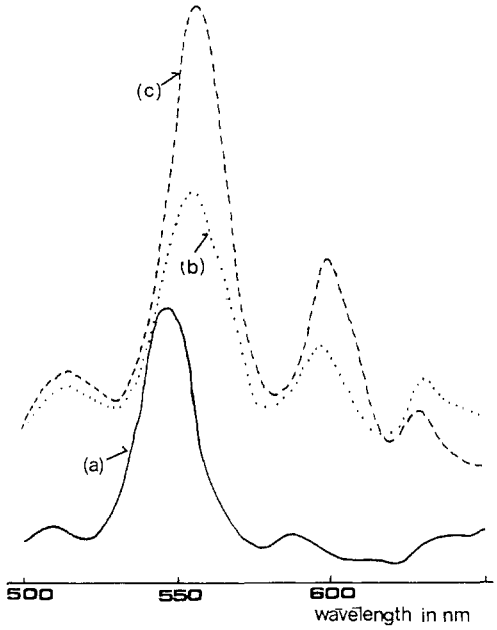

Figure 3. UV–vis spectra of (TPP)AlCl in (a) CH_2Cl_2, (b) acetone, and (c) 2-propanol under N_2 at room temperature.

for the signals of 2-propanol are also ascribed to the coordinative interaction with (TPP)AlCl.

The UV–vis spectral patterns for (TPP)AlCl in acetone and 2-propanol (Figures 3b and 3c) were both different from that in CH_2Cl_2 (Figure 3a) but similar to those for the six-coordinate complexes from 1 and Lewis bases such as 1-methylimidazole and tetraethylammonium acetate in CH_2Cl_2.[3,12] This observation and the NMR profiles mentioned above clearly demonstrate the possible coordinations of ketone and alcohol with (TPP)AlCl from the back side to generate the six-coordinate complexes. In sharp contrast, no change was observed for the NMR spectra of ketone and alcohol upon mixing with (TPP)AlOCH$(CH_3)_2$, which is much inferior to (TPP)AlCl in terms of both catalytic activity and stereoselectivity. Thus, in the reduction catalyzed by the chloroaluminum porphyrins, (TPP)AlCl and (EtioP)AlCl, the hydrogen transfer from carbinol to carbonyl group is affected by the coordinative interactions of substrates with the Lewis acidic metal center of the catalyst. The attempted reaction of cyclohexanone and 2-propanol with (TPP)AlCl in basic solvents such as tetrahydrofuran and pyridine resulted in no reduction of the substrate, probably due to the neutralization of the Lewis acidity of the catalyst by the preferential coordination of the solvent molecule.

The reduction of methylcyclohexanones with secondary alcohols catalyzed by aluminum porphyrin involves two competitive hydrogen-transfer processes, one of which leads to the reduction of methylcyclohexanones to the axial alcohols and the other results in the slow epimerization of the axial alcohols once produced to the equatorial alcohols (Table I and Figure 1). High stereoselectivities observed in both processes suggest that these two reactions proceed with a prominent steric effect of the bulky catalyst, chloroaluminum porphyrin.

Conclusion

Diastereoselective and enantioselective hydrogen-transfer reactions were observed in the reduction of ketones with alcohols by using the chloroaluminum porphyrins, (TPP)AlCl and (EtioP)AlCl, as catalysts. Coordinative interactions are present both for the ketones and alcohols with the Lewis acidic aluminum atom of the catalyst, leading to the facile hydrogen transfer under mild conditions. The reactions take place with a marked steric effect of the bulky porphyrin ligand around the metal center. Apart from the biological viewpoint, limited attempts have been reported to utilize metalloporphyrins as catalyst for synthetic reactions. The present development discloses *a potential utility of metalloporphyrins as catalysts for the steric control in organic syntheses.*

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Construction of Medium- and Large-Sized Cyclic β-Keto Esters (or Nitriles) via One-Pot Three-Carbon Ring Expansion of Carbocyclic β-Keto Esters and Its Application to the Synthesis of (−)-Muscone

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A one-pot, three-carbon ring expansion involving intramolecular aldol condensation and subsequent retro-aldol cleavage is induced by treatment of β-keto esters with potassium *tert*-butoxide in dimethyl sulfoxide to afford functionalized 8-, 9-, 10-, and 15-membered rings, respectively. The stereochemistry of intermediate **21** was established to be a cis-fused carbocyclic ring system with the methyl ketone in the cis position. The mechanism for the three-carbon ring expansion is explained by considering the dual function of the electron-withdrawing group (EWG). An iterative ring expansion was accomplished by the facile conversion of **8** to **20**. Application of this ring expansion method to the synthesis of (−)-muscone further attests to the generality of this reaction.

We recently found a one-pot, three-carbon ring expansion by treatment of carbocyclic β-keto esters with a 4-oxopentyl function at the α-position with potassium *tert*-butoxide in dimethyl sulfoxide.[1a] Medium-sized cy-

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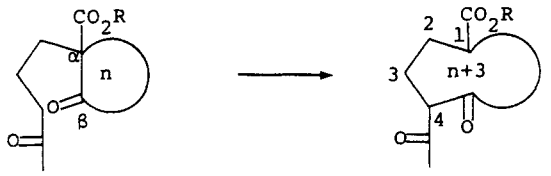
Scheme I



(1) n=5, R=Et (4)

(2) n=6, R=Et (5)

(3) n=7, R=Me (6)

cloalkanones are now easily prepared from preexisting smaller rings, using this ring expansion technique. As a part of our studies on ring conversion,[1] we sought to improve the three-carbon ring expansion and apply it to a variety of carbocyclic β-keto esters. We envisaged that the ring expansion of carbocyclic β-keto esters with (ethoxycarbonyl)propyl or cyanopropyl function at the α-position would be more synthetically useful, because the ring expanded β-keto esters or β-keto nitriles can undergo further elaboration such as alkylation[2] and decarboxylation[3] as well as iterative[4] ring expansion. Therefore, this reaction would be complementary to the Dieckmann (or Thorpe–Ziegler) reaction,[5] an important synthetic procedure to prepare carbocyclic five- and six-membered ring ketones with an ester or a nitrile at the α-position.

Now, we describe the construction of functionalized medium- and large-sized cyclic β-keto esters (or nitriles) using this reaction. The stereochemistry of the intermediate **21** initially formed by intramolecular aldol condensation was chemically established, and mechanistic considerations are discussed. Finally, a facile synthesis of (−)-muscone attests to the generality of this ring-expansion procedure.

