Journal of the Serbian Chemical Society
JSCS@tmf.bg.ac.yu • www.shd.org.yu/JSCS
J. Serb. Chem. Soc. *73* (2) 131–138 (2008)
JSCS–3695
UDC 547.78+542.913:547.334:547.77
Original scientific paper

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

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(Received 21 June, revised 1 August 2007)

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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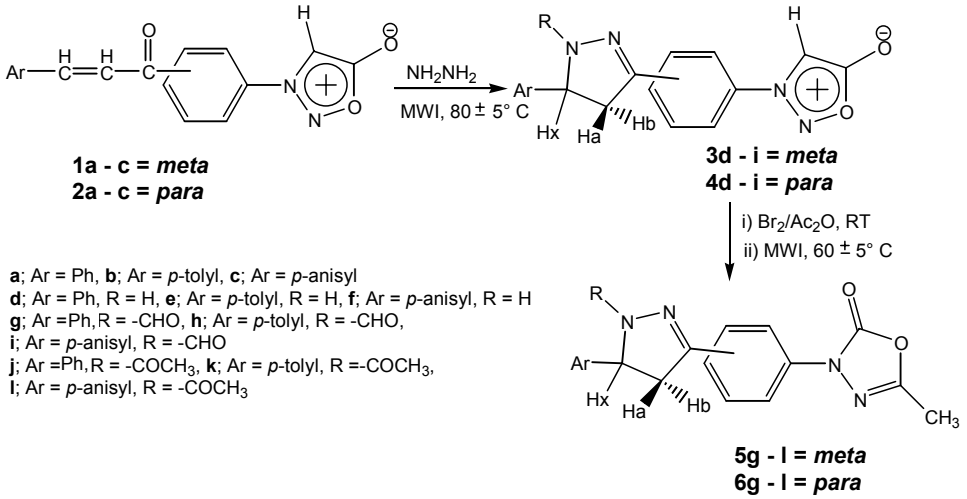
doi: 10.2298/JSC0802131K

RESULTS AND DISCUSSION

Chalcones (*meta* and *para* isomers), which were prepared according to a previously reported method,[23] undergo a rapid cyclization with hydrazine hydrate under microwave irradiations at 80±5 °C (240 W) to give pyrazolines **3d–i**/**4d–i** quantitatively in 4–12 min (Scheme 1). Poly(ethylene glycol) (PEG 200) and formic acid were used as the solvent for the preparation of **3d–f**/**4d–f** and **3g–i**/**4g–i**, respectively. Compounds **3d–i**/**4d–i** on bromination at 0–5 °C and heating under microwave at 60±5 °C (210 W) in acetic anhydride afforded **5g–l**/**6g–l**. The sydnone ring which is mesoionic undergoes 1,3-dipolar cyclo-addition reaction[24] with acetic anhydride to 1,3,4-oxadiazole. In addition, compounds **3d–i**/**4d–i** undergo *N*-acetylation of the pyrazoline ring to form **5j–l**/**6j–l**. These heterocyclic products were characterized based on their IR, ^{1}H-NMR, mass spectral and elemental analyses.



Scheme 1. The starting chalcones **1a–c**/**2a–c** and the intermediates 3-[3/4-(1-substituted-5--aryl-4,5-dihydro-1*H*-pyrazol-3-yl)phenyl]sydnone (**3d–i**/**4d–i**) and the final products after 1,3-dipolar cycloaddition, 5-methyl-3-[3/4-(1-substituted-5-aryl-4,5-dihydro--1*H*-pyrazol-3-yl)phenyl]-1,3,4-oxadiazol-2(3*H*)-ones (**5g–l**/**6g–l**).

On comparison of the synthesis by the microwave assisted method with that by the conventional method (randomly selected compounds),[25] 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.[26] 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 $CDCl_3$ (δ, 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. 1on UIC 002002 spectrometers.

