Diastereoselective Synthesis of Pinacols from Aromatic Aldehydes Using the System Pentacarbonyliron–Hexamethylphosphoric Triamide. Dual Reactivity of Pentafluorobenzaldehyde

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Abstract—The system $Fe(CO)_5$–HMPA effectively promotes diastereoselective reductive dimerization of aromatic aldehydes to the corresponding pinacols having preferentially or exclusively *dl* configuration. In the reaction with pentafluorobenzaldehyde, the product structure strongly depends on the presence of traces of moisture in the reaction system.
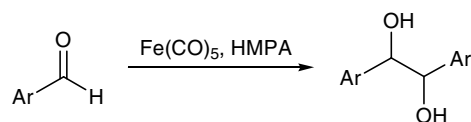
In the preliminary communication [1] we showed that the system $Fe(CO)_5$–HMPA can be successfully used to promote diastereoselective reductive dimerization of aromatic aldehydes to give the corresponding 1,2-dihydrobenzoins (pinacols) on heating the reactants for 3–4 h in boiling benzene. This procedure is more advantageous than the known methods [2–5] in several aspects which were considered in detail in [1]. Decafluoroethane-1,2-diol formed as a by-product in the addition of bromoform and methyl bromopropionate to pentafluorobenzaldehyde in the presence of $Fe(CO)_5$ [6] was a mixture of *dl* and *meso* diastereoisomers which were isolated and characterized. Only the use of $Fe(CO)_5$–HMPA ensured preparation of that diol exclusively as *dl* diastereoisomer.

Further studies in this line revealed some interesting specific features of the above reaction. Primarily,

we have found that diols like **I** can be obtained with a good yield and high diastereoselectivity in the system $Fe(CO)_5$–HMPA–aldehyde (Scheme 1) at room temperature in 3–4 days; therefore, the use of chiral cocatalysts in this reaction could give rise to enantioselective processes. Pentafluorobenzaldehyde (see table, run no. 1) and 4-chlorobenzaldehyde (run no. 2) reacted most effectively to produce exclusively *dl* isomers of diols like **I**, while in the reaction with benzaldehyde, the *dl*-to-*meso* isomer ratio was 80:20 (run no. 3).

Scheme 1.

Ar = C_6F_5, 4-ClC_6H_4, Ph, 4-$MeOC_6H_4$.

The structure, purity, configuration, and crystal lattice parameters of diol **I** (Fig. 1) were determined on the basis of a combination of data obtained by GLC analysis, ^{1}H NMR spectroscopy, and X-ray analysis. As shown in Fig. 2, molecules of diol **I** in crystal are linked to dimers via intermolecular hydrogen bonds. The X-ray diffraction data for the *dl* isomer of **I** are well consistent with those reported for D-1,2-diphenyl-ethane-1,2-diol [7].

The formation of pinacol-like structures may be rationalized by a scheme including one-electron trans-

Yields and diastereoisomer ratios of diols **I** in the reductive dimerization of aromatic aldehydes

Run no.	Ar	Yield of diol **I**,[a] %	Ratio *dl*:*meso*[b]
1	C_6F_5	92	>99:1
2	4-ClC_6H_4	91	>99:1
3	Ph	50	80:20
4	4-$MeOC_6H_4$	51	80:20

[a] Isolated and purified product.
[b] According to the ^{1}H NMR data.

[†] Deceased.

fer from Fe(0) to aldehyde to give radicals **A** in the iron coordination sphere; their dimerization, followed by hydrolysis, yields diol **I** (Scheme 2).

Scheme 2.
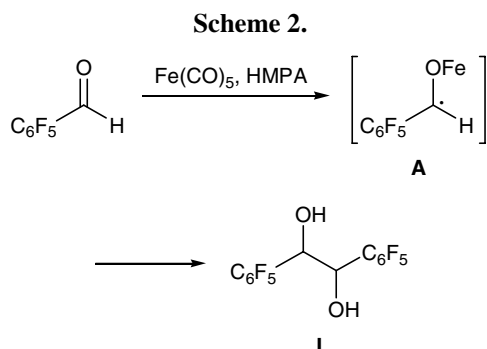
The reactions performed in anhydrous solvents (benzene and toluene) at room temperature resulted in the same composition of the reaction mixtures, and the yields of the corresponding diols were similar to those obtained using solvents without preliminary dehydration. Unexpected results were obtained in the dimerization of pentafluorobenzaldehyde in anhydrous benzene and toluene at 80°C. The reaction mixture contained decafluorostilbene **II** as the major product, 1,2-bis-(pentafluorophenyl)ethanone (**III**), and 2,3-bis(pentafluorophenyl)oxirane (**IV**), while no diol **I** was detected (Scheme 3). When the reaction was carried out in a dilute solution (the substrate concentration was lower by a factor of 3 to 5), stilbene **II** was the only product.

