Expeditious synthesis of 1,3,4-oxadiazole derivatives via sydnones

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Abstract: The clean cyclization of chalcones (1a–c/2a–c) with hydrazine hydrate under microwave irradiation afforded pyrazolines derivatised with sydnone (3d–i/4d–i), which underwent 1,3-dipolar cyclo-addition with acetic anhydride to form pyrazolines appended with 1,3,4-oxadiazoles (5g–l/6g–l). The newly synthesized compounds were confirmed by spectral and elemental analyses. In comparison to classical heating, the results indicate that microwave irradiation affords higher yields, shorter reaction times (4–12 min) and cleaner reactions.

Keywords: microwave irradiation; sydnones; chalcones; pyrazolines; 1,3,4-oxadiazoles.

INTRODUCTION

In recent years, a significant portion of the research in heterocyclic chemistry has been devoted to sydnones containing different moieties, as evident from the literature.1–4 Sydnones have played a crucial role in the development of theory in heterocyclic chemistry and have been used extensively as synthons in organic synthesis. It was reported that 1,3,4-oxadiazole derivatives, suitably substituted at the 2 and 5 positions, exhibited considerable antibacterial and antifungal activity.5–8 These heterocycles are of great interest to medicinal chemists for molecular manipulation and to biologists for further pharmacological evaluation. Pyrazolines and their derivatives are important biological agents and a significant amount of research activity has been directed towards this class of compounds. In particular, they are used as antitumor, antibacterial, antifungal, antiviral, antiparasitic, antitubercular and insecticidal agents.9–18 Some of these compounds also have anti-inflammatory, antidiabetic, anaesthetic and analgesic properties.19–22 As a result of studies related to the development of synthetic protocols using microwave irradiation, a novel and easy access to pyrazolines appended to 1,3,4-oxadiazoles is reported herein.

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RESULTS AND DISCUSSION

Chalcones (meta and para isomers), which were prepared according to a previously reported method, undergo a rapid cyclization with hydrazine hydrate under microwave irradiations at 80±5 °C (240 W) to give pyrazolines quantitatively in 4–12 min (Scheme 1). Poly(ethylene glycol) (PEG 200) and formic acid were used as the solvent for the preparation of and , respectively. Compounds on bromination at 0–5 °C and heating under microwave at 60±5 °C (210 W) in acetic anhydride afforded . The sydnone ring which is mesoionic undergoes 1,3-dipolar cyclo-addition reaction with acetic anhydride to 1,3,4-oxadiazole. In addition, compounds under N-acetylation of the pyrazoline ring to form . These heterocyclic products were characterized based on their IR, 1H-NMR, mass spectral and elemental analyses.

![Scheme 1. The starting chalcones and the intermediates and the final products after 1,3-dipolar cycloaddition, 5-methyl-3-[3/4-(1-substituted-5-aryl-4,5-dihydro-1H-pyrazol-3-yl)phenyl]sydnone (i) and the final products after 1,3-dipolar cycloaddition, 5-methyl-3-[3/4-(1-substituted-5-aryl-4,5-dihydro-1H-pyrazol-3-yl)phenyl]1,3,4-oxadiazol-2(3H)-ones (j).](image)

On comparison of the synthesis by the microwave assisted method with that by the conventional method (randomly selected compounds), it was observed that the reaction progressed very fast with excellent yields using the former method (Table I). Microwave irradiation facilitates polarisation of the molecule under irradiation, causing rapid reaction to occur.

EXPERIMENTAL

Materials

The microwave irradiations were performed using a commercial microwave oven M-2735A. The temperature approximation was realised using sealed capillaries containing compounds of
known melting points according to a reported method. The approximate temperature along with the power in watts is given in the experimental procedures. TLC was run on silica gel G plates using acetone–benzene (1:3) as the irrigant. The melting points were determined in open capillaries and are uncorrected. The IR (KBr) spectra were recorded on a Nicolet Impact-410 FT-IR spectrometer and the NMR spectra in CDCl$_3$ ($\delta,$ ppm downfield from TMS) were recorded on a Bruker Varian-300 MHz FT-NMR spectrometer. $J$ values are given in Hz. Elemental analyses were performed on a CEST 1106 elemental analyser. The mass spectra were recorded on EI-70 eV and FR ver. 1 on UIC 002002 spectrometers.

