ISSN 1070-4280, Russian Journal of Organic Chemistry, 2012, Vol. 48, No. 7, pp. 918–923. © Pleiades Publishing, Ltd., 2012.
Original Russian Text © B.A. Shainyan, M.Yu. Moskalik, V.V. Astakhova, 2012, published in Zhurnal Organicheskoi Khimii, 2012, Vol. 48, No. 7, pp. 923–928.

Oxidative Addition of Trifluoromethanesulfonamide to Vinylcyclohexane and *p*-Chlorostyrene

B. A. Shainyan, M. Yu. Moskalik, and V. V. Astakhova

Favorskii Irkutsk Institute of Chemistry, Siberian Division, Russian Academy of Sciences, ul. Favorskogo 1, Irkutsk, 664033 Russia
e-mail: bagrat@irioch.irk.ru

Received February 8, 2012

Abstract—Trifluoromethanesulfonamide reacted with vinylcyclohexane in the system *t*-BuOCl–NaI to give a mixture of 2,6-dicyclohexyl-1,4-bis(trifluoromethylsulfonyl)piperazine and 2-iodo-1-cyclohexylethanol. Conformational behavior of the heterocyclization product was studied by dynamic NMR. The reaction of *p*-chlorostyrene with trifluoromethanesulfonamide under analogous conditions produced the corresponding bis-adduct, *N*-[2-(4-chlorophenyl)-2-(trifluoromethylsulfonylamino)ethyl]trifluoromethanesulfonamide and 1-(4-chlorophenyl)-2-iodoethanol. A probable reaction mechanism was proposed, which rationalizes difference in the behavior of the examined alkenes.

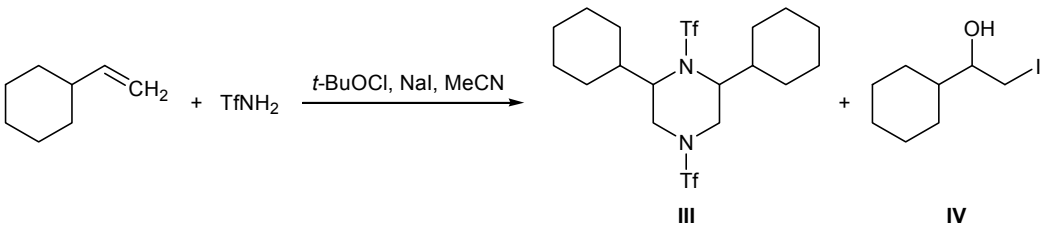
DOI: 10.1134/S1070428012070056

We previously showed that, depending on the conditions, the reaction of trifluoromethanesulfonamide with styrene leads to the formation of one of two isomeric piperazine derivatives, 2,5-diphenyl-1,4-bis(trifluoromethylsulfonyl)piperazine (**I**) (in the system *t*-BuOCl–NaI·2H_2O [1]) or 2,6-diphenyl-1,4-bis(trifluoromethylsulfonyl)piperazine (**II**) (in the presence of anhydrous NaI [2]). The major products were trifluoro-*N*-[2-phenyl-2-(trifluoromethylsulfonylamino)ethyl]methanesulfonamide and 2-iodo-1-phenylethanol. Compound **I** was also formed via dehydrobromination of *N*-(2-bromo-2-phenylethyl)trifluoromethanesulfonamide by the action of triethylamine [3]. No heterocyclic products were formed in the oxidative addition of trifluoromethanesulfonamide to α-methylstyrene and 2-methylpent-1-ene [4].

There are only a few published data on the formation of piperazine derivatives via addition of sulfonyl azides (precursors of sulfonyl nitrenes) to alkenes. For instance, trace amounts of 2,5-dialkoxy-1,4-bis(phenylsulfonyl)piperazines were formed by thermal decomposition of phenylsulfonyl azide in the presence of vinyl ethers [5]. It is also known that perfluoroalkylsulfonyl azides react with alkyl vinyl ethers to give the corresponding dihydro-1,2,3-triazoles which slowly decompose at room temperature with formation of symmetrically substituted 2,5-dialkoxy-1,4-bis(perfluoroalkylsulfonyl)piperazines [6]. 1,4-Bis(trifluoromethylsulfonyl)piperazine having no substituents on carbon atoms is the only known representative of *N*-trifluoromethylsulfonyl-substituted piperazines [7]. Apart from acylation of NH-piperazine, 1,4-substituted piperazines can be obtained by dimerization of the corresponding nonactivated aziridines by the action of various reagents [8].

