Thioformaldehyde *S*-Methylide and Thioacetone *S*-Methylide: An Ab Initio MO Study of Structure and Cycloaddition Reactivity

Reiner Sustmann,*[a] Willi Sicking,[a] and Rolf Huisgen[b]

Abstract: The mechanisms of cycloaddition of thioformaldehyde *S*-methylide and thioacetone *S*-methylide, as models for an alkyl-substituted ylide, to thioformaldehyde and thioacetone, as well as to ethene as a model for a C=C double bond have been studied by ab initio calculations. Restricted and unrestricted B3LYP/6–31G* calculations were performed for the geometries of ground states, transition structures, and intermediates. Although basis sets with more polarization functions were tested, the 6–31G* basis set was applied throughout. Single-point CASPT2 calculations are reported for analysis of the unsubstituted system. The stabilities of structures with high biradical character seem to be overestimated by DFT methods in comparison to CASPT2. The general trends of the results are independent of the level of theory. Thioformaldehyde adds to thioformaldehyde *S*-methylide without activation energy, and the activation energies for two-step biradical pathways to 1,3-dithiolane are low. *C*,*S* biradicals are more stable than *C*,*C* biradicals. The two-step cycloaddition is not competitive with the concerted cycloaddition. Methyl substitution in the 1,3-dipole and the dipolarophile does not change the mechanistic relationships. TSs for the concerted formation of the regioisomeric cycloadducts of thioacetone *S*-methylide and thioacetone were located. Concerted addition remains the preferred reaction. The reactivity of the C=S double bond is high relative to that of the C=C double bond.

Keywords: ab initio calculations · cycloaddition · density functional calculations · reaction mechanisms · thiocarbonyl ylides · transition states

Introduction

Cycloadditions of thiocarbonyl ylides, members of the class of 1,3-dipoles of allyl anion character, have been studied extensively by Kellogg, Huisgen, Mloston et al.; some reviews[1–5] and recent mechanistic contributions[6–10] are quoted. It was found that 2,5-dihydro-1,2,4-thiadiazoles, products of 1,3-dipolar cycloadditions between diazoalkanes and thiones, lose nitrogen on warming. This N_2 extrusion, a 1,3-dipolar cycloreversion, provides an easy route to thiocarbonyl ylides. These 1,3-dipoles are not isolable, and their cycloadditions have to be carried out in situ in the presence of suitable dipolarophiles.

1,3-Dipolar cycloadditions are generally described as pericyclic processes,[11, 12] or in other words the formation of the two new σ bonds is allowed to be concerted by the rules of orbital symmetry for $_{\pi}4_s + _{\pi}2_s$ cycloadditions.[13] Calculations have been carried out to explore the limitations of concerted and stepwise mechanisms, in particular for Diels–Alder reactions.[14–17] Over the course of time, experimental investigations on $_{\pi}4_s + _{\pi}2_s$ cycloadditions have shown that the mechanisms of these reactions are not universally concerted, but depend on the electronic structures of the 1,3-diene and dienophile, or of the 1,3-dipole and dipolarophile, respectively. Diels–Alder cycloadditions have been studied extensively as functions of the substituents in the 1,3-diene and the dienophile,[18] and—depending on the substitution pattern—these cycloadditions can take place either by concerted or by stepwise mechanisms. Zwitterions[19, 20] and biradicals[21–23] have been suggested as intermediates.

A reactivity model for concerted 1,3-dipolar cycloadditions can be convincingly rationalized on the basis of FMO theory.[24] Numerous MO theoretical calculations at different levels of sophistication, semiempirical and ab initio, have confirmed the concerted character of many of these cycloadditions.[25–37]

In 1,3-dipolar cycloadditions, the mechanistic picture is influenced not only by the nature of the substituents, but also by the kind and number of heteroatoms in the 1,3-dipole. In this study we begin an analysis of cycloadditions of thiocar-

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bonyl ylides, preferably those to C=S double bonds. For the purpose of systematics and computational economy, the unsubstituted thioformaldehyde *S*-methylide and thioacetone *S*-methylide have been chosen to allow comparisons with experimentally studied examples. Incidentally, the parent thiocarbonyl ylide **1** (see Figure 1) has been prepared from a silylated precursor and subjected to cycloadditions to C–C multiple bonds.[38] The structures of thioformaldehyde *S*-methylide and thioacetone *S*-methylide, their reactivity, and the mechanisms of their cycloadditions to thioformaldehyde and thioacetone, respectively, are therefore analyzed by ab initio methods.

Computational Methods

Semiempirical calculations at the PM3 level were initially performed,[39] as extension from unsubstituted to highly substituted thiocarbonyl ylides and thiocarbonyl compounds was planned. However, it soon became obvious that not only closed-shell structures, but also biradicals, had to be included. The reliability of semiempirical methods for these structures is low and the results are not reported here.

Ab initio methods at different levels of sophistication were therefore applied. The calculations were carried out with the aid of the Gaussian98 suite of programs[40] and the program MOLCAS.[41] For most of the calculations we used the 6–31G* basis set, which includes polarization functions for first and second row elements. In some cases (see below) tests were made of whether basis sets with more polarization functions yielded improved results. Molecules with obvious closed-shell character were evaluated by DFT theory with the B3LYP functional. In cases in which biradical character was assumed, UB3LYP was applied, including the keywords guess = alter or guess = mix in Gaussian. Biradical character (BRC) was determined by CASSCF calculation with the active space specified in the text. The evaluation of BRC was carried out by literature procedures. The values calculated in this contribution compare well with BRCs determined in other cases (for a discussion see ref. [42]). Whenever B3LYP and UB3LYP gave identical results, although a finite biradical character was found or assumed, the keyword stable = opt was applied to search for an improved UB3LYP wave function with a lower total energy. In general, B3LYP and UB3LYP yielded the same results when the biradical character was less than 30%. The reduction of the UB3LYP to the RB3LYP solution is observed when the diradical character is small.[17] All stationary points were checked by frequency calculations to determine whether they represented minima or maxima on the potential energy surface. All transition states (TSs) are characterized by only one imaginary frequency. TSs were tested for whether they properly connected the ground state of the reactant(s) and the product. Some calculations were carried out at the CBS-QB3 level. MOLCAS was used for single-point calculations on the geometries of DFT calculations, and the results of MOLCAS calculations were ZPVE-corrected (ZPVE = zero-point vibrational energy) by the values obtained by DFT.

RASSCF and CASPT2 calculations were performed with MOLCAS, with the 6–31G* basis set. This is particularly important for structures with presumed biradical character. The RASSCF and CASPT2 approach has been reported to be particularly valuable for biradical and biradicaloid structures.[43, 44] We first carried out CAS(6,5) calculations, and chose those natural orbitals showing the highest occupancy for the final CAS evaluation. Generally, these are the HOMO and LUMO of the SCF calculation. The biradical characters reported are based throughout on CAS(2,2) for reasons of comparison. As a consequence, the CAS(2,2) energies are not directly comparable between one another, since they include different degrees of CI, depending on the slightly different occupation numbers of HOMO and LUMO. The CASPT2 energies relative to the CASPT2 energy of **1**, however, are almost independent of the active space chosen as long as HOMO and LUMO are included.

Results and Discussion

Structures and energies of C_2H_4S molecules and thioformaldehyde

Thioformaldehyde *S*-methylide (1) and related structures 2–4: The geometry of thioformaldehyde *S*-methylide (**1**), the parent thiocarbonyl ylide, was determined by restricted and unrestricted B3LYP calculations with the 6–31G* and 6–31+G** basis sets. Although the geometries remain identical, the 6–31+G** basis set yields a slightly lower energy (Table 1). The planar ground state can be described as a roof-shaped structure (C_{2v} symmetry), characterized by a CSC angle of 116°, and the C–S bond length of 1.64 Å is only a little smaller than that in thioaldehyde **7**. The HCH angle is 121°, C–H bond lengths are 1.08 Å (Figure 1). Natural population analysis (B3LYP/6–31G*) of the charge distribution reveals that the carbon atoms each carry a negative charge of −0.84 electrons, the sulfur atom a positive charge of +0.72, and the four hydrogen atoms charges of +0.25 (*exo*) and +0.23 (*endo*). A dipole moment of only 0.13 D (B3LYP/6+31G**) demonstrates the allylic distribution of negative charge on either side of the positive one. The results agree with those obtained by Fabian by DFT, QCISD(T), and CASPT2 methods.[45] A CAS(2,2)/6–31G*//B3LYP/6–31G* single-

Table 1. Energies relative to **1** (0.0) [kcal mol^{-1}], dipole moments, and percentage biradical character of structures **1**–**7** according to different levels of ab initio calculations. If not mentioned otherwise, the basis set is 6–31G*.

