Synthesis of Six-Membered Compounds by Environmentally Friendly Cyclization Using Indirect Electrolysis

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[Ni(cyclam)]$(ClO_4)_2$-catalyzed indirect electroreduction of olefinic bromides produced six-membered compounds in low to high yields. The synthetic intermediate **49** of *Ipecac* and *Corynanthe* alkaloids was obtained in 88% yield in a highly stereoselective manner. Lactam **66**, the synthetic precursor of tacamonine, was prepared in 49% yield as a mixture of two diastereoisomers. The electrolysis of the bromoacetates gave the debrominated compounds in good yields.

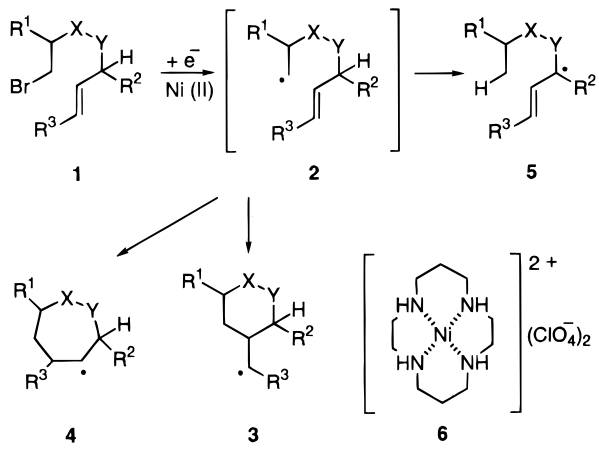
Introduction

Radical cyclization has emerged as one of the premier methods for the creation of new carbon−carbon bonds.[1,2] The majority of useful radical-mediated addition reactions have been carried out using organostannane,[3] organomercury,[4] or organosilane[5] radical initiators. However, a stoichiometric amount of chemical reagents and high dilution conditions are required in order to minimize the quenching of the initial radical centers by hydrogen radical abstraction. Furthermore, separating cyclized products and byproducts derived from the reagents is sometimes a troublesome task. In the course of our synthetic study of polycyclic natural products utilizing radical cyclization as a key step, we focused on the cathodic carbon−carbon bond formation[6,7] as an environmentally friendly method. We describe in detail the successful results of the electrolysis mediated with the Ni(II) complex.[8]

Results and Discussion

Although it is known that radical cyclizations are particularly useful for the construction of four- and five-membered ring systems, we were interested in the synthesis of six-membered compounds as an extension

Scheme 1



of our previous studies.[9,10] Radicals **2**, formed from bromides **1**, would lead to the formation of the six-membered **3** and seven-membered radicals **4** by the intramolecular addition reaction or to the formation of allylic radical **5** by a 1,5-hydrogen shift (Scheme 1). It was expected from literature results[6,7] that the formation of radicals from halides could be carried out using Ni(II)- or Co(III)-catalyzed electroreduction. Among the various mediators, we chose [Ni(cyclam)]$(ClO_4)_2$ (**6**) since the complex was readily prepared from commercially available 1,4,8,11-tetraazacyclotetradecane (cyclam).[11] In order to investigate the influence of substituents in substrates on the indirect electroreductive cyclization, various types of substrates **1** were prepared.

Preparations of Substrates. It was observed from our preliminary experiments that the indirect electrolysis of iodides and thioesters gave poor results. Therefore, a number of bromides were prepared as radical precursors. Alcohol **8**, derived from **7**, was converted into olefins **9**−**11** in three steps (Scheme 2). The (*Z*)-**10** and (*E*)-**11** olefins were selectively synthesized by Wittig reactions. The treatment of **9**−**11** with ethyl vinyl ether and NBS[12] furnished bromoacetals **12**−**14**, while reactions of **9**−**11**

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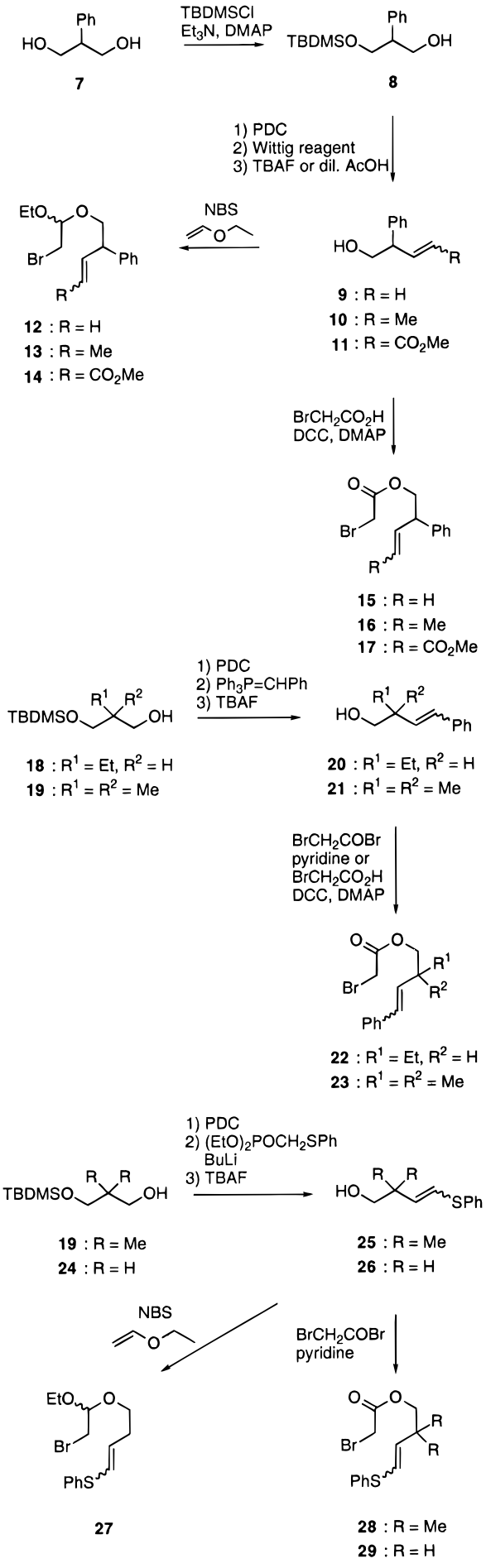
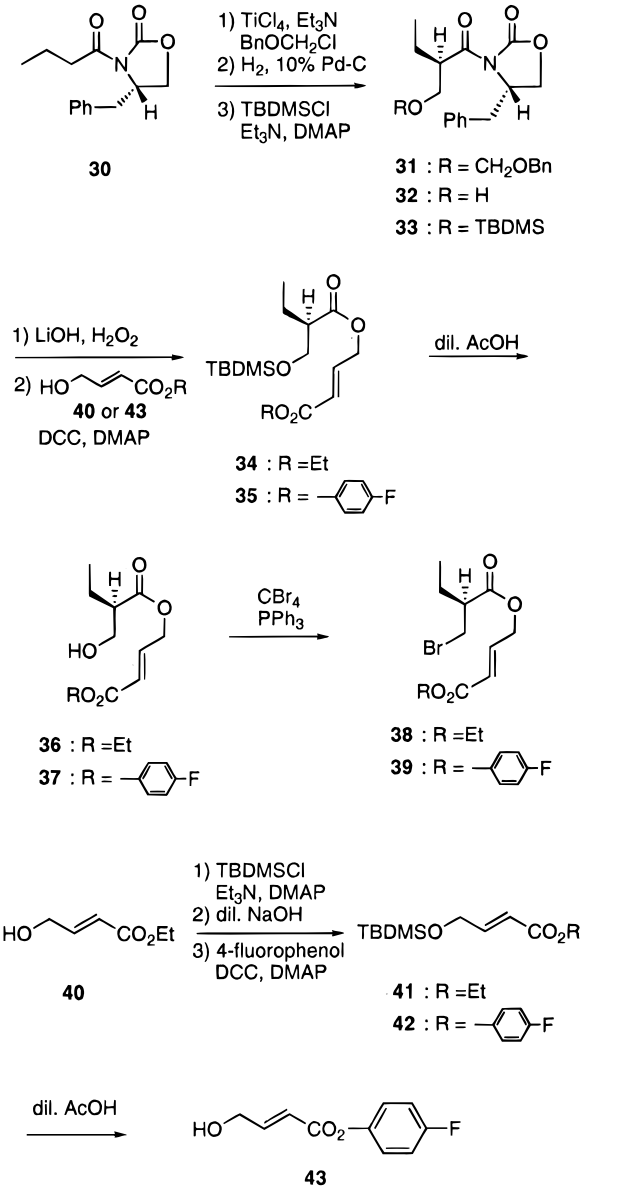
Scheme 2



Scheme 3



with bromoacetic acid in the presence of DCC and DMAP[13] gave bromoacetates **15**−**17**.

Olefins **20** and **21** were prepared as geometrically isomeric mixtures from **18**[10] and **19**[14] and then converted into bromoacetates **22** and **23**. Vinyl sulfides **25** and **26**, obtained from **19** and **24**,[15] were transformed into bromoacetal **27** and bromoacetates **28** and **29**.

