Cycloadditions and Methylene Transfer in Reactions of Substituted Thiocarbonyl *S*-Methylides with Thiobenzophenone: A Computational Study

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Regiochemistry and methylene transfer reactions in cycloadditions of aliphatic thiocarbonyl *S*-methylides and thiobenzophenone are analyzed by ab initio [(U)HF/3-21G*] and DFT calculations [(U)B3LYP/6-31G*//(U)HF/3-21G* and (U)B3LYP/6-31G*]. The formation of regioisomeric 1,3-dithiolanes is explained by the competition of concerted (2,4-substituted 1,3-dithiolane) and stepwise cycloaddition via *C*,*C*-biradicals (4,5-substituted 1,3-dithiolane). Aliphatic thiocarbonyl *S*-methylides with sterically demanding substituents undergo substantial methylene transfer in the reaction with thiobenzophenone. This process involves dissociation of the *C*,*C*-biradical intermediate with liberation of thiobenzophenone *S*-methylide which, in turn, combines with a second molecule of thiobenzophenone. Calculated activation parameters for the different processes are in agreement with the experimental observations.

Introduction

The formation of five-membered rings by 1,3-dipolar cycloadditions constitutes a powerful way of synthesizing heterocyclic compounds.[1] The variability of 1,3-dipoles and dipolarophiles provides access to a multitude of different heterocycles. Thiocarbonyl *S*-ylides belong to the class of 1,3-dipoles with allyl anion character. In situ cycloadditions take place with a variety of *CC* and *C*-hetero multiple bonds.[2] As cycloadditions of $_{\pi}4_s + _{\pi}2_s$ character, they are allowed to be concerted processes.[3] This has been suggested by the stereospecificity of their cycloadditions to *E*,*Z*-isomeric *CC*-double bonds.[4] However, it has also been demonstrated that under special steric and electronic conditions in 1,3-dipole and dipolarophile the mechanism of these reactions can change to a two-step process.[5] Thus, the cycloaddition of very electron deficient olefins may occur in a two-step manner via zwitterionic intermediates,[5] which has recently been confirmed by quantum chemical calculations.[6] In addition, it has been shown for cycloadditions of suitably substituted thiocarbonyl *S*-methylides to thiones that biradical pathways become feasible.[7] Quantum chemical calculations on the cycloaddition of thiobenzophenone *S*-methylide to thiobenzophenone support this mechanistic change.[8] Obviously, the mechanism depends on the substitution pattern of 1,3-dipole and dipolarophile. A continuous change from concerted pathways to two-step processes via zwitterionic or biradical intermediates seems to be possible,[9] a picture which had also been unveiled for the Diels–Alder reacton, likewise a $_{\pi}4_s + _{\pi}2_s$ cycloaddition.[10]

It was shown by high level ab initio and DFT calculations that the cycloaddition of thioformaldehyde *S*-methylide to thioformaldehyde should take place in a concerted fashion without activation energy, but that a biradical pathway might become feasible if radical stabilizing substituents are introduced in 1,3-dipole and dipolarophile.[7] Methyl groups are not sufficient, the concerted cycloaddition is still preferred. However, the cycloaddition of thiobenzophenone *S*-methylide to thiobenzophenone constitutes a case where the stability of biradical intermediates induces a change in mechanism. DFT calculations provided a satisfactory rationalization of mechanism and regiochemistry via a 1,5-*CC*-biradical as an intermediate.[8]

A mechanistic diversity seems to be indicated in the cycloadditions of aliphatic thiocarbonyl *S*-methylides to thiobenzophenone. Both positional isomers, the 2,4-substituted and the 4,5-substituted 1,3-dithiolane are formed (Scheme 1). In addition, the more sterically demanding the substituents on the 1,3-dipole are, the higher becomes the participation of a "methylene transfer reaction" from the aliphatic thiocarbonyl *S*-methylide to thiobenzophenone, forming thiobenzophenone *S*-methylide, which then undergoes cycloaddition to thiobenzophenone. Since the latter reaction takes place with hardly any activation barrier,[8] the competition between the aliphatic thione and thiobenzophenone ends in favor of the cycloaddition of the latter thione. Experimental results on methylene transfer reactions are described in the accompanying publication.[11] Here we present a computational study of cycloadditions of aliphatic thiocarbonyl *S*-methylides to thiobenzophenone in

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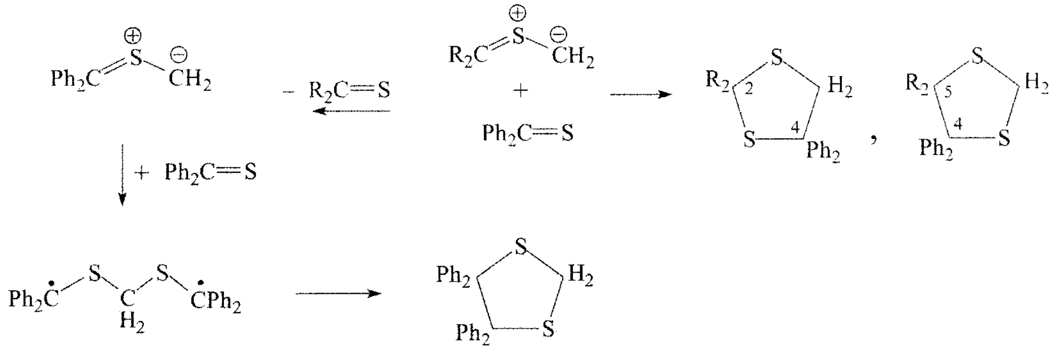


Scheme 1. Formation of regioisomers and methylene transfer in thiocarbonyl *S*-ylide cycloadditions.

order to unravel the mechanistic implications of the experimental results.

We will first describe calculations, carried out for the reaction of thioadamantane *S*-methylide with thiobenzophenone and for thiobenzophenone *S*-methylide with adamantanethione. Then calculations are reported for cycloadditions of thioacetone *S*-methylide and of 2,2,5,5-tetramethylcyclopentanethione *S*-methylide to thiobenzophenone as well as those of thiobenzophenone *S*-methylide to thioacetone and 2,2,5,5-cyclopentanethione.

Computational Methods

DFT calculations were carried out with the Gaussian98 suite of programs.[12] Due to the size of the systems, geometry optimizations were done originally on the (U)HF level, using the 3-21G* basis set. Single point calculations of stationary points, obtained by these calculations were performed with (U)B3LYP/6-31G*. As indicated below, we later preferred optimizations by (U)B3LYP/6-31G*.

Molecules with closed-shell character were evaluated by DFT theory using the B3LYP functional. In cases where biradical character was assumed, UB3LYP was applied including the key words guess = alter and guess = mix in Gaussian. When B3LYP and UB3LYP gave identical results, the key word stable = opt was additionally applied, in order to look for an improved UB3LYP wave function with a lower total energy. Biradical character (BRC) was determined by CAS(2,2)/3-21G* calculations.[13] CAS(2,2) is the minimum configuration interaction to calculate BRC. This approach does not, however, take proper account of the dynamic electron correlation, which may lead to an overestimation of the true biradical character.[14] As a check on the quality of the CAS(2,2) determined BRC, the total energies calculated by restricted and unrestricted methods are compared. If this difference is small, 2–3 kcal mol^{-1}, the biradical contribution to the total wave function must be small. This must also be the case when RB3LYP und UB3LYP both indicate a closed shell configuration.[15] In general RB3LYP and UB3LYP yielded identical results when the CAS(2,2) calculated biradical character did not exceed 30% appreciably. The BRC should parallel the magnitude of the energy difference between a restricted and an unrestricted calculation, in our case RB3LYP and UB3LYP. High BRC should be present when this difference exceeds 10 kcal mol^{-1}. Small energy differences of singlet and triplet biradical wave functions can be taken as a criterion for a high BRC.

Stationary points which could be determined were checked by frequency calculations to see whether they constituted minima or maxima on the potential energy surface. True transition structures (TSs) are characterized by only one imaginary frequency. These TSs were checked whether they connected properly the ground state of reactant(s) and product. The results were corrected by ZPVE. Proper TSs in UB3LYP/6-31G* calculations were evaluated for structures **37a** and **38**. The corresponding ΔZPVE corrections were applied to related transition structures (indicated in Table 1, Table 2, Table 3, Table 4), which were calculated by use of a reaction coordinate (indicated as TS_{RC} in Figures, Schemes and Tables). ZPVE corrections for B3LYP/6-31G*//RHF/3-21G* calculations (Table 1) result from the RHF/3-21G* wave function. In the case of UB3LYP/6-31G*//UHF/3-21G* determined biradicals in Table 1, the corrections derive from **27** (UB3LYP/6-31G*) optimizations (Table 2, structure similar to **12**, see Supporting Information; for Supporting Informations see also the footnote on the first page of this article). NPA charges and dipole moments were determined by (U)B3LYP/6-31G* calculations.

