New derivatives of fluorine-containing phenazines

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1,2-Epoxyperfluorocyclohexane reacts with 3,3′,4,4′-tetra-aminobiphenyl (1:1 mol/mol) to give 4-(6,6,7,7,8,8,9,9-octa-fluoro-6,7,8,9-tetrahydrophenazin-2-yl)benzene-1,2-diamine whose structure was determined by X-ray crystallography. Reactions of the latter with 1,2-epoxyperfluorocyclohexane or benzil bring about new fluorinated phenazine derivatives.
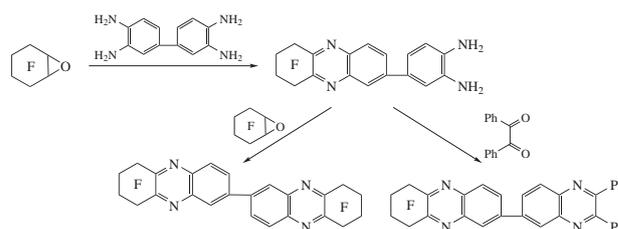
Oxides of terminal and internal perfluoroalkenes have a wide synthetic potential.[1–14] However, only a few representatives of perfluorocycloalkene oxides are known, therefore their reactivity has been studied insufficiently.
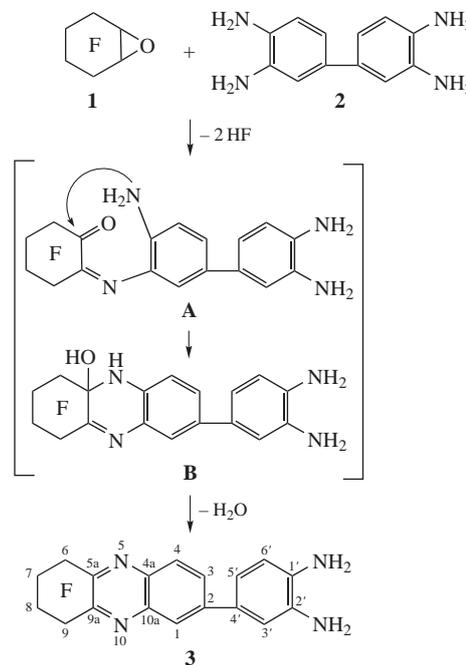
Previously, we used hypohalite epoxidation to obtain 1,2-epoxyperfluorocyclohexane **1**[13,14] and showed that it readily reacts with nucleophilic reagents to give products of epoxy ring opening.[14,15] The reactivity of compound **1** toward bi- and polynucleophilic reagents is little-studied. To date, only three examples of reactions of oxirane **1** with binucleophilic reagents are known, namely, with urea, thiourea and *o*-phenylenediamine. All of them occur with epoxy ring opening followed by formation of new fluorinated heterocyclic compounds (Scheme 1).[16]
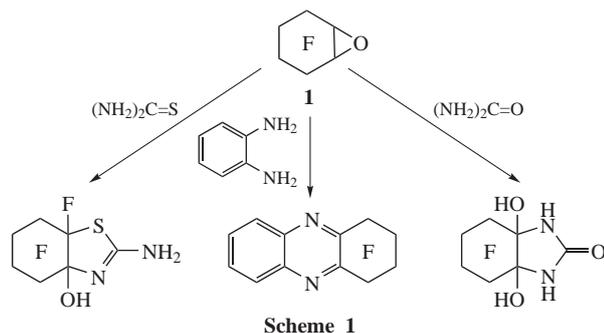
Scheme 1

In this study, we extended the scope of epoxide **1** reactions from *o*-phenylenediamine towards its binuclear analogue, 3,3′,4,4′-tetra-aminobiphenyl **2** (Scheme 2). Actually, oxirane **1** reacts with an equimolar amount of tetramine **2** to afford a new fluorinated phenazine derivative **3**.[†] The reaction apparently occurs *via* intermediates

A and **B**. The latter is stabilized by elimination of a water molecule to give a more stable aromatic system (see Scheme 2). Diaminophenylphenazine **3** comprises perfluorocyclic, aromatic and heterocyclic moities and can be of interest as a building block in the construction of conjugated fluorinated heterocyclic systems possessing biological activity and luminescent properties.

Scheme 2

reflectance attachment or a diffusion reflectance attachment (DRA). Elemental analyses were carried out using a Perkin Elmer PE 2400 analyzer.

Reaction of 1,2-epoxyperfluorocyclohexane **1** *with 3,3′,4,4′-tetraaminobiphenyl* **2**.

