Unexpected Rearrangement; A Novel Route to 3-Thiazoline

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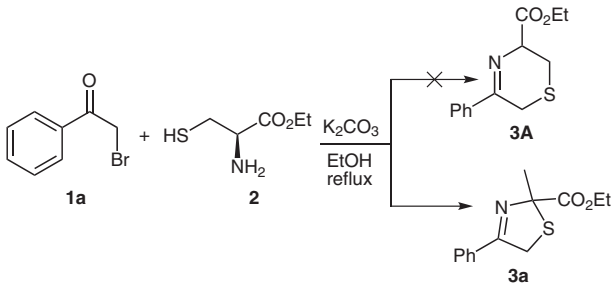
Abstract: An unexpected and novel rearrangement was discovered and used to synthesize a series of 3-thiazoline derivatives. The structures of the new compounds were determined by HRMS, IR, NMR and X-ray analyses.

Key words: rearrangement, amino acids, synthesis, thiazoline, X-ray

Thiazoline rings had been found in a large number of natural products with biological activities, and have been studied extensively.[1] Thiazolines have also been used as building blocks in pharmaceutical drug discovery[2] because some thiazoline derivatives present interesting activities such as anti-HIV, anti-cancer, antimitotic, and antibiotic effects.[3] New procedures for preparing such compounds have attracted the attention of many researchers,[4] especially for 3-thiazolines. For example, 2,4,5-trimethyl-3-thiazoline (TMT), a component of fox feces, has been widely used as an odorant to induce innate fear behavior in rats and mice.[5] In contrast to 2-thiazolines, the methods available for synthesizing 3-thiazoline derivatives are limited. Standard synthetic routes to 3-thiazolines involve the Asinger reaction, in which α-mercaptoketone, aldehyde, and ammonia react together at high temperature, or through modified Asinger reactions.[6] However, for these methods, byproducts are typically produced that are not easy to separate, and the 4-position of 3-thiazolines cannot be substituted by an ester group. There are a few reports on the synthesis of alkyl-substituted 3-thiazoline-carboxylates by a MnO_2-mediated oxidation reaction of thiazolidines. For 3-thiazolines substituted by an ester group, there has only been one study; in this case, the substitution occurred at the 2-position.[7]

Investigations aimed at discovering and developing anticancer reagents have been carried out in our laboratory,[8] and these have especially focused on the synthesis of novel, structurally diverse small molecules. In order to expand our small molecule library, a method to obtain 1,4-thiazine derivatives was designed that involved the condensation of cysteine and 1-aryl-2-bromoethanones, which were typically used to build heterocycle compounds.[9] However, during the synthesis, an unexpected product, 3-thiazoline, instead of 1,4-thiazine, was obtained. In this paper, this intriguing discovery is discussed.



Scheme 1 The reaction of α-bromoacetophenone and ethyl L-cysteine ester

It was reported that methyl (3*R*)-5-phenyl-1,4-thiazane-3-carboxylate can be obtained by the reaction of α-bromoacetophenone with methyl L-cysteine ester in a solution of potassium hydroxide in methanol, followed by sodium borohydride mediated reduction.[10] In our study, as shown in Scheme 1, when the reaction of α-bromoacetophenone (**1a**) and ethyl L-cysteine ester (**2**) was conducted with potassium carbonate instead of potassium hydroxide under reflux in ethanol for one hour, the unexpected product **3a** was found with a yield of 60%, rather than the expected product **3A**. The structure of **3a** was deduced from the HRMS, IR, and NMR spectroscopic data. The mass spectra displayed molecular ion peaks at *m/z* values consistent with **3a** (*m/z* $[M + H]^+$ calcd for $C_{13}H_{16}NO_2S$: 250.0902; found: 250.0905). The IR spectrum indicated the presence of C=O and C=N bonds from the existence of peaks at 1736 and 1631 cm^{-1}, respectively. The ^1H NMR spectrum of compound **3a** showed a singlet signal arising from a methyl group appearing at δ = 1.98 ppm. Signals from one methylene pair were observed at δ = 4.45 and 4.54 ppm as doublet peaks with a geminal coupling of 15.6 Hz. Similarly, by using this method and starting from 2-bromo-1-(4-chlorophenyl)ethanone, compound **3b** was obtained with a yield of 63%. For further structure elucidation of compound **3b**, two-dimensional NMR spectroscopy (COSY) were also obtained. The protons of the CH_2 in the ethyl group had strong and weak correlations with protons appearing at δ = 1.27 and 4.42 ppm, respectively, which were unambiguously assigned to the CH_3 in the ethyl group and H-5_{cis} in the 3-thiazoline ring. The correlations of H-5_{cis} in the 3-thiazoline ring with the protons of the CH_2 in the ethyl group could be seen by long distance coupling.

