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An Unprecedented Chemospecific and Stereoselective Tandem Nucleophilic Addition/Cycloaddition Reaction of Nucleophilic Carbenes with Ketenimines

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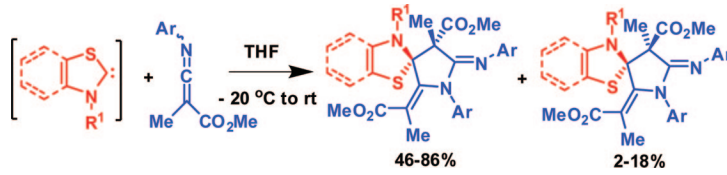

The first study of the reaction between nucleophilic carbenes and ketenimines is reported. The interaction of thiazole and benzothiazole carbenes with ketenimines proceeded in a chemospecific and stereoselective manner to produce thiazole- and benzothiazole-spiro-pyrrole derivatives generally in good yields. The reaction was proposed to proceed via a tandem nucleophilic addition of carbene to the C═N bond of ketenimine followed by a stepwise [3+2] cycloaddition of the 1,3-dipolar intermediate with the C═C bond of ketenimine. This reaction provides a powerful protocol for the construction of novel polyfunctional thiazole-spiro-pyrrole or benzothiazole-spiro-pyrrole compounds that are not readily accessible by other methods.

Introduction

Nucleophilic carbenes, especially the *N*-heterocyclic carbenes, have attracted considerable attention in recent years, not only because they can be used as organocatalysts[1] and as ligands in organometallic catalysts,[2] but also because they are versatile intermediates in the construction of novel multifunctional heterocycles.[3] Among the reactions of nucleophilic carbenes, those with various heterocumulenes have the most important applications in organic synthesis. For example, depending on the structures of both reactants, the reaction of nucleophilic carbenes with isocyanates can either form 1+1 adducts indole-2-one (or hydrogenated indole-2-one)[4] or 1+2 adducts imidazoline-2,4-dione derivatives.[5] Cyclization between nucleophilic carbenes and vinyl ketenes affords a concise method for the preparation of cyclopentenones.[6] Rigby and co-workers have successfully applied the reaction of bis(alkylthio)carbene with vinyl and indolyl isocyanates in the total syntheses of alkaloid Mesembrine[7a] and Phenserine.[7b] In addition to cycloaddition with heterocumulenes to afford cyclic products, *N*-heterocyclic carbenes can also undergo nucleophilic addition to cumulenes and heterocumulenes including allenoates,[8] isothiocyanates,[9] carbon dioxide,[10] and carbon disulfide[11] to form stable dipolar inner salts. In 2006, we found for the first time that the inner salts derived from *N*-heterocyclic carbenes and aryl isothiocyanates were unique ambident C^+-C-S^- and C^+-C-N^- bisdipoles.[12a] Since then, these *N*-heterocyclic carbene-derived 1,3-

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dipoles have been developed into versatile synthons in the construction of novel spiro and fused heterocycles by our group.[12]

Ketenimines,[13] the heterocumulenes that are structurally similar to isocyanates and ketenes, have numerous synthetic potentialities. For instance, [2+2],[14] [3+2],[15] and [4+2][14a,16] cycloadditions of ketenimines have become one of the most useful protocols for the construction of cyclic compounds. Furthermore, addition reactions constitute another important feature of ketenimines. Depending on the substituents attached to the cumulated double bonds, ketenimines are known to act either as electrophiles to react with nucleophilic reagents such as water,[17] alcohols and thiols,[18] thioketone,[19] amines,[20] enamines,[19,21] isonitriles,[22] and Grignard reagent,[23] or act as nucleophiles toward arylsulfenyl, arylsulfinyl, and arylsulfonyl chloride, trimethylhalosilane, and acid chlorides.[18,24] Although both ketenimines and nucleophilic carbenes have found applications in organic synthesis, surprisingly, to the best of our knowledge, the reaction between these two electrophiles and nucleophiles has never been reported so far.

