REACTIVITY OF N-ALKYLTHIIRANIMINES TOWARD SIMPLE NUCLEOPHILES AND ISO(THIO)CYANATES

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Abstract – Hydrolysis of N-(1-dimethylcarbamoyl-1-methylethyl)-thiiranimines occurs with S-C(sp²) ring cleavage while attack of hydrochloric acid results in S-C(sp³) ring opening. The latter mode of ring opening is also observed in [3+2] cycloaddition reactions with iso(thio)cyanates where the heterocumulene reacts via the C-chalcogen bond; only a sterically less hindered isopropyl substituted thiiranimine adds to the C=N bond in isocyanates to yield 4-thiohydantoins. The cycloadducts give a variety of hydrolysis products, in particular imidazo[2,1-b]oxazoles and –thiazoles, oxazolones, and stable thietes. Insertion of a thiocarbonyl into an isopropyl CH bond is observed yielding an annulated cyclopropane unit.

INTRODUCTION

The study of small ring compounds has played an important role in the development of our understanding of reactivity and bonding in organic chemistry.¹ In handling these systems, problems resulting from ring strain are less pronounced for sulfur-containing compounds because bonds to carbon are long and smaller angles are tolerated.² So α-thiolactones can be isolated in contrast to their unstable oxygen congeners³ and, in contrast to the unknown oxiranimines,⁴ stable N-sulfonyl-thiiranimines (2) can be obtained from arenesulfonyl isothiocyanates (1) and diphenyldiazomethane (Scheme 1).⁵,⁶ A thiadiazoline as [3+2] cycloadduct can be assumed as intermediate and a thiadiazoline also allows access to a silyl substituted thiiranimine where the exocyclic nitrogen is part of an azine unit.⁷ In contrast to these “rational” methods,
an unexpected route to thiiranimines 6 employs the reaction of thioketene S-oxides 3 with aminoazirines such as 4. The reaction is apparently initiated by a [3+2] cycloaddition of the sulfine unit in 3 to the C=N bond to give oxathiazolidines 5 as intermediates. This reactivity of S-oxides 3 is remarkable as non-cumulated sulfines only rarely react as 1,3-dipoles. So far, only the reactivity of sulfonyl derivatives 2 was probed. The uniform feature is ring-opening by cleavage of the S-C(sp³) bond. This is in line with a polarization as in diheterotrimethylenemethanes 2A,B where the negative charge is efficiently stabilized by the electron-withdrawing sulfonyl group (Scheme 1). In contrast, in thiiranimines 6 the electronic effect of the carboxamido group is certainly negligible and so the N-substituent is of the alkyl type. This should lead to a different reaction behavior. This consideration marks the starting point of the present study.

![Scheme 1. Syntheses of thiiranimines 2, 6](image)

**RESULTS AND DISCUSSION**

In contrast to thiiranimines 2, the bulky C-alkyl substituents in 6 prevent an uncatalyzed reaction with methanol, but hydrolytic ring-opening of 6 is achieved under catalysis by trifluoroacetic acid (Scheme 2). The spectroscopic data allow to assign structure 7 to the water addition product. Thus, ring opening occurs via primary attack of water at the imino carbon and leads to S-C(sp³) ring opening. Aqueous hydrochloric acid and 6 give only trace amounts of 7, but mainly thiazolinones 9. This means that a nucleophilic attack of chloride on C-3 prevails in spite of the extreme steric screening of this carbon
and then sulfur is the best possible leaving group leading to 8 as a result of S-C(sp³) bond cleavage formally as in thiiranamines 2. The nucleophilic thiol sulfur in 8 finally displaces the amino group to give recyclization product 9 (Scheme 2). The structure of 9a was unambiguously established by a single-crystal X-ray study (Figure 1).

Scheme 2. Attack of simple nucleophiles on thiiranamines 6

N-Sulfonyl-thiiranamines 2 give [3+2] cycloadducts with enamines, ynamines, and aldehydes, but do not react with iso(thio)cyanates. In contrast, thiiranamines 6 proved unreactive toward ynamines, acetylene
dicarboxylate, isonitriles, or tetracyanoethylene, but undergo a smooth reaction with isocyanates as well with isothiocyanates. Thus, the symmetrically substituted thiraninines \(6a,b\) react with sulfonylisocyanates \(10a,b\) at 0 °C and with aryl isocyanates \(10c,d\) on gentle warming to give 1:1 cycloadducts \(11\) (Scheme 3). This structure is derived from the spectroscopic data and from an X-ray investigation of \(11a\) (Figure 2).\(^{13}\) So the isocyanates \(10\) show the unusual reaction across their carbonyl group.\(^{14}\) The same reaction behavior is seen for the very reactive sulfonylisocyanates \(10e,f\). However, here the exocyclic sulfonyl moiety is easily hydrolyzed on chromatographic work-up and so yields are low (starting from \(10e\)) or cycloadducts \(11h,i\) (starting from \(10f\)) are only seen in the crude reaction mixture. Hydrolytic loss of the sulfonyl moiety leads to bicyclic compounds \(12\); apparently the initial product of hydrolysis is an imino compound (\(11\) with \(R^3 = H\)) which then attacks the exocyclic amide unit with extrusion of dimethylamine and cyclization (Scheme 3). This reaction pathway is substantiated by independent hydrolysis experiments with \(11a,b\) to give \(12a,b\). Structure \(12\) is proven by the X-ray structural investigation of \(12a\) (Figure 3).\(^{15}\) Under the more forcing conditions of half-concentrated hydrochloric acid, also the \(N\)-aryl-substituted oxazolin-4-thiones \(11d,e\) can be hydrolyzed. These reaction conditions result in complete displacement of the exocyclic imino group by the oxo unit of \(14\) and by a transition from the dimethylcarbamoyl to a monosubstituted amide derived from the original isocyanate (Scheme 3). Here, we assume the intermediacy of \(13\) with a tetrahedral carbon resulting from attack of water on the imino carbon. The high density of heteroatoms again called for a single-crystal X-ray study which proved the structure of \(14a\) (Figure 4).\(^{16}\)
The sterically less hindered thiiranimine 6c gives two isomeric 1:1 cycloadducts with isocyanates 10. One and the only one starting from 10c is again a 2-imino-oxazolidine-4-thione 11 (Scheme 4). The second product is the corresponding product 15 of cycloaddition across the C=N bond of the isocyanate as finally confirmed by an X-ray study (Figure 5). 17 It appears that due to the smaller substituent on C-5 of the five-membered ring Pitzer tension is reduced and allows the C-5 substituents to be accommodated next to the substituted ring nitrogen N1. However, a relatively long N1-C5 bond of 151.6 pm should be noted.

