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Reformatsky-type addition of esters of α-halogeno carboxylic acids to aldehydes and ketones in the presence of $Fe(CO)_5$

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Reformatsky-type addition of esters of α-halogeno carboxylic acids to aldehydes and ketones in the presence of $Fe(CO)_5$ and an activating agent ($CBrCl_3$ or I_2) afforded the corresponding esters of β-hydroxy acids in good yields. Possible reaction mechanisms are discussed.

Key words: iron pentacarbonyl, Reformatsky reaction, methyl α-bromopropionate, esters of β-hydroxy acids, reaction mechanism.

The formation of C—C bonds by reactions promoted with metals in low oxidation states or with their compounds is widely used in organic synthesis.[1,2] The preparation of esters of β-hydroxy carboxylic acids, which are important intermediates in the synthesis of natural compounds, by the Reformatsky reaction promoted with various metals (Zn, Cd, Sn, Ni, Ge, *etc.*)[1] is well developed. However, there are problems associated with the activation of the metal surface and heterogeneity of reagents.[1] Therefore, the use of soluble salts and metal complexes possessing redox potentials sufficiently high for the reaction to proceed is an alternative approach. Homogeneous reagents, such as $CrCl_2$ and $Co(R_3P)_4$, are used. The chemistry of SmI_2 has assumed particularly great importance.[2]

In the preliminary communication,[3] we have demonstrated for the first time that $Fe(CO)_5$ can promote Reformatsky-type reaction.

In the present work, we studied this reaction in more detail and extended its scope. We used methyl α-bromopropionate (**1a**), methyl dibromoacetate (**1b**), methyl trichloroacetate (**1c**), and various aromatic and aliphatic aldehydes and ketones as the initial compounds.

Results and Discussion

It was established that the reactivities of mono- (**1a**) and polyhalogenated derivatives (**1b** and **1c**) are substantially different. Hence, it is worthwhile to consider the reaction of carbonyl compounds with ester **1a** promoted with $Fe(CO)_5$ separately (Scheme 1).

Ester **1a** and a carbonyl compound were mixed in a solution of benzene or toluene in the presence of $Fe(CO)_5$ and then $CBrCl_3$ or I_2 was added as an activating agent. The reaction mixture was boiled until evolution of CO ceased. Special experiments with the use of GLC and ^1H NMR spectroscopy (Fig. 1) demonstrated that cessation of CO evolution was associated with the virtually complete conversion (98%) of the initial bromo ester **1a**. The presence of an activating agent is necessary for the reaction to occur (Table 1, runs *7—9*). Thus reactions

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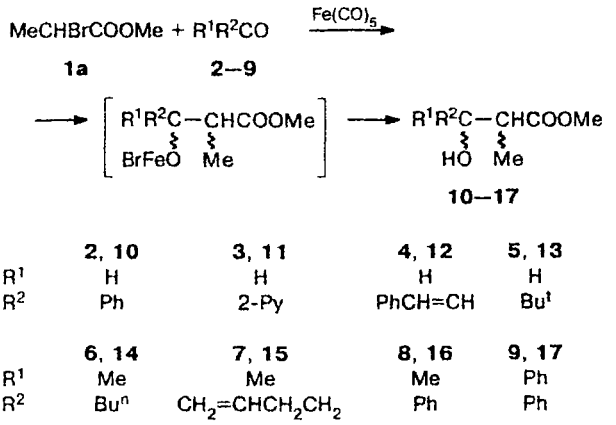
Scheme 1



	2, 10	3, 11	4, 12	5, 13
R^1	H	H	H	H
R^2	Ph	2-Py	PhCH=CH	Bu^t
	6, 14	**7, 15**	**8, 16**	**9, 17**
R^1	Me	Me	Me	Ph
R^2	Bu^n	CH_2=$CHCH_2CH_2$	Ph	Ph

with the use of freshly distilled reagents under an Ar atmosphere in the absence of oxidizing agents did not proceed (see Table 1, run *7*).

Bromo ester **1a** smoothly reacted with PhCHO (**2**) to give methyl 3-hydroxy-2-methyl-3-phenylpropionate (**10**) in nearly quantitative yield in 2—3 h (see Scheme 1; Table 1, runs *1*—*3*). However, pyridine-2-carbaldehyde (**3**) did not react with ester **1a** in benzene, while if a 2 : 1 PhH/DMF mixture was used, the formation of product **11** was completed in 4 h (see Table 1, run *4*). Apparently, the necessity of adding DMF stems from the fact that pyridine bases can occupy coordination sites in intermediate iron-containing compounds, thus inhibiting the desired reaction, while DMF, unlike nonpolar benzene, can destroy these complexes. The reaction of bromo ester **1a** with cinnamaldehyde **4** was virtually completed in 1 h. The yield of adduct **12** was ~70% (see Table 1, run *5*). Under the reaction conditions, aliphatic aldehydes gave a complex mixture of self-condensation products as a resin rather than β-hydroxy esters. The exception was 2,2-dimethylpropanal **5**, which gave adduct **13** (in 2 h) isolated in 10% yield (see Table 1, run 6), which is associated exclusively with incomplete conversion of the initial compounds (data of GLC analysis) rather than with side reactions.

