Electroorganic Chemistry. 140. Electroreductively Promoted Intra- and Intermolecular Couplings of Ketones with Nitriles[1]

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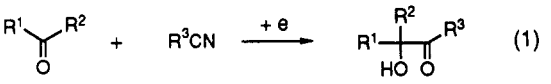
Electroreduction of γ- and δ-cyano ketones in i-PrOH with Sn cathode gave α-hydroxy ketones and their dehydroxylated ketones as the intramolecularly coupled products. Guaiazulene, (−)-valeranone, polyquinanes, dihydrojasmone, methyl dihydrojasmonate, and rosaprostol have been synthesized by utilizing this electroreductive intramolecular coupling of γ- and δ-cyano ketones in one of the key steps. Similarly, electroreduction of a mixture of ketone and nitrile gave the corresponding intermolecularly coupled product. The product obtained by the electroreductive intermolecular coupling of (+)-dihydrocarvone with acetonitrile has been found to be the precursor of an effective chiral ligand for the enantioselective addition of diethylzinc to aldehydes.

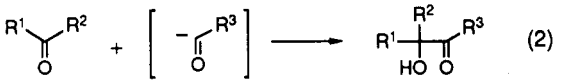
The coupling reaction of a carbonyl group with certain unsaturated systems which are not necessarily activated by typical activating groups is undoubtedly one of the most important types of reactions in organic synthesis. In our previous studies, the intramolecular coupling of a carbonyl group with a nonactivated carbon–carbon double[2] or triple bond[3] or an aromatic ring[4] and the intermolecular coupling of a carbonyl group with a nonactivated carbon–carbon double bond[5] or with the carbon–nitrogen double bond of an *O*-methyloxime[6] have been found to be successfully promoted by electroreduction.

It has been found in the present study that the coupling of a carbonyl group with a carbon–nitrogen triple bond (eq 1) is also effectively promoted by electroreduction, and this is a novel reaction corresponding to the reaction of an acyl anion with a carbonyl compound.



(1)

Since the acyl anion equivalent is one of the most important synthons in organic synthesis, a variety of acyl anion equivalents have already been synthesized and applied to the preparation of a variety of compounds such as α-hydroxycarbonyl compounds (eq 2).[7] Although the



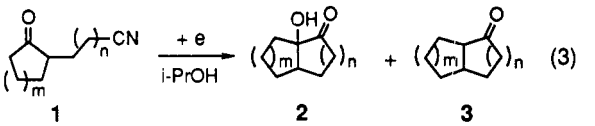
(2)

acyl anion equivalent is very effective for the development of new methods in organic synthesis, it is virtually limited to the intermolecular reaction. The intramolecular reaction of an acyl anion equivalent with a carbonyl group, for instance, is not achievable, due to the extreme difficulty involved in generating the acyl anion equivalent when a carbonyl group is present in the same molecule. On the other hand, the product synthesized by the electroreductively promoted coupling of a carbonyl group with a cyano group is equivalent to the compound formed by the reaction of an acyl anion equivalent with a carbonyl group, as shown in eqs 1 and 2. Hence, the electroreductively promoted coupling is a very useful equivalent to the reaction of the acyl anion.

The intramolecular coupling of γ- or δ-cyano ketones, for instance, was effectively promoted by electroreduction[8] and was found to be a new synthetic method for the preparation of polycyclic compounds or 2,3-disubstituted cyclopentanones. Indeed, guaiazulene, (−)-valeranone, polyquinanes, dihydrojasmone, methyl dihydrojasmonate, and rosaprostol have been synthesized by means of this new coupling method in the key step. The intermolecular coupling of ketones with nitriles was also promoted by electroreduction.[11] One of the more remarkable examples of intermolecular coupling was the coupling of (+)-dihydrocarvone with acetonitrile, and the product proved to be the precursor of an effective chiral ligand for the enantioselective addition of diethylzinc to aldehydes.

Results and Discussion

Electroreductive Intramolecular Coupling of γ- and δ-Cyano Ketones. The reaction conditions were scrutinized using 2-(2-cyanoethyl)cyclohexanone, **1a** (m = 2, n = 1), as a typical starting material (eq 3, Table I).



(3)

When the electroreduction was carried out in i-PrOH at 25 °C at a controlled potential of −2.8 V vs SCE using a divided cell equipped with a ceramic diaphragm and a Sn cathode, the intramolecularly coupled product **2a** was obtained in 76% yield together with a small amount of its dehydroxylated product **3a** (run 1). The electroreduction could also be carried out at a constant current of 0.2 A (run 2) or without a diaphragm (run 3), though the selectivity in product distribution was decreased to some extent. The reduction with a Ag cathode gave a similar result (run 4). Using other materials as the cathode (Cd: **2a** 64%, **3a** 2%; Pb: **2a** 40%, **3a** 15%; Zn: **2a** 30%, **3a** trace; C-fiber: **2a** 37%, **3a** 10%) or DMF as the solvent (Sn: **2a** 20%) resulted in a decrease in the yield. The results obtained with other cyclic γ- and δ-cyano ketones **1b–f** are shown in

(1) Preliminary report: Shono, T.; Kise, N. *Tetrahedron Lett.* **1990**, *31*, 1303.
(2) (a) Shono, T.; Mitani, M. *J. Am. Chem. Soc.* **1971**, *93*, 5284. (b) Shono, T.; Nishiguchi, I.; Ohmizu, H.; Mitani, M. *J. Am. Chem. Soc.* **1978**, *100*, 545.
(3) Shono, T.; Nishiguchi, I.; Ohmizu, H. *Chem. Lett.* **1976**, 1233.
(4) Shono, T.; Kise, N.; Suzumoto, T.; Morimoto, T. *J. Am. Chem. Soc.* **1986**, *108*, 4676.
(5) Shono, T.; Kashimura, S.; Mori, Y.; Hayashi, T.; Soejima, T.; Yamaguchi, Y. *J. Org. Chem.* **1989**, *54*, 6001.
(6) Shono, T.; Kise, N.; Fujimoto, T. *Tetrahedron Lett.* **1991**, *32*, 525.
(7) For reviews: (a) Lever, O. W., Jr. *Tetrahedron* **1976**, *32*, 1943. (b) Grobel, B. T.; Seebach, D. *Synthesis* **1977**, 357. (c) Martin, S. F. *Synthesis* **1979**, 633.
(8) The reductive cyclization of γ-cyano ketones with Zn–TMSCl[9] or SmI_2[10] has been reported.
(9) Corey, E. J.; Pyne, S. G. *Tetrahedron Lett.* **1983**, *24*, 2821.
(10) (a) Kraus, G. A.; Sy, J. O. *J. Org. Chem.* **1989**, *54*, 77. (b) Molander, G. M.; Kenny, C. *J. Am. Chem. Soc.* **1989**, *111*, 8236.
(11) Ytterbium metal promoted coupling reaction of diaryl ketones with nitriles has been reported.[12]
(12) Hou, Z.; Takamine, K.; Aoki, O.; Shiraishi, H.; Fujiwara, Y.; Taniguchi, H. *J. Org. Chem.* **1988**, *53*, 6077.

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Table I. Electroreductive Intramolecular Coupling of Cyclic γ- and δ-Cyano Ketones

run		m	n	temp, °C	F/mol	% yield[a] of 2 (ds)[b]		% yield of 3	
1	**1a**	2	1	25	3	**2a**	76[c]	**3a**	2
2[d]				25	3.5		63[c]		16
3[e]				25	4		65[c]		11
4[f]				25	4		74[c]		2
5				65	6		5[c]		64
6	**1b**	1	1	25	3	**2b**	68[c]		
7	**1c**	3	1	25	4	**2c**	76 (67:33)[g]	**3c**	8
8				65	8				71
9	**1d**	8	1	25	6	**2d**	55 (88:12)[h]	**3d**	22
10				65	10		4		54
11	**1e**	1	2	25	3	**2e**	60[c]		
12	**1f**	2	2	25	4	**2f**	69 (67:33)[g]	**3f**	3
13				65	8		3		60

[a] Isolated yields. [b] Diastereomeric ratios. [c] Obtained as a single stereoisomer (>99% based on ^{13}C NMR analysis). [d] At constant current of 0.2 A. [e] Without using a diaphragm. [f] Using Ag cathode. [g] Cis:trans ratio determined by isolation of each isomer. [h] Trans:cis ratio determined by ^{13}C NMR.

Scheme I

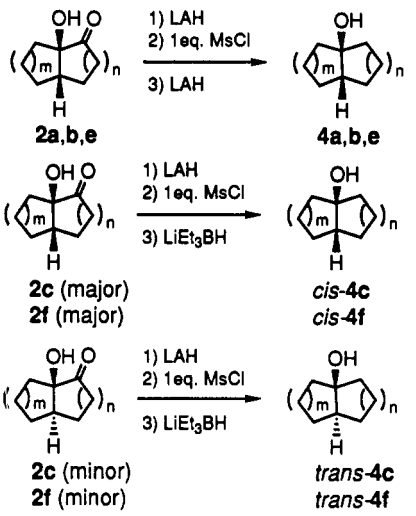
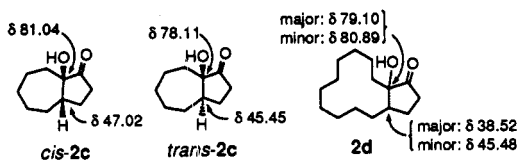


Table I (runs 6–13), in which it is clearly shown that the ratio of the products **2** and **3** was controlled by the reaction temperature. When the reaction was carried out at 25 °C, the α-hydroxy ketone **2** was obtained almost exclusively, whereas the dehydroxylated ketone **3** was the primary product at 65 °C.

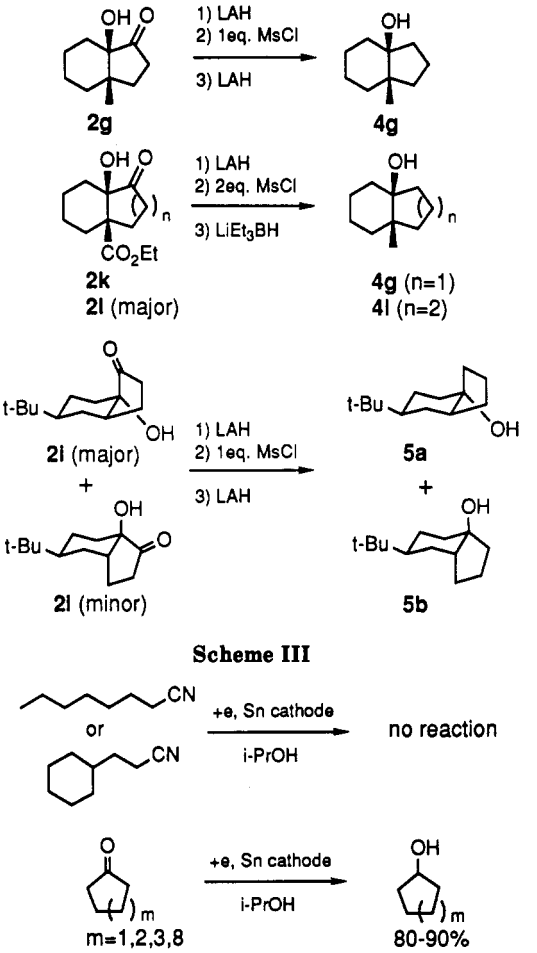
The stereoconfigurations of **2a–c,e,f** were determined by their transformations to the known compounds **4a–c,e,f**[13] and comparison of their ^{13}C NMR spectra with the reported data (Scheme I). Bicyclic α-hydroxy ketone **2a,b**, or **2e** was obtained as a single stereoisomer and assigned as cis. Due to the strain of trans-fused bicyclo[3.3.0] or -[4.3.0] skeleton, the exclusive formation of the cis isomer is reasonable. On the other hand, a 2:1 mixture of cis and trans isomers was obtained when the skeleton of the α-hydroxy ketone was bicyclo[5.3.0] (**2c**) or -[4.4.0] (**2f**). Furthermore, the major isomer of **2d** having a bicyclo-[10.3.0] skeleton was assigned to be trans by the comparison of its ^{13}C NMR with that of **2c**.[14]

(13) Molander, G. A.; Etter, J. B. *J. Org. Chem.* **1986**, *51*, 1778.

(14) The chemical shifts of bridgehead carbons of **2c** and **2d** are shown below. The major isomer of **2d** was determined to be trans on the basis of chemical shifts of *cis*- and *trans*-**2c**.



Scheme II



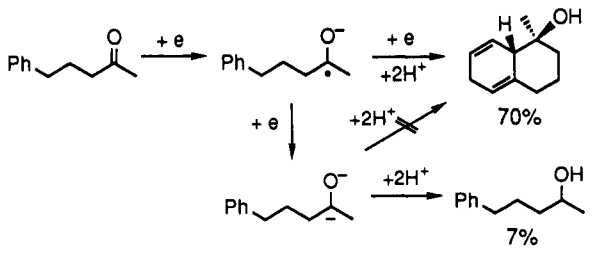
Scheme III

Other starting cyano ketones and coupling products obtained under the same reaction conditions are summarized in Table II. The coupling reaction was not hindered by alkyl (runs 1–4) and 2-ethoxycarbonyl substituents (runs 5, 6). The stereoconfigurations of **2g,i,k,l** (major) were determined to be cis-fused by the method described above (Scheme II), and it seemed probable that the other bicyclo[4.3.0] products **2h** and **2j** were also cis-fused isomers.

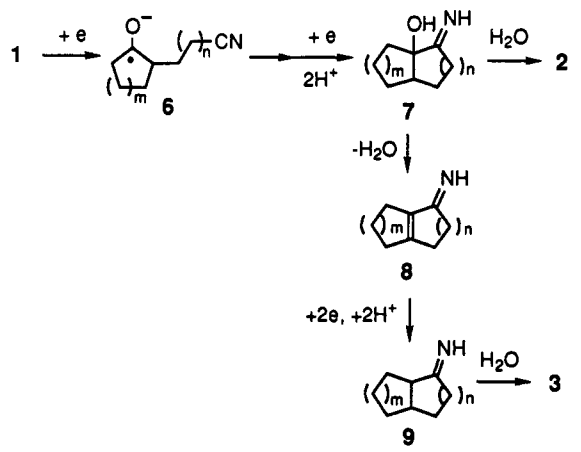
Acyclic γ- and δ-cyano ketones **1m–o** similarly gave the corresponding cyclized products **2m–o** (runs 7–9).

Reaction Mechanism. It is reasonable to assume that the initiation of the electroreductive intramolecular coupling of γ- and δ-cyano ketones is the reduction of the carbonyl group rather than the cyano group, since nitriles

Scheme IV



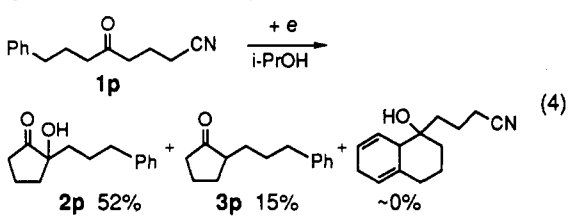
Scheme V



were completely inert under the present reaction conditions whereas ketones were easily reduced to the corresponding alcohols under the same conditions (Scheme III).

Furthermore, the electroreductive coupling of γ- and δ-cyano ketones was achieved in a protic solvent such as i-PrOH, and further, the addition of 1 equiv of water to the reaction system did not show any negative effect on the coupling.[15] These results suggest that the key active intermediate in this coupling is not an anionic species, but rather a radical species. As we have already reported the electroreductive intramolecular coupling of a carbonyl group with a phenyl group,[4] it is not unusual to find that the radical species formed by electroreduction of a carbonyl group couples with an unsaturated system (Scheme IV).

