2168 *J. Org. Chem.* **1998,** *63,* 2168−2171

The First Example of Addition of a 1,2-Dication to a C−C Multiple Bond. Reaction of S−S Dications with Alkenes and Alkynes

Valentine G. Nenajdenko,* Nikolai E. Shevchenko, and Elizabeth S. Balenkova*

Department of Chemistry, Moscow State University, Moscow 119899, Russia

Received September 29, 1997

The reactions of a bicyclic dithioether dication, generated from 1,4-dithiane 1-oxide, with a carbon−carbon multiple bond proceed as conjugated addition of two sulfonium groups and gives rise to derivatives of dithioniabicyclo[2.2.2]octane. The reaction is sensitive to electronic and steric factors. In all cases investigated the reactions of 1,2-disubstituted arylalkene proceed with retention of the relative arrangement of substituents at the double bond of the original alkene. A possible explanation of the obtained results is discussed.

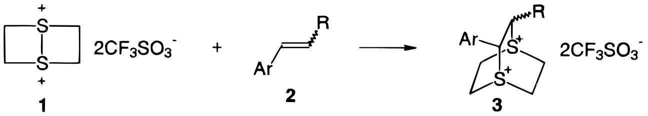
Introduction

Organic molecules possessing two positively charged adjacent atoms are relatively rare, and their chemistry and structures are of considerable theoretical interest. Several compounds having two positively charged heteroatoms ($N^+{-}N^+$,[1] $S^+{-}N^+$,[2] $Se^+{-}N^+$,[3] $S^+{-}S^+$,[4] $Se^+{-}Se^+$,[5] $S^+{-}Se^+$,[5] $Te^+{-}Te^+$ [6]) have been thoroughly investigated in recent years.

Dithioether dications are the most studied class of dications. Their formation as intermediates was initially proposed by Musker et al.[7] in 1977 in the course of kinetic studies of monosulfoxide reduction. Later these authors reported the first preparative synthesis of $S^+{-}S^+$ dications by oxidation of disulfides with $NOBF_4$.[5] Further progress in the synthesis and the chemistry of dithioether dications was achieved by Furukawa and co-workers [8] who elaborated a convenient approach to $S^+{-}S^+$ dications based on the reaction of cyclic monosulfoxides of bissulfides with trifluoromethanesulfonic anhydride. This new method allowed the first unambiguous X-ray structure determination of a $S^+{-}S^+$ dication, namely 1,5-dithioniabicyclo[3.3.0]octane ditriflate.[9]

The unusual structure of the $S^+{-}S^+$ dications results in their high reactivity. It was found that $S^+{-}S^+$ dications are able to behave either as oxidants (in the case of reaction with organometallics, alcohols, hydrazines, and mercaptans[10]) or as electrophilic reagents (with such nucleophiles as water, bromide anion, and electron-rich aromatic compounds).[10] Recently analogous compounds having $S^+{-}Se^+$,[11] $Se^+{-}Se^+$,[12] and $Te^+{-}Te^+$ [6] fragments have been found to be reactive toward aromatics. Nevertheless, the reactions of $S^+{-}S^+$ dications with alkenes and alkynes have not been described earlier. Moreover, we could not find examples of addition of any dicationic species to a multiple carbon−carbon bond in the literature.

Scheme 1



Results and Discussion

In this article we describe the first example of a reaction of a dication with a multiple C−C bond. We have found that the reaction of S−S dication **1**[13] with different vinyl arenes and vinylcyclopropane proceeds as conjugate addition of two sulfonium groups to form the corresponding sulfonium salts—the derivatives of dithioniabicyclo[2.2.2]octane (Scheme 1).

Only alkenes having a double bond conjugated with an aromatic or cyclopropane ring react with dication **1**. Such alkenes as 1-hexene and cyclohexene do not react. The reaction only proceeding with a cation-stabilizing group on the olefin indicates localization of positive charge at one carbon of the olefin in transition state.

α-Methylstyrene reacts with compound **1** to form a complex mixture of sulfonium salts (possibly due to the significant steric hindrance for the transition state). It should be noted that in the case of vinylcyclopropane only the product of conjugate 1,2-addition **3i** was isolated. No rearrangement products were detected. We believe that the exclusive formation of **3i** is due to homoallyl carbocation is not able to form six-membered ring.

