 138.36, 136.76, 134.37, 132.01, 129.59, 129.49, 129.03, 128.50, 127.71, 124.56, 123.71, 120.08, 112.42, 21.01, 20.90, 20.40, 10.75.
IR: 3423.09 cm⁻¹, 2923.53 cm⁻¹, 2853.23 cm⁻¹, 1632.99 cm⁻¹, 1595.22 cm⁻¹, 1510.27 cm⁻¹, 1380.42 cm⁻¹, 1108.11

cm⁻¹, 815.22 cm⁻¹, 515.66 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{25}H_{26}N_3([M+H]^+)$ 368.2121, found 368.2125.



5b was prepared according to the general procedure 3B, colorless waxy solid, 54% yield

(26 mg).

¹**H NMR** (400 MHz, CDCl₃): δ (ppm) 7.52 (d, *J* = 8.0 Hz, 2 H), 7.10-7.30 (m, 8 H), 6.75 (t, *J* = 8.0 Hz, 2 H), 6.52 (d, *J* = 8.0 Hz, 2 H), 6.42-6.46 (m, 2 H), 1.89 (s, 3 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 149.00, 145.25, 138.35, 136.20, 128.72, 128.68, 128.20, 127.81, 127.34, 125.41, 123.15, 122.59, 121.69, 118.77, 110.34, 11.09.

IR: 3448.42 cm⁻¹, 3056.81 cm⁻¹, 2924.68 cm⁻¹, 1624.51 cm⁻¹, 1567.51 cm⁻¹, 1494.27 cm⁻¹, 1400.80 cm⁻¹, 1200.89 cm⁻¹, 757.79 cm⁻¹, 690.75 cm⁻¹.

HRMS m/z (ES⁺): calcd for C₂₂H₂₀N₃ ([M+H]⁺) 326.1652, found 326.1651.



5e and 5e' were prepared according to the general procedure 3B,

slightly yellow waxy solid, 61% yield (35 mg, 5e/5e' = 1/2).

¹**H NMR** (400 MHz, CDCl₃): δ (ppm) 7.35 (t, *J* = 8.0 Hz, 2.09 H), 7.07-7.09 (m, 4.81 H), 6.73 (d, *J* = 8.0 Hz, 1.39 H), 6.58 (d, *J* = 8.0 Hz, 1.38 H), 6.33-6.45 (m, 3.74 H), 3.74 (s, 2.04 H), 3.59 (s, 0.98 H), 2.28-2.29 (m, 4.19 H), 2.06 (s, 2.02 H), 1.86-1.87 (m, 3.00 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 158.73, 153.05, 149.39, 145.48, 145.38, 145.28, 145.20, 141.95, 141.87, 137.38, 135.73, 135.59, 135.56, 135.51, 135.45, 133.46, 133.38, 129.42, 129.39, 129.35, 129.31, 128.69, 128.42, 128.10, 128.01, 123.50, 123.35, 123.21, 122.79, 122.61, 121.44, 121.36, 114.00, 113.50, 110.66, 55.70, 55.42, 20.99, 20.88, 20.44, 10.89, 10.84.

IR: 2924.20 cm⁻¹, 2853.79 cm⁻¹, 1631.33 cm⁻¹, 1510.59 cm⁻¹, 1401.82 cm⁻¹, 1247.61 cm⁻¹, 1033.15 cm⁻¹, 820.39 cm⁻¹, 525.83 cm⁻¹.

HRMS m/z (ES⁺): calcd for C₂₅H₂₆N₃O ([M+H]⁺) 384.2070, found 384.2053.



 GH_3 GH_3 Sf and Sf' were prepared according to the general procedure **3B**, colorless waxy solid, 68% yield (42 mg, Sf/5f' = 1/1).

