JOC Article

Zinc- and Indium-Mediated Ring-Expansion Reaction of α-Halomethyl Cyclic β-Keto Esters in Aqueous Alcohol

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Radical ring-expansion reaction of various α-halomethyl cyclic β-keto esters and α-halomethyl benzocyclic β-keto esters and chain-extension reaction of α-halomethyl β-keto esters with zinc powder and indium powder in refluxing aqueous alcohol were carried out to generate the corresponding ring-expansion and chain-extension products. As the results indicate, it was found zinc powder was more effective than indium powder to give the corresponding ring-expanded products in quite good yields. Moreover, the addition of zinc bromide as Lewis acid showed an increase of the yields, depending on the substrates. The present reaction conditions are highly effective, simple, and environmentally friendly.

Introduction

Free radical reactions are very important in organic synthesis, since functional group conversion of organic compounds can be easily carried out under mild reaction conditions.[1] Tributyltin hydride,[2] [tris(trimethylsilyl)]-silane,[3] and 1,1,2,2-tetraphenyldisilane[4] (TPDS) are well-known reagents for these radical reactions, though the first reagent is highly toxic and the second one is a less stable oil under aerobic conditions for storage. Among various types of radical reactions, radical cyclization reactions in the *5-exo-trig* and *6-exo-trig* manners are the most powerful and versatile methods for the construction of five- and six-membered ring systems.[5] However, the direct construction of a medium-sized ring skeleton by radical cyclization is normally not so useful because of poor yields of the cyclization products.[6] In 1987, Dowd reported a very interesting free radical ring expansion of α-halomethyl and α-halopropyl cyclic β-keto esters to one-carbon and three-carbon ring-expanded cyclic keto esters, respectively, by the slow addition of a mixture of tributyltin hydride and AIBN in refluxing benzene solution.[7] Here, the reaction proceeds through the formation of carbon-centered radicals, *3-exo-trig* or *5-exo-trig* cyclization of the formed carbon-centered radicals, and subsequent β-cleavage to provide the ring-expanded products. Baldwin has also reported a radical ring expansion of α-(haloalkyl)-β-stannylcyclohexanone with tributyltin hydride to form the corresponding ring-expanded cycloalkenones.[8] These methods are very efficient for the construction of medium-sized cyclic compounds, and the reactions are very attractive, since these types of ring expansion are specific radical reactions. Recently, treatment of α-halomethyl cyclic β-keto esters

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(1) (a) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon−Carbon Bonds*; Pergamon Press: Oxford, 1986. (b) Motherwell, W. B.; Crich, D. *Free Radical Chain Reactions in Organic Synthesis*; Academic Press: New York, 1992. (c) Fossey, J.; Lefort, D.; Sorba, J. *Free Radicals in Organic Chemistry*; John Wiley & Sons: Paris, 1995. (d) Renaud, P., Sibi, M. P., Eds. *Radicals in Organic Synthesis*; Wiley-VCH: Weinheim, Germany, 2001. (e) Togo, H. *Chemistry in Organic Free Radicals*; Kodansha: Tokyo, 2001.

(2) (a) Neumann, W. P. *Synthesis* **1987**, 665. (b) Curran, D. P. *Synthesis* **1988**, 417. (c) Curran, D. P. *Synthesis* **1988**, 489.

(3) (a) Chatgilialoglu, C. *Acc. Chem. Res.* **1992**, *25*, 188. (b) Chatgilialoglu, C.; Ferreri, C.; Gimisis, T. *The Chemistry of Organic Silicon Compounds*; John Wiley & Sons: New York, 1998; Vol. 2, Chapter 25.

(4) (a) Yamazaki, O.; Togo, H.; Matsubayashi, S.; Yokoyama, M. *Tetrahedron Lett.* **1998**, *39*, 1921. (b) Yamazaki, O.; Togo. H.; Matsubayashi, S.; Yokoyama, M. *Tetrahedron* **1999**, *55*, 3735. (c) Yamazaki, O.; Togo. H.; Yokoyama, M. *J. Chem. Soc., Perkin Trans 1* **1999**, 2891. (d) Yamazaki, O.; Togo, H.; Yamaguchi, K.; Yokoyama, M. *J. Org. Chem.* **2000**, *65*, 5440. (e) Togo, H.; Matsubayashi, S.; Yamazaki, O.; Yokoyama, M. *J. Org. Chem.* **2000**, *65*, 2816. (f) Ryokawa, A.; Togo, H. *Tetrahedron* **2001**, *57*, 5915. (g) Sugi, M.; Togo, H. *Tetrahedron* **2002**, *58*, 3171.

