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Novel (4-oxothiazolidine-2-ylidene)benzamide derivatives: synthesis, characterization and crystal structures

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Abstract A convenient, one-pot, multicomponent synthesis of new (4-oxothiazolidine-2-ylidene)benzamide derivatives by unsymmetrical thioureas, various amines and methyl bromoacetate has been developed. These new compounds were characterized by IR, ^{1}HNMR, ^{13}CNMR, mass spectrometry, CHNS elemental analysis, and single-crystal X-ray analysis.

Keywords (4-Oxothiazolidin-2-ylidene)benzamide · Amine · Thioureas · Methyl bromoacetate · Multi-component reactions (MCRs)

Introduction

The design and the synthesis of new drugs based on combinations of hybrid molecules are one of the important methods in modern chemistry. These compounds are synthesized by combining various pharmacophore fragments, and the obtained products have interesting biological activity.

Thiazoles and their derivatives have a heterocyclic ring containing nitrogen and sulphur. These compounds are important scaffolds in chemistry and have been found in the structure of many drugs because they have various biological properties [1], such as anticancer [2, 3], antifungal [4], anti-inflammatory [5], antibacterial [6, 7], anticonvulsant [8], antidiabetic [9] and anti-HIV [10]. On the other hand, amides are known as important components in supramolecular chemical anion

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sensors. Furthermore, amides can be selectively connected via hydrogen bonds to anionic substrates, such as DNA, and reveal new biological properties [11].

In general, thiazoles are synthesized by Hantzsch synthesis [12], where the cyclization of α-halocarbonyl compounds is carried out with a great variety of reactants including thioamides and thioureas. In recent decades, several methods have been reported to produce thiazole derivatives, such as the cyclization of thioureas with acetylenedicarboxylates or phenacyl bromide [13], the reaction between isothiocyanatobenzene and 1, 4-dithiane-2, 5-diol [14], and the cyclocondensation of thionyl chloride with enaminones [15]. Other methods include reactions of amines with benzaldehyde and an excess of mercaptoacetic acid in the presence of different catalysts [16–18]. Dömling et al. have also reported multicomponent reactions (MCRs) by using special isocyanide, thiocarboxylic acid, aldehyde and a primary amine for the synthesis of these compounds [19].

The thiazole derivatives containing amide groups may have interesting properties. Reactions of amine with ethyl cyanoacetate and aryl isothiocyanate have been reported to produce new compounds such as dual anti-inflammatory and antimicrobial agents [20]. Shahvelayati et al. used α-amino acids, aroyl isothiocyanates, and α-bromoketones in an ionic liquid [21]. The synthesis of these compounds by reactions between acetohydrazide derivatives and aldehyde with mercaptoacetic acid has also been investigated [22, 23].

In this paper, we describe an efficient one-pot method for the synthesis of some (4-Oxothiazolidine-2-ylidene) benzamide derivatives via condensation benzoyl isothiocyanate derivatives, suitable heterocyclic (aromatic) amines and methyl bromoacetate.

Experimental

Methods and materials

The reagents and solvents were purchased from Merck and Aldrich Chemical companies and were used as received. The samples were analyzed by FT-IR spectroscopy (JASCO FT/IR-460 plus spectrometer) and melting points were detected by Electro thermal 9100 apparatus. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DRX-400 Avance instrument in $CDCl_3$. The mass spectra were recorded on an Agilent Technology HP 5973 MSD mass spectrometer operating at an ionization potential of 70 eV, and elemental analyses were performed using a Heraeus CHN-Rapid analyzer.

General procedure for the synthesis of (4-oxothiazolidine-2-ylidene) benzamide derivatives

A mixture of 1 mmol benzoyl isothiocyanate derivatives (**1**) and 1.0 mmol appropriate (hetero) aromatic amine (**2**) in 5 ml acetonitrile as solvent under reflux conditions was stirred. Then, methyl bromoacetate (**3**) (1.1 mmol) and triethylamine (1.0 mmol, 0.10 g) were added to the reaction mixture. The progress of the reaction

was monitored by thin-layer chromatography (TLC). The reaction mixture was cooled to room temperature and microcrystalline powder was filtered and washed with a small amount of cold ethanol, and then recrystallized from suitable solvents.

