1,3-Dithiolanes from Cycloadditions of Alicyclic and Aliphatic Thiocarbonyl Ylides with Thiones: Regioselectivity**

Rolf Huisgen,*[a] Grzegorz Mloston,[b] Kurt Polborn,[a] and Reiner Sustmann[c]

Dedicated to Emanuel Vogel on the occasion of his 75th birthday

Abstract: The regiochemistry of 1,3-dithiolanes obtained from thiocarbonyl ylides **9** and thiones **10** shows a striking dependence on substituents. Previously and newly performed experiments indicate that sterically hindered cycloalkanethione *S*-methylides and dialkylthioketone *S*-methylides react with alicyclic and aliphatic thiones to give the 2,2,4,4-tetrasubstituted 1,3-dithiolanes **11** exclusively. Aryl groups in one or both reactants lead to a preference for, or even complete formation of, 4,4,5,5-tetrasubstituted 1,3-dithiolanes **12**. Several mechanisms appear to be involved, but the paucity of experimental criteria is troubling. Quantum-chemical calculations (see preceding paper) on the cycloaddition between thioacetone *S*-methylide and thioacetone furnish lower activation energies for the concerted process than for the two-step pathways via *C*,*S*- or *C*,*C*-biradicals; the favoring of the 2,4-substituted 1,3-dithiolanes over the 4,5-substituted type would be expected to increase with growing bulk of substituents. Aryl groups stabilize intermediate biradicals. Experimental criteria for the differentiation of regioisomeric dithiolanes are discussed. Thiocarbonyl ylides **9** are prepared by 1,3-cycloadditions between diazomethane and thioketones and subsequent N_2 elimination from the usually isolable 2,5-dihydro-1,3,4-thiadiazoles **17**; different ratios of the two rate constants lead to divergent product formation scenarios.

Keywords: cycloaddition · 1,3-dithiolanes · reaction mechanisms · regioselectivity · thiocarbonyl ylides

Introduction

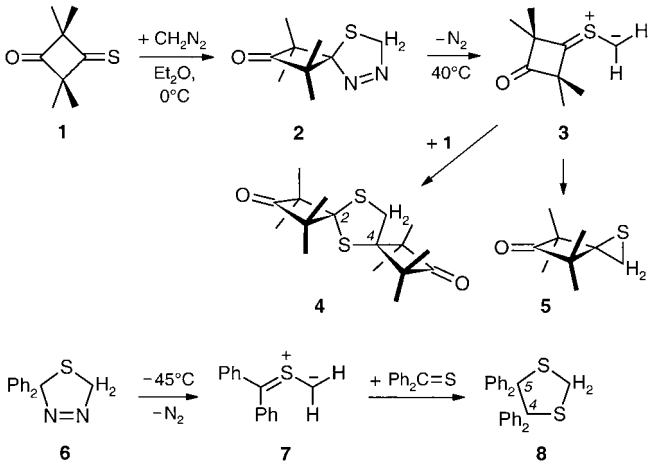
1,3-Cycloadditions between diazoalkanes and thioketones and subsequent N_2 elimination offer the most convenient and variable pathway to thiocarbonyl ylides (reviews:[1, 2]). In 1970, Diebert studied the reaction between the easily accessible 2,2,4,4-tetramethyl-3-thioxocyclobutanone (**1**) and diazomethane, and identified the primary adduct as 2,5-dihydro-1,3,4-thiadiazole **2**;[3] the "white solid" (no analyses) lost nitrogen on warming and furnished thiirane **5** (Scheme 1). Treatment of **1** with 0.8 equivalents of diazomethane provided some 1,3-dithiolane **4** as well as **5**, but the intermediacy of the thiocarbonyl *S*-methylide **3** remained unrecognized.

[a] Prof. R. Huisgen, Dr. K. Polborn
Department of Chemistry
Ludwig-Maximilians-Universität
Butenandtstrasse 5–13 (Haus F)
81377 München (Germany)
Fax (+49) 89-2180-77717
E-mail: rolf.huisgen@cup.uni-muenchen.de,
kvp@cup.uni-muenchen.de

[b] Prof. G. Mloston
Section of Heteroorganic Compounds
University of Lodz
Narutowicza 68, 90-136 Lodz (Poland)
E-mail: gmloston@krysia.uni.lodz.pl

[c] Prof. R. Sustmann
Institut für Organische Chemie der Universität
Universitätsstrasse 5, 45117 Essen (Germany)
E-mail: reiner.sustmann@uni-essen.de

[**] 1,3-Dipolar Cycloadditions, Part 127. Part 126: R. Huisgen, G. Mloston, E. Langhals, T. Oshima, *Helv. Chim. Acta* **2002**, *85*, 2668–2685.



Scheme 1. Thiocarbonyl ylides and thiones: classic examples of differing regioselectivity.

DOI: 10.1002/chem.200204659

Thiocarbonyl ylides such as **3** cannot be isolated, but can be intercepted with suitable dipolarophiles. Cycloadditions between the sterically hindered **3**, an electron-rich 1,3-dipole, and acceptor-substituted ethylenes have served as a model system to probe the borderline crossing from the *concerted mechanism* to the *two-step process* via zwitterionic intermediates.[4, 5]

In 1930/31, two groups reported the formation of 4,4,5,5-tetraphenyl-1,3-dithiolane (**8**), produced in high yield from thiobenzophenone and diazomethane at 0 °C.[6, 7] The mechanism, involving 2,2-diphenyl-2,5-dihydro-1,3,4-thiadiazole (**6**) and thiobenzophenone *S*-methylide (**7**) as intermediates, was established 50 years later.[8] This clarification led to the insight that thiones are "superdipolarophiles", with respect not only to thiocarbonyl ylides, but also to diazoalkanes, nitrones, and other 1,3-dipoles (review:[9]). Rate measurements on Diels–Alder reactions similarly revealed the "superdienophilic" character of thiones.[10]

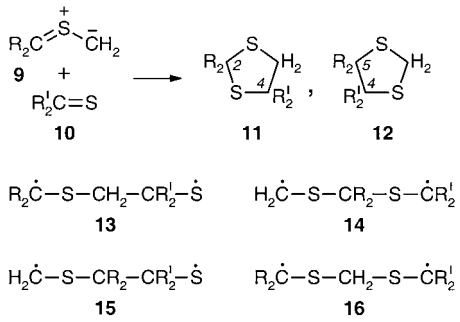
A fascinating problem of regioselectivity emerges: thiocarbonyl ylide **3** + thione **1** gave rise to the 2,2,4,4-tetrasubstituted dithiolane **4**, whereas **7** and thiobenzophenone exclusively afforded the 4,4,5,5-tetrasubstituted type **8**. Reactant pairs with other sets of substituents followed one or the other path, or furnished mixtures of regioisomers. Undoubtedly, several mechanisms are participating in dithiolane formation, but experimental criteria are scarce. The retention of dipolarophile configuration—so informative for additions to C=C bonds[4]—is not applicable to C=S bonds.

All the more welcome, therefore, were the quantum-chemical calculations reported in the preceding paper, which brought to light that account has to be taken of two-step mechanisms with *C*,*S* and *C*,*C* biradicals as intermediates as well as the concerted cycloaddition.[11] The outcome of transition state (TS) calculations is to be compared with experimental results in several publications, and this first set presents thiocarbonyl ylides + thiones with alicyclic and aliphatic substituents.

