Synthesis Q.-Z. Li et al. Special Topic

Silver-Catalyzed *para*-Selective C–H Amination of 1-Naphthylamides with Azodicarboxylates at Room Temperature

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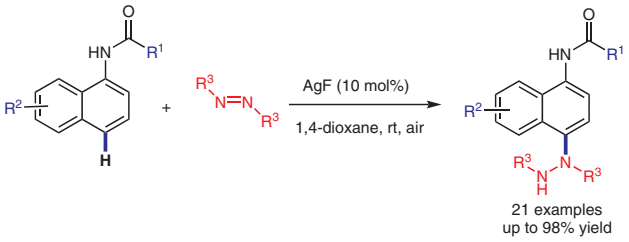

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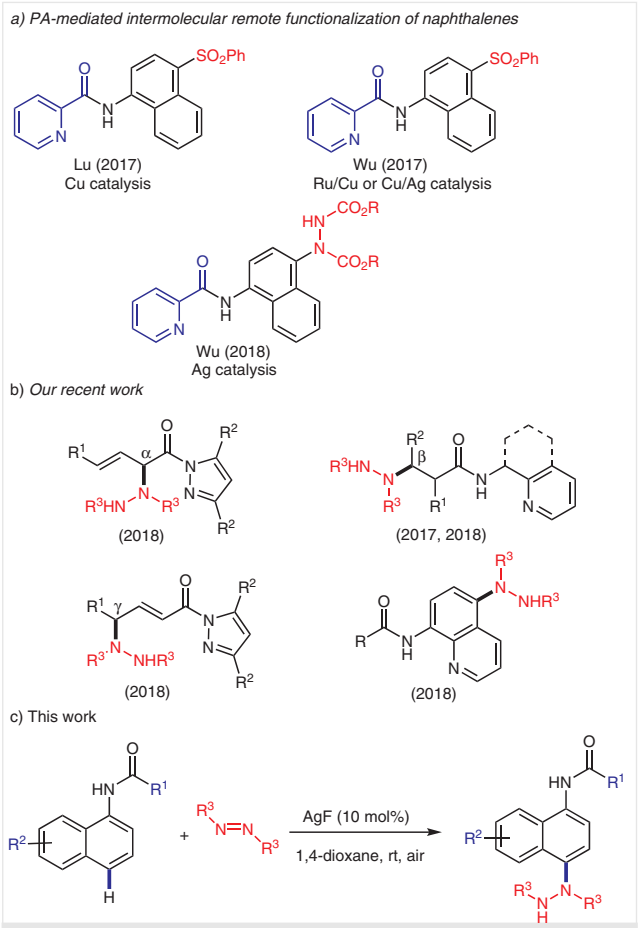
Abstract A simple and efficient protocol for *para*-selective C–H amination of 1-naphthylamide derivatives under silver catalysis is described. This reaction system could proceed without the help of directing group and a broad range of substrates were proved to be well tolerated. In addition, control experiments suggested that this reaction might not proceed via a single-electron-transfer process.

Key words transition metal, azodicarboxylates, regioselective, amination

Transitional-metal-catalyzed C–H functionalization has emerged as a reliable and robust tool for C–N formation in organic synthesis. [1] Naphthalenes are important structural unit in pharmaceuticals, agrochemicals, and functional materials [2] and considerable efforts have been directed toward the simple and efficient construction of substituted naphthalenes.[3] Significant advances have been made in the direct functionalization of 1-naphthylamines, especially for the highly selective C2–H and C8–H functionalization of 1-naphthylamine via the directing group (DG)-assisted C–H bond activation strategy.[4,5] However, the remote aromatic C–H functionalization remains extremely difficult, due to the limitation of directing group.

In recent years, some researchers focused on the development of the *para* C–H functionalization of naphthylamines (Scheme 1a). In 2017, Lu's group developed an efficient protocol catalyzed by copper for C–H functionalization of 1-naphthylamine derivatives at C4–H site directed by picolinic acid (PA).[6] Then Wu and co-workers reported two types of catalysis (Cu/Ru photoredox catalysis or Cu/Ag cocatalysis) for the remote C–H sulfonylation of 1-naphthylamides at room temperature with PA as the directing group.[7] In 2018, Wu's group discussed a silver-catalyzed PA directed C4–H amination of 1-naphthylamine derivatives with azodicarboxylates.[8] These synthetic methods all need a directing group and proceed via a single-electron-transfer (SET) mechanism; however, the introduction and subsequent removal of protecting groups not only require additional operations but also significantly decrease functional group compatibility. C4-substituted 1-naphthylamine framework exists in many pharmaceutical agents such as myeloid cell leukemia 1 (Mcl-1) inhibitor, chemokine receptor 8 (CCR8) antagonist, and 5-hydroxytryptamine receptor 6 (5-HT6) antagonist.[9] Therefore, it is meaningful and challenging to develop a straightforward and practical approach for the direct C4–H amination of 1-naphthylamides without a directing group.

