

# Benzyl Bromide Addition to Pentafluorobenzaldehyde by Zaitsev–Barbier Reaction Promoted with Complex Systems Underlain by Iron Pentacarbonyl

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**Abstract**—Iron pentacarbonyl promotes addition of benzyl bromide to benzaldehydes by Zaitsev–Barbier reaction only in the presence of nucleophilic additives [HMPT or (*S*)-*N*-benzoyl-2-methoxycarbonylpyrrolidine].

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Benzyl bromide as a rule does not enter into the radical addition and telomerization reactions under the conditions of peroxide initiation [1] but it is possible to attain a selective homolysis of the C–Br bond with subsequent addition to a C=C bond at the use metal complex catalysts: systems CuBr–dipyridyl [2] or Fe(CO)<sub>5</sub>–HMPT [3, 4], and also of the other metal complexes. In all events alongside the addition products a large quantity of dibenzyl is formed, sometimes it is the main reaction product.

The extension of the addition of alkyl halides to the C=C bond in the presence of systems including Fe(CO)<sub>5</sub> to the C=O bonds (by the Zaitsev–Barbier reaction [5–9]) proved to be very successful [10]. For instance, in the presence of Fe(CO)<sub>5</sub> under standard conditions reactions were effectively carried out with benzaldehyde (**IIa**), pentafluorobenzaldehyde (**IIb**), 4-chlorobenzaldehyde (**IIc**) to add to these compounds various aliphatic organohalogen substances [11] except for benzyl bromide (**Ia**).

In this study we for the first time succeeded in addition of substituted benzyl bromides **Ia** and **Ib** to benzaldehydes **IIa–IIc** by the Zaitsev–Barbier reaction with the promotion by complex system underlain by Fe(CO)<sub>5</sub> and containing a series of nucleophilic cocatalysts.

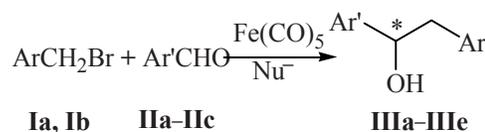
Whereas in the absence of nucleophilic additives the reaction did not occur, at their addition [0.5 mol per 1 mol

† Deceased.

of Fe(CO)<sub>5</sub>] and at higher temperature (110 instead of 80°C) we succeeded in preparation of reaction products of benzyl bromide (**Ia**) and pentafluorobenzyl bromide (**Ib**) with aldehydes **IIa–IIc**, secondary alcohols **IIIa–IIIe**, although in low yields (see the scheme and the table).

We applied as nucleophilic additives HMPT and a chiral amide, (*S*)-*N*-benzoyl-2-methoxycarbonylpyrrolidine (**IV**), in chlorobenzene or heptane. Alongside the target product practically always dibenzyl and decafluorodibenzyl were obtained (runs nos. 2, 3, 5, 6, 9, 10), and the best yields of alcohols **III** were attained at the use of pentafluorobenzaldehyde (**IIb**) (runs nos. 6, 7). Yet although the use of amide (*S*)-(**IV**) instead of HMPT in chlorobenzene did not result in qualitative changes (runs nos. 5, 6), the application of amide (*S*)-(**IV**) in heptane prevented the dibenzyl formation with the retention of the yield of alcohol **IIIc** (run no. 7).

## Scheme.



**I**, Ar = C<sub>6</sub>H<sub>5</sub> (**a**), C<sub>6</sub>F<sub>5</sub> (**b**); **II**, Ar' = C<sub>6</sub>H<sub>5</sub> (**a**), C<sub>6</sub>F<sub>5</sub> (**b**), 4-C<sub>6</sub>H<sub>4</sub>Cl (**c**); **III**, Ar = Ar' = C<sub>6</sub>H<sub>5</sub> (**a**), C<sub>6</sub>F<sub>5</sub> (**b**); Ar = C<sub>6</sub>H<sub>5</sub>, Ar' = C<sub>6</sub>F<sub>5</sub> (**c**), Ar = C<sub>6</sub>H<sub>5</sub>, Ar' = 4-ClC<sub>6</sub>H<sub>4</sub> (**d**); Ar = C<sub>6</sub>F<sub>5</sub>, Ar' = C<sub>6</sub>H<sub>5</sub> (**e**).

