Cyclization of allyl α-halocarboxylates in the presence of metallocomplex initiators

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Allyl trichloroacetate and allyl 2,2-dichloropropionate, unlike allyl bromoacetate and allyl 2-bromopropionate, undergo cyclization into γ-lactones in the presence of a $Fe(CO)_5$—amide system. All these esters undergo reductive dehalogenation under the action of the Bu^n_3SnH—AIBN system.

Key words: cyclization, allyl esters, iron pentacarbonyl, halocarboxylic acids.

Metallocomplex systems based on $Fe(CO)_5$ are effective initiators of the addition of derivatives of haloorganic acids to different unsaturated compounds[1] but still remain poorly studied as initiators of intramolecular addition leading to substituted lactones. The known examples involve the cyclization of allyl tri- and dichloroacetates initiated by $Fe(CO)_5$ combined with bipyridyl; in contrast to common addition, these reactions are not initiated by peroxides.[2] Intramolecular cyclization in such systems results most often in the formation of a five-membered ring.[3]

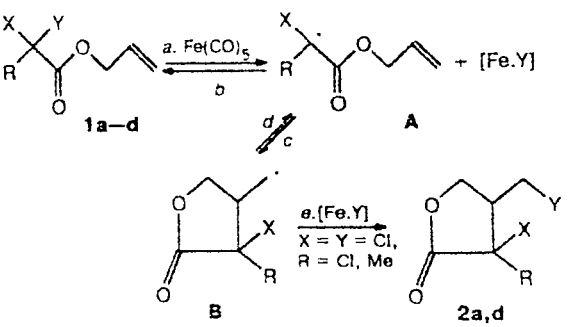
In the present work, we studied the possibility of cyclization, under comparable conditions, allyl trichloroacetate, allyl monobromoacetate, allyl 2-bromopropionate, and allyl 2,2-dichloropropionate (**1a—d**) in the presence of $Fe(CO)_5$—amide and Bu^n_3SnH—AIBN systems as initiators of radical reactions.

Results and Discussion

The intramolecular cyclization of allyl α-halocarboxylates **1a—d** includes stages *a*, *c*, and *e* (Scheme 1). Intermolecular chain transfer to a halogen-containing complex [Fe.Y] followed by regeneration of the initial compounds (Scheme 1, pathway *b*) competes with the intramolecular addition of the radicals A formed after the detachment of a halogen atom (Scheme 1, pathway *c*). The ease of ring-closure depends on the presence and the character of substituents at the radical center of the cyclic radical-adduct **B** involved in the chain transfer.

Taking into account that the course of these reactions is substantially influenced by the nature of the radical center formed and that, in principle, cyclization can occur stereoselectively, we used the methyl ester of *N*-benzoyl-L-proline (**3**) as a chiral cocatalyst in the $Fe(CO)_5$—amide system.

Scheme 1



a: R = X = Y = Cl
b: R = X = H, Y = Br
c: R = Me, X = H, Y = Br
d: R = Me, X = Y = Cl

We have established that benzoyl peroxide did not initiate the cyclization of esters **1a—d**, though normal intermolecular addition of similar alkyl esters to unsaturated compounds occurs in rather high yields under these conditions. Special experiments with ester **1c** as an example demonstrated that trimethylvinylsilane adds at the C—Br bond of this ester in the presence of both $(BzO)_2$ and systems based on $Fe(CO)_5$ (Scheme 2) to give the corresponding adduct **5**, and bromotrichloromethane easily adds to the double bond of ester **1c** in the presence of AIBN at 80 °C to form tetrahalobutyl ester **4**, which means that both reaction centers of this ester are active in the addition reactions.

It follows from these data that in all the examples studied either the radicals (**B**) generated do not affect chain transfer to the initial ester **1** at the C—halogen bond or the chain-transfer rate is considerably lower than that of ring-opening of the cyclic radical (see Scheme 1, pathway *d*).

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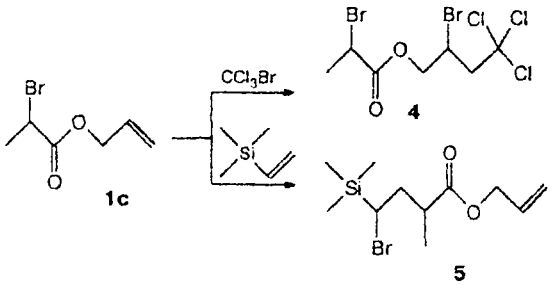
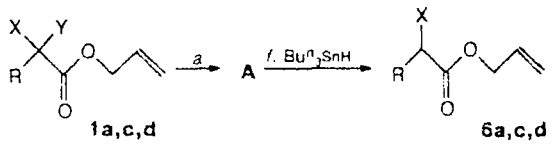
Scheme 2



Bu^n_3SnH, which is widely applied to other objects, in combination with irradiation or with AIBN also did not initiate the cyclization of allyl α-halocarboxylates.[4,5] These systems only caused reductive dehalogenation leading to the formation of esters **6a,c,d** (Scheme 3). It could be assumed that the rate of detachment of the hydrogen atom from tin hydride (see Scheme 3, pathway *f*) by the intermediate linear radicals A generated (Schemes 1 and 3, pathway *a*) is significantly higher than that of cyclization (see Scheme 1, pathway *c*).