Azodicarboxylates, which contain a central azo functional group, are very popular substrates for C–N bond-forming reactions and many derivatives thereof are also commercially available.[10] Over the past three years, our laboratory has introduced several novel C–H aminations[11] using azodicarboxylates as the amino source with different directing groups (Scheme 1b). To the best of our knowledge, there is no report on the C–H amination at the C4 position of 1-naphthylamide without the help of a directing group. Herein, we have developed a straightforward and practical approach for the direct C–H amination at the definite C4 position of 1-naphthylamides (Scheme 1c). The reactions proceed under simple and mild conditions without any additional directing group at room temperature and air atmo-

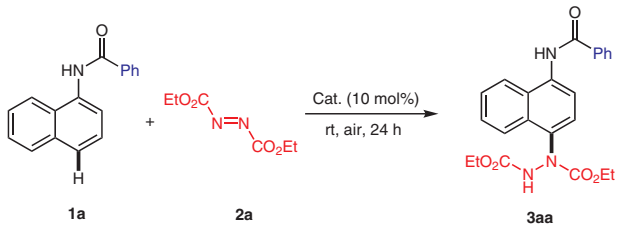


Scheme 1 a) PA-mediated intermolecular remote functionalization of naphthalenes b) Our previous work c) This work

sphere, providing desired products in good to excellent yields.

Initially, we commenced our investigation by the reaction of *N*-(naphthalen-1-yl)benzamide (**1a**) and diethyl azodicarboxylate (DEAD, **2a**) as the model reaction. As shown in Table 1, various metals such as Cu, Co, Ni were employed for this remote C4-amination of 1-naphthylamide. But no product could be acquired, indicating the chosen catalysts had no catalytic activity (Table 1, entries 1–3). When using AgOAc as the catalyst, the desired product could be produced in 39% yield. Then we chose different Ag salts as the catalyst, and AgF was proved to be the optimal catalyst, affording **3aa** in 98% yield (entries 4–8). Subsequently, various solvents were screened and the highest yield was achieved in 1,4-dioxane (entries 9–14). Finally, the effect of the catalyst amount was explored. The results showed that when the catalyst amount was decreased to 5% or increased to 15%, the yield of desired product **3aa** decreased (entries 15, 16)). So, the optimal catalyst amount was determined at 10%, indicating that AgF played an important effect in this model reaction. From all the above results, the condition showed in entry 7 was chosen as the optimized one.

Table 1 Optimization of the Reaction Conditions[a]

