Cycloaddition−Elimination Reactions of 5-Imino-1,2,4-thiadiazolidin-3-ones and 5-Imino-1,2,4-dithiazolidin-3-ones with Electron-Rich Double Bonds ☆

Franz Tittelbach*[a], Siegfried Vieth[b], and Matthias Schneider[a]

Institut für Angewandte Chemie Berlin-Adlershof e.V.[a],
Rudower Chaussee 5, D-12484 Berlin, Germany
E-mail: tittelbach@aca.fta-berlin.de

Brandenburgische Technische Universität Cottbus, Lehrstuhl für Anorganische Chemie[b],
Karl-Marx-Str. 17, D-03044 Cottbus, Germany

Received September 29, 1997

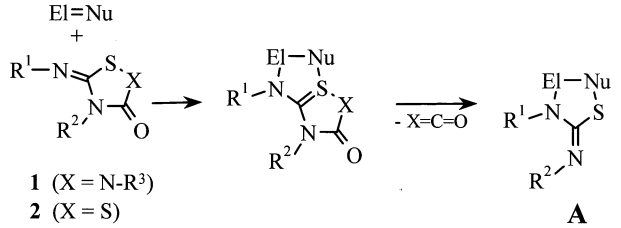
Keywords: Cycloaddition / Elimination / Heterocycles / 1,2,4-Thiadiazolidines / 1,2,4-Dithiazolidines

5-Imino-1,2,4-thiadiazolidin-3-ones **1** react with compounds containing electron-rich double bonds such as enamines and ester enolates to afford the 2-iminothiazolidines **3**, **4**, and **10** in cycloaddition−elimination reactions. The less reactive 5-imino-1,2,4-dithiazolidin-3-ones **2** only give the 2-iminothiazolidines **3** or **4** with enamines; with ester enolates the 5-alkylidene-1,2,4-dithiazolidines **12** are formed. The reaction products with enamines undergo hydrolysis and elimination to form the corresponding hydroxy compounds **5**, **6** or the unsaturated compounds **7**, **8**, depending on the size of the fused ring.

Introduction

5-Imino-1,2,4-thiadiazolidin-3-one **1** and 5-imino-1,2,4-dithiazolidin-3-one **2** undergo cycloaddition−elimination reactions with unsaturated systems of the type El=Nu, yielding heterocycles A according to Scheme 1.[1][2][3][4]

Scheme 1. General reaction of 5-imino-1,2,4-thiadiazolidin-3-one and 5-imino-1,2,4-dithiazolidin-3-one derivatives with dipolarophiles



In almost all cases, El=Nu is an electrophile. Isocyanates[1][3][4], isothiocyanates[1][2][4], activated nitriles[2][4], ketenes[1][2] as well as CS_2[4] have been used. In a single experiment we showed that benzimidazole **1d** reacts with nucleophilic enamines[5]. In this paper, we present the first systematic study of the reactions of thiadiazolidines **1** and dithiazolidines **2** with electron-rich enamines and ester enolates.

Results and Discussion

The reactivity of **1** and **2** towards electrophilic dipolarophiles decreases with decreasing electrophilic power of the dipolarophiles[1][2][3][4][5]. Only **1a** reacts slowly with CS_2[5], non-polar olefins and the less nucleophilic enol ethers do not react with **1** or **2**. However, more nucleophilic dipolarophiles such as enamines and ester enolates react readily with **1** and **2**.

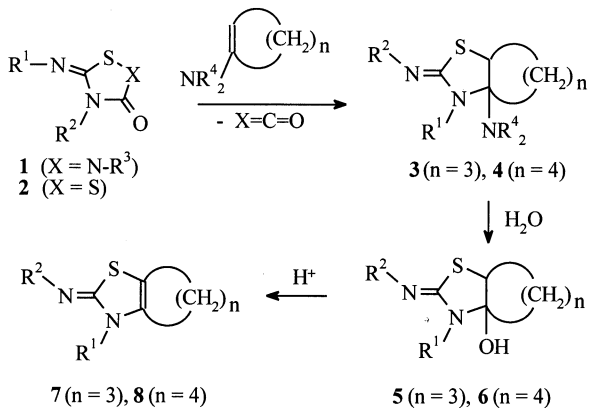
Treatment of **1** or **2** with *N*-substituted 1-aminocyclohexenes or 1-aminocyclopentenes furnishes, in a formally identical cycloaddition−elimination reaction, the adducts **3** and **4**, respectively. Obviously, the reactivity of the heterocycles **1** or **2** is determined by the electrophilic properties of the S atom. Thiadiazolidines **1** are more reactive than dithiazolidines **2**. Electron-withdrawing substituents attached to **1** or **2** improve the reactivity. Thus, diaryl-substituted thiadiazolidines (**1a**, **1d**) react most rapidly, while compounds **1b**, **c** with $R^1 = R^2$ = alkyl react more slowly. Dialkyl-substituted dithiazolidines **2** do not react with enamines under the conditions used.

As cyclic N,N-acetals, the primary products **3** and **4** are not very stable and are not isolable in all cases. They undergo hydrolysis, giving the hemiaminals **5** and **6**. The 6-ring-anellated hemiaminals **6** are able to eliminate water, yielding the unsaturated compounds **8**. The reaction pathway depends on the size of the carbocycle. The cyclopentane derivatives **3** can be isolated by column chromatography. They are easily transformed into the quite stable hemiaminals **5** by treatment with dilute acids. Surprisingly, **5** does not undergo elimination of water, even in the presence of hot, concentrated hydrochloric acid. However, the synthesis of the corresponding unsaturated products **7** is possible, as illustrated by the reaction of **1a** with 1-morpholinocyclopentene in the presence of dry $CuCl_2$ (see Experimental Section).

