at 120 °C, 8 h. Purification was carried out by successive SiO_2 column chromatographies—the first chromatography by eluting with cyclohexane, benzene, AcOEt, and then EtOH, successively, and the second chromatography by eluting with cyclohexane, benzene, and then AcOEt, successively—affording 0.35 g (0.38 mmol, 22%) of pure $4\cdot O^2$: IR ν_{max} (neat) 1780 ($\nu_{C=O}$), 1210 (ν_{CO}) cm^{-1}. Anal. Calcd for $C_{48}H_{78}O_{18}$: C, 61.13; H, 8.34. Found: C, 61.42; H, 8.52.

Hexakis[(2-methoxyoctanoyl)oxy]benzene (5). 3 (0.15 g, 0.86 mmol) and 2-methoxyoctanoyl chloride (2.0 g, 10 mmol) in the presence of dry pyridine (0.5 g, 6.3 mmol) and a solvent (decalin, 5 mL) were heated at 80–105 °C, 24 h. After a chromatographic purification through a SiO_2 column, HPLC analysis indicated that the crude **5** still contained four minor impurities, which were not easily eliminated by attempts of recrystallizations. Therefore, the final purification was performed by a preparative HPLC (SiO_2 column, CH_2Cl_2–CH_3CN = 100:3.5 (v/v), affording pure **5** (15%): IR ν_{max} (neat) 1790 ($\nu_{C=O}$) 1092 (ν_{CO}) cm^{-1}. Anal. Calcd for $C_{60}H_{102}O_{18}$: C, 64.84; H, 9.25. Found: C, 64.96; H, 9.26.

Hexakis[(3-thiaoctanoyl)oxy]benzene ($4\cdot S^3$) was prepared in a manner similar to that described for $4\cdot O^3$. $4\cdot S^3$: 64% yield; IR ν_{max} (KBr) 1774 ($\nu_{C=O}$) 1102 (ν_{CO}) cm^{-1}. Anal. Calcd for $C_{48}H_{78}O_{12}S_6$: C, 55.46; H, 7.56; S, 18.51. Found: C, 55.55; H, 7.62; S, 18.37.

Differential Scanning Calorimetry. DSC thermal analyses were performed with a Seiko DSC calorimeter (I&E Mode DSC-10 or DSC-20 calorimeter combined with a Seiko SSC/580 thermal controller). For the low temperature DSC measurements, a cooling accessory, Seiko 56 US-400, was employed with liquid N_2 as a coolant. Each sample (0.8–13 mg) was sealed in a Al pan with a sealer. The heating rate was 1–5°/min. The DSC scanning was made consecutively (more than twice) on each compound until good reproducibility of phase-transition temperatures (see also text) was observed. In the case of $4\cdot O^3$, a crystal–crystal transition appeared at 48 °C only in the first heating. In the second heating two new transitions appeared at 47 °C and 57 °C, which were reproducible and reserved in the consecutive scannings. The observed good reproducibility of the phase-transition temperatures (±1.5 °C) suggests that a degradation of compound was not appreciable at all in the presence DSC measurements. The phase-transition temperatures were not changed when the sample was sealed in the Al pan under Ar atmosphere.

Acknowledgment. This work was supported by the Japan Ministry of Education, Science and Culture, Grant-in-Aid for Specially Promoted Research No. 61065003. We thank Prof. T. Higuchi, Osaka City University, for helping with the X-ray analysis.

Supplementary Material Available: Proton NMR data for hexaesters $4\cdot O^{2,3,4,5,7}$, $4\cdot S$, and **5** (1 page). Ordering information is given on any current masthead page.

Carbon Monosulfide as Reagent in Organic Synthesis. A Mechanism Study Based on the Frontier Orbital Approach

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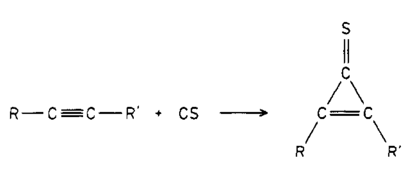
The cycloaddition and insertion reactions of CS have been studied by using the frontier orbital approach. Calculations of the symmetry, HOMO and LUMO energies and the atomic net charge at carbon for CS lead to a comparison in reaction pattern with singlet CR_2 (carbenes). For the cycloaddition reaction it is suggested that the first step is an electrophilic attack of the vacant p orbital of the CS carbon on the π bond of the acetylene. The reactivity of CS toward acetylenes is analyzed by using electrostatic as well as frontier overlap considerations. For the insertion reactions a similar approach is used. The results obtained are discussed in relation to experiments.