Abstract in German: *Die Regiochemie der 1,3-Dithiolan-Bildung aus Thiocarbonyl-yliden **9** and Thionen **10** zeigt eine auffallende Abhängigkeit vom Substitutionsmuster. Alte und neue Experimente lehren, daß sich sterisch gehinderte Cycloalkanthion-S-methylide und Dialkylthioketon-S-methylide mit alicyclischen und aliphatischen Thionen ausschließlich zu 2,2,4,4-tetrasubstituierten 1,3-Dithiolanen **11** vereinigen. Arylreste in einem oder beiden Reaktanten führen vorzugsweise oder gar vollständig zu 4,4,5,5-tetrasubstituierten 1,3-Dithiolanen **12**. Mehrere Mechanismen scheinen beteiligt zu sein, aber der Mangel an experimentellen Kriterien ist schmerzlich. Quantenchemische Rechnungen (vorstehende Arbeit) zur Cycloaddition des Thioaceton-S-methylids mit Thioaceton ergeben niedrigere Aktivierungsenergien für den konzertierten Prozeß als für die zweistufigen Wege über C,S- und C,C-Biradikale; der Vorzug der 2,4-substituierten 1,3-Dithiolane vor den 4,5-substituierten Typen sollte mit zunehmender Substituentengröße steigen. Arylreste stabilisieren intermediäre Biradikale. Experimentelle Kriterien für die Unterscheidung der regioisomeren 1,3-Dithiolane werden diskutiert. Thiocarbonyl-ylide **9** bereitet man durch 1,3-Cycloaddition des Diazomethans an Thioketone und anschließende N_2-Abspaltung aus den meist isolierbaren 2,5-Dihydro-1,3,4-thiadiazolen **17**; unterschiedliche Verhältnisse der beiden Geschwindigkeitskonstanten beeinflussen Reaktionsablauf und Produktspiegel.*

Results and Discussion

According to the calculations for thioformaldehyde *S*-methylide (**9**, R = H; Scheme 2), concerted cycloaddition to ethene has to overcome a well-defined barrier lower than the



Scheme 2. Regiochemistry of 1,3-dithiolane formation and conceivable biradical intermediates.

activation energy of biradical formation.[11, 12] In contrast, the concerted addition between **9** and thioformaldehyde (**10**, R′ = H) shows no sign of a potential energy barrier. Starting from the energy level of the reactants, the energy of the four-center reaction complex goes down, and—a rare feature—no TS can be defined on the route to 1,3-dithiolane. Two-center reactions lead to *C*,*S* and *C*,*C* biradicals, formed via barriers of +3.4 and 4.7 kcal mol^{-1}, respectively.

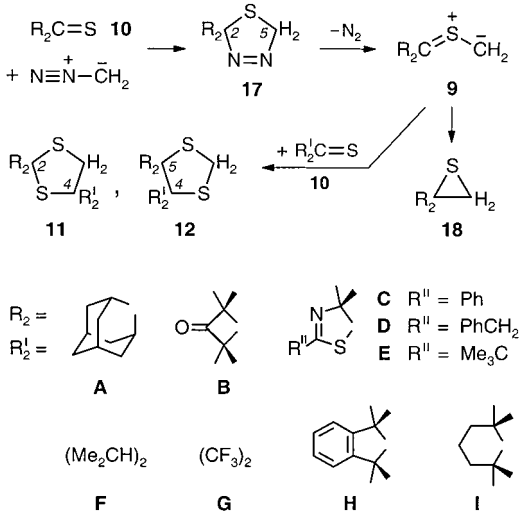
For the reaction between thioacetone *S*-methylide (**9**, R = Me) and thioacetone (**10**, R′ = Me), the second model used for calculation, two addition directions produce 1,3-dithiolanes **11** and **12**. The formation of **11** is 5 kcal mol^{-1} more exothermic than that of **12**, reflecting steric hindrance by the adjacent *gem*-dimethyl groups in **12**. Now the concerted processes for the formation of **11** and **12** (R = R′ = Me) show small activation barriers: 3.1 and 4.4 kcal mol^{-1}, respectively. In the framework of the two-step pathways, *C*,*S* biradical **13** and *C*,*C* biradical **14** lead to **11**, whereas the cyclizations of **15** and **16** give rise to **12**. The activation energies of biradical formation are still higher than those of the four-center cycloadditions.[11]

Generally, the substituents in **9** and **10** (Scheme 2) will influence the energy profile of cycloaddition in several respects: 1) substituents lose conjugation energy present in the reactants, 2) conjugation may stabilize the terminal carbon atom(s) of biradicals, and 3) steric hindrance in TSs and products will increase. The expectation that aryl substitution should work in favor of the biradical pathways is borne out by further calculations.[13]

All experimentally studied systems of **9** + **10** bear substituents R and R′ larger than Me. The difference of

1.3 kcal mol^{-1} in the activation energies of the two *concerted* paths leading to **11** and **12** (R = R′ = Me) will increase with growing steric interference in the TS in favor of formation of **11**.

The mechanism via the *C*,*S*-biradical **13**, which requires bonding of the reactants between CH_2 and CR'_2, likewise produces **11**. The formation of **13** (R = R′ = Me) passes through a TS at 7.1 kcal mol^{-1}: 4.0 kcal mol^{-1} higher than the TS of the concerted pathway to **11**. However, with increasing steric demands of R and R′, this energy difference should diminish because the TS(concerted) would be expected to rise more rapidly than the TS(*C*,*S* biradical). The two pathways to **11** should therefore become competitive, and the change of mechanism may even go unnoticed. (U)B3LYP calculations with the aliphatic and alicyclic residues R_2 and R'_2 employed experimentally (**A**–**I** in Scheme 3) are not yet feasible.



Scheme 3. The dithiolane formation reaction scheme and the substituents employed.

Clearly, 1,3-dithiolanes **11** are the only cycloadducts found for combinations of non-aromatic reactants published to date (Table 1). Most examples use thiocarbonyl *S*-methylides **9** (Scheme 3) derived from adamantanethione (**A**) or 2,2,4,4-tetramethyl-3-thioxocyclobutanone (**B**). The selection of thiones **10** is broader and includes 1,3-thiazole-5(4*H*)-thiones **C**–**E**. The yields of the spirocyclic adducts in Table 1 are based on ^{1}H NMR analysis with weight standard. Since the corresponding regioisomers **12** are unknown, small amounts may have escaped the analysis. In cases of moderate yields in Table 1, side products have been analyzed. A preliminary communication on some cycloadducts of **9B**[14] is supplemented here by spectroscopic and analytical data.

Competing with the cycloaddition is the electrocyclization of **9**, which irreversibly furnishes thiiranes **18**. Increasing yields of **18** signal weak dipolarophilic activity (e.g., 30% of **18F** along with 39% of **11FF** in the example with two diisopropyl groups[15]). The sterically most demanding thiocarbonyl ylides, **9H** and **9I**, no longer react with thione **1** (= **10B**); quantitative yields of thiiranes **18H** and **18I** indicate

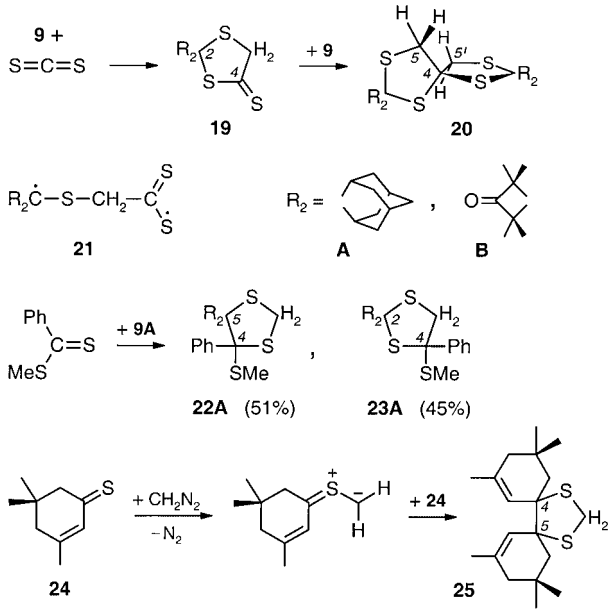
Table 1. Formation of 2,4-substituted 1,3-dithiolanes **11** from thiocarbonyl ylides **9** and thiones **10;** for symbols **A**–**G** see Scheme 3.

