Intramolecular Reductive Cyclization of Unsaturated Keto- or Aldo-esters by Samarium(II) Di-iodide: A Ready Synthesis of Bicyclic γ-Lactones

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Treatment of unsaturated keto- or aldo-esters with Sml_2 in tetrahydrofuran (THF) or THF-hexamethylphosphoramide affords bicyclic γ -lactones in moderate to good yields.

Numerous efforts have been made to prepare bicyclic γ -lactones, not only because their abundant occurrence in Nature, but also because of their usefulness as versatile synthons. As a result, various methods have been developed, *e.g.*, electrophilic ring-opening of a cyclopropanecarboxylic acid ester,¹ or spiro-oxirane;² the free-radical cyclization of a bromoacetal;³ the intramolecular lactonization of an unsaturated ester by PhSeCl;⁴ and the oxidative cyclization of an alkene containing a tertiary hydroxy-group by chromium(v).⁵

We have recently reported the intermolecular reductive coupling of α , β -unsaturated esters and carbonyl compounds by samarium(II) di-iodide (SmI₂), to give γ -lactones.⁶ We thought that if this procedure could be extended to an intramolecular reaction, bicyclic γ -lactones would be produced in one step; and indeed, they may be obtained from unsaturated keto- and aldo-esters in moderate to good yields under mild conditions.

Several *trans*-unsaturated keto- or aldo-esters were prepared by standard procedures.⁷ Treatment of these substrates with SmI₂ in tetrahydrofuran (THF) or THF-hexamethylphosphoramide (HMPA) (10:1) afforded moderate to good yields of bicyclic γ -lactones.[†] Reaction of *trans*-ethyl 8-oxonon-2-enoate (1; R = Me; n = 2) with SmI₂ was examined under a variety of conditions (changing solvent, temperature, time, amount of SmI₂, and addition of Fe^{III} catalyst). Results are shown in Table 1 (entries 2—6). Reaction proceeded either at room temperature or at reflux; reflux conditions usually gave higher yields. HMPA was not essential as co-solvent, but its addition tended to improved the product yields. Addition of a trace of FeCl₃ is effective for the Barbier-type reaction involving the use of SmI₂,⁸ but the yield was not improved in this case. The use of an excess of SmI₂ gave more satisfactory results.

Table 1. Intramolecular reductive cyclization of unsaturated keto- or aldo-esters by $SmI_{2,a}$

(1)			Isolated Isomer ratiob	
Entry	n	R Reaction conditions	yield (%)	trans : cis
1	1	$Me 2SmI_2$, THF, reflux, 4 h	92	90:10
2	2	Me 2 SmI ₂ , THF, reflux, 4 h	56	64:36
3	2	Me 2SmI ₂ , THF-HMPA, 25 °C, 5 h	36 (42)°	70:30
4	2	Me 2SmI ₂ , THF-HMPA, reflux, 1 h	47 (54)°	79:21
5	2	$Me 2SmI_2$, THF-HMPA, reflux,	38 (43)°	66:34
		$1 h, FeCl_3(1\%)$		
6	2	Me 4SmI ₂ , THF-HMPA, reflux, 1 h	66 (75)°	70:30
7	3	Me 4SmI ₂ , THF, reflux, 1 h	45	80:20
8	3	Me 2SmI ₂ , THF-HMPA, reflux, 1 h	40	75:25
9	8	Me 4SmI ₂ , THF-HMPA, reflux, 1 h	40 ^d	
10	1	H $4SmI_2$, THF-HMPA, reflux, 1 h	43	e
11	2	H 4SmI ₂ , THF-HMPA, 25 °C, 5 h	30	75:25
12	2	H 4 SmI ₂ , THF-HMPA, reflux, 1 h	34	70:30

^a (1) (1 mmol), BuⁱOH (1 mmol), THF (10 ml) or THF-HMPA (10 ml-1 ml). ^b Determined by ¹H n.m.r. and g.l.c. ^c G.l.c. yield. ^d 14-Hydroxypentadec-2-enoate was produced. ^e Not determined.