Previously,[10] *tert*-butyldimethylsilyl (TBDMS) ether **33** was synthesized in 48% overall yield *via* the hydroxymethylation of oxazolidone **30**.[16] On the other hand, the reaction of **30** with (benzyloxy)methyl chloride (BOMCl) in the presence of $TiCl_4$ and Et_3N at 0 °C produced **31**, mp 75−76 °C, as a single stereoisomer in 77% yield (Scheme 3). Hydrogenolysis of **31**, followed by protection of the resulting alcohol **32** with the TBDMS group, quantitatively provided **33**. After hydrolysis, esterification of the resulting acid with **40** in the presence of DCC

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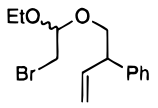
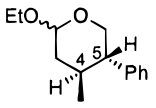
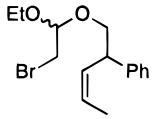
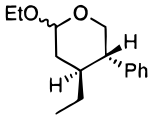
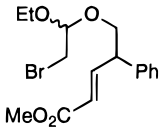
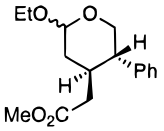
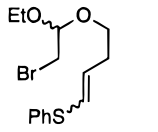
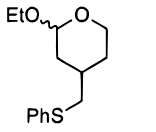
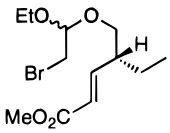
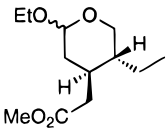
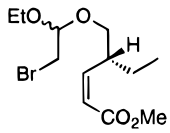
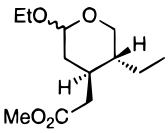
and DMAP[13] gave **34**. Similarly, the corresponding 4-fluorophenyl ester **35** was prepared using **43**, derived from **40** *via* **41** and **42**. TBDMS ethers **34** and **35** were transformed into bromides **38** and **39** by deprotection of the silyl group, followed by the bromination of **36** and **37** using CBr_4 and PPh_3.

Ni(II)-Catalyzed Electroreduction. Electrolysis was carried out in DMF containing 0.1 M Et_4NClO_4 (TEAP) as a supporting electrolyte, bromide as the substrate of the reaction, NH_4ClO_4 as a proton source, and [Ni(cyclam)]$(ClO_4)_2$[11] as the mediator in an H-shaped divided cell under N_2. Poor results were obtained without NH_4ClO_4. When the reaction was performed at −1.5 V vs Ag/AgCl, 10 mol % Ni(II) catalyst was enough to consume the starting material within several hours. The indirect electrolysis, carried out at −1.2 V vs Ag/AgCl, required 50 mol % of the Ni(II) catalyst to obtain similar results. The cathodic reactions, tested in the present study, are divided into three sections: (A) bromoacetals, (B) bromoacetates, and (C) other bromides.

(A) Bromoacetals. The results of the cyclization of bromoacetals are summarized in Table 1. Tetrahydro-2*H*-pyrans **44** and **45** were obtained in 16 and 29% yields, respectively, from **12** and **13** (entries 1 and 2). Cyclized products **46** were obtained in a significantly increased yield (75%) from **14** possessing an electron-withdrawing ester function (entry 3). The presence of the electron-releasing phenylthio group decreased the yield of cyclized product **47** (27% yield) (entry 4). The production of the pyrans **44**, **45**, and **47** supports the fact that cyclization proceeds in a radical manner. Further studies are in progress in order to determine the exact mechanism. Only *trans*-substituted products **44**−**46** were obtained by the above cyclizations because of the presence of a bulky phenyl group. The ratios of the diastereoisomers of **44**−**46** due to the stereogenic centers at the C-4 and C-5 positions were determined after conversions into lactones **51**−**53**, respectively, as depicted in Scheme 4. Indirect electrolysis of (*E*)-esters **48**[9] produced **49** in 83% yield, and the ratio of diastereoisomers at the C-4 and C-5 positions was proved to be 4:1 after transformation into the corresponding lactones.[9] *Trans*-substituted products **49** were exclusively obtained in 88% yield from (*Z*)-isomers **50**.[9] Tetrahydropyrans **49** had been produced in 96 and 97% yields from **48** and **50**, respectively, in similar stereoselectivities by the reaction utilizing Bu_3SnH and AIBN.[9] The selective formation of **49** from **50** was explained in terms of lessening the 1,3-allylic strain.[9] It was thus clarified that cyclization of bromoacetals having an α,β-unsaturated ester group can be carried out in high yields by the Ni(II)-catalyzed electrolysis (entries 3, 5, and 6). The product **49** had been correlated with (−)-protoemetine,[9] (−)-protoemetinol,[9] (−)-emetine,[9] (−)-tubulosine,[9] (−)-dihydrocorynantheol,[17] dihydroantirhine,[18] and quinine alkaloids.[18]

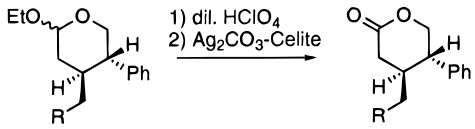
(B) Bromoacetates. Electrolysis of bromoactates **15**−**17**, **22**, **23**, **28**, and **29**, carried out under the same conditions as above, provided only acetates **54**−**60** (Figure 1) in good yields. No formation of cyclized products was detected in all reactions. Debrominated esters **58** and **59** were produced by hydrogen abstraction at the initial radical centers derived from olefins **23** and **28**

Table 1. Ni(II)-Mediated Electroreductive Cyclization of Bromoacetals[a]

entry	substrate	product	yield (%)	ratio of isomers[b]
1	 **12**	 **44**	16	> 99 : 1
2	 **13**	 **45**	29	> 99 : 1
3	 **14**	 **46**	75	> 99 : 1
4	 **27**	 **47**	27	
5	 **48**	 **49**	83	> 4 : 1
6	 **50**	 **49**	88	> 99 : 1

[a] Reaction conditions: −1.5 V vs Ag/AgCl, 10 mol % [Ni(cyclam)]$(ClO_4)_2$, NH_4ClO_4, 0.1 M TEAP−DMF. [b] The ratio of diastereoisomers at C-4 and C-5 positions was determined by ^1H NMR (300 or 500 MHz) after conversion into lactones.

Scheme 4



44 : R = H
45 : R = Me
46 : R = CO_2Me

51 : R = H
52 : R = Me
53 : R = CO_2Me

having dimethyl groups at the allylic position; this result supports the fact that the process does not involve a 1,5-hydrogen shift.

(C) Other Bromides. The treatment of **61**[10] under the same conditions as above gave a 1:1 mixture of 5-pentanolides **62** in 17% yield. A considerable amount of polymers was obtained by reductive coupling at the electron deficient olefinic carbons (entry 1 of Table 2). The coupling reaction was suppressed in the case of **38**, and a 2:1 mixture of **63** was obtained in 39% yield (entry

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(18) Taniguchi, N.; Ihara, M.; Fukumoto, K. *Heterocycles* **1992**, *33*, 545−548.

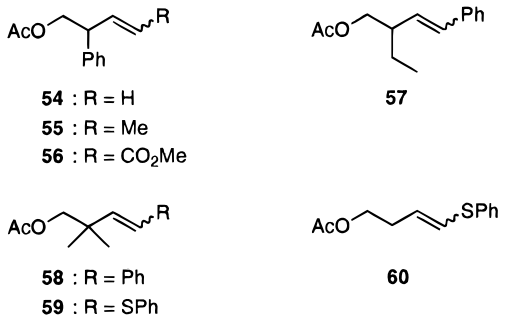

Figure 1.

2). The corresponding 4-fluorophenyl ester **39** was subjected to the cyclization reaction in the hope of improving yield, but the yield of **64** was not changed (entry 3). Lactam **66** was obtained in 49% yield by the electrolysis of **65** (entry 4).[10] The ratio of the two isomers was not determined by ^{1}H NMR spectroscopy because they are rotational isomers. The moderate yield of **66** may be largely attributable to the slow rotation of the OC−N bond in the intermediate radicals as suggested by Curran and Tamine.[19] The lactam **66** had been obtained in 44% yield from **65** by the reaction using Bu_3-SnH and AIBN.[10] The optically active indole alkaloid, tacamonine, had been synthesized in three steps starting with **66**.[10]

In conclusion, the usefulness of radical cyclization by electrolysis mediated with [Ni(cyclam)]$(ClO_4)_2$ was demonstrated for the construction of six-membered ring systems. Bromoacetals possessing an electron deficient olefin function are particularly suitable substrates for the cyclization reaction. High dilution conditions were not required to achieve the intramolecular addition reaction, and the purification of products was easily performed. Thus, the present procedure provides a useful method for a convenient and clean radical cyclization.

Experimental Section

General Procedure. All reactions were carried out under a positive atmosphere of N_2 or Ar unless otherwise indicated. Solvents were distilled prior to use. THF and benzene were distilled from sodium benzophenone while CH_2Cl_2 and DMF were distilled from CaH_2 and stored over 4-Å molecular sieves. All new compounds are homogeneous on TLC, and their purities were further verified by 300 or 500 MHz ^{1}H NMR spectra. NMR spectra were measured in $CDCl_3$.

