spectrophotometer in a temperature-controled cuvette with an iron-Constantan thermocouple, in a thin layer between the NaCl substrates. GLC was performed on a LKhM-8MD-2 chromatograph on a steel column (2000×3 mm) filled with Porapak Q, with catharometer as the detector; the carrier gas was He (1.2 L h^{-1}).

Acids **1**, **6** were distilled before use; CE were used without special purification. The TD and kinetic investigations were carried out according to known procedures.[4] In typical experiments, a mixture of 1 mmol of **1** or **6** and 3 mmol of CE was homogenized (except for the systems containing **4**) and heated under isothermal conditions. The resultant gases were identified by chromatography using reference samples. The retention times (min) are: 4.5 (CO_2) and 6.5 (**7**) at 60 °C, 1.5 (CO_2); 3 (**9b**, **c**); 3.4 (**9a**) and 5.5 (**8**) at 170 °C. The ratio of **9a** to **9b** was determined from the ^{19}F NMR spectra.

^{19}F NMR ($CDCl_3$, relative to $CFCl_3$); δ: **8**, 79.12 (tt, J = 9.3 Hz; 2.2 Hz, 3 F, CF_3); 126.39 (m, 2 F, CF_3); 128.95 (m, 2 F, CF_2); 136.22 (dm, J = 51.9 Hz, 2 F, CF_2H); **9a**, ($F^{-1}F^{-2}C{=}CF^{-3}{-}CF_2{}^{-4}{-}CF_3{}^{-5}$); 85.64 (3 F, CF_3); 86.36 (1 F, $=CF^{-2}$); 103.10 (1 F, $=CF^{-1}$, 120.46 (2 F, CF_2); 191.42 (1 F, J_{1-2} = 52.7 Hz, J_{1-3} = 117.8 Hz, J_{1-4} = 27.8 Hz, J_{1-5} = 3.2 Hz, J_{2-3} = 39.5 Hz, J_{2-4} = 5.6 Hz, J_{3-4} = 14.8 Hz, J_{3-5} = 6.6 Hz, J_{4-5} = 2.4 Hz); **9b**, 64.55, (m, 3 F, CF_3); 141.50 (m, 1 F, =CF); **9c**, 6712 (m, 3 F, CF_3); 159.84 (m, 1 F, =CF).

The reaction conditions and the yield of gases are given in Table 1, and the kinetic parameters are given in Table 2.

References

1. N. Nae and J. Jagur-Grodzinski, *J. Chem. Soc., Farad. Trans.1*, 1977, **73**, 1951.
2. H.-J. Buschman, *Polyhedron*, 1987, **6**, 1469.
3. V. S. Khomenko and L. I. Krasovskaya, *Koordinats. Khimiya*, 1991, **17**, 994 [*Coordination Chem.*, 1991, **17** (Engl. Transl.)].
4. A. V. Podolskii, T. G. Khonina, T. I. Filyakova, M. I. Kachalkova, and M. I. Kodess, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1991, 2259 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1991, **40**, 1977 (Engl. Transl.)].
5. R. N. Griffin and M. I. Bro, *J. Org. Chem.*, 1960, **25**, 1068.
6. E. N. Eremin, *Osnovy khimicheskoy kinetiki v gasakh i rastvorakh* [*Fundamentals of Chemical Kinetics in Gases and in Solution*], Moscow State University Press, Moscow, 1971, 43 (in Russian).
7. J. Villepin, A. Laute, and M.-L. Josien, *Anal. Chim.*, 1966, **1**, 365.
8. N. K. Dalley, J. S. Smith, S. B. Lanson, J. J. Christensen, and R. M. Izatt, *Chem. Communs.*, 1975, 43.
9. J. Jagur-Grodzinski, *Isr. J. Chem.*, 1985, **25**, 39.
10. G. W. Gokel, D. M. Goli, C. Minganti, and Echegoyen, *J. Am. Chem. Soc.*, 1983, **105**, 6786.
11. V. V. Yakshin and B. N. Laskorin, *Dokl. Akad. Nauk SSSR*, 1984, **274**, 868 [*Dokl. Chem.*, 1984, **274** (Engl. Transl.)].

