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THE STEREOCHEMISTRY OF ELECTROLYSIS AND SAMARIUM DIIODIDE-INDUCED CYCLIZATION BETWEEN CARBONYL AND ENONE SYSTEM IN INTER- AND INTRAMOLECULAR COUPLING

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Abstract – Both the inter- and intramolecular cyclization of the carbonyl compounds with α,β-unsaturated carbonyl system using samarium diiodide and electrolysis were carried out. The stereochemistry of the products was compared each other.

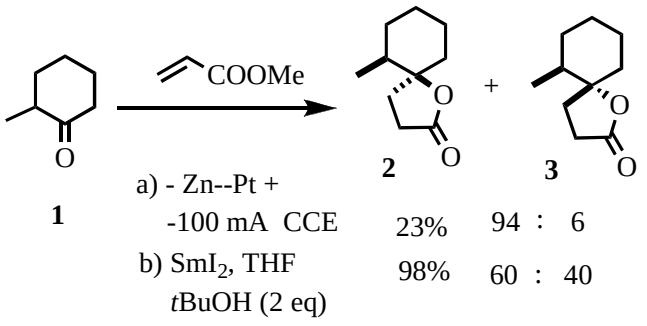
INTRODUCTION

Electrolysis can be carried out in water as a solvent without expensive reagents at ambient temperature costing only electricity.[1] Thus, it is cost-effective and environmentally benign.[1] The reaction mechanism is thought to be through a radical or an anion.[1] Samarium (II) also induces radical coupling of various carbonyl groups, which is well documented.[2] Cyclohexanone was reacted with methyl acrylate to form a lactone by the action of SmI_2, which was reported by Inanaga et al.[3] We are interested in carrying out this type of reaction using electrolysis. At the same time we have already reported several cyclization reactions using SmI_2 to form hydrindanones[4-6] and perhydronaphthalenones.[7] We are interested in carrying out these reactions using electrolysis in order to compare them with the reaction by SmI_2. Now we report our results in detail.

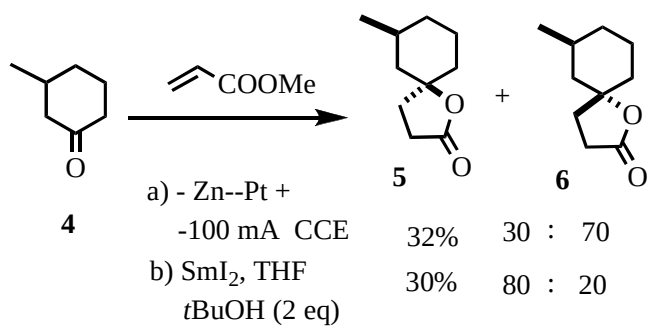
RESULTS AND DISCUSSION

Although cyclohexanone was reported to afford a lactone with methyl acrylate under reductive cyclization conditions,[3] stereoselectivity of the reaction was not studied. We would like to know the stereochemistry (relative to the existing substituents) of the coupling reactions. Therefore, we applied this reaction to 2-methylcyclohexanone (**1**) to study the stereochemistry of the lactone ring and found the isomer ratio was 3:2, whose stereochemistry was determined by derivatization of the products into the

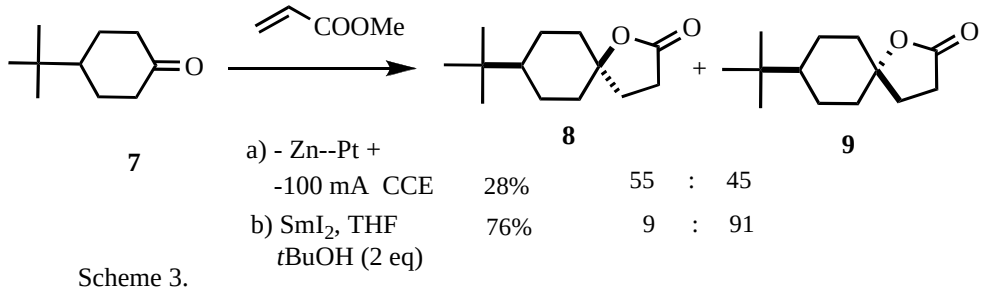
acetate.[8] The selectivity of addition of an alkyl group to the carbonyl group of 2-methylcyclohexanone (**1**) is well known,[9] that is, the alkyl groups always approach from the backside of a 2-methyl group to yield 1,2-*trans*-dialkylated cyclohexanol derivatives. Yamamoto *et al*. used an aluminium complex to prevent the predominant attack by coordination to the carbonyl group.[10] However, this methodology works only in the case of methyl and other small alkyl groups. Large alkyl groups do not work very well. In the SmI_2-induced coupling, syn-product **3** was obtained in *ca*. 40% yield (Scheme 1), which is the highest yield of the syn-product, to the best of our knowledge. We carried out electrolysis of 2-methylcyclohexanone (**1**) with methyl acrylate in *t*BuOH-H_2O (2:3) with Et_4NOTs as an electrolyte. However, the yield was not so high as expected and the ratio of syn-product **3** was similar to that of addition of an alkyl group to 2-methylcyclohexanone (**1**).[9] 3-Methylcyclohexanone (**4**) was next reacted with methyl acrylate. The yield of electrolysis was almost the same as that of **1**, but the ratio was completely opposite to that of **1**. SmI_2-induced cyclization afforded **5** and **6** in poor yield and the ratio was opposite to that of electrolysis. The stereochemistry of the products was determined by analysis of the NOESY spectrum.[11]



Scheme 1.



Scheme 2.