Controlled-potential electrolysis was carried out using a potentiostat (Hokuto Denko HAB-151), and the quantity of electricity consumed was recorded with a coulometer (Hokuto Denko HF-201).

(±)-3-(*tert*-Butyldimethylsiloxy)-2-phenylpropan-1-ol (8). To a stirred solution of **7** (4.21 g, 27.7 mmol), *tert*-butyldimethylsilyl chloride (TBDMSCl) (4.38 g, 29.1 mmol), and 4-(*N*,*N*-dimethylamino)pyridine (DMAP) (34 mg, 0.28 mmol) in dry CH_2Cl_2 (50 mL) at 0 °C was added Et_3N (4.35 mL, 31.2 mmol), and the mixture was stirred for 12 h at rt. The resulting mixture was partitioned between CH_2Cl_2 and H_2O. The organic layer was dried ($MgSO_4$) and evaporated to give a residue, which was purified by column chromatography on silica gel with hexane−AcOEt (4:1 v/v) as the eluent to afford **8** (3.87 g, 52%) as a colorless oil: IR (neat) 3400 cm^{-1}; ^{1}H NMR (300 MHz) δ 0.00 (s, 6H), 0.85 (s, 9H), 2.64−2.68 (m, 1H), 2.98−3.07 (m, 1H), 3.77−3.91 (m, 3H), 3.97−4.04 (m, 1H), 7.14−7.28 (m, 5H); MS *m*/*z* 209 (M^+ − *t*-Bu). Anal. Calcd for $C_{15}H_{26}O_2Si$: C, 67.62; H, 9.83. Found: C, 67.69; H, 9.79.

(±)-2-Phenyl-3-buten-1-ol (9). To a stirred solution of **8** (329 mg, 1.24 mmol) in dry CH_2Cl_2 (10 mL) at 0 °C were added 4-Å molecular sieves (698 mg) and PDC (698 mg, 1.86 mmol). The mixture was then stirred for 1.5 h at rt. After dilution with Et_2O followed by filtration through Celite, evaporation of the filtrate gave the crude aldehyde, which was used in the following reaction without purification.

To a suspension of methyltriphenylphosphonium bromide (883 mg, 2.47 mmol) in dry THF (5 mL) at 0 °C was added 1.56 M BuLi−hexane (1.19 mL, 1.86 mmol), and the mixture was stirred for 30 min at 0 °C. To the stirred mixture was added a solution of the above product in dry THF (10 mL), and the mixture was stirred for 3 h at 0 °C. After dilution with Et_2O, the mixture was washed with H_2O and brine, dried ($MgSO_4$), and evaporated to give a residue, which was subjected to the following reaction without purification.

To a stirred mixture of the above product in THF (5 mL) was added 1.0 M Bu_4NF−THF (2.47 mL, 2.47 mmol), and the mixture was stirred for 24 h at rt. The reaction mixture was partitioned between Et_2O and H_2O. The organic solution was washed with brine, dried ($MgSO_4$), and evaporated. Column chromatography of the product on silica gel with hexane−AcOEt (4:1 v/v) provided **9** (110 mg, 60% from **8**) as a colorless oil. Its spectral data supported the structure of the known compound.[20]

(±)-(3*Z*)-2-Phenyl-3-penten-1-ol (10). Using the same procedure as above, **8** (445 mg, 1.67 mmol) was converted into **10** (102 mg, 38%) as a colorless oil: IR (neat) 3600−3200, 1655 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.70 (d, 3H, J = 6.6 Hz), 3.65−3.90 (m, 3H), 5.57−5.83 (m, 2H), 7.20−7.49 (m, 5H); ^{13}C NMR (75 MHz) δ 141.6, 130.1, 128.7, 127.8, 127.3, 126.7, 67.0, 46.1, 13.4; HRMS calcd for $C_{10}H_{11}$ (M^+ − CH_2OH) 131.0861, found 131.0862.

Methyl (±)-(2*E*)-5-Hydroxy-4-phenyl-2-pentenoate (11). To a suspension of 60% NaH (165 mg, 4.13 mmol) in dry THF (5 mL) was added trimethyl phosphonoacetate (0.84 mL, 5.17 mmol), and the mixture was then stirred for 30 min at rt. After the addition of the crude aldehyde, prepared from **8** (550 mg, 2.07 mmol) as above in dry THF (15 mL), the mixture was stirred for 24 h at rt. After dilution with Et_2O, the resulting mixture was washed with H_2O and brine, dried ($MgSO_4$), and evaporated to give a residue, which was used in the next reaction without purification.

A mixture of the above product and AcOH−H_2O (3:1 v/v, 8 mL) in THF (2 mL) was stirred for 24 h at rt. After dilution with Et_2O followed by neutralization with saturated $NaHCO_3$ under cooling with ice, the combined extracts were washed with saturated $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated. Column chromatography of the product on silica gel with hexane−AcOEt (2:1 v/v) as an eluent provided **11** (213 mg, 50% from **8**) as a colorless oil: IR (neat) 3600−3200, 1730, 1655 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.76−1.85 (br s, 1H), 3.60−4.08 (m, 3H), 3.72 (s, 3H), 5.90 (d, 1H, J = 15.8 Hz), 7.14 (dd, 1H, J = 7.7, 15.8 Hz), 7.21−7.49 (m, 5H); ^{13}C NMR (75 MHz) δ 166.7, 148.6, 139.0, 128.5, 127.8, 126.9, 121.9, 65.0, 51.3, 50.7; MS *m*/*z* 144 (M^+ − CH_2OH − OMe). Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 69.79; H, 6.84.

(±)-(1*E* and 1*Z*)-3-(Hydroxymethyl)-1-phenyl-1-pentenes (20). Using the same procedure as for the preparation of **9**, **18**[10] (606 mg, 2.78 mmol) was transformed into a mixture of **20** (228 mg, 47%) in a ratio of 3:1 (*E*/*Z*) as a colorless oil: IR (neat) 3600−3200, 1655 cm^{-1}; ^{1}H NMR (300 MHz) δ 0.86−0.96 (m, 3H), 1.25−1.72 (m, 3H), 2.24−2.43 (m, 1H), 3.48−3.68 (m, 2H), 5.35−5.43 (m, 0.25H), 5.94−6.02 (m, 0.75H), 6.49 (d, 0.75H, J = 15.8 Hz), 6.61 (d, 0.25H, J = 11.4 Hz), 7.19−7.45 (m, 5H); HRMS calcd for $C_{12}H_{16}O$ (M^+) 176.1201, found 176.1215.

(3*E* and 3*Z*)-2,2-Dimethyl-4-phenyl-3-buten-1-ols (21). Using the same procedure as above, **19**[14] (688 mg, 3.15 mmol) was transformed into a mixture of **21** (311 mg, 60%) in a ratio of 7:3 (*Z*/*E*) as a colorless oil: IR (neat) 3600−3200, 1655 cm^{-1}; ^{1}H NMR (300 MHz) δ 0.96 (s, 4.2H), 1.13 (s, 1.8 H), 3.31 (s, 1.4H), 3.43 (s, 0.6H), 5.54 (d, 0.7H, J = 12.6 Hz), 6.17 (d, 0.3H,

(19) Curran. D. P.; Tamine, J. *J. Org. Chem.* **1991**, *56*, 2746−2750.

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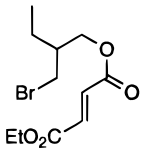
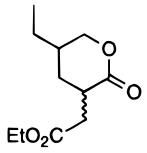
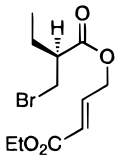
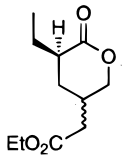
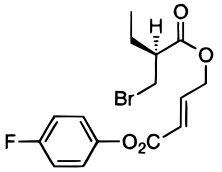
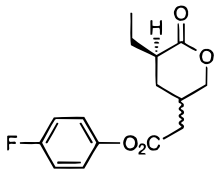
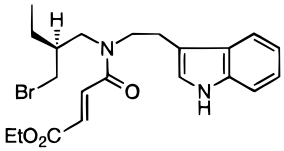
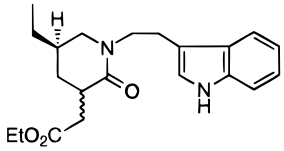
Table 2. Ni(II)-Mediated Electroreductive Cyclization of Bromoesters[a]

entry	substrate	product	yield (%)	ratio of isomers[b]
1	 **61**	 **62**	17	1 : 1
2	 **38**	 **63**	39	2 : 1
3	 **39**	 **64**	40	2 : 1
4	 **65**	 **66**	49	–[c]

[a] Reaction conditions: −1.5 V vs Ag/AgCl, 10 mol % [Ni(cyclam)]$(ClO_4)_2$, NH_4ClO_4, 0.1 M TEAP−DMF. [b] Determined by ^{1}H NMR (500 MHz). [c] Unclear due to rotational isomers.

