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A Diastereoselective Synthesis of Functionalized 3-Pyrazolidinones from Hydrazines, Aromatic Aldehydes, and Acylketene

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Abstract: A practical microwave-assisted, one-pot method for the construction of 4-acetyl-2-phenyl-5-aryl-3-pyrazolidinones via a tandem reaction between phenylhydrazine, aromatic aldehydes, and but-1-ene-1,3-dione (acylketene), in moderate to good yields, is reported. When methylhydrazine and 4-methylphenylhydrazine hydrochloride were used instead of phenylhydrazine, the reaction led to the formation of 3-oxobutanohydrazide derivatives.

Key words: hydrazines, aromatic aldehydes, 1,3-dioxinone, microwave irradiation, acylketene

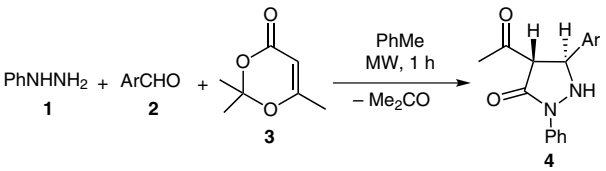
3-Pyrazolidinones are an interesting class of heterocyclic compounds which exhibit distinct bioactivity, and some of them have attracted much attention in drug development.[1–4] They belong to the family of pyrazoles that serve as products and intermediates in analytical, agricultural, and biological chemistry.[5–7] Hence, the development of efficient synthetic methods for this class of heterocycles is an important target in current organic synthesis. In recent years, several methods have been developed for the synthesis of 3-pyrazolidinones.[8–11]

As part of our current studies on the development of new routes to heterocyclic synthesis,[12–14] we describe a microwave-assisted, three-component reaction for the diastereoselective synthesis 3-pyrazolidinones using acylketene. Acylketene, which is significantly more reactive than ketenes, has found widespread interest in organic chemistry over years.[15–21] Acylketenes are highly reactive molecules which often cannot be isolated under ordinary reaction conditions and in the absence of trapping reagents rapidly undergo dimerization reaction. Synthetically useful procedures for the generation of acylketenes include solution thermolysis or photolysis of 1,3-dioxinone β-keto esters, acid chloride, and α-diazocarbonyl compounds.[8,22–27]

Initially, phenylhydrazine (**1**), 4-nitrobenzaldehyde (**2g**), and 1,3-dioxinone (**3**) were selected as prototypical reactants. Compound **3** is stable at room temperature but when heated above 100 °C in the absence of catalyst,[28,29] it extrudes acetone to generate acylketene which undergoes a smooth reaction with the hydrazone, generated in situ from **1** and **2g** to afford the pyrazolidinone **4g** in 90% yield. In order to optimize the reaction conditions, a variety of different conditions were employed. First the reaction was tested in the presence of Lewis acids as catalyst at 70 °C. Simple heating of a mixture of components **1**, **2g**, and **3** with 10 mol% of CuBr in toluene led to the desired product **4g** in 55% yield. Other catalysts such as CuI, CuCl, and $AgNO_3$ showed similar results under identical conditions. Also increasing the amount of catalyst to 30 mol% did not improve the yield. The reaction did not proceed at room temperature even in the presence of Lewis acids. Interestingly, when the reaction was carried out under microwave irradiation, the target compound **4g** was obtained in 93% yield. The use of microwave radiation reduces the time of reaction and provides higher yields.

Finally, the generality of this transformation was examined by using various aldehydes under optimized conditions, and the results are summarized in Table 1.[30]

Table 1 Synthesis of Compounds **4a**–**h** under the Optimized Conditions[a]



Entry	Aldehyde **2**, Ar	Product **4**	Yield (%)[b]
1	**2a** Ph	**4a**	83
2	**2b** *p*-Tol	**4b**	82
3	**2c** 2-ClC_6H_4	**4c**	85
4	**2d** 3-ClC_6H_4	**4d**	81
5	**2e** 4-ClC_6H_4	**4e**	84
6	**2f** 3-$O_2NC_6H_4$	**4f**	94
7	**2g** 4-$O_2NC_6H_4$	**4g**	93
8	**2h** 1-naphthyl	**4h**	80

[a] Reaction conditions: phenylhydrazine (1 mmol), aldehyde **2** (1.2 mmol), **3** (1.3 mmol), toluene (5 mL).
[b] Yield of the isolated product.