Primary adducts **4**, containing a cyclohexane ring, are less stable. For example, **4a** is only isolable as a crystalline compound when traces of acids are strictly excluded. Purification by column chromatography on silica failed − a mixture of the hydroxy compound **6a** and the elimination product **8a** was formed. **6a** could be isolated chromatograph-

  1434−193X/98/0303−0515 $ 17.50+.50/0

Scheme 2. Reaction of 5-imino-1,2,4-thiadiazolidin-3-ones and 5-imino-1,2,4-dithiazolidin-3-ones with enamines



1 (X = N-R3)
2 (X = S)

3 (n = 3), 4 (n = 4)

7 (n = 3), 8 (n = 4)

5 (n = 3), 6 (n = 4)

	R1	R2	R3
1a	C_6H_5	C_6H_5	C_6H_5
1b	C_6H_5-CH_2-CH-CO_2Et	CH_3	C_6H_5
1c	CH_3-CH-CO_2Et	CH_3	C_6H_5
1d	o-C_6H_4		C_2H_5
2a	C_6H_5	C_6H_5	
2b	p-Cl-C_6H_4	C_6H_5	

	R1	R2	HNR^4_2
3a	C_6H_5	C_6H_5	morpholine
3b	p-Cl-C_6H_4	C_6H_5	piperidine
3c	C_6H_5	p-Cl-C_6H_4	piperidine
3d	C_6H_5	C_6H_5	N-methyl-N-(1-phenylethyl)amine
3e	C_6H_5	C_6H_5	methyl prolinate
3f	o-C_6H_4		morpholine
4a	C_6H_5	C_6H_5	pyrrolidine
5a	C_6H_5	C_6H_5	
5b	o-C_6H_4		
6a	C_6H_5	C_6H_5	
6b	o-C_6H_4		
7a	C_6H_5	C_6H_5	
8a	C_6H_5	C_6H_5	
8b	p-Cl-C_6H_4	C_6H_5	
8c	C_6H_5	p-Cl-C_6H_4	
8d	CH_3	C_6H_5-CH_2-CH-CO_2Et	
8e	CH_3	CH_3-CH-CO_2Et	
8f	o-C_6H_4		

ically. However, further attempts at purification by recrystallisation led to elimination of water, yielding **8a**. Furthermore, the first detectable product from aminocyclohexenes and the benzimidazole derivative **1d** was the hemiaminal **6b**. Tetracyclic **6b** is stable towards dilute acid and will be transformed to **8f** with concentrated hydrochloric acid only. Its greater stability compared with bicyclic **6a** is due to the greater ring tension of elimination product **8f** compared with that of **8a**.

Structural assignments for new compuonds were made by interpretation of the ^{13}C-NMR spectra mainly. Phenyl substituents show the typical pattern (bound to an imino group: $\delta \approx 151/122/129/123$; bound at N-3: $\delta \approx 140/128/128/127$ for *ipso*-/*o*-/*m*-/*p*-C atoms)[6][7][8], important to distinguish between structures **3b/3c** and **8b/8c** for instance. Structural assignments for compounds **8d** and **8e** were made on the basis of the signals of the 3-methyl groups. The measured values of around $\delta = 30$ are typical for bonding to sp^3-N atoms; bonding to an exocyclic imino group would be expected to lead to a value of around $\delta = 38$[9].

The reversibility of analogous reactions of **1** (or **A**) with electrophilic unsaturated compounds such as isocyanates or isothiocyanates is known[3][4][9][10]. However, treatment of cyclopentane derivatives **3** with aminocyclohexenes or of cyclohexane derivatives **4** with aminocyclopentenes resulted in no reaction, indicating the irreversibility of addition−elimination reactions with enamines.

According to the mechanism of addition−elimination reactions, the imino-N atom and the endocyclic N atom change positions, as indicated by the interchange of R^1 and R^2 (see Scheme 1). However, the examples described above where the starting compounds **1** or **2** have identical R^1 and R^2 groups do not allow a proof of the mechanism. Using 5-(*p*-chlorophenyl)imino-4-phenyl-1,2,4-dithiazolidin-3-one (**2b**) in the reaction with piperidinocyclopentene we obtained a mixture of **3b** and **3c**, which proved inseparable by chromatographic means (see Scheme 3). ^{13}C-NMR experiments in different solvents and at different temperatures indicated a dynamic equilibrium with the non expected isomer **3c** being the main component. In a similar process, **2b** was treated with pyrrolidinocyclohexene. As expected (see above), the olefinic products **8b** and **8c** were formed and could be fully separated by chromatography. Again, the non expected isomer **8c**, with the substituents in formally unchanged positions, was found to be the main product. This behaviour can be understood by postulating an intermediate such as **B** (Scheme 3), which allows both N atoms of **3** (or **4**, respectively) the opportunity of ring closure by nucleophilic attack, leading to accumulation of the more stable isomer as the main component. Such a dynamic equilibrium may also be assumed for the hemiaminals **5** and **6**. However, no such equilibrium can occur for the unsaturated **8**.

Moreover, reaction of the alkyl-substituted thiadiazolidinones **1b** and **1c** with enamines gave **8d** and **8e**, respectively. Again, the positions of the substituents remained unchanged, certainly as a result of steric effects. The smaller group (Me) is situated at the endocyclic N atom[9]. Basically, C atoms 4 and 5 of the thiazolidine rings in **3** and **4** (or **5** and **6**, respectively) represent new stereocentres, giving the possibility of the formation of two diastereomers. However, ^{13}C-NMR spectra reveal the presence of only one isomer. X-ray analysis of 3-phenyl-2-phenylimino-4-pyrrolidino-4,5-tetramethylene-thiazolidine (**4a**) verifies the expected *cis* orientation of the anellated rings.

