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Organofluorine compounds and fluorinating agents Part 17: Sonochemical-forced preparation of perfluoroalkanals and their use for non-conventional acetalations of carbohydrates [1, 2]

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Abstract

The homologous 1-iodo-perfluoroalkanes **1a–1c** and α,ω-dibromo-perfluoroalkanes **4a, 4b** were carbonylated with DMF in the presence of $Al/SnCl_2$ or $Al/PbBr_2$ under sonication in a short reaction time. The hydrated aldehydes **2a–2c** and **5a, 5b** respectively were obtained in good yields allowing dehydration to **3a–3c** and **6a, 6b**. Some of the fluorinated aldehydes were selected as substrates in a Wittig–Horner olefination assisted by ultrasound and in non-conventional acetalations of methyl α-L-rhamnopyranoside (**9**). Thus, (*E*)-1-perfluorooctyl-2-phenylsulphonyl-ethene (**8**) was prepared from **3c** and the phosphonate **7** by Wittig–Horner synthesis. Acetalations of **9** were carried out with the aldehydes (**3a, 3b, 6a**), hydrated aldehydes (**2a, 2b**), and the aldehyde hemiacetal **12** respectively, in the presence of dicyclohexylcarbodiimide (DCC). In all cases, a selective epimerization was observed at the C-atom 3 of the monosaccharide, i.e. polyfluoroalkylidenated 6-deoxy-α-L-altropyranosides **10, 11, 13**, and **14** were obtained.

Keywords: Ultrasound; Perfluoroalkanals; Acetals; Carbohydrates; Alkenes

1. Introduction

Perfluoroalkanals are useful 'building blocks' in the synthesis of resins, polymers, dyes, medicinals and insecticides [2]. Recently, two research groups reported convenient procedures to prepare perfluoroaldehydes and dialdehydes by alkylation of DMF with 1-iodo-perfluoroalkanes and α,ω-dihalo-perfluoroalkanes respectively in the presence of zinc–copper metal couple/radical initiator [3], $Al/PbBr_2$ [4] or $Al/SnCl_2$ [5]. Radical and electron transfer processes are supposed to be the key steps of the reactions. As is generally known, ultrasound especially favours and accelerates radical and single electron transfer (SET) processes [6,7]. Furthermore, ultrasound has been applied successfully in heterogeneous reactions, especially involving metals [8]. Therefore, we investigated the influences of sonication on C-alkylations of DMF with 1-halo-perfluoroalkanes and α,ω-dihalo-perfluoroalkanes; applications of ultrasound in fluorine chemistry were reviewed recently [9]. The target products, homologous perfluorinated alkanals (**3a–3c**) and α,ω-dialkanals (**6a, 6b**), are useful precursors for a Wittig–Horner synthesis and for acetalations of carbohydrates.

Benefice-Malouet et al. [3] have observed an induction time of 5 min in 'silent' syntheses of perfluoroalkanals in the presence of zinc–copper metal couple/radical initiator. The total time of the reactions was relatively short (ca. 20 min) but following the described procedure we had some difficulties in the reproducibility of satisfying yields. Compared with that, the metal/initiator system $Al/PbBr_2$ used by Hu and Tang [4] required significantly longer reaction times, but the reaction was more convenient and reliable.

We compared 'silent' and sonicated perfluoroalkylations of DMF with the 1-halo-perfluoroalkanes **1a–1c** and **4a, 4b** in the presence of $Al/SnCl_2$ and $Al/PbBr_2$ respectively. Unlike the corresponding 'silent' procedures which have an induction time, the ultrasound assisted perfluoroalkylations started immediately at room temperature. After a reaction time of 4–24 h ('silent' procedures) and 0.25–3 h ('sonicated' procedures) respectively (see Table 1), the reaction mixtures were hydrolysed by aqueous acid to generate the hydrated perfluoroalkanals **2a–2c** and **5a, 5b** respectively (Scheme 1). It is noticeable that 1-H-perfluoroalkanes

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[1] For Part 16, see [1].

[2] Dedicated to Professor Dr. Alois Haas on the occasion of his 65th birthday.

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Table 1
Ultrasonically forced synthesis of perfluoroalkanals and corresponding monohydrates (reagent DMF/Al)