J = 16.3 Hz), 6.41 (d, 0.3H, J = 16.3 Hz), 6.61 (d, 0.7H, J = 12.6 Hz), 7.19−7.39 (m, 5H); MS m/z 176 (M^+). Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.89; H, 9.09.

(3*E*)-2,2-Dimethyl-4-(phenylthio)-3-buten-1-ol (25). Similarly, **19**[14] (541 mg, 2.48 mmol) was converted into **25** (260 mg, 50%) as a colorless oil: IR (neat) 3700−3100 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.08 (s, 6H), 3.38 (br s, 2H), 5.90 (d, 1H, J = 15.4 Hz), 6.20 (d, 1H, J = 15.4 Hz), 7.18−7.43 (m, 5H); MS m/z 208 (M^+). Anal. Calcd for $C_{12}H_{16}OS$: C, 69.19; H, 7.74. Found: C, 69.22; H, 7.86.

4-(Phenylthio)-3-buten-1-ol (26). Similarly, **24**[15] (878 mg, 4.62 mmol) was transformed into a mixture of **26** (380 mg, 46%) in a ratio of 1.5:1 (*E*/*Z*) as a colorless oil: IR (neat) 3600−3200, 1650, 1645 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.71 (br s, 1H), 2.39−2.46 (m, 1.2H), 2.50−2.57 (m, 0.8H), 3.67−3.76 (m, 2H), 5.81−6.01 (m, 1H), 6.27 (dt, 0.6H, J = 1.1, 15.0 Hz), 6.35 (dt, 0.4H, J = 1.1, 9.5 Hz), 7.18−7.49 (m, 5H); HRMS calcd for $C_{10}H_{12}OS$ (M^+) 180.0609, found 180.0580.

(±)-1-(2′-Bromo-1′-ethoxyethoxy)-2-phenyl-3-butenes (12). To a stirred solution of **9** (110 mg, 0.741 mmol) and ethyl vinyl ether (10 mL) at 0 °C was slowly added NBS (396 mg, 2.22 mmol), and the mixture was stirred for 2 h at rt. Evaporation of the mixture gave a residue, which was taken up into Et_2O. The organic solution was washed with brine, dried ($MgSO_4$), and evaporated. Column chromatography of the product on silica gel with hexane−AcOEt (33:1 v/v) provided **12** (137 mg, 62%) as a pale yellowish oil: IR (neat) 1640, 1120 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.11−1.36 (m, 3H), 3.30−3.96 (m, 7H), 4.63−4.69 (m, 1H), 5.09−5.17 (m, 2H), 5.99−6.10 (m, 1H), 7.22−7.50 (m, 5H). Anal. Calcd for $C_{14}H_{19}BrO_2$: C, 56.20; H, 6.40. Found: C, 56.13; H, 6.40.

(±)-(3*Z*)-1-(2′-Bromo-1′-ethoxyethoxy)-2-phenyl-3-pentenes (13). Using the same means as above, **10** (54 mg, 0.33 mmol) was transformed into **13** (52 mg, 50%) as a pale yellowish oil: IR (neat) 1655, 1130 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.15−1.26 (m, 3H), 1.62−1.72 (m, 3H), 3.29−3.95 (m, 7H), 4.61−4.68 (m, 1H), 5.62−5.68 (m, 2H), 7.18−7.39 (m, 5H). Anal. Calcd for $C_{15}H_{21}BrO_2$: C, 57.52; H, 6.76. Found: C, 57.61; H, 6.77.

Methyl (±)-(2*E*)-5-(2′-Bromo-1′-ethoxyethoxy)-4-phenyl-2-pentenoates (14). Using the same procedure as above, **11** (234 mg, 1.14 mmol) was transformed into **14** (255 mg, 63%) as a pale yellowish oil: IR (neat) 1730, 1655, 1130 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.17 (t, 3H, J = 7.0 Hz), 3.22−4.00 (m, 7H), 3.72 (s, 3H), 4.64−4.70 (m, 1H), 5.89 (d, 1H, J = 15.4 Hz), 7.05−7.46 (m, 6H); MS m/z 311 (M^+ − OEt). Anal. Calcd for $C_{16}H_{21}BrO_4$: C, 53.79; H, 5.92. Found: C, 53.75; H, 5.96.

1-(2′-Bromo-1′-ethoxyethoxy)-4-(phenylthio)-3-butenes (27). Using the same procedure as above, **26** (109 mg, 0.604 mmol) was converted into **27** (111 mg, 55%) as a colorless oil: IR (neat) 1645, 1130 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.21−1.35 (m, 3H), 2.43−2.60 (m, 2H), 3.36−3.80 (m, 6H), 4.67−4.73 (m, 1H), 5.86−5.99 (m, 1H), 6.23−6.33 (m, 1H), 7.18−7.36 (m, 5H); HRMS calcd for $C_{14}H_{19}BrO_2S$ (M^+) 330.0289, found 330.0330.

(±)-1-(Bromoacetyloxy)-2-phenyl-3-butene (15). To a stirred solution of **9** (495 mg, 3.34 mmol), bromoacetic acid (488 mg, 3.51 mmol), and DMAP (4.1 mg, 33 μmol) in dry CH_2Cl_2 (20 mL) at 0 °C was slowly added a solution of DCC (828 mg, 4.01 mmol) in dry CH_2Cl_2 (10 mL), and the mixture was stirred for 1.5 h at rt. After dilution with Et_2O followed by filtration through Celite, the filtrate was washed with H_2O, dried ($MgSO_4$), and evaporated. Column chromatography of the product on silica gel with hexane−AcOEt (9:1 v/v) yielded **15** (542 mg, 61%) as a colorless oil: IR (neat) 1740, 1640 cm^{-1}; ^{1}H NMR (300 MHz) δ 3.68−3.85 (m, 3H), 4.35−4.47 (m, 2H), 5.07−5.20 (m, 2H), 5.93−6.05 (m, 1H), 7.21−7.44 (m, 5H); HRMS calcd for $C_{11}H_{11}BrO_2$ (M^+ − Me + H) 253.9942, found 253.9954.

(±)-(2*Z*)-1-(Bromoacetoxy)-2-phenyl-3-pentene (16). Using the same method as above, **10** (190 mg, 1.18 mmol) was converted into **16** (278 mg, 84%) as a colorless oil: IR (neat) 1740, 1650 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.68 (d, 3H, J = 5.5 Hz), 3.77 (s, 2H), 4.00−4.08 (m, 1H), 4.33−4.43 (m, 2H), 5.55−

5.72 (m, 2H), 7.23−7.34 (m, 5H). Anal. Calcd for $C_{13}H_{15}BrO_2$: C, 55.14; H, 5.34. Found: C, 55.29; H, 5.35.

Methyl (±)-(2*E*)-5-(Bromoacetoxy)-4-phenyl-2-pentenoate (17). Using the same method as above, **11** (142 mg, 0.69 mmol) was transformed into **17** (164 mg, 73%) as a colorless oil: IR (neat) 1745, 1735, 1660 cm^{-1}; ^1H NMR (300 MHz) δ 3.74 (s, 3H), 3.80 (s, 2H), 3.84−3.92 (m, 1H), 4.43−4.47 (m, 2H), 5.90 (dd, 1H, J = 1.4, 15.7 Hz), 7.11 (dd, 1H, J = 7.4, 15.7 Hz), 7.20−7.41 (m, 5H); Anal. Calcd for $C_{14}H_{15}BrO_4$: C, 51.40; H, 4.62. Found: C, 51.67; H, 4.64.

(±)-(1*E* and 1*Z*)-3-[(Bromoacetoxy)methyl]-1-phenyl-1-pentenes (22). To a stirred solution of **20** (228 mg, 1.29 mmol) and pyridine (0.12 mL, 1.42 mmol) in dry CH_2Cl_2 (5 mL) at 0 °C was added bromoacetyl bromide (0.12 mL, 1.36 mmol), and the mixture was stirred for 2 h at rt. After neutralization with 10% HCl under cooling with ice, the mixture was thoroughly extracted with Et_2O. The extract was washed with saturated $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated to give a residue, which was subjected to column chromatography on silica gel. Elution with hexane−AcOEt (19:1 v/v) yielded a mixture of **22** (317 mg, 82%) in a ratio of 3:1 (*E*/*Z*) as a colorless oil: IR (neat) 1740, 1655 cm^{-1}; ^1H NMR (300 MHz) δ 0.86−0.97 (m, 3H), 1.27−1.65 (m, 2H), 2.45−2.53 (m, 0.75H), 2.88−3.02 (m, 0.25H), 3.77−3.85 (m, 2H), 4.10−4.23 (m, 2H), 5.35−5.43 (m, 0.25H), 5.93−6.01 (m, 0.75H), 6.45 (d, 0.75H, J = 15.8 Hz), 6.61 (d, 0.25H, J = 11.4 Hz), 7.19−7.37 (m, 5H); MS m/z 296 (M^+). Anal. Calcd for $C_{14}H_{17}BrO_2$: C, 56.58; H, 5.77. Found: C, 56.50; H, 5.87.

