Journal of Fluorine Chemistry 129 (2008) 669–673

Contents lists available at ScienceDirect

Journal of Fluorine Chemistry

journal homepage: www.elsevier.com/locate/fluor

Pentafluorophenyl carbonyl compounds in the Reformatsky-type reactions promoted with $Fe(CO)_5$-based metal complex systems

A.B. Terent'ev, T.T. Vasil'eva, O.V. Chahovskaya, N.E. Mysova, H.H. Hambardzumyan, K.A. Kochetkov *

A.N. Nesmeyanov Institute of Organoelement Compounds, The Russian Academy of Sciences, Vavilov Str. 28, 119991 Moscow, Russian Federation

ARTICLE INFO

Article history:
Received 7 December 2007
Received in revised form 30 May 2008
Accepted 30 May 2008
Available online 5 June 2008

Keywords:
Pentafluorophenyl-containing compounds
The Reformatsky-type reaction
Iron pentacarbonyl
Reductive coupling

ABSTRACT

Iron pentacarbonyl is an effective promoter for additions of halogenated acid esters and nitriles to pentafluorophenyl carbonyl compounds **1**, **4**, and **5** by the Reformatsky-type reaction and reductive coupling of compound **1**. The electron-withdrawing character of the pentafluorophenyl group has a significant effect on the reaction pathway and the type of the reaction products. The reactions involving metal complex systems derived from $Fe(CO)_5$ have a number of advantages such as a simple procedure for carrying out, the lack of necessity to use anhydrous solvents and an inert atmosphere. The schemes of the reactions have been proposed and the conditions for preparative syntheses of most products have been optimized.

1. Introduction

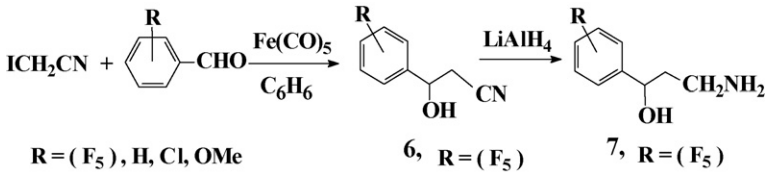
Today the expanding circle of reactions including metal insertion into carbon–halogen bond followed by interaction with compounds containing reactive groups such as carbonyl, nitrile, *etc.* are assigned to Zaitsev–Barbier–Reformatsky reactions [1–5]. Various metals are involved in these reactions such as zinc [4], magnesium [6] and more recently samarium [7], silicon [8], indium [5], *etc.* Although the common conditions for above reactions are continuously being improved, certain difficulties exist for carrying out them such as the need to use anhydrous and volatile solvents and inert atmosphere, low temperatures, heterogeneous medium, effective agitating and activating a metal surface. A search for new approaches to realization of additions of organohalogen compounds, specifically organofluorine compounds, to the carbonyl group of aldehydes and ketones is still being continued [9,10]. Taking into account the fact that introduction of fluorine atoms into organic compounds often leads to essential changes in their physical, chemical and biological properties [2,3,11–14] it is of great interest to develop a new methodology for the synthesis of multifunctional organofluorine compounds that would be experimentally simple.

Most metal complexes widely used in the organic synthesis are either expensive or not easily available [5,7,10]. On the other hand, iron oxides, salts and complexes are cheap and recently they have been proposed as catalysts and promoters for organic synthesis [15–19], at the same time the available metal carbonyls are used as reagents much more rarely [20]. We reported the first examples that $Fe(CO)_5$ and homogenous $Fe(CO)_5$-based metal complex systems are effective promoters for the Reformatsky-type reactions [21–23]. The above reactions are characterized by high yields, high selectivity, and they can be carried out under simple conditions such as either refluxing in benzene for several hours or standing at room temperature, there is no need to use anhydrous solvents and inert atmosphere. We studied these reactions by the example of various types of carbonyl compounds and concluded that the presence of $Fe(CO)_5$ is most effective in the case of pentafluorobenzaldehyde **1**, this made it possible to perform additions of various organohalogen compounds to **1** [24]. For instance, a striking example of the $Fe(CO)_5$-promoted reaction is addition of allyl iodide to aldehyde **1** that occurs under mild conditions to give secondary alcohol $CH_2{=}CHCH_2$-CH(OH)-C_6F_5 (**2**) in almost quantitative yield [24]. We have also showed that aldehyde **1** undergoes diastereoselective reductive coupling in the presence of [$Fe(CO)_5$ + HMPA] system to form the corresponding decafluorodihydrobenzoine C_6F_5–CH(OH)–CH(OH)–C_6F_5 (**3**) [25].

In this work we have first performed the reaction of the Reformatsky-type with perfluoro- and pentafluoroacetophenones (**4** and **5**) in the presence of $Fe(CO)_5$. Taking into account the new examples of additions of organohalogen compounds to aldehyde **1**, we have compared the reactivity of pentafluorophenyl carbonyl compounds **1**, **4**, and **5** in the reactions of the above type and proposed the reaction mechanism.