Results and Discussion

Reactions of adamantanethione *S*-methylide (2) with thiobenzophenone (3) and of thiobenzophenone *S*-methylide (1) with adamantanethione (4) ((U)B3LYP/6-31G*//(U)HF/3-21G*): Concerted or stepwise, two reaction centers in both 1,3-dipole and dipolarophile – many pathways are conceivable.[7] For a first critical survey, we applied (U)HF/3-21G* for geometry optimizations. After selecting the mechanistic paths with the lowest activation energies by single point (U)B3LYP/6-31G* calculations on the (U)HF/3-21G* geometries, the calculations were repeated for the optimization of structures on the more demanding (U)B3LYP/6-31G* level (next chapter). Recently, we published a detailed computational study of the reaction of **1** with **3**.[8] The structures of **1** and **3** are reported for convenience in Scheme 2. The analysis showed the high reactivity of the

Table 1. Reaction of adamantanethione *S*-methylide (**2**) with thiobenzophenone (**3**), and of thiobenzophenone *S*-methylide (**1**) with adamantanethione (**4**). ((U)B3LYP/6-31G*//(U)HF/3-21G*) Energies relative to **2** + **3** in kcal mol^{-1}.

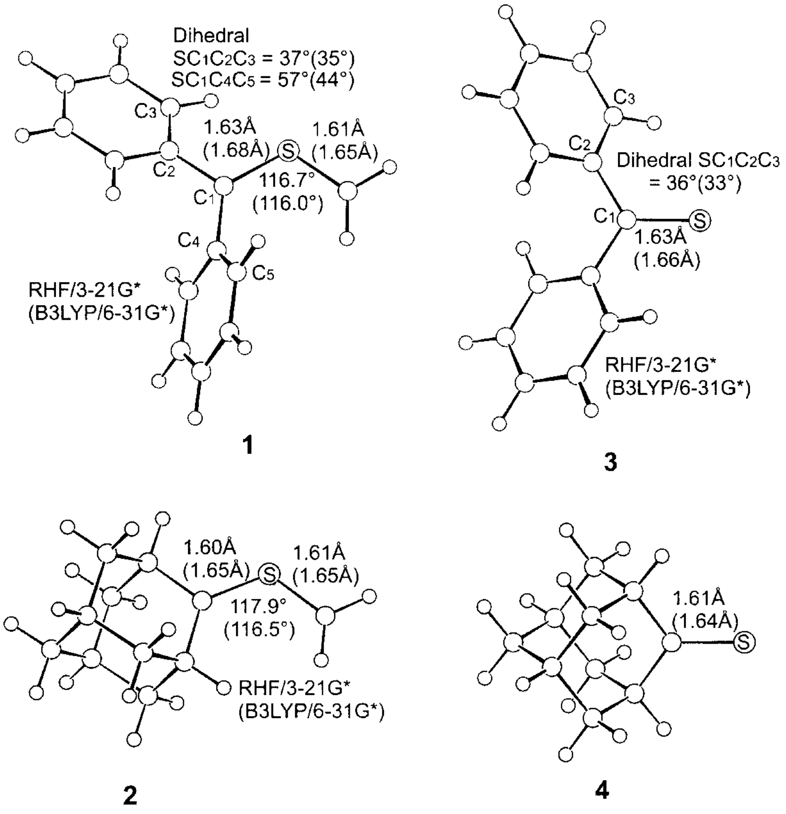
Structure	Δ ZPVE	BRC, CAS(m,n)/3-21G*	(m,n)	μ [D]	E_{rel}	E_{rel} +Δ ZPVE
2		19.7	4.3	1.3		
3		9.9	2.2	3.4		
2+**3**	0.0					0.0
1		18.6	4.3	0.7		
4		9.7	2.2	3.6		
1+**4**	–0.1				–4.5	–4.6
5 (TS)[a]	0.8			3.7	3.5	4.3
6 (TS)	(1.0)[b]			4.3	6.4	(7.4)[b]
7 (TS)	0.8			2.2	2.9	3.7
8 (TS)	1.0			1.6	9.7	10.7
9 (Prod)[a]	4.4			0.8	–57.0	–52.6
10 (Prod)	5.1			1.2	–31.4	–26.3
11 (I)[a]	1.3[c]	90	2.2	2.6	–9.9	–8.6
12 (I)	1.3[c]	99	2.2	0.7	–12.9	–11.6
13 (TS$_{\text{RC}}$)	0.8[d]	41	2.2	2.5	1.4	2.2
14 (TS$_{\text{RC}}$)	1.6[e]	41	2.2	1.4	–6.6	–5.0
15 (TS)	0.9	18	2.2	7.8	9.0	9.9
16 (I)	1.3	100	2.2	10.5	–5.3	–4.0
17 (I)	1.3[c]	86	2.2	1.0	–0.4	0.9
18 (TS$_{\text{RC}}$)	0.8[d]			2.1	7.2	8.0
19 (TS$_{\text{RC}}$)	0.8[d]			2.6	–1.3	–0.5
20 (Prod)	4.3			1.6	–55.8	–51.5
21 (I)	3.5			3.1	–18.8	–15.3
22 (TS)	0.9			3.1	7.8	8.7
21a (I)	[f]			16.0		
22a (TS)	1.0			6.7	7.9	8.9
23 (I)	1.3[c]			0.7	16.2	17.5

[a] TS = transition structure, TS$_{\text{RC}}$ = TS determined by reaction coordinate calculation, I = intermediate, Prod = product. [b] See text. [c] Δ ZPVE from **27**. [d] Δ ZPVE from **37a**. [e] Δ ZPVE from **38**. [f] SCRF CPCM calculation in THF.

reactants and established a biradical pathway of the cycloaddition to yield 4,4,5,5-tetraphenyl-1,3-dithiolane as the only product. Likewise, we determined structures of **2** and **4** by HF/3-21G* and by B3LYP/6-31G* calculations (values in brackets in Scheme 2). The HF/3-21G* geometrical parameters of the reactive parts of **2** and **4** are very similar to those of **1** and **3** (bond lengths deviate at most by 0.03 Å). The dipole part of **2** and the CS double bond of **4** are planar. The TSs **5**–**8** for the concerted cycloadditions of **2** to **3** and of **1** to **4** to give the 2,4- and the 4,5-substituted 1,3-dithiolanes **9** and **10** are shown in Scheme 3 and Scheme 4. Detailed structural information and total energies are given in the Figures, the Tables, and as Supporting Information. A comment on the magnitude of the activation parameters in the Figures and Tables seems to be appropriate. Many activation energies are low, i. e., the corresponding reactions should be almost diffusion controlled. It has to be remembered, however, that the numbers are not free energies of activation (ΔG^*), not even ΔH^* values, but ZPVE corrected energies. If entropies, which are highly negative for typical bimolecular reactions, are included, the activation parameters will be raised by ca. 10 kcal mol^{-1} (approximate ΔG^*). The activation energies will still be low, but in accordance with the "superdipolarophilic" character of the CS double bond.[16]

Relative energies of transition structures (TS), intermediates (I), and products (Prod) in Figures 1–4 and Tables 1–4 are based on the sum of reactant energies (zero energy level) in the upper level of the diagrams. This applies also to the energies of the structures formed from the cycloaddends of the lower level. On the other hand, activation energies are always related to the specific level. In Figures 1 (a,b) the upper level constitutes the sum of the energies of adamantanethione *S*-methylide (**2**) and thiobenzophenone (**3**). The sum of the energies of the second pair of reactants, thiobenzophenone *S*-methylide (**1**) and adamantanethione (**4**), is 4.6 kcal mol^{-1} lower, reflecting a slight preference in stability of the second pair.

TS **5** connects reactants **2** and **3** with spiro compound **9** and is located at +4.3 kcal mol^{-1} relative to the reactants. Minute elongations of the CS bonds compared to the ground state structures of the reactants and rather high lengths of bonds under formation speak for an early TS. The forming CS bond of 3.19 Å in **5** is longer than the CC bond of 2.46 Å, reflecting the fact that the CS bond has a length of 1.84 Å and the CC bond a length of 1.54 in **9**. In TS **5** the two incipient bonds approximately define a plane which cuts the C–S–C plane at an angle of 108°, i. e., only slightly higher than 90° for the arrangement of the two reactants in parallel planes. Furthermore, the pyramidalization



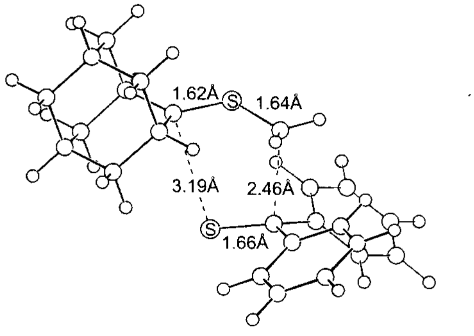
Scheme 2. Ground-state structures of **1**–**4**.

at the formerly planar reactive centers of **2** and **3** is small in TS **5**. Thus, most of the structural changes leading to product **9** occur on the downhill ride of the energy profile, underlining the mentioned early TS.

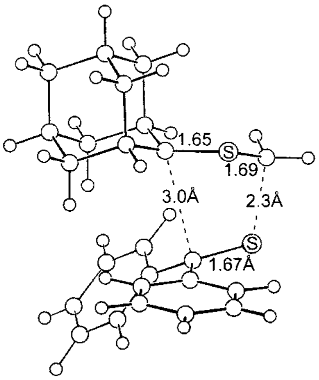
The cycloaddition is highly exothermic (–52.6 kcal mol^{-1}). A comparison of the calculated structure of **9** (Scheme 4) with the X-ray structure[17] reveals an interesting divergence between gas phase and crystal, probably as a result of lattice forces. The five-membered ring comes close to a perfect envelope in both structures. The dihedral angle C-5,S-1–C-2,S-3 in the calculated **9** is 1.6°, demonstrating the almost planar arrangement of the four atoms, and C-4 with the two phenyl groups is the flap, whereas the X-ray structure shows the methylene carbon C-5 as the flap. The folding angle in **9** is 134° as compared to 127°; C-4 is 0.74 Å above the plane and C-5 0.78 Å in the X-ray structure. The bond lengths in Scheme 4 show an excellent agreement between measured and calculated values. The RHF/3-21G* values seem to be slightly superior to the B3LYP/6-31G* distances.