Acid-catalyzed hydrolysis of cycloadducts 11k,l with \( R^2 = i\text{-Pr} \) should be expected to give again oxazolidinones 14. However, in striking contrast to expectation, the reaction mixture turns immediately orange and work-up leads to an orange-colored oil with a complex \(^1\)H-NMR spectrum. From this oil, colorless crystals can be isolated which allowed an X-ray structural investigation to reveal thiete structure 19a (Figure 6). 18 Now the color of the oil can be explained by the thione unit in valence tautomer 18 (Scheme 4). We see here an amazing \( \beta \)-elimination involving an alkyl CH bond from 16 to 17 and then an enethione/thiete (18/19) equilibrium. Such equilibria have been seen before, 19 but the present case is unusual as it involves the thiocarbonyl of a thioamide moiety other than the usual stabilization of thiotes
by aryl substituents. In previous studies, this type of thiete has only been invoked as an intermediate.\(^\text{20}\)

![Thiete structure](image)

\[\text{R}^3\text{NCO} \rightarrow \text{Me}_2\text{N} \quad \text{Et}_2\text{O or CHCl}_3\]

**Scheme 4.** Cycloaddition of thiranimine 6c to isocyanates 10 and hydrolysis products 18/19

The noteworthy generation of a thiete from the vicinal thione/isopropyl units in 11k,l motivated to search for the same effect in related structures such as in 15. But when 15c is treated with aqueous hydrochloric acid just as it had been done for 11k,l, there is no orange color at all. From the complex product mixture, a compound lacking the dimethylamino unit can be isolated. But the \(^{13}\)C NMR spectrum shows three quaternary aliphatic carbons which is not compatible with 18 or other compounds found earlier. The solution is again brought by an X-ray structural investigation (Figure 7).\(^\text{21}\) We are dealing with a tricyclic compound 21 where the original isopropyl structural units show up as annulated cyclopropane (Scheme 5). Our rational is the unusual insertion of the thiocarbonyl group into the isopropyl CH bond to give intermediate 20. This may look like a light-induced process rather than acid-catalyzed,\(^\text{22}\) but in a control experiment the conversion of 15c into 21 could not be induced photochemically. The thiol in 20 finally attacks the amide unit, displaces the dimethylamino group and leads to formation of a \(\gamma\)-thiolactone.
Figure 5. Perspective ORTEP presentation of the molecular structure of 4-thioxo-imidazolidin-2-one \(15b\) (hydrogen atoms not shown).

Figure 6. Perspective ORTEP presentation of the molecular structure of thiete \(19a\) (hydrogen atoms not shown).

Scheme 5. Hydrolysis of imidazolinone \(15c\) to give tricycle \(21\).
Scheme 6. Cycloaddition of thiiranimines 6a,b to isothiocyanates 22 and hydrolysis products

![Scheme 6](image)

Figure 7. Perspective ORTEP presentation of the molecular structure of tricycle 21
(hydrogen atoms not shown)

Isothiocyanates are known to be less reactive than isocyanates, but cycloadduct formation with thiiranimines 6 is possible, though for 4-nitrophenyl isothiocyanate (22b) heating to 60 °C is required. After isocyanates 10 show the preference for cycloaddition across the C=O bond, it is no surprise that isothiocyanates also enter into the reaction via their C-chalcogen bond to give [3+2] cycloadducts 23
(Scheme 6). Structure assignment is suggested by the similarity of spectroscopic data, especially $^{13}$C NMR shifts, to those of isocyanate cycloadducts 11 (vide supra). In some cases trace amounts of hydrolysis products are detected and hydrolysis can also be induced deliberately. Thus, the action of hydrochloric acid on $N$-tosyl derivatives 23a-c yields bicycles 24a-c as suggested by the similarity of spectroscopic data with those of 12a,b and also the analogous reaction mechanism is invoked (cf. Scheme 3). Starting from 4-nitrophenyl derivatives 23d,e, products 25 are formed by analogy with hydrolysis products 14 and again an intermediate of type 13 is plausible.

**CONCLUSION**

Thiiranimines 6 with their alkyl type $N$-substituent show a widely different reaction pattern from their $N$-sulfonyl congeners 2 though except for the trifluoroacetic acid-catalyzed hydrolysis of 6 both types of thiiranimines enter into reactions via cleavage of the C(sp$^3$)-S bond which is also the longest bond in the molecular structures.\(^5\),\(^8\) However, the contrasting reactivity toward iso(thio)cyanates demonstrates that $N$-sulfonyl-thiiranimines 2 are mainly electrophilic while the thiiranimines 6 of the present study are in the first place nucleophilic. Thus, a wealth of heterocyclic structures is provided by the cycloaddition reactions and the subsequent hydrolysis experiments. A limitation is the need for bulky substituents to make thioketene S-oxides 3 isolable and use them in the synthesis of 6. However, the different bond selectivity of 6a,b vs. 6c toward isocyanates shows that even with the presently possible substitution pattern different steric effects are seen. Moreover, it should not be underestimated that the bulky substituents certainly increase the stability of the products and e. g. may be crucial in the formation and stabilization of thietes 19 or to allow the highly unusual thermal insertion reaction in the formation of 21.