The reaction with benzaldehyde in anhydrous solvent gave only the corresponding diol, i.e., the presence of moisture did not affect the reaction direction. In order to elucidate the role of water, we carried out the reaction with pentafluorobenzaldehyde in anhydrous benzene in the presence of an equimolar amount of water. In this case, the product was diol **I**, whereas stilbene **II** was almost absent. The formation of stilbenes from aldehydes in the presence of metal complexes was reported previously [8, 9], but no details of the reaction mechanism were given.

We presumed that the reaction performed by heating in anhydrous solvents includes the following transformations (Scheme 3): formation of metal carbenoid **B**, followed by inner-sphere dimerization to stilbene **II** (path *b*); and reaction of carbenoid complex **B** with aldehyde via insertion into the C–H or C=O bond to give ketone **III** or oxirane **IV**, respectively (path *c*). Presumably, the presence of moisture hampers formation of metal carbenoid **B**, so that the major product is diol **I** (path *a*).
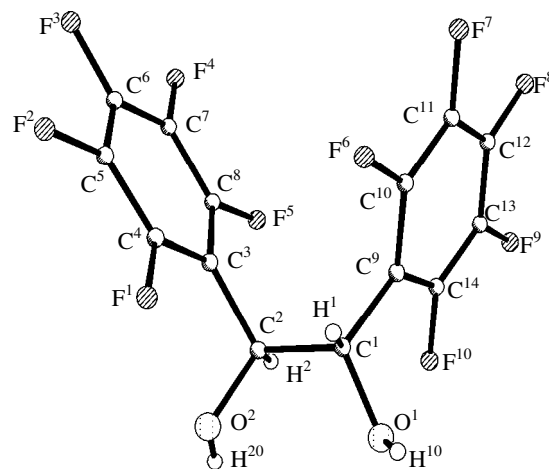
Fig. 1. Structure of the molecule of 1,2-bis(pentafluoro-phenyl)ethane-1,2-diol (**I**) with atom numbering according to the X-ray diffraction data .
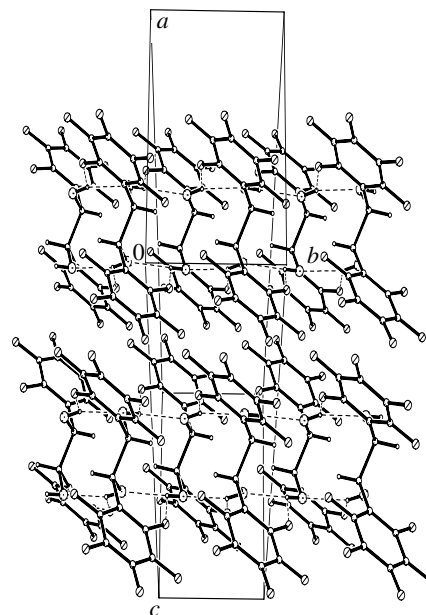
Fig. 2. Packing of 1,2-bis(pentafluorophenyl)ethane-1,2-diol (**I**) molecules in crystal (projection along the *a* axis).

The fact that stilbene **II** is formed as the only product in the reaction with pentafluorobenzaldehyde under 3–5-fold dilution indicates inner-sphere formation of stilbene **II** (path *b*) and intermolecular mechanism of formation of adducts **III** and **IV** (path *c*). The observed considerable difference in the results of the reactions with pentafluorobenzaldehyde and benzaldehyde in anhydrous solvents is likely to reflect effect of polar substituents in the benzene ring of the substrate. Unlike the phenyl group in unsubstituted benzaldehyde, electron-withdrawing pentafluorophenyl group favor stabilization of complex **B**. Thus pentafluorobenzalde-

Scheme 3.