TABLE I. Comparison of the reaction time required and yield

<table>
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<th>Microwave</th>
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</tr>
<tr>
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<td>52</td>
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<tr>
<td>6l</td>
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</table>

Methods

General procedure for 3d–i/4d–i: The hydrazine hydrate (0.012 mol) was added to a stirred solution of chalcone 1a–c/2a–c (0.010 mol) in 5 ml of poly(ethylene glycol) (PEG 200) or formic acid (5 ml). The mixture was subjected to microwave heating at 80$^\circ$C (240 W) for several minutes, which after workup afforded the pyrazoline derivatives 3d–i/4d–i. The crude products after crystallization using absolute ethanol gave the pure compounds in 80–95% yield.

3-[3-(4,5-Dihydro-5-phenyl-1H-pyrazol-3-yl)phenyl]sydnone (3d): pale yellow crystals, m.p. 170–171$^\circ$C. Anal. Calcd. for C$_{17}$H$_{14}$N$_4$O$_2$: C, 66.66; H, 4.58; N, 18.30. Found: C, 66.60 H, 4.52, N, 18.28. IR (KBr, cm$^{-1}$): 3400, 3103, 1715, 1599. $^1$H-NMR (300 MHz, CDCl$_3$, $\delta$, ppm): 3.40 (1H, $\text{dd}$, C$_4'/g_237H_b$), 3.75 (1H, $\text{dd}$, C$_4'/g_237H_a$), 4.85 (1H, $\text{dd}$, C$_5'/g_237H_x$), 5.20 (1H, s, NH), 6.75 (1H, s, C$_4$/g_237H), 6.9–7.8 (8H, $\text{bm}$, Ar/$g_237H$), 7.98 (1H, s, C$_2'/g_237Ar/g_237H$). MS ($m$/z (relative abundance, %)): 306 (M+, 55), 276 (32), 248 (45), 221 (100), 144 (90), 77 (55).

3-[3-(4,5-Dihydro-5-4-p-tolyl-1H-pyrazol-3-yl)phenyl]sydnone (3e): pale yellow crystals, m.p. 154–155$^\circ$C. Anal. Calcd. for C$_{18}$H$_{16}$N$_4$O$_2$: C, 67.50; H, 5.00; N, 17.50. Found: C, 67.45 H, 4.96, N, 17.46. IR (KBr, cm$^{-1}$): 3410, 3100, 1724, 1595. $^1$H-NMR (300 MHz, CDCl$_3$, $\delta$, ppm): 2.10 (3H, s, CH$_3$), 3.15 (1H, $\text{dd}$, C$_4'/g_237H_b$), 3.60 (1H, $\text{dd}$, C$_4'/g_237H_a$), 4.90 (1H, $\text{dd}$, C$_5'/g_237H_x$), 5.05 (1H, s, NH), 6.60 (1H, s, C$_4$/g_237H), 7.0–7.75 (7H, $\text{bm}$, Ar/$g_237H$), 8.05 (1H, s, C$_2'/g_237Ar/g_237H$). MS ($m$/z (relative abundance, %)): 320 (M+, 64), 290 (40), 262 (50), 235 (100), 144 (82), 91 (50).

3-[3-(5-p-Anisyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl]sydnone (3f): yellow crystals, m.p. 184–190$^\circ$C. Anal. Calcd. for C$_{18}$H$_{16}$N$_4$O$_3$: C, 64.29; H, 4.71, N, 16.62. IR (KBr, cm$^{-1}$): 3400, 3110, 1730, 1600. $^1$H-NMR (300 MHz, CDCl$_3$, $\delta$, ppm): 3.05 (1H, $\text{dd}$, C$_4'/g_237H_b$), 3.30 (1H, $\text{dd}$, C$_4'/g_237H_a$), 3.75 (3H, s, −OCH$_3$), 4.74 (1H, $\text{dd}$, C$_5'/g_237H_x$), 5.50 (1H, s, NH), 6.85 (1H, s, C$_4$/g_237H), 7.15–7.90 (7H, $\text{bm}$, Ar/$g_237H$), 7.95 (1H, s, C$_2'/g_237Ar/g_237H$). MS ($m$/z (relative abundance, %)): 336 (M$^+$, 70), 309 (45), 281 (49), 254 (100), 144 (85), 107 (47).

