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Sulfur- and DABCO-Promoted Reaction between Alkylidene Rhodanines and Isothiocyanates: Access to Aminoalkylidene Rhodanines

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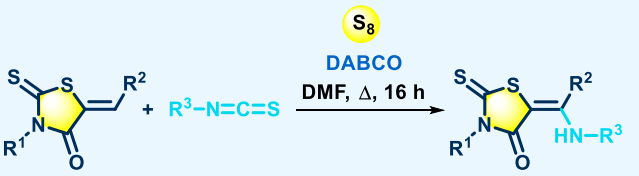
ABSTRACT: In this work, an efficient sulfur- and DABCO-promoted reaction for the synthesis of aminoalkylidene rhodanines from available alkylidene rhodanines and isothiocyanates is reported. A tandem process including sulfurative annulation/ring-opening by liberation of a CS_2 molecule/olefination allows the synthesis of aminoalkylidene rhodanines with acceptable functional group tolerance. Chemo- and stereoselectivity, operational simplicity, and synthetically useful yields are some highlighted advantages of these transformations.



- Heterocyclic motif of medicinal and material interest
- Readily available starting materials
- One-pot and metal-free procedure
- Synthetically useful yields

INTRODUCTION

Substituted heterocyclic molecules are identified as a privileged class of compounds in contemporary organic and medicinal chemistry. These frameworks constitute an inspiration for chemists owing to their extensive biological and synthetic relevance.[1] Among various important heterocyclic scaffolds, rhodanines are interesting key units found in many biological active compounds and therapeutic agents.[2] The structures of rhodanine (A) and some pharmacophores (B−E) containing the rhodanine subunit are depicted in Figure 1.[3] Furthermore, rhodanine derivatives are responsive to photons and have the potential to be used as photocatalysts. In this regard, substituted rhodanines attract significant attention due to their considerable value as building blocks and synthetic targets.[4] Over the past years, rhodanine-based compounds have been employed as nucleophilic or electrophilic synthons for the synthesis of high-added-value molecules.[5] Among various rhodanine derivatives, alkylidene rhodanines (Figure 1F) are very interesting starting materials and they have been used in several cycloaddition transformations.[6]

Alizadeh et al. reported the ultrasound-promoted [4 + 2] annulation/aromatization/nucleophilic acyl substitution reaction of alkylidene rhodanines and alkylidene malononitriles toward the synthesis of phthalimides.[7] Preparation of spirocyclohexanonerhodanines using a diamine-catalyzed asymmetric tandem reaction between alkylidene rhodanines and α,β-unsaturated ketones was disclosed by Ye and co-workers.[8] Yavari et al. reported the synthesis of spiropyrrolizidine-linked rhodanines through [3 + 2] cycloaddition reactions of azomethine ylides, prepared *in situ* from L-proline and acetylenic esters and alkylidene rhodanines.[9] As a part of our ongoing studies directed toward developing practical and novel synthetic protocols for heterocycles, we decided to employ alkylidene rhodanines for the synthesis of novel rhodanine-based molecules.[10]

Interestingly, Nguyen's group developed several elegant methods for the synthesis of heterocyclic compounds using elemental sulfur as a stable, readily accessible, and user-friendly (nontoxic, nonodorous, and nonvolatile) reagent.[11] In 2021, they reported a base-catalyzed three-component synthesis of thiazole-2-thiones via the reaction of chalcones with isothiocyanates and elemental sulfur (Scheme 1A).[12] Inspired by this research, we decided to investigate the reaction of alkylidene rhodanines,[13] in the place of simple chalcones, with isothiocyanates[14] and elemental sulfur for the synthesis of novel rhodanine-based compounds. To our surprise, compared with the report by Nguyen's group, the base-catalyzed three-component reaction of alkylidene rhodanines with isothiocyanates and elemental sulfur progressed differently and novel aminoalkylidene rhodanines were synthesized (Scheme 1B).

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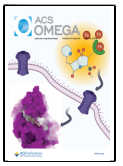


