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Regiochemistry in Cycloadditions of Diazomethane to Thioformaldehyde and Thioketones

Reiner Sustmann* and Willi Sicking

Institut für Organische Chemie der Universität Essen, Postfach 103 764, 4300 Essen 1, F.R.G.

Rolf Huisgen

Institut für Organische Chemie der Universität München, Karlstr. 23, 8000 München 2, F.R.G.

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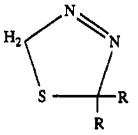
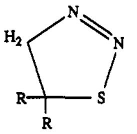
In cycloadditions of open-chain aliphatic thiones ($R_2C{=}S$, R = ethyl, *n*-propyl, isopropyl, and *tert*-butyl) to diazomethane mixtures of regioisomers were obtained; the ratio depends on R and solvent polarity. Ab initio RHF and CASSCF calculations (3-21G*, 6-31G*, CAS/3-21G*) and semiempirical calculations (AM1 and MNDO-PM3) are carried out on ground states, possible transition structures, and intermediates. Extensive ab initio calculations on the reaction of diazomethane with thioformaldehyde suggest that both regioisomers should be formed via concerted pathways. In contrast, AM1 and MNDO-PM3 advocate a concerted formation of the 1,3,4-thiadiazoline and a two-step reaction to the 1,2,3-isomer involving the electrocyclic ring closure of an intermediate of pentadienyl anion type. The ab initio calculations (3-21G*) favor the 1,2,3- over the 1,3,4-thiadiazoline for thioformaldehyde as dipolarophile by $\Delta\Delta H^{\ddagger} = 2.4$ kcal mol^{-1}, for dimethyl thioketone the $\Delta\Delta H^{\ddagger}$ value decreases to 0.5 kcal mol^{-1}, and for the diethyl compound both $\Delta H^{\ddagger}$ values are identical. A similar trend is observed for the 6-31G* basis set: the CASSCF single-point calculations of the 3-21G* transition structure for the reaction of thioformaldehyde reduces the difference in favor of the 1,2,3-isomer to 0.5 kcal mol^{-1}. The preference for the 1,2,3-thiadiazoline structure in more polar solvents is explained by the higher dipole moment (ca. 5 D as compared to ca. 2 D) of the transition structure. The ab initio calculations seem to be in better agreement with experiment than the AM1 or MNDO-PM3 results.

Thiones, recently termed superdipolarophiles in 1,3-dipolar cycloadditions,[1] add diazomethane not uniformly but lead to mixtures of regioisomers 1 and 2.[2-4] The ratio of regioisomers depends on solvent polarity and steric effects. Rising polarity of the solvent favors the production of 1,2,3-thiadiazolines 2 whereas increasing steric demand of the thione assists formation of the 1,3,4-isomer 1 (Table I). An explanation was attempted on the basis of competing concerted pathways; the polarity of the transition states and the energy gain by FMO interactions oppose each other as directing forces.[4]



1a: R=H
1b: R=Et
1c: R=*i*-Pr
1d: R=*t*-Bu



2a: R=H
2b: R=Et
2c: R=*i*-Pr
2d: R=*t*-Bu

A detailed quantum chemical analysis of ground states, transition structures, and possible intermediates is reported in which both semiempirical AM1 and MNDO-PM3 calculations and ab initio calculations on different levels (3-21G*, 6-31G*, CASSCF) are compared.

Table I. Cycloadditions of Diazomethane to Dialkyl Thioketones at 0 °C: Ratio of Regioisomeric Thiadiazolines 1/2[4]

	solvent		
$R_2C{=}S$, R =	pentane	diethyl ether	methanol
CH_2CH_3	75:25	62:38	13:87
$CH_2CH_2CH_3$	77:23	73:27	19:81
$CH(CH_3)_2$	87:13	85:15	40:60
$C(CH_3)_2$	100:0	100:0	100:0

Semiempirical Calculations

Using the PM3 parametrization of the MNDO method[5] we searched by RHF calculations the potential energy surface for the interaction of diazomethane with thioformaldehyde and some of its alkyl derivatives. Stationary points were also determined with AM1.[6] The RHF method imposes a closed-shell nature on the reaction path and says nothing about the occurrence of biradical intermediates. As the biradical character turns out to be rather small in the ab initio CASSCF calculations (see below), the chosen approach seems to be reasonable. Before a systematic analysis of the potential energy surface was undertaken, preliminary calculations were carried out. The product structure served as a starting point, and two movements were performed: (1) One of the newly formed bonds was elongated systematically while allowing all other parameters to be optimized. (2) The same procedure was

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Table II. MNDO-PM3 and AM1 (in Parentheses) Calculated Properties of Ground States of Reactants and Products, Transition Structures, and Intermediates in the Cycloaddition of Diazomethane to Thioketones[a]