(3*E* and 3*Z*)-1-(Bromoacetoxy)-2,2-dimethyl-4-phenyl-3-butenes (23). Using the same method as for the preparation of **15**, **21** (231 mg, 1.31 mmol) was transformed into a mixture of **23** (328 mg, 84%) in a ratio of 7:3 (*Z*/*E*) as a colorless oil: IR (neat) 1730, 1645 cm^{-1}; ^1H NMR (300 MHz) δ 1.00 (s, 4.2 H), 1.18 (s, 1.8H), 3.82−3.84 (m, 2H), 3.90 (s, 1.4H), 4.04 (s, 0.6H), 5.55 (d, 0.7H, J = 12.5 Hz), 6.18 (d, 0.3H, J = 16.3 Hz), 6.40 (d, 0.3H, J = 16.3 Hz), 6.58 (d, 0.7H, J = 12.5 Hz), 7.15−7.37 (m, 5H); HRMS calcd for $C_{14}H_{17}BrO_2$ (M^+) 296.0412, found 296.0408.

(3*E*)-1-(Bromoacetoxy)-2,2-dimethyl-4-(phenylthio)-3-butene (28). Using the same method as for the preparation of **22**, **25** (120 mg, 0.58 mmol) was transformed into **28** (184 mg, 97%) as a colorless oil: IR (neat) 1730 cm^{-1}; ^1H NMR (300 MHz) δ 1.13 (s, 6H), 3.85 (s, 2H), 3.98 (s, 2H), 5.90 (d, 1H, J = 15.4 Hz), 6.20 (d, 1H, J = 15.4 Hz), 7.20−7.37 (m, 5H); HRMS calcd for $C_{14}H_{17}BrO_2S$ (M^+) 328.0133, found 328.0103.

(3*E* and 3*Z*)-1-(Bromoacetoxy)-4-(phenylthio)-3-butenes (29). Using the same means as above, **26** (109 mg, 0.61 mmol) was converted into a mixture of **29** (154 mg, 84%) in a ratio of 1.5:1 (*E*/*Z*) as a colorless oil: IR (neat) 1740 cm^{-1}; ^1H NMR (300 MHz) 2.49−2.56 (m, 1.2H), 2.60−2.67 (m, 0.8H), 3.83−3.84 (m, 2H), 4.21−4.30 (m, 2H), 5.75−5.94 (m, 1H), 6.28 (dt, 0.6H, J = 1.4, 15.1 Hz), 6.36 (dt, 0.4H, J = 1.4, 9.3 Hz), 7.17−7.40 (m, 5H); HRMS calcd for $C_{12}H_{13}BrO_2S$ (M^+) 299.9820, found 299.9780.

(+)-(4*S*)-3-[(2′*R*)-2′-((Benzyloxy)methyl)butanoyl]-4-benzyl-2-oxazolidinone (31). To a stirred solution of **30**[16] (2.04 g, 8.25 mmol) in dry CH_2Cl_2 (20 mL) at 0 °C was added $TiCl_4$ (0.905 mL, 8.25 mmol). After 10 min of stirring at 0 °C followed by addition of Et_3N (1.15 mL, 8.25 mmol), the mixture was stirred for 30 min at the same temperature. To the mixture was added BOMCl (2.29 mL, 16.5 mmol), and the resulting mixture was further stirred for 2 h at the same temperature. After dilution with CH_2Cl_2, the mixture was washed with 10% aqueous NH_4Cl, saturated $NaHCO_3$, and brine and dried (Na_2SO_4). Filtration through a pad of silica gel, followed by evaporation of the filtrate, gave a residue, which was crystallized from AcOEt−hexane to afford **31** (2.34 g, 77%) as crystals, mp 75−76 °C: $[\alpha]^{22}_D$ +40.9° (*c* 0.94, $CHCl_3$); IR ($CHCl_3$) 1780, 1700 cm^{-1}; ^1H NMR (300 MHz) δ 0.93 (t, 3H, J = 7.5 Hz), 1.54−1.82 (m, 2H), 2.69 (dd, 1H, J = 9.5, 13.5 Hz), 3.23 (dd, 1H, J = 3.1, 13.5 Hz), 3.66 (dd, 1H, J = 3.1, 9.5 Hz), 3.81 (t, 1H, J = 9.1 Hz), 4.10−4.22 (m, 3H), 4.54 (s, 2H), 4.64−4.76 (m, 1H), 7.18−7.38 (m, 10H); MS m/z 367 (M^+). Anal. Calcd for $C_{22}H_{25}NO_4$: C, 71.91; H, 6.86; N, 3.81. Found: C, 71.90; H, 6.83; N, 3.79.

(+)-(4*S*)-3-[(2′*R*)-2′-(Hydroxymethyl)butanoyl]-4-benzyl-2-oxazolidinone (32). A mixture of **31** (7.70 g, 21.0 mmol) and 10% Pd on carbon (500 mg) in EtOH (100 mL) was stirred for 3 days at rt under H_2 (1 atm). Filtration through Celite, followed by evaporation of the filtrate, gave a residue, which was subjected to chromatography on silica gel. Elution with hexane−AcOEt (3:2 v/v) provided **32** (5.80 g, 100%) as a colorless oil: $[\alpha]^{25}_D$ +71.6° (*c* 0.83, $CHCl_3$); IR (neat) 3450, 1770, 1690 cm^{-1}; ^1H NMR (300 MHz) δ 0.97 (t, 3H, J = 7.3 Hz), 1.57−1.77 (m, 2H), 2.20 (br s, 1H), 2.82 (dd, 1H, J = 9.3, 13.4 Hz), 3.30 (dd, 1H, J = 3.1, 13.4 Hz), 3.84−3.90 (m, 3H), 4.17−4.25 (m, 2H), 4.67−4.74 (m, 1H), 7.22−7.36 (m, 5H); MS m/z 277 (M^+); HRMS calcd for $C_{15}H_{19}NO_4$ (M^+) 277.1314, found 277.1300.

(+)-(4*S*)-3-[(2′*R*)-2′-((*tert*-Butyldimethylsiloxy)methyl)-butanoyl]-4-benzyl-2-oxazolidinone (33). To a stirred solution of **32** (5.80 g, 21.0 mmol), TBDMSCl (4.74 g, 31.4 mmol), and DMAP (256 mg, 2.10 mmol) in dry CH_2Cl_2 (20 mL) at 0 °C was added Et_3N (5.80 mL, 41.6 mmol), and the mixture was stirred for 5 h at rt. The mixture was washed with H_2O and brine, dried (Na_2SO_4), and evaporated to give a residue, which was purified by column chromatography on silica gel. Elution with hexane−AcOEt (9:1 v/v) afforded **33** (8.21 g, 100%) as a colorless oil, physical properties of which were identical with those of the authentic compound.[10]

(−)-Ethyl (2*E*)-4-[((2′*R*)-2′-((*tert*-Butyldimethylsiloxy)-methyl)butanoyl)oxy]-2-butenoate (34). To a stirred solution of **33** (1.04 g, 2.66 mmol) in THF−H_2O (3:1 v/v, 52 mL) at 0 °C were slowly added 30% H_2O_2 (2.4 mL, 21.2 mmol) and $LiOH·H_2O$ (223 mg, 5.31 mmol), and the mixture was stirred for 2 h at rt. After addition of 1.5 N Na_2SO_3, the resulting mixture was concentrated under reduced pressure to remove THF. After being washed with Et_2O, followed by acidification of the aqueous solution with 5% HCl at 0 °C, the mixture was thoroughly extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4) and evaporated to give a residue, which was used in the following reaction without purification.

To a stirred solution of the above product, **40** (680 mg, 5.31 mmol), and DMAP (97 mg, 0.79 mmol) in dry CH_2Cl_2 (20 mL) at 0 °C was slowly added a solution of DCC (1.37 g, 6.64 mmol) in dry CH_2Cl_2 (5 mL), and the mixture was stirred for 12 h at rt. After dilution with Et_2O followed by filtration through Celite, the filtrate was evaporated to give a residue, which was subjected to column chromatography on silica gel. Elution with hexane−AcOEt (19:1 v/v) yielded **34** (913 mg, 100%) as a colorless oil: $[\alpha]^{21}_D$ −4.1° (*c* 0.90, $CHCl_3$): IR (neat) 1720, 1655 cm^{-1}; ^1H NMR (300 MHz) δ 0.02 (s, 6H), 0.82 (s, 9H), 0.91 (t, 3H, J = 7.3 Hz), 1.29 (t, 3H, J = 7.1 Hz), 1.50−1.70 (m, 2H), 2.52−2.64 (m, 1H), 3.68 (dd, 1H, J = 5.7, 9.5 Hz), 3.78 (dd, 1H, J = 8.0, 9.5 Hz), 4.19 (q, 2H, J = 7.1 Hz), 4.74−4.75 (m, 2H), 6.01 (dt, 1H, J = 2.0, 15.5 Hz), 6.92 (dt, 1H, J = 4.4, 15.5 Hz); MS m/z 287 (M^+ − *t*-Bu); HRMS calcd for $C_{17}H_{32}O_5Si$ (M^+ − *t*-Bu) 287.1315, found 287.1324.