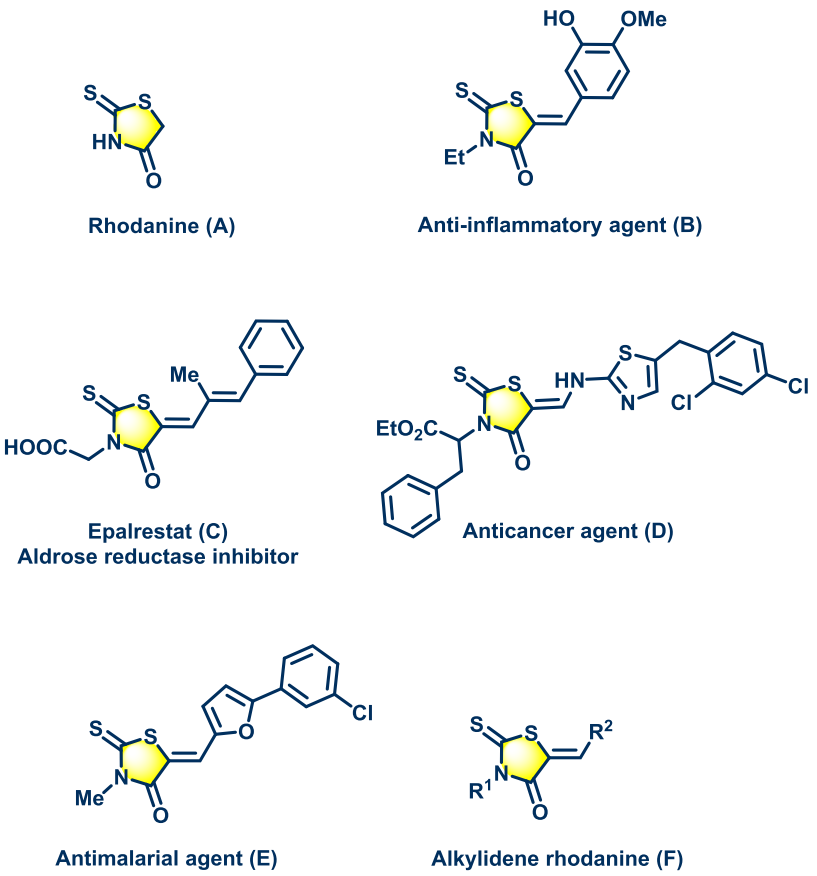
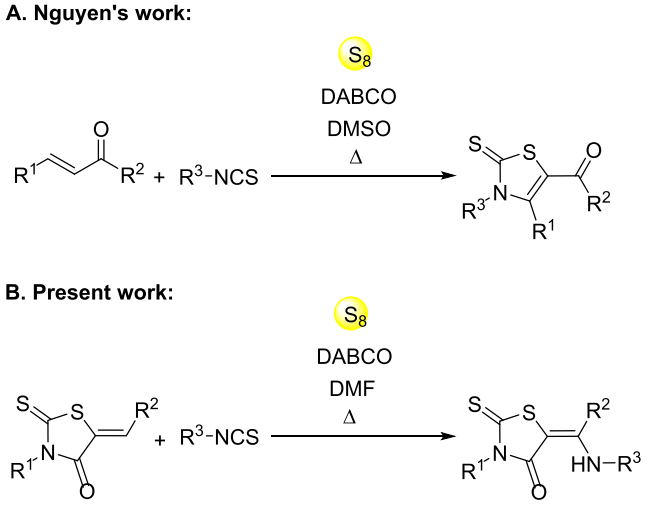


Figure 1. Structures of rhodanine (A), some bioactive molecules containing a rhodanine unit (B–E), and alkylidene rhodanine (F).

Scheme 1. Sulfur- and DABCO-Promoted Reaction between Chalcones and Isothiocyanates



Seemingly, this transformation is based on the following three steps (Figure 2): (1) sulfur- and base-promoted formation of zwitterion intermediate **I**; (2) nucleophilic attack of the intermediate **I** to alkylidene rhodanine **1** followed by the formation of spiro intermediate **II**; and (3) base-promoted CS_2 cleavage and final product preparation.

Interestingly, there are some reports on the synthesis of aminoalkylidene rhodanine scaffolds. In 2009, Favi's group described the three-component reaction of aliphatic primary amines and carbon disulfide with 1,2-diaza-1,3-dienes, in which the final product bears an aminoalkylidene rhodanine framework (Scheme 2A).[15] Lesyk et al. demonstrated a facile method for the synthesis of pharmaceutically active aminoalkylidene rhodanine derivatives *via* the reaction of ethoxyalkylidene rhodanines with amines (Scheme 2B).[16] Moreover, aminoalkylidene rhodanine frameworks were synthesized through reactions between 3-alkyl rhodanines and formamidines (Scheme 2C).[17]

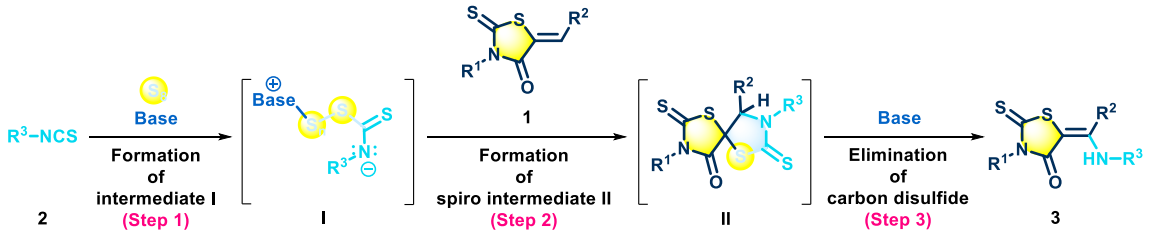


Figure 2. Proposed reaction path for the synthesis of aminoalkylidene rhodanines.

