REACTIONS OF A TETRASUBSTITUTED THIOCARBONYL YLIDE; NEW EVIDENCE FOR TWO-STEP CYCLOADDITIONS

Rolf Huisgen* and Grzegorz Mloston [1]

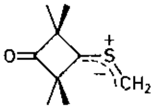
Institut für Organische Chemie der Universität München
Karlstr. 23, D-8000 München 2, Federal Republic of Germany

Dedicated to the memory of Professor Tetsuji Kametani

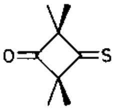
Abstract - Zwitterionic intermediates from aliphatic thiocarbonyl ylides and tetrasubstituted acceptor olefins can close the 5-membered ring (thiolane) or the 7-membered ring (ketene imine), undergo rotation, and - shown here - furnish cyclopropane and thione in an intramolecular nucleophilic substitution.

The 1,3-cycloadditions of 2,2,4,4-tetramethyl-3-thioxocyclobutanone *S*-methylide (1) to highly electron-deficient ethylenes served as models for the two-step mechanism; 1 adds nonstereospecifically to dimethyl 2,3-dicyanofumarate and 2,3-dicyanomaleate.[2,3] Besides an extreme difference of π-MO energies of 1,3-dipole and dipolarophile, massive steric screening of *one* terminus of the 1,3-dipole was regarded as prerequisite for the two-step mechanism of cycloaddition. What would be the effect of steric hindrance at *both* termini of the 1,3-dipole ?

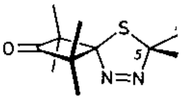
Thione 2 and 2-diazopropane in pentane at 0°C furnished the 1,3,4-thiadiazoline 3 (84%, mp 54-55°C).[4] With $t_{1/2}$ = 18 min in toluene and 37 min in acetonitrile at 70°C, 3 extrudes N_2 slower than the thiadiazoline without the 5-methyl groups.[5] According to ^{1}H nmr analysis with standard, the tetrasubstituted thiocarbonyl ylide 4 afforded 38% of thiirane 5 and 33% of the thioenol ether 6 in toluene, and 94% 5 + a trace of



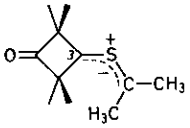
1



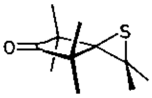
2



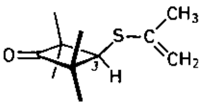
3



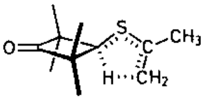
4



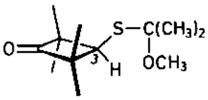
5



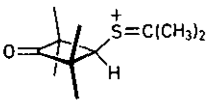
6



7



8



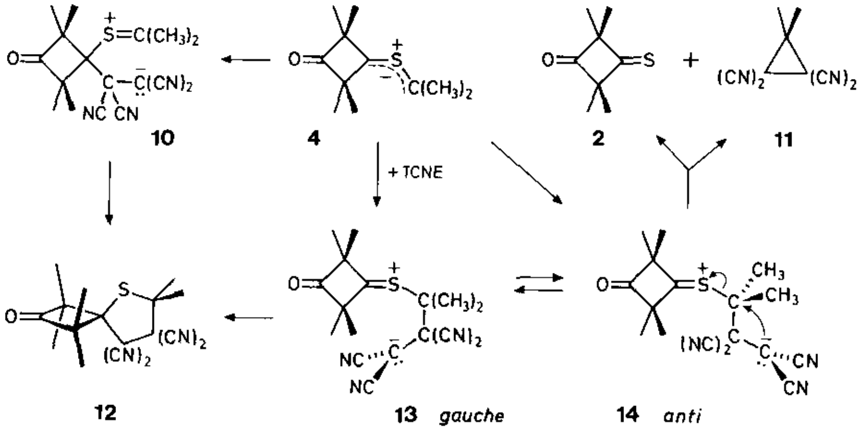
9

6 in acetonitrile at 70°C. The conrotatory electrocyclization producing the thiirane 5 appears to pass a more polar transition state than the suprafacial 1,4-shift via 7, both being allowed by the Woodward-Hoffmann rules.

