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Synthesis of 2,3-bis(perfluoroalkyl)quinoxalines and 2,3-bis(perfluoroalkyl)-1,4-benzoxazines from oxides of internal perfluoroolefins

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Abstract

The reactions of oxides of internal *trans*-, *cis*-perfluoroolefins with *o*-phenylenediamine and 2-aminophenol in dioxane gave 2,3-bis(perfluoroalkyl)quinoxalines and 2,3-bis(perfluoroalkyl)-2H-1,4-benzoxazin-2-ols respectively in yields of 23–67%. When *N*,*N*-dimethylacetamide was used as a solvent an anionic isomerization of the oxides into ketones, which further yielded 2-(perfluoroalkyl)benzimidazoles in the case of *o*-phenylenediamine and 2-hydroxy-*N*-perfluoroalkanoylanilines in the case of 2-aminophenol, became the main path of these reactions. Unusual cyclization resulting in 2-pentafluoroethyl-2-pentafluoropropanoylbenzoxazolidine occurs on interaction between dodecafluoro-3,4-epoxyhexane and 2-aminophenol in *N*,*N*-dimethylacetamide.

Keywords: Oxides of internal perfluoroolefins; *O*-phenylenediamine; 2-Aminophenol; 2,3-Bis(perfluoroalkyl)quinoxalines; 2,3-Bis(perfluoroalkyl)-1,4-benzoxazines; 2-(Perfluoroalkyl)benzimidazoles; 2-Hydroxy-*N*-perfluoroalkanoylanilines

1. Introduction

It is known that quinoxalines and benzoxazines belong to natural biomolecules, there are physiologically active substances [1–3] and pesticides [4] among compounds of such structures; therefore synthesis of fluorocontaining analogs of the former is of great interest for search of biologically active substances.

One of not numerous examples of ones is the reaction of hexafluoro-1,2-epoxypropane with *o*-phenylenediamine and 2-aminophenol affording 3-(trifluoromethyl)-2(1H)-quinoxalinone and 3-(trifluoromethyl)-2H-1,4-benzoxazin-2-one, respectively [5].

At the same time, we have shown that the oxirane cycle can be converted into *N*,*O*,*S*-containing heterocycles by reactions of internal perfluoroolefin oxides with *N*,*O*,*S*-bifunctional nucleophilic reagents [6–8]. Thus, reactions between perfluoro-2,3-epoxyalkanes and nucleophiles such as ethylenediamine, 2-aminoethanol, thiourea, thiosemicarbazide and thiosemicarbazones of carbonyl compounds afforded corresponding fluoroalkyl-containing diazines, oxazines, 2-amino- and 2-hydrazinothiazolines, thiazolinylhydrazones of ketones and camphor. However, reactions of the former with aromatic bifunctional nucleophiles are unknown.

In this work we have studied the interaction of internal octafluoro-2,3-epoxybutane (**1**) (*trans*:*cis* ~ 90:10), dodecafluoro-3,4-epoxyhexane (**2**) (*trans*:*cis* ~ 90:10) and dodecafluoro-2,3-epoxyhexane (**3**) (*trans*:*cis* ~ 90:10) [9] with *o*-phenylenediamine and 2-aminophenol for the purpose of the

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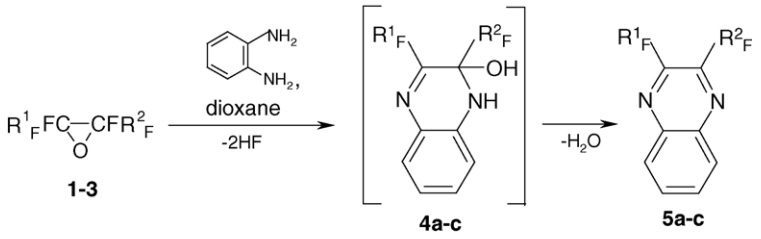


	R^1_F	R^2_F
1, 4a, 5a	CF_3	CF_3
2, 4b, 5b	CF_2CF_3	CF_2CF_3
3, 4c, 5c	CF_3	$CF_2CF_2CF_3$

Scheme 1.

preparing of heterocyclic compounds containing two perfluoroalkyl substituents along with an aromatic fragment, 2,3-bis(perfluorialkyl)quinoxalines and 2,3-bis(perfluorialkyl)benzoxazines. To study the effect of a solvent polarity on the heterocyclization process the aprotic solvents possessing different polarity, dioxane and *N*,*N*-dimethylacetamide, have been used in the reactions.

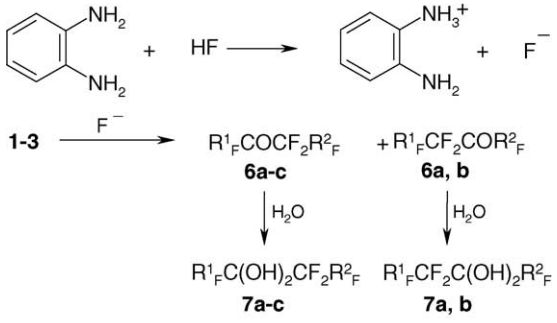
2. Results and discussion

In contrast to hexafluoro-1,2-epoxypropane easily interacting with *o*-phenylenediamine and 2-aminophenol in aprotic solvents [5] oxiranes (**1**–**3**) react with *o*-phenylenediamine in dioxane only under heating (~100 °C, sealed tubes) for several hours to yield 2,3-bis(trifluoromethyl)-quinoxaline (**5a**), 2,3-bis(pentafluoroethyl)quinoxaline (**5b**) and 2-heptafluoropropyl-3-trifluoromethylquinoxaline (**5c**) in high yields (Scheme 1). The reaction is likely to proceed via formation of intermediates – 2,3-bis(perfluoroalkyl)-2(1H)-quinoxalinols (**4a**–**c**) which losing a molecule of water yield more stable aromatic systems – quinoxalines (**5a**–**c**). This is in contrast to 2,3-bis(perfluoroalkyl)diazinols prepared earlier by the reaction of perfluoro-2,3-epoxyalkanes with ethylenediamine [6]. The structure of quinoxalines (**5a**–**c**) was determined by IR, ^{19}F, ^{1}H NMR spectroscopy and elemental analysis, in the case of compound (**5a**) – additionally by ^{13}C NMR spectroscopy.

