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Acid–base reactions of adamantanethione *S*-methylide and its spiro-1,3,4-thiadiazoline precursor

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Dedicated to Professor Ivar Ugi, München, on the occasion of his 70th birthday

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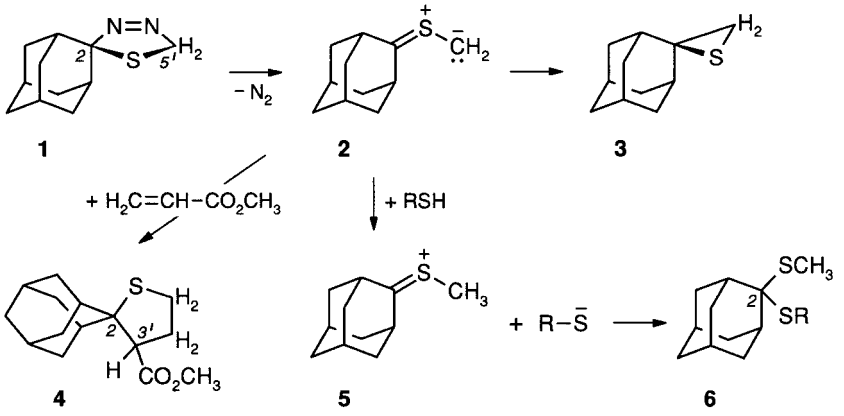
Abstract—The spiro-1,3,4-thiadiazoline **1** loses N_2 at 45°C, and, as recently reported, the short-lived adamantanethione *S*-methylide (**2**) is an active 1,3-dipole. Interception of **2** by acids HX consists of CH_2-protonation and ion recombination. Even **1** acts as HX vs **2** and—after electrocyclic ring opening of the anion (**13** →**15**)—affords the dithioacetal $C_{22}H_{32}N_2S_2$ (**14**). The Δ^3-thiadiazoline **1** is converted by base or acid catalysis to the Δ^2-tautomer **21**. Amidrazones (**25**, **26**) are formed from **1** and *sec*-amines. The mechanisms are discussed and the structures elucidated.

1. Introduction

2′,5′-Dihydrospiro[adamantane-2,2′-(1,3,4)-thiadiazole] (**1**) is easily available by 1,3-cycloaddition of diazomethane with adamantanethione.[1] The N_2 elimination from **1** (half-life 90 min at 40°C in THF) is a 1,3-dipolar cycloreversion which furnishes adamantanethione *S*-methylide (**2**). We chose **2** as one of the model compounds for studying the reactivity of thiocarbonyl ylides. 1,3-Dipolar cycloadditions with CC-multiple bonds[2] and heterodouble bonds C═O, C═S, C═N,[3,4] N═S,[5] and N═N[6] have recently been described (Scheme 1).

The *S*-methylide **2** cannot be isolated. In the absence of intercepting reagents, it undergoes electrocyclization and affords spirothiirane **3**.[1] As an isoelectronic heteroatom analogue of the allyl anion, **2** shows basic and nucleophilic properties. Although the anionic charge is distributed over the two termini of thiocarbonyl ylides, formula **2** symbolises the reactivity. The cycloaddition with methyl acrylate gives rise to **4**,[2] and the CH_2 group is the basic centre in the reaction with thiols affording dithioacetals **6** via thionium ion **5**.[1] Further HX additions to other thiocarbonyl ylides have been reported.[7,8]

The CH_2 group of the 1,3,4-thiadiazoline **1** is acidic. It is well known that 1-pyrazolines are converted to the thermodynamically more stable 2-pyrazolines by base or acid



Scheme 1.

Keywords: Δ^3- and Δ^2-1; 3; 4-thiadiazolines; thiocarbonyl ylides; acid–base reaction; adamantane derivatives.

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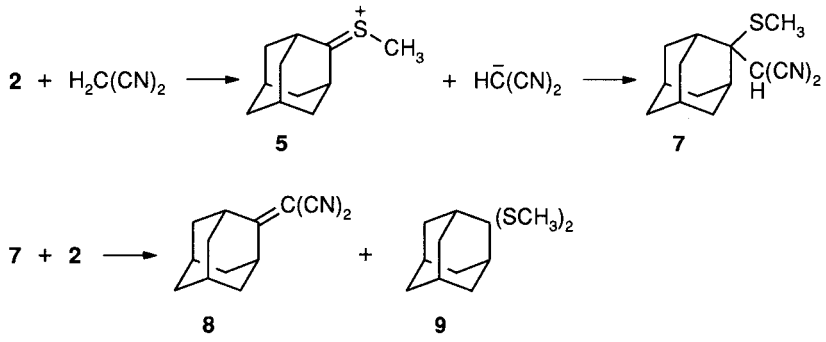


Scheme 2.

catalysis.[9,10] A similar prototropy is expected to convert Δ^3-(1,3,4)-thiadiazolines to the Δ^2-isomers. We report here on a variety of acid–base reactions of **1** and **2**.[11]

2. Results and discussion

When **1** was reacted with 1.3 equiv. of malononitrile in THF at 40°C for 8 h, 0.94 equiv. of N_2 was set free; 2-(dicyanomethylene)adamantane (**8**, 60%) and 2,2-bis(methylthio)-adamantane (**9**, 24%) were isolated. A plausible conjecture asserts deprotonation of malononitrile by *S*-methylide **2** and recombination of the ions to yield the HX-type adduct **7**. The latter still contains acidic hydrogen and reacts with a second molecule of **2**, thus furnishing **8**+**9** (Scheme 2).