Spectral data

(Z)-N-(3-(furan-2-ylmethyl)-4-oxothiazolidine-2-ylidene)benzamide ***(4a)*** Brown solid; Yield = 86%, m.p. = 199–201 °C; IR (KBr): 3003, 3051 (C–H aromatic), 2976 (C–H aliphatic), 1737 (C=O), 1642 (C=O thiazol), 1596, 1448, 1367 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.35$ (2H, d $J = 7.2$ Hz, Ar–H), 7.62 (1H, t $J = 7.6$ Hz, Ar–H), 7.52 (2H, t, $J = 7.2$ Hz, $J = 7.6$ Hz, Ar–H), 7.38 (1H, d $J = 1.2$ Hz CH-fouran) 4.48 (1H, d $J = 3.2$ Hz CH-fouran), 6.35 (1H, q, $J = 1.2$ Hz CH-fouran), 5.20 (2H, s CH_2 thiazol), 3.86 (2H, s CH_2) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): 177.20 (C=O), 172.30 (C=O), 171.80 (N–C–S), 148.25 (C), 142.83 (CH), 135.04 (C), 133.12 (CH), 130 (2CH), 128.20 (2CH), 110.80 (CH), 109.85 (CH), 40 (CH2 thiazol), 32 (CH_2) ppm; MS (EI, 70 eV) m/z (%): 300 (M^+), 195, 105, 77, 51; Anal. calcd. for $C_{15}H_{12}N_2O_3S$; C: 59.99, H: 3.99, N: 9.33, S: 10.68, Found: C: 60.09, H: 3.95, N: 9.43, S: 10. 57.

(Z)-4-chloro-N-(3-(furan-2-ylmethyl)-4-oxothiazolidin-2-ylidene)benzamide ***(5a)*** Dark yellow solid; Yield = 89%, m.p. = 196–197 °C; IR (KBr): 3084 (C–H aromatic), 2964 (C–H aliphatic), 1743 (C=O), 1640 (C=O thiazol), 1590, 1482, 1359 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.28$ (2H, d $J = 8.4$ Hz, Ar–H), 7.48 (2H, d $J = 8.4$ Hz, Ar–H), 7.38 (1H, d $J = 1.2$ Hz CH-fouran), 6.46 (1H, d $J = 3.2$ Hz CH-fouran), 6.35 (1H, q $J = 1.2$ Hz CH-fouran), 5.20 (2H, s CH_2 thiazol), 3.85 (1H, s CH_2) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): 176.40 (C=O), 172.50 (C=O), 172.20 (N–C–S), 148.30 (C), 142.80 (CH), 139.67 (C), 133.71 (C), 131.51 (2CH), 128.80 (2CH), 110.90 (CH), 110.95 (CH),40 (CH_2 thiazol), 32 (CH_2) ppm; MS (EI, 70 eV) m/z (%): 334 (M^+), 336 (M + 2), 195, 141,139, 111, 81; Anal. calcd. for $C_{15}H_{11}ClN_2O_3S$; C: 53.79, H: 3.28, N: 8.36, S: 9.58, Found: C: 53. 90, H, 3.35, N: 8. 29, S: 9.53.

(Z)-N-(3-(furan-2-ylmethyl)-4-oxothiazolidine-2-ylidene)-4-methylbenzamide ***(6a)*** Light brown solid; Yield = 82%, m.p. = 196–197 °C, IR (KBr): 3116 (C–H aromatic), 2926 (C–H aliphatic), 1736 (C=O), 1684 (C=O thiazol), 1605, 1497, 1568, 1516 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.25$ (2H, d $J = 8.00$ Hz, Ar–H), 7.37 (1H, d), 7.31 (2H, d, $J = 8.00$ Hz, Ar–H), 6.46 (1H, d $J = 3.2$ Hz CH-fouran), 6.34 (1H, q $J = 3.2$ Hz CH-fouran), 5.18 (2H, s CH_2 thiazol), 3.84 (2H, s CH_2), 2.46 (3H, s CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): 177.17 (C=O), 172.56 (C=O), 171.17 (N–C–S), 148.57 (C), 144.14 (C), 142.58 (CH), 132.62 (C), 130.24 (2CH), 129.23 (2CH), 127.45 (CH), 110.57 (CH), 109.88 (CH), 109.12 (CH), 39.95 (CH_2 thiazol), 33.03 (CH_2), 21.83 (CH_3). MS (EI, 70 eV) m/z (%): 314 (M^+), 300, 195, 119,105, 91; Anal. calcd. for $C_{16}H_{14}N_2O_3S$; C: 61.14, H: 4.45, N: 8.91, S: 10.21, Found: C: 61.09, H: 4.47, N: 8.87, S: 10.17.