The structures of pyrazolidinones **4a**–**h** were verified by ^{1}H NMR, ^{13}C NMR, and IR spectroscopy and mass spectrometry. Unambiguous evidence for the structure and stereochemistry of **4c** was obtained from a single-crystal X-

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ray analysis (Figure 1). The structure deduced from the crystallographic experiment by analogy can be applied to the other products on account of their NMR-spectroscopic similarities. For details of the structure determination and refinement, see the experimental section.[30]

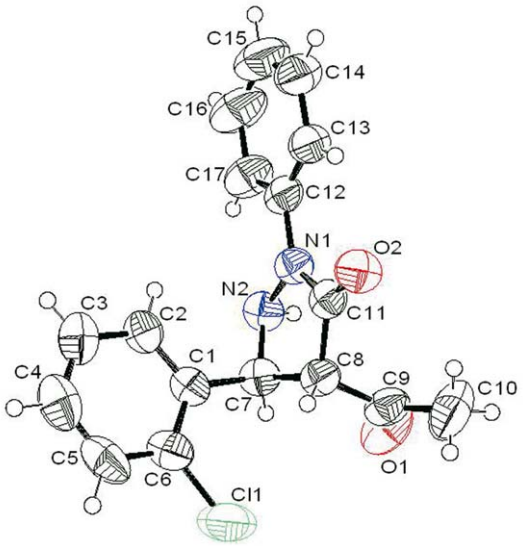


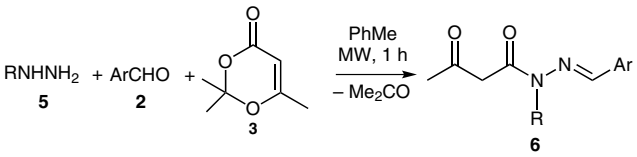
Figure 1 X-ray crystal structure of **4c**, ORTEP-III plot;[31] crystallographic numbering shown

Products **4** possess two stereogenic centers and can exist as two diastereoisomers, namely *trans* and *cis*. In this work, only the *trans* isomer is isolated from the reaction mixtures. The results of density functional theory (DFT) calculations[32] at B3LYP/6-31++G level for the two diastereoisomers of product **4a** show that the *trans* isomer is 5.97 kcal/mol more stable than the *cis* isomer. Thus, the observed *trans* isomer of **4a** is thermodynamically more stable.

To extend our knowledge of this transformation, we performed the same reaction with methylhydrazine (**5a**) and 4-methylphenylhydrazine hydrochloride (**5b**) instead of **1** but cyclization did not occur and the reaction afforded **6a–d** in good yields (Table 2). The products were again fully characterized with their IR, ^{1}H NMR, and ^{13}C NMR spectra. Moreover, phenylhydrazines with electron-withdrawing groups, such as 2-nitrophenylhydrazine and 2,4-dinitrophenylhydrazine, were unsuccessful.

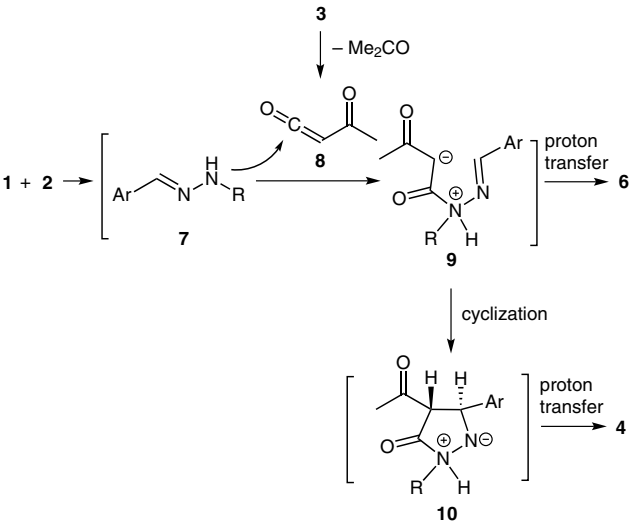
A plausible mechanism of this transformation is proposed in Scheme 1. Presumably, hydrazone **7**, formed from **1** and **2**, reacts with acylketene **8**, generated in situ from **3**, to produce intermediate **9**. This intermediate can undergo cyclization and proton-transfer reaction to afford pyrazolidinone **4**. Alternatively, intermediate **9** is converted into product **6** by proton-transfer reaction.

