Phase-transfer catalyzed, energy-efficient and facile synthesis of 5-arylidene-1,3-thiazolidine-2,4-diones was developed. Three independent variables (temperature, bases and phase-transfer catalyst (PTC)) were screened through one-factor-at-a time (OFAT) study. The optimum reaction conditions suggested by the OFAT analysis were the use of tetrabutylammonium bromide (8 mol%) and potassium carbonate (1 mmol) for the reaction at 100°C. The nitrogen of PTC stabilizes carbonyl groups of thiazolidine-2,4-dione (TZD). The active methylene hydrogen of TZD forms potassium salt with potassium carbonate and generates 5-arylidene-1,3-thiazolidine-2,4-diones (1–16) through nucleophilic attack on the carbonyl carbon of arylaldehydes. The prominent advantages of this new process are economic viability, shorter reaction time (15 min), simple product isolation (non-chromatographic method), good to excellent yields (78–96%) and solvent-free conditions.

Keywords: phase-transfer catalyst; Knoevenagel condensation; 5-arylidene-1,3-thiazolidine-2,4-dione; OFAT study; green synthesis

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1. Introduction

Design of benign organic transformations to reduce, eliminate and replace hazardous resources (energy and solvents) is a major concern of green chemistry.[1] Knoevenagel condensation generates carbon–carbon (C–C) bonds and plays a pivotal role in synthetic transformations of medicinal chemistry research.[2] Knoevenagel condensation is useful in the construction of clinical candidates [3] such as pioglitazone, rosiglitazone and englitazone (PPARγ agonists), epalrestat (aldose reductase inhibitor), nifedipine (calcium channel blocker), atorvastatin (HMG-CoA reductase inhibitor), entacapone (COMT inhibitor), sulindac (anti-inflammatory agent) and lumefantrin (antimalarial agent).

The Knoevenagel condensation of the active methylene group of thiazolidinone (1,3-thiazolidine-2,4-dione/rhodanine) and aryl aldehydes generates 5-aryldene-thiazolidinones. These scaffolds exhibited antidiabetic,[4] antimicrobial [5] and anti-cancer [6] properties. The literature demonstrates the aldose reductase,[7] β-lactamase,[8] hepatitis C virus protease,[9] JNK stimulatory phosphatase 1 (JSP 1), [10] tyrosine phosphatase,[11] protein mannosyl transferase 1 (PMT1) [12] and enoyl-acyl carrier protein (enoyl-ACP) reductase [13] inhibitory potentials of 5-arylidene-thiazolidinones. The representative analogues are under clinical development for their inhibitory potential against phospholipase A2, cyclooxygenase-2 and 5-lipoxygenase.[14] The agonistic activity of these molecules on peroxisome proliferator-activated receptor gamma (PPARγ) and free fatty acid receptors (FFAR1 and FFAR2) is well appreciated.[15,16]

These prominent properties prompted medicinal chemists to develop a facile and efficient process for the generation of 5-arylidene-1,3-thiazolidine-2,4-diones. Several bases such as piperidine,[17] piperidinium acetate,[18] sodium acetate [19] and ammonium acetate [20] were utilized to accelerate the Knoevenagel condensation. The catalytic function of urea and thiourea,[16] benzoic acid,[21] polyethylene glycol-300,[22] potash alum,[23] L-proline,[23] boric acid,[23] oxalic acid,[23] ionic liquids,[24] Bakers yeast,[25] Mg-doped Ce–Zr [26] and morpholine [27] were utilized in the improved syntheses.

Microwave,[28] ultrasonication [29] and grinding-assisted methods [30] were also utilized to improve the yield of 5-arylidene-1,3-thiazolidine-2,4-diones. However, these methods are associated with limitations, such as low yield, prolonged heating, toxic residues, carcinogenic amines, expensive catalysts and are of important environmental concern. Hence, an efficient and versatile procedure (mild reaction conditions) to construct 5-arylidene-1,3-thiazolidine-2,4-diones is in great demand. Phase-transfer catalysts (PTCs) are one of the most powerful greener tools in fine chemical synthesis.[31]

In light of the above-mentioned facts, the effect of eight PTCs in the synthesis of 5-arylidene-1,3-thiazolidine-2,4-diones was investigated and were found to be effective promoters.