¹H NMR (400 MHz, CDCl₃): δ (ppm) 7.43 (d, J = 8.0 Hz, 0.96 H), 7.35 (J = 8.0 Hz, 1.02 H), 6.96-7.08 (m, 6.43 H), 6.54-6.57 (m, 2.00 H), 6.36-6.44 (m, 3.00 H), 2.51 (t, J = 8.0 Hz, 1.12 H), 2.26-2.33 (m, 5.70 H), 2.04 (s, 1.52 H), 1.87 (s, 3.00 H), 1.50 (sept, 1.16 H), 1.19-1.39 (m, 3.57 H), 0.88-0.93 (m, 3.36 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 146.22, 145.95, 145.36, 145.22, 137.20, 135.87, 135.22, 135.21, 135.15, 133.67, 133.57, 133.33, 133.27, 129.34, 129.30, 129.25, 128.58, 128.31, 128.08, 128.01, 127.89, 127.73, 127.66, 123.33, 123.26, 123.19, 122.68, 122.65, 121.60, 121.54, 110.48, 110.31, 35.14, 34.75, 34.26, 33.68, 21.98, 20.98, 20.89, 20.87, 20.45, 14.01, 13.94, 10.98, 10.96.

IR: 2924.89 cm⁻¹, 2859.45 cm⁻¹, 1592.93 cm⁻¹, 1511.06 cm⁻¹, 1397.11 cm⁻¹, 1202.82 cm⁻¹, 1035.25 cm⁻¹, 819.28 cm⁻¹, 517.31 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{28}H_{32}N_3$ ([M+H]⁺) 410.2591, found 410.2592.



5g and $5g^\prime$ were prepared according to the general procedure 3B,

colorless waxy solid, 63% yield (35 mg, 5g/5g'=2/1).

¹**H NMR** (400 MHz, CDCl₃): δ (ppm) 7.39-7.44 (m, 2.03 H), 6.96-7.13 (m, 6.19 H), 6.71 (d, *J* = 8.0 Hz, 0.32 H), 6.55 (d, *J* = 8.0 Hz, 1.73 H), 6.33-6.45 (m, 3.06 H), 2.30 (s, 3.00 H), 2.26 (s, 0.98 H), 2.17 (s, 2.03 H), 2.10 (s, 0.99 H), 2.04 (s, 2.07 H), 1.84 (s, 0.82 H), 1.75 (s, 2.02 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 147.66, 146.07, 144.82, 144.19, 137.05, 136.92, 135.97, 135.12, 134.97, 134.86, 133.53, 130.51, 129.19, 129.06, 129.01, 128.97, 128.12, 128.09, 127.82, 123.21, 123.02, 122.31, 122.17, 122.10, 121.63, 119.29, 110.04, 109.95, 20.96, 20.87, 20.44, 18.73, 17.82, 10.92, 10.49.

IR: 3447.08 cm⁻¹, 2959.71 cm⁻¹, 2921.78 cm⁻¹, 1616.66 cm⁻¹, 1579.44 cm⁻¹, 1537.39 cm⁻¹, 1454.44 cm⁻¹, 1259.89 cm⁻¹, 1081.64 cm⁻¹, 800.76 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{25}H_{26}N_3([M+H]^+)$ 368.2121, found 368.2121.



5h and 5h' were prepared according to the general procedure 3B,

slightly yellow waxy solid, 73% yield (40 mg, 5h/5h' = 1.3/1).

¹**H NMR** (400 MHz, CDCl₃): δ (ppm) 7.34-7.38 (m, 2.15 H), 6.93-7.12 (m, 6.49 H), 6.69 (t, *J* = 8.0 Hz, 0.61 H), 6.57 (d, *J* = 8.0 Hz, 0.85 H), 6.38-6.58 (m, 2.32 H), 6.28 (m, 1.08 H), 2.28-2.29 (m, 3.00 H), 2.26 (s, 1.71 H), 2.20 (s, 1.22 H), 2.05 (s, 1.26 H), 1.98 (s, 1.62 H), 1.88-1.89 (m, 2.83 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 148.16, 145.75, 145.30, 145.23, 138.52, 137.33, 136.88, 135.74, 135.63, 135.43, 135.33, 133.30, 129.24, 129.20, 129.18, 129.11, 128.33, 128.18, 128.06, 128.00, 127.81, 127.66, 123.28, 118.60, 110.71, 110.63, 20.99, 20.94, 20.86, 20.41, 10.92, 10.88.

IR: 3421.75 cm⁻¹, 2992.89 cm⁻¹, 2854.09 cm⁻¹, 1589.80 cm⁻¹, 1401.75 cm⁻¹, 1206.86 cm⁻¹, 815.01 cm⁻¹, 742.28 cm⁻¹, 517.57 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{25}H_{26}N_3([M+H]^+)$ 368.2121, found 368.2113.



