ISSN 1070-4280, Russian Journal of Organic Chemistry, 2019, Vol. 55, No. 5, pp. 734–736. © Pleiades Publishing, Ltd., 2019.
Russian Text © The Author(s), 2019, published in Zhurnal Organicheskoi Khimii, 2019, Vol. 55, No. 5, pp. 810–813.

SHORT COMMUNICATIONS

Reaction of *N*,*N*'-Methylenebis(trifluoromethanesulfonamide) with Styrene under Oxidative Conditions

M. Yu. Moskalik[a], V. V. Astakhova[a], A. S. Ganin[a], and B. A. Shainyan[a,*]

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

Received January 18, 2019; revised February 10, 2019; accepted February 12, 2019

Abstract—The reaction of *N*,*N*'-methylenebis(trifluoromethanesulfonamide) with styrene in the oxidative system *t*-BuOCl/NaI affords triflamide, 2-iodo-1-phenylethanol, *N*,*N*'-bis(trifluoromethanesulfonyl)urea, and the product of styrene bistriflamidation. The mechanism is proposed involving hydrolysis and oxidation of the starting *N*,*N*'-methylenebis(trifluoromethanesulfonamide).

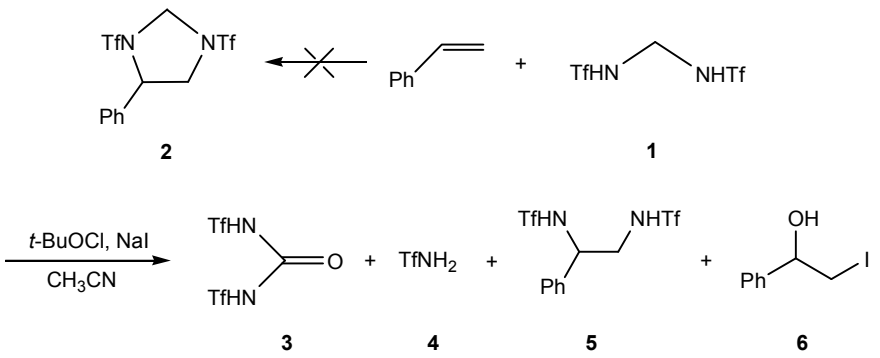
Keywords: *N*,*N*'-methylenebis(trifluoromethanesulfonamide), oxidation, styrene, triflamidation, oxyiodination

DOI: 10.1134/S1070428019050270

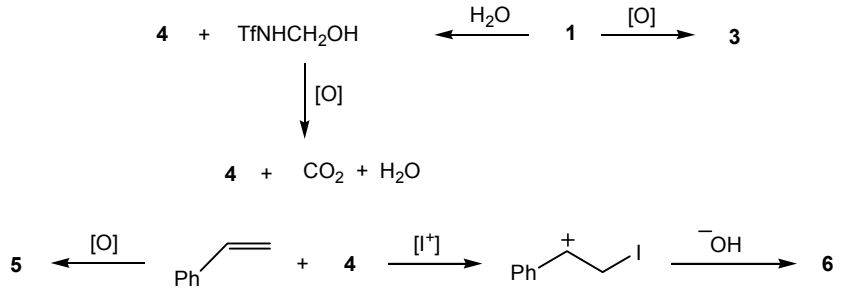
Many sulfonamides are important drugs. However, design of new, more active and less toxic, sulfonamide drugs still remains a topical issue. One the methods of synthesis of novel sulfonamide derivatives, providing a great variety of linear and cyclic products, is oxidative sulfamidation [1–6]. Our previous research on this synthetic approach showed that fluorinated sulfonamide (triflamide) often behaves quite differently from its nonfluorinated analogs [4–6]. Taking into account that the reactions of triflamide with unsaturated compounds in the oxidative system *t*-BuOCl/NaI results in preferential formation of bistriflamidation products, in the present work we decided to study the reaction of *N*,*N*'-methylenebis-(trifluoromethanesulfonamide) $(TfNH)_2CH_2$ **1** with styrene in the same oxidative system as a potential approach to the synthesis of imidazolidine derivatives by a [2+3] cycloaddition reaction involving both the triflamide moieties in compound **1** (Scheme 1).

