CONVENIENT SYNTHESIS OF 2,3-DIHYDRO-1,2,4-THIADIAZOLES, 4,5-DIHYDRO-1,3-THIAZOLES, AND 1,3-THIAZOLES THROUGH A [4+1]-TYPE OXIDATIVE RING CLOSURE OF 1,3-THIAZA-1,3-BUTADIENES

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Abstract – 1,3-Thiaza-1,3-butadienes bearing an N,N-dimethylamino group at the C-2 position were efficiently converted into 5H-1,2,4-oxathiazoles, 2,3-dihydro-1,2,4-thiadiazoles, 4,5-dihydro-1,3-thioazoles, and 1,3-thiazoles through an oxidative ring closure by treating with mCPBA, chloramine-T, metal carbenoids, or dichlorocarbene, respectively, via the ring closure of in situ generated heterocumulene-type reactive species involving thione S-oxides, thione S-imides, and thiocarbonyl ylides.

INTRODUCTION

Recently, sulfur- and nitrogen-containing five-membered heterocyclic ring systems are widely recognized as important ring systems of a variety of biologically-active natural products such as bacteriocides, fungicides, herbicides, and antibiotics, and numerous preparative methods for these compounds have been reported to date. However, in contrast to the preparation of 3,5-disubstituted 1,2,4-thiadiazole derivatives bearing the same substituents through oxidative dimerization of primary thioamides, syntheses of 1,2,4-thiadiazoles and 1,3-thiazoles bearing different substituents was not simple due to the requirement of regioselectivity in the formal [3+2] coupling, formal [4+1] coupling, or ring closure of some nonsymmetrical precursors in the key steps. The divergent synthetic utility of 1,3-chalcogenaza-1,3-butadienes as the four-atom building blocks of a variety of sulfur- and nitrogen-containing heterocyclic ring systems has been widely recognized along with the progress in the chemistry of 1,3-thiaza-1,3-butadienes during these decades, and, recently, much interest have been focused onto their oxidized variants in the light of their functionalized heterocumulene-like structures and
the potential reactivity as the new versatile building blocks of such five-membered heterocycles. However, in spite of the wide synthetic potentiality of these compounds originated from their characteristic structures bearing the nucleophile-sensitive and electrophile-sensitive moieties in one molecules, only limited studies on the [4+1]-type oxidative ring closure of 1,3-thiaza-1,3-butadienes have been carried out to date.\(^4\)

In the course of the studies on chalcogenocarbonyl functionalities connecting with \(\pi\)-conjugation systems, limited studies on the convenient routes for the generation of 1,3-thiaza-1,3-butadienes \(A\) have been carried out only through thermal cycloreversion of \(6H\)-1,3,5-oxathiazines, and we also reported the extension of the methodology to their oxidized variants, such as 1,3-thiaza-1,3-butadiene \(S\)-oxides and 1,3-thiaza-1,3-butadiene \(S\)-sulfides, for the synthesis of \(5H\)-1,2,4-oxathiazoles and \(3H\)-1,2,4-dithiazoles, respectively.\(^5\) These successful results urged us to the \textit{in situ} generation and of other oxidized variants of 1,3-thiaza-1,3-butadienes by using the same methodology in the light of the synthetic utilities of such compounds as the building blocks of a variety of heterocycles. However, \(6H\)-1,3,5-oxathiazines were unreactive toward chloramine-T, carbenes, and metal carbenoids in contrast to \(m\)CPBA, and several attempts for generation of 1,3-thiaza-1,3-butadiene \(S\)-imides and \(S\)-ylides through the retro [4+2]-type methodology from \(6H\)-1,3,5-oxathiazine derivatives afforded the unsuccessful results in all cases. In order to realize a new synthesis of 2,3-dihydro-1,2,4-thiadiazoles and 5,6-dihydro-1,3-thiazoles by using a similar [4+1]-type protocol to our previous results, we just had an expectation that the use of isolable 1,3-thiaza-1,3-butadienes \(A\) would enable us to realize the methodology. Our previous findings on the conversion of \(6H\)-1,3,5-oxathiazines into \(5H\)-1,2,4-oxathiazoles and \(3H\)-1,2,4-dithiazoles also supported us to generation and the subsequent ring closure of intermediary oxidized variants \(B\) from 1,3-thiaza-1,3-butadienes \(A\) bearing a highly reactive thiocarbonyl functionality as the new precursors of five-membered ring heterocycles \(C\). In this paper, we report a preparation of 1,3-thiaza-1,3-butadienes and the subsequent [4+1]-type coupling reactions by the treatment of various oxidizing agents toward the sulfur atom of the heterodiienes to form 2,3-dihydro-1,2,4-thiadiazoles, 4,5-dihydro-1,3-thiazoles, and 1,3-thiazoles.
RESULTS AND DISCUSSION

\(N,N\)-Dimethylthiourea (1, \(R^1 = \text{NMe}_2\)), prepared from \(N,N\)-dimethylcyanamide and \(\text{H}_2\text{S}\) gas, was treated with pivalaldehyde (3a) and \(\text{BF}_3\cdot\text{OEt}_2\) to afford the corresponding heterodiene 5a bearing an \(N,N\)-dimethylamino group at the C-2 position in high yield. Product 5a was stable enough toward the exposure to air and sunlight, but was unstable toward the contact with silica gel. A similar reaction of 1 with aromatic aldehydes 3b-e also afforded the corresponding heterodienes 5b-e in moderate yields, and the use of aliphatic aldehydes, such as 2-methylpropanal and cyclohexanecarbaldehyde, as the substrates, in turn, resulted in the formation of complex mixture. Therefore, it is assumed that the stability of the heterodienes would be affected by the steric bulkiness and/or the aromatic stabilization of substituent \(R^2\).

Heterodienes, 5f (\((N'\text{-dimethylaminothiocarbamoyl})-N,N\)-dimethylformamidine, \(R^1 = R^2 = \text{NMe}_2\)) and 6 (\((N'\text{-thiobenzoyl})-N,N\)-dimethylformamidine, \(R^1 = \text{C}_6\text{H}_5\), \(R^2 = \text{NMe}_2\)), both bearing an \(N,N\)-dimethylamino group at the C-4 position, were also synthesized by treating compound 1 or thiobenzamide (2) with \(N,N\)-dimethylformamide dimethyl acetal (4) according to the reported methods. All the results of the reactions of 1 with aldehydes 2a-e are summarized in Table 1.

Table 1. Preparation of 1,3-Thiaza-1,3-butadienes 5 and 6 bearing an \(N,N\)-Dimethylamino Group at the C-2 or C-4 Position

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Reagent</th>
<th>Lewis Acid</th>
<th>Temp</th>
<th>Time</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>(R^1)</td>
<td>(R^2)</td>
<td>3 or 4 (mol amt.)</td>
<td>(mol amt.)</td>
<td>(^{\circ}\text{C})</td>
<td>h</td>
</tr>
<tr>
<td>NMe$_2$</td>
<td>1</td>
<td>(t)-C$_8$H$_9$</td>
<td>3a (4.0)</td>
<td>BF$_3$•OEt$_2$ (3.2)</td>
<td>0</td>
</tr>
<tr>
<td>NMe$_2$</td>
<td>1</td>
<td>t-C$_8$H$_9$</td>
<td>3a (4.0)</td>
<td>SnCl$_4$ (2.5)</td>
<td>0</td>
</tr>
<tr>
<td>NMe$_2$</td>
<td>1</td>
<td>C$_6$H$_5$</td>
<td>3b (4.0)</td>
<td>BF$_3$•OEt$_2$ (4.0)</td>
<td>0</td>
</tr>
<tr>
<td>NMe$_2$</td>
<td>1</td>
<td>(p)-ClC$_6$H$_4$</td>
<td>3c (2.0)</td>
<td>BF$_3$•OEt$_2$ (4.0)</td>
<td>0</td>
</tr>
<tr>
<td>NMe$_2$</td>
<td>1</td>
<td>C$_6$H$_5$CH=CH</td>
<td>3d (2.0)</td>
<td>BF$_3$•OEt$_2$ (2.5)</td>
<td>rt</td>
</tr>
<tr>
<td>NMe$_2$</td>
<td>1</td>
<td>Mes</td>
<td>3e (2.0)</td>
<td>BF$_3$•OEt$_2$ (1.8)</td>
<td>0</td>
</tr>
<tr>
<td>NMe$_2$</td>
<td>1</td>
<td>NMMe$_2$</td>
<td>4 (2.5)</td>
<td>-</td>
<td>reflux</td>
</tr>
<tr>
<td>C$_6$H$_5$</td>
<td>2</td>
<td>NMe$_2$</td>
<td>4 (2.0)</td>
<td>-</td>
<td>rt</td>
</tr>
</tbody>
</table>

$^a$Isolated yields.