* Corresponding author. Tel.: +7 499 1355033; fax: +7 499 1355085.
E-mail address: const@ineos.ac.ru (K.A. Kochetkov).

0022-1139/$ – see front matter © 2008 Elsevier B.V. All rights reserved.
doi:10.1016/j.jfluchem.2008.05.017



Scheme 1.

2. Results and discussion

The use of pentafluorobenzaldehyde **1** in the Reformatsky-type reactions allowed us to open the route to a wide circle of functionally substituted secondary alcohols containing a pentafluorophenyl group [24]. A sharp increase in the yields of the adducts was observed when going from perfluorobutyl iodide to allyl iodide; this is associated with the fact that electrophilic pentafluorobenzaldehyde **1** much more readily reacts with a nucleophilic reagent than with an electrophilic one.

The reaction with iodoacetonitrile does make it possible to obtain β-hydroxy nitrile **6** in high yield whose reduction allows one to prepare easily γ-oxyamine **7** (Scheme 1).

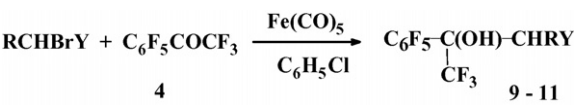
Application of PASS Software [27] to fluorinated γ-amino alcohols predicted (with a probability exceeding 95%) the pronounced anti-ischemic activity for amine **7**. Chiral amino alcohols obtained from β-hydroxy nitriles are of great importance because of their biological activity and the possible applicability to asymmetric synthesis as ligands [28,29].

The addition of methyl bromoacetate, the typical Reformatsky reagent, to aldehyde **1** occurs at 110 °C to give 3-hydroxy-3-pentafluorophenylpropionic acid methyl ester (**8**) in good yield; it is accompanied by the formation of **3** as a by-product in the form of a mixture of *meso*- and D,L-forms.

Involving the less reactive pentafluorophenyl ketones **4** and **5** in the Reformatsky reaction makes it possible to synthesize functionally substituted tertiary alcohols with a pentafluorophenyl group. Perfluoroacetophenone **4** undergoes the reaction with halogenated compounds on heating in chlorobenzene; the reaction is not virtually accompanied by formation of by-products such as unsaturated compounds and diols unlike reaction with aldehyde **1** (Table 1).

In the case of pentafluoroacetophenone **5** the yields of the target products are somewhat lower than those in the case of ketone **4** (Table 2) and a by-product, namely 1,2-bis(pentafluorophenyl)propen-1-ol (**12**), is formed as a result of aldol condensation in about 10% yield. Unlike the reductive coupling of aldehyde **1**, diastereoselectivity of the above reactions (Tables 1 and 2) is not high, and the diastereoisomer ratio is about 2:1.

Table 1
Reaction of brominated esters and nitriles with perfluoroacetophenone **4**



Entry	R	Y	Product	Yield (%)
1[a]	H	$COOCH_3$	8	65
2	CH_3	$COOCH_3$	9	70
3	CH_3	CN	10	65
4	H	$COOCH_3$	11	71

[a] Addition of methyl bromoacetate to pentafluorobenzaldehyde **1** has been performed that was accompanied by the formation of diol **3** (5%) and unsaturated compound.

Therefore, we have proposed a one-step process for preparation of tertiary hydroxy esters and nitriles containing pentafluorophenyl group in combination with methyl and trifluoromethyl groups. In our opinion, the special properties of polyfluorinated carbonyl compounds **1**, **4**, and **5** are associated with strong electron-withdrawing character of the pentafluorophenyl group, this indicates that the role of polar factors is significant in the reactions under consideration. The results we have obtained supplement well the existing opportunities for the synthesis of secondary and tertiary fluorinated hydroxy compounds reported in literature [9].

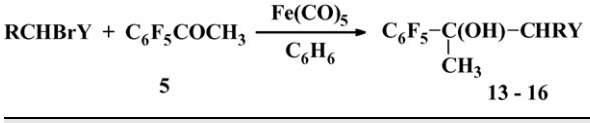
It is well known that organomagnesium compounds derived from perfluoroalkyl halides can be obtained mainly as a result of the exchange reaction of a perfluoroalkyl halide with an alkylmagnesium halide; and it is difficult to use the Grignard reactions for synthesizing pentafluorinated hydroxy compounds of the considered series [30]. In this case reduction of substrate often takes place and sometimes the reduction becomes the major reaction, this results in low yields of the target products—secondary and tertiary alcohols. At the same time, under the conditions studied that result in products **8–16**, there were not found the substances corresponding to the reduction products of the initial polyfluorinated compounds (according to GC–MS data) such as diols or stilbenes.

When we considered the possible reaction mechanism (Scheme 2), we reasoned from the fact that the charge-transfer complexes of the (**A**) type are formed in systems including $Fe(CO)_5$ and organohalogen compounds as we showed earlier using UV spectroscopy. Decomposition of the above complexes provides initiation of the reactions [26].

