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A simple approach to pyrazol-3-ones via diazenes

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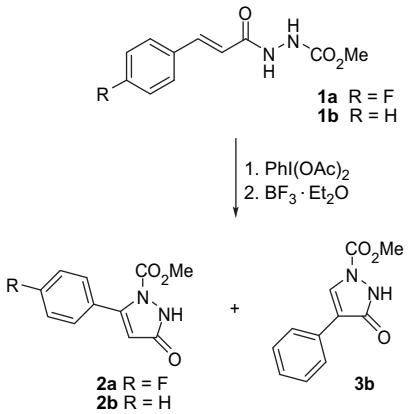
ABSTRACT

An efficient entry into pyrazol-3-ones is described starting from propenoic acids that were first transformed into the corresponding hydrazides. Oxidation of the hydrazides gave the diazenes and the latter cyclized to pyrazol-3-ones on treatment with $ZrCl_4$. The methoxycarbonyl protection of the N-1 of the pyrazolone derivatives was easily removed under mild reaction conditions.

1. Introduction

The pyrazole moiety[1] is present in a plethora of natural and synthetic compounds.[2] It is involved in a number of biologically active molecules[3] and can act as an efficient coordinating ligand.[4] Pyrazol-3-ones are typical representatives of the pyrazole derivatives. Their syntheses, reactivity, and numerous applications are well documented.[5] They belong to a broad family of compounds that serve as products and intermediates in analytical, agricultural, biological, and pharmaceutical chemistry. Some of them are used as important pharmaceutical agents (antipyrine and its congeners).[6] Recently, 4,5-diaryl-1*H*-pyrazole-3-ol was utilized as a versatile template for synthesizing the compounds that act as potential cyclooxygenase-2 (COX-2) inhibitors and also show good selectivity for COX-2 versus COX-1 enzymes.[7] Some pyrazolones showed inhibition of TNF-α production in response to the tumor promotor TPA on HL-60 cells.[8] Denis et al. very recently reported on the synthesis and biological activity of new pyrazol-3-ones.[9] They found that these compounds effectively inhibited heptosyltransferase WaaC, which represents an attractive target for the discovery of new Gram-negative antibacterial drugs based on an antivirulence mechanism. In addition, pyrazolone derivatives were demonstrated as inhibitors of the accumulation of the abnormal protease-resistant form of prion protein (PrP-res).[10]

In the light of the above-mentioned properties, there is a permanent need for new approaches toward pyrazol-3-ones. Usually, the synthesis of pyrazol-3-ones relies on the reaction of the appropriate C_3 synthon with hydrazine or its derivative, which leads to the formation of the C3–N2 bond of the pyrazole ring in the final step. Examples of an alternative option, i.e., C5–N1 ring-closure, are rare and are limited by the pool of starting materials.[5a] A recent paper by Prata et al. describes the cyclization of 3-arylpropanoylhydrazides leading to the mixtures of the corresponding 1-azaspiro[4.5]deca-6,9-diene-2,8-diones and 3,4-dihydroquinolin-2(1*H*)-ones.[11] They also report on two experiments involving 3-arylpropenoylhydrazides that gave another type of products (Scheme 1). Thus, the oxidation of 4-fluorocinnamic hydrazide **1a** with (diacetoxyiodo)benzene, followed by the treatment with $BF_3 \cdot Et_2O$ resulted in rather poor yield (23%) of the pyrazol-3-one **2a**. The same reaction sequence starting from cinnamic hydrazide **1b** gave the mixture of pyrazol-3-ones **2b** and **3b** in 45% and 9%



Scheme 1.

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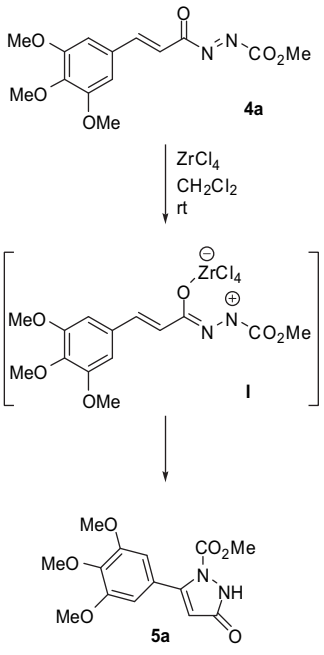
yields, respectively. The reason for the poor yield of pyrazol-3-one **2a** in the first case and the mixture of products in the second experiment seemed to be an unsuitable choice of reagents employed in the procedure. In order to check this hypothesis and to improve the outcome of the reaction sequence we first performed on the same substrates the oxidation with NBS, followed by the cyclization in the presence of $ZrCl_4$. Our results were indeed essentially better: (i) the pyrazol-3-one **2a** was isolated in 91% yield; (ii) the cyclization of **1b** led to **2b** in 65% yield accompanied by only 3% of **3b**.

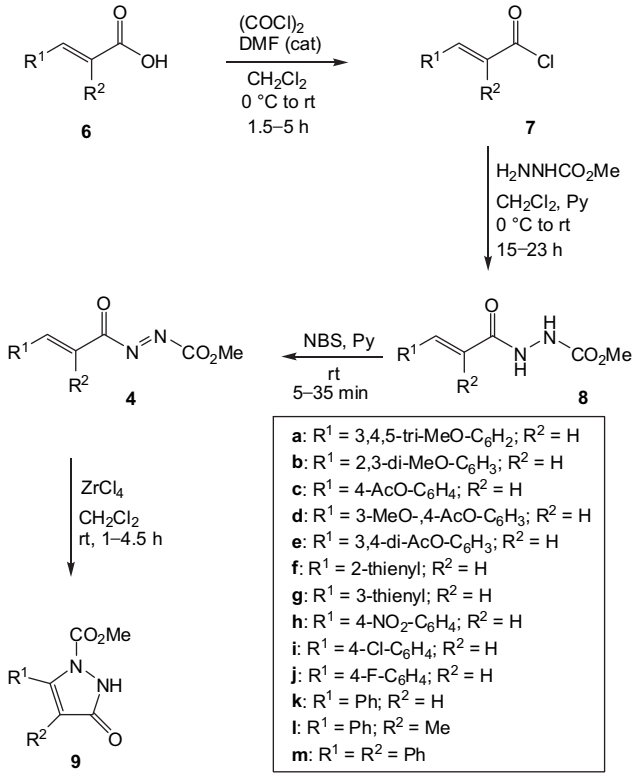
2. Results and discussion

Based on our previous experiences with diazenes[12] we became interested in intramolecular cyclizations of 3-substituted propenoyldiazenecarboxylates, which can be considered as the dehydro-analogues of the hydrazides **1**. For the initial studies concerning the ring-closure reactions we selected the diazene **4a** (Scheme 2), having three donating groups at the benzene ring but otherwise related to the diazenes that are probably formed from **1** on oxidation. To perform the cyclization of **4a** we chose $ZrCl_4$ as a Lewis acid because its catalytic power has already been proven in various electrophilic aminations.[13] Although it is impossible to a priori exclude another reaction that would eventually lead to the different product, we isolated the pyrazol-3-one **5a** as the sole product in a high yield (Scheme 2). The exclusive formation of the product **5a** may be explained by the initial attack of the $ZrCl_4$ at the carbonyl oxygen to give the dipolar species **I**, which serves as an internal nitrogen electrophile yielding the product **5a** upon cyclization. We have already demonstrated the use of $ZrCl_4$ for intramolecular electrophilic aminations of diazenes, i.e., arylaminocarbonyldiazenedicarboxylates that led to the formation of the 2-imidazolone ring as a consequence of the Lewis acid's attack at the ester carbonyl oxygen.[13a] It seems that the site of the $ZrCl_4$ binding regulates the outcome of the process.