[†] A typical experimental procedure is as follows. To a refluxing blue-green solution of SmI₂ (0.4 m; 10 ml) in THF-HMPA (9–1 ml) was added a THF (1 ml) solution of 8-oxonon-2-enoate (1; R = Me, n = 2, 198 mg, 1 mmol) and t-butyl alcohol (1 mmol) with stirring. The refluxing was continued for 1 h, during which period the solution turned yellow-green. After the usual work-up, the bicyclic γ -lactone (2; R = Me, n = 2, 104 mg, 0.66 mmol) was obtained in 66% yield by flash column chromatography on silica gel (hexane-ethyl acetate, 10:1, as eluant). The isomer ratio was determined by ¹H n.m.r.⁹ and g.l.c. The product gave satisfactory analytical results, and the i.r. spectrum (v_{CO} 1765 cm⁻¹) and mass spectrum (M^+ 154) were in accord with the structure assigned.





The bicyclic γ -lactone (2; R = Me, n = 2) was obtained as a mixture of *trans*- and *cis*-isomers in a *trans* to *cis* ratio of 70:30. The ratio was determined by the relative intensity of methyl proton absorption and g.l.c.⁹ It was almost independent of the reaction conditions; thus we infer that the bicyclic γ -lactone was the kinetic product of the reaction.

The analogous reaction occurred with ethyl 7-oxo-oct-2enoate (1; R = Me, n = 1), ethyl 9-oxodec-2-enoate (1; R = Me, n = 3), ethyl 7-oxohept-2-enoate (1; R = H, n = 1), and ethyl 8-oxo-oct-2-enoate (1; R = H, n = 2) to produce the corresponding bicyclic γ -lactones as mixtures of *trans*- and *cis*-isomers in good yields (Table 1, entries 1, 7---8, 10---12).¹⁰ However, the longer-chain unsaturated keto-esters such as ethyl 14-oxopentadec-2-enoate (1; R = Me, n = 8) did not yield (2); simple carbonyl reduction occurred instead (entry 9).

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References

- 1 S. P. Brown and B. S. Bal, Tetrahedron Lett., 1981, 22, 4891.
- 2 L. Sterkowski and M. A. Batliste, Tetrahedron Lett., 1981, 22, 279.
- 3 G. Stork, R. Mook, Jr., S. A. Biller, and S. D. Rychrovsky, J. Am. Chem. Soc., 1983, 105, 3741.
- 4 K. C. Nicolaou, S. P. Seitz, W. J. Sipio, and J. F. Blount, J. Am. Chem. Soc., 1979, 101, 3884.
- 5 T. K. Chakraborty and S. C. Sekaran, *Tetrahedron Lett.*, 1984, 27, 2895.
- 6 S. Fukuzawa, A. Nakanishi, T. Fujinami, and S. Sakai, J. Chem. Soc., Chem. Commun., 1986, 624. See also preceding communication.
- 7 trans-Unsaturated keto-esters were prepared by a chemoselective Wittig reaction of the corresponding keto-aldehydes with ethyl (triphenylphosphoranylidene)acetate. trans-Unsaturated aldoesters were prepared from δ -valero- and ε -capro-lactone according to the literature methods. (a) J. M. Takacs, M. A. Helle, and F. L. Seely, *Tetrahedron Lett.*, 1986, **27**, 1257; (b) R. D. Little and G. W. Mueller, J. Am. Chem. Soc., 1981, **103**, 2744.
- 8 P. Girard, J. L. Namy, and H. B. Kagan, J. Am. Chem. Soc., 1980, 102, 2693.
- 9 (a) J. Ficini and A. Manjean, Bull. Soc. Chim. Fr., 1971, 219; (b) T. K. D. Gupta, D. Felix, U. M. Kempe, and A. Eschenmoser, Helv. Chim. Acta, 1972, 55, 2198. trans-CH₃ appears at higher field, δ 1.32, than cis-CH₃, δ 1.44.
- 10 P. Buldt, W. Thieleche, and J. Etzenmueler, Chem. Ber., 1969, 102, 4157.