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Short Communication

Ultrasonics promoted synthesis of thiazolidinones from 2-aminopyridine and 2-picolilamine

Daniela P. Gouvêa, Valéria D.O. Bareño, Juliano Bosenbecker, Bruna B. Drawanz, Patrícia D. Neuenfeldt, Geonir M. Siqueira, Wilson Cunico *

Núcleo de Química Aplicada (NuQuiA), Universidade Federal de Pelotas - UFPel, Campus Universitário, s/n°, 96010-900 Pelotas, RS, Brazil

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ABSTRACT

The efficient multicomponent synthesis of thiazolidinones from the reaction of arenealdehydes, mercaptoacetic acid and 2-picolilamine or 2-aminopyridine under ultrasound irradiation are reported. The reaction with 2-aminopyridine needs a Lewis acid catalysis to afford the corresponding 2-aryl-3-(pyridin-2-yl)-1,3-thiazolidin-4-ones. All novel compounds were identified and characterized by ^{1}H and ^{13}C NMR spectra. Applying the sonochemical methodology, two series of heterocyclic thiazolidinones were synthesized in good yields after short reaction times.

1. Introduction

Ultrasound irradiation has been utilized to accelerate a number of synthetically useful reactions during the last few years. Cavitation is the formation, growth and collapse of bubbles in an irradiated liquid. This effect induces very high local pressure and temperatures inside the bubbles and enhances mass transfer and turbulent flow in the liquid [1]. Ultrasound has been utilized to accelerate a number of synthetically useful reactions, especially in heterocyclic chemistry. The literature reports the sonochemistry synthesis of 1,2,4-oxadiazoles [2], benzoxazoles [3], pyrazoles [4], thiazoles [5], isoxazoles [6], imidazolines [7], thiazolidinones [8], triazoles [9], pyrimidines [10], pyrazolopyridines [11], thiazinanones [12].

For the past five years, our research program has extensively studied the formation five-membered heterocyclic thiazolidinones [13]. Thiazolidinones have valuable biological activities as antitumor [14], antidiabetes [15], antioxidant [16], anti-hepatitis C virus [17], antiinflamatory [18], antimicrobial [19], antitubercular [20], and anti-HIV agents [21]. More recently, we also showed the tuberculostatic activity of such heterocycles [22] and improved the methodologies to synthesis thiazolidinones under solvent-free [13d] and using ultrasound irradiation [13e]. Now, we aim to explore the potential synthetic of different amines (2-aminopyridine and 2-picolilamine) as precursor to the thiazolidinones by sonochemical synthesis.

2. Results and discussion

The study of reaction conditions to afford the thiazolidinone **5k** using ultrasound irradiation was summarized in Table 1. The progresses of reactions were monitored by TLC and GC analysis. It can see clearly that the best condition were achieved when the mercaptoacetic acid were added after the reaction of 3-methoxybenzaldehyde **1k** with 2-aminopyridine 3 (entry 4, 5 and 6). Due the low nucleophilic reactivity of 2-aminopyridine 3, the presence of a Lewis acid (BF_3:MeOH 50%) was necessary and 10 min in ultrasound irradiation to complete the formation of the imine. When the reaction was carried out in a one-pot methodology, low concentration of the desire thiazolidinone **5k** was identified due the formation of the common by-product 2-(3-methoxyphenyl)-1,3-oxathiolan-5-one (entry 1, 3 and 7) [13c]. The complete imine formation decreases the concentration of aldehyde and avoids the formation of by-product.

All (pyridin-2-yl)thiazolidinones **5a–o** were synthesized from the reaction of intermediate imines (formed in situ from arenealdehyde **1a–o** and 2-aminopyridine 3 with a 50% solution of boron trifluoride in methanol for 10 min) with mercaptoacetic acid 2 using ultrasound irradiation for 25 min in good yields (Scheme 1 and Table 2). In this condition, the compounds **5a**, **5b**, **5c**, **5e**, **5g** and **5h** showed low yields due the formation of by-product oxathiolane. The thiazolidinones **5a–o** were also obtained via conventional methodology after 16 h of reaction using catalytic BF_3 to

* Corresponding author.
E-mail addresses: wjcunico@yahoo.com.br, wilson.cunico@ufpel.edu.br (W. Cunico).

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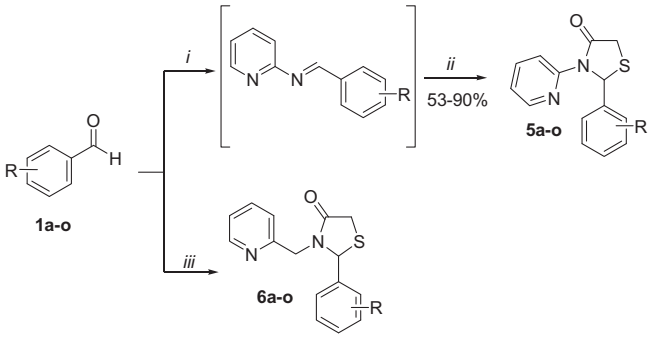
Table 1
Optimization of reaction medium for the synthesis of thiazolidinone **5k** under ultrasonic irradiation.

