Samarium(II) Di-iodide Induced Reductive Coupling of α,β-Unsaturated Esters with Carbonyl Compounds Leading to a Facile Synthesis of γ-Lactone

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Samarium(II) di-iodide, which is a strong one-electron transfer reducing agent, is effective for the reductive coupling of α,β-unsaturated esters with carbonyl compounds, whereby substituted γ-lactones can easily be prepared in good to excellent yields under very mild conditions. Two mole equiv. of samarium(II) di-iodide to each mole equiv. of starting substrate always give reasonable yields. The presence of an alcohol is essential in the reaction, complex unidentified products being formed in the absence of an alcohol; t-butyl alcohol gave more satisfactory results than methanol and ethanol. The alcohol acts as a proton donor, the use of MeOD leading to a deuteriated γ-lactone. The reaction is applicable to both aliphatic and aromatic ketones or aldehydes, whereas the electrochemical method is limited to aliphatic substrates. The diastereoselectivity is examined in the reaction of 4-t-butylcyclohexanone with ethyl acrylate; an *anti*-isomer is produced predominantly (*syn*:*anti* = 1:9) as the result of selective axial attack. The reaction may proceed by a radical mechanism, and reaction may not involve a samarium ester homoenolate. The reaction is extended to the intramolecular reaction of an α,β-unsaturated keto ester (8-oxonon-2-enoate) leading to the ready synthesis of a bicyclic γ-lactone.

There have been several recent examples of the use of lanthanoid reagents in organic synthesis.[1] Pioneering studies by Kagan and co-workers demonstrated the particular effectiveness of samarium(II) di-iodide (SmI_2) as a strong one-electron transfer reducing agent.[2] Barbier-type reactions of organic halides with carbonyl substrates were investigated and these served as the basis for the current study; for example, hydroxylation[3] and iodomethylation of carbonyl compounds,[4] and intramolecular annelation of 2-(ω-iodoalkyl)cycloalkanones.[5] We have reported in a preliminary fashion that SmI_2 is effective for the reductive coupling of α,β-unsaturated esters with carbonyl compounds to give γ-lactones in good yields.[6] In this connection, the synthesis of lactones, is important not only because they occur widely in Nature, but also because they constitute a particularly useful class of synthons. Recent useful examples for the two-component synthesis of γ-lactone frameworks are as follows. (i) A radical oxidative coupling of olefins with carboxylic acids by manganese(III) or cerium(IV) salts;[7] (ii) a radical coupling of a stannyl α-iodo ester with olefins;[8] (iii) a metal ester homoenolate addition to carbonyl compounds;[9,10] and a reductive coupling between α,β-unsaturated esters and carbonyl substrates by (iv) an electrolytic method[11] and (v) by zinc[12] or zinc–chlorotrimethylsilane.[13] The present reaction with SmI_2 results in 'umpolung' (a polarity inversion) of α,β-unsaturated esters likewise to previous examples of (**4**) and (**5**). We believe that the SmI_2 induced γ-lactone synthesis should prove to be one of the most facile and effective methods available since the reaction procedure is quite simple and the conditions are very mild. We here report the details of this reaction.

Results and Discussion

Reaction of α,β-Unsaturated Esters with Carbonyl Compounds.—As shown in Table 1, SmI_2 induced reductive coupling of α,β-unsaturated esters and carbonyl compounds proceeded smoothly under mild conditions to give substituted γ-lactones in good to excellent yields. These results demonstrate that the reaction is applicable to both aliphatic and aromatic ketones or aldehydes, whereas the electrochemical method is limited to aliphatic compounds.[11] For ketones, the reaction may be carried out at room temperature, while the aldehydes lower temperatures (< 0 °C) are necessary at the initiation of the reaction; otherwise yields of the desired product were less, many by-products being formed. Two mole equiv. of SmI_2 were necessary for each starting substrate to ensure a reasonable yield; 1 equiv. to a carbonyl compound and 1 equiv. to an α,β-unsaturated ester. Spectral and combustion analytical data for the γ-lactones prepared are summarized in Table 2.

α- and β-Substituted γ-lactones were prepared from ethyl methacrylate (**2b**) and crotonate (**2c**), respectively, as a mixture of *cis* and *trans* isomers with respect to the R^1 (R^2) and R^3 and R^4 groups; isomer ratios were determined on the basis of ^1H n.m.r. results and by reference to the literature.[14]

Table 1. Reductive coupling of carbonyl compound with α,β-unsaturated esters[a]

