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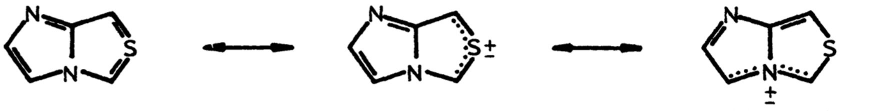
A NOVEL TETRAVALENT SULFUR COMPOUND, 1,3,6-TRIPHENYLIMIDAZO[1,2-c]THIA^{IV}ZOLE; SYNTHESIS AND PERIPHERAL CYCLOADDITION REACTION

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 novel tetravalent sulfur compound, 1,3,6-triphenylimidazo[1,2-c]thia^{IV}zole, was synthesized, which reacted with N-(p-tolyl)maleimide as both an azomethine ylide and a thiocarbonyl ylide 1,3-dipole yielding four 1:1 adducts that contained each endo and exo isomers. The cycloadducts of azomethine ylide were found to isomerize into those of thiocarbonyl ylide through a retro 1,3-dipolar cycloaddition reaction. It was offered that this nitrogen-bridged tetravalent sulfur compound was to be designated as a *bi-perifunctional* compound.

In the previous papers, it has been reported that the thiocarbonyl ylide 1,3-dipole of 1,3-diphenylthia^{IV}zolo[3,4-a]benzimidazole reacts with electron-deficient acetylenes and olefins in a stereo- and regioselective manner.[1,2] The imidazo[1,2-c]thia^{IV}zole A, a benzo-free analog of the above tetravalent sulfur compound, is expected to function not only as a thiocarbonyl ylide B but also an azomethine ylide 1,3-dipole C.



A B C

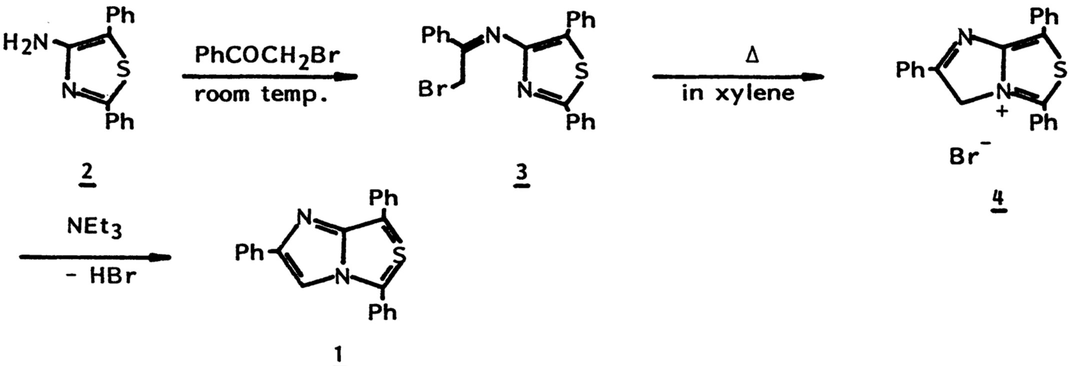
Three examples for the synthesis of nitrogen-bridged tetravalent sulfur compound that carries two functional parts of periphery have been reported,[3-5] two of them actually demonstrating the contribution of both functionalities. Thus a thia^{IV}zolo[3,4-b]indazole[4] and pyrrolo[1,2-c]thia^{IV}zole derivative[5] cycloadded to N-phenylmaleimide as an azomethine imine and azomethine ylide, respectively, while both of them reacted with dimethyl acetylenedicarboxylate as a thiocarbonyl ylide. No conceivable explanation, however, has been represented about what led to such different reactions.

In the present communication, we wish to report the synthesis of 1,3,6-triphenylimidazo[1,2-c]thia^{IV}zole, a new tetravalent sulfur system with a bridgehead nitrogen atom, and its unusual reactions in which it has contributed in two ways, as an azomethine ylide and a thiocarbonyl ylide 1,3-dipole, toward a dipolarophile, N-(p-tolyl)maleimide. In addition, we would like to propose that a word "*bi-perifunctional*" is to be used to express the unique nature of this kind of compound.[6]

Synthesis of 1,3,6-Triphenylimidazo[1,2-c]thia^{IV}zole 1.

Treatment of 4-amino-2,5-diphenylthiazole 2[7] with an equivalent amount of phenacyl bromide in ethanol at room temperature precipitated 3, mp 122-123 °C (dec.), as a colorless solid in 60 % yield. The product 3 is rather unstable suffering a decomposition on its purification by recrystallization.