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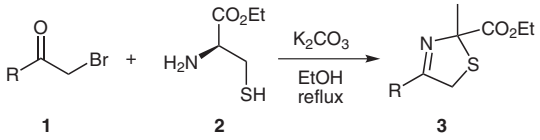
To further investigate the reaction, other substituted α-bromoacetophenones were used. The reactions of ethyl L-cysteine ester (**2**) with a series of α-bromoacetophenone derivatives **1b–h** and α-bromoacetofuran (**1i**) were carried out as shown in Scheme 2, and the yields were about 50–69% (Table 1). The reaction of bromomethyl ketones instead of 1-aryl-2-bromoethanones was also carried out but, unfortunately, none of the desired product was obtained. To our knowledge, except for our studies, ester substitutions at the 2-position of 3-thiazolines **3a–i** has not previously been reported.



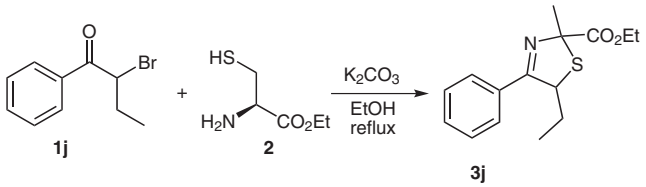
1 2 3

Scheme 2 Synthesis of 3-thiazoline derivatives

Table 1 Synthesis of 3-Thiazoline Derivatives

Entry	R	Time (h)	Product	Yield (%)
1	Ph	1	**3a**	60
2	4-ClC_6H_4	0.8	**3b**	63
3	4-$MeOC_6H_4$	1.5	**3c**	60
4	4-$NO_2C_6H_4$	1	**3d**	50
5	3-$NO_2C_6H_4$	1	**3e**	57
6	4-MeC_6H_4	1	**3f**	57
7	4-(*t*-Bu)C_6H_4	1	**3g**	69
8	4-MeO-3-$NO_2C_6H_3$	1	**3h**	56
9	2-furyl	1.5	**3i**	54

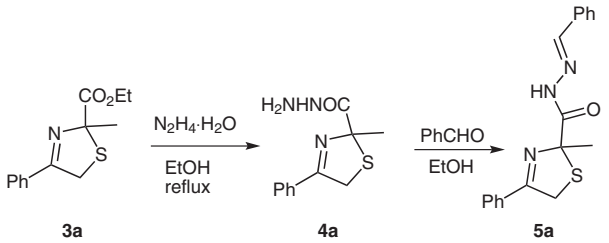
Interestingly, when 2-bromo-1-phenylbutan-1-one (**1j**) was used as starting material, two compounds were obtained in 1:1 ratio, which were diastereomers arising from different groups on C2 and C5 (Scheme 3). The mixture could be easily separated by column chromatography on silica gel to obtain two stereoisomers, which were racemic because of the C2 chirality.