structure	ΔH_f° (kcal/mol)	μ (D)	selected bond lengths (Å) MNDO-PM3	
1a	47.0 (44.4)	0.60 (0.76)	$r_{CS} = 1.84$	$r_{CN} = 1.49$
1b	32.4 (29.8)	0.87 (1.12)	1.83	1.53
1c	27.1 (25.5)	0.86 (1.00)	1.83	1.52
1d	28.1 (27.9)	0.89 (1.02)	1.83	1.52
2a	33.6 (37.8)	3.50 (3.41)	$r_{NS} = 1.76$	$r_{CC} = 1.54$
2b	19.6 (22.9)	3.76 (3.70)	1.76	1.56
2c	12.1 (18.9)	3.95 (3.83)	1.76	1.56
2d	13.0 (25.9)	3.86 (3.77)	1.76	1.56
3a	107.1 (94.3)	3.62 (2.29)	$r_{CS} = 1.98$	$r_{CN} = 2.71$
3b	82.7 (68.9)	1.76 (1.64)	1.87	2.74
3c	78.2 (65.0)	1.62 (1.92)	1.86	2.72
3d	79.1 (70.2)	1.70 (1.41)	1.89	2.74
4a	103.1 (101.5)	1.81 (0.93)	$r_{NS} = 2.40$	$r_{CC} = 5.54$
4b	78.0 (72.0)	1.54 (3.08)	2.38	5.51
4c	72.1 (67.9)	1.50 (3.04)	2.37	5.55
4d	70.9 (70.6)	1.20 (2.09)	2.35	5.64
5a	84.1 (70.7)	4.07 (2.85)	$r_{NS} = 1.69$	$r_{CC} = 3.27$
5b	60.3 (47.7)	4.74 (2.71)	1.71	3.90
5c	55.2 (56.1)	4.73 (1.84)	1.71	4.05
5d	59.7 (46.2)	2.81 (1.48)	1.75	4.33
7a	100.1 (95.0)	2.71 (2.31)	$r_{NS} = 1.76$	$r_{CC} = 2.56$
7b	78.6 (72.1)	3.45 (2.45)	1.80	2.79
7c	71.7 (68.1)	3.69 (2.59)	1.80	2.85
7d	72.4 (73.5)	3.47 (2.51)	1.80	2.85
9a	116.7 (98.7)	6.06 (4.42)	$r_{NS} = 2.75$	$r_{CC} = 2.13$
9b	(77.3)	(4.20)	2.41	2.29[b]
9c	(77.4)	(4.16)	2.39	2.34[b]
9d	(81.0)	(3.86)	2.41	2.36[b]
H_2CN_2	61.0 (62.6)	1.92 (1.33)	$r_{CN} = 1.296$	$r_{NN} = 1.137$
H_2CS	37.6 (29.9)	2.07 (1.84)	$r_{CS} = 1.538$	
Et_2CS	12.1 (2.1)	3.01 (2.65)	$r_{CS} = 1.576$	
i-Pr_2CS	5.3 (−2.4)	3.06 (2.82)	$r_{CS} = 1.588$	
t-Bu_2CS	5.4 (−1.4)	2.95 (2.66)	$r_{CS} = 1.598$	

[a] Notation **a**–**d** refers to formulas **1** and **2**. [b] AM1 calculation.

followed for the second new bond. This procedure allows one to overview the energy surface, and in particular hints at a concerted versus closed-shell stepwise process.

Now starting at separations of the reactants of ca. 5.5 Å, the potential energy surface was established systematically. A grid was obtained representing the distances between the reacting centers. At each point of the grid a complete geometry optimization was performed with the restriction that the separation of the reacting atoms was kept constant. The location of the saddle points was refined with gradient techniques of the program package SCAMP.[7] Each saddle point is characterized by one negative vibrational frequency, thus characterizing it as a true transition structure. The data for starting molecules, saddle points, intermediates, and final products are collected in Table II.

The reaction of diazomethane with thioformaldehyde giving 1,3,4-thiadiazoline **1a** (R = H) displays a shallow potential energy surface (Figure 1). At a separation of 5.5 Å for the C–N bond and 4.0 Å for the S–C bond, the ΔH°_f of the molecular complex is 0.2 kcal mol^{-1} above that of the sum of the separated molecules. We first investigated the formation of the two new bonds separately. The C–N distance of 5.5 Å was chosen to permit a linear structure of the complex. One-bond formations correspond to pathways along the rear and the right border of the grid. One distance is shortened systematically while allowing all other degrees of freedom of the complex to be optimized. The energy increases steadily in both directions without passing through a maximum which might indicate an intermediate.

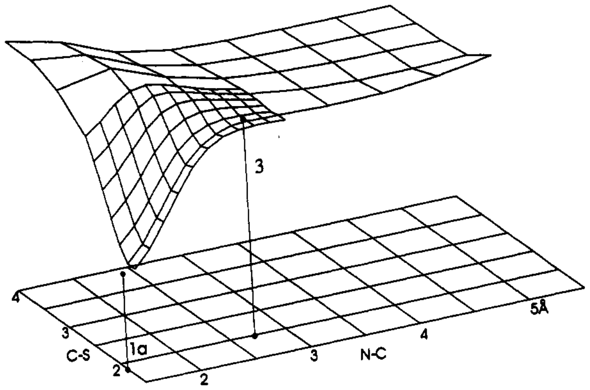
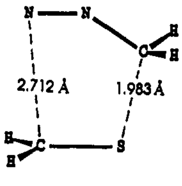


Figure 1. MNDO-PM3 potential energy surface for the formation of 1,3,4-thiadiazoline from diazomethane and thioformaldehyde. Numbers refer to structural formulas.

If the separation of both atom pairs was shortened simultaneously, corresponding to a walk across the surface, the saddle point **3** is located at a C–N distance of 2.71 Å and a S–C distance of 1.98 Å; thus, the S–C bond has been formed to a greater extent than the C–N bond. Diazomethane is slightly bent and the hydrogen atoms point away from the thione. This distortion is very similar to that found for the cycloaddition of diazomethane to ethyl vinyl ether and ethoxyacetylene.[8] Thioformaldehyde on the other hand does not yet show sizable geometrical changes. In the final product **1a** the bond lengths were determined as 1.84 Å for S–C and 1.49 Å for C–N. The corresponding ab initio calculated valued are (3-21G*) S–C = 1.82 Å and C–N = 1.50 Å. A pictorial representation of the MNDO-PM3 transition structure is given in **3**, the heat of formation can be found in Table II.