The dependences of elimination of CO and accumulation of the product on the reaction time were studied in the reaction of ester **1a** with benzaldehyde (**2**) (see Fig. 1; Table 1, run *3*). The general view of these dependences suggests autocatalysis by the reaction products. Under the reaction conditions, the activating agent (I_2) immediately reacted with $Fe(CO)_5$, the color of iodine disappeared, and an equivalent amount of CO (~5 moles of CO per mole of I_2) was eliminated, followed by an induction period (~1 h) during which ~10% of CO (with respect to the theoretical volume) was eliminated and 10% of the target condensation product was formed. Then, vigorous evolution of CO accompanied by accu-

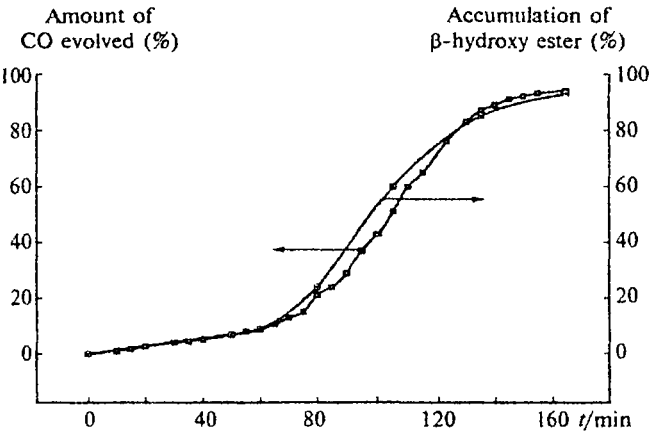


Fig. 1. Dependence of the accumulation of β-hydroxy ester and the amount of CO evolved in the reaction **1a** + **2** on time.

Table 1. Results of the reactions of methyl ester (**1a**) with carbonyl compounds promoted with $Fe(CO)_5$ (benzene, 80 °C)

Run	Carbonyl compound	Reaction product	Activating agent (0.5 mol.%)	*threo/erythro*	*t*/h	Yield of β-hydroxy ester (%)
1	**2**	**10**	I_2	1/1.5	2.0	87
2[a]	**2**	**10**	—	1/1.5	2.0	95
3[b]	**2**	**10**	I_2	1/1.5	3.0	93
4[c]	**3**	**11**	I_2	1/1	4.0	76
5	**4**	**12**	I_2	3/1	1.0	70
6[d]	**5**	**13**	I_2	1/1	2.0	10
7	**6**	**14**	—	—	6.0	0
8	**6**	**14**	$BrCCl_3$	1/1	4.0	30
9	**6**	**14**	I_2	1/1	2.0	50
10	**7**	**15**	I_2	1.2/1	1.5	30
11	**8**	**16**	I_2	3/1	2.0	36
12	**9**	**17**	I_2	—	2.0	84

[a] $Fe_2(CO)_9$ as the promoter. [b] $PhCH_3$, 90 °C. [c] A 2 : 1 PhH/DMF mixture as the solvent. [d] The conversion of **1a** was 12%.

mulation of an adduct as a colored precipitate (apparently, iron alkoxide) was observed. The solution over the precipitate, which was studied by GLC, did not contain the reaction product. Treatment of the precipitate with 3*M* HCl and extraction of the aqueous solution afforded the target β-hydroxy ester **10**.

Polynuclear iron carbonyl clusters,[4] for example, iron nonacarbonyl $Fe_2(CO)_9$, can be used as a promoter (see Table 1, run *2*). In this case, there is no need for addition of an activating agent. The reaction started immediately upon heating without an induction period. Polynuclear clusters possess higher redox potentials than $Fe(CO)_5$. For example, $E_p^{ox}Fe(CO)_5$ = 0.64 V and $E_p^{ox}Fe_3(CO)_{12}$ = 0.5 V (acetone). Consequently, these clusters should be more active in reduction of alkyl halides.[5]

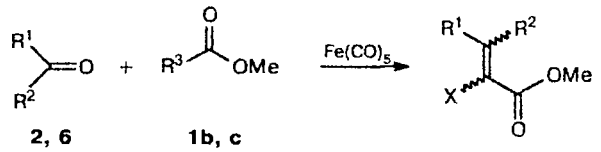
Aromatic and aliphatic ketones also reacted with ester **1a** in the presence of $Fe(CO)_5$ (see Table 1, runs *8—12*). The structures of all compounds were established by spectral methods as well as by comparing with the published data.

As can be seen from Table 1, the yields of the reaction products of bromo ester **1a** with aldehydes and ketones depend on their structures. Thus in the case of complete conversion of the initial **1a** (GLC) and enolizable ketones, the yields of β-hydroxy esters were 30—50% (see Table 1, runs *8—11*). Quantitative analysis of the reaction mixture by GLC and ^1H NMR spectroscopy demonstrated that a portion of bromide **1a**, which did not enter into the condensation reaction, was reduced to methyl propionate. Apparently, the enolizable ketones yielded iron enolates, which formed as a precipitate (in the case of acetophenone), or gave products of crotonic condensation as a mixture of *E*/*Z* isomers (in the case of aliphatic ketones). The material balance of the process with respect to the total amount of β-hydroxy ester and methyl propionate that formed was indicative of complete conversion of **1a**.