Spectroscopic examination (^{19}F NMR) of the reaction mixtures produced by oxiranes (**1**–**3**) and *o*-phenylenediamine in dioxane indicated the presence of ketones (**6a**–**c**) (~25–28%). They were identified as the corresponding hydrates (**7a**–**c**), which apparently are formed as a result of anionic isomerization of the starting oxiranes under the action of F^- (Scheme 2) [6,10,11].

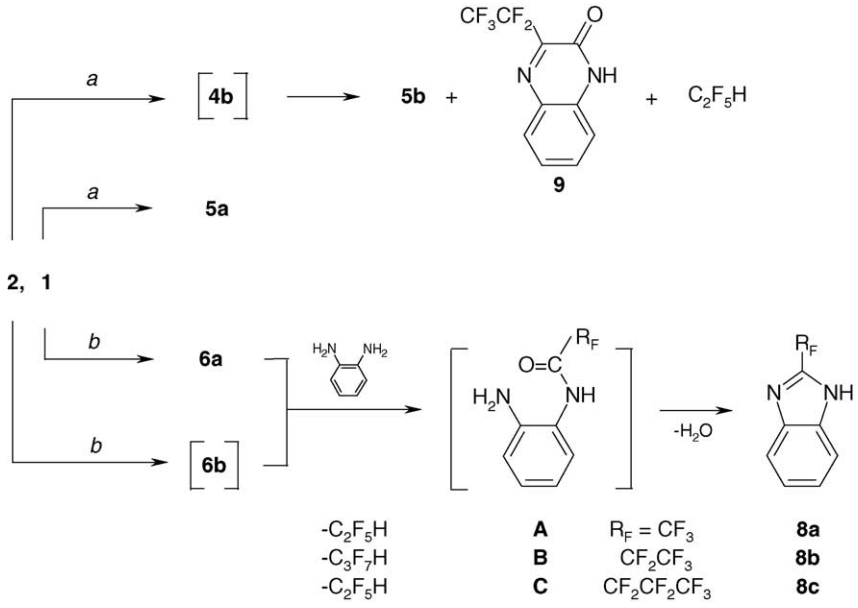
Using the more polar solvent, *N*,*N*-dimethylacetamide, in the reaction gave lower yields of quinoxalines (**5a**–**c**); relative amounts of the isomerization products increased. Thus, in the case of compound (**1**) (Scheme 3) octafluoro-2-butanone (**6a**) has been obtained as a major reaction product which in part underwent haloform decomposition under the action of *o*-phenylenediamine to afford pentafluoroethane and the intermediate 2-amino-*N*-trifluoroacetylaniline (**A**). The latter, being unstable under the reaction conditions, eliminated a molecule of water to give 2-trifluoromethylbenzimidazole (**8a**) (path *b*). Thus, quinoxaline (**5a**) has been obtained as a minor product (path *a*, yield ~8%, Table 1, run 2).

A similar reaction between oxirane **2** and *o*-phenylenediamine in *N*,*N*-dimethylacetamide gave poor yields of quinoxaline (**5b**) and 3-pentafluoroethyl-2(1H)-quinoxalinone (**9**) which seems to be the result of pentafluoroethane elimination from intermediate (**4b**) (Scheme 3, path *a*). The latter has been detected by GCMS to support the proposed scheme of the reaction (Scheme 1). But the main direction of the reaction was anionic isomerization of oxirane (**2**) into dodecafluoro-2-hexanone (**6b**) (Scheme 3, path *b*) yielding further 1-hydroheptafluoropropane, pentafluoroethane and



	R^1_F	R^2_F
6a, 7a	CF_3	CF_3
6b, 7b	CF_2CF_3	CF_2CF_3
6c, 7c	CF_3	$CF_2CF_2CF_3$

Scheme 2.



Scheme 3. (a) *O*-phenylenediamine, DMAA, −2HF; (b) F^-, DMAA.

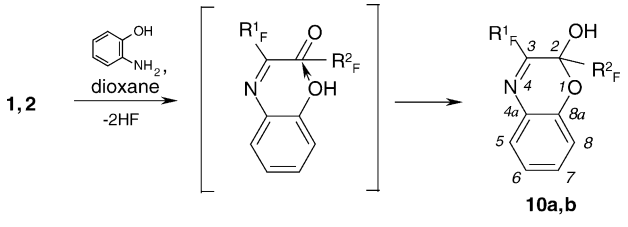
Table 1
Composition of the products of the reactions of oxiranes **1**–**3** with *o*-phenylenediamine and 2-aminophenol at the molar ratio oxirane:nucleophile = 1:2

Run no.	Starting oxirane, nucleophile	Solvent in the reaction	Reaction products (molar ratio (%), from ^{19}F NMR)
1	**1**, *o*-phenylenediamine	Dioxane	**5a**, **6a** (∼75:25)
2	**1**, *o*-phenylenediamine	*N*,*N*-dimethylacetamide	**5a**, **8a**, **6a** (∼8:15:77)
3	**2**, *o*-phenylenediamine	Dioxane	**5b**, **6b** (∼72:28)
4	**2**, *o*-phenylenediamine	*N*,*N*-dimethylacetamide	**5b**, **8b**, **8c**, **9** (∼8:72:14:6)
5	**3**, *o*-phenylenediamine	Dioxane	**5c**, **6b**, **6c** (∼82:9:9)
6	**1**, 2-aminophenol	Dioxane	**10a**
7	**1**, 2-aminophenol	*N*,*N*-dimethylacetamide	**10a**, **6a**, **11a** (∼32:61:7)
8	**2**, 2-aminophenol	Dioxane	**10b**
9	**2**, 2-aminophenol	*N*,*N*-dimethylacetamide	**12**, **11b**, **11c** (∼15:73:12)
10	**3**, 2-aminophenol	Dioxane	**10c**, **10d** (∼51:49)

amides (**B** and **C**) as a result of haloform decomposition. On reacting the amides, probably, lost a molecule of water to yield 2-pentafluoroethyl (**8b**) and 2-heptafluoropropylbenzimidazole (**8c**) (Table 1, run 4).