	Method/Basis Set	E [au]	E_{rel} + ZPVE	%BRC cas(m,n)	μ [D]
1	B3LYP	−476.7116			0.21
	UB3LYP	−476.7116			0.21
	B3LYP/6–31+G**	−476.7271			0.13
	CAS(2,2)//B3LYP	−475.4890		24	
	CASPT2//B3LYP	−475.8674			
	CBS-QB3	−476.1139			
2	UB3LYP	−476.6772	19.3		1.24
	CAS(2,2)//UB3LYP	−475.4616	14.9	99	
	CASPT2//UB3LYP	−475.8238	25.1		
3	B3LYP	−476.6249	54.4[a]		0
	B3LYP/6–31+G**	−476.6386	54.5[a]		0
	CAS(2,2)//B3LYP	−475.3835	66.2[a]	17	
	CASPT2//B3LYP	−475.7726	59.7[a]		
4	UB3LYP	−476.5800	82.6[a]		0
	UB3LYP/6–31+G**	−476.5940	83.5[a]		0
	CAS(2,2)//UB3LYP	−475.3338	97.4[a]	100	
	CASPT2//UB3LYP	−475.7199	92.6[a]		
5	B3LYP	−476.6844	17.2		0.93
	UB3LYP	−476.6863	15.3		1.15
	CAS(2,2)//B3LYP	−475.4753	8.7	35	
	CASPT2//B3LYP	−475.8444	14.5		
	CBS-QB3	−476.0886	15.9		
6	B3LYP	−476.7835	−42.1		2.15
	CAS(2,2)//B3LYP	−475.5852	−57.4	2	
	CASPT2//B3LYP	−475.9379	−41.2		
	CBS-QB3	−476.1698	−35.1		
7	B3LYP	−437.4623			1.89
	CAS(2,2)//B3LYP	−436.5341		12	
	CASPT2//B3LYP	−436.7643			
	CBS-QB3	−436.9382			

[a] Constrained geometry optimization, no ZPVE.

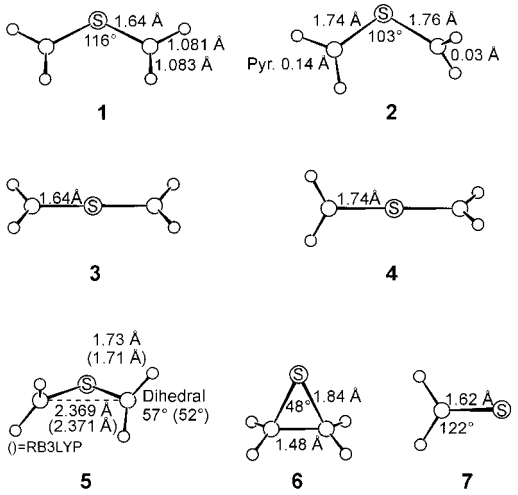

Figure 1. Structures of thioformaldehyde *S*-methylide, thioformaldehyde, and related molecules calculated at the (U)B3LYP/6–31G* level.

point calculation showed 24% biradical character (BRC) for the thiocarbonyl ylide structure. Because of the small level of biradical character, the UB3LYP/6–31G* evaluation yielded the same structure and wavefunction as the closed shell variant.[17] As far as the total energy is concerned, CASPT2 yields a less negative value than that obtained in the CBS-QB3 approximation. The geometries remain almost identical to those from the B3LYP evaluation. In conclusion, it can be stated that thioformaldehyde *S*-methylide in its ground state is best described as a singlet with some BRC.

Several other potential structures of **1** were considered for purposes of comparison. Thus, a structure **2**, in which one methylene group of **1** assumes an orthogonal position (rotation of CH_2 by 90°), was analyzed to determine the rotational barrier of the CH_2 group. Structure **2**, the TS for rotation of a CH_2 group, is a true biradical (99% BRC) and is characterized by one negative vibrational frequency in the Hessian matrix. The most remarkable structural differences from **1** are: reduction of the C-S-C angle from 116 to 103°, elongation and slightly different C–S bond lengths of 1.76 and 1.74 Å, and a slight pyramidalization of the CH_2 groups. The barrier height of 25.1 (CASPT2) and 19.3 kcal mol^{-1} (UB3LYP) can be taken as an approximation to the resonance energy of the planar thioformaldehyde *S*-methylide. Barriers of this remarkable size are not unusual for 1,3-dipoles of the allyl type. Even higher values have been determined for substituted nitrones[46, 47] and azomethine ylides.[48] Further, a linear planar structure **3**—a kind of inversion TS—was calculated by the same methods (Table 1). Except for the constraint of linearity, all geometrical degrees of freedom were optimized. The C–S bond length was determined to 1.64 Å, no different from that in **1**. The energy relative to **1** is +59.7 (CASPT2) or +54.4 kcal mol^{-1} (B3LYP). The biradical character according to a CAS(2,2)/6–31G*//UB3LYP/6–31G* calculation is 17%. The relative high deformation energy required to linearize structure **1** can be explained by the required sp hybridization of sulfur, which forces the residual lone pair on sulfur into a p orbital, in contrast to **1**, in which the lone pair occupies a sp^2 orbital.

The linear structure **3** was modified by rotation of one of the methylene groups by 90°, leading to an allene type molecule **4**. In VB terms it can be regarded as a singlet diradical, BRC equaling 100% according to CAS(2,2)/6–31G*//UB3LYP/6–31G* (i.e., one electron is present in each of the HOMO and the LUMO of the UB3LYP calculation). Energetically, **4** is 92.6 (CASPT2/6–31G*//UB3LYP/6–31G*) and 82.6 kcal mol^{-1} (UB3LYP/6–31G*) above **1**. In comparison with **3**, the π-electronic system can be described as consisting of two orthogonal C=S double bonds in which two orbitals are doubly occupied and the two others singly occupied, being localized at the terminal carbon atoms according to the CAS calculation. The destabilization of **4** relative to **3** results from the transformation of the two different π systems.

Electrocyclization of 1 to 6: In the absence of cycloaddition partners, thiocarbonyl ylides undergo electrocyclic ring-closure to give thiiranes. This is a competing reaction pathway. Although this ring-closure had already been analyzed by ab initio methods[45, 49] we redetermined the barrier of this reaction to have consistent results. TS **5** displays the expected conrotatory movement of the two CH_2 groups. The dihedral angle HC-SC is 57°, and the C–S bond lengths are 1.73 Å (i.e., intermediate between the corresponding bond lengths in the thiocarbonyl ylide **1** and the thiirane **6**). The CASPT2 barrier height was found to be 14.5 kcal mol^{-1}, the values obtained by the other methods being slightly higher, although all are close to the previously determined barrier height.[45] TS **5** has a biradical character of 35%, which is higher than that in the ground state of thioformaldehyde *S*-methylide. As would be anticipated, the biradical character of **6** is negligible. Structures **1**, **5**, and **6** were also calculated by use of Gaussian98's high quality CBS-QB3 procedure. The relative energies—in particular with respect to the barrier of electrocyclization of **1**—are comparable to the values obtained by the other methods, however (Table 1).