But, it was given a satisfactory analysis as well as spectral data[8] for the assigned structure, 4-(2-bromo-1-phenylethylideneamino)-2,5-diphenylthiazole. When heated under reflux in xylene for 0.5 h, 3 readily cyclized into 1,3,6-triphenyl-5H-imidazo[1,2-c]thiazolium bromide 4, mp 236.5-240 °C, in 83 % yield. This salt 4 corresponds to a protonated form of the tetravalent sulfur compound 1 (Scheme 1).



Scheme 1

Deprotonation of 4 with triethylamine in chloroform gave a halogen-free product 1, mp 194-196.5 °C, as orange needles (from ethanol) in 97 % yield. Structural determination of 1, 1,3,6-triphenylimidazo[1,2-c]thia^{iv}zole, was based on the analysis and spectral data,[9] especially on the electronic spectrum that showed an absorption maximum at 487 nm ($\log\varepsilon$ 3.92). This nitrogen-bridged tetravalent sulfur compound 1, the second isolated example of this kind of compounds,[10] has such a remarkable thermal stability that it is recovered unchanged even when refluxed in xylene for 6 h.[11]

Peripheral Cycloaddition Reactions of 1 with N-(p-Tolyl)maleimide 5.

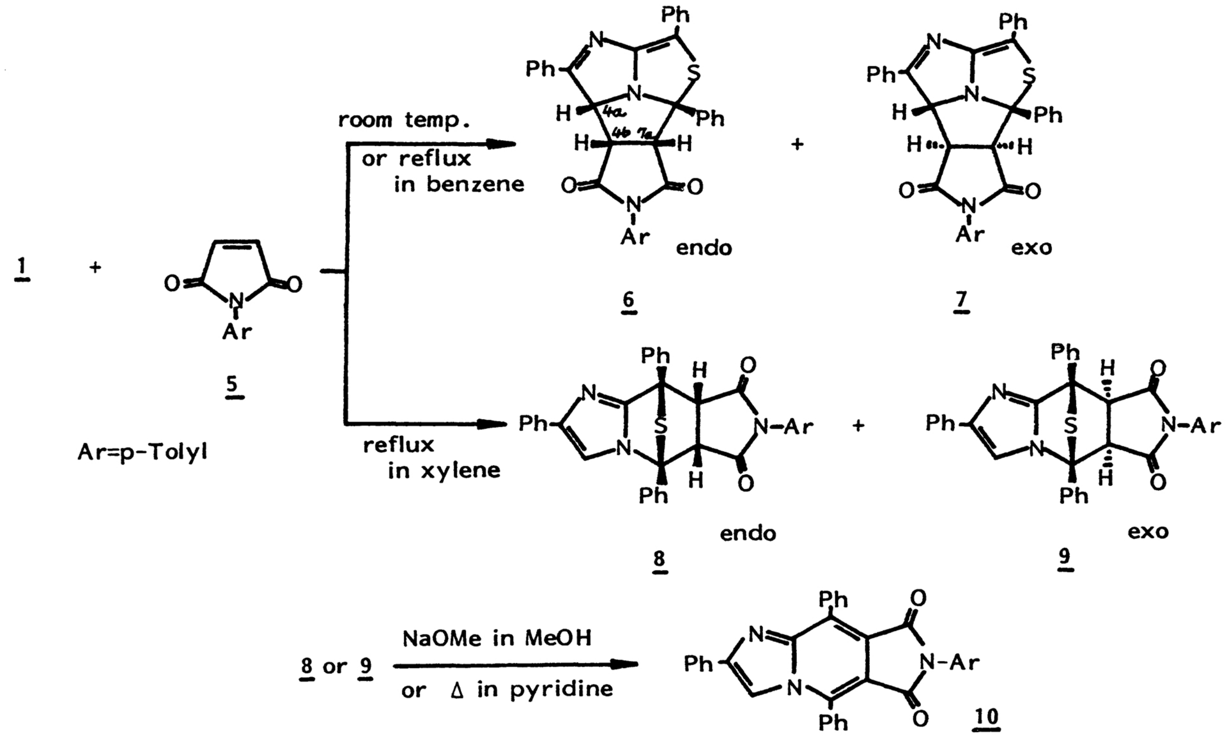
The reaction of 1 with an equivalent amount of N-(p-tolyl)maleimide 5 in dry benzene, under nitrogen at room temperature for 24 h, gave a mixture of two isomeric 1:1 adducts which were isolated through a column chromatography on silica gel using benzene as an eluent: 6, mp 172.5-174 °C, as yellow needles in 26 % yield and 7, mp 197-199 °C, as red prisms in 47 % yield (Scheme 2).

