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Reaction of *o*-Benzyne with Tropothione Involving Biradical Processes†

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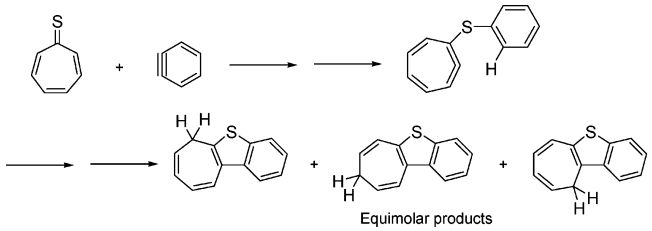

A benzyne−tropothione reaction was studied experimentally and computationally. Three isomeric products were detected by a careful experiment using two benzyne sources. The three equimolar products were identified. The expected symmetry-allowed [4 + 2] or [8 + 2] cycloadduct was not detected. In order to explain the unexpected products, density functional calculations and complete active space self-consistent field (CASSCF) calculations were carried out. The benzyne is, first, added to the tropothione via one-center C−S bond formation. Then a singlet biradical intermediate is formed. In the biradical, an α hydrogen atom of the tropothione moiety is moved to the benzyne moiety. A closed-shell intermediate is generated. This allene-type intermediate is isomerized to the second intermediate. The intramolecular proton shift in the latter leads to the three products. The biradical character of the benzyne has a key role in the present reaction and was discussed in reference to other benzyne reactions.

I. Introduction

o-Benzyne (**1**, bisdehydrobenzene) is a potential intermediate in organic chemical reactions.[2] On account of its transient nature, precise experimental characterizations have been difficult. Species **1** is usually represented as similar to benzene. However, it has a weak π bond in the plane of the ring and the π bond is formed from two sp^2 orbitals.[3] Chemical reactions involving **1**[4] have been carried out for over 100 years, and there were sporadic suggestions of the possibility of such a short-lived and highly reactive intermediate. However, conclusive proof for the existence of **1** was not obtained until Roberts et al.[2a] demonstrated it on the conversion of [1-^{14}C]chlorobenzene to [1-^{14}C]- and [2-^{14}C]aniline with potassium amide in liquid ammonia.

† This paper is dedicated to Professor Rolf Huisgen for his extensive studies of cycloadditions.[1]

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(1) Huisgen, R. The Adventure Playground of Mechanisms and Novel Reactions. In *Profiles, Pathways, and Dreams: Autobiographies of Eminent Chemists*; Seeman, J. I., Ed.; American Chemical Society: Washington, DC, 1994.

(2) (a) Roberts, J. D.; Simmons, H. E.; Carismith, L. A.; Vaughan, C. W. *J. Am. Chem. Soc.* **1953**, *75*, 3290−3291. (b) Washburn, W. N. *J. Am. Chem. Soc.* **1975**, *98*, 1615−1616. (c) Washburn, W. N.; Zahler, R. *J. Am. Chem. Soc.* **1976**, *98*, 7827−7828. (d) Washburn, W. N.; Zahler, R. *J. Am. Chem. Soc.* **1976**, *98*, 7828−7830. (e) Jones, R. R; Bergman, R. G. *J. Am. Chem. Soc.* **1972**, *94*, 660−661. (f) Breslow, R.; Napierski, J.; Clarke, T. C. *J. Am. Chem. Soc.* **1975**, *97*, 6275−6276.

(3) (a) Simmons, H. E. *J. Am. Chem. Soc.* **1961**, *83*, 1657−1664. (b) Berry, R. S.; Spokes, G. N.; Stiles, M. *J. Am. Chem. Soc.* **1962**, *84*, 3570−3577. (c) Chapman, O. L.; Mattes, K.; McIntosh, C. L.; Pacansky, J.; Calder, G. V.; Orr, G. *J. Am. Chem. Soc.* **1973**, *95*, 6134−6135. (d) Laing, J. W.; Berry, R. S. *J. Am. Chem. Soc.* **1976**, *98*, 660−664. (e) Brown, R. D.; Godfrey, P. D.; Rodler, M. *J. Am. Chem. Soc.* **1986**, *108*, 1296−1297.

(4) (a) Hoffmann, R. W. *Dehydrobenzene and Cycloalkynes*; Academic: New York, 1967; Chapt. 2, pp 99−193. (b) Sharp, J. T. In *Comprehensive Organic Chemistry: The Synthesis and Reactions of Organic Compounds*; Barton, D., Ollis, W. D., Eds.; Pergamon: Oxford, U.K., 1979; Vol. 1, Chapt. 2.8, pp 477−490.

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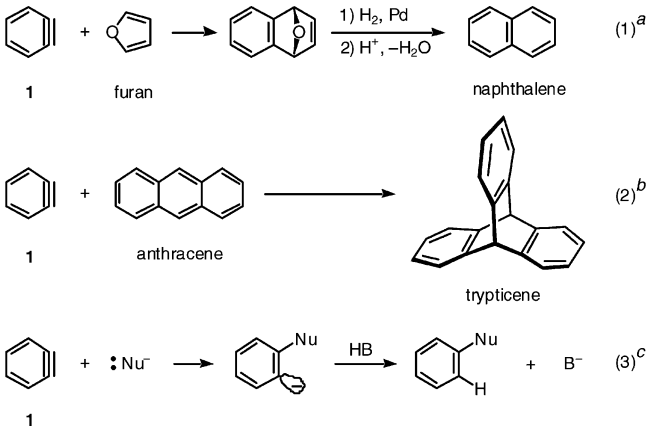
SCHEME 1. Typical Reactions of Benzyne as a Dienophilic or Electrophilic Reagent Reported So Far



[a] Reference 8. [b] Reference 9. [c] Reference 10.

They proposed the provocative formula **1** for the intermediate, benzyne. Almost simultaneously, as an alternative proof, Huisgen and Rist[5] reported on rearrangements in the aryl fluoride with a phenyl-lithium system, which likewise required an elimination−addition sequence. Theoretical analyses[6] of the electronic structure and vibrational frequencies (e.g., 2085 vs 1860 cm^{-1})[6f] of **1** have been extensively made.

Some typical reactions of **1** are shown in Scheme 1. In particular, eq 2 of Scheme 1 shows that **1** is an excellent dienophile in the normal electron demand.[7] Interestingly, there are also many "symmetry-forbidden" [2 + 2] cycloadditions of **1** to attain benzocyclobutanes.[11]

Tropothione[12] (**2**) is one of the simplest possible molecules in novel nonbenzenoid aromatic compounds.[13] The compound **2** shows almost exclusively [8 + 2] cycloadditions toward dienophiles (2π system),[12c,e] diene (4π),[12a] fulvene (6π),[12d] and tropothione (8π) itself (Scheme 2).[14] We reported the first explicit consideration of the secondary orbital interaction leading to a cycloadduct from the reaction of fulvenes with tropothione or tropone.[12d] A prominent shape of the highest occupied molecular orbital (HOMO) of **2** controlling the product configuration was described, and the large electron-donating strength of the sulfur $3p_\pi$ orbital of HOMO was demonstrated. The nucleophile **2** would react very efficiently with the electrophilies to afford [8 + 2] adducts in view of Scheme 2.

In this work, the **1** + **2** reaction was studied both experimentally and computationally. Great care was taken with the purity of **1** and the source of **2**, because both species are so reactive that many side reactions will occur by quenching impurity components. The reaction might give a zwitterionic intermediate in the strong donor (**2**)−acceptor (**1**) relationship (pathway a in Scheme 3).[15] Otherwise, a Diels−Alder ([4 + 2]) reaction will be brought about in pathway b of Scheme 3.

According to frontier molecular orbital (FMO) theory,[16a] [8 + 2] and [4 + 2] products in Scheme 3 may be obtained via concerted cycloadditions (Scheme 4). Apparently, the **1** + **2** reaction is a simple problem of either [8 + 2] or [4 + 2] cycloaddition.

Scheme 5 shows that tropone (**8**) reacts with benzyne **1**[17] (generated in situ from thermolysis of benzenediazonium-2-carboxylate) at 40 °C to give a [4 + 2] cycloadduct predominantly in 40% yield,[18] accompanied by an unidentified material

(5) (a) Huisgen, R.; Rist, H. *Naturwissenschaften* **1954**, *41*, 358−359. (b) Huisgen, R.; Rist, H. *Justus Liebigs Ann. Chem.* **1955**, *594*, 137−158.