3-[3-(1-Formyl-4,5-dihydro-5-phenyl-1H-pyrazol-3-yl)phenyl]sydnone (3g): yellow crystals, m.p. 108–109$^\circ$C. Anal. Calcd. for C$_{18}$H$_{14}$N$_4$O$_3$: C, 64.67; H, 4.19; N, 16.72. IR (KBr, cm$^{-1}$): 3138, 1745, 1600, 1580. $^1$H-NMR (300 MHz, CDCl$_3$, $\delta$, ppm):
δ, ppm): 3.18 (1H, dd, C4-H), 3.39 (1H, dd, C5-H), 4.45 (1H, dd, C6-H), 6.70 (1H, s, C7-H), 6.78–7.40 (8H, bm, Ar-H), 7.75 (1H, s, C2- Ar-H), 8.9 (1H, s, −CHO); MS (m/z (relative abundance, %)): 334 (M+ , 75), 306 (64), 276 (49), 248 (100), 221 (14), 144 (58), 77 (50).

3-[3-Formyl-4,5-dihydro-5-p-tolyl-1H-pyrazol-3-ylphenyl]sydnone (3b): yellow crystals, m.p. 184–185 °C. Anal. Calcd. for C19H16N4O3: C, 65.54; H, 4.61; N, 16.09. Found: C, 65.47; H, 4.54; N, 16.06. IR (KBr, cm−1): 3145, 1737, 1605, 1405. 1H-NMR (300 MHz, CDCl3, δ, ppm): 2.4 (3H, s, CH3), 3.05 (1H, dd, C4-H), 3.45 (1H, dd, C5-H), 4.75 (1H, dd, C6-H), 6.70 (1H, s, C7-H), 6.85–7.35 (7H, bm, Ar-H), 8.0 (1H, s, C2-Ar-H), 9.0 (1H, s, −CHO); MS (m/z (relative abundance, %)): 366 (M+ , 39), 338 (60), 308 (54), 280 (100), 144 (87), 107 (44).

3-[3-(5-P-Anisyl-1-formyl-4,5-dihydro-1H-pyrazol-3-ylphenyl]sydnone (3c): yellow crystals, m.p. 160–161 °C. Anal. Calcd. for C19H16N4O3: C, 63.66; H, 4.48; N, 18.30. Found: C, 63.65 H, 4.48; N, 18.30. IR (KBr, cm−1): 3395, 3114, 1725, 1600. 1H-NMR (300 MHz, CDCl3, δ, ppm): 2.23 (3H, s, CH3), 3.20 (1H, dd, C4-H), 3.39 (1H, dd, C5-H), 4.60 (1H, dd, C6-H), 6.50 (1H, s, C7-H), 6.70–7.25 (8H, bm, Ar-H). MS (m/z (relative abundance, %)): 306 (M+ , 62), 145 (24), 131 (26), 117 (100), 103 (15), 90 (50), 67 (75).

3-[3-(4,5-Dihydro-5-phenyl-1H-pyrazol-3-ylphenyl]sydnone (4d): yellow crystals, m.p. 127–128 °C. Anal. Calcd. for C21H16N4O3: C, 64.29; H, 4.76; N, 16.66. Found: C, 64.30, H, 4.75, N, 16.67. IR (KBr, cm−1): 3100, 1730, 1600. 1H-NMR (300 MHz, CDCl3, δ, ppm): 3.18 (1H, dd, C4-H), 3.25 (1H, dd, C5-H), 3.80 (3H, s, −OCH3), 4.75 (1H, dd, C6-H), 4.95 (1H, s, NH), 6.60 (1H, s, C7-H), 6.65–7.64 (8H, bm, Ar-H). MS (m/z (relative abundance, %)): 336 (M+ , 65), 175 (35), 148 (100), 131 (32), 121 (22), 103 (54).