2. Results and discussion

In continuation of our research interest on PTCs,[32,33] herein we report that the PTC promoted efficient synthesis of 5-arylidene-1,3-thiazolidine-2,4-diones (Scheme 1) through Knoevenagel condensation. The condensation of anisaldehyde and 2,4-thiazolidinedione generated 5-(4-methoxybenzylidene)-1,3-thiazolidine-2,4-dione (compound 1) and was selected as our model reaction. The effects of temperature, bases and catalysts (PTCs) in the model reaction were examined. The reaction at room temperature with tetrabutylammonium bromide (TBAB) and piperidine gave trace yields (detected in TLC) and the reaction at 60°C produced 38% yield (requires purification). However, the reaction at 100°C gave higher yield (52%) of compound 1.
Table 1. TBAB catalyzed condensation of 4-methoxybenzaldehyde and thiazolidine-2,4-dione using different bases.

| Entry | Bases                | Concentration (mmol) | Yield (%) |
|-------|----------------------|----------------------|-----------|
| 1     | Piperidine           | 2                    | 52        |
| 2     | Potassium carbonate  | 2                    | 69        |
| 3     | Potassium carbonate  | 1.5                  | 81        |
| 4     | Potassium carbonate  | 1                    | 91        |
| 5     | Potassium carbonate  | 0.5                  | 43        |
| 6     | Tyrosine             | 2                    | Trace*    |
| 7     | Ammonium acetate     | 2                    | 47        |
| 8     | Potassium hydroxide  | 2                    | 58        |
| 9     | Potassium phosphate  | 2                    | Trace*    |
| 7     | Triethyl amine       | 2                    | 26        |

Note: Reaction conditions: 4-methoxybenzaldehyde (5 mmol), thiazolidine-2,4-dione (5 mmol), TBAB (10 mol%), heated with stirring at 100°C for 15 min; * = detected in TLC.

At higher temperatures, collision of molecules is appreciable due to their substantial kinetic energy and enhances the reaction yield.

The effect of seven different bases, namely piperidine, potassium carbonate, tyrosine, ammonium acetate, potassium hydroxide, potassium phosphate and triethyl amine at 2 mmol concentration was studied. In the presence of potassium carbonate, the reaction gave a good yield (69%, Table 1, entry 2) of compound 1. The reaction with potassium hydroxide, piperidine and ammonium acetate produced fairly good yields (58%, 52% and 47%, respectively), while triethyl amine produced a very poor yield (26%). However, tyrosine and potassium phosphate gave only trace yields. Potassium carbonate was chosen as the suitable base from this analysis for further investigation and it was examined at four different concentrations (0.5, 1, 1.5 and 2 mmol). The reaction with 1 mmol concentration of potassium carbonate gave excellent yield (91%, Table 1, entry 4).

The catalytic potential of eight PTCs, namely TBAB, benzyltriethylammonium chloride (BTEAC), benzyltrimethylammonium chloride (BTMAC), tetrapropylammonium bromide
Table 2. Condensation of 4-methoxybenzadehyde and thiazolidine-2,4-dione using different PTCs.

| Entry | Catalysts | Concentration (mol%) | Yield (%) |
|-------|-----------|----------------------|-----------|
| 1     | TBAB      | 10                   | 91        |
| 2     | TBAB      | 12                   | 72        |
| 3     | TBAB      | 8                    | 96        |
| 4     | TBAB      | 6                    | 69        |
| 5     | BTEAC     | 10                   | 51        |
| 6     | BTMAC     | 10                   | 45        |
| 7     | TPAB      | 10                   | 49        |
| 8     | CTAB      | 10                   | 21        |
| 9     | TBAI      | 10                   | 53        |
| 10    | TPEAC     | 10                   | 48        |
| 11    | TEAB      | 10                   | 37        |

Note: Reaction conditions: 4-methoxybenzadehyde (5 mmol), thiazolidine-2,4-dione (5 mmol), potassium carbonate (10 mol%), heated with stirring at 100°C for 15 min.

