# Difference in the behavior of methyl (S)- $\alpha$ -bromopropionate in its addition to trimethylvinylsilane depending on the method of initiation

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The addition of methyl  $(\mathcal{S})$ -2-bromopropionate to trimethylvinylsilane initiated by systems based on iron pentacarbonyl affords a racemic adduct and is accompanied by racemization of the unreacted chiral ester. In the presence of benzoyl peroxide, the reaction proceeds similarly, but no racemization of the starting chiral ester occurs.

Key words: addition, iron pentacarbonyl, racemization, methyl (S)-2-bromopropionate.

The addition of halogen-containing compounds to a double bond under the action of metal-complex initiators is a well known method for constructing a carbon skeleton.<sup>1</sup> Various mechanisms for the metal-complex activation of the halogen-containing telogen have been suggested. They vary from a free-radical mechanism to a metal-complex mechanism, including a number of intermediate variants.<sup>2-5</sup>

Data supporting one or another mechanism of this reaction have been reported. Although the mechanisms of initiation and chain transfer involving metals should obviously vary depending on the natures of the reactants and initiating systems used and also depending on the conditions under which the reaction is conducted, the mechanism generally accepted at present is redox catalysis.<sup>4</sup> Nevertheless, some experimental facts, such as asymmetric induction in the step of transfer of the halogen atom from a chiral complex to a radical adduct<sup>6</sup> and different  $\rho$  values for the reaction series involving different metals,<sup>7</sup> cannot be explained satisfactorily in terms of the conventional redox scheme. To develop a unified description of this process, additional studies in the field of metal redox catalysis are needed.

We believed that the use of new types of halogencontaining substrates may be useful for the solution of this problem. In the present work, we used optically active halogen-containing compounds as these substrates and then studied the stereochemical result of the addition and determined the configuration of the unreacted starting compound. In view of the fact that systems based on iron pentacarbonyl have been most thoroughly studied as initiators of the addition and telomerization reactions,<sup>4</sup> we used these initiators in the series of studies that we have begun. The present study deals with the addition of methyl (S)- $\alpha$ -bromopropionate (1) to trimethylvinylsilane (TMVS) in the presence of peroxide or metal-complex initiators.

## **Results and Discussion**

In all of the cases studied, the addition of compound 1 to TMVS occurred with a satisfactory yield according to Scheme 1, no matter what initiating system was employed.



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**Table 1.** Addition of methyl (S)- $\alpha$ -bromopropionate to trimethylvinylsilane (1:1, 100 °C, 2 h, 10 mol. % IPC)

Run	Initiator	Cocatalyst	Yield of 2 (%)	(S):(R) ratio in 1 after the reaction
1	BP	_	82	75:254
2	IPC	_	40	ь
3	IPC	DMF	17	ь
4	IPC	Ph <sub>1</sub> P	13	50:50ª
5	IPC	6 <sup>c</sup>	73	51:49
6	IPC	7ª	88	50:50
7	Mn <sub>2</sub> (CO) <sub>10</sub> <sup>e</sup>	_	80	90:10⁄

<sup>a</sup> The (S):(R) ratio in the starting compound was 80:20; the ratio between the stereoisomers does not change on heating without an initiator (140 °C, 2 h). <sup>b</sup> Runs 2 and 3 were carried out with racemic 1. <sup>c</sup> N-Benzoyl-1-methoxycarbonylpyrrolidine 6. <sup>d</sup> N-(2-Bromopropionyl)pyrrolidine 7. <sup>e</sup> At 140 °C. <sup>f</sup> The (S):(R) ratio in the starting compound was 98:2.

The structures of adduct 2 and its homolog 5 prepared by the addition of methyl  $\alpha$ -bromobutyrate to TMVS were confirmed by their <sup>13</sup>C NMR spectra using the DEPT-135 and INADEQUATE techniques. The latter technique allows one to distinguish signals corresponding to individual diastereomers in a mixture of diastereomers (see experimental).