3-[4-Formyl-4,5-dihydro-5-p-tolyl-1H-pyrazol-3-ylphenyl]sydnone (4a): yellow crystals, m.p. 140–141 °C. Anal. Calcd. for C19H16N4O3: C, 64.67; H, 4.19; N, 16.76. Found: C, 64.60, H, 4.17, N, 16.78. IR (KBr, cm−1): 3100, 1725, 1605, 1595. 1H-NMR (300 MHz, CDCl3, δ, ppm): 3.16 (1H, dd, C4-H), 3.35 (1H, dd, C5-H), 4.57 (1H, dd, C6-H), 6.70 (1H, s, C7-H), 6.9–7.40 (8H, bm, Ar-H), 10.50 (1H, s, −CHO); MS (m/z (relative abundance, %)): 334 (M+ , 21), 306 (47), 145 (25), 131 (30), 117 (100), 103 (46), 95 (15), 90 (43), 67 (14), 29 (4), 40 (5).

3-[4-Formyl-4,5-dihydro-5-p-tolyl-1H-pyrazol-3-ylphenyl]sydnone (4h): yellow crystals, m.p. 161–162 °C. Anal. Calcd. for C21H16N4O3: C, 65.52; H, 4.60; N,16.09. Found: C, 65.54, H, 4.61, N, 16.13. IR (KBr, cm−1): 3110, 1725, 1610, 1625. 1H-NMR (300 MHz, CDCl3, δ, ppm): 2.34 (3H, s, CH3), 3.12 (1H, dd, C4-H), 3.47 (1H, dd, C5-H), 4.80 (1H, dd, C6-H), 6.54 (1H, s, C7-H), 6.67–7.40 (8H, bm, Ar-H). MS (m/z (relative abundance, %)): 350 (M+ , 52), 322 (28), 159 (16), 131 (100), 104 (6), 67 (20), 40 (7), 29 (10).
3-[4-(5-p-Anisyl-1-formyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl]syrnone (4i): yellow crystals, m.p. 154–155 °C. Anal. Calcd. for C_{19}H_{18}N_{4}O_{3}: C, 62.64; H, 4.40; N, 15.38. Found: C, 62.61; H, 4.38; N, 15.36. IR (KBr, cm^{-1}): 3127, 1732, 1597, 1620. ^1H-NMR (300 MHz, CDCl_3, δ, ppm): 3.18 (1H, dd, C_{5}′–H_{b}), 3.35 (1H, dd, C_{4}′–H_{a}), 3.90 (3H, s, –OCH_3), 4.45 (1H, dd, C_{5}′–H_{x}), 6.85 (1H, s, C_{2}–H), 7.0–7.57 (8H, bm, Ar–H). 10.5 (1H, s, –CHO); MS (m/z (relative abundance, %)): 366 (M^+, 34), 338 (24), 177 (15), 131 (87), 150 (100), 123 (7), 67 (18), 40 (8), 29 (11).

General procedure for the synthesis of 5g-16g-l: A solution of bromine (0.011 mol) in 5 ml of acetic anhydride was added to the compound 3d-14d-l (0.010 mol) in 5 ml of acetic anhydride at 0–5 °C over 30 min. The mixture was subjected to microwave heating at 60–65 °C (210 W) until the evolution of carbon dioxide fumes had ceased and then allowed to attain room temperature. The reaction mixture was poured into ice water and filtered. The crude product was filtered and crystallized using hot methanol to obtain pale yellow crystals of 5g-16g-l in 90–95 % yield.