The reaction was performed under cooling (–30°C) or at room temperature, as, according to our previous findings [6–8], the temperature can strongly affect the composition of the reaction products. The expected 1,3-bis(trifluoromethanesulfonyl)-4-phenylimidazolidine **2** was not detected in the reaction mixture at neither low nor room temperature. In both cases, individual compounds **3–6** were isolated by column chromatography and identified as *N*,*N*'-bis(trifluoromethanesulfonyl)-urea **3**, triflamide **4**, styrene bistriflamidation product **5** [5], and iodo alcohol **6** by means of IR and NMR spectroscopy and a comparison with the published

Scheme 1.



Scheme 2.



data. The effect of the temperature is manifested in that the total isolable yield of products **3–6** decreases from 80% at –30°C to 51% at room temperature, probably, because of a lower tarring of the reaction mixture at the negative temperature, and also the **3** : **4** : **5** : **6** product changes from 29 : 26 : 19 : 6 at –30°C to 10 : 18 : 8 : 15 at room temperature. Compound **3** was previously prepared by hydrolysis of bis(triflyl)-chloroformamidine TfNHC(Cl)=NTf [9]. It was reasonable to suggest that substituted urea **3** is formed by the oxidation of *N*,*N*'-methylenebis(trifluoromethanesulfonamide), which occurs under the reaction conditions and does not involve styrene. To obtain evidence for this suggestion, we performed this reaction under the same conditions (at –30°C) but in the absence of styrene and isolated compounds **3** (77%) and **4** (21%) with a nearly quantitate total yield. This result implies independent formation of urea **3** and products **4**–**6** and allows us to propose the following reaction mechanism (Scheme 2).

Thus, the reaction of *N*,*N*'-methylenebis(trifluoromethanesulfonamide) with styrene in the oxidative system *t*-BuOCl/NaI involves two independent routes. The first consists in the oxidation of the reagent to *N*,*N*'-bis(trifluoromethanesulfonyl)urea, as well as its hydrolysis with traces of water to triflamide and an *N*-(hydroxymethyl)triflamide intermediate, and the second, in the bistriflamidation of styrene and formation of a iodo alcohol, as we described earlier.

Reaction of *N*,*N*'-methylenebis(trifluoromethanesulfonamide) with styrene in an oxidative system. A solution of *N*,*N*'-methylenebis(trifluoromethanesulfonamide) (2.00 g, 6.5 mmol), styrene (0.68 g, 6.5 mmol), and NaI (2.93 g, 19.5 mmol) in 60 mL of acetonitrile was cooled to –30°C and protected from light, after which *t*-BuOCl (2.12 g, 19.5 mmol) was added dropwise to it in the dark. The mixture was stirred for a day under argon. The solvent was then removed in a vacuum, the residue was dissolved in 60 mL of ether and treated with aqueous $Na_2S_2O_3$, and the extract was dried over $CaCl_2$. The solvent was removed in a vacuum, and the residue was treated with ether. The residue insoluble in ether was recrystallized from hexane to obtain 0.60 g (29%) of *N*,*N*'-bis-(trifluoromethanesulfanyl)urea **3**. The liquid residue (1.6 g) was applied on a column of silica gel (AcrosOrganics, 0.060–0.200 nm) and eluted with hexane to isolate 0.10 g (6%) of 2-iodo-1-phenylethanol **6**, then with hexane–ether (1 : 1) to isolate 0.50 g (26%) of triflamide **4**, and finely with pure ether to isolate 0.50 g (19%) of *N*-[2-phenyl-2-(trifluoromethanesulfonyl)aminoethyl]triflamide **5**.

Oxidation of *N*,*N*'-methylenebis(trifluoromethanesulfonamide). A solution of NaI (0.72 g, 4.8 mmol) and *N*,*N*'-methylenebis(trifluoromethanesulfonamide) (0.50 g, 1.6 mmol) in 30 mL of acetonitrile was cooled to –30°C, after which *t*-BuOCl (0.52 g, 4.8 mmol) was added dropwise to it. The mixture was stirred for a day under argon. The solvent was then removed in a vacuum, the residue was dissolved in 30 mL of ether, treated with aqueous $Na_2S_2O_3$, and the extract was dried over $CaCl_2$. The solvent was removed in a vacuum, and the residue (0.3 g) was recrystallized from hexane to obtain 0.20 g (77%) of *N*,*N*'-bis-(trifluoromethanesulfonyl)urea **3** and 0.05 g (21%) of triflamide **4**.

