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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.0c00378 • Publication Date (Web): 05 Jun 2020

Just Accepted

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Rhodium(II)-Catalyzed Annulative Coupling of β-Ketothioamides with α-Diazo compounds: Access to Highly Functionalized Thiazolidin-4-ones and Thiazolines

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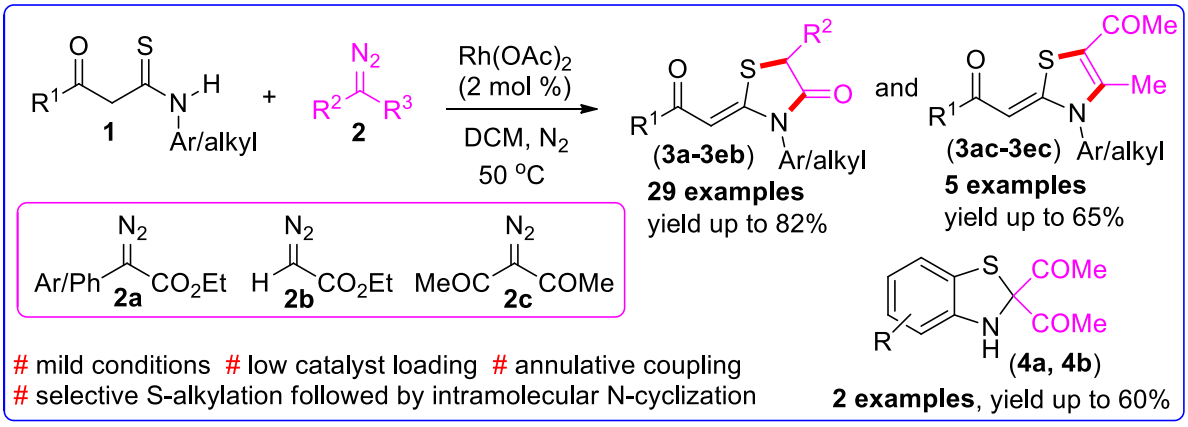


ABSTRACT: An operationally simple and efficient one-pot protocol for the synthesis of highly functionalized thiazolidin-4-ones and thiazolines has been devised via $Rh(OAc)_2$-catalyzed annulative coupling of β-ketothioamides with diazo compounds under mild reaction conditions for the first time. This double functionalization of diazo compounds proceeds via selective S-alkylation followed by intramolecular N-cyclization enabling the formation of C–S and C–N bonds at moderate temperature. Notably, the products possess *Z*-stereochemistry with regard to the exocyclic C=C double bond at the 2-position of the ring. Further, the synthetic utility of the strategy has been revealed to access 2,3-dihydrobenzo[*d*]thiazoles. Remarkably, atom-economy and tolerance of a wide range of functional groups are added characteristics to this strategy.

INTRODUCTION

The utility of nitrogen/sulfur heterocycles has become prevalent in medicinal and agricultural industries. Thiazolidine-4-one/thiazoline derivatives represent an important class of heterocycles, which are ubiquitous core structural motifs in many natural products, pharmaceuticals and functional materials.[1] The thiazolidine derivatives exhibit extensive pharmacological property such as anticancer,[2a] antihistaminic,[2b] anti-HIV[2c] activities, and selective COX-2 inhibitors.[2d] Thiazolidin-4-one scaffold has been considered as a magic moiety because it possesses almost all types of biological properties such as antifungal, antitubercular, antimicrobial, antioxidant, antibacterial, cytotoxic, anti-inflammatory, analgesic and anti-YFV (yellow fever virus) activities.[3] Among the various available reports for the synthesis of thiazolidine-4-ones, the most common and general approach involves the reaction between aldehyde, amine (or Schiff's base) and mercaptoacetic acid.[4a] Bolognese and co-workers[4b] synthesized the thiazolidine 4-ones via microwave technique, while Lingampalle *et al*.[4c] constructed thiazolidines utilizing ionic liquid. Jagodzinski *et al*.[5a] and our group[5b,c] synthesized the thiazolidin-4-ones by the reaction of β-ketothioamides with different coupling partners. Despite the aforesaid approaches for the synthesis of thiazolidin-4-ones, most of them suffer from one or more limitations such as use of excess base, lack of generality, pre-functionalization of starting materials, limited functional group tolerability, and poor yield. Therefore, it is still challenging and highly desirable to explore an operationally simple, efficient and widely applicable general approach for the synthesis of thiazolidin-4-one derivatives.

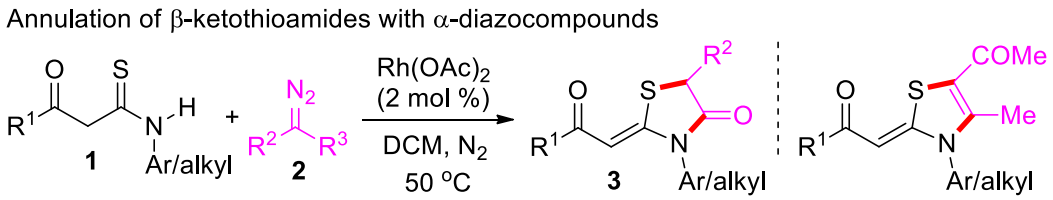
Over the past several decades, the decomposition of diazo compounds generating carbenes or metal-stabilized carbenoids provided synthetic chemist a valuable tool for the selective construction of both C−C and C−heteroatom bonds.[6] Diazo compounds are amphiphilic, and the negatively polarized diazo carbon atom is nucleophilic, while the metal carbene species generated from a diazo compound has an electron-deficient carbene center.[7] The utility of α-diazocarbonyl compounds as versatile synthon has been established in various areas of organic synthesis such as Wolff rearrangements,[8] cyclopropanation reactions,[9a-c] benzannulation,[9d] cycloaddition chemistry,[10] and C−H/heteroatom−H inser-

tion/functionalization reactions.[11] Furthermore, diazo compounds are widely used for the synthesis of heterocyclic frameworks.[12] Very recently, Wang *et al*.[13a] reported sulfhydryl-directed iridium-catalyzed C−H/diazo coupling with naphthalene-1-thiols to construct naphtho fused thiopyrans. Koenigs *et al*.[13b] reported iron-catalysed S-alkylation of thioether with diazoalkane. $Rh(OAc)_2$ introduced by Teyssie and co-workers[14] in the early 1970s, is still the catalyst of choice for metal carbenoid formation.[15]

In contrast, the coupling reactions involved metal carbenes and thiocarbonyl (C=S) group are not often explored. In this regard, Zeng[16a] and Moody[16b] developed Rh-catalyzed intermolecular coupling reaction of carbonyl group (C=O) with diazo compounds, in which nucleophilic attack of carbonyl oxygen of amide to Rh-carbenes generated carbonyl ylides, which upon further intramolecular cyclization afforded oxazole derivatives. In addition to above approaches the reaction of diazo compounds with thioamides for the synthesis of heterocyclic motifs have been reported but most of them suffer from generality, poor yield of desired products and vigorous conditions.[16c,d] To date, the intermolecular coupling reaction between diazo compounds and thiocarbonyl C=S of β-ketothioamides has not been explored, while this type of transformation could provide an alternative approach for the gathering of structurally diverse molecules.

The success of carbenoid insertion/annulation strategy relies on the judicious choice of starting material, which requires two orthogonal reactivity types: a site for insertion and a compatible electrophile, which will not undergo reaction with the metal carbenoid. One such simple substrate is β-ketothioamide that has been well-documented as an intriguing synthon to access valuable heterocyclic scaffolds.[17] Site-selectivity in β-ketothioamide functionalizations has been achieved by leveraging several factors.[18] Against this background and our experience towards the chemistry of β-ketothioamides,[18] it was envisioned that the marriage of the carbenoid insertion/annulation with β-ketothioamides would provide access to interesting and potentially useful heterocyclic frameworks. To this end, herein we disclose the $Rh(OAc)_2$-catalyzed annulative coupling of β-ketothioamides with diazo compounds for the synthesis of highly functionalized thiazolidinones and thiazolines (Scheme 1).