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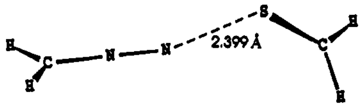

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The MNDO-PM3 analysis of the regioisomeric approach led to an unexpected result. The search was started at a C–C distance of 6.0 Å and a N–S distance of 4.0 Å (upper right edge of the grid in Figure 2). At these separations the heat of formation equals that of the sum of the values for the isolated molecules. The separation of the two reacting carbon atoms being decreased, one moves along the rear border of the grid. A steady increase of the heat of formation is observed, i.e., no intermediate is found. If, on the other hand, the N and S atoms approach each other, a transition structure **4**, 4.5 kcal mol^{-1} higher in energy than the reactants, is discovered at a N–S bond distance of 2.40 Å and a C–C separation of 5.54 Å. Both molecules almost retain their ground-state geometry. If one continues from this saddle point, the reacting complex falls into the trough of intermediate **5**. Bond distances and

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[7] We thank Dr. T. Clark, Universität Erlangen-Nürnberg for a copy of the program SCAMP in which we incorporated the MNDO-PM3 parameters.

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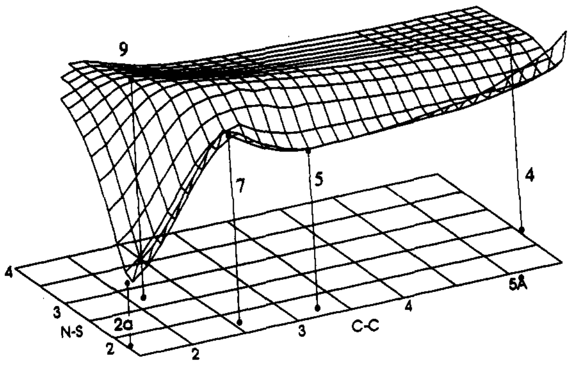
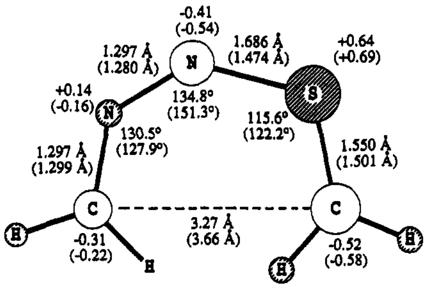


Figure 2. MNDO-PM3 potential energy surface for the formation of 1,2,3-thiadiazoline from diazomethane and thioformaldehyde. Numbers refer to structural formulas.

angles calculated by MNDO-PM3 and AM1 (in brackets) are given in **5**; the area of the circles is a measure of the MNDO-PM3 charge distribution. The structure is very similar to that of the CAS(6,5)/3-21G* calculation for **20** (see below).



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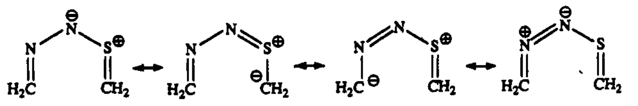
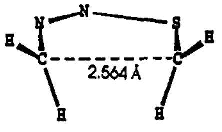
All atoms in the U-shaped molecule lie in one plane, including the hydrogen atoms of the CH_2 groups. Almost no change in the CN bond length in the former diazomethane subunit is observed, whereas the NN bond is elongated by 0.16 Å. The CS bond of the thione remains almost untouched, the new NS bond is by 0.07 Å (MNDO-PM3) shorter than in the final product. The polar nature of the molecule can be derived from the total charges at the individual atoms, visualized by the area of the circles around the atoms. Sulfur is positive, underlining its onium character. The terminal carbon atoms on the other hand are negatively charged. This charge distribution can be rationalized most easily by drawing resonance structures **6a–d** which are participating with decreasing weight. The steric interaction of the inward-pointing methylene group hydrogens results in a widening of the inner bond angles to 134.8° (MNDO-PM3) and 151.2° (AM1); no out of plane rotation of the methylene groups is observed.



6a 6b 6c 6d

The existence of lone pair electrons at S and sp hybridization at the terminal N atom of diazomethane enable a structure where through-conjugation exists. It is easily recognized that intermediate **5** harbors a conjugated 6π system of the pentadienyl anion type. In the classification of heterosubstituted pentadienyl anions,[9] **5** shows two isoionic exchanges (N atoms) and one isoelectronic exchange (S atom). The structures **6a–c** reveal the sulfonium-substituted pentadienyl anion in accordance with the +0.6 to +0.7 charge of S in **5**. The conversion **5** → **2a** constitutes an electrocyclic ring closure the transition state of which is shown for R = H in **7**. Electrocyclizations of heterosubstituted pentadienyl anions and the corresponding ring openings of cyclopentenyl anion type compounds justify a superlative in their importance for heterocyclic chemistry.[9] The rules of conservation of orbital symmetry impose a disrotatory course; this was experimentally established by a stereospecificity of >99.7%.[10] The HOMO symmetry of **8**—S is located in the nodal plane—leaves no doubt that the bonding of the terminal centers requires disrotation.



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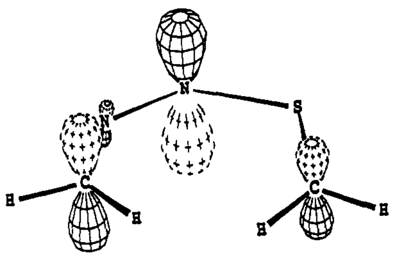

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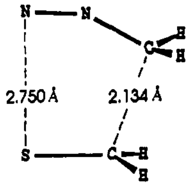

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The evaluation of the potential energy surface revealed also a saddle point **9** for the concerted formation of the cycloadduct. This mechanism, however, requires an activation enthalpy which is higher than that for the two-step process by 13.5 kcal mol^{-1} (MNDO-PM3). The AM1 calculation leads qualitatively to a result analogous to the ab initio analysis (see below). The concerted pathway is preferred by 2.8 kcal mol^{-1}. Schematically the situation is represented in Figure 3. According to MNDO-PM3 the 1,2,3-thiadiazoline (**2a**) should be formed via the two-step process, whereas AM1 favors the 1,3,4-thiadiazoline (**1a**) via the concerted reaction pathway. The two parameterizations of the MNDO method thus lead to opposite results. Obviously, this is the consequence of different parameterization procedures. In our analysis we relied originally only on that of MNDO-PM3, because at that