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Studies of transformations of 4-X-2,3,5,6-tetrafluoro-2′-amino-substituted diphenyl ethers in DMF

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The rate of cyclization of pentafluoro- (**1**) and 4-Cl-2,3,5,6-tetrafluoro-2′-NHY-diphenyl ethers (**2a**, Y=Ac; **2b**, Y=H; **2c**, Y=Me) to form phenoxazines on refluxing in DMF increases with an increase in the nucleophilicity of the amino group. The cyclization of the N-acetyl derivative **2a** is followed by the Smiles rearrangement, whereas the transformation of ethers **2b** and **c**, containing free amino and N-methylamino groups, respectively, includes mainly an attack on the amino group at the *ortho*-position of the fluorinated ring. In the case of ether **2c**, introduction of K_2CO_3 into the reaction mixture results in cyclization with the Smiles rearrangement.

Key words: 2-aminopolyfluorodiphenyl ether; DMF; cyclization; Smiles rearrangement, polyfluorophenoxazine.

We have shown previously that 4-X-2,3,5,6-tetrafluoro-2′-acetylaminodiphenyl ethers **1a** (X = F) and **2a** (X = Cl) undergo cyclization into phenoxazines[1,2] on heating to 80 °C in DMF in the presence of potash. The

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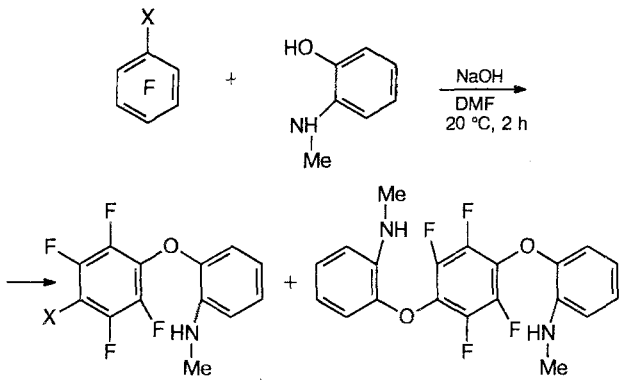
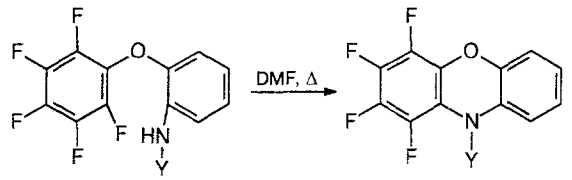
Scheme 1



1c (82 %)
2c (21 %)**

3 (18 %)*

Scheme 2



1a—c

Y = Ac (**a**), H (**b**), Me (**c**)

4a (20 %)
4b (70 %)
4c (70 %)**

structure of the phenoxazine derivative obtained from ether **2a** indicates that the Smiles rearrangement precedes the cyclization step.[2] On the other hand, it has been shown that 2,3,4,5,6-pentafluoro-2′-aminodiphenyl ether (**1b**) remains intact on heating in DMF at 100 °C.[3] Since the nucleophilicity of an attacking group is known to be one of the factors which determine the possibility of realization of the Smiles rearrangement,[4—6] we have studied the transformation of 4-X-2,3,5,6-tetrafluoro-2′-NHY-diphenyl ethers **1a—c** (X = F) and **2a—c** (X = Cl; Y = Ac, H, Me) in DMF.

The synthesis of diphenyl ethers **1a,b** and **2a,b** has been reported previously.[1,2] The use of DMF (instead of pyridine) as the solvent for the synthesis of compound **2b** made it possible to carry the reaction out at room temperature (for 2 h) and to increase the yield of the target product (*cf.* ref. 2). The previously unknown diphenyl ethers **1c** and **2c**, containing the methylamino group at the 2′ position, were prepared by the interaction of C_6F_6 or C_6F_5Cl with *o*-methylaminophenol in DMF in the presence of NaOH. Apart from compound **1c**, the reaction with C_6F_6 gave a product of the substitution of two fluorine atoms (**3**). Isomeric diphenylamines were absent in the reaction mixture (Scheme 1).

It was shown in the present study that the prolonged boiling of compounds **1a—c** in DMF results in their transformation into phenoxazines (**4a—c**) (Scheme 2); diphenylamines (products of the possible Smiles rearrangement of the original ethers) were not found in the reaction mixture. According to ^{19}F NMR spectra, compounds **4a** and **4b** are identical with those obtained previously.[1] The structure of phenoxazine **4c** was established on the basis of elemental analysis data, IR and ^{19}F NMR spectra. It should be noted that in the latter, the signal of the F(1) atom, which is located in the *peri*-position relative to the Me group, is additionally split due to spin-spin coupling with the H atoms of the methyl group (J = 5.5 Hz). Accordingly, the signal of the Me group in the ^1H NMR spectrum of phenoxazine **4c** is displayed as a doublet with J = 5.5 Hz.