Scheme 3

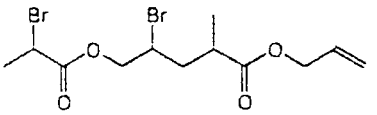


a: R = X = Cl
c: R = Me, X = H
d: R = Me, X = Cl

When $Fe(CO)_5$ was used as the initiator, a significant difference in the behavior of mono- and polyhalogenated esters was observed. When heated with the $Fe(CO)_5$—amide **3** system, esters **1a** and **1d** form tri- and dichlorolactones **2a,d** (see Scheme 1). Taking into account the results of experiments with benzoyl peroxide, this can be explained by the relative ease of chain transfer to a halogen-containing metal-carbonyl particle [Fe.Y] by the corresponding radicals **B** (see Scheme 1, pathway *e*). In these examples, one or two chlorine atoms are localized at the β-position to the radical center. They probably stabilize radical **B** (X = Cl) in the cyclic transition state and confer a relative electrophilic character on it, which facilitates chain transfer to an iron-carbonyl particle containing a chlorine atom. The cyclization of ester **1d** is of special interest in connection with the formation of two chiral centers in the molecule during the cyclization, which allows one to clarify the possible stereospecificity of the reaction. In fact, in this case, two cyclic, diastereomeric products (**2d**) are formed in a 1 : 3 ratio. This ratio is retained on going from the chiral cocatalyst **3** to DMF in the initiator system, *i.e.*, the stereospecificity manifests itself during ring-closure and is not related to the chirality of the cocatalyst.

A completely different pattern was observed when cyclization of monobromocarboxylates **1b,c** was attempted. These esters did not enter into intramolecular addition and were recovered unchanged.

When experiments with ester **1c** were carried out in the absence of a solvent, regardless of the initiation conditions allyl 4-bromo-5-(2-bromopropionyloxy)-2-methylpentanate (**7**) was identified (yield 15—24%, GLC) as a product of the interaction of two ester molecules, one of which served as a halogen derivative, while the other served as an olefin.



With regard to cyclization, esters **1c** and **1d** are very close analogs from the viewpoint of the character of the transition state **B**, and the substantial difference in their behavior under the reaction conditions may be due to the absence of a halogen atom at the β-position to the radical center in ester **1c**. The relative nucleophilicity of this radical is an unfavorable factor, which decreases the reaction rate at the stage of chain transfer to a halogen-containing iron-carbonyl particle (see Scheme 1, pathway *e*). Thus, reversible ring-opening and chain transfer by a linear radical can determine the reaction outcome (see Scheme 1, pathway *d,b*).

The actual existence of such a pathway of the reaction was confirmed experimentally with the intermolecular addition of methyl (*S*)-2-bromopropionate to trimethylvinylsilane as an example. When the reaction was carried out with benzoyl peroxide, along with the formation of an adduct, the unconsumed initial ester remained, which mainly retained the (*S*)-configuration. It is recovered in the form of a racemate in the presence of $Fe(CO)_5$, *i.e.*, the radical $MeC\dot{H}CO_2Me$ formed from the (*S*)-configuration of the ester detaches the bromine atom from the [Fe.Y] complex nonstereoselectively.[6]

Experimental

The mass spectra were obtained on a VG-7070E chromato-mass spectrometer with a DB-5 column (50 m). The temperature regime was 30—220 °C (2.5 deg min^{-1}), and the m/z value of ions are given for ^{79}Br and ^{35}Cl isotopes. The GLC analysis was performed on an LKhM-80 chromatograph with a steel column (1300 mm × 3 mm) with SKTFT-50X (15%) on Chromaton N-AW and helium as the carrier gas (60 mL min^{-1}). A katharometer was the detector, and the temperature was programmed in the range of 50—250 °C (6 deg min^{-1}). Preparative GLC was performed on a steel column (1300 mm × 9 mm) with 20% SKTFT-50X on the same stationary phase and helium as the carrier gas (120 mL min^{-1}), 180 °C. The ^1H and ^{13}C NMR spectra were

recorded on a Bruker WP-200 instrument (200 MHz) in C_6D_6; the chemical shifts are given with respect to tetramethylsilane.

