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Samarium(II) iodide-induced cascade reaction for tricyclic γ-lactone synthesis from acyclic keto diesters

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ABSTRACT

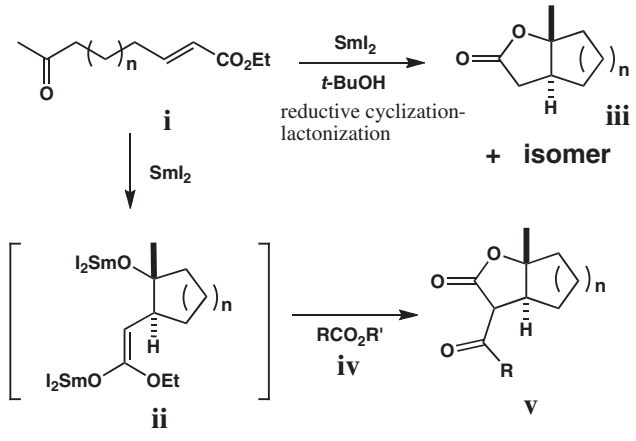
Cascade reaction involving reductive cyclization, Dieckmann condensation, and lactonization of *E*- and *Z*-dimethyl 2-methyl-8-oxoundec-2-enedioates and *Z*-dimethyl 2-methyl-7-oxodec-2-enedioate with samarium(II) iodide was found to stereospecifically produce *cis* and *trans* bicyclo[4.4.0]decane (decalin) ring systems and *trans* bicyclo[4.3.0]nonan (perhydroindane) ring system each consisting of γ-lactone, respectively.

Polycyclic γ-lactones are structural constituents present in various natural products such as C_{19}-gibberellins,[1] ginkgolide B,[2] 3-methoxy-15-oxozoapatlin,[3] each of which possessing biological significance. The samarium(II) iodide (SmI_2) -induced sequential reductive coupling–lactonization of acyclic keto ester **i** is effective for forming bicyclic γ-lactones **iii**,[4] but to our knowledge, this process has not yet to be shown to bring about the further functionalization through capture of enolate **ii** with ester **iv** to produce γ-lactone **v** (Scheme 1).

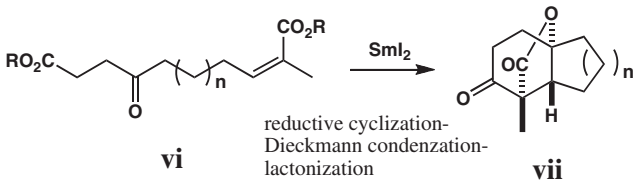
Samarium enolates generated from bis-α,β-unsaturated esters with SmI_2 or from dimethyl 1,2-cyclobutanedicarboxylates with SmI_2–HMPA have recently been shown at this laboratory to react intramolecularly with the ester carbonyl group to provide α-methoxycarbonylcyclopentanones.[5] Thus possibly, samarium enolate **ii** may react with an ester placed at an appropriate position in the same molecule so as to produce tricyclic γ-lactones. In this study, the authors conducted a one-step synthesis of bicyclo[4.2+n.0]-alkan-3-ones **vii** ($n = 1, 2$) each bearing a γ-lactone from acyclic keto diesters **vi** ($n = 1, 2$) via Sm(II)-induced stereospecific cascade reaction involving reductive coupling, Dieckmann condensation, and lactonization (Scheme 2).

The results of the cyclization reactions of keto diesters **3** to **6** with SmI_2 are presented in Table 1.

The substrate **3**[6] bearing *E*-olefin and its *Z* isomer **4**[7] possessing a ketone, an ester, and an α,β-unsaturated ester were prepared selectively from methyl 3-chloroformylpropionate in a three-step



Scheme 1.



Scheme 2.