(5) Giese, B.; Kopping, B.; Gobel, T.; Dickhaut, J.; Thoma, G.; Kulicke, K. J.; Trach, F. Radical Cyclization Reactions. *Organic Reactions*; John Wiley & Sons: New York, 1996; Vol. 48, Chapter 2.

(6) *Endo-trig* cyclization of iodoalkyl vinyl ketones and iodoalkyl acrylates with Bu_3SnH/AIBN gave the corresponding medium-sized cyclic ketones and lactones in moderate to low yields. (a) Porter, N. A.; Magnin, D. R.; Wright, B. T. *J. Am. Chem. Soc.* **1986**, *108*, 2787. (b) Porter, N. A.; Chang, V. H. T. *J. Am. Chem. Soc.* **1987**, *109*, 4976. (c) Porter, N. A.; Chang, V. H. T.; Magnin, D. R.; Wright, B. T. *J. Am. Chem. Soc.* **1988**, *110*, 3554. (d) Porter, N. A.; Lacker, B.; Chang, V. H. T.; Magnin, D. R. *J. Am. Chem. Soc.* **1989**, *111*, 8309. (e) Cox, N. J. G.; Mills, S. D.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1313. 8-*Endo-trig* cyclization of 4-pentenyl α-bromoacetate with Bu_3-SnH/AIBN proceeded to give lactones in moderate to low yields. (f) Lee, E.; Yoon, C. H.; Lee, T. H. *J. Am. Chem. Soc.* **1992**, *114*, 10981. (g) Lee, E.; Yoon, C. H.; Lee, T. H.; Kim, S. Y. Ha, T. J.; Sung, Y. S.; Park, S. H.; Lee, S. *J. Am. Chem. Soc.* **1998**, *120*, 7469. (h) Oh, Heong-S.; Lee, H. I.; Cha, J. K. *Org. Lett.* **2002**, *4*, 3708.

(7) (a) Beckwith, A. L. J.; Kazlauskas, R.; Syner-Lyons, M. R. *J. Org. Chem.* **1983**, *48*, 4718. (b) Dowd, P.; Choi, S. C. *J. Am. Chem. Soc.* **1987**, *109*, 6548. (c) Dowd, P.; Choi, S. C. *J. Am. Chem. Soc.* **1987**, *109*, 3493. (d) Beckwith, A. L. J.; O'Shea, D. M. Gerba, S.; Westwood, S. W. *J. Chem. Soc., Chem. Commun.* **1987**, 666. (e) Beckwith, A. L. J.; O'Shea, D. M.; Westwood, S. W. *J. Am. Chem. Soc.* **1988**, *110*, 2565. (f) Dowd, P.; Choi. S. C. *Tetrahedron Lett.* **1989**, *30*, 6129. (g) Dowd, P.; Choi, S. C. *Tetrahedron* **1989**, *45*, 77. (h) Dowd, P.; Choi, S. C. *Tetrahedron Lett.* **1991**, *32*, 565. (i) Zhang, W.; Dowd, P. *Tetrahedron Lett.* **1992**, *33*, 3285. (j) Reviews: Dowd, P.; Zhang, W. *Chem. Rev.* **1993**, *93*, 2091. (k) Yet, L. *Tetrahedron* **1999**, *55*, 9349.

(8) (a) Baldwin, J. E.; Adlington, R. M. Robertson, J.*J. Chem. Soc., Chem. Commun.* **1988**, 1404. (b) Baldwin, J. E.; Adlington, R. M.; Robertson, J. *Tetrahedron* **1989**, *45*, 909.