The transformation rate of ethers **1** increased with an increase in the nucleophilicity of the amino group. Thus, the reaction mixtures prepared by boiling compounds **1a** and **1b** in DMF for 12 h contained 80 and 30 % of the original product, respectively. The transformation of ether **1c** proceeded completely in 2 h.

One may assume two pathways for the formation of phenoxazines **4a—c** from diphenyl ethers **1a—c**. Path A involves the Smiles rearrangement *via* a spirocomplex **5**. Path B involves attack on the amino group at position 2 of the fluorinated ring followed by the elimination of a fluoride ion. For pentafluorodiphenyl ethers **1**, both of these routes lead to the same product, phenoxazine **4**. In order to find which path is preferable, we studied the transformations of the ethers **2**.

Thus, the prolonged heating (36 h) of diphenyl ether **2a** in DMF was shown to result in the formation of a mixture of phenoxazines **6a** and **6b** (65 and 20 %, respectively). The presence of the latter in the reaction product is due to deacetylation of compound **6a** under the reaction conditions.[7] The absence of a **7a** type structure in the mixture of phenoxazine derivatives indicates that the transformation of diphenyl ether **2a** on boiling in DMF proceeds exclusively *via* path A, which involves the Smiles rearrangement.

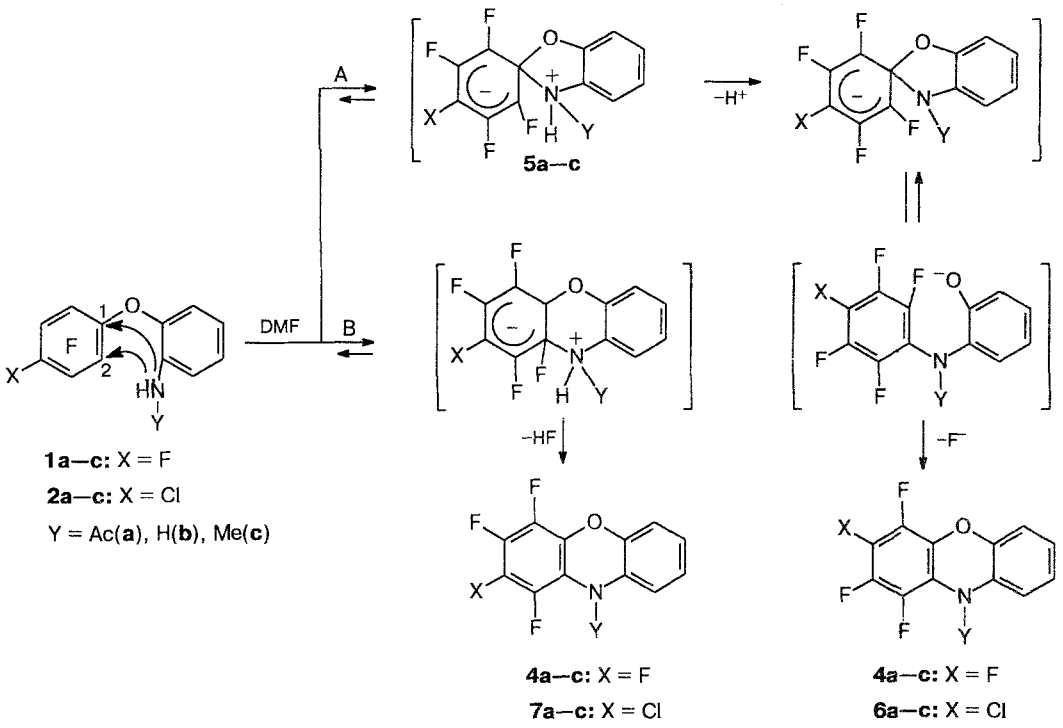
The transformation of compound **2b**, containing a nonsubstituted amino group, proceeds faster and results in the formation of phenoxazine **7b** as the main product (80 %); the amount of compound **6b** in the mixture is only ~10 %. Phenoxazine **6b** is identical with that obtained previously (according to the ^{19}F NMR spectrum).[2] The structure of compound **7b** was established on the basis of mass spectrometry and IR and ^{19}F NMR spectroscopy.

