Cycloaddition-Elimination Reactions of 5-Imino-1,2,4-dithiazolidin-3-ones with Heterocumulenes

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5-Benzylimino-1,2,4-dithiazolidin-3-one (**2a**) reacts with heterocumulenes (isocyanates, isothiocyanates, ketenes) with elimination of carbonyl sulfide, yielding the heterocycles **6-8**. The thiadiazolidine **6a**, obtained from **2a** and phenyl isocyanate, underwent similar reactions but under milder conditions, indicating that phenyl isocyanate is a better leaving group than carbonyl sulfide.

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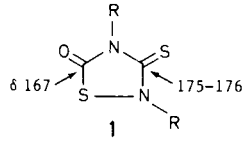
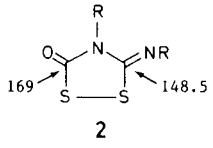
The bromine-oxidation of isothiocyanates in the presence of water gives so-called "isothiocyanate oxides" of empirical formula $(RNCS)_2O$, whose structures have been debated over a long period starting with Freund in 1895 [1]. The oxides were formulated either as thiadiazolidines **1** or as dithiazolidines **2** until Bradsher *et al.* [2] divided them into two classes according to the presence or absence of a C=N absorption at *ca* 1640 cm^{-1} in the ir spectra. Thus, simple alkyl derivatives (methyl, ethyl) correspond to **1**, whereas aralkyl and aryl derivatives have structure **2**. These structures have been confirmed by their C=S (δ ~ 170) and C=N (δ ~ 150) chemical shifts in the ^{13}C nmr spectra, comparable with our model compound **3** [3] (see drawings, deuteriochloroform as solvent).



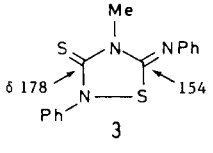
1

R = Me, Et



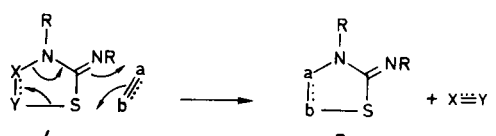
2

a: R = $PhCH_2$ (δ given)
b: R = Ph



3

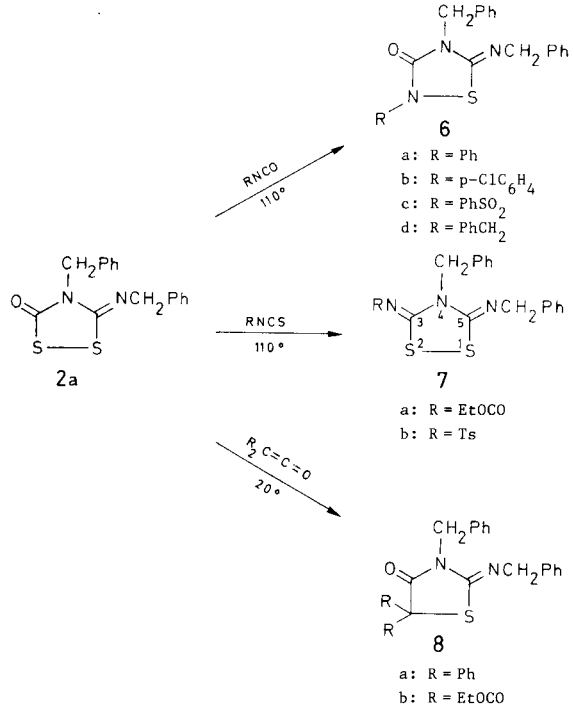
The heterocycles **2a,b** possess an imine function adjacent to a ring-sulfur atom and, hence, should undergo cycloaddition-elimination reactions with unsaturated systems according to the general equation **4** → **5**. Previous studies have shown that this type of ring transformation can be carried out when the extruded XY molecule is a nitrile [4], dinitrogen [5,6], a sulfene [5] or an isothiocyanate [7]. In the case of **2**, carbonyl sulfide would be eliminated.