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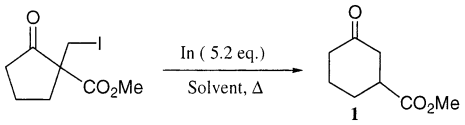
with SmI_2 in THF in the presence of an activator such as MeOH, HMPA, or NiI_2 was reported to give the corresponding one-carbon ring-expanded products in good to moderate yields.[9] However, SmI_2 is rather sensitive to air, and has to be kept in a tightly closed container under an inert atmosphere. So, it is not so easy to handle, because the yields of the ring-expanded products with SmI_2 are rather variable and depend on the ring size, on the basis of our follow-up experiments. We have also reported 1,1,2,2-tetraphenyldisilane (TPDS)-mediated radical ring expansion of α-haloalkyl cyclic β-keto esters to form ring-expanded cyclic keto esters through the same radical pathway, and compared the reactivities for ring expansion among tributyltin hydride, tris(trimethylsilyl)-silane, and TPDS.[4g] There, generally the yields of ring-expanded products are better than those with tributyltin hydride, because of the lower hydrogen-donating ability of TPDS. However, there are still problems because of the operationally troublesome purification of the ring-expanded products from the reaction mixtures. Recently, environmentally friendly organic synthesis has become very important and is required, such as solvent-free organic synthesis, or organic reactions in room temperature ionic liquids as new reaction media, or in water, aiming toward green chemistry.[10] Here, as a part of our study on environmentally friendly organic synthesis via radical reactions,[4] we report efficient zinc- and indium-mediated radical ring-expansion reactions of various α-halomethyl cyclic β-keto esters and chain-extension reaction of α-halomethyl β-keto esters in aqueous alcohol.

Results and Discussion

Barbier-type indium- and zinc-mediated reactions have become popular in allylation of carbonyl compounds with allylic halides in water-containing media,[11] and recently two-atom carbocyclic enlargement based on indium-mediated Barbier-type reaction in water was reported.[11e] Indium and zinc are stable under air, and it is much easier to run their reactions than those with SmI_2, and the toxicity is quite low. Moreover, the metal species can be easily removed from the reaction mixtures by simple filtration and washing with water, not like tributyltin hydride, tris(trimethylsilyl)silane, and TPDS. Thus, methyl 1-bromomethyl-2-oxocyclopentanecarboxylate was treated with indium powder in various refluxing solvents such as MeOH, dioxane, *tert*-amyl alcohol (*t*AA), THF-containing water, etc., under an argon atmosphere as shown in Table 1. As a result, when this reaction was carried out in refluxing *t*AA, the corresponding ring-expanded product was obtained in the best yield (entry 3). Moreover, the reaction was not retarded by the addition of water, and showed the same reactivity as in *t*AA alone (entry 5).

TABLE 1. Indium-Mediated Ring Expanion in Various Solvents



1

entry	solvent	time (h)	yield (%)
1	methanol	5	10
2	dioxane	5	45
3	*t*AA[a]	2	59
4	dioxane/H_2O (2:1)	3	42
5	TAA/H_2O (2:1)	1	55
6	THF/H_2O (5:1)	24	3 (42)[b]

[a] *t*AA = *tert*-amyl alcohol. [b] Starting material was recovered.

The same reactions with other ring-sized α-iodomethyl cyclic β-keto esters in a mixture of *t*AA and water (2:1) were examined to give the corresponding ring-expanded products in varying yields, depending on the ring size, as shown in Table 2. Thus, yields in the formation of eight- and nine-membered rings are good in both cyclic and benzocyclic β-keto esters, while yields in other membered rings and acyclic β-keto ester are decreased. Moreover, the reaction with six-membered α-iodomethyl β-keto ester gave a bicyclic cyclopropanol as a major product, together with a ring-expanded product as a minor product (entry 3). Here, the corresponding α-bromomethyl cyclic β-keto esters did not react with indium powder under the same reaction conditions.

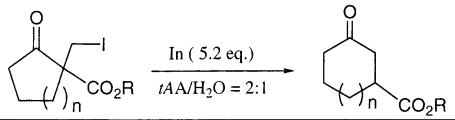
Next, the same ring expansion of α-halomethyl cyclic β-keto esters with zinc powder, instead of indium powder, was examined in a mixture of *t*AA and water (1:1), as shown in Table 3. Here again, the same reaction products as with indium powder were obtained. However, the yields were surprisingly much increased. The presence of water in this reaction was found to be essential for an effective and high yield of the ring-expanded products. Moreover, both bromomethyl and iodomethyl cyclic β-keto esters can be used for the ring-expansion reaction effectively to provide the corresponding ring-expanded 6-membered, 8-membered, 9-membered, 13-membered, and 16-membered products in good yields. When the amount of zinc powder was reduced to 2.6 equiv, the corresponding ring-expanded product was also obtained (entry 3). However, the yield was decreased. Thus, it is better to use an excess amount of zinc powder (5.2 equiv) for effective ring-expansion reactions. Chain extension of α-iodomethyl β-keto ester also proceeded effectively to generate γ-keto ester in good yield (entries 16 and 17). Surprisingly, the addition of a Lewis acid, $ZnBr_2$, increased the yields of the ring-expanded products, depending on the substrates, though $Yb(OTf)_3$ and $Mg(ClO_4)_2$ were not effective. Probably, this effect derives from the fact that the increasing electrophilicity of the carbonyl

