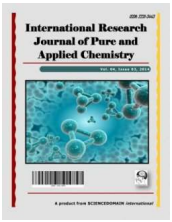


International Research Journal of Pure & Applied Chemistry
11(4): 1-8, 2016, Article no.IRJPAC.25957
ISSN: 2231-3443, NLM ID: 101647669

SCIENCEDOMAIN *international*
www.sciencedomain.org

Synthesis of Novel 2-amino-6-oxo-3-(piperidinylamidino)-4-aryl-6,7-dihydro-pyrano[2,3-d]-5,7-thiazol Derivatives by Domino Reaction under Microwave Irradiation

Hong-Shun Sun[1,2*], Jian-Qiang Wang[1], Da-Wei Gu[1], Cheng Guo[1] and Lin-Jiang Shen[1*]

[1]College of Chemistry and Molecular Engineering, Nanjing Tech University, Nanjing 211816, China.
[2]Department of Chemical Engineering, Nanjing Polytechnic Institute, Nanjing 210048, China.

Authors' contributions

This work was carried out in collaboration between all authors. Authors LJS and CG designed the study and wrote the protocol. Author HSS was involved in the synthesis of all compounds and carried out the structure determination. All authors contributed to the writing of the paper and have read and approved the final manuscript.

Article Information

DOI: 10.9734/IRJPAC/2016/25957
Editor(s):
(1) Martin Kroger, Department of Materials, Computational Polymer Physics, Swiss Federal Institute of Technology (ETH Zürich), Switzerland.
Reviewers:
(1) Claudia Araceli Contreras Celedon, Universidad Michocana de San Nicolás de Hidalgo, Morelia, Mexico.
(2) Manohar V. Lokhande, Sathaye College, Mumbai, India.
(3) S. Srinivas Rao, JNT University Hyderabad, India.
Complete Peer review History: http://sciencedomain.org/review-history/14293

Original Research Article

Received 28th March 2016
Accepted 13th April 2016
Published 21st April 2016

ABSTRACT

Seven novel 2-amino-6-oxo-3-(piperidinylamidino)-4-aryl-6,7-dihydro-pyrano[2,3-d]-5,7-thiazol derivatives, which are different with the products of 2-amino-3-cyano-6-oxo-4-aryl-6,7-dihydro-pyrano[2,3-d]-5,7-thiazol derivatives in the conventional heating conditions, were synthesized by using arylidenemalononitrile, 2,4-thiazolidinedione and piperidine in one-pot via microwave irradiation techniques. The reaction condition is mild and we get these new compounds high-efficiently in a very short reaction times, which provides an elegant methodology for the synthesis of highly functionalized pyrano[3,2-d]-5,7-thiazole derivatives. At the end, the reaction mechanism was

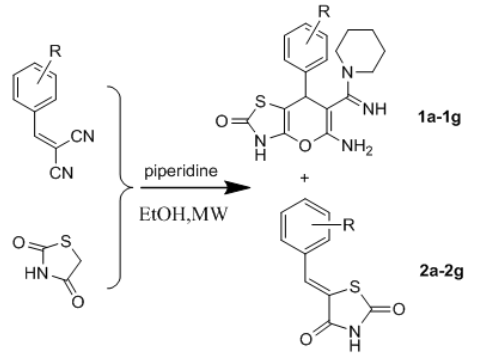
**Corresponding author: E-mail: njutshs@126.com, ljshen@njtech.edu.cn;*

discussed. The structures of these compounds were characterized by ^{1}H NMR, IR, MS and elemental analysis.

Keywords: 2,4-thiazolidinedione; pyrano[2,3-d]-5,7-thiazol; piperidine; microwave irradiation; domino reactions.

1. INTRODUCTION

Modern organic synthesis has benefited from the development of high-efficient synthetic strategy for the selective construction of potentially useful target compounds. Multi-component domino reactions (MDRs) have been successfully applied to total synthesis of natural and natural-like products [1-3], becoming one of the key tools that allows the creation of several bonds in a one pot manner and offers remarkable advantages like convergence, operational simplicity, and facile automation [4-7]. These reactions not only can enable constructing complex structures in a single operation but also avoid tedious isolation and purification work-up. Among these methodologies, MDRs toward the formation of various heterocycles have been extensively studied [8-10]. Therefore, they have played an important role in modern synthetic organic chemistry and drug-discovery research.