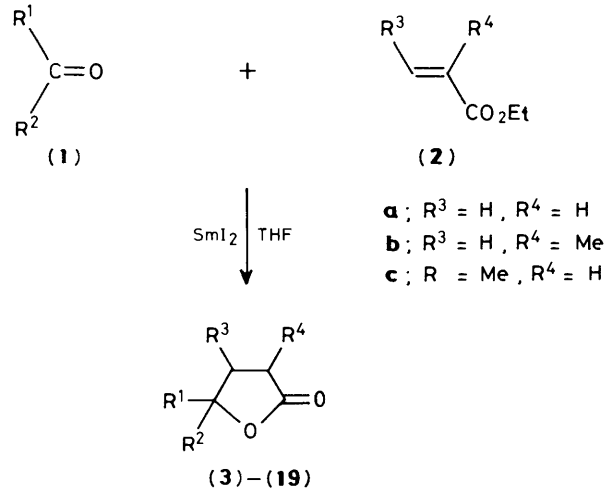
Entry	α,β-Unsaturated ester	Carbonyl compound	Product and isolated yield (%)
1	Ethyl acrylate	Acetophenone	(**3**), 70
2		Benzophenone	(**4**), 47
3		Diethyl ketone	(**5**), 40
4		Octan-2-one	(**6**), 71
5		Cyclohexanone	(**7**), 76
6		Cyclododecanone	(**8**), 76
7		4-t-Butylcyclohexanone	(**9**), 71
8		Hex-5-en-2-one	(**10**), 70
9		Benzaldehyde	(**11**), 82
10		Propanal[b]	(**12**), 65
11		Isobutyraldehyde[b]	(**13**), 63
12		Hexanal[b]	(**14**), 57
13	Ethyl methacrylate	Acetophenone	(**15**),[c] 75
14		Benzaldehyde	(**16**),[d] 75
15		Cyclohexanone	(**17**), 63
16	Ethyl crotonate	Pentanal[b]	(**18**),[e] 70
17		Hexanal[b]	(**19**),[f] 70

[a] α,β-Unsaturated ester (2 mmol), carbonyl compound (2 mmol), SmI_2 (0.4M; 10 ml, 4 mmol), THF (10 ml); room temperature, 2 h. [b] The reaction was carried out at 0 °C for 10 h. [c] Isomer ratio, *ca.* 55:45. [d] *cis*:*trans* = *ca.* 75:25. [e] *cis*:*trans* = *ca.* 65:35.[14] [f] *cis*:*trans* = *ca.* 70:30.[14]

