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KO*t*-Bu promoted homocoupling and decomposition of *N*′-aryl acylhydrazines: synthesis of unsymmetric *N*′,*N*′-diaryl acylhydrazines

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ABSTRACT

The KO*t*-Bu promoted homocoupling and decomposition of *N*′-aryl acylhydrazines has been achieved. The method allows for a novel and efficient synthesis of unsymmetric *N*′,*N*′-diaryl acylhydrazines under mild reaction conditions. The reaction probably proceeds via the generation of *N*′-centered acylhydrazine radicals and the subsequent homolytic aromatic substitution.

1. Introduction

The nitrogen radicals are useful intermediates for the synthesis of various amines and nitrogen heterocycles.[1,2] However, their synthetic applications are still limited comparing with carbon radicals. There are two general approaches for generating nitrogen radicals: (1) the scission of a weak N–X bond (X is a halogen, a nitrogen, an oxygen, or a sulfur); (2) the break of a N–H bond in the presence of oxidants. Acylhydrazine radicals can be generated in the presence of bases and oxidants.[3,4] They are reported to be *N*-centered (the unpaired electron is localized at the nitrogen atom connected to the acyl group). Most acylhydrazine radicals are easily oxidized to diazenes, which decompose to give the corresponding carbon radicals. Bowman and co-workers reported Ag(I)-catalyzed oxidation reaction of acylhydrazines. The *N*-centered acylhydrazine radicals were suggested to be the intermediates. Mason and co-workers observed the existence of short-lived acylhydrazine radicals via the fast-flow technique by electron paramagnetic resonance (EPR) spectroscopy.[4] To the best of our knowledge, the direct addition or substitution reactions via *N*-centered or *N*′-centered acylhydrazine radicals have never been reported.[5] Herein, we report the KO*t*-Bu promoted homocoupling and decomposition of *N*′-aryl acylhydrazines. A series of unsymmetric *N*′,*N*′-diaryl acylhydrazines were prepared in good yields. The experiment evidences approve a reaction mechanism involving the generation of *N*′-centered acylhydrazine radicals and consequent homolytic aromatic substitution.[6]

Recently we found that KO*t*-Bu/DMF promotes inter- and intramolecular additions of α-aryl substituted amides to alkenes (Scheme 1, eq. 1).[7] The formation of α-amido alkyl radicals was proposed based on the experiment evidences. We speculate that the structurally analogues acylhydrazine can generate the acylhydrazine radicals under the similar reaction conditions. The subsequent intramolecular addition with alkenes will provide diazepinone derivatives. Initially, we examined the reaction of acylhydrazide **1** in KO*t*-Bu/DMF at 90 °C. Diazepinone and 2-(phenylamino)-dihydroisoquinolinone were obtained with a ratio of about 2/1. When the reaction was carried out at room temperature, almost no diazepinone and 2-(phenylamino)-dihydroisoquinolinone were obtained. Unexpectedly we got *N*′,*N*′-diphenyl benzohydrazide **2** in 20% yield (Scheme 1, eq. 2). The yield could be increased to 62% while THF was used as the solvent. The result uncovered a new synthetic pathway of *N*′,*N*′-diaryl acylhydrazines from *N*′-aryl acylhydrazines.[8]

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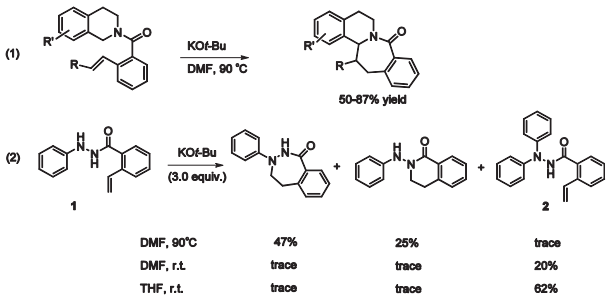
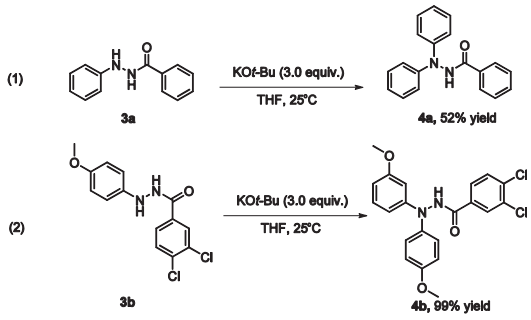


Scheme 1. Previous study of amides and reaction of *N*′-aryl acylhydrazine **1** with KO*t*-Bu.

We then examined the reaction of *N*′-phenyl-benzohydrazide **3a** in KO*t*-Bu/THF. The expected product **4a** was obtained in a moderate yield (Scheme 2, eq. 1). However, the reaction of 3,4-dichloro-*N*′-(4-methoxyphenyl)-benzohydrazide **3b** provided the product **4b** in an almost quantitative yield (Scheme 2, eq. 2). Interestingly, the substituted position of methoxyl group on the two phenyl group was found to be different. Recently, Li, Lu and co-workers reported copper (II)-catalyzed reaction of *N*′-aryl acylhydrazines, respectively.[9] Symmetric *N*′,*N*′-diaryl acylhydrazines were obtained in good yields. The diazenes were proposed to be the intermediates in the reactions. The generation of unsymmetric *N*′,*N*′-diaryl acylhydrazine **4b** implicated the existence of a different reaction pathway in our study.



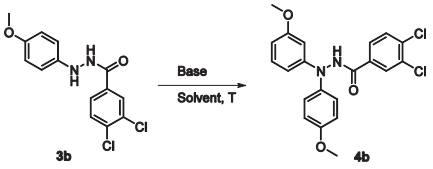
Scheme 2. Reaction of *N*′-aryl acylhydrazines **3a**–**b** in KO*t*-Bu/THF.

2. Results and discussion

Using **3b** as the substrate, the effect of bases, solvents, and temperature was examined. The reactions were carried out in the Radleys reaction tube under a nitrogen atmosphere and the results are summarized in Table 1. Other base such as NaO*t*-Bu, LiO*t*-Bu, KOMe, K_2CO_3 were less effective (Table 1, entries 2–5). The reaction in DMF, DMSO, dioxane and toluene provided lower yields (Table 1, entries 6–9). Protonic solvent such as HO*t*-Bu was incompatible (Table 1, entry 10). Lower reaction temperature (0 °C) or higher reaction temperature (reflux) resulted in lower yields (Table 1, entries 11–12). The loading of KO*t*-Bu could be decreased to 1.5 equiv without eroding the yield, but the further decrease of the loading lead to the significant loss of the yield (Table 1, entries 13–14). The ultra-pure KO*t*-Bu (>99.99% purity) was also examined, and the same yield of **4b** was obtained. The result confirmed that the residual transition metal in KO*t*-Bu did not exert the crucial effect on the reaction (Table 1, entry 15).

The O_2 concentration was found to exert the amazing effect on the reaction. No product **4b** was obtained with the strict exclusion of O_2 (Table 1, entry 16). On the other hand, the reaction with an O_2 balloon gave only trace amount of **4b** (Table 1, entry 17). A close examination of the influence of O_2 concentration was carried out and the results are listed in Fig. 1. The optimal O_2 concentration was found to be about 2% (v/v). The higher O_2 concentration led to a significant loss of the yield. The successful reaction in the Radleys reaction tube could be ascribed to the slow penetration of O_2 through the septum.[10]

Table 1
Optimization of reaction conditions[a]



Entry	Base (equiv.)	Solvent	T (°C)	Yield[b] (%)
1	KO*t*-Bu (3.0)	THF	25	99
2	NaO*t*-Bu (3.0)	THF	25	45
3	LiO*t*-Bu (3.0)	THF	25	0
4	KOMe (3.0)	THF	25	52
5	K_2CO_3 (3.0)	THF	25	0
6	KO*t*-Bu (3.0)	DMF	25	86
7	KO*t*-Bu (3.0)	DMSO	25	86
8	KO*t*-Bu (3.0)	Dioxane	25	79
9	KO*t*-Bu (3.0)	Toluene	25	53
10	KO*t*-Bu (3.0)	HO*t*-Bu	90	0
11	KO*t*-Bu (3.0)	THF	0	60
12	KO*t*-Bu (3.0)	THF	Reflux	31
13	KO*t*-Bu (1.5)	THF	25	99
14	KO*t*-Bu (1.0)	THF	25	40
15[c]	KO*t*-Bu (1.5)	THF	25	99
16[d]	KO*t*-Bu (1.5)	THF	25	0
17[e]	KO*t*-Bu (1.5)	THF	25	6

[a] Reaction conditions: **3b** (0.3 mmol), base, solvent (1.5 mL), in a 20 mL Radleys reaction tube at the indicated temperature for 24 h.
[b] Isolated yields of **4b** after column chromatography.
[c] KO*t*-Bu (>99.99% purity, 0.45 mmol) was used.
[d] The reaction was carried out with the strict exclusion of O_2.
[e] The reaction was carried out with an O_2 balloon.