Table 1 presents the yields of adduct 2 obtained with various initiating systems. High yields were obtained with both benzoyl peroxide (BP) (Table 1, run 1) and dimanganese decacarbonyl (Table 1, run 7). When the reaction was carried out in the presence of Mn<sub>2</sub>(CO)<sub>10</sub> at 140 °C, Me<sub>3</sub>SiCH<sub>2</sub>CH<sub>2</sub>CH(CH<sub>3</sub>)COOMe (3) (resulting from the chain transfer at hydrogen) and  $Me_3SiCH(CH_3)CH(CH_3)COOMe$  (4) (resulting from the inverse addition) were obtained, along with adduct 2. High yields were also attained by using iron pentacarbonyl Fe(CO)<sub>5</sub> (IPC) with the addition of N-(benzoyl-1-methoxycarbonyl)pyrrolidine (6) or N-(2-bromopropionyl)pyrrolidine (7) as a cocatalyst (Table 1, runs 5 and 6). The systems incorporating IPC combined with DMF or PPh<sub>3</sub> proved to be less effective (Table 1, runs 3 and 4), which is unusual for reactions of this type.<sup>5</sup>

In all the cases, adduct 2 was formed as a mixture of two racemic diastereomers in approximately equal proportions. This indicates that the reactive species formed from compound 1 through the action of either metalcomplex or peroxide initiators loses completely its initial configuration before it adds to TMVS. If the reaction occurred by a metal-complex pathway, the configuration of the starting 1 would apparently be retained, at least partly, in the reaction product.<sup>6</sup> It is obvious that the alternative reaction mechanisms<sup>3,4</sup> can describe the observed regularities, because, according to these mechanisms, the carbon-centered radical generated from compound 1 acts as the intermediate reactive species. In this aspect, the metal-complex initiation does not differ fundamentally from the peroxide initiation.

The principal distinction in the behavior of BP, IPC, and  $Mn_2(CO)_{10}$  is manifested in the GLC analysis of the starting 1 (Table 1). When the process is initiated by BP or  $Mn_2(CO)_{10}$ , the unreacted ether 1 is mostly the (S)-isomer (racemization occurs to a small extent, Table 1, runs 1 and 7); the same result was obtained on heating the starting compound for 2 h at 140 °C without an initiator. However, when initiating systems based on IPC are used, the unreacted 1 is virtually completely racemized (Table 1, run 3 and 4). This indicates that the addition of the intermediate radical formed from compound 1 to TMVS occurs more slowly than the abstraction of the halogen atom from the intermediate [Fe-Br] catalytic species (Scheme 2). In other words, in the case when IPC is used, the first step of the generation of the radical from comound 1 is reversible.

### Scheme 2



In order to juxtapose the course of the racemization and addition under strictly comparable conditions, we studied the time dependences of the accumulation of the (R)-isomer 1 and adduct 2 during the reaction carried out in a dilute solution (in order to decrease its rate) and initiated by the  $Fe(CO)_5-DMF$  system.

As can be seen from Fig. 1, the curves of the accumulation of adduct 2 and the (R)-isomer of 1 are analogous and differ only in quantitative parameters. Moreover, both processes have identical induction periods and saturation periods. This indicates that both processes are initiated by iron carbonyl species of the same nature and that the concentration of these species decreases rather quickly under the reaction conditions.

It should be noted that the use of the chiral telogen made it possible for the first time to detect experimentally during racemization the chain transfer by the radical, formed initially from the telogen, with the participation of halogen-containing iron-carbonyl species. This



Fig. 1. Time ( $\tau$ ) dependence of the accumulation (Y) of methyl (R)-2-bromopropionate 1 (curve I) and adduct 2 (curve 2) (1 M benzene solution; 1:TMVS molar ratio 1:1; 10 mol. % IPC, 30 mol. % DMF).

was also supported by the fact that almost no racemization of (S)-1 is observed when the reaction is carried out in the presence of BP, although the addition occurs rather effectively under similar conditions.