The electroreduction of a γ-cyano-γ'-phenyl ketone **1p** under the same reaction conditions as shown in Scheme IV proved interesting, as the radical species preferentially coupled with the cyano group as shown in eq 4.

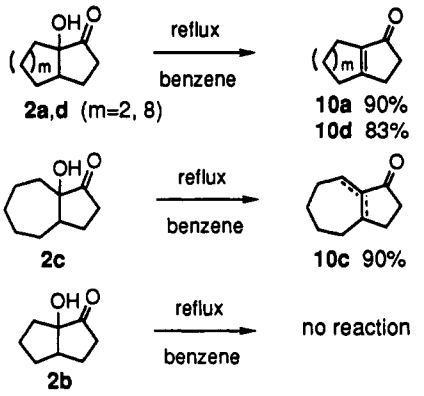


(4)

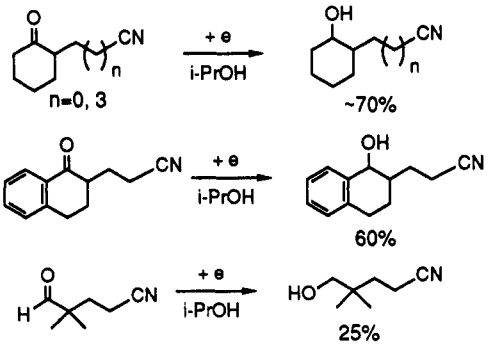
Hence, the overall reaction scheme of the intramolecular coupling of γ- and δ-cyano ketones is depicted in Scheme V.[17] The first active species, namely an anion radical **6** or its protonated analog, attacks the cyano group intramolecularly, and subsequent one-electron transfer and protonation gives the α-hydroxy imine **7**. At an elevated temperature, dehydration of **7** takes place, forming α,β-unsaturated imine **8**, which is immediately reduced to imine **9**.

Workup of **7** and **9** with water gives the products **2** and **3**, respectively. The fact that **7** was thermally dehydrated

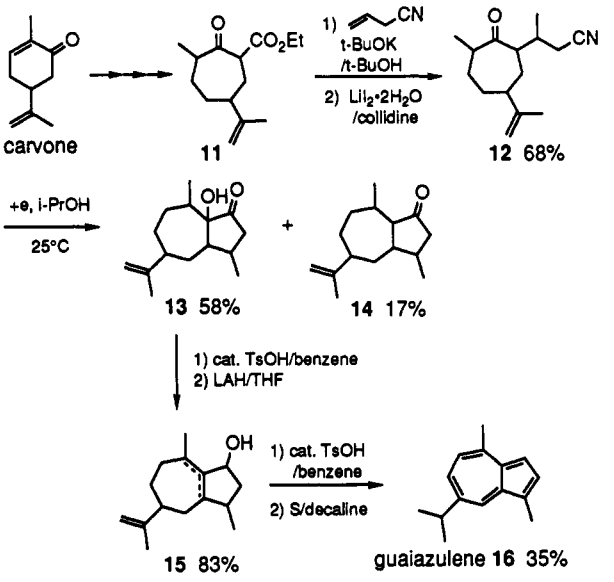
Scheme VI



Scheme VII



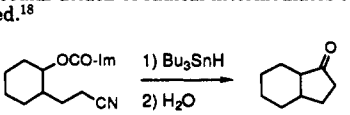
Scheme VIII



(15) The electroreductive intermolecular coupling of cycloheptatriene with acetone (Sn cathode: solvent DMF) has also been shown to be a radical addition reaction in which the radical species formed from the carbonyl group adds to the triene,[5] and this reaction is not inhibited by water (DMF containing 4 wt % water) at all. On the other hand, the electroreductive alkylation of cycloheptatriene with alkyl chloride (Pt cathode: solvent DMF) is a substitution reaction in which the alkyl chloride is substituted by an anion formed by electroreduction of cycloheptatriene.[16] This reaction is completely inhibited by water (DMF containing 4 wt % water).

(16) Shono, T.; Kashimura, S.; Yamaguchi, Y.; Ishifune, M.; Sakaguchi, M.; Masuda, H. *Tetrahedron Lett.* **1991**, *32*, 1051.

(17) Intramolecular attack of radical intermediates to a cyano group has been reported.[18]



(18) Clive, D. L. J.; Beaulieu, P. L.; Set, L. *J. Org. Chem.* **1984**, *49*, 1313.

Table II. Electroreductive Intramolecular Coupling of Substituted Cyclic and Acyclic γ- and δ-Cyano Ketones[a]

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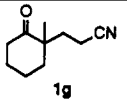
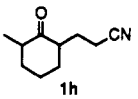
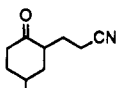
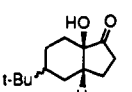
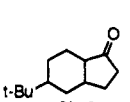
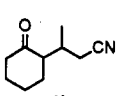
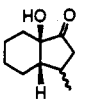
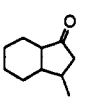
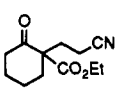
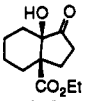
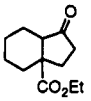
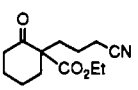
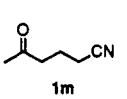
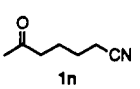
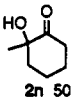
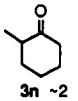
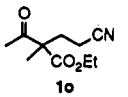
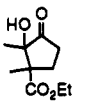
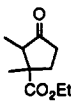
1	 1g	4.5	 2g 60	 3g 5
2	 1h	4.5	 2h 62 (>95:5)[d]	 3h ~2
3	 1i	4.5	 2i 58 (88:12)[d]	 3i 8
4	 1j	4.5	 2j 62 (75:25)[d]	 3j 9
5[e]	 1k	4.5	 2k 52	 3k 20
6[e]	 1l	4.5	 2l 72 (64:36)[f]	
7	 1m	4.5	 2m 55	 3m ~2
8	 1n	4.0	 2n 50	 3n ~2
9[e]	 1o	4.5	 2o 43 (67:33)[d]	 3o 10

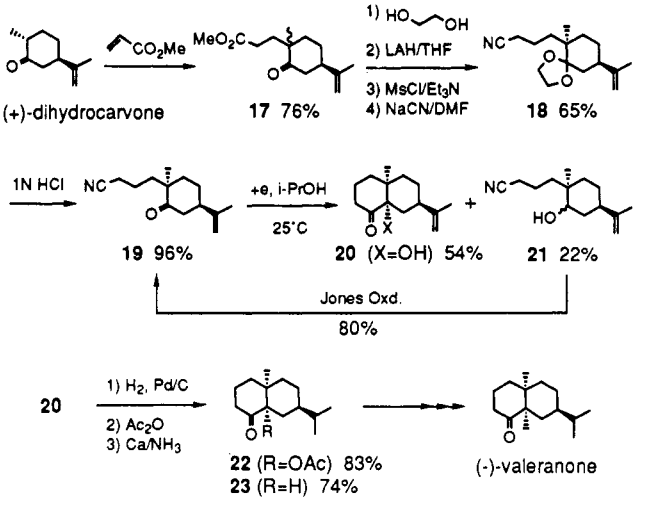
[a] Electroreduction was carried out using a Sn cathode in i-PrOH at 25 °C under a controlled cathode potential (−2.8 V vs SCE). [b] Isolated yields. [c] Diastereomeric ratios. [d] Determined by ^1H or ^{13}C NMR. [e] Without using a diaphragm. [f] Cis:trans ratio determined by isolation of each isomer.

to 8 is supported by the fact that α-hydroxy ketones **2** were easily dehydrated to α,β-unsaturated ketones **10** by refluxing in benzene (Scheme VI). That the electroreduction of **1b** did not give dehydroxylated ketone **3b** even at 65 °C is consistent with the fact that **2b** was inert under reflux in benzene.

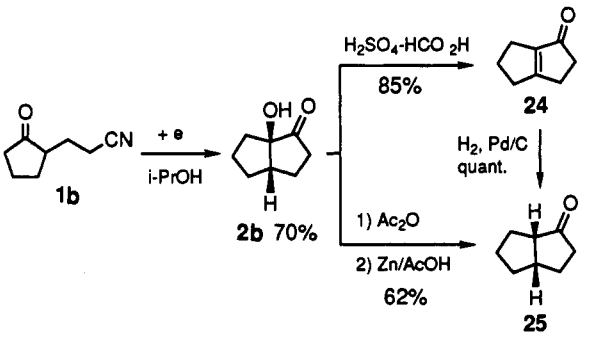
The other cyano ketones such as β- and ϵ-cyano ketones, aromatic γ-cyano ketone, and γ-cyano aldehydes gave noncyclized alcohols under the same reaction conditions (Scheme VII).

Synthesis of Guaiazulene. The electroreductive intramolecular coupling of cyclic γ- and δ-cyano ketones is an effective method for the construction of bicyclo[*m.n.*0] skeletons ($m \geq 3$, $n = 3, 4$). For example, synthesis of guaiazulene **16** was achieved using the electroreduction of γ-cyano ketones as a key step (Scheme VIII). β-Keto ester

Scheme IX



Scheme X



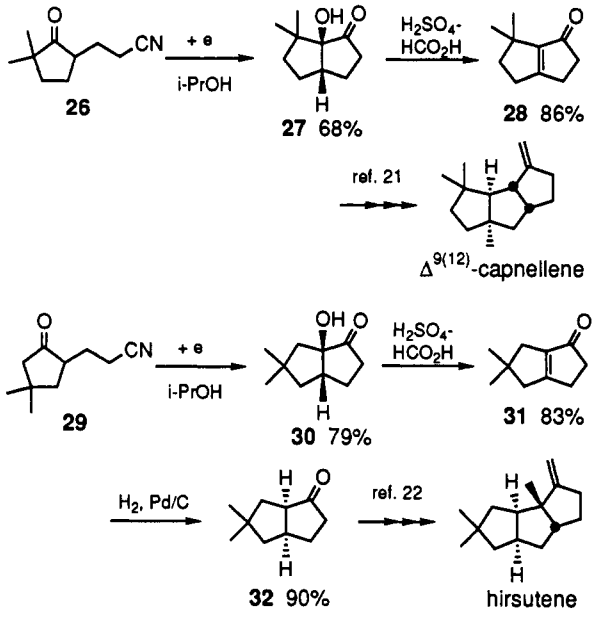
11 was prepared from carvone by a known method.[19] Cyanoalkylation of **11** with allylcyanide followed by decarbethoxylation gave the starting material γ-cyano ketone **12**. Electroreduction of **12** at 25 °C under the conditions described above afforded cyclized α-hydroxy ketone **13** together with **14**. Dehydration of **13** and subsequent LAH reduction gave **15**. Guaiazulene **16** was obtained by dehydration of **15** followed by aromatization of the dehydrated product with sulfur.

Formal Synthesis of (−)-Valeranone. As shown in Scheme IX, the electroreductive cyclization of δ-cyano ketones was found to be useful for the synthesis of (−)-valeranone,[20] a sesquiterpene possessing the bicyclo[4.4.0] skeleton. Specifically, the Michael reaction of (+)-dihydrocarvone with methyl acrylate gave **17** as an 86:14 mixture of two diastereomers. After a ketal of **17** was prepared, the methoxycarbonyl group of the ketal was reduced with LAH, the resultant alcohol was mesylated, and finally the sulfonate was cyanated with NaCN to give δ-cyano ketal **18** (β-Me) and its diastereomer. The major isomer **18** was separated by column chromatography on silica gel and hydrolyzed to give δ-cyano ketone **19**. Electroreduction of **19** afforded the cyclized product **20** (X = OH) together with a noncyclized alcohol **21**, which was easily transformed to **19** by oxidation. Since the dehydroxylated product (**23**, X = H) was not formed even by the electroreduction carried out at 65 °C, dehydroxylation of **20** (X = OH) was achieved in three steps, i.e., hydrogenation, acetylation of OH group, and reduction of the acetate **22** with Ca in liquid NH_3. Transformation of

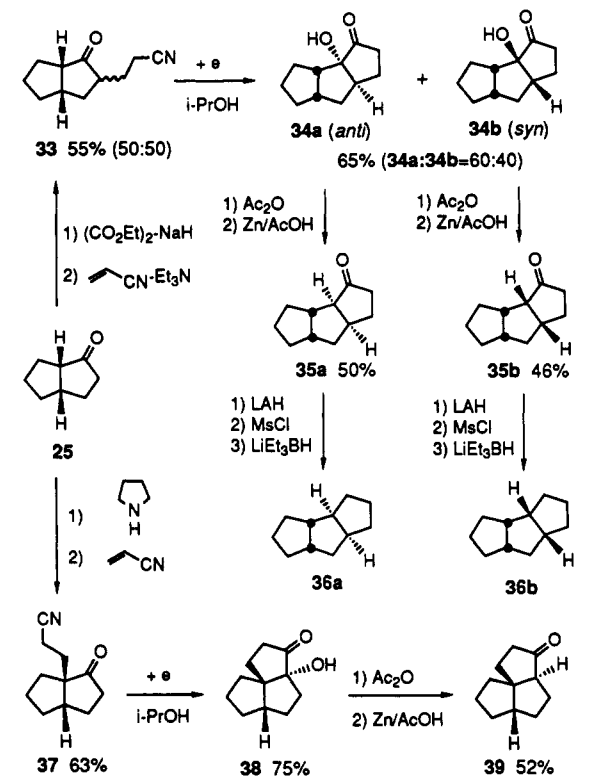
(19) Jacob, T. M.; Vatakencherry, P. A.; Dev, S. *Tetrahedron* **1964**, *20*, 2821.

(20) (a) Stool, A.; Seebeck, E.; Stauffacher, D. *Helv. Chim. Acta* **1957**, *40*, 1205. (b) Theobald, D. W. *Tetrahedron* **1966**, *22*, 2869. (c) Marshall, J. A.; Bundy, D. L.; Fanta, W. I. *J. Org. Chem.* **1968**, *33*, 3913.