TABLE 1. The Reaction of 3-Ethyl-4-methylthiazolium Salt 1a with Methyl 2-Methyl-3-(phenylimino)acrylate 3a under Different Conditions

	reaction conditions					
entry	**1a**:**3a**	base	solvent	temp	time	yield of **4a-I**[a]
1	1:1	NaH	THF	rt	4 h	57[b]
2	1:2	NaH	THF	−20 °C	8 h	71
3	1:2	NaH	THF	rt	4 h	68
4	1:2	NaH	THF	reflux	3 h	65
5	1:2	NaH	acetone	rt	40 min	64
6	1:2	NaH	benzene	reflux	24 h	45
7	1:2	NaH	CH_2Cl_2	reflux	24 h	20
8	1:2	*t*-BuOK	THF	rt	24 h	45
9	1:2	$(i\text{-Pr})_2$NEt	THF	reflux	36 h	7

[a] Isolated yield. [b] Calculation of the yield of product **4a-I** was based on 0.5 equiv of **1a** due to **4a-I** being a 1+2 adduct of **1a** with **3a**.

Our continuous interests in the reactivity and applications of nucleophilic and ambiphilic carbenes[12,25] have led us to investigate the reactions of carbenes with heterocumulenes. We envisioned that the reaction of nucleophilic carbenes with ketenimines would produce interesting multifunctional compounds. The reaction pathways and selectivity would also be intriguing. We report herein the unprecedented chemospecific and stereoselective reaction of thiazole and benzothiazole carbenes with ketenimines.

Results and Discussion

We started the investigation with the reaction of thiazole carbenes with 2-methyl-3-(arylimino)acrylates **3**, the highly electrophilic ketenimines readily available from the reaction of aryl isocyanates with methyl 2-(triphenylphosphoranylidene)propanoate.[26] At room temperature and in dry THF, the reaction of 3-ethyl-4-methylthiazole carbene **2a**, which was generated in situ from treatment of 3-ethyl-4-methylthiazolium salt **1a** with sodium hydride, with 1 equiv of methyl 2-methyl-3-(phenylimino)acrylate **3a** produced a yellow thiazole-spiro-pyrrole **4a-I** in 57% yield. Having realized the formation of adduct **4a-I** from reactants in a 1:2 ratio, the reaction employing 2 equiv of ketenimine **3a** was optimized by varying bases, solvents, and reaction temperature. As indicated in Table 1, the best yield of **4a-I** (71%) was obtained from the reaction of **1a** with **3a** with NaH as a base in THF at −20 °C (Table 1, entry 2). High reaction temperature led to a slight decrease of chemical yield (entries 3 and 4). Acetone proved to be a good medium for the reaction, but benzene and dichloroethane did not facilitate the reaction (entries 5−7). Strong base *t*-BuOK led to poor chemical yield of **4a-I** (entry 8), while Hünig's base was not efficacious in this reaction (entry 9).

The scope of the reaction was then studied under the optimized conditions, using thiazolium salts **1** and ketenimines **3** that bear different substituents. As illustrated in Scheme 1

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SCHEME 1. The Reaction of Thiazolium Salts 1 with Ketenimines 3 in the Presence of NaH

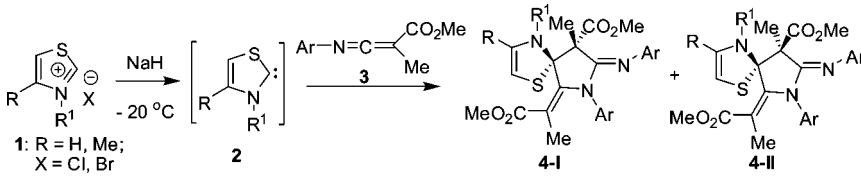


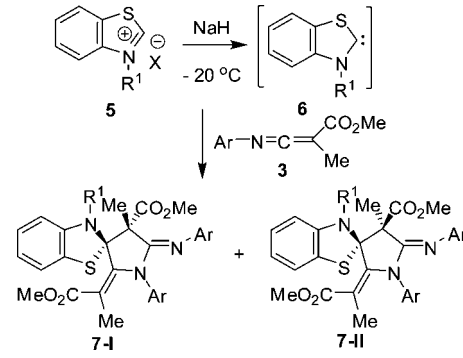
TABLE 2. The Reaction of Thiazolium Salts 1 with Ketenimines 3 in the Presence of NaH in THF