Substrate	Catalyst	))))[a]	Time (h)	Product	m.p.(solvent) (b.p.) (°C)	Yield(%)
C_4F_9I	$SnCl_2$	+	0.25	C_4F_9CHO (**3a**)	(47–49 [4])	41
$C_6F_{13}I$	$SnCl_2$	–	24	$C_6F_{13}CH(OH)_2$ (**2b**)	77–78 ($CHCl_3$)	80
				$C_6F_{13}CHO$ (**3b**)		60
$C_6F_{13}I$	$SnCl_2$	+	0.25	$C_6F_{13}CH(OH)_2$ (**2b**)	77–78 ($CHCl_3$)	82
				$C_6F_{13}CHO$ (**3b**)	(103–105)[b]	65
$C_8F_{17}I_2$	$SnCl_2$	+	0.25	$C_8F_{17}CH(OH)_2$ (**2c**)	91–94 ($CHCl_3$)	78
				$C_8F_{17}CHO$ (**3c**)	(125–126.5 [4])	65
$BrC_6F_{12}Br$	$SnCl_2$	+	3	$(HO)_2CHC_6F_{12}CH(OH)_2$ (**5a**)	125–128 (toluene: ethyl acetate 3:1)	87
				$OCHC_6F_{12}CHO$ (**6a**)	(144–146 [4])	60
$BrC_8F_{16}Br$	$SnCl_2$	+	3	$(HO)_2CHC_8F_{16}CH(OH)_2$ (**5b**)	116–118 (toluene: ethyl acetate 3:1)	90
				$OCHC_8F_{16}CHO$ (**6b**)	68–70 [4]	57
C_4F_9I	$PbBr_2$	+	0.25	C_4F_9CHO (**3a**)		50
$C_6F_{13}I$	$PbBr_2$	–	16	$C_6F_{13}CH(OH)_2$ (**2b**)		74
				$C_6F_{13}CHO$ (**3b**)		65
$C_6F_{13}I$	$PbBr_2$	+	0.25	$C_6F_{13}CH(OH)_2$ (**2b**)		70
				$C_6F_{13}CHO$ (**3b**)		62
$C_8F_{17}I$	$PbBr_2$	+	0.25	$C_8F_{17}CH(OH)_2$ (**2c**)		70
				$C_8F_{17}CHO$ (**3c**)		60
$BrC_6F_{12}Br$	$PbBr_2$	–	4	$(HO)_2CHC_6F_{12}CH(OH)_2$ (**5a**)		80
				$OCHC_6F_{12}CHO$ (**6a**)		65
$BrC_6F_{12}Br$	$PbBr_2$	+	1.5	$(HO)_2CHC_6F_{12}CH(OH)_2$ (**5a**)		87
				$OCHC_6F_{12}CHO$ (**6a**)		60
$BrC_8F_{16}Br$	$PbBr_2$	+	1.5	$(HO)_2CHC_8F_{16}CH(OH)_2$ (**5b**)		83
				$OCHC_8F_{16}CHO$ (**6b**)		60

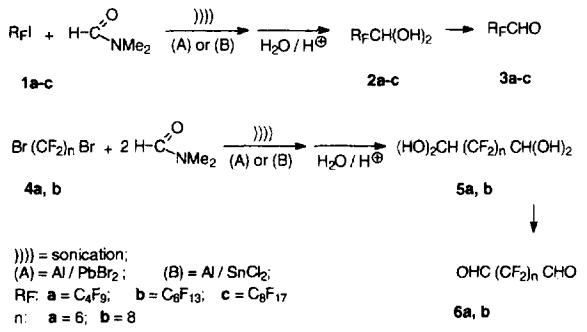
[a]Sonication; [b]132 °C, 90–92 °C [4].

(R_FH) were formed in 3%–5% yield; other by-products were not further investigated.

Two different procedures could be used to separate the hydrated perfluoroalkanals **2a–2c** from the reaction mixtures. One possibility is to extract the compounds directly from the hydrolysed reaction mixtures with diethyl ether. After evaporation of ether, light-brown solids were obtained. The hydrated perfluoroalkanals **2a–2c** could be purified by sublimation yielding colourless crystalline sublimates.

Another possibility is to purify the hydrates of monoaldehydes **2a–2c** by steam distillation followed by extraction with ether. In this case, light-yellow products were obtained.

The overall yields of **2a–2c** are somewhat higher if steam distillation is used instead of sublimation. The hydrated dialdehydes **5a** and **5b** are sublimable but not steam volatile, i.e. only the first procedure could be used for separation and purification.



Scheme 1.

Dehydration of the compounds **2a–2c** and **5a**, **5b** was carried out as reported [3,4,10] by distillation from P_2O_5 giving the aldehydes **3a–3c** and **6a**, **6b** respectively in good yields.

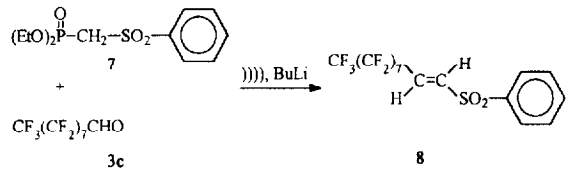
The structures of the compounds **2a–2c**, **3a–3c**, **5a**, **5b** and **6a**, **6b** were confirmed by their ^1H and ^{19}F NMR spectroscopic data summarized in Table 2. The chemical shifts of the corresponding aldehyde protons were found to be $\delta = 5.36–5.40$ (aldehyde hydrates) and $\delta = 9.50–9.58$ (aldehydes). The H atoms of the CHO groups coupled with α-CF_2 and β-CF_2 so that two $J_{H,F}$ coupling constants were found ($^3J_{H,F}$ 3.4 Hz and $^4J_{H,F}$ 1.0 Hz respectively). In previous reports [3,10] only the couplings of 1 Hz were given. The aldehyde protons of aldehyde hydrates **2a–2c** and **5a**, **5b** gave $^3J_{H,F}$ couplings of 8.3 Hz (Table 2).