Clearly, as described in the literature[11], *trans* products are disfavoured energetically and therefore cannot be detected by NMR. With this in mind, the different elimination behaviour of **3** and **4** can be explained; *trans* anellation offers the better geometry for elimination. Compounds **3**, with two anellated five-membered rings follow the rule of *trans* connection of fused rings more strictly. They can only

Scheme 3. Isomerisation of products of enamine addition

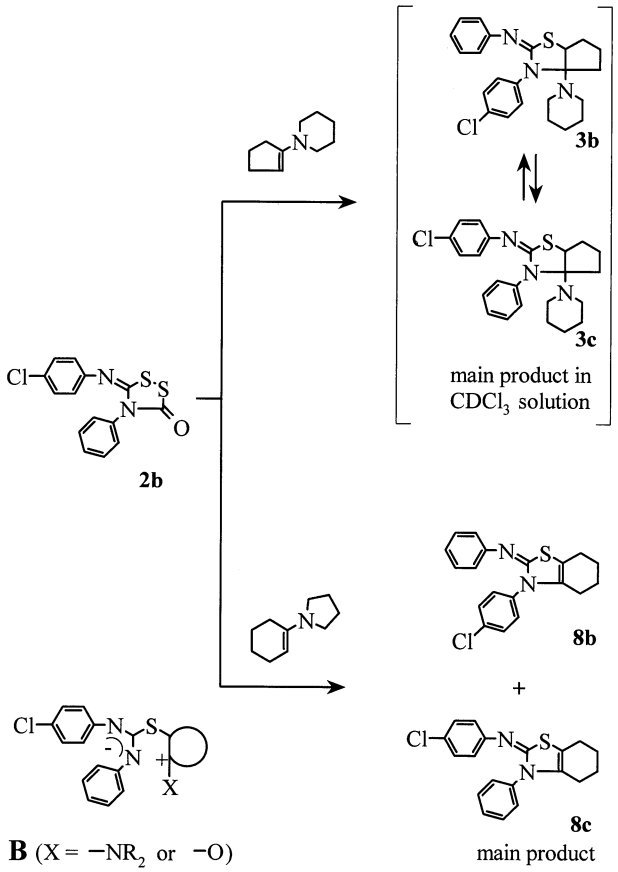
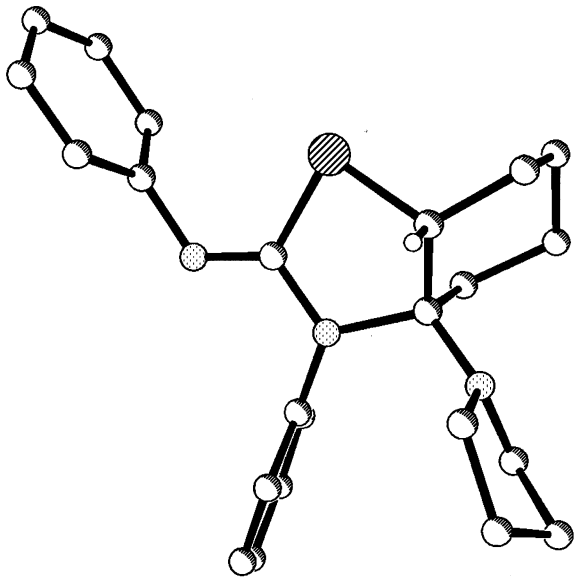


Figure 1. X-ray crystal structure of **4a**[16]

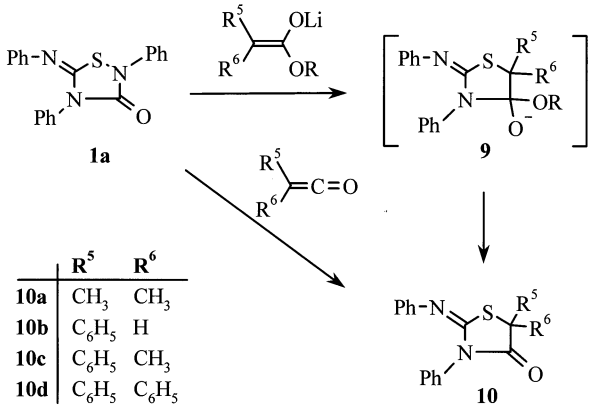


be hydrolysed to **5**. Compounds **4** (or **6**), with a six-membered ring anellated to the thiazolidine can, however, form (via **B**, X = NR_2 or OH) small amounts of the *trans* isomers in the equilibrium, which undergo elimination more readily.

The diastereoselectivity of ring anellation prompted us to test the chiral induction of enamines with proline ester or *N*-methylphenylethylamine substituents as auxiliaries. The products **3d** and **3e**, respectively, were formed as the appropriate mixtures of two diastereomers. However, we could not detect any diastereoselectivity by analysis of the ^{13}C-NMR spectra. The starting materials **1b** and **1c**, with amino acid ester functions, afforded the corresponding unsaturated compounds **8d** and **8e** as the first isolable products with loss of the two new stereocentres, due to reduced reactivity of the aliphatic substituted starting materials.

Furthermore, we tested other electron-rich unsaturated systems in the reaction with **1** or **2**. Enol ethers were found to be insufficiently nucleophilic, but ester enolates reacted, showing different reaction pathways for the starting compounds **1** and **2**. The more reactive thiadiazolidines **1** follow the general route (Scheme 1), yielding thiazolidinones **10** (Scheme 4). For a quantitative transformation, two equivalents of enolate are necessary, because the isocyanate product also reacts with the enolate. As expected, the hemiacetal intermediate **9** could not be isolated.