The transition state of the reactions can be represented in the form of organoiron complex (B), including either **1** (or **4** or **5**) and anion resulted from the electron transfer in the system $Fe(CO)_5$–RX (X = Hal) [24]. The strong electron-accepting effect of the pentafluorophenyl group facilitates the nucleophilic attack of the anion at the electrophilic centre of the carbonyl compound.

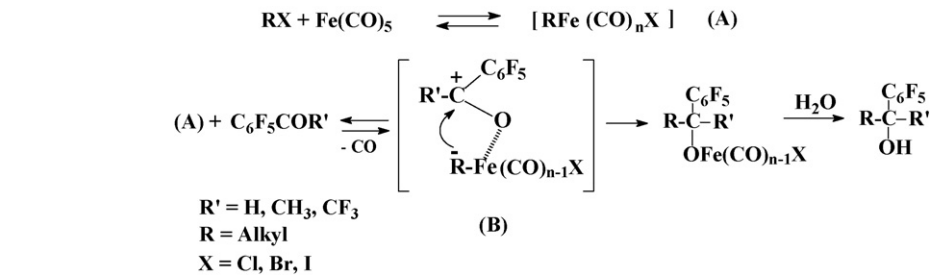
Our studies of reaction mixtures resulted from Reformatsky-type reactions involving aldehyde **1**, showed the presence of traces of decafluorodihydrobenzoine **3** [25]. The formation of the corresponding dihydrobenzoines from ketones **4** and **5** was not observed under the similar conditions unlike aldehyde **1**.

Table 2
Reaction of halogenated esters and nitriles with pentafluoroacetophenone **5**

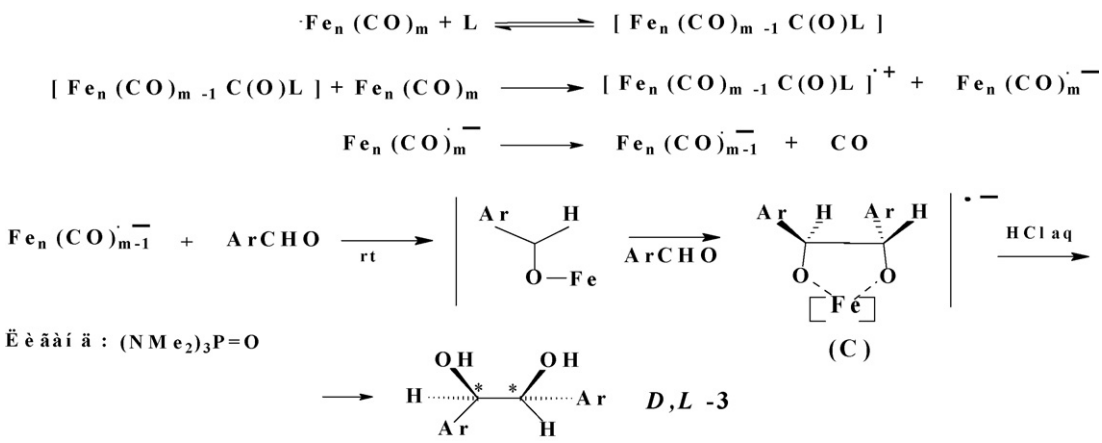


Entry	R	Y	Solvent	Product	Yield(%)
1[a]	H	$COOCH_3$	ClC_6H_5	13	35
2	H	CN	C_6H_6	14	25
3	CH_3	$COOCH_3$	C_6H_6	15	70
4	CH_3	CN	ClC_6H_5	16	45

[a] The reaction with JCH_2CN occurs similarly.



Scheme 2.



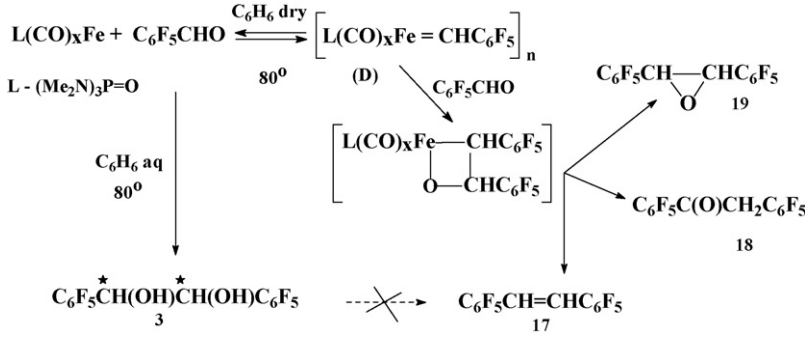
Scheme 3.

The formation of product **3** made it possible to study the conditions for the reductive coupling of aldehyde **1** in detail. We have shown that in the presence of [$Fe(CO)_5$ + HMPA] system, aldehyde **1** gives corresponding **3** as D,L-isomer in almost quantitative yield.

