Reactions of Keto–Enol Tautomers of 2-Thiazolyl-, 2-Oxazolyl-, 2-Benzoxazolyl-, or 2-Benzothiazolyl-1-phenylethenols with α,β-Alkynyl Esters: Syntheses of Highly Functionalized Fused-Ring Heterocycles

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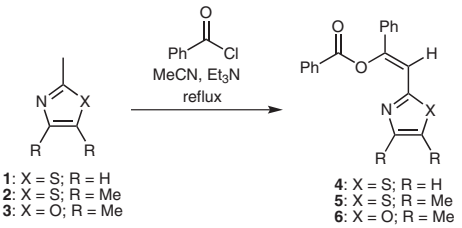
Abstract: 2-Methyl-1,3-thiazole, 2,4-dimethyl-1,3-thiazole, 2,4,5-trimethyl-1,3-thiazole, 2,4,5-trimethyl-1,3-oxazole, 2-methyl-1,3-benzoxazole and 2-methyl-1,3-benzothiazole were each treated with benzoyl chloride in acetonitrile containing triethylamine to give the corresponding (*Z*)-2-(heterocyclic)-1-phenylvinyl benzoates. Base hydrolysis of these vinyl benzoates gave the corresponding 2-(heterocyclic)-1-phenylethenols, which exist in both keto and enol tautomeric forms. These tautomers were used as starting materials for the syntheses of fused-ring heterocycles. The reactivity of the keto–enol tautomers depends on the nature of the heteroatom and the substituents that are present on the ring. Each tautomeric pair reacts with dimethyl acetylenedicarboxylate (DMAD) in methanol to give the 5,6-ring-fused 8-benzoyl-5-oxo-5*H*-thiazolo- and 8-benzoyl-5-oxo-5*H*-oxazolopyridinecarboxylate, 4-benzoyl-1-oxo-1*H*-pyrido[2,1-*b*]benzoxazolecarboxylate and 4-benzoyl-1-oxo-1*H*-pyrido[2,1-*b*]benzothiazolecarboxylate derivatives. Two novel 5,7-ring-fused compounds, tetramethyl 9-benzoyl-2,3-dimethyl-5,6-dihydrothiazolo[3,2-*a*]azepine-5,6,7,8-tetracarboxylate and its oxazole analogue, were also obtained when the tautomers formed from 2,4,5-trimethyl-1,3-thiazole and 2,4,5-trimethyl-1,3-oxazole, respectively, were treated with DMAD. Reactions of the tautomers with methyl propiolate did not, however, give satisfactory results.

Key words: tautomerism, heterocycles, polycycles, Michael additions, cyclocondensations

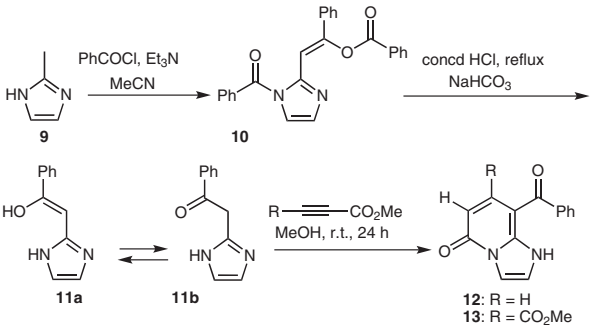
Derivatives of thiazole, oxazole, benzoxazole, and benzothiazole form an important class of heterocyclic units that are found in antiviral, antifungal, antibacterial, anti-inflammatory, and anticancer agents.[1–4] This wide range of biological activities justifies the syntheses of novel heterocyclic compounds that contain such ring structures.

We have previously reported reactions of 2-methyl-1,3-thiazole (**1**), 2,4,5-trimethyl-1,3-thiazole (**2**), and 2,4,5-trimethyl-1,3-oxazole (**3**) with benzoyl chlorides in the presence of a base to give the corresponding (*Z*)-2-(heterocyclic)-1-phenylvinyl benzoates **4**–**6** (Scheme 1).[5] 2-Methyl-1,3-benzoxazole (**7**) and 2-methyl-1,3-benzothiazole (**8**) have also been reported to give similar vinyl benzoates.[6]

Acid hydrolysis of (*Z*)-2-(1-benzoyl-1*H*-imidazol-2-yl)-1-phenylvinyl benzoate (**10**), prepared from 2-methyl-1*H*-imidazole (**9**), gave (*Z*)-2-(1*H*-imidazol-2-yl)-1-phenylethenols (**11a**), which exists in both keto and enol tautomeric forms **11a** and **11b**, respectively (Scheme 2).[7] The 5,6-ring-fused products **12** and **13** were obtained when the tautomeric pair was treated with methyl propiolate or dimethyl acetylenedicarboxylate (DMAD), respectively (Scheme 2).[7]



Scheme 1 Reactions of heterocycles **1**–**3** with benzoyl chloride[5]



Scheme 2 Synthesis of 5,6-ring-fused products **12** and **13**[7]

We hypothesized that hydrolysis of (*Z*)-2-(heterocyclic)-1-phenylvinyl benzoates of thiazoles, oxazoles, benzoxazoles, or benzothiazoles followed by reaction of the resultant 2-(heterocyclic)-1-phenylethenols with α,β-alkynyl esters might give highly functionalized fused-ring heterocycles, in a similar manner to the syntheses of **12** and **13** (Scheme 2). In this manner, we were able to prepare six novel 5,6-ring-fused and two novel 5,7-ring-fused compounds.

Treatment of 2-methyl-1,3-thiazole (**1**), 2,4-dimethyl-1,3-thiazole (**14**), 2,4,5-trimethyl-1,3-thiazole (**2**), 2,4,5-trimethyl-1,3-oxazole (**3**), 2-methyl-1,3-benzoxazole (**7**), or 2-methyl-1,3-benzothiazole (**8**) with benzoyl chloride in the presence of triethylamine in refluxing acetonitrile gave the corresponding (*Z*)-2-(heterocyclic)-1-phenylvinyl benzoates **4**–**6** and **15**–**17** (shown in Table 1). Com-

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pounds **4**–**6**, **16**, and **17** followed from our earlier work,[5] and the new preparation of **15** from thiazole **14** provided a sixth model vinyl benzoate.

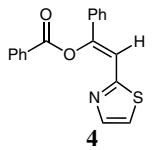
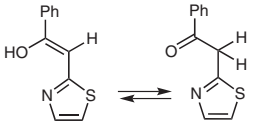
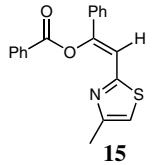
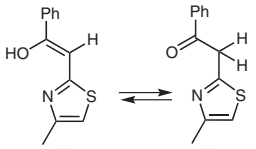
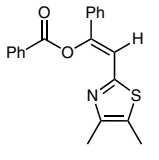
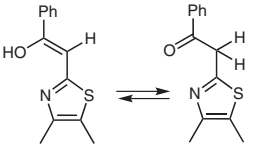
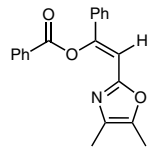
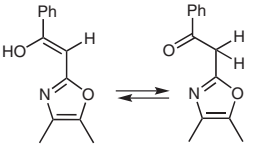
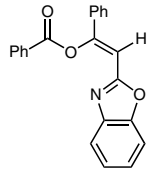
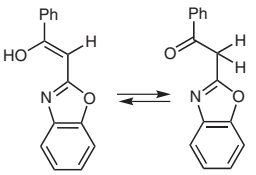
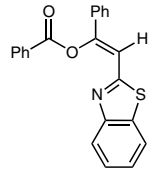
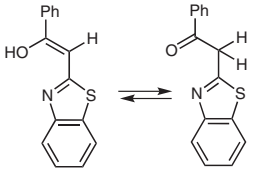
Benzoates **4**–**6** and **15**–**17** (Table 1) were hydrolyzed with a solution of potassium hydroxide in anhydrous methanol to give the equilibrated 2-(heterocyclic)-1-phenylethenols **18a**–**23a** and their corresponding keto tautomers **18b**–**23b** in good yields.[8] All the hydrolyzed products showed two sets of resonances in their ^{1}H and ^{13}C NMR spectra in chloroform-d_1 at 20 °C. The presence of a methylene proton and the ^{13}C signals at δ = 4.38–4.81 and 43.81–38.81 ppm confirmed that each hydrolyzed product contained the appropriate keto tautomer **18b**–**23b**. This was further confirmed by the presence of distinct carbonyl carbon signals between δ = 192.38 and δ = 194.79 ppm. Vinyl proton signals of the enol forms (δ = 5.98–6.35 ppm) were also observed for each hydrolyzed product. The ^{1}H NMR spectra of the hydrolyzed products of **4**, **5**, **15**, **16**, and **17** each showed a broad downfield signal (δ = 12.62–13.91 ppm) from the strong intramolecularly hydrogen-bonded enol hydroxy proton, except in the case of the hydrolyzed product from **6**. Hydrolysis of **4**, **15**, **5**, and **6** afforded the keto forms **18b**–**21b**, respectively, as the major tautomers (Table 1, entries 1–4). In contrast, hydrolysis of the benzoxazole and benzothiazole derivatives **16** and **17** gave the corresponding enol forms **22a** and **23a** as the major tautomers.

The ^{13}C NMR carbonyl resonances were used to confirm the presence of enol tautomers rather than enaminones. The enaminone carbonyl carbon of **23** appears 12.9 ppm upfield from the keto tautomer **23b**, which appears at δ = 192.4 ppm.[9] Enolic carbons (=C–OH) of the intramolecularly hydrogen-bonded enol tautomers **22a** and **23a** appeared even further upfield (δ = 166.3 and 163.5 ppm, respectively) than the enaminone carbonyl carbons.[9,10] The absence of ^{13}C NMR responses in the δ = 170–190 ppm region for the hydrolysis products of **16** and **17** excluded the presence of the corresponding enaminones and confirmed the presence of the enol forms **22a** and **23a**, respectively. Hydrolysis products of **4**–**6** and **15** also showed no ^{13}C peaks in the δ = 170–190 ppm region, confirming that only keto and enol tautomers were present in chloroform-d_1.

The equilibrating tautomers **18a**,**b**–**23a**,**b** were then treated with dimethyl acetylenedicarboxylate in anhydrous methanol at either room temperature or at reflux. The products and their isolated yields are shown in Tables 2–4, together with the appropriate reaction conditions.

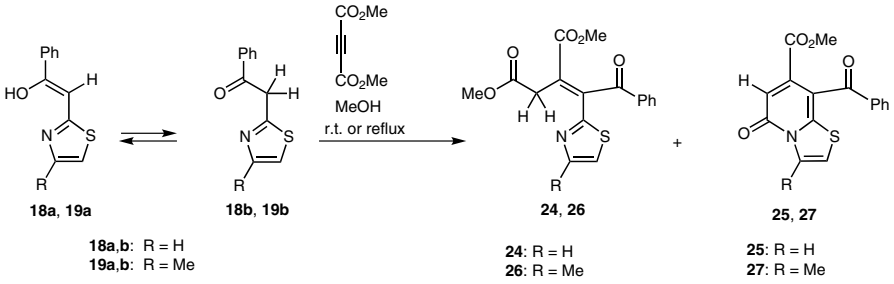
Tautomers **18a**,**b** gave the 5,6-ring-fused product methyl 8-benzoyl-5-oxo-5*H*-thiazolo[3,2-*a*]pyridine-7-carboxylate (**25**) in moderate-to-good yields (42–70%) under various reaction conditions (Table 2, entries 1–3). The open-chain product **24**, a possible intermediate in the formation of **25**, was also isolated in 9–26% yield under all three sets of conditions. The isolated yield of **24** was higher when

Table 1 Keto–Enol Tautomeric Ratios of **18a**,**b**–**23a**,**b** in Chloroform-d_1 Solution at 20 °C, and Their Isolated Yields

Entry[a]	Substrate	Product	Enol/keto ratio[b]	Yield (%)[c]
1	 **4**	 **18a** **18b**	1:2.0	90
2	 **15**	 **19a** **19b**	1:1.32	67
3	 **5**	 **20a** **20b**	1:1.41	85
4	 **6**	 **21a** **21b**	1:3.57	74
5	 **16**	 **22a** **22b**	1.06:1	73
6	 **17**	 **23a** **23b**	1.63:1	92

[a] Reactions were carried out in anhyd MeOH for 24 h at r.t.
[b] Ratios were determined by NMR spectral integrations. The total concentrations of the enol and keto tautomers in $CDCl_3$ were between 0.184 M and 0.0186 M. Enol/keto ratios were calculated based on the =CH peak area of the enol and the methylene protons of the keto tautomer. The keto/enol ratios in the solid state are not known and might be significantly different from the solution values given in this table.
[c] Isolated yields were calculated by considering **4**–**6** and **15**–**17** as the limiting reagents.