Scheme 4. Reaction of 5-imino-1,2,4-thiadiazolidin-3-ones with ester enolates



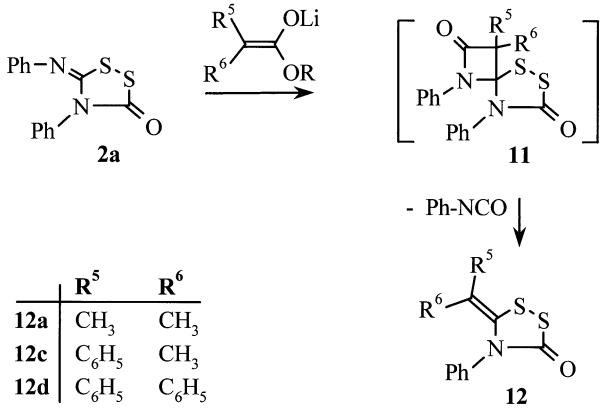
	R^5	R^6
10a	CH_3	CH_3
10b	C_6H_5	H
10c	C_6H_5	CH_3
10d	C_6H_5	C_6H_5

Noteworthily, the thiazolidinones **10** can be prepared by treatment of **1** with either a nucleophilic or an electrophilic unsaturated species. They are also accessible from **1** and ketenes[12].

Dithiazolidines **2** are generally less reactive in cycloaddition–elimination processes and follow a different reaction pathway with ester enolates, yielding alkylidene dithiazolidines **12** (Scheme 5). The products are formed by nucleophilic attack of the enolate on the iminocarbonyl group of **2**. We assume the well-known ring closure to β-lactams **11** to be the next step[13]. The spiro compound **11** is unstable and eliminates phenyl isocyanate, which is scavenged with a second equivalent of enolate.

The formation of **12** from **2** is only possible if disubstituted enolates are used (R^3 and $R^4 \neq H$). Hydrogen at the β position of the enolate causes decomposition. This behaviour can be explained considering the necessary stabilisation of the β-lactam ring in **11** by large substituents[14], which is absent if R^3 or R^4 = H.

Scheme 5. Reaction of 5-imino-1,2,4-dithiazolidin-3-ones with ester enolates



	R^5	R^6
12a	CH_3	CH_3
12c	C_6H_5	CH_3
12d	C_6H_5	C_6H_5

In conclusion, we have shown that 5-imino-1,2,4-thiadiazolidin-3-one (**1**) and 5-imino-1,2,4-dithiazolidin-3-one (**2**) undergo cycloaddition reactions with both electrophilic and nucleophilic unsaturated compounds (dipolarophiles). This is, on the one hand, typical behaviour of 1,3-dipoles[15], and supports the interpretation that −N=C−S−, the reacting moiety of **1** and **2**, can be viewed as a masked 1,3-dipole[2]. In all the investigated cycloadditions of **1** and **2**, electron-rich as well as electron-poor dipolarophiles approach with the more negative part of the double bond oriented towards the electrophilic S atom of **1** or **2**. This, on the other hand, makes it difficult to ascertain whether the ring closure is a concerted or a two-step process.

Experimental Section

General: Unless otherwise noted, materials were obtained from commercial suppliers and were used without further purification. For column chromatography silica gel Merck KG 60 was used. THF was distilled from sodium prior to use; diisopropylamine and dichloromethane were distilled from calcium hydride. All reactions involving organometallic reagents were conducted under argon. Melting points are uncorrected. − ^{1}H- and ^{13}C-NMR spectra were recorded with a Bruker WP 200 SY spectrometer. Chemical shifts are expressed in ppm downfield from internal tetramethylsilane. − Mass spectra were determined with a Fisons Instruments VG Auto Spec. All compounds gave the appropriate M^+ peak. − Elemental analyses were determined with a Carlo Erba 1406 analyzer. − X-ray analysis was performed with a Turbo CAD4 diffractometer (Enraf-Nonius); the structure was solved and refined using the program SHELX-97[16]. Further details of the crystal structure determination are available[17].

The syntheses of **1a**[4], **1d**[5], **2a**[18][19], **2b**[19] and **6b**[5] are described in the literature.

(1′-RS)-5-[(1-Ethoxycarbonyl-2-phenylethyl)imino]-4-methyl-2-phenyl-1,2,4-thiadiazolidin-3-one (**1b**) was prepared in two steps:

1. *(1′-RS)-5-[(1-Ethoxycarbonyl-2-phenylethyl)imino]-4-methyl-1,2,3,4-thiatriazoline:* (1′-*RS*)-5-[(1-Ethoxycarbonyl-2-phenylethyl)-amino]-1,2,3,4-thiatriazole[20] was methylated with trimethyloxonium tetrafluoroborate according to ref.[21]. The product was isolated by column chromatography (heptane/acetone, 5:1) as an oil, yield (51%). − ^{13}C NMR ($CDCl_3$): δ = 171.3, 158.5, 137.7, 129.7, 128.5, 126.9, 73.8, 61.3, 39.8, 34.4, 14.1.

2. **1b**: 1.0 g (3.42 mmol) of (1′-*RS*)-5-[(1-ethoxycarbonyl-2-phenylethyl)imino]-4-methyl-1,2,3,4-thiatriazoline and 0.5 g (4.20 mmol) of phenyl isocyanate were dissolved in 10 ml of dry dichloromethane. After 24 h at room temperature, the solvent was removed under reduced pressure. **1b** was isolated as an oil by column chromatography (heptane/acetone, 5:1); yield 1.2 g (91%). − ^{13}C NMR ($CDCl_3$): δ = 171.0, 152.8, 150.6, 137.6, 137.0, 129.6, 129.7, 128.5, 126.9, 126.3, 123.0, 67.5, 61.3, 40.0, 30.2, 14.1.

(1′-RS)-5-[(1-Ethoxycarbonylethyl)imino]-4-methyl-2-phenyl-1,2,4-thiadiazolidin-3-one (**1c**): This compound was prepared in two steps analogously to **1b**:

1. *(1′-RS)-5-[(1-Ethoxycarbonylethyl)imino]-4-methyl-1,2,3,4-thiatriazoline:* From (1′-*RS*)-5-[(1-ethoxycarbonylethyl)amino]-1,2,3,4-thiatriazole[20] and trimethyloxonium tetrafluoroborate according to ref.[21]. The product was isolated by column chromatography (heptane/acetone, 5:1) as an oil; yield (56%). − ^{13}C NMR ($CDCl_3$): δ = 171.9, 157.3, 66.6, 60.8, 33.9, 18.2, 13.9.