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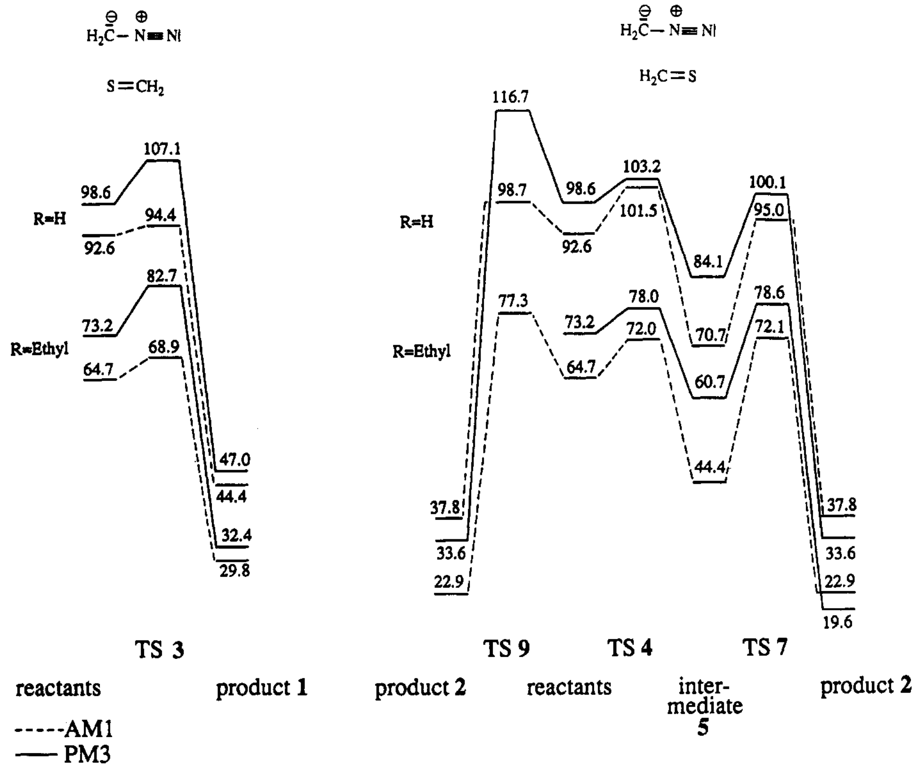

Figure 3. Schematic representation of heats of formation (MNDO-PM3 and AM1) for various stages of the cycloaddition of thioformaldehyde and diethyl thioketone to diazomethane.

time the AM1 parameters for sulfur were unknown yet. In the AM1 calculations reported here we used the newly determined S parameters.[11]

The scheme of Figure 3 indicates that intermediate **5** (R = H) is located below the level of the reactants. In the experimental work,[4] diazomethane was not reacted with thioformaldehyde but rather with thioketones $R_2C{=}S$, R = ethyl, *n*-propy, isopropyl, and *tert*-butyl (Table I). On extending the calculations to the cycloadditions of dialkyl thioketones (Table II), we could not locate transition structures for the concerted formation of the substituted 1,2,3-thiadiazolines by the MNDO-PM3 procedure. Therefore, only AM1-calculated heats of formation are reported in Table II and Figure 3. In Figure 3 we display the results for diethyl thioketone. Both semiempirical schemes favor the two-step formation of **2b** (R = ethyl). In the overall preference, however, they lead to the opposite conclusion. MNDO-PM3 would predict **2b**; AM1 on the other hand shows preference for **1b**. As can be deduced from Table II the general picture is not altered for R = isopropyl and *tert*-butyl in $R_2C{=}S$.

The intermediate **5** from the reaction of diazomethane and thioformaldehyde presents itself in a planar structure, thus allowing for maximum delocalization (MNDO-PM3). Geometry optimization of the U conformation for the substituted cases unveiled likewise planar structures for the ethyl- and isopropyl-substituted examples. As long as one hydrogen atom remains at C_α of the CS double bond strong steric interaction with the methylene group of diazomethane can be avoided. The *tert*-butyl-substituted thioketone lacking such a hydrogen atom does not allow the U conformation; the pentadienyl unit assumes a nonplanar conformation.

Ab Initio Calculations

Using the Gaussian 90 program[12] extensive RHF calculations were done with a 3-21G* basis set on the hypothetical cycloaddition of diazomethane to thioformaldehyde. After locating stationary points on the potential energy surface for this system, we included the methyl- and ethyl-substituted thione in the analysis. Some stationary points were reoptimized with a 6-31G* basis set, and single-point CAS(6,5) calculations pertain to the 3-21G* transition structures. Ground states of reactants and intermediates were analyzed on different theoretical levels. The results are collected in Table III.

The structural data for diazomethane for which other calculations have been reported[13] are in agreement with experimental findings.[14] No direct comparison with experimental data is possible for the dienophiles; the CS double bond length, however, conforms to related bonds.[15] The dipole moment of 2.05 D (3-21G*) for thioformaldehyde demonstrates a polarity which is comparable to that of formaldehyde (μ = 2.33 D)[16] although the origin of the polarity is different. In formaldehyde it is mainly due to the polarization of the π electrons whereas in thioformaldehyde the lone-pair electrons at sulfur cause the polarity.

