Development of a New Reaction System for the Synthesis of Highly Optically Active α,γ-Substituted γ-Butyrolactones

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A highly useful method for the synthesis of optically active α,γ-substituted γ-butyrolactones has been developed. The SmI_2-induced reductive coupling of chiral 2-alkyl acrylates derived from isosorbide with ketones in the presence of (1*S*)-(−)-2,10-camphorsultam as a proton source give the chiral α,γ-substituted γ-butyrolactones in good yields and high enantiomeric purities (up to >99% ee for *trans* and 75% ee for *cis*). The reaction system has been investigated with various ketones, and it is demonstrated that this system is very effective for *trans*-α,γ-substituted γ-butyrolactones. Both the chiral auxiliary and the hindered proton source in this system are necessary for the observed excellent ee values of the products. The absolute configuration of the *trans* products is assigned on the basis of the X-ray crystal structure.

Introduction and Background

Optically active γ-butyrolactones have attracted much attention owing to their presence in a large variety of biologically active compounds and their use as important intermediates for fine chemicals and pharmaceuticals.[1] For instance, they have been reported as building blocks for the synthesis of many natural products such as alkaloids,[2] antibiotics,[3] pheromones,[4] and flavor components.[5] Interest in the synthesis of these and other applications of γ-butyrolactones has fueled and stimulated the effort to develop improved methodology for the construction of substituted γ-butyrolactones in an enantioselective manner.

Among the methods for generating chiral γ-butyrolactones,[6] the approach based on SmI_2-mediated reductive radical reactions developed by Fukuzawa and co-workers[7] in 1997 is one of the most facile and effective methods for preparing chiral γ-butyrolactones. Using optically pure *N*-methylephedrines as chiral auxiliaries, their acrylate or crotonate derivatives were coupled with carbonyl compounds to afford chiral γ-substituted or *cis*-β,γ-substituted γ-butyrolactones in high enantiomeric purities. Although this method is efficient, there are still some drawbacks and limitations. In most cases, the yields are low, in the range of 40−60%.[8] Also this reaction system was found to be limited for the synthesis of chiral α,γ-substituted γ-butyrolactones in high enantiomeric purities.[9] To the best of our knowledge, there has been no report concerning the highly enantioselective synthesis of α,γ-substituted γ-butyrolactones.[10]

In their former studies,[11a] Fukuzawa and co-workers found that the presence of an alcohol is essential for the

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(8) GC yield, not isolated yield.

(9) See the results shown below.

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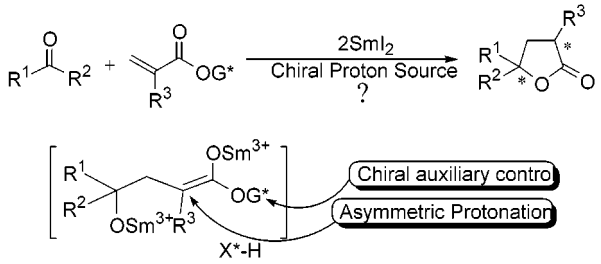
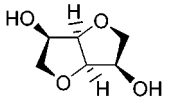
Scheme 1

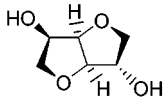


formation of the γ-butyrolactones in the reaction of α,β-unsaturated esters with ketones mediated by SmI_2 as an electron-transfer agent. The effect of an alcohol was examined, and *tert*-butyl alcohol was found to give the most satisfactory results. Further deuterium exchange experiments confirmed the role of the alcohol as a proton donor, and the proton was introduced into the α-C of lactone. Although a free radical mechanism has been assumed,[11] we are interested in the possibility that the reaction actually proceeds by an enolate intermediate. Therefore, it is desirable to construct the α-carbon chiral center of the γ-butyrolactone by asymmetric protonation of the samarium enolate using a chiral proton source. On the basis of this hypothesis, we further envisage that if both the chiral auxiliary and chiral proton source are present in the reaction, it might be possible to obtain the optically active α,γ- substituted γ-butyrolactones in high enantiomeric purities (Scheme 1).

In seeking the new type of chiral auxiliaries, we are interested in two wedge-shaped molecules—isomannide and isosorbide. They are easily accessible and inexpensive carbohydrate derivatives[12] and can be considered unique diol auxiliaries with one or two hydroxyl groups *endo*-orientated in the molecule, where the two *cis*-fused tetrahydrofuran rings form a wedge. Previously, asymmetric synthesis of optically active γ-methyl-γ-phenyl-γ-butyrolactone using their derivatives as chiral auxiliaries was carried out.[13] Herein, we wish to report detailed studies on the development of a new reaction system for the asymmetric synthesis of chiral α,γ-substituted γ-butyrolactones using a wedge-shaped isosorbide derivative as a chiral auxiliary.[14]



Isomannide

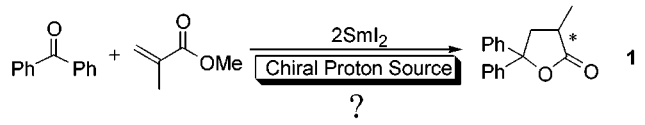


Isosorbide

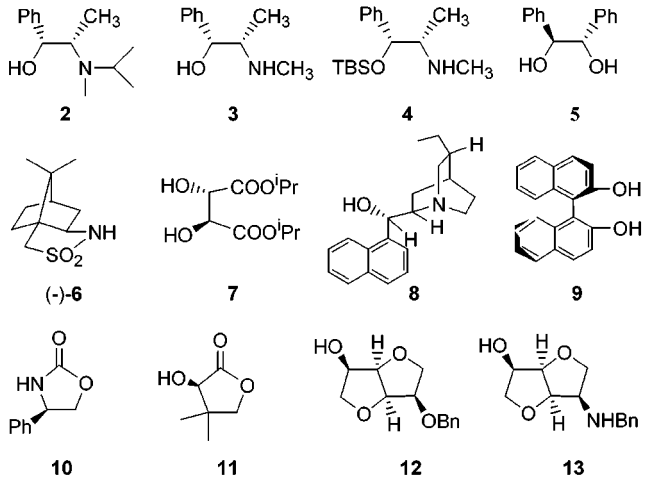
Results and Discussions

Preliminary Study on the Chiral Proton Source Induced Enantioselective Protonation of Samarium Enolate.[15] To begin addressing the previous hypothesis of asymmetric protonation, we first sought to find a simple reaction that would allow the easy detection of the enantioselectivity of the product. Thus, the reaction of methyl methacrylate with benzophenone was chosen and examined (Scheme 2). In an asymmetric protonation, the choice of a chiral proton source is a key factor in attaining a good level of asymmetric induction. *N*-Isopropylephedrine was chosen as the chiral proton source because of reports[16] of its success in this function and its simple preparation. When *N*-isopropylephedrine was employed, the reaction gave the product with an enantiomeric excess of about 9% under the optimized conditions at temperatures from −78 to −10 °C. Although this ee value is low, it seems likely that *N*-isopropylephedrine did function as a chiral proton source, implying that asymmetric protonation at this stage is possible. Furthermore, it reveals that a samarium enolate might be formed as a key intermediate in this process.