(TPAB), cetyltrimethylammonium bromide (CTAB), tetrabutylammonium iodide (TBAI), triphenylethylammonium chloride (TPEAC) and tetaethylammonium bromide (TEAB) at 10 mol% was investigated next. The reaction with potassium carbonate (1 mmol) and TBAB (10 mol%) exhibited the highest catalytic potential (91%, Table 2, entry 1). This analysis permitted the ranking of catalysts as TBAB > TBAI > BTEAC > TPAB > TPEAC > TEAB > BTMAC > CTAB. Higher catalytic potential of TBAB, TBAI and BTEAC reactions can be correlated with their substrate extraction potential (TBAB > TBAI > BTEAC). The reason for the lower catalytic function of CTAB is the high aliphatic load.[34,35] The catalytic potential of TBAB at four different concentrations (6, 8, 10 and 12 mol%) was explored further. TBAB at 8 mol% in the presence of potassium carbonate (1 mmol) produced a very high yield (96%, Table 2, entry 3).

Scheme 2. Phase transfer catalysis mechanism involved between the two phases in the Knoevenagel condensation [14, 26].
Further increase in the catalyst concentration did not produce a significant effect on the yield enhancement.

The synthesis of 5-(4-hydroxybenzylidene)-1,3-thiazolidine-2,4-dione (2) under the heterogeneous system ($n$-butanol and water, 1:1) was performed in order to investigate the substrate extraction potential of PTC. PTC shuttles between two phases and activates the carbonyl groups of TZD and aryl aldehydes (Scheme 2). It combines with the active methylene group of TZD present in the aqueous phase and transfers it into the organic phase (seat of reaction). The migrated PTC-TZD undergoes nucleophilic attack with aryl aldehydes and produce 5-arylidene-1,3-thiazolidine-2,4-dione.[14,26] This investigation produced a similar trend to that of the homogenous reaction (Table 3).

The available literature describes only small-scale synthesis. Hence, the condensation of multifold concentrations (1, 2, 5 and 10 folds) of 4-hydroxybenzaldehyde and thiazolidine-2,4-dione under the optimized conditions was carried out to test the utility of the reaction for process development programs. The trends indicated linearity between 2-fold and 10-fold concentration increases (Table 4). The yields are appreciable and high (> 69%). The $R^2$ values of curvelinear trend (0.9177) and log scale (0.9991) are indicative of the significance of prediction. Therefore, the present work demonstrates that the optimized conditions can be applied to multifold reaction.

Sixteen 5-arylidene-1,3-thiazolidine-2,4-dione analogues were prepared using the optimized conditions. The yields of 5-arylidene-1,3-thiazolidine-2,4-diones were found to be in the range of 78–96% (Table 5). The synthesis of 5-arylidene-1,3-thiazolidine-2,4-diones was compared with methods reported in the literature (Table 6). All catalysts gave very good yields (> 82); however, a few have distinct disadvantages. The major limiting factors are large reaction time and laborious workup. The toxicological studies revealed the genotoxic nature of urea and thiourea, which also produce dermatitis.[36,37] Ionic liquids and PEG300 are carcinogenic, while cerrium

| Entry | Catalysts (8 mol%) | Yield (%) |
|-------|-------------------|-----------|
| 1     | TTBAB             | 92        |
| 2     | BTEAC             | 78        |
| 3     | BTMAC             | 71        |
| 4     | TPAB              | 74        |
| 5     | CTAB              | 29        |
| 6     | TBAI              | 85        |
| 7     | TPEAC             | 73        |
| 8     | TEAB              | 70        |

Note: Reaction conditions: 4-methoxybenzaldehyde (5 mmol), thiazolidine-2,4-dione (5 mmol), potassium carbonate (10 mol%), refluxed with stirring for 60 min.