1j 2 3j

Scheme 3 Reaction of 2-bromo-1-phenylbutan-1-one (**1j**) and ethyl L-cysteine ester (**2**)

To determine the exact structure of these novel and unexpected compounds, a single crystal of product **3** would clearly have been ideal, unfortunately, the experiment was not successful. Thus, derivatives such as carbohydrazone were then investigated. Fortunately, a single crystal of the derivative of 3-thiazoline, (*E*)-*N*′-benzylidene-2-methyl-4-phenyl-2,5-dihydrothiazole-2-carbohydrazide (**5a**), which was synthesized from **3a**, was successfully obtained. In the approach, compound **3a** reacted with hydrazine hydrate to afford compound **4a**; the latter then reacted with benzaldehyde to give compound **5a** (Scheme 4). The molecular view of **5a**[11] is shown in Figure 1. Based on the X-ray analysis of **5a**, the structure of **3a** was thus confirmed.



3a 4a 5a

Scheme 4 Synthesis of carbohydrazone **5a**

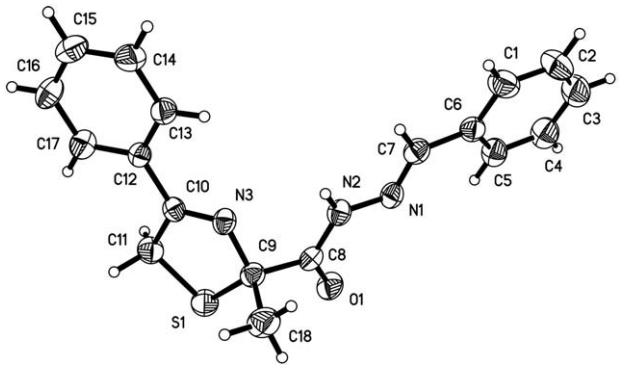
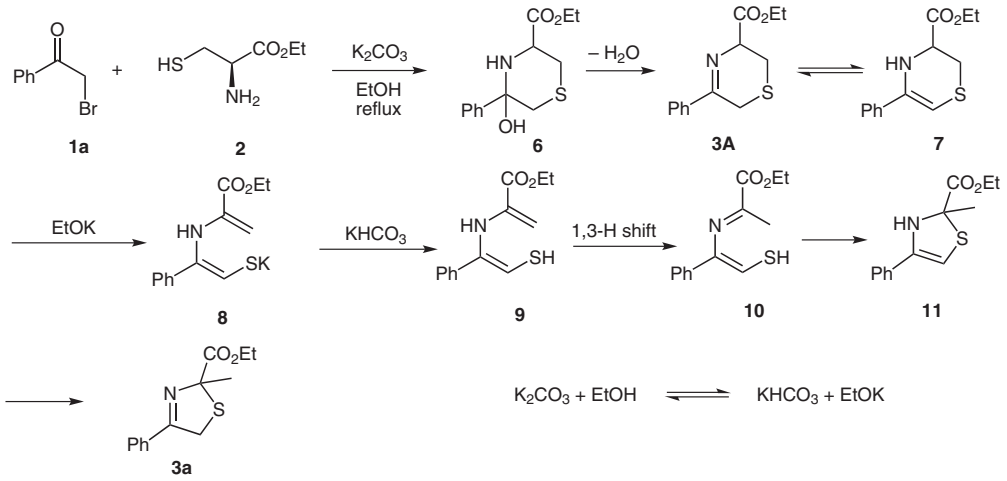


Figure 1 X-ray crystal structure of compound **5a**

To explain the unexpected formation of the 3-thiazoline ring, a mechanism for the reaction is proposed, as shown in Scheme 5. The expected six-membered-ring product (**3A**) was initially formed by the dehydration of intermediate **6**. Compound **3A** then tautomerizes to **7** and the α-hydrogen next to the ester group is removed by potassium ethoxide (generated from potassium carbonate and ethanol),[12] which induces cleavage of C–S bond to form **8**. Intermediate **8** is converted into **9** by reaction with potassium hydrocarbonate (formed from potassium carbonate and ethanol).[12] A 1,3-hydrogen shift then forms an imino ester **10**, which is conjugated with the enethiol. Addition of the thio moiety to the imine generates the racemic enamine **11**. Double bond migration around the five-membered-ring finally generates the product **3a**. Attempts were made to isolate the proposed intermediate **3A**, however, this was unsuccessful.

