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Three component solvent-free synthesis of 1*H*-pyrazol-5(4*H*)-one-based heterocyclic ketene aminal derivatives†

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An efficient one-pot three-component synthesis of novel 1*H*-pyrazol-5(4*H*)-one-based heterocyclic ketene aminal libraries was performed by simply refluxing a mixture of heterocyclic ketene aminals (HKAs), 1-phenyl-1*H*-pyrazol-5(4*H*)-ones and triethoxymethane under solvent-free and catalyst-free conditions. The protocol has the advantages of being highly efficient and environmentally benign, with excellent yields and easy work-up, making it suitable for large-scale and parallel combination synthesis. These compounds are promising candidates for drug discovery. Consequently, a library of diverse 1*H*-pyrazol-5(4*H*)-one-based HKAs was rapidly constructed using this method.

Introduction

The major challenges in modern drug discovery at the beginning of 21st century are the design of highly efficient protocols to provide structural complexity and diversity in compounds. Recently, more and more strategies and technologies have been developed to obtain novel compounds to meet the demands of drug chemists. Multicomponent reactions (MCRs) have been widely studied, which allow the quick assembly of several simple components into complex structures in one pot.[1] MCRs are powerful tools in the modern drug discovery process.[2] In addition, solvent-free conditions (SFC) have been used with great success, thus avoiding complicated and time-consuming purification operations.[3]

Pyrazolone is a structural motif present in many important natural products and synthetic drugs.[4] The heterocyclic nucleus containing pyraolones, such as edaravone (MCI-186, Fig. 1), has been widely used for treating brain[5] and myocardial ischemia.[6] Phenazone and propheazone (Fig. 1) have been widely used as antipyretic and analgesic agents.[7] Recently, medical chemists have begun to pay attention to the α,β-unsaturated pyrazolones, which have potent bioactivities such as HIV-1 integrase inhibition[8] (compound A, Fig. 1), BAF-3/TPO luciferase activity[9] (compound B), and so on.[10]

Consequently, the search for efficient, concise and environmentally friendly methods for the synthesis of this type of compound is an interesting field in chemistry.

Heterocyclic ketene aminals (HKAs) are versatile building blocks in heterocyclic synthesis,[11] which have been widely used in the synthesis of heterocyclic compounds including anticancer agents,[12] herbicides, pesticides,[13] antianxiety agents,[14] antileishmanial agents,[15] and antibacterial and antitherapeutic drugs.[16] Our group have a long-standing interest in this field, and we have developed MCRs to obtain compounds with these biological activities using a convenient and rapid synthetic procedure.[12] Encouraged by these results, we believe that hybrid molecules based on pyrazolone and HKAs maybe have potent biological activity.

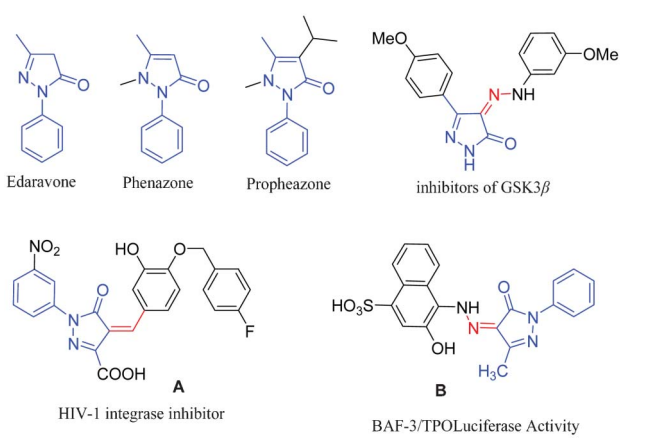

Fig. 1 Some biologically active pyrazolones and α,β-unsaturated pyrazolones.

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The structure of HKAs is described in Fig. 2, with the conjugation of electro-donating amino groups and the electron-withdrawing carbonyl group. Thus, HKAs have a highly polarized double bond (C=C).[11a,11b] This leads to the electron density of the α-carbon (C3) being higher than that of the secondary amino groups (N1 and N5). As a result, the substituted targets of the α-carbon have been obtained with high selectivity *via* alkylation,[17] acylation,[18] glycosylation[19] and halogenation reactions.[20] However, the selective formation of α,β-unsaturated double bonds *via* MCRs has not been reported to date (Fig. 2).

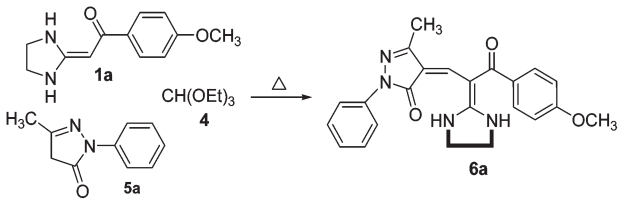
We believe that these hybrid molecules, with a combination of the pharmaceutical properties of pyrazolone and the biological activities of HKAs, may have potent activities. So, an efficient and concise one-pot MCR approach to obtain novel regio- and stereoselective targets is particularly promising as well as strongly desired.

Herein, we describe a facile, eco-friendly method for efficient synthesis of α,β-unsaturated pyrazolone-based HKAs in SFC based on MCRs of HKAs, triethoxymethane and 3-pyrazol-5(4*H*)-ones. This method has some advantages such as high yields, a broad scope, time efficiency and easy work-up.

Results and discussion

First, the MCR reaction of HKA **1a**, triethoxymethane **4** and 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one **5a** was evaluated. The materials were composed of a 1 : 2 : 1.2 ratio of **1a** : **4** : **5a**, which were treated under various conditions including different solvents and catalysts (Table 1, entries 1–9). The results indicate that the reaction could not proceed in water (Table 1, entry 1), nor could it proceed in the presence of *t*-BuOK in EtOH (Table 1, entry 5). We obtained the target compound **6a** under solvent-free and catalyst-free conditions with the best yield of 93% (Table 1, entry 9). Solvent-free conditions are optimal to prepare these target compounds. The product was carefully identified by spectroscopic data and high-resolution mass spectroscopy.

Table 1 Optimization of the reaction conditions[a]



Entry	Solvent	Catalyst	*t* (°C)	Time (min)	Yield[b] (%)
1	Water	—	Reflux	10	n.r.
2	EtOH	—	Reflux	10	85
3	MeCN	—	Reflux	10	83
4	Dioxane	—	Reflux	10	78
5	EtOH	*t*-BuOK	Reflux	10	n.r.
6	EtOH	*p*-TSA	Reflux	10	68
7	EtOH	AcOH	Reflux	10	83
8	EtOH	L-pyridine	Reflux	10	30
9	—	—	110	10	93

[a] The reaction was performed with **1a** (1 mmol), **4** (2 mmol), **5a** (1.2 mmol) and the solvent (15 mL) under reflux. [b] Isolated yield based on HKA **1a**. n.r. = no reaction.

With the optimization conditions in hand, we wanted to examine the scope and limitations of this method. Thus, a number of five-membered ring HKAs **1b–1f** were used as substrates to react with triethoxymethane **4** and pyrazolones **5a–5b** (Table 2, entries 2–12). The results demonstrate that the five-membered HKAs, with various substituents, were all good substrates for the cascade reaction in one pot (Table 2, entries 1–12). The reactions usually took 10 min at 110 °C to complete, and gave the products in excellent yields. Based on this, other five-membered HKAs **1g** and **1h** were reacted with triethoxymethane **4** and 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one **5a** under the same conditions (Scheme 1), and also gave the target compounds in good yields. All in all, various substituted HKAs could be smoothly reacted with substrates **4** and **5** to obtain the target compounds in good to excellent yields (82–95%) (Table 2, entries 1–12, and Scheme 1).

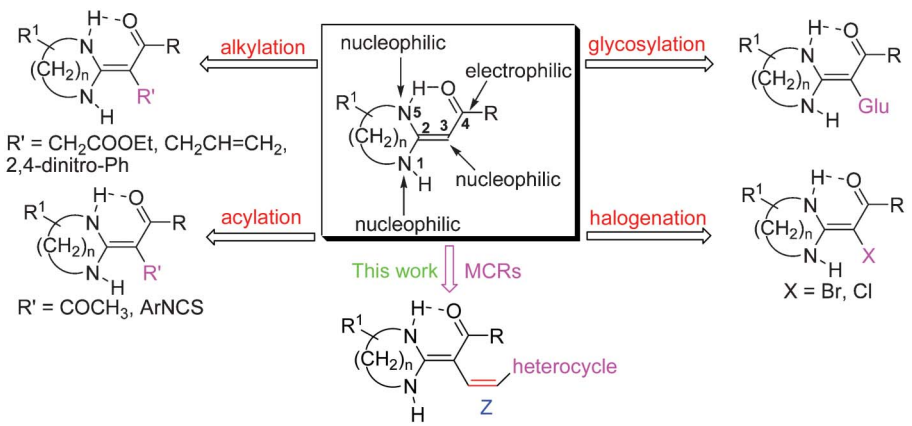
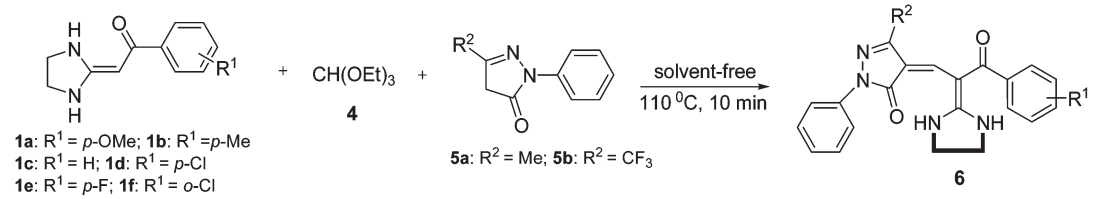


Fig. 2 Routes based on the one-pot cascade reaction of HKAs to give 1*H*-pyrazol-5(4*H*)-one-based HKA derivatives.