3-[3-(1-Formyl-4,5-dihydro-5-phenyl-1,3,4-oxadiazol-2-2(3H)-one (5g): pale yellow crystals, m.p. 111–112 °C. Anal. Calcd. for C_{19}H_{16}N_{4}O_{3}: C, 65.52; H, 4.60; N, 16.09. Found: C, 65.48; H, 4.58, N, 16.05. IR (KBr, cm^{-1}): 1775, 1652, 1599. ^1H-NMR (300 MHz, CDCl_3, δ, ppm): 1.94 (3H, s, C_{5}–C_{4}–CH_3), 3.10 (1H, dd, C_{4}′–H_{a}), 4.1 (1H, dd, C_{5}′–H_{x}), 5.5 (1H, dd, C_{3}′–H_{b}), 7.2–8.1 (9H, bm, Ar–H). 8.2 (1H, s, C_{2}–Ar–H); 9.0 (1H, s, –CHO); MS (m/z (relative abundance, %)): 348 (M^+, 67), 277 (63), 117 (100), 105 (22), 90 (67), 43 (23).

3-[3-(4,5-dihydro-5-p-tolyl-1,3,4-oxadiazol-2(3H)-one (5h): pale yellow crystals, m.p. 165–166 °C. Anal. Calcd. for C_{20}H_{18}N_{4}O_{3}: C, 66.30; H, 4.97; N, 15.46. Found: C, 66.27; H, 4.92, N, 15.42. IR (KBr, cm^{-1}): 1773, 1640, 1585. ^1H-NMR (300 MHz, CDCl_3, δ, ppm): 2.0 (3H, s, C_{5}–C_{4}–CH_3), 2.4 (3H, s, Ph–CH_{3}), 3.05 (1H, dd, C_{4}′–H_{a}), 4.0 (1H, dd, C_{5}′–H_{x}), 5.4 (1H, dd, C_{3}′–H_{b}), 7.0–7.9 (8H, bm, Ar–H). 8.0 (1H, s, C_{2}–Ar–H); 8.9 (1H, s, –CHO); MS (m/z (relative abundance, %)): 362 (M^+, 74), 291 (65), 131 (100), 105 (20), 104 (87), 90 (67), 77 (12), 43 (23).

3-[1-(5-p-Anisyl-1-formyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl]-5-methyl-1,3,4-oxadiazol-2(3H)-one (5i): yellow crystals, m.p. 215–216 °C. Anal. Calcd. for C_{23}H_{36}N_{4}O_{3}: C, 63.49; H, 4.76; N, 14.81. Found: C, 63.45; H, 4.74, N, 14.79. IR (KBr, cm^{-1}): 1765, 1645, 1597. ^1H-NMR (300 MHz, CDCl_3, δ, ppm): 2.20 (3H, s, CH_3), 3.0 (1H, dd, C_{5}′–H_{b}), 3.80 (1H, dd, C_{4}′–H_{a}), 5.0 (1H, dd, C_{5}′–H_{x}), 6.90–7.60 (8H, bm, Ar–H). 7.89 (1H, s, C_{2}–Ar–H); 9.0 (1H, s, –CHO); MS (m/z (relative abundance, %)): 378 (M^+, 42), 307 (65), 147 (100), 120 (78), 105 (20), 104 (87), 90 (68), 43 (20).

3-[1-(Acetyl-4,5-dihydro-5-phenyl-1,3,4-oxadiazol-2(3H)-one (5j): pale yellow crystals, m.p. 301–302 °C. Anal. Calcd. for C_{20}H_{18}N_{4}O_{3}: C, 66.29; H, 4.97; N, 15.46. Found: C, 66.25; H, 4.95, N, 15.42. IR (KBr, cm^{-1}): 1765, 1648, 1600. ^1H-NMR (300 MHz, CDCl_3, δ, ppm): 2.15 (3H, s, C_{5}–C_{4}–CH_3), 2.62 (3H, s, COCH_3), 3.4 (1H, dd, C_{4}′–H_{a}), 3.9 (1H, dd, C_{5}′–H_{x}), 5.0 (1H, dd, C_{3}′–H_{b}), 6.95–7.9 (8H, bm, Ar–H). 7.85 (1H, s, C_{2}–Ar–H); 10.0 (1H, s, –CHO); MS (m/z (relative abundance, %)): 362 (M^+, 66), 291 (47), 263 (23), 117 (100), 105 (24), 90 (50), 43 (45).