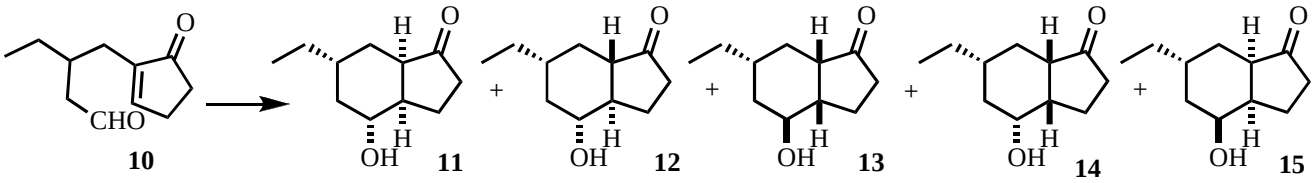
Scheme 3.

Next, we carried out the reaction of 4-*t*-butylcyclohexanone (**7**) and methyl acrylate with the aid of SmI_2 and electrolysis. It is very interesting to note that SmI_2-induced reaction gave two lactones, **8** and **9**, in the ratio of 9:91 in 76% yield. However, electrolysis yielded the same products in the ratio of 55:45 in 28% yield. The stereochemistry was determined by analysis of the 2D NMR spectra and also by derivatization.[12]

Samarium diiodide transfers one-electron to the carbonyl group to yield a radical in the axial manner, in which samarium still coordinates to the carbonyl oxygen atom. Thus, acrylate attacks the radical from the axial side to give compounds **5** and **9** as the major product. In the case of 2-methylcyclohexanone (**1**), the samarium-coordinated group is close to the 2-methyl group, and thus, the selectivity is not as high as **4** and **7**. However, electrolysis provides a radical or an anion of acrylate and it attacks the carbonyl group from the equatorial side to yield an axial alcohol followed by lactonization.[9,13,14]

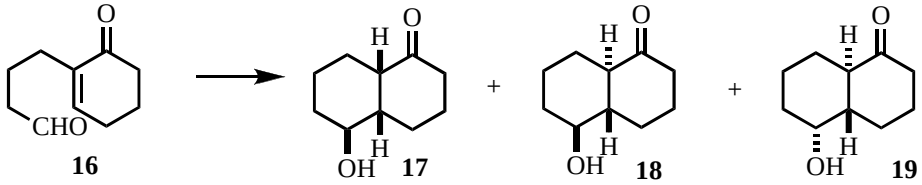
We have previously reported SmI_2-induced intramolecular cyclization to yield hydrindanones[4-6] and perhydronaphthalenones.[7] Aldehyde **10** cyclized under the SmI_2 conditions with a proton source (MeOH) into four kinds of hydrindanones **11**, **12**, **14**, **15** in the ratio of 32:12:17:39 in moderate yield as reported in the literature (Table 1).[5] Here, we carried out electrolysis of compound **10** to yield **11**, **14**, and **15** in the ratio of 17:64:19 in 31% yield. Unfortunately, the yield was much less than that of SmI_2-induced cyclization. The predominant compound **14** had *cis*-ring junction with the ethyl and hydroxy groups in the opposite side. Thus, the results are very diverse and complicated, and different in each case.[15]

Table 1. Cyclization of compound **10** to bycyclic ketols **11**-**15**.



Reagent	Solvent	Additive	Time(h)	Ratio (**11**:**12**:**13**:**14**:**15**)	Yield(%)
electrolysis	*t*BuOH-H_2O (4:6)	Et_4NTsO	4	17:0:0:64:19	31
SmI_2	THF	-	2	47:20:21:12:0	64
SmI_2	THF	MOH (10 equiv.)	1	32:12:0:17:39	69

Table 2. Cyclization of compound **16** to bicyclic ketols **17**-**19**.

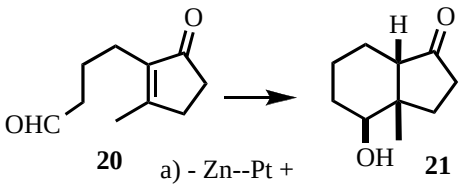


Reagent	Solvent	Additive	Time(h)	Ratio (**17**:**18**:**19**)	Yield(%)
electrolysis	*t*BuOH-H_2O (4:6)	Et_4NTsO	3	22:14:63	60
SmI_2	THF	-	1	28:61:11	100
SmI_2	THF	NiI_2	4	55:45:0	98

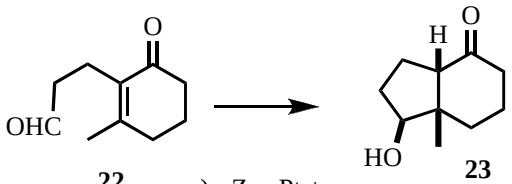
Next, we studied the reaction of compounds having a 6-membered ring. Aldehyde **16** was reported to give **17**, **18**, and **19** in quantitative yield in the ratio of 28:61:11 by the action of SmI_2 without additive.[7]

Electrolysis afforded three products as well, in the ratio of 22:14:63 in favor of compound **19**, which was a remarkable contrast to the results of SmI_2. Compound **19** has *trans* stereochemistry concerning the hydroxy group and the juncture proton, while compounds **17** and **18** have *cis*-arrangement.

The next two examples are the case of compounds having a methyl group at the juncture position. Compound **20**[16] cyclized into *cis*-arranged hydrindanolone **21**[17] in 80% yield by SmI_2, and in 39% yield by electrolysis (Scheme 4). Similar results were obtained in the case of compound **22** (Scheme 5).[18,19] Therefore, the 6-Endo Trig mode or 5-Endo Trig mode of cyclization reaction by electrolysis and SmI_2 both gave the same product in these examples.



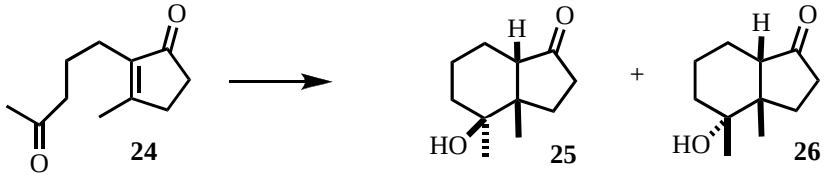
Scheme 4.