Carbon monosulfide, CS, has been known for more than a century, and in spite of its unstable nature it has been the subject of numerous investigations, mainly in the spectroscopic[1] and theoretical[2] fields, but also the reactions of CS with O and O_2 have been the subject of much interest.[3] Recently CS has been introduced as a new reagent in organic synthesis as a reaction partner in cycloadditions[4] as well as α insertions.[5] The reaction of CS with acetylenic derivatives, **1**, leads to cyclopropenethiones, **2**, (eq 1). The reaction 1, however, is mainly restricted to amino- and diaminoacetylenes whereas aminothioacetylenes ($R_2NC\equiv CSR'$), bis(ethylthio)acetylene, di-*tert*-butoxyacetylene, bis(methylseleno)acetylene, strained acetylenes, anthracene, cyclooctatetraene, and azulene did not react with CS under the standard reaction conditions.[4,5]



1 2 (1)

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† Present address: H. Ludbeck A/S, DK-2500 Valby, Denmark.

(1) See, e.g.: (a) Cossart, D.; Horani, M.; Rostas, J. *J. Mol. Spectrosc.* **1977**, *67*, 283. (b) Yang, S. C.; Freedman, A.; Kawasaki, M.; Bersohn, R. *J. Chem. Phys.* **1980**, *72*, 4058. (c) Saever, M.; Hudgens, J. W.; De Corpo, J. J. *J. Chem. Phys.* **1982**, *70*, 63. (d) Schofield, K. *J. Phys. Chem. Ref. Data* **1979**, *8*, 723. (e) Obase, H.; Tsuji, M.; Nishimura, U. *Chem. Phys.* **1981**, *57*, 89; **1984**, *87*, 93.

(2) See, e.g.: (a) Robbe, J. M.; Schamp, J. *J. Chem. Phys.* **1976**, *65*, 5420. (b) Cossart, D.; Bergeman, T.; *J. Chem. Phys.* **1976**, *65*, 5462. (c) Wilson, S. *J. Chem. Phys.* **1977**, *67*, 4491. (d) Green, S. *Chem. Phys.* **1978**, *31*, 425; **1979**, *40*, 1. (e) Raine, G. P.; Schaefer, H. F., III; Haddon, R. C. *J. Am. Chem. Soc.* **1983**, *105*, 194.

(3) See, e.g.: (a) Hsu, D. S. Y.; Shaub, W. M.; Burks, T. L.; Lin, M. C. *Chem. Phys.* **1979**, *44*, 143. (b) Black, G.; Jusinski, L. E.; Slanger, T. G. *Chem. Phys. Lett.* **1983**, *102*, 63. (c) Lilenfeld, H. V.; Richardson, R. J. *J. Chem. Phys.* **1977**, *67*, 3991.

(4) (a) Krebs, A.; Güntner, A.; Senning, A.; Moltzen, E. K.; Klabunde, K. J.; Kramer, M. P. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 729. (b) Lütjens, H.; Moltzen, E. K.; Krebs, A.; Senning A., unpublished results. (c) Moltzen, E. K. Cand. Scient. Theses, Aarhus University, 1985.

(5) (a) Klabunde, K. J.; Kramer, M. P.; Senning, A.; Moltzen, E. K. *J. Am. Chem. Soc.* **1984**, *106*, 263. (b) Moltzen, E. K.; Senning, A.; Kramer, M. P.; Klabunde, K. J. *J. Org. Chem.* **1984**, *49*, 3854. (c) Moltzen, E. K.; Senning, A.; Kramer, M. P.; Klabunde, K. J. *J. Org. Chem.* **1987**, *52*, 1156. (d) Moltzen, E. K.; Jensen, B.; Senning, A. *Sulfur Lett.* **1986**, *4*, 203. (e) Moltzen, E. K.; Jensen, B.; Senning, A. *Acta Chem. Scand., Ser. B* **1986**, *B40*, 609.