In continuation of our studies on reactions of trifluoromethanesulfonamide with unsaturated compounds, in the present work we examined its reactions

Scheme 1.



III IV

Tf = CF_3SO_2.

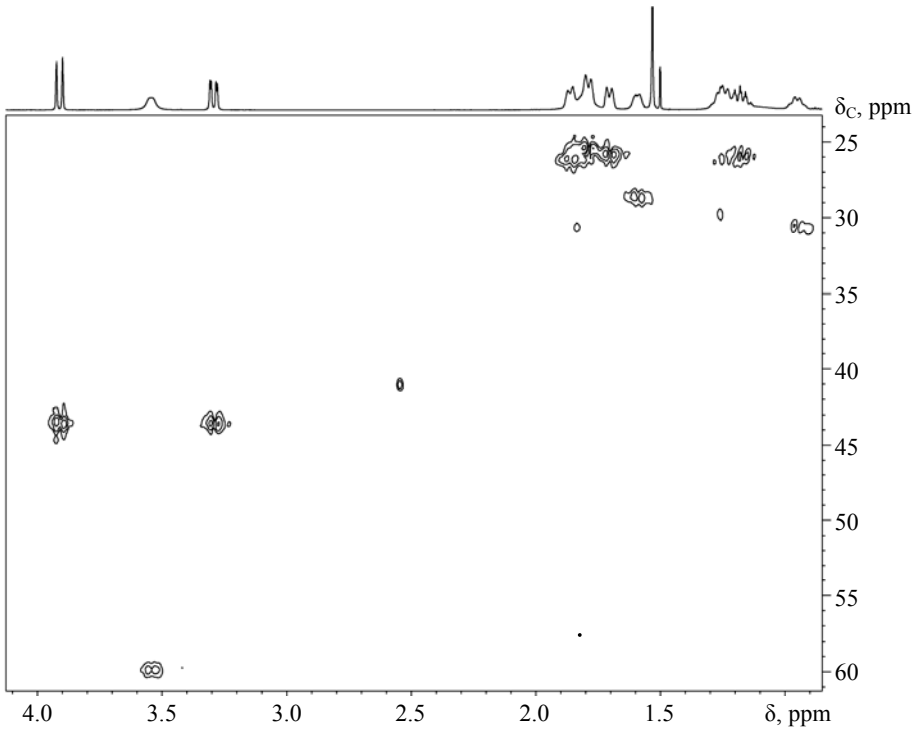


Fig. 1. Two-dimensional ^{1}H–^{13}C HMQC spectrum of compound **III**.