Scheme 5.

The last two examples are the case of reaction between ketone and the α,β-unsaturated ketone system having a methyl group at the juncture position (Table 3).[20] Electrolysis did not give a good yield, but the predominant product was compound **26** in the ratio of 1:4. SmI_2-induced reaction also afforded compound **26** as a major product without an additive. SmI_2 reduces the carbonyl group to give -OSm group and it coordinates to the oxygen atom of the enone carbonyl group to yield compound **26**. However, SmI_2 with a proton source (MeOH) gave an almost 1:1 mixture of diastereomeric products **25** and **26**.[21] In this case, the -OSm group does not coordinate to the carbonyl oxygen atom to afford compounds **25** and **26**, in almost 1:1 ratio.[4]

Table 3. Cyclization of compound **24** to bicyclic ketols **25** and **26**.

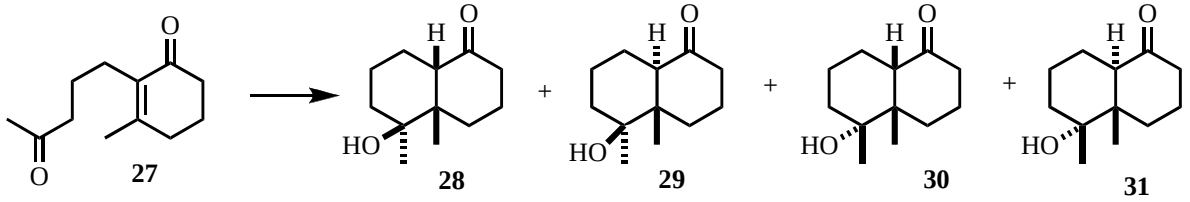


Reagent	Solvent	Additive	Time(h)	Ratio (**25**:**26**)	Yield(%)
electrolysis	*t*BuOH-H_2O (4:6)	Et_4NTsO	3	20:80	34
SmI_2	THF	-	1	11:89	50
SmI_2	THF	MOH (20 equiv.)	1.5	55:45	100

In the case of perhydronaphthalenones, the yield of the electrolysis reaction was excellent and the products were only **28** and **29**, in the ratio of *ca.* 1:1 (Table 4). SmI_2-induced reaction of compound **27** gave four kinds of products as reported.[7] Since compounds **28** and **29** are the isomers concerning the

juncture position, it is easier to isomerize **28** into the *trans*-fused ketone **29**. In this respect, the whole process of electrolysis is highly selective and gives high yield, which can be utilized in the synthesis.

Table 4. Cyclization of compound **27** to bicyclic ketols **28**-**31**.



Reagent	Solvent	Additive	Time(h)	Ratio (**28**:**29**:**30**:**31**)	Yield(%)
electrolysis	*t*BuOH-H_2O (4:6)	Et_4NTsO	4.5	43:57:0:0	100
SmI_2	THF	-	3.5	69:19:3:9	100
SmI_2	THF	MOH (20 equiv.)	1.5	30:51:11:8	91

Here, we reported three examples of intermolecular coupling and six examples of intramolecular cyclization by both electrolysis and SmI_2-induced reaction. Since the enone system is more susceptible to reduction, the resulting anion or radical attacks the other carbonyl group. Samarium can coordinate to both carbonyl groups and it adopts an equatorial or energetically more stable position leading to the stereoselective products. Electrolysis can provide high stereoselectivity and high yield of products, if the conditions fit the reaction system. It should be noted here again, water can be used as a solvent for electrolysis without expensive reagents at ambient temperature costing only electricity and it is cost-effective and environmentally benign.[1]

EXPERIMENTAL

GENERAL

IR spectra were measured on a JASCO FT/IR-5300 spectrophotometer. The ^1H and ^{13}C NMR spectra were taken on a Varian Unity 600 (600 MHz and 150 MHz, respectively) and a Varian Unity 200 (200 MHz and 50 MHz, respectively) spectrometer. MS spectra including high-resolution mass spectra were recorded on a JEOL JMS-700 MStation. Chemcopak Nucleosil 50-5 (4.8×250 mm) was used for HPLC (JASCO pump system). Silica gel 60 (70-230 mesh, Fuji Sylisia) was used for column chromatography and silica gel 60 F_{254} plates (Merck) were used for TLC.

General procedure for electrolysis

Zn and Pt were used for cathode and anode, respectively, with Et_4NOTs in *t*BuOH-H_2O (2:3) (20 mL), at 100 mA and 13.94 V at rt. Work-up: Benzene was added and most of the water was removed under

reduced pressure. The residue was extracted with AcOEt and the organic layer was washed with Sat. NaCl solution. The organic layer was dried ($MgSO_4$), and the filtrate was evaporated to give a residue, which was purified by silica-gel column chromatography or HPLC.

General procedure for SmI_2 reduction

A solution of substrate in dry THF was introduced into a solution of SmI_2 at a certain temperature. Saturated solution of sodium potassium tartrate was added and the solvent was evaporated. The mixture was extracted with ether and worked up as usual. The residue was purified by silica-gel column chromatography.

2: colorless oil; IR (FT) 1770 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.94 (3H, d, *J* = 6.2 Hz), 1.30-1.93 (10H, m), 2.20 (1H, m), 2.58 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.9 (CH_3), 22.3 (CH_2), 24.8 (CH_2), 29.0 (CH_2), 30.7 (CH_2) 31.5 (CH_2), 38.3 (CH_2), 39.9 (CH), 88.0 (C), 177.4 (CO); MS *m/z* 168 (M^+), 150, 139, 125, 111 (base), 98, 83; HRMS Found *m/z* 168.1150. Calcd for $C_{10}H_{16}O_2$ 168.1150.