Thiones are superdipolarophiles[12] and avidly receive **2** to afford spiro-1,3-dithiolanes.[3] In the case of thiocampher (**10**), however, steric hindrance to cycloaddition cannot be overcome, and deprotonation at position 3 by **2** takes place instead. Combination of ene-thiolate **11** with **5** furnished the mixed dithioacetal **12**. Cleavage of the latter with 2,4-DNPH in ethanolic sulfuric acid afforded the 2,4-dinitrophenylhydrazones of adamantanone and campher (Scheme 3).

In a kinetic experiment with 0.20 M **1** in xylene at 80°C, the N_2 evolution (96%) followed the first-order law with a half-reaction time of 55 s, and 94% of thiirane **3** was found as reaction product.[1] In an experiment at 45°C, however, only 0.64 equiv. of N_2 was evolved, and the deviation from the first-order plot began, after ~60% of **1** was consumed. Colourless crystals $C_{22}H_{32}N_2S_2$ (**14**) were isolated in 31% yield according to the stoichiometry:

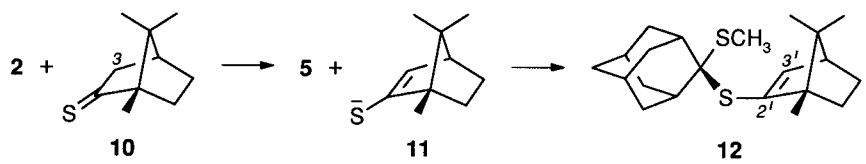
$$2\ C_{11}H_{16}N_2S\ (1) \rightarrow C_{22}H_{32}N_2S_2 + N_2$$

The NMR spectra of **14** are in accordance with an SCH_3 group (s, δ_H 2.01 and q, δ_C 10.9) and a thioformimidate function, –N=CH–S– (s, δ_H 8.10 and d, δ_C 150.6). The C-2 signal (δ_C 175.9) is comparable to 171.0 ppm of azino-2,2′-bis(adamantane) (**17**). The ^{13}C parameters of the adamantylidene group reveal a plane of symmetry in **14** by means of two sets of 3 CH signals (2:1:1) and 3 CH_2 signals (2:2:1). The base peak in the MS of **14**, *m*/*z* 181, comes from thionium ion **5**, as confirmed by the intensities of isotope peaks. The second *S*-function can also appear as thionium ion, but [$\mathbf{14}^+$–SCH_3] reaches only 0.1% intensity. Chemical evidence for **14** was provided by cleavage with 2,4-DNPH, which furnished 1.96 equiv. of hydrazone **16** (Scheme 4).

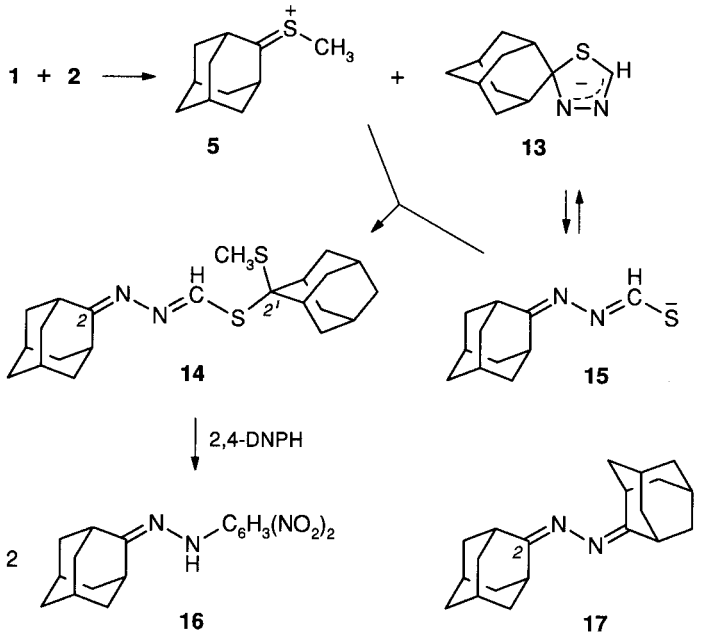
Obviously, the intermediate thiocarbonyl ylide **2** has a sufficient life-time at 45°C to deprotonate the precursor molecule, the thiadiazoline **1**. The anion of the latter, **13**, undergoes an electrocyclic ring-opening of type 'cyclopentenyl anion→pentadienyl anion'.[13] The nucleophilic thiolate function of **15** fits into the electrophilic centre of **5**, and **14** is formed.

At first glance, it might astonish that an abundance of interception reactions of **2** suppresses the simple straightforward cyclization **2**→**3**. The formal simplicity of the latter is deceptive, however. In fact, the electrocyclic ring closure of the quasi-planar thiocarbonyl ylide involves two 90° rotations about the two C–S bonds. Most of the resonance energy of the 1,3-dipole **2** has to be sacrificed, before the new C–C bond notably contributes to the bond energy. The enthalpic barrier to cyclization is high enough to allow trapping reactions. These interceptions are burdened with the large negative activation entropies of bimolecular reactions. As cyclization competes with interception of **2**, the first-order reaction **2**→**3** is expected to show the steeper rise of the rate constant with increasing temperature. Not at 80°C, but at 45°C, the protonation of **2** by the second molecule of **1** successfully competes with the cyclization **2**→**3**.