Table 2 Synthesis of Compounds **6a–d** under the Optimized Conditions[a]



Entry	Hydrazine **5**, R	Aldehyde **2**, Ar	Product **6**	Yield (%)[b]
1	**2a** Me	**2a** *p*-Tol	**6a**	81
2	**2b** Me	**2b** 4-$O_2NC_6H_4$	**6b**	95
3	**2c** *p*-Tol	**2c** 4-ClC_6H_4	**6c**	67[c]
4	**2d** *p*-Tol	**2d** 3-$O_2NC_6H_4$	**6d**	71[c]

[a] Reaction conditions: hydrazine **5** (1 mmol), aldehyde **2** (1.2 mmol), **3** (1.3 mmol), toluene (5 mL).
[b] Yield of the isolated product.
[c] Et_3N (1 mmol) added.



Scheme 1 A plausible mechanism for the formation of compounds **4** and **6**

In summary, utilizing arylhydrazines, aromatic aldehydes, and acylketene we have demonstrated a practical microwave-assisted reaction for the synthesis of functionalized 3-pyrazolidinones in moderate to good yields. When methylhydrazine and 4-methylphenylhydrazine hydrochloride was used instead of phenylhydrazine, the reaction led to the formation of 3-oxobutanohydrazide derivatives in good yields.