Reactants		1,3-Dithiolane **11**				Ref.
9, R_2	**10**, R'_2	Formula	Yield [%]	M.p. [°C]	δ(^{13}C) of C5	
A	**A**	**11AA**	86	165–166	45.5	[16]
A	**B**	**11AB**	80	128–129	41.9	[16]
A	Me, SMe		64	43–45	48.2	[16]
A	$(SPh)_2$		85	122–124	45.9	[16]
A	S=C=	**19A**	89	108–110	55.9	[16]
A	**19A**	**20A**	81	230–231	48.2	[16]
A	**D**	**11AD**	94	oil	47.8	[17]
B	**A**	**11BA**	88	139–141	47.0	[14][a]
B	**B**	**11BB**	73	159–161	43.4	[3, 14][a]
B	**C**	**11BC**	87	108–109	49.1	[17]
B	**D**	**11BD**	84	oil	48.7	[17]
B	**E**	**11BE**	85	123–124	48.5	[17]
B	S=C=	**20B**	66,*b*	132–134	50.2	[a]
F	**F**	**11FF**	39	oil	44.3	[15][a]
G	**G**	**11GG**	29	b.p. 143–144		[18]

[a] This paper. [b] In dilute solution (0.005 M **17B** in CS_2) 30% **19B** + 16% **20B**.

that the *intramolecular* reaction course is less hindered than the *intermolecular* one.

Carbon disulfide is a weaker dipolarophile towards **9A** than its monoadduct **19A** (Scheme 4). The high yield of **19A** (89% in Table 1) was observed in dilute CS_2 solution (0.005 M **17A**); **19A** (now in the role of R'_2C=S) reacted >300 times more



Scheme 4. Carbon disulfide reacts "normally", but aromatic and olefinic unsaturation change the regiochemistry.

rapidly than CS_2 with **9A**.[16] The chiral bisadduct **20A** shows equivalent adamantane systems, due to the presence of a C_2 axis; both dithiolane rings belong to type **11**. When **9B** was treated with carbon disulfide (as solvent), the corresponding monoadduct **19B** and bisadduct **20B** were identified by ^{1}H NMR spectroscopy, but only the latter compound was isolated pure and crystalline. Four ^{1}H and four ^{13}C signals for

eight methyl groups in the NMR spectra of **20B** testify to C_2 symmetry. Should the pathway via the attractive *C*,*S*-biradical **21** be discussed? This is not clear because the extra stabilization of S=C=S (like that of CO_2) lowers the reactivity.

The dithiocarboxylic esters (methyl dithioacetate), dithiolactones **19**, 1,3-thiazole-5(*4H*)-thiones **10C**–**10E**, and diphenyl trithiocarbonate in Table 1 correspond to aliphatic or alicyclic thioketones in their regiochemical behavior, affording 1,3-dithiolanes **11**. However, **9A** reacts with methyl dithiobenzoate to give the regioisomers **22A** and **23A**,[16] so the presence of one phenyl group among the four substituents is sufficient to bring out the biradical pathway,[13] at least partially (Scheme 4).

In the reaction between the unsaturated thioketone **24** and diazomethane, Metzner obtained **25** (*meso* + *dl*) in 85% yield.[19] Dithiolane **25** corresponds to type **12**, the vinylic unsaturation in both reactants probably sharing the phenyl group's capacity to stabilize an intermediate *C*,*C* biradical of type **16**.

Direct measurements of cycloaddition rates of **9** are not obtainable, since the rate-determining step is always the loss of N_2 from the precursor 2,5-dihydro-1,3,4-thiadiazole **17**. The solvent dependence of rate constants is also not accessible, thus further diminishing the applicable mechanistic criteria. However, it is not necessary to dispense completely with structure/rate relationships, which are a valuable mechanistic criterion. Competition constants between pairs of dipolarophiles with thiobenzophenone *S*-methylide (**7**) have provided relative rates and indicated the superiority of thiones as dipolarophiles.[20]

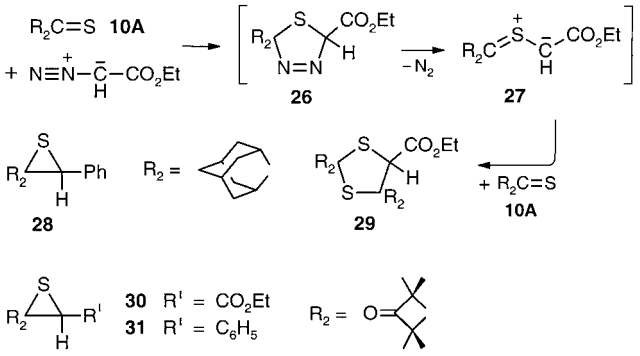
The tools allowing the assignments of structures **11** and **12** are mentioned briefly:

Symmetry: The ^{13}C NMR spectrum of the 4,4,5,5-tetraphenyl-1,3-dithiolane (**8**) shows only one set of Ph signals, due to C_{2v} symmetry. In the regioisomer **11** (R = R′ = Ph), only one σ plane is left, and two different phenyl spectra would be expected. The dithiolane **11AA** similarly belongs to the point group C_s. The two adamantane residues are different, but both reveal the presence of the mirror plane through a reduction in the number of ^{13}C signals. For the same reason, **11BB** meets the same expectation, with four NMR signals for eight methyl groups, and not two signals, as would be expected for the (unknown) **12BB**.

Matched pairs: Reactants **9A** + **10B** and **9B** + **10A** give different 2,4-substituted thiolanes (**11AB** and **11BA**), whereas regioisomers **12AB** and **12BA** would be identical.

^{13}C chemical shift of ring-CH_2: The triplet for C5 in **11** appears at higher frequencies ($\delta = 42-56$ ppm in Table 1) than that of C2 in **12** ($\delta = 28-31$ ppm).[16] The deshielding effect exerted by the quaternary C4 on C5 of **11** is stronger than that of the second thioether function acting on C2 of **12**. For example, C5 signal in **22A** was found at $\delta = 28.1$, and the C2 signal of **23A** at $\delta = 47.3$ ppm (Scheme 4).

The 2,5-dihydro-1,3,4-thiadiazoles (i.e., the cycloadducts of diazoalkanes and thiones) are not always isolable. Whereas adamantanethione (**10A**) rapidly reacted with diazomethane in pentane at −30 °C to give **17A**,[21] the less reactive ethyl diazoacetate required 2 h at 60 °C for the addition, which was immediately followed by N_2 extrusion from **26**. Thiocarbonyl ylide **27** combined with a second molecule of **10A** and provided the dispirodithiolane **29** in 87% yield (Scheme 5); although the ratio of reactants was 1:1, two molecules of **10A**



Scheme 5. "Schönberg reaction": cycloreversion (N_2 extrusion) of 2,5-dihydro-1,3,4-thiadiazole is faster than its formation.

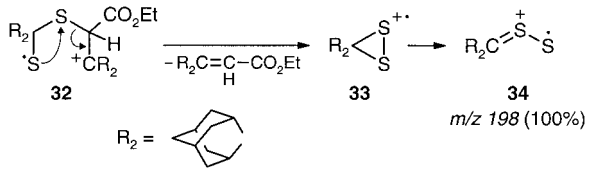
entered into the formation of **29**, and 0.5 equivalents of ethyl diazoacetate remained unconsumed. When the reaction was repeated at room temperature and at −28 °C, the disappearance of the red color of thione **10A** required 12 h and six weeks, respectively, and NMR monitoring did not bring any **26** to light.

The reaction shown in Scheme 5 corresponds to that in Scheme 3, consisting of two 1,3-dipolar cycloadditions separated by a 1,3-dipolar cycloreversion (extrusion of N_2), but the rate ratio of the first two steps is reversed here. The cycloaddition of ethyl diazoacetate is rate-determining, and only the 1:2 product **29** can be isolated. We have proposed the term "Schönberg reaction" for this 1:2 stoichiometry[8] to honor the pioneer of thione chemistry, who studied the formation of dithiolane **8** in the reaction between diazomethane and thiobenzophenone.[7] Two differences are notable, however: 2,2-diphenyl-2,5-dihydro-1,3,4-thiadiazole (**6**) was isolable at −78 °C, and eliminated N_2 at −45 °C (Scheme 1).[8] The second difference lies in the regiochemistry: **8** and **29** belong to dithiolane types **12** and **11**, respectively. The highly hindered **8** may originate from a pathway with a *C*,*C* biradical intermediate of type **16**.[13] In contrast, **29** could well be the result of a concerted cycloaddition, although a path via a *C*,*C* biradical of type **14** with the carboxylate as stabilizing substituent is also conceivable.