To support the mechanism, NMR experiments were carried out, however, the NMR spectra were too complex to provide any valuable information. LC-MS was also employed to obtain mass spectra at different reaction time-



Scheme 5 Proposed mechanism of the reaction

points, which might support the proposed mechanism. Samples taken during the initial stage of the reaction (20 min) and analyzed by HRMS gave signals at *m/z* = 268.1012 and 250.1000, which are consistent with intermediate **6** and either **3A** or **3a**, respectively.

In conclusion, an unexpected and novel rearrangement in the reaction of α-bromoacetophenone and ethyl L-cysteine ester in the presence of potassium carbonate was discovered and used to synthesize a series of new 3-thiazoline derivatives. The study provides a simple and versatile method for the synthesis of relatively rare 3-thiazolines.

Thin-layer chromatography (TLC) was carried out on silica gel 60 F_{254} plates (Merck KGaA). ^{1}H NMR spectra were recorded with Bruker Avance 300 (300 MHz) and 400 (400 MHz) spectrometers, using $CDCl_3$ or DMSO as solvents and tetramethylsilane (TMS) as internal standard. Melting points were determined with an XD-4 digital micro melting point apparatus. IR spectra were recorded with an Avtar 370 FT-IR (Termo Nicolet) spectrophotometer. LC-MS measurements were carried out using a C18 column (2.1 × 150 mm, 5 μm) from Agilent. HRMS spectra were recorded with a Q-TOF6510 spectrograph.

Preparation of Ethyl 2,5-Dihydrothiazole-2-carboxylate Derivatives 3a–j; General Procedure

2-Bromo-1-phenylethanone (1 mmol), L-cysteine ethyl ester (1.1 mmol), K_2CO_3 (4 mmol), and absolute EtOH (50 mL) were added to a flask and the mixture was stirred and heated to reflux under N_2 (the reaction was monitored by TLC until complete). The mixture was then filtered and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc–petroleum ether) to obtain the product.

Ethyl 2-Methyl-4-phenyl-2,5-dihydrothiazole-2-carboxylate (3a)

Yield: 60%; yellow solid; mp 54–56 °C.

IR (KBr): 1736 (C=O), 1631 (C=N) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 6.9 Hz, 3 H, CH_3), 1.98 (s, 3 H, CH_3), 4.17–4.27 (m, 2 H, CH_2), 4.45 (d, *J* = 15.6 Hz, 1 H, SCH_AH_B), 4.54 (d, *J* = 15.6 Hz, 1 H, SCH_AH_B), 7.41–7.52 (m, 3 H, ArH), 7.89 (dt, *J* = 6.3, 1.5 Hz, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.6, 170.0, 133.2, 131.5, 128.7 (2C), 128.6 (2C), 89.0, 61.8, 44.2, 27.5, 14.0.

HRMS: *m/z* [M + H]$^+$ calcd for $C_{13}H_{16}NO_2S$: 250.0902; found: 250.0905.

Ethyl 4-(4-Chlorophenyl)-2-methyl-2,5-dihydrothiazole-2-carboxylate (3b)

Yield: 63%; yellow oil.

IR (KBr): 1734 (C=O), 1636 (C=N) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.97 (s, 3 H, CH_3), 4.17–4.26 (m, 2 H, CH_2), 4.42 (d, *J* = 15.6 Hz, 1 H, SCH_AH_B), 4.45 (d, *J* = 15.6 Hz, 1 H, SCH_AH_B), 7.42 (d, *J* = 8.6 Hz, 2 H, ArH), 7.85 (d, *J* = 8.6 Hz, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.4, 168.9, 137.7, 131.5, 129.9 (2C), 128.9 (2C), 88.9, 61.9, 44.0, 27.4, 14.0.

