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ORIGINAL PAPER

$AlCl_3·6H_2O$-catalyzed Schiff-base reaction between aryl ketones and aromatic acylhydrazines/hydrazines in water

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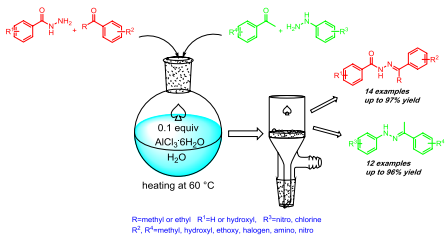
Abstract

Schiff-bases have important applications in the field of analysis, biomedicine, as well as material sciences. Hydrazones and acylhydrazones are two representative types of Schiff-bases. In this study, a green synthesis of aromatic hydrazones and acylhydrazones via Schiff-base reaction of aryl ketones and aromatic acylhydrazines/hydrazines had been reported. In the synthesis, water was used as solvent and $AlCl_3·6H_2O$ was used as catalyst. The reaction is simple, highly efficient, and eco-friendly.

Graphic abstract



Keywords Green synthesis · Acylhydrazone · Hydrazone · $AlCl_3·6H_2O$

Introduction

Environment-friendly chemical processes and products are essential in the sustainable development of mankind. Green chemistry is one of the most attractive concepts in organic chemistry because of its low pollution and low cost. Environmentally friendly solvent is an important research area of green chemistry with great merits [1]. In this study, a variety of Schiff-bases were prepared with an efficient and green synthetic method.

Schiff-base reaction was discovered by Hugo Schiff in 1864 [2], which refers to the reaction between carbonyls (aldehydes and ketones) and amines (primary amine, hydrazine, acylhydrazine, and hydroxylamine) condensed into imine groups (–C=N–). The formation of C=N bond belongs to dynamic covalent reactions [3], and Schiff-base's structure has obvious reversibility with the change of pH [4], which makes it useful in many fields. Over the last few decades, Schiff-bases had been widely used in analysis [5, 6], biomedicine [7–9], and material sciences [10, 11].

Conventionally, Schiff-bases can be prepared in organic solvents [12, 13]. For example, Enthaler et al. [14] and Lu et al. [15] prepared acylhydrazones by the reaction between aromatic ketones and acylhydrazines in EtOH and THF, respectively. Rathelot et al. [16] prepared hydrazones in organic solvent with AcOH as catalyst in high yield and short reaction time. However, green synthetic methods for Schiff-bases with water as solvent seem to be more attractive in terms of cost and environmental protection. $AlCl_3$ had

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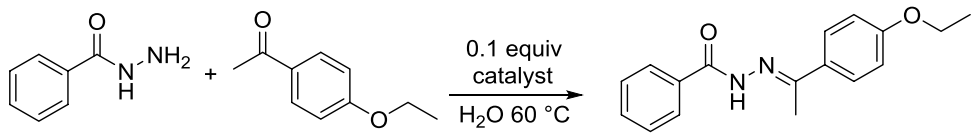
Table 1 Examination of reaction conditions



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

Entry	Catalyst (0.1 equiv)	Time/h	Yield/%
1	CH_3COOH	12	–
2	HCl	12	–
3	$ZnCl_2$	12	–
4	$ZnBr_2$	12	–
5	$CuCl_2{\cdot}2H_2O$	7	56
6	$FeCl_3$	4	68
7	$AlCl_3{\cdot}6H_2O$	2.5	74

been reported as an efficient Lewis acid catalyst. However, it is generally thought to be unstable in aqueous medium and recommended to be used as catalyst in organic solvents under anhydrous conditions [17]. Fringuelli et al. [18] discovered that 1 mol% of $AlCl_3$ effectively catalyzed the azidolysis of α,β-epoxycarboxylic acids in water at pH 4.0. In this study, a novel, simple, and green method was first developed to obtain various aromatic acylhydrazones by reacting ketones with acylhydrazines and adding 0.1 equiv $AlCl_3{\cdot}6H_2O$ as new catalyst in water. High purity products were collected by filtration and drying. It is delightful that a considerable number of aromatic hydrazone compounds had also been prepared using the same method. Most important of all, $AlCl_3{\cdot}6H_2O$ slowly dissociates in water and the reactions are mild and safe. This methodology has a wider range of substrate suitability and more simple operation.