Scheme 2.

Encouraged by the above-mentioned result we focused our attention on the scope of this ring-closure with regard to the synthesis of various pyrazol-3-ones. Initial experiments confirmed that the cyclization can serve as the final step in a general route to 1-methoxycarbonyl-5-aryl substituted pyrazol-3-ones. This multistep approach starting from simple compounds is outlined in Scheme 3. Thus, easily available propenoic acids **6** reacted with oxalyl chloride in the presence of catalytic amounts of DMF to give the acid chlorides **7**. The latter were not isolated but were immediately exposed to methyl carbazate to obtain the hydrazides **8**. Oxidation of the NHNH moiety in **8** was conducted with NBS using pyridine as a base to yield the diazenes **4** that usually appeared as red, oily products.



Scheme 3.

Although the diazenes **4** were generally not isolated, as they were quite unstable, we did succeed in the purification and characterization of the diazene **4d**. The last step of the above sequence that involved the treatment of the diazenes **4** with $ZrCl_4$ at room temperature gave the pyrazol-3-ones **9** in good-to-excellent yield (Table 1).

Table 1
Pyrazol-3-ones prepared from propenoic acids **6** via their hydrazides

Entry	Propenoic acid	Hydrazide	Yield[a] (%)	Pyrazol-3-one	Yield[a] (%)
1	**6a**	**8a**	94	**9a**	97
2	**6b**	**8b**	94	**9b**	97
3	**6c**	**8c**	98	**9c**	76
4	**6d**	**8d**	88	**9d**	95
5	**6e**	**8e**	91	**9e**	76
6	**6f**	**8f**	98	**9f**	89
7	**6g**	**8g**	97	**9g**	90
8	**6h**	**8h**	93	**9h**	77
9	**6i**	**8i**	99	**9i**	86
10	**6j**	**1a**	88	**2a**	91
11	**6k**	**1b**	95	**2b**	64[b]
12	**6l**	**8l**	96	**9l**	92
13	**6m**	**8m**	99	**9m**	96

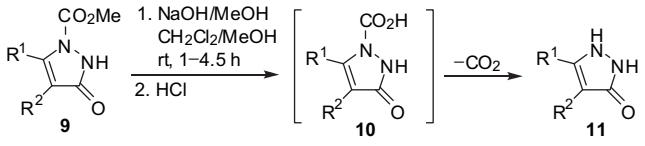
[a] Yields of isolated products are given.
[b] After chromatographic separation from 4-phenyl isomer **3b** (3%).

Most of the products (entries 1–11) are representatives of the pyrazole derivatives that are unsubstituted at the position 4. As demonstrated by the conversion of **6l** and **6m** into **9l** and **9m**

(entries 12 and 13) this approach works equally well if 2,3-disubstituted propenoic acids are applied as the starting materials and give the corresponding 4,5-disubstituted pyrazol-3-ones **9l** and **9m**.

The methoxycarbonyl functionality in the product **9** can be considered as an N-1 protecting group. It seemed reasonable to perform the hydrolysis of the pyrazol-3-ones **9** as well as **2a** and **2b**. The application of trimethylsilyl iodide is well documented[14] and was the first method we selected for this purpose. Although the reaction of pyrazol-3-ones with trimethylsilyl iodide in methylene chloride led to the deprotection of the N-1 under microwaves in a moderate yield (a 53% yield starting from **9l**) we also checked an elegant method recently described by Theodorou et al.[15] Namely, they developed a mild and efficient procedure for the alkaline hydrolysis of esters under non-aqueous conditions that also worked well in our case (Table 2). Thus, pyrazol-3-ones were treated with a methanolic solution of NaOH in the mixture CH_2Cl_2/MeOH at room temperature for 1–4 h. The resulting mixture was evaporated to dryness and the residue acidified with aqueous HCl to give, via the unstable acids **10**, the final products **11**. This process is accompanied by the hydrolysis of the acetoxy functionality when the latter is attached to the benzene ring giving a free phenolic OH group (Table 2, entries 3–5).

Table 2
Hydrolysis of 1-methoxycarbonyl substituted pyrazol-3-ones



Entry	Starting material	Product	Yield[a] (%)
1	**9a**	**11a**	80
2	**9b**	**11b**	94
3	**9c**	**11c**[b]	97
4	**9d**	**11d**[c]	97
5	**9e**	**11e**[d]	99
6	**9f**	**11f**[5b]	97
7	**9g**	**11g**	80
8	**9h**	**11h**	82
9	**9i**	**11i**	96
10	**2a**	**11j**	89
11	**2b**	**11k**	93
12	**9l**	**11l**	83
13	**9m**	**11m**	99

[a] Yields of isolated products are given.
[b] R^1=4-HO–C_6H_4.
[c] R^1=3-MeO–, 4-HO–C_6H_3.
[d] R^1=3,4-di-HO–C_6H_3.

3. Conclusions

In conclusion, we have described an efficient entry into pyrazolones, applying commercially available propenoic acids as the starting materials. This is a simple method for constructing of the pyrazole ring by forming the N1–C5 bond. The diazenes formed by the oxidation of the corresponding hydrazides do not need to be isolated and cyclize in the presence of $ZrCl_4$ to the desired pyrazol-3-ones. As far as we know, there are no reports in the literature concerning a general route to pyrazol-3-ones via a regioselective ring-closure of the diazenes. This simple and straightforward method is useful for the preparation of various N-1 protected pyrazol-3-ones. The protecting group, i.e., methoxycarbonyl, can be easily removed under mild reaction conditions, which enables further modifications of the pyrazolone molecule. The mild reaction conditions applied in the all steps, the simple procedures, the relatively rapid conversions, and the good-to-excellent yields are all notable characteristics of this protocol.

4. Experimental

4.1. General methods

Solvents and starting compounds were obtained from commercial sources (Fluka, Sigma, and Aldrich). TLC was carried out on Fluka silica-gel TLC-cards. All mps were determined on a hot stage apparatus and are uncorrected. IR spectra were recorded on a Bio-Rad FTS 3000MX instrument. NMR spectra were recorded on a Bruker Avance 300 DPX spectrometer at 302 K. Chemical shifts are reported in δ ppm, referenced to an internal TMS standard for ^{1}H NMR, DMSO-d_6 (δ 39.5) for ^{13}C NMR. Microanalyses were performed on a Perkin–Elmer 2400 series II CHNS/O analyser. Mass spectra and high-resolution mass measurements were performed on a VG-Analytical Autospec EQ instrument.