Thioformaldehyde (7): The structure and energy of thioformaldehyde as the dipolarophile for the cycloaddition to the thicarbonyl ylides were determined by different approximations. Its biradical character is small (12%), and the structure (B3LYP/6–31G*) is very close to that obtained earlier.[26, 50]

Cycloaddition between thioformaldehyde *S*-methylide and thioformaldehyde: The interaction between thioformaldehyde *S*-methylide and thioformaldehyde was studied to search the potential energy surface for possible concerted and two-step cycloadditions. For this purpose, different approaches of the two molecules, suited for either a concerted or a non-concerted cycloaddition, were chosen. This was done because in real situations the molecules collide statistically in different orientations, which might have consequences for the reaction mechanism. As biradical intermediates can be anticipated as intermediates, all calculations except those for the final product were carried out at the UB3LYP/6–31G* level. The energies relative to those of the isolated molecules were corrected for ZPVE. RASSCF and CASPT2 procedures were applied to the geometry optimized structures as single-point calculations. The energies discussed are those from the

CASPT2 approximation. The BRC is evaluated by CAS(2,2) and is given, together with the energies, in Table 2. Most of the stationary points are characterized by high BRCs. On comparing the UB3LYP/6–31G* and the CASPT2 energies it can be seen that the DFT calculations consistently display higher biradical stabilities, between 4 and 7 kcal mol^{-1}, than those obtained by the CASPT2 procedure.

Table 2. Energies relative to reactants [kcal mol^{-1}], ΔZPVE [kcal mol^{-1}], biradical character according to cas(m,n), and dipole moments of structures **8a**–**8f**, **9a**–**9f**, **10**, and **11**.[a]

Structure		E_{rel} (U)B3LYP + ZPVE	E_{rel} CASPT2 + ZPVE	%BRC cas(m,n) /6–31G*	(m,n)	μ [D]
8a	TS	2.2	3.4	23	(6,5)	4.88
8b	I	−22.2	−17.0	87	(2,2)	3.04
8c	TS	−18.2	−12.6	95	(2,2)	2.41
8d	TS	−20.3	−13.2	90	(2,2)	3.54
8e	I	−28.3	−25.1	23	(2,2)	3.93
8f	TS	−17.4	−11.6	88	(2,2)	3.38
9a	TS	2.9	4.7	31	(6,5)	2.14
9b	I	−5.9	−1.6	80	(2,2)	1.66
9c	TS	−5.2	0.5	86	(2,2)	1.49
9d	I	−6.5	−1.2	93	(2,2)	0.25
9e	TS	−4.6	0.5	81	(2,2)	0.37
9f	TS	−4.3	1.4	98	(2,2)	1.52
10	PROD	−76.0	−74.6	2	(2,2)	1.34
11		−7.7	−7.7	18	(6,5)	3.15

[a] The basis set is 6–31G*. TS = transition state, I = intermediate, PROD = product.

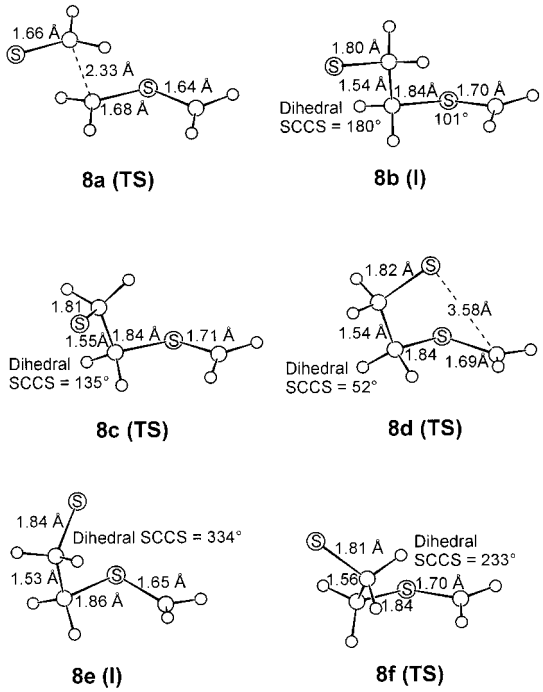

Figure 2. (U)B3LYP/6–31G*-calculated transition states and intermediates for the two-step cycloaddition between thioformaldehyde *S*-methylide and thioformaldehyde via *C*,*S* biradicals.

Biradical intermediates: Studies were also made of two modes of approach of thioformaldehyde to **1** that cannot lead immediately to the cycloadduct, but should provide intermediates, possibly of high BRC. Thioformaldehyde can attack the terminal C atom of **1** either through its carbon atom (Figure 2) or through its sulfur atom (Figure 3). Geometries of approach in which the intermediates (**8b** and **9b**) formed from TSs **8a** and **9a** are incapable of closing to form a five-membered ring without further conformational changes are chosen. TS **8a** is characterized by a length of 2.33 Å for the new C–C bond and somewhat elongated C–S bonds relative to those in the ground state structures **1** and **7**. The energy is 3.4 kcal mol^{-1} above the reactants, and the BRC of **8a** remains identical to that of **1** (Table 2). A search for the closest intermediate brings **8b** to light. The SC-CS dihedral angle of 180° shows that **8b** assumes a staggered conformation at the new C–C bond. According to a CAS(2,2) calculation, **8b** is a true biradical (87% BRC) with the unpaired electrons at sulfur and carbon, and is located −17.0 kcal mol^{-1} below the energies of the reactants.

To effect ring-closure, rotations about the C–C bond have to occur. Structures **8c** and **8d** are the two TSs for ring-closure obtained from **8b** (dihedral angle 180°) by clockwise and counterclockwise rotation about the new C–C bond. The dihedral angles SC-CS are 135° and 52° in **8c** and **8d**. The BRC remains ≥90%. For the conversion of **8b** into TS **8d**, clockwise rotation about the C–C bond leads via TS **8f** to intermediate **8e**. Ring-closure to form **10** takes place when this intermediate passes through TS **8d** (BRC 90%) on further rotation. The well in which **10** is found lies −74.6 kcal below the level of the reactants, so the total reaction is strongly exothermic.

A comment on the low biradical character of **8e** (23% as compared to **8b**–**d** and **8f**) is appropriate. The small separation of the two sulfur atoms in **8e** (2.50 Å) leads to overlap of the sulfur orbitals and concomitantly to covalent interactions that reduce the biradical character. For comparison, the S–S single bond length in H_2S_2 is 2.02 Å[51] so a sizable overlap already exists in **8e**, supporting the presumption. In terms of valence bond theory, sulfonium thiolate structures contribute to the ground state of structures **8**, which becomes apparent in the natural population analysis (NPA) and the C–S distances. The sulfur in the C–S single bond (1.80 Å (**8b**) and 1.84 Å (**8e**)) either carries no charge (**8b**) or is slightly negatively charged (−0.21, **8e**), whereas the sulfur atom in the sulfonium C–S bond (1.70 Å (**8b**) and 1.65 Å (**8e**)) is positively charged (+0.40 (**8b**) and +0.66 (**8e**)). Intermediate **8e** (S–S distance 2.50 Å) is therefore more strongly stabilized by Coulombic interactions than **8b** (S–S distance 4.83 Å). This contribution to the stabilization of **8e** can be regarded as the reason for the lower energy of **8e** relative to **8b**. The explanation for the increase in BRC in TS **8d** in relation to the intermediate **8e** follows the same line of arguments. The S–S distance increases to 3.32 Å, reducing the S,S overlap, and the Coulombic interaction becomes smaller, leading to the increase in energy. It should be mentioned that the flat saddle occurs at the still large C–S distance of 3.58 Å, which is even greater than in **8e** (3.34 Å).