2. **1c**: From (1′-*RS*)-5-[(1-ethoxycarbonylethyl)imino]-4-methyl-1,2,3,4-thiatriazoline and phenyl isocyanate according to the synthesis of **1b**; isolated by column chromatography (heptane/acetone, 5:1); yield (98%), m.p. 74−75°C (EtOH). − ^{13}C NMR ($CDCl_3$): δ = 172.1, 153.0, 149.9, 137.2, 129.5, 126.4, 123.1, 61.4, 60.8, 30.3, 19.1, 14.2.

General Procedure for Reaction of **1** *or* **2** *with Enamines:* A solution of 1 mmol of thiadiazolidinone **1** or dithiazolidinone **2** and 2 mmol of the appropriate enamine in 15 ml of chloroform was stirred for 24 h at room temperature. The solvent was then removed under reduced pressure and the residue was crystallised from ethanol or purified by column chromatography.

4-(Morpholin-1-yl)-3-phenyl-2-phenylimino-4,5-trimethylenethiazolidine (**3a**): From **1a** and 1-morpholinocyclopentene; yield quantitative; m.p. 178−180°C (MeCN/water). − $C_{22}H_{25}N_3OS$ (379.5): calcd. C 69.62, H 6.64, N 11.07; found C 69.75, H 6.62, N 11.07. − ^{13}C NMR ([D$_6$]DMSO): δ = 160.0, 151.8, 139.9, 128.6 (2 C), 128.2, 126.5, 123.0, 122.1, 96.4, 67.2, 46.6, 42.3, 37.9, 34.6, 24.0.

3-(p-Chlorophenyl)-2-phenylimino-4-(piperidin-1-yl)-4,5-trimethylenethiazolidine (**3b**) *and 2-(p-Chlorophenylimino)-3-phenyl-4-(piperidin-1-yl)-4,5-trimethylenethiazolidine* (**3c**): From dithiazolidinone **2b** and pyrrolidinocyclohexene. **3b** and **3c** were isolated by column chromatography (heptane/ethyl acetate, 10:1) as an inseparable mixture; yield 63%, m.p. 146−152°C (MeCN). − $C_{23}H_{26}ClN_3S$ (412.0): calcd. C 67.05, H 6.36, N 10.20; found C 67.17, H 6.54, N 10.23.

3b (minor component): ^{13}C NMR ($CDCl_3$): δ = 160.1, 151.7, 138.6, 131.7, 129.4, 128.7, 128.6, 123.0, 122.1, 96.9, 47.1, 42.0, 38.0, 35.6, 26.4, 24.8, 24.2.

3c (major component): ^{13}C NMR ($CDCl_3$): δ = 160.6, 150.6, 140.0, 128.6, 128.5, 128.4, 127.8, 126.5, 123.7, 97.1, 47.1, 42.5, 38.0, 35.6, 26.4, 24.8, 24.2.

(1′-RS)-4-[N-Methyl-N-(1-phenylethyl)amino]-3-phenyl-2-phenylimino-4,5-trimethylenethiazolidine (**3d**): From **1a** and (1′-*RS*)-[*N*-methyl-*N*-(1-phenylethyl)amino]cyclopentene; isolated as an oil by column chromatography (heptane/acetone, 5:1); yield 88.7%. − $C_{27}H_{29}N_3S$ (427.6): calcd. C 75.84, H 6.84, N 9.83; found C 75.55, H 6.54, N 9.67. − ^{13}C NMR ($CDCl_3$): δ = 159.8/160.0, 152.0, 144.0/144.4, 139.8/140.0, 127.0/127.6, 126.6/127.0, 126.7/126.8, 122.4, 122.7, 55.0/55.9, 97.6/98.1, 127.9/128.6, 128.4, 128.2/128.7, 129.1/129.6, 46.7/47.4, 37.2/37.2, 35.1/35.3, 28.9/30.1, 23.3/23.4, 15.1/20.2.

(2′-S)-4-(2-Methoxycarbonylpyrrolidin-1-yl)-3-phenyl-2-phenylimino-4,5-trimethylenethiazolidine (**3e**): From **1a** and (2′-*S*)-(2-methoxycarbonylpyrrolidin-1-yl)aminocyclopentene; isolated as an oil by column chromatography (heptane/acetone, 10:3); yield 93%. − $C_{24}H_{27}N_3O_2S$ (421.6): calcd. C 68.38, H 6.64, N 9.97; found C 68.38, H 6.67, N 9.71. − ^{13}C NMR ($CDCl_3$): δ = 176.3/176.3, 159.5/159.8, 151.9/152.0, 139.7/140.0, 128.8/128.9, 128.3/128.3, 128.1/128.5, 126.3/127.0, 122.5/122.6, 122.0/122.1, 94.8/95.3, 59.1/60.5, 51.8/51.9, 48.9/49.1, 46.0/47.1, 37.0/37.1, 36.5/35.8, 31.1/32.1, 24.1/24.1, 23.2/23.8.

2,3-Dihydro-3-(morpholin-1-yl)-2,3-trimethylenebenzimidazo[2,1-b]thiazole (**3f**): From **1d** and 1-morpholinocyclopentene; yield 61%, m.p. 178−180°C ($CHCl_3$/heptane). − $C_{16}H_{19}N_3OS$ (421.6): calcd. C 63.76, H 6.35, N 13.94; found C 63.46, H 6.45, N 13.72. − ^{13}C NMR ([D$_6$]DMSO): δ = 157.9, 150.0, 133.0, 122.1, 121.4, 118.6, 110.2, 92.7, 67.0, 55.8, 48.2, 37.3, 34.8, 24.5.

