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ACID-BASE REACTIONS OF 1,3,4-THIADIAZOLINES AND THIOCARBONYL YLIDES; 1,3,4-THIADIAZOLINE-2-SPIRO-2'-ADAMANTANE

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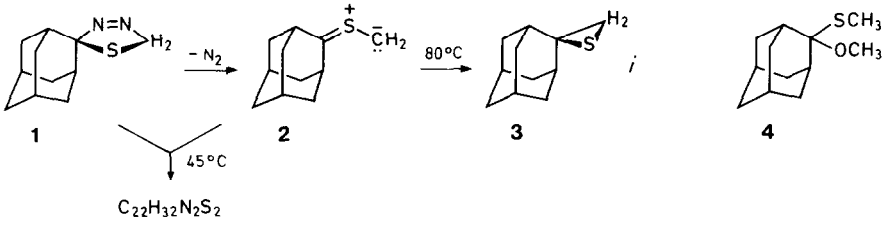
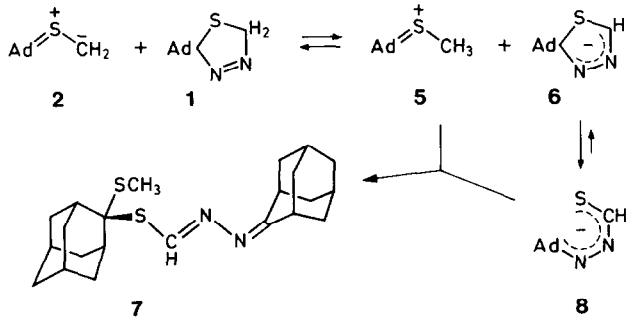
Summary The surprising formation of $C_{22}H_{32}N_2S_2$ from the title compound 1 at 45°C involves the interaction of the basic adamantanethione *S*-methylide (2) with its acidic precursor 1, in the course of which the anion 6 undergoes electrocyclic ring opening; the acid and base functions offer the clue to a prolific chemistry of the thiadiazoline 1 and the thiocarbonyl ylide 2.

When the 1,3,4-thiadiazoline 1 was heated in xylene *at 80°C*, 96% N_2 were extruded in 10 min and 94% of the spiro-thiirane 3 was formed *via* 2.[1] In the same reaction *at 45°C*, the N_2 evolution was finished with 64% after 7 h and the CH_2 signal of 3 was missing in the ^1H NMR spectrum. Instead, a compound $C_{22}H_{32}N_2S_2$, colorless crystals with mp 194-195°C,[2] was produced in 32% yield; the stoichiometry requires 2 equiv. of 1 with elimination of 1 equiv. N_2. On running the decomposition of 0.2 M (or 0.013 M) 1 in methanol at 45°C, ^1H NMR analysis indicated 56% (33%) of $C_{22}H_{32}N_2S_2$ along with 30% (45%) of 2-methoxy-2-(methylthio)adamantane (4). Distillation and tlc afforded 4 as a colorless oil, bp 40-45°C/0.01 Torr.



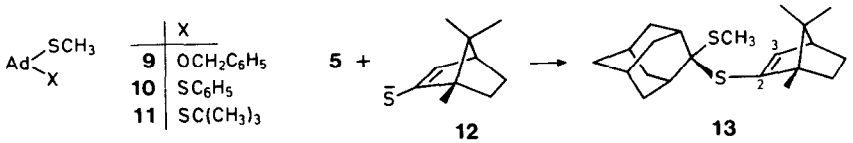
The dependence on temperature and concentration suggests that a bimolecular reaction of adamantanethione *S*-methylide (2) with the precursor 1 competes with the unimolecular electrocyclization 2 → 3. The interplay of activation enthalpy and entropy allows one to expect that the conversion 2 → 3 has the higher temperature coefficient. The ^1H NMR spectrum of $C_{22}H_{32}N_2S_2$ ($CDCl_3$) indicates a SCH_3 group at δ 2.02 and a 1H singlet at 8.12, whereas the ^{13}C NMR spectrum shows signals at δ 10.9 (q, SCH_3), 150.3 (d, HC=N-), and 175.5 (s, C-2 of Ad=N). In accordance with structure 7, 1.96 equiv. of adamantanone 2,4-dinitrophenylhydrazone, mp 212-214°C, were formed with 2,4-DNPH in ethanolic sulfuric acid. The conversion to 2,2-dimethoxyadamantane in methanol with trifluoroacetic acid tallies with the structure of the *O,S*-dimethylacetal 4; δ_H = 1.87 (s,

