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REVIEW

Dedicated to Full Member of the Russian Academy of Sciences I.P. Beletskaya on Her Jubilee

New Synthetic Capabilities of Sulfonium Salts

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Abstract—The review summarizes published data on the synthesis and reactivity of new functionally substituted sulfonium salts: dimethyl(trifluoromethylsulfonyloxy)sulfonium trifluoromethanesulfonate, dimethyl(trifluoromethylsulfonyl)sulfonium trifluoromethanesulfonate, various disulfonium dications, dimethyl sulfide–sulfur trioxide complex, acyl(dimethyl)sulfonium salts, dimethyl(trifluoroacetyl)sulfonium salts, and boron trifluoride complexes with alkylthio-substituted acyl fluorides as intramolecular analogs of acylsulfonium salts. A theoretical approach is described, which explains electrophilic reactivity of sulfonium salts.

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I. INTRODUCTION

A considerable progress in the field of organic synthesis during the last two decades would be impossible without continuous development of new reagents and improvement of already existing ones. Great demands in new synthetic approaches, methods, and reactions require persistent and hard work on elaboration of new reagents for chemo-, regio, and stereoselective transformations.

In the recent years, our research team was the first to obtain several new functionally substituted sulfonium salts and study them as electrophilic reagents. These were dimethyl(trifluoromethylsulfonyloxy)sulfonium triflate, dimethyl(trifluoromethylsulfonyl)sulfonium triflate, various disulfonium dications, acyl(dimethyl)sulfonium salts, dimethyl(trifluoroacetyl)sulfonium salts, boron trifluoride complexes with alkylthio-substituted acyl fluorides (as intramolecular analogs of acylsulfonium salts), and dimethyl sulfide complex with sulfur trioxide:

$Me_2\overset{+}{S}OSO_2CF_3\ OTf^-$ $Me_2\overset{+}{S}SO_2CF_3\ OTf^-$

$R_2\overset{+}{S}—\overset{+}{S}R_2\ 2OTf^-$ $Me_2\overset{+}{S}COR\ BF_4^-$

$Me_2\overset{+}{S}COCF_3\ CF_3COOBF_3$ $C_2H_5S(CH_2)_nCOF–BF_3$

$Me_2\overset{+}{S}\ SO_3^-$

$n = 1, 2.$

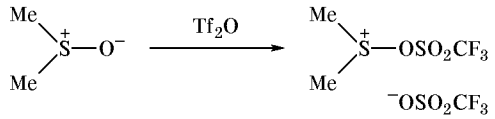
These compounds turned out to be very promising electrophilic reagents. They play an important role in a number of chemical reactions and attract interest from both synthetic and theoretical viewpoints. These reagents are quite versatile. Despite common origin, their reactions with nucleophiles can take radically different pathways: the electrophilic center therein may be either the cationic sulfur atom or another electrophilic group.

Although there are extensive experimental data on the synthesis and reactivity of sulfonium salts (for reviews, see [1–4]), no general concept of the electrophilic reactivity of sulfonium salts have been proposed so far. Therefore, in addition to the development of methods for synthesis of sulfonium salts and study of their structure, reactivity, and synthetic potential, we made an attempt to summarize the available published data with a view to advance a general theoretical approach which could substantiate the reactivity of sulfonium salts as electrophiles.

II. DIMETHYL SULFIDE DITRIFLATE (DMSD)

One of the examined sulfonium salts was dimethyl sulfide ditriflate [or dimethyl(trifluoromethylsulfonyloxy)sulfonium trifluoromethanesulfonate, DMSD]. This reagent was synthesized for the first time by reaction of dimethyl sulfoxide with trifluoromethanesulfonic anhydride [5] (Scheme 1).

Scheme 1.



DMSD

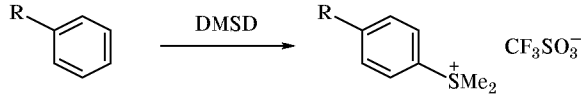
In the recent time, trifluoromethanesulfonic anhydride has received a very wide application in organic synthesis due to unique electronic and nucleofugic properties of the trifluoromethylsulfonyl group [6]. The latter is among the most readily departing groups, and it gives rise to enhanced electrophilicity of the sulfur atom in DMSD, as compared, e.g., with chloro(dimethyl)sulfonium chloride. However, the use of trifluoromethanesulfonic anhydride in the synthesis of sulfonium salts was so far fairly limited. Dimethyl sulfide ditriflate was previously studied as oxidant in the transformation of alcohols into carbonyl compounds [5] and of aromatic amines into sulfimides [7, 8]. Reactions of dimethyl sulfide ditriflate with carbon-centered nucleophiles were studied very poorly, although its reactions with unsaturated and aromatic compounds open wide prospects for various further transformations.

II.1. Reactions of DMSD with Arenes

Dimethyl sulfoxide activated by various acids (HCl, H_2SO_4, $HClO_4$, P_2O_5) was used in the synthesis of aryl(dimethyl)sulfonium salts, but these reactions occurred only with electron-rich aromatic substrates, such as anisole, indole, and azulene. Weakly reactive arenes cannot be involved in a similar process [9].

Dimethyl sulfide ditriflate is a highly reactive S-electrophile in electrophilic substitution reactions. It reacts even with such low active substrates as benzene and toluene. In reactions with arenes, DMSD acts as a synthetic equivalent of the doubly charged synthon Me_2S^{2+}. The reactions occur under mild conditions and yield aryl(dimethyl)sulfonium salts (Scheme 2). Benzene was the least reactive among the arenes involved; fluorobenzene and chlorobenzene failed to react with DMSD. Attempts to effect the reaction by raising the temperature or increasing the reaction time were unsuccessful because of limited thermal stability of the reagent [10]. The reactions of DMSD with arenes are regioselective. The electrophile attacks *para* position of the aromatic ring; an exception is toluene which gives rise to a mixture of *para*- and *ortho*-substituted products at a ratio of 1.5 : 1. The observed regioselectivity is explained in terms of a large size of the electrophilic species. The reaction with naphthalene yields the corresponding 1-substituted derivative.

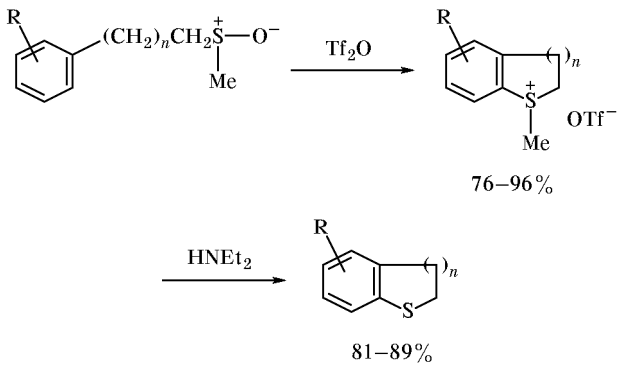
Scheme 2.



55–81%

We also examined an intramolecular version of the reaction of arenes with sulfoxides activated by trifluoromethanesulfonic anhydride. The latter promoted cyclization of methyl sulfoxides having 2-arylethyl, 3-phenylpropyl, and 4-phenylbutyl substituents to give, respectively, 5-, 6-, and 7-membered cyclic sulfonium salts [10] (Scheme 3).

Scheme 3.



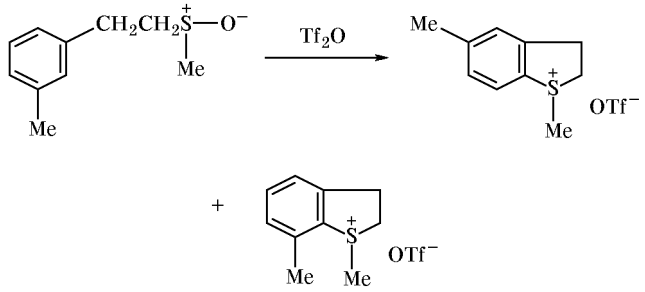
76–96%

81–89%

R = H, Me; *n* = 1, 2, 3.

The reaction with methyl 2-(3-methylphenyl)ethyl sulfoxide occurred at both *ortho* and *para* positions of the aromatic ring with respect to the methyl group, yielding the corresponding isomers at a ratio of 1 : 3 (Scheme 4).

Scheme 4.



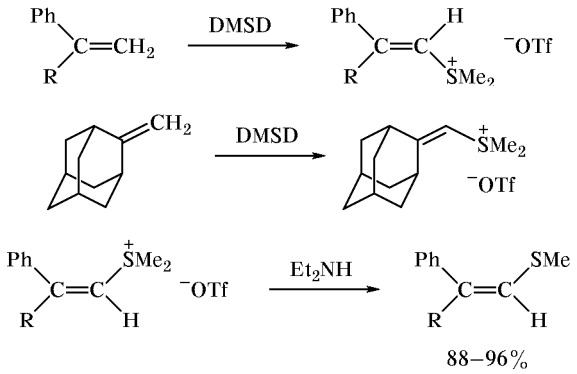
Cyclic sulfonium salts are readily converted in high yield into sulfur-containing heterocyclic compounds by the action of excess diethylamine. Also, a one-step synthesis of sulfur-containing heterocycles has been developed. In this case, the yields of the target heterocyclic sulfides were 70–88%.

II.2. Reactions of DMSD with Alkenes

Reactions of DMSD with alkenes involve replacement of the olefinic proton by dimethylsulfonium group with formation of dimethyl(vinyl)sulfonium salts (Scheme 5). With cyclohexene and cyclopentene as substrates, complex mixtures of sulfonium salts are obtained. It should be noted that products of conjugate addition of the electrophile (dimethylsulfonium group) and nucleophile (trifluoromethanesulfonate anion) are not formed. Intermediate carbocations possess an acceptor dimethylsulfonium group in the α-position with respect to the cationic center, and their stabilization via elimination of proton is faster than addition of such a weak nucleophile as triflate ion [11]. Dimethyl(vinyl)sulfonium salts readily undergo demethylation by treatment with diethylamine. Vinyl sulfides can also be synthesized without intermediate isolation of sulfonium salts, and the yields as a rule are not reduced.

The reaction of DMSD with α-methylstyrene gave the corresponding vinylsulfonium salt as a single *E* isomer. However, detailed study of this reaction

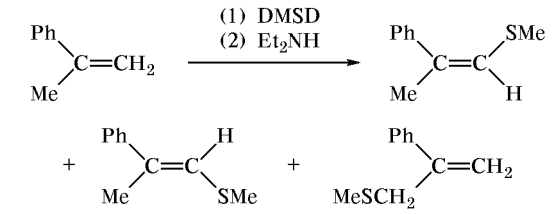
Scheme 5.



R = H, Me, Ph.

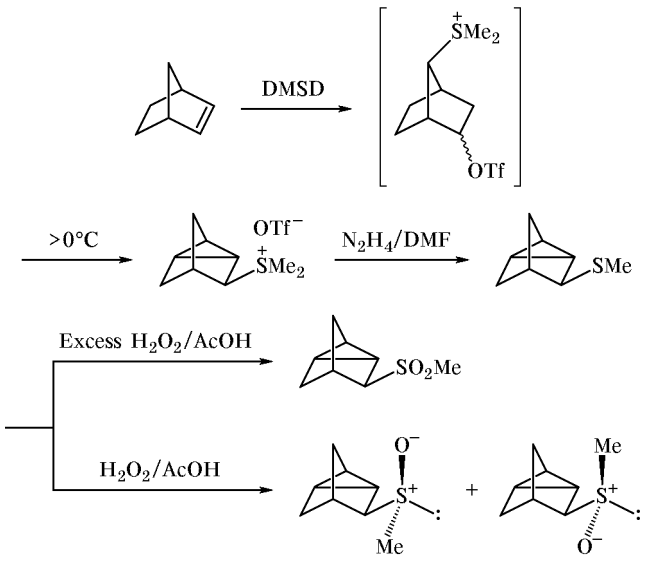
showed that in fact a complex mixture of sulfonium salts is formed. Its subsequent demethylation yields two isomeric (*E*)- and (*Z*)-vinyl sulfides and allyl sulfide (ene reaction product) at a ratio of 5:1:1 (Scheme 6).

Scheme 6.



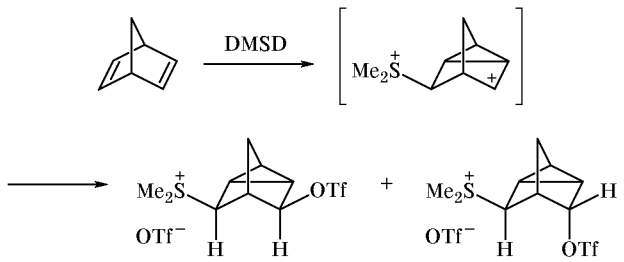
The reaction of DMSD with norbornene is accompanied by Wagner–Meerwein rearrangement, leading to nortricyclane with a dimethylsulfonium group.

Scheme 7.



The resulting sulfonium salt was converted into other nortricyclane derivatives: sulfide, diastereoisomeric sulfoxides, and sulfone (Scheme 7). A mixture of diastereoisomeric sulfonium salts at a ratio of 3:2 was obtained in the reaction of DMSD with norbornadiene (Scheme 8). Addition of the electrophilic species (Me_2S^+) to norbornadiene gives carbocationic intermediate with *exo*-oriented dimethylsulfonium group. The subsequent addition of triflate ion as nucleophile occurs from both *exo* and *endo* side to afford a mixture of sulfonium salts. The Wagner–Meerwein rearrangement is followed by removal of carbocationic center from the dimethylsulfonium group, so that stabilization via formation of the corresponding trifluoromethanesulfonate becomes possible. Presumably, intermediate trifluoromethanesulfonate formed in the reaction with norbornene is insufficiently stable; therefore, it is converted into nortricyclane sulfonium salt via elimination of trifluoromethanesulfonic acid.

Scheme 8.



The reaction of DMSD with dimethoxybenzonorbornadiene was also examined. This substrate is known to readily undergo Wagner–Meerwein rearrangement by the action of electrophiles. It was quite surprising that its reaction with DMSD gave sulfonium salt as a result of electrophilic attack at the aromatic ring rather than at the double bond. A possible reason is steric factor: the attack by electrophile on the double bond is sterically hindered (Scheme 9).

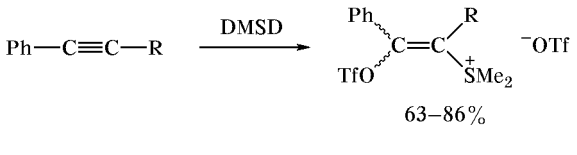
Scheme 9.

II.3. Reactions of DMSD with Acetylenes

Dimethyl sulfide ditriflate reacts with phenylacetylenes under mild conditions, yielding products of conjugate addition of dimethylsulfonium group

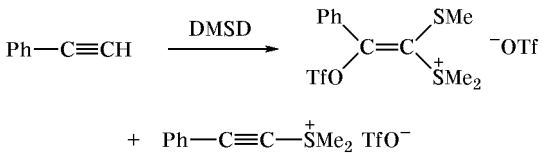
(electrophile) and triflate ion (nucleophile). This reaction provides a synthetic route to vinyl trifluoromethanesulfonates having a strong electron-acceptor group (dimethylsulfonio) in the β-position at the double bond [12] (Scheme 10).

Scheme 10.



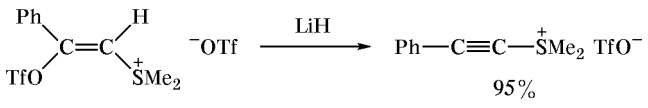
Vinyl trifluoromethanesulfonates play an important role in modern organic synthesis [13]. They are effective precursors of vinyl cations, alkylidenecarbenes (primary vinyl trifluoromethanesulfonates), acetylenes, and allenes (secondary vinyl trifluoromethanesulfonates) [14]. These compounds are widely used in cross-coupling reactions catalyzed by low-valence platinum, palladium, and nickel [15, 16]. In the reaction with 1-phenyl-1-propyne, a mixture of *E* and *Z* isomers is formed at a ratio of 1:5. From phenylacetylene and 1-phenyl-1-butyne, only the corresponding *Z* isomers are obtained. By contrast, the reaction with diphenylacetylene yields (*E*)-dimethyl(1,2-diphenyl-2-trifluoromethylsulfonyloxyethenyl)sulfonium trifluoromethanesulfonate. The stereochemistry of the addition is governed by steric factors. In the reaction of DMSD with diphenylacetylene, steric effect of the bulky phenyl groups is crucial. The reaction of DMSD with phenylacetylene gives a mixture of the corresponding vinyl trifluoromethanesulfonate and ethynylsulfonium salt at a ratio of 2:3 (Scheme 11).

Scheme 11.



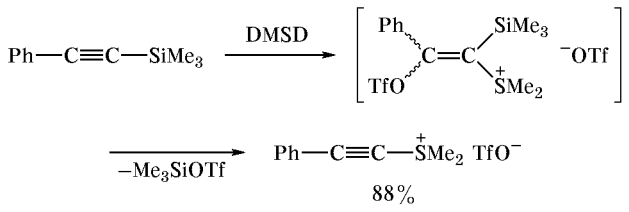
Vinyl trifluoromethanesulfonate derived from phenylacetylene can undergo spontaneous transformation into ethynylsulfonium salt via elimination of trifluoromethanesulfonic acid. This reaction is also promoted by lithium hydride (Scheme 12).

Scheme 12.



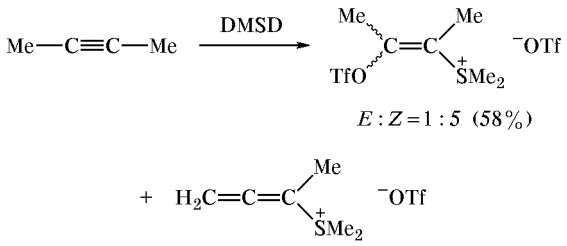
The same sulfonium salt was obtained in a good yield from phenyl(trimethylsilyl)acetylene. Presumably, the primary adduct is unstable, and fast elimination of trimethylsilyl trifluoromethanesulfonate occurs (Scheme 13).

Scheme 13.



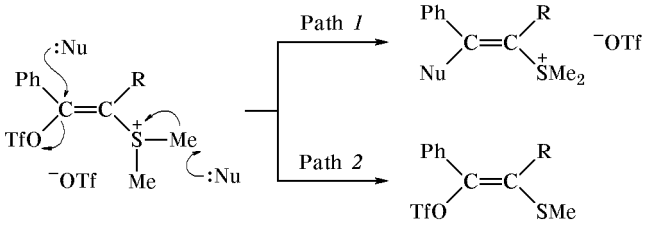
The reaction of DMSD with 2-butyne afforded a mixture of vinyl trifluoromethanesulfonate and allenylsulfonium salt (Scheme 14).

Scheme 14.



Vinyl trifluoromethanesulfonates possess several reaction centers: they can react with nucleophiles either at the carbon atom attached to the trifluoromethylsulfonyloxy group (path *1*) or at the sulfonium group (path *2*, Scheme 15).

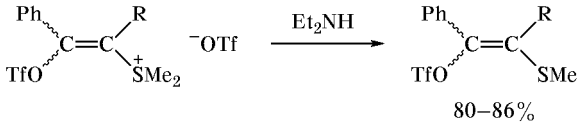
Scheme 15.



Reactions of vinyl trifluoromethanesulfonates with various amines occur in a chemoselective manner, namely as nucleophilic substitution at the sulfonium group to give sulfides (path *2*), whereas the sulfonate moiety is not involved. Diethylamine ensures the largest yields in demethylation of sulfonium salts. The resulting sulfides do not react with amines, presumably because of donor effect of the methylthio group. Sulfides can also be obtained without inter-

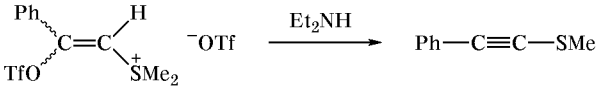
mediate isolation of sulfonium salts, by treatment of reaction mixtures with diethylamine (Scheme 16).

Scheme 16.



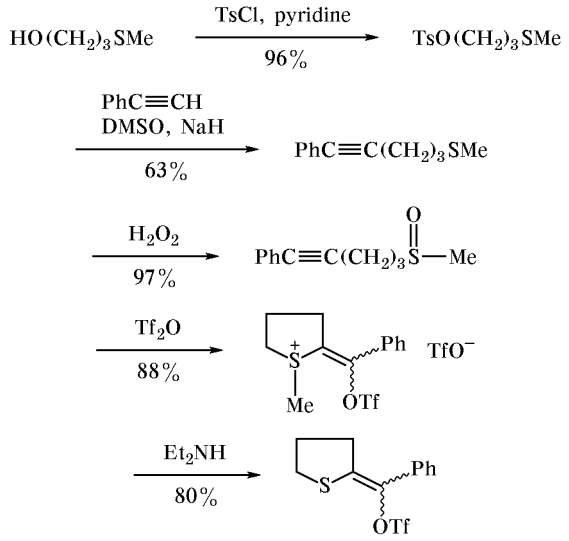
In the reaction of DMSD with phenylacetylene, demethylation leads to formation of methyl phenylethynyl sulfide, and the corresponding vinyl trifluoromethanesulfonate could not be isolated (Scheme 17).

Scheme 17.



With a view to obtain thiophene derivatives, we studied intramolecular cyclization of methyl 5-phenyl-4-pentynyl sulfoxide by the action of trifluoromethanesulfonic anhydride. Cyclic sulfonium salt was obtained as a mixture of *E* and *Z* isomers at a ratio of 2:3. The reaction follows the Markownikoff and Baldwin patterns [12] (*exo*-cyclization with formation of five-membered ring, Scheme 18).