The formation of product **3** can be explained by the scheme that includes one-electron transfer from the iron atom to aldehyde **1** to form an anion-radical in the iron ligand sphere, addition of the new aldehyde molecule to the anion-radical particle (this step may be sterically hindered in the case of ketones **4** and **5**) to give alkoxide (**C**), and its hydrolysis leading to diol (Scheme 3). The first step is confirmed by the data concerning the charge-transfer complexes [6], and formation of the similar anion-radical particles was observed by ESR in particular in the $Fe(CO)_5$ system with amines, amides, phosphines, *etc.* [20,31].

We obtained unexpected results when the reductive coupling of **1** was carried out in anhydrous benzene at 80 °C. The reaction mixture was found to contain decafluorostilbene **17** as the major identified reaction product as well as 1,2-di(pentafluorophenyl)ethanone **18** и decafluorostilbene **19**, whereas diol **3** was absent (Scheme 4). It should be noted that stilbene **17** was registered as the only reaction product when a fivefold decrease of the initial concentration of **1** in the solution was used. To clarify the role of water in the above abnormalities we carried out the reaction with aldehyde **1** in the presence of the water added in the equivalent amount (1 mmol). In this case product **3** was obtained again, and stilbene **17** was virtually absent. Therefore, in reductive coupling pentafluorobenzaldehyde **1** exhibits the dual reactivity depending on the presence of water in the system (even in trace amounts). The synthesis of stilbenes from various aldehydes was earlier reported in the presence of either $AlCl_3$ + Zn [32] or $InCl_3$ + Zn [33] systems, where the reactions were carried out in anhydrous acetonitrile under refluxing, and the mechanisms were not considered.

We assume the following steps of the reaction when it is carried out in an anhydrous solvent on heating (Scheme 4): the formation of metallocarbene followed by intracomplex coupling



Scheme 4.

to give stilbene **17**, reacting the carbene complex (**D**) with aldehyde, i.e. insertion of the carbine into C–H and C=O bonds to yield ketone **18** and oxirane **19**, respectively. The presence of moisture hinders the carbine formation and as a result diol **3** became the major product.

In our opinion, the fact that stilbene **17** is the only product when the reaction is carried out at fivefold dilution, indicates that the formation of stilbene is of intracomplex character and products **18** and **19** are formed in an intermolecular manner.

The substantial distinctions in the results of the reactions with perfluorobenzaldehyde **1** (Scheme 4) and benzaldehyde [23] reflects the effect of the polar substituents in the benzene ring of aldehyde **1**. Judging from the experimental data, the electron-withdrawing pentafluorophenyl group facilitates stabilization of the carbene complex **D**, unlike the phenyl group in benzaldehyde; this can explain the dual character of the reactivity of pentafluorobenzaldehyde **1** depending on the reaction conditions.

3. Conclusion

Therefore, we have demonstrated the opportunity to use $Fe(CO)_5$-based systems for promoting the Reformatsky-type reactions and diastereoselective reductive coupling for organofluorine carbonyl compounds to give polyfunctional compounds containing groups with potential biological activity. The reactions involving metal complex systems derived from $Fe(CO)_5$ have a number of advantages such as a simple procedure for carrying out (refluxing in either benzene or chlorobenzene for several hours), the lack of necessity to use anhydrous solvents and an inert atmosphere. The schemes of the reactions have been proposed and the conditions for preparative syntheses of most products have been optimized.

4. Experimental

GC–MS measurements were carried out on a VG-7070E instrument (EI, 70 eV). Because the mass spectra of the diastereoisomers are almost identical, the spectrum of one of them is given. GLC analysis was conducted on a LKhM-80 chromatograph, a steel column (1300 × 3 mm) with 15% SKTFT-50X on Chromaton-N-AW, detector-catharometer, helium was used as a gas-carrier (60 ml/min), temperature programming in the range of 50–250 °C (6°/min), the yields were determined by internal standard method. The ^1H and ^{19}F NMR spectra were recorded on a Bruker WP-300 and 400 in $CDCl_3$, the chemical shifts are given for either TMC or CF_3CO_2H standards, respectively. All organic reagents were purified by distillation. Compounds **1**, **4** and **5** were delivered from Scientific Industrial Association "P & M" (Russia). $Fe(CO)_5$ from Fluka was used without additional purification.

4.1. General procedures for the synthesis of hydroxy carbonyl compounds. Reactions of pentafluorophenyl carbonyl compounds 1, 4, and 5 with halogenated esters and nitriles

A solution of a mixture of halogenated derivative (1 mmol), carbonyl compound (1 mmol), $Fe(CO)_5$ (2 mmol) in 1 ml of benzene (or chlorobenzene) was heated with stirring for 4 h at 80 °C (or at 110 °C, respectively). Then the reaction mixture was diluted with 2 ml of the solvent, treated with 1N hydrochloric acid, twice washed with water, and dried over $MgSO_4$. The reaction products were isolated either by crystallization (solids) or preparative GLC (liquids) using the phase that was used in GLC analysis. The yields were determined by GLC using an internal standard [24].