a R=H, b R=3-NO_2, c R=2-Cl, d R=4-Cl, e R=2-F, f R=3-F, g R=4-OCH_3

Scheme 1. Reactions of the domino synthesis under MW

Recently, we have reported a domino reaction of arylidenemalononitrile, 2,4-thiazolidinedione and ammonium acetate under microwave irradiation, and we got a series of new thiazolo[4,5-b]pyridine-6-carboxamide derivatives [11]. Considering that many pyran derivatives have been reported to be used as promoting development, antiallergic, antifungal and anticancer drugs [12-15]. On the other hand, thiazoles are known to be highly biologically active reagents [16-19]. Therefore, compounds containing both the pyran and thiazole moities are expected to posses potential biological activities. Thus we report herein the synthesis of heterocyclic compounds containing the two mentioned rings via the domino reaction of arylidenemalononitrile, 2,4-thiazolidinedione and piperidine under microwave irradiation. This reaction is very interesting because the piperidine participated in the reaction lastly and there is an unexpected byproduct of 5-arylidenethiazolidine-2,4-dione (Scheme 1) above.

2. EXPERIMENTAL DETAILS

2.1 General

Microwave irradiation was carried out with an initiator from Biotage, Sweden. Melting points were determined in open capillaries and were uncorrected. IR spectra were taken on a FT-IR-Tensor 27 spectrometer in KBr pellets and reported in cm-1. 1H NMR spectra were measured on a Bruker DPX 500 MHz spectrometer in CDCl3 with chemical shift (d) given in ppm relative to TMS as internal standard. MS (ESI) was determined by using microTOF-Q II HRMS/MS instrument (Bruker). Element analysis was determined by using a Perkin–Elmer 240c elemental analysis instrument.

Arylidenemalononitriles were prepared according to the reported procedures [11]. Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification.

2.2 General Procedure for the Synthesis of Compounds 1 and 2 with Microwave Irradiation

2.2.1 Microwave heating

A mixture of arylidenemalononitrile (10 mmol), 2,4-thiazolidinedione (10 mmol) and piperidine (10 mmol) in ethanol (20 ml)was introduced in a 50 mL Initiator reaction vial. Subsequently, the reaction vial was capped and then pre-stirred for 20 s. The mixture was irradiated (time: 10 min, temperature: 80℃; Absorption Level: High; Fixed

Hold Time) until TLC (petroleum ether: acetic ether 2:1) revealed that conversion of the starting material was completed. The reaction mixture was cooled to room temperature. The resulting precipitate was collected by filtration and washed with heated ethanol. The crude product was recrystallized with a mixture of acetonitrile and N,N-dimthylforamide to give the pure product (**1a–g**). Next, the filtrate was poured to cold water (50 mL). The solid product was collected by Büchner filtration and was purified by recrystallization from 95% ethanol to afford the pure yellow solid (**2a–g**).

2.3 Characterization Data of Selected Compounds

2-amino-6-oxo-3-(piperidinylamidino)-4-phenyl-6,7-dihydro-pyrano[2,3-d]-5,7-thiazol (**1a**): yellow solid; M.p.: 223.1 ~ 223.2℃; ^{1}H NMR($CDCl_3$, 500 MHz) δ: 1.41~1.44(m, 4H, CH_2), 1.49~1.51(m, 2H, CH_2), 3.21~3.31(m, 4H, CH_2), 4.39(br, 1H, =NH), 4.57(s, 1H, CH), 7.06(br 2H, NH_2) 7.26~7.28(m, 3H, ArH),. 7.33 ~7.36(m, 2H, ArH), 9.93(br, 1H, NH); IR (KBr) υ: 3400, 3309, 3248, 3195, 2944, 2854, 1684, 1655, 1589, 1579, 1493, 1468, 1450, 1383, 1264, 1247, 1230, 1212, 1138, 697, 649 cm^{-1}; MS m/z: 356.13, 379.5$(M+Na)^+$, 355.5$(M-H)^-$; Anal. Calcd for $C_{18}H_{20}N_4O_2S$: C, 60.65; H, 5.66; N, 15.72; Found: C, 60.60; H, 5.62; N, 15.76.