Table 2 Preparation of 1*H*-pyrazol-5(4*H*)-one-based HKA derivative **6**[a]



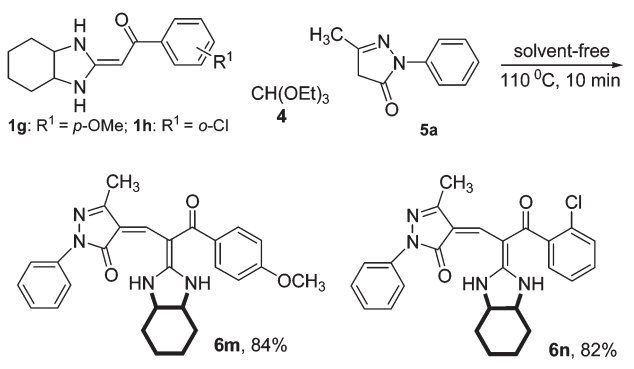
Entry	R^1	R^2	1	5	6	Yield[b](%)
1	*p*-OMe	CH_3	**1a**	**5a**	**6a**	93
2	*p*-Me	CH_3	**1b**	**5a**	**6b**	92
3	H	CH_3	**1c**	**5a**	**6c**	90
4	*p*-Cl	CH_3	**1d**	**5a**	**6d**	87
5	*p*-F	CH_3	**1e**	**5a**	**6e**	85
6	*o*-Cl	CH_3	**1f**	**5a**	**6f**	85
7	*p*-OMe	CF_3	**1a**	**5b**	**6g**	95
8	*p*-Me	CF_3	**1b**	**5b**	**6h**	94
9	H	CF_3	**1c**	**5b**	**6i**	93
10	*p*-Cl	CF_3	**1d**	**5b**	**6j**	92
11	*p*-F	CF_3	**1e**	**5b**	**6k**	88
12	*o*-Cl	CF_3	**1f**	**5b**	**6l**	90

[a] The reaction was performed with **1** (1 mmol), **4** (2 mmol), and **5** (1.2 mmol). [b] Isolated yield based on HKA **1**.

Encouraged by these results, ring size was also investigated in our work. Thus, the six-membered HKAs **2a–2f** were reacted with triethoxymethane **4** and pyrazolones **5a–5b** (Table 3, entries 1–12). At the same time, multifunctional pyrazolone **5c** was used as the substrate and reacted with HKA **2b** and triethoxymethane **4** under the same conditions. We also obtained compound **7m** in excellent yield (Scheme 2). On the whole, the six-membered HKAs provided higher yields than those of the five-membered HKAs (Table 2 and Scheme 1 *vs.* Table 3 and Scheme 2).

To explore the scope and limitations of this method, the seven-membered HKAs **3a–3e** were used as substrates to react with triethoxymethane **4** and pyrazolones **5a–5b** (Table 4, entries 1–10).

We concluded that HKAs, with various substituents and different ring sizes, were all good substrates for the cascade reaction in one pot (Tables 2–4 and Schemes 1–2). The reactions were complete in about 10 min at 110 °C, and provided products in excellent yields (82–96%). In general, the different substituents of the same ring sizes of HKAs provided similar yields (Table 2, entries 1–12; Table 3, entries 1–12; Table 4, entries 1–10). On the whole, the seven-membered HKAs were more favorable in terms of yields than the five-membered or six-membered HKAs (Table 4 *vs.* Table 2 and Table 3).



Scheme 1 One-pot synthesis of HKA derivatives **6m–6n**.

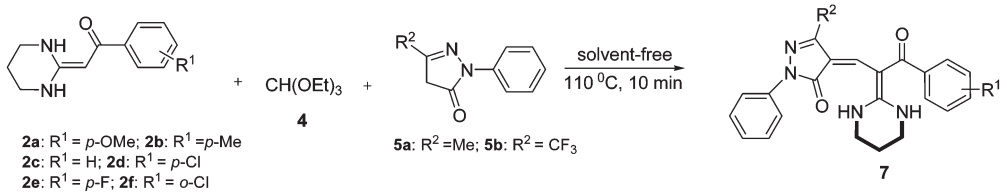
To verify the structure of the product 1*H*-pyrazol-5(4*H*)-one-based HKAs, **6c** was selected as a representative compound and characterized by X-ray crystallography, as shown in Fig. 3 (CCDC 917318).[21]

A proposed mechanism for the cascade reaction is depicted in Scheme 3. HKA **1c** reacted with triethoxymethane **4** to form intermediate **9** *via* an aza-ene reaction mechanism[22] and lost one molecular ethanol. Then, **9** underwent a process of imine–enamine tautomerization to obtain compound **10**. 3-Methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one **5a** gave **11** though keto-enol tautomerism. Intermediate **10** reacted with **11** to form compound **12** *via* an aldol condensation accompanied by the loss of one molecular ethanol. Finally, **12** formed the final product **6c** by an aromatization mechanism.

Conclusions

To summarize, we have developed a method for the synthesis of diverse 1*H*-pyrazol-5(4*H*)-one-based HKAs with potent bioactivity using a one-pot three-component reaction. By this method, a diverse 1*H*-pyrazol-5(4*H*)-one-based HKA library was rapidly constructed with excellent regio- and *cis*/*trans* stereoselectivity by simply heating a mixture of HKA, triethoxy-

Table 3 One-pot synthesis of 1*H*-pyrazol-5(4*H*)-one-based HKA derivative **7** under solvent-free conditions[a]



Entry	R^1	R^2	2	5	7	Yield[b](%)
1	*p*-OMe	CH_3	**2a**	**5a**	**7a**	95
2	*p*-Me	CH_3	**2b**	**5a**	**7b**	95
3	H	CH_3	**2c**	**5a**	**7c**	93
4	*p*-Cl	CH_3	**2d**	**5a**	**7d**	92
5	*p*-F	CH_3	**2e**	**5a**	**7e**	90
6	*o*-Cl	CH_3	**2f**	**5a**	**7f**	91
7	*p*-OMe	CF_3	**2a**	**5b**	**7g**	96
8	*p*-Me	CF_3	**2b**	**5b**	**7h**	95
9	H	CF_3	**2c**	**5b**	**7i**	92
10	*p*-Cl	CF_3	**2d**	**5b**	**7j**	91
11	*p*-F	CF_3	**2e**	**5b**	**7k**	89
12	*o*-Cl	CF_3	**2f**	**5b**	**7l**	91

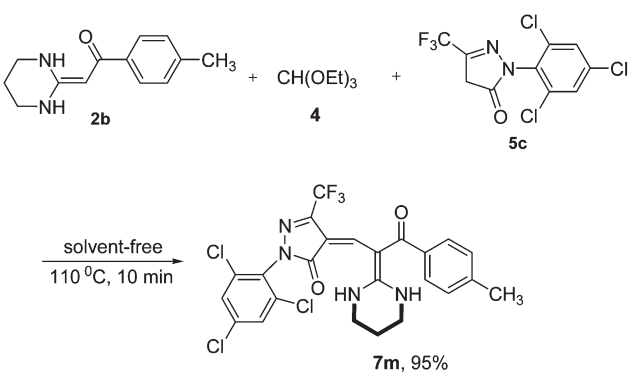
[a] The reaction was performed with **2** (1 mmol), **4** (2 mmol) and **5** (1.2 mmol). [b] Isolated yield based on HKA **2**.

methane and pyrazolones under solvent-free and catalyst-free conditions. Furthermore, the generality with respect to the substrate scope and facile accessibility to the starting materials are also highly appealing.