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Scheme 2. Reported Strategies for the Formation of Aminoalkylidene Rhodanine Derivatives

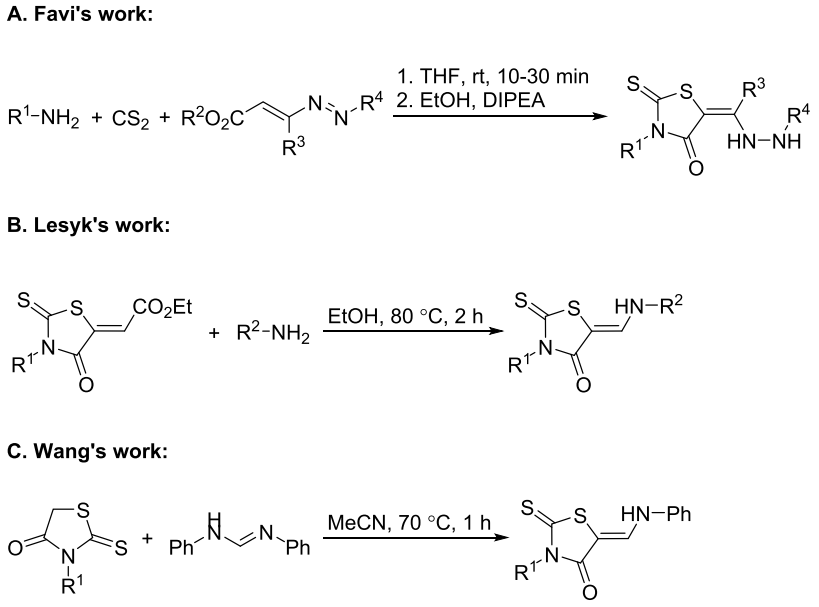
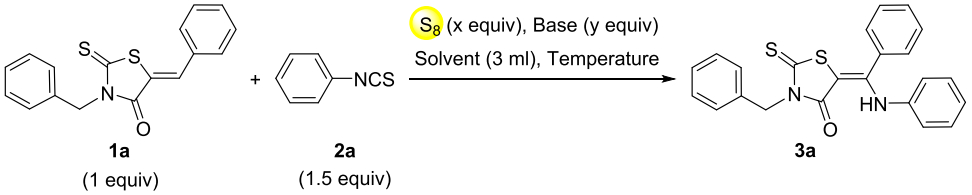


Table 1. Survey on the Conditions for the Synthesis of 3a[a]



entry	*x*	base	*y*	solvent	temperature (°C)	time	yield (%)[b]
1	2	DABCO	0.2	MeCN	80	24	0
2	2	DABCO	0.2	MeCN	100	48	trace
3	2	DABCO	0.2	DMSO	100	24	37
4	2	DABCO	0.2	DMF	100	24	44
5	2	DABCO	0.2	DMA	100	24	40
6	2	DABCO	0.2	toluene	100	24	0
7	2	DABCO	0.2	1,4-dioxane	100	24	10
8	2	DABCO	0.2	EtOH	80	24	0
9	2	DABCO	0.2	DMF	120	20	51
10	2	triethylamine	1	DMF	120	24	32
11	2	*N*-methylpiperidine	1	DMF	120	24	35
12	2	Pyridine	1	DMF	120	24	0
13	2	DABCO	0.5	DMF	120	19	58
14	2	DABCO	1	DMF	120	17	62
15	3	DABCO	1	DMF	120	16	67
16	**4**	**DABCO**	**1**	**DMF**	**120**	**16**	**74**
17	4	DABCO	1	DMF	140	14	69
18	0	DABCO	1	DMF	120	24	0

[a]Reaction conditions: **1a** (311 mg, 1.0 mmol), **2a** (202 mg, 1.5 mmol), S_8 (*x* equiv, *x* mmol, 32 mg/mmol), base (*y* equiv, *y* mmol), and solvent (3 mL) were added to the reaction vessel. The reaction mixture was magnetically stirred at the mentioned temperature in an oil bath. After the mentioned time, the target product was purified by column chromatography on silica gel using *n*-hexane/EtOAc (9:1 v/v) as the eluent. [b]Isolated yields.

To the best of our knowledge, this base-catalyzed reaction of alkylidene rhodanines with isothiocyanates and elemental sulfur to direct the synthesis of aminoalkylidene rhodanines has never been documented, which represents an interesting reaction mode and extends the application of alkylidene rhodanines in organic synthesis.

RESULTS AND DISCUSSION

At the outset of our study, alkylidene rhodanine **1a** (1 equiv) and isothiocyanate **2a** (1.5 equiv) were selected for the initial reaction in the presence of S_8 (2 equiv) and DABCO (0.2 equiv) in MeCN (Table 1, entry 1). The reaction mixture was magnetically stirred at reflux temperature for 24 h, but no product was obtained. Increasing the reaction temperature to

