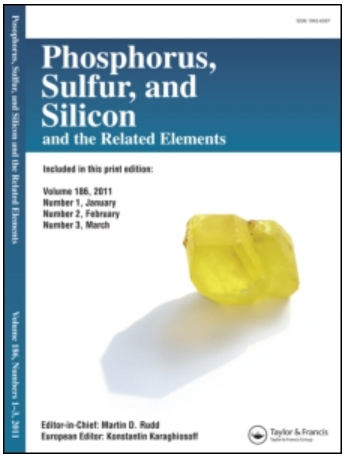


## Phosphorus, Sulfur, and Silicon and the Related Elements

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# Acid-Catalyzed Isomerization of 1-Halo-2-Arylthioalk-1-Enes

Nikolai V. Zyk[a]; Elena K. Beloglazkina[a]; Maria A. Belova[a]; Stanislav V. Zatonsky[a]; Nikolai S. Zefirov[a]
[a] Faculty of Chemistry, Moscow State University, Moscow, Russia

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# ACID-CATALYZED ISOMERIZATION OF 1-HALO-2-ARYLTHIOALK-1-ENES

*Nikolai V. Zyk, Elena K. Beloglazkina, Maria A. Belova, Stanislav V. Zatonsky, and Nikolai S. Zefirov*
*Faculty of Chemistry, Moscow State University, Vorob'evy gory, Moscow, 119899 Russia*

(Received August 2, 2001)

*1-Halo-2-arylthioalk-1-enes, the anti-Markovnikov adducts of 1,2-halosulfenylation of terminal alkynes containing propargyl hydrogen atoms, were found to transform into a mixture of* E- *and* Z-*isomers of 1-halo-2-arylthioalk-2-enes under acid catalysis conditions. A plausible mechanism of rearrangement is proposed. The Markovnikov adducts 2-halo-1-arylthioalk-1-enes were partially converted into their* cis-*form under similar conditions. The halosulfenylation products of 1-phenylpent-1-yne did not show the signs of double-bond migration in the presence of an acid; only partial isomerization of the* E- *to the* Z-*isomers took place.*

*Keywords:* Acid catalysis; 1-halo-2-arylthioalk-1-enes; 1-halo-2-arylthioalk-2-enes; isomerization

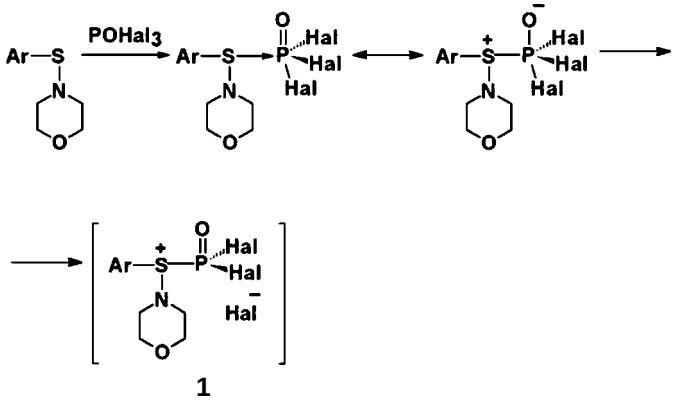
## INTRODUCTION

In previous studies[1–3] we proposed a new method for chloro- and bromosulfenylation of alkenes,[1] alkynes,[2] and dienes[3] with arylsulfenamides in the presence of phosphorus oxyhalides. The simplicity of experimental design, high yields, and stability of the reactants allow this method to be considered an alternative to the existing techniques.

Arylsulfenamides as such are weak electrophilic agents incapable of adding across multiple bonds; however, when reacted with $POCl_3$ or $POBr_3$, they form reactive complexes of type **1** in which a positive charge on the sulfur atom is higher than on the reactant sulfenamide (see Scheme 1).