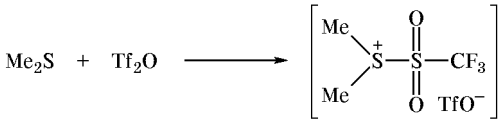
Scheme 18.



III. DIMETHYL(TRIFLUOROMETHYLSULFONYL)SULFONIUM TRIFLATE

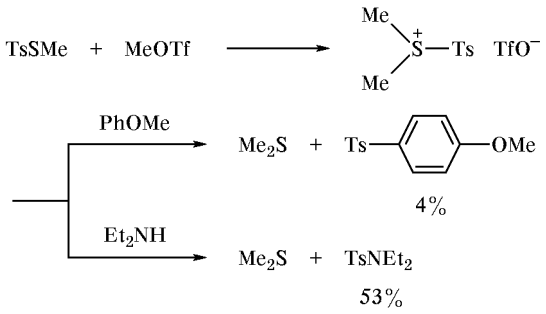
The reaction of trifluoromethanesulfonic anhydride, as well of other sulfonic anhydrides, with dimethyl sulfide was studied [17]. In methylene chloride at –60°C a colorless crystalline complex was obtained. No reaction occurred between dimethyl sulfide and less electrophilic methanesulfonic anhydride or *p*-toluenesulfonic anhydride even at room temperature over a long time. The crystalline complex formed in the reaction of dimethyl sulfide with trifluoromethanesulfonic anhydride was dimethyl(trifluoromethylsulfonyl)sulfonium triflate (Scheme 19).

Scheme 19.



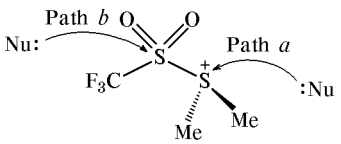
Such sulfonium salts were almost not studied. The only example of the synthesis of a sulfonylsulfonium salt was reported in [18]. Dimethyl(tosyl)sulfonium triflate was synthesized previously by methylation of *S*-methyl *p*-toluenethiosulfonate with methyl trifluoromethanesulfonate (Scheme 20).

Scheme 20.



Dimethyl(trifluoromethylsulfonyl)sulfonium triflate possesses two electrophilic centers, the sulfonium and sulfonate sulfur atoms; therefore, its reactions with nucleophiles can occur at both these sites (path *a* or path *b*). As shown in [18], dimethyl(tosyl)sulfonium triflate reacts with anisole or diethylamine at the sulfonate sulfur atom, i.e., according to path *b* (Scheme 21).

Scheme 21.

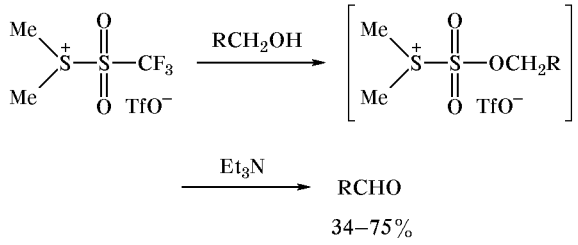


III.1. Reactions with O-Nucleophiles

The complex dimethyl sulfide–trifluoromethanesulfonic anhydride reacts with primary and secondary alcohols exclusively at the sulfonium sulfur atom

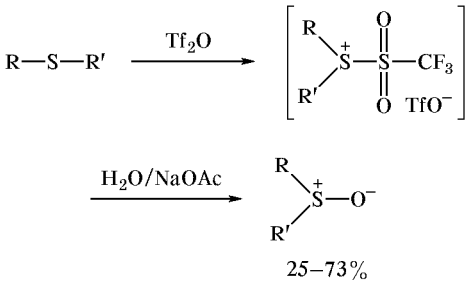
(path *a*) to give the corresponding alkoxysulfonium salts. Subsequent treatment of the reaction mixtures with triethylamine leads to formation of carbonyl compounds in 34–75% yield [17]. These reactions underlie a new procedure for oxidation of alcohols into carbonyl compounds (Scheme 22).

Scheme 22.

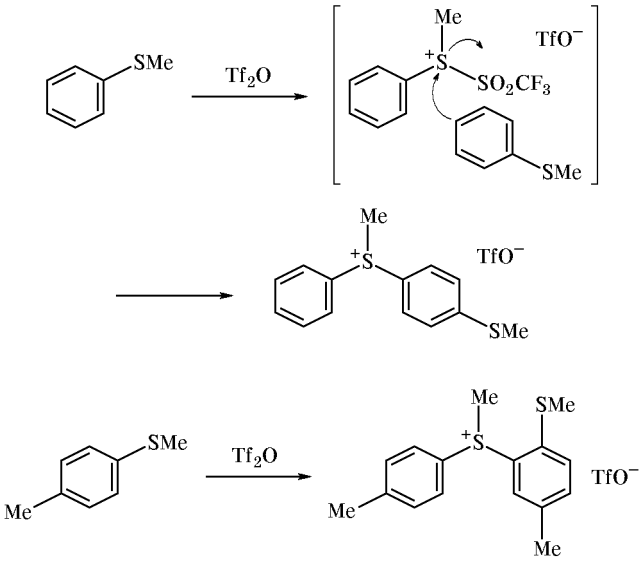


Reactions of trifluoromethanesulfonic anhydride with various sulfides make it possible to obtain sulfoxides without overoxidation to sulfones [17] (Scheme 23). The process is quite sensitive to electronic and steric factors. In the oxidation of methyl phenyl sulfide, the corresponding sulfoxide was obtained in a poor yield (25%). It was found that the oxidation is accompanied by electrophilic substitution to give diaryl(methyl)sulfonium salt. This means that intermediate sulfonylsulfonium salts acts as sulfonium electrophile. In the reaction with methyl *p*-tolyl sulfide, the corresponding sulfonium salt is formed in 73% yield (Scheme 24).

Scheme 23.

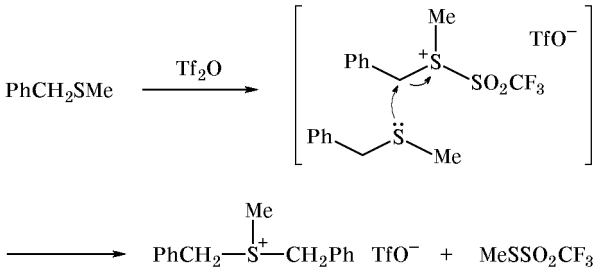


Scheme 24.



No sulfoxide was obtained in the reaction of benzyl methyl sulfide with trifluoromethanesulfonic anhydride. In this case, the anomalous reaction pathway is explained by enhanced mobility of the benzyl group in nucleophilic substitution. As a result, the only reaction pathway is transbenzylation (Scheme 25).

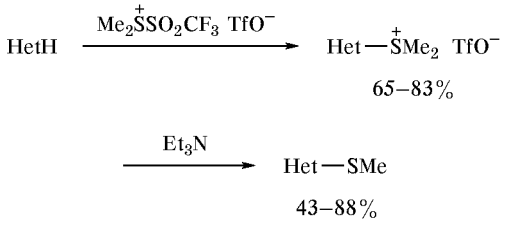
Scheme 25.



III.2. Reactions with C-Nucleophiles

A new mild procedure for the preparation of dimethyl(hetaryl)sulfonium salts was developed on the basis of the reaction of dimethyl(trifluoromethylsulfonyl)sulfonium triflate with aromatic heterocycles [19]. The simplest synthetic route to such salts, which involves alkylation of aryl alkyl sulfides, cannot be regarded as universal, for synthesis of the latter is a separate task [9]. The known methods for preparation of aryl alkyl sulfides are based on oxidative activation of dimethyl sulfide [20] or electrophilic activation of dimethyl sulfoxide [21]. We have found that the complex dimethyl sulfide–trifluoromethanesulfonic anhydride reacts with a number of heteroaromatic compounds under mild conditions (on

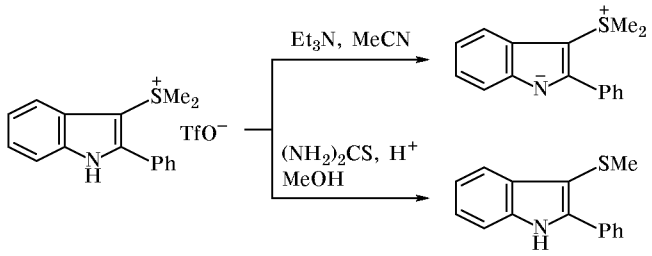
Scheme 26.



cooling), affording the corresponding aryl(dimethyl)sulfonium salts. In most cases, only one regioisomer is formed via electrophilic substitution at the most nucleophilic carbon atom of the heteroring. The resulting sulfonium salts can readily be converted into hetaryl methyl sulfides by treatment with triethylamine [19] (Scheme 26).

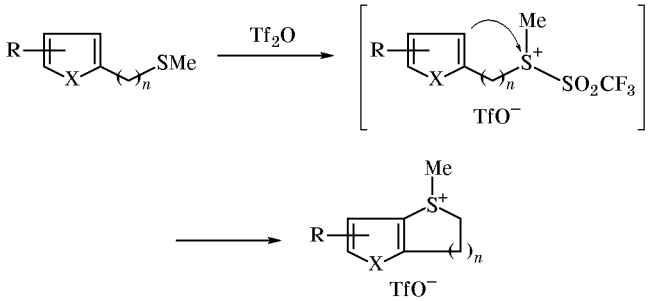
Unexpected results were obtained in an attempt to effect demethylation with triethylamine of the sulfonium salt derived from 2-phenylindole. Instead of the desired sulfide, we isolated sulfonium ylide [19]. Although deprotonation of both sulfonium salts and unsubstituted indole requires strong bases [22], pyrrole and indole derivatives exhibit enhanced NH acidity, so that the formation of the corresponding ylides becomes possible in the presence of weaker bases [23, 24]. In the above case, the transformation occurred in the presence of thiourea and $HClO_4$, and methyl 2-phenylindol-3-yl sulfide was isolated in 84% yield (Scheme 27).

Scheme 27.



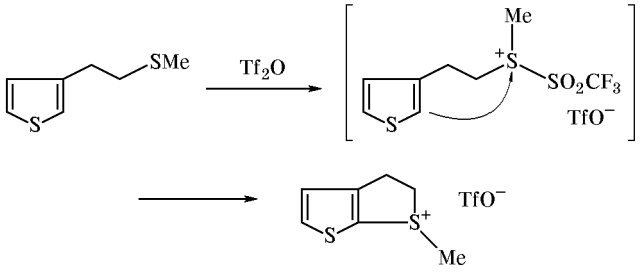
An intramolecular version of aromatic electrophilic substitution in (trifluoromethylsulfonyl)sulfonium salts leads to cyclic sulfonium salts whose subsequent dealkylation gives various fused sulfur-containing heterocycles. Direct activation by trifluoromethanesulfonic anhydride of appropriate dialkyl sulfides having a heteroaromatic fragment extends the potential of previously known methods for preparation of sulfur-containing heterocycles. It was found that the reaction of trifluoromethanesulfonic anhydride with model sulfides gives cyclic five- or six-membered sulfonium salts (Scheme 28). A probable mechanism includes intermediate formation of sulfonylsulfonium salt and subsequent electrophilic substitution at the neighboring *ortho* position of the heteroring, e.g., as shown in Scheme 29.

Scheme 28.



n = 1, 2.

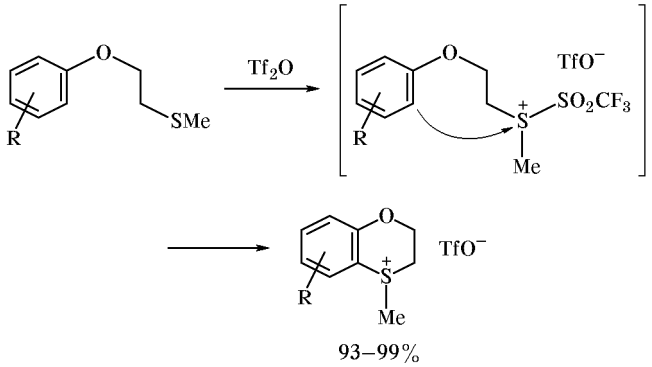
Scheme 29.



The procedure turned out to be fairly general. It is applicable to various electron-rich aromatic heterocycles. Cyclic sulfonium salts were synthesized from labile indole derivatives. However, an attempt to carry out cyclization of furan derivative resulted in strong tarring of the reaction mixture.

Cyclization of ω-(methylthio)alkyl phenyl and naphthyl ethers by the action of trifluoromethanesulfonic anhydride was studied. In these cases, only the corresponding six-membered rings were obtained (Scheme 30). Cyclization of N-substituted aromatic heterocyclic sulfides by the action of Tf_2O provides the possibility for synthesizing heterocycles of the thiazine, thiazole, and thiazepine series.

Scheme 30.

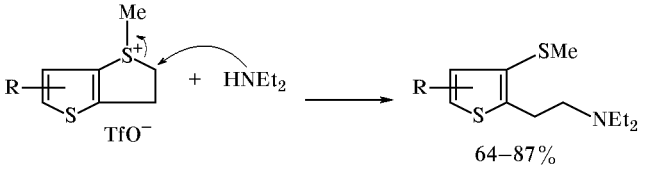


With the goal of obtaining sulfur-containing heterocycles, demethylation of cyclic sulfonium salts was studied. Triethylamine turned out to be the most appropriate reagent. It ensured mild conditions and

acceptable rate of the process which was not accompanied by side formation of ring opening products. As a result, the corresponding fused sulfur-containing heterocycles were formed. They can also be synthesized in one step without preliminary isolation of sulfonium salts.

An unusual pattern was observed while studying demethylation of five-membered cyclic sulfonium salts. Their treatment with triethylamine resulted in formation of products of nucleophilic ring opening, methylthio derivatives of the corresponding heterocyclic compounds having a 2-diethylaminoethyl fragment (Scheme 31). On the other hand, treatment of six-membered cyclic sulfonium salts with diethylamine afforded the same products as those obtained with the use of triethylamine, the corresponding heterocycles. Nucleophilic substitution at the methyl or benzyl carbon atom is the most facile; the reaction at other alkyl carbon atoms is more difficult: Bzl > Me > Alk. A probable reason for ring opening in five-membered sulfonium salts by the action of diethylamine is considerable angular strain which is typical of pyrrole and thiophene derivatives fused to a five-membered ring [25].

Scheme 31.



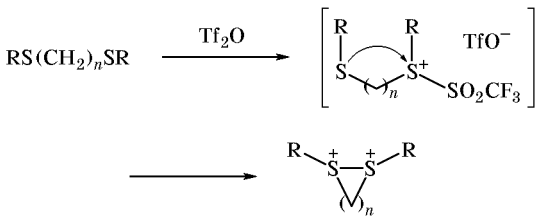
Similar reactions with triethylamine, which is a more hindered nucleophile, lead to selective formation of the corresponding fused sulfur-containing heterocycles.

IV. S–S DICATIONS

IV.1. Oxidation of Bis-Sulfides with Trifluoromethanesulfonic Anhydride. Synthesis of Disulfonium Dications

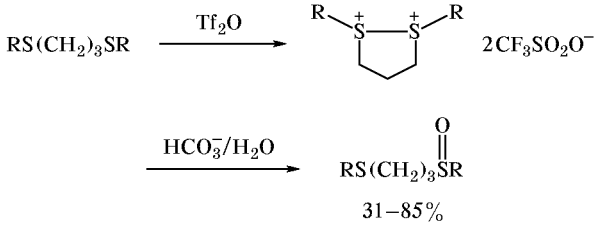
Reactions of trifluoromethanesulfonic anhydride with cyclic and acyclic bis-sulfides give disulfonium dications (Scheme 32). Compounds having two directly linked positively charged heteroatoms are very specific and rare. They are characterized by maximal mutual influence of the two positively charged reaction centers, which gives rise to unusual properties as compared to monocations or dications with spatially separated centers. Among such structures, disulfonium dications are studied most extensively. However, taking into account their increased lability, most known methods of synthesis of S–S dications [26–31] give low yields of the target products and are not selective or require special equipment. The most general procedure for generation of disulfonium dications is based on the reaction of trifluoromethanesulfonic anhydride with bis-sulfides [26]. Obviously, direct oxidation of bis-sulfides makes the synthesis of S–S dications simpler, for it avoids selective oxidation of initial bis-sulfides to monosulfoxides (the more so there is no well-developed procedure for preparation of monosulfoxides [32]).

Scheme 32.



In order to determine the scope of application of the above method for generation of disulfonium dications, we studied oxidation with trifluoromethanesulfonic anhydride of a series of cyclic and acyclic bis-sulfides [32]. In most cases, dications thus formed were very labile; therefore, they were characterized as the hydrolysis products, the corresponding sulfoxides [33] (Scheme 33). The procedure is very sensitive to angular strains appearing in new rings upon formation of an additional S–S bond. Five- and six-membered cyclic structures are formed most readily, and closure of four-membered ring is considerably more difficult. In going from eight-membered bis-sulfide (the corresponding dication contains two five-membered rings) to dithiane (which gives rise to disulfonium dication with two four-membered rings), the yield of the respective sulfoxide decreases from 71 to 31%. The same applies to disulfonium dications derived from acyclic bis-sulfides.

Scheme 33.



The reaction of bis-sulfides with trifluoromethanesulfonic anhydride, followed by hydrolysis, may be

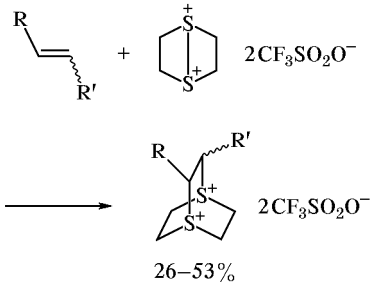
regarded as a new selective method for oxidation of bis-sulfides to the corresponding monosulfoxides, which avoids side formation of bis-sulfoxides.

IV.2. Reactions of Disulfonium Dications with Unsaturated Compounds

Disulfonium dications are the most extensively studied 1,2-dications. Fujihara *et al.* previously showed that S–S dications act as oxidants toward organometallic compounds [34], alcohols, hydrazines [35], and thiols [36]. Disulfonium dications are fairly reactive electrophiles with respect to such nucleophiles as water [33], bromide ion [37], and electron-rich aromatic compounds [38]. Despite a great number of publications on S–S dications, their reactions with compounds having multiple carbon–carbon bonds were not studied. The most extensively studied and stable dication generated from 1,5-dithiocane turned out to be inactive toward styrene. No positive results were obtained with a more strained dication generated from 1,4-dithiepane [39].

Disulfonium dication derived from 1,4-dithiane is more reactive. Its reactions with alkenes lead to conjugate addition products of two sulfonium groups at the double bond, namely bicyclic sulfonium salts of the 1,4-dithioniabicyclo[2.2.2]octane series [39] (Scheme 34).

Scheme 34.

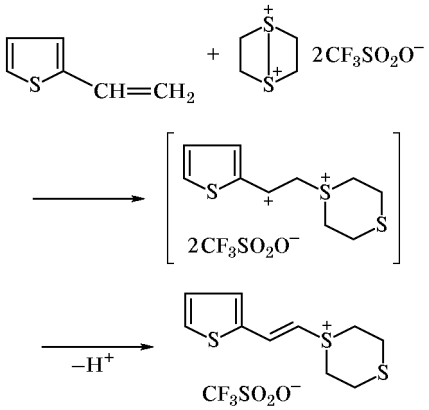


26–53%

Alkenes with an activated double bond (due to conjugation with an aromatic or cyclopropane ring) can also be involved in this reaction. By contrast, such alkenes as 1-hexene or cyclohexene failed to react. Enhanced reactivity of the dication generated from 1,4-dithiane is explained by considerable steric strain in the system consisting of two fused four-membered rings. It should be noted that in the reaction with vinylcyclopropane, only the 1,2-addition product was isolated. No rearrangement products (with participation of the cyclopropane ring) were detected. Presumably, intramolecular reaction of intermediate carbocation with the resulting sulfide is faster than its rearrangement.

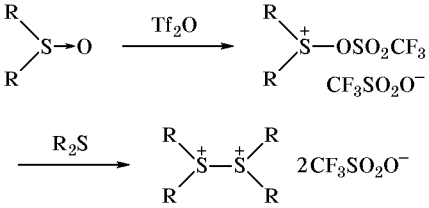
Reactions with 2-substituted 1-phenylethenes give only one stereoisomer, the relative configuration of substituents in the initial alkene being retained. For example, *trans*-disubstituted sulfonium salts were isolated in reactions of cyclic disulfonium dications with alkenes having *E* configuration of the double bond. The reaction with indene gives the corresponding *cis* adduct. Unusual reaction occurs with 2-vinylthiophene. Unlike the other vinylarene studied, the isolated product was β-substituted vinylthiophene (Scheme 35).

Scheme 35.



To get a deeper insight into the reactivity of S–S dications, we examined simple acyclic disulfonium dications in which the sulfur atoms are not linked by polymethylene bridges. Tetramethyldisulfonium ditriflate was synthesized for the first time by reaction of dimethyl sulfide with DMSD. Likewise, the corresponding dication was obtained from tetrahydrothiophene [40] (Scheme 36).

Scheme 36.