Scheme XI



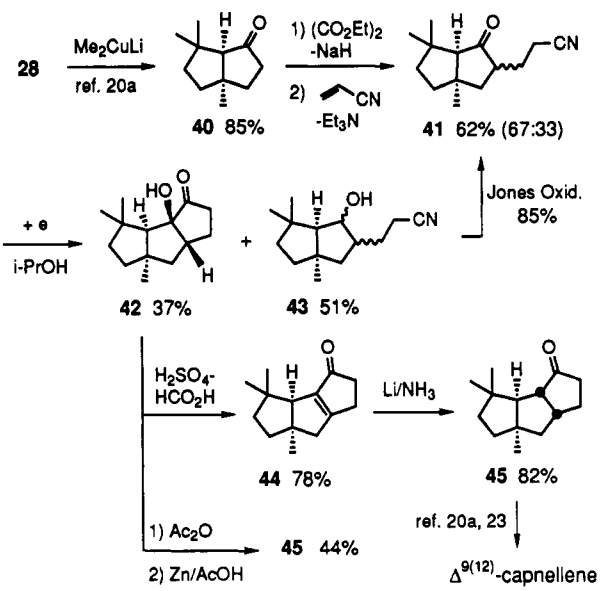
Scheme XII



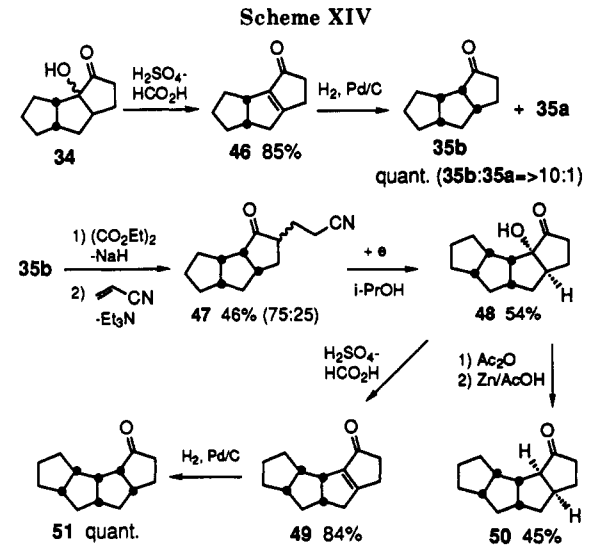
23 to (−)-valeranone is a known procedure.[20c]

Synthesis of Polyquinans. As described above, electroreduction of **1b** effectively gave the bicyclo[3.3.0] type compound **2b**, which was easily converted to α,β-unsaturated ketone **24** and dehydroxy ketone **25** (Scheme X) by dehydration and acetylation followed by reduction with zinc, respectively. The ketone **25** was also obtained by hydrogenation of **24**. This reaction sequence was effective for the synthesis of diquinanes **28** and **32** which are known as precursors for the synthesis of triquinane sesquiterpenes, $\Delta^{9(12)}$-capnellene[21] and hirsutene[22] (Scheme XI). Regioselective cyanoethylation of **25** followed by electroreductive cyclocoupling of the resulting γ-cyano ketones **33** and **37** led to the selective synthesis of linear and angular triquinanes, **34** and **38** (Scheme XII). The stereoconfiguration of each isomer of **34** was confirmed by its transformation to the known compound **36**.[23] Angular triquinane **38** was obtained as a single stereoisomer.

Scheme XIII



Scheme XIV



According to the reaction sequence shown in Scheme XII, $\Delta^{9(12)}$-capnellene was prepared from **28** (Scheme XIII). Electroreduction of γ-cyano ketone **41** (about 2:1 mixture of two diasteromers) gave the cyclized product **42** together with the simply reduced alcohol **43**. The anti isomer of triquinane **42** was preferentially obtained due to the steric hindrance of dimethyl substituents in **41**. The byproduct **43** was easily transformed to the starting material **41** by simple oxidation. Dehydroxylation of **42** was achieved by dehydration followed by reduction of the resultant enone **44**. The dehydroxylation product **45** was also obtained by acetoxylation of **42** and subsequent reduction with zinc, though the yield of **45** was lower than that obtained with the dehydration–reduction method. Transformation of **45** to $\Delta^{9(12)}$-capnellene has already been reported.[21a,24]

(21) (a) Paquette, L. A.; Stevens, K. E. *Can. J. Chem.* **1984**, *62*, 2415. (b) Iyoda, M.; Kushida, T.; Kitami, S.; Oda, M. *J. Chem. Soc., Chem. Commun.* **1987**, 1607.

(22) Cossy, J.; Belotti, T.; Pete, J. P. *Tetrahedron Lett.* **1987**, *28*, 4547.

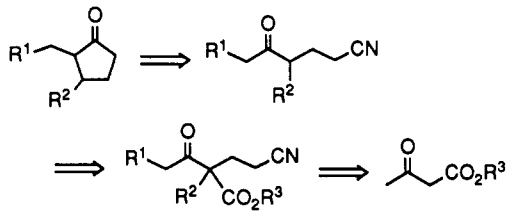
(23) Wu, T.-C.; Houk, K. N. *J. Am. Chem. Soc.* **1985**, *107*, 5308.

Table III. Electroreductive Intermolecular Coupling of Ketones with Nitriles[a]

run	ketone[b]	solvent[c]	% yield[d] 65	66	67
1	cyclohexanone	CH_3CN			90
2		CH_3CN/i-PrOH = 5/1	**65a**, 57	11	25
3		CH_3CN/i-PrOH = 2/1	**65a**, 67	18	8
4		CH_3CN/i-PrOH = 1/3	**65a**, 49	21	2
5		CH_3CN/EtOH = 10/1	**65a**, 65	19	3
6	4-*tert*-butylcyclohexanone	CH_3CN/i-PrOH = 5/1	**65b**, 68	9	15
7	cycloheptanone	CH_3CN/i-PrOH = 5/1	**65c**, 44	24	7
8	cyclopentanone	CH_3CN/EtOH = 10/1	**65d**, 39	14	
9	2-pentanone	CH_3CN/i-PrOH = 5/1	**65e**, 38		21
10	cyclohexanone	CH_3CH_2CN/i-PrOH = 10/1	**65f**, 54	38	2
11		$CH_3CH_2CH_2CN$/i-PrOH = 1/2	**65g**, 29	14	21
12		$(CH_3)_2CHCN$/i-PrOH = 2/1	**65h**, 16	45	10

[a] Electroreduction was carried out using a Sn cathode at constant current of 0.2 A (2.5 F/mol based on ketone) at 5 °C. [b] 5 mmol. [c] 40 mL. [d] Isolated yields.

Scheme XV



Furthermore, linear tetraquinanes could be synthesized from linear triquinanes by the same reaction sequence as above. The ketone **35b** (syn) was stereoselectively obtained from **34** and it was transformed to two types of linear tetraquinanes **50** and **51**, as shown in Scheme XIV.

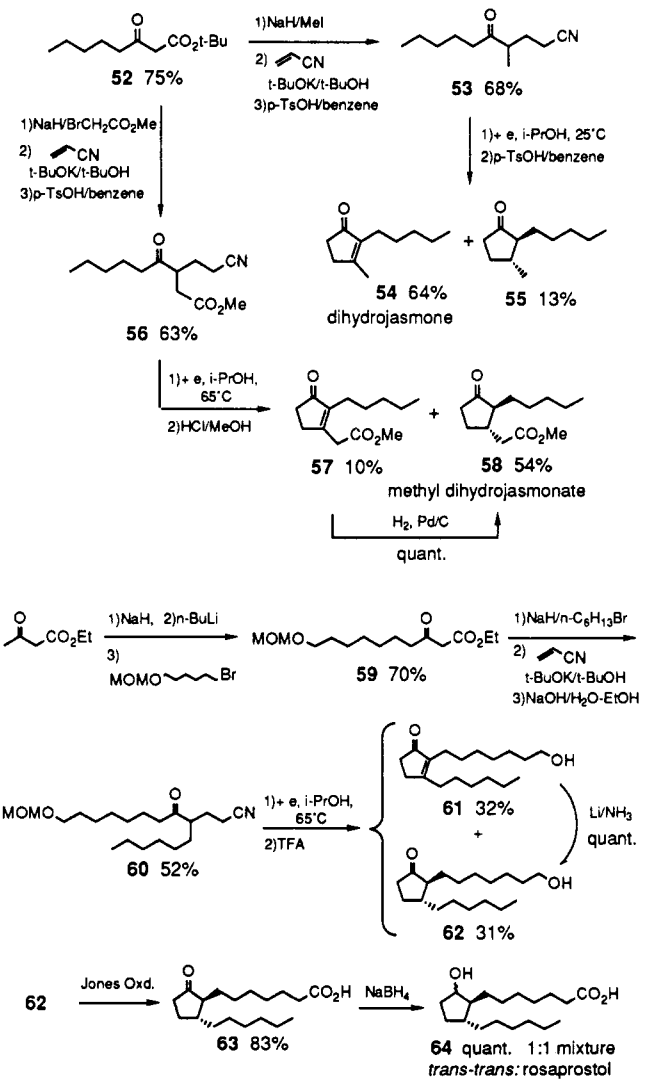
Synthesis of Dihydrojasmone, Methyl Dihydrojasmonate, and Rosaprostol. Since a variety of γ-cyano ketones are easily prepared from alkyl acetoacetates, the electroreductive coupling of γ-cyano ketones is a new and effective synthetic method for the preparation of 2,3-disubstituted cyclopentanones according to the retrosynthesis outlined in Scheme XV. Synthesis of dihydrojasmone (**54**), methyl dihydrojasmonate (**58**), and rosaprostol (**64**)[25] were all achieved according to this methodology (Scheme XVI).

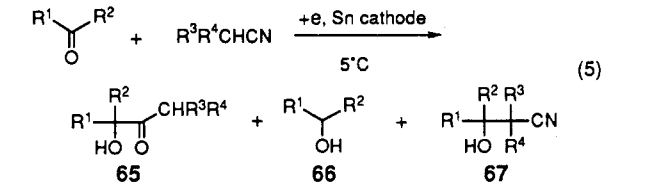
γ-Cyano ketones **53** and **56** were easily prepared from *tert*-butyl acetoacetate. Electroreduction of **53** at 25 °C and subsequent treatment of the product with acid gave dehydrojasmone **54** and a hydrogenated ketone **55**. Methyl dihydrojasmonate (**58**) was obtained by electroreduction of **56** at 65 °C followed by dehydration. The byproduct **57** was easily transformed to **58** quantitatively by hydrogenation.

Similarly, γ-cyano ketone **60** was prepared from ethyl acetoacetate, and electroreduction of **60** gave a mixture of 2,3-disubstituted cyclopentenone **61** and cyclopentanone **62**. Although the ratio of **62** and **61** was about 1:1 even when the electroreduction was carried out at 65 °C, **61** was easily reduced to **62**. Jones oxidation of **62** and subsequent reduction with $NaBH_4$ gave hydroxy carboxylic acid **64** as a 1:1 mixture of two stereoisomers. The trans,trans isomer of **64** is rosaprostol.

Electroreductive Intermolecular Coupling of Ketones with Nitriles. Electroreductive intermolecular coupling of ketones with nitriles was examined under conditions similar to those used in the intramolecular coupling (eq 5). A mixture of the nitrile and either i-PrOH

Scheme XVI

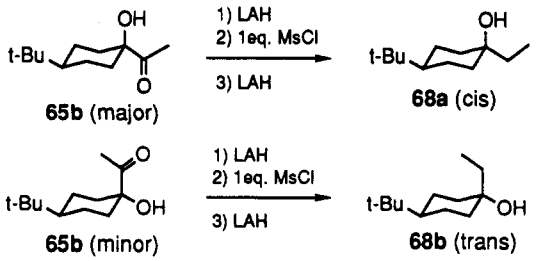




(5)

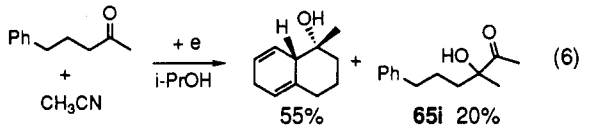
(24) Stille, J. R.; Grubbs, R. H. *J. Am. Chem. Soc.* **1986**, *108*, 855.
(25) A prostaglandin analog possessing antiulcer activity.[26]
(26) (a) Valcavi, U.; Caponi, R.; Brambilla, A.; Parlmira, M.; Minoja, F.; Bernini, F.; Musanti, R.; Fumagalli, R. *Arzneim. Forsch.* **1982**, *32*, 657; *Chem. Abstr.* **1982**, *97*, 85067c. (b) Adami, M.; Scarpignato, C.; Signorini, G.; Coruzzi, G.; Bertaccini, G. *Farmaco, Ed. Prat.* **1984**, *39*, 409; *Chem. Abstr.* **1985**, *102*, 18341w.

Scheme XVII



or EtOH was used as solvent. The results are summarized in Table III. As typified by the reaction of cyclohexanone with acetonitrile (runs 1–5), the ratio of nitrile/alcohol is important to suppress the formation of unexpected byproducts **66** and **67**. Some other ketones and nitriles also gave the corresponding coupling products **65** when appropriate mixtures of nitrile and alcohol were used as the solvent system (runs 6–12). The yields of **65** decreased with increasing bulkiness of the nitriles (runs 3, 10–12).

In contrast to the corresponding intramolecular coupling (eq 4), the intermolecular coupling of γ-phenyl ketone with acetonitrile was slower than the intramolecular coupling of γ-phenyl ketone itself[4] as shown in eq 6.



Electroreduction of 4-*tert*-butylcyclohexanone with acetonitrile gave **65b** as a 65/35 mixture of two diastereomers. The stereoconfiguration of each isomer was determined by its conversion to known compound **68**[27] (Scheme XVII). This result shows that the addition of the intermediate radical to acetonitrile takes place preferentially at the less hindered side (equatorial side) to give cis alcohol **68a**.

Stereoselective Synthesis of a Chiral Ligand for the Enantioselective Addition of Diethylzinc to Aldehydes. Chiral β-amino alcohol **72** was synthesized from (+)-dihydrocarvone and acetonitrile by electroreductive intermolecular coupling (Scheme XVIII). Electroreduction of (+)-dihydrocarvone with acetonitrile gave the corresponding coupling product α-hydroxy ketone as a mixture of stereoisomers. The major isomer (**69**) could be isolated by column chromatography on silica gel in 45% yield. The stereoconfiguration of **69** was assigned after it was found that *tert*-alcohol **70** derived from **69** was consistent with the major product of the reaction of (+)-dihydrocarvone with ethylmagnesium bromide.[28] This result showed that the electroreductive coupling occurs predominantly at the equatorial side of (+)-dihydrocarvone. Conversion of **69** to the *O*-methyloxime and subsequent LAH reduction of the oxime gave β-amino alcohol **71** as a sole product. The compound **71** was converted to oxazoline **73**, and its stereoconfiguration was determined by

Scheme XVIII

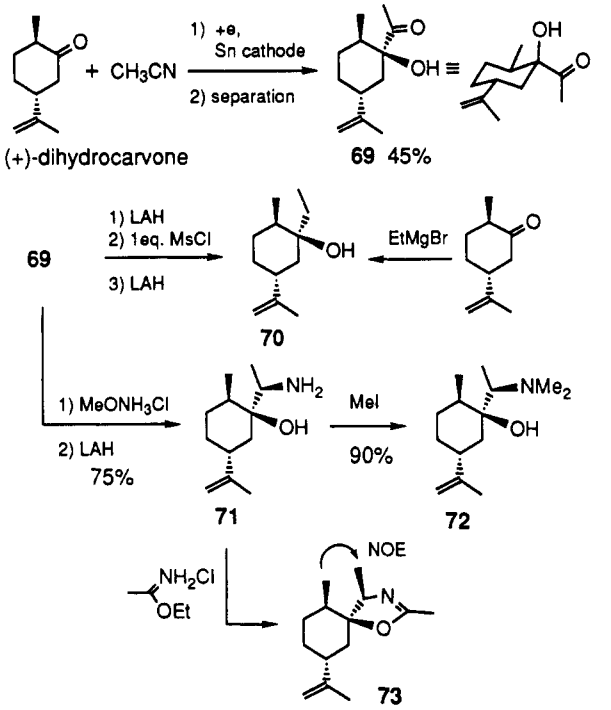


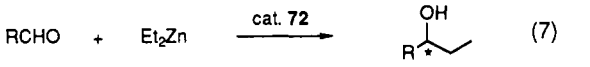
Table IV. Enantioselective Addition of Diethylzinc to Aldehydes

aldehyde	% yield[a]	% ee (config)[b]	$[\alpha]^{25}_D$ (c, solvent)
PhCHO	89	>99[c] (*S*)	−45.4 (4.3, $CHCl_3$)
PhCH=CHCHO	87	82[c] (*S*)	−7.2 (4.1, $CHCl_3$)
n-$C_6H_{13}CHO$	74	80[d] (*S*)	+7.8 (3.8, $CHCl_3$)

[a] Isolated yields. [b] Determined by their optical rotations. Reported values are as follows: $[\alpha]_D$ −45.45 (*c* 5.15, $CHCl_3$) for (*S*)-1-phenylpropanol;[31] $[\alpha]^{23}D$ −6.6 (*c* 3.2, $CHCl_3$) for (*S*)-1-phenylpent-1-en-3-ol in 75% ee;[32] $[\alpha]^{24}_D$ +9.6 (*c* 8.3, $CHCl_3$) for (*S*)-3-nonanol.[33] [c] Determined by ^1H NMR of acetates of alcohols using Eu(hfc)$_3$. [d] Based on the optical rotation.

analysis of the NOE enhancement between two doublets at δ 0.86 and 1.32 in the ^1H NMR spectrum of **73**. N,N-Dimethylation of **71** gave β-*N*,*N*-dimethylamino alcohol **72**.