2-amino-6-oxo-3-(piperidinylamidino)-4-(3-nitrophenyl)-6,7-dihydro-pyrano[2,3-d]-5,7-thiazol (**1b**) : yellow solid; M.p.: 235.0 ~ 235.9°C; ^{1}H NMR(DMSO-d_6, 500 MHz) δ: 1.45~1.46(m, 4H, CH_2), 1.53~1.54 (m, 2H, CH_2), 3.31~3.34(m, 4H, CH_2), 4.47(br, 1H, =NH), 4.77(d, *J* =2.3Hz, 1H, CH), 7.25(s, 2H, NH_2). 7.68~7.71(t, *J* =9Hz, 1H, ArH), 7.80(d, *J* =7.7Hz, 1H, ArH), 8.16~8.18(m, 2H, ArH). 9.99(s, 1H, NH); IR (KBr) υ: 3404, 3316, 3233, 3203, 2947, 2935, 2850, 1693, 1666, 1644, 1573, 1528, 1479, 1444, 1383, 1353, 1328, 1262, 1250, 1232, 1204, 813, 737 cm^{-1}; MS m/z: 401.12, 402.5 $(M+H)^+$, 424.5$(M+Na)^+$; Anal. Calcd for $C_{18}H_{19}N_5O_4S$: C, 53.85; H, 4.77; N, 17.45; Found: C, 53.80; H, 4.72; N, 17.51.

2-amino-6-oxo-3-(piperidinylamidino)-4-(2-chlorophenyl)-6,7-dihydro-pyrano[2,3-d]-5,7-thiazol (**1c**) : white solid; M.p.: 239.1 ~ 240.2°C; ^{1}H NMR($CDCl_3$, 500 MHz) δ: 1.43~1.47(m, 4H, CH_2), 1.53~1.56 (m, 2H, CH_2), 3.32~3.40(m, 4H, CH_2), 4.30(br, 1H, =NH), 4.99(s, 1H, CH), 7.25(br, 2H, NH_2). 7.31 ~7.33(m, 1H, ArH), 7.35 ~7.38(m, 1H, ArH), 7.42~7.45(m, 1H, ArH). 7.51 (d, *J* =7.8Hz, 1H, ArH), 10.06(br, 1H, NH); IR (KBr) υ: 3412, 3317, 3210, 3093, 3068, 3056, 3010, 2944, 2925, 2852, 1687, 1650, 1586, 1569, 1497, 1467, 1445, 1435, 1369, 1311, 1265, 1245, 1228, 1206, 1189, 1167, 1139, 1120, 1054, 1037, 1024, 996, 758, 743, 725, 704 cm^{-1}; MS m/z: 390.09, 389.3$(M-H)^-$; Anal. Calcd for $C_{18}H_{19}ClN_4O_2S$: C, 55.31; H, 4.90; N, 14.33; Found: C, 55.25; H, 4.96; N, 14.37.

2-amino-6-oxo-3-(piperidinylamidino)-4-(4-chlorophenyl)-6,7-dihydro-pyrano[2,3-d]-5,7-thiazol (**1d**) : yellow solid; M.p.: 221.8 ~ 222.5°C; ^{1}H NMR($CDCl_3$, 500 MHz) δ: 1.44~1.47(m, 4H, CH_2), 1.52~1.54(m, 2H, CH_2), 3.30~3.32 (m, 4H, CH_2), 4.40(br, 1H, =NH), 4.60(d, *J* =2.9Hz, 1H, CH), 7.14(br 2H, NH_2). 7.32(t, *J* =4.6Hz, 2H, ArH), 7.42 ~7.44 (m, 2H, ArH), 9.98(br, 1H, NH); IR (KBr) υ: 3546, 3403, 3331, 3314, 3222, 2937, 2925, 2856, 1724, 1682, 1667, 1627, 1582, 1573, 1490, 1473, 1449, 1343, 1244, 1206, 1091, 1015, 651 cm^{-1}; MS m/z: 390.09, 391.3$(M+H)^+$, 413.3$(M+Na)^+$, 389.1$(M-H)^-$; Anal. Calcd for $C_{18}H_{19}ClN_4O_2S$: C, 55.31; H, 4.90; N, 14.33; Found: C, 55.22; H, 4.97 ; N, 14.30.