3: colorless oil; IR (FT) 1765 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.91 (3H, d, *J* = 6.6 Hz), 1.30-1.93 (10H, m), 2.12 (1H, m), 2.56 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.8 (CH_3), 23.1 (CH_2), 24.2 (CH_2), 26.0 (CH_2), 29.3 (CH_2), 31.0 (CH_2), 37.1 (CH_2), 39.5 (CH), 89.6 (C), 177.0 (CO); MS (EI) *m/z* 168 (M^+), 150, 139, 125, 111 (base), 98, 83; HRMS Found *m/z* 168.1159. Calcd for $C_{10}H_{16}O_2$ 168.1150.

5: colorless oil; IR (FT): 1770 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.89 (1H, dddd, *J* = 13.2, 11.5, 11.5, 3.6 Hz), 0.96 (3H, d, *J* = 6.6 Hz), 1.34 (1H, qt, *J* = 13.2, 3.6 Hz), 1.39 (1H, t, *J* = 12.4 Hz), 1.50 (1H, m), 1.62 (1H, td, *J* = 13.2, 3.6 Hz), 1.66 (1H, m), 1.77 (1H, m), 1.75 (1H, m), 1.79 (1H, dquint, *J* = 13.2, 3.6 Hz), 2.06 (2H, td, *J* = 8.8, 2.2 Hz), 2.59 (2H, t, *J* = 8.8 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 22.1 (CH_3), 22.6 (CH_2), 28.7 (CH_2), 29.9 (CH) 30.7 (CH_2), 33.5 (CH_2), 36.1 (CH_2), 45.1 (C), 87.3 (C), 176.7 (CO); MS (EI) *m/z* 168 (M^+), 153, 140, 125 (base), 111, 95; HRMS Found *m/z* 168.1158. Calcd for $C_{10}H_{16}O_2$ 167.1150.

6: colorless oil; IR (FT): 1775 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 0.86 (1H, m), 0.89 (3H, d, *J* = 6.6 Hz) 1.09 (1H, t, *J* = 12.4 Hz) 1.36 (1H, ddd, *J* = 13.2, 13.2, 4.9 Hz), 1.64 (1H, m), 1.67 (1H, m), 1.74 (1H, m), 1.80 (1H, m), 1.84 (1H, m), 1.97 (2H, m), 2.59 (2H, t, *J* = 8.40 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 22.0 (CH_2), 22.3 (CH_3), 28.4 (CH), 28.6 (CH_2), 33.8 (CH_2), 34.5 (CH_2) 36.6 (CH_2), 45.5 (CH_2), 86.4 (C), 176.9 (CO); MS (EI) *m/z* 168 (M^+), 140, 125 (base), 111, 95; HRMS Found *m/z* 168.1149. Calcd for $C_{10}H_{16}O_2$ 168.1150

8: colorless amorphous; IR (FT): 1760 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 0.86 (9H, s), 1.02 (1H, tt, *J* = 11.8, 3.0 Hz), 1.38-1.49 (4H, m), 1.65-1.68 (2H, m), 1.93-1.96 (2H, m), 1.97 (2H, t, *J* = 8.4 Hz), 2.59 (2H, t, *J* = 8.40 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 23.1 (CH_2), 27.5 (CH_3), 28.7 (CH_2), 32.4 (C), 34.1 (CH_2), 37.6 (CH_2), 47.2 (CH), 85.6 (C), 177.0 (C); MS (EI) *m/z* 210 (M^+), 195, 154 (base), 136, 94, 81, 57; HRMS Found *m/z* 210.1600. Calcd for $C_{13}H_{22}O_3$ 210.1620.

9: colorless amorphous; IR (FT): 1770 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 0.87 (9H, s), 1.05-1.13 (3H, m), 1.74 (2H, m), 1.82 (4H, m), 2.06 (2H, t, *J* = 8.2 Hz), 2.58 (2H, t, *J* = 8.2 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 24.1 (CH_2), 27.5 (CH_3), 28.6 (CH_2), 30.2 (CH_2), 32.2 (C), 36.8 (CH_2), 46.7 (CH), 87.2 (C), 176.7 (C); MS (EI) *m/z* 210 (M^+), 195, 167, 155, 136, 111, 94, 81, 57 (base); HRMS Found *m/z* 210.1597. Calcd for $C_{13}H_{22}O_3$ 210.1620.

Preparation of 4-(2-methyl-5-oxocyclopent-1-enyl)butanal (**20**)

To a stirred solution of *t*BuOK in THF (72.6 mL) was added 3-methylcyclopent-2-en-1-one (2.90 g, 30.2 mmol) and the mixture was stirred for 30 min at rt. 1-Bromo-3-(*t*-butyldimethylsilyloxy)propane (12.0 g, 45.2 mmol) was added and the mixtrure was heated at 100°C under reflux for 1 h. After cooling, NH_4Cl solution was added and the solvent was evaporated. The residue was extracted with ether and the organic phase was washed with brine. The organic layer was dried ($MgSO_4$), and evaporated under reduced pressure to afford a residue. The residue was purified by silica-gel column chromatography to give 2-(4-*t*-butyldimethylsilyloxybutyl)-3-methylcyclopent-2-en-1-one (**20b**) (1.20 g, 9.2%): oil; IR (FT): 1700, 1640 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ -0.01 (6H, s), 0.84 (9H, s), 1.20-1.52 (4H, m), 2.00 (3H, s), 2.14 (2H, t, *J* = 7.0 Hz), 2.25-2.32 (2H, m), 2.42-2.47 (2H, m), 3.55 (2H, t, *J* = 6.2 Hz); ^{13}C NMR (200 MHz, $CDCl_3$) δ –5.4 (CH_3), 17.1 (CH_3), 18.2 (C), 22.6 (CH_2), 24.5 (CH_2), 25.8 (CH_3), 31.4 (CH_2), 32.6 (CH_2), 34.2 (CH_2), 62.8 (CH_2), 140.5 (C), 170.2 (C), 209.6 (CO); MS (EI) *m/z* 282 (M^+), 267, 225 (base); HRMS Found *m/z* 282.2017. Calcd for $C_{16}H_{30}O_2Si$ 282.2015.