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Table III. Energies and Dipole Moments of ab Initio Calculations on Ground States of Reactants and Products

molecule	basis set	method	dipole moment (D)	total energy (au)	ZPVE[a] (kcal mol^{-1})
diazomethane	3-21G*	RHF	1.50	−146.995 821	21.42
	6-31G*	RHF	1.54	−147.843 784	21.57
	3-21G*//	CAS(4,4)	1.75	−147.040 151	
	3-21G*	CAS(4,4)	1.79	−147.040 602	
thioformaldehyde	3-21G*	RHF	2.05	−434.446 459	16.82
	6-31G*	RHF	2.23	−436.506 457	16.85
	3-21G*//	CAS(2,2)	1.69	−434.476 325	
dimethyl thioketone	3-21G*	RHF	3.15	−512.101 664	55.20
	6-31G*	RHF	3.34	−514.593 988	55.08
diethyl thioketone	3-21G*	RHF	3.16	−589.738 223	94.24
1,3,4-thiadiazoline	3-21G*	RHF	1.60	−581.499 515	44.13
1,2,3-thiadiazoline	3-21G*	RHF	4.12	−581.500 981	44.19
2,2-dimethyl-1,3,4-thiadiazoline	3-21G*	RHF	1.55	−659.148 826	81.70
5,5-dimethyl-1,2,3-thiadiazoline	3-21G*	RHF	4.44	−659.143 639	81.85
2,2-diethyl-1,3,4-thiadiazoline	3-21G*	RHF	1.69	−736.780 959	120.21
5,5-diethyl-1,2,3-thiadiazoline	3-21G*	RHF	4.52	−736.774 469	120.42

[a] ZPVE = zero point vibrational energy.

Table IV. Energies and Dipole Moments of ab Initio Calculations on Transition Structures 10–19

transition structure	basis set	total energy (au)	ZPVE[a] (kcal mol^{-1})	dipole moment (D)	ΔH^*, kcal mol^{-1}	$\Delta\Delta H^*$, kcal mol^{-1}
10	3-21G*	−581.429 496	41.33	2.80	8.0	2.4
11	3-21G*	−581.433 329	41.03	5.40	5.6	
12	3-21G*	−659.074 573	79.05	2.53	14.4	0.6
13	3-21G*	−659.075 395	78.88	5.52	13.8	
14	3-21G*	−736.709 924	117.73	2.33	15.1	0.0
15	3-21G*	−736.709 940	117.59	5.31	15.1	
16	6-31G*	−584.324 757	41.47	2.62	16.0	6.2
17	6-31G*	−584.334 569	41.24	6.14	9.8	
18	6-31G*	−662.399 905	79.11	2.15	23.7	5.1
19	6-31G*	−662.408 192	79.04	6.38	18.6	
10	CAS(6,5)//3-21G*	−581.495 317		2.58	9.0	0.5
11	CAS(6,5)//3-21G*	−581.496 133		4.78	8.5	

[a] ZPVE = zero point vibrational energy.

RHF calculations on 1,3-dipoles have often been criticized because these molecules are supposed to possess more or less biradical character.[13] This had been shown by more advanced calculational procedures. Only recently the difference in energy between RHF and UHF calculations was proposed as a measure of the biradical contribution to the ground state.[17] Proper account of this feature can be taken only in MCSCF calculations. We carried out CASSCF calculations where the active space was defined as consisting of the occupied and unoccupied π MOs of diazomethane which take part in the cycloaddition process. Besides the three π MOs of the heteroallyl system a fourth unoccupied MO having a small π contribution had to be included in the CASSCF calculation in order to achieve convergence in the geometry optimization. According to this analysis (CAS(4,4)/3-21G* calculation) the wave function has the structure: $\Psi = 0.97\Phi_1 - 0.22\Phi_2$ with negligible contributions from other electronic configurations. Φ_1 corresponds to the ground-state electronic configuration of the 4π-electron heteroallyl system, in Φ_2 the two HOMO electrons have been promoted to the LUMO. Taking 2 × fraction $\Phi_2{}^2$ in Ψ as a measure of the biradical character,[18] we must conclude that diazomethane carries only 10% biradical character. This is also in agreement with the RHF–UHF approach[17] and other calculations.[13] In ozone, on the other hand, the same electron configurations contribute according to a CAS(4,4)/3-21G* calculation 64% (Φ_1) and 34% (Φ_2).[19] Thus, this 1,3-dipole has a much higher biradical character (23%) in its ground state as was postulated some time ago.[20] *It has to be remembered, however, that the notion biradical cannot be interpreted in terms of a structure with two unpaired electrons where these behave like electrons in mono radicals, a common misunderstanding.*

A CASSCF calculation (CAS(2,2)//3-21G*) for thioformaldehyde with the π and π^* MO as active space gave about 6% contribution of the configuration with both π electrons in the π^* MO, i.e. the biradical character (12%) is small.

An interesting trend is observed for the stability of the regioisomeric thiadiazolines. For thioformaldehyde as dipolarophile the 1,2,3-isomer is slightly more stable than the 1,3,4-isomer (0.9 kcal mol^{-1}). Methyl and ethyl substitution reverse this trend; the 2,2-diethyl-1,3,4-thiadiazoline is 4.1 kcal mol^{-1} more stable than its regioisomer. This observation seems to reflect the influence of the size of the alkyl group, i.e., a steric effect. If some of this phenomenon were already present in the

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[20] Hay, P. J.; Dunning, T. H., Jr.; Goddard, W. A. III. *Chem. Phys. Lett.* **1973**, *23*, 457. Hay, P. J.; Dunning, T. H., Jr.; Goddard, W. A. III. *J. Chem. Phys.* **1975**, *62*, 3912. Hay, P. J.; Dunning, T. H., Jr. *J. Chem. Phys.* **1977**, *67*, 2290. Goddard, W. A. III; Dunning, T. H., Jr.; Hunt, W. J.; Hay, P. J. *Acc. Chem. Res.* **1973**, *6*, 368.