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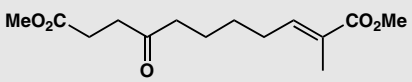
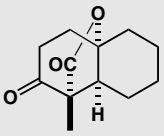
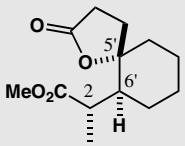
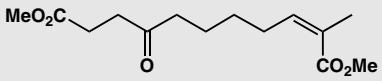
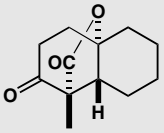
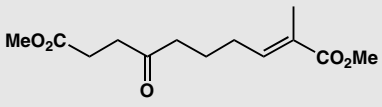
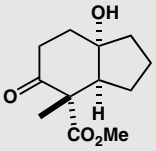
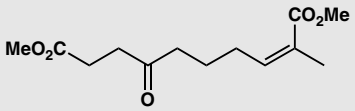
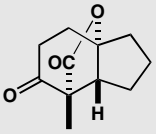
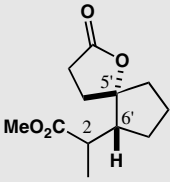
Table 1
Sequential reductive coupling–Dieckmann Condensation–lactonization to yield bicyclo[4.4.0]decanones and bicyclo[4.3.0]nonanones[a]

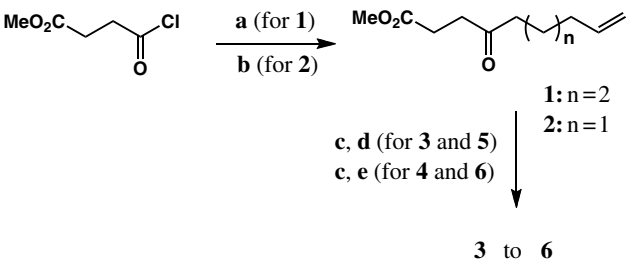
Entry	Esters	Additive	Time	Products (Yield)[b]
1	 **3**	None	1 h	 **7**[c] (63%) +  **8**[d] (11%)
2	**3**	HMPA[e]	30 min	**7** (61%)
3	 **4**	None	2 h	 **9**[c] (59%)
4	**4**	None	15 h[f]	**9** (75%)
5	**4**	HMPA[e]	30 min	**9** (37%)[g]
6	 **5**	None	30 min	 **10**[c] (88%)
7	**5**	HMPA[e]	10 min	**10** (52%)[g]
8	 **6**	None	1 h	**10** (21%) +  **11** (57%) +  **12**[h] (6%)
9	**6**	HMPA[e]	10 min	**10** (43%) + **11** (8%) + **12** (11%)

[a] Reactions were conducted at 0.25–0.50 mmol scale and carried out at room temperature, and 3.0 equiv of SmI_2 was used.
[b] Isolated yield.
[c] Stereochemistry was determined by X-ray analysis.
[d] The relative configurations at C-2, C-5′, and C-6′ were determined by NOE experiment.
[e] 5.0 equiv of HMPA was used.
[f] This reaction was carried out at 0 °C.
[g] This reaction produced small amount (10–20% yield) of highly polar compounds, but the structures of them were not identified.
[h] The relative configuration at C-5′ and C-6′ was determined by NOE experiment, but that of C-2 and C-6′ was not determined.

sequence, which involves an introduction of hexenyl group using 5-hexenyl magnesium bromide-CuI in THF to give **1**,[8] ozonolysis, and Wittig reaction for preparing **3** or modified Horner–Emmons reaction[9] for preparing **4** (Scheme 3). Substrates **5**[10] and **6**,[11] each of whose methylene chains was one unit shorter, were prepared from the same starting material via **2** in the same manner as above, except for the use of 4-pentenyl magnesium bromide-CuI instead of 5-hexenyl magnesium bromide-CuI.

On treating keto diester **3** having the *E* olefin with 3 equiv of SmI_2[12] prepared from samarium metal and 1,2-diiodoethane in THF at room temperature, tricyclic compound **7**[13] comprising a *cis* bicyclo[4.4.0]decane (decalin) ring system and γ-lactone was obtained as the major product in 63% yield along with spiro γ-lactone **8**[14] (entry 1). Treatment of **4** bearing the *Z* olefin with SmI_2 in THF gave **9**[15] consisting of a *trans* decalin ring system and γ-lactone as the major product (entries 3 and 4). The stereochemistries of ring junctures in **7** and **9** were determined by X-ray crystallography (Fig. 1).[16]

Treatment of *E* isomer **5** with SmI_2 in THF gave stereoselectively bicyclic keto ester **10**[17] possessing a *cis* perhydroindan ring system