Entry	Equimolar proportion			Reaction time (min)	BF_3:MeOH	GC-Analyses (%)
	Amine	Aldehyde	Acid			**5k**
1	1	1	3	25	No	46
2	1	1	3	5 + 20[a]	No	52
3	1	1	3	25	10 drops	45
4	1	1	3	5 + 20[a]	10 drops	67
5	1	1	3	10 + 25[a]	10 drops	98
6	1	1	1	10 + 25[a]	10 drops	94
7	1	2	3	10 + 25[a]	10 drops	30

[a] Mercaptoacetic acid added after.



Scheme 1. (i) 2-Aminopyridine **3**, toluene, BF_3:MeOH, ultrasonic irradiation, 10 min. (ii) $HSCH_2COOH$ **2**, ultrasonic irradiation, 25 min. (iii) 2-Picolilamine **4**, toluene, $HSCH_2COOH$ **2**, ultrasonic irradiation, 10 min.

better yields (Table 2). The compounds were confirmed by GC–MS and by melting points and are in agreement with literature data [23–27]. The novel compounds **5d**, 5j and **5n** were also fully characterized by ^1H and ^{13}C NMR (see experimental part).

As expected, the (pyridin-2-ylmethyl)thiazolidinones **6a–o** required less time for complete consumption of the starting materials due the more reactivity of the aliphatic nitrogen of 2-picolilamine **4**. So, those one-pot reactions were carried out in toluene using ultrasound irradiation for 10 min in good yields without any further purification (Scheme 1 and Table 2). Only a few amount of by-product was observed in GC (up to 5%). The heterocycles **6a–o** were confirmed and characterized by ^1H and ^{13}C NMR (see experimental part).

3. Experimental

Unless otherwise indicated, all common reagents and solvents were used as obtained from commercial suppliers without further purification. The reactions were carried out with a microtip probe (3 mm) connected to a 500 Watt Sonics Vibra-cell ultrasonic processor operating at 20 kHz at 25% of the maximum power output. The progress of reactions and the purity of compounds were monitored by thin layer chromatography (TLC, using silica gel 60F253 aluminum sheets; visualization by ultraviolet light 254 nm) and by a Shimadzu Gas Chromatograph GC-2010, Column I.D., 0.25 mm; Column length, 30 m; Column Head Pressure, 14 psi, program: $T_0 = 50\ ^\circ C$; $t_0 = 2.0$ min; rate 16.0 °C/min; $T_f = 250\ ^\circ C$; $t_f = 10.0$ min; Inj. = 250 °C; Det. = 270 °C. Melting points were determined using open capillaries on a Fisatom model 430 apparatus and are uncorrected. GC–MS analyses were performed on a GC 2010-plus GC–MS-QP2010SE System AOC-20i – auto injector. ^1H and ^{13}C NMR spectra were recorded using a Bruker DRX 400 spectrometer (^1H at 400.14 MHz and ^{13}C at 100.61 MHz) or a Bruker Avance 500 spectrometer (^1H at 500.13 MHz and ^{13}C at 125.75 MHz) in $CDCl_3$ containing TMS as in internal standard. Elemental analysis was carried out using a CHN EA 1110; percentages of C, H and N agreed with the product formula (within ±0.4% of theoretical values for elements).

3.1. Conventional synthesis of 2-aryl-3-(pyridin-2-yl)-1,3-thiazolidin-4-ones 5a-o

A mixture of 2-aminopyridine 3 (1 mmol), BF_3:MeOH 50% (10 drops) and corresponding arenaldehyde 1a–o (1 mmol) in toluene (30 mL) was heated at 110 °C with a Dean–Stark trap for 3 h. Afterward, the mercaptoacetic acid 2 (1 mmol) was added and the mixture was heated until the reaction was complete, as shown by TLC (about 16 h). The organic layer was washed with a saturated solution of $NaHCO_3$ (3 x 30 mL), dried with $MgSO_4$ and concentrated to give the products. When necessary, the compounds were washed with a hot solution of hexane:ethyl acetate (9:1) to furnished the pure products.

Table 2
Yields and melting points of 3-(pyridin-2-yl)thiazolidinones **5a–o** and 3-(pyridin-2-ylmethyl)thiazolidinones **6a–o**.