Table 2. Spectral and combustion analytical results for the γ-lactones

	γ-Lactone						Found (%) (Required)		
	R^1	R^2	R^3	R^4	$\nu_{max.}$/cm^{-1}	δ_H (60 MHz)	C	H	R_F[a] value
(3)	Ph	Me	H	H	1 787	1.58 (s, CH_3, 3 H) 2.30 (br s CH_2CH_2, 4 H), 7.14 (br s, Ph, 5 H)	75.1 (74.97)	7.0 (6.86)	0.50
(4)	Ph	Ph	H	H	1 782	2.32 (m, CH_2CH_2C=O, 2 H),[b] 2.80 (m, CH_2CH_2C=O, 2 H),[b] 6.8—7.4 (m, Ph, 10 H)	80.75 (80.65)	5.85 (5.92)	0.55
(5)	Et	Et	H	H	1 782	0.85 (t, *J* 7.0 CH_3CH_2, 3 H), 1.53 (q, *J* 7.0 CH_3CH_2, 2 H), 1.86 (m, CH_2CH_2C=O, 2 H),[b] 2.39 (m, CH_2CH_2C=O, 2 H)[b]	67.3 (67.57)	10.0 (9.92)	0.48
(6)	C_6H_{13}	Me	H	H	1 783	0.89 (t, *J* 7.0, CH_3CH_2, 3 H) 1.37 (s, CH_3, 3 H), 1.1—1.7 (m, alkyl CH_2, 10 H) 2.00 (m, CH_2CH_2C=O, 2 H),[b] 2.62 (m, CH_2CH_2C=O, 2 H)[b]	71.25 (71.70)	11.05 (10.94)	0.40
(7)	$-(CH_2)_5-$		H	H	1 779	1.2—1.8 (m, alkyl CH_2, 10 H), 2.01 (m, CH_2CH_2C=O, 2 H),[b] 2.53 (m, CH_2CH_2C=O, 2 H)[b]	70.55 (70.09)	9.7 (9.15)	0.50
(8)	$-(CH_2)_{11}-$		H	H	1 762	0.9—1.3 (m, alkyl CH_2, 22 H), 1.60 (m, CH_2CH_2C=O, 2 H),[b] 2.01 (m, CH_2CH_2C=O, 2 H)[b]	75.1 (75.58)	11.25 (10.99)	0.40
(9)	$-[(CH_2)_2C(Bu^t)(CH_2)_2]-$		H	H	1 776	0.87 (s, Bu^t, 9 H), 1.0—2.1 (m, alkyl CH_2, 9 H) 2.28—2.6 (m, CH_2CH_2C=O, 4 H)[b]	70.1 (70.24)	10.25 (10.54)	0.40
(10)	CH_2=$CH(CH_2)_2$	Me	H	H	1 776	1.41 (s, CH_3, 3 H) 1.5—2.7 (m, alkyl and lactone CH_2, 8 H), 5.1—5.5 (m, CH_2=, 2 H), 5.8—6.4 (m, =CH, 1 H)	70.3 (70.09)	9.3 (9.21)	0.50
(11)	Ph	H	H	H	1 788	1.7—2.6 (m, CH_2CH_2C=O, 4 H), 5.20 (t, *J* 7.0, CHO, 1 H), 7.08 (br s, Ph, 5 H)	74.45 (74.06)	6.6 (6.22)	0.45
(12)	Pr	H	H	H	1 780	0.91 (t, *J* 7.0, CH_3, 1 H), 1.1—1.7 (m, alkyl and lactone CH_2, 4 H), 4.0—4.6 (m, CHO, 1 H)	65.9 (65.60)	9.35 (9.44)	0.40
(13)	Pr^i	H	H	H	1 789	0.83 (d, *J* 4.0, CH_3, 6 H) 1.2—2.6 [m, CH_2CH_2C=O and $CH(Me)_2$, 5 H], 4.03 (dt, *J* 4.0, 7.0, 1 H)	65.4 (65.60)	9.65 (9.44)	0.45
(14)	C_5H_{11}	H	H	H	1 781	0.85 (t, *J* 7.0, CH_3, 3 H), 1.0—1.6 (m, alkyl CH_2, 8 H), 1.7—2.6 (m, CH_2CH_2C=O, 4 H), 4.04 (m, CHO, 1 H)	69.2 (69.19)	10.45 (10.32)	0.45
(15)[c]	Ph	Me	H	Me	1 765	1.09 and 1.12 (d, *J* 7.5, CH_3CH, 3 H), 1.53 and 1.58 (s, CH_3, 3 H), 1.6—2.7 (m, lactone H, 3 H), 7.12 (br s, Ph, 5 H)	75.5 (75.76)	7.7 (7.42)	0.50
(16)[c]	Ph	H	H	Me	1 784	1.13 and 1.31 (d, *J* 7.4 Hz, 3 H), 2.3—2.9 (m, CH_2, 2 H), 3.0—3.5 (m, CHO=O, 1 H), 5.34 (dd, *J* 5.8 10.2) and 5.55 (dd, *J* 4.8, 6.8) (CHO, 1 H), 7.0—7.5 (m, Ph, 5 H)	74.75 (74.98)	7.1 (6.86)	0.45
(17)[c]	$-(CH_2)_2-$		H	Me	1 750	1.15 (d, *J* 7.5, CH_3, 3 H), 1.3—1.8 (m, CH_2, 10 H), 1.9—2.5 (m, lactone H, 3 H)	71.3 (71.31)	9.3 (9.59)	0.40
(18)[c]	C_4H_9	H	Me	H	1 770	0.90 (t, *J* 6.8, CH_3CH_2, 3 H) 1.13 (d, *J* 7.0, CH_3CH, 3 H), 1.3—1.7 (m, alkyl CH_2, 6 H), 1.9—2.3 (m, lactone H, 3 H), 3.90 and 4.33 (m, 1 H)	69.2 (69.19)	10.3 (10.32)	0.40
(19)[c]	C_5H_{11}	H	Me	H	1 774	0.95 (t, *J* 6.8, CH_3CH_2, 3 H), 1.11 (d, *J* 7.0, CH_3CH, 3 H), 1.2—1.7 (m, alkyl CH_2, 6 H), 2.0—2.9 (m, lactone H, 3 H), 3.92 and 4.40 (m, 1 H)	70.45 (70.54)	10.7 (10.66)	0.40

[a] On silica gel with hexane–diethyl ether (1:1) as eluant. [b] AA'BB' Type coupling. [c] *cis* and *trans* Mixture.



Scheme 1.

Table 3. Effect of a proton source and additives on the reaction of ethyl acrylate with acetophenone[a]

Entry	Alcohol	Additive	Isolated yield (%) of (3)
1	MeOH	None	66
2	EtOH	None	55
3	Pr^{i}OH	None	69
4	Bu^{t}OH	None	70
5	Bu^{t}OH	TMEDA[b]	72
6	Bu^{t}OH	TEGDME[c]	62
7	Bu^{t}OH	HMPA[d]	75[e]

[a] Ethyl acrylate (2 mmol), acetophenone (2 mmol), alcohol (2 mmol), THF (10 ml), additive (1 ml); room temperature, 2 h. [b] Tetramethylethylenediamine. [c] Tetraethylene glycol dimethyl ether. [d] Hexamethylphosphoramide. [e] The reaction was completed within 10 min.

Biologically interesting and natural γ-lactones were produced in one step. For example, *Quercus* lactone (whisky lactone) (**18**),[14] which is present in oak woods and aged spirits, was readily synthesized from (**2c**) and pentanal in a high yield by a simpler method than that used previously (entry 16, Table 1).

