Synthesis of polyfluorinated ketones *via* the ate-complexes

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Asymmetric polyfluorinated ketones R^FCOR are formed by treating various derivatives of (polyfluoro)alkanoic acids (esters, anhydrides, acid chlorides) with lithium tetraalkylaluminates ("ate-complexes"). The highest yields of the ketones (65—78 %) were obtained from (polyfluoro)alkanoyl chlorides.

Key words: fluorinated ketones, synthesis; lithium tetraalkylaluminates, reaction with (polyfluoro)alkanoyl chlorides.

Fluorinated ketones are used as fire-resistant solvents for polymers as well as synthons for obtaining biologically active compounds and thermo-, light-, and chemically stable polymers. Traditionally, ketones of the R^FCOR type are obtained by treating fluorocarboxylic acids or their derivatives (esters, nitriles, acid halides) with organomagnesium and organolithium compounds.[1] Surprisingly, the much more available organoaluminum compounds have not been utilized for this purpose. Moreover, the records of their use for the synthesis of organofluorine compounds are rather scarce.[2,3]

We have elaborated an efficient method for the synthesis of nonsymmetric ketones of the general formula $R^FCOCH_2CH_2R$ (**1a—f**) by treating the derivatives of (polyfluoro)alkanoic acids of the general formula R^FCOX (**2a—d**, X = Cl, MeO or EtO, 4-$NO_2C_6H_4O$, CF_3COO) with lithium tetraalkylaluminates ("ate-complexes") of general type **3**. The latter are readily formed from terminal alkenes and $LiAlH_4$ in the presence of a $TiCl_4$ catalyst (Scheme 1, *A*). The reaction is easy to perform and, unlike most reactions involving organoaluminum compounds, does not require that the synthesis be performed under a stream of argon.

The reactions of fluorine-substituted substrates (**2a—d**) (X = Cl, OMe, OEt, 4-$NO_2C_6H_4O$, CF_3COO) with ate-complexes **3a—d** result exclusively in asymmetric ketones **1a—f** (Scheme 1, *B*; Tables 1 and 2), the yield of which strongly depends on the reactivity of the carbonyl component, *i.e.*, on the nature of the ligand X in compounds **2a—d**. When X = OMe or OEt, the yields of compounds **1a—d** are as small as 7—10 %. If *p*-nitrophenyl fluorocarboxylates are used, the yields of compounds **1a—f** increase significantly, but these substrates tend to decompose on storage. The anhydrides (X = CF_3COO) react satisfactorily, but a sixfold excess of these compounds with respect to **3** is required. The best yields of fluoroketones are attained using the acid chlorides, **2a—d** (X = Cl), at a molar ratio ate-complex : acid chloride = 1 : 3.

Scheme 1

$$CH_2{=}CHR + LiAlH_4 \xrightarrow[20\ ^\circ C,\ 48\ h]{TiCl_4(cat)/THF} \underset{\mathbf{3a{-}d}}{Li[Al(CH_2CH_2R)_4]} \quad (A)$$

R = n-C_7H_{15}(**a**), n-C_6H_{13}(**b**),
n-C_3H_7(**c**), n-C_4H_9(**d**)

$$\mathbf{3(a{-}d)} + \underset{\mathbf{2a{-}d}}{R^FCOX} \xrightarrow[24\ h]{-10^\circ \longrightarrow 20\ ^\circ C} \underset{\mathbf{1a{-}f}}{R^FCOCH_2CH_2R} \quad (B)$$

R^F = CHF_2 (**a**), CF_3 (**b**),
n-C_4F_9(**c**), n-C_6F_{13}(**d**)
(X = Cl, OMe, OEt, 4-$NO_2C_6H_4O$, CF_3COO)

Tables 1 and 2 present the parameters of the hitherto unknown products synthesized in this work.

Experimental

IR spectra were recorded on a Specord-75 IR spectrophotometer in a 5 mm-thick layer. ^1H NMR spectra were recorded on a Tesla BS-567A spectrometer (100 MHz) using Me_4Si as the internal standard. Elemental analysis data are in accordance with the structures presented.

Preparation of ate-complexes (general procedure). 1-Nonene (56 g, 0.48 mol) and $TiCl_4$ (0.5 g, 3.7 mmol) were added dropwise with stirring to a suspension of $LiAlH_4$ (4.7 g, 0.12 mol) in THF (200 mL) in such a way that the temperature did not exceed 40 °C. The mixture was kept for one day at ~20 °C and then used in reactions with derivatives of fluorocarboxylic acids.

Synthesis of fluoro-substituted ketones. Method 1. The reaction of perfluorovaleroyl chloride with lithium tetraoctylaluminate (**3b**).