Structure **6** where the substituents wind up at neighboring positions does not correspond to a true TS. Despite numerous attempts, it has not been possible to locate a TS. So, finally a structure was chosen in which the lengths of the forming bonds were approximately adapted to the distances determined for the proper TS **8**, which leads to the same product; in **8** the phenyl groups and the adamantane ring are interchanged. All other geometrical variables were optimized for **6**, and the ZPVE correction was assumed to be the same as in **8**. The strong steric repulsion of the bulky groups is partly reflected in **6** (+7.4 kcal mol^{-1}), but is demonstrated much better in product **10** (Scheme 4). Its formation produces only half of the energy (–26.3 kcal mol^{-1}) as that of **9**. In **10** the envelope is not as perfect as in **9**, due to the steric crowding of the substituents at C-4 and C-5. The dihedral angle S-1,C-2–S-3,C-4 is 12.5°, the flap is C-5, 0.86 Å above the quasi plane. The X-ray structure of **10**[17] reveals S-1 as flap of a distorted envelope. If two concerted cycloadditions would be responsible for product formation, then 2,4-substituted dithiolane **9** should be experimentally preferred. However, the experiment leads to isolated 42% of **9** and 50% of **10**.[17] This suggests, that another mechanistic pathway is responsible for the 50% of**10**.

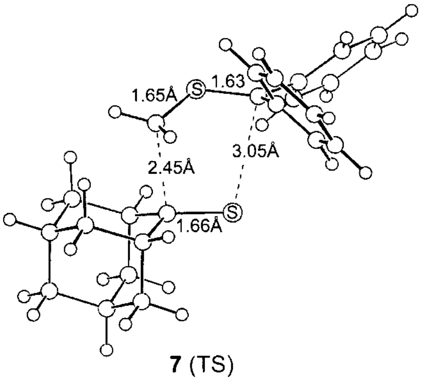
Figure 1 reveals a *C,C*-biradical (Scheme 5) as solution to this problem. One end is a diphenylmethyl radical and the other an adamantyl radical; two conformations of such a biradical are displayed in **11** (– 8.6 kcal mol^{-1}, BRC = 90%, not shown in Figure 1a) and **12** (BRC = 99%). Biradical **12** is located 11.6 kcal mol^{-1} below the reactants, and its barrier of formation (TS, **13**) amounts to only 2.2 kcal mol^{-1}. That is 2.1 kcal mol^{-1} lower than the activation energy for the concerted formation of the 2,4-substituted 1,3-dithiolane **9** (+4.3 kcal mol^{-1}) in this approximation. Cyclization of **12** to **10** occurs via TS **14**, which can be generated from **12** by rotation about one of the CH_2–S bonds (left one in **12**). Structure **14** is the result of a calculation, where the CC bond in **10** has been chosen as reaction coordinate and its length increased incrementally until the en-



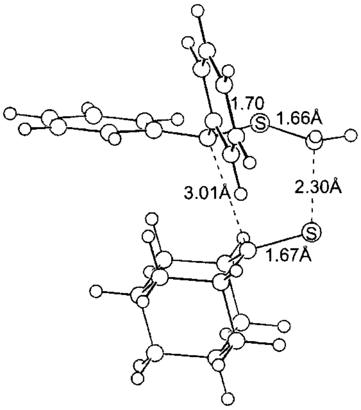
5 (TS)



6 (TS)

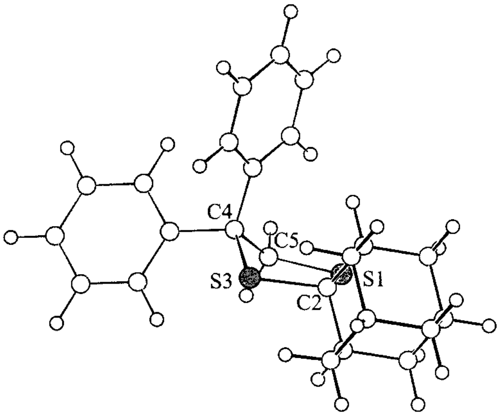


7 (TS)



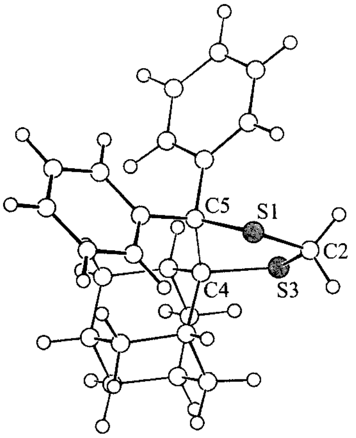
8 (TS)

Scheme 3. Regioisomeric transitions states (TSs) **5**–**8** for the concerted cycloadditions of **2** + **3** and for **1** + **4**.



9 (Prod)

Bond length [Å]	X-Ray Structure	RHF/ 3-21G*	B3LYP/ 6-31G*
S1-C2	1.83	1.85	1.88
C2-S3	1.86	1.84	1.87
S3-C4	1.84	1.83	1.88
C4-C5	1.53	1.54	1.54
C5-S1	1.80	1.81	1.83



10 (Prod)

Bond length [Å]	X-Ray Structure	RHF/ 3-21G*	B3LYP/ 6-31G*
S1-C2	1.78	1.80	1.81
C2-S3	1.80	1.81	1.83
S3-C4	1.88	1.86	1.90
C4-C5	1.62	1.63	1.64
C5-S1	1.85	1.85	1.89

Scheme 4. Comparison of calculated product structures **9** and **10** with data from X-ray analyses.

ergy reached a maximum. Structure **14** (BRC = 41%) is, therefore, not a true TS, characterized by one negative vibrational frequency; its energy (–5.0 kcal mol^{-1}) should, however, be close to that of the proper TS (see below structures **37** and **37a**). Considering that the energy profile of Figure 1a) for the different pathways of the reaction of **2** with **3** is based on (U)B3LYP/6-31G* single point calculations on (U)HF/3-21G* geometries, the evolving picture is in satisfactory agreement with the experimental observa-

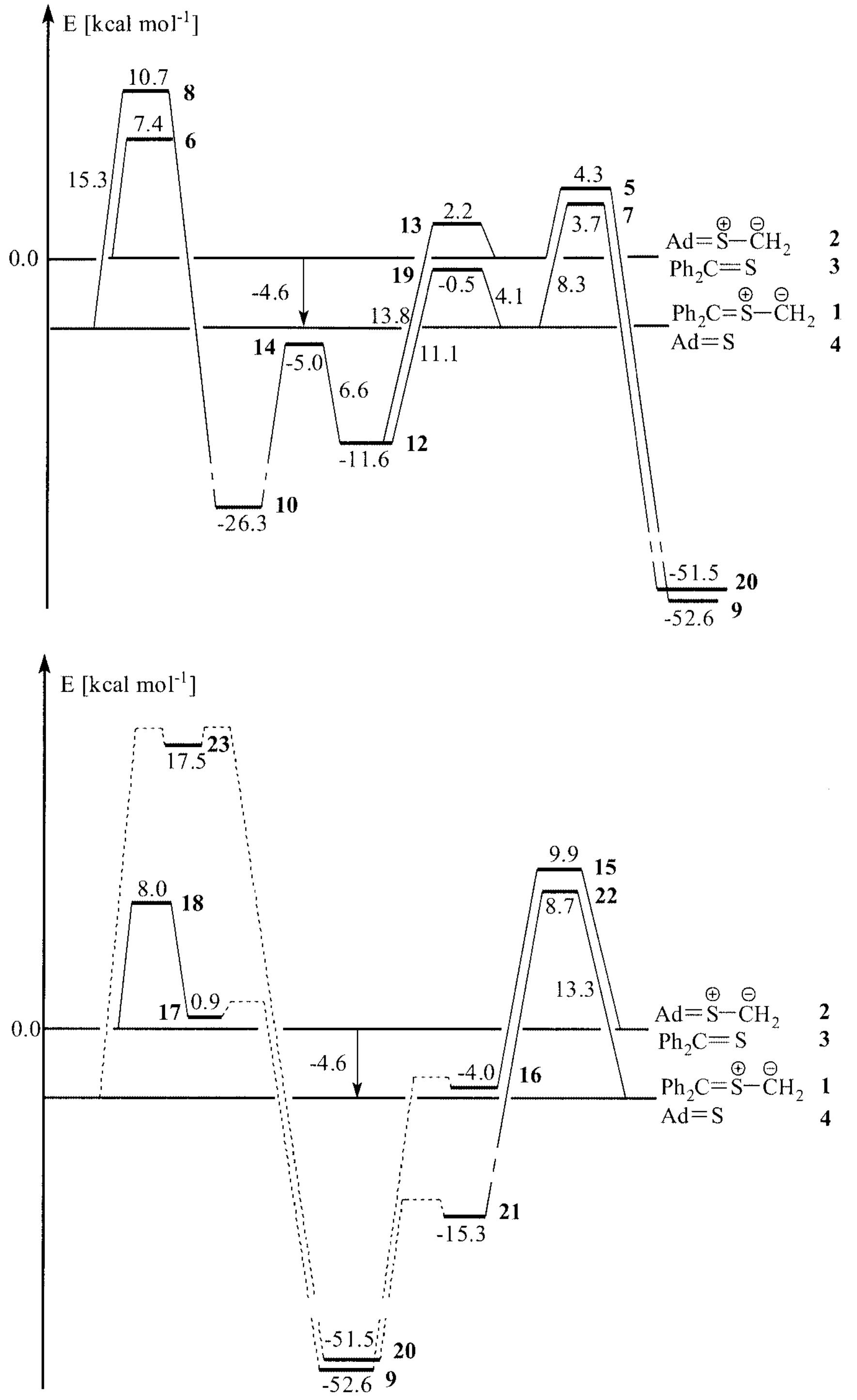
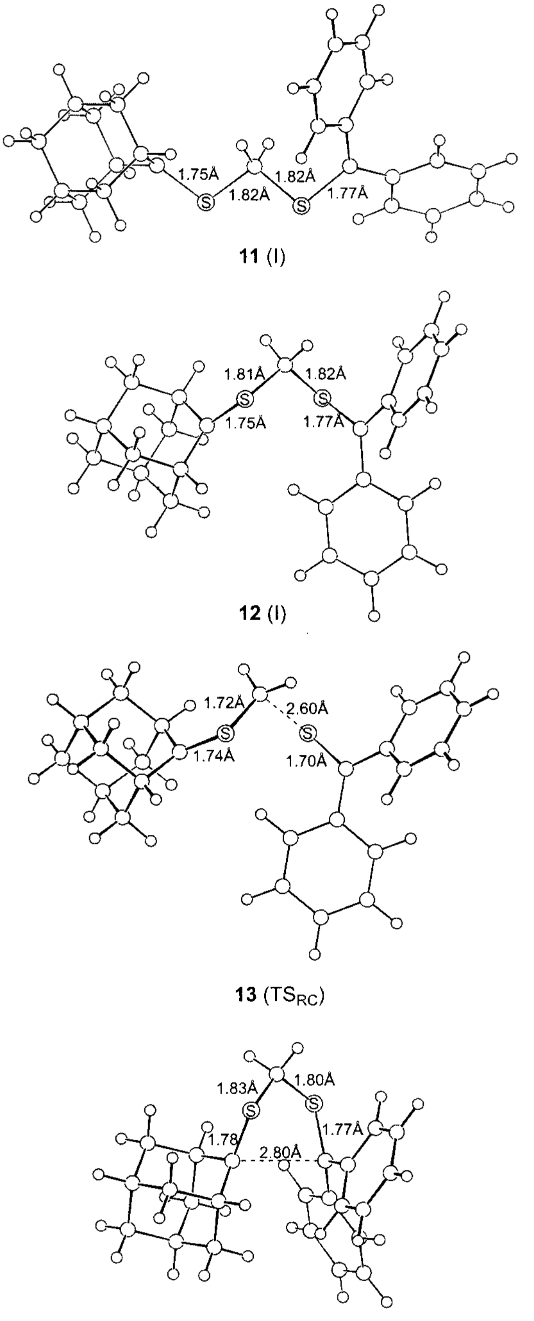