In the concerted elimination of N_2 from **17**, the substituents gain conjugation when the thiocarbonyl ylide **9** is formed. Thus, the rate constants of the first-order N_2 elimination reflect the stabilizing influence of substituents in **9**. The spirothiadiazolines **17A** and **17B** lose N_2 with half-reaction times of 89 and 86 min at 40 °C (THF),[5b, 21] respectively, while the formation of **7** from **6** ($t_{1/2} = 56$ min *at* −45 °C in THF)[8b] profits from the incipient phenyl conjugation. The carboxylate group should stabilize the anionic charge of thiocarbonyl ylide **27**, but the rate constant of N_2 extrusion from **26** is not accessible, for reasons given above.

On slow addition of phenyldiazomethane to adamantanethione, decolorization and N_2 evolution took place simultaneously. The formation of 92% of thiirane **28** shows that electrocyclic ring-closure won over the cycloaddition. Correspondingly, the "Schönberg reaction" failed for interaction between thione **1** and ethyl diazoacetate or phenyldiazomethane. The thiiranes **30** (93%) and **31** (93%) were obtained instead of the cycloadducts.

Dithiolane **29** may be singled out for a brief structural comment. As a consequence of the chirality, the ^{13}C NMR shows 20 signals for the 20 C atoms of two adamantane systems. We have previously discussed the mass spectra of 1,3-dithiolanes[16] and assumed an open-chain structure—here **32** (Scheme 6)—for the molecular ion. Splitting of radical cation



Scheme 6. Suggested pathway of mass spectral fragmentation of dithiolane **29**.

32 leads to $C_{10}H_{14}S_2^+$ as base peak, together with an olefinic compound (*m*/*z* 220, $C_{14}H_{20}O_2^+$). The first fragment is tentatively assigned the structure (**34**) of a *distonic* ion; distonic species are those with separate centers of charge and spin density.[22, 23] Scheme 6 outlines a plausible pathway. 1,3-Dipoles related to **34** are thiocarbonyl *S*-sulfides.[24, 25] A second, minor mode of fragmentation follows the cycloaddition path: $\mathbf{27}^+$ (*m*/*z* 252, 12%) and $\mathbf{10A}^+$ (*m*/*z* 166, 11%), so both fragments can bear the positive charge.

We determined the X-ray structure of **4** (= **11BB**) to learn about the influence of the space-filling spiro-annulated substituents on the conformation of the 1,3-dithiolane ring. Whereas the X-ray analysis of 2,2′-bis(1,3-dithiolane) revealed a half-chair,[26] the hetero ring of **4** shows a pronounced envelope conformation (Figure 1). The dihedral angle at C4-S5-C6-S10 (= −4.9°) defines a quasi-plane, and C11 as a "flap" is located 0.78 Å above that plane. The puckering displacement of the cyclopentane envelope amounts to 0.46 Å (gas-phase electron diffraction).[27] The bond angle at the bivalent S atom is smaller than that at sp^3-hybridized carbon and easier to deform. Previous NMR studies indicate that 1,3-dithiolanes are more strongly puckered than 1,3-dioxolanes.[28]

Five-membered rings such as 1,3-dithiolanes have ten conformers each for half-chair and envelope in the pseudorotation circuit. Bulky substituents may strongly confine favorable conformations.[29] The envelope structure resembles that observed for the cycloadduct obtained from **9A** and **10** (R = Ph).[16]

The two four-membered rings in **4** are virtually planar, as the sums of the intracyclic bond angles (359.4°, 360.0°) demonstrate. The intracyclic angles at the carbonyl C atoms are compressed to 95.6° and 95.9°. The C–C bond length for C1–C4 in the cyclobutanone ring (1.598 Å) exceeds that of

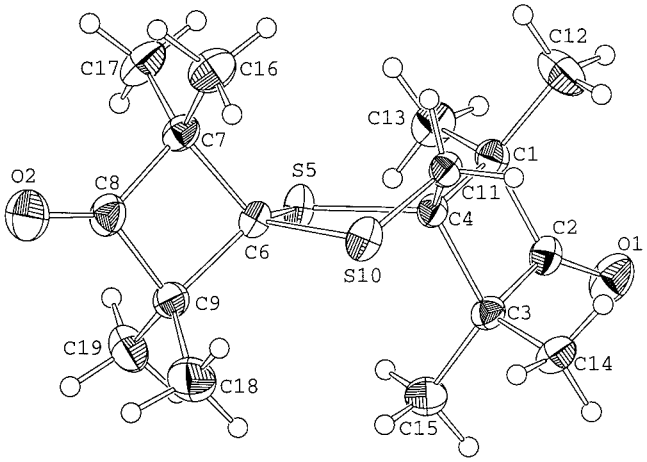


Figure 1. Structure of 1,3-dithiolane **4** (ZORTEP plot; thermal ellipsoids at 30% probability level) showing the envelope conformation of the heterocycle. Selected bond lengths [Å]: C4–S5 1.817(2), S5–C6 1.826(2), C6–S10 1.813(2), S10–C11 1.793(2), C11–C4 1.526(3), C3–C4 1.598(2), C6–C9 1.601(3); bond angles [°]: C4–S5–C6 100.37(9), S5–C6–S10 106.4(1), C6–S10–C11 95.04(9), S10–C11–C4 106.7(1), C11–C4–S5 104.3(1); dihedral angles [°] within heterocycle at: C4–S5 −27.6(2), S5–C6 −4.9(1), C6–S10 29.8(1), S10–C11 −51.5(1), C11–C4 51.4(1).

C4–C11 (1.526 Å) in the dithiolane ring, probably as a consequence of van der Waals pressure.

The puckering angle of cyclobutane (28°)[30] is reduced in cyclobutanone (gas phase) to 10.4 ± 2.7°[31] or 11.5°;[32] its evaluation by electron diffraction, microwave, or IR data is rendered difficult by a low inversion barrier. Possibly, lattice forces contribute to the planarization of the four-membered rings in the crystal of **4**.

Conclusions

The formation of 2,2,4,4-tetrasubstituted 1,3-dithiolanes **11** in 1,3-dipolar cycloadditions between alicyclic or aliphatic thiocarbonyl ylides **9** and thiones **10** is in accordance with the concerted pathway indicated by quantum-chemical TS calculations as most favorable for R = R′ = Me, the barrier height being 3.1 kcal mol^{-1}. Two biradical pathways similarly furnish dithiolanes **11**. The activation energies for biradical formation were calculated, and were found to be 7.1 kcal mol^{-1} for *C*,*S* biradical **13** and 9.1 kcal mol^{-1} for *C*,*C* biradical **14** (R = R′ = Me).[11] It is to be expected that all these barriers should increase for more voluminous substituents R and R′, probably to a higher extent for the sensitive concerted process than for the two-center reactions leading to biradicals. Since computer resources prohibit calculations on the larger systems, there remains an uncertainty about the extent to which one- and two-step processes contribute to the favored formation of dithiolanes **11**. Free of this ambiguity, however, are reactions of type **9** + **10** (R = R′ = Ph).[13]

Experimental Section

General: IR spectra were recorded on Perkin–Elmer 125 or Beckmann FT model IFS 45 instruments. NMR spectra were taken on Bruker

WP80CW (80 MHz) for ^{1}H and WP80DS (20 MHz) for ^{13}C (multiplicities by comparison of ^{1}H decoupled with off-resonance spectra), or Varian XR400S for ^{1}H (400 MHz) and ^{13}C (100 MHz) with DEPT. Solvent was acid-free $CDCl_3$, stored over dry K_2CO_3, if not otherwise stated. As weight standard for quantitative ^{1}H NMR analysis (usually ±4%, relative), *sym*-tetrachloroethane ($\delta = 5.92$ ppm) or trichloroethylene ($\delta = 6.70$ ppm) were used. The MS are EI spectra with 70 eV, recorded on AET 909 or Finnigan MAT 90 machines; intensities of isotope peaks are reported as, for example, ^{13}C% calcd/%found; HR = high-resolution (by peak-matching with perfluorokerosine). CC = column chromatography; PLC = preparative layer chromatography: 20 × 20 cm glass plates, 2 mm Merck silica gel $60PF_{254}$.