Experimental

General information

All compounds were fully characterized by spectroscopic methods. NMR spectra were recorded on a Bruker DRX400 or DRX500, chemical shifts (δ) are expressed in ppm, and J values are given in Hz; DMSO-d_6 and $CDCl_3$ were used as solvents. IR spectra were recorded on a FT-IR Thermo Nicolet Avatar 360 using a KBr pellet. The reactions were monitored by thin-layer chromatography (TLC) using silica gel GF_{254}. The melting points were determined on XT-4A melting point apparatus and are uncorrected. High resolution mass spectrometry (HRMS) was performed on an Agilent LC/MSD TOF and monoisotopic mass instrument. All chemicals and solvents were used as received without further purification unless otherwise stated. Column chromatography was performed on silica gel (200–300 mesh). The raw materials **1–3** were synthesized according to the literature.[23]



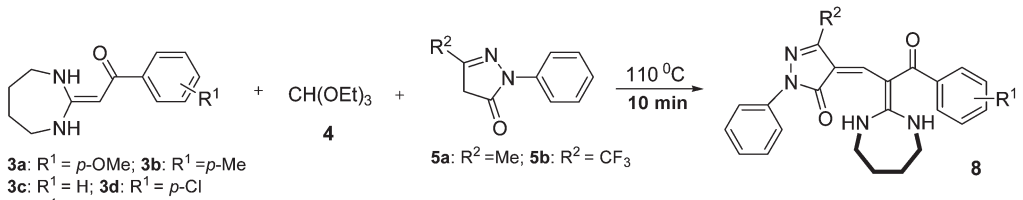
Scheme 2 One-pot synthesis of HKA derivative **7m**.

General procedure. HKAs **1–3** (1.0 mmol), triethoxymethane **4** (2.0 mmol) and 1-phenyl-1*H*-pyrazol-5(4*H*)-one derivatives **5** (1.2 mmol) were placed into a 25 mL round-bottom flask and the mixture was heated to 110 °C for about 10 min and monitored by TLC until the HKA substrate was used up. Then the reaction mixture was cooled to room temperature, filtered and washed with 95% EtOH to give the pure product with 82–96% yield. The products were further identified by FT-IR, NMR and HRMS, being in good agreement with the assigned structures.

(*Z*)-4-(2-(Imidazolidin-2-ylidene)-3-(4-methoxyphenyl)-3-oxopropylidene)-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (6a). Saffron yellow solid; m.p. 204–205.5 °C; IR (KBr): 3307, 2965, 1625, 1593, 1496, 1427, 1392, 1294, 1252, 1176, 1127, 992, 841, 765 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 1.95 (s, 3H, CH_3), 3.76–3.79 (m, 4H, NCH_2CH_2N), 3.78 (s, 3H, OCH_3), 6.95–6.97 (m, 2H, ArH), 7.00–7.04 (m, 1H, ArH), 7.28–7.32 (m, 2H, ArH), 7.42 (s, 1H, CH), 7.52–7.55 (m, 2H, ArH), 7.89–7.91 (m, 2H, ArH), 9.67 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 13.3 (CH_3), 43.4 (NCH_2), 43.4 (CH_2N), 55.3 (OCH_3), 113.3, 117.9, 122.9, 128.5, 130.8, 130.8 (=CH), 132.7, 139.9, 142.9, 150.4, 161.4 (HNC=), 162.8 (CH_3OC=), 165.9 (NC=O), 191.8 (C=O); HRMS (EI): m/z calcd for $C_{23}H_{22}N_4O_3$ [M], 402.1692; found, 402.1690.

(*Z*)-4-(2-(Imidazolidin-2-ylidene)-3-oxo-3-*p*-tolylpropylidene)-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (6b). Saffron yel-

Table 4 One-pot synthesis of 1*H*-pyrazol-5(4*H*)-one-based HKA derivative **7** under solvent-free conditions[a]



3a: R^1 = *p*-OMe; **3b**: R^1 = *p*-Me
3c: R^1 = H; **3d**: R^1 = *p*-Cl
3e: R^1 = *o*-Cl

5a: R^2 = Me; **5b**: R^2 = CF_3

Entry	R^1	R^2	3	5	8	Yield[b](%)
1	*p*-OMe	CH_3	**3a**	**5a**	**8a**	96
2	*p*-Me	CH_3	**3b**	**5a**	**8b**	95
3	H	CH_3	**3c**	**5a**	**8c**	94
4	*p*-Cl	CH_3	**3d**	**5a**	**8d**	93
5	*o*-Cl	CH_3	**3e**	**5a**	**8e**	93
6	*p*-OMe	CF_3	**3a**	**5a**	**8f**	96
7	*p*-Me	CF_3	**3b**	**5b**	**8g**	96
8	H	CF_3	**3c**	**5b**	**8h**	96
9	*p*-Cl	CF_3	**3d**	**5b**	**8i**	94
10	*o*-Cl	CF_3	**3e**	**5b**	**8j**	94

[a] The reaction was performed with **3** (1 mmol), **4** (2 mmol) and **5** (1.2 mmol). [b] isolated yield based on HKA **3a**.

low solid; m.p. 238–241 °C; IR (KBr): 3321, 1625, 1593, 1496, 1397, 1257, 1185, 1128, 1048, 990, 763 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6 + $HClO_4$): δ = 2.26 (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 3.82–3.85 (m, 4H, NCH_2CH_2N), 7.27–7.29 (m, 3H, CH and ArH), 7.43–7.49 (m, 5H, ArH), 7.59–7.61 (m, 2H, ArH), 9.72 (br, 2H, NH); ^{13}C NMR (125 MHz, DMSO-d_6 + $HClO_4$): δ = 11.5 (CH_3), 21.4 ($PhCH_3$), 44.4 (NCH_2), 44.4 (CH_2N), 100.8, 114.3, 120.9, 126.7, 129.4, 129.5, 129.5 (=CH), 135.2, 135.7, 139.7, 143.3, 150.7, 158.8 (HNC=), 165.7 (NC=O), 191.8 (C=O); HRMS (EI): *m*/*z* calcd for $C_{23}H_{22}N_4O_2$ [M], 386.1743; found, 386.1735.

(*Z*)-4-(2-(Imidazolidin-2-ylidene)-3-oxo-3-phenylpropylidene)-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (6c). Saffron yellow solid; m.p. 231–235 °C; IR (KBr): 3288, 2878, 1623, 1585, 1495, 1428, 1258, 1130, 1037, 994, 751 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.84 (s, 3H, CH_3), 3.87–3.90 (m, 4H, NCH_2CH_2N), 7.18–7.22 (m, 1H, ArH), 7.42–7.55 (m, 7H, ArH), 7.63 (s, 1H, CH), 7.89–7.92 (m, 2H, ArH), 11.34 (br, 2H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.2 (CH_3), 43.8 (NCH_2), 43.8 (CH_2N), 101.5, 106.5, 120.4, 125.0, 128.3, 128.7, 128.7, 130.9, 138.8, 140.8, 147.9, 152.8, 163.5 (HNC=), 165.5 (NC=O), 198.1 (C=O); HRMS (EI): *m*/*z* calcd for $C_{22}H_{20}N_4O_2$ [M], 372.1586; found, 372.1590.

(*Z*)-4-(3-(4-Chlorophenyl)-2-(imidazolidin-2-ylidene)-3-oxopropylidene)-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (6d). Saffron yellow solid; m.p. 233–237 °C; IR (KBr): 3321, 2886, 1631, 1591, 1494, 1428, 1392, 1254, 1182, 1128, 1088, 1044, 993, 823, 763 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 2.27 (s, 3H, CH_3), 3.81–3.86 (m, 4H, NCH_2CH_2N), 7.23–7.26 (m, 1H, ArH), 7.41–7.45 (m, 4H, ArH), 7.47–7.50 (m, 3H, ArH), 7.52 (s, 1H, CH), 7.67–7.69 (m, 2H, ArH), 9.71 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 11.2 (CH_3), 44.0 (NCH_2), 44.0 (CH_2N), 100.9, 112.5, 120.5, 126.2, 128.5, 129.1, 129.2, 130.9, 135.4, 136.5, 137.2, 150.5, 158.6 (HNC=), 165.1 (NC=O), 190.6 (C=O);

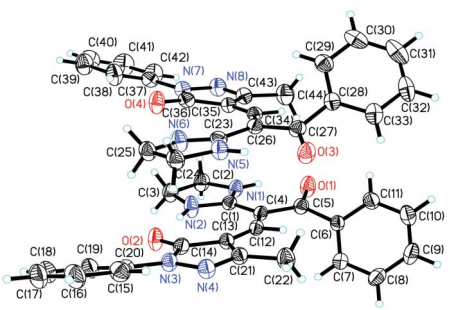
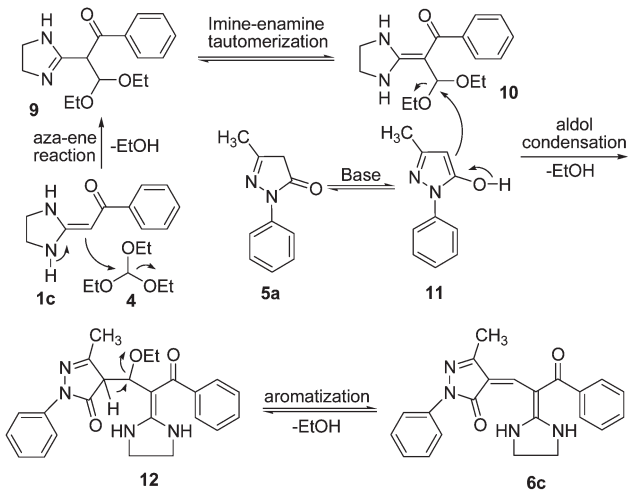


Fig. 3 X-ray crystal structures of **6c**; ellipsoids are drawn at the 30% probability level.