---

[1] (a) Nelsen, S. F.; Wang, Y. *J. Am. Chem. Soc.* **1991**, *113*, 5905. (b) Nelsen, S. F.; Tran, H. Q.; Hiyashi, R. K.; Powell, D. R.; Neugebauer, F. A. *J. Org. Chem.* **1995**, *60*, 6756. (c) Alder, R. W. *Tetrahedron* **1990**, *46*, 687.

[2] Williams, K. A.; Doi, J. T.; Musker, W. K. *J. Org. Chem.* **1985**, *50*, 4.

[3] Fujihara, H.; Mima, H.; Erata, T.; Furukawa, N. *J. Chem. Soc., Chem. Commun.* **1991**, *2*, 98.

[4] Doi, J. T.; Musker, W. K. *J. Am. Chem. Soc.* **1978**, *100*, 3533.

[5] Musker, W. K. *Acc. Chem. Res.* **1980**, *13*, 200.

[6] Fujihara, H.; Ninoi, T.; Akaishi, R.; Erata, T.; Furukawa, N. *Tetrahedron Lett.* **1991**, *32*, 4537.

[7] Musker, W. K.; Wolford, T. L.; Roch, P. B. *J. Am. Chem. Soc.* **1978**, *100*, 6416.

[8] (a) Furukawa, N.; Kawada, A.; Kawai, T. *J. Chem. Soc., Chem. Commun.* **1984**, 1151. (b) Fujihara, H.; Akaishi, R.; Furukawa, N. *J. Chem. Soc., Chem. Commun.* **1987,** 930.

[9] Iwasaki, F.; Toyoda, N.; Akaishi, R.; Fujihara, H.; Furukawa, N. *Bull. Chem. Soc. Jpn.* **1988,** *61*, 2563.

[10] (a) Fujihara, H.; Akaushi, R.; Furukawa, N. *J. Chem. Soc., Chem. Commun.* **1989**, 147. (b) Fujihara, H.; Akaishi, R.; Furukawa, N. *Chem. Lett.* **1988**, 709. (c) Fujihara, H.; Akaishi, R.; Furukawa, N. *Tetrahedron* **1992**, *49*, 1605.

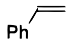
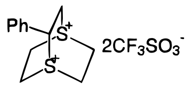
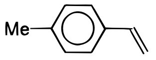
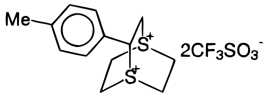
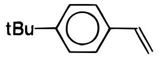
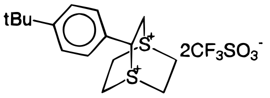
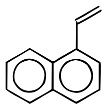
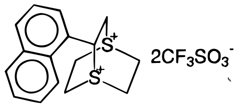
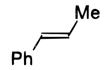
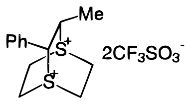
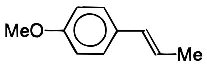
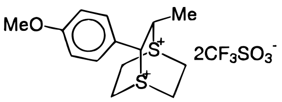
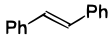
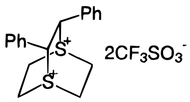
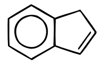
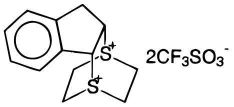
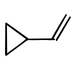
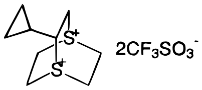
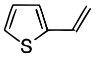
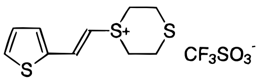
[11] Fujihara, H.; Akaishi, R.; Furukawa, N. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 616.

[12] (a) Fujihara, H.; Nakamura, A.; Akaishi, R.; Furukawa, N. *Chem. Lett.* **1990**, 393. (b) Fujihara, H.; Mima, H.; Chiu, J.-J.; Furukawa, N. *Tetrahedron Lett.* **1990**, *31*, 2307.