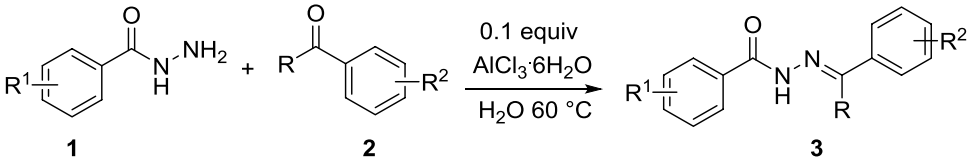
To explore and optimize reaction conditions, we begin our study with the model reaction between benzoylhydrazine (**1a**) and 1-(4-ethoxyphenyl)ethanone (**2a**) in water. It is worth mentioned that all the aromatic ketones can easily soluble in water under heating conditions in this study. It is reported that weak acid condition can promote the formation of –C=N– [4], so the reaction was first carried out in water with CH_3COOH and HCl as catalyst, but no product was formed. To find a suitable catalyst, the reaction was performed using different Lewis acid such as $ZnCl_2$, $ZnBr_2$, $CuCl_2{\cdot}2H_2O$, $FeCl_3$, and $AlCl_3{\cdot}6H_2O$ as catalyst in water at 60 °C. As shown in Table 1, desired product **3aa** was obtained with 56% yield using $CuCl_2{\cdot}2H_2O$ as catalyst. Although the reaction was done within 7 h, the yield of product was difficult to improve by changing the reaction temperature. To our delight, the reaction in the presence of $FeCl_3$ afforded **3aa** in 68% yield. Fortunately, further studies revealed that the catalyst $AlCl_3{\cdot}6H_2O$ was more effective for achieving this reaction, and the corresponding adduct **3aa** was obtained in 74% yield and faster reaction rate.

Results and discussion

In accordance with the optimized conditions, we then explored the scope of this Schiff-base reaction with various ketones and acylhydrazines (Table 2). Aryl ketones with a hydroxyl in the *para*-position and *meta*-position had a fast reaction rate and ordinary yield (**3ab**, **3ac**). Furthermore, benzoic acid [1-(2-hydroxyphenyl)ethylidene]hydrazide (**3ad**) and 4-hydroxybenzoic acid 2-[1-(2-hydroxylphenyl)-ethylidene]hydrazide (**3bd**) were obtained in higher yields but the reaction time is longer. Perhaps it is the formation of intramolecular hydrogen bond between *ortho*-hydroxyl group and carbonyl oxygen that makes carbonyl more active, and thus facilitates to decompose. Meanwhile, *ortho* steric hindrance leads to longer reaction time to exhaust reactant. Besides, the reaction of **2e** bearing a strong electron-withdrawing nitro group at *meta*-position of phenyl with benzoylhydrazine leads to the product **3ae** in good yield and short reaction time. Maybe, electron-withdrawing group on the aromatic ketone is beneficial to the reaction.

Halogen groups such as Br and F, electron-donating groups such as ethoxyl, methyl, and amino in the phenyl unit in the ketones were all well tolerated in this reaction. Benzoylhydrazine reacted smoothly with 1-(4-bromophenyl)-ethanone (**2f**) and 1-(3,4-difluorophenyl)ethanone (**2g**) to furnish the corresponding products in good yields, respectively (Table 2, **3af** and **3ag**). This trend may be attributed to the weak electron-withdrawing capability of halogen groups, which may promote the reaction between carbonyl and benzoylhydrazines. But if with C-F bond adjacent to methyl