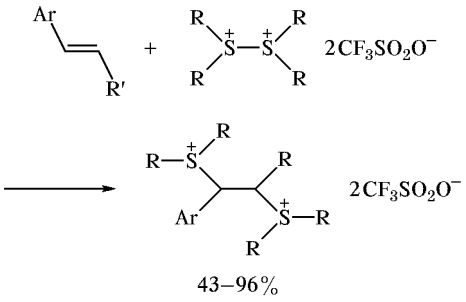


R = Me, RR = $(CH_2)_4$.

These two dications react with olefins under mild conditions and yield disulfonium salts as 1,2-addition products. However, identifiable products were obtained only from alkenes in which the double bond is

conjugated with an aromatic ring. The stereochemistry of addition of disulfonium dications across double C=C bond was studied using 1,2-disubstituted ethylenes. The addition was not stereoselective, and mixtures of *erythro* and *threo* isomers were obtained (Scheme 37).

Scheme 37.



R = Me, RR = $(CH_2)_4$.

IV.3. Mechanism of Reactions of S–S Dications with Alkenes

Comparison of the data on the reactivities of cyclic and acyclic disulfonium dications toward alkenes allowed us to draw some conclusions concerning the reaction mechanism. As hypotheses we considered synchronous addition involving a four-membered cyclic transition state and consecutive electrophilic addition with formation of carbocationic intermediates. Oxidative properties of S–S dications [28, 36] do not exclude radical cation mechanism, but ESR study of the reaction revealed no radical species. The lack of stereoselectivity in the addition of acyclic disulfonium dications to 1,2-disubstituted ethylenes evidences in favor of the consecutive mechanism. By contrast, conservation of the relative arrangement of substituents at the double bond in the alkene adducts with cyclic S–S dication may be the result of synchronous process (Scheme 38).

An additional information on the reaction mechanism was obtained by *ab initio* calculations of a series of disulfonium dications in the HF/6-31G* approximation [41, 42]. The bond lengths and interatomic distances in the optimized structures are given in Table 1. The data for 1,5-dithioniabicyclo[3.3.0]octane are well consistent with those found experimentally [43, 44]. The calculated energies of the lowest unoccupied molecular orbitals of dications correlate with their electrophilic reactivity. Thus, 1,4-dithioniabicyclo[2.2.0]hexane (E_{LUMO} = –0.3616) is the only bicyclic dication capable of reacting with alkenes. Dications with higher LUMO energies, 1,4-dithioniabicyclo[2.3.0]heptane and 1,5-dithioniabicyclo[3.3.0]octane (E_{LUMO} = –0.3270 and –0.2919, respectively) do not react with alkenes. Acyclic tetramethyldisulfonium dication (E_{LUMO} = –0.3000) falls out from the given series. Probably, its high reactivity originates from weakening of the S–S bond as a result of uncompensated van der Waals repulsion of the methyl groups. This is well illustrated by increase of the calculated S–S bond length relative to cyclic dications (Table 1). Figure 1 shows a correlation diagram of frontier orbitals for reactions of S–S dications with alkenes. The highest occupied molecular orbital (HOMO) of 1,4-dithioniabicyclo[2.2.2]octane is an in-phase *n*[S] + *n*[S] combination corresponding to the 1-HOMO of the initial dication, and its LUMO is the next following occupied orbital of the dication. The reason is repulsion of the electron density on the sulfur atoms and on the σ-C–C bonds. An analogous pattern was observed for 1,4-diazabicyclo[2.2.2]octane [45]. In compounds with an open S–C–C–S chain, such energetically unfavorable orbital interactions is minimized for conformations with transoid orientation of the dimethylsulfonium groups.

Simulation of the frontal attack by ethylene on 1,4-dithioniabicyclo[2.2.0]hexane gave no optimal structure of intermediate complex. In this case, the synchronous addition should involve an antiaromatic suprasurface transition state possessing 8 electrons and corresponding to the Hückel topology of the basis orbital set (two nodes) [46]. This means that, in keeping with the generalized Woodward–Hoffmann

Scheme 38.

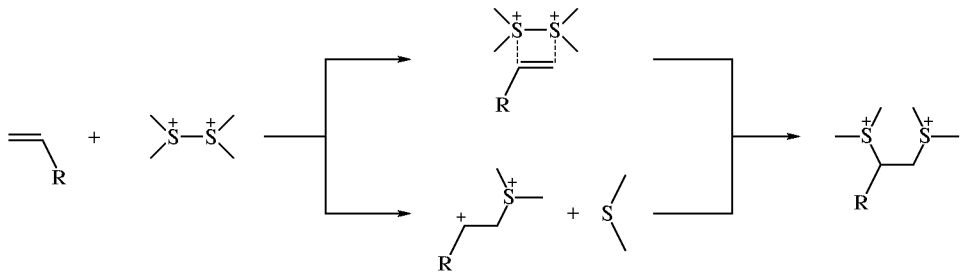


Table 1. Calculated bond lengths in disulfonium dications

Structure	C–S bond length, Å	S···S distance, Å
$Me_2\overset{+}{S}-\overset{+}{S}Me_2$, (*ap–ap*)	1.832	2.128
$Me_2\overset{+}{S}-\overset{+}{S}Me_2$, (*sp–sp*)	1.829	2.157
1,4-Dithiane (*boat*)	1.813	3.152
1,4-Dithioniabicyclo[2.2.0]hexane	1.862	2.116
1,4-Dithioniabicyclo[3.2.0]heptane	1.864 (4-membered ring) 1.868 (5-membered ring)	2.109
1,5-Dithioniabicyclo[3.3.0]octane[a]	1.862 (1.842, 1.828)	2.114 (2.126)
1,4-Dithioniabicyclo[2.2.2]octane	1.818	3.119

[a] In parentheses, experimental data from [43] are given.

rule, synchronous addition of disulfonium dications at the double C=C bond of alkenes is a thermally forbidden process; therefore, it is hardly probable.

On the other hand, in the lateral approach of the reactants, orbital factors favor attack of the double bond by one of the sulfonium sulfur atoms of the

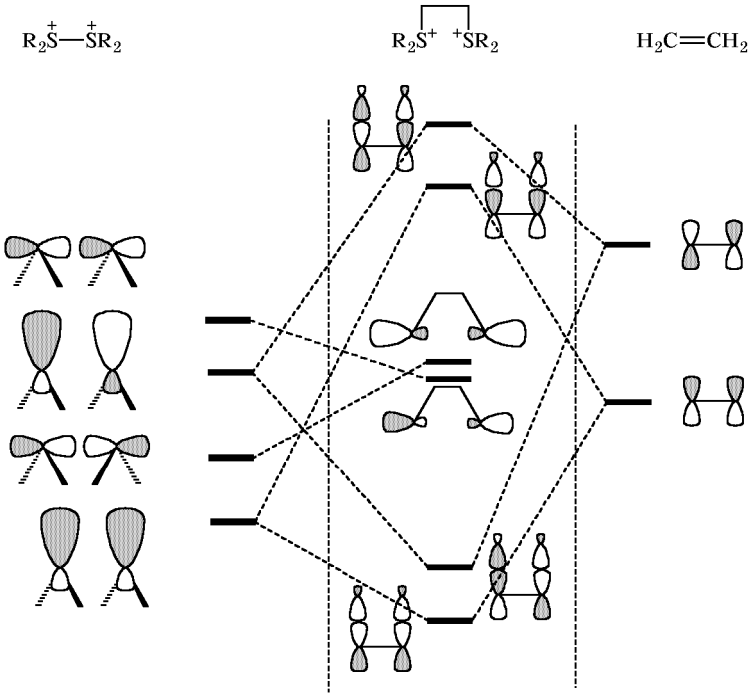


Fig. 1. Correlation diagram of frontier orbitals for reactions of disulfonium dications with alkenes.

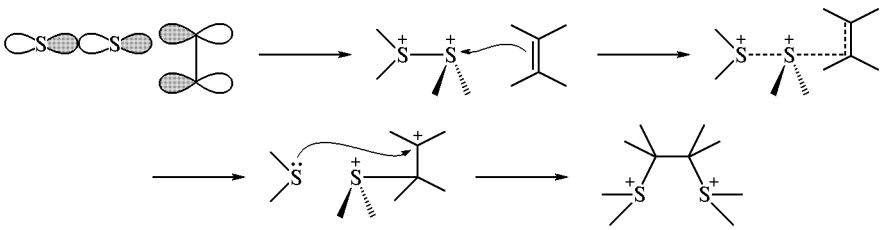
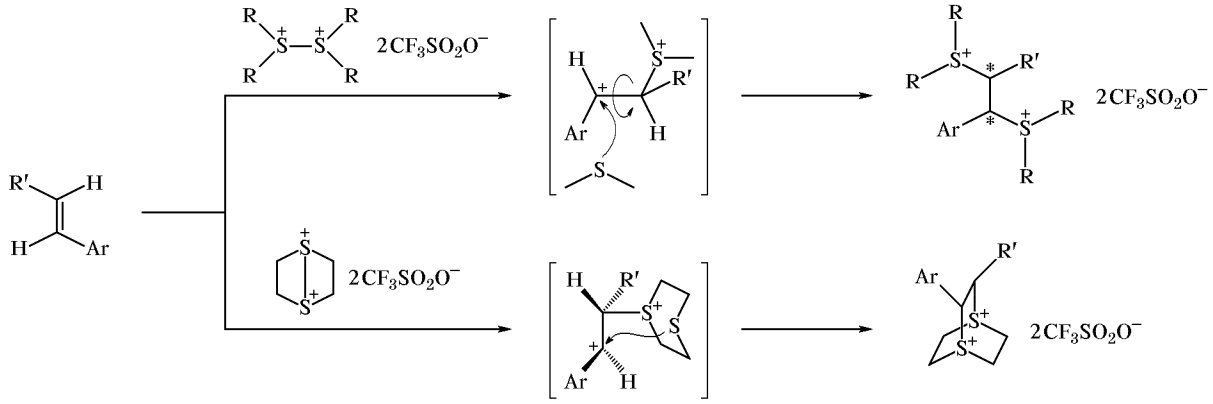


Fig. 2. Reaction scheme of disulfonium dications with alkenes.

Scheme 39.



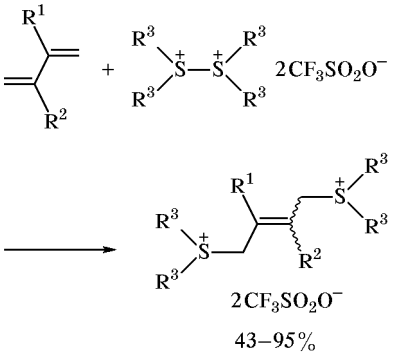
dication. This pattern corresponds to S_N2-like substitution at sulfur atom [S_N2(S)] (Fig. 2). Using such reactant orientation, the structure of intermediate π-complex was successfully optimized. The distances between the reaction centers in the complex, i.e., between the carbon atoms of the ethylene fragment and the nearest sulfur atom of the dication are 2.74 and 2.96 Å, respectively.

Thus, interpretation of the experimental data in terms of the consecutive electrophilic mechanism seems to be more reasonable. In this case, different stereochemical results of the reactions of cyclic and acyclic disulfonium dications are explained by higher rates of intramolecular processes as compared to intermolecular (Scheme 39).

IV.4. Reactions of Disulfonium Dications with Conjugated Dienes

Reactions of disulfonium dications with conjugated dienes provide an additional information on the mechanism of their reaction with unsaturated compounds, for in this case the orbital symmetry favors concerted process. All the examined disulfonium dications do react with dienes, but from cyclic S–S dications and butadiene or its derivatives complex mixtures of oligomeric sulfonium salts are formed. Reactions of acyclic disulfonium dications with 1,3-dienes lead to formation of unsaturated salts as a result of conjugate 1,4-addition of two sulfonium groups (Scheme 40). No 1,2-addition products were isolated [40]. The most probable explanation may be given in terms of the consecutive electrophilic addition mechanism. In the first step, allylic carbocation with a terminal sulfonium group is formed; due to Coulomb interaction between two positive charges, the contribution of mesomeric structure with maximally distant charges should predominate. The reaction of this carbocation with liberated sulfide should result in selective formation of the 1,4-addition product

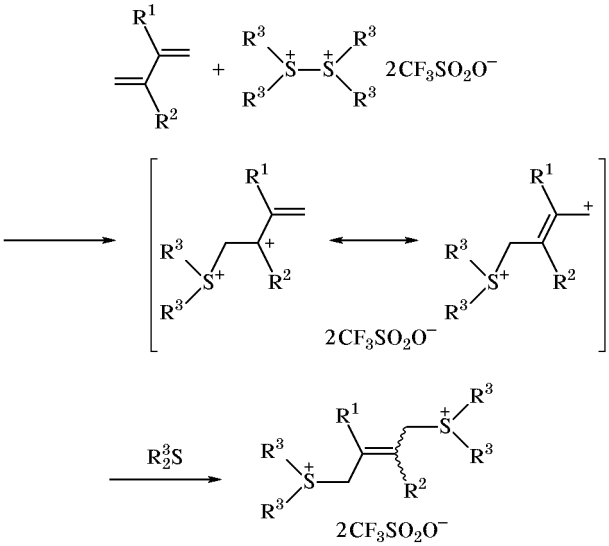
Scheme 40.



43–95%

R^3 = Me, R^3R^3 = $(CH_2)_4$.

Scheme 41.



R^3 = Me, R^3R^3 = $(CH_2)_4$.

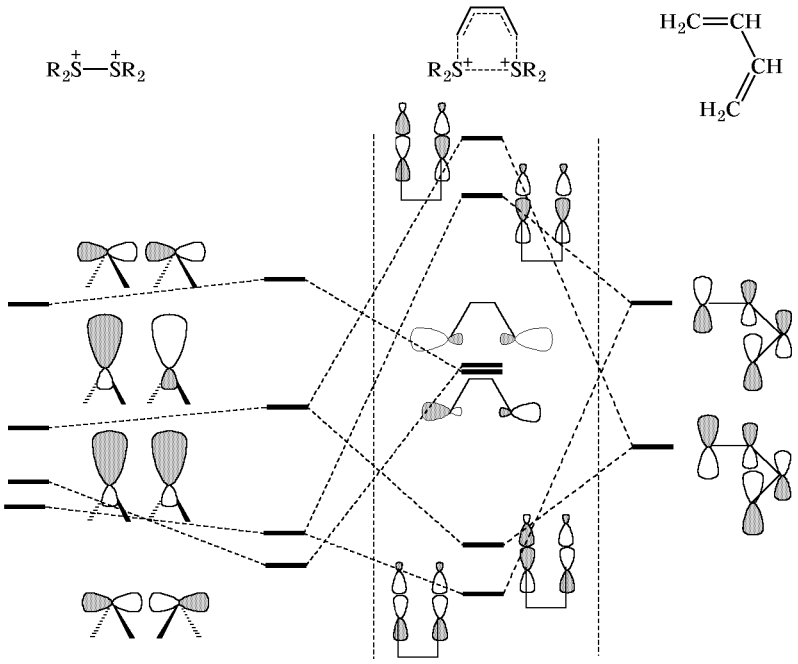


Fig. 3. Diagram of orbital interaction between 1,3-butadiene and disulfonium dications.

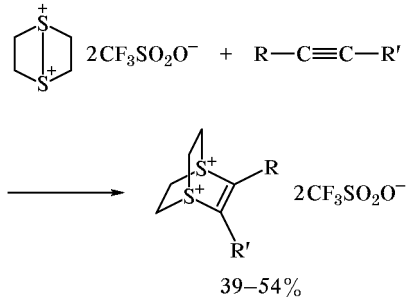
(Scheme 41). The reaction is very sensitive to steric factors. Dienes having alkyl or aryl groups at the terminal carbon atoms of the conjugated system react with acyclic disulfonium dications to form complex mixtures of oligomeric sulfonium salts. An exception is 1,3-cyclohexadiene which gives rise to the corresponding 1,4-disulfonium salts in good yields, presumably due to lower steric hindrances in the transition state. In all cases, the new C=C bond has mainly *E* configuration, where strains originating from the Coulomb and van der Waals interactions between the sulfonium groups are minimal. Increase in the fraction of the *Z* isomer in going from butadiene to isoprene and 2,3-dimethylbutadiene is likely to result from decrease in the energy difference between the *cis* and *trans* isomers upon replacement of hydrogen atoms at the double bond by larger methyl groups.

Treatment of the reaction of disulfonium dications with 1,3-dienes (using 1,3-butadiene as an example) in terms of the molecular orbital theory leads to the diagram shown in Fig. 3. Despite the fact that the orbital symmetry favors concerted process, the lack of *cis*-selectivity in the addition of acyclic dications suggests consecutive reaction mechanism.

IV.5. Reactions of Disulfonium Dications with Acetylenes

Alkynes in which the triple bond is conjugated with an aromatic or heteroaromatic ring react with strained 1,4-dithioniabicyclo[2.2.0]hexane ditriflate. The products are cage-like sulfonium salts of the bicyclooctane series [39, 47] (Scheme 42). Acetylenes of the aliphatic series, e.g., 1-hexyne, do not react with the same dications. Disulfonium dications generated from 1,5-dithiocane and 1,4-dithiepane turned out to be inactive toward alkynes.

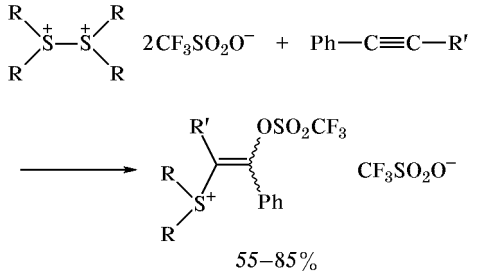
Scheme 42.



Reactions of simple acyclic disulfonium dications with acetylenes give not 1,2-disulfonium salts but products of conjugate addition of the dimethylsulfonium and trifluoromethylsulfonyloxy groups. The structure of the products and the observed regioselectivity indicate that triflate ion acts as nucleophile in the second stage of the process [47]. The different behaviors of cyclic and acyclic disulfonium dications in reactions with acetylenes may also be interpreted in favor of the consecutive electrophilic mechanism. According to the latter, carbocationic intermediate

formed in reactions of 1,4-dithioniabicyclo[2.2.0]-hexane with acetylenes is stabilized via intramolecular process. In reactions with acyclic dications, this stage is an intermolecular process which assumes competition with other nucleophilic species present in the mixture. Although trifluoromethanesulfonate ion is a much weaker nucleophile than sulfide, the formation of vinyl trifluoromethanesulfonates may be explained by steric factors (Scheme 43).

Scheme 43.



R = Me, RR = $(CH_2)_4$; R′ = H, Me, Et, Ph.

V. MODIFICATION OF ELECTROPHILES WITH SULFIDES. DIMETHYL SULFIDE–SULFUR TRIOXIDE COMPLEX

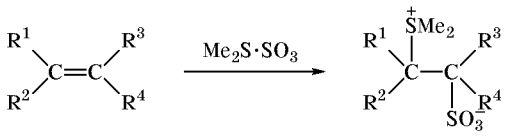
In the preceding sections we considered reactions of sulfonium salts at the sulfur atom, which involve sulfonium group transfer to nucleophile. Further on, we shall discuss reactions of electrophile complexes with sulfides, where another center of the sulfonium salt acts as electrophile. Such reagents can be regarded as sulfide-modified initial electrophile in which the electrophilic center is retained. An example is the complex of dimethyl sulfide with sulfuric anhydride $Me_2S \cdot SO_3$; it is formed by mixing sulfuric anhydride with dimethyl sulfide in methylene chloride or dichloroethane at –10 to 0°C [48]. The enthalpy of formation of $Me_2S \cdot SO_3$ from the components is 92 kJ/mol, which suggests the presence of a dative S–S bond [49].

Complexes of sulfuric anhydride with several nucleophiles are known, e.g., with dioxane, pyridine, DMF, etc. [50]; their use allows variation of the electrophilicity of sulfuric anhydride, which extends synthetic potential of the sulfonation reaction. However, the problem of controlled sulfonation remains unsolved. The dimethyl sulfide–sulfuric anhydride complex ensures selective sulfonation of various hydrocarbons, such as alkenes, acetylenes, and conjugated and unconjugated dienes.

V.1. Reactions of $Me_2S \cdot SO_3$ with Alkenes

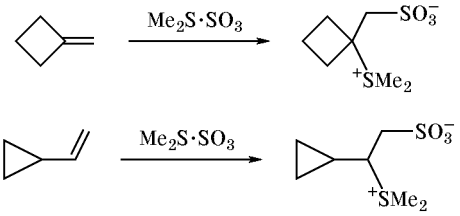
Reactions of $Me_2S \cdot SO_3$ with various olefins were studied. The set of the examined substrates was sufficiently wide to determine the regio- and stereochemistry of the addition, as well as the possibility for skeletal rearrangements to occur. In all cases, $Me_2S \cdot SO_3$ reacted with alkenes under mild conditions in the temperature range from 20 to 80°C, and the corresponding 1,2-adducts were formed in 57–80% yield [51–53] (Scheme 44).

Scheme 44.



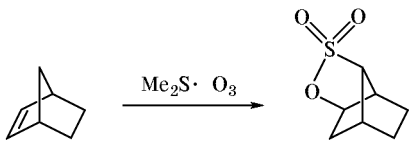
All reactions with unsymmetrically substituted olefins were regioselective: they followed the Markownikoff pattern. No polymeric products were formed in reactions with such readily polymerizable olefins as styrene, 2-methylpropene, and vinylcyclopropane. Small-ring olefins, methylenecyclobutane and vinylcyclopropane did not undergo skeletal rearrangements [53] (Scheme 45).