Product	R	m.p.(°C)[a]	Ultrasound yield (%)[b]	Conventional yield (%)[b]	Product	R	m.p.(°C)[a]	Ultrasound yield (%)[b]	Conventional yield (%)[b]
5a [23]	2-NO_2	162–164	61	81	**6a**	2-NO_2	109–112	95	74
5b [23,24]	3-NO_2	153–155	54	74	**6b**	3-NO_2	Oil	79	58
5c [23]	4-NO_2	152–154	57	89	**6c**	4-NO_2	Oil	54	88
5d	2-F	78–80	59	75	**6d**	2-F	Oil	52	70
5e [23]	3-F	Oil	45	50	**6e**	3-F	78–80	83	75
5f [24,17]	4-F	79–82	62	59	**6f**	4-F	Oil	58	43
5g [25]	2-Cl	108–111	29	88	**6g**	2-Cl	53–55	52	98
5h [24]	3-Cl	Oil	30	83	**6h**	3-Cl	Oil	62	98
5i [24]	4-Cl	Oil	50	87	**6i**	4-Cl	88–90	72	59
5j	2-OCH_3	112–115	55	64	**6j**	2-OCH_3	73–74	70	83
5k [24]	3-OCH_3	129–131	69	72	**6k**	3-OCH_3	Oil	70	90
5l [26]	4-OCH_3	102–105	74	64	**6l**	4-OCH_3	Oil	59	99
5m [27]	2-OH	118–120	57	59	**6m**	2-OH	Oil	89	91
5n	3-OH	Oil	53	50	**6n**	3-OH	Oil	63	89
5o [24]	4-CH_3	128–130	73	62	**6o**	4-CH_3	Oil	90	93

[a] Melting points are uncorrected.
[b] Yields of pure compounds.

3.2. Ultrasonics synthesis of 2-aryl-3-(pyridin-2-yl)-1,3-thiazolidin-4-ones 5a-o

In a 25 mL beaker was added a mixture of 2-aminopyridine 3 (1 mmol), BF_3:MeOH 50% (10 drops), and the corresponding arenaldehyde **1a–o** (1 mmol) in toluene (10 mL). The mixture was then sonicated by an ultrasonic probe with a frequency of 20 kHz at room temperature for 10 min. The mercaptoacetic acid 2 (1 mmol) was added and the mixture was sonicated for 25 more minutes until the complete consumption of reagents, as monitored by TLC and GC. The solution was washed with saturated solution of $NaHCO_3$ (3 x 10 mL), dried with $MgSO_4$ and concentrated to give the pure products without any further purification. For thiazolidinones **5a**, **5b**, **5c**, **5e**, 5g and **5h** the pure product were obtained after washed with hot hexane / ethyl acetate 9:1 (3 x 10 mL).

3.2.1. Selected data for 2-(2-fluorophenyl)-3-(pyridin-2-yl)1,3-thiazolidin-4-one **5d**

^{1}H NMR δ (400 MHz, ppm, J_{H-H} = Hz): 8.22 (d, 2H, py and Ph, ^3J = 7.4); 7.70 (dt, 1H, py, ^3J = 8.6, ^4J = 1.8); 7.22 (m, 1H, py); 7.13 (td, 1H, aryl, ^3J = 7.8, ^4J = 1.5); 7.07 (s, 1H, H2); 7.02 (m, 3H, aryl); 4.05 (dd, 1H, H5a, ^2J = 16.0, ^4J = 1.2); 3.78 (d, 1H, H5b, ^2J = 16.0). ^{13}C NMR δ (100 MHz, ppm, J_{C-F} = Hz): 171.5 (C4); 159.9 (d, $^1J_{C-F}$ = 248.4); 150.6; 147.7; 137.8; 129.5 (d, ^3J = 8,8); 126.4; 124.1; 120.6; 116.0 (d, ^2J = 28.0); 57.6 (C2); 34.1 (C5). GC–MS m/z (%): 274 (M, 38); 232 (37), 181 (28), 125 (55), 79 (100).

3.2.2. Selected data for 2-(2-methoxyphenyl)-3-(pyridin-2-yl)1,3-thiazolidin-4-one **5j**

^{1}H NMR δ (400 MHz, ppm, J_{H-H} = Hz): 8.27 (d, 1H, aryl, ^3J = 7.8); 8.23 (dd, 1H, py, ^3J = 5.1, ^4J = 1.9); 7.70 (dt, 1H, py, ^3J = 7.4, ^4J = 1.9); 7.22 (td, 1H, py, ^3J = 7.9, ^4J = 1.5); 7.10 (s, 1H, H2); 6.99 (m, 2H, aryl); 6.90 (d, 1H, aryl, ^3J = 7.8); 6.80 (t, 1H, aryl, ^3J = 7.4); 3.95 (d, 1H, H5a, ^2J = 16.0); 3.92 (s, 3H, OCH_3); 3.70 (d, 1H, H5b, ^2J = 16.0). ^{13}C NMR δ (100 MHz, ppm): 172.1 (C4); 156.3; 150.9; 147.8; 137.7; 129.3; 128.9; 124.8; 120.3; 116.1; 110.9; 58.6 (C2); 55.6 (OCH_3); 34.0 (C5). GC–MS m/z (%): 286 (M, 60); 211 (66), 181 (32), 125 (75), 105 (31), 79 (100).