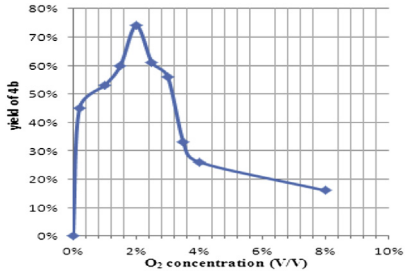
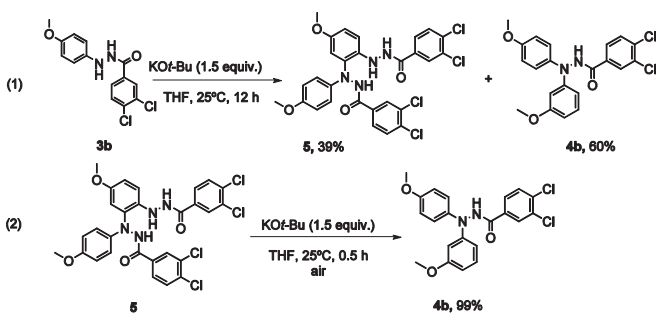


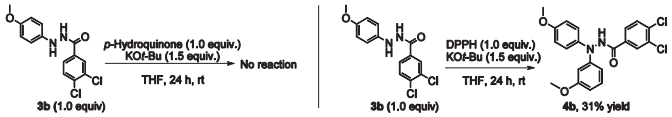
Fig. 1. Influence of O_2 concentration.

When the reaction of **3b** was stopped in 12 h, a homocoupling compound **5** was isolated and characterized (Scheme 3). The treatment of **5** under the reaction conditions gave the product **4b** in almost quantitative yield. The result indicated that compound **5** is the primary product in the reaction.



Scheme 3. Isolation and decomposition of homocoupling compound.

To explore the reaction mechanism, the control experiments with free radical scavengers were examined (Scheme 4). The reaction was found to be inhibited by hydroquinone and DPPH (1,1-diphenyl-2-picrylhydrazyl).



Scheme 4. Controlled experiments with free radical scavengers.

The electron paramagnetic resonance (EPR) spectra of substrate **3b** and **3e** in KOt-Bu/THF were detected. The strong EPR signals were observed in both solutions. The data suggested the generation of acylhydrazine radicals (see Fig. 2).

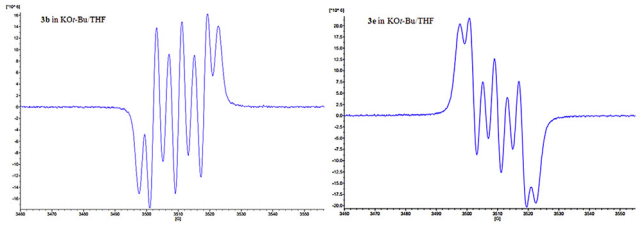
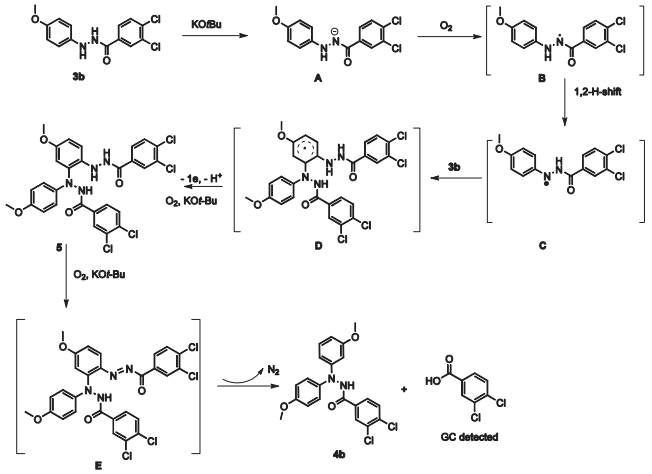


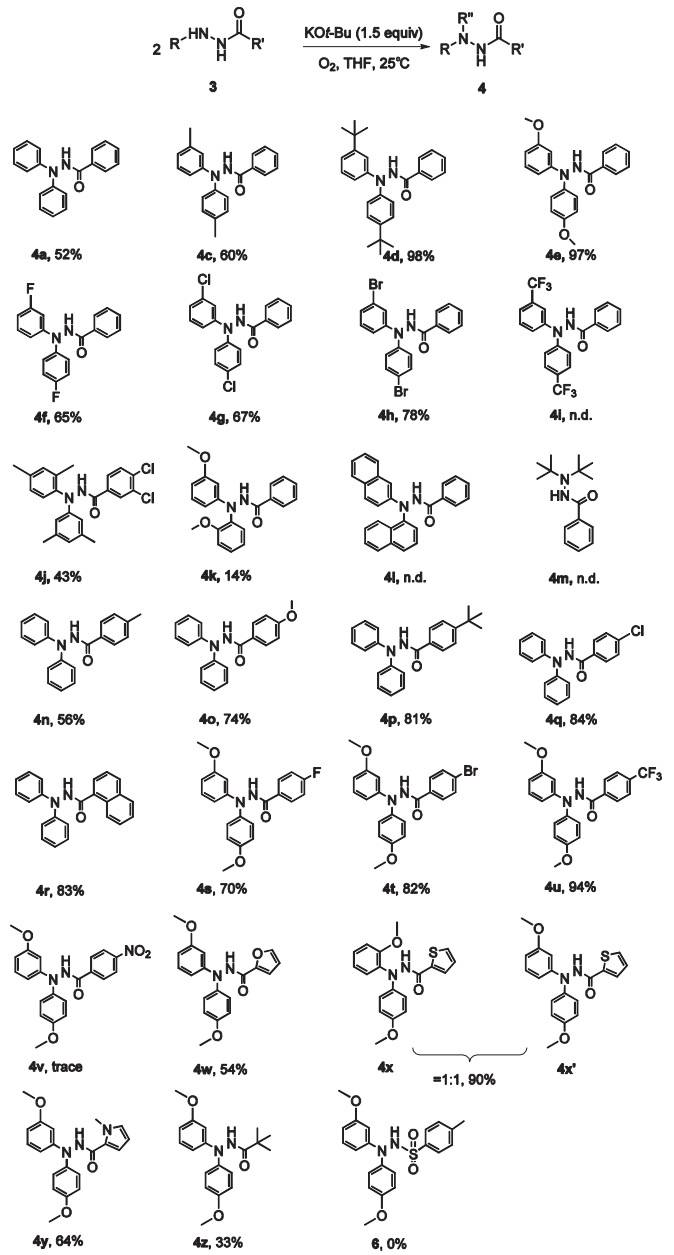
Fig. 2. EPR spectra (X band, 9.875 GHz) of **3b** and **3e** in KO*t*-Bu/THF at room temperature.

Based on the experiment data, a reaction mechanism was proposed in Scheme 5. Firstly, an anion **A** is generated after the deprotonation of the substrate **3b** with KO*t*-Bu. The *N*-centered acylhydrazine radical **B** is formed via a single-electron-transfer (SET) to O_2. After a 1,2-hydrogen migration, the *N′*-centered acylhydrazine radical **C** is produced. The addition of **C** to **3b** gives an aryl radical **D**. Homocoupling product **5** is generated via a PCET (proton coupled electron transfer) step. Again, O_2 works as a single-electron-transfer acceptor. Such a reaction can be ascribed to a homolytic aromatic substitution (HAS) involving nitrogen radical.[6] **5** is further oxidized to a diazene **E**. The decomposition of **E** provides product **4b** and dichlorobenzoic acid, which was detected by a GC–MS analysis.



Scheme 5. Tentative reaction mechanism.

The substrate scope of the reaction was then examined and the results are summarized in Scheme 6. The 4-substitutions on *N′*-phenyl with alkyl, methoxyl and halogen were well tolerated. Excellent yields were obtained for 4-*tert*-butyl and 4-methoxyl substituted substrates **3d**–**3e**. The 4-trifluoromethyl substituted substrate **3i** was unreactive. Comparing with the electronic property of the substituent, the steric effect is more significant. 3,5-Dimethyl substituted substrate **3j** gave low yield of the product **4j**. 2-Methoxyl substituted substrate **3k** provided only 14% yield. More sterically demanding *N′*-naphthyl-*N*-benzohydrazide **3l** was completely unreactive. When the *N′*-aryl group was changed to *N′*-*tert*-butyl, no expected reaction occurred.



