ORGANIC
LETTERS

2005
Vol. 7, No. 13
2739−2742

Evidence for a Transition State Model Compound of In-Plane Vinylic S$_N$2 Reaction

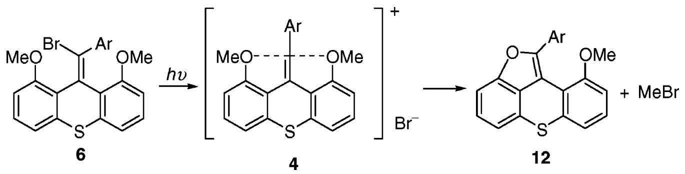
Torahiko Yamaguchi,[†] Yohsuke Yamamoto,*,[†] Yoshihisa Fujiwara,[‡] and Yoshifumi Tanimoto[‡]

*Department of Chemistry, Graduate School of Science, Hiroshima University,
1-3-1 Kagamiyama, Higashi-Hiroshima 739-8526, Japan, and Department of
Mathematical and Life Science, Graduate School of Science, Hiroshima University,
1-3-1 Kagamiyama, Higashi-Hiroshima 739-8526, Japan*

yyama@sci.hiroshima-u.ac.jp

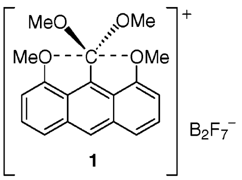
Received April 29, 2005

ABSTRACT

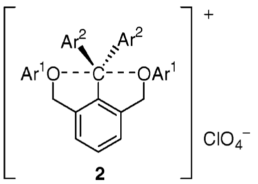


To isolate a transition state model compound of an in-plane vinylic S$_N$2 reaction, vinyl bromide 6 bearing a newly synthesized tridentate ligand derived from 1,8-dimethoxythioxanthen-9-one (5) was prepared as a precursor. Although irradiation of 6 gave demethylated benzofuran 12, a transient broad peak which indicates formation of the desired transition state model compound was observed in the laser flash photolytic study.

A bimolecular nucleophilic substitution (S$_N$2) reaction at an sp^3 carbon atom proceeds via a five-coordinate carbon compound as a transition state.[1] Recently, we reported the synthesis and crystal structure of hypervalent pentacoodinate carbon compounds bearing a sterically rigid anthracene ligand **1**[2] or a flexible van Koten type ligand **2**[3] as a transition state model compound of the S$_N$2 reaction.

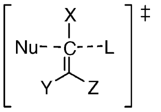


1



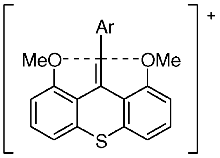
2

An example of an in-plane S$_N$2 reaction at an sp^2 vinylic carbon atom, which proceeds with complete inversion of the reaction center, has been reported by Ochiai et al.[4] Recently, Okuyama et al. concluded that the transition state of this reaction should be a four-coordinate carbon compound **3** based on detailed analysis of the kinetics.[5] However, the four-coordinate carbon compound as the transition state model of the in-plane vinylic S$_N$2 reaction has not been detected or isolated. Herein, we report the observation of the transition state model compound **4** using laser flash photolysis although the lifetime is very short (several hundreds microseconds).



3

Nu : nucleophile
L : leaving group



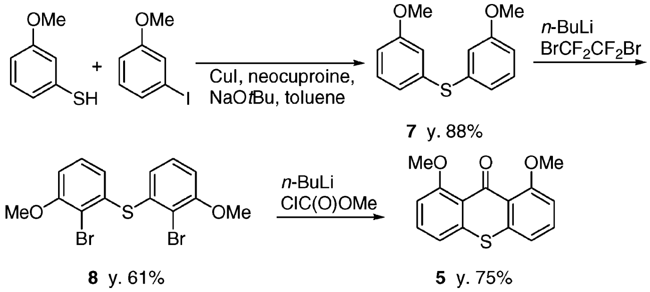
4

To isolate the transition state model compound, we synthesized 1,8-dimethoxythioxanthen-9-one (**5**) first as shown in Scheme 1.

[†] Department of Chemistry.
[‡] Department of Mathematical and Life Science.
(1) Morrison, R. T.; Boyde, R. N. *Organic Chemistry*, 6th ed.; Prentice Hall, Inc.: New Jersey, 1992; Chapter 5.