**EXPERIMENTAL**

Melting points were determined on a Leitz hot-stage microscope and are uncorrected. IR spectra were recorded as KBr pellets or for oils as films between NaCl plates on Perkin-Elmer instruments 257, 299, and 399. $^1$H- and $^{13}$C-NMR spectra were recorded on Bruker spectrometers WH 270 and WM 400 with TMS as internal reference at $\delta = 0.00$ and using CDCl$_3$ as solvent. For $^{13}$C-NMR spectra, only the significant shifts with $\delta > 50$ are given for characterization and all are inactive in the DEPT mode (quaternary carbons). MS spectra were obtained with a Varian CH7 with ionization energy 70 eV. X-ray measurements were carried out using a single-crystal CAD 4 (Enraf-Nonius; Cu-$K_{\alpha}$ radiation) or a Hilger & Watts instrument (Mo-$K_{\alpha}$ radiation). Preparative TLC (layer ca. 2 mm) was performed using silica PF$_{254}$ (Merck). Isolated products were recrystallized from dichloromethane/$n$-hexane or diethyl ether/$n$-hexane unless noted otherwise. Petroleum ether (PE) had boiling point range 60-70 °C. Thiiranimines 6 were synthesized as reported before.\(^8\) Isocyanates 10 were commercially available.
Isothiocyanate 22a\textsuperscript{24} and 22b\textsuperscript{25} were obtained using literature procedures.

**Trifluoroacetic Acid-catalyzed Hydrolysis of Thiiranimines 6a,b.**

A suspension of 6 (1 mmol) in CF\textsubscript{3}COOH (1 mL) and H\textsubscript{2}O (10 mL) was stirred at rt for 5 h when TLC showed no more 6. The reaction mixture was extracted with CHCl\textsubscript{3}. The extract was shaken with sat. aq. NaHCO\textsubscript{3} and dried (Na\textsubscript{2}SO\textsubscript{4}). The filtrate was concentrated in vacuo and the product purified by preparative TLC (PE/EtOAc 1:2 v/v) to give 7a (96\%) and 7b (99\%).

\textbf{N,N,2-Trimethyl-2-(2,2,6,6-tetramethyl-1-thio-cyclohexanecarbonyl)aminopropionamide (7a):} mp 132 °C; IR 3320, 2560, 1640, 1450, 1005 cm\textsuperscript{-1}; \textsuperscript{1}H NMR \(\delta\) 0.93, 1.28 (each s, 6H, ring-CMe\textsubscript{2}), 1.66 (s, 6H, CMe\textsubscript{2}), 1.77 (s, 1H, SH), 2.6-1.6 (br, 6H, 3 CH\textsubscript{2}), 3.06 (s, 6H, NMe\textsubscript{2}), 9.0 (br, 1H, NH); \textsuperscript{13}C NMR \(\delta\) 57.7(C-NH), 70.8 (C-SH), 171.9 (C=O), 173.6 (C=O). Anal. Calcd for C\textsubscript{17}H\textsubscript{32}N\textsubscript{2}O\textsubscript{2}S; C, 62.14; H, 9.84; N, 8.53; S, 9.76. Found: C, 62.18; H, 9.77; N, 8.36; S, 9.69.

\textbf{2-(1-tert-Butyl-2,2-dimethyl-1-thio-butyryl)amino-N,N-2-trimethylpropionamide (7b):} mp 102 °C; IR 3300, 1630, 1400 - 1500 cm\textsuperscript{-1}; \textsuperscript{1}H NMR \(\delta\) 1.27 (s, 18H, t-Bu\textsubscript{2}), 1.65 (s, 6H, CMe\textsubscript{2}), 2.00 (s, 1H, SH), 3.06 (s, 6H, NMe\textsubscript{2}), 8.57 (br, 1H, NH); \textsuperscript{13}C NMR \(\delta\) 57.5, 73.6 (C-SH), 171.0, 173.5. Anal. Calcd for C\textsubscript{16}H\textsubscript{32}N\textsubscript{2}O\textsubscript{2}S; C, 60.70; H, 10.21; N, 8.85; S, 10.13. Found: C, 60.88; H, 10.01; N, 8.59; S, 9.86.

**Hydrochloric Acid-catalyzed Hydrolysis of Thiiranimines 6a-c.**

6 (1 mmol) in Et\textsubscript{2}O (5 mL) and 2 M HCl (2 mL) were mixed at rt. Control by TLC showed immediate reaction. The mixture was washed with sat. aq. NaHCO\textsubscript{3} and dried (Na\textsubscript{2}SO\textsubscript{4}). After preparative TLC (PE/EtOAc 1:2 v/v) gave 9a (86\%), 9b (50\%), and 9c (85\%).

\textbf{2-(1-Chloro-2,2,6,6,-tetramethylcyclohexyl)-4,4-dimethyl-2-thiazolin-5-one (9a):} mp 98 °C; IR 1700, 1600 cm\textsuperscript{-1}; \textsuperscript{1}H NMR \(\delta\) 1.08, 1.32, 1.42 (each s, 6H, ring-CMe\textsubscript{2}), 2.63 – 1.63 (br, 6H, 3 CH\textsubscript{2}); \textsuperscript{13}C NMR \(\delta\) 86.6, 91.1, 169.6 (C=N), 213.0 (C=O); MS m/z 273 (M\textsuperscript{+} - CO, 20), 237 (M\textsuperscript{+} - CO - HCl, 100). Anal. Calcd for C\textsubscript{15}H\textsubscript{24}ClNOS; C, 59.67; H, 8.03; N, 4.64; S, 10.64, Cl 11.74. Found: C, 59.43; H, 8.00; N, 4.55; S, 10.68, Cl 11.41.

\textbf{2-(1-tert-Butyl-1-chloro-2,2-dimethylpropyl)-4,4-dimethyl-2-thiazolin-5-one (9b):} mp 66 °C; IR (film) 1710, 1600 cm\textsuperscript{-1}; \textsuperscript{1}H NMR \(\delta\) 1.32 (s, 18H, t-Bu\textsubscript{2}), 1.42 (s, 6H, ring-CMe\textsubscript{2}). Anal. Calcd for C\textsubscript{14}H\textsubscript{24}ClNOS; C, 58.00; H, 8.36; N, 4.83; S, 11.06, Cl 12.24. Found: C, 58.21; H, 8.31; N, 4.58; S, 10.56, Cl 12.12.