(Z)-N-(4-oxo-3-(pyridin-2-ylmethyl)thiazolidine-2-ylidene)benzamide ***(4b)*** Green solid; Yield = 82%, m.p. = 216–218 °C; IR (KBr): 3080 (C–H aromatic), 2976,

2933 (C–H aliphatic), 1733 (C=O), 1640 (C=O thiazol), 1595, 1484, 1374 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.59$ (1H, d $J = 4.4$ CH-pyridine), 8.13 (2H, d $J = 7.6$ Ar–H), 7.72 (1H, t $J = 7.6$, $J = 8$ Ar–H), 7.57 (1H, d $J = 7.6$ CH-pyridine), 7.43 (2H, t $J = 7.6$, $J = 7.6$ Ar–H), 7.35 (1H d $J = 8$ CH-pyridine), 7.23 (1H t $J = 5.2$ CH-pyridine), 5.33 (2H, s CH_2 thiazol), 3.48 (2H, s CH_2) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): 177.21 (C=O), 172.99 (C=O), 172.02 (N–C–S), 154.49 (C), 149.96 (CH), 136.87 (CH), 135 (C), 133.11 (CH), 130.04 (2CH) 128.35 (2CH), 122.80 (CH), 121.50 (CH), 49 (CH_2 thiazol), 32 (CH_2) ppm; MS (EI, 70 eV) m/z (%): 311 (M^+), 206, 105,92, 77; Anal. calcd. for $C_{16}H_{13}N_3O_2S$; C: 61.69, H: 4.17, N: 13.49, S: 10.30, Found: C: 61. 58, H: 4.20, N: 13.59, S: 10.21.

(Z)-4-chloro-N-(4-oxo-3-(pyridin-2-ylmethyl)thiazolidin-2-ylidene)benzamide ***(5b)*** Green solid; Yield = 85%, m.p. = 225–226 °C, IR (KBr): 3082 (C–H aromatic), 2955 C–H aliphatic),, 1740 (C=O), 1641 (C=O thiazol), 1591, 1483, 1376 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.58$ (1H, d $J = 4.8$ Hz CH-pyridine), 8.16 (2H, d $J = 8.4$ Hz Ar–H), 7.70 (1H, t $J = 7.6$ Hz CH-pyridine), 7.39 (2H, d $J = 8.4$ Hz Ar–H), 7.30 (1H, d CH-pyridine), 7.23 (1H, t $J = 4.8$ Hz CH -pyridine), 5.31 (2H, s CH_2 thiazol), 4.00 (2H, s CH_2) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): 176.26 (C=O), 172.91 (C=O), 172.53 (N–C–S), 154.4 (C), 149.96 (CH), 139.53 (C), 136.75 (C & CH), 133.59 (CH), 131.42 (2CH), 128.64 (2CH), 48.49 (CH_2), 33.22 (CH_2) ppm; MS (EI, 70 eV) m/z (%): 345 (M^+), 347 (M + 2), 271, 206, 139, 111, 92, 75. Anal. calcd. for $C_{16}H_{12}ClN_3O_2S$; C: 55.59, H: 3.47, N: 12.15, S: 9.27, Found: C: 55. 49, 3. 49, N: 12.23, S: 9.17.

(Z)-4-methyl-N-(4-oxo-3-(pyridin-2-ylmethyl)thiazolidin-2-ylidene)benzamide ***(6b)*** Green solid, Yield = 79%, m.p. = 224–225 °C, IR (KBr): 3098 (C–H aromatic), 2986 (C–H aliphatic), 1741 (C=O), 1637 (C=O thiazol), 1605, 1515, 1600, 1479 cm^{-1}, ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.60$ (1H, d $J = 4.8$ Hz CH-pyridine), 8.03 (2H, d $J = 8.4$ Hz Ar–H), 7.70 (1H, t CH-pyridine), 7.32 (1H, d CH-pyridine), 7.28 (1H, t), 7.21 (2H, d $J = 8$ Hz Ar–H), 5.33 (2H, S CH_2 thiazol), 3.97 (2H, S CH_2), 2.41 (3H, S CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): 177.15 (C=O), 173.02 (C=O), 171.45 (N–C–S), 154.57 (C), 194.54 (CH), 144.02 (C), 136.84 (CH), 132.47 (C), 130.15 (2CH), 129.09 (2CH), 122.67 (CH), 121.47 (CH), 48.40 (CH_2), 33.21 (CH_2), 21.78 (CH_3) ppm; MS (EI, 70 eV) m/z (%): 325 (M^+), 206, 119, 91. Anal. calcd. for $C_{17}H_{15}N_3O_2S$; C: 62.76, H: 4.61, N: 12.92, S: 9.86, Found: C: 62.69, H: 4.60, N: 12.88, S: 9.78.