Ethyl (2*E*)-4-(*tert*-Butyldimethylsiloxy)-2-butenoate (41). To a stirred mixture of **40** (859 mg, 6.61 mmol), TBDMSCl (1.50 g, 9.95 mmol), and DMAP (81 mg, 0.66 mmol) in dry CH_2Cl_2 (20 mL) at 0 °C was added Et_3N (1.80 mL, 12.9 mmol), and the mixture was stirred for 1 h at rt. The mixture was washed with H_2O and brine, dried (Na_2SO_4), and evaporated. Column chromatography of the residue on silica gel with hexane−AcOEt (9:1 v/v) as the eluent gave **41** (1.50 g, 99%) as a colorless oil: IR (neat) 1720, 1655 cm^{-1}; ^1H NMR (300 MHz) δ 0.06 (s, 6H), 0.92 (s, 9H), 1.32 (t, 3H, J = 7.4 Hz), 4.20 (q, 2H, J = 7.4 Hz), 4.35 (dd, 2H, J = 2.0, 3.2 Hz), 6.10 (dt, 1H, J = 2.0, 15.3 Hz), 7.00 (dt, 1H, J = 3.2, 15.3 Hz); MS m/z 244 (M^+). Anal. Calcd for $C_{12}H_{24}O_3Si$; C, 58.97; H, 9.90. Found: C, 59.16; H, 9.96.

***p*-Fluorophenyl (2*E*)-4-Hydroxy-2-butenoate (43)**. A mixture of **41** (1.01 g, 4.15 mmol) and 0.5 N NaOH (9.13 mL) in MeOH (15 mL) was stirred for 5 h at rt. After concentration of the reaction mixture under reduced pressure followed by dilution with CH_2Cl_2, the mixture was acidified with 10% aqueous $KHSO_4$ under ice cooling, and the combined CH_2Cl_2 layers were dried (Na_2SO_4) and evaporated to give the crude acid, which was used in the next reaction without purification.

To a stirred mixture of the above product, 4-fluorophenol (512 mg, 4.57 mmol), and DMAP (46.6 mg, 0.38 mmol) in dry $ClCH_2CH_2Cl$ (10 mL) at 0 °C was slowly added a solution of DCC (1.03 g, 4.99 mmol) in $ClCH_2CH_2Cl$ (5 mL), and the mixture was stirred for 14 h at rt. After dilution with Et_2O, the mixture was filtered through Celite and then evaporated. Column chromatography of the product on silica gel with hexane−AcOEt (19:1 v/v) as the eluent provided **42** (572 mg, 44% for two steps) as a colorless oil: IR (neat)1740, 1660 cm^{-1}; ^1H NMR (300 MHz) δ 0.08 (s, 6H), 0.96 (s, 9H), 4.41 (dd, 2H, J = 2.5, 3.3 Hz), 6.30 (dt, 1H, J = 2.5, 15.3 Hz), 7.07−7.08 (m, 4H), 7.25 (dt, 1H, J = 3.3, 15.3 Hz); MS m/z 310 (M^+); HRMS calcd for $C_{16}H_{23}FO_3Si$ (M^+) 310.1401, found 310.1443.

A mixture of **42** (570 mg, 1.84 mmol) and AcOH−H_2O (3:1 v/v, 16 mL) in THF (4 mL) was stirred for 10 h at rt. After dilution with AcOEt, the mixture was neutralized with saturated $NaHCO_3$ under cooling with ice. The organic layer was washed with brine, dried (Na_2SO_4), and evaporated to give a residue, which was purified by column chromatography on silica gel. Elution with hexane−AcOEt (3:1 v/v) afforded **43** (324 mg, 90%) as a colorless oil: IR (neat) 3400, 1740, 1660 cm^{-1}; ^1H NMR (300 MHz) δ 2.22−2.38 (br s, 1H), 4.41 (m, 2H), 6.30 (dt, 1H, J = 2.2, 15.8 Hz), 7.06−7.08 (m, 4H), 7.25 (dt, 1H, J = 3.6, 15.8 Hz); MS m/z 196 (M^+); HRMS calcd for $C_{10}H_9FO_3$ (M^+) 196.0536, found 196.0554.

(−)-*p*-Fluorophenyl (2*E*)-4-[((2′*R*)-2′-((*tert*-Butyldimethylsiloxy)methyl)butanoyl)oxy]-2-butenoate (35). To a stirred solution of the crude acid, which was prepared from **33** (305 mg, 0.78 mmol) as in the previous description, **43** (210 mg, 1.07 mmol), and DMAP (13 mg, 0.11 mmol) in dry $ClCH_2CH_2Cl$ (5 mL) at 0 °C was slowly added a solution of DCC (287 mg, 1.39 mmol) in dry $ClCH_2CH_2Cl$ (1 mL), and the mixture was stirred for 12 h at rt. Dilution with Et_2O, followed by filtration through Celite and evaporation of the filtrate, gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane−AcOEt (19:1 v/v) yielded **35** (441 mg, 100%) as a colorless oil: $[\alpha]^{21}_D$ −0.96° (*c* 0.94, $CHCl_3$); IR (neat) 1740, 1720, 1660 cm^{-1}; ^1H NMR (300 MHz) δ 0.05 (s, 6H), 0.87 (s, 9H), 0.96 (t, 3H, J = 7.5 Hz), 1.52−1.72 (m, 2H), 2.55−2.64 (m, 1H), 3.76 (dd, 1H, J = 5.5, 9.8 Hz), 3.82 (dd, 1H, J = 8.0, 9.8 Hz), 4.83−4.86 (m, 2H), 6.23 (dt, 1H, J = 1.8, 15.3 Hz), 7.06−7.08 (m, 4H), 7.15 (dt, 1H, J = 4.4, 15.3 Hz); MS m/z 353 (M^+ − *t*-Bu); HRMS calcd for $C_{21}H_{31}FO_5Si$ (M^+ − *t*-Bu) 353.1221, found 353.1222.

(−)-Ethyl (2*E*)-4-[((2′*R*)-2′-(Hydroxymethyl)butanoyl)oxy]-2-butenoate (36). A mixture of **34** (706 mg, 2.05 mmol) and AcOH−H_2O (1:1 v/v, 6 mL) in THF (3 mL) was stirred for 12 h at 40 °C. After neutralization with saturated $NaHCO_3$ under cooling with ice, the mixture was thoroughly extracted with Et_2O. The combined extracts were washed with brine, dried (Na_2SO_4), and evaporated. Column chromatography of the product on silica gel with hexane−AcOEt (3:1 v/v) provided **36** (472 mg 96%) as a colorless oil: $[\alpha]^{21}_D$ −1.1° (*c* 0.93, $CHCl_3$); IR (neat) 3450, 1720, 1655, cm^{-1}; ^1H NMR (300 MHz) δ 0.98 (t, 3H, J = 7.2 Hz), 1.29 (t, 3H, J = 7.2 Hz), 1.59−1.81 (m, 2H), 2.09−2.22 (br s, 1H), 2.56−2.66 (m, 1H), 3.72−3.82 (m, 2H), 4.21 (q, 2H, J = 7.2 Hz), 4.80 (dd, 2H, J = 2.2, 4.5 Hz), 6.05 (dt, 1H, J = 2.2, 15.4 Hz), 6.95 (dt, 1H, J = 4.5, 15.4 Hz). Anal. Calcd for $C_{11}H_{18}O_5$: C, 57.38; H, 7.88. Found: C, 57.26; H, 7.84.

(−)-Ethyl (2*E*)-4-[((2′*R*)-2′-(Bromomethyl)butanoyl)oxy]-2-butenoate (38). A mixture of **36** (112 mg, 0.49 mmol), CBr_4 (242 mg, 0.73 mmol), and PPh_3 (153 mg, 0.58 mmol) in dry CH_2Cl_2 (5 mL) was stirred for 3.5 h at rt. Evaporation of the solvent, followed by column chromatography of the product on silica gel with hexane−AcOEt (9:1 v/v) as the eluent, provided **38** (135 mg, 95%) as a pale yellowish oil: $[\alpha]^{21}_D$ −4.9° (*c* 0.91, $CHCl_3$); IR (neat) 1720, 1655 cm^{-1}; ^1H NMR (300 MHz) δ 0.97 (t, 3H, J = 7.5 Hz), 1.30 (t, 3H, J = 7.2 Hz), 1.68−1.84 (m, 2H), 2.76−2.84 (m, 1H), 3.48 (dd, 1H, J = 5.1, 9.9 Hz), 3.59 (dd, 1H, J = 8.1, 9.9 Hz), 4.21 (q, 2H, J = 7.2 Hz), 4.79−4.84 (m, 2H), 6.05 (dt, 1H, J = 1.9, 15.7 Hz), 6.95 (dt, 1H, J = 3.8, 15.7 Hz). Anal. Calcd for $C_{11}H_{17}BrO_4$: C, 45.07; H, 5.84. Found: C, 45.25; H, 5.73.

