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ORIGINAL ARTICLE

Catalyst-, solvent- and desiccant-free three-component synthesis of novel C-2,N-3 disubstituted thiazolidin-4-ones

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Green synthesis;
Thiazolidin-4-ones

Abstract Herein it is provided an efficient, environmentally friendly and one-pot procedure for the synthesis of a library of new and diversely substituted 1,3-thiazolidin-4-ones in short reaction times and good yields through a solvent-, catalyst- and desiccant-free three-component process. Reactions proceeded by treatment of primary benzyl(aryl)amines with aromatic aldehydes (and ketones) and 2-mercaptoacetic acid acting as both reagent and self-catalyst. All reactions were performed in sand bath instead of the commonly used oil bath avoiding the generation of undesired volatile materials proceeding of the thermal decomposition of the oils. IR, Mass and NMR experiments as well as X-ray diffraction confirmed structures of the obtained products.

1. Introduction

The structural and therapeutic diversity of small heterocyclic molecules coupled with their commercial availability has fascinated organic and medicinal chemists. For this reason, the design of new substances based on privileged scaffolds is one of the successful directions in drug discovery. According to this approach, thiazolidin-4-one scaffold has been gaining prominence in recent years, due to the fact that many of them have proved interesting activity profiles namely anti-inflammatory (Look et al., 1996), anti-histaminic (Diurno et al., 1992), antibacterial (Anders et al., 2000; Kucukguzel et al., 2002), anti-fungal (Karali et al., 1998; Fahmy, 2001), anticonvulsant (Ergenc and Capan, 1994; Capan et al., 1966), antituberculosis (Bukowski et al., 1998; Ulusoy, 2002; Babaoglu et al., 2003), anticancer (Lesyk et al., 2011; Kaminsky et al., 2011; Kaminsky and Lesyk, 2010; Gududuru et al., 2004a, 2004b; Ottanà et al., 2005), antiviral (Rawal et al., 2007, 2008; Barreca et al., 2001; Rao et al., 2002, 2003, 2004) and

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anti-Candida and antioxidant (Secci et al., 2016; De Monte et al., 2016). Fig. 1 shows some representative examples of this family of compounds.

Compound **1** showed a potent activity as a non-nucleoside inhibitor of the hepatitis C virus NS5B RNA-dependant RNA polymerase (Rawal et al., 2008). Compound **2** displayed a superior *in vitro* anticancer activity than other related compounds, showing its highest susceptibility against the *Leukemia* panel (Kaminsky et al., 2011), compounds **3** exhibited high COX-2 inhibitory selectivity and potency (Unsal-Tan et al., 2012), while compound **4** and some of its analogues have been reported as promising and selective HIV-1 reverse transcriptase inhibitors. From a structure-activity relationship (SAR) point of view, the anti-HIV activity displayed by this family of compounds is strongly dependent on the nature of the substituents at C-2 and N-3 of the thiazolidin-4-one ring (Rao et al., 2003, 2004; Barreca et al., 2001).

Because of the high reaction rates, selectivity and efficiency, as well as the low cost and small environmental impact, multicomponent reactions (MCRs) have become a powerful tool to access a vast number of synthetic and pharmaceutically relevant compounds (Dömling, 2005a; Dömling et al., 2012; Jarusiewicz et al., 2009). MCRs are convergent reactions in which three or more starting materials react in a single chemical step to form a product that incorporates substantial portions of all components. Thus, there is a network of reaction equilibria, which all finally flow into an irreversible step that leads to the formed products (Tietze, 1996; Dömling, 2005b; Coquerel et al., 2010).

Usually the synthesis of the thiazolidin-4-ones has been carried out via two- and three-component reactions involving primary amines, an oxo-compound and thiolic acids, commonly under harsh and environmentally unfriendly reaction conditions. In this sense, several synthetic approaches, with minor or major success, have been reported, as shown in Scheme 1, entry (a).

In contrast, we are proposing here an environmentally friendly synthesis of new C-2 and N-3 disubstituted thiazolidin-4-ones through a catalyst-, solvent- and desiccant-free three-component approach, as shown in Scheme 1, entry (b).

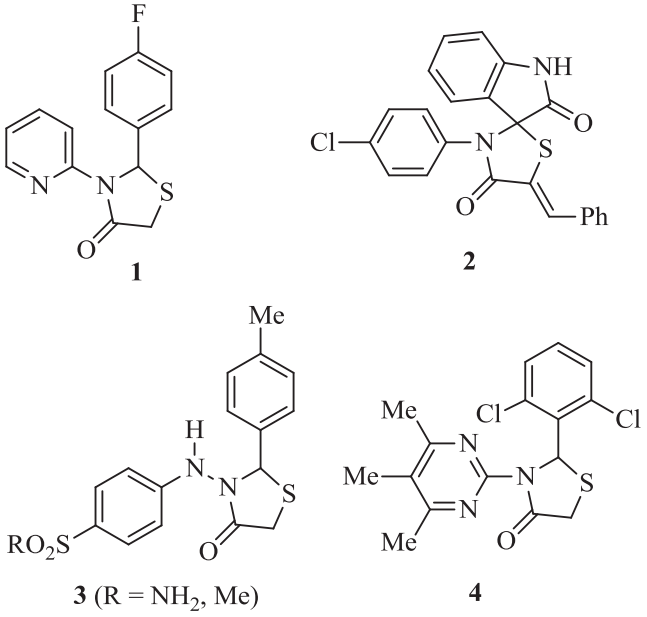


Figure 1 Some 1,3-thiazolidin-4-one derivatives of biological interest.

2. Results and discussion

Continuing with our current studies on the synthetic utility of benzylamines (Castillo et al., 2009; Abonia et al., 2010a, 2013) and 2-mercaptoacetic acid (Abonia, 2014), herein, we report an efficient synthetic procedure to prepare 1,3-thiazolidin-4-ones in good to excellent yield starting from primary benzylamines and anilines through a three-component approach without using solvent, catalyst or desiccant agents, constituting the main advantage with respect to the previous reported methods.

Recently, we found that the heating of a solvent- and catalyst-free three-component mixture of 5-aminopyrazoles **5**, benzaldehydes **6** and 2-mercaptoacetic acid **7a** at 120 °C, afforded the respective pyrazolothiazepinones **8** in good to excellent yields (Scheme 2) (Abonia, 2014). In order to evaluate the effect of replacing the 5-aminopyrazole motifs **5** by primary benzylamines **9**, a mixture of benzylamine **9a** (R^1 = H) (1 equiv), 3,4,5-trimethoxybenzaldehyde **6a** (R = 3,4,5-$(OCH_3)_3$) (1 equiv) and 2-mercaptoacetic acid **7a** (1.1 equiv) was subjected to the above reaction conditions as a model approach (Scheme 2). Upon consumption of the starting materials after 30 min of heating (monitored by thin-layer chromatography, TLC), the obtained residue was purified from aqueous ethanol, affording a yellow solid. After analysis by spectroscopic techniques, interestingly we noticed the formation of the thiazolidin-4-one derivative **10a** in 78% yield instead of its corresponding eightmembered thiazocinone **11** structurally related to the structure **8**.

The most relevant spectroscopic features to confirm the structure proposed for compound **10a** corresponded to the presence of NC═O and C─O absorption bands at 1675 and (1237, 1007) cm^{-1}, respectively, in the IR spectrum. Two doublets at 3.71 and 5.08 ppm (J = 14.8 Hz and J = 14.8 Hz, respectively) corresponding to the $PhCH_2$ protons, a double-doublet integrating for 1H at 3.78 ppm (J = 1.0, 15.6 Hz) assigned to Ha-5, a multiplet integrating for 10H in the range of 3.82–3.88 ppm assigned to $(OCH_3)_3$ and Hb-5, and a doublet integrating for 1H at 5.36 ppm (J = 1.5 Hz) assigned to H-2, along with the remaining 7H aromatic protons are the most relevant signals in the ^{1}H NMR spectrum of **10a**. The absence of a NH signal in both IR and ^{1}H NMR spectra also agrees with the proposed structure **10a**. The presence of two methylene carbon atoms at 33.1 and 46.5 ppm assigned to C-5 and $PhCH_2$ respectively, two types of (OCH_3) carbon atoms at 56.2 and 63.5 ppm, the C-2 signal at 60.8 ppm and the NC═O signal at 171.2 ppm are the most relevant features in the ^{13}C NMR spectrum of **10a**. Finally, a molecular ion with m/z 359 (88%), and a base peak with m/z 284 [M-75] (100%), also confirmed the proposed structure for compound **10a**.

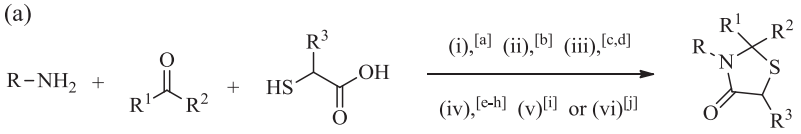
Given the success of the model reaction, we decided to evaluate the scope of this multicomponent approach by extending our synthetic methodology to the benzaldehydes chemset **6a–d** and the benzylamines and anilines chemset **9a–f**, Fig. 2.

Similar to our first test, the reactions proceeded smoothly and a set of diversely substituted thiazolidin-4-ones **10** was obtained in moderate to excellent yields, Table 1.

A further exploration of the scope and limitations of this methodology consisted in trying the reaction with heterocyclic aldehydes **6e–g** and ketones **6h,i** chemsets as carbonylic precursors, Fig. 3.

Previous work: Harsh and environmentally unfriendly reaction conditions

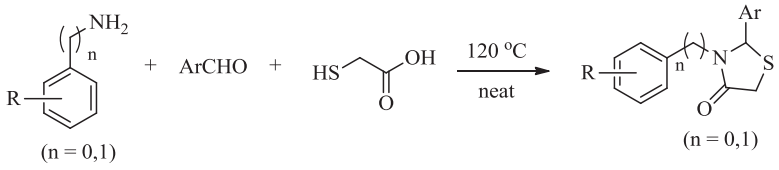
(a)



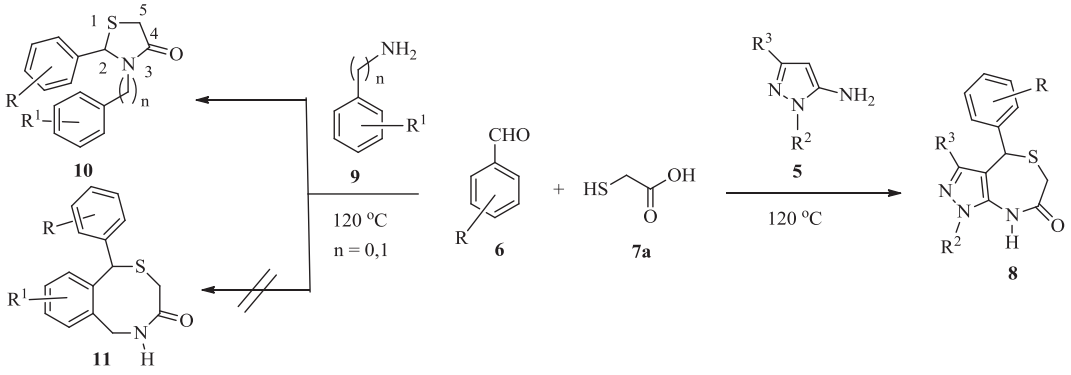
(i) = refluxing anhydrous benzene/AcOH/Dean-Stark trap, (ii) = refluxing dry toluene at 120 °C, (iii) = DCC/THF/rt or toluene/4Å MS/*p*-TSA/120 °C, (iv) = refluxing toluene then $NaHCO_3$ solution, (v) = MW assisted synthesis or (vi) = ionic liquid (IL)/N_2/80 °C then $NaHCO_3$ solution.