The attack on **1** by the sulfur atom of thioformaldehyde leads to TS **9a**, 4.7 kcal mol^{-1} above the reactants (Figure 3). The BRC of 31% is comparable to that of **1**. Intermediate **9b**

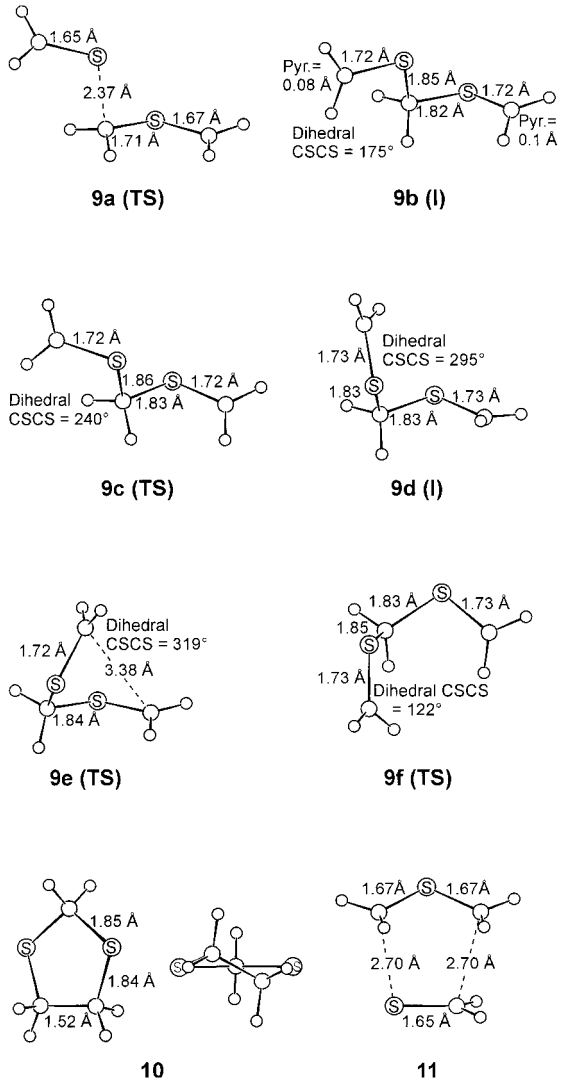

Figure 3. (U)B3LYP/6–31G*-calculated transitions states, intermediates, and cycloadduct for the two-step cycloaddition between thioformaldehyde *S*-methylide and thioformaldehyde via *C*,*C* biradicals. Structure **11** simulates a concerted cycloaddition (see text for details).

(BRC 80%), similar in its structure to **8b**, is a *C*,*C* biradical and lies -1.6 kcal mol^{-1} below the reactants. The small stabilization demonstrates that a *C*,*S* biradical (**8b**) is superior in stability to a *C*,*C* biradical, by 15.4 kcal mol^{-1}, so sulfur is a better radical-stabilizing atom than a carbon atom with an adjacent thioether function. The CS-CS dihedral angle of 175° in **9b** shows that ring-closure requires rotation about the C–S bond. Two modes of rotation to reach a conformation suitable for ring-closure are possible. Rotation about the newly formed C–S bond leads to TS **9c**, $+0.5$ kcal mol^{-1} above the reactants and with a CS-CS dihedral angle of 240°, and further rotation provides the energy minimum of **9d** at a dihedral angle of 295°. The rotational barrier is 2.1 kcal mol^{-1}, so the minimum of **9d** is at -1.2 kcal mol^{-1}. On further increasing of the dihedral angle to 319°, TS **9e** ($+0.5$ kcal mol^{-1}) leads to product **10**. If the dihedral angle in **9b** is altered in the opposite direction (from 175° to 122°), TS **9f**—which also leads to 1,3-dithiolane **10**—is found at $+1.4$ kcal mol^{-1}. The calculated half-chair conformation of **10** compares favorably with the reported X-ray structure, although the calculation refers to a gas-phase molecule.[52]

In Figure 4 the CASPT2 energies of TSs, intermediates, and product relative to the energies of the reactants (0.0) are represented graphically for attack at carbon (**8a**–**8f**) or sulfur (**9a**–**9f**) of thioformaldehyde on **1**. The approach to the potential energy surface was chosen in such a way that the elongated biradicals **8b** and **9b** are formed. Obviously, geometrical approaches of the reactants leading directly to the rotameric forms **8e** and **9d** can also be envisioned. No attempts to locate these TSs were made. The concerted cycloaddition of **1** to **7**, which requires no activation energy, is not shown in Figure 4.

Concerted cycloaddition: Different modes of approach of **1** and **7** were studied to enforce the formation of intermediates in the cycloaddition. The main result is that attack on **1** through the carbon of thioformaldehyde leads to a *C*,*S* biradical of sizable stability when the two molecules meet in a conformation in which direct formation of a cycloadduct is not possible. Attack by the sulfur of thioformaldehyde on **1** in similar arrangement gives rise to biradicals that are only slightly stabilized. There is, however, a window in the conformational space in which the two molecules might react to give the cycloadduct directly without formation of an intermediate biradical. For the attack at **1** through the carbon of thioformaldehyde, this should occur when the dihedral

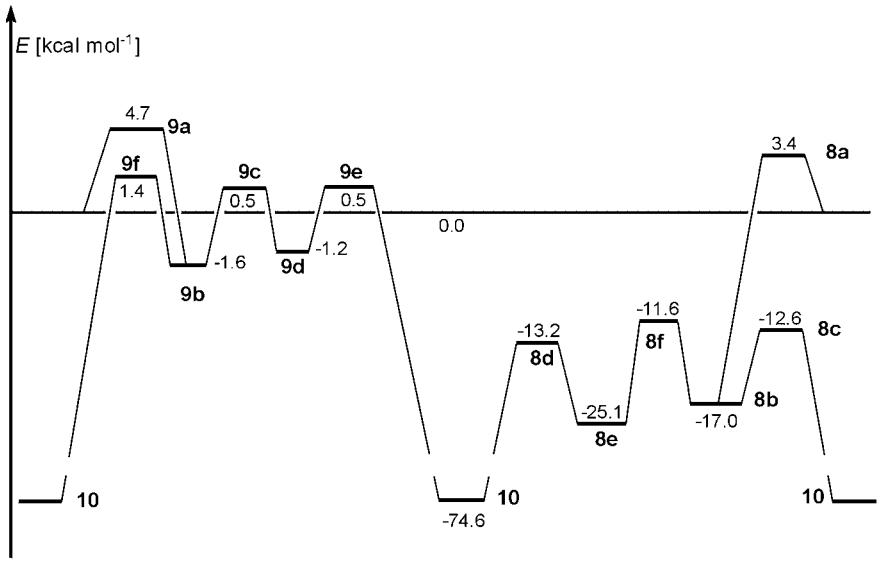

Figure 4. CASPT2 potential energy diagram for the cycloaddition between thioformaldehyde *S*-methylide and thioformaldehyde, showing transition states, intermediates, and product relative to the energies of the reactants.

angle in **8c** becomes smaller than 135°, and in the case of the *C*,*C* biradical the dihedral angles should either be smaller than 122° (**9f**) or greater than 319° (**9e**). Structure **11**, with equal bond lengths for the two new bonds, is within this window, and arbitrarily chosen distances of 2.70 Å are greater than normally observed for TSs of concerted cycloadditions. Therefore, **11** should be on the way to the TS and should have a more positive energy than the reactants. The total energy for **11**, however, is lower than that of the reactants by 7.7 kcal mol^{-1}. Optimization to find a true TS always led to the reactants. As no TS could be found, it must be concluded that there is no activation barrier for the concerted cycloaddition between thioformaldehyde *S*-methylide and thioformaldehyde.

An *energy profile* is a kind of shorthand for a reaction mechanism, and the *minimum energy pathway* on the polydimensional potential energy surface, despite its fictitiousness, is the more subtle version. Here, no minimum energy path can be defined, and a plurality of relative arrangements of the two reactants is funneled down to dithiolane **10**.