The N_2 extrusion of **1** remains to be the rate-determining step. The reaction at 45°C should *kinetically* still be of first



Scheme 3.



Scheme 4.

order, but *stoichiometrically* of second order. However, the capturing of **2** by **1** is incomplete, especially when the concentration of **1** becomes small. Initially, 2 [**1**] enters the rate equation of $-d[\mathbf{1}]/dt$, and successively diminishes to [**1**].

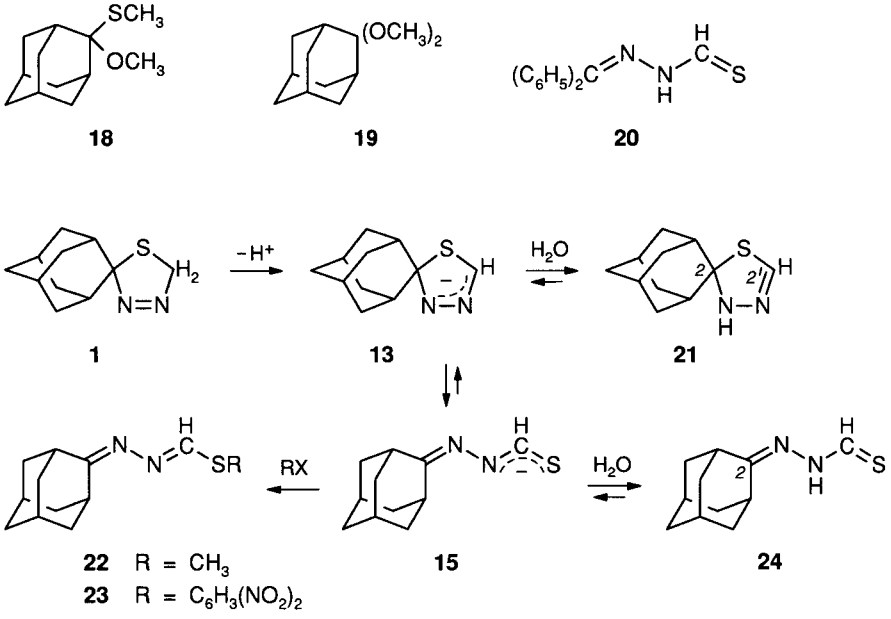
In the decomposition of 0.2 M **1** at 45°C, the percentage of **14** depends on the solvent: methanol 56%, xylene 31%, hexane 30%, benzene 26%, THF <5% (^{1}H NMR analysis). In addition to 56% of **14**, the experiment in methanol produced 30% of *S*,*O*-dimethylacetal **18** (2 s at δ_H 1.87 and 3.31 for SCH_3 and OCH_3). The result of the competition suggests that **1** is a stronger acid than methanol versus **2**. The expected dependence of the product ratio on $[\mathbf{1}]_0$ was confirmed (45°C):

0.20 M**1** → 56% of **14** and 30% of **18**

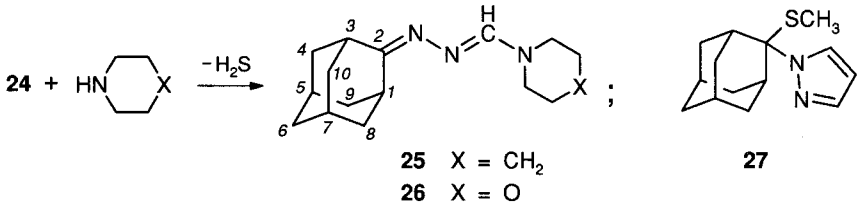
0.013 M**1** → 33% of **14** and 45% of **18**

An experiment with 0.20 M **1** in methanol was run at 45°C in the presence of trifluoroacetic acid and provided 84% of the *O*,*O*-dimethylacetal **19**. This is due to the fact that **2** is protonated by the strong acid, and the thionium ion **5** attacks methanol (Scheme 5).

To study reactions of the thiadiazoline anion **13**, **1** was



Scheme 5.



Scheme 6.

deprotonated by 1 equiv. of LDA in THF at 0°C. Methyl iodide converted the lithium salt to the open-chain *S*-methyl derivative **22** (s at δ_H 2.37 for SCH_3, s at 7.65 for –N=CH–S–). On the other hand, treating the lithium salt with water furnished the 4,5-dihydro-1,3,4-thiadiazole **21**. The IR absorption at 3355 cm^{-1} and the broad s at δ_H 6.2 indicate NH; the NMR spectra are in accordance with **21**. However, tiny δ_C signals suggest a small equilibrium concentration (about 1%) of the open-chain tautomer **24**: We assign the s at δ_C 168.7 to the adamantane–C-2 (171.0 in **17**), and the d at δ_C 189.0 corresponds to 189.6 ppm for the thioformyl C-atom of **20**.[14]

The ring-chain tautomerism of 4,5-dihydro-1,3,4-thiadiazoles with N^{β}-thioacylhydrazones of aldehydes and ketones has been carefully studied by Zelenin et al.[15] and by Evans and Taylor.[16] The equilibria are rapidly established at room temperature, and their position depends markedly on the substituents. It is noteworthy that **20**, prepared on a pathway analogous to that of **21/24**, exists completely in the thioformylhydrazone form.[14] The phenyl conjugation is sufficient to shift the equilibrium to the side of the open-chain form.