Heating of 5a or 5b in an ethanolic media afforded the corresponding 1,4-adducts 7a or 7b, respectively. In contrast, a similar heating of 5f or 6 in ethanol only gave the recovery of substrates. These results suggested that the electron-donating \(N,N\)-dimethylamino group bound to the C-4 position of heterodienes
5f and 6 affects the lowering of the reactivity toward the nucleophilic attack at the C-4 position. Similar heating of a toluene solution of 5a and dienophiles 8 under refluxing temperature also afforded the corresponding [4+2] cycloadducts 9a-11a in high yields, and these results indicated that heterodiienes 5 shows the similar reactivity to that of the previously reported 1,3-thiaza-1,3-butadienes. Interestingly, thermal reaction of 5f in the presence of methyl propiolate (8a) afforded thienamid 12 in 27% yield via a plausible pathway involving cycloaddition of 5f and 8a and the subsequent hydrolytic ring cleavage of the intermediary [4+2] cycloadduct. All results are summarized in Scheme 1 and Scheme 2.

Scheme 1. Reaction of 1,3-Thiaza-1,3-butadienes 5a, b with Ethanol or Acetylenic Dienophiles 8

Scheme 2. Reaction of 1,3-Thiaza-1,3-butadiene 5f with Ethanol or Methyl Propiolate (8a)

When a CHCl3 solution of 1,3-thiaza-1,3-butadiene 5a (R1 = NMe2, R2 = t-C4H9) was treated with mCPBA (1.5 mol amt.) at 0°C, 5H-1,2,4-oxathiazoles 13a was obtained in moderate yields in a similar manner to our previous cases starting from mCPBA oxidation of 6H-1,3,5-oxathiazine derivatives. On the other hand, a similar mCPBA oxidation of 5b or 5c resulted in the formation of complex mixture, and the intermediary thione S-oxides (sulfines) were not detected through NMR monitoring of the reaction of 5a and mCPBA in an NMR tube at all. Standing of 13a under an aerobic condition at rt for a long time also caused gradual decomposition to afford the complex mixture containing pivalaldehyde (3a), N,N-dimethylthiourea (1), and a trace amount of 1,2,4-thiadiazole 14 bearing two N,N-dimethylamino
groups at the C-3 and C-5 positions.\textsuperscript{10} Compound 1 was assumed to be formed from 13\texttext{a} through oxidative S-O bond cleavage and the subsequent hydrolytic cleavage, and compound 14 was recognized to be an oxidative dimerization product from thiourea 1.\textsuperscript{2} Therefore, it is assumed that these results supported the structure of the compound to be 5\texttext{H}-1,2,4-oxathiazole ring arrangement of sulfur and oxygen atoms in the ring system of the product and the alternative pathway involving the formation of oxathiirane intermediate to form 3\texttext{H}-1,2,4-oxathiazole ring was excluded.\textsuperscript{11}

A similar treatment of a CHCl\texttext{3} solution of 5\texttext{a-e} with chloramine-T (1.5 mol amt.) at 0 °C to rt for 24-48 h afforded 2,3-dihydro-1,2,4-thiadiazoles 15\texttext{a-e} in moderate to high yields as sole products, and in these cases any other byproducts assignable to thione S-imides were not found at all in the crude mixture.\textsuperscript{12} All physical and spectral data of 15\texttext{a-e} involving MS, IR, \texttext{1}H NMR, and \texttext{13}C NMR spectra, as well as the elemental analysis data, were fully consistent with the desired 2,3-dihydro-1,2,4-thiadiazole derivatives. On the other hand, 5\texttext{f} was unreactive to chloramine-T, and a similar treatment of isomeric heterodiene 6 (R\texttext{1} = C\texttext{6}H\texttext{5}, R\texttext{2} = NMe\texttext{2}) with chloramine-T just afforded 1,3-diazadiene 16 in 46% yield along with the formation of elemental sulfur. All the results of the reactions of 1,3-thiaza-1,3-butadienes 5 and 6 with chloramine-T are summarized in Table 2. Especially, standing of 13\texttext{a} and 15\texttext{e} under an aerobic exposure at rt for a long time caused gradual decomposition to afford the complex mixture containing aldehyde 3\texttext{a} or 3\texttext{e}, N,N-dimethylthiourea (1), and a trace amount of 1,2,4-thiadiazole 14 as shown in Scheme 3. It is assumed that these products were also formed through hydrolytic cleavage of 15, and, therefore, the isomeric structure of these compounds, as 4,5-dihydro-1,2,4-thiadiazole ring system, was excluded through these results.

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Oxidizing Agent</th>
<th>Solvent</th>
<th>Temp / °C</th>
<th>Time / h</th>
<th>Yield / %</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>mCPBA (1.5)</td>
<td>CHCl\texttext{3}</td>
<td>rt</td>
<td>48</td>
<td>56 (13\texttext{a})</td>
<td>0</td>
</tr>
<tr>
<td>5b</td>
<td>mCPBA (1.5)</td>
<td>CHCl\texttext{3}</td>
<td>0</td>
<td>5</td>
<td>complex mixture</td>
<td>0</td>
</tr>
<tr>
<td>5c</td>
<td>mCPBA (1.5)</td>
<td>CHCl\texttext{3}</td>
<td>0</td>
<td>5</td>
<td>complex mixture</td>
<td>0</td>
</tr>
<tr>
<td>5a</td>
<td>Chloramine-T (1.5)</td>
<td>CHCl\texttext{3}</td>
<td>0</td>
<td>48</td>
<td>47 (15\texttext{a})</td>
<td>0</td>
</tr>
<tr>
<td>5a</td>
<td>Chloramine-T (1.5)</td>
<td>CHCl\texttext{3}</td>
<td>rt</td>
<td>48</td>
<td>56 (15\texttext{a})</td>
<td>0</td>
</tr>
<tr>
<td>5b</td>
<td>Chloramine-T (1.5)</td>
<td>CHCl\texttext{3}</td>
<td>rt</td>
<td>24</td>
<td>63 (15\texttext{b})</td>
<td>0</td>
</tr>
<tr>
<td>5c</td>
<td>Chloramine-T (1.5)</td>
<td>CHCl\texttext{3}</td>
<td>rt</td>
<td>24</td>
<td>52 (15\texttext{c})</td>
<td>0</td>
</tr>
<tr>
<td>5d</td>
<td>Chloramine-T (1.5)</td>
<td>CHCl\texttext{3}</td>
<td>rt</td>
<td>48</td>
<td>72 (15\texttext{d})</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Chloramine-T (1.5)</td>
<td>CHCl₃</td>
<td>rt</td>
<td>24</td>
<td>53 (15e)</td>
<td>0</td>
</tr>
<tr>
<td>---</td>
<td>--------------------</td>
<td>-------</td>
<td>-----</td>
<td>-----</td>
<td>----------</td>
<td>-----</td>
</tr>
<tr>
<td>5e</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>5f</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>6</td>
<td>Chloramine-T (1.5)</td>
<td>CHCl₃</td>
<td>rt</td>
<td>48</td>
<td>0</td>
<td>46</td>
</tr>
</tbody>
</table>

*Isolated yields. *Commercially available mCPBA containing 30% water was used.