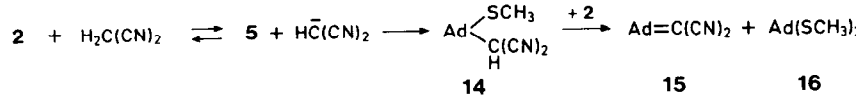
SCH_3) and 3.31 (s, OCH_3) contribute NMR evidence.



The mystery of the 7 formation is solved in the formula scheme on recognizing the fact that the thiocarbonyl ylide 2 is a *base* and the thiadiazoline 1 an *acid*. Proton transfer leads to the sulfonium ion 5 and a cyclic allyl anion 6, which undergoes an *electrocyclic* ring opening of the type cyclopentenyl anion → pentadienyl anion;[3] the superior stabilization of the anion 8 by nitrogen *and sulfur* is responsible for the ring cleavage. The thioformhydrazone derivative 7 results from the combination of the electrophile 5 with the ring-opened anion 8. Structure 7 is in accordance with the properties mentioned above for compound $C_{22}H_{32}N_2S_2$.

The nucleophilic [1] and *basic properties* of 2 are a function of the low-lying HOMO of thiocarbonyl ylides.[4] Methanol is likewise able to protonate 2; the *O,S*-dimethylacetal 4 emerges from the ion recombination, 5 + CH_3O^-. Correspondingly, warming of 0.2 M 1 in benzyl alcohol at 45°C produced 96% N_2 and 83% of the mixed *O,S*-acetal 9, mp 70.5-72°C. Analogous reactions of 1 *via* 2 with thiophenol or *tert*-butyl mercaptan gave rise to mixed dithioacetals 10 (100%, mp 82-84°C) and 11 (94%, oil), respectively.

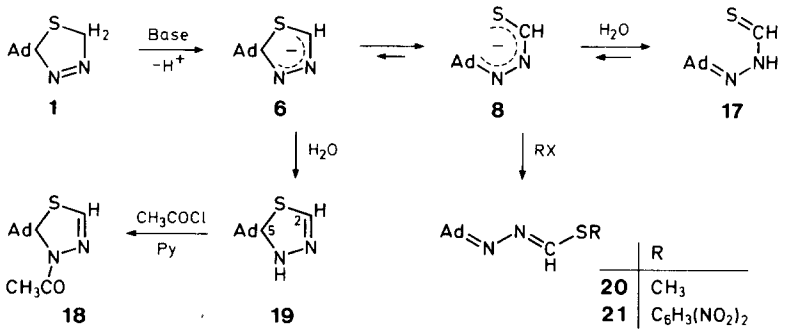




When 1 was heated with *thiocampher* in THF (8 h 40°C, 94% N_2), the 1,3-cycloaddition of 2 to the C=S bond was probably sterically hindered. Instead, the scenario is set for an acid-base reaction providing sulfonium ion 5 + bornene-2-thiolate (12). Ion recombination furnished the mixed dithioacetal 13, mp 86-87°C in 25% yield. ^{1}H NMR ($CDCl_3$): 0.77, 0.82, 1.00 (3s, 3 CH_3), 2.05 (s,

SCH_3), 6.15 (d, $J_{3,4}$ = 3.3 Hz, 3-H). The base peak of the MS was $C_{11}H_{17}S^+$ (181), *i.e.*, the sulfonium ion 5. From the solution of 13 and 2,4-DNPH in ethanolic sulfuric acid at 20°C crystallized 0.9 equiv. adamantanone 2,4-dinitrophenylhydrazone in 10 min and 0.6 equiv camphor 2,4-dinitrophenylhydrazone in 5 days.

On extruding N_2 from 1 in THF in the presence of *malononitrile* at 40°C, 56% of 2-dicyanomethyleneadamantane (15) and 25% of the dimethyl dithioacetal 16 were isolated. Proton transfer and ion recombination yielded 14, and a subsequent E2 reaction, probably induced by a second molecule of 2, afforded 15 + 16. The dinitrile 15, mp 179-181°C, was identified with an authentic specimen.[5] The 2,2-bis(methylthio)adamantane (16) showed δ_H = 1.93 ($CDCl_3$) for the two SCH_3 groups.



