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Barbier-Type Addition of Alkyl Halides to Aldehydes Promoted by Pentacarbonyliron

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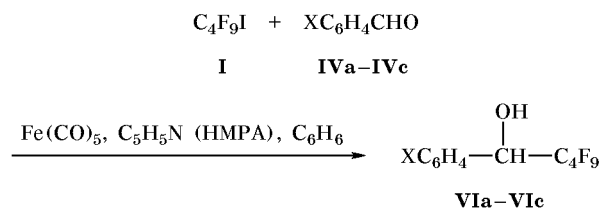*ul. Vavilova 28, Moscow, 119991 Russia*
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Abstract—The yield and structure of products of the Barbier-type addition of alkyl halides (perfluorobutyl iodide, allyl bromide, allyl iodide, and hexyl iodide) to *para*-substituted benzaldehydes in the presence of pentacarbonyliron are essentially determined, on the one hand, by the ability of alkyl halide to be reduced to carbanion and, on the other, by the electrophilicity of the aldehyde reaction center which in turn depends on the nature of *para*-substituent in the aromatic ring.

We previously showed [1] that pentacarbonyliron is an efficient promotor of the addition of halogen-substituted esters to aldehydes and ketones, following a Reformatsky-like reaction pattern. We revealed a considerable effect on the process of substituents both in aromatic aldehyde and in halogen-containing carboxylic acid ester: Electron-acceptor substituents (such as Cl and Br) favor the reaction, while electron-donor groups (Me, MeO) decelerate the process [2]. No such effect was observed when analogous reactions were carried out under usual conditions [3].

In the present communication we report on the first examples of pentacarbonyliron-promoted addition of alkyl halides to aldehydes, following the Barbier-like reaction pattern. We used a set of reactants which allowed us to elucidate the possibility for Barbier-type reaction to occur in the presence of Fe(CO)$_5$, as well as to reveal a significant effect of substituents in both alkyl halide and aldehyde on the yield and structure of the products; this effect is untypical of such reactions [4].
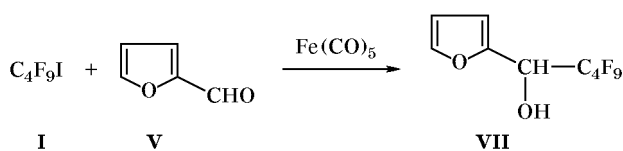
Alkyl halides, namely perfluorobutyl iodide (**I**), allyl bromide (**IIa**), allyl iodie (**IIb**), and hexyl iodide (**III**) were brought into reactions with benzaldehyde (**IVa**), *p*-chlorobenzaldehyde (**IVb**), and *p*-methoxybenzaldehyde (**IVc**). The reaction of iodide **I** with 2-furaldehyde (**V**) was also examined. Perfluorobutyl iodide (**I**) reacted with aldehydes **IVa**–**IVc** in the presence of Fe(CO)$_5$ and pyridine, following a usual Barbier-type addition scheme and resulting in formation of secondary alcohols **VIa**–**VIc** (Scheme 1). A specific effect of *para*-methoxy group in the aromatic ring was observed. The yields of adducts **VIa** and **VIb** from benzaldehyde (**IVa**) and *p*-chlorobenzaldehyde (**IVb**), respectively, were 18–20% or 65–90% on the reacted aldehyde, whereas from aldehyde **IVc** only 6% of addition product **VIc** was obtained (18% on the reacted aldehyde). Iodide **I** reacted with 2-furaldehyde (**V**) in a way similar to the reaction with benzaldehyde (**IVa**). As a result, 2,2,3,3,4,4,5,5,5-nonafluoro-1-(2-furyl)pentanol (**VII**) was obtained (Scheme 2).

Scheme 1.

C$_4$F$_9$I + XC$_6$H$_4$CHO

I   IVa–IVc

Fe(CO)$_5$, C$_5$H$_5$N (HMPA), C$_6$H$_6$
$\xrightarrow{\hspace{3cm}}$

OH
|
XC$_6$H$_4$—CH—C$_4$F$_9$

VIa–VIc

IV, **VI**, X = H (**a**), *p*-Cl (**b**), *p*-MeO (**c**).
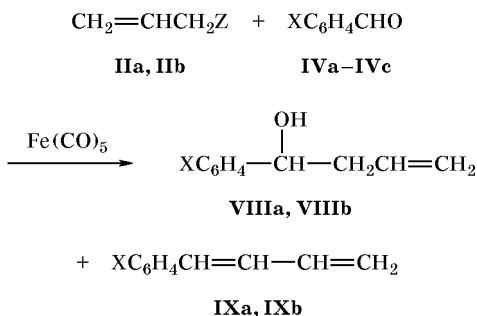
Scheme 2.