(6) (a) Noell, J. O.; Newton, M. D. *J. Am. Chem. Soc.* **1979**, *101*, 51−57. (b) Rondon, N. G.; Domelsmith, L. N.; Houk, K. N.; Bowne, A. T.; Levin, R. H. *Tetrahedron Lett.* **1979**, 3237−3240. (c) Radom, L.; Nobes, R. H.; Underwood, D. J.; Li, W.-K. *Pure Appl. Chem.* **1986**, *58*, 75−88. (d) Rigby, K.; Hillier, I. H.; Vincent, M. A. *J. Chem. Soc., Perkin Trans. 2* **1987**, 117−119. (e) Hillier, I. H.; Vincent, M. A.; Guest, M. F.; Niessen, W. V. *Chem. Phys. Lett.* **1987**, *134*, 403−406. (f) Scheiner, A. C.; Schaefer, H. F., III; Liu, B. *J. Am. Chem. Soc.* **1989**, *111*, 3118−3124. (g) Burton, N. A.; Quelch, G. E.; Gallo, M. M.; Schaefer, H. F., III. *J. Am. Chem. Soc.* **1991**, *113*, 764−769. (h) Scheiner, A. C.; Schaefer, H. F., III. *Chem. Phys. Lett.* **1991**, *177*, 471−476. (i) Liu, R.; Zhou, X.; Pulay, P. *J. Phys. Chem.* **1992**, *96*, 8336−8339. (j) Radziszewski, J. G.; Hess, B. A., Jr.; Zahradnik, R. *J. Am. Chem. Soc.* **1992**, *114*, 52−57. (k) Kraka, E.; Cremer, D. *Chem. Phys. Lett* **1993**, *216*, 333−340. (l) Wierschke, S.; Nash, J. J.; Squires, R. R. *J. Am. Chem. Soc.* **1993**, *115*, 11958−11967. (m) Nicolaides, A.; Borden, W. T. *J. Am. Chem. Soc.* **1993**, *115*, 11951−11957. (n) Hobza, P.; Zahradnik, R.; Hess, B. A., Jr.; Radziszewski, J. G. *Theor. Chim. Acta.* **1994**, *88*, 233−241. (o) Lindh, R.; Lee, T. J.; Bernhardsson, A.; Persson, B. J.; Karlstrom, G. *J. Am. Chem. Soc.* **1995**, *117*, 7186−7194. (p) Hess, B. A., Jr.; Smentek, L. *Int. J. Quantum Chem. Quant. Chem. Symp.* **1995**, *29*, 647−656. (q) Liu, R.; Tate, D. R.; Clark, J. A.; Moody, P. R.; Van Buren, A. S.; Krauser, J. A. *J. Phys. Chem.* **1996**, *100*, 3430−3434. (r) Lindh, R.; Schutz, M. *Chem. Phys. Lett.* **1996**, *258*, 409−415. (s) Orendt, A. M.; Facelli, J. C.; Radziszewski, J. G.; Horton, W. J.; Grant, D. M.; Michl, J. *J. Am. Chem. Soc.* **1996**, *118*, 846−852. (t) Jiao, H.; Schleyer, P. von R.; Beno, B. R.; Houk, K. N.; Warmuth, R. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2761−2764. (u) Cramer, C. J.; Nash, J. J.; Squires, R. R. *Chem. Phys. Lett.* **1997**, *277*, 311−320. (v) Johnson, W. T. G.; Cramer, C. J. *J. Phys. Org. Chem.* **2001**, *14*, 597−603. (w) Wenk, H. H.; Winkler, M.; Sander, W. *Angew. Chem., Int. Ed.* **2003**, *42*, 502−528. (x) Clark, A. E.; Davidson, E. R. *J. Am. Chem. Soc.* **2001**, *123*, 10691−10698. (y) Salem, L.; Rowland, C. *Angew. Chem. Int. Ed.* **1972**, *11*, 92−111. (z) Hernandez-Trujillo, J.; Garcia-Cruz, I.; Martinez-Magadan, J. M. *Chem. Phys.* **2005**, *308*, 181−192.

(7) Fleming, I. *Frontier orbitals and organic chemical reactions*; John Wiley: London, 1976.

(8) Wittig, G.; Pohmer, L. *Angew. Chem.* **1955**, *67*, 348−348.

(9) (a) Wittig, G. *Org. Synth.* **1959**, *39*, 75−77. (b) Friedman, L.; Dogullo, F. M. *J. Org. Chem.* **1969**, *34*, 3089−3092.

(10) (a) Bunnett, J. F.; Happer, D. A.; Patsch, M.; Pyun, C.; Takayama, H. *J. Am. Chem. Soc.* **1966**, *88*, 5250−5254. (b) Bunnett, J. F.; Kim, J. K. *J. Am. Chem. Soc.* **1973**, *95*, 2254−2259.

(11) (a) Tabushi, I.; Oda, R.; Okazaki, K. *Tetrahedron Lett.* **1968**, 3743−3747. (b) Jones, M., Jr.; Levin, R. H. *Tetrahedron Lett.* **1968**, 5593−5595. (c) Wasserman, H. H.; Solodar, A. J.; Keller, L. S. *Tetrahedron Lett.* **1968**, 5597−5600. (d) Friedman, L.; Osiewicz, R. J.; Rabideau, P. W. *Tetrahedron Lett.* **1968**, 5735−5737. (e) Gassman, P. G.; Benecke, H. P. *Tetrahedron Lett.* **1969**, 1089−1092. (f) Bowne, A. T.; Christopher, T. A.; Levin, R. H. *Tetrahedron Lett.* **1976**, 4111−4114. (g) Jones, M., Jr.; Levin, R. H. *J. Am. Chem. Soc.* **1969**, *91*, 6411−6415. (h) Gregoire, B.; Carre, M. C.; Caubere, P. *J. Org. Chem.* **1986**, *51*, 1419−1427. (i) Hosoya, T.; Hasegawa, T.; Kuriyama, Y.; Suzuki, K. *Tetrahedron Lett.* **1995**, *36*, 3377−3380.

(12) (a) Machiguchi, T.; Hasegawa, T.; Otani, H.; Ishii, Y. *J. Chem. Soc., Chem. Commun.* **1987**, 1375−1376. (b) Machiguchi, T.; Hasegawa, T.; Itoh, S.; Mizuno, H. *J. Am. Chem. Soc.* **1989**, *111*, 1920−1921. (c) Higashi, M.; Yamaguchi, H.; Machiguchi, T.; Hasegawa, T.; Baumann, H. *Helv. Chim. Acta.* **1992**, *75*, 1880−1884. (d) Machiguchi, T.; Hasegawa, T.; Ishii, Y.; Yamabe, S.; Minato, T. *J. Am. Chem. Soc.* **1993**, *115*, 11536−11541. (e) Minato, T.; Yamabe, S.; Ishiwata, A.; Hasegawa; T. Machiguchi, T. *J. Mol. Struct.* **1999**, *461−462*, 359−377. (f) Machiguchi, T. *Tetrahedron* **1995**, *51*, 1133−1142. (g) Yamabe, S.; Kawajiri, S.; Minato, T.; Machiguchi, T. *J. Org. Chem.* **1993**, *58*, 1122−1127.

(13) Asao, T.; Oda, M. In *Carbocyclische π-Electronen-Systeme: Houben-Weyl, Methoden der organischen Chemie*; Müller, E., Bayer, Ollis, W. D., Eds.; Georg Thieme, Stuttgart, Germany, 1986; Vol. 15, Chapt. 2c, pp 49−85 and 710−780.

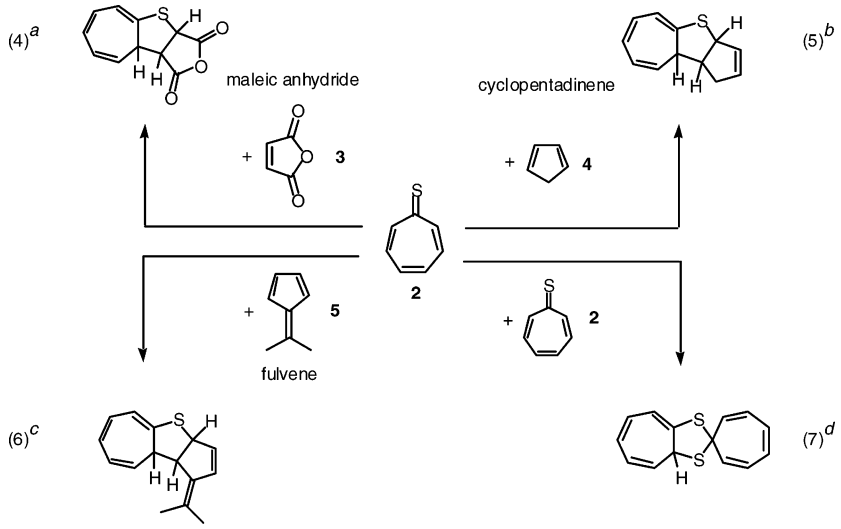
(14) Tropothione (**2**) dimerizes to give a [8 + 2] cycloadduct in the molten or solution state. In the solid state of **2**, a novel [8 + 8]-type dimer was formed spontaneously, showing nontopochemically controlled cyclodimerization.[12b]

(15) Huisgen, R. *Acc. Chem. Res.* **1977**, *16*, 199−206.