Scheme 1. Synthesis of Thiazolidinones and Thiazolines

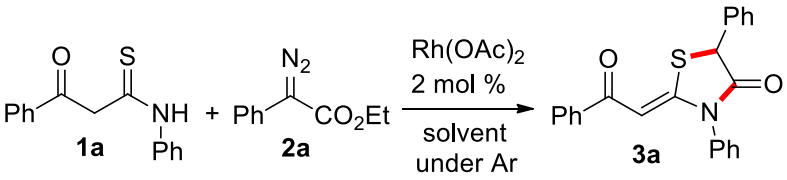


RESULTS AND DISCUSSION

In general, most of the reactions in organic chemistry are reagent/catalyst-controlled, and their regio- and stereoselectivity are directed by the inherent nature of the reagent or catalyst. While in substrate-directed reactions, the selectivity is determined by the functional group on the substrate. In this perspective, one of the simple substrate is β-ketothioamide, which exerts amazing reactivity and emerged as novel multi-role-synthon for the construction of various heterocyclic motifs.[17,18] In continuation of our ongoing research toward the development of powerful synthetic strategies to assemble different heterocyclic scaffolds employing β-ketothioamide as a reaction partner, we turned our attention to react β-ketothioamide with diazoalkane, which could generate hitherto unknown heterocyclic motif via one-pot cascade annulation. To validate our hypothesis, we commenced our study employing β-ketothioamide **1a** and diazoalkane **2a** as model substrates to examine various reaction parameters to optimize the reaction conditions. The results are summarized in Table 1.

Initially, the reaction of **1a** and **2a** in equimolar ratio in the presence of 2 mol % of $Rh(OAc)_2$ in dichloromethane (DCM) at room temperature under inert atmosphere could provide only a trace of the desired product **3a** after 24 h (Table 1, entry 1). The above result encouraged us to continue our investigations for the formation of desired product **3a** in good yield. To this end, the test reaction was carried out at 50 ^{o}C, which afforded the desired product **3a** in 82% isolated yield (Table 1, entry 2). Further increasing the temperature not only decreased the yield, but also made the reaction messy (Table 1, entry 3).

Table 1. Optimization of Reaction Conditions[a]



entry	conditions	solvent	temp (°C)	yield (%)[b] **3a**
1	as shown	DCM	25	Trace
2	as shown	DCM	50	82
3	as shown	DCM	60	65[c]
4	as shown	DCE	50	NR
5	as shown	CH_3CN	50	NR
6	as shown	DMSO	50	NR
7	as shown	DMF	50	NR
8	as shown	Dioxane	50	NR
9	$[Rh(COD)Cl]_2$	DCM	50	NR
10	$[RhCl(PPh_3)]_3$	DCM	50	60
11	CuCl	DCM	50	65
12	CuBr	DCM	50	65
13	$Cu(OAc)_2$	DCM	50	60
14	$AgSbF_6$	DCM	50	NR
15	No catalyst	DCM	50	NR

[a]Unless otherwise noted all the reaction were carried out using 0.5 mmol of each **1a** and **2a** in the presence of 2 mol % of catalyst in 5 mL of solvent. [b]Isolated yields. [c]Complex TLC pattern. NR = No reaction.

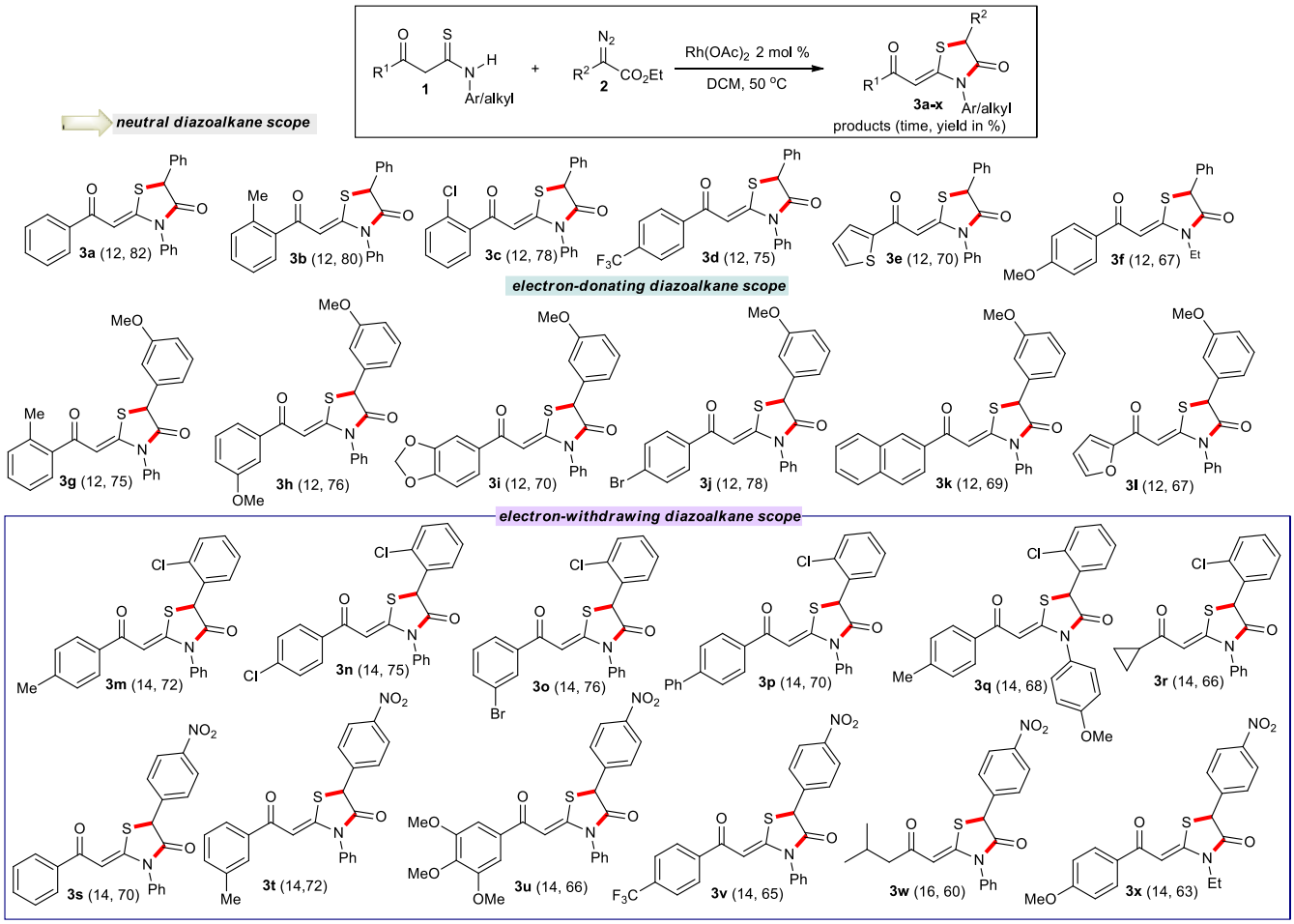
Inspired by the above result, we intended to see the effect of some other solvents. Thus, the test reaction is performed in various solvents such as dichloroethane (DCE), CH_3CN, DMSO, DMF and diox-

ane, but none of them did trigger the reaction (Table 1, entries 4-8). After optimizing DCM as a choice of solvent, next we screened some other rhodium catalysts such as $Rh(COD)Cl]_2$ and $RhCl(PPh_3)_3$. Notably, $Rh(COD)Cl]_2$ did not trigger the reaction, while $RhCl(PPh_3)_3$ triggered the reaction producing the desired product **3a** albeit in lower yield (Table 1, entries 9 & 10). Keeping in mind the use of relatively inexpensive and less toxic copper salts, we screened some copper catalysts such as CuCl, CuBr, and $Cu(OAc)_2$, which also could not provide better result than rhodium (Table 1, entries 11-13). To check the generality of the protocol, we also screened $AgSbF_6$, which did not trigger the reaction (Table 1, entry 14). In the absence of a catalyst, the reaction did not occur at all revealing the significance of catalyst to the success of the reaction (Table 1, entry 15). Thus, the optimum condition for the synthesis of **3a** was achieved by employing **1a** (0.5 mmol), **2a** (0.5 mmol), $Rh(OAc)_2$ (2 mol %), in 5 mL of DCM at 50 °C under inert atmosphere (Table 1, entry 2).