Chiral β-amino alcohol **72** performed as an effective ligand for the enantioselective addition of diethylzinc to aldehydes[30] (eq 7), and chiral secondary alcohols were



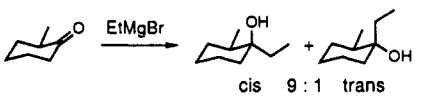
obtained with high enantioselectivity when the reaction was carried out in the presence of a catalytic amount of **72** (Table IV).

Experimental Section

^1H NMR spectra were measured on a Varian EM-390 or a Varian Gemini-200 spectrometer. ^{13}C NMR spectra were measured on a Varian Gemini-200 spectrometer.

(27) Meakins, G. D.; Percy, R. K.; Richards, E. E.; Young, R. N. *J. Chem. Soc. C* **1968**, 1106.

(28) It has been reported that the addition of ethylmagnesium bromide to 2-methylcyclohexanone gave predominantly cis alcohol by equatorial attack.[29]



(29) Ficini, J.; Maujean, A. *Bull. Soc. Chim. Fr.* **1971**, 219.

(30) Recent studies on the enantioselective addition of diethylzinc to aldehydes in the presence of chiral amino alcohols: (a) Oguni, N.; Matsuda, Y.; Kaneko, T. *J. Am. Chem. Soc.* **1988**, *110*, 7877. (b) Kitamura, M.; Okada, S.; Suga, S.; Noyori, R. *Ibid.* **1989**, *111*, 4208. (c) Soai, K.; Niwa, S. *Chem. Lett.* **1989**, 481. (d) Shono, T.; Kise, N.; Shirakawa, E.; Matsumoto, H.; Okazaki, E. *J. Org. Chem.* **1991**, *56*, 3063.

(31) Pickard, R. H.; Kenyon, J. *J. Chem. Soc.* **1914**, 1115.

(32) Sato, T.; Gotoh, Y.; Wakabayashi, Y.; Fujisawa, T. *Tetrahedron Lett.* **1983**, *24*, 4123.

(33) Mukaiyama, T.; Hojo, K. *Chem. Lett.* **1976**, 893.

Starting Materials. Cyclic γ-cyano ketones **1a–d** and **1h–j** were prepared in the usual way by alkylation of the corresponding enamines with acrylonitrile or allyl cyanide.[34] Other cyclic γ-cyano ketones **1g**, **1k**, and **1o** were obtained by the cyanoethylation of the corresponding ketones with acrylonitrile according to known methods.[35] Cyclic δ-cyano ketone **1l** was prepared by the alkylation of 2-(ethoxycarbonyl)cyclohexanone with 4-bromobutyronitrile.[36] Decarbethoxylation of **1l** gave **1f**, and **1e** and **1n** were prepared by the same method. 5-Ketohexanenitrile (**1m**) is commercially available (Tokyo Kasei Kogyo). (+)-Dihydrocarvone (90% purity) was obtained from Aldlich Chemical Co.

General Procedure for Electroreduction of γ- and δ-Cyano Ketones. A solution of Et_4NOTs (10 g) in i-PrOH (40 mL) was put into a divided cell (50-mL beaker) equipped with a Sn cathode (5 × 10 cm^2), a carbon rod anode, and a ceramic diaphragm. To the catholyte was added cyano ketone **1** (5 mmol). The electricity was passed while the cathode potential was controlled at −2.8 V vs SCE or with a constant current of 0.2 A until almost all of the cyano ketone was consumed. The catholyte was poured into water (200 mL) and extracted with Et_2O. The products were isolated by column chromatography on silica gel. The products **2a**,[37] **3a**,[18] **2c**,[37] **3c**,[37] **3d**,[38] **3f**, **2m**,[39] **3m**, **2n**,[39] and **3n** were identified by comparison of their spectroscopic behaviors with those described in the references or with those of authentic samples. The other products were confirmed by spectroscopic and elemental analyses.

2a: R_f 0.2 (hexane–AcOEt, 5:1); ^{13}C NMR ($CDCl_3$) δ 20.67 (2 C, t), 20.94 (t), 24.40 (t), 29.11 (t), 33.15 (t), 40.77 (d), 77.67 (s), 219.94 (s).

2b: R_f 0.4 (hexane–AcOEt, 2:1); IR (neat) 3450 (brd), 1740 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.20–3.00 (m, 12 H); ^{13}C NMR ($CDCl_3$) δ 23.90 (t), 24.30 (t), 31.87 (t), 35.02 (t), 37.14 (t), 48.21 (d), 88.06 (s), 220.21 (s). Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.49; H, 8.61.

***cis*-2c** (major): R_f 0.3 (hexane–AcOEt, 5:1); ^{13}C NMR ($CDCl_3$) δ 21.75 (t), 25.71 (t), 25.74 (t), 30.59 (t), 32.38 (t), 32.52 (t), 34.84 (t), 47.02 (d), 81.04 (s), 221.78 (s).

***trans*-2c** (minor): R_f 0.35 (hexane–AcOEt, 5:1); ^{13}C NMR ($CDCl_3$) δ 23.90 (t), 26.27 (t), 26.32 (t), 26.47 (t), 27.01 (t), 34.67 (t), 36.32 (t), 45.45 (d), 78.11 (s), 219.02 (s).

2d (88:12 mixture of two diastereomers): R_f 0.35 (hexane–AcOEt, 5:1); mp 73–74 °C; IR (KBr) 3450 (br s), 1740 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.00–2.70 (m, 26 H); ^{13}C NMR (major, $CDCl_3$) δ 19.40 (t), 21.71 (t), 22.08 (t), 22.11 (t), 22.39 (t), 24.03 (t), 24.11 (t), 25.23 (t), 25.89 (t), 26.13 (t), 30.84 (t), 36.84 (t), 38.52 (d), 79.10 (s), 218.81 (s); ^{13}C NMR (minor, $CDCl_3$) δ 19.62 (t), 23.02 (t), 23.27 (t), 23.80 (t), 24.06 (t), 24.17 (t), 24.48 (t), 25.35 (t), 25.96 (t), 26.01 (t), 27.16 (t), 32.81 (t), 45.48 (d), 80.89 (s), 219.55 (s). Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 11.00. Found: C, 75.39; H, 10.94.

3d (>95% single stereoisomer): R_f 0.7 (hexane–AcOEt, 5:1); ^{13}C NMR ($CDCl_3$) δ 22.01 (t), 22.40 (t), 22.88 (t), 23.49 (t), 23.51 (t), 23.55 (2 C, t), 24.06 (t), 24.87 (t), 26.97 (t), 30.25 (t), 37.60 (2 C, d and t), 51.61 (d), 222.05 (s).

2e: R_f 0.35 (hexane–AcOEt, 5:1); IR (neat) 3500 (brd), 1710 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.00–2.70 (m, 13 H), 3.93 (s, 1 H, OH); ^{13}C NMR ($CDCl_3$) δ 21.33 (t), 26.11 (t), 30.03 (t), 30.59 (t), 37.18 (t), 37.26 (t), 52.64 (d), 86.44 (s), 214.33 (s). Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.01; H, 9.18.

***cis*-2f** (major): R_f 0.5 (hexane–AcOEt, 5:1); mp 59–60 °C; IR (KBr) 3480 (br s), 1710 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.00–2.70 (m, 15 H), 3.85 (s, 1 H, OH); ^{13}C NMR ($CDCl_3$) δ 20.10 (t), 21.14 (t), 26.01 (t), 26.39 (t), 27.47 (t), 31.39 (t), 37.24 (t), 44.62 (d), 78.05 (s), 214.40 (s). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.26; H, 9.51.

***trans*-2f** (minor): R_f 0.35 (hexane–AcOEt, 5:1); IR (neat) 3450 (br s), 1710 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.00–2.33 (m, 15 H), 2.80–3.25 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 20.84 (t), 25.44 (t), 26.38 (t), 27.10 (t), 27.41 (t), 31.16 (t), 37.46 (t), 46.72 (d), 76.19 (s), 213.43 (s). Anal. Calcd for $C_9H_{14}O_2$: C, 71.39; H, 9.59. Found: C, 71.22; H, 9.49.

2g: R_f 0.3 (hexane–AcOEt, 5:1); IR (neat) 3450 (brd), 1745 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.91 (s, 3 H), 1.00–2.50 (m, 13 H); ^{13}C NMR ($CDCl_3$) δ 20.51 (t), 20.99 (t), 22.09 (q), 27.57 (t), 30.27 (t), 30.92 (t), 32.68 (t), 40.27 (s), 80.21 (s), 220.44 (s). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.33; H, 9.51.

3g (>95% single stereoisomer): R_f 0.6 (hexane–AcOEt, 5:1); IR (neat) 1740 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.18 (s, 3 H), 1.00–2.50 (m, 13 H); ^{13}C NMR ($CDCl_3$) δ 20.75 (t), 21.39 (t), 22.59 (t), 25.68 (q), 33.50 (t), 34.12 (t), 34.93 (t), 38.20 (s), 55.78 (d), 221.37 (s). Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.78; H, 10.54.

2h (>95% single stereoisomer): R_f 0.25 (hexane–AcOEt, 5:1); IR (neat) 3450 (br s), 1740 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.18 (s, 3 H), 0.65–2.70 (m, 13 H); ^{13}C NMR ($CDCl_3$) δ 14.43 (q), 22.26 (t), 23.14 (t), 28.48 (t), 30.82 (t), 34.39 (t), 37.62 (d), 43.58 (d), 79.32 (s), 218.66 (s). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.35; H, 9.60.

3h (80:20 mixture of two diastereomers): R_f 0.6 (hexane–AcOEt, 5:1); IR (neat) 1740 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.60–2.50 (m, 16 H); ^{13}C NMR (major, $CDCl_3$) δ 19.09 (q), 25.72 (t), 26.95 (t), 32.34 (t), 32.81 (d), 35.98 (t), 37.15 (t), 42.94 (d), 60.22 (d), 218.69 (s); ^{13}C NMR (minor, $CDCl_3$) δ 18.58 (q), 25.24 (t), 25.50 (t), 27.94 (t), 30.31 (t), 32.22 (d), 35.65 (t), 38.16 (d), 54.47 (d), 219.68 (s). Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.75; H, 10.64.

2i (90:10 mixture of two diastereomers): R_f 0.3 (hexane–AcOEt, 5:1); IR (neat) 3450 (br s), 1740 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.83 (s, 0.81 H), 0.87 (s, 0.09 H), 1.00–2.60 (m, 13 H); ^{13}C NMR (major, $CDCl_3$) δ 24.14 (t), 24.63 (t), 27.47 (3 C, q), 30.54 (t), 30.84 (t), 32.18 (s), 32.60 (t), 43.26 (d), 46.17 (d), 77.78 (s), 217.74 (s); ^{13}C NMR (minor, $CDCl_3$) δ 21.14 (t), 21.38 (t), 24.76 (t), 27.43 (3 C, q), 30.18 (t), 32.32 (t), 33.50 (s), 41.49 (d), 41.56 (d), 77.67 (s), 220.79 (s). Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.11; H, 10.62.

3i (50:50 mixture of two diastereomers): R_f 0.65 (hexane–AcOEt, 5:1); IR (neat) 1745 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.81 (s, 0.45 H), 0.88 (s, 0.45 H), 0.60–2.55 (m, 13 H); ^{13}C NMR ($CDCl_3$) δ 22.87 (t), 23.49 (t), 24.33 (t), 25.83 (t), 26.34 (t), 27.04 (q), 27.35 (t), 27.42 (q), 29.79 (t), 31.98 (s), 32.12 (s), 33.18 (t), 34.05 (t), 37.00 (d), 37.15 (t), 43.41 (d), 46.39 (d), 47.70 (d), 49.42 (d), 55.53 (d), 218.33 (s), 220.19 (s). Anal. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.36; H, 11.45.

2j (75:25 mixture of two diastereomers): R_f 0.2 (hexane–AcOEt, 5:1); IR (neat) 3450 (br s), 1745 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.03 (d, 0.75 H, J = 7.0 Hz), 1.10 (d, 2.25 H, J = 6.0 Hz), 0.80–2.90 (m, 13 H); ^{13}C NMR (major, $CDCl_3$) δ 18.62 (q), 19.93 (2 C, t), 20.31 (t), 26.63 (d), 29.35 (t), 41.99 (t), 48.06 (d), 78.35 (s), 220.07 (s); ^{13} NMR (minor, $CDCl_3$) δ 14.73 (q), 22.98 (t), 23.09 (t), 23.72 (t), 28.30 (d), 30.16 (t), 40.32 (t), 46.34 (d), 79.18 (s), 217.27 (s). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.27; H, 9.62.

3j (mixture of diastereomers): R_f 0.6 (hexane–AcOEt, 5:1); IR (neat) 1740 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.80–2.70 (m, 16 H). Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.81; H, 10.64.

2k: R_f 0.2 (hexane–AcOEt, 5:1); IR (neat) 3480 (br s), 1750 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.28 (t, 3 H, J = 7.0 Hz), 1.0–2.70 (m, 12 H), 3.30 (br s, 1 H, OH), 4.23 (q, 2 H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 13.90 (q), 20.31 (t), 20.93 (t), 24.75 (t), 27.34 (t), 30.53 (t), 31.40 (t), 51.45 (s), 60.97 (t), 79.18 (s), 175.55 (s), 215.84 (s). Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.55; H, 7.93.

3k (>95% single stereoisomer): R_f 0.45 (hexane–AcOEt, 5:1); IR (neat) 1740, 1730 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.30 (t, 3 H, J = 7.0 Hz), 0.70–2.50 (m, 12 H), 2.63–2.83 (m, 1 H), 4.22 (q, 2 H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 13.93 (q), 21.20 (t), 21.89 (t), 22.32 (t), 29.97 (t), 30.03 (t), 34.41 (t), 49.30 (s), 51.92 (d), 60.75 (t), 175.95 (s), 217.57 (s). Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.46; H, 8.65.

***cis*-2l** (major): R_f 0.6 (hexane–AcOEt, 2:1); IR (neat) 3500 (br s), 1730 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.22 (t, 3 H, J = 7.0 Hz), 1.00–2.70 (m, 15 H), 4.13 (q, 2 H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 13.38 (q), 19.79 (t), 20.04 (t), 21.02 (t), 28.33 (t), 28.52

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(t), 32.88 (t), 35.14 (t), 53.42 (s), 60.19 (t), 77.22 (s), 174.60 (s), 212.30 (s). Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 65.01; H, 8.38.

***trans*-2l** (minor): R_f 0.5 (hexane–AcOEt, 2:1); IR (neat) 3480 br s), 1730 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.23 (t, 3 H, J = 7.0 Hz), 1.00–3.10 (m, 15 H), 4.17 (q, 2 H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 13.71 (q), 20.00 (t), 20.98 (t), 22.57 (t), 27.81 (t), 29.50 (t), 29.75 (t), 35.33 (t), 55.05 (s), 60.48 (t), 74.43 (s), 174.69 (s), 209.15 (s). Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.90; H, 8.41.