L = (Me$_2$N)$_3$PO.
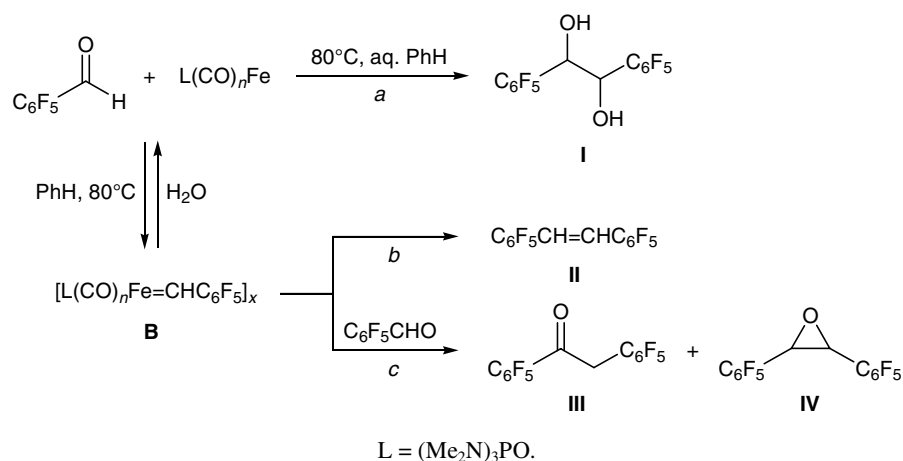
hyde exhibits dual reactivity in the reductive dimerization, depending on the presence of even traces of water in the reaction system.

EXPERIMENTAL

The mass spectra were recorded on a Finnigan MAT Magnum GC–MS system (25-m Ultra-2 column, oven temperature programming from 30 to 220°C at a rate of 2.5 deg/min). GLC analysis was performed on an LKhM-80 chromatograph equipped with a thermal conductivity detector and a 1300×3-mm steel column packed with 15% of SKTFT-50Kh on Chromaton-N-AW; carrier gas helium, flow rate 60 ml/min; oven temperature programming from 50 to 250°C at a rate of 6 deg/min. The ^{1}H and ^{13}C NMR spectra were measured on a Bruker WP-200 instrument (200 MHz for ^{1}H) relative to TMS; CDCl$_3$ was used as solvent. X-Ray analysis was performed at the X-Ray Analysis Laboratory (Nesmeyanov Institute of Organometallic Compounds, Russian Academy of Sciences).

All organic reagents were purified by distillation; commercial Fe(CO)$_5$ with a purity of 97% (from Fluka) was used without additional purification; the solvents were dehydrated over CaCl$_2$ and were then distilled over metallic sodium.

X-Ray diffraction data for 1,2-bis(pentafluorophenyl)ethane-1,2-diol (I). C$_{14}$H$_4$F$_{10}$O$_2$, M 394.17; monoclinic crystals with the following unit cell parameters (120 K): $a = 8.950(1)$, $b = 5.6865(9)$, $c = 25.834(4)$ Å, $\beta = 93.606(3)°$; $V = 1312.3(4)$ Å^3; $Z = 4$; $d_{calc} = 1.995$ g/cm^3; space group $P2_1/c$. Total of 10706 reflections were measured on a Bruker SMART 1000 CCD diffractometer at 120 K. After averaging of equivalent reflections, 3460 independent reflections ($R_{int} = 0.0184$) were obtained and used in the structure

determination and refinement. The structure was solved by the direct method; non-hydrogen atoms were localized by the difference Fourier syntheses and were refined in anisotropic approximation. The positions of hydrogen atoms H(C) were calculated (hydroxy hydrogen atoms were localized by the difference syntheses) and refined in isotropic approximation using the riding model. The final divergence factors were $R_1 = 0.0448$ [calculated by F_{hkl} from 2806 reflections with $I > 2\sigma(I)$] and $wR_2 = 0.1350$ (calculated by F_{hkl}^2 from all 3460 independent reflections); GOF 1.004; 251 independent parameters. The coordinates of atoms and their temperature factors were deposited to the Cambridge Crystallographic Data Center (entry no. CCDC 637471).