3-Phenyl-2-phenylimino-4-(pyrrolidin-1-yl)-4,5-tetramethylenethiazolidine (**4a**): From **1a** or **2a** and 1-pyrrolidinocyclohexene; yield from **1a**/**2a** 91.5/64.5%, m.p. 144−146°C (MeCN). − $C_{23}H_{27}N_3S$ (377.6): calcd. C 73.17, H 7.21, N 11.13; found C 73.39, H 7.23, N 11.11. − ^{13}C NMR ([D$_6$]DMSO): δ = 157.5, 152.2, 140.8, 130.7, 128.9, 128.5, 127.6, 122.7, 122.5, 86.0, 45.5, 45.0, 30.2, 25.2, 24.9, 21.7, 19.2.

4-Hydroxy-3-phenyl-2-phenylimino-4,5-trimethylenethiazolidine (**5a**): 1.0 g (2.64 mmol) of **3a** was dissolved in 20 ml of warm ethanol. Then, 0.2 ml of concentrated hydrochloric acid was added and the solution was left to stand for 24 h at room temperature. The solvent was removed under reduced pressure and the residue was redissolved in 40 ml of 0.1 M HCl. Addition of an excess of $KHCO_3$ gave the solid products; yield 800 mg (98%), m.p. 127−128°C ($CHCl_3$/heptane). − $C_{18}H_{18}N_2OS$ (310.4): calcd. C 69.65, H 5.84, N 9.03; found C 69.39, H 5.75, N 9.12. − ^{13}C NMR ([D$_6$]DMSO): δ = 158.2, 151.3, 138.6, 129.0, 128.7, 128.4, 127.1, 123.3, 122.1, 103.2, 53.2, 36.4, 35.8, 23.2.

2,3-Dihydro-3-hydroxy-2,3-trimethylenebenzimidazo[2,1-b]thiazole (**5b**): From **3f** according to the hydrolysis of **3a** to **5a**; yield quantitative, m.p. 178−180°C (MeCN). − $C_{12}H_{12}N_2OS$ (232.3): calcd. C 62.04, H 5.21, N 12.06; found C 62.12, H 5.30, N 12.21. − ^{13}C NMR ([D$_6$]DMSO): δ = 157.2, 148.9, 131.4, 122.1, 121.6, 117.4, 109.6, 99.2, 62.6, 38.1, 36.3, 24.2.

4-Hydroxy-3-phenyl-2-phenylimino-4,5-tetramethylenethiazolidine (**6a**): From **2a** and 1-pyrrolidinocyclohexene after chromatographic work-up (heptane/acetone, 10:3) as oil; yield 22%. − ^{13}C NMR (CD_3CN): δ = 140.2, 122.4, 130.3*, 123.6 (iminophenyl, *ipso*, *o*, *m*, *p*), 130.1*, 129.6*, 129.8*, 128.2 (4-phenyl, *ipso*, *o*, *m*, *p*), 152.7 (C-2), 92.6 (C-4), 53.4 (C-5), 35.7, 34.4, 25.0, 22.6 (tetramethylene) (* may be interchanged).

3-Phenyl-2-phenylimino-4,5-trimethylenethiazoline-Δ^4 (**7a**): To 500 mg (1.45 mmol) of **1a** in 5 ml of MeCN, 195 mg of dry $CuCl_2$ and 597 mg (4.35 mmol) of pyrrolidinocyclopentene were added. After 7 days at room temperature, the solvent was removed under reduced pressure and the product was isolated by column chromatography (heptane/diethyl ether, 5:2); yield 252 mg (59.6%), m.p. 133−135°C (EtOH). − $C_{18}H_{16}N_2S$ (292.4): calcd. C 73.94, H 5.52, N 9.58; found C 73.90, H 5.52, N 9.58. − ^{13}C NMR ([D$_6$]DMSO): δ = 163.3, 151.3, 140.1, 138.0, 129.3, 129.1, 127.2, 126.6, 123.0, 121.6, 110.2, 28.4, 28.1, 24.7.

3-Phenyl-2-phenylimino-4,5-tetramethylenethiazoline-Δ^4 (**8a**): Obtained from **4a** and diluted hydrochloric acid analogously to **5a**; yield 92%, m.p. 122−123°C (EtOH). − $C_{18}H_{16}N_2S$ (306.4): calcd. C 74.47, H 5.92, N 9.14; found C 74.78, H 5.99, N 9.09. − ^{13}C NMR ([D$_6$]DMSO): δ = 159.9, 152.7, 137.7, 131.9, 129.5, 129.3, 129.0, 128.2, 123.0, 122.0, 107.0, 24.3, 23.7, 23.0, 22.3.

3-(p-Chlorophenyl)-2-phenylimino-4,5-tetramethylene-1,3-thiazoline-Δ^4 (**8b**) *and 2-(p-Chlorophenylimino)-3-phenyl-4,5-tetramethylenethiazoline-Δ^4* (**8c**): From 500 mg (1.56 mmol) of **2b** and 471 mg (3.11 mmol) of 1-pyrrolidinocyclohexene. The two isomers were separated by column chromatography (heptane/ethyl acetate, 10:1).

8b: Yield 28 mg (5.3%), m.p. 125−126°C (MeCN). − $C_{19}H_{17}ClN_2S$ (340.9): calcd. C 66.59, H 5.03, N 8.22; found C 66.60, H 5.13, N 8.35. − ^{13}C NMR ($CDCl_3$): δ = 159.6, 152.0, 135.8, 133.9, 131.3, 130.1, 129.6, 129.2, 123.1, 121.7, 107.4, 24.3, 23.6, 23.0, 22.2.