Scheme 45.



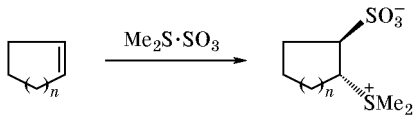
The only reaction accompanied by rearrangement was that between the $Me_2S \cdot SO_3$ complex and norbornene. It resulted in formation of γ-sultone but no addition of dimethyl sulfide occurred (Scheme 46).

Scheme 46.



The reaction of $Me_2S \cdot SO_3$ with cyclic olefins is stereoselective: *anti*-addition of the dimethyl sulfide and sulfonate moieties at the double bond yields the corresponding (*E*)-1,2-adducts [48, 54] (Scheme 47).

Scheme 47.

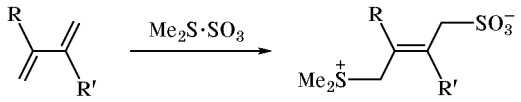


n = 1, 2.

V.2. Reactions of $Me_2S \cdot SO_3$ with Dienes

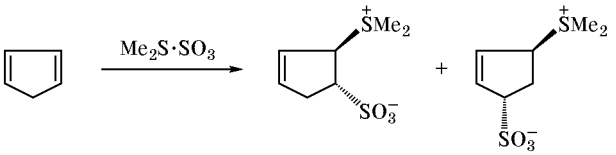
The $Me_2S \cdot SO_3$ complex readily reacts with acyclic 1,3-dienes, following the conjugate addition pattern. The corresponding (*E*)-1,4-adducts are formed in preparative yield with high regio- and stereoselectivity [55, 56] (Scheme 48).

Scheme 48.



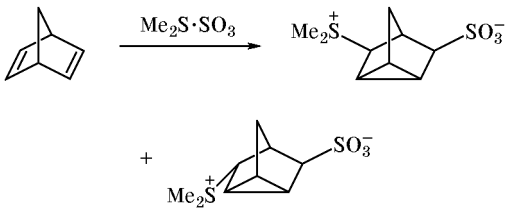
In the reaction with a cyclic conjugated diene, cyclopentadiene, an equimolar mixture of *trans*-1,2- and *trans*-1,4-adducts was obtained. The 1,2-isomer is completely converted into the 1,4-isomer on heating in boiling alcohol or dichloroethane or on prolonged storage of its solution (Scheme 49).

Scheme 49.



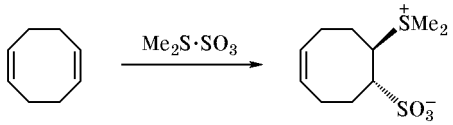
The reaction of $Me_2S \cdot SO_3$ with norbornadiene leads to formation of two nortricyclane adducts at a ratio of 12 : 1 (the diexo isomer prevailing) in an overall yield of 40% (Scheme 50).

Scheme 50.



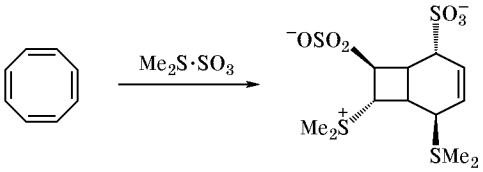
1,5-Cyclooctadiene reacts with $Me_2S \cdot SO_3$ at one of the double bond to give conjugate *trans*-1,2-adduct in 59% yield (Scheme 51); its structure was determined by X-ray analysis.

Scheme 51.



An unexpected pattern was observed in the reaction of $Me_2S \cdot SO_3$ with cyclooctatetraene. The only isolated product was bicyclic bis-adduct as a single isomer. The structure of the product was established on the basis of the X-ray diffraction data [57]. Its formation implies successive addition of two $Me_2S \cdot SO_3$ species to the substrate (Scheme 52).

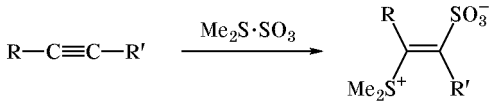
Scheme 52.



V.3. Reactions of $Me_2S \cdot SO_3$ with Acetylenes

Sulfonation of acetylenes almost was not studied. Only a few examples of sulfonation of alkynes have been reported [58]. Acetylenic hydrocarbons react with the $Me_2S \cdot SO_3$ complex in a way similar to olefins. The reaction is stereo- and regioselective, and the corresponding *E*-1,2-adducts are formed in 55–80% yield (Scheme 53). Both terminal and internal alkynes can be involved. The addition of $Me_2S \cdot SO_3$ to cyclopropylacetylene is not accompanied by rearrangement [53, 59].

Scheme 53.



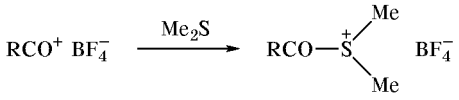
The sulfonation of unsaturated hydrocarbons with $Me_2S \cdot SO_3$ is considerably more advantageous than the corresponding reactions with other complexes [50]. The most important are the general character of the process, high yields, and high stereoselectivity.

VI. ACYL(DIMETHYL)SULFONIUM SALTS

Another kind of sulfonium salts in which the sulfur atom acts as nucleophile are acyl(dimethyl)sulfonium salts. They are formed by reaction of acylium salts

with sulfides (Scheme 54) and can be regarded as a new type of sulfonium salts with the sulfur atom linked to carbonyl group [60]. According to spectral data, a chemical reaction between dimethyl sulfide and acylium salt occurs and gives rise to a new covalent bond [60]. Acyl(dimethyl)sulfonium salts are milder acylating reagents than the initial acylium salts due to the presence of dimethyl sulfide moiety which is capable of binding to carbocations, thus preventing cationic polymerization.

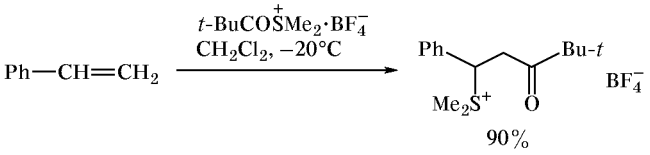
Scheme 54.



VI.1. Acylation of Alkenes

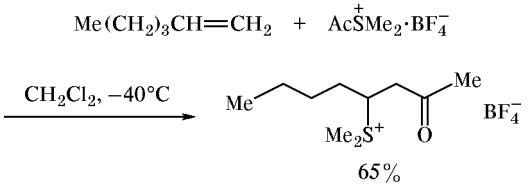
The reaction of styrene with acetyl(dimethyl)sulfonium tetrafluoroborate leads to formation of a mixture of two sulfonium salts and unsaturated ketone. Such reaction pattern is explained by the fact that the presence of an acceptor $COCH_3$ group in primary adduct **A** increases the acidity of α-protons. Therefore, there are two possible ways for stabilization of intermediate **A**: addition of nucleophile (dimethyl sulfide) or proton elimination to give unsaturated ketone. Protonation of the other styrene molecule, followed by addition of dimethyl sulfide, yields sulfonium salt as conjugate addition product of proton and dimethyl sulfide at the styrene double bond. Treatment of the reaction mixture with aqueous sodium hydrogen carbonate yields benzylideneacetone as the only acylation product which can readily be separated from sulfonium salts [60] (Scheme 55). The acylation of styrene with dimethyl(pivaloyl)sulfonium tetrafluoroborate occurs in a similar way with the difference that the only reaction product is sulfonium salt formed by conjugate addition of the acyl and dimethylsulfonium groups (Scheme 56).

Scheme 56.



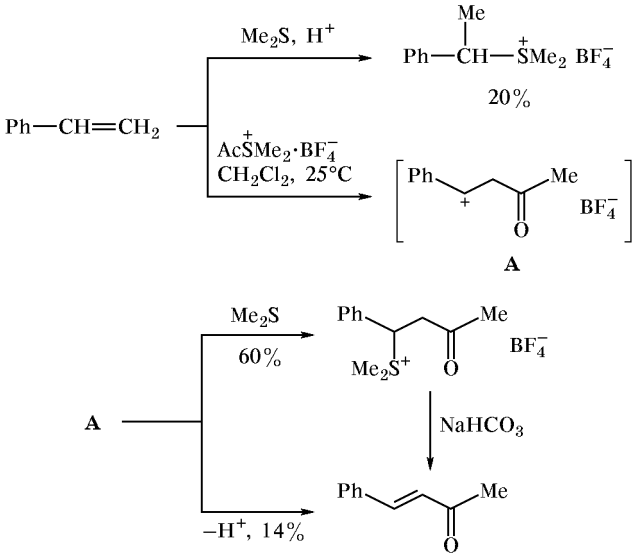
Acetyl(dimethyl)sulfonium tetrafluoroborate selectively reacts with 1-hexene, yielding product of conjugate addition of the acetyl and dimethyl sulfide groups (Scheme 57); the reaction is not accompanied by formation of protonation product.

Scheme 57.

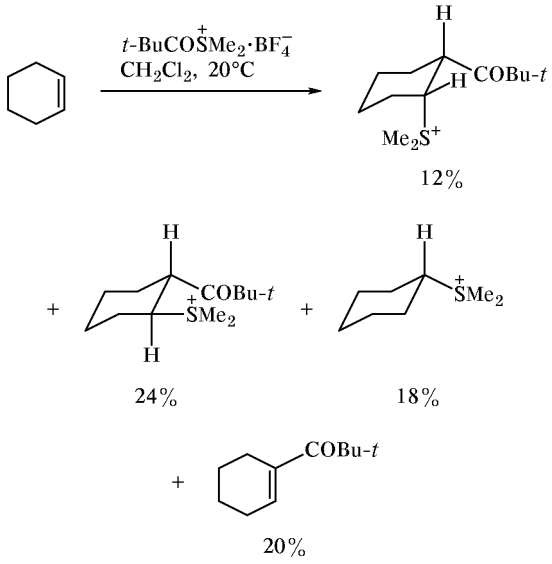


Three sulfonium salts and α,β-unsaturated ketone are formed in the acylation of cyclohexene with dimethyl(pivaloyl)sulfonium tetrafluoroborate. *tert*-

Scheme 55.



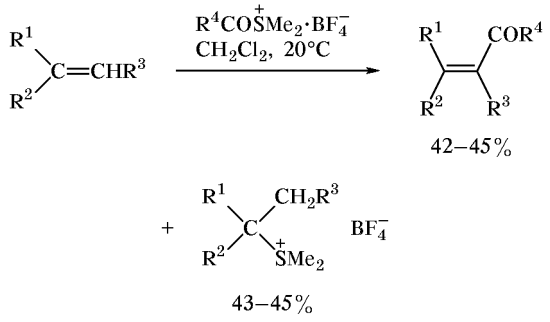
Scheme 58.



Butyl 1-cyclohexenyl ketone can readily be separated from the sulfonium salts. Two sulfonium salts are products of conjugate *cis*- and *trans*-addition of the acyl and dimethyl sulfide groups at the double bond (Scheme 58).

Alkenes capable of giving rise to tertiary carbocations react with acyl(dimethyl)sulfonium tetrafluoroborates with formation of unsaturated ketones together with the corresponding sulfonium salts as products of conjugate addition of proton and dimethyl sulfide to the alkene (Scheme 59).

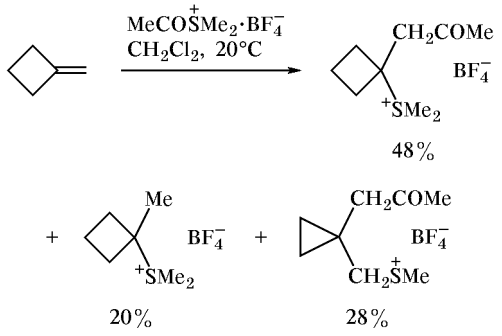
Scheme 59.



R^4 = Me, *t*-Bu.

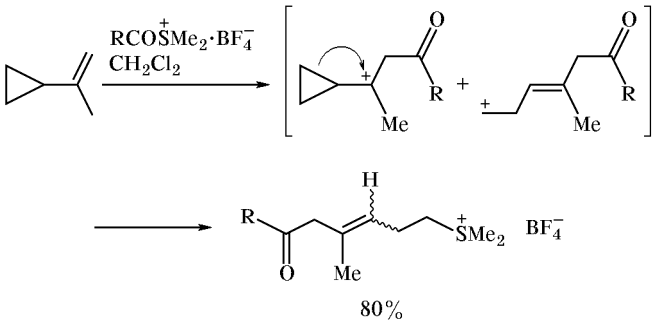
Unlike acylation of alkenes forming secondary carbocations, the reaction does not involve conjugate addition of the acyl and dimethyl sulfide groups at the double bond but proton replacement by the acyl group to give α,β-unsaturated ketones. The most probable reason is steric hindrance in the tertiary carbocation which hampers attack by dimethyl sulfide, so that the carbocation is stabilized via elimination of proton. The reaction with methylenecyclobutane leads to formation of three sulfonium salts in almost quantitative yield (Scheme 60).

Scheme 60.



The dimethyl sulfide complexes with acetyl- and pivaloyl tetrafluoroborates react with isopropenylcyclopropanol through opening of the three-membered ring. As a result, stabilization product of intermediate homoallyl cation is formed (Scheme 61).

Scheme 60.



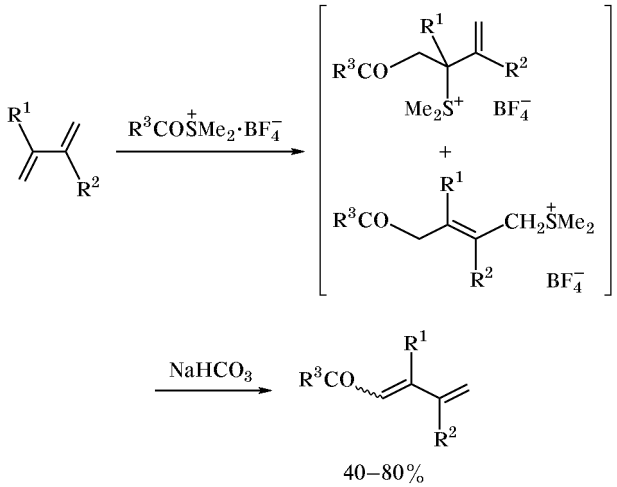
R = Me, *t*-Bu.

The occurrence of skeletal rearrangements in the reactions of acyl(dimethyl)sulfonium tetrafluoroborates with small-ring alkenes indicates a considerable electrophilicity of the reagent and carbocationic character of the intermediate.

VI.2. Acylation of Conjugated Dienes

Acyl(dimethyl)sulfonium salts are especially convenient reagents for acylation of conjugated dienes. Salts derived from dimethyl sulfide and acetyl, isovaleryl, or pivaloyl tetrafluoroborate ensure preparative acylation of 1,3-butadiene, isoprene, and dimethylbutadiene. After treatment of the reaction mixture with an aqueous solution of sodium hydrogen

Scheme 62.



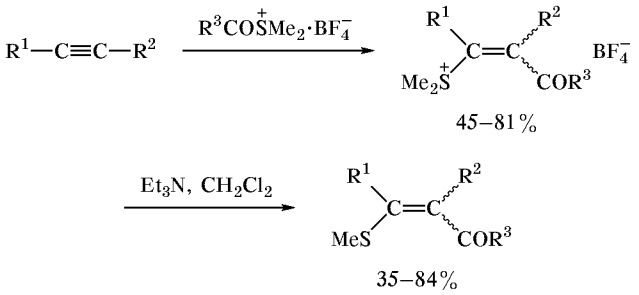
R^1, R^2 = H, Me; R^3 = Me, *t*-Bu.

carbonate, the corresponding dienones are isolated, as a rule, as mixtures of *E* and *Z* isomers (Scheme 62). The reaction is regioselective (the acyl group adds at the terminal position) but not stereoselective [61]. The products, conjugated dienones, are key starting compounds in the synthesis of various natural substances.

VI.3. Acylation of Acetylenes

Acylsulfonium salts react with arylacetylenes, following the conjugate addition pattern at the triple bond with the acyl group as electrophile and dimethyl sulfide as nucleophile. The corresponding sulfonium salts are formed in a regioselective fashion (the addition gives a more stable carbocation), while no stereoselectivity is observed: both *syn*- and *anti*-addition products are obtained (Scheme 63). Treatment of the resulting alkenylsulfonium salts with triethylamine results in their dealkylation and formation of the corresponding sulfides. This reaction may be regarded as nucleophilic substitution at the methyl group of dimethylsulfonium salt, where the sulfide is a departing group.

Scheme 63.

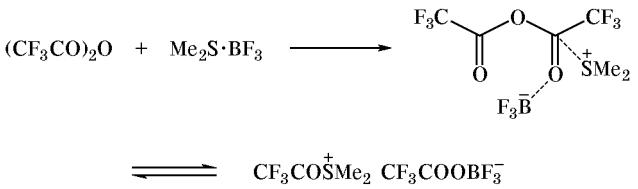


VII. DIMETHYL(TRIFLUOROACETYL)-SULFONIUM SALT

Up to now, electrophilic perfluoroacylation of unsaturated hydrocarbons with nonactivated multiple bonds have not been known, despite the fact that the acylation of unsaturated hydrocarbons was extensively studied since the beginning of XXth century. The set of available perfluoroacylating agents is very limited, and their electrophilicity is insufficient for the reaction with alkenes to occur. Acylating agents widely used in organic synthesis cannot be applied to perfluoroacylation. Perfluorinated acylium salts are unstable, and they decompose on attempted isolation [63–65]. There are no well-developed procedures for the synthesis of unsaturated ketones with a perfluoroacyl group; therefore, their use in organic synthesis as synthons for preparation of trifluoromethyl-substituted heterocycles was not studied.

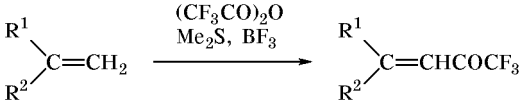
The $(CF_3CO)_2O$–BF_3–SMe_2 complex is a new reagent, which allowed development of a procedure for direct electrophilic perfluoroacylation of unsaturated compounds. The complex is obtained by addition of trifluoroacetic anhydride to a solution of dimethyl sulfide in methylene chloride, saturated with boron trifluoride. Physicochemical study of the system $(CF_3CO)_2O$–BF_3–SMe_2 showed that the chemical reaction occurring therein and activation of trifluoroacetic anhydride involve coordination of BF_3–SMe_2 at the carbonyl group [66] (Scheme 64).

Scheme 64.



The electrophilicity of the new trifluoroacetylating reagent was found to be higher than that of trifluoroacetic anhydride. The latter is capable of reacting only with electron-rich alkenes which contain a heteroatom at the double bond [67–72]. The $(CF_3CO)_2O$–BF_3–SMe_2 complex considerably extends synthetic potential in the preparation of unsaturated ketones having a perfluoroacyl group, but its electrophilicity is insufficient to react with any alkene. Here, reactive alkenes are only those which give rise to carbocations stabilized by phenyl or cyclopropyl group or those forming tertiary carbocations [73–77] (Scheme 65).

Scheme 65.



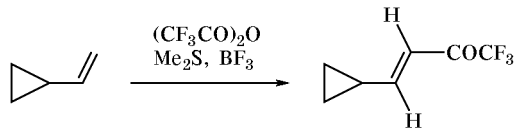
VII.1. Trifluoroacetylation of Alkenes

With the goal of studying the effect of alkene structure, the nature of intermediate carbocations, the reaction mechanism, and the scope of its application, we examined the behavior of alkenes with mono-, 1,1-di-, 1,2-di-, tri-, and tetrasubstituted double bond, as well as of cyclic alkenes with exo- and endocyclic double bond [66, 73]. Trifluoroacetylation of styrene led to formation of α,β-unsaturated ketone and sulfonium

salt, the latter being the product of conjugate addition of proton and dimethyl sulfide at the styrene double bond. The reaction pattern is similar to that observed in the acylation of styrene with acyl(dimethyl)sulfonium salts. It is important that the target trifluoroacylation products, ketones having a perfluoroacyl group, can readily be separated from by-products (sulfonium salts) by treatment of the reaction mixture with ether.

Less reactive terminal alkenes, such as 1-hexene and 1-octene, failed to react with the above complex. Trifluoroacetylation of vinylcyclopropane stereoselectively yields the corresponding *E*-isomeric ketone (Scheme 66); no opening of the three-membered ring or rearrangement into cyclobutane is observed [75].

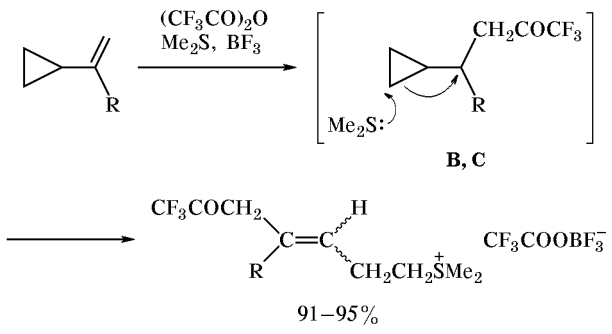
Scheme 66.



32%

Trifluoroacetylation of isopropenylcyclopropane and dicyclopropylethylene [76] follows a different pathway. The reaction quantitatively yields the corresponding sulfonium salts as stabilization products of intermediate cations formed by homoallyl opening of cyclopropylmethyl cations **B** and **C**.

Scheme 67.