Scheme 2



To achieve a high level of enantioselectivity, various chiral compounds (**2**−**13**) including chiral alcohols, amides, and amino alcohols were examined as proton sources; the results are summarized in Table 1.



Among the chiral proton sources tested, low enantioselectivity was observed in most cases and **6** and **10** provided relatively higher enantioselectivity and yield. The best ee (47%) was achieved when (1*R*)-(+)-2,10-camphorsultam **6** was used. As shown in entries 5 and 6, the configuration of the product was determined by the stereochemistry of the proton source employed; this could be explained by enantiofacial discrimination in the protonation step.

Study on Chiral Auxiliary Induced Asymmetric Synthesis of γ-Butyrolactone. As our initial attempts at improving the performance of the chiral proton source failed, further research efforts were concentrated on the asymmetric synthesis induced by a chiral auxiliary.

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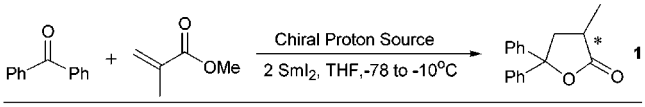
Table 1. Initial Examination of the Asymmetric Protonation Using Various Chiral Compounds as Proton Sources



entry	chiral proton source	yield (%)[a]	ee (%)[b]	$[\alpha]_D$ sign
1	**2**	53	9	(+)
2	**3**	18	15	(+)
3	**4**	20	2	(−)
4	**5**	43	9	(+)
5	(−)-**6**	90	39	(−)
6	(+)-**6**	83	47	(+)
7	**7**	<10	14	(+)
8	**8**	48	1	(+)
9	**9**	<10	6	(+)
10	**10**	63	16	(+)
11	**11**	49	1	(−)
12	**12**	61	1	(+)
13	**13**	68	3	(+)

[a] Isolated yield. [b] The ee values were determined by HPLC analysis on a Chiralcel AD column.

Considering that *N*-methylephedrine and *N*-isopropylephedrine were effective chiral auxiliaries in the SmI_2-mediated asymmetric synthesis of γ-substituted or *cis*-β,γ-substituted γ-butyrolactones, we first synthesized methacrylates **14** and **15** from commercial ephedrine by simple procedures. We treated them with benzophenone in the presence of ^{t}BuOH at −78 °C to room temperature. The reaction proceeded well; however, low ee values were observed in both cases. Interestingly, the configuration of the product was largely determined by the substituent of the amino group, suggesting that the enantioselectivity could be influenced by steric hindrance or chelation control. In an attempt to improve enantioselectivity, we synthesized substrates **16**−**20** from easily available isomannide or isosorbide and investigated their utility under the same reaction conditions. As we can see from the table, **18** appears to be the most favorable substrate and gave the highest enantioselectivity (60%). It is notable that the reaction temperature was very important. The enantioselectivity increased when the reaction was quenched at a lower temperature; for example, the reaction of benzophenone with **7** provided lactone with 79% ee when quenched at −10 °C as opposed to 60% ee when quenched at room temperature (Table 2, entries 5 and 6). Further examinations were carried out by using substrates **19** and **20**, both bearing one free hydroxy group. We predicted that these kinds of substrates might also act as chiral proton sources in the reaction. In fact, the reaction did proceed smoothly in the absence of ^{t}BuOH but did not give improved enantioselectivity, resulting in respective ee of only 38% and 19%.

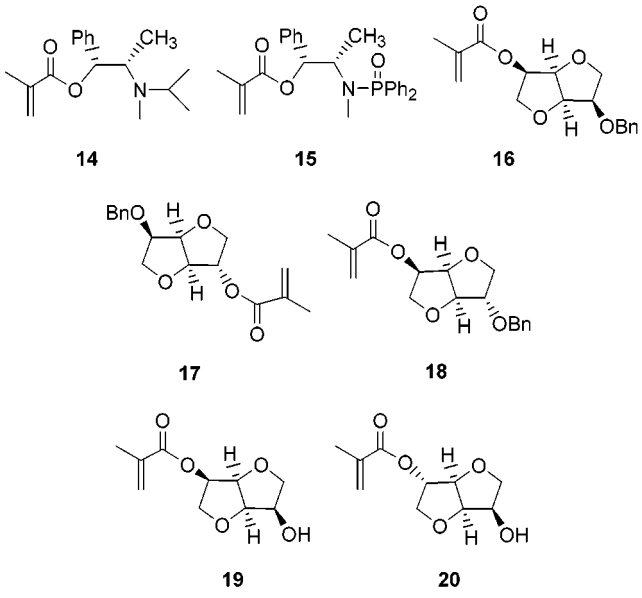
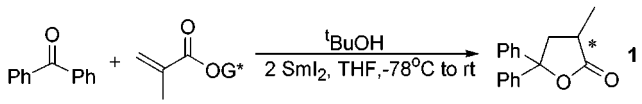


Table 2. Chiral Auxiliary Induced Asymmetric Synthesis of γ-Butyrolactone 1

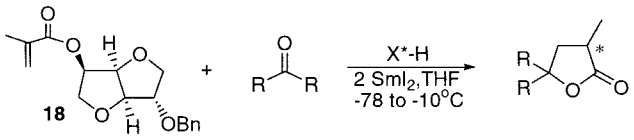


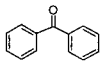
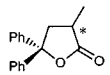
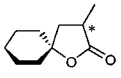
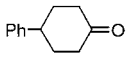
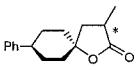
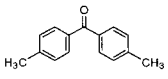
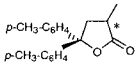
entry	substrate	yield (%)[a]	ee (%)[b]	$[\alpha]_D$ sign
1	**14**	49	30	(−)
2	**15**	42	25	(+)
3	**16**	51	49	(+)
4	**17**	68	8	(−)
5	**18**	55	60	(+)
6[c]	**18**	55	79	(+)
7	**19**	45	38	(+)
8	**20**	60	19	(+)

[a] Isolated yield. [b] The ee values were determined by HPLC analysis on a Chiralcel AD column. [c] The reaction was quenched at −10 °C.

