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1,3-CYCLOADDITIONS OF A THIONITROSO *S*-SULFIDE [1]

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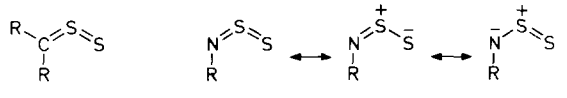
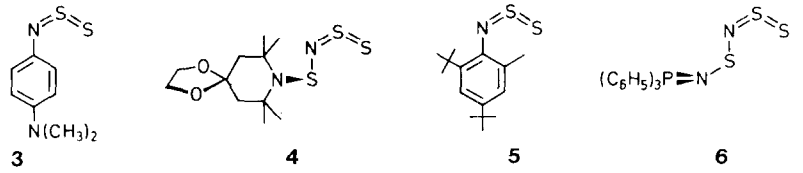
Summary The thionitroso *S*-sulfide 5 adds to (*E*)-cyclooctene, (*E,Z*)-1,5-cyclooctadiene, and norbornene to give 1,2,3-dithiazolidines, whereas enamines undergo electrophilic substitution.

In contrast to thiocarbonyl *S*-sulfides 1,[2,3] the *N* analogues 2 are isolable. X-Ray analyses of crystalline "thiosulfinylamines" 4-6 [4-6] revealed double bond character of the N=S and S=S bond. The resonance structures 2b and 2c are probably meaningful; 2 undergoes 1,3-dipolar cycloadditions and shares the preference for cis configuration with substituted allyl anions. In the nomenclature of 1,3-dipoles,[7] compounds 2 are thionitroso *S*-sulfides.



1 2a b c

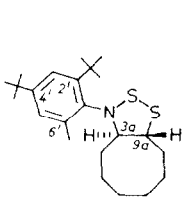


3 4 5 6

Barton and Robson [8] described 1,3-cycloadditions of the purple 3 to norbornadiene and cyclopentadiene. Inagaki, Okazaki, and Inamoto [9] prepared 5 (dark ruby-red crystals) from the arylamine and S_2Cl_2; the careful study of the chemistry of 5 [10] did not include cycloadditions.

The deep color of the $CHCl_3$ solution of 5 and 1.1 equiv of *trans-cyclooctene* faded in 4 h at 20°C; the 1:1 adduct 7 (mp 114-115°C, 50%) [11] crystallized in yellow needles. Similarly, *trans,cis-1,5-cyclooctadiene* afforded 83% of 8, mp 126-127°C. The M^+ ions are the strongest peaks in the MS of 7 and 8; m/e 249 and 230 occur in both spectra and are ascribed to 9 and 10.

Reduction of 7 by $LiAlH_4$ in THF resulted in removal of one sulfur; in situ reaction with acetyl chloride furnished 38% of 11. IR bands ($CHCl_3$) at 3440 (N-H) and 1675 cm^{-1} (C=O) as well as δ_C = 196.2 for CH_3-CO-S (194.1 for *S*-butyl thioacetate, δ_C of CH_3-CO-N lower by ∿20 ppm) fit 11 better than the isome-



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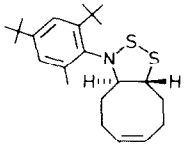

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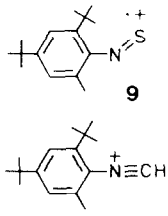

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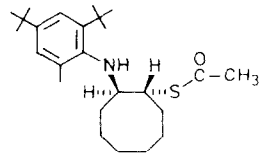
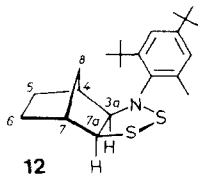


11

ric *N*-acetyl compound. Why does the thioacetic ester 11 - thioesters are acylating reagents - not transfer the acetyl group to the neighboring NH function ? Steric hindrance of the acyl shift is conceivable, but we prefer a thermodynamic reason: The loss of resonance energy in a highly twisted acetamide derivative may change the energy balance in favor of 11.



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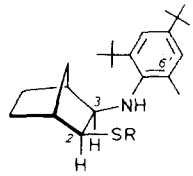


13 R = H
14 R = $COCH_3$

The cycloaddition of 5 to the less active *norbornene* required 3 d at 50°C and yielded 73% of the yellow 12, mp 135-136°C. MS: m/e = 375 (M^+, 100%), 311 (M^+- 2S, 56%), 296 (M^+- 2S - CH_3, 80%), 230 (10, 80%).

$LiAlH_4$ converted 12 into the oily aminothiol 13; m/e = 345 (M^+, 33%), 330 (M^+- CH_3, 18%), 230 (10, 100%). The crystalline *S*-acetyl derivative 14, mp 129 -130°C (64%), was obtained from 12 and $LiAlH_4$, followed by acetyl chloride. N-H at 3445 cm^{-1} (CCl_4), the lack of an S-H vibration, and δ_C 195.9 for CH_3-CO-S again excludes the acetanilide derivative. In the ^1H NMR spectrum ($CDCl_3$) of 14 after removal of NH by D_2O, the doublets for 2-H and 3-H at δ 3.65 and 3.93, J = 7 Hz, indicate the *exo* cycloaddition of the 1,3-dipole 5 to norbornene.