HRMS: *m/z* [M + H]$^+$ calcd for $C_{13}H_{15}ClNO_2S$: 284.0512; found: 284.0505.

Ethyl 4-(4-Methoxyphenyl)-2-methyl-2,5-dihydrothiazole-2-carboxylate (3c)

Yield: 60%; yellow oil.

IR (KBr): 1732 (C=O), 1605 (C=N) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 6.8 Hz, 3 H, CH_3), 1.99 (s, 3 H, CH_3), 3.89 (s, 3 H, OCH_3), 4.16–4.30 (m, 2 H, CH_2), 4.44 (d, *J* = 15.2 Hz, 1 H, SCH_AH_B), 4.53 (d, *J* = 15.2 Hz, 1 H, SCH_AH_B), 6.96 (t, *J* = 8.8 Hz, 2 H, ArH), 7.88 (d, *J* = 8.8 Hz, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.8, 169.3, 162.2, 130.3 (2C), 125.8, 114.0 (2C), 88.8, 61.7, 55.4, 44.0, 27.5, 14.0.

HRMS: *m/z* [M + H]$^+$ calcd for $C_{14}H_{18}NO_3S$: 280.1007; found: 280.1001.

Ethyl 2-Methyl-4-(4-nitrophenyl)-2,5-dihydrothiazole-2-carboxylate (3d)

Yield: 50%; yellow solid; mp 71–73 °C.

IR (KBr): 1731 (C=O), 1639 (C=N) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.99 (s, 3 H, CH_3), 4.17–4.31 (m, 2 H, CH_2), 4.47 (d, *J* = 15.6 Hz, 1 H, SCH_AH_B), 4.55 (d, *J* = 15.6 Hz, 1 H, SCH_AH_B), 8.07 (d, *J* = 8.7 Hz, 2 H, ArH), 8.30 (d, *J* = 8.7 Hz, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0, 168.2, 149.5, 138.6, 129.6 (2C), 123.8 (2C), 89.0, 62.1, 44.1, 27.3, 14.0.

HRMS: *m/z* [M + H]$^+$ calcd for $C_{13}H_{15}N_2O_4S$: 295.0753; found: 295.0755.

Ethyl 2-Methyl-4-(3-nitrophenyl)-2,5-dihydrothiazole-2-carboxylate (3e)
Yield: 57%; yellow oil.

IR (KBr): 1734 (C=O), 1640 (C=N) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.99 (s, 3 H, CH_3), 4.18–4.28 (m, 2 H, CH_2), 4.49 (d, *J* = 15.5 Hz, 1 H, SCH_AH_B), 4.56 (d, *J* = 15.5 Hz, 1 H, SCH_AH_B), 7.65 (t, *J* = 8.0 Hz, 1 H, ArH), 8.26 (dt, *J* = 8.0, 0.8 Hz, 1 H, ArH), 8.36 (ddd, *J* = 8.0, 2.0, 0.8 Hz, 1 H, ArH), 8.71 (t, *J* = 2.0 Hz, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 168.0, 148.4, 134.7, 134.3, 129.8, 125.9, 123.5, 88.9, 62.1, 44.0, 27.3, 14.0.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{15}N_2O_4S$: 295.0753; found: 295.0741.

Ethyl 2-Methyl-4-(*p*-tolyl)-2,5-dihydrothiazole-2-carboxylate (3f)
Yield: 57%; yellow solid; mp 52–53 °C.