4.2. General procedure for the synthesis of hydrazides 8

Oxalyl chloride (15.543 g, 120 mmol) was slowly added to a stirred mixture of the acid **6** (60 mmol) and *N*,*N*-dimethylformamide (2–3 drops) in dry CH_2Cl_2 (90 mL) at 0 °C under argon. The reaction mixture was stirred at room temperature for an additional 2–5 h and evaporated to dryness to give the corresponding acid chloride **7** in a quantitative yield. Then, a solution of **7** in dry CH_2Cl_2 (100 mL) was slowly added to a stirred solution of methyl carbazate (5.515 g, 60 mmol) and pyridine (4.986 mL, 62.4 mmol) in dry CH_2Cl_2 (100 mL) at 0 °C. The reaction mixture was then stirred at room temperature for 15–23 h, water was added (50 mL), the mixture was left at room temperature for 3 h, and the solid material (**8**) was filtered off. If no precipitation occurred, the organic phase was separated, dried over anhydrous sodium sulfate, and evaporated to dryness to give the hydrazide **8** in an excellent yield.

*4.2.1. Methyl 2-[(2E)-3-(3,4,5-trimethoxyphenyl)prop-2-enoyl]hydrazinecarboxylate (**8a**).* Reaction time: 2 h (for **7a**) and 18 h. White needles; mp 82.1–84.6 °C (MeOH). IR (KBr): 3496, 3302, 1728, 1618, 1586, 1277, 1235, 1126. ^{1}H NMR (DMSO-d_6): δ 3.63 (s, 3H), 3.71 (s, 3H), 3.84 (s, 6H), 6.60 (d, J=15.9 Hz, 1H), 6.95 (s, 2H), 7.51 (d, J=15.9 Hz, 1H), 9.19 (br s, 1H), 9.83 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 52.0, 56.0, 60.1, 105.3, 118.7, 130.2, 139.1, 140.6, 153.2, 156.7, 165.0. MS (EI) m/z (%) 310 (M^+, 34), 221 (100), 190 (35), 163 (21). HRMS calcd for $C_{14}H_{18}N_2O_6$ (M^+): 310.1165. Found: 310.1170.

*4.2.2. Methyl 2-[(2E)-3-(2,3-dimethoxyphenyl)prop-2-enoyl]hydrazinecarboxylate (**8b**).* Reaction time: 3 h (to obtain **7b**) and 20 h (transformation of **7b** into **8b**). White needles; mp 133.0–134.0 °C (EtOAc). IR (KBr): 3464, 3275, 1724, 1655, 1620, 1481, 1274, 1229. ^{1}H NMR (DMSO-d_6): δ 3.64 (s, 3H), 3.78 (s, 3H), 3.84 (s, 3H), 6.69 (d, J=15.9 Hz, 1H), 7.15 (m, 3H), 7.76 (d, J=15.9 Hz, 1H), 9.21 (br s, 1H), 9.96 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 52.0, 55.8, 60.7, 114.2, 118.8, 120.6, 124.4, 128.1, 134.9, 147.6, 152.9, 156.7, 165.0. MS (EI) m/z (%) 280 (M^+, 5), 191 (100), 176 (38), 148 (12). Anal. Calcd for $C_{13}H_{16}N_2O_5$ (280.28): C, 55.71; H, 5.75; N, 9.99. Found: C, 55.91; H, 5.93; N, 10.05.

*4.2.3. Methyl 2-[(2E)-3-(4-acetoxyphenyl)prop-2-enoyl]hydrazinecarboxylate (**8c**).* Reaction time: 3 h 30 min (for **7c**) and 21 h. White needles; mp 166.8–168.5 °C (EtOAc). IR (KBr): 3326, 1751, 1660, 1625, 1489, 1214, 1199, 1166. ^{1}H NMR (DMSO-d_6): δ 2.29 (s, 3H), 3.65 (s, 3H), 6.65 (d, J=15.9 Hz, 1H), 7.21 and 7.68 (AA′XX′, J=8.7 Hz, 4H), 7.60 (d, J=15.9 Hz, 1H), 9.24 (br s, 1H), 9.97 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 20.8, 52.0, 119.4, 122.5, 129.0, 132.3, 139.6, 151.6, 156.8, 164.9, 169.1. MS (EI) m/z (%) 278 (M^+, 1), 189 (51), 147 (100), 69 (41). Anal. Calcd for $C_{13}H_{14}N_2O_5$ (278.26): C, 56.11; H, 5.07; N, 10.07.

Found: C, 56.25; H, 5.26; N, 9.75. HRMS calcd for $C_{13}H_{14}N_2O_5$ (M^+): 278.0903. Found: 278.0908.

*4.2.4. Methyl 2-[(2E)-3-(4-acetoxy-3-methoxyphenyl)prop-2-enoyl]-hydrazinecarboxylate (**8d**).* Reaction time: 5 h (for **7d**) and 23 h. White needles; mp 178.8–180.5 °C (CH_2Cl_2). IR (KBr): 1765, 1717, 1669, 1631, 1517, 1264, 1231, 1198. ^{1}H NMR (DMSO-d_6): δ 2.27 (s, 3H), 3.62 (s, 3H), 3.83 (s, 3H), 6.63 (d, J=15.9 Hz, 1H), 7.14 (d, J=8.4 Hz, 1H), 7.22 (dd, J_1=8.4 Hz, J_2=1.5 Hz, 1H), 7.37 (d, J=1.5 Hz, 1H), 7.54 (d, J=15.9 Hz, 1H), 9.19 (br s, 1H), 9.89 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 20.4, 51.9, 55.8, 111.9, 119.6, 120.2, 123.3, 133.5, 139.8, 140.4, 151.1, 156.6, 164.7, 168.4. MS (EI) m/z (%) 308 (M^+, 4), 219 (45), 177 (100), 145 (26). Anal. Calcd for $C_{14}H_{16}N_2O_6$ (308.29): C, 54.54; H, 5.23; N, 9.09. Found: C, 54.73; H, 5.19; N, 8.79. HRMS calcd for $C_{14}H_{16}N_2O_6$ (M^+): 308.1008. Found: 308.1015.

*4.2.5. Methyl 2-[(2E)-3-(3,4-diacetoxyphenyl)prop-2-enoyl]hydrazine-carboxylate (**8e**).* Reaction time: 3 h (for **7e**) and 15 h. White needles; mp 181.4–183.9 °C (MeOH). IR (KBr): 3309, 3214, 1766, 1737, 1622, 1249, 1213, 1184. ^{1}H NMR (DMSO-d_6): δ 2.29 (s, 3H), 2.30 (s, 3H), 3.63 (s, 3H), 6.62 (d, J=15.9 Hz, 1H), 7.34 (m, 1H), 7.55 (m, 3H), 9.21 (br s, 1H), 9.95 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 20.3, 52.0, 120.4, 122.6, 124.2, 126.1, 133.4, 138.8, 142.4, 143.0, 156.7, 164.6, 168.1, 168.2. MS (EI) m/z (%) 336 (M^+, 3), 247 (33), 205 (60), 163 (100). Anal. Calcd for $C_{15}H_{16}N_2O_7$ (336.30): C, 53.57; H, 4.80; N, 8.33. Found: C, 53.61; H, 4.83; N, 8.24.