[13] The dication **1** was obtained according to the literature procedure by the reaction of 1,4-dithiane 1-oxide with triflic anhydride and its spectroscopic characteristics are consistent with early reported.[8]

S0022-3263(97)01801-X CCC: $15.00

Table 1. Reaction of 1 with Alkenes

Alkene		Product		Isolated yield, %
	**2a**		**3a**	45
	**2b**		**3b**	46
	**2c**		**3c**	48
	**2d**		**3d**	38
	**2e**		**3e**	40
	**2f**		**3f**	45
	**2g**		**3g**	26
	**2h**		**3h**	53
	**2i**		**3i**	43
	**2j**		**3j**	42

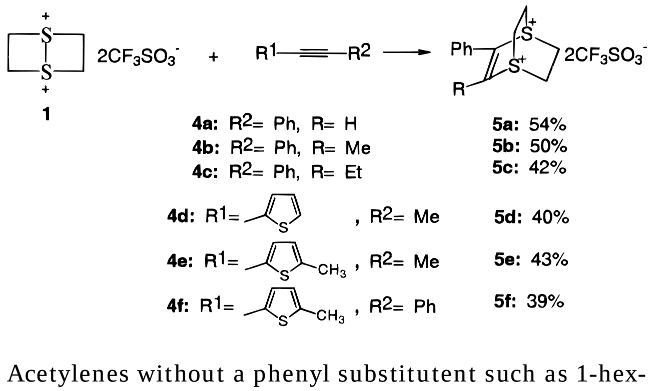
We have investigated stereochemistry of the dication addition to a double bond. In the case of reaction **1** with 1,2-disubstituted alkenes only one diastereomer was formed. The addition of dication **1** in all cases investigated proceeded with formation of the most stable product. The reaction of alkenes **2e**−**g** with and *E*-double bond results in trans-substituted bicyclic products **3e**−**g**, whereas the reaction with indene **2h** gives rise to *cis*-**3h**. The difference between the vicinal coupling constant for compounds **3e**−**g** having trans configuration (11.2 Hz) and the coupling constant for compound **3h** having cis configuration (8.5 Hz) is not very significant. Therefore, configurations of **3e** and **3h** were confirmed in addition by 2D NOESY experiments.

Reaction of **1** with vinylthiophene does not result in a bicyclic sulfonium salt, unlike in the cases of other vinyl arenes. Only the *E*-isomer of vinylsulfonium salt **3j** (the product of formal proton substitution by a sulfonium moiety) is isolated.

We have also found that **1** reacts with terminal and internal arylacetylenes. The reaction proceeds similarly to the reaction with alkenes as a conjugate addition to form bicyclic sulfonium salts with the dithioniabicyclo[2.2.2]octene skeleton (Scheme 2).

It should be noted that formation of vinyl triflates (they can be intermediates of the reaction) does not take place.

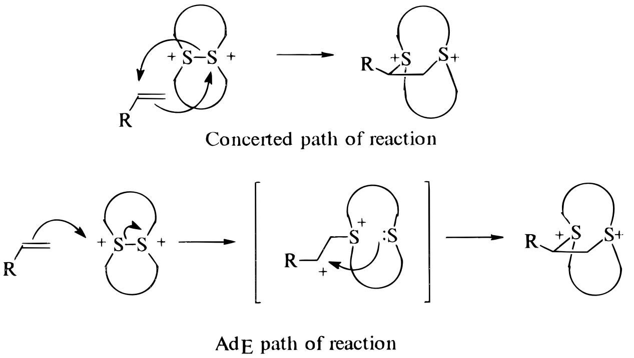
Scheme 2



Acetylenes without a phenyl substitutent such as 1-hexyne and 1-heptyne do not react.