Table V. Total Energies from ab Initio Calculations (au), Heats of Formations from MNDO-PM3 Calculations (kcal mol^{-1}), Relative Energies (kcal mol^{-1}) with Respect to Minimum Energy Structure (in Parentheses), and Dipole Moments in Brackets) for Adducts 20–23 from Diazomethane and Thioformaldehyde

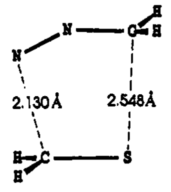
method	20	21	22	23
RHF 3-21G*	−581.391 348 (+17.8)[a] [4.72]	−518.419 750 (0.0) [1.28]	−581.386 506 (+20.8)[a] [4.56]	−581.412 352 (+4.6) [1.46]
CAS(6,5)//3-21G*	−581.463 514 (+18.4) [4.43]	−581.492 921 (0.0) [1.09]	−581.463 997 (+18.1) [3.67]	−581.487 574 (+3.3) [0.76]
CAS(6,5)/3-21G*	−581.466 348 (+18.6) [4.43]	−581.496 089 (0.0) [1.04]	−581.468 225 (+17.5) [3.50]	−581.491 173 (+3.1) [0.70]
MNDO-PM3 (kcal mol^{-1})	84.1 (+3.4) [4.07]	80.7 (0.0) [2.11]	88.5 (+7.8) [4.10]	84.1 (+3.4) [2.57]

[a] The molecule was kept planar because 20 and 22 are not minima on the potential energy surface; all other parameters optimized.

transition state of the cycloadditions it would represent a simple rationalization of the experimental results where the 1,3,4-thiadiazoline is preferred with increasing bulk of the substituent. The cycloaddition of thioformaldehyde to diazomethane is exothermic by about 36–37 kcal mol^{-1}.

The following procedure was adopted to locate transition structures for cycloaddition. In order to save computation time, we first carried out semiempirical MNDO-PM3 calculations[5,7] (see above) and then started the ab initio calculations with the so obtained structures (3-21G*). The stationary points were true saddle points characterized by only one negative vibrational frequency. For thioformaldehyde as dipolarophile the transition structures were refined by 6-31G* calculations. CASSCF calculations on the 3-21G* geometries were performed in order to study the influence of configuration interaction. Six electrons in five MOs were included where the latter were those which originated from the heteroallyl system and the CS π-bond. The results in Table IV correspond to the structural features in formulas 10–19.

It is not surprising that the complexes display different separations of the reacting atoms. Due to the lack of symmetry, the lengths of the two new bonds are rather different in the transition structures. The structures leading to the 1,3,4-thiadiazolines are more compact than those giving the 1,2,3-isomer. In the latter case the forming SN bond is 0.6–0.9 Å longer than the CC bond. The 6-31G* basis set leads to a slightly more symmetrical transition structure for the 1,3,4- and to a less symmetrical one for the 1,2,3-regioisomer as compared to the 3-21G* calculation. Diazomethane is bent and nonplanar; the thiones assume a pyramidalized C-atom at the double bond. The bond lengths of the reactants have been elongated slightly, the effect being more pronounced for the CS double bond.



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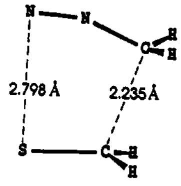

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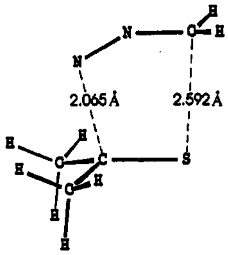

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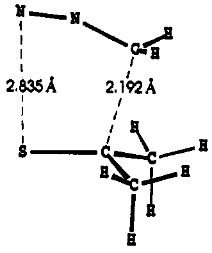

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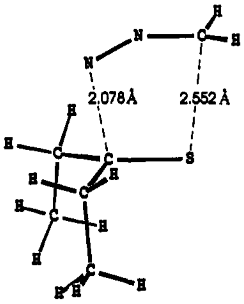

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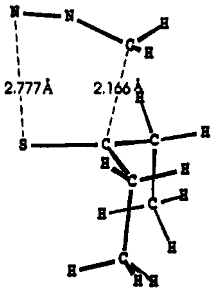

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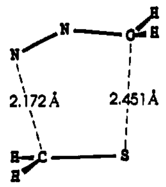

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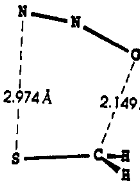

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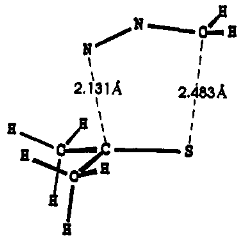

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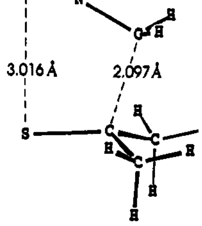

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The activation enthalpies (3-21G* basis set) are low and favor the 1,3,4-isomer by 2.4 kcal mol^{-1} for thioformaldehyde as dipolarophile; this is unaffected by including the zero point vibrational energy (ZPVE). The difference decreases to 0.6 kcal mol^{-1} or zero, respectively, for dimethyl and the diethyl thioketone. The same trend was noticed for the energies of the products. The calculations with the 6-31G* basis set display higher activation enthalpies, greater $\Delta\Delta H^{\ddagger}$ values, and percentage-wise a smaller decrease in $\Delta\Delta H^{\ddagger}$ for the unsubstituted and dimethyl-substituted thione. Higher activation enthalpies for calculations with the 6-31G* basis set as compared to the 3-21G* basis set have been observed before and are quite common.[21] The single-point CAS(6,5) calculation with the 3-21G* transition structure leads to a preference of 0.5 kcal mol^{-1} for the 1,2,3-thiadiazoline with thioformaldehyde as dipolarophile. There are small differences in total energy for CASSCF calculations which were carried out as a single-point calculation on a 3-21G* optimized structure and a calculation where the structure was refined by CASSCF. This, however, seems to be not relevant in our case. At the moment the GAUSSIAN 90

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(21) Houk, K. N. *Pure Appl. Chem.* 1989, *61*, 643.