Allyl iodide (**IIb**) reacted with benzaldehyde on heating in boiling benzene to afford a mixture of

alcohol **VIIIa** and product of its dehydration, phenyl-butadiene **IXa** (Scheme 3). An analogous reaction with *p*-chlorobenzaldehyde gave 1-(*p*-chlorophenyl)-3-buten-1-ol (**VIIIb**) and 1-*p*-chlorophenyl-1,3-butadiene (**IXb**) in an overall yield of 30%. No corresponding adducts were formed from *p*-methoxybenzaldehyde under the same conditions.
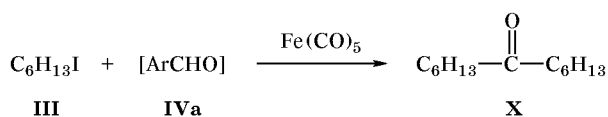
Scheme 3.

$$CH_2{=}CHCH_2Z \ + \ XC_6H_4CHO$$

IIa, IIb   **IVa–IVc**

$$\xrightarrow{\text{Fe(CO)}_5} \ XC_6H_4-\overset{\overset{\displaystyle OH}{|}}{CH}-CH_2CH{=}CH_2$$

VIIIa, VIIIb

$$+ \ XC_6H_4CH{=}CH-CH{=}CH_2$$

IXa, IXb

II, Z = Br (**a**), I (**b**); **IV**, **VIII**, **IX**, X = H (**a**), *p*-Cl (**b**), *p*-MeO (**c**).

In a control experiment, iodide **IIb** was brought into reaction with an equimolar mixture of aldehydes **IVa** and **IVc**. Only benzaldehyde adduct **VIIIa** was detected in the reaction mixture. We succeeded in obtaining adducts of allyl bromide (**IIa**) with aldehydes **IVa** and **IVb** only in HMPA, while aldehyde **IVc** failed to react with bromide **IIa**.

In the reactions of hexyl iodide (**III**) with aldehydes **IVa**–**IVc** in the presence of Fe(CO)$_5$ we isolated about 30% of dihexyl ketone (**X**) instead of the expected adducts like **VIII** (Scheme 4). Ketone **X** was also obtained in a blank experiment (with no aldehyde).

Scheme 4.

$$C_6H_{13}I \ + \ [ArCHO] \ \xrightarrow{\text{Fe(CO)}_5} \ C_6H_{13}-\overset{\overset{\displaystyle O}{\|}}{C}-C_6H_{13}$$

III   **IVa**   **X**

We previously [1, 2] proposed and substantiated a scheme of reactions promoted by Fe(CO)$_5$. According to this scheme, organohalogen substrate initially gives rise to the corresponding radical which is reduced to carbanion. The latter reacts with relatively electrophilic aldehyde carbonyl group inside the iron carbonyl complex. In reactions with iodide **I**, perfluorobutyl radical generated in the first stage is strongly electrophilic. It is capable of being reduced to carbanion which could attack carbonyl carbon atom of

aldehyde. In the reaction of iodide **III** with Fe(CO)$_5$ nucleophilic hexyl radical is formed, and its oxidation to the corresponding carbocation is more probable. As a result, a different reaction path is observed.

Presumably, just favorable combination of polar factors in the transition state like **A** in the case of perfluorobutyl iodide (which is unfavorable in the case of hexyl iodide) determines the final result of the reaction with aldehydes.

A
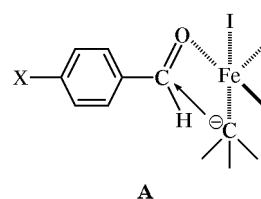
Probably, allyl halides occupy an intermediate place between perfluoroalkyl and alkyl iodides, and the electrophilicity of aldehyde is significant. Electron-donor methoxy group reduces the electrophilicity of the reaction center, and no reaction occurs.