We have found that the structure of the S−S dication imposes restrictions in the reaction with alkenes and alkynes. The dication derivative of 1,5-dithiacyclooctane is the most investigated S^+-S^+ dication due to stability of this compound at room temperature.[9] However, we could not introduce this dication in reactions with various alkenes and alkynes. We tried also to carry out the reaction of alkenes with the S−S dication derivative of 1,4-dithiacycloheptane, which sould have an intermediate reactivity in comparison with the dicationic derivatives

Scheme 3



of 1,5-dithiacyclooctane and 1,4-dithiane. But this compound turned out to be unreactive toward alkenes as well. We believe that the enhanced reactivity of dication **1** obtained from 1,4-dithiane 1-oxide is due to the considerable strain of its structure. Although early reported data for dithioniabicyclo[2.2.0]hexane bis(hydrosulfate) suggest that in solution there are both intramolecular and intermolecular forms,[14] dithioniabicyclo[2.2.0]hexane bis(trifluoromethanesulfonate) is derived from a monomer dication.[8] We believe that the driving force of this reaction is the minimization of Coulomb repulsion between the two charged sulfur atoms and a decrease of ring strain of the S−S dication **1.**

The S^+-S^+ dication molecule seems to be an interesting model in the Ad_E reaction (Scheme 3). Both sulfur atoms in the molecule of the dithioether dication are positively charged. At the same time one of these sulfur atoms should act as an electrophilic center but the other one as a nucleophilic center in the reaction with multiple bond. Therefore in the frame of the usual mechanism of electrophilic addition this reaction should be considered as a conjugate addition of double-charged sulfur electrophile S^{2+} and sulfide as the nucleophile. We believe that it is more understandable to consider this reaction as a nucleophilic substituion at the sulfur atom. The first step is substitution of the sulfide moiety by alkene or alkyne as a nucleophile. The next step can be either direct trapping of the carbocation with newly formed sulfide or intermediate trapping of the carbocation with triflate anion followed by substitution of the triflate group with sulfide. In the case of stronger electron-donating aromatics, which stabilize the intermediate benzylic cation, deprotonation followed by formation of a conjugated alkene can be observed as well (the path leading to compound **3j**.

In summary, we have studied the reactions of some bicyclic dithioether dications with a multiple carbon-carbon bond. It has been found that only the dication generated from 1,4-dithiane 1-oxide is active in these reactions. Moreover, the reaction seems to be very sensitive to electronic and steric factors. Exposure of the dication to the arylakenes or arylalkynes led to the formation of 1,2-disulfonium salts with the dithioniabicyclo[2.2.2]octane skeleton. In the case of 1,2-disubstituted alkenes the sulfonium salts were formed as one diastereomer.

Experimental Section

Melting points were determined in sealed capillaries and are uncorrected. All solvents were dried and distilled according to the standard procedure. Triflic anhydride was prepared according to literature procedure[15] from trifluoromethanesulfonic acid (Merck).

General Procedure for Reaction of Dithioether Dication 1 with Alkenes and Alkynes. A solution of 1.7 g (6 mmol) of triflic anhydride in 30 mL of anhydrous dichloromethane was cooled to −60 °C. Over a period of 10 min, 0.73 g (5 mmol) of 1,4-dithiane 1-oxide in 10 mL of dichloromethane was added dropwise. A white precipitate formed. The reaction mixture was allowed to warm to −20 °C followed by dropwise addition of an eqimolar solution of the corresponding alkene (or acetylene) in 10 mL of dichloromethane. The resulting mixture was allowed to react at −20 °C for 1−12 h (TLC monitoring). Then 50 mL of ether was added followed by filtration of precipitate. The products should be kept at 0 °C.

2-Phenyl-1,4-dithioniabicyclo[2.2.2]octane Bis(trifluoromethanesulfonate) (3a). Yield 45%, mp 158−160 °C dec. IR (Nujol) 1300−1100, 1040 cm^{-1}; ^1H NMR (CD_3CN) δ 7.92−7.54 (m, 5H), 6.04 (t, 1H, $J = 9.6$ Hz), 4.73−3.70 (m, 10H); ^{13}C NMR (CD_3CN) δ 131.96, 130.77, 130.69, 129.98, 121.80, (q, $J = 319.2$ Hz), 45.34, 29.00, 25.72, 25.60, 24.38. Anal. Calcd for $C_{14}H_{16}F_6O_6S_4$: C, 32.18; H, 3.09. Found: C, 32.45; H, 3.04.