*4.2.6. Methyl 2-[(2E)-3-(2-thienyl)prop-2-enoyl]hydrazinecarboxylate (**8f**).* Reaction time: 4 h 30 min (for **7f**) and 20 h. Off-white needles; mp 136.1–137.7 °C (EtOAc). IR (KBr): 3346, 3190, 1734, 1719, 1661, 1651, 1616, 1231. ^{1}H NMR (DMSO-d_6): δ 3.63 (s, 3H), 6.40 (d, J=15.6 Hz, 1H), 7.13 (dd, J_1=5.1 Hz, J_2=3.5 Hz, 1H), 7.44 (d, J=3.5 Hz, 1H), 7.64 (d, J=5.1 Hz, 1H), 7.73 (d, J=15.6 Hz, 1H), 9.21 (br s, 1H), 9.88 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 52.0, 117.8, 128.4, 128.5, 131.3, 133.4, 139.5, 156.7, 164.7. MS (EI) m/z (%) 226 (M^+, 8), 137 (100), 109 (41), 65 (20). Anal. Calcd for $C_9H_{10}N_2O_3S$ (226.25): C, 47.78; H, 4.45; N, 12.38. Found: C, 47.84; H, 4.52; N, 12.45.

*4.2.7. Methyl 2-[(2E)-3-(3-thienyl)prop-2-enoyl]hydrazinecarboxylate (**8g**).* Reaction time: 4 h 30 min (for **7g**) and 19 h 30 min. White needles; mp 147.8–149.5 °C (EtOAc). IR (KBr): 3343, 3194, 1733, 1717, 1657, 1621, 1272, 1228. ^{1}H NMR (DMSO-d_6): δ 3.63 (s, 3H), 6.46 (d, J=15.6 Hz, 1H), 7.39 (d, J=5.1 Hz, 1H), 7.57 (d, J=15.6 Hz, 1H), 7.62 (dd, J_1=5.1 Hz, J_2=3.0 Hz, 1H), 7.87 (d, J=3.0 Hz, 1H), 9.18 (br s, 1H), 9.86 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 52.0, 118.7, 125.2, 127.8, 128.2, 134.4, 137.6, 156.7, 165.2. MS (EI) m/z (%) 226 (M^+, 4), 137 (100), 109 (44), 65 (20). Anal. Calcd for $C_9H_{10}N_2O_3S$ (226.25): C, 47.78; H, 4.45; N, 12.38. Found: C, 47.91; H, 4.52; N, 12.36.

*4.2.8. Methyl 2-[(2E)-3-(4-nitrophenyl)prop-2-enoyl]hydrazinecarboxy-late (**8h**).* Reaction time: 4 h (for **7h**) and 17 h. Off-white needles; mp 238–241 °C (EtOAc/MeOH). IR (KBr): 3287, 1744, 1721, 1662, 1623, 1511, 1350, 1252. ^{1}H NMR (DMSO-d_6): δ 3.67 (s, 3H), 6.84 (d, J=15.9 Hz, 1H), 7.69 (d, J=15.9 Hz, 1H), 7.90 and 8.28 (AA′XX′, J=8.9 Hz, 4H), 9.31 (br s, 1H), 10.11 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 52.0, 123.6, 124.1, 128.8, 138.1, 141.0, 147.7, 156.6, 164.2. MS (ES^+) m/z (%) 266.1 (MH^+). Anal. Calcd for $C_{11}H_{11}N_3O_5$ (265.23): C, 49.81; H, 4.18; N, 15.84. Found: C, 49.94; H, 3.98; N, 15.86.

*4.2.9. Methyl 2-[(2E)-3-(4-chlorophenyl)prop-2-enoyl]hydrazinecarboxy-late (**8i**).* Reaction time: 4 h (for **7i**) and 16 h. White platelets; mp 192.0–193.2 °C (EtOAc). IR (KBr): 3258, 3028, 1716, 1665, 1634, 1523, 1492, 1245. ^{1}H NMR (DMSO-d_6): δ 3.65 (s, 3H), 6.66 (d, J=15.9 Hz, 1H), 7.49 and 7.65 (AA′XX′, J=8.6 Hz, 4H), 7.57 (d, J=15.9 Hz, 1H), 9.25 (br s, 1H), 9.97 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 52.0, 120.1, 129.0, 129.4, 133.5, 134.3, 139.1, 156.7, 164.6. MS (ES^+) m/z (%) 277.0 (M+Na)$^+$. Anal. Calcd for $C_{11}H_{11}ClN_2O_3$ (254.67): C, 51.88; H, 4.35; N, 11.00. Found: C, 51.96; H, 4.15; N, 11.04.

*4.2.10. Methyl 2-[(2E)-(2-methyl-3-phenyl)prop-2-enoyl]hydrazinecar-boxylate (**8l**).* Reaction time: 4 h 30 min (for **7l**) and 19 h 30 min. White cubes; mp 115.4–117.3 °C (EtOAc). IR (KBr): 3347, 3290, 1713, 1659, 1524, 1508, 1290, 1266. ^{1}H NMR (DMSO-d_6): δ 2.05 (s, 3H), 3.64 (s, 3H), 7.38 (m, 6H), 9.12 (br s, 1H), 9.93 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 14.2, 51.9, 128.0, 128.5, 129.3, 130.6, 133.5, 135.7, 156.9, 168.8. MS (EI) m/z (%) 234 (M^+, 2), 145 (100), 117 (79), 91 (29). Anal. Calcd for $C_{12}H_{14}N_2O_3$ (234.25): C, 61.53; H, 6.02; N, 11.96. Found: C, 61.29; H, 6.19; N, 12.10.

*4.2.11. Methyl 2-[(2E)-(2,3-diphenyl)prop-2-enoyl]hydrazinecarboxy-late (**8m**).* Reaction time: 2 h (for **7m**) and 20 h. White platelets; mp 147.6–148.9 °C (EtOAc/heptane). IR (KBr): 3290, 3216, 1741, 1655, 1610, 1501, 1248, 1217. ^{1}H NMR (DMSO-d_6): δ 3.62 (s, 3H), 7.04 (m, 2H), 7.19 (m, 5H), 7.36 (m, 4H), 9.17 (br s, 1H), 9.72 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 51.9, 128.0, 128.2, 128.4, 128.7, 129.4, 129.6, 134.0, 134.7, 135.3, 135.6, 156.8, 168.0. MS (ES^+) m/z (%) 297.1 (MH^+). Anal. Calcd for $C_{17}H_{16}N_2O_3$ (296.32): C, 68.91; H, 5.44; N, 9.45. Found: C, 69.14; H, 5.53; N, 9.52.

The hydrazides **1a**, **1b** were prepared from the acids **6j**, **6k** following the above general procedure:

*4.2.12. Methyl 2-[(2E)-3-(4-fluorophenyl)prop-2-enoyl]hydrazinecar-boxylate (**1a**).* Reaction time: 1 h 30 min (for **7j**) and 17 h. White platelets; mp 178.5–180.1 °C (EtOAc). Lit. mp 180–183 °C.[11] IR (KBr): 3257, 1719, 1663, 1628, 1603, 1524, 1509, 1226. ^{1}H NMR (DMSO-d_6): δ 3.64 (s, 3H), 6.59 (d, J=15.9 Hz, 1H), 7.27 (m, 2H), 7.57 (d, J=15.9 Hz, 1H), 7.69 (m, 2H), 9.22 (br s, 1H), 9.93 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 52.0, 115.9 (d, J=21.7 Hz), 119.2, 129.9 (d, J=8.5 Hz), 131.1 (d, J=3.0 Hz), 139.2, 156.7, 162.9 (d, J=246.2 Hz), 164.7.