The experimental data obtained by us imply that in terms of the character of their effects on the course of racemization, the studied initiating systems can be divided into two groups: BP and dimanganese decacarbonyl constitute one group, and IPC-based initiators belong to the second group.

A study of addition and telomerization reactions involving polyhaloalkanes and functionally substituted organohalogen compounds showed that in this case, too, the characters of the participation of initiating systems in the reaction are dissimilar. BP and  $Mn_2(CO)_{10}$  act only as initiators, whereas IPC + DMF not only initiates the reaction, but also participates in the chain transfer step, due to the ability of the halogen-containing metal-carbonyl complex to donate the halogen atom to the radicals formed intermediately. Perhaps, this is the reason for the dissimilar effects of the natures of initiating systems on the course of racemization: the initiator can only abstract the bromine atom from a minor portion of the molecules, but the process does not develop further; a system based on IPC operates according to the principle of chain process, since it "works over" all or almost all the chiral compound.

### Experimental

Mass spectra were obtained on a VG-7070E GC/MS using a DB-5 (50 m) column, under  $30 \rightarrow 220$  °C temperature condi-

tions (2.5 deg. min<sup>-1</sup>); the m/z values for ions are given for the <sup>79</sup>Br and <sup>35</sup>Cl isotopes. GLC analysis was carried out on an LKhM-80 chromatograph using a steel column (1300×3 mm) with 15 % SKTFT-50X on Chromaton N-AW, helium as the carrier gas (60 mL min<sup>-1</sup>), and a katharometer as the detector; the temperature was programmed in the 50-250 °C region (6 deg. min<sup>-1</sup>). GLC of optical isomers was performed on a capillary quartz column with the DP-TFA-y-cD chiral phase (with a length of 32 m, an inner diameter of 0.20 mm, and a thickness of the layer of 0.12 mm; at a helium pressure of 1.8 bar and at 100 °C). Specific optical rotation was measured on a Perkin-Elmer-241 polarimeter (in CHCl<sub>3</sub>). The <sup>13</sup>C NMR spectra were recorded on a Jeol JNM GSX 270 FT spectrometer in CDCl<sub>3</sub>; the signals were assigned using the DEPT-135 and 2D <sup>13</sup>C-<sup>13</sup>C INADEQUATE methods (see Tables 2 and 3).

(S)- $\alpha$ -Bromopropionic acid (prepared similarly to the procedure described in Ref. 8). L-Alanine (8.9 g, 0.1 mol) and calcined KBr (41.6 g, 0.35 mol) were placed in a threenecked flask equipped with a stirrer and a reflux condenser, and preliminarily cooled 2.5 N sulfuric acid (416 mL, 0.52 mol) was added. The solution was cooled to -10 °C, and a solution of NaNO<sub>2</sub> (11 g, 0.16 mol) in 15 mL of water was added over a period of 2.5 h, the temperature being maintained between -8 and -5 °C; then the mixture was stirred for an additional 3 h at ~20 °C. The reaction mixture was extracted with ether, and the extract was washed with a 5 % solution of Na<sub>2</sub>SO<sub>3</sub> and with water and was dried with MgSO<sub>4</sub>. The ether was evaporated. The yield of crude acid was 8.0 g (52 %).  $[\alpha]_D^{25} =$ -28.53 (c 1, CHCl<sub>3</sub>); cf. Ref. 9: for (S)- $\alpha$ -bromopropionic acid,  $[\alpha]_D^{25} = -29.0$ .

