A STABLE SEVEN-MEMBERED RING KETENE IMINE FROM A THIOCARBONYL YLIDE AND AN ACCEPTOR OLEFIN

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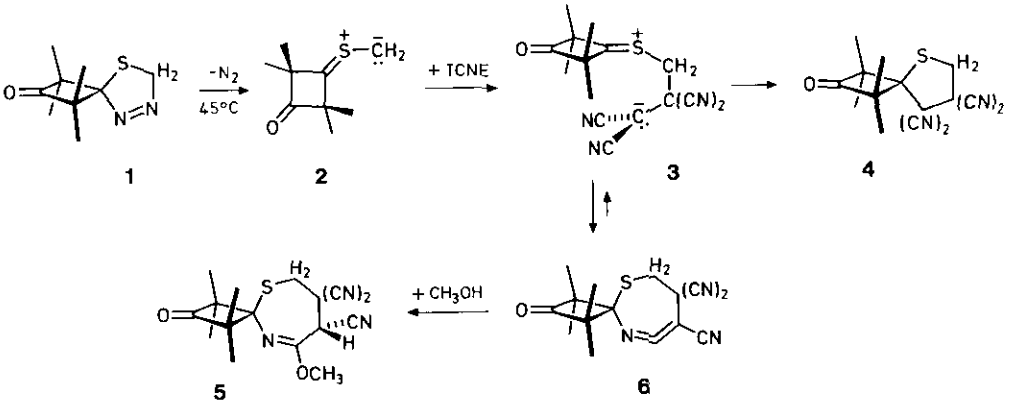
Dedicated to Professor Michael J.S. Dewar on the occasion of his seventieth birthday

Abstract - 2,2,4,4-Tetramethyl-3-thioxocyclobutanone *S*-methylide (2), generated from the 1,3,4-thiadiazoline 1 by N_2 extrusion, combines with trans- and cis-1,2-dicyano-1,2-bis(trifluoromethyl)ethylene (7) furnishing nonstereospecifically five-membered thiolanes (8, 16) and a strained cyclic ketene imine in parallel reactions. The results of a mechanistic study are interpreted by zwitterionic intermediates.

The *concerted* pathway of 1,3-dipolar cycloaddition is replaced by a *two-step mechanism* via a zwitterionic intermediate if two requirements are fulfilled: extreme difference of HO-LU-energies of 1,3-dipole and dipolarophile, and high steric hindrance at *one* terminus of the 1,3-dipole. The reaction of thiocarbonyl ylide 2 - generated by N_2 extrusion from the easily available thiadiazoline 1 [1] - and tetracyanoethylene (TCNE) fulfills the prerequisites. It is in the ratio of 65:35 that the zwitterionic intermediate 3 enters into the reversible formation of the ketene

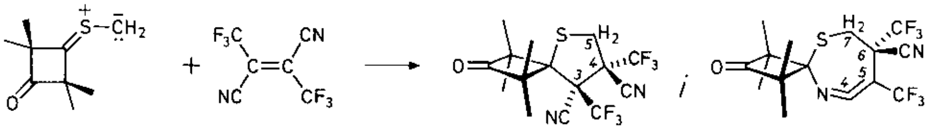


imine 6 and the irreversible ring closure giving the thiolane 4.[2] In THF + 2 Vol% methanol as solvent, 6 is intercepted furnishing the lactim ether 5.

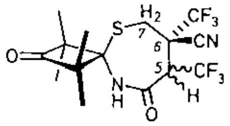
The evidence for the occurrence of the ketene imine 6 is *indirect*. No infrared absorption in the region of 2000 cm^{-1} - characteristic of cumulated systems - was observed during the reaction (without methanol). Now we report the isolation of a crystalline cyclic ketene imine when 1,2-dicyano-1,2-bis(trifluoromethyl)ethylene (7) [3] served as acceptor olefin.

A. Isolation of the Ketene Imine and Its Reactions

When thiocarbonyl ylide 2 was generated from 1 in the presence of 1.2 equiv. of trans-7 in $CDCl_3$ (40°C, 11 h), the ^{1}H nmr spectrum showed ketene imine 9 and thiolane 8 in a 78:22 ratio. A strong ir absorption at 2030 cm^{-1} disappeared upon adding a drop of methanol.