\textbf{2-(1-Chloro-1-isopropyl-2,2-dimethylpropyl)-4,4-dimethyl-2-thiazolin-5-one (9c):} oil; IR (film) 1710, 1600 cm\textsuperscript{-1}; \textsuperscript{1}H NMR \(\delta\) 1.01, 1.13 (each d, \(J = 7\) Hz, 6H, i-Pr), 1.20 (s, 9H, t-Bu), 1.38 (s, 6H, CMe\textsubscript{2}), 2.83 (septet, \(J = 7\) Hz, 1H, i-Pr). Anal. Calcd for C\textsubscript{13}H\textsubscript{22}ClNOS; C, 56.60; H, 8.06; N, 5.08; S, 11.62, Cl 12.85. Found: C, 57.05; H, 8.46; N, 4.81; S, 11.40, Cl 12.72.
General Procedure for the Reaction of Thiiranimines 6 with Iso(thio)cyanates 10, 22.

6 (1 mmol) in dry Et₂O (5 mL) or dry CHCl₃ (5 mL) and 10 or 22 (1.1 mmol) were mixed at 0 °C. Sulfonyl iso(thio)cyanates reacted at this temperature, while aryl derivatives required gentle heating up to 60 °C in CHCl₃. The reaction was monitored by TLC. In some cases, yellow crystals separated from the reaction mixture which were nevertheless purified by preparative TLC (PE/EtOAc 1:2 v/v) as were, after evaporation, the crude reaction mixtures. Solid products 11, 15, and 23 were further purified by recrystallization from PE/EtOAc. By chromatography of the N-sulfonyl derivatives of 11a-c, traces of hydrolysis products 12 or 14 were detected (vide infra); starting from chlorosulfonyl isocyanate (10e), considerable hydrolysis to 12a,b occurred and, starting from 10f, only products 12 were isolated. Also the reaction products from isothiocyanate 22a gave considerable hydrolysis to 24.

2-(6,6,10,10-Tetramethyl-4-thioxo-2-tosylimino-1-oxa-3-azaspiro[4,5]decan-3-yl)-N,N-2-trimethylpropionamide (11a): yield 87% from 6a and 10a; mp 131 °C; IR 1655 (br) cm⁻¹; ¹H NMR δ 0.77, 1.22, (each s, 6H, CMe₂), 1.52 (br s, 6H, (CH₂)₃), 1.83 (s, 6H, CMe₂), 2.38 (s, 3H, Ar-Me), 2.83 (s, 6H, NMe₂), 7.50 (mc, 4H, Ar); ¹³C NMR δ 67.9, 106.0, 126.9, 129.3, 139.1, 143.2, 156.9 (C=O), 169.7 (C=N), 202.9 (C=S). Anal. Calcd for C₂₅H₃₇N₃O₄S₂; C, 59.14; H, 7.35; N, 8.28; S, 12.63. Found: C, 58.99; H, 7.37; N, 8.15; S, 12.47.

2-(5,5-Di-tert-butyloxy-4-thioxo-2-tosylimino-oxazolidin-3-yl)-N,N-2-trimethylpropionamide (11b): yield 96% from 6b and 10a; mp 152-3 °C; IR 1640 (br) cm⁻¹; ¹H NMR δ 1.08 (s, 18H, t-Bu₂), 1.83 (s, 6H, CMe₂), 2.35 (s, 3H, Ar-Me), 2.80 (s, 6H, NMe₂), 7.43 (mc, 4H, Ar-Me); ¹³C NMR δ 68.1, 106.6, 126.8, 129.2, 138.9, 143.2, 157.4 (C=O), 169.8 (C=N), 204.6 (C=S). Anal. Calcd for C₂₅H₃₇N₃O₄S₂; C, 58.15; H, 7.52; N, 8.48; S, 12.94. Found: C, 58.02; H, 7.65; N, 8.44; S, 12.66.

2-(2-Mesylimino-6,6,10,10-tetramethyl-4-thioxo-1-oxa-azaspiro[4,5]decan-3-yl)-N,N-2-trimethylpropionamide (11c): yield 86% from 6a and 10b; mp 144 °C; IR 1640 (br) cm⁻¹; ¹H NMR δ 0.95, 1.32 (each s, 6H, CMe₂), 1.15 (br, 6H, (CH₂)₃), 1.87 (s, 6H, CMe₂), 2.90 (s, 6H, NMe₂), 3.17 (s, 3H, Ms); ¹³C NMR δ 67.5, 102.00, 123.5, 124.6, 143.8, 150.6, 151.1 (C=O), 170.6 (C=N), 202.4 (C=S). Anal. Calcd for C₁₉H₂₇N₃O₄S₂; C, 52.86; H, 7.72; N, 9.74; S 14.85. Found: C, 52.47; H, 8.02; N, 9.87; S, 14.98.

2-(6,6,10,10-Tetramethyl-2-p-nitrophenylimino-4-thioxo-1-oxa-3-azaspiro[4,5]decan-3-yl)-N,N-2-trimethylpropionamide (11d): yield 98% from 6a and 10c; mp 129-130 °C; IR 1710, 1630, 1600, 1580 cm⁻¹; ¹H NMR δ 0.97, 1.30 (each s, 6H, CMe₂), 1.60 (s, br, 6H, (CH₂)₃), 2.00 (s, 6H, CMe₂), 3.00 (s, 6H, NMe₂), 7.70 (mc, 4H, Ar); ¹³C NMR δ 67.5, 102.00, 123.5, 124.6, 143.8, 150.6, 151.1 (C=O), 170.6 (C=N), 202.4 (C=S). Anal. Calcd for C₂₄H₂₆N₃O₄S; C, 60.74; H, 7.22; N, 11.80; S, 6.76. Found: C, 60.51; H, 7.64; N, 11.76; S, 6.87.