Table 2 Reactions of Tautomeric Pairs **18a**,**b** and **19a**,**b** with Dimethyl Acetylenedicarboxylate in Anhydrous Methanol for 24 Hours under Various Conditions



Entry	Substrate	Tautomeric pair /DMAD ratio [molarities (M)]	Temp	Yield[a] (%)			
				24	**25**	**26**	**27**
1[b]	**18a**,**b** R = H	1:1.1 [0.18:0.16]	r.t.	26	42		
2	**18a**,**b** R = H	1:1.5 [0.18:0.26]	reflux	9	70		
3[c]	**18a**,**b** R = H	1:2.5 [0.18:0.44]	reflux	13	51		
4[d]	**19a**,**b** R = Me	1:2.5 [0.18:0.44]	reflux			12	65
5[e]	**19a**,**b** R = Me	1:1 [0.08:0.08]	reflux			25	32

[a] Yields of isolated products were calculated by considering the sum of both tautomers as the limiting reagent.
[b] 10% of the starting equilibrating tautomers were recovered at a **18a**/**18b** ratio of 1:1.89, as determined by NMR in $CDCl_3$.
[c] 0.135 g of a solid byproduct was isolated but not identified.
[d] Traces of both dimethyl (*E*)-2-methoxymaleate (**28**) and dimethyl (*Z*)-2-methoxymaleate (**29**) were also isolated.[11]
[e] 15% of the starting equilibrating tautomeric pair were recovered in a **19a**/**19b** ratio of 1:1.25, as determined by NMR in $CDCl_3$.

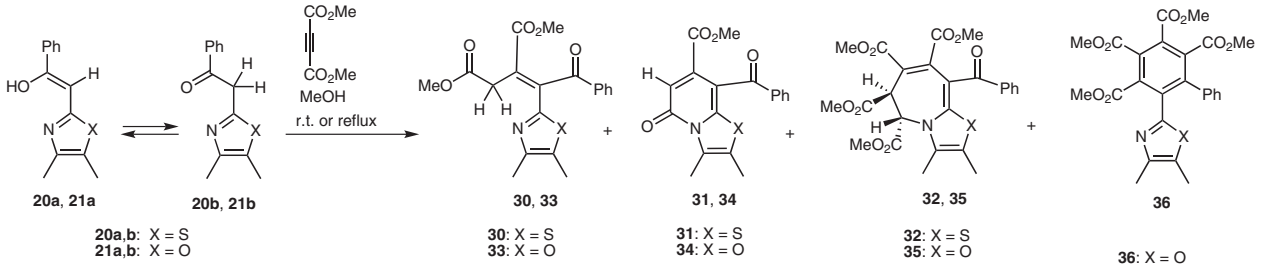
the reaction was carried out at 20–25 °C, whereas formation of **25** was favored in refluxing methanol (Table 1, entries 1 vs. 2).

When 2.5 equivalents of dimethyl acetylenedicarboxylate were refluxed with tautomeric pair **19a**,**b** in methanol, methyl 8-benzoyl-3-methyl-5-oxo-5*H*-[1,3]thiazolo[3,2-*a*]pyridine-7-carboxylate (**27**), an analogue of **25**, was isolated in moderate yield (65%), along with a small amount (12%) of the open-chain product **26** (Table 2, entry 4). The use of lower concentrations of **19a**,**b** and dimethyl acetylenedicarboxylate in methanol resulted in an increased yield of **26** but a lower yield of **27** and a lower combined yield of both products (Table 2, entry 5).

Tautomeric pairs **20a**,**b** and **21a**,**b** reacted with dimethyl acetylenedicarboxylate in methanol in a different manner to **18a**,**b** or **19a**,**b** (Table 3). Interestingly, the novel, highly functionalized, 5,7-ring-fused compounds **32** and **35** were isolated in addition to the open-chain products **30** and **33** and the 5,6-ring-fused products **31** and **34**. The low isolated yields of **31** and **34** suggest that the C-4 and C-5 methyl groups of the thiazole and oxazole rings slow the cyclization of **30** to **31** and of **33** to **34**. This allows **30** and **32** to add a second equivalent of dimethyl acetylenedicarboxylate before cyclizing, resulting in 5,7-ring fusion. A trace (1%) of a new compound **36** was isolated in addition to **33**, **34**, and **35**. The yield of both **32** and **35** increased when more than two equivalents of dimethyl acetylenedicarboxylate were used (Table 3, entries 2 vs. 1 and 3 vs. 4).

The yields of isolated products from reactions of dimethyl acetylenedicarboxylate with benzoxazole- and benzothiazole-derived tautomeric pairs **22a**,**b** and **23a**,**b** in anhydrous methanol are summarized in Table 4. Tautomeric pair **22a**,**b** with 1.5 equivalents of dimethyl acetylenedicarboxylate in refluxing methanol gave the 5,6-ring-fused product methyl 4-benzoyl-1-oxo-1*H*-pyrido[2,1-*b*][1,3]benzoxazole-3-carboxylate (**38**) in excellent yield (Table 4, entry 1). The yield of **38** decreased from 93% to 11%, whereas that of the open-chain product **37** increased from 2% to 35% at lower concentrations of the tautomeric pair and dimethyl acetylenedicarboxylate (Table 4, Entries 1 and 2). The 5,6-ring-fused product methyl 4-benzoyl-1-oxo-1*H*-pyrido[2,1-*b*][1,3]benzothiazole-3-carboxylate (**40**) was isolated exclusively on treating **23a**,**b** with dimethyl acetylenedicarboxylate (entries 3 and 4). The open-chain product **39**, a probable precursor of **40**, was not observed, even when the tautomeric pair **23a**,**b** was treated with dimethyl acetylenedicarboxylate at low concentrations at room temperature.

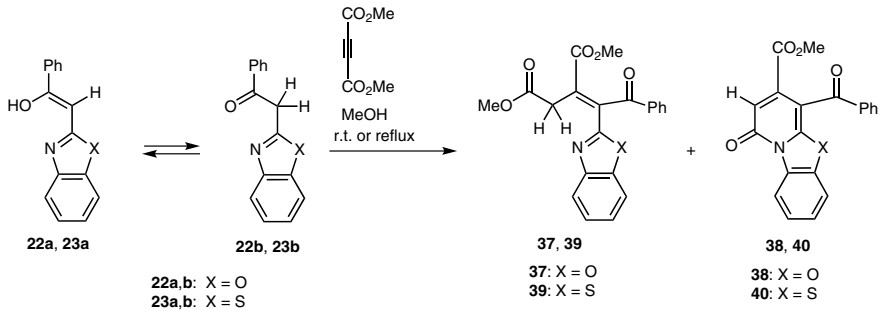
Table 3 Reactions of Tautomers **20a**,**b** and **21a**,**b** with Dimethyl Acetylenedicarboxylate in Anhydrous Methanol for 24 Hours under Various Conditions



Entry	Substrate	Tautomeric pair/DMAD ratio [molarities (M)]	Temp	Yield[a] (%)						
				30	**31**	**32**	**33**	**34**	**35**	**36**
1	**20a**,**b** (X = S)	1:1.5 [0.22:0.15]	reflux	46	21	7				
2[b]	**20a**,**b** (X = S)	1:2.5 [0.15:0.44]	reflux	32[b]	16	23				
3[b]	**21a**,**b** (X = O)	1:2.5 [0.15:0.44]	reflux				36[b]	4	47	1
4[c]	**21a**,**b** (X = O)	1:1 [0.17:0.17]	r.t.				44[c]	–	20	–

[a] Yields of isolated products were calculated by considering the sum of both tautomers as the limiting reagent.
[b] Traces of both dimethyl (*E*)-2-methoxymaleate (**28**) and dimethyl (*Z*)-2-methoxymaleate (**29**) were also isolated.[11]
[c] 17% of the starting equilibrating tautomeric pair was recovered in a **21a**/**21b** ratio of 1:2.73, as determined by NMR in $CDCl_3$.

Table 4 Reactions of Tautomers **22a**,**b** and **23a**,**b** with Dimethyl Acetylenedicarboxylate in Anhydrous Methanol for 24 Hours under Various Conditions



Entry	Substrate	Tautomeric pair/DMAD ratio [molarities (M)]	Temp	Yield[a] (%)			
				37	**38**	**39**	**40**
1	**22a**,**b** (X = O)	1:1.5 [0.14:0.22]	reflux	2	93		
2[b]	**22a**,**b** (X = O)	1:1.5 [0.05:0.08]	reflux	35	11		
3[c]	**23a**,**b** (X = S)	1:2.5 [0.18:0.44]	reflux			–	85
4[d]	**23a**,**b** (X = S)	1:1 [0.08:0.08]	r.t.			–	65

[a] Yields of isolated products were calculated by considering the sum of both tautomers as the limiting reagent.
[b] 41% of the starting tautomers were recovered at a **22a**/**22b** ratio of 1.11:1, as determined by NMR in $CDCl_3$.
[c] Traces of both dimethyl (*E*)-2-methoxymaleate (**28**) and dimethyl (*Z*)-2-methoxymaleate (**29**) were also isolated.[11]
[d] 22% of the starting tautomeric pair was recovered at a **23a**/**23b** ratio of 1.62:1, as determined by NMR in $CDCl_3$.

The presence of a single vinyl proton and one ester methoxy group in the ^{1}H NMR spectra and of three carbonyl carbons (corresponding to the ketone, ester, and amide functions) in the ^{13}C NMR spectra were characteristic of each of the 5,6-ring-fused structures **25**, **27**, **31**, **34**, **38**, and **40**. The IR spectra of each of these compounds showed three distinct absorptions for unsaturated ester, amide, and unsaturated aromatic ketone carbonyl groups. X-ray crystal structures were obtained for compounds **25**, **34**, and **38** (Figures 1–3), thereby completing the definitive identification of these structures.

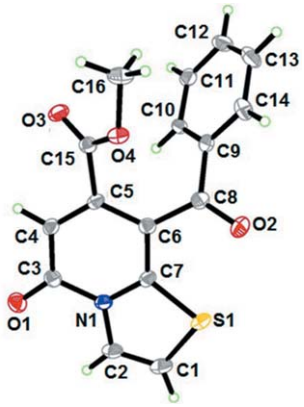


Figure 1 The X-ray crystal structure of **25** (CCDC 888329)

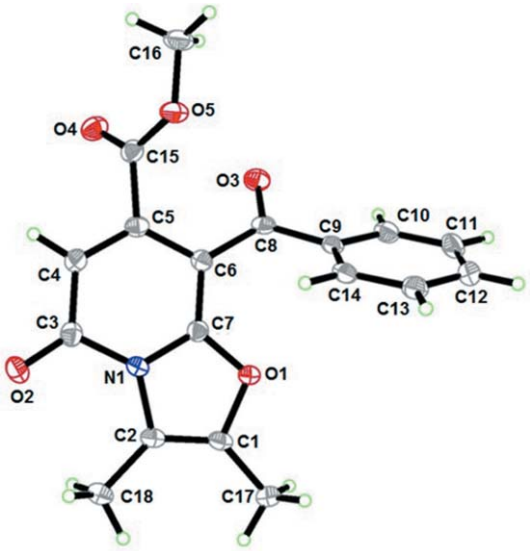


Figure 2 The X-ray crystal structure of **34** (CCDC 888334)

The presence of a methylene proton and of ^{13}C signals at δ = 4.38–4.12 and 43.81–38.81 ppm in the NMR spectra of all the open-chain products **24**, **26**, **30**, **33**, and **37** (Tables 2–4) excluded the two other possible tautomeric structures (**41** and **42**, Scheme 3). The X-ray crystal structure of the oxazole derivative **33** confirmed the *Z*-geometry of the C4–C5 double bond (Figure 4) in the solid state. The existence of the *Z*-geometrical isomers of **33** and **37** and the analogous *E*-geometries in **24**, **26**, **30**, and **39** are

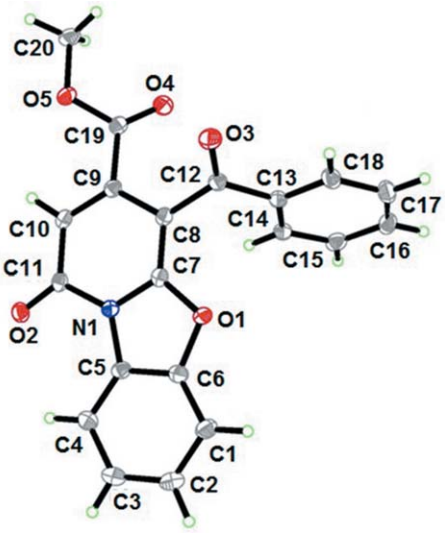
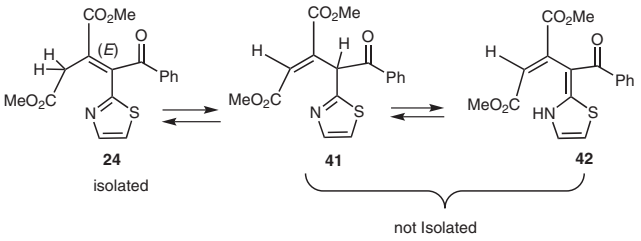


Figure 3 The X-ray crystal structure of **38** (CCDC 888333)

necessary to permit cyclization to the 5,6-ring-fused structures **34**, **38**, **25**, **27**, **31**, and **40**, respectively. If these double bonds had the opposite geometries, then cyclization at the nitrogen would only be possible for the ester carbonyl carbon substituting this double bond, which would lead to 5,5-ring fusion.