4 5

Compound **2a** reacts with a series of heterocumulenes in toluene to give the heterocycles **6-8** in good to high yields (Scheme 1). Diphenylketene and bis(ethoxycarbonyl)ketene [8] react at room temperature, whereas isocyanates and isothiocyanates require refluxing conditions.

Scheme 1



2a

6
a: R = Ph
b: R = p-ClC_6H_4
c: R = $PhSO_2$
d: R = $PhCH_2$

7
a: R = EtOCO
b: R = Ts

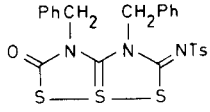
8
a: R = Ph
b: R = EtOCO

Mechanistically, the cycloaddition-elimination reactions probably proceed *via* thiapentalene-like intermediates such as **9**. Support for this was found when the reaction of **2a** (0.25 *M*) with tosyl isothiocyanate (5 equivalents) was monitored in deuterated toluene at 90° by ^1H nmr spectroscopy. Besides the methylene resonances of **2a** (δ 4.16 and 4.73) and **7b** (δ 4.13 and 4.90), singlet absorptions were observed at δ 4.67 and 5.03, which constituted the major product peaks at the early stage (~20% after 2 hours) but disappeared as the reaction progressed. We confidently assign them to the benzyl methylene resonances of **9**.

Table 1
Spectral Characterization of the new Heterocylces [a]

Compound	IR		^{1}H NMR		^{13}C NMR				
	C=N	C=O	>NCH$_2$	=NCH$_2$	>NCH$_2$ [b]	=NCH$_2$ [c]	C=N	C=O ring	other absorptions [d]
6a	1655	1715	5.05	4.35	46.9	55.9	147.6	152.9	
6b	1660	1710	5.05	4.35	47.0	56.0	147.0	152.6	
6c	1660	1740	4.80	4.30	46.9	55.5	145.5	151.1	
6d	1650	1705	4.75 5.00	4.20	46.8 49.3	56.0	148.7	155.2	
7a	1640		5.45	4.50	51.9	56.9	151.8 172.6		14.3, 63.0 (Et) 164.1 (CO)
7b	1645		5.25	4.50	52.1	57.0	150.2 165.8		21.6 (Me)
7c	1625		5.60	4.50	52.3	57.3	152.4 172.9		177.4 (CO)
7d	1620		5.35	4.55	51.2	56.1	150.5 154.0		
8a	1655	1720	5.05	4.55	46.5	55.4	149.8	173.7	67.3 (C-5)
8b	1650	1750	5.00	4.50	47.0	55.4	147.9	165.1	13.7, 63.8 (Et) 65.2 (C-5), 163.9 (CO)

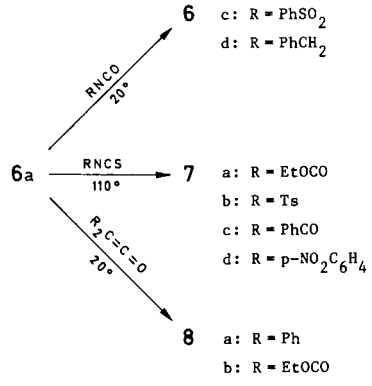
[a] The ir spectra (cm^{-1}) were taken in potassium bromide discs. The nmr spectra (δ-values from tetramethylsilane) were recorded in deuteriochloroform. [b] Coupling constant $^1J_{CH}$ = 141-143 Hz. [c] Coupling constant $^1J_{CH}$ = 133-134 Hz. [d] The phenyl absorptions are at the expected positions and are omitted.



9

Compound **6a** also possesses a thioimidate structural unit which is capable of undergoing cycloaddition-eliminations with heterocumulenes. The reactions, summarized in Scheme 2, occur under milder conditions than do those of **2a**. In particular, **2a** does not react with *p*-nitrophenyl isothiocyanate, whereas **6a** furnishes **7d** in high yield (77%). The ring-degenerate transformation of **6a** into **6c** is promoted by the electrophilicity of the isothiocyanate since the reverse reaction **6c** → **6a** does not take place in toluene at 90°.