Preparation of 2,5-dihydro-1,3,4-thiadiazoles

Compound 17A:[21]

Compound 17B: This compound was described by Diebert[3] without m.p. and elemental analyses; it was later characterized[33] (m.p. 40–42 °C) and keeps well in the deep-freeze.

Compound 17H:[34]

2,2-Diisopropyl-2,5-dihydro-1,3,4-thiadiazole (17F): Treatment of 2,4-dimethylpentane-3-thione (**10F**)[35] with diazomethane in Et_2O at 0° furnished **17F** and the regioisomeric 4,5-dihydro-1,2,3-thiadiazole in 85:15 ratio.[36] Colorless prisms of **17F** crystallized from the crude product in MeOH at −78 °C, m.p. −12 to −10 °C; ^{1}H NMR (80 MHz): $\delta =$ 0.90, 0.97 (2 × d, $^3J = 6.5$ Hz; 4 × Me), 2.60 (sept., $^3J = 6.5$ Hz; 2 × CH), 5.62 (s, 2H; 5-H_2) ppm; IR (KBr): $\tilde{\nu} = 1577$ m (N=N) cm^{-1}; MS: *m*/*z* (%): 172 (< 1) $[M]^+$, 144 (100) $[M - N_2]^+$, 129 (14) [144 − Me], 111 (32), 101 (57), 97 (45); elemental analysis calcd (%) for $C_8H_{16}N_2S$ (172.29): C 55.77, H 9.36, N 16.26, S 18.61; found: C 55.82, H 9.09, N 16.26, S 18.59.

6,6,10,10-Tetramethyl-4-thia-1,2-diazaspiro[4,5]dec-1-ene (17I): Analogously, 2,2,6,6-tetramethylcyclohexanethione[37] (dark red oil, b.p. 84 °C/12 Torr) was converted with diazomethane into **17I**, which was isolated as colorless crystals (72%), m.p. 104–105 °C; ^{1}H NMR (80 MHz): $\delta =$ 0.54, 1.21 (2 × s, 12H; 2 × 2Me), 1.5–2.2 (m, 6H; 3 × CH_2), 5.60 (s, 2H; 3-H_2) ppm; ^{13}C NMR (20.2 MHz): $\delta = 19.0$ (t; C8), 27.2, 28.1 (2 × q; 2 × 2Me), 38.6 (t; C7, C9), 41.1 (s; C6, C10), 83.9 (t; C3), 129.6 (s; C5) ppm; IR (KBr): $\tilde{\nu} = 1576$ m (N=N) cm^{-1}; MS (20 °C): *m*/*z* (%): 212 (3) $[M]^+$, 184 (76) $[M - N_2]^+$, 169 (34) [184 − Me], 152 (13) [184 − S, $C_{11}H_{20}]^+$, 137 (93) $[C_{10}H_{17}]^+$, 123 (84) $[C_9H_{15}]^+$, 109 (47) $[C_8H_{13}]^+$, 95 (82) $[C_7H_{11}]^+$, 82 (100) $[C_6H_{10}]^+$, 81 (77) $[C_6H_9]^+$, 69 (69), 55 (49); elemental analysis calcd (%) for $C_{11}H_{20}N_2S$ (212.35): C 62.21, H 9.49, N 13.19, S 15.10; found: C 62.47, H 9.47, N 13.43, S 15.10.

1,3-Cycloadditions and electrocyclizations

1,1,3,3-Tetramethylcyclobutane-2-spiro-2′-1,3-dithiolane-4′-spiro-2″-adamantane (11BA): Freshly recrystallized thiadiazoline **17B** (396 mg, 2.00 mmol) and adamantanethione[38] (**10A**, 365 mg, 2.20 mmol) in absolute THF (4 mL) were heated in a 40 °C bath for 8 h; a gas burette indicated the liberation of N_2 (2 mmol). After removal of the solvent under vacuum, the residue was subjected to ^{1}H NMR analysis in $CDCl_3$ with weight standard, and the integral of the singlet at $\delta = 3.12$ ppm indicated 88% of cycloadduct **11BA**. Twice crystallized from EtOH, pure **11BA** (463 mg, 69%) was obtained as lustrous leaflets, m.p. 139–141 °C; ^{1}H NMR (80 MHz): $\delta =$ 1.31 (s, br., 12H; 4 × Me), 1.62–2.32 (m, 14H), 3.12 (s, 2H; 5′-H_2) ppm; ^{13}C NMR (20.2 MHz): $\delta = 22.4$, 24.7 (2 × q; 2 × 2Me), 26.8, 27.4, 37.9 (3 × d, 1:1:2; 4 × CH of adamantane), 34.8, 36.9, 38.2 (3 × t, 1:2:2; 5 × CH_2 of adamantane), 47.0 (t; C5′), 66.1 (s; C1, C3), 73.5, 74.3 (2 × s; C2′, C4′), 220.6 (s; C=O) ppm; IR (KBr): $\tilde{\nu} = 1777$ s (C=O), 2855 m, 2913 s, 2978 s (C–H) cm^{-1}; MS (60 °C): *m*/*z* (%): 336 (8) $[M]^+$, 266 (100) [*M* − dimethylketene, $C_{15}H_{22}S_2]^+$, 188 (15) $[C_8H_{12}OS_2]^+$, 180 (8) $[C_{11}H_{16}S^+$, **18A**$]^+$, 148 (15) $[C_{11}H_{16}$, 2-methyleneadamantane$]^+$, 86 (53%) $[C_4H_6S$, dimethylthioketene$]^+$, 71 (9), 70 (9) $[C_4H_6O$, dimethylketene$]^+$; elemental analysis calcd (%) for $C_{19}H_{28}OS_2$ (336.55): C 67.80, H 8.39, S 19.06; found: C 67.75, H 8.18, S 19.05.

1,1,3,3,7,7,9,9-Octamethyl-5,10-dithiadispiro[3.1.3.2]undecane-2,8-dione (4; = 11BB): The crude product, obtained analogously from **17B** and **1**,[39] contained 73% of **11BB** according to ^{1}H NMR analysis of the singlet at $\delta =$ 3.17 ppm; thiirane **5** was a side product. Dithiolane **11BB** (442 mg, 68%) crystallized from EtOH, m.p. 159–161 °C after recrystallization. Diebert[3] obtained 31% with m.p. 162–164 °C. ^{1}H NMR (400 MHz): $\delta = 1.305$, 1.308, 1.35, 1.36 (4 × s, 12H; 8 × Me), 3.22 (s, 2H; 11-H_2) ppm; ^{13}C NMR (100 MHz, DEPT): $\delta = 19.8$, 21.8, 25.14, 25.24 (4 × 2Me), 43.5 (CH_2; C11), 63.5, 66.4 (C1 + C3, C7 + C9), 71.6, 73.6 (C4, C6), 219.9, 220.3 (2 × C=O) ppm; IR (KBr): $\tilde{\nu} = 1030$ m, 1461 s, 1775 vs (C=O), 2926 m, 2968 s (C–H) cm^{-1}; MS (30 °C): *m*/*z* (%): 326 (0.4) $[M]^+$, 298 (0.6) $[M - CO]^+$ (^{13}C 0.11/0.12), 256 (34) $[M - C_4H_6O]^+$ (^{13}C 5.0/5.3; $^{13}C_2 + {}^{34}$S 3.4/3.3), 186 (100) $[C_9H_{14}S_2$, M − 2 × dimethylketene$]^+$ (^{13}C 10/11; $^{13}C_2 + {}^{34}$S 9.3/9.3), 171 (9) [186 − Me]$^+$, 86 (12) $[C_4H_6S$; dimethylthioketene$]^+$, 85 (5), 70 (3) $[C_4H_6O]^+$; elemental analysis calcd (%) for $C_{17}H_{26}O_2S_2$ (326.51): C 62.53, H 8.03, S 19.64; found: C 62.51, H 8.03, S 19.69.