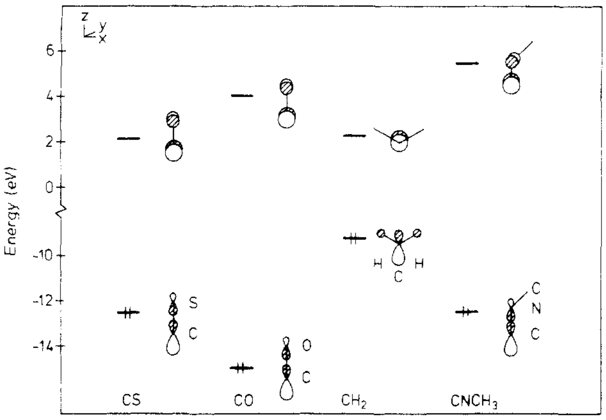
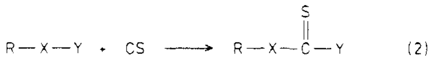


Figure 1. Energies and shapes of the frontier orbitals of CS, CO, CH_2, and CH_3NC.

The insertion reactions of CS (eq 2) have also been found to be of limited scope under the standard reaction conditions and seem not to be as general a reaction type as



$$R{-}X{-}Y + CS \longrightarrow R{-}X{-}\overset{\overset{S}{\|}}{C}{-}Y \qquad (2)$$

observed for the isoelectronic counterparts of CS: carbenes[6] and isocyanides.[7] CS has been found to insert into the nitrogen–hydrogen bond of amines,[5c] the sulfur–hydrogen bond of thiols,[5c] and the sulfur–chlorine bonds.[5a,b,d,e] Diazo compounds have also been found to react with CS, giving the corresponding thioketenes.[4b]

The aim of this paper is to try to give a coherent picture of the reactivity of CS, based on theoretical calculations, in relation to the experimental results.[4,5] For this purpose symmetry arguments, the frontier orbital approach[8] and ab initio calculations[9] will be used. Considering the CS reactions as being purely charge controlled leads to contradictions; e.g., amines and aminoacetylenes are electron-rich (nucleophilic) systems, while sulfenyl chlorides are electron-poor (electrophilic) systems, but CS reacts with both types of substrates. The frontier orbital approach gives a better explanation of the observed reactivity of CS.

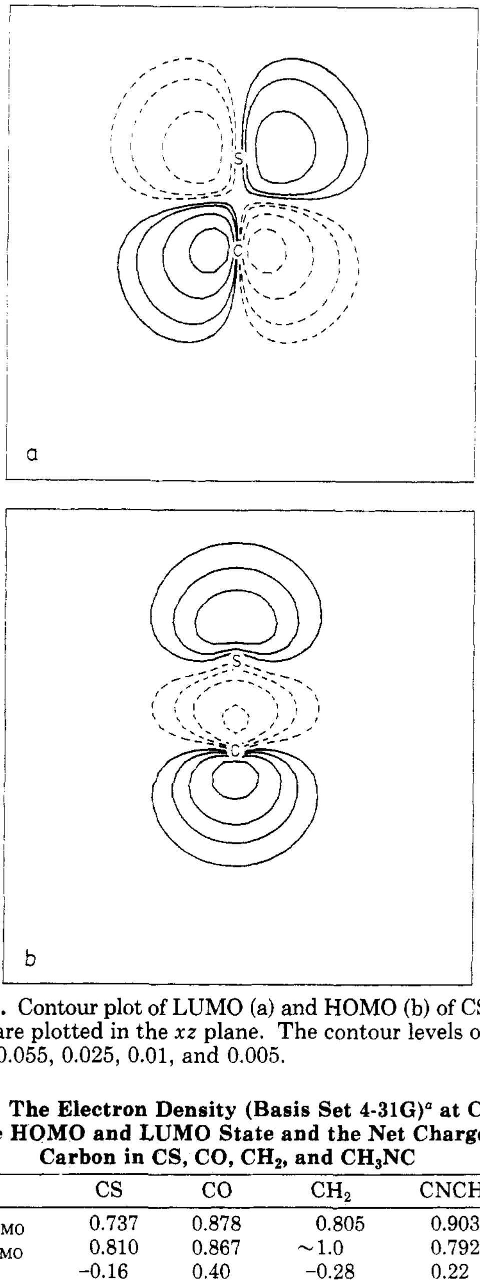


Figure 2. Contour plot of LUMO (a) and HOMO (b) of CS. The orbitals are plotted in the *xz* plane. The contour levels of ψ are 0.2, 0.1, 0.055, 0.025, 0.01, and 0.005.

Table I. The Electron Density (Basis Set 4-31G)[a] at Carbon in the HOMO and LUMO State and the Net Charge at Carbon in CS, CO, CH_2, and CH_3NC

	CS	CO	CH_2	$CNCH_3$
C_{HOMO}	0.737	0.878	0.805	0.903
C_{LUMO}	0.810	0.867	~1.0	0.792
q	−0.16	0.40	−0.28	0.22

[a] Calculation of the atomic net charge at carbon in CS using a better basis set (6-31G*) gives −0.03, indicating that the atomic net charge depends on the basis set used.