General procedure for reductive dimerization of aromatic aldehydes. A solution of 1 mmol of the corresponding aldehyde, 2 mmol of Fe(CO)$_5$, and 4 mmol of HMPA in 1 ml of benzene was heated for 4 h at 80°C and was then left to stand for 3 days at room temperature. The mixture was diluted with benzene, washed with dilute hydrochloric acid and water, and dried. The solvent was distilled off, and the residue was analyzed by GC–MS and GLC using authentic samples as references; crystalline products were purified by recrystallization or by column chromatography on silica gel using hexane–ethyl acetate (4:1) as eluent.

1,2-Bis(pentafluorophenyl)ethane-1,2-diol (I). *a.* The reaction was carried out at 80°C (4 h) in 1 ml of benzene (without preliminary dehydration) [1]. Yield ~90%, mp 185°C (from benzene). According to the ^{1}H NMR data, only one isomer was formed and was identified as *dl* by X-ray analysis. ^{1}H NMR spectrum, δ, ppm: 5.38 d and 5.40 d (1H each, CH, $J = 6$ Hz; the signals are split due to nonequivalence of those protons in that isomer), 2.50 d and 2.52 d (1H each, OH, $J = 6$ Hz). Found, %: C 42.94; H 1.20; F 46.81; OH 9.75.

$C_{14}H_4F_{10}O_2$. Calculated, %: C 42.6; H 1.0; F 48.2; OH 8.6.

1,2-Diphenylethane-1,2-diol, 1,2-bis(4-chlorophenyl)ethane-1,2-diol, and 1,2-bis(4-methoxyphenyl)-ethane-1,2-diol [1] were obtained in a similar way.

b. The reaction was carried out at 20°C (3 days) using 1 ml of anhydrous or non-dehydrated benzene. Yield of **I** ~90% (65% in anhydrous benzene), *de* 100%.

1,2-Diphenylethane-1,2-diol (yield 30%, *de* 80%) and 1,2-bis(4-chlorophenyl)ethane-1,2-diol (yield 75%, *de* 100%) were obtained in a similar way.

c. The reaction was carried out at 80°C (4 h) in 1 ml of anhydrous benzene containing 1 mmol of water. Yield of **I** 60%, *de* 100%.

The products were identified by GLC using authentic samples [1]. No reaction occurred with 4-methoxybenzaldehyde, and the initial compound was recovered from the reaction mixture.

1,2-Bis(pentafluorophenyl)ethene (II). *a.* The reaction was carried out at 80°C (4 h) in 1 ml of anhydrous benzene. Yield 25%. ^{1}H NMR spectrum: δ 7.37 ppm, s (2H, CH=); published data [10]: δ 7.10 ppm (CCl$_4$). Mass spectrum, *m/z* (I_{rel}, %): *cis* isomer: 360 $[M]^+$ (100), 341 $[M - F]^+$ (5), 192 $[M - C_6F_5H]^+$ (12), 180 $[C_6F_5CH]^+$ (10), 168 $[C_6F_5H]^+$ (7); *trans* isomer: 360 $[M]^+$ (100), 341 $[M - F]^+$ (25), 192 $[M - C_6F_5H]^+$ (25), 180 $[C_6F_5CH]^+$ (35), 168 $[C_6F_5H]^+$ (12).

1,2-Bis(pentafluorophenyl)ethanone (III). ^{13}C NMR spectrum, δ$_C$, ppm: 211.9 (C=O), 29.7 (CH$_2$). Mass spectrum, *m/z* (I_{rel}, %): 376 $[M]^+$ (5), 358 $[M - H_2O]^+$ (100), 195 $[C_6F_5CO]^+$ (7).

2,3-Bis(pentafluorophenyl)oxirane (IV). ^{1}H NMR spectrum: δ 4.14 ppm, s (2H, CH). ^{13}C NMR spectrum:

δ$_C$ 62.4 ppm (CHO). Mass spectrum, *m/z* (I_{rel}, %): 376 $[M]^+$ (1), 358 $[M - H_2O]^+$ (100), 195 $[C_6F_5CO]^+$ (15).

b. The reaction was carried out at 80°C (4 h) in 5 ml of anhydrous benzene. Yield 20%. No adducts **III** and **IV** were present in the reaction mixture.

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