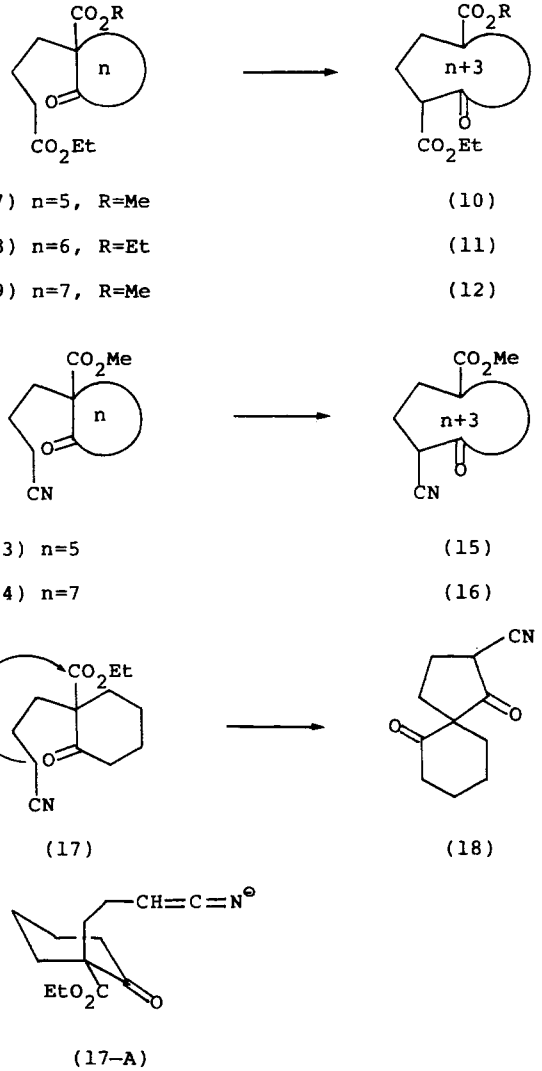
Results and Discussion

Ring Expansion of Carbocyclic β-Keto Esters (5-, 6-, and 7-Membered Rings) with a 4-Oxopentyl Function at the α-Position. Compounds **1–3** were prepared via alkylation of the corresponding carbocyclic β-keto esters with 5-chloropentan-2-one ethylene acetal (*t*-BuOK/DMSO) and subsequent treatment with 10% hydrochloric acid in methanol. Treatment of **3** with potassium *tert*-butoxide in dimethyl sulfoxide at room temperature followed by quenching with acetic acid yielded regioselective ring-expansion product **6** in 78% yield. The structure of **6** is based on its spectral analysis, a double doublet of C_4 proton appearing at 3.42 ppm in the ^1H NMR spectrum, and the signal of newly formed two tertiary carbons (C_4 and C_1) at 59.6 and 52.4 ppm in the ^{13}C NMR spectrum. An $FeCl_3$ test on **6** was positive, indicating the presence of a 1,3-dicarbonyl function. In a manner similar to that described above, **1** and **2** gave **4** and **5** in 62% and 54% yields, respectively (Scheme I).

Ring Expansion of Carbocyclic β-Keto Esters with an (Ethoxycarbonyl)propyl or a Cyanopropyl Function at the α-Position. Compounds **7–9** and **13–14** afforded the expected ring-expansion products, (**10**, 55%; **11**, 49%; **12**, 58%; **15**, 63%; **16**, 57%). The characteristic structure of these compounds could be assigned by 270-MHz ^1H NMR and ^{13}C NMR spectroscopy in each case. For example, in the ^1H NMR spectra of compounds **10**, **11**, **12**, **15**, and **16**, the signals for C_4-H were observed at δ 3.25 (m), 3.16 (t, J = 7.4 Hz), 3.33 (t, J = 7.3 Hz), 3.18 (m), and 3.42 (m), respectively. The ratio of diastereomers was estimated to be 1:1–1:2 on the basis of the ester signals.

But, only **17** preferred Thorp–Ziegler condensation to give the spiro-ring **18** in 52% yield to the ring expansion. The structure of spiro compound **18** was supported by disappearance of the ethoxy unit in its MS and ^1H NMR spectra (Scheme II). Examination of Dreiding stereomodels[6] suggests that the anion adjacent to the cyano

Scheme II



(7) n=5, R=Me (10)

(8) n=6, R=Et (11)

(9) n=7, R=Me (12)

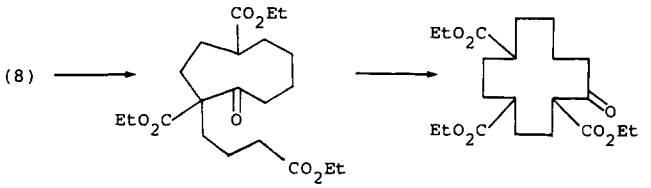
(13) n=5 (15)

(14) n=7 (16)

(17) (18)

(17–A)

Scheme III



(19) (20)

(1) (a) Xie, Z.-F.; Suemune, H.; Sakai, K. *J. Chem. Soc., Chem. Commun.* **1988**, 612. (b) For recent examples of three carbon ring expansion, see: Baldwin, J. E.; Adlington, R. M.; Robertson, J. *J. Chem. Soc., Chem. Commun.* **1988**, 1404. Dowd, P.; Choi, S.-C. *J. Am. Chem. Soc.* **1987**, *109*, 6548. For a recent review, see: Stach, H.; Hesse, M. *Tetrahedron* **1988**, *44* 1573.

(2) For alkylation of β-keto ester, see: Singh, J. *J. Org. Chem.* **1980**, *45*, 3368 and early references cited therein.

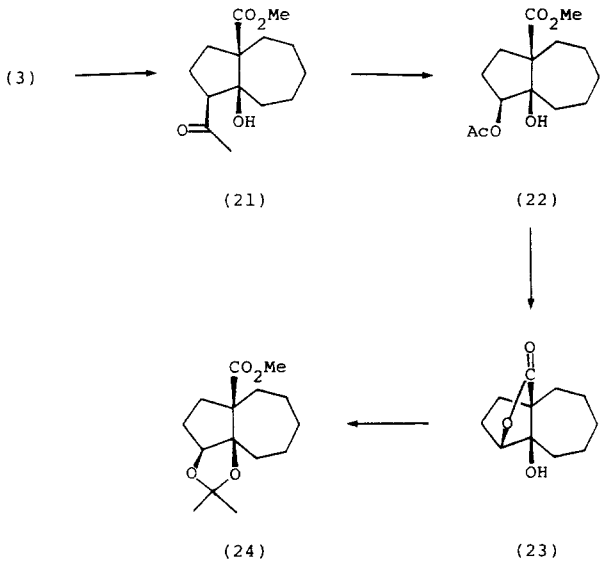
(3) For decarboxylation of β-keto ester, see: Krapcho, A. P. *Synthesis* **1982**, 805.

(4) Bartlett, P. A.; Ting, P. C. *J. Org. Chem.* **1986**, *51*, 2230.

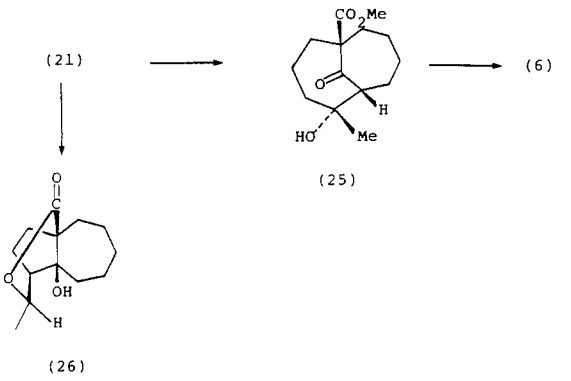
(5) Schaeffer, J. P.; Bloomfield, J. *J. Org. React.* **1965**, *15*, 1.

(6) Dreiding Steromodels; Büchi-Laboratotiums-Technik AG (Swiss).

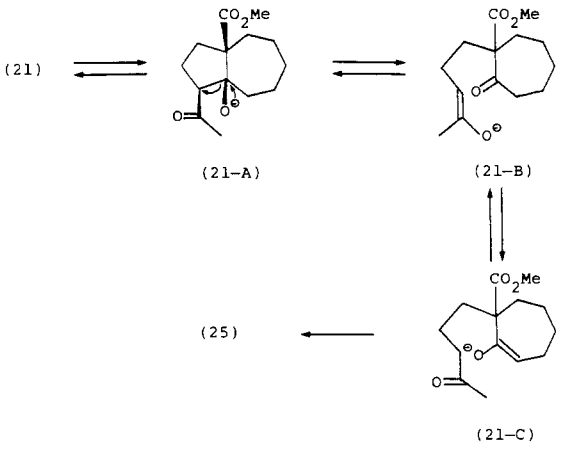
Scheme IV



Scheme V



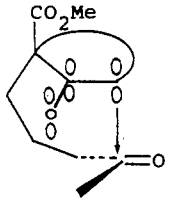
Scheme VI



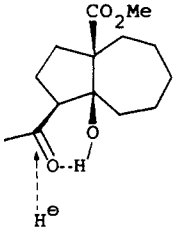
group occupies a sterically favorable position to attack the ester function rather than the ketone (see **17-A**). Ring expansion of **8** followed by trapping with ethyl 4-bromobutyrate afforded **19** in 67% yield. On treatment with t-BuOK, **19** was further enlarged to 12-membered ring ketone **20** in 51% yield (Scheme III). The ^{1}H NMR spectrum of **20** showed a triplet signal at 3.30 ppm for C_7-H, in addition to a tertiary carbon of C_7 at 52.18 ppm in the ^{13}C NMR spectrum. Thus, this iterative ring expansion provides a novel three-carbon ring-expansion method.

