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Samarium(II)-induced ring-expansion reaction of 1,2-cyclobutanedicarboxylates to produce cyclopentanones

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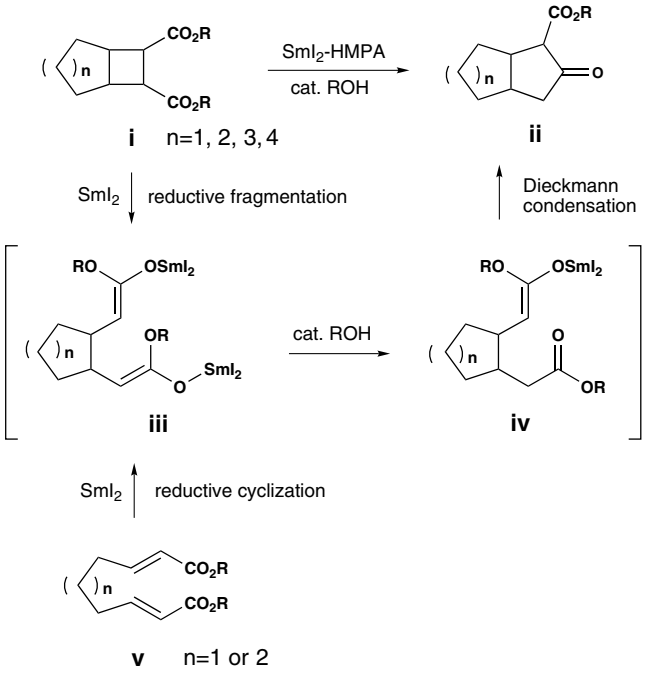
Abstract—Novel ring-expansion reaction of 1,2-cyclobutanedicarboxylates with Sm(II) in the presence of HMPA with a catalytic amount of methanol was found to provide 2-oxocyclopentanecarboxylates.

Cyclopentanones are structural constituents present in numerous natural products, which serve to make up a polycyclic framework or isolated ring. Tandem reductive coupling-Dieckmann condensation of bis-α,β-unsaturated ester **v** was recently noted to produce bicyclic cyclopentanones **ii** ($n=1$ or 2), a process induced by samarium(II)iodide (SmI_2) via **iii** and **iv** (Scheme 1).[1] The formation of oxocyclopentanecarboxylates **ii** ($n=3$, 4) failed to occur by the above cyclization, though it was considered that reductive ring cleavage of the cyclobutane ring activated by a 1,2-bis(alkoxycarbonyl) group would possibly serve as an alternative means for generating intermediate **iii** to produce cyclopentanones **ii** bearing carbocycles of various sizes. The present paper describes novel ring-expansion reaction of 1,2-cyclobutanedicarboxylates **i** to afford **ii** ($n=1$–4) via Sm(II)-induced tandem reductive fragmentation-Dieckmann condensation.[2]



Scheme 1.

Ring transformation precursors **2**, **3**, **4** and **5** were prepared from the corresponding cycloalkenes **1** ($n=1$–4) in three steps,[3] (1) photocycloaddition with maleic anhydride,[4] (2) methanolysis and (3) methylation, as shown in Scheme 2. Precursors **6**[5], **7**[6] and **8**[7] were prepared according to the literature.

The results of reactions of dimethyl 1,2-cyclobutanedicarboxylates **2**–**8** with Sm(II) are summarized in Table 1. On treating cyclobutanedicarboxylate **2** possessing a *cis* ring juncture with SmI_2 (3 equiv), HMPA (12 equiv) and methanol in trace amount in THF at 0 °C, methyl 3-oxobicyclo[3.3.0]octane-2-carboxylate **9a**[8] was obtained as a single isomer in 44% yield (entry 1). Higher reaction temperature (50 °C) gave a mixture of **9a** (45%) and unexpected **9b**[9,10] (12%) possessing a *trans* ring juncture, but the total yield of **9** was noted to have increased (entry 2). HMPA addition is crucial for this reaction and