*4.2.13. Methyl 2-[(2E)-3-phenylprop-2-enoyl]hydrazinecarboxylate (**1b**).* Reaction time: 2 h (for **7k**) and 19 h. White needles; mp 161.0–162.6 °C (EtOAc). Lit. mp 164–166 °C.[11] IR (KBr): 3328, 3193, 1729, 1716, 1672, 1633, 1557, 1232. ^{1}H NMR (DMSO-d_6): δ 3.62 (s, 3H), 6.62 (d, J=15.9 Hz, 1H), 7.42 (m, 3H), 7.54 (d, J=15.9 Hz, 1H), 7.61 (m, 2H), 9.18 (br s, 1H), 9.90 (br s, 1H).

4.3. General procedure for the transformations of 8 into 9

NBS (1.978 g, 11 mmol) was slowly added to a stirred solution of the hydrazide **12** (2.343 g, 10 mmol) and pyridine (1.598 g, 20 mmol) in CH_2Cl_2 (130 mL) at room temperature. The reaction mixture was then stirred at the same temperature for 10–35 min (TLC evidence), treated successively with a 12% aqueous solution of HCl (33 mL), a 5% aqueous solution of $Na_2S_2O_3\cdot 5H_2O$ (33 mL), saturated aqueous $NaHCO_3$ (33 mL), and H_2O (33 mL), and dried over anhydrous Na_2SO_4 (for the characterization of the diazene **4d**, see Section 4.3.14). An organic phase containing the diazene **4** was added dropwise to a stirred suspension of $ZrCl_4$ (3.56 g, 15 mmol) in dry CH_2Cl_2 (10 mL) at room temperature. After stirring at room temperature for an additional 1–4.5 h (TLC evidence) the reaction mixture was quenched with H_2O (150 mL) and neutralized with saturated aqueous $NaHCO_3$. The two phases were separated, and the aqueous solution was extracted with CH_2Cl_2 (3×100 mL). The organic phase was dried over anhydrous Na_2SO_4 and evaporated to dryness to give the pyrazol-3-one **9** in a good-to-excellent yield.

*4.3.1. Methyl 3-oxo-5-(3,4,5-trimethoxyphenyl)-2,3-dihydro-1H-pyr-azole-1-carboxylate (**9a**).* Reaction time: (oxidation) 10 min, (cyclization) 2 h. Off-white amorphous powder; mp 188.7–191.0 °C (EtOAc). IR (KBr): 1757, 1585, 1533, 1447, 1362, 1346, 1267, 1132. ^{1}H NMR (DMSO-d_6): δ 3.72 (s, 3H), 3.80 (s, 9H), 6.04 (s, 1H), 6.79 (s, 2H),

10.97 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 53.8, 56.1, 60.1, 100.8, 106.9, 126.2, 138.0, 147.7, 149.9, 152.3, 162.4. MS (EI) m/z (%) 308 (M^+, 100), 293 (48), 265 (13), 177 (10). Anal. Calcd for $C_{14}H_{16}N_2O_6$ (308.29): C, 54.54; H, 5.23; N, 9.09. Found: C, 54.69; H, 5.44; N, 8.84.

*4.3.2. Methyl 5-(2,3-dimethoxyphenyl)-3-oxo-2,3-dihydro-1H-pyrazole-1-carboxylate (**9b**).* Reaction time: (oxidation) 10 min, (cyclization) 4 h 30 min. White platelets; mp 218–220 °C (MeOH). IR (KBr): 1754, 1589, 1532, 1434, 1341, 1269, 1000, 790. ^{1}H NMR (DMSO-d_6): δ 3.56 (s, 3H), 3.70 (s, 3H), 3.83 (s, 3H), 5.93 (s, 1H), 6.84 (dd, J_1=7.2 Hz, J_2=1.8 Hz, 1H), 7.10 (m, 2H), 10.91 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 53.8, 55.8, 60.1, 100.5, 113.9, 121.6, 123.5, 125.5, 143.4, 146.2, 149.7, 152.0, 162.4. MS (EI) m/z (%) 278 (M^+, 100), 247 (16), 188 (33), 161 (47). Anal. Calcd for $C_{13}H_{14}N_2O_5$ (287.26): C, 56.11; H, 5.07; N, 10.07. Found: C, 55.96; H, 4.94; N, 9.95.

*4.3.3. Methyl 5-(4-acetoxyphenyl)-3-oxo-2,3-dihydro-1H-pyrazole-1-carboxylate (**9c**).* Reaction time: (oxidation) 10 min, (cyclization) 4 h. White needles; mp 192.8–194.8 °C (EtOAc). IR (KBr): 1750, 1536, 1440, 1375, 1344, 1238, 1218, 1204. ^{1}H NMR (DMSO-d_6): δ 2.29 (s, 3H), 3.77 (s, 3H), 6.05 (s, 1H), 7.17 and 7.50 (AA′XX′, J=8.4 Hz, 4H), 11.06 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 20.8, 53.9, 101.0, 121.2, 128.2, 130.2, 147.0, 150.0, 150.8, 162.5, 169.1. MS (EI) m/z (%) 276 (M^+, 12), 234 (100), 189 (35), 118 (38). Anal. Calcd for $C_{13}H_{12}N_2O_5$ (276.24): C, 56.52; H, 4.38; N, 10.14. Found: C, 56.48; H, 4.47; N, 9.87.

*4.3.4. Methyl 5-(4-acetoxy-3-methoxyphenyl)-3-oxo-2,3-dihydro-1H-pyrazole-1-carboxylate (**9d**).* Reaction time: (oxidation) 35 min, (cyclization) 1 h 5 min. White platelets; mp 192.2–194.1 °C (EtOAc). IR (KBr): 1766, 1595, 1587, 1326, 1224, 1210, 1139, 1118. ^{1}H NMR (DMSO-d_6): δ 2.28 (s, 3H), 3.77 (s, 3H), 3.79 (s, 3H), 6.07 (s, 1H), 7.03 (dd, J_1=8.1 Hz, J_2=1.8 Hz, 1H), 7.10 (d, J=8.1 Hz, 1H), 7.26 (d, J=1.8 Hz, 1H), 11.00 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 20.4, 53.9, 56.0, 101.1, 113.9, 121.4, 122.1, 129.4, 139.7, 147.1, 149.9, 150.1, 162.5, 168.5. MS (EI) m/z (%) 306 (M^+, 4), 264 (100), 205 (12), 148 (16). Anal. Calcd for $C_{14}H_{14}N_2O_6$ (306.27): C, 54.90; H, 4.61; N, 9.15. Found: C, 54.92; H, 4.66; N, 8.93.

*4.3.5. Methyl 5-(3,4-diacetoxyphenyl)-3-oxo-2,3-dihydro-1H-pyrazole-1-carboxylate (**9e**).* Reaction time: (oxidation) 25 min, (cyclization) 1 h 45 min. White needles; mp 186.5–187.8 °C (EtOAc). IR (KBr): 1770, 1754, 1373, 1359, 1331, 1245, 1214, 1185. ^{1}H NMR (DMSO-d_6): δ 2.28 (s, 3H), 2.30 (s, 3H), 3.76 (s, 3H), 6.07 (s, 1H), 7.29 (dd, J_1=7.8 Hz, J_2=0.9 Hz, 1H), 7.39 (m, 2H), 11.01 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 20.29, 20.35, 54.0, 101.3, 123.0, 124.4, 127.3, 129.1, 141.3, 142.4, 146.0, 149.9, 162.5, 168.15, 168.16. MS (EI) m/z (%) 334 (M^+, 4), 292 (30), 250 (100), 205 (19). Anal. Calcd for $C_{15}H_{14}N_2O_7$ (334.28): C, 53.89; H, 4.22; N, 8.38. Found: C, 53.63; H, 4.03; N, 8.12.

