Russian Journal of Organic Chemistry, Vol. 39, No. 10, 2003, pp. 1517–1521. Translated from Zhurnal Organicheskoi Khimii, Vol. 39, No. 10, 2003, pp. 1583–1587.

Dedicated to Full Member of the Russian Academy of Sciences B.A. Trofimov on the 65th Anniversary of His Birth

Reactions of 1,2,3-Triazoles with Trifluoromethanesulfonyl Chloride and Trifluoromethanesulfonic Anhydride

V. I. Meshcheryakov, B. A. Shainyan, L. L. Tolstikova, and A. I. Albanov

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

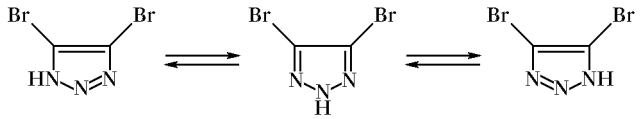
Received May 28, 2003

Abstract—Reactions of 4,5-dibromo-1,2,3-triazole, 1*H*-1,2,3-benzotriazole, and 2-phenyl-2*H*-1,2,3-triazole-4-carbonyl chloride with trifluoromethanesulfonyl chloride and trifluoromethanesulfonic anhydride were studied. 4,5-Dibromo-1,2,3-triazole sodium salt reacted with CF_3SO_2Cl in tetrahydrofuran to give 4,5-dibromo-2-(2-tetrahydrofuryl)-2*H*-1,2,3-triazole rather than expected 4,5-dibromo-2-trifluoromethylsulfonyl-2*H*-1,2,3-triazole. The latter was synthesized by treatment of 4,5-dibromo-1,2,3-triazole sodium salt with trifluoromethanesulfonic anhydride. The reaction of benzotriazole with $(CF_3SO_2)_2O$ afforded 1-trifluoromethylsulfonyl-1*H*-1,2,3-benzotriazole and 1,2,3-benzotriazolium trifluoromethanesulfonate. 2-Phenyl-2*H*-1,2,3-triazole-4-carbonyl chloride reacted with trifluoromethanesulfonamide sodium salt in DMF, yielding *N*-(dimethylaminomethylene)trifluoromethanesulfonamide. Possible ways for formation of the unexpected products were proposed.

In continuation of our studies on trifluoromethylsulfonyl derivatives of azoles [1], in the present work we examined the possibility for introduction of a trifluoromethylsulfonyl group into the heteroring or side chain of various 1,2,3-triazoles. Preliminary experiments showed that 4-nitro-1,2,3-triazole sodium salt, whose nucleophilicity is reduced due to the presence of a nitro group, does not react with trifluoromethanesulfonyl chloride. Sodium salt derived from 1,2,3-triazole does react with CF_3SO_2Cl, but the products thus formed are unstable, and they undergo spontaneous thermal decomposition on attempted isolation. Taking the above into account, as substrates we selected 4,5-dibromo-1,2,3-triazole (**I**), 1*H*-1,2,3-benzotriazole (**II**), and 2-phenyl-2*H*-1,2,3-triazole-4-carbonyl chloride (**III**). On the one hand, these compounds should be more reactive toward electrophiles than 4-nitro-1,2,3-triazole, and on the other, the corresponding trifluoromethylsulfonyl derivatives were expected to be more stable due to the presence of bulky substituents.

Like other 1,2,3-triazoles having no substituents on the nitrogen atoms, 4,5-dibromo-1,2,3-triazole (**I**) can exist as 1*H*- and 2*H*-tautomers, as follows from analysis of the ^{13}C NMR spectra recorded in various solvents at different temperature. The ^{13}C NMR spectrum of a solution of **I** in acetone-d_6 contains two signals: a narrow peak at δ_C 124.2 ppm and a broadened signal at δ_C 125.3 ppm with an intensity ratio of ~1 : 4. In DMSO-d_6, only one broadened signal is present at δ_C 123.7 ppm with a halfwidth of 37 Hz. On heating to 100°C, it becomes narrower (to 8 Hz) and shifts by 0.9 ppm upfield. The observed pattern may be interpreted in terms of the equilibrium shown in Scheme 1. In going from polar acetone to even more polar DMSO, the equilibrium shifts completely toward the more polar 1(3)*H*-tautomer.