Development a New Reaction System for the Efficient Synthesis of Chiral α,γ-Substituted γ-Butyrolactones. We previously demonstrated the use of asymmetric protonation and chiral auxiliary in the synthesis of chiral α-methyl-γ,γ-diphenyl-γ-butyrolactones; therefore, it was reasonable to expect double asymmetric induction by using both a chiral proton source and a chiral auxiliary in the reaction. In light of the above results, this possibility was explored by employing both chiral substrate **18** and a chiral proton source. As shown in Table 3, when chiral compounds **2** and **10** were used as the proton sources in place of achiral ^{t}BuOH in the reaction of **18** with benzophenone, the enantiomeric excesses were improved to 85% and 86%, respectively. When (−)-**6** was employed, we were surprised and delighted to find that the reaction provided **1** with a very high enantiomeric excess (95%, Table 3, entry 3). This high enantioselectivity was unexpected, because chiral proton source (−)-**6** and chiral substrate **18** favored different enantiomers (compare Table 1, entry 5 with Table 2, entries 5 and 6). An equally high enantioselectivity (93% ee) was also observed when (+)-**6** was used as the chiral proton source (entry 4). These findings suggest that the enantioselectivity of the reaction may be unrelated to double asymmetric induction. To confirm this consideration, the use of racemic sultam [(±)-**6**] was examined. A high degree of enantioselectivity was attained (95% ee, entry 5), similar to that with the achiral sterically bulky trityl alcohol (entry 6). These two results supported the idea that double asymmetric induction was not exerted in this reaction. Moreover, in all cases, we found that the configurations of the main products were the same. Thus, it can be concluded that the enantioselectivity of the reaction was strongly controlled by the stereochemistry of the chiral substrate and that the chirality of the proton source was not a determining factor. In addition, the above results suggest that che-

Table 3. Highly Enantioselective Synthesis of γ-Butyrolactones with Chiral Substrate 18 and Symmetrical Ketones



entry	ketone	proton source	product	yield (%)[a]	*ee* (%)[b]	$[\alpha]_D$ sign
1		**2**		43	85	(+)
2		**10**		51	86	(+)
3		(-)-**6**		66	95	(+)
4		(+)-**6**	**1**	67	93	(+)
5		(±)-**6**		60	95	(+)
6		TrOH		53	87	(+)
7		(-)-**6**	 **21**	99	76[c]	(-)
8		(-)-**6**	 **22**	79	87[d]	(-)
9		(-)-**6**	 **23**	71	90	(+)

[a] Isolated yield. [b] The ee values were determined by HPLC analysis on a Chiralcel AD column unless otherwise noted. [c] Determined by GC analysis on a G-PN (astec) column. [d] Determined by HPLC analysis on a Chiralcel AS column.

lation of the samarium atom and the oxygen atoms in the substrate may play an important role in the asymmetric induction. The exact transition-state model and mechanistic explanation of this study remain unclear at this time.[17]

Encouraged by these results, we tested other symmetrical ketone substrates, including cyclohexanone, 4-phenylcyclohexanone, and 4,4′-dimethylbenzophenone in the presence of (−)-**6**.[18] Their results are presented in Table 3, entries 7−9. For the aliphatic cyclohexanone, the reaction afforded spiro lactone **21** in quantitative yield and 76% ee. Changing the 4-substituent from hydrogen to a phenyl group led to a slightly lower yield and an increase to 87% ee.

The success in the synthesis of highly optically active **1**, **21**, **22**, and **23** prompted us to extend this new reaction system to the preparation of γ-butyrolactones with two chiral centers, α-C and γ-C. Treatment of chiral methacrylate **18** with unsymmetrical ketones under optimized conditions for several hours afforded the diastereomeric *trans* and *cis* lactones, which could be separated by column chromatography. Table 4 summarizes the results of this asymmetric coupling reaction. The diastereoselection of the *trans* products are superior to their *cis* analogues with ratios up to 79:21. The *trans* isomers were obtained with excellent ee values in all cases; extremely high *ee* values (>99%) were achieved with acetophenone and propiophenone (entries 1 and 2). In contrast, for the *cis* products, much lower enantioselectivities were observed; the ee values were found to be largely dependent on the structure of the ketones. Interestingly, when α-tetralone was used, both *trans* and *cis* spiro lactones **31** were obtained with very good enantiomeric excesses of 97% and 75%, respectively (entry 8).

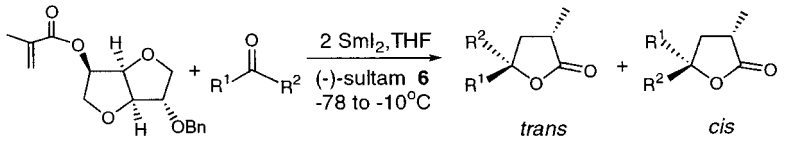
The configuration of this type of *trans* product was solved by X-ray diffraction. Using 4′-bromoacetophenone as starting material, we fortunately obtained the corresponding product *trans*-**27** as a white solid. The absolute configuration was then determined as (2*S*,4*R*) according to X-ray analysis of the single crystal of *trans*-**27** obtained from ethyl acetate−hexane (Figure 1).

Further Extension of the New Reaction System. To gain further insight into the application of this new reaction system, we synthesized 2-ethylacrylate **32** and 2-phenylacrylate **33** from their corresponding 2-alkenoic

(17) A plausible transition state model is shown in Supporting Information.

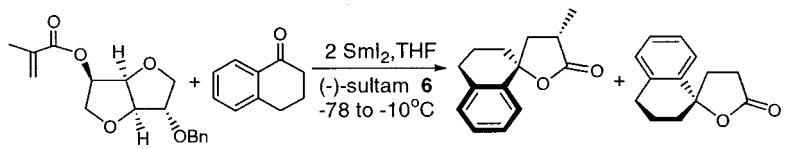
(18) Since (1*S*)-(−)-2,10-camphorsultam (**6**) is commercially available and not expensive, we still use it as the chiral proton source instead of (±)-sultam.

Table 4. Asymmetric Synthesis of α,γ-Substituted γ-Butyrolactones with Chiral Substrate 18 and Unsymmetrical Ketones

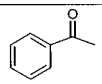
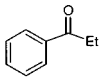
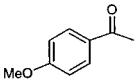
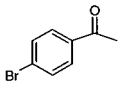
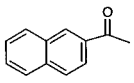
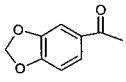


18

24 R^1=Ph, R^2=Me; **25** R^1= Ph, R^2=Et
26 R^1=*p*-MeO-C_6H_4, R^2=Me; **27** R^1=*p*-Br-C_6H_4, R^2=Me
28 R^1=2-naphthyl, R^2=Me; **29** R^1=*o*-MeO-C_6H_4, R^2=Me
30 R^1=3,4-methylenedioxy-phenyl, R^2=Me



18 *trans*-**31** *cis*-**31**

entry	ketone	product	*trans*/*cis*[a]	*trans* *ee*(%)[b]	*cis* *ee*(%)[b]	yield (%)[c]
1		**24**	79/21	>99[d]	---[f]	74
2		**25**	61/39	>99	19	73
3		**26**	76/24	95	24[e]	81
4		**27**	77/23	96	14[d]	61
5		**28**	68/32	98	52	84
6		**29**	61/39	93	35[d]	68
7		**30**	73/27	96	4	84
8		**31**	69/31	97	75	58

[a] *Trans* and *cis* were confirmed by $^1H-^1H$ NOESY in light of their NOE effect; the ratio of *trans*/*cis* were determined by HPLC or GC. [b] The ee values were determined by HPLC analysis on a Chiralcel AD column unless otherwise noted. [c] Total isolated yield of *trans* and *cis* products. [d] Determined by HPLC analysis on a Chiralcel OJ column. [e] Determined by HPLC analysis on a Chiralcel OD column. [f] Not detected.

acids[19] by a reaction with monobenzylated isosorbide in the presence of DCC and DMAP. Examinations were carried out by using **32** or **33** with a variety of ketone substrates in the presence of (−)-**6** as the proton source under the optimized conditions.