The introduction of an electron-donating methyl substituent into the amino group accelerats the process. Thus, the complete transformation of **2c** into a mixture of phenoxazines **6c** and **7c** with predominance of the latter (5:95) was achieved in 3 h by boiling in DMF.

* Hereinafter, the compositions of mixtures given are based on ^{19}F NMR spectral data.

** Isolated yield.

Scheme 3



Thus, in contrast to the N-acylated ether **2a**, the cyclization of diphenyl ethers **2b** and **c**, which contain free or N-methylated amino groups, mostly occurs by substitution of the fluorine atom at position 2 of the fluorinated ring without the Smiles rearrangement.

The results obtained were rationalized on the basis of the above Scheme 3. Taking into account the orientation rules in the nucleophilic substitution in the polyfluoroaromatic series,[8] one may assume that process A is preferred. Its first step involves attack on the amino group at position 1 to form spirocomplex **5**. The sequence of further transformations leads to a phenoxazine **6**. This route is realized for ether **2a**, which contains an acylamino group that possesses comparatively low nucleophilicity. In our opinion, the change in the direction of the reaction in the case of compounds **2b** and **2c**, which contain the more nucleophilic amino and N-methylamino groups, is caused by difficulties in the realization of the second step, *i.e.*; deprotonation of spirocomplex **5**. Reaction route B, which begins with an intramolecular attack on the amino group at the less electrophilic position 2, appears to be preferable for ethers **2b** and **2c**. The reversibility of the formation of spirocomplex **5** is the prerequisite for the realization of process B (*cf.* ref. 9). The comparative reactivities of compounds **2b** and **2c** are in agreement with the data that the formation of a σ-complex[10] is the rate-limiting step in the nucleophilic substitution in the polyfluoroaromatic series.

There are some literature examples of the Smiles rearrangement, in which the rate of the process was determined by the deprotonation of the spirocomplex, and such rearrangements have been shown to be subject to base catalysis.[9,11] This suggests that the introduction of a base into the reaction medium would result in the transformation of ethers **2b,c** by route A with the Smiles rearrangement.

We found that boiling **2b** in DMF in the presence of K_2CO_3 resulted in the formation of complex mixtures of products, among which phenoxazine **6b** (~10 %) was identified by ^{19}F NMR spectroscopy. The only product isolated was compound **8** (37 %), which we believe on the basis of IR and mass-spectral data, as well as literature analogies to be N,C-biphenoxazine.[7] Phenoxazine **7b** was not found in the reaction mixtures.

The transformation of compound **2c** in the presence of K_2CO_3 proceeded under milder conditions (130 °C, 1 h) and more smoothly to give a reaction mixture with a predominance of phenoxazine **6c** (90 %). In the absence of the base under the same conditions only phenoxazine **7c** was formed (40 %) together with the recovered ether **2c**.

Experimental

IR spectra were recorded on UR-20 and Specord M 80 instruments in $CHCl_3$. ^1H and ^{19}F NMR spectra were obtained on Bruker WP-200 SY and Bruker AC-200 (188.28

MHz) spectrometers. Chemical shifts are given in ppm with respect to TMS and C_6F_6, respectively. Molecular weights were determined on a Finnigan MAT 8200 instrument.

Preparation of 2,3,4,5,6-pentafluoro-2′-methylaminodiphenyl ether (1c) and 1,4-bis(2-methylamino)phenoxy-2,3,5,6-tetrafluorobenzene (3). A mixture of 2-methylaminophenol (0.28 g) and ground NaOH (0.10 g) in 6 mL of DMF was stirred for 15 min at ~20 °C. Then, C_6F_6 (0.26 mL, 0.41 g) in 1 mL of DMF was added. The reaction mixture was stirred for 2 h, poured into water and neutralized with 10 % HCl, and the products were extracted with ether. The ethereal layer was washed with water and dried with $CaCl_2$. After evaporation of the ether, the residue contained compounds **1c** and **3** in the ratio of 82:18 (according to the ^{19}F NMR spectrum), which were isolated by column chromatography (SiO_2, L 100/250) in benzene.