2-(4-Methylphenyl)-1,4-dithioniabicyclo[2.2.2]octane Bis(trifluoromethanesulfonate) (3b). Yield 42%, mp 115−116 °C dec. IR (Nujol) 1300−1100, 1040 cm^{-1}; ^1H NMR (CD_3CN) δ 7.59 (d, 2H, $J = 9.5$ Hz), 7.40 (d, 2H, $J = 9.5$ Hz), 5.52 (dd, 1H, $J = 8.5$ and 10.6 Hz), 4.31 (dd, 1H, $J = 15.4$ and 8.5 Hz), 4.22 (dd, 1H, $J = 15.4$ and 10.6 Hz), 4.16−3.73 (m, 8H), 2.88 (s, 3H); ^{13}C NMR (CD_3CN) δ 141.70, 130.30, 128.40, 125.00, 120.10 (q, $J = 321.1$ Hz), 43.80, 28.50, 28.40, 24.10, 24.00, 22.70, 19.90. Anal. Calcd for $C_{15}H_{18}F_6O_6S_4$: C, 34.58; H, 3.46. Found: C, 34.19; H, 3.71.

2-(4-*tert*-Butylphenyl)-1,4-dithioniabicyclo[2.2.2]octane Bis(trifluoromethanesulfonate) (3c). Yield 48%, mp 148−149 °C dec. IR (Nujol) 1300−1100, 1030 cm^{-1}; ^1H NMR (CD_3CN) δ 7.65 (s, 4H), 5.54 (dd, 1H, $J = 8.4$ and 10.5 Hz), 4.33 (dd, 1H, $J = 15.3$ and 8.4 Hz), 4.23 (dd, 1H, $J = 15.3$ and 10.5 Hz), 4.18−3.74 (m, 8H), 1.38 (s, 9H); ^{13}C NMR (CD_3CN) δ 154.41, 128.10, 126.52, 125.37, 121.07 (q, $J = 321.1$ Hz), 43.56, 34.30, 28.38, 27.48, 23.94, 23.85, 22.61, 29.70. Anal. Calcd for $C_{18}H_{24}F_6O_6S_4$: C, 37.36; H, 4.18. Found: C, 37.60; H, 4.20.

2-(1-Naphthyl)-1,4-dithioniabicyclo[2.2.2]octane Bis(trifluoromethanesulfonate) (3d). Yield 38%, mp 101−102 °C dec. IR (Nujol) 1300−1100, 1030 cm^{-1}; ^1H NMR (CD_3CN) δ 8.28−7.67 (m, 7H), 6.25 (dd, 1H, $J = 8.5$ and 10.1 Hz), 4.60−3.70 (m, 10H); ^{13}C NMR (CD_3CN) δ 139.54, 137.68, 135.39, 134.98, 133.58, 132.63, 132.60, 130.83, 127.47, 122.04 (q, $J = 319.6$ Hz), 46.52, 34.11, 33.24, 29.99, 29.90, 29.18 Anal. Calcd for $C_{18}H_{18}F_6O_6S_4$: C, 37.76; N, 3.17. Found: C, 37.60; H, 3.21.

***trans*-3-Methyl-2-phenyl-1,4-dithioniabicyclo[2.2.2]octane Bis(trifluoromethanesulfonate) (3e).** Yield 40%, mp 115−116 °C dec. IR (Nujol) 1300−1100, 1040 cm^{-1}; ^1H NMR (CD_3CN) δ 7.58−7.73 (m, 5H), 5.25 (d, 1H, $J = 11.2$ Hz), 4.69 (dq, 1H, $J = 11.2$ and 6.9 Hz), 4.45−3.88 (m, 8H), 1.65 (d, 3H, $J = 6.9$ Hz), 1.38 (s, 9H); ^{13}C NMR (CD_3CN) δ 131.35, 129.90, 128.84, 127.80, 121.24 (q, $J = 318.4$ Hz), 49.88, 40.97, 27.99, 25.96, 23.10, 22.50, 14.01. Anal. Calcd for $C_{15}H_{18}F_6O_6S_4$: C, 34.58; H, 3.46. Found: C, 34.32; H, 3.46.