3.2.3. Selected data for 2-(3-hydroxyphenyl)-3-(pyridin-2-yl)1,3-thiazolidin-4-one **5n**

^{1}H NMR δ (400 MHz, ppm, J_{H-H} = Hz):8.24 (m, 1H, py); 8.06 (d, 1H, py, ^3J = 8.3); 7.70 (td, 1H, py, ^3J = 7.4 Hz, ^4J = 1.9); 7.13 (t, 1H, aryl, ^3J = 7.8); 7.00 (ddd, 1H, aryl, ^3J = 7.4, ^3J = 5.1, ^4J = 1.2); 6.84 (d, 1H, aryl, ^3J = 7.8); 6.81 (s, 1H, H2); 6.76 (t, 1H, aryl, ^4J = 1.9); 6.68 (ddd, 1H, aryl, ^3J = 5.5, ^4J = 2.5, ^4J = 1.2); 4.02 (dd, 1H, H5a, ^2J = 16.4, ^4J = 1.2); 3.79 (d, 1H, H5b, ^2J = 16.0). ^{13}C NMR δ (100 MHz, ppm): 171.5 (C4); 156.1; 150.6; 147.8; 142.8; 137.8; 130.0; 120.9; 118.1; 115,3; 112.7; 62.7 (C2); 34.1 (C5). GC–MS m/z (%): 272 (M, 47); 230 (35), 197 (55), 125 (52), 105 (20), 79 (100).

3.3. Conventional synthesis of 2-aryl-3-(pyridin-2-ylmethyl)-1,3-thiazolidin-4-ones **6a–o**

A mixture of 2-picolilamine **4** (1 mmol), corresponding arenaldehyde **1a–o** (1 mmol) and mercaptoacetic acid 2 (3 mmol) in toluene (30 mL) was heated at 110 °C with a Dean–Stark trap for 16 h. The organic layer was washed with saturated solution of $NaHCO_3$ (3 x 30 mL), dried with $MgSO_4$ and concentrated to give the products. When necessary, the compounds were washed with a hot solution of hexane:ethyl acetate (9:1) to furnished the pure products.

3.4. Ultrasonics synthesis of 2-aryl-3-(pyridin-2-ylmethyl)-1,3-thiazolidin-4-ones **6a–o**

In a 25 mL beaker was added a mixture of 2-picolilamine **4** (1 mmol) the corresponding arenaldehyde **1a–o** (1 mmol) and the mercaptoacetic acid 2 (3 mmol) in toluene (10 mL). The reaction mixture was sonicated by an ultrasonic probe with a frequency of 20 kHz at room temperature for 10 min (until complete consumption of starting materials, as monitored by TLC and GC). The solution was washed with saturated solution of $NaHCO_3$ (3 x 10 mL), dried with $MgSO_4$ and concentrated to give the pure products without any further purification.

3.4.1. Selected data for 2-(2-nitrophenyl)-3-(pyridin-2-ylmethyl)1,3-thiazolidin-4-one **6a**

^{1}H NMR δ (400 MHz, ppm, J_{H-H} = Hz): 8.49 (d, 1H, py, ^3J = 5.1); 8.19 (m, 1H, aryl); 8.14 (t, 1H, py, ^4J = 2.0); 7.65 (m, 2H, py and aryl); 7.56 (t, 1H, aryl, ^3J = 8.2); 7.22 (m, 2H, aryl); 5.89 (d, 1H, H2, ^4J = 2.0); 5.02 (d, 1H, CH_2a, ^2J = 15.2); 3.96 (d, 1H, CH_2b, ^2J = 15.2); 3.93 (dd, 1H, H5a, ^2J = 15.6, ^4J = 2.0); 3.82 (d, 1H, H5b, ^2J = 15.6). ^{13}C NMR δ (100 MHz, ppm): 171.4 (C4); 154.9; 149.4; 141.6; 137.1; 133.4; 130.0; 124.0; 122.9; 122.6; 62.7 (C2); 48.1 (CH_2); 32.7 (C5).

3.4.2. Selected data for 2-(3-nitrophenyl)-3-(pyridin-2-ylmethyl)1,3-thiazolidin-4-one **6b**

^{1}H NMR δ (400 MHz, ppm, J_{H-H} = Hz): 8.47 (m, 1H, py); 8.11 (dd, 1H, aryl, ^3J = 8.2, ^4J = 1.8); 7.70 (dd, 1H, py, ^3J = 7.6, ^4J = 1.8); 7.49 (m, 2H, py and aryl); 7.24 (m, 2H, aryl); 7.19 (m, 1H, aryl); 6.28 (d, 1H, H2, ^4J = 1.2); 5.24 (d, 1H, CH_2a, ^2J = 15.0); 3.86 (d, 1H, H5a, ^2J = 14.6); 3.75 (d, 2H, CH2b and H5b, ^2J = 15.0 Hz). ^{13}C NMR δ (100 MHz, ppm): 171.0 (C4); 163.9; 154.5; 148.1; 142.3; 135.9; 132.0; 123.3; 121.8; 121.5; 117.5; 114.9; 62.9 (C2); 47.8 (CH_2); 32.6 (C5).