The structures of 6 and 7 were determined as the endo and exo [3 + 2] cycloadducts to the azomethine ylide 1,3-dipole of 1, respectively, on the basis of the spectral data.[12] The ^{1}H-NMR spectra indicate the presence of three consecutive methine hydrogens whose coupling constants are 9.5 (J_{4a-4b}) and 9.0 Hz (J_{4b-7a}) for 6, and 3.0 (J_{4a-4b}) and 9.5 Hz (J_{4b-7a}) for 7, supporting the endo and exo configurations.

The relative yields between 6 and 7 were found to depend on the reaction conditions such as reaction temperature, time and solvent as shown in Table 1. Below 80 °C, the only isolated products are 6 and 7. The reaction in pyridine at room temperature is favorable for the formation of endo adduct 6, whereas the reaction in benzene at 80 °C predominantly gives the exo adduct 7. At 110 °C

Table 1. The Reaction of 1 with 5.

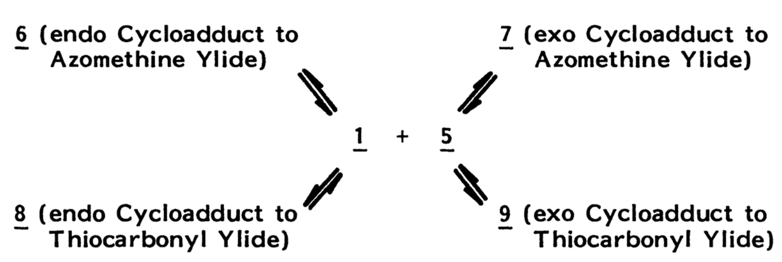
Reaction Conditions				Products (yield %)			
Temperature	Solvent	Time	Total Yield(%)	6	7	8	9
room temp.	benzene	24 h	73	26	47	-	-
room temp.	pyridine	24	89	52	37	-	-
reflux (80 °C)	benzene	3	70	10	60	-	-
80 °C	pyridine	0.5	73	34	39	-	-
reflux (110 °C)	toluene	2	68	+	9	11	48
reflux (115 °C)	pyridine	1.5	68	3	6	8	51
reflux (140 °C)	xylene	1	70	-	-	10	60



Scheme 2

(reflux in toluene) or at 115 °C (reflux in pyridine), the other two products, 8 and 9, are formed together with small amounts of two adducts 6 and 7.

When the same reaction was carried out in xylene under reflux for 1 h, no traces of 6 and 7 were obtained but instead the two isomeric 1:1 adducts were afforded by a column chromatography on silica gel: 8, mp 215-216 °C, as colorless needles in 10 % yield and 9, mp 259.5-262 °C, as colorless needles in 60 % yield. The structures of 8 and 9 were elucidated as the endo and exo [3 + 2] cycloadducts to the thiocarbonyl ylide 1,3-dipole of 1, respectively, on the basis of the spectral data.[13] In the ^{1}H-NMR spectrum the methine hydrogens of 8 (4.65 and 4.82 ppm) are observed in considerably lower fields than those of 9 (3.84 and 4.07 ppm) since those of 8 are deshielded by the sulfur atom.[14] When treated with sodium methoxide in methanol or refluxed in pyridine for 48 h, both 8 and 9 easily eliminated hydrogen sulfide to give the imidazo[1,2-a]pyrrolo[3',4'-c]pyridine 10, mp >300 °C, in excellent yields. The formation of 10 is consistent with the structures of 8 and 9.



Scheme 3

It is concluded that the four isomeric cycloadducts, 6 to 9, all lie in a thermal equilibrium, and that 6 is the initial kinetically controlled product and 9 is the final thermodynamically controlled one, on the basis of the following isomerization reactions: i) At the very initial stage of the reaction of 1 with 5 in benzene at 80 °C, 6 is the only product (by ^{1}H-NMR); ii) A mixture of 6 and 7 (6/7=1/12) is obtained by refluxing 6 or 7 in benzene for 18 h; iii) A mixture of 8 and 9 (8/9=1/2) is obtained by refluxing 6 or 7 in xylene for 4 h; iv) A mixture of 8 and 9 (8/9=1/6) is obtained by refluxing 8 or 9 in xylene for 24 h. The corresponding exo cycloadducts 7 and 9 are found to be more thermally stable than the endo ones 6 and 8 from the equilibrium compositions between 6 and 7 (1:12) and 8 and 9 (1:6).