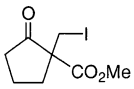
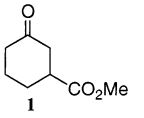
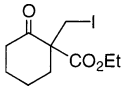
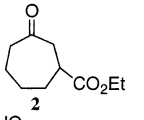
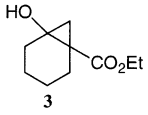
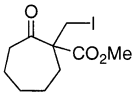
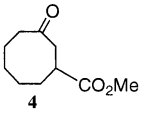
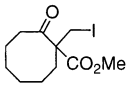
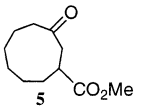
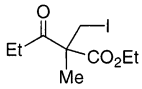
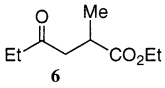
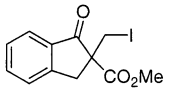
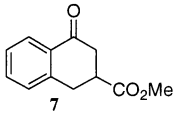
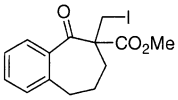
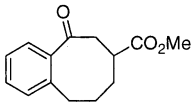
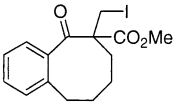
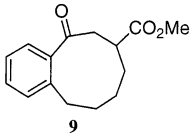
(9) (a) Hasegawa, E.; Kitazume, T.; Suzuki, K.; Tosaka, E. *Tetrahedron Lett.* **1998**, *39*, 4059. (b) Chung, S. H.; Cho, M. S.; Choi, J. Y.; Kwon, D. W.; Kim, Y. H. *Synlett* **2001**, 1266.

(10) (a) Loupy, A.; Petit, A.; Hamelin, J.; Texier-Boullet, F.; Jacquault, P.; Mathe, D. *Synthesis* **1998**, 1213. (b) Welton, T. *Chem. Rev.* **1999**, *99*, 2071. (c) Wasserscheid, P.; Keim, W. *Angew. Chem., Int. Ed.* **2000**, *39*, 3772. (d) Sheldon, R. A. *Pure Appl. Chem.* **2000**, *72*, 1233. (e) Sheldon, R. *Chem. Commun.* **2001**, 2399. (f) Ren, R. X.; Zueva, L. D.; Ou, W. *Tetrahedron Lett.* **2001**, *42*, 8441. (g) Morrison, D. W.; Forbes, D. C.; Davis, J. H., Jr. *Tetrahedron Lett.* **2001**, *42*, 6053. (h) Sharghi, H.; Hosseini, M. *Synthesis* **2002**, 1057. (i) Melucci, M.; Barbarella, B.; Sotgiu, G. *J. Org. Chem.* **2002**, *67*, 8877. (j) Mayo, K. G.; Nearhoof, E. H.; Kiddle, J. J. *Org. Lett.* **2002**, *4*, 1567. (k) Yanada, R.; Takemoto, Y. *Tetrahedron Lett.* **2002**, *43*, 6849. (l) Ansari, I. A.; Gree, R. *Org. Lett.* **2002**, *4*, 1507. (m) Fukuyama, T.; Shinmen, M.; Nishitani, S.; Sato, M.; Ryu, I. *Org. Lett.* **2002**, *4*, 1691. (n) Xie, Yuan-Y.; Chen, Zhen-C. Zheng, Qin-G. *Synthesis* **2002**, 1505.

(11) (a) Li, Chao-J.; Chan, Tak-H. *Organic Reactions in Aqueous Media*; John Wiley & Sons: New York, 1997. (b) Cintas, P. *Synlett* **1995**, 1087. (c) Li, Chao-J. *Tetrahedron* **1996**, *52*, 5643. (d) Li, Chao-J.; Chen, Dong-Li.; Lu, Yue-Q.; Haberman, J. X.; Mague, J. T. *J. Am. Chem. Soc.* **1996**, *118*, 4216. (e) Li, Chao-J.; Chan, Tak-H. *Tetrahedron* **1999**, *55*, 11149.