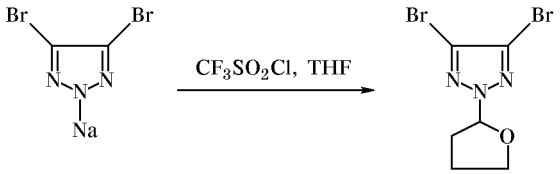
Scheme 1.



Our attempts to replace the bromine atoms in **I** by CF_3SO_2 or CF_3SO_2NH group via reaction with sodium trifluoromethanesulfinate or trifluoromethane-

sulfonamide sodium salt were unsuccessful. Compound **I** turned out to be inactive toward nucleophilic substitution by such weak nucleophiles. The reaction of triazole **I** with sodium hydrogen carbonate gave sodium salt 2Na-**I** which was then treated with trifluoromethanesulfonyl chloride in tetrahydrofuran with a view to obtain 4,5-dibromo-2-trifluoromethylsulfonyl-2*H*-1,2,3-triazole. Surprisingly, the isolated product was 4,5-dibromo-2-(2-tetrahydrofuryl)-2*H*-1,2,3-triazole (**IV**) (Scheme 2).

Scheme 2.

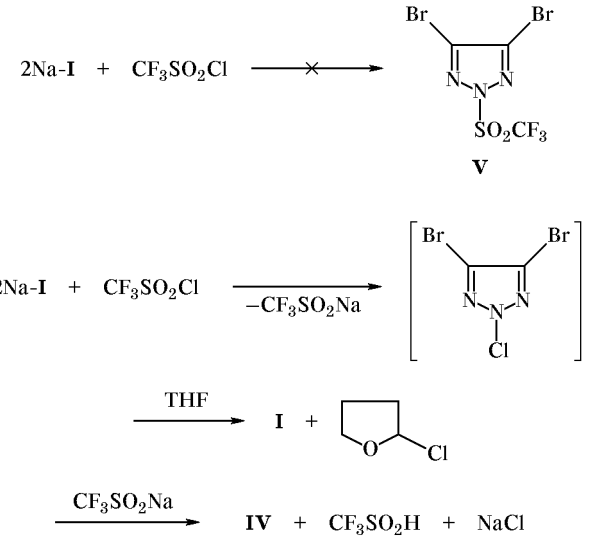


2Na-**I** **IV**

The structure of compound **IV** was unambiguously proved by the ^1H and ^{13}C (proton-coupled) NMR spectra, mass spectrum, and elemental analysis. The symmetric structure of 2-substituted triazole **IV** follows from the presence of only one signal from the triazole ring carbon atoms in the ^{13}C NMR spectrum (δ_C 125 ppm).

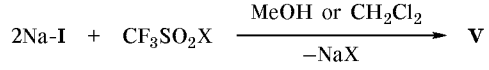
Giller *et al.* reported on the synthesis of *N*-(2-tetrahydrofuryl)-substituted heterocycles exhibiting a high anticarcinogenic activity [such as Ftorafur, 5-fluoro-1-(2-tetrahydrofuryl)-1,2,3,4-tetrahydropyrimidine-2,4-dione] by reaction of N-mercurated [2] or N-silylated [3] heterocycles with 2-chlorotetrahydrofuran. Taking into account that tetrahydrofuran readily undergoes chlorination at the α-position by the action of, e.g., sulfuryl chloride [4] and that trifluoromethanesulfonyl chloride is capable of acting as chlorinating agent [5, 6], intermediate formation of 2-chlorotetrahydrofuran in the reaction of CF_3SO_2Cl with THF could be presumed. In fact, tetrahydrofuran reacts with CF_3SO_2Cl, but the reaction is fairly slow and is accompanied by almost complete tarring. On the other hand, addition of CF_3SO_2Cl to a solution of 2Na-**I** in THF results in almost instantaneous separation of a white solid. It is known [7] that 2-chlorotetrahydrofuran is also formed by reaction of THF with *N*-chlorotriazoles. Therefore, we propose Scheme 3 as a possible way of formation of compound **IV**.