Scheme 3. Standing of 13a and 15e under an Aerobic Condition

Subsequently, direct observation of reactive intermediates of the reaction of the heterodiienes with chloramine-T was attempted. When a CDCl₃ solution of heterodiene 5a (R¹ = NMe₂, R² = t-C₄H₉) was treated with chloramine-T (1.5 mol amt.) in an NMR tube and the reaction was monitored by measuring ¹H NMR spectra of the reaction mixture at room temperature, only the ¹H NMR signals of substrate 5a, chloramine-T, and the product 15a revealed as soon as adding chloramine-T to the solution, and no signals assignable to 1,3-thiaza-1,3-butadiene S-imide B (X = NTs) were observed in the ¹H NMR spectra at all both in the case of a short reaction time and the case of a prolonged reaction time. These results suggested that intermediary 1,3-thiaza-1,3-butadiene S-imides B (X = NTs) underwent facile ring closure to form 15 through the nucleophilic attack of the nitrogen atom of the intermediates onto the C-4 position of the heterodiienes as shown in Scheme 4. In contrast, a similar treatment of isomeric heterodiene 6 (R¹ = C₆H₅, R² = NMe₂) with chloramine-T just afforded 1,3-diazadiene 16 in 46% yield along with the formation of elemental sulfur, and ring closure product 15 was not found at all in the crude products. This result indicated that compound 16 was formed through sulfonylimidation of 1,3-thiaza-1,3-butadienes primarily at the sulfur atom of heterodiene 6 forming 1,3-thiaza-1,3-butadiene S-imide B (X = NTs) and the subsequent ring closure of B and the final extrusion of elemental sulfur from the thiaziridine intermediate D as shown in Scheme 4. The lack of ring closure products in this case was explained by the low feasibility of the C-4 position of the heterodiienes bearing an N,N-dimethylamino group at the C-4 position of 6 toward the intramolecular nucleophilic attack of the nitrogen atom due to the
electron-donating character of the \textit{N},\textit{N}-dimethylamino group bound directly onto the azomethine carbon of the heterodiienes.

**Scheme 4.** Plausible Pathways for the Formation of Compounds 15 and 16 through the Reaction of Heterodiienes 5 or 6 with Chloramine-T

A similar treatment of a CH$_2$Cl$_2$ solution of heterodiienes 5a or 5e with ethyl diazoacetate (17, 1.5 mol amt.) in the presence of Cu$_2$Cl$_2$ (1.5 mol amt.) or Rh$_2$(OAc)$_4$ (0.01 mol amt.) at rt afforded \textit{cis/trans} mixtures of 4,5-dihydro-1,3-thiazoles 18 bearing an ester moiety at the C-5 position and 1,3-thiazoles 19a or 19e, respectively, in moderate yields. The \textit{trans} stereochemistry of 18a and 18e between the \textit{t}-butyl or mesityl goup on the C-4 and the ester moiety at the C-5 position was confirmed by using an NOE experiment of the compounds, and, for instance, the 7% NOE was observed between the \textit{t}-butyl group at the C-4 position and the methane proton at the C-5 position in the case of \textit{trans}-18a. It is assumed that the predominant formation of \textit{trans}-18 would be rationalized by the plausible pathway involving more favorable transition state E with a less steric repulsion of the substituents in the stage of ring closure of intermediary thiocarbonyl ylide B formed through the reaction of 5 with ethyl diazoacetate (17) and Rh$_2$(OAc)$_4$ as shown in Scheme 5. In addition, it is worth noting that neither isomeric heterocyclic compounds nor acyclic isomeric products or desulfurized olefinic products were found at all in the crude products. All the results of the synthesis of 4,5-dihydro-1,3-thiazoles 18 and 1,3-thiazoles 19 are shown in Table 3. Dehydrogenation of a \textit{cis/trans} mixture of 18e was also achieved efficiently by treating with DDQ (2.0 mol amt.) to give thiazole 19e in 65% yield as a sole product as shown in Scheme 6. Furthermore, ethyl ester 19b (R$^2$ = C$_6$H$_5$, R$^3$ = CO$_2$Et) was hydrolyzed through a usual manner to give the corresponding free carboxylic acid. In contrast, a similar treatment of heterodiene 6 (R$^1$ = C$_6$H$_5$, R$^2$ = NMe$_2$) with ethyl diazoacetate and Cu$_2$Cl$_2$ just resulted in the formation of a complex mixture.
Table 3. Synthesis of 4,5-Dihydro-1,3-thiazoles 18 and 1,3-Thiazoles 19 through the Reaction of 1,3-Thiaza-1,3-butadienes 5 with Metal Carbenoids

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Catalyst</th>
<th>Temp</th>
<th>Time</th>
<th>Yield / %</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>R²</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>t-C₄H₉</td>
<td>CuCl₂ (1.5)</td>
<td>rt</td>
<td>48</td>
<td>45 (18a)</td>
<td>0</td>
</tr>
<tr>
<td>t-C₄H₉</td>
<td>Rh₂(OAc)₄ (0.01)</td>
<td>rt</td>
<td>120</td>
<td>63 (18a)</td>
<td>0</td>
</tr>
<tr>
<td>C₆H₅</td>
<td>CuCl₂ (1.5)</td>
<td>rt</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>C₆H₅</td>
<td>Rh₂(OAc)₄ (0.01)</td>
<td>rt</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mes</td>
<td>CuCl₂ (2.0)</td>
<td>rt</td>
<td>36</td>
<td>27 (18e)</td>
<td>6 (18e)</td>
</tr>
<tr>
<td>NMe₂</td>
<td>CuCl₂ (2.0)</td>
<td>reflux</td>
<td>48</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

¹Isolated yields. ²The relative stereochemistry of trans-18 and cis-18 concerning the substituents of the C-4 and C-5 positions was confirmed through the NOE experiments. ³A complex mixture was obtained. ⁴Compound 19f (R² = H) was obtained.

Scheme 5. Plausible Pathway for the Ring Closure of Thiocarbonyl Ylides B (X = CHCO₂Et)

Scheme 6. Dehydrogenation of 18e to form 1,3-Thiazole 19e

When a hexane solution of 5a or 5e was treated with CHCl₃ (10.0 mol amt.) and then with potassium t-butoxide (5.0 mol amt.) at 0 °C for several hours, the corresponding 1,3-thiazoles 20a (Y = Cl) and 20e (Y = Cl) were afforded beside aldehydes 3a and 3e, respectively, among several uncharacterized byproducts. However, in spite of the efforts of optimization of the experimental procedures and reaction conditions, the yields of compounds 20 remained in a moderate level, and neither the recovered substrates 5 nor the precursory 5,5-dichloro-4,5-dihydro-1,3-thiazole (F) was not found in the crude mixture in all
cases. 5-Chloro-1,3-thiazoles 20 were assumed to form through a plausible pathway involving the ring closure of \textit{in situ} generation of thiocarbonyl ylides B\textsuperscript{15f,18} and the subsequent dehydrochlorination of ring closure product F under a basic condition as shown in Scheme 7. In contrast, a similar treatment of 5e with CHBr\textsubscript{3} in place of CHCl\textsubscript{3} at 0 °C or -78 °C only afforded aldehyde 3e or a complex mixture, and 5-bromo-1,3-thiazole 21e (Y = Br) was not found at all in the crude reaction mixture. All the results of the reaction of 1,3-thiaza-1,3-butadienes 5 with \textit{in situ} generated dichlorocarbene forming 5-chloro-1,3-thiazoles 20 are shown in Table 4. Alternative attempts for the conversion of 5e into 5-phenyl-1,3-thiazoles by treating with benzal chloride (C\textsubscript{6}H\textsubscript{5}CHCl\textsubscript{2}) and potassium t-butoxide in a similar manner just resulted in the formation of aldehyde 3e in all cases.