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(30) **General Procedure for the Synthesis of Compounds 4 and 6**
A solution of aryl(alkyl)hydrazine (1 mmol) and aldehydes **2** (1.2 mmol) was stirred in toluene (5 mL) for 10 min. Then, **3** (0.19 g, 1.3 mmol) was added, irradiated under microwave at 900 W. After completion of the reaction [about 1 h; TLC monitoring (EtOAc–hexane, 1: 5)], the solvent was evaporated, and the residue was purified by column chromatography [silica gel (230–400 mesh; Merck), EtOAc–hexane, 1:5] to give pure product.
4-Acetyl-2,5-diphenylpyrazolidin-3-one (4a)
Yellow powder; mp 124–126 °C; yield: 0.23 g (83%). IR (KBr): 3384, 3051, 2923, 1691, 1618, 1500, 1457 cm^{-1}. ^1H NMR (500.1 MHz, $CDCl_3$): δ = 2.51 (3 H, s, Me), 3.96 (1 H, d, ^3J = 4.4 Hz, CH), 5.17 (1 H, d, ^3J = 4.4 Hz, CH), 5.35 (1 H, br s, NH), 7.18 (1 H, d, ^3J = 7.4 Hz, CH), 7.33–7.37 (2 H, m, CH), 7.39 (2 H, t, ^3J = 8.0 Hz, CH), 7.48 (2 H, d, ^3J = 7.9 Hz, CH), 7.58 (1 H, m, CH),7.92 (2 H, d, ^3J = 7.8 Hz, CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 29.7 (Me), 58.2 (CH), 66.2 (CH), 124.9 (2 CH), 125.9 (2 CH), 126.8 (C), 128.1 (CH), 128.5 (CH), 128.9 (2 CH), 129.0 (2 CH), 132.9 (C), 138.9 (C), 165.5 (C), 201.7 (C) ppm. MS (EI): *m*/*z* (%) = 280 (24) [M^+], 278 (80), 263 (59), 91 (25), 77 (52). Anal. Calcd for $C_{17}H_{16}N_2O_2$ (280.32): C, 72.84; H, 5.75; N, 9.99. Found: C, 72.39; H, 5.84; N, 10.08.
4-Acetyl-2-phenyl-5-*p*-tolylpyrazolidin-3-one (4b)
Yellow powder; mp 123–125 °C; yield: 0.24 g (82%). IR (KBr): 3395, 3032, 2919, 1685, 1619, 1505 cm^{-1}. ^1H NMR (500.1 MHz, $CDCl_3$): δ = 2.34 (3 H, s, Me), 2.50 (3 H, s, Me), 3.96 (1 H, d, ^3J = 4.6 Hz, CH), 5.12 (1 H, d, ^3J = 4.6 Hz, CH), 5.23 (1 H, br s, NH), 7.16–7.19 (3 H, m, CH), 7.24 (2 H, d, ^3J = 8.0 Hz, CH), 7.38 (2 H, d, ^3J = 7.7 Hz, CH), 7.91 (2 H, d, ^3J = 8.0 Hz, CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 21.1 (Me), 29.7 (Me), 58.2 (CH), 66.0 (CH), 118.8 (2 CH), 120.9 (C), 124.6 (CH), 126.1 (2 CH), 128.9 (2 CH), 129.8 (2 CH), 138.0 (C), 138.4 (C), 165.7 (C), 201.8 (C) ppm. MS (EI): *m*/*z* (%) = 294 (14) [M^+], 292 (80), 277 (58), 91 (43), 77 (24). Anal. Calcd for $C_{18}H_{18}N_2O_2$ (294.35): C, 73.45; H, 6.16; N, 9.52. Found: C, 73.78; H, 6.07; N, 9.57.
4-Acetyl-5-(2-chlorophenyl)-2-phenylpyrazolidin-3-one (4c)
Yellow powder; mp 113–115 °C; yield: 0.27 g (85%). IR (KBr): 3424, 3059, 2924, 1698, 1625, 1554, 1497 cm^{-1}. ^1H NMR (500.1 MHz, $CDCl_3$): δ = 2.53 (3 H, s, Me), 3.85 (1 H, d, ^3J = 3.2 Hz, CH), 5.30 (1 H, d, ^3J = 3.2 Hz, CH), 5.38 (1 H, br s, NH), 7.19–7.25 (3 H, m, CH), 7.38 (2 H, d, ^3J = 6.5 Hz, CH), 7.42–7.47 (2 H, m, CH), 8.01 (2 H, d, ^3J = 7.9 Hz, CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 31.9 (Me), 56.0 (CH), 66.3 (CH), 118.1 (2 CH), 124.9 (CH), 127.0 (CH), 127.4 (CH), 129.0 (2 CH), 129.1 (CH), 129.8 (CH), 131.8 (C), 137.3 (C), 138.2 (C), 165.0 (C), 201.8 (C) ppm. MS (EI): *m*/*z* (%) = 314 (15) [M^+], 312 (55), 297 (35), 91 (15), 77 (63). Anal. Calcd for $C_{17}H_{15}ClN_2O_2$ (314.77): C, 64.87; H, 4.80; N, 8.90. Found: C, 65.15; H, 4.74; N, 9.01.
X-ray Crystal-Structure Determination of 4c – Structure-Determination and Refinement Data
Formula: $C_{17}H_{15}ClN_2O_2$; M_r 314.76; triclinic, space group: $P\overline{1}$, a = 9.863(1), b = 10.850(1), c = 15.029(2) Å, α = 94.69(1)°, δ = 90.35(1)°, γ = 96.32(1)°; Z = 2, V = 1593.0(3) Å^3, D_{calcd} = 1.312 mg/m^3; Mo-Kα radiation (0.71073 Å); T = 293(2) K. 6580 reflections collected on a Bruker P4 diffractometer, 5545 unique (R_{int} = 0.0284). All heavy atoms have been located by difference Fourier maps and refined anisotropically. All hydrogen atoms except that of the NH group have been placed on calculated positions and refined isotropically by using the riding model. The NH proton has been located by difference Fourier maps and refined isotropically. Final indices for 2287 reflections with $I > 2\sigma(I)$: $R1$ = 0.0588, $wR2$ = 0.1142, GOF = 1.008. The crystallographic data of **4c** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 912090. Copies of the data can be obtained, free of charge, via the internet (http://www.ccdc.cam.ac.uk/data_request/cif), e-mail (data_request@ccdc.cam.ac.uk), or fax [+44(1223)336033].
4-Acetyl-5-(3-chlorophenyl)-2-phenylpyrazolidin-3-one (4d)
Yellow powder; mp 118–120 °C; yield: 0.25 g (81%). IR (KBr): 3421, 3063, 2922, 1695, 1593, 1497 cm^{-1}. ^1H NMR