This work: Solvent-, catalyst- and dessicant-free three-component approach

(b)



Scheme 1 Synthetic approaches for preparing 1,3-thiazolidin-4-ones. [a]Kaminsky et al. (2011), [b]Rawal et al. (2007), [c]Rawal et al. (2008), [d]Srivastava et al. (2002), [e]Rao et al. (2004), [f]Barreca et al. (2001), [g]Rao et al. (2003), [h]Rao et al. (2002), [i]Dandia et al. (2006), Gududuru et al. (2004a, 2004b), Bolognese et al. (2004), Pawełczyk and Zaprutko (2009), [j]Yadav et al. (2009).



Scheme 2 Amine-dependent three-component synthesis of pyrazolothiazepinones **8** or thiazolidin-4-one derivative **10a** (R = 3,4,5-$(OCH_3)_3$; R^1 = H; n = 1).

In all cases, reaction proceeded in similar manner and the expected products **10p–w** were obtained in good yields, Table 2. Interestingly, the six-membered 1,3-thiazin-4-one **12** was obtained when 3-mercaptopropionic acid **7b** was used instead of the 2-mercaptoacetic one **7a**.

The presence of the NC═O functionality (evidenced in the range of 1652–1736 cm^{-1} in IR and 170.6–172.8 ppm in ^{13}C NMR spectra), two double-doublets for C-5(Ha)/C-5(Hb) proton [carbon] (in the range of 3.62–3.88/3.75–5.16 ppm and [31.3–33.4] ppm) in the ^1H and ^{13}C NMR spectra respectively, and a narrow doublet (singlet for structures **10e**, **10g**, **10i**, **10j**, **10m**, **10p** and **10r–10t**) assigned to C-2(H) proton [carbon] (in the range of 5.34–6.57, and [54.3–65.2] ppm), were the determinant structural features of the thiazolidin-4-one skeleton in compounds **10**. Particularly, in the case of the spiro-derivatives **10u–w**, the quaternary C-2 carbon atoms appeared in the range of 70.5–74.4 ppm in their ^{13}C NMR spectra. In the case of the 1,3-thiazin-4-one **12**, its NC═O functionality appeared at 1645 cm^{-1} in the IR and 169.5 ppm in ^{13}C NMR spectra, while the C-2(H) proton [carbon] appeared as singlet at 5.38 ppm in the ^1H NMR and 61.2 ppm in the ^{13}C NMR spectra, respectively.

In addition to the above spectroscopic experiments and in order to unequivocally demonstrate the formation of the thiazolidin-4-one derivatives **10**, single crystals suitable for X-ray diffraction of compounds **10a** (Fig. 4) and **10l** (Moreno-Fuquen et al., 2014), were grown by slow evaporation in ethanol at room temperature, as shown in Fig. 4 and Tables 3 and 4. According to the results there is no doubt that, the obtained compounds effectively corresponded to 1,3-thiazolidin-4-ones **10** as proposed in Scheme 1 and Tables 1 and 2.

The more likely mechanism for the formation of the thiazolidin-4-one **10** and thiazin-4-one **12** skeletons is described in Scheme 3.

According to this mechanistic approach, formation *in situ* of the iminium species **13** is suggested as the first step, followed by a nucleophilic attack of the ─SH moiety of **7** on the

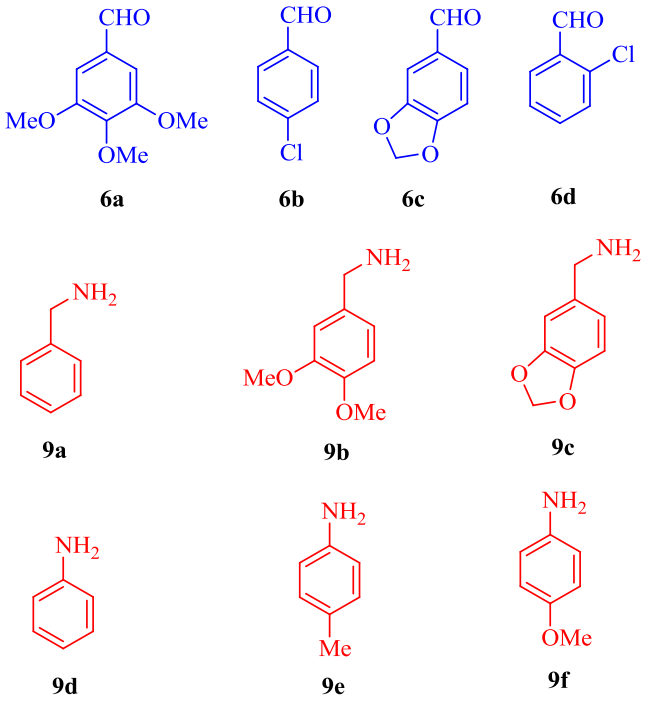


Figure 2 Diverse aldehydes **6** and amines **9** employed for the synthesis of product **10**.

activated azomethinic carbon atom in **13** affording the γ-amino-acid **14**. This latter, suffers an intramolecular amidation process releasing a molecule of water to afford the isolated compounds **10**, **12**. Interestingly, the source of protons during the process is supplied by the mercapto-acids **7a,b** themselves. Therefore, this process certainly corresponds to a self-catalyzed three-component approach with a double role of the mercapto-acids **7a,b** acting as both the reagents and the catalysts. The last step in Scheme 3 is associated with the rate limiting for obtaining low or high yields of thiazolidin-4-ones **10** (Srivastava et al., 2002) and for instance thiazin-4-ones **12**. Consequently, to enhance the efficiency of this reaction, a variety of desiccants has been employed for removing the water during the cyclization process. Currently, either azeotropic distillation or molecular sieves have been used with this purpose (Kaminsky et al., 2011; Rawal et al., 2008; Holmes et al., 1995). Additionally, anhydrous $ZnCl_2$ (Srinivas et al., 2008), trimethylorthoformate (Holmes et al., 1995) or sodium sulfate (Sharma and Kumar, 2000) have also worked as desiccants. Particularly, in our case the use of a desiccant was unnecessary because our methodology proceeded without using solvent and the mixture was heated at 120 °C in open vessel glassware. This fact guaranteed the removal of the water as soon as it was forming during the reaction progress.

The general character of this approach was confirmed by using not only primary benzylamines (products **10a**–**10l**, **10p**–**10v** and **12**) but also primary anilines (products **10m**–**10o** and **10w**) which worked well although with relative lower yields. The reaction worked well not only with the ordinary aldehydes (products **10a**–**10o** and **12**) but also with heterocyclic aldehydes (products **10p**–**10t**) and ketones (products **10u**–**10w**) as the carbonyl reagents. Interestingly, no limitation was found when 2-mercaptoacetic acid **7a** was replaced by 3-mercaptopropionic acid **7b**. As expected, the larger six-membered thiazin-4-one ring **12** was effectively obtained, extending moreover the scope of this simple methodology and opening a future research line on thiazin-4-one derivatives under the established reaction conditions.

It is worth mentioning that all reactions were performed in a sand bath instead of the commonly recommended oil baths. This fact avoided the generation of undesired volatile materials associated with the thermal decomposition of the utilized oils. Consequently, no final disposition of the bath was required. It is also remarkable, that in this three-component procedure, three new bonds were formed during the process. This finding is in agreement with the atomic economy and bond-forming efficiency (BFE) concepts characteristic of the multicomponent reactions (Dömling, 2005a, 2005b; Dömling et al., 2012; Jarusiewicz et al., 2009; Tietze, 1996; Coquerel et al., 2010). Moreover, production of water as the unique by-product during the overall process, brings this approach effectively near to an environmentally friendly three-component synthesis.

3. Conclusions

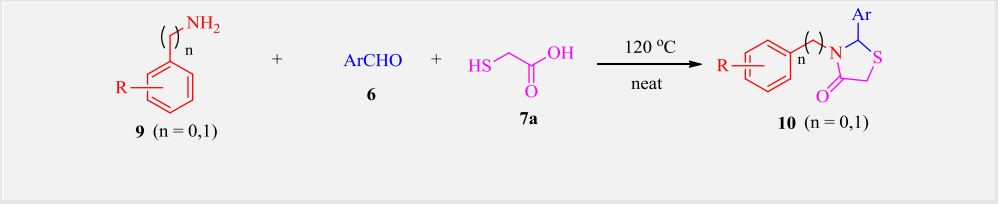
In summary, we have implemented a simple, efficient and environmentally friendly solvent-, catalyst- and desiccant-free three-component approach for the synthesis of a library of new and diversely disubstituted 1,3-thiazolidin-4-ones in short reaction times and good yields. Reaction proceeded by the heating at 120 °C, in a sand bath, a mixture of benzyl(aryl)amines **9**, aromatic aldehydes (and ketones) **6** and 2-mercaptoacetic acid **7a** acting as both a reagent and a self-catalyst. When acid **7a** was replaced by 3-mercaptopropionic acid **7b**, the six-membered thiazin-4-one **12** was obtained as unique product. Although most previous reports have required acid catalysts and/or desiccant agents to remove the releasing water to guarantee good yields, our open vessel methodology proceeded efficiently without using any of these additives.