2,3,4,5,6-Pentafluoro-2′-methylaminodiphenyl ether (1c) was isolated in a yield of 47 %; MS, *m/z* (found) 289.0527, *m/z* (calculated for $C_{13}H_8F_5NO$) 289.0526. IR, ν/cm^{-1}: 2825 (CH_3), 3460 (NH). ^{19}F NMR spectrum (DMF), δ: −0.4, 0.9, and 7.1, the ratio of the intensities is 2:1:2.

1,4-Bis(2-methylaminophenoxy)tetrafluorobenzene (3) was isolated in a yield of 7 %, m.p. 137—141 °C (from light petroleum); MS, *m/z* (found): 392.1153, *m/z* (calculated for $C_{20}H_{16}F_4N_2O_2$): 392.1148. IR, ν/cm^{-1}: 2825 (CH_3), 3460 (NH). ^{19}F NMR spectrum in THF contained a singlet at 7.0 ppm.

Transformation of compounds (1). Compounds **1a—c** (0.1 g) were refluxed in 0.3 mL of DMF for 12 h. After cooling to ~20 °C, the reaction mixtures were analyzed by ^{19}F NMR spectroscopy. Phenoxazines **4a** and **4b** were identified in the reaction mixtures on the basis of ^{19}F NMR spectra.[2]

1,2,3,4-Tetrafluoro-10-methylphenoxazine (4c) was isolated in a yield of 70 %, m.p. 118—121 °C (from aqueous ethanol). Found (%): C, 58.26; H, 2.42; F, 28.38; N, 5.20. Calculated for $C_{13}H_7F_4NO$ (%): C, 58.00; H, 2.62; F, 28.23; N, 5.20. IR, ν/cm^{-1}: 2850 (br, NH). ^{19}F NMR spectrum (DMF), δ: −6.8 (td, F(3), $J_{F(3),F(2)} = J_{F(3),F(4)} = 22$ Hz, $J_{F(3),F(1)} = 5.5$ Hz); −3.9 (td, F(2), $J_{F(2),F(1)} = J_{F(2),F(3)} = 22$ Hz, $J_{F(2),F(4)} = 4$ Hz); −1.4 (ddd, F(4), $J_{F(4),F(3)} = 22$ Hz, $J_{F(4),F(1)} = 5.5$ Hz, $J_{F(4),F(2)} = 4$ Hz); 4.6 (dq, F(1), $J_{F(1),F(2)} = 22$ Hz, $J_{F(1),F(3)} = J_{F(1),F(4)} = J_{F(1),CH} = 5.5$ Hz). ^1H NMR (DMSO-d_6), δ: 3.3 (d, 3H, CH_3, $J_{CH_3,F(1)} = 5.5$ Hz) and 6.8—7.1 (4 H, C_6H_4).

Preparation of diphenyl ethers (2b,c). Finely ground NaOH (5.4 mmol) was added to a solution of the corresponding aminophenol (5 mmol) in 15 mL of DMF, and the mixture was stirred for 15—20 min at ~20 °C. Then, a solution of C_6F_5Cl (1.1 g, 5.2 mmol) in 1 mL of DMF was added dropwise. The reaction mixture was stirred for 2 h, poured into water, and neutralized with 10 % HCl. The precipitated product **2b** was filtered off; product **2c** was extracted with ether. Compounds **2b,c** were purified by chromatography on SiO_2 (L 100/160) in benzene.

4-Chloro-2,3,5,6-tetrafluoro-2′-aminodiphenyl ether 2b was prepared in a yield of 21 %, m.p. 63—66 °C. The IR and ^{19}F NMR spectra were identical with those of the product obtained previously.[5]

4-Chloro-2,3,5,6-tetrafluoro-2′-methylaminodiphenyl ether 2c, yield 50 %; MS, *m/z*, found: 305.0228, *m/z*, calculated for $C_{13}H_8ClF_4NO$: 305.0230. IR, ν/cm^{-1}: 2815 (CH_3), 3450 (NH). ^{19}F NMR spectrum (DMF), δ: 8.3 and 20.8; the ratio of the intensities is 1:1.

Transformation of diphenyl ethers 2 in DMF. Ethers **2a—c** (0.12 g) were refluxed in 3 mL of DMF for the time indicated in Table 1. The reaction mixtures were poured into water and the products were extracted with ether. The residue obtained after evaporation of ether (0.10 g) was analyzed by ^{19}F NMR spectroscopy in $CDCl_3$ (Table 1).