Table 2 $AlCl_3{\cdot}6H_2O$ catalyzed Schiff-base reaction of acylhydrazines and ketones in water

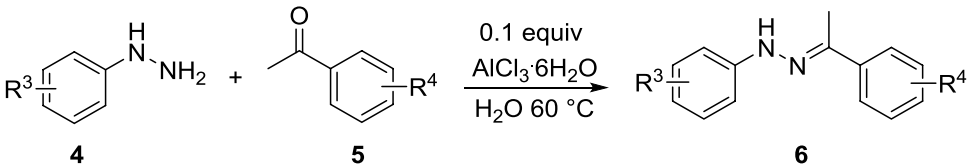


1 2 3

Entry	R^1	R^2	Time/h	Yield/%	References
3aa	H (**1a**)	4-Ethoxy (**2a**)	2.5	74	–
3ab	H (**1a**)	4-Hydroxy (**2b**)	1	71	[19]
3ac	H (**1a**)	3-Hydroxy (**2c**)	1	74	–
3ad	H (**1a**)	2-Hydroxy (**2d**)	5	95	[20]
3ae	H (**1a**)	4-Methyl-3-nitro (**2e**)	1.5	97	–
3af	H (**1a**)	4-Bromo (**2f**)	1.5	95	[21]
3ag	H (**1a**)	3,4-Difluoro (**2g**)	1.5	80	–
3ah	H (**1a**)	2-Fluoro (**2h**)	1	76	–
3ai[a]	H (**1a**)	4-Methyl (**2i**)	7.5	73	–
3ba	4-Hydroxy (**1c**)	4-Ethoxy (**2a**)	13	90	–
3bd	4-Hydroxy (**1c**)	2-Hydroxy (**2d**)	2.5	82	[22]
3bl	4-Hydroxy (**1c**)	4-Amino (**2l**)	12	80	–
3cc	Nicotinic hydrazide (**1c**)	3-Hydroxyl (**2c**)	3	86	–
3cl	Nicotinic hydrazide (**1c**)	4-Amino (**2l**)	10	79	[23]

[a]R = ethyl

Table 3 $AlCl_3{\cdot}6H_2O$ catalyzed Schiff-base reactions of hydrazines and ketones in water

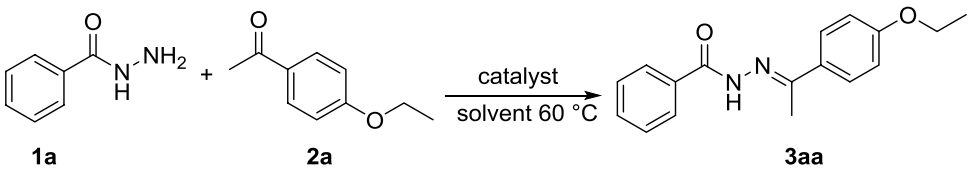


4 5 6

Entry	R^3	R^4	Time	Yield/%	References
6aa	H (**4a**)	4-Amino (**5a**)	15 min	68	[24]
6ab	H (**4a**)	4-Hydroxy (**5b**)	10 min	91	[25]
6ac	H (**4a**)	3-Hydroxy (**5c**)	1 h	91	[26]
6ad	H (**4a**)	2-Hydroxy (**5d**)	2.5 h	70	[27]
6ae	H (**4a**)	3,4-Difluoro (**5e**)	3 h	96	–
6af	H (**4a**)	4-Bromo (**5f**)	4 h	85	[25]
6ba	4-Chloro (**4b**)	4-Amino (**5a**)	1.5 h	76	–
6cc	2,4-Dinitro (**4c**)	3-Hydroxy (**5c**)	1.5 h	87	–
6da	4-Nitro (**4d**)	4-Amino (**5a**)	10 min	66	[29]
6dc	4-Nitro (**4d**)	3-Hydroxy (**5c**)	10 min	84	[28]
6dg	4-Nitro (**4d**)	2-Methyl (**5g**)	1.5 h	56	–
6dh	4-Nitro (**4d**)	H (**5h**)	20 min	72	[30]

phenyl ketone **2h**, both yield and reaction time will decrease. Maybe less hindered C-F bond has a negative effect on yield (Table 2, **3ah**). In addition, we employed a series of methyl phenyl ketones with electron-donating groups in phenyl. As shown in Table 2, the reactions between aryl ketones **2a**, **2b**, and **2i** and benzoylhydrazine afford to corresponding

