$C_{28}H_{49}N_6O_6$ calc. 593.4027, found 593.4009. ^1H NMR ($CDCl_3$), δ(ppm) 0.75-0.97 (m,12H,4CH_3 Val and Ile); 1.23 (d,J=7Hz,3H, CH_3 Ala); 1.2-1.6 (m,5H,$CH_2\gamma$ Ile and $CH_3\delta$ Nva); 1.6-2.5 (m,10H,CHβ Ile, $CH_2\beta$ and $CH_2\gamma$ Pro, $CH_2\gamma$ Nva,CHβ Val and CH_2-CO βAla); 2.67 (s,3H,N-CH_3 Ala); 3.05-3.25 and 3.92-4.02 (2m,2H,N-CH_2 βAla); 3.05 (s,3H,N-CH_3 Nva); 3.15 (s,3H,N-CH_3 Val); 3.4-3.55 and 3.9-4.1 (2m,2H,N-CH_2 Pro); 4.55-4.65 (m,1H,CHα Nva); 4.63 (m,1H,CHα Pro); 4.75-4.8 (m,1H,CHα Ile); 4.94 (d,J=11Hz,1H,CHα Val); 5.14 (q,J=7Hz,1H,CHα Ala); 7.1 (d,J=9Hz,1H,NH Ile); 8.0-8.1 (m,1H,NH β Ala).

c(Ile-NMeVal-NMeAla-βAla-(L)Nva-Pro) (8e): m.p.=110-115°C; Yield=78%; TLC: R_f=0.4 ($CHCl_3$/isopropanol 92.5/7.5); HPLC (CH_3CN/H_2O 50/50) retention time=5.8 min; (CH_3CN/H_2O 40/60) retention time=8.5; MS FAB(+) (GT) $(M+H)^+$=579; FAB(-) (G) $(M-H)^-$=577. MS (HR-FAB) : $(M+H)^+$ $C_{29}H_{51}N_6O_6$ calc. 579.3870, found 579.3900. ^1H NMR ($CDCl_3$), δ(ppm) 0.7-0.9 (m,12H,4CH_3 Val and Ile); 1.27 (d,J=7Hz,3H,CH_3 Ala); 1.1-1.5 (m,5H,$CH_2\gamma$ Ile and $CH_3\delta$ Nva); 1.61-1.63 (m,2H,$CH_2\gamma$ Nva); 1.8-2.5 (m,8H,CHβ Ile,$CH_2\beta$ and $CH_2\gamma$ Pro,CHβ Val and CH_2-CO βAla); 2.65 (s,3H,N-CH_3 Ala); 3.06-3.08 and 3.90-3.92 (2m,2H,N-CH_2 βAla); 3.2 (s,3H,N-CH_3 Val); 3.5-3.52 and 4.10-4.12 (2m,3H,N-CH_2 Pro and CHα Nva); 4.26 (m,1H,CHα Pro); 4.61(m,1H,CHα Ile); 4.9-5.05 (m,2H,CHα Val and CHα Ala); 7.75-7.85 (m,1H,NH Ile); 8.65-8.75 (m,1H,NH βAla).

c(Ile-NMeVal-NMeAla-βAla-(D)Nva-Pro) (8f): m.p.=145-150°C; Yield=74%; TLC: R_f=0.37 ($CHCl_3$/isopropanol 92.5/7.5); HPLC (CH_3CN/H_2O 50/50) retention time=5.2 min; (CH_3CN/H_2O 40/60) retention time=11.7; MS FAB(+) (GT) $(M+H)^+$=579; FAB(-) (G) $(M-H)^-$=577. MS (HR-FAB) : $(M+H)^+$ $C_{29}H_{51}N_6O_6$ calc. 579.3870, found 579.3839. ^1H NMR ($CDCl_3$), δ(ppm) 0.75-1.0 (m,12H,4CH_3 Val and Ile); 1.26 (d,J=7Hz,3H,CH_3 Ala); 1.2-1.5 (m,5H,$CH_2\gamma$ Ile and $CH_3\delta$ Nva); 1.71-1.73 (m,2H,$CH_2\gamma$ Nva); 1.8-2.1 (m,4H,CHβ Ile,HCHβ and $CH_2\gamma$ Pro); 2.31-2.33(m,1H,CHβ Val); 2.3-2.5 (m,3H,HCHβ Pro and CH_2-CO βAla); 2.7 (s,3H,N-CH_3 Ala); 3.14-3.16 and 3.94-3.96 (2m,2H, N-CH_2 βAla); 3.2 (s,3H,N-CH_3 Val); 3.5-3.52 and 4.09-4.11 (2m,2H,N-CH_2 Pro); 4.25-4.35 (m,1H,CHα Nva) 4.53 (m,1H,CHα Pro); 4.79-4.81 (m,1H,CHα Ile); 5.0 (d,J=9Hz,1H,CHα Val); 5.18 (q,J=7Hz,1H,CHα Ala); 6.05 (d,J=5Hz,1H,NH Ile); 8.2-8.3 (m,1H,NH βAla).

c(Ile-NMeVal-NMeAla-βAla-(D)NMeAla-Pro)$_2$ (9b): m.p.=220°C; TLC: R_f=0.17 ($CHCl_3$/isopropanol 92.5/7.5); HPLC (CH_3CN/H_2O 50/50) retention time=6.7 min; (CH_3CN/H_2O 40/60) retention time=16.6 min; MS FAB(+) (G) $(M+H)^+$=1129; FAB(-) (G) $(M-H)^-$=1127. MS (HR-FAB) : $(M+H)^+$ $C_{56}H_{97}N_{12}O_{12}$ calc. 1129.7349, found 1129.7472. ^1H NMR ($CDCl_3$), δ(ppm) 0.7-1.05 (m,24H,8 CH_3 Val and Ile); 1.3 and 1.4 (2d,J=7Hz,12H,4 CH_3 Ala); 1.15-3.7 (m,28H,2$CH_2\gamma$ and 2Cβ Ile,2$CH_2\beta$,2$CH_2\gamma$ and 2N-CH_2 Pro,2CHβ Val,2CH_2CO and 2N-CH_2 βAla); 2.83 (s,6H,2N-CH_3 Ala); 3.12 and 3.17 (2s,12H,4N-CH_3 (D)Ala and Val); 4.67 (q,J=7Hz,2H,2CHα (D)Ala); 4.9-5.45 (m,8H,2X4CHα Pro,Ile,Val and Ala); 7.3 (m,2H,NH Ile); 8.75 (d,J=9Hz,2H,NH βAla).

REFERENCES

1. Fargues, J.; Robert, P-H.; Vey, A. *Entomophaga* **1985**, *30*, 353-364.
2. Fargues, J.; Robert, P-H.; Vey, A.; Païs, M. *C. R. Acad. Sci.* **1986**, *303*, série III, 83-86.
3. Robert P-H.; Fargues J. *C. R. Acad. Sci.* **1986**, *303*, série III, 641.
4. Calmès,M.; Cavelier-Frontin, F.; Jacquier,R.; Mercadier, J-L.; Sabil, S.; Verducci, J.; Quiot, J-M.; Vey, A. *Int. J. Peptide Protein Res.* **1993**, *41*, 528-535.
5. Anteunis, M. J. O.; Van Der Auwera, C. *Int. J. Peptide Protein Res.* **1988**, *31*, 301-310.
6. Coste, J.; Dufour, M-N.; Pantaloni, A.; Castro, B. *Tetrahedron Lett.* **1990**, *31*, 669-672.
7. Diago-Meseguer, J.; Palomo-Coll, A. L. *Synthesis* **1980**, 547-551.
8. Tung, R. D.; Rich, D. H. *J. Am. Chem. Soc.* **1985**, *107*, 4342-4343.
9. Tung, R. D.; Dhaon, M. K.; Rich, D. H. *J. Org. Chem.* **1986**, *51*, 3350-3354.
10. Van Der Auwera, C.; Van Damme, S.; Anteunis, M. J. O. *Bull. Soc. Chim. Belg.* **1986**, *95*, 203-205.
11. Van Der Auwera, C.; Van Damme, S.; Anteunis, M. J. O. *Int. J. Peptide Protein Res.* **1987**, *29*, 464-471.
12. Van Der Auwera, C.; Anteunis, M. J. O. *Int. J. Peptide Protein Res.* **1987**, *29*, 574-588.
13. Cheung, S. T.; Benoiton, N. L. *Can. J. Chem.* **1977**, *55*, 906-910.
14. Freidinger, R. M.; Hinkle, J. S.; Perlow, D. S.; Arison, B. H. *J. Org. Chem.* **1983**, *48*, 77-81.
15. Cruisi, E.; Huerta, J. M.; Andreu, D. *Tetrahedron Lett.* **1990**, *29*, 4191-4194.
16. Schmitt, R.; Neubert, K. *Int. J. Peptide Protein Res.* **1991**, *37*, 502-507.
17. Hoffmann, E.; Beck-Sickinger, A. G.; Jung, G. *Liebigs Ann. Chem.* **1991**, 585-590.
18. Ehrlich, A.; Rothermund, S.; Brudel, M.; Beyermann, M.; Carpino, L.A.; Bienert, M. *Tetrahedron Lett.* **1993**, *34*, 4781-4784.
19. Ehrlich, A.; Brudel, M.; Beyermann, M.; Winter, R.; Carpino, L.A.; Bienert, M. *Peptides* **1994**, ESCOM, editor H.L.S. Maia, p.167-168.
20. Shiori, T.; Ninomuja, K; Yamada, S. *J. Am. Chem. Soc.* **1972**, *94*, 6203-6206.
21. Freidinger, R. M.; Brady, S. F.; Swenk, D. A.; Mendlowski, M.; Varga S. L.; Holly F. W.; Veber D. F. *J. Org. Chem.* **1979**, *44*, 3101.
22. Spatola, A. F.; Amwer, M. K.; Rockwell, A. L.; Gierasch, J. M. *J. Am. Chem. Soc.* **1986**, *108*, 825-831.
23. Boger, D. L.; Yohannes, D. *J. Org. Chem.* **1990**, *55*, 6000-6017.
24. Bergeron, R. J.; McManis, J. S.; Perumal, P. T.; Algee, S. E. *J. Org. Chem.* **1991**, *56*, 5560-5563.
25. Bailey, P. D.; Crofts, G. A. *Tetrahedron Lett.* **1992**, *33*, 3207-3208.
26. Boger, D. L.; Myers, Jr J. B.,*J. Org. Chem.* **1991**, *56*, 5385.
27. Steh, L.; Mokotoff, M. *Tetrahedron Lett.* **1985**, *26*, 5755-5758.
28. Vey A., INRA-URA CNRS 11840, Research Station for Comparative Pathology, 30195 Saint-Christol-lez-Alès, France.
29. Courtiade B, Biochimie Agro Vétérinaire, ROUSSEL UCLAF, 102-111 Route de Noisy, 92230 Romainville, France.
30. Beyerman, H. C.; De Leer, E.W. B.; Floor, J., *Rec. Trav. Chim.* **1973**, *92*, 481-492.