As revealed in Table 5, this new reaction system was successful again for the highly enantioselective synthesis of *trans* lactones **34**−**41**, implying a broad substrate scope. An exchange of the R^3 substitutent (from Me to Et to Ph) gave no significant change in the enantioselectivity of the corresponding *trans* products. For example, *trans* lactones **27**, **34**, and **35** were obtained with very similar enantiomeric excesses of 95%, 92%, and 92%,

(19) 2-Alkenoic acids were prepared from the corresponding aldehyde by a literature procedure, see: Outurquin, F.; Paulmier, C. *Synthesis* **1989**, *9*, 690.

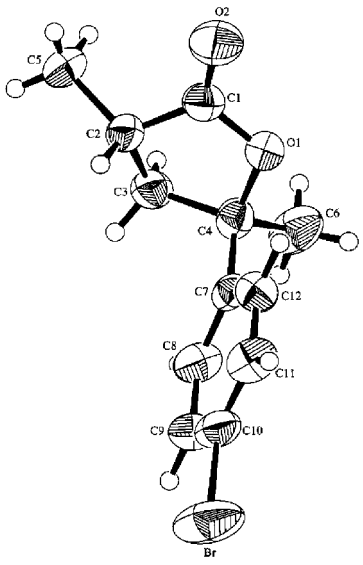
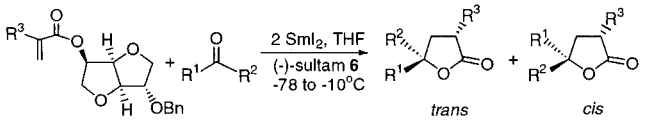


Figure 1. X-ray crystal structure of *trans*-**27**.

Table 5. Application of the New Reaction System in the Asymmetric Synthesis of α,γ-Substituted γ-Butyrolactones Bearingan α-Ethyl or Phenyl Substituent



32 R^3=Et
33 R^3=Ph

34 R^1=*p*-bromo-C_6H_4, R^2=Me, R^3=Et
35 R^1=*p*-bromo-C_6H_4, R^2=Me, R^3=Ph
36 R^1=2-naphthyl, R^2=Me, R^3=Et
37 R^1=2-naphthyl, R^2=Me, R^3=Ph
38 R^1=*o*-MeO-C_6H_4, R^2=Me, R^3=Et
39 R^1=*o*-MeO-C_6H_4, R^2=Me, R^3=Ph
40 R^1=3,4-methylenedioxy-phenyl, R^2=Me, R^3=Et
41 R^1=3,4-methylenedioxy-phenyl, R^2=Me, R^3=Ph

entry	product	*trans*/*cis*[a]	*trans* ee (%)[b]	*cis* ee (%)[b]	yield (%)[c]
1	**34**	69/31	92	*g*	59
2	**35**	64/36	92	22[d]	79
3	**36**	76/24	96	14	61
4	**37**	65/35	89	37[d]	82
5	**38**	80/20	92	*g*	88
6	**39**	56/44	95	0.3[e]	84
7	**40**	78/22	95	30	66
8	**41**	63/37	95	46[f]	84

[a] *Trans* and *cis* were confirmed by $^1H-^1H$ NOESY in light of their NOE effect; the ratio of *trans*/*cis* were determined by HPLC. [b] The ee values were determined by HPLC analysis on a Chiralcel AD column unless otherwise noted. [c] Total isolated yield of *trans* and *cis* products. [d] Determined by HPLC analysis on a Chiralcel OD column. [e] Determined by HPLC analysis on a Chiralcel OJ column. [f] Determined by HPLC analysis on a Chiralcel AS column. [g] Not detected.

respectively (Table 4, entry 4, and Table 5, entries 1 and 2). On the other hand, changing the R^3 substitutent influenced the enantioselectivity of the *cis* products but without the expected improvements (compare Table 4, entries 4, 5, 6, and 7 with Table 5), the best ee was only 46% (entry 8).

Conclusion

In summary, we have developed an efficient, general method for the synthesis of optically active α,γ-substituted γ-butyrolactones by using an excellent reaction system. The combination of a chiral 2-alkylacrylate (**18**, **32**, or **33**) derived from isosorbide and a hindered proton source ((−)-**6**) were crucial to the success of the asymmetric synthesis. By this protocol, a series of chiral α,γ-substituted γ-butyrolactones were efficiently prepared and excellent *e*e values of their *trans* diastereomers were obtained in all cases (up to >99% ee). We believe that this new reaction system should be broadly applicable to the synthesis of other chiral α,γ-substituted γ-butyrolactones. Further studies are currently underway to extend this strategy to prepare more challenging fully substituted optically active γ-butyrolactones.

Experimental Section

General Methods. The ^1H NMR spectra were recorded in $CDCl_3$ at 300 and 400 MHz, and ^{13}C NMR spectra were recorded at 75 or 100 MHz. Chemical shifts are given in ppm relative to internal standard TMS (^1H, 0.0 ppm) or $CDCl_3$ (^{13}C, 77.23 ppm). Mass spectra were recorded by the EI method, and HRMS was measured on a Finnigan MAT-8430 mass spectrometer. IR spectra were recorded on a Digibal FT-IR spectrometer. Elemental analysis was performed on Heraeus Rapid-CHNO. Optical rotations were measured on a Perkin-Elmer 241MC polarimeter. Melting points are uncorrected. THF was dried with sodium/benzophenone, CH_2Cl_2 was distilled from CaH_2 prior to use, and commercially available reagents were used without further purification. All reactions were monitored by TLC with Huanghai analytical silica gel GF_{254} plates. Purification of reaction products was carried out by flash chromatography using 300−400 mesh silica gel.

General Procedure for Preparation of Chiral Methacrylate 18, 2-Ethylacrylate 32 and 2-Phenylacrylate 33. To a solution of 0.5 g of monobenzylated isosorbide in dichloromethane (10 mL) were added DMAP (60 mg) and the corresponding 2-alkenoic acid (1.2 equiv) at 0 °C under nitrogen. After being stirred for 5 min, DCC (1.1 equiv) was slowly added into the reaction flask. The mixture was stirred at 0 °C for 5 h and then allowed to warm to room temperature for another 5 h. The solution was filtered on Celite, and the obtained clear solution was washed with 10% aqueous HCl and then aqueous $NaHCO_3$. The organic layer was dried over anhydrous Na_2SO_4 and evaporated to an oil residue. Silica gel chromatography afforded the pure ester.