The ultrasound-assisted Wittig–Horner synthesis of aryl- and alkylsulphonyl phosphonates with carbonyl compounds [11] including trifluoroacetophenone [12] has been proved a useful access to vinylsulphones. The reaction in general leads to the trans isomer as major product, in some cases even as the only product [11,13]. We synthesized the perfluoroalkyl substituted vinylsulphone **8** by Wittig–Horner olefination from the phosphonate **7** and the perfluorononanal **3c** assisted by sonication. The reaction proceeds readily and yields 53% (isolated) of (*E*)-1-perfluorooctyl-2-phenylsulphonyl-ethene (**8**) (Scheme 2). NMR spectra showed the presence of only one isomer which is the trans isomer. In fluorinated alkenes of the type XCF_2–CH=CHR, the observed couplings $^4J_{H,F}$ are always less than 1 Hz (0.4–0.9 Hz) if the α-CF_2 group and the corresponding hydrogen are

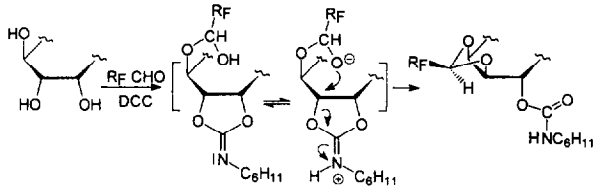
Table 2
^1H and ^{19}F NMR spectra of the perfluoroalkanals **3a–3c**, **6a**, **6b** and corresponding monohydrates **2a–2c**, **5a**, **5b**

Compound	^1H NMR	^{19}F NMR (δ)
2a $C_4F_9CH(OH)_2$[a]	δ=5. 39 (t, 1H, $^3J_{H,F}\approx$8.3 Hz)[b]	81.5 (3F), 123.8 (2F), 126.6 (2F), 128.8 (2F)
3a C_4F_9CHO[c,d]	δ=9.54 (tt, 1H, $^3J_{H,F}\approx$3.4 $^4J_{H,F}\approx$1.0 Hz)	80.9 (3F), 124.3 (2F), 125.4 (2F), 125.8 (2F)
2b $C_6F_{13}CH(OH)_2$[a]	δ=5.36 (t, 1H, $^3J_{H,F}\approx$8.3 Hz)[b]	81.5 (3F), 122.3 (2F), 122.7 (2F), 123.0 (2F), 126.5 (2F), 128.2 (2F)
3b $C_6F_{13}CHO$[c,d]	δ=9.50 (tt, 1H, $^3J_{H,F}\approx$3.4 Hz, $^4J_{H,F}\approx$1.0 Hz)	81.9 (3F), 122.1 (2F), 123.3 (2F), 124.0 (2F), 126.2(2F), 126.8 (2F)
2c $C_8F_{17}CH(OH)_2$[a]	δ=5.40 (t, 1H, $^3J_{H,F}\approx$8.3 Hz)[b]	81.5 (3F), 122.1 (6F), 122.7 (2F), 122.9 (2F), 126.4 (2F), 128.2 (2F)
3c $C_8F_{17}CHO$[c,d]	δ=9.50 (tt, 1H, $^3J_{H,F}\approx$3.4 Hz, $^4J_{H,F}\approx$1.0 Hz)	81.5 (3F), 121.7 (2F), 122.1 (4F), 122.9 (2F), 123.7 (2F), 125.8 (2F), 126.5 (2F)
5a $(HO)_2CHC_6F_{12}CH(OH)_2$[a]	δ=5.40 (t, 2H, $^3J_{H,F}\approx$8.3 Hz)[b]	122.2 (4F), 122.7 (4F), 128.3 (4F)
6a $OCHC_6F_{12}CHO$[c,d]	δ=9.58 (t, 2H, $^3J_{H,F}\approx$3.4 Hz)	121.4 (4F), 123.3 (4F), 125.3 (4F)
5b $(HO)_2CHC_8F_{16}CH(OH)_2$[a]	δ=5.40 (t, 2H, $^3J_{H,F}\approx$8.3 Hz)[b]	122.1 (8F), 122.7 (4F), 128.2 (4F)
6b $OCHC_8F_{16}CHO$[c,d]	δ=9.58 (t, 2H, $^3J_{H,F}\approx$3.4 Hz)	121.2 (4F), 121.5 (4F), 123.1 (4F), 125.1 (4F)

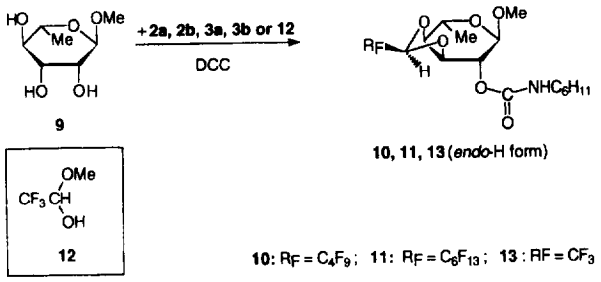
[a]Recorded in acetone-d_6;
[b]the chemical shifts of the OH protons are found at $\delta\approx$6.2–6.3;
[c]recorded in $CDCl_3$;
[d][3,10] $J_{H,F}\approx$1.0 Hz.



Scheme 2.



Scheme 3.



Scheme 4.

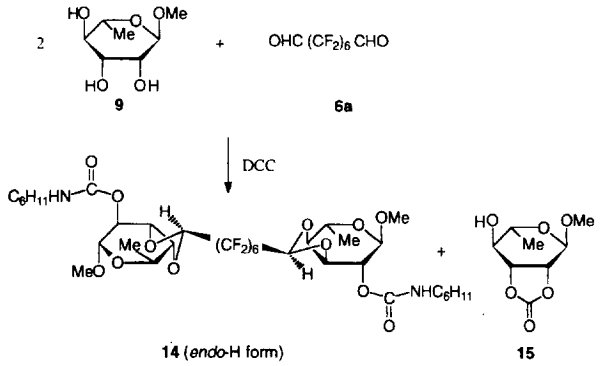
trans arranged. If they are on the same side (cis), values of $^4J_{H,F}\approx$1.5–2.5 Hz are observed [14]. In similarity to this, $^4J_{H,F}$ couplings of 1.5 Hz were found for the vinylsulphone **8** indicating a trans arrangement of the perfluoroalkyl and the phenylsulphonyl group.