2,2,4,4-Tetraisopropyl-1,3-dithiolane (11FF): Thiadiazoline **17F** (517 mg, 3.00 mmol) and thione **10F** (568 mg, 3.30 mmol) in THF (3 mL) were stirred at 65 °C for 6 h. ^{1}H NMR analysis of the s at $\delta = 3.05$ indicated 39% of **11FF** and about 30% of thiirane **18F**. 2,4-Dimethyl-3-methylthio-2-pentene, the second product of **17F** thermolysis,[36] was also present, but could not be quantified. After separation by PLC (pentane/Et_2O), the colorless oil (318 mg) crystallized from MeOH at −78 °C. Rapid filtering and dissolving in pentane (3 mL) allowed the isolation of pure **11FF**, m.p. ≈20–22 °C; ^{1}H NMR (80 MHz): $\delta = 1.07$, 1.10, 1.12, 1.20 (4 × d, 6 lines visible, 24H; 4 pairs of diastereoisotopic Me), 2.32 (sept, $^3J = 7.0$ Hz, 4H; CH of 4 × *i*Pr), 3.05 (s, 2H; 5-H_2) ppm; ^{13}C NMR (20.2 MHz): $\delta = 20.3$, 20.5 (2 × q; 2 × 2Me), 20.9 (q; 4 × Me), 35.3, 37.6 (2 × d; 2 × CH of 4 × *i*Pr), 44.3 (t; C5), 77.0, 81.2 (2 × s; C2, C4) ppm; IR (film): $\tilde{\nu} = 1382$ m, 1462 m, 1477 m; 2963 s (C–H) cm^{-1}; MS (60 °C): *m*/*z* (%): 274 (2) $[M]^+$, 231 (100) $[M - i\text{Pr}]^+$, 187 (1) [231 − C_3H_8, $C_9H_{15}S_2]^+$, 133 (3), 129 (5) $[C_7H_{13}S$, **10F** − H$]^+$, 111 (19) $[C_8H_{15}]^+$, 97 (4), 87 (26) $[C_4H_7S$, *i*Pr−CS$]^+$, 43 (10) $[i\text{Pr}]^+$, 41 (15) [allyl]$^+$; elemental analysis calcd (%) for $C_{15}H_{30}S_2$ (274.52): C 65.62, H 11.02, S 23.36; found: C 65.81, H 10.68, S 23.20.

1,1,4,4-Tetramethyl-6-thioxo-5,8-dithiaspiro[3,4]octane-2-one (19B) and 1,1,3,3,9,9,11,11-octamethyl-5,7,12,15-tetrathia-trispiro[3.1.1.3.2.2]pentadecane-2,10-dione (20B): a) Thiadiazoline **17B** (396 mg, 2.0 mmol) in CS_2 (10 mL, 166 mmol) was stirred in a bath at 45 °C for 6 h; after evaporation, ^{1}H NMR analysis in $CDCl_3$ with weight standard indicated 66% of **20B** (doublet at $\delta = 3.32$ ppm, 2H) and 21% of thiirane **5** (singlet at $\delta =$ 2.29 ppm, 2H). The colorless bisadduct **20B** (240 mg, 58%) crystallized from methanol, m.p. 132–134 °C; ^{1}H NMR (80 MHz): $\delta = 1.29$, 1.35, 1.39, 1.43 (4 × s; 8 × Me), 3.32, 3.62 (AB, $^2J = 12.2$ Hz; 13-H_2 + 14-H_2) ppm; ^{13}C NMR (20 MHz, Tesla BS 687): $\delta = 21.9$, 22.2, 24.7, 25.1 (4 × 2Me), 50.2 (C13, C14), 65.4, 67.9 (C1, C3, C9, C11), 75.7 (C6), 83.8 (C4, C8), 219.1 (2 × C=O) ppm; IR (KBr): $\tilde{\nu} = 1026$ m, 1459 s; 1778 vs (C=O) cm^{-1}; MS (50 °C): *m*/*z* (%): 346 (0.4) $[M - C_4H_6O]^+$, 276 (50) $[M - 2 \times C_4H_6O$; $C_{11}H_{16}S_4]^+$ (^{13}C 6.1/7.3, $^{13}C_2 + {}^{34}$S 9.26/9.26), 158 (100) [276 − $Me_2C{=}CS_2$; $C_7H_{10}S_2]^+$ ($^{13}C_2 + {}^{34}$S 9.1/8.4), 157 (78) $[C_7H_9S_2]^+$, 143 (16) $[C_6H_7S_2]^+$ ($^{13}C_2 + {}^{34}$S 1.4/1.6), 86 (14) $[Me_2C{=}C{=}S]$ ($^{13}C_2 + {}^{34}$S 0.63/0.67), 85 (10), 71 (11) $[C_4H_7O]^+$, 70 (10) $[Me_2C{=}C{=}O]^+$; elemental analysis calcd (%) for $C_{19}H_{28}O_2S_4$ (416.69): C 54.76, H 6.77, S 30.78; found: C 54.74, H 6.75, S 30.76.

b) After N_2 elimination from **17B** (2.0 mmol) in CS_2 (400 mL, 6.64 mol) at 45 °C, ^{1}H NMR analysis with the standard showed 25% of **5**, 16% of **20B**, and 30% of **19B** (s, 4.09, 2H). The red semisolid contained monoadduct **19B**, the isolation of which failed because it decomposed on silica gel during PLC. ^{1}H NMR (80 MHz): $\delta = 1.42$, 1.48 (2 × 2Me), 4.09 (s, ring CH_2, assigned in analogy to 4.17 for CH_2 of **19A**[16]).

Ethyl dispiro[1,3-dithiolane-2′,2;4′,2″-bis(adamantane)]-5′-carboxylate (29): a) Adamantanethione (**10A**, 333 mg, 2.00 mmol) and ethyl diazoacetate (228 mg, 2.00 mmol) in THF (4 mL) were allowed to react at 60 °C. After 2 h, the red color of **10A** had disappeared, and only the faint yellow of the excess of ethyl diazoacetate persisted; 27 mL of N_2 were evolved. ^{1}H NMR analysis in $CDCl_3$ established 87% of **29** (s, $\delta = 4.37$). Crystals (255 mg, 61%) from EtOH, m.p. 150–151 °C. ^{1}H NMR (80 MHz): $\delta = 1.25$ (t, $^3J = 7.0$ Hz, 3H; Me), 1.50–2.87 (m, 28H), 4.10, 4.15 (2 × q, $^3J = 7.0$ Hz, 2H; diastereotopic H of Et), 4.37 (s, 1H; 5′-H) ppm; ^{13}C NMR (20.2 MHz): $\delta = 14.1$ (q; Me), 26.17 (2 ×), 26.81, 27.23, 34.01, 34.47, 34.62, 36.14, 36.20, 36.38, 36.47, 37.13, 37.56, 37.92, 38.19, 38.38, 41.31, 44.89 (18C of two nonequivalent adamantane systems), 59.1 (d; C-5′), 60.8 (t; OCH_2), 73.9, 76.5 (2 × s; C2′, C4′), 171.3 (s; C=O) ppm; IR (KBr): $\tilde{\nu} = 1098$ m, 1147 s (C–O), 1736 s (C=O), 2854 s, 2987 vs (C–H) cm^{-1}; MS (100 °C), *m*/*z* (%): 418 (27) $[M]^+$, 345 (2) $[M - CO_2Et]^+$, 252 (12) $[C_{14}H_{20}O_2S$, *M* − **10A**$]^+$, 220 (3) $[C_{14}H_{20}O_2$, $C_9H_{14}CH{=}CH{-}CO_2Et]^+$, 198 (100) $[C_{10}H_{14}S_2]^+$ (**34**; HR calcd 198.0537, found 198.0544), 166 (11) [**10A**$]^+$, 133 (22) $[C_{10}H_{13}$, **10A** − SH$]^+$, 91 (15) $[C_7H_7]^+$, 79 (8); elemental analysis calcd (%) for $C_{24}H_{34}O_2S_2$ (418.64): C 68.85, H 8.19, S 15.32; found: C 69.00, H 8.09, S 15.35.

b) The reaction was also run at lower temperatures. According to the color test and ^{1}H NMR monitoring, the completion required about 12 h at 25 °C,

6 d at +5 °C, and six weeks at −28 °C. Dithiolane **29** was the only defined product.