The structure of the anion (deprotonated **1**) is unknown, but the stabilization of the negative charge by nitrogen and sulfur is good reason to prefer **15** to **13**. The cyclic form **21** is favoured for the protonated species. The hydrazone group of **21** is superior in bond energy to the cyclic azo group in **1**, thus reflecting the energetic preference of 2-pyrazolines over 1-pyrazolines. As in pyrazoline chemistry,[9,10] bases *and* acids catalyse equilibration. When **1** was treated with CF_3CO_2H in $CDCl_3$ at 4°C (no N_2 extrusion at this temperature), the ^1H NMR signals of **1** were replaced by those of **21** within 3 weeks. By-the-way, **21** is a sensitive substance. In hot ethanol, some azine **17** is generated by an unknown route. The *N*-acetyl derivative of **21** was obtained analytically pure.

The methanolic solution of **1** and 1 equiv. of sodium methanolate did not liberate N_2 at 45°C, i.e. the deprotonation of **1** is virtually complete; this confirms that **1** is more acidic than methanol. The reaction of anion **15** with 2,4-dinitrochlorobenzene furnished the thioimidate **23** in 63% yield. When **1** was dissolved in an excess of piperidine or morpholine at 20°C, de- and reprotonation led to Δ^2-thiadiazoline **21** and its open-chain isomer **24**. Like thioformamides, N^{β}-thioformylhydrazone **24** rapidly interacts with the *sec*-amines and affords the amidrazones **25** and **26**. Isolated **21** and piperidine likewise afforded **25** (85% yield). A direct interaction of **21** with the *sec*-amine is also conceivable, but less probable than the path via **24** (Scheme 6).

The central C-atom of the formamidrazone group appears at δ_C 158.6 (**25**) and 156.1 (**26**), whereas the C-2 of the adamantylidene group resonates at higher frequency (s at 171.6 and 173.2 ppm). The ^{13}C parameters of the adamantylidene group reveal a σ-plane for **25** and **26**. Comparing with the ^{13}C NMR spectrum of azino-2,2′-bis(adamantane) (**17**) allowed us to sort out the ^{13}C signals of the cyclic amine and to unequivocally assign all adamantylidene C-atoms. Both coalescence phenomena and a second set of NMR parameters were missing, which indicates that eventual conformational changes of **25** and **26** (*syn–anti*) are fast compared with the NMR time scale.

The NH group of azoles (pyrazole, imidazole, 1,2,4-triazole) no longer reacts with **1**, but rather intercepts **2**, as was recently described.[17] e.g. **1** reacted with pyrazole at 45°C to afford the *S*,*N*-acetal **27** in 41% yield.

The main preparative value of thiocarbonyl ylides probably rests on their 1,3-cycloadditions. However, the colourful assortment of acid–base reactions of thiocarbonyl ylides and their 1,3,4-thiadiazoline precursors is of mechanistic interest and provides manifold modifications of the original thione function.

3. Experimental

3.1. General[3]

3.1.1. 2′,5′-Dihydrospiro[adamantane-2,2′-(1,3,4)-thiadiazole] (1).[1] ^{13}C NMR (20 MHz): δ 26.9, 27.4, 2×40.6 (4 CH) and 2×35.4, 36.8, 2×37.5 (5 CH_2) indicate a σ-plane; 81.4 (C-5′), 119.6 (C-2).

3.1.2. Reaction of 2 with malononitrile. Compound **1** (300 mg, 1.44 mmol) and freshly distilled malononitrile (120 mg, 1.82 mmol) in absol. THF (3 mL) were stirred at 40°C (bath) for 8 h (34 mL of N_2, 94%). After evaporation of the solvent, the residue was subjected to preparative layer chromatography (PLC, 2 mm silica gel, petroleum ether/CH_2Cl_2 3:2). The first fraction, namely fine needles (160 mg, 60%) from ethanol, mp 179–181°C, was identified with **2-(dicyanomethylene)adamantane (8)** by mixed mp and ^1H NMR spectrum; the authentic sample, mp 183–185°C,[18] was prepared from adamantanone, malononitrile, and piperidine. The second fraction (40 mg, 24%), mp 48–49°C, was NMR-identical with **bis(methylthio)adamantane (9)**.[1]

3.1.3. 2-[(Born-2-en-2-yl)thio]-2-(methylthio)adamantane (12). (a) **1** (416 mg, 2.00 mmol) and (±)-thiocampher[19] (**10**, 353 mg, 2.10 mmol) in THF (6 mL) + a drop of

triethylamine were heated to 40°C for 8 h (47 mL of N_2, 94%). PLC (cyclohexane/CH_2Cl_2 9:1) furnished **12** (178 mg, 24%), colourless crystals (ethanol), mp 86–87°C. IR (KBr): ν 781 (cm^{-1}) m, 1100 m, 1385 m, 1453 st, 1473 m; 1561 m, br (S–C═C). ^{1}H NMR: δ 0.77, 0.82, 1.00 (3s, 3 CH_3), 1.0–2.75 (m, 19H), 2.05 (s, SCH_3), 6.15 (d, J=3.3 Hz, 3′-H). MS (60°C); *m/z* (%): 348 (~1) [M^+], 301 (<1) [M^+-SCH_3], 181 (100) [**5**], 166 (2) [$C_{10}H_{14}S^+$], 133 (3) [166–SH], 91 (9) [$C_7H_7^+$], 79 (4). Anal. calcd for $C_{21}H_{32}S_2$ (368.60): C 72.35, H 9.25, S 18.40; found: C 72.38, H 8.98, S 18.81.

