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STEREOSPECIFIC REVERSIBLE CYCLOADDITION REACTIONS OF A BIPERIFUNCTIONAL COMPOUND, 1,3,6-TRIPHENYLIMIDAZO[1,2-c]THIA^{IV}ZOLE

Otohiko TSUGE*, Shuji KANEMASA, and Takayoshi HAMAMOTO
Research Institute of Industrial Science, and Department of Molecular Science
and Technology, Interdisciplinary Graduate School of Engineering Sciences,
Kyushu University, Kasuga, Kasuga-shi, Fukuoka 816

A nitrogen-bridged tetravalent sulfur compound, 1,3,6-triphenylimidazo[1,2-c]-thia^{IV}zole, undergoes highly stereospecific cycloaddition reactions to some acyclic olefinic dipolarophiles giving the [3 + 2] cycloadducts to the thiocarbonyl ylide of the imidazothia^{IV}zole in good yields. The formation of the [3 + 2] cycloadducts is explained to have arisen from the reversible cycloaddition reactions in a concerted manner.

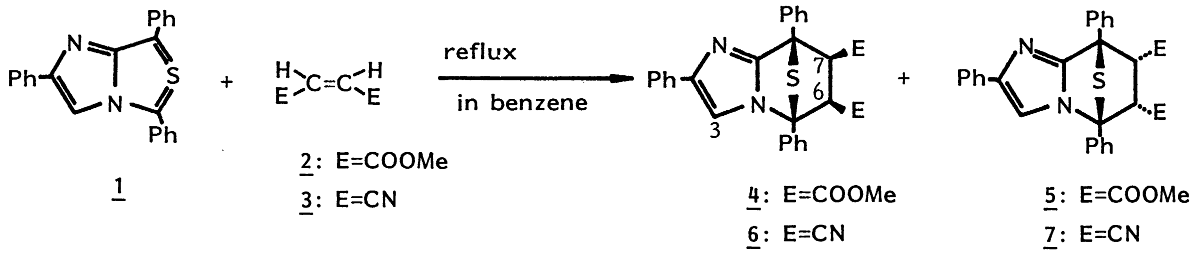
The previous communication has presented the first demonstration of biperifunctional character of 1,3,6-triphenylimidazo[1,2-c]thia^{IV}zole 1, a new type of nitrogen-bridged tetravalent sulfur compound, in the cycloaddition reactions with N-(p-tolyl)maleimide.[1] Both of the azomethine ylide and the thiocarbonyl ylide 1,3-dipole along the periphery of the imidazothia^{IV}zole 1 have participated in the cycloaddition reactions to give four isomeric [3 + 2] cycloadducts. In addition, the cycloaddition reactions toward both the peripheral 1,3-dipoles take place in a reversible fashion, the kinds and the relative yields of cycloadducts depending upon the reaction conditions (temperature and time).

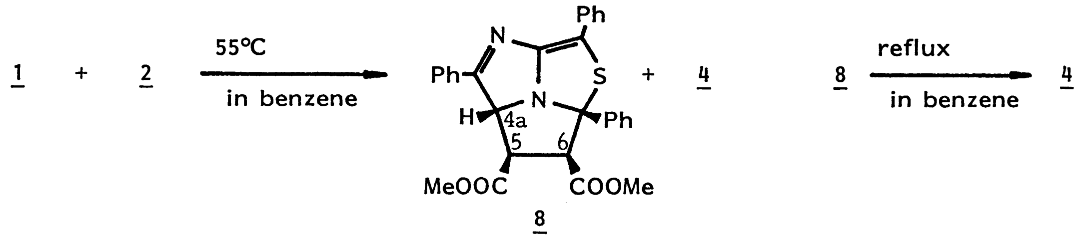
However the use of such a limited dipolarophile as N-(p-tolyl)maleimide gave us no any suggestive information on the stereochemical transformation of dipolarophile-configuration during the reversible cycloaddition reaction of 1. The mechanism for this rare cycloaddition reaction may be established on the basis of the stereochemical investigation of the reactions with acyclic olefinic dipolarophiles.

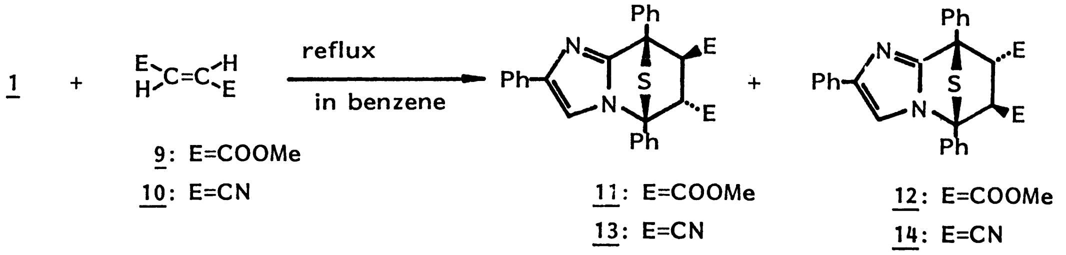
We would like to report in the present communication some examples of highly stereospecific 1,3-dipolar cycloaddition reactions of 1,3,6-triphenylimidazo[1,2-c]thia^{IV}zole 1 to symmetrically substituted olefinic dipolarophiles. It is proposed here that the reversible 1,3-dipolar cycloaddition reactions of the above system are most likely to proceed in a concerted manner.