Figure 1. a) (U)B3LYP/3-21G*//(U)HF/3-21G* energies for the cycloadditions of adamantanethione *S*-methylide (**2**) + thiobenzophenone (**3**) and of thiobenzophenone *S*-methylide (**1**) + adamantanethione (**4**): Concerted reactions and those via *C,C*-biradicals (kcal mol^{-1}); b) (U)B3LYP/3-21G*//(U)HF/3-21G* energies for further two-step reactions of adamantanethione *S*-methylide (**2**) to thiobenzophenone (**3**) and of thiobenzophenone *S*-methylide (**1**) to adamantanethione (**4**) (kcal mol^{-1}).

tions. It will be shown below that full (U)B3LYP/6-31G* calculations will provide an even closer agreement between theory and experiment.

Figure 1b) provides information on two-step pathways to **9** and **20** (structure of **20**, see Supporting Information). When the methylide C-atom of **2** attacks the C-atom of the thiocarbonyl group of thiobenzophenone (**3**), intermediate **16** is generated. The structure of **16** (Scheme 6) which is formed via TS **15** (BRC = 18%) needs comment. In comparison with the relevant CS bond lengths of *C,C*-biradical **12** (1.75 and 1.77 Å), those of **16** show greater differences: 1.63 and 1.85 Å. These values are those of a CS double and



11 (I)

12 (I)

13 (TS_{RC})

14 (TS_{RC})

Scheme 5. Two-step cycloaddition of **2** + **3**: *C*,*C*-biradical and TSs of formation and cyclization.

single bond, respectively, and suggest a 1,5-*C*,*S*-zwitterion, i. e., a sulfonium thiolate structure. This finds strong support by the dipole moments of **12** and **16**: The value of **16** is 10.5 D, that of **12** 0.7 D (Table 1).

On the other hand, 100% BRC was calculated by CAS(2,2). The phenomenon that CAS(2,2) grossly overestimates the BRC had been observed in our previous study on the reaction of **1** with **3**.[8] We wonder whether the closed-shell structure with some biradical participation is the best description.

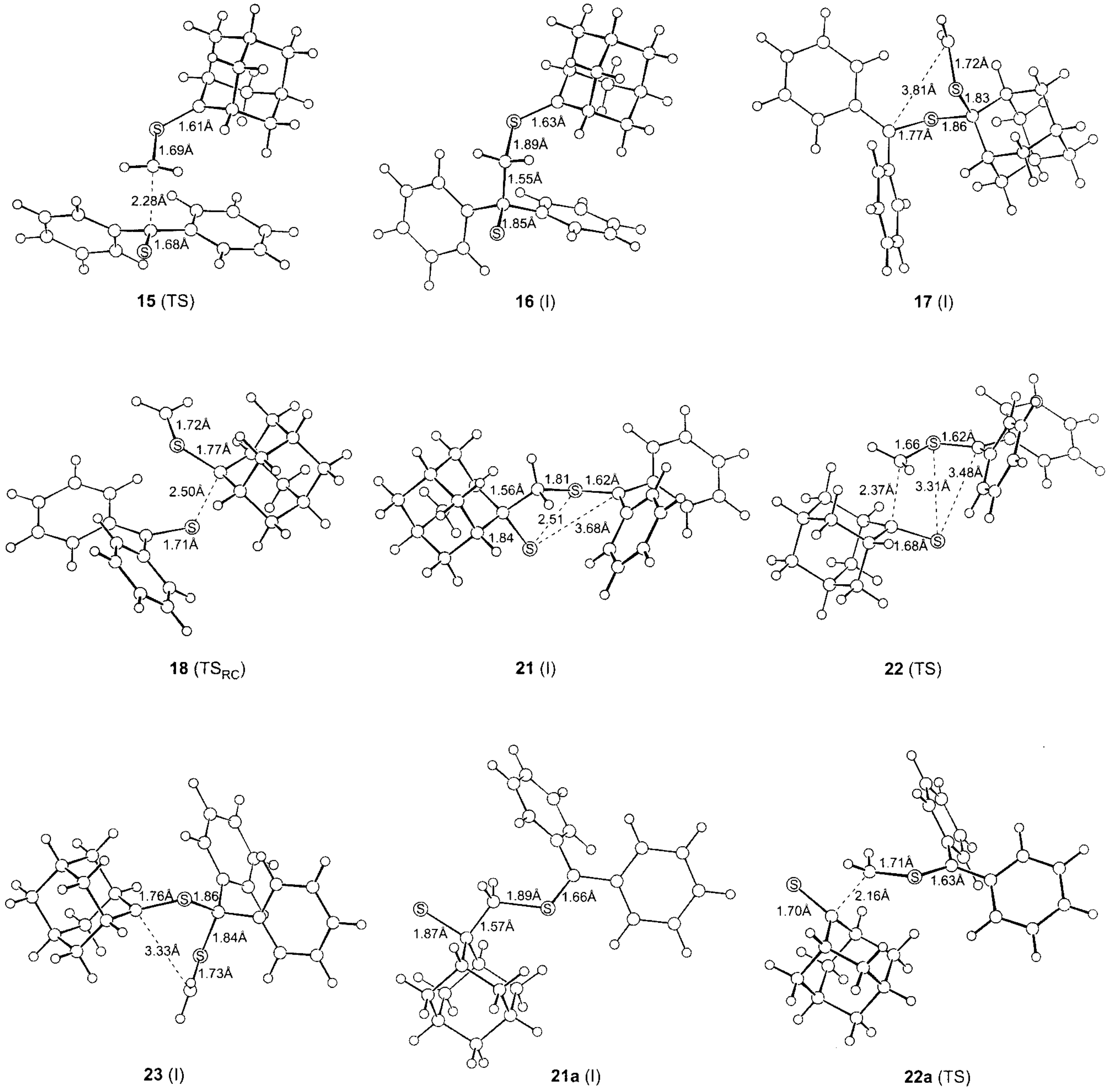
Since the barrier of formation of **16** (+9.9 kcal mol^{-1}) is higher than that for the concerted formation of **9** (+4.3 kcal mol^{-1}), we did not pursue this pathway and did not attempt to calculate a TS for cyclization of **16**. Furthermore, dithiolane **9** might also be the result of ring closure of *C*,*C*-biradical **17** (BRC = 86%) which is formed by attack of the substituted terminus of **2** on the sulfur atom of **3**. An activation energy of 8.0 kcal mol^{-1} (TS, **18**) for the formation of **17** (Figure 1b), harms this pathway in the competition with the concerted cycloaddition or the reaction via *C*,*C*-biradical **12**. Therefore, this path was also disregarded.