Compound **20b** (1.20 g) was dissolved in THF (8 mL) and TBAF (8.5 mL, 2 equiv.) was added and the mixture was stirred for 1 h at rt. Work-up as usual and purification by silica-gel column chromatography afforded 4-(2-methyl-5-oxocyclopent-1-enyl)butanol (**20c**) (479 mg, 73%): oil; IR (FT): 3450, 1680, 1640 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.34-1.66 (4H, m), 2.07 (3H, s), 2.20 (2H, t, *J* = 7.6 Hz), 2.32-2.41 (2H, m), 2.42-2.56 (3H, m), 3.64 (2H, t, *J* = 6.2 Hz); ^{13}C NMR (200 MHz, $CDCl_3$) δ 17.1 (CH_3), 22.4 (CH_2), 24.4 (CH_3), 31.5 (CH_2), 32.2 (CH_2), 34.2 (CH_2), 62.3 (CH_2), 140.4 (C), 171.0 (C), 210.2 (CO); MS (EI) *m/z* 168 (M^+), 150, 135 (base), 123, 109, 93, 79, 67, 55; HRMS Found *m/z* 168.1158. Calcd for $C_{10}H_{16}O_2$ 168.1152.

The alcohol **20c** (617 mg, 3.68 mmol) was oxidized with PDC (2.77 g, 7.36 mmol) and molecular sieves (3A, 615 mg) in CH_2Cl_2 (64 mL) at rt for 7 h. Work-up and purification afforded aldehyde **20** (409 mg, 71%): oil; IR (FT): 1720, 1690, 1640 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.65-1.82 (2H, m), 2.07 (3H, s), 2.23 (2H, t, *J* = 7.2 Hz), 2.26-2.58 (6H, m), 9.75 (1H, t, *J* = 1.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 17.1 (CH_3), 20.6 (CH_2), 22.1 (CH_2), 31.5 (CH_2), 34.2 (CH_2), 43.3 (CH_2), 139.5 (C), 171.4 (C), 202.3 (CO), 209.6 (CO); MS (EI) *m/z* 166 (M^+), 137, 123 (base), 110; HRMS Found *m/z* 166.0989. Calcd for $C_{10}H_{14}O_2$ 166.0994.

21: colorless oil; IR (FT): 3450, 1740 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 1.17 (1H, m), 1.19 (3H, s), 1.39 (1H, m), 1.44 (1H, 1H, m), 1.51 (1H, m), 1.58 (1H, m), 1.64 (1H, m), 1.99 (1H, br d, *J* = 14 Hz), 2.04 (1H, m), 2.24-2.37 (3H, m), 3.28 (1H, dd, *J* = 12, 4.2 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 18.7 (CH_3), 19.7 (CH_2), 21.8 (CH_2), 30.1 (CH_2), 34.6 (CH_2), 43.7 (C), 57.3 (CH), 71.0 (CH), 219.3 (CO); MS (EI) *m/z* 168 (M^+), 150, 135, 111, 97 (base); HRMS Found *m/z* 168.1152. Calcd for $C_{10}H_{16}O_2$ 168.1150.

Preparation of 3-(2-methyl-6-oxocyclohex-1-enyl)propanal (**22**)

Compound **22** was prepared following the procedure for **20** starting from 3-methylcyclohex-2-en-1-one. **22b**: oil; IR (FT): 1660, 1620 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.02 (6H, s), 0.87 (9H, s), 1.43-1.57 (2H, m), 1.93 (3H, s), 1.82-1.95 (2H, m), 2.27-2.37 (6H, m), 3.57 (2H, t, *J* = 6.2 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ -5.3 ($CH_3\times2$), 18.3 (C), 21.1 (CH_3), 21.6 (CH_2), 22.3 (CH_2), 25.9 ($CH_3\times3$), 32.2 (CH_2), 32.8 (CH_2), 37.9 (CH_2), 62.9 (CH_2), 135.4 (C), 155.3 (C), 198.7 (C); MS (CI) *m/z* 283 $[M+H]^+$, 282, 281, 267, 225 (base), 151, 133, 107, 91; CI-HRMS Found *m/z* 283.2063. Calcf for $C_{16}H_{31}SiO_2$ 283.2093. **22c**: oil; IR (FT): 3400,1660, 1620 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.59 (2H, quint, *J* = 6.0 Hz), 1.98 (3H, s), 1.88-2.01 (2H, m), 2.34-2.45 (6H, m), 3.75 (2H, t, *J* = 6.2 Hz); ^{13}C NMR (200 MHz, $CDCl_3$) δ 20.3 (CH_2), 21.2 (CH_3), 22.3 (CH_2), 31.6 (CH_2), 32.9 (CH_2), 37.6 (CH_2), 60.9 (CH_2), 134.8 (C), 157.6 (C), 200.6 (CO); MS (CI) *m/z* 169 $[M+H]^+$, 151 (base), 135, 123, 79; CI-HRMS Found *m/z* 169.1214. Calcd for $C_{10}H_{17}O_2$ 169.1228. **22**: oil; IR (FT) 2710, 1720, 1660, 1630 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.98 (3H, s), 1.87-2.00 (2H, m), 2.31-2.66 (8H, m), 9.55 (1H, t, *J* = 1.6 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.3 (CH_2), 21.2 (CH_3), 32.8 (CH_2), 37.6 (CH_2), 43.0 (CH_2), 133.7 (C), 156.8 (C), 198.6 (C), 202.3 (CH); MS (EI) *m/z* 166 (M^+), 138 (base), 110, 95, 79, 67; HRMS Found *m/z* 166.0979. Calcd for $C_{10}H_{14}O_2$ 166.0994.

