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Rotaxane-Stabilized Thiophosphonium Salt from Disulfide and Phosphine

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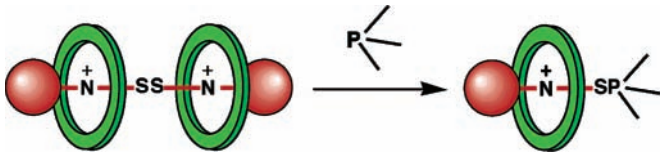
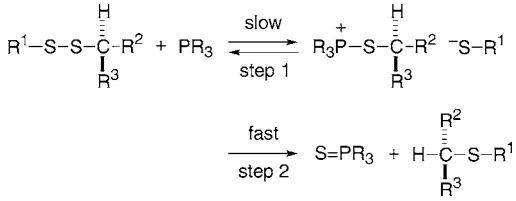
ABSTRACT



The reaction of a rotaxanated disulfide with hexamethylphosphorustriamide afforded a stable thiophosphonium salt in rotaxanated form. The structure of the thioposphonium salt was confirmed by spectroscopic and X-ray crystal structure analyses. The successful isolation of this salt was attributed to the special stabilization capability of the rotaxane structure.

Alkylthiophosphonium salt is a reactive species possessing contiguous reactive centers of phosphorus, sulfur, and carbon atoms adjacent to the sulfur toward the nucleophiles.[1] In the desulfurization of dialkyl disulfides with phosphines, alkylthiophosphonium salt acts as a key intermediate.[2] Desulfurization proceeds as shown in Scheme 1.[2] Generally, it is

Scheme 1



extremely difficult to isolate thiophosphonium salt[3] because the second step of the reaction proceeds much faster than the first. In addition, the axle component of rotaxanes is characterized as "a molecule laid under a specific environment" due to its highly protected structure resulting from the presence of wheel components interlocking each other. Some groups have reported that wheel components greatly reduce the reactivity of axle components in rotaxanes.[4]

We have recently succeeded in isolating an alkylthiophosphonium salt having a rotaxane structure in an attempted desulfurization reaction of a disulfidic [3]rotaxane[5] with a phosphine. This paper describes the isolation and structure

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(1) (a) Omelanczuk, J.; Mikolajczyk, M. *J. Am. Chem. Soc.* **1979**, *101*, 7292 and references therein. (b) Ohmori, H.; Nakai, S.; Sekiguchi, M.; Masui, M. *Chem. Pharm. Bull.* **1980**, *20*, 910. (c) Omelanczuk, J.; Mikolajczyk, M. *Tetrahedron Lett.* **1984**, *25*, 2493. (d) Krafft, G. A.; Siddal, T. L. *Tetrahedron Lett.* **1985**, *26*, 4867. (e) Omelanczuk, J. *Tetrahedron Lett.* **1993**, *49*, 39.

(2) Harpp, D. N.; Gleason, J. G. *J. Am. Chem. Soc.* **1971**, *93*, 2437 and references therein.

(3) Masui et al. isolated thiophosphonium salts from disulfide and phosphines by using controlled potential electrolysis (ref 1b).