Table 4 Control experiments for the $AlCl_3.6H_2O$-Catalyzed formation of C=N bond



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

Entry	Solvent (10 cm^3)	Catalyst (0.1 equiv)	Time/h	Yield/%
1	CH_3CH_2OH	$AlCl_3.6H_2O$	12	29
2	CH_3CH_2OH	None	12	29
3	H_2O	HCl/CH_3COOH	12	0
4	H_2O	$AlCl_3.6H_2O$	2.5	74

products **3aa**, **3ab**, and **3ai** in lower yields, respectively. Maybe electron-donating groups of aryl ketones are not conductive to the progress of the reaction. Moreover, benzoylhydrazine bearing electron-donating groups, such as 4-hydroxybenzoylhydrazine, provides corresponding products **3ba** and **3bl** in high yields, which confirms that the electron-donating groups of benzoylhydrazines may improve the nucleophilicity of acylhydrazine.

This green synthetic method inspires us to further expand its applications to more types of reactions. In the light of the procedure of forming acylhydrazones, $AlCl_3{\cdot}6H_2O$ plays a key role in forming C=N bond. It is well-known that hydrazones, imines and oximes are Schiff-bases with a structure of C=N. We next applied the same conditions to try to synthesize these three Schiff-bases. It is satisfied that it is easier to prepare hydrazones by the reaction of various aromatic ketones and hydrazines, and the corresponding results are displayed in Table 3. Compounds **6ac**, **6cc**, and **6dc** bearing a *meta*-hydroxy-substituted phenyl ring could be prepared in a high yield as well as fast reaction rate. Maybe it is due to electron-withdrawing of *meta*-hydroxyl group on the benzene ring, which makes the carbonyl group more susceptible to decomposition. However, 1-(2-hydroxyphenyl)ethanone (**5d**) leads to a lower yield and longer reaction time. Maybe electron-donating and sterically hindered *ortho*-hydroxyl groups of benzene ring are not conductive to the formation of hydrazones.

Moreover, we investigated this reaction process by the reaction of aromatic hydrazines and ketones with electron-donating substituents including amino (**5a**) and methyl (**5g**). Notably, the aromatic ketones with *para*-amino and *ortho*-methyl produced corresponding hydrazones in lower yields (**6aa**, **6ba**, **6da**, and **6dg**). This confirms a rule that the electron-donating group on the aromatic ketone is not conductive to the condensation reaction. Besides, the low yield of compound **6dg** is consistent with that of compound **6ad**. It is further proved that aromatic ketones with *ortho*-position electron-donating group are not conductive to the formation of hydrazones. Interestingly, halogen groups, such as F and Br, in the aryl unit in the ketones give a good yield (**6ae** and **6af**); perhaps weak electron-withdrawing halogen group increases the reactivity of the carbonyl group.

To have a good insight into the reaction mechanism, we carried out a few control experiments for the $AlCl_3.6H_2O$-catalyzed reaction between **1a** and **2a**. First, the reaction was performed in CH_3CH_2OH under refluxing,but reactants **1a** and **2a** cannot be exhausted completely after 12 h. The product was collected by silica gel column chromatography and the yield was shown in Table 4. It can be inferred that perhaps $AlCl_3.6H_2O$ cannot activate carbonyl in this reaction. If the reaction was performed in water used the same $AlCl_3.6H_2O$ as catalyst, the desired product **3aa** was easily obtained in 74% after 2.5 h. To identify whether acidic condition is important to cause the reaction happens, control group experiments were also performed in the presence of HCl or CH_3COOH (Table 4), but no product **3aa** was formed in these two reactions. It is reported that $AlCl_3$ dissociates in water and forms the corresponding aqua ion $Al(H_2O)_6^{3+}$ [18]. We believe $Al(H_2O)_6^{3+}$ plays a critical role in this reaction and it is the real catalyst. Maybe it can activate carbonyl carbon by interacting with the arylketonic oxygen. Thus, nucleophile aromatic arylhydrazines/hydrazines are easier to react with arylketones to afford C=N bond.