5i was prepared according to the general procedure 3B, colorless waxy solid, 17%

yield (10 mg).

¹**H NMR** (400 MHz, CDCl₃): δ (ppm) 8.09-8.12 (m, 1 H), 7.52-7.56 (m, 1 H), 7.44 (d, *J* = 8.0 Hz, 2 H), 7.29-7.33 (m, 2 H), 6.93-7.03 (m, 3 H), 6.74-6.86 (m, 3 H), 6.51 (d, *J* = 8.0 Hz, 2 H), 6.50 (d, *J* = 4.0 Hz, 1 H), 6.39 (s, 1 H), 2.27 (s, 3 H), 2.15 (s, 3 H), 1.84 (s, 3 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 145.69, 145.00, 137.07, 135.85, 135.18, 134.20, 133.09, 129.12, 128.71, 127.68, 127.30, 125.53, 124.77, 124.45, 123.76, 123.20, 122.35, 118.98, 116.90, 20.88, 20.86, 10.85.

IR: 2923.15 cm⁻¹, 2855.77 cm⁻¹, 1598.97 cm⁻¹, 1510.97 cm⁻¹, 1404.69 cm⁻¹, 1204.20 cm⁻¹, 1103.37 cm⁻¹, 817.73 cm⁻¹, 773.94 cm⁻¹, 505.90 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{28}H_{26}N_3$ ([M+H]⁺) 404.2121, found 404.2121.



⁵¹ CH₃ 5i' was prepared according to the general procedure **3B**, colorless waxy solid, 41% yield (25 mg).

¹**H NMR** (400 MHz, CDCl₃): δ (ppm) 7.61-7.74 (m, 3 H), 7.52 (d, *J* = 8.0 Hz, 2 H), 7.41-7.49 (m, 2 H), 7.22-7.28 (m, 2 H), 7.15 (d, *J* = 8.0 Hz, 2 H), 6.52 (d, *J* = 4.0 Hz, 1 H), 6.27 (d, *J* = 8.0 Hz, 2 H), 6.21 (d, *J* = 8.0 Hz, 2 H), 2.33 (s, 3 H), 1.91 (s, 3 H), 1.72 (s, 3 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 145.64, 145.43, 136.02, 135.13, 134.09, 132.81, 131.14, 129.43, 128.46, 128.34, 128.17, 128.05, 127.74, 126.81, 126.15, 125.13, 123.46, 123.07, 122.98, 121.82, 110.19, 20.99, 20.39, 10.42.

IR: 2923.15 cm⁻¹, 2855.77 cm⁻¹, 1598.97 cm⁻¹, 1510.97 cm⁻¹, 1404.69 cm⁻¹, 1204.20 cm⁻¹, 1103.37 cm⁻¹, 817.73 cm⁻¹, 773.94 cm⁻¹, 505.90 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{28}H_{26}N_3$ ([M+H]⁺) 404.2121, found 404.2121.



5j and 5j' were prepared according to the general procedure 3B,

colorless waxy solid, 63% yield (38 mg, 5j/5j' = 1/1.3).

¹H NMR (400 MHz, CDCl₃): δ (ppm) 7.58-7.78 (m, 1.42 H), 7.51 (s, 0.45 H), 7.30-7.50 (m, 4.76 H), 7.19-7.24 (m, 2.58 H), 7.02-7.11 (m, 1.19 H), 6.91 (d, *J* = 8.0 Hz, 1.19 H), 6.79-6.84 (m, 1.13 H), 6.76-6.69 (m, 1.12 H), 6.41-6.43 (m, 2.74 H), 2.29 (s, 1.38 H), 2.19 (s, 1.60 H), 2.07 (s, 1.57 H), 1.89 (m, 3.00 H), 1.82 (s, 1.34 H).
¹³C NMR (100 MHz, CDCl₃): δ (ppm) 147.07, 146.20, 145.88, 145.48, 137.45, 135.95, 135.81, 135.52, 135.26, 134.38, 133.74, 133.47, 133.09, 132.19, 129.32, 128.55, 128.26, 128.22, 128.13, 127.90, 127.85, 127.52, 127.19, 127.12, 127.07, 126.28, 126.20, 126.17, 120.05, 124.88, 123.93, 123.34, 122.67, 122.46, 121.63, 116.60, 110.79, 110.64, 20.98, 20.89, 20.29, 11.17, 11.04.