3-Phenyl-[thiirane-2-spiro-2′-adamantane] (28):[40] Thione **10 A** (365 mg, 2.2 mmol) in $CDCl_3$ (2 mL) was treated dropwise with phenyldiazomethane[41] in pentane at room temperature until the orange-red color faded; N_2 was immediately set free. ^{1}H NMR analysis indicated 92% of thiirane **28** (s, $\delta = 3.91$ ppm). Evaporation and trituration with MeOH gave crystalline **28** (413 mg, 73%); recrystallization from pentane, m.p. 67–68 °C (oil[40]): ^{1}H NMR (80 MHz): $\delta = 1.2-2.1$ (m, 14H), 3.91 (s, 3-H), 7.1–7.5 (m, 5H; Ph) ppm; IR (KBr): $\tilde{\nu} = 702$ s, 754 s (arom. out-of-plane deform.), 1447 s, 1492 m, 1599 w (arom. ring vibr.), 2849 s, 2910 vs (C–H) cm^{-1}; elemental analysis calcd (%) for $C_{17}H_{20}S$ (256.40): C 79.63, H 7.86, S 12.51; found: C 79.81, H 7.86, S 12.48.

Ethyl 4,4,6,6-tetramethyl-5-oxo-1-thiaspiro[2.3]hexane-2-carboxylate (30): a) Thione **1** (2.0 mmol) and ethyl diazoacetate (2.2 mmol) in $CDCl_3$ (2 mL) were magnetically stirred at room temperature; after 10 h, 48 mL N_2 (2.0 mmol) had evolved; ^{1}H NMR analysis: 93% of **30**. CC (silica gel, CH_2Cl_2) gave **30** (328 mg, 68%) as a colorless oil, and Kugelrohr distillation at 80 °C/0.05 Torr furnished the analytical sample; ^{1}H NMR (80 MHz): $\delta =$ 1.11, 1.25, 1.30, 1.32 (4 × s, 12H; 4 Me), 1.40 (t, $^3J = 7.0$ Hz, 3H; Me of Et), 3.50 (s; 2-H), 4.19 (q, $^3J = 7.0$ Hz, 2H; OCH_2) ppm; IR (KBr): $\tilde{\nu} = 1027$ s, 1180 s, 1275 m, br. (C–O), 1724 s, 1746 s (C=O, ester), 1788 vs (C=O, ketone), 2929 m, 2967 s (C–H) cm^{-1}; MS (130 °C): *m/z* (%): 242 (5) $[M]^+$, 210 (3) $[M-S]^+$, 197 (8) $[M-OEt]^+$, 182 (40) [197 − Me], 172 (25) $[C_8H_{12}O_2S$; M − dimethylketene$]^+$, 169 (100) $[M-CO_2Et]^+$, 141 (27), 126 (79), 107 (16), 99 (20) $[169-C_4H_6O]$, 81 (11), 70 (12) $[C_4H_6O]^+$; elemental analysis calcd (%) for $C_{12}H_{18}O_3S$ (242.33): C 59.47, H 7.49, S 13.23; found: C 59.13, H 7.42, S 13.37. b) An experiment at −28 °C was completed after three weeks; ^{1}H NMR monitoring did not reveal signals of the intermediate dihydrothiadiazole derivative.

4,4,6,6-Tetramethyl-2-phenyl-1-thiaspiro[2.3]hexane-5-one (31): Thione **1** was treated with phenyldiazomethane as described for **30**; 96% N_2 evolution. ^{1}H NMR analysis indicated 93% of **31** (s, $\delta = 4.17$ ppm); crystals (67%) from MeOH, m.p. 90.5–92.5 °C; ^{1}H NMR (80 MHz): $\delta = 0.60$, 1.17, 1.25, 1.35 (4 × s, 12H; 4 × Me), 4.17 (s; 2-H), 7.1–7.3 (m; Ph) ppm; IR (KBr): $\tilde{\nu} = 703$, 762 m (arom. out-of-plane deform.), 1456 s, 1493 w (arom. ring vibr.), 1780 vs (C=O), 2925 m, 2965 s (C–H) cm^{-1}; elemental analysis calcd (%) for $C_{15}H_{18}OS$ (246.36): C 73.13, H 7.37, S 13.02; found: C 73.16, H 7.47, S 13.07.

2,3-Dihydro-1,1,3,3-tetramethylspiro[1*H*-indene-2.2′-thiirane] (18H): Thiadiazoline **17H** (150 μmol) and thione **1** (402 μmol) in $CDCl_3$ (0.5 mL) were heated at 80 °C in an NMR tube for 10 min. After the sample had cooled and dibenzyl had been added (s, $\delta =$ 2.92 ppm), ^{1}H NMR analysis showed 100% of **18H** (s, $\delta = 2.54$ ppm);[42] ^{1}H NMR: identical with a sample prepared without **1**.[34]

4,4,8,8-Tetramethyl-1-thiaspiro[2.5]octane (18I): The analogous experiment with **1** and **17I** in octane (15 min at 130 °C) provided 100% of **18I**[42] (i.e., thiocarbonyl ylide **9I** likewise refused to undergo cycloaddition with **1**). In a preparative experiment, **18I** was obtained from Et_2O as needles, m.p. 78–79 °C. ^{1}H NMR (80 MHz): $\delta = 0.93$, 1.15 (2 × s, 12H; 4 × Me), 1.30–1.75 (m, 6H), 2.43 (s, 2H; 2-H_2) ppm; ^{13}C NMR (20.2 MHz): $\delta = 19.0$ (t, C6), 28.5, 30.4 (2 × q, 2 × 2Me), 29.1 (t, C2), 37.0 (s, C4, C8), 41.7 (t, C5, C7), 63.2 (s, C3) ppm; MS (20 °C): *m/z* (%): 184 (18) $[M]^+$, 169 (9) $[M-Me]^+$, 152 (16) $[M-S]^+$, 137 (44) [152 − Me], 123 (14), 109 (45) $[C_8H_{13}]^+$, 96 (46), 95 (43) $[C_7H_{11}]^+$, 82 (100) $[C_6H_{10}]^+$, 69 (34) $[C_5H_9]^+$, 55 (28) $[C_4H_7]^+$; elemental analysis calcd (%) for $C_{11}H_{20}S$ (184.34): C 71.67, H 10.94, S 17.40.

X-ray diffraction analysis of 4 (Figure 1): monoclinic, space group $P2_1$, no. 4. Unit cell dimensions: $a = 8.0034(12)$, $b = 11.691(2)$, $c = 9.571(3)$ Å, $\beta = 96.39(2)°$, $V = 890.0(4)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.218$ Mg m^{-3}, $F(000) = 352$, $T = 295(2)$ K, $\mu(Mo_{K\alpha}) = 0.301$ mm^{-1}. Data collection: Nonius MACH3 diffractometer, colorless block (0.27 × 0.47 × 0.53 mm), mounted in a glass capillary, cell constants from 25 centered reflections. $Mo_{K\alpha}$ radiation, $\lambda = 0.71073$ Å, graphite monochromator, ω-2θ scan, scan width (0.66 + 0.55 tan θ)°, maximum measuring time 60 s, intensity of three standard reflections checked every 2 h, θ range 2.56–23.96° for all $\pm h$, $\pm k$, $\pm l$ reflections, 3277 reflections measured, 2785 unique, and 2659 reflections with $I > 2\sigma(I)$. Lorentz, polarization, and absorption corrections (T_{min}/T_{max} 0.8960 and 0.9984). Structure solution by SHELXS-86 and refinement by SHELXL-93.[43] Final $R_1 = 0.0263$ and $wR2 = 0.0673$ for 2659 reflections with $I > 2\sigma(I)$ and 198 variable and 1 restraint. $R1 = 0.0285$ and $wR2 =$ 0.0696 for all data. Weight: SHELXL-93. Absolute structure parameter: −0.03(6). Maximum and minimum of the final difference Fourier synthesis 0.176 and −0.149 eÅ^{-3}. ZORTEP plot.[44] CCDC-192837 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 IEZ, UK; fax: (+44)1223–336–033; email: deposit@ccdc.cam.ac.uk).