With the established optimal conditions in hand, we explored the scope and generality of the protocol. A wide range of β-ketothioamides (KTAs) with diverse substituents at R^1 moiety irrespective of their substitution pattern (*ortho*, *meta*, or *para*) are found to be compatible well under the optimized conditions showing no obvious electronic/steric hindrance (Table 2). The KTAs bearing substituents like Cl, Br, OMe, Me, CF_3, and $-OCH_2O-$ at phenyl group of R^1 moiety participated well with neutral, electron-donating and electron-withdrawing diazoalkanes affording the corresponding thiazolidinones in good to excellent yields (Table 2). The introduction of halogen (e.g., chloro and bromo) substituents into target product is attractive because of their potential for further synthetic elaborations. Different thioamides (**1a**-**1f**, SI Table S4) were well tolerated with ethyl 2-diazo-2-phenylacetate furnishing the desired thiazolidinones up to 82% yield (Table 2, entries **3a**-**3f**). After effective implementation of the neutral diazoalkane, next we employed the electron-rich diazoalkane, which was found to be viable participant with different thioamides (**1g**-**1l**, SI Table S4) and afforded the corresponding products in good yields (Table 2, entries **3g**-**3l**). Further, we examined the scope of this transformation with electron-poor diazo-

alkanes with diverse KTAs (**1m-1x**, SI Table S4), which also delivered the corresponding thiazolidinones in excellent yield (Table 2, entries **3m-3x**).

Table 2. Scope of β-Ketothioamides and α-Diazoacetates to Access Diverse Thiazolidinones[a]



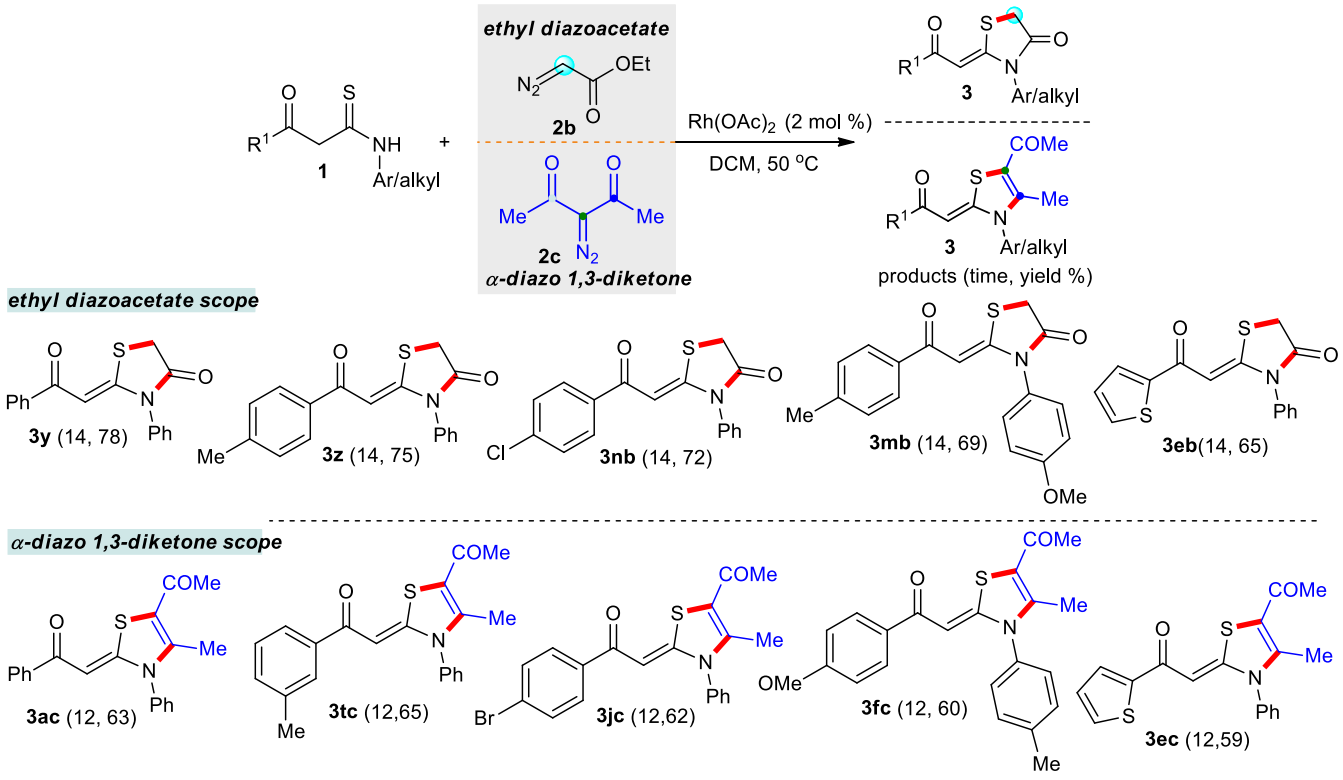
[a]All the reaction were performed with 0.5 mmol of each thioamides (**1**) and diazo compounds (**2**).

Remarkably, KTAs bearing not only aromatic, extended aromatic, and heteroaromatic entrants at R^1 moiety were found to be highly amenable to this protocol, but also alicyclic and aliphatic groups like cyclopropyl and *iso*-butyl at R^1 moiety were also tolerated well under the standard conditions affording the corresponding thiazolidinones in good yields (Table 2, entries **3r** and **3w**). Interestingly, thioamides bearing three strong electron-donating methoxy groups and strong electron-withdrawing CF_3 group at R^1 moiety were also coupled well with electron-poor diazoalkane furnishing the desired products in good yields (Table 2, entries **3u** and **3v**). After successful utilization of β-ketothioamides containing ar-

omatic moiety at nitrogen atom, next we employed the thioamides bearing alkyl substituents at nitrogen like ethyl group and found to be compatible well affording the corresponding thiazolidinones in good yield (Table 2, entries **3f** and **3x**).

Next, the protocol generality was investigated by carrying out the reaction of thioamides **1** with different diazo compounds with a view to add further diversity to thiazolidinone ring (Table 3). Notably, the α-diazocarbonyl (**2b**) and α-diazo 1,3-diketone (**2c**) also underwent the reaction smoothly with diverse β-ketothioamides bearing R^1 moiety as phenyl and aryl (substituted with both electron-withdrawing and electron-donating groups) substituents under optimized conditions affording the corresponding thiazolidinones and thiazolines in good yields (Table 3, entries **3y**-**3ec**).

Table 3. Scope of ethyl diazoacetate (2b) and α-diazo 1,3-diketone (2c)[a]



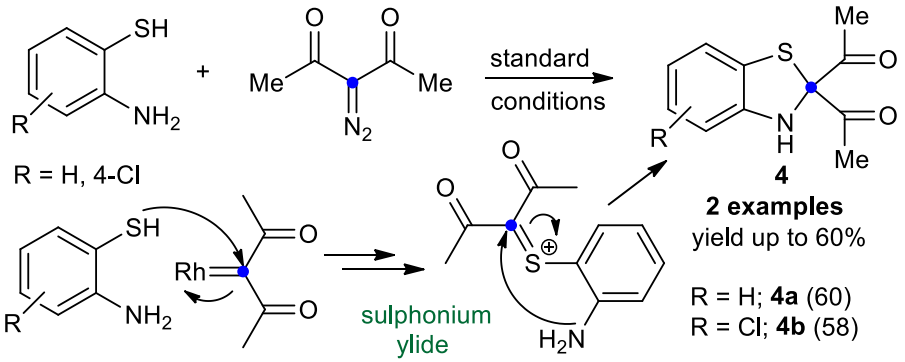
[a]All the reaction were performed with 0.5 mmol of each thioamides (**1**) and diazocompounds (**2**).

Importantly, thioamide bearing π-electron excessive group like 2-thienyl substituent at R^1 moiety was also well tolerated under standard conditions affording the corresponding thiazolidinone and thiazoline

in good yields (Table 3, **3eb** and **3ec**). It has been observed that thioamides with α-diazocarbonyl as coupling partner provided the desired products up to 78% yield, while with α-diazo 1,3-diketone as coupling partner afforded slightly decreased yield (up to 65%).