It was suggested that perfluoroalkyl-containing sugars could be used as surfactants and co-surfactants for biomedical uses [15]. Generally, fluorine containing carbohydrates are important sensors in studies of transport, metabolism, and enzymology of sugars [16,17].

In 1994 it was reported that the reaction of hexafluoroacetone and dicyclohexylcarbodiimide (DCC) with bis-vicinal triols (pyranosides) having a cis, trans sequence of hydroxyl groups resulted in the formation of cyclic acetals in which the central carbon of the triol had the inverted configuration [18]. Moreover, we have shown that chloral likewise generates cyclic acetals from suitable pyranosides in the presence of DCC [19]. The non-classical pathway of these acetalations involves the in situ formation of a cyclic imidocarbonic ester intermediate followed by an intramolecular S_N2-attack by a deprotonated neighbouring hemiacetal moiety [19].

Now, we investigated the introduction of perfluoroalkyl chains into a monosaccharide moiety by acetalation (Scheme 3). Thus, methyl α-L-rhamnopyranoside (**9**) was heated for 4.5 h in 1,2-dichloroethane with two equivalents of the perfluoroalkanals **3a** or **3b** in the presence of DCC generating the corresponding methyl 2-*O*-cyclohexylcarbamoyl-6-deoxy-3,4-*O*-polyfluoroalkylidene-α-L-altropyranosides **10** and **11** in moderate yields (40%–50% after chromatographic purification) (Scheme 4).

Unlike acetalations with chloral [20], even the hydrated aldehydes **2a**, **2b** could be used to generate the polyfluoroalkylidene derivatives **10** and **11** by acetalations of **9** in the presence of DCC using the same procedure given in Section 2. The yields are decreased (20% and 33% for **10** and **11** respectively). Furthermore, it is noticeable that 2,2,2-trifluoroethanal (fluoral) could not be used in non-conventional acetalations of **9**, because polymerization occurred when DCC was added. However, using the hemiacetal **12** instead of fluoral, the acetalation was successful. Thus, rhamnoside **9** treated with 2,2,2-trifluoroethanal methylhemiacetal (**12**) and DCC gave the altrose derivative **13** in a yield of 55%. It is noticeable that exclusively the *endo*-H diastereomer was formed (Scheme 4).



Scheme 5.

Finally, methyl rhamnoside **9** was acetalated with the α,ω-dialdehyde **6a** under analogous reaction conditions as described for monoaldehydes. In this case, a mixture of *endo*-H/*endo*-H and *endo*-H/*exo*-H diastereomers (approximately 10:1) was formed. The *endo*-H/*endo*-H major isomer **14** was obtained in pure form by recrystallization of the mixture from heptane:ethanol. The molecular mass of **14** was determined by mass spectrometry (*m/z* 928 (M^+)). Furthermore, the structure of compound **14** could be supported by its ^1H, ^{13}C, and ^{19}F NMR spectra. Thus, only three different signals ($\delta = -127, -123, -122.2$) were observed for the six CF_2-groups, showing the symmetrical arrangement of the molecule. The chemical shifts and coupling constants of the two altrose moieties of **14** are identical; the observed H,H-couplings correspond to reported data of methyl 2-*O*-cyclohexylcarbamoyl-6-deoxy-3,4-*O*-(2,2,2-trichloroethylidene)-α-L-altropyranoside [21] and to the values of the polyfluoroalkylidene derivatives **10** and **11**. The triplet of the two *endo*-H acetal protons is found at $\delta = 5.70$. It is important to mention that two by-products were obtained in acetalation of **9** with the α,ω-dialdehyde **6a**. Thus, methyl α-L-rhamnopyranoside 2,3-carbonate (**15**) could be separated after quenching the reaction mixture with 2% aqueous HCl (c.f. Section 2) (Scheme 5). Its melting point (167–169 °C) and the value of the optical rotation ($[\alpha]_D^{21} = -57.2°$) correspond with literature data reported for this compound [22]. Compound **15** could be formed by hydrolysis of a cyclic imidocarbonic ester intermediate (c.f. Scheme 3). This separation of the cyclic carbonate **15** is a further important indication of the correctness of the postulated non-classical pathway of acetalation [19].

Another by-product was observed when the reaction mixture was worked up by treatment with 10% aqueous acetic acid instead of HCl. The observed compound seems to be an intermediate of the hydrolysis occurring previously leading to the formation of **15**. It is less stable than **15** and contains a perfluoroalkyl group. Unfortunately, this by-product could not be exactly characterized so far.

2. Experimental

Sonication was carried out in an ultrasonic bath Sonorex RK 102 H (Bandelin), 35 kHz, 2 × 120 W electrical input in order to prepare the perfluoroalkanals; a VIBRACELL VCX-400, 20 kHz, 6 or 13 mm probe, 120 W electrical input was used in the Wittig–Horner synthesis. All the ultrasound assisted reactions were carried out under an argon atmosphere. Column chromatography utilized silica gel 60 (63–200 μm, Merck) and thin-layer chromatography (TLC) silica gel foils 60 F_{254} (Merck). The NMR spectra were recorded by Bruker AC 250 and ARX 300 equipment: ^1H NMR, internal standard TMS; ^{19}F {H} NMR, referred to $CFCl_3$. A polarizing microscope Leitz (Laborlux 12 Pol) equipped with a hot stage (Mettler FP 90) was used for determination of melting points. Chemicals: 1,1,1-trifluoroethanal methylhemiacetal (Hoechst AG).