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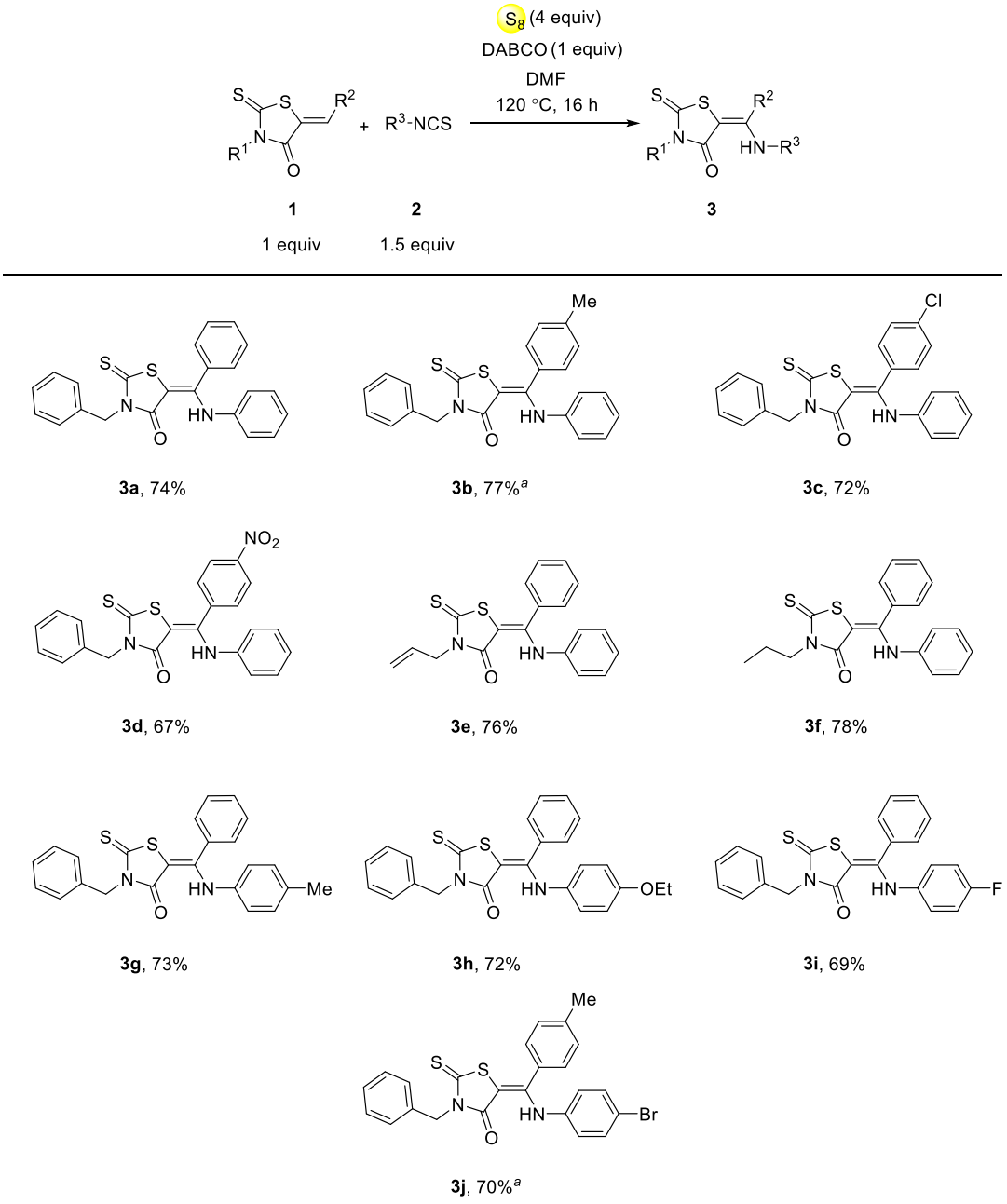
Scheme 3. Synthesis of Aminoalkylidene Rhodanines



[a]Reaction temperature: 140 °C.

100 °C led to the formation of product **3a** with a negligible yield, and the reaction remained incomplete even after 48 h. Gratifyingly, a moderate yield of **3a** was obtained when the reaction was heated at 100 °C in dimethyl sulfoxide (DMSO) (entry 3). Encouraged by this result, other solvents were tested, and the best yield was gained when using dimethylformamide (DMF) as the solvent (entries 4−8). Notably, increasing the reaction temperature to 120 °C led to a higher yield (entry 9).

In the next step, bases were screened. Different bases including triethylamine, pyridine, and *N*-methylpiperidine were inferior to DABCO (entries 10−12). Moreover, a significant improvement in the reaction yield and time was observed by using 1 equiv of DABCO (entry 14). Notably, no transformation occurred in the absence of S_8 in DMF at 120 °C overnight (entry 18).

Further investigation revealed that the ratio of starting materials is crucial, and the best result, 74%, was gained when the ratio of **1a**, **2a**, and S_8 was adjusted to 1:1.5:4. It should be noted that the role of the isothiocyanate component in this conversion was investigated by a control experiment. In the absence of the isothiocyanate component, upon keeping the mixture of alkylidene rhodanine **1a** and aniline under identical reaction conditions, no sign of aminoalkylidene rhodanine formation was observed. In this regard, we deduced that the presence of the isothiocyanate component is necessary for this transformation.

To gain insight into the tolerance of this transformation, we evaluated the reaction scope using various alkylidene

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rhodanines and isothiocyanates under the optimized reaction conditions. We first investigated the reaction scope with respect to the alkylidene rhodanines. As indicated in Scheme 3, either an electron-donating substituent or an electron-withdrawing substituent on the phenyl ring of alkylidene rhodanines was well-tolerated, giving the expected products in synthetically useful yields (**3b** and **3c**).