Methyl (S)- $\alpha$ -bromopropionate (S-1). Thionyl chloride (1.8 mL, 24 mmol) was added dropwise to a stirred solution of (S)- $\alpha$ -bromopropionic acid (3.8 g, 24 mmol) in 10 mL of anhydrous MeOH cooled to -15 °C; during the addition the

 
 Table 2.
 <sup>13</sup>C NMR spectra of methyl 4-bromo-2-methyl-4-trimethylsilylbutyrate (2)

	2	3	4	
СН,-	-CH-	-CH,	-CHBr-Si(CH	)_
3	1		·	· 3
	CO	CH.		
		3		

C atom	δ, (tetramethyl-	I <sub>rel</sub> (%)	Assignment of diastereomers		
	silane)	_	A	B	
COOR	176.88	10.78	176.88		
COOR	176.34	10.08		176.34	
CH <sub>3</sub> O	51.66	31.12	51.66	—	
CH <sub>3</sub> O	51.56	23.98	-	51.56	
CH(4)	42.52	38.75		42.52	
CH(4)	40.88	48.35	40.88		
CH(2)	38.63	51.28		38.63	
CH(2)	37.98	57.45	37.98		
$CH_{2}(3)$	37.46	47.69	-	37.46	
$CH_{2}(3)$	36.13	57.97	36.13		
CH <sub>3</sub>	18.29	50.32		18.29	
CH	14.74	59.59	14.74		
Si(ĆH <sub>3</sub> ) <sub>3</sub>	-3.11	100.00	-3.11		
Si(CH <sub>3</sub> ) <sub>3</sub>	-3.24	68.65		-3.24	

 
 Table 3.
 <sup>13</sup>C NMR spectra of methyl 4-bromo-2-ethyl-4-trimethylsilylbutyrate (5)

$$CH_3 - CH_2 - CH_2 - CH_2 - CHBr - Si(CH_3)_3$$
  
cooch<sub>3</sub>

C atom	δ, (tetramethyl-	/ <sub>rel</sub> (%)	Assignment of diastereomers		
	silane)		A	B	
COOR	176.21	11.36		176.21	
COOR	175.86	17.02	175.86	-	
CH <sub>1</sub> O	51.49	31.46		51.49	
CHIO	51.40	45.22	51.40	-	
CH(2)	46.02	93.51	46.02	-	
CH(2)	45.25	62.03	_	45.25	
CH(4)	42.48	99.15	42.48		
CH(4)	41.00	53.58		41.00	
CH <sub>2</sub> (3)	35.45	100.00	35.45		
$CH_{2}(3)$	34.41	58.37		34.41	
CH <sub>2</sub>	26.17	96.22	26.17		
CH <sub>2</sub>	22.83	57.71		22.83	
CH	11.64	82.19	11.64		
CH	11.03	57.68		11.03	
Si(CH <sub>1</sub> ) <sub>1</sub>	-3.09	77.15	_	-3.09	
Si(CH <sub>3</sub> ) <sub>3</sub>	-3.24	98.98	-3.24		

temperature of the reaction mixture was maintained below -15 °C. Then the mixture was stirred for 2 h at -15 °C and for 2 h at 20 °C, 10 mL of ether was added, the mixture was cooled to -10 °C, and water was added with stirring and cooling until the mixture no longer warmed up on the addition of water. The mixture was washed with water and with a sodium carbonate solution, and the organic layer was dried with Na<sub>2</sub>SO<sub>4</sub>. After evaporation of the solvent, the residue was distilled *in vacuo*. The yield of (S)-1 was 2 g (50 %),  $[\alpha]_D^{25} = -46.65$  (c 1, CHCl<sub>1</sub>).