				yield of product (%)		
entry	**1**: R, R^1	**3**: Ar	reaction conditions	**4-I** + **4-II**[a]	**4-I**[b,c]	**4-II**[c,d]
1	**1a**: Me, Et	**3a**: Ph	−20°C, 8 h	71	**4a-I**: 69	**4a-II**: 2
2	**1a**: Me, Et	**3b**: *p*-MeOPh	−20°C, 8 h	75	**4b-I**: 73	**4b-II**: 2
3	**1a**: Me, Et	**3c**: *p*-MePh	−20°C, 8 h	61	**4c-I**: 59	**4c-II**: 2
4	**1a**: Me, Et	**3d**: *p*-ClPh	−20°C, 3 h	85	**4d-I**: 80	**4d-II**: 5
5	**1a**: Me, Et	**3e:** *p*-CF_3Ph	−20°C, 3 h	86	**4e-I**: 83	**4e-II**: 3
6	**1b**: Me, *n*-Bu	**3d**: *p*-ClPh	−20°C, 4 h	80	**4f-I**: 75	**4f-II**: 5
7	**1b**: Me, *n*-Bu	**3e:** *p*-CF_3Ph	−20°C, 3 h	80	**4g-I**: 75	**4g-II**: 5
8	**1c**: Me, Bn	**3a**: Ph	−20°C, 5 h	82	**4h-I**: 66	**4h-II**: 16
9	**1d**: Me, *p*-MeOBn	**3d**: *p*-ClPh	−20°C, 3 h	75	**4i-I**: 65	**4i-II**: 10
10	**1e**: Me, *p*-BrBn	**3d**: *p*-ClPh	−20°C, 5 h	70	**4j-I**: 65	**4j-II**: 5
11	**1f**: Me, *p*-MeBn	**3a**: Ph	−20°C, 3 h	70	**4k-I**: 62	**4k-II**: 8
12	**1e**: Me, *p*-BrBn	**3b**: *p*-MeOPh	−20°C,12 h	77	**4*l*-I**: 66	**4*l*-I**: 11
13	**1g**: h, Bn	**3a**: Ph	−20°C, 8 h	70	**4m-I**:**4m-II**: ∼**10**:**1**[e]	
14	**1h**: h, Et	**3a**: Ph	−20°C, 8 h	67	**4n-I**:**4n-II**: ∼**2**:**1**[e]	

[a] Isolated yield. [b] Pure major products **4-I** were obtained by recrystallization of the mixture of isomers from ethyl acetate and petroleum ether. [c] Yields were determined by ^{1}H in CD_3COCD_3 or DMSO-d_6. [d] Pure byproduct **4-II** was not isolated. [e] Pure **4m-I** and **4n-I** were not obtained by both chromatography and recrystallization purifications.

and Table 2, the reaction showed tolerance for the substituent on both reactants. In all cases examined, thiazolium salts **1** substituted by either a small or a large alkyl group on the nitrogen atom reacted efficiently with ketenimines **3** bearing either an electron-rich or an electron-deficient aryl group on the nitrogen atom of the cumulated double bond furnishing thiazole-spiro-pyrrole derivatives **4** in moderate to good yields. On the bases of structures, thiazole-spiro-pyrrole products **4** should have diastereomers and cis−trans stereoisomers due to the fact that there are two chiral centers and one exocyclic C=C and one C=N bonds. However, these isomers were not separated on TLC. After isolation of products by column chromatography on neutral Al_2O_3, ^{1}H spectra indicated indeed that the crude products without recrystallization were a mixture of isomers. As determined by ^{1}H in CD_3COCD_3 or DMSO-d_6 solution, the yields of major products **4-I** ranged from 48% to 83%, while the minor ones **4-II** were in 2% to 16% yields (Table 2). Interestingly, the minor products **4-II** were found unstable and they were converted into the major ones **4-I** in $CDCl_3$. For example, in the case of products **4n** derived from *N*-ethylthioazole carbenes **2g** and ketenimine **3a**, the ratio of **4n-I** over **4n-II** was about 2:1 in CD_3COCD_3 or DMSO-d_6. The ratio was changed, however, to about 10:1 in $CDCl_3$. Pure products **4a-I** to **4l-I** derived from 4-methylthioazole carbenes were easily obtained from recrystallization of mixtures of isomers from ethyl acetate and petroleum ether (Table 2, entries 1−12), however, pure **4m-I** and **4n-I** derived from thioazole carbenes were not obtained by both chromatography and recrystallization purifications, and byproduct **4-II** could not be isolated and fully characterized. Although **4-II** were not isolated, the fact that the mixtures of **4-I** and **4-II** gave satisfactory element analysis results allowed us to suggest **4-II** to be isomers of **4-I**. On the basis of the isolation of diastereomeric byproduct in the reaction of benzothiazole carbenes with ketenimines (vide infra), and on the observation of similar transformation from minor to major