(b) *Acid cleavage of **12**.* 2,4-Dinitrophenylhydrazine (90 mg, 0.45 mmol), dissolved in ethanol (2.2 mL), water (0.7 mL), and conc. H_2SO_4 (0.45 mL), was heated with **12** (74 mg, 0.20 mmol) on the steam bath for 10 min; after 10 min at room temperature, adamantanone 2,4-dinitrophenylhydrazone (**16**, 60 mg, 91%) was filtered, mp 213–215°C, mixed mp without depression (213.5–214.5).[20] Within 5 days at room temperature, (±)-campher 2,4-dinitrophenylhydrazone crystallised as a second fraction (40 mg, 60%), mp 155–159°C; recryst. from ethanol, mp 163–165°C, mixed mp (166–167°C).[21] The rate difference in crystallization was used for separation. TLC (silica gel, CH_2Cl_2) gave R_f 0.44 for the campher derivative and R_f 0.52 for the adamantanone derivative.

3.1.4. Adamantanone N^{β}-[2′-(Methylthio)adamantyl-(2′)-thio]-methylenehydrazone (14). (a) The solution of **1** (416 mg, 2.00 mmol, freshly prepared) in xylene (10 mL) evolved 32 mL of N_2 (64%, nitrometer) in a thermostated 45°C-bath in 7 h; the half-life of the N_2 extrusion was 32 min. The residue after removal of the solvent was triturated with diethyl ether and gave **14** as colourless crystals (120 mg, 31%), mp 178–182°C; after recrystallization (ethanol/CH_2Cl_2 4:1) mp 194–195°C. UV (CH_2Cl_2): λ_{max} 271 nm (log ϵ 5.0), 2.54 (4.96). IR (KBr): ν 745 cm^{-1} m, 776 m, 1098 m, 1449 st, 1548 st; 1625 vst (C═N); 2852 st, 2906 vst (C–H). ^{1}H NMR (400 MHz); δ 1.62–1.73 (m, 5H), 1.81–2.08 (m, 18H), 2.01 (s, SCH_3), 2.38–2.58 (m, 3H), 2.73, 3.37 (2s, br., 1-H, 3-H), 8.10 (s, N═CH–S). ^{13}C NMR (100 MHz, DEPT): δ 10.9 (SCH_3); 26.9, 27.0, 2×27.9, 32.8, 2×36.2, 39.3 (2 sets of 4 CH, 2:1:1); 2×33.26, 2×33.34, 36.6, 2×38.3, 38.8, 2×39.4 (2 sets of 5 CH_2, 2:2:1); 70.2 (C-2′), 150.6 (N═CH–S), 175.9 (C-2). MS (110°C); *m/z* (%): 388 (0.02) [M^+], 341 (0.10) [$C_{21}H_{29}N_2S^+$, M^+-SCH_3], 296 (1.1), 208 (2.7) [$C_{11}H_{16}N_2S^+$, $C_9H_{14}C$═N–NH–CH═S^+; ^{13}C calcd 0.33, found 0.35], 181 (100) [**5**; ^{13}C 12.2/13.7, $^{13}C_2+^{34}S$ 5.1/5.0], 175 (2.1) [208–HS, $C_9H_{14}C$═N–N^+≡CH possible], 166 (4.3) [$C_{10}H_{14}S^+$, adamantanethione$^+$], 148 (2.7) [181–HS, $C_{11}H_{16}^+$], 133 (5.3) [166–HS], 91 (12) [$C_7H_7^+$], 79 (8) [$C_6H_7^+$], 77 (4) [$C_6H_5^+$]. Anal. calcd for $C_{22}H_{32}N_2S_2$ (388.62): C 67.99, H 8.30, N 7.21, S 16.50; found: C 67.86, H 8.30, N 7.13, S 16.51.

(b) *Acid cleavage of **14**.* Short refluxing of **13** (180 mg, 0.46 mmol) with 2,4-DNPH in ethanolic H_2SO_4 afforded adamantanone 2,4-dinitrophenylhydrazone (**16**, 295 mg, 0.89 mmol), mp 212–214°C (mixed mp, IR).

(c) *Competing reactions of **2** in Methanol.* In two experiments, **1** (208 mg, 1.00 mmol) each was dissolved in 5 mL (75 mL) of methanol. After 7 h at 45°C, the solvent was removed, and the residue in $CDCl_3$ NMR-analysed. The integrals of the s at δ_H 8.10 (**14**) and the s at 3.31 (**18**) were compared with that of *sym*-tetrachloroethane (δ 5.97) as weight standard (results given above). The separation of **14** and **18** was achieved by triturating the combined residues with ether, leaving **14** undissolved. Distillation of the mother liquor at 40–45°C (bath)/0.01 Torr gave **2-methoxy-2-(methylthio)adamantane (18)** as a colourless oil, which was further purified by PLC (ether/pentane 3:2). IR (neat): ν 844 cm^{-1} m, 885 st; 1075, 1086, 1101 st (C–O); 1454 st; 2860 st sharp, 2905 vst, br (C–H). ^{1}H NMR: 1.37–1.90, 1.95–2.42 (2 m, 14H), 1.87 (s, SCH_3), 3.31 (s, OCH_3). MS (80°C); *m/z* (%): 212 (0.7) [M^+], 180 (3), 165 (100) [M^+-SCH_3], 150 (28) [$C_{10}H_{14}O^+$, adamantanone$^+$], 133 (4) [$C_{10}H_{13}^+$], 91 (20) [$C_7H_7^+$], 80 (13), 79 (20). Anal. calcd for $C_{12}H_{20}OS$ (212.35): C 67.87, H 9.49, S 15.10; found: C 68.17, H 9.40, S 15.09.