Scheme 3.



We succeeded in synthesizing the target product, 4,5-dibromo-2-trifluoromethylsulfonyl-2*H*-1,2,3-triazole (**V**), by reaction of sodium salt 2Na-**I** with trifluoromethanesulfonyl chloride in methanol or with trifluoromethanesulfonic anhydride in methylene chloride according to the procedure described in [8] (Scheme 4). In the ^{13}C NMR spectrum of **V** we observed only one signal from the triazole carbon atoms (δ_C 137 ppm).

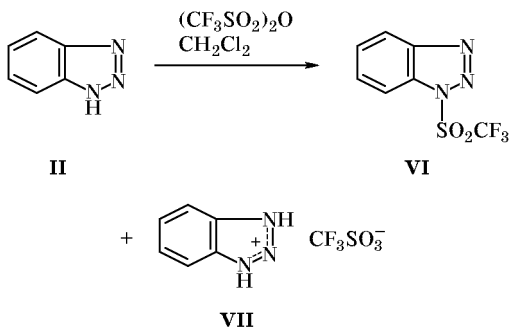
Scheme 4.



X = Cl, CF_3SO_3.

Due to the presence of fused benzene ring, benzotriazole (**II**) exists exclusively as the 1*H*-tautomer. It smoothly reacted with trifluoromethanesulfonic anhydride under mild conditions, leading to 1-trifluoromethylsulfonyl-1*H*-1,2,3-benzotriazole (**VI**) and 1,2,3-benzotriazolium trifluoromethanesulfonate (**VII**) (Scheme 5). Compound **VI** showed in the ^{13}C NMR spectrum a quartet signal from the CF_3 group and six signals from the benzene ring carbon atoms, while

Scheme 5.



II VI

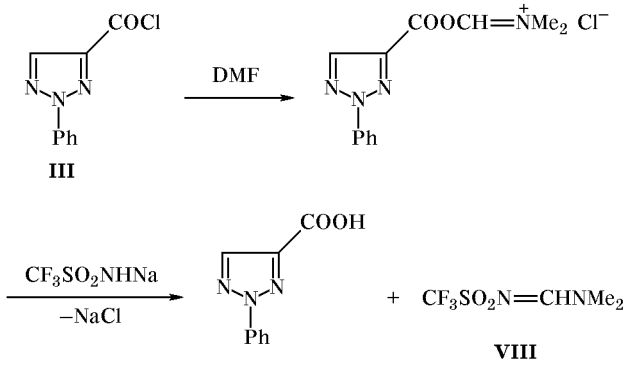
VII

only three aromatic carbon signals were present in the spectrum of **VII**. These data indicate asymmetric structure of *N*-trifluoromethylsulfonyl derivative **VI** and symmetric structure of salt **VII**.

Thus the trifluoromethylsulfonylation of 1,2,3-triazoles and their sodium salts can occur in both usual way, leading to the corresponding *N*-trifluoromethylsulfonyl derivatives (compounds **V** and **VI**), and anomalous mode, leading to oxidative coupling product **IV** with reduction of sulfonate moiety to sulfinate.

We also tried to synthesize a mixed imide, *N*-trifluoromethylsulfonyl-2-phenyl-2*H*-1,2,3-triazole-4-carboxamide (which was expected to be a very strong NH acid), by reaction of 2-phenyl-2*H*-1,2,3-triazole-4-carbonyl chloride (**III**) with trifluoromethanesulfonamide sodium salt in dimethylformamide. However, the products were *N*-(dimethylaminomethylene)trifluoromethanesulfonamide (**VIII**) and 2-phenyl-2*H*-1,2,3-triazole-4-carboxylic acid (Scheme 6).