Effect of a Proton Source and Additives on the Reaction.—Since the presence of an alcohol was essential, complex unidentified products being formed in its absence, the effect of a proton source on the reaction was examined; the results are shown in Table 3. Methanol, ethanol, isopropyl alcohol, and t-butyl alcohol were used as a proton source, the last-named giving the most satisfactory results. All reactions were, therefore, performed by using t-butyl alcohol as a proton source. Next, the effect of additives was examined (Table 3). The complexation of the additives with SmI_2 may be expected to suppress the simple reduction and/or reductive homo-coupling of the ketone or increase the reducing ability of SmI_2.[3] Addition of tetramethylethylenediamine (TMEDA) or tetraethyleneglycol dimethyl ether (TEGDME) did not improve the yield, but hexamethylphosphoramide (HMPA) effectively promoted the reaction when used as a co-solvent; the reaction was complete within a few minutes.[15]

Deuterium Exchange Experiment.—To confirm the role of the alcohol as a proton donor, deuteriated methanol (MeOD) was employed to the reaction and, because of the ease of assigning their ^1H and ^{13}C n.m.r. spectra, the γ-lactones (**3**) and (**16**) were chosen. In the ^1H n.m.r. spectrum of (**3**) the lactone ring signal appears at δ 2.20 as a broad 4 H singlet; the intensity of the peak was diminished to 3 H when MeOD was used. In the ^{13}C n.m.r. spectrum of (**3**), the C-2 signal is a triplet at δ 28.7 p.p.m.; the use of MeOD resulted in a remarkable decrease of the carbon peak (see Figure 1).*[16] This result indicates the incorporation of

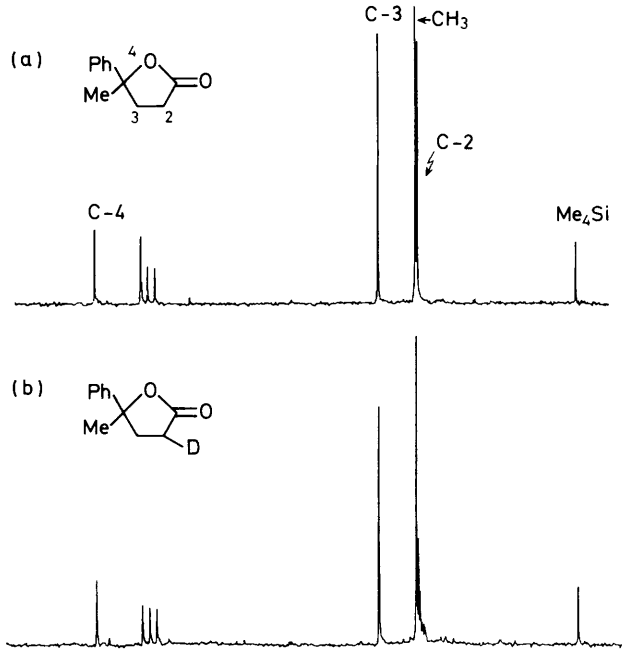


Figure 1. ^{13}C N.m.r. spectra of (a) 4-methyl-4-phenyl-γ-butyrolactone (**3**); (b) 2-deuterio-4-methyl-4-phenyl-γ-butyrolactone (**3′**) in $CDCl_3$

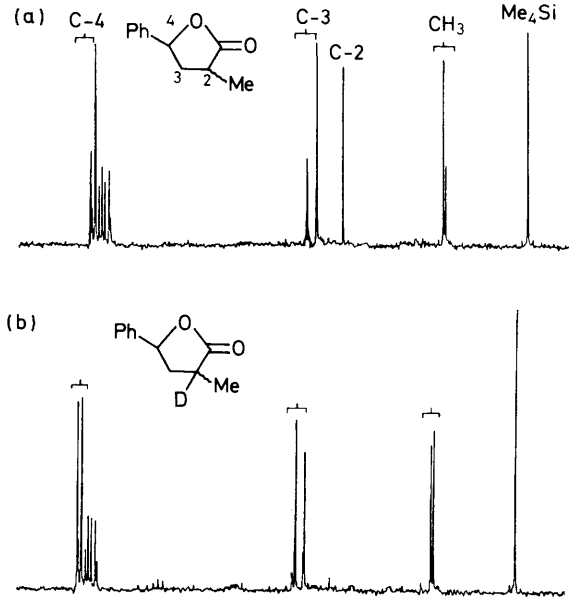
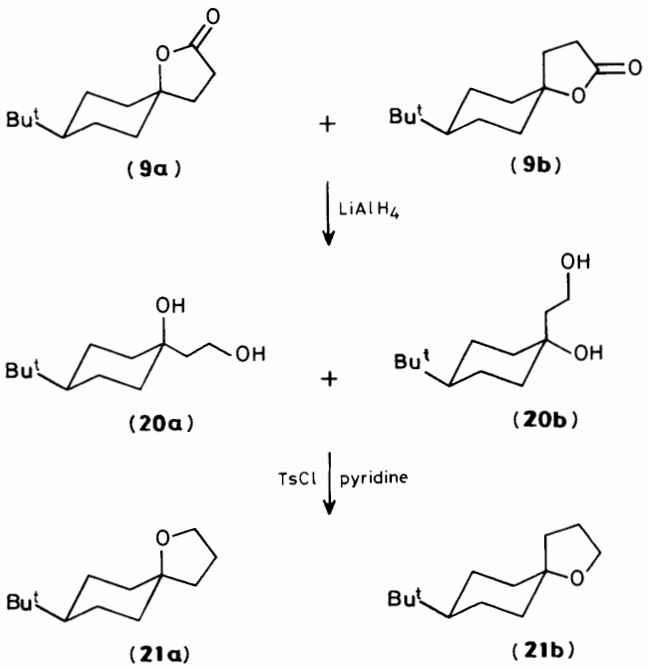