10.1021/ol050961o CCC: $30.25

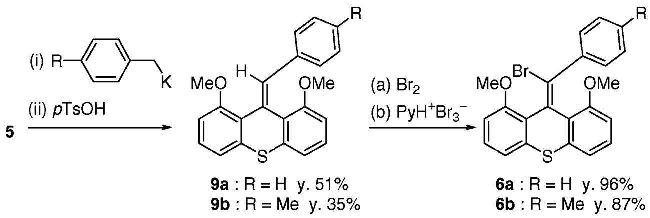
Scheme 1



Bis(3-methoxyphenyl) sulfide (**7**) was synthesized by a copper-catalyzed coupling reaction[6] of commercially available 3-iodoanisole and 3-methoxybenzenthiol. The sulfide **7** was selectively dilithiated by refluxing in *n*-hexane, and bis(2-bromo-3-methoxyphenyl) sulfide (**8**) was obtained after treatment with 1,2-dibromotetrafluoroethane. The sulfide **8** was then converted to **5** via dilithiation followed by treatment with methyl chloroformate.

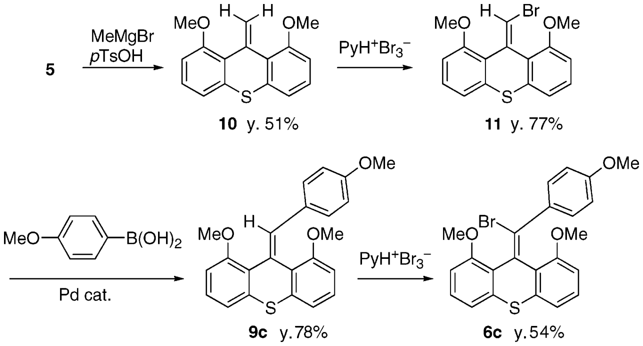
Because it was known that a vinyl halide affords a vinyl cation by photolysis,[7] we synthesized vinyl bromide **6** as a precursor as shown in Scheme 2.

Scheme 2



The reaction of thioxanthone **5** with benzylpotassium[8] afforded an alcohol which was treated with *p*-toluenesulfonic acid to give olefin **9**. Subsequent bromination of **9a** proceeded using Br$_2$, and the desired vinyl bromide **6a** was obtained (Scheme 2). In the case of **9b**, bromination using Br$_2$ afforded a byproduct, but it proceeded cleanly using pyridinium hydrobromide perbromide, and **6b** was obtained. However *p*-methoxybenzylpotassium could not be generated by similar procedures, so *p*-methoxy derivative **6c** was synthesized by another route (Scheme 3). Thioxanthone **5** was converted to **10** via treatment with MeMgBr and *p*-toluenesulfonic acid, followed by bromination with pyridinium hydrobromide perbromide. A Pd-catalyzed cross-coupling reaction of **11** with *p*-methoxyphenylboronic acid and subsequent bromination with pyridinium hydrobromide perbromide afforded **6c**. Colorless crystals suitable for X-ray analysis of **6c** were obtained by recrystallization from *n*-hexane/CH$_2$Cl$_2$, and the X-ray structure is shown in Figure 1. Daylight irradiation of vinyl bromide **6a** was carried out in chloroform-*d*. Analysis of the ^{1}H NMR spectroscopic data of the reaction mixture indicated the formation of benzofuran

Scheme 3



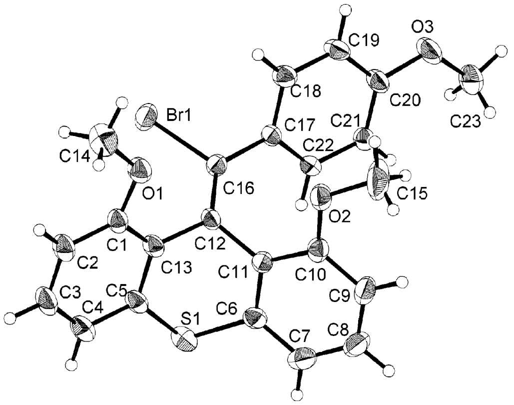
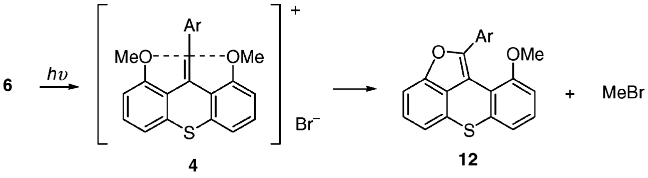


Figure 1. Crystal structure (30% thermal ellipsolids) of **6c**.

Scheme 4



---

(2) (a) Akiba, K.-y.; Yamashita, M.; Yamamoto, Y.; Nagase, S. *J. Am. Chem. Soc*. **1999**, *121*, 10644−10645. (b) Yamashita, M.; Yamamoto, Y.; Akiba, K.-y.; Hashizume, D.; Iwasaki, F.; Takagi, N.; Nagase, S. *J. Am. Chem. Soc*. **2005**, *127*, 4354−4371.