(−)-*p*-Fluorophenyl (2*E*)-4-[((2′*R*)-2′-(Bromomethyl)butanoyl)oxy]-2-butenoate (39). Using the same procedure as above, **35** (441 mg, 1.07 mmol) was converted into **37** (308 mg, 97%) as a colorless oil: $[\alpha]^{21}_D$ +2.4° (*c* 1.23, $CHCl_3$); IR (neat) 3500, 1740, 1720, 1660 cm^{-1}; ^1H NMR (300 MHz) δ 0.99 (t, 3H, J = 7.5 Hz), 1.52−1.80 (m, 2H), 2.28−2.42 (br s, 1H), 2.57−2.70 (m, 1H), 3.75−3.90 (m, 2H), 4.88 (dd, 2H, J = 1.8, 4.4 Hz), 6.24 (dt, 1H, J = 1.8, 15.7 Hz), 7.04−7.06 (m, 4H), 7.15 (dt, 1H, J = 4.4, 15.7 Hz); MS m/z 296 (M^+); HRMS calcd for $C_{15}H_{17}FO_5$ (M^+) 296.1060, found 296.1056.

Using the same method as above, **37** (61 mg, 0.20 mmol) was transformed into **39** (63 mg, 85%) as a colorless oil: $[\alpha]^{21}_D$ −3.8° (*c* 0.80, $CHCl_3$); IR (neat) 1750, 1730, 1660 cm^{-1}; ^1H NMR (300 MHz) δ 0.99 (t, 3H, J = 7.4 Hz), 1.64−1.88 (m, 2H), 2.79−2.90 (m, 1H), 3.52 (dd, 1H, J = 5.1, 10.3 Hz), 3.61 (dd, 1H, J = 8.2, 10.3 Hz), 4.88−4.91 (m, 2H), 6.26 (dt, 1H, J = 1.9, 15.7 Hz), 7.03−7.09 (m, 4H), 7.15 (dt, 1H, J = 4.4, 15.7 Hz); MS m/z 358 (M^+); HRMS calcd for $C_{15}H_{16}BrFO_4$ (M^+) 358.0216, found 358.0200.

Standard Procedure for Indirect Electroreduction. The electrolysis was carried out in dry DMF (about 10 mL) containing a supporting electrolyte (0.1 M Et_4NClO_4), the substrate (amount used is shown in each experiment), a proton source (NH_4ClO_4 200 mol %), and $[Ni(cyclam)](ClO_4)_2$ (10 mol %), potentionstatically at −1.5 V vs Ag/AgCl using glassy carbon graphite (0.5 × 0.5 × 0.5 cm^3) as the cathode, under N_2 bubbling using an H-type divided cell separated by a cationic exchange membrane (Nafion 117) at rt. The reaction was monitored by TLC. After the reaction, the mixture was diluted with H_2O and then thoroughly extracted with Et_2O. The combined extracts were washed with brine, dried ($MgSO_4$), and evaporated. The product was purified by column chromatography on silica gel.

(±)-(4*R,5*R**)-2-Ethoxy-4-methyl-5-phenyl-3,4,5,6-tetrahydro-2*H*-pyrans (44).** Using the standard procedure, **12** (144 mg, 0.48 mmol) was converted to **44** (17 mg, 16%) as a colorless oil: ^1H NMR (300 MHz) δ 0.71−0.79 (m, 3H), 1.19−1.30 (m, 3H), 1.85−1.91 (m, 1H), 2.39−2.49 (m, 1H), 3.44−3.54 (m, 2H), 3.72−3.85 (m, 2H), 4.90−4.91 (m, 1H), 7.19−7.34 (m, 5H); HRMS calcd for $C_{14}H_{20}O_2$ (M^+) 220.1463, found 220.1474.

(±)-(4*R,5*R**)-2-Ethoxy-4-ethyl-5-phenyl-3,4,5,6-tetrahydro-2*H*-pyrans (45).** The indirect electroreduction of **13** (193 mg, 0.62 mmol) provided **45** (42 mg, 29%) as a colorless oil: ^1H NMR (300 MHz) δ 0.74 (t, 3H, J = 7.4 Hz), 1.20−1.33 (m, 3H), 1.40−1.50 (m, 1H), 1.65−1.75 (m, 1H), 1.91−2.00 (m, 1H), 2.13−2.18 (m, 1H), 2.51−2.70 (m, 1H), 3.45−3.58 (m, 2H), 3.72−3.83 (m, 2H), 4.80−4.95 (m, 1H), 7.19−7.34 (m, 5H); HRMS calcd for $C_{15}H_{22}O_2$ (M^+) 234.1620, found 234.1603.

(±)-(4*S,5*R**)-2-Ethoxy-4-[(methoxycarbonyl)methyl]-5-phenyl-3,4,5,6-tetrahydro-2*H*-pyrans (46).** Similarly, **14** (123 mg, 0.35 mmol) was transformed into **46** (72 mg, 75%) as a colorless oil: ^1H NMR (300 MHz) δ 1.23−1.29 (m, 3H), 1.90−2.13 (m, 2H), 2.19−2.29 (m, 1H), 2.34−2.74 (m, 2H), 3.53−3.55 (m, 3H), 3.71−4.00 (m, 2H), 4.57−4.91 (m, 1H), 7.15−7.36 (m, 5H); HRMS calcd for $C_{15}H_{19}O_4$ (M^+ − Me) 263.1284, found 263.1292.

(±)-2-Ethoxy-4-[(phenylthio)methyl]-3,4,5,6-tetrahydro-2*H*-pyrans (47). Similarly, **27** (48 mg, 0.14 mmol) was converted into **47** (10 mg, 27%) as a colorless oil: IR ($CHCl_3$) 1130 cm^{-1}; ^1H NMR (300 MHz) δ 1.20 (t, 3H, J = 7.0 Hz), 2.16−2.27 (m, 1H), 2.73−2.90 (m, 2H), 3.39−3.81 (m, 4H), 4.85 (br s, 1H), 7.14−7.40 (m, 5H); HRMS calcd for $C_{14}H_{20}O_2S$ (M^+) 252.1184, found 252.1177.

(4*R*,5*R*)-2-Ethoxy-5-ethyl-4-[(methoxycarbonyl)methyl]-3,4,5,6-tetrahydro-2*H*-pyrans (49). (A) Using the same method as above, **48**[9] (29 mg, 0.09 mmol) was transformed into a 4:1 mixture of **49** (18.0 mg, 83%), the spectral data of which were consistent with those of the authentic sample.[9]

(B) Similarly, **50**[9] (32 mg, 0.10 mmol) was converted into the *trans*-substituted **49** (21 mg, 88%), all properties of which were identical with those of authentic sample.[9]

4-Acetoxy-2-phenyl-1-butene (54). The electrolysis of **15** (103 mg, 0.38 mmol) gave **54** (42 mg, 58%) as a colorless oil: IR (neat) 1730, 1635 cm^{-1}; ^1H NMR (300 MHz) δ 2.01 (s, 3H), 3.64−3.72 (m, 1H), 4.25−4.38 (m, 2H), 5.09−5.18 (m, 2H), 5.93−6.05 (m, 1H), 7.20−7.38 (m, 5H). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.71; H, 7.54.

(2*Z*)-5-Acetoxy-4-phenyl-2-pentene (55). The electrolysis of **16** (93 mg, 0.33 mmol) provided **55** (53 mg, 78%) as a colorless oil: IR (neat) 1740, 1650 cm^{-1}; ^1H NMR (300 MHz) δ 1.67 (d, 3H, J = 5.1 Hz), 2.00 (s, 3H), 3.96−4.04 (m, 1H), 4.20−4.33 (m, 2H), 5.55−5.70 (m, 2H), 7.19−7.38 (m, 5H). Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.89. Found: C, 76.26; H, 7.87.

Methyl (2*E*)-5-Acetoxy-4-phenyl-2-pentenoate (56). The electrolysis of **17** (92 mg, 0.28 mmol) gave **56** (32 mg, 46%) as a colorless oil: IR (neat) 1745, 1730, 1655 cm^{-1}; ^1H NMR (300 MHz) δ 2.03 (s, 3H), 3.73 (s, 3H), 3.80−3.87 (m, 1H), 4.34−4.36 (m, 2H), 5.88 (dd, 1H, J = 1.4, 15.9 Hz), 7.12 (dd, 1H, J = 7.4, 15.9 Hz), 7.19−7.37 (m, 5H); HRMS calcd for $C_{11}H_{12}O_2$ ($M^+ - C_3H_4O_2$) 176.0837, found 176.0802.