Synthesis of allyl halocarboxylates (1a—d). *A.* A mixture of methyl or ethyl carboxylate (0.05 mol), allyl alcohol (0.5 mol), and several drops of conc. H_2SO_4 was boiled for 5 h with removal of alkyl alcohol. The excess allyl alcohol was removed *in vacuo* (water aspirator pump). The residue was dissolved in ether and washed with a Na_2CO_3 solution to neutral pH and then with water. The ethereal solution was dried with Na_2SO_4, and the ether was removed. The residue was distilled *in vacuo*.

B. A mixture of a carboxylic acid (0.05 mol) and allyl alcohol (0.5 mol) was cooled to −10 °C, and $SOCl_2$ (0.055 mol) was added dropwise with stirring. The reaction mixture was stirred for 2 h with cooling and then for an additional 2 h at ~20 °C. Ether was added, and the mixture was cooled again and treated with water. The ethereal layer was washed with a Na_2CO_3 solution, then with water, and dried with Na_2SO_4. The ether was removed, and the residue was distilled *in vacuo*.

Allyl trichloroacetate (1a) was obtained according to procedure *A*, b.p. 118—120 °C (40 Torr), yield 66%; ^{1}H NMR, δ: 4.31 (d, 2 H, CH_2O); 4.86 (m, 2 H, CH_2); 5.28 (m, 1 H, CH).

Allyl monobromoacetate (1b) was obtained according to procedure *B*, ^{1}H NMR, δ: 3.31 (s, 2 H, CH_2Br); 4.57 (d, 2 H, CH_2O); 5.27 (m, 2 H, CH_2); 5.84 (m, 1 H, CH).

Allyl 2-bromopropionate (1c) was obtained according to procedure *A*, b.p. 91—93 °C (40 Torr), yield 76%; ^{1}H NMR, δ: 1.75 (d, 3 H, CH_3); 4.32 (q, 1 H, CHBr); 4.60 (d, 2 H, CH_2O); 5.29 (m, 2 H, CH_2); 5.88 (m, 1 H, CH).

Allyl 2,2-dichloropropionate (1d) was obtained according to procedure *B*, b.p. 74—75 °C (25 Torr), yield 60%, n_D^{20} 1.4520, d_4^{20} 1.2038; ^{1}H NMR, δ: 2.15 (s, 3 H, CH_3); 4.60 (d, 2 H, CH_2O); 5.23 (m, 2 H, CH_2); 5.78 (m, 1 H, CH); MS: *m/z* (I_{rel}(%)), the number of halogen atoms: 182 $[M]^+$ (0.5), 2 Cl; 147 $[M-Cl]^+$ (0.5), 1 Cl; 97 $[CH_3CCl_2]^+$ (34), 2 Cl; 41 $[CH_2CH=CH_2]^+$ (100).

The reduction of esters 1a,c,d in the presence of Bu^n_3SnH. A solution of ester **1** (1 mmol), tin hydride (1.2 mmol), and AIBN (0.02 g) in 10 mL of benzene was refluxed for 4 h in an atmosphere of dry argon. The benzene was distilled off, ether (10 mL) and a solution of KF (0.5 g) in 10 mL of water were added, and the reaction mixture was stirred for 30 min. The ethereal layer was separated, washed with water, and dried with Na_2SO_4. The ether was removed, and the residue was analyzed by GLC, ^{1}H NMR, and chromato-mass spectrometry. The reduction was quantitative. Compounds **6a,c,d** were identified in the corresponding reaction mixtures.

Allyl dichloroacetate (6a), ^{1}H NMR, δ: 4.0 (s, 1 H, $CHCl_2$); 4.67 (d, 2 H, CH_2O); 5.3 (m, 2 H, CH_2); 5.9 (m, 1 H, CH) (*cf.* Ref. 2).

Allyl propionate (6c), MS, *m/z* (I_{rel}(%)): 114 $[M]^{+\cdot}$ (1); 85 $[M-C_2H_5]^+$ (2); 75 $[C_2H_5COOH_2]^+$ (6); 57 $[C_2H_5CO]^+$ (100); 41 $[C_3H_5]^+$ (29); 29 $[C_2H_5]^+$ (44).

Allyl 2-chloropropionate (6d), ^{1}H NMR, δ: 1.59 (d, 3 H, CH_3); 4.31 (q, 1 H, CHCl); 4.55 (d, 2 H, CH_2O); 5.22 (m, 2 H, CH_2); 5.83 (m, 1 H, CH).