Scheme 2



The structures of the new heterocycles were elucidated by spectral analyses and the pertinent data are summarized in Table 1.

EXPERIMENTAL

4-Benzyl-5-benzylimino-2-phenyl-1,2,4-thiadiazolidin-3-one (**6a**).

This compound was obtained by heating **2a** (2 g, 6.4 mmoles) with phenyl isocyanate (3.8 g, 32 mmoles) in toluene (50 ml) at reflux temperature for 24 hours, followed by crystallization of the reaction mixture from *n*-heptane (50 ml), yield 94% (2.25 g), mp 98° (ether).

Anal. Calcd. for $C_{22}H_{19}N_3OS$ (mol wt 373): C, 70.75; H, 5.13. Found: C, 70.69; H, 5.17.

4-Benzyl-5-benzylimino-2-(*p*-chlorophenyl)-1,2,4-thiadiazolidin-3-one (**6b**).

This compound was obtained by heating **2a** (1 g, 3.2 mmoles) with *p*-chlorophenyl isocyanate (2.4 g, 16 mmoles) in toluene (25 ml) at reflux temperature for 24 hours, followed by crystallization of the reaction mixture from *n*-heptane (25 ml), yield 97% (1.25 g), mp 107° (ether).

Anal. Calcd. for $C_{22}H_{18}ClN_3OS$ (mol wt 408): C, 64.78; H, 4.44. Found: C, 64.63; H, 4.52.

4-Benzyl-5-benzylimino-2-phenylsulfonyl-1,2,4-thiadiazolidin-3-one (**6c**).

This compound was obtained by heating **2a** (1 g, 3.2 mmoles) with phenylsulfonyl isocyanate (2.9 g, 16 mmoles) in toluene (25 ml) at reflux temperature for 2 hours, followed by cooling off the solution, yield 85% (1.15 g), mp 112° (chloroform).

This compound was also obtained in 98% yield by reacting **6a** (0.2 g, 0.54 mmole) with phenylsulfonyl isocyanate (0.5 g, 2.7

mmoles) in toluene (20 ml) at room temperature for 1 day.

Anal. Calcd. for $C_{22}H_{19}N_3O_3S_2$ (mol wt 438): C, 60.39; H, 4.52. Found: C, 60.24; H, 4.42.

5-Benzylimino-2,4-dibenzyl-1,2,4-thiadiazolidin-3-one (**6d**).

This compound was obtained by heating **2a** (0.5 g, 1.6 mmoles) with benzyl isocyanate (1.06 g, 8 mmoles) in toluene (50 ml) at reflux temperature for one week, followed by column chromatography on silica gel with ether/*n*-hexane (20:80) as the eluent, yield 36% (220 mg), mp 65° (ether).

This compound was also obtained in 82% yield by reacting **6a** (0.5 g, 13 mmoles) with benzyl isocyanate (0.86 g, 65 mmoles) in toluene (50 ml) at room temperature for 2 hours, followed by crystallization of the reaction mixture from *n*-heptane (50 ml).

Anal. Calcd. for $C_{23}H_{21}N_3OS$ (mol wt 387.5): C, 71.29; H, 5.46. Found: C, 71.28; H, 5.41.

4-Benzyl-5-benzylimino-3-ethoxycarbonylimino-1,2,4-dithiazolidine (**7a**).

This compound was obtained by heating **2a** (1 g, 3.2 mmoles) with ethoxycarbonyl isothiocyanate (4.2 g, 32 mmoles) in toluene (25 ml) at reflux temperature for 4 days, followed by crystallization of the reaction mixture from *n*-heptane (25 ml), yield 73% (0.87 g), mp 97° (ether).

This compound was also obtained in 100% yield (0.20 g) by heating **6a** (0.2 g, 0.54 mmole) with ethoxycarbonyl isothiocyanate (0.42 g, 3.2 mmoles) in toluene (20 ml) at reflux temperature for 2 hours.

Anal. Calcd. for $C_{19}H_{19}N_3O_2S_2$ (mol wt 385): C, 59.20; H, 4.97. Found: C, 59.27; H, 4.92.