(500.1 MHz, $CDCl_3$): δ = 2.53 (3 H, s, Me), 3.92 (1 H, d, ^3J = 3.7 Hz, CH), 5.14 (1 H, d, ^3J = 3.7 Hz, CH), 5.27 (1 H, br s, NH), 7.19 (1 H, d, ^3J = 7.5 Hz, CH), 7.23–7.26 (2 H, m, CH), 7.28 (2 H, d, ^3J = 7.3 Hz, CH), 7.40 (2 H, t, ^3J = 7.7 Hz, CH), 7.94 (2 H, t, ^3J = 8.7 Hz, CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 30.4 (Me), 57.8 (CH), 66.7 (CH), 119.0 (2 CH), 124.3 (CH), 125.6 (CH), 126.8 (CH), 128.8 (CH), 129.5 (2 CH), 130.9 (CH), 135.3 (C), 138.6 (C), 141.7 (C), 165.3 (C), 201.9 (C) ppm. MS (EI): *m/z* (%) = 314 (27) [M^+], 312 (80), 297 (57), 91 (23), 77 (48). Anal. Calcd for $C_{17}H_{15}ClN_2O_2$ (314.77): C, 64.87; H, 4.80; N, 8.90. Found: C, 64.63; H, 4.86; N, 9.00.

4-Acetyl-5-(4-chlorophenyl)-2-phenylpyrazolidin-3-one (4e)

Yellow powder; mp 105–107 °C; yield: 0.26 g (84%). IR (KBr): 3415, 3051, 2930, 1701, 1580 cm^{-1}. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.53 (3 H, s, Me), 3.88 (1 H, d, ^3J = 3.4 Hz, CH), 5.13 (1 H, d, ^3J = 3.4 Hz, CH), 5.21 (1 H, br s, NH), 7.18 (1 H, d, ^3J = 7.3 Hz, CH), 7.28 (2 H, d, ^3J = 8.5 Hz, CH), 7.32 (2 H, d, ^3J = 8.5 Hz, CH), 7.39 (2 H, d, ^3J = 8.0 Hz, CH), 7.90 (2 H, d, ^3J = 8.0 Hz, CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 29.6 (Me), 57.4 (CH), 66.3 (CH), 118.5 (2 CH), 125.1 (CH), 127.2 (2 CH), 128.8 (2 CH), 129.1 (2 CH), 130.7 (C), 138.2 (C), 138.2 (C), 165.7 (C=O), 201.4 (C=O) ppm. MS (EI): *m/z* (%) = 314 (27) [M^+], 312 (78), 297 (61), 91 (27), 77 (53). Anal. Calcd for $C_{17}H_{15}ClN_2O_2$ (314.77): C, 64.87; H, 4.80; N, 8.90. Found: C, 64.57; H, 4.89; N, 9.02.

4-Acetyl-5-(3-nitrophenyl)-2-phenylpyrazolidin-3-one (4f)