(16) (a) Fukui, K. *Theory of Orientation and Stereoselection*; Springer-Verlag: Heidelberg, Germany, 1970. (b) Inagaki, S.; Fujimoto, H.; Fukui, K. *J. Am. Chem. Soc.* **1976**, *98*, 4054−4061.

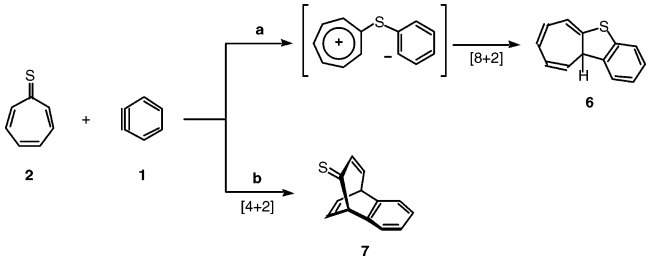
(17) Stiles, M.; Miller, R. G. *J. Am. Chem. Soc.* **1960**, *82*, 3802−3802.

SCHEME 2. Reactions of Tropothione (2) with Conjugated Systems To Give [8 + 2] Cycloadducts Reported So Far

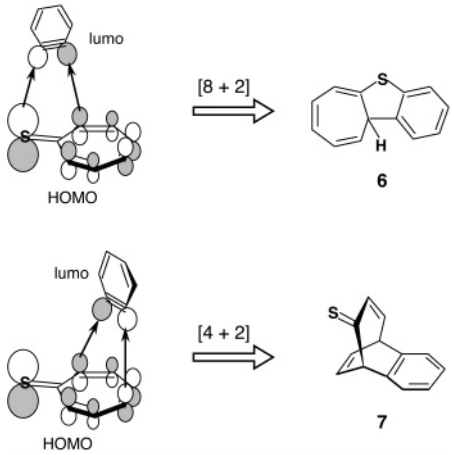


[a] Reference 12e. [b] Reference 12a. [c] Reference 12d. [d] Reference 12b.

SCHEME 3. Candidates for Reaction Routes between 1 and 2



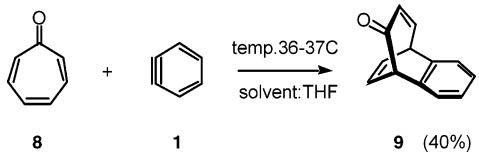
SCHEME 4. (HOMO → lumo) Antisymmetric Charge-Transfer Interactions Leading to [8 + 2] and [4 + 2] Cycloadducts[a]



[a] HOMO is the highest occupied molecular orbital of **2** and lumo is the lowest unoccupied molecular orbital of **1**.

of 2:1 adduct (*m*/*z* 258). This reaction constitutes the first example of Diels−Alder reactions and the representative one in troponoid reactions.

SCHEME 5. Reaction between Tropone (8) and Benzyne (1) To Give Diels−Alder Adduct 9 Predominantly[a]



[a] Reported by Kende et al.[18]

However, the present reaction has given three products entirely different from what is expected in Scheme 4. This work will show a novel reaction route (Scheme 6) initiated by scission of the C_α−H bond of **2** by **1**. The biradical character in the **1** + **2** complex causes the present reaction. Our goal is to explain how and why the unexpected products **10a**−**10c** are formed in high yield.

II. Experimental Results

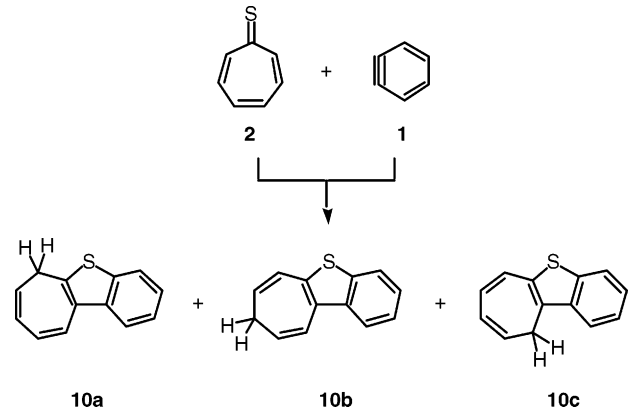
We have examined the reaction of benzyne (**1**) with tropothione (**2**). In the reaction performed, **1** was generated in situ (from thermolysis of benzenediazonium-2-carboxylate)[17] in refluxing dichloromethane at 40 °C for 1 h. The reaction gave an inseparable mixture of benzo-2*H*-cyclohepta[*b*]thiophenes (87% yield). The mixture consists of three components, **10a**−**c**, in an approximately equimolar ratio of the total three products according to ^{1}H NMR spectroscopy. We have also obtained the same equimolar mixture of products **10a**−**c** when the reaction was carried out at 10 °C for 1 h with **1** generated in situ from thermolysis of 1,2,3-benzothiadiazole-1,1-dioxide.[19] Scheme 7 shows the experimental results.

Structures of the inseparable products **10a**−**c** were elucidated by ^{13}C and ^{1}H NMR spectroscopies with an aid of a selective decoupling (SEL) and 2D NMR ^{13}C−^{1}H heteronuclear correlation spectroscopy (^{13}C−^{1}H COSY) as well as a quantitative analysis of nuclear Overhauser effect (NOE). The structure of

(18) Ciabattoni, J.; Crowley, J. E.; Kende, A. S. *J. Am. Chem. Soc.* **1967**, *89*, 2778−2779.

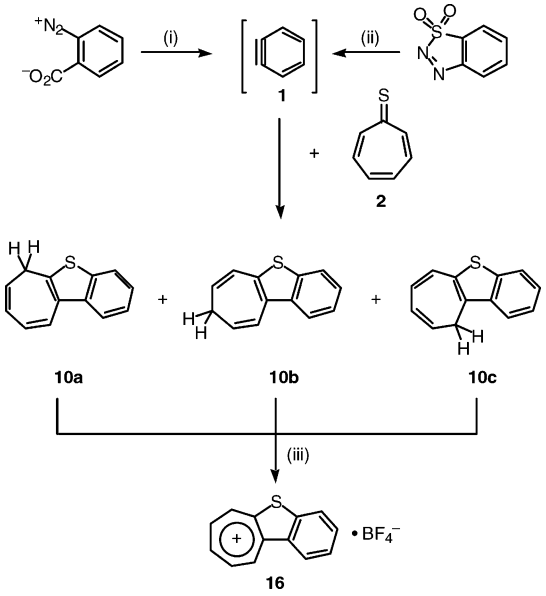
(19) Wittig, G.; Hoffmann, R. W. *Organic Syntheses*; Wiley & Sons: New York, 1973; Collect. Vol. 5, pp 60−66.

SCHEME 6. Present Result of the Reaction 1 + 2, Which Gives Three *Equimolar* Products[a]



[a] Neither [8 + 2] adduct **6** nor [4 + 2] adduct **7** in Scheme 3 has been detected.

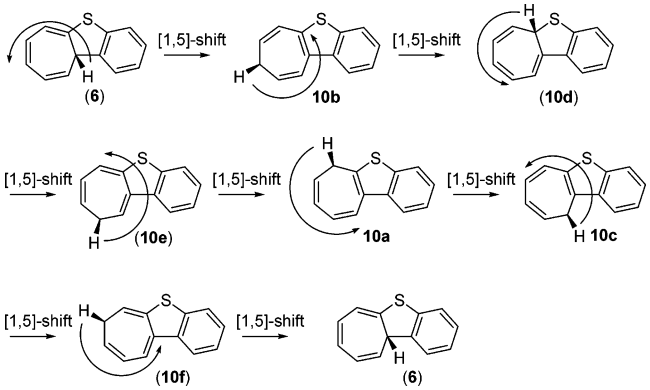
SCHEME 7. Results for the Reaction of Benzyne (1) with Tropothione (2) To Give a Mixture of Three Products (10a−c)[a]



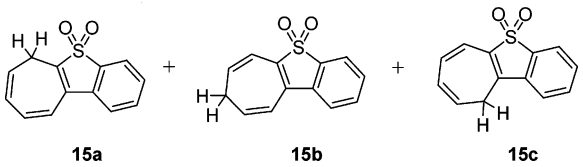
[a] Reagents and conditions: (i) Benzenediazonium-2-carboxylate generated in Situ from anthranilic acid and *iso*-amylnitrate, refluxing CH_2Cl_2 or tetrahydrofuran, 40 °C, 3 h, **10a−c** (87% isolated yield). (ii) 1,2,3-Benzothiadiazole 1,1-dioxide generated from sodium 2-aminobenzenesulfinate, CH_2Cl_2, 10 °C, 1 h, **1** + **2** → **10a−c** (equimolar mixture, 98% total yield isolated). (iii) Ph_3CBF_4, $CHCl_3$, 25 °C, 45 min, **16** (92% total yield isolated).