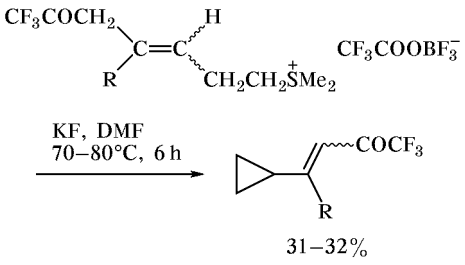
91–95%

R = Me, cyclopropyl.

The reaction is sereoselective: from isopropenylcyclopropane (R = Me), only one sulfonium salt isomer is formed. The observed stereochemistry of cyclopropane ring opening is explained by predominant conformation of cyclopropylcarbinyl cation in which the cyclopropyl group is oriented toward less bulky methyl group. Ring opening in that conformer, followed by stabilization of homoallyl cation via addition of dimethyl sulfide, gives *E*-isomeric sulfonium salt.

The presence of an electron-acceptor trifluoroacetyl group and readily departing dimethyl sulfide group in the resulting sulfonium salts makes it possible to effect intramolecular nucleophilic substitution by the action of a base, e.g., potassium fluoride in dimethylformamide [76] (Scheme 68).

Scheme 68.

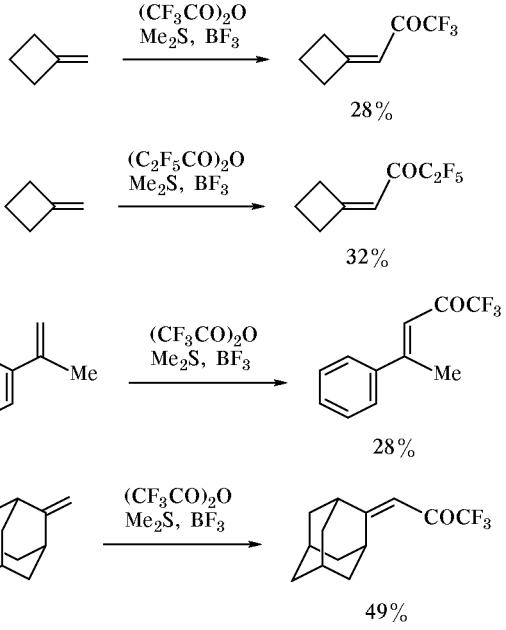


31–32%

R = Me, cyclopropyl.

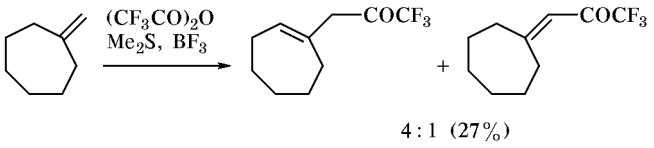
1,1-Disubstituted alkenes readily undergo perfluoroacylation at –40 to –50°C. The products are the corresponding unsaturated ketones [66, 73]. Trifluoroacetylation of methyleneadamantane gives 49% of 2-adamantylidenemethyl trifluoromethyl ketone. The yield is almost equal to the theoretically possible one, for a half of the unsaturated substrate is consumed for acylation while the other half reacts with proton to give sulfonium salts as products of conjugate addition of proton and dimethyl sulfide (Scheme 69).

Scheme 69.



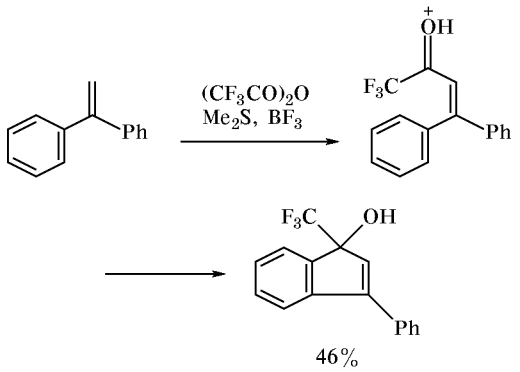
In the acylation of methylenecycloheptane, the main reaction pathway is formation of β,γ-unsaturated ketones, whereas the corresponding conjugated ketone is formed in a small amount (Scheme 70).

Scheme 70.



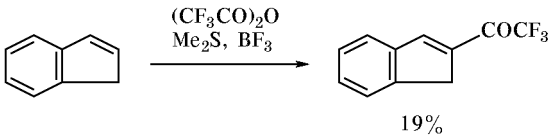
The reaction with 1,1-diphenylethylene does not stop at the stage of formation of unsaturated ketone. Spatial proximity of the carbonyl group and aromatic ring favors intramolecular alkylation to give trifluoromethylindenol (Scheme 71).

Scheme 71.



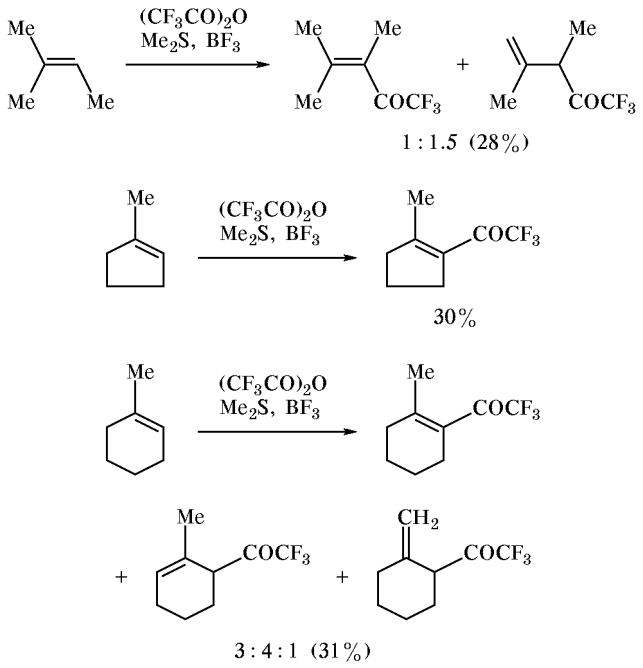
Trifluoroacetylation of indene is regioselective, and it gives a cation in which the positively charged center is conjugated with the aromatic ring. However, the yield of the target unsaturated ketone is poor because of strong polymerization. No reaction occurred with less active 1,2-disubstituted alkenes, such as cyclohexene and cyclopentene (Scheme 72).

Scheme 72.



Trisubstituted alkenes are less reactive than their 1,1-disubstituted analogs. The trifluoroacetylation occurs at –20 to 0°C, in spite of the possibility for formation of stable tertiary carbocations. Presumably, the double bond is sterically shielded by alkyl groups. Trisubstituted alkenes show a stronger tendency to form α,β-unsaturated ketones (Scheme 73). In the trifluoroacylation of some alkenes, elimination of proton is likely to involve a six-membered transition state.

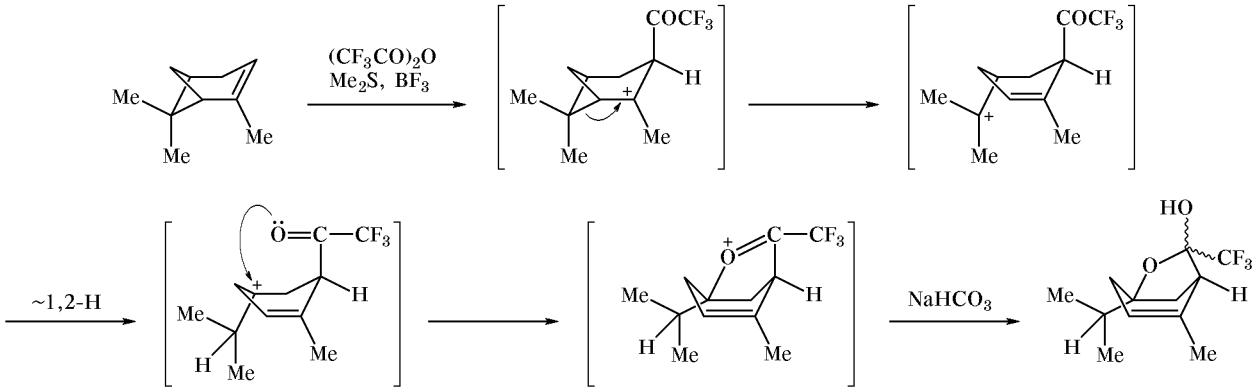
Scheme 73.



A considerable difference in the results of trifluoroacylation of 1-methylcyclopentene and 1-methylcyclohexene should be emphasized. In the first case, almost pure α,β-unsaturated ketone is formed, while from 1-methylcyclohexene a mixture of unsaturated ketones is obtained. Presumably, the corresponding intermediates have different geometries. The conformation of cation derived from 1-methylcyclohexene favors formation of a six-membered transition state for elimination of proton from the γ-position with respect to the carbonyl group. Proton elimination from the methyl group (provided that the trifluoroacetyl group is equatorial) leads to β,γ-unsaturated ketone, while elimination from the methylene group in position *3* (axial trifluoroacetyl group) leads to another β,γ-unsaturated ketone with endocyclic double bond [73]. 1-Methylcyclopentene gives rise to a more rigid cation conformation, in which the distance between the carbonyl oxygen atom and proton in the γ-position is considerably longer. Therefore, the probability for elimination through a six-membered transition state is much lower, and the corresponding β,γ-unsaturated ketone almost is not formed.

The trifluoroacetylation of α-pinene follows an unusual pattern [77]. The major product is CF_3-containing bicycic semiacetal with the menthane rather than

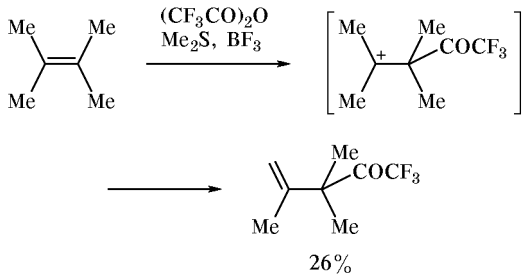
Scheme 74.



pinane skeleton. It is formed as a result of electrophilic rearrangement of the primary product of attack by CF_3CO species. The direction of rearrangement in the acylation of pinene is determined by the possibility for formation of five-membered carboxonium salt (Scheme 74). The stereochemistry of this process is very interesting. Despite a series of consecutive carbocation transformations, the reaction is enantioselective, and the product is optically active ($[\alpha]_D^{20} = -56°C$).

Trifluoroacetylation of tetramethylethylene gives β,γ-unsaturated ketone and sulfonium salt as by-product (via addition of proton and dimethyl sulfide; Scheme 75). Obviously, the addition of dimethyl sulfide to intermediate carbocation is hindered for steric reasons.

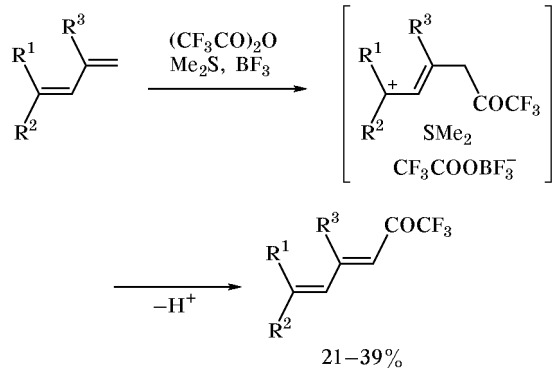
Scheme 75.



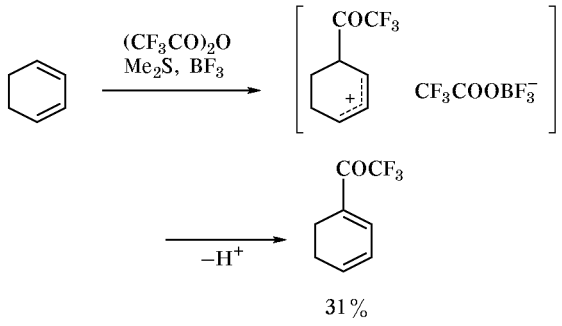
VII.2. Trifluoroacetylation of Dienes

Conjugated dienes are capable of reacting with the system $(CF_3CO)_2O$–BF_3–Me_2S to afford the corresponding triconjugated dienones [78]. Substituted dienes react regioselectively at the terminal double bond. The process is also stereoselective: the respective (*E*)-dienones are formed. The stereochemistry of the reaction is likely to be determined by steric factor: the trifluoroacetyl group occupies the *trans*-position with respect to the bulkiest substituent (Scheme 76).

Scheme 76.



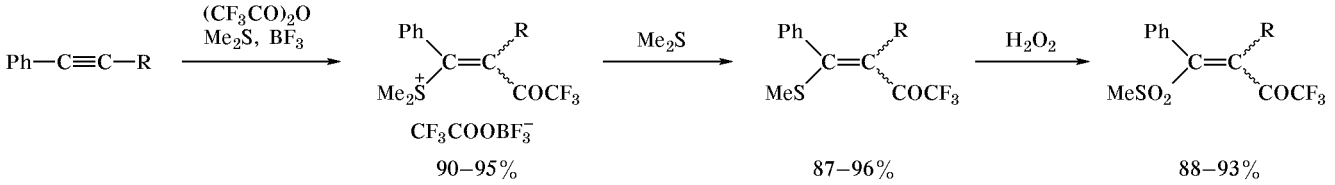
$R^1 = R^2 = R^3 = H$; $R^1 = Ph$, $R^2 = R^3 = H$; $R^1 = R^2 = R^3 = Me$.



VII.3. Trifluoroacetylation of Acetylenes

The reaction occurs only with sufficiently active acetylenes having a phenyl substituent [79]. Less reactive 1-decyne and 1-hexyne remain unchanged. The reaction yields the corresponding sulfonium salts via conjugate addition of trifluoroacetyl and dimethyl sulfide groups across the triple bond. In all the examined cases, (*Z*)-alkenylsulfonium salts were mainly formed (Scheme 77). The salts can readily be

Scheme 77.



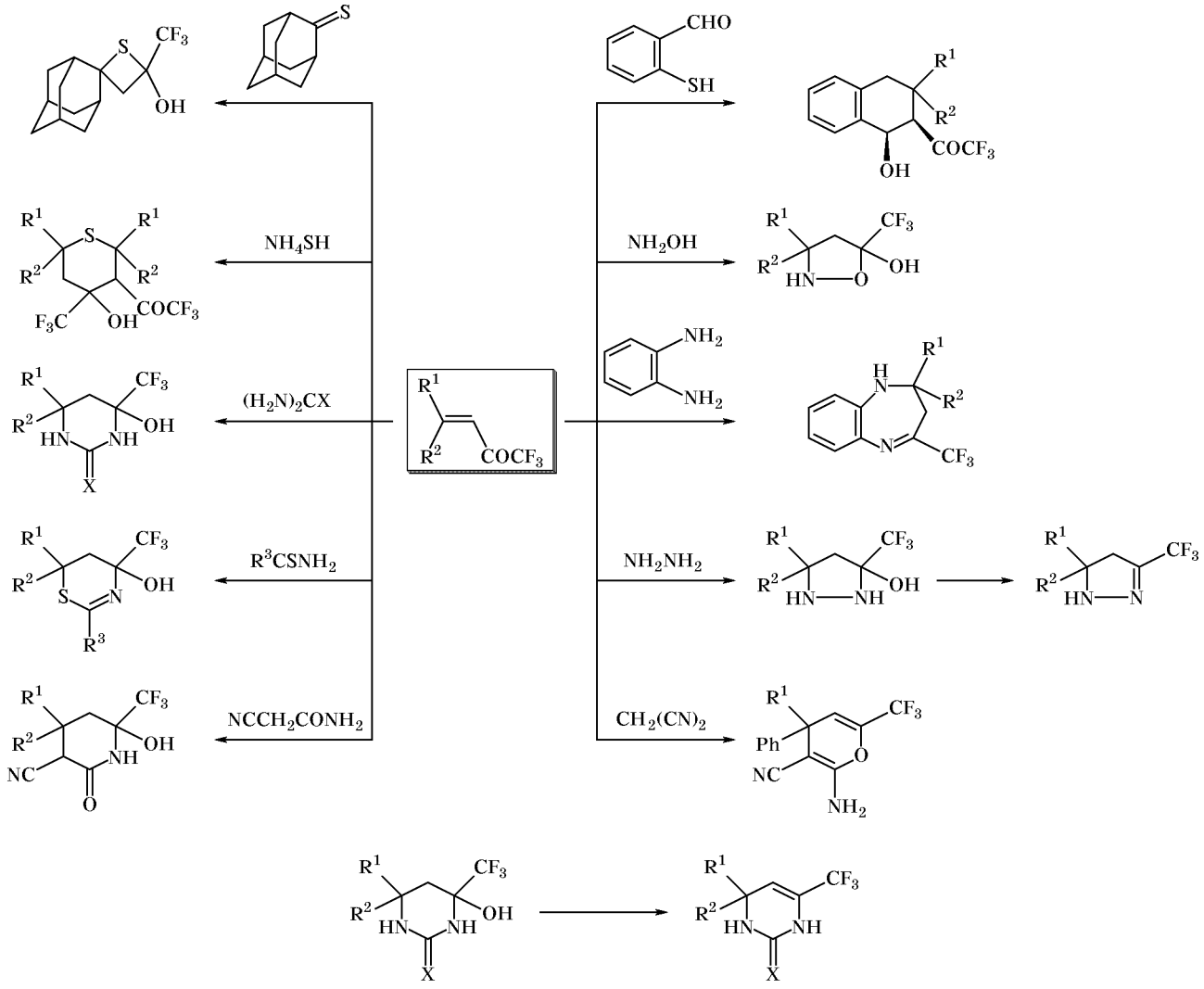
R = H, Me, Et.

converted into β-trifluoroacetylvinyl sulfides in almost quantitative yield by treatment with dimethyl sulfide under mild conditions. The subsequent oxidation with hydrogen peroxide gives the respective sulfones in very high yield. These compounds possess two electron-acceptor groups at the double bond and are interesting as potential multipurpose synthons.

VII.4. Synthesis of Trifluoromethyl-Substituted Heterocycles

Reactions of α,β-unsaturated ketones with difunctional nucleophiles constitute a classical method of synthesis of heterocycic compounds. However, reactions of CF_3-containing enones, specifically of those

Scheme 78.



having no alkoxy or amino group, almost were not studied up to now. α,β-Unsaturated ketones having a trifluoromethyl group are very convenient "building blocks" for the synthesis of various CF_3-containing derivatives, including four-, five-, six-, and seven-membered heterocycles [80–92] (Scheme 78). Trifluoromethyl enones are more reactive than their nonfluorinated analogs. Therefore, some reactions of the former take different pathways or such reactions do not occur with nonfluorinated enones. Fluorinated enones give products with a stable semiacetal, semithioacetal, or semiaminal fragment due to electron-acceptor effect of the trifluoromethyl group. Their reactions with a number of nucleophiles are stereoselective, and the trifluoromethyl group in the products (due to its high conformational energy) occupies equatorial or pseudoequatorial position [91, 92].

VIII. INTRAMOLECULAR ANALOGS OF ACYLSULFONIUM SALTS

Intramolecular analogs of acylsulfonium salts are Lewis acid (BF_3) complexes with alkylthio-substituted carboxylic acid fluorides. The complexes $BF_3 \cdot EtSCH_2CH_2COF$ and $BF_3 \cdot EtSCH_2COF$ are formed by saturation with boron trifluoride of a solution of the corresponding acyl fluoride in methylene chloride at –60°C (Scheme 79). The complex $EtSCH_2COF \cdot BF_3$ is stable below –30°C, and $EtSCH_2CH_2COF \cdot BF_3$ is stable below 0°C. Study of their structure by IR and NMR spectroscopy showed that the complexes exist as intra- or/and intermolecular sulfonium salts.

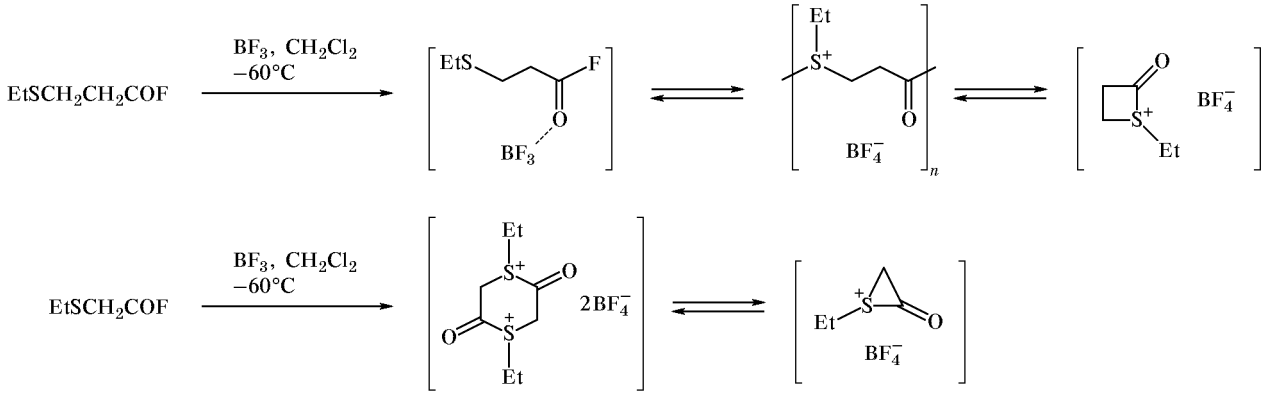
VIII.1. Reactions of $EtSCH_2CH_2COF \cdot BF_3$ and $EtSCH_2COF \cdot BF_3$ with Alkenes and 1,3-Dienes

Reactions of $EtSCH_2CH_2COF \cdot BF_3$ with various alkenes lead to formation of six-membered cyclic sulfonium salts, products of conjugate addition of the acyl and sulfide fragment to the double bond [93, 94] (Scheme 80). Bases are capable of abstracting proton from the α-position with respect to the carbonyl group of six-membered sulfonium salt. The reaction is accompanied by ring opening at the C–S bond to afford α,β-unsaturated ketones having an ethylthio group. Depending on the initial alkene structure, two types of ring opening products can be obtained. The first of these (*A*) arises from addition of the ethylthio and acryloyl groups at the double bond, and the second (*B*) is formed by replacement of proton at the double bond by 3-ethylthiopropionyl group.