(*Received in Belgium* 26 *December* 1995; *accepted* 22 *February* 1996)

Pergamon

Tetrahedron, Vol. 52, No. 17, pp. 6187-6200, 1996

0040-4020/96 $15.00 + 0.00

S0040-4020(96)00243-8

Sequential Radical Perfluoroalkylation - Nucleophilic Cyclization. Synthesis of 2-Perfluoroalkylidenemethyl and 2-Perfluoroalkylmethyl-1,4-dioxanes from 1-*O*-allyl-1,2-diols.

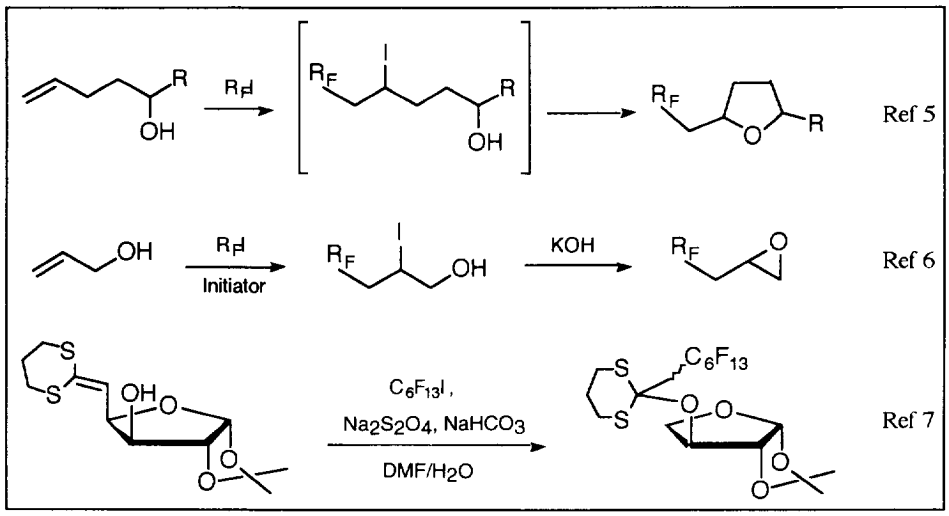
Gaëlle Foulard, Thierry Brigaud and Charles Portella*

Laboratoire des Réarrangements Thermiques et Photochimiques, Associé au CNRS
UFR Sciences. BP 1037. 51087 REIMS CEDEX 2.

Abstract. The title compounds were synthesized by radical addition of perfluoroalkyl iodide to 1-*O*-allyl-1,2-diols and subsequent nucleophilic cyclization according to one of the following procedures. Basic treatment of the iodo F-alkyl adduct gave an olefinic compound which is stereoselectively cyclized with an excess of base into the corresponding 2-perfluoroalkylidenemethyl-1,4-dioxane through a S_N' process. The direct cyclization of the adduct into 2-perfluoroalkylmethyl-1,4-dioxane was achieved by a new and simple method using molecular iodine or positive halogen reagents (DBH, NBS) for the activation of the carbon-iodine bond. Copyright © 1996 Elsevier Science Ltd

The synthesis of new perfluoroalkylated (F-alkylated) compounds is a permanent matter of interest owing to their various applications.[1] The radical chain addition of F-alkyl iodide to an unsaturated substrate is widely used for this purpose. The addition to a double bond gives a 1-F-alkyl-2-iodo product which is often transformed by hydrogenolysis of the C-I bond or by elimination of HI.[2] The addition works very well on heteroatom substituted alkenes (enriched alkenes) owing to the electrophilic character of the F-alkyl radical. In these cases, the easy solvolysis of the C-I bond or elimination of hydrogen iodide leads to non iodinated functionalized products.[3]

However, the presence of the C-I bond could be exploited for further elaboration into cyclized compounds. Some papers have reported the tandem radical addition-radical cyclization from diallylether as a mechanistic probe of a radical mechanism or for synthetic purposes,[4] but very few reports take advantage of the nucleofugal ability of the iodide for nucleophilic inter-or intramolecular displacement: formation of a tetrahydrofuran ring by radical addition of R_FI to penten-4-ol in basic medium has been described;[5] F-alkylmethylepoxyde was obtained from addition of R_FI to allylic alcohol followed by a basic treatment;[6] we observed the formation of protected α-F-alkyl-γ-lactones by addition of R_FI to γ-hydroxylated ketenedithioacetals.[7] (Scheme 1).

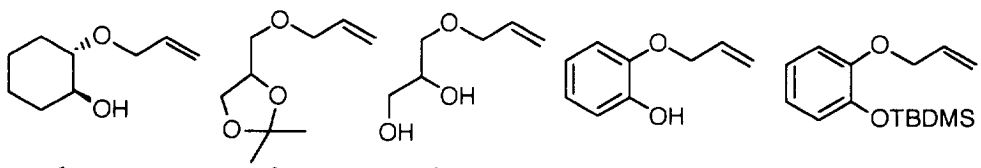


Scheme 1

Considering that such a consecutive radical addition-nucleophilic cyclization could be a method of choice for the synthesis of new F-alkylated heterocycles, and that polyhydroxylated natural products would be interesting substrates for later applications, we have undertaken a program on the radical addition of F-alkyliodide on 1-*O*-allyl-1,2-diols in order to have access, after nucleophilic intramolecular displacement of iodide, to 2-F-alkylmethyl-1,4-dioxanes. We report here the results obtained from model simple 1,2-diols and from glycerol, which will show: (i) how we have taken advantage of a competing elimination to prepare F-alkylidenmethyl-1,4-dioxanes; (ii) a new method of cyclisation to prepare F-alkylmethyl-1,4-dioxanes.[8]

Results and discussion

The starting compounds **1**-**5** were prepared by opening of the activated epoxide by allylic alcohol (for **1**) or by Williamson reactions of the alkoxide with allyl bromide (for **2** and **4**). The deprotection of the solketal derived allylether **2** gave 1-*O*-allyl glycerol **3**. Protection of *O*-allyl catechol **4** gave the silylether **5**.

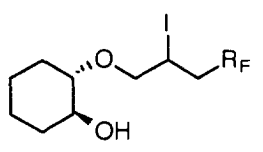


1 racemic *trans* **2** **3** **4** **5**

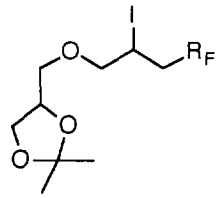
Radical addition of R_FI

The addition of F-alkyliodide was first initiated with azobisisobutyronitrile (AIBN) in the presence of 2,6-lutidine to favour a possible subsequent cyclization of the adduct.[5a] Only addition was observed and reactions were further carried out without adding a base in the medium, under initiation with AIBN or with triethylborane[9] (1 M in hexane)-O_2. Results are summarized in Table 1. All reactions with AIBN were carried

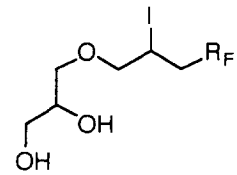
out without solvent. Reactions with Et_3B were carried out at room temperature either in pentane as solvent or, particularly for the poorly soluble compound **3**, without solvent. The reactions with AIBN are slow and it is sometimes difficult to obtain a total conversion of the starting material, even after further addition of initiator. Generally, the reaction was much faster with Et_3B as initiator. Satisfactory yields of adducts were usually obtained (table 1), except for the catechol derivative **4**. The difficult formation of **9** may be explained by an inhibition of the chain reaction by the phenol moity. Conversion of **4** into the silyl ether **5** and a subsequent addition of R_FI led efficiently to the adduct **10**. Compound **9** was easily obtained from **10** by treatment with tetrabutylammonium fluoride (TBAF) under acidic conditions in order to avoid elimination *(vide infra)*.