Scheme 6. Reaction of *N′*-aryl acylhydrazines[a,b].

[a]Reaction conditions: *N′*-aryl acylhydrazines **3** (0.3 mmol), KO*t*-Bu (0.45 mmol), THF (1.5 mL), 25 °C, in a 20 mL Radleys reaction tube, stirred under a nitrogen atmosphere for 24 h.

[b] Isolated yields after column chromatography.

We also explored the influence of acyl group. Both the substitutions with alkyl, alkoxyl and halogen (**4n**–**q**) provided the products in good yields. The re-placement of benzoyl group with a naphthoyl group (**3r**) also led to a good yield. However, the substrate **3v** with a nitro group provided only trace amount of the

product. A series of heteroaryl substituted substrates **3w**–**y** were also examined. Furan-carbohydrazide and *N*-methyl-pyrrole-carbohydrazide (**3w** and **3y**) gave the products in moderate yields. Thiophene-carbohydrazide **3x** gave a mixture of **4x** and **4x′**. Pivalohydrazide **3z** is also applicable. The product **4z** was obtained in a low yield. The reaction of toluenesulfonohydrazide **6** was unsuccessful. Although the complete consumption of the substrate was observed, no expected product was obtained.

3. Conclusions

In conclusion, we have developed KO*t*-Bu promoted homocoupling and decomposition of *N′*-aryl acylhydrazines. A variety of unsymmetric *N′*,*N′*-diaryl acylhydrazines were prepared in moderate to excellent yields. The O_2 concentration was found to exert the crucial effect on the reaction. The experiment data approve a reaction mechanism involving the generation of nitrogen radical and a homolytic aromatic substitution. The finding provides a new strategy for the generation and reaction of *N′*-centered acylhydrazine radicals.

4. Experimental section

4.1. General

^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer. Chemical shifts of protons are reported in parts per million downfield from tetramethylsilane. Chemical shifts of carbon are referenced to the carbon resonances of the solvent ($CDCl_3$: δ 77.0). Peaks are labeled as single (s), broad singlet (br), doublet (d), triplet (t), double doublet (dd), multiplet (m). Melting points were determined with a commercially available melting point apparatus. The IR spectra were recorded as thin films with KBr and reported in wavenumbers (cm^{-1}). High-resolution mass spectra (HRMS) were acquired using an electron spray ionization time-of-flight (ESI-TOF) mass spectrometer in positive mode. Copies of their ^{1}H NMR and ^{13}C NMR spectra were provided. EPR spectra were recorded on a X-band spectrometer. The samples were taken out by a capillary (borosilicate glass, 3 mm), and then recorded by EPR spectrometer at indicated temperature and parameters. All reagents were used without further purification as received from commercial suppliers unless otherwise noted. All solvents were dried and distilled prior to use according to the standard protocols.

4.2. General procedure for the preparation of substrates (1, 3a–z)[11]

To a solution of benzoic acid (610.6 mg, 5 mmol) and phenylhydrazine hydrochloride (723.0 mg, 5 mmol) in DMF (10.0 mL) was added HCTU (5-Chloro-1-[bis(dimethylamino)methylene]-1*H*-benzotriazolium 3-oxide hexafluorophosphate) (2275.3 mg, 5.5 mmol) and Et_3N (2085.0 mL, 15 mmol). The reaction mixture was stirred at room temperature for overnight. Then the reaction mixture was washed with saturated NH_4Cl (aq), $NaHCO_3$ (aq) and brine. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by column chromatography to give **1a** as a white solid (955.2 mg, 90%).

*4.2.1. N′-Phenyl-2-vinylbenzohydrazide (**1**).* White solid (953.2 mg, 80% yield), mp 130.1–131.6 °C. ^{1}H NMR (400 MHz, DMSO): δ 10.13 (d, *J*=2.7 Hz, 1H), 7.94 (d, *J*=2.9 Hz, 1H), 7.75 (d, *J*=7.6 Hz, 1H), 7.49 (t, *J*=7.4 Hz, 2H), 7.38–7.42 (m, 1H), 7.19 (dd, *J*=8.4, 7.4 Hz, 2H), 6.98 (dd, *J*=17.6, 11.1 Hz, 1H), 6.83 (dd, *J*=8.5, 0.9 Hz, 2H), 6.74 (dd, *J*=10.4, 4.1 Hz, 1H), 5.86 (dd, *J*=17.6, 1.0 Hz, 1H), 5.34 (dd, *J*=11.1, 0.9 Hz, 1H). ^{13}C NMR (100 MHz, DMSO): δ 168.5, 149.4, 135.2, 134.4, 133.7, 129.9, 128.8, 127.6, 127.5, 125.2, 118.6, 116.2, 112.2. IR (KBr) ν/cm^{-1}: 3280, 3035, 1650, 993, 912, 750, 710. HRMS (ESI) calculated for $C_{15}H_{15}N_2O$ $(M+H)^+$: 239.1179, found: 239.1168.

*4.2.2. 3,4-Dichloro-N′-(4-methoxyphenyl)benzohydrazide (**3b**).* Off-white solid (933.5 mg, 60%), mp 143.5–146.2 °C. ^{1}H NMR (400 MHz, DMSO): δ 10.52 (s, 1H), 8.13 (d, *J*=2.0 Hz, 1H), 7.87 (dd, *J*=8.4, 2.0 Hz, 1H), 7.79 (d, *J*=8.4 Hz, 1H), 7.65 (s, 1H), 6.74–6.80 (m, 4H), 3.65 (s, 3H). ^{13}C NMR (100 MHz, DMSO): δ 164.6, 153.3, 143.5, 134.9, 133.9, 131.9, 131.4, 129.7, 128.0, 114.7, 114.4, 55.7. IR (KBr) ν/cm^{-1}: 3253, 3055, 1660, 2960, 2870, 1650, 1490, 850, 750.7, 1510. HRMS (ESI) calculated for $C_{14}H_{12}Cl_2N_2NaO_2$ $(M+Na)^+$: 333.0168, found: 333.0159.

*4.2.3. N′-(4-(tert-Butyl)Phenyl)benzohydrazide (**3d**).* White solid (872.2 mg, 65%), mp 149.6–150.9 °C. ^{1}H NMR (400 MHz, DMSO): δ 10.36 (d, *J*=3.0 Hz, 1H), 7.91 (d, *J*=7.4 Hz, 2H), 7.76 (d, *J*=3.0 Hz, 1H), 7.57 (d, *J*=7.2 Hz, 1H), 7.50 (t, *J*=7.5 Hz, 2H), 7.17 (d, *J*=8.5 Hz, 2H), 6.72 (d, *J*=8.5 Hz, 2H), 1.23 (s, 9H). ^{13}C NMR (100 MHz, DMSO): δ 166.8, 147.7, 141.4, 133.6, 132.1, 128.9, 127.7, 125.8, 112.7, 34.1, 31.9. IR (KBr) ν/cm^{-1}: 3263, 3055, 2960, 2870, 1647, 1514, 1255, 1285, 850, 692, 752. HRMS (ESI) calculated for $C_{17}H_{21}N_2O$ $(M+H)^+$: 269.1648, found: 269.1635.

*4.2.4. N′-(4-(Trifluoromethyl)phenyl)benzohydrazide (**3i**).* White solid (700.6 mg, 50%), mp 142.1–142.6 °C. ^{1}H NMR (400 MHz, DMSO): δ 10.51 (s, 1H), 8.59 (s, 1H), 7.93 (d, *J*=7.4 Hz, 2H), 7.60 (t, *J*=7.3 Hz, 1H), 7.48–7.54 (m, 4H), 6.88 (d, *J*=8.5 Hz, 2H). ^{13}C NMR (100 MHz, DMSO): δ 166.8, 153.1, 133.1, 132.3, 129.5 (*J*=270 Hz), 129.0, 127.8, 126.7 (*J*=4 Hz), 119.2 (*J*=32 Hz), 112.1. IR (KBr) ν/cm^{-1}: 3242, 3043, 1653, 1525, 835, 748, 696. HRMS (ESI) calculated for $C_{14}H_{11}F_3N_2NaO$ $(M+Na)^+$: 303.0716, found: 303.0702.