A preliminary conclusion might be drawn at this point: The experimental product ratio of **9** and **10** should be the result of a competition between a concerted cycloaddition via TS **5** and a two-step pathway via TS **13** and *C*,*C*-biradical **12**, respectively. Methylene transfer from **2** to **3** should not take place as the activation energy for fragmentation of **12** to **1** and **4** via TS **19** (+11.1 kcal mol^{-1}) (see Supporting Information) is higher than that of the cyclization of **12** leading via TS **14** to **10** (+6.6 kcal mol^{-1}) (Figure 1a).

Figure 1a,b also deal with the interaction of thiobenzophenone *S*-methylide (**1**) with adamantanethione (**4**). Starting point for the different reaction pathways is the energy level of –4.6 kcal mol^{-1} relative to that of the reactants **2** and **3**. The two concerted cycloadditions (Figure 1a) require activation energies of 8.3 kcal mol^{-1} (TS, **7**) for the formation of a third positional isomer, the spiro compound **20** (see Supporting Information), and 15.3 kcal mol^{-1} (TS, **8**) for the formation of **10**. When the substituents in 1,3-dipole and dipolarophile are interchanged, compared with **2** + **3**, the 4,5-substituted 1,3-dithiolane **10** occurs again, but the 2,4-substituted 1,3-dithiolanes **9** and **20** are different. Their energies of formation are very similar, i. e., the exothermicity remains ca. 52 kcal mol^{-1}. The activation energy to the formation of biradical **12** from **1** and **4** via TS **19** is 4.1 kcal mol^{-1}, i. e., considerably smaller than those for the two concerted processes. The only cycloadduct formed should be **10** (Figure 1a); that was indeed experimentally observed, albeit in low yield (22%) in an unpleasant reaction.[18]

The reaction of **1** and **4** to produce **21**, which leads to **20** via TS **22**, is the result of one, out of a multitude of different possible approaches of the reactants. Intermediate **21** is characterized by a CC bond length of 1.56 Å, somewhat longer than a regular CC σ-bond, by a SS distance of 2.51 Å, and by a SC separation (C atom of diphenylmethyl) of 3.68 Å. Compared to **22**, not only the CC but also the SS distance has shortened. The SS distance suggests some bonding, which seems to be of ionic (coulombic) and not covalent character. The thiolate sulfur (CS, 1.84 Å) carries a negative charge (–0.17, by NPA analysis) and the sulfonium sulfur (CS, 1.62 Å) a positive charge (+0.73, by NPA analysis), which supports an ionic stabilization. If there were a covalent bond, the SS distance should be ca. 2.05 Å.

The dipole moment of **21** (3.1 D, Table 1) seems to be at variance with the sulfonium thiolate structure, suggested by the unequal CS bond lengths. The dipole moment, however, is defined as the product of charge times separation of the charge centers. Therefore, a smaller dipole moment is ex-



Scheme 6. Selected TSs and intermediates for the cycloadditions of **2** + **3** and of **1** + **4**. See Table 1 and Figure 1a,b.

pected for **21** (short SS separation) than for **16** (extended sulfonium thiolate (NPA charges: thiolate sulfur –0.30, sulfonium sulfur +0.55).

Another TS for the putative formation of an extended intermediate can be located, if the reactants approach as in **22a**. TS **22a**, however, leads to the thiirane of adamantanethione *S*-methylide (structure, see Supporting Information) besides thiobenzophenone, a process which is exothermic by 46.6 kcal mol^{-1}. There is no intermediate involved in this reaction.

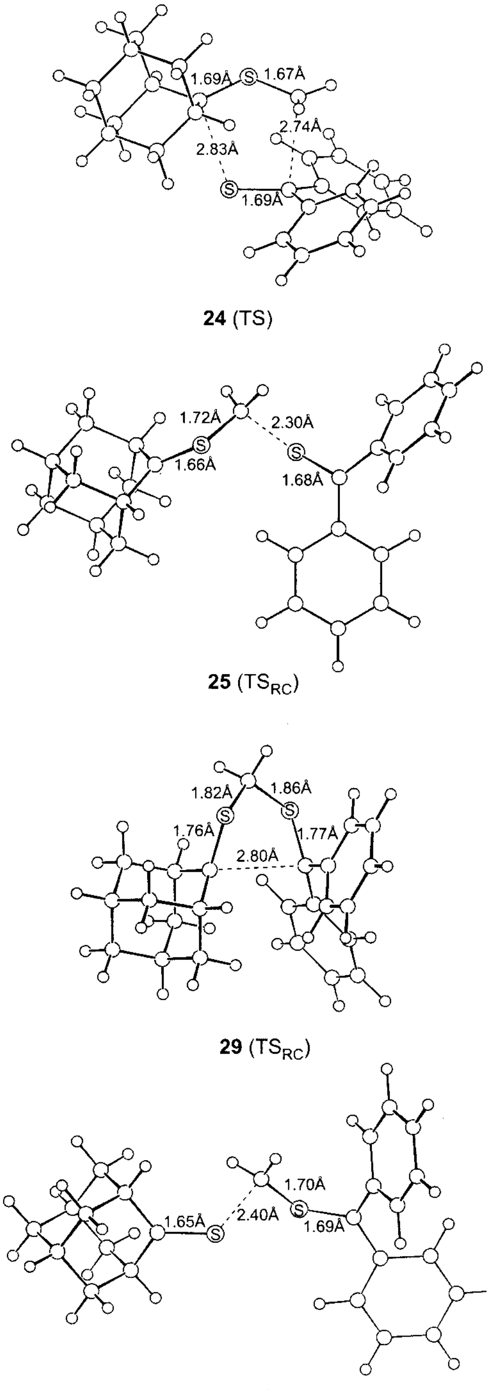
TS **22a** does not lead to a stable zwitterion under the "gas-phase" condition of the calculation. In an earlier study on the cycloaddition of polar dienes to polar dienophiles,[19] it had been observed that "gas-phase" conditions are sometimes not suited to describe zwitterion formation properly. Only, when SCRF calculations[20] with a solvent of dielectric constant 8.9 (dichloromethane) were carried out, stable zwitterionic structures were obtained. The occurrence of a stable intermediate from TS **22a** was, therefore, tested by carrying out a SCRF calculation for the elongated intermediate in THF (ε = 7.6), the solvent which was used in the experimental study.[17] The CPCM model, implemented in GAUSSIAN98,[12] was applied.[21] Now a stable structure **21a** is determined, which is characterized by a high dipole moment (ε = 16.0 D in solution) and unequal CS bond lengths (1.66 Å and 1.87 Å), confirming a zwitterionic sulfonium thiolate. The onium sulfur carries a charge of +0.52, the thiolate sulfur is negative (–0.48 electrons), as obtained by a natural population analysis (NPA). Although the evaluation of the two-step cycloaddition of **1** and **4** has led to interesting insights, the pathways via *C*,*S*-zwitterions **21**, **21a** (not shown in Figure 1b), or *C*,*C*- biradical **23** (Figure 1b) are not competitive with the reaction via *C*,*C*-biradical **12**.

Refined calculations on reactions of adamantanethione *S*-methylide (2) with thiobenzophenone (3) and of thiobenzophenone *S*-methylide (1) with adamantanethione (4) [(U) B3LYP/6-31G*]: The previous section provided evidence that the competition between the concerted formation of the 2,4-substituted 1,3-dithiolane and the formation of the 4,5-substituted 1,3-dithiolane via a biradical route constitutes the essential part of the potential energy surface. Therefore, we restricted the more demanding (U)B3LYP/6-31G* calculations to this part of the hypersurface (Scheme 7, Figure 2, Table 2).

When the extended basis set and DFT instead of (U) HF calculations were used for finding stationary points, the energies and structures have been somewhat altered, compared to the previous calculations (Figure 1a,b, Table 1). In the reactants **1–4** the calculated CS bonds are slightly longer than determined by HF/3-21G* (see values in brackets in formulae **1–4**). In the TS **24** for the concerted cycloaddition of **2** + **3** producing **26** (**9** in Scheme 4) (structure see Supporting Information), the formation of the new CS bond is more progressed (2.83 Å) than in TS **5** (3.19 Å, Scheme 3), whereas the CC bond shows the opposite trend (2.74 Å versus 2.46 Å). Energy changes are small in this rather flat part of the surface. As expected for an early TS, the bonds of the reactants remain almost unaltered. The activation energy is lowered from 4.3 to 3.7 kcal mol^{-1}.

The biradical pathway leading to the 4,5-substituted 1,3-dithiolane **28** (**10** in Scheme 3) is likewise modified. The activation energy for the formation of the biradical **27** (**12** in Scheme 5) (structures of **27** and **28** see Supporting Information) via TS **25** remains 2.2 kcal mol^{-1} (compare with TS **13**, Figure 1a) and, therefore, approaches the activation energy for the concerted formation of the 2,4-substituted 1,3-dithiolane **26** (**10** in Scheme 3); the difference shrinks from the previous 2.1 to now 1.5 kcal mol^{-1}. This is a move in the right direction in order to reproduce the modest experimental preference of formation of the 4,5-substituted 1,3-dithiolane.