2-amino-6-oxo-3-(piperidinylamidino)-4-(2-fluorophenyl)-6,7-dihydro-pyrano[2,3-d]-5,7-thiazol (**1e**) : white solid; M.p.: 226.9 ~ 227.2°C; ^{1}H NMR($CDCl_3$, 500 MHz) δ: 1.43~1.47(m, 4H, CH_2), 1.52~1.55(m, 2H, CH_2), 3.31~3.36(m, 4H, CH_2), 4.43(br, 1H, =NH), 4.93(s, 1H, CH), 7.18(br, 2H, NH_2). 7.21 ~7.27(m, 2H, ArH), 7.31 ~7.40(m, 2H, ArH), 10.04(br, 1H, NH); IR (KBr) υ: 3405, 3313, 3204, 3090, 3065, 3004, 2943, 2924, 2875, 2856, 1685, 1657, 1616, 1591, 1581, 1484, 1454, 1382, 1375, 1363, 1264, 1247, 1231, 1212, 1167, 1139, 1093, 1023, 997, 758, 745, 730 cm^{-1}; MS m/z:374.12, 413.3$(M+K)^+$, 373.1$(M-H)^-$; Anal. Calcd for $C_{18}H_{19}FN_4O_2S$: C, 57.74; H, 5.11; N, 14.96; Found: C, 57.76; H, 5.20; N, 14.90.℃

2-amino-6-oxo-3-(piperidinylamidino)-4-(3-fluorophenyl)-6,7-dihydro-pyrano[2,3-d]-5,7-thiazol (**1f**) : white solid; M.p.: 230.7 ~ 231.9°C; ^{1}H NMR(DMSO-d_6, 500 MHz) δ: 1.44~1.47(m, 4H, CH2), 1.52~1.54(m, 2H, CH_2), 3.21~3.40(m, 4H, CH_2), 4.43(br, 1H, =NH), 4.62(d, *J* =2.5Hz, 1H, CH), 7.09~7.17(m, 5H, ArH and -NH_2), 7.40~7.45(m, 1H, ArH), 9.98(br, 1H, NH); IR (KBr) υ: 3410, 3327, 3277, 3232, 3091, 3062, 2992, 2929, 2855, 1693, 1670, 1633, 1613, 1589, 1572, 1487, 1471, 1449, 1355, 1312, 1259, 1247, 1229, 1201, 1164, 1141, 1025,

1003, 995, 958, 792, 773, 737 cm^{-1}; MS m/z: 374.12, 375.4$(M+H)^+$, 397.4$(M+Na)^+$, 373.1$(M-H)^-$; Anal. Calcd for $C_{18}H_{19}FN_4O_2S$: C, 57.74; H, 5.11; N, 14.96; Found: C, 57.70; H, 5.18; N, 14.90.

2-amino-6-oxo-3-(piperidinylamidino)-4-(4-methoxyphenyl)-6,7-dihydro-pyrano[2,3-d]-5,7-thiazol (**1g**) : yellow solid; M.p.: 222.3 ~ 223.5°C; ^1H NMR($CDCl_3$, 500 MHz) δ: 1.44~1.46(m, 4H, CH_2), 1.52~1.54(m, 2H, CH_2), 3.27~3.32(m, 4H, CH_2), 3.74(s, 3H, CH_3), 4.37(br, 1H, =NH), 4.55(d, *J* =3.3Hz, 1H, CH), 6.91~6.94(m, 2H, ArH), 7.05(br, 2H, NH_2). 7.18~7.21(m, 2H, ArH), 9.95(br, 1H, NH); IR (KBr) u: 3404, 3314, 3222, 2955, 2926, 2857, 1683, 1668, 1626, 1579, 1512, 1472, 1449, 1439, 1344, 1304, 1244, 1227, 1207, 1177, 1144, 1033, 1012, 993, 825, 803, 775, 748, 725 cm^{-1}; MS m/z: 386.14, 387.5$(M+H)^+$,409.6$(M+Na)^+$. Anal. Calcd for $C_{19}H_{22}N_4O_3S$: C, 59.05; H, 5.74; N, 14.50; Found: C, 59.15; H, 5.70; N, 14.53.

(Z)-5-benzylidenethiazolidine-2,4-dione (**2a**): yellow solid;. M.p.: 240.5 ~ 241.7°C (241 ~ 242°C[20]); ^1H NMR (DMSO-d_6, 300 MHz) δ: 7.46 ~ 7.57 (m, 3H, ArH), 7.59 ~ 7.62 (m, 2H, ArH), 7.80 (s, 1H, CH), 12.62 (br, 1H, NH).