Scheme 3 Proposed mechanism for the three-component reaction.

HRMS (EI): *m*/*z* calcd for $C_{22}H_{19}ClN_4O_2$ [M], 406.1197; found, 406.1191.

(*Z*)-4-(3-(4-Fluorophenyl)-2-(imidazolidin-2-ylidene)-3-oxopropylidene)-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (6e). Saffron yellow solid; m.p. 202–204 °C; IR (KBr): 3333, 2900, 1626, 1591, 1496, 1429, 1395, 1338, 1254, 1127, 1044, 993, 841, 765 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 1.97 (s, 3H, CH_3), 3.74–3.78 (m, 4H, NCH_2CH_2N), 6.99–7.03 (m, 1H, ArH), 7.19–7.24 (m, 2H, ArH), 7.27–7.31 (m, 2H, ArH), 7.41 (s, 1H, CH), 7.57–7.61 (m, 2H, ArH), 7.84–7.86 (m, 2H, ArH), 9.49 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 13.1 (CH_3), 43.4 (NCH_2), 43.4 (CH_2N), 105.1, 114.8 (d, *J* = 21.5 Hz), 117.8, 123.0, 128.5, 131.0, 137.1, 139.8, 142.9, 150.3, 162.1, 162.7 (HNC=), 164.5, 165.8 (NC=O), 191.0 (C=O); HRMS (EI): *m*/*z* calcd for $C_{22}H_{19}FN_4O_2$ [M], 390.1492; found, 390.1492.

(*Z*)-4-(3-(2-Chlorophenyl)-2-(imidazolidin-2-ylidene)-3-oxopropylidene)-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (6f). Saffron yellow solid; m.p. 204–207 °C; IR (KBr): 3278, 1886, 1625, 1588, 1497, 1434, 1282, 1243, 1133, 1042, 996, 759 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 1.69 (s, 3H, CH_3), 3.80–3.83 (m, 4H, NCH_2CH_2N), 7.04–7.08 (m, 2H, ArH), 7.31–7.35 (m, 3H, CH and ArH), 7.41–7.48 (m, 2H, ArH), 7.53–7.55 (m, 1H, ArH), 7.88–7.89 (m, 2H, ArH), 10.09 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 12.6 (CH_3), 43.4 (NCH_2), 43.4 (CH_2N), 101.4, 105.2, 118.3, 123.6, 127.4, 128.6, 128.6, 129.4, 129.5, 130.6, 139.4, 139.9, 144.6, 150.7, 162.7 (HNC=), 164.3 (NC=O), 190.9 (C=O); HRMS (EI): *m*/*z* calcd for $C_{22}H_{19}ClN_4O_2$ [M], 406.1197; found, 406.1191.

(*Z*)-4-(2-(Imidazolidin-2-ylidene)-3-(4-methoxyphenyl)-3-oxopropylidene)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5-(4*H*)-one (6g). Saffron yellow solid; m.p. 227–230 °C; IR (KBr): 3205, 2965, 1640, 1594, 1500, 1414, 1285, 1112, 1033, 982, 837, 761 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 3.87 (s, 3H, OCH_3), 3.90–3.94 (m, 4H, NCH_2CH_2N), 6.92–6.95 (m, 2H, ArH), 7.24–7.27 (m, 1H, ArH), 7.42–7.46 (m, 2H, ArH), 7.59–7.62 (m, 2H, ArH), 7.81 (s, 1H, CH), 7.89–7.91 (m, 2H, ArH), 11.18 (br, 2H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 44.0 (NCH_2), 44.0 (CH_2N), 55.5 (OCH_3), 99.6, 105.3, 113.6, 119.5, 121.3, 126.0, 128.8, 128.8, 131.7, 131.9, 131.9, 138.5, 146.9, 162.9 (HNC=), 165.5 (NC=O), 197.1 (C=O); HRMS (EI): *m*/*z* calcd for $C_{23}H_{19}F_3N_4O_3$ [M], 456.1409; found, 456.1407.

(*Z*)-4-(2-(Imidazolidin-2-ylidene)-3-oxo-3-*p*-tolylpropylidene)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5(4*H*)-one (6h). Saffron yellow solid; m.p. 207–209 °C; IR (KBr): 3292, 1889, 1634, 1531, 1499, 1441, 1376, 1278, 1180, 1122, 1040, 972, 766 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 2.42 (s, 3H, CH_3), 3.90–3.94 (m, 4H, NCH_2CH_2N), 7.23–7.27 (m, 3H, ArH), 7.41–7.49 (m, 4H, ArH), 7.83 (s, 1H, CH), 7.88–7.89 (m, 2H, ArH), 11.18 (br, 2H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.6 ($PhCH_3$), 44.0 (NCH_2), 44.0 (CH_2N), 99.9, 105.3, 119.2, 121.3, 121.9, 126.1, 128.8, 129.0, 129.4, 136.6, 138.4, 142.6, 147.5, 163.0 (HNC=), 165.4 (NC=O), 198.3 (C=O); HRMS (EI): *m*/*z* calcd for $C_{23}H_{19}F_3N_4O_2$ [M], 440.1460; found, 440.1452.

(*Z*)-4-(2-(Imidazolidin-2-ylidene)-3-oxo-3-phenylpropylidene)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5(4*H*)-one (6i). Saffron yellow solid; m.p. 233–235 °C; IR (KBr): 3288, 2886, 1632, 1523, 1499, 1437, 1370, 1272, 1183, 1121, 968, 758 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 3.91–3.95 (m, 4H, NCH_2CH_2N), 7.24–7.28 (m, 1H, ArH), 7.41–7.47 (m, 4H, ArH), 7.52–7.56 (m, 3H, ArH), 7.82 (s, 1H, CH), 7.87–7.89 (m, 2H, ArH), 11.19 (br, 2H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 43.9 (NCH_2), 43.9 (CH_2N), 100.2, 105.0, 119.1, 121.3, 121.8, 126.1, 128.4, 128.8, 128.9, 131.6, 138.4, 139.6, 147.8, 163.5 (HNC=), 165.3 (NC=O); HRMS (EI): *m*/*z* calcd for $C_{22}H_{17}F_3N_4O_2$ [M], 426.1304; found, 426.1296.

(*Z*)-4-(3-(4-Chlorophenyl)-2-(imidazolidin-2-ylidene)-3-oxopropylidene)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5(4*H*)-one (6j). Saffron yellow solid; m.p. 230–233 °C; IR (KBr): 3221, 2969, 1640, 1583, 1499, 1403, 1282, 1176, 1114, 982, 836, 757 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 3.80–3.87 (m, 4H, NCH_2CH_2N), 7.14 (m, 1H, ArH), 7.37 (m, 3H, ArH), 7.54 (m, 4H, CH and ArH), 7.89 (m, 2H, ArH), 9.59 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 43.7 (NCH_2), 43.7 (CH_2N), 106.3, 118.9, 120.0, 122.7, 124.4, 125.4, 128.4, 128.7, 130.2, 135.9, 137.9, 139.3, 141.1, 161.7 (HNC=), 166.3 (NC=O), 190.3 (C=O); HRMS (EI): *m*/*z* calcd for $C_{22}H_{16}ClF_3N_4O_2$ [M], 460.0914; found, 460.0915.

(*Z*)-4-(3-(4-Fluorophenyl)-2-(imidazolidin-2-ylidene)-3-oxopropylidene)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5(4*H*)-one (6k). Saffron yellow solid; m.p. 237–240 °C; IR (KBr): 3305, 2900, 1633, 1606, 1523, 1500, 1442, 1377, 1274, 1236, 1184, 1123, 1044, 972, 841, 765 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 3.82–3.87 (m, 4H, NCH_2CH_2N), 7.12–7.14 (m, 1H, ArH), 7.28–7.40 (m, 5H, CH and ArH), 7.57–7.62 (m, 2H, ArH), 7.88–7.94 (m, 2H, ArH), 9.61 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 43.7 (NCH_2), 43.7 (CH_2N), 96.7, 106.5, 115.3 (d, *J* = 23.6 Hz), 118.9, 120.1, 122.8, 124.4, 128.7, 131.1, 135.7, 139.4, 141.1, 161.7, 162 (HNC=).4, 166.5 (NC=O), 190.4 (C=O); HRMS (EI): *m*/*z* calcd for $C_{22}H_{16}F_4N_4O_2$ [M], 444.1209; found, 444.1212.