The reaction of complex **1** with multiple bonds follows the electrophilic addition mechanism. The addition to alkynes is *trans*-stereospecific

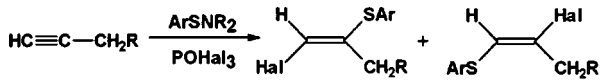
Address correspondence to Elena K. Beloglazkina, Faculty of Chemistry, Moscow State University, Vorob'evy gory, Moscow, 119899 Russia. E-mail: bel@org.chem.msu.su



1

**SCHEME 1**

and yields $\beta$-halovinylaryl sulfides,[2] a mixture of Markovnikov and anti-Markovnikov addition products with the prevalence of the latter products being formed in the case of non-symmetric substrates (in particular, terminal alkynes):

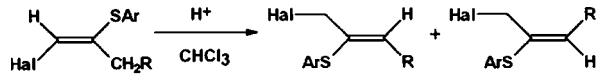


a (*E*) b (*E*)

aM M

**SCHEME 2**

However, we have found that 1-halo-2-arylthioalk-1-enes, the halosulfenylation products of terminal alkynes containing propargyl hydrogen atoms, are capable of isomerizing into 1-halo-2-arylthioalk-2-enes by the action of a catalytic amount of an acid.



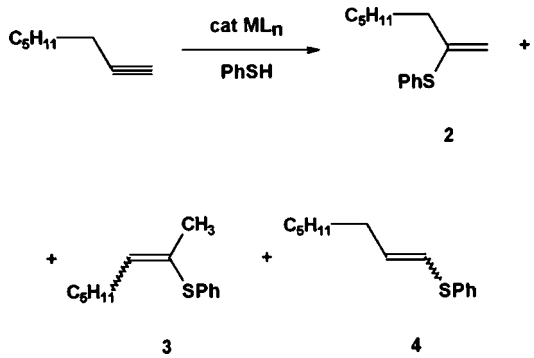
a (*E*) c (*Z*) c (*E*)

aM

**SCHEME 3**

The only example of similar double-bond migration in the reaction of alkynes having the propargyl hydrogen atoms has been reported in the literature: thiophenol in the presence of the metal complex catalysts ($PdCl_2(PhCN)_2$, $RhH(CO)(PPh_3)_3$, $Pt(PPh_3)_2(CH_2{=}CH_2)$) primarily

yields the Markovnikov products (**2**) which undergo isomerization under the reaction conditions to give products of type **3** (see Scheme 4). If an alkyne does not contain propargyl hydrogen atoms, there is no isomerization of **2**.[4]




**SCHEME 4**



## RESULTS AND DISCUSSION

To study in more detail the acid-catalyzed isomerization of 1-halo-2-arylthioalk-1-enes into 1-halo-2-arylthioalk-2-enes, we examined the reactions of three arylsulfenamides: *p*-nitrophenyl-thiomorpholine (**5a**), *o*-nitrophenylthiomorpholine (**5b**), and phenylthiomorpholine (**5c**), activated by $POCl_3$ or $POBr_3$, with some terminal alkynes (hex-1-yne (**6a**), hept-1-yne (**6b**), and oct-1-yne (**6c**)) and the non-terminal alkyne 1-phenylpent-1-yne (**6d**) which possesses propargyl hydrogen atoms.

As noted above, the sulfenylation of terminal alkynes **6a–6c** usually produces two regioisomers (**a**) 1-halo-2-arylthioalk-1-ene (the anti-Markovnikov addition product) and (**b**) 2-halo-1-arylthioalk-1-ene (the Markovnikov addition product). No other products are observed when the reaction is activated by phosphorus oxychloride. However, if $POBr_3$ (either freshly distilled or commercial without additional purification) is used as an activator, the isomerization products (*Z*/*E*)-1-bromo-2-arylthioalk-2-enes appear in the solution immediately after completion of the reaction. We assumed that the isomerization is mediated by catalytic amounts of HBr produced upon degradation of $POBr_3$. Such isomerization must also be catalyzed by other strong protic acids. To verify this assumption, we heated the isolated mixture of the 1,2-addition products chlorosulfides **a** and **b** in chloroform in the presence of *p*-toluenesulfonic acid. As a result, the predicted isomerization products (**c**) were obtained. The products yields and the isomer ratios of the reactions are given in Table I.