Biradical **27** is structurally very similar to the corresponding **12** (Scheme 4 and Figure 1a), but slightly less stable, a trend, which was also observed in our study on the cycloaddition of **1** to **3**, where, however, the biradical formation needed almost no activation. In this previous investigation,[8] it was reasoned that the stability of the biradical relative to that of the product is overestimated by DFT. Calculations on bond dissociation energies on different levels confirmed this conclusion. Here, biradical **27** lies 16.3 kcal mol^{-1} above product **28**. The barrier for ring closure of **27** to give cycloadduct **28** via TS **29** is 6.1 kcal mol^{-1}. As in Figure 1a, this value is substantially smaller than the activation energy needed to cleave the biradical. Thus, once formed, the biradical should end up as cycloadduct, and methylene transfer from **1** to **4** should be negligible. In general, the (U)B3LYP/6-31G* calculations seem to reproduce the experimental findings quantitatively slightly better than the (U)B3LYP/6-31G*//(U)HF/3-21G* calculations. Qualitatively the conclusions remain the same.



Scheme 7. TSs [(U)B3LYP/6-31G*] for concerted and two-step cycloadditions of **2** + **3** and **1** + **4**.

Reactions of Thioacetone *S*-Methylide (31) with Thiobenzophenone (3) and of Thiobenzophenone *S*-Methylide (1) with Thioacetone (32) [(U)B3lyp/6-31g*]: How does a replacement of the adamantylidene by the isopropylidene group

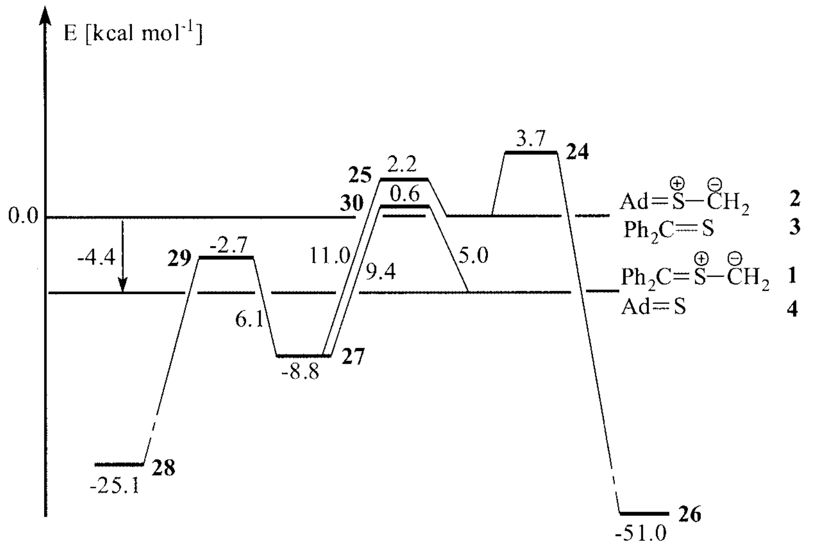


Figure 2. Section of the (U)B3LYP/6-31G* potential energy surface of the reaction of adamantanethione *S*-methylide (**2**) with thiobenzophenone (**3**) and of thiobenzophenone *S*-methylide (**1**) with adamantanethione (**4**) (kcal mol^{-1}).

Table 2. Reaction of adamantanethione *S*-methylide (**2**) with thiobenzophenone (**3**), and of thiobenzophenone *S*-methylide (**1**) with adamantanethione (**4**). ((U)B3LYP/6-31G*) Energies relative to **2** + **3** in kcal mol^{-1}.

Structure	Δ ZPVE	μ [D]	E_{rel}	E_{rel} +Δ ZPVE
2+3	0.0			0.0
1+4	0.1		–4.5	–4.4
24 (TS)[a]	0.9	3.2	2.8	3.7
25 (TS$_{RC}$)	0.8[b]	4.0	1.4	2.2
26 (Prod)[a]	4.3	0.7	–55.3	–51.0
27 (I)[a]	1.3	0.8	–10.1	–8.8
28 (Prod)	4.6	1.3	–29.7	–25.1
29 (TS$_{RC}$)	1.6[c]	1.4	–4.3	–2.7
30 (TS$_{RC}$)	0.8[b]	1.5	–0.2	0.6

[a] TS = Transition structure, TS$_{RC}$ = TS determined by reaction coordinate calculation, I = intermediate, Prod = product. [b] Δ ZPVE from **37a**. [c] Δ ZPVE from **38**.

change the reaction profile? Again the competition of the concerted cycloaddition producing the 2,4-substituted 1,3-dithiolane **34** via TS **33** and the formation of biradical **36** via TS **37**, the result of a reaction coordinate calculation, is considered (Figure 3, Table 3, Scheme 8); subsequently, intermediate **36** cyclizes to give dithiolane **35** (structure in Supporting Information) via TS **38**. As all other biradicals, treated in this contribution, were obtained from reaction coordinate calculations as a consequence of the size of the systems, we followed the same procedure here. However, it was also possible to determine in this less highly substituted case the proper TS **37a** (Table 3) with slightly higher energy, 3.6 instead of 2.7 kcal mol^{-1} (Scheme 8); it is a UB3LYP/6-31G* determined TS, from which a ZPVE correction could be obtained. This ΔZPVE was used in related structures, obtained by reaction coordinate calculations and indicated in the Tables. The fair agreement of **37** and **37a** in structure and energy justifies the other reaction coordinate calculations of this paper. As **37a**, the TS for biradical formation, and TS **33**, concerted cycloaddition of thioacetone *S*-methylide to thiobenzophenone (2,4-substituted dithiolane), could be determined properly, it was possible to calculate the Gibbs free energies of activation for both processes. The $\Delta G^{\neq}$ values are 17.3 kcal mol^{-1} for **33** and 15.2 kcal mol^{-1} for **37a**. The corresponding activation entropies are –47 (**33**) and –39 cal K^{-1} mol^{-1} (**37a**). This result confirms the presumption (see above) that consideration of activation entropy raises the calculated activation energies by ca. 10 kcal mol^{-1}.

In order to account for a possible methylene transfer by cleavage of biradical **36** to give thiobenzophenone *S*-methylide (**1**) and thioacetone (**32**), the energy of TS **39** for formation of biradical **36** from **1** + **32** was calculated (4.4 kcal mol^{-1}). From this barrier the activation energy of dissociation, **36** → **1** + **32**, results as 10.5 kcal mol^{-1}. Thus, methylene transfer is not competitive to ring closure. The structures and energies of **31** and **32** occurred in our previous paper,[7] but are repeated in the new context (Supporting Information).

Astonishingly, the activation barrier for the concerted addition of **31** + **3** (3.6 kcal mol^{-1}, TS **33**) is virtually identical with that for the reaction of **2** +**3** (3.7 kcal mol^{-1}, TS **24** in Figure 2), but these TSs, **24** and **33**, reveal an intriguing – and surprising – difference in their structure. While in **24** the incipient CS bond (2.83 Å) is longer than the CC σ-bond (2.74 Å), the opposite was observed for **33** (2.63 Å for CS, 2.95 Å for CC). The formation of the 2,4-substituted dithiolane **34** is with 50.8 kcal mol^{-1} exothermic, compared with 51 kcal mol^{-1} for the reaction of **2** + **3** to give **26**. Obviously, the change of van der Waals strain which is connected with the replacement of spiro(adamantylidene) by isopropylidene, influences reactants, TSs, and products to the same extent.

Alas, the 4,5-substituted dithiolanes differ in their cycloaddition energies: –25.1 kcal mol^{-1} for **28** (Figure 2) versus –35.9 kcal mol^{-1} for **35** (Figure 3) (structures **28** and **35**, see

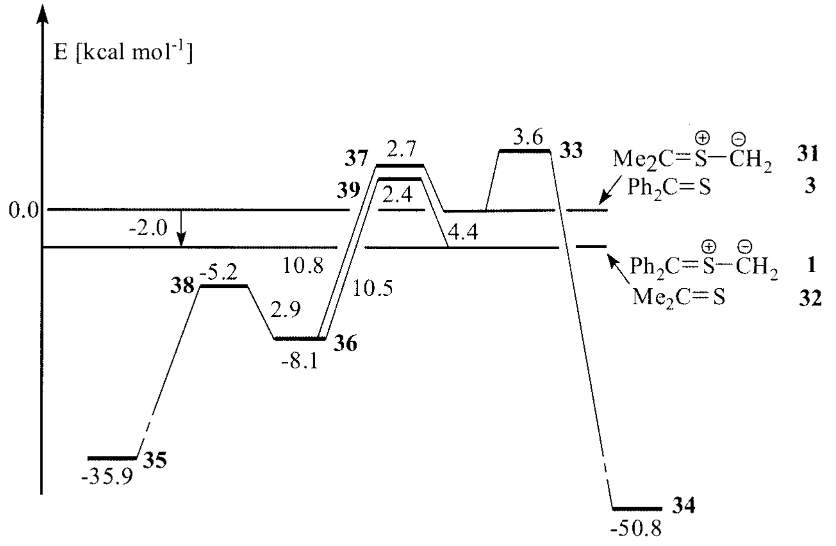


Figure 3. Section of the (U)B3LYP/6-31G* potential energy surface of the reaction of thioacetone *S*-methylide (**31**) with thiobenzophenone (**3**) and of thiobenzophenone *S*-methylide (**1**) with thioacetone (**32**) (kcal mol^{-1}).