2o (67:33 mixture of two diastereomers): R_f 0.45 (hexane–AcOEt, 2:1); IR (neat) 3450 (br s), 1740, 1725 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.20 (s, 2 H), 1.21 (s, 1 H), 1.23 (s, 1 H), 1.24 (t, 2 H, J = 7.2 Hz), 1.30 (t, 1 H, J = 7.2 Hz), 1.33 (s, 2 H), 1.65 (br s, 2 H, OH), 1.70–2.00 (m, 1 H), 2.22–2.60 (m, 3 H), 3.00 (br s, 1 H, OH), 4.15 (q, 1.33 H, J = 7.2 Hz), 4.23 (q, 0.67 H, J = 7.2 Hz); ^{13}C NMR (major, $CDCl_3$) δ 13.49 (q), 17.12 (q), 18.80 (q), 28.63 (t), 31.36 (t), 51.81 (s), 60.76 (t), 80.49 (s), 175.17 (s), 217.53 (s); ^{13}C NMR (minor, $CDCl_3$) δ 13.67 (q), 17.35 (q), 19.21 (q), 27.25 (t), 30.81 (t), 52.03 (s), 60.65 (t), 79.55 (s), 174.69 (s), 216.73 (s). Anal. Calcd for $C_9H_{14}O_2$: C, 59.98; H, 8.05. Found: C, 59.87; H, 8.01.

3o (>95% single stereoisomer): R_f 0.45 (hexane–AcOEt, 5:1); IR (neat) 1740, 1725 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.03 (d, 3 H, J = 7.0 Hz), 1.12 (s, 3 H), 1.29 (t, 3 H, J = 7.1 Hz), 1.93–2.10 (m, 1 H), 2.15–2.50 (m, 3 H), 2.69 (q, 1 H, J = 7.0 Hz), 4.20 (q, 2 H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 8.53 (q), 13.93 (q), 16.80 (q), 31.40 (t), 34.35 (t), 48.94 (s), 51.82 (d), 60.88 (t), 176.40 (s), 218.19 (s). Anal. Calcd for $C_9H_{14}O_2$: C, 65.19; H, 8.75. Found: C, 65.10; H, 8.69.

2p: R_f 0.3 (hexane–AcOEt, 2:1); IR (neat) 3400, 1740, 1600, 730, 695 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.50–2.10 (m, 9 H), 2.30 (t, 2 H, J = 7.2 Hz), 2.63 (t, 2 H, J = 7.5 Hz), 7.10–7.35 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 16.76 (t), 24.30 (t), 34.41 (t), 34.63 (t, 2 C), 35.58 (t), 78.57 (s), 125.74 (d), 128.28 (d, 4 C), 141.82 (s), 220.04 (s). Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.96; H, 8.43.

3p: R_f 0.5 (hexane–AcOEt, 5:1); IR (neat) 1730, 740, 695 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.00–2.40 (m, 11 H), 2.50–2.70 (m, 2 H), 7.10–7.35 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 20.51 (t), 29.28 (t, 2 C), 35.79 (t), 35.94 (t), 37.97 (t), 48.90 (d), 125.82 (d), 128.32 (d, 2 C), 128.46 (d, 2 C), 142.37 (s), 221.71 (s). Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 83.10; H, 9.05.

Transformation of 2a, 2b, 2e, 2g, and 2i to 4a, 4b, 4e, 4g, and 5. A mixture of an α-hydroxy ketone (1 mmol) and LAH (1 mmol) in THF (5 mL) was stirred for 1 h at room temperature. The obtained diol was treated with MsCl (1.2 mmol) and Et_3N (1.2 mmol) in CH_2Cl_2 (5 mL) at 0 °C for 2 h. The crude monomesylate was reduced with LAH (1 mmol) in refluxing THF (5 mL) for 6 h. The products **4a**, **4b**, **4e**, **4g**, and **5** were purified by column chromatography on neutral Al_2O_3 (activity III), and the ^{13}C NMR spectra of these compounds were compared with reported data[13] or with those of authentic samples.[27]

Transformation of 2c, 2f, 2k, and 2l to 4c, 4f, 4g, and 4l. A mixture of an α-hydroxy ketone (1 mmol) and LAH (1 or 2 mmol) in THF (5 mL) was stirred for 2 h at room temperature. The obtained diol or triol was treated with MsCl (1.2 or 2.2 mmol) and DMAP (cat.) in pyridine (5 mL) at room temperature for 6 h. The crude mono- or dimesylate was reduced with $LiEt_3BH$ (3 or 4 mL of a 1.0 M THF solution) in refluxing THF (5 mL) for 6 h. The products **4c**, **4f**, **4g**, and **4l** were purified by column chromatography on neutral Al_2O_3 (activity III), and their ^{13}C NMR spectra were compared with reported data.[13]

Dehydration of 2a, 2c, and 2d. A solution of α-hydroxy ketone (2 mmol) was refluxed in benzene (5 mL) with continuous removal of water using a Dean–Stark apparatus. The addition of catalytic amounts of *p*-TsOH accelerated the dehydration (**2a**, 10 min; **2c**, 30 min; **2d**, 2 h). After evaporation of benzene, α,β-unsaturated ketone **10** was isolated by column chromatography on silica gel. The products **10a**,[40] **10c**,[37] and **10d**[38] were identified by comparison with authentic samples.

Synthesis of 12. β-Keto ester **11** was prepared from carvone by the reported method.[19] A solution of **11** (20 mmol), allyl cyanide (24 mmol), and t-BuOK (1 mmol) was refluxed in t-BuOH (30 mL) for 24 h. The crude product was heated with $LiI{\cdot}2H_2O$ (20 mmol) under reflux in collidine (20 mL) for 8 h. γ-Cyano ketone **12** was isolated as a mixture of diastereomers by distillation (68% yield).

12 (mixture of diastereomers): bp 130–133 °C (2 mmHg); R_f 0.25 (hexane–AcOEt, 10:1); IR (neat) 2250, 1710, 1645, 890 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.90–3.00 (m, 21 H), 4.67 (br s, 2 H). Anal. Calcd for $C_{15}H_{23}ON$: C, 77.20; H, 9.94; N, 6.00. Found: C, 77.01; H, 9.98; N, 5.87.

Electroreduction of 12 was carried out at 25 °C according to the method described above (−2.8 V vs SCE, 6 F/mol). The products **13** (58%) and **14** (17%) were isolated by column chromatography on silica gel.

13 (mixture of diastereomers): R_f 0.2–0.25 (hexane–AcOEt, 10:1); IR (neat) 3500 (br d), 1740, 1645, 890 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.60–3.00 (m, 22 H), 4.67 (br s, 2 H). Anal. Calcd for $C_{15}H_{24}O_2$: C, 76.22; H, 10.24. Found: C, 76.09; H, 10.25.

14 (mixture of diastereomers): R_f 0.5 (hexane–AcOEt, 10:1); IR (neat) 1740, 1645, 890 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.60–3.00 (m, 22 H), 4.67 (br s, 2 H). Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.58; H, 10.93.

Synthesis of 15. Dehydration of **13** (5 mmol) under reflux in benzene (10 mL) in the presence of catalytic amounts of *p*-TsOH for 2 h gave α,β-unsaturated ketone which was reduced with LAH (2.5 mmol) in THF (10 mL) at room temperature for 1 h. The product **15** was isolated by column chromatography on silica gel (83% yield).

15 (mixture of diastereomers): R_f 0.25–0.3 (hexane–AcOEt, 10:1); IR (neat) 3350 (br s), 1650, 895 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.70–2.80 (m, 24 H), 4.67 (br s, 2 H). Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.48; H, 11.09.

Synthesis of Guaiazulene 16. Dehydration of **15** (2 mmol) was carried out under the same conditions as described above (30 min). The crude triene was heated with excess amounts of sulfur (20 mmol) under reflux in decalin (5 mL) for 2 h. The product **16** was isolated by column chromatography on Al_2O_3 (activity I) in 35% yield and identified by comparison with authentic guaiazulene.

Synthesis of 17. To a solution of (+)-dihydrocarvone (30 mmol) and t-BuOK (3 mmol) in t-BuOH (30 mL) was added methyl acrylate (30 mmol) slowly at 0 °C, and the mixture was stirred at 0 °C for 2 h. After the usual workup, the product **17** was isolated by distillation (76% yield).

17 (86:14 mixture of two diastereomers): bp 138–140 °C (4 mmHg); ^1H NMR (200 MHz, $CDCl_3$) δ 1.03 (s, 2.57 H), 1.15 (s, 0.43 H), 1.75 (s, 3 H), 1.50–2.54 (m, 11 H), 3.67 (s, 3 H), 4.73 (s, 1 H), 4.79 (t, 1 H, J = 2 Hz).

Synthesis of 19. Ketalization of **17** (10 mmol) was carried out by refluxing with ethylene glycol (12 mmol) in benzene (10 mL) in the presence of catalytic amounts of *p*-TsOH with continuous removal of water using a Dean–Stark apparatus. LAH reduction of the obtained ketal and subsequent mesylation were carried out according to the same method used in the transformation of **2** to **4**. The mesylate was heated with NaCN (10 mmol) in DMF (10 mL) at 0 °C for 6 h. The major isomer **18** was isolated by column chromatography on silica gel (65% yield from **17**).

18: R_f 0.4 (hexane–AcOEt, 5:1); IR (neat) 2240, 1640, 885 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.86 (s, 3 H), 1.15–1.40 (m, 2 H), 1.48–1.68 (m, 8 H), 1.72 (s, 3 H), 2.14–2.38 (m, 3 H), 3.87–4.10 (m, 4 H), 4.70 (s, 2 H).

A solution of **18** (5 mmol) in 1 N HCl (5 mL) and THF (5 mL) was stirred at 60 °C for 1 h. The product **19** was isolated by column chromatography on silica gel (96% yield).

19: R_f 0.3 (hexane–AcOEt, 2:1); $[\alpha]^{20}_D$ +105 (*c* 2.5, $CHCl_3$); IR (neat) 2245, 1700, 1640, 890 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.06 (s, 3 H), 1.20–2.00 (m, 9 H), 1.75 (s, 3 H), 2.35 (t, 2 H, J = 6.5 Hz), 2.35–2.50 (m, 2 H), 4.72 (s, 1 H), 4.80 (t, 1 H, J = 1 Hz); ^{13}C NMR ($CDCl_3$) δ 17.20 (t), 19.75 (t). 20.30 (q), 21.82 (q), 25.38 (t), 35.91 (t), 37.55 (t), 43.04 (t), 45.59 (d), 47.36 (s), 110.08 (t), 119.25 (s), 147.17 (s), 214.58 (s). Anal. Calcd for $C_{14}H_{21}O$: C, 76.66; H, 9.65; N, 6.39. Found: C, 76.56; H, 9.60; N, 6.33.

Electroreduction of 19 was carried out at 25 °C according to the method described above (0.1 A, 6 F/mol). The products **20** (54%) and **21** (22%) were isolated by column chromatography on silica gel.

(40) Johnson, W. S.; Davis, C. E.; Hunt, R. H.; Stork, G. *J. Am. Chem. Soc.* **1948**, *70*, 3021.

20: R_f 0.7 (hexane–AcOEt, 5:1); $[\alpha]^{20}_D$ −48 (*c* 2.8, $CHCl_3$); IR (neat) 3470, 1700, 1640, 880 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.83 (s, 3 H), 1.17–1.30 (m, 1 H), 1.37–1.50 (m, 2 H), 1.60–1.88 (m, 3 H), 1.74 (s, 3 H), 1.88–2.05 (m, 3 H), 2.25–2.50 (m, 3 H), 2.57–2.75 (m, 1 H), 3.89 (s, 1 H, OH), 4.73 (br s, 2 H); ^{13}C NMR ($CDCl_3$) δ 20.88 (q), 21.71 (t and q, 2 C), 25.89 (t), 32.01 (t), 35.43 (t), 36.12 (t), 37.84 (t), 39.00 (d), 41.21 (s), 80.64 (s), 108.67 (t), 149.57 (s), 215.20 (s). Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.55; H, 9.94.

21 (88:12 mixture of two diastereomers): R_f 0.35 (hexane–AcOEt, 2:1); IR (neat) 3450 (br s), 2250, 1640, 885 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.95 (s, 0.36 H), 1.01 (s, 2.64 H), 1.05–1.83 (m, 11 H), 1.73 (s, 3 H), 1.92–2.10 (m, 1 H), 2.36 (t, 2 H, J = 6.5 Hz), 3.38–3.50 (m, 0.88 H), 3.55–3.61 (m, 0.12 H), 4.71 (s, 2 H).

Oxidation of 21 to 19. To a solution of **21** (2 mmol) in acetone (5 mL) was added Jones' reagent (25 mmol) at 0 °C for 10 min. After the usual workup, **19** was isolated by column chromatography on silica gel (80% yield).

Synthesis of 23. A solution of **20** (3 mmol) in AcOEt (5 mL) was stirred under H_2 (1 atm) in the presence of catalytic amounts of Pd/C at room temperature for 1 h. The crude product was treated with *p*-TsOH (cat.) and acetic anhydride (3 mL) at room temperature for 30 min. The acetate was isolated by column chromatography on silica gel (83% yield).

22: R_f 0.25 (hexane–AcOEt, 10:1); IR (neat) 1740, 1720 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.87 (d, 6 H, J = 6.6 Hz), 0.88 (s, 3 H), 1.10–1.30 (m, 2 H), 1.30–2.00 (m, 8 H), 2.12 (s, 3 H), 2.27–2.45 (m, 2 H), 2.60–2.78 (m, 1 H), 2.90–3.00 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 19.24 (q), 19.38 (q), 21.40 (q, 2 C), 22.43 (t), 23.82 (t), 30.12 (t), 31.82 (t), 31.94 (d), 35.14 (t), 37.95 (d and t, 2 C), 42.57 (s), 90.83 (s), 169.63 (s), 206.21 (s). Anal. Calcd for $C_{16}H_{26}O_3$: C, 72.14; H, 9.84. Found: C, 72.01; H, 9.78.

To a solution of Ca (5 mmol) of liquid NH_3 (10 mL) was added a solution of **22** (2 mmol) in Et_2O (2 mL), and the mixture was stirred for 15 min. After the usual workup, the product **23** was isolated by column chromatography on silica gel (74% yield).

23: R_f 0.5 (hexane–AcOEt, 10:1); $[\alpha]^{20}_D$ −76 (*c* 0.7, $CHCl_3$), (lit.[20b] $[\alpha]^{20}_D$ +76 for enantiomer); IR (neat) 1705 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.86 (d, 3 H, J = 6.8 Hz), 0.87 (d, 3 H, J = 6.8 Hz), 0.89 (s, 3 H), 0.95–1.64 (m, 5 H), 1.78–2.22 (m, 9 H), 2.37–2.56 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 19.55 (q), 19.60 (q), 21.64 (t), 24.66 (t), 27.75 (q), 28.41 (t), 30.16 (t), 32.52 (d), 36.01 (s), 36.59 (t), 39.68 (t), 43.38 (d), 59.53 (d), 216.76 (s). Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.69; H, 11.58.

Dehydration of 2a, 27, 30, 34, 42, and 48. A solution of **2a** (2 mmol) in HCO_2H (5 mL) containing three drops of H_2SO_4 was refluxed for 15 min. After addition of water (20 mL), the mixture was extracted with ether. The product **24**[41] was isolated by column chromatography on silica gel. The other α-hydroxy ketones **27**, **30**, **34**, **42**, and **48** were dehydrated by the same method.