Scheme 3. Reagents and conditions: (a) $CH_2{=}CHCH_2CH_2CH_2CH_2MgBr$, CuI, THF, 1 h, 0 °C, 80%; (b) $CH_2{=}CHCH_2CH_2CH_2MgBr$, CuI, THF, 1 h, 0 °C, 80%; (c) O_3, CH_2Cl_2, −78 °C then Ph_3P; (d) $Ph_3P{=}C(Me)CO_2Me$, CH_2Cl_2, rt, **3**, 75% from **1**, **5**, 81% from **1**; (e) $(CF_3CH_2O)_2P(O)CH(Me)CO_2Me$,[9] $KN(TMS)_2$, 18-Crown-6, THF, −78 °C, **4**, 72% from **2**, **6**, 88% from **2**.

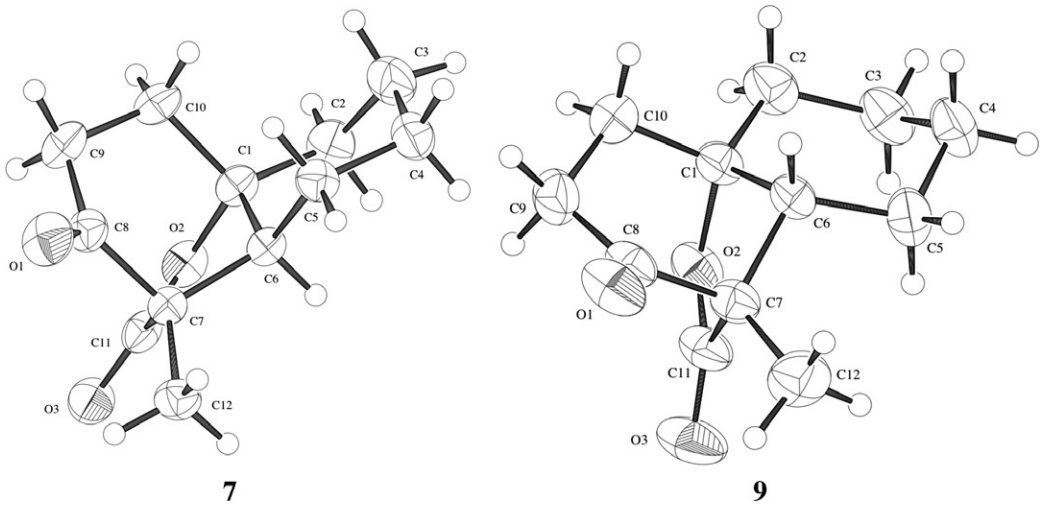


Figure 1. X-ray structures of **7** and **9**.