Before proceeding to the theoretical analysis a few facts should be mentioned about the generation of CS: CS is prepared by dissociation of CS_2 in a high-voltage AC discharge. The CS is passed into the reaction flask containing a stirred solution of the appropriate reagent kept at low temperature (−78 to 0 °C).[4,5] In the analysis presented here it will be assumed that the reactive form of CS is in its singlet ground state, $X^1\Sigma^+$. Dissociation of CS_2 in a high-voltage discharge is known to produce CS in both the excited singlet state, $A^1\pi$, and in the excited triplet states, $a^3\pi$, $a'^3\pi$, $e^3\Sigma^-$, and $d^3\Delta$,[10] but considering both the very short lifetimes of excited CS[11] and the fact that CS_2 is an effective quencher of excited CS[11d,12] it is reasonable to assume that singlet ground-state CS is the most important reactive species although the participation of excited CS, especially CS in the $a^3\pi$ state,[11a,d] cannot be completely excluded.

A comparison of the frontier orbitals of CS with those of some of its better known isoelectronic counterparts is a good starting point for the theoretical analysis. Figure 1 shows the energies and shapes of the frontier orbitals (HOMO and LUMO) of CS, carbon monoxide (CO), singlet methylene (CH_2), and methyl isocyanide (CH_3CN), respectively.[9] The HOMO and LUMO in CS (as well as in its isoelectric counterparts) in Figure 1 are of σ and π symmetry, respectively. Thus, CS has the possibility to act as a σ donor as well as a π acceptor. Figure 2 shows contour plots of the HOMO and LUMO wave functions

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(6) See, e.g.: Kirmse, W. *Carbene Chemistry*; Academic: New York, 1971.

(7) See, e.g.: Saegusa, T.; Ito, Y. In *Isonitrile Chemistry*; Ugi, I., Ed.; Academic: New York, 1971: p 65 ff.

(8) See, e.g.: Klopman, G. *Chemical Reactivity and Reaction Paths*; Wiley: New York, 1974.

(9) All calculations have been performed with a GAUSSIAN 80 program (Birkley, J. S.; Whiteside, R. A.; Krishan, R.; Seager, R.; DeFries, D. J.; Schegel, H. B.; Topiol, S.; Kahn, L. R.; Pople, J. A. *QCPE* 446). A 4-31G basis set has been used for all the calculations and the geometries of the compounds have been taken from the literature or optimized.

(10) Cossart, D. *J. Chim. Phys. Phys.-Chim. Biol.* 1981, *78* (1981) 711.

(11) (a) Fournier, J.; Deson, J.; Vermeil, C.; Robbe, J. M.; Schamps, J. *J. Chem. Phys.* **1979**, *70*, 5703. (b) Hynes, A. J.; Brophy, J. H. *Chem. Phys. Lett.* **1979**, *63*, 93. (c) Carlson, T. A.; Copley, J.; Duric, N.; Erman, P.; Larsson, M. *Chem. Phys.* **1978**, *42*, 81. (d) Same as ref 1d.

(12) Ashfold, M. N. R.; Quinton, A. M.; Simons, J. P. *J. Chem. Soc., Faraday Trans 2* **1980**, *76*, 915.

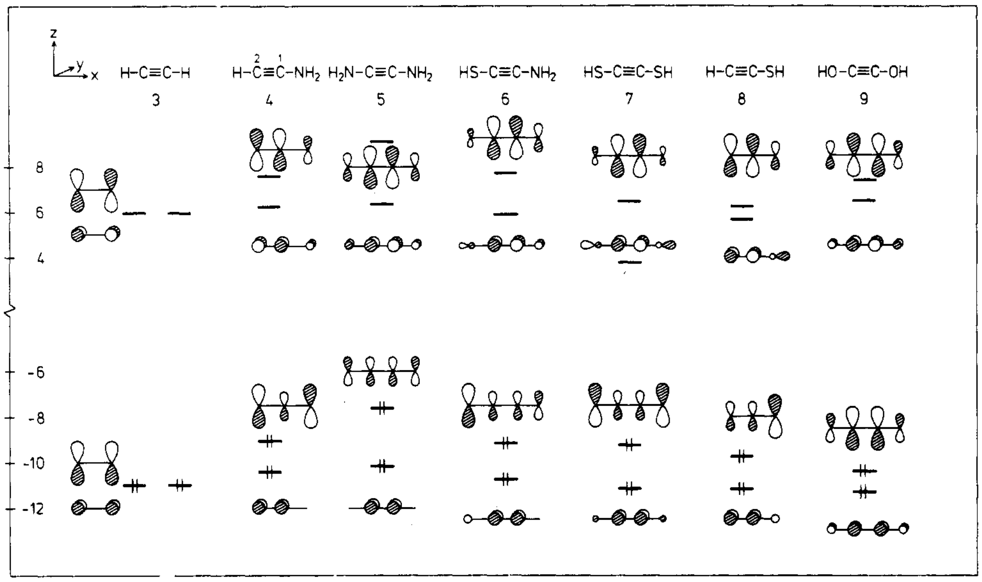
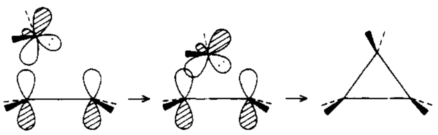