Keywords: Samarium and compounds; Radicals and radical reactions; Ring transformation; Cyclobutanes; Cyclopentanones.
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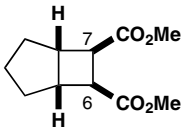
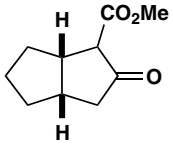
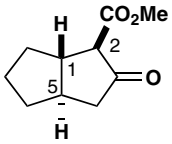
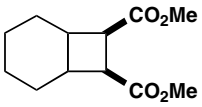
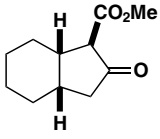
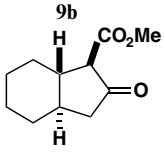
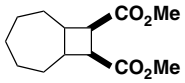
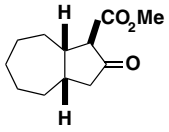
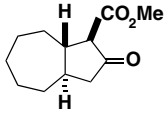
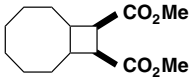
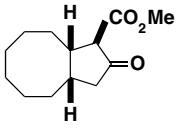
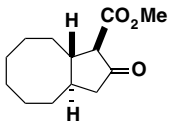
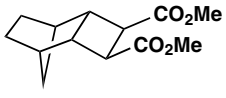
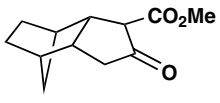
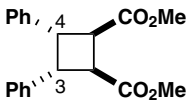
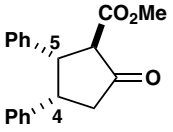
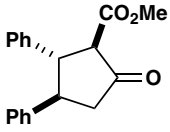
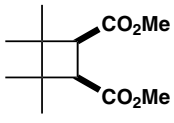
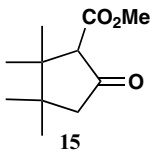
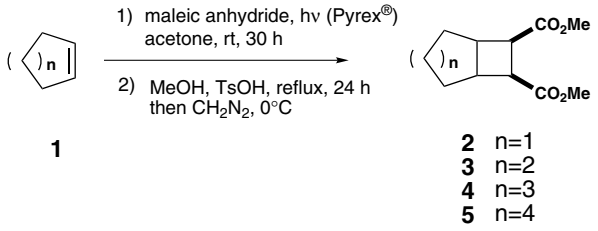
Table 1. Sm(II)-induced ring-expansion reaction of dimethyl 1,2-cyclobutanedicarboxylates[a]

Entry	Esters	Conditions		Products		Yield[b] (ratio of **a**:**b**)
		Temp (°C)	Time			
1	 **2**	0 °C	2 h	 **9a**[c]		44%
2	**2**	50 °C	1 h	**9a**	 **9b**	57% (3.8:1)[d]
3	 **3**[e]	50 °C	1 h	 **10a**	 **10b**	71% (2.6:1)[d,f]
4	 **4**[e]	50 °C	3 h	 **11a**	 **11b**	79% (1.6:1)[d]
5	 **5**[e]	50 °C	1.5 h	 **12a**	 **12b**	68% (1:1.5)[d]
6	 **6**	50 °C	1.5 h	 **13**[c]		38%
7[g]	 **7**	50 °C	1 h	 **14a**	 **14b**	39% (1:1.5)[d]
8[h]	 **8**	rt	2.5 h	 **15**		41%

[a] SmI_2 (3 equiv), HMPA (12 equiv) and trace amount of MeOH were used.
[b] Isolated yield.
[c] This compound has the enol form.
[d] Compounds **10a/10b** were inseparable. Compounds **9a/9b**, **11a/11b**, **12a/12b** and **14a/14b** could be separated.
[e] A mixture of diastereomers was used.
[f] Determined by ^1H NMR (300 MHz) analysis.
[g] SmI_2 (5 equiv), HMPA (20 equiv) and trace amount of MeOH were used.
[h] $SmBr_2$ (5 equiv), HMPA (20 equiv) and trace amount of MeOH were used.



Scheme 2.