Methacrylate 18. Yield 77%. $[\alpha]^{20}_D$ +54.7 (*c* 1.01, $CHCl_3$); FT-IR (film) ν 2929, 1722, 1455, 1297, 1167, 1097, 738, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.96 (s, CH_3, 3H), 3.80−4.00 (m, 3H), 4.01−4.11 (m, 2H), 4.54 (d, J = 4.8 Hz, 1H), 4.57 (s, CH_2Ph, 2H), 4.87 (t, J = 5.1 Hz, 1H), 5.18 (dd, J_1 = 5.4 Hz, J_2 = 10.9 Hz, 1H), 5.61 (s, 1H), 6.15 (s, 1H), 7.28−7.34 (m, PhH, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.43, 70.44, 71.48, 73.17, 74.36, 80.89, 83.37, 86.46, 126.31, 127.82, 127.82, 128.62, 135.91, 137.73, 166.81; EIMS (*m*/*z*, %) 305 (M^+ + 1, 3.84), 304 (M^+, 0.79), 235 (15.24), 181 (6.07), 112 (19.78), 91 (100.00), 69 (59.99), 41 (29.35); HRMS calcd for $C_{17}H_{20}O_5$ 304.1311, found 304.1322.

2-Ethylacrylate 32. Yield 62%. $[\alpha]^{20}_D$ +60.5 (*c* 0.92, $CHCl_3$); FT-IR (film) ν 2971, 2935, 2875, 1722, 1633, 1455, 1369, 1306, 1280, 1258, 1166, 1097, 1062, 975, 946, 738, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.09 (t, 3H, J = 7.5 Hz), 2.34 (q, 2H, J = 7.3 Hz), 3.73−4.10 (m, 5H), 4.52−4.57 (m, 3H), 4.87 (t, 1H, J = 5.1 Hz), 5.19 (q, 1H, J = 5.5 Hz), 5.57 (d, 1H, J = 1.4 Hz), 6.17 (s, 1H), 7.28−7.37 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.70, 24.91, 70.46, 71.48, 73.17, 74.28, 80.90, 83.34, 86.45, 124.40, 127.84, 128.01, 128.64, 137.71, 141.81, 166.73; EIMS (*m*/*z*, %) 319 (M^+ + 1, 13.29), 235 (29.73), 173 (20.18), 145 (17.01), 91 (100.00), 83 (37.69), 69 (14.01), 55 (17.19); HRMS calcd for $C_{18}H_{22}O_5$ 318.1467, found 318.1436.

2-Phenylacrylate 33. Yield 83%. $[\alpha]^{20}_D$ +54.1 (*c* 1.11, $CHCl_3$); FT-IR (film) ν 1725, 1497, 1455, 1311, 1193, 1095, 1028, 777, 739, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.78−4.11 (m, 5H), 4.54−4.57 (m, 3H), 4.93 (t, 1H, J = 5.1 Hz), 5.27 (q, 1H, J = 5.4 Hz), 5.94 (d, 1H, J = 0.85 Hz), 6.37 (d, 1H, J = 0.86 Hz), 7.29−7.46 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ

70.57, 71.56, 73.20, 74.85, 80.91, 83.42, 86.57, 127.21, 127.87, 128.05, 128.28, 128.42, 128.48, 128.68, 136.63, 137.77, 141.08, 166.32; EIMS (*m*/*z*, %) 366 (M^+, 7.85), 235 (38.14), 193 (21.70), 132 (23.16), 103 (80.90), 91 (100.00), 77 (15.15); HRMS calcd for $C_{22}H_{22}O_5$ 366.1467, found 366.1427.

General Procedure of the SmI_2-Mediated Asymmetric Reductive Coupling Reaction for the Preparation of Chiral α,γ-Substituted γ-Butyrolactones. To samarium metal powder (230 mg, 1.5 mmol) in a Schlenk flask was added a solution of diiodomethane (freshly distilled, 0.081 mL, 1.0 mmol) in THF (5 mL) at room temperature under nitrogen. After approximately 1 h, the color of the mixture solution turned to deep blue, indicating the formation of samarium diiodide. The solution was then cooled to −78 °C, and a mixture of α-alkylacrylate (0.5 mmol), ketone (0.5 mmol), and proton source (0.5 mmol) in THF (5 mL) was added. The resulting mixture was stirred for 2 h at the same temperature and then allowed to warm slowly; the reaction was subsequently quenched at −10 °C with 5% aqueous HCl, extracted with diethyl ether, washed with aqueous $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, and then concentrated under reduced pressure. The resulting residue was finally purified by flash-column chromatography on silica gel to afford the optically active γ-butyrolactones.

Determination of the Enantiomeric Excess. The enantiomeric excess was determined by HPLC analysis on a chiralcel OJ, AD, AS, OD column (detected at 254 nm; eluent *n*-hexane/isopropyl alcohol). For comparison, racemic γ-butyrolactones were prepared by the reaction of methyl methacrylate, methyl 2-ethylacrylate, and methyl 2-phenylacrylate with corresponding ketones in the presence of *tert*-butyl alcohol.

(+)-α-Methyl-γ,γ-diphenyl-γ-butyrolactone (1).[20] Mp 118−120 °C; $[\alpha]^{20}_D$ +26.0 (*c* 0.495, $CHCl_3$) for 97% ee; FT-IR (KBr) ν 1774, 1451, 1304, 1230, 1191, 1167, 1039, 987, 935, 749, 707 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.27(d, *J* = 7.0 Hz, CH_3, 3H), 2.47 (t, *J* = 12.1 Hz, 1H), 2.61−2.72 (m, 1H), 3.23 (dd, J_1 = 7.6 Hz, J_2 = 12.3 Hz, 1H), 7.26−7.46 (m, PhH, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.78, 35.28, 44.04, 87.36, 125.44, 125.49, 127.94, 127.97, 128.67, 128.79, 142.80, 144.07, 178.75; EIMS (*m*/*z*, %) 252 (M^+, 47.47), 224 (1.65), 183 (65.03), 175 (33.28), 115 (15.06), 105 (100.00), 77 (34.11), 42 (12.81). Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 80.73; H, 6.50. HPLC (Chiralcel AD, hexane/*i*-PrOH = 80:20 (v/v), flow rate = 0.7 mL/min) t_R = 8.8 min (major), t_R = 10.7 min (minor).

(−)-3-Methyl-1-oxaspiro[4,5]-2-decanone (21).[21] $[\alpha]^{20}_D$ −0.5 (*c* 0.33, $CHCl_3$) for 76% ee; FT-IR (KBr) ν 2929, 2858, 1765, 1449, 1380, 1216, 1137, 969, 956, 931 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.27 (d, 7.2 Hz, 3H), 1.39−1.81 (m, 11H), 2.34 (dd, J_1 = 12.7 Hz, J_2 = 9.2 Hz, 1H), 2.74−2.80 (m, 1H); EIMS (*m*/*z*, %) 169 (M^+ + 1, 12.58), 168 (M^+, 100.00), 150 (29.43), 125 (32.93), 95 (59.08), 87 (76.48), 81 (86.98), 41 (84.68). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.72; H, 9.56. GC (G-PN(astec) 20 m × 0.25 mm, oven 120 °C, det FID, 240 °C, inj 240 °C, carrier N_2, 8.0 psi) t_R = 30.6 min (major), t_R = 33.2 min (minor).