2-(5,5-Di-tert-butyloxynaphthylimino-4-thioxo-oxazolidin-3-yl)-N,N-2-trimethylpropionamide (11e): yield 62% from 6b and 10d; mp 139 °C; IR 1695, 1640, 1580 cm⁻¹; ¹H NMR δ 1.22 (s, 18H, t-Bu₂), 2.00 (s, 6H, 2H, t-Bu₂).
CMe$_2$), 2.90 (s, 6H, NMe$_2$), 7.10 (s, 5H, Ph); $^{13}$C NMR δ 67.5, 102.4, 123.4, 123.9, 128.7, 144.2, 148.8 (C=O), 171.2 (C=N), 203.7 (C=S). Anal. Calcd for C$_{23}$H$_{35}$N$_3$O$_2$S; C, 66.14; H, 8.36; N, 10.06; S, 7.68. Found: C, 66.13; H, 8.20; N, 9.86; S, 8.08.

2-(3-Chlorosulfonylimino-6,6,10,10-tetramethyl-4-thioxo-1-oxa-3-azaspiro[4,5]-decan-3-yl)-N,N-$^2$-trimethylpropionamide (11f): yield 59% from 6a and 10e; mp 92 °C; IR 1650, 1580, 1450, 1180 cm$^{-1}$; $^1$H NMR δ 0.98, 1.32 (each s, 6H, CMe$_2$), 1.70 (br, 6H, (CH$_2$)$_3$), 1.88 (s, 6H, CMe$_2$), 2.91 (s, 6H, NMe$_2$); $^{13}$C NMR δ 68.5, 108.7, 161.3 (C=O), 169.0 (C=N), 202.6 (C=S). Anal. Calcd for C$_{18}$H$_{30}$ClN$_3$O$_4$S$_2$; C, 47.82; H, 6.70; N, 9.30; S, 14.18; Cl, 8.33. Found: C, 47.68; H, 6.52; N, 9.23; S, 14.05; Cl, 8.33.

2-(5,5-Di-$^t$-butyl-3-chlorosulfonylimino-4-thioxo-oxazolidin-3-yl)-N,N-$^2$-2-trimethylpropionamide (11g): yield 16% from 6b and 10e; mp 99 °C; IR 1660, 1640, 1360, 1300 cm$^{-1}$; 1H NMR δ 1.30 (s, 18H, $^t$-Bu$_2$), 1.95 (s, 6H, CMe$_2$), 2.98 (s, 6H, NMe$_2$). Anal. Calcd for C$_{17}$H$_{30}$ClN$_3$O$_4$S$_2$; C, 46.40; H, 6.88; N, 9.55. Found: C, 46.68; H, 6.78; N, 5.57.

2-(5-$^t$-Butyl-5-isopropyl-2-mesylimino-4-thioxo-oxazolidin-3-yl)-N,N-$^2$-2-trimethylpropionamide (11j): yield 34% from 6c and 10b; mp 105 °C; IR 1700, 1600 cm$^{-1}$; 1H NMR δ 0.94, 1.18 (each d, J = 6 Hz, 6H, $^i$-Pr), 1.18 (s, 9H, $^t$-Bu), 2.00 (s, 6H, CMe$_2$), 2.65 (sept, 1H, $^i$-Pr), 2.92 (s, 6H, NMe$_2$), 3.02 (s, 3H, Ms); $^{13}$C NMR δ 67.9, 106.07, 157.6 (C=O), 169.7 (C=N), 206.2 (C=S). Anal. Calcd for C$_{17}$H$_{31}$N$_3$O$_4$S$_2$; C, 50.35; H, 7.70; N, 10.36; S, 15.81. Found: C, 50.03; H, 7.77; N, 10.27; S, 16.30.

2-(5-$^t$-Butyl-5-isopropyl-2-phenylimino-4-thioxo-oxazolidin-3-yl)-N,N-$^2$-2-trimethylpropionamide (11l): yield 59% from 6c and 10d, mp 144-145 °C; IR 1700, 1640, 1580 cm$^{-1}$; 1H NMR δ 0.91, 1.11 (each d, J = 9 Hz, 6H, $^i$-Pr), 1.17 (s, 9H, $^t$-Bu), 2.00 (s, 6H, CMe$_2$), 2.70 (sept, 1H, $^i$-Pr), 2.95 (s, 6H, NMe$_2$), 7.17 (s, 5H, Ph). Anal. Calcd for C$_{22}$H$_{33}$N$_3$O$_2$S; C, 65.47; N, 8.24; N, 10.41; S, 7.94. Found C, 65.66; H, 8.12; N, 10.15; S, 8.06.

2,2,5´,5´,6,6-Hexamethyl-3´-thioxo-3'H-spirocyclohexane-1,2'-(7'H)-imidazol[2,1-b]oxazol-6'(5'H)-one (12a): yield 8% from 6a and 10e, 47% from 6a and 10f; mp 135 °C; IR 1700, 1600, 1580, 1370, 1360 cm$^{-1}$; $^1$H NMR δ 0.90, 1.20, 1.57, 1.60 (each s, 6H, CMe$_2$ and Me$_2$C(CH$_2$)$_3$CMe$_2$), ca. 1.7 (br, 6H, (CH$_2$)$_3$); $^{13}$C NMR δ 68.2, 116.0, 176.7, 190.5 (C=O, C=N), 194.8 (C=S); MS m/z 308 (M$^+$, 43), 293 (M$^+$ - Me, 18), 182 (54), 167 (100). Anal. Calcd for C$_{16}$H$_{24}$N$_2$O$_2$S; C, 62.29; H, 7.86; N, 9.08; S, 10.39. Found: C, 62.49; H, 7.97; N, 9.65; S, 10.59.
2,2-Di-tert-butyl-2,3,5,6-tetrahydro-5,5-dimethyl-3-thioxo-imidazo[2,1-b]oxazol-6-one (12b): yield 44% from 6b and 10e, 25% from 6b and 10f; mp 95 °C; IR 1760, 1600, 850 cm⁻¹; ¹H NMR δ 1.27 (s, 18H, t-Bu₂), 1.67 (s, 6H, CMe₂); ¹³C NMR δ 68.3, 116.6, 177.3, 190.8 (C=O, C=N), 196.3 (C=S). Anal. Calcd for C₁₅H₂₄N₂O₂S; C, 60.77; H, 8.18; N, 9.45; S, 10.81. Found: C, 60.57; H, 8.34; N, 9.33; S, 10.51.