Reactions of benzyl bromides **Ia** and **Ib** with benzaldehydes **IIa–IIc**

Run no.	Benzyl bromide	Aldehyde	Cocatalyst	Solvent (temperature)	Dibenzyl (decafluorodibenzyl), %	Reaction products (yield, %)
1	<b>Ia</b>	<b>IIb</b>	( <i>S</i> )-( <b>IV</b> )	C <sub>6</sub> H <sub>6</sub> (80°C)	–	–
2	<b>Ia</b>	<b>IIa</b>	HMPT	C <sub>6</sub> H <sub>5</sub> (110°C)	10	<b>IIIa</b> (15)
3	<b>Ia</b>	<b>IIc</b>	HMPT	C <sub>6</sub> H <sub>5</sub> (110°C)	5	<b>IIIc</b> (17)
4	<b>Ia</b>	<b>IIb</b>	–	C <sub>6</sub> H <sub>5</sub> (110°C)	–	–
5	<b>Ia</b>	<b>IIb</b>	HMPT	C <sub>6</sub> H <sub>5</sub> (110°C)	6	<b>IIIc</b> (18)
6	<b>Ia</b>	<b>IIb</b>	( <i>S</i> )-( <b>IV</b> )	C <sub>6</sub> H <sub>5</sub> (110°C)	5	<b>IIIc</b> (20)
7	<b>Ia</b>	<b>IIb</b>	( <i>S</i> )-( <b>IV</b> )	C <sub>7</sub> H <sub>16</sub> (98°C)	–	<b>IIIc</b> (28)
8	<b>Ia</b>	<b>IIb</b>	HMPT	C <sub>7</sub> H <sub>16</sub> (98°C)	–	–
9	<b>Ib</b>	<b>IIb</b>	HMPT	C <sub>6</sub> H <sub>5</sub> (110°C)	(10–12)	<b>IIIb</b> (3.5)
10	<b>Ib</b>	<b>IIa</b>	HMPT	C <sub>6</sub> H <sub>5</sub> (110°C)	(11–13)	<b>IIIe</b> (5)

Formerly in Zaitsev–Barbier reactions involving pentafluorobenzaldehyde (**IIb**) [11] a strong reduction in adducts yields was observed in the process with an electrophilic reagent as compared to a nucleophilic one. Analogous trend we also observed in reactions of aldehydes with electrophilic pentafluorobenzyl bromide (**Ib**) resulting in the prevailing formation of decafluorodibenzyl (runs nos. 9, 10).

We showed earlier by UV spectroscopy that in the systems containing Fe(CO)<sub>5</sub> and nucleophilic additives charge-transfer complexes were observed [12], and especially in the system Fe(CO)<sub>5</sub>–(*S*)-(**IV**) formed a complex with an intensive charge transfer band [13]. Proceeding from the data on these complexes [14] arising from the interaction between Fe(CO)<sub>5</sub> and Lewis bases and from the data on the formation of anion-radical species which were observed by ESR method [15, 16] it was presumable that the benzylation of aldehydes occurred by the standard route of addition products formation we had suggested previously [17]. Therewith first the activating complexing occurs [15] at the addition of a number of compounds reacting with Fe(CO)<sub>5</sub>, like DMF, HMPT, or amide **IV** [13]. Apparently other nucleophiles may act like these activating additives [15], and we actively look for these compounds. The use of amide (*S*)-(**IV**) did not result in the stereoselectivity of the process, and the secondary alcohol **IIIc** was obtained in a racemic form.

The organomagnesium compounds from perfluoroalkyl halides are known to be commonly prepared by an exchange between perfluoroalkyl halides with

alkylmagnesium halide, and it is difficult to apply the Grignard reaction for preparation of perfluoro-containing hydroxy compounds of the series under consideration [18]. The developed mode of alkylation of compound **IIb** supplements the known procedures of preparation of secondary polyfluorinated hydroxy compounds by nucleophilic perfluoroalkylation [19] and by employing derivatives of difficultly available iron tetracarbonyl iodides [20].