Scheme 3 Two possible tautomers of **24**

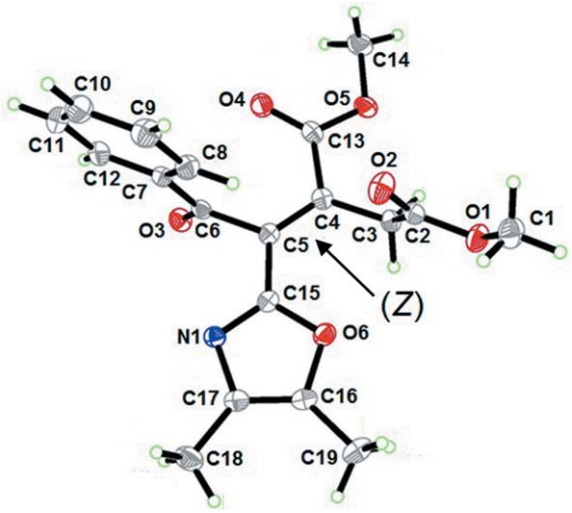


Figure 4 The X-ray crystal structure of **33** (CCDC 888330)

The ^{1}H NMR spectra of the highly functionalized 5,7-ring-fused compounds **32** and **35** (Table 3) showed the presence of four ester methoxy groups and two methyl groups on the C4 and C5 atoms of the thiazole and oxazole rings. Two downfield doublets (J = 5.2 Hz in **32** and J = 4.9 Hz in **35**) appeared, each of which integrated as one proton. The X-ray crystal structure of **35** confirmed this structure (Figure 5). The two ester groups on the two adjacent tertiary ring carbons are oriented *trans* to one another. The structures of **32** and **35** indicate that two equivalents of dimethyl acetylenedicarboxylate had reacted with one equivalent of the tautomeric pairs **20a**,**b** and **21a**,**b**, respectively.

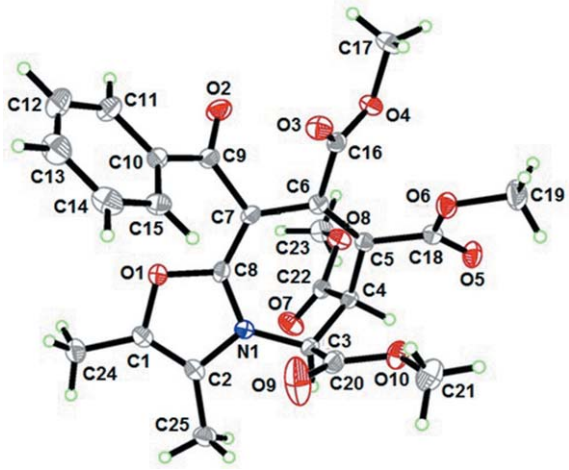


Figure 5 X-ray crystal structure of **35**. This crystal structure contains a 1:1 ratio of two slightly different geometries of **35** (see Supporting Information). Solvent molecules (acetone) are omitted for clarity (CCDC 888332).

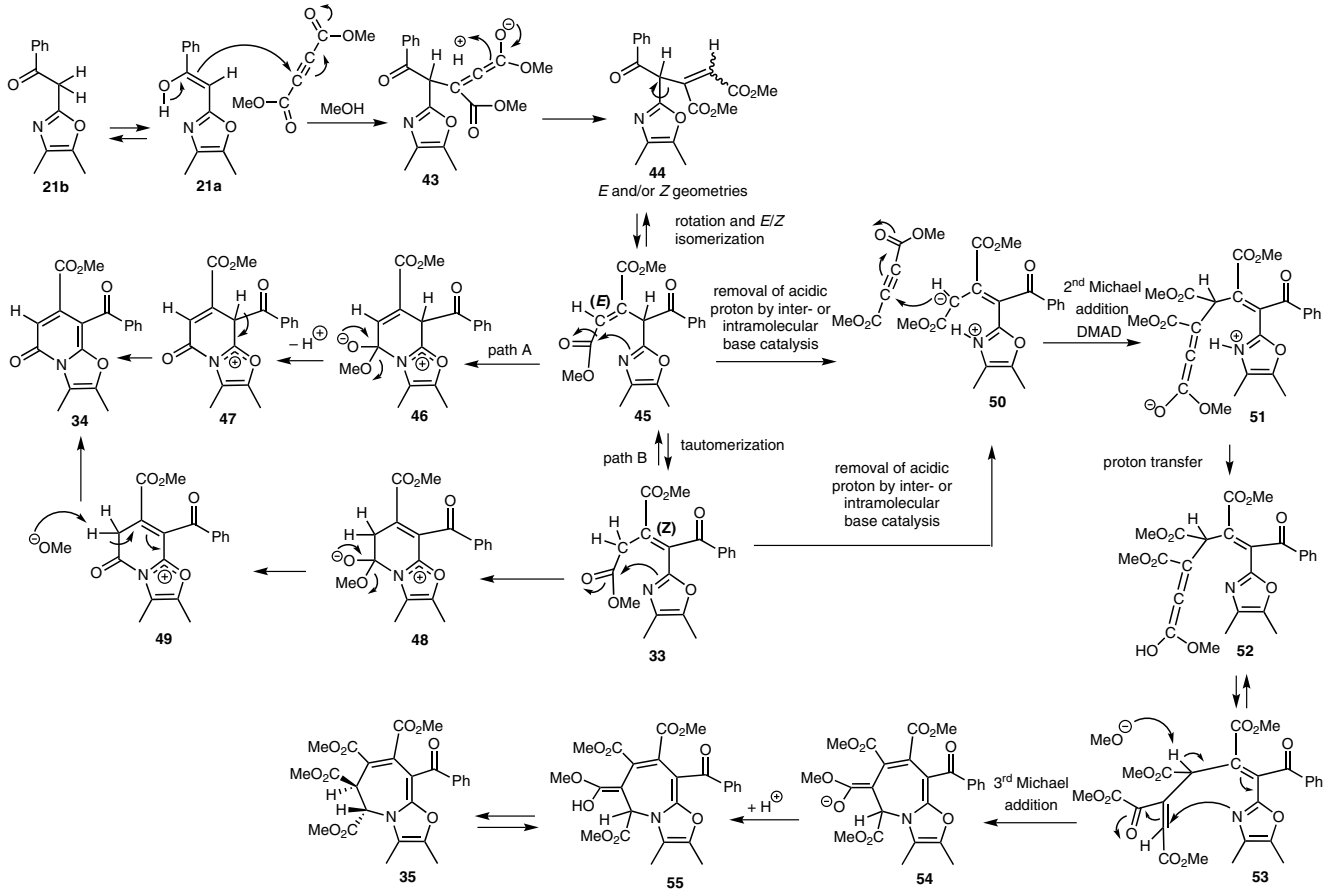
Possible reaction paths for the 5,6- and 5,7-ring fusion processes are shown in Scheme 4. The formation of compounds **34** and **35** from the tautomeric pair **21a**,**b** is used as an example. All the steps to **45** are common for paths to the open-chain and the 5,6- and 5,7-ring-fused products. Enol **21a**, or the corresponding enolate anion induced by the action of the oxazole nitrogen as a base, undergoes Michael addition to dimethyl acetylenedicarboxylate to give the allenic intermediate **43**. Protonation of the central carbon of the allene group of **43** results in the formation of enedioate **44**, which can have either an *E*- or a *Z*-geometry at the C=C bond. The *Z*-isomer cannot give the observed 5,6-ring-fused compound. Therefore, if the *Z*-isomer is present, it isomerizes to the *E*-isomer **45** before undergoing 5,6-ring fusion. Two possible pathways (A and B) starting from **45** can lead to the desired cyclocondensation. Nucleophilic attack by nitrogen on the terminal ester carbonyl carbon of **45** (path A) gives the zwitterionic intermediate **46**, which then expels a methoxy group to give oxazolium cation **47**. Finally, **47** is converted into the fused product **34** by loss of the acidic β-proton. In the alternative path B, *E*-isomer **45** first tautomerizes to give **33**, the isolated open-chain product mentioned in Table 3. The ester carbonyl of **33** is more electrophilic than the α,β-unsaturated ester carbonyl of **45** in Path A, but the ring nitrogen of **33** is less nucleophilic, because it is conjugated. Cyclocondensation of **33** through nitrogen nucleophilic attack gives **48**, which loses a methoxy group to form **49**. Subsequent loss of the acidic proton gives **34**.

The path to 5,7-ring fusion starts with removal of the acidic methylene proton of **45** with inter- or intramolecular base catalysis to form the zwitterionic intermediate **50**. Alternatively, tautomerization of **45** to **33**, also with inter- or intramolecular base catalysis, is followed by deprotonation of **33** to form zwitterion **50**. If **50** undergoes Michael addition to a second molecule of dimethyl acetylenedicarboxylate to give **51**, in competition with cyclization of **33** or **45** (leading to 5,6-ring fusion), the formation of the 5,7-ring-fused products become possible. Proton transfer from **51**, followed by keto–enol tautomerization of **52**, results in the formation of the enetetracarboxylate **53**. This can undergo intramolecular cyclization through a third Michael addition to give the fused derivative **54**. Protonation of **54** followed by keto–enol tautomerization of the product **55** gives the 5,7-ring-fused compound **35**.

Isolations of the open-chain products **24**, **26**, **30**, **33**, and **37** confirmed that the β-carbons of the starting tautomers can undergo Michael additions to dimethyl acetylenedicarboxylate (Scheme 5). We needed to determine whether **24**, **26**, **30**, **33**, **37**, and **39** are the actual precursors to the 5,6-ring-fused products **25**, **27**, **31**, **34**, **38** and **40**, respectively. To answer this question, we refluxed **37** in anhydrous methanol (Scheme 5). The fused product **38** was observed exclusively on a thin-layer chromatogram after refluxing **37** for 15 hours, and **38** was isolated in 99% yield, thereby confirming our hypothesis.

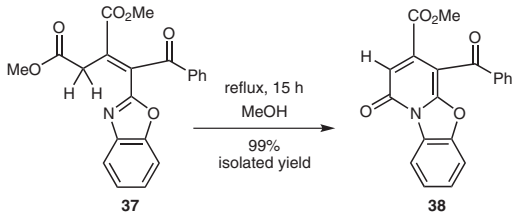
We envisioned that reactions of isolated open-chain products, such as **24**, with a base might facilitate the cyclocondensation (Scheme 6). To test this hypothesis, the isolated intermediates **24**, **30**, **33**, and **37** were refluxed in tetrahydrofuran containing the strong base sodium hydride, which should convert these intermediates quantitatively into their enolate anions (Table 5).

Intermediates **24**, **30**, and **37** were converted entirely into the corresponding 5,6-ring-fused compounds **25**, **31**, and **38**, respectively, when treated with sodium hydride in refluxing tetrahydrofuran for seven to eight hours (Table 5, entries 1, 2, and 5). No other products were observed by thin-layer chromatography (TLC). The reported yields are the isolated yields after workup, including column chromatography. Compound **33** was only partially converted into **34** after refluxing for 24 hours in tetrahydrofuran (Table 5, entry 3). Only a 40% yield of **34** was isolated, along with 39% of the unreacted starting intermediate **33**. Reaction in refluxing 1,4-dioxane (boiling point 101 °C) instead of tetrahydrofuran (boiling point 66 °C) gave only a 7% yield of **34**, along with 32% of unreacted **33**, after 24 hours (entry 4). Increasing the temperature may have destroyed the starting material **33**, the 5,6-ring-fused prod-



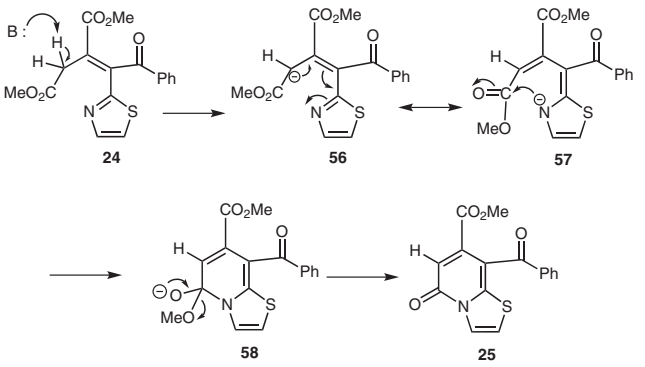
Scheme 4 Plausible mechanisms for the formation of 5,6- and 5,7-ring-fused compounds **34** and **35**, respectively

uct **34**, or both, thereby reducing the yield of **34**. Neither **33** nor **34** was refluxed in 1,4-dioxane in the absence of sodium hydride to test their thermal stability in this solvent.