IR (KBr): 1739 (C=O), 1632 (C=N) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.26 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.96 (s, 3 H, CH_3), 2.40 (s, 3 H, CH_3), 4.15–4.25 (m, 2 H, CH_2), 4.42 (d, *J* = 15.6 Hz, 1 H, SCH_AH_B), 4.51 (d, *J* = 15.6 Hz, 1 H, SCH_AH_B), 7.24 (d, *J* = 8.4 Hz, 2 H, ArH), 7.77 (d, *J* = 8.4 Hz, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.7, 169.9, 141.9, 130.5, 129.4 (2C), 128.6 (2C), 88.9, 61.8, 44.2, 27.5, 21.5, 14.0.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{18}NO_2S$: 264.1058; found: 264.1034.

Ethyl 4-[4-(*tert*-Butyl)phenyl]-2-methyl-2,5-dihydrothiazole-2-carboxylate (3g)
Yield: 69%; yellow oil.

IR (KBr): 1735 (C=O), 1609 (C=N) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.26 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.34 [s, 9 H, $C(CH_3)_3$], 1.96 (s, 3 H, CH_3), 4.15–4.25 (m, 2 H, CH_2), 4.43 (d, *J* = 15.3 Hz, 1 H, SCH_AH_B), 4.53 (d, *J* = 15.3 Hz, 1 H, SCH_AH_B), 7.46 (d, *J* = 8.4 Hz, 2 H, ArH), 7.82 (d, *J* = 8.4 Hz, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.7, 169.8, 155.0, 130.4, 128.5 (2C), 125.6 (2C), 89.0, 61.7, 44.2, 35.0, 31.2 (3C), 27.5, 14.0.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{24}NO_2S$: 306.1528; found: 306.1515.

Ethyl 4-(4-Methoxy-3-nitrophenyl)-2-methyl-2,5-dihydrothiazole-2-carboxylate (3h)
Yield: 56%; yellow solid; mp 99–101 °C.

IR (KBr): 1739 (C=O), 1618 (C=N) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.96 (s, 3 H, CH_3), 4.03 (s, 3 H, OCH_3), 4.17–4.26 (m, 2 H, CH_2), 4.41 (d, *J* = 15.4 Hz, 1 H, SCH_AH_B), 4.49 (d, *J* = 15.4 Hz, 1 H, SCH_AH_B), 7.15 (d, *J* = 8.8 Hz, 1 H, ArH), 8.12 (dd, *J* = 8.8, 2.2 Hz, 1 H, ArH), 8.34 (d, *J* = 2.2 Hz, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.3, 167.4, 155.0, 139.5, 134.2, 126.0, 125.7, 113.5, 88.8, 62.0, 56.9, 43.8, 27.4, 14.0.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{17}N_2O_5S$: 325.0858; found: 325.0851.

Ethyl 4-(Furan-2-yl)-2-methyl-2,5-dihydrothiazole-2-carboxylate (3i)
Yield: 54%; yellow oil.

IR (KBr): 1733 (C=O), 1638 (C=N) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.97 (s, 3 H, CH_3), 4.13–4.28 (m, 2 H, CH_2), 4.35 (d, *J* = 15.4 Hz, 1 H, SCH_AH_B), 4.43 (d, *J* = 15.4 Hz, 1 H, SCH_AH_B), 6.54 (dd, *J* = 3.5, 1.5 Hz, 1 H, ArH), 6.99 (d, *J* = 3.5 Hz, 1 H, ArH), 7.59 (d, *J* = 1.5 Hz, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.4, 160.5, 148.3, 145.6, 115.2, 112.1, 88.9, 61.9, 43.4, 27.3, 14.0.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{14}NO_3S$: 240.0694; found: 240.0689.

(2*S*,5*R*)-Ethyl 5-Ethyl-2-methyl-4-phenyl-2,5-dihydrothiazole-2-carboxylate (3j$_{cis}$)
Yield: 27%; yellow oil.