The side reaction of reduction of bromo ester **1a** is excluded if the carbonyl compound does not contain a labile α-proton (as, for example, in PhCHO or Ph_2CO). In this case, the yields of β-hydroxy esters varied from 84 to 95% (see Table 1, runs *2*, *3*, and *12*). The *threo*/*erythro* ratios in the corresponding β-hydroxy esters were determined from the ^1H NMR spectra. This ratio was 1 : 1 for aliphatic ketones and aldehydes, 3 : 1 for acetophenone and cinnamaldehyde, and 1 : 1.5 for benzaldehyde. The identical degree of diastereoselectivity was observed in the Reformatsky reaction with Zn.[6]

Polyhalogeno esters **1b** and **1c** also reacted with carbonyl compounds in the presence of two equivalents of $Fe(CO)_5$. Esters **1b** and **1c** are more reactive than **1a** and reacted with aldehydes and ketones in the absence of an activating agent. In this case, the reactions afforded products of formal elimination of Fe_2OHal_2 to form esters of substituted acrylic acids as a mixture of *E*/*Z* isomers (Scheme 2, Table 2) rather than hydroxy esters. A decrease in the amount of $Fe(CO)_5$ resulted in a mixture of esters of acrylic and β-hydroxy carboxylic acids. Apparently, the reaction proceeded in several steps. Iron alkoxide was formed in the initial stage followed by elimination to yield derivatives of acrylic acid. It is worthy of note that the reactions of polyhalogenated esters **1b** and **1c** with aliphatic ketones possessing a labile α-hydrogen atom gave only insignificant amounts of products of reductive dehalogenation. The yields of Reformatsky adducts were rather high (see Table 2, runs *1* and *2*). Apparently, this is indicative of a higher nucleophilicity of polyhalogeno intermediates compared to the intermediate formed from ester **1a** in the stage of addition at the carbonyl group of ketone.

Scheme 2



2, 6 **1b, c** **18—20**

	18	**19**	**20**
R^1	Me	Me	Ph
R^2	Bu	Bu	H
X	H	Cl	Cl

R^3 = $CHBr_2$ (**1b**), CCl_3 (**1c**)

It is well known that the $Fe(CO)_5$—DMF system serves as a catalyst of radical telomerization and radical addition of alkyl halides at the C=C bond.[7] However, $Fe(CO)_5$ has not been previously used in the Grignard and Reformatsky reactions. Although a detailed mechanism of the above reactions with the use of metallic Zn and Mg is open to discussion, the formation of organometallic compounds as key intermediates in these classical cases was confirmed experimentally.[1b] We found that prolonged boiling (3 h) of ester **1a** with $Fe(CO)_5$ either in the presence or in the absence of oxidizing agents neither changed ester **1a** nor resulted in noticeable elimination of CO. In other words, organoiron compounds were not formed from **1a** under the reaction conditions in the absence of an aldehyde or a ketone.

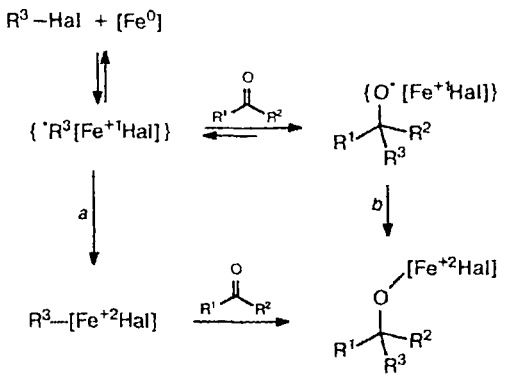
Table 2. Products of condensation of esters of polyhalogeno carboxylic acids **1b** and **1c** with carbonyl compounds

Ester	Carbonyl compound	Reaction product	*E*/*Z*[a]	Yield of esters of acrylic acids[b] (%)
1b	**6**	**18**	4/1	95
1c	**6**	**19**	2.4/1	80
1c	**2**	**20**	1.8/1	35

[a] According to the ^1H NMR spectral data.
[b] Preparative yield.

Apparently, the mechanism of condensation of ester **1a** with carbonyl compounds in the presence of $Fe(CO)_5$ differs from the classical one. Several alternative mechanisms are possible by analogy with those proposed for the Barbier reaction.[8] The results of the latter have been considered previously in detail.[9] Notwithstanding the fact that the last-cited study discussed the behavior of SmI_2 as a mediator of the reaction, the proposed models have a general character. In the case of iron pentacarbonyl, the possible mechanisms are those involving intermediate formation of an α-carbon center (which is either planar or undergoes rapid inversion) in the initial ester because the reaction, performed with the use of optically pure allyl (*S*)-α-bromopropionate ((*S*)-**1d**) and allylacetone, afforded completely racemic β-hydroxy ester, and the unconsumed bromo ester (the conversion was 50%) also represented a racemic mixture, which was confirmed by GLC using a capillary column with a chiral stationary phase. Therefore, the most probable models of the reaction mechanisms are as follows (Scheme 3):

Scheme 3



a. Organometallic mechanism.
b. Radical mechanism.