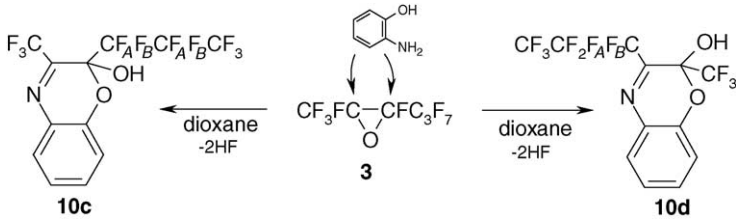
To identify benzimidazoles (**8a–c**) by ^{19}F NMR spectroscopy the former have been prepared by independent synthesis from corresponding perfluorinated carboxylic acids and *o*-phenylenediamine in the presence of hydrochloric acid using the Phillips reaction [12,13]. Quinoxalinone (**9**) was identified using IR [14], ^{19}F NMR spectroscopy and GCMS. Detection of gaseous pentafluoroethane and 1-hydroheptafluoropropane [15] in part dissolved in the reaction mixture together with compounds (**5b**), (**8b**) and (**c**) and (**9**) by ^{19}F NMR spectroscopy confirms the reaction scheme.

The reaction of oxiranes (**1**) and (**2**) with 2-aminophenol in *N*,*N*-dimethylacetamide has been carried out under similar conditions (∼100 °C, sealed tubes). We have found it to proceed with high selectivity affording benzocyclic products, 2,3-bis(trifluoromethyl)-2H-1,4-benzoxazin-2-ol (**10a**) and 2,3-bis(pentafluoroethyl)-2H-1,4-benzoxazin-2-ol (**10b**), in good yields (Scheme 4). In this case the anionic isomerization of oxiranes to ketones was not observed probably due to the lower basicity of 2-aminophenol compared with *o*-phenylenediamine. The structure of compounds (**10a** and **b**) was



	R^1_F	R^2_F
10a	CF_3	CF_3
10b	$CF_AF_BCF_3$	$CF_AF_BCF_3$

Scheme 4.



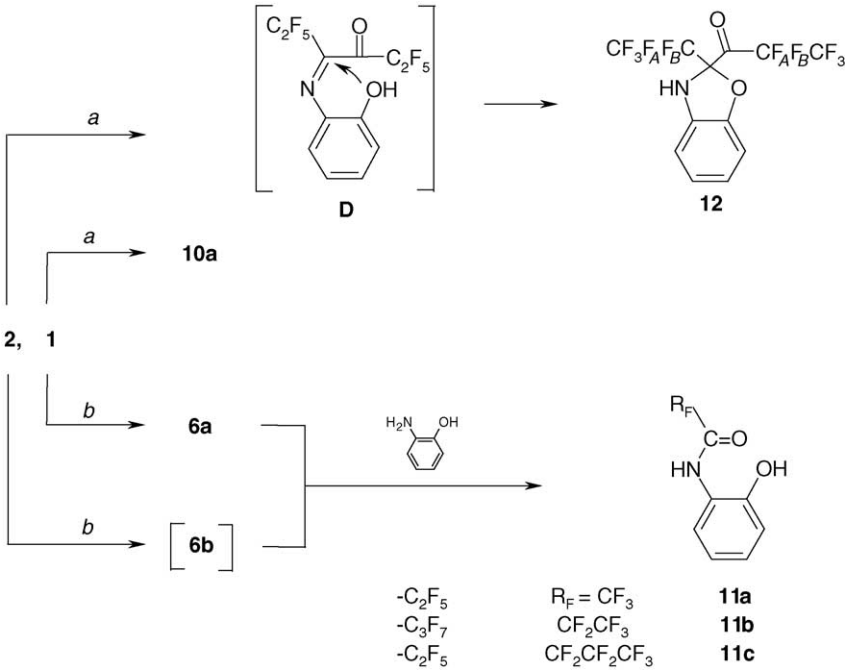
Scheme 5.

determined by IR, ^{1}H, ^{19}F NMR spectroscopy, mass spectrometry, elemental analysis and in the case of compound (**10a**) additionally by ^{13}C NMR spectroscopy.

Nucleophilic ring opening of unsymmetrical dodecafluoro-2,3-epoxyhexane (**3**) with 2-aminophenol under the same conditions occurred in both possible directions to yield two regioisomers, 2-heptafluoropropyl-3-trifluoromethyl-2H-1,4-benzoxazin-2-ol (**10c**) and 3-heptafluoropropyl-2-trifluoromethyl-2H-1,4-benzoxazin-2-ol (**10d**) (Scheme 5). Almost identical yields of the resulting regioisomers have demonstrated an equal probability of 2-aminophenol attack on both epoxide carbon atoms C-2 and C-3. It is possible to explain this by the predominant influence of electronic factors (the approximately equal stability of the corresponding intermediate O-anions [6]). Benzoxazine (**10c**) can be isolated from the regioisimer mixtures in individual state by crystallization.

Treating oxirane (**1**) with 2-aminophenol in *N*,*N*-dimethylacetamide gave octafluoro-2-butanone (**6a**) as a major product (path *b*, ~61%), benzoxazine (**10a**) (path *a*, ~32%) and 2-hydroxy-*N*-trifluoroacetylaniline (**11a**) (path *b*, ~7%) as minor products of the reaction (Scheme 6, Table 1, run 7). The latter has probably resulted from haloform decomposition of isomeric ketone (**6a**) under the action of 2-aminophenol. Similar scheme of amide formation has been also proposed in the case of interaction of internal perfluoroolefin oxides with ethylenediamine and 2-aminoethanol in polar aprotic solvents [6].

With an increase in length of the perfluoroalkyl substituents in the starting oxiranes, an unusual course of the reaction with 2-aminophenol in *N*,*N*-dimethylacetamide is observed. Thus, a similar reaction of oxirane (**2**) yielded amides (**11b** and **c**) and the unexpected 2-pentafluoroethyl-2-pentafluoropropanoyl-1,3-benzoxazolidine (**12**) (Scheme 6, Table 1, run 9). Obviously, the first step of the reaction is the nucleophilic attack of NH_2 group on the epoxide carbon atom of compound (**2**) followed by the ring opening and formation of intermediate (**D**) (Scheme 6, path *a*). However, the subsequent attack of the OH group and cyclization occur at the imine but not at the carbonyl carbon atom, like in the case of compound (**1**) (Scheme 4), resulting in benzoxazolidine (**12**). This may be explained by the weaker solvation of C=N as compared with the C=O group. The predominant formation of 2-



Scheme 6. (a) 2-Aminophenol, DMAA, −2HF; (b) F^{-}, DMAA.

hydroxy-*N*-pentafluoropropanoylaniline (**11b**) and 2-hydroxy-*N*-heptafluorobutanoylaniline (**11c**) in the reaction (a molar ratio **11b**:**11c**:**12** ~ 73:12:15) is a result of haloform decomposition of the isomeric dodecafluoro-2-hexanone (**6b**) and shows that oxirane **2** is more reactive to F^- than to 2-aminophenol under these reaction conditions.