Table 4. Reaction of 1,3-Thiaza-1,3-butadienes 5 with \textit{in situ} Generated Dihalocarbenes

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Haloform</th>
<th>Temp / °C</th>
<th>Time / h</th>
<th>Yield / %a</th>
</tr>
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<tbody>
<tr>
<td>(t\text{-C}_\text{4}H_9)</td>
<td>5a</td>
<td>Cl</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Mes</td>
<td>5e</td>
<td>Cl</td>
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</tr>
<tr>
<td>Mes</td>
<td>5e</td>
<td>Br</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Mes</td>
<td>5e</td>
<td>Br</td>
<td>-78</td>
<td>3</td>
</tr>
</tbody>
</table>

\(a\) Isolated yields.

**Scheme 7.** Plausible Pathway for the Formation of 5-Chloro-1,3-thiazoles 20

**CONCLUSION**

In conclusion, we found a generation and the subsequent facile ring closure of novel heterocumulene-type oxidized variants of 1,3-thiaza-1,3-butadienes 5 to afford \(5H\)-1,2,4-oxathiazoles, 2,3-dihydro-1,2,4-thiadiazoles, 4,5-dihydro-1,3-thiazoles, and 1,3-thiazoles. It is recognized that these methodology afford a new and convenient synthetic protocol for the short step synthesis of naturally occurring and biologically active 1,3-thiazole derivatives. Further attempts for the conversion of the products of oxidative ring closure of 1,3-thiaza-1,3-butadienes 5 into various pharmaceutically active compounds are expected in our laboratory.
EXPERIMENTAL SECTION

Instruments:
The melting points were determined with a Barnstead International MEL-TEMP, and were uncorrected.

\(^1\)H NMR spectra were recorded on a Bruker DRX 400-P spectrometer (400 MHz), and the chemical shifts of the \(^1\)H NMR spectra are given in δ relative to internal tetramethylsilane (TMS). \(^{13}\)C NMR spectra were recorded using a Bruker DRX-400P (101 MHz). Mass spectra were recorded on a JEOL JMS-700T mass spectrometer with electron-impact ionization or electrospray ionization. High resolution mass spectra (HRMS) were also recorded on a JEOL JMS-700T spectrometer. IR spectra were measured as thin-film (neat) or KBr disks on a JASCO FT/IR-7300 spectrometer. Elemental analyses were performed using a Yanagimoto CHN corder MT-5.

Starting Materials. Column chromatography was performed using silica gel (Merck, Cat. No. 7734 or 9385) without pretreatment. Dichloromethane (CH\(_2\)Cl\(_2\)) and chloroform (CHCl\(_3\)) were dried over P\(_4\)O\(_{10}\) and were freshly distilled before use. Hexane, benzene, toluene, and EtOAc were dried over CaH\(_2\) and were freshly distilled before use. Ethanol was dried over MgO and was freshly distilled before use. All substrates and reagents including pivalaldehyde, benzaldehyde, p-chlorobenzaldehyde, 2,4,6-trimethylbenzaldehyde, cinnamaldehyde, thiobenzamide, triethylamine, boron trifluoride diethyl ether complex (BF\(_3\)•OEt\(_2\)), iron sulfide (Fe(II)S), hydrochloric acid, N,N-dimethylcyanamide, N,N-dimethylformamide dimethyl acetal, m-chloroperbenzoic acid (mCPBA, 70%), chloramine-T, elemental sulfur, ethyl diazoacetate (15% toluene solution), methyl propiolate, dimethyl acetylenedicarboxylate (DMAD), copper(I) chloride (Cu\(_2\)Cl\(_2\)), rhodium acetate (Rh\(_2\)(OAc)\(_4\)), 2,3-dichloro-2,3-dicyano-1,4-benzoquinone (DDQ), benzal chloride, potassium \(t\)-butoxide (\(t\)-C\(_4\)H\(_9\)OK), and anhydrous sodium sulfate powder (Na\(_2\)SO\(_4\)) were commercially available reagent grade and were used without any pretreatment.

A Typical Procedure for the Preparation of 1,3-Thiaza-1,3-butadienes 5. A dry CHCl\(_3\) solution of N,N-dimethylthiourea 1 (80 mg, 0.77 mmol) was treated with pivalaldehyde (3a, 190 mg, 4.0 mol amt.) and boron trifluoride diethyl ether complex (BF\(_3\)•OEt\(_2\)) (350 mg, 3.2 mol amt.) at rt for 12 h. The reaction was quenched by addition of an aqueous NaHCO\(_3\) solution, and the reaction mixture was extracted with CHCl\(_3\). The organic layer was dried over anhydrous Na\(_2\)SO\(_4\) powder, and then the organic solvent was evaporated in vacuo to obtain 1,3-thiaza-1,3-butadiene 5a (R\(^1\) = NMe\(_2\), R\(^2\) = \(t\)-C\(_4\)H\(_9\), 276 mg, 93% yield) as yellow oil.

5a (R\(^1\) = NMe\(_2\), R\(^2\) = \(t\)-C\(_4\)H\(_9\)): Yellow oil, MS (m/z) 172 (M\(^+\); 45%), 140 (M\(^+\)-S; 5%), 115 (M\(^+\)-\(t\)-C\(_4\)H\(_9\); 13%), 89 (Me\(_2\)NCS+1; bp), 44 (NMe\(_2\); 95%); IR (neat) 2961, 2934, 2868, 1658, 1526, 1125 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) δ 1.15 (9H, s), 3.25 (3H, s), 3.47 (3H, s), 8.19 (1H, s); \(^{13}\)C NMR (CDCl\(_3\)) δ 26.2 (q), 37.1
Anal. Calcd for C₈H₁₆N₂S: C, 54.30; H, 9.85, N, 12.76%. Found: C, 54.18; H, 9.75; N, 12.83%.

5b (R¹ = NMe₂, R² = C₆H₅): Orange oil; MS (m/z) 192 (M⁺; bp), 148 (M⁺-NMe₂; 28%), 89 (Me₂NCS+1; 47%); IR (neat) 2931, 1630, 1522, 759, 692 cm⁻¹; ¹H NMR (CDCl₃) δ 3.38 (3H, s), 3.55 (3H, s), 7.48 (2H, br. t, J = 7.4 Hz), 7.55 (1H, br. t, J = 7.4 Hz), 7.90 (2H, br. t, J = 7.4 Hz), 8.99 (1H, s); ¹³C NMR (CDCl₃) δ 40.3 (q), 43.7 (q), 128.9 (d), 130.2 (d), 133.1 (d), 134.6 (s), 165.6 (d), 193.6 (s). HRMS Calcd for C₁₀H₁₂N₂S: m/z 192.0721. Found: m/z 192.0715.