The generation of 4 from 3 in methanol (6 h, 60°C) provided 51% 6 and 37% of the *O,S*-acetal 8, but *no thiirane* 5. Our guess that the vinyl sulfide 6 is now the result of another pathway which exceeds the sigmatropic reaction via 7 in rate, found support in the behavior of 4 towards CH_3OD at 60°C. The 60:40 ratio of 6 and 8 was unchanged, and the D incorporation in 3-position of the ring amounted to 80% in 6 and 81% in 8; the 3-H compounds 6 and 8 were stable to CH_3OD at 60°C. The lack of an isotope effect in the product ratio suggests the sulfonium ion 9 as the *common intermediate* which either loses a proton or adds CH_3O^-.

Thiocarbonyl ylides are bases; remarkably, the CH_2 group was the basic center in the thione *S*-methylide 1, and the addition of methanol took place in the *opposite* direction.[5]

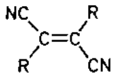
The thiirane 5, mp 61-62.5°C, showed three ^1H singlets for three pairs of methyl groups. Separated by thick-layer chromatography, 6 and 8 were liquids. The t at δ_C 107.9 and s at 141.3 ($CDCl_3$) characterize the olefinic carbons of 6; the CH_3 of the unsaturated C-atom occurs at δ_H 1.97. Three ^1H singlets for 3 x 2 CH_3 groups in 8 leave no doubt, that CH_3O is located in the side chain and 3-H appears as s at δ 3.05.

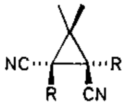


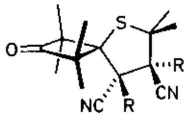
The interaction of 4 with tetracyanoethylene (1.1 equiv, toluene, 6 h, 60°C) gave rise to 58% of thiolane 12 along with 40% of 3,3-dimethylcyclopropane-1,1,2,2-tetracarbonitrile (11) and 27% of thione 2; the expected equivalence of 11 and 2 was disturbed by the volatility of 2 during work-up. Three s at δ_H 1.42, 1.92, 1.97 for 6 methyl groups reveal the plane of symmetry in 12, mp 174-176°C. Cyclopropane

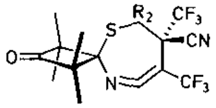
11, mp 209.5-210°C, was independently synthesized (63%) from TCNE and 2-diazopropane.[6] Thiolane 12 is stable even at 200°C and cannot be the precursor of 11 + 2.

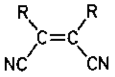
In an attractive scheme, thiolane 12 originates from the electrostatically favored *gauche* zwitterion 13, whereas the *anti* conformation 14 enters into a nucleophilic substitution with thione 2 as leaving group. The latter is a new variant of the cyclopropane synthesis devised by W.H. Perkin jr. in 1884.[7] The yields are somewhat solvent-dependent: 54% 12 + 34% 11 in THF and 80% 12 + 12% 11 in CD_3CN at 50°C.[6] Instead of 13, the structurally different zwitterion 10 - attack of the electrophile at the ring position - could likewise be the precursor of 12, but not of 2 + 11.

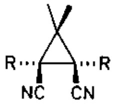

15

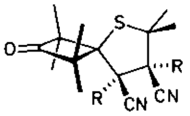

16


17


21 R = CH_3
22 R = H


18


19


20

a: R = CO_2CH_3 b: R = CF_3

Cis,trans isomeric acceptor olefins served as *stereochemical probe*. The N_2 extrusion of 1 in the presence of 1.1 equiv. of dimethyl 2,3-dicyanofumarate (15a, 1 h, 80°C in $CDCl_3$, closed tube) afforded 68% of trans-cyclopropane 16a, 18% of trans-thiolane 17a, and 9% of thiirane 5. The experiment with the cis isomer 18a furnished 57% cis-cyclopropane 19a, 25% cis-thiolane 20a, 7% trans-thiolane, and some of trans-cyclopropane 16a. Thus, 4 appears to combine more stereospecifically than 1[3] with 15a and 18a; however, the 60 MHz nmr analysis is not very precise. A small extent of a preceding cis,trans isomerization, 18a $\rightleftharpoons$ 15a, catalyzed by 3,[3] cannot be excluded.