TABLE I. Comparison of the reaction time required and yield

Compound	Thermal		Microwave	
	Time, h	Yield, %	Time, min	Yield, %
3d	4.0	60	5.0	82
3i	6.0	67	8.0	90
4d	4.5	65	7.0	92
4i	6.0	70	10.0	87
5g	1.0	66	7.0	90
5l	1.5	60	5.0	95
6g	1.0	52	8.0	90
6l	1.5	57	5.0	92

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±5 °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-1*H*-pyrazol-3-yl)phenyl]sydnone* (**3d**): pale yellow crystals, m.p. 170–171 °C. Anal. Calcd. for $C_{17}H_{14}N_4O_2$: 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, $CDCl_3$, δ, ppm): 3.40 (1H, *dd*, $C_{4'}$–H_b), 3.75 (1H, *dd*, $C_{4'}$–H_a), 4.85 (1H, *dd*, $C_{5'}$–H_x), 5.20 (1H, *s*, NH), 6.75 (1H, *s*, C_4–H), 6.9–7.8 (8H, *bm*, Ar–H), 7.98 (1H, *s*, $C_{2'}$–Ar–H). MS (*m*/*z* (relative abundance, %)): 306 (M^+, 55), 276 (32), 248 (45), 221 (100), 144 (90), 77 (55).

*3-[3-(4,5-Dihydro-5-*p*-tolyl-1*H*-pyrazol-3-yl)phenyl]sydnone* (**3e**): pale yellow crystals, m.p. 154–155 °C. Anal. Calcd. for $C_{18}H_{16}N_4O_2$: 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, $CDCl_3$, δ, ppm): 2.10 (3H, *s*, CH_3), 3.15 (1H, *dd*, $C_{4'}$–H_b), 3.60 (1H, *dd*, $C_{4'}$–H_a), 4.90 (1H, *dd*, $C_{5'}$–H_x), 5.05 (1H, *s*, NH), 6.60 (1H, *s*, C_4–H), 7.0–7.75 (7H, *bm*, Ar–H), 8.05 (1H, *s*, $C_{2'}$–Ar–H). 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-1*H*-pyrazol-3-yl)phenyl]sydnone* (**3f**): yellow crystals, m.p. 184–190 °C. Anal. Calcd. for $C_{18}H_{16}N_4O_3$: C, 64.29; H, 4.76; N, 16.66. Found: C, 64.23, H, 4.71, N, 16.62. IR (KBr, cm^{-1}): 3400, 3110, 1730, 1600. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 3.05 (1H, *dd*, $C_{4'}$–H_b), 3.30 (1H, *dd*, $C_{4'}$–H_a), 3.75 (3H, *s*, –OCH_3), 4.74 (1H, *dd*, $C_{5'}$–H_x), 5.50 (1H, *s*, NH), 6.85 (1H, *s*, C_4–H), 7.15–7.90 (7H, *bm*, Ar–H), 7.95 (1H, *s*, $C_{2'}$–Ar–H). 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-1*H*-pyrazol-3-yl)phenyl]sydnone* (**3g**): yellow crystals, m.p. 108–109 °C. Anal. Calcd. for $C_{18}H_{14}N_4O_3$: C, 64.67; H, 4.19; N, 14.67. Found: C, 64.65, H, 4.14, N, 16.72. IR (KBr, cm^{-1}): 3138, 1745, 1600, 1580. ^{1}H-NMR (300 MHz, $CDCl_3$,

δ, ppm): 3.18 (1H, *dd*, $C_{4'}$–H_b), 3.39 (1H, *dd*, $C_{4'}$–H_a), 4.45 (1H, *dd*, $C_{5'}$–H_x), 6.70 (1H, *s*, C_4–H), 6.78–7.40 (8H, *bm*, Ar–H), 7.75 (1H, *s*, $C_{2'}$–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-(1-Formyl-4,5-dihydro-5-*p-*tolyl-1*H-*pyrazol-3-yl)phenyl]sydnone* (**3h**): yellow crystals, m.p. 184–185 °C. Anal. Calcd. for $C_{19}H_{16}N_4O_3$: C, 65.52; H, 4.60; N, 16.09. Found: C, 65.47, H, 4.54, N, 16.06. IR (KBr, cm^{-1}): 3145, 1737, 1605, 1610. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 2.4 (3H, *s*, CH_3), 3.05 (1H, *dd*, $C_{4'}$–H_b), 3.45 (1H, *dd*, $C_{4'}$–H_a), 4.75 (1H, *dd*, $C_{5'}$–H_x), 6.70 (1H, *s*, C_4–H), 6.85–7.35 (7H, *bm*, Ar–H), 8.0 (1H, *s*, $C_{2'}$–Ar–H), 9.0 (1H, *s*, –CHO); MS (*m*/*z* (relative abundance, %)): 350 (M^+, 42), 322 (63), 292 (34), 264 (100), 144 (90), 107 (40).

