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Microwave-assisted reactions of 4-[(4-oxochromen-3-yl)methylene]-2-phenyl-1,3-oxazol-5(4*H*)-ones with nitrogen bases

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Abstract: The microwave-assisted reactions of 4-[(6-R-4-oxochromen-3-yl)methylene]-2-phenyl-1,3-oxazol-5(4*H*)-ones **1a-1c** with *N*-bases are described. Substituted benzamides **2a-2c** were prepared by reaction of **1a** with primary amines in the presence of acetic acid and potassium acetate. Benzamides **3a** and **3b** were synthesized by reaction of **1b** with piperidine and morpholine, respectively. Oxazolone **1** reacted with *o*-phenylenediamine to give benzoimidazole derivative **4**. 3-Benzamido-1-[(pyridin-4-yl)carboxamido]-2,5-dioxo-3,10a-dihydro-2*H*-chromeno[2,3-*b*]pyridine **5** was prepared by reaction of **1a** with isoniazid in acetic acid and 5-[(6-bromo-4-oxochromen-3-yl)methylene]-3-phenyl-2,5-dihydro-1*H*-[1,2,4]triazine-6-one **6** was synthesized by reaction of **1c** with hydrazine in methanol.

Keywords: microwave irradiation, 1,3-oxazol-5(4*H*)-one, *N*-bases

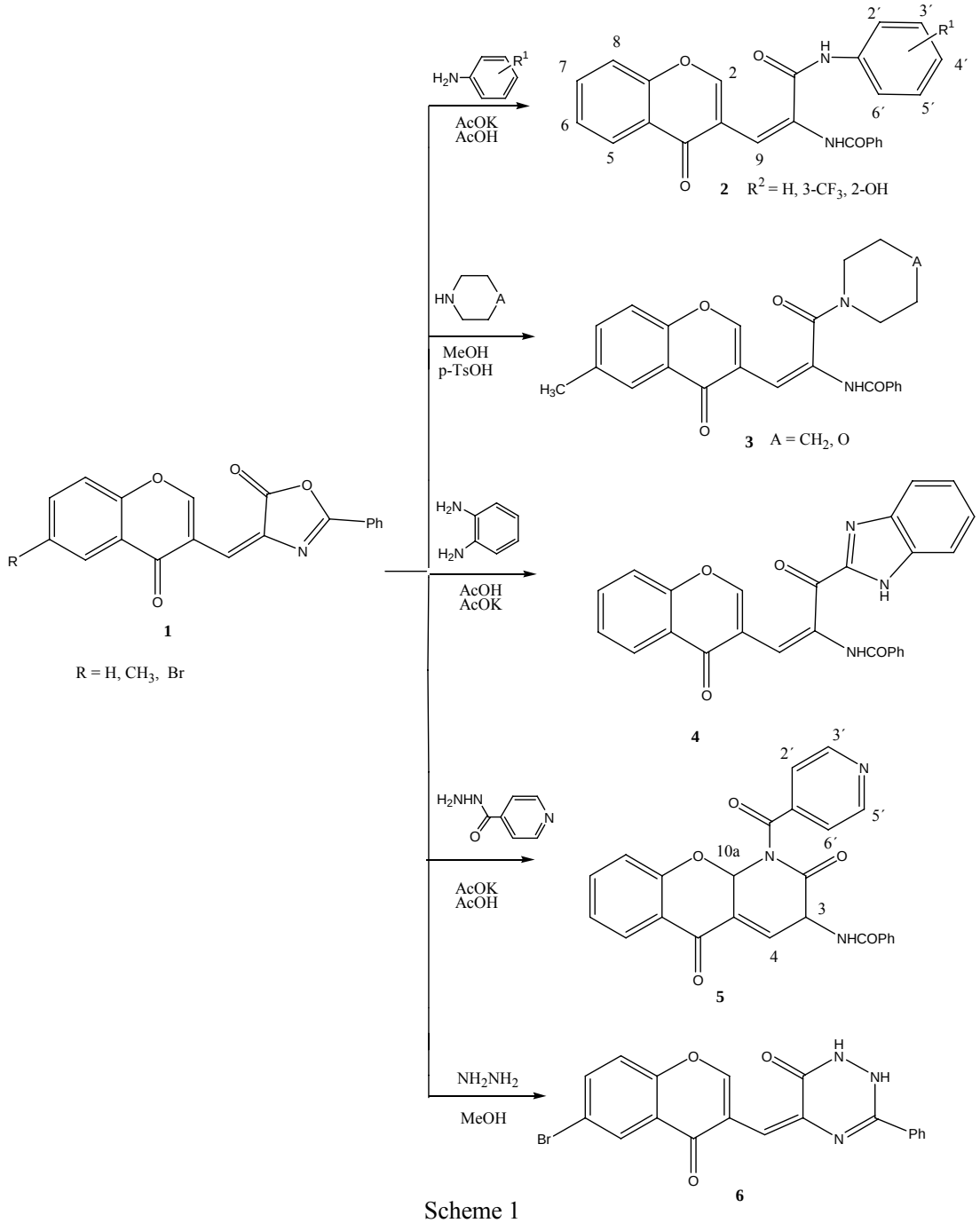
Introduction

1,3-Oxazol-5(4*H*)-one derivatives react easily with nitrogen nucleophiles, therefore they can serve as a convenient reagents for synthesis of new nitrogen heterocycles. They react with ammonia to give tetrazoles [1], with primary or secondary amines to give imidazoles or acrylamides [2]. Reactions of 1,3-oxazol-5(4*H*)-ones with hydrazine led to pyridazine or oxadiazole derivatives [3]. 1,2,4-Triazines were prepared by reaction of 1,3-oxazol-5(4*H*)-ones with phenylhydrazine [2]. Finally, the reaction of 1,3-oxazol-5(4*H*)-ones with o-phenylenediamine gave either benzimidazole or imidazole derivatives [4,5]

Results and discussion

N-{1-[(R-4-phenylamino)carbonyl]-2-(4-oxochromen-3-yl)vinyl}benzamides **2a – 2c** were synthesized in 50 - 78 % yields by microwave-assisted reaction of **1a** with substituted