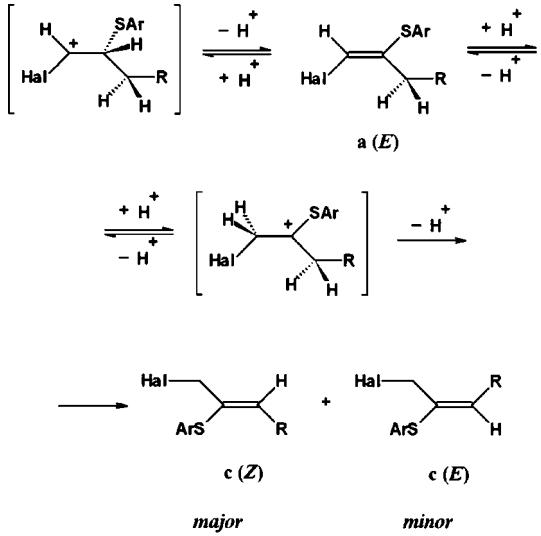
**TABLE I** Product Yields in the Reactions of Phosphorus(V) Oxyhalide-Activated Sulfenamides with Alkynes[a]

| Alkyne | | $POHal_3$ | | | | Isomer ratio (%) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| $R^1$ | $R^2$ | Hal | Sulfenamide Ar | Product | Total yield | a(*E*) | b(*E*) | c(*Z*) | c(*E*) | a(*Z*) | b(*Z*) |
| H | $C_4H_9$ | Cl | 4-$O_2N$—$C_6H_4$ | 7 | 87 | 80/10 | 20/14 | —/51 | —/16 | —/— | —/9 |
| | | Br | 4-$O_2N$—$C_6H_4$ | 8 | 63 | 2 | 11 | 58 | 29 | — | — |
| H | $C_5H_{11}$ | Cl | 4-$O_2N$—$C_6H_4$ | 9 | 68 | 80/— | 20/12 | —/66 | —/16 | —/— | —/6 |
| | | Br | 4-$O_2N$—$C_6H_4$ | 10 | 71 | 15 | 19 | 36 | 19 | — | 11 |
| | | | 2-$O_2N$—$C_6H_4$ | 11 | 66 | 53 | 28 | 11 | 8 | — | — |
| | | | $C_6H_5$ | 12 | 41 | — | 42 | 42 | 16 | — | — |
| H | $C_6H_{13}$ | Cl | 4-$O_2N$—$C_6H_4$ | 13 | 70 | 79/9 | 21/20 | —/42 | —/29 | —/— | —/— |
| | | Br | 4-$O_2N$—$C_6H_4$ | 14 | 60 | 2 | 27 | 54 | 17 | — | — |
| Ph | $C_3H_7$ | Cl | 4-$O_2N$—$C_6H_4$ | 15 | 67 | 83/62 | 17/14 | —/— | —/— | —/17 | —/6 |
| | | Br | 4-$O_2N$—$C_6H_4$ | 16 | 86 | 73 | 10 | — | — | 10 | 7 |

[a]The shaded boxes show the yields of chlorosulfides/the yields of chlorosulfides after heating in $CHCl_3$ in the presence of catalytic amounts of *p*-toluenesulfonic acid.

To describe the mechanism of the acid-catalyzed isomerization of 1-halo-2-arylthioalk-1-enes, we propose Scheme 5.

The key step in the rearrangement is the protonation of the double bond of compound **a** and subsequent proton elimination yielding a




**SCHEME 5**

mixture of isomeric alkenes **a**, **c**(*Z*), and **c**(*E*) in the ratio determined by their relative thermodynamic stability. Note that only one of the initially formed halovinyl sulfide, the anti-Markovnikov isomer **a**, undergoes isomerization into the mixture of 1-halo-2-arylthioalk-2-ene *E*- and *Z*-isomers under acid catalysis conditions.