Alkylidene rhodanines bearing electron-donating groups gave yields higher than those bearing electron-withdrawing groups. Moreover, substrate **1**, with a strong electron-withdrawing substituent on the phenyl ring, such as nitro, gave a relatively lower yield (**3d**, 67%). Subsequently, the effect of the substituent at N-3 of the rhodanine substrate **1** was explored. Both N-allyl and -propyl substituted alkylidene rhodanines reacted smoothly, delivering **3e** and **3f** in 76 and 78% yields, respectively.

Next, the scope of isothiocyanates was explored. Differently substituted isothiocyanates, derived from anilines,[14] were subjected to the reaction with **1a** under the optimized reaction conditions. In most cases, the transformation also worked smoothly, affording the desired aminoalkylidene rhodanines in good yields (**3g−j**, 69−73%).

Notably, the reactions of isothiocyanates with an electron-deficient substituent, such as $-CF_3$, $-CN$, and $-NO_2$ groups, failed to afford the expected products. In the case of aliphatic isothiocyanates including benzyl isothiocyanate and propyl isothiocyanate, the target products were formed in trace amounts, and the isolation was difficult. To obtain satisfactory results, some reactions were carried out at a higher temperature (140 °C), except where noted in Scheme 3.

The structures of all products were characterized by high-resolution mass spectrometry (HRMS) analysis and NMR spectroscopy. Moreover, the structure of **3f** was undeniably confirmed by X-ray crystallographic analysis (Figure 3). It is

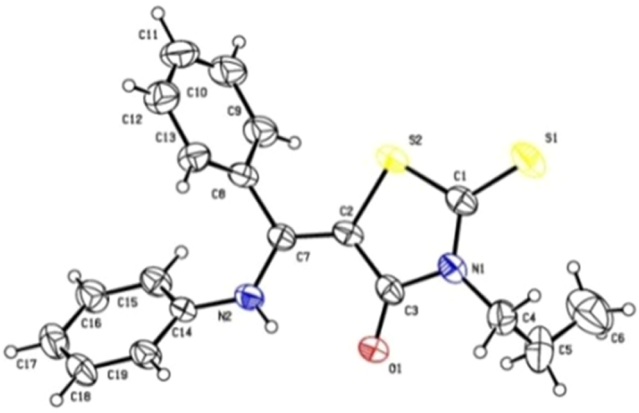

Figure 3. Oak ridge thermal ellipsoid plot (ORTEP) of the crystal structure of **3f.** One of the two molecules in the asymmetric unit is present. Thermal ellipsoids are at the 30% probability level. CCDC No. 2330745.

noteworthy that there are two possible *E* and *Z* diastereomeric structures for **3**. To our delight, the transformations exhibited excellent diastereoselectivity and exclusively generated the E-isomers (according to NMR and X-ray results as well as experimental observations).

On the basis of the above results and relevant studies, a possible mechanism for the formation of **3** is proposed (Scheme 4). This process could be initiated by the formation of DABCO-sulfur adduct **A**. Next, the nucleophilic attack of **A** to isothiocyanate **2** would lead to the zwitterion dithiocarbamate intermediate **B**. Subsequent nucleophilic addition of the intermediate **B** to alkylidene rhodanine **1** followed by elimination of S_n and cyclization would generate the spiro intermediate **C**. Finally, DABCO-catalyzed liberation of a CS_2 molecule from **C** would provide **3**.

CONCLUSIONS

In summary, a versatile sulfur- and DABCO-promoted reaction of available alkylidene rhodanines with isothiocyanates under simple heating conditions has been disclosed, yielding a series of novel aminoalkylidene rhodanine derivatives in synthetically useful yields.

The new C−N bond of the product is efficiently formed between the β-carbon of the alkylidene rhodanine and the nitrogen atom of the isothiocyanate through the sulfurative annulation/ring-opening by cleavage of a CS_2 molecule/olefination sequence.

Further development of this interesting method, especially in the case of other heterocyclic-based chalcones, is underway in our laboratory.

EXPERIMENTAL SECTION

General Information. All reactions were monitored by thin-layer chromatography (TLC) on Merck silica gel 60 F254 plates. The temperatures were monitored using a mercury laboratory thermometer. Column chromatography purification was carried out on silica gel (63−200-mesh ASTM). Melting points were measured on an Electrothermal 9100 apparatus. ^{1}H NMR (600 MHz) and ^{13}C{^{1}H} NMR (150 MHz) spectra were obtained using a Bruker spectrometer. NMR spectra were recorded at rt in $CDCl_3$. Chemical shifts are reported in parts per million (δ) downfield from an internal tetramethylsilane (TMS) reference. Coupling constants (J values) are reported in hertz (Hz), and standard abbreviations were used to indicate spin multiplicities (s, singlet; d, doublet; t, triplet; q, quartet; sext, sextet; br, broad; m multiplet). High-resolution mass spectra (HRMS) were obtained on an Agilent HRMS-ESI/QTOF instrument. All chemicals and solvents were used without further purification, purchased from Merck or Aldrich. Starting materials were synthesized according to the procedures reported in the literature.[13,14] Single crystals of compound **3f** were formed in the mixture of CH_2Cl_2 and *n*-hexane (1:1 v/v).