Stereochemistry of Intermediate 21 and Mechanistic Consideration. Intermediate **21** was isolated by treatment of **3** with t-BuOK/THF at −78 °C. To clarify the stereochemistry of **21** concerning in the pathway of ring expansion, we embarked on the following chemical transformation (Scheme IV). Baeyer–Villiger oxidation of **21** with CF_3CO_3H followed by methanolysis with K_2CO_3/MeOH afforded the five-membered lactone **23**. The lactone structure of **23** is supported by a 1760 cm^{-1} absorption in the IR spectrum, in addition to the disappearance of methyl signal in the ^{1}H NMR spectrum. Facile formation of **23** indicates that the methyl ketone in **21** should be cis relative to the angular methyl ester. By treatment with 2,2-dimethoxypropane/*p*-$MeC_6H_4SO_3H$, **23** was converted to acetonide **24**. Compound **24** showed a characteristic singlet at 3.68 ppm assignable to angular methyl ester in the ^{1}H NMR spectrum. Therefore, the stereochemistry of **21** was confirmed to be a cis-fused carbocyclic ring system with the methyl ketone in the cis position. An examination of molecular models strongly suggested that intramolecular aldol condensation of **3** would take place from the anti direction to the angular methyl ester to form the cis-fused ring system.

The chemistry of **21** proved intriguing (Scheme V). For example, treatment of **21** with L-Selectride (Aldrich) or $NaBH_4$ at −78 °C afforded bicyclo[4.4.1]undecanone derivative **25**, and the expected reduction product was not obtained. The two quaternary carbons (C_1 and C_5) and two carbonyl carbons for **25** were observed as singlets at 66.5, 81.5, 176.4, and 218.5 ppm in the off-resonance spectrum, respectively. The formation of **25** could be explained as follows (Scheme VI). The generated O-anion as shown in **21-A** induced facile retro aldol condensation to give **21-B**, the ketone of which may be somehow masked by chelation with lithium (or sodium) to reduce its carbonyl character. It is reasonable to presume an equilibrium occurs between enolates **21-B** and **21-C**, the latter undergoing intramolecular aldol condensation to yield exclusively **25**. Based on the assumption that the attack of the carbanion would take place on the *si* face of the methyl ketone to achieve the required trajectory,[7] the stereochemistry for **25** was temporarily assigned as 5*R* configuration. Reaction of **21** with lithium acetylide also

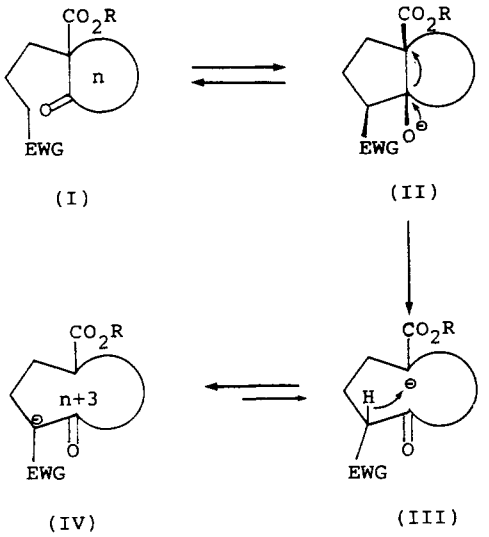


afforded **25**, and the addition product was not obtained. When **21** was subjected to reduction with $NaBH_4$ at room temperature, lactone **26** was isolated in 60% yield. Based on the assumption that attack of hydride ion from the *re* face of the methyl ketone, in which hydrogen bond may be formed between the carbonyl and OH functions, the (*S**)-OH configuration may be predominantly obtained.



(7) Baldwin, J. E. *Tetrahedron* **1982**, *38*, 2939.

Scheme VII

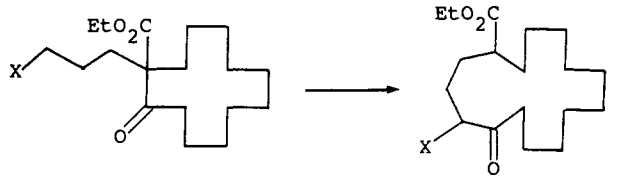


Treatment of **25** with t-BuOK or MeONa gave exclusively the ring-expanded product **6**. Compound **21** could be also converted to **6** by treatment with t-BuOK. This finding suggests that the three-carbon ring expansion process is thermodynamically preferable to the dehydration process. On the other hand, Hesse[1b] failed to observe the ring expansion from α-nitrocyclopentanone or α-nitrocyclohexanone with methyl 3-oxo-4-pentenoate since a thermodynamically favorable proton transfer from the β-keto ester occurs instead of retro aldol cleavage (ring expansion).[8] Trost explained the difficulty of ring enlargement in his reaction, on the basis of strain energy calculations showing that ring expansion from a simple cyclohexanone is 6 kcal/mol endothemic and that of a cycloheptanone is 1 kcal/mol endothemic.[9] We have rationalized the successful three-carbon ring expansion by taking the dual function of EWG in I into consideration (Scheme VII). One is that cis–cis interaction of ester, O-anion, and EWG in II should facilitate the cleavage of bond. The other is that the anion of ring-expanded product III is rapidly trapped by intramolecular acidic proton of β-keto ester. As a consequence, the carbanion of the ring-expanded product is highly stabilized by the enolization of the 1,3-dicarbonyl group (IV).

Application of the Three-Carbon Ring Expansion to the Synthesis of (−)-Muscone. The new approach to ring expansion provides a practical route to the hitherto difficult preparation of medium-sized rings. To test the feasibility of this reaction, we undertook the ring expansion of 12-membered ring β-keto esters **27** and **28** with cyanopropyl or (ethoxycarbonyl)propyl function at the α-position. As expected, the ring-expanded cyclopentadecanones **29** and **30** were obtained in 64% and 61% yields, respectively (Scheme VIII).

This finding allowed us to apply this ring expansion to a novel total synthesis of (−)-Muscone.[10] According to this strategy (Scheme IX), ethoxycarbonylation of commercially available **31** with ethyl cyanoformate afforded **32** in 89% yield. Alkylation of **32** with (*S*)-4-bromo-3-methylbutanenitrile[11] gave **33** (85% yield), which was exposed to

Scheme VIII



(27) X=CN (29)

(28) X=CO_2Et (30)

the ring-expansion conditions to afford **34** in 70% yield. Keto aldehyde **37** was obtained via acid hydrolysis followed by reduction with $LiAlH_4$, then oxidation with pyridinium chlorochromate (overall yield 50%). Compound **37** was characterized by absorptions at 2720, 1730, and 1710 cm^{-1} in its IR spectrum. Decarbonylation of **37** with Wilkinson's complex[12] afforded (−)-muscone in 40% yield. This synthesis provides novel access to (−)-muscone (seven steps from **31**, overall yield 13%) in its natural form.

Conclusion

We have developed a one-pot, three-carbon ring-expansion reaction to synthesize medium- and large-sized rings. A new mechanism for this process is proposed by considering the dual function of the EWG in I. Among synthetic approaches[13] to medium- and large-sized rings, the reported method is simple and affords functionalized medium- to large-sized cyclic β-keto esters (or nitriles). Furthermore, the facile synthesis of (−)-muscone demonstrates the usefulness and generality of the reaction.