IR: 3421.75 cm⁻¹, 2922.89 cm⁻¹, 2854.09 cm⁻¹, 1589.80 cm⁻¹, 1401.75 cm⁻¹, 1206.86 cm⁻¹, 815.01 cm⁻¹, 742.28 cm⁻¹, 517.57 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{28}H_{26}N_3([M+H]^+)$ 404.2121, found 404.2114.



51 and 51' were prepared according to the general procedure 3B,

colorless waxy solid, 61% yield (35 mg, 51/51' = 1/3.7).

¹**H NMR** (400 MHz, CDCl₃): δ (ppm) 7.42 (d, *J* = 8.0 Hz, 0.41 H), 7.36 (d, *J* = 8.0 Hz, 1.53 H), 7.05-7.08 (m, 2.03 H), 6.95-7.00 (m, 1.66 H), 6.87-6.89 (m, 1.55 H), 6.51-6.56 (m, 1.76 H), 6.42 (d, *J* = 8.0 Hz, 1.53 H), 6.28-6.35 (m, 1.38 H), 2.29-2.30 (m, 3.12 H), 2.25-2.26 (m, 3.00 H), 2.12 (s, 2.34 H), 2.04-2.06 (m, 3.51 H), 1.83 (s, 0.56 H), 1.75 (s, 2.26 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 146.12, 144.94, 144.86, 144.16, 138.03, 136.98, 136.48, 136.02, 134.93, 134.76, 133.57, 132.45, 131.17, 129.53, 129.14, 129.02, 128.92, 128.64, 128.57, 128.02, 127.85, 127.85, 126.90, 125.70, 123.24, 123.05, 122.34, 122.31, 122.01, 121.65, 109.91, 109.86, 20.93, 20.85, 20.43, 18.62, 17.73, 10.90, 10.47.

IR: 2921.17, 2859.39 cm⁻¹, 1631.82 cm⁻¹, 1509.12 cm⁻¹, 1397.13 cm⁻¹, 1157.64 cm⁻¹, 1036.83 cm⁻¹, 817.20 cm⁻¹,

514.78 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{26}H_{28}N_3([M+H]^+)$ 382.2278, found 382.2275.



5m and 5m' were prepared according to the general procedure 3B,

slightly yellow waxy solid, 57% yield (32 mg, 5m/5m' = 1/1.4).

¹H NMR (400 MHz, CDCl₃): δ (ppm) 7.39-7.42 (m, 1.96 H), 7.03-7.07 (m, 2.14 H), 6.90-6.97 (m, 3.40 H), 6.46-6.50 (m, 1.62 H), 6.28-6.39 (m, 3.04 H), 2.27 (s, 3.00 H), 2.22 (s, 1.36 H), 2.11 (s, 1.89 H), 1.99-2.00 (m, 3.63 H), 1.94 (s, 2.47 H), 1.80 (s, 1.19 H), 1.74 (s, 1.71 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 147.81, 146.05, 144.99, 144.26, 137.74, 136.95, 136.11, 136.08, 135.83, 135.47, 135.19, 134.91, 134.72, 133.53, 129.42, 129.23, 129.01, 128.73, 128.05, 127.92, 127.85, 127.61, 127.22, 125.64, 124.56, 123.11, 123.00, 122.51, 122.07, 121.65, 121.24, 120.34, 109.76, 20.93, 20.89, 20.42, 20.06, 14.44, 10.91, 10.49.

IR: 3421.73 cm⁻¹, 2923.04 cm⁻¹, 1599.49 cm⁻¹, 1412.91 cm⁻¹, 1470.55 cm⁻¹, 1400.34 cm⁻¹, 1209.06 cm⁻¹, 816.35 cm⁻¹, 714.78 cm⁻¹, 521.26 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{26}H_{28}N_3([M+H]^+)$ 382.2286, found 382.2278.



5n and 5n' were prepared according to the general procedure 3B,

slightly yellow waxy solid, 65% yield (47 mg, 5n/5n' = 1.5/1).