10b exhibits an approximate AA′BB′X_2 pattern, including triplet signals of the methylene protons [δ 2.52 (t, 2H, J = 6.8 Hz) for X], in its ^{1}H NMR spectrum, different from ABCDX_2 patterns involving doublet signals [δ 3.26 (d, 2H, J = 6.5 Hz) and 3.27 (d, 2H, J = 6.5 Hz)] of X for **10a** and **10c**, respectively. The assignments for those products are further supported by spectroscopic evidence for a mixture of their oxidation products, benzothiophene *S*-dioxides (**15a−c**) (equimolar mixture from 400-MHz ^{1}H NMR spectroscopy). For details, see Supporting Information. Among the three components of **15a−c**, the methylene signal (δ 2.51) of **15a** shifts largely downfield to δ 2.99 due to the strong influence by the anisotropic effect of an S=O group. In contrast, CH_2 signals of **15b** and **15c** are not largely influenced by the effect.

SCHEME 8. Hypothetical Consecutive [1,5] Hydrogen Shifts along a Counterclockwise Rotation, Which Must Involve the [8 + 2] Cycloadduct 6[a]



[a] Species in parentheses were not detected in the present experiment.



In seven-membered-ring triene compounds, [1,5]-hydrogen shifts are thought to be difficult usually. It has been known that such conversion needs relatively high temperatures above 100 °C.[20] We have attempted to detect the [8 + 2] cycloadduct (**6**), which would afford the products **10a−c** via [1,5] hydrogen shifts in Scheme 8The benzenediazonium-2-sulfate was used as a precursor of **1** in Scheme 7, step ii. We carried out the reaction at 10 °C and worked up below 10 °C carefully. However, we have obtained only the same mixture products **10a−c** in almost quantitative yield as those obtained at 40 °C in Scheme 7, step i. The [8 + 2] cycloadduct **6** has not been detected at all. The absence of the adduct **6** and the almost equimolar yield of three isomers, **10a**, **10b**, and **10c**, suggest either that the isomers are not derived from **6** or that **10a−c** are much more stable than **6**. The hypothetical [1,5] shifts in Scheme 8 will be traced in the next subsection. The present reaction between benzyne (**1**) and tropothione (**2**) is in remarkable contrast with the reported [4 + 2] reaction between tropone (**8**) and **1** to give **9** (Scheme 5).[18]

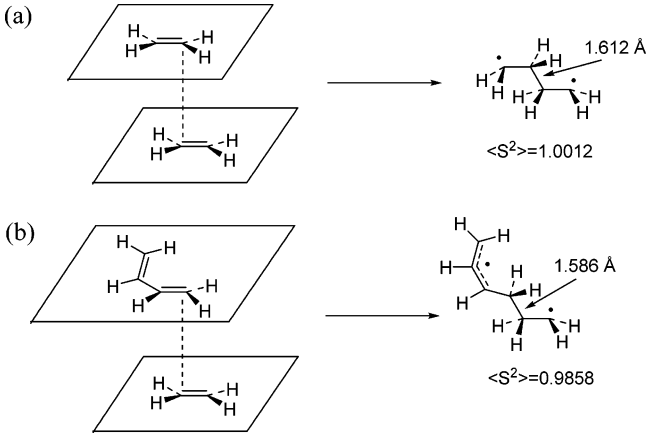
III. Computational Results of the Reaction Path

Whereas the present experimental result did not give the [4 + 2] cycloadduct **7**, the presence or absence of the [4 + 2] cycloaddition path was examined first. Computational methods are described in Supporting Information section III. We traced the potential-energy surfaces of the reactions by (U)B3LYP/6-31G* with self-consistent reaction field (SCRF) = dipole. This method is not necessarily of high accuracy, especially for open-shell singlet biradical species shown in Scheme 9. However,

(20) Nozoe, T.; Takahashi, K. *Bull. Chem. Soc. Jpn.* **1965**, *38*, 665−674.

(21) Goldstein, E.; Beno, B.; Houk, K. N. *J. Am. Chem. Soc.* **1996**, *118*, 6036−6043.

SCHEME 9. One-Center Addition Reactions Leading to Singlet Biradical Intermediates[a]



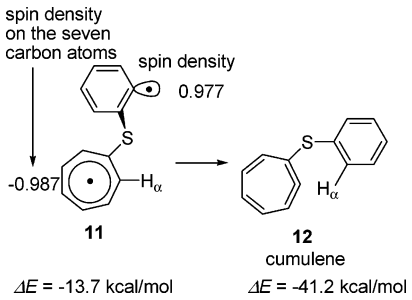
[a] (a) The ethylene dimer by Ub3LYP/6-31G* is taken from ref 24. (b) The ethylene-butadiene intermediate by Ub3LYP/6-31G* is from ref 21. Note that the additional moieties have the transoid geometries. $\langle S^2 \rangle$ is the spin expectation value.

the systems dealt with in this work are large and the better computational methods are hardly feasible in the potential-surface search. Figure 1 shows the reaction path, which corresponds to the [4 + 2] FMO interaction in Scheme 4. In the cycloaddition transition state (TS), the reaction-−coordinate vectors indicate correctly the concerted process. In Figure 1, a reaction between tropothione (**2**) and a typical electrophilic olefin, maleic anhydride (**3**), is also shown.[12e] Two [4 + 2] cycloaddition TS geometries are compared. While TS (**2** + **3**) has intermolecular C···C distances, 2.120 and 2.305 Å, TS (**1** + **2**) has appreciably large ones, 2.554 and 2.708 Å. In the C_s symmetric cycloaddition TS between ethylene and butadiene, the B3LYP/6-31G* distance is 2.273 Å.[21] In view of the geometry of this parent reacting system, TS (**2** + **3**) is normal and TS (**1** + **2**) is very *early*.[22] This early TS is consistent with the reasonable in-phase [4 + 2] HOMO−LUMO (lowest unoccupied molecular orbital) overlap in Scheme 4. Since the [4 + 2] cycloadduct **7** has not been detected in the present experiment, a more probable route needs to be considered.

According to the [8 + 2] HOMO−LUMO overlap in Scheme 4, second, we attempted to obtain the [8 + 2] cycloaddition TS yielding the adduct **6**. However, by the RB3LYP/6-31G* method, the [8 + 2] cycloaddition path could not be obtained.[23] The reason why the symmetry-allowed [8+2] path is unlikely will be explained in section IV.

It is well-known that the one-center addition path leading to a singlet biradical intermediate coexists with the cycloaddition path regardless of the condition that the latter is symmetry-allowed or symmetry-forbidden. Scheme 9 presents two parent systems calculated by the symmetry-broken UB3LYP/6-31G* geometry optimizations.[21,24]

The one-center addition occurs in the transoid orientation. According to the orientation, third, we searched a singlet biradical intermediate composed of **1** and **2**. The biradical (**11**) was obtained without the activation energy barrier and its geometry is shown in Figure 2. As expected, the $C_{16}-C_{15}-S_1-C_2$ moiety has a trans shape. One radical spin density is localized at C_{16} of the six-membered ring and the other is delocalized on the seven-membered ring. The intermediate **11** is not a zwitterionic species but a biradical, because the weight of configuration interaction (CI) coefficients is not limited to the adiabatic electron configuration. The CI coefficient of the adiabatic electron configuration was calculated to be −0.706 by CASSCF(4,4)/6-31G* [0.871 by CISD/6-31+G(d)] and that of the doubly excited one is 0.689. The biradical species **11** is −13.7 kcal/mol more stable than (**1** + **2**) by UB3LYP/6-31G* SCRF = dipole and is −6.2 kcal/mol more stable than the corresponding closed-shell species of RB3LYP/6-31G* SCRF = dipole.