| Entry | Number of folds | Yield (%) |
|-------|-----------------|-----------|
| 1     | 1               | 91        |
| 2     | 2               | 84        |
| 3     | 5               | 76        |
| 4     | 10              | 69        |

Note: Reaction conditions: 4-hydroxybenzaldehyde (5 mmol), thiazolidine-2,4-dione (5 mmol), TBAB (8 mol%), potassium carbonate (1 mmol), heated with stirring at 100°C for 15 min.
Table 5. TBAB catalyzed synthesis of 5-arylidene-1,3-thiazolidine-2,4-diones (1-16).

| Compound code | Ar                  | Rf  | Yield (%) | Melting range (°C) |
|---------------|---------------------|-----|-----------|--------------------|
| 1             | 4-OCH₃C₆H₄          | 0.70| 96        | 214–216            |
| 2             | 4-OH₂C₆H₄           | 0.68| 91        | 280–281            |
| 3             | C₆H₅                 | 0.60| 93        | 239–240            |
| 4             | 4-Cl–C₆H₄           | 0.47| 94        | 222–224            |
| 5             | 4-F-C₆H₄            | 0.64| 90        | 216–217            |
| 6             | 4-N,N–CH₃–C₆H₄      | 0.66| 92        | 274–276            |
| 7             | 2,4-Cl–C₆H₃         | 0.73| 81        | 219–220            |
| 8             | 2-OHC₆H₄            | 0.64| 95        | 276–277            |
| 9             | 4-OH, 3-OCH₃–C₆H₃   | 0.71| 83        | 194–195            |
| 10            | 2-Furyl             | 0.49| 78        | 234–236            |
| 11            | 2-Thienyl           | 0.72| 87        | 239                |
| 12            | 4-NO₂–C₆H₄          | 0.65| 86        | 281–283            |
| 13            | 3-OHC₆H₄            | 0.76| 89        | 246–248            |
| 14            | 3,4-OCH₃–C₆H₃       | 0.70| 84        | 234–236            |
| 15            | 5-CH₃–Furfuryl       | 0.70| 86        | 228–230            |
| 16            | 2,5-OCH₃–C₆H₃       | 0.81| 92        | 210–212            |

Table 6. Comparison of proposed and literature methods for the synthesis of 5-(4-methoxybenzylidene-1,3-thiazolidine-2,4-dione (compound 1).

| Catalyst (concentration) | TBAB (8 mol%) + K₂CO₃ | Urea/thiourea (10 mol%) | PEG300 (5 mL) | Alum (10 mol%) | Bmim[Cl] (0.5 mol) | Bakers yeast (2 g) | Mg-doped Ce–Zr (200 mg) |
|--------------------------|------------------------|-------------------------|---------------|----------------|-------------------|--------------------|-------------------------|
| Solvent                  | Solvent free           | Solvent free            | Water (10 mL) | Solvent free   | Ethanol (30 mL)   | Ethanol + water (20 mL) |
| Time (min)               | 15                     | 10                      | 180           | 90             | 12                | 2400               | 90                      |
| Yield (%)                | 96                     | 93                      | 82            | 88             | 94                | 50                 | 92                      |
| Reference Comments       | Present Practicability, viable | Ref. [16] | Ref. [22] | Ref. [23] | Ref. [24] | Ref. [25] | Ref. [26] |
|                         | Dermatitis, explosive, genotoxic | - | - | Carcinogenic | Carcinogenic | Laborious work up | Expensive and eco pollutant |

and zirconium are expensive.[38,39] In the present method, purification of the compounds is done through simple washing (non-chromatographic method) with cold toluene–ethanol mixture (1:1, 1 mL), and this is a major advantage of our method.