(d) ***14** and CF_3CO_2H in Methanol.* **14** (50 mg) was treated with methanol (5 mL) and 2 drops of CF_3CO_2H at room temperature for 24 h. Work-up with Na_2CO_3/CH_2Cl_2 afforded **2,2-dimethoxyadamantane** (**19**, 35 mg) as a colourless oil, ^{1}H NMR-identified (s, δ 3.15, 2 OCH_3) with an authentic sample.[22]

3.1.5. 4′,5′-Dihydrospiro[adamantane-2,5′-(1,3,4)-thiadiazole] (21). (a) *From **1** via anion **15**.* Lithium diisopropylamide (LDA, 3.1 mmol, freshly prepared) in THF (25 mL) was slowly introduced to the ice-cooled solution of **1** (625 mg, 3.00 mmol) in THF (50 mL) under argon. After 1 h at room temperature, THF was evaporated, and the residue treated with water (50 mL) and CH_2Cl_2 (25 mL). Removal of CH_2Cl_2 in vacuo and trituration with cold ethanol furnished **21** as colourless crystals (380 mg, 61%), mp 141–143°C. **21** is sensitive; attempted recrystallization from hot ethanol afforded azino-2,2′-bis(adamantane) (**17**). Properties of **21**: IR (KBr): ν 863 cm^{-1} m, 885 m, 896 m, 1255 st, 1279 st, br; 1455 vst, 1520 vst, 1629 st (C═N), 3120 st, br (N–H); ($CHCl_3$): 3355 w (N–H). ^{1}H NMR (80 MHz): δ 1.43–2.07 (m, 12H), 2.07–2.35 (m, 1-H, 3-H), 6.2 (br, s, NH, disappears with D_2O), 7.04 (s, 2′-H). ^{13}C NMR (20.2 MHz): δ 26.2, 26.8, 2×39.0 (4 CH), 2×33.9, 2×36.8, 37.3 (5 CH_2); 91.4 (s, C-2), 134.8 (d, C-2′); minor participation of **24** is suggested by small signals: 168.7 (s, C-2), 189.0 (d, thioformyl-C). MS (60°C); *m/z* (%): 208 (75) [M^+], 181 (73) [M^+–HCN], 175 (50), 165 (19), 149 (73), 113 (51), 91 (42), 87 (100) [$C_2H_3N_2S^+$, thiadiazolium ?]. Anal. calcd for $C_{11}H_{16}N_2S$ (208.32): C 63.42, H 7.74, N 13.45, S 15.39; found: C 62.64, H 7.92, N 13.30, S 15.73.

(b) *From **1** via protonation.* **1** (416 mg, 2.00 mmol) in $CDCl_3$ (3 mL) was treated with **4** drops of CF_3CO_2H and stored at 4°C. The ^{1}H NMR spectra, taken from time to time, indicated that **1** had disappeared after 3 weeks. ^{1}H NMR analysis with as-tetrachloroethane (δ 4.28) as standard showed 73% of **21**. H_2S (smell) and azino-2,2′-bis(adamantane) (**17**) were side products.

(c) *N-Acetyl derivative:* **21** (2.00 mmol) and acetyl chloride (2.1 mmol) were reacted in pyridine/CH_2Cl_2. The crude product was purified by PLC (CH_2Cl_2/acetone 95:5) and recrystallized from ethanol, mp 71–72°C. IR (KBr): ν

852 cm^{-1} st, 1318 st, 1328 st, 1366 st, 1551 m (C═N), 1690 vst, br (amide I). ^1H NMR: δ 1.5–2.75 (2 m, 14H), 2.22 (s, CH_3CO), 7.62 (s, 2′-H). MS (40°C); *m/z* (%): 250 (12) [M^+], 208 (100) [$M^+-H_2C{=}CO$], 181 (23), 175 (14), 149 (60) [$C_{10}H_{15}N^+$], 91 (16), 87 (28). Anal. calcd for $C_{13}H_{18}N_2OS$ (250.36): C 62.36, H 7.25, N 11.19, S 12.81; found: C 62.50, H 7.30, N 11.15, S 12.79.

3.1.6. Adamantanone N^{β}-(Methylthiomethylene)hydrazone (22). The dry lithium salt of **1** (3.00 mmol), as prepared above, and methyl iodide (10 mL) were refluxed for 90 min. After evaporation, work-up with aq. NH_3/CH_2Cl_2 and subsequent PLC (petroleum ether/acetone 7:3) provided **22** (453 mg, 68%), mp 56–57°C (isopropyl alcohol). UV (CH_2Cl_2): 253 (5.05). IR (KBr): ν 817 cm^{-1} st, 832 m, 1077 st, 1290 m, br, 1433 m, 1440 st, 1451 st; 1556+1565 vst, br, 1636 vst (C═N). ^1H NMR: δ 1.75–2.19 (appar. d, 12H), 2.69, 3.30 (2 appar. s, br, 2H), 2.37 (s, SCH_3), 7.65 (s, HC═N). MS (30°C); *m/z* (%): 222 (45) [M^+], 207 (9) [M^+-CH_3], 175 (100) [M^+-SCH_3, $C_9H_{14}C{=}N{-}N^+{\equiv}CH$], 149 (37) [$C_{10}H_{15}N^+$], 121 (12), 119 (12), 106 (18), 95 (18), 93 (19), 91 (19), 79 (48). Anal. calcd for $C_{12}H_{18}N_2S$ (222.34): C 64.82, H 8.16, N 12.60, S 14.42; found: C 64.83, H 8.24, N 12.45, S 14.37.