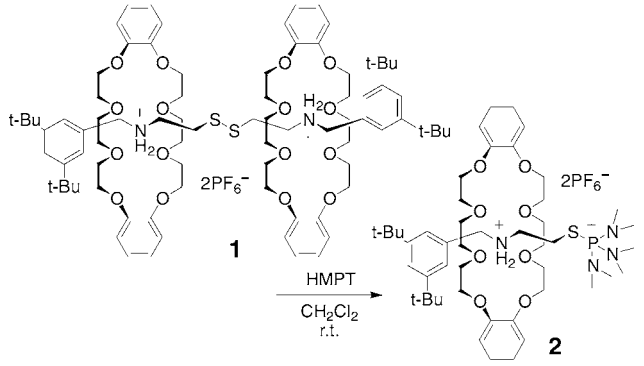
(4) (a) Buchecker, C. O. D,; Sauvage, J. P. *J. Am. Chem. Soc.* **1984**, *106*, 3043. (b) Leigh, D. A.; Murphy, A.; Smart, J. P.; Slawin, A. M. Z. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 728. (c) Anderson, S.; Claridge, T. D. W.; Anderson, H. L. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1310. (d) Asakawa, M.; Brown, C. L.; Menzer, S.; Raymo, F. M.; Stoddart, J. F.; Williams, D. J. *J. Am. Chem. Soc.* **1997**, *119*, 2614. (e) Parham, A. H.; Windisch, B.; Vögtle, F. Eur. *J. Org. Chem.* **1999**, 1233. (f) Reuter, C.; Vögtle, F. *Org. Lett.* **1999**, *2*, 593. (g) Kihara, N.; Tachibana, Y.; Kawasaki, H.; Takata, T. *Chem. Lett.* **2000**, 56. (h) Craig, M. R.; Hutchings, M. G.; Claridge, T. D. W.; Anderson, H. L. *Angew. Chem., Int. Ed.* **2001**, *40*, 1071. (i) Zehnder, D. W., II; Smithrud, D. B. *Org. Lett.* **2001**, *3*, 2485.

(5) (a) Kolchinski, A. G.; Alcock, N. W.; Roesner, R. A.; Busch, D. H. *Chem. Commun.* **1998**, 1437. (b) Furusho, Y.; Hasegawa, T.; Tsuboi, A.; Kihara, N.; Takata, T. *Chem. Lett.* **2000**, *18*. (c) Furusho, Y.; Oku, T.; Hasegawa, T.; Tsuboi, A.; Kihara, N.; Takata, T. *Chem. Eur. J.* **2003**, *9*, 2895. (d) Takata, T. *Expected Mater. Future* **2002**, *2*, 10.

of a thiophosphonium salt having a rotaxane skeleton by utilizing the transformation of a rotaxane structure while maintaining the interlocked structure[6] in light of the significant stabilization effect that a rotaxane structure has on reactive species.

Rotaxane **1** was synthesized by utilizing the thiol−disulfide interchange reaction and the ammonium−crown rotaxane system[7] as previously described.[5−b,c] When the desulfurization of a rotaxanated disulfide (**1**) was carried out by treatment with hexamethylphosphorustriamide (HMPT, 1.1 equiv) as a phosphine in dichloromethane at room temperature for 67 h, a crystalline product (**2**) was obtained in 40% yield (Scheme 2, Table 1, run 1) and 10% of **1** was

Scheme 2



recovered. The shortened reaction period (Table 1, run 2) resulted in both the enhancement of the yield of **2** and the isolation of [2]rotaxane **5** and axle **6** (Scheme 3).

Table 1. Isolated Yield of Rotaxanated Thiophosphonium Salt (**2**) in the Reaction of Rotaxanated Disulfide (**1**) and Phosphines[a]

run	phosphine (M)	time (h)	yield (%)
1	HMPT (0.11)	67	40
2	HMPT (0.11)	32	58
3	HMPT (0.20)	32	trace
4[b]	HMPT (0.11)(+ NH_4PF_6 0.1)	32	65
5	Ph_3P (0.11)	24	0
6	$(EtO)_3P$ (0.11)	24	0

[a] Reactions were carried out in CH_2Cl_2 at room temperature under an argon atmosphere. [**1**] = 0.10 M. [b] CH_3CN was used as the solvent. NH_4PF_6 (1 equiv) was added.

The above time-dependent phenomenon can be accounted for by the assumption that **3**, once formed during the reaction, reacts further with **1** and **5** to give **5** and **6**, respectively, via the thiol−disulfide interchange reaction. The attack of **3** at the P atom of **2** forms an unstable thiophosphonium salt **4**, which may decompose shortly thereafter. Therefore, the prolonged reaction time (run 1), as well as the excess amount of HMPT (run 3), cause a reduction in the yield of **2**, according to the mechanism proposed. The addition of an equimolar amount of ammonium hexafluorophosphate increased the yield of **2**, presumably due to the enhanced concentration of PF_6^- (run 4). Triphenylphosphine and triethyl phosphite gave no corresponding thiophosphonium salt-type product (Table 1, runs 5 and 6). HMPT should be distinguished from other phosphines by its high nucleophilicity and cation-stabilizing effect; also, it is bulky enough to act as an end-capping group capable of preventing the dethreading of the wheel component in the rotaxane.