(Z)-N-(3-(5-chloro-2-phenoxyphenyl)-4-oxothiazolidin-2-ylidene)benzamide ***(4c)*** light yellow solid; Yield = 80%, m.p. = 167–168 °C; IR (KBr): 3042 (C–H aromatic), 2965 (C–H aliphatic), 1740 (C=O), 1642 (C=O thiazol), 1590, 1577, 1485, 1356 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.10$ (2H, d $J = 7.2$ Hz Ar–H), 7.57 (1H, t $J = 7.2$, $J = 7.6$ Hz Ar–H), 7.45-7.42 (3H, m), 7.26-6.98 (7H, m CH phenoxyphenyl), 3.34 (2H, q, *diastereotopic* thiazol) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): 177.22 (C=O), 17.50 (C=O), 155.90 (N–C–S), 152.11 (C), 134.90 (C), 133.35 (C), 131.09 (CH), 130.13 (2CH), 130.06 (2CH), 129.95 (2CH), 128.43 (2CH), 128.10 (C), 126.18 (CH), 124.57 (CH), 122.11 (CH), 119.45 (2CH), 31.50 (CH_2) ppm; MS (EI, 70 eV) m/z (%): 423 (M^+), 425 (M + 2), 405 329, 331, 105,

77; Anal. calcd. for: $C_{22}H_{15}ClN_2O_3$: C: 62.50, H: 3.54, N: 6.62, S: 7.58, Found: C: 62.59, H: 3. 45, N: 6.73, S: 7.49.

(Z)-4-chloro-N-(3-(5-chloro-2-phenoxyphenyl)-4-oxothiazolidin-2-ylidene) benzamide (***5c***) yellow solid; Yield = 78%, m.p. = 210–211 °C; IR (KBr): 3094 (C–H aromatic), 2978, 2934 (C–H aliphatic), 1736 (C=O), 1649 (C=O thiazol), 1587, 1571, 1479, and 1359 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.02$ (2H, d $J = 8.4$ Hz Ar–H), 7.46 (H, S), 7.43 (2H d $J = 8.4$ Hz Ar–H), 7.30-6.97 (7H, m phenoxyphenyl), 3.90 (2H, q *diastereotopic*) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): 176.33 (C=O), 172.15 (C=O), 171.41 (N–C–S), 155.71 (C), 152.11 (C), 139.92 (C), 133.42 (C), 131.49 (2CH), 131.16 (CH), 129.99 (2CH), 128.76 (2CH), 128 11 (2CH), 126.02 (CH). 124.64 (CH), 120.10 (CH), 119.41 (2CH), 32 (CH_2) ppm; MS (EI, 70 eV) m/z (%): 457 (M^+), 459 (M + 2), 461 (M + 4), 363, 365, 367, 139, 111, 75; Anal. calcd. for: $C_{22}H_{14}Cl_2N_2O_3$: C: 57. 79, H: 3.06, N: 6.12, S: 7.01, Found: C: 58. 77, H: 3.13, N: 6.19, S: 6. 96.

(Z)-N-(3-(5-chloro-2-phenoxyphenyl)-4-oxothiazolidin-2-ylidene)-4-methylbenzamide (***6c***) Yellow crystal, Yield = 71%, m.p. = 160 °C, Yield = 80%, IR (KBr): 3060 (C–H aromatic), 2931 (C–H aliphatic), 1748 (C=O), 1685 (C=O thiazol), 1608, 1495, 1584, 1513 cm^{-1}, ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.98$ (2H, d, $J = 8.2$ Hz Ar–H), 7.46-7.41 (2H, m phenoxyphenyl), 7.24-7.29 (2H Ar–H), 7.25-6.98 (7H, m phenoxyphenyl), 7.00 3.89 (2H, q *diastereotopic* $J = 18$ Hz), 2.43 (3H. s CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): 177.22 (C=O), 171.55(C=O), 170.98 (N–C–S), 155.78 (C), 152.17(C), 144.19(C), 132.33(C), 131.02 (CH), 130.23 (2CH), 130.09 (CH), 129.94 (2CH), 129.18 (2CH), 128.06 (CH), 126.20 (CH), 124.55 (CH), 120.08 (CH), 119.46 (2CH), 33.10 (CH_2), 21.82 (CH_3) ppm; MS (EI, 70 eV) m/z (%): 437 (M^+), 439 (M + 2), 364, 347, 343, 119, 91; Anal. calcd. for: $C_{23}H_{17}ClN_2O_3$: C: 63.15, H: 3.89, N: 6.40, S: 7.33. Found: C: 63.14, H: 3.86, N: 6.43, S: 7.29.