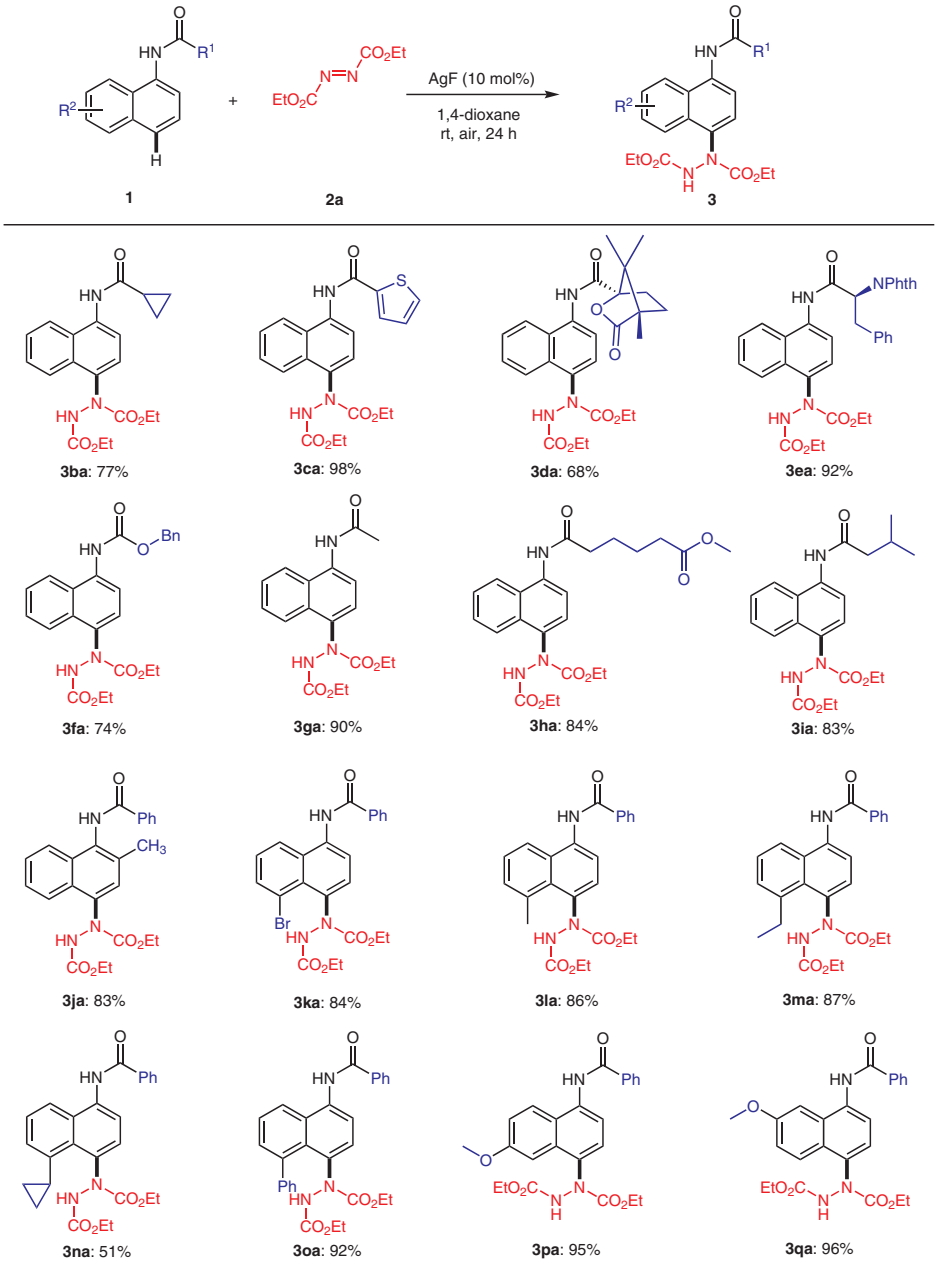


1a **2a** **3aa**

Entry	Catalyst	Solvent	Yield (%)[b]
1	$Cu(OAc)_2$	1,4-dioxane	trace
2	$Co(OAc)_2$	1,4-dioxane	trace
3	$Ni(acac)_2$	1,4-dioxane	trace
4	AgOAc	1,4-dioxane	39
5	Ag_2CO_3	1,4-dioxane	13
6	AgTFA	1,4-dioxane	<5
7	**AgF**	**1,4-dioxane**	**98**
8	AgOTf	1,4-dioxane	<5
9	AgF	DCM	72
10	AgF	DCE	80
11	AgF	toluene	22
12	AgF	MeOH	10
13	AgF	acetone	75
14	AgF	MeCN	69
15[c]	AgF	1,4-dioxane	76
16[d]	AgF	1,4-dioxane	90

[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), and catalyst (10 mol%) in solvent (1 mL) stirred under air for 24 h.
[b] Isolated yields.
[c] AgF: 5 mol%.
[d] AgF: 15 mol%.

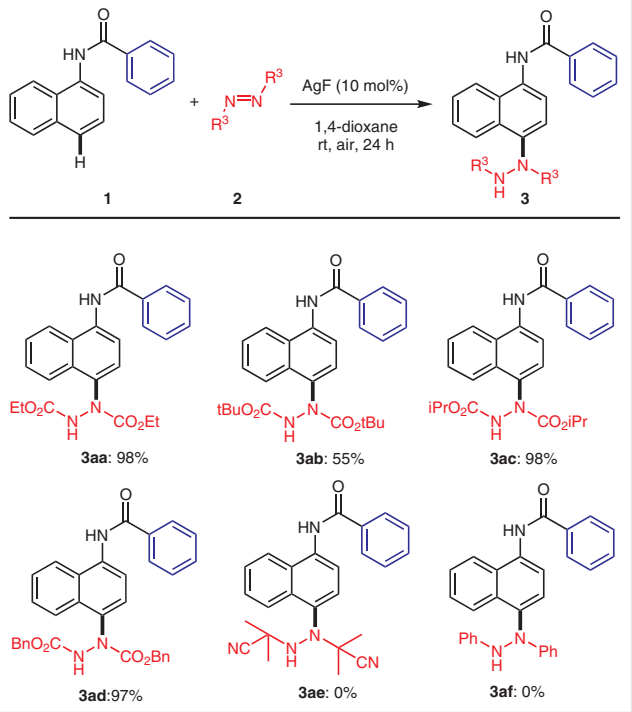
Under the optimized conditions, we then explored the applicability of the present amination protocol for *N*-(naphthalen-1-yl)amide derivatives (Scheme 2). 1-Naphthylamides with various substituted groups at R^1 position were first examined. All tested linear and cyclic carboxamides were well tolerated and gave **3ba–ia** in high isolated yields (68–98%). Then various substituents at different positions of naphthalene were examined, which generated the corresponding products **3ja–qa** efficiently. Different substituted groups like MeO, Me, Br, Et, Ph could provide the corresponding amination products in excellent yields (83–96%), indicating that the electronic effect has no evident influence. But for the substrate containing a cyclopropyl substituent, the product **3na** was obtained in relatively lower yield of 50%. The results could be attributed to the steric effect.



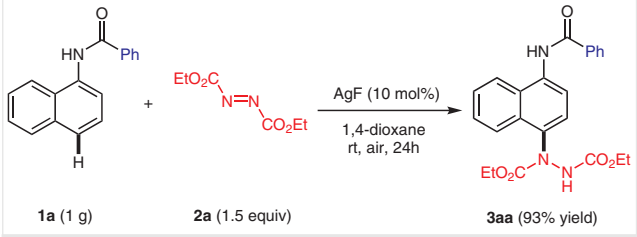
Scheme 2 Substrate scope of 1-naphthylamides. *Reagents and conditions*: **1** (0.1 mmol), **2** (0.15 mmol), AgF (10 mol%), and 1,4-dioxane (1 mL) at rt for 24 h. Isolated yields are shown. The reaction was conducted at 80 °C for the formation of compounds **3da** and **3ha**.

Under the optimized conditions, the scope of azodicarboxylates was also examined (Scheme 3). The ethyl-substituted, isopropyl-substituted, and benzyl-substituted azodicarboxylates afforded the corresponding products **3aa**, **3ac**, and **3ad** in excellent yields. However, the *tert*-butyl-substituted azodicarboxylate proceeded worse and led to the product **3ab** in only 55% yield, which could be attributed to the steric hindrance of *tert*-butyl group. Unfortunately, azo derivatives **2e** and **2f** was not suitable for this reaction, indicating the importance of carboxyl group in azodicarboxylates.