3. Conclusion

The utility of PTC in the straightforward synthesis of 5-arylidene-1,3-thiazolidine-2,4-diones by Knoevenagel condensation was established for the first time. This solvent-free (benign) methodology is applicable to a wide range of substrates (aryl aldehydes and heteroaryl aldehydes). This energy-efficient procedure is consistent with high atom economy (economic viability) of a green chemistry strategy. The multifold reactions substantiated the utility of this protocol in pharmaceutical process chemistry. The attractive features of this new protocol are shorter reaction time, simple product isolation (non-chromatographic method) and good to excellent yields.
4. Experimental section

Melting points were determined in the DBK program melting point apparatus and expressed in °C and were uncorrected. Aluminum-backed plates coated with silica 60 F254 (Merck) were used for reactions monitoring by thin layer chromatography. The chromatograms were visualized under UV light (254 and 366 nm) and by staining with iodine. The structures of the synthesized compounds were established using IR, NMR (1H and 13C) and mass spectra. The IR spectra were recorded on an IR affinity-1 spectrophotometer (Schimadzu, Japan) using DRS 8000 and are expressed in cm\(^{-1}\). 1H NMR and 13C NMR spectra were recorded on an Avance 300 NMR spectrophotometer (Bruker, Switzerland). The chemical shifts were reported as parts per million (δ ppm), using tetramethylsilane as an internal standard. Mass spectrum was recorded on GC-AccuTOF (Jeol, USA, Inc).

4.1. General method for one-factor-at-a-time investigations

A mixture of anisaldehyde (5 mmol), thiazolidine-2,4-dione (5 mmol), base and PTC loaded in the 25 ml flat bottom flask was heated with stirring. The reaction mixture was cooled to room temperature, poured into a beaker containing crushed ice (5 g). The isolated precipitate was washed with cold toluene–ethanol mixture (1:1, 1 mL) and air dried.

4.2. Phase-transfer catalysis in heterogeneous (liquid–liquid) system

4-Hydroxy benzaldehyde (5 mmol) and thiazolidine-2,4-dione (5 mmol) were dissolved in n-butanol–water mixture (10 mL, 1:1) loaded in the flask. PTC (8 mol%) and potassium carbonate (1 mmol) were added to the flask and refluxed with stirring for 60 min. The organic layer was washed with water (several times), isolated product was washed with cold toluene–ethanol mixture (1:1, mL) and air dried.

4.3. Synthesis of 5-arylidene-1,3-thiazolidine-2,4-diones (1–17)

Thiazolidine-2,4-dione was prepared by condensing equimolar quantities of urea and chloroacetic acid. A mixture of aryl/heteroaryl aldehyde (5 mmol), thiazolidine-2,4-dione (5 mmol) and potassium carbonate (1 mmol) was heated with stirring at 100°C in the presence of TBAB (8 mol%) for 15 min. The reaction mixture was cooled to room temperature, poured into a beaker containing crushed ice (5 g). The precipitate was separated by filtration under vacuum. The isolated product was washed with cold toluene–ethanol mixture (1:1, 1 mL) and air dried.

\[(\text{5Z})-5-(4-\text{Methoxybenzylidene})-1,3-\text{thiazolidine-2,4-dione} \text{ (1)}: \text{ FT-IR (KBr, cm}^{-1}\text{)}: 3226 (\text{NH symmetric stretching}), 3050 (\text{ArCH stretching}), 1728 (\text{C}=\text{O stretching}), 1696 (\text{C}=\text{O stretching}), 1510 (\text{C}=\text{C stretching}), 1340 (\text{C}–\text{O}–\text{C stretching}), 1317 (\text{C}–\text{N stretching}), 701 (\text{C}–\text{S}–\text{C stretching}). \text{1H NMR (300 MHz, DMSO-d}6\text{)}: \delta 11.72 (\text{s, 1H, NH}), 7.43 (\text{s, 1H, =CH}), 7.08 (\text{d, 2H, } J=6.0 \text{ Hz, Ar-H}), 6.62 (\text{d, 2H, } J=6.0 \text{ Hz, Ar-H}), 2.70 (\text{s, 3H, OCH}_3). \text{ MS } m/z (\%) : 235.07 (M}^+\text{, 3), 164 (34), 149 (44), 121 (48), 93 (23), 77 (23), 69 (4). \]