*4.2.5. 3, 4-Dichloro-N′-(3,5-dimethylphenyl)benzohydrazide (**3j**).* White solid (773.0 mg, 50%), mp 203.7–205.1 °C. ^{1}H NMR (400 MHz, DMSO): δ 10.50 (s, 1H), 8.15 (s, 1H), 7.89 (d, *J*=8.4 Hz, 1H), 7.80 (d, *J*=8.3 Hz, 2H), 6.39 (s, 2H), 6.37 (s, 1H), 2.16 (s, 6H). ^{13}C NMR (100 MHz, DMSO): δ 164.5, 149.7, 138.2, 135.0, 133.8, 131.9, 131.4, 129.7, 128.1, 121.2, 110.7, 39.5, 21.7. IR (KBr) ν/cm^{-1}: 3263, 3055, 2960, 2870, 1647, 1514, 1255, 1285, 850, 752. HRMS (ESI) calculated for $C_{15}H_{15}N_2OCl_2$ $(M+H)^+$: 309.0556, found: 309.0557.

*4.2.6. N′-(Naphthalen-2-yl)benzohydrazide (**3l**).* White solid (786.9 mg, 60%), mp 185.8–186.6 °C. ^{1}H NMR (400 MHz, DMSO): δ 10.57 (d, *J*=1.5 Hz, 1H), 8.48 (d, *J*=1.4 Hz, 1H), 8.29–8.30 (m, 1H), 8.00 (d, *J*=7.3 Hz, 2H), 7.83–7.86 (m, 1H), 7.61 (t, *J*=7.2 Hz, 1H), 7.54 (t, *J*=7.5 Hz, 2H), 7.49 (dd, *J*=9.2, 5.3 Hz, 2H), 7.31 (d, *J*=4.3 Hz, 2H), 6.77 (t, *J*=4.3 Hz, 1H). ^{13}C NMR (100 MHz, DMSO): δ 166.8, 144.7, 134.3, 133.5, 132.2, 129.0, 128.5, 127.8, 126.8, 126.3, 125.0, 122.7, 122.2, 119.0, 105.5. IR (KBr) ν/cm^{-1}: 3260, 3118, 2954, 2865, 1655, 1508, 1245, 1298, 852. HRMS (ESI) calculated for $C_{17}H_{14}N_2NaO$ $(M+Na)^+$: 285.0998, found: 285.0994.

*4.2.7. 4-Methyl-N′-phenylbenzohydrazide (**3n**).* White solid (1006.9 mg, 89%), mp 180.8–181.6 °C. ^{1}H NMR (400 MHz, DMSO): δ 10.29 (s, 1H), 7.87 (d, *J*=2.2 Hz, 1H), 7.83 (d, *J*=8.2 Hz, 2H), 7.31 (d, *J*=8.0 Hz, 2H), 7.15 (dd, *J*=8.4, 7.4 Hz, 2H), 6.77–6.79 (m, 2H), 6.71 (t, *J*=7.3 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, DMSO): δ 166.2, 149.6, 141.5, 130.2, 129.0, 128.7, 127.3, 118.6, 112.3, 21.0. IR (KBr) ν/cm^{-1}: 3284, 3028, 2960, 2870, 1649, 1497, 1380, 1305, 902, 690, 750. HRMS (ESI) calculated for $C_{14}H_{14}N_2NaO$ $(M+Na)^+$: 249.0998, found: 249.0984.

*4.2.8. 4-(tert-Butyl)-N′-phenylbenzohydrazide (**3p**).* White solid (1207.6 mg, 90%), mp 220.6–221.7 °C. ^{1}H NMR (400 MHz, DMSO): δ 10.30 (d, *J*=2.9 Hz, 1H), 7.88 (dd, *J*=7.8, 5.7 Hz, 3H), 7.52 (d, *J*=8.5 Hz, 2H), 7.15 (dd, *J*=8.3, 7.5 Hz, 2H), 6.78 (d, *J*=7.7 Hz, 2H), 6.71

(t, *J*=7.3 Hz, 1H), 1.31 (s, 9H). ^{13}C NMR (100 MHz, DMSO): δ 166.2, 154.4, 149.6, 130.2, 128.7, 127.1, 125.2, 118.5, 112.3, 34.6, 30.9. IR (KBr) ν/cm^{-1}: 3251, 3155, 2964, 2870, 1649, 1496, 1395, 1365, 748, 688. HRMS (ESI) calculated for $C_{17}H_{19}N_2O$ $(M-H)^-$: 267.1503, found: 267.1508.

*4.2.9. 4-Chloro-N′-phenylbenzohydrazide (**3q**).* White solid (1048.4 mg, 85%), mp 140.5–141.6 °C. ^{1}H NMR (400 MHz, DMSO): δ 10.44 (d, *J*=2.7 Hz, 1H), 7.95 (d, *J*=1.8 Hz, 1H), 7.93 (d, *J*=2.6 Hz, 2H), 7.57–7.60 (m, 2H), 7.15 (t, *J*=7.9 Hz, 2H), 6.79 (d, *J*=7.7 Hz, 2H), 6.72 (t, *J*=7.3 Hz, 1H). ^{13}C NMR (100 MHz, DMSO): δ 165.3, 149.3, 136.5, 131.7, 129.2, 128.7, 128.6, 118.7, 112.3. IR (KBr) ν/cm^{-1}: 3238, 3047, 1649, 1490, 852, 750, 700. HRMS (ESI) calculated for $C_{13}H_{12}ClN_2O$ $(M+H)^+$: 247.0633, found: 247.0633.

*4.2.10. N′-Phenyl-1-naphthohydrazide (**3r**).* White solid (1049.2 mg, 80%), mp 192.9–193.4 °C. ^{1}H NMR (400 MHz, DMSO): δ 10.34 (d, *J*=2.9 Hz, 1H), 8.20–8.23 (m, 1H), 8.07–8.09 (m, 2H), 8.00–8.03 (m, 1H), 7.78 (dd, *J*=7.0, 1.1 Hz, 1H), 7.57–7.63 (m, 3H), 7.22 (dd, *J*=8.4, 7.4 Hz, 2H), 6.90 (d, *J*=7.6 Hz, 2H), 6.77 (t, *J*=7.3 Hz, 1H). ^{13}C NMR (100 MHz, DMSO): δ 168.9, 149.9, 133.6, 133.2, 130.8, 130.4, 129.3128.8, 127.4, 126.8, 126.1, 125.5, 125.4, 119.1, 112.7. IR (KBr) ν/cm^{-1}: 3246, 3049, 3107, 1637, 1484, 1311, 912, 770, 779. HRMS (ESI) calculated for $C_{17}H_{14}N_2NaO$ $(M+Na)^+$: 285.0998, found: 285.0982.

*4.2.11. 4-Fluoro-N′-(4-methoxyphenyl)benzohydrazide (**3s**).* White solid (650.7 mg, 50%), mp 150.6–151.7 °C. ^{1}H NMR (400 MHz, DMSO): δ 10.38 (s, 1H), 7.80–7.96 (m, 2H), 7.60 (s, 1H), 7.34 (t, *J*=8.2 Hz, 2H), 6.77 (s, 4H), 3.66 (s, 3H). ^{13}C NMR (100 MHz, DMSO): δ 165.8 (*J*=247 Hz), 165.7, 153.2, 143.8, 130.4 (*J*=9 Hz), 130.0, 116.0 (*J*=22 Hz), 114.7, 114.3, 55.7. IR (KBr) ν/cm^{-1}: 3282, 3133, 2953, 2868, 3030, 1650, 1520, 1245, 1298, 840. HRMS (ESI) calculated for $C_{14}H_{13}FN_2NaO_2$ $(M+Na)^+$: 283.0853, found: 283.0844.

*4.2.12. 4-Bromo-N′-(4-methoxyphenyl)benzohydrazide (**3t**).* White solid (802.9 mg, 50%), mp 159.1–159.8 °C. ^{1}H NMR (400 MHz, DMSO): δ 10.44 (d, *J*=3.4 Hz, 1H), 7.85 (d, *J*=8.5 Hz, 2H), 7.72 (d, *J*=8.4 Hz, 2H), 7.63 (d, *J*=3.4 Hz, 1H), 6.74–6.79 (m, 4H), 3.66 (s, 3H). ^{13}C NMR (100 MHz, DMSO): δ 165.9, 153.2, 143.7, 132.67, 132.0, 129.8, 125.8, 114.7114.3, 55.7. IR (KBr) ν/cm^{-1}: 3226, 3110, 2960, 2870, 1633, 1510, 1247, 1032, 831. HRMS (ESI) calculated for $C_{14}H_{12}N_2O_2Br$ $(M-H)^-$: 319.0088, found: 319.0078.