Table 3. Reaction of thioacetone *S*-methylide (**31**) with thiobenzophenone (**3**), and of benzophenone *S*-methylide (**1**) with thioacetone (**32**). ((U)B3LYP/6-31G*) Energies relative to **3** + **32** in kcal mol^{-1}.

Structure	Δ ZPVE	μ [D]	E_{rel}	E_{rel} +Δ ZPVE
3+31	0.0			0.0
1+32	–0.2		–1.8	–2.0
33 (TS)[a]	1.0	2.7	2.6	3.6
34 (Prod)[a]	4.9	1.1	–55.7	–50.8
35 (Prod)	5.5	1.3	–41.4	–35.9
36 (I)[a]	1.1	0.3	–9.2	–8.1
37 (TS_{RC})	0.8[b]	3.0	1.9	2.7
37a (TS)[c]	0.8	3.8	2.8	3.6
38 (TS)	1.6	1.0	–6.8	–5.2
39 (TS_{RC})	0.8[b]	1.4	1.6	2.4

[a] TS = Transition structure, TS_{RC} = TS determined by reaction coordinate calculation, I = intermediate, Prod = product. [b] Δ ZPVE from **37a**. [c] True Ts, s^2 = 0, (RB3LYP = UB3LYP).

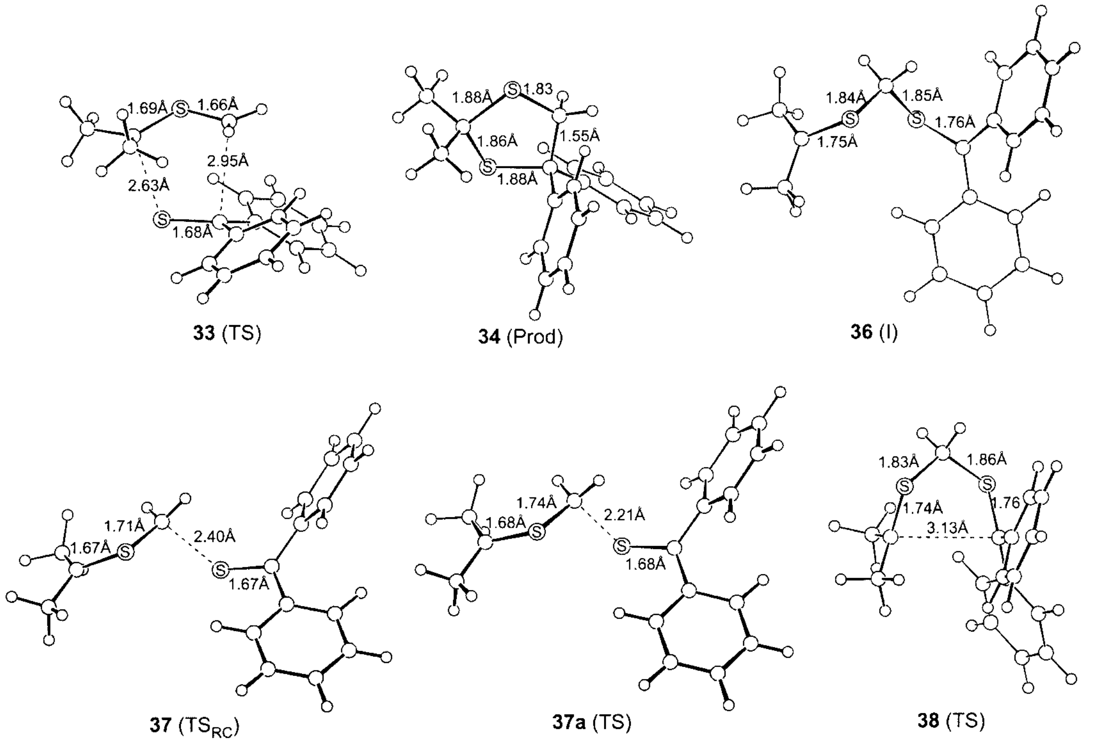
Supporting Information). Thus, the front strain between the voluminous substituents in 4- and 5-position of **28** claims an extra 10.8 kcal mol^{-1}. On the favored pathway to **35**, a barrier of 2.7 kcal mol^{-1} (TS, **37**) has to be overcome for the formation of *C*,*C*-biradical **36**,the formationof which is exothermic with –8.1 kcal mol^{-1}. The corresponding energies for the reaction of **2** + **3**, 2.2 kcal mol^{-1} for TS **25** and –8.8 kcal mol^{-1} for **27** (Figure 2), are surprisingly similar. On the other hand, the cyclization barriers of the biradicals reflect the developing front strain: 2.9 kcal mol^{-1} (TS, **38**) for **35** versus 6.1 kcal mol^{-1} (TS, **29**) for **28**.

It is to be expected that an experimental study (not carried out) would lead to a mixture of cycloadducts **34** and **35** with a slight preference for the biradical pathway. A conceivable methylene transfer would involve a return from biradical **36** to the second reactant level (**1** + **32**). The formation of **36** from **1** + **32** passes TS **39** (structure see Supporting Information) (Figure 3), 2.4 kcal mol^{-1} above the zero level. The activation energy of fragmentation of **36** to the level of **1** and **32**is 10.5 kcal mol^{-1}. Thus, again not competitive to ring closure.

Reactions of 2,2,5,5-tetramethylcyclopentanethione *S*-methylide (40) with thiobenzophenone (3) and of thiobenzophenone *S*-methylide (1) with 2,2,5,5-tetramethylcyclopentanethione (41) ((U)B3LYP/6-31G*): The reaction of 2,2,5,5-tetramethylcyclopentanethione *S*-methylide (**40**) with thiobenzophenone (**3**) leads to 95% of 4,4,5,5-tetraphenyl-1,3-dithiolane with liberation of 98% of tetramethylcyclopentanethione (**41**).[11] This is a consequence of complete methylene transfer from the aliphatic *S*-methylide to **3** yielding thiobenzophenone *S*-methylide (**1**), which then undergoes rapid cycloaddition to a second molecule of **3**. Can (U)B3LYP/6-31G* calculations reproduce this experimental observation (Figure 4, Table 4 and Scheme 9)?

The 1,3-dipolar part of the calculated structure of *S*-methylide **40** has C_s symmetry, and both CS bonds are 1.65 Å. The five-membered ring is twisted and the methylene group of **40** is arranged symmetrically between two methyl groups of the 2,2,5,5-tetramethylcyclopentane unit. Among the alkyl-substituted *S*-methylides **2**, **31**, and **40**, it is the latter, which carries the bulkiest alkyl group. This is reflected in the angle CSC, which increases from 113.6° in **31** to 116.5° in**2**and to 118.2° in **40**. Thione **41** has a normal CS bond length of 1.64 Å. Inspection of structure **40** indicates that the approach to the substituted terminus of the thiocarbonyl *S*-methylide should be highly sterically hindered. As in the previous cases, we restricted the calculations to the concerted formation of the 2,4-substituted 1,3-dithiolane **42** and the two-step pathway to the 4,5-substituted 1,3-dithiolane **43** via biradical **44**.

TS **45** for the concerted reaction leading to product **42** is located 9.4 kcal mol^{-1} above the energies of the reactants. It is characterized by lengths of 3.16 Å for the new CS and 2.37 Å for the new CC bond. It is interesting to note, that the corresponding bond lengths are 2.83 Å (CS) and 2.74 Å



33 (TS) **34** (Prod) **36** (I)

37 (TS_{RC}) **37a** (TS) **38** (TS)

Scheme 8. Selected TSs and intermediates in the cycloadditions of **31** + **3**. See Figure 3 and Table 3; additional structures can be found in the Supporting Information.

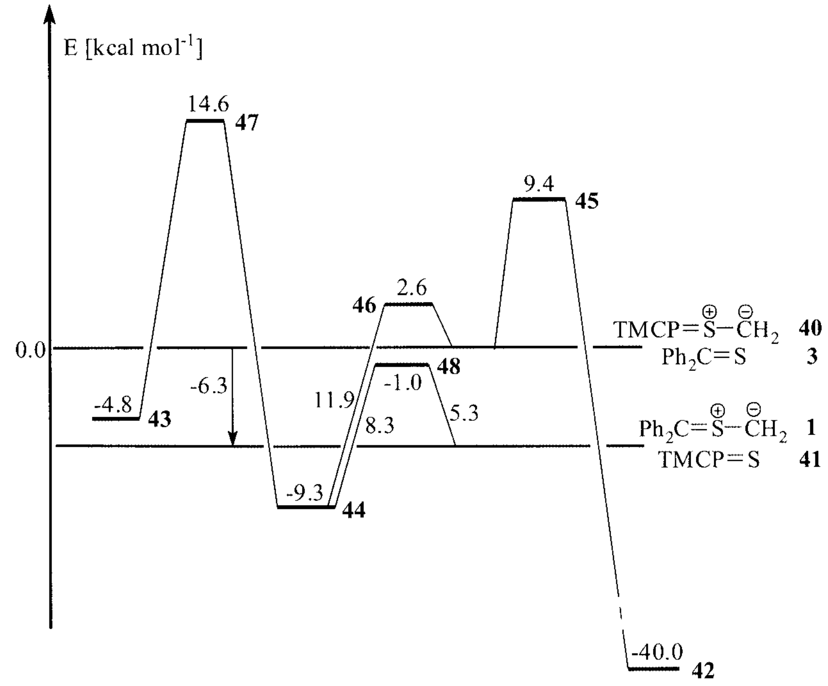


Figure 4. Section of the (U)B3LYP/6-31G* potential energy surface of the reaction of 2,2,5,5-tetramethylcyclopentanethione *S*-methylide (**40**) with thiobenzophenone (**3**) and of thiobenzophenone *S*-methylide (**1**) with 2,2,5,5-tetramethylcyclopentanethione (**41**) ($kcal\,mol^{-1}$).