3.4.3. Selected data for 2-(4-nitrophenyl)-3-(pyridin-2-ylmethyl)1,3-thiazolidin-4-one **6c**

^{1}H NMR δ (400 MHz, ppm, J_{H-H} = Hz): 8.48 (d, 1H, py, ^3J = 4.2); 7.63 (dd, 1H, py, ^3J = 7.8, ^4J = 2.0); 7.28 (d, 2H, aryl, ^3J = 7.8); 7.20 (m, 1H, py); 7.15 (m, 1H, aryl); 6.92 (d, 2H, aryl, ^3J = 8.0); 5.88 (s, 1H, H2); 5.12 (d, 1H, CH_2a, ^2J = 14.6); 3.91 (d, 2H, CH_2b and H5a, ^2J = 14.8); 3.81 (d, 1H, H5b, ^2J = 15.2). ^{13}C NMR δ (100 MHz, ppm): 169.9 (C4); 161.4; 154.6; 149.8; 141.8; 136.6; 130.1; 123.5; 123.0; 122.1; 116.9; 115.4; 62.5 (C2); 49.1 (CH_2); 33.0 (C5).

3.4.4. Selected data for 2-(2-fluorophenyl)-3-(pyridin-2-ylmethyl)1,3-thiazolidin-4-one **6d**

^{1}H NMR δ (400 MHz, ppm, J_{H-H} = Hz): 8.51 (d, 1H, py, ^3J = 4.0); 7.66 (dd, 1H, py, ^3J = 8.0, ^4J = 1.9); 7.37 (dd, 1H, py, ^3J = 8.0, ^4J = 2.0); 7.25 (dd, 1H, aryl, ^3J = 7.8, ^4J = 1.8); 7.25 (m, 2H, aryl); 7.10 (m, 1H, aryl); 5.79 (s, 1H, H2); 5.08 (d, 1H, CH_2a, ^2J = 14.8); 3.86 (d, 2H, CH_2b and H5a, ^2J = 14.8); 3.71 (d, 1H, H5b, ^2J = 15.0). ^{13}C NMR δ (100 MHz, ppm, J_{C-F} = Hz): 170.4 (C4); 163.4 (d, $^1J_{C-F}$ = 248.4); 156.0; 149.1; 144.1 (d, $^4J_{C-F}$ = 5.8); 135.1; 130.2 (d, $^3J_{C-F}$ = 9.4); 122.9; 122.0; 121.2; 117.3 (d, $^2J_{C-F}$ = 22.4); 115.6 (d, $^2J_{C-F}$ = 22.0); 62.7 (C2); 48.3 (CH_2); 33.0 (C5). Anal. Calcd for $C_{15}H_{13}FN_2OS$: C, 62.48; H, 4.54; N, 9.72. Found: C, 62.40; H, 4.79; N, 9.81.

3.4.5. Selected data for 2-(3-fluorophenyl)-3-(pyridin-2-ylmethyl)1,3-thiazolidin-4-one **6e**

^{1}H NMR δ (500 MHz, ppm, J_{H-H} = Hz): 8.53 (d, 1H, py, ^3J = 3.9); 7.63 (dd, 1H, py, ^3J = 7.8, ^4J = 1.9); 7.33 (dd, 1H, py, ^3J = 7.8, ^4J = 1.9); 7.18 (m, 2H, aryl); 7.00 (m, 2H, aryl); 7.07 (d, 1H, aryl, ^3J = 7.8 Hz); 7.02 (m, 1H, aryl); 5.75 (s, 1H, H2); 5.06 (d, 1H, CH_2a, ^2J = 14.6); 3.88 (d, 2H, CH_2b and H5a, ^2J = 14.6); 3.79 (d, 1H, H5b, ^2J = 15.6). ^{13}C NMR δ (125 MHz, ppm, J_{C-F} = Hz): 171.6 (C4);

163.2 (d, $^1J_{C-F}$ = 249.2); 155.5; 149.7; 142.0 (d, $^4J_{C-F}$ = 5.5); 136.9; 130.8 (d, $^3J_{C-F}$ = 9.1); 123.1; 122.8; 122.6; 116.3 (d, $^2J_{C-F}$ = 22.0); 114.4 (d, $^2J_{C-F}$ = 22.0); 63.0 (C2); 48.1 (CH_2); 32.8 (C5). Anal. Calcd for $C_{15}H_{13}FN_2OS$: C, 62.48; H, 4.54; N, 9.72. Found: C, 62.46; H, 4.89; N, 9.80.