8c: Yield 210 mg (40%), m.p. 113−114°C (MeCN). − $C_{19}H_{17}ClN_2S$ (340.9): calcd. C 66.59, H 5.03, N 8.22; found C 66.70, H 5.20, N 8.31. − ^{13}C NMR ($CDCl_3$): δ = 160.0, 151.0, 137.2, 131.9, 129.4, 129.2, 128.7, 128.2, 127.6, 123.2, 107.0, 24.3, 23.6, 23.0, 22.2.

(1′-RS)-2-[(1-Ethoxycarbonyl-2-phenylethyl)imino]-3-methyl-4,5-tetramethylenethiazoline-Δ^4 (**8d**): 1.0 g (2.61 mmol) of **1b** and 1.0 g (6.61 mmol) of pyrrolidinocyclohexene were dissolved in 15 ml of chloroform. After 5 d at room temperature, the solvent was removed under reduced pressure. **8d** was isolated as an oil by column chromatography (heptane/acetone, 10:3); yield 1.09 g (48%). − $C_{19}H_{17}ClN_2S$ (344.5): calcd. C 66.25, H 7.02, N 8.13; found C 66.06, H 6.97, N 7.82. − ^{13}C NMR ($CDCl_3$): δ = 172.7, 160.9, 138.4, 131.8, 129.3, 127.8, 125.9, 105.1, 69.0, 60.1, 40.0, 29.8, 23.2, 22.8, 22.6, 21.7, 13.8.

(1′-RS)-2-[(1-Ethoxycarbonylethyl)imino]-3-methyl-4,5-tetramethylene-1,3-thiazoline-Δ^4 (**8e**): Obtained from **1c** and 1-pyrrolidinocyclohexene analogously to **8d**; isolated as an oil by column chromatography (hexane/ethyl acetate, 10:3), yield 40%. − $C_{13}H_{20}N_2O_2S$ (268.4): calcd. C 58.18, H 7.51, N 10.44; found C 57.91, H 7.33, N 10.27. − ^{13}C NMR ($CDCl_3$): δ = 174.4, 161.5, 131.8, 105.9, 62.4, 60.8, 30.4, 23.6, 23.3, 23.1, 22.2, 19.2, 14.3.

2,3-Tetramethylenebenzimidazo[2,1-b]thiazole (**8f**): A solution of 200 mg (0.81 mmol) of **6b** in 3 ml of concentrated hydrochloric acid was heated to reflux. After cooling, the solution was diluted with water and neutralised with sodium bicarbonate. Extraction with $CHCl_3$ and removal of the solvent gave 185 mg of the product (99.8%); m.p. 146−147°C (ethyl acetate). − $C_{13}H_{20}N_2O_2S$ (228.3): calcd. C 68.39, H 5.30, N 12.27; found C 68.44, H 5.27, N 12.29. − ^{13}C NMR ([D$_6$]DMSO): δ = 155.5, 147.7, 129.9, 127.1, 122.6, 120.3, 119.0, 118.7, 110.3, 24.2, 23.1, 22.6, 21.6.

Exchange Experiments: 500 mg (1.32 mmol) of 3-phenyl-2-phenylimino-4,5-tetramethylene-5-pyrrolidinothiazolidine (**4a**) was treated with 2.0 g (13.2 mmol) of morpholinocyclopentene. After 14 d at room temperature, no change could be observed according to TLC analysis. The same result was obtained with **3a** and pyrrolidinocyclohexene.

Synthesis of Thiazolidinones **10** *and 1,2,4-Dithiazolidinones* **12**. − *General Procedure:* A solution of lithium diisopropylamide was prepared from 222 mg of diisopropylamine (2.2 mmol) in 7 ml of THF and 1.375 ml of a 1.6 M solution of *n*BuLi in hexane (2.2 mmol). The mixture was cooled to −78°C and 2 mmol of the appropriate ester was added over 3 min. After stirring at −78°C for 15 min, a solution of 1 mmol of the heterocycle **1a** or **2a** in 3 ml of THF was added over a period of 7 min. Stirring at −78°C was continued for a further 30 min (1.5 h for **10d** and **12d**, R^5 = R^6 = Ph), and then the mixture was allowed to warm to room temperature. Saturated aqueous NH_4Cl solution (20 ml) and diethyl ether

(20 ml) were added. The organic layer was separated, washed with brine, and dried (Na_2SO_4). The solvent was removed under reduced pressure. The products **10** were isolated by crystallisation from a suitable solvent, the products **12** by chromatographic work-up.

5,5-Dimethyl-3-phenyl-2-phenyliminothiazolidin-4-one (**10a**): Yield 75%; m.p. 132−134°C (EtOH). − $C_{17}H_{16}N_2OS$ (296.4): calcd. C 68.89, H 5.44, N 9.45; found C 68.94, H 5.66, N 9.39. − ^{13}C NMR ($CDCl_3$): δ = 177.7, 153.1, 148.4, 135.0, 129.2, 129.0, 128.7, 127.9, 124.4, 120.9, 52.0, 28.6.

3,5-Diphenyl-2-phenyliminothiazolidin-4-one (**10b**): Yield 66%; m.p. 132−134°C (aq. EtOH). − $C_{21}H_{16}N_2OS$ (344.4): calcd. C 73.23, H 4.68, N 8.13; found C 73.20, H 4.76, N 8.21. − ^{13}C NMR ($CDCl_3$): δ = 172.7, 153.8, 148.3, 135.9, 135.2, 129.5, 129.4, 129.3, 129.1, 129.0, 128.4, 128.3, 124.9, 121.2, 51.7.