Figure 2. ^{13}C N.m.r. spectra of (a) 2-methyl-4-phenyl-γ-butyrolactone (**16**); (b) 2-deuterio-2-methyl-4-phenyl-γ-butyrolactone (**16′**) in $CDCl_3$

* The carbon bearing one deuterium should, in principle, appear as a triplet. It was not, however, observed since the concentration of the sample is low (5—10%) and the peak may be concealed in the noise.

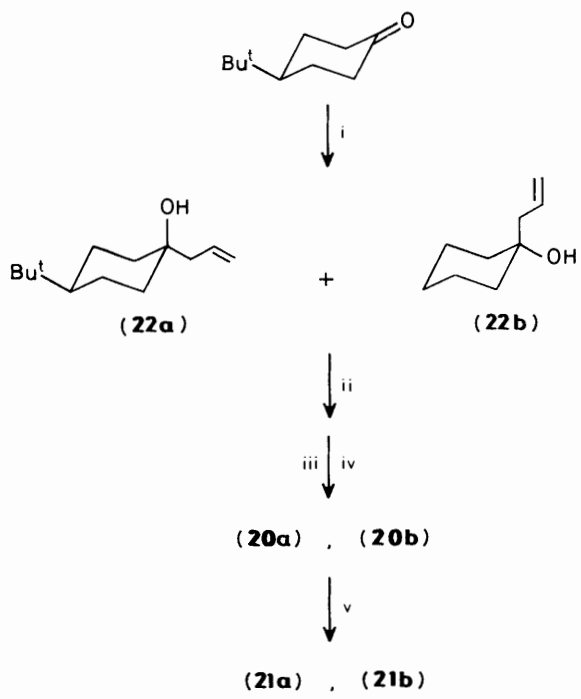
deuterium into C-2 of the γ-lactone. As a further example, the use of MeOD changed the original doublet of the methyl group in (**16**) to a broad singlet. The ^{13}C n.m.r. spectra shows the complete disappearance of the original C-2 carbon of (**16**) as seen in that of (**3**) (Figure 2).* This certainly indicates deuteriation of (**16**) at C-2. Consequently, an alcohol undoubtedly acted as a proton donor and a proton is introduced into C-2 of the lactone ring.

Stereochemical Aspects.—Diastereoselectivity was examined in the reaction with 4-t-butylcyclohexanone. Since their spectra were closely similar and could not be distinguished the stereochemical assignment of *syn*-(**9a**) and *anti*-(**9b**) were based on the transformation of the compounds to a mixture of tetrahydrofuran derivatives according to Trost's method.[17] Lithium aluminium hydride reduction of the lactones leading to the diols (**20a**) and (**20b**) followed by annelation with toluene-*p*-sulphonyl chloride in pyridine resulted in a mixture of the tetrahydrofurans (**21a**) and (**21b**). The authentic tetrahydrofuran was separately prepared as follows (Scheme 3). Allylation of 4-t-butylcyclohexanone with allylmagnesium bromide affords the axial (**22a**) and equatorial (**22b**) homoallylic alcohols in an approximately equimolar ratio. After separation of these alcohols by preparative t.l.c. each of them is converted into a diol by hydroboration. Subsequent cyclization of each alcohol with toluene-*p*-sulphonyl chloride in pyridine yields a single tetrahydrofuran (**21a**) or (**21b**).



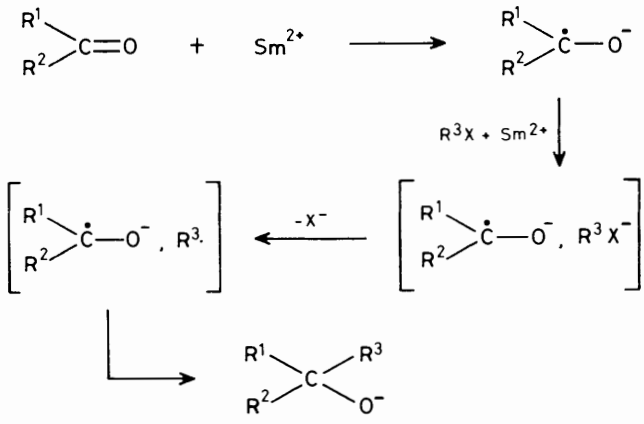
Scheme 2.