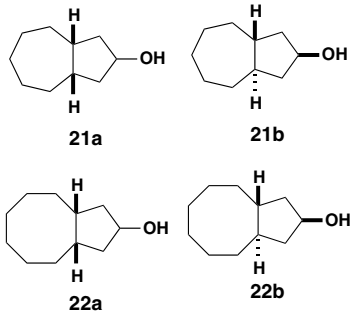


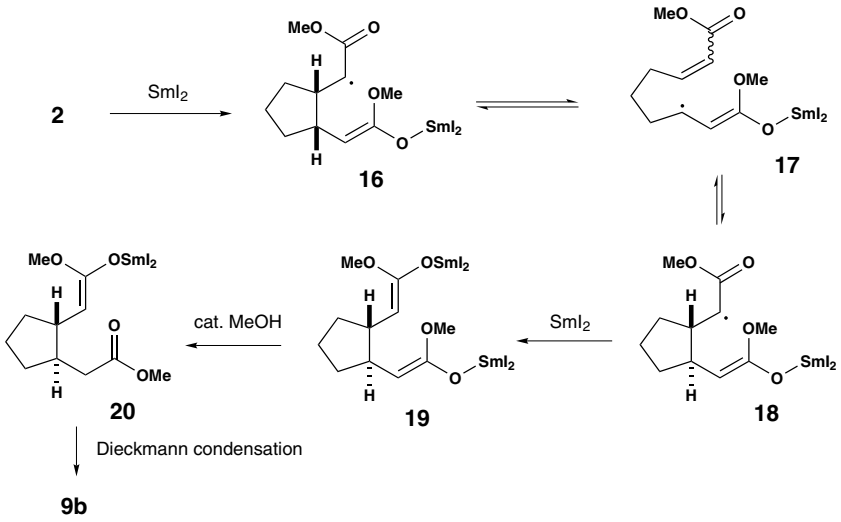
Figure 1.

in the absence of which the reaction virtually fails to occur. SmI_2-HMPA treatment of cyclobutanes **3**, **4** and **5**, having cyclohexane, cycloheptane and cyclooctane rings, respectively, and each of these cyclobutanes being a diastereomeric mixture comprised of three components,[11] provided bicyclic cyclopentanones **10** (**10a**:**10b** = 2.6:1),[8] **11** (**11a**:**11b** = 1.6:1)[9,12] and **12** (**12a**:**12b** = 1:1.5)[9,12] in 71, 79 and 68% yields, respectively (entries 3, 4 and 5). Neither bicyclo[5.3.0]decane **11** nor bicyclo[6.3.0]undecane **12** could be obtained by the previously reported SmI_2-induced tandem cyclization of bis-α,β-unsaturated ester.[1] The tricyclo[5.2.1.$0^{2,6}$]decane derivative and monocyclic cyclopentanones could also be obtained by the present method. Reaction of dicarboxylate **6** with SmI_2-HMPA and catalytic amount of MeOH provided tricyclic keto ester **13**[1] as a single isomer (entry 6), while that of 3,4-*cis*-dicarboxylate **7**[6] resulted in a mixture of 4,5-*cis*-cyclopentanone **14a**[1] and 4,5-*trans*-isomer **14b**.[1] Sterically congested 3,3,4,4-tetrasubstituted cyclobutanedicarboxylate **8** does not react with SmI_2-HMPA, but on treating **8** with $SmBr_2$[13]-HMPA, cyclopentanone **15**[9] was obtained.

Unexpected isomerization at the ring junction via ring-expansion reaction of **2** (entry 2) to give **9b** may be explained as due to generation of allylic radical **17** by radical fragmentation of the cyclopentane ring in **16** and recyclization of **17** to produce radical **18**, the *trans* isomer of **16**, as shown in Scheme 3.