The structure of **2** was fully determined by the ^{1}H NMR, FAB MS spectra, and X-ray crystal structure analysis. Figure 1[8] clearly suggests the rotaxane structure of thiophosphonium

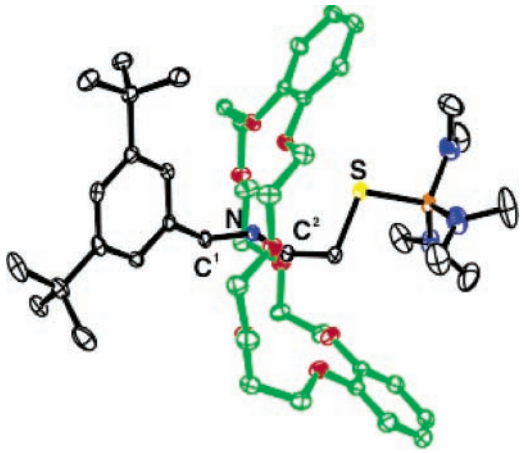


Figure 1. X-ray crystal structure of **2**. Counteranion PF_6^- and the solvent molecule have been omitted for clarity.

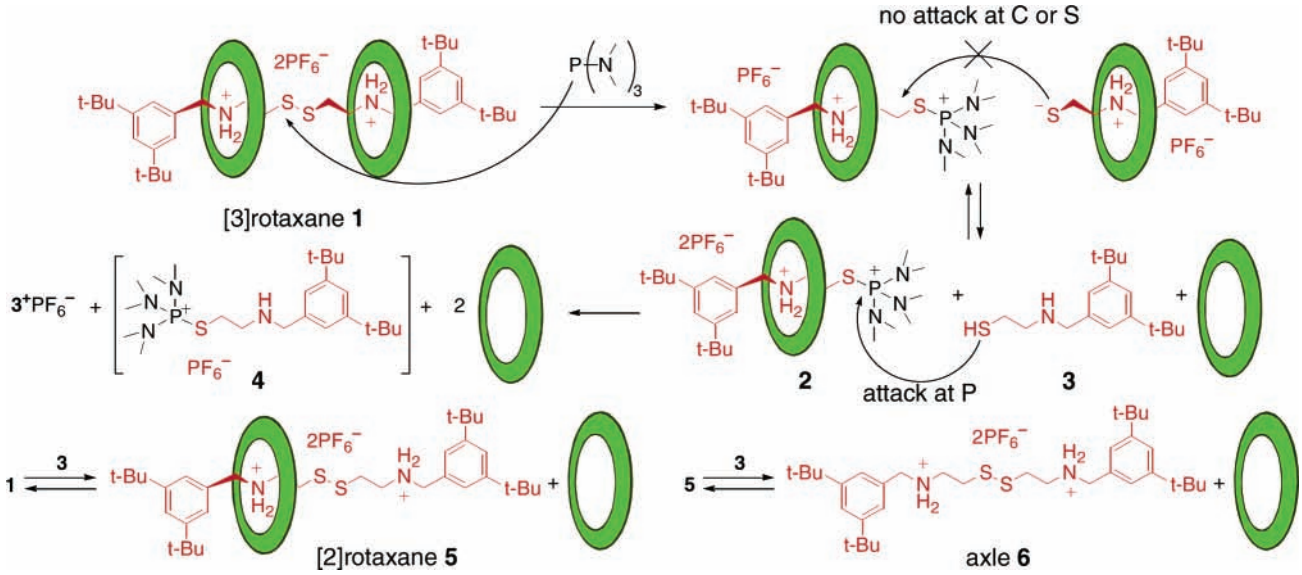
salt **2**. The crown ether oxygen atoms have some interaction with both the ammonium (N) protons and the methylene (C^1 and C^2) protons adjacent to the nitrogen atom. Interaction was also observable in the ^{1}H NMR spectrum (see Supporting Information), indicating that interaction takes place even in a solution state. Namely, there may be downfield shifts of the ammonium and methylene protons, consistent with the occurrence of intramolecular hydrogen bonding. The S−P bond length of **2** (2.07 A) shows that the S−P bond is a single bond and that a positive charge lies on the phosphorus atom. The S−C bond length of **2** (1.836 Å), which is longer than that (1.82 Å) of disulfide [3]rotaxane **1**, suggests that **2**