Figure 3. The frontier orbitals of 3–9.

Scheme I



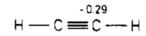
of CS, and the π acceptor and σ donor properties are shown in Figure 2a,b, respectively.

Table I gives the electron densities at carbon in the HOMO and LUMO states as well as the net atomic charge at carbon for CS, CO, CH_2, and CH_3NC. It appears from Table I that the electron densities in the HOMO and LUMO states of the systems are of the same magnitude while differences in net atomic charges at carbon are observed: The carbons in CS and singlet CH_2 are negative (−0.16 and −0.28, respectively) and the relevant carbons in CO and CH_3NC are positive (0.40 and 0.22, respectively) with the basis set used here (4-31G). The data for CS from Figure 1 and Table I allow the use of the singlet methylene reaction pattern approach to interpret the observed reactivity of CS.

The reactions of singlet carbenes with ethylenes are well studied from both an experimental[6,13] and a theoretical[13,14] point of view. Skell and Doering found that the transition state of singlet carbene cycloadditions to alkenes involves electrophilic attack of the vacant p orbital of the carbene on the π bond of the alkene.[13] Later Hoffmann confirmed this result both in the methylene–ethylene reaction[14a] and in the difluoromethylene–ethylene reaction.[14b] Recently Houk et al.[15] as well as others[15] have studied this type of reaction in more detail. The proposed mechanism is shown in Scheme I.

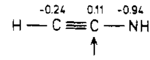
The unoccupied orbital of p character of singlet carbene approaches the alkene along the π axis to form a loose charge-transfer-type complex, which then collapses to produce the cyclopropane (Scheme I).

In the following this approach will be used to interpret the reactions of CS with acetylenic derivatives; as a starting point the electrostatic interaction[16] between the carbon atom of CS and the acetylenes is considered. The net atomic charges at the different atoms in the different model acetylenes 3–9 are shown below.



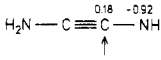
$$\mathrm{H{-}C{\equiv}\overset{-0.29}{C}{-}H}$$

3



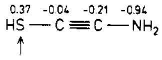
$$\mathrm{H{-}\overset{-0.24}{C}{\equiv}\underset{\uparrow}{\overset{0.11}{C}}{-}\overset{-0.94}{NH_2}}$$

4



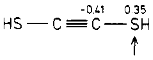
$$\mathrm{H_2N{-}C{\equiv}\underset{\uparrow}{\overset{0.18}{C}}{-}\overset{-0.92}{NH_2}}$$

5



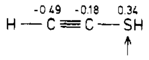
$$\mathrm{\underset{\uparrow}{\overset{0.37}{HS}}{-}\overset{-0.04}{C}{\equiv}\overset{-0.21}{C}{-}\overset{-0.94}{NH_2}}$$

6



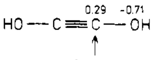
$$\mathrm{HS{-}C{\equiv}\overset{-0.41}{C}{-}\underset{\uparrow}{\overset{0.35}{SH}}}$$

7



$$\mathrm{H{-}\overset{-0.49}{C}{\equiv}\overset{-0.18}{C}{-}\underset{\uparrow}{\overset{0.34}{SH}}}$$

8



$$\mathrm{HO{-}C{\equiv}\underset{\uparrow}{\overset{0.29}{C}}{-}\overset{-0.71}{OH}}$$