Acknowledgements

We are greatly indebted to the Fonds der Chemischen Industrie, Frankfurt, for the support of our research program. G. M. thanks the Alexander von Humboldt Foundation for the prolongation of a stipend. Sincere thanks are expressed to Helmut Huber for his help in NMR spectroscopy, to Reinhard Seidl for the mass spectra, as well as to Helmut Schulz and Magdalena Schwarz for the elemental analyses.

[1] R. Huisgen, C. Fulka, I. Kalwinsch, X. Li, G. Mloston, J. R. Moran, A. Pröbstl, *Bull. Soc. Chim. Belg.* **1984**, *93*, 511–532.
[2] G. Mloston, H. Heimgartner, in *The Chemistry of Heterocyclic Compounds*, *Vol. 59*, *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products* (Eds.: A. Padwa, W. H. Pearson), Wiley, New York, **2002**, pp. 360.
[3] C. E. Diebert, *J. Org. Chem.* **1970**, *35*, 1501–1505.
[4] a) R. Huisgen, G. Mloston, E. Langhals, *J. Am. Chem. Soc.* **1986**, *108*, 6401–6402; b) G. Mloston, E. Langhals, R. Huisgen, *Tetrahedron Lett.* **1989**, *30*, 5373–5376; c) R. Huisgen, G. Mloston, H. Giera, E. Langhals, *Tetrahedron* **2002**, *58*, 507–519.
[5] a) R. Huisgen, G. Mloston, E. Langhals, *J. Org. Chem.* **1986**, *51*, 4085–4087; b) R. Huisgen, G. Mloston, E. Langhals, *Helv. Chim. Acta* **2001**, *84*, 1805–1820.
[6] E. Bergmann, M. Magat, D. Wagenberg, *Ber. Dtsch. Chem. Ges.* **1930**, *63*, 2576–2584.
[7] a) A. Schönberg, D. Cernik, W. Urban, *Ber. Dtsch. Chem. Ges.* **1931**, *64*, 2577–2581; b) A. Schönberg, B. König, E. Singer, *Chem. Ber.* **1967**, *100*, 767–777.
[8] a) I. Kalwinsch, X. Li, J. Gottstein, R. Huisgen, *J. Am. Chem. Soc.* **1981**, *103*, 7032–7033; b) R. Huisgen, I. Kalwinsch, X. Li, G. Mloston, *Eur. J. Org. Chem.* **2000**, 1685–1694.
[9] L. Fisera, R. Huisgen, I. Kalwinsch, E. Langhals, X. Li, G. Mloston, K. Polborn, J. Rapp, W. Sicking, R. Sustmann, *Pure Appl. Chem.* **1996**, *68*, 789–798.
[10] a) J. Sauer, J. Schatz, *Tetrahedron Lett.* **1994**, *35*, 4767–4770; b) J. Breu, P. Höcht, U. Rohr, J. Schatz, J. Sauer, *Eur. J. Org. Chem.* **1998**, 2861–2874; c) U. Rohr, J. Schatz, J. Sauer, *Eur. J. Org. Chem.* **1998**, 2875–2883.
[11] See preceding paper: R. Sustmann, W. Sicking, R. Huisgen, *Chem. Eur. J.* **2003**, *9*, 2245–2255.
[12] J. Fabian, *J. Mol. Struct. (Theochem)* **1997**, *398*, 411–416.
[13] R. Sustmann, W. Sicking, R. Huisgen, unpublished results.
[14] R. Huisgen, G. Mloston, C. Fulka, *Heterocycles* **1985**, *23*, 2207–2212.
[15] R. Huisgen, G. Mloston, *Tetrahedron Lett.* **1989**, *30*, 7041–7044.
[16] G. Mloston, R. Huisgen, K. Polborn, *Tetrahedron* **1999**, *55*, 11475–11494.
[17] G. Mloston, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **1991**, *74*, 1386–1398.
[18] W. J. Middleton, W. H. Sharkey, *J. Org. Chem.* **1965**, *30*, 1384–1390.
[19] P. Metzner, *Bull. Soc. Chim. Fr.* **1973**, 2297–2300.
[20] R. Huisgen, X. Li, H. Giera, E. Langhals, *Helv. Chim. Acta* **2001**, *84*, 981–999.
[21] R. Huisgen, G. Mloston, *Polish J. Chem.* **1999**, *73*, 635–644.
[22] B. F. Yates, W. J. Bouma, L. Radom, *Tetrahedron* **1986**, *42*, 6225–6234.
[23] Review: K. M. Stirk, L. K. M. Kiminkinen, H. I. Kentämaa, *Chem. Rev.* **1992**, *92*, 1649–1665.
[24] R. Huisgen, J. Rapp, *Tetrahedron* **1997**, *53*, 939–960.
[25] A. Senning, H. C. Hansen, M. F. Abdel-Meged, W. Mazurkiewicz, B. Jensen, *Tetrahedron* **1986**, *42*, 739–746.

[26] L. B. Brahde, *Acta Chem. Scand.* **1954**, *8*, 1145–1151.
[27] W. J. Adams, H. J. Geise, L. S. Bartell, *J. Am. Chem. Soc.* **1970**, *92*, 5013–5019.
[28] a) L. A. Sternson, D. A. Coviello, R. S. Egan, *J. Am. Chem. Soc.* **1971**, *93*, 6529–6532.
[29] W. E. Willey, G. Binsch, E. L. Eliel, *J. Am. Chem. Soc.* **1970**, *92*, 5394–5402.
[30] T. Egawa, T. Fukuyama, S. Yamamoto, F. Takabayashi, H. Kambara, T. Ueda, K. Kuchitsu, *J. Chem. Phys.* **1987**, *86*, 6018–6026.
[31] K. Tamagawa, R. L. Hilderbrandt, *J. Phys. Chem.* **1983**, *87*, 5508–5514.
[32] K. C. Cole, D. F. R. Gilson, *Can. J. Chem.* **1976**, *54*, 657–664.
[33] R. Huisgen, J. Penelle, G. Mloston, A. Bruyle Padias, H. K. Hall, *J. Am. Chem.Soc.* **1992**, *114*, 266–274.
[34] H. Giera, R. Huisgen, E. Langhals, K. Polborn, *Helv. Chim. Acta* **2002**, *85*, 1523–1545.
[35] P. Metzner, R. Rakotonirina, *Tetrahedron* **1985**, *41*, 1289–1298.
[36] G. Mloston, R. Huisgen, *Tetrahedron Lett.* **1989**, *30*, 7045–7048.
[37] R. Huisgen, L. Fisera, H. Giera, R. Sustmann, *J. Am. Chem. Soc.* **1995**, *117*, 9671–9678.
[38] J. W. Greidanus, *Can. J. Chem.* **1970**, *48*, 3530–3536.
[39] E. U. Elam, H. E. Davis, *J. Org. Chem.* **1967**, *32*, 1562–1565.
[40] T. Katada, S. Eguchi, T. Sasaki, *J. Chem. Soc. Perkin Trans. 1* **1984**, 2641–2647.
[41] D. G. Farnum, *J. Org. Chem.* **1963**, *28*, 870–872.
[42] H. Giera, Ph.D. Thesis, Universität München, **1991**.
[43] G. M. Sheldrick, Programs for the solution and refinement of X-ray structures, University of Göttingen, **1986** and **1993**.
[44] L. Zsolnai, G. Huttner, Program ZORTEP, University of Heidelberg, **1994**.

Received: December 10, 2002 [F4659]