A gram-scale reaction of *N*-(naphthalen-1-yl)benzamide (**1a**) was conducted to demonstrate the synthetic application of this protocol, and the C4–H anination product was obtained in 93% yield under the same reaction conditions (Scheme 4), indicating the successful scale-up of this process.



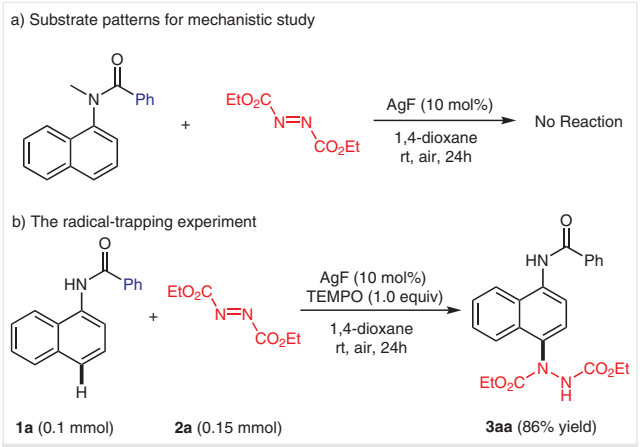
Scheme 3 Substrate scope of azodicarboxylates. *Reagents and conditions*: **1** (0.1 mmol), **2** (0.15 mmol), AgF (10 mol%), and 1,4-dioxane (1 mL) at rt for 24 h. Isolated yields are shown.



Scheme 4 Synthetic application

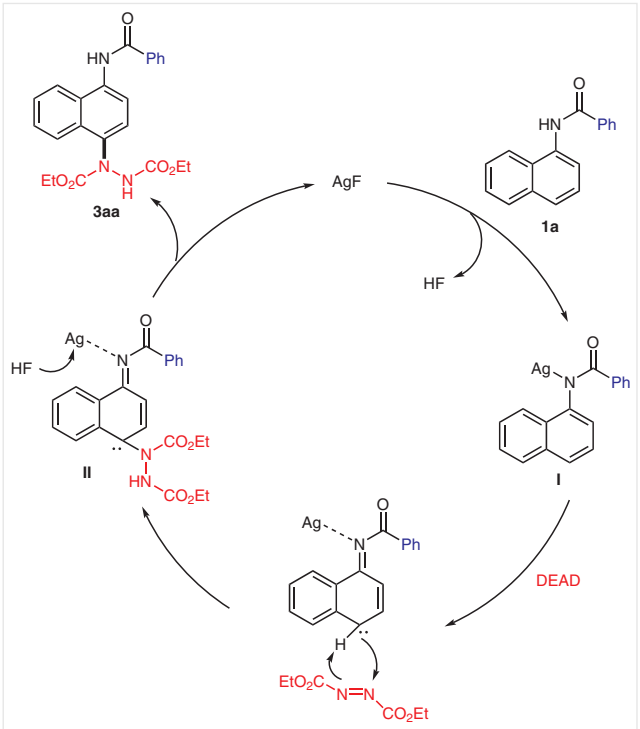
In order to gain insight into the mechanism for this reaction, the substrate with the hydrogen atom substituted by methyl at the amide nitrogen was used to react with DEAD (Scheme 5a). However, the desired product could not be obtained, showing that the hydrogen atom was indispensable and played a critical role in this process. Then, a radical-trapping experiment was also performed by the addition of 1.0 equivalent of TEMPO as radical scavenger (Scheme 5b), and this reaction did not evidently inhibit the formation of desired product **3aa**, indicating our protocol may not involve a SET mechanism.

Although the details of this amination reaction mechanism need to be elucidated, a plausible proposal could be put forward as in Scheme 6. First, the amide **1a** reacts with AgF to give the intermediate **I** and releases HF. Then intermediate **I** progresses electron delocalization and proceeds



Scheme 5 Control experiments

with DEAD to give rise to intermediate **II**. Finally, the rearomatization beomes favorable and the N–Ag bond is severed by HF to regenerate AgF for the next cycle, and the desired amination product **3aa** is obtained.



Scheme 6 Proposed reaction mechanism

In conclusion, we have developed an efficient silver-catalyzed direct amination of 1-naphthylamides with an excellent degree of regioselectivity at C4-position based on the direct C–H bond functionalization. This protocol is operationally simple, scalable, displays a broad substrate scope, and uses commercially available azodicarboxylates as the

aminating agents. Notably, the amination reaction needs no directing group compared with the former reported methods. The control experiments suggested that this amination of 1-naphthylamide may not involve a SET mechanism. Further investigation to extend the application of this method is still in progress.

^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Varian MERCURY plus-400 spectrometer with TMS as an internal standard. HRMS was performed at the Analysis Center of Shanghai Jiao Tong University. All commercially available substrates were used as received. Amide substrates were prepared according to literature[12] (see also: Supporting Information).

Ag-Catalyzed Amidation Reactions; General Procedure

A mixture of amide **1** (0.1 mmol, 1 equiv), AgF (0.01 mmol, 0.1 equiv), and azodicarboxylate **2** (0.15 mmol, 1.5 equiv) in 1,4-dioxane (1 mL) in a 10 mL glass vial (sealed with a PTFE cap) was stirred at rt under air for 24 h. The reaction mixture was concentrated in vacuo. The resulting residue was purified by flash chromatography on silica gel to give the desired product **3**.