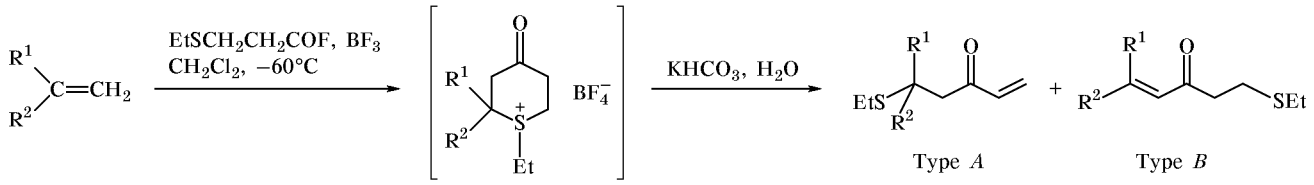
Analysis of the available data allows us to trace the relation between the structure of initial alkene and the way of opening of intermediate sulfonium salt, i.e., the ratio of type *A* and *B* ketones. The pathway of ring opening can be determined by steric factors, as well as by the possibility for conjugation between the new double bond and aromatic ring. For example, in the reaction of $EtSCH_2CH_2COF \cdot BF_3$ with styrene, the only product has structure like *B*. The regioselectivity of this reaction may be explained in terms of conformation of intermediate sulfonium salt in which the phenyl ring occupies equatorial position. Here, the phenyl ring and carbonyl group are antiperiplanar with respect to each other, so that *anti*-elimination of the sulfonium group leads to *trans*-arrangement of the carbonyl group and phenyl ring in the product. Introduction of a substituent, e.g., methyl or phenyl group, creates steric hindrance at position *3*, and the fraction of type *A* product increases (as in the case of α-methylstyrene and 1,1-diphenylethylene; Scheme 81).

Reactions of $EtSCH_2CH_2COF \cdot BF_3$ with *trans*-1-methyl-2-phenylethene and *trans*-1,2-diphenylethene are chemoselective and stereospecific; they give products of conjugate addition of the acryloyl and ethylthio groups at the double bond. The resulting ketone is a single diastereoisomer (Scheme 82).

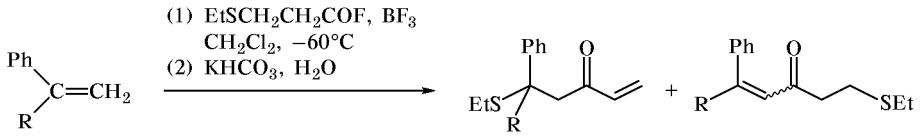
Scheme 79.



Scheme 80.

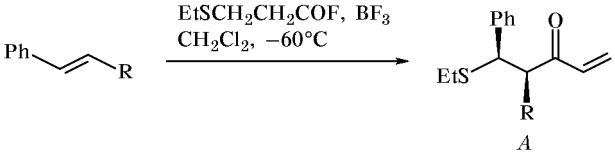


Scheme 81.



R = H	(*E*)	34%
R = Me	*A*:*B* (*E*):(*Z*) 2:1:1	68%
R = Ph	*A*:*B* 2:1	87%

Scheme 82.



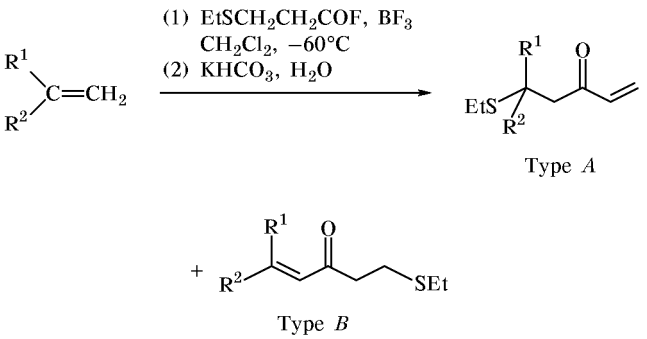
R = Ph (yield 30%); R = Me (67%).

The product ratio in reactions with cyclic hydrocarbons having an exocyclic double bond is determined mainly by steric factor. The reaction of 2-methyleneadamantane with $EtSCH_2CH_2COF \cdot BF_3$ gives the corresponding 2,2-disubstituted adamantane (type *A*). In the reaction with methylenecyclobutane, protons on C^3 in the intermediate sulfonium salt are not shielded so strongly as in the intermediate derived from methyleneadamantane; therefore, both possible products (*A* and *B*) are obtained (Scheme 83).

Reactions of $EtSCH_2CH_2COF \cdot BF_3$ with cyclic alkenes were studied using cyclopentene and cyclohexene as examples. The reaction with cyclopentene afforded a single product, type *B* ketone, while from cyclohexene a mixture of products was obtained. Presumably, the different reaction patterns are explained by conformational features of intermediate sulfonium salts (Scheme 84).

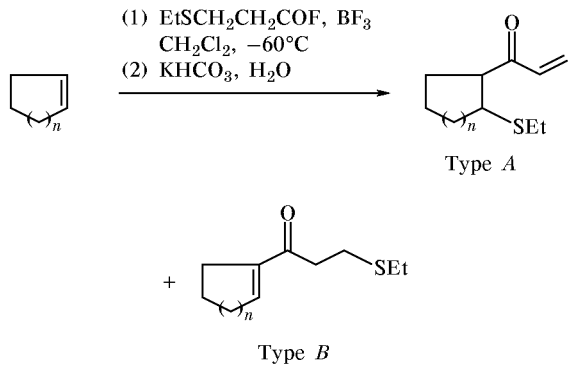
The complex $EtSCH_2COF \cdot BF_3$ reacts with alkenes through formation of five-membered cyclic sulfonium

Scheme 83.



R^1R^2C = adamantan-2-ylidene (*A*); $R^1R^2 = (CH_2)_3$, *A*:*B* = 1:1, yield 54%.

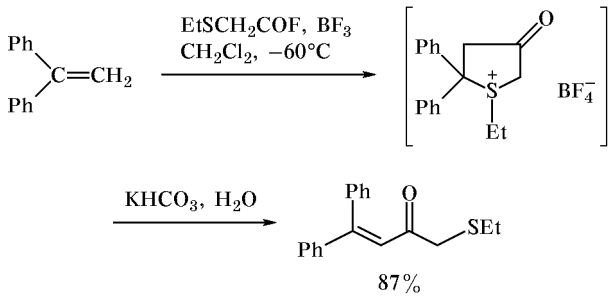
Scheme 84.



n = 1 (*B*, 62%); *n* = 2 (*A*:*B* = 1:1, 23%).

salts. Obviously, ring opening in such salts can occur in only one mode with formation of type *B* products. The reaction of 1,1-diphenylethene with $EtSCH_2COF \cdot BF_3$ yields the corresponding α,β-unsaturated ketone without isolation of intermediate sulfonium salt [94] (Scheme 85).

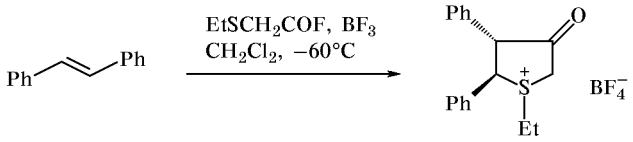
Scheme 85.



87%

Five-membered cyclic sulfonium salt was isolated in the reaction of $EtSCH_2COF \cdot BF_3$ with *trans*-1,2-diphenylethene. The phenyl groups in the product occupy pseudoequatorial positions (Scheme 86).

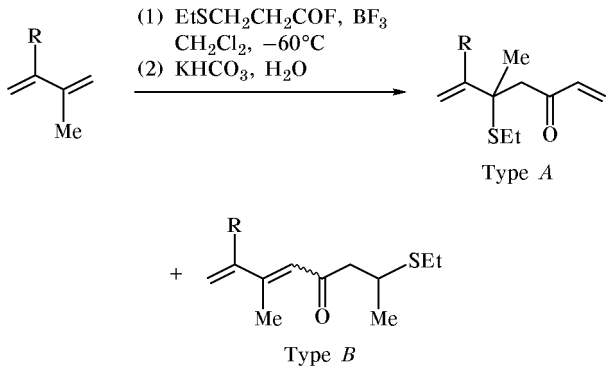
Scheme 86.



59%

1,3-Dienes react with $EtSCH_2CH_2COF \cdot BF_3$ under mild conditions, usually yielding mixtures of type *A* and *B* products (Scheme 87). No 1,4-adducts were isolated [94].

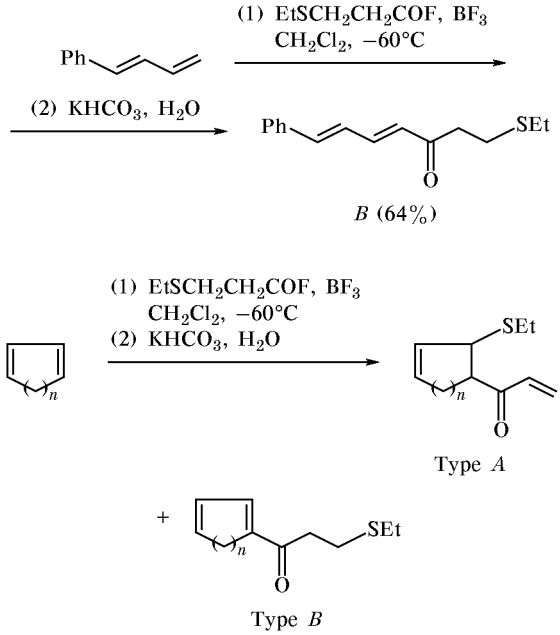
Scheme 87.



R = H, *A*:*B* = 7:1, yield 47%; R = Me, *A*:*B* (*E*:*Z*) = 6:1:1, yield 55%.

The only product, type *B* ketone possessing an extended conjugated bond system, was isolated from the reaction of $EtSCH_2CH_2COF \cdot BF_3$ with (*E*)-1-phenyl-1,3-butadiene. 1,3-Cyclohexadiene and 1,3-cyclooctadiene gave rise to mixtures of two products (Scheme 88).

Scheme 88.

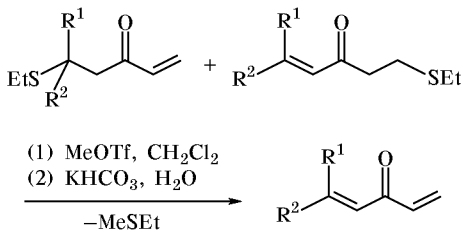


n = 2, *A*:*B* = 1:1, yield 40%; *n* = 4, *A*:*B* = 5:1, yield 55%.

VIII.2. Synthesis of Polyconjugated Unsaturated Ketones

Elimination of the ethylthio group from ketones gives polyconjugated ketones. The transformation was effected by successive S-methylation and elimination of methyl ethyl sulfide by the action of a base. These reactions are characterized by high yields and almost complete absence of by-products. The optimal reagent is methyl trifluoromethanesulfonate which ensures

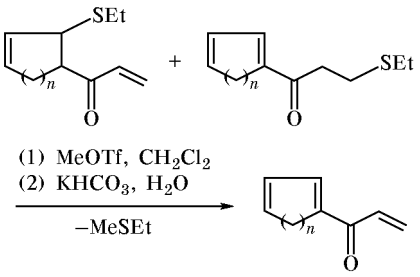
Scheme 89.



R^1R^2C = adamantan-2-ylidene (*A*, 98%); R^1 = Ph, R^2 = H (*B*, 73%); R^1 = R^2 = Ph (*A*, *B*, 91%).

the process to be complete in 1–2 h. Even mixtures of type *A* and *B* ketones give rise to the only reaction product [94] (Schemes 89, 90).

Scheme 90.

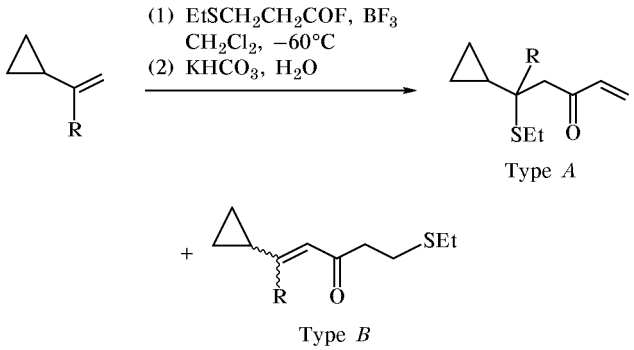


n = 2, *A*, B, 88%; *n* = 4, *A*, B, 76%.

VIII.3. Reactions with Cyclopropyl-Substituted Alkenes

Reactions of cyclopropyl-containing alkenes with electrophiles are usually accompanied by isomerization and polymerization [95–97]. The presence in the complexes of ethylthio group, which is capable of forming covalent bonds in carbocation reactions, suppresses the above side processes. In the acylation with $EtSCH_2CH_2COF \cdot BF_3$ and $EtSCH_2COF \cdot BF_3$ of various hydrocarbons of the vinylcyclopropane series, such as vinylcyclopropane, 1-cyclopropyl-1-methylethene, 1,1-dicyclopropylethene, and 1-cyclopropyl-1-phenylethene, opening of the three-membered ring was observed only in the case of $EtSCH_2CH_2COF \cdot BF_3$ and 1-cyclopropyl-1-phenylethylene; in all other cases, neither rearrangement nor ring opening products were isolated [98] (Scheme 91).

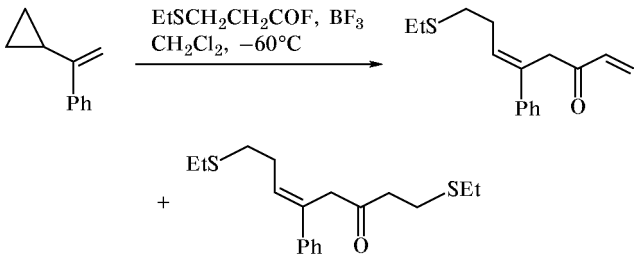
Scheme 91.



R = H, *A*:*B* (*E*) = 1.2:1, 53%; R = Me, *A*:*B* (*E*:*Z*) = 5:1:1, 45%.

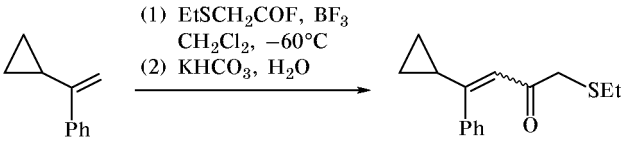
The reaction of $EtSCH_2CH_2COF \cdot BF_3$ with 1-cyclopropyl-1-phenylethene afforded two ketones, both these being products of cyclopropane ring opening. Each ketone had *E* configuration of the double bond at C^5 (Scheme 92).

Scheme 92.



Cyclopropyl-substituted alkenes react with the $EtSCH_2COF \cdot BF_3$ complex to give α,β-unsaturated ketones in high yields (Scheme 93). The reactions are not accompanied by opening or rearrangement of the three-membered ring.

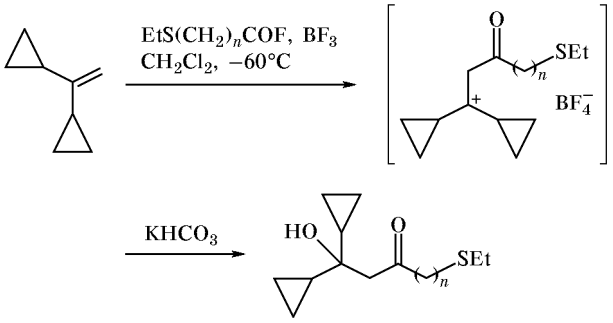
Scheme 93.



R = H, *E*, 77%; R = Me, *E*:*Z* = 1.2:1, 82%; R = Ph, *E*:*Z* = 1:1, 87%.

Unusual products were obtained by reactions of 1,1-dicyclopropylethene with the boron trifluoride–ethylthio-substituted carboxylic acid fluoride complexes. These reactions gave exclusively β-hydroxyketones (Scheme 94). Intermediate tertiary dicyclopropylcarbenium ion is fairly stable and also sterically hindered, so that its lifetime is sufficiently long to react with potassium hydrogen carbonate upon subsequent treatment of the reaction mixture.

Scheme 94.

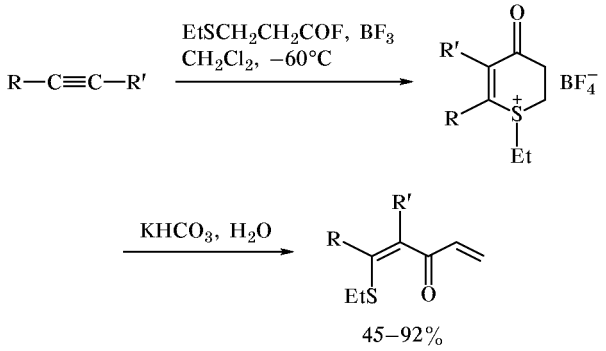


n = 1, yield 52%; *n* = 2, 34%.

VIII.4. Reactions with Acetylenes

The complex $EtSCH_2CH_2COF \cdot BF_3$ reacts with acetylenes, following the conjugate addition pattern. The acyl and sulfide moieties of the complex add to the triple bond, yielding cyclic sulfonium salts. The latter undergo ring cleavage by the action of $KHCO_3$ to give the corresponding (*Z*)-1-ethylthio-1,4-pentadien-3-ones [99, 100] (Scheme 95).

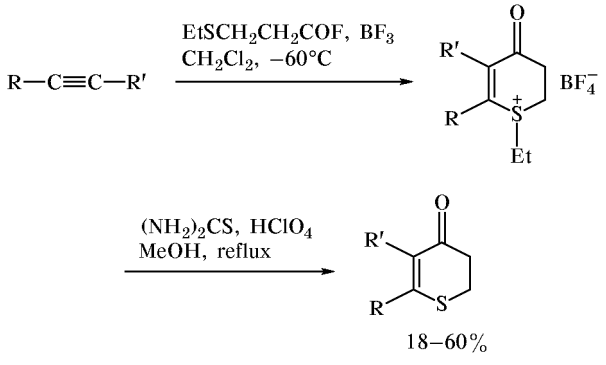
Scheme 95.



It was shown that opening of sulfonium salts derived from acetylenes, as well as of those obtained from alkenes, is a reversible process. Treatment with perchloric acid of the ketone prepared from 1-phenylbutyne gives in high yield six-membered sulfonium perchlorate, and the latter reacts with an aqueous solution of $KHCO_3$ to afford the initial ketone in quanttitative yield.

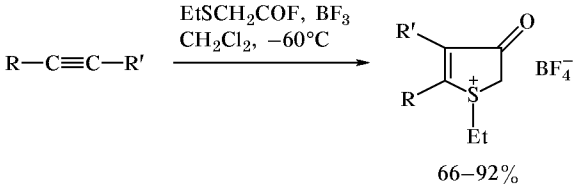
Treatment of cyclic sulfonium salts with thiourea in the presence of a catalytic amount of perchloric acid results in selective deethylation with formation of 2,3-dihydro-4*H*-thiopyran-4-ones [99] (Scheme 96).

Scheme 96.



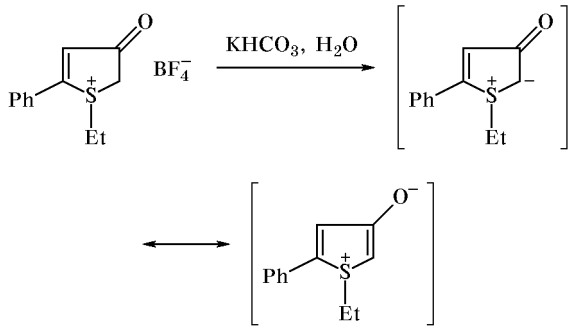
The complex of (ethylthio)acetyl fluoride with boron trifluoride reacts with acetylenes in a way similar to the $EtSCH_2CH_2COF \cdot BF_3$ complex. The reaction occurs as conjugate addition of the acyl and sulfide fragments to the triple bond, and the resulting five-membered cyclic sulfonium salts are fairly stable substances [101] (Scheme 97).

Scheme 97.



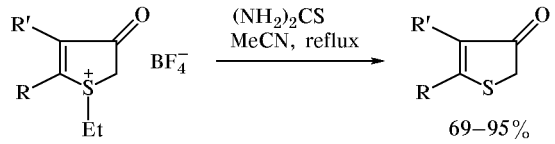
Reactions of $EtSCH_2COF \cdot BF_3$ with various terminal and internal alkynes having both aryl and alkyl substituents, as well as with with cyclooctyne and phenylthioacetylene, were studied. In all these cases, five-membered cyclic sulfonium tetrafluoroborates were formed. The reactions are regioselective, the contribution of side processes is small, and the yields are good. Some reactions of the resulting sulfonium salts were examined. Treatment of a solution of sulfonium salt in methylene chloride with an aqueous solution of potassium hydrogen carbonate changes the color of the organic phase which turns bright orange. Presumably, an ylide is thus formed (Scheme 98). Attempts to isolate it were unsuccessful, though such ylides should be fairly stable due to effect of the carbonyl group [102]. Treatment of the salt with sodium hydride in DMSO (with a view to isolate the ylide) resulted in complete tarring of the reaction mixture.