***trans*-3-Methyl-2-(4-methyloxyphenyl)-1,4-dithioniabicyclo[2.2.2]octane Bis(trifluoromethanesulfonate) (3f).** Yield 45%, mp 110−111 °C dec. IR (Nujol) 1300−1100, 1040 cm^{-1}; ^1H NMR (CD_3CN) δ 7.64 (d, 2H $J = 9.5$ Hz), 7.12 (d, 2H, $J = 9.5$ Hz), 5.20 (d, 1H, $J = 11.2$ Hz), 4.1−3.50 (m, 9H), 3.88 (s, 3H), 1.52 (d, 3H, $J = 8.5$ Hz); ^{13}C NMR (CD_3CN) δ 130.43, 118.82, 115.22, 121.26 (q, $J = 320.5$ Hz), 50.09, 41.05, 27.87, 25.90, 22.85, 22.44, 14.00. Anal. Calcd for $C_{16}H_{20}F_6O_6S_4$: C, 34.91; H, 3.66. Found: C, 34.32; H, 3.70.

***trans*-2,3-Diphenyl-1,4-dithioniabicyclo[2.2.2]octane Bis(trifluoromethanesulfonate) (3g).** Yield 26%, mp 142−

---

(14) Fujihara, H.; Kawada, A.; Furukawa, N. *J. Org. Chem.* **1987**, *52*, 4254.

(15) Stang, P. J.; Hanack, M.; Subramanian, L. R. *Synthesis* **1982**, 85.

143 °C dec. IR (Nujol) 1300−1100, 1040 cm^{-1}; ^{1}H NMR (CD$_3$CN) δ 7.60−7.42 (m, 10H), 6.02 (s, 2H), 4.38−4.06 (m, 4H), 3.40−3.62 (m, 4H); ^{13}C NMR (CD$_3$CN) δ 132.75, 131.21, 130.64, 129.43, 119.80 (q, J = 321.00 Hz), 58.99, 39.48, 39.22, 24.71, 24.06. Anal. Calcd for $C_{18}H_{20}F_6O_6S_4$: C, 37.63; H, 3.51. Found: C, 37.22; H, 3.53.

1,11-Dithioniatetracyclo[9.2.2.0^{2,10}.0^{3,8}]pentadeca-3,5,7-triene Bis(trifluoromethanesulfonate) (3h). Yield 53%, mp 134−136 °C dec. IR (Nujol) 1300−1100, 1040 cm^{-1}; ^{1}H NMR (CD$_3$CN) δ 7.68−7.52 (m, 4H), 5.86 (d, 2H, J = 9.6 Hz), 5.04 (dt, 1H J = 9.6 and 6.5 Hz), 4.25−3.65 (m, 10H); ^{13}C NMR (CD$_3$CN) δ 145.69, 137.05, 134.62, 134.48, 134.42, 121.10 (q, J = 319.1 Hz), 55.25, 46.38, 39.24, 31.39, 30.63, 26.40, 25.82. Anal. Calcd for $C_{15}H_{16}F_6O_6S_4$: C, 34.72; H, 3.09. Found: C, 34.84; H, 3.10.

2-Cyclopropyl-1,4-dithioniabicyclo[2.2.2]octane Bis(trifluoromethanesulfonate) (3i). Yield 43%, mp 161−162 °C dec. IR (Nujol) 1300−1100, 1040 cm^{-1}; ^{1}H NMR (CD$_3$CN) δ 4.11−3.43 (m, 11H), 1.39−1.30 (m, 1H), 0.98−0.67 (m, 4H); $_{13}$C NMR (CD$_3$CN) δ 122.50 (q, J = 320.3 Hz), 47.91, 30.73, 27.74, 25.57, 25.24, 23.88, 12.47, 8.07, 6.26. Anal. Calcd for $C_{11}H_{16}F_6O_6S_4$: C, 27.16; H, 3.32. Found: C, 27.19; H, 3.27.