The structure of compounds (**11b**) and (**12**) isolated was confirmed by IR, ^{19}F, ^{1}H NMR spectroscopy, mass spectrometry and elemental analysis. Amides (**11a** and **c**) were identified using ^{19}F NMR spectroscopy and GCMS [16,17].

3. Conclusion

Thus, reactions of oxides of internal perfluoroolefins with *o*-phenylenediamine and 2-aminophenol in dioxane give 2,3-bis(perfluoroalkyl)quinoxalines and 2,3-bis(perfluoroalkyl)-2H-1,4-benzoxazin-2-ols respectively in high yields, providing a route to perfluoroalkylated quinoxalines and unknown type of benzoxazines with two perfluoroalkyl substituents. Using more polar *N*,*N*-dimethylacetamide results in lower yields of benzocyclic compounds; quinoxalines and benzoxazines are minor products in this case. The main direction of the reactions becomes the anionic isomerization of starting oxiranes to ketones which as a result of the further transformations give 2-perfluoroalkylbenzimidazoles in the case of *o*-phenylenediamine or 2-hydroxy-*N*-perfluoroalkanoylanilines in the case of 2-aminophenol.

4. Experimental

^{1}H, ^{13}C (^{1}H decoupled), ^{19}F NMR spectra were recorded on Bruker DRX-400 spectrometer operating at 400, 100 and 376 MHz, respectively. Chemical shifts are reported in ppm (δ) from internal $(CH_3)_4Si$ for hydrogen and carbon and internal CCl_3F for fluorine [$(CD_3)_2CO$, $CDCl_3$, $(CD_3)_2SO$]. Mass spectra were obtained on a Varian MAT-311 mass spectrometer and a Fisions GCMS instrument with detector MD 800, quartz capillary column HP-5, 25 m × 0.25 mm, thickness of a stationary phase film 0.25 mcm, the carrier-gas—helium, ionization energy 70 eV. Infrared spectra were obtained on a Perkin-Elmer Spectrum One FT-IR spectrometer in Nujol. The ν_{max} are reported in cm^{-1}. Elemental analyses were carried out on a Carlo Erba CHNS-OEA 1108 elemental analyzer. Thin-layer chromatography (TLC) was performed on Silufol UV-254 plates, column chromatography—on silica-gel L 100/250. Melting points were measured in open capillaries and are reported uncorrected. Oxiranes (**1**–**3**) [9] were prepared according to reported procedures.

4.1. The reaction of oxirane *1* with o-phenylenediamine

4.1.1. Procedure 1

A mixture of oxirane (**1**) (3 g, 13.9 mmol), *o*-phenylenediamine (3.0 g, 28 mmol) and dioxane (20 ml) was heated in a sealed tube in a boiling water bath for 8 h, with intermittent shaking. After cooling (−70 °C), the tube was opened and ^{19}F NMR spectrum of the reaction mixture was recorded (Table 1, run 1). After that the contents were poured into ice water (200 ml) and the lower organic layer was separated and washed with water once more. The resultant precipitate was collected by filtration, dried at room temperature and purified by a column chromatography (eluent: $CHCl_3$; R_f **5a** = 0.9). Crystallization from aqueous EtOH afforded colorless crystals of quinoxaline (**5a**). Yield 1.9 g (51%), mp 121–121.5 °C (lit. mp 118 °C [18]). ^{1}H NMR [$(CD_3)_2CO$]: δ 8.23–8.27 (2H, m, 2CH), 8.36–8.40 (2H, m, 2CH). ^{13}C NMR [$(CD_3)_2CO$]: δ 121.5 (q, $^{1}J_{CF}$ = 274.9 Hz, CF_3-2, CF_3-3), 130.6 (s) (C-5, C-8), 135.3 (s) (C-6, C-7), 140.0 (q, $^{2}J_{CF}$ = 37.8 Hz, C-2, C-3), 141.7 (s, C-4a, C-8a). ^{19}F NMR [$(CD_3)_2CO$]: δ −63.5 (s, $2CF_3$). Anal. Calcd for $C_{10}H_4F_6N_2$: C, 45.1; H, 1.5; F, 42.9; N, 10.5. Found: C, 45.2; H, 1.2; F 42.8; N 10.6.

*4.1.1.1. 1,1,1,3,3,4,4,4-Octafluoro-2,2-dihydroxybutane (**7a**).* ^{19}F NMR [$(CD_3)_2SO$]: δ −124.7 (2F, q, $^{4}J_{FF}$ = 10.6 Hz, CF_2), −80.3 (3F, tq, $^{4}J_{FF}$ = 10.6, $^{5}J_{FF}$ = 3.6 Hz, $CF_3C(OH)_2$), −79.0 (3F, q, $^{5}J_{FF}$ = 3.6 Hz, $CF_2\mathbf{CF_3}$).

4.1.2. Procedure 2

In a similar manner to Section 4.1.1, oxirane (**1**) (5.8 g, 27 mmol) was treated with *o*-phenylenediamine (5.8 g, 54 mmol) in 20 ml of DMAA for 1.5 h. The reaction mixture (Table 1, run 2) was worked up as described above in Section 4.1.1. The resulting precipitate (0.9 g) [a mixture of quinoxaline (**5a**) and benzimidazole (**8a**) (~2:1, from ^{19}F NMR)], was collected by filtration, dried at room temperature, then heated at 90–95 °C (760 Torr) to isolate quinoxaline (**5a**) by sublimation. Yield of compound (**5a**) 0.5 g (7%). The solid residue (mainly benzimidazole **8a**) was purified by column chromatography (eluent: $CHCl_3$–MeOH, 10: 0.1, R_f **8a** = 0.39). Additional quantity of compound **8a** was obtained by $CHCl_3$ extraction of aqueous solution of the reaction mixture. The extract containing benzimidazole **8a** and *o*-phenylenediamine (from ^{1}H and ^{19}F NMR) was dried over $MgSO_4$, evaporated and purified by column chromatography as above. Recrystallization from aqueous EtOH gave colorless crystals of compound (**8a**), mp 208–210 °C (lit. mp 210 °C [13]), yield 0.6 g (12%). ^{1}H NMR [$(CD_3)_2SO$]: δ 7.38–7.41 (2H, m, 2CH), 7.74 (2H, m, 2CH), 13.93 (1H, br.s, NH). ^{19}F NMR [$(CD_3)_2SO$]: δ −63.0 (s, CF_3).