1. Radical addition. The iron carbonyl complex can rapidly reversibly reduce alkyl halide R^3Hal through a one-electron transfer to form the $\cdot R^3$ radical (as evidenced by racemization of unconsumed (*S*)-**1d**) and iron(+1) halide (the existence of compounds L_5Fe^+ containing Fe(+1) as intermediates has been assumed previously[10]). Then the $\cdot R^3$ radical attacks the C=O bond to form an *O*-centered radical as an intermediate. It is known that *O*-radicals are unstable and can undergo β-fragmentation.[11] However, the complexation with metal (and hence the stabilization of the radical[12]) increases the probability of the reaction *via* the *O*-centered radical. If the radical is formed in the first stage, it apparently remains in the coordination sphere of the metal atom rather than exiting into the solution. Otherwise, the attack by the radical would occur substantially more rapidly on the C=C bond than on the C=O bond (for example, in the reaction with allylacetone, see Table 1, run *10*), which in fact did not occur as evidenced by the absence of the addition product at the C=C bond. In addition, the reaction in toluene and with benzaldehyde, which contain benzylic hydrogen atoms, would afford the reduction product of the initial **1a**, which is inconsistent with the experimental results (see Table 1, runs *1*—*4*). The formation of the intermediate *O*-centered radical is also highly improbable.

2. Formation of an organoiron compound and its addition at the carbonyl group. As in the case of radical addition, the reaction proceeds through reversible intermediate formation of the $\cdot R^3$ radical. The rate of its reduction to the free anion or to the organoiron compound, which add at the C=O group of the carbonyl compound, governs the overall mechanism of the process. The side reduction involving the detachment of the proton from the ketone as a CH-acid counts in favor of the formation of anionic particles, *i.e.*, in favor of the organometallic mechanism. Thus when the reaction was carried out with the enolizable deuterated ketone (acetone-d_6), the reduction product of **1a** (methyl propionate) contained deuterium (26%), which was established by GLC-mass spectrometry. On the other hand, from Fig. 1 it follows that the accumulation of β-hydroxy ester **10** and decomposition of $Fe(CO)_5$ occurred virtually simultaneously. These facts indicate that organoiron compounds containing the C—Fe bond, if ever formed, are very unstable under the experimental conditions and react with the C=O group immediately after formation rather than being accumulated in the solution.

Although it is difficult to choose between the radical and organometallic mechanisms because both mechanisms can afford identical intermediates and the final product, the absence of free-radical reactions with ester **1a** and the existence of side reactions of reduction and enolization typical of the organometallic mechanism suggest that the key stage is, apparently, the formation of an intermediate anionic organometallic species.

To summarize the above evidence, we can say that iron pentacarbonyl acts as a promoter of the reactions of esters of α-halogeno carboxylic acids with carbonyl compounds and extends the series of soluble reagents in Reformatsky-type reactions both with respect to availability and ease of the experimental procedure. Apparently, this first example of the use of carbonyl compounds in reactions of this type will draw attention to application of other metal carbonyls. The yields of the products obtained give promise that this method will find wider use.

Experimental

The mass spectra (EI, 70 eV) were obtained on an EVG-7070E GLC-mass spectrometer equipped with a 50-m DB-5 column in the temperature range of 30—220 °C (2.5 deg min^{-1}). The *m/z* values of ions are given for the ^{79}Br isotope. The IR

spectra were recorded on a UR-20 instrument in KBr pellets. The GLC analysis was performed on an LKhM-80 chromatograph equipped with a steel column (1300×3 mm) with 15% SKTFT-50Kh or with a column with Carbowax-20000 on Chromaton-N-AW (helium as the carrier gas; the flow rate was 60 mL min^{-1}); the katharometer was used as the detector; the temperature was varied in the range of 50—250 °C (6 deg min^{-1}). Preparative GLC was carried out with the use of a steel column (1300×9 mm) with 20% SKTFT-50Kh on the same support (helium as the carrier gas; the flow rate was 120 mL min^{-1}). The enantiomeric composition was determined on a quartz capillary column with a DP-TFA-γ-D chiral phase (the length was 32 m, the inner diameter was 0.20 mm, the thickness of the layer was 0.12 μm, 1.8 bar helium, 100 °C, ester **11** was analyzed at 170 °C). The ^1H and ^{13}C NMR spectra (in $CDCl_3$) were recorded on a Bruker WP-200 SY instrument (200 MHz). The chemical shifts are given in the δ scale relative to Me_4Si. The constants J are given in Hz. Column chromatography was performed on SiO_2 60 (Merck). Iron pentacarbonyl (Fluka) was used without additional purification. Benzene and toluene were distilled over P_2O_5.