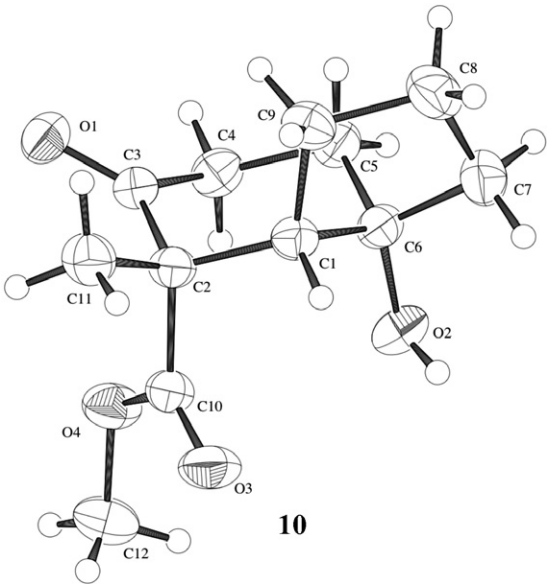
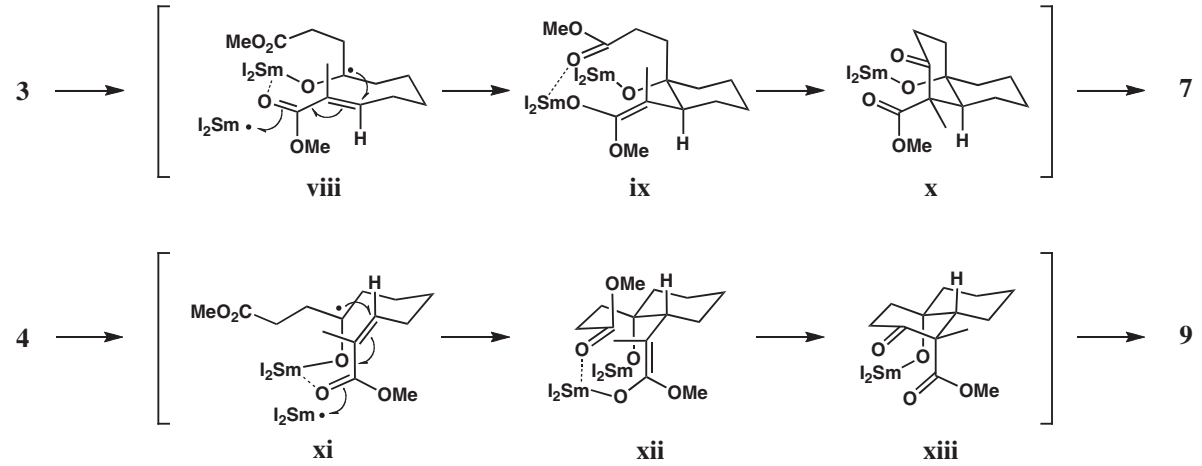


Figure 2. X-ray structure of **10**.

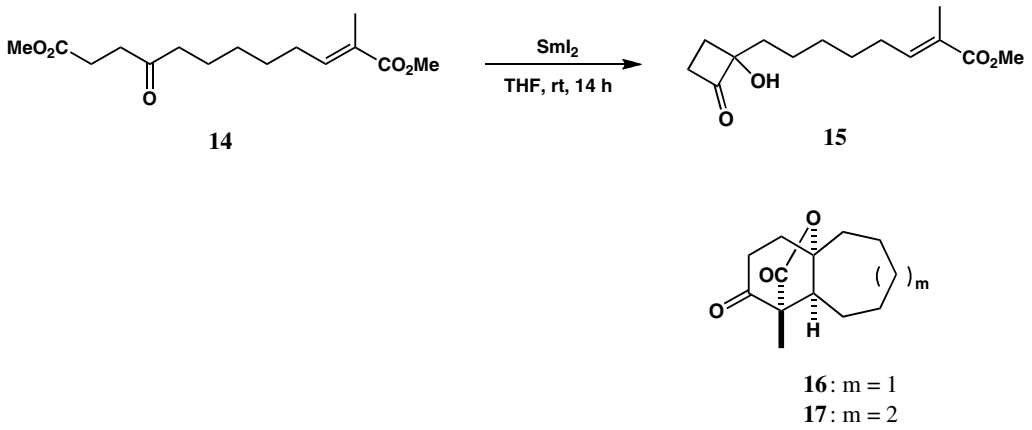
in high yield, though the lactonization step failed to proceed, as expected, owing to the excessive strain of the corresponding lactone (entry 6). The stereochemistry of **10** was determined by X-ray crystallography (Fig. 2).[16] Reaction of **6** bearing the *Z* olefin with SmI_2 in THF provided the corresponding tricyclic compound **11**[18] consisting of a trans ring juncture and γ-lactone as the major product (entry 8).

Each stereoisomer related to the ring juncture in the decalin system or perhydroindan system may thus be obtained selectively by appropriately selecting the geometry of the double bond in a cyclization substrate. HMPA as an additive has been shown to augment the rate of the reaction and inhibit the formation of spirolactone, but yields of the desired products were seen to be somewhat less compared to the case without HMPA (entries 2, 5, and 7).[19] But in the reaction of **6** with SmI_2, stereoselectivity appeared strongly affected by the addition of HMPA (entry 9).[20]

Stereoselectivity in the sequential cyclization of **3** and **4** with SmI_2 in THF may be explained as due to the generation of a favored chelated intermediate, as shown in Scheme 4. The first single electron reduction of **3** with SmI_2 should provide a ketyl radical **viii**. C–C bond formation in the chelated intermediate **viii** would consequently take place with high stereoselectivity to produce **ix**. The Dieckmann condensation of **ix** may produce keto ester **x** likely



Scheme 4.