Yellow powder; mp 137–139 °C; yield: 0.31 g (94%). IR (KBr): 3415, 3080, 1704, 1619, 1532 cm^{-1}. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.55 (3 H, s, Me), 3.92 (1 H, d, ^3J = 3.5 Hz, CH), 5.26 (1 H, br s, NH), 5.30 (1 H, d, ^3J = 3.5 Hz, CH), 7.19 (1 H, t, ^3J = 7.4 Hz, CH), 7.42 (2 H, t, ^3J = 7.3 Hz, CH), 7.53 (1 H, t, ^3J = 7.9 Hz, CH), 7.72 (1 H, d, ^3J = 7.7 Hz, CH), 7.91 (2 H, d, ^3J = 7.6 Hz, CH), 8.15 (1 H, d, ^3J = 8.0 Hz, CH), ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 29.7 (Me), 57.0 (CH), 66.4 (CH), 118.4 (2 CH), 121.3 (CH), 123.0 (CH), 125.3 (CH), 129.3 (2 CH), 130.0 (CH), 132.1 (CH), 137.9 (C), 141.6 (C), 148.6 (C), 164.4 (C), 201.0 (C) ppm. MS (EI): *m/z* (%) = 325 (5) [M^+], 323 (75), 308 (55), 308 (61), 91 (51), 77 (55). Anal. Calcd for $C_{17}H_{15}N_3O_4$ (325.32): C, 62.76; H, 4.65; N, 12.92. Found: C, 63.07; H, 4.71; N, 13.04.

4-Acetyl-5-(4-nitrophenyl)-2-phenylpyrazolidin-3-one (4g)

Yellow powder; mp 156–158 °C; yield: 0.30 g (93%). IR (KBr): 3418, 3067, 2923, 1702, 1602, 1520 cm^{-1}. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.53 (3 H, s, Me), 3.86 (1 H, d, ^3J = 2.8 Hz, CH), 5.14 (1 H, t, ^3J = 2.8 Hz, CH), 5.42 (1 H, br s, NH), 7.19 (1 H, t, ^3J = 7.4 Hz, CH), 7.40 (2 H, t, ^3J = 7.7 Hz, CH), 7.54 (2 H, d, ^3J = 8.5 Hz, CH), 7.90 (2 H, d, ^3J = 8.0 Hz, CH), 8.18 (2 H, d, ^3J = 8.7 Hz, CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 29.6 (Me), 57.1 (CH), 66.5 (CH), 118.4 (2 CH), 124.0 (2 CH), 125.3 (CH), 127.0 (2 CH), 129.0 (2 CH), 130.4 (C), 138.0 (C),146.7 (C), 164.4 (C), 200.9 (C) ppm. MS (EI): *m/z* (%) = 325 (14) [M^+], 323 (80), 308 (55), 91 (22), 77 (57). Anal. Calcd for $C_{17}H_{15}N_3O_4$ (325.32): C, 62.76; H, 4.65; N, 12.92. Found: C, 62.58; H, 4.72; N, 12.98.

4-Acetyl-5-(naphthalen-1-yl)-2-phenylpyrazolidin-3-one (4h)

Pale yellow powder; mp 115–117 °C; yield: 0.26 g (80%). IR (KBr): 3424, 3230, 2923, 1668, 1606, 1549, 1497 cm^{-1}. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.55 (3 H, s, Me), 3.93 (1 H, d, ^3J = 2.9 Hz, CH), 5.43 (1 H, br s, NH), 5.87 (1 H, d, ^3J = 2.9 Hz, CH), 7.20 (1 H, t, ^3J = 7.5 Hz, CH), 7.40–7.45 (3 H, m, CH), 7.52 (2 H, t, ^3J = 7.6 Hz, CH), 7.59 (1 H, d, ^3J = 7.2 Hz, CH), 7.70 (1 H, d, ^3J = 7.3 Hz, CH), 7.80 (1 H, d, ^3J = 7.5 Hz, CH), 7.90 (1 H, d, ^3J = 7.6 Hz, CH), 8.03 (2 H, d, ^3J = 7.2 Hz, CH) ppm. MS (EI): *m/z* (%) = 330 (6) [M^+], 328 (77), 313 (62), 91 (14), 77 (33). Anal. Calcd for $C_{21}H_{18}N_2O_2$ (330.38): C, 76.34; H, 5.49; N, 8.48. Found: C, 76.69; H, 5.55; N, 8.57.