Table 1. Transformation of aminodiphenyl ethers **2a—c** into phenoxazines **6** and **7**

Compound	Reaction time /h	Composition of the reaction mixture according to the ^{19}F NMR (%)		
		2	**6**	**7**
2a	36	15	65*	—
2b	12	10	10	80
2c	3	—	5	95

* The mixture also contains ~20 % of compound **6b**.

According to the ^{19}F NMR spectra, compounds **6a,b** are identical to phenoxazines obtained previously.[5]

Compounds **7b,c** were isolated from the reaction mixtures (Table 1) by column chromatography (SiO_2, L 100/160) in light petroleum (b.p. 70—100 °C).

2-Chloro-1,3,4-trifluorophenoxazine (7b) was obtained in 73 % yield. MS, *m/z* (exp.) 271.0008. $C_{12}H_5ClF_3NO$. MS, *m/z* (calc.) 271.0012. IR, ν/cm^{-1}: 3415 (NH). ^{19}F NMR ($CDCl_3$), δ: −0.7, 12.8, and 17.2, the ratio of the intensities is 1:1:1.

2-Chloro-1,3,4-trifluoro-10-methylphenoxazine (7c). A. The yield was 72 %, m.p. 99—102 °C, (from hexane). Found (%): C, 54.40; H, 2.45; Cl, 14.59; F, 19.60; N, 4.77. Calculated for $C_{13}H_7ClF_3NO$ (%): C, 54.66; H, 2.47; Cl, 14.41; F, 19.95; N, 4.90. IR, ν/cm^{-1}: 2830 (CH_3). ^{19}F NMR ($CDCl_3$), δ: −0.8 (dd, F(4), $J_{F(4),F(3)} = 22$ Hz, $J_{F(4),F(1)} = 7$ Hz); 15.5 (dd, F(3), $J_{F(3),F(4)} = 22$ Hz, $J_{F(3),F(1)} = 6$ Hz); 27.7 (ddq, F(1), $J_{F(1),F(4)} = 7$ Hz, $J_{F(1),F(3)} = 6$ Hz, $J_{F(1),CH3} = 5$ Hz). ^1H NMR ($CDCl_3$), δ: 3.3 (d, 3H, CH_3, $J_{CH_3,F(1)} = 5$ Hz); and 3 6.6—7.0 (4 H, C_6H_4).

B. Ether **2c** (0.12 g) was stirred in 3 mL of DMF for 1 h at 130 °C. The reaction mixture was poured into water and the product was extracted with ether. The residue obtained after evaporation of ether (0.11 g) contained the starting compound **2c** and phenoxazine **7c** in the ratio of 60:40 (according to the ^{19}F NMR spectrum).

Transformation of diphenyl ethers 2b,c in DMF in the presence of K_2CO_3. A. Ether **2b** (0.12 g) and K_2CO_3 (0.12 g) were refluxed in 3 mL of DMF for 12 h. The reaction mixture was poured into water, neutralized with 10 % HCl, and the products were extracted with ether. Evaporation of the solvent gave a dark oil (0.10 g) containing ~10 % of phenoxazine **6b** according to the ^{19}F NMR spectrum. Biphenoxazine **8** (0.08 g, 36 %) was isolated by column chromatography on SiO_2 (L 100/200) in benzene; *m/z*, found: 522. The pattern of the mass spectrum is characteristic for compounds with two Cl atoms; *m/z*, calculated for $C_{24}H_9Cl_2F_5N_2O_2$: 522.

B. Ether **2c** (0.12 g) and K_2CO_3 (0.12 g) were stirred in 3 mL of DMF for 1 h at 130 °C. The reaction mixture was poured into water, neutralized with 10 % HCl, and the products were extracted with ether. Evaporation of ether gave 0.10 g of phenoxazines **6c** and **7c** in the ratio of 90:10 according to ^{19}F NMR spectral data. **6c** (0.09 g, 82 %) was isolated by column chromatography on SiO_2 (L 100/160).