Cycloaddition between thioformaldehyde *S*-methylide and ethene: Although the cycloaddition between thioformaldehyde *S*-methylide and ethylene has been analyzed in a previous theoretical study,[44] the calculations were repeated for reasons of consistency (Figure 5 and Table 3). The concerted TS, the reaction product, and a biradical pathway were considered, similarly to the case of the cycloaddition between **1** and **7**. From (U)B3LYP/6–31G*-optimized geometries (Figure 5), RASSCF and CASPT2 single-point calculations were performed. In contrast to the cycloaddition between **1** and **7**, a TS for the concerted cycloaddition is obtained here. The structure **12** shows the characteristics of TSs of the cycloaddition of a 1,3-dipole of allyl type (i.e., there is an angle between the plane (CSC) of the dipole and the plane (CCCC) of the carbon atoms). From a starting point of 90° ("orientation complex"), this folding angle widens to 121° in the TS, retaining C_s symmetry. The forming bonds have lengths of 2.56 Å and the bond lengths in the reactants are only slightly elongated, so we are dealing with an early TS. The carbon atoms show some degree of pyramidalization. The activation energy of 6.6 kcal mol^{-1} (Becke3LYP) or 4.2 kcal mol^{-1} (CASPT2) is slightly lower than the reported values.[45] Thiolane **13**, two representations of which are given in Figure 5, is a puckered five-membered ring with bond lengths typical of single bonds. The same half-chair conformation of **13** with C–S–C in the central plane has also been found in the gas phase by electron diffraction.[53] The reaction energy is −78.3 (B3LYP) or −79.3 kcal mol^{-1} (CASPT2).

Table 3. Energies relative to reactants [kcal mol^{-1}], biradical character according to cas(m,n), and dipole moments of the cycloaddition between **1** and ethene.[a]

Structure		E_{rel} (U)B3LYP + ZPVE	E_{rel} CASPT2 + ZPVE	%BRC cas(m,n) /6–31G*	(m,n)	μ [D]
12	TS	6.6	4.2	23	(6,5)	0.79
13	PROD	−78.3	−79.3	2	(2,2)	2.21
14	TS	13.5	16.1	29	(6,5)	0.64
15	I	−4.8	−2.9	84	(2,2)	1.24
16	TS	−1.6	0.7	82	(2,2)	1.65

[a] The basis set is 6–31G*. TS = transition State, I = intermediate, PROD = product.

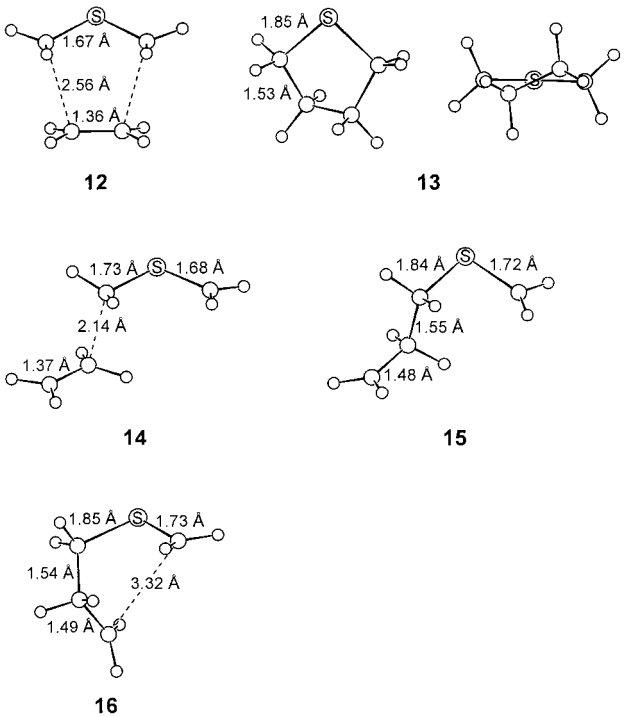

Figure 5. Structures ((U)B3LYP/6–31G*) of transition states, intermediates, and product for the cycloaddition between thioformaldehyde *S*-methylide and ethene.

No less interesting than the allowed concerted pathway is the possible existence of a two-step cycloaddition. A TS for the formation of a linear biradical (**14**) shows only small deformations of the reactants and a separation of 2.14 Å for the new C–C bond. Its energy is 13.5 (UB3LYP) or 16.1 kcal mol^{-1} (CASPT2) (the first differs from Fabian's value of 18.9 kcal mol^{-1}),[45] and demonstrates that the concerted TS is favored by 6.9 or 11.9 kcal mol^{-1}, respectively. The biradical intermediate **15** assumes a stretched structure in which the terminal radical centers are slightly pyramidalized. The energy of formation, −4.8 kcal mol^{-1} (UB3LYP) or −2.9 kcal mol^{-1} (CASPT2), provides a small stabilization with respect to the reactants. Rotation about the new bond leads to a TS **16** at −1.6 kcal mol^{-1} (UB3LYP) or +0.7 kcal mol^{-1} (CASPT2) for ring-closure, with a C–C distance of 3.32 Å.

The conclusion from comparison of thioformaldehyde (**7**) and ethene in their behavior towards **1** is that **7** displays a much higher reactivity. Thiones have therefore been termed "superdipolarophiles" in cycloadditions of various 1,3-dipoles.[54] On the other hand, it is also found, for the cycloaddition between thioformaldehyde and **1**, that biradical intermediates are favored over equivalent intermediates in the two-step cycloaddition of ethene. This could have been expected from the results for the cycloaddition between **1** and thioformaldehyde, as the attack at the carbon atom of **7** on **1** produced the *C*,*S* biradical **8b**, which is more stable than the biradical formed by attack through the sulfur of **7** on **1** (*C*,*C*

biradical **9b**). The results will be modified if substituents are incorporated in the 1,3-dipole and/or dipolarophile, in particular if they are able to stabilize radical centers.

Cycloaddition between thioacetone *S*-methylide (17) and thioacetone (18): How do alkyl substituents in a thiocarbonyl *S*-methylide and a dipolarophile influence the cycloaddition pathways for C=S and C=C double bonds? The presence of two methyl groups at one end of the ylide **17** (thioacetone *S*-methylide) and the dipolarophile **18** (thioacetone) moderately increases the size of the system, while still allowing high level calculations with (U)B3LYP/6–31G* (the CASPT2 procedure was not applied, for reasons concerning computer resources). Comparison of the results with those found for the unsubstituted system, for which CASPT2 results are available (see above), should allow assessment of the influence of the higher level calculation. Experimental studies have been performed with alkyl groups bulkier than *gem*-dimethyl in the 1,3-dipole and the dipolarophile.[55]

Ground states of thioacetone *S*-methylide, thioacetone, and cycloadducts: Because of the substitution, the C–S bonds (Figure 6) in **17** are slightly longer (1.66 Å) than those in **1**. The C-S-C angle is 114°. According to CAS(4,3) the biradical character is 24%, similar to that of **1**. The C=S double bond in thioacetone (**18**) is also somewhat longer (1.64 Å) than in thioformaldehyde (**7**).

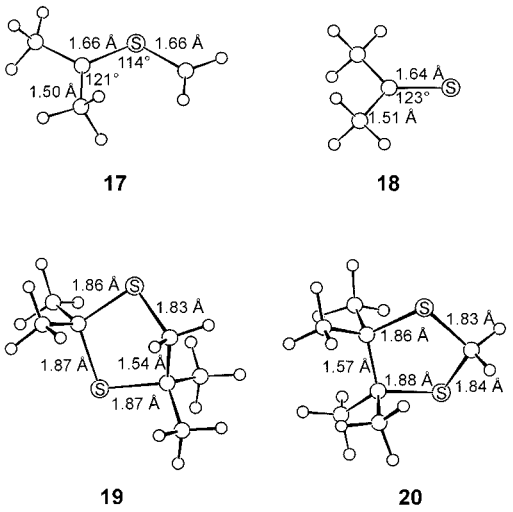

Figure 6. Cycloaddition between thioacetone *S*-methylide and thioacetone. (U)B3LYP/6–31G* structures of reactants and products.