Thus we succeeded for the first time in addition of benzyl bromide to the C=O bond of benzaldehydes **IIa–IIc** in the presence of Fe(CO)<sub>5</sub> and a nucleophilic additive [HMPT or (*S*)-(**IV**)] and in developing the conditions where the target alcohol **IIIc** formed in heptane solution without dibenzyl.

## EXPERIMENTAL

Mass spectra were measured on an instrument VG-7070E (ionizing electrons energy 70 eV). The analysis of reaction mixtures by GLC was carried out on a chromatograph LKhM-80, steel column (1300 × 3 mm), stationary phase 15% SKTFT-50X on Chromaton-N-AW, carrier gas helium, flow rate 60 cm<sup>3</sup>/min, detector catharometer, ramp 50–250°C at a rate 6 deg/min. <sup>1</sup>H and <sup>19</sup>F NMR spectra were registered on a spectrometer Bruker WP-300 at 300 and 282 MHz respectively from solutions in CDCl<sub>3</sub>, chemical shifts were reported with respect to TMS and CF<sub>3</sub>CO<sub>2</sub>H. All organic reagents were purified by distillation. Pentafluorobenzyl bromide and pentafluorobenzaldehyde were purchased from PIM,

Russia.  $\text{Fe}(\text{CO})_5$  from Fluka (97%) was used without additional purification.

**1-(Pentafluorophenyl)-2-phenylethanol (IIIc).** (a) (see the table, run no. 7). A solution of 0.2 g (1 mmol) of compound **IIb**, 0.18 ml (1 mmol) of benzyl bromide (**Ia**), 0.27 ml (2 mmol) of  $\text{Fe}(\text{CO})_5$ , and 0.10 g of (*S*)-(**IV**) in 1 ml of heptane was heated at reflux (98°C) for 4 h. Vigorous evolution of CO proceeded for 2 h. The mixture was diluted with 2 ml of benzene, treated with 1 N hydrochloric acid, washed thrice with water, the water layer was extracted with benzene, the combined benzene extracts were dried with  $\text{MgSO}_4$ . The residue was evaporated, then filtered through a silica gel bed (eluent hexane–ethyl acetate, 10:1). According to GLC data the product did not contain initial compounds. Yield 0.081 g 28%, mp 59–60°C [18].  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 2.65–2.67 d (2H, OH,  $J$  6.18 Hz), 3.13–3.41 q.d (2H,  $\text{CHCH}_2$ , *AB* part of *ABX* system,  $J_{AB}$  13.47,  $J_{AX}$  6.3,  $J_{BX}$  8.1 Hz), 5.30 m (1H,  $\text{CHCH}_2$ , *X* part of *ABX* system), 7.22–7.24 m (2H, Ar), 7.25–7.37 m (3H, Ar).  $^{19}\text{F}$  NMR spectrum,  $\delta$ , ppm: –65.72q–65.77 q.d (2F, Ar,  $J$  14.4 Hz), –77.23 t (1F, Ar,  $J$  20.8 Hz), –84.34...–84.21 q.d (2F, Ar,  $J$  20.8 Hz). Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): 288 [ $M$ ]<sup>+</sup> (0), 270 [ $M - \text{H}_2\text{O}$ ]<sup>+</sup> (6), 250 [ $M - \text{H}_2\text{O} - \text{HF}$ ]<sup>+</sup> (8), 197 [ $\text{C}_6\text{F}_5\text{CHOH}$ ]<sup>+</sup> (89), 167 [ $\text{C}_6\text{F}_5$ ]<sup>+</sup> (14), 99 (30), 92 [ $\text{C}_7\text{H}_8$ ]<sup>+</sup> (100), 91 [ $\text{C}_7\text{H}_7$ ]<sup>+</sup> (100), 65 (79), 51 (51), 39 [ $\text{C}_3\text{H}_3$ ]<sup>+</sup> (64), 29 [ $\text{C}_2\text{H}_5$ ]<sup>+</sup> (10). Found, %: C 58.74; H 3.07; F 32.26.  $\text{C}_{14}\text{H}_9\text{F}_5\text{O}$ . Calculated, %: C 58.34; H 3.15; F 32.96.

The reaction in chlorobenzene occurred with strong tarring, the yield of compound **IIIc** 20%.