3.4.6. Selected data for 2-(4-fluorophenyl)-3-(pyridin-2-ylmethyl)1,3-thiazolidin-4-one ***6f***

^{1}H NMR δ (400 MHz, ppm, J_{H-H} = Hz): 8.49 (d, 1H, py, ^3J = 3.8); 7.60 (dd, 1H, py, ^3J = 7.8, ^4J = 2.2); 7.29 (d, 2H, aryl, ^3J = 7.8); 7.18 (m, 1H, py); 7.13 (m, 1H, aryl); 6.89 (d, 2H, aryl, ^3J = 7.8); 5.85 (s, 1H, H2); 5.15 (d, 1H, CH_2a, ^2J = 14.8); 3.88 (d, 2H, CH_2b and H5a, ^2J = 14.8); 3.74 (d, 1H, H5b, ^2J = 15.2). ^{13}C NMR δ (100 MHz, ppm, J_{C-F} = Hz): 169.9 (C4); 164.6 (d, $^1J_{C-F}$ = 247.8); 157.0; 149.1; 141.8 (d, $^4J_{C-F}$ = 6.0); 136.7; 131.2 (d, $^3J_{C-F}$ = 9.4); 123.1; 122.7; 122.6; 117.5 (d, $^2J_{C-F}$ = 21.8); 115.4 (d, $^2J_{C-F}$ = 22.0); 64.1 (C2); 49.3 (CH_2); 32.5 (C5). Anal. Calcd for $C_{15}H_{13}FN_2OS$: C, 62.48; H, 4.54; N, 9.72. Found: C, 62.53; H, 4.62; N, 9.88.

3.4.7. Selected data for 2-(2-chlorophenyl)-3-(pyridin-2-ylmethyl)1,3-thiazolidin-4-one ***6g***

^{1}H NMR δ (400 MHz, ppm, J_{H-H} = Hz): 8.55 (d, 1H, py, ^3J = 3.8); 7.62 (dd, 1H, py, ^3J = 8.0, ^4J = 2.0); 7.30 (dd, 1H, py, ^3J = 8.0, ^4J = 2.0); 7.20 (dd, 1H, aryl, ^3J = 7.8, ^4J = 2.0); 7.16 (m, 2H, aryl); 7.08 (dd, 1H, aryl, ^3J = 8.0, ^4J = 2.0); 5.71 (s, 1H, H2); 5.11 (d, 1H, CH_2a, ^2J = 14.8); 3.89 (d, 2H, CH_2b and H5a, ^2J = 14.6); 3.69 (d, 1H, H5b, ^2J = 15.0). ^{13}C NMR δ (100 MHz, ppm): 170.0 (C4); 164.1; 155.1; 149.6; 141.5; 136.0; 130.1; 122.9; 122.4; 120.6; 118.4; 115.5; 63.1 (C2); 48.1 (CH_2); 33.1 (C5). Anal. Calcd for $C_{15}H_{13}ClN_2OS$: C, 59.11; H, 4.30; N, 9.19. Found: C, 59.00; H, 4.41; N, 9.12.

3.4.8. Selected data for 2-(3-chlorophenyl)-3-(pyridin-2-ylmethyl)1,3-thiazolidin-4-one ***6h***

^{1}H NMR δ (400 MHz, ppm, J_{H-H} = Hz): 8.39 (d, 1H, py, ^3J = 4.2); 7.66 (m, 1H, py); 7.27 (dd, 1H, py, ^3J = 8.0, ^4J = 2.0); 7.15 (m, 2H, aryl); 7.01 (m, 2H, aryl); 6.96 (d, 1H, aryl, ^3J = 8.0); 6.90 (m, 1H, aryl); 5.62 (s, 1H, H2); 5.06 (d, 1H, CH_2a, ^2J = 14.0); 4.01 (d, 2H, CH_2b and H5a, ^2J = 14.8); 3.77 (d, 1H, H5b, ^2J = 15.0). ^{13}C NMR δ (100 MHz, ppm): 171.4 (C4); 162.4; 152.9; 148.2; 142.2; 138.5; 130.0; 123.4; 122.6; 121.9; 116.3; 114.5; 59.9 (C2); 47.5 (CH_2); 32.9 (C5). Anal. Calcd for $C_{15}H_{13}ClN_2OS$: C, 59.11; H, 4.30; N, 9.19. Found: C, 59.20; H, 4.39; N, 9.22.