(E)-(2-(Thien-2-yl)vinyl)-1,4-dithianium Bis(trifluoromethanesulfonate) (3j). Yield 42%, mp 85−86 °C. IR (Nujol) 1610, 1300−1100, 1040 cm^{-1}; ^{1}H NMR (CD$_3$CN) δ 7.86 (d, 1H, J = 15.1 Hz), 7.76 (d, 1H, J = 5.0 Hz), 7.57 (d, 1H, J = 3.7 Hz), 7.22 (dd, 1H, J = 5.0 and 3.7 Hz), 6.80 (d, 1H, J = 15.1 Hz), 3.80 (ddd, 2H, J = 13.3, 2.5 and 8.5 Hz), 3.62 (ddd, 2H, J = 13.3, 8.4 and 2.3 Hz), 3.34 (ddd, 2H, J = 15.7, 2.3 and 8.5 Hz), 3.11 (ddd, 2H, J = 15.7, 2.5 and 8.4 Hz); ^{13}C NMR (CD$_3$CN) δ 143.30, 136.40, 132.00, 128.40, 133.40, 119.70 (q, J = 320.0 Hz), 104.20, 39.50, 22.20. Anal. Calcd for $C_{11}H_{13}F_3O_3S_4$: C, 34.91; H, 3.46. Found: C, 34.84; H, 3.48.

2-Phenyl-1,4-dithioniabicyclo[2.2.2]oct-2-ene Bis(trifluoromethanesulfonate) (5a). Yield 54%, mp 108−110 °C dec. IR (Nujol) 1620, 1300−1100, 1040 cm^{-1}; ^{1}H NMR (CD$_3$CN) δ 8.47 (s, 1H), 8.10−8.02 (m, 2H), 7.72−7.58 (m, 3H), 4.91 (ddd, 2H, J = 13.4, 8.5 and 4.5 Hz), 4.65 (ddd, 2H, J = 13.2, 8.2 and 4.5 Hz), 4.42−3.95 (m, 4H),; ^{13}C NMR (CD$_3$CN) δ 146.20, 133.70, 131.64, 130.01, 128.57, 126.36, 118.10 (q, J = 319.20 Hz), 32.89, 30.89. Anal. Calcd for $C_{14}H_{14}F_6O_6S_4$: C, 32.31; N, 2.71. Found: C, 32.80; H, 2.60.

3-Methyl-2-phenyl-1,4-dithioniabicyclo[2.2.2]oct-2-ene Bis(trifluoromethanesulfonate) (5b). Yield 50%, mp 137−138 °C dec. IR (Nujol) 1620, 1300−1100, 1040 cm^{-1}; ^{1}H NMR (CD$_3$COCD$_3$) δ 7.92−7.80 (m, 2H), 7.68−7.50 (m, 3H), 4.85−4.62 (m, 4H), 4.43−4.18 (m, 4H), 2.90 (s, 3H); ^{13}C NMR (CD$_3$COCD$_3$) δ 143.04, 139.62, 132.28, 131.55, 130.64, 129.68, 120.10 (q, J = 320.20 Hz), 32.71, 31.43, 22.89. Anal. Calcd for $C_{15}H_{16}F_6O_6S_4$: C, 33.71; H, 3.02. Found: C, 34.04; H, 3.28.

3-Ethyl-2-phenyl-1,4-dithioniabicyclo[2.2.2]oct-2-ene Bis(trifluoromethanesulfonate) (5c). Yield 42%, mp 132−133 °C dec. IR (Nujol) 1610, 1300−1100, 1020 cm^{-1}; ^{1}H NMR (CD$_3$CN) δ 7.90−7.78 (m, 2H), 7.69−7.48 (m, 3H), 4.80−4.68 (m, 4H), 4.40−4.23 (m, 4H), 3.20 (q, 2H, J = 7.7 Hz), 1.28 (t, 3H, J = 7.7 Hz); ^{13}C NMR (CD$_3$CN) δ 142.15, 138.51, 131.17, 130.44, 129.53, 128.57, 119.90 (q, J = 320.10 Hz), 31.60, 30.32, 25.56, 15.62. Anal. Calcd for $C_{16}H_{18}F_6O_6S_4$: C, 35.04; H, 3.28. Found: C, 35.64; H, 3.23.

Acknowledgment. We are grateful to Dr. I. D. Gridnev for the recording of high resolution NMR spectra. We thank Dr. I. V. Alabugin for helpful discussion. The research described in this publication was supported by Russian Fundamental Investigation Foundation (Grant N 97-03-32959a).

JO971801W