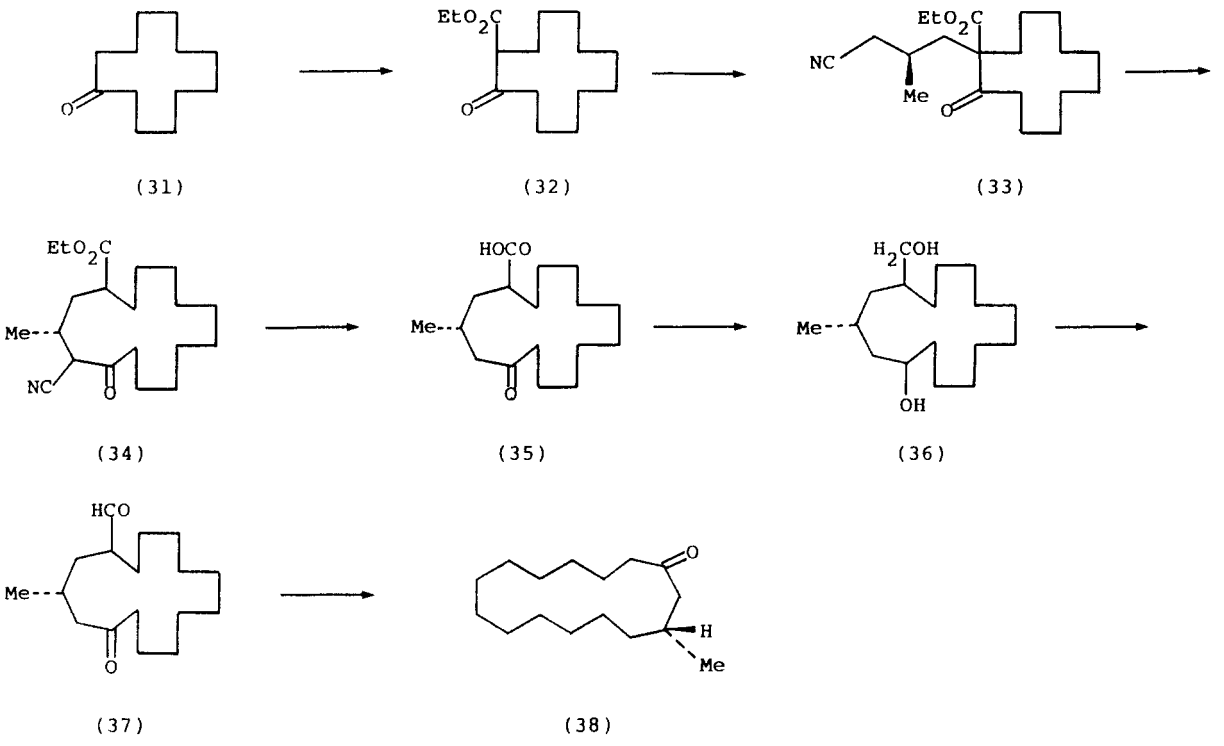
Experimental Section

General Methods. NMR spectra were obtained in $CDCl_3$ solution at 270 MHz. Each reaction was carried out under an N_2 atmosphere and monitored by TLC (silica gel 60F-254 plates). DMSO was distilled in the presence of CaH_2 before use. All organic solvent extracts were washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure on a rotary evaporator. Unless otherwise indicated, each product was purified by flash chromatography (230–400 mesh silica gel) and obtained as oily substances. The purity of all title compounds was judged to be >95% by TLC and GC.

General Ring-Expansion Procedure: Methyl 4-Acetyl-5-oxocyclodecanecarboxylate (6). To a freshly distilled DMSO solution (8 mL) of sublimed t-BuOK (265 mg, 2.36 mmol) at 25 °C under an N_2 atmosphere was added dropwise a DMSO solution (5 mL) of methyl 2-oxo-1-(4-oxopentyl)cycloheptanecarboxylate (500 mg, 1.97 mmol). After 5 h at 25 °C, acetic acid (0.5 mL) was added to quench the reaction. The reaction mixture was diluted with brine (5 mL), followed by extraction with EtOAc. The organic layer was washed with 5% aqueous $NaHCO_3$ (5 mL). The crude product was purified by flash column chromatography (20% EtOAc–hexane) to give 390 mg (78% yield) of **6** as a colorless oil: R_f 0.48 in EtOAc–hexane (2:1); IR 1740–1690 (br), 1635, 1440, 1360, 1220 cm^{-1}; ^1H NMR δ 1.40–2.45 (m, 15 H), 2.24 (s, 3 H), 3.42 (dd, 1 H, J = 7.4, 14.6 Hz), 3.74 (s, 3 H); ^{13}C NMR δ 24.2, 25.1, 25.9, 28.7, 29.4, 29.8, 31.4, 43.0, 51.8, 52.4, 59.6, 170.1, 202.9, 215.5; MS m/e (relative intensity) 254 (M^+, 1), 223 (2), 211 (1), 194 (7), 178

(8) Nakashita, Y.; Hesse, M. *Helv. Chim. Acta* **1983**, *66*, 845.
(9) Trost, B. M.; Vincent, J. E. *J. Am. Chem. Soc.* **1980**, *102*, 5680.
(10) For the synthesis of optically active (*R*)-(−)-muscone, see: Terunuma, D.; Motegi, M.; Tsuda, M.; Sawada, T.; Nozawa, H.; Nohira, H. *J. Org. Chem.* **1987**, *52*, 1630. Branca, Q.; Fischli, A. *Helv. Chim. Acta* **1977**, *60*, 925. Stallberg-Stenhagen, S. *Arkiv Kemi.* **1951**, *3*, 517.
(11) This chiral building block was readily obtained by chemo-enzymatic approach, see: Xie, Z.-F.; Suemune, H.; Sakai, K. *J. Chem. Soc., Chem. Commun.* **1988**, 1638.
(12) Tsuji, J.; Ohno, K. *Tetrahedron Lett.* **1965**, 3969.
(13) For approaches to medium- and large-sized rings, see: (a) Molander, G. A.; Shubert, D. C. *J. Am. Chem. Soc.* **1987**, *109*, 6877. (b) Adams, J.; Frenette, R.; Beley, M.; Chibante, F.; Springer, J. P. *Ibid.* **1987**, *109*, 5432. (c) Oppolzer, W. *Acc. Chem. Res.* **1982**, *15*, 135. (d) Kocovsky, P.; Turecek, F.; Jajicek, J. *Synthesis of Natural Products: Problems of Stereoselectivity*; CRC: Boca Raton, FL, **1986**; Volume 1, p 135. (e) Patel, H. A.; Dev, S. *Tetrahedron* **1981**, *37*, 1577. See also ref 1.

Scheme IX



(15), 112 (76); HRMS for $C_{14}H_{22}O_4$ (M^+) calcd m/z 254.3263, found 254.3251.

Ethyl 4-Acetyl-5-oxocyclooctanecarboxylate (4). According to general ring expansion procedure described above, **4** was obtained as a colorless oil in 62% yield: R_f 0.60 in EtOAc–hexane (1:1); IR 1740, 1710, 1440, 1360 cm^{-1}; ^1H NMR δ 1.40–2.40 (m, 11 H), 1.28 (t, 3 H, J = 7.2 Hz), 2.24 (s, 3 H), 3.40 (t, 1 H, J = 6.9 Hz), 4.18 (q, 2 H, J = 7.2 Hz); ^{13}C NMR δ 14.2, 20.7, 26.1, 27.4, 29.0, 29.4, 38.0, 48.9, 59.8, 61.5, 169.6, 202.9, 213.5; MS m/e 240 (M^+, 2), 212 (2), 195 (12), 166 (11), 149 (100); HRMS for $C_{13}H_{20}O_4$ (M^+) calcd m/z 240.2994, found 240.2971.