Scheme 5.

to undergo lactonization to afford cis isomer **7**. The reaction of **4** would then appear to possibly produce the chelated intermediate **xi**, from which trans isomer **9** may be formed via **xii** and **xiii**.

The present method was found unsuitable for preparing bicyclo[5.4.0]undecan-8-one **16** or bicyclo[6.4.0]dodecan-9-one **17**. Treatment of **14**[21] with SmI_2 in THF gave cyclobutanone **15**[22] in low yield (27%), and the expected **16** ($m = 1$) was not produced at all (Scheme 5).[23]

In a typical experiment, a suspension of Sm (292 mg, 1.94 mmol) and 1,2-diiodoethane (469 mg, 1.67 mmol) in THF (17 mL) was sonicated for 2 h at room temperature under argon and cooled to −78 °C. To the mixture, a solution of keto diester **3** (150 mg, 0.556 mmol) in THF (1.4 mL) was added dropwise over 1 min and then the mixture was warmed to room temperature. After 1 h at this temperature, the reaction was quenched with bubbling air. The resulting mixture was diluted with ether, washed with 1N hydrochloric acid, water, saturated sodium thiosulfate, saturated sodium bicarbonate, and brine, dried over magnesium sulfate and concentrated. The crude product was separated by silica gel column chromatography eluted with ethyl acetate: hexane = 1:5 to give keto lactone **7** (73.1 mg, 63% yield) as colorless crystals and spirolactone **8** (15.0 mg, 11% yield) as a colorless oil.

The authors have thus established a new process for obtaining tricyclic γ-lactones from readily available acyclic keto diesters, which is conducted by SmI_2-induced cascade reaction. The mild reaction conditions in this method should render it applicable for the synthesis of complex molecules possessing sensitive functional groups in the final stage.