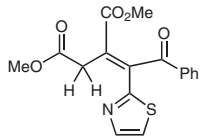
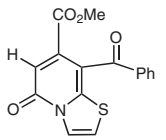
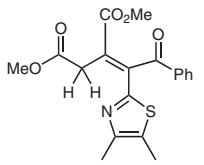
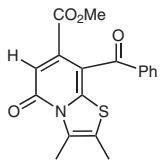
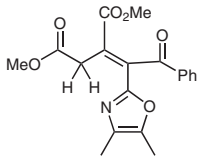
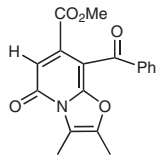
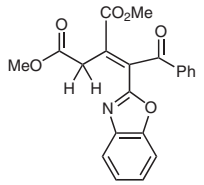
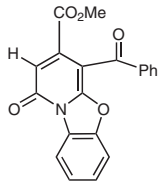
Scheme 5 Conversion of the open-chain product **37** into fused-ring product **38**

In an attempt to increase the yields of the 5,6-ring-fused compounds **31** and **34** and those of the 5,7-ring-fused compounds **32** and **35**, we added a stronger base (sodium methoxide) at the start of the reaction with the starting tautomers (Scheme 7). We speculated that this might enhance the rate of both the initial Michael addition to dimethyl acetylenedicarboxylate and of the cyclization step in a manner analogous to the conversion of **24** into **25** in Scheme 6. Tautomeric pairs **20a**,**b** and **21a**,**b** were independently treated with 2.5 equivalents of dimethyl acetylenedicarboxylate in methanol containing 0.32 or 0.28 equivalents of sodium methoxide, respectively (Scheme 7). The yields of **31** and **34** did increase (to 44 and 36%, respectively) compared with those reported in Table 3. The amount of **36** increased from 1 to 17%, and product **59** was observed for the first time. The 5,7-ring-fused compounds **32** or **35** were not detected by TLC.

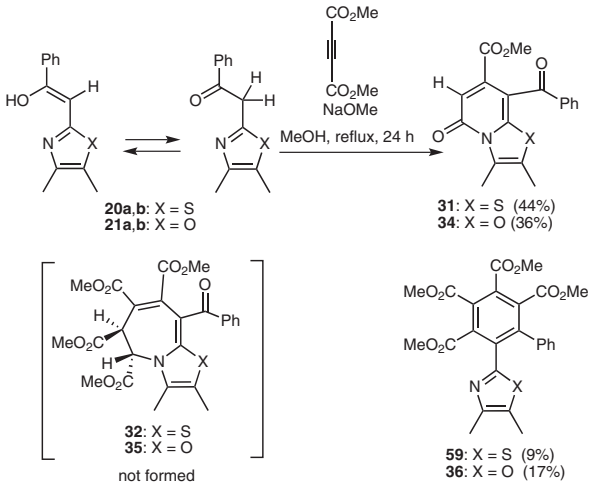


Scheme 6 Conversion of **24** into **25** in the presence of sodium hydride

Table 5 Synthesis of 5,6-Ring-Fused Heterocycles **25**, **31**, **34**, and **38** Starting from **24**, **30**, **33**, and **37**, Respectively, in the Presence of Sodium Hydride

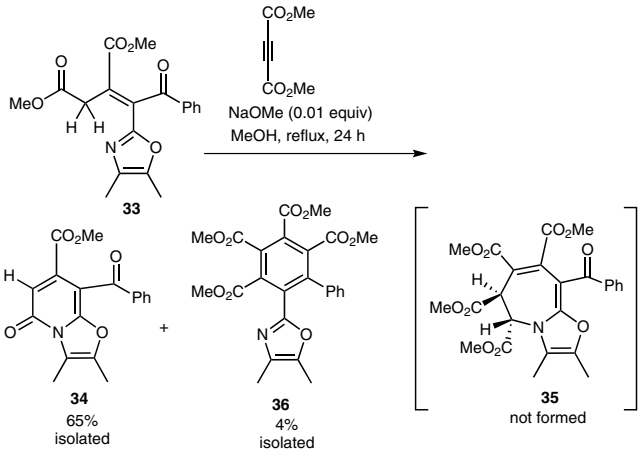
Entry	Substrate	Time (h)	Product	Yield[a] (%)
1	 **24**	7	 **25**	76
2	 **30**	8	 **31**	61
3[b]	 **33**	24	 **34**	40
4[c]		24		7
5	 **37**	8	 **38**	79

[a] Isolated yields were calculated by assuming 100% conversion of the open-chain product into the corresponding 5,6-ring-fused compound.
[b] 39% of **33** was recovered.
[c] 32% of **33** was recovered.



Scheme 7 Reactions of the tautomeric pairs **20a**,**b** and **21a**,**b** with dimethyl acetylenedicarboxylate in the presence of sodium methoxide

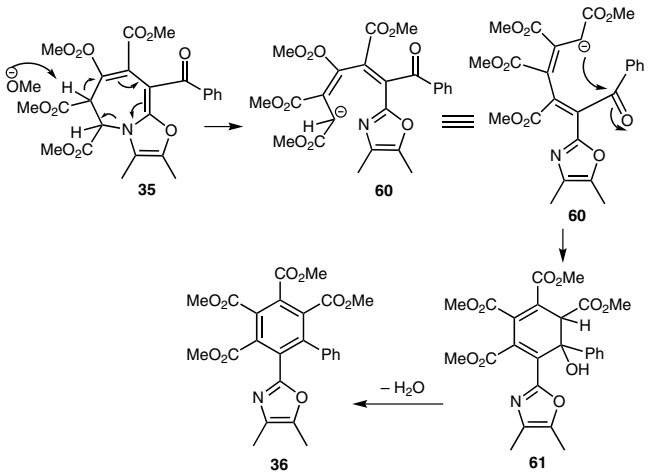
We also speculated that the reaction of intermediate **33** with dimethyl acetylenedicarboxylate in the presence of a base might increase the yield of the 5,7-ring-fused compound **35**. We therefore treated **33** with 1.1 equivalents of dimethyl acetylenedicarboxylate in the presence of small amount of sodium methoxide in refluxing methanol for 24 hours (Scheme 8). However, no **35** was detected and the 5,6-ring-fused products **34** (65%) and **36** (4%), together with unreacted **33** (18%), were isolated after workup. This absence of the 5,7-ring-fused product **35** is consistent with the results summarized in Scheme 7, starting from tautomers **21a**,**b** and 2.5 equivalents of dimethyl acetylenedicarboxylate.



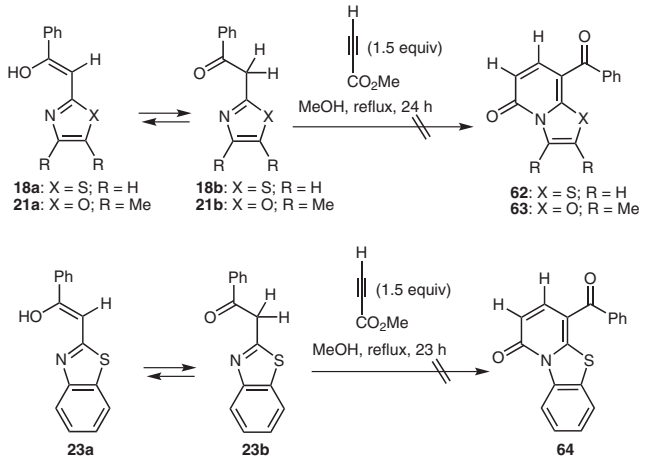
Scheme 8 Reaction of **33** with dimethyl acetylenedicarboxylate in the presence of sodium methoxide

This led us to postulate that the methoxide ion might induce reopening of the seven-membered ring of **35** to form the corresponding open-chain enolate anion **60**, which might then reclose by an aldol condensation to give the aryloxazole **36** (Scheme 9). To test this hypothesis, we treated **35** with ~0.9 equivalents of sodium methoxide in methanol at room temperature and we monitored the reaction by TLC. The TLC spot for **35** disappeared after only 15 min and a new spot appeared and was identified as aryloxazole **36**, which was isolated in 37% yield. This showed that if **35** had formed from **21a**,**b** (Scheme 7) or from **33** (Scheme 8) in the presence of methoxide, it might have been converted into to **36**.

Methyl propiolate is an α,β-alkynyl monoester analogous to dimethyl acetylenedicarboxylate. It was used in an attempt to extend the successful preparation of the 5,6-ring-fused compounds **25**, **27**, **31**, **34**, **38**, and **40** from tautomeric pairs **18a**,**b**–**23a**,**b** and dimethyl acetylenedicarboxylate. Methyl propiolate is a weaker electrophile than dimethyl acetylenedicarboxylate. When tautomeric pairs **18a**,**b**, **21a**,**b**, or **23a**,**b** were treated with methyl propiolate in methanol (Scheme 10), the expected 5,6-ring-fused compounds **62**, **63**, and **64** were not obtained.

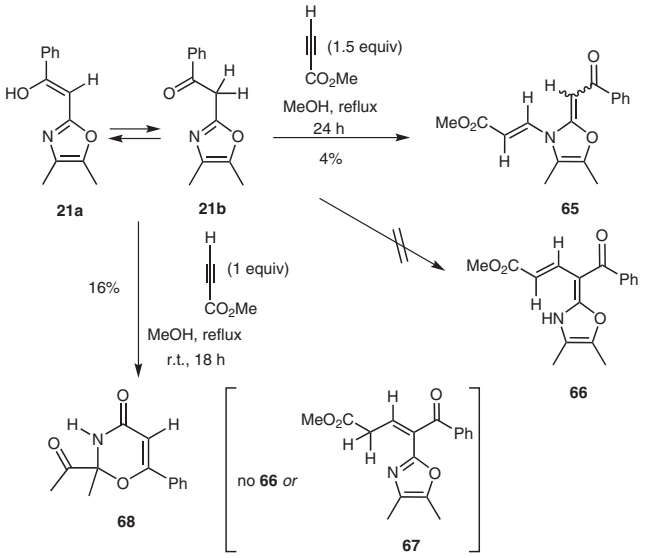


Scheme 9 Possible mechanism for the formation of aryloxazole **36** by ring opening of **35** with sodium methoxide in methanol



Scheme 10 Attempted reactions of the tautomeric pairs **18a**,**b**, **21a**,**b**, and **23a**,**b** with methyl propiolate

Unreacted tautomers were isolated along with unidentified byproducts when the thiazole-based tautomeric pair **18a**,**b** or the benzothiazole-based tautomeric pair **23a**,**b** was treated with 1.5 equivalents of methyl propiolate in refluxing methanol for 24 or 23 hours, respectively (see Supporting Information). No attempt was made at further purification or analysis of these unidentified fractions. One new compound **65** was isolated in 4% yield when the oxazole-based tautomeric pair **21a**,**b** was treated with 1.5 equivalents of methyl propiolate in refluxing methanol for 24 hours (Scheme 11). The ^{1}H NMR spectrum of **65** showed the presence of one ester methoxy group, three vinyl protons, five phenyl protons, and six methyl protons. Two vinyl protons were doublets with a 15-Hz coupling constant, consistent with vicinal *trans* vinyl proton coupling. This ruled out structure **67**. The presence of nine carbon signals in the DEPT 135 spectrum (see Supporting Information) excluded the other possible structure **66**, as only eight signals should be seen for **66**. The NOESY spectrum of **65** did not show clear evidence for an NOE interaction between the vinyl protons on the β-carbon and the carbon next to the nitrogen of the side-chain alkene. This might be due to a low rotational barrier about the exocyclic double bond, which could prevent observation of an NOE interaction. Therefore, the geometry of the *exo*-ring double bond at the β-carbon of **65** is unknown.



Scheme 11 Reactions of the tautomeric pair **21a**,**b** with methyl propiolate in methanol at the reflux or at room temperature

When tautomeric pair **21a**,**b** was treated with a single equivalent of methyl propiolate in methanol at room temperature, a new compound **68** was isolated in 16% yield, along with the recovered tautomers **21a**,**b** (39%). The structure of **68** was confirmed by X-ray crystallography (Figure 6).

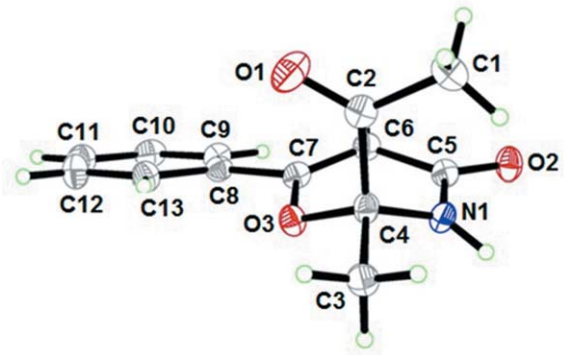


Figure 6 The X-ray crystal structure of **68**. This crystal structure contains two independent enantiomeric molecules (see Supporting Information) (CCDC 888331).

In conclusion, we prepared the (*Z*)-2-(heterocyclic)-1-phenylvinyl benzoates **4**, **15**, **5**, **6**, **16**, and **17** by treating the appropriate methylated heterocycles with benzoyl chloride. Hydrolysis of **4**, **15**, **5**, **6**, **16** and **17** with methanolic potassium hydroxide gave the corresponding 2-(heterocyclic)-1-phenylethenols **18a**–**23a** and their tautomers **18b**–**23b** These tautomeric pairs afforded a wide variety of products, including highly functionalized 5,6- and 5,7-

ring-fused heterocycles, when treated with dimethyl acetylenedicarboxylate. The reactivity of the keto–enol tautomeric pairs **18a**,**b**–**23a**,**b** depends on the nature of their heteroatoms and the substituents present on the ring. However, the corresponding 5,6-ring-fused heterocycles were not isolated when methyl propiolate, a weaker electrophile than dimethyl acetylenedicarboxylate, was used as a dielectrophile.