2-(5-tert-Butyl-5-isopropyl-2-oxo-4-thioxo-imidazolidin-3-yl)-N,N-trimethylpropionamide (15a): yield 85% from 6a and 10a; mp 153-4 °C; IR 1750, 1675, 1275, 1170 cm⁻¹; ¹H NMR δ 1.08, 1.24 (each d, J = 5 Hz, 6H, i-Pr), 1.33 (s, 9H, t-Bu), 1.72, 1.80 (each s, 3H, CMe₂), 2.43 (s, 3H, Ts), 2.70 (s, 6H, NMe₂), 3.53 (m, 1H, i-Pr), 7.70 (mc, 4H, Ar); ¹³C NMR δ 66.4, 93.3, 128.9, 129.4, 130.5, 145.3, 154.2 (C=O), 170.6 (C=O), 201.7 (C=S). Anal. Calcd for C₂₃H₃₅N₃O₄S₂; C, 57.35; H, 7.32; N, 8.72; S, 13.31. Found: C, 57.28; H, 7.32; N, 8.62; S, 13.35.

2-(5-tert-Butyl-5-isopropyl-1-mesyl-2-oxo-4-thioxo-imidazolidin-3-yl)-N,N-2-trimethylpropionamide (15b): yield 62% from 6c and 10b; mp 160-1 °C; IR 1740, 1630 cm⁻¹; ¹H NMR δ 1.23 (br, d, 6H, i-Pr), 1.87 (s, 6H, CMe₂), 2.92 (s, 6H, NMe₂), 3.52 (s, 3H, Ms); ¹³C NMR δ 66.9, 92.8, 155.9 (C=O), 170.5 (C=O), 203.1 (C=S). Anal. Calcd for C₁₇H₃₁N₃O₄S₂; C, 50.35; H, 7.70; N, 10.36; S, 15.81. Found: C, 50.53; H, 8.03; N, 10.21; S, 15.43.

2-(5-tert-Butyl-5-isopropyl-2-oxo-1-phenyl-4-thioxo-imidazolidin-3-yl)-N,N-2-trimethylpropionamide (15c): yield 37% from 6c and 10d; mp 50 °C (decomp); IR 1730, 1650, 1590 cm⁻¹; ¹H NMR δ 1.2 (mc, 6H, i-Pr), 2.85, 2.92 (2s, br, 6H, CMe₂), 2.95 (s, 3H, Ts), 2.98 (s, 6H, NMe₂), 7.82 (s, 5H, Ph); ¹³C NMR δ 65.8, 100.2, 120.3, 124.7, 129.1, 137.2, 155.4 (C=O), 169.0, 208.4 (C=S). Anal. Calcd for C₂₂H₃₃N₃O₂S; C, 65.47; H, 8.24; N, 10.41; S, 7.94. Found: C, 65.66; H, 8.12; N, 10.15; S, 8.06.

2-(6,6,10,10-Tetramethyl-4-thioxo-2-tosylimino-1-thia-3-azaspiro[4,5]decan-3-yl)-N,N-2-trimethylpropionamide (23a): yield 96% from 6a and 22a; mp 162 °C; IR 1640, 1550 cm⁻¹; ¹H NMR δ 0.9 – 2.0 (br, 12H), 1.25 (s, 6H, CMe₂), 1.83 (s, 6H, CMe₂), 2.43 (s, 3H, Ts), 2.78 (s, 6H, NMe₂), 7.48 (mc, 4H, Ar); ¹³C NMR δ 71.5, 82.8, 126.9, 129.2, 137.0, 143.6, 169.0, 170.6 (C=O, C=N), 207.8 (C=S). Anal. Calcd for C₂₅H₃₇N₃O₃S₃; C, 57.32; H, 7.14; N, 10.82; S, 18.36. Found: C, 56.19; H, 7.40; N, 8.00; S, 18.55.

2-(5,5-Di-tert-butyl-4-thioxo-2-tosylimino-thiazolidin-3-yl)-N,N-2-trimethylpropionamide (23b): yield 94% from 6b and 22a; mp 146 °C; IR 1645, 1590 cm⁻¹; ¹H NMR δ 1.27 (s, 18H, t-Bu₂), 1.87 (br, 6H, CMe₂), 2.43 (s, 3H, Ts), 2.80 (s, 6H, NMe₂), 7.53 (mc, 4H, Ar); ¹³C NMR δ 71.6, 85.0, 127.0, 129.2, 137.3, 143.6, 169.1 (C=O), 170.8 (C=N), 207.7 (C=S). Anal. Calcd for C₂₄H₃₇N₃O₃S₃; C, 56.27; H, 7.30; N, 8.21; S, 18.79. Found: C, 56.19; H, 7.40; N, 8.00; S, 18.68.

2-(5-tert-Butyl-5-isopropyl-4-thioxo-2-tosylimino-thiazolidin-3-yl)-N,N-2-trimethylpropionamide (23c): yield 96% from 6c and 22a; mp 142 °C; IR 1645, 1550, 1600 cm⁻¹; ¹H NMR δ 1.2 (br,mc, 6H, i-Pr), 1.22 (s, 9H, t-Bu), 2.42 (s, 3H, Ts), 2.80 (s, 6H, NMe₂), 7.50 (mc, 4H, Ar); ¹³C NMR δ 71.2, 83.0,
127.0, 129.2, 137.0, 143.7, 168.7 (C=O), 170.6 (C=N), 210.9 (C=S). Anal. Calcd for C_{23}H_{35}N_{3}O_{3}S_{3}; C, 55.50; H, 7.10; N, 8.44; S, 19.32. Found: C, 55.50; H, 7.29; N, 8.44; S, 19.54.

