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A Facile Synthesis of 5-Arylidene-2-imino-4-thiazolidinones Under Microwave Irradiation

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Abstract: A series of 5-arylidene-2-imino-4-thiazolidinone derivatives were synthesized by the cross-aldol condensation of aromatic aldehydes with 2-imino-4-thiazolidinone in sodium acetate/acetic acid under microwave irradiation. The reactions were completed in 10 min with 63–91% yields, were environmental benign, and had easy workup.

Keywords: Aromatic aldehyde, 2-imino-4-thiazolidinone, microwave irradiation

Thiazolidin-4-ones derivatives have been proven to be attractive compounds because of their outstanding biological activities.[1–8] Therefore, the syntheses of these compounds are of considerable interest. Continuing our interest in the development of efficient reagents and simple procedures for the synthesis of organic compounds, we reported previously an efficient synthesis of 5-benzylidenerhodamines.[9] Herein, we report a facile synthesis of 5-arylidene-2-imino-4-thiazolidinone by the cross-aldol condensation of aromatic aldehydes with 2-imino-4-thiazolidinone using sodium acetate as catalyst in acetic acid under microwave irradiation (Scheme 1). The reactions were completed in 10 min with 63–91% yields, were environmentally benign, and had easy workup.

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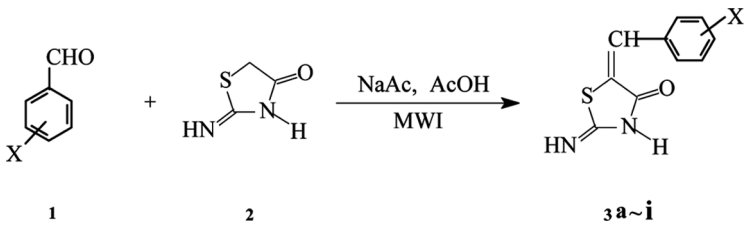

1 2 3a~i

Scheme 1. Synthesis of 5-arylidene-2-imino-4-thiazolidinone under microwave irradiation.

RESULTS AND DISCUSSION

When a mixture of aromatic aldehyde **1**, 2-imino-4-thiazolidinone **2**, and ammonium acetate was irradiated in a microwave (Scheme 1), the reactions were completed in 10 min. The crude products were purified by recrystallization from 95% ethanol to afford products with mild to good yields (63–91%). However, conventional approaches for the synthesis of these compounds often involve long reaction times, harsh reaction conditions, unsatisfactory yields, and environmentally unfavorable solvents. For example, the condensation of aromatic aldehyde with 2-imino-4-thiazolidinone has been performed using piperidine as catalyst in ethanol at reflux for 20–24 h,[10] using sodium acetate in glacial acetic acid under reflux for 0.5–12 h,[11] or using pyridine in xylene at 150–160 °C for 3 h,[12] and so on. The results as summarized in Table 1 clearly reveal the scope and generality of the reaction with respect to various substituted

Table 1. Microwave irradiation synthesis of **3a–i**

Compounds	X	Reaction temperature[a] (°C)	Reaction time (min)	Yields[b] (%)	Mp (°C)
3a	H	170	10	77	275–276
3b	4-Cl	160	10	77	>300
3c	4-NO_2	150	10	74	>300
3d	3-NO_2	150	10	79	292–293
3e	4-HO	140	10	63	295–297
3f	4-CH_3	170	10	78	281–283
3g	4-CH_3O	170	10	91	257–258
3h	4-$(CH_3)_2N$	170	10	83	276–278
3i	3,4-(OCH_2O)	170	10	78	287–288

[a]Microwave power: 150 W.
[b]Yields of the isolated products.

aromatic aldehyde and that reasonable yields (63–94%) of the products were achieved after only 10 min of microwave irradiation.

In conclusion, we have described a rapid and environmentally friendly procedure for the synthesis of 5-arylidene-2-imino-4-thiazolidinone derivatives from the corresponding aromatic aldehyde with 2-imino-4-thiazolidinone under microwave irradiation.

EXPERIMENTAL

Melting points were determined in a WRS-1B digital melting-point instrument and are uncorrected. IR spectra were recorded on a Nicolet Avatar 360 FT-IR instrument. ^{1}H NMR were measured on a Burke 400-MHz spectrometer in DMSO-d_6 with TMS as internal standard. Mass spectra (MS) were recorded on an LCQ Advantage instrument. Reactions under microwaves were performed in a CEM Discover® monomode microwave reactor. All the reagents are commercially available.

General Procedure for 5-Arylidene-2-imino-4-thiazolidinones (3a–i)

A 10-mL process vial was charged with a mixture of the aromatic aldehyde (1 mmol), 2-imino-4-thiazolidinone (1 mmol), sodium acetic (1.5 mmol), and acetic acid (5 mL) and sealed with a cap containing a septum. The loaded vial was then placed into the cavity of the microwave reactor and heated at 150 W, 140–170 °C for 10 min (as indicated by thin-layer chromatography, TLC). The reaction mixture was allowed to stand at room temperature to solidify. The crude product was collected, washed with water, and recystallized from 95% ethanol.

Data

Compound **3a**

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.44 (s, 1H, =NH), 9.17 (s, 1H, NH), 7.81 (s, 1H, CH=), 7.54 (s, 5H, ArH); IR (KBr): 3184, 3018, 1673, 1508, 1278, 1143 cm^{-1}; MS: m/e $(M+H)^+$ 204.2. Anal. Calcd. for $C_{10}H_8N_2OS$: C, 58.81; H, 3.95; N, 13.72. Found: C, 59.06; H, 3.97; N, 13.79.