Addition of methyl (S)- $\alpha$ -bromopropionate to trimethylvinylsilane. Methyl (S)- $\alpha$ -bromopropionate (S-1) (6.68 g, 0.04 mol), trimethylvinylsilane (4 g, 0.04 mol), and BP (0.48 g, 0.002 mol) were placed into a 25-mL glass tube. The mixture was heated in the sealed tube in a boiling water bath for 2 h, dissolved in ether, washed with a sodium carbonate solution and with water, and dried with CaCl<sub>2</sub>. After evaporation of the ether and the unreacted starting compounds, the residue was distilled *in vacuo* to give 4.6 g of methyl 4-bromo-2-methyl-4-trimethylsilylbutyrate (2), yield 43 % of the theoretical yield, b.p. 75-76 °C (1 Torr),  $n_D^{20}$  1.4677,  $d_4^{20}$  1.1734, Found (%): C, 40.58; H, 7.31; Br, 29.50; Si, 10.48; MR 63.3. C9H<sub>19</sub>BrO<sub>2</sub>Si. Calculated (%): C, 40.40; H, 7.20; Br, 30.00; Si, 10.53; MR 63.0.

Methyl 4-bromo-2-ethyl-4-trimethylsilylbutyrate (5) was prepared in a similar way from methyl  $\alpha$ -bromobutyrate, yield 26 % of the theoretical yield, b.p. 78 °C (1 Torr),  $n_D^{20}$  1.4687,  $d_4^{20}$  1.1497. Found (%): C, 43.2; H, 7.61; Br, 27.74; Si, 9.95; MR 68.1.  $C_{10}H_{21}BrO_2Si$ . Calculated (%): C, 42.70; H, 7.50; Br, 28.40; Si, 10.00; MR 67.6.

Analytical experiments. The experiments presented in Table 1 and Fig. 1 were carried out in 4.5-mL glass tubes sealed under argon by the "freezing—evacuation—thawing" procedure. The tubes were placed into metallic chucks and heated in an oil bath with stirring (the conditions under which the experiments were conducted are given in Table 1). Table 1 also presents the results of the runs on the addition of the racemic and (S)-esters to TMVS in which the character of the initiator varied. The yields of compound 2 were determined from the GLC data, and the ratios between the (S)- and (R)-isomers were found by measuring the optical rotation angles and by GLC on the optically active phase. The results obtained by these two methods were in good agreement.

The mass spectra of the compounds obtained, m/z ( $I_{rel}$ (%)), the number of halogen atoms: 2 (one of the diastereomers): 266, 268 [M]<sup>+</sup> (0); 251, 253 [M-CH<sub>3</sub>]<sup>+</sup> (4.2), 1 Br; 235, 237 [M-OCH<sub>3</sub>]<sup>+</sup> (6.4), 1 Br; 160 [M-C<sub>2</sub>H<sub>3</sub>Br]<sup>+</sup> (85.1); 137, 139 [(CH<sub>3</sub>)<sub>3</sub>SiBr]<sup>+</sup> (17.0), 1 Br; 73 [Si(CH<sub>3</sub>)<sub>3</sub>]<sup>+</sup> (100); 3: 188 [M]<sup>+</sup> (0); 173 [M-CH<sub>3</sub>]<sup>+</sup> (29.8); 160 [M-C<sub>2</sub>H<sub>4</sub>]<sup>+</sup> (48.9); 89 [(CH<sub>3</sub>)<sub>3</sub>SiO]<sup>+</sup> or [(CH<sub>3</sub>)<sub>2</sub>SiOCH<sub>3</sub>]<sup>+</sup> (91.5); 73 [(CH<sub>3</sub>)<sub>3</sub>Si]<sup>+</sup> (100); 4 (one of the diastereomers): 188 [M]<sup>+</sup> (0); 157 [M-OCH<sub>3</sub>]<sup>+</sup> (2.0); 144 [M-CO<sub>2</sub>]<sup>+</sup> (36.2); 129 [M-COOCH<sub>3</sub>]<sup>+</sup> (51.0); 101 [M-C<sub>2</sub>H<sub>4</sub>-COOCH<sub>3</sub>]<sup>+</sup> (38.3); 75 [(CH<sub>3</sub>)<sub>2</sub>SiOH]<sup>+</sup> (51.0); 73 [(CH<sub>3</sub>)<sub>3</sub>Si]<sup>+</sup> (100)

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