3.4.9. Selected data for 2-(4-chlorophenyl)-3-(pyridin-2-ylmethyl)1,3-thiazolidin-4-one ***6i***

^{1}H NMR δ (400 MHz, ppm, J_{H-H} = Hz): 8.53 (d, 1H, py, ^3J = 4.2); 7.64 (td, 1H, py, ^3J = 7.4, ^4J = 1.5); 7.33 (d, 2H, aryl, ^3J = 8.2); 7.21 (m, 4H, py and aryl); 5.74 (br, 1H, H2); 5.04 (d, 1H, CH_2a, ^2J = 15.2); 3.88 (dd, 1H, H5a, ^2J = 15.6, ^4J = 1.9); 3.85 (d, 1H, CH_2b, ^2J = 15.2); 3.79 (d, 1H, H5b, ^2J = 15.6). ^{13}C NMR δ (100 MHz, ppm, J_{C-F} = Hz): 171.4 (C4); 155.3; 149.5; 137.5; 136.8; 129.2; 128.8; 122.6; 122.5; 62.8 (C2); 47.8 (CH_2); 32.8 (C5). Anal. Calcd for $C_{15}H_{13}ClN_2OS$: C, 59.11; H, 4.30; N, 9.19. Found: C, 58.98; H, 4.21; N, 9.33.

3.4.10. Selected data for 2-(2-methoxyphenyl)-3-(pyridin-2-ylmethyl) 1,3-thiazolidin-4-one ***6j***

^{1}H NMR δ (400 MHz, ppm, J_{H-H} = Hz): 8.51 (d, 1H, py, ^3J = 3.9); 7.67 (td, 1H, py, ^3J = 7.8, ^4J = 2.0); 7.29 (dd, 1H, py, ^3J = 8.2, ^4J = 1.5); 7.21 (m, 2H, py and aryl); 7.11 (dd, 1H, aryl ^3J = .7.9, ^4J = 1.6); 6.93 (td, 1H, aryl, ^3J = 7.4, ^4J = 1.1); 6.86 (d, 1H, aryl, ^3J = 7.8); 5.95 (d, 1H, H2, ^4J = 1.6); 5.13 (d, 1H, CH_2a, ^2J = 15.7); 3.97 (d, 1H, CH_2b, ^2J = 15.7); 3.83 (dd, 1H, H5a, ^2J = 15.6, ^4J = 1.6); 3.77 (s, 3H, OMe); 3.70 (d, 1H, H5b, ^2J = 15.6). ^{13}C NMR δ (100 MHz, ppm): 172.5 (C4); 157.0; 155.5; 149.0; 137.2; 129.9; 127.0; 122.7; 120.8; 111.1; 58.5 (C2); 55.5 (OMe); 48.0 (CH_2); 32.5 (C5). Anal. Calcd for $C_{16}H_{16}N_2O_2S$: C, 63.98; H, 5.37; N, 9.33. Found: C, 64.05; H, 5.21; N, 9.57.

3.4.11. Selected data for 2-(3-methoxyphenyl)-3-(pyridin-2-ylmethyl) 1,3-thiazolidin-4-one ***6k***

^{1}H NMR δ (400 MHz, ppm, J_{H-H} = Hz): 8.53 (d, 1H, py, ^3J = 4.0); 7.63 (dd, 1H, py, ^3J = 8.0, ^4J = 1.9); 7.32 (dd, 1H, py, ^3J = 7.8, ^4J = 1.9); 7.20 (m, 2H, aryl); 7.01 (m, 2H, aryl); 6.89 (d, 1H, aryl, ^3J = 8.0); 7.02 (m, 1H, aryl); 5.78 (s, 1H, H2); 5.03 (d, 1H, CH_2a, ^2J = 15.0); 3.93 (d, 2H, CH_2b and H5a, ^2J = 14.8); 3.81 (s, 3H, OCH_3); 3.77 (d, 1H, H5b, ^2J = 15.6). ^{13}C NMR δ (100 MHz, ppm): 170.6 (C4); 163.2; 155.4; 149.6; 139.9; 136.4; 130.2; 124.6; 122.5; 121.9; 117.3; 114.4; 62.3 (C2); 55.9 (OCH_3); 48.6 (CH_2); 32.5 (C5). Anal. Calcd for $C_{16}H_{16}N_2O_2S$: C, 63.98; H, 5.37; N, 9.33. Found: C, 64.25; H, 5.55; N, 9.45.

3.4.12. Selected data for 2-(4-methoxyphenyl)-3-(pyridin-2-ylmethyl) 1,3-thiazolidin-4-one ***6l***

^{1}H NMR δ (500 MHz, ppm, J_{H-H} = Hz): 8.52 (d, 1H, py, ^3J = 4.9); 7.62 (td, 1H, py, ^3J = 7.8, ^4J = 1.9); 7.22 (d, 2H, aryl, ^3J = 8.8); 7.18 (m, 1H, py); 7.15 (m, 1H, aryl); 6.87 (d, 2H, aryl, ^3J = 8.8); 5.71 (s, 1H, H2); 5.02 (d, 1H, CH_2a, ^2J = 15.6); 3.88 (m, 2H, CH_2b and H5a); 3.81 (s, 3H, OCH_3); 3.79 (d, 1H, H5b, ^2J = 14.6). ^{13}C NMR δ (125 MHz, ppm): 171.6 (C4); 160.4; 155.8; 149.7; 130.8; 129.1; 128.0; 122.6; 122.5; 114.5; 63.4 (C2); 55.5 (OCH_3); 47.9 (CH_2); 33.2 (C5). Anal. Calcd for $C_{16}H_{16}N_2O_2S$: C, 63.98; H, 5.37; N, 9.33. Found: C, 63.87; H, 5.31; N, 9.20.