The scope of this work is not limited to 2-(heterocyclic)-1-phenylethenols and their keto tautomers, such as **11**, **18**–**23**, etc. We have previously shown[5] that aroyl chlorides, in general, can be used to prepare aryl derivatives of compounds **4**–**6**. Therefore, these aryl derivatives and their benzoxazole and benzothiazole analogues could be synthesized[6] and hydrolyzed to give the corresponding aryl-substituted keto and enol tautomeric analogues of **11** and **18**–**23**, thereby extending the scope of this synthetic route. However, aliphatic acid chlorides, with the exception of 2,2-dimethylpropanoyl chloride, failed in these reactions.[5]

Future efforts in this research area will involve attempts to optimize the reaction conditions for using methyl propiolate. Furthermore, this work could be extended to α,β-unsaturated esters, nitriles, ketones, or aldehydes, to explore the synthesis of new fused-ring heterocycles.

Chemicals and solvents were purchased from commercial suppliers and used as received, except for MeCN and Et_3N, which were distilled from CaH_2 under N_2. All reactions were carried out under N_2. Silica gel (230–400 mesh; pore size 60 Å; Sorbent Technologies) was used as the stationary phase for flash chromatography. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AVANCE III-300 or -600 spectrometer operating at 300 MHz or 600 MHz for protons, and at 75 MHz or 150 MHz for carbon-13. Chemical shifts are reported relative to the TMS as an internal standard for ^{1}H (δ = 0 ppm) and to the centerline of the deuterated solvent for ^{13}C ($CDCl_3$: δ = 77.0 ppm; DMSO-d_6: δ = 39.43 ppm). High-resolution mass spectra were recorded on a Bruker UHPLC-micro-Q/T MS/MS spectrometer in the ESI mode. Melting points were recorded with a Mel-Temp apparatus and are uncorrected. IR spectra were recorded on a Nicolet 6700 FT-IR spectrometer. A Bruker AXS Smart 1000 diffractometer, upgraded with an APEX II detector and software that incorporates SHELX components,[12] was employed for crystal-structure determinations at –173 °C.

(*Z*)-1-Phenyl-2-(thiazol-2-yl)vinyl Benzoate[5] (4): Typical Procedure

Et_3N (1.83 g, 18.1 mmol, 3.6 equiv) was added to a stirred soln of thiazole **1** (0.496 g, 5 mmol, 1 equiv) in MeCN (25 mL) at r.t. under N_2. BzCl (2.13 g, 15 mmol, 3 equiv) in MeCN (20 mL) was added dropwise at r.t. under N_2. The resulting soln was refluxed for 7 h, then cooled to r.t. MeCN was removed by rotary evaporation and the residue was dissolved in CH_2Cl_2 (30 mL), washed with sat. aq $NaHCO_3$ (2 × 30 mL), dried (Na_2SO_4), filtered, and concentrated by rotary evaporation. The crude product was purified by column chromatography [silica gel, EtOAc–hexane (1:3)] to give a yellow solid; yield: 1.364 g (89%); mp 105–106 °C; R_f = 0.39 (EtOAc–hexane, 1:3).

IR (neat): 3116, 3069, 3032, 2981, 1732, 1642, 1599, 1448, 1235, 1175, 1076, 1058, 1023, 762, 707, 692 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.33 (d, *J* = 7.48 Hz, 2 H), 7.82 (d, *J* = 3.0 Hz, 1 H), 7.71 (t, *J* = 7.40 Hz, 1 H), 7.63–7.55 and 7.37–7.40 (m, 8 H), 7.25 (d, *J* = 3.0 Hz, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 163.68, 161.42, 150.18, 142.77, 134.13, 133.85, 130.57, 129.63, 128.89, 128.85, 128.82, 124.96, 119.66, 112.08.

(*Z*)-2-(4,5-Dimethylthiazol-2-yl)-1-phenylvinyl Benzoate (5)[5]

By following the typical procedure, starting from thiazole **2** (0.636 g, 5 mmol, 1 equiv), Et_3N (1.84 g, 18 mmol, 3.6 equiv), and BzCl (2.13 g, 15 mmol, 3 equiv), benzoate **5** was isolated as a yellow solid; yield: 1.11 g (66%); mp 156–158 °C; R_f = 0.50 (EtOAc–hexane 1:3).

IR (neat): 3066, 3045, 2951, 2915, 1741, 1655, 1537, 1450, 1432, 1227, 1076, 1050, 1023, 885, 767, 694 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.33 (d, *J* = 7.55 Hz, 2 H), 7.72 (t, *J* = 7.40 Hz, 1 H), 7.62–7.56 and 7.38–7.35 (m, 7 H), 7.23 (s, 1 H), 2.31 (s, 3 H), 2.28 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 163.84, 156.69, 148.75, 148.38, 134.03, 134.01, 130.54, 129.29, 129.00, 128.85, 128.79, 127.80, 124.73, 112.24, 14.54, 11.35.

(*Z*)-2-(4,5-Dimethyloxazol-2-yl)-1-phenylvinyl Benzoate (6)[5]

By following the typical procedure, starting from oxazole **3** (0.585 g, 5 mmol, 1 equiv), Et_3N (1.87 g, 18.5 mmol, 3.7 equiv), and BzCl (2.15 g, 15.1 mmol, 3 equiv), benzoate **6** was isolated as a sticky oil; yield: 1.26 g (79%); R_f = 0.54 (EtOAc–hexane, 1:3).

IR (neat): 3062, 2978, 2953, 2923, 2858, 1738, 1633, 1449, 1236, 1175, 1082, 1064, 1024, 1000, 760, 705, 689 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.27 (d, *J* = 7.47 Hz, 2 H), 7.69–7.37 (m, 8 H), 6.83 (s, 1 H), 2.01 (s, 3 H), 1.92 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 164.62, 155.83, 149.71, 143.42, 133.82, 133.42, 132.00, 130.16, 129.54, 129.73, 128.69, 128.37, 124.86, 103.10, 10.92, 9.59.

(*Z*)-2-(4-Methylthiazol-2-yl)-1-phenylvinyl Benzoate (15)

By following the typical procedure, starting from thiazole **14** (2.29 g, 20 mmol, 1 equiv), Et_3N (7.29 g, 72 mmol, 3.6 equiv), and BzCl (8.54 g, 61 mmol, 3 equiv), benzoate **15** was isolated as a yellow solid; yield: 3.95 g (62%); mp 125–126 °C; R_f = 0.40 (EtOAc–hexane, 1:4).

IR (neat): 3107, 3073, 2971, 2929, 1731, 1635, 1599, 1510, 1448, 1421, 1232, 1079, 1059, 1025, 1000, 968, 871, 765, 750, 692 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.33 (d, *J* = 7.19 Hz, 2 H), 7.71 (t, *J* = 7.42 Hz, 1 H), 7.62–7.57 and 7.42–7.36 (m, 7 H), 7.30 (s, 1 H), 6.80 (s, 1 H), 2.43 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.73, 160.64, 152.69, 149.87, 134.06, 133.88, 130.50, 129.52, 128.88, 128.78, 124.84, 114.63, 111.95, 16.90.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{16}NO_2S$: 322.0900; found: 322.0880.

(*Z*)-2-(Benzoxazol-2-yl)-1-phenylvinyl Benzoate (16)

By following the typical procedure, starting from benzoxazole **7** (2.69 g, 20 mmol, 1 equiv), Et_3N (7.48 g, 74 mmol, 3.7 equiv), and BzCl (8.51 g, 60.5 mmol, 3 equiv), benzoate **16** was isolated as a white crystalline solid; yield: 2.94 g (43%); mp 97–98 °C; R_f = 0.58 (EtOAc–hexane, 1:4).

IR (neat): 3078, 1731, 1644, 1605, 1540, 1451, 1234, 1181, 1152, 1084, 1067, 1027, 946, 848, 790, 746, 701, 687 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.32 (d, *J* = 7.68 Hz, 2 H), 7.71–7.67, 7.60–7.54, 7.41–7.40 and 7.24–7.18 (m, 11 H), 7.11 (d, *J* = 8.04 Hz, 1 H), 7.04 (s, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 164.47, 159.75, 154.09, 150.06, 141.57, 133.67, 133.58, 130.45, 130.41, 129.37, 128.87, 128.56, 125.48, 125.19, 124.39, 119.95 and 110.12, 103.22.

(*Z*)-2-(Benzothiazol-2-yl)-1-phenylvinyl Benzoate (17)
By following the typical procedure, starting from benzothiazole **8** (1.51 g, 10 mmol, 1 equiv), Et_3N (3.71 g, 36.7 mmol, 3.7 equiv), and BzCl (4.26 g, 30 mmol, 3 equiv), benzoate **17** was isolated as yellow solid; yield: 1.89 g (53%); mp 146–148 °C; R_f = 0.54 (EtOAc–hexane, 1:4).

IR (neat): 3061, 2981, 1739, 1641, 1596, 1452, 1445, 1432, 1227, 1209, 1175, 1080, 1055, 1023, 1000, 850, 754, 656 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 8.36 (d, *J* = 7.80 Hz, 2 H), 7.97 (d, *J* = 8.19 Hz, 1 H), 7.73 (dd, *J* = 7.80, 7.61 Hz, 2 H), 7.65 (d, *J* = 7.65 Hz, 2 H), 7.60 (dd, *J* = 7.65, 7.56 Hz, 2 H), 7.45–7.39 (m, 5 H), 7.31 (t, *J* = 7.56 Hz, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 163.71, 161.38, 152.57, 152.48, 135.05, 134.20, 133.73, 130.63, 130.05, 128.95, 128.88, 128.80, 126.25, 125.32, 125.21, 123.00, 121.29, 112.44.

(*Z*)-1-Phenyl-2-(thiazol-2-yl)ethenol (18a) and 1-Phenyl-2-(thiazol-2-yl)ethanone (18b): Typical Procedure
A soln of KOH (0.788 g, 14.04 mmol, 2 equiv) in MeOH (10 mL) was added dropwise to a soln of benzoate **4** (2.144 g, 6.98 mmol, 1 equiv) in anhyd MeOH (15 mL), and the mixture was stirred for 24 h at r.t. MeOH was then removed by rotary evaporation and the residue was dissolved in H_2O (30 mL). The soln was neutralized with 1 M H_2SO_4 and extracted with CH_2Cl_2 (2 × 25 mL). The organic layer was washed with H_2O (30 mL), dried (Na_2SO_4), filtered, and concentrated by rotary evaporation. The crude product was purified by column chromatography [silica gel, EtOAc–hexane (1:4)] to give a dark-green oil; yield: 1.273 g (90%); R_f = 0.48 (EtOAc–hexane, 1:3). ^1H and ^{13}C NMR in $CDCl_3$ confirmed that the isolated product consists of the tautomers **18a** and **18b** in a 1:2.0 ratio.

IR (neat): 3117, 3084, 3060, 1687, 1622, 1598, 1576, 1494, 1483, 1449, 1263, 1210, 1100, 1070, 752, 686, 632 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 13.18 (br s, 1 H), 7.99 (d, *J* = 7.56 Hz, 2 H), 7.74 (d, *J* = 7.95 Hz, 2 H), 7.70 (d, *J* = 3.25 Hz, 1 H), 7.61 (d, *J* = 3.32 Hz, 1 H), 7.53 (t, *J* = 7.37 Hz, 2 H), 7.42 (t, *J* = 7.70 Hz, 2 H), 7.35–7.31 (m, 2 H), 7.26 (d, *J* = 3.25 Hz, 1 H), 7.00 (d, *J* = 3.32 Hz, 1 H), 6.28 (s, 1 H), 4.69 (s, 2 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 194.46, 168.35, 162.15, 160.64, 142.10, 140.11, 135.71, 134.60, 133.71, 129.63, 128.74, 128.52, 128.34, 125.42, 120.04, 114.39, 90.99, 42.65.

(*Z*)-2-(4-Methylthiazol-2-yl)-1-phenylethenol (19a) and 2-(4-Methylthiazol-2-yl)-1-phenylethanone (19b)
By following the typical procedure, starting from benzoate **15** (1.045 g, 3.25 mmol, 1 equiv) in anhyd MeOH (15 mL) and KOH (0.365 g, 6.51 mmol) in MeOH (10 mL), tautomers **19a**,**b** were isolated as a yellow solid; yield: 0.473 g (66.9%); mp 96–97 °C; R_f = 0.42 (EtOAc–hexane, 1:7). In $CDCl_3$, the ratio of **19a** to **19b** was 1:1.32.

IR (neat): 3106, 3053, 2956, 2918, 1608, 1574, 1519, 1492, 1454, 1259, 1035, 836, 758 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 13.44 (br s, 1 H), 7.98 (d, *J* = 7.23 Hz, 2 H), 7.74–7.72 (d, *J* = 7.73 Hz, 2 H), 7.52 (t, *J* = 6.90 Hz, 1 H), 7.42 (t, *J* = 7.79 Hz, 2 H), 7.37–7.42 (m, 3 H), 6.79 (d, *J* = 0.71 Hz, 1 H), 6.53 (d, *J* = 0.74 Hz, 1 H), 6.21 (s, 1 H), 4.63 (s, 2 H), 2.37 (s, *J* = 0.75 Hz, 3 H), 2.35 (d, *J* = 0.78 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 194.58, 167.58, 161.37, 160.52, 152.02, 150.11, 135.61, 134.67, 133.70, 129.53 128.27, 128.44, 128.37, 125.30, 114.56, 108.92, 91.06, 42.68, 16.95, 16.68.