The major lactone was shown to be the *anti*-isomer (**9b**) resulting from predominantly axial attack by ethyl acrylate; this suggested a high degree of diastereoselectivity for the reaction (*syn*:*anti* = 1:9). This result contrasts with the stereoselectivity shown on allylation[2a] and iodomethylation[4b] of 4-t-butylcyclohexanone with SmI_2 where attack is predominantly equatorial, an axial alcohol being the major product. The *syn*-lactone is prepared selectively with lithium β-lithiopropionate (lithium ester homoenolate)[10a] or by a spiro-oxirane route;[17] a selective *anti*-lactone synthesis has seldom been reported.



Scheme 3. *Reagents:* i, CH_2=$CHCH_2MgBr$–Et_2O; ii, separation; iii, BH_3; iv, H_2O_2–NaOH; v, TsCl–pyridine

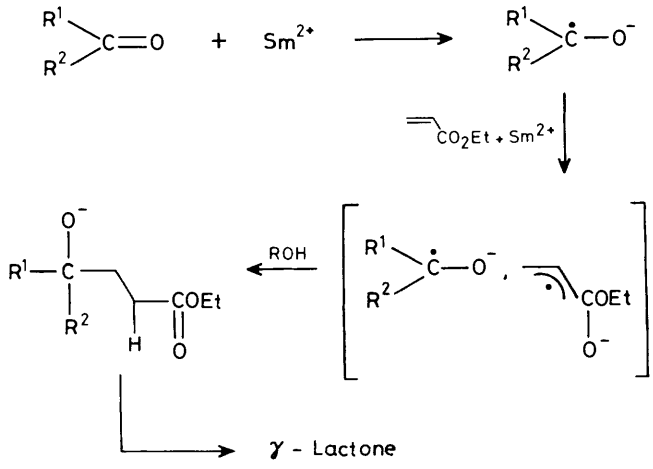
Mechanistic Considerations.—An SmI_2 induced coupling reaction of organic halides with carbonyl compounds was studied by Kagan and co-workers,[2b] who showed that the main route for the reaction involves both a ketyl radical and a halide anion radical; this is consistent with all available data. Since simple reduction and reductive coupling products are by-products in the γ-lactone synthesis, it is reasonable to assume that the reaction may also proceed mainly by a radical mechanism;[18] one possible pathway is shown in Scheme 5. The reaction involves reduction of a carbonyl compound to a ketyl with subsequent coupling of this to an allylic radical resulting from a one-electron transfer from Sm^{2+} to ethyl acrylate. A proton of an alcohol is then incorporated into the α-carbon from the ester group followed by cyclization to provide a γ-lactone.



Scheme 4.

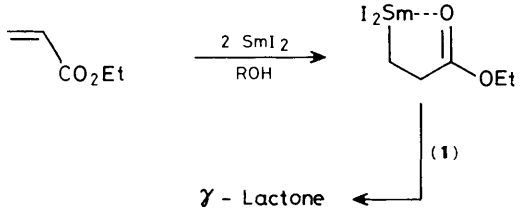
The ionic mechanism involving a samarium ester homo-

* See footnote on p. 1671.



Scheme 5.

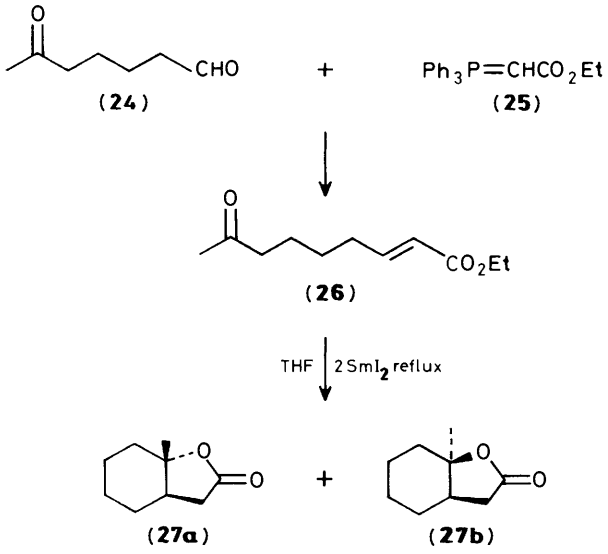
enolate (**23**), should also be considered. This involves successive double one-electron transfers from 2 equiv. of SmI_2 to ethyl acrylate to afford a samarium ester homoenolate (**23**); during



Scheme 6.

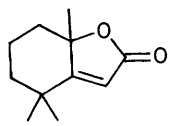
this, hydrogen abstraction from an alcohol takes place. This path, however, is not likely because the stepwise addition of ethyl acrylate and then a carbonyl compound failed to produce a reasonable yield of γ-lactone. Consequently, the major reaction path involved is considered to be a radical one.