2 *trans* - **7** **8** **9**



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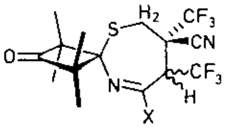
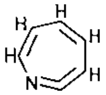


	X
11	OCH_3
12	NHC_6H_5



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The separation of 9 from 8 succeeded by crystallization from dry carbon disulfide at low temperature. The pale-yellow needles of the 7-membered cyclic ketene imine show mp 87-88°C.[4] The ir absorption at 2031 cm^{-1} (nujol) exceeds even the C=O band at 1791 cm^{-1} in intensity; open-chain ketene imines absorb at ~2000 cm^{-1}.[5] The $\delta(7\text{-}H_2)$ of 9 appeared at 2.83 and 3.41 with J = 15.2 Hz ($CDCl_3$); in contrast to the thiolanes 8 and 16, J_{gem} was 15-16 Hz in all the 7-membered rings discussed here. The ^{19}F-nmr spectrum exhibits quartets at δ -54.4 ($6\text{-}CF_3$) and -71.8 ($5\text{-}CF_3$) with J_{F-F} = 4.3 Hz ($CDCl_3$). $\delta(^{13}C)$ at 188.9 (C-4) and 63.5 (C-5) is in harmony with data of open-chain ketene imines: δ 187-196 for α-C and 37-78 for β-C.[6]

The mother liquor contained the trans-thiolane 8 which crystallized from pentane at -78°C, mp 78-80°C: ^{1}H Nmr ($CDCl_3$): AB at 3.48 and 3.64 with J = 11.8 Hz for $5\text{-}H_2$. The ^{19}F shifts at δ -56.1 and -66.9 with J_{F-F} = 7.8 Hz (C_6D_6) suggest trans-CF_3

groups. In the ms of both 8 and 9 m/z = 70 (dimethylketene$^+$) occurs as base peak.

The ketene imine is sensitive to moisture. The exothermic reaction with water in THF furnished the lactam 10 in two diastereoisomers (4:1) with respect to C-5. The major product, mp 213-214°C, shows δ(5-H) as q at 3.98 with $J_{H,F}$ = 7.0 Hz, and the broad NH signal at 6.55. Ir (KBr): 3403 (N-H), 1786 (C=O, cyclobutanone), 1695 (amide I). Triethylenediamine in $CDCl_3$ catalyzed a slow epimerization at C-5; after 3 d a 17:83 equilibrium was established. Thus, the less favorable diastereoisomer of 10 was preferred in the kinetic protonation.

Ketene imine 9 combined with methanol in $CDCl_3$ affording a 1:1 mixture of diastereoisomeric lactim methyl ethers 11; δ(5-H) was 4.58 and 4.83 with $J_{H,F}$ = 8.0 Hz. Diazomethane - usually unreactive vs. carboxamides - converted the acidic lactam 10 (mp 213-214°C) into the diastereoisomers of 11 (7:3). Ir (KBr): C=N at 1685 and C=O at 1784 cm^{-1}. Correspondingly, 9 added aniline at the C=C bond producing the amidines 12; the NH signals at δ 5.30 and 6.52 ($CDCl_3$) disappeared with D_2O.

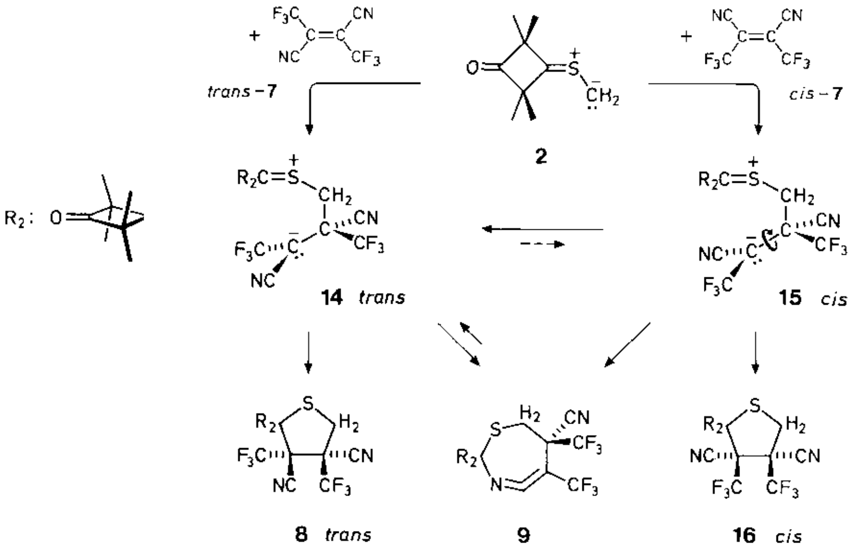
Cycloocta-1,2-diene is the smallest isolable ring to harbor an allene system,[7] although the 6- and 7-membered cyclic allenes occur as transient intermediates.[8] It may well be that the cumulated bond system of ketene imines allows some deformation more easily. X-Ray analysis of open-chain ketene imines shows deviations of C=C=N from linearity by 5 - 10°,[9] crystal lattice forces probably being responsible. The only 7-membered cyclic ketene imine known appears to be 1-azacyclohepta-1,2,4,6-tetraene (13) which is formed on irradiation of phenyl azide in a matrix at 8 K;[10] it is highly thermolabile.