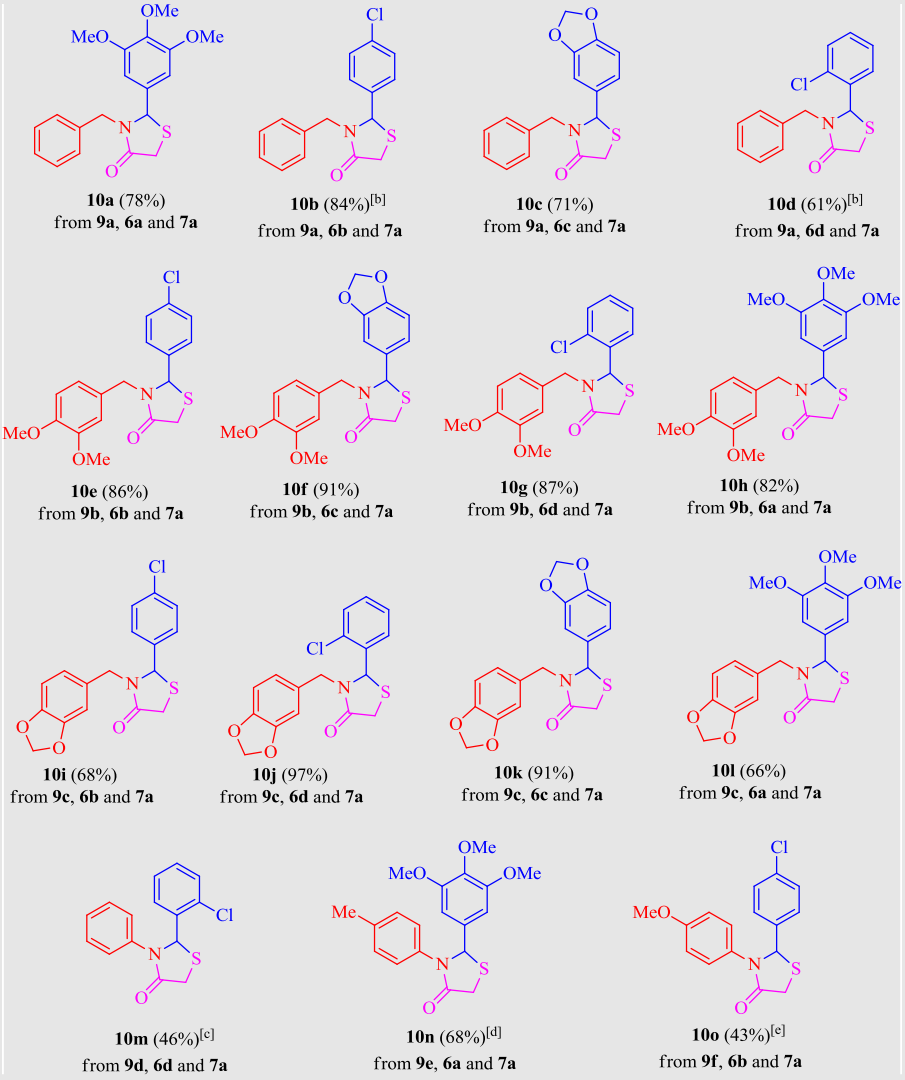
4. Material and methods

4.1. Materials

Melting points were determined on a Büchi melting point B-450 apparatus and are uncorrected. IR spectra were recorded on a Shimadzu FTIR 8400 spectrophotometer in KBr disks and films. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 400 spectrophotometer operating at 400 MHz and 100 MHz respectively, and using $CDCl_3$ as solvent and tetramethylsilane as internal standard. Mass spectra were run on a SHIMADZU-GCMS 2010-DI-2010 spectrometer (equipped with a direct inlet probe) operating at 70 eV. Single-crystal X-ray data for compound **10a** were collected at temperature (120 K) on a Kappa-CCD diffractometer, Monochromator graphite, CCD rotation images, using MoKα radiation (0.71073 Å) and deposited at Cambridge Crystallographic Data Center (CCDC reference: 1471083). Microanalyses were performed on an Agilent elemental analyzer and the values are within ±0.4% of the theoretical values. Silica gel aluminum plates (Merck 60 F_{254}) were used for analytical TLC. The starting amines **9** and the remaining reagents and solvents were purchased from Aldrich, Fluka and Acros (analytical reagent grades) and were used without further purification. Due to the heterocyclic aldehyde **6e** is commercially unavailable, and it was synthesized following a similar procedure described earlier (Abonia et al., 2010b).

Table 1 Solvent-, catalyst- and desiccant-free three-component synthesis of the new 1,3-thiazolidin-4-ones **10**.[a]





[a]Yields are based on isolated products after crystallization. [b–e]These compounds have previously been reported. Please see: [b]Raval and Trivedi (1960), [c]Yadav et al. (2009), [d]Kumar et al. (2012), [e]Tu et al. (2009).

*4.2. General procedure for the synthesis of thiazolidin-4-ones **10** and thiazin-4-one **12***

A 5 mL pyrex test tube was charged with a mixture of aldehyde **6** (0.74 mmol), 2-mercaptoacetic acid **7a** (0.82 mmol) and amine **9** (0.74 mmol) in the absence of solvent. The mixture was heated in a sand bath at 120 °C for 20–30 min until the starting materials were no longer detected by TLC. The obtained residues were purified from aqueous ethanol. In the case of thiazin-4-one **12**, 2-mercaptoacetic acid **7a** was replaced by 3-mercaptopropionic acid **7b**.

*4.2.1. (±)-3-Benzyl-2-(3,4,5-trimethoxyphenyl)thiazolidin-4-one **10a***

This compound was obtained from benzylamine **9a** (109 mg, 1.02 mmol), 3,4,5-trimethoxybenzaldehyde **6a** (201 mg,

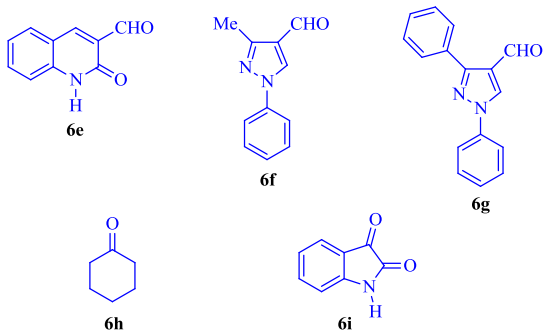


Figure 3 Additional aldehydes **6e-g** and ketones **6h,i** employed for the synthesis of a further family of product **10**.

1.02 mmol) and 2-mercaptoacetic acid **7a** (105 mg, 1.14 mmol) as a yellow solid. Yield: 78% (285 mg). Mp 100–102 °C. Data: FTIR (KBr): ν = 2937, 2839, 1675 (C═O), 1237 and 1007 (C─O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.71 (d, J = 14.8 Hz, 1H, Bn-H), 3.78 (dd, J = 0.6, 15.6 Hz, 1H, H-5a), 3.82 (s, 6H, OCH_3 x 2), 3.86–3.90 (m, 4H, OCH_3, H-5b), 5.08 (d, J = 14.8 Hz, 1H, Bn-H), 5.36 (d, J = 1.5 Hz, 1H, H-2), 6.42 (s, 2H, Ar-H), 7.09–7.13 (m, 2H, Ph-H), 7.28–7.31 (m, 3H, Ph-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.1 (CH_2), 46.5 ($PhCH_2$), 56.2 (OCH_3 x 2), 60.8 (C-2), 63.5 (OCH_3), 104.3, 127.9, 128.4, 128.6, 134.1 (Cq), 135.5 (Cq), 138.7 (Cq), 153.7 (Cq), 171.2 (C═O) ppm. MS (70 eV, EI): m/z (%) = 359 $[M]^+$ (88), 284 (100), 268 (25), 212 (23), 146 (6), 147 (11), 104 (5), 91 (79) [$PhCH_2$]. $C_{19}H_{21}NO_4S$ (359,12): calcd. C 63.49, H 5.89, N 3.90; found: C 63.32, H 5.67, N 4.08.

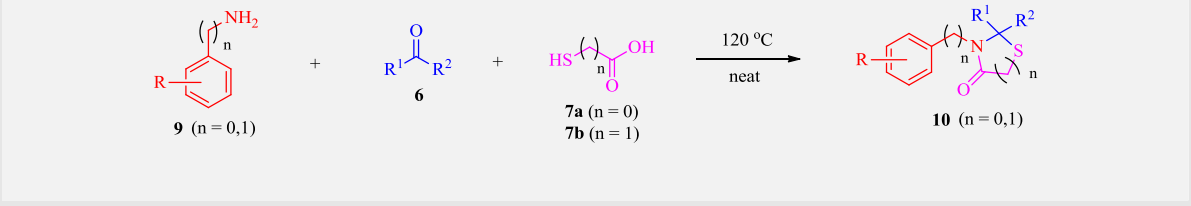
4.2.2. (±)-3-Benzyl-2-(4-chlorophenyl)thiazolidin-4-one ***10b***

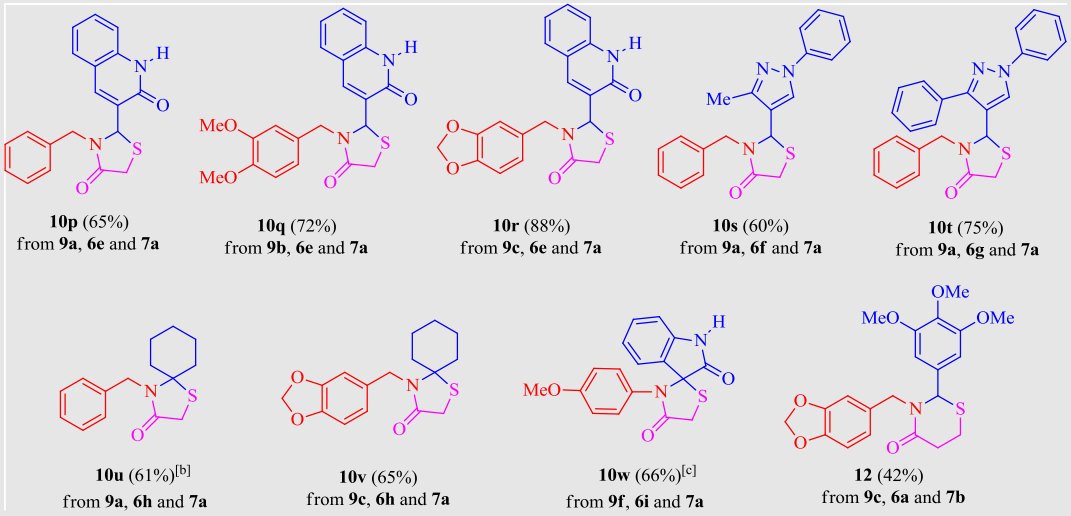
This compound was obtained from benzylamine **9a** (104 mg, 0.97 mmol), *p*-chlorobenzaldehyde **6b** (137 mg, 0.98 mmol) and 2-mercaptoacetic acid **7a** (98 mg, 1.06 mmol) as a yellow solid. Yield: 84% (247 mg). Mp 100–101 °C (73 °C by Raval and Trivedi, 1960). FTIR (KBr): ν = 2925, 2832, 1679 (C═O) cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ = 3.66 (d, J = 15.3 Hz, 1H, Bn-H), 3.78 (d, J = 15.7 Hz, 1H, H-5a), 3.97 (dd, J = 1.4, 15.6 Hz, 1H, H-5b), 4.83 (d, J = 15.1 Hz, 1H, Bn-H), 5.59 (d, J = 1.6 Hz, 1H, H-2), 7.09 (d, J = 7.2 Hz, 2H, Ph-H), 7.25–7.34 (m, 3H, Ph-H), 7.34 (d, J = 8.4 Hz, 2H, Ar-H), 7.43 (d, J = 8.4 Hz, 2H, Ar-H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 31.6 (CH_2), 45.6 ($PhCH_2$), 61.0 (C-2), 127.5, 127.6, 128.5, 128.8 (2 x C), 133.2 (Cq), 135.7 (Cq), 139.1 (Cq), 170.8 (C═O) ppm. MS (70 eV, EI): m/z (%) = 305/303 $[M]^+$ (1/3), 230/228 (6/17), 214/212 (6/17), 178 (11), 146 (25), 147 (31), 104 (16), 91 (100) [$PhCH_2$]. $C_{16}H_{14}ClNOS$ (303,05): calcd. C 63.25, H 4.64, N 4.61; found: C 63.39, H 4.45, N 4.36.

4.2.3. (±)-2-(Benzo[d][1,3]dioxol-5-yl)-3-benzylthiazolidin-4-one ***10c***

This compound was obtained from benzylamine **9a** (97 mg, 0.91 mmol), benzo[*d*][1,3]dioxole-5-carbaldehyde **6c** (137 mg,

Table 2 Additional examples obtained from the three-component procedure described in Scheme 1, entry (b).[a]





[a]Yields are based on isolated products after crystallization. [b,c]These compounds have previously been reported. Please see: [b]El-Zohry et al. (1993)), [c]Joshi et al. (1981).