4-Benzyl-5-benzylimino-3-tosylimino-1,2,4-dithiazolidine (**7b**).

This compound was obtained by heating **2a** (0.5 g, 1.6 mmoles) with tosyl isothiocyanate (1.7 g, 8 mmoles) in dry toluene (50 ml) at reflux temperature for 1 week, followed by crystallization of the reaction mixture from *n*-heptane (400 ml), yield 66% (330 mg), mp 161° (ether).

This compound was also obtained in 62% yield (155 mg) by heating **6a** (0.2 g, 0.54 mmole) with tosyl isothiocyanate (0.58 g, 2.7 mmoles) in dry toluene (25 ml) at reflux temperature for 24 hours.

Anal. Calcd. for $C_{23}H_{21}N_3O_2S_3$ (mol wt 468): C, 59.08; H, 4.53. Found: C, 58.92; H, 4.49.

3-Benzoylimino-4-benzyl-5-benzylimino-1,2,4-dithiazolidine (**7c**).

This compound was obtained by heating **6a** (1 g, 2.7 mmoles) with benzoyl isothiocyanate (2.2 g, 13.5 mmoles) in toluene (25 ml) at reflux temperature for 5 hours, followed by crystallization of the reaction mixture from *n*-heptane (50 ml), yield 92% (1.04 g), mp 127° (ether).

Anal. Calcd. for $C_{23}H_{19}N_3OS_2$ (mol wt 417.6): C, 66.16; H, 4.59. Found: C, 66.32; H, 4.53.

4-Benzyl-5-benzylimino-3-(*p*-nitrophenyl)imino-1,2,4-dithiazolidine (**7d**).

This compound was obtained by heating **6a** (0.5 g, 1.3 mmoles) with *p*-nitrophenyl isothiocyanate (0.24 g, 1.3 mmoles, freshly crystallized from dry carbon tetrachloride) in toluene (50 ml) at reflux temperature for 3 days, followed by crystallization from *n*-heptane (200 ml), yield 77% (435 mg), mp 139° (chloroform/ether).

Anal. Calcd. for $C_{22}H_{18}N_4O_2S_2$ (mol wt 434.5): C, 60.81; H, 4.18. Found: C, 60.88; H, 4.12.

3-Benzyl-2-benzylimino-5,5-diphenylthiazolidin-4-one (**8a**).

This compound was obtained by reacting **2a** (0.5 g, 1.6 mmoles) with diphenylketene (0.63 g, 3.2 mmoles) in dry toluene (50 ml) at room temperature for 3 days, followed by crystallization of the reaction mixture from *n*-heptane (100 ml), yield 75% (535 mg), mp 121° (chloroform).

This compound was also obtained in 70% yield (405 mg) by reacting **6a** (0.5 g, 1.3 mmoles) with diphenylketene (0.5 g, 2.6 mmoles) in dry toluene (50 ml) at room temperature for 30 minutes.

Anal. Calcd. for $C_{29}H_{24}N_2OS$ (mol wt 449): C, 77.65; H, 5.39. Found: C, 77.40; H, 5.30.

3-Benzyl-2-benzylimino-5,5-di(ethoxycarbonyl)thiazolidin-4-one (**8b**).

This compound was obtained by reacting **2a** (0.5 g, 1.6 mmoles) with bis(ethoxycarbonyl)ketene (0.60 g, 3.2 mmoles) in dry toluene (50 ml) at room temperature for 2 days, followed by crystallization of the reaction mixture from ether (30 ml); yield 61% (430 mg), mp 57° (ether).

This compound was also obtained in 73% yield (400 mg) by reacting **6a** (0.5 g, 1.3 mmoles) with bis (ethoxycarbonyl)ketene (0.48 g, 2.6 mmoles) in dry toluene (50 ml) at room temperature for 30 minutes.

Anal. Calcd. for $C_{23}H_{24}N_2O_5S$ (mol wt 440.5): C, 62.71; H, 5.49. Found: C, 62.90; H, 5.42.

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