5c (R¹ = NMe₂, R² = p-ClC₆H₄): Orange oil; MS (m/z) 226 (M⁺; bp), 89 (Me₂NCS+1; 68%); IR (neat) 3164, 2924, 1623, 1527, 1398, 1269, 1087, 864, 725 cm⁻¹; ¹H NMR (CDCl₃) δ 3.38 (3H, s), 3.55 (3H, s), 7.55 (2H, d, J = 8.4 Hz), 7.85 (2H, d, J = 8.4 Hz), 8.96 (1H, s); ¹³C NMR (CDCl₃) δ 40.3 (q), 43.7 (q), 129.3 (d), 131.3 (d), 133.1 (s), 139.3 (s), 164.4 (d), 192.5 (s). HRMS Calcd for C₁₀H₁₁N₂SCl: m/z 226.0331. Found: m/z 226.0329.

5d (R¹ = NMe₂, R² = C₆H₅CH=CH): Orange oil; MS (m/z) 218 (M⁺; bp), 115 (M⁺-C₆H₅CH=CH; 28%), 89 (Me₂NCS+1; 81%); IR (neat) 2927, 1674, 1615, 1525, 1274, 1122, 759, 694 cm⁻¹; ¹H NMR (CDCl₃) δ 3.34 (3H, s), 3.52 (3H, s), 7.01 (1H, dd, J = 16.0, 9.6 Hz), 7.36 (1H, d, J = 16.0 Hz), 7.38-7.45 (3H, m), 7.54-7.58 (2H, m), 8.78 (1H, br. d, J = 9.6 Hz); ¹³C NMR (CDCl₃) δ 39.1 (q), 42.6 (q), 127.0 (d), 128.0 (d), 129.4 (d), 148.0 (d), 151.8 (d), 164.4 (d), 192.5 (s). HRMS Calcd for C₁₂H₁₄N₂S: m/z 218.0878. Found: m/z 218.0877.

5e (R¹ = NMe₂, R² = Mes): Yellow oil; MS (m/z) 234 (M⁺; bp), 146 (MesCNH; 57%), 89 (Me₂NCS+1; 68%); IR (neat) 2923, 1606, 1518, 1454, 1387, 1274, 1115 cm⁻¹; ¹H NMR (CDCl₃) δ 2.24 (3H, s), 2.51 (6H, s), 3.30 (3H, s), 3.48 (3H, s), 6.84 (2H, s), 9.45 (1H, s); ¹³C NMR (CDCl₃) δ 20.4 (q), 20.9 (q), 34.0 (q), 45.8 (q), 130.3 (d), 140.3 (s), 165.3 (d), 193.4 (s). HRMS Calcd for C₁₃H₁₈N₂S: m/z 234.1191. Found: m/z 234.1183.

A Typical Procedure for the Reaction of 1,3-Thiaza-1,3-butadienes 5 with Ethanol. An ethanolic solution of 1,3-thiaza-1,3-butadiene 5a (R¹ = NMe₂, R² = t-C₄H₉, 86 mg, 0.50 mmol) was heated under refluxing temperature for 5 h. The reaction mixture was cooled and the solvent was evaporated in vacuo. The crude mixture was separated by using chromatography on silica gel to obtain compound 7a (21 mg, 24% yield) as yellow oil.
182.4 (s). Anal. Calcd for C_{10}H_{22}N_{2}O_{3}S: C, 55.00; H, 10.16; N, 12.83%. Found: C, 54.56; H, 10.33; N, 12.60%.

**7b** (R^1 = NMe_2, R^2 = C_6H_5): Yellow oil; IR (neat) 2960, 1526, 1370, 1116, 1069 cm\(^{-1}\); \(^1\)H NMR (CDCl_3) \(\delta\) 1.21 (3H, t, J = 7.0 Hz), 3.29 (6H, s), 3.72 (1H, dq, J = 10.0, 7.0 Hz), 3.86 (1H, dq, J = 10.0, 7.0 Hz), 5.80 (1H, d, J = 8.5 Hz), 6.94 (1H, d, J = 8.5 Hz), 7.30-7.40 (2H, m), 7.40-7.60 (3H, m); \(^{13}\)C NMR (CDCl_3) \(\delta\) 15.2 (q), 40.3 (q), 43.7 (q), 64.1 (t), 85.8 (d), 126.0 (d), 128.3 (d), 130.2 (d), 140.1 (s), 181.7 (s). Anal. Calcd for C_{12}H_{18}N_{2}O_{3}S: C, 60.47; H, 7.61; N, 11.75%. Found: C, 60.01; H, 7.46; N, 11.64%.

**A Typical Procedure for the Reaction of 1,3-Thiaza-1,3-butenediene 3 with an Acetylenic Dienophile.**

A toluene solution of 1,3-thiaza-1,3-butenediene 3a (R^1 = NMe_2, R^2 = t-C\(_4\)H\(_9\), 90 mg, 0.52 mmol) was treated with methyl propiolate (8a, R^3 = H, 132 mg, 1.57 mmol, 3.0 mol amt.) under refluxing temperature for 1 h. The reaction mixture was cooled and the solvent was evaporated in vacuo. The crude mixture was separated by using chromatography on silica gel to obtain [4+2] cycloadduct 9a (93 mg, 71% yield) as yellow oil.

**9a** (R^1 = NMe_2, R^2 = t-C\(_4\)H\(_9\), R^3 = H, R^4 = CO_2Me): Yellow oil; MS (m/z) 257 (M^+1; bp), 199 (M^+-C\(_4\)H\(_9\); 1%); IR (neat) 2951, 2374, 1702, 1632, 1593, 1327, 1195 cm\(^{-1}\); \(^1\)H NMR (CDCl_3) \(\delta\) 0.94 (9H, s), 3.01 (6H, s), 3.74 (3H, s), 4.66 (1H, s), 5.97 (1H, s); \(^{13}\)C NMR (CDCl_3) \(\delta\) 26.4 (q), 36.3 (q), 39.5 (q), 51.6 (q), 87.9 (d), 108.9 (d), 159.4 (s), 165.8 (s), 166.0 (s). Anal. Calcd for C_{12}H_{20}N_{2}O_{3}S: C, 56.22; H, 7.86; N, 10.93%. Found: C, 55.91; H, 7.65; N, 10.81%.

**10a** (R^1 = NMe_2, R^2 = t-C\(_4\)H\(_9\), R^3 = R^4 = CO_2Me): Yellow oil; MS (m/z) 315 (M^+1; bp), 257 (M^+-t-C\(_4\)H\(_9\); 21%); IR (neat) 2952, 1726, 1635, 1434, 1363, 1134, 1257, 1039, 734 cm\(^{-1}\); \(^1\)H NMR (CDCl_3) \(\delta\) 0.94 (9H, s), 3.01 (6H, s), 3.76 (3H, s), 3.82 (3H, s), 4.78 (1H, s); \(^{13}\)C NMR (CDCl_3) \(\delta\) 26.6 (q), 38.8 (q), 41.5 (s), 52.4 (q), 53.1 (q), 69.2 (d), 130.0 (s), 131.6 (s), 148.6 (s), 164.8 (s), 167.9 (s). HRMS (Cl) Calcd for C_{12}H_{14}N_{2}O_{3}S: m/z 314.1300. Found: m/z 315.1381 (M^+1). Anal. Calcd for C_{14}H_{22}N_{2}O_{3}S: C, 53.48; H, 7.05; N, 8.91%. Found: C, 53.02; H, 6.88; N, 8.78%.