31: R_f 0.25 (hexane–AcOEt, 5:1); IR (neat) 1690, 1640 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.18 (s, 6 H), 2.18–2.23 (m, 2 H), 2.35–2.40 (m, 2 H), 2.47–2.57 (m, 2 H), 2.67–2.73 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 25.68 (t), 29.72 (q, 2 C), 39.44 (t), 39.95 (t), 44.53 (s), 47.07 (t), 146.91 (s), 185.49 (s), 204.85 (s). Anal. Calcd for $C_{10}H_{14}O$: C, 79.96; H, 9.36. Found: C, 80.02; H, 9.38.

44: R_f 0.4 (hexane–AcOEt, 5:1); IR (neat) 1690, 1635 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.84 (s, 3 H), 1.13 (s, 3 H), 1.22 (s, 3 H), 1.40–1.50 (m, 2 H), 1.63–1.72 (m, 2 H), 2.32 (t, 2 H, J = 2.4 Hz), 2.41–2.56 (m, 3 H), 2.69 (t, 2 H, J = 4.5 Hz); ^{13}C NMR ($CDCl_3$) δ 25.54 (q), 25.64 (t), 29.58 (q), 30.09 (q), 39.77 (t), 40.42 (t), 41.34 (t), 42.17 (s), 48.06 (t), 57.24 (s), 62.39 (d), 148.92 (s), 185.17 (s), 206.11 (s). Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.37, H, 9.91.

46: R_f 0.25 (hexane–AcOEt, 5:1); IR (neat) 1685, 1635 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.20–1.90 (m, 7 H), 2.08–2.24 (m, 1 H), 2.28–2.88 (m, 4 H), 3.10–3.25 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 25.03 (t), 25.36 (t), 30.01 (t), 34.85 (t), 39.37 (t), 40.79 (t), 42.56 (d), 46.83 (d), 150.48 (s), 186.34 (s), 204.18 (s). Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.41; H, 8.66.

49: R_f 0.3 (hexane–AcOEt, 5:1); IR (neat) 1685, 1625 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.84–1.09 (m, 1 H), 1.00–1.84 (m, 7 H), 1.97–2.12 (m, 1 H), 2.17–2.33 (m, 1 H), 2.33–2.90 (m, 6 H), 3.07–3.40 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 25.57 (t), 26.23 (t), 28.63 (t), 30.01 (t), 37.80 (t), 40.74 (t, 2 C), 46.32 (d, 2 C), 46.57 (d), 50.10 (d), 149.65 (s), 186.38 (s), 201.75 (s). Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 83.02; H, 8.92.

Dehydroxylation of 2a, 34, 38, 42, and 48. Acetoxylation of **2a** (2 mmol) was carried out by stirring a solution of **2a** in acetic anhydride (5 mL) containing catalytic amounts of *p*-TsOH at room temperature for 30 min. The obtained crude acetate was treated with zinc powder (0.65 g, 10 mmol) in acetic acid (6 mL) and concd HCl (2 mL) at 80 °C for 1 h. The product **25**[41,42] was isolated by column chromatography on silica gel. The other α-hydroxy ketones, **34**, **38**, **42**, and **48**, were dehydroxylated by the same method.

35a: R_f 0.4 (hexane–AcOEt, 10:1); IR (neat) 1740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.20–2.92 (m, 16 H); ^{13}C NMR ($CDCl_3$) δ 24.35 (t), 26.41 (t), 33.40 (t), 34.67 (t), 36.27 (t), 38.29 (t), 41.80 (d), 44.02 (d), 46.95 (d), 61.22 (d), 223.31 (s). Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.35; H, 9.88.

35b: R_f 0.4 (hexane–AcOEt, 10:1); IR (neat) 1740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.01–2.95 (m, 16 H); ^{13}C NMR ($CDCl_3$) δ 24.63 (t), 26.70 (t), 28.12 (t), 31.36 (t), 37.76 (t), 39.15 (t), 44.36 (d), 46.37 (d), 47.56 (d), 54.76 (d), 223.20 (s). Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.38; H, 9.91.

39: R_f 0.5 (hexane–AcOEt, 10:1); IR (neat) 1740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.23–2.49 (m, 16 H); ^{13}C NMR ($CDCl_3$) δ 26.66 (t), 30.45 (t), 34.05 (t), 34.31 (t), 34.78 (t), 39.40 (t), 40.75 (t), 51.27 (d), 59.01 (s), 60.29 (d), 223.99 (s). Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.40; H, 9.77.

50: R_f 0.7 (hexane–AcOEt, 5:1); IR (neat) 1730 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.80–0.98 (m, 1 H), 1.20–1.95 (m, 11 H), 1.95–3.00 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 24.66 (t), 26.58 (t), 29.21 (t), 31.07 (t), 36.27 (t, 2 C), 38.97 (t), 41.73 (d), 46.38 (d), 47.68 (d), 48.54 (d), 50.39 (d), 55.60 (d), 224.12 (s). Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.37; H, 9.86.

Hydrogenation of 24, 31, 46, and 49. Hydrogenation of **24** (2 mmol) was carried out in EtOH (10 mL) in the presence of 5% Pd/C catalyst under H_2 (1 atm) at room temperature for 1 h. The product **25** was isolated by column chromatography on silica gel. The other α,β-unsaturated ketones **31**, **46**, and **49** were hydrogenated by the same method.

51: R_f 0.7 (hexane–AcOEt, 5:1); IR (neat) 1730 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.98–3.08 (m, 20 H); ^{13}C NMR ($CDCl_3$) δ 25.28 (t), 25.50 (t), 29.55 (t), 30.33 (t), 36.31 (t), 39.02 (t), 42.64 (t), 44.86 (d), 47.41 (d), 49.30 (t), 49.77 (t), 52.15 (t), 53.66 (t), 224.18 (s). Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.22; H, 9.81.

Synthesis of 26, 29, 33, 41, and 47. A suspension of 2,2-dimethylcyclopentanone[43] (50 mmol), diethyl oxalate (60 mmol), and NaH (60 mmol) in benzene (50 mL) was stirred at room temperature for 12 h. To the solution was added 1 N HCl (50 mL), and the mixture was extracted with ether. The crude keto ester was treated with acrylonitrile (60 mmol) in a mixed solvent of Et_3N (15 mL), EtOH (20 mL), and H_2O (20 mL) at room temperature for 5 days. The mixture was diluted with water (100 mL) and extracted with ether. The product **26** was isolated by distillation. The other γ-cyano ketones, **29**, **33**, **41**, and **47**, were prepared by the same method from 3,3-dimethylcyclopentanone,[44] **25**, **40**,[21a] and **35b**, respectively.

26: bp 115 °C (5 mmHg); IR (neat) 2250, 1730 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.99 (s, 3 H), 1.20 (s, 3 H), 1.45–2.68 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 15.24 (t), 23.71 (q), 24.44 (q), 25.39 (t), 26.19 (t), 36.05 (t), 45.00 (s), 46.83 (d), 119.47 (s), 223.43 (s). Anal. Calcd for $C_{10}H_{15}ON$: C, 72.69; H, 9.15; N, 8.48. Found: C, 72.78; H, 9.22; N, 8.37.

29: bp 124 °C (5 mmHg); IR (neat) 2250, 1725 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.10 (s, 3 H), 1.20 (s, 3 H), 1.39–2.57 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 15.38 (t), 26.20 (t), 27.67 (q), 29.54 (q), 33.98 (s), 43.41 (t), 46.39 (d), 52.73 (t), 119.44 (s), 219.86 (s). Anal. Calcd for $C_{10}H_{15}ON$: C, 72.69; H, 9.15; N, 8.48. Found: C, 72.75; H, 9.26; N, 8.40.

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33 (50:50 mixture of two diastereomers): R_f 0.3 (hexane–AcOEt, 5:1); IR (neat) 2250, 1730 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.85–2.88 (m, 15 H); ^{13}C NMR ($CDCl_3$) δ 14.77 (t), 24.33 (t), 25.31 (t), 26.74 (t), 28.34 (t), 30.78 (t), 32.34 (t), 32.99 (t), 33.23 (t), 33.32 (t), 37.15 (d), 37.96 (d), 44.68 (d), 48.28 (d), 50.75 (d), 51.82 (d), 119.26 (s), 119.36 (s), 220.21 (s), 222.81 (s). Anal. Calcd for $C_{11}H_{15}ON$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.68; H, 8.66; N, 7.78.

41 (67:33 mixture of two diastereomers): R_f 0.35 (hexane–AcOEt, 5:1); IR 2250, 1730 (neat) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.93 (s, 2 H), 0.95 (s, 1 H), 1.13 (s, 2 H), 1.16 (s, 1 H), 1.25 (s, 3 H), 1.42–1.94 (m, 7 H), 1.99–2.24 (m, 2 H), 2.35–2.60 (m, 3 H); ^{13}C NMR (major, $CDCl_3$) δ 15.03 (t), 24.80 (t), 25.61 (q), 28.14 (q), 31.02 (q), 38.89 (t), 41.71 (t), 41.95 (t), 43.84 (s), 46.50 (s), 47.81 (d), 69.16 (d), 119.34 (s), 220.44 (s). Anal. Calcd for $C_{14}H_{21}ON$: C, 76.67; H, 9.65; N, 6.39. Found: C, 76.73; H, 9.71; N, 6.30.

47 (75:25 mixture of two diastereomers): R_f 0.3 (hexane–AcOEt, 5:1) IR (neat) 2250, 1720 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.88–1.90 (m, 10 H), 2.00–3.00 (m, 9 H); ^{13}C NMR (major, $CDCl_3$) δ 14.88 (t), 25.10 (t), 26.34 (t), 27.61 (t), 30.19 (t), 30.52 (t), 39.25 (t), 41.43 (d), 45.00 (d), 46.25 (d), 47.59 (d), 54.62 (d), 119.33 (s), 221.49 (s). Anal. Calcd for $C_{14}H_{19}ON$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.56; H, 8.90; N, 6.32.

Synthesis of 37. A solution of **25** (20 mmol) and pyrrolidine (22 mmol) in benzene (50 mL) was refluxed for 8 h with continuous removal of water. After evaporation of benzene, the crude enamine was treated with acrylonitrile (22 mmol) in dioxane (50 mL) under reflux for 10 h. After the usual workup, the product **37** was isolated by column chromatography on silica gel (63% yield).

37: R_f 0.25 (hexane–AcOEt, 5:1); IR (neat) 2250, 1725 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.47–2.58 (m, 15 H); ^{13}C NMR ($CDCl_3$) δ 12.86 (t), 24.66 (t), 24.84 (t), 31.14 (t), 32.88 (t), 35.43 (t), 37.22 (t), 45.99 (d), 58.58 (s), 119.62 (s), 222.91 (s). Anal. Calcd for $C_{11}H_{15}ON$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.61, H, 8.58; N, 7.87.

Electroreduction of 26, 29, 33, 37, 41, and 47 was carried out by the same method as described above (–2.8 V vs SCE). The products were isolated by column chromatography on silica gel.

27: R_f 0.3 (hexane–AcOEt, 5:1); IR (neat) 3440, 1720 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.92 (s, 3 H), 1.04 (s, 3 H), 1.59–2.48 (m, 9 H), 2.69 (br s, 1 H, OH); ^{13}C NMR ($CDCl_3$) δ 14.91 (q), 22.66 (q), 31.54 (t), 32.12 (t), 35.76 (t), 40.30 (t), 47.66 (s), 49.05 (s), 89.63 (s), 221.35 (s). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.69. Found: C, 71.41; H, 9.68.

30: R_f 0.25 (hexane–AcOEt, 5:1); IR (neat) 3450, 1740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.09 (s, 3 H), 1.18 (s, 3 H), 1.34–2.78 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 23.84 (t), 29.03 (q), 30.23 (q), 34.10 (t), 40.77 (s), 47.60 (d and t, 2 C), 51.30 (s), 87.63 (s), 220.69 (s). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.69. Found: C, 71.34; H, 9.66.

34a: R_f 0.65 (hexane–AcOEt, 2:1); IR (neat) 3450, 1740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.20–2.85 (m, 16 H); ^{13}C NMR ($CDCl_3$) δ 21.84 (t), 26.19 (t), 27.15 (t), 33.00 (t), 33.89 (t), 36.31 (t), 43.37 (d), 48.57 (d), 50.06 (d), 87.77 (s), 220.84 (s). Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.33; H, 8.94.

34b: R_f 0.5 (hexane–AcOEt, 2:1); IR (neat) 3450, 1730 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.10–2.98 (m, 16 H); ^{13}C NMR ($CDCl_3$) δ 23.50 (t), 26.99 (t), 28.04 (t), 33.13 (t), 37.14 (t), 38.34 (t), 44.68 (d), 50.76 (d), 57.16 (d), 89.10 (s), 221.72 (s). Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.18; H, 8.87.

38: R_f 0.35 (hexane–AcOEt, 5:1); mp 65–67 °C; IR (KBr) 3450, 1740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.20–2.55 (m, 16 H); ^{13}C NMR ($CDCl_3$) δ 27.17 (t), 30.68 (t), 33.06 (t), 34.05 (t), 34.53 (t), 35.51 (t), 37.98 (t), 52.80 (s), 60.44 (s), 86.82 (s), 222.19 (s). Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.25; H, 8.97.

42: R_f 0.3 (hexane–AcOEt, 5:1); IR (neat) 3450, 1730 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.04 (s, 3 H), 1.12 (s, 3 H), 1.21 (s, 3 H), 1.40–2.15 (m, 10 H), 2.37–2.45 (m, 2 H), 2.69–2.83 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 22.73 (t), 23.74 (q), 31.07 (q), 31.79 (q), 32.82 (t), 42.10 (t), 42.82 (t), 43.62 (s), 45.34 (t), 47.74 (d), 49.41 (s), 63.53 (d), 88.00 (s), 220.62 (s). Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.59; H, 9.93.

43 (mixture of diastereomers): R_f 0.1–0.25 (hexane–AcOEt, 5:1); IR (neat) 3450, 2250 cm^{-1}.

48: R_f 0.4 (hexane–AcOEt, 5:1); IR (neat) 3450, 1735 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.12–2.20 (m, 12 H), 2.25–2.80 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 24.01 (t), 27.06 (t), 28.48 (t), 30.49 (t), 33.69 (t), 36.02 (t), 40.53 (t), 45.74 (d), 46.57 (d), 47.78 (d), 49.27 (d), 51.56 (d), 88.14 (s), 221.13 (s). Anal. Calcd for $C_{10}H_{14}O$: C, 76.33; H, 9.15. Found: C, 76.25; H, 9.07.

Transformation of 35 to 36. Each isomer of **35** was transformed to **36** by the same method as the transformation of **2c** to **4c**. Each isomer of **36** was identified by comparison of its ^{13}C NMR spectrum with the reported data.[23]

Oxidation of 43. To a solution of **43** (1 mmol) in acetone (5 mL) was added Jones' reagent (1.5 mmol) at 0 °C, and the mixture was stirred for 30 min at the temperature. After the usual workup, the γ-cyano ketone **41** was isolated by column chromatography on silica gel (85% yield).

Reduction of 44. To a solution of Li (3 mmol) in NH_3 (10 mL) was added a solution of **44** (1 mmol) in ether (1 mL) at –70 °C, and the mixture was stirred for 15 min. After the usual workup, the ketone **45** was isolated by column chromatography on silica gel (82% yield).

Synthesis of 52 and 59. According to the known alkylation method of dianion of alkyl acetoacetate,[45] β-keto ester **52** (75% yield) and **59** (70% yield) were prepared.