To validate the further synthetic utility of the present protocol, and in order to extend the substrate scope, we intended to employ 2-aminothiophenol instead of β-ketothioamide with different diazo compounds under above optimized conditions. It has been observed that only α-diazo 1,3-diketone gave the expected product with 2-amino thiophenol, while α-diazocarbonyl and α-diazoalkane could not provide even a trace of the anticipated product under standard conditions. In this regard, we employed 2-aminothiophenols, which underwent reaction efficiently with α-diazo 1,3-diketone under standard conditions providing the desired 2,3-dihydrobenzo[*d*]thiazoles in satisfactory yield (Scheme 2, **4a** and **4b**). As one of the most important exponents, 2-substituted benzothiazoles are of huge interest since they have been used as antimicrobial, antitumor, anticonvulsant, and neuroprotective agents.[19]

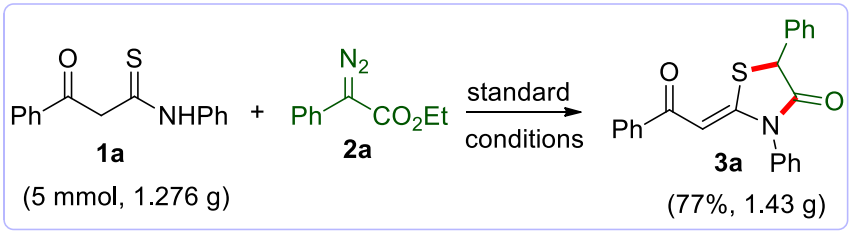
Scheme 2. Application towards Benzo[*d*]thiazoles



The structural determination of all the newly synthesized compounds was achieved by their satisfactory spectral (^{1}H, ^{1}H decoupled ^{13}C NMR, and HRMS) studies. The structure of one of the representative compound (Z)-2-(2-oxo-2-(thiophen-2-yl)ethylidene)-3,5-diphenylthiazolidin-4-one (**3e**) was further unambiguously established by the single crystal X-ray crystallography (see Supporting Information Figure S1 for details).[20]

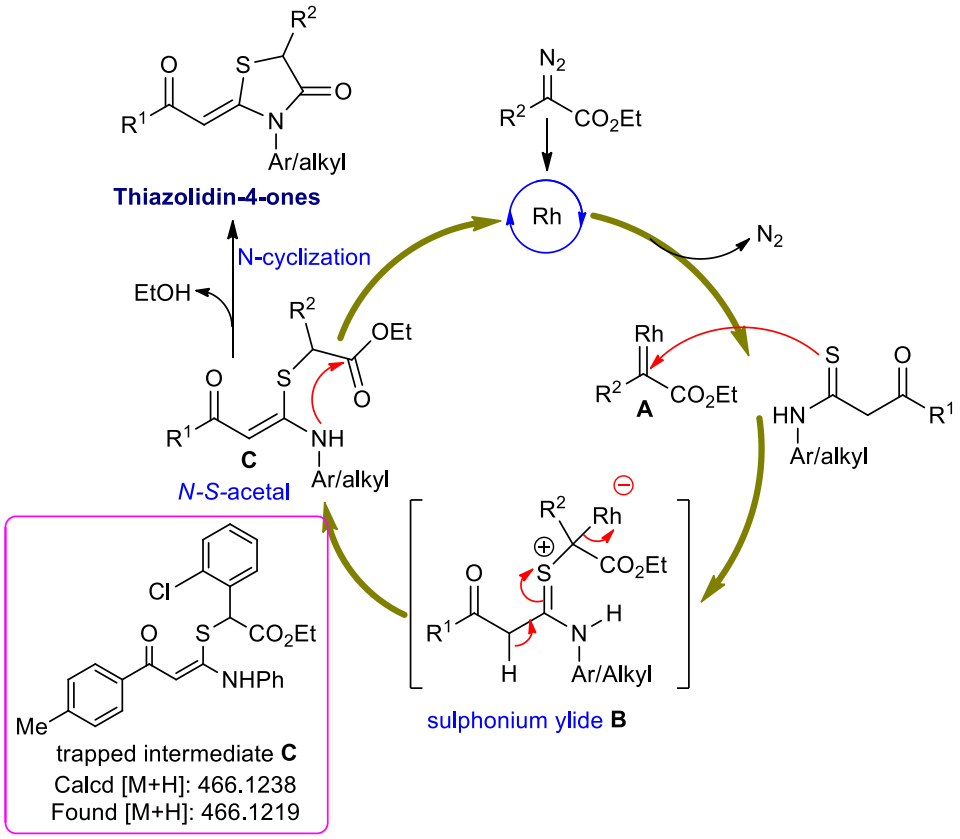
Further to check the practical efficacy of this protocol, we performed the large scale reaction employing β-ketothioamide **1a** (5 mmol) and α-diazoacetate **2a** (5 mmol) under optimized reaction conditions (Scheme 3). The desired thiazolidinone **3a** was obtained in 77% yield (1.43 g), which was found to be comparable to the small scale reaction. This observation indicated that the present method could be easily implemented for a large scale preparation of thiazolidinones.

Scheme 3. Gram-scale Synthesis of Compound 3a



Based on our experimental observation, a plausible mechanism is proposed in Scheme 4. The first step is believed to be the reaction between $Rh(OAc)_2$ and diazo compound to generate rhodium carbenoid species **A** via the extrusion of nitrogen. Next, the rhodium carbenoid species **A** reacts with thioamide sulfur to form the sulphonium ylide **B**, which in turn follows proton transfer to form *N,S*-acetal intermediate **C** by the regeneration of rhodium catalyst. Finally, in situ generated *N,S*-acetal intermediate **C** undergoes intramolecular N-cyclization by elimination of ethanol to give the desired thiazolidinones and thiazolines, respectively. To validate the proposed reaction mechanism, we recorded the mass spectrum of the reaction mixture, which shows the existence of intermediate **C** (See SI, Figure S2). The above observation supported that reaction proceeds via intermediate **C**.

Scheme 4. Proposed Mechanism for the Reaction



CONCLUSION

In summary, we have developed a concise and efficient protocol for the synthesis of diverse thiazolidinones and thiazolines via Rh(II)-catalyzed annulative coupling of β-ketothioamides with diazo compounds for the first time. Moreover, the described methodology is not limited to only β-ketothioamides but was also applicable to 2-amino thiophenols, which enabled direct approach to substituted benzo[*d*]thiazoles. The clean reaction profile, flexible structural modification, broad substrate scope, good functional group tolerance, and alcohol being the only byproduct are additional attributes to this one-pot strategy. Our method enables the synthesis of a broad range of highly functionalized thiazolidinones and thiazolines in good to excellent yield under mild reaction conditions.

EXPERIMENTAL SECTION

Commercially available chemicals used in this manuscript were used without further purification and were purchased from TCI, Sigma-Aldrich and Alfa Aesar. Solvents used for reactions were p.A. grade, and solvents for column chromatography were technical grade and distilled before use; solvent mixtures are understood as volume/volume. All the reactions were carried out in a flame or oven dried glass wares with freshly distilled dry solvents under anhydrous conditions. All the reactions were monitored by analytical thin layer chromatography (TLC) using Merck precoated aluminium sheets and visualized by UV lamp. Column chromatography using silica gel (100-200 mesh) was performed for the purification of products. The ^{1}H and ^{13}C NMR spectra were recorded on JEOL 500 FT-NMR spectrometer operating at 500 and 125 MHz, respectively. Chemical shifts (δ) for ^{1}H and $^{13}C\{^{1}H\}$ NMR are given in parts per million (ppm) using the residual solvent peaks as reference relative to tetramethylsilane (TMS). Coupling constant (J) values are reported in Hz. Mass spectra were recorded on Sciex X500R Q-TOF instruments. Melting points are uncorrected.

Materials: All solvents were distilled under argon and dried before use. Catalysts used in this protocol $Rh(OAc)_2$, $[Rh(COD)Cl]_2$, $RhCl(PPh_3)_3$, CuCl, CuBr, $Cu(OAc)_2$ and $AgSbF_6$ were purchased from Sigma-Aldrich Chemicals Pvt. Ltd. The β-ketothioamides[21a] and diazocompounds[21b,c] were synthesized by reported procedures.