SCHEME 2. The Reaction of Benzothiazolium Salts 5 with Ketenimines 3 in the Presence of NaH



products derived from both thioazole and benzothiazole carbenes (vide infra), we assigned the byproduct **4-II** to be the diastereomers of **4-I**.

To further examine the generality of the reaction, we then extended the carbene substrates to benzothiazole carbenes **6**. At −20 °C or room temperature depending on the alkyl groups substituted on benzothiazole ring, the reaction of benzothiazolium salts **5** with ketenimines **3** in the presence of NaH proceeded smoothly to produce benzothiazole-spiro-pyrroles **7-I** and **7-II** in 46−86% and 3−18% yields, respectively (Scheme 2, Table 3). Both products **7-I** and **7-II** were separated by chromatography on a silicon gel column, while no separation was achieved when Al_2O_3 was used. It was noted that byproducts **7-II** were unstable and were converted into the major ones **7-I** upon heating, or in $CDCl_3$ solution or on silicon gel. The isolated yields of **7-II** were therefore strongly depended on their stabilities and on the workup process. Although the stereoselectivity of reaction was not satisfied in some cases at low temperature, this disadvantage was overcome by transformation

TABLE 3. The Reaction of Benzothiazolium Salts 5 with Ketenimines 3 in the Presence of NaH in THF

entry	5: R^1	3: Ar	reaction conditions	yield of product (%)[a] 7-I	7-II
1	**5a**: Et	**3a**: Ph	−20 °C, 8 h	**7a-I**: 70	**7a-II**: 12
2	**5a**: Et	**3b**: *p*-MeOPh	−20 °C, 12 h	**7b-I**: 52	**7b-II**: 10[b]
3	**5a**: Et	**3c**: *p*-MePh	−20 °C, 15 h	**7c-I**: 58	**7c-II**: 18
4	**5a**: Et	**3d**: *p*-ClPh	−20 °C, 10 h	**7d-I**: 73	**7d-II**: 3[b]
5	**5a**: Et	**3e:** *p*-CF_3Ph	−20 °C, 5 h	**7e-I**: 86	**7e-II**: −
6	**5b**: *n*-Bu	**3d**: *p*-ClPh	rt, 10 h	**7f-I**: 72	**7f-II**: 4[b]
7	**5b**: *n*-Bu	**3e:** *p*-CF_3Ph	rt, 12 h	**7g-I**: 70	**7g-II**: 4[b]
8	**5c**: Bn	**3d**: *p*-ClPh	rt, 24 h	**7h-I**: 56	**7h-II**: 13[b]
9	**5d**: *p*-BrBn	**3d**: *p*-ClPh	rt, 24 h	**7i-I**: 46	**7i-II**: 16
10	**5a**: Et	**3a**: Ph	rt, 5 h; reflux, 8 h	**7a-I**: 77	**7a-II**: −[c]
11	**5a**: Et	**3b**: *p*-MeOPh	rt, 8 h; reflux, 8 h	**7b-I**: 75	**7b-II**: −[c]
12	**5a**: Et	**3c**: *p*-MePh	rt, 8 h; reflux, 8 h	**7c-I**: 72	**7c-I**: −[c]
13	**5a**: Et	**3d**: *p*-ClPh	rt, 5 h; reflux, 8 h	**7d-I**: 80	**7d-II**: −[c]
14	**5a**: Et	**3e:** *p*-CF_3Ph	rt, 3 h; reflux, 8 h	**7e-I**: 87	**7e-II**: −[c]
15	**5b**: *n*-Bu	**3d**: *p*-ClPh	rt, 10 h; reflux, 10 h	**7f-I**: 76	**7f-II**: −[c]
16	**5b**: *n*-Bu	**3e:** *p*-CF_3Ph	rt, 12 h; reflux, 8 h	**7g-I**: 77	**7g-II**: −[c]
17	**5c**: Bn	**3d**: *p*-ClPh	rt, 24 h; reflux, 12 h	**7h-I**: 68	**7h-II**: −[c]
18	**5d**: *p*-BrBn	**3d**: *p*-ClPh	rt, 24 h; reflux, 24 h	**7i-I**: 62	**7i-II**: 6[c]