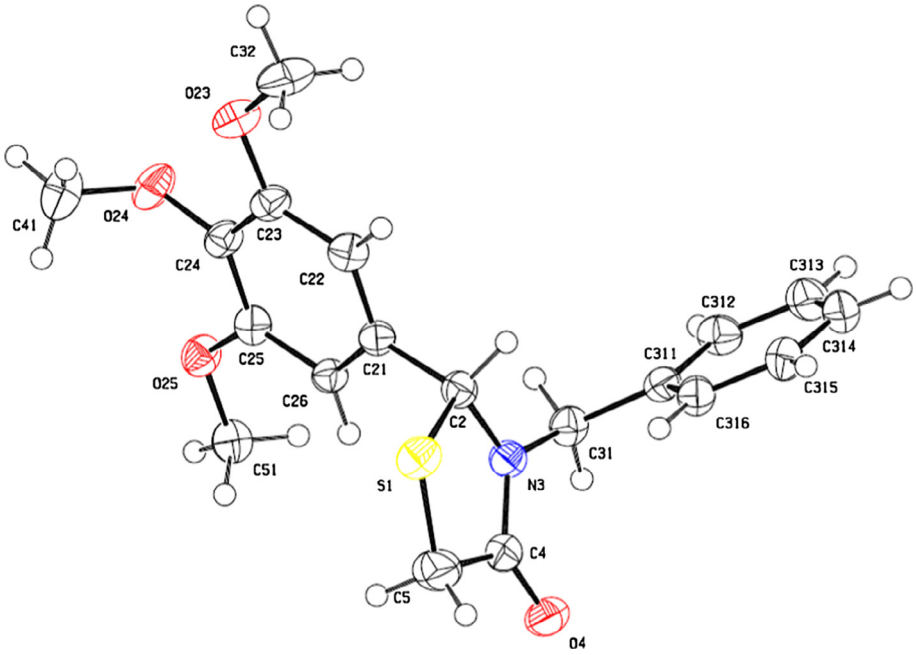


Figure 4 ORTEP drawing of the asymmetric unit for compound **10a**; ellipsoids are displayed at the 50% probability level.

Table 3 Crystal data and structure refinement for compound **10a.**

Empirical formula	$C_{19}H_{21}NO_4S$
Formula weight	359.4
Temperature	120 (2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P − 1
Unit cell dimensions	a = 8.316(5) Å α = 100.72(4)° b = 10.297(3) Å β = 110.25(6)° c = 11.781(8) Å γ = 96.74(4)°
Volume	911.6(9) $Å^3$
Z	2
Density (calculated)	1.309 Mg/m^3
Absorption coefficient	0.200 mm^{-1}
F(000)	380
Crystal size	0.12 × 0.31 × 0.36 mm^3
Theta range for data collection	2.62–27.5°
Index ranges	$-10 \leqslant h \leqslant 10$, $-13 \leqslant k \leqslant 13$, $-15 \leqslant l \leqslant 15$
Reflections collected	22,225
Independent reflections	4189 [R(int) = 0.0742]
Completeness to theta = 27.5°	99.9%
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	4189/0/229
Goodness-of-fit on F2	1.028
Final R indices [I > 2sigma(I)]	R1 = 0.0696, wR2 = 0.1830
R indices (all data)	R1 = 0.0944, wR2 = 0.2056
Largest diff. peak and hole	1.833 and −0.374 e.$Å^{-3}$

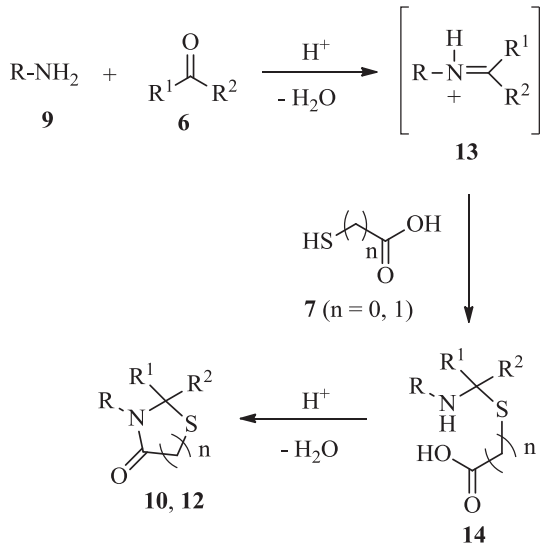
Table 4 Selected bond lengths [Å], angles [°] and torsion angles [°] for compound **10a.**

Bond lengths	
S(1)-C(5); 1.792(4)	N(3)-C(2); 1.449(4)
S(1)-C(2); 1.860(3)	O(4)-C(4); 1.220(4)
N(3)-C(4); 1.361(4)	
Angles	
C(5)-S(1)-C(2); 92.60(15)	N(3)-C(4)-C(5); 111.4(3)
C(4)-N(3)-C(2); 119.6(2)	C(4)-C(5)-S(1); 107.6(2)
N(3)-C(2)-S(1); 104.90(18)	
Torsion angles	
C(4)-N(3)-C(31)-C(311); 99.8(3)	C(4)-N(3)-C(2)-S(1); −8.5(3)
C(4)-N(3)-C(2)-C(21); 114.4(3)	C(31)-N(3)-C(2)-S(1); 165.05(19)
N(3)-C(2)-C(21)-C(22); 160.3(2)	

0.91 mmol) and 2-mercaptoacetic acid **7a** (93 mg, 1.01 mmol) as a yellow solid. Yield: 71% (201 mg). Mp 77 °C. Data: FTIR (KBr): ν = 2915, 2849, 1678 (C═O), 1246 and 1037 (C─O) cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ = 3.66 (d, J = 15.3 Hz, 1H, Bn-H), 3.74 (d, J = 15.5 Hz, 1H, H-5a), 3.97 (dd, J = 1.6, 15.5 Hz, 1H, H-5b), 4.80 (d, J = 15.3 Hz, 1H, Bn-H), 5.50 (d, J = 1.6 Hz, 1H, H-2), 6.03 (d, J = 5.0 Hz, 2H, OCH_2O), 6.77 (dd, J = 1.6, 7.9 Hz, 1H, Ar-H), 6.87 (d, J = 7.8 Hz, 1H, Ar-H), 6.91 (d, J = 1.8 Hz, 1H, Ar-H), 7.12 (d, J = 7.4 Hz, 2H, Ph-H), 7.25–7.35 (m, 3H, Ph-H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 31.7 (CH_2), 45.5 ($PhCH_2$), 61.8 (C-2), 101.3 (OCH_2O), 107.0, 107.9, 120.9, 127.4, 127.6, 128.5, 133.5 (Cq), 135.8 (Cq), 147.7 (Cq), 147.9 (Cq), 170.6 (C═O) ppm. MS (70 eV, EI): m/z (%) = 313 $[M]^+$ (39), 238 (100), 222 (31), 146 (16), 147 (19), 104 (9), 91 (90) $[PhCH_2]$. $C_{17}H_{15}NO_3S$ (313,08): calcd. C 65.16, H 4.82, N 4.47; found: C 65.09, H 5.03, N 4.33.

4.2.4. (±)-3-Benzyl-2-(2-chlorophenyl)thiazolidin-4-one ***10d***

This compound was obtained from benzylamine **9a** (93 mg, 0.87 mmol), *o*-chlorobenzaldehyde **6d** (123 mg, 0.88 mmol)



Scheme 3 Proposed mechanistic sequence for the formation of products **10** and **12** via the iminium intermediate **13.**

and 2-mercaptoacetic acid **7a** (88 mg, 0.96 mmol) as a yellow solid. Yield: 61% (160 mg). Mp 105–106 °C (75 °C by Raval and Trivedi, 1960). Data: FTIR (KBr): ν = 2946, 2837, 1690 (C═O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.67 (d, J = 14.8 Hz, 1H, Bn-H), 3.72 (d, J = 15.6 Hz, 1H, H-5a), 3.84 (dd, J = 1.0, 15.6 Hz, 1H, H-5b), 5.22 (d, J = 14.8 Hz, 1H, Bn-H), 5.88 (d, J = 1.0 Hz, 1H, H-2), 7.14–7.17 (m, 2H, Ar-H), 7.23 (dd, J = 2.0, 7.0 Hz, 1H, Ar-H), 7.29–7.35 (m, 5H, Ph-H), 7.41 (dd, J = 2.0, 7.2 Hz, 1H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.3 (CH_2), 46.7 ($PhCH_2$), 62.7 (C-2), 127.6, 128.0, 128.3 (2 x C), 128.8, 129.7, 130.3, 132.8 (Cq), 134.9 (Cq), 136.6 (Cq), 171.7 (C═O) ppm. MS (70 eV, EI): m/z (%) = 305/303 $[M]^+$ (0.5/1), 230/228 (1/3), 214/212 (2/6), 147 (7), 146 (8), 104 (12), 91 (100) [$PhCH_2$]. $C_{16}H_{14}ClNOS$ (303,05): calcd. C 63.25, H 4.64, N 4.61; found: C 63.59, H 4.79, N 4.45.

4.2.5. (±)-3-(3,4-Dimethoxybenzyl)-2-(4-chlorophenyl) thiazolidin-4-one ***10e***

This compound was obtained from 3,4-dimethoxybenzylamine **9b** (94 mg, 0.56 mmol), *p*-chlorobenzaldehyde **6b** (80 mg, 0.57 mmol) and 2-mercaptoacetic acid **7a** (58 mg, 0.63 mmol) as a yellow solid. Yield: 86% (176 mg). Mp 102 °C. Data: FTIR (KBr): ν = 2933, 2834, 1679 (C═O), 1239, 1157, 1140 and 1027 (C—O) cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ = 3.59 (d, J = 14.8 Hz, 1H, Bn-H), 3.68 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 3.76 (d, J = 15.7 Hz, 1H, H-5a), 3.95 (d, J = 15.7 Hz, 1H, H-5b), 4.69 (d, J = 14.8 Hz, 1H, Bn-H), 5.57 (s, 1H, H-2), 6.61–6.62 (d, 2H, Ar-H), 6.87 (d, J = 8.6 Hz, 1H, Ar-H), 7.34 (d, J = 8.2 Hz, 2H, Ar-H), 7.43 (d, J = 8.2 Hz, 2H, Ar-H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 31.7 (CH_2), 45.5 ($PhCH_2$), 55.3 (OCH_3), 55.5 (OCH_3), 61.0 (C-2), 111.7, 111.8, 120.2, 127.9 (Cq), 128.8, 128.9, 133.1 (Cq), 139.2 (Cq), 148.3 (Cq), 148.7 (Cq), 170.7 (C═O) ppm. MS (70 eV, EI): m/z (%) = $[M]^+$ 365/363 (7/18), 207 (38), 176 (100), 164 (16), 151 (73). $C_{18}H_{18}ClNO_3S$ (363,07): calcd. C 59.42, H 4.99, N 3.85; found: C 59.36, H 5.05, N 3.91.