2.1. Perfluoroalkanals (general procedure)

40 mmol of the corresponding 1-iodo-perfluoroalkane **1a–1c** (or α,ω-dibromoperfluoroalkane **4a**, **4b**) were added to a suspension of Al-powder [3] (48 mmol) and $SnCl_2$[3] (4 mmol) (or 1 mmol of $PbBr_2$[3]) in 80 ml of dry DMF at room temperature. The reaction mixture was stirred (or sonicated, Table 1), poured into 2% aq. HCl, filtered and extracted with diethyl ether (8 times). The organic solution was washed with 0.5% aq. HCl, dried with Na_2SO_4 [4] and the solvent was evaporated. Dehydration of the residue with P_2O_5 and distillation (analogously to Refs. [3–5]) gave the corresponding aldehyde; for further experimental details and NMR data see Table 1 and Table 2.

(E)-1-Perfluorooctyl-2-phenylsulphonyl-ethene (**8**) (according to [11,12]). Under sonication butyl lithium (1.1 mmol of a 1.6 M solution in hexane) was slowly added under argon to a solution of phosphonate **7** (292 mg, 1 mmol) in 25 ml THF. After further sonication (30 min) perfluorononanal (**3c**) (448 mg, 1 mmol) was added and the irradiation was continued for 30 min. To work up, a saturated NH_4Cl solution (25 ml) and CH_2Cl_2 (25 ml) were added, the organic phase was separated, washed with a saturated $NaHCO_3$ solution (25 ml) and water (25 ml). After drying with Na_2SO_4 and evaporation of the solvent, the residue (crude yield 86%) was chromatographed by preparative circular thin layer chromatography (Harrison Research Chromatotron 8924, Merck silica gel containing gypsum, heptane:ethyl acetate 1:1) yielding 155 mg (53%) of sulphone **8**. Recrystallization from pentane gave needles of m.p. 100–103 °C. ^1H NMR (250 MHz, $CDCl_3$): $\delta = 6.89$ (dt, 1H, $^3J_{H,F} \approx 22.0$ Hz, $^3J_{H,H} \approx 15.3$ Hz, =CH), 7.06 (dt, 1H, $^4J_{H,F} \approx 1.5$ Hz, =CH), 7.60–7.90 (m, 5H, aromat.). ^{19}F {H} NMR (235 MHz, $CDCl_3$): $\delta = -125.7$ (2F, CF_2), -122.6 (2F, CF_2), -122.3 (2F, CF_2), -121.5 (4F, CF_2), -121.0 (2F,CF_2), -112.7 (2F, CF_2), -80.5 (3F, CF_3). $C_{16}H_7F_{17}O_2S$ (586.26): calculated C 32.78, H 1.20, S 5.47; found C 32.82, H 1.28, S 5.38.

[3] For α,ω-dibromoperfluoroalkane, 96 mmol of Al, 10 mmol of $SnCl_2$ and 2 mmol of $PbBr_2$.

[4] Purification of the hydrated perfluoroalkanals **2a–2c** was possible by steam distillation followed by extraction with diethyl ether.

2.2. *Perfluoroalkylidene derivatives of 6-deoxy-L-altropyranosides (general procedure)*

Methyl 2-O-cyclohexylcarbamoyl-6-deoxy-3,4-O-perfluoroalkylidene-α-L-altropyranosides (**10, 11**). A mixture of methyl α-L-rhamnopyranoside (**9**) (0.92 g, 5.2 mmol), DCC (2.14 g, 10.4 mmol), perfluoroalkanal **2a, 2b, 3a, 3b** or **12** (10.4 mmol) and 1,2-dichloroethane (10 ml) was refluxed for 4.5 h (1,1,1-trifluoroethanal methylhemiacetal 8–10 h). Then the solution was cooled to room temperature and shaken for 30 min with 2% aqueous HCl (or 10% aqueous acetic acid) in order to destroy remaining DCC (the precipitated *N,N'*-dicyclohexylurea is filtered off). Finally, dichloromethane (20 ml) was added, the organic phase was washed with saturated $NaHCO_3$ solution (twice with 20 ml) and water (twice with 30 ml), dried over Na_2SO_4 and concentrated in a rotary evaporator. The residue was dissolved in acetone (15 ml), whereby the remaining *N,N'*-dicyclohexylurea can be separated. After concentration the syrupy yellowish crude product was purified by column chromatography (eluent toluene:ethyl acetate 6–10:1 v/v).