anilines in acetic acid in the presence of potassium acetate with a power output of 90 W over the period given in Table 1. The ^{1}H NMR spectra of compounds **2a-2c** displayed signals of H-2 protons in the 8.68-8.73 ppm range and signals due to CH= bonded protons in 6.79 – 6.86 ppm range (Table 2).



Scheme 1

N-[2-(6-methyl-4-oxochromen-3-yl)-1-{[(piperidn-1-yl)carbonyl]vinyl}benzamide **3a** and *N*-[2-(6-methyl-4-oxochromen-3-yl)-1-{[(morpholin-4-yl)carbonyl]vinyl}benzamide **3b** were prepared in 80 and 98% yields by microwave-assisted reaction of **1b** with piperidine or

morpholine in methanol in the presence of p-toluenesulfonic acid with a power output of 90 W over the period given in Table 1. ^{1}H NMR spectra of compounds **3a**, **3b** displayed the signals of H-2 protons at 8.30 and 8.71 ppm while the signal of CH= bonded protons at 5.45 and 5.82 ppm, respectively (Table 2).

N-[1-(1*H*-Benzoimidazol-2-yl)-2-(4-oxochromen-3-yl)-vinyl]benzamide **4** was synthesized in 76% yield by microwave-assisted reaction of **1a** with o-phenylenediamine in acetic acid – potassium acetate medium. The reaction needed 10 min to completion at 160 W power output (Table 1). The ^{1}H NMR spectrum of **4** displays signal of H-2 bonded proton at 8.65 ppm and signal of CH= bonded proton at 6.89 ppm (Table 2).

3-Benzamido-1-[(pyridin-4-yl)carboxamido]-2,5-dioxo-3,10a-dihydro-2*H*-chromeno[2,3-*b*]pyridine **5** was synthesized in 60% yield by microwave-assisted reaction of **1a** with isoniazid in acetic acid in the presence of potassium acetate with a power output of 90 W for 10 min (Table 1). The ^{1}H NMR spectrum of **5** displays singlet signal of H-10a proton at 7.46 ppm range and signals due to H-3 and H-4 protons in 7.61 – 7.56 ppm range (Table 2).

When **1c** was irradiated in microwave oven with hydrazine at 90W for 10 min, 5-[(6-bromo-4-oxochromen-3-yl)methylene]-3-phenyl-2,5-dihydro-1*H*-[1,2,4]triazin-6-one **6** was prepared in 51% yield. The ^{1}H NMR spectrum of **5** displays singlet signal of H-2 at 8.76 ppm and signal of CH= bonded proton at 6.99 ppm (Table 2).