Diethyl 1-(4-Benzamidonaphthalen-1-yl)hydrazine-1,2-dicarboxylate (3aa)

White solid; yield: 41.1 mg (98%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.39 (s, 1 H), 8.08 (s, 1 H), 8.02–7.99 (m, 3 H), 7.97–7.93 (m, 1 H), 7.70 (br, 1 H), 7.64–7.53 (m, 5 H), 7.40 (br, 1 H), 4.23–4.21 (m, 4 H), 1.29–1.11 (m, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 167.4, 156.7, 156.3, 136.1, 134.2, 133.3, 133.2, 132.0, 130.6, 129.0, 128.6, 128.5, 127.5, 127.4, 126.8, 126.4, 125.4, 123.4, 122.3, 63.0, 61.9, 14.3.

HRMS (ESI): *m*/*z* calcd for $C_{23}H_{23}N_3O_5$ [M + H]$^+$: 422.1710; found: 422.1711.

Diethyl 1-[4-(Cyclopropanecarboxamido)naphthalen-1-yl]hydrazine-1,2-dicarboxylate (3ba)

Light yellow oil; yield: 29.7 mg (77%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.28–9.88 (m, 2 H), 8.18–8.14 (m, 2 H), 7.74–7.72 (m, 1 H), 7.74–7.59 (m, 3 H), 4.20–4.04 (m, 4 H), 2.10 (pent, *J* = 6.3 Hz, 1 H), 1.32–0.84 (m, 10 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 177.8, 161.6, 160.5, 140.6, 140.3, 139.1, 135.4, 135.3, 133.3, 131.8, 131.3, 130.4, 128.7, 128.2, 128.1, 126.4, 67.3, 66.4, 66.2, 19.7, 19.6, 19.4, 12.6.

HRMS (ESI): *m*/*z* calcd for $C_{20}H_{23}N_3O_5$ [M + H]$^+$: 386.1710; found: 386.1715.

Diethyl 1-[4-(Thiophene-2-carboxamido)naphthalen-1-yl]hydrazine-1,2-dicarboxylate (3ca)

White flocs; yield: 41.7 mg (98%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.56 (s, 1 H), 10.34–9.94 (m, 1 H), 8.18 (d, *J* = 3.8 Hz, 2 H), 8.05–8.03 (m, 1 H), 7.91 (d, *J* = 5.0 Hz, 1 H), 7.70–7.60 (m, 4 H), 7.29 (dd, *J* = 5.0, 3.8 Hz, 1 H), 4.23–4.04 (m, 4 H), 1.29–0.99 (m, 6 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 161.3, 156.8, 155.7, 140.0, 137.2, 137.0, 133.9, 132.4, 130.7, 130.3, 129.9, 128.7, 127.1, 126.8, 125.6, 124.3, 124.1, 62.6, 61.7, 61.5, 14.9.

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{21}N_3O_5S$ [M + H]$^+$: 428.1275; found: 428.1272.

Diethyl 1-{4-[(1*R*,4*S*)-4,7,7-Trimethyl-3-oxo-2-oxabicyclo[2.2.1]heptane-1-carboxamido]naphthalen-1-yl}hydrazine-1,2-dicarboxylate (3da)

Light yellow oil; yield: 33.6 mg (68%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.33–9.92 (m, 2 H), 8.16 (br, 1 H), 7.93–7.88 (m, 1 H), 7.67–7.61 (m, 3 H), 7.54–7.50 (m, 1 H), 4.22–4.08 (m, 4 H), 2.59–2.53 (m, 1 H), 2.09–2.01 (m, 2 H), 1.69–1.63 (m, 1 H), 1.31–1.01 (m, 15 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 178.5, 166.8, 156.8, 155.7, 137.2, 133.4, 130.7, 130.3, 127.1, 126.8, 125.6, 124.8, 123.9, 92.7, 62.6, 61.7, 61.5, 55.1, 54.1, 30.6, 28.9, 17.1, 17.0, 14.9, 10.1.

HRMS (ESI): *m*/*z* calcd for $C_{26}H_{31}N_3O_7$ [M + H]$^+$: 498.2235; found: 498.2232.

Diethyl (*S*)-1-{4-[2-(1,3-Dioxoisoindolin-2-yl)-3-phenylpropanamido]naphthalen-1-yl}hydrazine-1,2-dicarboxylate (3ea)

Light yellow oil; yield: 54.4 mg (92%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.33–9.93 (m, 2 H), 8.15–8.04 (m, 2 H), 7.89–7.81 (m, 4 H), 7.68–7.61 (m, 3 H), 7.52–7.50 (m, 1 H), 7.25–7.11 (m, 5 H), 5.42 (dd, *J* = 11.6, 4.7 Hz, 1 H), 4.20–4.05 (m, 4 H), 3.73 (dd, *J* = 14.0, 4.8 Hz, 1 H), 3.48 (t, *J* = 12.8 Hz, 1 H), 1.28–0.96 (m, 6 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 168.3, 168.0, 156.8, 155.7, 138.0, 137.0, 136.9, 135.0, 134.1, 131.9, 130.7, 130.2, 129.4, 128.8, 127.1, 127.0, 126.7, 125.6, 124.3, 123.9, 123.6, 62.6, 61.7, 61.5, 55.0, 38.7, 34.7, 14.9.

HRMS (ESI): *m*/*z* calcd for $C_{33}H_{30}N_4O_7$ [M + H]$^+$: 595.2187; found: 595.2187.