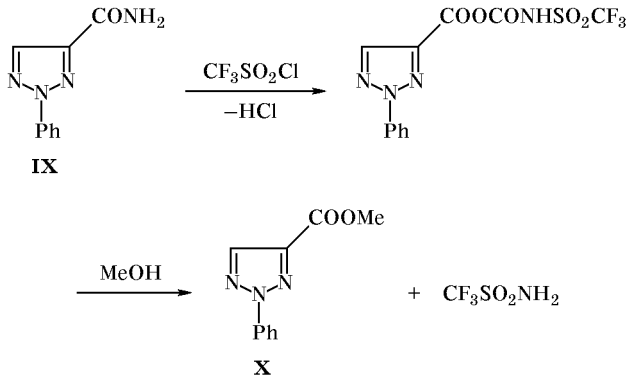
Scheme 6.



The synthesis *N*-perfluoroalkylsulfonylamidines of the general formula $RFSO_2N{=}C(R)NR^1R^2$ was described in [9–11]. These compounds are obtained by reaction of *N*-trimethylsilylamide $C_4F_9SO_2NHSiMe_3$ with dimethylformamide in the presence of CsF [9], by reaction of sodium salt $C_4F_9SO_2NHNa$ with the Vilsmeier reagent ($POCl_3$ + DMF) [10], and by reaction of perfluoroalkanesulfonyl azides with ketones and secondary amines [11]. Obviously, in our case, acyl chloride **III** initially reatcs with DMF to give an adduct analogous to the Vilsmeier reagent. Its subsequent reaction with trifluoromethanesulfonamide sodium salt yields formamidine **VIII** and triazolecarboxylic acid.

An alternative route is the reaction of 2-phenyl-2*H*-1,2,3-triazole-4-carboxamide (**IX**) with CF_3SO_2Cl in methanol. However, it afforded methyl 2-phenyl-2*H*-1,2,3-triazole-4-carboxylate (**X**) and trifluoromethanesulfonamide instead of the desired mixed imide. Taking into account that amide **IX** does not react with methanol, the reaction is likely to follow a nucleophilic catalysis pattern with formation of intermediate having a highly nucleofugal CF_3SO_2NH group, which then undergoes methanolysis (Scheme 7).

Scheme 7.



EXPERIMENTAL

The IR spectra were recorded on an IKS-29 spectrometer from samples prepared as KBr pellets or dispersed in mineral oil. The NMR spectra were obtained on a Bruker DPX-400 instrument at 400 MHz for ^1H, 100 MHz for ^{13}C, and 376 MHz for ^{19}F; the chemical shifts were measured relative to TMS (^1H and ^{13}C; HMDS was used as internal reference) and CCl_3F (^{19}F). The mass spectra (70 eV) were run on a Hewlett–Packard HP 5971A mass-selective detector coupled with an HP 5890 gas chromatograph (Ultra-2 column, 5% of phenylmethylsilicone; injector temperature 250°C; oven temperature programming from 70 to 280°C at 20 deg/min). The progress of reactions was monitored by thin-layer chromatography using Silufol UV-254 plates.

Reaction of 4-nitro-2*H*-1,2,3-triazole sodium salt with trifluoromethanesulfonyl chloride. To a solution of 4-nitro-2*H*-1,2,3-triazole sodium salt in acetone we added dropwise under stirring and cooling an equimolar amount of trifluoromethanesulfonyl chloride in dioxane. The mixture was stirred for 1 h and was then heated for 2 h under reflux. After appropriate treatment, initial 4-nitro-2*H*-1,2,3-triazole was isolated.

Reaction of 1,2,3-triazole sodium salt with trifluoromethanesulfonyl chloride. To a solution of 1,2,3-triazole sodium salt in tetrahydrofuran we added dropwise under stirring and cooling an equimolar amount of trifluoromethanesulfonyl chloride in THF.

The mixture was stirred for 1 h, heated for 2 h under reflux, and cooled. The precipitate was filtered off, and the filtrate was evaporated. The viscous semicrystalline residue underwent spontaneous decomposition with strong heat evolution and tarring on exposure to air (in an attempt to dry the product).