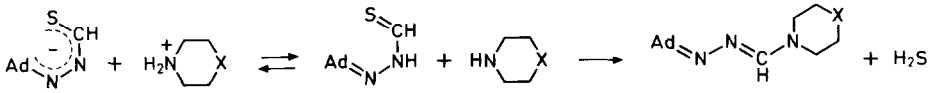
The *acid character* of the Δ^3-1,3,4-thiadiazoline 1 was the second postulate of our interpretation of 7 formation above. When 1 was deprotonated by 1 equiv. of lithium diisopropylamide at 0°C in THF, subsequent treatment with methyl iodide gave rise to 2-(methylthiomethylene)hydrazono-adamantane (20), isolated in 68% yield, mp 56-57°C. The occurrence of *S*-methyl (δ_H 2.37) established the derivative of the *open-chain anion* 8; s of S-CH= at δ 7.65. The base peak of the MS was observed at m/e = 175 ($M^+ - SCH_3$).

A base as strong as LDA is not required. The solution of 1 and 1 equiv. of sodium methoxide in methanol did not evolve N_2 at 45°C, *i.e.*, the anion formation must be complete. After treatment with 2,4-dinitrochlorobenzene, 63% of the golden-yellow 21, mp 115-116°C, was isolated following tlc on silica gel.

Hydrolysis of the lithium salt (1 + LAD) provided the Δ^2-1,3,4-thiadiazoline 19 which crystallized from ethanol in 47% yield, mp 141-143°C. In hot ethanol the sensitive 19 was converted to adamantanone azine, mp 314-316°C. The IR frequencies of 19 at 3120 and 1629 cm^{-1} are assigned to N-H and C=N; the broad ^1H NMR singlet at δ 6.2 (NH) disappears with D_2O and the 2-H is found at 7.02. Evidence for the cyclic structure came from the ^{13}C NMR spectrum: δ 134.8 (d, C-2), 91.4 (s, C-5); the C-2 of Ad=N in an open-chain structure, the adamantanone N-thioformylhydrazone (17), should occur at a much higher field. The *N*-acetyl derivative 18, mp 70-71°C, shows the amide I band at 1690 cm^{-1}.

Nevertheless, we suppose 17 is the primary hydrolysis product of 8. The literature offers evidence for ring-chain tautomerism of Δ^2-1,3,4-thiadiazolines,[6-8] although 2-unsubstituted 5,5-dialkyl-Δ^2-1,3,4-thiadiazolines have not been described. Our conclusion: the equilibrium of the anions is far on the side of the *open-chain* 8, and kinetically controlled reactions (alkylation, arylation) afford open-chain compounds. The neutral species, however, favors thermodynamically the *cyclic* form, *i.e.*, 17 → 19.

The higher bond energy of the cyclic hydrazone 19 compared with the azo compound 1 finds its precedent in the different stabilities of 2- and 1-pyrazolines. The analogy includes the base *and acid* catalysis of tautomerization. Trifluoroacetic acid (10 vol%) in $CDCl_3$ isomerized the Δ^3-1,2,3-thiadiazoline 1 to the Δ^2-form 19 in 30 min.



8 **22** **17** **23** X = CH_2, **24** X = O

Piperidine and morpholine are sufficiently basic to induce ring-opening of the Δ^3-thiadiazoline 1 at 20°C in 3 h furnishing the formamidrazones 23, mp 84-85°C, and 24, mp 72-73°C, respectively; of course, the Δ^2-tautomer 19 was also converted by piperidine to 23 (85%). The ^{13}C NMR signals of 23 at δ 171.6 (s) for C-2 of adamantane and at 158.6 (d) for the formyl C-atom as well as C=N stretching frequencies at 1605 and 1636 cm^{-1} secured the structure. The mechanism ? Base catalysis establishes an equilibrium of the thiadiazolines 1 and 19 *via* the ion pair 8 + 22 with a modest concentration of 17, which, in turn, is substituted by the secondary amine with H_2S elimination.

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