9

Since the carbon atom in CS has a net negative atomic charge (−0.16), one might expect an electrostatic interaction with the positive centers in the model acetylenes 3–9 to take place. The positive centers in 3–9 are indicated by arrows. With 4 and 5, the amino- and diaminoacetylenes, an initial attack of CS on carbon is possible, which might lead to the corresponding cyclopropenethione, 2, whereas the sulfur atoms in 6–8 are the preferred sites of attack, leading to transition states from which no stable products can be formed. Ethynediol, 9, should, according to the net positive atomic charge on carbon, be able to react with CS, but no reaction has been observed under the conditions applied.[4b] The inertness of dialkoxyacetylenes toward CS might be explained in terms of frontier orbital considerations (see later) or might be due to steric reasons. These "simple" considerations purely based on electrostatic interactions explain to some extent the observed[4,5] reactivity of CS in cycloadditions.

As mentioned above there is a similarity between CS and methylene both with respect to orbital symmetry and with

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[13] Skell, P. S.; Cholod, M. S. *J. Am. Chem. Soc.* **1969**, *91*, 7131 and references therein.

[14] (a) Hoffmann, R. *J. Am. Chem. Soc.* **1968**, *90*, 1475. (b) Hoffmann, R.; Hayes, D. M.; Skell, P. S. *J. Phys. Chem.* **1972**, *76*, 664.

[15] Rondan, N. G.; Houk, K. N.; Moss, R. A. *J. Am. Chem. Soc.* **1980**, *102*, 1770. See ref 13 for some references.

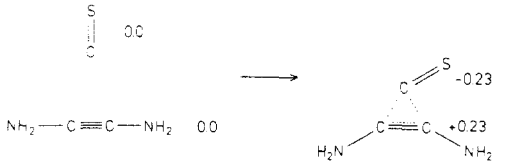
[16] The concept of charge and frontier controlled reactions introduced by G. Klopman (ref 8) will be used here.

respect to electron density. It is, therefore, obvious to use a frontier orbital approach, similar to the mechanism shown in Scheme I, for the CS reactions. Figure 3 shows the frontier orbitals of **3**–**9**. The frontier orbitals of acetylene (**3**) are shown with the expected symmetry of HOMO and LUMO (π,π^* symmetry); the HOMO of acetylene (−10.97 eV) is the lowest lying in the depicted model compounds. Since the reaction of CS with an acetylene involves electrophilic approach of the unoccupied p orbital of CS toward the π bond of the acetylene, the reaction of **3** with CS can be expected to be less favorable than the reactions of CS with the other acetylenes shown in Figure 3. This finding combined with the previously discussed electrostatic interactions explains the observed inertness of CS toward, e.g., the strained acetylenes.[4b]

The amino- and diaminoacetylenes should, according to the electrostatic interaction approach, be able to react with CS. The HOMO of both systems is of p_z symmetry in the coordinate system used in Figure 3 and located higher in energy than the HOMO for **3**; the HOMOs of amino- and diaminoacetylene are located at −9.14 and −7.70 eV, respectively. For aminoacetylene (**4**) the HOMO is mainly located at C-2 and the nitrogen; the unoccupied p orbital of CS then has the possibility of overlap with both the C-2 p_z orbital and the nitrogen p_z orbital. An overlap of CS with the nitrogen will not lead to any stable products and is, furthermore, hindered by electrostatic repulsion whereas overlap with carbon will lead to an intermediate of the type shown in Scheme I. The reaction is completed by interaction of the σ donor orbital of CS with the LUMO of p_z symmetry located at C-1. It should be noted that CS attacks C-1 according to the electrostatic interaction approach.

The HOMO of diaminoacetylene (**5**) is more or less evenly distributed over both carbons and nitrogens, so attack of CS is possible both at carbon and nitrogen. However, attack at nitrogen is electrostatically unfavorable and will, furthermore, not lead to stable products, whereas attack at either of the carbons will lead to the corresponding cyclopropenethione.

From the location of the HOMO energy in **4** and **5** one might expect **5** to be the most reactive since the HOMO in **5** is located 1.44 eV higher in energy than the HOMO in **4**. Calculation of a transition-state-like diaminoacetylene–CS complex[17] **10** shows that a charge transfer from the π orbital of diaminoacetylene to the p acceptor orbital of CS has taken place. A similar observation has been made in the reactions of carbenes with alkenes,[13–15] and such a charge-transfer complex might also explain the Hammett ρ value obtained in the reactions of isocyanides with acetylenes.[18]



10

In the acetylenes **6**–**8** the HOMO is mainly located on sulfur and is lower in energy than in the aminoacetylenes **4** and **5**. This location of the HOMO at sulfur favors an electrophilic attack of the carbon atom of CS at this site, thus leading to a transition state from which no stable product can be formed. The lower energy of the HOMOs of **6**–**8** compared to the HOMOs of **4** and **5** also indicates **6**–**8** to be less reactive than **4** and **5**. These frontier orbital reasonings are in accord with the predictions based on the electrostatic interaction approach and the observed inertness of CS toward sulfur substituted acetylenes is, therefore readily understood.