The results of reactions of 1 with some symmetrically substituted olefinic dipolarophiles are summerized in Table 1, and the characteristic spectral data of the cycloadducts obtained are listed in Table 2.

The reaction of 1 with an equimolar amount of dimethyl maleate 2 under reflux in benzene for 24 h afforded the single 1:1 adduct 4 in 77 % yield. The structure of 4 was assigned to be the cis exo [3 + 2] cycloadduct to the thiocarbonyl ylide of 1 mainly on the basis of the ^{1}H-NMR spectrum which showed an olefin singlet at 6.80 ppm and two methine hydrogens in considerably high fields[2] as each doublet with the coupling constants of 9.0 Hz. Although no essential change of the yields was observed between the two reaction times (Table 1), the same reaction under the milder conditions (55 °C) allowed us to isolate the cis exo [3 + 2] cycloadduct 8[3] to the azomethine ylide of 1 in 27 % yield together with the previous product 4 (37 %).[4] The rather unstable cycloadduct 8 was convertible into







4 in 57 % yield when refluxed in benzene for 24 h. These results indicate that the thiocarbonyl ylide adduct 4 was formed via the azomethine ylide adduct 8 through a reversible 1,3-dipolar cycloaddition reaction as have been reported in the case of N-(p-tolyl)maleimide,[1] and that this reversible cycloaddition reaction proceeds in a highly stereospecific manner.

Interestingly the two 1:1 adducts 6 and 7 were obtained in the similar reaction of 1 with maleonitrile 3. The major product 6 and the minor one 7 were identified to be the cis exo and cis endo [3 + 2] cycloadducts to the thiocarbonyl ylide of 1, respectively, on the ground of the chemical shifts

Table 1. The Cycloaddition Reactions of 1,3,6-Triphenylimidazo[1,2-c]thia^{IV}zole 1 to Olefinic Dipolarophiles.

Dipolarophiles	Reaction Conditions[a]		Products (yield)	
2	reflux	24 h	4 (77 %)	
2	reflux	48 h	4 (79 %)	
2	55 °C	48 h	4 (37 %),	8 (27 %)
3	reflux	24 h	6 (43 %),	7 (38 %)
3	reflux	48 h	6 (70 %),	7 (13 %)
9	reflux	24 h	11 (51 %),	12 (32 %)
9	reflux	48 h	11 (52 %),	12 (32 %)
10	reflux	24 h	13 (52 %),	14 (26 %)

a) All the reactions were carried out in benzene.

and the coupling constants of two methine hydrogens of the products as well as the comparison of the ^{1}H-NMR spectra with those for the trans [3 + 2] cycloadducts 13 and 14 obtained in the reaction with fumaronitrile 10: The methine hydrogens (4.46 and 4.74 ppm with a coupling constant of 10.5 Hz) of 7 appear downfield of those (3.79 ppm) of 6 owing to the deshielding effect by the bridged sulfur atom.[2]

In a prolonged reaction, the yield of 6 increased by the decreased yield of 7 meaning that 7 gradually changed into 6 through a reversible 1,3-dipolar cycloaddition reaction. The relative yields between the exo and endo [3 + 2] cycloadducts to the thiocarbonyl ylide of 1 seem to depend upon the relative stability of them. No formation of the corresponding endo adduct 5 in the case of the maleate 2 would result from the high steric hindrance caused by the bulky ester substituents both at the endo positions.

Table 2. The [3 + 2] Cycloadducts to the Thiocarbonyl Ylide of 1.

Products	Mp (°C)[a]	^{1}H-NMR in $CDCl_3$ (δ ppm, Hz)					IR (cm^{-1})	M^+ (m/e)
		3-H	6-H	7-H	J_{6-7}	COOMe		
4	192-193	6.80 s	3.90 d	3.84 d	9.0[b]	3.25, 3.47	1750(CO)	496
6	182.5-185	6.70 s	3.79 s	3.79 s			2200(CN)	430
7	124-128.5	c)	4.74 d	4.46 d	10.5		2220(CN)	430
11	149.5-151	c)	5.04 d	3.74 d	4.5	3.29, 3.48	1740(CO)	496
12	161-163	6.94 s	4.22 d	4.58 d	4.0	3.42, 3.47	1740(CO)	496
13	142.5-144	c)	4.68 d	3.80 d	4.0		2220(CN)	430
14	d)	6.69 s	3.95 d	4.42 d	4.0			

a) All the compounds melt with decomposition.