(CC) in TS **24** (Figure 2 and Scheme 7, cycloaddition of **2** and **3**), and 2.63 Å (CS) and 2.95 Å (CC) in TS **33** (Figure 3 and Scheme 8, cycloaddition of **31** and **3**). Not unexpectedly, the activation energy, here 9.4 $kcal\,mol^{-1}$, is the highest in the series of TSs for the concerted formation of 2,4-substituted 1,3-dithiolanes. The presumption is that the voluminous group on the side of **40** leads to an elongation of the forming CS bond, which causes the increase in TS energy. In the least symmetric TS **45**, the van der Waals repulsion is insufficiently balanced by the energy of the incipient

Table 4. Reaction of 2,2,5,5-tetramethylcyclopentanethione *S*-methylide (**40**) with thiobenzophenone (**3**) and of thiobenzophenone *S*-methylide (**1**) with 2,2,5,5-tetramethylcyclopentanethione (**41**). [(U)B3LYP/6-31G*] Energies relative to **3** + **40** in kcal mol^{-1}.

Structure	Δ ZPVE	μ [D]	E_{rel}	E_{rel} +Δ ZPVE
3+40	0.0			0.0
1+41	–0.17		–6.1	–6.3
42 (Prod)[a]	4.2	0.6	–44.2	–40.0
43 (Prod)	5.1	1.2	–9.9	–4.8
44 (I)[a]	1.0	1.0	–10.3	–9.3
45 (TS)[a]	1.3	3.7	8.1	9.4
46 (TS$_{\text{RC}}$)	0.8[b]	3.4	1.8	2.6
47 (TS$_{\text{RC}}$)	1.6[c]	1.2	13.0	14.6
48 (TS$_{\text{RC}}$)	0.8[b]	1.1	–1.8	–1.0

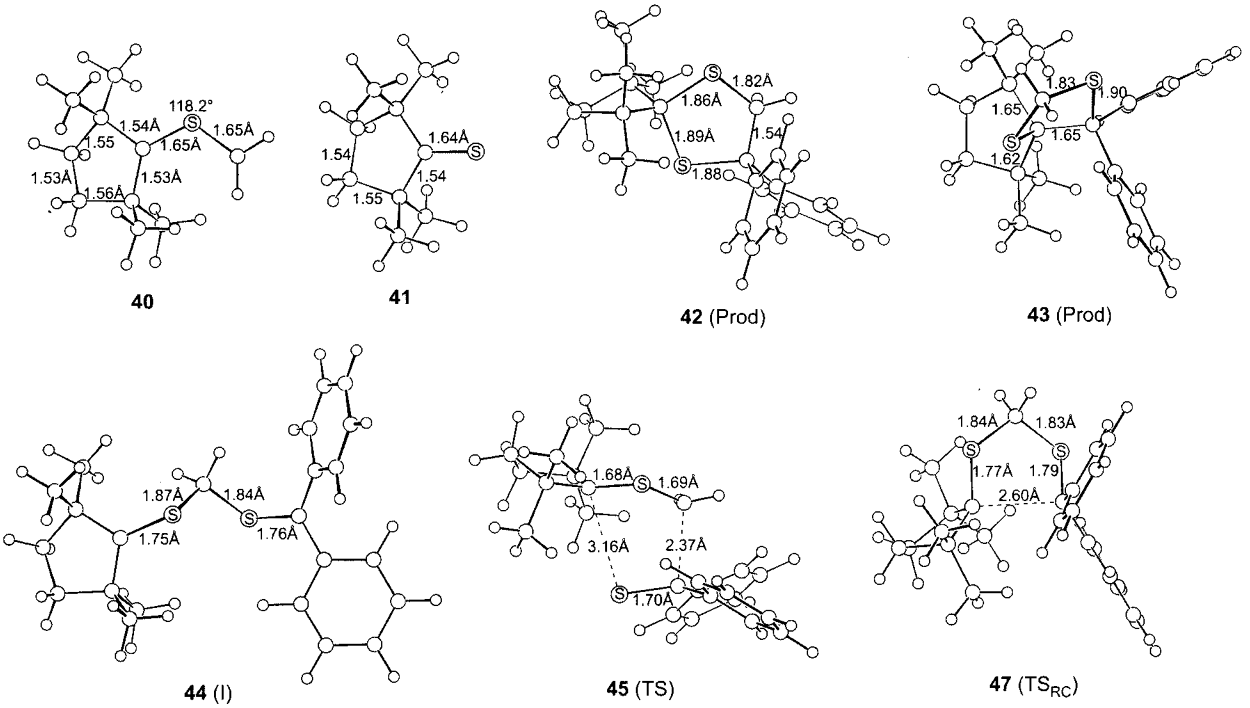
[a] TS = Transition structure, TS$_{\text{RC}}$ = TS determined by reaction coordinate calculation, I = intermediate, Prod = product. [b] Δ ZPVE from **37a**. [c] Δ ZPVE from **38**.

σ-bonds. The 2,4-substituted dithiolane **42**is likewise affected by the bulky aliphatic group, its energy level is at –40 kcal mol^{-1}, compared with –51.0 and –50.8 kcal mol^{-1} for the examples discussed above.

Biradical formation requires an activation energy of 2.6 kcal mol^{-1} (TS, **46**, structure see Supporting Information), as determined by a calculation taking the CS distance as reaction coordinate. Biradical **44** is found at –9.3 kcal mol^{-1}, which might be too low, due to the overestimation of biradical stability by the (U)B3LYP method.[7] However, more alarming is the barrier to ring closure of biradical **44**, again determined by a reaction coordinate calculation. The CC bond of **43** was successively elongated until – with an investment of 19.4 kcal mol^{-1} - the energy maximum **47** was reached at a CC separation of 2.6 Å (approximate TS for biradical formation). The energy is +14.6 kcal mol^{-1}, even higher than the activation energy of the concerted formation of **42** (TS, **45** at 9.4 kcal mol^{-1}). Thus, the cyclization barrier of *C*,*C*-biradical **44** amounts to a remarkable 23.9 kcal mol^{-1}.The energy level of cycloadduct **43** is obtained at –4.8 kcal mol^{-1}, slightly below the level of the reactants, showing a high CC bond length of 1.65 Å, i. e., by 0.11 Å longer than the CC bond of the positional isomer **42**. The difference in energy of **42** and **43**, 35.2 kcal mol^{-1}, is an approximate and impressive figure for the front strain in **43**.

As mentioned above, methylene transfer from the cycloaliphatic ylide **40** to thiobenzophenone (**3**) supersedes the cycloaddition. The open-chain *C*,*C*-biradical **44** exceeds dithiolane **43** by 4.5 kcal mol^{-1} in bond energy (or somewhat less). Nevertheless, **44** escapes a conceivable accumulation by flowing off through the channel of dissociation (Figure 4). Over a barrier of 8.3 kcal mol^{-1} (or less) and a stretching of the CS bond to 2.40 Å in TS **48** (for the structure see Supporting Information), the energy level of **1** + **41** is reached. Rapid cycloaddition of thiobenzophenone *S*-methylide (**1**) with an excess of **3** (no activation energy, irreversible under the reaction conditions) siphons off the *C*,*C*-biradical **44**. When two reactions with activation energies of 2.6 and 9.4 kcal mol^{-1} compete for **40** + **3**, the dominance of the methylene transfer is secured. The (U)B3LYP calculations are in complete agreement with the experimental findings.

In the three corresponding reactant pairs, the energy differences increase with the bulk of R_2C: –2.2 kcal mol^{-1} for



Scheme 9. Reactants, TSs, intermediate, and products from the reaction of **40** + **3**, and of **1** + **41**. See Figure 4 and Table 4; additional structures can be found in the Supporting Information.

isopropylidene (**31** + **3** minus **1** + **32**, Figure 3), –4.4 kcal mol^{-1} for adamantylidene (Figure 2), and –6.3 kcal mol^{-1} for tetramethylcyclopentylidene (Figure 4). The major contributor is probably the increased van der Waals strain in the *S*-methylides, **31** < **2** < **40**.

Conclusions

(U)B3LYP/6-31G* evaluation of the potential energy surface for the cycloadditions of adamantanethione *S*-methylide, thioacetone *S*-methylide, and 2,2,5,5-tetramethylcyclopentanethione *S*-methylide to thiobenzophenone leads to a consistent explanation of the experimental observations.

The ratio of regioisomeric dithiolanes and the switch from cycloaddition to methylene transfer are determined by two rate ratios, both of which are functions of the steric hindrance exerted by the aliphatic residues. The activation energy of the concerted mechanism (→ 2,4-substituted dithiolane) jumps up on going from thiocarbonyl ylide **2** to **40**, whereas the barriers of biradical formation on the two-step pathway change only little. The switching from the formation of the crowded 4,5-substituted dithiolane to methylene transfer occurs on the level of the *C*,*C*-biradical, when the barrier to cyclization surpasses that of dissociation.

Supporting Information (see also footnote on the first page of this article): Additional structures not mentioned in this article in the Figures, Tables of total energies, and coordinates of optimized structures.

Acknowledgments

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