Scheme 98.



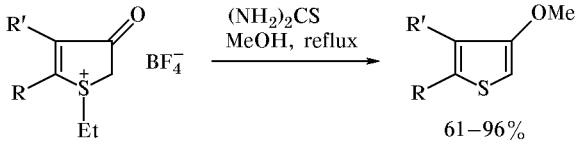
The reaction with thiourea was used to convert five-membered cyclic sulfonium salts into the corresponding heterocycles. When the reaction was carried out in methanol, 3-methoxythiophene was isolated instead of the expected thiophen-3-one. The latter was obtained by heating with thiourea in boiling acetonitrile (Scheme 99).

Scheme 99.



Later on, it was found that reactions with thiourea in acetonitrile and methanol are general: in the first case, thiophen-3(2*H*)-one derivatives are formed, and in the second, 3-methoxythiophenes (Scheme 100).

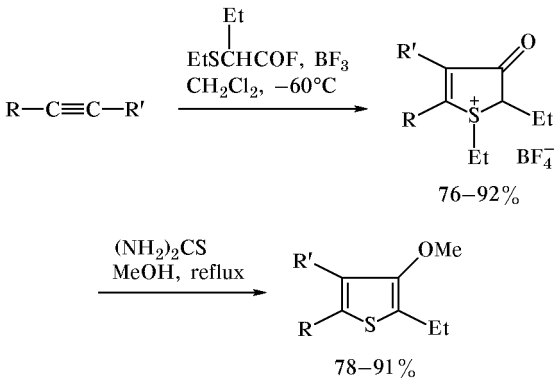
Scheme 100.



3-Hydroxythiophenes are usually synthesized by various versions of the Fiesselmann procedure, which is based on the condensation of ethyl mercaptoacetate with propynoic acid derivatives. This reaction gives 3-hydroxythiophenes having electron-acceptor substituents [103, 104]. There are almost no published data on the synthesis of thiophene ring from the C–C–S and C–C fragments [105, 106]; Here, the source of the C–C–S moiety is (ethylthio)acetyl fluoride, and the C–C fragment is taken from acetylene.

Thus the reaction of the $EtSCH_2COF \cdot BF_3$ complex with acetylenes underlies a general procedure for the synthesis of various 4- and 5-substituted tiophen-3(2*H*)-ones and 3-methoxythiophenes. Both acylation and dealkylation of sulfonium salts with thiourea occur under very mild conditions. The proposed procedure can be applied to preparation of a wide series of thiophene derivatives having substituents in various positions: the substituents in positions *4* and *5* are controlled by the nature of initial acetylene. The 2-position in 3-methoxythiophenes is additionally activated by the methoxy group, and it can readily be functionalized by the action of various electrophiles. It was also shown that the substituent in position *2* of 3-methoxythiophenes can be introduced by using appropriately substituted (ethylthio)acetyl fluoride in reactions with acetylenes (Scheme 101).

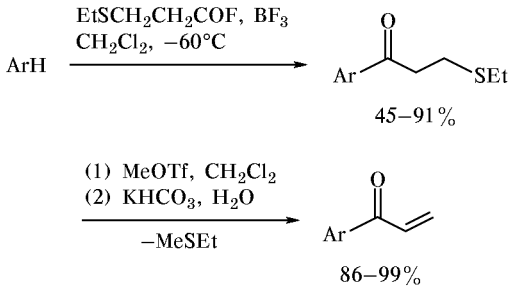
Scheme 101.



VIII.5. Reactions of $EtSCH_2CH_2COF \cdot BF_3$ with Aromatic Compounds

Reactions of $EtSCH_2CH_2COF \cdot BF_3$ with a wide series of aromatic and heteroaromatic compounds were studied. These reactions occur under mild conditions and give the corresponding 3-ethylthio-1-aryl-(hetaryl)propan-1-ones [107, 108] (Scheme 102). Attempts to effect acylation of weakly reactive aromatic compounds, such as toluene, xylene, mesitylene, and anthracene, were unsuccessful. No reaction was observed below 0°C, while raising the temperature resulted in fast decomposition of $EtSCH_2CH_2COF \cdot BF_3$ into the initial acyl fluoride and boron trifluoride. It was also impossible to involve in the reaction with $EtSCH_2CH_2COF \cdot BF_3$ nitrogen-containing aromatic heterocycles (such as pyrrole, *N*-methylpyrrole, and *N*-methylindole) and aromatic amines (*N*,*N*-dimethylaniline). Presumably, decomposition of the complex $EtSCH_2CH_2COF \cdot BF_3$ occurs even at a temperature below –60°C, and boron trifluoride coordinates at the nitrogen atom of the sulbstrate.

Scheme 102.



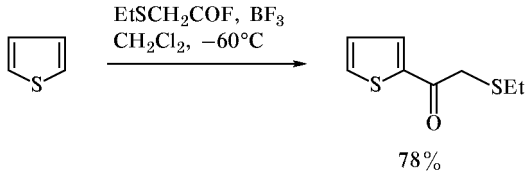
Vinyl ketones are widely used in organic synthesis as Michael acceptors, dienophiles, dienes, and monomers [109–111]. However, no procedure was reported for direct acylation of aromatic compounds with acrylic acid derivatives.

The synthesis of aryl vinyl ketones from 3-ethylthio-1-arylpropan-1-ones was studied. For this purpose, the same procedure was applied as in the synthesis of various polyconjugated enones, namely

S-methylation and subsequent elimination of methyl ethyl sulfide by the action of a base. As previously, the best results were obtained with methyl trifluoromethanesulfonate as methylating agent. The procedure requires the simplest equipment, the resulting vinyl ketones are sufficiently pure, and their yields are almost quantitative [107]. The reaction provides one more example of the application of $EtSCH_2CH_2COF \cdot BF_3$ as synthetic equivalent of acryloyl cation.

The complex $EtSCH_2COF \cdot BF_3$ also reacts with aromatic compounds. For instance, its reaction with thiophene afforded 2-ethylthio-1-(2-thienyl)ethan-1-one (Scheme 103).

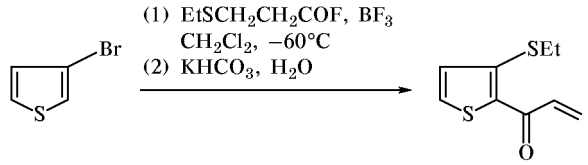
Scheme 103.



VIII.6. Reactions of $EtSCH_2CH_2COF \cdot BF_3$ with Halogen-Containing Aromatic Compounds

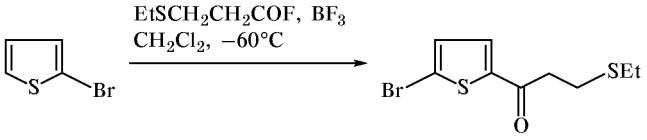
Some halogen-containing aromatic compounds react with $EtSCH_2CH_2COF \cdot BF_3$ in an unusual way [112]. For example, the reaction of 3-bromothiophene with $EtSCH_2CH_2COF \cdot BF_3$, followed by treatment of the reaction mixture with an aqueous solution of $KHCO_3$, gave 2-acryloyl-3-ethylthiothiophene as the only product (Scheme 104).

Scheme 104.



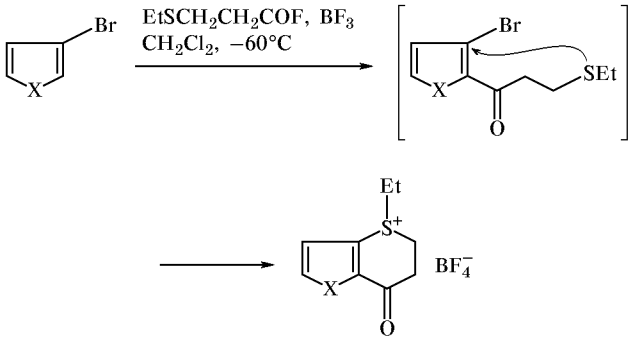
On the other hand, the reaction with 2-bromothiophene resulted in formation of "usual" product, 1-(5-bromothienyl)-3-ethylthiopropan-1-one (Scheme 105).

Scheme 105.



Further study of the reaction with 3-bromothiophene showed that the primary product is six-membered cyclic sulfonium salt (Scheme 106).

Scheme 106.

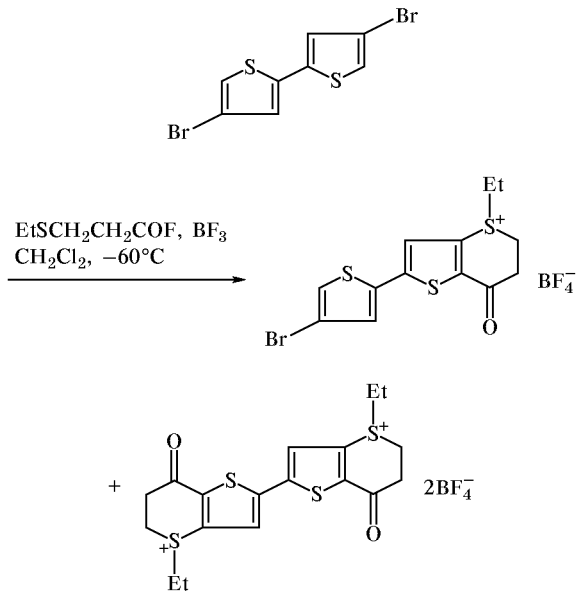


X = S, 33%; X = O, 19%.

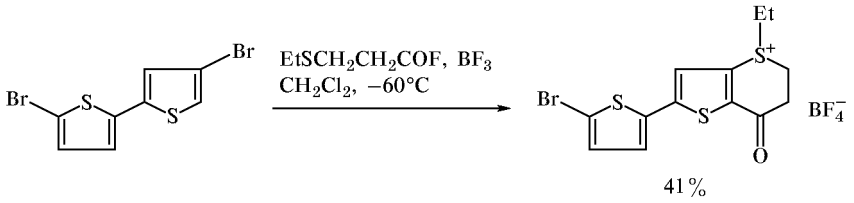
The scheme of formation of such sulfonium salt may be represented as follows: in the first stage, acylation of 3-bromothiophene at the 2-position occurs. In the second stage, the bromine atom is replaced by sulfonium group via intramolecular nucleophilic reaction. Taking into account that no open-chain acylation product, 1-(3-bromo-2-thienyl)-3-ethylthiopropan-1-one, was isolated, we can conclude that the second stage (intramolecular ring closure) is fast due to additional activation of the bromine atom by the neighboring carbonyl group. These transformations constitute previously unknown type of aromatic substitution reactions, tandem electrophilic and nucleophilic substitution.

3-Bromofuran and 4-bromo-1,2-dimethoxybenzene react in a similar way, yielding the corresponding sulfonium salts. *m*-Bromoanisole failed to react with

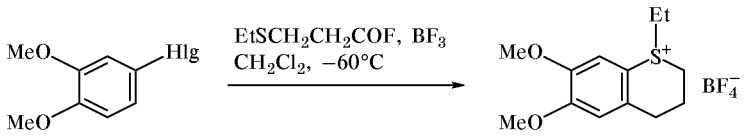
Scheme 107.



Scheme 108.

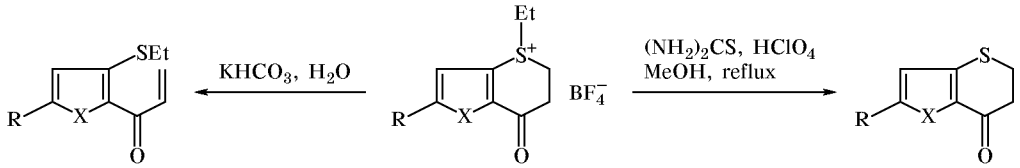


Scheme 109.

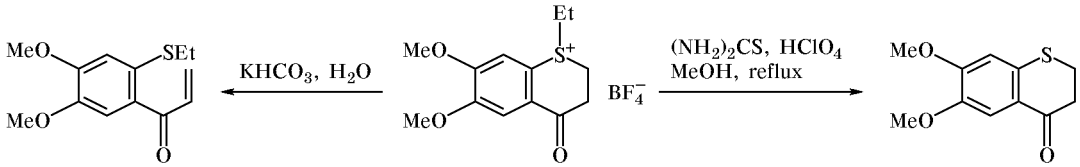


Hlg = Cl (yield 12%), Br (38%), I (45%).

Scheme 110.



83%	R = H, X = S	89%
95%	R = H, X = O	42%
86%	R = 4-bromo-2-thienyl, X = S	48%
95%	R = 5-bromo-2-thienyl, X = S	70%



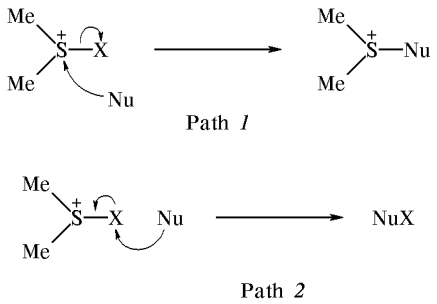
$EtSCH_2CH_2COF \cdot BF_3$, while from 4,4′-dibromo-2,2′-bithiophene a mixture of mono- and diacylation products was obtained at a ratio of 3:1 in an overall yield of 64% (Scheme 107). The reaction of 4,5′-dibromo-2,2′-bithiophene with $EtSCH_2CH_2COF \cdot BF_3$ gave 41% of the corresponding sulfonium tetrafluoroborate (Scheme 108). Reactions with 4-halo-1,2-dimethoxybenzenes with $EtSCH_2CH_2COF \cdot BF_3$ were studied with the goal of elucidating the effect of the halogen nature (Scheme 109). The yields of the sulfonium salts turned out to decrease in the series I > Br > Cl.

Cyclic sulfonium salts were subjected to ring opening and deethylation. Treatment of the salts with a base (aqueous potassium hydrogen carbonate) gave ethylthio-substituted aryl vinyl ketones. Their reaction with thiourea in acid medium afforded fused thiopyran-4-ones (Scheme 110).

IX. CONCLUSION

The available data on the reactivity of sulfonium salts lead us to presume that the direction of nucleophilic attack is determined by several factors. One of

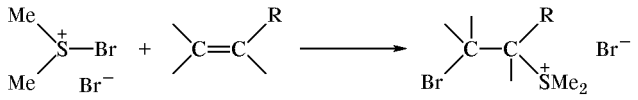
Scheme 111.



the main factors is nucleofugality of the X group (Scheme 111). Obviously, path *1* is possible only when X is a readily departing group. Path *1* is quite impossible for acyl(dimethyl)sulfonium salts: here, the nucleofuge should be acyl anion RCO^-. On the other hand, dimethyl sulfide itself is a good leaving group, so that path *2* is possible for all sulfonium salts in which X can act as electrophile. In some cases, the nucleofugalities of dimethyl sulfide and X group may be comparable; then, both reaction paths are theoretically probable. Such a situation is typical of dimethyl(sulfonyl)sulfonium salts [17]. The data on the reactivity of dimethyl(trifluoromethylsulfonyl)-sulfonium trifluoromethanesulfonate show that nucleophilic attack is directed at the sulfonium sulfur atom. According to Minato *et al.* [18], sulfonate sulfur atom can also act as electrophilic center, e.g., as in dimethyl(*p*-tolylsulfonyl)sulfonium trifluoromethanesulfonate. Probably, complete alteration of the reaction is explained by the fact that trifluoromethanesulfinate ion is a better leaving group than *p*-toluenesulfinate ion. An example of sulfonium salts in which the nucleofugalities of dimethyl sulfide and group X are equal is tetramethyldisulfonium dication where the two positions are degenerate.

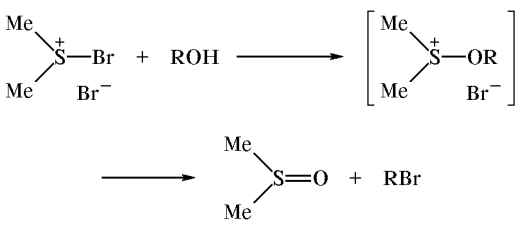
Another important factor responsible for the reactivity of sulfonium electrophiles is spatial accessibility of the electrophilic center. The most typical example is likely to be the complex of dimethyl sulfide with bromine (X–Br). Here, the nucleofugalities of dimethyl sulfide and bromide ion are comparable; however, greater accessibility of the halogen center makes it more active in reactions with alkenes (path *2*), which occur as conjugate addition of the halogen and dimethyl sulfide [113] (Scheme 112).

Scheme 112.



The nature of nucleophile can also affect the reaction direction, i.e., will it occur at one or another electrophilic center of sulfonium salt. For example,

Scheme 113.



the same complexes of halogens with dimethyl sulfide act as S-electrophiles (path *1*) in reactions with alcohols [114] (Scheme 113).

In order to get a deeper insight into the nature of sulfonium salts and elucidate the effect of substituent on their chemical properties, we performed detailed quantum-mechanical calculations of a series of sulfonium salts, including both known and unknown ones. The calculations were performed in the MP2/6-31G approximation using PC-GAMESS program [42]. We analyzed the effect of substituents in sulfonium cations on their electronic and geometric structure and reactivity. It was presumed that these data will allow us to determine the main factors responsible for the direction of nucleophilic attack. Here, the dual reactivity of sulfonium salts and ambident character of some sulfonium reagents should be emphasized once more. The calculated parameters are collected in Table 2.

Attempts were made to correlate the reactivity of sulfonium salts with the energy of the S–X bond, which should decrease as the bond lengthens. Figure 4 shows the diagram of the S–X and S–C bond lengths in $Me_2\overset{+}{S}X$ sulfonium salts. It is seen that the X substituent almost does not affect the length of the bond between the sulfur atom and methyl carbon atom, which remains approximately equal to 1.80 Å. On the other hand, the S–X bond length changes very strongly. Direct comparison of the S–X distances is hardly correct, for the nature of the X atom changes. Nevertheless, some correlations are observed for sulfonium salts having substituents of the same nature. In the series of halogen-substituted sulfonium salts, the S–X bond shortens in going from bromine to fluorine (Br > Cl > F). However, such a relation might be expected. More interesting is variation of the S–X bond length in acyl- and sulfonylsulfonium salts: increase in the acceptor power of the substituent leads to some characteristic changes of the bond length. In going from acetyl to trifluoroacetyl group, the S–C bond shortens by 0.16 Å (~8%). Even greater changes are observed in the series of sulfonylsulfonium salts. The S–S bond length in $Me_2\overset{+}{S}SO_2CF_3$ is 2.244 Å; reduction of the acceptor power of the substituent results in considerable elongation of the S–S bond, to 2.340 and 2.551 Å in $Me_2\overset{+}{S}SO_2CH_3$ and in the complex of dimethyl sulfide with sulfur trioxide, respectively. Thus the S–X bond length in sulfonium salts shows a weak correlation with the direction of nucleophilic attack.

Another factor which could affect the reactivity is geometric structure of sulfonium reagents. Reaction

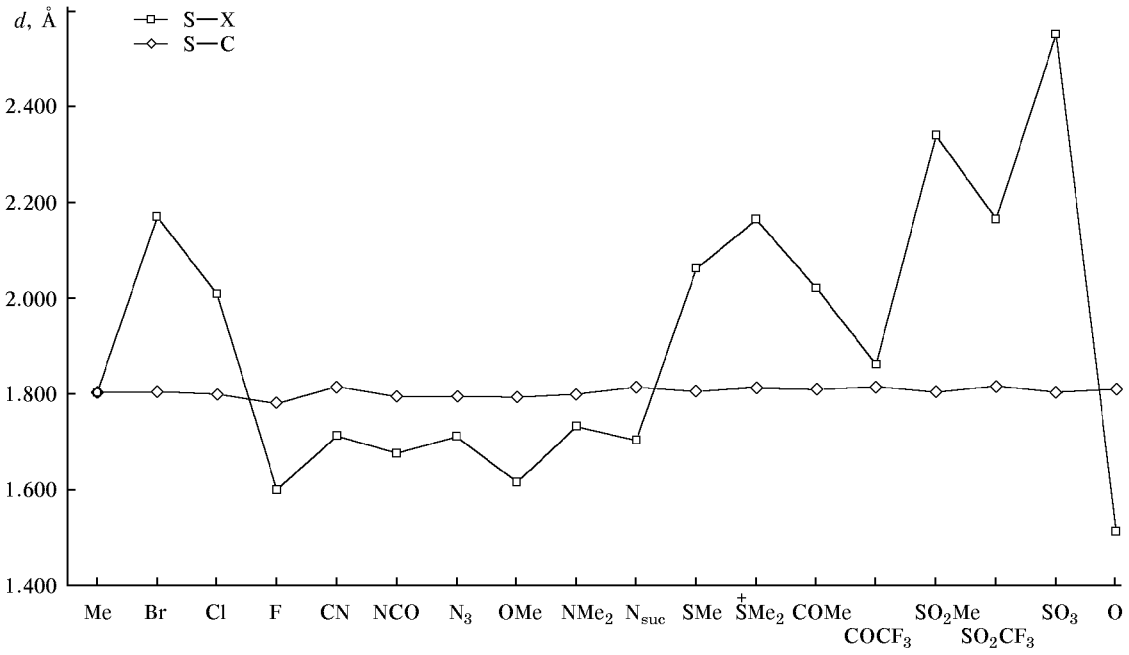
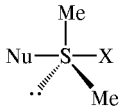


Fig. 4. Lengths of the S−X and S−CH_3 bonds in sulfonium salts.

of a nucleophile with sulfonium salt at the sulfur atom of the latter can be regarded as nucleophilic substitution at that sulfur atom. In the corresponding transition state, the dihedral angle between the substituent which acts as the leaving group and the CH_3-S-CH_3 plane should be 90°:



It was presumed that the pyramidal configuration of sulfonium salts can be distorted, i.e., the dihedral angle $X-CH_3-S-CH_3$ decreases to 90°, thus preparing the transition state for nucleophilic attack at the sulfur atom. However, according to the calculated dihedral angles (Fig. 5), the situation is even the reverse. For example, in the complex of dimethyl sulfide with sulfur trioxide, the above angle is 97.9°, but the reaction occurs at the sulfonate rather than sulfonium sulfur atom. Unfortunately, the calculations did not include topological analysis of the electron density, which could make it possible to characterize the position of unshared electron pair on the sulfonium sulfur atom. Probably, in the future such analysis will elucidate the effect of geometry on the reactivity of sulfonium salts. However, our data on the geometry of sulfonium salts do not allow us to draw a direct correlation with their reactivity.