Methyl 2-O-cyclohexylcarbamoyl-6-deoxy-3,4-O-(2,2,-3,3,4,4,5,5,5-nonafluoropentylidene)-α-L-altropyranoside (**10**). R_f = 0.65 (toluene:ethyl acetate 3:1 v/v); yield 1.07 g (38% as mixture of *endo*-H/*exo*-H diastereomers 5:1); m.p. 94–96 °C (hexane). ^{1}H NMR (250 MHz, $CDCl_3$): δ ≈ 1.16 (m, 3H, cyclohexyl CH_2), ≈ 1.32 (m, 2H, cyclohexyl CH_2), 1.35 (d, 3H, $J_{5/6\text{-}CH3}$ ≈ 6.1 Hz, 6-CH_3), ≈ 1.65 (m, 3H, cyclohexyl CH_2), ≈ 1.97 (m, 2H, cyclohexyl CH_2), 3.37 (s, 3H, OCH_3), 3.46 (m, 1H, cyclohexyl CH), 3.79 (dq, 1H, $J_{4/5}$ ≈ 8.8 Hz, 5-H), 4.09 (dd, 1H, $J_{3/4}$ ≈ 6.1 Hz, 4-H), 4.31 (dd, 1H, $J_{2/3}$ ≈ 5.2 Hz, 3-H), 4.58 (d, 1H, $J_{1/2}$ ≈ 3.0 Hz, 1-H), 4.65 (m, 1H, NH), 5.05 (dd, 1H, 2-H), 5.31 (t, 1H, $J_{H/F}$ ≈ 7.6 Hz, *exo*-acetal H), 5.52 (t, 1H, $J_{H/F}$ ≈ 8.5 Hz, *endo*-acetal H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 18.6 (C6), 24.7, 24.7, 25.4, 25.4, 33.2 (cyclohexyl CH_2), 50.2 (cyclohexyl CH), 55.6 (OCH_3), 63.3 (C5), 69.6 (C2), 76.4 (C3), 77.6 (C4), 98.2 (t, $J_{C/F}$ ≈ 26.0 Hz, acetal C), 99.2 (C1), 105–120 (m, CF_2, CF_3), 153.8 (carbamoyl C=O). ^{19}F {H} NMR (235 MHz, $CDCl_3$): δ = −128.1 (d, 1F, $J_{F/F}$ ≈ 282 Hz, CF_2–CH), −126.6 (d, 1F, $J_{F/F}$ ≈ 282 Hz, CF_2–CH), −125.9, −123.6 (s, 2F, CF_2), −80.7 (CF_3). $C_{19}H_{24}F_9NO_6$ (533.38): calculated C 42.78, H 4.54, N 2.63; found C 42.62, H 4.48, N 2.61. MS (auto-Cl, 100 eV): m/z = 533 (M^+).

Methyl 2-O-cyclohexylcarbamoyl-6-deoxy-3,4-O-(2,2,-3,3,4,4,5,5,5,6,6,7,7,7-tridecafluoroheptylidene)-α-L-altropyranoside (**11**). R_f = 0.62 (toluene:ethyl acetate 3:1 v/v); yield 1.58 g (48%, as mixture of *endo*-H/*exo*-H diastereomers 5:1); m.p. 91–93 °C (hexane). ^{1}H NMR (250 MHz, $CDCl_3$): δ ≈ 1.16 (m, 3H, cyclohexyl CH_2), ≈ 1.32 (m, 2H, cyclohexyl CH_2), 1.35 (d, 3H, $J_{5/6\text{-}CH3}$ ≈ 6.1 Hz, 6-CH_3), ≈ 1.65 (m, 3H, cyclohexyl CH_2), ≈ 1.97 (m, 2H, cyclohexyl CH_2), 3.38 (s, 3H, OCH_3), 3.43 (m, 1H, cyclohexyl CH), 3.79 (dq, 1H, $J_{4/5}$ ≈ 8.8 Hz, 5-H), 4.09 (dd, 1H, $J_{3/4}$ ≈ 6.1 Hz, 4-H), 4.31 (dd, 1H, $J_{2/3}$ ≈ 5.2 Hz, 3-H), 4.58 (d, 1H, $J_{1/2}$ ≈ 3.0 Hz, 1-H), 4.65 (m, 1H, NH), 5.06 (dd, 1H, 2-H), 5.31 (*exo*-acetal H), 5.53 (t, 1H, $J_{H/F}$ ≈ 8.8 Hz, *endo*-acetal H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 18.6 (C6), 24.6, 24.6, 25.4, 33.2 (cyclohexyl CH_2), 50.2 (cyclohexyl CH), 55.4 (OCH_3), 63.5 (C5), 69.7 (C2), 76.5 (C3), 77.8 (C4), 98.3 (t, $J_{C/F}$ ≈ 25.5 Hz, acetal C), 99.2 (C1), 105–120 (m, CF_2, CF_3), 153.8 (carbamoyl C=O). ^{19}F {H} NMR (235 MHz, $CDCl_3$): δ = −127.8 (d, 1F, $J_{F/F}$ ≈ 282 Hz, CF_2–CH), −126.4 (d, 1F, $J_{F/F}$ ≈ 282 Hz, CF_2–CH), −125.8, −122.5, −122.5, −121.7 (s, 2F, CF_2), −80.6 (CF_3). $C_{21}H_{24}F_{13}NO_6$ (633.40): calculated C 39.82, H 3.82, N 2.21; found C 40.06, H 3.76, N 2.26. MS (auto-Cl, 100 eV): m/z = 633 (M^+).