The endo-exo isomerizations described above are confirmed to take place through a retro 1,3-dipolar cycloaddition reaction by the facts that the parent compounds 1 and 5 have been detected during the isomerization of 6 or 7 into their mixture in benzene-d_6 at 80 °C and of 8 or 9 into their mixture in xylene at 140 °C (by ^{1}H-NMR and thin layer chromatography). The isomerization into regio isomers would have taken the same reaction pathways (Scheme 3).

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2. O. Tsuge, H. Shiraishi, and M. Noguchi, Chem. Lett., 213 (1981).
3. H. Shimoharada, S. Ikeda, S. Kajigaeshi, and S. Kanemasa, Chem. Lett., 1237 (1977).
4. K. T. Potts and J. L. Marshall, J. Org. Chem., 41, 129 (1976).
5. J. M. Kane, J. Org. Chem., 45, 5396 (1980).
6. A bi-perifunctional compound is designated to be the one that carries two functionalities along the periphery of cyclic system. The first bi-perifunctional compound has been reported by Potts and his co-worker: K. T. Potts and D. McKeough, J. Amer. Chem. Soc., 96, 4268 (1974).
7. E. C. Taylor, Jr., J. A. Anderson, and G. A. Berchtold, J. Amer. Chem. Soc., 77, 5444 (1955).
8. 3: IR 1610 cm^{-1}; ^{1}H-NMR (CDCl$_3$) δ4.89 (2H, s), 7.00-8.30 (15H, m); MS m/e 352 (M$^+$-HBr).
9. 1: IR 1585 cm^{-1}; ^{1}H-NMR (CDCl$_3$) δ6.80-8.50 (16H, m, ArH + =CH-); UV λ_{max}^{EtOH} (logε) 487 (3.92), 310 (3.85), 255 nm (4.04); MS m/e 352 (M$^+$).
10. The first isolated example for tetravalent sulfur compounds with bridgehead nitrogens has been shown by Potts and his co-worker (see ref. 4).
11. Any spot other than that of 1 has not been detected in the TLC, while 1 partly decomposed to give a few spots after 24 h.
12. 6: IR 1775, 1705 cm^{-1} (CO); ^{1}H-NMR (CDCl$_3$) δ2.19 (3H, s), 3.72 (1H, dd, J=9.5, 9.0 Hz, 4b-H), 4.16 (1H, d, J=9.0 Hz, 7a-H), 5.14 (1H, d, J=9.5 Hz, 4a-H), 6.25-8.00 (19H, m); MS m/e 539 (M$^+$).
    7: IR 1780, 1710 cm^{-1} (CO); ^{1}H-NMR (CDCl$_3$) δ2.26 (3H, s), 3.31 (1H, dd, J=9.5, 3.0 Hz, 4b-H), 4.24 (1H, d, J=9.5 Hz, 7a-H), 5.48 (1H, d, J=3.0 Hz, 4a-H), 6.20-8.25 (19H, m); MS m/e 539 (M$^+$).
13. 8: IR 1780, 1710 cm^{-1} (CO); ^{1}H-NMR δ2.06 (3H, s), 4.65, 4.82 (each 1H, d, J=9.0 Hz, CH), 6.80 (1H, s, =CH-), 6.54-8.22 (19H, m); MS m/e 539 (M$^+$).
    9: IR 1770, 1720 cm^{-1} (CO); ^{1}H-NMR δ2.25 (3H, s), 3.84, 4.07 (each 1H, d, J=6.5 Hz, CH), 6.88 (1H, s, =CH-), 6.90-7.88 (19H, m); MS m/e 539 (M$^+$).
14. The deshielding effect of the bridged sulfur atom in this kind of system has been discussed in the following reports: M. P. Cava, M. Behforouz, G. E. M. Husbands, and M. Srinivasan, J. Amer. Chem. Soc., 95, 2561 (1973) and K. T. Potts and D. McKeough, J. Amer. Chem. Soc., 96, 4268 (1974). See also refs. 1 and 2.

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