*4.2.13. N′-(4-Methoxyphenyl)-4-(trifluoromethyl)benzohydrazide (**3u**).* White solid (775.7 mg, 50%), mp 169.4–170.6 °C. ^{1}H NMR (400 MHz, DMSO): δ 10.58 (s, 1H), 8.10 (d, *J*=8.1 Hz, 2H), 7.89 (d, *J*=8.2 Hz, 2H), 7.69 (s, 1H), 6.78 (s, 4H), 3.66 (s, 3H). ^{13}C NMR (100 MHz, DMSO): δ 165.6, 153.3, 143.5, 137.4, 132.1 (*J*=32 Hz), 128.7, 126.0 (*J*=4 Hz), 125.7 (*J*=272 Hz), 114.7, 114.4, 55.7. IR (KBr) ν/cm^{-1}: 3244, 3097, 2999, 1647, 1510, 1331, 1238, 831. HRMS (ESI) calculated for $C_{15}H_{13}F_3N_2NaO_2$ $(M+Na)^+$: 333.0821, found: 333.0799.

*4.2.14. N′-(4-Methoxyphenyl)-4-nitrobenzohydrazide (**3v**).* Yellow solid (718.2 mg, 50%), mp 209.6–210.5 °C. ^{1}H NMR (400 MHz, DMSO): δ 10.66 (s, 1H), 8.34 (d, *J*=8.8 Hz, 2H), 8.12–8.14 (m, 2H), 7.71 (s, 1H), 6.78 (s, 4H), 3.66 (s, 3H). ^{13}C NMR (100 MHz, DMSO): δ 164.7, 152.9, 149.2, 142.9, 138.8, 128.8, 123.6, 114.3, 113.9, 55.2. IR (KBr) ν/cm^{-1}: 3296, 3025, 2999, 2833, 1643, 1520, 1340, 1232, 1033, 831. HRMS (ESI) calculated for $C_{14}H_{12}N_3O_4$ $(M-H)^-$: 286.0833, found: 286.0839.

*4.2.15. N′-(4-Methoxyphenyl)furan-2-carbohydrazide (**3w**).* White solid (580.6 mg, 50%), mp 140.4–142.6 °C. ^{1}H NMR (400 MHz, DMSO): δ 10.23 (s, 1H), 7.88 (d, *J*=1.0 Hz, 1H), 7.22 (d, *J*=3.4 Hz, 1H), 6.77 (d, *J*=9.0 Hz, 2H), 6.71 (d, *J*=9.0 Hz, 2H), 6.65 (dd, *J*=3.4, 1.7 Hz, 1H), 3.65 (s, 3H). ^{13}C NMR (100 MHz, DMSO): δ 158.0, 152.7, 146.6, 145.4, 143.1, 114.2, 113.8, 113.7, 111.7, 55.2. IR (KBr) ν/cm^{-1}: 3225, 3080, 2960, 2810, 1630, 1505, 1247, 820. HRMS (ESI) calculated for $C_{12}H_{12}N_2NaO_3$ $(M+Na)^+$: 255.0740, found: 255.0726.

*4.2.16. N′-(4-Methoxyphenyl)thiophene-2-carbohydrazide (**3x**).* Yellow solid (682.8 mg, 55%), mp 178.2–179.2 °C. ^{1}H NMR (400 MHz, DMSO): δ 10.37 (d, *J*=2.4 Hz, 1H), 7.88 (d, *J*=3.4 Hz, 1H), 7.82 (d, *J*=4.9 Hz, 1H), 7.64 (d, *J*=2.5 Hz, 1H), 7.19 (t, *J*=4.2 Hz, 1H), 6.78 (d, *J*=8.7 Hz, 2H), 6.73 (d, *J*=8.8 Hz, 2H), 3.65 (s, 3H). ^{13}C NMR (100 MHz, DMSO): δ 161.8, 153.2, 143.7, 138.4, 131.7, 128.8, 128.6, 114.7, 114.2, 55.7. IR (KBr) ν/cm^{-1}: 3224, 3079, 2960, 2870, 1635, 1506, 1245, 825. HRMS (ESI) calculated for $C_{12}H_{12}N_2O_2S$ $(M+Na)^+$: 271.0512, found: 271.0491.

*4.2.17. N′-(4-Methoxyphenyl)-1-methyl-1H-pyrrole-2-carbohydrazide (**3y**).* White solid (735.8 mg, 60%), mp 127.1–127.9 °C. ^{1}H NMR (400 MHz, DMSO): δ 9.81 (s, 1H), 7.39 (s, 1H), 6.91 (d, *J*=2.8 Hz, 2H), 6.70 (q, *J*=9.0 Hz, 4H), 6.00 (t, *J*=2.8 Hz, 1H), 3.76 (s, 3H), 3.61 (s, 3H). ^{13}C NMR (100 MHz, DMSO): δ 162.0, 153.0, 144.3, 128.7, 124.2, 114.7, 114.1, 113.1, 107.3, 55.7, 36.6. IR (KBr) ν/cm^{-1}: 3236, 3055, 2956, 1635, 1510, 1329, 1246, 1032, 825. HRMS (ESI) calculated for $C_{13}H_{15}N_3NaO_2$ $(M+Na)^+$: 268.1056, found: 268.1035.

*4.2.18. N′-(4-Methoxyphenyl)pivalohydrazide (**3z**).* White solid (666.8 mg, 60%), mp 140.7–141.6 °C. ^{1}H NMR (400 MHz, DMSO): δ 9.45 (d, *J*=3.7 Hz, 1H), 7.23 (d, *J*=3.7 Hz, 1H), 6.74–6.77 (m, 2H), 6.65–6.68 (m, 2H), 3.65 (s, 3H), 1.16 (s, 9H). ^{13}C NMR (100 MHz, DMSO): δ 177.0, 152.5, 143.7, 114.1, 113.6, 55.2, 37.4, 27.2. IR (KBr) ν/cm^{-1}: 3280, 3109, 2960, 1657, 1510, 1395, 1365, 1294, 1243, 1035, 831. HRMS (ESI) calculated for $C_{12}H_{18}N_2NaO_2$ $(M+Na)^+$: 245.1260, found: 245.1244.

4.3. General procedure for the preparation of substrates (2, 4a–z)

To a dried 20 mL Radleys reaction tube was added **3a** (63.7 mg, 0.3 mmol), KO*t*-Bu (50.5 mg, 0.45 mmol) and THF (1.5 mL). The reaction mixture was stirred at 25 °C for 24 h. The solvent was removed under reduced pressure and the residue was purified by column chromatography to give **4a** as a white solid (22.5 mg, 52%).

*4.3.1. N′,N′-diphenyl-2-vinylbenzohydrazide (**2**).* White solid (29.3 mg, 62%), mp 120.5–121.69 °C. ^{1}H NMR (400 MHz, DMSO): δ 11.02 (s, 1H), 7.76 (d, *J*=7.7 Hz, 1H), 7.52 (dd, *J*=13.9, 7.5 Hz, 2H), 7.42 (t, *J*=7.4 Hz, 1H), 7.34 (t, *J*=7.5 Hz, 4H), 7.20 (d, *J*=8.0 Hz, 4H), 7.03 (t, *J*=7.1 Hz, 2H), 6.91 (dd, *J*=17.4, 11.0 Hz, 1H), 5.84 (d, *J*=17.6 Hz, 1H), 5.32 (d, *J*=11.1 Hz, 1H). ^{13}C NMR (100 MHz, DMSO): δ 168.0, 145.7, 135.5, 133.6, 133.4, 130.3, 129.1, 127.7, 127.4, 125.4, 122.3, 118.8, 116.6.

*4.3.2. N′,N′-Diphenylbenzohydrazide (**4a**).* White solid (22.5 mg, 52%), mp 159.7–160.9 °C. ^{1}H NMR (400 MHz, DMSO): δ 11.22 (s, 1H), 7.95 (dd, *J*=5.2, 3.3 Hz, 2H), 7.59–7.63 (m, 1H), 7.52 (dd, *J*=10.3, 4.6 Hz, 2H), 7.28–7.32 (m, 4H), 7.17 (dd, *J*=8.6, 1.0 Hz, 4H), 6.99 (dd, *J*=10.5, 4.1 Hz, 2H). ^{13}C NMR (100 MHz, DMSO): δ 166.3, 146.2, 132.9, 132.5, 129.5, 129.1, 127.9, 122.6, 119.2. This is a known compound and the spectral data are identical to those reported in the literature.[9b]

*4.3.3. 3,4-Dichloro-N′-(3-methoxyphenyl)-N′-(4-methoxyphenyl) benzohydrazide (**4b**).* Off-white solid (62.6 mg, quant), mp 158.3–159.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (s, 1H), 7.89 (s, 1H), 7.61 (d, *J*=8.3 Hz, 1H), 7.45 (d, *J*=8.3 Hz, 1H), 7.29 (d, *J*=8.7 Hz,

2H), 7.11 (t, *J*=8.1 Hz, 1H), 6.85 (d, *J*=8.6 Hz, 2H), 6.46 (t, *J*=7.7 Hz, 2H), 6.42 (s, 1H), 3.80 (s, 3H), 3.71 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.7, 160.4, 157.5, 148.3, 138.1, 136.6, 133.2, 132.1, 130.7, 129.9, 129.5, 126.4, 126.1, 114.7, 107.9, 105.6, 101.7, 55.5, 55.2. IR (KBr) ν/cm^{-1}: 3207, 3113, 2953, 2833, 1660, 1508, 1250, 1032, 839, 690. HRMS (ESI) calculated for $C_{21}H_{18}Cl_2N_2NaO_3$ $(M+Na)^+$: 439.0587, found: 439.0564.