Reaction of methyl α-bromopropionate (1a) with butyl methyl ketone (6) (a general procedure for the preparation of preparative amounts of adducts). A solution of ester **1a** (3.3 g, 20 mmol), $Fe(CO)_5$ (7.8 g, 40 mmol), ketone **6** (4.0 g, 40 mmol), and CCl_3Br (0.1 mL, 1 mmol) in PhH (10 mL) was refluxed for 4 h. After 1.5 h, evolution of CO started and the solution turned dark green. After completion of the reaction, 6*M* HCl (10 mL) was added, the reaction mixture was extracted with benzene (3×5 mL), and the organic extracts were combined, washed with water, dried with Na_2SO_4, and concentrated *in vacuo*. Distillation of the residue afforded methyl 3-hydroxy-2,3-dimethylheptanoate **14** in a yield of 1.2 g (30%), b.p. 114 °C (16 Torr), n_D^{20} 1.4430, d_4^{20} 0.9626. Found (%): C, 64.33; H, 10.80. $C_{10}H_{20}O_3$. Calculated (%): C, 63.79; H, 10.71. ^1H NMR, δ: 3.68 (s, 3 H, CH_3O); 2.81 (s, 1 H, OH); 2.53 (m, 1 H, CH); 1.45—1.40 and 1.33—1.24 (both m, 6 H, 3 CH_2); 1.17, 1.15 (both d, 3 H, $C\underline{H}_3$—CH, J = 6.0 Hz); 1.10 (s, 3 H, CH_3—C); 0.86 (m, 3 H, $C\underline{H}_3$—CH_2). ^{13}C NMR, δ: 177.1 (COO); 72.8 (C—OH); 51.6 (CH_3O); 47.1 (CH); 41.1 ($\underline{C}H_2$—C); 25.6 (CH_2); 23.0 ($\underline{C}H_2$—CH_3); 22.9 ($\underline{C}H_3$—C); 13.9 ($\underline{C}H_3$—CH_2); 12.3 ($\underline{C}H_3$—CH). MS, m/z (I_{rel} (%)): 173 $[M - CH_3]^+$ (6.3); 157 (4.3); 131 (100); 101 (42.6); 99 (62.0); 88 (70.3); 59 (8.5); 43 (77.3); 31 (3.6); 29 (14.5). IR, ν_{max}/cm^{-1}: 3516 (OH); 1720 (C=O). The product of crotonic condensation of two molecules of ketone **6**, *viz.*, butyl 2-methylpent-1-enyl ketone, was isolated by column chromatography (SiO_2, 5 : 1 n-C_6H_{14} : $CHCl_3$ as the eluent) as a mixture of *E*/*Z* isomers in a 2 : 1 ratio. ^1H NMR, δ: 6.05 (s, 1 H, CH=); 2.54 and 2.41 (both m, 1 H and 2 H, CH_2—C=O); 2.09 and 1.84 (both s, 2 H and 1 H (slight allylic splitting into a doublet is observed), $C\underline{H}_3$—C=CH); 2.6—1.15 (m, 8 H, $4CH_2$—); 0.88 (br.t, 6 H, $2CH_3$, J = 7.4 Hz).

The yield of product **14** can be increased to 50% and the reaction time can be decreased to 2 h using I_2 or Br_2 as a promoter.

Reaction of 1a with allylacetone (7) in the presence of $Fe(CO)_5$ (a general procedure for the preparation of analytical amounts of adducts). Ester **1a** (0.17 g, 1 mmol), $Fe(CO)_5$ (0.4 g, 2 mmol), ketone **7** (0.2 g, 2 mmol), CCl_3Br (0.01 g, 0.05 mmol), and PhH (1 mL) were mixed. The mixture was refluxed for 3 h and then passed through a layer of SiO_2 to remove iron salts. Methyl 3-hydroxy-2,3-dimethylhept-6-enoate (**15**) was isolated by preparative GLC in 30% yield, n_D^{20} 1.4529, d_4^{20} 0.984. Found (%): C, 64.26; H, 9.51. $C_{10}H_{18}O_3$. Calculated (%): C, 64.49; H, 9.74. ^1H NMR, δ: 5.76 (m, 1 H, CH=); 4.93 (m, 2 H, CH_2=); 3.64 (s, 3 H, CH_3O); 3.06 (s, 1 H, OH); 2.49 (m, 1 H, CH); 2.08 (m, 2 H, CH_2); 1.50 (m, 2 H, CH_2); 1.13 (s, 3 H, CH_3—C); 1.10 (d, 3 H, $C\underline{H}_3$—CH, J = 6.0 Hz). ^{13}C NMR, δ: 177.5 (CO_2); 139.2 (CH=); 115.0 (CH_2=); 73.3 (C—OH); 52.3 (CH_3O); 48.1 (CH); 40.9 ($\underline{C}H_2$—C); 28.6 ($\underline{C}H_2$—CH); 23.5 ($\underline{C}H_3$—C); 12.9 ($\underline{C}H_3$—CH). MS, m/z (I_{rel} (%)): 171 $[M - CH_3]^+$ (11.76); 131 (81.66); 99 (100); 88 (99.88); 59 (10.83); 57 (48.24); 55 (30.30); 43 (98.33); 41 (26.90).

Reaction of allyl α-bromopropionate (1d) with allylacetone. The reaction of **1d** (0.2 g, 1 mmol) with ketone **7** (0.2 g, 2 mmol) in the presence of $Fe(CO)_5$ (0.2 g, 1 mmol) and CCl_3Br (0.01 g, 0.05 mmol) in PhH (1 mL) was performed as described above. The reaction product, *viz.*, allyl 3-hydroxy-2,3-dimethylhept-6-enoate (**21**), was isolated by preparative GLC in 30% yield, n_D^{20} 1.4630, d_4^{20} 0.974. Found (%): C, 67.71; H, 9.89. $C_{12}H_{20}O_3$. Calculated (%): C, 67.89; H, 9.50. ^1H NMR, δ (400 MHz): 1.16 and 1.14 (both d, 3 H, CH_3); 1.09 (s, 3 H, CH_3); 1.50 (m, 2 H, CH_2); 2.08 (m, 2 H, CH_2); 2.53 (m, 1 H, CH); 3.15 (s, 1 H, OH); 4.55 (d, 2 H, CH_2O); 4.93 (m, 1 H, CH_2=); 5.23 (m, 1 H, CH_2=); 5.78 (m, 1 H, CH=). ^{13}C NMR, δ: 175.9 (COO); 138.4, 131.6 (CH=); 118.5 (CH_2=); 72.6 (C—OH); 65.0 (CH_2O); 47.3 (CH); 40.2 ($\underline{C}H_2$—C); 27.8 (CH_2); 25.2 ($\underline{C}H_3$—C); 12.2 (CH_3). MS, m/z (I_{rel} (%)): 197 $[M - CH_3]^+$ (0.26); 170 (2.28); 157 (31.79); 114 (11.27); 99 (23.59); 57 (14.81); 43 (100); 41 (53.5). IR, ν_{max}/cm^{-1}: 3511 (OH); 3098 (=CH_2); 1716 (C=O); 1642 (C=CH_2).