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6. *Data for* **3**: IR (neat) ν_{max}: 2951, 1740, 1717, 1653 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 1.44 (quin, 2H, $J = 7.5$ Hz), 1.58–1.68 (m, 2H), 1.82 (s, 3H), 2.18 (q, 2H, $J = 7.3$ Hz), 2.47 (t, 2H, $J = 7.3$ Hz), 2.56–2.73 (m, 4H), 3.67 (s, 3H), 3.73 (s, 3H), 6.72 (t, 1H, $J = 7.3$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.4, 23.5, 27.8, 28.1, 28.5, 37.1, 42.5, 51.7, 51.8, 127.8, 141.8, 168.5, 173.1, 208.4; FABMS *m/z*: 271 (M+1); HR-FABMS Calcd for $C_{14}H_{23}O_5$: 271.1545; found: 271.1542.
7. *Data for* **4**: IR (neat) ν_{max}: 2953, 1740, 1717, 1647 cm^{-1}; ^1H-NMR (300 MHz, $CDCl_3$) δ: 1.35–1.45 (m, 2H), 1.56–1.65 (m, 2H), 1.87 (d, 3H, $J = 1.3$ Hz), 2.42–2.48 (m, 4H), 2.55–2.73 (m, 4H), 3.66 (s 3H), 3.72 (s 3H), 5.90 (dt, 1H, $J = 1.3$, 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.6, 23.3, 27.7, 28.8, 29.2, 37.0, 42.4, 51.2, 51.7, 127.1, 142.9, 168.4, 173.3, 208.8; FABMS *m/z*: 271 (M+1); HR-FABMS Calcd for $C_{14}H_{23}O_5$: 271.1545; found: 271.1546.
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10. *Data for* **5**: IR (neat) ν_{max}: 2953, 1740, 1715, 1651 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 1.75 (quin, 2H, $J = 7.5$ Hz), 1.82 (d, 3H, $J = 1.3$ Hz), 2.15–2.22 (m, 2H), 2.48 (t, 2H, $J = 7.3$ Hz), 2.56–2.73 (m, 4H), 3.67 (s 3H), 3.73 (s 3H), 6.71 (dt, 1H, $J = 1.3$, 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 12.4, 22.5, 27.7, 27.8, 37.1, 41.9, 51.7, 51.8, 128.4, 141.2, 168.5, 173.2, 208.3; EIMS *m/z*; 256 (M^+, 0.64), 224 (100), 192 (83), 165 (35), 127 (41), 115(57), 109(69), 98 (87); HR-MS Calcd for $C_{13}H_{20}O_5$: 256.1311; found: 256.1315.
11. *Data for* **6**: IR (neat) ν_{max}: 2953, 1740, 1717, 1647 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 1.70 (quin, 2H, $J = 7.5$ Hz), 1.89 (d, 3H, $J = 1.4$ Hz), 2.45 (q, 2H, $J = 7.5$ Hz), 2.47 (t, 2H, $J = 7.5$ Hz), 2.56–2.73 (m, 4H), 3.67 (s 3H), 3.72 (s 3H), 5.88 (dt, 1H, $J = 1.4$, 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.6, 23.2, 27.7, 28.8, 37.1, 42.0, 51.2, 51.8, 127.7, 142.1, 168.3, 173.3, 208.6; EIMS *m/z*; 256 (M^+, 0.55), 224 (100), 192 (87), 165 (46), 127 (39), 115 (66), 109 (75), 98 (81); HR-MS Calcd for $C_{13}H_{20}O_5$: 256.1311; found: 256.1310.
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13. *Data for* **7**: mp: 122 °C; IR (KBr) ν_{max}: 2941, 1765, 1715 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 1.22 (dq, 1H, $J = 13.1$, 3.6 Hz), 1.24 (S, 3H), 1.36 (tq, 1H, $J = 13.7$, 4.6 Hz), 1.53 (tq, 1H, $J = 13.1$, 4.6 Hz), 1.69 (ddt, 1H, $J = 13.1$, 3.7, 1.2 Hz) 1.80 (dt, 1H, $J = 12.5$, 4.9 Hz), 1.85–1.93 (m, 2H), 2.11 (m, 1H), 2.17 (m, 1H), 2.26 (ddd, 1H, $J = 3.6$, 1.8 Hz), 2.46–2.55 (m, 2H), 2.61 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 12.4, 22.7, 22.8, 25.0, 28.5, 34.1, 34.7, 58.2, 60.0, 84.2, 175.7, 202.1; EIMS *m/z*: 208 (M^+, 14), 164 (82), 153 (3), 122 (100), 55 (12); HR-MS Calcd for $C_{12}H_{16}O_3$: 208.1099; found: 208.1091.
14. *Data for* **8**: EIMS *m/z*; 240 (M^+, 31), 208 (100), 180 (60), 150 (42), 111 (61); HR-MS calcd for $C_{13}H_{20}O_4$: 240.1362, found: 240.1363; IR (neat) ν_{max}: 2937, 1774, 1740 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 0.94 (dq, 1H, $J = 12.5$, 3.6 Hz), 1.15 (d, 3H, $J = 6.8$ Hz), 1.19–1.43 (m, 2H), 1.63–1.82 (m, 4H), 1.84–2.00 (m, 2H), 2.07–2.28 (m, 2H), 2.37 (dq, 1H, $J = 9.9$, 6.8 Hz), 2.55–2.60 (m, 2H), 3.66 (s, 3H,); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 15.8, 23.2, 24.7, 24.9, 25.9, 28.4, 38.0, 40.0, 47.9, 51.9, 88.9, 176.2, 176.9; EIMS *m/z*; 240 (M^+, 31), 208 (100), 180 (60), 150 (42), 111 (61); HR-MS Calcd for $C_{13}H_{20}O_4$: 240.1362; found: 240.1363.
15. *Data for* **9**: mp: 61 °C; EIMS *m/z*: 208 (M^+, 100), 164 (61), 153 (14), 122 (76), 95 (73), 55 (20); HR-MS calcd for $C_{12}H_{16}O_3$: 208.1099, found: 208.1091; IR (KBr) ν_{max}: 2933, 1774, 1724, 1713 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 1.13–1.17 (m,

