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A Direct Synthesis of γ-, δ-, and ε-Lactones Utilizing SmI_2-induced Barbier-type Reaction in the Presence of Hexamethylphosphoric Triamide (HMPA)[1)]

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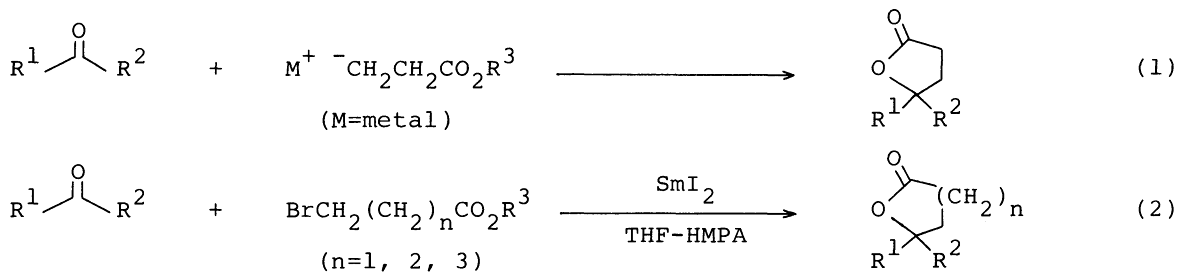
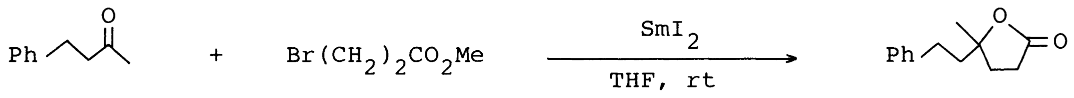
By using an efficient reduction system of SmI_2-THF-HMPA, the coupling reaction of β-, γ-, or δ-bromoesters with carbonyl compounds was completed within a minute at room temperature affording γ-, δ-, or ε-lactones, respectively, in good yields. Cp_2ZrCl_2 was also found to be effective for the coupling with ketones.

One of the important functions of β-metalloesters and their equivalents[2)] as versatile homoenolate species is that they provide a direct way to γ-lactones[3)] from carbonyl compounds, and the preparation of lithium,[3a)] titanium,[3b)] zinc,[3c)] or lanthanide metal homoenolates[3d)] has been reported. (Eq. 1) However, they are sometimes not prepared straightforwardly or not always effective for both aldehydes and ketones. Furthermore, there have been almost no similar methods for the one step synthesis of δ- as well as ε-lactones from easily available materials.



In the preceding paper, we reported that one electron transfer reduction of organic halides by SmI_2 was remarkably accelerated by the addition of HMPA.[4)] We then found that the Barbier-type condensation of organic halides with carbonyl compounds by SmI_2, which had been rather sluggish in the absence of HMPA[5a,b)] except for some activated halides,[5c,e,f)] was also promoted to a large extent by the addition of HMPA,[6)] making the method a quite useful one. In this communication, we wish to report a mild, convenient, and general method for the direct synthesis of γ-,[3e,f)] δ-, and ε-lactones from commercially available β-bromopropionate, γ-bromobutyrate, or δ-bromovalerate and aldehydes or ketones by utilizing the above HMPA-promoted Barbier-type reaction with SmI_2, where intermediary radical species[7)] may be involved instead of carbanion species such as metal homoenolates. (Eq. 2) It should be noted that Fukuzawa et al.[3d)] have already reported the use of metallic Sm for this type of γ-lactone synthesis, though without the use of HMPA.