Ethyl 4-acetyl-5-oxocyclononanecarboxylate (5): 54% yield; R_f 0.53 in EtOAc–hexane (1:1); IR 1710 (br), 1640, 1440, 1360 cm^{-1}; ^1H NMR δ 1.28 (t, 3 H, J = 7.3 Hz), 1.40–2.50 (m, 13 H), 2.24 (s, 3 H), 3.40 (t, 1 H, J = 7.1 Hz), 4.18 (q, 2 H, J = 7.3 Hz); ^{13}C NMR δ 14.1, 25.0, 25.3, 25.9, 27.2, 28.8, 34.1, 42.1, 50.5, 59.9, 61.3, 169.7, 203.2, 212.7; MS m/e 254 (M^+, 2), 211 (2), 209 (12), 181 (2), 124 (49); HRMS for $C_{14}H_{22}O_4$ (M^+) calcd m/z 254.3263, found 254.3291.

Methyl 4-(ethoxycarbonyl)-5-oxocyclooctanecarboxylate (10): 55% yield, a colorless oil; R_f 0.42 in EtOAc–hexane (1:2); IR 1730 (br), 1660, 1450, 1370, 1250 cm^{-1}; ^1H NMR δ 1.25 (t, 2 H, J = 7.2 Hz), 1.28 (t, 1 H, J = 7.2 Hz), 1.50–2.50 (m, 11 H), 3.25 (m, 1 H), 3.67 (s, 2 H), 3.73 (s, 1 H), 4.16 (q, $^4/_3$ H, J = 7.2 Hz), 4.18 (q, $^2/_3$ H, J = 7.2 Hz); MS m/e 256 (M^+, 2), 228 (2), 224 (36), 210 (12), 197 (12), 192 (2), 123 (100); HRMS for $C_{13}H_{20}O_5$ (M^+) calcd m/z 256.2988, found 256.2998.

Ethyl 4-(ethoxycarbonyl)-5-oxocyclononanecarboxylate (11): 49% yield, a colorless oil; R_f 0.52 in EtOAc–hexane (1:2); IR 1710 (br), 1660, 1450, 1370, 1250 cm^{-1}; ^1H NMR δ 1.26 (t, 3 H, J = 7.1 Hz), 1.28 (t, 3 H, J = 7.1 Hz), 1.40–2.30 (m, 10 H), 2.30–2.90 (m, 3 H), 3.13 (t, 0.5 H, J = 7.6 Hz), 3.16 (t, 0.5 H, J = 7.4 Hz), 4.16 (q, 2 H, J = 7.1 Hz), 4.19 (q, 2 H, J = 7.1 Hz); MS m/e 284 (M^+, 1), 238 (36), 210 (24), 136 (47), 108 (51); HRMS for $C_{15}H_{24}O_5$ (M^+) calcd m/z 284.3526, found 284.3543.

Methyl 4-(ethoxycarbonyl)-5-oxocyclodecanecarboxylate (12): 58% yield, a colorless oil; R_f 0.53 in EtOAc–hexane (1:2); IR 1740, 1710, 1450, 1370, 1230 cm^{-1}; ^1H NMR δ 1.27 (t, 3 H, J = 7.2 Hz), 1.35–2.00 (m, 12 H), 2.29–2.65 (m, 3 H), 3.33 (t, 1 H, J = 7.3 Hz), 3.73 (s, 3 H), 4.19 (q, 2 H, J = 7.2 Hz); MS m/e 284 (M^+, 4), 239 (1), 224 (1), 179 (9), 146 (30); HRMS for $C_{15}H_{24}O_5$ (M^+) calcd m/z 284.3526, found 284.3549.

Methyl 4-cyano-5-oxocyclooctanecarboxylate (15): 63% yield, a colorless oil; R_f 0.56 in EtOAc–hexane (1:1); IR 2250, 1720 (br), 1650, 1460, 1340, 1200 cm^{-1}; ^1H NMR δ 1.60–2.15 (m, 8 H), 2.20–2.50 (m, 3 H), 3.18 (m, 1 H), 3.74 (s, 1 H), 3.76 (s, 2 H); MS m/e 209 (M^+, 3), 178 (16), 150 (8), 122 (17), 110 (39); HRMS for $C_{11}H_{15}NO_3$ (M^+) calcd m/z 209.2451, found 209.2446.

Methyl 4-cyano-5-oxocyclodecanecarboxylate (16): 57% yield, a colorless liquid; R_f 0.49 EtOAc–hexane (1:1); IR 2250, 1740, 1710, 1640, 1460, 1370, 1260 cm^{-1}; ^1H NMR δ 1.20–2.00 (m, 12 H), 2.10–2.90 (m, 3 H), 3.42 (m, 1 H), 3.81 (s, 1.5 H), 3.82 (s, 1.5 H); MS m/e 237 (M^+, 9), 209 (3), 181 (16), 141 (39), 112 (100); HRMS for $C_{13}H_{19}NO_3$ (M^+) calcd m/z 237.2988, found 237.2969.

1,6-Dioxospiro[5.4]decane-2-carbonitrile (18): 52% yield, a yellow oil; R_f 0.30 in EtOAc–hexane (1:10); IR 2950, 2250, 1760, 1710, 1640, 1460, 1370, 1260, 1200, 1140 cm^{-1}; ^1H NMR δ 1.60–2.30 (m, 6 H), 2.35–2.50 (m, 2 H), 2.60–2.90 (m, 2 H), 3.34 (m, 1 H); MS m/e 191 (M^+, 28), 164 (54), 136 (19), 120 (24); HRMS for $C_{11}H_{13}NO_2$ (M^+) calcd m/z 191.2284, found 191.2296.

Iterative Ring Expansion of Ethyl 1-(3-(Ethoxycarbonyl)propyl)-2-oxocyclohexanecarboxylate (8). To a solution of t-BuOK (554 mg, 4.94 mmol) in DMSO (10 mL) compound **8** (1.17 g, 4.12 mmol) in DMSO (5 mL) was added dropwise at 30 °C. After 2 h at 30 °C, ethyl 4-bromobutyrate (0.65 mL, 4.53 mmol) was added. The whole mixture was stirred for 14 h and quenched with 20% acetic acid (5 mL). The mixture was extracted with EtOAc (2 × 50 mL) and washed with aqueous $NaHCO_3$ (20 mL). The resulting crude oil was purified via flash chromatography on silica gel (elution with EtOAc/hexane, 1:4) to afford 845 mg (48% yield) of ethyl 4-(ethoxycarbonyl)-4-(3-(ethoxycarbonyl)propyl)-5-oxocyclononanecarboxylate (**19**) as a colorless oil: R_f 0.52 in EtOAc/hexane (1:2); IR 2950, 1740, 1720, 1450, 1370, 1340, 1260, 1180, 1100, 1030 cm^{-1}; ^1H NMR δ 1.20–1.38 (m, 9 H), 1.40–2.05 (m, 14 H), 2.05–2.60 (m, 5 H), 4.00–4.38 (m, 6 H); MS m/e 398 (M^+, 1), 370 (1), 352 (6), 307 (7), 274 (5), 201 (10).

According to general ring-expansion procedure described above, ethyl 4,7-bis(ethoxycarbonyl)-8-oxocyclododecanecarboxylate (**20**) was obtained from **19**: 51% yield, a colorless oil; R_f 0.49 in EtOAc/hexane (1:2); IR 2945, 1730 (br), 1710, 1450, 1370, 1250, 1180, 1100, 1030 cm^{-1}; ^1H NMR δ 1.10–1.36 (m, 9 H), 1.35–2.70 (m, 18 H), 3.30 (t, 1 H, J = 7.3 Hz), 3.96–4.28 (m, 6 H); FDMS m/e 398 (M^+, 22), 35 (100).