4.2. The reaction of oxirane *2* with o-phenylenediamine

4.2.1. Procedure 1

In a similar manner to Section 4.1.1, oxirane 2 (4.7 g, 15 mmol) was treated with *o*-phenylenediamine (3.2 g, 30 mmol) in 20 ml of dioxane for 4.5 h. The reaction mixture (Table 1, run 3) was worked up as above in Section 4.1.1. The solid obtained was dried at room temperature,

purified by column chromatography (eluent—$CHCl_3$, R_f **5b** = 0.9) and recrystallized from aquaous EtOH to give 1.7 g (31%) of quinoxaline (**5b**) as colorless crystals, mp 53–53.5 °C (subl.) (new compound). ^{1}H NMR [$(CD_3)_2SO$]: δ 8.24–8.28 (2H, m, 2CH), 8.35–8.39 (2H, m, 2CH). ^{19}F NMR [$(CD_3)_2SO$]: δ −108.5 (4F, s, $2CF_2$), −79.7 (6F, s, $2CF_3$). IR: ν 1564, 1612 (C=C, C=N). Anal. Calcd for $C_{12}H_4F_{10}N_2$: C, 39.3; H, 1.1; F, 51.9; N, 7.6. Found: C, 39.2; H, 1.0; F, 51.7; N, 7.4.

*4.2.1.1. 1,1,1,2,2,4,4,5,5,6,6,6-Dodecafluoro-3,3-dihydroxyhexane (**7b**).* ^{19}F NMR [$(CD_3)_2SO$]: δ −123.7 (2F, m, $CF_2\mathbf{CF_2}CF_3$), −123.3 [2F, tt, $^4J_{FF}$ = 13.5, $^5J_{FF}$ = 7.4 Hz, $CF_3\mathbf{CF_2}C(OH)_2$], −120.4 (2F, m, $\mathbf{CF_2}CF_2CF_3$), −80.2 (3F, t, $^4J_{FF}$ = 10.2 Hz, $CF_2CF_2\mathbf{CF_3}$), −78.5 [3F, t, $^5J_{FF}$ = 5.4 Hz, $\mathbf{CF_3}CF_2C(OH)_2$].

4.2.2. Procedure 2

In a similar manner, oxirane (**2**) (3.9 g, 12 mmol) was treated with *o*-phenylenediamine (2.7 g, 25 mmol) in 16 ml of DMAA for 2.5 h. The reaction mixture (Table 1, run 4) was worked up as above in Section 4.1.1. The resulting precipitate was collected by filtration, dried at room temperature and heated at 50–60 °C (760 Torr) [at this temperature quinoxaline (**5b**) sublimed, yield 0.2 g (4.4%)]. After that the solid residue was purified by column chromatography (eluent: $CHCl_3$–MeOH, 10:0.1, R_F **8b** = 0.63) and twice recrystallized from aqueous EtOH to give 1.5 g (52%) of benzimidazole (**8b**) as colorless crystals, mp 210–212 °C (lit. mp 212–214 °C [12]). ^{1}H NMR [$(CD_3)_2SO$]: δ 7.40–7.42 (2H, m, 2CH), 7.67–7.90 (2H, m, 2CH), 14.0 (1H, br.s, NH). ^{19}F NMR [$(CD_3)_2SO$]: δ −113.0 (2F, q, $^3J_{FF}$ = 3.0 Hz, CF_2,), −83.0 (3F, t, $^3J_{FF}$ = 3.0 Hz, CF_3). GCMS, *m/z* (rel. int.): 237 (5.4, $[M+1]^+$), 236 (70.9, M^+), 217 (10.0, $[M-F]^+$), 168 (7.4), 167 (100, $[M-CF_3]^+$), 147 (28.7, $[M-CF_3\text{-}HF]^+$), 140 (18.4), 116 (5.7, $[M-C_2F_5H]^+$), 102 (14.6, $[C_6H_4NC]^+$), 95 (16.4), 90 (16.5, $[C_6H_4N]^+$), 69 (11.8, $[CF_3]^+$), 64 (8.0), 63 (13.0). Anal. Calcd for $C_9H_5F_5N_2$: C, 45.8; H, 2.1; F, 40.3; N, 11.9. Found: C, 45.5; H, 2.0; F, 40.6; N, 11.6.

*4.2.2.1. Benzimidazole (**8c**).* ^{19}F NMR [$(CD_3)_2SO$]: δ −126.6 (2F, m, $CF_2\mathbf{CF_2}CF_3$), −111.6 (2F, m, $\mathbf{CF_2}CF_2CF_3$), −80.1 (3F, tt, $^4J_{FF}$ = 8.9, $^3J_{FF}$ = 1.1 Hz, CF_3). GCMS, *m/z* (rel. int.): 286 (49.6, M^+), 267 (9.5, $[M-F]^+$), 186 (15.0), 168 (7.6), 167 (100, $[M-C_2F_5]^+$), 166 (11.3, $[M-C_2F_5H]^+$), 147 (23.7), 140 (15.0), 116 (9.1, $[M-C_3F_7H]^+$), 102 (12.6, $[C_6H_4NC]^+$), 95 (15.2), 90 (16.8, $[C_6H_4N]^+$), 69 (14.4, $[CF_3]^+$), 64 (9.9), 63 (13.3).

*4.2.2.2. Quinoxalinone (**9**).* ^{19}F NMR [$(CD_3)_2SO$]: δ −115.9 (2F, q, $^3J_{FF}$ = 1.4 Hz, CF_2), −80.7 (3F, t, $^3J_{FF}$ = 1.4 Hz, CF_3). GCMS, *m/z* (rel. int.): 264 (59.9, M^+), 245 (7.7, $[M-F]^+$), 195 (22.7, $[M-CF_3]^+$), 168 (7.4), 167 (100, $[M-CF_3\text{-}CO]^+$), 147 (29.1), 145 (16.1, $[M-C_2F_5]^+$), 140 (15.0), 119 (7.0, $[C_2F_5]^+$), 117 (5.2), 116 (6.4), 102 (15.0, $[C_6H_4NC]^+$), 95 (14.7), 90 (37.9, $[C_6H_4N]^+$), 76 (8.7, $[C_6H_4]^+$), 75 (6.4), 69 (19.4, $[CF_3]^+$), 64 (15.4), 63 (21.2).