(Z)-5-(3-nitrobenzylidene)thiazolidine-2,4-dione (**2b**) : yellow solid; M.p.: 186.4 ~ 187.7°C(187 ~ 189°C[20]); ^1H NMR (CD_3COCD_3, 300 MHz) δ: 7.87 (t, *J* = 8.01 Hz, 1H, ArH), 7.94 (s, 1H, CH), 8.05 (t, *J* = 0.66 Hz, 1H, ArH), 8.32 ~ 8.35 (m, 1H, ArH), 8.48 (d, *J* = 2.07 Hz, 1H, ArH), 11.27 (br, 1H, NH).

(Z)-5-(2-chlorobenzylidene)thiazolidine-2,4-dione (**2c**) : yellow solid; M.p.: 219.9 ~ 221.8°C(241 ~ 242°C[20]); ^1H NMR ($CDCl_3$, 500 MHz) δ: 7.36 ~ 7.39 (m, 2H, ArH), 7.48 ~ 7.53 (m, 2H, ArH), 8.22 (s, 1H, CH), 8.62 (br, 1H, NH).

(Z)-5-(4-chlorobenzylidene)thiazolidine-2,4-dione (**2d**) : yellow solid; M.p.: 224.5 ~ 226.0°C(226 ~ 228°C[20]); ^1H NMR (DMSO- d_6, 300 MHz) δ: 7.36 ~ 7.43 (m, 2H, ArH), 7.65 ~ 7.70 (m, 2H, ArH), 7.81 (s, 1H, CH), 12.63 (br, 1H, NH).

(Z)-5-(2-fluorobenzylidene)thiazolidine-2,4-dione (**2e**) : yellow solid; M.p.: 225.7 ~ 226.8°C(226.4 ~ 227.5°C[21]); ^1H NMR ($CDCl_3$, 500 MHz) δ: 7.16 ~ 7.20 (m, 1H, ArH), 7.27 ~ 7.30 (m, 1H, ArH), 7.43 ~ 7.46 (m, 1H, ArH), 7.47 ~ 7.51 (m, 1H, ArH), 8.10 (s, 1H, CH), 8.28 (br, 1H, NH).

(Z)-5-(3-fluorobenzylidene)thiazolidine-2,4-dione (**2f**) : yellow solid; M.p.: 167.7 ~ 168.8°C(169 ~ 172°C[21]); ^1H NMR ($CDCl_3$, 500 MHz) δ: 7.45~7.49(m, 1H, ArH), 7.29~7.30(m, 1H, ArH), 7.19~7.21(m, 1H, ArH), 7.14~7.18(m, 1H, ArH), 7.81(s, 1H, CH), 3.50(br, 1H, NH).

(Z)-5-(4-methoxybenzylidene)thiazolidine-2,4-dione (**2g**) : yellow solid; M.p.: 217.8 ~ 219.1°C(218 ~ 220°C[20]); ^1H NMR ($CDCl_3$, 500 MHz) δ: 3.87 (m, 3H, OCH_3), 6.92 ~ 7.01 (m, 2H, ArH), 7.28 ~ 7.98 (m, 2H, ArH), 7.80 (s, 1H, CH), 8.19(br, 1H, NH).

3. RESULTS AND DISCUSSION

It has been reported that when a mixture of arylidenemalononitrile, 2,4-thiazolidinedione, and piperidine was refluxed in ethanol, a cycloadduct 2-amino-3-cyano-6-oxo-4-aryl-6,7-dihydro-pyrano[2,3-d] -5,7-thiazol (Chart **1**) was produced in high yields [22]. We repeated the experiment at reflux condition, and we got the same result. On the other hand, when the mixture of arylidenemalononitrile, 2,4-thiazolidinedione and piperidine was stired at room temperature for 48 h, we did not find any chang by monitoring with TLC (petroleum ether: acetic ether 2:1).

Since the reaction time at reflux condition is long, we thought to develop the reaction under microwave irradiation. We started this study by subjecting a preformed arylidenemalononitrile, 2,4-thiazolidinedione and piperidine in ethanol at 60°C for 10 minutes under microwave irradiation. In that time, yellow precipitates were observed. After filtration and analysis, it was surprising to find that the product is not the expected pyrano[3,2-d]-5,7-thiazole. All of the analytical data showed that a piperidine unit was introduced in the final product, and a novel polysubstituted pyrano[3,2-d]-5,7-thiazole derivative containing piperidinylamidino (**1a**) was produced in 55% yield (Scheme 1). In this reaction, piperidine behaves both as a base catalyst and as a nucleophile. When the filtrate

was diluted with cold water, another surprising result occurred, we got a byproduct of 5-benzylidenethiazolidine-2,4-dione **2a** (Scheme 1).