(3) Akiba, K.-y.; Moriyama, Y.; Mizozoe, M.; Inohara, H.; Nishii, T.; Yamamoto, Y.; Minoura, M.; Hashizume, D.; Iwasaki, F.; Takagi, N.; Ishimura, K.; Nagase, S. *J. Am. Chem. Soc.* **2005**, *127*, 5893−5901.

(4) Ochiai, M.; Ohshima, K.; Masaki, Y. *J. Am. Chem. Soc.* **1991**, *113*, 7059−7061.

(5) (a) Okuyama, T.; Takino, T.; Sato, K.; Ochiai, M. *J. Am. Chem. Soc.* **1998**, *120*, 2275−2282. Okuyama, T.; Takino, T.; Sato, K.; Oshima, K.; Imamura, S.; Yamataka, H.; Asano, T.; Ochiai, M. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 243−257. (b) Okuyama, T.; Yamataka, H. *Can. J. Chem.* **1999**, *77*, 577−583.

(6) Bates, C. G.; Gujadhur, R. K.; Venkataraman, D. *Org. Lett.* **2002**, *4*, 2803−2806.

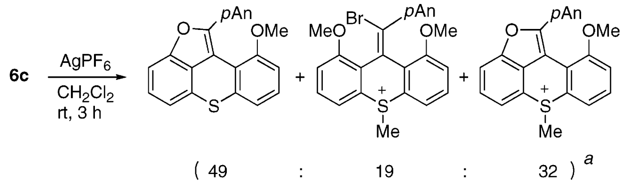
(7) Suzuki, T.; Kitamura, T.; Sonoda, T.; Kobayashi, S.; Taniguchi, H. *J. Org. Chem.* **1981**, *46*, 2275−2282.

(8) Schlosser, M.; Hartmann, J. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 508−509.

12a and MeBr (Scheme 4). In the photolysis by 266 nm laser light in CD_2Cl_2, the formation of **12a** was also observed.

To exchange the counteranion, we attempted reaction of **6** with $AgPF_6$,[9] but the reaction gave the mixture shown in Scheme 5.

Scheme 5



[a] estimated by ^{1}H NMR spectra.

Therefore, to detect the transient species in the photolysis of **6**, a laser flash photolytic study[10] was carried out. Figure 2 shows the transient absorption spectra of **6a** and non-methoxy derivative **13** recorded after 266 nm pulse laser irradiation (8 ns fwhm). The spectrum recorded in dichloromethane solution (Figure 2a) at a 0.4 μs delay time has a broad peak at ca. 400−650 nm which includes two components. One component appears at 400−500 nm and has a lifetime of less than 10 μs (**A**). Another has a spectrum widely spread over 400−650 nm and a lifetime of several hundreds μs (**B**). In the presence of oxygen, **B** is still present but **A** is absent (Figure 2b). Because the lifetime of **B** is hardly affected by O_2 bubbling, this peak should not be derived from either a radical species or a triplet state which should be quenched in the presence of O_2. The results strongly suggest that the spectrum of 400−650 nm observed after a 10 μs delay time should be assigned to a cation species. In our study on the hypervalent pentacoodinate carbon compound of **2**, a similar broad peak at 500−800 nm, which was considered to be derived from a charge transfer (CT) between apical aryloxy groups and the central carbocation, was observed.[3] Based on the formation of **12a** after photolysis of **6**, the intermediate should be the desired cation **4**, and the broad peak at ca. 400−650 nm should be derived from CT between ambilateral methoxy groups to the vinyl cation center. Consistent with the discussion, non-methoxy derivative **13** did not show a similar broad peak during the laser photolytic study (Figure 2c). In addition, the optimized structure of **4a** with the hybrid density functional theory (DFT) at the B3PW91/6-31G(d) level[11] using the Gaussian 98 program[12] showed that the symmetrically coordinated structure is the energy minimum (Figure 3). The two C−O distance are almost identical (2.292