Method A. Tetramine **2** (1.92 g, 9 mmol), NaHCO$_3$ (1.5 g, 18 mmol) and dioxane (20 ml) were placed in a glass tube. The tube was cooled with dry ice, and oxirane **1** (2.5 g, 9 mmol) was then added. The tube was

The activity of amino groups in compound **3** is sufficient for reactions with equimolar amounts of oxirane **1** or 1,2-diphenyl-ethanedione (benzil) to afford new polycyclic compounds **4** and **5** (Scheme 3).‡ Note that the reaction between oxirane **1** and tetramine **2**, even at their equimolar ratio, gives up to 10% of compound **4** (Methods A and B) along with diaminophenylphenazine **3** as the major product. Biphenazinyl **4** can be obtained from oxirane **1** without preliminary isolation of compound **3**. In this case, the 1:2 molar ratio should be of 2:1 (Method C).
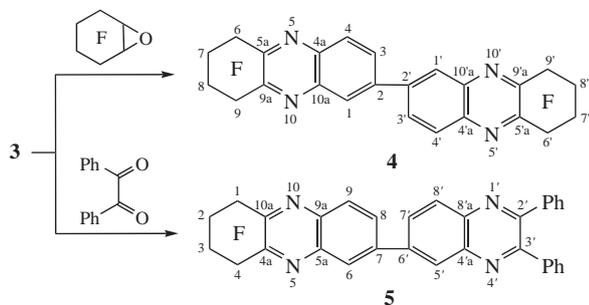
Scheme 3

Figure 1 The molecular structure of diaminophenylphenazine **3**.

The compositions and structures of compounds **3**–**5** were confirmed by ^{1}H, ^{13}C, ^{19}F NMR, IR spectroscopy and elemental analyses.

The crystal structure of compound **3** was determined by single crystal X-ray diffraction analysis (Figure 1).§ It is crystallized in

sealed. The reaction mixture was brought to room temperature and heated in a boiling water bath for 6 h. Once in a while, the tube was carefully removed from the water bath and shaken. After that, the tube was cooled to room temperature and cautiously unsealed. The precipitate was filtered off, the filtrate was poured into a Petri dish, and the solvent was evaporated to leave 3.2 g of a brown solid residue, which was purified by column chromatography on silica gel using first CH_2Cl_2–hexane (6:1) and then $CHCl_3$–MeOH–hexane (10:1:1) as the eluents. The following compounds were obtained (in the order in which the compounds were eluted from the column).

6,6,7,7,8,8,9,9,6',6',7',7',8',8',9',9'-Hexadecafluoro-6,7,8,9,6',7',8',9'-octahydro[2,2']biphenazinyl **4**: yield 0.21 g (7%). Light-yellow crystals, mp 195–196 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 8.67 (d, 2H, H$^{4,4'}$, *J* 9.0 Hz), 9.01 (dd, 2H, H$^{3,3'}$, *J* 9.0, 2.0 Hz), 9.22 (d, 2H, H$^{1,1'}$, *J* 2.0 Hz). ^{19}F NMR (470.5 MHz, DMSO-d_6) δ: 29.4 (m, 8F, F$^{7,7',8,8'}$), 54.3 (m, 8F, F$^{6,6',9,9'}$). ^{13}C NMR (126 MHz, DMSO-d_6) δ: 106.18–110.88 (m, 8CF$_2$), 128.63 (C$^{1,1'}$), 130.68 (C$^{4,4'}$), 134.61 (C$^{3,3'}$), 138.12 (tm, C$^{9a,9'a(5a,5'a)}$, J_{CF} 21.5 Hz), 138.20 (tm, C$^{5a,5'a(9a,9'a)}$, J_{CF} 20.4 Hz), 143.19 (C$^{2,2'}$), 143.57 (C$^{10a,10'a(4a,4'a)}$), 143.74 (C$^{4a,4'a(10a,10'a)}$). IR (ν/cm^{-1}): 1615, 1490, 1426 (C=C, C=N), 1320, 1180, 1113, 1092, 1007, 993 (C–F). Found (%): C, 43.90; H, 0.92; N, 8.59; F, 46.57. Calc. for C$_{24}$H$_6$N$_4$F$_{16}$ (%): C, 44.06; H, 0.92; N, 8.56; F, 46.46.