(b) (see the table, run no. 5). A solution of 0.20 g (1 mmol) of compound **IIb**, 0.18 ml (1 mmol) of benzyl bromide (**Ia**), 0.27 ml (2 mmol) of  $\text{Fe}(\text{CO})_5$ , and 0.09 ml of HMPT in 1 ml of chlorobenzene was heated at 110°C while stirring for 4 h. In the course of the process CO evolution was observed that finished to the end of the reaction. According to GLC data the final reaction mixture did not contain initial compounds. The mixture was diluted with 2 ml of benzene, treated with 1 N hydrochloric acid, washed thrice with water, the water layer was extracted with benzene, the combined benzene extracts were dried with  $\text{MgSO}_4$ . The residue was evaporated. Yield of alcohol **IIIc** 18%, of dibenzyl, 6%.

The other experiments were performed in a similar way. The yields are reported in the table. The compounds obtained were identified by mass spectrometry.

**1,2-Diphenylethanol (IIIa)** [21]. Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): 198 [ $M$ ]<sup>+</sup> (1), 180 [ $M - \text{H}_2\text{O}$ ]<sup>+</sup> (1), 107

[ $\text{C}_6\text{H}_5\text{CHOH}$ ]<sup>+</sup> (70), 92 [ $\text{C}_7\text{H}_8$ ]<sup>+</sup> (100), 79 [ $\text{C}_6\text{H}_7$ ]<sup>+</sup> (45), 77 [ $\text{C}_6\text{H}_5$ ]<sup>+</sup> (24).

**1,2-Bis(pentafluorophenyl)ethanol (IIIb)** [18]. Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): 378 [ $M$ ]<sup>+</sup> (0), 197 [ $\text{C}_6\text{F}_5\text{CHOH}$ ]<sup>+</sup> (100), 181 [ $\text{C}_6\text{F}_5\text{CH}_2$ ]<sup>+</sup> (38), 169 (26), 149 [ $\text{C}_6\text{F}_5$ ]<sup>+</sup> (20), 119 (23), 99 (19).

**1-(4-Chlorophenyl)-2-phenylethanol (IIIId)** [22]. Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): 232/234 [ $M$ ]<sup>+</sup> (<1), 214/216 [ $M - \text{H}_2\text{O}$ ]<sup>+</sup> (19), 179 [ $M - \text{OH} - \text{Cl}$ ]<sup>+</sup> (15), 178 [ $M - \text{H}_2\text{O} - \text{Cl}$ ]<sup>+</sup> (17), 141 [ $\text{C}_6\text{H}_4\text{ClCHOH}$ ]<sup>+</sup> (62), 139 [ $\text{C}_6\text{H}_4\text{ClCO}$ ]<sup>+</sup> (16), 92 (100), 91 [ $\text{C}_7\text{H}_7$ ]<sup>+</sup> (26), 77 [ $\text{C}_6\text{H}_5$ ]<sup>+</sup> (37).

**2-(Pentafluorophenyl)-1-phenylethanol (IIIe)** [23]. Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): 288 [ $M$ ]<sup>+</sup> (0), 270 [ $M - \text{H}_2\text{O}$ ]<sup>+</sup> (12), 250 [ $M - \text{H}_2\text{O} - \text{HF}$ ]<sup>+</sup> (9), 219 (7), 201 (4), 181 [ $\text{C}_6\text{F}_5\text{CH}_2$ ]<sup>+</sup> (13), 108 (11), 107 [ $\text{C}_6\text{H}_5\text{CHOH}$ ]<sup>+</sup> (87), 79 [ $\text{C}_6\text{H}_7$ ]<sup>+</sup> (100), 77 [ $\text{C}_6\text{H}_5$ ]<sup>+</sup> (59), 51 [ $\text{CF}_2\text{H}$ ]<sup>+</sup> (23), 39 [ $\text{C}_3\text{H}_3$ ]<sup>+</sup> (6).

**Decafluorobenzyl.** Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): 362 [ $M$ ]<sup>+</sup> (11), 291 (1), 181 [ $M/2$ ]<sup>+</sup> (100), 161 [ $\text{C}_7\text{HF}_4$ ]<sup>+</sup> (1).

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