Next, the isomerization paths from the biradical species were investigated. The radical **11** undergoes a surprising isomerization with TS(**11** → **12**) (Figure 2). The α hydrogen of the tropothione ring is snapped off by the radical center of the benzyne ring. The driving force of the α hydrogen migration is, of course, formation of the C−H bond in the benzyne ring. Such a C−H scission in the cyclic conjugated compounds is unprecedented. The resultant closed-shell species **12** has a cumulene fragment in the seven-membered ring. The π electron density of the phenyl group of **12** is nucleophilic and the central carbon of the cumulene is electrophilic. A C−C bond formation reaction is expected.

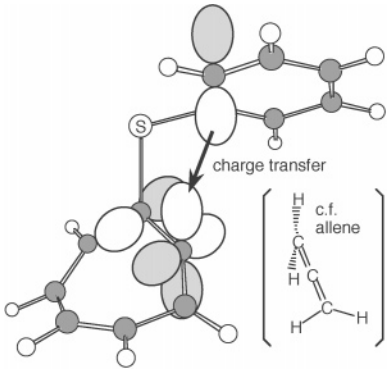
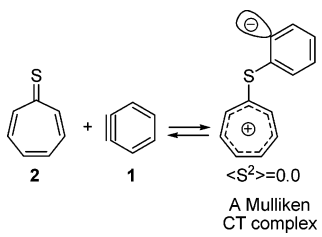


Figure 3 shows that the electrophilic center of the cumulene bond is linked with the phenyl α carbon via TS(**12** → **13**), yielding a tricyclic intermediate, **13**. The cumulene conformation

(22) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334−338.

(23) Alternatively, the TS search gave a Mulliken CT complex that does not lead to the subsequent reaction.



(24) Bernardi, F; Ross, I. *J. Am. Chem. Soc.* **1998**, *120*, 7770−7775.

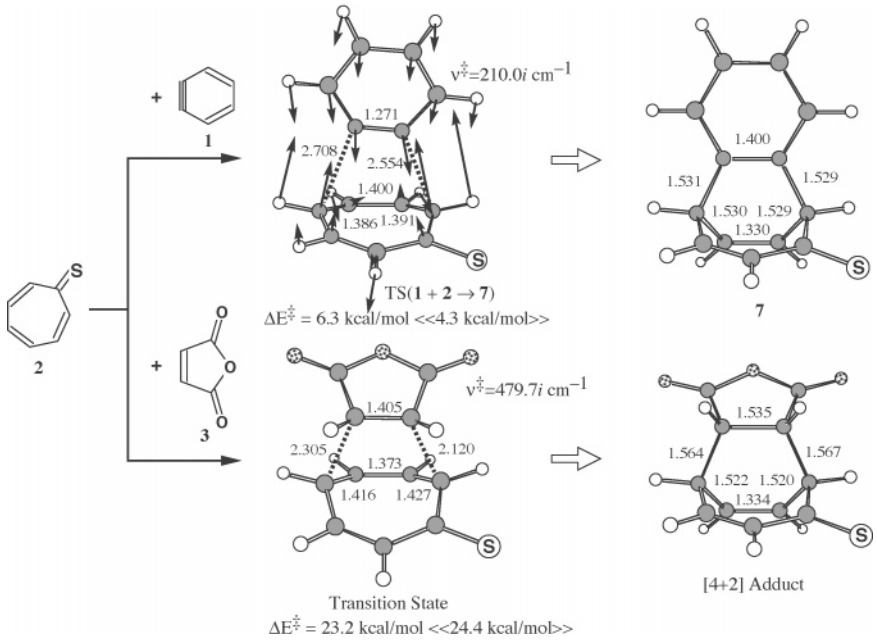
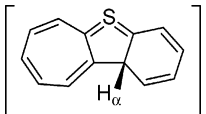


FIGURE 1. B3LYP/6-31G* SCRF calculated geometries of the [4 + 2] cycloaddition between **1** and **2** and its product **7**. Distances are in angstroms. The activation energy, $\Delta E^{\ddagger}$, is relative to the sum of total energies of the reactants. For TS, the reaction-coordinate vectors corresponding to the sole imaginary frequency, $\nu^{\ddagger} = 210.0i$ cm^{-1}, are sketched. In the lower side, the [4 + 2] cycloaddition TS geometry of the reaction between **2** and maleic anhydride **3** is shown for comparison. The notation ⟨⟨energy⟩⟩ indicates those in the gas phase, which are similar to those containing SCRF=dipole.

of **12** has made it possible to undergo the intramolecular addition. Noteworthy is the large C−H$_\alpha$ distance, 1.120 Å, in **13**. The proton H$_\alpha$ would shift either intermolecularly or intramolecularly.



intermediate **13**

First, the intermolecular shift was considered. From the transient and unstable intermediate **13**, a double and mutual proton transfer is likely in the $\pi-\pi$ stack conformation of a dimer of intermediate **13** (Figure 4). The proton transfer occurs in a stepwise process with an ion-pair intermediate **14**.[25]

Through the intermolecular double proton transfer, two neutral molecules, **10a** and **10b**, are obtained. The proton attachment to the seven-membered ring takes place so that a thiophene five-membered ring fused to the benzene one is attained. On account of the mobility of the plane of intermediate **13**, the double proton transfer shown in Scheme 10 might give possibly three structural isomers **10a**, **10b**, and **10c**. However, the intermolecular reactions are usually unfavorable owing to the entropy loss by the association. They need to be compared with unimolecular ones in Gibbs free energies.

The energy diagram of the novel reaction paths is shown in Figure 5 along with that of the [4 + 2] cycloaddition. The product of the multistep process is more stable than that of the

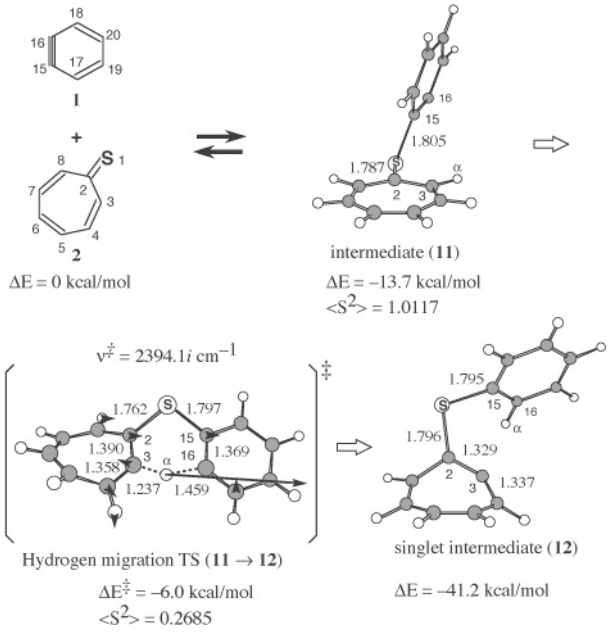


FIGURE 2. Reaction between **1** and **2** involving a singlet biradical intermediate **11** to arrive at an allene intermediate **12**. (U)B3LYP/6-31G* distances are shown.

Diels−Alder one, and the rate-determining step of the former process is TS(**11** → **12**) (hydrogen migration).[26]

Second, the intramolecular process of **13** → **10** was considered. Paths of H$_\alpha$ 1,2 and 1,5 shifts were calculated and their energies are shown in Figure 6. From the intermediate **13**, a [1,2] shift leads to the [8 + 2] cycloadduct, **6**. Since the step **13** → **6** is very exothermic, the transient species **6** may be

(25) While TS of the first transfer, TS(**13** + **13** → **14**) was obtained successfully, that of the second one could not be obtained in spite of many attempts. Probably, the neutralization process from **14** to the product (**10a** + **10b**) has a particularly small activation energy. In general, neutral reactions from ion-pair species are difficult to describe by the calculations which can not include the bulk solvent effect.

(26) The one-center addition process, **1** + **2** → **11**, was calculated to be of the monotonic energy decrease.

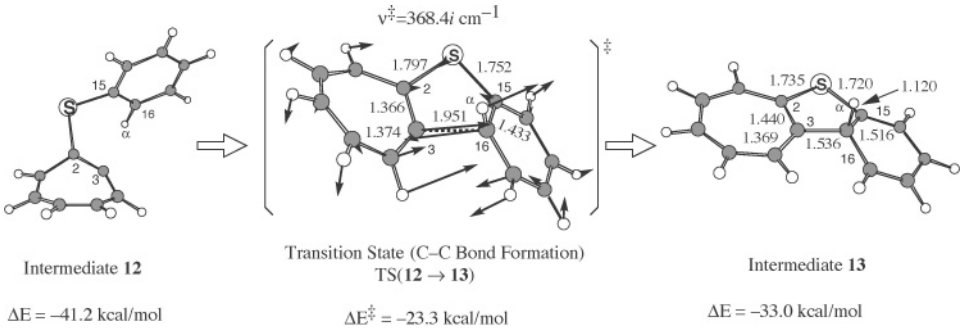


FIGURE 3. C−C bond-forming path leading to an intermediate **13** with the hypervalent sulfur.