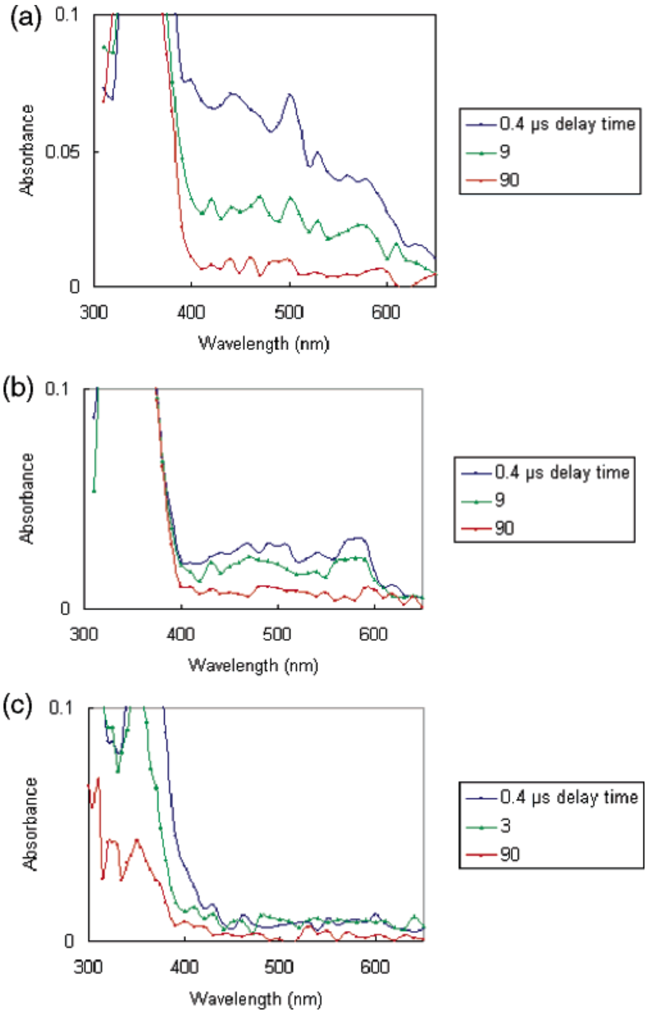


Figure 2. Transient absorption spectra of **6a** in CH_2Cl_2 in the (a) absence and (b) presence of O_2. (c) Transient absorption spectra of **13** in CH_2Cl_2.

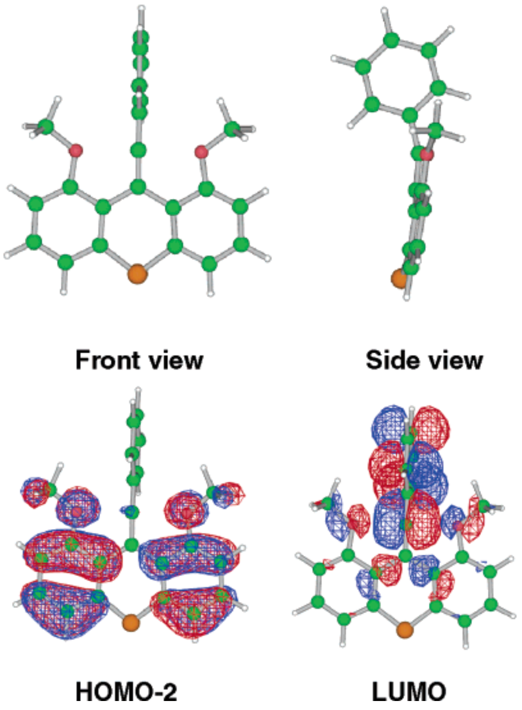


Figure 3. Optimized structure (upper) and orbitals (lower) of **4a** calculated at the B3PW91/6-31G(d) level.

and 2.313 Å). It should be noted that the calculated λ_{max} (529.1 nm: HOMO-2 to LUMO) of the optimized structure at the TD-B3PW91/6-311+G(2d, p) level is quite consistent with the observed spectra of **B**.

In conclusion, the transient species **B** should be the transition state model compound of the in-plane vinylic S_N2 reaction.

To prohibit the demethylation reaction, attempts at preparation of the compounds bearing aryloxy groups instead of the methoxy groups are in progress.

Acknowledgment. This work was supported by a Grant-in-Aid (No. 14078220) for Scientific Research provided by the Ministry of Education, Culture, Sports, Science and Technology of the Japanese Government. We thank Professor Tsugio Kitamura (University of Saga) for helpful discussions.

Supporting Information Available: Experimental procedures and CIF files of **6c**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL050961O

---

(9) Kitamura, T.; Kobayashi, S.; Taniguchi, H.; Rapoport, Z. *J. Org. Chem.* **1982**, *47*, 5003−5009.

(10) Tanimoto, Y.; Udagawa, H.; Katsuda, Y.; Itoh, M. *J. Phys. Chem.* **1983**, *87*, 3976.

(11) (a) Becke, A. D. *Phys. Rev.* **1988**, *A38*, 3098−3100. (b) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648−5652. (c) Perdew, J. P.; Wang, Y. *Phys. Rev.* **1992**, *B45*, 13244−13249.

(12) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A.; Stratmann, R. E., Jr.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniel, A. D.; Kudin, S. K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.5; Gaussian, Inc.: Pittsburgh, PA, 1998.