4-(6,6,7,7,8,8,9,9-Octafluoro-6,7,8,9-tetrahydrophenazin-2-yl)benzene-1,2-diamine **3**: yield 2.5 g (64%). Deep red crystals, mp 170–172 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 4.72 (br. s, 2H, NH$_2$), 5.20 (br. s, 2H, NH$_2$), 6.67 (d, 1H, H$^{6'}$, *J* 8.1 Hz), 7.21 (dd, 1H, H$^{5'}$, *J* 8.1, 2.1 Hz), 7.26 (d, 1H, H$^{3'}$, *J* 2.1 Hz), 8.34 (d, 1H, H^4, *J* 9.1 Hz), 8.36 (d, 1H, H^1, *J* 1.9 Hz), 8.52 (dd, 1H, H^3, *J* 9.1, 1.9 Hz). ^{19}F NMR (470.5 MHz, DMSO-d_6) δ: 29.33 (m, 4F, F^{7,8}), 53.79 (m, 2F, F$^{6(9)}$), 54.60 (m, 2F, F$^{9(6)}$). ^{13}C NMR (126 MHz, DMSO-d_6) δ: 106.16–111.17 (m, 4CF$_2$), 112.76, 114.39, 117.92, 121.54, 124.61, 129.63, 134.06, 135.13 (t, C$^{5a(9a)}$, *J* 23.9 Hz), 135.32, 137.56 (t, C$^{9a(5a)}$, *J* 21.8 Hz), 138.24, 142.50, 144.47, 147.44. IR (ν/cm^{-1}): 3445, 3409, 3344 (NH$_2$), 1614, 1494, 1427 (C=C, C=N), 1309, 1178, 1111, 1092, 1014, 996 (C–F). Found (%): C, 49.56; H, 2.38; N, 12.63; F, 34.52. Calc. for C$_{24}$H$_6$N$_4$F$_{16}$ (%): C, 49.78; H, 2.32; N, 12.90; F, 34.10.

Analytical samples of compounds **3**, **4** were obtained by recrystallization from a benzene–hexane (1:1) mixture.

Method B. Tetramine **2** (1.7 g, 7.9 mmol), NaHCO$_3$ (1.33 g, 15.8 mmol) and acetonitrile (25 ml) were placed into a flask equipped with a low-temperature reflux condenser, a dropping funnel and a magnetic stirrer, then oxirane **1** (2.2 g, 7.9 mmol) was added dropwise. The mixture was refluxed under continuous stirring for 5 h and cooled. The precipitate was filtered off, the filtrate was poured into a Petri dish and the solvent was evaporated to leave 2.82 g of a solid brown residue that mainly consisted of compound **3** (according to ^{19}F NMR data). The residue was treated similarly to Method A to give products **3** (2.24 g, 65%) and **4** (0.26 g, 10%).
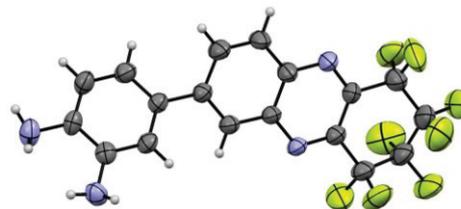
Method C. Similarly to Method A, the reaction of tetramine **2** (0.96 g, 4.5 mmol), epoxide **1** (2.5 g, 9 mmol), NaHCO$_3$ (1.5 g, 18 mmol) and dioxane (25 ml) carried out for 8 h gave 2.56 g of a solid brown residue mainly containing biphenazinyl **4** (^{19}F NMR data). The residue was treated similarly to the previous experiments to give products **4** (1.86 g, 63%) and **3** (0.23 g, 6%).

Reaction of diaminophenylphenazine **3** *with oxirane* **1**. Compound **3** (0.72 g, 1.66 mmol), NaHCO$_3$ (0.3 g, 3.5 mmol) and acetonitrile (15 ml) were placed in a glass tube, cooled with dry ice, and epoxide **1** (0.6 g, 2.1 mmol) was then added. The tube was sealed. The reaction mixture was brought to room temperature and heated in a boiling water bath under intermittent shaking for 8 h, then cooled and unsealed. The precipitate was filtered off, the filtrate was poured into a Petri dish and the solvent was evaporated to leave 1.2 g of a solid brown residue containing mainly biphenazinyl **4** (^{19}F NMR data). The residue was treated similarly to the previous experiment to give 0.87 g (81%) of pure biphenazinyl **4**.