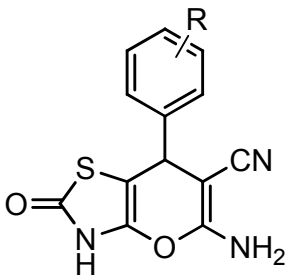


Chart 1. The product structure at reflux condition

To optimize the reaction conditions, the influences of solvent, reaction temperature and amount of piperidine were investigated by using the reaction of benzylidenemalononitrile as an example. The reaction was observed using various solvents, such as ethanol, methanol, acetone, dichloromethane, chloroform, acetonitrile and DMF. Ethanol was proven to be the best solvent (Table 1, entry 1). Subsequently, the reaction was performed and repeated many times in different temperatures in a sealed vessel under microwave irradiation for 10 min. The best yield of product **1a** (65%) was obtained in ethanol as the reaction temperature was increased to 80℃ (Table 1, entry 9). A further increase in reaction temperature failed to improve the yield of the desired product **1a**. On the other hand, we found that an excess of piperidine (1.0, 1.5, or 2.0 times) did not increase the yield of the product **1a**.

Encouraged by the above interesting results, a library of new multi-functionalized pyrano[3,2-d]-5,7-thiazole derivatives **1** was synthesized in order to evaluate the scope of the protocol (Table 2). From these results, we could see that all of the reactions proceeded smoothly to afford the corresponding pyrano[3,2-d]-5,7-thiazole derivatives containing piperidinylamidino in moderate yields (62-75%). At the same time, the byproducts 5-benzylidenethiazolidine-2,4-dione **2** were also separated in low yields(18-28%). Arylidenemalononitrile carrying either electron-donating or electron- withdrawing substituents showed similar reactivity and reacted efficiently to yield the desired product. At the same time, we find that the latter is more beneficial to the reaction than the former. The structures of pyrano[3,2-d]-5,7-thiazole derivatives containing piperid-nylamidino were fully characterized by elemental analysis, ^{1}H NMR, MS, and IR spectra.

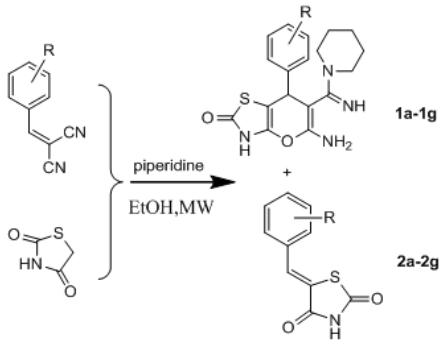
On the basis of experimental results, a reaction mechanism for this domino reaction is postulated in Scheme 2. The first step is a Michael addition of the carbanion of 2,4-thiazolidinedione to arylidenemalononitrile to yield adduct A. This intermediate (A) reacts further by two different paths that yield two different products.