\[(\text{5Z})-5-(4-\text{Hydroxybenzylidene})-1,3-\text{thiazolidine-2,4-dione} \text{ (2)}: \text{ FT-IR (KBr, cm}^{-1}\text{)}: 3428 (\text{OH stretching}), 3162 (\text{NH symmetric stretching}), 3033 (\text{ArCH stretching}), 1739 (\text{C}=\text{O stretching}), 1681 (\text{C}=\text{O stretching}), 1365 (\text{C}–\text{N stretching}), 1281 (\text{C}–\text{O}–\text{C stretching}), 676 (\text{C}–\text{S}–\text{C stretching}). \text{1H NMR (300 MHz, DMSO-d}6\text{)}: \delta 9.70 (\text{brs, 2H, OH phenolic, TZD-NH}), 7.58 (\text{d, 2H, } J=6.0 \text{ Hz, Ar-H}), 6.62 (\text{d, 2H, } J=6.0 \text{ Hz, Ar-H}), 2.70 (\text{s, 3H, OCH}_3). \text{ MS } m/z (\%) : 235.07 (M}^+\text{, 3), 164 (34), 149 (44), 121 (48), 93 (23), 77 (23), 69 (4). \]
(2C, C2, C3, Ar), 159.90 (2C, C5, C6, Ar), 167.54 (1C, −C=O, C2 of TZD ring), 168.09 (1C, −C=O, C4 of TZD ring); MS m/z (%): 221 (M+, 24), 150 (100), 121 (20), 77 (9), 69 (15), 55 (17).

(5Z)-5-Benzylidene-1,3-thiazolidine-2,4-dione (3): FT-IR (KBr, cm−1): 3223 (NH symmetric stretching), 3034 (ArCH stretching), 1698 (C=O stretching), 1632 (C=O stretching), 1431 (C−N−C stretching), 638 (C=S−C stretching). 1H NMR (300 MHz, DMSO-d6): δ 12.63 (s, 1H, NH), 7.80 (s, 1H, =CH), 7.59-7.61 (d, 2H, J = 8.49 Hz, Ar-H), 7.48-7.56 (m, 3H, Ar-H); MS m/z (%): 205 (M+, 4), 134 (72), 108 (9), 89 (37), 63 (46).

(5Z)-5-(4-Chlorobenzylidene)-1,3-thiazolidine-2,4-dione (4): FT-IR (KBr, cm−1): 3189 (NH symmetric stretching), 3021 (ArCH stretching), 1712 (C=S−C stretching), 1465 (C=N stretching), 634 (C=S−C stretching). 1H NMR (300 MHz, DMSO-d6): δ 12.50 (s, 1H, NH), 7.73 (s, 1H, =CH), 7.52 (d, 2H, J = 8.82 Hz, Ar-H), 7.06 (d, 2H, J = 7.11 Hz, Ar-H).

(5Z)-5-(4-Fluorobenzylidene)-1,3-thiazolidine-2,4-dione (5): FT-IR (KBr, cm−1): 3109 (NH symmetric stretching), 3043 (ArCH stretching), 1753 (C=O stretching), 1698 (C=O stretching), 1443 (C=N stretching), 1146 (C−F stretching), 639 (C=S−C stretching). 1H NMR (300 MHz, DMSO-d6): δ 12.61 (s, 1H, NH), 7.65 (s, 1H, =CH), 7.34–7.68 (m, 4H, Ar-H); MS m/z (%): 223.12 (M+ +, 4), 222.08 (100).

(5Z)-5-(4-(Dimethylamino)benzylidene)-1,3-thiazolidine-2,4-dione (6): FT-IR (KBr, cm−1): 3109 (NH symmetric stretching), 3007 (ArCH stretching), 1725 (C=O stretching), 1680 (C=O stretching), 1517 (C=C stretching), 1340 (C=N−C stretching), 647 (C=S−C stretching). 1H NMR (300 MHz, DMSO-d6): δ 12.30 (s, 1H, NH), 10.51 (s, 1H, OH), 7.34 (d, 2H, J = 8.73 Hz, Ar-H), 3.00 (s, 6H, N,N(CH3)2). MS m/z (%): 248 (M+, 11), 177 (100), 161 (15), 134 (12), 89 (24), 63 (10).