General Procedure for Preparation of 3a−j. DABCO (1.0 mmol, 112 mg) and elemental sulfur powder (4 mmol, 128 mg) were added to a solution of alkylidene rhodanine **1** (1.0 mmol) and isothiocyanate **2** (1.5 mmol) in DMF (3.0 mL). The reaction mixture was magnetically stirred at 120 °C in an oil bath. The final reaction mixture was concentrated under reduced pressure, and the residue was purified by column chromatography on silica gel using *n*-hexane/EtOAc (9:1 v/v) as the eluent. (Exceptionally, derivatives **3b** and **3j** were formed at 140 °C.)

*(E)-3-Benzyl-5-(phenyl(phenylamino)methylene)-2-thioxothiazolidin-4-one (**3a**).* The reaction mixture was purified by column chromatography using *n*-hexane/EtOAc (9:1 v/v) as the eluent to afford the product as a pale-yellow solid (297 mg, 74% yield), mp 168−170 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.27 (1H, s, NH), 7.52 (d, 2H, J = 7.3 Hz), 7.42 (t, 1H, J = 7.3 Hz), 7.37 (t, 2H, J = 7.8 Hz), 7.33−7.25 (m, 5H),

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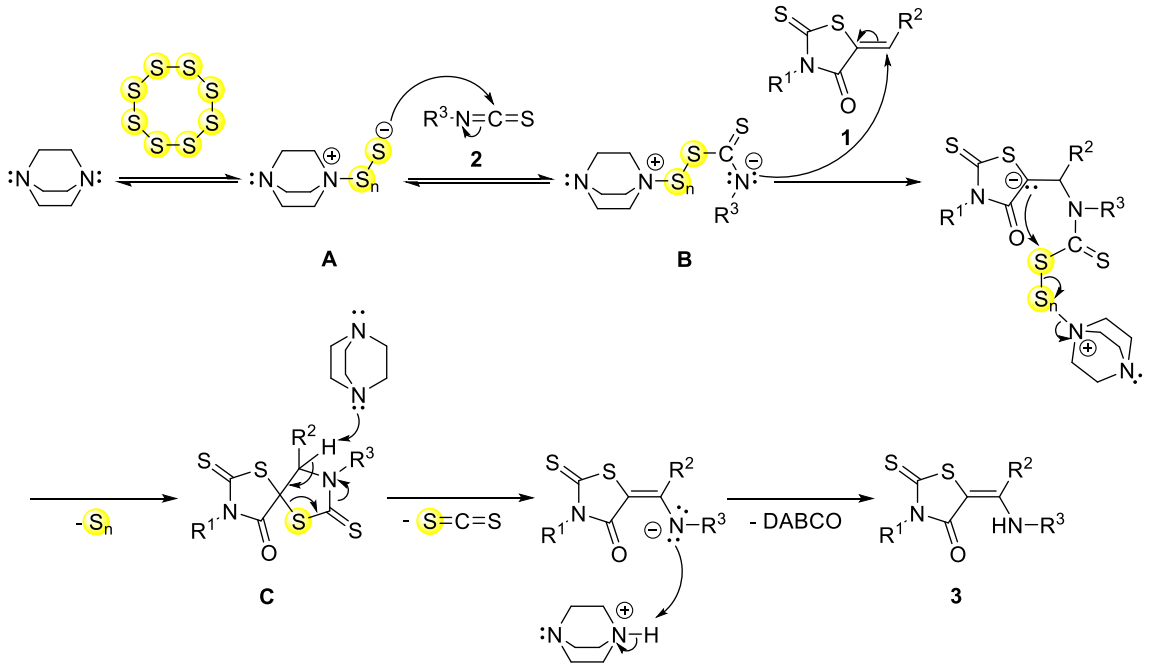
Scheme 4. Plausible Reaction Mechanism



7.09 (t, 2H, J = 7.6 Hz), 6.99 (t, 1H, J = 7.3 Hz), 6.70 (d, 2H, J = 7.9 Hz), 5.33 (s, 2H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 191.6, 167.3, 153.0, 138.0, 135.5, 132.7, 130.9, 129.2, 129.0, 128.7, 128.4, 128.3, 127.8, 125.0, 122.9, 96.6, 47.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{23}H_{19}N_2OS_2$ 403.0933; found 403.0930.

*(E)-3-Benzyl-5-((phenylamino)(p-tolyl)methylene)-2-thioxothiazolidin-4-one (**3b**).* The reaction mixture was purified by column chromatography using *n*-hexane/EtOAc (9:1 v/v) as the eluent to afford the product as a pale-yellow solid (320 mg, 77% yield), mp 129−131 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 11.25 (s, 1H, NH), 7.51 (d, 2H, J = 7.3 Hz), 7.31 (t, 2H, J = 7.2 Hz), 7.26 (t, 1H, J = 7.3 Hz), 7.19−7.15 (m, 4H), 7.10 (t, 2H, J = 7.8 Hz), 7.00 (t, 1H, J = 7.5 Hz), 6.71 (d, 2H, J = 7.8), 5.33 (s, 2H), 2.35 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 191.6, 167.2, 153.3, 141.4, 138.1, 135.5, 129.9, 129.7, 128.9, 128.7, 128.4, 128.2, 127.8, 124.9, 122.9, 96.5, 47.2, 21.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{24}H_{21}N_2OS_2$ 417.1090; found 417.1093.