(*Z*)-2-(4,5-Dimethylthiazol-2-yl)-1-phenylethenol (20a) and 2-(4,5-Dimethylthiazol-2-yl)-1-phenylethanone (20b)
By following the typical procedure, starting from benzoate **5** (0.502 g, 1.50 mmol, 1 equiv) in anhyd MeOH (10 mL) and KOH (0.168 g, 2.99 mmol, 2 equiv) in MeOH (10 mL), tautomers **20a**,**b** were isolated as a yellow solid; yield: 0.308 g (85%); mp 80–81 °C; R_f = 0.44 (EtOAc–hexane, 1:6). In $CDCl_3$, the ratio of **20a** to **20b** was 1:1.41.

IR (neat): 3089, 3055, 3038, 2980, 2918, 1630, 1573, 1555, 1492, 1454, 1268, 1146, 1060, 817, 770, 747, 687, 648 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 13.52 (br s, 1 H), 8.04 (d, *J* = 7.66 Hz, 2 H), 7.79 (d, *J* = 7.41 Hz, 2 H), 7.58 (t, *J* = 7.38 Hz, 1 H), 7.48 (t, *J* = 7.57 Hz, 2 H), 7.41–7.35 (m, 3 H), 6.19 (s, 1 H), 4.61 (s, 2 H), 2.32, 2.31, 2.30 (s, 12 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 194.79, 164.01, 160.45, 157.33, 147.50, 145.00, 135.86, 135.10, 133.57, 129.32, 128.69, 128.52, 128.33, 127.27, 125.25, 121.56, 90.64, 42.92, 14.52, 14.24, 11.14.

(*Z*)-2-(4,5-Dimethyloxazol-2-yl)-1-phenylethenol (21a) and 2-(4,5-Dimethyloxazol-2-yl)-1-phenylethanone (21b)
By following the typical procedure, starting from benzoate **6** (1.6 g, 5.1 mmol, 1 equiv) in anhyd MeOH (15 mL) and KOH (0.578 g, 10.3 mmol, 2 equiv) in MeOH (10 mL), tautomers **21a**,**b** were isolated as a dark-green oil; yield: 0.811 g (74%); R_f = 0.57 (EtOAc–hexane, 1:6). In $CDCl_3$, the ratio of **21a** to **21b** was 1:3.57.

IR (neat): 3059, 2980, 2953, 2924, 2882, 1693, 1633, 1598, 1578, 1532, 1496, 1449, 1293, 1201, 1066, 1012, 756, 713, 688, 639, 618 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 7.66 Hz, 2 H), 7.71 (d, *J* = 7.72 Hz, 2 H), 7.51 (m, 5 H), 7.32 (t, *J* = 7.56 Hz, 1 H), 5.91 (s, 1 H), 4.37 (s, 2 H), 2.17 (s, 3 H), 2.14 (s, 3 H), 2.03 (s, 3 H), 2.02 (s, 3 H); OH peak not seen.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 193.28, 161.23, 160.92, 155.28, 143.98, 140.21, 135.63, 134.42, 133.49, 130.61, 129.41, 128.88, 128.57, 128.36, 128.22, 125.08, 84.01, 38.81, 10.88, 10.73, 9.75, 9.63.

(*Z*)-2-(Benzo[*d*]oxazol-2-yl)-1-phenylethenol (22a) and 2-(Benzo[*d*]oxazol-2-yl)-1-phenylethanone (22b)
By following the typical procedure, starting from benzoate **16** (0.844 g, 2.47 mmol, 1 equiv) in anhyd MeOH (15 mL) and KOH (0.28 g, 5.2 mmol, 2.1 equiv) in MeOH (10 mL), tautomers **22a**,**b** were isolated as a greenish-white solid; yield: 0.541 g (92%); mp 87–89 °C; R_f = 0.64 (EtOAc–hexane, 1:5). In $CDCl_3$, the ratio of **22a** to **22b** was 1.06:1.

IR (neat): 3065, 3032, 3044, 2979, 1625, 1576, 1530, 1453, 1277, 1250, 1164, 1064, 850, 792, 743, 762, 702, 685 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 12.62 (br s, 1 H), 8.05 (d, *J* = 7.74 Hz, 2 H), 7.88 (m, 2 H), 7.72 (m, 1 H), 7.61 (m, 2 H), 7.52–7.45 (m, 7 H), 7.34–7.31 (m, 3 H), 7.28 (t, *J* = 7.66 Hz, 1 H), 6.21 (s, 1 H), 4.64 (s, 2 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 192.38, 166.19, 165.68, 160.41, 151.24, 148.69, 141.26, 139.85, 135.66, 134.03, 133.91, 130.56, 128.85, 128.53, 128.53, 125.82, 124.98, 124.61, 124.32, 124.08, 119.95, 117.85, 110.61, 110.19, 83.66, 39.56.

(*Z*)-2-(Benzo[*d*]thiazol-2-yl)-1-phenylethenol (23a) and 2-(Benzo[*d*]thiazol-2-yl)-1-phenylethanone (23b)
By following the typical procedure, starting from benzoate **17** (1.008 g, 2.82 mmol, 1 equiv) in anhyd MeOH (15 mL) and KOH (0.316 g, 5.63 mmol, 2 equiv) in MeOH (10 mL), tautomers **23a**,**b** were isolated as a yellowish-green solid; yield: 0.516 g (73%); mp 111–112 °C; R_f = 0.64 (EtOAc–hexane, 1:5). In $CDCl_3$, the ratio of **23a** to **23b** was 1.63:1.

IR (neat): 3057, 2922, 1610, 1596, 1573, 1494, 1473, 1436, 1378, 1264, 1249, 1136, 1057, 751, 729, 687, 668 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 13.91 (br s, 1 H), 8.07 (d, *J* = 7.68 Hz, 2 H), 7.99 (d, *J* = 8.13 Hz, 1 H), 7.85–7.87 (m, 3 H), 7.80 (d, *J* = 8.10 Hz, 1 H), 7.76 (d, *J* = 7.93 Hz, 1 H), 7.58 (dd, *J* = 8.13, 7.91 Hz, 1 H), 7.48 (dd, *J* = 7.68, 7.53 Hz, 2 H), 7.41–7.46 (m, 5 H), 7.36 (t, *J* = 7.53 Hz, 1 H), 7.27 (t, *J* = 7.53 Hz, 1 H), 6.35 (s, 1 H), 4.81 (s, 2 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 194.05, 168.07, 165.46 163.44, 152.68, 150.38, 135.88, 135.78, 134.74, 133.82, 131.37, 130.28, 128.81, 128.64, 128.48, 126.46, 125.96, 125.89, 125.05, 124.11, 122.85, 121.51, 121.37, 119.95, 90.83, 43.81.

Reaction of Tautomers 18a,b with Dimethyl Acetylenedicarboxylate: Typical Procedure

A soln of DMAD (0.63 g, 4.4 mmol, 2.5 equiv) in anhyd MeOH (5 mL) was added dropwise to a stirred soln of the tautomers **18a**,**b** (0.357 g, 1.76 mmol, 1 equiv) in anhyd MeOH (5 mL) at r.t. under N_2. (The molarities of DMAD and tautomers **18a**,**b** were 0.44 M and 0.18 M, respectively.) The soln was refluxed for 24 h under N_2 and then MeOH was removed by rotary evaporation. The residue was dissolved in CH_2Cl_2 (40 mL), washed with H_2O (2 × 40 mL), and dried (Na_2SO_4). CH_2Cl_2 was removed by rotary evaporation to give a crude product that was purified by column chromatography [silica gel, EtOAc–hexane (1:3 then 3:1)]. The open-chain intermediate product **24** eluted first and was followed by the 5,6-ring-fused product **25**. An orange-colored solid (0.135 g) was also isolated but not identified.

Dimethyl (2*E*)-2-[2-Oxo-2-phenyl-1-(1,3-thiazol-2-yl)ethylidene]succinate (24)

Yellow solid; yield: 0.079 g, 13%; mp 130–131 °C; R_f = 0.42 (EtOAc–hexane, 1:2).

IR (neat): 3134, 3112, 3096, 3040, 3001, 2951, 2843, 1733, 1712, 1679, 1663, 1612, 1448, 1256, 1198, 1176, 1113, 1102 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.08 (d, *J* = 7.73 Hz, 2 H), 7.96 (d, *J* = 2.64 Hz, 1 H), 7.55 (t, *J* = 7.26 Hz, 1 H), 7.45 (m, 3 H), 4.12 (s, 2 H), 3.79 (s, 3 H), 3.57 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 194.59, 171.01, 166.17, 160.50, 144.62, 143.84, 135.55, 133.55, 128.97, 128.80, 127.17, 122.73, 52.54, 52.54, 35.11.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{16}NO_5S$: 346.0749; found: 346.0740.

Methyl 8-Benzoyl-5-oxo-5*H*-[1,3]thiazolo[3,2-*a*]pyridine-7-carboxylate (25)

Yellow solid; yield: 0.278 g (51%); mp 145–146 °C; R_f = 0.42 (EtOAc–hexane, 1:1).

IR (neat): 3158, 3125, 3091, 3062, 3030, 3008, 2953, 1725, 1681, 1663, 1619, 1595, 1472, 1439, 1409, 1331, 1252, 1159, 1096, 1077 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.36 (d, *J* = 4.27 Hz, 1 H), 7.59 (d, *J* = 7.95 Hz, 2 H), 7.53 (t, *J* = 7.28 Hz, 1 H), 7.46 (m, 2 H), 7.31 (d, *J* = 4.27 Hz, 1 H), 6.67 (s, 1 H), 3.18 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 191.20, 166.43, 158.12, 154.89, 42.89, 139.37, 131.86, 128.54, 127.85, 124.14, 117.00, 109.81, 108.09, 52.39.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{12}NO_4S$: 314.0487; found: 314.0455.

Single crystals for X-ray crystallography were grown by the vapor-diffusion method by diffusing hexane into a soln of ester **25** in $CHCl_3$.

Reaction of Tautomers 19a,b with Dimethyl Acetylenedicarboxylate

The open-chain product **26** and the 5,6-ring-fused product **27** were prepared by treating DMAD (0.638 g, 4.44 mmol, 2.49 equiv) in anhyd MeOH (5 mL) with the tautomers **19a**,**b** (0.386 g, 1.78 mmol) in MeOH (5 mL) in accordance with the typical procedure described above. The molarities of DMAD and tautomers **19a**,**b** were 0.44 M and 0.18 M, respectively.

Dimethyl (2*E*)-2-[1-(4-Methyl-1,3-thiazol-2-yl)-2-oxo-2-phenylethylidene]succinate (26)

Yellow solid; yield: 0.073 g (12%); mp 114–115 °C; R_f = 0.47 (EtOAc–hexane, 1:2).

IR (neat): 3100, 2997, 2949, 2933, 1733, 1711, 1679, 1604, 1505, 1446, 1257, 1231, 1198, 1172 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 6.74 Hz, 2 H), 7.54 (t, *J* = 6.39 Hz, 1 H), 7.45 (dd, *J* = 6.74, 6.39 Hz, 2 H), 7.26 (s, 1 H), 4.12 (s, 2 H), 3.80 (s, 3 H), 3.57 (s, 3 H), 2.47 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 194.52, 171.19, 166.23, 159.22, 155.04, 143.81, 135.54, 133.42, 128.86, 128.69, 126.30, 117.87, 52.42, 51.98, 35.15, 17.02.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{18}NO_5S$: 360.0906; found: 360.0908.

Methyl 8-Benzoyl-3-methyl-5-oxo-5*H*-[1,3]thiazolo[3,2-*a*]pyridine-7-carboxylate (27)

Yellow solid; yield: 0.379 g (65%); mp 203–204 °C; R_f = 0.53 (EtOAc–hexane, 1:1).

IR (neat): 3128, 3066, 2981, 2951, 1723, 1667, 1625, 1594, 1475, 1435, 1406, 1304, 1255, 1144, 1126 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.57 (d, *J* = 7.14 Hz, 2 H), 7.51 (t, *J* = 7.38 Hz, 1 H), 7.44 (dd, *J* = 7.38, 7.14 Hz, 2 H), 6.74 (s, 1 H), 6.53 (s, 1 H), 3.16 (s, 3 H), 2.92 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 190.97, 166.35, 161.18, 157.55, 142.18, 139.56, 138.93, 131.64, 128.42, 127.78, 112.36, 111.34, 107.46, 52.26, 18.25.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{13}NO_4S$: 328.0663; found: 328.0644.

Reaction of Tautomers 20a,b with Dimethyl Acetylenedicarboxylate

The open-chain product **30**, the 5,6-ring-fused product **31**, and the 5,7-ring-fused product **32** were prepared by treating DMAD (0.638 g, 4.44 mmol, 2.49 equiv) in anhyd MeOH (5 mL) with tautomers **20a**,**b** (0.337 g, 1.46 mmol) in MeOH (5 mL) in accordance with the typical procedure described above. The molarities of DMAD and tautomers **20a**,**b** were 0.44 M and 0.15 M, respectively.