[a] Isolated yield. [b] Byproducts **7-II** were isolated without full characterization due to their instability. [c] None or a tiny amount of byproduct was detected by using TLC.

of **7-II** to **7-I** at the higher temperature. In practice, the reaction of benzothiazolium salts **5** with ketenimines **3** in the presence of NaH was first carried out at ambient temperature until the consumption of starting materials (note: ketenimines **3** were not stable at high temperature), and the reaction mixture was then heated in refluxing THF for a period of time. Under these conditions, products **7-I** were obtained predominantly in 62−87% yields, while only a tiny amount of **7-II** was detected with TLC in some cases.

The structures of products **4-I**, **7-I**, and **7-II** were elucidated on the basis of spectroscopic data and microanalysis. The NMR spectra, mass data, and elemental analyses indicated all products being adducts of one carbene intermediate with two ketenimine molecules. To determine the products beyond doubt, the structures of **4d-I**, **7a-I**, and **7a-II** were determined unambiguously by single-crystal X-ray diffraction analysis (see Figure S1 in the Supporting Information). From the single-crystal structures of **4d-I**, **7a-I**, and **7a-II**, we found that both the major products **4-I** and **7-I** have the (*S*,*R*) or (*R*,*S*) configurations at chiral centers, while the minor one **7-II** has the (*R*,*R*) or (*S*,*S*) configurations. In the major products **4-I** and **7-I**, the ester group of the pyrrole ring and the nitrogen-bearing alkyl group of thiazole or benzothiazole are in a trans relationship. Apparently, such orientation can reduce the repulsion between the ester and alkyl group attached respectively to the pyrrole and thiazole rings. Another important feature is that the exocyclic C=C and C=N bonds of all products **4-I**, **7-I**, and **7-II** are *E*-configured. It is clear that this steric preference could avoid the huge steric repulsion between the vinyl ester or the imine aryl and the aryl group attached to the pyrrole ring. Thus, the stereoselectivity of the reaction between thiazole or benzothiazole carbenes and ketenimines can be best explained by predominant formation of thermodynamically stable products. The thermal conversion of **7-II** to **7-I** also supports our interpretation.

To account for the formation of thiazole- or benzothiazole-spiro-pyrroles **4** or **7**, a tandem nucleophilic addition/cycloaddition reaction mechanism was proposed (Scheme 3, eq 1). Nucleophilic addition of carbenes **2** or **6** to ketenimines **3** forms 1,3-dipolar intermediates **8**. A concerted cycloaddition or a stepwise addition−cyclization of 1,3-dipoles **8** with the C=C bond of ketenimines gives rise to thiazole- or benzothiazole-spiro-pyrroles **4** or **7**. The thermal transformation of byproduct **4-II** or **7-II** to the major ones **4-I** or **7-I** that was most probably via the 1,4-dipoles **9** supports the stepwise cycloaddition mechanism. The transformation of **4-II** or **7-II** to **4-I** or **7-I** in acidic media such as $CDCl_3$ or silicon gel was probably via the intermediate **10** or **11**, since the C−N or C−S bond of the spiro-carbon atom of **4** or **7** (a analogous structure of a ketal) might be easily broken under acidic conditions (eq 1 in Scheme 3).