*3-[3-(5-*p-*Anisyl-1-formyl-4,5-dihydro-1*H-*pyrazol-3-yl)phenyl]sydnone* (**3i**): yellow crystals, m.p. 201–202 °C. Anal. Calcd. for $C_{19}H_{16}N_4O_3$: C, 62.64; H, 4.40; N, 15.38. Found: C, 62.61, H, 4.38, N, 15.36. IR (KBr, cm^{-1}): 3132, 1740, 1585, 1595. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 3.20 (1H, *dd*, $C_{4'}$–H_b), 3.49 (1H, *dd*, $C_{4'}$–H_a), 3.74 (3H, *s*, –OCH_3), 4.60 (1H, *dd*, $C_{5'}$–H_x), 6.78 (1H, *s*, C_4–H), 6.90–7.45 (7H, *bm*, Ar–H), 7.90 (1H, *s*, $C_{2'}$–Ar–H), 10.0 (1H, *s*, –CHO). MS (*m*/*z* (relative abundance, %)): 366 (M^+, 39), 338 (60), 308 (54), 280 (100), 144 (87), 107 (44).

*3-[4-(4,5-Dihydro-5-phenyl-1*H-*pyrazol-3-yl)phenyl]sydnone* (**4d**): yellow crystals, m.p. 160–161 °C. Anal. Calcd. for $C_{17}H_{14}N_4O_2$: C, 66.66; H, 4.58; N, 18.30. Found: C, 66.65 H, 4.54, N, 18.30. IR (KBr, cm^{-1}): 3395, 3114, 1730, 1600. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 3.24 (1H, *dd*, $C_{4'}$–H_b), 3.45 (1H, *dd*, $C_{4'}$–H_a), 4.62 (1H, *dd*, $C_{5'}$–H_x), 5.15 (1H, *s*, NH), 6.50 (1H, *s*, C_4–H), 6.75–7.27 (9H, *bm*, Ar–H). MS (*m*/*z* (relative abundance, %)): 306 (M^+, 62), 145 (24), 131 (26), 117 (100), 103 (15), 90 (50), 67 (75).

*3-[4-(4,5-Dihydro-5-*p-*tolyl-1*H-*pyrazol-3''-yl)phenyl]sydnone* (**4e**): yellow crystals, m.p. 178–179 °C. Anal. Calcd. for $C_{18}H_{16}N_4O_2$: C, 67.50; H, 5.00; N, 17.50. Found: C, 67.48 H, 5.05, N, 17.55. IR (KBr, cm^{-1}): 3096, 1725, 1605. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 2.23 (3H, *s*, CH_3), 3.20 (1H, *dd*, $C_{4'}$–H_b), 3.39 (1H, *dd*, $C_{4'}$–H_a), 4.60 (1H, *dd*, $C_{5'}$–H_x), 5.0 (1H, *s*, NH), 6.54 (1H, *s*, C_4–H), 6.70–7.25 (8H, *bm*, Ar–H); MS (*m*/*z* (relative abundance, %)): 320 (M^+, 64), 159 (28), 132 (100), 105 (19), 103 (50), 67 (75), 40 (13).

*3-[4-(5-*p-*Anisyl-4,5-dihydro-1*H-*pyrazol-3-yl)phenyl]sydnone* (**4f**): yellow crystals, m.p. 127–128 °C. Anal. Calcd. for $C_{18}H_{16}N_4O_3$: 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. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 3.18 (1H, *dd*, $C_{4'}$–H_b), 3.25 (1H, *dd*, $C_{4'}$–H_a), 3.80 (3H, *s*, –OCH_3), 4.75 (1H, *dd*, $C_{5'}$–H_x), 4.95 (1H, *s*, NH), 6.60 (1H, *s*, C_4–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-(1-Formyl-4,5-dihydro-5-phenyl-1*H-*pyrazol-3-yl)phenyl]sydnone* (**4g**): yellow crystals, m.p. 140–141 °C. Anal. Calcd. for $C_{18}H_{14}N_4O_3$: 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. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 3.16 (1H, *dd*, $C_{4'}$–H_b), 3.35 (1H, *dd*, $C_{4'}$–H_a), 4.57 (1H, *dd*, $C_{5'}$–H_x), 6.70 (1H, *s*, C_4–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 (44), 40 (5).