‡ *7-(2,3-Diphenylquinoxalin-6-yl)-1,1,2,2,3,3,4,4-octafluoro-1,2,3,4-tetrahydrophenazine* **5**. Diaminophenylphenazine **3** (0.21 g, 4.8 mmol) and EtOH (4 ml) were placed in a flask equipped with a reflux condenser, a dropping funnel and a magnetic stirrer, then a solution of benzil (0.1 g, 4.8 mmol) in EtOH (4 ml) was added dropwise. The reaction mixture was refluxed for 2 h under continuous stirring and cooled to room temperature. The precipitate was filtered and dried in air to give 0.29 g of a solid light-brown residue which was then purified on a column with silica gel using CH_2Cl_2–hexane (10:1) as the eluent to afford 0.24 g (82%) of compound **5** as greenish-yellow crystals, mp 227–228 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ: 7.34–7.42 (m, 6H, 4H$_m$, 2H$_p$), 7.55–7.58 (m, 4H, 4H$_o$), 8.17 (dd, 1H, H$^{7'}$, *J* 8.7, 2.1 Hz), 8.33 (d, 1H, H$^{8'}$, *J* 8.7 Hz), 8.49 (d, 1H, H^9, *J* 8.9 Hz), 8.52 (dd, 1H, H^8, *J* 8.9, 1.9 Hz), 8.58 (d, 1H, H$^{5'}$, *J* 2.1 Hz), 8.72 (d, 1H, H^6, *J* 1.9 Hz). ^{19}F NMR (470.5 MHz, CDCl$_3$) δ: 27.95–28.09 (m, 4F, F^{2,3}), 52.07 and 52.30 (2m, 2F, F^{1,4}). ^{13}C NMR (126 MHz, CDCl$_3$) δ: 108.86 (tm, 4CF$_2$, $^1J_{CF} \approx$ 267 Hz), 127.69, 128.34, 128.37, 128.84, 129.16, 129.80, 129.84, 130.50, 130.80, 134.06, 138.65, 138.67, 138.94 (t, C$^{4a(10a)}$, J_{CF} 23.9 Hz), 139.15, 139.71 (t, C$^{10a(4a)}$, J_{CF} 23.4 Hz), 141.21, 141.34, 143.33, 144.05, 145.77, 154.43, 154.56. IR (ν/cm^{-1}): 1616, 1544, 1509, 1506, 1495, 1484, 1444, 1431, 1393 (C=C, C=N), 1320, 1304, 1178, 1114, 1092, 1012, 994 (C–F). Found (%): C, 63.16; H, 2.52; N, 9.22; F, 24.94. Calc. for C$_{32}$H$_{16}$F$_8$N$_4$ (%): C, 63.17; H, 2.65; N, 9.21; F, 24.98.

§ *Crystal data for* **3**. The XRD analysis was accomplished on the automated four-circled diffractometer Xcalibur 3 with CCD-detector by standard procedure [295(2) K, MoKα-irradiation, graphite monochromator, ω-scans with 1° steps], absorption correction was not applied. The structure was solved and refined with SHELXTL program package.[17] All non-hydrogen atoms were refined in anisotropic approximation, the H-atoms were placed in the calculated positions and refined using a riding model with dependent isotropic displacement parameters.

The crystal (C$_{18}$H$_{10}$F$_8$N$_4$, *M* = 434.30) is orthorhombic, space group *Pna*2$_1$, *a* = 35.855(3), *b* = 5.6351(6) and *c* = 8.6308(10) Å, *V* = 1743.8(3) Å^3, *T* = 295(2) K, *Z* = 4, μ(MoKα) = 0.161 mm^{-1}, 9561 reflections measured, 2630 unique (R_{int} = 0.0619) which were used in all calculations. The final wR_2 = 0.2070 (all data) and R_1 = 0.0652 [*I* > 2σ(*I*)]. Largest diff. peak/hole: 0.30/–0.22 eÅ^{-3}.

CCDC 1524102 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.

non-centrosymmetric space group. All bond lengths and angles are close to the typical values for compounds of this class. The NH$_2$ groups are non-planar; the benzene ring is rotated towards the quinoxaline moiety by 35.6°. The perfluorocyclohexene moiety has a (pseudo)sofa conformation. In this part of the molecule, disorder is not observed; however, significant $\Delta\rho_e = 0.297/{-}0.224$ e Å^{-3} and high value of $R_1 = 0.0652$ can be caused by unresolved disorder of the perfluoroalkyl moiety. In addition, bulky perfluoroalkyl moieties avert the formation of intermolecular H-bonds, and only shortened NH$\cdots$N contacts in the crystal packing are available. In particular, both amino groups form 'chelated' short contacts with N(1) atoms of quinoxaline [$-x$, $-1-y$, $z-0.5$] with distances N(18)$\cdots$N(1) 3.58 Å and N(23)$\cdots$N(1) 3.13 Å. The second type of short contacts is observed between the N(18)–H and N(23) [x, $y-1$, z] atoms.