23: oil; IR (FT): 3420, 1700 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 1.09 (3H, s), 1.52 (1H, ddd, *J* = 14.0, 7.4, 4.1 Hz), 1.61 (1H, m), 1.67 (1H, ddd, *J* = 14.0, 8.5, 4.1 Hz), 1.87 (1H, m), 1.90 (1H, m), 1.95 (1H, m), 2.07 (1H, m), 2.19 (1H, m), 2.26 (1H, m), 2.43 (1H, m), 2.46 (1H, dd, *J* = 8.1, 6.0 Hz), 3.81 (1H, t, *J* = 5.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.2 (CH_3), 21.9 (CH_2), 22.6 (CH_2), 31.2 (CH_2), 31.6 (CH_2), 38.9 (CH_2), 50.2 (C), 57.1 (CH), 77.8 (CH), 213.2 (CO); MS (EI) *m/z* 168 (M^+), 153, 138, 124, 111 (base), 97; HRMS Found *m/z* 168.1158. Calcd for $C_{10}H_{16}O_2$ 168.1150.

Preparation 5-(2-methyl-5-oxocyclopent-2-enyl)-2-pentanone (**24**)

Compound **24** was prepared from 2-methyl-2-(3-bromopropyl)-1,3-dioxolane in two steps. 3-Methylcyclopent-2-en-1-one was alkylated in the presence of *t*BuOK in THF to afford **24a**: oil; IR (FT) 1700, 1650 cm^{-1}; MS *m/z* 224 (M^+), 209, 115, 87 (base); ^1H NMR (200 MHz, $CDCl_3$) δ 1.29 (3H, s), 1.42-1.48 (4H, m), 2.05 (3H, br s), 2.18 (2H, m), 2.37 (2H, m), 2.63 (2H, m), 3.92 (4H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 17.2 (CH_3), 22.7 (CH_2), 22.8 (CH_2), 23.7 (CH_3), 31.4 (CH_2), 34.2 (CH_2), 38.8 (CH_2), 64.4

(CH_2), 109.6 (C), 140.2 (CH), 170.4 (C), 209.5 (CO); HRMS Found *m/z* 224.1401. Cacld for $C_{13}H_{20}O_3$ 224.1412. This was treated with TsOH to afford **24**: oil; IR (FT): 1720, 1695, 1650 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.66 (2H, quint, *J* = 5.2 Hz), 2.07 (3H, s), 2.13 (3H, s), 2.16 (1H, m), 2.34-2.54 (5H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 17.2 (CH_3), 22.1 (CH_2), 22.4 (CH_2), 29.8 (CH_3), 31.5 (CH_2), 34.2 (CH_2), 43.1 (CH_2), 139.8 (CO), 171.1 (CO), 208.7 (CO), 209.5 (CO); MS (EI) *m/z* 180 (M^+), 137, 123 (base), 110, 96; HRMS Found *m/z* 180.1162. Calcd for $C_{11}H_{16}O_2$ 180.1150.

25: oil; ^1H NMR (600 MHz, $CDCl_3$) δ 1.16 (3H, s), 1.17 (3H, s), 1.36 (1H, m), 1.39 (1H, m), 1.46 (1H, m), 1.53 (1H, ddd, *J* = 13.2, 11.0, 8.0 Hz), 1.62 (1H, m), 1.64 (1H, m), 1.90 (1H, m), 2.03 (1H, m), 2.20 (1H, dddd, *J* = 18.1, 11.0, 3.0, 1.6 Hz), 2.31 (1H, ddd, *J* = 13.2, 10.2, 3.0 Hz), 2.41 (1H, ddd, *J* = 18.1, 10.2, 8.0 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 18.0 (CH_2), 19.4 (CH_2), 25.0 (CH_3), 26.2 (CH_3), 29.5 (CH_2), 36.2 (CH_2), 36.6 (CH_2), 45.0 (C), 55.4 (CH), 74.3 (C), 218.4 (CO); MS *m/z* 182 (M^+), 167, 164, 154, 149, 124, 109, 97 (base), 84; HRMS Found *m/z* 182.1305. Calcd for $C_{11}H_{18}O_2$ 182.1307.

26: oil; ^1H NMR (600 MHz, $CDCl_3$) δ 1.03 (3H, s), 1.18 (3H, s), 1.21 (1H, m), 1.55-1.71 (6H, m), 2.02 (1H, dt, *J* = 12.6, 9.6 Hz), 2.09 (1H, dd, *J* = 12.2, 6.3 Hz), 2.29 (1H, dt, *J* = 19.5, 10.4 Hz), 2.38 (1H, ddd, *J* = 19.5, 9.9, 2.2 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 19.6 (CH_2), 20.7 (CH_3), 24.3 (CH_2), 24.9 (CH_3), 28.8 (CH_2), 33.9 (CH_2), 35.9 (CH_2), 45.2 (C), 54.7 (CH), 71.9 (C), 220.3 (CO); MS *m/z* 182 (M^+), 167, 164, 154, 149, 124, 111, 106, 97 (base), 84; HRMS Found *m/z* 182.1334. Calcd for $C_{11}H_{18}O_2$ 182.1307.

ACKNOWLEDGEMENTS

We thank Miss Yasuko Okamoto, of this University, for measurement of MS spectra.

REFERENCES AND NOTES

* This paper is dedicated to Professor Yoshito Kishi on the occasion of his 70th birthday.