**11a** (R^1 = NMe_2, R^2 = R^3 = t-C\(_4\)H\(_9\), R^4 = COCO_2Et): Yellow oil; MS (m/z) 355 (M^+; bp); 297 (M^+-t-C\(_4\)H\(_10\); 21%); IR (neat) 2957, 1727, 1600, 1457, 1365, 1134, 719 cm\(^{-1}\); \(^1\)H NMR (CDCl_3) \(\delta\) 1.11 (9H, s), 1.30 (3H, t, J = 7.2 Hz), 1.41 (9H, s), 2.68 (6H, s), 3.95 (1H, s), 4.21 (2H, q, J = 7.2 Hz); \(^{13}\)C NMR (CDCl_3) \(\delta\) 14.1 (q), 27.0 (q), 28.4 (q), 34.9 (q), 40.7 (q), 40.9 (s), 61.6 (t), 77.2 (d), 121.0 (s), 164.6 (s), 165.4 (s), 180.7 (s), 189.1 (s). HRMS Calcd for C_{18}H_{31}N_{2}O_{3}S: m/z 355.2055. Found: m/z 355.2067.

**Preparation of Thiobenzamide 12 from Heterodiene 5f and Methyl Propiolate (8a).** A CHCl_3 solution of 1,3-thiaza-1,3-butenediene 5f (R^1 = NMe_2, R^2 = NMe_2, 100 mg, 0.63 mmol) was treated with methyl propiolate (8a, R^3 = H, 79 mg, 0.94 mmol, 1.5 mol amt.) at rt for 5 days. The reaction mixture was
cooled and the solvent was evaporated in vacuo. The crude mixture was separated by using chromatography on silica gel to obtain thioenamide 12 (37 mg, 27% yield) as yellow oil besides the recovery of 3a (47 mg, 48% yield).

12: Yellow oil; MS (m/z) 216 (M+; 4%), 187 (M+-CHO; bp), 89 (Me₂NCS+; 20%); IR (neat) 3486, 2949, 2377, 1716, 1532, 1241, 779 cm⁻¹; ¹H NMR (CDCl₃) δ 3.42 (3H, s), 3.58 (3H, s), 3.85 (3H, s), 9.13-9.22 (1H, m), 10.0 (1H, d, J = 4.0 Hz), 13.1 (1H, br. s); ¹³C NMR (CDCl₃) δ 39.6 (q), 44.3 (q), 51.8 (s), 106.4 (s), 152.9 (d), 166.3 (s), 179.2 (s), 193.5 (d). HRMS Calcd for C₈H₁₂N₂O$: m/z 216.0569. Found: m/z 216.0571 (M+;+1).

A Typical Procedure for the Reaction of 1,3-Thiaza-1,3-butadienes 5 with mCPBA. A CHCl₃ solution of 1,3-thiaza-1,3-butadiene 5a (R¹ = NMe₂, R² = t-C₄H₉, 122 mg, 0.71 mmol) was treated with mCPBA (70%, 260 mg, 1.5 mol amt.) and NaHCO₃ powder (100 mg, 2.0 mol amt.) at rt for 48 h. The reaction was quenched by addition of an excess amount of saturated Na₂SO₃ solution, and the reaction mixture was extracted with CHCl₃. The organic layer was dried over anhydrous Na₂SO₄ powder, and then the organic solvent was evaporated in vacuo. The crude products were separated by using chromatography on silica gel to obtain 5H-1,2,4-oxathiazole 13a (76 mg, yield 56%) as colorless oil.

13a (R¹ = NMe₂, R² = t-C₄H₉): Colorless oil; MS (m/z) 156 (M+-S; 53%), 139 (M+-SOH; bp), 57 (t-C₄H₉; 68%); IR (neat) 2960, 2935, 2876, 1668, 1126 cm⁻¹; ¹H NMR (CDCl₃) δ 0.97 (9H, s), 3.16 (6H, s), 6.20 (1H, s); ¹³C NMR (CDCl₃) δ 25.1 (q), 35.6 (s), 39.3 (q), 123.3 (d), 165.0 (s). Anal. Calcd for C₈H₁₆N₂OS: C, 51.03; H, 8.56; N, 14.88%. Found: C, 50.54; H, 8.21; N, 14.67%.

A Typical Procedure for the Reaction of 1,3-Thiaza-1,3-butadienes 5 with Chloramine-T. A CHCl₃ solution of 1,3-thiaza-1,3-butadiene 5a (R¹ = NMe₂, R² = t-C₄H₉, 76 mg, 0.44 mmol) was treated with chloramine-T (0.189 g, 1.5 mol amt.) at rt for 48 h. The reaction was quenched by addition of an excess amount of water, and the reaction mixture was extracted with CHCl₃. The organic layer was dried over anhydrous Na₂SO₄ powder, and then the organic solvent was evaporated in vacuo. The crude products were separated by using chromatography on silica gel and the subsequent recrystallization from CHCl₃-EtOAc to obtain 2,3-dihydro-1,2,4-thiadiazole 15a (20 mg, yield 56%) as colorless prisms.

15a (R¹ = NMe₂, R² = t-C₄H₉): Colorless prisms, mp 185.1-188.2 °C; MS (m/z) 284 (M+-t-C₄H₉; bp), 155 (M+-p-TolSO₂; 85%), 91 (Tol; 90%); IR (KBr) 2964, 2929, 2869, 1644, 1344, 1165, 809 cm⁻¹; ¹H NMR (CDCl₃) δ 1.00 (9H, s), 2.41 (3H, s), 2.70 (6H, s), 5.58 (1H, s), 7.27 (2H, br. d, J = 8.0 Hz), 7.78 (2H, br. d, J = 8.0 Hz); ¹³C NMR (CDCl₃) δ 21.5 (q), 26.3 (q), 39.8 (q), 39.9 (s), 101.7 (d), 129.0 (d), 129.3 (d), 130.9 (s), 144.2 (s), 160.4 (s). Anal. Calcd for C₁₅H₂₃N₃O₂S₂: C, 52.50; H, 6.72; N, 11.83%. Found: C, 52.76; H, 6.79; N, 12.30%.
15b (R¹ = NMe₂, R² = C₆H₅): Colorless prisms, mp 122.3-124.8 °C; MS (m/z) 361 (M⁺; 10%), 291 (M⁺-C₆H₅NCN; 5%), 227 (M⁺-C₆H₅NCN-C₆H₅; bp), 206 (M⁺-p-TolSO₂; 27%), 91 (Tol; 59%); IR (KBr) 2959, 2927, 2900, 1641, 1345, 1167, 816, 769 cm⁻¹; ¹H NMR (CDCl₃) δ 2.45 (3H, s), 2.75 (6H, s), 7.02 (1H, s), 7.31-7.33 (5H, m), 7.46-7.47 (2H, m), 7.86 (2H, d, J = 8.4 Hz); ¹³C NMR (CDCl₃) δ 21.7 (q), 40.1 (q), 93.1 (d), 126.6 (d), 128.1 (d), 128.5 (d), 129.0 (d), 129.3 (d), 131.3 (s), 137.5 (s), 144.8 (s), 162.3 (s). Anal. Calcd for C₁₇H₁₉N₃O₂S: C, 56.48; H, 5.30; N, 11.62%. Found: C, 56.36; H, 5.19; N, 11.63%.

15c (R¹ = NMe₂, R² = p-ClC₆H₄): Colorless needles, mp 156.3-157.6 °C; IR (KBr) 2918, 2326, 1627, 1345, 1160, 1052, 558 cm⁻¹; ¹H NMR (CDCl₃) δ 2.46 (3H, s), 2.78 (3H, s), 6.97 (1H, s), 7.30 (2H, d, J = 8.4 Hz), 7.34 (2H, d, J = 8.4 Hz), 7.41 (2H, d, J = 8.4 Hz), 7.86 (2H, d, J = 8.4 Hz); ¹³C NMR (CDCl₃) δ 21.7 (q), 40.4 (q), 91.7 (d), 126.5 (d), 128.2 (d), 128.3 (d), 129.1 (d), 129.4 (d), 129.7 (d), 131.1 (s), 134.4 (s), 135.8 (s), 145.0 (s), 161.2 (s). Anal. Calcd for C₁₇H₁₈ClN₃O₂S: C, 51.57; H, 4.58; N, 10.61%. Found: C, 51.94; H, 4.41; N, 10.18%.