Table 1. Effect of Additives on γ-Lactone Synthesis using SmI_2[a)]



Run	Additive[b)]	Reaction time/min	Yield/%[c)]
1	none	120	39
2[d)]	$FeCl_3$	120	50
3	Cp_2ZrCl_2	30	98
4	HMPA	1	85

a) The reactions were carried out by using 4-phenyl-2-butanone (0.1 mmol), methyl β-bromopropionate (0.2 mmol), and a SmI_2-THF solution (0.1 mol dm^{-3}, 4 ml) at room temperature with or without an additive. b) $FeCl_3$ (3.3 mg, 20 mol%), Cp_2ZrCl_2 (35 mg, 1.2 equiv.), or HMPA (0.1 ml) was used as an additive. c) Isolated yield. d) Methyl β-bromopropionate (0.3 mmol) and a SmI_2-THF solution (0.1 mol dm^{-3}, 5 ml) was used.

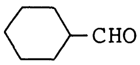
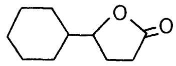
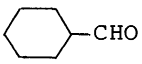
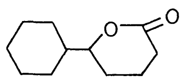
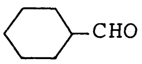
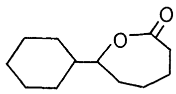
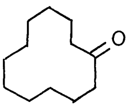
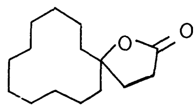
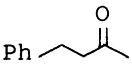
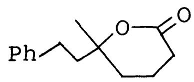
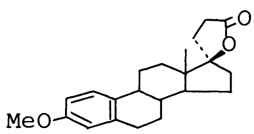
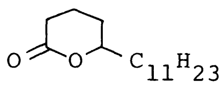
In Table 1 are shown the effect of some additives on the formation of a γ-lactone from 4-phenyl-2-butanone and β-bromopropionate. Interestingly, other than HMPA (Run 4), Cp_2ZrCl_2 also gave a high yield of the product (Run 3), probably because of its carbonyl activating property. On the other hand, $FeCl_3$ which has been known to be an efficient catalyst for Barbier-type reaction,[8)] did not give a notable effect (Run 2).

Other results are given in Table 2. Aldehydes produced a considerable amount of pinacols as by-products[9)] in the presence of Cp_2ZrCl_2 (e.g. Runs 1 and 3). A proper concentration of the ketyl radicals in the reaction media seems to be important for the present cross-coupling reaction.

The method is also applicable to the one-pot synthesis of δ- and ε-lactones other than γ-lactones. Although the yields of δ- or ε-lactones are not very high, it is noteworthy that γ-bromobutyrate or δ-bromovalerate has been formally converted into a bishomoenolate[2b)] or a δ-carbanionic ester equivalent, respectively, neither of which is easily obtainable.

Thus, a general and very convenient method for the direct synthesis of γ-, δ-, and ε-lactones was established. It should be noted that the reaction can be conducted under extremely mild conditions since the coupling reaction initiated by one electron transfer from SmI_2 proceeds rapidly at room temperature under essentially neutral conditions.

Table 2. SmI_2-induced Coupling Reaction of Carbonyl Compounds with β-, γ-, or δ-Bromoester[a)]

Run	Carbonyl compound	Bromoester	Additive	Time/min	Product[b)]	Yield/%[c)]
1		$Br(CH_2)_2CO_2Me$	Cp_2ZrCl_2	30		49[d)]
2		$Br(CH_2)_2CO_2Me$	HMPA	1		88
3		$Br(CH_2)_3CO_2Et$[e)]	Cp_2ZrCl_2	40		29[d)]
4		$Br(CH_2)_3CO_2Et$[e)]	HMPA	1		54[d)]
5		$Br(CH_2)_4CO_2Et$	HMPA	1		53[f)]
6		$Br(CH_2)_2CO_2Me$	Cp_2ZrCl_2	20		80
7		$Br(CH_2)_2CO_2Me$	HMPA	1		75
8		$Br(CH_2)_3CO_2Et$[e)]	Cp_2ZrCl_2	40		42[d)]
9		$Br(CH_2)_3CO_2Et$[e)]	HMPA	1		55[d)]
10	3-O-methyl-estrone	$Br(CH_2)_2CO_2Me$	Cp_2ZrCl_2	30	 g)	26[h)]
11		$Br(CH_2)_2CO_2Me$	HMPA	1		41[h)]
12	$C_{11}H_{23}CHO$	$Br(CH_2)_3CO_2Et$	HMPA	1	 i)	44