(5Z)-5-(2,4-Dichlorobenzylidene)-1,3-thiazolidine-2,4-dione (7): FT-IR (KBr, cm−1): 3223 (NH symmetric stretching), 3072 (ArCH stretching), 1725 (C=O stretching), 1680 (C=O stretching), 1517 (C=C stretching), 1340 (C=N−C stretching), 647 (C=S−C stretching). 1H NMR (300 MHz, DMSO-d6): δ 12.80 (s, 1H, NH), 7.65 (s, 1H, =CH), 7.39 (d, 2H, J = 9 Hz, Ar-H), 6.78 (d, 2H, J = 8.73 Hz, Ar-H), 3.00 (s, 6H, N,N−CH3). MS m/z (%): 251.99 (M+, 15), 274.05 (63), 272.04 (100).

(5Z)-5-(2-Hydroxybenzylidene)-1,3-thiazolidine-2,4-dione (8): FT-IR (KBr, cm−1): 3421 (NH symmetric stretching), 3030 (ArCH stretching), 1776 (C=O stretching), 1678 (C=O stretching), 1454 (C=C stretching), 1334 (C−O−C stretching), 1247 (C=N−C stretching), 748 (C=S−C stretching). 1H NMR (300 MHz, DMSO-d6): δ 12.47 (s, 1H, NH), 10.51 (s, 1H, OH), 8.01 (s, 1H, =CH), 7.31 (t, 2H, Ar-H), 6.97 (q, 2H, Ar-H); MS m/z (%): 221 (M+, 11), 196 (8), 178 (12), 150 (24), 121 (55), 107 (77), 91 (100), 78 (75), 65 (30).

(5Z)-5-(4-Hydroxy-3-methoxybenzylidene)-1,3-thiazolidine-2,4-dione (9): FT-IR (KBr, cm−1): 3480 (OH stretching), 3192 (NH symmetric stretching), 3034 (ArCH stretching), 1737 (C=O), 1678 (C=O), 1516 (C=C), 1290 (C−O−C stretching). 1H NMR (300 MHz, DMSO-d6): δ 9.77 (br, s, 2H, OH, NH), 7.57 (s, 1H, =CH), 7.15 (d, 1H, J = 1.6 Hz, Ar-H), 7.02 (dd, J = 1.6, 1.6 Hz, 1H, Ar-H), 6.87 (d, 2H, J = 8.00 Hz, Ar-H); MS m/z (%): 215.1 (M+, 12), 250.1 (100).

(5Z)-5-(Furan-2-ylmethylidene)-1,3-thiazolidine-2,4-dione (10): FT-IR (KBr, cm−1): 3123 (NH symmetric stretching), 3032 (ArCH stretching), 1728 (C=O stretching), 1681 (C=O stretching), 1475 (C=N stretching), 1284 (C−O−C stretching), 685 (C=S−C stretching). 1H NMR (300 MHz, DMSO-d6): δ 12.44 (s, 1H, NH), 8.03 (s, 1H, =CH), 7.06-7.59 (m, 3H, Ar-H); MS m/z (%): 195 (M+, 8), 124 (100), 96 (57), 69 (52).

(5Z)-5-(Thiophen-2-ylmethylidene)-1,3-thiazolidine-2,4-dione (11): FT-IR (KBr, cm−1): 3124 (NH symmetric stretching), 3045 (ArCH stretching), 1732 (C=O stretching), 1681 (C=O stretching), 1595 (C=C stretching), 1415 (C=N stretching), 634 (C=S−C stretching). 1H NMR (300 MHz, DMSO-d6): δ 12.55 (s, 1H, NH), 8.04 (s, 1H, =CH), 7.98 (d, 1H, J = 4.98 Hz, Ar-H), 7.65 (d, 1H, J = 3.48 Hz, Ar-H), 7.25 (q, 1H, Ar-H); MS m/z (%): 211 (M+, 2), 140 (26), 96 (17), 82 (30), 69 (48).
(5Z)-5-(4-Nitrobenzylidene)-1,3-thiazolidine-2,4-dione (12): FT-IR (KBr, cm\(^{-1}\)): 3268 (NH symmetric stretching), 3034 (ArCH stretching), 1678 (C=O stretching), 1610 (C=O stretching), 1411 (C−N stretching), 631 (C−S−C stretching). \(^1\)H NMR (300 MHz, DMSO-\(d_6\)):\(\delta\) 12.75 (s, 1H, NH), 7.91 (s, 1H, =CH), 7.83 (d, 2H, \(J = 8.40\) Hz, Ar-H).