Dimethyl (2*E*)-2-[1-(4,5-Dimethyl-1,3-thiazol-2-yl)-2-oxo-2-phenylethylidene]succinate (30)

Brown sticky oil; yield: 0.175 g (32%); R_f = 0.50 (EtOAc–hexane, 2:1).

IR (neat): 3060, 3023, 2997, 2981, 2951, 2925, 2847, 1736, 1714, 1672, 1628, 1294, 1254, 1491, 1407, 1205, 1170, 1121, 939, 785, 729, 689 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 7.50 Hz, 2 H), 7.55 (t, *J* = 7.21 Hz, 1 H), 7.45 (dd, *J* = 7.50, 7.21 Hz, 2 H), 4.12 (s, 2 H), 3.79 (s, 3 H), 3.55 (s, 3 H), 2.33 (s, 3 H), 2.30 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 195.67, 171.33, 166.34, 154.98, 151.20, 144.00, 135.61, 133.32, 131.79, 128.83, 128.66, 129.95, 52.35, 51.94, 35.10, 14.70, 11.17.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{20}NO_5S$: 374.1062; found: 374.1074.

Methyl 8-Benzoyl-2,3-dimethyl-5-oxo-5*H*-[1,3]thiazolo[3,2-*a*]pyridine-7-carboxylate (31)

Yellow solid; yield: 0.08 g (16%); mp 172–174 °C; R_f = 0.58 (EtOAc–hexane, 1:1).

IR (neat): 3081, 3030, 2970, 2981, 2951, 2936, 1733, 1683, 1608, 1598, 1539, 1480, 1443, 1413, 1323, 1310, 1280, 1249, 1174, 1123, 981, 947, 847, 780, 694 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.56 (d, *J* = 7.84 Hz, 2 H), 7.51 (t, *J* = 7.02 Hz, 1 H), 7.44 (dd, *J* = 7.84, 7.02 Hz, 2 H), 6.53 (s, 1 H), 3.15 (s, 3 H), 2.82 (s, 3 H), 2.35 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 191.07, 166.55, 161.06, 155.57, 141.50, 139.73, 133.24, 131.61, 128.44, 127.85, 122.59, 111.68, 107.19, 52.25, 15.11, 11.61.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{16}NO_4S$: 342.0800; found: 342.0773.

Tetramethyl (5*S,6*S**)-9-Benzoyl-2,3-dimethyl-5,6-dihydro[1,3]thiazolo[3,2-*a*]azepine-5,6,7,8-tetracarboxylate (32)**
Yellowish-orange solid; yield: 0.173 g (23%); mp 216–218 °C: R_f = 0.45 (EtOAc–hexane, 3:1).

IR (neat): 1996, 2949, 2840, 1738, 1709, 1549, 1449, 1333, 1348, 1213, 1137, 997, 786, 740, 700, 662 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 7.16 Hz, 2 H), 7.38 (t, *J* = 7.34 Hz, 1 H), 7.31 (dd, *J* = 7.34, 7.16 Hz, 2 H), 5.76 (d, *J* = 5.2 Hz, 1 H), 4.98 (d, *J* = 5.2 Hz, 1 H), 3.71 (s, 3 H), 3.68 (s, 3 H), 3.67 (s, 3 H), 3.03 (s, 3 H), 2.24 (s, 3 H), 2.21 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 189.64, 169.06, 167.73, 167.70, 167.08, 160.25, 142.15, 140.86, 132.81, 130.45, 129.34, 127.53, 119.90, 116.90, 97.59, 64.12, 53.16, 53.07, 52.35, 51.93, 46.32, 12.51, 11.43.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{26}NO_9S$: 516.1328; found: 516.1286.

Reaction of Tautomeric Pair 21a,b with Dimethyl Acetylenedicarboxylate
The open-chain product **33**, the 5,6-ring-fused product **34**, and the 5,7-ring-fused product **35** were prepared by treating DMAD (0.601 g, 4.19 mmol, 2.51 equiv) in anhyd MeOH (5 mL) with tautomers **21a**,**b** (0.360 g, 1.67 mmol, 1 equiv) in MeOH (5 mL) in accordance with the typical procedure described above. The molarities of DMAD and tautomers **21a**,**b** were 0.42 M and 0.17 M, respectively.

Dimethyl (2*Z*)-2-[1-(4,5-Dimethyl-1,3-oxazol-2-yl)-2-oxo-2-phenylethylidene]succinate (33)
Yield: 0.212 g (36%); yellow solid; mp 110–111 °C; R_f = 0.65 (EtOAc–hexane, 1:1).

IR (neat): 3084, 3066, 3029, 2959, 2935, 2850, 1736, 1708, 1601, 1434, 1361, 1335, 1279, 1248, 1216, 1195, 1174, 1120, 942, 968, 896, 866 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 7.92 Hz, 2 H), 7.55 (t, *J* = 7.30 Hz, 1 H), 7.46 (dd, *J* = 7.92, 7.30 Hz, 2 H), 4.22 (s, 2 H), 3.78 (s, 3 H), 3.55 (s, 3 H), 2.16 (s, 3 H), 2.07 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 192.63, 171.13, 166.14, 154.61, 145.93, 138.17, 136.16, 134.06, 133.22, 128.77, 128.65, 126.95, 52.44, 52.09, 34.94, 11.19, 10.05.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{20}NO_6$: 358.1291; found: 358.1261.

Single crystals for X-ray crystallography were grown by the vapor-diffusion method by diffusing hexane into a soln of compound **33** in $CHCl_3$.

Methyl 8-Benzoyl-2,3-dimethyl-5-oxo-5*H*-[1,3]oxazolo[3,2-*a*]pyridine-7-carboxylate (34)
Yellow solid; yield: 0.023 g (4%); mp 162–164 °C; R_f = 0.44 (EtOAc–hexane, 2:1).

IR (neat): 3079, 2993, 2973, 2950, 2933, 1733, 1706, 1663, 1640, 1444, 1428, 1270, 1154, 971 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.56 (d, *J* = 8.42 Hz, 2 H), 7.50 (t, *J* = 7.38 Hz, 1 H), 7.44 (dd, *J* = 8.42, 7.38 Hz, 2 H), 6.54 (s, 1 H), 3.16 (s, 3 H), 2.83 (s, 3 H), 2.35 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 189.57, 166.08, 158.48, 153.22, 142.76, 142.10, 138.43, 132.84, 128.69, 128.45, 119.38, 109.85, 97.77, 52.62, 9.95, 9.79.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{16}NO_5$: 326.1028; found: 326.0998.

Single crystals for X-ray crystallography were grown by the vapor-diffusion method by diffusing hexane into a soln of compound **34** in $CHCl_3$.

Tetramethyl (5*S,6*S**)-9-Benzoyl-2,3-dimethyl-5,6-dihydro[1,3]oxazolo[3,2-*a*]azepine-5,6,7,8-tetracarboxylate (35)**
Intense yellow solid; yield: 0.392 g (47%); mp 170 °C (dec); R_f = 0.35 (EtOAc–hexane, 4:1).

IR (neat): 2997, 2991, 2980, 2930, 1729, 1683, 1657, 1570, 1515, 1430, 1232, 1227, 1225, 1170, 1120, 1097, 1000, 855, 768, 716, 695 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.60 (d, *J* = 7.58 Hz, 2 H), 7.39 (t, *J* = 7.25 Hz, 1 H), 7.31 (dd, *J* = 7.58, 7.25 Hz, 2 H), 5.42 (d, *J* = 4.9 Hz, 1 H), 5.26 (d, *J* = 4.9 Hz, 1 H), 3.74 (s, 3 H), 3.73 (s, 3 H), 3.69 (s, 3 H), 3.65 (s, 3 H), 2.05 (s, 3 H), 1.83 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 192.37, 170.38, 168.76, 167.08, 166.58, 158.96, 144.31, 141.85, 138.12, 130.69, 128.40, 127.71, 121.44, 110.70, 89.79, 60.29, 53.28, 53.16, 52.32, 52.25, 44.93, 9.59, 7.59.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{26}NO_{10}$: 500.1557; found: 500.1530.

Single crystals for X-ray crystallography were grown by the vapor-diffusion method by diffusing hexane into a soln of compound **35** in acetone.

Tetramethyl 6-(4,5-Dimethyl-1,3-oxazol-2-yl)biphenyl-2,3,4,5-tetracarboxylate (36)
Off-white solid; yield: 0.011 g (1%); mp 124–126 °C; R_f = 0.35 (EtOAc–hexane, 2:3).

IR (neat): 3023, 3018, 3001, 2981, 2956, 2928, 1735, 1438, 1335, 1209, 1187, 1176, 1153, 1094, 924, 857, 715 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.29 (m, 3 H), 7.06 (d, *J* = 7.19 Hz, 2 H), 3.90 (s, 3 H), 3.88 (s, 3 H), 3.76 (s, 3 H), 3.50 (s, 3 H), 1.99 (s, 3 H), 1.92 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.71, 166.42, 165.85, 165.82, 154.26, 144.52, 142.90, 136.44, 135.98, 135.27, 131.75, 131.48, 130.99, 129.89, 53.24, 53.20, 52.88, 52.51, 11.08, 9.57.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{24}NO_9$: 482.1451; found: 482.1435.

Reaction of Tautomeric Pair 22a,b with Dimethyl Acetylenedicarboxylate
The open-chain product **37** and the 5,6-ring-fused product **38** were prepared by treating DMAD (0.308 g, 2.15 mmol, 1.5 equiv) in anhyd MeOH (5 mL) with tautomers **22a**,**b** (0.339 g, 1.43 mmol, 1 equiv) in MeOH (5 mL) in accordance with the typical procedure. The molarities of DMAD and tautomers **22a**,**b** were 0.22 M and 0.14 M, respectively.

Dimethyl (2*Z*)-2-[1-(1,3-Benzoxazol-2-yl)-2-oxo-2-phenylethylidene]succinate (37)
Yellow solid; yield: 0.01 g (2%); mp 130–132 °C; R_f = 0.48 (EtOAc–hexane, 1:2).

IR (neat): 3086, 3067, 2981, 2952, 2923, 2849, 1743, 1720, 1694, 1596, 1534, 1449, 1434, 1296, 1243, 1209, 1181, 1001, 944, 753, 725, 692 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.08 (d, *J* = 8.53 Hz, 2 H), 7.77–7.73 (m, 1 H), 7.57 (t, *J* = 7.93 Hz, 1 H), 7.50–7.47 (m, 3 H), 7.37–7.33 (m, 2 H), 4.38 (s, 2 H), 3.81 (s, 3 H), 3.61 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 192.12, 170.72, 165.75, 158.21, 150.05, 141.13, 138.43, 135.96, 133.64, 132.39, 128.93, 128.90, 126.92, 125.25, 121.12, 111.10, 52.86, 52.47, 35.45.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{18}NO_6$: 380.1134; found: 380.1115.

Methyl 4-Benzoyl-1-oxo-1*H*-pyrido[2,1-*b*][1,3]benzoxazole-3-carboxylate (38)

Pale-yellow solid; yield: 0.46 g (93%); mp 193–195 °C; R_f = 0.48 (EtOAc–hexane, 1:1).

IR (neat): 3081, 3040, 3006, 2952, 1739, 1687, 1648, 1634, 1599, 1516, 1441, 1418, 1297, 1250, 1164, 1050, 1000, 850, 790, 782, 757, 623 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 8.64 (d, *J* = 7.49 Hz, 2 H), 7.85 (d, *J* = 7.74 Hz, 1 H), 7.61 (t, *J* = 7.31 Hz, 1 H), 7.50–7.44 (m, 5 H), 6.89 (s, 1 H), 3.61 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 189.40, 165.57, 158.07, 152.87, 147.03, 143.08, 137.96, 133.34, 128.99, 128.69, 127.72, 126.44, 125.56, 117.37, 112.76, 110.96, 98.16, 52.94.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{14}NO_5$: 348.0872; found: 348.0829.

Single crystals for X-ray crystallography were grown by the vapor-diffusion method by diffusing hexane into a soln of compound **38** in $CHCl_3$.

Reaction of Tautomeric Pair 23a,b with Dimethyl Acetylenedicarboxylate

The 5,6-ring-fused product **40** was synthesized by treating DMAD (0.226 g, 1.57 mmol, 1.5 equiv) in anhyd MeOH (5 mL) with tautomers **23a**,**b** (0.261g, 1.03 mmol, 1 equiv) in MeOH (15 mL) in accordance with the typical procedure. The molarities of tautomers **23a**,**b** and DMAD were 0.05 M and 0.08 M, respectively.

Methyl 4-Benzoyl-1-oxo-1*H*-pyrido[2,1-*b*][1,3]benzothiazole-3-carboxylate (40)

Intense-yellow solid; yield: 0.317 g (85%); mp 234–236 °C; R_f = 0.43 (EtOAc–hexane, 1:2).