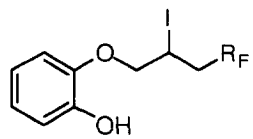
6



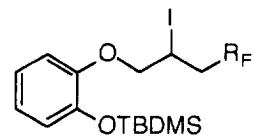
7



8



9



10

Table 1. Radical addition of R_FI to *O*-allyl diols **1- 5**

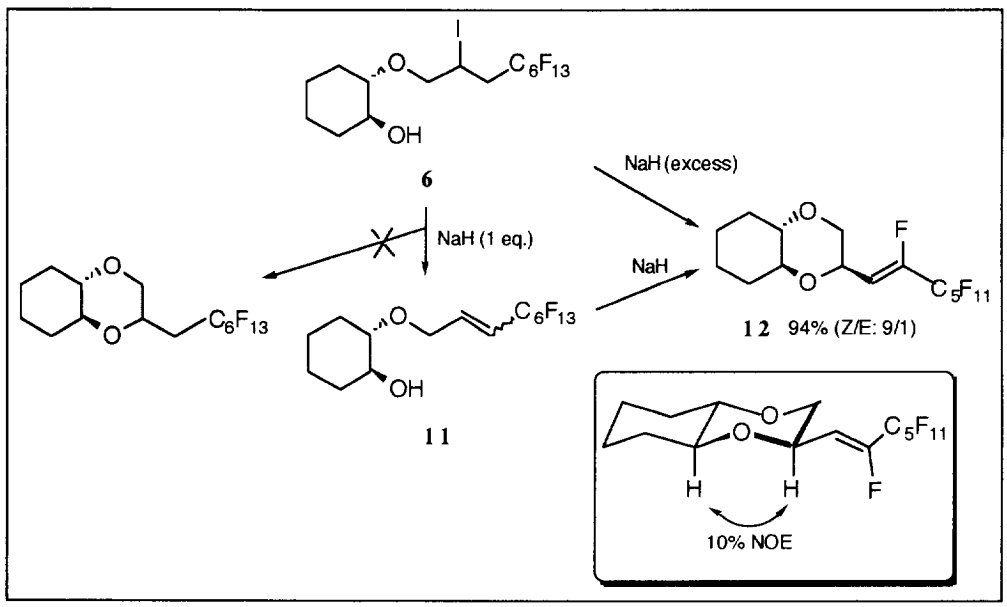
Starting compound	Initiator (eq)	conditions	Product	yield (%)[a]
1	AIBN (0.4)	2,6-lutidine (1.2 eq.)/ 90- 100°C	**6**	61
1	AIBN (0.1)	90- 100°C	**6**	62[b]
1	Et_3B/ O_2 (0.06)	pentane, RT	**6**	68
2	Et_3B/ O_2 (0.1)	pentane, RT	**7**	66
3	AIBN (0.1)	90- 100°C	**8**	77
3	Et_3B/ O_2 (0.2)	no solvent, RT	**8**	75
4	AIBN	90- 100°C	**9**	0
5	Et_3B/ O_2 (0.5)	pentane, RT	**10**	64

a) isolated yield of pure product. b) 90% conversion

Elimination and cyclization to F-alkylidenemethyl dioxanes

As mentioned above, 2,6-lutidine was too weak a base for initiating nucleophilic cyclizations. The treatment of **6** with various stronger bases such as NaH, DBU or KOH at room temperature, or triethylamine at 65°C led, instead of the cyclodehydroiodidation product, to the elimination product **11** (Scheme 2). The

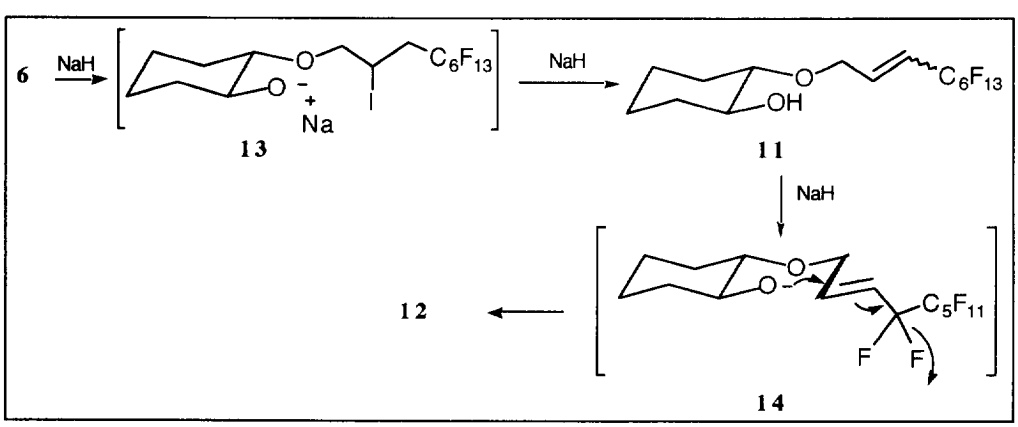
treatment of **11** or **6** with an excess of NaH, led to the F-alkylidenemethyl-1,4-dioxane **12** in high yield. The cyclisation step was completely diastereoselective giving the all equatorial compound as shown by a 10% NOE between H-2 and H-6 of the dioxane moiety.[10] The ratio Z/E = 9/1 was determined by NMR: the signal with the higher coupling constant was attributed to the Z isomer (trans relationship between H and F).



Scheme 2

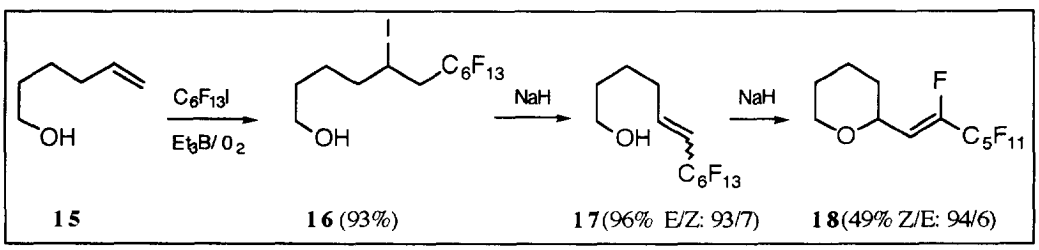
Owing to the lability of the C-H bonds between the R_F and I groups, the abstraction of one of these protons by the alkoxide **13** (probably by intermolecular processes) competes with intramolecular substitution of iodide. Compound **12** arose from an intramolecular $S_{N'}$ substitution via the alkoxide **14** (Scheme 3).[11]

An attempt of iodo-cyclisation of **11** (3 eq. I_2, 3 eq. $NaHCO_3$, CH_3CN, rt) was unsuccessful because of deactivation of the double bond.



Scheme 3

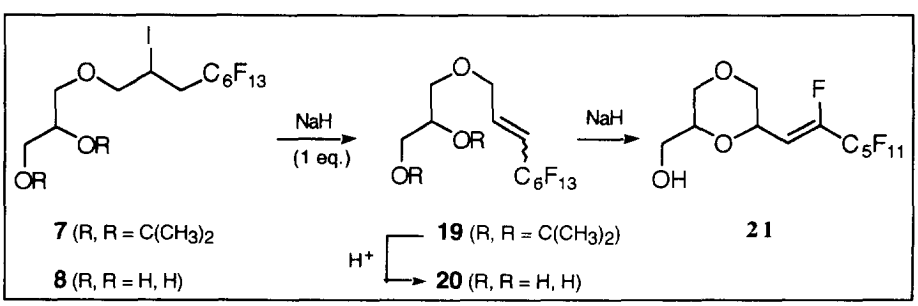
Surprisingly, elimination has not been mentioned in previous examples of cyclisation under basic conditions. In order to discriminate a possible role of an additional oxygen and/or the length between the two functional carbon atoms, hex-5-en-1-ol **15** was submitted to the same reaction sequence. The various reactions proceeded similarly and efficiently to give the corresponding compounds **16-18** (Scheme 4), showing that a heteroatom in the chain does not induce particular reactivity and that our conditions are of general use for heterocyclic synthesis.



15 **16** (93%) **17** (96% E/Z: 93/7) **18** (49% Z/E: 94/6)

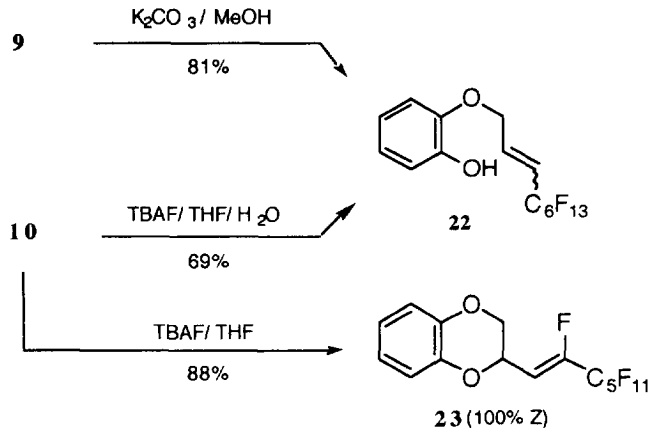
Scheme 4

Treated with one equivalent of NaH in THF, glycerol derivatives **7** and **8** gave cleanly the corresponding allylic ethers **19** (82 %) and **20** (86 %) respectively. Compound **20** was also prepared by acid hydrolysis of **19**. The S_N' type cyclisation with an excess of base also occurred, giving the dioxane **21**, but with a lower yield (35 %) than above (Scheme 5). Compound **21** was obtained as a mixture of diastereomers (overall Z/E = 90/10). The diastereoselectivity of the cyclization was 90/10, but we have not determined unambigously the relative configurations.