¹**H** NMR (400 MHz, CDCl₃): δ (ppm) 7.52 (d, *J* = 8.0 Hz, 0.80 H), 7.30-7.34 (m, 2.07 H), 6.97-7.09 (m, 5.90 H), 6.89 (d, *J* = 8.0 Hz, 0.81 H), 6.58 (d, *J* = 8.0 Hz, 0.79 H), 6.36-6.39 (m, 1.76 H), 6.24-6.26 (m, 1.23 H), 2.31-2.32 (d, *J* = 4.0 Hz, 3.78 H), 2.29 (s, 1.23 H), 2.10 (s, 1.22 H), 1.88-1.89 (m, 3.00 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 149.05, 145.58, 145.54, 144.73, 137.77, 136.38, 135.89, 135.79, 135.58, 135.52, 135.48, 133.16, 130.01, 129.50, 129.39, 129.30, 128.65, 128.46, 127.86, 123.94, 123.40, 123.31, 122.65, 121.91, 121.54, 111.13, 110.66, 92.39, 80.13, 21.10, 20.95, 20.91, 20.54, 10.99, 10.92.

IR: 3448.71 cm⁻¹, 2922.36 cm⁻¹, 2854.76 cm⁻¹, 1626.73 cm⁻¹, 1566.05 cm⁻¹, 1513.01 cm⁻¹, 1403.18 cm⁻¹, 1201.13

cm⁻¹, 1040.53 cm⁻¹, 817.97 cm⁻¹, 710.84 cm⁻¹, 520.18 cm⁻¹.

HRMS m/z (ES⁺): calcd for C₂₄H₂₃IN₃ ([M+H]⁺) 480.0931, found 480.0923.



50 CH_3 **50** CH_3 **50** and **50** were prepared according to the general procedure **3B**, slightly yellow waxy solid, 69% yield (41 mg, **50/50'** = 1/5).

¹**H** NMR (400 MHz, CDCl₃): δ (ppm) 7.39 (d, *J* = 12.0 Hz, 2.05 H), 7.06 (d, *J* = 8.0 Hz, 2.14 H), 6.96-7.00 (m, 2.42 H), 6.50-6.56 (m, 3.49 H), 6.40 (d, *J* = 8.0 Hz, 2.08 H), 6.29-6.34 (m, 1.39 H), 2.88 (s, 5.14 H), 2.65 (s, 0.98 H), 2.28 (s, 3.11 H), 2.26 (s, 0.58 H), 2.05 (s, 2.56 H), 1.86 (s, 3.00 H).

¹³**C NMR** (100 MHz, CDCl₃): δ (ppm) 149.72, 146.51, 145.57, 144.98, 141.05, 136.70, 136.14, 136.05, 134.88, 134.70, 133.88, 129.16, 129.11, 128.91, 128.15, 128.08, 127.35, 125.23, 123.13, 123.07, 122.44, 122.25, 121.60, 115.11, 112.36, 110.09, 109.74, 42.61, 40.65, 20.99, 20.87, 20.47, 10.02, 10.91.

IR: 3536.18 cm⁻¹, 2922.33 cm⁻¹, 2857.09 cm⁻¹, 1594.69 cm⁻¹, 1513.99 cm⁻¹, 1213.72 cm⁻¹, 1045.96 cm⁻¹, 816.80 cm⁻¹, 522.11 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{26}H_{29}N_4([M+H]^+)$ 397.2387, found 397.2387.



5p' CH_3 **5p'** CH_3 **5p'** CH_3 **5p** and **5p'** were prepared according to the general procedure **3B**, colorless waxy solid, 40% yield (27 mg, **5p/5p'** < 1/5) was obtained for **5p'**.

¹**H NMR** (400 MHz, CDCl₃): δ (ppm) 7.27 (s, 1.03 H), 7.17-7.19 (m, 0.96 H), 7.11 (d, *J* = 8 Hz, 2.02 H), 6.94-6.99 (m, 4.03 H), 6.62 (d, *J* = 8 Hz, 2.00 H), 6.55 (d, *J* = 8 Hz, 2.01 H), 6.38 (s, 0.97 H), 2.69 (s, 2.90 H), 2.24 (s, 2.99 H), 2.05 (s, 3.09 H), 1.89 (s, 3.00 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 145.40, 143.08, 140.47, 136.91, 135.09, 134.48, 130.07, 129.74, 129.23, 128.77, 124.40, 124.07, 122.87, 121.20, 120.76, 120.68, 112.68, 39.14, 20.90, 20.48, 10.57.