2H), 1.20 (s, 3H), 1.43–1.53 (m, 2H), 1.68 (m,1H), 1.73–1.83 (m, 2H), 1.89 (ddd, 1H, J = 14.0, 11.0, 7.8 Hz), 2.14 (dd, 1H, J = 11.3, 5.8 Hz), 2.29 (dt, 1H, J = 11.0, 2.1 Hz), 2.32 (ddd, 1H, J = 14.0, 8.9, 1.2 Hz), 2.59 (ddd, 1H, J = 16.5, 7.6, 1.5 Hz), 2.66 (ddd, 1H, J = 16.8, 11.0, 8.9 Hz);^{13}C NMR (75 MHz, $CDCl_3$) δ: 9.5, 20.4, 23.2, 24.9, 32.5, 35.5, 36.7, 49.5, 63.7, 82.4, 175.7, 201.7; EIMS m/z; 208 (M^+, 100), 164 (61), 153 (14), 122 (76), 95 (73), 55 (20); HR-MS Calcd for $C_{12}H_{16}O_3$: 208.1099; found: 208.1091.

16. *Crystallographic data of* **7**: $C_{12}H_{16}0_3$, M_w = 208.26, monoclinic, primitive, a = 13.055(3), b = 8.305(2), c = 9.974(2) Å, β = 94.65(2)°, V = 1077.8(4) Å^3, space group $P2_1/a$ (#14), Z = 4, D_c = 1.283 g/cm^3, Rigaku AFC7S Diffractometer, Radiation CuKα (λ = 1.54178 Å, T = 296 K), R = 0.066, Rw = 0.158, R_1 = 0.041, GOF = 1.30 for 2094 reflections with $I > 2.0\sigma(I)$ out of 2250 reflections collected. CCDC 650890 contains the supplementary crystallographic data for **7**.
Crystallographic data of **9**: $C_{12}H_{16}0_3$, M_w = 208.26, triclinic, primitive, a = 11.1716(9), b = 11.941(3), c = 8.538(1) Å, α = 105.59(2), β = 91.744(8), γ = 84.59(1)°, V = 1092.1(3) Å^3, space group $P1$ (#2), Z = 4, D_c = 1.266 g/cm^3, Rigaku AFC7S Diffractometer, Radiation CuKα (λ = 1.54178 Å, T = 297 K), R = 0.068, Rw = 0.247, R_1 = 0.050, GOF = 1.74 for 4062 reflections with $I > 2.0\sigma(I)$ out of 4269 reflections collected. CCDC 650891 contains the supplementary crystallographic data for **9**.*Crystallographic data of* **10**: $C_{12}H_{18}0_4$, M_w = 226.27, triclinic, primitive, a = 12.513(1), b = 12.616(3), c = 8.219(1) Å, α = 106.66 (1)°, β = 93.044(10)°, γ = 72.08(1)°, V = 81.9(3)Å^3, space group $P1$ (#2), Z = 4, D_c = 1.272 g/cm^3, Rigaku AFC7S Diffractometer, Radiation Cu Kα (λ = 1.54178 Å, T = 291 K), R = 0.087, Rw = 0.214, R_1 = 0.050, GOF = 1.33 for 4519 reflections with $I > 2.0\sigma(I)$ out of 4519 reflections collected. CCDC 650892 contains the supplementary crystallographic data for **10**.These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