3.1.7. Adamantanone N^{β}-[(2,4-Dinitrophenylthio)methylene]hydrazone (23). **1** (417 mg, 2.00 mmol) and sodium methanolate (2.00 mmol) in methanol (20 mL) were reacted at 45°C for 30 min (no N_2 elimination). 2,4-Dinitrochlorobenzene (2.00 mmol) in methanol (10 mL) was slowly added and heated to 45°C for another 30 min. Work-up with water/CH_2Cl_2 and PLC (silica gel, CH_2Cl_2) furnished **23** (470 mg, 63%) as golden-yellow leaflets, mp 115–116°C (isopropyl alcohol). IR (KBr): ν 731 cm^{-1} m, 832 m; 1344, 1530 vst (NO_2); 1452 m, 1598 st, 1634 st (C═N, arom. ring vibr.). ^1H NMR: same appearance of adamantane-H as for **22**, δ 2.00 (d, br, 12H); 2.78, 3.44 (2s, br, 1-H, 3-H), 7.25, 7.87 (2s, CH═N, probably two conformations), 7.88 (d, *J*=9.0 Hz, 6′-H), 8.48 (dd, *J*=9.0, 2.2 Hz, 5′-H), 8.90 (d, *J*=2.2 Hz, 3′-H). MS (110°C); *m/z* (%): 374 (1.4) [M^+], 328 (41) [M^+-NO_2], 301 (18), 150 (47) [$C_{10}H_{16}N^+$], 148 (51) [$C_{10}H_{14}N^+$], 121 (29), 93 (37) [$C_7H_9^+$], 91 (48) [$C_7H_7^+$], 81 (42), 80 (52), 79 (100) [$C_6H_7^+$]. Anal. calcd for $C_{17}H_{18}N_4O_4S$ (374.41): C 54.53, H 4.85, N 14.97, S 8.56; found: C 54.12, H 4.73, N 14.74, S 8.58.

3.1.8. Adamantanone N^{β}-(Piperidinomethylene)hydrazone (25). (a) The solution of **1** (2.00 mmol) in piperidine (10 mL) developed H_2S, but no N_2, in 3 h at 20°C. Work-up with H_2O/CH_2Cl_2 and PLC (CH_2Cl_2/ethanol 9:1) afforded colourless **25** (275 mg, 53%), mp 84–85°C (acetone). IR (KBr): ν 1009 cm^{-1} st, 1198 st; 1605 vst, 1635 vst (C═N). ^1H NMR (400 MHz): δ 1.52–1.66 (m, 6H), 1.80–1.94 (m, 12H), 2.54 (s, 1H), 3.28–3.35 (m, 2 H_2C–N), 3.86 (s, br, 1H), 7.92 (s, N═CH–N). ^{13}C NMR (20.2 MHz, H-decoupled and off-resonance): δ 24.7 (C-4′), 25.6 (C-3′/5′), 47.2 (C-2′/6′ of piperidino); 4 CH of adamantylidene: 28.3 (C-5/7), 31.9, 39.7 (C-1, C-3); 5 CH_2 of adamantylidene: 37.0 (C-6), 38.1, 39.3 (C-4/10, C-8/9); 158.6 (d, CH═N), 171.6 (s, C-2). MS (30°C); *m/z* (%): 259 (79) [M^+; ^{13}C 14.1/15.0], 175 (93) [$M^+-NC_5H_{10}$], 150 (96) [$C_{10}H_{16}N^+$, $C_9H_{14}C{=}NH_2^+$; ^{13}C 10.7/9.9], 149 (16) [$C_{10}H_{15}N^+$], 111 (29) [$C_6H_{11}N_2^+$, $C_5H_{10}N{-}C{\equiv}NH^+$], 110 (6), 95 (5), 84 (100) [$C_5H_{10}N^+$, piperidino$^+$; ^{13}C 5.6/6.1], 83 (10) [$C_5H_9N^+$], 79 (10) [$C_6H_7^+$], 77 (6) [$C_6H_5^+$]. Anal. calcd for $C_{16}H_{25}N_3$ (259.38): C 74.08, H 9.72, N 16.20; found: C 74.10, H 9.72, N 15.95.

(b) **21** (208 mg, 1.00 mmol) in piperidine (5 mL) reacted at room temperature for 10 h. Work-up as above gave **25** (220 mg, 85%) after recrystallization from acetone, mp 83–84°C (mixed mp, IR).

3.1.9. Adamantanone N^{β}-(morpholinomethylene)hydrazone (26). The compound was analogously prepared; 320 mg, 61%, mp 72–73°C (pentane). IR (KBr): ν 865 cm^{-1} m, 922 m, 990 m, 1029 st, 1119 st, 1231 m, 1270 m, 1450 st; 1608 vst, 1640 vst (C═N). ^1H NMR: 1.6–4.0 (several m, 22H), 7.92 (s, CH═N). ^{13}C NMR (100 MHz, DEPT): Adamantylidene, δ 28.2, 31.9, 39.7 (4 CH, 2:1:1), 36.9, 38.1, 39.3 (5 CH_2, 1:2:2), 173.2 (C-2); morpholino, 46.5 (2 N–CH_2), 66.6 (2 O–CH_2); 156.1 (CH═N). MS (30°C): *m/z* (%): 261 (29) [M^+; ^{13}C 4.9/5.1], 175 (100) [$M^+-NC_4H_8O$], 150 (27) [$C_{10}H_{16}N^+$, $C_9H_{14}C{=}NH_2^+$; ^{13}C 3.0/2.9], 113 (9) [$HN^+{\equiv}C{-}NC_4H_8O$], 86 (10) [$OC_4H_8N^+$, morpholino$^+$], 85 (7), 79 (5), 77 (3). Anal. calcd for $C_{15}H_{23}N_3O$ (261.36): C 68.93, H 8.87, N 16.08; found: C 68.59, H 8.85, N 15.94.