*4.3.6. Methyl 3-oxo-5-(2-thienyl)-2,3-dihydro-1H-pyrazole-1-carboxylate (**9f**).* Reaction time: (oxidation) 10 min, (cyclization) 3 h 30 min. Light-brown plates; mp 176.3–177.9 °C (EtOAc). IR (KBr): 1747, 1603, 1443, 1374, 1352, 1322, 1211, 704. ^{1}H NMR (DMSO-d_6): δ 3.85 (s, 3H), 6.16 (s, 1H), 7.12 (dd, J_1=5.1 Hz, J_2=3.8 Hz, 1H), 7.43 (dd, J_1=3.8 Hz, J_2=0.9 Hz, 1H), 7.68 (dd, J_1=5.1 Hz, J_2=0.9 Hz, 1H), 11.09 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 54.1, 101.4, 127.0, 128.2, 129.8, 130.0, 140.6, 150.0, 162.4. MS (EI) m/z (%) 224 (M^+, 100), 179 (33), 109 (62), 65 (44). Anal. Calcd for $C_9H_8N_2O_3S$ (224.24): C, 48.21; H, 3.60; N, 12.49. Found: C, 48.18; H, 3.58; N, 12.45.

*4.3.7. Methyl 3-oxo-5-(3-thienyl)-2,3-dihydro-1H-pyrazole-1-carboxylate (**9g**).* Reaction time: (oxidation) 10 min, (cyclization) 1 h 10 min. Off-white needles; mp 184.0–186.2 °C (EtOAc). IR (KBr): 1749, 1605, 1557, 1438, 1378, 1355, 1334, 777. ^{1}H NMR (DMSO-d_6): δ 3.81 (s, 3H), 6.07 (s, 1H), 7.29 (dd, J_1=5.1 Hz, J_2=1.2 Hz, 1H), 7.54 (dd, J_1=3.0 Hz, J_2=5.1 Hz, 1H), 7.75 (dd, J_1=3.0 Hz, J_2=1.2 Hz, 1H), 11.01 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 53.9, 100.6, 125.2, 125.9, 128.9, 130.4, 142.8, 150.0, 162.5. MS (EI) m/z (%) 224 (M^+, 100), 179 (37), 151 (17), 109 (53). Anal. Calcd for $C_9H_8N_2O_3S$ (224.24): C, 48.21; H, 3.60; N, 12.49. Found: C, 47.92; H, 3.61; N, 12.20.

*4.3.8. Methyl 5-(4-nitrophenyl)-3-oxo-2,3-dihydro-1H-pyrazole-1-carboxylate (**9h**).* Reaction time: (oxidation) 5 min, (cyclization) 1 h. White amorphous powder; mp 202–204 °C (EtOAc/MeOH). IR (KBr): 3030, 1750, 1586, 1518, 1442, 1337, 1283, 1138. ^{1}H NMR (DMSO-d_6): δ 3.77 (s, 3H), 6.19 (s, 1H), 7.77 and 8.24 (AA′XX′, J=8.7 Hz, 4H), 11.13 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 54.1, 102.0, 122.8, 130.4, 137.2, 145.4, 147.4, 149.9, 162.6. MS (ES^+) m/z (%) 264.1 (MH^+). Anal. Calcd for $C_{11}H_9N_3O_5$ (263.21)·1/5H_2O: C, 49.52; H, 3.55; N, 15.75. Found: C, 49.40; H, 3.25; N, 15.54.

*4.3.9. Methyl 5-(4-chlorophenyl)-3-oxo-2,3-dihydro-1H-pyrazole-1-carboxylate (**9i**).* Reaction time: (oxidation) 5 min, (cyclization) 1 h. White needles; mp 196.8–199.0 °C (EtOAc). IR (KBr): 1753, 1609, 1590, 1524, 1439, 1368, 1336, 1284. ^{1}H NMR (DMSO-d_6): δ 3.78 (s, 3H), 6.06 (s, 1H), 7.48 (m, 4H), 11.07 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 53.9, 101.1, 127.7, 129.6, 130.8, 133.6, 146.4, 149.9, 162.5. MS (ES^+) m/z (%) 253.0 (MH^+). Anal. Calcd for $C_{11}H_9ClN_2O_3$ (252.66): C, 52.29; H, 3.59; N, 11.09. Found: C, 52.14; H, 3.37; N, 11.01.

*4.3.10. Methyl 4-methyl-3-oxo-5-phenyl-2,3-dihydro-1H-pyrazole-1-carboxylate (**9l**).* Reaction time: (oxidation) 20 min, (cyclization) 1 h 15 min. White cubes; mp 156.1–157.2 °C (EtOAc). IR (KBr): 2966, 1755, 1540, 1445, 1336, 1280, 1213, 1177. ^{1}H NMR (DMSO-d_6): δ 1.74 (s, 3H), 3.71 (s, 3H), 7.38 (m, 5H), 11.12 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 6.8, 53.5, 107.9, 127.8, 128.3, 129.4, 130.8, 143.2, 149.9, 162.3. MS (EI) m/z (%) 232 (M^+, 100), 187 (62), 115 (52), 77 (22). Anal. Calcd for $C_{12}H_{12}N_2O_3$ (232.24): C, 62.06; H, 5.21; N, 12.06. Found: C, 62.29; H, 5.20; N, 12.19.

*4.3.11. Methyl 4,5-diphenyl-3-oxo-2,3-dihydro-1H-pyrazole-1-carboxylate (**9m**).* Reaction time: (oxidation) 5 min, (cyclization) 1 h. White needles; mp 213–216 °C (MeOH). IR (KBr): 1762, 1754, 1543, 1440, 1347, 1262, 1160, 703. ^{1}H NMR (DMSO-d_6): δ 3.72 (s, 3H), 7.17 (m, 5H), 7.34 (m, 5H), 11.50 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 53.8, 112.5, 126.7, 127.88, 127.92, 128.5, 128.7, 129.8, 130.0, 130.8, 142.8, 149.7, 160.7. MS (ES^+) m/z (%) 295.1 (MH^+). Anal. Calcd for $C_{17}H_{14}N_2O_3$ (294.30): C, 69.38; H, 4.79; N, 9.52. Found: C, 69.64; H, 4.65; N, 9.55.

The pyrazole-3-ones **2a**, **2b** were prepared from the hydrazides **1a**, **1b** following the above general procedure:

*4.3.12. Methyl 5-(4-fluorophenyl)-3-oxo-2,3-dihydro-1H-pyrazole-1-carboxylate (**2a**).* Reaction time: (oxidation) 5 min, (cyclization) 1 h 15 min. White needles; mp 191.7–193.8 °C (EtOAc). Lit. mp 175–177 °C.[11] IR (KBr): 1749, 1613, 1535, 1440, 1374, 1346, 1223, 783. ^{1}H NMR (DMSO-d_6): δ 3.77 (s, 3H), 6.03 (s, 1H), 7.23 (m, 2H), 7.51 (m, 2H), 11.05 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 53.9, 101.0, 114.6 (d, J=21.7 Hz), 127.2 (d, J=3.2 Hz), 131.2 (d, J=8.4 Hz), 146.7, 149.9, 162.3 (d, J=244.4 Hz), 162.5.