Diethyl 1-(4-{[(Benzyloxy)carbonyl]amino}naphthalen-1-yl)hydrazine-1,2-dicarboxylate (3fa)

White solid; yield: 33.4 mg (74%).

^{1}H NMR (500 MHz, DMSO-d_6): δ = 10.31–9.85 (m, 2 H), 8.14–8.12 (m, 2 H), 7.71–7.57 (m, 4 H), 7.49 (d, *J* = 7.5 Hz, 2 H), 7.43 (t, *J* = 7.5 Hz, 2 H), 7.39–7.35 (m, 1 H), 5.23 (s, 2 H), 4.23–4.03 (m, 4 H), 1.29–0.98 (m, 6 H).

^{13}C NMR (126 MHz, DMSO-d_6): δ = 156.8, 155.7, 155.2, 137.2, 135.6, 134.4, 130.7, 128.9, 128.8, 128.53, 128.51, 127.1, 126.6, 125.7, 123.9, 123.5, 121.2, 66.5, 62.5, 61.7, 61.4, 14.92, 14.87, 14.8.

HRMS (ESI): *m*/*z* calcd for $C_{24}H_{25}N_3O_6$ [M + H]$^+$: 452.1816; found: 452.1814.

Diethyl 1-(4-Acetamidonaphthalen-1-yl)hydrazine-1,2-dicarboxylate (3ga)

Brown oil; yield: 32.2 mg (90%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.26–9.86 (m, 2 H), 8.14–8.11 (m, 2 H), 7.72–7.71 (br, 1 H), 7.63–7.58 (m, 3 H), 4.18–4.03 (m, 4 H), 2.22 (s, 3 H), 1.32–1.01 (m, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.3, 161.5, 160.5, 140.5, 139.2, 135.4, 133.5, 131.7, 131.2, 130.4, 128.7, 128.3, 126.6, 67.3, 66.4, 66.2, 28.7, 19.7, 19.6.

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{21}N_3O_5$ [M + H]$^+$: 360.1554; found: 360.1555.

Diethyl 1-[4-(6-Methoxy-6-oxohexanamido)naphthalen-1-yl]hydrazine-1,2-dicarboxylate (3ha)

Colorless oil; yield: 38.7 mg (84%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.28–9.87 (m, 2 H), 8.11–8.08 (m, 2 H), 7.71–7.57 (m, 4 H), 4.20–4.02 (m, 4 H), 3.61 (s, 3 H), 2.54–2.50 (m, 2 H), 2.41 (t, *J* = 6.8 Hz, 2 H), 1.72–1.63 (m, 4 H), 1.32–0.98 (m, 6 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 173.8, 172.3, 156.7, 155.7, 135.7, 134.3, 130.7, 128.8, 127.0, 126.5, 125.7, 124.0, 123.5, 121.9, 62.5, 61.7, 61.4, 51.7, 36.0, 33.5, 25.2, 24.6, 14.90, 14.85.

HRMS (ESI): *m*/*z* calcd for $C_{23}H_{29}N_3O_7$ [M + H]$^+$: 460.2078; found: 460.2077.

Diethyl 1-[4-(3-Methylbutanamido)naphthalen-1-yl]hydrazine-1,2-dicarboxylate (3ia)

White solid; yield: 33.4 mg (83%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.30–9.89 (m, 2 H), 8.13–8.08 (m, 2 H), 7.72–7.59 (m, 4 H), 4.22–4.05 (m, 4 H), 2.39 (d, *J* = 7.2 Hz, 2 H), 2.22–2.12 (m, 1 H), 1.38–0.91 (m, 12 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 171.9, 156.8, 155.7, 135.7, 134.3, 130.7, 128.9, 127.0, 126.5, 125.7, 124.0, 123.5, 122.1, 62.5, 61.7, 61.4, 45.6, 26.3, 22.8, 14.91, 14.86.

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{27}N_3O_5$ [M + H]$^+$: 402.2023; found: 402.2028.

Diethyl 1-(4-Benzamido-3-methylnaphthalen-1-yl)hydrazine-1,2-dicarboxylate (3ja)

White flocs; yield: 36 mg (83%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.34–9.96 (m, 2 H), 8.15–8.07 (m, 3 H), 7.96–7.92 (m, 1 H), 7.68–7.56 (m, 6 H), 4.22–4.10 (m, 4 H), 2.39 (d, *J* = 4.8 Hz, 3 H), 1.30–1.03 (m, 6 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 166.3, 156.8, 155.7, 137.5, 134.6, 133.5, 132.4, 132.3, 132.2, 131.9, 129.3, 129.0, 128.2, 127.1, 126.2, 123.9, 62.6, 61.7, 61.5, 18.7, 14.9.

HRMS (ESI): *m*/*z* calcd for $C_{24}H_{25}N_3O_5$ [M + H]$^+$: 436.1867; found: 436.1866.