4.2.6. (±)-3-(3,4-Dimethoxybenzyl)-2-(benzo[d][1,3]dioxol-5-yl)thiazolidin-4-one ***10f***

This compound was obtained from 3,4-dimethoxybenzylamine **9b** (106 mg, 0.63 mmol), benzo[*d*][1,3]dioxole-5-carbaldehyde **6c** (96 mg, 0.64 mmol) and 2-mercaptoacetic acid **7a** (65 mg, 0.71 mmol) as a yellow solid. Yield: 91% (216 mg). Mp 112 °C. Data: FTIR (KBr): ν = 2933, 2835, 1677 (C═O), 1244, 1156, 1140 and 1033 (C—O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.54 (d, J = 14.3 Hz, 1H, Bn-H), 3.73 (d, J = 15.6 Hz, 1H, H-5a), 3.83 (s, 3H, OCH_3), 3.87 (dd, J = 1.6, 15.4 Hz, 1H, H-5b), 3.87 (s, 3H, OCH_3), 5.06 (d, J = 14.6 Hz, 1H, Bn-H), 5.34 (d, J = 1.5 Hz, 1H, H-2), 6.00 (s, 2H, OCH_2O), 6.62–6.68 (m, 3H, Ar-H), 6.76–6.80 (m, 3H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.1 (CH_2), 46.0 ($PhCH_2$), 55.9 (OCH_3 x 2), 62.8 (C-2), 101.5 (OCH_2O), 107.1, 108.1, 111.1, 111.7, 121.0, 121.2, 127.8 (Cq), 132.9 (Cq), 148.4 (Cq), 148.6 (Cq), 148.8 (Cq), 149.1 (Cq), 171.0 (C═O) ppm. MS (70 eV, EI): m/z (%) = 373 $[M]^+$ (17), 207 (60), 192 (13), 176 (100), 164 (13), 151 (70), 135 (11), 121 (13), 107 (21). $C_{19}H_{19}NO_5S$ (373,10): calcd. C 61.11, H 5.13, N 3.75; found: C 61.05, H 5.02, N 3.61.

4.2.7. (±)-3-(3,4-Dimethoxybenzyl)-2-(2-chlorophenyl) thiazolidin-4-one ***10g***

This compound was obtained from 3,4-dimethoxybenzylamine **9b** (116 mg, 0.69 mmol), *o*-chlorobenzaldehyde **6d** (98 mg, 0.70 mmol) and 2-mercaptoacetic acid **7a** (71 mg, 0.77 mmol) as a yellow solid. Yield: 87% (219 mg). Mp 108–109 °C. Data: FTIR (KBr): ν = 2923, 2840, 1668 (C═O), 1235, 1142 and 1030 (C—O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.60 (d, J = 14.5 Hz, 1H, Bn-H), 3.71 (d, J = 15.5 Hz, 1H, H-5a), 3.83 (s, 3H, OCH_3), 3.84 (d, J = 15.5 Hz, 1H, H-5b), 3.88 (s, 3H, OCH_3), 5.15 (d, J = 14.5 Hz, 1H, Bn-H), 5.87 (s, 1H, H-2), 6.65–6.68 (m, 2H, Ar-H), 6.79 (d, J = 8.5 Hz, 1H, Ar-H), 7.23 (dd, J = 1.7, 7.1 Hz, 1H, Ar-H), 7.30–7.37 (m, 2H, Ar-H), 7.42 (dd, J = 1.7, 7.5 Hz, 1H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.5 (CH_2), 46.6 ($PhCH_2$), 55.8 (OCH_3), 55.9 (OCH_3), 59.0 (C-2), 111.2, 111.6, 121.1, 127.2, 127.4 (Cq), 127.6, 129.8, 130.3, 132.8 (Cq), 136.8 (Cq), 148.8 (Cq), 149.2 (Cq), 171.7 (C═O) ppm. MS (70 eV, EI): m/z (%) = 365/363 $[M]^+$ (0.5/3), 176 (42), 151 (46), 107 (25), 91 (10) [$PhCH_2$], 28 (100). $C_{18}H_{18}ClNO_3S$ (363,07): calcd. C 59.42, H 4.99, N 3.85; found: C 59.59, H 4.85, N 3.91.

4.2.8. (±)-3-(3,4-Dimethoxybenzyl)-2-(3,4,5-trimethoxyphenyl)thiazolidin-4-one ***10h***

This compound was obtained from 3,4-dimethoxybenzylamine **9b** (89 mg, 0.53 mmol), 3,4,5-trimethoxybenzaldehyde **6a** (106 mg, 0.54 mmol) and 2-mercaptoacetic acid **7a** (55 mg, 0.60 mmol) as a yellow solid. Yield: 82% (183 mg). Mp 104–105 °C. Data: FTIR (KBr): ν = 2937, 2836, 1688 (C═O), 1237, 1124, 1027 and 1005 (C—O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.62 (d, J = 14.3 Hz, 1H, Bn-H), 3.76 (d, J = 15.1 Hz, 1H, H-5a), 3.82 (s, 3H, OCH_3), 3.83 (s, 6H, OCH_3 x 2), 3.84–3.89 (m, 7H, H-5b, OCH_3 x 2), 5.05 (d, J = 14.3 Hz, 1H, Bn-H), 5.35 (d, J = 1.5 Hz, 1H, H-2), 6.42 (s, 2H, Ar-H), 6.61 (dd, J = 1.9, 8.0 Hz, 1H, Ar-H), 6.64 (d, J = 1.8 Hz, 1H, Ar-H), 6.77 (d, J = 8.0 Hz, 1H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.2 (CH_2), 46.3 ($PhCH_2$), 55.9 (OCH_3 x 2), 56.2 (OCH_3 x 2), 60.8 (OCH_3), 63.3 (C-2), 104.2, 111.1, 111.8, 121.0, 127.9 (Cq), 134.3 (Cq), 138.6 (Cq),

148.8 (Cq), 149.2 (Cq), 153.7 (Cq), 171.2 (C═O) ppm. MS (70 eV, EI): *m/z* (%) = 419 $[M]^+$ (34), 344 (11), 268 (12), 207 (35), 176 (100), 151 (82), 107 (12). $C_{21}H_{25}NO_6S$ (419,14): calcd. C 60.13, H 6.01, N 3.34; found: C 60.21, H 5.85, N 3.19.

*4.2.9. (±)-3-((Benzo[d][1,3]dioxol-6-yl)methyl)-2-(4-chlorophenyl)thiazolidin-4-one **10i***

This compound was obtained from 3,4-methylenedioxybenzylamine **9c** (107 mg, 0.71 mmol), *p*-chlorobenzaldehyde **6b** (100 mg, 0.71 mmol) and 2-mercaptoacetic acid **7a** (73 mg, 0.79 mmol) as a white solid. Yield: 61% (167 mg). Mp 115–116 °C. Data: FTIR (KBr): *v* = 2924, 2895, 1672 (C═O), 1244, 1092 and 1038 (C—O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.45 (d, *J* = 14.6 Hz, 1H, Bn-H), 3.73 (d, *J* = 15.6 Hz, 1H, H-5a), 3.86 (d, *J* = 15.8 Hz, 1H, H-5b), 5.02 (d, *J* = 14.6 Hz, 1H, Bn-H), 5.37 (s, 1H, H-2), 5.95 (s, 2H, OCH_2O), 6.48 (d, *J* = 7.8 Hz, 1H, Ar-H), 6.61 (s, 1H, Ar-H), 6.70 (d, *J* = 7.8 Hz, 1H, Ar-H), 7.17 (d, *J* = 8.3 Hz, 2H, Ar-H), 7.35 (d, *J* = 8.3 Hz, 2H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.9 (CH_2), 46.1 ($PhCH_2$), 62.0 (C-2), 101.1 (OCH_2O), 108.2, 108.7, 121.9, 128.5, 128.8 (Cq), 129.3, 135.0 (Cq), 137.7 (Cq), 147.4 (Cq), 148.1 (Cq), 171.0 (C═O) ppm. MS (70 eV, EI): *m/z* (%) = 349/347 $[M]^+$ (3/9), 191 (58), 161 (45), 148 (42), 135 (100), 105 (17), 77 (52). $C_{17}H_{14}ClNO_3S$ (347,04): calcd. C 58.70, H 4.06, N 4.03; found: C 58.95, H 4.24, N 4.18.

*4.2.10. (±)-3-((Benzo[d][1,3]dioxol-6-yl)methyl)-2-(2-chlorophenyl)thiazolidin-4-one **10j***

This compound was obtained from 3,4-methylenedioxybenzylamine **9c** (107 mg, 0.71 mmol), *o*-chlorobenzaldehyde **6d** (102 mg, 0.73 mmol) and 2-mercaptoacetic acid **7a** (73 mg, 0.79 mmol) as a white solid. Yield: 97% (238 mg). Mp 119 °C. Data: FTIR (KBr): *v* = 2927, 2839, 1677 (C═O), 1247 and 1038 (C-O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.50 (d, *J* = 14.8 Hz, 1H, Bn-H), 3.62 (d, *J* = 15.6 Hz, 1H, H-5a), 3.75 (d, *J* = 0.9, 15.5 Hz, 1H, H-5b), 5.03 (d, *J* = 14.6 Hz, 1H, Bn-H), 5.82 (s, 1H, H-2), 5.86 (s, 2H, OCH_2-O), 6.48 (dd, *J* = 1.2, 7.6 Hz, 1H, Ar-H), 6.62 (d, *J* = 1.5 Hz, 1H, Ar-H), 6.64 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.16 (dd, *J* = 2.1, 7.2 Hz, 1H, Ar-H), 7.19–7.26 (m, 2H, Ar-H), 7.33 (dd, *J* = 1.6, 7.6 Hz, 1H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.1 (CH_2), 46.2 ($PhCH_2$), 58.8 (C-2), 100.8 (OCH_2O), 107.9, 108.4, 121.6, 126.9, 127.3, 128.4 (Cq), 129.5, 130.0, 132.5 (Cq), 136.4 (Cq), 147.1 (Cq), 147.7 (Cq), 171.3 (C═O) ppm. MS (70 eV, EI): *m/z* (%) = 349/347 $[M]^+$ (6/12), 214/212 (14/27), 191 (70), 161 (52), 148 (42), 135 (100), 105 (21), 77 (50), 46 (88). $C_{17}H_{14}ClNO_3S$ (347,04): calcd. C 58.70, H 4.06, N 4.03; found: C 58.93, H 4.21, N 4.16.