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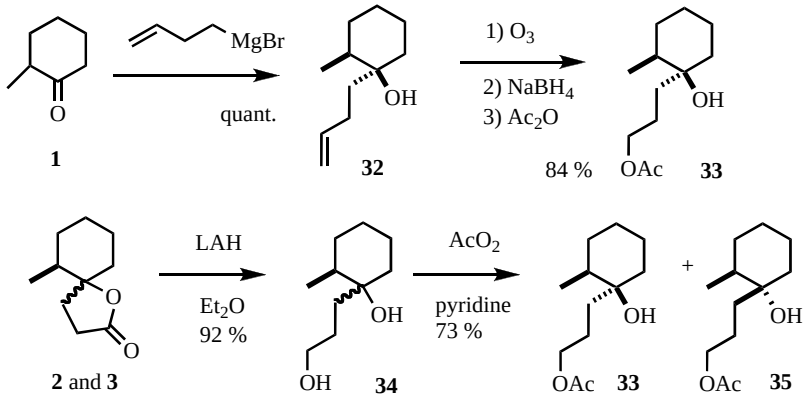
8. The stereochemistry was established as follows. Grignard reaction of 4-bromo-1-butene to 2-methylcyclohexanone gave **32**, whose stereochemistry is well known. Compound **32** was further derived into acetate **33** by a three step-transformation [(i) O_3, CH_2Cl_2, -78ºC, (ii) $NaBH_4$, MeOH, 0ºC, (iii) Ac_2O, Py, rt]. Then, a lactone mixture of **2** and **3** was reduced ($LiAlH_4$, Et_2O) to diol **34** as a mixture followed by acetylation (Ac_2O, Py) and separation to yield **33** as a major compound, with the same stereochemistry as that from **32**. **33**: amorphous: IR(FT): 3520, 1730 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.87 (3H, d, *J* = 6.2 Hz), 1.24-1.74 (14H, m), 2.05 (3H, s), 4.07 (2H, td, *J* = 6.6, 1.8 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.8 (CH_3), 20.9 (CH_3), 21.7 (CH_2), 22.9 (CH_2), 25.6 (CH_2), 30.5 (CH_2), 35.8 (CH_2), 36.8 (CH_2), 38.2 (CH), 65.0 (CH_2), 72.6 (C), 171.2 (CO); MS (EI) *m/z* 214 (M^+), 154, 113, 97 (base); HRMS Found *m/z* 214.1556 Calcd for $C_{12}H_{22}O_3$ 214.1569. **35**: amorphous: IR (FT): 3480, 1740, 1720 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.97 (3H, d, *J* = 6.6 Hz), 1.14-1.84 (14H, m), 2.06 (3H, s), 4.09 (2H, t, *J* = 6.6 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.0 (CH_3), 21.0 (CH_3), 21.8 (CH_2), 23.1 (CH_2), 23.9 (CH_2), 30.1 (CH_2), 30.9 (CH_2), 35.9 (CH_2), 41.4 (CH), 65.2 (CH_2), 73.8 (C), 171.3 (CO); MS (EI) *m/z* 214 (M^+), 154, 113, 97 (base); HRMS Found *m/z* 214.1549 Calcd for $C_{12}H_{22}O_3$ 214.1569.



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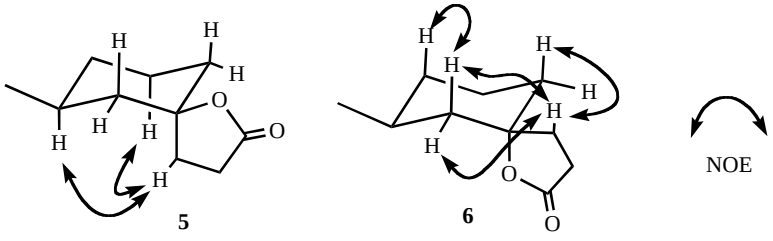
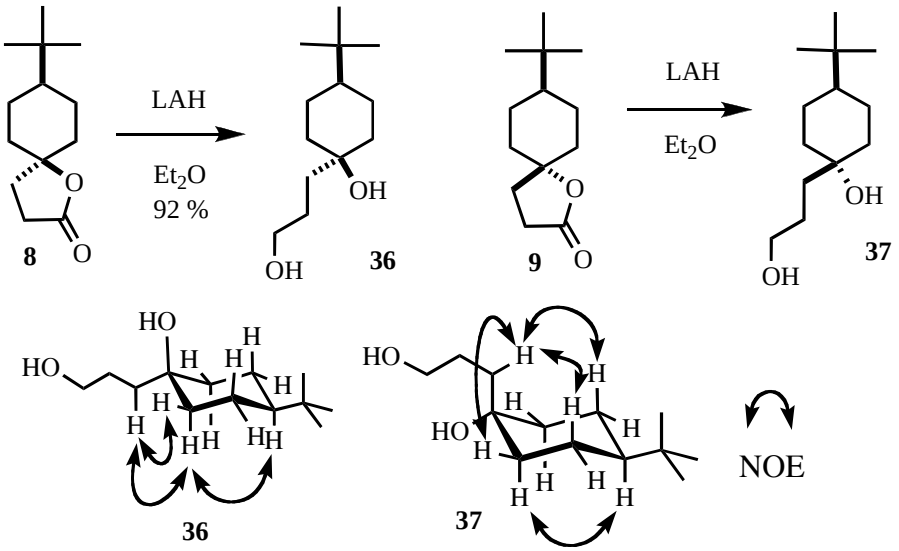
11. The stereochemistry of compounds **5** and **6** was determined by NOESY spectra. The selected correlations were shown here.



