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Triflamides and Triflates of Six-membered Heterocyclic Amines

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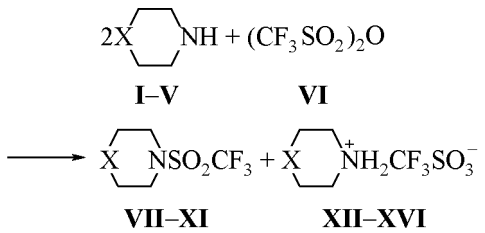
Abstract—Reactions of secondary cyclic amines (piperidine, morpholine, thiomorpholine, 1λ⁶,4-thiazinane-1,1-dione) with trifluoromethanesulfonic anhydride or with *N*-phenyltriflimide both in the presence and in the absence of a base (Et_3N) result in formation of corresponding triflamides and triflates of the initial amines. The triflates and triflamides can be distinguished by their ^{19}F and ^{15}N NMR spectra and the presence in the IR spectra of salts of absorption bands in the region 3270–3000 cm^{-1} lacking in the spectra of triflamides.

Triflamides CF_3SO_2NHR and triflimide $(CF_3SO_2)_2NH$ are strong NH-acids which find application as catalysts in various chemical processes, and their lithium salts are used nowadays as electrolytes in the high-voltage current sources [1–3]. When treated with nucleophiles these compounds are capable to be cleaved both at the R–N and S–N bonds [4], and sometimes even at the C–S bond [5, 6]. Triflamides and triflimides are readily obtained in reaction of amines with one or two equiv of trifluoromethanesulfonic anhydride $(CF_3SO_2)_2O$ in the presence of triethylamine used for binding the liberated acid and preventing the formation of the initial amine triflate salt [4, 7]. In the absence of the binding base the reaction affords a mixture of triflamide and triflate salt as in the synthesis of 1-trifluoromethylsulfonyl-1*H*-imidazole currently applied as triflating agent [8]. As an alternative triflating agent for aliphatic and primary aromatic amines was suggested *N*-phenyltriflimide $(CF_3SO_2)_2NPh$ [7]. The reaction with primary amines and piperidine occurred with a high yield, but the secondary amines failed to react [9]. Although the procedure was obviously simple, sometimes mistakes still arose: For instance, a compound obtained from piperidine and *N*-phenyltriflimide and described as piperidine triflamide [9] turned actually to be its triflate salt (see below), and the conclusion on "unexpected selectivity of the reaction" was also wrong. In the present study in extension of the investigation of N-triflated derivatives from heterocyclic series [10] we carried out reactions of piperidine, morpholine, piperazine, thiomorpholine, λ⁶,4-thiazinane-1,1-dione) with trifluoromethanesulfonic anhydride and *N*-phenyltriflimide aiming, firstly, at comparison of characteristics of the corresponding triflamides and triflates and at establishing spectral criteria for their distinguishing, and, secondly, at elucidating whether the heterocyclic secondary amines may be brought into reaction with *N*-phenyltriflimide. The reaction of compounds **I–V** with $(CF_3SO_2)_2O$ was performed in the absence of triethylamine or any other substance for binding the liberated acid in order to obtain both types of reaction products, triflamides and triflate salts. The reaction follows the general equation



X = CH_2 (**I, VII, XII**); O (**II, VIII, XIII**); NH (**III**); S (**IV, X, XV**); CF_3SO_2N (**IX**); $CF_3SO_3^-\ N_{H_2}^+$ (**XIV**); SO_2 (**V, XI, XVI**).

The triflate salts precipitate if the reaction is carried out in a mixture Et_2O–CH_2Cl_2 and thus are easily separated from triflamides. Triflamides **VII–XI** and salts **XII–XVI** have very similar ^1H and ^{13}C NMR spectra (save the very easily exchangeable NH-protons of the salts), their elemental composition also is much alike. As criteria for distinguishing may serve the position of the signal in the ^{19}F NMR spectra that for triflamides **VII–XI** is located downfield (–76 ppm) with respect to that of salts **XII–XVI** (–79 ppm), and the chemical shift of ^{15}N quite dissimilar for these types of compounds (see table). As

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Physicochemical constants and NMR spectra of compounds **VII**–**XVI**