The cyclization of esters 1a—d in the presence of a $Fe(CO)_5$—cocatalyst system. A mixture of ester **1** (1 mmol), $Fe(CO)_5$ (0.1 mmol), and **3** (0.1 mmol) in 10 mL of benzene was placed in glass tubes, degassed by freezing—evacuating—thawing, and sealed in an atmosphere of argon. The tubes were placed into metal holders and kept with stirring at 145 °C for 3 h. The reaction mixture was passed through a layer of silica gel and analyzed by GLC, ^{1}H NMR, and chromato-mass spectrometry. Preparative experiments with esters **1a** and **1d** resulted in the corresponding lactones (**2a,d**).

2,2-Dichloro-3-chloromethylbutyrolactone (2a),[2] yield 85% (GLC), m.p. 73—74 °C (from a hexane—ether mixture). ^{1}H NMR (one diastereomer), δ: 3.31 (m, 1 H, CH); 3.81 (m, 2 H, CH_2Cl); 4.19 and 4.61 (both 2 t, 2 H, CH_2O) (*cf.* Ref. 2). MS, *m/z* (I_{rel}(%)), the number of halogen atoms: 139 $[M-Cl-CO]^+$ (4), 2 Cl; 123 $[M-Cl-CO_2]^+$ (37), 2 Cl; 109 $[M-CO_2-CH_2Cl]^+$, $[M-COCl-CH_2O]^+$ (100.0), 2 Cl; 73 $[M-CO_2-CH_2Cl-HCl]^+$ (11), 1 Cl.

2-Methyl-2-chloro-3-chloromethylbutyrolactone (2d), yield 80% (GLC), was isolated from the reaction mixture by preparative GLC. ^{1}H NMR, δ: 1.73 (s, 3 H, CH_3); 2.75 (m, 1 H, CH); 3.66 (m, 2 H, CH_2Cl); 3.95 and 4.49 (both 2 t, 2 H, CH_2O). MS: *m/z* (I_{rel}(%)), the number of halogen atoms: 117 $[M-CH_2O-Cl]^+$ (1), 1 Cl; 103 $[M-CO_2-Cl]^+$ (100), 1 Cl; 89 $[M-CO_2-CH_2Cl]^+$ (75), 1 Cl.

Ester 7. MS, *m/z* (I_{rel}(%)), the number of halogen atoms: 384 $[M]^+$ (1), 2 Br; 305 $[M-Br]^+$ (6), 1 Br; 232 $[M-CH_3CHBrCOOH]^{+\cdot}$ (8), 1 Br; 153 $[M-CH_3CHBrCOOH-Br]^+$ (25); 135 $[CH_3CHBrCO]^+$ (15), 1 Br; 107 $[CH_3CHBr]^+$ (21), 1 Br; 41 $[CH_2CH=CH_2]^+$ (100).

The addition of CCl_3Br to ester 1c. A solution of **1c** (2.6 g), $BrCCl_3$ (4.04 g), and benzoyl peroxide (0.4 g) in 8 mL of benzene was heated in a sealed tube at 80 °C for 3 h. The reaction mixture was diluted with $CHCl_3$, washed with a Na_2CO_3 solution and water, and dried. **2-Bromo-4,4,4-trichlorobutyl 2-bromopropionate (4)** was isolated by distillation, yield 78%, b.p. 127—128 °C (1 Torr), n_D^{20} 1.5295, d_4^{20} 1.8337. Found (%): C, 21.71; H, 2.34; Hal, 68.20. $C_7H_9Br_2Cl_3O_2$. Calculated (%): C, 21.48; H, 2.32; Hal, 68.02. ^{13}C NMR, δ: 21.6 (CH_3); 39.3 (CHBrCO); 169.4 (CO); 58.7 (CH_2O); 42.3, 42.4 (CHBr); 67.6, 67.7 (CH_2); 96.4 (CCl_3).

The addition of ester 1c to trimethylvinylsilane. The reaction was carried out under conditions similar to those of cyclization, but in the presence of an equivalent (with respect to the ester) amount of trimethylvinylsilane. Allyl 4-bromo-2-methyl-4-trimethylsilylbutyrate (**5**) was obtained, yield 17% (GLC). MS, *m/z* (I_{rel}(%)), the number of halogen atoms: 277 $[M-CH_3]^+$ (4), 1 Br; 235 $[M-CH_3-CH_3CH=CH_2]^+$ (5), 1 Br; 186 $[M-Br-C_2H_3]^{+\cdot}$ (12); 137 $[Me_2SiBr]^{+\cdot}$ (14), 1 Br; 73 $[SiMe_3]^+$ (100).

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