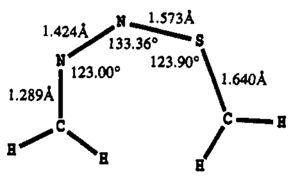
program does not allow the refinement of the transition structure under CASSCF conditions. The values for $\Delta H^{\ddagger}$ and $\Delta\Delta H^{\ddagger}$ in Table IV support the experimental results as well as can be expected from isolated molecule evaluations. A direct comparison is possible for the diethyl-substituted thione where the calculation with the 3-21G* basis set indicates a 1:1 mixture of the regioisomers. In pentane the experimental ratio is 75:25 (Table I).[4]

The dipole moments of the transition structures for the regioisomeric thiadiazolines differ by 2.6–4.2 D (Table IV). This suggests that structures **11**, **13**, **15**, **17**, and **19** will be more stabilized in polar solvents than the others which lead to the 1,3,4-thiadiazoline structure. This is again in line with the experimental findings (Table I) and resembles the alignment of dipole moments of the reactants invoked earlier.[4]

The AM1 and MNDO-PM3 calculation (see above) favored a two-step process for the formation of the 1,2,3-thiadiazoline; first, a pentadienyl anion-like structure is generated which undergoes electrocyclic ring closure. Different conformations of pentadienyl anion-like structures which might be intermediates in the cycloaddition were not only calculated by MNDO-PM3 (ΔH°_{f} values for optimized structures in Table V) but also by ab initio procedures. On the basis of the MNDO-PM3 results ab initio calculations for the pentadienyl anion type structures **20**–**23** were performed (Table V). Formulas **20**–**23** represent CAS(6,5)/3-21G* calculated structures. Two of the four possible conformations (**21** and **23**) are energy minima on the 3-21G* energy surface; the U-form **20** becomes a minimum in the CASSCF calculation. If all geometrical parameters are optimized with the 3-21G* basis set, then the CH_2N unit in **20** rotates about the NN bond to end up in the S form **21** which is the most stable one. Structure **22** likewise is not a minimum on the 3-21G* potential energy surface, since it transforms to the extended conformation **23**. Relative to transition structures **10** and **11**, **20** which constitutes a possible intermediate for electrocyclic ring closure is 24–26 kcal mol^{-1} (3-21G*) or 20 kcal mol^{-1} (CAS(6,5)//3-21G*) higher in energy.

In connection with the mechanistic problem it is important to note that the transition structures for both reactions are lower in energy than the ground state structure **20**. This excludes **20** as intermediate, at least for the unsubstituted thione and under isolated molecule conditions. Only the *S* form **21** from which product formation without rotation about the NN bond is not possible is energetically comparable to **10** and **11** (CAS(6,5)//3-21G*). However, such open-chain molecules might become intermediates in the formation of cycloadducts for suitably substituted cases and in solution and should not be excluded a priori.

CASSCF/3-21G* calculations enable an assessment of the biradical character of the structures. With the inclusion of the π MOs of the pentadienyl system the active space comprises 6 electrons in 5 MOs. The wave function of the most stable structure **21** can be written as $\Psi = 0.92\Phi_1 - 0.29\Phi_2 - 0.17\Phi_3$; other individual electron configurations contribute less than 1% to the total wave function. Φ_1 is the ground-state configuration with the three lowest π MOs doubly occupied $(\pi_1\pi_2\pi_3)^2$, Φ_2 has the two electrons in the HOMO moved to the LUMO $(\pi_1\pi_2\pi_4)^2$, and Φ_3 is the configuration $(\pi_2\pi_3\pi_5)^2$. According to the above procedure the biradical character is 17%.



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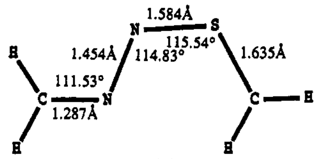

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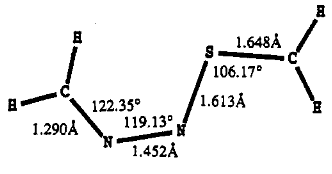

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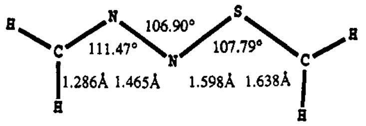

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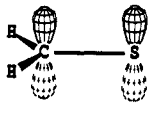
Discussion

The formation of regioisomeric 1,2,3- and 1,3,4-thiadiazolines in cycloadditions of diazomethane to thiones was qualitatively explained on the basis of concerted mechanisms.[4] This hypothesis has now been corroborated by the ab initio calculations. The transition structures (TS) for the formation of both regioisomers have been located (3-21G* and partly 6-31G* basis set). The products are formed via unsymmetrical TS, and their formation requires only little activation. The 1,2,3-thiadiazoline is favored for thioformaldehyde, but this preference vanishes in going to thioacetone and diethyl thioketone. In the latter case direct comparison with experiment is possible: 3-21G* calculations suggest a 1:1 mixture of the two thiadiazolines. Energywise, neglecting contributions from $\Delta S^{\ddagger}$, this is very close to the 3:1 ratio in favor of the 2,2-diethyl-1,3,4-thiadiazoline (**1b**) observed in pentane as solvent. The CASSCF calculations attribute only little biradical character to the TS.