*4.2.2.3. Benzodiazinol (**4b**).* GCMS, *m/z* (rel. int.): 384 (9.1, M^+), 265 (100, $[M-C_2F_5]^+$), 245 (18.2, $[M-C_2F_5\text{-}HF]^+$), 217 (45.5), 197 (10.0), 196 (16.4, $[M-CF_3\text{-}C_2F_5]^+$), 195 (10.0), 167 (33.6), 147 (6.4), 129 (6.4), 120 (16.4), 119 (16.4, $[C_2F_5]^+$), 90 (27.3, $[C_6H_4N]^+$), 69 (30.0, $[CF_3]^+$), 65 (10.0), 52 (9.0).

4.2.2.4. HCF_2CF_3. ^{19}F NMR [$(CD_3)_2SO$]: δ −139.5 (2F, dq, $^2J_{HF}$ = 51.1, $^3J_{FF}$ = 3.0 Hz, HCF_2), −85.1 (3F, dt, $^3J_{HF}$ = $^3J_{FF}$ = 3.0 Hz, CF_3).

4.2.2.5. $HCF_2CF_2CF_3$. ^{19}F NMR [$(CD_3)_2SO$]: δ −139.0 (2F, dtq, $^2J_{HF}$ = 50.2, $^3J_{FF}$ = 4.9, $^4J_{FF}$ = 7.0 Hz, HCF_2), −132.2 (2F, dt, $^3J_{HF}$ = $^3J_{FF}$ = 4.9 Hz, CF_2), −81.7 (3F, t, $^4J_{FF}$ = 7.0 Hz, CF_3).

*4.3. The reaction of oxirane **3** with o-phenylenediamine*

In a similar manner, oxirane (**3**) (4.7 g, 15 mmol) was treated with *o*-phenylenediamine (3.2 g, 30 mmol) in 20 ml of dioxane for 6 h. The reaction mixture (Table 1, run 5) was worked up as above in Section 4.1.1. The resulting solid was dried at room temperature and purified by column chromatography (eluent: $CHCl_3$–hexane, 10:1, R_f **5c** = 0.9). The subsequent recrystallization of the obtained solid from aqueous EtOH afforded 2.0 g (38%) of quinoxaline (**5c**) as colorless crystals, mp 40–40.5 °C (subl.) (new compound). ^{1}H NMR [$(CD_3)_2CO$]: δ 8.25–8.29 (2H, m, 2CH), 8.36–8.41 (2H, m, 2CH). ^{19}F NMR [$(CD_3)_2CO$]: δ: −122.1 (2F, m, $CF_2\mathbf{CF_2}CF_3$), −106.6 (2F, m, $\mathbf{CF_2}CF_2CF_3$), −78.5 (3F, t, $^4J_{FF}$ = 10.0 Hz, $CF_2CF_2\mathbf{CF_3}$), −62.6 (3F, tt, CF_3CN, $^5J_{FF}$ = 18.7, $^6J_{FF}$ = 6.2 Hz). IR: ν 1550, 1600, 1650 (C=C, C=N). Anal. Calcd for $C_{12}H_4F_{10}N_2$: C, 39.3; H, 1.1; F, 51.9; N, 7.7. Found: C, 39.3; H, 1.2; F, 52.2; N, 7.6.

*4.3.1.1. 1,1,1,3,3,4,4,5,5,6,6,6-Dodecafluoro-2,2-dihydroxyhexane (**7c**)*

^{19}F NMR [$(CD_3)_2SO$]: δ −125.5 (2F, m, $CF_2CF_2\mathbf{CF_2}CF_3$), −121.0 (2F, m, $CF_2\mathbf{CF_2}CF_2CF_3$), −120.8 (2F, m, $\mathbf{CF_2}CF_2CF_2$-CF_3), −80.5 (3F, tt, $^4J_{FF}$ = 9.9, J_{FF} = 2.9 Hz, $CF_2CF_2CF_2\mathbf{CF_3}$), −80.1 (3F, tt, $^4J_{FF}$ = 10.7, $^5J_{FF}$ = 5.4 Hz, $CF_3C(OH)_2$).

The ^{19}F NMR spectrum of compound (**7b**) is identical to that described above (Section 4.2.1).

*4.4. The reaction of oxirane **1** with 2-aminophenol*

4.4.1. Procedure 1

In a similar manner, oxirane (**1**) (4.6 g, 21 mmol) was treated with 2-aminophenol (4.7 g, 43 mmol) in 60 ml of dioxane for 3.5 h. The reaction mixture (Table 1, run 6) was worked up as above in Section 4.1.1. The resulting solid was dried (∼40 °C), purified by column chromatography (eluent:$CHCl_3$, R_F **10a** = 0.51) and recrystallized from

hexane–benzene (3:1) to give 4.1 g (67%) of colorless crystals of benzoxazinol (**10a**), mp 126–127 °C (new compound). ^{1}H NMR [$(CD_3)_2CO$]: δ 7.19–7.21 (1H, m, CH), 7.26–7.30 (1H, m, CH), 7.53–7.57 (1H, m, CH), 7.64–7.66 (1H, m, CH), 8.73 (1H, br.s, OH). ^{19}F NMR [$(CD_3)_2CO$]: δ: −80.7 (3F, q, $^5J_{FF}$ = 8.5 Hz, CF_3CO), −65.5 (3F, q, $^5J_{FF}$ = 8.5 Hz, CF_3CN). ^{13}C NMR [$(CD_3)_2CO$]: δ 91.2 (q, $^2J_{CF}$ = 36.2 Hz, C-2), 117.3 (s, C-8), 120.1 (q, $^1J_{CF}$ = 276.2 Hz, CF_3-2), 122.1 (q, $^1J_{CF}$ = 288 Hz, CF_3-3), 124.9 (s, C-5), 129.4 (s, C-4a), 134.4 (s, C-7), 130.5 (s, C-6), 143.8 (q, $^2J_{CF}$ = 35.9 Hz, C-3), 144.2 (s, C-8a). IR: ν 1585, 1600, 1635 (C=C, C=N), 2770, 3120 broad (OH). GCMS, *m/z* (rel. int.): 285 (39.2, M^+), 268 (12.5, $[M - OH]^+$), 256 (19.6), 246 (27.5), 218 (7.5), 217 (8.1), 216 (94.8, $[M - CF_3]^+$), 196 (90.0, $[M - CF_3\text{-}HF]^+$), 188 (78.5), 168 (100, $[M - CF_3\text{-}CO\text{-}HF]^+$), 140 (24.5, $[M - CF_3\text{-}C_6H_4]^+$), 132 (10.0), 103 (7.5), 102 (93.5, $[C_6H_4NC]^+$), 90 (20.0, $[C_6H_4N]^+$), 76 (26.5, $[C_6H_4]^+$), 69 (50.2, $[CF_3]^+$), 65 (31.5), 64 (21.2), 63 (32.0), 50 (20.8). Anal. Calcd for $C_{10}H_5F_6NO_2$: C, 42.1; H, 1.8; F, 40.0; N, 4.9. Found: C, 42.3; H, 1.8; F, 39.9; N, 4.9.