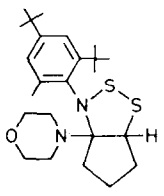
The cycloadducts 7, 8, and 12 are pure compounds. In solution, *double sets of NMR signals* at 32°C indicate unequal populations of two conformations. Single sets for the *S*-acetyl compounds 11 and 14 testify that after ring opening conformational changes are fast on the NMR time scale. The ^1H NMR spectrum of 7 in quinoline (80 MHz, 32°C) displays 2 s for 2'-$C(CH_3)_3$ ($\Delta\nu$ 14.9 Hz), 2 s for 6'-CH_3 (4.4 Hz), and only one s for 4'-$C(CH_3)_3$. Adduct 12 in quinoline showed $\Delta\nu$ 18.1 Hz for 2'-$C(CH_3)_3$, 2.2 Hz for 4'-$C(CH_3)_3$, and 15.8 Hz for 6'-CH_3. The ratios of integrals, 62:38 for 7 and 82:18 for 12 are not precise due to superposition by CH_2 signals.

The ^{13}C NMR spectra ($CDCl_3$, 20.15 MHz, 32°) disclose fair agreement in 11 intensity ratios of signal pairs: 58:42 for 7, 61:39 for 8, and 78:22 for 12. The largest $\Delta\nu$ were found for the ring junctions: 90.3 Hz for C-3a and 47.6 Hz

for C-9a of 7 as well as 92.2 Hz for C-3a and 17.7 Hz for C-7a of 12. The 6'-CH_3 shifts differ by 43.3 Hz for 7 and 15.9 Hz for 12.

On heating 7 in quinoline, the ^1H methyl singlets coalesced at 90±5°C ($\Delta\nu$ 2.0 Hz), and T_C 125°C ($\Delta\nu$ 12.5 Hz) was estimated for the 2'-$C(CH_3)_3$ signals (decomp. <110°C); $\Delta G^{\ddagger}$ 20.7 and 21.1 kcal mol^{-1} refer to the major conformation.[12] For adduct 12, $\Delta G^{\ddagger}$ 20.6 and 21.1 kcal mol^{-1}, respectively, were calculated from T_C 99±3°C ($\Delta\nu$ 13.0 Hz, 6'-CH_3) and T_C 108±4°C (13.2 Hz, 2'-$C(CH_3)_3$).

Apart from the stable stereocenters (3a,9a in 7; 3a,7a in 12), the cycloadducts harbor *four stereolabile configurational units*: the hindered torsions about S-S, S-N, N-Ar and the inversion at pyramidal nitrogen. $\Delta G^{\ddagger}$ 14 kcal mol^{-1} was reported for S-S torsion of 1,2-dithiolane-4-carboxylic acid [13] and <12 kcal mol^{-1} is estimated for the S-N barrier in dithiazolidines from values of open-chain sulfenamides.[14] Although the activation energies of the stereomutations of the ring members could be additive to some extent, the highly hindered N-Ar rotation [15] is probably responsible for the observed barriers.



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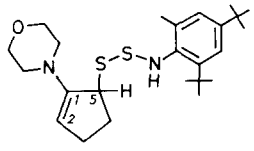

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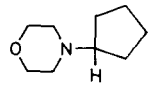

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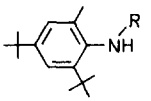
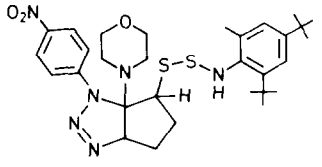


18 R = H

19 R = $COCH_3$



20

The reaction of 5 with *1-morpholinocyclopentene* (3.5 h, ether, 20°C) furnished 80% of a labile, light-yellow 1:1 adduct, mp 106-107°C. Structure 15 was ruled out by the N-H frequency at 3430 cm^{-1} (CCl_4) and δ_H (NH) 5.50 (D_2O test). A broad singlet at δ_H 4.50 is low for a vinylic proton, but fits the β-H of an enamine. The ^{13}C NMR spectrum (-21°C) showed s δ 131.6 and d 102.0 for C-1 and C-2 of the enamine formula 16. The multiplet of 5-H cannot be clearly located, but the assignment of d δ_C 54.2 to C-5 is unambiguous. In contrast to the 1,2,3-dithiazolidines, 16 displays a single set of NMR data.

Chemical properties accord with the open chain structure 16. Hydrogenolysis by Raney nickel (ethanol/ethyl acetate, 5 h 20°C) produced 82% of *N*-cyclopentylmorpholine (17) and 73% of 2,4-di-*tert*-butyl-6-methylaniline (18). In 1895, Michaelis [16] noticed the acid sensitivity of R_2N-S-S-NR_2 which is shared by 16. At room temperature, acetic acid converted 16 into 18, and 19 resulted from 16 and acetic anhydride. Enamines add organic azides very fast.[17] Indeed, 16 and 4-nitrophenyl azide (3 h 20°C, CCl_4) yielded 96% of 20, mp 137°C (dec.).

Formation of 16 is conceivable via 15 with subsequent ring opening. An al-

ternative is *nucleophilic attack* of the enamine on the terminal sulfur of 5 followed by 1,3-prototropy. We chose *1-morpholinocycloheptene* as a second example; the adduct (33%, mp 99-101°C) behaved similar to 16.

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