(*Z*)-4-(3-(2-Chlorophenyl)-2-(imidazolidin-2-ylidene)-3-oxopropylidene)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5(4*H*)-one (6l). Saffron yellow solid; m.p. 224–226 °C; IR (KBr): 3316, 2893, 1633, 1591, 1431, 1377, 1289, 1249, 1184, 1114, 1044, 971, 826, 757 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 3.86–3.90 (m, 4H, NCH_2CH_2N), 7.10 (s, 1H, CH), 7.11–7.15 (m, 1H, ArH), 7.32–7.40 (m, 3H, ArH), 7.44–7.49 (m, 2H, ArH), 7.54–7.56 (m, 1H, ArH), 7.87–7.89 (m, 2H, ArH), 9.64 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 43.7 (NCH_2), 43.7 (CH_2N), 97.2, 106.9, 119.0, 119.8, 122.5, 124.5, 127.3, 128.6, 128.7, 129.6, 130.9, 138.8, 139.3, 142.2, 161.7 (HNC=), 165.2 (NC=O), 190.1 (C=O); HRMS (EI): *m*/*z* calcd for $C_{22}H_{16}ClF_3N_4O_2$ [M], 460.0914; found, 460.0912.

(*Z*)-4-(2-(1*H*-benzo[*d*]imidazol-2(3*H*,3*aH*,4*H*,5*H*,6*H*,7*H*,7*a*-*H*)-ylidene)-3-(4-methoxyphenyl)-3-oxopropylidene)-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (6m). Saffron yellow solid; m.p. 206–207.5 °C; IR (KBr): 3264, 2933, 1617, 1583, 1500, 1444, 1388, 1349, 1257, 1171, 1138, 1095, 779 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 1.27–1.30 (m, 2H, CH_2), 1.45–1.49 (m, 2H, CH_2), 1.71–1.75 (m, 2H, CH_2), 2.06–2.11 (m, 2H, CH_2), 2.28 (s, 3H, CH_3), 3.42–3.46 (m, 2H, NCHCHN), 3.82 (s, 3H, OCH_3), 6.96–6.99 (m, 2H, ArH), 7.22–7.26 (m, 1H, ArH), 7.39–7.47 (m, 4H, ArH), 7.51 (s, 1H, CH), 7.67–7.69 (m, 2H, ArH), 9.99 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 11.2 (CH_3), 23.4 ($NCHCH_2CH_2$), 23.4 (CH_2CH_2CHN), 28.3 ($NCHCH_2$, 28.3 (CH_2CHN), 55.5 (NCH), 55.5 (CHN), 64.1, 100.9, 113.7, 120.5,

121.4, 126.2, 129.1, 129.3, 130.3, 131.5, 135.4, 150.4, 158.5, 162.8 (HNC=), 166.9 (NC=O), 190.5 (C=O); HRMS (EI): *m*/*z* calcd for $C_{27}H_{28}N_4O_3$ [M], 456.2161; found, 456.2157.

(*Z*)-4-(2-(1*H*-benzo[*d*]imidazol-2(3*H*,3*aH*,4*H*,5*H*,6*H*,7*H*,7*a*-*H*)-ylidene)-3-(2-chlorophenyl)-3-oxopropylidene)-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (6n). Saffron yellow solid; m.p. 204–207.5 °C; IR (KBr): 3283, 2933, 1624, 1583, 1537, 1494, 1437, 1396, 1367, 1277, 1137, 756 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 1.31–1.34 (m, 2H, CH_2), 1.38–1.39 (m, 2H, CH_2), 1.57 (m, 2H, CH_2), 1.69 (s, 3H, CH_3), 1.73 (m, 2H, CH_2), 4.11 (m, 2H, NCHCHN), 7.04–7.09 (m, 2H, ArH), 7.31–7.36 (m, 2H, ArH), 7.38 (s, 1H, CH), 7.41–7.47 (m, 2H, ArH), 7.52–7.54 (m, 1H, ArH), 7.86–7.88 (m, 2H, ArH), 10.06 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 12.6 (CH_3), 19.3 ($NCHCH_2CH_2$), 19.3 (CH_2CH_2CHN), 25.8 ($NCHCH_2$), 25.8 (CH_2CHN), 54.3 (NCH), 54.3 (CHN), 101.6, 105.4, 118.2, 123.6, 127.4, 128.6, 128.7, 129.4, 129.5, 130.5, 139.4, 140.0, 144.1, 150.7, 162.7 (HNC=), 164.2 (NC=O), 191.0 (C=O); HRMS (EI): *m*/*z* calcd for $C_{26}H_{25}ClN_4O_2$ [M], 460.1666; found, 460.1679.

(*Z*)-4-(3-(4-Methoxyphenyl)-3-oxo-2-(tetrahydropyrimidin-2-(1*H*)-ylidene)propylidene)-3-methyl-1-phenyl-1*H*-pyrazol-5-(4*H*)-one (7a). Saffron yellow solid; m.p. 224–229 °C; IR (KBr): 3263, 2962, 1635, 1597, 1500, 1461, 1359, 1309, 1265, 1166, 1030, 997, 837, 754 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 1.99 (s, 3H, CH_3), 1.97–2.06 (m, 2H, CH_2), 3.39–3.43 (m, 4H, NCH_2CH_2N), 3.84 (s, 3H, OCH_3), 6.99–7.04 (m, 3H, ArH), 7.27 (s, 1H, CH), 7.31–7.34 (m, 2H, ArH), 7.53–7.55 (m, 2H, ArH), 8.03–8.04 (m, 2H, ArH), 9.03 (br, 2H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.6 (CH_3), 17.8 (CH_2), 38.2 (NCH_2), 38.2 (CH_2N), 55.7 (OCH_3), 101.1, 109.9, 113.6, 117.7, 122.4, 128.7, 130.7, 133.2, 141.0, 141.3, 150.0, 161.3, 161.8 (HNC=), 163.3 (NC=O), 189.8 (C=O); HRMS (EI): *m*/*z* calcd for $C_{24}H_{24}N_4O_3$ [M], 416.1848; found, 416.1855.

(*Z*)-3-Methyl-4-(3-oxo-2-(tetrahydropyrimidin-2(1*H*)-ylid-ene)-3-*p*-tolylpropylidene)-1-phenyl-1*H*-pyrazol-5(4*H*)-one (7b). Saffron yellow solid; m.p. 249–252 °C; IR (KBr): 3266, 2958, 1635, 1502, 1439, 1352, 1274, 1204, 1142, 1069, 997, 794, 754 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 1.93 (s, 3H, CH_3), 1.96–1.98 (m, 2H, CH_2), 2.35 (s, 3H, $ArCH_3$), 3.29–3.33 (m, 4H, NCH_2CH_2N), 6.96–6.99 (m, 1H, ArH), 7.22–7.31 (m, 5H, CH and ArH), 7.39–7.42 (m, 2H, ArH), 7.96–7.98 (m, 2H, ArH), 9.00 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 13.2 (CH_3), 17.4 (CH_2), 21.1 ($PhCH_3$), 37.8 (NCH_2), 37.8 (CH_2N), 100.9, 109.6, 117.4, 122.2, 128.4, 128.4, 128.5, 137.7, 140.2, 140.5, 141.2, 149.7, 161.2 (HNC=), 162.8 (NC=O), 190.3 (C=O); HRMS (EI): *m*/*z* calcd for $C_{24}H_{24}N_4O_2$ [M], 400.1899; found, 400.1906.

(*Z*)-3-Methyl-4-(3-oxo-3-phenyl-2-(tetrahydropyrimidin-2-(1*H*)-ylidene)propylidene)-1-phenyl-1*H*-pyrazol-5(4*H*)-one (7c). Saffron yellow solid; m.p. 257–262 °C; IR (KBr): 3256, 3016, 1632, 1594, 1500, 1442, 1381, 1310, 1269, 1204, 1138, 1066, 990, 946, 758 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 1.92 (s, 3H, CH_3), 1.95–1.98 (m, 2H, CH_2), 3.30–3.36 (m, 4H, NCH_2CH_2N), 6.96–6.99 (m, 1H, ArH), 7.21 (s, 1H, CH), 7.27–7.31 (m, 2H, ArH), 7.43–7.49 (m, 5H, ArH), 7.98–8.00 (m, 2H, ArH), 9.04 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 13.1 (CH_3), 17.4 (CH_2), 37.8 (NCH_2), 37.8 (CH_2N), 101.1, 109.4, 117.3, 122.2, 127.9, 128.0, 128.4, 130.1, 140.6, 140.7, 141.2, 149.6, 161.2 (HNC=), 162.8 (NC=O), 190.3 (C=O); HRMS (EI): *m*/*z* calcd for $C_{23}H_{22}N_4O_2$ [M], 386.1743; found, 386.1742.