Reaction of 1a with benzaldehyde (2). Ester **1a** (0.84 g, 5 mmol), **2** (0.53 g, 5 mmol), $Fe(CO)_5$ (1.18 g, 6 mmol), several crystals of I_2 (<10 mg), and PhH (2 mL) were mixed. The reaction mixture was refluxed for 2.0 h (until liberation of CO ceased) and cooled. Then 3*M* HCl (6 mL) was added. The reaction mixture was extracted with PhH (3×4 mL) and the extract was washed with water, dried with Na_2SO_4, and concentrated *in vacuo*. The residue was chromatographed on a column with SiO_2 (5 ×1.5 cm); a 4 : 1 n-C_6H_{14} : Et_2O mixture was used as the eluent; after elution of an admixture of benzaldehyde (TLC control), Et_2O was used as the eluent. Methyl 3-hydroxy-2-methyl-3-phenylpropionate (**10**)[6,13] was isolated in 88% yield. Found (%): C, 68.20; H, 7.18. $C_{11}H_{14}O_3$. Calculated (%): C, 68.02; H, 7.26. ^1H NMR [*threo*/*erythro*], δ: 7.50/7.28 (m, 5 H, C_6H_5); 4.62/5.05 (d, 1 H, CH); 3.59/3.66 (s, 3 H, CH_3O)); 3.22 (s, 1 H, OH); 0.93/1.10 (d, 3 H, CH_3). MS, m/z (I_{rel} (%)): 194 $[M]^+$ (1.29); 176 $[M - 18]^+$ (2.6); 162 (2.7); 117 (9.4); 88 (100); 77 (58.0); 51 (27).

Reaction of 1a with pyridine-2-carbaldehyde (3). Ester **1a** (0.84 g, 5 mmol), **3** (0.54 g, 5 mmol), $Fe(CO)_5$ (1.18 g, 6 mmol), several crystals of I_2 (<10 mg), PhH (2 mL), and DMF (1 mL) were mixed. The reaction mixture was refluxed for 4 h (until liberation of CO ceased) and cooled. Then 3*M* HCl (2×6 mL) was added and the organic layer was washed with water. The aqueous layer was neutralized with K_2CO_3, an EDTA solution was added, and the reaction mixture was extracted with $CHCl_3$ (5×4 mL). The extracts were dried with K_2CO_3 and concentrated *in vacuo*. The residue was chromatographed on a column with SiO_2 (5×1.5 cm) with a 6 : 1 $CHCl_3$: MeOH, mixture as the eluent. Methyl 3-hydroxy-2-methyl-3-(2-pyridyl)propionate (**11**) was isolated in 76% yield. Found (%): C, 61.12; H, 6.71; N, 7.18. $C_{10}H_{13}NO_3$. Calculated (%): C, 61.52; H, 6.64; N, 7.23. ^1H NMR, δ: 1.03 and 1.12 (both d, 3 H, $C\underline{H}_3$—CH, J = 7.1/J = 7.1 Hz); 2.96 (m, 1 H, $C_\alpha H$); 3.67 and 3.72 (both s, 3 H, $C\underline{H}_3$—O); 4.87 and 5.20 (d, 1 H, J = 5.8 Hz and br.s, 1 H, C<u>H</u>—Py); 7.20—7.38 (m, 2 H, Py); 7.70 (m, 1 H, Py); 8.56 (m, 1 H, Py).

Reaction of 1a with cinnamaldehyde (4). Ester **1a** (0.84 g, 5 mmol), **4** (0.60 g, 5 mmol), $Fe(CO)_5$ (1.18 g, 6 mmol), several crystals of I_2 (<10 mg), and PhH (2 mL) were mixed. The reaction mixture was refluxed for 1 h. Then 3*M* HCl (3 mL) and PhH (8 mL) were added and the organic layer was separated, washed with water (2×3 mL), dried with Na_2SO_4, and concentrated *in vacuo*. The residue was chromatographed as described above for the experiment with benzaldehyde. Methyl 3-hydroxy-2-methyl-5-phenylpent-4-enoate (**13**) was isolated in 70% yield. Found (%): C, 70.78; H, 7.31. $C_{13}H_{16}O_3$. Calculated (%): C, 70.88; H, 7.32. ^{1}H NMR, δ: 1.21 and 1.19 (both d, 3 H, CH_3—CH, J = 7.2/J = 7.2 Hz); 2.62—2.75 (m, 1 H, $C_\alpha H$); 2.80 (br.d, 1 H, OH, J = 3.8 Hz); 4.37 and 4.56 (both m, 1 H, CH—OH); 6.22 and 6.13 (both dd, 1 H, CH=, J_1 = 6.1 Hz, J_2 = 15.3/J_1 = 6.9 Hz, J_2 = 15.6 Hz); 6.67 and 6.66 (both d, 1 H, CH=, J = 15.3/J = 15.6 Hz); 7.39—7.24 (m, 5 H, Ph).