(−)-3-Methyl-8-phenyl-1-oxaspiro[4,5]-2-decanone 22. $[\alpha]^{20}_D$ −11 (*c* 0.27, $CHCl_3$) for 87% ee; FT-IR (KBr): ν 2934, 2858, 1759, 1601, 1494, 1452, 1184, 1064, 1018, 975, 932, 757, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.31 (d, 7.1 Hz, 3H), 1.56−1.69 (m, 3H), 1.83−2.05 (m, 6H), 2.59−2.66 (m, 2H), 2.77−2.83 (m, 1H), 7.20−7.34 (m, 5H); EIMS (*m*/*z*, %) 245 (M^+ + 1, 14.80), 244 (M^+, 49.85), 171 (44.04), 157 (35.94), 143 (30.56), 104 (100.00), 91 (67.42), 55 (38.67). Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.49; H, 8.15. HPLC (Chiralcel AS, hexane/*i*-PrOH = 60:40 (v/v), flow rate = 0.6 mL/min) t_R = 13.6 min (major), t_R = 22.6 min (minor).

(+)-α-Methyl-γ,γ-di(*p*-tolyl)-γ-butyrolactone 23.[20a] $[\alpha]^{20}_D$ +17 (*c* 0.15, $CHCl_3$) for 90% ee; FT-IR (KBr) ν 1774, 1511, 1452, 1304, 1235, 1037, 983, 939 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.27 (d, 7.0 Hz, 3H), 2.31 (s, 6H), 2.42 (t, 12.2 Hz, 1H), 2.61−2.68 (m, 1H), 3.17 (dd, J_1 = 12.2 Hz, J_2 = 7.7 Hz, 1H), 7.11−7.32 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.82, 21.11, 21.15, 35.39, 44.11, 87.45, 125.39, 125.43, 129.28, 129.41, 137.63, 137.66, 140.05, 141.41, 178.94; EIMS (*m*/*z*, %) 280 (M^+, 82.46), 221 (31.45), 211 (100.00), 195 (29.28), 189 (32.05), 129 (12.38), 119 (83.03), 91 (27.20). Anal. Calcd for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19. Found: C, 81.85; H, 7.15. HPLC (Chiralcel AD, hexane/*i*-PrOH = 80:20 (v/v), flow rate = 0.7 mL/min) t_R = 9.9 min (major), t_R = 12.6 min (minor).

(2*S*,4*R*)-(+)-*trans*-α,γ-Dimethyl-γ-phenyl-γ-butyrolactone (*trans*-24). $[\alpha]^{20}_D$ +39.0 (*c* 0.32, $CHCl_3$) for >99% ee; FT-IR (film) ν 2980, 1771, 1448, 1228, 1142, 1047, 953, 768, 701 cm^{-1}; ^1H NMR(400 MHz, $CDCl_3$) δ 1.25 (d, 7.1 Hz, C-2 CH_3, 3H), 1.73 (s, C-4 CH_3, 3H), 2.04 (dd, J_1 = 10.1 Hz, J_2 = 12.2 Hz, H_3, 1H), 2.46−2.54 (m, H_2, 1H), 2.78 (dd, J_1 = 8.1 Hz, J_2 = 12.2 Hz, $H_{3'}$, 1H), 7.28−7.37 (m, PhH, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.90, 30.51, 35.19, 45.24, 84.69, 124.41, 127.77, 128.78, 144.11, 179.38; EIMS (*m*/*z*, %) 190 (M^+, 2.15), 175 (71.94), 145 (2.25), 131 (27.06), 105 (100.00), 91 (16.04), 77 (26.88), 43 (31.11); HRMS calcd for $C_{12}H_{14}O_2$ 190.0994, found 190.1008. HPLC (Chiralcel OJ, hexane/*i*-PrOH = 80:20 (v/v), flow rate = 0.7 mL/min) t_R = 10.6 min (major), t_R = 12.9 min (minor).

***cis*-α,γ-Dimethyl-γ-phenyl-γ-butyrolactone (*cis*-24).** FT-IR (film) ν 2976, 1772, 1448, 1308, 1219, 1155, 1110, 953, 765, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.25 (d, *J* = 7.1 Hz, C-2 CH_3, 3H), 1.67 (s, C-4 CH_3, 3H), 2.04−2.12 (dd, J_1 = 10.8 Hz, J_2 = 12.5 Hz, H_3, 1H), 2.71 (dd, J_1 = 8.8 Hz, J_2 = 12.6 Hz, $H_{3'}$, 1H), 2.89−2.97 (m, H_2, 1H), 7.29−7.40 (m, PhH, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.58, 28.95, 35.44, 44.15, 84.60, 124.06, 127.67, 128.72, 145.54, 178.97; EIMS (*m*/*z*, %)190 (M^+, 2.91), 175 (100.00), 145 (5.08), 105 (85.88), 91 (18.27), 77 (30.93), 51 (13.92), 43 (16.74); HRMS calcd for $C_{12}H_{14}O_2$ 190.0994, found 190.1010.

(2*S*,4*R*)-*trans*-α-Methyl-γ-ethyl-γ-phenyl-γ-butyrolactone (*trans*-25). FT-IR (film) ν 2974, 1776, 1450, 1205, 965, 930, 762, 708 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.81 (t, *J* = 7.4 Hz, CH_2CH_3, 3H), 1.25 (d, 7.0 Hz, C-2 CH_3, 3H), 1.90−2.10 (m, CH_2, H_3, 3H), 2.43−2.57 (m, H_2, 1H), 2.72 (dd, J_1 = 8.2 Hz, J_2 = 12.2 Hz, $H_{3'}$, 1H), 7.25−7.47 (m, PhH, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 8.43, 14.86, 34.83, 35.86, 43.53, 87.60, 125.11, 127.71, 128.65, 142.39, 179.53; EIMS (*m*/*z*, %) 205 (M^+ + 1, 0.19), 204 (M^+, 0.10), 175 (49.21), 131 (8.62), 105 (100.00), 91 (12.06), 77 (32.43), 51 (13.21); HRMS calcd for $C_{13}H_{16}O_2$ 204.1150, found 204.1193. HPLC (Chiralcel AD, hexane/*i*-PrOH = 80:20 (v/v), flow rate = 0.7 mL/min) t_R = 5.9 min (major), t_R = 7.1 min (minor).