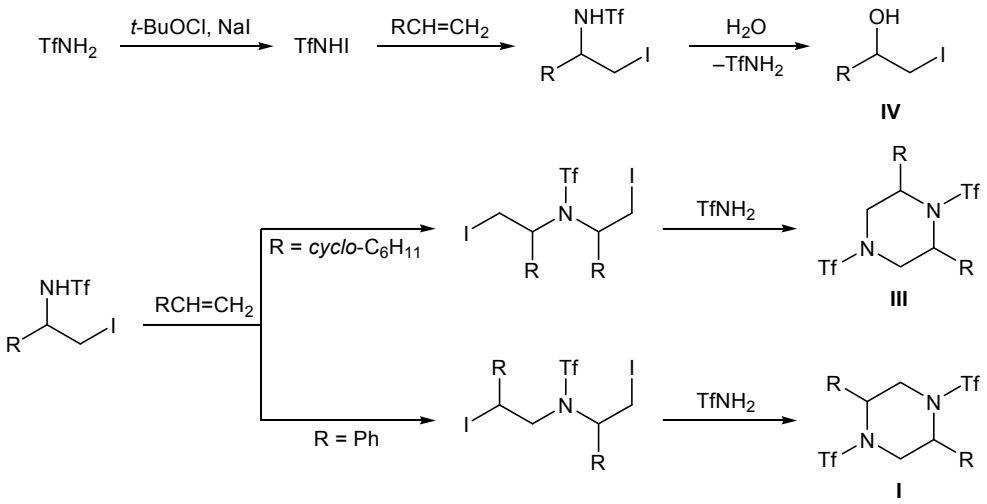
with vinylcyclohexane and *p*-chlorostyrene in acetonitrile in the presence of *t*-BuOCl–NaI as oxidative system with a view to extend the series of alkenes involved and compare their reactivity with the reactivity of styrene studied previously. The reaction with vinylcyclohexane was carried out at room temperature or on cooling to –10°C. In all cases, two products were formed. They were isolated by column chromatography and identified as 2,6-dicyclohexyl-1,4-bis(trifluoromethylsulfonyl)piperazine (**III**) and 1-cyclohexyl-2-iodoethanol (**IV**) at a ratio of 1 : 3 (Scheme 1).

The structure of compound **III** was determined by comparing its ^{1}H NMR spectrum with those of 2,5-diphenyl- [1] and 2,6-diphenyl-substituted analogs [2]. In all cases, protons in the piperazine ring gave rise to an *ABX* pattern, and their signals were assigned on the basis of the 2D ^{1}H–^{13}C HMQC data (Fig. 1). The upfield CH_2 signal appeared as a slightly split doublet (J = 14.5, 3.3 Hz), which was very similar to the corresponding signal in the spectrum of **II** (J = 13.8, 3.6 Hz) but considerably different from that observed for compound **I** (J = 15.5, 11.2 Hz). The downfield signal in the spectra of **II** and **III** was a doublet (J = 14.5 Hz), in contrast to the doublet of doublets in the spectrum of **I** (J = 15.5, 6.8 Hz). The CH proton in **II** and **III** resonated as a broadened singlet or a weakly split doublet against distinct doublet of doublets for compound **I** (J = 11.2, 6.8 Hz). Strong similarity of the spectral patterns of **II** and **III** and their appreciable difference from that observed for compound **I**, as well as the presence of two CF_3 signals in the ^{19}F NMR spectrum of **III**, allowed us to identify compound **III** as 2,6-disubstituted piperazine derivative. The difference in the fluorine chemical shifts in the ^{19}F NMR spectrum of **III** is small ($\Delta\delta_F$ = 0.9 ppm), and the corresponding carbon signals coincide in the ^{13}C NMR spectrum (a single quartet is observed).

The structure of iodo-substituted alcohol **IV** was confirmed by the presence of a triplet at δ_C 11.14 ppm (CH_2I) and a doublet at δ_C 68.22 ppm (CH_2OH) in its ^{13}C NMR spectrum recorded without decoupling from protons.

Unlike the reaction with styrene [1, 2], even traces of linear bis-adduct $CF_3SO_2NHCH(R)CH_2NHSO_2CF_3$ (R = cyclo-C_6H_{11}) were not detected. Let us consider a probable reaction mechanism to rationalize the observed differences in the behavior of styrene [1, 2] and vinylcyclohexane. The formation of isomeric piperazines was presumed previously to result from opening of intermediate aziridines generated by addition of trifluoromethanesulfonyl nitrene to styrene [1, 2]. However, taking into account that intermediate aziridines were not detected and that perfluoroalkanesulfonyl nitrenes are formed (at least from the corresponding

Scheme 2.



Tf = CF_3SO_2; R = *cyclo*-C_6H_{11}, Ph.

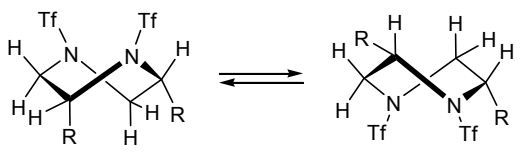
azides) only at elevated temperature [9], alternative mechanisms should be considered.