*(E)-3-Benzyl-5-((4-chlorophenyl)(phenylamino)-methylene)-2-thioxothiazolidin-4-one (**3c**).* The reaction mixture was purified by column chromatography using *n*-hexane/EtOAc (9:1 v/v) as the eluent to afford the product as a pale-yellow solid (314 mg, 72% yield), mp 164−166 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 11.22 (1H, s, NH), 7.51 (d, 2H, J = 7.2 Hz), 7.35 (d, 2H, J = 8.5 Hz), 7.32 (t, 2H, J = 7.2 Hz), 7.27 (t, 1H, J = 7.2 Hz), 7.24 (d, 2H, J = 8.4 Hz), 7.13 (t, 2H, J = 7.8 Hz), 7.03 (t, 1H, J = 7.5 Hz), 6.71 (d, 2H, J = 7.8 Hz), 5.32 (s, 2H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 191.3, 167.3, 151.5, 137.8, 137.1, 135.4, 131.8, 129.8, 129.6, 129.1, 128.8, 128.5, 127.9, 125.3, 123.1, 96.8, 47.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{23}H_{18}ClN_2OS_2$ 437.0544; found 437.0496.

*(E)-3-Benzyl-5-((4-nitrophenyl)(phenylamino)methylene)-2-thioxothiazolidin-4-one (**3d**).* The reaction mixture was purified by column chromatography using *n*-hexane/EtOAc (9:1 v/v) as the eluent to afford the product as a pale-orange solid (299 mg, 67% yield), mp 194−196 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 11.21 (s, 1H, NH), 8.22 (d, 2H, J = 8.7 Hz), 7.52−7.50 (m, 4H), 7.32 (t, 2H, J = 7.2 Hz), 7.28 (t, 1H, J = 7.2 Hz), 7.13 (t, 2H, J = 7.8 Hz), 7.04 (t, 1H, J = 7.3 Hz), 6.70 (d, 2H, J = 7.8 Hz), 5.32 (s, 2H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 191.0, 167.5, 149.6, 148.7, 138.9, 137.4, 135.2, 129.7, 129.3, 128.8, 128.5, 128.0, 125.7, 124.4, 123.3, 97.4, 47.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{23}H_{18}N_3O_3S_2$ 448.0784; found 448.0742.

*(E)-3-Allyl-5-(phenyl(phenylamino)methylene)-2-thioxothiazolidin-4-one (**3e**).* The reaction mixture was purified by column chromatography using *n*-hexane/EtOAc (9:1 v/v) as the eluent to afford the product as a pale-yellow solid (267 mg, 76% yield), mp 143−145 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 11.30 (s, 1H, NH), 7.43 (t, 1H, J = 7.5 Hz), 7.37 (t, 2H, J = 7.8 Hz,), 7.31 (d, 2H, J = 7.2 Hz), 7.10 (t, 2H, J = 7.8 Hz,), 7.00 (t, 1H, J = 7.5 Hz), 6.71 (d, 2H, J = 7.8 Hz), 5.95−5.89 (m, 1H), 5.30 (dd, 1H, J = 17.1 Hz, J = 1.2 Hz), 5.25 (dd, 1H, J = 10.2 Hz, J = 1.0 Hz), 4.75 (d, 2H, J = 5.7 Hz).$^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 191.3, 167.1, 153.0, 138.0, 132.7, 130.9, 130.2, 129.2, 129.0, 128.3, 125.0, 122.9, 118.6, 96.7, 46.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{17}N_2OS_2$ 353.0777; found 353.0778.

*(E)-5-(Phenyl(phenylamino)methylene)-3-propyl-2-thioxothiazolidin-4-one (**3f**).* The reaction mixture was purified by column chromatography using *n*-hexane/EtOAc (9:1 v/v) as the eluent to afford the product as a pale-orange solid (276 mg, 78% yield), mp 146−148 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 11.33 (s, 1H, NH), 7.42 (t, 1H, J = 7.4 Hz), 7.37 (t, 2H, J = 7.8 Hz), 7.30 (d, 2H, J = 7.2 Hz), 7.10 (t, 2H, J = 7.8 Hz), 7.00 (t, 1H, J = 7.4 Hz), 6.71 (d, 2H, J = 7.8 Hz), 4.08 (t, 2H, J = 7.6 Hz), 1.77 (sext, 2H, J = 7.6 Hz), 0.98 (t, 3H, J = 7.4 Hz). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 191.6, 167.5, 152.7, 138.1, 132.8, 130.8, 129.2, 129.0, 128.3, 124.9, 122.8, 96.9, 45.7, 20.4, 11.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{19}N_2OS_2$ 355.0933; found 355.0935.