4.2. Pentafluorophenyl hydroxy compounds derived from 1

4.2.1. 3-Hydroxy-3-pentafluorophenylpropionic acid methyl ester (8)

(110 °C, ClC_6H_5, 4 h). Yield 62%, mp 53–55 °C, diastereoisomer ratio 1:1.5. ^1H NMR (400 MHz, $CDCl_3$): δ 2.76–3.14 (2H, AB part of ABX system, J_{AB} = 22.32 Hz, J_{AX} = 12.64 Hz, J_{BX} = 12.64 Hz), 3.50 (1H, s), 5.47–5.51 (1H, m, X part of ABX system). ^{19}F NMR (282 MHz, $CDCl_3$): δ −64.92 (m, 2F), −76.35 (t, 1F, J = 20.8 Hz), −83,75 (m, 2F). GC–MS: m/z (I_{rel}): 270 $[M]^+$ (0.4), 252 $[M-H_2O]^+$ (25.7), 197 $[C_6F_5CH(OH)]^+$ (83.3), 195 $[C_6F_5CO]^+$ (52.4), 167 $[C_6F_5]^+$ (24), 74 $[CH_3COOCH_3]^+$ (55.1), 43 $[CH_3CO]^+$ (100). Anal. Calcd for $C_{10}H_7F_5O_3$: C, 44.44; H, 2.59; F, 35.18. Found: C, 44.17; H, 2.40; F, 35.67.

4.3. Pentafluorophenyl hydroxy compounds derived from 4

4.3.1. 4,4,4-Trifluoro-3-hydroxy-2-methyl-3-pentafluorophenylbutyric acid methyl ester (9)

(110 °C, ClC_6H_5, 4 h). Yield 70%, mp 54–56 °C, diastereoisomer ratio 1:1.5. ^1H NMR (300 MHz, $CDCl_3$): δ 1.58 (3H, d, J = 7 Hz), 3.71–3.77 (1H, m), 4.87 (1H, s), 3.88 (3H, s). ^{19}F NMR (282 MHz, $CDCl_3$): δ −1.43 (t, 3F, J = 8 Hz), −59.78 (m, 2F), −73.88 (t, 1F, J = 21 Hz), −83.18 (m, 2F). GC–MS: m/z (I_{rel}): 352 $[M]^{\bullet+}$ (2.40), 321 $[M-OCH_3]^+$ (1.28), 283 $[M-OCH_3]^+$ (7.70), 265 $[C_6F_5(CF_3)OH]^+$ (10.6), 195 $[C_6F_5CO]^+$ (100.0), 88 $[C_2H_5COOCH_3]^+$ (65.7). Anal. Calcd for $C_{12}H_8F_8O_3$: C, 40.90; H, 2.27; F, 43.18. Found: C, 40.62; H, 2.41; F, 43.02.

4.3.2. 4,4,4-Trifluoro-3-hydroxy-2-methyl-3-pentafluorophenylbutyronitrile (10)

(110 °C, ClC_6H_5, 4 h). Yield 65%, mp 150 °C, diastereoisomer ratio 1:3. ^1H NMR (300 MHz, $CDCl_3$): δ 1.52 (3H, d, J = 7 Hz), 3.90 (1H, q, J = 14 Hz), 4.21 (1H, s). ^{19}F NMR (282 MHz, $CDCl_3$): δ −1,43 (t, 3F, J = 8 Hz), −61.35 (m, 2F), −70.53 (t, 1F, J = 21 Hz), −80.58 (m, 2F). GC–MS: m/z (I_{rel}): 319 $[M]^{\bullet+}$ (1.5), 265 $[C_6F_5(CF_3)COH]^+$ (20.5), 250 $[M-CF_3]^+$ (1.4), 195 $[C_6F_5CO]^+$ (100.0), 167 $[C_6F_5]^+$ (11.9), 69 $[CF_3]^+$ (5.1), 55 $[CH_3CH_2CN]^+$ (48.1). Anal. Calcd for $C_{11}H_5F_8NO$: C, 41.39; H, 1.58; F, 47.62; N, 4.38. Found: C, 41.51; H, 1.55; F, 47.70; N, 4.36.

4.3.3. 4,4,4-Trifluoro-3-hydroxy-3-pentafluorophenylbutyric acid methyl ester (11)

(110 °C, ClC_6H_5, 4 h). Yield 71%, mp 79 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 3.15 (1H, d, J = 17.4 Hz), 3.65 (1H, d, J = 17.4 Hz), 3.80 (3H, s), 5.05 (1H, s). ^{19}F NMR (282 MHz, $CDCl_3$): δ −4.12 (t, 3F, J = 8 Hz), −60.34 (m, 2F), −73.88 (t, 1F, J = 20.71 Hz), −83.27 (m, 2F). GC–MS: m/z (I_{rel}): 338 $[M]^{\bullet+}$ (1.0), 269 $[M-CF_3]^+$ (70.0), 265 $[C_6F_5(CF_3)OH]^+$ (23.7), 196 $[C_6F_5C-OH]^+$ (16.7), 195 $[C_6F_5CO]^+$ (100.0), 74 $[CH_3COOCH_3]^+$ (4.6), 69 $[CF_3]^+$ (10.5), 43 $[C_2H_3O]^+$ (32.1), 42 $[C_2H_2O]^+$ (11.8). Anal. Calcd for $C_{11}H_6F_8O_3$: C, 39.07; H, 1.77; F, 44.95. Found: C, 39.23; H, 1.83; F, 45.05.