3-[1-(Acetyl-4,5-dihydro-5-p-tolyl-1,3,4-oxadiazol-2(3H)-one (5k): pale yellow crystals, m.p. 181–182 °C. Anal. Calcd. for C_{23}H_{36}N_{4}O_{3}: C, 67.02; H, 5.32; N, 14.89. Found: C, 67.00; H, 5.29, N, 14.85. IR (KBr, cm^{-1}): 1770, 1655, 1605. ^1H-NMR (300 MHz, CDCl_3, δ, ppm): 2.12 (3H, s, C_{5}–C_{4}–CH_3), 2.4 (3H, s, Ph–CH_{3}), 2.50 (3H, s, COCH_3), 3.12 (1H, dd, C_{4}′–H_{a}), 3.8 (1H, dd, C_{5}′–H_{x}), 4.57 (1H, dd, C_{5}′–H_{x}), 7.05–7.75 (8H, bm, Ar–H). 7.9 (1H, s, C_{2}–Ar–H); 9.7 (1H, s, –CHO); MS (m/z (relative abundance, %)): 376 (M^+, 58), 348 (25), 305 (28), 131 (100), 105 (39), 43 (28).
3-[3-(1-acetyl-5-p-anisyl-4,5-dihydro-1H-pyrazol-3-ylphenyl)-5-methyl-1,3,4-oxadiazol-2(3H)-one (5b): yellow crystals, m.p. 224–225 °C. Anal. Calcd. for C_{19}H_{16}N_{4}O_{4}: C, 64.28; H, 5.10; N, 14.28. Found: C, 64.25; H, 5.07; N, 14.25. IR (KBr, cm⁻¹): 1762, 1648, 1592. ¹H-NMR (300 MHz, CDCl₃, δ ppm): 2.15 (3H, s, C₅=CH₂), 2.36 (3H, s, COCH₃), 3.30 (1H, dd, C₆=H₅), 3.67 (3H, s, OCH₃), 3.85 (1H, dd, C₆=H₅), 4.85 (1H, dd, C₆=H₅), 6.82–7.70 (8H, Ar–H), 7.90 (1H, s, C₂–Ar–H), 10.05 (1H, s, –CHO); MS (m/z (relative abundance, %)): 392 (M⁺, 20), 364 (45), 321 (30), 147 (100), 120 (58), 105 (42).

3-[4-(1-Formyl-4,5-dihydro-5-phenyl-1H-pyrazol-3-ylphenyl)-5-methyl-1,3,4-oxadiazol-2(3H)-one (6g): pale yellow crystals, m.p. 185–186 °C. Anal. Calcd. for C_{20}H_{18}N_{4}O_{3}: C, 65.52; H, 4.60; N, 16.09. Found: C, 65.51; H, 4.56; N, 16.10. IR (KBr, cm⁻¹): 1772, 1648, 1603. ¹H-NMR (300 MHz, CDCl₃, δ ppm): 1.9 (3H, s, C₅=CH₂), 3.25 (1H, dd, C₆=H₅), 3.96 (1H, dd, C₆=H₅), 4.98 (1H, dd, C₆=H₅), 7.0–8.4 (9H, bm, Ar–H), 10.0 (1H, s, –CHO); MS (m/z (relative abundance, %)): 348 (M⁺, 46), 305 (37), 130 (58), 103 (100), 90 (67), 29 (15).

3-[4-(1-Formyl-4,5-dihydro-5-phenyl-1H-pyrazol-3-ylphenyl)-5-methyl-1,3,4-oxadiazol-2(3H)-one (6h): pale yellow crystals, m.p. 220–221 °C. Anal. Calcd. for C_{20}H_{18}N_{4}O_{3}: C, 66.30; H, 4.97; N, 15.46. Found: C, 66.35; H, 5.00 N, 15.44. IR (KBr, cm⁻¹): 1765, 1635, 1602. ¹H-NMR (300 MHz, CDCl₃, δ ppm): 1.99 (3H, s, C₅=CH₂), 2.47 (3H, s, Ph–CH₃), 3.24 (1H, dd, C₆=H₅), 3.65 (1H, dd, C₆=H₅), 5.0 (1H, dd, C₆=H₅), 6.95–7.45 (8H, bm, Ar–H), 9.0 (1H, s, –CHO); MS (m/z (relative abundance, %)): 362 (M⁺, 63), 319 (33), 144 (100), 117 (60), 104 (21), 29 (17).