*4.3.4. N′-(3-Tolyl)-N′-(4-tolyl)benzohydrazide (**4c**).* White solid (28.5 mg, 60%), mp 179.7.1–180.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (s, 1H), 7.84 (d, *J*=7.7 Hz, 2H), 7.54 (d, *J*=7.3 Hz, 1H), 7.45 (t, *J*=7.5 Hz, 2H), 7.15 (t, *J*=6.6 Hz, 3H), 7.10 (d, *J*=8.5 Hz, 2H), 6.90–6.93 (m, 2H), 6.79 (d, *J*=7.4 Hz, 1H), 2.31 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 146.3, 143.4, 139.0, 133.4, 132.6, 132.2, 129.9, 129.0, 128.8, 127.3, 123.1, 121.1, 118.7, 115.2, 21.6, 20.9. IR (KBr) ν/cm^{-1}: 3267, 3110, 2920, 1657, 1510, 1305, 690, 602. HRMS (ESI) calculated for $C_{21}H_{21}N_2O$ $(M+H)^+$: 317.1648, found: 317.1626.

*4.3.5. N′-(3-(tert-Butyl)phenyl)-N′-(4-(tert-butyl)phenyl)benzohydrazide (**4d**).* White solid (58.9 mg, 98%), mp 207.8–208.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (s, 1H), 7.85 (d, *J*=7.8 Hz, 2H), 7.54 (d, *J*=7.2 Hz, 1H), 7.46 (t, *J*=7.5 Hz, 2H), 7.27–7.31 (m, 3H), 7.21 (t, *J*=7.9 Hz, 1H), 7.14 (d, *J*=8.4 Hz, 2H), 7.06 (d, *J*=7.7 Hz, 1H), 7.00 (d, *J*=7.8 Hz, 1H), 1.30 (s, 9H), 1.27 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.5, 152.3, 145.8, 145.7, 143.5, 132.8, 132.2, 128.9, 128.8, 127.2, 126.1, 120.1, 119.1, 116.7, 116.4, 34.8, 34.3, 31.4, 31.3. IR (KBr) ν/cm^{-1}: 3278, 3113, 2960, 2870, 1659, 1514, 1309, 1279, 800, 775, 696. HRMS (ESI) calculated for $C_{27}H_{33}N_2O$ $(M+H)^+$: 401.2587, found: 401.2573.

*4.3.6. N′-(3-Methoxyphenyl)-N′-(4-methoxyphenyl)benzohydrazide (**4e**).* White solid (50.7 mg, 97%), mp 201.5–202.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33 (s, 1H), 7.81–7.83 (m, 2H), 7.54 (t, *J*=7.4 Hz, 1H), 7.43 (t, *J*=7.6 Hz, 2H), 7.32–7.36 (m, 2H), 7.12 (t, *J*=8.1 Hz, 1H), 6.85–6.89 (m, 2H), 6.53–6.54 (m, 1H), 6.49 (t, *J*=2.2 Hz, 1H), 6.45 (dd, *J*=8.1, 1.9 Hz, 1H), 3.80 (s, 3H), 3.71 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 160.5, 157.4, 148.6, 138.5, 132.6, 132.2, 129.9, 128.8, 127.3, 126.1, 114.7, 108.0, 105.7, 101.7, 55.5, 55.2. IR (KBr) ν/cm^{-1}: 3236, 3113, 2926, 2865, 1659, 1510, 1244, 1030, 845, 735, 688. HRMS (ESI) calculated for $C_{21}H_{21}N_2O_3$ $(M+H)^+$: 349.1547, found: 349.1554.

*4.3.7. N′-(3-Fluorophenyl)-N′-(4-fluorophenyl)benzohydrazide (**4f**).* White solid, 31.7 mg, 65% yield, mp 185.7–186.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.56 (s, 1H), 7.81 (d, *J*=7.4 Hz, 2H), 7.55 (t, *J*=7.4 Hz, 1H), 7.42 (t, *J*=7.6 Hz, 2H), 7.32 (dd, *J*=8.8, 4.8 Hz, 2H), 7.14 (dd, *J*=14.8, 7.9 Hz, 1H), 7.01 (t, *J*=8.6 Hz, 2H), 6.69 (d, *J*=8.1 Hz, 1H), 6.62 (dd, *J*=16.0, 9.7 Hz, 2H). ^{13}C NMR (100 MHz, DMSO): δ 166.2, 166.1, 164.6 (*J*=242 Hz), 160.7 (*J*=242 Hz), 149.1 (*J*=10 Hz), 141.6, 132.6 (*J*=5 Hz), 131.2 (*J*=10 Hz), 129.1, 128.0, 125.3 (*J*=9 Hz), 116.7 (*J*=23 Hz), 111.8, 107.4 (*J*=21 Hz), 102.7 (*J*=26 Hz). IR (KBr) ν/cm^{-1}: 3257, 3116, 3062, 1659, 1504, 1269, 1169, 1169, 833, 712. HRMS (ESI) calculated for $C_{19}H_{14}F_2N_2NaO$ $(M+Na)^+$: 347.0966, found: 347.0945.

*4.3.8. N′-(3-Chlorophenyl)-N′-(4-chlorophenyl)benzohydrazide (**4g**).* White solid (35.9 mg, 67%), mp 192.7–193.4 °C. ^{1}H NMR (400 MHz, DMSO): δ 11.36 (s, 1H), 7.94 (d, *J*=7.4 Hz, 2H), 7.63 (t, *J*=7.3 Hz, 1H), 7.54 (t, *J*=7.6 Hz, 2H), 7.40 (d, *J*=8.8 Hz, 2H), 7.32 (t, *J*=8.4 Hz, 1H), 7.24 (d, *J*=8.8 Hz, 2H), 7.02–7.07 (m, 3H). ^{13}C NMR (100 MHz, DMSO): δ 166.3, 147.5, 144.3, 134.1, 132.8, 132.4, 131.3, 129.7, 129.2, 128.0, 127.5, 122.2, 122.1, 117.5, 116.8. IR (KBr) ν/cm^{-1}: 3267, 3055, 3103, 1659, 1485, 1255, 1093, 827, 773, 683. HRMS (ESI) calculated for $C_{19}H_{14}Cl_2N_2NaO$ $(M+Na)^+$: 379.0375, found: 379.0357.

*4.3.9. N′-(3-Bromophenyl)-N′-(4-bromophenyl)benzohydrazide (**4h**).* White solid (52.2 mg, 78%), mp 220.2–222.3 °C. ^{1}H NMR (400 MHz, DMSO): δ 11.34 (s, 1H), 7.92–7.94 (m, 2H), 7.61 (d, *J*=7.4 Hz, 1H), 7.49–7.53 (m, 4H), 7.22–7.27 (m, 2H), 7.11–7.18 (m, 4H). HRMS (ESI) calculated for $C_{19}H_{14}Br_2N_2NaO$ $(M+Na)^+$: 466.9365, found: 466.9339. ^{13}C NMR (100 MHz, DMSO): δ 166.3, 147.5, 144.8, 132.8, 132.6, 132.4, 131.6, 129.2, 128.0, 125.3, 122.5, 122.2, 120.8, 117.6, 115.2. IR (KBr) ν/cm^{-1}: 3260, 3080, 1659, 1510, 1260, 835, 755, 705. HRMS (ESI) calculated for $C_{19}H_{14}Br_2N_2NaO$ $(M+Na)^+$: 466.9365, found: 466.9339.