***cis*-α-Methyl-γ-ethyl-γ-phenyl-γ-butyrolactone (*cis*-25).** FT-IR (film) ν 2974, 1774, 1450, 1198, 1114, 967, 937, 761, 703 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.81 (t, *J* = 7.4 Hz, CH_2CH_3, 3H), 1.23 (d, *J* = 7.1 Hz, CH_3, 3H), 1.86−2.12 (m, CH_2, H_3, 3H), 2.76 (dd, J_1 = 9.2 Hz, J_2 = 12.5 Hz, $H_{3'}$, 1H), 2.84−2.97 (m, H_2, 1H), 7.26−7.41 (m, PhH, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 8.39, 16.00, 34.90, 35.34, 42.79, 87.47, 124.64, 127.48, 128.46, 143.97, 179.23; EIMS (*m*/*z*, %) 205 (M^+ + 1, 10.29), 187 (4.46), 175 (51.15), 159 (5.01), 105 (100.00), 91 (14.47), 77 (29.81), 51 (12.47); HRMS calcd for $C_{13}H_{16}O_2$ 204.1150, found 204.1122. HPLC (Chiralcel AD, hexane/*i*-PrOH = 90:10 (v/v), flow rate = 0.7 mL/min) t_R = 7.8 min (major), t_R = 8.5 min (minor).

(2*S*,4*R*)-(+)-*trans*-α,γ-Dimethyl-γ-(4-methoxyphenyl)-γ-butyrolactone (*trans*-26). $[\alpha]^{20}_D$ +17.6 (*c* 0.55, $CHCl_3$) for 95% ee; FT-IR (KBr) ν 1769, 1512, 1257, 1228, 1140, 1030, 953, 832 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.25 (d, 7.1 Hz, C-2 CH_3, 3H), 1.70 (s, CH_3, 3H), 2.00 (dd, J_1 = J_2 = 12.2 Hz,, H_3, 1H), 2.47−2.56 (m, H_2, 1H), 2.74 (dd, J_1 = 8.2 Hz, J_2 = 12.4 Hz, $H_{3'}$, 1H), 6.89 (m, PhH, 2H), 7.28 (m, PhH, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.90, 30.70, 35.30, 45.15, 55.53, 84.68, 114.08, 125.68, 136.08, 159.15, 179.55; EIMS (*m*/*z*, %) 220 (M^+, 19.76), 205 (66.92), 175 (3.40), 161 (15.43), 151 (16.85), 135 (100.00), 77 (19.29), 41 (17.30); HRMS calcd for $C_{13}H_{16}O_3$ 220.1100, found 220.1095. HPLC (Chiralcel AD, hexane/*i*-PrOH = 80:20 (v/v), flow rate = 0.7 mL/min) t_R = 7.4 min (major), t_R = 9.8 min (minor).

(20) Known as a racemic compound, see: (a) Baddar, F. G.; El-Assal, L. S.; Habashi, A. *J. Chem. Soc.* **1957**, 1690. (b) Fujimoto, N.; Nishino, H.; Kurosawa, K. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 3161.

(21) Known as a racemic compound, see: Piva, O. *Tetrahedron* **1994**, *50*, 13687.

***cis*-α,γ-Dimethyl-γ-(4-methoxyphenyl)-γ-butyrolactone (*cis*-26).** FT-IR (KBr) ν 1770, 1614, 1515, 1322, 1250, 1035, 948, 915, 828 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (d, 7.1 Hz, C-2 CH_3, 3H), 1.66 (s, CH_3, 3H), 2.08 (dd, J_1 = 11.0 Hz, J_2 = 12.4 Hz,, H_3, 1H), 2.68 (dd, J_1 = 8.8 Hz, J_2 = 12.5 Hz, $H_{3'}$, 1H), 2.90−2.98 (m, H_2, 1H), 6.88−6.93 (m, PhH, 2H), 7.27−7.35 (m, PhH, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.63, 28.95, 35.56, 44.29, 55.48, 84.54, 114.03, 125.43, 137.71, 159.09, 179.07; EIMS (*m*/*z*, %) 220 (M^+, 15.87), 205 (72.28), 175 (2.09), 161 (11.31), 151 (14.43), 135 (100.00), 77 (16.60), 43 (22.10); HRMS calcd for $C_{13}H_{16}O_3$ 220.1100, found 220.1136; HPLC (Chiralcel OD, hexane/*i*-PrOH = 90:10 (v/v), flow rate = 0.7 mL/min) t_R = 11.7 min (major), t_R = 12.7 min (minor).

(2*S*,4*R*)-(+)-*trans*-α,γ-Dimethyl-γ-(4-bromophenyl)-γ-butyrolactone (*trans*-27). $[\alpha]^{20}_D$ +19.2 (*c* 0.49, $CHCl_3$) for 96% ee; FT-IR (KBr) ν 1771, 1484, 1449, 1228, 1142, 1087, 1009, 957, 823 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (d, 7.0 Hz, C-2 CH_3, 3H), 1.71 (s, C-4 CH_3, 3H), 2.04 (dd, J_1 = J_2 = 12.2 Hz,, H_3, 1H), 2.43−2.57 (m, H_2, 1H), 2.73 (dd, J_1 = 8.2 Hz, J_2 = 12.3 Hz, $H_{3'}$, 1H), 7.26 (m, PhH, 2H), 7.50 (m, PhH, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.91, 30.44, 35.14, 45.07, 84.27, 121.86, 126.31, 131.95, 143.22, 179.09; EIMS (*m*/*z*, %) 271 (M^+ + 2, 27.38), 269 (M^+, 31.09), 255 (87.54), 253 (89.43), 185 (69.67), 183 (74.58), 130 (54.98), 76 (33.02), 42 (100.00); HRMS calcd for $C_{12}H_{13}O_2Br$ 268.0099, found 268.0061; HPLC (Chiralcel AD, hexane/*i*-PrOH = 80:20 (v/v), flow rate = 0.7 mL/min) t_R = 7.0 min (major), t_R = 8.1 min (minor).

Data for the X-ray structure analysis: crystals from EtoAc/hexane, $C_{12}H_{13}O_2Br$ (M_r = 269.14); colorless, prismatic; crystal dimensions 0.20 × 0.20 × 0.30 mm^3; orthorhombic; space group $P2_12_12_1$ (No. 19); a = 8.101(3), b = 25.457(3), and c = 5.886(3) Å, Z = 4, V = 1213.8(8) Å^3, F(000)=544.00, ρ_{calcd} = 1.473 g/cm^3,; T = 293K; $2\theta_{max}$ = 55.0 °C; 3348 reflections measured, 1674 were unique (R_{int} = 0.066), and 1338 observed ($I > 3\sigma(I)$); Rigaku AFC7R diffractometer, Mo Kα radiation (λ = 0.71069 Å), graphite monochromator; Lorentz-polarization absorption correction (μ = 33.75 cm^{-1}). The structure was solved by Patterson methods and refined with the full-matrix least-squares method; R = 0.054, wR = 0.061; reflection/parameter ratio 9.77; residual electon density +0.74/−0.45 e Å^{-3}.