15d (R¹ = NMe₂, R² = C₆H₅CH=CH): Yellow oil; MS (m/z) 388 (M⁺+1; bp), 317 (M⁺-C₆H₅NCN; 33%), 232 (M⁺-p-TolSO₂; 48%), 162 (M⁺-p-TolSO₂-CH₃CN; 37%); IR (neat) 2984, 1694, 1630, 1522, 1261, 1081, 755 cm⁻¹; ¹H NMR (CDCl₃) δ 2.43 (3H, s), 2.71 (6H, s), 6.11 (1H, d, J = 16.0 Hz), 6.56 (1H, dd, J = 4.8, 1.2 Hz), 6.64 (1H, d, J = 0.8 Hz), 7.22-7.25 (1H, m), 7.29-7.31 (4H, m), 7.37 (2H, d, J = 7.2 Hz), 7.83 (2H, d, J = 8.0 Hz); ¹³C NMR (CDCl₃) δ 21.6 (q), 40.1 (q), 92.5 (d), 124.3 (d), 126.9 (d), 128.0 (d), 128.5 (d), 128.9 (d), 131.3 (d), 131.1 (s), 134.4 (s), 135.8 (s), 144.7 (s), 161.9 (s). HRMS Calcd for C₁₉H₂₁N₃O₂S²: m/z 387.1075. Found: m/z 388.1160 (M⁺+1).

15e (R¹ = NMe₂, R² = Mes): Yellow prisms, mp 164.2-166.5 °C; IR (KBr) 2984, 2379, 1937, 1384, 1350, 1160, 666 cm⁻¹; ¹H NMR (CDCl₃) δ 2.16 (3H, s), 2.38 (3H, s), 2.42 (6H, s), 6.75 (2H, s), 7.06 (1H, s), 7.22 (2H, d, J = 8.0 Hz), 7.79 (2H, d, J = 8.0 Hz); ¹³C NMR (CDCl₃) δ 20.8 (q), 21.2 (q), 21.7 (q), 39.7 (q), 93.4 (d), 129.4 (d), 129.7 (d), 130.6 (d), 131.5 (s), 132.3 (s), 137.2 (s), 137.8 (s), 144.6 (s), 158.8 (s). Anal. Calcd for C₂₀H₂₅N₃O₂S²: C, 59.52; H, 6.24; N, 10.41%. Found: C, 59.10; H, 6.21; N, 10.23%.

**Procedure for the Reaction of 1,3-Thiaza-1,3-butadiene 6 with Chloramine-T.** A CHCl₃ solution of 1,3-thiaza-1,3-butadiene 6 (R¹ = C₆H₅, R² = NMe₂, 100 mg, 0.52 mmol) was treated with chloramine-T (210 mg, 1.5 mol atm.) at rt for 48 h. The reaction was quenched by addition of an excess amount of water, and the reaction mixture was extracted with CHCl₃. The organic layer was dried over anhydrous Na₂SO₄ powder, and then the organic solvent was evaporated in vacuo. The crude crystalline solids were purified by using chromatography on silica gel and the subsequent recrystallization from CHCl₃-EtOAc to obtain product 16 (79 mg, yield 46%) as pale yellow needles.
16: Pale yellow needles, mp 124.3-124.8 °C; MS (m/z) 329 (M⁺; 30%), 328 (M⁺-1; 40%), 162 (M⁺-NO₂Tol; bp), 91 (M⁺-C₆H₁₃N₃O₂S; 69%); IR (KBr) 2927, 2363, 2868, 1497, 1147, 665 cm⁻¹; ¹H NMR (CDCl₃) δ 2.40 (3H, s), 3.15 (3H, s), 3.20 (3H, s), 7.65 (2H, t, J = 4 Hz), 7.36 (2H, t, J = 8.5 Hz), 7.46 (1H, t, J = 7.0 Hz), 7.88 (2H, d, J = 7.0 Hz), 7.93 (2H, d, J = 8.5 Hz), 8.04 (1H, s); ¹³C NMR (CDCl₃) δ 21.5 (q), 35.2 (q), 41.2 (q), 126.7 (d), 128.1 (d), 129.0 (d), 129.6 (d), 132.0 (d), 136.6 (s), 140.4 (s), 142.1 (s), 157.7 (d), 169.9 (s). Anal. Calcd for C₁₂H₁₉N₃O₂S: C, 61.98; H, 5.81; N, 12.76%. Found: C, 61.77; H, 5.73; N, 12.70%.

A Typical Procedure for the Reaction of 1,3-Thiaza-1,3-butadienes 5 with Ethyl Diazoacetate in the Presence of a Catalytic Amount of Rh₂(OAc)₄. A CH₂Cl₂ solution of 1,3-thiaza-1,3-butadiene 5a (R¹ = NMe₂, R² = t-C₄H₉, 93 mg, 0.54 mmol) was treated with a toluene solution of ethyl diazoacetate (0.8 mL, 1.08 mmol, 2.0 mol amt.) and a toluene solution of Rh₂(OAc)₄ (0.44 mg, 1.0 μmol, 0.01 mol amt.) at rt for 120 h. The solvent was removed by evaporation from the reaction mixture, and the crude mixture was separated by using chromatography on silica gel to obtain trans-18a (88 mg, 63% yield) as yellow oil.

A Typical Procedure for the Reaction of 1,3-Thiaza-1,3-butadienes 5 with Ethyl Diazoacetate in the Presence of Cu₂Cl₂. A CH₂Cl₂ solution of 1,3-thiaza-1,3-butadiene 5e (R¹ = NMe₂, R² = Mes, 100 mg, 0.43 mmol) was treated with a toluene solution of ethyl diazoacetate (0.86 mmol, 2.0 mol amt.) and Cu₂Cl₂ (84 mg, 0.86 mmol, 2.0 mol amt.) at rt for 36 h. Then, the solvent was removed by evaporation from the reaction mixture, and the crude brown solid was separated by using chromatography on silica gel to obtain trans-18e (38 mg, 27% yield, yellow oil), cis-18e (8 mg, 6% yield, yellow oil), and 19e (7 mg, 5% yield, colorless solid) as yellow oil.

A Typical Procedure for the Reaction of 1,3-Thiaza-1,3-butadienes 5 with Ethyl Diazoacetate in the Presence of Cu₂Cl₂. A CH₂Cl₂ solution of 1,3-thiaza-1,3-butadiene 5e (R¹ = NMe₂, R² = Mes, 100 mg, 0.43 mmol) was treated with a toluene solution of ethyl diazoacetate (0.86 mmol, 2.0 mol amt.) and Cu₂Cl₂ (84 mg, 0.86 mmol, 2.0 mol amt.) at rt for 36 h. Then, the solvent was removed by evaporation from the reaction mixture, and the crude brown solid was separated by using chromatography on silica gel to obtain trans-18e (38 mg, 27% yield, yellow oil), cis-18e (8 mg, 6% yield, yellow oil), and 19e (7 mg, 5% yield, colorless solid) as yellow oil.

trans-18a (R¹ = NMe₂, R² = t-C₄H₉): Yellow oil; MS (m/z) 258 (M⁺; 14%), 201 (M⁺-t-C₄H₉; bp); IR (neat) 2955, 1739, 1635, 1368, 1171, 1030, 605 cm⁻¹; ¹H NMR (CDCl₃) δ 0.94 (9H, s), 1.27 (3H, t, J = 7.2 Hz), 2.97 (6H, s), 4.20 (2H, q, J = 7.2 Hz), 4.25 (1H, d, J = 4.0 Hz), 4.40 (1H, d, J = 4.0 Hz); ¹³C NMR (CDCl₃) δ 14.1 (q), 26.2 (q), 36.2 (s), 40.1 (q), 53.3 (d), 61.1 (t), 86.3 (d), 158.9 (s), 172.6 (s). HRMS Calcd for C₁₂H₂₃N₂O₂S: m/z 259.1480. Found: m/z 259.1482.