Compd no.	bp (mp), °C × mm^{-1} Hg^{-1}	^{1}H NMR spectrum, δ, ppm			^{13}C NMR spectrum, δ, ppm				^{19}F NMR spectrum, δ, ppm	^{15}N NMR spectrum, δ, ppm
		X	XCH_2	CH_2N	X	XCH_2	CH_2N	CF_3 (*J*, Hz)		
VII	63–64/1	1.68	1.68	3.50	23.76	26.33	48.19	121.16 (323.1)	–76.82	–292.3
VIII	59–60/1	–	3.75	3.50	–	67.00	47.39	121.11 (323.0)	–77.05	–295.8
IX	133	–	3.78	3.78	–	47.26	47.26	120.87 (322.3)	–76.82	
X	–[a]	–	2.89	3.50	–	27.64	49.33	120.61 (322.4)	–76.99	
XI	162	–	3.35	4.08	–	52.24	46.74	120.63 (322.0)	–77.34	
XII	145	1.72	1.88	3.33	22.58	23.17	45.94	121.72 (319.0)	–79.05	–341.93
XIII	101	–	3.99	3.46	–	64.30	45.03	121.63 (319.8)	–79.23	–345.0
XIV	370	–	3.67	3.67	–	41.61	41.61	121.03 (319.4)	–78.87	
XV	103	–	3.66	3.06	–	24.75	47.17	121.77 (320.3)	–78.88	
XVI	207	–	3.65	4.02	–	49.10	45.18	121.55 (319.8)	–78.90	

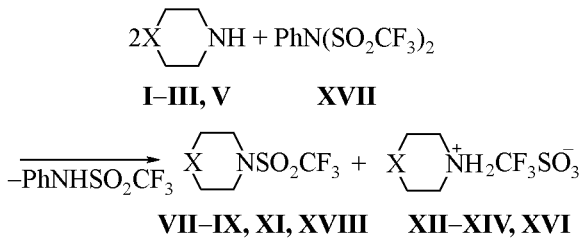
[a] The physicochemical constants of 1-trifluoromethylsulfonyl)thiomorpholine (X) were not determined because of its easy tarring. The structure was proved by ^{1}H, ^{13}C, and ^{19}F NMR spectra.

independent criterium serves the presence in the IR spectra of salts **XII**–**XVI** of the characteristic bands of vibrations from the H_2N^+ group in the region 3270–3000 cm^{-1} lacking in the spectra of triflamides.

Triflamide **VII** was previously prepared from piperidine and *N*-phenyltriflimide in the presence of triethylamine and described (almost simultaneously) both as a liquid (without mentioning the boiling point) [11] and as crystalline substance of mp 134–135°C [9].

According to our data triflamide **VII** is a liquid boiling at 63–64°C at 1 mm Hg. But both in the presence and in the absence triethylamine formed also piperidinium triflate (**XII**). The N-triflamide reacted similarly also with the other secondary amines **II, III, V** in the absence of triethylamine affording both types of products, triflamides **VII**–**XI** and salts **XII**–**XVI**, the latter prevailing.

In the ^{19}F NMR spectrum of the reaction mixture obtained from piperazine **III** and N-phenyltriflimide



X = CH_2 (**I, VII, XII**); O (**II, VIII, XIII**); NH (**III, XVIII**); CF_3SO_2N (**IX**); $CF_3SO_3^-NH_2$ (**XIV**); SO_2 (**V, XI, XVI**).

in the "triflamide" region besides the signal of compound **IX** is observed a less strong peak located around –76.41 ppm that is tentatively assigned to monosubstituted compound **XVIII**.

EXPERIMENTAL

IR spectra were recorded on spectrophotometer IKS-29 from thin film, KBr pellets, or mulls in mineral oil. ^{1}H, ^{13}C, ^{15}N, and ^{19}F NMR spectra were registered on spectrometer Bruker DPX 400 (400 MHz for protons) from solutions in $CDCl_3$, internal reference HMDS, the chemical shifts are presented with respect to TMS (^{1}H, ^{13}C), CH_3NO_2 (^{15}N), and CCl_3F (^{19}F). Chemical shifts of ^{15}N signals were obtained from the two-dimensional spectra 2D(^{1}H–^{15}N)with the use of a gradient probe in a mode *hmbcgp*. N-Phenyltriflimide was prepared by procedure [7], mp 95–96°C. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 7.6–7.7 m (Ph). ^{13}C NMR spectrum (acetone-d_6), δ, ppm: 120.16 q (CF_3, $^1J_{CF}$ 324.3 Hz), 131.03 (C_o), 131.95 (C_m), 132.64 (C_1), 133.27 (C_n). ^{19}F NMR spectrum (acetone-d_6), δ, ppm: –72.49.

Reaction of amines with trifluoromethanesulfonic anhydride (general procedure). To a solution of 0.01–0.02 mol of amine in 10–20 ml of dichloromethane cooled to –78°c was added dropwise at stirring 0.005–0.01 mol (with piperazine equimolar amount) of solution of trifluoromethansulfonic anhydride in dichloromethane. The cooling was removed, the reaction mixture was stirred at room

temperature and left standing for 24 h. The precipitated amine triflate salt was filtered off, and evaporation of the filtrate afforded the corresponding triflamide. If the salt did not precipitate, the reaction mixture was evaporated, treated with anhydrous ether, and the precipitated amine triflate was separated.