52: bp 80 °C (2 mmHg); IR (neat) 1740, 1720, 1640 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.91 (t, 3 H, J = 6.0 Hz), 1.00–1.80 (m, 6 H), 1.47 (s, 9 H), 2.47 (t, 2 H, J = 6.0 Hz), 3.20 (s, 2 H). Anal. Calcd for $C_{12}H_{22}O_3$: C, 67.25; H, 10.35. Found: C, 67.18; H, 10.33.

59: R_f 0.3 (hexane–AcOEt, 5:1); IR (neat) 1750, 1720, 1630 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.05–1.85 (m, 10 H), 2.54 (t, 2 H, J = 7.0 Hz), 3.37 (s, 3 H), 3.44 (s, 2 H), 3.51 (t, 2 H, J = 6.0 Hz), 3.75 (s, 3 H), 4.63 (s, 2 H). Anal. Calcd for $C_{13}H_{24}O_5$: C, 59.98; H, 9.29. Found: C, 59.87; H, 9.31.

Synthesis of 53, 56, and 60. Alkylation of **52** and **59** was carried out by the usual method, i.e., treatment of **52** or **59** (10 mmol) with NaH (11 mmol) in DMF (10 mL) and subsequent reaction with an alkyl halide (12 mmol) at 50 °C. After cyanoethylation of the alkylated product with acrylonitrile, the usual decarboalkoxylation gave **53** (68%), **56** (63%), and **60** (52%).

53: R_f 0.35 (hexane–AcOEt, 5:1); IR (neat) 2250, 1735 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.90 (t, 3 H, J = 6.0 Hz), 1.16 (d, 2 H, J = 7.0 Hz), 1.10–3.00 (m, 14 H). Anal. Calcd for $C_{11}H_{19}ON$: C, 72.88; H, 10.57; N, 7.73. Found: C, 72.88; H, 10.56; N, 7.65.

56: R_f 0.6 (hexane–AcOEt, 2:1); IR (neat) 2250, 1735, 1715 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.90 (t, 3 H, J = 6.0 Hz), 1.25 (t, 3 H, J = 7.0 Hz), 1.10–3.20 (m, 15 H), 4.13 (q, 2 H, J = 7.0 Hz). Anal. Calcd for $C_{14}H_{23}O_3N$: C, 66.37; H, 9.15; N, 5.53. Found: C, 66.31; H, 9.18; N, 5.38.

60: R_f 0.3 (hexane–AcOEt, 5:1); IR (neat) 2250, 1715 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.88 (t, 3 H, J = 6.0 Hz), 1.10–2.00 (m, 22 H), 2.00–2.85 (m, 5 H), 3.37 (s, 3 H), 3.53 (t, 2 H, J = 6.0 Hz), 4.63 (s, 2 H). Anal. Calcd for $C_{20}H_{37}O_3N$: C, 70.75; H, 10.99; N, 4.13. Found: C, 70.59; H, 11.01; N, 4.05.

Synthesis of Dihydrojasmone (54). Electroreduction of **53** (5 mmol) was carried out at 25 °C according to the method described above (–2.8 V vs SCE, 6 F/mol). The mixture of crude products was refluxed in benzene (10 mL) in the presence of catalytic amounts of *p*-TsOH for 1 h. After evaporation of benzene, the products **54** (64%) and **55** (13%) were isolated by column chromatography on silica gel, and **54** was identified by comparison with authentic dihydrojasmone.

55: R_f 0.7 (hexane–AcOEt, 5:1); IR (neat) 1740 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.88 (t, 3 H, J = 6.0 Hz), 1.15 (d, 3 H, J = 6.0 Hz), 1.05–2.50 (m, 14 H); ^{13}C NMR ($CDCl_3$) δ 13.82 (q), 19.50 (q), 22.30 (t), 26.35 (t), 27.54 (t), 29.39 (t), 31.97 (t), 36.64 (d), 37.96 (t), 56.40 (d), 221.85 (s). Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.47; H, 12.00.

Synthesis of Methyl Dihydrojasmonate (58). Electroreduction of **56** (5 mmol) was carried out at 65 °C according to the method described above (0.2 A, 8 F/mol). The mixture of products was stirred in saturated HCl/MeOH (10 mL) at room temperature for 12 h. After removal of MeOH, **57** (10%) and **58** (54%) were isolated by column chromatography on silica gel. A solution of **57** (0.5 mmol) in MeOH (5 mL) was stirred under H_2 (1 atm) in the presence of catalytic amounts of Pd/C at room temperature for 6 h to give **58** (quant.). The product **58** was identified by comparison with authentic methyl dihydrojasmonate.

57: R_f 0.2 (hexane–AcOEt, 5:1); IR (neat) 1745, 1705, 1650 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.86 (t, 3 H, J = 6.0 Hz), 1.05–1.80 (m, 8 H), 2.00–2.75 (m, 8 H), 3.45 (s, 2 H), 3.73 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 13.64 (q), 22.15 (t), 22.88 (t), 27.70 (t), 29.41 (t), 31.47 (t), 34.02 (t), 36.31 (t), 52.04 (q), 143.28 (s), 163.70 (s), 169.74 (s), 209.49 (s). Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.49; H, 8.87.

Synthesis of 62. Electroreduction of **60** (5 mmol) was carried out at 65 °C according to the method described above (0.2 A, 6 F/mol). The crude mixture of products was treated with TFA (10 mL) at room temperature for 1 h. After removal of TFA, **61** (32%) and **62** (31%) were isolated by column chromatography on silica gel. The α,β-unsaturated ketone **61** (1.5 mmol) was reduced to **62** (quant.) by treatment with Li (4 mmol)/NH_3 (10 mL) at −70 °C for 1 h.

61: R_f 0.2 (hexane–AcOEt, 2:1); IR (neat) 3400 (br s), 1700, 1640 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.90 (t, 3 H, J = 6.0 Hz), 1.10–1.80 (m, 19 H), 2.00–2.60 (m, 8 H), 3.63 (t, 2 H, J = 6.0 Hz); ^{13}C NMR ($CDCl_3$) δ 13.71 (q), 22.22 (t), 22.76 (t), 25.35 (t), 27.21 (t), 28.27 (t), 28.70 (t), 28.88 (t), 29.07 (t), 29.32 (t), 30.93 (t), 31.32 (t), 32.41 (t), 33.98 (t), 62.56 (t), 140.44 (s), 174.62 (s), 210.65 (s). Anal. Calcd for $C_{18}H_{32}O_2$: C, 77.09; H, 11.50. Found: C, 76.87; H, 11.55.

62: R_f 0.45 (hexane–AcOEt, 2:1); IR (neat) 3400 (br s), 1740 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.90 (t, 3 H, J = 6.0 Hz), 1.00–2.00 (m, 26 H), 2.00–2.50 (m, 3 H), 3.60 (t, 2 H, J = 6.0 Hz); ^{13}C NMR ($CDCl_3$) δ 13.85 (q), 22.41 (t), 25.43 (t), 26.52 (t), 26.87 (2 C, t), 27.75 (t), 29.00 (t), 29.31 (t), 29.66 (t), 31.64 (t), 32.52 (t), 34.58 (t), 37.76 (t), 41.34 (d), 54.95 (d), 62.79 (t), 222.22 (s). Anal. Calcd for $C_{18}H_{34}O_2$: C, 76.54; H, 12.13. Found: C, 76.51; H, 12.13.

Synthesis of 63. To a solution of **62** (2 mmol) in acetone (5 mL) was added Jones' reagent (3 mmol) at 0 °C for 10 min. After the usual workup, the product **63** was isolated by column chromatography on silica gel (83% yield).

63: R_f 0.5 (hexane–AcOEt, 1:1); IR (neat) 3500–2500 (br s), 1740, 1715 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.90 (t, 3 H, J = 6.0 Hz), 1.00–2.00 (m, 23 H), 2.00–2.50 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 14.02 (q), 22.57 (t), 24.54 (t), 26.59 (t), 26.97 (t), 27.01 (t), 27.90 (t), 28.80 (t), 29.43 (t), 29.47 (t), 31.76 (t), 33.96 (t), 34.70 (t), 37.83 (t), 41.50 (d), 54.98 (d), 179.88 (s), 221.75 (s). Anal. Calcd for $C_{18}H_{32}O_3$: C, 72.92; H, 10.88. Found: C, 72.78; H, 10.79.

Synthesis of Rosaprostol (64). To a solution of **63** (1 mmol) in MeOH (5 mL) was added $NaBH_4$ (1 mmol) at 0 °C, and the mixture was stirred for 1 h. After the usual workup, the product was isolated as a 1:1 mixture of rosaprostol (**64**) and its diastereomer by column chromatography on silica gel (quant.).

64 (50:50 mixture of two diastereomers): R_f 0.2 (hexane–AcOEt, 1:1); IR (neat) 3600–2500 (br s), 1715 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.90 (t, 3 H, J = 6.0 Hz), 1.00–2.20 (m, 27 H), 2.37 (t, 2 H, J = 7.0 Hz), 3.77–4.00 (m, 0.5 H), 4.10–4.33 (m, 0.5 H); ^{13}C NMR ($CDCl_3$) δ 13.89 (q), 22.48 (t), 24.45 (t), 27.43 (t), 27.96 (t), 28.13 (t), 28.81 (t), 29.18 (t), 29.47 (t), 31.74 (t), 33.21 (t), 33.36 (t), 33.88 (t), 34.01 (t), 34.95 (t), 35.84 (t), 41.68 (d), 44.46 (d), 51.37 (d), 54.23 (d), 74.49 (d), 79.18 (d), 179.46 (s). Anal. Calcd for $C_{18}H_{34}O_3$: C, 72.43; H, 11.48. Found: C, 72.39; H, 11.53.

Electroreduction of Ketones and Nitriles. Electroreduction of a ketone (5 mmol) and a nitrile was carried out at 5 °C in a solvent as depicted in Table III according to the method described above (constant current of a 0.2 A). The products were isolated by column chromatography on silica gel. The products **66** and **67** were assigned by comparison with authentic samples.

65a: R_f 0.3 (hexane–AcOEt, 5:1); IR (neat) 3450 (br s), 1710 cm^{-1}; ^1H NMR (90 MHz, CCl_4) δ 1.25–1.94 (m, 10 H), 2.09 (s, 3 H), 3.33 (s, 1 H, OH); ^{13}C NMR ($CDCl_3$) δ 20.66 (2 C, t), 23.42 (q), 24.88 (t), 33.35 (2 C, t), 77.81 (s), 213.27 (s). Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.93. Found: C, 67.51; H, 9.88.

65b (cis): R_f 0.45 (hexane–AcOEt, 5:1); mp 71–72 °C; IR (KBr) 3500, 1720 cm^{-1}; ^1H NMR (90 MHz, CCl_4) δ 0.88 (s, 9 H), 1.39–1.66 (m, 9 H), 2.08 (s, 3 H), 3.35 (br s, 1 H, OH); ^{13}C NMR ($CDCl_3$) δ 21.75 (2 C, t), 23.42 (q), 27.21 (3 C, q), 32.23 (s), 34.21 (2 C, t), 47.19 (d), 77.65 (s), 213.52 (s). Anal. Calcd for $C_{12}H_{22}O_3$: C, 72.68; H, 11.18. Found: C, 72.66; H, 11.18.

65b (trans): R_f 0.35 (hexane–AcOEt, 5:1); mp 81–82 °C; IR (KBr) 3440, 1700 cm^{-1}; ^1H NMR (90 MHz, CCl_4) δ 0.86 (s, 9 H), 1.08–1.99 (m, 9 H), 2.07 (s, 3 H), 2.43 (br s, 1 H, OH); ^{13}C NMR ($CDCl_3$) δ 24.03 (2 C, t), 24.40 (q), 27.34 (3 C, q), 32.03 (s), 35.38 (2 C, t), 46.86 (d), 77.14 (s), 211.64 (s). Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.69; H, 11.21.

65c: R_f 0.35 (hexane–AcOEt, 5:1); IR (neat) 3450 (br s), 1710 cm^{-1}; ^1H NMR (90 MHz, CCl_4) δ 1.40–1,89 (m, 12 H), 2.08 (s, 3 H), 3.37 (s, 1 H, OH); ^{13}C NMR ($CDCl_3$) δ 22.77 (2 C, t), 23.35 (q), 28.83 (2 C, t), 37.38 (2 C, t), 80.67 (s), 213.01 (s). Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.08; H, 10.35.

65d: R_f 0.15 (hexane–AcOEt, 5:1); IR (neat) 3450 (br s), 1710 cm^{-1}; ^1H NMR (90 MHz, CCl_4) δ 1.60–1.95 (m, 8 H), 2.13 (s, 3 H), 3.67 (s, 1 H, OH); ^{13}C NMR ($CDCl_3$) δ 23.43 (q), 25.28 (2 C, t), 38.75 (2 C, t), 87.01 (s), 212.64 (s). Anal. Calcd for $C_7H_{12}O_2$: C, 65.59; H, 9.44. Found: C, 65.71; H, 9.35.

65e: R_f 0.55 (hexane–AcOEt, 5:1); IR (neat) 3470 (br s), 1710 cm^{-1}; ^1H NMR (90 MHz, CCl_4) δ 0.94 (t, 3 H, J = 7.2 Hz), 1.12–1.72 (m, 4 H), 1.28 (s, 3 H), 2.10 (s, 3 H), 3.54 (s, 1 H, OH); ^{13}C NMR ($CDCl_3$) δ 13.71 (q), 16.18 (t), 23.21 (q), 24.84 (q), 41.22 (t), 78.53 (s), 212.58 (s). Anal. Calcd for $C_7H_{14}O_2$: C, 64.58; H, 10.84. Found: C, 64.55; H, 10.71.

65f: R_f 0.35 (hexane–AcOEt, 5:1); IR (neat) 3470 (br s), 1710 cm^{-1}; ^1H NMR (90 MHz, CCl_4) δ 1.06 (t, 3 H, J = 7.0 Hz), 1.30–1.90 (m, 10 H), 2.51 (q, 2 H, J = 7.0 Hz), 3.34 (s, 1 H, OH); ^{13}C NMR ($CDCl_3$) δ 7.34 (q), 20.67 (2 C, t), 24.92 (t), 28.56 (t), 33.57 (2 C, t), 77.69 (s), 215.71 (s). Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.05; H, 10.28.

65g: R_f 0.5 (hexane–AcOEt, 5:1); IR (neat) 3460 (br s), 1700 cm^{-1}; ^1H NMR (90 MHz, CCl_4) δ 0.89 (t, 3 H, J = 7.0 Hz), 1.22–1.74 (m, 12 H), 2.41 (t, 2 H, J = 7.0 Hz), 3.32 (s, 1 H, OH); ^{13}C NMR ($CDCl_3$) δ 13.48 (q), 16.91 (t), 20.84 (t), 25.10 (t), 33.58 (t), 37.40 (t), 77.84 (s), 215.16 (s). Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66. Found: C, 70.48; H, 10.69.

65h: R_f 0.5 (hexane–AcOEt, 5:1); IR (neat) 3470 (br d), 1710 cm^{-1}; ^1H NMR (90 MHz, CCl_4) δ 1.06 (d, 6 H, J = 6.6 Hz), 1.30–1.90 (m, 10 H), 2.80–3.30 (m, 1 H), 3.32 (s, 1 H, OH); ^{13}C NMR ($CDCl_3$) δ 19.37 (2 C, q), 20.77 (2 C, t), 25.07 (t), 33.00 (2 C, t), 33.32 (d), 78.31 (s), 219.15 (s). Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66. Found: C, 70.46; H, 10.62.

65i could not be separated from intramolecularly coupled product: R_f 0.35 (hexane–AcOEt, 5:1); ^{13}C NMR ($CDCl_3$) δ 23.28 (q), 24.81 (t), 25.13 (q), 35.47 (t), 38.45 (t), 78.67 (s), 125.88 (d), 128.36 (d), 141.78 (s), 212.65 (s).