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Table 1. Yields and characteristics of asymmetric polyfluorinated ketones **1**

Compound	R^F	R	Method of synthesis	Yield (%)	B.p./°C (*p*/Torr)
1,1-Difluoro-2-undecanone (**1a**)	HCF_2	C_7H_{15}	1	73	94—95 (34)
1,1,1-Trifluoro-2-decanone (**1b**)	HF_3	C_6H_{13}	1	65	96—97 (41)
1,1,1,2,2,3,3,4,4-Nonafluoro-5-decanone (**1c**)	C_4F_9	C_3H_7	1	68	81—82 (50)
1,1,1,2,2,3,3,4,4-Nonafluoro-5-undecanone (**1d**)	C_4F_9	C_4H_9	1	76	92—93 (45)
1,1,1,2,2,3,3,4,4-Nonafluoro-5-tridecanone (**1e**)	C_4F_9	C_6H_{13}	3	42	111—112 (23)
1,1,1,2,2,3,3,4,4,5,5,6,6-Tridecafluoro-7-pentadecanone (**1f**)	C_6F_{13}	C_6H_{13}	1	72	110—111 (7)

Table 2. Spectroscopic characteristics of polyfluorinated ketones **1**

Ketone	IR, ν/cm^{-1}	^{1}H NMR, δ (*J*/Hz)
1a	1755	0.88 (t, 3 H, CH_3, $J_{CH_3CH_2}$ = 6.0); 1.2—1.36 (m, 12 H, $(CH_2)_6$); 1.46—1.80 (m, 2 H, $COCH_2\underline{CH_2}$); 2.64 (t, 2 H, $COCH_2$, $J_{CH_2CH_2}$ = 7.0)
1b	1765	0.70 (t, 3 H, CH_3, $J_{CH_3CH_2}$ = 6.1); 0.92—1.18 (m, 10 H, $(CH_2)_5$); 1.26—1.54 (m, 2 H, $COCH_2\underline{CH_2}$); 2.71 (t, 2 H, $COCH_2$, $J_{CH_2CH_2}$ = 6.8)
1c	1760	0.85 (t, 3 H, CH_3, $J_{CH_3CH_2}$ = 6.0); 0.90—1.19 (m, 6 H, $(CH_2)_3$); 1.35—1.68 (m, 2 H, $COCH_2\underline{CH_2}$); 2.70 (t, 2 H, $COCH_2$, $J_{CH_2CH_2}$ = 6.8)
1d	1757	0.91 (t, 3 H, CH_3, $J_{CH_3CH_2}$ = 5.4); 1.26—1.48 (m, 6 H, $(CH_2)_3$); 1.57—1.84 (m, 2 H, $COCH_2\underline{CH_2}$); 2.76 (t, 2 H, $COCH_2$, ($J_{CH_2CH_2}$ = 6.8)
1e	1750	0.89 (t, 3 H, CH_3, $J_{CH_3CH_2}$ = 5.4); 1.24—1.50 (m, 10 H, $(CH_2)_5$); 1.56—1.84 (m, 2 H, $COCH_2\underline{CH_2}$); 2.75 (t, 2 H, $COCH_2$, $J_{CH_2CH_2}$ = 6.8)
1f	1755	0.92 (t, 3 H, CH_3, $J_{CH_3CH_2}$ = 5.4); 17.6—1.44 (m, 10 H, $(CH_2)_5$); 1.56—1.86 (m, 2 H, $COCH_2\underline{CH_2}$); 2.75 (t, 2 H, CH_2, $J_{CH_2CH_2}$ = 7.0)

Perfluorovaleroyl chloride (**2c**, X = Cl) (102 g, 0.36 mol) was added at −10 °C with stirring to the ate-complex **3b** (R = C_6H_{13}) obtained by the above procedure. The mixture was kept for one day at ~20 °C, then cooled to 0 °C. Water and 20 % aqueous H_2SO_4 were added dropwise until the inorganic salts dissolved. The mixture was extracted with ether and the extract was dried with $MgSO_4$ and concentrated, after which the product **1e** was isolated by distillation *in vacuo*.

Method 2. Reaction of trifluoroacetic anhydride with lithium tetraoctylaluminate. Trifluoroacetic anhydride (**2b**, X = $OCOCF_3$) (75.6 g, 0.36 mol) was added dropwise at −20 °C to a stirred solution of the ate-complex **3b** obtained from $LiAlH_4$ (2.28 g, 0.06 mol), 1-octene (28 g, 0.25 mol), and $TiCl_4$ (0.25 g, 1.85 mmol). The mixture was kept for one day at ~20 °C and worked up according to method 1 to give ketone **1b**.

Method 3. Reaction of *p*-nitrophenyl perfluorovalerate with Li[AlOct$_4$]. *p*-Nitrophenyl ester **2c** (X = $4\text{-}NO_2C_6H_4O$) (69.3 g, 0.18 mol) was added dropwise at −5 °C with stirring to a solution of the ate-complex **3b** obtained as described above. The mixture was kept for one day at −20 °C and worked up as above. Ketone **1e** was isolated according to *method* 1.

Method 4. Reaction of **3b** with ethyl perfluorovalerate. Ester **2c** (X = OEt) (52.5 g, 0.18 mol) was added dropwise at ~20 °C to a stirred solution of the ate-complex **3b** obtained as described above. The mixture was refluxed for 3 h. Subsequent work-up and isolation of ketone **1e** were carried out according to method 1.

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