Table 1. Optimization of reaction conditions for 1a

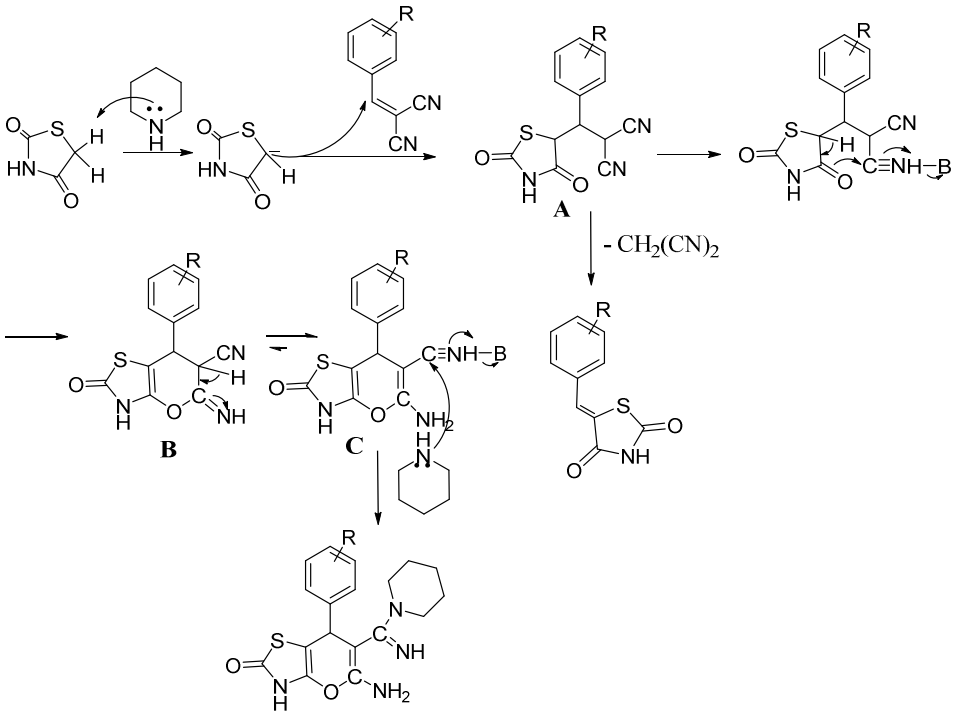
Entry	Solvent	Base(equiv)	T(℃)	Time(min)	Yield (%)
1	EtOH	Piperidine(1.0)	60	10	55
2	MeOH	Piperidine(1.0)	60	10	45
3	CH_3COCH_3	Piperidine(1.0)	60	10	40
4	CH_2Cl_2	Piperidine(1.0)	60	10	20
5	$CHCl_3$	Piperidine(1.0)	60	10	34
6	CH_3CN	Piperidine(1.0)	60	10	50
7	DMF	Piperidine(1.0)	60	10	48
8	EtOH	Piperidine(1.0)	70	10	58
9	EtOH	Piperidine(1.0)	80	10	65
10	EtOH	Piperidine(1.0)	90	10	60
11	EtOH	Piperidine(1.0)	100	10	55
12	EtOH	Piperidine(1.5)	80	10	65
13	EtOH	Piperidine(2.0)	80	10	65

On the first reaction path, the intramolecular cyclization of intermediate A form a pyran ring intermediate (B). Then, H transfer/tautomerism of B gets intermediate (C). Finally the piperidine attacks the cyano group to form the product 1. In this process, piperidine behaves both as a base catalyst and as a nucleophile. On the second path, the intermediate (A) loses a malononitrile molecular to form the byproduct 2.

Table 2. Results of the domino synthesis under MW



Entry	R	Compd	Yield (%)	Compd	Yield (%)
1	H	1a	65	2a	25
2	3-NO_{24}	1b	75	2b	18
3	3-Cl	1c	68	2c	20
4	4-Cl	1d	70	2d	19
5	2-F	1e	73	2e	22
6	3-F	1f	71	2f	21
7	4-OCH_3	1g	62	2g	28



Scheme 2. Formation mechanism for pyrano [3,2-d]-5,7-thiazole derivatives and 5-arylidenethiazolidine-2,4-dione

4. CONCLUSION

In summary, we have developed an interesting domino reaction of 2,4-thiazolidinedione, arylidenemalononitrile and piperidine, and seven new 2-amino-6-oxo-3-(piperidinylamidino)-4-aryl-6,7-dihydro-pyrano[2,3-d]-5,7-thiazol derivatives were synthesized under microwave irradiation which are different with the products of 2-amino-3-cyano- 6-oxo-4-aryl-6,7-dihydro-pyrano[2,3-d]-5,7-thiazol derivatives got in the conventional heating conditions. The mild conditions, the maximum efficiency of a process and short reaction periods as well as operational simplicity are clearly represented in this one-pot transformation that provides an elegant methodology for the synthesis of highly functionalized pyrano[3,2-d]-5,7-thiazole derivatives. Further investigations to evaluate the applicability of this process to a broad range of substrates, synthesizing more complex products and testing their biological activity is an ongoing goal of research in our laboratory.