Transformation of 65b to 68[27] was carried out by the same method as that of **2** to **4**.

68a (cis): R_f 0.5 (hexane–AcOEt; 5:1); ^{13}C NMR ($CDCl_3$) δ 7.20 (q), 22.19 (2 C, t), 27.33 (3 C, q), 32.16 (s), 36.32 (2 C, t), 36.66 (t), 47.85 (d), 70.56 (s).

68b (trans): R_f 0.3 (hexane–AcOEt, 5:1); ^{13}C NMR ($CDCl_3$) δ 6.61 (q), 24.07 (2 C, t), 27.33 (3 C, q), 28.34 (t), 31.90 (s), 37.99 (2 C, t), 47.30 (d), 71.90 (s).

Synthesis of 69. Electroreduction of (+)-dihydrocarvone (5 mmol) was carried out in acetonitrile/i-PrOH = 2/1 (40 mL) according to the method described above (0.2 A, 5 F/mol). The major isomer (**69**) was isolated by column chromatography on silica gel (45% yield).

69: R_f 0.5 (hexane–AcOEt, 10:1); $[\alpha]^{20}_D$ −6.1 (*c* 3.8, $CHCl_3$); IR (neat) 3450 (br s), 1700, 1640, 885 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.70 (d, 3 H, J = 6.6 Hz), 1.18–1.68 (m, 6 H), 1.73 (s, 3 H), 1.75–1.90 (m, 2 H), 2.24 (s, 3 H), 2.27–2.44 (m, 1 H), 3.81 (s, 1 H, OH), 4.71 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.84 (q), 20.80 (q), 23.21 (q), 29.67 (t), 30.88 (t), 36.33 (d), 38.78 (d), 39.80 (t), 80.74 (s), 108.74 (t), 149.54 (s), 212.58 (s). Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.40; H, 10.28.

Transformation of 69 to 70. Transformation of **69** to **70** was carried out by the same method as that used in the conversion of **2** to **4**. The product **70** was consistent with the major isomer obtained from the reaction of (+)-dihydrocarvone with ethylmagnesium bromide.[29]

70: R_f 0.35 (hexane–AcOEt, 10:1); IR (neat) 3480 (br s), 1640, 975, 945, 885 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.87 (d, 3 H, J = 6.1 Hz), 0.88 (t, 3 H, J = 7.5 Hz), 1.10–1.80 (m, 10 H), 1.72 (s, 3 H), 2.18–2.35 (m, 1 H), 4.69 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 7.88 (q), 14.31 (q), 20.80 (q), 30.34 (t), 31.25 (t), 33.47 (t), 36.95 (d), 39.88 (d), 40.68 (t), 73.50 (s), 108.34 (t), 150.61 (s). Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 79.06; H, 12.11.

Synthesis of 71. A solution of **69** (2 mmol) and *O*-methylhydroxylamine hydrochloride (2.4 mmol) in pyridine (10 mL) was stirred at room temperature for 12 h. The obtained *O*-methyl-

oxime was treated with LAH (2 mmol) in refluxing THF (10 mL). After the usual workup, the product **71** was isolated by Kugelrohr distillation (120 °C (2 mmHg); 75% yield).

71: IR (neat) 3350 (br s), 1640, 885 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.87 (d, 3 H, J = 6.2 Hz), 1.17 (d, 3 H, J = 6.8 Hz), 1.00–1.85 (m, 10 H), 1.72 (s, 3 H), 2.20–2.40 (m, 1 H), 2.80 (q, 1 H, J = 6.8 Hz), 4.69 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 15.27 (q), 18.37 (q), 20.66 (q), 30.82 (t), 30.93 (t), 35.07 (d), 38.27 (t), 39.88 (d), 54.14 (d), 73.51 (s), 108.20 (t), 150.52 (s). Anal. Calcd for $C_{12}H_{23}ON$: C, 73.04; H, 11.75; N, 7.10. Found: C, 72.81; H, 11.65; N, 6.87.

Synthesis of 72. A mixture of **71** (1 mmol), methyl iodide (2.2 mmol), and K_2CO_3 (2.2 mmol) in EtOH (5 mL) was stirred at room temperature for 2 days. The product **72** was isolated by column chromatography on silica gel (90% yield).

72: R_f 0.3 (hexane–AcOEt, 1:1); $[\alpha]^{20}_D$ −12.4 (c 2.8, $CHCl_3$); IR (neat) 3350 (br s), 2780, 1640, 885 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.86 (d, 3 H, J = 6.6 Hz), 1.00 (d, 3 H, J = 7.3 Hz), 1.10–1.80 (m, 8 H), 1.72 (s, 3 H), 2.16–2.33 (m, 1 H), 2.29 (s, 6 H), 2.54 (q, 1 H, J = 7.3 Hz), 4.69 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 6.35 (q), 15.62 (q), 20.77 (q), 31.18 (t), 31.28 (t), 35.00 (d), 39.78 (t), 40.17 (d), 43.62 (q), 65.61 (d), 75.07 (s), 108.25 (t), 150.81 (s). Anal. Calcd for $C_{14}H_{27}ON$: C, 74.61; H, 12.08; N, 6.22. Found: C, 74.40; H, 11.85; N, 5.98.

Synthesis of 73. A mixture of **71** (1 mmol), ethyl acetimidate hydrochloride (1.2 mmol), and Et_3N (1.2 mmol) in CH_2Cl_2 (5 mL) was stirred at room temperature for 12 h. After the usual workup, the product **73** was isolated by column chromatography on silica gel (70% yield).

73: R_f 0.3 (hexane–AcOEt, 2:1); IR (neat) 1680, 1645, 930, 915, 885 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.86 (d, 3 H, J = 5.8 Hz), 1.10–1.92 (m, 7 H), 1.32 (d, 3 H, J = 7.4 Hz), 1.73 (s, 3 H), 1.96 (d, 3 H, J = 1.7 Hz), 2.15–2.32 (m, 1 H), 3.70 (dq, 1 H, J = 1.7, 7.4 Hz), 4.71 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.92 (q), 14.20 (q), 16.53 (q), 20.62 (q), 30.56 (t), 31.42 (t), 35.03 (d), 41.22 (d), 43.19 (t), 71.48 (d), 89.56 (s), 108.70 (t), 149.61 (s), 164.21 (s). Anal. Calcd for $C_{14}H_{23}ON$: C, 75.97; H, 10.47; N, 6.33. Found: C, 75.72; H, 10.33; N, 6.09.

General Procedure for Enantioselective Addition of Diethylzinc to Aldehydes. A mixture of diethylzinc (1 M hexane solution, 0.32 mL) and a chiral β-amino alcohol **72** (0.16 mmol) in toluene (5 mL) was refluxed for 30 min. Diethylzinc (1 M hexane solution, 4.8 mL) and an aldehyde (3.2 mmol) were added to the mixture at 0 °C. The mixture was stirred for 6–12 h at this temperature. After 1 N HCl (20 mL) was added, the mixture was extracted with CH_2Cl_2. The products, secondary alcohols, were isolated by PTLC (silica gel, hexane–AcOEt).

Registry No. (±)-**1a**, 58769-43-0; (±)-**1b**, 58734-78-4; (±)-**1c**, 144178-54-1; (±)-**1d**, 144126-62-5; (±)-**1e**, 144126-63-6; (±)-**1f**, 144126-64-7; (±)-**1g**, 144126-65-8; **1h**, 21197-29-5; **1i**, 21197-28-4; **1j**, 7647-27-0; (±)-**1k**, 98263-14-0; (±)-**1l**, 124355-57-3; **1m**, 10412-98-3; **1n**, 18458-15-6; (±)-**1o**, 123187-58-6; **1p**, 144126-66-9; (±)-**1** (m = 2, n = 0), 74629-98-4; (±)-**1** (m = 2, n = 3), 144126-67-0; (±)-**2a**, 128893-51-6; (±)-**2b**, 128893-50-5; (±)-*cis*-**2c**, 128893-52-7; (±)-*trans*-**2c**, 128893-56-1; (±)-*cis*-**2d**, 144178-55-2; (±)-*trans*-**2d**, 128893-53-8; (±)-**2e**, 144126-68-1; (±)-*cis*-**2f**, 128893-55-0; (±)-*trans*-**2f**, 128893-58-3; (±)-**2g**, 144126-69-2; (±)-**2h** (isomer 1), 144126-70-5; (±)-**2h** (isomer 2), 144126-71-6; (±)-**2i** (isomer 1), 144126-72-7; (±)-**2i** (isomer 2), 144178-56-3; (±)-**2j** (isomer 1), 144126-73-8; (±)-**2j** (isomer 2), 144126-74-9; (±)-**2k**, 144126-75-0; (±)-*cis*-**2l**, 144126-76-1; (±)-*trans*-**2l**, 144126-77-2; (±)-**2m**, 144178-57-4; (±)-**2n**, 144178-58-5; (±)-*cis*-**2o**, 123187-59-7; (±)-*trans*-**2o**, 144126-78-3; (±)-**2p**, 144126-79-4; **3a**, 29927-85-3; **3c**, 10407-30-4; **3d**, 15210-26-1; **3f**, 4832-16-0; **3g**, 16938-81-1; **3h**, 92015-41-3; **3i**, 58567-79-6; **3j**, 64558-16-3; **3k**, 144126-80-7; **3m**, 32854-37-8; **3n**, 24965-84-2; **3o**, 144126-81-8; **3p**, 144126-82-9; (±)-**4a**, 144126-83-0; **4b**, 52318-93-1; (±)-*cis*-**4c**, 144126-84-1; (±)-*trans*-**4c**, 144126-85-2; (±)-*cis*-**4f**, 3574-58-1; (±)-*trans*-**4f**, 1654-87-1; (±)-**4g**, 144126-86-3; **4l**, 5173-74-0; (±)-**5a**, 144126-87-4; (±)-**5b**, 144126-88-5; **10a**, 22118-00-9; **10c** (isomer 1), 769-32-4; **10c** (isomer 2), 144126-89-6; **10d**, 15210-25-0; **11**, 144126-90-9; **12**, 144126-91-0; **13**, 144126-92-1; **14**, 144126-93-2; **15** (isomer 1), 144126-94-3; **15** (isomer 2), 144126-95-4; **16**, 489-84-9; **17** (isomer 1), 144126-96-5; **17** (isomer 2), 144178-59-6; **18**, 144126-97-6; **19**, 144126-98-7; **20**, 144126-99-8; **21** (isomer 1), 144127-00-4; **21** (isomer 2), 144127-01-5; **22**, 144127-02-6; **23**, 22451-64-5; **24**, 10515-92-1; (±)-**25**, 88931-54-8; (±)-**26**, 144127-03-7; (±)-**27**, 144127-04-8; **28**, 81332-19-6; (±)-**29**, 144127-05-9; (±)-**30**, 144127-06-0; **31**, 83180-75-0; (±)-**32**, 115580-56-8; (±)-**33** (isomer 1), 144127-07-1; (±)-**33** (isomer 2), 144178-60-9; (±)-**34a**, 144127-08-2; (±)-**34b**, 144178-61-0; (±)-**35a**, 144178-62-1; (±)-**35b**, 144178-63-2; (±)-**36a**, 120052-74-6; **36b**, 58116-67-9; (±)-**37**, 144127-09-3; (±)-**38**, 144127-10-6; (±)-**39**, 104833-04-7; (±)-**40**, 81332-20-9; (±)-**41** (isomer 1), 144127-11-7; (±)-**41** (isomer 2), 144178-64-3; (±)-**42**, 144127-12-8; **43**, 144127-13-9; (±)-**44**, 115895-85-7; (±)-**45**, 81331-89-7; (±)-**46**, 119245-21-5; (±)-**47** (isomer 1), 144127-14-0; (±)-**47** (isomer 2), 144178-65-4; (±)-**48**, 144127-15-1; (±)-**49**, 144127-16-2; (±)-**50**, 144127-17-3; (±)-**51**, 144178-66-5; **52**, 66720-07-8; (±)-**53**, 144127-18-4; **54**, 1128-08-1; (±)-**55**, 128893-60-7; (±)-**56**, 144127-19-5; **57**, 24863-70-5; (±)-**58**, 2570-03-8; **59**, 128893-62-9; (±)-**60**, 144127-20-8; **61**, 128893-64-1; (±)-**62**, 128893-65-2; (±)-**63**, 56695-64-8; (±)-*trans,trans*-**64**, 128948-49-2; (±)-*trans,cis*-**64**, 128948-48-1; **65a**, 1123-27-9; *cis*-**65b**, 6555-57-3; *trans*-**65b**, 6555-58-4; **65c**, 73642-06-5; **65d**, 17160-89-3; (±)-**65e**, 144127-21-9; **65f**, 1124-90-9; **65g**, 68487-06-9; **65h**, 1126-99-4; (±)-**65i**, 144127-22-0; **66a**, 108-93-0; **66b**, 98-52-2; **66c**, 502-41-0; **66d**, 96-41-3; **67a**, 14368-55-9; **67b**, 71750-16-8; **67c**, 144127-23-1; (±)-**67e**, 144127-24-2; (±)-**67f**, 144127-25-3; (±)-**67g**, 144127-26-4; **67h**, 7178-96-3; **68a**, 17328-78-8; **68b**, 25143-76-4; **69**, 144127-27-5; **70**, 144127-28-6; **71**, 144127-29-7; **72**, 144127-30-0; **73**, 144127-31-1; Et_2Zn, 557-20-0; PhCHO, 100-52-7; PhCH=CHCHO, 104-55-2; n-$C_6H_{13}CHO$, 111-71-7; CH_3CN, 75-05-8; CH_3CH_2CN, 107-12-0; $CH_3(CH_2)_2CN$, 109-74-0; $(CH_3)_2CHCN$, 78-82-0; $OHCC(CH_3)_2(CH_2)_2CN$, 6140-61-0; $HOCH_2C(CH_3)_2(CH_2)_2CN$, 25252-68-0; (*S*)-PhCH)OH)Et, 613-87-6; (*S*)-PhCH=CHCH(OH)Et, 103729-97-1; (*R*)-PhCH=CHCH(OH)Et, 110611-22-8; (*S*)-n-$C_6H_{13}CH(OH)Et$, 61925-49-3; (*R*)-n-$C_6H_{13}CH(OH)Et$, 61925-50-6; $Br(CH_2)_3CN$, 5332-06-9; CH_2=CHCN, 107-13-1; $Ph(CH_2)_2COCH_3$, 2235-83-8; CH_2=$CHCO_2Me$, 96-33-3; $CH_3COCH_2CO_2Et$, 141-97-9; cyclohexanone, 108-94-1; 4-*tert*-butylcyclohexanone, 98-53-3; cycloheptanone, 502-42-1; cyclopentanone, 120-92-3; 2-pentanone, 107-87-9; (±)-2-(2-cyanoethyl)-1-tetralone, 144127-32-2; 2-(cyanomethyl)cyclohexanol, 90242-33-4; 2-(4-cyanobutyl)cyclohexanol, 144127-33-3; 2-(2-cyanoethyl)-1-tetralol, 144127-34-4; hirsutene, 59372-72-4; $\Delta^{9(12)}$-capnellene, 68349-51-9; (−)-valeranone, 5090-54-0; (+)-dihydrocarvone, 5524-05-0; carvone, 99-49-0; 2-(ethoxycarbonyl)cyclohexanone, 1655-07-8; 2,2-dimethylcyclohexanone, 1193-47-1; (±)-*trans*-1,2,3,4,6,8a-hexahydro-1-methyl-1-naphthol, 144127-35-5.