*3-[4-(1-Formyl-4,5-dihydro-5-*p-*tolyl-1*H-*pyrazol-3-yl)phenyl]sydnone* (**4h**): yellow crystals, m.p. 161–162 °C. Anal. Calcd. for $C_{19}H_{16}N_4O_3$: 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. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 2.34 (3H, *s*, CH_3), 3.12 (1H, *dd*, $C_{4'}$–H_b), 3.47 (1H, *dd*, $C_{4'}$–H_a), 4.80 (1H, *dd*, $C_{5'}$–H_x), 6.54 (1H, *s*, C_4–H), 6.67–7.40 (8H, *bm*, Ar–H) 9.5 (1H, *s*, –CHO); 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-1*H*-pyrazol-3-yl)phenyl]sydnone* (**4i**): yellow crystals, m.p. 154–155 °C. Anal. Calcd. for $C_{19}H_{16}N_4O_3$: 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. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 3.18 (1H, *dd*, $C_{4'}$–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_4–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–l/6g–l***: A solution of bromine (0.011 mol) in 5 ml of acetic anhydride was added to the compound **3d–i**/**4d–i** (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±5 °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–l**/**6g–l** in 90–95 % yield.

*3-[3-(1-Formyl-4,5-dihydro-5-phenyl-1*H*-pyrazol-3-yl)phenyl]-5-methyl-1,3,4-oxadiazol-2(3*H*)-one* (**5g**): pale yellow crystals, m.p. 111–112 °C. Anal. Calcd. for $C_{19}H_{16}N_4O_3$: 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. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 1.94 (3H, *s*, C_5–CH_3), 3.10 (1H, *dd*, $C_{4'}$–H_b), 4.1 (1H, *dd*, $C_{4'}$–H_a), 5.5 (1H, *dd*, $C_{5'}$–H_x), 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-(1-Formyl-4,5-dihydro-5-*p*-tolyl-1*H*-pyrazol-3-yl)phenyl]-5-methyl-1,3,4-oxadiazol-2(3*H*)-one* (**5h**): pale yellow crystals, m.p. 165–166 °C. Anal. Calcd. for $C_{20}H_{18}N_4O_3$: 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. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 2.0 (3H, *s*, C_5–CH_3), 2.4 (3H, *s*, Ph–CH_3), 3.05 (1H, *dd*, $C_{4'}$–H_b), 4.0 (1H, *dd*, $C_{4'}$–H_a), 5.4 (1H, *dd*, $C_{5'}$–H_x), 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-[3-(5-*p*-Anisyl-1-formyl-4,5-dihydro-1*H*-pyrazol-3-yl)phenyl]-5-methyl-1,3,4-oxadiazol-2(3*H*)-one* (**5i**): yellow crystals, m.p. 215–216 °C. Anal. Calcd. for $C_{20}H_{18}N_4O_4$: 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, 1599. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 2.20 (3H, *s*, CH_3), 3.0 (1H, *dd*, $C_{4'}$–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-[3-(1-Acetyl-4,5-dihydro-5-phenyl-1*H*-pyrazol-3-yl)phenyl]-5-methyl-1,3,4-oxadiazol-2(3*H*)-one* (**5j**): pale yellow crystals, m.p. 301–302 °C. Anal. Calcd. for $C_{20}H_{18}N_4O_3$: 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. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 2.15 (3H, *s*, C_5–CH_3), 2.62 (3H, *s*, $COCH_3$), 3.4 (1H, *dd*, $C_{4'}$–H_b), 3.9 (1H, *dd*, $C_{4'}$–H_a), 5.0 (1H, *dd*, $C_{5'}$–H_x), 6.95–7.8 (9H, *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-[3-(1-Acetyl-4,5-dihydro-5-*p*-tolyl-1*H*-pyrazol-3-yl)phenyl]-5-methyl-1,3,4-oxadiazol-2(3*H*)-one* (**5k**): pale yellow crystals, m.p. 181–182 °C. Anal. Calcd. for $C_{21}H_{20}N_4O_3$: 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. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 2.12 (3H, *s*, C_5–CH_3), 2.4 (3H, *s*, Ph–CH_3), 2.50 (3H, *s*, $COCH_3$), 3.12 (1H, *dd*, $C_{4'}$–H_b), 3.8 (1H, *dd*, $C_{4'}$–H_a), 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-yl)phenyl]-5-methyl-1,3,4-oxadiazol--2(3H)-one* (**5l**): yellow crystals, m.p. 224–225 °C. Anal. Calcd. for $C_{21}H_{20}N_4O_4$: 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. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 2.15 (3H, *s*, C_5–CH_3), 2.36 (3H, *s*, $COCH_3$), 3.30 (1H, *dd*, $C_{4'}$–H_b), 3.67 (3H, *s*, OCH_3), 3.85 (1H, *dd*, $C_{4'}$–H_a), 4.85 (1H, *dd*, $C_{5'}$–H_x), 6.82–7.70 (8H, *bm*, Ar–H), 7.90 (1H, *s*, $C_{2'}$–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-1*H*-pyrazol-3-yl)phenyl]-5-methyl-1,3,4-oxadiazol--2(3H)-one* (**6g**): pale yellow crystals, m.p. 185–186 °C. Anal. Calcd. for $C_{19}H_{16}N_4O_3$: 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. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 1.9 (3H, *s*, C_5–CH_3), 3.25 (1H, *dd*, $C_{4'}$–H_b), 3.96 (1H, *dd*, $C_{4'}$–H_a), 4.98 (1H, *dd*, $C_{5'}$–H_x), 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-*p*-tolyl-1*H*-pyrazol-3-yl)phenyl]-5-methyl-1,3,4-oxadiazol--2(3H)-one* (**6h**): pale yellow crystals, m.p. 220–221 °C. Anal. Calcd. for $C_{20}H_{18}N_4O_3$: 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. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 1.99 (3H, *s*, C_5–CH_3), 2.47 (3H, *s*, Ph–CH_3), 3.24 (1H, *dd*, $C_{4'}$–H_b), 3.65 (1H, *dd*, $C_{4'}$–H_a), 5.0 (1H, *dd*, $C_{5'}$–H_x), 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*-Anisyl-1-formyl-4,5-dihydro-1*H*-pyrazol-3-yl)phenyl]-5-methyl-1,3,4-oxadiazol--2(3H)-one* (**6i**): yellow crystals, m.p. 148–149 °C. Anal. Calcd. for $C_{20}H_{18}N_4O_4$: 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. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 2.06 (3H, *s*, C_5–CH_3), 3.52 (1H, *dd*, $C_{4'}$–H_b), 3.74 (3H, *s*, –OCH_3), 3.95 (1H, *dd*, $C_{4'}$–H_a), 5.0 (1H, *dd*, $C_{5'}$–H_x), 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-1*H*-pyrazol-3-yl)phenyl]-5-methyl-1,3,4-oxadiazol--2(3H)-one* (**6j**): pale yellow crystals, m.p. 170–171 °C. Anal. Calcd. for $C_{20}H_{18}N_4O_3$: 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. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 1.98 (3H, *s*, CH_3), 2.43 (3H, *s*, $COCH_3$), 3.26 (1H, *dd*, $C_{4'}$–H_b), 3.87 (1H, *dd*, $C_{4'}$–H_a), 4.98 (1H, *dd*, $C_{5'}$–H_x), 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-1*H*-pyrazol-3-yl)phenyl]-5-methyl-1,3,4-oxadiazol--2(3H)-one* (**6k**): pale yellow crystals, m.p. 218–219 °C. Anal. Calcd. for $C_{21}H_{20}N_4O_3$: C, 67.02; H, 5.32; N, 14.89. Found: C, 67.00; H, 5.29, N, 14.85. IR (KBr, cm^{-1}): 1785, 1637, 1584. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 2.0 (3H, *s*, C_5–CH_3), 2.30 (3H, *s*, Ph–CH_3), 2.47(3H, *s*, $COCH_3$), 3.12 (1H, *dd*, $C_{4'}$–H_b), 3.8 (1H, *dd*, $C_{4'}$–H_a), 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^+, 40), 334 (50), 201 (100), 174 (88), 104 (14), 43 (11).

*3-[4-(1-Acetyl-5-*p*-anisyl-4,5-dihydro-1*H*-pyrazol-3-yl)phenyl]-5-methyl-1,3,4-oxadiazol--2(3H)-one* (**6l**): yellow crystals, m.p. 162–163 °C. Anal. Calcd. for $C_{21}H_{20}N_4O_4$: 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. ^{1}H-NMR (300 MHz, $CDCl_3$, δ, ppm): 2.15 (3H, *s*, C_5–CH_3), 2.55 (3H, *s*, $COCH_3$), 3.30 (1H, *dd*, $C_{4'}$–H_b), 3.64 (3H, *s*, –OCH_3), 3.94 (1H, *dd*, $C_{4'}$–H_a), 5.12 (1H, *dd*, $C_{5'}$–H_x), 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.