Diethyl 1-(4-Benzamido-8-bromonaphthalen-1-yl)hydrazine-1,2-dicarboxylate (3ka)

White solid; yield: 42 mg (84%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.63 (d, *J* = 10.1 Hz, 1 H), 9.59 (d, *J* = 51.1 Hz, 1 H), 8.15–8.11 (m, 3 H), 8.07–7.95 (m, 2 H), 7.74 (d, *J* = 8.0 Hz, 1 H), 7.68–7.57 (m, 3 H), 7.49–7.44 (m, 1 H), 4.24–3.98 (m, 4 H), 1.29–1.01 (m, 6 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 166.8, 157.2, 157.1, 155.6, 155.1, 136.4, 136.1, 135.73, 135.71, 134.8, 134.53, 134.51, 132.8, 132.40, 132.38, 129.4, 129.2, 129.90, 128.98, 128.4, 128.3, 128.2, 127.9, 127.1, 127.0, 125.7, 125.0, 116.6, 62.54, 62.51, 61.8, 61.7, 15.1, 15.90, 14.95.

HRMS (ESI): *m*/*z* calcd for $C_{23}H_{22}BrN_3O_5$ [M + H]$^+$: 500.0816; found: 500.0819.

Diethyl 1-(4-Benzamido-8-methylnaphthalen-1-yl)hydrazine-1,2-dicarboxylate (3la)

Brownish yellow powder; yield: 37.5 mg (86%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.54–10.52 (m, 1 H), 10.14–10.03 (m, 1 H), 8.13 (d, *J* = 7.4 Hz, 2 H), 7.96 (d, *J* = 8.1 Hz, 2 H), 7.67–7.57 (m, 4 H), 7.48–7.40 (m, 2 H), 4.26–4.07 (m, 4 H), 2.78–2.76 (m, 3 H), 1.33–1.03 (m, 6 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 166.7, 157.0, 156.9, 156.2, 155.5, 138.2, 137.7, 135.4, 134.8, 133.7, 132.3, 131.89, 131.86, 131.0, 130.7, 130.5, 129.05, 128.97, 128.3, 127.4, 126.2, 124.8, 123.0, 62.6, 61.7, 61.6, 23.0, 22.7, 15.1, 15.00, 15.4.96.

HRMS (ESI): *m*/*z* calcd for $C_{24}H_{25}N_3O_5$ [M + H]$^+$: 436.1867; found: 436.1866.

Diethyl 1-(4-Benzamido-8-ethylnaphthalen-1-yl)hydrazine-1,2-dicarboxylate (3ma)

White powder; yield: 39.1 mg (87%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.51 (d, *J* = 7.9 Hz, 1 H), 10.11–10.00 (m, 1 H), 8.13 (d, *J* = 7.5 Hz, 2 H), 8.04–7.89 (m, 2 H), 7.67–7.57 (m, 4 H), 7.54–7.48 (m, 2 H), 4.25–4.10 (m, 4 H), 3.33–3.23 (m, 1 H), 3.21–3.10 (m, 1 H), 1.30–1.04 (m, 9 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 166.7, 157.0, 156.9, 156.1, 155.6, 139.7, 137.8, 137.1, 135.5, 134.8, 132.2, 132.0, 130.0, 129.7, 129.0, 128.3, 127.6, 126.2, 124.5, 122.7, 62.6, 62.5, 61.6, 26.7, 15.15, 15.08, 14.94, 14.90.

HRMS (ESI): *m*/*z* calcd for $C_{25}H_{27}N_3O_5$ [M + H]$^+$: 450.2023; found: 450.2024.

Diethyl 1-(4-Benzamido-8-cyclopropylnaphthalen-1-yl)hydrazine-1,2-dicarboxylate (3na)

White solid; yield: 23.6 mg (51%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.49 (d, *J* = 9.4 Hz, 1 H), 9.93–9.84 (m, 1 H), 8.11–8.08 (m, 2 H), 7.98–7.91 (m, 2 H), 7.67–7.56 (m, 4 H), 7.47–7.39 (m, 2 H), 4.25–3.98 (m, 4 H), 2.75–2.74 (br, 1 H), 1.28–1.16 (m, 4 H), 1.09–1.01 (m, 3 H), 0.90–0.82 (m, 2 H), 0.43–0.29 (m, 1 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 166.7, 157.3, 155.9, 155.8, 138.3, 138.1, 137.9, 137.1, 135.4, 134.8, 134.7, 132.2, 131.9, 131.8, 131.5, 131.2, 129.0, 128.9, 128.4, 128.29, 128.26, 127.4, 127.2, 126.1, 126.0, 124.6, 123.0, 62.5, 62.2, 61.7, 61.6, 16.2, 16.0, 15.01, 14.99, 14.95, 14.85, 9.4, 5.7.

HRMS (ESI): *m*/*z* calcd for $C_{26}H_{27}N_3O_5$ [M + H]$^+$: 462.2023; found: 462.2023.

Diethyl 1-(4-Benzamido-8-phenylnaphthalen-1-yl)hydrazine-1,2-dicarboxylate (3oa)

Light yellow solid; yield: 53.1 mg (92%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.64–10.62 (m, 1 H), 8.18–8.13 (m, 3 H), 7.84–7.50 (m, 8.5 H), 7.43–7.31 (m, 3 H), 7.27–7.22 (m, 1 H), 7.12–7.09 (m, 0.5 H), 4.20–3.63 (m, 4 H), 1.21–1.00 (m, 6 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 166.9, 166.8, 156.2, 156.1, 154.4, 153.8, 143.1, 142.9, 138.4, 138.3, 137.0, 136.4, 135.2, 135.0, 134.8, 134.7, 132.33, 132.30, 131.7, 131.6, 131.4, 131.3, 129.00, 128.98, 128.6, 128.5, 128.37, 128.35, 128.2, 128.0, 127.7, 127.5, 127.2, 127.0, 125.8, 125.7, 124.8, 124.5, 124.3, 62.6, 62.1, 62.0, 14.9, 14.8, 14.6.