Experimental Part

All experiments were performed inWhirpool M401 type microwave oven. The apparatus was adapted for laboratory applications – n-hexane was used as coolant for the condenser. ^{1}H NMR spectra were obtained on a 300 MHz spectrometer VARIAN GEMINI 200 in DMSO-d_6 with tetramethylsilane as an internal standard. Melting points of products were determined on a Kofler hot plate apparatus and are uncorrected. All solvents were predistilled and dried appropriately prior to use. The course of reactions was monitored by TLC chromatography in ethyl acetate / n-hexane. The protocol in [6] was followed for the synthesis of oxazolones **1**.

General procedure

Synthesis of 2a-2c, 4, 5

The mixture of 4-[(4-oxochromen-3-yl)methylene]-2-phenyl-1,3-oxazol-5(4*H*)-one (**1a**) (0.3 g, 0.95 mmol), substituted aniline (*o*-phenylenediamine or isoniazid) (0.95 mmol) and catalytic amount of freshly fused potassium acetate in acetic acid (5 ml) was irradiated in

microwave oven at 90W (160W for **4**) for time period, given in Table 1. After cooling, the solid product was filtered off, dried and crystallized from ethanol.

Table 1 Characteristic data of compounds **2-6**

Compound	**R** **R^1 (A)**	**Formula** **Mw**	**Mp** (°C)	**Yield** (%)	**React. time** (min.)
2a	H H	$C_{25}H_{18}N_2O_4$ 410.4	231-234	78	5
2b	H 3-CF_3	$C_{26}H_{17}F_3N_2O_4$ 478.4	222-225	76	6
2c	H 2-OH	$C_{25}H_{18}N_2O_5$ 426.4	130-132	50	8
3a	CH_3 (CH_2)	$C_{25}H_{24}N_2O_4$ 416.5	225-230	98	5
3b	CH_3 (O)	$C_{24}H_{22}N_2O_5$ 418.4	248-250	80	6
4	H -	$C_{25}H_{17}N_3O_3$ 407.1	152-156	79	10
5	H	$C_{25}H_{18}N_4O_5$ 410.4	315-318	60	10
6	Br -	$C_{19}H_{12}BrN_3O_3$ 410.2	260-265	51	10

Synthesis of 3a, 3b

The mixture of 4-[(6-methyl-4-oxochromen-3-yl)methylene]-2-phenyl-1,3-oxazol-5(4*H*)-one (**1b**) (0.3 g, 0.91 mmol), piperidine (or morpholine) (0.91 mmol) and catalytic amount *p*-toluenesulfonic acid in methanol (5 ml) was irradiated in microwave oven at 90W for time period, given in Table 1. After cooling, the solid product was filtered off, dried and crystallized from ethanol.

Synthesis of 6

The mixture of 4-[(6-bromo-4-oxochromen-3-yl)methylene]-2-phenyl-1,3-oxazol-5(4*H*)-one (**1c**) (0.3 g, 0.76 mmol), hydrazine (0.03g, 0.94 mmol) in methanol (4 ml) was irradiated in microwave oven at 90W for time period, given in Table 1. After cooling, the solid product was filtered off, dried and crystallized from ethanol.

Table 2. ^{1}H NMR spectra (DMSO-d_6)