In a typical experiment, a suspension of Sm (142 mg, 0.946 mmol) and 1,2-diiodoethane (243 mg, 0.861 mmol) in THF (5.7 mL) was sonicated for 1 h at room temperature under argon. Following addition of HMPA (0.60 mL, 3.4 mmol) and a solution of cyclobutanedicarboxylate **4** (69 mg, 0.287 mmol) and methanol (37 μg) in THF (2.5 mL), the mixture was stirred for 3 h at 50 °C and the reaction was terminated with few drops of 30% hydrogen peroxide[14] and 1 N HCl. The system was then diluted with ether, washed with saturated $NaHCO_3$, saturated $Na_2S_2O_3$ and water, dried and concentrated. The crude product was purified by silica gel column chromatography to give keto ester **11a** (29 mg, 48% yield) and **11b** (19 mg, 31% yield).

In the present study, a method was established to bring about novel ring-expansion reaction of 1,2-cyclobutanedicarboxylates, readily accessible from the corresponding cycloalkenes, to produce cyclopentanones, through application of the one electron transfer reagent Sm(II) in the presence of HMPA and methanol in trace amount. This paper reports the first instance of the transformation of cyclobutanes to cyclopentanes via tandem reductive fragmentation-Dieckmann condensation.



Scheme 3.