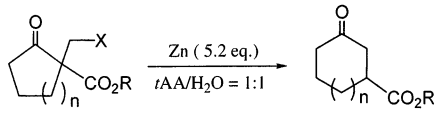
TABLE 2. Indium-Mediated Ring Expansion of α-Iodomethyl Cyclic β-Keto Esters

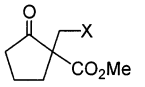
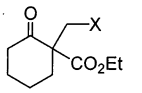
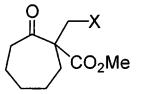
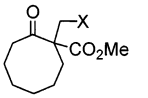
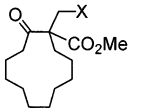
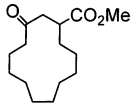
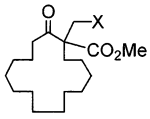
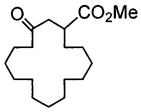
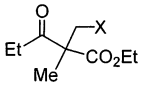
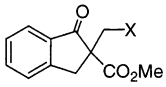
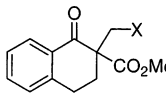
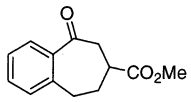
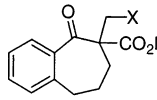
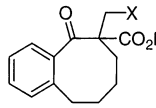


Entry	Substrate	Time	Product	Yield(%)
1		1 h	 **1**	55
2		2 h[a)]		59
3		2 h	 **2**	23
			 **3**	36
4		2 h	 **4**	69
5		3 h[a)]		64
6		2 h	 **5**	74
7		1 h	 **6**	20
8		2 h	 **7**	15
9		2 h	 **8**	45
10		2 h	 **9**	64

[a] *t*AA was used as a solvent, instead of *t*AA/H_2O.

TABLE 3. Zinc-Mediated Ring Expansion of α-Halomethyl Cyclic β-Keto Esters



Entry	Substrate	X	Time	Product	Yield (%)
1		Br	2 h	**1**	54
2		Br	2 h[a)]		73
3		I	2 h		81 (73)[b)]
4		Br	6 h	**2**	27[c)]
5		I	2 h		34[d)]
6		Br	6 h	**4**	73
7		Br	6 h[a)]		86
8		I	2 h		91
9		Br	6 h	**5**	70
10		Br	6 h[a)]		82
11		I	2 h		86
12		I	3 h		24
13		I	3 h[a)]		56
14		I	3 h		59
15		I	3 h[a)]		92
16		I	1 h	**6**	65
17		I	1 h[a)]		87
18		Br	3 h	**7**	36
19		Br	3 h[a)]		41
20		I	3 h		56
21		Br	3 h		61
22		Br	3 h[a)]		60
23		I	3 h		63
24		Br	3 h	**8**	59
25		Br	3 h[a)]		86
26		I	3 h		75
27		Br	3 h	**9**	77
28		Br	3 h[a)]		93
29		I	3 h		87

[a] $ZnBr_2$ was added. [b] (2.6 equiv) Zinc powder was used. [c] Compound **3** was obtained in 41% yield. [d] Compound **3** was obtained in 53% yield.

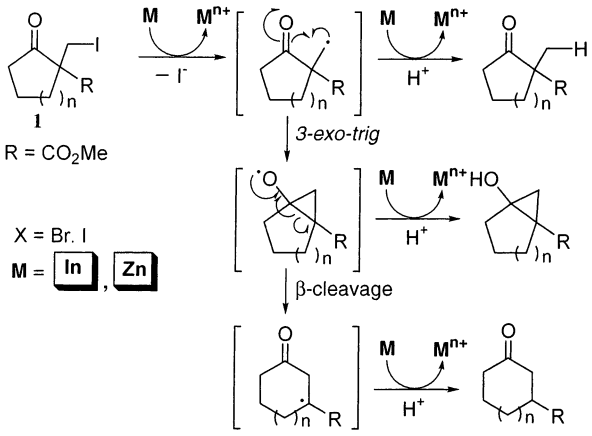
carbon by the coordination of the carbonyl oxygen onto $ZnBr_2$ accelerates *3-exo-trig* cyclization of the methyl radical derivative formed, to generate the corresponding cyclopropoxyl radical. The reactions are extremely clean and operationally simple for isolation of products. In six-membered α-halomethyl cyclic β-keto ester, the effect of $ZnBr_2$ was not observed, and again the ring-expanded product was obtained in low yield, together with bicyclic cyclopropanol **3**. Unfortunately, the same treatment of α-halopropyl cyclic β-keto esters with zinc powder gave the corresponding direct reduction products alone, not three-carbon ring-expanded product.