4.4.2. Procedure 2

In a similar manner, oxirane (**1**) (4.6 g, 21 mmol) was treated with 2-aminophenol (4.7 g, 43 mmol) in 20 ml of DMAA for 1 h. After the volatiles were removed ^{19}F NMR spectrum of the reaction mixture was recorded (Table 1, run 7) and the contents were worked up as described above in Section 4.1.1. The resultant precipitate was dried (∼50–60 °C) and recrystallized from hexane–benzene (3:1). Yield of compound (**10a**) 0.7 g (12%).

*4.4.2.1. Amide (**11a**).* ^{19}F NMR [$(CD_3)_2SO$]: δ −74.1 (s, CF_3).

4.5. The reaction of oxirane **2** with 2-aminophenol

4.5.1. Procedure 1

In a similar manner, oxirane (**2**) (3.0 g, 9 mmol) was treated with 2-aminophenol (2.0 g, 18 mmol) in 40 ml of dioxane for 4 h. The reaction mixture (Table 1, run 8) was worked up as described above (Section 4.1.1) and extracted with $CHCl_3$. The extract was dried over $MgSO_4$, $CHCl_3$ was distilled off and the residue was subjected to vacuum distillation to afford 1.5 g (42%) of benzoxazinole (**10b**) as oil, bp 76–80 °C (10 Torr) (new compound). ^{1}H NMR ($CDCl_3$): δ 4.50 (1H, br.s, OH), 7.01–7.03 (1H, m, CH), 7.15–7.19 (1H, m, CH), 7.38–7.40 (1H, m, CH), 7.56–7.59 (1H, m, CH). ^{19}F NMR ($CDCl_3$): δ: −125.0 (1F, ddd, $^2J_{FF}$ = 282.8, $^5J_{FF}$ = 29.4, 19.8 Hz, $CF_3CF_A\mathbf{F_B}CO$), −124.2 (1F, ddd, $^2J_{FF}$ = 282.8, $^5J_{FF}$ = 15.2, 10.2 Hz, $CF_3C\mathbf{F_A}F_BCO$), −114.3 (1F, ddd, $^2J_{FF}$ = 300.5, $^5J_{FF}$ = 29.4, 15.2 Hz, $CF_3CF_A\mathbf{F_B}CN$), −111.8 (1F, ddd, $^2J_{FF}$ = 300.5, $^5J_{FF}$ = 19.8, 10.2 Hz, $CF_3C\mathbf{F_A}F_BCN$), −81.8 (3F, s, $\mathbf{CF_3}CF_AF_BCO$), −80.0 (3F, d, J = 1.8 Hz, $\mathbf{CF_3}CF_AF_BCN$). IR: ν 1589, 1598, 1625 (C=C, C=N), 3182 broad, 3445, 3595, 3687 (OH). GCMS, *m/z* (rel. int.): 385 (9.9, M^+), 368 (6.9, $[M - OH]^+$), 356 (6.1), 346 (6.7), 267 (7.5), 266 (100, $[M - C_2F_5]^+$), 246 (24.7, $[M - C_2F_5\text{-}HF]^+$), 238 (21.8), 218 (43.0), 190 (9.1), 169 (6.5), 168 (51.3), 119 (18.6, $[C_2F_5]^+$), 102 (40.6, $[C_6H_4NC]$), 93 (5.5, $[C_6H_5O]^+$), 91 (10.6, $[C_6H_4NH]^+$), 76 (12.2, $[C_6H_4]^+$), 75 (5.4), 69 (13.6, $[CF_3]^+$), 65 (14.2), 64 (8.7), 63 (11.8), 52 (5.5), 51 (9.4), 50 (7.9). Anal. Calcd for $C_{12}H_5F_{10}NO_2$: C, 37.4; H, 1.3; F, 49.4; N, 3.6. Found: C, 37.8; H, 1.7; F, 49.6; N, 3.9.

4.5.2. Procedure 2

In a similar manner, oxirane (**2**) (5.5 g, 17 mmol) was treated with 2-aminophenol (3.5 g, 32 mmol) in 20 ml of DMAA for 1 h. Volatiles were removed (HC_2F_5 and HC_3F_7) and the reaction mixture (Table 1, run 9) was worked up as described above (Section 4.1.1). The resulting precipitate consisting of compounds (**12**) and (**11b**) and (**11c**) (∼26: 57: 17, from ^{19}F NMR and GCMS) was collected by filtration and dried at room temperature. Recrystallization from hexane–benzene (1:1) afforded 1.4 g (31.8%) of amide (**11b**), mp 115–116 °C (lit. mp 117–118 °C [5]) and 0.8 g of mixture of amides (**11b** and **c**) (∼7:3, from ^{19}F NMR). The filtrate was concentrated under reduced pressure, and the residue was twice recrystallized from hexane to give 0.2 g (3%) of benzoxazolidine (**12**) as colorless crystals, mp 97–98 °C (new compound). ^{1}H NMR ($CDCl_3$): δ 4.61 (1H br.s, NH), 6.83–6.85 (1H, m, CH), 6.92–6.96 (1H, m, CH), 7.06–7.13 (2H, m, 2CH). ^{19}F NMR ($CDCl_3$): δ −119.6 (2F, dm, $CF_A\mathbf{F_B}CN$, $^2J_{FF} \approx 288$, $CF_A\mathbf{F_B}CO$, $^2J_{FF} \approx 288$ Hz), −114.2 (2F, dm, $C\mathbf{F_A}F_BCN$, $^2J_{FF} \approx 288$, $C\mathbf{F_A}F_BCO$, $^2J_{FF} \approx 288$ Hz), −70.09 (3F, t, $^3J_{FF}$ = 2.1 Hz, CF_3), −79.08 (3F, t, $^3J_{FF}$ = 2.1 Hz, CF_3). IR: ν 1504, 1605, 1632 (C=C), 1763 (C=O), 3315 (NH). EIMS, *m/z* (rel. int.): 385 (27.8, M^+), 267 (11.3), 266 (100, $[M - C_2F_5]^+$), 238 (12.4, $[M - C_2F_5CO]^+$), 218 (9.9), 169 (6.1, $[M - C_2F_5CO\text{-}CF_3]^+$), 168 (13.5), 119 (5.8, $[C_2F_5]^+$), 102 (14.2, $[C_6H_4NC]^+$), 93 (7.2, $[C_6H_5O]^+$), 69 (7.0, $[CF_3]^+$), 65 (17.5), 52 (6.0). Anal. Calcd for $C_{12}H_5F_{10}NO_2$: C, 37.4; H, 1.3; F, 49.4; N, 3.6. Found: C, 37.3; H, 1.4; F, 49.6; N, 3.4.