Intramolecular Reaction.[19].—We next applied the reaction intramolecularly for the synthesis of a bicyclic γ-lactone. The



Scheme 7.

starting unsaturated keto ester (**26**) was prepared by a chemoselective Wittig reaction of 6-oxoheptanal (**24**) with ethyl(triphenylphosphoranylidene)acetate (**25**).[20] Treatment of (**26**) with 2 mole equiv. of SmI_2 in refluxing THF for 4 h afforded a 56% yield of the bicyclic γ-lactone as a mixture of *cis*-(**27a**) and *trans*-(**27b**) isomers in the ratio of *cis*:*trans* = 3:7; unchanged (**26**) was recovered in 30% yield. Product stereochemistry was assigned by comparing the ^1H n.m.r. chemical shifts for the methyl proton for each isomer with those described in the literature.[21] Compound (**27**) is interesting because of the similarity of its molecular skelton to that of the dihydroactinidiolite (**28**), a natural γ-lactone isolated from tobacco or the leaves of *Actinidia polygama*, and a potent inhibitor of seed germination and root length elongation.[22]



(**28**)

Experimental

General.—I.r. spectra were recorded on a JASCO Model A-1 spectrometer in carbon tetrachloride (CCl_4). ^1H N.m.r. spectra were taken in CCl_4 or $CDCl_3$ at 60 MHz on a Hitachi R-600 or R-24 instruments. The chemical shifts are recorded in p.p.m. relative to tetramethylsilane as an internal standard. ^{13}C N.m.r. spectra were taken in the laboratory of Professor S. Uemura, Institute for Chemical Research, Kyoto University. Microanalyses were carried out at the Microanalytical Centre of Kyoto University. G.l.c. analyses were performed by a Shimadzu GC 8A or GC 6AM apparatus on EGSS-X(3%)-Chromosorb-W(60—80 mesh)(2 m), Silicon GUM SE-30(3%)-Chromosorb-W(60—80 mesh)(2 m), and Silicon DC QF-1(5%)-Chromosorb-W(60—80 mesh)(3 m) columns using nitrogen as carrier gas. Flash column chromatography was performed on a EYELA EF-10 apparatus using E. Merck Kieselgel 60 (230—400 mesh) or Wako silica gel C-300. Preparative t.l.c. separation was conducted using 20 × 20 cm glass plates coated with a 2.0 mm thick layer of Merck Kieselgel PF_{254}. R_F Values record the positions of spots. Microdistillation was performed by using a Shibata glass tube oven GTO 250 RS apparatus.

Materials.—Samarium powder was purchased from Nippon Yttrium Co. Ltd. 1,2-Di-iodoethane (Tokyo Kasei Chemicals) in chloroform was washed with aqueous sodium thiosulphate and then with brine; the solution was then dried ($MgSO_4$) and evaporated to provide pure 1,2-di-iodoethane as a white powder. Di-iodomethane was purchased from Tokyo Kasei Chemicals and distilled before use under reduced pressure. THF was distilled under nitrogen from sodium benzophenone ketyl prior to use. Commercial HMPA was dried over CaH_2, distilled under reduced pressure, and stored on molecular sieve 5A. TMEDA was dried over NaOH, and TEGDME was stored on molecular sieve 5A. Methanol, ethanol, isopropyl alcohol, and t-butyl alcohol were distilled on magnesium ribbon; methan[^2H]ol was purchased from the CEA company. 6-Oxoheptanal[22] was prepared by ozonolysis of 1-methylcyclohex-1-ene and ethyl (triphenylphosphoranylidene)acetate was prepared by a reported method.[18] All organic compounds were commercially available and used without further purification unless otherwise noted. All reactions were run under an nitrogen atmosphere employing standard techniques for handling air-sensitive materials.

Reaction of α,β-Unsaturated Esters with Carbonyl Compounds by SmI_2: General Procedure.—A THF (5 ml) solution of 1,2-di-iodoethane (1.13 g, 4 mmol) or di-iodomethane (1.07 g, 4 mmol) was added at room temperature to samarium metal powder (0.60 g, 4 mmol). The mixture was then stirred at ambient temperature until the colour of the solution became deep green (0.5—1 h). A mixture of ethyl acrylate (0.20 g, 2 mmol), a carbonyl compound (2 mmol), and t-butyl alcohol (0.14 g, 2 mmol) in THF (5 ml) was then added simultaneously at 0 °C (for aldehydes) or at room temperature (for ketones). The resulting mixture was stirred for 2—10 h at the same temperature, during which time its colour changed to brownish yellow. The solution was poured into a dilute HCl and the aqueous layer was extracted with ether (20 ml × 3); the extract was dried ($MgSO_4$) and evaporated to leave a yellow oil which was subjected to flash column chromatography; hexane–diethyl ether (1:1) eluted a γ-lactone. The product was further purified by preparative t.l.c. and microdistillation. Spectral and combustion analytical data for the γ-lactones are summarized in Table 2.