Conclusion

In summary, we have developed a new strategy for the efficient and green synthesis of various aromatic acylhydrazones and hydrazones via an efficient C=N bond formation pathway, water was used as the solvent. Various electron-withdrawing groups and electron-donating groups were well tolerated. Meanwhile, catalyst $AlCl_3{\cdot}6H_2O$ plays a vital role in this reaction. This green synthesis of aromatic hydrazones and acylhydrazones will have a broad application prospects.

Experimental

All reagents were purchased from commercial suppliers without further purification. Experiments were monitored by thin layer chromatography (TLC) and the TLC was performed on pre-coated silica gel plates. The ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance III 500 MHz spectrometer with DMSO-d_6 as the solvent and tetramethylsilane (TMS) as an internal standard at room temperature. Chemical shifts are given in δ relative to TMS, and the coupling constants J values are given in Hertz (Hz). HRMS were obtained from solariX.

Synthesis of aromatic acylhydrazones and hydrazones

Acylhydrazines (1 mmol), aromatic ketones (1 mmol), and $AlCl_3·6H_2O$ (0.1 mmol) were first charged to a round-bottom flask. 10 cm^3 water was also added to the flask. Then the reaction mixture was heated to 60 °C and stirred. TLC was used to monitor reaction progress. After the reaction was completed, solids were collected by filtration; the filtrate was washed by water. The product was drained by vacuum pump to afford desired compound.

Benzoic acid [1-(4-ethoxyphenyl)ethylidene]hydrazide (3aa, $C_{17}H_{18}N_2O_2$) White solid; m.p.: 157–158 °C; yield: 208 mg (74%); ^1H NMR (500 MHz, DMSO-d_6): $\delta = 10.72$ (s, 1H), 8.05-7.68 (m, 4H), 7.62–7.47 (m, 3H), 6.98 (d, $J = 6.7$ Hz, 2H), 4.14–3.97 (m, 2H), 2.34 (s, 3H), 1.34 (t, $J = 6.8$ Hz, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): $\delta = 164.08$, 160.20, 156.27, 134.61, 131.85, 130.80, 128.76, 128.42, 128.26, 128.24, 128.14, 114.60, 63.64, 15.06 ppm; HRMS (ESI): *m/z* calcd for $C_{17}H_{18}N_2O_2$ ($[M+H]^+$) 283.1441, found 283.1441.

Benzoic acid [1-(3-hydroxyphenyl)ethylidene]hydrazide (3ac, $C_{15}H_{14}N_2O_2$) White solid; m.p.: 180–181 °C; yield: 188 mg (74%); ^1H NMR (500 MHz, DMSO-d_6): $\delta = 10.74$ (s, 1H), 9.58 (s, 1H), 7.96-7.82 (m, 2H), 7.59 (t, $J = 7.3$ Hz, 1H), 7.52 (t, $J = 7.5$ Hz, 2H), 7.35 (s, 1H), 7.24 (d, $J = 8.7$ Hz, 2H), 6.85 (d, $J = 7.0$ Hz, 1H), 2.34 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): $\delta = 164.35$, 157.75, 155.97, 139.93, 134.57, 131.85, 129.80, 128.76, 128.31, 117.94, 117.11, 113.44, 15.06 ppm; HRMS (ESI): *m/z* calcd for $C_{15}H_{14}N_2O_2$ ($[M+H]^+$) 255.1128, found 255.1135.