Acknowledgements. One of the authors (RRK) wishes to acknowledge the financial support of the University of Mysore and to the Principal, Yuvaraja's College, Mysore for the laboratory facilities. In addition, the authors would like to thank USIC, University of Mysore, for performing the spectral analyses.

И З В О Д

ЕФИКАСНА СИНТЕЗА 1,3,4-ОКСАДИАЗОЛСКИХ ДЕРИВАТА ПРЕКО СИДНОНА

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Чистом циклизацијом халкона **1a–c**/**2a–c** са хидразин-хидратом под дејством микро-таласног зрачења добијени су пиразолини **3d–i**/**4d–i** дериватизовани сидноном. 1,3-Диполарном циклоадицијом са анхидридом сирћетне киселине граде се пиразолини **5g–l**/**6g–l** који садрже 1,3,4-оксадиазолски фрагмент. Структура ових једињења потврђена је на основу спектралних података и елементалне анализе. У поређењу са стандардним загревањем, добијени резултати указују на то да се микро-таланим зрачењем, у реакцијама које су чистије, постиже већи принос, уз краће реакционо време (4–12 min).

(Примљено 21. јуна, ревидирано 1. августа 2007)

REFERENCES

1. C. V. Yelamaggad, U. S. Hiremath, B. V. Badami, *Indian J. Chem*. **33B** (1994) 674
2. B. M. Patil, B. V. Badami, G. S. Puranik, *Indian Drugs* **32 (**1995) 439
3. J. R. Kavali, B. V. Badami, *Farmaco* **55** (2000) 406
4. J. R. Kavali, B. V. Badami, *J. Chem. Res.* (2000) 546
5. K. Mogliah, D. S. Chowdary R. B. Rao, *Indian J. Chem*. **40B** (2001) 43
6. V. R. Shah, M. Vadodaria, A. R. Parikh, *Indian J. Chem*. **36B** (1997) 100
7. K. Ladva, P. Patel, P. Upadhyay, H. Parekh, *Indian J. Chem*. **35B** (1996) 1062
8. X. W. Su, X. P. Hui, C. H. Chu, Z. Y. Zhang, *Indian J. Chem*. **40B** (2001) 15
9. E. C. Taylor, H. Patel, H. Kumar, *Tetrahedron* **48** (1992) 8089
10. S. G. Roelfvan, C. Arnold, K. Wellnga, *J. Agric. Food Chem*. **84** (1979) 406
11. G. H. Keats, GB 1,209,631 (1970)
12. R. M. Kedar, N. N. Vidhale, M. M. Chincholkar, *Orient. J. Chem*. **13** (1997) 143
13. A. Singh, S. Rathod, B. N. Berad, S. D. Patil, A. G. Dosh, *Orient. J. Chem*. **16** (2000) 315
14. H. Z. Katri, S. A. Vunii, *J. Indian Chem. Soc*. **58** (1981) 168
15. N. B. Das, A. S. Mitra, *Indian J. Chem*. **16B** (1978) 638
16. D. Azarifar, M. Shaebanzadeh, *Molecules* **7** (2002) 885
17. B. Shivarama Holla, P. M. Akberali, M. K. Shivananda, *Farmaco* **55** (2000) 256
18. E. Palaska, M. Aytemir, I. Tayfun, K. Erol, E. Dilek, *Eur. J. Med. Chem. Chim. Ther*. **36** (2001) 539

19. H. G. Garge, Chandraprakash, *J. Pharm. Sci*. **14** (1971) 649
20. H. A. Regaila, A. K. El-Bayonk, M. Hammad, *Egypt. J. Chem*. **20** (1979) 197
21. R. Krishna, B. R. Pande, S. P. Bharthwal, S. S. Parmar, *Eur. J. Med. Chem*. **15** (1980) 567
22. M. I. Husain, S. Shukla, *Indian J. Chem*. **25B** (1986) 983
23. R. R. Kamble, B. S. Sudha, *Indian J. Pharm. Sci*. **68** (2006) 249
24. R. R. Kamble, S. B. Sudha, *J. Serb. Chem. Soc*. **71** (2006) 331
25. Conventional method was done according to the report; R. R. Kamble, *Ph.D. Thesis*, Karnatak University, Dharwad, India, 2001, p. 122
26. R. J. Giguere, T. L. Bray, S. M. Duncan, *Tetrahedron Lett*. **27** (1986) 4949.