(Z)-N-(3-(naphthalene-2-yl)-4-oxothiazolidine-2-ylidene)benzamide (***4d***) Almond green solid; Yield = 80%, m.p. = 170–171 °C, IR (KBr): 3057 (C–H aromatic), 2971 (C–H aliphatic), 1748 (C=O), 1643 (C=O thiazol), 1598, 1511, 1483, 1347 cm^{-1}, ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.08$ (1H, d $J = 8.4$ Hz, naphthalene), 8.02 (1H, d $J = 8.8$ Hz, naphthalene), 7.78 (2H, d $J = 7.2$ Hz ArH), 7.68 (1H, t $J = 7.2$ Hz Ar–H), 7.58-7.24 (7H, m), 4.16 (2H, q *diastereotopic* $J = 18.4$ Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): 177.50 (C=O), 172.50 (C=O), 171.98 (N–C–S), 134.80 (C), 134.44 (C), 133.15 (CH), 131.60 (C), 130.32 (CH), 130.03 (2CH), 129.30 (CH), 128.22 (2CH), 127.47 (C), 126.60 (CH), 126.70 (CH), 125.55 (CH), 122.95 (CH), 30.35 (CH_2) ppm, MS (EI, 70 eV) m/z (%): 346 (M^+), 241, 105, 77. Anal. calcd. for: $C_{20}H_{14}N_2O_2S$: C: 69.37, H: 4.04, N: 8.08, S: 9.25, Found: C: 69.45, H: 4.10, N: 8.02, S: 9.31.

(Z)-N-4-chloro-N-(3-(naphthalene-2-yl)-4-oxothiazolidine-2-ylidene)benzamide (***5d***) Green solid; Yield = 83%, m.p. = 155–156 °C, IR (KBr): 3055 (C–H aromatic), 2971 (C–H aliphatic), 1742 (C=O), 1644 (C=O thiazol), 1599, 1521, 1488 cm^{-1}, ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.08$ (1H, d $J = 8.4$ Hz naphthalene) 8.03 (1H, d

$J = 7.6$ Hz naphthalene), 7.68 (2H, d $J = 8.4$ Hz Ar–H), 7.61-7.48 (5H, m naphthalene), 7.25 (2H, d $J = 8.4$ Hz Ar–H), 4.18 (2H, q *diastereotopic* $J = 18.4$ Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): 176.49 (C=O), 172.54 (C=O), 172.44 (N–C–S), 139.51 (C), 134.43(C), 133.32 (C), 131.48 (C), 131.38 (2CH),130.39 (CH), 129.19 (CH), 128.78 (CH), 128.53 (2CH), 127.49 (CH), 126.73 (C), 126.52 (CH), 125.50 (CH), 121.89 (CH), 33.46 (CH_2) ppm; MS (EI, 70 eV) m/z (%): 380 (M^+), 382 (M + 2), 241, 139, 111. Anal. calcd. for: $C_{20}H_{13}ClN_2O_2S$: C: 63.15, H: 3.42, N: 7.3, S: 8.43, Found: C: 63.18, H: 3.41, N: 7.29, S: 8.42.

(Z)-4-methyl-N-(3-(naphthalen-1-yl)-4-oxothiazolidin-2-ylidene) benzamide ***(6d)*** Light gray; Yield = 77%, m.p. = 174–175 °C, IR (KBr): 3057 (C–H aromatic), 2978 (C–H aliphatic), 1729 (C=O), 1635 (C=O thiazol), 1516, 1608, and 1494 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.08$ (1H, d, $J = 8.4$ Hz naphthalene), 8.02 (1H, d, $J = 8.0$ Hz naphthalene), 7.67 (2H, d $J = 8$ Ar–H) 7.64-7.49 (1H, m naphthalene), 7.05 (2H d $J = 8$ Ar–H) 4.20 (2H, q *diastereotopic* $J = 18.4$ Hz), 2.32 (3H, S CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): 177.40 (C=O), 172.57 (C=O), 171.35 (N–C–S), 143.98 (C), 134.43 (C), 132.23 (C), 131.64 (C), 130.26 (C), 130.12 (2CH), 129.28 (CH), 128.96 (2CH), 128.71 (2CH), 127.42 (CH), 126.66 (CH), 126.57 (CH), 125.48 (CH), 122.00 (CH), 33.45 (CH_2), 21.70 (CH_3) ppm; MS (EI, 70 eV) m/z (%): 360 (M^+), 240, 119, 91; Anal. calcd. for: $C_{12}H_{16}N_2O_2S$, C: 70, H: 4.4, N: 7.7, S: 8.9. Found: C: 72.10, H: 4.38, N: 7.69, S: 8.91.

X-ray crystal structure determination of compounds 4a and 4c

The crystallographic data for both complexes were collected at room temperature on a Bruker Smart Apex II single-crystal diffractometer working with monochromatic Mo-Kα radiation and equipped with an area detector [26]. The structures were solved by direct methods and refined against F^2 with SHELXL-2014/7 [27] with anisotropic thermal parameters for all non-hydrogen atoms. Idealized geometries were assigned to the hydrogen atoms. Details for the X-ray data collection are reported in Table 1. Complete crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as a supplementary publication [28].