***N*-Methyl-*N*′-[1-(4-methylphenyl)methylidene]-3-oxobutanohydrazide (6a)**

Pale yellow powder; mp 82–84 °C; yield: 0.18 g (77%). IR (KBr): 3430, 2924, 2857, 1687, 1607 cm^{-1}. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.26 (3 H, s, Me), 2.37 (3 H, s, Me), 3.39 (3 H, s, CH_3N), 3.93 (2 H, s, CH_2), 7.19 (2 H, d, ^3J = 8.0 Hz, CH), 7.50 (2 H, d, ^3J = 8.0 Hz, CH), 7.66 (1 H, s, CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 21.4 (Me), 27.7 (Me), 29.9 (CH_3N), 50.4 (CH_2), 125.6 (C), 127.0 (2 CH), 128.5 (2 CH), 131.5 (C), 140.3 (CH), 168.9 (C), 202.0 (C) ppm. MS (EI): *m/z* (%) = 232 (18) [M^+], 148 (55), 91 (28), 84 (80), 77 (10), 51 (55). Anal. Calcd for $C_{13}H_{16}N_2O_2$ (232.28): C, 67.22; H, 6.94; N, 12.06. Found: C, 66.89; H, 6.97; N, 12.15.

***N*-Methyl-*N*′-[1-(4-nitrophenyl)methylidene]-3-oxobutanohydrazide (6b)**

Pale yellow powder; mp 156–158 °C; yield: 0.25 g (95%). IR (KBr): 3425, 2930, 1687, 1607 cm^{-1}. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.27 (3 H, s, Me), 3.43 (3 H, s, CH_3N), 3.97 (2 H, s, CH_2), 7.66 (2 H, d, ^3J = 7.1 Hz, CH), 8.27 (2 H, d, ^3J = 7.1 Hz, CH) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 28.1 (Me), 29.9 (CH_3N), 50.4 (CH_2), 124.2 (2 CH), 127.6 (2 CH), 140.2 (C), 148.2 (C), 169.0 (C), 201.4 (C) ppm. MS (EI): *m/z* (%) = 263 (13) [M^+], 136 (25), 91 (21), 77 (11). Anal. Calcd for $C_{12}H_{13}N_3O_4$ (263.2): C, 54.75; H, 4.98; N, 15.96. Found: C, 55.03; H, 5.06; N, 16.08.

***N*′-[1-(4-Chlorophenyl)methylidene)]-*N*-(4-methylphenyl)-3-oxobutanohydrazide (6c)**

Yellow solid; mp 94–96 °C; yield: 0.21 g (67%). IR (KBr): 3435, 2920, 2861, 1701, 1607 cm^{-1}. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.33 (3 H, s, Me), 2.43 (3 H, s, Me), 4.06 (2 H, s, CH_2), 7.08 (2 H, d, ^3J = 7.9 Hz, CH), 7.21 (1 H, s, CH), 7.33 (2 H, d, ^3J = 8.1 Hz, CH), 7.36 (2 H, d, ^3J = 7.9 Hz, CH), 7.43 (2 H, d, ^3J = 8.1 Hz, CH) ppm. MS (EI): *m/z* (%) = 328 (3) [M^+], 271 (21), 77 (13). Anal. Calcd for $C_{18}H_{17}ClN_2O_2$ (328.80): C, 65.75; H, 5.21; N, 8.52. Found: C, 65.38; H, 5.28; N, 8.61.

***N*′-[1-(3-Nitrophenyl)methylidene)]-*N*-(4-methylphenyl)-3-oxobutanohydrazide (6d)**

Yellow solid; mp 105–107 °C; yield 0.24 g (71%). IR (KBr): 3425, 2930, 1687, 1607 cm^{-1}. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.40 (3 H, s, Me), 2.54 (1 H, d, ^3J = 3.5 Hz, CH), 2.95 (2 H, s, CH_2), 7.41–45 (2 H, m, CH), 7.16 (1 H, s, CH), 7.65 (1 H, d, ^3J = 7.6 Hz, CH), 7.83 (2 H, d, ^3J = 7.6 Hz, CH), 8.30 (1 H, d, ^3J = 7.6 Hz, CH) ppm. MS (EI): *m/z* (%) = 339 (4) [M^+], 282 (14), 77 (11). Anal. Calcd for $C_{18}H_{17}N_3O_4$ (339.35): C, 63.71; H, 5.05; N, 12.38. Found: C, 63.96; H, 5.08; N, 12.46.

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