*4.5.2.1. Amide (**11b**).* ^{1}H NMR [$(CD_3)_2SO$]: δ 6.14 (1H, br.s, OH), 6.91–7.00 (1H, m, CH), 7.10–7.14 (1H, m, CH), 7.12 (1H, m, CH), 7.98–8.00 (1H, m, CH), 8.58 (1H, br.s, NH). ^{19}F NMR [$(CD_3)_2SO$]: δ −121.6 (2F, q, $^3J_{FF}$ = 1.6 Hz, CF_2), −82.4 (3F, t, $^3J_{FF}$ = 1.6 Hz, CF_3). IR: ν 1509, 1552, 1598, 1618 (C=C), 1695 (C=O), 3325, 3383 (OH, NH). EIMS, *m/z* (rel. int.): 255 (39.5, M^+), 168 (10.0), 137 (6.8), 136 (100, $[M - C_2F_5]^+$), 119 (11.8, $[C_2F_5]^+$), 108 (35.1, $[M - C_2F_5CO]^+$), 90 (6.3, $[C_6H_4N]^+$), 80 (48.1), 79 (7.4), 69 (10.4). Calcd for $C_9H_6F_5NO_2$: C, 42.35; H, 2.35; F, 37.25; N, 5.49. Found: C, 42.23; H, 2.39; F, 37.55; N, 5.54.

*4.5.2.2. Amide (**11c**).* ^{19}F NMR [$(CD_3)_2SO$]: δ −126.7 (2F, s, $CF_2\mathbf{CF_2}CF_3$), −119.3 (2F, q, $^4J_{FF}$ = 8.5 Hz, $\mathbf{CF_2}CF_2CF_3$,), −80.3 (3F, t, $^4J_{FF}$ = 8.5 Hz, CF_3,).

4.6. The reaction of oxirane **3** with 2-aminophenol

In a similar manner, oxirane (**3**) (3.5 g, 11 mmol) was treated with 2-aminophenol (2.4 g, 22 mmol) in 55 ml of dioxane for 4.5 h. The reaction mixture (Table 1, run 10) was worked up as above in Section 4.1.1. The solid obtained consisting of regioisomers (**10c** and **d**) (51:49) was purified by column chromatography (eluent–$CHCl_3$, R_f **10c**, **d** = 0.45) and recrystallized from hexane three times to afford benzoxazinole (**10c**) (1.0 g, 23%) as colorless crystals, mp 115 °C (subl.) (new compound). ^{1}H NMR ($CDCl_3$): δ 4.51 (1H, br.s, OH), 7.04–7.07 (1H, m, CH), 7.19–7.22 (1H, m, CH), 7.40–7.44 (1H, m, CH), 7.60–7.62 (1H, m, CH). ^{19}F NMR ($CDCl_3$): δ −126.1 (1F, dd, $^2J_{FF}$ = 293.6, $^3J_{FF}$ = 11.2 Hz, $CF_AF_BCF_A\mathbf{F_B}CF_3$), −124.8 (1F, dddq, $^2J_{FF}$ = 293.6, $^3J_{FF}$ = 11.4, 4.1; $^6J_{FF}$ = 2.5 Hz, $CF_AF_BC\mathbf{F_A}F_BCF_3$), −122.6 (1F, dqdq, $^2J_{FF}$ = 289.6, $^5J_{FF}$ = 15.4, $^3J_{FF}$ = 11.4, $^4J_{FF}$ = 10.0 Hz, $CF_A\mathbf{F_B}CF_ACF_BCF_3$), −120.4 (1F, ddqqd, $^2J_{FF}$ = 289.6, $^3J_{FF}$ = 11.2, $^5J_{FF}$ = $^4J_{FF}$ = 10.0, $^3J_{FF}$ = 4.1 Hz, $C\mathbf{F_A}F_BCF_AF_BCF_3$), −82.0 (3F, t, $^4J_{FF}$ = 10.0 Hz, $CF_AF_BCF_AF_B\mathbf{CF_3}$), −67.2 (3F, ddd, $^5J_{FF}$ = 15.4, 10.0; $^6J_{FF}$ = 2.5 Hz, CF_3CN). IR: ν 1580, 1590, 1630 (C=C, C=N), 2660, 2710, 3150 broad (OH). Anal. Calcd For $C_{12}H_5F_{10}NO_2$: C, 37.4; H, 1.3; F, 49.4; N, 3.6. Found: C, 37.4; H, 1.4: F, 49.5; N, 3.6.

4.6.1.1. Benzoxazinole (**10d**) (new compound)

^{19}F NMR ($CDCl_3$): δ −124.9 (2F, br.s, $CF_3\mathbf{CF_2}CF_AF_B$), −112.0 (1F, dqq, $^2J_{FF}$ = 298.1, $^5J_{FF}$ = 13.6; $^4J_{FF}$ = 9.9 Hz, $CF_3CF_2CF_A\mathbf{F_B}$), −109.1 (1F, dqq, $^2J_{FF}$ = 298.1, $^5J_{FF}$ = 11.0, $^4J_{FF}$ = 9.9 Hz, $CF_3CF_2C\mathbf{F_A}F_B$), −84.2 (3F, ddt, $^5J_{FF}$ = 13.6, 11.0; $^6J_{FF}$ = 1.2 Hz, CF_3CO), −80.8 (3F, t, $^4J_{FF}$ = 9.9 Hz, $\mathbf{CF_3}CF_2CF_AF_B$).

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