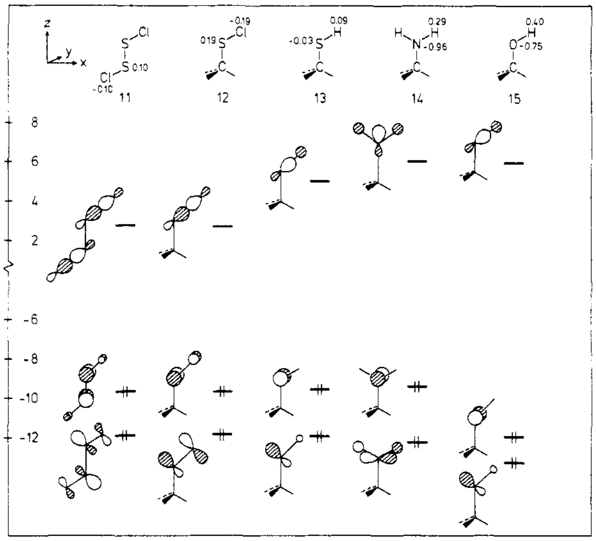


Figure 4. The frontier orbitals of **11**–**15**.

Ethynediol (**9**) occupies an exceptional position in the acetylene series. Both the electrostatic interactions and frontier orbital considerations are in favor of the reaction of CS with **9** although the reaction rate might be rather lower compared with **4** and **5** due to the relatively lower energy of the HOMO of **9**, but nonetheless CS seems to be completely inert toward dialkoxyacetylenes. This inertness might have steric reasons since the reaction was carried out with di-*tert*-butoxyacetylene[4b] and steric repulsion between the *tert*-butyl groups and CS might reduce the overlap of the unoccupied p orbital of CS with one of the π orbitals of the acetylene moiety, thus preventing the reaction from taking place. Further work with other alkoxyacetylenes is in progress in order to clarify this point.

CS has also been used in potential insertion reactions. Figure 4 shows the frontier orbitals and net atomic charges of a series of compounds **11**–**15** with which CS insertion has been tried.

The frontier orbitals of S_2Cl_2 (**11**) and CH_3SCl (**12**) (a model compound for RSCl) look very similar. The HOMO is mainly of p_y symmetry located as a lone pair at sulfur at −9.79 and −9.77 eV, respectively. The LUMO of interest of **11** and **12** is mainly of σ antibonding sulfur–chlorine character at 2.72 and 2.74 eV, respectively. The net atomic charge on sulfur in **11** and **12** is 0.10 and 0.19, respectively, while the atomic charge on chlorine is −0.10 and −0.19, respectively.

According to both electrostatic interaction and frontier orbital considerations, **11** and **12** are ideal substrates for CS. The net positive atomic charges at sulfur favor the approach of the negatively charged carbon atom in CS, and the interaction of the unoccupied p orbital of CS with the substrate HOMO is also highly favored considering that the HOMO mainly is a lone pair orbital of p_y symmetry on sulfur, thus giving **16**. The next step takes place as a donation of electron density from the σ orbital of CS to the σ^*_{S-Cl} orbital according to eq 3. This donation of electron density weakens the sulfur–chlorine bond and allows CS to be inserted. With this approach the insertions

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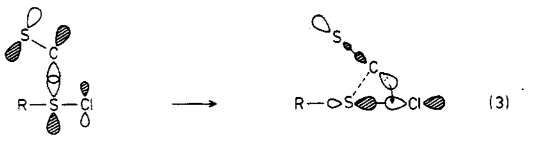
[17] The transition-state calculation has been performed at a geometry which is similar to the transition state for cycloaddition of carbene to ethylene (see ref 15).

[18] Krebs, A.; Güntner, A.; Versteylen, S.; Schultz, S. *Tetrahedron Lett.* 1984, *25*, 2333.