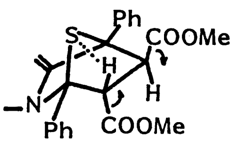
b) The coupling constant was measured in the ^{1}H-NMR spectrum taken in deuteriobenzene (the 6- and 7-H were observed at 3.82 and 3.58 ppm, respectively).

c) The signals are overlapping with aromatic signals.

d) The analytically pure sample was not available.

Two kinds of thiocarbonyl ylide adducts 11 and 12 were afforded in the reaction of 1 with dimethylfumarate 9. Similarly fumalonitrile 10 gave the corresponding cycloadducts 13 and 14 in about the same yields as the above case. The small coupling constants (4.0 to 4.5 Hz) between the adjacent methine hydrogens of all the cycloadducts show that the trans configuration of the starting olefins 9 and 10 have been retained in the reactions.

The major product 11 (and 13) and the minor one 12 (and 14) were assigned to be the 6-endo-7-exo and 6-exo-7-endo dicarboxylates (and dinitriles), respectively, on the basis of the ^{1}H-NMR spectra as well as the inspection of the molecular models: Compared to the smaller cyano substituents in 13 and 14, the bulky ester ones in 11 and 12 would induce the torsion around the C_6-C_7 bond[5] in order that the 6-exo hydrogen of 11 and both the 6-endo and 7-exo hydrogens of 12 may be shifted relatively downfield by the increased deshielding effects from the bridged sulfur and the bridgehead nitrogen atoms.



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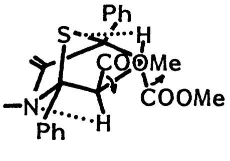

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Thus, in the cycloaddition reactions of 1,3,6-triphenylimidazo[1,2-c]thia^{IV}zole 1 to some symmetrically substituted olefinic dipolarophiles the configurations of starting olefins have been exclusively retained regardless of the kinds of [3 + 2] cycloadducts. Based on the fact that the four [3 + 2] cycloadducts of 1 to N-(p-tolyl)maleimide, each the endo and exo cycloadducts to the azomethine ylide and the thiocarbonyl ylide of 1, lie in a thermal equilibrium,[1] it is easily assumed that the most stable [3 + 2] cycloadducts such as 6 might have been formed via some unstable ones.

We would like to conclude that all the processes for the [3 + 2] cycloaddition reactions and the retro reactions of a rare nitrogen-bridged tetravalent sulfur compound, 1,3,6-triphenylimidazo[1,2-c]thia^{IV}zole 1, would proceed in a stereospecific manner. This high stereospecificity is most probably explained by a concerted mechanism.

References.

1. O. Tsuge, S. Kanemasa, and T. Hamamoto, Chem. Lett., 1982, 1491.
2. Among the methine hydrogens at the 6- and 7-positions of the [3 + 2] cycloadducts to the thiocarbonyl ylide of 1, the exo ones are known to appear downfield of the endo ones owing to the deshielding effect by the bridged sulfur atom (see ref. 1 and the references cited therein). The inspection of molecular models indicates that the 6-exo hydrogen is slightly closer to the sulfur atom than the 7-exo one, and that the 6-endo hydrogen can be deshielded by the bridgehead nitrogen atom. Thus, the assignment of the methine hydrogens in 4 and 7 has been accomplished as shown in Table 2.
3. 8: IR (KBr) 1720 cm^{-1} (CO); ^{1}H-NMR ($CDCl_3$) δ2.95 (1H, dd, J=4.5 and 10.0 Hz, 5-H), 3.37 and 3.44 (each 3H, s, COOMe), 4.02 (1H, d, J=10.0 Hz, 6-H), 5.41 (1H, d, J=4.5 Hz, 4a-H), and 7.20-8.07 ppm (15H, m, aromatics).
4. In the reaction with N-(p-tolyl)maleimide under reflux in benzene, 1 gave only the [3 + 2] cycloadducts to the azomethine ylide in good yields (see ref. 1).
5. In the both cases, the steric hindrance between the endo ester substituent and the fused imidazole ring and between the exo one and the bridged sulfur atom causes the torsion in the direction to reduce the dihedral angle between the two ester groups. Subsequently the 6-exo hydrogen of 11 and the 7-exo one of 12 are forced to come closer to the sulfur atom, and the 6-endo hydrogen of 12 to the bridgehead nitrogen atom.

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