(*Z*)-4-(3-(4-Chlorophenyl)-3-oxo-2-(tetrahydropyrimidin-2-(1*H*)-ylidene)propylidene)-3-methyl-1-phenyl-1*H*-pyrazol-5-(4*H*)-one (7d). Saffron yellow solid; m.p. 265–269 °C; IR (KBr): 3270, 2973, 1634, 1497, 1359, 1271, 1200, 1146, 1088, 997, 834, 747 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 1.94–1.98 (m, 5H, CH_3 and CH_2), 3.30–3.37 (m, 4H, NCH_2CH_2N), 6.96–7.00 (m, 1H, ArH), 7.21 (s, 1H, CH), 7.27–7.31 (m, 2H, ArH), 7.48–7.54 (m, 4H, ArH), 7.98–7.99 (m, 2H, ArH), 9.05 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 13.2 (CH_3), 17.4 (CH_2), 37.8 (NCH_2), 37.8 (CH_2N), 101.7, 108.9, 117.3, 122.2, 128.1, 128.4, 129.9, 134.7, 139.5, 140.5, 141,0, 149.8, 161.1 (HNC=), 162.8 (NC=O), 188.6 (C=O); HRMS (EI): *m*/*z* calcd for $C_{23}H_{21}ClN_4O_2$ [M], 420.1353; found, 420.1354.

(*Z*)-4-(3-(4-Fluorophenyl)-3-oxo-2-(tetrahydropyrimidin-2-(1*H*)-ylidene)propylidene)-3-methyl-1-phenyl-1*H*-pyrazol-5-(4*H*)-one (7e). Saffron yellow solid; m.p. 263–266 °C; IR (KBr): 3266, 2969, 1635, 1598, 1497, 1359, 1268, 1147, 1073, 997, 845, 754 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 1.93–1.96 (m, 5H, CH_2 and CH_3), 3.28–3.34 (m, 4H, NCH_2CH_2N), 6.96–7.00 (m, 2H, ArH), 7.20 (s, 1H, CH), 7.26–7.31 (m, 4H, ArH), 7.53–7.56 (m, 2H, ArH), 7.96–7.98 (m, 2H, ArH), 9.03 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 13.1 (CH_3), 17.4 (CH_2), 37.8 (NCH_2), 37.8 (CH_2N), 101.4, 109.1, 114.9 (d, J = 21.5 Hz), 117.4, 122.3, 128.4, 130.5, 137.1, 140.4, 141.1, 149.8, 161.1 (HNC=), 162.8 (NC=O), 163.0 (d, J = 245.9 Hz), 188.9 (C=O); HRMS (EI): *m*/*z* calcd for $C_{23}H_{21}FN_4O_2$ [M], 404.1649; found, 404.1641.

(*Z*)-4-(3-(2-Chlorophenyl)-3-oxo-2-(tetrahydropyrimidin-2-(1*H*) -ylidene)propylidene)-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (7f). Saffron yellow solid; m.p. 252–254.5 °C; IR (KBr): 3299, 2969, 1634, 1584, 1502, 1436, 1356, 1283, 1200, 1149, 1088, 993, 750 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 1.83 (s, 3H, CH_3), 1.98–2.04 (m, 2H, CH_2), 3.36–3.44 (m, 4H, NCH_2CH_2N), 6.88 (s, 1H, ACH), 6.99–7.03 (m, 1H, ArH), 7.31–7.36 (m, 3H, ArH), 7.42–7.47 (m, 2H, CH and ArH), 7.53–7.54 (m, 1H, ArH), 8.00–8.02 (m, 2H, ArH), 9.05 (br, 2H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.1 (CH_3), 17.8 (CH_2), 38.3 (NCH_2), 38.3 (CH_2N), 102.1, 109.9, 117.7, 122.7, 127.2, 128.7, 129.3, 129.8, 130.1, 130.5, 140.5, 140.8, 141.8, 149.7, 160.5 (HNC=), 163.2 (NC=O), 188.6 (C=O); HRMS (EI): *m*/*z* calcd for $C_{23}H_{21}ClN_4O_2$ [M], 420.1353; found, 420.1348.

(*Z*)-4-(3-(4-Methoxyphenyl)-3-oxo-2-(tetrahydropyrimidin-2-(1*H*)-ylidene)propylidene)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5(4*H*)-one (7g). Saffron yellow solid; m.p. 291–293 °C; IR (KBr): 3278, 2965, 1641, 1595, 1501, 1465, 1292, 1258, 1172, 1113, 1069, 975, 838, 761 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 1.99–2.01 (m, 2H, CH_2), 3.33–3.37 (m, 4H, NCH_2CH_2N), 3.81 (s, 3H, OCH_3), 7.01–7.03 (m, 2H, ArH), 7.11–7.14 (m, 1H, ArH), 7.33–7.37 (m, 2H, ArH), 7.39 (s, 1H, CH), 7.52–7.54 (m, 2H, ArH), 7.94–7.96 (m, 2H, ArH), 9.19 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 17.3 (CH_2), 37.8 (NCH_2), 37.8 (CH_2N), 55.4 (OCH_3), 95.0, 113.4, 114.3, 118.8, 121.6 (d, J = 268.7 Hz), 124.1, 128.7, 130.7, 139.0, 139.2, 139.6, 139.7, 160.3, 161.5 (HNC=), 161.8 (NC=O), 190.9 (C=O); HRMS (EI): *m*/*z* calcd for $C_{24}H_{21}F_3N_4O_3$ [M], 470.1566; found, 470.1566.

(*Z*)-4-(3-Oxo-2-(tetrahydropyrimidin-2(1*H*)-ylidene)-3-*p*-tolylpropylidene)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5(4*H*)-one (7h). Saffron yellow solid; m.p. 296–298 °C; IR (KBr): 3299, 3013, 1640, 1595, 1499, 1454, 1288, 1179, 1115, 1066, 979, 830, 750 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 1.97–2.01 (m, 2H, CH_2), 2.36 (s, 3H, $ArCH_3$), 3.33–3.37 (m, 4H, NCH_2CH_2N), 7.11–7.14 (m, 1H, ArH), 7.27–7.29 (m, 2H, ArH), 7.34–7.38 (m, 2H, ArH), 7.39 (s, 1H, ArH), 7.43–7.45 (m, 2H, ArH), 7.94–7.96 (m, 2H, ArH), 9.21 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 17.3 (CH_2), 21.1 ($PhCH_3$), 37.8 (NCH_2), 37.8 (CH_2N), 95.1, 114.2, 118.8, 120.2, 122.9, 124.1, 128.5, 128.7, 136.5, 139.3, 139.4, 139.6, 140.9, 160.2 (HNC=), 161.8 (NC=O), 191.7 (C=O); HRMS (EI): *m*/*z* calcd for $C_{24}H_{21}F_3N_4O_2$ [M], 454.1617; found, 454.1613.

(*Z*)-4-(3-Oxo-3-phenyl-2-(tetrahydropyrimidin-2(1*H*)-ylidene)-propylidene)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5-(4*H*)-one (7i). Saffron yellow solid; m.p. 276–285 °C; IR (KBr): 3297, 3013, 1640, 1591, 1500, 1288, 1182, 1118, 1073, 986, 834, 696 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 1.97–2.01 (m, 2H, CH_2), 3.33–3.37 (m, 4H, NCH_2CH_2N), 7.11–7.15 (m, 1H, ArH), 7.32 (s, 1H, CH), 7.36–7.39 (m, 2H, ArH), 7.45–7.55 (m, 5H, ArH), 7.93–7.95 (m, 2H, ArH), 9.23 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 17.3 (CH_2), 37.8 (NCH_2), 37.8 (CH_2N), 95.3, 114.1, 118.8, 120.2, 122.9, 124.2, 128.1, 128.2, 128.7, 130.8, 139.3, 139.4, 139.7, 160.1 (HNC=), 161.8 (NC=O), 192.0 (C=O); HRMS (EI^+): *m*/*z* calcd for $C_{23}H_{19}F_3N_4O_2$ [M], 440.1460; found, 440.1457.

(*Z*)-4-(3-(4-Chlorophenyl)-3-oxo-2-(tetrahydropyrimidin-2-(1*H*) -ylidene)propylidene)-1-phenyl-3-(trifluoromethyl)-1*H*-pyr-azol-5(4*H*)-one (7j). Saffron yellow solid; m.p. > 300 °C; IR (KBr): 3027, 2581, 1640, 1600, 1499, 1465, 1398, 1291, 1181, 1116, 982, 834, 756 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 1.96–1.98 (m, 2H, CH_2), 3.32–3.35 (m, 4H, NCH_2CH_2N), 7.11–7.15 (m, 1H, ArH), 7.29 (s, 1H, CH), 7.38–7.39 (m, 2H, ArH), 7.50–7.57 (m, 4H, ArH), 7.91–7.93 (m, 2H, ArH), 9.24 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 17.2 (CH_2), 37.8 (NCH_2), 37.8 (CH_2N), 95.6, 113.6, 118.8, 121.5, 123.0, 124.2, 128.3, 128.7, 130.0, 135.5, 138.2, 139.6, 159.9 (HNC=), 161.7 (NC=O), 190.5 (C=O); HRMS (EI): *m*/*z* calcd for $C_{23}H_{18}ClF_3N_4O_2$ [M], 474.1070; found, 474.1073.