4.4. Pentafluorophenyl hydroxy compounds derived from 5

4.4.1. 1,3-Bis(pentafluoropheny)but-2-en-1-one (12)

^{19}F NMR (282 MHz, $CDCl_3$): δ −63.23 (m, 2F), −71.61 (t, 1F, J = 20.5 Hz), −82.64 (m, 2F). GC–MS: m/z (I_{rel}): 402 $[M]^{\bullet+}$ (49.0), 383 $[M-F]^+$ (63.2), 235 $[M-C_6F_5]^+$ (32.7), 207 $[M-C_6F_5C(O)]^+$ (26.7), 195 $[C_6F_5CO]^+$ (100.0), 167 $[C_6F_5]^+$ (45.4), 40 $[M-C_6F_5C(O)-C_6F_5]^+$ (59.0).

4.4.2. 3-Hydroxy-3-pentafluorphenylbutyric acid methyl ester (13)

(110 °C, ClC_6H_5, 4 h). Yield 35% (GLC). ^1H NMR (300 MHz, $CDCl_3$): δ 1.73 (3H, s), 2.86 (1H, d, J = 17 Hz), 3.28 (1H, d, J = 17 Hz), 3.73 (3H, s), 4.69 (1H, s). ^{19}F NMR (282 MHz, $CDCl_3$): δ −63.23 (m, 2F), −78.38 (t, 1F, J = 21 Hz), −84.45 (m, 2F). GC–MS: m/z (I_{rel}): 269

$[M-CH_3]^+$ (6.9), 266 $[M-H_2O]^+$ (3.4), 237 $[M-COF]^+$ (3.3), 211 $[C_6F_5C(CH_3)OH]^+$ (24.8), 195 $[C_6F_5CO]$ (54.9), 181 $[C_6F_5CH_2]^+$ (7.5), 167 $[C_6F_5]^+$ (19.4), 117 $[C_5F_3]^+$ (13.4), 74 $[CH_3COOCH_3]^+$ (21.8), 69 $[CF_3]^+$ (6.3), 59 $[COOCH_3]^+$ (10.1), 43 $[C_2H_3O]^+$ (100), 42 $[C_2H_2O]^+$ (27.1). Anal. Calcd for $C_{11}H_9F_5O$: C, 46.48; H, 3.17; F, 33.45. Found: C, 45.83; H, 3.02; F, 33.17.

*4.4.3. 3-Hydroxy-3-pentafluorphenylbutyronitrile (**14**)*

(80 °C, C_6H_6, 4 h). Yield 25%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.90 (3H, s), 3.03 (1H, d, J = 16.7 Hz), 3.16 (1H, d, J = 16.7 Hz), 3.42 (1H, s). ^{19}F NMR (282 MHz, $CDCl_3$): δ −62.36 (m, 2F), −75.86 (t, 1F, J = 20.5 Hz), −82.76 (m, 2F). GC–MS: m/z (I_{rel}): 233 $[M-H_2O]^+$ (35.0), 211 $[C_6F_5C(CH_3)OH]^+$ (71.0), 195 $[C_6F_5CO]^+$ (67.2), 167 $[C_6F_5]^+$ (25.0), 117 (17.0), 41 (40.0), 43 $[CH_3CO]^+$ (100). Anal. Calcd for $C_{10}H_6F_5NO$: C, 47.81; H, 2.35; F, 37.85; N, 5.57. Found: C, 47.46; H, 2.49; F, 38.10; N, 5.70.

*4.4.4. 3-Hydroxy-2-methyl-3-pentafluorphenylbutyric acid methyl ester (**15**)*

(80 °C, C_6H_6, 4 h). Yield 70%. Product **15** exists in the form of two diastereoisomers (ratio 1:1.5), which were isolated by preparative GLC.

Diastereoisomer I: n_D^{20} = 1.4512; d_4^{20} = 1.4052. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.34 (3H, d, J = 6 Hz), 1.62 (3H, s), 3.13 (1H, q, J = 14.3 Hz), 3.60 (3H, s), 4.49 (1H, s). ^{19}F NMR (282 MHz, $CDCl_3$): δ −63.13 (m, 2F), −78.18 (t, 1F, J = 20.8 Hz), −84.18 (m, 2F). GC–MS: m/z (I_{rel}): 211 $[C_6F_5C(CH_3)OH]^+$ (68.0), 195 $[C_6F_5CO]^+$ (65.0), 167 $[C_6F_5]^+$ (19.8), 88 $[CH_3CH_2COOCH_3]^+$ (100), 43 $[CH_3CO]^+$ (68.0). Anal. Calcd for $C_{12}H_{11}F_5O_3$: C, 48.33; H, 3.72; F, 31.86. Found: C, 47.80; H, 3.65; F, 32.80.