2-(6,6,10,10-Tetramethyl-2-p-nitrophenylimino-4-thioxo-1-thia-3-azaspiro[4,5]decan-3-yl)-N,N-2-trimethylpropionamide (23d): yield 77% from 6a and 22b; mp 190 °C; IR 1640, 1590 cm^{-1}; ^{1}H NMR δ 0.87, 1.03, 1.20, 1.57 (each s, 3H, ring-Me_{2}C), 1.67 (s, 6H, (CH_{2})_{3}), 2.00 (s, 6H, CMe_{2}), 2.97 (s, 6H, NMe_{2}), 7.57 (mc, 4H, Ar); ^{13}C NMR δ 70.7, 82.9, 121.1, 125.3, 144.4, 154.2, 158.3 (C=O), 171.7 (C=N), 207.0 (C=S). Anal. Calcd for C_{24}H_{34}N_{4}O_{3}S_{2}; C, 58.74; H, 7.00; N, 11.42; S, 13.07. Found: C, 58.64; H, 7.16; N, 11.23; S, 12.80.

General Procedure for the Hydrochloric Acid-catalyzed Hydrolysis of Cycloadducts 11, 15, 23.

A compound 11, 15, or 23 including crude 11h,i (0.5 mmol) in CHCl_{3} (10 mL) and half-concentrated (5 M) aq. HCl (coned aq. HCl for 11k,l) were mixed at rt and kept at this temperature for up to 24 h while the progress of the reaction was monitored by TLC. If required, the reaction mixture was refluxed till TLC showed no more starting material. The reaction mixture was washed with sat. aq. NaHCO_{3}, concentrated in vacuo and the crude product purified by preparative TLC (PE/EtOAc 1:2 v/v) to give the following products:

12a: yield 65% from 11a, 36% from 11c, 20% from 11d, 20% from 11f, 48% from 11h. Data see above.
12b: yield 68% from 11b, 60% from 11e, 20% from 11g, 20% from 11i. Data see above.

2-(6,6,10,10-Tetramethyl-2-oxo-4-thioxo-1-thia-3-azaspiro[4,5]decan-3-yl)-2-methyl-N-(4-nitrophenyl)propionamide (14a): yield 80% from 11d; mp 170 °C; IR 3400, 1770, 1700, 1600, 1590, 1530, 1500, 1340 cm^{-1}; ^{1}H NMR δ 1.00, 1.20 (each s, 6H, ring-Me_{2}C), 1.60 (s, 6H, (CH_{2})_{3}), 1.90 (s, 6H, CMe_{2}), 7.73 (mc, 4H, Ar); ^{13}C NMR δ 65.8, 100.0, 119.3, 125.0, 143.2, 143.8, 154.6 (C=O), 169.3 (C=O), 205.4 (C=S); MS m/z 447 (M^{+}, 3), 310 (M^{+} - Ar-NH, 100), 266 (76). Anal. Calcd for C_{22}H_{29}N_{3}O_{5}S_{2}; C, 59.03; H, 6.54; N, 9.39; S, 7.16. Found: C, 58.78; H, 6.47; N, 9.23; S, 7.20.

2-(5,5-Di-tert-butyl-2-oxo-4-thioxo-oxazolidin-3-yl)-2-methyl-N-(4-nitrophenyl)propionamide (14b): yield 60% from 11e; mp 207 °C; IR 3300, 1800, 1640, 1600, 1345, 1290 cm^{-1}; ^{1}H NMR δ 1.20 (s, 18H, t-Bu_{2}), 1.83 (s, 6H, CMe_{2}), 7.13 (m, 5H, Ph); ^{13}C NMR δ 65.7, 100.3, 120.3, 124.7, 129.1, 137.4, 155.4 (C=O), 169.1 (C=O), 206.5 (C=S). Anal. Calcd for C_{21}H_{30}N_{2}O_{5}; C, 64.57; H, 7.84; N, 7.17; S, 8.21. Found: C, 63.62; H, 7.58; N, 6.94; S, 8.36.
1-(3-tert-Butyl-2,2-dimethyl-2H-thiet-4-yl)-5,5-dimethyl-3-phenyl-imidazolidine-2,4-dione (19a): yield 90% from 11k; mp 103 °C; IR 1770, 1720, 1635, 1600, 1350–1390 cm⁻¹; ¹H NMR δ 1.20 (s, 9H, t-Bu), 1.63, 1.84 (each s, 6H, CMe₂), 7.40 (s, 5H, Ph); ¹³C NMR δ 55.0, 63.2, 121.0, 126.0, 128.1, 128.9, 131.6, 151.1, 152.1 (C=O), 174.7 (C=O); MS m/z 358 (M⁺, 94), 343 (M⁺ - Me, 68), 301 (M⁺ - t-Bu, 70), 196 (33), 139 (100). Anal. Calcd for C₂₀H₂₆N₂O₂S; C, 66.99; H, 7.32; N, 7.82; S, 8.94. Found: C, 67.10; H, 7.47; N, 7.76; S, 8.98.

1-(3-tert-Butyl-2,2-dimethyl-2H-thiet-4-yl)-5,5-dimethyl-3-(4-nitrophenyl)imidazolidine-2,4-dione (19b): yield 90% from 11l; mp 129 °C; IR 1780, 1740, 1640, 1620, 1600, 1520, 1380 cm⁻¹; ¹H NMR δ 1.20 (s, 9H, t-Bu), 1.67, 1.87 (each s, 6H, CMe₂), 8.08 (mc, 4H, Ar); ¹³C NMR δ 55.3, 63.3, 120.5, 124.2, 125.8, 137.3, 146.4, 151.2, 151.7 (C=O), 174.1 (C=O); MS m/z 403 (M⁺, 84), 388 (M⁺ - Me, 78), 346 (M⁺ - t-Bu, 48), 196 (41), 139 (100). Anal. Calcd for C₂₀H₂₅N₃O₄S; C, 59.52; H, 6.26; N, 10.42; S, 7.95. Found: C, 59.52; H, 6.32; N, 10.13; S, 7.52.