A plausible mechanism of these reactions is shown in Scheme 1. The reaction pathway is similar to that of the TPDS-mediated radical ring expansion.[4g] However, the reaction is initiated by the first single electron transfer from metal to α-halomethyl cyclic β-keto esters to form the corresponding methyl radical derivative, followed by *3-exo-trig* cyclization and its radical β-cleavage. Here, ring-expansion products were effectively formed, since there is no good hydrogen donor such as TPDS, tris(trimethylsilyl)silane, or tributyltin hydride.

Conclusion

The present ring-expansion reactions of α-halomethyl cyclic β-keto esters and chain-extension reaction of α-halomethyl β-keto esters with zinc or indium powder in refluxing aqueous alcohol are highly effective and envi-

SCHEME 1



ronmentally friendly. Thus, zinc powder and indium powder are the most notable metals in terms of both reactivity and environmental point of view.

Experimental Section

General Methods. ^{1}H NMR spectra were recorded on 400 and 500 MHz spectrometers, and ^{13}C NMR spectra were recorded on 100 and 125 MHz spectrometers. Chemical shifts are expressed in parts per million downfield from that of TMS in δ units. In the ^{13}C NMR spectra, p, s, t, and q mean primary, secondary, tertiary, and quaternary. Silica gel 60 was used for column chromatography, and Wakogel B-5F was used for preparative TLC. $CHCl_3$ was used in recycling preparative HPLC.

Materials. Zinc powder and indium powder were obtained commercially.

General Procedure for Ring Expansion with Indium Powder. Indium powder (2.08 mmol) was added to a refluxing solution of α-halomethyl cyclic *β*-keto ester (0.4 mmol) in *tert*-amyl alcohol (2 mL) and water (1 mL) under an argon atmosphere. The mixture was stirred for 2 h at the same temperature. After the reaction, the reaction mixture was filtered through Celite, then the solvent was removed, and the residue was purified by preparative TLC or column chromatography on silica gel.

General Procedure for Ring Expansion with Zinc Powder. Zinc powder (2.08 mmol) was added to a refluxing solution of α-halomethyl cyclic *β*-keto ester (0.4 mmol) in *tert*-amyl alcohol (2 mL) and water (2 mL) under an argon atmosphere. The mixture was stirred for 2 h at the same temperature. After the reaction, the reaction mixture was filtered through Celite, then the solvent was removed, and the residue was purified by preparative TLC or column chromatography on silica gel.

Methyl 3-Oxocyclohexanecarboxylate: oil; IR (neat) 2950, 2870, 1740, 1720 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.71 (3H, s), 2.81 (1H, m), 2.56 (2H, d, J = 8.2 Hz), 2.44−2.28 (2H, m), 2.16−2.02 (2H, m), 1.90−1.69 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 209.2 (q), 174.2 (q), 52.1 (p), 43.13 (s), 43.11 (t), 40.16 (s), 27.7 (s), 24.5 (s); MS (EI) *m*/*z* 156; HRMS (EI) *m*/*z* found 156.0789, calcd for $C_8H_{12}O_3$ (M^+) 156.0786.

Ethyl 3-Oxocycloheptanecarboxylate: oil; IR (neat) 2980, 2940, 2860, 1740, 1700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.15 (2H, q, J = 7.2 Hz), 2.81 (1H, dd, J = 11.0, 15.6 Hz), 2.73−2.66 (2H, m), 2.58−2.44 (2H, m), 2.10 (1H, m), 1.98−1.61 (5H, m), 1.26 (3H, t, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 212.2 (q), 174.5 (q), 60.8 (s), 45.5 (s), 43.5 (s), 41.2 (t), 33.2 (s), 28.3 (s), 27.9 (s), 14.1 (p); MS (FAB) *m*/*z* 185; HRMS (FAB) *m*/*z* found 185.1160, calcd for $C_{10}H_{17}O_3$ (M + H) 185.1178.