Diastereoisomer II: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.25 (3H, d, J = 6 Hz), 1.80 (3H, s), 3.15 (1H, q, J = 14.3 Hz), 3.65 (3H, s), 3.98 (1H, s). Anal. Calcd for $C_{12}H_{11}F_5O_3$: C, 48.33; H, 3.72; F, 31.86. Found: C, 48.21; H, 3.80; F, 32.59.

*4.4.5. 3-Hydroxy-2-methyl-3-pentafluorphenylbutyronitrile (**16**)*

(110 °C, ClC_6H_5, 4 h). Yield 45%, mp 54–56 °C, diastereoisomer ratio 1.5:1. GC–MS: m/z (I_{rel}): 211 $[C_6F_5C(CH_3)OH]^+$ (97.0), 195 $[C_6F_5CO]^+$ (42.30), 167 $[C_6F_5]^+$ (16.20), 55 $[CH_3CH_2CN]^+$ (17.30), 43 $[CH_3CO]^+$ (100). Anal. Calcd for $C_{11}H_8F_5NO$: C, 49.81; H, 3.01; F, 35.85; N, 5.28. Found: C, 50.24; H, 3.00; F, 35.47; N, 5.16.

Diastereoisomer I: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.40 (3H, d, J = 7.08 Hz), 1.87 (d, 3H, J = 4.92 Hz), 3.10 (1H, s), 3.34–3.38 (1H, m). ^{19}F NMR (282 MHz, $CDCl_3$): δ −62.30 (m, 2F), −75.48 (t, 1F, J = 21 Hz), −82.62 (m, 2F).

Diastereoisomer II: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.44 (3H, d, J = 7.05 Hz), 1.96 (d, 3H, J = 5 Hz), 3.25 (1H, s), 3.37–3.41 (1H, m); ^{19}F NMR (282 MHz, $CDCl_3$): δ −62.79 (m, 2F), −75.71 (t, 1F, J = 21 Hz), −82.72 (m, 2F).

4.5. Reductive coupling of aldehyde **1**

A solution of aldehyde **1** (1 mmol), $Fe(CO)_5$ (2 mmol), and HMPA (4 mmol) in benzene (1 ml) was heated at 80 °C for 4 h or kept at room temperature for 3 days. Then the reaction mixture was diluted with benzene, treated with diluted hydrochloric acid, washed with water, and dried. After the solvent was evaporated, the resulting mixture was analyzed and crystallized from benzene to give D,L-1,2-di(pentafluorophenyl)-1,2-dihydroxyethane (**3**) in ~90% yield, mp 185 °C (185 °C lit. [25]). ^{1}H NMR ($CDCl_3$): δ 5.38, 5.40 (2H, d, J = 6 Hz, CH), 2.50, 2.52 (2H, d, J = 6Hz, OH). GC–MS: m/z (I_{rel}): 197 $[1/2M]^+$ (100). Anal. Calcd for $C_{14}H_4F_{10}O_2$: C, 42.6, H, 1.0, F, 48.2. Found: C, 42.94, H, 1.20, F, 46.81.

When the reaction was carried out in anhydrous benzene, compound **17** (yield 25%) and small amounts of **18** and **19** were isolated.

Decafluorostilbene (**17**). GC–MS: m/z (I_{rel}): (*cis*-) 360 $[M]^+$ (100), 341 $[M-F]^+$ (5), 192 $[M-C_6F_5H]^{\bullet+}$ (12), 180 $[C_6F_5CH]^{\bullet+}$ (10); (*trans*-) 360 $[M]^+$ (100), 341$[M-F]^+$ (25), 192 $[M-C_6F_5H]^+$ (25), 180 $[C_6F_5CH]^+$ (35).

1,2-di(pentafluorophenyl)ethanone (**18**). ^{13}C NMR ($CDC1_3$): δ 211.9 (C=O), 29.7 (CH_2). GC–MS: m/z (I_{rel}): 376 $[M]^+$ (5), 358 $[M-F+H]^+$ (100), 195 $[C_6F_5C(O)]^+$ (7).

1,2-di(pentafluorophenyl)ethylene oxide (**19**). ^{13}C NMR ($CDC1_3$): δ 62.4 (CHO). GC–MS: m/z (I_{rel}): 376 $[M]^+$ (1), 358 $[M-F+H]^+$ (100), 195 $[C_6F_5C(O)]^+$ (15).

Acknowledgements

This work was supported by Russian Foundation for Basic Research (Project 06-03-32820) and Russian Academy of Sciences (Grant P-8).