It is known that carboxylic acid amides react with *tert*-butyl hypochlorite in the presence of NaI to give *N*-iodo amides [10]. It is also known that reactions of *N*-halo amides with alkenes in the absence of water lead to the corresponding haloamidation products [11]. *N*-Halo amides react with terminal alkenes in the presence of water to afford 1-alkyl-2-iodoethanols [12]. The above data led us to presume that compounds **III** and **IV** are formed according to Scheme 2.

Different regioselectivities in the addition of trifluoro-*N*-iodomethanesulfonamide to vinylcyclohexane and styrene (electrophilic attack by iodine at the terminal or internal double-bonded carbon atom, respectively) may be related to different localizations of the highest occupied molecular orbitals (HOMO) in vinylcyclohexane and styrene. According to HF/6-311G** calculations, the HOMO in vinylcyclohexane is localized mainly on the terminal olefinic carbon atom, whereas in styrene, on the internal carbon atom. Closure of ε-diiodo derivatives to six-membered piperazine ring by the action of trifluoromethanesulfonamide is analogous to the ring closure of organosilicon ε-dichloro [13] and ε-dibromo compounds [14].

The fact that *cyclo*-$C_6H_{11}CH(NHTf)CH_2NHTf$ {linear bis-adduct analogous to $PhCH(NHTf)CH_2NHTf$ [1, 2]} is not formed may be related to very weak nucleophilicity of trifluoromethanesulfonamide which is incapable of replacing iodine in intermediate adduct *cyclo*-$C_6H_{11}CH(NHTf)CH_2I$ (Scheme 2). In the reaction with styrene, replacement of iodine in analogous intermediate $PhCH(NHTf)CH_2I$ is facilitated due to anchimeric assistance by the phenyl group.

Low-temperature ^1H NMR spectra of **III** revealed conformational equilibrium which was "frozen" at –80°C (Fig. 2). The observed pattern indicated the existence of equilibrium between energetically equivalent conformers. The two $CHCH_2$ fragments in the piperazine ring of each conformer are magnetically nonequivalent. The most informative was the presence of four doublets from piperazine CH protons at δ 3.4–3.6 ppm with coupling constants of 9.0 and 10.4 Hz (in pairs); these data correspond to coupling of these protons with the cyclohexyl CH protons, whereas no coupling with the piperazine CH_2 protons exists (Fig. 3). Splitting of the CH_B signal (δ 3.8–3.9 ppm, J = 15 Hz) is likely to result from coincidence of signals of one of these protons in two conformers (δ 3.83 and 3.85 ppm) and their different positions for the other (δ 3.81/3.84 and 3.84/3.86 ppm). The CH_A signal at δ 3.2–3.3 ppm appears as a complex unresolved multiplet, obviously due to weak long-range couplings. The absence of vicinal coupling in the $CHCH_2$ fragments of the piperazine ring (small coupling constants) is possible in the *twist* conformation which was found for the diphenyl-substituted analog of **III** [2]; the dihedral angles $HCCH_A$ and $HCCH_B$



R = *cyclo*-C_6H_{11}.