Results and discussion

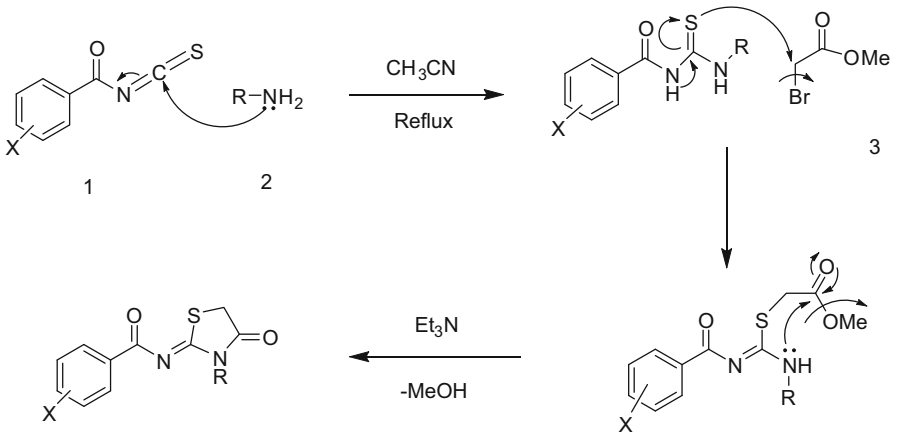
Chemistry

In this article, a one-pot, multicomponent synthesis of thiazole derivatives bearing an amide moiety have been performed by using benzoyl isothiocyanate derivatives (1), the suitable heterocyclic (aromatic) amines (2) and methyl bromoacetate (3) in the presence of triethylamine as a catalyst and bromine scavenger in acetonitrile as a solvent. A proposed mechanism for the reaction is outlined in Scheme 1.

Table 1 Details for the X-ray data collection for compounds **4a** and **4c**

Compound	**4a**	**4c**
Formula	C_{15} H_{12} N_2 O_3 S	C_{22} H_{15} Cl N_2 O_3 S
Molecular weight	300.33	422.87
Crystal system	Triclinic	Triclinic
Space group	P-1	P-1
a/Å	8.468 (4)	10.577(7)
b/Å	8.993 (4)	10.759(7)
c/Å	9.768 (5)	11.262 (7)
a/°	83.209 (7)	62.670 (9)
b/°	73.129 (7)	63.120 (10)
c/°	70.881 (7)	81.479 (10)
Volume, Å^3	672.4 (6)	1012.8 (11)
Z	2	2
D_{calc}/g cm^{-3}	1.483	1.387
F (000)	312	436
μ(Mo-Kα)/mm^{-1}	0.252	0.318
Reflections collected	10,967	10,975
Unique reflections	4118	3614
Observed reflections [$I > 2\sigma(I)$]	3034;[$R_{int} = 0.0341$]	2855; [$R_{int} = 0.0397$]
R, *wR* [$I > 2\sigma(I)$]	$R = 0.0434$; $wR = 0.1119$	$R = 0.0468$; $wR = 0.1232$
R, *wR* [all data]	$R = 0.0616$; $wR = 0.1237$	$R = 0.0587$; $wR = 0.1338$

$$R = \sum |Fo - Fc| / \sum |Fo|; \quad wR = \left[\sum \left[w(Fo^2 - Fc^2)^2 \right] / \sum \left[w(Fo^2)^2 \right] \right]^{1/2}$$



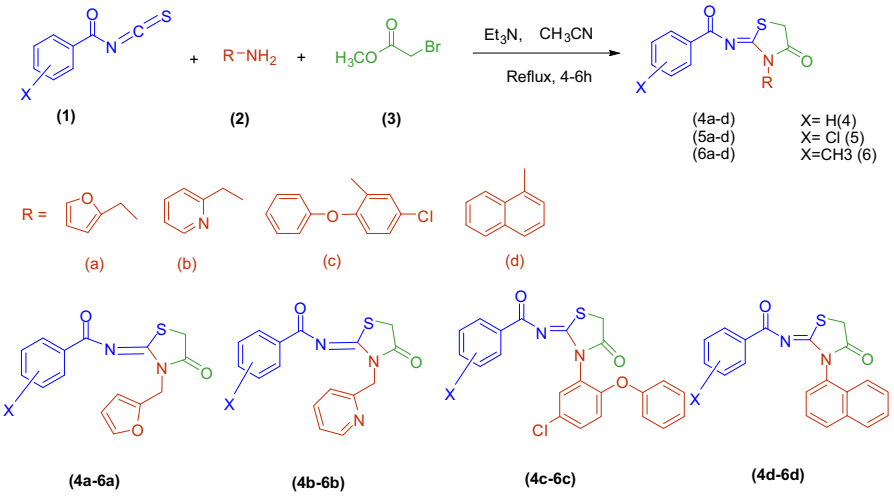
Scheme 1 Proposed mechanism for the formation of (4-oxothiazolidine-2-ylidene)benzamide derivatives