Compound **3b**

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.54 (s, 1H, =NH), 9.27 (s, 1H, NH), 7.93 (s, 1H, CH=), 7.62 (d, 2H, $J = 8.8$ Hz, ArH), 7.51 (d, 2H, $J = 8.8$ Hz,

ArH); IR (KBr): 3206, 3010, 1670, 1559, 1274, 1139 cm^{-1}; MS: *m/e* $(M+H)^+$ 239.9. Anal. calcd. for $C_{10}H_7ClN_2OS$: C, 50.32; H, 2.96; N, 11.74. Found: C, 50.55; H, 2.98; N, 11.80.

Compound **3c**

^1H NMR (400 MHz, DMSO-d_6): δ 9.63 (s, 1H, =NH), 9.35 (s, 1H, NH), 8.34 (d, 2H, $J = 8.8$ Hz, ArH), 7.83 (d, 2H, $J = 8.8$ Hz, ArH), 7.71 (s, 1H, CH=); IR (KBr): 3217, 3020, 1671, 1528, 1279, 1136 cm^{-1}; MS: *m/e* $(M+H)^+$ 250.5. Anal. calcd. for $C_{10}H_7N_3O_3S$: C, 48.20; H, 2.83; N, 16.86. Found: C, 48.42; H, 2.85; N, 16.95.

Compound **3d**

^1H NMR (400 MHz, DMSO-d_6): δ 9.61 (s, 1H, =NH), 9.23 (s, 1H, NH), 8.42 (s, 1H, ArH), 8.26 (d, 1H, $J = 8.0$ Hz, ArH), 8.04 (d, 1H, $J = 8.0$ Hz, ArH), 7.81 (s, 1H, CH=); IR (KBr): 3228, 3011, 1689, 1530, 1268, 1141 cm^{-1}; MS: *m/e* $(M+H)^+$ 250.5. Anal. calcd. for $C_{10}H_7N_3O_3S$: C, 48.20; H, 2.83; N, 16.86. Found: C, 48.41; H, 2.85; N, 16.96.

Compound **3e**

^1H NMR (400 MHz, DMSO-d_6) δ 10.09 (s, 1H, OH), 9.29 (s, 1H, =NH), 9.04 (s, 1H, NH), 7.71 (s, 1H, CH=), 7.42 (d, 2H, $J = 8.8$ Hz, ArH), 6.90 (d, 2H, $J = 8.8$ Hz, ArH); IR (KBr): 3207, 3010, 1648, 1588, 1260, 1143 cm^{-1}; MS: *m/e* $(M+H)^+$ 221.5. Anal. calcd. for $C_{10}H_8N_2O_2S$: C, 54.53; H, 3.66; N, 12.72. Found: C, 54.78; H, 3.68; N, 12.78.

Compound **3f**

^1H NMR (400 MHz, DMSO-d_6) δ 9.39 (s, 1H, =NH), 9.12 (s, 1H, NH), 7.76 (s, 1H, CH=), 7.47 (d, 2H, $J = 8.0$ Hz, ArH), 7.33 (d, 2H, $J = 8.0$ Hz, ArH), 2.35 (s, 3H, CH_3); IR (KBr): 3186, 3016, 1677, 1507, 1277, 1145 cm^{-1}; MS: *m/e* $(M+H)^+$ 219.3. Anal. calcd for $C_{11}H_{10}N_2OS$: C, 60.53; H, 4.62; N, 12.83. Found: C, 60.80; H, 4.65; N, 12.90.

Compound **3g**

^1H NMR (400 MHz, DMSO-d_6) δ 9.36 (s, 1H, =NH), 9.09 (s, 1H, NH), 7.76 (s, 1H, CH=), 7.53 (d, 2H, $J = 8.8$ Hz, ArH), 7.10 (d, 2H, $J = 8.8$ Hz, ArH), 3.32 (s, 3H, OCH_3); IR (KBr): 3198, 3003, 1696, 1505, 1255,

1146 cm^{-1}; MS: m/e $(M+H)^+$ 235.6. Anal. calcd. for $C_{11}H_{10}N_2O_2S$: C, 56.40; H, 4.30; N, 11.96. Found: C, 56.65; H, 4.32; N, 12.02.

Compound **3h**

^1H NMR (400 MHz, DMSO-d_6) δ 9.18 (s, 1H, = NH), 8.94 (s, 1H, NH), 7.67 (s, 1H, CH=), 7.43 (d, 2H, $J = 8.8$ Hz, ArH), 6.81 (d, 2H, $J = 8.8$ Hz, ArH), 3.32 [s, 3H, $N(CH_3)_2$]; IR (KBr): 3100, 3002, 1684, 1523, 1269, 1145 cm^{-1}; MS: m/e $(M+H)^+$ 248.6. Anal. calcd. for $C_{12}H_{13}N_3OS$: C, 58.29; H, 5.30; N, 17.00. Found: C, 58.55; H, 5.33; N, 17.09.

Compound **3i**

^1H NMR (400 MHz, DMSO-d_6): δ 9.81 (s, 1H, =NH), 9.44 (s, 1H, NH), 7.76 (s, 1H, CH=), 7.61 (s, 1H, ArH), 7.16 (d, 1H, $J = 8.0$ Hz, ArH), 7.07 (d, 2H, $J = 8.0$ Hz, ArH), 6.02 (s, 2H, OCH_2O); IR (KBr): 3200, 3002, 1666, 1495, 1255, 1144 cm^{-1}; MS: m/e $(M+H)^+$ 249.5. Anal. calcd. for $C_{11}H_8N_2O_3S$: C, 53.21; H, 3.25; N, 11.28. Found: C, 53.44; H, 3.27; N, 11.33.

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