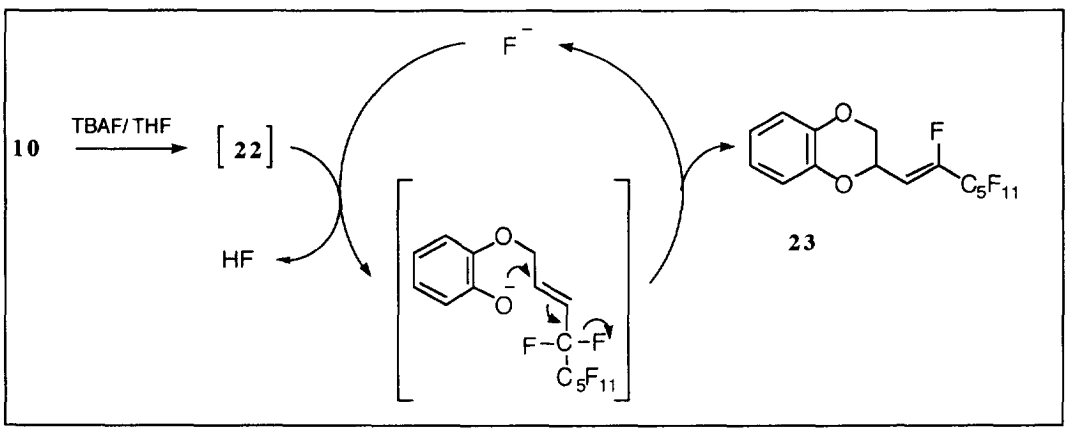


Scheme 5

Compound **9** was efficiently converted into the allylic ether **22** (81%) when treated with potassium carbonate in methanol. The reaction of the silyl protected analogue **10** with tetrabutylammonium fluoride depended on the conditions. Hydrated TBAF in THF converted **10** into **22** (69%) whereas dry TBAF in THF gave a high yield (88%) of the corresponding dioxane **23** in a pure Z-configuration (scheme 6). It is noteworthy that only one equivalent of TBAF was required, indicating that fluoride is basic enough to initiate the intramolecular S_N' substitution which is a catalytic process (Scheme 7). The benzodioxane moiety is found in various bioactive molecules.[12] By our methodology fluorosubstituted derivatives could be obtained from synthons such as **23**.



Scheme 6

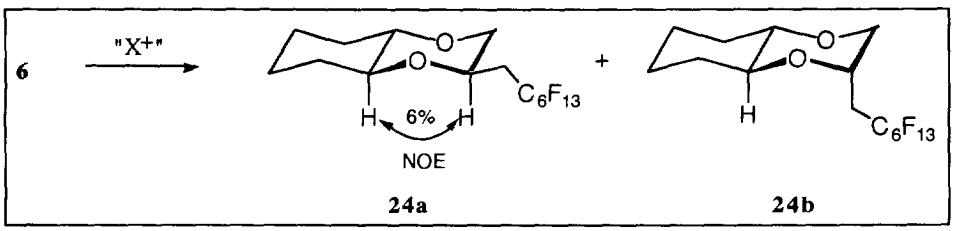


Scheme 7

Direct cyclization to F-alkylmethyldioxanes

Owing to the impossibility to achieve the direct cyclization of adducts by activation of the nucleophilic moiety in basic medium (S_N2 conditions), we have attempted to favour a S_N1 process by activation of the dissociation of the C-I bond. Results are described in the scheme 8 and Table 2. Activaton with silver oxide was unsuccessful. Compound **6** was warmed in a polar aprotic solvent, DMSO, and no reaction was observed below 150°C. At this temperature some cyclization was obtained giving the F-alkylmethyl dioxane **24** as a minor product in a mixture containing also the unsaturated product **11**. Better results were observed when the reaction was performed in the presence of pyridine in order to neutralize the strong hydroiodic acid, dioxane **24** being now the major product (51 %). To avoid high temperatures, which could be hazardous for other substrates, additives which would enhance the leaving group ability of the iodide were tested. Iodine exchange between alkyl iodide and molecular iodine is a known process[13] and iodine can act as an efficient Lewis acid.[14] This prompted us to attempt the activation of the carbon iodine bond by molecular iodine. Indeed, in DMSO in the presence of one equivalent of iodine and one equivalent of pyridine, cyclization occurred at 90°C, but

elimination still competed. Other sources of positive halogen and other solvents were tested. Good results were obtained using dibromodimethylhydantoin (DBH) in CH_3CN. Very mild conditions were required with DBH since total conversion occurred using 0.5 equivalent at room remperature in acetonitrile. One equivalent of N-bromosuccinimide gave similar results.



Scheme 8

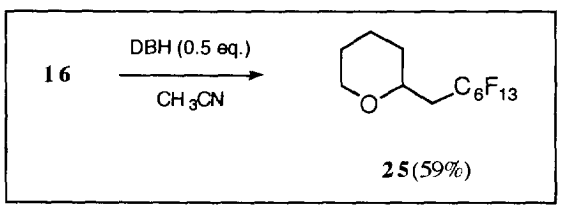
Table 2. Direct cyclisation of compound 6 in various conditions.

Reaction medium	Conditions	Yield of **24** (%)	Comments
Ag_2O, Monoglyme	80°C, 24 h	0	
DMSO	90°C, 3h	0	
DMSO	150°C, 3h	19[a]	+ **11** (10%)
DMSO - Pyridine (1 eq)	150°C, 3h	51[a]	+ **11** (13%)
DMSO - Pyridine (1 eq) - I_2 (1 eq)	90°C	20[a]	+ **11** (35%)
CH_3CN - I_2 (1eq)	80°C	0	
CH_3CN - DBH (0.5 eq)	rt	62[b]	
CH_3CN - NBS (1 eq)	rt	69[c]	

a/ **24a+24b** (ratio not determined); b/ **24a/24b** = 70/30; c/ **24a/24b** = 65/35

Compound **24** was obtained as a mixture of two separable diastereomers **24a** and **24b**. Isomer **24a**, the major one, corresponds to the all equatorial substituted dioxane, as confirmed by the observation of a NOE (6%) between the two axial tertiary protons (Scheme 8) of the dioxane (irradiation of H-2).

Unfortunately, attempted cyclization of the adducts **8** and **9** under the same conditions was unsuccessful, giving a complex mixture of products. The failure of a clean reaction was probably due to side reactions with the highly reactive dihalogen generated in the medium, but attempts to improve the process in the presence of reductive agents have been unsuccessful so far. In contrast, the simple hexenol derivative **16** was efficiently cyclized into the corresponding 2-(F-alkylmethyl)tetrahydropyran **25** (Scheme 9).



Scheme 9

Conclusion

Two classes of fluorinated 1,4-dioxanes were synthesized from adducts obtained from radical addition of R_FI to 1-*O*-allyl-1,2-diols. Under basic treatment, HI elimination and subsequent intramolecular S_N' reaction led to 2-F-alkylidenemethyl-1,4-dioxanes in high yields and stereoselectivity. Direct cyclization into 2-F-alkylmethyl-1,4-dioxane has been achieved by activation of the C-I bond with halonium ions. This original procedure, very efficient for simple model molecules, remains to be improved for polyhydroxylated ones. Further investigations in this area are in progress.

EXPERIMENTAL SECTION

General methods.

Melting points are uncorrected. FT-IR spectra were run on a MIDAS corporation apparatus. ^1H, ^{19}F, and ^{13}C NMR spectra were recorded on a BRUCKER AC-250 spectrometer. All chemical shifts are reported in parts per million against internal tetramethylsilane for ^1H and ^{13}C NMR spectra and $CFCl_3$ for ^{19}F NMR spectra. MS data were obtained on a JEOL D 300 apparatus at 70 eV in the electron impact mode. Elemental analyses were performed with a Perkin Elmer CHN 2400 apparatus. All reactions were monitored by TLC (Merck F 254) or GC. GC analyses were performed on a HP 5890 chromatograph equipped with a polydimethylsiloxane HP ultra I column and a flame ionization detector. Silicagel Merck 9385 (40-63 μm) was used for flash chromatography.

Starting materials

Starting *Trans*-2-(allyloxy)cyclohexanol **1** was prepared according to reported procedures.[15] Hex-5-en-1-ol **15** is commercially available.

1,2-*O*-isopropylidene-3-(allyloxy)propane-1,2-diol (2). To a stirred solution of solketal (12.4 mL, 0.1 mol) in 200 mL of a mixture toluene-DMSO 20/80 was added crushed potassium hydroxide (14 g, 0.25 mol) and allylbromide (10.4 mL, 0.12 mol). The resulting mixture was stirred overnight at room temperature, filtered and washed with a saturated solution of ammonium chloride until neutralization. The aqueous layer was extracted with toluene (3x 50 mL). The solution was dried over anhydrous Na_2SO_4 and toluene removed under vacuum to give **2** as an oil (16.3 g, 95% yield).

^1H NMR δ 1.33 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 3.45 (dd, 1H, J_{AB} = 9.9 Hz, ^3J = 5.7 Hz, H_3), 3.52 (dd, 1H, J_{AB} = 9.9 Hz, ^3J = 5.7 Hz, H_3'), 3.73 (dd, 1H, J_{AB} = 8.4 Hz, ^3J = 6.5 Hz, H_1), 4.02 (dd, 2H, ^3J = 5.5 Hz, ^4J = 1.1 Hz, O-CH_2C=C), 4.05 (dd, 1H, J_{AB} = 8.4 Hz, ^3J = 6.5 Hz, H_1'), 4.28 (quintuplet, 1H, ^3J = 6.1 Hz, H_2), 5.18 (ddt, 1H, $^3J_{cis}$ = 10.3 Hz, J_{gem} = 1.9 Hz, ^4J = 1.1 Hz, C=CH_2), 5.27 (ddt, 1H, $^3J_{trans}$ = 17.2 Hz, J_{gem} = 1.9 Hz, ^4J = 1.5 Hz, C=CH_2), 5.90 (ddt, 1H, $^3J_{trans}$ = 17.2 Hz, $^3J_{cis}$ = 10.3 Hz, ^3J = 5.5 Hz, CH=C); ^{13}C NMR δ 25.4 and 26.7 (C(CH_3)2), 66.8 (C_3), 71.1 (O-CH_2), 72.5 (C_1), 74.7 (C_2), 109.4 ($C(CH_3)_2$), 117.2 (=CH_2), 134.5 (CH=).