Important Safety Note. Diazo compounds should only be handled in a well-ventilated fume cupboard. An additional blast shield is recommended. Although we did not realise any problem in the handling of diazo compounds, extreme care should be taken when manipulating them due to their potentially explosive nature. However, the reader should be aware of hazards of the diazo compounds. Safety precautions should be followed and strict risk assessment and proper safety precautions are recommended.

General Procedures for the Synthesis of Thiazolidinones and Thiazolines. In a two neck round bottom flask 0.5 mmol of β-ketothioamides **1**, 0.5 mmol of diazo compounds (**2a/2b/2c**) and 2 mol % of $Rh(OAc)_2$ were taken and sealed with double channel balloon adopter and flushed with argon for 5 to 6 times with the help of vacuum pump. Thereafter dichloromethane (5 mL) was added with the help of syringe. Now, the whole reaction mixture was put into pre-heated oil bath at 50 °C and stirred for stipulated period of time till completion. After the completion of the reaction (monitored by TLC), aqueous work up of reaction mixture was performed using ethyl acetate as organic phase. Organic phase was separated and dried over anhydrous Na_2SO_4 and solvent was evaporated under vacuum. Thus crude reaction mixture obtained was purified by column chromatography using hexane-ethyl acetate (8:2) as eluent to afford the pure final product.

The spectral and analytical data of all the compounds are given as follows:

*(Z)-2-(2-oxo-2-phenylethylidene)-3,5-diphenylthiazolidin-4-one (**3a**)*: The product was obtained as brown solid (82%, 152 mg); mp 205-206 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, J = 5.0 Hz, 2H), 7.61-7.53 (m, 3H), 7.51-7.46 (m, 3H), 7.43-7.34 (m, 7H), 6.40 (s, 1H), 5.16 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 188.9, 173.4, 160.7, 138.2, 135.6, 135.3, 132.3, 130.3, 130.0, 129.2, 128.8, 128.5, 128.4, 128.0, 127.6, 97.5, 50.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{18}NO_2S$ 372.1053; Found 372.1031.

*(Z)-2-(2-oxo-2-(o-tolyl)ethylidene)-3,5-diphenylthiazolidin-4-one (**3b**):* The product was obtained as brown solid (80%, 154 mg); mp 144-145 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.54 (t, J = 7.5 Hz, 2H), 7.49 (d, J = 5.0 Hz, 2H), 7.43-7.41 (m, 2H), 7.36 (d, J = 5.0 Hz, 1H), 7.31-7.26 (m, 4H), 7.18-7.13 (m, 3H), 6.07 (s, 1H), 5.16 (s, 1H), 2.44 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 193.1, 173.4, 159.7, 139.7, 137.2, 135.6, 135.3, 131.5, 130.8, 130.6, 130.3,129.9, 129.3, 128.8, 128.5, 128.0, 127.8, 126.9, 125.7, 101.5, 101.2, 50.3, 31.7, 22.7, 20.7, 14.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{20}NO_2S$ 386.1209; Found 386.1183.

*(Z)-2-(2-(2-chlorophenyl)-2-oxoethylidene)-3,5-diphenylthiazolidin-4-one (**3c**)*: The product was obtained as white solid (78%, 158 mg); mp 149-150 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (t, J = 7.5 Hz, 2H), 7.51-7.47 (m, 5H), 7.39-7.36 (m, 1H), 7.32-7.31 (m, 2H), 7.29-7.28 (m, 2H), 7.29-7.18 (m, 2H), 6.19 (s, 1H), 5.18 (s, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 189.9, 173.4, 160.1, 139.5, 135.4, 135.1, 131.5, 131.3, 130.8, 130.4, 130.2, 130.0, 129.9, 129.3, 128.9, 128.5, 128.0, 127.0, 101.8, 50.5; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{17}ClNO_2S$ 406.0663; Found 406.0645.

*(Z)-2-(2-oxo-2-(4-(trifluoromethyl)phenyl)ethylidene)-3,5-diphenylthiazolidin-4-one (**3d**)*: The product was obtained as white solid (75%, 165 mg); mp 198-199 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, J = 5.0 Hz, 2H), 7.55-7.45 (m, 5H), 7.39 (d, J = 10.0 Hz, 2H), 7.33-7.25 (m, 5H+1H of $CDCl_3$), 6.26 (s, 1H), 5.08 (s, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 187.5, 173.3, 162.2, 141.1, 135.3, 135.1, 133.5 (q, $^{2}J_{CF3}$ = 32.5 Hz), 130.4, 130.1, 129.5, 129.3, 128.9, 128.6, 128.4, 128.0, 127.9, 126.6, 125.6, 125.6, 123.7 (q, $^{1}J_{CF3}$ = 271.2 Hz), 97.2, 50.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{17}F_3NO_2S$ 440.0927; Found 440.0897.

*(Z)-2-(2-oxo-2-(thiophen-2-yl)ethylidene)-3,5-diphenylthiazolidin-4-one (**3e**)*: The product was obtained as yellow solid (70%, 132 mg); mp 204-205 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50-7.39 (m, 6H), 7.33-7.17 (m, 6H+1H of $CDCl_3$), 6.93 (t, J = 5.0, 1H), 6.13 (s, 1H), 5.06 (s, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 181.5, 173.2, 159.9, 145.5, 135.6, 135.2, 132.7, 130.3, 130.0, 129.9, 129.2, 128.8, 128.4, 128.1, 128.0, 97.6, 50.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{16}NO_2S_2$ 378.0617; Found 378.0593.

*(Z)-3-ethyl-2-(2-(4-methoxyphenyl)-2-oxoethylidene)-5-phenylthiazolidin-4-one (**3f**)*: The product was obtained as white solid (67%, 118 mg); mp 142-143 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, J = 10.0 Hz, 2H), 7.28-7.24 (m, 5H+1H of $CDCl_3$), 6.88 (d, J = 10.0 Hz, 2H), 6.66 (s, 1H), 4.86 (s, 1H), 3.81 (q, J = 6.6 Hz, 2H), 3.78 (s, 3H), 1.24 (t, J = 5.0 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ

187.6, 173.5, 163.0, 158.6, 135.7, 131.3, 131.1, 129.7, 129.1, 128.6, 128.4, 114.0, 113.8, 95.1, 55.5, 50.1, 39.1, 12.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{20}NO_3S$ 354.1158; Found 354.1132.

*(Z -)-5-(3-methoxyphenyl)-2-(2-oxo-2-(o-tolyl)ethylidene)-3-phenylthiazolidin 4-one (**3g**):* The product was obtained as yellow solid (75%, 156 mg); mp 134-135 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.53 (t, J = 7.5 Hz, 2H), 7.47 (t, J = 7.5 Hz, 1H), 7.33-7.24 (m, 5H+1H of $CDCl_3$), 7.17-7.12 (m, 2H), 7.07 (d, J = 5.0 Hz, 1H), 7.02 (s, 1H), 6.90-6.88 (m, 1H), 6.06 (s, 1H), 5.12 (s, 1H), 3.81 (s, 3H), 2.44 (s,3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 193.0, 173.1, 160.1, 159.6, 139.6, 137.1, 137.0, 135.2, 131.5, 130.5, 130.2, 130.2, 129.9, 127.9, 127.8, 125.6, 120.6, 114.3, 114.1, 101.2, 55.4, 50.1, 20.6; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{22}NO_3S$ 416.1315; Found 416.1287.

*(Z)-5-(3-methoxyphenyl)-2-(2-(3-methoxyphenyl)-2-oxoethylidene)-3-phenylthiazolidin-4-one (**3h**):* The product was obtained as yellow solid (76%, 164 mg); mp 166-167 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.58-7.52 (m, 3H), 7.37 (s, 1H), 7.33-7.21 (m, 5H+1H of $CDCl_3$), 7.07 (d, J = 5.0 Hz, 1H), 7.02 (s, 2H), 6.90-6.88 (m, 1H), 6.36 (s, 1H), 5.11 (s, 1H), 3.81 (s, 3H), 3.80 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 188.6, 173.2, 160.8, 160.2, 159.8, 139.7, 137.0, 135.3, 130.3, 130.3, 130.0, 129.5, 128.0, 120.6, 119.9, 118.7, 114.3, 114.2, 112.2, 97.7, 55.4, 50.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{22}NO_4S$ 432.1264; Found 432.1235.