*4.2.11. (±)-2-(Benzo[d][1,3]dioxol-5-yl)-3-((benzo[d][1,3]dioxol-6-yl)methyl)thiazolidin-4-one **10k***

This compound was obtained from 3,4-methylenedioxybenzylamine **9c** (99 mg, 0.66 mmol), 3,4-methylenedioxybenzaldehyde **6c** (100 mg, 0.67 mmol) and 2-mercaptoacetic acid **7a** (66 mg, 0.72 mmol) as a brown solid. Yield: 91% (213 mg). Mp 129–130 °C. Data: FTIR (KBr): *v* = 2931, 2897, 1670 (C═O), 1609, 1244, 1097 and 1037 (C—O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.50 (d, *J* = 14.6 Hz, 1H, Bn-H), 3.73 (d, *J* = 15.6 Hz, 1H, H-5a), 3.86 (dd, *J* = 1.2, 15.4 Hz, 1H, H-5b), 5.02 (d, *J* = 14.6 Hz, 1H, Bn-H), 5.35 (d, *J* = 1.8 Hz, 1H, H-2), 5.96 (s, 2H, OCH_2O), 6.00 (s, 2H, OCH_2O), 6.54 (dd, *J* = 1.4, 7.7 Hz, 1H, Ar-H), 6.65 (d, *J* = 1.5 Hz, 1H, Ar-H), 6.67 (dd, *J* = 1.9, 7.8 Hz, 1H, Ar-H), 6.72 (d, *J* = 8.0 Hz, 1H, Ar-H), 6.75–6.79 (m, 2H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.0 (CH_2), 45.9 ($PhCH_2$), 62.7 (C-2), 101.1 (OCH_2O), 101.5 (OCH_2O), 107.1, 108.1, 108.2, 108.8, 121.2, 122.0, 129.1 (Cq), 132.8 (Cq), 147.3 (Cq), 148.0 (Cq), 148.4 (Cq), 148.6 (Cq), 170.9 (C═O) ppm. MS (70 eV, EI): *m/z* (%) = 357 $[M]^+$ (37), 165 (21), 148 (16), 135 (100), 121 (26), 105 (17), 77 (39), 46 (51). $C_{18}H_{15}NO_5S$ (357,07): calcd. C 60.49, H 4.23, N 3.92; found: C 60.38, H 4.40, N 3.98.

*4.2.12. (±)-3-((Benzo[d][1,3]dioxol-6-yl)methyl)-2-(3,4,5-trimethoxyphenyl)thiazolidin-4-one **10l***

This compound was obtained from 3,4-methylenedioxybenzylamine **9c** (111 mg, 0.74 mmol), 3,4,5-trimethoxybenzaldehyde **6a** (145 mg, 0.74 mmol) and 2-mercaptoacetic acid **7a** (75 mg, 0.82 mmol) as a white solid. Yield: 66% (196 mg). Mp 122–123 °C. Data: FTIR (KBr): *v* = 2934, 2841, 1672 (C═O), 1240, 1121 and 1037 (C—O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.60 (d, *J* = 14.6 Hz, 1H, Bn-H), 3.75 (d, *J* = 15.8 Hz, 1H, H-5a), 3.83–3.89 (m, 10H, H-5b, OCH_3 x 3), 4.98 (d, *J* = 14.6 Hz, 1H, Bn-H), 5.36 (d, *J* = 1.5 Hz, 1H, H-2), 5.95 (s, 2H, OCH_2O), 6.44 (s, 2H, Ar-H), 6.52 (dd, *J* = 1.4, 7.8 Hz, 1H, Ar-H), 6.64 (d, *J* = 1.2 Hz, 1H, Ar-H), 6.71 (d, *J* = 8.0 Hz, 1H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.1 (CH_2), 46.3 ($PhCH_2$), 56.2 (OCH_3 x 2), 60.8 (C-2), 63.4 (OCH_3), 101.1 (OCH_2O), 104.3, 108.1, 108.9, 122.0, 129.2 (Cq), 134.2 (Cq), 138.7 (Cq), 147.3 (Cq), 148.0 (Cq), 153.7 (Cq), 171.2 (C═O) ppm. MS (70 eV, EI): *m/z* (%) = 403 $[M]^+$ (7), 212 (17), 191 (28), 161 (32), 148 (29), 135 (100), 105 (17), 77 (52). $C_{20}H_{21}NO_6S$ (403,11): calcd. C 59.54, H 5.25, N 3.47, found: C 59.87, H 5.34, N 3.23.

*4.2.13. (±)-2-(2-Chlorophenyl)-3-phenylthiazolidin-4-one **10m***

This compound was obtained from aniline **9d** (104 mg, 1.12 mmol), 2-chlorobenzaldehyde **6d** (158 mg, 1.13 mmol) and 2-mercaptoacetic acid **7a** (114 mg, 1.24 mmol) as a yellow solid. Yield: 46% (149 mg). Mp 115 °C (117–118 °C by Yadav et al., 2009). Data: FTIR (KBr): *v* = 2922, 2841, 1693 (C═O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.82 (d, *J* = 15.8 Hz, 1H, H-5a), 3.94 (d, *J* = 15.8 Hz, 1H, H-5b), 6.57 (s, 1H, H-2), 7.16–7.37 (m, 9H, Ph-H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.0 (CH_2), 61.8 (C-2), 124.1, 126.7, 127.4, 129.1 (2 x C), 129.6, 130.2, 132.4 (Cq), 137.1 (Cq), 137.5 (Cq), 171.3 (C═O) ppm. MS (70 eV, EI): *m/z* (%) = 291/289 $[M]^+$ (0.5/1.4), 214 (9), 135 (9), 104 (17), 77 (63), 46 (100). $C_{15}H_{12}ClNOS$ (289,03): calcd. C 62.17, H 4.17, N 4.83; found: C 62.18, H 4.36, N 4.73.

*4.2.14. (±)-2-(3,4,5-Trimethoxyphenyl)-3-p-tolylthiazolidin-4-one **10n***

This compound was obtained from *p*-methylaniline **9e** (106 mg, 0.99 mmol), 3,4,5-trimethoxybenzaldehyde **6a** (198 mg, 1.01 mmol) and 2-mercaptoacetic acid **7a** (101 mg, 1.10 mmol) as a yellow solid. Yield: 68% (242 mg). Mp 116 °C (160–162 °C by Kumar et al., 2012). Data: FTIR (KBr): *v* = 2937, 2837, 1681 (C═O), 1235 and 1004 (C—O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.29 (s, 3H, CH_3), 3.80 (s, 6H, OCH_3 x 2), 3.81 (s, 3H, OCH_3), 3.87 (dd,

J = 0.5, 16.0 Hz, 1H, H-5a), 3.98 (dd, J = 1.5, 15.8 Hz, 1H, H-5b), 6.00 (d, J = 1.0 Hz, 1H, H-2), 6.50 (s, 2H, Ar-H), 7.06 (d, J = 8.5 Hz, 2H, Ar-H), 7.11 (d, J = 8.5 Hz, 2H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0 (CH_3), 33.4 (CH_2), 56.2 (OCH_3 x 2), 60.8 (C-2), 65.9 (OCH_3), 104.0, 125.6, 129.8, 134.9 (Cq), 137.2 (Cq), 138.3 (Cq), 143.8 (Cq), 153.5 (Cq), 171.1 (C═O) ppm. MS (70 eV, EI): m/z (%) = 359 $[M]^+$ (54), 285 (5), 284 (5), 222 (100), 211 (16), 195 (46), 168 (5), 91 (3) [$PhCH_2$]. $C_{19}H_{21}NO_4S$ (359,12): calcd. C 63.49, H 5.89, N 3.90; found: C 63.39, H 5.71, N 3.73.

4.2.15. (±)-2-(4-Chlorophenyl)-3-(4-methoxyphenyl) thiazolidin-4-one ***10o***

This compound was obtained from *p*-methoxylaniline **9f** (103 mg, 0.84 mmol), *p*-chlorobenzaldehyde **6b** (119 mg, 0.85 mmol) and 2-mercaptoacetic acid **7a** (85 mg, 0.92 mmol) as a yellow solid. Yield: 43% (115 mg). Mp 165–166 °C (169–170 °C by Tu et al., 2009). Data: FTIR (KBr): ν = 2932, 2836, 1671 (C═O), 1247 and 1029 (C─O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.74 (s, 3H, OCH_3), 3.88 (d, J = 15.8 Hz, 1H, H-5a), 3.98 (dd, J = 1.8, 15.8 Hz, 1H, H-5b), 5.98 (d, J = 1.5 Hz, 1H, H-2), 6.81 (d, J = 9.0 Hz, 2H, Ar-H), 7.02 (d, J = 9.0 Hz, 2H, Ar-H), 7.24 (d, J = 8.8 Hz, 2H, Ar-H), 7.28 (d, J = 8.8 Hz, 2H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.3 (CH_2), 55.3 (OCH_3), 65.2 (C-2), 114.5, 127.4, 128.6, 129.0, 129.8 (Cq), 134.7 (Cq), 138.1 (Cq), 158.5 (Cq), 170.9 (C═O) ppm. MS (70 eV, EI): m/z (%) = 321/319 $[M]^+$ (15/38), 247/245 (4/10), 232/230 (7/25), 153 (67), 135 (100), 127/125 (5/18), 77 (16). $C_{16}H_{14}ClNO_2S$ (319,04): calcd. C 60.09, H 4.41, N 4.38; found: C 59.95, H 4.58, N 4.31.

4.2.16. (±)-3-(3-Benzyl-4-oxothiazolidin-2-yl)quinolin-2 (1H)-one ***10p***

This compound was obtained from benzylamine **9a** (102 mg, 0.95 mmol), 1,2-dihydro-2-oxoquinoline-3-carbaldehyde **6e** (168 mg, 0.97 mmol) and 2-mercaptoacetic acid **7a** (97 mg, 1.05 mmol) as a yellow solid. Yield: 65% (208 mg). Mp 190–192 °C. Data: FTIR (KBr): ν = 3503 (N-H), 2921, 2859, 1688 (C═O), 1656 (C═O), 1565 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.72 (d, J = 15.3 Hz, 1H, H-5a), 3.91–3.96 (m, 2H, Bn-H), 5.16 (d, J = 15.1 Hz, 1H, H-5b), 5.68 (s, 1H, H-2), 7.21 (d, J = 7.8 Hz, 2H, Ph-H), 7.24–7.32 (m, 4H, Ph-H, quinolin-H), 7.40 (d, J = 8.3 Hz, 1H, quinolin-H), 7.55–7.61 (m, 3H, quinolin-H), 12.27 (s, 1H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.6 (CH_2), 47.0 ($PhCH_2$), 58.6 (C-2), 116.0, 119.4 (Cq), 123.5, 127.9, 128.0, 128.1, 128.7, 129.5 (Cq), 131.4, 135.0 (Cq), 136.4, 137.4 (Cq), 162.6 (C═O, quinolin), 172.9 (C═O, thiazolidin) ppm. MS (70 eV, EI): m/z (%) = 336 $[M]^+$ (1), 263 (6), 245 (9), 171 (11), 153 (6), 130 (5), 91 (100) [$PhCH_2$]. $C_{19}H_{16}N_2O_2S$ (336,09): calcd. C 67.84, H 4.79, N 8.33; found: C 67.61, H 4.91, N 8.28.