3-(allyloxy)propane-1,2-diol (3). To a solution containing **2** (2 g, 11.6 mmol) in EtOH-H_2O 95/5 (v/v, 20 mL) was added activated Amberlyst® 15 (wet) H^+ (1.5 g). The mixture was stirred 4 h at 40° C and one night at rt. The resin was filtered off, washed with EtOH and the solution was concentrated. The crude product was diluted in CH_2Cl_2, dried over anhydrous Na_2SO_4 and the solvent was removed. Purification by flash chromatography (AcOEt-petroleum ether 1/1) afforded **3** as a liquid (1.37g, 89%).

^1H NMR δ 2.76 (t, ^3J = 6.1 Hz, 1H, OH), 3.13 (d, ^3J = 5 Hz, 1H, OH), 3.49 (dd, 1H, J_{AB} = 9.9 Hz, ^3J = 6 Hz, H_3), 3.52 (dd, J_{AB} = 9.9 Hz, ^3J = 4.6 Hz, H_3'), 3.61 (dd, J_{AB} = 11.5 Hz, ^3J = 6.1 Hz, 1H, H_1), 3.69 (dd, 1H, J_{AB} = 11.5 Hz, ^3J = 4.0 Hz, H_1'), 3.87 (tt, ^3J = 4 Hz, ^3J = 6 Hz, H_2), 4.02 (ddd, 2H, ^3J = 5.7 Hz, ^4J = 1.5 Hz, ^4J = 1.1 Hz, O-CH_2C=C), 5.20 (ddt, 1H, $^3J_{cis}$ = 10.3 Hz, J_{gem} = 1.9 Hz, ^4J = 1.1 Hz, C=CH_2), 5.27 (ddt, $^3J_{trans}$ = 17.2 Hz, J_{gem} = 1.5 Hz, ^4J = 1.5 Hz, C=CH_2), 5.90 (ddt, 1H, $^3J_{trans}$ = 17.2 Hz, $^3J_{cis}$ = 10.3 Hz, ^3J = 5.7 Hz, CH=C); ^{13}C NMR δ 64.0 (C_3), 70.7 (C_2), 71.6 (O-CH_2), 72.4 (C_1), 117.4 (=CH_2), 134.3 (CH=).

2-allyloxyphenol (4) Allylbromide (7.9 mL, 0.09 mol) and K_2CO_3 (7.53 g, 0.05 mol) were added to a solution of catechol (10 g, 0.09 mol) in acetone (250 mL). The mixture was stirred and heated at reflux overnight. After

filtration, ether (200 mL) was added and the solution was washed with a saturated aq NH_4Cl. After drying over $MgSO_4$, the solvent was removed and the crude product was purified by flash chromatography (AcOEt-petroleum ether 5/95) to afford **4** as a liquid (8.57 g, 63%).
^1H NMR δ 4.58 (dt, 2H, J = 5.6 Hz, ^4J = 1.5 Hz, O-CH_2C=C), 5.28 (ddt, 1H, $^3J_{cis}$ = 10.3 Hz, Jgem = ^4J = 1.5 Hz, C=CH_2), 5.39 (ddt, 1H, $^3J_{trans}$ = 17.2 Hz, J_{gem} = ^4J = 1.5 Hz, C=CH_2), 5.71 (s, 1H, OH), 6.05 (ddt, 1H, $^3J_{trans}$ = 17.2 Hz, $^3J_{cis}$ = 10.3 Hz, ^3J = 5.6 Hz, CH=C), 6.77-6.96 (m, 4H, H-Ar); ^{13}C NMR δ 69.8 (O-CH_2), 112.2 and 114.7 (C-Ar), 118.2 (=CH_2), 120.0 and 121.7 (C-Ar), 132.9 (CH=), 145.5 (C_2), 145.9 (C_1).

1-allyloxy-2-*tert*-butyldimethylsilyloxybenzene (5). A mixture of 2-allyloxyphenol **4** (1.76 g, 11.7 mmol), imidazole (1.99 g, 29.3 mmol) and *tert*-butyldimethylsilyl chloride (2.12 g, 14.1 mmol) in DMF (12 mL) was stirred 3h at rt under argon. Water (10 mL) was added and the solution was extracted with petroleum ether (3x 50 ml). The combined organic layers were washed with brine and dried over $MgSO_4$. The solvent was removed to give **5** (3.23 g, quantitative) as a colorless liquid.
^1H NMR δ 0.18 (s, 6H, 2xCH_3), 1.03 (s, 9H, C(CH_3)$_3$), 4.54 (dt, 2H, ^3J = 5.3 Hz, ^4J = 1.5 Hz, O-CH_2), 5.28 (ddt, 1H, $^3J_{cis}$ = 10.5 Hz ,^3J = J_{gem} = 1.3 Hz, =CH_2), 5.42 (ddt, 1H, $^3J_{trans}$ = 17.2 Hz, ^3J = J_{gem} = 1.5 Hz, =CH_2), 6.10 (ddt, 1H, $^3J_{cis}$ = 10.5 Hz, $^3J_{trans}$ = 17.2 Hz, ^3J = 5.3 Hz, CH=), 6.84-6.95 (m, 4H, H-Ar); ^{13}C NMR δ -4.6 (Si(CH_3)$_2$), 18.4 (Si*C*(CH_3)$_3$), 25.8 (C(CH_3)$_3$), 69.7 (O-CH_2), 114.1 (C-Ar), 117.5 (=CH_2), 121.3 (2C, C-Ar), 121.7 (C-Ar), 133.7 (CH=), 145.4 (*C*-O-CH_2), 150.1 (C-O-Si); IR (film): 3073, 2922 (s), 2861 (s), 1591 (m), 1505 (s), 1265 (s), 1115 (m), 928 (s), 839 (s), 739 (s).

Perfluoroalkylation: general procedures
Method A. A round bottom flask was charged with the starting *O*-allyl-1,2-diol (5-10 mmol) and perfluorohexyl iodide (1.5 eq). AIBN (0,05 eq) was added and the mixture was stirred in the dark at 90-100° C. The reaction was monitored by GC and an additional amount of AIBN (0.05 eq) was sometimes added to complete the reaction. After completion of the reaction (2.5-8h) the excess of perfluorohexyl iodide was removed *in vacuo* and the crude product was purified by flash chromatography .
Method B. To a suspension of the starting *O*-allyl-1,2-diol (3 mmol) in pentane (3 mL) were added perfluorohexyl iodide (1.3 eq) and Et_3B 1M in hexane (0.1 eq). The mixture is stirred in the dark and the reaction is monitored by GC. After completion of the reaction (1.5-2h) , the solution was poured in brine and extracted with ether. The combined organic layers were washed with brine and dried over Na_2SO_4. The solvent was removed and the crude product was purified by flash chromatography.
Method C. The procedure was the same as in method B except that no solvent was added.

***trans*-2-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-2-iodononyloxy)cyclohexan-1-ol (6).**
method A: 62%; method B: 68%. White solid, mixture of diastereomers. Chromatography: petroleum ether- AcOEt 9/1.
^1H NMR δ 1.15-1.35 (m, 4H, H_4 and H_5), 1.68-1.74 (m, 2H, H_3 and H_6), 2.00-2.05 (m, 2H, H_3 and H_6), 2.61-3.18 (m, 3H, CH_2-CF_2, *CH*-O-CH_2), 2.70 (d, 1H, ^3J = 1.9 Hz, OH) and 2.84 (d, 1H, ^3J = 1.5 Hz, OH), 3.50 (m, 1H, *CH*-OH), 3.60-3.67 (m, 1H, O-CH_2), 3.78-3.91 (m, 1H, O-CH_2), 4.38 (quint, 1H, ^3J = 6.1 Hz, CHI) and 4.44 (m, 1H, CHI); ^{13}C NMR δ 16.1 and 16.7 (C-I), 23.7 and 24.1 (C_4 and C_5), 29.3, 29.4 and 32.0 (C_3 and C_6), 37.9 (t, $^2J_{CF}$ = 20.7 Hz, CH_2-CF_2), 73.3 and 73.5 (O-CH_2), 73.7 and 73.9 (C_1), 84.4 and 84.7 (C_2); ^{19}F NMR δ -81.3 (t, 3F, $^3J_{FF}$ = 9 Hz, CF_3), -113 (dm, 1F, J_{AB} = 280 Hz, F_4) and -114.3 (dm, 1F, J_{AB} = 280 Hz, F_4), one diastereomer, -113.5 (dm, 1F, J_{AB} = 280 Hz, F_4) and -114.5 (dm, 1F, J_{AB} = 280 Hz, F_4), other diastereomer, -122.2 (2F, F_5), -123.3 (2F, F_6), -124.0 (2F, F_7), -126.6 (2F, F_8); IR (KBr): 3387 (s, br), 2936 (s), 2861 (m), 1454, 1366 (m), 1203 (s, br), 1140 (s), 1078 (s), 702 (s), 650 (s) cm^{-1}; MS m/z (%) 602 (M^+, 1), 585, 487 (29), 457 (15), 359 (6), 289 (7), 173 (12), 99 (100); Anal. calc. for $C_{15}H_{16}O_2F_{13}I$: C, 29.92; H, 2.68. Found C, 30.01; H, 2.52.