12. The structures of **8** and **9** were determined as follows. Both lactones **8** and **9** were reduced with $LiAlH_4$ to afford **36** and **37**, respectively, and their structures were analyzed by NOESY spectra. **36**: colorless oil: IR (FT) 3300 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 0.87 (9H, s), 0.94 (1H, m), 1.28 (2H, m), 1.29 (2H, m), 1.52 (2H, t, *J* = 6.0 Hz), 1.61 (2H, m), 1.67 (1H, m), 1.69 (1H, m), 1.74 (2H, m), 3.66 (2H, t, *J* = 6.0 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 22.4 (CH_2), 26.4 (CH_2), 27.5 (CH_3), 32.4 (C), 37.5 (CH_2), 40.9 (CH_2), 47.9 (CH), 63.5 (CH_2), 70.4 (C); MS (CI) *m/z* 215 $[M+H]^+$, 214, 19 (base), 179, 155, 115, 97; HRMS Found *m/z* 214.1914. Calcd for $C_{13}H_{26}O_2$ 214.1932. **37**: colorless oil: IR (FT) 3300 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 0.82 (9H, s), 1.03 (2H, m), 1.05 (1H, m), 1.37 (2H, m) 1.60-1.69 (6H, m), 1.83 (2H, br d, *J* = 11.8 Hz), 3.65 (2H, t, *J* = 5.8 Hz), ^{13}C NMR (150 MHz, $CDCl_3$) δ 24.4 (CH_2), 26.0 (CH_2), 27.6 (CH_3), 32.2 (C), 33.0 (CH_2), 38.7 (CH_2), 47.5 (CH), 63.0 (CH_2), 71.9(C); MS (CI) *m/z* 214 (M^+), 197 (base), 179, 155, 115, 97; CI-HRMS Found *m/z* 214.1951. Calcd for $C_{13}H_{26}O_2$ 214.1933.



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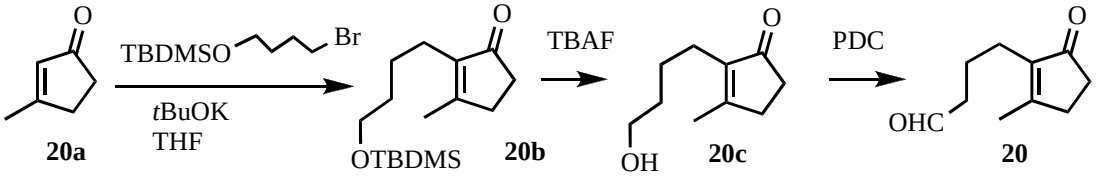
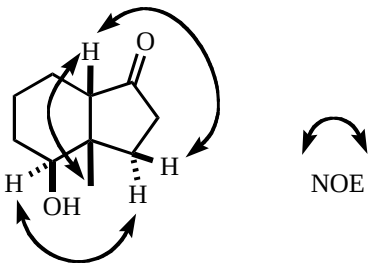
15. The reason why compounds **12** and **13** were not produced in electrolysis was not clear now. The trend of stereoselectivity in SmI_2-induced cyclization was discussed in ref. 5.
16. Compound **20** was prepared from 3-methylcyclopent-2-en-1-one in three steps (see Experimental).

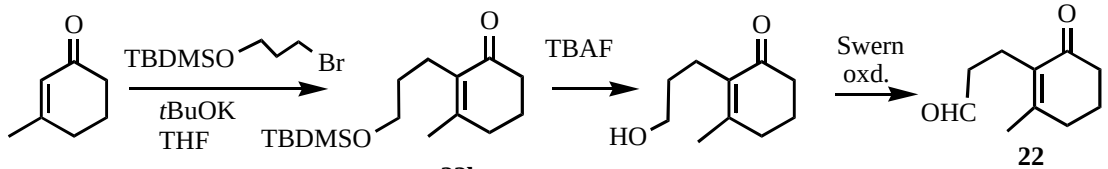


17. The stereochemistry of **21** was established by NOESY spectrum.



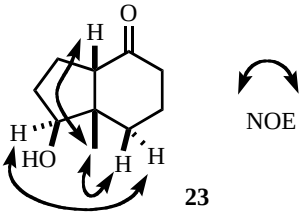
21

18. Compound **22** was prepared from 3-methylcyclohex-2-en-1-one in three steps (see Experimental).



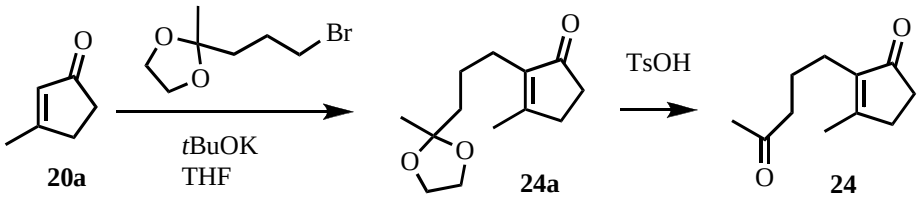
22a **22b** **22c** **22**

19. The stereochemistry of **23** was established by NOESY spectrum.



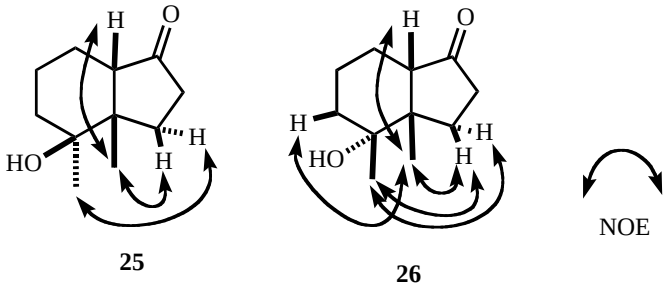
23

20. Compound **24** was prepared from 3-methylcyclopent-2-en-1-one in two steps (see Experimental).



20a **24a** **24**

21. The stereochemistry of compounds **25** and **26** was established by NOESY spectrum.



25 **26**