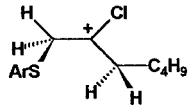
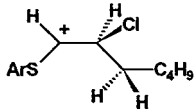
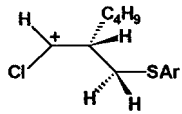
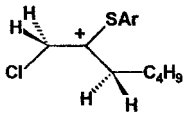
Theoretically, four carbocations can be formed from two $\beta$-halovinylaryl sulfide isomers **a** and **b** by protonation. To estimate the relative stability of these cations, we optimized their geometry and calculated their heats of formation by the semiempirical AM1 method. The heats of formation of cations thus obtained are presented in Table II.

As regards the Markovnikov adducts 2-halo-1-arylthioalk-1-enes (**b**), they partially transform into their *Z*-isomers under the acid catalysis conditions (see Scheme 6).

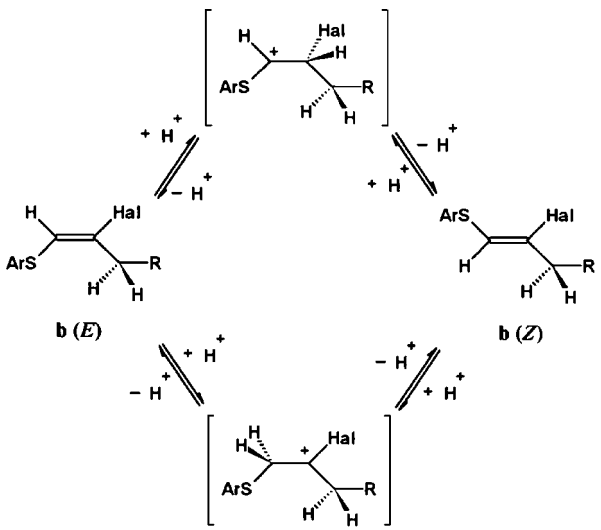
It is likely that the driving force of isomerization in both cases is the formation of more thermodynamically stable alkenes.

By analogy with the published data,[4] we may expect that similar isomerization will take place for the products of addition to 1-phenylpent-1-yne **(6d)**. However, the halosulfenylation products

**TABLE II** Heats of Formation of Cations

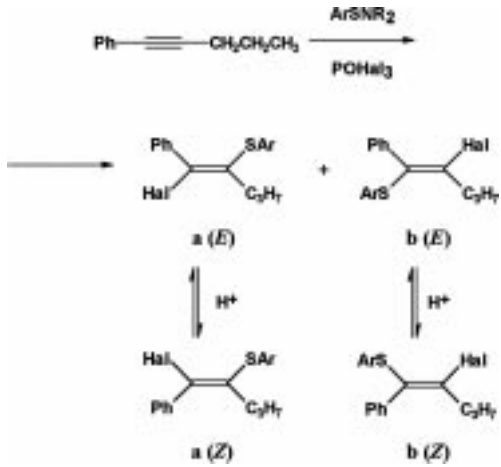
| | Carbocation | Heat of formation (kcal/mol) |
|---|---|---|
| 1 |  **17a** | 184.71 |
| 2 |  **17b** | 170.07 |
| 3 |  **17c** | 183.48 |
| 4 |  **17d** | 166.60 |

Ar = 4-$O_2N$—$C_6H_4$.



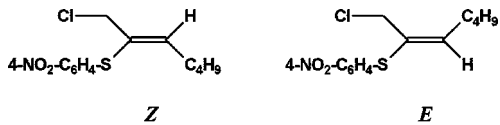
**SCHEME 6**

obtained in this case do not show the occurrence of double-bond migration under acid catalysis conditions, except for the partial isomerization of the *E*-isomers of **a** and **b** into the *Z*-isomers (see Scheme 7).