*4.3.10. 3,4-Dichloro-N′-(2,4-dimethylphenyl)-N′-(3,5-dimethylphenyl)benzohydrazide (**4j**).* White solid (26.7 mg, 43%), mp 199.1–120.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (s, 1H), 7.81 (s, 1H), 7.50 (d, *J*=8.3 Hz, 1H), 7.28 (d, *J*=8.3 Hz, 1H), 7.23 (d, *J*=7.6 Hz, 1H), 7.04 (s, 1H), 6.95 (d, *J*=8.2 Hz, 1H), 6.49 (s, 1H), 6.26 (s, 2H), 2.32 (s, 4H), 2.22 (s, 4H), 2.17 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.5, 147.2, 140.8, 138.9, 136.9, 136.4, 136.0, 133.2, 132.4, 132.0, 130.7, 129.4, 128.0, 126.7, 126.4, 122.3, 111.7, 21.6, 21.1, 18.2. IR (KBr) ν/cm^{-1}: 3250, 3082, 2960, 2870, 1660, 1509, 810, 755. HRMS (ESI) calculated for $C_{23}H_{21}N_2OCl_2$ $(M-H)^-$: 411.1036, found: 411.1032.

*4.3.11. N′-(2-Methoxyphenyl)-N′-(3-methoxyphenyl)benzohydrazide (**4k**).* White solid (7.4 mg, 14%), mp 202.6–202.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (s, 1H), 7.82 (d, *J*=7.2 Hz, 2H), 7.66 (dd, *J*=7.7, 1.4 Hz, 1H), 7.52 (d, *J*=7.4 Hz, 1H), 7.44 (t, *J*=7.5 Hz, 2H), 7.29 (dd, *J*=7.9, 1.3 Hz, 1H), 7.09 (t, *J*=8.1 Hz, 1H), 7.02 (dd, *J*=13.3, 7.4 Hz, 2H), 6.40 (dd, *J*=13.8, 5.1 Hz, 2H), 6.35–6.42 (m, 1H), 3.83 (s, 3H), 3.71 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 160.5, 155.7, 149.9, 133.0, 132.3132.0, 130.8, 129.7, 128.8, 128.7, 127.3, 121.4112.4, 106.1, 104.7, 99.8, 55.8, 55.2. IR (KBr) ν/cm^{-1}: 3236, 3113, 2926, 2865, 1659, 1510, 1244, 1030, 845, 750, 700. HRMS (ESI) calculated for $C_{21}H_{21}N_2O_3$ $(M+H)^+$: 349.1547, found: 349.1554.

*4.3.12. 4-Methyl-N′,N′-diphenylbenzohydrazide (**4n**).* White solid (25.4 mg, 56%), mp 183.7–184.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (s, 1H), 7.74 (d, *J*=7.7 Hz, 2H), 7.26–7.28 (m, 5H), 7.21 (t, *J*=8.8 Hz, 5H), 7.02 (t, *J*=7.1 Hz, 2H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 145.8, 142.9, 129.5, 129.2, 127.3, 123.0, 119.5, 21.6. IR (KBr) ν/cm^{-1}: 3280, 3030, 2960, 2870, 1660, 1515, 1380, 830, 750, 700. HRMS (ESI) calculated for $C_{20}H_{18}N_2NaO$ $(M+Na)^+$: 325.1311, found: 325.1297.

*4.3.13. 4-Methoxy-N′,N′-diphenylbenzohydrazide (**4o**).* White solid (35.4 mg, 74%), mp 197.7–198.6 °C. ^{1}H NMR (400 MHz, DMSO): δ 10.22 (s, 1H), 7.92 (d, *J*=2.0 Hz, 1H), 7.90 (d, *J*=2.8 Hz, 1H), 7.13–7.17 (m, 2H), 7.04 (d, *J*=1.9 Hz, 1H), 7.02 (d, *J*=2.8 Hz, 1H), 6.79 (d, *J*=1.0 Hz, 1H), 6.77 (d, *J*=0.9 Hz, 1H), 6.70–6.73 (m, 1H), 3.82 (s, 3H). ^{13}C NMR (100 MHz, DMSO): δ 165.8, 161.9, 149.7, 129.1, 128.7, 125.1, 118.5, 113.7, 112.3, 55.4. This is a known compound and the spectral data are identical to those reported in the literature.[9b]

*4.3.14. 4-(tert-Butyl)-N′,N′-diphenylbenzohydrazide (**4p**).* White solid (41.9 mg, 81%), mp 250.0–250.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (s, 1H), 7.80 (d, *J*=8.0 Hz, 2H), 7.45 (d, *J*=8.0 Hz, 2H), 7.27 (t, *J*=7.1 Hz, 4H), 7.20 (d, *J*=8.0 Hz, 4H), 7.03 (d, *J*=7.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.3, 155.9, 145.9, 129.5, 129.2, 127.2, 125.8, 123.0, 119.5, 35.1, 31.2. IR (KBr) ν/cm^{-1}: 3273, 3113, 2962, 2873, 1657, 1497, 1396, 1362, 850, 746, 700. HRMS (ESI) calculated for $C_{23}H_{24}N_2NaO$ $(M+Na)^+$: 367.1781, found: 367.1786.

*4.3.15. 4-Chloro-N′,N′-diphenylbenzohydrazide (**4q**).* White solid (40.7 mg, 84%), mp 175.5–178.6 °C. ^{1}H NMR (400 MHz, DMSO): δ 11.29 (s, 1H), 7.94–7.97 (m, 2H), 7.60–7.63 (m, 2H), 7.28–7.32 (m, 4H), 7.15 (dd, *J*=8.6, 1.0 Hz, 4H), 6.99 (dd, *J*=10.5, 4.1 Hz, 2H). ^{13}C NMR (100 MHz, DMSO): δ 164.8, 145.6, 136.9, 131.2, 129.4, 129.1, 128.7, 122.2, 118.7. IR (KBr) ν/cm^{-1}: 3246, 3041, 1655, 1494, 897, 746,

692. HRMS (ESI) calculated for $C_{19}H_{15}ClN_2NaO$ $(M+Na)^+$: 345.0765, found: 345.0744.

*4.3.16. N′,N′-Diphenyl-1-naphthohydrazide (**4r**).* White solid (48.4 mg, 83%), mp 175.5–178.6 °C. ^{1}H NMR (400 MHz, DMSO): δ 11.22 (s, 1H), 8.10–8.15 (m, 2H), 8.01–8.04 (m, 1H), 7.82 (d, *J*=7.0 Hz, 1H), 7.59–7.65 (m, 3H), 7.37 (t, *J*=7.7 Hz, 4H), 7.26 (d, *J*=8.2 Hz, 4H), 7.04 (t, *J*=7.2 Hz, 2H). ^{13}C NMR (100 MHz, DMSO): δ 168.4, 146.2, 133.7, 132.4, 131.2, 130.4, 129.7, 128.9, 127.7, 127.0, 126.2, 125.5, 125.3, 122.8, 119.2. IR (KBr) ν/cm^{-1}: 3250, 3050, 3106, 1650, 1490, 750, 700. HRMS (ESI) calculated for $C_{23}H_{18}N_2NaO$ $(M+Na)^+$: 361.1311, found: 361.1285.

*4.3.17. 4-Fluoro-N′-(3-methoxyphenyl)-N′-(4-methoxyphenyl)benzohydrazide (**4s**).* White solid (38.5 mg, 81%), mp 182.6–183.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.56 (s, 1H), 7.81 (dd, *J*=7.5, 5.6 Hz, 2H), 7.29 (d, *J*=8.4 Hz, 2H), 7.10 (t, *J*=8.2 Hz, 1H), 7.04 (t, *J*=8.3 Hz, 2H), 6.83 (d, *J*=8.4 Hz, 2H), 6.47 (dd, *J*=18.6, 7.8 Hz, 3H), 3.79 (s, 3H), 3.70 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4 (*J*=251 Hz), 165.55, 160.5, 157.5, 148.6, 138.4, 129.9, 129.8 (*J*=9 Hz), 128.6, 126.1, 116.0 (*J*=22 Hz), 114.7, 107.9, 105.5, 101.7, 55.5, 55.2. IR (KBr) ν/cm^{-1}: 3260, 3118, 2954, 2865, 1655, 1508, 1245, 1298, 852. HRMS (ESI) calculated for $C_{21}H_{19}FN_2NaO_3$ $(M+Na)^+$: 389.1272, found: 389.1255.

*4.3.18. 4-Bromo-N′-(3-methoxyphenyl)-N′-(4-methoxyphenyl)benzohydrazide (**4t**).* White solid (52.6 mg, 82%), mp 152.6–153.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (s, 1H), 7.66 (d, *J*=8.1 Hz, 2H), 7.50 (d, *J*=8.2 Hz, 2H), 7.29 (d, *J*=8.6 Hz, 2H), 7.11 (t, *J*=8.3 Hz, 1H), 6.84 (d, *J*=8.7 Hz, 2H), 6.46 (dd, *J*=13.0, 7.5 Hz, 3H), 3.79 (s, 3H), 3.71 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6, 160.5, 157.5, 148.5, 138.3, 132.0, 131.3, 129.9, 128.9, 127.0, 126.1, 114.7, 107.9, 105.6, 101.7, 55.5, 55.2. IR (KBr) ν/cm^{-1}: 3253, 3111, 2953, 2863, 1657, 1508, 1245, 1299, 1035, 892. HRMS (ESI) calculated for $C_{21}H_{19}BrN_2NaO_3$ $(M+Na)^+$: 449.0471, found: 449.0466.