(5Z)-5-(3-Hydroxybenzylidene)-1,3-thiazolidine-2,4-dione (13): FT-IR (KBr, cm\(^{-1}\)): 3302 (NH symmetric stretching), 3070 (ArCH stretching), 1753 (C=O stretching), 1691 (C=O stretching), 1591 (C=C stretching), 1448 (C−O−C stretching), 1236 (C−N stretching), 790 (C−S−C stretching). \(^1\)H NMR (300 MHz, DMSO-\(d_6\)):\(\delta\) 9.89 (s, 1H, NH), 7.65 (s, 1H, =CH), 7.30 (s, 1H, OH), 7.02 (d, 2H, \(J = 9\) Hz, Ar-H).

(5Z)-5-(3,4-Dimethoxybenzylidene)-1,3-thiazolidine-2,4-dione (14): FT-IR (KBr, cm\(^{-1}\)): 3216 (NH symmetric stretching), 3044 (ArCH stretching), 1731 (C=O stretching), 1693 (C=O stretching), 1501 (C=C stretching), 1332 (C−O−C stretching), 1315 (C−N stretching), 714 (C−S−C stretching). \(^1\)H NMR (300 MHz, DMSO-\(d_6\)):\(\delta\) 12.52 (s, 1H, NH), 7.75 (s, 1H, =CH), 7.17 (d, 2H, \(J = 6.8\) Hz, Ar-H), 7.11 (d, 2H, \(J = 12.0\) Hz, Ar-H), 3.81 (s, 6H, 3,4-OCH\(_3\)). MS \(m/z\) (%): 265.2 (M\(^+\), 23), 264.1 (100).

(5Z)-5-(3-Methylfuran-2-yl)methylidene)-1,3-thiazolidine-2,4-dione (15): FT-IR (KBr, cm\(^{-1}\)): 3185 (NH symmetric stretching), 3037 (ArCH stretching), 1681 (C=O stretching), 1616 (C=O stretching), 1411 (C−N stretching), 1284 (C−O−C stretching), 686 (C−S−C stretching). \(^1\)H NMR (300 MHz, DMSO-\(d_6\)):\(\delta\) 12.41 (s, 1H, NH), 8.03 (s, 1H, =CH), 7.13 (d, 2H, \(J = 8.70\) Hz, Ar-H), 2.71 (s, 3 H, CH\(_3\)). MS \(m/z\) (%): 209 (M\(^+\), 30), 138 (100), 109 (10), 95 (15), 81 (13), 69 (7), 51 (9).

(5Z)-5-(2,5-Dimethoxybenzylidene)-1,3-thiazolidine-2,4-dione (16): FT-IR (KBr, cm\(^{-1}\)): 3444 (NH symmetric stretching), 3028 (ArCH stretching), 1732 (C=O stretching), 1680 (C=O stretching), 1591 (C=C stretching), 1344 (C−O−C stretching), 1220 (C=N stretching), 680 (C−S−C stretching). \(^1\)H NMR (300 MHz, DMSO-\(d_6\)):\(\delta\) 12.85 (s, 1H, NH), 7.89 (s, 1H, =CH), 7.06 (s, 2H, Ar-H), 6.89 (s, 1H, Ar-H), 3.81 (s, 3H, OCH\(_3\)), 3.73 (s, 3H, OCH\(_3\)); MS \(m/z\) (%): 265 (M\(^+\), 100), 179 (100), 151 (23), 136 (23), 108 (12), 97 (17), 82 (13), 69 (5).

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Supplemental data

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