4.2.17. (±)-3-(3-(3,4-Dimethoxybenzyl)-4-oxothiazolidin-2-yl)quinolin-2(1H)-one ***10q***

This compound was obtained from 3,4-dimethoxybenzylamine **9b** (103 mg, 0.62 mmol), 1,2-dihydro-2-oxoquinoline-3-carbal dehyde **6e** (109 mg, 0.63 mmol) and 2-mercaptoacetic acid **7a** (63 mg, 0.68 mmol) as a green solid. Yield: 72% (176 mg). Mp 208–211 °C. Data: FTIR (KBr): ν = 3508 (N-H), 2936, 2837, 1721 (C═O), 1652 (C═O), 1568, 1238, 1157, 1140 and 1024 (C─O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.72 (d, J = 15.3 Hz, 1H, H-5a), 3.81–3.87 (m, 7H, Bn-H, OCH_3 x 2), 3.96 (d, J = 15.3 Hz, 1H, H-5b), 5.14 (d, J = 14.6 Hz, 1H, Bn-H), 5.69 (d, J = 0.7 Hz, 1H, H-2), 6.72–6.79 (m, 3H, Ar-H), 7.27 (t, J = 8.0 Hz, 1H, quinolin-H), 7.42 (d, J = 8.0 Hz, 1H, quinolin-H), 7.53 (s, 1H, quinolin-H), 7.54–7.61 (m, 2H, quinolin-H), 12.46 (s, 1H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.0 (CH_2), 46.8 ($PhCH_2$), 55.9 (OCH_3 x 2), 58.7 (C-2), 111.1, 111.4, 116.0, 119.2 (Cq), 120.8, 123.2, 127.8 (Cq), 128.0, 130.0 (Cq), 131.3, 135.8, 138.0 (Cq), 148.8 (Cq), 149.3 (Cq), 162.5 (C═O, quinolin), 172.5 (C═O, thiazolidin) ppm. MS (70 eV, EI): m/z (%) = 396 $[M]^+$ (19), 245 (100), 208 (32), 176 (32), 171 (19), 151 (52). $C_{21}H_{20}N_2O_4S$ (396,11): calcd. C 63.62, H 5.08, N 7.07; found: C 63.60, H 5.22, N 7.31.

4.2.18. (±)-3-(3-((Benzo[d][1,3]dioxol-6-yl)methyl)-4-oxothiazolidin-2-yl)quinolin-2(1H)-one ***10r***

This compound was obtained from 3,4-methylenedioxybenzylamine **9c** (115 mg, 0.76 mmol), 1,2-dihydro-2-oxoquinoline-3-carbaldehyde **6e** (132 mg, 0.76 mmol) and 2-mercaptoacetic acid **7a** (79 mg, 0.86 mmol) as a yellow solid. Yield: 88% (255 mg). Mp 212–214 °C. Data: FTIR (KBr): ν = 3508 (N-H), 2931, 2860, 1681 (C═O), 1655 (C═O), 1565, 1249 and 1033 (C─O) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.62 (d, J = 15.3 Hz, 1H, H-5a), 3.82 (d, J = 14.6 Hz, 1H, Bn-H), 3.88 (d, J = 14.8 Hz, 1H, Bn-H), 4.84 (d, J = 15.1 Hz, 1H, H-5b), 5.54 (s, 1H, H-2), 5.96 (d, J = 3.3 Hz, 2H, OCH_2O), 6.67 (dd, J = 1.2, 8.0 Hz, 1H, Ar-H), 6.76 (d, J = 1.2 Hz, 1H, Ar-H), 6.82 (d, J = 7.8 Hz, 1H, Ar-H), 7.20 (t, J = 8.0 Hz, 1H, quinolin-H), 7.33 (d, J = 8.0 Hz, 1H, quinolin-H), 7.51 (t, J = 7.6 Hz, 1H, quinolin-H), 7.66–7.71 (m, 2H, quinolin-H), 11.94 (s, 1H, NH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 31.5 (CH_2), 45.7 ($PhCH_2$), 57.4 (C-2), 101.0 (OCH_2O), 108.2 (C × 2), 114.9, 118.7 (Cq), 121.2, 122.0, 128.3, 129.8 (Cq), 130.4 (C + Cq), 134.4, 138.2 (Cq), 146.7 (Cq), 147.4 (Cq), 160.4 (C═O, quinolin), 171.6 (C═O, thiazolidin) ppm. MS (70 eV, EI): m/z (%) = 380 $[M]^+$ (5), 245 (88), 190 (25), 171 (50), 161 (20), 135 (100), 105 (14), 77 (42). $C_{20}H_{16}N_2O_4S$ (380,08): calcd. C 63.14, H 4.24, N 7.36; found: C 63.01, H 4.37, N 7.30.

4.2.19. (±)-3-Benzyl-2-(3-methyl-1-phenyl-1H-pyrazol-4-yl) thiazolidin-4-one ***10s***

This compound was obtained from benzylamine **9a** (101 mg, 0.94 mmol), 3-methyl-1-phenyl-1*H*-pyrazole-4-carboxaldehyde **6f** (177 mg, 0.95 mmol) and 2-mercaptoacetic acid **7a** (99 mg, 1.08 mmol) as a white solid. Yield: 60% (198 mg). Mp 131 °C. Data: FTIR (KBr): ν = 2984, 2830, 1695 (C═O), 1599 and 1562 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.22 (s, 3H, CH_3), 3.80–3.90 (m, 3H, Bn-H, H-5a, H-5b), 5.14 (d, J = 14.8 Hz, 1H, Bn-H), 5.59 (s, 1H, H-2), 7.15 (d, J = 7.6 Hz, 2H, Ph-H), 7.29–7.36 (m, 4H, Ph-H), 7.48 (t, J = 7.9 Hz, 2H, Ph-H), 7.64 (d, J = 7.8 Hz, 2H, Ph-H), 7.78 (s, 1H, pyrazol-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.1 (CH_3), 33.1 (CH_2), 46.1 ($PhCH_2$), 54.3 (C-2), 118.7 (C + Cq), 126.5, 126.9, 127.9, 128.2, 128.7, 129.4, 135.3 (Cq), 139.5 (Cq), 148.8 (Cq), 170.7 (C═O) ppm. $C_{20}H_{19}N_3OS$ (349,12): calcd. C 68.74, H 5.48, N 12.02; found: C 68.89, H 5.64, N 12.06.

4.2.20. (±)-3-Benzyl-2-(1,3-diphenyl-1H-pyrazol-4-yl) thiazolidin-4-one **10t**

This compound was obtained from benzylamine **9a** (96 mg, 0.90 mmol), 3-phenyl-1-phenyl-1*H*-pyrazole-4-carboxaldehyde **6g** (220 mg, 0.89 mmol) and 2-mercaptoacetic acid **7a** (93 mg, 1.01 mmol) as a white solid. Yield: 75% (277 mg). Mp 168–169 °C. Data: FTIR (KBr): ν = 2938, 2850, 1686 (C═O), 1597 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.73 (d, J = 15.6 Hz, 1H, H-5a), 3.78 (dd, J = 0.9, 15.8 Hz, 1H, H-5b), 3.92 (d, J = 14.8 Hz, 1H, Bn-H), 4.96 (d, J = 14.8 Hz, 1H, Bn-H), 5.71 (s, 1H, H-2), 6.98–7.01 (m, 2H, Ph-H), 7.14–7.19 (m, 3H, Ph-H), 7.34 (t, J = 7.5 Hz, 1H, Ph-H), 7.38–7.44 (m, 3H, Ph-H), 7.46–7.51 (m, 4H, Ph-H), 7.72 (d, J = 7.8 Hz, 2H, Ph-H), 7.93 (s, 1H, pyrazol-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33.0 (CH_2), 46.5 ($PhCH_2$), 54.5 (C-2), 119.1, 120.0 (Cq), 127.0, 127.3, 127.7, 128.2, 128.4, 128.5, 128.6, 128.7, 129.4, 132.0 (Cq), 135.2 (Cq), 139.5 (Cq), 151.9 (Cq), 170.8 (C═O) ppm. $C_{25}H_{21}N_3OS$ (411,14): calcd. C 72.97, H 5.14, N 10.21; found: C 72.91, H 5.28, N 10.09.

4.2.21. 4-Benzyl-1-thia-4-azaspiro[4.5]decan-3-one **10u**

This compound was obtained from benzylamine **9a** (103 mg, 0.96 mmol), cyclohexanone **6h** (96 mg, 0.98 mmol) and 2-mercaptoacetic acid **7a** (98 mg, 1.06 mmol) as a yellow solid. Yield: 61% (153 mg). Mp 92–93 °C (115–117 °C by El-Zohry et al., 1993). Data: FTIR (KBr): ν = 2929, 2855, 1674 (C═O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.02–1.10 (m, 1H, cyclohexyl-H), 1.52–1.83 (m, 9H, cyclohexyl-H), 3.63 (s, 2H, H-5), 4.59 (s, 2H, Bn-H), 7.24–7.34 (m, 5H, Ph-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.4 (CH_2), 24.4 (CH_2), 31.3 (CH_2), 38.3 (CH_2), 45.1 ($PhCH_2$), 74.3 (Cq, C-2), 127.0, 127.1, 128.4, 137.9 (Cq), 171.7 (C═O) ppm. $C_{15}H_{19}NOS$ (261,12): calcd. C 68.93, H 7.33, N 5.36; found: C 68.78, H 7.40, N 5.19.

4.2.22. 4-(1,3-Benzodioxol-5-ylmethyl)-1-thia-4-azaspiro[4.5] decan-3-one **10v**

This compound was obtained from 3,4-methylenedioxybenzylamine **9c** (97 mg, 0.64 mmol), cyclohexanone **6h** (64 mg, 0.65 mmol) and 2-mercaptoacetic acid **7a** (65 mg, 0.71 mmol) as a white solid. Yield: 65% (127 mg). Mp 109–111 °C. Data: FTIR (KBr): ν = 2925, 2855, 1670 (C═O), 1241 and 1036 (C—O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.00–1.10 (m, 1H, cyclohexyl-H), 1.53–1.83 (m. 9H, cyclohexyl-H), 3.60 (s, 2H, H-5), 4.49 (s, 2H, Bn-H), 5.94 (s, 2H, OCH_2O), 6.72–6.74 (d, 2H, Ar-H), 6.81 (s, 1H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.5 (CH_2), 24.6 (CH_2), 31.3 (CH_2), 38.4 (CH_2), 45.0 ($PhCH_2$), 74.4 (Cq, C-2), 101.0 (OCH_2O), 107.9, 108.1, 120.4, 132.1 (Cq), 146.8 (Cq), 147.9 (Cq), 171.7 (C═O) ppm. MS (70 eV, EI): m/z (%) = 305 $[M]^+$ (8), 191 (9), 161 (11), 148 (9), 135 (100), 105 (8), 77 (27). $C_{16}H_{19}NO_3S$ (305,11): calcd. C 62.93, H 6.27, N 4.59; found: C 63.05, H 6.43, N 4.64.

4.2.23. (±)-3′-(4-methoxyphenyl)spiro[indoline-3–2′-thiazolidine]-2,4′-dione **10w**

This compound was obtained from *p*-methoxyaniline **9f** (88 mg, 0.72 mmol), isatin **6i** (103 mg, 0.70 mmol) and 2-mercaptoacetic acid **7a** (80 mg, 0.87 mmol) as a yellow solid. Yield: 66% (151 mg). Mp 206–207 °C (210 °C by Joshi et al., 1981). Data: FTIR (KBr): ν = 3268 (N-H), 2941, 2837, 1736 (C═O), 1682 (C═O), 1616, 1193 and 1032 (C—O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.66 (s, 3H, OCH_3), 3.87 (d, J = 15.3 Hz, 1H, H-5a), 4.32 (d, J = 15.3 Hz, 1H, H-5b), 6.69 (d, J = 9.0 Hz, 2H, Ar-H), 6.74 (d, J = 7.8 Hz, 1H, Ar-H), 6.97 (d, J = 9.0 Hz, 2H, Ar-H), 7.09 (td, J = 1.0, 7.6 Hz, 1H, Ar-H), 7.22 (td, J = 1.1, 7.8 Hz, 1H, Ar-H), 7.48 (d, J = 7.5 Hz, 1H, Ar-H), 8.55 (s, 1H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.9 (CH_2), 55.2 (OCH_3), 70.5 (Cq, C-2), 110.9, 114.6, 123.5, 125.2 (Cq), 126.6, 128.2 (Cq), 129.7, 131.1, 140.6 (Cq), 159.4 (Cq), 172.8 (C═O, thiazolidin), 177.1 (C═O) ppm. $C_{17}H_{14}N_2O_3S$ (326,07): calcd. C 62.56, H 4.32, N 8.58; found: C 62.71, H 4.50, N 8.72.