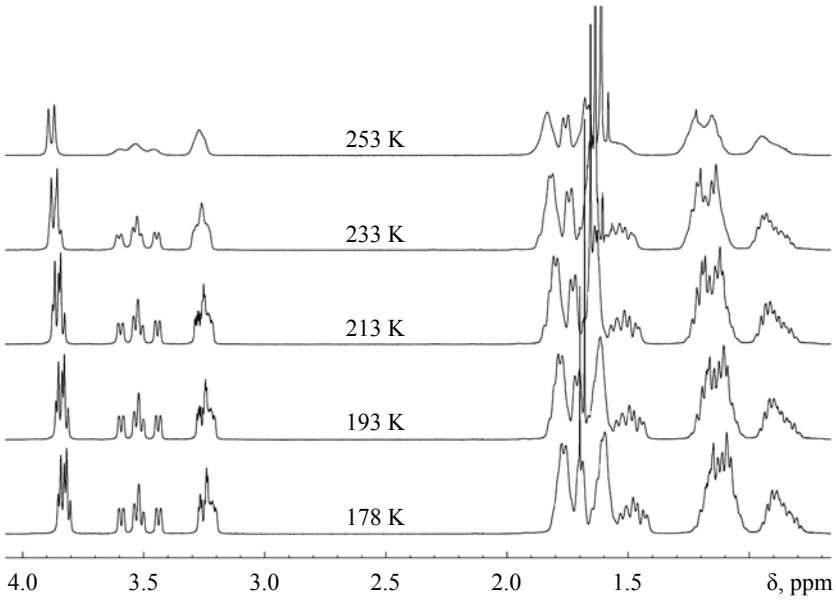


Fig. 2. Low-temperature ^{1}H NMR spectra of compound **III**.

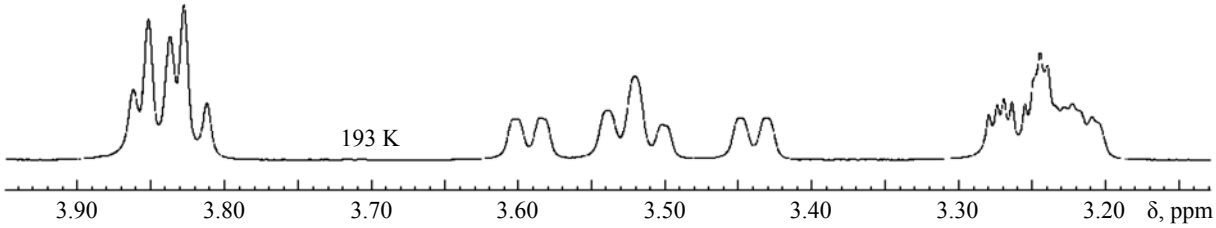


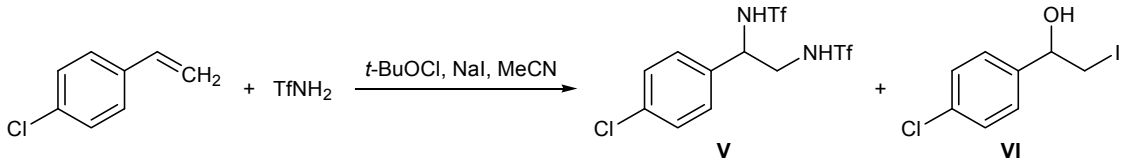
Fig. 3. Signals from protons in the piperazine ring of compound **III** in the ^{1}H NMR spectrum under maximal resolution.

therein approach 70°. Thus variations observed in the NMR spectra at low temperature may be explained by conformational equilibrium.

The reaction of *p*-chlorostyrene with trifluoromethanesulfonamide in acetonitrile in the presence of *t*-BuOCl–NaI gave a mixture of bis-adduct, *N*,*N*′-[1-(4-chlorophenyl)ethane-1,2-diyl]bis(trifluoromethanesulfonamide) (**V**), and 1-(4-chlorophenyl)-2-iodoethanol (**VI**) at a ratio of ~1:1 (Scheme 3). Unlike the reactions with vinylcyclohexane (Scheme 1) and styrene [1, 2], no piperazine derivatives were detected in the reaction mixture. The structure of compound **V** was confirmed by the presence in its IR spectrum of absorption bands typical of NH stretching vibrations (3380 cm^{-1}) and characteristic signals in the ^{1}H and ^{13}C NMR spectra. Two nonequivalent CF_3 groups in molecule **V** gave rise to two quartets in the ^{13}C NMR spectrum and two signals in the ^{19}F NMR spectrum.

The ratio of the corresponding bis-adduct and iodo alcohol in the reaction with styrene [1] was 5:2. The smaller fraction of bis-adduct **V** formed in the reaction with *p*-chlorostyrene conforms to the above assumption implying anchimeric assistance by the aryl group, for the effect of *p*-chlorophenyl group is weaker as compared to phenyl. In keeping with Scheme 2, piperazines are formed via electrophilic iodoamidation of the second alkene molecule with intermediate TfN(I)CH(R)CH_2I; therefore, reduction of the electron

Scheme 3.