*4.3.13. Methyl 3-oxo-5-phenyl-2,3-dihydro-1H-pyrazole-1-carboxylate (**2b**).* Reaction time: (oxidation) 5 min, (cyclization) 1 h. White cubes; mp 182.6–184.9 °C (EtOAc). Lit. mp 155–159 °C.[11] IR (KBr): 1748, 1596, 1530, 1442, 1367, 1334, 1134, 766. ^{1}H NMR (DMSO-d_6): δ 3.76 (s, 3H), 6.02 (s, 1H), 7.42 (m, 5H), 11.03 (br s, 1H). ^{13}C NMR (DMSO-d_6): δ 53.8, 100.8, 127.7, 128.7, 128.9, 130.8, 147.8, 150.0, 162.5.

The diazene **4d** was obtained by the oxidation of the hydrazide **8d** in 99% yield:

*4.3.14. Methyl 2-[(2E)-3-(4-acetoxy-3-methoxyphenyl)prop-2-enoyl]-diazenecarboxylate (**4d**).* Reaction time: 5 min. Orange amorphous

powder; mp 76.8–84.4 °C (CH_2Cl_2/*i*-Pr_2O). IR (KBr): 1763, 1692, 1509, 1261, 1217, 1199, 1156, 1121. ^{1}H NMR (DMSO-d_6): δ 2.29 (s, 3H), 3.86 (s, 3H), 4.10 (s, 3H), 7.18 (d, J=16.2 Hz, 1H), 7.21 (d, J=8.1 Hz, 1H), 7.44 (dd, J_1=8.1 Hz, J_2=1.8 Hz, 1H), 7.66 (d, J=1.8 Hz, 1H), 7.86 (d, J=16.2 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 20.3, 55.7, 56.1, 112.7, 116.3, 123.2, 123.4, 132.4, 142.4, 150.4, 151.3, 160.6, 168.2, 180.1. MS (EI) *m*/*z* (%) 308 ($(M+2H)^+$, 0.3), 219 (38), 177 (100), 145 (27). Anal. Calcd for $C_{14}H_{14}N_2O_6$ (306.27): C, 54.90; H, 4.61; N, 9.15. Found: C, 54.79; H, 4.54; N, 8.72. HRMS calcd for $C_{14}H_{15}N_2O_6$ (MH^+): 307.0930. Found: 307.0922.

4.4. Hydrolysis of 1-methoxycarbonylpyrazol-3-ones into 11

A methanolic solution of NaOH (2 M, 6 mL; 12 mL in the case of **9e**) was added to a stirred mixture of 1-methoxycarbonylpyrazol-3-one (5 mmol) in CH_2Cl_2/MeOH (9:1; 20 mL) at room temperature. Stirring was continued at the same temperature for an additional 1–4.5 h and the reaction mixture was evaporated to dryness. The residue was treated with water (50 mL), acidified with aqueous HCl (1:2, v/v), and extracted with EtOAc (4×100 mL). The combined EtOAc extracts were dried over anhydrous sodium sulfate and evaporated to dryness to give unprotected pyrazol-3-ones **11**. A modified procedure (applied for the isolation of **11c**–**11e**): the reaction mixture after the addition of aqueous HCl was evaporated to dryness, treated with isopropanol (75 mL), filtered through a short column of silica gel, and evaporated to dryness.

*4.4.1. 5-(3,4,5-Trimethoxyphenyl)-1,2-dihydro-3H-pyrazol-3-one (**11a**).* Reaction time: 4 h. Pale yellow amorphous powder; mp 233–235 °C (EtOAc). Lit. mp 230–232 °C.[16] IR (KBr): 3327, 1595, 1572, 1527, 1501, 1260, 1247, 1136. ^{1}H NMR (DMSO-d_6): δ 3.67 (s, 3H), 3.82 (s, 6H), 5.91 (s, 1H), 6.97 (s, 2H), 9.81 (br s, 1H), 11.89 (br s, 1H). Anal. Calcd for $C_{12}H_{14}N_2O_4$ (250.25): C, 57.59; H, 5.64; N, 11.19. Found: C, 57.30; H, 5.54; N, 10.80.

*4.4.2. 5-(2,3-Dimethoxyphenyl)-1,2-dihydro-3H-pyrazol-3-one (**11b**).* Reaction time: 4 h. Pale yellow small cubes; mp 176.5–177.9 °C (EtOAc). IR (KBr): 3352, 1568, 1536, 1506, 1482, 1266, 1055, 771. ^{1}H NMR (DMSO-d_6): δ 3.71 (s, 3H), 3.83 (s, 3H), 5.95 (s, 1H), 7.01 (dd, J_1=8.1 Hz, J_2=1.5 Hz, 1H), 7.10 (dd, J_1=8.1 Hz, J_2=7.8 Hz, 1H), 7.24 (dd, J=7.8, 1.5 Hz, 1H), 10.73 (br s, 2H). ^{13}C NMR (DMSO-d_6): δ 55.8, 59.7, 89.8, 112.3, 118.7, 123.9, 124.2, 139.2, 145.5, 153.1, 161.0. MS (EI) *m*/*z* (%) 220 (M^+, 100), 189 (21), 175 (19), 134 (20). HRMS calcd for $C_{11}H_{12}N_2O_3$ (M^+): 220.0848. Found: 220.0850.

*4.4.3. 5-(4-Hydroxyphenyl)-1,2-dihydro-3H-pyrazol-3-one (**11c**).* Reaction time: 4 h. Large off-white plates; mp 273–277 °C (EtOAc/MeOH). IR (KBr): 2957, 1626, 1601, 1567, 1536, 1507, 1470, 1265. ^{1}H NMR (DMSO-d_6): δ 6.12 (s, 1H), 6.89 and 7.70 (AA′XX′, J=8.7 Hz, 4H), 10.06 (br s, 3H). ^{13}C NMR (DMSO-d_6): δ 86.7, 116.0, 117.6, 128.3, 147.4, 158.0, 159.8. MS (EI) *m*/*z* (%) 178 ($(MH_2)^+$, 75), 147 (100), 119 (34), 91 (25). HRMS calcd for $C_9H_9N_2O_2$ (MH^+): 177.0664. Found: 177.0670.

*4.4.4. 5-(4-Hydroxy-3-methoxyphenyl)-1,2-dihydro-3H-pyrazol-3-one (**11d**).* Reaction time: 2 h 25 min. Light-brown oil. IR (KBr): 3169, 1633, 1623, 1608, 1514, 1479, 1289, 1266. ^{1}H NMR (DMSO-d_6): δ 3.91 (s, 3H), 6.31 (s, 1H), 6.99 (d, J=8.3 Hz, 1H), 7.40 (dd, J_1=8.3 Hz, J_2=1.5 Hz, 1H), 7.62 (d, J=1.5 Hz, 1H), 13.16 (br s, 3H). ^{13}C NMR (DMSO-d_6): δ 56.1, 86.9, 110.6, 116.0, 117.9, 120.3, 147.6, 148.1, 149.2, 157.9. MS (EI) *m*/*z* (%) 206 (M^+, 100), 191 (16), 163 (15), 149 (46). HRMS calcd for $C_{10}H_{10}N_2O_3$ (M^+): 206.0691. Found: 206.0686.