**SCHEME 7**

The *Z*/*E*-isomer ratio was determined from $^1$H NMR data. The assignment of signals from the *Z*/*E*- isomers of 1-halo-2-arylthioalk-2-enes (**c**) was based on the results of nuclear Overhauser effect (NOE) measurements. We measured NOE for a mixture of (*E*)-**9c** and (*Z*)-**9c**. The presence of the effect $\eta_{H(4)}(H(1)) = 6.6\%$ and $\eta_{H(4)}(H(3)) = 6.6\%$ for (*E*)-**9c** and the lack of response to H(3) upon irradiation of H(1) suggest the *E*-orientation of H(3) and the $ClCH_2$ group with respect to the double bond.

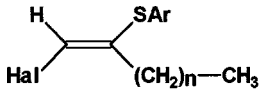



*Z* *E*

The H(1) signal of (*Z*)-**9c** in the $^1$H NMR spectrum exhibits coupling ($J_{H(1)-H(3)} = 1.1$ Hz) to H(3) at the double bond, which is consistent with the published coupling constant ($^4J = 1.0$–$2.0$ Hz[5]) for allyl protons with the *cis*-proton of the C=C bond. Moreover, the stronger NOE effect $\eta_{H(3)}(H(1)) = 8.6\%$ unequivocally proves the *Z*-configuration of (*Z*)-**9c**.

In summary, a new example of the rearrangement of arylthio substituted 1-enes into corresponding 2-enes has been revealed. The occurrence of rearrangement for only one of the halovinyl sulfide isomers suggests the preferable formation of the carbocationic center stabilized

**TABLE III** Chemical Shifts of $^1$H (ppm) in Compounds **7–14a**




| Compound | $H^1$ | $H^3$ | $H^4$ | $H^5$ | $H^6$ | $H^7$ | $H^8$ | H(Ar) |
|---|---|---|---|---|---|---|---|---|
| **7** (*E*) | 6.61 | 2.41 | 1.49 | 1.30 | 0.87 | — | — | 8.20–7.40 |
| **8** (*E*) | 6.76 | 2.40 | 1.60–1.20 | | 0.90 | — | — | 8.16–7.28 |
| **9** (*E*) | 6.61 | 2.40 | 1.50 | 1.45–1.20 | | 0.85 | — | 8.16–7.30 |
| **10** (*E*) | 6.76 | 2.41 | 1.54 | 1.34–1.20 | | 0.87 | — | 8.16–7.30 |
| **11** (*E*) | 6.89 | 2.40 | 1.54 | 1.36–1.20 | | 0.88 | — | 8.24–7.24 |
| **13** (*E*) | 6.63 | 2.40 | 1.50 | | 1.30–1.10 | | 0.85 | 8.16–7.30 |
| **14** (*E*) | 6.77 | 2.40 | 1.55 | | 1.30–1.10 | | 0.85 | 8.16–7.30 |

by the mesomeric effect of the arylthio group, rather than the carbocation stabilized by the mesomeric effect of a halogen.

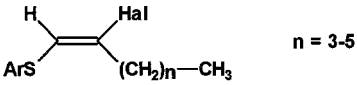


## EXPERIMENTAL

$^1$H NMR spectra were recorded with a Varian VXR-400 instrument operated on 400 MHz at a temperature of 28°C. $CDCl_3$ was used as a solvent. NOE measurements were made in the difference mode (program NOEDIF). Arylsulfenamides were synthesized according to the literature procedure.[6]

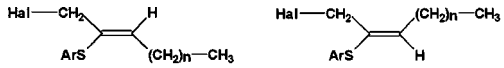
AM1 quantum-chemical calculations were performed using the program package Hyperchem (Hypercube Inc., Gainesville, FL USA) with