Methyl 2-O-cyclohexylcarbamoyl-6-deoxy-3,4-O-(2,2,2-trifluoroethylidene)-α-L-altropyranoside (**13**). R_f = 0.58 (toluene:ethyl acetate 6:1 v/v); yield 1.10 g (55%, pure *endo*-H diastereomer); m.p. 158–159 °C (ethanol); $[\alpha]_D^{22.5}$ −49.02° (c = 0.865, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ ≈ 1.03–1.23 (m, 4H, cyclohexyl CH_2), 1.33 (d, 3H, $J_{5/6\text{-}CH3}$ ≈ 6.0 Hz, 6-CH_3), 1.51–1.73 (m, 4H, cyclohexyl CH_2), 1.85–1.99 (m, 2H, cyclohexyl CH_2), 3.36 (s, 3H, OCH_3), 3.44–3.55 (m, 1H, cyclohexyl CH), 3.77 (dq, 1H, $J_{5/6\text{-}CH3}$ ≈ 6.0 Hz, 5-H), 4.06 (dd, 1H, $J_{4/5}$ ≈ 8.8 Hz, 4-H), 4.29 (dd, 1H, $J_{3/4}$ ≈ 5.9 Hz, 3-H), 4.56 (d, 1H, $J_{1/2}$ ≈ 2.7 Hz, 1-H), 4.68 (d, 1H, $J_{NH/CH}$ ≈ 7.2 Hz, NH), 5.04 (dd, 1H, $J_{2/3}$ ≈ 5.4 Hz, 2-H), 5.70 (q, 1H, $J_{H/F}$ ≈ 4.3 Hz, *endo*-acetal H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 18.9 (C6), 25.1, 25.8, 33.6 (cyclohexyl CH_2), 50.6 (cyclohexyl CH), 56.0 (OCH_3), 63.4 (C5), 69.7 (C2), 76.4 (C3), 77.1 (C4), 97.9 (q, $J_{C/F}$ ≈ 36.2 Hz, acetal C), 99.5 (C1), 122.0 (q, $J_{C/F}$ ≈ 285 Hz, CF_3), 154.2 (carbamoyl C=O). ^{19}F {H} NMR (235 MHz, $CDCl_3$): δ = −82.7 (CF_3). $C_{16}H_{24}F_3NO_6$ (383.15): calculated C 50.11, H 6.31, N 3.65; found C 50.14, H 6.38, N 3.70. MS (auto-Cl, 100 eV): m/z = 384 (M^+ + 1).

1,6-Bis-(methyl 2-O-cyclohexylcarbamoyl-6-deoxy-3,4-O-methylidin-α-L-altropyranoside) dodecafluorohexane (**14**). A mixture of methyl α-L-rhamnopyranoside (**9**) (1.0 g, 5.6 mmol), DCC (2.3 g, 11.2 mmol), 2,2,3,3,4,4,5,5,6,6,7,7-dodecafluorooctane-1,8-dial (**6a**) (1.0 g, 2.8 mmol) and 1,2-dichloroethane (10 ml) was refluxed for 5 h. The mixture was worked up (under shaking with 2% aqueous HCl) as described in the general procedure. The compounds **14** (R_f = 0.31) and **15** (R_f = 0.15) were separated by column chromatography (toluene:ethyl acetate 3:1 v/v).

Yield of **14**, 0.28 g (11%, mixture of *endo*-H/*endo*-H and *endo*-H/*exo*-H diastereomers). Recrystallization from heptane:chloroform (3:1) gave the pure *endo*-H/*endo*-H diastereomer **14**: m.p. 191–193 °C; $[\alpha]_D^{23}$ = +38.4° (c = 1.0, $CHCl_3$).

Yield of methyl α-L-rhamnopyranoside 2,3-carbonate (**15**), 0.21 g (18%); m.p. 167–169 °C (heptane:ethanol 10:1); $[\alpha]_D^{21}$ = −57.2° (c = 1.0, $CHCl_3$), Literature data [22] m.p. 169–171 °C, $[\alpha]_D^{24}$ = −59.0° (c = 1.0, $CHCl_3$).

14. ^{1}H NMR (250 MHz, acetone-d_6): δ ≈ 1.26 (m, 5H, cyclohexyl CH_2), 1.30 (d, 3H, $J_{5/6\text{-}CH3}$ ≈ 6.4 Hz, 6-CH_3), ≈ 1.58 (m, 1H, cyclohexyl CH_2), ≈ 1.70 (m, 2H, cyclohexyl CH_2), ≈ 1.88 (m, 2H, cyclohexyl CH_2), 3.34 (s, 3H, OCH_3),

≈3.38 (m, 1H, cyclohexyl CH), 3.83 (dq, 1H, $J_{4/5}$≈8.9 Hz, 5-H), 4.13 (dd, 1H, $J_{3/4}$≈5.2 Hz, 4-H), 4.33 (dd, 1H, $J_{2/3}$≈4.9 Hz, 3-H), 4.54 (d, 1H, $J_{1/2}$≈2.7 Hz, 1-H), 4.98 (dd, 1H, 2-H), 5.70 (t, $J_{H/F}$≈8.9 Hz, *endo*-acetal H), 6.25 (m, 1H, NH). ^{13}C NMR (62.9 MHz, acetone-d_6): δ=18.9 (CH_3), 25.7, 26.3, 33,7 (cyclohexyl CH_2),51.1 (cyclohexyl CH), 55.4 (OCH_3), 64.2 (C5), 70.3 (C2), 77.8 (C3), 78.9 (C4), 99.0 (t, $J_{C,F}$≈25.5 Hz, acetal-C), 100.1 (C1), 155.0 (C=O). ^{19}F {H} NMR (235 MHz, acetone-d_6): δ= −122.2 (s, 4F, γ, γ'-CF_2), −123.0 (s, 4F, β, β'-CF_2), −127.7 (s, 4F, α,α'-CF_2). $C_{36}H_{48}F_{12}N_2O_{12}$ (928.80): calculated C 46.55, H 5.21, N 3.02; found C 46.64, H 5.23, N 3.02. MS (70 eV): m/z=928 (M^+).