The results of the present work led us to conclude that the nature of substituents in both reactants, aldehyde and alkyl halide, exerts a considerable effect on Fe(CO)$_5$-promoted Barbier-type reactions.

sec-Perfluoropropylarylcarbinols are known to be obtained in ~40% yield with the use of preliminarily prepared (perfluoroalkyl)(tetracarbonyl)iron iodides which are fairly difficultly accessible [5, 6]; moreover, organometallic syntheses require low temperatures (–20 to –80°C) and long time (30–50 h), while the yields of the target products are poor (10–30%) [7]. We believe that the proposed procedure involving pentacarbonyliron, despite relatively low yields, can be regarded as an alternative to the known methods. Its advantages are experimental simplicity (heating of a mixture of reactants in benzene at 65–70°C for 2–3 h) and sufficiently high selectivity.

EXPERIMENTAL

The mass spectra were obtained on a Magnum Finnigan MAT mass spectrometer coupled with a gas chromatograph (25-m Ultra-2 column; oven temperature programming from 30 to 220°C at 2.5 deg/min). GLC analysis was performed on an LKhM-80 chromatograph (1300 × 3-mm steel column packed with 15% of SKTFT-50Kh on Chromaton-N-AW; carrier gas helium at a flow rate of 60 cm^3/min; thermal-conductivity detector; oven temperature programming from 50 to 250°C at 6 deg/min). The ^{1}H NMR spectra

were recorded on a Bruker WP-200 spectrometer at 200 MHz using $CDCl_3$ as solvent; the chemical shifts were measured relative to tetramethylsilane. All organic reagents were purified by distillation; $Fe(CO)_5$ (97%, Fluka) was used without additional purification. The yields of the products were determined from the GLC data using ethyl benzoate as reference.

Reaction of perfluorobutyl iodide (I) with benzaldehydes in the presence of $Fe(CO)_5$. A solution of 1 mmol of perfluorobutyl iodide (**I**), 1 mmol of aldehyde **IVa**–**IVc**, 2 mmol of $Fe(CO)_5$, and 4 mmol of pyridine in 1 ml of benzene was heated for 3 h at 65°C. The mixture was treated with dilute hydrochloric acid and extracted with benzene, the extract was dried over Na_2SO_4, and the solvent and unreacted initial compounds were distilled off.

2,2,3,3,4,4,5,5,5-Nonafluoro-1-phenyl-1-pentanol (VIa). Yield 18%; conversion of aldehyde **IVa** 20%; yield on the reacted aldehyde **IVa** 90%. Mass spectrum, m/z (I_{rel}, %): 326 $[M]^{+\cdot}$ (1.2), 107 $[M-C_4F_9]^+$ (100), 79 (55), 77 (35), 69 (5).

1-(p-Chlorophenyl)-2,2,3,3,4,4,5,5,5-nonafluoro-1-pentanol (VIb). Yield 20%; conversion of aldehyde **IVb** 30%; yield on the reacted aldehyde **IVb** 65%. Mass spectrum, m/z (I_{rel}, %): 360 $[M]^{+\cdot}$ (10), 141, 143 $[M-C_4F_9]^+$ (100), 77 (57), 69 (15).

2,2,3,3,4,4,5,5,5-Nonafluoro-1-(p-methoxyphenyl)-1-pentanol (VIc). Yield 6%; converson of aldehyde **IVc** 35%; yield on the reacted aldehyde **IVc** 18%. Mass spectrum, m/z (I_{rel}, %): 356 $[M]^{+\cdot}$ (20), 137 $[M-C_4F_9]^+$ (100), 77 (10), 69 (1).

2,2,3,3,4,4,5,5,5-Nonafluoro-1-(2-furyl)-1-pentanol (VII). Yield 18%. $n_D^{20} = 1.3760$, $d_4^{20} = 1.5789$. ^{1}H NMR spectrum, δ, ppm: 2.69 br.s (1H, OH); 5.20 m (1H, CH); 5.40 s, 6.60 s, and 7.40 s (1H each, CH, furyl). Mass spectrum, m/z (I_{rel}, %): 316 $[M]^{+\cdot}$ (10), 97 $[M-C_4F_9]^+$ (100), 69 (20). Found, %: C 34.11; H 1.62; F 52.00. $C_9H_5F_9O_2$. Calculated, %: C 34.19; H 1.59; F 54.09.