a) The reactions were carried out by using carbonyl compounds (0.1—1 mmol), bromoesters (0.2—2 mmol), and a SmI_2-THF solution (0.1 mol dm^{-3}, 4—40 ml) in THF (1—5 ml) with Cp_2ZrCl_2 (0.12—1.2 mmol) or HMPA (0.1—1 ml) at room temperature under an atmosphere of nitrogen. The reaction products were stirred with aq. HCl solution (1 mol dm^{-3}, 0.1—1 ml) and SiO_2 (1—10 g) for 10 min and then worked up in the usual manner. b) Satisfactory ^1H NMR, IR, and analytical data were obtained. c) Isolated yield. d) The major byproduct was the corresponding pinacol. e) 4 equiv. of bromoester was used. f) A mixture of ε-lactone and the corresponding hydroxy ester (ca. 3:2). g) This spirolactone has been synthesized in 5 steps from the same starting ketone (25% overall yield) [E.Ehlinger and P.Magnus, J. Am. Chem. Soc., 102, 5004 (1980)]. See also Ref. 3f. h) The starting ketone (50—60%) was recovered. i) A pheromone of the oriental hornet. [For recent syntheses of this lactone: See D.B.Gerth and B.Giese, J. Org. Chem., 51, 3726 (1986) and references cited therein.]

References

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4) J.Inanaga, M.Ishikawa, and M.Yamaguchi, the preceding paper.
5) Previous examples of SmI_2-induced Barbier-type reactions without the use of HMPA. a) P.Girard, J.L.Namy, and H.B.Kagan, J. Am. Chem. Soc., 102, 2693 (1980); b) H.B.Kagan, J.L.Namy, and P.Girard, Tetrahedron, 37, Suppl. No 1, 175 (1981); c) For benzyloxymethylation of carbonyl compounds: T.Imamoto, T.Takeyama, and M.Yokoyama, Tetrahedron Lett., 25, 3225 (1984); d) For intramolecular Barbier-type reaction: G.A.Molander and J.B.Etter, ibid., 25, 3281 (1984); G.A.Molander, J.B.Etter, and P.W.Zinke, J. Am. Chem. Soc., 109, 453 (1987); e) For iodomethylation of carbonyl compounds: T.Imamoto, T.Takeyama, and H.Koto, Tetrahedron Lett., 27, 3243 (1986); T.Tabuchi, J.Inanaga, and M.Yamaguchi, ibid., 27, 3891 (1986); f) For intramolecular Reformatsky-type reaction: T.Tabuchi, K.Kawamura, J.Inanaga, and M.Yamaguchi, ibid., 27, 3889 (1986).
6) The reaction of 2-octanone with n-BuBr or sec-BuBr in a SmI_2-THF-HMPA solution gave the corresponding coupling products within 1 min in 92 or 90% yield, respectively, which are much better than the results without HMPA (67%, refl, 1 day or 27%, refl, 1.5 days, respectively: see Ref. 5a).
7) SmI_2-induced Barbier-type reaction has been suggested to proceed through radical process (Ref. 5b), and a coupling reaction of ethyl β-bromopropionate with cyclohexanone by the aid of SmI_2 in the absence of HMPA has also been reported to give the corresponding γ-hydroxy ester in 28% yield under reflux in THF for 1 day (Ref. 5a). See also B.Giese and H.Horler, Tetrahedron, 41, 4025 (1985) and references cited therein.
8) Cp_2ZrCl_2 is not reduced by SmI_2 whereas Fe(III) species have been known to be reduced under the conditions and to participate in the generation of a ketyl radical (Refs. 5a, b, and d).
9) J.L.Namy, J.Souppe, and H.B.Kagan, Tetrahedron Lett., 24, 765 (1983).

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