J. Org. Chem. **1987**, *52*, 2509-2517



(3)

16 16′

of CS into the sulfur–chlorine bonds of S_2Cl_2 and $RSCl$[4,5,19] are readily understood.

The frontier orbitals of thiols are somewhat similar to the frontier orbitals of the sulfenyl chlorides and insertion of CS into the sulfur–hydrogen bond should, therefore, be possible. There are, however, some significant differences. The sulfur in the thiol has, contrary to the sulfur atoms in **11** and **12**, a net negative atomic charge which might lead to a lowering (although it is very small) of the reactivity toward CS. Furthermore, the LUMO of the thiol lies higher in energy than the LUMOs of **11** and **12**, thus increasing the energy gap between this LUMO and the filled σ orbital of CS (cf. Figures 1 and 4). This energy gap reduces the rate of the insertion (eq 3). As a result of these considerations the thiols should be less reactive toward CS than, e.g., **11** and **12**, and, indeed, this prediction fits nicely with the experimental result. CS does react with thiols but very sluggishly under the standard conditions.[5c] The primary insertion products are unstable so that only secondary products are obtained in very low yield.[19]

The picture that emerges from the analysis of primary amines is very similar to the result of the analysis of the thiols. The main difference is the significantly larger net negative atomic charge on nitrogen compared to the sulfur in thiols. The reactivity of primary amines toward CS should, therefore, be comparable to the reactivity of thiols, and the experimental results are in complete accord with the prediction. The resulting stable thioformamides are obtained in very low yield.

Secondary amines, however, are very reactive toward CS. The resulting stable thioformamides are obtained in high yields[5a] and the only limiting factor seems to be the steric bulk of the R groups in R_2NH. The observed difference in reactivity between primary and secondary amines can be traced to the HOMO energy of the amines: Secondary amines have generally a higher HOMO energy than primary[20] amines and should then according to the perturbation theory[8] be expected to be more reactive toward electrophiles than primary amines.

Alcohols have very low-lying HOMO orbitals and, furthermore, a significant amount of net negative atomic charge on oxygen. The reactivity of alcohols toward CS should, therefore, be very low which is in accord with the experimental results. No reactions between CS and alcohols have been observed and alcohols have been used as solvents in several CS reactions.[4b]

Conclusion

The analysis presented here shows that the frontier orbital approach, combined with the electrostatic interaction approach, gives a satisfactory coherent explanation of the reactivity of CS. This analysis can also be useful for future choices of substrates for CS. The ideal substrate should have an energetically high-lying HOMO orbital of a symmetry which allows overlap with the empty p orbital of CS, and the major part of the electron density of this HOMO orbital should be located on the atom which is attacked by CS. This specific atom should also have a net positive atomic charge and not be sterically hindered. A further requirement for a successful reaction is that there has to be a pathway from the initially formed transition state, e.g., **16**, to a chemically possible product.

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(19) M. P. Kramer, Ph.D. Thesis, Kansas State University, 1985.

(20) See, e.g., the ionization potentials ($\simeq$–HOMO energy) for secondary and primary amines in: *Handbook of Chemistry and Physics*, 55th ed.; CRC: Boca Raton, FL, 1974.

Stereospecific Skeletal Rearrangement Reactions in Bridgehead-Substituted Bicyclo[2.2.2] Systems under Neutral Conditions

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General and stereospecific pinacolic-type rearrangement reactions of vicinal methoxy mesylates under neutral conditions have been developed for the construction of functionalized bicyclo[3.2.1]octanes. For instance, *exo*-5,5-dimethyl-1-methoxy-6-[(methylsulfonyl)oxy]bicyclo[2.2.2]oct-2-ene rearranged to 8,8-dimethylbicyclo-[3.2.1]oct-6-en-2-one when treated with NaI in DMF. The tolerance of various functional groups to these reaction conditions was demonstrated in the transformation of the C ring of thebaine to the corresponding bicyclo-[3.2.1]octenone. The quadrone skeleton (ABC rings) was also constructed by utilizing this pinacol-type rearrangement reaction.

Introduction

Our interest in functionalized bicyclo[3.2.1]octene systems stemming from our synthetic work directed toward the taxane diterpenes,[1] exemplified by taxol (**1**),[1b] prompted us to investigate a mild and effective skeletal rearrangement reaction of 1-methoxybicyclo[2.2.2]octenes. Scheme I outlines the retrosynthetic plan for the synthesis of the taxane ring system.

The pinacolic-type rearrangement of vicinal *cis*-glycol monotosylates[2] would provide a method to prepare bicy-

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