*4.3.19. N′-(3-Methoxyphenyl)-N′-(4-methoxyphenyl)-4-(trifluoromethyl)benzohydrazide (**4u**).* White solid (58.8 mg, 94%), mp 181.9–182.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58 (s, 1H), 7.91 (d, *J*=8.0 Hz, 2H), 7.64 (d, *J*=8.0 Hz, 2H), 7.31 (d, *J*=8.6 Hz, 2H), 7.12 (t, *J*=8.1 Hz, 1H), 6.85 (d, *J*=8.6 Hz, 2H), 6.48 (dd, *J*=13.0, 7.8 Hz, 3H), 3.80 (s, 3H), 3.71 (s, 3H). ^{13}C NMR (100 MHz, DMSO): δ 164.6, 160.0, 156.6, 148.5, 138.1, 136.4, 132.2 (*J*=32 Hz), 129.8, 128.4, 127.9 (*J*=272 Hz), 125.6 (*J*=7 Hz), 125.3, 114.5, 107.4, 104.8, 100.9, 55.2, 54.9. IR (KBr) ν/cm^{-1}: 3255, 3010, 2998, 1650, 1509, 1237, 835. HRMS (ESI) calculated for $C_{22}H_{19}F_3N_2NaO_3$ $(M+Na)^+$: 439.1240, found: 439.1226.

*4.3.20. N′-(3-Methoxyphenyl)-N′-(4-methoxyphenyl)furan-2-carbohydrazide (**4w**).* White solid (27.5 mg, 54%), mp 155.9–156.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58 (s, 1H), 7.42 (s, 1H), 7.32 (d, *J*=8.9 Hz, 2H), 7.16 (d, *J*=3.4 Hz, 1H), 7.10 (t, *J*=8.1 Hz, 1H), 6.85 (d, *J*=8.9 Hz, 2H), 6.42–6.52 (m, 4H), 3.78 (s, 3H), 3.70 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.5, 157.6, 157.3, 148.7, 146.6, 144.5, 138.5, 129.8, 126.3, 116.0, 114.7, 112.3, 108.0, 105.7, 101.8, 55.5, 55.2. IR (KBr) ν/cm^{-1}: 3225, 3080, 2960, 2810, 1630, 1505, 1247, 820. HRMS (ESI) calculated for $C_{19}H_{18}N_2NaO_4$ $(M+Na)^+$: 361.1159, found: 361.1135.

*4.3.21. N′-(3-methoxyphenyl)-N′-(4-methoxyphenyl)thiophene-2-carbohydrazide (**4x**) and N′-(2-methoxyphenyl)-N′-(4-methoxyphenyl)thiophene-2-carbohydrazide (**4x′**).* Off-white solid (47.9 mg, 90%), mp 152.0–152.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (s, 1H), 8.05 (d, *J*=2.3 Hz, 1H), 7.66 (d, *J*=2.3 Hz, 1H), 7.52 (d, *J*=4.8 Hz, 2H), 7.48 (s, 1H), 7.34 (d, *J*=8.4 Hz, 2H), 7.20 (dd, *J*=19.5, 8.4 Hz, 3H), 7.07–7.13 (m, 3H), 6.69–6.88 (m, 4H), 6.68 (d, *J*=8.3 Hz, 1H), 6.65 (s, 1H), 6.58 (d, *J*=8.0 Hz, 1H), 6.52 (d, *J*=8.2 Hz, 1H), 6.48 (s, 1H), 6.44 (d, *J*=8.1 Hz, 1H), 3.79 (s, 6H), 3.74 (s, 3H), 3.71 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.8, 161.0, 160.5, 157.5, 149.1, 148.6, 139.7, 138.4, 136.0, 135.4, 133.7, 131.3, 130.8, 130.0, 129.9, 129.4, 127.9, 126.8, 126.2, 124.3, 114.7, 110.4, 108.0, 107.9, 105.7, 104.1, 101.7, 55.5, 55.3, 55.2. IR (KBr) ν/cm^{-1}: 3235, 3083, 2958, 2840, 1665, 1509, 1312, 1250, 830. HRMS (ESI) calculated for $C_{19}H_{18}N_2NaO_3S$ $(M+Na)^+$: 377.0930, found: 377.0919.

*4.3.22. N′-(3-Methoxyphenyl)-N′-(4-methoxyphenyl)-1-methyl-1H-pyrrole-2-carbohydrazide (**4y**).* White solid (33.8 mg, 64%), mp 153.8–154.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (s, 1H), 7.32 (d, *J*=8.0 Hz, 2H), 7.11 (t, *J*=8.1 Hz, 1H), 6.87 (d, *J*=8.4 Hz, 2H), 6.78 (s, 1H), 6.70 (s, 1H), 6.55 (d, *J*=8.2 Hz, 1H), 6.51 (s, 1H), 6.43 (d, *J*=7.8 Hz, 1H), 6.10 (s, 1H), 3.92 (s, 3H), 3.79 (s, 3H), 3.71 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.8, 160.5, 157.2, 148.8, 138.7, 129.8, 129.0, 125.5, 123.2, 114.6, 112.2, 108.0, 107.6, 105.6, 101.6, 55.5, 55.2, 36.8. IR (KBr) ν/cm^{-1}: 3259, 3091, 2966, 2933, 1655, 1603, 1489, 1240, 1031, 833. HRMS (ESI) calculated for $C_{20}H_{21}N_3NaO_3$ $(M+Na)^+$: 374.1475, found: 374.1463.

*4.3.23. N′-(3-Methoxyphenyl)-N′-(4-methoxyphenyl)pivalohydrazide (**4z**).* White solid (16.3 mg, 33%), mp 185.6–186.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (s, 1H), 7.25 (d, *J*=9.0 Hz, 2H), 7.10 (t, *J*=8.0 Hz, 1H), 6.86 (d, *J*=8.6 Hz, 2H), 6.40–6.44 (m, 3H), 3.80 (s, 3H), 3.72 (s, 3H), 1.28 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.6, 160.4, 157.1, 148.6, 138.6, 129.8, 125.5, 114.6, 107.8, 105.6, 101.4, 55.5, 55.2, 38.3, 27.5. IR (KBr) ν/cm^{-1}: 3244, 3107, 2954, 1664, 1491, 1395, 1365, 1228, 1101, 832. HRMS (ESI) calculated for $C_{19}H_{25}N_2O_3$ $(M+H)^+$: 329.1860, found: 329.1847.

*4.3.24. 3,4-Dichloro-N′-(2-(2-(3,4-dichlorobenzoyl)hydrazinyl)-5-methoxyphenyl)-N′-(4-methoxyphenyl)benzohydrazide (**5**).* White solid (36.3 mg, 39%), mp 146.6–147.6 °C. ^{1}H NMR (400 MHz, DMSO): δ 11.08 (s, 1H), 10.64 (d, *J*=3.5 Hz, 1H), 8.18 (d, *J*=2.0 Hz, 1H), 8.11 (d, *J*=2.0 Hz, 1H), 7.91 (dd, *J*=8.4, 2.0 Hz, 1H), 7.85 (td, *J*=5.1, 2.5 Hz, 2H), 7.79 (d, *J*=8.4 Hz, 1H), 7.67 (d, *J*=3.4 Hz, 1H), 6.85–6.88 (m, 3H), 6.83 (d, *J*=2.2 Hz, 2H), 6.70–6.74 (m, 2H), 3.69 (s, 3H), 3.65 (s, 3H). ^{13}C NMR (100 MHz, DMSO): δ 164.5, 163.9, 153.5, 153.1, 141.2, 140.4, 134.8, 134.5, 133.2, 132.7, 132.4, 131.5, 131.4, 131.0, 130.9, 129.4, 129.2, 127.9, 127.5, 115.6, 114.3, 114.1, 113.7, 55.4, 55.3. IR (KBr) ν/cm^{-1}: 3250, 3084, 2960, 2870, 1644, 1506, 1242, 1033, 758, 700. HRMS (ESI) calculated for $C_{28}H_{21}Cl_4N_4O_4$ $(M-H)^-$: 617.0322, found: 617.0300.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2015.10.023. These data include MOL files and InChiKeys of the most important compounds described in this article.

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