*(Z)-2-(2-(benzo[d][1,3]dioxol-5-yl)-2-oxoethylidene)-5-(3-methoxyphenyl)-3-phenylthiazolidin-4-one (**3i**)*: The product was obtained as brown solid (70%, 156 mg); mp 194-195 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.59-7.52 (m, 3H), 7.33-7.25 (m, 5H+1H of $CDCl_3$), 7.07 (d, J = 10.0 Hz, 1H), 7.01 (s, 1H), 6.89-6.88 (m, 1H), 6.75 (d, J = 5.0 Hz, 1H), 6.28 (s, 1H), 5.99 (s, 2H), 5.10 (s, 1H), 3.81 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 187.1, 173.2, 160.2, 160.1, 151.2, 148.1, 137.1, 135.3, 133.0, 130.3, 130.3, 130.0, 128.1, 123.3, 120.7, 114.3, 114.2, 107.9, 107.8, 101.8, 97.4, 55.4, 50.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{20}NO_5S$ 446.1057; Found 446.1057.

*(Z)-2-(2-(4-bromophenyl)-2-oxoethylidene)-5-(3-methoxyphenyl)-3-phenylthiazolidin-4-one (**3j**)*: The product was obtained as yellow solid (78%, 187 mg); mp 182-183 ^{o}C;^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59-7.50 (m, 7H), 7.32 (t, J = 7.5 Hz, 3H), 7.0 (d, J = 5.0 Hz, 1H), 7.0 (s, 1H), 6.90-6.88 (m, 1H), 6.30 (s, 1H), 5.11 (s, 1H), 3.81 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 187.6, 173.2, 161.4, 160.2, 137.0, 136.8, 135.2, 131.8, 130.4, 130.3, 130.1, 129.1, 128.0, 127.2, 120.6, 114.3, 114.2, 97.1, 55.4, 50.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{19}BrNO_3S$ 480.0264; Found 480.0258.

*(Z)-5-(3-methoxyphenyl)-2-(2-(naphthalen-2-yl)-2-oxoethylidene)-3-phenylthiazolidin-4-one (**3k**)*: The product was obtained as light brown solid (69%, 156 mg); mp 194-195 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.87-7.82 (m, 4H), 7.62-7.47 (m, 5H), 7.36-7.31 (m, 3H), 7.08 (d, J = 10.0 Hz, 1H), 7.04 (s, 1H), 6.89 (d, J = 5.0 Hz, 1H), 6.53 (s, 1H), 5.13 (s, 1H), 3.82 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 188.8, 173.3, 160.7, 160.2, 137.0, 135.6, 135.4, 135.2, 132.6, 130.4, 130.3, 130.0, 129.5, 128.6, 128.4, 128.1, 127.8, 126.7, 123.9, 120.7, 114.3, 114.2, 97.8, 55.4, 50.3; HRMS (ESI-TOF) m/z: $[M + H]^+$Calcd for $C_{28}H_{22}NO_3S$ 452.1315; Found 452.1302.

*(Z)-2-(2-(furan-2-yl)-2-oxoethylidene)-5-(3-methoxyphenyl)-3-phenylthiazolidin-4-one (**3l**)*: The product was obtained as yellow solid (67%, 131 mg); mp 177-178 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59-7.52 (m, 3H), 7.43 (s, 1H), 7.31 (t, J = 10.0 Hz, 3H), 7.07-06 (m, 2H), 7.01 (s, 1H), 6.89-6.88(m, 1H), 6.45 (d, J = 5.0 Hz, 1H), 6.27 (s, 1H), 5.11 (s, 1H), 3.81 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 177.8, 173.1, 160.2, 160.0, 153.5, 145.4, 137.0, 135.2, 130.3, 129.9, 128.1, 120.6, 115.5, 114.2, 112.4, 97.4, 55.4, 50.3; HRMS (ESI-TOF) m/z: $[M + H]^+$Calcd for $C_{22}H_{18}NO_4S$ 392.0951; Found 392.0923.

*(Z)-5-(2-chlorophenyl)-2-(2-oxo-2-(p-tolyl)ethylidene)-3-phenylthiazolidin-4-one (**3m**)*: The product was obtained as yellow solid (72%, 151 mg); mp 203-204 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (t, J = 10.0 Hz, 4H), 7.56 (t, J = 7.5 Hz, 1H), 7.45-7.43 (m, 1H), 7.41-7.36 (m, 3H), 7.31-7.28 (m, 2H), 7.16 (d, J = 10.0 Hz, 2H), 6.36 (s, 1H), 5.53 (s, 1H), 2.36 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 188.6,

172.7, 160.4, 143.0, 135.6, 135.4, 134.5, 133.7, 130.5, 130.3, 130.1, 130.0, 129.2, 128.0, 127.7, 127.6, 97.6, 48.6, 21.6; HRMS (ESI-TOF) m/z: $[M + H]^+$Calcd for $C_{24}H_{19}ClNO_2S$ 420.0820; Found 420.0801.

*(Z)-5-(2-chlorophenyl)-2-(2-(4-chlorophenyl)-2-oxoethylidene)-3-phenylthiazolidin-4-one (**3n**)*: The product was obtained as white solid (75%, 165 mg); mp 209-210 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, J = 10.0 Hz, 2H), 7.61 (d, J = 10.0 Hz, 2H), 7.58-7.55 (m, 1H), 7.46-7.44 (m, 1H), 7.40-7.36 (m, 3H), 7.34-7.32 (m, 2H), 7.31-7.29 (m, 2H), 6.30 (s, 1H), 5.53 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 187.4, 172.6, 161.6, 138.6, 136.5, 135.2, 134.5, 133.5, 130.6, 130.5, 130.4, 130.2, 130.1, 129.0, 128.8, 127.9, 127.6, 97.1, 48.6; HRMS (ESI-TOF) m/z: $[M + H]^+$Calcd for $C23H_{16}Cl_2NO_2S$ 440.0273; Found 440.0255.

*(Z)-2-(2-(3-bromophenyl)-2-oxoethylidene)-5-(2-chlorophenyl)-3-phenylthiazolidin-4-one (**3o**)*: The product was obtained as yellow solid (76%, 184 mg); mp 166-167 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.63-7.56 (m, 5H), 7.45-7.43 (m, 1H), 7.40-7.36 (m, 3H), 7.31-7.29 (m, 2H), 7.22 (t, J = 7.5 Hz, 1H), 6.28 (s, 1H), 5.33 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 187.1, 172.6, 161.9, 140.0, 135.1, 135.0, 134.4, 133.4, 130.6, 130.5, 130.4, 130.2, 130.2, 130.1, 127.8, 127.6, 126.0, 122.9, 97.0, 48.6; HRMS (ESI-TOF) m/z: $[M + H]^+$Calcd for $C_{23}H_{16}BrClNO_2S$ 483.9768; Found 483.9757.

*(Z)-2-(2-([1,1'-biphenyl]-4-yl)-2-oxoethylidene)-5-(2-chlorophenyl)-3-phenylthiazolidin-4-one (**3p**)*: The product was obtained as yellow solid (70%, 169 mg); mp 207-208 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, J = 10.0 Hz, 2H), 7.64-7.56 (m, 7H), 7.46-7.44 (m, 3H), 7.43-7.36 (m, 4H), 7.32-7.30 (m, 2H), 6.40 (s, 1H), 5.55 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 188.4, 172.7, 160.9, 145.0, 140.0, 136.9, 135.4, 134.5, 133.7, 130.5, 130.4, 130.2, 130.1, 129.0, 128.4, 128.2, 128.2, 128.0, 127.6, 127.4, 127.3, 127.2, 97.6, 48.6; HRMS (ESI-TOF) m/z: $[M + H]^+$Calcd for $C_{29}H_{21}ClNO_2S$ 482.0976; Found 482.0975.

(Z)-5-(2-chlorophenyl)-3-(4-methoxyphenyl)-2-(2-oxo-2-(p-tolyl)ethylidene)thiazolidin-4-one (***3q***): The product was obtained as yellow solid (68%, 153 mg); mp 176-177 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, J = 5.0 Hz, 2H), 7.45-7.43 (m, 1H), 7.40-7.38 (m, 1H), 7.31-7.27 (m, 4H), 7.17 (d, J = 5.0 Hz, 2H), 7.11-7.09 (m, 2H), 6.37 (s, 1H), 5.52 (s, 1H), 3.90 (s, 3H), 2.36 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 188.6, 172.9, 160.8, 160.5, 143.0, 135.7, 134.5, 133.9, 130.5, 130.1, 129.2, 127.8, 127.7, 127.6, 115.6, 97.6, 55.7, 48.5, 21.7; HRMS (ESI-TOF) m/z: $[M + H]^+$Calcd for $C_{25}H_{21}ClNO_3S$ 450.0925; Found 450.0896.