**TABLE IV** Chemical Shifts of $^1$H (ppm) in Compounds **7–14b**




| Compound | $H^1$ | $H^3$ | $H^4$ | $H^5$ | $H^6$ | $H^7$ | $H^8$ | H(Ar) |
|---|---|---|---|---|---|---|---|---|
| **7** (*E*) | 6.31 | 2.62 | 1.58 | 1.32 | 0.90 | — | — | 8.20–7.40 |
| **7** (*Z*) | 6.30 | 2.50 | 1.60–1.25 | | 0.90 | — | — | 8.20–7.40 |
| **8** (*E*) | 6.40 | 2.68 | 1.60–1.20 | | 0.98 | — | — | 8.16–7.28 |
| **9** (*E*) | 6.32 | 2.60 | 1.60 | 1.45–1.20 | | 0.85 | — | 8.16–7.28 |
| **9** (*Z*) | 6.30 | 2.50 | 1.60 | 1.45–1.20 | | 0.85 | — | 8.16–7.28 |
| **10** (*E*) | 6.56 | 2.69 | 1.60 | 1.34–1.20 | | 0.87 | — | 8.16–7.28 |
| **10** (*Z*) | 6.32 | 2.63 | 1.60 | 1.34–1.20 | | 0.87 | — | 8.16–7.28 |
| **11** (*E*) | 6.52 | 2.76 | 1.60 | 1.34–1.20 | | 0.88 | — | 8.24–7.24 |
| **12** (*E*) | 6.04 | 2.38 | 1.60 | 1.40–1.20 | | 0.90 | — | 7.60–7.10 |
| **13** (*E*) | 6.30 | 2.62 | 1.60 | | 1.30–1.10 | | 0.85 | 8.16–7.30 |
| **14** (*E*) | 6.55 | 2.70 | 1.60 | | 1.30–1.10 | | 0.85 | 8.16–7.30 |

**TABLE V** Chemical Shifts of $^1$H (ppm) in Compounds **7–14c**




*Z* *E* n = 2-4

| Compound | $H^1$ | $H^3$ | $H^4$ | $H^5$ | $H^6$ | $H^7$ | $H^8$ | H(Ar) |
|---|---|---|---|---|---|---|---|---|
| **7** (*E*) | 4.19 | 6.36 | 2.33 | 1.55 | 0.90 | — | — | 8.16–7.28 |
| **7** (*Z*) | 4.17 | 6.62 | 2.32 | 1.45 | 0.90 | — | — | 8.16–7.28 |
| **8** (*E*) | 4.12 | 6.32 | 2.28 | 1.43 | 0.90 | — | — | 8.16–7.28 |
| **8** (*Z*) | 4.14 | 6.64 | 2.28 | 1.40 | 0.90 | — | — | 8.16–7.28 |
| **9** (*E*) | 4.19 | 6.36 | 2.33 | 1.65–1.20 | | 0.85 | — | 8.16–7.28 |
| **9** (*Z*) | 4.16 | 6.61 | 2.32 | 1.65–1.20 | | 0.85 | — | 8.16–7.28 |
| **10** (*E*) | 4.09 | 6.32 | 2.30 | 1.60–1.20 | | 0.88 | — | 8.16–7.28 |
| **10** (*Z*) | 4.11 | 6.64 | 2.30 | 1.60–1.20 | | 0.88 | — | 8.16–7.28 |
| **11** (*E*) | 4.07 | 6.40 | 2.39 | 1.66–1.20 | | 0.84 | — | 8.24–7.24 |
| **11** (*Z*) | 4.09 | 6.70 | 2.39 | 1.66–1.20 | | 0.84 | — | 8.24–7.24 |
| **12** (*E*) | 4.00 | 6.32 | 2.20 | 1.40–1.20 | | 0.90 | — | 7.60–7.10 |
| **12** (*Z*) | 3.99 | 6.82 | 2.18 | 1.40–1.20 | | 0.90 | — | 7.60–7.10 |
| **13** (*E*) | 4.19 | 6.36 | 2.32 | 1.65–1.15 | | | 0.85 | 8.16–7.28 |
| **13** (*Z*) | 4.16 | 6.61 | 2.32 | 1.65–1.15 | | | 0.85 | 8.16–7.28 |
| **14** (*E*) | 4.08 | 6.36 | 2.30 | 1.56–1.22 | | | 0.90 | 8.11–7.31 |
| **14** (*Z*) | 4.11 | 6.65 | 2.30 | 1.56–1.22 | | | 0.90 | 8.11–7.31 |

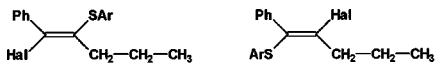


full optimization of molecular geometry. The condition of convergence was a gradient value of $<10$ cal mol$^{-1}$Å$^{-1}$.