17. *Data for* **10**: mp 84 °C; IR (KBr) ν_{max}: 3427, 2964, 1738, 1693 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.03–1.09 (m, 1H), 1.25 (s, 3H), 1.63–2.02 (m, 7H), 2.21 (ddd, 1H, J = 16.0, 7.3, 5.0 Hz), 2.39 (br d, 1H), 2.82 (ddd, 1H, J = 16.0, 9.2, 6.1 Hz), 2.83–2.88 (m, 1H), 3.76 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 19.3, 20.3, 27.3, 34.4, 35.4, 39.7, 53.0, 55.2, 57.2, 78.3, 174.8, 207.9; EIMS m/z; 226 (M^+, 18), 208(20), 153 (4), 149 (100), 55 (19); HR-MS Calcd for $C_{12}H_{18}O_4$: 226.1205; found: 226.1202; EIMS m/z: 226 (M^+, 18), 208 (20), 153 (4), 149 (100), 55 (19); HR-MS calcd for $C_{12}H_{18}O_4$: 226.1205, found: 226.1202.
18. *Data for* **11**: IR (neat) ν_{max}: 2939, 1771, 1717 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.26 (s, 3H), 1.62 (ddt, 1H, J = 13.1, 9.8, 7.3 Hz), 1.80–1.95 (m, 2H), 1.98 (ddd, 2H, J = 13.7, 9.8, 7.9 Hz), 2.06 (m, 1H), 2.31(m, 1H), 2.39 (t, 1H, J = 8.9 Hz), 2.54 (m, 1H), 2.62 (dd, 1H, J = 7.9, 2.4 Hz), 2.64 (dd, 1H, J = 9.8, 7.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 10.7, 24.5, 26.4, 31.4, 34.0, 35.1, 56.3, 63.5, 93.4, 174.5, 201.5; EIMS m/z; 194 (M^+, 51), 139 (7), 111 (100), 55 (23); HR-MS Calcd for $C_{11}H_{14}O_3$: 194.0943; found: 194.0941.
19. Based on the results, it seems that HMPA does not inhibit the chelation of carbonyl group to samarium atom in these reactions. Similar observations were detected in the reactions of keto ester **i** with SmI_2 to give γ-lactone **iii**.[4]
20. *Data for* **12**: IR (neat) ν_{max}: 2961, 1771, 1732 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.20 (d, 3H, J = 6.7 Hz), 1.46–1.56 (m, 3H), 1.59–1.68 (m, 1H), 1.71–1.80 (m, 3H), 1.90–2.01 (m, 3H), 2.23 (dt, 1H, J = 12.8, 9.8 Hz), 2.52 (q, 1H, J = 8.5 Hz), 2.52–2.59 (m, 2H), 2.62–2.69 (m, 1H), 3.67 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.6, 19.8, 26.8, 27.5, 29.1, 38.0, 40.5, 48.7, 51.8, 94.8, 175.7, 176.2; EIMS m/z; 226 (M^+, 12), 194 (100), 166 (72), 124 (57), 111 (67), 55 (26); HR-MS. Calcd for $C_{12}H_{18}O_4$: 226.1205; found: 226.1202.
21. *Data for* **14**: IR (neat) ν_{max}: 2937, 2860, 1740, 1715, 1651 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.27–1.36 (m, 2H), 1.39–1.49 (m, 2H), 1.60 (quin, 2H, J = 7.5 Hz), 1.81 (d, 3H, J = 1.3 Hz), 2.16 (q, 2H, J = 7.5 Hz), 2.45 (t, 2H, J = 7.5 Hz), 2.56–2.73 (m, 4H), 3.67 (s, 3H), 3.72 (s, 3H), 6.73 (dt, 1H, J = 1.3, 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 12.3, 23.5, 27.7, 28.3, 28.4, 37.0, 42.6, 51.7, 51.8, 127.6, 142.3, 168.7, 173.3, 208.8; FABMS m/z: 285 (M+1); HRFABMS Calcd for $C_{15}H_{25}O_5$: 285.1702; found: 285.1706.
22. *Data for* **15**: IR (neat) ν_{max}: 3447, 2936, 1784, 1715, 1647 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.32–1.51 (m, 6H), 1.64–1.79 (m, 2H), 1.82 (d, 3H, J = 1.3 Hz), 1.97 (m, 1H), 2.11–2.21 (m, 3H), 2.50 (br d, 1H), 2.80 (ddd, 1H, J = 5.3, 10.6, 17.6 Hz), 2.91 (ddd, 1H, J = 9.7, 10.6, 17.6 Hz), 3.73 (s, 3H), 6.74 (qt, 1H, J = 1.3, 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 12.4, 23.3, 26.9, 28.4, 28.5, 29.4, 35.7, 39.9, 51.7, 91.5, 127.6, 142.3, 168.7, 210.8; FABMS m/z: 255 (M+1), HR-FABMS calcd for $C_{14}H_{23}O_4$: 255.1518; found: 255.1591.
23. In this reaction 39% of the starting material was recovered.