B. Stereochemistry of Thiolane Formation

The trans- and cis-isomers of acceptor olefin 7 served as probes for the steric course of the (3+2) cycloaddition; nucleophilic catalysts establish a 95:5 equilibrium (CH_2Cl_2) of trans- and cis-7.[11]

The cycloreversion of thiadiazoline 1 into 2 + N_2 proceeded in C_6D_6 at 40°C with $t_{1/2}$ = 75 min. Upon warming 0.5 M 1 and 1.0 M cis-7 in C_6D_6 for 6 h (20 h) to 40°C, the unconsumed 7 revealed some isomerization with cis/trans = 84:16 (80:20). Is the thiadiazoline 1 the nucleophilic catalyst or is it the thiocarbonyl ylide 2 ? In the latter case, the cis and trans conformers of the zwitterion, 14 and 15, should dissociate back to the reactants. However, our conclusion that the precursor 1 was the "culprit" responsible for the disturbing cis,trans isomerization is based on twofold evidence.

1. Where bimolecular catalysis and unimolecular N_2 extrusion from 1 are competing, the negative $\Delta S^{\ddagger}$ of the bimolecular reaction results in a lower temperature dependence vs. the N_2 elimination. Indeed, after completing the reaction of 0.43 M 1 and 0.63 M cis-7 in $[D_{12}]$cyclohexane at the higher temperature of 80°C (10 min), a cis,trans ratio of 95:5 for the excess of 7 signalled little isomerization. ^{19}F Nmr analysis with standard indicated 71% of ketene imine 9, 16% trans-thiolane 8, and 10% cis-thiolane 16. Under the same conditions, trans-7 furnished 48% 9, 35% 8, and 0.5% 16, likewise *kinetically controlled.*



2. A trace of conc. H_2SO_4 in $CDCl_3$ (7.6 mM after shaking $CDCl_3$ with sulfuric acid) was found to protect cis-7, i.e., to suppress the thiadiazoline catalysis of cis → trans isomerization. The reaction of 1 with 1.2 equiv. cis-7 in this medium for 6 min at 80°C provided 9, 8, and 16 in the ratio 81:10:9.

In the reaction mixture obtained with cis-BTE, the ketene imine 9 was converted to lactam 10 by aqueous acetone. Distillation of the remainder at 90°C/0.4 Torr gave an oily 64:36 mixture of 8 and 16 which allowed a characterization of 16 by nmr spectra. $\delta(^{19}F)$ occurs at -63.0 and -66.5; J_{F-F} = 15 Hz is larger than 7.8 Hz for 8 and confirms greater proximity of the cis-located CF_3 groups.

Even at 160°C in CD_3CN, a stereoisomerization of thiolane 8 was not observed. Reactants and products being stable, we must conclude from the steric course that *an intermediate rotates* before ring closure takes place. Starting from cis-BTE, the cis-zwitterion 15 - cis with respect to the CF_3 groups - is the logical first intermediate which can either cyclize to 16 or undergo rotation. The double bond of the acceptor olefin has become a single bond in 15 allowing two directions of rotation, one with CN and the other with CF_3 on the "inside". With CN inside, the electrophilic carbenium-sulfonium ion snatches the nitrogen of the cyano group and forms the ketene imine 9. Thus, 9 results from a *half-way stop* between cis- and trans-zwitterions, 15 and 14. In the other rotation, illustrated by the arrow in formula 15, the bulkier CF_3 group passes on the inside until the trans-zwitterion 14 is reached after 180°C. Gauche conformations with respect to the newly formed σ-bond of 14 and 15 should be favored over anti zwitterions by Coulombic attraction.

Rotation of a zwitterionic intermediate was likewise made accountable for the non-stereospecificity of the 1,3-cycloadditions of 2 (and related thiocarbonyl ylides) to dimethyl 2,3-dicyanofumarate [12,13] and 2,3-dicyanomaleate.[14] What makes the reaction with 7 furnish such valuable *information is the combination of the steric* course of the (3+2) cycloaddition with the isolation of the cyclic ketene imine 9.

Why is the strained 9 *stable* in contrast to the transient character of 6 ? Two cyano groups better stabilize the anionic terminus of zwitterion 3 than CN + CF_3 in 14 and 15; as a consequence, the ring opening 6 → 3 is less endothermic than that of 9. A pertinent observation: a competition experiment established that thiocarbonyl ylide 2 combines 11 times faster with TCNE than with trans-7 (C_6D_6, 40°C).

A major factor, however, may be the stabilizing effect of trifluoromethyl groups on strained molecules. Although ample precedents are known,[15-17] it still remains somewhat of a *"magic phenomenon". Of course, the thiolane 8 is more stable than 9,* and slowly 9 rearranges to 8; the subsequent paper deals with the mechanistic implications of this ring contraction. It should be emphasized that the product ratios described above are not noticeably falsified by the ensuing isomerization of ketene imine 9.

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