Cycloaddition between **17** and thioacetone can produce two regioisomeric products: **19** and **20** (2,2,4,4-tetramethyl-1,3-dithiolane and 4,4,5,5-tetramethyl-1,3-dithiolane). Both reactions are strongly exothermic (Table 4): -61.1 kcal mol^{-1} for the formation of **19** and -56.2 kcal mol^{-1} for **20**. The difference in stability, of 5.0 kcal mol^{-1}, can be attributed to steric destabilization of **20** by the four methyl groups at adjacent C atoms. It is interesting to note that the formation of **10**, the cycloadduct of **1** and **7**, is 15 kcal mol^{-1} more exothermic than that of **19**. The five-membered rings are puckered and display normal C–C and C–S bond lengths (Figure 6).

Table 4. Energies relative to reactants [kcal mol^{-1}], biradical character according to cas(m,n), and dipole moments of structures **17**–**27**.[a]

Structure		E_{rel} (U)B3LYP + ZPVE	%BRC cas(m,n)	(m,n)	μ [D]
17			24.4	(4,3)	1.0
18			10.1	(2,2)	3.05
19	PROD	-61.1			1.05
20	PROD	-56.2			1.54
21a	TS	5.9	46.6	(4,4)	2.13
21b	I	0.7	92.7	(2,2)	0.11
22a	TS	9.1		(4,4)	2.29
22b	I	6.8	100.5	(2,2)	0.67
23	TS	1.9	79.4	(2,2)	0.62
24a	TS	7.1	24.8	(4,4)	6.58
24b	I	-10.6		(2,2)	5.60
25a	TS	14.8		(4,4)	5.71
25b	I	2.4		(2,2)	3.24
26	TS	3.1	23.9	(4,4)	2.64
27	TS	4.4	24.2	(4,4)	3.27

[a] The basis set is 6–31G*. TS = transition State, I = intermediate, PROD = product.

Biradical pathways to 19 and 20: Biradicals might be generated if thioacetone were to attack ylide **17** either at the dimethyl-substituted carbon atom or at the unsubstituted side. As this can proceed through reaction of either the sulfur or the carbon of the C=S double bond, four different biradicals can be anticipated. All possibilities were considered, with modes of attack being chosen so as to produce conformations of biradicals that would not be able to undergo cyclization without rotation (see the above discussion of biradical formation between thioformaldehyde and thioformaldehyde *S*-methylide). In all cases, stationary points for biradicals were found on the potential energy surface. The calculations were not carried out in such detailed fashion as for the unsubstituted 1,3-dipole and dipolarophile: rotameric forms of the biradicals were not evaluated. A TS to ring-closure was looked for only in the case of biradical **21b**, as the expected mechanistic insight did not seem to justify the necessary computational expense in other cases. The general picture of the potential energy surface should be similar to that of the cycloaddition of **1** to **7**.

***C*,*C* biradicals**: Formulae **21a/b**–**22a/b** (Figure 7) show TSs and biradicals generated by attack of the sulfur atom of thioacetone on either the substituted (**22**) or the unsubstituted side (**21**) of thioacetone *S*-methylide. Ring-closure of **22b** produces **19**, while that of **21b** leads to **20**. In TS **21a**, attack of the sulfur atom at the unsubstituted side, the length of the forming bond is 2.28 Å, and the relevant ylide C–S bonds are elongated to 1.70 Å and 1.74 Å when compared to **17**; the former C=S double bond of **18** is 1.67 Å in TS **21a**. According to the UB3LYP/6–31G* calculation, TS **21a** is at $+5.9$ kcal mol^{-1} relative to the reactants, and biradical **21b**—with an energy of $+0.7$ kcal mol^{-1}—is slightly less stable than the reactants. Ring-closure to give **20** may take place after rotation about the substituted C–S bonds. TS **23**, characterized by one negative vibrational frequency, leads to **20**. At the TS the separation of the two carbon atoms forming the new bond is 3.54 Å, and the energy of TS **23** is

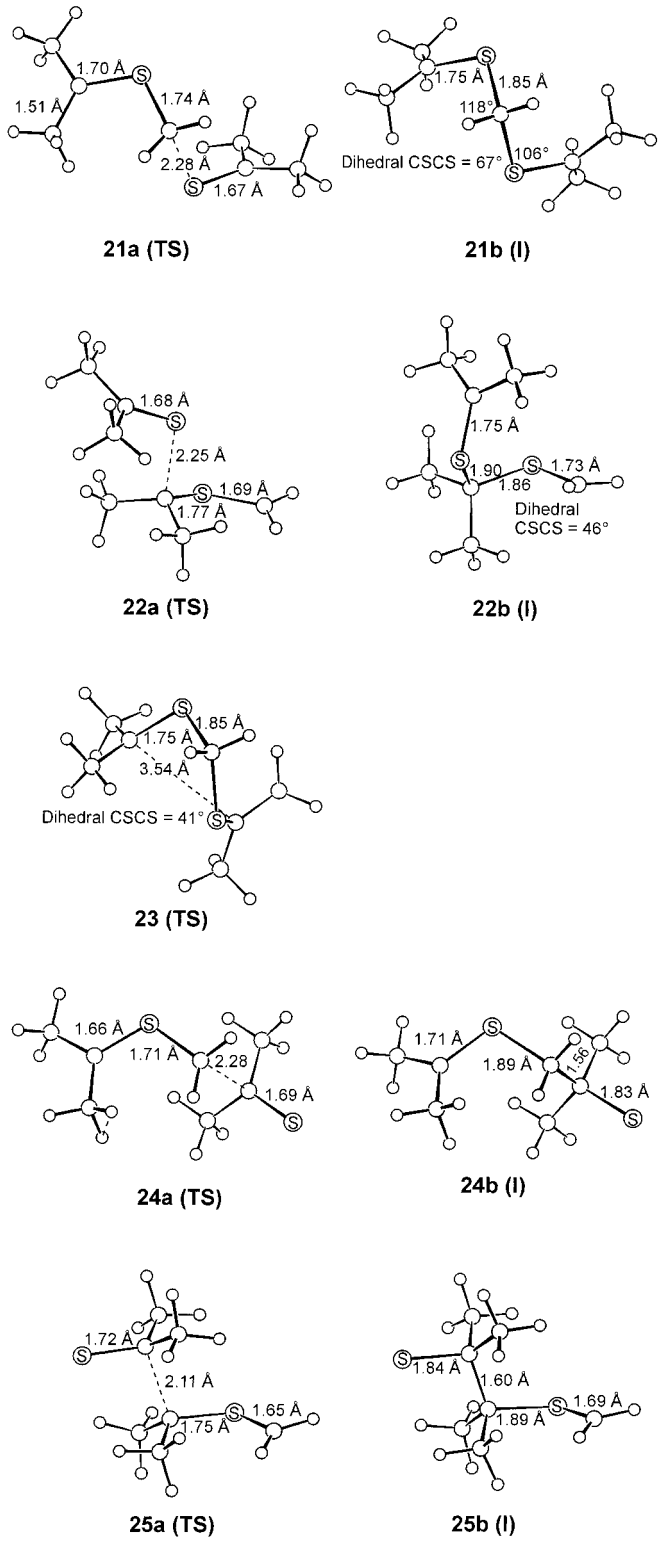

Figure 7. Transition states and possible biradical intermediates (I) in a two-step cycloaddition between thioacetone and thioacetone *S*-methylide.

only 1.2 kcal mol^{-1} above the energy of intermediate **21b**. According to CAS evaluations, the BRCs of the TS and the intermediates are: **21a** 47%, **21b** 93%, and **23** 79%. It is not surprising that TSs **21a** and **23** have less biradical character than **21b**, both TSs retain mainly the BRC of their starting molecule(s).