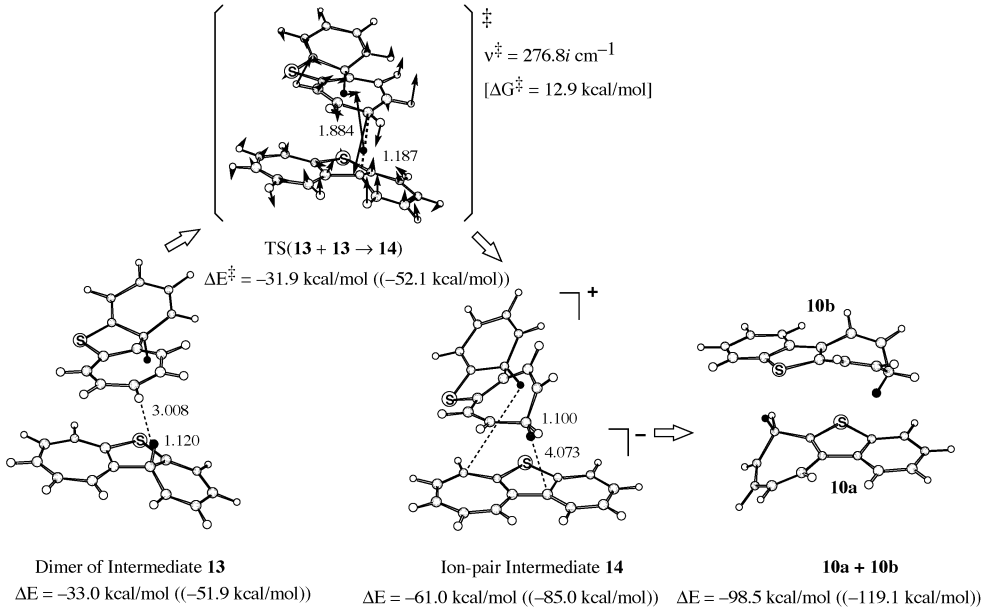


FIGURE 4. Stepwise proton-transfer process via an ion-pair intermediate **14** in the stack configuration of the two intermediates **13**. Half energies of dimeric species calculated by B3LYP/6-31G* SCRF=dipole, TS(**13** + **13** → **14**) and **14**, are shown. In double parentheses, the MP2/6-31G* SCRF=dipole energies are also shown.

subject to further isomerization, i.e., [1,5] shifts. Activation energies of the [1,5] shifts are not so different, and they would occur repeatedly. Among the eight isomers, **13**, **6**, **10b**, **10d**, **10e**, **10a**, **10c**, and **10f**, three (**10b**, **10a,** and **10c**) are most stable. Therefore, after the repetitious isomerizations, eventually three species with similar stabilities could be obtained. This result is consistent with the present experimental evidence.

In the top right portion of Figure 4, the activation barrier ($\Delta G^{\ddagger}$) of Gibbs free energy of TS(**13** + **13** → **14**) is shown in brackets, [$\Delta G^{\ddagger}$ = 12.9 kcal/mol, T = 298.15 K, and P = 1 atm]. Although the energy barrier of $\Delta E^{\ddagger}$ of TS(**13** + **13** → **14**) is small, 2.0 kcal/mol, the bracketed value is large owing to the entropy loss of the dimer association. In the top left portion of Figure 6, the $\Delta G^{\ddagger}$ value of TS(**13** → **6**) is also shown in brackets, [$\Delta G^{\ddagger}$ = 7.5 kcal/mol, T = 298.15 K, and P = 1 atm]. Comparison of the two bracketed values indicates that the intramolecular H_{α} shift (Figure 6) is more likely than the intermolecular one (Figure 4). Aside from the proton shift processes, the similar stabilities of **10a**, **10b** and **10c** correspond reasonably to their equimolar yields.

IV. Discussions of Sources of the Anomalous Reactions in Figures 2, 3, and 6

Prior to experiments, the [4 + 2] or [8 + 2] cycloaddition between **1** and **2** in Scheme 4 was expected. According to the large sulfur 3pπ lobe of the tropothione HOMO, the [8 + 2] addition is more likely than the [4 + 2] one. However, not the cycloaddition but the peculiar multistep route of Figures 2, 3 and 6 has been obtained. The absence of the direct [8 + 2] cycloaddition is considered first.

In Scheme 11, the shape of lumo of **1** is drawn. The sp^2 lobe of the lumo has rigid 120° directionality. In general, cycloadditions require the $sp^2 \rightarrow sp^3$ rehybridization at reaction centers. The rigid sp^2 directionality of the lumo of **1** cannot satisfy the requirement. In the upper portion of Scheme 11, the maximum HOMO−lumo orbital overlap at one site sacrifices that at the other site. That is, the direction of the sp^2 lobe of C_{16} cannot be adjusted to make the $C_{16}-C_3$ bond. The [8 + 2] cycloaddition is unlikely due to the rigid orbital extension of lumo. That is, in the [8 + 2] cycloaddition path, the overlap cannot contribute to the C···C bond formation. Giving up the in-phase π approach, benzyne approaches tropothione in the one-center addition orientation to form the singlet biradical **11**.

In order to check the biradical character of the one-center benzyne adduct, two other intermediates **17** and **18** were considered (Scheme 12). The species **17** is composed of **1** and a nucleophilic model olefin, 1,1-dimethoxyethene [$H_2C{=}C(OMe)_2$]. The intermediate **18** is composed of an electrophilic olefin, 1,1-dicyanoethene [$(NC)_2C{=}CH_2$], and the nucleophilic olefin.

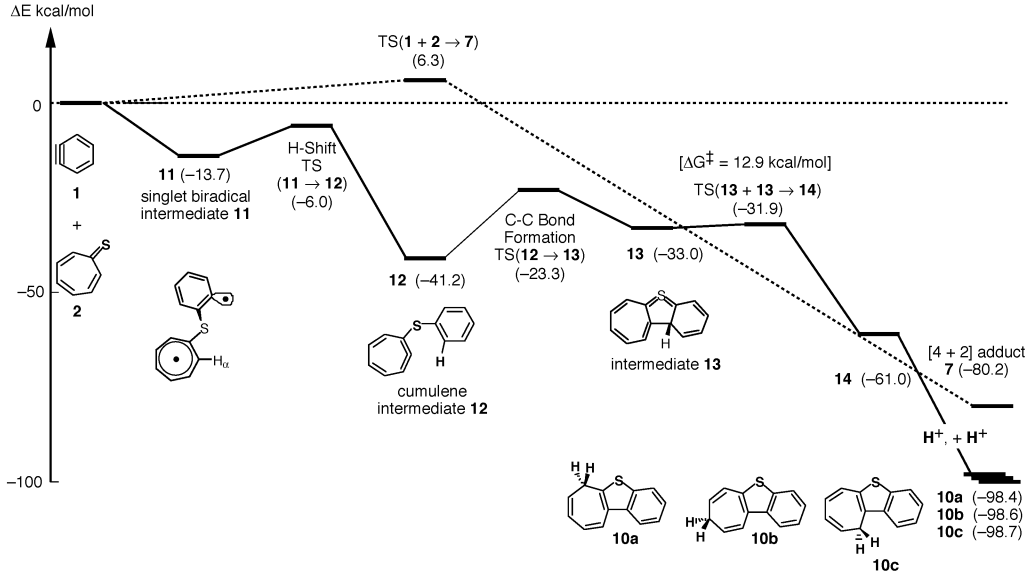
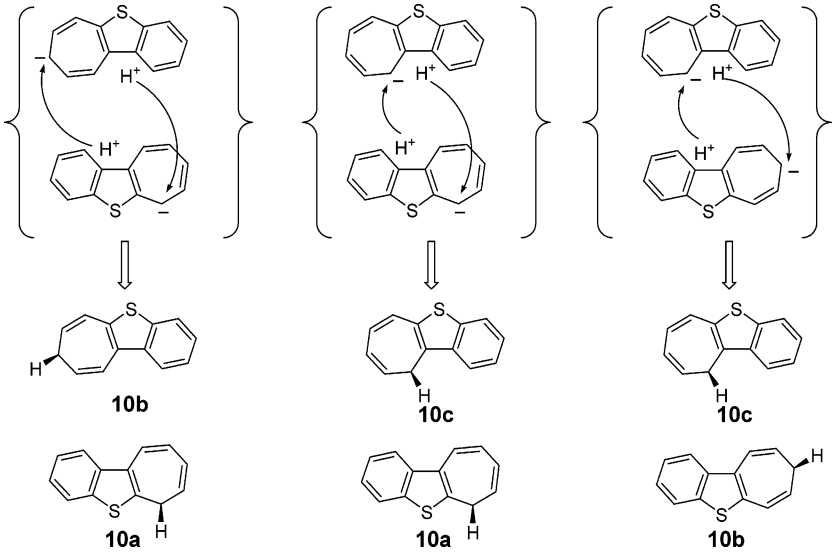


FIGURE 5. Energy changes in kilocalories/mole [R(U)B3LYP/6-31G* SCRF=dipole] along the reactions in Figures 1−4. Half energies of dimeric species, TS(**13** + **13** → **14**) and **14**, are shown.