ACKNOWLEDGEMENTS

We gratefully acknowledge the financial support from the National Natural Science Foundation of China (No. 21106069) and Top-notch Academic Programs Project of Jiangsu Higher Education Institutions (TAPP).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Touré BB, Hall DG. Natural product synthesis using multicomponent reaction strategies. Chem. Rev. 2009;109:4439-4486 .
2. Groenendaal B, Ruijter E, Orru RVA. 1-Azadienes in cycloaddition and multicomponent reactions towards N-heterocycles. Chem. Commun. 2008;43: 5474 -5489.
3. Ismabery N, Lavilla R. Heterocycles as key substrates in multicomponent reactions: The fast lane towards molecular complexity. Chem. Eur. J. 2008;14:8444-8454.
4. Sunderhaus JD, Martin SF. Applications of multicomponent reactions to the synthesis of diverse heterocyclic scaffolds. Chem. Eur. J. 2009;15:1300-1308.
5. Ganem B. Strategies for innovation in multicomponent reaction design. Acc. Chem. Res. 2009;42:463-472.
6. Santra S, Andreana PR. A bioinspired ugi/michael/aza-michael cascade reaction in aqueous media: Natural-product-like molecular diversity. Angew. Chem. Int. Ed. 2011;50:9418-9422.
7. Dömling A, Wang W, Wang K. Chemistry and biology of multicomponent reactions. Chem. Rev. 2012;112:3083-3135.
8. Fustero S, Sánchez-Roselló M, Barrio P, Simón-Fuentes A. From 2000 to mid-2010: A fruitful decade for the synthesis of pyrazoles. Chem. Rev. 2011;111:6984-7034.
9. Li G, Wei HX, Kim SH, Carducci MD. A novel electrophilic diamination reaction of alkenes. Angew. Chem. Int. Ed. 2001;40: 4277-4280.
10. Jiang B, Rajale JT, Wever W, Tu SJ, Li G. Multicomponent reactions for the synthesis of heterocycles. Chem. Asian J. 2010;5: 2318-2335.
11. Sun HS, Wang JQ, Guo C, Shen LJ. The synthesis of 5-amino-2-oxo-7-aryl-2,3,4,7-tetrahydro-1,3-thiazolo[4,5-b] pyridine-6-carboxamide derivatives under microwave irradiation. Chin. J. Org. Chem. 2013;33: 2220-2225.
12. Montandon JB, Zijlatra FJ, Wilson JHP. *In-vitro* versus i*n-vivo* activities of new 5-lipoxygenase inhibitors with antiinflammatory activity. Int J Tissue React. 1989;11:107-112.
13. Brooks GT, Ottridge AP. The effect of some furochromene and benzochromene analogues of 2,2-dimethyl-7-methoxychromene (precocene I) and benzofuran precursors on *Oncopeltus fasciatus* (dallas) and *Locusta migratoria* migratorioides (R&F). Pestic Sci. 1988;22: 41-50.
14. Witte EC, Neubert P. 7-(Piperazinylpropoxy)-2H-1-benzopyran-2-ones. DE3427985; 1986.
15. Sun HB, Hua WY. Studies on potassium channel openers(I)—synthesis and cardiovascular activity of substituted trans-4-amino-3, 4-dihydro-2, 2-dimethyl-2H-1-benzopyran-3-ols. Chem J Chinese U. 1997;18:730-733.
16. Yoshioka T. Fujita T, Kanai TJ. Studies on hindered phenols and analogs. 1. Hypolipidemic and hypoglycemic agents

with ability to inhibit lipid peroxidation. J Med Chem. 1989;32:421-428.
17. Lei Q, Guang B, Wang LB. Synthesis of rosiglitazone. Journal of Sichuan University. 2003;35:107-109.
18. Lu XP. Antidiabetic medicine rosiglitazone. Progress in Pharmaceutical Sciences. 2000;24:122-124.
19. Sohda T. Mizuno K, Imamiya E. Studies on antidiabetic agents. II. synthesis of 5-[4-(1-methylcyclohexylme- thoxy)-benzyl]thiazolidine-2,4-dione (ADD-3878) and its derivatives. Chem. Pharm. Bull. 1982;30:3580-3600.
20. Zhang YL, Zhou ZQ. A solvent-free protocol for the green synthesis of 5-arylidene-2,4-thiazolidinediones using ethylenediamine diacetate as catalyst. Organic Chemistry International. 2012;2012:1-5.
21. Yang DC, An JF, Zhang K. 5-aryl methylene thiazolidine-2,4-diones as PPAR agonist and their preparation. CN102731429; 2012.
22. Rao VS, Grupta SVS, Giridhar P, Ganesh N, Reddy BS. Synthesis of pyranothiazoles and spiro-thiazolidinediones. Indian J. Heterocycl. Chem. 2000;9:247–250.

Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/14293