Methyl (1*S,3a*R**,8a*S**)-1-Acetyloctahydro-8a-hydroxy-3a(1*H*)-azulenecarboxylate (21).** To a suspension of t-BuOK (490 mg, 43 mmol) in THF (10 mL) was added dropwise at −78 °C **3** (1 g, 3.9 mmol). The stirring was continued for 2 h at −78

°C, and then the reaction was quenched with acetic acid (1 mL) at −78 °C. The mixture was diluted with water (10 mL) and extracted with ether (2 × 50 mL). The combined extracts were washed with aqueous $NaHCO_3$ (20 mL). The crude oil was subjected to flash chromatography (elution with EtOAc/hexane, 1:3) to give 640 mg of **21** (64%) as a colorless liquid: R_f 0.58 in EtOAc/hexane (1:2); IR 3460, 1710, 1690, 1430, 1350, 1230 cm^{-1}; ^1H NMR δ 1.40–2.10 (m, 15 H), 2.22 (s, 3 H), 2.97 (dd, 1 H, J = 7.6, 10.7 Hz), 3.71 (s, 1 H); MS m/e 254 (M^+, 3), 236 (28), 223 (3), 211 (2), 194 (19), 176 (39); HRMS for $C_{14}H_{22}O_4$ (M^+) calcd m/z 254.3263, found 254.3245.

Methyl (1*S,3a*R**,8a*S**)-1-(Acetyloxy)octahydro-8a-hydroxy-3a(1*H*)-azulenecarboxylate (22).** To a solution of CF_3CO_3H (prepared from $(CF_3CO)_2O$ (1.35 mL) and 30% H_2O_2 (200 mg) in CH_2Cl_2 (2 mL)) was added dropwise at 0 °C **21** (150 mg, 0.59 mmol) in CH_2Cl_2 (1 mL). The whole mixture was stirred at 25 °C for 5 h and quenched with addition of $Na_2S_2O_3$ (1 g) and aqueous $NaHCO_3$ (20 mL). The mixture was extracted with CH_2Cl_2 (2 × 30 mL). The crude oil was purified by preparative chromatography (developer with EtOAc/hexane, 1:2) to afford 97 mg of **22** (61%) as a colorless liquid: R_f 0.42 in EtOAc/hexane (1:2); IR 3450, 1710, 1700, 1430, 1230 cm^{-1}; ^1H NMR δ 1.40–2.08 (m, 13 H), 2.10 (s, 3 H), 2.40–2.55 (m, 2 H), 3.73 (s, 3 H), 5.05 (dd, 1 H, J = 7.1, 9.1 Hz); HRMS for $C_{14}H_{22}O_5$ (M^+) calcd m/z 270.3257, found 270.3215.

(1*S,3a*R**,8a*S**)-Hexahydro-8a-hydroxy-3*H*-1,3a-ethano-1*H*-cyclohepta[*c*]furan-3-one (23).** The suspension of **22** (95 mg, 0.36 mmol) and anhydrous K_2CO_3 (138 mg, 1 mmol) in dry MeOH (2 mL) was stirred at 25 °C for 6 h. The mixture was diluted with water (5 mL) and extracted with EtOAc (2 × 30 mL). After usual workup, the resulting residue was subjected to preparative chromatography (EtOAc/hexane, 1:1) to give 62 mg of **23** (85%) as a colorless oil: R_f 0.60 in EtOAc/hexane (1:1); IR 3450, 1770, 1440, 1200 cm^{-1}; ^1H NMR δ 1.20–2.20 (m, 15 H), 4.3 (t, 1 H, J = 1.5 Hz); MS m/e 196 (M^+, 15), 178 (24), 134 (37), 112 (100); HRMS for $C_{11}H_{16}O_3$ (M^+) calcd m/z 196.2462, found 196.2491.

Methyl (3a*S,5a*R**,10a*S**)-Octahydro-2,2-dimethyl-5*H*-azuleno[1,8a-*d*]-1,3-dioxole-5a-carboxylate (24).** A solution of **23** (50 mg, 0.26 mmol), 2,2-dimethoxypropane (1 mL), acetone (0.5 mL), and *p*-TsOH (5 mg) in dimethylformamide was stirred at 30 °C for 20 h. The mixture was diluted with aqueous $NaHCO_3$ (5 mL) and extracted with EtOAc (30 mL). The crude product was purified by flash chromatography (elution with EtOAc/hexane, 1:3) to afford 27 mg of **24** (40%) as well as the recovery of **23** (25 mg, 50%): R_f 0.66 in EtOAc/hexane (1:1); IR 1705, 1440, 1370, 1200 cm^{-1}; ^1H NMR δ 1.33 (s, 3 H), 1.35 (s, 3 H), 1.40–2.35 (m, 14 H), 3.68 (s, 3 H), 4.46 (d, 1 H, J = 3.8 Hz); MS m/e 268 (M^+, 72), 253 (100), 211 (39), 193 (52), 161 (27), 151 (95); HRMS for $C_{15}H_{24}O_4$ (M^+) calcd m/z 268.3532, found 268.3561.

Methyl (1*R,5*R**,6*R**)-5-Hydroxy-5-methyl-11-oxobicyclo[4.4.1]undecane-1-carboxylate (25).** To a solution of **21** (100 mg, 0.4 mmol) in THF (1 mL) was added L-Selectride (0.6 mL, 0.6 mmol) dropwise at −78 °C. After being stirred for 2 h at −78 °C, the mixture was quenched with 3% HCl (5 mL) at −78 °C and extracted with EtOAc (2 × 30 mL). The combined extracts were washed with aqueous $NaHCO_3$ dropwise at −78 °C. After being stirred for 2 h at −78 °C, the mixture was quenched with 3% HCl (5 mL) at −78 °C and extracted with EtOAc (2 × 30 mL). The combined extracts was washed with aqueous $NaHCO_3$ (5 mL). The crude product was purified by preparative chromatography (EtOAc/hexane, 1:2) to give 80 mg of **25** (80%) as a colorless liquid: R_f 0.55 in EtOAc/hexane (1:2); IR 3460, 1690, 1430, 1360, 1200 cm^{-1}; ^1H NMR δ 1.22 (s, 3 H), 1.40–2.05 (m, 14 H), 2.91 (dd, 1 H, J = 9.1, 10.4 Hz), 3.71 (s, 3 H), 3.77 (s, 1 H); ^{13}C NMR δ 22.7, 25.4, 26.1, 27.2, 30.5, 30.8, 34.0, 43.9, 51.2, 51.8, 66.5, 81.5, 176.4, 218.5; MS m/e 254 (M^+, 4), 236 (2), 205 (20), 177 (18), 138 (100); HRMS for $C_{14}H_{22}O_4$ (M^+) calcd m/z 254.3263, found 254.3275.

(3*S*,4*R,4a*S**,9a*R**)-Octahydro-4a-hydroxy-3-methyl-1*H*-4,9a-ethanocyclohepta[*c*]pyran-1-one (26).** To a solution of **21** (100 mg, 0.4 mmol) in MeOH (1 mL) was added $NaBH_4$ (17 mg, 0.44 mmol) in one portion at 0 °C. The whole was stirred for 2 h at 0 °C to room temperature. The reaction mixture was diluted with brine and then extracted with EtOAc (30 mL). After usual workup, the resulting residue was purified by preparative chromatography (EtOAc/hexane, 1:2) to afford 25 mg of **25** (35%) and 54 mg of **26** (60%) as colorless needles recrystallized from hexane/CH_2Cl_2: mp 118–120 °C; IR ($CHCl_3$) 3450 (br), 1710, 1440, 1370, 1160 cm^{-1}; ^1H NMR δ 1.30 (d, 3 H, J = 6.6 Hz), 1.50–2.20 (m, 15 H), 5.07 (dq, 1 H J = 6.6, 1.4 Hz); ^{13}C NMR δ 17.8, 18.2, 20.3, 20.4, 27.3, 29.5, 31.6, 34.5, 50.4, 55.4, 75.2, 81.2, 177.5; MS m/e 224 (M^+, 2), 202 (8), 180 (19), 151 (87), 135 (90).