Deuterium Exchange Reaction using Methan[^{2}H]*ol.*—This reaction was carried out in manner similar to that of the general procedure except for a non-aqueous work-up. A mixture of ethyl methacrylate (0.23 g, 2 mmol), benzaldehyde (0.20 g, 2 mmol), and MeOD (66 mg, 2 mmol) in THF (5 ml) was added at room temperature to a stirred THF (5 ml) solution of SmI_2 (1M; 4 mmol). After 2 h, the resulting mixture was filtered through a Celite bed and the precipitate washed with CCl_4 several times; the filtrate and the washing were combined. Evaporation of the solvent followed by preparative t.l.c. separation gave 2-deuterio-2,3-dimethyl-4-phenyl-γ-butyrolactone (**16′**); δ_H(60 MHz; $CDCl_3$) 1.29 (br s, CH_3, 3 H), 2.31—2.86 (m, CH_2CHO, 3 H), 5.33 t, *J* 8 Hz, CHO, 1 H), and 7.3—7.4 (m, Ph, 5 H). ^{13}C N.m.r. indicates the presence of *cis* and *trans* isomers of (**16′**) with respect to methyl and phenyl groups; δ_C 14.8 and 15.3 (q, CH_3), 38.1 and 39.7 (t, C-3), 78.5 and 79.2 (d, C-4), 125.0, 125.5, 126.8, 127.2, and 128.6 (Ph), and 179.3 and 180.0 (s, C=O). The original C-2 atom at 33.5 p.p.m. (d) is greatly diminished, and scarcely observed.

2-Deuterio-4-methyl-4-phenyl-γ-butyrolactone (**3′**).—The title compound was prepared from the reaction of ethyl acrylate with acetophenone in the presence of MeOD by the same procedure; δ_H(60 MHz; $CDCl_3$) 1.30 (s, CH_3 3 H), 2.20 (br s, CH_2CHD, 3 H), and 7.20 (s, Ph, 5 H); δ_C 29.3 (q, CH_3), 35.9 (t, C-3), 86.6 (s, C-4), 124.0, 127.5, and 128.5 (Ph), and 176.3 (s, C=O). The original C-2 signal at 28.7 p.p.m. (t) had virtually disappeared.

Preparation of trans-*Ethyl 8-Oxonon-2-enoate* (**26**).—6-Oxoheptanol (0.67 g, 5 mmol) was added to a suspension of ethyl (triphenylphosphoranylidene)acetate (2.00 g, 5 mmol) in dichloromethane (10 ml) at room temperature with magnetic stirring. The resulting solution was stirred for 12 h and then evaporated under reduced pressure. Light petroleum was added to the residue and the insoluble fraction filtered off through a Celite bed. The filtrate was concentrated and the residue was purified by microdistillation to give the product (0.64 g, 3.3 mmol, 66%); δ_H(60 MHz; CCl_4) 1.22 (t, *J* 7.5 Hz, CH_2CH_3, 3 H), 1.3—1.7 (m, 6 H), 2.03 (s, CH_3CO, 3 H), 2.19—2.5 (m, 2 H), 4.11 (q, *J* 7.5 Hz, CH_2CH_3, 2 H), 5.73 (d, *J* 16.0 Hz, =$CHCO_2$Et, 1 H), and 6.85 (dt, *J* 16.0, 7.0 Hz, CH_2CH=); $\nu_{max.}$(neat) 1 730 and 1 706 cm^{-1} (Found: C, 66.25; H, 9.05. $C_{11}H_{19}O_3$ requires C, 66.64; H, 9.15%).

Cyclization of Compound (**26**) *with* SmI_2.—Compound (**26**) (0.40 g, 2 mmol) in THF (5 ml) was added a THF solution of SmI_2 prepared in the manner described above (0.4M; 10 ml, 4 mmol) at reflux. The colour of the solution rapidly changed to dark orange, and the resulting mixture was stirred for 4 h. The solution was quenched with aqueous sodium thiosulphate, extracted with diethyl ether (20 ml × 3), dried ($MgSO_4$), and evaporated under reduced pressure. The crude product was subjected to flash column chromatography [hexane–diethyl ether (1:1) as eluant] to give a mixture of *cis* and *trans* isomers of the bicyclic γ-lactone (**27**) (0.17 g, 1.1 mmol, 55%; starting material compound (**26**) was recovered (0.12 g, 0.6 mmol, 30%). The product was further purified by preparative t.l.c. [R_F 0.30, hexane–diethyl ether (1:1)]; δ_H(60 MHz; $CDCl_3$) 1.0—2.0 (m, 9 H), 1.32 (*trans*-CH_3) and 1.40 (*cis*-CH_3) (s, 3 H), and 2.2—2.7 (m, 2 H); $\nu_{max.}$(CCl_4) 1 774 cm^{-1}; *m/z* 154 (M^+) (Found: C, 70.05; H, 9.15. $C_9H_{14}O_2$ requires C, 70.10; H, 9.15%).

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