4,5-Dibromo-2-(2-tetrahydrofuryl)-2*H*-1,2,3-triazole (IV). A solution of 1.5 g (0.006 mol) of 4,5-dibromo-2*H*-1,2,3-triazole sodium salt (4,5-dibromo-2*H*-1,2,3-triazole was synthesized by the procedure described in [12]) in 20 ml of tetrahydrofuran was cooled to 10–15°C, and a solution of 1 g (0.006 mol) of trifluoromethanesulfonyl chloride in 5 ml of THF was added dropwise. The mixture slightly warmed up, and a colorless solid precipitated. When the addition was complete, the mixture was stirred for 2 h at room temperature and for 1 h at 60°C, cooled, poured into ice water, and extracted with two portions of diethyl ether. The combined ether extracts were washed with a solution of sodium carbonate and with water, dried over $MgSO_4$, and evaporated to isolate 1.68 g (94%) of crude product **IV** which was purified by recondensation under reduced pressure. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.03 m (1H, $NCCH_B$), 2.34 m (2H, $OCCH_2$), 2.54 m (1H, $NCCH_A$), 4.00 d.t (1H, OCH_B, J = 6.8, 7.6 Hz), 4.11 d.t (1H, OCH_A, J = 6.4, 7.6 Hz), 6.16 d.d (1H, CH, J = 2.4, 6.4 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 23.95 t ($OCH_2\mathbf{C}H_2$, J_{CH} = 131.9 Hz), 31.10 t (N**C**, J_{CH} = 133.2 Hz), 69.76 t (OCH_2, J_{CH} = 149.4 Hz), 93.57 d (NCO, J_{CH} = 169.4 Hz), 125.02 (C=N). Mass spectrum, *m/z* (I_{rel}, %): 295 (2) $[M]^+$, 117 (4) $[C_2NBr]^+$, 79 (4) $[Br]^+$, 71 (100) $[C_4H_7O]^+$, 43 (20) $[C_2H_3O]^+$. Found, %: C 23.76; H 2.31; N 14.10. $C_6H_7Br_2N_3O$. Calculated, %: C 24.27; H 2.38; N 14.15.

4,5-Dibromo-2-trifluoromethylsulfonyl-2*H*-1,2,3-triazole (V). *a*. A solution of 2.5 g (0.01 mol) of 4,5-dibromo-2*H*-1,2,3-triazole sodium salt in 5 ml of methanol was added dropwise over a period of 30 min to a solution of 2.54 g (0.015 mol) of trifluoromethanesulfonyl chloride in 10 ml of methanol, cooled to 3–5°C. A white solid gradually precipitated during the addition. The mixture was stirred for 2–3 h at room temperature, the progress of the reaction being monitored by TLC. The precipitate was filtered off and washed with cold methanol, and the solvent was distilled off from the filtrate to isolate 3.42 g (95%) of compound **V** as slightly yellowish crystals. ^{13}C NMR spectrum (acetone-d_6), δ_C, ppm: 119.47 q (CF_3, J_{CF} = 324.0 Hz), 136.83 (X=N). ^{19}F NMR spectrum: δ_F –73.58 ppm. Found, %: C 10.67; H 11.56. $C_3Br_2F_3N_3O_2S$. Calculated, %: C 10.04; H 11.71.

b. 4,5-Dibromo-2*H*-1,2,3-triazole sodium salt, 1.5 g (0.006 mol), was added in portions to a solution of 0.93 g (0.0033 mol) of trifluoromethanesulfonic anhydride in 30 ml of methylene chloride, cooled to –78°C, the mixture was stirred for 30 min at that temperature, the cooling bath was removed, and the mixture was stirred for 1 h at room temperature. The precipitate of sodium trifluoromethanesulfonate was filtered off and washed with methylene chloride, the filtrate was combined with the washings, and the solvent was distilled off to obtain 1.54 g (71%) of compound **V** as an orange viscous material. The ^{13}C and ^{19}F NMR spectra of the product coincided with those of a sample prepared as described in *a*.