Methyl 3-Oxocyclooctanecarboxylate: oil; IR (neat) 2940, 2860, 1730, 1700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.70 (3H, s), 2.94 (1H, s), 2.94 (1H, m), 2.80 (1H, t, J = 13.2 Hz), 2.58 (1H, m), 2.42 (2H, m), 2.04−1.63 (8H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 214.5 (q), 174.8 (q), 51.9 (p), 42.9 (s), 42.8 (s), 42.7 (t), 29.7 (s), 27.2 (s), 24.8 (s), 23.2 (s); MS (EI) *m*/*z* 184; HRMS (EI) *m*/*z* found 184.1085, calcd for $C_{10}H_{16}O_3$ (M^+) 184.1099.

Methyl 3-Oxocyclononanecarboxylate: oil; IR (neat) 2930, 2870, 1740, 1700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.66 (3H, s), 3.02 (1H, m), 2.85 (1H, dd, J = 11.3, 13.8 Hz), 2.63 (1H, dd, J = 2.7, 13.8 Hz), 2.49 (2H, m), 1.96−1.32 (10H, dd, J = 11.0, 15.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 215.0 (q), 175.7 (q), 52.0 (p), 44.3 (s), 45.5 (s), 43.7 (s), 41.2 (t), 29.2 (s), 25.6 (s), 25.5(s), 24.1 (s), 22.9 (s); MS (EI) *m*/*z* 198; HRMS (EI) *m*/*z* found 198.1064, calcd for $C_{11}H_{18}O_3$ (M^+) 198.1256.

Methyl 3-Oxocyclotridecanecarboxylate: oil; IR (neat) 2930, 2860, 1740, 1710 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.69 (3H, s), 2.98 (1H, m), 2.85 (1H, dd, J = 8.9, 16.9 Hz), 2.94 (1H, dd, J = 3.4, 16.9 Hz), 2.55 (1H, m), 2.35 (1H, m), 1.79−1.11 (18H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 210.2 (q), 175.7 (q), 51.9 (p), 43.5 (s), 42.5 (s), 39.6 (t), 29.5 (s), 26.2 (s), 26.14 (s), 26.11 (s), 25.5 (s), 24.6 (s), 24.3 (s), 23.8 (s), 23.7 (s); MS (EI) *m*/*z* 254; HRMS (EI) *m*/*z* found 254.1863, calcd for $C_{15}H_{26}O_3$ (M^+) 254.1882.

Methyl 3-Oxocyclohexadecanecarboxylate: oil; IR (neat) 2930, 2860, 1740, 1700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.69 (3H, s), 2.96 (1H, m), 2.74 (2H, m), 2.50 (1H, m), 2.35 (1H, m), 1.81−1.44 (4H, m), 1.42−1.20 (20H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 209.5 (q), 175.9 (q), 51.7 (p), 43.1 (s), 42.1 (s), 38.9 (t), 30.2 (s), 27.4 (s), 26.9 (s), 26.8 (t), 26.6 (s), 26.4 (s), 26.36 (s), 26.35 (s), 26.2 (s), 25.2 (s), 23.6; MS (FAB) *m*/*z* 297; HRMS (FAB) *m*/*z* found 297.2418, calcd for $C_{18}H_{33}O_3$ (M + H) 297.2430.

Ethyl 2-Methyl-4-oxohexanoate: oil; IR (neat) 2980, 2940, 1730, 1720 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.13 (2H, q, J = 7.1 Hz), 2.99−2.84 (2H, m), 2.55−2.37 (3H, m), 2.58−2.44 (2H, m), 1.25 (3H, t, J = 7.1 Hz), 1.18 (3H, d, J = 7.0 Hz), 1.06 (3H, t, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 195.8 (q), 173.5 (q), 141.5 (q), 134.8 (t), 134.4 (q), 133.9 (t), 131.8 (q), 128.8 (t), 127.8 (t), 127.2 (t), 52.2 (p), 40.7 (s), 40.1 (s), 32.0 (s); MS (EI) *m*/*z* 172; HRMS (EI) *m*/*z* found 172.1094, calcd for $C_9H_{16}O_3$ (M^+) 172.1098.