*(E)-3-Benzyl-5-(phenyl(p-tolylamino)methylene)-2-thioxothiazolidin-4-one (**3g**).* The reaction mixture was purified

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by column chromatography using *n*-hexane/EtOAc (9:1 v/v) as the eluent to afford the product as a pale-yellow solid (303 mg, 73% yield), mp 180−182 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.25 (s, 1H, NH), 7.52 (d, 2H, J = 7.3 Hz), 7.41 (t, 1H, J = 7.4 Hz), 7.36 (t, 2H, J = 7.8 Hz), 7.32 (t, 2H, J = 7.2), 7.28 (d, 2H, J = 7.2), 7.26 (t, 1H, J = 7.4 Hz), 6.89 (d, 2H, J = 8.3 Hz), 6.59 (d, 2H, J = 8.3 Hz), 5.33 (s, 2H), 2.20 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 191.5, 167.2, 153.3, 135.6, 135.3, 135.0, 132.8, 130.8, 129.5, 129.2, 128.7, 128.4, 128.3, 127.8, 123.0, 96.0, 47.2, 20.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{24}H_{21}N_2OS_2$ 417.1090; found 417.1097.

(E)-3-Benzyl-5-(((4-ethoxyphenyl)amino)(p-tolyl)-methylene)-2-thioxothiazolidin-4-one (***3h***). The reaction mixture was purified by column chromatography using *n*-hexane/EtOAc (9:1 v/v) as the eluent to afford the product as a pale-yellow solid (321 mg, 72% yield), mp 148−150 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.22 (s, 1H, NH), 7.52 (d, 2H, J = 7.4 Hz), 7.39 (t, 1H, J = 7.4 Hz), 7.34 (t, 2H, J = 7.6 Hz), 7.32 (t, 2H, J = 7.6 Hz), 7.27−7.25 (m, 3H), 6.65 (d, 2H, J = 8.9 Hz), 6.61 (d, 2H, J = 8.9 Hz), 5.33 (s, 2H), 3.89 (q, 2H, J = 7.0 Hz), 1.33 (3H, t, J = 7.0 Hz). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 191.4, 167.1, 156.5, 153.8, 135.6, 132.7, 130.7, 129.1, 128.7, 128.4, 128.3, 127.8, 124.8, 114.7, 95.4, 63.6, 47.2, 14.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{25}H_{23}N_2O_2S_2$ 447.1195; found 447.1197.

(E)-3-Benzyl-5-(((4-fluorophenyl)amino)(phenyl)-methylene)-2-thioxothiazolidin-4-one (***3i***). The reaction mixture was purified by column chromatography using *n*-hexane/EtOAc (9:1 v/v) as the eluent to afford the product as a pale-yellow solid (289 mg, 69% yield), mp 162−164 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.20 (s, 1H, NH), 7.52 (d, 2H, J = 7.4 Hz), 7.42 (t, 1H, J = 7.4 Hz), 7.37 (t, 2H, J = 7.7 Hz), 7.32 (t, 2H, J = 7.2 Hz), 7.28−7.26 (m, 3H), 6.80 (t, 2H, J = 8.5), 6.70−6.68 (m, 2H), 5.33 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 191.6, 167.4, 159.9 (d, C_{ipso}-F, J = 244.0 Hz), 153.1, 135.5, 134.1 (d, C_{ipso}-NH, J = 3.2 Hz), 132.4, 130.9, 129.3, 128.8, 128.5, 128.3, 127.8, 124.9 (d, 2CH, J = 8.2 Hz), 115.9 (d, 2CH, J = 22.9 Hz), 96.5, 47.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{23}H_{18}FN_2OS_2$ 421.0839; found 421.0839.

(E)-3-Benzyl-5-(((4-bromophenyl)amino)(p-tolyl)-methylene)-2-thioxothiazolidin-4-one (***3j***). The reaction mixture was purified by column chromatography using *n*-hexane/EtOAc (9:1 v/v) as the eluent to afford the product as a pale-yellow solid (345 mg, 70% yield), mp 203−205 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.22 (s, 1H), 7.55 (d, 2H, J = 7.0 Hz), 7.38−7.30 (m, 3H), 7.26 (d, 2H, J = 7.7 Hz), 7.23−7.19 (m, 4H), 6.61 (d, 2H, J = 7.2 Hz), 5.36 (s, 2H), 2.41 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 191.7, 167.4, 152.5, 141.6, 137.4, 135.5, 132.0, 130.1, 129.4, 128.7, 128.5, 128.2, 127.8, 124.2, 118.0, 97.4, 47.2, 21.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{24}H_{20}BrN_2OS_2$ 495.0195; found 495.0193.

■ ASSOCIATED CONTENT

Data Availability Statement

The data and spectra underlying this study are available in the published article and its Supporting Information.

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.4c03341.

Crystallographic data (CIF)

Copies of ^{1}H and ^{13}C{^{1}H} NMR spectra for all products and X-ray structure for the compound **3f** and crystal structure description of **3f** (PDF)

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Notes

The authors declare no competing financial interest.

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