3-(4,4,5,5,6,6,7,7,8,8,9,9,9-Tridecafluoro-2-iodononyloxy)-1,2-*O*-isopropylidenepropane-1,2-diol (7).
Method B: 66 %. Colorless oil, mixture of diastereomers 50/50. Chromatography: petroleum ether- AcOEt 9/1.
^1H NMR δ 1.36 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 2.69 (m, 1H, CH_2-CF_2), 3.06 (m, 1H, CH_2-CF_2), 3.56 (dd, 1H, J_{AB} = 10.3 Hz, ^3J = 5.3 Hz, H_3), 3.60 (dd, 1H, J_{AB} = 10.3 Hz, ^3J = 5.3 Hz, H_3'), 3.68-3.85 (m, 3H, H_1, H_1' and O-CH_2-CHI), 4.06 (m, 1H, O-CH_2-CHI), 4.22-4.42 (m, 2H, H_2 and CHI); ^{13}C NMR δ 14.1 (CHI), 25.3 and 26.6 (C(CH_3)$_2$), 37.6 (t, $^2J_{CF}$ = 21.7Hz, CH_2-CF_2), 37.7 (t, $^2J_{CF}$ = 21.7 Hz, CH_2-CF_2), 66.6 (C_1), 71.8 (C_3), 74.6

(C_2), 76.3 (O-CH_2), 109.5 ($C(CH_3)_2$); ^{19}F NMR δ -81.3 (t, 3F, $^3J_{FF}$ = 10.0 Hz, CF_3), -114.0 (2F, F_4), -122.2 (2F, F_5), -123.3 (2F, F_6), -124.1 (2F, F_7), -126.6 (2F, F_8); IR (film): 2986 (m), 2936 (m), 2872 (m), 1203 (s), 1078 (s) cm^{-1}; Anal. calc. for $C_{15}H_{16}O_3F_{13}I$: C, 29.14; H, 2.61. Found C, 29.46; H, 2.43.

3-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-2-iodononyloxy)propan-1,2-diol (8).
Method A: 77%. Method B: 57%. Method C: 75%. Solid, one diastereomer. mp: 34-36°C. Chromatography: petroleum ether- AcOEt 1/1.
^1H NMR δ 2.87 (m, 2H, CH_2-CF_2), 3.16 (s, 1H, OH), 3.41 (s, 1H, OH), 3.60 (dd, 2H, ^3J = 5.7 Hz, ^3J = 2.3 Hz, H_3, H_3'), 3.57-3.79 (m, 6H, H_3, H_3', H_1, H_1' and CH_2-CHI), 3.91 (quint., 1H, ^3J = 4.6 Hz, H_2), 4.40 (quint., 1H, ^3J = 6.1 Hz, CHI); ^{13}C NMR δ 14.8 (CHI), 37.8 (t, $^3J_{CF}$ = 20.9 Hz, CH_2-CF_2), 63.8 (C_1), 70.8 (C_2), 72.3 (C_3), 76.0 (OCH_2-CHI); ^{19}F NMR: -81.5 (t, 3F, $^3J_{FF}$ = 11.5 Hz, CF_3), -113.2 (dm, 1F, J_{AB} = 274 Hz, F_4), -114.4 (dm, 1F, J_{AB} = 274 Hz, F_4), -122.2 (2F, F_5), -123.3 (2F, F_6), -123.9 (2F, F_7), -126.6 (2F, F_8); IR (KBr): 3399 (s, br), 2936 (m), 2872 (m), 1366, 1240, 1190 (s, br), 1140 (s), 702 cm^{-1}; MS m/z (%) 580, 487 (100), 467 (29), 451 (66), 391 (33), 377 (8), 340 (19), 313 (13), 289 (27), 245 (12), 173 (35), 75 (97); Anal. calc. for $C_{12}H_{12}O_3F_{13}I$: C, 24.93; H, 2.09. Found C, 25.04; H, 2.06.

1-(*tert*-butyldimethylsilyloxy)-2-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-2-iodononyloxy)benzene (10).
Method B: 64% . Oil. Chromatography: petroleum ether.
^1H NMR δ 0.22 (s, 3H, CH_3), 0.23 (s, 3H, CH_3), 1.03 (s, 9H, $C(CH_3)_3$), 2.78 (dqm, 1H, J_{gem} = $^3J_{HF}$ = 18.0 Hz, $^3J_{HH}$ = 7.6 Hz, CH_2-CF_2), 3.30 (dqm, 1H, J_{gem} = $^3J_{HF}$ = 18.0 Hz, $^3J_{HH}$ = 5 Hz, CH_2-CF_2), 4.21 (dd, 1H, J_{AB} = 10.7 Hz, $^3J_{HH}$ = 7.6 Hz, OCH_2), 4.34 (dd, 1H, J_{AB} = 10.7 Hz, $^3J_{HH}$ = 5 Hz, OCH_2), 4.51 (tt, 1H, $^3J_{HH}$ = 5 Hz, $^3J_{HH}$ = $^3J_{HH}$ = 7.6 Hz, CHI), 6.86-6.94 (m, 4H, H-Ar); ^{13}C NMR δ -4.4 ($Si(CH_3)_2$), 12.8 (CHI), 18.3 ($SiC(CH_3)_3$), 25.7 ($C(CH_3)_3$), 37.6 (t, $^2J_{CF}$ = 20.7 Hz, CH_2-CF_2), 74.2 (OCH_2), 115.3, 121.2, 121.7 and 122.5 (C-Ar), 145.7 (C-O-CH_2), 149.2 (C-O-Si); ^{19}F NMR δ -81.3 (t, 3F, $^3J_{FF}$ = 9.5 Hz, CF_3), -114.1 (tt, 2F, $^3J_{HF}$ = $^3J_{FF}$ = 15.26 Hz, F_4), -122.2 (2F, F_5), -123.3 (2F, F_6), -124.0 (2F, F_7), -126.6 (2F, F_8); IR (film): 2968, 2864, 1591, 1500, 1240 (s) cm^{-1}; Anal. calc. for $C_{21}H_{24}O_2F_{13}I$: C, 35.51; H, 3.40. Found C, 35.74; H, 3.17.

7,7,8,8,9,9,10,10,11,11,12,12,12-tridecafluoro-5-iodo-dodecanol (16).
Method C: 93%. Oil. Chromatography: petroleum ether-AcOEt 4/1.
^1H NMR δ 1.4-1.9 (m, 7H, H_2, H_3, H_4 and OH), 2.65-3.1 (m, 2H, CH_2-CF_2), 3.6-3.8 (t, 2H, ^3J = 6.1 Hz, CH_2-OH), 4.35 (tt, 1H, ^3J = 8 Hz, ^3J = 5.3 Hz, CHI); ^{13}C NMR δ 20.2 (CHI), 25.9, 31.4 and 40.0 (C_2, C_3 and C_4), 41.6 (t, $^2J_{CF}$ = 21.7 Hz, CH_2-CF_2), 62.4 (C_1); ^{19}F NMR δ -81.3 (t, 3F, $^3J_{FF}$ = 9.5 Hz, CF_3), -112.2 (dm, 1F, J_{AB} = 271 Hz, CH_2-CF_2), -114.9 (dm, 1F, J_{AB} = 271 Hz, CH_2-CF_2), -122.2 (2F, F_8), -123.3 (2F, F_9), -124.1 (2F, F_{10}), -126.6 (2F, F_{11}).

2-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-2-iodononyloxy)phenol (9). To a solution of **10** (1.065 g, 1.5 mmol) in THF/H_2O 9/1 (15 mL) were added 35% aq HCl (0.3 mL) and tetrabutylammonium fluoride hydrate (1.419 g, 4.5 mmol) at 0°C. After 2 days at rt, the reaction mixture was extracted with ether (200 mL). The organic layer was dried over Na_2SO_4 and the solvent evaporated. The crude product was purified by flash chromatography (petroleum ether-AcOEt 95/5) to give **9** (62%) as a white solid. mp: 70°C. ^1H NMR δ 2.79-3.18 (m, 2H, CH_2CF_2), 4.22 (dd, 1H, J_{AB} = 10.7 Hz, $^3J_{HH}$ = 5.3 Hz, O-CH_2), 4.25 (dd , 1H, J_{AB} = 10.7 Hz,$^3J_{HH}$ = 5,5 Hz, O-CH_2), 4.59 (ddt, 1H, $^3J_{HH}$ = 7.25 Hz, $^3J_{HH}$ = 5.4 Hz, $^3J_{HH}$ = 2.9 Hz, CHI), 5.64 (s, 1H, OH), 6.83-7.00 (m, 4H, H-Ar); ^{13}C NMR δ 13.7 (CHI), 38.3 (t, $^2J_{CF}$ = 21.7 Hz, CH_2CF_2), 73.6 (O-CH_2), 113.3, 115.5, 120.4 and 123.1 (C-Ar), 144.7 and 146.2 (C-O); ^{19}F NMR δ -81.3 (t, 3F, $^3J_{FF}$ = 9.5 Hz, CF_3), -112.6 (dm, 1F, J_{AB} = 270.8 Hz, F_4), -114.6 (dm, 1F, J_{AB} = 270.8 Hz, F_4), -122.2 (2F, F_5), -123.3 (2F, F_6), -123.9 (2F, F_7), -126.6 (m, 2F, F_8); IR (KBr): 3445 (br), 2936 (s), 1599, 1514 (s), 1464 (s), 1370, 1319, 1234 (s, br), 1204 (s, br), 1138 (s), 1111 (s), 1045, 743, 698 cm^{-1}; MS m/z (%) 596 (M^+, 47), 487 (79), 450 (5), 359 (7), 313 (7), 295 (12), 236 (23), 173 (16), 128 (14), 109 (100), 81 (33).