Reaction of 1*H*-1,2,3-benzotriazole (II) with trifluoromethanesulfonic anhydride. To a solution of 0.6 g (5 mmol) of 1*H*-1,2,3-benzotriazole in 8 ml of methylene chloride we added dropwise under stirring at room temperature 0.71 g (2.5 mmol) of trifluoromethanesulfonic anhydride, and the mixture was stirred for 1 h and was left to stand for 24 h. The precipitate was filtered off, washed with anhydrous diethyl ether, and dried. The product was 1,2,3-benzotriazolium trifluoromethanesulfonate (**VII**), yield 0.77 g (100%), colorless crystals with mp 144°C. IR spectrum, ν, cm^{-1}: 3100–2700, 1620, 1430, 1290–1130, 1030, 1010, 900, 780, 760, 640, 510. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 7.99 m (2H, 5-H, 6-H), 8.32 m (2H, 4-H, 7-H), 13.0–15.5 br.s (2H, NH). ^{13}C NMR spectrum (acetone-d_6), δ_C, ppm: 115.07 (C^4, C^7), 131.85 (C^5, C^6), 135.02 (C^8, C^9), 121.78 q (CF_3, $^1J_{CF}$ = 319.30 Hz). ^{19}F NMR spectrum (acetone-d_6): δ_F –79.09 ppm. Found, %: C 31.71; H 2.23; F 19.89; N 15.74; S 11.80. $C_7H_6F_3N_3O_3S$. Calculated, %: C 31.23; H 2.25; F 21.17; N 15.61; S 11.91.

Evaporation of the filtrate gave 0.56 g (89%) of 1-trifluoromethylsulfonyl-1*H*-1,2,3-benzotriazole (**VI**) as brownish crystals with mp 35°C. IR spectrum, ν, cm^{-1}: 1600, 1490, 1440, 1280–1110, 1060, 900, 780, 750, 680, 610, 580, 550, 520. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 7.77 d.d.d (1H, 6-H, $J_{4,6}$ = 1.3, $J_{5,6}$ = 7.0, $J_{6,7}$ = 8.3 Hz), 7.97 d.d.d (1H, 5-H, $J_{4,5}$ = 8.3, $J_{5,7}$ = 1.1 Hz), 8.01 d.d.d (1H, 4-H, $J_{4,7}$ = 0.9 Hz), 8.34 d.d.d (1H, 7-H). ^{13}C NMR spectrum (acetone-d_6), δ_C, ppm: 112.66 (C^4), 120.11 q (CF_3, $^1J_{CF}$ = 322.8 Hz), 122.51 (C^7), 128.49 (C^6), 133.08 (C^8), 133.59 (C^5), 145.60 (C^9). ^{19}F NMR spectrum (acetone-d_6): δ_F –76.09 ppm. Found, %: C 33.65; H 1.65; F 22.06; N 16.40; S 13.67. $C_7H_4F_3N_3O_2S$. Calculated, %: C 33.47; H 1.61; F 22.69; N 16.73; S 12.76.