Benzoic acid [1-(4-methyl-3-nitrophenyl)ethylidene]-hydrazide (3ae, $C_{16}H_{15}N_3O_3$) White solid; m.p.: 203–204 °C; yield: 288 mg (97%); ^1H NMR (500 MHz, DMSO-d_6): $\delta = 10.91$ (s, 1H), 8.42 (d, $J = 17.3$ Hz, 1H), 8.13–8.02 (m, 1H), 7.90 (s, 2H), 7.59 (d, $J = 7.5$ Hz, 2H), 7.53 (t, $J = 7.2$ Hz, 2H), 2.55 (s, 3H), 2.41 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): $\delta = 164.55$, 153.08, 149.51, 137.81, 134.42, 133.99, 133.42, 132.00, 131.15, 128.73, 128.44, 122.21, 19.82, 14.71 ppm; HRMS (ESI): *m/z* calcd for $C_{16}H_{15}N_3O_3$ ($[M+H]^+$) 298.1186, found 298.1189.

Benzoic acid [1-(4-bromophenyl)ethylidene]hydrazide (3af, $C_{15}H_{13}BrN_2O$) White solid; m.p.: 220–221 °C; yield: 300 mg (95%); ^1H NMR (500 MHz, DMSO-d_6): $\delta = 10.82$ (s, 1H), 7.85 (d, $J = 40.8$ Hz, 4H), 7.61 (dd, $J = 26.4$, 6.2 Hz, 3H), 7.52 (t, $J = 7.1$ Hz, 2H), 2.37 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): $\delta = 164.50$, 154.41, 137.80, 134.48, 131.78, 128.87, 128.77, 128.39, 123.36, 40.53, 14.76 ppm; HRMS (ESI): *m/z* calcd for $C_{15}H_{13}BrN_2O$ ($[M+H]^+$) 317.0284, found 317.0287.

Benzoic acid [1-(3,4-difluorophenyl)ethylidene]hydrazide (3ag, $C_{15}H_{13}F_2N_2O$) White solid; m.p.: 206–207 °C; yield: 219 mg (80%); ^1H NMR (500 MHz, DMSO-d_6): $\delta = 10.86$ (s, 1H), 7.89 (s, 3H), 7.72 (s, 1H), 7.59 (d, $J = 6.8$ Hz, 1H), 7.52 (t, $J = 7.3$ Hz, 3H), 2.37 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): $\delta = 164.50$, 153.38, 150.74, 148.89, 136.30, 134.43, 132.00, 128.74, 128.43, 123.89, 117.94, 117.80, 115.79, 115.64, 14.84 ppm; HRMS (ESI): *m/z* calcd for $C_{15}H_{13}F_2N_2O$ ($[M+H]^+$) 275.0990, found 275.0997.

Benzoic acid [1-(2-fluorophenyl)ethylidene]hydrazide (3ah, $C_{15}H_{13}FN_2O$) White solid; m.p.: 157–159 °C; yield: 195 mg (76%); ^1H NMR (500 MHz, DMSO-d_6): $\delta = 10.83$ (s, 1H), 7.95-7.83 (m, 2H), 7.59 (s, 2H), 7.51 (dd, $J = 17.9$, 11.3 Hz, 3H), 7.28 (t, $J = 9.5$ Hz, 2H), 2.38 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): $\delta = 161.41$, 159.44, 153.71, 134.40, 132.00, 131.58, 131.51, 130.27, 128.74, 128.45, 127.82, 127.73, 124.90, 116.51, 18.28 ppm; HRMS (ESI): *m/z* calcd for $C_{15}H_{13}FN_2O$ ($[M+H]^+$) 257.1085, found 257.1090.