IR: 2924.19 cm⁻¹, 1596.88 cm⁻¹, 1512.07 cm⁻¹, 1402.94 cm⁻¹, 1330.49 cm⁻¹, 1153.51 cm⁻¹, 970.98 cm⁻¹, 798.56 cm⁻¹, 697.28 cm⁻¹, 519.55 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{25}H_{27}N_4O_2S$ ([M+H]⁺) 447.1849, found 447.1849.



colorless waxy solid, 42% yield (25mg, **5q/5q'** > 5/1) was obtained for **5q**. ¹**H NMR** (400 MHz, CDCl₃): δ (ppm) 7.34 (d, *J* = 8 Hz, 2.03 H), 6.98-7.08 (m, 8.21 H), 6.88 (t, *J* = 8 Hz, 1.04 H), 6.81 (d, *J* = 4 Hz, 1.00 H), 6.41 (s, 0.97 H), 2.38 (s, 2.91 H), 2.27 (s, 3.10 H), 2.25 (s, 3.13 H), 1.91 (s, 3.00 H). ¹³**C NMR** (100 MHz, CDCl₃): δ (ppm) 198.89, 149.26, 145.85, 137.73, 136.52, 135.96, 135.45, 133.17, 129.51, 129.42, 128.04, 127.87, 126.50, 123.60, 122.97, 121.00, 118.62, 111.02, 26.59, 21.03, 20.95, 10.93. **IR:** 2923 24 cm⁻¹, 1567.12 cm⁻¹, 1514.49 cm⁻¹, 1403.38 cm⁻¹, 1194.99 cm⁻¹, 816.57 cm⁻¹, 692.65 cm⁻¹, 521.29 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{26}H_{26}N_3O([M+H]^+)$ 396.2070, found 396.2076.



5r and 5r' were prepared according to the general procedure 3B,

colorless waxy solid, 49% yield (30 mg, 5r/5r' = 2/1)

¹**H NMR** (400 MHz, CDCl₃): δ (ppm) 7.76-7.82 (m, 0.62 H), 7.42 (d, *J* = 4 Hz, 0.63 H), 7.33-7.36 (m, 1.72 H), 7.24-7.28 (m, 0.55 H), 7.08-7.12 (m, 4.84 H), 7.01 (d, *J* = 4 Hz, 1.42 H), 6.82 (m, 0.72 H), 6.73 (d, *J* = 12 Hz, 0.70 H), 6.52 (d, *J* = 8 Hz, 0.64 H), 6.39 (d, *J* = 8 Hz, 1.62 H), 3.90 (s, 0.9 H), 3.81 (s, 2.01 H), 2.30 (s, 1.16 H), 2.27 (s, 2.25 H), 2.24 (s, 2.17 H), 2.01 (s, 0.95 H), 1.88 (d, *J* = 8 Hz, 3.00 H).

¹³C NMR (100 MHz, CDCl₃): δ (ppm) 167.65, 166.11, 149.24, 145.90, 145.78, 144.97, 137.54, 136.46, 135.70, 135.65, 135.51, 135.31, 133.22, 132.56, 130.59, 129.38, 129.31, 129.12, 128.37, 128.19, 127.85, 127.71, 126.24, 123.50, 123.20, 122.20, 121.97, 121.63, 119.50, 110.95, 110.74, 52.16, 51.60, 20.95, 20.88, 20.38, 10.99, 10.88. IR: 2923.29 cm⁻¹, 1568.73 cm⁻¹, 1513.78 cm⁻¹, 1357.94 cm⁻¹, 1282.14 cm⁻¹, 1103.89 cm⁻¹, 815.97 cm⁻¹, 732.39 cm⁻¹, 522.01 cm⁻¹.

HRMS m/z (ES⁺): calcd for $C_{26}H_{26}N_3O_2([M+H]^+)$ 412.2020, found 412.2020.

NMR spectra of 2-aminoimidazoles and 2-iminoimidazoles:





4b:



4c:



4d:

29



7.01 7.01 7.15 7.19 7.19 7.19 7.19 7.15 7.15 7.15 7.15 7.15 7.15 7.15 7.03 7.70 7.70 7.70 7.70















H₃C







4k/4k':

-2.41-2.2171.997











4l/4l':







4m:





4n/4n':







4p':



4q':



4s/4s':

-2.44-2.25-2.2











CH3

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5a:







5b:



















5g/5g':











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51/51':

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5q:

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