(4-Oxothiazolidine-2-ylidene) benzamide derivatives are synthesized via one-pot, two-step cyclocondensation reaction. In the first step, benzoyl isothiocyanate (1) reacts with heterocyclic aliphatic or aromatic amines (2) to produce N-(carbamothioyl) benzamide as an unsymmetrical thiourea. In the next step, methyl bromoacetate (3) is attacked by nucleophiles.

First, the reactions were investigated at room temperature for 8–10 h, but no suitable progress of the reaction was observed. In order to improve the reaction efficiency, the reaction was carried out under reflux conditions. The compounds were characterized by IR, ^{1}H NMR, ^{13}C NMR spectra, mass spectrometry and CHNS elemental analysis. In the case of compounds **4a** and **4c**, single crystals adapted for X-ray diffraction analysis were obtained.

First, (Z)-4-chloro-N-(3-(furan-2-ylmethyl)-4-oxothiazolidine-2-ylidene) benzamide (**5a**) was synthesized and characterized. In the IR spectrum, C–H aliphatic and aromatic bands were observed at 3084 and 2964 cm^{-1}, and strong absorptions at 1743 and 1640 cm^{-1} were due to carbonyl groups. The ^{1}H NMR spectrum showed the presence of 2 aliphatic protons at 5.20 ppm ($C_{\text{furan ring}}$–CH_2–N), 3.85 ppm (CH_2 $_{\text{thiazole}}$), while aromatic protons of phenyl and furan rings appear at 8.28–6.35 ppm. The ^{13}CNMR spectrum of this compound showed carbonyl groups and carbon of the thiazole ring at 176.40, 172.50 and 172.20 ppm, respectively. The mass spectrometry and CHNS elemental analysis confirmed the proposed formula.

Various amines, such as substituted 2-furanmethylamine (a) 2-(aminomethyl) pyridine (b), 5-chloro-2-phenoxyaniline (c), and 1-naphthylamine (d) were used to give thiazolidinone derivatives (Scheme 2). Interestingly, in the ^{1}HNMR spectra, AB quartet systems were observed when aromatic compounds (1-naphthylamine and 5-chloro-2-phenoxyaniline) were used. Aliphatic hydrogens in the thiazole ring are diastereotopic, and they have different chemical shifts in the ^{1}HNMR spectrum. When the hydrogens are diastereotopic, they frequently split from each other, but in



Scheme 2 Synthesis of (4-oxothiazolidine-2-ylidene)benzamide derivatives

the case of aliphatic amines [2-furanmethylamine, 2-(aminomethyl) pyridine], the rotation around the C—N bond inhibits the observation of the AB quartet system.

Crystal structure analysis for compounds 4a, 4c

The molecular structures of compounds **4a** and **4c** were established by single crystal X-ray diffraction methods. The molecular structures of the compounds are reported in Figs. 1 and 2 together with the atomic labeling scheme.

A list of the most important bond distances and angles are reported in the figure captions. In both structures, the thiazolidinone group, the amide system, and the aromatic rings are almost coplanar with a dihedral angle between the aromatic rings and the mean plane of the thiazolidinone group of 6.54(2)° and 10.63(2)° for **4a** and **4c**, respectively. On the other hand, the furfuryl and the 1-chloro-4-phenoxybenzene moieties in **4a** and **4c**, respectively, tend to dispose in order to minimize the steric hindrance with the planar system. In particular, in **4a** the mean plane defined by the furfuryl group forms a dihedral angle of 71.65(2)° with the planar system, while in **4c** the mean plane defined by the chlorophenyl moiety forms a dihedral angle of 76.64(2)° with the analogous planar system. This fact prevents stacking molecules assisted by pi–pi interactions as observed in other similar structures found in the Crystallographic Data Base [24, 25]. Nevertheless, hydrogen bonds and Van der Waals interactions are present between adjacent molecules in the crystal packing of both structures. In particular, the oxygen atoms of the thiazolidinone and of the amide groups are involved in interactions with hydrogen