HRMS (ESI): *m*/*z* calcd for $C_{29}H_{27}N_3O_5$ [M + H]$^+$: 498.2023; found: 498.2024.

Diethyl 1-(4-Benzamido-7-methoxynaphthalen-1-yl)hydrazine-1,2-dicarboxylate (3pa)

Light yellow floc; yield: 43.0 mg (95%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.52–10.33 (m, 2 H), 8.15–8.13 (m, 2 H), 8.00 (d, *J* = 9.2 Hz, 1 H), 7.70–7.39 (m, 6 H), 7.29–7.26 (m, 1H), 4.26–3.93 (m, 4 H), 3.96 (s, 3 H), 1.34–1.06 (m, 6 H).

^{13}C NMR (101 MHz, DMSO): δ = 166.8, 158.5, 157.0, 155.8, 135.8, 134.8, 134.7, 132.5, 132.2, 128.9, 128.3, 126.7, 126.1, 125.7, 121.7, 119.3, 102.2, 62.6, 61.7, 61.5, 55.9, 14.9.

HRMS (ESI): *m*/*z* calcd for $C_{24}H_{25}N_3O_6$ [M + H]$^+$: 452.1816; found: 452.1816.

Diethyl 1-(4-Benzamido-6-methoxynaphthalen-1-yl)hydrazine-1,2-dicarboxylate (3qa)

Brownish yellow powder; yield: 43.5 mg (96%); mp: 183 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.46 (s, 1 H), 10.31–9.94 (m, 1 H), 8.14–8.12 (m, 3 H), 7.66–7.54 (m, 5 H), 7.38–7.37 (m, 1 H), 7.33 (dd, *J* = 9.3, 2.5 Hz, 1 H), 4.25–4.06 (m, 4 H), 3.88 (s, 3 H), 1.30–1.02 (m, 6 H).

^{13}C NMR (101 MHz, DMSO): δ = 166.8, 158.0, 156.8, 155.7, 137.0, 135.0, 133.4, 132.2, 131.6, 129.0, 128.3, 126.2, 126.0, 124.9, 123.0, 119.3, 102.8, 62.6, 61.7, 61.5, 55.7, 14.92, 13.89.

HRMS (ESI): *m*/*z* calcd for $C_{24}H_{25}N_3O_6$ [M + H]$^+$: 452.1816; found: 452.1819.

Di-*tert*-butyl 1-(4-Benzamidonaphthalen-1-yl)hydrazine-1,2-dicarboxylate (3ab)

White flocs; yield: 26.3 mg (55%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.52 (s, 1 H), 9.91–9.46 (m, 1 H), 8.20–8.12 (d, *J* = 7.5 Hz, 3 H), 8.03 (d, *J* = 7.9 Hz, 1 H), 7.65–7.57 (m, 7 H), 1.52–1.25 (m, 18 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 166.7, 155.9, 154.8, 154.4, 137.6, 134.8, 134.1, 133.9, 132.2, 130.7, 130.2, 128.9, 128.3, 126.6, 126.5, 125.7, 124.2, 124.0, 81.2, 80.7, 80.2, 28.5, 28.5, 28.3, 28.2.

HRMS (ESI): *m*/*z* calcd for $C_{27}H_{31}N_3O_5$ [M + H]$^+$: 478.2336; found: 478.2339.

Diisopropyl 1-(4-Benzamidonaphthalen-1-yl)hydrazine-1,2-dicarboxylate (3ac)

Light yellow flocs; yield: 43.8 mg (98%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.55 (s, 1 H), 10.20 (d, *J* = 10.8 Hz, 1 H), 8.21–8.14 (m, 3 H), 8.09–8.07 (m, 1 H), 7.73–7.68 (m, 2 H), 7.66–7.58 (m, 5 H), 4.94–4.88 (m, 2 H), 1.35–1.01 (m, 12 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 166.8, 156.5, 155.4, 137.3, 137.1, 134.8, 134.4, 132.2, 130.8, 130.3, 129.0, 128.3, 127.0, 126.7, 125.7, 125.6, 124.2, 70.3, 69.0, 22.4, 22.1.

HRMS (ESI): *m*/*z* calcd for $C_{25}H_{27}N_3O_5$ [M + H]$^+$: 450.2023; found: 450.2019.

Dibenzyl 1-(4-Benzamidonaphthalen-1-yl)hydrazine-1,2-dicarboxylate (3ad)

White flocs; yield: 52.9 mg (97%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.69–10.24 (m, 2 H), 8.26–8.10 (m, 4 H), 7.83–7.16 (m, 17 H), 5.32–5.17 (m, 4 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 166.8, 156.8, 155.7, 136.7, 134.83, 134.81, 132.3, 130.8, 130.6, 130.4, 129.0, 128.9, 128.8, 128.6, 128.5, 128.45, 128.38, 128.0, 127.9, 127.2, 126.8, 125.8, 124.3, 124.2, 124.0, 67.9, 67.4, 67.0.

HRMS (ESI): *m*/*z* calcd for $C_{33}H_{27}N_3O_5$ [M + H]$^+$: 546.2023; found: 546.2026.

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Supporting Information

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