Benzoic acid [1-(4-methylphenyl)propylidene]hydrazide (3ai, $C_{17}H_{18}N_2O$) White solid; m.p.: 146–147 °C; yield: 194 mg (73%); ^1H NMR (500 MHz, DMSO-d_6): $\delta = 10.80$ (s, 1H), 7.80 (d, $J = 54.4$ Hz, 4H), 7.63–7.56 (m, 1H), 7.53 (d, $J = 7.6$ Hz, 2H), 7.30–7.15 (m, 2H), 2.91 (q, $J = 7.6$ Hz, 2H), 2.35 (d, $J = 4.7$ Hz, 3H), 1.08 (t, $J = 7.6$ Hz, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): $\delta = 164.63$, 159.76, 139.29, 134.63, 131.81, 129.50, 128.72, 128.38, 127.56, 126.98, 21.30, 20.24, 11.41 ppm; HRMS (ESI): *m/z* calcd for $C_{17}H_{18}N_2O$ ($[M+H]^+$) 267.1491, found 267.1492.

4-Hydroxybenzoic acid 2-[1-(4-ethoxyphenyl)propylidene]-hydrazide (3ba, $C_{17}H_{18}N_2O_3$) White solid; m.p.: 225–226 °C; yield: 268 mg (90%); ^1H NMR (500 MHz, DMSO-d_6): $\delta = 10.44$ (s, 1H), 10.07 (s, 1H), 7.79 (d, $J = 8.4$ Hz, 4H), 6.96 (d, $J = 8.7$ Hz, 2H), 6.86 (d, $J = 8.6$ Hz, 2H), 4.07 (q, $J = 6.9$ Hz, 2H), 2.31 (s, 3H), 1.34 (t, $J = 7.0$ Hz, 3H)

ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 163.72, 160.84, 160.02, 148.49, 130.96, 130.32, 128.28, 125.09, 115.28, 114.58, 63.62, 15.07, 14.59 ppm; HRMS (ESI): *m/z* calcd for $C_{17}H_{18}N_2O_3$ ($[M+H]^+$) 299.1390, found 299.1395.

4-Hydroxybenzoic acid 2-[1-(4-aminophenyl)propylidene]-hydrazide (3bl, $C_{15}H_{15}N_2O_3$) Light yellow solid; m.p.: 272–274 °C; yield: 215 mg (80%); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 10.33 (s, 1H), 10.05 (s, 1H), 7.87–7.71 (m, 2H), 7.58 (s, 2H), 6.92–6.81 (m, 2H), 6.65–6.53 (m, 2H), 5.48 (s, 2H), 2.25 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 163.48, 160.70, 156.73, 150.69, 130.15, 128.09, 125.80, 125.30, 115.30, 113.67, 14.45 ppm; HRMS (ESI): *m/z* calcd for $C_{15}H_{15}N_2O_3$ ($[M+H]^+$) 270.1237, found 270.1237.

3-Pyridinecarboxylic acid [1-(3-hydroxyphenyl)propylidene]-hydrazide (3cc, $C_{14}H_{13}N_2O_3$) White solid; m.p.: 191–192 °C; yield: 219 mg (86%); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 10.94 (s, 1H), 9.59 (s, 1H), 9.06 (s, 1H), 8.79–8.73 (m, 1H), 8.25 (d, J = 7.9 Hz, 1H), 7.58–7.53 (m, 1H), 7.36 (s, 1H), 7.25 (d, J = 9.0 Hz, 2H), 6.86 (d, J = 7.3 Hz, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 162.96, 157.77, 156.37, 152.44, 149.24, 139.79, 136.18, 130.34, 129.82, 123.90, 118.04, 117.29, 113.47, 15.24 ppm; HRMS (ESI): *m/z* calcd for $C_{14}H_{13}N_2O_3$ ($[M+H]^+$) 256.1081, found 256.1082.