*4.4.5. 5-(3,4-Dihydroxyphenyl)-1,2-dihydro-3H-pyrazol-3-one (**11e**).* Reaction time: 4 h. Brown oil. IR (KBr): 3151, 1626, 1531, 1514, 1473, 1384, 1293, 1242. ^{1}H NMR (DMSO-d_6): δ 5.83 (s, 1H), 6.80 (d, J=8.1 Hz, 1H), 7.03 (dd, J_1=8.1 Hz, J_2=2.1 Hz, 1H), 7.10 (d, J=2.1 Hz, 1H), 9.23 (br s, 4H). ^{13}C NMR (DMSO-d_6): δ 86.6, 113.5, 116.2, 117.6, 120.1, 145.7, 146.0, 146.9, 159.9. MS (EI) *m*/*z* (%) 192 (M^+, 100), 163 (8), 135 (41), 89 (10). HRMS calcd for $C_9H_8N_2O_3$ (M^+): 192.0535. Found: 192.0537.

*4.4.6. 5-(2-Thienyl)-1,2-dihydro-3H-pyrazol-3-one (**11f**).* Reaction time: 3 h 10 min. Gray amorphous powder; mp 200–201 °C (EtOAc). Lit. mp 203–204 °C.[5b] IR (KBr): 2590, 1615, 1571, 1524, 1440, 770, 743, 712. ^{1}H NMR (DMSO-d_6): δ 5.69 (s, 1H), 7.07 (dd, J_1=5.1 Hz, J_2=3.6 Hz, 1H), 7.33 (dd, J_1=3.6 Hz, J_2=1.1 Hz, 1H), 7.46 (dd, J_1=5.1 Hz, J_2=1.1 Hz, 1H), 10.23 (br s, 2H). Anal. Calcd for $C_7H_6N_2OS$ (166.20): C, 50.59; H, 3.64; N, 16.86. Found: C, 50.38; H, 3.64; N, 16.56.

*4.4.7. 5-(3-Thienyl)-1,2-dihydro-3H-pyrazol-3-one (**11g**).* Reaction time: 4 h 30 min. Light-pink small needles; mp 215–217 °C (EtOAc). IR (KBr): 2722, 1616, 1589, 1526, 1491, 777, 717, 702. ^{1}H NMR (DMSO-d_6): δ 5.82 (s, 1H), 7.44 (dd, J_1=5.0 Hz, J_2=0.9 Hz, 1H), 7.59 (dd, J_1=5.0 Hz, J_2=2.9 Hz, 1H), 7.74 (dd, J_1=2.9 Hz, J_2=0.9 Hz, 1H), 10.87 (m, 2H). ^{13}C NMR (DMSO-d_6): δ 87.1, 120.5, 125.5, 126.9, 132.0, 139.5, 160.9. MS (EI) *m*/*z* (%) 166 (M^+, 100), 137 (5), 109 (48), 65 (11). Anal. Calcd for $C_7H_6N_2OS$ (166.20): C, 50.59; H, 3.64; N, 16.86. Found: C, 50.34; H, 3.67; N, 16.58.

*4.4.8. 5-(4-Nitrophenyl)-1,2-dihydro-3H-pyrazol-3-one (**11h**).* Reaction time: 2 h 30 min. Yellow amorphous powder; mp 240–243 °C (EtOAc). Lit. mp 248–249 °C.[17] IR (KBr): 3369, 1604, 1575, 1541, 1511, 1349, 1331, 855. ^{1}H NMR (DMSO-d_6): δ 6.07 (s, 1H), 7.95 and 8.25 (AA′XX′, J=8.7 Hz, 4H), 10.30 (br s, 1H), 12.47 (br s, 1H).

*4.4.9. 5-(4-Chlorophenyl)-1,2-dihydro-3H-pyrazol-3-one (**11i**).* Reaction time: 2 h. White needles; mp 243–245 °C (EtOAc/MeOH). Lit. mp 242 °C.[18] IR (KBr): 2810, 1626, 1555, 1519, 1493, 1467, 1092, 797. ^{1}H NMR (DMSO-d_6): δ 6.40 (s, 1H), 7.60 and 8.00 (AA′XX′, J=8.6 Hz, 4H), 13.76 (br s, 2H). ^{13}C NMR (DMSO-d_6): δ 88.2, 126.2, 128.3, 129.2, 135.0, 145.4, 158.1.

*4.4.10. 5-(4-Fluorophenyl)-1,2-dihydro-3H-pyrazol-3-one (**11j**).* Reaction time: 2 h 30 min. White amorphous powder; mp 230–235 °C. Lit. mp 168–170 °C.[19] IR (KBr): 1621, 1601, 1553, 1514, 1493, 1451, 1224, 844. ^{1}H NMR (DMSO-d_6): δ 5.93 (s, 1H), 7.26 (m, 2H), 7.75 (m, 2H), 10.18 (br s, 2H). ^{13}C NMR (DMSO-d_6): δ 86.8, 115.7 (d, J=21.6 Hz), 126.9 (d, J=8.2 Hz), 127.3 (d, J=2.7 Hz), 143.1, 160.6, 161.7 (d, J=244.8 Hz). MS (ES^+) *m*/*z* (%) 179 (MH^+). HRMS calcd for $C_9H_8FN_2O$ (MH^+): 179.0621. Found: 179.0626.

*4.4.11. 5-Phenyl-1,2-dihydro-3H-pyrazol-3-one (**11k**).* Reaction time: 2 h 30 min. White amorphous powder; mp 237–240 °C (EtOAc). Lit. mp 236–238 °C.[20] IR (KBr): 3061, 1624, 1600, 1541, 1510, 1490, 1465, 758. ^{1}H NMR (DMSO-d_6): δ 5.80 (br s, 2H), 6.02 (s, 1H), 7.43 (m, 3H), 7.73 (m, 2H).

*4.4.12. 4-Methyl-5-phenyl-1,2-dihydro-3H-pyrazol-3-one (**11l**).* Reaction time: 1 h 20 min. White cubes; mp 206–212 °C (EtOAc). Lit. mp 201–205 °C.[21] IR (KBr): 3272, 1619, 1599, 1535, 1509, 1478, 767, 694. ^{1}H NMR (DMSO-d_6): δ 1.99 (s, 3H), 7.43 (m, 5H), 9.52 (br s, 1H), 11.67 (br s, 1H). Anal. Calcd for $C_{10}H_{10}N_2O$ (174.20): C, 68.95; H, 5.79; N, 16.08. Found: C, 68.96; H, 5.91; N, 16.18.

*4.4.13. 4,5-Diphenyl-1,2-dihydro-3H-pyrazol-3-one (**11m**).* Reaction time: 3 h. White platelets; mp 235–236 °C (EtOAc/heptane). Lit. mp 236–238 °C.[22] IR (KBr): 3470, 3406, 3314, 3250, 1616, 1513, 758, 695. ^{1}H NMR (DMSO-d_6): δ 7.25 (m, 10H), 11.08 (br s, 2H). ^{13}C NMR

(DMSO-d_6): δ 102.8, 125.6, 127.5, 128.1, 128.6, 128.9, 130.7, 132.8, 139.8, 159.1.

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