SCHEME 10. Double Proton Transfer from the Intermediate 13 Leading to the Three Products 10a, 10b, and 10c



In their optimized transoid geometries, CI coefficients of CASSCF(4,4)/6-31G* were examined. In **17**, that of the adiabatic electron configuration (Ψ_0) is −0.702, and that of the doubly excited one [Ψ(HOMO → LUMO, HOMO → LUMO)] is 0.689. The almost equal weight of two configurations means that **17** is a singlet biradical intermediate. In contrast, in **18**, the coefficient of Ψ_0 is 0.997. The species **18** can be described by a Hartree−Fock configuration and is a zwitterionic intermediate. Thus, **1** is basically a biradical reagent toward olefins [e.g., $H_2C{=}C(OMe)_2$].

The "triple" bond of **1** has been studied extensively, and it has been established spectroscopically that the bond is actually somewhere between a double and triple bond.[6s] On account of the rigid directionality of two in-plane sp^2 orbitals, their combination does not lead to such a typical triple bond as in acetylene with a large $\pi-\pi^*$ energy gap.[27] The incomplete in-plane π bond means a partial biradical character, which was estimated to be 11% by CCSD(T) calculations.[6j] The character of **1** is activated by interactions with olefins and conjugated systems. In this respect, the combination of **1** and **2** is fit to generate the singlet biradical **11**. For formation of **11**, the sulfur atom of **2** has a large out-of-plane $3p_\pi$ orbital, which may capture *one* sp^2 orbital of **1** without failure.

V. Concluding Remarks

Benzyne (**1**) is usually known as an electrophilic reagent toward conjugated and olefinic compounds. The benzyne−tropothione reaction was expected to be a typical cycloaddition.

However, the present experiment and calculation have revealed a novel multistep process in Figures 5 and 6. Benzyne (**1**) has a lumo with a rigid orbital extension. lumo is, by nature, composed of two rather independent sp^2 orbitals and is not fit for cycloadditions in some cases either with the unfavorable

(27) The singlet ($\tilde{x}\ ^1A_1$)−triplet ($\tilde{a}\ ^3B_2$) energy splitting in **1** was determined by photoelectron spectrum to be 37.7 kcal/mol: Leopold, D. G.; Miller, A. E. S.; Lineberger, W. C. *J. Am. Chem. Soc.* **1986**, *108*, 1379−1384.

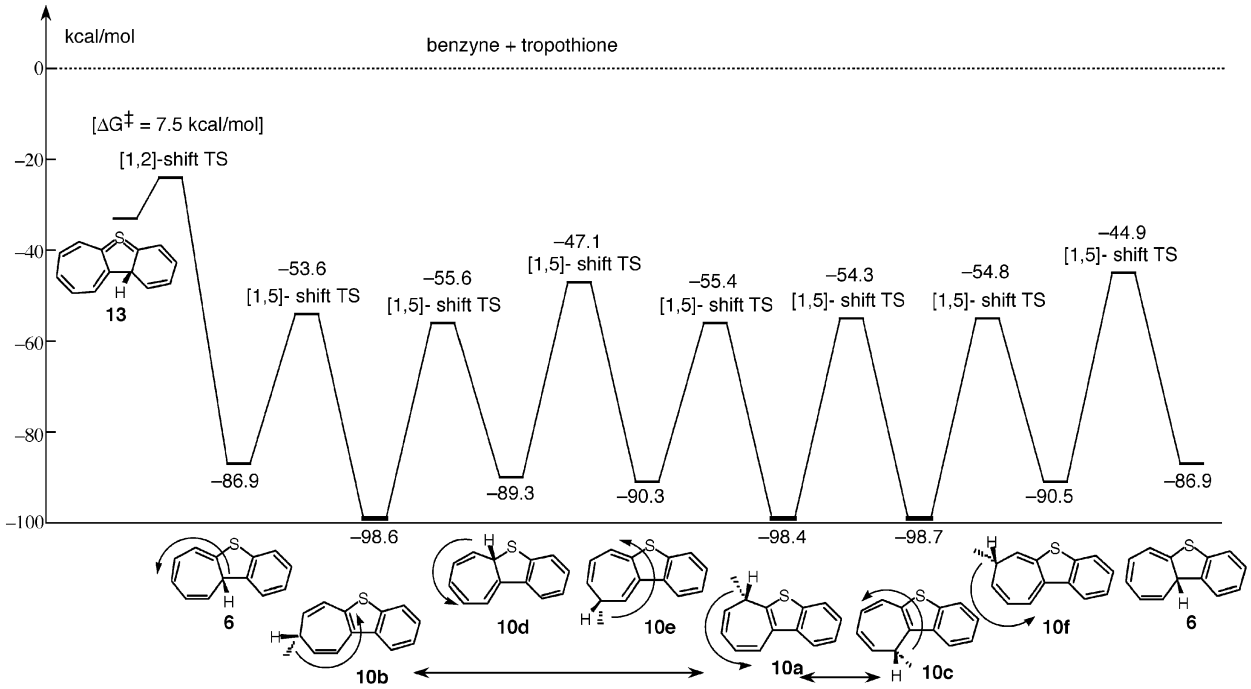
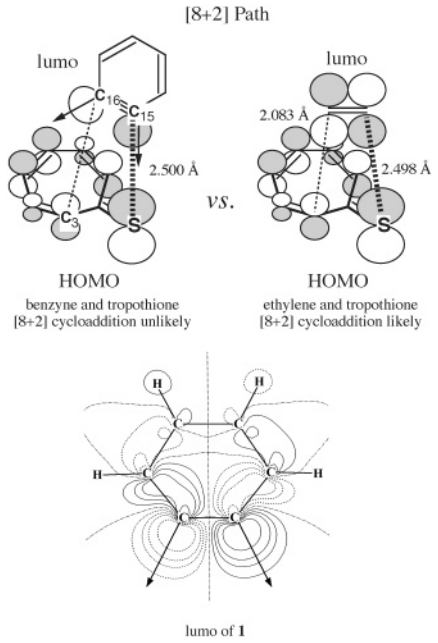


FIGURE 6. Energetics of H_α [1,2]- and [1,5] shifts.

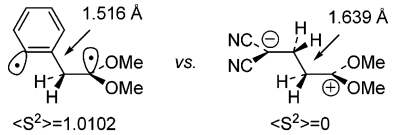
SCHEME 11. Rigid sp² Directionality of the LUMO of 1 Precludes the [8 + 2] Cycloaddition[a]



[a] This was not taken into account in Scheme 4. The C_{15}−S distance, 2.5 Å, is taken from the TS geometry of a [8 + 2] cycloaddition between ethylene and **2**.[12g] The atom numbering in the **1** + **2** model follows that in Figure 2. The arrows of benzyne show the direction of the sp² lobe of the lumo. The arrow starting from C_{16} cannot be adjusted to make the C_{16}−C_3 covalent bond.

FMO overlap or with the other likely reaction channel. The independent and biradical function causes the C−Hα bond rupture at TS(**11** → **12**). In general, it is unlikely that the C(sp²)−H bond is cleaved to form a cumulene bond, and the present reaction would be quite novel. Another striking point is that the products are converged to the three, **10a**−**c**, in spite

SCHEME 12. Geometries of One-Center Adducts Optimized by the Symmetry-Broken UB3LYP/6-31G* Calculations



of radical reactions involved. The tropothione (**2**) has induced the biradical character of **1** toward conjugated systems. The apparent Diels−Alder cycloadduct **9** in Scheme 5 has been found to be yielded in a biradical process, which will be reported elsewhere. Benzyne (**1**) is regarded *as a phenyl biradical reactant rather than as an electrophile toward the nucleophile* ***2***.