Besides the aforementioned stereoselectivity, the chemoselectivity of the tandem 1+2 cyclization reaction of carbenes with ketenimines also deserves comment. Theoretically, the nucleophilic additions of carbenes **2** or **6** and the consequent 1,3-dipolar intermediates **8** to ketenimines **3** could take place both at C=N bonds and at electron-deficient C=C bonds of **3** to form different types of spiro products. In fact, only products **4** or **7** that were derived from addition of carbenes to C=N bonds followed by cycloaddition of 1,3-dipoles **8** with C=C bonds of ketenimines were isolated, while other types of products were not detected at all in this work. The specific formation of products **4** and **7** can be explained by electronic or/and steric effects of the intermediates and products. First, the nucleophilic addition of carbenes to ketenimines formed ambident $C^+-C-N^-$and C^+-C-C^-1,3-dipoles **8**, whose nitrogen anions should be more reactive than the carbanions because carbanions are directly stabilized by the ester and imine groups and are also more sterically hindered than the nitrogen anions. Second, the steric effects of products probably accounts for the selective cycloaddition of C^+-C-N^- dipolar specie of **8** with the C=C bond rather than the C=N bond of ketenimines **3**, since spiro-pyrrole **4** or **7** could reduce the steric repulsions among the substituents of the pyrrole ring through the formation of *Z*-configured C=C and C=N bonds, whereas spiro-imidazoles **12** could not avoid the repulsion between ester and aryl groups whatever the configurations of two exocyclic C=C bonds would be (Scheme 3, eq 2).

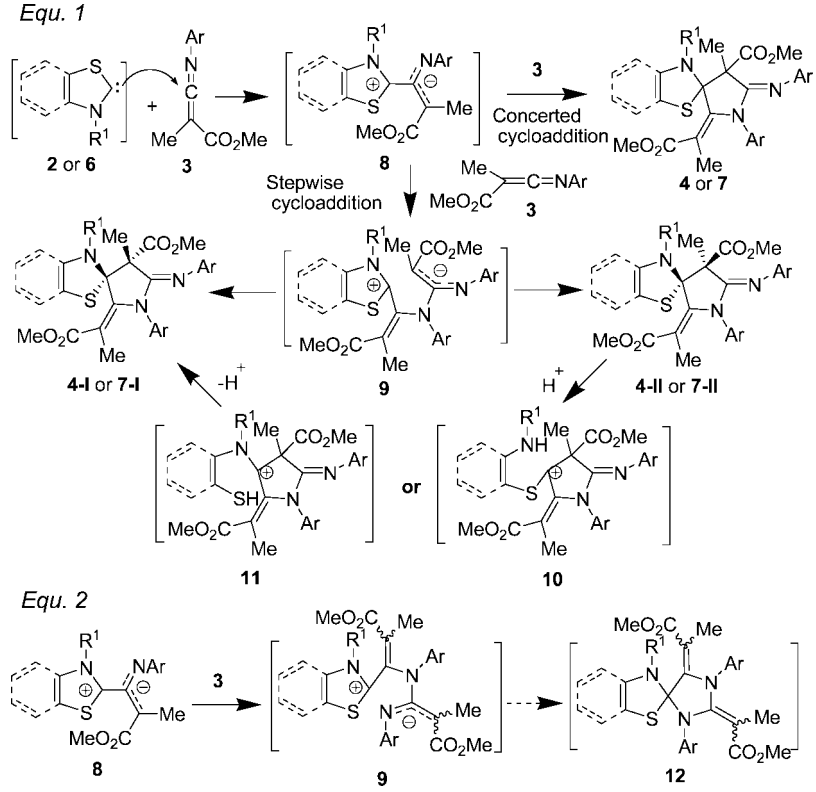
Conclusion

In conclusion, we have shown that thiazole and benzothiazole carbenes underwent chemospecific and stereoselective 1+2 cyclization reaction with 2 equiv of ketenimines to afford thiazole- or benzothiazole-spiro-pyrrole derivatives in moderated to good yields. The reaction mechanism can be best explained by a tandem nucleophilic addition of carbene to the C=N bond of ketenimine followed by a stepwise [3+2] cycloaddition of the 1,3-dipolar intermediate with the C=C bond of ketenimine. The chemospecificity and stereoselectivity of the reaction originated from electronic or/and steric effects of dipolar intermediates and products. The easy availability of thiazole and benzothiazole carbene precursors and the high efficiency in the reaction of carbenes with ketenimines render this reaction a powerful protocol for the construction of novel polyfunctional thiazole-spiro-pyrrole or benzothiazole-spiro-pyrrole compounds that are not readily accessible by other methods.