As indicated in the introduction (Table I), the regioselectivity of the addition of diazomethane to thioketones shifts toward the 1,2,3-thiadiazoline in polar solvents. In our calculations this is rationalized in terms of the polarity of the TS. The TS leading to **2** display dipole moments of ca. 5 D as compared to ca. 2 D for the TS giving rise to **1**; therefore, **2** should be favored in more polar solvents.

A rationalization of regioselectivity in terms of frontier MOs is popular: **24**–**27** are the FMOs of diazomethane and thioformaldehyde as obtained by the 3-21G* basis set. Their structures are very similar to those calculated with the MNDO-PM3 or AM1 method and reported for diazomethane in ref 8. For thiones results are reported in ref 22. This demonstrates that semiempirical procedures which can be applied much easier and to much bigger systems lead here to results comparable with ab initio calculations. Within the framework of FMO theory, the MNDO-PM3 energies of the frontier molecular orbitals of diazomethane (HOMO = −9.23 eV, LUMO = +0.88 eV) and thioformaldehyde (HOMO = −12.21 eV, LUMO = −1.44 eV) classify the cycloadditions as $\mathrm{HOMO}_{CH_2N_2}$ − LUMO_{CH_2S} controlled. According to the magnitude of the eigenvector coefficients, which can be deduced qualitatively from the size of the p-AOs, no preference would be predicted for the formation of the regioisomeric thiadiazolines. The structure of the MOs suggests a mixture of regioisomers.



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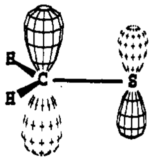

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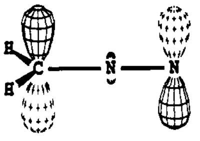

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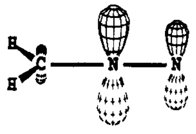

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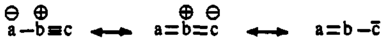
The semiempirical calculations suggest a change of mechanism for the formation of 1,2,3-thiadiazolines. Both the AM1 and the MNDO-PM3 procedures favor a pentadienyl anion type intermediate which subsequently undergoes electrocyclization. This pathway requires, however, more activation than the concerted cycloaddition on the 3-21G* potential energy surface. It has been possible to locate the TS for the concerted formation of the substituted 1,2,3-thiadiazolines only by the AM1 and not by the MNDO-PM3 method. In contrast to the ab initio calculations, they are on a higher energy level. Both approaches, ab initio and semiempirical, indicate the formation of the 1,2,4-thiadiazolines via concerted reactions. It should be noted that semiempirical calculations seem to have a tendency to favor asymmetrical TS or intermediates.[23] In one case, however, it was possible to demonstrate that an X-ray analysis of an intermediate in a 1,3-dipolar cycloaddition[24] reflects closely the structure of the intermediate obtained for the cycloaddition by a MNDO-PM3 calculation.[25]

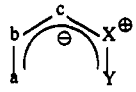
Although the primary formation of an open-chain structure of a pentadienyl anion type and subsequent electrocyclization seems to be excluded on the basis of the ab initio energies, it has to be remembered that our calculations refer to the gas phase. A quantitative account of the influence of the solvent polarity is out of reach presently; the appealing possibility of a stepwise reaction cannot be ruled out. In particular, a change of the substitution pattern of 1,3-dipole and/or dipolarophile might divert the cycloadditions toward this reaction channel. Without an extensive search of the potential energy surface by semiempirical methods, the feasibility of a two-step reaction via electrocyclization of a pentadienyl anion like structure would probably not have been discovered. The advantage of the semiempirical procedures is that they can be used for larger systems and for a very detailed analysis of the potential energy surface. However, we learn the lesson that it is necessary to check the semiempirical results by ab initio calculations.

Although the stepwise reaction does not seem to be realized in these cycloadditions, it opens up an attractive alternative which might come into play in suitably substituted diazoalkanes and thiones or, more generally, in other 1,3-dipolar cycloadditions. This type of reaction is imaginable for all 1,3-dipoles of the propargyl–allenyl type (**28**) and hetero double bonds Y=X. Besides the zwitterionic structures **28a,b**, a structure **28c** with an electron sextet at c is conceivable, although its contribution may be negligible. It is just center c which has formally the chance of interacting with X of the dipolarophile; a pentadienyl type anion **29** with onium center X would result. Preliminary calculations confirm this generalization.



$$\overset{\ominus}{a}-\overset{\oplus}{b}\equiv c \longleftrightarrow a=\overset{\oplus}{b}=\overset{\ominus}{c} \longleftrightarrow a=b-\bar{c}$$

28a 28b 28c



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Among the cycloadditions which might pass intermediates of type **29**, pentazole formation from benzenediazonium ion and azide anion[26] may be quoted. The kinetics did not allow for the distinction between a concerted and a two-step process. However, the analogy with the system imino azide ⇄ tetrazole was so close that the mechanism via benzene diazo azide, a type **29** intermediate, was preferred.[9,26]

It should be mentioned that the two-step 1,3-dipolar cycloadditions of certain thicarbonyl ylides published recently[27] do not pass type **29** intermediates; the charge centers of the zwitterion are separated by a tetrahedral carbon function. An extreme difference of FMO energies of 1,3-dipole and dipolarophile coupled with steric hindrance are responsible for this transgression from the orthodox concerted pathway. The same is true of the isolable zwitterionic intermediates in the reaction of methylsulfonyl azide and 5-alkylidenedihydrotetrazoles.[24,25]

Acknowledgment. This work was supported by the Deutsche Forschungsgemeinschaft. Computer time was provided by the HLRZ of the KFA Jülich and the computation center of the RWTH Aachen.

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(22) For 3-21G calculations on thioaldehydes including thioformaldehyde, see: Vedejs, E.; Perry, D. A.; Houk, K. N.; Rondan, N. G. *J. Am. Chem. Soc.* **1983**, *105*, 6999.

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