Ethyl 4-cyano-5-oxocyclopentadecanecarboxylate (29): 64% yield, a colorless oil; R_f 0.36 in EtOAc/hexane (1:4); IR 2250, 1745, 1710, 1470, 1440, 1370, 1250, 1200, 1045 cm^{-1}; ^1H NMR δ 1.24 (t, 3 H, J = 7.4 Hz), 1.25–1.98 (m, 22 H), 2.11–2.78 (m, 3 H), 3.45 (dd, 1 H, J = 6.7, 12.5 Hz), 4.27 (q, 2 H, J = 7.4 Hz); MS m/e 321 (M^+, 6), 293 (5), 275 (29), 247 (6), 220 (4), 197 (11).

Ethyl 4-(ethoxycarbonyl)-5-oxocyclopentadecanecarboxylate (30): 61% yield, a colorless liquid; R_f 0.45 in EtOAc/hexane (1:4); IR 1740, 1710, 1470, 1445, 1370, 1340, 1250, 1150 cm^{-1}; ^1H NMR δ 1.23 (t, 6 H, J = 7.2 Hz), 1.30–1.90 (m, 22 H), 2.35–2.64 (m, 3 H), 3.29 (t, 1 H, J = 7.1 Hz), 4.19 (q, 4 H, J = 7.2 Hz); FDMS m/e 368 (M^+, 100), 322 (12).

Synthesis of (−)-Muscone. Ethyl 2-Oxocyclododecanecarboxylate (32). To a solution of lithium diisopropylamide (prepared from *n*-BuLi (16.5 mL 26.4 mmol) and diisopropylamine (3.7 mL, 26.4 mmol) in THF (20 mL)) was added cyclododecanone (4 g, 22 mmol) in THF (20 mL) dropwise at −78 °C. The mixture was stirred for 30 min at −78 °C and then hexamethylphosphoramide (2.24 mL, 22 mmol) was added, followed by dropwise addition of ethyl cyanoformate (2.6 mL, 26.4 mmol). After 2 h at −78 °C, the mixture was warmed up to 0 °C and then poured into cold water (20 mL). After extraction with ether (4 × 50 mL) followed by usual workup, the resulting residue was purified by flash chromatography (elution with EtOAc/hexane, 1:5) to afford 4.97 g of **32** (89%) as a colorless oil: R_f 0.45 in EtOAc/hexane (1:8); IR 2950, 1745, 1710, 1470, 1440, 1370, 1260, 1240, 1180, 1020 cm^{-1}; ^1H NMR δ 1.35 (t, 3 H, J = 7.1 Hz), 1.30 (br, 18 H); 2.30–2.70 (m, 3 H), 3.61 (dd, 1 H, J = 3.7, 11.5 Hz), 4.16 (q, 2 H, J = 7.1 Hz); MS m/e 254 (M^+, 1), 209 (3), 182 (31), 139 (15), 111 (42).

Ethyl 1-((2*S*)-3-Cyano-2-methylpropyl)-2-oxocyclododecanecarboxylate (33). To a solution of t-BuOK (530 mg, 4.72 mmol) in DMSO (8 mL) was added **32** (1 g, 3.9 mmol) dropwise at 25 °C. After 30 min, (*S*)-4-bromo-3-methylbutanenitrile (430 mg, 4.33 mmol) was added dropwise. The stirring was continued for 16 h, quenched with water (10 mL), and extracted with EtOAc (3 × 30 mL). The crude product was purified by flash chromatography (elution with EtOAc/hexane, 1:10) to afford 925 mg of **33** (71%) as a colorless liquid: R_f 0.36 in EtOAc/hexane (1:5); IR 2250, 1735, 1710, 1470, 1440, 1370, 1240, 1200, 1180 cm^{-1}; ^1H NMR δ 1.12 (d, 1.5 H, J = 7.2 Hz), 1.17 (d, 1.5 H, J = 7.2 Hz), 1.30–2.10 (m, 21 H), 2.10–2.60 (m, 4 H), 4.17 (q, 1 H, J = 7.2 Hz), 4.18 (q, 1 H, J = 7.2 Hz); MS m/e 335 (M^+, 8), 320 (5), 307 (3), 289 (52), 261 (6), 81 (28); HRMS for $C_{20}H_{33}NO_3$ (M^+) calcd m/z 335.4856, found 335.4866.

Ethyl (3*R*)-4-Cyano-3-methyl-5-oxocyclopentadecanecarboxylate (34). According to general ring expansion procedure, **34** (70%) was obtained as a colorless liquid: R_f 0.31 in EtOAc/hexane (1:5); IR 2250, 1740, 1710, 1470, 1445, 1370, 1240, 1190, 1030 cm^{-1}; ^1H NMR δ 1.11 (d, 1.5 H, J = 6.6 Hz), 1.12 (d, 1.5 H, J = 6.6 Hz), 1.35 (br, 23 H), 2.20–2.70 (m, 2 H), 2.88 (m, 1 H), 3.48 (m, 1 H), 4.22 (m, 2 H); MS m/e 335 (M^+, 15), 326 (6), 289 (79), 262 (15), 221 (6); HRMS for $C_{20}H_{33}NO_3$ (M^+) calcd m/z 335.4856, found 335.4870.

(3*R*)-3-Methyl-5-oxocyclopentadecanecarboxaldehyde (37). A mixture of **34** (300 mg, 0.9 mmol) in concentrated HCl was heated under reflux for 48 h. The mixture was poured into water (5 mL) and then extracted with EtOAc (3 × 50 mL). The solvent was removed to leave a residue, which was purified by flash chromatography using a short column (elution with EtOAc/hexane, 2:1) to afford 131 mg of (3*R**)-5-(hydroxycarbonyl)-3-methyl-1-cyclopentadecanone (**35**) as a yellow oil: R_f 0.31 in EtOAc/hexane (2:1); IR 3500–3000 (br), 1750, 1710 cm^{-1}.

To a suspension of $LiAlH_4$ (67 mg, 1.75 mmol) in dry ether (10 mL), **35** (100 mg, 0.35 mmol) in ether (1 mL) was added dropwise at 0 °C. The mixture was stirred for 5 h at 25 °C and further refluxed for 1 h. The reaction was quenched with 5% H_2SO_4 (10 mL) and then extracted with ether (3 × 50 mL). After usual workup, the resulting residue was purified by flash chromatog-

raphy (elution with EtOAc/hexane, 2:1) to give 82 mg of (3*R**)-5-(hydroxymethyl)-3-methyl-1-cyclopentadecanol (**36**) (87%) as a colorless liquid: IR 3400 (br) cm^{-1}; FDMS *m/e* 270 (M^+, 100), 252 (11).

A mixture of **36** (60 mg, 0.22 mmol) and pyridinium chlorochromate (142 mg, 0.66 mmol) in CH_2Cl_2 (5 mL) was stirred at 25 °C for 15 h and filtrated on Celite. The filtrate was subjected to the usual workup to leave a residue, which was purified by a short flash column eluted with ether to afford 53 mg of **37** (90% yield) as a colorless liquid: R_f 0.39 in EtOAc/hexane (1:5); IR 2940, 2720, 1730, 1710, 1470, 1440, 1365, 1240, 1190, 1125 cm^{-1}; ^1H NMR δ 0.95 (d, 0.75 H, J = 6.6 Hz), 0.96 (d, 2.25 H, J = 6.6 Hz), 1.29 (br, 23 H), 2.10–2.70 (m, 4 H), 2.90 (m, 1 H), 9.74 (d, 0.25 H, J = 2 Hz), 9.75 (d, 0.75 H, J = 2.2 Hz); FDMS *m/e* 266 (M^+, 100), 265 (6), 238 (19), 125 (10), 110 (4); HRMS for $C_{17}H_{30}O_2$ (M^+) calcd *m/z* 266.4228, found 266.4231.