Tf = CF_3SO_2.

density on the vinyl group in going from R = Ph to R = *p*-ClC_6H_4 is also consistent with the proposed mechanism and the absence of heterocyclization product in the reaction with *p*-chlorostyrene (Scheme 3).

EXPERIMENTAL

The IR spectra were recorded on a Varian 3100 FT-IR spectrometer. The NMR spectra were measured on a Bruker DPX-400 spectrometer at 400 (^{1}H), 100 (^{13}C), and 376 MHz (^{19}F); the chemical shifts are given relative to tetramethylsilane (^{1}H, ^{13}C) and CCl_3F (^{19}F). The low-temperature ^{1}H NMR spectra and two-dimensional HMBC and HSQC experiments were run on a Bruker AV-600 instrument (600 MHz for ^{1}H and 150.95 MHz for ^{13}C). The mass spectrum (electron impact, 70 eV) was obtained on a Shimadzu GCMS-QP5050A mass spectrometer with quadrupole mass analyzer (direct sample admission into the ion source) The progress of reactions was monitored by TLC on silica gel 60 F_{254} using hexane–diethyl ether (1:2) as eluent.

Reaction of trifluoromethanesulfonamide with vinylcyclohexane in acetonitrile in the presence of *t*-BuOCl and NaI. *tert*-Butyl hypochlorite, 4.24 g (39 mmol), was added dropwise to a solution of 2 g (13 mmol) of trifluoromethanesulfonamide, 2.86 g (26 mmol) of vinylcyclohexane, and 5.85 g (39 mmol) of anhydrous NaI in 78 ml of acetonitrile. The mixture was stirred for 24 h at 20°C in the dark under argon, treated with 80 ml of a concentrated solution of $Na_2S_2O_3$, and extracted with 100 ml of chloroform. The extract was dried over $CaCl_2$, the solvent was distilled off under reduced pressure, and the tarry residue, 4.83 g, was subjected to column chromatography on silica gel using hexane as eluent.

2,6-Dicyclohexyl-1,4-bis(trifluoromethylsulfonyl)piperazine (III). Yield 120 mg (4%), white crystals, mp 193°C. IR spectrum, ν, cm^{-1}: 3433, 3025, 2947, 2938, 2859, 1454, 1391, 1380, 1221, 1108, 1068, 976, 952, 777, 652, 594. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.15 m (5H) and 1.74 m (6H) (C_6H_{11}), 3.30 d (1H, CH_2, J = 14.7 Hz), 3.54 br.s (1H, CH_2), 3.93 (1H, CH, J = 14.7 Hz). ^{13}C NMR spectrum (CD_3CN), δ_C, ppm: 25.6 t ($C^{4'}$, J = 125.3 Hz), 25.8 t ($C^{3'}$, J = 129.2 Hz), 26.3 t ($C^{5'}$, J = 128.0 Hz), 28.77 t ($C^{2'}$, J = 123.8 Hz), 30.84 t ($C^{6'}$, J = 126.9 Hz), 34.17 d ($C^{1'}$, J = 120.8 Hz), 43.72 t (C^4, C^5, J = 143.6 Hz), 59.9 t (C^2, C^6, J = 143.6 Hz), 119.62 q (CF_3, J = 322.3 Hz). ^{19}F NMR spectrum (CD_3CN): δ_F –74.5 ppm. Mass spectrum, *m*/*z* (I_{rel}, %): 514 (16) $[M]^+$, 431 (9) $[M - C_6H_{11}]^+$, 349 (28) $[431 - C_6H_{10}]$, 299 (5), 215 (11), 165 (9), 124 (7), 95 (11), 83 (78) $[C_6H_{11}]^+$, 82 (40) $[C_6H_{11} - 1]^+$, 69 (28), 55 (100), 41 (44). Found: *m*/*z* 514.1374 $[M]^+$. $C_{18}H_{28}F_6N_2O_4S_2$. Calculated: *M* 514.1368.