trans-Cyclopropane 16a (mp 148°C, δ_H 1.62 for 2 CH_3) and cis-cyclopropane 19a (mp 90-92°C, δ_H 1.54, 1.70 for 2 CH_3) were identified with specimens prepared from 15a and 18a with 2-diazopropane. The configurational assignment of the thiolanes 17a (mp 213-214°C) and 18a (mp 132-134°) rests on the retention principle.

Cyclopropane formation via the anti zwitterion became even more prominent in the interaction of 4 with trans- and cis-1,2-dicyano-1,2-bis(trifluoromethyl)ethylenes, 15b and 18b. After reaction of 3 with 1.1 equiv. of 15b in $CDCl_3$ for 1 h at 80°C, ^1H and ^{19}F nmr analysis indicated 90% trans-cyclopropane 16b, 5% of ketene imine 21, and

5% thiirane 5. The cis acceptor olefin 18b is sensitive to bases which establish a cis,trans equilibrium of 5:95.[8] However, on reacting 3 with 1.1 equiv. of 18b for 1 h at 80°C, the unconsumed 18b did not contain 15b; thus, the formation of 94% cis-cyclopropane 19b and 5% of the trans isomer 16b denoted some nonstereospecificity.

One methyl s at δ_H 1.75 for 16b (mp 52-53°C) and two s at 1.69 and 1.82 for 19b (mp 81-82°C) were in accord with the structures. An ir absorption at 2035 cm^{-1} in the reaction solutions pointed to the ketene imine 21 which was not isolated; ^{19}F nmr signals at -59.6 and -65.3 with J_{FF} = 6.4 Hz were tentatively assigned to 21. The 7-membered ketene imine 22 was the main product in the reactions of 1 with 15b or 18b;[9] it results from a cyclization of the gauche zwitterion of type 13.

The intramolecular substitution furnishing cyclopropane + thione offers new evidence for the *occurrence of zwitterionic intermediates;* both this S_N2 type process and thiolane formation are irreversible. The loss of stereochemical integrity in the cycloadditions of 4 with 15 and 18 is smaller than observed for *S*-methylide 1. It is hard to predict the relative heights of rotational barriers in persubstituted zwitterions of type 13 and 14 in which steric hindrance plays such a dominant role. Stereoretention may be violated in two-step cycloadditions, *but not necessarily.*

ACKNOWLEDGMENT

We express our gratitude to the *Fonds der Chemischen Industrie* for support.

REFERENCES

1. Present address: Department of Organic Synthesis, Institute of Chemistry, University of Lodz, Poland.
2. R. Huisgen, G. Mloston, and E. Langhals, *J.Am.Chem.Soc.* 1986, *108*, 6401.
3. G. Mloston, E. Langhals, and R. Huisgen, *Tetrahedron Lett.*, submitted.
4. Satisfactory elemental analyses and spectra were obtained for all new compounds.
5. R. Huisgen, G. Mloston, and C. Fulka, *Heterocycles*, 1985, *23*, 2207.
6. Experiments by E. Langhals and J. Rapp, Munich 1986/87.
7. W.H. Perkin jr., *Ber.Dtsch.Chem.Ges.*, 1884, *17*, 54.
8. G. Urrutia Desmaison, Ph.D. Thesis, University of Munich, 1986.
9. R. Huisgen, E. Langhals, G. Mloston, and T. Oshima, *Heterocycles*, 1989, *29* ,2069.

Received, 14th August, 1989