Reaction of 1a with 2,2-dimethylpropanal (5). Ester **1a** (0.17 g, 1 mmol), **5** (0.09 g, 1 mmol), $Fe(CO)_5$ (0.2 g, 1 mmol), and PhH (1 mL) were mixed and several crystals of I_2 (<10 mg) were added. The reaction mixture was refluxed for 2 h and treated with 3*M* HCl. The organic layer was passed through SiO_2 and concentrated *in vacuo*. The residue was purified by preparative GLC and methyl 3-hydroxy-2,4,4-trimethylpentanoate (**13**) was isolated in 10% yield, n_D^{20} 1.4360, d_4^{20} 0.967. Found (%): C, 62.09; H, 10.28. $C_9H_{18}O_3$. Calculated (%): C, 62.03; H, 10.41. ^{1}H NMR, δ: 0.83 and 0.89 (both s, 9 H, CH_3—C); 1.17 and 1.29 (both d, 3 H, CH_3—CH, J = 7.2/J = 7.1 Hz); 2.68 (m, 1 H, CH—C); 3.13 (s, 1 H, OH); 3.58 (m, 1 H, CH—O); 3.63 (s, 3 H, CH_3O). ^{13}C NMR, δ: 177.7 (COO); 82.4 (CH—OH); 51.6 (CH_3O); 38.1 (CH); 35.8 (C); 25.9 (CH_3—C); 17.8 (CH_3—CH). MS, *m/z* (I_{rel} (%)): 174 $[M]^+$ (0.23); 159 (7.87); 156 (0.96); 143 (16.40); 117 (61.98); 88 (84.80); 85 (100); 57 (89.40).

Reaction of 1a with acetophenone (8). Ester **1a** (0.84 g, 5 mmol), **8** (0.6 g, 5 mmol), $Fe(CO)_5$ (1.18 g, 6 mmol), several crystals of I_2 (<10 mg), and PhH (2 mL) were mixed. The reaction was conducted as described above. The residue was chromatographed on a column with a 2 : 1 n-C_6H_{14} : Et_2O mixture as the eluent. After elution of acetophenone (TLC control), Et_2O was used as the eluent. Methyl 3-hydroxy-2-methyl-3-phenylbutyrate (**16**)[6,14] was isolated in 36% yield. Found (%): C, 69.46; H, 7.70. $C_{12}H_{16}O_3$. Calculated (%): C, 69.20; H, 7.75. ^{1}H NMR [*threo*/*erythro*], δ: 7.61/7.23 (m, 5 H, C_6H_5); 3.85/4.05 (s, 1 H, OH); 3.40/3.69 (s, 3 H, CH_3O); 3.05/2.88 (m, 1 H, CH); 1.41/1.51 (s, 3 H, CH_3); 1.27/0.95 (d, 3 H, CH_3—CH, J = 7.1/J = 7.06 Hz). MS, *m/z* (I_{rel} (%)): 207 $[M - H]^+$ (0.49); 191 $[M - 17]^+$ (0.21); 145 (20); 115 (30); 105 (87); 77 (69); 69 (12); 51 (26); 44 (100).

Reaction of 1a with benzophenone (9). Ester **1a** (0.84 g, 5 mmol), **9** (0.9 g, 5 mmol), $Fe(CO)_5$ (1.18 g, 6 mmol), several crystals of I_2 (<10 mg), and PhH (2 mL) were mixed. The reaction was conducted as described above. Methyl 3-hydroxy-2-methyl-3,3-diphenylpropionate (**17**)[15] was isolated in 84% yield. Found (%): C, 75.59; H, 6.82. $C_{17}H_{18}O_3$. Calculated (%): C, 75.53; H, 6.71. M.p. 122—123 °C (hexane). ^{1}H NMR, δ: 7.50—7.42 (m, 10 H, C_6H_5); 4.68 (s, 1 H, OH); 3.64 (m, 1 H, CH); 3.58 (s, 3 H, CH_3O); 1.15 (d, 3 H, CH_3—CH, J = 7.0 Hz). MS, *m/z* (I_{rel} (%)): 270 $[M]^+$ (0.04); 252 $[M - 18]^+$ (0.36); 193 (0.79); 183 (98.1); 105 (100); 77 (91.9); 51 (26.2).