When the sulfur atom of **18** reacts at the substituted side of **17**, TS **22a**, in which the bond-forming atoms are separated by 2.25 Å, is identified. The other geometrical parameters are similar to those in **21a**. The substitution of the ylide carbon atom by two methyl groups should generate some steric hindrance on approach of **18**, and the new C–S bond in **22a** is somewhat shorter than in **21a** (Figure 7). The energy of **22a** is about 3 kcal mol^{-1} higher than that of **21a**: 9.1 as compared to 5.9 kcal mol^{-1}. The biradical **22b** is at an energy level of 6.8 kcal mol^{-1}, hence 6.1 kcal mol^{-1} above **21b**. The TS to ring-closure, which was not determined, is assumed to be only slightly higher in energy than intermediate **22b**, as the C–C bond is formed between one dimethyl-substituted carbon atom and one unsubstituted carbon atom, differently from the TS **23**, in which both carbon atoms are dimethyl-substituted. In this case dithiolane **19** is the product of reaction.

***C,S* Biradicals**: The dimethyl-substituted carbon atom of thioacetone can attack ylide **17**, which leads to *C,S* instead of *C,C* biradicals. If the new bond is generated between the unsubstituted carbon of **17** and the dimethyl-substituted one of **18**, TS **24a** is found at a separation of 2.28 Å between the reacting atoms and an energy of +7.1 kcal mol^{-1}. The corresponding biradical **24b** is located at −10.6 kcal mol^{-1}, and so is more stable than the reactants, which parallels the reaction of the unsubstituted dipole and dipolarophile, in which it was found to be 17 kcal mol^{-1} more stable. The BRCs of **24a** and **24b** are 25 and 100%, respectively. Ring-closure of this biradical leads to **19**, the 2,2,4,4-tetramethyl-1,3-dithiolane. The TS of ring-formation has not been determined. However, it is supposedly close to the biradical in energy. If **24b** is compared to the pathway via *C,C* biradical **22b**, leading to **19**, considered above, this *C,S* biradical is 17.4 kcal mol^{-1} more stable.

Attack of the carbon atom of **18** at the substituted side of **17** creates steric congestion, but the pathway has to be considered for reasons of completeness. The reaction leads via TS **25a**, energetically the highest considered in the series, to *C,S* biradical **25b**, which is close in energy (2.4 kcal mol^{-1}) to *C,C* biradical **21b** (0.7 kcal mol^{-1}). The reason for the small difference in the stability of biradicals **25b** and **21b** is the compensation of the unfavorable steric effect by the greater radical-stabilizing power of sulfur in **25b**. Ring-closure of **25b** provides dithiolane **20**.

Concerted pathways to 19 and 20: While no TS could be located for concerted cycloaddition between thioformaldehyde *S*-methylide and thioformaldehyde, the cycloaddition between **17** and **18** has to pass through TSs **26** and **27** (Figure 8) for the formation of the regioisomeric adducts **19** and **20**. Different basis sets and two density functionals were tested and RHF calculations were performed. Table 5 lists the separations of the reacting atoms as well as the activation and reaction energies for the two cycloadditions. As expected from experience with other calculations, the activation energies are highest by the RHF/3-21G* approach and, on comparison with experimentally obtained results in other cases, come out too high.[56] Generally, the low activation energies in the other calculations illustrate the high reactivity

Table 5. ZPVE-corrected activation energies (E_a), reaction energies (ΔH), and lengths of the forming bonds in transition states **26** and **27**.

Method/Basis Set	**26** r_{cc} [Å]	r_{cs} [Å]	E_a [kcal mol^{-1}]	**19** ΔH [kcal mol^{-1}]	**27** r_{cc} [Å]	r_{cs} [Å]	E_a [kcal mol^{-1}]	**20** ΔH
B3LYP/6–31G*	2.71	3.05	3.1	–61.1	2.81	2.74	4.4	–56.2
B3LYP/6–31+G*	2.66	3.03	4.7	–57.7	2.78	2.70	6.1	–52.2
B3LYP/6–311+G**	2.63	2.97	4.8	–55.3	2.74	2.69	6.2	–50.1
BLYP/6–31G*	2.74	3.05	3.2	–50.4	2.90	2.71	3.9	–44.9
RHF/3–21G*	2.50	3.14	7.8	–82.4	2.54	2.83	11.9	–78.1

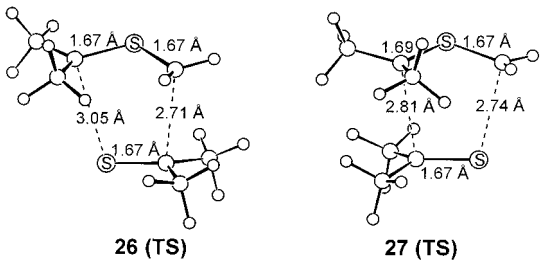

Figure 8. Transition states for the concerted cycloaddition between thioacetone and thioacetone *S*-methylide.

of the C=S double bond. The formation barrier of **19** is favored over that of **20** by energy differences of 0.7 to 1.5 kcal mol^{-1}, depending on basis set and density functional. The small preference in $\Delta E^{\neq}$ for **19** over **20** is probably due to some steric interference by the two *gem*-dimethyl groups. This is reflected in the greater C–C distance in TS **27**; interestingly, the C–S distance is 0.24 Å greater in **26** than in **27**. Folding angles of ca. 110° demonstrate early TSs on the reaction coordinate, as would be expected for the very low activation energies.

The different pathways of formation of intermediates and products during the reaction between thioacetone *S*-methylide (**17**) and thioacetone (**18**) are shown schematically in Figure 9, in which energies ((U)B3LYP/6–31G*) are plotted relative to those of the reactants. The concerted cycloaddition is the most favorable way to both regioisomers. In contrast to the cycloaddition of the unsubstituted reactants, alkyl substitution produces low but finite activation energies for the concerted cycloaddition. Biradicals constitute energy minima on the potential energy surface. However, three of the four possible biradicals display an energy higher than that of the reactants. Only biradical **24b**, generated by attack of the carbon of thioacetone on the unsubstituted carbon of thioacetone *S*-methylide to form a *C*,*S* biradical, shows a negative energy of formation. The activation energies for the formation of all the biradicals, however, are too high to be competitive to the concerted cycloaddition.

It has to be concluded that substitution with four methyl groups hardly changes the qualitative picture obtained for the cycloaddition between the parent 1,3-dipole and dipolarophile. Yet the results suggest that competition between concerted and stepwise processes might become feasible if substituents other than methyl were present. Would the general picture have changed if CASPT2 calculations had been performed? Analysis of the (U)B3LYP and CASPT2 results for the unsubstituted system tells that the differences between the two methods increase with the %BRC of the structures considered. With values $\geq$80% the CASPT2 method furnishes less biradical stabilization than (U)B3LYP by about 5–7 kcal mol^{-1}. As the former method constitutes the higher level (i.e., producing more reliable results), it has to be concluded that the density functional procedure overestimates biradical stability in these cases. If this is true for the unsubstituted and the methyl-substituted biradicals, it is then to be expected that the use of CASPT2 calculations would produce biradicals **21b**–**24b** still less stable, which in turn means that the preference for the concerted pathway would become even stronger. However, this does not have to be the case for other systems, as reference [44] demonstrates.

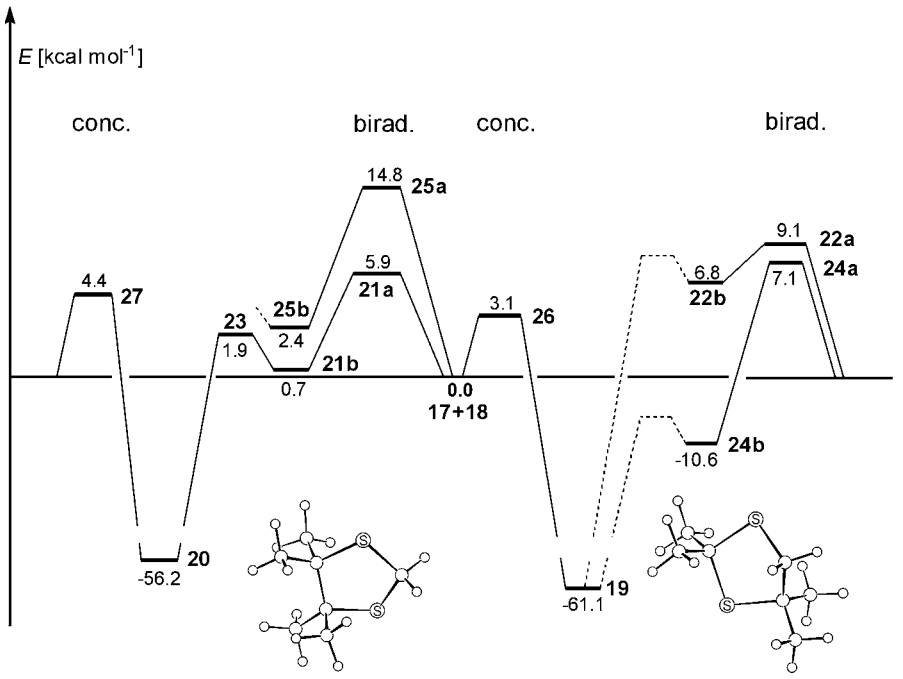

Figure 9. (U)B3LYP potential energy diagram for cycloaddition between thioacetone and thioacetone *S*-methylide, showing transition states, intermediates, and products relative to the energies of the reactants.