(Z)-5-(2-chlorophenyl)-2-(2-cyclopropyl-2-oxoethylidene)-3-phenylthiazolidin-4-one (***3r***): The product was obtained as yellow solid (66%, 122 mg); mp 156-157 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.69 (t, J = 7.5 Hz, 2H), 7.64 (t, J = 7.5 Hz, 1H), 7.54 (t, J = 5.0 Hz, 1H), 7.48-7.46 (m, 1H), 7.43 (d, J = 10.0 Hz, 2H), 7.40-7.38 (m, 2H), 5.40 (s, 1H), 5.60 (s, 1H), 1.84-1.80 (m, 1H), 1.05 (t, J = 5.0 Hz, 2H), 0.81 (t, J = 5.0 Hz, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 198.4, 172.7, 157.4, 135.3, 134.5, 133.9, 130.4, 130.3, 130.1, 129.9, 128.0, 127.6, 101.1, 48.5, 21.5, 10.9, 10.9; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{17}ClNO_2S$ 370.0663; Found 370.0638.

(Z)-5-(4-nitrophenyl)-2-(2-oxo-2-phenylethylidene)-3-phenylthiazolidin-4-one (***3s***): The product was obtained as brown solid (70%, 146 mg); mp 178-179 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, J = 10.0 Hz, 2H), 7.74-7.70 (m, 4H), 7.62-7.57 (m, 4H), 7.50 (t, J = 7.5 Hz, 1H), 7.40 (t, J = 7.5 Hz, 3H), 6.43 (s, 1H), 5.25 (s, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 189.1, 172.2, 159.5, 148.1, 142.6, 137.9, 135.0, 132.6, 130.5, 130.3, 129.6, 128.7, 127.9, 127.7, 124.4, 98.3, 49.6; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{17}N_2O_4S$ 417.0904; Found 417.0887.

(Z)-5-(4-nitrophenyl)-2-(2-oxo-2-(m-tolyl)ethylidene)-3-phenylthiazolidin-4-one (***3t***): The product was obtained as brown solid (72%, 155 mg); mp 139-140 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, J = 10.0 Hz, 2H), 7.71 (d, J = 5.0 Hz, 2H), 7.66-7.56 (m, 5H), 7.47 (d, J = 5.0 Hz, 1H), 7.32-7.27 (m, 3H),

6.41 (s, 1H), 5.25 (s, 1H), 2.36 (s, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 189.3, 172.2, 159.3, 148.2, 142.7, 138.6, 138.0, 135.0, 133.5, 130.5, 130.3, 129.6, 128.5, 128.3, 128.0, 124.8, 124.4, 98.5, 49.6, 21.5; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{19}N_2O_4S$ 431.1060; Found 431.1033.

(Z)-5-(4-nitrophenyl)-2-(2-oxo-2-(3,4,5-trimethoxyphenyl)ethylidene)-3-phenylthiazolidin-4-one ***(3u)***: The product was obtained as brown solid (66%, 167 mg); mp 141-142 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, J = 10.0 Hz, 2H), 7.72 (d, J = 10.0Hz, 2H), 7.61-7.42 (m, 5H), 6.98 (s, 2H), 6.35 (s, 1H), 5.26 (s, 1H), 3.88 (s, 3H), 3.82 (s, 6H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 188.0, 172.1, 159.4, 153.2, 148.2, 142.5, 142.4, 135.0, 133.3, 130.4, 130.3, 129.6, 128.0, 124.4, 105.4, 98.1, 61.0, 56.4, 56.2, 49.7; HRMS (ESI-TOF) m/z: $[M + H]^+$Calcd for $C_{26}H_{23}N_2O_7S$ 507.1220; Found 507.1192.

(Z)-5-(4-nitrophenyl)-2-(2-oxo-2-(4-(trifluoromethyl)phenyl)ethylidene)-3-phenylthiazolidin-4-one ***(3v)***: The product was obtained as brown solid (65%, 157 mg); mp 171-172 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, J = 10.0 Hz, 2H), 7.82 (d, J = 5.0 Hz, 2H), 7.71 (d, J = 5.0 Hz, 2H), 7.67-7.59 (m, 5H), 7.36-7.31 (m, 2H), 6.40 (s, 1H), 5.28 (s, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 187.84, 172.18, 161.00, 148.23, 142.28, 140.81, 138.12, 134.82, 133.8 (q, $^{2}J_{CF3}$ J = 32.5), 131.72, 130.62, 130.49, 130.40, 129.65, 128.02, 127.91, 125.78, 125.76, 124.49, 123.7 (q, $^{1}J_{CF3}$ J = 270.8 Hz), 97.90, 49.65; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{16}F_3N_2O_4S$ 485.0777; Found 485.0767.

(Z)-2-(4-methyl-2-oxopentylidene)-5-(4-nitrophenyl)-3-phenylthiazolidin-4-one ***(3w)***: The product was obtained as dark brown solid (60%, 119 mg); mp 135-136 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, J = 10.0 Hz, 2H), 7.68 (d, J = 10.0 Hz, 2H), 7.58-7.55 (m, 1H), 7.41 (t, J = 7.5 Hz, 3H), 7.29 (t, J = 7.5 Hz, 1H), 5.67 (s, 1H), 5.19 (s, 1H), 2.24 (d, J = 5.0 Hz, 2H), 2.11-2.04 (m, 1H), 0.89 (d, J = 5.0 Hz, 6H) ; $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 172.2, 156.6, 142.7, 134.9, 130.4, 129.7, 129.6, 127.9, 127.3, 125.4, 124.4, 101.7, 52.3, 49.5, 25.5, 22.7; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{21}N_2O_4S$ 397.1217; Found 397.1204.

*(Z)-3-ethyl-2-(2-(4-methoxyphenyl)-2-oxoethylidene)-5-(4-nitrophenyl)thiazolidin-4-one (**3x**)*: The product was obtained as white solid (63%, 125 mg); mp 183-184 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (d, J =5.0 Hz, 2H), 7.96 (d, J = 5.0 Hz, 2H), 7.59 (d, J = 5.0 Hz, 2H), 6.98 (d, J = 7.5 Hz, 2H), 6.79 (s, 1H), 5.06 (s, 1H), 3.93 (d, J = 3.33, 2H), 3.89 (s, 3H), 1.36 (t, J = 5.0 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 187.8, 172.3, 163.3, 157.4, 148.0, 142.9, 131.0, 129.9, 129.6, 124.3, 114.0, 95.8, 55.6, 49.5, 39.5, 12.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{19}N_2O_5S$ 399.1009; Found 399.0997.

*(Z)-2-(2-oxo-2-phenylethylidene)-3-phenylthiazolidin-4-one (**3y**)*: The product was obtained as brown solid (78%, 115 mg); mp 190-191 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72-7.70 (m, 2H), 7.62-7.56 (m, 3H), 7.45 (d, J = 5.0 Hz, 1H), 7.37 (t, J = 7.5 Hz, 2H), 7.32-7.30 (m, 2H), 6.32 (s, 1H), 3.90 (s, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 188.9, 172.6, 162.3, 138.3, 135.2, 132.3, 130.4, 130.1, 128.6, 128.0, 127.6, 97.8, 32.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{14}NO_2S$ 296.0740; Found 296.0725.

*(Z)-2-(2-oxo-2-(p-tolyl)ethylidene)-3-phenylthiazolidin-4-one (**3z**)*: The product was obtained as brown solid (75%, 116 mg); mp 215-216 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62-7.56 (m, 5H), 7.30 (d, J = 5.0 Hz, 2H), 7.17 (d, J = 10.0 Hz, 2H), 6.30 (s, 1H), 3.90 (s, 2H), 2.36 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 188.6, 172.7, 161.9, 143.0, 135.7, 135.2, 130.4, 130.0, 129.3, 128.0, 127.7, 97.9, 32.2, 21.7; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{16}NO_2S$ 310.0896; Found 310.0883.