(6) (a) Rowan, S. J.; Stoddart, J. F. *J. Am. Chem. Soc.* **2000**, *122*, 164. (b) Chiu, S.-H.; Rowan, S. J.; Cantrill, S. J.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Chem. Eur. J.* **2002**, *8*, 5170.

(7) System using *sec*-ammonium salt and crown ether was first reported by Busch and then Stoddart. (a) Kolchinski, A. G.; Busch, D. H.; Alcock, N. W. *Chem. Commun.* **1995**, 1289. (b) Ashton, P. R.; Glink, P. T.; Stoddart, J. F.; Tasker, P. A.; White, A. J. P.; Williams, D. J. *Chem. Eur. J.* **1996**, *2*, 729. (c) Fyfe, C. T.; Stoddart, J. F. In *Advances in Supramolecular Chemistry*; Gokel, G. W., Ed.; JAI Press: Greenwich, CT, 1999; Vol. 5, pp 1−53.

(8) Single crystals suitable for X-ray analysis were grown by recrystallization from MeOH/ether/chloroform. Crystal data: $C_{47}H_{79}F_{12}N_4O_8P_3S$, M = 1181.31, monoclinic, a = 22.2201(3) Å, b = 12.7238(2) Å, c = 41.0667(4) Å, β = 91.6132(5)°, V = 11605.9(3) Å^3, space group $P2_1/n$, Z = 8, ρ = 1.352 g/cm^3, R = 0.082, R_w = 0.110, GOF = 0.91, reflection/parameter ratio = 24.87, max shift/error in final cycle = 0.002.

Scheme 3



is more reactive than **1**, similar to common thiophosphonium salts that are much more reactive than disulfide.[9]

The independent reaction of axle **6** with HMPT under the same conditions gave various products that contained no thiophosphonium salt (See Supporting Information). This result reveals that the wheel component (DB24C8) plays a crucial role in the isolation of roxanated thiophosphonium salt **2**. That is, the wheel component of the rotaxane sterically protects the reactive axle component so as to make possible the isolation of the reactive species.

(9) To investigate the protective effect of the wheel on the sulfur and the neighboring carbon atom of the axle, reactions of **2** with nucleophiles (Grignard reagent, diethylmalonate anion, and thiolate anion) were carried out. No new rotaxane was obtained and only the decomposition of the rotaxane structure was observed by ^{1}H NMR spectra. This seems to suggest that the nucleophiles preferentially attacked the P atom. If the nucleophiles attack the sulfur or the neighboring carbon atom, a new rotaxane is expected to be formed. This result shows that crown ether acts as an effective protecting group for both the sulfur and the contiguous carbon atoms that have strong electrophilicity to prevent the desulfurization reaction and to stabilize the thiophosphonium salt.

In this study, we have demonstrated that thiophosphonium salt, a reactive intermediate, can be isolated as a stable species after adopting a rotaxane structure during the reaction of the rotaxanated disulfide with a phosphine. The protective effect of the wheel component in a rotaxane system such as that described here is sufficiently large to allow for the isolation of thiophosphonium salt; it is therefore of interest as a new type of steric protection method. The protective function of the wheel toward the axle seems not only static but also dynamic in terms of both translation and circumrotation.

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Supporting Information Available: Experimental procedures for the synthesis of **1** and its reactions with HMPT and ^{1}H NMR and FAB MS spectra of **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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