Entropic contributions to the reactivity might be important in these cases. The TSs for concerted cycloaddition and biradical formation—one-bond versus two-bond formation—should have different activation entropies. For concerted cycloaddition between thioacetone *S*-methylide and thioacetone, yielding **19** and **20**, activation entropies of -46 e.u. and -50 e.u., respectively, were determined from the ΔH and ΔG values calculated by Gaussian98. A $\Delta S^{\neq}$ value of -36 e.u. characterizes the formation of biradical **21b**. Qualitatively, the smaller $\Delta S^{\neq}$ for biradical formation is expected. Quantitatively, the values obtained for the concerted cycloaddition are higher than experimentally determined activation entropies.[57] Generally, calculated free energies of activation are 10–14 kcal mol^{-1} more positive than the electronic energies + ZPVE. The conclusions to be drawn from both sets of energies are the same in these cases. The calculation of $\Delta S^{\neq}$, however, is based on approximations. The reliability of the calculated values is thus uncertain. The discussion throughout this work is therefore based on ZPVE-corrected energies.

Cycloaddition between thioacetone S-methylide (17) and ethene: Do the two methyl groups in **17** decrease or increase the barrier to concerted cycloaddition of ethene, or favor or disfavor the biradical pathway? Figure 10 displays TSs, product, and a biradical intermediate, in which ethene attacks the unsubstituted side of **17**; Table 6 contains the relevant data. The TS for concerted cycloaddition is characterized by distances of 2.53 and 2.58 Å of the forming bonds, the C–C and C–S bonds of thioacetone *S*-methylide and ethene are slightly elongated relative to the ground-state structures, and the angle between the planes C-C-C-C and C-S-C is 120°. The calculated activation energy is 9.6 kcal mol^{-1}, 3.0 kcal mol^{-1} higher than for the cycloaddition between **1** and ethene. From Table 6 it can be seen that the formation of biradical **31** requires a higher activation energy than the concerted cycloaddition: the TS is at 13.8 kcal mol^{-1} and has a BRC of 42%. The forming C–C bond is 2.13 Å long. The biradical itself (BRC 84%) is below the energies of the reactants (-4.5 kcal mol^{-1}). As this is the result of a UB3LYP evaluation, the value has to be compared with the UB3LYP value of **15**, which is -4.8 kcal mol^{-1}. Ring-closure of **31** takes place via TS **32**, which is located at -1.4 kcal mol^{-1}. In **32** (BRC 80%) the distance between the ring-forming carbon atoms is 3.36 Å, so the TS is early on the reaction coordinate, as is also demonstrated by the high BRC of **32**. The corresponding value for **16** (BRC 82%), the TS of ring closure in the unsubstituted case, is -1.6 kcal mol^{-1}. The final result is that the substituted ylide **17** behaves similarly to **1** in the cycloaddition to ethene, but that the barriers for both mechanistic pathways are higher for **17**.

Table 6. Energies relative to reactants [kcal mol^{-1}], biradical character according to cas(m,n), and dipole moments of the cycloaddition between **17** and ethene. Basis set is 6–31G*. (TS) = transition state, (I) = intermediate, (PROD) = product.

Structure		E_{rel} (U)B3LYP + ZPVE	%BRC cas(m,n) /6—31G*	(m,n)	μ [D]
28	TS	9.6	24.9	(4,4)	1.11
29	PROD	-74.1			2.07
30	TS	13.8	42.1	(4,4)	1.39
31	I	-4.5	83.7	(2,2)	1.19
32	TS	-1.4	80.0	(2,2)	1.55

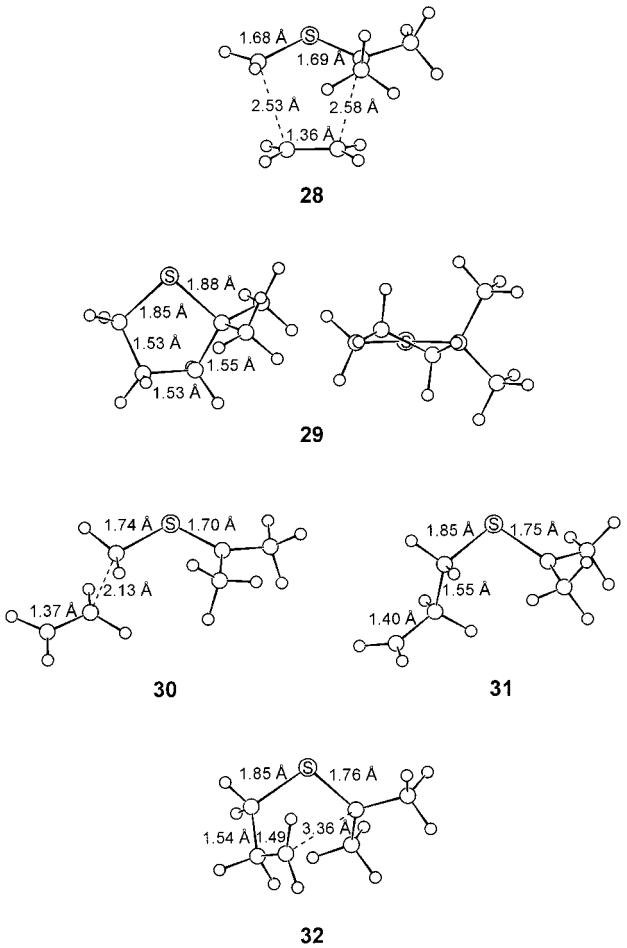

Figure 10. Cycloaddition between thioacetone *S*-methylide and ethene. (U)B3LYP/6–31G* structures of transition states, intermediates, and product.

Conclusion

Concerted cycloadditions of thioformaldehyde *S*-methylide (**1**) and thioacetone S-methylide (**17**) to thioformaldehyde (**7**) and thioacetone (**18**), respectively, are the preferred reaction pathways. Concerted cycloaddition between **1** and **7** occurs without activation energy. The formation of 2,2,4,4-tetramethyl 1,3-dithiolane (**19**) shows a small, but still lower activation energy than the formation of 4,4,5,5-tetramethyl-1,3-dithiolane (**20**), although the difference (1.2 kcal mol^{-1}) is so small that mixtures of regioisomers might be obtained. Biradical pathways are amenable, but require activation energies not competitive with the four-center pathways. *C*,*S* biradicals are more stable than *C*,*C* biradicals, showing the good radical-stabilizing properties of sulfur.

The differences in activation energies between concerted and stepwise cycloadditions are modest. This suggests that

competition between the two cycloaddition modes might favor a biradical pathway if radical-stabilizing substituents were introduced in 1,3-dipole and/or dipolarophile. Diverse basis sets were tested in some cases, but the differences in the energies of intermediates and TSs in no case qualitatively altered the picture. CASPT2 calculations did not change the conclusions arrived at from the density functional calculations, but have less tendency to overestimate biradical stability.

Acknowledgement

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