15. ^{1}H NMR (250 MHz, acetone-d_6): δ=1.28 (d, 3H, $J_{5/6\text{-}CH3}$≈6.4 Hz, 6-CH_3), 3.35 (ddd, 1H, $J_{4/5}$≈9.8 Hz, 4-H), 3.37 (s, 3H, OCH_3), 3.64 (dq, 1H, 5-H), 4.64 (dd, 1H, $J_{3/4}$≈7.0 Hz, 3-H), 4.72 (dd, 1H, $J_{2/3}$≈7.0 Hz, 2-H), 4.92 (d, 1H, $J_{1/2}$≈0.6 Hz, 1-H), 4.95 (d, 1H, $J_{4/OH}$≈5.8 Hz OH). ^{13}C NMR (62.9 MHz, acetone-d_6): δ=17.5 (CH_3), 55.1 (OCH_3), 65.7 (C5), 74.0 (C4), 77.5 (C2), 80.5 (C3), 97.0 (C1), 154.5 (C=O). $C_8H_{12}O_6$ (204.18): calculated C 47.06, H 5.92; found C 47.36, H 5.92. MS (70 eV): m/z=204 (M^+).

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References

[1] O. Klenz, R. Evers, R. Miethchen and M. Michalik, *J. Fluorine Chem.,81* (1997) 205.
[2] R.E. Banks, B.E. Smart and J.C. Tatlow (Eds.), *Organofluorine Chemistry, Principles and Commercial Applications*, Plenum, New York, 1994.
[3] S. Benefice-Malouet, H. Blancou and A. Commeyras, *J. Fluorine Chem., 63* (1993) 217.
[4] C.-M. Hu and X.-Q. Tang, *J. Fluorine Chem., 61* (1993) 217.
[5] C.-M. Hu and J. Chen, *J. Fluorine Chem., 67* (1994) 189.
[6] C. Einhorn, J. Einhorn and J.-L. Luche, *Synthesis* (1989) 787; G.J. Price (Ed.), *Current Trends in Sonochemistry*, Royal Society of Chemistry, Cambridge, 1992.
[7] J.-L. Luche, C. Einhorn and J.V. Sinisterra-Gago, *Tetrahedron Lett., 31* (1990) 4125.
[8] K.S. Suslick, *Ultrasound — Its Chemical, Physical, and Biological Effects*, VCH, Weinheim, 1988; G.J. Price (Ed.), *Current Trends in Sonochemistry*, Royal Society of Chemistry, Cambridge, 1992.
[9] D. Peters and R. Miethchen, *J. Prakt. Chem., 337* (1995) 615.
[10] S. Benefice-Malouet and A. Commeyras, *J. Fluorine Chem., 70* (1995) 103.
[11] H. ElFakih, F. Pautet, H. Fillion and J.-L. Luche, *Tetrahedron Lett., 33* (1992) 4909.
[12] D. Peters, F. Pautet, H. ElFakih, H. Fillion and J.-L. Luche, *J. Prakt. Chem., 337* (1995) 363.
[13] W.S. Wadsworth, *Org. React., 25* (1977) 73.
[14] J.M. Emsley, L. Phillips and V. Wray, *Fluorine Coupling Constants*, Pergamon, Oxford, 1977.
[15] J.R. Riess and J. Greiner, in G. Descotes (Ed.), *Carbohydrates as Organic Raw Materials II*, VCH, Weinheim, 1993, pp. 209–259.
[16] R. Filler and Y. Kobayashi (Eds.), *Biomedical Aspects of Fluorine Chemistry*, Kodansha, Tokyo, 1982; R.E. Banks (Ed.), *Preparation, Properties and Industrial Applications of Organofluorine Compounds*, Ellis Horwood, Chichester, 1982; N. Ishikawa (Ed.), *Synthesis and Reactivity of Fluoro-compounds*, Vol. 3, CMC, Tokyo, 1987; J.T. Welch and S. Eswarakrishnan, *Fluorine in Bioorganic Chemistry*, Wiley, New York, 1991.
[17] F. Micheel and A. Klemer, *Adv. Carbohydr. Chem., 16* (1961) 85; A.A.E. Penglis, *Adv. Carbohydr. Chem. Biochem., 38* (1981) 195; N.F. Taylor, *Fluorinated Carbohydrates*, Washington, DC, 1988; T. Tsuchiya, *Adv. Carbohydr. Chem. Biochem., 48* (1990) 91.
[18] R. Miethchen, D. Rentsch and M. Michalik, *Liebigs Ann. Chem.* (1994) 219.
[19] R. Miethchen and D. Rentsch, *Liebigs Ann. Chem.* (1994) 1191; R. Miethchen, D. Rentsch, M. Frank and A. Lipták, *Carbohydr. Res., 281* (1996) 61; R. Miethchen, D. Rentsch and M. Frank, *J. Carbohydr. Chem., 15* (1996) 15 and papers cited therein.
[20] D. Rentsch, *Dissertation*, Universtät Rostock, 1995.
[21] R. Miethchen and D. Rentsch, *Synthesis* (1994) 827.
[22] K. Tatsuta, K. Akimoto, M. Annaka, Y. Ohno and M. Kinoshita, *Bull. Chem. Soc. Jpn., 58* (1985) 1699.