IR (KBr): 1734 (C=O), 1633 (C=N) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.96 (t, *J* = 7.3 Hz, 3 H, CH_3), 1.29 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.64–1.75 (m, 1 H, SCH_AH_B), 1.90–1.99 (m, 1 H, SCH_AH_B), 1.96 (s, 3 H, CH_3), 4.16–4.30 (m, 2 H, CH_2), 5.01 (dd, *J* = 9.8, 3.0 Hz, 1 H, SCH), 7.42–7.48 (m, 3 H, ArH), 7.81 (d, *J* = 6.5 Hz, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.2, 171.9, 133.0, 130.6, 129.1 (2C), 128.8 (2C), 87.1, 62.6, 61.8, 28.6, 28.3, 14.0, 11.6.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{20}NO_2S$: 278.1215; found: 278.1208.

(2*S*,5*S*)-Ethyl 5-Ethyl-2-methyl-4-phenyl-2,5-dihydrothiazole-2-carboxylate (3j$_{trans}$)
Yield: 27%; yellow solid; mp 57–59 °C.

IR (KBr): 1735 (C=O), 1637 (C=N) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.96 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.26 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.61–1.72 (m, 1 H, SCH_AH_B), 1.88–2.04 (m, 1 H, SCH_AH_B), 1.95 (s, 3 H, CH_3), 4.15–4.26 (m, 2 H, CH_2), 5.07 (dd, *J* = 8.7, 3.2 Hz, 1 H, SCH), 7.42–7.48 (m, 3 H, ArH), 7.75 (d, *J* = 6.4 Hz, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.3, 172.0, 132.9, 130.8, 129.3 (2C), 128.9 (2C), 86.4, 63.3, 61.7, 28.9, 28.3, 14.0, 12.7.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{20}NO_2S$: 278.1215; found: 278.1210.

Preparation of (*E*)-*N*′-Benzylidene-2-methyl-4-phenyl-2,5-dihydrothiazole-2-carbohydrazide (5a); General Procedure
Ethyl 2-methyl-4-phenyl-2,5-dihydrothiazole-2-carboxylate (**3a**; 1 mmol) and absolute EtOH (25 mL) were added to a flask, then hydrazine hydrate (5 mL) was added and the mixture was stirred and heated to reflux under N_2 (the reaction was monitored by TLC). Upon completion, the mixture was concentrated under reduced pressure, deionized H_2O (10 mL) was added and the aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and evaporated. The equivalent amount of benzaldehyde (1 mmol) and EtOH (20 mL) were added to the residue, and the mixture was heated to reflux for 4 h. The mixture was concentrated to remove a portion of EtOH under reduced pressure, then the mixture was kept overnight and the formed solid was collected by filtration and washed with EtOH to obtain the product **5a**. A sample for X-ray analysis was prepared by evaporating a solution of **5a** in EtOH.

(*E*)-*N*′-Benzylidene-2-methyl-4-phenyl-2,5-dihydrothiazole-2-carbohydrazide (5a)
Yield: 56%; yellow solid; mp 212–214 °C.

IR (KBr): 3225 (NH), 1677 (C=O), 1638 (C=N) cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 1.82 (s, 3 H, CH_3), 4.58 (d, *J* = 16.2 Hz, 1 H, SCH_AH_B), 4.64 (d, *J* = 16.2 Hz, 1 H, SCH_AH_B), 7.43–7.46 (m, 3 H, ArH), 7.51–7.60 (m, 3 H, ArH), 7.66–7.69 (m, 2 H,

ArH), 8.05 (d, *J* = 7.7 Hz, 2 H, ArH), 8.47 (s, 1 H, =CH), 10.68 (s, 1 H, NH).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 170.4, 168.0, 149.3, 134.1, 132.8, 131.5, 130.1, 128.9 (2C), 128.7 (2C), 128.4 (2C), 127.0 (2C), 90.8, 42.2, 29.5.

HRMS: *m/z* [M + H]$^+$ calcd for $C_{18}H_{18}N_3OS$: 324.1171; found: 324.1168.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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