VI. Experimental Section

Reaction of Tropothione (2) with Benzyne (1): (i) Generation in Situ from 1,2,3-Benzothiadiazole 1,1-dioxide. A mixture of tropothione (815.4 mg, 6.67 mmol) and 1,2,3-benzothiadiazole 1,1-dioxide[19] [prepared from 2.31 g (12.89 mmol) of sodium 2-aminobenzenesulfinate[10]] in ether (70 mL) was heated at 10 °C with stirring for 2 h. After filtration of the resulting precipitates, the filtrate was washed with water and the organic layer was dried over magnesium sulfate. Solvent removal left 2.01 g of viscous oil composed of an equimolar mixture of benzothiophene **10a**−**c**. Silica-gel column chromatography (20 × 100 cm i.d., eluted from dichloromethane) left 1.20 g (90%) of oily product. Kugelrohr distillation gave 1.14 g (86%) of pale yellow oil.

(ii) Generation in Situ from Benzenediazonium-2-carboxylate. The above procedure was followed, with **2** (1.06 g, 8.67 mmol) and benzenediazonium-2-carboxylate[9,28] (1.28 g, 8.67 mmol, 1.0 equiv, prepared from anthranilic acid and *iso*-amylnitrate). Workup left 2.01 g of oily product. Column chromatographic purification (silica gel, dichloromethane) gave the same products of equimolar mixture of benzothiophenes **10a**−**c** (1.65 g, 96%). Kugelrohr distillation of the mixture of **10a**−**c** gave 1.49 g (87%) of pale yellow oil.

Triphenylmethyl fluoroborate (421 mg, 1.27 mmol) was added into a solution of **10a−c** (243 mg, 1.23 mmol) in chloroform (10 mL). Resulting reddish precipitates were washed with chloroform and recrystalized from acetonitrile to give tropylium cation **16** (321 mg, 92%).

An equimolar mixture of **10a−c**: Colorless liquid, bp 65−66 °C (0.05 mmHg); IR (neat) ν_{max} 3020 (s), 2950 (m), 1580 (w), 1430 (m), 1320 (m), 740 (vs), 720 (vs), 700 (s), 635 (s), 500 (m), 445 (m), 420 (m) cm^{-1}; EI-MS (75 eV) *m*/*z* 199 ($M^+ + 1$, 16.9%), 198 (M^+, 93, $C_{13}H_{10}S$), 197 ($M^+ - 1$, 100, $C_{10}H_9S$), 165 (17, $C_{13}H_9$), 152 (11, $C_{12}H_8$), 122 (2, C_7H_6S), 121 (3, C_7H_5S), 89 (3, C_7H_5), 76 (6, C_6H_4). Anal. Calcd for $C_{13}H_{10}S$: C, 78.74; H, 5.08; S, 16.17. Found: C, 78.70; H, 5.12; S, 16.09.

NMR data for **10a**: ^{1}H NMR δ 3.24 (d, 2H, J = 6.6 Hz, H-3), 5.57 (dd, 1H, J = 9.5, 6.6 Hz, H-4), 6.13 (dd, 1H, J = 9.5, 5.8 Hz, H-5), 6.40 (dd, 1H, J = 11.3, 5.8 Hz, H-6), 6.99 (d, 1H, J = 11.3 Hz, H-7), 7.16−7.46 (m, 2H, H-11,12), 7.62−7.88 (m, 2H, H-10,-13); ^{13}C NMR δ 25.5 (t, C-3), 123.0 (d, C-4), 125.4 (d, C-7), 127.7 (d, C-5), 128.1 (d, C-6). For **10b**: ^{1}H NMR δ 2.51 (t, 2H, J = 6.8 Hz, H-5), 5.62 (dd, 1H, J = 9.7, 6.8 Hz, H-6), 5.66 (dd, 1H, J = 9.6, 6.8 Hz, H-4), 6.77 (d, 1H, J = 9.7 Hz, H-7), 6.94 (d, 1H, J = 9.6 Hz, H-3), 7.16−7.46 (m, 2H, H-11,12), 7.62−7.88 (m, 2H, H-10,13); ^{13}C NMR δ 27.1 (t, C-5), 122.6 (d, C-3), 123.0 (d, C-4), 123.4 (d, C-7), 124.4 (d, C-6). For **10c**: ^{1}H NMR δ 3.25 (d, 2H, J = 6.6 Hz, H-7), 5.59 (dd, 1H, J = 9.5, 6.6 Hz, H-6), 6.15 (dd, 1H, J = 9.5, 5.8 Hz, H-5), 6.40 (dd, 1H, J = 11.3, 5.8 Hz, H-4), 7.24 (d, 1H, J = 11.3 Hz, H-3), 7.16−7.46 (m, 2H, H-11,12), 7.62−7.88 (m, 2H, H-10,13); ^{13}C NMR δ 28.2 (t, C-7), 121.1 (d, C-6), 124.7 (d, C-3), 127.1 (d, C-5), 129.6 (d, C-4).[29]

Tropylium cation **16**: Reddish solid, mp 181−182 °C; IR (KBr) ν_{max} 3081 (m), 3067 (m), 1592 (s), 1467 (s), 1441 (s), 1419 (s), 1341 (s), 1054 (br vs), 745 (vs), 679 (m), 594 (m) cm^{-1}; UV−vis (CH_3CN) λ_{max} 197.5 (log ϵ 4.17), 221 (4.35), 241.5 (4.29), 268.5 (3.83), 284.0 (3.84), 332 (4.24); ^{1}H NMR (400 MHz, CD_3CN) δ 7.94 (ddd, J = 8.6, 7.5, 1.1 Hz, H-2), 8.06 (ddd, J = 8.0, 7.5, 1.1 Hz, H-3), 8.38 (dd, J = 8.0, 1.1 Hz, H-4), 8.84 (ddd, J = 10.2, 9.6, 1.1 Hz, H-7), 8.85 (dd, J = 8.6, 1.1 Hz, H-1), 8.96 (td, J = 9.6, 1.1 Hz, H-9), 9.05 (tt, J = 9.6, 1.1 Hz, H-8), 9.68 (dd, J = 10.2, 1.1 Hz, H-6), 9.91 (dd, J = 9.6, 1.1 Hz, H-10); ^{13}C NMR (100.6 MHz, CD_3CN) δ123.9 (d, C-4), 126.0 (d, C-1), 128.2 (d, C-2), 134.3 (d, C-3), 135.4 (d, C-10b), 142.3 (d, C-7), 143.6 (d, 2C, C-9 and C-10), 144.3 (s, C-4a), 147.2 (d, C-6), 150.9 (d, C-8), 152.6 (d, C-10a), 166.2 (d, C-5a). Anal. Calcd for $C_{13}H_9SBF_4$: C, 54.96; H, 3.19; S, 11.29; B, 3.81; F, 26.75. Found: C, 54.97; H, 3.12.

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Supporting Information Available: One-dimensional ^{1}H NMR, 2D NMR (^{1}H−^{1}H COSY), 1D ^{13}C NMR, and 2D NMR (^{13}C−^{1}H COSY) charts of the three products **10a−c**, the sulfones **15a−c**, and the tropylium cation **16**; and Cartesian coordinates of the optimized geometries in Figures 1−4 and 6. This information is available free of charge via the Internet at http://pubs.acs.org.

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(28) (a) Berry, R. S.; Spokes, G. N.; Stiles, M. *J. Am. Chem. Soc.* **1962**, *84*, 3570−3577. (b) Friedman, L.; Logullo, F. M. *J. Am. Chem. Soc.* **1963**, *85*, 1549−1549. (c) *Organic. Syntheses*; Wiley & Sons: New York, 1973. (d) Logullo, F. M.; Seitz, A. H.; Friedman, L. *Organic Syntheses*; Wiley & Sons: New York, 1973; Collect. Vol. 5, pp 54−59.

(29) Unassignable signals in the aromatic region in ^{13}C NMR to individual component **10a−c**: δ 120.8 (d, C-10 or C-13), 121.5, 121.6, 122.1, 122.4, 122.4, 123.6 (d, C-11 or C-12), 124.0, 124.2 (3C), 124.8, 128.4 (s, C-8), 129.5, 130.2, 133.6 (s, C-2), 133.6, 135.2, 137.9 (s, C-9 or C-14), 138.1, 138.2, 139.1, 140.0, and 141.7.