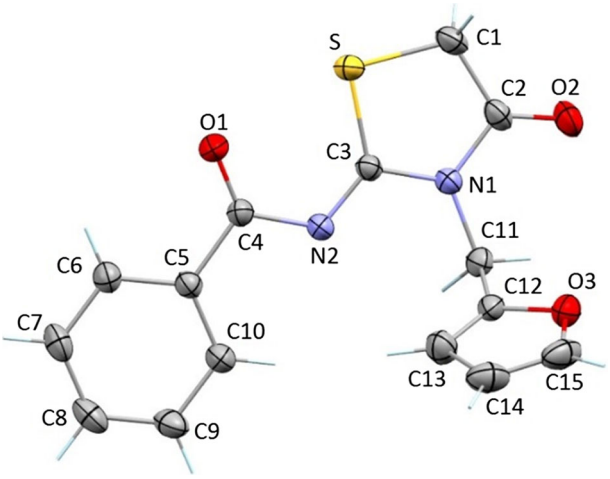


Fig. 1 Ortep view of molecular structure of compound **4a**. *Ellipsoids* are drawn at their 30% probability level. Selected bond distances (Å) and angles (deg): C1-C2 1.498(2), C1-S 1.8019(17), C2-O2 1.2010(18), C2-N1 1.3867(18), C3-N2 1.2855(17), C3-N1 1.3736(17), C3-S 1.7405(14), C4-O1 1.2228(17), C4-N2 1.3890(18), C4-C5 1.487(2), C11-N1 1.4666(18), C2-C1-S 108.40(10), O2-C2-N1 123.03(15), O2-C2-C1 126.28(14), N1-C2-C1 110.69(12), N2-C3-N1 119.02(12), N2-C3-S 128.98(11), N1-C3-S 112.01(10), O1-C4-N2 123.85(13), O1-C4-C5 122.07(13), N2-C4-C5 114.08(12), C3-N1-C2 116.97(12), C3-N1-C11 121.37(11), C2-N1-C11 121.65(12), C3-N2-C4 118.34(12), C3-S-C1 91.85(7)

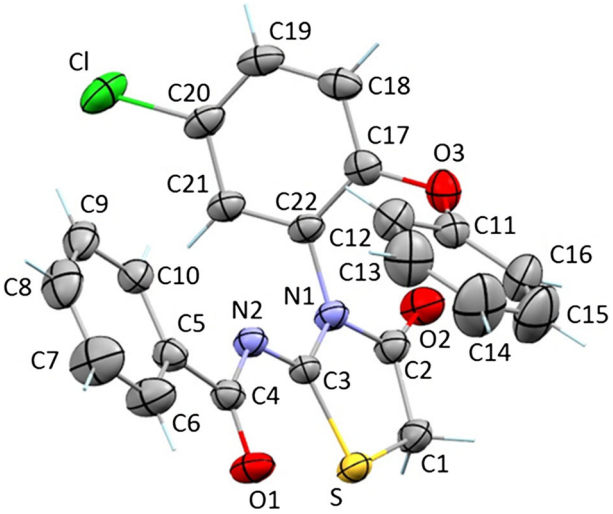


Fig. 2 Ortep view of molecular structure of compound **4c**. *Ellipsoids* are drawn at their 30% probability level. Selected bond distances (Å) and angles (deg): C1-C2 1.498(3), C1-S 1.804(2), C2-O2 1.208(3), C2-N1 1.389(3), C3-N2 1.289(2), C3-N1 1.384(3), C3-S 1.743(2), C4-O1 1.222(2), C4-N2 1.385(3), C4-C5 1.489(3), C22-N1 1.438(2), C2-C1-S 108.62(14), O2-C2-N1 123.7(2), O2-C2-C1 125.59(18), N1-C2-C1 110.75(18), N2-C3-N1 118.67(17), N2-C3-S 129.41(15), N1-C3-S 111.92(13), O1-C4-N2 124.65(18), O1-C4-C5 121.74(18), N2-C4-C5 113.61(17), C3-N1-C2 116.80(17), C3-N1-C22 121.09(15), C2-N1-C22 121.52(16), C3-N2-C4 118.00(17), C17-O3-C11 117.30(15), C3-S-C1 91.91(9)

atoms of the aromatic rings of adjacent molecules with O···C (H) distances ranging from 3.335(2) to 3.590(3) Å.

Conclusions

In summary, we have introduced a novel and efficient method for the synthesis of new derivatives of (4-oxothiazolidine-2-ylidene)benzamide via a one-pot reaction between benzoyl isothiocyanate, various amines and methyl bromoacetate. The single crystal X-ray diffraction analysis unequivocally reveals the exact identity of the compounds. The procedure is extremely useful in synthetic and medicinal chemistry as it provides the desired products in a one-pot process in excellent to good yield.

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28. Copies of the data can be obtained free of charge on application to the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, U.K. (fax, (+44) 1223 336033; e-mail, deposit@ccdc.cam.ac.uk)