3-[4-(5-p-tolyl-1H-pyrazol-3-ylphenyl)-5-methyl-1,3,4-oxadiazol-2(3H)-one (6i): yellow crystals, m.p. 148–149 °C. Anal. Calcd. for C_{23}H_{20}N_{4}O_{3}: C, 63.49; H, 4.76; N, 14.81. Found: C, 63.48; H, 4.77, N, 14.80. IR (KBr, cm⁻¹): 1780, 1655, 1588. ¹H-NMR (300 MHz, CDCl₃, δ ppm): 2.06 (3H, s, C₅=CH₂), 3.52 (1H, dd, C₆=H₅), 3.74 (3H, s, –OCH₃), 3.95 (1H, dd, C₆=H₅), 5.0 (1H, dd, C₆=H₅), 6.95–7.52 (8H, bm, Ar–H), 9.3 (1H, s, –CHO); MS (m/z (relative abundance, %)): 378 (M⁺, 52), 335 (77), 160 (94), 133 (100), 120 (21), 29 (14).

3-[4-(1-acetyl-4,5-dihydro-5-phenyl-1H-pyrazol-3-ylphenyl)-5-methyl-1,3,4-oxadiazol-2(3H)-one (6j): pale yellow crystals, m.p. 170–171 °C. Anal. Calcd. for C_{21}H_{18}N₄O₄: C, 66.29; H, 4.97; N, 15.46. Found: C, 66.30; H, 4.90, N, 15.50. IR (KBr, cm⁻¹): 1774, 1657, 1606. ¹H-NMR (300 MHz, CDCl₃, δ ppm): 1.98 (3H, s, CH₃), 2.43 (3H, s, COCH₃), 3.26 (1H, dd, C₆=H₅), 3.87 (1H, dd, C₆=H₅), 4.98 (1H, dd, C₆=H₅), 6.97–7.72 (9H, bm, Ar–H), 10.4 (1H, s, –CHO). MS (m/z (relative abundance, %)): 362 (M⁺, 67), 320 (54), 187 (100), 144 (90), 90 (45), 43 (56).

3-[4-(1-acetyl-4,5-dihydro-5-p-tolyl-1H-pyrazol-3-ylphenyl)-5-methyl-1,3,4-oxadiazol-2(3H)-one (6k): yellow crystals, m.p. 162–163 °C. Anal. Calcd. for C_{24}H_{24}N₄O₄: C, 64.28; H, 5.10; N, 14.28. Found: C, 64.27; H, 5.12, N, 14.32. IR (KBr, cm⁻¹): 1762, 1648, 1592. ¹H-NMR (300 MHz, CDCl₃, δ ppm): 2.15 (3H, s, C₅=CH₂), 2.55 (3H, s, COCH₃), 3.30 (1H, dd, C₆=H₅), 3.64 (3H, s, –OCH₃), 3.94 (1H, dd, C₆=H₅), 5.12 (1H, dd, C₆=H₅), 6.80–7.54 (8H, bm, Ar–H), 9.45 (1H, s, –CHO); MS (m/z (relative abundance, %)): 392 (M⁺, 66), 350 (48), 217 (100), 147 (75), 120 (64), 43 (10).
CONCLUSION

This work demonstrated a rapid, efficient and environmentally friendly method of synthesis of bisheterocycles containing sydnone and 1,3,4-oxadiazole derivatized with pyrazoline under microwave heating. The method is convenient, inexpensive with good yields and is useful for the synthesis the bioactive molecules. The pharmacological assay of the newly synthesized molecules is in progress.

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