Reaction of methyl dibromoacetate (1b) with 6. Ester **1b** (0.55 g, 2.35 mmol), **6** (0.2 g, 2 mmol), $Fe(CO)_5$ (0.78 g, 4 mmol), and PhH (1 mL) were mixed. The reaction was conducted as described above. Methyl 3-methylhept-2-enoate (**18**) was isolated as a mixture of *E*/*Z* isomers in 95% yield. Found (%): C, 68.60; H, 10.03. $C_9H_{16}O_2$. Calculated (%): C, 69.19; H, 10.32. ^{13}C NMR, δ: 166.5 (COO); 161.0 (C=); 115.2 (CH); 50.4 (CH_3O); 32.9 (CH_2—C); 30.1 (CH_2); 24.9 (CH_3—C); 22.6 (CH_2—CH_3); 13.7 (CH_3). MS, *m/z* (I_{rel} (%)): 156 $[M]^+$ (63.76); 127 (100); 114 (48.04); 99 (13.68); 95 (84.71); 82 (47.91); 55 (54.54). Both stereoisomers were isolated in individual form by preparative GLC. The major isomer: n_D^{20} 1.4495, d_4^{20} 0.9094. ^{1}H NMR, δ: 0.70 (t, 3 H, CH_3, J = 8.0 Hz); 1.18 (m, 4 H, $2CH_2$); 1.66 (s, 3 H, CH_3C); 2.41 (t, 2 H, CH_2—C, J = 8.0 Hz); 3.45 (s, 3 H, CH_3O); 5.58 (s, 1 H, CH). Minor isomer: n_D^{20} 1.4510, d_4^{20} 0.9138. ^{1}H NMR, δ: 0.85 (t, 3 H, CH_3, J = 8.0 Hz); 1.20—1.41 (m, 4 H, $2CH_2$); 2.01 (t, 2 H, CH_2C, J = 6.0 Hz); 2.06 (s, 3 H, CH_3C); 3.60 (s, 3 H, CH_3O); 5.58 (s, 1 H, CH).

Reaction of methyl trichloroacetate (1c) with 6. Ester **1c** (0.15 g, 0.9 mmol), **6** (0.10 g, 1 mmol), $Fe(CO)_5$ (0.39 g, 2 mmol), and PhH (1 mL) were mixed. The reaction was conducted as described above. Methyl 3-methyl-2-chlorohept-2-enoate (**19**) was isolated as a mixture of *E*/*Z*-isomers in 80% yield, n_D^{20} 1.4700, d_4^{20} 1.070. Found (%): Cl, 18.77. $C_9H_{17}ClO_3$. Calculated (%): Cl, 18.63. ^{1}H NMR, δ: 3.74 (s, 3 H, CH_3O); 2.46 and 2.30 (both t, 2 H, CH_2, J = 6.5/J = 8.0 Hz); 2.07 and 1.93 (both s, 3 H, CH_3—C); 1.36 (m, 4 H, $2CH_2$); 0.86 (m, 3 H, CH_3—CH_2). ^{13}C NMR, δ: 164.0 (COO); 151.3 (CCl=); 117.8 (C=); 53.6 (CH_3O); 37.4, 30.1, 22.4 (CH_2); 22.2 (CH_3—C); 13.6 (CH_3). MS, *m/z* (I_{rel} (%)): 190 $[M]^+$ (1 Cl) (47.45), 161 (1 Cl) (70.78), 155 (15.39), 148 (1 Cl) (100), 135 (1 Cl) (70.94), 129 (1 Cl) (44.13), 116 (53.23). In addition, small amounts of methyl dichloroacetate (6%) and dimethyl tetrachlorosuccinate (10%) were identified in the reaction mixture. The latter was isolated by preparative GLC. ^{1}H NMR, δ: 3.81 (s, 3 H, CH_3O); ^{13}C NMR, δ: 55.1 (CH_3O), 87.1 (CCl_2), 162.9 (COO).

Reaction of 1c with 2. Ester **1c** (0.16 g, 0.9 mmol), **3** (0.12 g, 1.2 mmol), $Fe(CO)_5$ (0.39 g, 2 mmol), and PhH (1 mL) were mixed. After the reaction was over, methyl 2-chloro-3-phenylacrylate (**20**)[16] was isolated in 35% yield. ^{1}H NMR of the mixture of isomers, δ: 7.88 and 7.32 (both m, 5 H, C_6H_5); 3.85 (s, 3 H, OCH_3); 3.82 and 3.70 (both s, 2 H, CH=).

Investigation of the possibility of formation of an organoiron compound from 1a and $Fe(CO)_5$. Ester **1a** (0.84 g, 5 mmol), $Fe(CO)_5$ (1.18 g, 6 mmol), several crystals of I_2 (20 mg, $7.9 \cdot 10^{-5}$ mol), and PhH (2 mL) were mixed in a two-neck flask equipped with a septum and a reflux condenser under an Ar atmosphere (three freezing—evacuation—gas filling cycles). The reaction mixture was heated to boiling. A precipitate was formed in a few minutes and CO (~10 mL) was liberated. Then the reaction mixture was refluxed for 2.0 h (no elimination of CO was observed). The reaction was terminated by adding an excess of water (1 mL). The organic phase was analyzed by GLC (Carbowax 20000).

Study of the stereochemistry of the reaction of allyl (*S*)-2-bromopropionate [(*S*)-1d] with 7 in the presence of $Fe(CO)_5$. Ester (*S*)-**1d**[17] (0.193 g, 1 mmol) and compound **7** (0.196 g, 2 mmol) were mixed. Then $Fe(CO)_5$ (0.195 g, 1 mmol) and PhH (0.5 mL) were added and $BrCCl_3$ (0.01 g, 0.05 mmol) was used as an activating agent. The reaction mixture was refluxed for 1 h until the conversion of the initial (*S*)-**1d** amounted to 50% (GLC control) and was worked up as described above for the experiment with racemic **1d**. The yield of the adduct (determined by GLC) was 54%. The enantiomeric analysis of the reaction mixture was performed by chiral GLC. According to the results obtained, the unconsumed initial (*S*)-**1d** (*ee* > 98%) underwent complete racemization in the course of the reaction. In addition, the resulting β-hydroxy ester **7d** is a racemate with respect to two chiral centers.

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