In keeping with the molecular orbital perturbation theory, the reaction selectivity is determined by a combination of orbital and charge interactions between the sulfur atom and the neighboring center in sulfonium salts. The calculated charges (Mulliken's q_M and Lawdin's q_L) on the sulfonium center are as a rule considerably greater than on the neighboring electrophilic center. Moreover, in some cases the calculated charges are negative, e.g., on the carbon atom in the cyanosulfonium salt or on the nitrogen atom in the azidosulfonium salt. The charge on the neighboring center is considerably greater in sulfonium salts with a sulfonate group; the charges on the sulfonate sulfur atoms are generally greater than unity (Table 2, Fig. 6). It should be noted that, in terms of quantum-mechanical methods, charges are ill-conditioned formal quantities [115]. In addition, the charge on the sulfur atom in S(VI) derivatives is usually overestimated to a strong extent. Therefore, the calculated charges provide no interpretation of the reactivity of sulfonium electrophiles. Presumably, reactions of sulfonium salts with nucleophiles are not charge-controlled. The energy of the lowest unoccupied molecular orbital (LUMO) is known to characterize the electrophilicity of reagents: the lower the LUMO energy, the more electrophilic the reagent. As is seen from Table 2 and Fig. 7, all sulfonium salts are fairly strong electrophiles. For most of them, the LUMO energy ranges from –3 to 0 eV. However, in our case the above quantities provide only qualitative informa-

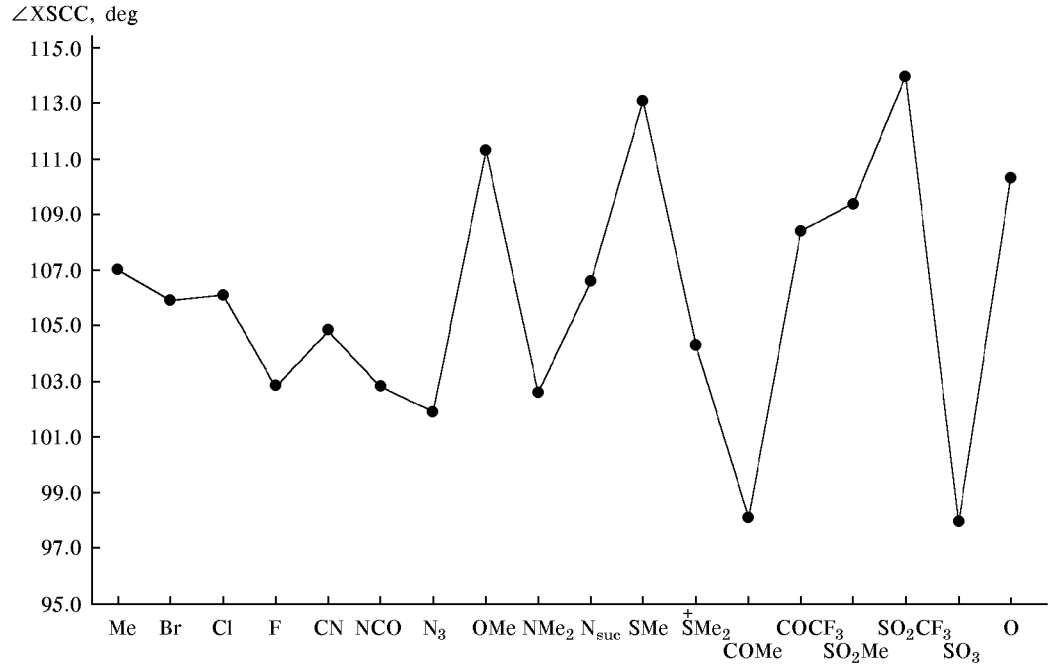


Fig. 5. Dihedral angles between the S−X bond and SCC plane in sulfonium salts.

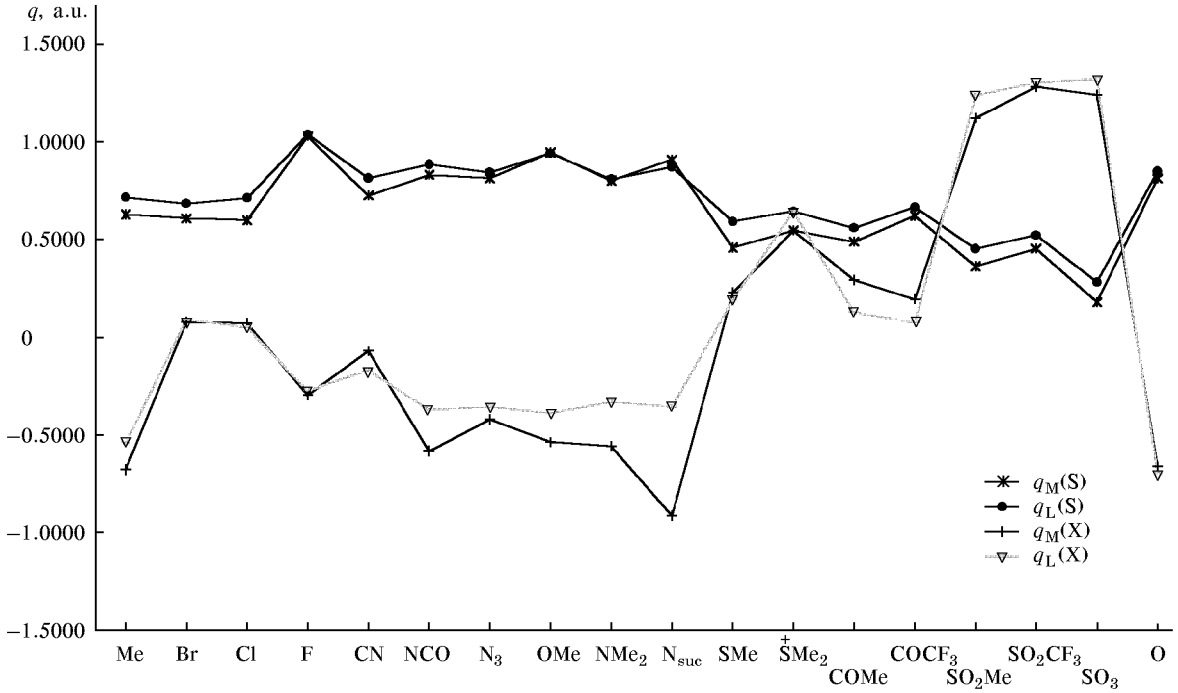


Fig. 6. Charges on the sulfur and X atoms (Mulliken's q_M and Lawdin's q_M) in sulfonium salts.

tion, and they cannot unambiguously correlate with the reactivity of sulfonium salts.

The LUMO energies of disulfonium dication and dimethyl sulfoxide complex with sulfur trioxide fall out from the general series. The low E_{LUMO} value of S−S dication is likely to result from its double positive charge, and the high E_{LUMO} value of the complex $SMe_2 \cdot SO_3$ may be explained by the fact that the calculated structure is not a sulfonium salt (which exists as dipolar ion) but a coordination compound

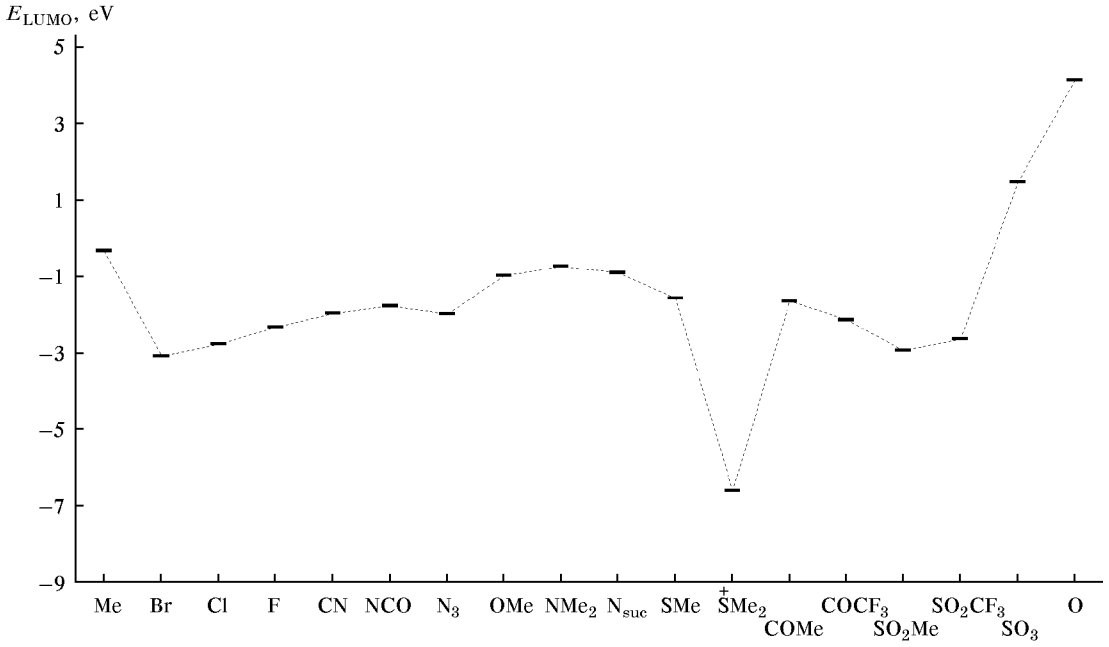


Fig. 7. LUMO energies of sulfonium salts.

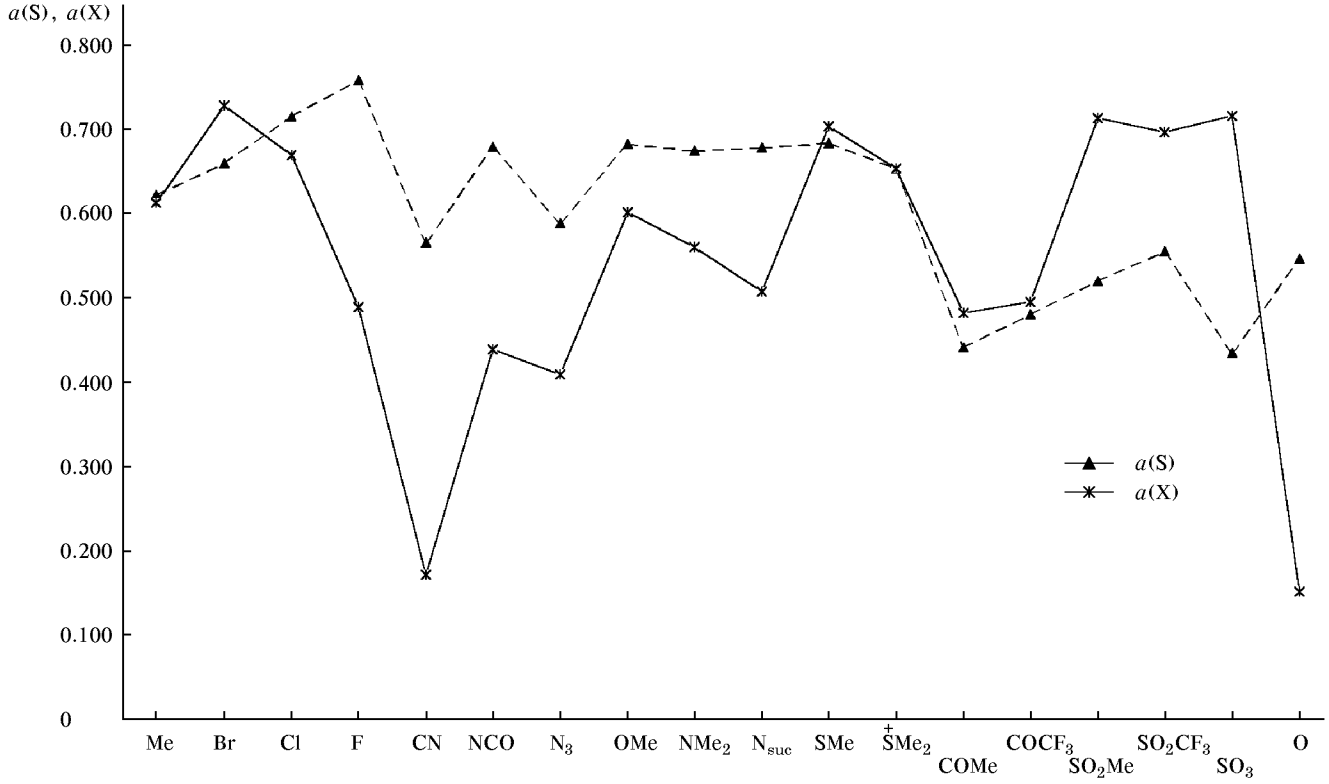


Fig. 8. Orbital coefficients in the LUMO of sulfonium salts.

with a fairly long and weak S–S bond. Unfortunately, there are no published structural data on the $SMe_2 \cdot SO_3$ complex, which could clarify the nature of the S–S bond in this compound.

It turned out to be most reasonable to consider orbital coefficients in the LUMO of the sulfur atom or neighboring electrophilic center in sulfonium salts (Fig. 8). The direction of nucleophilic attack correlates

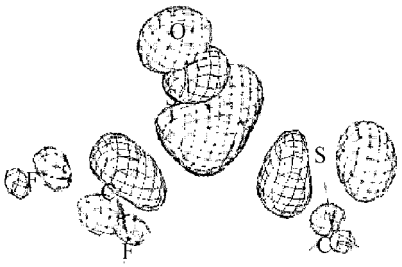
Table 2. Calculated geometric and electronic structure parameters[a] of sulfonium salts $Me_2\overset{+}{S}X$

Substituent X	d(S–X), Å	d(S–C), Å	∠XSCC, deg	q_M(S), a.u.	q_L(S), a.u.	q_M(X), a.u.	q_L(X), a.u.	E_{LUMO}, eV	a(S)	a(X)
Me	1.802	1.802	107.0	0.6300	0.7172	–0.6766	–0.5407	–0.34	0.621	0.612
Br	2.170	1.804	106.9	0.6100	0.6849	0.0786	0.0917	–3.09	0.659	0.728
Cl	2.008	1.798	106.1	0.6001	0.7140	0.0733	0.0507	–2.78	0.715	0.669
F	1.599	1.779	102.8	1.0302	1.0388	–0.2953	–0.2720	–2.34	0.758	0.489
CN	1.711	1.814	104.8	0.7260	0.8152	–0.0694	–0.1681	–1.97	0.565	0.172
NCO	1.675	1.794	102.8	0.8330	0.8852	–0.5827	–0.3718	–1.78	0.678	0.439
N_3	1.710	1.795	101.9	0.8152	0.8447	–0.4201	–0.3550	–1.99	0.588	0.409
OMe	1.615	1.792	111.3	0.9464	0.9425	–0.5370	–0.3894	–0.99	0.682	0.602
NMe_2	1.731	1.798	102.6	0.8027	0.8087	–0.5580	–0.3303	–0.74	0.674	0.560
N_{suc}	1.702	1.813	106.6	0.9108	0.8739	–0.9143	–0.3552	–0.91	0.678	0.507
SMe	2.062	1.804	113.1	0.4595	0.5937	0.2301	0.1906	–1.58	0.683	0.703
$\overset{+}{S}Me_2$	2.164	1.813	104.3	0.5480	0.6444	0.5480	0.6444	–6.62	0.653	0.653
COMe	2.021	1.808	98.1	0.4903	0.5603	0.2936	0.1275	–1.65	0.441	0.482
$COCF_3$	1.861	1.814	108.4	0.6233	0.6671	0.1954	0.0753	–2.14	0.480	0.495
SO_2Me	2.340	1.803	109.4	0.3633	0.4537	1.1243	1.2399	–2.94	0.519	0.713
SO_2CF_3	2.165	1.816	114.0	0.4545	0.5223	1.2821	1.3066	–2.65	0.555	0.696
SO_3	2.551	1.802	97.9	0.1802	0.2822	1.2415	1.3252	1.46	0.434	0.715
O	1.511	1.809	110.3	0.8143	0.8503	–0.6613	–0.6965	4.14	0.545	0.162

[a] q_M(S), q_L(S), q_M(X), and q_L(X) are charges on the sulfur and X atoms according to Mulliken and Lawdin (Fig. 6); a(S) and a(X) are orbital coefficients in the LUMO of sulfonium salts (Fig. 8).

well with these quantities. In fact, the larger the orbital coefficient, the more probable nucleophilic attack at the respective center. The orbital coefficient of the X atom in the LUMO of halosulfonium salts increases in the series of halogens. The largest a[X] value was obtained for the bromosulfonium salt which acts as brominating agent. When nucleophilic reaction occurs at the center neighboring to the sulfonium sulfur atom, the orbital coefficient of that center in the LUMO is comparable to or greater than the orbital coefficient of the sulfonium sulfur atom. Such reactions are typical of the following sulfonium cations: Me_3S^+, $Me_2\overset{+}{S}Br$, $Me_2\overset{+}{S}SMe$, $Me_2\overset{+}{S}\overset{+}{S}Me_2$ (here, both reaction centers are equivalent), $Me_2\overset{+}{S}COMe$, $Me_2\overset{+}{S}COCF_3$, and $Me_2\overset{+}{S}SO_3$. However, the results of calculations predict nucleophilic reaction at the sulfonate sulfur atom of trifluoromethylsulfonylsulfonium salts, while in fact such reactions occur at the sulfonium center. This means that, despite a good agreement with the experimental data, in some cases deviations are observed, which require other factors to be taken into account.

Nevertheless, the orbital factor is crucial in reactions of sulfonium salts with nucleophiles. Analysis of the LUMO coefficients could have a significant predictive power. We can anticipate that some previously unknown sulfonium salts, e.g., those having a cyano, cyanato, or azido group at the sulfonium center, would react with a high probability at the sulfur atom rather than at carbon or nitrogen (which is more interesting from the synthetic viewpoint).



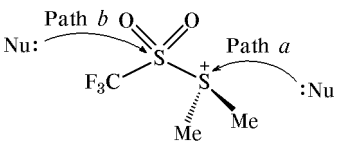


Fig. 9. Structure of the LUMO of dimethyl(trifluoromethylsulfonyl)sulfonium cation and paths of its reactions with nucleophiles.

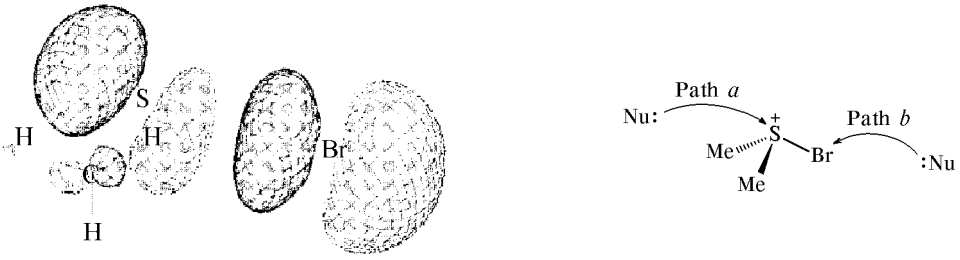


Fig. 10. Structure of the LUMO of bromo(dimethyl)sulfonium cation and paths of its reactions with nucleophiles.

Thus the results of quantum-mechanical calculations of sulfonium salts show that orbital control is the main factor determining the direction of their reactions with nucleophiles. Apart from orbital coefficients in the LUMO, very important are spatial accessibility of orbitals and hardness–softness ratio of the reaction centers. Presumably, steric factors are crucial in the reactions of sulfonylsulfonium salts with nucleophiles.

Figure 10 shows that the orbital factor favor S_N2-like attack by nucleophile on the S(II) atom, followed by cleavage of the S(II)–S(VI) bond. Oxygen atoms of the sulfonyl group, which possess a negative charge, also contribute to the reaction according to path *a*. In this connection, very interesting is ambident properties of bromosulfonium salts. Large size and softness of alkenes (compared to alcohols) force the reaction to occur at the more accessible and softer (smaller charge) bromine atom (Fig. 10).

It is quite obvious that sulfonium salts are very interesting compounds from both synthetic and purely theoretic viewpoints. Undoubtedly, the chemistry of reagents on the basis of sulfonium salts should receive extensive development.

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