3-Chloro-1,2,4-trifluoro-10-methylphenoxazine (6c), m.p. 115—118 °C (from hexane). Found (%): C, 54.29; H, 2.33; Cl, 13.97; F, 19.49; N, 4.68. Calculated for $C_{13}H_7ClF_3NO$ (%):

C, 54.66; H, 2.47; Cl, 14.41; F, 19.95; N, 4.90. IR, ν/cm^{-1}): 2850 (CH_3). ^{19}F NMR ($CDCl_3$), δ: 4.1 (ddq, F(1), $J_{F(1),F(2)}$ = 21 Hz, $J_{F(1),F(4)}$ = 7 Hz, $J_{F(1),CH3}$ = 5 Hz); 17.2 (dd, F(2), $J_{F(2),F(1)}$ = 21 Hz, $J_{F(2),F(4)}$ = 5 Hz); 18.7 (dd, F(4); $J_{F(4),F(1)}$ = 7 Hz, $J_{F(4),F(2)}$ = 5 Hz). ^1H NMR ($CDCl_3$), δ: 3.3 (d, 3 H, CH_3, $J_{CH_3,F(1)}$ = 5 Hz); 6.6—7.0 (4H, C_6H_4).

References

1. T. V. Mikhalina, E. F. Kolchina, T. N. Gerasimova, and E. P. Fokin, *Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk*, 1984, **1**, 113 (in Russian).
2. E. F. Kolchina, I. Yu. Kargapolova, and T. N. Gerasimova, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1986, 1855 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1986, **35**, 1685 (Engl. Transl.)].
3. T. N. Gerasimova, E. F. Kolchina, and I. Yu. Kargapolova, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1987, 2814 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1987, **36**, 2611 (Engl. Transl.)].
4. E. W. Truce, E. M. Kreider, and W. W. Brand, *Organic Reactions*, J.Wiley, New York—London—Sydney—Toronto, 1970, **18**, 99.
5. K. C. Roberts, C. G. M. Worms, and H. B. Clark, *J. Chem. Soc.*, 1935, 196.
6. J. F. Bunnett and R. E. Zahler, *Chem. Rev.*, 1951, **49**, 273.
7. E. F. Kolchina and T. N. Gerasimova, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1990, 850 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1990, **39**, 759 (Engl. Transl.)].
8. L. S. Kobrina, *Fluor. Chem. Rev.*, 1974, **7**, 1.
9. A. C. Knipe, J. Lound-Keast, and N. Sridhar, *J. Chem. Soc., Perkin Trans. 2*, 1984, 1885.
10. R. D. Chamders, J. S. Waterhouse, and D. L. H.Williams, *J. Chem. Soc., Perkin Trans. 2*, 1977, 585.
11. C. F. Bernascone and C. L. Gehriger, *J. Am. Chem. Soc.*, 1974, **96**, 1092.

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Synthesis of 2- and 4-chloropyrimidines with hydroxyphenyl substituents by the interaction of Vilsmeier—Haack reagents with (hydroxyphenyl)dihydropyrimidin-2- and -4-ones

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The reaction of 2- and 4-hydroxypyrimidines containing *ortho*- and *para*-hydroxyphenyl substituents with Vilsmeier—Haack reagents generated *in situ* from DMF and $SOCl_2$ or $POCl_3$ results in the chemoselective replacement of the heterocyclic hydroxyl group by chlorine and formylation of the phenolic hydroxyl group. Aryl formates are hydrolyzed under the conditions of their isolation to give the corresponding phenols, especially if the pyrimidyl fragment is *ortho* to the formyloxy group.

Key words: thionyl chloride, phosphoryl chloride, dimethylformamide, Vilsmeier—Haack reagents, dihydropyrimidinones, chloropyrimidines, phenols, aryl formates, ^1H NMR.

Chloropyrimidines are important starting compounds in the synthesis of various pyrimidine derivatives due to the high reactivity of chlorine atoms at the even positions of the ring. The main method for the synthesis of these compounds is the action of $POCl_3$ (normally, in the presence of dialkylanilines) or Vilsmeier—Haack complexes on hydroxypyrimidines.[1]

Earlier,[2] we suggested a one-step method for the synthesis of chloropyrimidines with *ortho*-hydroxyphenyl substituents by treating (*o*-hydroxyphenyl)dihydropyrimidin-2- and -4-ones with the $SOCl_2$/DMF reagent in $SOCl_2$. Data on this type of compound in the azine series and their benzo-analogs is severely limited. The case when a labile chlorine atom and an *ortho*-phenolic fragment are simultaneously present in a pyrimidine molecule is undoubtedly of scientific and practical interest since the formation of a strong intramolecular hydrogen bond between the phenolic hydroxyl and the aza

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