Experimental Section

General Procedure for the Reaction of Thiazolium Salts 1 with Ketenimines 3 in the Presence of NaH. Under nitrogen

SCHEME 3[a]



[a] (1) The proposed mechanisms for the formation of thiazole- or benzothiazole-spiro-pyrroles **4** or **7** from the reaction of carbenes **2** or **6** with ketenimines **3** and for the transformation of **4-II** or **7-II** to **4-I** or **7-I** (eq 1). (2) Another plausible pathway for the reaction of thiazole or benzothiazole carbenes with ketenimines (eq 2).

atmosphere and at −20 °C, NaH (4 mmol, 50% in mineral oil) was added in portions to the mixture of thiazolium salts **1** (2.2 mmol) with ketenimines **3** (4 mmol) in dry THF (30 mL). The reaction mixture was stirred at −20 °C for 3−12 h. After removal of the solvent under vacuum at room temperature, the residue was chromatographed on a neutral Al_2O_3 column eluting with a mixture of petroleum ether (30−60 °C) and ethyl acetate (8:1) to afford the mixtures of isomers **4-I** and **4-II.** Pure major products **4-I** were obtained by recrystallization of the mixtures of **4-I** and **4-II** from petroleum ether and ethyl acetate.

(2*R*,2′*E*,4′*S*,5′*E*) or (2*S*,2′*E*,4′*R*,5′*E*)-Methyl 3-Ethyl-2′-(1-methoxycarbonylethylidene)-4,4′-dimethyl-1′-phenyl-5′-(phenylimino)-3*H*-spiro[thiazole-2,3′-pyrrolidine]-4′-carboxylate, 4a-I. Yield 69%, mp 147−148 °C; IR υ (cm^{-1}) 1739, 1690, 1663, 1609; ^{1}H NMR (300 MHz, CD_3COCD_3) δ (ppm) 7.46−7.48 (m, 4H), 7.34−7.37 (m, 1H), 7.19 (t, J = 7.3 Hz, 2H), 6.95 (t, J = 7.3 Hz, 1H), 6.55 (d, J = 7.8 Hz, 2H), 4.65 (s, 1H), 3.82 (s, 3H), 3.62−3.80 (m, 1H), 3.62 (s, 3H), 3.32−3.37 (m, 1H), 1.90 (s, 3H), 1.41 (s, 3H), 1.37 (t, J = 7.2 Hz, 3H), 1.05 (s, 3H); ^{13}C NMR (75 MHz, CD_3COCD_3) δ (ppm) 171.0, 170.2, 148.1, 147.4, 139.2, 136.6, 128.9, 128.6, 127.3, 122.5, 120.3, 109.6, 90.0, 85.7, 67.8, 52.7, 52.0, 40.1, 17.4, 16.8, 14.6, 14.0; MS (ESI) 506 (M + 1). Anal. Calcd for $C_{28}H_{31}N_3O_4S$: C 66.51, H 6.18, N 8.31. Found: C 66.57, H 6.22, N 8.26.

General Procedures for the Reaction of Benzothiazolium Salts 5 with Ketenimines 3 in the Presence of NaH. Method A. Under nitrogen atmosphere and at −20 °C or at room temperature, NaH (4 mmol, 50% in mineral oil) was added in portions to the mixture of benzothiazolium salts **5** (2.2 mmol) with ketenimines **3** (4 mmol) in dry THF (30 mL). The reaction mixture was stirred at −20 °C or at room temperature for 8−24 h. After removal of the solvent under vacuum at room temperature, the residue was chromatographed on a silica gel column eluting with a mixture of petroleum ether (30−60 °C) and ethyl acetate (15:1) to afford products **7-I** in 46−86% yields, while byproducts **7-II** were obtained in 3−18% yields (note: isomers **7-I** and **7-II** could not be well separated by chromatography on a Al_2O_3 column).