References

[1] L. Keinicke, P. Fristrup, P.-O. Norrby, R. Madsen, J. Am. Chem. Soc. 127 (2005) 15756–15761.
[2] F. Huguenot, T. Brigaud, J. Org. Chem. 71 (2006) 2159–2162.
[3] R. Moumne, S. Laveielle, P. Karoyan, J. Org. Chem. 71 (2006) 3332–3334.
[4] L.-T. Yu, M.-T. Ho, Ch.-Y. Chang, T.-K. Yang, Tetrahedron: Asymm. 18 (2007) 949–962.
[5] S.A. Babu, M. Yasuda, I. Shibata, A. Baba, J. Org. Chem. 70 (2005) 10408–11411.
[6] K.H. Yong, N.J. Taylor, J.M. Chong, Org. Lett. 4 (2002) 3553–3556.
[7] F. Orsini, G. Sello, A.M. Manzo, E.M. Lucci, Tetrahedron: Asymm. 16 (2005) 1913–1918.
[8] S.E. Denmark, J. Fu, D.M. Coe, X. Su, N.E. Pratt, B.D. Griedel, J. Org. Chem. 71 (2006) 1513–1522.
[9] Ch. Pooput, W.R. Dolbier, M. Medebielle, J. Org. Chem. 71 (2006) 3564–3568.
[10] K. Mikami, Y. Itoh, M. Yamanaka, Chem. Rev. 104 (2004) 1–16.
[11] M. Schlosser, Angew. Chem., Int. Ed. 110 (1998) 1496–1513.
[12] V.P. Kukhar, V.A. Soloshonok, Fluorine Containing Amino Acids: Synthesis and Properties, Wiley, New York, 1995.
[13] H. Yamamoto (Ed.), Organofluorine Compounds, Chemistry and Applications, Springer-Verlag, Berlin and Heidelberg, Germany, 2000.
[14] B.E. Smart, J. Fluor. Chem. 109 (2001) 3–11.
[15] C. Bolm, J. Legros, J.L. Paih, L. Zani, Chem. Rev. 104 (2004) 6217–6621.
[16] T. Watahiki, Y. Akabane, S. Mori, T. Oriyarna, Org. Lett. 5 (2003) 3045–3048.
[17] J. Vela, J.M. Smith, N.A. Ketterer, C.J. Flaschenriem, R.J. Lachicotte, P.L. Holland, J. Am. Chem. Soc. 127 (2005) 7857–7870.
[18] A. Ghosh, F.T. de Olivera, T. Yano, T. Nishioka, E.S. Beach, I. Kinoshita, E. Munck, A.D. Ryabov, C.P. Horwitz, T.J. Collins, J. Am. Chem. Soc. 127 (2005) 2505–2513.
[19] J.L. Gorczynski, J. Chen, C.L. Fraser, J. Am. Chem. Soc. 127 (2005) 14956–14957.
[20] Y.N. Belousov, Russ. Chem. Rev. 76 (2007) 46–65.
[21] A.B. Terent'ev, T.T. Vasil'eva, N.A. Kuzmina, E.I. Mysov, N.Yu. Kuznetsov, Yu.N. Belokon, J. Chem. Res. S (1998) 306–308;
A.B. Terent'ev, T.T. Vasil'eva, N.A. Kuzmina, E.I. Mysov, N.Yu. Kuznetsov, Yu.N. Belokon, J. Chem. Res. M (1998) 1281.
[22] A.B. Terent'ev, T.T. Vasil'eva, N.A. Kuzmina, E.I. Mysov, N.Yu. Kuznetsov, Yu.N. Belokon, Russ. Chem. Bull. (1999) 1121–1123.
[23] T.T. Vasil'eva, O.V. Chakhovskaya, N.E. Mysova, A.B. Terent'ev, Russ. J. Org. Chem. 38 (2002) 1014–1017.
[24] A.B. Terent'ev, T.T. Vasil'eva, O.V. Chakhovskaya, N.E. Mysova, K.A. Kochetkov, Russ. J. Org. Chem. 41 (2005) 1615–1617.
[25] T.T. Vasil'eva, O.V. Chakhovskaya, A.B. Terent'ev, K.A. Kochetkov, Russ. J. Org. Chem. 41 (2005) 1553–1555.
[26] L.V. Balabanova, A.B. Terent'ev, T.T. Vasil'eva, S.I. Gapusenko, T.D. Churkina, Russ. J. Gen. Chem. 63 (1993) 2267–2269.
[27] V. Poroikov, D. Filimonov, PASS: prediction of biological activity, in: Ch. Helma (Ed.), Predictive Toxicology, Marcel Dekker, New York, 2005, pp. 459–478.
[28] Z. Szokonji, A. Balazs, T.A. Martinek, F. Fulop, Tetrahedron: Asymm. 17 (2006) 199–204.
[29] J.R. Dehli, V. Gotor, Tetrahedron: Asymm. 11 (2000) 3693–3700.
[30] R.P. Singh, B. Twamley, L. Fabry-Asztalos, D.S. Matteson, J.M. Shreeve, J. Org. Chem. 65 (2000) 8123–8126.
[31] Y.N. Belousov, T.A. Belousova, Polyhedron 18 (1999) 2605–2608.
[32] D.K. Dutta, D. Konwar, Tetrahedron Lett. 41 (2000) 6227–6228.
[33] D.C. Barman, A.J. Thakur, D. Prajapati, J.S. Sandhu, Synlett 4 (2001) 515–516.