IR (neat): 3126, 3094, 3068, 3013, 2981, 2952, 1719, 1672, 1621, 1559, 1492, 1434, 1409, 1289, 1264, 1244, 1196, 1120, 1066, 996, 945, 858, 805, 762, 679, 620 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 9.32 (d, *J* = 8.14 Hz, 2 H), 7.81 (d, *J* = 7.32 Hz, 1 H), 7.63 (t, *J* = 7.5 Hz, 1 H), 7.60–7.53 (m, 3 H), 7.47 (dd, *J* = 8.14, 7.50 Hz, 2 H), 6.83 (s, 1 H), 3.23 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 191.72, 166.09, 161.13, 154.90, 141.70, 139.25, 137.20, 132.12, 128.61, 128.35, 127.98, 127.48, 127.06, 121.66, 120.34, 113.92, 108.16, 52.46.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{14}NO_4S$: 364.0644; found: 364.0600.

Conversion of the Open-Chain Product 37 into the 5,6-Ring-Fused Product 38

A soln of open-chain product **37** (0.20 g, 0.53 mmol) in anhyd MeOH (3 mL) was refluxed and the reaction was monitored by TLC. When the spot for **37** disappeared after 15 h, the MeOH was removed by rotary evaporation and the residue was dissolved in CH_2Cl_2 (10 mL) and washed with H_2O (2 × 10 mL). The organic layer was dried (Na_2SO_4), filtered, and concentrated; yield: 0.182 g (99%).

Synthesis of the 5,6-Fused-Ring Product 25 from the Open-Chain Product 24 by Treatment with Sodium Hydride: Typical Procedure

A soln of the open-chain product **24** (0.301 g, 0.84 mmol) in THF (10 mL) was added to a mixture of a 60% suspension of NaH in mineral oil (0.051 g, 1.28 mmol, 1.5 equiv) and THF (10 mL) at r.t. under N_2. Bubbles of H_2 evolved. When the mixture had been refluxed for 7 h and unreacted **24** was no longer observed by TLC, the THF was removed by rotary evaporation. The residue was dissolved in CH_2Cl_2 (30 mL), washed with H_2O (2 × 20 mL), dried (Na_2SO_4), and concentrated by rotary evaporation. The crude product was purified by column chromatography [silica gel, EtOAc–hexane (1:1)]; yield: 0.086 g (76%).

Synthesis of Other 5,6-Ring-Fused Products from Open-Chain Products by Treatment With Sodium Hydride

By following the typical procedure, refluxing **31** (0.114 g, 0.31 mmol, 1 equiv) and NaH (0.02 g, 0.5 mmol, 1.6 equiv) in THF (20 mL) for 8 h gave **30**; yield: 0.064 g (61%).

By following the typical procedure, refluxing **33** (0.203 g, 0.57 mmol) and NaH (0.034 g, 0.85 mmol, 1.5 equiv) in THF (20 mL) for 24 h gave **34**; yield: 0.073 g (40%). Unreacted **33** (38.6%) was also recovered. On refluxing **33** (0.208 g, 0.58 mmol) and NaH (0.035 g, 0.88 mmol, 1.5 equiv) in 1,4-dioxane (20 mL) for 24 h, **34** was obtained in 7% yield (0.013 g) with 31.6% recovery of **33**.

By following the typical procedure, refluxing **37** (0.121 g, 0.32 mmol) and NaH (0.02 g, 0.5 mmol, 1.6 equiv) in THF (20 mL) for 8 h gave **38**: yield: 0.088 g (79%).

Tetramethyl 6-(4,5-Dimethyl-1,3-thiazol-2-yl)biphenyl-2,3,4,5-tetracarboxylate (59)

A soln of DMAD (0.523 g, 3.64 mmol, 2.5 equiv) in anhyd MeOH (5 mL) was added dropwise to a soln of the tautomers **20a**,**b** (0.337 g, 1.46 mmol) in anhyd MeOH (5 mL) at r.t. under N_2. A 25 wt% soln of NaOMe in MeOH (0.1 mL, 0.5 mmol, 0.32 equiv) was then added and the mixture was refluxed for 24 h under N_2. MeOH was removed by rotary evaporation, and the residue was dissolved in CH_2Cl_2 (40 mL), washed with H_2O (2 × 40 mL), dried (Na_2SO_4), and concentrated by rotary evaporation. The crude product was purified by column chromatography [silica gel, EtOAc–hexane (1:2)]. The 5,6-ring-fused product **31** [yield: 0.221 g (44%)] eluted first, and this was followed by the open-chain product **59** as an off-white solid; yield: 0.067 g (9%); mp 165–166 °C; R_f = 0.50 (EtOAc–hexane, 1:2).

IR (neat): 3081, 3030, 2981, 2951, 2936, 1733, 1683, 1608, 1598, 1539, 1480, 1443, 1310, 1413, 1323, 1280, 1249, 947, 789, 747, 726, 694 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 7.36–7.29 (m, 3 H), 7.11 (d, *J* = 7.68 Hz, 2 H), 3.89 (s, 3 H), 3.87 (s, 3 H), 3.72 (s, 3 H), 3.47 (s, 3 H), 2.26 (s, 3 H), 2.20 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.95, 166.81, 166.08, 165.78, 156.93, 148.01, 141.68, 135.96, 135.81, 135.28, 134.94, 131.41, 130.18, 130.99, 129.50, 128.55, 128.14, 53.15, 53.10, 52.49, 52.40, 14.41, 11.18.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{25}H_{24}NO_8S$: 498.1223; found: 498.1182.

Reaction of the Tautomeric Pair 21a,b with Dimethyl Acetylenedicarboxylate in the Presence of Sodium Methoxide in Methanol

The reaction of DMAD (0.599 g, 4.17 mmol, 2.5 equiv) with tautomers **21a**,**b** (0.359 g, 1.67 mmol) in the presence of NaOMe (0.1 mL, 0.5 mmol, 0.28 equiv) in MeOH (10 mL) for 24 h gave the 5,6-ring-fused product **34** [yield: 0.286 g (36%)] and tetracarboxylate **36** yield: 0.089 g (17%).

Reaction of Succinate 33 with Dimethyl Acetylenedicarboxylate in the Presence of Sodium Methoxide

A soln of DMAD (0.112 g, 0.78 mmol, 1.1 equiv) in anhyd MeOH (2 mL) was added dropwise to a soln of succinate **33** (0.255 g, 0.71 mmol) in anhyd MeOH (2 mL) at r.t. under N_2. A 25 wt% soln of NaOMe in MeOH (1.5 μL, 0.01 equiv) was added and the resulting soln was refluxed for 24 h under N_2. MeOH was removed by rotary evaporation, and the residue was dissolved in CH_2Cl_2 (40 mL), washed with H_2O (2 × 40 mL), dried (Na_2SO_4), and concentrated by rotary evaporation. The crude product was purified by column chromatography [silica gel, EtOAc–hexane (1:2)]. The 5,7-ring-fused product **35** was not detected by TLC but, instead, the 5,6-ring-fused product **34** [yield: 0.15 g (65%)] and the tetracarboxylate **36** [yield: 0.012 g (4%)] were obtained. In addition, 18% of the starting succinate **33** was also recovered.

Reaction of 5,7-Ring-Fused Product 35 with Sodium Methoxide in Methanol

A soln of NaOMe in MeOH (0.09 mL, 0.4 mmol, 0.9 equiv) was added to a soln of **35** (0.2 g, 0.4 mmol) in MeOH at r.t. The intense yellow color of the **35** in MeOH changed to a dark brown. After stirring for 15 min at r.t., the soln was analyzed by TLC. The spot for the starting 5,7-ring-fused **35** had disappeared while a new spot appeared on the TLC plate and was identified as corresponding to tetracarboxylate **36**. After 15 min, MeOH was removed by rotary evaporation and the products were purified according to the general workup procedure and by column chromatography [silica gel, EtOAc–hexane (1:1) to give tetracarboxylate **36**; yield: 0.072 g (37.1%).

Reaction of Tautomeric Pair 21a,b with Methyl Propiolate in Refluxing Methanol

A soln of methyl propiolate (0.264 g, 3.11 mmol, 1.51 equiv) in anhyd MeOH (15 mL) was added dropwise to a stirred soln of tautomers **21a**,**b** (0.444 g, 2.06 mmol, 1 equiv) in anhyd MeOH (10 mL) at r.t. under N_2. The molarities of methyl propiolate and tautomers **21a**,**b** were 0.21 M and 0.14 M, respectively. The resulting soln was refluxed for 24 h under N_2, and then MeOH was removed by rotary evaporation. In addition to a spot for the unreacted **21a**,**b**, two new spots were detected by TLC (EtOAc–hexane, 1:2). The products were isolated and purified by following the general workup procedure. The crude product was further purified by column chromatography [silica gel, EtOAc–hexane (1:3 then 1:1)]. Unreacted **21a**,**b** [0.291g (66%)] was eluted first (**21a**/**21b** ratio 1:3.03 in $CDCl_3$), followed by oxazole **65**; yield: 0.022 g (4%). A more polar intense-yellow solid (0.026 g), corresponding to the third spot on the TLC, was also isolated; R_f = 0.29 (EtOAc–hexane, 1:2).

Repetition of this reaction with **21a**,**b** (0.37 g, 1.7 mmol, 1 equiv) and methyl propiolate (0.222 g, 2.61 mmol, 1.52 equiv) in refluxing MeOH (10 mL) for 27 h gave the unreacted starting tautomers **21a**,**b** [0.15 g (41%)], **65** [yield: 0.03 g (6%)], and the same unidentified intense-yellow solid (0.058 g).

Methyl (2*E*)-3-[4,5-Dimethyl-2-(2-oxo-2-phenylethylidene)-1,3-oxazol-3(2*H*)-yl]acrylate (65)

Yellow solid; yield: 0.022 g (4%); mp 150–152 °C; R_f = 0.40 (EtOAc–hexane, 1:2).

IR (neat, cm^{-1}): 3084, 3001, 2951, 2850, 1699, 1635, 1597, 1573, 1450, 1351, 1326, 1289, 1239, 1222, 1152, 1123, 1064, 978, 924, 861, 834, 763, 680.

^1H NMR (600 MHz, $CDCl_3$): δ = 8.09 (d, *J* = 14.95 Hz, 1 H), 7.46 (m, 5 H), 6.70 (s, 1 H), 5.32 (d, *J* = 14.95 Hz, 1 H), 3.75 (s, 3 H), 2.03 (s, 3 H), 1.72 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 203.52, 168.84, 167.46, 162.13, 134.10, 131.51, 129.44, 129.39, 127.24, 120.34, 99.73, 75.44, 51.57, 23.39, 18.21.

HRMS (ESI): *m/z* $[M + 2H]^+$ calcd for $C_{17}H_{19}NO_4$: 301.1314; found: 301.1407.

Reaction of Tautomeric Pair 21a,b with Methyl Propiolate in Methanol at Room Temperature

A soln of methyl propiolate (0.097 g, 1.1 mmol, 1 equiv) in anhyd MeOH (10 mL) was added dropwise to a stirred soln of the tautomers **21a**,**b** (0.24 g, 1.1 mmol, 1 equiv) in anhyd MeOH (15 mL) at r.t. under N_2. (The molarities of methyl propiolate and tautomers **21a**,**b** were both 0.05 M.) The soln was stirred for 18 h under N_2 and then MeOH was removed by rotary evaporation. Workup according to the general procedure gave a crude product that was further purified by column chromatography [silica gel, EtOAc–hexane (1:3 then 2:1)] to give oxazinone **68** [yield: 0.042 g (16%)], along with unreacted **21a**,**b** [0.096 g (39%)]; the **21a**/**21b** ratio was 1:2.86.

The reaction of **21a**,**b** (0.269 g, 1.25 mmol, 1 equiv) with methyl propiolate (0.109 g, 1.28 mmol, 1 equiv) in MeOH (20 mL) at r.t. for 24 h gave **68** in 13% (0.036 g) yield.

2-Acetyl-2-methyl-6-phenyl-2,3-dihydro-4*H*-1,3-oxazin-4-one (68)

Pale-yellow solid; yield: 0.042 g (16%); mp 142–144 °C; R_f = 0.45 (EtOAc–hexane, 1:2).

IR (neat): 3168, 3055, 2895, 1727, 1652, 1451, 1394, 1197, 1108, 1053, 1021, 952, 900, 825, 769, 684, 664 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.37 (s, 1 H), 7.78 (d, *J* = 7.37 Hz, 2 H), 7.54–7.44 (m, 3 H), 5.83 (s, 1 H), 2.33 (s, 3 H), 1.79 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.48, 165.55, 164.12, 131.67, 131.45, 128.76, 126.56, 96.55, 91.09, 24.80, 22.09.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{13}H_{14}NO_3$: 232.0974; found: 232.0992.

Single crystals for X-ray crystallography were grown by the vapor-diffusion method by diffusing hexane into a soln of compound **68** in $CHCl_3$.

Crystallographic data for compounds **25**, **33**, **34**, **35** **38**, and **68** have been deposited with the accession numbers CCDC 88832, CCDC 888330, CCDC 888334, CCDC 888332, CCDC 888333, and CCDC 888331, respectively, and can be obtained free of charge from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44(1223)336033; E-mail: deposit@ccdc.cam.ac.uk; Web site: www.ccdc.cam.ac.uk/conts/retrieving.html.

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Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis. This contains details of the experimental procedures discussed in this article, along with detailed peak assignments for ^1H and ^{13}C NMR spectra and DEPT 135 data.

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