2a	10.41 (s, 1H, NH); 10.19 (s, 1H, NH); 8.71 (s, 1H, H-2); 8.19-8.16 (dd, 1H, ^{3}J=6.9 Hz, ^{4}J=1.6 Hz, H-5); 7.99-7.97 (m, 2H, H-2″, H-6″); 7.89-7.87 (m, 1H, ^{3}J=6.9 Hz, ^{4}J=1.64 Hz, H-7); 7.73-7.69 (m, 3H, H-8, H-2′, H-6′); 7.61-7.53 (m, 5H, H-6, H-3′, H-5′, H-3″, H-5″); 7.36-7.30 (m, 1H, H-4″); 7.11-7.06 (m, 1H, H-4′); 6.79 (s, 1H, H-9).
2b	10.52 (s, 1H, NH); 10.49 (s, 1H, NH); 8.73 (s, 1H, H-2); 8.19-8.16 (m, 2H, H-2″, H-6″); 7.99-7.95 (m, 3H, H-2′, H-4′, H-5); 7.90-7.84 (m, 1H, ^{3}J=7.2 Hz, ^{4}J=1.5 Hz, H-7); 7.73-7.71 (d, 1H, H-8, ^{3}J=8.4 Hz); 7.62-7.54 (m, 5H, H-5′, H-6′, H-3″, H-4″, H-5″); 7.45-7.43 (d, 1H, H-6, ^{3}J=8.4 Hz); 6.81 (s, 1H, H-9).
2c	10.45 (s, 1H, OH); 10.00 (s, 1H, NH); 9.85 (s, 1H, MH); 8.68 (s, 1H, H-2); 8.23-8.21 (m, 3H, H-5, H-2″, H-6″); 7.62-7.69 (m, 7H, H-6, H-7, H-8, H-3′, H-4′, H-5′, H-6′); 7.43-7.31 (m, 3H, H-3″, H-4″, H-5″); 6.86 (s, 1H, H-9).
3a	11.16 (s, 1H, NH); 8.71 (s, 1H, H-2); 7.98-7.94 (m, 3H, H-5, H-2″, H-6″); 7.71-7.55 (m, 5H, H-7, H-8, H-3″, H-4″, H-5″); 5.82 (s, 1H, H-9); 3.55-3.49 (m, 4H, CH_2); 2.49 (s, 3H, CH_3); 1.58-1.56 (m, 6H, CH_2).
3b	12.17 (s, 1H, NH); 8.14-8.11 (m, 3H, H-5. H-2″, H-6″); 8.30 (s, 1H, H-2); 7.58-7.48 (m, 5H, H-7. H-8. H-3″, H-4″, H-5″); 5.45 (s, 1H, H-9); 3.79-3.63 (m, 8H, CH_2); 2.51 (s, 3H, CH_3).
4	12.63 (s, 1H, NH); 10.30 (s, 1H, NH); 8.65 (s, 1H, H-2); 8.16. 8.14 (d, 1H, H-5. ^{3}J=8.8 Hz); 8.06-7.95 (m, 2H, H-2″, H-6″); 7.68-7.39 (m, 7H, H-4′, H-7′, H-6, H-7, H-8, H-5′, H-6′); 7.23-7.19 (m, 3H, H-3″, H-4″, H-5″); 6.89 (s, 1H, H-9).
5	11.94 (s, 1H, NH); 9.85 (s, 1H, NH); 8.85-8.83 (dd, 2H, H-3′, H-5′;^{3}J=6.9 Hz, ^{4}J=1.5 Hz); 8.21-8.18 (dd, 1H, H-6, ^{3}J=6.6 Hz, ^{4}J=1.8 Hz); 8.13-8.09 (dd, 2H, H-2′, H-6′, ^{3}J=6.6 Hz, ^{4}J=1.5 Hz); 7.94-7.88 (tt, 1H, H-7); 7.81-7.76 (m, 4H, H-2″, H-6″, H-8, H-9); 7.61-7.56 (m, 5H, H-3. H-4. H-3″, H-4″, H-5″); 7.46 (s, 1H, H-10a).
6	10.56 (bs, 2H, NH); 8.76 (s, 1H, H-2); 8.15-8.01 (m, 3H, H-5, H-7, H-8); 7.70-7.47 (m, 5H, Ph); 6.99 (s, 1H, H-9).

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References

[1] Behringer H., Grimme W.: *Chem. Ber.*, 92, **1959**, 2967-2972.

[2] Ghosh C. K., Bandyopadhyay C.: *Indian J. Chem.*, 23B, **1984**, 1048 - 1053.

[3] Hamad A. S. S., Hashem A. I.: *Molecules*, 5, **2000**, 895 – 907.

[4] Tikdari A. M., Mukerjee A. K.: *J. Prakt. Chem.*, 330, **1988**, 647 – 649.

[5] Girges M. M., El.Zahab M. M. A. , Hanna M. A.: *Collect. Czech. Chem. Commun.*, 54, **1989**, 1096 – 1103.

[6] Fitton A. O., Frost J. R., Suschitsky H., Houghton P. G.: *Synthesis* **1977**, 133 - 135.