In conclusion, starting from a preparatively available fluorinated synthon, 1,2-epoxyperfluorocyclohexane, we synthesized a new diamino derivative of fluorinated phenazines, *i.e.*, 4-(6,6,7,7,8,8,9,9-octafluoro-6,7,8,9-tetrahydrophenazin-2-yl)benzene-1,2-diamine, determined its structure and found the first examples of its use as a building block in the formation of polycyclic structures.

References

1 P. Tarrant, C. G. Allison, K. P. Barthold and E. C. Stump, Jr., *Fluorine Chem. Rev.*, 1971, **5**, 77.
2 H. Millauer, W. Schwertfeger and G. Siegemund, *Angew. Chem.*, 1985, **97**, 164.
3 H. S. Eleuterio, *J. Macromol. Sci., Chem.*, 1972, **6**, 1027.
4 V. A. Ponomarenko, S. P. Krukovskii and A. Yu. Alybina, *Ftorsoderzhashchie geterotsepnye polimery (Fluorine-containing Heterochain Polymers)*, Nauka, Moscow, 1973 (in Russian).
5 *Novoe v tekhnologii soedinenii ftora (Flourine Compounds. Modern Technology and Applications)*, ed. N. Ishikawa, Mir, Moscow, 1984 (in Russian).
6 G. G. Furin, *Ftorsoderzhashchie geterotsiklicheskie soedineniya. Sintez i primenenie (Fluorine-containing Heterocyclic Compounds. Synthesis and Application)*, Nauka, Novosibirsk, 2001 (in Russian).
7 L. V. Saloutina, A. Ya. Zapevalov, M. I. Kodess and V. I. Saloutin, *Russ. J. Org. Chem.*, 1997, **33**, 265 (*Zh. Org. Khim.*, 1997, **33**, 299).
8 L. V. Saloutina, A. Ya. Zapevalov, M. I. Kodess, V. I. Saloutin, G. G. Aleksandrov and O. N. Chupakhin, *Russ. J. Org. Chem.*, 2000, **36**, 887 (*Zh. Org. Khim.*, 2000, **36**, 921).
9 L. V. Saloutina, A. Ya. Zapevalov, V. I. Saloutin, M. I. Kodess, V. E. Kirichenko, M. G. Pervova and O. N. Chupakhin, *Russ. J. Org. Chem.*, 2006, **42**, 558 (*Zh. Org. Khim.*, 2006, **42**, 577).
10 T. I. Filyakova, A. Ya. Zapevalov, M. I. Kodess, P. A. Slepukhin and V. I. Saloutin, *Russ. J. Org. Chem.*, 2009, **45**, 884 (*Zh. Org. Khim.*, 2009, **45**, 897).
11 T. I. Filyakova, M. I. Kodess, P. A. Slepukhin and A. Ya. Zapevalov, *Russ. J. Org. Chem.*, 2009, **45**, 1700 (*Zh. Org. Khim.*, 2009, **45**, 1706).
12 T. I. Filyakova, L. V. Saloutina, A. Ya. Zapevalov, P. A. Slepukhin, M. I. Kodess and V. I. Saloutin, *Russ. J. Org. Chem.*, 2011, **47**, 650 (*Zh. Org. Khim.*, 2011, **47**, 649).
13 T. I. Filyakova, A. Ya. Zapevalov and I. P. Kolenko, *Patent USSR 666176*, 1979.
14 A. Ya. Zapevalov, T. I. Filyakova, N. V. Peschanskii, I. P. Kolenko and M. I. Kodess, *Zh. Org. Khim.*, 1986, **22**, 2088 (*Chem. Abstr.*, 1987, **107**, 236099).
15 P. L. Coe, A. W. Mott and J. C. Tatlow, *J. Fluorine Chem.*, 1982, **20**, 659.
16 T. I. Filyakova, A. Ya. Zapevalov, M. I. Kodess, P. A. Slepukhin and V. I. Saloutin, *Russ. J. Org. Chem.*, 2014, **50**, 854 (*Zh. Org. Khim.*, 2014, **50**, 870).
17 G. M. Sheldrick, *Acta Crystallogr.*, 2008, **A64**, 112.