(1*E* and 1*Z*)-4-Acetoxy-3-ethyl-1-phenyl-1-butenes (57). The electrolysis of **22** (104 mg, 0.35 mmol) gave a mixture of **57** (61 mg, 80%) in a ratio of 3:1 (*E*/*Z*) as a colorless oil: IR (neat) 1740, 1655 cm^{-1}; ^1H NMR (300 MHz) δ 0.85−0.96 (m, 3H), 1.26−1.66 (m, 2H), 2.01 (s, 0.75H), 2.03 (s, 2.25H), 2.38−2.51 (m, 0.75H), 2.88−3.02 (m, 0.25H), 4.02−4.13 (m, 2H), 5.35−5.42 (m, 0.25H), 5.94−6.03 (m, 0.75H), 6.43 (d, 0.75H, J = 16.1 Hz), 6.59 (d, 0.25H, J = 11.7 Hz), 7.18−7.37 (m, 5H); MS m/z 218 (M^+). Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.91; H, 8.39.

(1*E* and 1*Z*)-5-Acetoxy-3,3-dimethyl-1-phenyl-1-butenes (58). The electrolysis of **23** (135 mg, 0.46 mmol) afforded a mixture of **58** (63 mg, 63%) in a raito of 7:3 (*Z*/*E*) as a colorless oil: IR (neat) 1740, 1655 cm^{-1}; ^1H NMR (300 MHz) δ 0.97 (s, 4.2H), 1.16 (s, 1.8H), 2.05 (s, 3H), 3.81 (s, 1.4H), 3.94 (s, 0.6H), 5.55 (d, 0.7H, J = 12.5 Hz), 6.19 (d, 0.3H, J = 16.3 Hz), 6.38 (d, 0.3H, J = 16.3 Hz), 6.56 (d, 0.7H, J = 12.5 Hz), 7.16−7.45 (m, 5H); MS m/z 218 (M^+). Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.14; H, 8.33.

(1*E*)-4-Acetoxy-3,3-dimethyl-1-(phenylthio)-1-butene (59). The electrolysis of **28** (85 mg, 0.26 mmol) yielded **59** (52 mg, 81%) as a colorless oil: IR (neat, cm^{-1}) 1740 cm^{-1}; ^1H NMR (300 MHz) δ 1.11 (s, 6H), 2.07 (s, 3H), 3.88 (s, 2H), 5.93 (d, 1H, J = 15.4 Hz), 6.17 (d, 1H, J = 15.4 Hz), 7.17−7.41 (m, 5H); HRMS calcd for $C_{14}H_{18}O_2S$ (M^+) 250.1028, found 250.0993.

(1*E* and 1*Z*)-4-Acetoxy-1-(phenythio)-1-butenes (60). The electrolysis of **29** (92 mg, 0.30 mmol) produced a mixture of **60** (49 mg, 73%) in a ratio of 1.5:1 (*E*/*Z*) as a colorless oil: IR (neat) 1735 cm^{-1}; ^1H NMR (300 MHz) δ 2.06 (s, 3H), 2.45−2.52 (m, 1.2H), 2.56−2.63 (m, 0.8H), 4.11−4.18 (m, 2H), 5.76−5.93 (m, 1H), 6.26 (d, 0.6H, J = 15.0 Hz), 6.34 (d, 0.4H, J = 9.5 Hz), 7.19−7.52 (m, 5H); HRMS calcd for $C_{12}H_{14}O_2S$ (M^+) 222.0715, found 222.0720.

(±)-4-Ethyl-2-[(ethoxycarbonyl)methyl]-5-pentanolides (62). The electrolysis of **61** (33 mg, 0.11 mmol) gave **62** (4 mg, 17%) as a colorless oil, which was identical with the authentic specimen[10] in all respects.

(−)-(2*R*)-Ethyl-4-[(ethoxycarbonyl)methyl]-5-pentanolides (63). The electrolysis of **38** (32 mg, 0.11 mmol) yielded a 2:1 mixture of **63** (9 mg, 39%) as a colorless oil: $[\alpha]^{25}_D$ −50.9° (*c* 0.43, $CHCl_3$); IR (neat) 1720 cm^{-1}; ^1H NMR (300 MHz) δ 0.95−1.01 (m, 3H), 1.27 (t, 3H, J = 7.1 Hz), 1.42−2.60 (m, 8H), 3.94−4.08 (m, 1H), 4.16 (q, 2H, J = 7.1 Hz), 4.32 (dd, 0.67H, J = 4.8, 11.4 Hz), 4.36−4.41 (m, 0.33H); MS m/z 214 (M^+); HRMS calcd for $C_{11}H_{18}O_4$ (M^+) 214.1205, found 214.1194.

(−)-(2*R*)-Ethyl-4-[((*p*-fluorophenoxy)carbonyl)methyl]-5-pentanolides (64). The electrolysis of **39** (32 mg, 0.09 mmol) gave a 2:1 mixture of **64** (10 mg, 40%) as a colorless oil: $[\alpha]^{25}_D$ −42.5° (*c* 0.44, $CHCl_3$); IR (neat)1740, 1720 cm^{-1}; ^1H NMR (500 MHz) δ 0.97−1.03 (m, 3H), 1.26−2.69 (m, 8H), 4.09−4.16 (m, 1H), 4.40 (dd, 0.66H, J = 4.9, 11.5 Hz), 4.42−4.46 (m, 0.34H), 7.01−7.11 (m, 4H); MS m/z 280 (M^+); HRMS calcd for $C_{15}H_{17}FO_4$ (M^+) 280.1111, found 280.1138.

(+)-(5*R*)-3-[(Ethoxycarbonyl)methyl]-5-ethyl-*N*-[2-(3-indolyl)ethyl]piperidin-2-ones (66). The electrolysis of **65**[10] (72 mg, 0.17 mmol) provided **66** (29 mg, 49%) as a colorless oil, which was identical with the authentic sample[10] in all respects.

(±)-(3*R,4*R**)-3-Methyl-4-phenyl-5-pentanolide (51).** The product **44**, obtained by the electrolysis of **12** (144 mg, 0.48 mmol), was dissolved in THF (4 mL) and then treated with 10% $HClO_4$ (2 mL) for 24 h at rt. The mixture was thoroughly extracted with Et_2O. The combined extracts were washed with saturated $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated to give a residue, which was used in the following reaction without purification.

A mixture of the above product and Ag_2CO_3 on Celite (17:15 v/v, 1.95 g, 1.95 mmol) in dry benzene (15 mL) was heated for 40 min under reflux. Filtration through Celite, followed by evaporation of the filtrate, afforded a residue, which was subjected to column chromatography on silica gel. Elution with hexane−AcOEt (3:1 v/v) provided **51** (12 mg, 13% from **12**) as colorless needles, mp 102−103 °C: IR ($CHCl_3$) 1730 cm^{-1}; ^1H NMR (500 MHz) δ 0.90 (d, 3H, J = 5.5 Hz), 2.28−2.35 (m, 2H), 2.69−2.74 (m, 1H), 2.84−2.91 (m, 1H), 4.25−4.41 (m, 2H), 7.15−7.38 (m, 5H); MS m/z 190 (M^+). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.73; H, 7.43.

(±)-(3*R,4*R**)-3-Ethyl-4-phenyl-5-pentanolide (52).** The product **45**, obtained by the electrolysis of **13** (193 mg, 0.62 mmol), was similarly converted into **52** (29 mg, 23% from **13**) as a colorless solid: IR (neat) 1740 cm^{-1}; ^1H NMR (300 MHz) δ 0.80−0.97 (m, 3H), 1.09−1.51 (m, 2H), 2.13−2.29 (m, 1H), 2.35 (dd, 1H, J = 9.5, 17.6 Hz), 2.81 (ddd, 1H, J = 5.1, 10.3, 10.3 Hz), 2.89 (dd, 1H, J = 6.2, 17.2 Hz), 4.23−4.40 (m, 2H), 7.15−7.47 (m, 5H); HRMS calcd for $C_{13}H_{16}O_2$ (M^+) 204.1150, found 204.1169.

(±)-(3*S,4*R**)-3-[(Methoxycarbonyl)methyl]-4-phenyl-5-pentanolide (53).** The product **46**, obtained by the electrolysis of **14** (123 mg, 0.35 mmol), was similarly transformed into **53** (38 mg, 45% from **14**) as a colorless oil: IR (neat) 1730 cm^{-1}; ^1H NMR (300 MHz) δ 2.08−2.17 (m, 1H), 2.35 (dd, 1H, J = 4.0, 16.1 Hz), 2.45 (dd, 1H, J = 9.9, 17.6 Hz), 2.67−2.79 (m, 1H), 2.92 (ddd, 1H, J = 5.1, 10.6, 10.6 Hz), 3.02 (dd, 1H, J = 6.2, 17.6 Hz), 3.59 (s, 3H), 4.27−4.45 (m, 2H), 7.20−7.46 (m, 5H); MS m/z 248 (M^+). Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.56; H, 6.57.

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Supporting Information Available: ^1H NMR spectra of **10**, **15**, **20**, **23**, **26**−**29**, **32**, **34**, **35**, **39**, **43**, **44**−**47**, **52**, **56**, **59**, **60**, **63**, and **64** (23 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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