19e (R¹ = NMe₂, R² = C₆H₅): Yellow needles, 33.1-34.0 °C; MS (m/z) 276 (M⁺; bp), 247 (M⁺-C₂H₅; 28%); IR (KBr) 2925, 1740, 1630, 1353, 1164, 1086, 682 cm⁻¹; ¹H NMR (CDCl₃) δ 2.35 (6H, s), 4.19 (2H, q, J = 7.2 Hz), 3.18 (6H, s), 4.19 (2H, q, J = 7.2 Hz), 7.38-7.39 (3H, m), 7.72-7.73 (2H, m).

trans-18e (R¹ = NMe₂, R² = Mes): Yellow oil; MS (m/z) 320 (M⁺; 54%), 247 (M⁺-CO₂Et; bp); IR (neat) 2925, 1740, 1633, 1373, 1160, 1029, 661 cm⁻¹; ¹H NMR (CDCl₃) δ 0.77 (3H, t, J = 7.0 Hz), 2.20 (3H, s), 2.35 (6H, s), 3.06 (6H, s), 3.50 (1H, dq, J = 11.0, 7.0 Hz), 3.67 (1H, dq, J = 11.0, 7.0 Hz), 4.84 (1H, d, J = 10.5 Hz), 6.14 (1H, d, J = 10.5 Hz), 6.74 (2H, s); ¹³C NMR (CDCl₃) δ 13.3 (q), 20.7 (q), 21.3 (1), 40.2 (q), 56.4 (d), 61.3 (t), 7.68 (d), 128.8 (d), 132.2 (s), 136.5 (s), 137.9 (s), 160.0 (s), 170.2 (s). HRMS Calcd for
C_{17}H_{24}N_{2}O_{2}S: m/z 320.1558. Found: m/z 320.1562.

cis-18e (R^1 = NMe_2, R^2 = Mes): Yellow oil; MS (m/z) 320 (M^+; 61%), 247 (M^+CO_2Et; bp); IR (neat) 2918, 1738, 1413, 1144, 1075, 756 cm^{-1}; \^1H NMR (CDCl_3) δ 1.24 (3H, t, J = 7.0 Hz), 2.23 (3H, s), 2.34 (6H, s), 2.99 (6H, s), 4.15 (1H, dq, J = 11.0, 7.0 Hz), 4.21 (1H, dq, J = 11.0, 7.0 Hz), 4.50 (1H, d, J = 8.0 Hz), 6.15 (1H, d, J = 8.0 Hz), 6.81 (2H, s); \^13C NMR (CDCl_3) δ 14.1 (q), 20.5 (q), 20.8 (q), 40.3 (q), 58.0 (d), 62.0 (t), 75.7 (d), 130.3 (d), 135.2 (s), 136.9 (s), 137.0 (s), 159.1 (s), 171.7 (s). HRMS Calcd for C_{17}H_{24}N_{2}O_{2}S: m/z 320.1558. Found: m/z 320.1558.

19e (R^1 = NMe_2, R^2 = Mes): Colorless solid, mp 116.0-119.0 °C; MS (m/z) 318 (M^+; 58%), 245 (M^+CO_2Et; bp); IR (KBr) 2918, 1738, 1698, 1560, 1413, 1144, 1075, 756 cm^{-1}; \^1H NMR (CDCl_3) δ 1.24 (3H, t, J = 7.0 Hz), 2.28 (6H, s), 3.17 (6H, s), 4.08 (2H, q, J = 7.0 Hz), 6.86 (2H, s); \^13C NMR (CDCl_3) δ 14.1 (q), 19.8 (q), 21.2 (q), 40.1 (q), 60.1 (t), 111.8 (t), 127.9 (d), 132.8 (s), 137.3 (s), 164.4 (s), 161.7 (s), 171.5 (s). HRMS Calcd for C_{17}H_{22}N_{2}O_{2}S: m/z 318.1402. Found: m/z 318.1406.

19f (R^1 = NMe_2, R^2 = H): Yellow needles, mp 33.1-34.0 °C (Lit. 17a 38.0-39.0 °C); MS (m/z) 201 (M^+1; bp). IR (KBr) 2925, 1724, 1630, 1353, 1164, 1086, 682 cm^{-1}; \^1H NMR (CDCl_3) δ 1.34 (3H, t, J = 7.2 Hz), 3.16 (6H, s), 4.29 (2H, q, J = 7.2 Hz), 7.88 (1H, s); \^13C NMR (CDCl_3) δ 14.4 (q), 40.2 (q), 116.4 (s), 148.3 (d), 162.2 (s), 174.5 (s). HRMS Calcd for C_{8}H_{12}N_{2}O_{2}S: m/z 200.0619. Found: m/z 201.0675 (M^+1).

A Typical Procedure for the Reaction of 1,3-Thiaza-1,3-butadienes 5 with Dichlorocarbene. A hexane solution of 5e (R^1 = NMe_2, R^2 = Mes, 92 mg, 0.39 mmol) was treated with dry CHCl_3 (469 mg, 10.0 mol amt.) and then with potassium t-butoxide (220 mg, 5.0 mol amt.) with vigorous stirring at 0 °C for 5 h. Then, the solvent was removed by evaporation from the reaction mixture, and the crude brown solid was separated by using chromatography on silica gel to obtain 5-chloro-1,3-thiazole 20e (28 mg, 25% yield) as yellow solids.

20a (R^1 = NMe_2, R^2 = t-C_4H_9): Brown oil; MS (m/z) 220 (M^+; 33%, 37Cl), 218 (M^+; 97%, 35Cl), 205 (M^+-Me; 34%, 37Cl), 203 (M^+-Me; bp, 35Cl), 57 (t-C_4H_9; 41%); IR (neat) 2927, 1653, 1363, 1182, 1085, 690 cm^{-1}; \^1H NMR (CDCl_3) δ 1.27 (9H, s), 3.27 (6H, s); \^13C NMR (CDCl_3) δ 29.8 (q), 35.6 (s), 39.9 (q), 104.0 (s), 155.3 (s) 164.9 (s). Anal. Calcd for C_{9}H_{15}ClN_{2}S: C, 49.42; H, 6.91; N, 12.81%. Found: C, 49.51; H, 6.80; N, 12.75%.

20e (R^1 = NMe_2, R^2 = Mes): Yellow solid, mp 125.0-128.0 °C; MS (m/z) 282 (M^+; 27%, 37Cl), 280 (M^+; 71%, 35Cl), 245 (M^+Cl; bp), 175 (64%); IR (KBr) 2953, 1651, 1349, 1186, 1090, 682 cm^{-1}; \^1H NMR (CDCl_3) δ 2.14 (6H, s), 2.28 (3H, s), 3.05 (6H, s), 6.89 (2H, s); \^13C NMR (CDCl_3) δ 29.8 (q), 35.6 (s), 39.9 (q), 107.7 (s), 128.2 (d), 130.0 (s), 137.6 (s), 138.1 (s), 148.1 (s), 166.7 (s). HRMS Calcd for C_{14}H_{17}N_{2}SCl: m/z 280.0801. Found: m/z 280.0800.
REFERENCES