Acknowledgements

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References and notes

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3. Cycloalkene **1** (2.0 equiv) and maleic anhydride (1.0 equiv) were used for photocycloaddition and overall yields of **2**, **3**, **4** and **5** were 13%, 35%, 43% and 37%, respectively, based on maleic anhydride. Compounds **2** and **3** can also be obtained by photocycloaddition of cyclopentene or cyclohexene with dimethyl maleate. De Mayo, P.; Reid, S. T.; Yip, R. W. *Can. J. Chem.* **1964**, *42*, 2828–2835.
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8. Taber, D. F.; Ruckle, R. E., Jr. *J. Am. Chem. Soc.* **1986**, *108*, 7686–7693.
9. Compound **9b**: EI-MS (*m*/*z*, %) 182 (M^+, 3), 94 (100); HR-MS calcd for $C_{10}H_{14}O_3$: 182.0943, found: 182.0936; IR ν_{max} (neat) 1761, 1732 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.29 (m, 2H), 1.67 (m, 1H), 1.85–2.19 (m, 6H), 2.48 (dd, $J = 17.4$, 6.4 Hz, 1H), 2.88 (d, $J = 12.7$ Hz, 1H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.5, 26.1, 26.8, 43.2, 45.8, 52.1, 52.3, 60.4, 169.9, 212.4.
Compound **11a**: EI-MS (*m*/*z*, %) 210 (M^+, 33), 178 (100), 121 (37); HR-MS calcd for $C_{12}H_{18}O_3$: 210.1256, found: 210.1253; IR ν_{max} (neat) 1755, 1732 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.15-1.55 (m, 5H), 1.70–2.05 (m, 5H), 2.17 (dd, $J = 18.5$, 4.0 Hz, 1H), 2.57 (m, 1H), 2.61 (dd, $J = 18.5$, 9.0 Hz, 1H), 2.84 (m, 1H), 3.01 (d, $J = 9.9$ Hz, 1H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.1, 29.2, 31.2, 32.0, 32.1, 38.2, 43.6, 47.1, 52.4, 61.2, 169.6, 211.4.
Compound **11b**: EI-MS (*m*/*z*, %) 210 (M^+, 82), 108 (100); HR-MS calcd for $C_{12}H_{18}O_3$: 210.1256, found: 210.1259; IR ν_{max} (neat) 1757, 1732 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.25–1.42 (m, 2H), 1.45–1.67 (m, 4H), 1.72 (m, 2H), 1.81–2.10 (m, 4H), 2.30 (qd, $J = 10.6$, 3.9 Hz, 1H), 2.52 (dd, $J = 18.2$, 7.0 Hz, 1H), 2.90 (d, $J = 11.9$ Hz, 1H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.6, 26.7, 26.9, 33.5, 34.2, 41.0, 47.3, 47.4, 52.4, 64.2, 169.5, 210.5.
Compound **12a**: EI-MS (*m*/*z*, %) 224 (M^+, 30), 192 (100); HR-MS calcd for $C_{13}H_{20}O_3$: 224.1412, found: 224.1411; IR ν_{max} (neat) 1757, 1732 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.35–1.83 (m, 12H), 2.15 (m, 1H), 2.41 (m, 1H), 2.50–2.75 (m, 2H), 2.93 (dd, $J = 10.1$, 1.3 Hz, 1H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.3, 26.3, 27.39, 27.41, 29.7, 30.2, 36.9, 44.5, 49.0, 52.5, 60.7, 169.7, 211.5.
Compound **12b**: EI-MS (*m*/*z*, %) 224 (M^+, 30), 192 (100); HR-MS calcd for $C_{13}H_{20}O_3$: 224.1412, found: 224.1411; IR ν_{max} (neat) 1757, 1732 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.45–1.78 (m, 10H), 1.84 (m, 2H), 1.97 (m, 1H), 2.11 (dd, $J = 17.6$, 11.7 Hz, 1H), 2.35 (m, 1H), 2.48 (dd, $J = 17.6$, 6.5 Hz, 1H), 2.94 (d, $J = 11.9$ Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.0, 26.8, 26.9, 31.7, 32.3, 39.6, 45.9, 47.5, 52.4, 64.2, 169.5, 210.0.
Compound **15**: EI-MS (*m*/*z*, %) 198 (M^+, 19), 151 (100); HR-MS calcd for $C_{11}H_{18}O_3$: 198.1256, found: 198.1253; IR ν_{max} (neat) 1749, 1732 cm^{-1} ^1H NMR (300 MHz, $CDCl_3$): δ 0.99 (s, 3H), 1.02 (s, 3H), 1.07 (s, 3H), 1.16 (s, 3H), 2.17 (d, $J = 18.4$ Hz, 1H), 2.39 (d, $J = 18.4$ Hz, 1H), 3.24 (s, 1H), 3.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.2, 22.60, 22.63, 25.3, 39.8, 44.8, 51.9, 52.1, 63.9, 169.4, 210.9.
10. Relative configuration of C1–C5 in **9b** was determined based on comparison of ^1H and ^{13}C NMR spectra of **9b** with those of **9a**,[8] ca 50% of which was found to exist in the enol form. The relative configuration of C1–C2 in **9b** was elucidated from the coupling constants of C2–H (2.88 ppm, $J = 12.7$ Hz) in ^1H NMR.
11. Compounds **3**, **4** and **5** were all diastereomeric mixtures but no determination was made of their respective amounts.
12. Configurations of ring junctures in **11a** and **11b** were found based on ^{13}C NMR analysis of **21a** and **21b** derived from **11a** and **11b** by decarbomethoxylation with NaCl, DMSO and H_2O at 140 °C for 1.5 h[15] and reduction of ketone with $NaBH_4$ in MeOH at 0 °C. The ^{13}C NMR spectrum of **21a** indicated six signals, while that of **21b**, ten signals. ^{13}C NMR (100 MHz, $CDCl_3$) of **21a**: δ 29.7, 31.5, 33.1, 40.8, 44.0, 72.9; ^{13}C NMR (100 MHz, $CDCl_3$) of **21b**: δ 26.5, 28.0, 28.1, 33.9, 34.9, 43.5, 44.9, 45.1, 45.2, 72.7. Configurations of ring junctures in **12a** and **12b** were clarified in same manner as above. The ^{13}C NMR spectrum of **22a** indicated six signals and that of **22b**, eight signals (more than six). ^{13}C NMR (100 MHz, $CDCl_3$) of **22a**: δ 25.9, 29.7, 30.6, 40.3, 45.7, 71.8; ^{13}C NMR (100 MHz, $CDCl_3$) of **22b**: δ 24.7, 27.2, 35.6, 36.5, 41.3, 42.3, 45.5, 72.2 (Fig. 1).
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14. Without hydrogen peroxide treatment, reduction of the ketone in **11** occurs to give a small amount of the corresponding cyclopentanols.
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