Reaction of allyl iodide (IIb) with benzaldehyde (IVa) in the presence of $Fe(CO)_5$. A solution of 0.17 g (1 mmol) of allyl iodide (**IIb**), 0.11 g (1 mmol) of benzaldehyde (**IVa**), and 0.39 g (2 mmol) of $Fe(CO)_5$ in 1 ml of benzene was refluxed for 2 h. The mixture was treated with dilute hydrochloric acid and extracted with benzene, and the extract was dried over Na_2SO_4 and evaporated. The reactions of **IIb** with aldehydes **IVb** and **IVc** were carried out in a similar way.

1-Phenyl-3-buten-1-ol (VIIIa). Yield 11%. ^{1}H NMR spectrum, δ, ppm: 2.48–2.55 m (3H, OH, CH_2);

4.68 t (1H, CH, $J = 6$ Hz); 5.08–5.17 m (2H, CH_2=); 5.68–5.88 m (1H, CH=); 7.30–7.35 m (5H, C_6H_5). ^{13}C NMR spectrum, $δ_C$, ppm: 127.4 (CH=); 118.2 (CH_2=); 73.2 (CHO); 43.7 (CH_2); 143.7, 134.4, 128.3, 125.7 (C_6H_5). Mass spectrum, m/z (I_{rel}, %): 130 $[M-H_2O]^{+\cdot}$ (9.5), 107 $[M-C_3H_5]^+$ (100), 77 (47). Found, %: C 79.55; H 8.25; $C_{10}H_{12}O$. Calculated, %: C 81.04; H 8.16.

1-Phenyl-1,3-butadiene (IXa). Yield 3%. Mass spectrum, m/z (I_{rel}, %): 130 $[M]^{+\cdot}$ (100), 115 (44), 103 (6), 77 (10).

1-(p-Chlorophenyl)-3-buten-1-ol (VIIIb). Yield 19.5%. Mass spectrum, m/z (I_{rel}, %): 182 $[M]^{+\cdot}$ (6), 164 $[M-H_2O]^{+\cdot}$ (95), 141 $[M-C_3H_5]$ (100); 77 (60).

1-(p-Chlorophenyl)-1,3-butadiene (IXb) (two isomers at a ratio of 1:1). Yield 11%. Mass spectrum, m/z (I_{rel}, %): 164 $[M]^{+\cdot}$ (95), 129 $[M-Cl]^{+\cdot}$ (100), 111 $[M-C_4H_5]^+$ (5); 77 (10).

According to the GLC data, no product was formed in the reaction of allyl iodide with *p*-methoxybenzaldehyde (**IVc**). In the reaction mixture obtained from a 1:1 mixture of aldehydes **IVa** and **IVc**, only 1-phenyl-3-buten-1-ol (**VIIIa**) was identified by GLC (by comparison with an authentic sample).

Reaction of allyl bromide (IIa) with benzaldehydes in the presence of $Fe(CO)_5$. All reactions were carried out by heating a solution of 1 mmol of allyl bromide (**IIa**), 1 mmol of aldehyde **IVa**–**IVc**, 2 mmol of $Fe(CO)_5$, and a catalytic amount of $CBrCl_3$ in 1 ml of HMPA at 60°C for 5 h.

1-Phenyl-3-buten-1-ol (VIIIa). Yield 19%.

1-(p-Chlorophenyl)-3-buten-1-ol (VIIIb). Yield 18%. In the reaction with aldehyde **IVc**, the mixture contained no any product (GLC).

Reaction of hexyl iodide (III) with pentacarbonyliron. A solution of 1 mmol of hexyl iodide (**III**), 2 mmol of $Fe(CO)_5$, and 2 mmol of HMPA in 1 ml of benzene was heated for 3 h at 80°C. The mixture was treated with dilute hydrochloric acid and extracted with benzene, the extract was dried over Na_2SO_4, and the solvent and unreacted initial compounds were distilled off.

Tridecan-7-one (X). Yield 32%. ^{1}H NMR spectrum, δ, ppm: 2.34 t (4H, CH_2CO, $J = 2$ Hz); 1.1–2.0 m (22H, C_5H_{11}). Mass spectrum, m/z (I_{rel}, %): 198 $[M]^{+\cdot}$ (5), 169 $[M-C_2H_5]^+$ (1), 141 $[M-C_4H_9]^+$ (15), 128 $[C_6H_{13}COCH_3]^{+\cdot}$ (30), 113 $[M-C_6H_{13}]^+$ (100), 85 $[C_6H_{13}]^+$ (45), 43 $[C_3H_7]^+$ (95).

The same product was obtained when the reaction was carried out in the presence of aldehyde **IVa**–**IVc**.

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