(*Z*)-4-(3-(4-Fluorophenyl)-3-oxo-2-(tetrahydropyrimidin-2-(1*H*)-ylidene)propylidene)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5(4*H*)-one (7k). Saffron yellow solid; m.p. 284–288.5 °C; IR (KBr): 3263, 3016, 1641, 1595, 1500, 1457, 1399, 1290, 1174, 1116, 1069, 979, 754 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 1.97–2.02 (m, 2H, CH_2), 3.33–3.36 (m, 4H, NCH_2CH_2N), 7.11–7.15 (m, 1H, ArH), 7.27–7.31 (m, 2H, CH and ArH), 7.32–7.40 (m, 3H, ArH), 7.56–7.60 (m, 2H, ArH), 7.93–7.95 (m, 2H, ArH), 9.24 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 17.3 (CH_2), 37.8 (NCH_2), 37.8 (CH_2N), 95.4, 113.8, 115.1, 115.3, 118.8, 121.5 (d, *J* = 268.7 Hz), 124.2, 128.7, 130.8, 130.9, 135.9, 139.6, 160.1 (HNC=), 161.8 (NC=O), 163.4 (d, *J* = 247.0 Hz), 190.6 (C=O); HRMS (EI): *m*/*z* calcd for $C_{23}H_{18}F_4N_4O_2$ [M], 458.1366; found, 458.1356.

(*Z*)-4-(3-(2-Chlorophenyl)-3-oxo-2-(tetrahydropyrimidin-2-(1*H*)-ylidene)propylidene)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5(4*H*)-one (7l). Saffron yellow solid; m.p. 283–287 °C; IR (KBr): 3322, 3009, 1641, 1594, 1541, 1504, 1297, 1185, 1119, 1037, 979 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 1.97–2.02 (m, 2H, CH_2), 3.35–3.39 (m, 4H, NCH_2CH_2N), 6.97–7.00 (s, 1H, CH), 7.13–7.15 (m, 1H, ArH), 7.32–7.39 (m, 3H, ArH), 7.43–7.49 (m, 2H, ArH), 7.52–7.54 (m, 1H, ArH), 7.89–7.92 (m, 2H, ArH), 9.23 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 17.3 (CH_2), 37.8 (NCH_2), 37.8 (CH_2N), 95.8, 114.3, 118.8, 119.9, 122.6, 124.3, 127.0, 128.7, 129.5, 129.7, 130.7, 138.9, 139.5, 139.6, 140.6, 159.1 (HNC=), 161.8 (NC=O), 190.2 (C=O); HRMS (EI): *m*/*z* calcd for $C_{23}H_{18}ClF_3N_4O_2$ [M], 474.1070; found, 474.1078.

(*Z*)-4-(3-Oxo-2-(tetrahydropyrimidin-2(1*H*)-ylidene)-3-*p*-tolylpropylidene)-1-(2,4,6-trichlorophenyl)-3-(trifluorometh-yl)-1*H*-pyrazol-5(4*H*)-one (7m). Saffron yellow solid; m.p. 286–289 °C; IR (KBr): 3279, 2918, 1633, 1591, 1498, 1345, 1272, 1142, 1091, 993, 747 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 1.86–1.90 (m, 2H, CH_2), 2.36 (s, 3H, $ArCH_3$), 3.26–3.35 (m, 4H, NCH_2CH_2N), 7.27–7.29 (m, 2H, ArH), 7.35 (s, 1H, CH), 7.42–7.44 (m, 2H, ArH), 7.84 (m, 2H, ArH), 9.23 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 17.3 (CH_2), 21.1 ($PhCH_3$), 37.6 (NCH_2), 37.6 (CH_2N), 93.3, 114.4, 121.4 (d, *J* = 268.8 Hz), 122.7, 128.4, 128.6, 133.9, 134.5, 135.8, 136.5, 139.6, 140.4, 140.8, 160.0 (HNC=), 161.8 (NC=O), 191.3 (C=O); HRMS (TOF ES^+): *m*/*z* calcd for $C_{24}H_{18}Cl_3F_3N_4O_2$ [$(M + H)^+$], 557.0520; found, 557.0519.

(*Z*)-4-(2-(1,3-Diazepan-2-ylidene)-3-(4-methoxyphenyl)-3-oxo-propylidene)-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (8a). Saffron yellow solid; m.p. 244–248.5 °C; IR (KBr): 3280, 2924, 1634, 1595, 1501, 1349, 1268, 1162, 1138, 1033, 993, 801, 755 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 1.74–1.78 (m, 4H, NCH_2CH_2N), 1.97 (s, 3H, CH_3), 3.33–3.36 (m, 4H, NCH_2CH_2N), 3.78 (s, 3H, OCH_3), 6.97–6.99 (m, 3H, CH and ArH), 7.25–7.31 (m, 3H, ArH), 7.47–7.49 (m, 2H, ArH), 7.94–7.96 (m, 2H, ArH), 8.81 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 13.3 (CH_3), 26.3 (CH_2CH_2), 26.3 (CH_2CH_2), 43.5 (NCH_2), 43.5 (CH_2N), 55.3 (OCH_3), 101.6, 110.9, 113.2, 117.4, 122.4, 128.4, 130.2, 133.1, 140.4, 141.5, 149.9, 160.9 (HNC=), 162.9 (NC=O), 167.3 (CH_3OC), 190.4 (C=O); HRMS (EI): *m*/*z* calcd for $C_{25}H_{26}N_4O_3$ [M], 430.2005; found, 430.2000.

(*Z*)-4-(2-(1,3-Diazepan-2-ylidene)-3-oxo-3-*p*-tolylpropylidene)-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (8b). Saffron yellow solid; m.p. 263–265 °C; IR (KBr): 3281, 2922, 1633, 1499, 1352, 1273, 1142, 1001, 790, 750 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 1.82–1.87 (m, 4H, CH_2CH_2), 2.19 (s, 3H, CH_3), 2.35 (s, 3H, $ArCH_3$), 3.39–3.43 (m, 4H, NCH_2CH_2N), 7.21 (s, 1H, CH), 7.27–7.37 (m, 3H, ArH), 7.46–7.49 (m, 3H, ArH), 7.54–7.57 (m, 3H, ArH), 9.27 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 11.0 (CH_3), 21.1 ($PhCH_3$), 25.9 (CH_2CH_2), 25.9 (CH_2CH_2), 43.6 (NCH_2), 43.6 (CH_2N), 99.8, 120.6, 122.7, 126.4, 129.0, 129.1, 129.3, 135.0, 135.4, 139.0, 142.5, 150.6, 158.5 (HNC=), 164.0 (NC=O), 192.6 (C=O); HRMS (EI): *m*/*z* calcd for $C_{25}H_{26}N_4O_2$ [M], 414.2056; found, 414.2053.

(*Z*)-4-(2-(1,3-Diazepan-2-ylidene)-3-oxo-3-phenylpropylidene)-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (8c). Saffron yellow solid; m.p. 223–227 °C; IR (KBr): 3274, 2926, 1633, 1499, 1341, 1268, 1138, 997, 805, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.86–1.93 (m, 4H, CH_2CH_2), 1.92 (s, 3H, CH_3), 3.17 (m, 2H, NCH_2), 3.49 (m, 2H, NCH_2), 7.07–7.11 (m, 1H, ArH), 7.26 (s, 1H, CH), 7.31–7.39 (m, 4H, ArH), 7.43–7.46 (m, 1H,

ArH), 7.51–7.52 (m, 2H, ArH), 7.76–7.78 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.9 (CH_3), 26.4 (CH_2CH_2), 26.4 (CH_2CH_2), 44.8 (NCH_2), 44.8 (CH_2N), 104.2, 109.5, 119.9, 124.5, 128.2, 128.6, 128.8, 131.2, 138.8, 140.1, 145.9, 151.5, 162.8 (HNC=), 166.6 (NC=O), 195.6 (C=O); HRMS (EI): *m*/*z* calcd for $C_{24}H_{24}N_4O_2$ [M], 400.1899; found, 400.1908.