HI elimination: general procedure.
To a suspension of sodium hydride (1.2 eq) in dry THF (15 mL) was added dropwise at 0°C under Argon a solution of the iodo F-alkylated adduct (2 mmol) in dry THF (20 mL). The reaction mixture was stirred at room temperature for 1 h, and then poured into water (25 mL) and extracted with diethyl ether (3x 50 mL). The organic

layer was washed with saturated aq NH_4Cl until neutralisation and dried over sodium sulfate . After removal of the solvent, crude product was purified by flash chromatography (AcOEt-Petroleum ether).

trans-2-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononon-2-enyloxy)cyclohexan-1-ol (11).
Yield: 87%. White solid, mixture of diastereomers (E/Z > 90/10). Chromatography: petroleum ether-AcOEt 9/1 then 4/1.
^1H NMR δ 1.15-1.39 (m, 4H, H_4 and H_5), 1.72 (m, 2H, H_3 and H_6), 2.04 (m, 2H, H_3 and H_6), 2.53 (d, 1H, ^3J = 1.9 Hz, OH), 3.13 (ddd, 1H, ^3J = 10.3 Hz, ^3J = 8.8, Hz ^3J = 4.6 Hz, C*H*-O-CH_2), 3.48 (ddd, 1H, ^3J = 10.3 Hz, ^3J = 8.4 Hz, ^3J = 4.6 Hz, C*H*-OH), 4.19 (dm, 1H, J_{AB} = 15.6 Hz, O-CH_2), 4.30 (dm, 1H, J_{AB} = 15.6 Hz, O-CH_2), 5.60 (m, 1H, CH-CF_2, Z), 5.95 (dt, 1H, $^3J_{trans}$ = 15.8 Hz, $^3J_{HF}$ = 12 Hz, CH-CF_2, E), 6.30 (m, 1H, CH=C-CF_2, Z), 6.49 (dtt, 1H, $^3J_{trans}$ = 15.8 Hz, ^3J = 4.2 Hz, $^3J_{HF}$ = 2.1 Hz, CH=C-CF_2, E); ^{13}C NMR δ 23.8 and 24.1 (C_4 and C_5), 29.2 and 32.2 (C_3 and C_6), 67.0 (O-CH_2), 73.8 (C-OH), 84.1 (*C*-O-CH_2), 117.0 (t, $^2J_{CF}$ = 23.6 Hz, CH-CF_2), 139.5 (*C*H=C-CF_2); ^{19}F NMR δ -81.4 (t, 3F, ^3J = 11.4 Hz, CF_3), -108.3 (2F, F_4, Z), -112.1 (d, 2F, ^3J = 12 Hz, F_4, E), -122.1 (2F, F_5), -123.3 (2F, F_6), -123.8 (m, 2F, F_7), -126.6 (m, 2F, F_8); IR (KBr): 3463 (w, br), 3073, 2938, 2866, 1684, 1454, 1366 (s), 1262 (s), 1190 (s), 1136 (s), 1069, 1047, 974, 791, 689 cm^{-1}; MS m/z (%) 474 (M^+, 2), 457 (16), 428 (11), 415 (12), 356 (18), 339 (6), 289 (16), 245 (9), 137 (22), 121 (18), 99 (87), 81 (100); Anal. calc. for $C_{15}H_{15}O_2F_{13}$: C, 37.99; H, 3.19. Found C, 37.91; H, 2.83.

7,7,8,8,9,9,10,10,11,11,12,12,12-tridecafluorododec-5-en-1-ol (17).
Yield: 96%. Oil, mixture of diastereomers (E/Z = 92/8).
^1H NMR δ 1.40-1.75 (m, 5H, 2x CH_2 and OH), 2.15-2.35 (m, 2H, CH_2), 3.6-3.7 (m, 2H, C*H*$_2$-OH), 5.51 (m, 1H, CH-CF_2, Z), 5.63 (dt, 1H, $^3J_{trans}$ = 15.6 Hz, $^3J_{HF}$ = 12.2 Hz, CH-CF_2, E), 6.12 (m, 1H, CH=C-CF_2, Z), 6.42 (ddt, 1H, $^3J_{trans}$ = 15.6 Hz, ^3J = 6.9 Hz, $^4J_{HF}$ = 2.3 Hz, CH=C-CF_2, E); ^{13}C NMR δ 24.2 (C_4), 31.6 and 31.9 (C_2 and C_3), 62.4 (C_1), 117.1 (t, $^2J_{CF}$ = 23.6 Hz, *C*H$_2$-CF_2), 142.7 (C_5); ^{19}F NMR δ -81.4 (t, 3F, $^3J_{FF}$ = 11.4 Hz, CF_3), -107.1 (m, 2F, F_7, Z), -111.7 (m, 2F, F_7, E), -122.1 (2F, F_8), -123.4 (2F, F_9), -124.0 (2F, F_{10}), -126.6 (2F, CF_{11}); IR (film): 3345 (br, OH), 2940, 2869, 1674, 1456, 1437, 1418, 1366, 1238 (s, br), 1200 (s, br), 1144 (s), 1121, 1067, 976, 849, 812, 708, 654 cm^{-1}.

1,2-*O*-isopropylidene-3-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononon-2-enyloxy)propane-1,2 diol (19).
Yield: 82%. Oil, mixture of diastereomers (E/Z = 75/25). Chromatography: Petroleum ether-AcOEt 9/1.
^1H NMR δ 1.36 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 3.44-3.50 (dd, 1H, J_{AB} = 9.9 Hz, ^3J = 5 Hz, H_3, Z), 3.49-3.54 (m, 1H, $H_{3'}$, Z), 3.51 (dd, 1H, J_{AB} = 10.1 Hz, ^3J = 5.3 Hz, H_3, E), 3.58 (dd, 1H, J_{AB} = 10.1 Hz, ^3J = 5.5 Hz, $H_{3'}$, E), 3.72 (dd, 1H, J_{AB} = 8.0 Hz, ^3J = 6.5 Hz, H_1, Z), 3.74 (dd, 1H, J_{AB} = 8.4 Hz, ^3J = 6.5 Hz, H_1, E), 4.05 (dd, 1H, J_{AB} = 8.0 Hz, ^3J = 6.5 Hz, H_1, Z), 4.06 (dd, 1H, J_{AB} = 8.4 Hz, ^3J = 6.5 Hz, H_1, E), 4.16-4.36 (m, 3H, H_2, O-CH_2-C=C), 5.59 (m, 1H, CH-CF_2, Z), 5.94 (dt, dt, 1H, $^3J_{trans}$ = 15.8 Hz, $^3J_{HF}$ = 12.2 Hz, CH-CF_2, E), 6.28 (m, 1H, CH=C-CF_2, Z), 6.43 (dtt, 1H, $^3J_{trans}$ = 15.8 Hz, ^3J = 4.2 Hz, $^3J_{HF}$ = 2.1 Hz, CH=C-CF_2, E); ^{13}C NMR δ 25.3, 26.6 (2x CH_3), 66.5 (C_1), 69.5 (O-*C*H$_2$-C=C), 71.9 (C_3), 74.7 (C_2), 109.6 (*C*(CH_3)$_2$), 117.3 (t, $^2J_{CF}$ = 23.6 Hz, CH-CF_2, Z), 117.4 (t, $^2J_{CF}$ = 23.6 Hz, CH-CF_2, E), 138.6 (t, $^2J_{CF}$ = 7.9 Hz, *C*H=C-CF_2); ^{19}F NMR δ -81.3 (t, 3F, ^3J = 8.5 Hz, CF_3), -108.4 (m, 2F, F_4, Z), -112.2 (m, 2F, F_4, E), -122.1 (2F, F_5), -123.3 (2F, F_6), -123.8 (m, 2F, F_7), -126.6 (m, 2F, F_8).

3-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononon-2-enyloxy)propane-1,2 diol (20).
Yield: 86%. Oil, mixture of diastereomers (E/Z = 82/18). Chromatography: petroleum ether-ethyl acetate 45/55. The compound **20** was also prepared in 87% yield from **19** using the same procedure than **3** from **2**.
^1H NMR δ 2.37 (m, 1H, OH), 2.81 (d, 1H, ^3J = 4.2 Hz, OH), 3.47-3.76 (m, 4H, H_1 and H_3), 3.91 (m, 1H, H_2), 4.18 (dd, 1H, J_{AB} = 3.8 Hz, ^3J = 2.1 Hz, O-CH_2-C=C, E), 4.21 (dd, 1H, J_{AB} = 3.8 Hz, ^3J = 2.1 Hz, O-CH_2-C=C, E), 4.32 (dd, 1H, J_{AB} = 3.8 Hz, ^3J = 2.1 Hz, O-CH_2-C=C, Z), 4.35 (dd, 1H, J_{AB} = 3.8 Hz, ^3J = 2.1 Hz, O-CH_2-C=C, Z), 5.63 (dm, 1H, $^3J_{cis}$ ~ 14.0 Hz, CH-CF_2, Z), 5.92 (dt broad, 1H, $^3J_{trans}$ = 15.6 Hz, $^3J_{HF}$ = 12.2 Hz, CH-CF_2, E), 6.27 (dtt, 1H, $^3J_{cis}$ = 12.2 Hz, ^3J = 5.5 Hz, $^4J_{HF}$ = 2.7 Hz, CH=C-CF_2, Z), 6.45 (dtt, 1H, $^3J_{trans}$ = 16.0 Hz, ^3J = 4.2 Hz, $^4J_{HF}$ = 2.1 Hz, CH=C-CF_2, E); ^{13}C NMR δ 63.8 (C_1), 69.5 (O-*C*H$_2$-C=C), 70.7 (C_2), 72.4 (C_3), 117.6 (t, $^2J_{CF}$ = 23.5 Hz, *C*H-CF_2), 138.5 (*C*H=CCF$_2$); ^{19}F NMR δ -81.4 (t, 3F, ^3J = 9.5, CF_3), -108.4 (d, 2F, ^3J = 15.3 Hz, F_4, Z), -112.2 (d, 2F, ^3J = 11.5 Hz, F_4, E), -122.1 (2F, F_5), -123.3 (2F, F_6), -123.8 (m, 2F, F_7, E), -124.2 (m, 2F, F_7, Z), -126.6 (2F, F_8); IR (film): 3372 (s, br), 2926 (br), 2876 (br), 1682, 1366, 1240 (s, br), 1202 (s, br), 1146 (s), 1121 (s), 1069 (s), 966, 735, 720 cm^{-1}.