(*R*)-3-Methyl-1-cyclopentadecanone (38). A mixture of **37** (20 mg, 0.075 mmol) and $RhCl(PPh_3)_3$ (75 mg, 0.11 mmol) in benzene (3 mL) was refluxed for 8 h. After cooling, EtOH (2 mL) was added. The mixture was diluted with brine (5 mL) and extracted with EtOAc (30 mL) followed by usual workup. The resulting crude product was purified by preparative chromatography developed with EtOAc/hexane (1:2) to afford 7.2 mg of **38** (40%) as a colorless liquid: $[\alpha]^{25}_D$ −11.4° (*c* = 0.70, MeOH); IR 2950, 1718, 1460, 1430, 1380, 1320, 1280 cm^{-1}; ^1H NMR δ 0.94 (d, 3 H, J = 6.1 Hz, 1.15–1.80 (m, 23 H), 1.80–2.45 (m, 4 H); MS *m/e* 238 (M^+, 10), 223 (3), 195 (23), 164 (4); HRMS for $C_{16}H_{30}O$ (M^+) calcd *m/z* 238.4136, found 238.4149.

Registry No. 1, 124355-45-9; **2**, 124355-46-0; **3**, 124355-44-8; **4**, 116487-76-4; **5**, 116487-77-5; **6**, 116487-78-6; **7**, 124355-47-1; **8**, 124355-49-3; **9**, 124355-51-7; **10** (isomer 1), 124355-48-2; **10** (isomer 2), 124379-61-9; **11** (isomer 1), 124355-50-6; **11** (isomer 2), 124439-17-4; **12** (isomer 1), 124355-52-8; **12** (isomer 2), 124439-97-0; **13**, 124355-53-9; **14**, 124355-55-1; **15** (isomer 1), 124355-54-0; **15** (isomer 2), 124355-67-5; **16** (isomer 1), 124355-56-2; **16** (isomer 2), 124439-18-5; **17**, 124355-57-3; **18**, 124355-58-4; **19**, 124355-59-5; **20**, 124379-60-8; **21**, 124355-60-8; **22**, 124355-61-9; **23**, 124439-14-1; **24**, 124439-15-2; **25**, 124439-16-3; **26**, 124355-62-0; **27**, 124355-63-1; **28**, 124355-64-2; **29**, 119725-14-3; **30**, 119708-20-2; **31**, 830-13-7; **32**, 75232-70-1; **33**, 119708-21-3; **34**, 119708-22-4; **35**, 124355-65-3; **36**, 124355-66-4; **37**, 119708-23-5; **38**, 10403-00-6; ethyl 4-bromobutyrate, 2969-81-5; cyclododecanone, 830-13-7; ethyl cyanoformate, 623-49-4.

Supplementary Material Available: Characterization for compounds not described above (4 pages). Ordering information is given on any current masthead page.

A Stereocontrolled Organopalladium Route to 2,5-Disubstituted Pyrrolidine Derivatives. Application to the Synthesis of a Venom Alkaloid of the Ant Species *Monomorium latinode*

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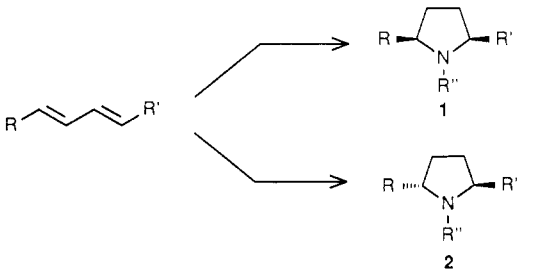
A general method for the preparation of cis- and trans-2,5-disubstituted pyrrolidines from conjugated dienes has been developed. The approach involves a stereocontrolled syn- or anti-1,4-addition of an amino and an oxygen function to the diene via palladium catalysis. Subsequent stereospecific cyclization produces the pure cis- and trans-2,5-disubstituted pyrrolidines, respectively. The method was applied to the synthesis of an ant venom alkaloid from the species *Monomorium latinode*.

Pyrrolidines that are stereospecifically substituted in the 2- and 5-positions have attracted interest for two reasons: (i) there are many natural products with this structure;[1-3] (ii) 2,5-disubstituted pyrrolidines have found use as chiral auxiliaries.[4,5]

A number of stereoselective methods for the synthesis of pyrrolidines have been reported during the last decade.[2,4-8] Although there are many procedures for the preparation of *cis*- and *trans*-2,5-dialkylpyrrolidines, both isomers are not usually available via the same approach. We have recently developed methodology for the functionalization of conjugated dienes, that offers a dual control of the 1,4-relative stereochemistry.[9,10] This is based on

Scheme I



(1) (a) Attygalle, A. B.; Morgan, E. D. *Chem. Soc. Rev.* **1984**, *13*, 245. (b) Jones, T. H.; Blum, M. S.; Fales, H. M. *Tetrahedron* **1982**, *38*, 1949. (c) Daly, J. W.; Spande, T. F.; Whittaker, N.; Highet, R. J.; Feigl, D.; Nishimori, N.; Tokuyama, T.; Myers, C. W. *J. Nat. Prod.* **1986**, *49*, 265.

(2) (a) Iida, H.; Yamazaki, N.; Kibayashi, C. *Tetrahedron Lett.* **1985**, *26*, 3255; *J. Org. Chem.* **1987**, *52*, 1956. (b) Yamazaki, N.; Kibayashi, C. *Tetrahedron Lett.* **1988**, *29*, 5767; *J. Am. Chem. Soc.* **1989**, *111*, 1396.

(3) Massiot, G.; Delaude, C. In *The Alkaloids*; Brossi, A., Ed.; Academic Press: New York, **1986**; Vol. 27, p 269.

(4) (a) Whitesell, J. K.; Minton, M. A.; Chen, K. M. *J. Org. Chem.* **1988**, *53*, 5383. (b) Whitesell, J. Kk. Felman, S. W. *Ibid.* **1980**, *45*, 755. (c) *Ibid.* **1977**, *42*, 1663.

(5) (a) Schlessinger, R. H.; Iwanowicz, E. J. *Tetrahedron Lett.* **1987**, *28*, 2083. (b) Kawanami, Y.; Ito, Y.; Kitagawa, T.; Taniguchi, Y.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1984**, *25*, 857. (c) Björkling, F.; Boutelje, J.; Hjalmarsson, M.; Hult, K.; Norin, T. *J. Chem. Soc., Chem. Commun.* **1987**, *1042*. (d) Short, R. P.; Kennedy, R. M.; Masamune, S. *J. Org. Chem.* **1989**, *54*, 1755.

(6) Weber, T.; Seebach, D. *Helv. Chim. Acta* **1985**, *68*, 155.

(7) (a) Shiosaki, K.; Rapoport, H. *J. Org. Chem.* **1985**, *50*, 1229. (b) Arseniyadis, S.; Huang, P. Q.; Pivetau, D.; Husson, H. P. *Tetrahedron* **1988**, *44*, 2457. (c) Gessner, W.; Takahashi, K.; Brossi, A.; Kowalski, M.; Kaliner, M. A. *Helv. Chim. Acta* **1987**, *70*, 2003.

(8) (a) Harding, K. E.; Marman, T. H. *J. Org. Chem.* **1984**, *49*, 2838. (b) Danishefsky, S.; Taniyama, E.; Webb, R. R. II *Tetrahedron Lett.* **1983**, *24*, 11. (c) Barluenga, J.; Jimenez, C.; Yus, M. *J. Chem. Soc., Perkin Trans. 1* **1984**, 721. (d) Tokuda, M.; Yamada, Y.; Suginome, H. *Chem. Lett.* **1988**, 1289.

(9) (a) Bäckvall, J. E.; Nyström, J. E.; Nordberg, R. E. *J. Am. Chem. Soc.* **1985**, *107*, 3676. (b) Bäckvall, J. E.; Byström, S. E.; Nyström, J. E. *Tetrahedron* **1985**, *41*, 5761. (c) Bäckvall, J. E. In *Organic Synthesis: an interdisciplinary challenge*; Streith, J., Prinzbach, H., Schill, G., Eds.; Blackwell Scientific Publications: Oxford, UK, **1985**; p 69. (d) Bäckvall, J. E. *Bull. Soc. Chim. Fr.* **1987**, 665.

0022-3263/90/1955-0826$02.50/0