4.2.24. (±)-3-((Benzo[d][1,3]dioxol-6-yl)methyl)-2-(3,4,5-trimethoxyphenyl)-1,3-thiazin-4-one **12**

This compound was obtained from 3,4-methylenedioxybenzylamine **9b** (101 mg, 0.67 mmol), 3,4,5-trimethoxybenzaldehyde **6a** (133 mg, 0.68 mmol) and 3-mercaptopropionic acid **7b** (79 mg, 0.74 mmol) as a yellow solid. Yield: 42% (117 mg). Mp 136–138 °C. Data: FTIR (KBr): ν = 2962, 2889, 1645 (C═O), 1591, 1234, 1130, 1035 and 1006 (C—O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.67–2.76 (m, 1H), 2.89–2.99 (m, 3H), 3.61 (d, J = 14.8 Hz, 1H, Bn-H), 3.84 (s, 6H, OCH_3 x 2), 3.87 (s, 3H, OCH_3), 5.38 (s, 1H, H-2), 5.54 (d, J = 15.1 Hz, 1H, Bn-H), 5.96 (s, 2H, OCH_2O), 6.42 (s, 2H, Ar-H), 6.64 (dd, J = 1.4, 8.0 Hz, 1H, Ar-H), 6.74 (d, J = 8.0 Hz, 1H, Ar-H), 6.76 (d, J = 1.5 Hz, 1H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.3 (CH_2), 34.6 (CH_2), 49.4 ($PhCH_2$), 56.3 (OCH_3 x 2), 60.8 (OCH_3), 61.2 (C-2), 101.1 (OCH_2O), 104.0, 108.2, 108.6, 121.5, 130.2 (Cq), 134.5 (Cq), 138.0 (Cq), 147.1 (Cq), 148.0 (Cq), 153.4 (Cq), 169.5 (C═O) ppm. $C_{21}H_{23}NO_6S$ (417,12): calcd. C 60.42, H 5.55, N 3.36; found: C 60.61, H 5.32, N 3.47.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.arabjc.2016.11.016.

References

Abonia, R., Castillo, J., Insuasty, B., Quiroga, J., Nogueras, M., Cobo, J., 2010a. Eur. J. Org. Chem., 6454–6463
Abonia, R., Castillo, J., Cuervo, P., Insuasty, B., Quiroga, J., Ortíz, A., Nogueras, M., Cobo, J., 2010b. Eur. J. Org. Chem., 317–325
Abonia, R., Castillo, J., Insuasty, B., Quiroga, J., Nogueras, M., Cobo, J., 2013. ACS Combust. Sci. 15, 2–9.
Abonia, R., 2014. Curr. Org. Synth. 11, 773–786.
Anders, C.J., Bronson, J.J., D'Andrea, S.V., Deshpande, S.M., Falk, P.J., Grant-Young, K.A., Harte, W.E., Ho, H., Misco, P.F.,

Robertson, Stock, D., Sun, Y., Walsh, A.W., . Bioorg. Med. Chem. Lett. 10, 715–717.
Babaoglu, K., Page, M.A., Jones, V.C., McNeil, M.R., Dong, C., Naismith, J.H., Lee, R.E., 2003. Bioorg. Med. Chem. Lett. 13, 3227–3230.
Barreca, M.L., Chimirri, A., De Luca, L., Monforte, A.M., Monforte, P., Rao, A., Zappalà, M., Balzarini, J., De Clercq, E., Pannecouque, C., Witvrouw, M., 2001. Bioorg. Med. Chem. Lett. 11, 1793–1796.
Bolognese, A., Correale, G., Manfra, M., Lavecchia, A., Novellino, E., Barone, V., 2004. Org. Biomol. Chem. 2, 2809–2813.
Bukowski, L., Janowiec, M., Zwolska-Kwiek, Z., Andrezejczyk, Z., 1998. Pharmazie 53, 373–376.
Capan, G., Ulusoy, N., Ergenc, N., Ekinci, A.C., Vidin, A., 1966. Farmaco 51, 729–732.
Castillo, J., Abonia, R., Cobo, J., Glidewell, C., 2009. Acta Cryst. C65, o303–o310.
Coquerel, Y., Boddaert, T., Presset, M., Mailhol, D., Rodriguez, J., 2010. Ideas in chemistry and molecular sciences. In: Pignataro, B. (Ed.), Advances in Synthetic Chemistry. Wiley-VCH, Weinheim, pp. 187–202.
Dandia, A., Singh, R., Khaturia, S., Mérienne, C., Morgant, G., Loupy, A., 2006. Bioorg. Med. Chem. 14, 2409–2417.
De Monte, C., Carradori, S., Bizzarri, B., Bolasco, A., Caprara, F., Mollica, A., Rivanera, D., Mari, E., Zicari, A., Akdemir, A., Secci, D., 2016. Eur. J. Med. Chem. 107, 82–96.
Diurno, M.V., Mazzoni, O., Calignano, P.E., Giordano, F., Bolognese, A., 1992. J. Med. Chem. 35, 2910–2912.
Dömling, A., 2005. Org. Chem. Highlights April 5.
Dömling, A., 2005b. In: Zhu, J., Bienaymé, H. (Eds.), Multicomponent Reactions. Wiley-VCH, Weinheim, pp. 76–80.
Dömling, A., Wang, W., Wang, K., 2012. Chem. Rev. 112, 3083–3135.
El-Zohry, M.F., Awad, I.M.A., Abdel-Hafez, A.A., 1993. Arch. Pharm. 326, 115–118.
Ergenc, N., Capan, G., 1994. Farmaco 49, 133–135.
Fahmy, H.T.Y., 2001. Boll. Chim. Farm. 140, 422–427.
Gududuru, V., Hurh, E., Dalton, J.T., Miller, D.D., 2004a. Bioorg. Med. Chem. Lett. 14, 5289–5293.
Gududuru, V., Nguyen, V., Dalton, J.T., Miller, D.D., 2004b. Synlett, 2357–2358.
Holmes, C.P., Chinn, J.P., Look, C.G., Gordon, E.M., Gallop, M.A., 1995. J. Org. Chem. 60, 7328–7333.
Jarusiewicz, J., Choe, Y., Yoo, K.S., Park, C.P., Jung, K.W., 2009. J. Org. Chem. 74, 2873–2876.
Joshi, K.C., Patni, R., Chand, P., 1981. Heterocycles 16, 1555–1559.
Kaminsky, D.V., Lesyk, R.B., 2010. Biopolym. Cell 26, 136–145.
Kaminsky, D., Khyluk, D., Vasylenko, O., Zaprutko, L., Lesyk, R., 2011. Sci. Pharm. 79, 763–777.
Karali, N., Ilhan, E., Gürsoy, A., Kiraz, M., 1998. Farmaco 53, 346–349.
Kucukguzel, S.G., Oruc, E.E., Rollas, S., Sahin, F., Ozbek, A., 2002. Eur. J. Med. Chem. 37, 197–206.
Kumar, K.S.S., Swaroop, T.R., Harsha, K.B., Narasimhamurthy, K. H., Ranga, K.S., 2012. Tetrahedron Lett. 53, 5619–5623.
Lesyk, R.B., Zimenkovsky, B.S., Kaminsky, D.V., Kryshchyshyn, A. P., Havryluk, D.Y., Atamanyuk, D.V., Subtel'na, I.Y., Khyluk, D. V., 2011. Biopolym. Cell 27, 107–117.
Look, G.C., Schullek, J.R., Holmes, C.P., Chinn, J.P., Gordon, E.M., Gallop, M.A., 1996. Bioorg. Med. Chem. Lett. 6, 707–712.
Moreno-Fuquen, R., Castillo, J.C., Abonia, R., Ellena, J., De Simone, C.A., 2014. Acta Cryst. E70, o1235–o1236.
Ottanà, R., Carotti, S., Maccari, R., Landini, I., Chiricosta, G., Caciagli, B., Vigorita, M.G., Mini, E., 2005. Bioorg. Med. Chem. Lett. 15, 3930–3933.
Pawełczyk, A., Zaprutko, L., 2009. Eur. J. Med. Chem. 44, 3032–3039.
Rao, A., Carbone, A., Chimirri, A., De Clercq, E., Monforte, A.M., Monforte, P., Pannecouque, C., Zappalà, M., 2002. Farmaco 57, 747–751.
Rao, A., Carbone, A., Chimirri, A., De Clercq, E., Monforte, A.M., Monforte, P., Pannecouque, C., Zappalà, M., 2003. Farmaco 58, 115–120.
Rao, A., Balzarini, J., Carbone, A., Chimirri, A., De Clercq, E., Monforte, A.M., Monforte, P., Pannecouque, C., Zappalà, M., 2004. Farmaco 59, 33–39.
Raval, B.K., Trivedi, J.J., 1960. J. Indian Chem. Soc. 37, 353–354.
Rawal, R.K., Tripathi, R., Katti, S.B., Pannecouque, C., De Clercq, E., 2007. Bioorg. Med. Chem. 15, 3134–3142.
Rawal, R.K., Katti, S.B., Kaushik-Basu, N., Arora, P., Pan, Z., 2008. Bioorg. Med. Chem. Lett. 18, 6110–6114.
Secci, D., Carradori, S., Bizzarri, B., Chimenti, P., De Monte, C., Mollica, A., Rivanera, D., Zicari, A., Mari, E., Zengin, G., Aktumsek, A., 2016. Eur. J. Med. Chem. http://dx.doi.org/10.1016/j.ejmech.2016.04.012.
Sharma, R.C., Kumar, D.J., 2000. Indian Chem. Soc. 77, 492–493.
Srinivas, A., Nagaraj, A., Sanjeeva-Reddy, Ch., 2008. J. Heterocycl. Chem. 45, 999–1003.
Srivastava, T., Haq, W., Katti, S.B., 2002. Tetrahedron 58, 7619–7624.
Tietze, L.F., 1996. Chem. Rev. 96, 115–136.
Tu, S.-J., Cao, X.-D., Hao, W.-J., Zhang, X.-H., Yan, S., Wu, S.-S., Han, Z.-G., Shi, F., 2009. Org. Biomol. Chem. 7, 557–563.
Ulusoy, N., 2002. Arzneim.-Forsch. Drug Res. 52, 565–571.
Unsal-Tan, O., Ozadali, K., Piskin, K., Balkan, A., 2012. Eur. J. Med. Chem. 57, 59–64.
Yadav, A.K., Kumar, M., Yadav, T., Jain, R., 2009. Tetrahedron Lett. 50, 5031–5034.