3.1.10. Azino-2,2′-bis(adamantane)[23] (17). The compound was prepared for spectroscopic comparison. Adamantanone (10.0 mmol) in ethanol (5 mL) was heated with hydrazine hydrate (50 mmol) and 2 drops of conc. HCl under reflux for 4 h. **17** (0.90 g, 61%) was isolated, mp 312–314°C, (mp>300°C)[23]. IR (KBr): ν 1443+1452 cm^{-1} m; 1648 st (C═N); 2854 st, sharp, 2910 vst, br (C–H). ^{13}C NMR (20.2 MHz): δ 2×28.0, 31.7, 39.6 (3 d, 4 CH), 36.7, 2×38.1, 2×39.4 (3 t, 5 CH_2), 171.0 (s, C-2); identical adamantylidene groups, σ-plane. Anal. calcd for $C_{20}H_{28}N_2$ (296.44): C 81.03, H 9.52, N 9.45; found: C 80.70, H 9.35, N 9.45.

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References

1. Huisgen, R.; Mloston, G. *Tetrahedron Lett.* **1985**, *26*, 1049–1052; *Polish J. Chem.* **1999**, *73*, 635–644.
2. Mloston, G.; Huisgen, R.; Huber, H.; Stephenson, D. S. *J. Heterocycl. Chem.* **1999**, *36*, 959–968.
3. Mloston, G.; Huisgen, R.; Polborn, K. *Tetrahedron* **1999**, *55*, 11475–11494.
4. Mloston, G.; Linden, A.; Heimgartner, H. *Helv. Chim. Acta* **1996**, *79*, 31–40.
5. Huisgen, R.; Mloston, G.; Polborn, K. *Heteroat. Chem.* **1999**, *10*, 662–669.

6. Huisgen, R.; Li, X.; Mloston, G.; Knorr, R.; Huber, H.; Stephenson, D. S. *Tetrahedron* **1999**, *55*, 12783–12796.
7. Hürzeler, M.; Bernet, B.; Mäder, T.; Vasella, A. *Helv. Chim. Acta* **1993**, *76*, 1779–1781.
8. Kägi, M.; Mloston, G.; Linden, A.; Heimgartner, H. *Helv. Chim. Acta* **1994**, *77*, 1299–1312.
9. von Auwers, K.; Cauer, E. *Liebigs Ann. Chem.* **1929**, *470*, 284–312.
10. Theobald, R. S. In *Rodds Chemistry of Carbon Compounds*, 2nd Ed.; Ansell, M. F., Ed.; Elsevier: Amsterdam, 1986; Vol. IVC, pp 54–64 Review.
11. Preliminary communication: Mloston, G.; Huisgen, R. *Tetrahedron Lett.* **1985**, *26*, 1053–1056.
12. Fisera, L.; Huisgen, R.; Kalwinsch, I.; Langhals, E.; Li, X.; Mloston, G.; Polborn, K.; Rapp, J.; Sicking, W.; Sustmann, R. *Pure Appl. Chem.* **1996**, *68*, 789–798 Review.
13. Review on 1,5-electrocyclizations: Huisgen, R. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 947–973.
14. Huisgen, R.; Kalwinsch, I.; Li, X.; Mloston, G. *Eur. J. Org. Chem.* **2000**, 1685–1694.
15. Zelenin, K. N.; Khrustalev, V. A.; Alekseev, V. V.; Sharbatyan, P. A.; Lebedev, A. T. *Khim. Geterosikl. Soedin.* **1982**, 904–910; *Chem. Abstr.* **1982**, *87*, 162877; Zelenin, K. N.; Alekseev, V. V.; Khrustalev, V. A. *J. Org. Chem. USSR (Engl. Transl.)* **1984**, *20*, 169–180.
16. Evans, D. M.; Taylor, D. R. *J. Chem. Soc., Chem. Commun.* **1982**, 188–189.
17. Mloston, G.; Gendek, T.; Heimgartner, H. *Pol. J. Chem.* **1998**, *72*, 66–72.
18. Dekkers, A. W. J. D.; Verhoeven, I. W.; Speckamp, W. N. *Tetrahedron* **1973**, *29*, 1691–1696.
19. Barton, D. H. R.; Guziec, F. S.; Shahak, I. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1794–1799.
20. Smith, G. H.; Williams, H. D. *J. Org. Chem.* **1961**, *26*, 2207–2212.
21. Kotake, M.; Nonaka, H. *Liebigs Ann. Chem.* **1957**, *607*, 153–159.
22. Gowenlock, B. G.; Pfab, J.; Kresze, G. *J. Chem. Soc., Perkin Trans. 2* **1974**, 511–518.
23. Funabashi, M.; Tanaka, A.; Anselme, J. P. *Bull. Chem. Soc. Jpn* **1972**, *45*, 2958.