1-(Trifluoromethanesulfonyl)piperidine (VII). Yield 43%. Colorless liquid, n_D^{22} 1.4134. IR spectrum, cm^{-1}: 3000–2860, 1460, 1390, 1230–1130, 1050, 950, 770, 710, 600, 500. Found, %: C 32.79; H 4.76; F 25.32; N 6.56; S 15.87. $C_6H_{10}F_3NO_2S$. Calculated, %: C 33.18; H 4.64; F 26.24; N 6.45; S 14.76.

1-(Trifluoromethanesulfonyl)morpholine (VIII). Yield 53%. Colorless liquid, n_D^{20} 1.4127. IR spectrum, cm^{-1}: 2980–2860, 1460, 1390, 1280–1110, 1070, 970, 770, 710, 620, 590, 500. Found, %: C 27.49; H 3.37; F 24.93; N 6.23; S 14.83. $C_5H_8F_3NO_3S$. Calculated, %: C 27.40; H 3.68; F 26.00; N 6.39; S 14.63.

1,4-Bis(trifluoromethanesulfonyl)piperazine (IX). Yield 66%. IR spectrum, cm^{-1}: 1390, 1350, 1230–1140, 1080, 950, 770, 710, 610, 590, 440. Found, %: C 20.61; H 2.34; N 7.38; S 18.74. $C_6H_8F_6N_2O_4S_2$. Calculated, %: C 20.58; H 2.30; N 8.00; S 18.31.

4-(Trifluoromethanesulfonyl)-1λ⁶,4-thiazinane-1,1-dione (XI). Yield 35%. IR spectrum, cm^{-1}: 1390, 1305, 1280–1110, 1080, 1020, 920, 700, 710, 600, 580, 450. Found, %: C 22.32; H 3.11; N 5.29; S 23.68. $C_5H_8F_3NO_4S_2$. Calculated, %: C 22.47; H 3.02; N 5.24; S 23.99.

Piperidinium trifluoromethanesulfonate (XII). Yield 100%. IR spectrum, cm^{-1}: 3270–3050, 1290–1230, 1165, 1120, 640. Found, %: 30.76; H 5.19; F 23.86; N 6.00; S 14.34. $C_6H_{12}F_3NO_3S$. Calculated, %: C 30.64; H 5.14; F 24.23; N 5.95; S 13.63.

Morpholinium trifluoromethanesulfonate (XIII). Yield 96%. IR spectrum, cm^{-1}: 3250–3000, 1600, 1460, 1310–1230, 1170, 1105, 1030, 900, 880, 640, 510. Found, %: C 25.88; H 4.46; N 5.99; S 14.13. $C_5H_{10}F_3NO_4S$. Calculated, %: C 25.32; H 4.25; N 5.91; S 13.52.

Piperazinium trifluoromethanesulfonate (XIV). Yield 100%. IR spectrum, cm^{-1}: 3240–3000, 1560, 1440, 1320–1240, 1170, 1080, 1030, 950, 870, 650, 590, 520. Found, %: C 19.79; H 3.14; F 27.43; N 7.85; S 15.79. $C_6H_{12}F_6N_2O_6S_2$. Calculated, %: C 18.66; H 3.13; F 29.51; N 7.25; S 16.60.

Thiomorpholinium trifluoromethanesulfonate (XV). IR spectrum, cm^{-1}: 3230–3070, 1600, 1330–1230, 1170, 1030, 630. Found, %: C 23.12; H 3.92; N 5.94; S 25.49. $C_5H_{10}F_3NO_3S_2$. Calculated, %: C 23.71; H 3.98; N 5.53; S 25.32.

1,1-Dioxo-1λ⁶,4-thiazinan-4-ium trifluoromethanesulfonate (XVI). Yield 87%. IR spectrum, cm^{-1}: 3250–3000, 1390–1170, 1070, 1020, 950, 840, 630, 520, 430. Found, %: C 21.86; H 3.59; N 4.86. $C_5H_{10}F_3NO_5S_2$. Calculated, %: C 21.05; H 3.53; N 4.91.

Reaction of amines I–III, V with *N*-phenyltriflimide (XVII) (general procedure). To a solution of *N*-phenyltriflimide (0.5 mmol) in dichloromethane (3 ml) was added at room temperature 0.5 mmol of amine. The reaction mixture was stirred at room temperature and left overnight. The solution was evaporated. The crystalline residue was a mixture of the initial *N*-phenyltriflimide (**XVII**), triflamide **VII–IX, XI**, triflate **XII–XIV, XVI**, and *N*-phenyltriflamide.

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