3-Pyridinecarboxylic acid [1-(4-aminophenyl)propylidene]-hydrazide (3cl, $C_{14}H_{14}N_4O$) Yellow solid; m.p.: 207–208 °C; yield: 201 mg (79%); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 10.82 (s, 1H), 9.05 (s, 1H), 8.71 (d, J = 25.8 Hz, 1H), 8.28–8.10 (m, 1H), 7.70–7.31 (m, 3H), 6.62 (s, 2H), 5.53 (s, 2H), 2.29 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 162.47, 158.40, 152.24, 151.04, 149.06, 135.98, 130.53, 128.37, 125.37, 123.93, 113.69, 14.79 ppm; HRMS (ESI): *m/z* calcd for $C_{14}H_{14}N_4O$ ($[M+H]^+$) 255.1240, found 255.1242.

1-(3,4-Difluorophenyl)ethanone phenylhydrazone (6ae, $C_{14}H_{12}F_2N_2$) Brown solid; m.p.: 130–134 °C; yield: 236 mg (96%); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 9.37 (s, 1H), 7.82-7.75 (m, 1H), 7.59 (s, 1H), 7.43-7.37 (m, 1H), 7.28-7.22 (m, 4H), 6.78 (t, J = 6.8 Hz, 1H), 2.24 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 150.96, 146.23, 138.81, 137.46, 129.37, 122.15, 119.61, 117.68, 117.55, 114.22, 114.08, 113.40, 13.11 ppm; HRMS (ESI): *m/z* calcd for $C_{14}H_{12}F_2N_2$ ($[M+H]^+$) 247.1041, found 247.1044.

1-(4-Amniophenyl)ethanone 2-(4-chlorophenyl)hydrazone (6ba, $C_{14}H_{14}ClN_3$) Yellow solid; m.p.: 159–160 °C; yield: 197 mg (76%); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 9.09 (s, 1H), 7.51 (d, J = 8.2 Hz, 2H), 7.20 (q, J = 8.7 Hz, 4H), 6.58 (d, J = 8.2 Hz, 2H), 5.28 (s, 2H), 2.17 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 149.27, 146.03, 143.35, 129.02, 127.16, 126.83, 121.72, 114.37, 113.92, 13.30 ppm; HRMS (ESI): *m/z* calcd for $C_{14}H_{14}ClN_3$ ($[M+H]^+$) 260.0949, found 260.0951.

1-(3-Hydroxyphenyl)ethanone 2-(2,4-dinitrophenyl)hydrazone (6cc, $C_{14}H_{12}N_4O_5$) Red solid; m.p.: 250–252 °C; yield: 275 mg (87%); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 10.99 (s, 1H), 9.59 (s, 1H), 8.79 (s, 1H), 8.35 (d, J = 12.0 Hz, 1H), 7.93 (d, J = 9.5 Hz, 1H), 7.23 (dq, J = 15.6, 7.8 Hz, 3H), 6.83 (d, J = 5.7 Hz, 1H), 2.33 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 157.90, 153.43, 149.58, 144.77, 138.63, 137.67, 130.50, 129.90, 123.29, 117.82, 117.47, 116.69, 113.37, 13.70 ppm; HRMS (ESI): *m/z* calcd for $C_{14}H_{12}N_4O_5$ ($[M+H]^+$) 317.0880, found 317.0885.

1-(2-Methylphenyl)ethanone 2-(4-nitrophenyl)hydrazone (6dg, $C_{15}H_{15}N_3O_2$) Yellow solid; m.p.: 147–151 °C; yield: 151 mg (56%); ^{1}H NMR (500 MHz, DMSO-d_6): δ = 10.13 (s, 1H), 8.12 (d, J = 9.3 Hz, 2H), 7.35 (d, J = 7.9 Hz, 1H), 7.29–7.24 (m, 5H), 2.41 (s, 3H), 2.31 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 151.97, 149.34, 140.15, 138.88, 135.52, 131.20, 128.62, 128.31, 126.33, 126.15, 112.23, 21.21, 18.08 ppm; HRMS (ESI): *m/z* calcd for $C_{15}H_{15}N_3O_2$ ($[M+Na]^+$) 292.1056, found 292.1057.

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