2-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononon-2-enyloxy)phenol (22). K_2CO_3 (17 mg, 0.12 mmol) was added to a solution of **9** (0.06 g, 0.1 mmol) in methanol (2 mL). The reaction mixture was stirred at rt for 2,5 h and then diluted with water and extracted with diethyl ether (40 mL). The organic layer was washed with saturated aq NH_4Cl until neutralization. After drying over $MgSO_4$ and concentration, flash chromatography (petroleum ether-AcOEt 9/1) gave **22** (38 mg, 81%) as a solid. Mixture of diastereomers (E/Z=93/7).
^1H NMR δ 4.76 (m, 2H, OCH_2, E), 4.94 (m, 2H, OCH_2, Z), 5.53 (1H, OH), 5.73 (m, 1H, CH-CF_2, Z), 6.00 (dtm, 1H, $^3J_{trans}$ = 15.6 Hz, $^3J_{HF}$ = 12.2 Hz, CH-CF_2, E), 6.40 (m, 1H, CH=C-CF_2, Z), 6.61 (dt, 1H, $^3J_{trans}$ = 15.6 Hz, ^3J = 4.6 Hz, $^4J_{HF}$ = 2.3 Hz, CH=C-CF_2, E), 6.80-7.00 (m, 4H, H-Ar); ^{13}C NMR δ 67.4 (O-CH_2), 112.4 and 115.4 (C-Ar), 118.8 (t, $^2J_{CF}$ = 21.7 Hz, C=*C*-CF_2), 120.4 and 122.7 (C-Ar), 137.0 (t, $^3J_{CF}$ = 9.9 Hz, *C*H=C-CF_2), 144.9 (C-OR), 145.9 (C-OH); ^{19}F NMR δ -81.3 (t, 3F, $^3J_{FF}$ = 9.5 Hz, CF_3), -108.9 (m, 2F, F_4, Z), -112.4 (m, 2F, F_4, E), -122.1 (2F, F_5), -123.3 (2F, F_6), -123.7 (2F, F_7, E), -124.2 (m, 2F, F_7, Z), -126.6 (2F, F_8); MS m/e (%) 468 (M^+, 100), 449 (11), 199 (3), 149 (6), 131 (14), 121 (30), 109 (100); Anal. calc. for $C_{15}H_9O_2F_{13}$: C, 38.48; H, 1.94. Found: C, 38.35; H, 1.61.

Cyclization into 2-(F-alkylidenemethyl)-1,4-dioxane: general procedure
A solution of the iodo F-alkylated adduct (1 mmol) in dry THF (10 mL) was added dropwise under Argon at 0°C to a dispersion of sodium hydride (3-4 eq) in dry tetrahydrofuran (6 mL). The resulting mixture was stirred 1 h at 0°C, 0.5 h at rt and then was quenched with saturated aq NH_4Cl and extracted with diethyl ether. The combined extracts were washed with saturated aq NH_4Cl and dried over $MgSO_4$. After concentration the residue was purified by flash chromatography.

2-(2,3,3,4,4,5,5,6,6,7,7,7-dodecafluorohept-1-enyl)-octahydrobenzo-1,4-dioxine (12).
Yield: 90%. White solid, mixture of diastereomers (Z/E=9/1). Chromatography: petroleum ether-CH_2Cl_2 7/3.
^1H NMR δ 1.2-1.45 (m, 4H, CH_2-*C*H_2-*C*H_2-CH_2), 1.65-2.00 (m, 4H, *C*H_2-CH_2-CH_2-*C*H_2), 3.08-3.33 (m, 2H, 2x CH-O), 3.45 (dd, 1H, J_{AB} = 11.4 Hz, ^3J = 10.5, O-*C*H_2-CH, E), 3.46 (dd, 1H, J_{AB} = 11.4 Hz, ^3J = 10.7 Hz, O-*C*H_2-CH, Z), 3.74 (dd, 1H, J_{AB} = 11.4 Hz, ^3J = 2.9 Hz, O-*C*H_2-CH, E), 3.80 (dd, 1H, J_{AB} = 11.4 Hz, ^3J = 3.0 Hz, O-*C*H_2-CH, Z), 4.57 (m, 1H, CH-C=C, E), 4.70 (dddd, 1H, ^3J = 10.7 Hz, ^3J = 7.6 Hz, ^3J = 3.0 Hz, $^4J_{HF}$ = 1.5 Hz, CH-C=C, Z), 5.61 (dd, 1H, ^3J = 7.6 Hz, $^3J_{HF}$ = 34.3 Hz, CH=C, Z), 5.81 (dd, 1H, $^3J_{HF}$ = 21.7 Hz, ^3J = 9.3 Hz, CH=C, E); ^{13}C NMR δ 24.1 (CH_2-*C*H_2-*C*H_2-CH_2), 29.6 and 30.0 (*C*H_2-CH_2-CH_2-*C*H_2), 69.0 (O-*C*H_2-CH), 69.8 (*C*H-C=C), 79.3 and 79.7 (2x CH-O), 113.1 (*C*H=C), 146.9 (dt, $^1J_{CF}$ = 265 Hz, $^2J_{CF}$ = 29.5 Hz, CH=*C*); ^{19}F NMR δ -81.4 (t, 3F, $^3J_{FF}$ = 9 Hz, CF_3), -118.2 (m, 2F, F_3), -123.3 (2F, F_4), -123.5 (2F, F_5), -125.0 (m, 1F, F_2), -126.7 (F_6); IR (KBr): 2953, 2940, 2868, 1719, 1389, 1352, 1231 (s), 1200 (s), 1188 (s), 1161 (s), 1144 (s), 1117 (s), 864, 723 (s) ; 646 cm^{-1}; MS m/e (%) 454 (M^+, 100), 425 (17), 405 (13), 356 (11), 341 (17), 289 (5), 169, 131, 97, 81; Anal. calc. for $C_{15}H_{14}O_2F_{12}$: C, 39.66; H, 3.11. Found: C, 39.73; H, 2.79.

2-(2,3,3,4,4,5,5,6,6,7,7,7-dodecafluorohept-1-enyl)-tetrahydropyran (18).
Yield: 50%. conv. 82%. Oil, mixture of diastereomers (E/Z = 6/94). Chromatography: petrol. ether - CH_2Cl_2 4/ 1.
^1H NMR δ 1.45-2.00 (m, 6H, *C*H_2-*C*H_2-*C*H_2-CH), 3.51 (m, 1H, O-CH_2), 4.00 (m, 1H, O-CH_2), 4.37 (m, 1H, CH-C=C), 5.70 (dd, 1H, $^3J_{HF}$ = 34.3 Hz, $^3J_{HH}$ = 7.6 Hz, CH=CF-CF_2, Z), 5.90 (dd, 1H, $^3J_{HF}$ = 21.4 Hz, $^3J_{HH}$ = 9.2 Hz, CH=CF-CF_2, E); ^{13}C NMR δ 22.8 (C_4), 25.4 (C_5) , 31.1 (C_3), 68.3 (C_6), 71.2 (C_2), 117.7 (*C*H=CF-R_F), 145.1 (dt, $^1J_{CF}$ = 293 Hz, $^2J_{CF}$ = 29.5 Hz, CF); ^{19}F NMR δ -81.4 (s, CF_3), -118.3 (m, 2F, F_3), -123.4 (m, 2F, F_4), -123.7 (m, 2F, F_5), -126.7 (m, 2F, F_6), -126.7 (m, 1F, F_2).

2-(2,3,3,4,4,5,5,6,6,7,7,7-dodecafluorohept-1-enyl)-6-hydroxymethyl-1,4-dioxane (21).
Yield: 36%. Oil, mixture of diastereomers (Z/E=90/10). Chromatography: petroleum ether- ethyl acetate 4/1.
^1H NMR δ 2.33 (s broad, 1H, OH), 3.24-3.90 (m, 7H, *C*H-*C*H_2-OH, 2x O-CH_2), 4.71 (m, 1H, CH-C=C), 5.62 (dd, 1H, $^3J_{HF}$ = 34.3 Hz, ^3J = 7.6 Hz, CH=CF, major Z), 5.80 (dd, 1H, $^3J_{HF}$ = 21.8 Hz, ^3J = 9.2 Hz, CH=CF, E), 6.08 (dd, 1H, $^3J_{HF}$ = 34.3 Hz, ^3J = 7.8 Hz, CH=CF, minor Z); ^{13}C NMR (major isomer) δ 62.3 (O-CH_2-CH-CH_2), 67.2 (CH_2-OH), 68.2 (O-*C*H_2-CH-C=C), 69.6 (*C*H-C=C), 75.8 (*C*H-CH_2-OH), 112.7 (C-*C*H=C), 147.3 (dt, $^1J_{CF}$ = 266 Hz, $^2J_{CF}$ = 29.5 Hz,); ^{19}F NMR δ -81.4 (t, $^4J_{FF}$ = 9.5 Hz, CF_3), -118.3 (m, CF-*C*F_2), -123.3 (CF_2), -123.5 (CF_2), -124.3 (m, 1F, C=CF), -126.7 (2F, CF_2); IR: (film): 3437 (br), 2971, 2928, 2874, 1715 (w), 1458, 1364 (s), 1321 (vs), 1234 (vs), 1204 (vs), 1144 (vs), 1078 (vs and br), 941, 820, 721 cm^{-1}; MS m/e (%) 431 (M^++1, 9), 413 (6), 399 (38), 381 (13), 369 (10), 341 (45), 295 (16), 169 (6), 151 (7), 131 (14), 121 (100); Anal. calc. for $C_{15}H_{14}O_2F_{12}$: C, 33.50; H, 2.34. Found: C, 33.79; H, 2.01.