5-Methoxycarbonyl-1,2-benzo-3-oxocyclohexenone: oil; IR (neat) 2960, 1740, 1680, 760 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.03 (1H, dd, J = 7.6, 1.2 Hz), 7.51 (1H, td, J = 7.6, 1.2 Hz), 7.34 (1H, td, J = 7.6, 0.6 Hz), 7.28 (1H, d, J = 7.6 Hz), 3.73 (3H, s), 3.28−3.16 (3H, m), 2.99−2.91 (1H, m), 2.89−2.78 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 195.8 (q), 173.5 (q), 141.5 (q), 133.9 (t), 131.8 (q), 128.8 (t), 127.8 (t), 127.2 (t), 52.2 (p), 40.7 (s), 40.1 (t), 32.0 (s); MS (FAB) *m*/*z* 205; HRMS (FAB) *m*/*z* found 205.0874, calcd for $C_{12}H_{13}O_3$ (M + H) 205.0865.

5-Methoxycarbonyl-1,2-benzo-3-oxocycloheptenone: oil; IR (neat) 2950, 1740, 1680, 770 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.71 (1H, dd, J = 7.6, 1.5 Hz), 7.43 (1H, td, J = 7.6, 1.5 Hz) 7.31 (1H, td, J = 7.6, 1.0 Hz), 7.21 (1H, d, J = 7.6 Hz), 3.64 (3H, s), 3.10−2.83 (5H, m), 2.32−2.21 (1H, m), 2.19−2.07 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 202.6 (q), 174.7 (q), 140.6 (q), 138.1 (q), 132.5 (t), 129.7 (t), 128.6 (t), 126.9 (t), 52.0 (p), 42.7 (s), 38.1 (p), 31.0 (s), 28.5 (s); MS (FAB) *m*/*z* 219; HRMS (FAB) *m*/*z* found 219.1028, calcd for $C_{13}H_{15}O_3$ (M + H) 219.1021.

5-Methoxycarbonyl-1,2-benzo-3-oxocyclooctenone: oil; IR (neat) 2950, 1740, 1670, 750 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.79 (1H, dd, J = 7.6, 1.5 Hz), 7.42 (1H, td, J = 7.6, 1.5 Hz), 7.30 (1H, td, J = 7.6, 1.2 Hz), 7.18 (1H, d, J = 7.6 Hz), 3.71 (3H, s), 3.42 (1H, dd, J = 13.6, 10.0 Hz), 3.35−3.24 (1H, m), 3.07−2.91 (3H, m), 2.02−1.89 (1H, m), 1.84−1.65 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 203.3 (q), 174.4 (q), 139.8 (q), 138.9 (q), 132.2 (t), 131.2 (t), 128.5 (t), 126.5 (t), 51.9 (p), 44.6 (s), 40.5 (t), 34.2 (s), 26.9 (s), 25.0 (s); MS (FAB) *m*/*z* 233; HRMS (FAB) *m*/*z* found 233.1185, calcd for $C_{14}H_{17}O_3$ (M + H) 233.1178.

5-Methoxycarbonyl-1,2-benzo-3-oxocyclononenone: oil; IR (neat) 2950, 1740, 1670, 760 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) $\delta = 7.41-7.34$ (2H, m), 7.26 (1H, td, $J = 7.5$, 1.2 Hz), 7.19 (1H, d, $J = 7.5$ Hz), 3.69 (3H, s), 3.25 (1H, dd, $J = 14.9$, 11.0 Hz), 3.09−2.96 (3H, m), 2.82. (1H, ddd, $J = 14.5$, 8.3, 3.1 Hz), 2.06−1.95 (1H, m), 1.86−1.62 (2H, m), 1.61−1.46 (2H, m), 1.40−1.28 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) $\delta = 207.9$ (q), 175.2 (q), 141.8 (q), 139.0 (q), 131.0 (t), 130.9 (t), 126.5 (t), 126.2 (t), 51.9 (p), 43.2 (s), 42.8 (t), 31.2 (s), 30.2 (s), 28.2 (s), 21.9 (s); MS (FAB) *m*/*z* 247; HRMS (FAB) *m*/*z* found 247.1316, calcd for $C_{15}H_{19}O_3$ (M + H) 247.1334.

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Supporting Information Available: ^1H NMR spectra for all ring-expanded products **1**−**9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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