1-Cyclohexyl-2-iodoethanol (IV). Yield 250 mg (8%), colorless liquid. Compound **IV** was described in [15]; however, its spectral parameters were not given therein. IR spectrum, ν, cm^{-1}: 2927, 2853, 2666, 1448, 1290, 1238, 1152, 1123, 966, 887, 704, 596, 572. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.20 m (5H) and 1.70 m (6H) (C_6H_{11}), 3.60 d.d (1H, OH, J = 6.02, 2.17 Hz), 4.00 d.d (1H, CHC**H**$_2$, J = 11.1, 8.9 Hz), 4.10 d.d (1H, CHC**H**$_2$, J = 11.1, 6.02 Hz), 4.30 m (1H, C**H**CH_2). ^{13}C NMR spectrum (CD_3CN), δ_C, ppm: 25.6 t ($C^{4'}$, J = 125.3 Hz), 25.8 t ($C^{3'}$, J = 129.2 Hz), 26.3 t ($C^{5'}$, J = 128.0 Hz), 28.77 t ($C^{2'}$, J = 123.8 Hz), 30.84 t ($C^{6'}$, J = 126.9 Hz), 34.17 d ($C^{1'}$, J = 120.8 Hz), 43.72 t (CH**C**H_2, J = 143.6 Hz).

Reaction of trifluoromethanesulfonamide with *p*-chlorostyrene in acetonitrile in the presence of *t*-BuOCl–NaI. *tert*-Butyl hypochlorite, 4.24 g (39 mmol), was added dropwise to a solution of 2 g (13 mmol) of trifluoromethanesulfonamide, 1.81 g (13 mmol) of *p*-chlorostyrene, and 5.85 g (39 mmol) of anhydrous NaI in 78 ml of acetonitrile (the mixture spontaneously warmed up to 50°C). The mixture was stirred for 24 h at room temperature in the dark under argon, treated with 80 ml of a concentrated solution of $Na_2S_2O_3$, and extracted with 80 ml of chloroform, the extract was dried over $CaCl_2$, and the solvent was distilled off under reduced pressure to obtain 2.57 g of a dark oily residue which was purified by column chromatography on silica gel using hexane and diethyl ether–hexane (1:1) as eluent. We thus isolated 1 g of an oily substance, 500 mg of which was applied to a column charged with fine-grained silica gel. Elution with methylene chloride–hexane (1:3) gave *N*,*N*′-[1-(4-chlorophenyl)ethane-1,2-diyl]bis(trifluoromethanesulfonamide) (**V**). The remaining 500 mg of the residue was subjected to column chromatography on fine-grained silica gel using diethyl ether–hexane (1:1) as eluent to isolate 1-(4-chlorophenyl)-2-iodoethanol (**VI**).

Compound **V**. Yield 400 mg (14%), white crystals, mp 125°C. IR spectrum, ν, cm^{-1}: 3483, 3295, 2953, 1913, 1500, 1462, 1373, 1229, 1201, 1146, 1093, 988, 615, 434. ^{1}H NMR spectrum (CD_3CN), δ, ppm: 3.60 (2H, CH_2, J = 6.4 Hz), 4.72 t (1H, CH, J = 6.4 Hz), 7.18 br.s (2H, NH), 7.37 d (2H, *m*-H, J = 8.4 Hz), 7.46 (2H, *o*-H, J = 8.4 Hz). ^{13}C NMR spectrum (CD_3CN), δ_C, ppm: 49.5 (CH_2), 59.9 (CH), 120.54 q (1-CF_3, J =

320.7 Hz), 120.7 q (2-CF_3, J = 320.6 Hz), 129.7 (C^m), 130.1 (C^o), 135.2 (C^p), 137.0 (C^i). ^{19}F NMR spectrum (CD_3CN), δ_F, ppm: –78.58 (1-CF_3), –78.79 (2-CF_3). Found, %: C 27.11; H 1.87; F 22.55; N 5.83; S 15.54. $C_{10}H_9ClF_6N_2O_4S_2$. Calculated, %: C 27.63; H 2.09; F 26.22; N 6.44; S 14.75.