## Reactions of Sulfenamides with Alkyne in the Presence of Phosphorus(V) Oxyhalides

To a sulfenamide solution (1.5 mmol) in absolute $CH_2Cl_2$ was slowly added a solution of 1.5 mmol of phosphorus(V) oxyhalide in the same

**TABLE VI** Chemical Shifts of $^1$H (ppm) in Compounds **15–16a**,**b**




**a** **b**

| Compound | $H^3$ | $H^4$ | $H^5$ | H(Ar) |
|---|---|---|---|---|
| **15a** (*E*) | 2.58 | 1.68 | 0.96 | 8.08; 7.44–7.20 |
| **15a** (*Z*) | 2.24 | 1.48 | 0.72 | 8.16; 7.44–7.20 |
| **15b** (*E*) | 2.92 | 1.74 | 1.00 | 7.99; 7.44–7.20 |
| **15b** (*Z*) | 2.43 | 1.70 | 0.84 | 7.82; 7.44–7.20 |
| **16a** (*E*) | 2.60 | 1.70 | 0.98 | 8.08; 7.44–7.18 |
| **16a** (*Z*) | 2.20 | 1.46 | 0.70 | 8.16; 7.44–7.18 |
| **16b** (*E*) | 3.03 | 1.70 | 1.01 | 7.99; 7.44–7.18 |
| **16b** (*Z*) | 2.50 | 1.70 | 0.82 | 7.92; 7.44–7.18 |

**TABLE VII** Elemental Analysis Data for Compounds **7–16**

| Compound | Found/Calculated (%)[a] | | | Formula |
|---|---|---|---|---|
| | C | H | N | |
| **7** | 52.95/53.03 | 5.30/5.15 | — | $C_{12}H_{14}ClNO_2S$ |
| **8** | 44.18/45.57 | 4.47/4.43 | — | $C_{12}H_{14}BrNO_2S$ |
| **9** | 55.29/54.64 | 5.63/5.60 | — | $C_{13}H_{16}ClNO_2S$ |
| **10** | 46.47/47.27 | 4.69/4.84 | — | $C_{13}H_{16}BrNO_2S$ |
| **13** | 56.34/56.09 | 6.40/6.01 | — | $C_{14}H_{18}ClNO_2S$ |
| **14** | 47.87/48.83 | 5.49/5.23 | — | $C_{14}H_{18}BrNO_2S$ |
| **15** | 60.88/61.17 | 4.89/4.80 | 3.95/4.19 | $C_{17}H_{16}ClNO_2S$ |
| **16** | 53.36/53.97 | 4.49/4.23 | — | $C_{17}H_{16}BrNO_2S$ |

[a]In each case the analysis was performed for the mixture of isomeric compounds.



solvent upon vigorous stirring at room temperature and stirred for 10 min. Then an alkyne (1 mmol) solution in absolute $CH_2Cl_2$ was slowly added, and the mixture was stirred until the completion of the reaction (the proceeding of the reaction was monitored by TLC on silica gel/aluminum sheets (Silufol)). The solvent was removed on a rotary evaporator and the residue was chromatographed on a $SiO_2$ column (with 1:3 chloroform-petroleum ether as an eluent).

## Isomerization of Alkyne Chlorosulfenylation Products

A mixture of isomers **a** and **b** (0.9–1.5 mmol) was dissolved in 20 ml of chloroform, 0.05 g of *p*-toluenesulfonic acid was added, and the solution was refluxed for 3 h. The resultant mixture was filtered by passing through an alumina column, and the solvent was evaporated on the rotary evaporator. The reaction mixture was analyzed by NMR spectroscopy.

The yields of products are given in Table I, and their physicochemical characteristics are shown in Tables III–VI. Elemental Analysis Data are given in Table VII.

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