5-Methyl-3,5-diphenyl-2-phenyliminothiazolidin-4-one (**10c**): Yield 71%; m.p. 144−145°C (EtOH). − $C_{22}H_{18}N_2OS$ (358.5): calcd. C 73.72, H 5.06, N 7.81; found C 73.82, H 5.07, N 7.72. − ^{13}C NMR ($CDCl_3$): δ = 176.2, 153.1, 148.5, 140.9, 135.3, 129.5, 129.3, 129.1, 129.1, 128.5, 128.3, 126.5, 124.8, 121.2, 58.4, 28.1.

3,5,5-Triphenyl-2-phenyliminothiazolidin-4-one (**10d**): Yield 82%; m.p. 165−166°C (EtOH). − $C_{27}H_{20}N_2OS$ (420.5): calcd. C 77.12, H 4.79, N 6.66; found C 77.48, H 4.79, N 6.51. − ^{13}C NMR ($CDCl_3$): δ = 173.8, 152.2, 148.1, 140.6, 135.0, 129.3, 129.1, 128.9, 128.6, 128.3, 128.2, 128.1, 124.7, 121.1, 67.0.

5-Isopropylidene-4-phenyl-1,2,4-dithiazolidin-3-one (**12a**): Isolated by column chromatography (heptane/diethyl ether, 5:1); yield 27%, m.p. 112−114°C (aq. EtOH). − $C_{11}H_{11}NOS_2$ (237.3): calcd. C 55.67, H 4.67, N 5.90; found C 55.88, H 4.98, N 5.77. − ^{13}C NMR ([D_6]DMSO): δ = 199.5, 179.4, 135.2, 129.6, 129.5, 128.3, 55.3, 27.3.

4-Phenyl-5-(1-phenylethylidene)-1,2,4-dithiazolidin-3-one (**12c**): Isolated by column chromatography (heptane/diethyl ether, 5:1), yield 25%, m.p. 116−117°C (aq. EtOH). − $C_{16}H_{13}NOS_2$ (299.4): calcd. C 64.18, H 4.38, N 4.68; found C 64.26, H 4.52, N 4.68. − ^{13}C NMR ([D_6]DMSO): δ = 199.0, 179.0, 138.7, 135.3, 129.7, 129.5, 129.1, 128.7, 128.4, 126.3, 61.7, 26.5.

5-Diphenylmethylene-4-phenyl-1,2,4-dithiazolidin-3-one (**12d**): Isolated by column chromatography (heptane/*t*BuOMe, 94:6); yield 27%, m.p. 137−139°C (EtOH). − $C_{21}H_{15}NOS_2$ (361.5): calcd. C 69.78, H 4.18, N 3.87; found C 69.67, H 4.08, N 3.57. − ^{13}C NMR ([D_6]DMSO): δ = 198.3, 175.8, 139.2, 136.6, 129.9, 129.7, 129.1, 128.9, 128.7, 128.5, 70.7.

☆ Dedicated to Professor *Dieter Martin* on the occasion of his 65th birthday.

[1] G. L'abbé, A. Vandendriessche, *J. Heterocycl. Chem*. **1990**, 1629−1631.
[2] G. L'abbé, N. Wayns, *Bull. Soc. Chim. Belg*. **1991**, *100*, 185−186.
[3] G. L'abbé, E. Albrecht, *Bull. Soc. Chim. Belg*. **1991**, *100*, 27−28.
[4] F. Tittelbach, *J. Prakt. Chem*. **1991**, *333*, 579−592.
[5] D. Martin, F. Tittelbach, *J. Chem. Soc., Perkin Trans.1* **1985**, 1007−1013.
[6] F. Tittelbach, *J. Prakt. Chem*. **1991**, *333*, 107−117.
[7] G. L'abbé, E. van Look, E. Verhelst, S. Toppet, *J. Heterocycl. Chem*. **1975**, *12*, 607−608.
[8] J. Llinares, J. Elguero, *Org. Magn. Reson*. **1980**, *14*, 20−24.
[9] G. L'abbé, N. Wayns, I. Sannen, P. Debelke, S. Toppet, *J. Heterocycl. Chem.* **1991**, *28*, 405−409.
[10] G. L'abbé, K. Buelens, *Tetrahedron* **1990**, *46*, 1281−1286.
[11] F. A. Carey, R. J. Sundberg, *Organische Chemie,* VCH Verlag, Weinheim, **1995**, p. 156.
[12] G. L'abbé, I. Sannen, A. Vandendriessche, *J. Heterocycl. Chem.* **1992**, *29*, 69−72.
[13] F. H. van der Steen, G. van Koten, *Tetrahedron* **1991**, *47*, 7503−7524.
[14] W. Lwowski in *Comprehensive Heterocyclic Chemistry* (Eds.: A. R. Katritzky, C. W. Rees), Pergamon Press, Oxford **1984**, vol. 7, p. 1−46.
[15] R. Huisgen in *1,3-Dipolar Cycloaddition Chemistry* (Ed.: A. Padwa), Wiley, **1984**, vol. 1, chapter 1.
[16] G. M. Sheldrick, *SHELX-97, Program Package for Determination and Refinement of Ccrystal Structures*, University of Göttingen, Germany, **1997**.
[17] A list of structure factors, anisotropic thermal parameters, atomic coordinates and tables of bond lengths and angles may be obtained from the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-76344 Eggenstein-Leopoldshafen, Germany, on quoting the depository number CSD-407624, the names of the authors, and the full journal citation.
[18] M. Freund, E. Asbrand, G. Bachrach, *Justus Liebigs Ann. Chem.* **1895**, *285*, 154−203.
[19] F. Tittelbach, *J. Prakt. Chem*. **1990**, *332*, 181−190.
[20] L. Floch, A. Martvon, M. Uher, J. Lesko, W. Weis, *Collect. Czechoslov. Chem. Commun.* **1977**, *42*, 2945−2952.
[21] N. H. Tuobro, A. Holm, *J. Chem. Soc., Perkin Trans.1* **1978**, 1440−1445.

[97297]