Compound **VI**. Yield 450 mg (5%), white crystals which readily decomposed on exposure to air, mp 80°C; published data: mp 78°C [16]. ^1H NMR spectrum (CD_3CN), δ, ppm: 3.39 d.d (1H, CHC**H**$_2$, J = 10.3, 6.8 Hz), 3.49 d.d (1H, CHC**H**$_2$, J = 10.1, 4.7 Hz), 3.84 d (1H, OH, J = 4.7 Hz), 4.73 d.d.d (1H, CH, J = 10.3, 6.8, 4.7 Hz), 7.37 m (4H, H_{arom}). ^{13}C NMR spectrum (CD_3CN), δ_C, ppm: 15.2 (CH_2), 73.1 (CH), 127.1 (C^m), 128.7 (C^o), 133.9 (C^p), 139.4 (C^i).

This study was performed under financial support by the Russian Foundation for Basic Research (project no. 10-03-00110). The authors thank Prof. E. Kleinpeter (University of Potsdam) for recording low-temperature ^1H NMR spectra, two-dimensional HMBC and HSQC spectra, high-resolution mass spectrum of **III**, and ESI MS spectra.

REFERENCES

1. Shainyan, B.A., Moskalik, M.Yu., Starke, I., and Schilde, U., *Tetrahedron*, 2010, vol. 66, p. 8383.
2. Moskalik, M.Yu. and Shainyan, B.A., *Russ. J. Org. Chem*., 2011, vol. 47, p. 568.
3. Shainyan, B.A. and Sterkhova, I.V., *Russ. J. Org. Chem*., 2010, vol. 46, p. 1743.
4. Moskalik, M.Yu., Shainyan, B.A., and Schilde, U., *Russ. J. Org. Chem*., 2011, vol. 47, p. 1271.
5. Franz, J.E., Dietrich, M.W., Henshall, A., and Osuch, C., *J. Org. Chem*., 1966, vol. 31, p. 2847.
6. Zhu, S.-Z., He, P., Zhao, Z.-W., and Cai, X., *J. Fluorine Chem*., 2004, vol. 125, p. 445.
7. Shainyan, B.A., Tolstikova, L.L., and Zhnikin, A.R., *Russ. J. Org. Chem*., 2003, vol. 39, p. 1180.
8. Okada, I., Itoh, N., and Sudo, R., *Bull. Chem. Soc. Jpn*,, 1969, vol. 42, p. 547.
9. Xu, Y. and Zhu, S., *Tetrahedron*, 2001, vol. 57, p. 669.
10. Barton, D.H.R., Beckwith, A.L.J., and Goosen, A., *J. Chem. Soc*., 1965, p. 181.
11. Touchard, D. and Lessard, J., *Tetrahedron Lett*., 1971, vol. 12, p. 4425; Touchard, D. and Lessard, J., *Tetrahedron Lett*., 1973, vol. 14, p. 3827; Lessard, J., Mondon, M., and Touchard, D., *Can. J. Chem*., 1981, vol. 59, p. 4313; Mackiewsz, P. and Furstoss, R., *Tetrahedron*, 1978, vol. 34, p. 3241.
12. Fieser, L.F. and Fieser, M., *Reagents for Organic Synthesis*, New York: Wiley, vol. 4, 1974. Translated under the title *Reagenty dlya organicheskogo sinteza*, Moscow: Mir, 1978, vol. 7, p. 55.
13. Suslova, E.N. and Shainyan, B.A., *Russ. J. Gen. Chem*., 2010, vol. 80, p. 2059.
14. Suslova, E.N. and Shainyan, B.A., *Russ. J. Gen. Chem*., 2010, vol. 80, p. 2061.
15. Gharpure, S.J. and Reddy, S.R.P., *Tetrahedron Lett*., 2010, vol. 51, p. 6093.
16. Assensio, G., Andreu, C., Boix-Bernardini, C., Mello, R., and González-Nuñez, M.-E., *Org. Lett*., 1999, vol. 1, p. 2125.