***N*-(Dimethylaminomethylene)trifluoromethanesulfonamide (VIII).** A solution of 1.63 g (9.5 mmol) of trifluoromethanesulfonamide sodium salt in 10 ml of DMF was added dropwise to a mixture of 1.95 g (9.5 mmol) of 2-phenyl-2*H*-1,2,3-triazole-4-carbonyl chloride (**III**) (prepared by treatment of 2-phenyl-2*H*-1,2,3-triazole-4-carboxylic acid [13] with $SOCl_2$) and 20 ml of DMF, cooled to 10–15°C. The mixture was stirred for 2 h at room temperature, the solvent was removed on a rotary evaporator, the residue was treated with an alcohol–hexane mixture, and the precipitate of 2-phenyl-2*H*-1,2,3-triazole-4-carboxylic acid, 1.07 g (60%), was filtered off, washed, and dried in air. The mother liquor was concentrated to isolate formamidine **VIII** which was purified by recrystallization from diethyl ether–hexane. Yield 1.83 g (94%), mp 90–92°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.15 s (3H, NCH_3), 3.24 s (3H, NCH_3), 8.05 s (1H, CH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 35.98 q (NCH_3, J_{CH} = 139.4 Hz), 41.94 q (NCH_3, J_{CH} = 139.8 Hz), 119.56 q (CF_3, J_{CF} = 320.5 Hz), 162.08 d (CH, J_{CH} = 186.3 Hz). ^{19}F NMR spectrum: δ_F –78.50 ppm. Found, %: C 23.68; H 3.77; F 27.55; N 13.66; S 15.48. $C_4H_7F_3N_2O_2S$. Calculated, %: C 23.53; H 3.46; F 27.92; N 13.72; S 15.70.

Methyl 2-phenyl-2*H*-1,2,3-triazole-4-carboxylate (X). A solution of 0.67 g (0.004 mol) of trifluoromethanesulfonyl chloride in 5 ml of methanol was added dropwise at room temperature to a mixture of 0.5 g (2.7 mmol) of 2-phenyl-2*H*-1,2,3-triazole-4-carboxamide (**IX**) [14] and 0.56 g (4 mmol) of K_2CO_3 in 10 ml of methanol. The mixture was stirred for 2 h and poured into ice water, and the precipitate was filtered off and dried in air. Yield 0.52 g (95%), mp 84–85°C; published data [13]: mp 85–86°C.

The authors thank Yu.A. Chuvashev for recording the mass spectrum of compound **IV**.

REFERENCES

1. Shainyan, B.A. and Meshcheryakov, V.I., *Russ. J. Org. Chem.*, 2001, vol. 37, p. 1797.
2. Giller, S.A., Zhuk, R.A., and Lidak, M.Yu., *Dokl. Akad. Nauk SSSR*, 1967, vol. 176, p. 332.
3. Giller, S.A., Lidak, M.Yu., Zhuk, R.A., Berzinya, A.E., Pets, K.Ya., Getsova, I.N., and Bruk, E.I., *Khim. Geterotsikl. Soedin.*, 1969, p. 375.
4. Hakimelahi, G.H. and Just, G., *Tetrahedron Lett.*, 1979, p. 3643.
5. Shainyan, B.A., Ustinov, M.V., and Nindakova, L.O., *Russ. J. Org. Chem.*, 2001, vol. 37, p. 1757.
6. Kruse, C.G., Broekhof, N.L.G.M., and van der Gen, A., *Tetrahedron Lett.*, 1976, p. 1725.
7. Becker, H.G.O., Eisenschmidt, V., Bubig, M., Jähnisch, K., Klein, N., Kowalski, W., Misselwitz, R., Muller, R., Reimann, P., Roth, C., Sauter, W.-D., Schlöβer W., and Thorein, B., *Z. Chem.* 1969, vol. 9, p. 325.
8. Hendrickson, J.B. and Sternbach, D.D., *J. Org. Chem.*, 1975, vol. 40, p. 3450.
9. Niederprum, H., Voss, P., and Beyl, V., *Justus Liebigs Ann. Chem.*, 1973, vol. 767, p. 20.
10. Xu, G., Xu, B., Qin, C., and Zhu, S., *J. Fluorine Chem.*, 1997, vol. 84, p. 25.
11. Xu, Y., Wang, Y., and Zhu, S., *Synthesis*, 2000, p. 513.
12. Huttel, R. and Gebhardt, A., *Justus Liebigs Ann. Chem.*, 1947, vol. 558, p. 34.
13. Riebsomer, J.L. and Sumrell, G., *J. Org. Chem.*, 1948, vol. 13, p. 807.
14. Meshcheryakov, V.I., Mikiya, D.V., Kirillova, L.P., Shul'gina, V.M., and Vereshchagin, L.I., *Russ. J. Org. Chem.*, 1997, vol. 33, p. 1641.