***N*,*N*′-Bis(trifluoromethanesulfonyl)urea (3).** Yield 0.5 g (29%). White water-soluble powder, mp 123.8–124.7°C (from hexane; 129–131°C [9]). IR spectrum, ν, cm^{-1}: 3232, 2691, 1952, 1787, 1729, 1630, 1543, 1430, 1328, 1204, 1126, 976, 817, 757, 645, 595, 561, 500, 486. ^{1}H NMR spectrum (CD_3CN), δ, ppm: 8.72 s (1H, NH). ^{13}C NMR spectrum (CD_3CN), δ, ppm: 119.82 q (CF_3, *J* 320.3 Hz), 174.54 (C=O). ^{19}F NMR spectrum (CD_3CN): δ –79.7 ppm.

***N*-[2-Phenyl-2-(trifluoromethanesulfonyl)aminoethyl]trifluoromethanesulfonamide (5).** Yield 0.5 g (19%). Colorless crystals. The melting point and IR and NMR spectra are identical to those reported in [4].

2-Iodo-1-phenylethanol (6). Yield 0.10 g (6%). Oil with crystals. The NMR spectra are identical to those reported in [5].

The ^{1}H, ^{13}C, and ^{19}F NMR spectra were measured on Bruker DPX 400 and Bruker AV-400 spectrometers (400.13, 101.61, and 376.50 MHz, respectively), internal references HMDS (^{1}H, ^{13}C) and $CFCl_3$ (^{19}F). The IR spectra were obtained on a Bruker IFS 25 spectrometer in thin films.

N,N′-Methylenebis(trifluoromethanesulfonamide) was prepared by the condensation of triflamide with Paraform by the procedure described in [10]. Monitoring of the reaction progress and column chromatography separation was performed by TLC on Merck silica gel 60 F_{254} plates, eluent hexane–ether, 1 : 1.

ACKNOWLEDGMENTS

The work was performed using the equipment of the Baikal Analytical Center for Collective Use, Siberian Branch, Russian Academy of Sciences.

FUNDING

The work was financially supported by the Russian Foundation for Basic Research (project no. 17-03-00213).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Minakata, S., Morino, Y., Oderaotoshi, Y., and Komatsu, M., *Chem. Commun*., 2006, p. 3337. doi 10.1039/B606499J
2. Zhang, G., An, G., Zheng, J., Pan, Y., and Li, G., *Tetrahedron Lett*., 2010, vol. 51, p. 987. doi 10.1016/j.tetlet.2009.12.059
3. Yu, W.Z., Chen, F., Cheng, Y.A., and Yeung, Y.Y., *J. Org. Chem*., 2015, vol. 80, p. 2815. doi 10.1021/jo502416r
4. Shainyan, B.A., Moskalik, M.Y., Starke, I., and Schilde, U., *Tetrahedron*, 2010, vol. 66, p. 8383. doi 10.1016/j.tet.2010.08.070
5. Astakhova, V.V., Moskalik, M.Yu., Ganin, A.S., Sterkhova, I.V., and Shainyan, B.A., *ChemistrySelect*, 2018, vol. 3, p. 5960. doi 10.1002/slct.201801379
6. Shainyan, B.A., Astakhova, V.V., Ganin, A.S., Moskalik, M.Y., and Sterkhova, I.V., *RSC Adv*., 2017, vol. 7, p. 38951. doi 10.1039/C7RA05831D
7. Moskalik, M.Yu., Astakhova, V.V., Schilde, U., Sterkhova, I.V., and Shainyan, B.A., *Tetrahedron*, 2014, vol. 70, p. 8636. doi 10.1016/j.tet.2014.09.050
8. Moskalik, M.Yu., Astakhova, V.V., Sterkhova, I.V., and Shainyan, B.A., *ChemistrySelect*, 2017, vol. 2, p. 4662. doi 10.1002/slct.201701147
9. Petrik, V.N., Kondratenko, N.V., and Yagupolskii, L.M., *J. Fluorine Chem.*, 2003, vol. 124, p. 151. doi 10.1016/S0022-1139(03)00202-1
10. Meshcheryakov, V.I., Albanov, A.I., and Shainyan, B.A., *Russ. J. Org. Chem*., 2005, vol. 41, p. 1381. doi 10.1007/s11178-005-0351-3