Method B. Under nitrogen atmosphere and at room temperature, NaH (4 mmol, 50% in mineral oil) was added in portions to the mixture of benzothiazolium salts **5** (2.2 mmol) with ketenimines **3** (4 mmol) in dry THF (30 mL). The reaction mixture was stirred at room temperature until the disappearance of ketenimines and was then stirred at the refluxing temperature of THF for another 8−24 h. After removal of the solvent under vacuum at room temperature, the residue was chromatographed on a silica gel column eluting with a mixture of petroleum ether (30−60 °C) and ethyl acetate (15:1) to afford products **7-I** in 62−87% yields, while a tiny amount of byproduct **7-II** was detected by TCL without isolation.

(2*R*,2′*E*,4′*S*,5′*E*)- or (2*S*,2′*E*,4′*R*,5′*E*)-Methyl 3-Ethyl-2′-(1-methoxycarbonylethylidene)-4′-methyl-1′-phenyl-5′-(phenylimino)-3*H*-spiro[benzo[*d*]thiazole-2,3′-pyrrolidine]-4′-carboxylate, 7a-I. Yield 70% (rt), 77% (THF, reflux); mp 185−186 °C; IR υ (cm^{-1}) 1744, 1708, 1668, 1611, 1593; ^{1}H NMR (300 MHz, CD_3COCD_3) δ (ppm) 7.50 (br s, 4H), 7.38 (br s, 1H), 7.18 (t, J = 7.6 Hz, 2H), 7.01 (t, J = 7.5 Hz, 2H), 6.95 (t, J = 7.3 Hz, 1H), 6.63 (d, J = 7.6, Hz, 1H), 6.57 (d, J = 7.9 Hz, 1H), 6.49 (d, J = 7.6 Hz, 1H), 3.87 (s, 3H), 3.81−3.86 (m, 1H), 3.46−3.53 (m, 1H), 3.07 (s, 3H), 1.49 (t, J = 7.1 Hz, 3H), 1.44 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.8, 169.8, 147.8, 147.5, 145.1, 139.1, 129.0, 128.6, 127.5, 125.9, 122.8, 122.7, 120.5, 120.2, 117.7, 109.5, 106.2, 88.5, 67.1, 53.0, 51.6, 40.9, 17.0, 14.3, 13.1; MS (ESI) 542 (M + 1). Anal. Calcd for $C_{31}H_{31}N_3O_4S$: C 68.74, H 5.77, N 7.76. Found: C 68.73, H 5.67, N 7.62.

(2*R*,2′*E*,4′*R*,5′*E*)- or (2*S*,2′*E*,4′*S*,5′*E*)-Methyl 3-Ethyl-2′-(1-methoxycarbonylethylidene)-4′-methyl-1′-phenyl-5′-(phenylimino)-3*H*-spiro[benzo[*d*]thiazole-2,3′-pyrrolidine]-4′-carboxylate, 7a-II. Yield 12%, mp 147−148 °C; IR υ (cm^{-1}) 1714, 1701, 1675, 1627, 1591; ^{1}H NMR (300 MHz, CD_3COCD_3) δ (ppm) 7.49 (br s,

4H), 7.36 (br s, 1H), 7.16−7.19 (m, 2H), 6.91−7.03 (m, 3H), 6.69 (d, $J = 7.3$ Hz, 2H), 6.61 (t, $J = 7.2$ Hz, 1H), 6.44 (d, $J = 7.8$ Hz, 1H), 3.53−3.69 (m, 2H), 3.18 (s, 3H), 3.13 (s, 3H), 1.70 (s, 3H), 1.43 (s, 3H), 1.38 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.9, 168.2, 147.9, 145.9, 144.7, 138.8, 129.1, 128.5, 127.6, 127.3, 125.6, 122.6, 122.1, 120.9, 120.4, 117.8, 109.5, 106.9, 92.8, 52.3, 52.0, 40.7, 21.8, 17.4, 13.0; MS (ESI) 542 (M + 1). Anal. Calcd for $C_{31}H_{31}N_3O_4S$: C 68.74, H 5.77, N 7.76. Found: C 68.72, H 6.01, N 7.72.

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Supporting Information Available: The experimental procedures for the reactions of thiazole and benzothiazole carbenes with ketenimines, full characterization for products **4-I**, **7-I**, and **7-II** excluding those byproduct without isolation, copies of ^{1}H and ^{13}C NMR spectra of products **4-I**, **7-I**, and **7-II,** as well as single crystal data of **4d-I**, **7a-I**, and **7a-II** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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