6a-tert-Butyl-3,3,7,7-tetramethyl-6-phenyl-cyclopropa[4,5]imidazo[5,1-b]thiazol-2,5(3H,6H)-dione (21): yield 10% from 15c; mp 105 °C; ¹H NMR δ 1.08 (s, 9H, t-Bu), 1.25 (s, 3H, Me), 1.50 (s, 6H, CMe₂), 2.85 (s, 3H, Me), 2.87 (s, 3H, Me), 7.37 (s, 5H, Ph); ¹³C NMR δ 55.7, 60.0, 66.0, 125.9, 126.1, 128.1, 138.6, 154.4 (C=O), 205.3 (C=O); MS m/z 358 (M⁺, 1.8), 301 (100), 273 (48). Anal. Calcd for C₂₀H₂₆N₂O₂S; C, 66.99; H, 7.32; N, 7.82; S, 8.94. Found: C, 67.11; H, 7.28; N, 7.86; S, 8.88.

5´,6´-Dihydro-2,2,5´,5´,6,6-hexamethyl-7´-thioxo-spirocyclohexane-1,1´-(7´H)-imidazo[2,1-b]thiazol-4´-one (24a): yield 89% from 23a; mp 146 – 7 °C; IR 1760, 1500, 1360, 1290, 1080 cm⁻¹; ¹H NMR δ 1.00, 1.33 (each s, 6H, cyclohexane-CH₃), 1.67 (s, 6H, CH₂), 2.13, 2.77 (each br s, 3H, Me); ¹³C NMR δ 68.08, 92.8, 185.2, 191.3 (C=O, C=N), 200.5 (C=S); MS m/z 324 (M⁺, 82), 242 (73), 200 (59), 167 (64), 91 (56), 41 (100). Anal. Calcd for C₁₆H₂₄N₂O₂S₂; C, 59.21; H, 7.47; N, 8.63; S, 19.76. Found: C, 59.14; H, 7.44; N, 8.37; S, 19.52.

5`-Di-tert-butyl-2,2,2,3,3,5,5,6-tetrahydro-5,5-dimethyl-3-thioxo-imidazo[2,1-b]thiazol-6-one (24b): yield 40% from 23b; mp 98 – 9 °C; IR 1760, 1500, 1360, 1290, 1080 cm⁻¹; ¹H NMR δ 1.33 (s, 18H, t-Bu₂), 1.67 (s, 6H, CMe₂). Anal. Calcd for C₁₅H₂₄N₂O₂S₂; C, 57.64; H, 7.76; N, 8.97; S, 20.52. Found: C, 57.72; H, 7.57; N, 8.91; S, 20.21.

2-tert-Butyl-2-isopropyl-2,3,5,6-tetrahydro-5,5-dimethyl-3-thioxo-imidazo[2,1-b]thiazol-6-one (24c): yield 91% from 23c; mp 117 °C; ¹H NMR δ 0.92, 1.55 (each d, J = 5 Hz, 6H, i-Pr), 1.27 (s, 9H, t-Bu), 1.70 (s, 6H, CMe₂), 2.90 (sept, J = 5 Hz, 1H, i-Pr), ¹³C NMR δ 67.7, 92.5, 186.3, 191.4 (C=N, C=O), 202.4 (C=S). Anal. Calcd for C₁₄H₂₂N₂O₂S₂; C, 56.33; H, 7.44; N, 9.39; S, 21.48. Found: C, 56.41; H, 7.64; N, 9.32; S, 21.65.

2-(6,6,10,10-Tetramethyl-2-oxo-4-thioxo-1-thia-3-azaaspiro[4,5]decan-3-yl)-2-methyl-N-(4-nitrophenyl)-propionamide (25a): yield 83% from 23d; mp 232 °C (decomp); IR 3400, 1700, 1615, 1530, 1500, 1480
cm\(^{-1}\); \(^1\)H NMR \(\delta\) 1.50 – 2.80 (br, 6H, (CH\(_2\))\(_3\)), 1.00, 1.30, 1.93 (3s, each 6H, CMe\(_2\)), 7.70 (mc, 4H, Ar); \(^{13}\)C NMR \(\delta\) 69.4, 81.2, 119.0, 125.1, 143.6, 143.7, 169.9 (C=O), 174.2 (C=O), 207.7 (C=S). Anal. Calcd for C\(_{22}\)H\(_{29}\)N\(_3\)O\(_4\)S\(_2\); C, 56.99; H, 6.32; N, 9.06; S, 13.83. Found: C, 56.76; H, 6.27; N, 9.05; S, 13.89.

2-(5,5-Di-tert-butyl-2-oxo-4-thioxo-thiazolidin-3-yl)-2-methyl-N-(4-nitrophenyl)propionamide (25b): yield 96% from 6b and 22b by hydrolysis on work-up; mp 180 °C; IR 3400, 1700, 1620, 1600, 1535, 1500, 1400, 1340, 1300 cm\(^{-1}\); \(^1\)H NMR \(\delta\) 1.33 (s, 18H, t-Bu\(_2\)), 1.93 (s, 6H, CMe\(_2\)), 7.07 - 8.10 (mc, 4H, Ar). Anal. Calcd for C\(_{21}\)H\(_{29}\)N\(_3\)O\(_4\)S\(_2\); C, 55.84; H, 6.49; N, 9.31; S, 14.20. Found: C, 55.63; H, 6.48; N, 9.31; S, 14.53.

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REFERENCES AND NOTES


12. Crystallographic data (excluding structure factors) for the structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-825077. The data can be obtained free of charge from the CCDC, *via* www.ccdc.cam.ac.uk/data_request/cif.

13. CCDC-825075; cf. ref. 12.


15. CCDC-825081; cf. ref. 12.

16. CCDC-825080; cf. ref. 12.

17. CCDC-825076; cf. ref. 12.

18. CCDC-825079; cf. ref. 12.


21. CCDC-825078; cf. ref. 12.