(*Z*)-4-(3-(4-Chlorophenyl)-2-(1,3-diazepan-2-ylidene)-3-oxopropylidene)-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (8d). Saffron yellow solid; m.p. 275–279 °C; IR (KBr): 3279, 2918, 1633, 1591, 1498, 1345, 1272, 1142, 1091, 933, 837, 747 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.82–1.86 (m, 4H, CH_2CH_2), 2.21 (s, 3H, CH_3), 3.40–3.45 (m, 4H, NCH_2CH_2N), 7.22 (s, 1H, CH), 7.26–7.30 (m, 1H, ArH), 7.46–7.49 (m, 2H, ArH), 7.56–7.58 (m, 4H, ArH), 7.63–7.65 (m, 2H, ArH), 9.29 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 11.1 (CH_3), 25.8 (CH_2CH_2), 26.0 (CH_2CH_2), 43.6 (NCH_2), 43.6 (CH_2N), 99.9, 120.6, 121.9, 126.3, 128.6, 129.3, 130.7, 135.4, 136.6, 136.8, 139.6, 150.8, 158.6 (HNC=), 163.9 (NC=O), 191.7 (C=O); HRMS (EI): *m*/*z* calcd for $C_{24}H_{23}ClN_4O_2$ [M], 434.1510; found, 434.1524.

(*Z*)-4-(3-(2-Chlorophenyl)-2-(1,3-diazepan-2-ylidene)-3-oxo propylidene)-3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one (8e). Saffron yellow solid; m.p. 244–249 °C; IR (KBr): 3317, 2922, 1635, 1581, 1504, 1443, 1349, 1283, 1146, 1055, 993, 750 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.76–1.96 (m, 7H, CH_3 and CH_2CH_2), 3.38–3.41 (m, 4H, NCH_2CH_2N), 6.99–7.02 (m, 1H, ArH), 7.29–7.32 (m, 2H, ArH), 7.38 (s, 1H, CH), 7.41–7.42 (m, 3H, ArH), 7.49 (m, 1H, ArH), 7.98–7.99 (m, 2H, ArH), 8.83 (br, 2H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.2 (CH_3), 26.4 (CH_2CH_2), 26.4 (CH_2CH_2), 43.4 (NCH_2), 43.4 (CH_2N), 102.7, 111.1, 117.7, 122.7, 127.1, 128.1, 128.7, 129.3, 129.7, 130.0, 130.4, 140.7, 141.4, 149.9, 163.3 (HNC=), 166.3 (NC=O), 188.7 (C=O); HRMS (EI): *m*/*z* calcd for $C_{24}H_{23}ClN_4O_2$ [M], 434.1510; found, 434.1502.

(*Z*)-4-(2-(1,3-Diazepan-2-ylidene)-3-(4-methoxyphenyl)-3-oxopropylidene)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5-(4*H*)-one (8f). Saffron yellow solid; m.p. 288–290.5 °C; IR (KBr): 3305, 2926, 1635, 1595, 1500, 1396, 1289, 1262, 1173, 1115, 1019, 982, 841, 754 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.85 (m, 4H, $2CH_2$), 3.44 (m, 4H, $2CH_2$), 3.79 (s, 3H, OCH_3), 7.00–7.02 (m, 2H, ArH), 7.11–7.15 (m, 1H, ArH), 7.32 (s, 1H, CH), 7.36–7.39 (m, 2H, ArH), 7.51–7.53 (m, 2H, ArH), 7.92–7.94 (m, 2H, ArH), 9.025 (s, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 26.2 (CH_2CH_2), 26.2 (CH_2CH_2), 43.2 (NCH_2), 43.2 (CH_2N), 55.4 (OCH_3), 95.3, 113.4, 115.9, 118.8, 120.6 (d, *J* = 268.7 Hz), 124.2, 128.7, 130.6, 131.6, 139.1, 139.3, 139.7, 161.5, 161.9 (HNC=), 165.7 (NC=O), 191.6 (C=O); HRMS (EI): *m*/*z* calcd for $C_{25}H_{23}F_3N_4O_3$ [M], 484.1722; found, 484.1727.

(*Z*)-4-(2-(1,3-Diazepan-2-ylidene)-3-oxo-3-*p*-tolylpropylidene)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5(4*H*)-one (8g). Saffron yellow solid; m.p. 298–300 °C; IR (KBr): 3300, 2929, 1636, 1498, 1396, 1285, 1178, 1115, 986, 834, 755 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.85–1.90 (m, 4H, CH_2CH_2), 2.38 (s, 3H, $ArCH_3$), 3.42–3.48 (m, 4H, NCH_2CH_2N), 7.14–7.17 (m, 1H, ArH), 7.29–7.31 (m, 2H, ArH), 7.37–7.42 (m, 4H, CH and ArH), 7.45–7.47 (m, 1H, ArH), 7.98–7.99 (m, 2H, ArH), 9.08 (br, 2H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 21.4 (CH_3), 26.6 (CH_2CH_2), 26.6 (CH_2CH_2), 43.6 (NCH_2), 43.6 (CH_2N), 95.8, 116.1, 119.0, 120.9, 123.0, 124.4, 128.7, 128.9, 137.2, 139.6, 140.1, 141.0, 162.0, 162.3 (HNC=), 166.1 (NC=O), 192.5 (C=O); HRMS (EI): *m*/*z* calcd for $C_{25}H_{23}F_3N_4O_2$ [M], 468.1773; found, 468.1767.

(*Z*)-4-(2-(1,3-Diazepan-2-ylidene)-3-oxo-3-phenylpropylidene)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5(4*H*)-one (8h). Saffron yellow solid; m.p. 267–272 °C; IR (KBr): 3305, 3023, 1640, 1537, 1499, 1396, 1286, 1178, 1116, 986, 827, 689 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.81–1.85 (m, 4H, NCH_2CH_2N), 3.39–3.50 (m, 4H, NCH_2CH_2N), 7.11–7.15 (m, 1H, ArH), 7.32 (s, 1H, CH), 7.36–7.39 (m, 3H, ArH), 7.45–7.54 (m, 4H, ArH), 7.93–7.95 (m, 2H, ArH), 9.08 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 26.2 (CH_2CH_2), 26.2 (CH_2CH_2), 43.2 (NCH_2), 43.2 (CH_2N), 95.6, 115.6, 118.7, 120.2, 124.2, 128.0, 128.1, 128.7, 130.7, 139.5, 139.6, 139.7, 161.9 (HNC=), 165.5 (NC=O), 192.5 (C=O); HRMS (EI): *m*/*z* calcd for $C_{24}H_{21}F_3N_4O_2$ [M], 454.1617; found, 454.1611.

(*Z*)-4-(3-(4-Chlorophenyl)-2-(1,3-diazepan-2-ylidene)-3-oxopropylidene)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5(4*H*)-one (8i). Saffron yellow solid; m.p. 291–294 °C; IR (KBr): 3300, 3023, 1635, 1591, 1498, 1396, 1288, 1179, 1117, 986, 834, 750 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.81–1.85 (m, 4H, CH_2CH_2), 3.41–3.60 (m, 4H, NCH_2CH_2N), 7.11–7.15 (m, 1H, ArH), 7.29 (s, 1H, CH), 7.36–7.39 (m, 2H, ArH), 7.49–7.52 (m, 2H, ArH), 7.54–7.57 (m, 2H, ArH), 7.90–7.94 (m, 2H, ArH), 9.09 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 26.2 (CH_2CH_2), 26.2 (CH_2CH_2), 43.2 (NCH_2), 43.2 (CH_2N), 95.9, 115.2, 118.8, 121.5 (d, *J* = 268.8 Hz), 124.3, 128.3, 128.7, 129.9, 135.4, 138.4, 139.3, 139.5, 139.7, 161.9, 165.3(HNC=), 165.3 (NC=O), 919.1 (C=O); HRMS (EI): *m*/*z* calcd for $C_{24}H_{20}ClF_3N_4O_2$ [M], 488.1227; found, 488.1227.

(*Z*)-4-(3-(2-Chlorophenyl)-2-(1,3-diazepan-2-ylidene)-3-oxo propylidene)-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5(4*H*) one (8j). Saffron yellow solid; m.p. 298–302 °C; IR (KBr): 3333, 2947, 1640, 1592, 1540, 1500, 1180, 1113, 982, 827, 758 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.80–1.90 (m, 4H, CH_2CH_2), 3.50–3.55 (m, 4H, NCH_2CH_2N), 7.07 (s, 1H, CH), 7.11–7.15 (m, 1H, ArH), 7.36–7.48 (m, 5H, ArH), 7.51–7.53 (m, 1H, ArH), 7.90–7.92 (m, 2H, ArH), 9.04 (br, 2H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 26.1 (CH_2CH_2), 26.1 (CH_2CH_2), 43.0 (NCH_2), 43.0 (CH_2N), 95.9, 106.5, 115.8, 118.8, 121.2 (d, *J* = 268.7 Hz), 124.3, 125.3, 126.9, 128.7, 128.8, 129.5, 129.6, 130.6, 139.1–140.0 (m), 139.3, 161.9 (HNC=), 164.4 (NC=O), 190.5 (C=O); HRMS (TOF ES$^+$): *m*/*z* calcd for $C_{24}H_{20}ClF_3N_4O_2$ [$(M + H)^+$], 489.1300; found, 489.1300.

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