*(Z)-2-(2-(4-chlorophenyl)-2-oxoethylidene)-3-phenylthiazolidin-4-one (**3nb**)*: The product was obtained as brown solid (72%, 119 mg); mp 160-161 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.63-7.54 (m, 4H), 7.43 (d, J = 10.0 Hz, 1H), 7.32-7.29 (m, 3H), 6.24 (s, 1H), 3.91 (s, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 169.2, 153.1, 139.3, 128.93, 128.6, 125.4, 123.2, 122.1, 121.3, 121.3, 121.2, 119.7, 119.7, 119.7, 119.7, 29.8, 20.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{13}ClNO_2S$ 330.0350; Found 330.0330.

*(Z)-3-(4-methoxyphenyl)-2-(2-oxo-2-(p-tolyl)ethylidene)thiazolidin-4-one (**3mb**)*: The product was obtained as brown solid (69%, 117 mg); mp 194-195 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, J = 10.0 Hz, 2H), 7.22-7.17 (m, 4H), 7.08 (d, J = 5.0 Hz, 2H), 6.32 (s, 1H), 3.89 (s, 3H), 3.87 (s, 2H), 2.36 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 188.6, 172.9, 162.2, 160.5, 143.0, 135.8, 129.2, 129.1, 127.7, 127.6, 115.6, 97.8, 55.7, 32.1, 29.8, 21.7; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{18}NO_3S$ 340.1002; Found 340.0985.

*(Z)-2-(2-oxo-2-(thiophen-2-yl)ethylidene)-3-phenylthiazolidin-4-one (**3eb**)*: The product was obtained as dark brown solid (65%, 98 mg); mp 139-140 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62-7.54 (m, 3H), 7.52 (d, J = 5.0 Hz, 1H), 7.35 (d, J = 5.0 Hz, 1H), 7.29 (d, J = 5.0 Hz, 2H), 7.01 (t, J = 5.0 Hz, 1H), 6.15 (s, 1H), 3.90 (s, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 181.5, 172.5, 161.6, 145.5, 135.1, 132.7, 130.4, 130.1, 129.8, 128.0, 128.0, 97.8, 32.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{12}NO_2S_2$ 302.0304; Found 302.0296.

*(Z)-2-(5-acetyl-4-methyl-3-phenylthiazol-2(3H)-ylidene)-1-phenylethanone (**3ac**)*: The product was obtained as yellow solid (63%, 106 mg); mp 229-230 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, J = 10.0 Hz, 2H), 7.67-7.61 (m, 3H), 7.40-7.29 (m, 5H), 6.07 (s, 1H), 2.51 (s, 3H), 2.31 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 191.0, 184.3, 162.3, 145.6, 139.1, 136.7, 130.9, 130.9, 130.6, 128.3, 128.1, 127.1, 116.7, 90.1, 30.4, 14.5; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{18}NO_2S$ 336.1053; Found 336.1053.

*(Z)-2-(5-acetyl-4-methyl-3-phenylthiazol-2(3H)-ylidene)-1-(m-tolyl)ethanone (**3tc**)*: The product was obtained as pale yellow solid (65%, 113 mg); mp 174-175 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68-7.63 (m, 3H), 7.59 (s, 1H), 7.48-7.46 (m, 1H), 7.31-7.30 (m, 2H), 7.22 (t, J = 7.5 Hz, 2H), 6.06 (s, 1H), 2.52 (s, 3H), 2.34 (s, 3H), 2.31 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 191.1, 184.5, 162.2, 145.6,

139.1, 138.0, 136.7, 131.7, 130.9, 130.5, 128.1, 128.1, 127.8, 124.1, 116.6, 90.2, 30.4, 21.5, 14.5; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{20}NO_2S$ 350.1209; Found 350.1186.

(Z)-2-(5-acetyl-4-methyl-3-phenylthiazol-2(3H)-ylidene)-1-(4-bromophenyl)ethanone (***3jc***): The product was obtained as pale yellow solid (62%, 128 mg); mp 215-216 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.68-764 (m, 3H), 7.59 (d, J = 10.0 Hz, 2H), 7.46 (d, J = 10.0 Hz, 2H), 7.30 (d, J = 5.0 Hz, 2H), 6.0 (s, 1H), 2.52 (s, 3H), 2.32 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 190.9, 182.8, 162.6, 145.7, 137.9, 136.5, 131.5, 130.9, 130.7, 128.7, 128.0, 125.5, 116.9, 89.7, 30.4, 14.5; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{17}BrNO_2S$ 414.0158; Found 414.0159.

(Z)-2-(5-acetyl-4-methyl-3-(p-tolyl)thiazol-2(3H)-ylidene)-1-(4-methoxyphenyl)ethanone (***3fc***): The product was obtained as yellow solid (60%, 104 mg); mp 205-206 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, J = 5.0 Hz, 2H), 7.22-7.19 (m, 2H), 7.16-7.11 (m, 4H), 6.08 (s, 1H), 3.93 (s, 3H), 2.51 (s, 3H), 2.36 (s, 3H), 2.31 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 191.1, 184.2, 162.4, 160.8, 146.2, 141.3, 136.5, 129.2, 129.1, 129.0, 127.2, 115.9, 90.0, 55.8, 30.4, 21.6, 14.5; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{22}NO_3S$ 380.1315; Found 380.1303.

(Z)-2-(5-acetyl-4-methyl-3-phenylthiazol-2(3H)-ylidene)-1-(thiophen-2-yl)ethanone (***3ec***): The product was obtained as yellow solid (59%, 101 mg); mp 218-219 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.68-7.63 (m, 3H), 7.40 (d, J = 5.0 Hz, 1H), 7.32-7.29 (m, 3H), 6.98 (t, J = 5.0 Hz, 1H), 5.90 (s, 1H), 2.50 (s, 3H), 2.31 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 190.9, 177.6, 161.8, 145.6, 136.6, 130.9, 130.6, 130.3, 128.1, 127.7, 127.6, 117.1, 89.9, 30.4, 14.5; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{16}NO_2S_2$ 342.0617; Found 342.0617.

1-(3-methyl-4H-benzo[b][1,4]thiazin-2-yl)ethanone (***4a***): The product was obtained as brown sticky solid (60%, 66 mg); ^1H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, J = 10.0 Hz, 1H), 7.88 (d, J = 5.0 Hz, 1H), 7.49 (t, J = 7.5 Hz, 1H), 7.39 (t, J = 7.5 Hz, 1H), 5.19 (s, 1H), 2.49 (s, 3H), 1.96 (s, 3H); $^{13}C\{^1H\}$ NMR

(125 MHz, $CDCl_3$) δ 206.7, 174.0, 153.8, 135.7, 132.0, 129.9, 127.8, 127.1, 126.2, 125.5, 125.3, 123.2, 122.5, 121.9, 81.3, 25.9, 23.5; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{12}NO_2S$ 222.0583; Found 222.0559.

1-(6-chloro-3-methyl-4H-benzo[b][1,4]thiazin-2-yl)ethanone ***(4b)***: The product was obtained as white solid (58%, 74 mg); mp 134-135 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 8.01 (s,1H), 7.80 (d, J = 10.0 Hz, 1H), 7.37 (dd, J = 10.0 Hz, 5.0 Hz, 1H), 5.17 (s, 1H), 2.50 (s, 3H), 1.93 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 206.4, 176.2, 154.7, 134.0, 132.3, 125.9, 123.1, 122.7, 81.4, 26.0, 23.5; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{11}ClNO_2S$ 256.0194; Found 256.0181.

ASSOCIATED CONTENT

Supporting Information

Experimental procedure, full characterization of products, copies of ^1H, ^{13}C NMR, HRMS spectra (PDF), and CIF information. The Supporting Information is available free of charge on the ACS Publications website.

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGEMENTS

We acknowledge the financial support from the Science and Engineering Research Board (SERB/EMR/2015/002482), the Council of Scientific and Industrial Research (02(0263)/16/EMR-II), and DST-PURSE programme, New Delhi. The authors acknowledge to SAIF IIT, Patna for providing single crystal X-Ray facility. The authors (M.A.A. & D.Y.) are thankful to University Grants Commission (UGC), New Delhi for fellowship.

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