3.4.13. Selected data for 2-(2-hydroxyphenyl)-3-(pyridin-2-ylmethyl) 1,3-thiazolidin-4-one ***6m***

^{1}H NMR δ (400 MHz, ppm, J_{H-H} = Hz): 8.51 (d, 1H, py, ^3J = 3.5); 7.68 (dt, 1H, py, ^3J = 7.4, ^4J = 1.9); 7.24 (m, 2H, py and aryl); 7.13 (t, 1H, aryl, ^3J = 7.8); 6.73 (m, 3H, aryl); 5.63 (d, 1H, H2, ^4J = 1.9); 5.07 (d, 1H, CH_2a, ^2J = 15.7); 3.96 (d, 1H, CH_2b, ^2J = 15.6); 3.87 (dd, 1H, H5a, ^2J = 15.6, ^4J = 1.6); 3.76 (d, 1H, H5b, ^2J = 15.6). ^{13}C NMR δ (100 MHz, ppm): 172.0 (C4); 157.5; 155.3; 148.9; 140.4; 137.4; 130.2; 122.9; 122.8; 118.4; 116.5; 113.9; 63.5 (C2); 47.7 (CH_2); 32.7 (C5). Anal. Calcd for $C_{15}H_{14}N_2O_2S$: C, 62.92; H, 4.93; N, 9.78. Found: C, 62.89; H, 5.11; N, 9.53.

3.4.14. Selected data for 2-(3-hydroxyphenyl)-3-(pyridin-2-ylmethyl) 1,3-thiazolidin-4-one ***6n***

^{1}H NMR δ (400 MHz, ppm, J_{H-H} = Hz): 8.57 (m, 1H, py); 7.63 (m, 1H, py); 7.28 (dd, 1H, py, ^3J = 8.2, ^4J = 1.9); 7.14 (m, 2H, aryl); 7.01 (m, 2H, aryl); 6.94 (d, 1H, aryl, ^3J = 8.0); 7.02 (m, 1H, aryl); 5.89 (d, 1H, H2, ^4J = 1.0); 5.10 (d, 1H, CH_2a, ^2J = 14.8); 3.88 (d, 2H, CH_2b and H5a, ^2J = 14.6); 3.72 (d, 1H, H5b, ^2J = 15.0). ^{13}C NMR δ (100 MHz, ppm): 172.9 (C4); 162.8; 155.9; 148.2; 141.9; 132.1; 129.4; 124.4; 121.9; 116.3; 113.9; 59.9 (C2); 49.9 (CH_2); 32.9 (C5). Anal. Calcd for $C_{15}H_{14}N_2O_2S$: C, 62.92; H, 4.93; N, 9.78. Found: C, 63.07; H, 5.15; N, 9.97.

3.4.15. Selected data for 2-(4-methylphenyl)-3-(pyridin-2-ylmethyl) 1,3-thiazolidin-4-one ***6o***

^{1}H NMR δ (400 MHz, ppm, J_{H-H} = Hz): 8.50 (d, 1H, py, ^3J = 4.0); 7.65 (td, 1H, py, ^3J = 8.0, ^4J = 1.9); 7.18 (d, 2H, aryl, ^3J = 8.2); 7.17 (m, 1H, py); 7.12 (m, 1H, aryl); 6.89 (d, 2H, aryl, ^3J = 8.2); 5.88 (s, 1H, H2); 5.02 (d, 1H, CH_2a, ^2J = 15.0); 3.88 (m, 2H, CH_2b and H5a); 3.76 (d, 1H, H5b, ^2J = 14.6); 2.31 (s, 3H, CH_3). ^{13}C NMR δ (100 MHz, ppm): 170.9 (C4); 163.8; 155.3; 150.7; 131.8; 129.6; 128.3; 123.0; 122.6; 115.1; 63.4 (C2); 47.9 (CH_2); 33.5 (C5); 20.8 (CH_3). Anal. Calcd for $C_{16}H_{16}N_2OS$: C, 67.58; H, 5.67; N, 9.85. Found: C, 67.76; H, 5.88; N, 9.91.

4. Conclusion

In summary, we applied the ultrasound methodology to promote the synthesis of heterocyclic thiazolidinones in good yields and good purities. The reaction times were lower than conventional synthetic methodology, however, even using ultrasound irradiation, the 3-(pyridin-2-yl) thiazolidinones **5a–o** needed a Lewis acid catalysis.

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