***cis*-α,γ-Dimethyl-γ-(4-bromophenyl)-γ-butyrolactone (*cis*-27).** FT-IR (film) ν 2972, 1769, 1488, 1378, 1316, 1224, 1206, 1158, 1057, 1009, 953, 916, 822 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26(d, 7.1 Hz, C-2 CH_3, 3H), 1.65 (s, C-4 CH_3, 3H), 2.04 (dd, J_1 = 11.0 Hz, J_2 = 9.0 Hz,, H_3, 1H), 2.70 (dd, J_1 = 8.8 Hz, J_2 = 12.6 Hz, $H_{3'}$, 1H), 2.87−2.99 (m, H_2, 1H), 7.26 (m, PhH, 2H), 7.50 (m, PhH, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.56, 28.83, 35.38, 44.05, 84.06, 121.64, 125.93, 131.85, 144.60, 178.61; EIMS (*m*/*z*, %) 270 (M^+ + 1, 12.31), 269 (M^+, 6.08), 268 (M^+ − 1, 12.85), 255 (100.00), 185 (79.40), 183 (80.29), 130 (37.17), 42 (61.34); HRMS calcd for $C_{12}H_{13}O_2Br$ 268.0099, found 268.0117; HPLC (Chiralcel OJ, hexane/*i*-PrOH = 90:10 (v/v), flow rate = 0.7 mL/min) t_R = 16.8 min (major), t_R = 18.9 min (minor).

(2*S*,4*R*)-(−)-*trans*-α,γ-Dimethyl-γ-(2-naphthyl)-γ-butyrolactone (*trans*-28). $[\alpha]^{20}_D$ −6.0 (*c* 0.725, $CHCl_3$) for 98% ee; FT-IR (KBr) ν 2979, 1768, 1460, 1381, 1228, 1137, 1030, 952, 822, 753 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (d, 7.0 Hz, C-2 CH_3, 3H), 1.81 (s, C-4 CH_3, 3H), 2.10 (t, 12.2 Hz, H_3, 1H), 2.51−2.63 (m, H_2, 1H), 2.88 (dd, J_1 = 12.4 Hz, J_2 = 8.1 Hz, H_3, 1H), 7.41−7.51 (m, ArH, 3H), 7.81−7.87 (m, ArH, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.95, 30.41, 35.23, 45.08, 84.84, 122.79, 123.02, 126.55, 126.84, 127.74, 128.40, 128.85, 132.80, 133.17, 141.26, 179.53; EIMS (*m*/*z*, %) 241 (M^+ + 1, 25.17), 240 (M^+, 63.51), 225 (91.57), 181 (26.18), 166 (15.97), 165 (21.66), 155 (100.00), 127 (38.02); HRMS calcd for $C_{16}H_{15}O_2$ 240.1151, found 240.1163; HPLC (Chiralcel AD, hexane/*i*-PrOH = 80:20 (v/v), flow rate = 0.7 mL/min) t_R = 7.7 min (major), t_R = 14.5 min (minor).

(+)-*cis*-α,γ-Dimethyl-γ-(2-naphthyl)-γ-butyrolactone (*cis*-28). $[\alpha]_D^{20}$ +10.2 (*c* 0.50, $CHCl_3$) for 52% ee; FT-IR (KBr) ν 2976, 1772, 1455, 1380, 1306, 1219, 1154, 1105, 1054, 954, 821, 751 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (d, 7.1 Hz, C-2 CH_3, 3H), 1.76 (s, C-4 CH_3, 3H), 2.18 (dd, J_1 = 12.3 Hz, J_2 = 10.8 Hz, H_3, 1H), 2.78 (dd, J_1 = 12.5 Hz, J_2 = 8.8 Hz, H_3, 1H), 2.92−3.03 (m, H_2, 1H), 7.43−7.51 (m, ArH, 3H), 7.82−7.88 (m, ArH, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.72, 28.96, 35.56, 44.21, 84.79, 122.52, 122.62, 126.43, 126.71, 127.79, 128.39, 128.75, 132.78, 133.26, 142.79, 179.09; EIMS (*m*/*z*, %) 241 (M^+ + 1, 36.95), 240 (M^+, 70.24), 225 (100.00), 195 (17.54), 181 (21.94), 165 (19.53), 155 (99.38), 127 (30.87); HRMS calcd for $C_{16}H_{15}O_2$ 240.1151, found 240.1160. HPLC (Chiralcel AD, hexane/*i*-PrOH = 90:10 (v/v), flow rate = 0.7 mL/min) t_R = 11.1 min (major), t_R = 12.0 min (minor).

(2*S*,4*R*)-(+)-*trans*-α,γ-Dimethyl-γ-(2-methoxyphenyl)-γ-butyrolactone (*trans*-29). $[\alpha]^{20}_D$ = +68.7 (*c* 0.255, $CHCl_3$) for 93% ee; FT-IR (film) ν 2975, 2937, 1774, 1601, 1585, 1490, 1438, 1374, 1305, 1290, 1262, 1241, 1228, 1179, 1145, 1132, 1074, 1044, 1027, 953, 757 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (d, 3H, J = 7.1 Hz), 1.78 (s, 3H), 1.92 (dd, 1H, J_1 = 12.8 Hz, J_2 = 11.6 Hz), 2.40−2.51 (m, 1H), 3.06 (dd, 1H, J_1 = 12.8 Hz, J_2 = 11.6 Hz), 3.87 (s, 3H), 6.91−6.96 (m, 2H), 7.26−7.30 (m, 1H), 7.41 (dd, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.19, 27.63, 35.33, 43.04, 55.33, 84.56, 111.42, 120.86, 125.67, 129.19, 131.72, 155.48, 180.05; EIMS (*m*/*z*, %) 220 (M^+, 35.37), 205 (99.68), 177 (49.10), 175 (16.60), 161 (19.95), 135 (100.00), 91 13.99), 77 (17.46); HRMS calcd for $C_{13}H_{16}O_3$ 220.1100, found 220.1142; HPLC (Chiralcel AD, hexane/*i*-PrOH = 90:10 (v/v), flow rate = 0.7 mL/min) t_R = 7.2 min (major), t_R = 8.1 min (minor).

(+)-*cis*-α,γ-Dimethyl-γ-(2-methoxyphenyl)-γ-butyrolactone (*cis*-29). $[\alpha]^{20}_D$ +24.5 (*c* 0.175, $CHCl_3$) for 35% ee; FT-IR (film) ν 2973, 2937, 1772, 1602, 1586, 1492, 1465, 1438, 1377, 1310, 1282, 1245, 1221, 1155, 1110, 1027, 953, 917, 817, 757 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23 (d, 3H, J = 6.6 Hz), 1.69 (s, 3H), 2.02−2.10 (m, 1H), 2.84−2.92 (m, 2H), 3.85 (s, 3H), 6.90−6.98 (m, 2H), 7.26−7.30 (m, 1H), 7.55 (dd, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.62, 26.55, 34.97, 43.13, 55.42, 84.43, 111.37, 120.86, 125.35, 128.96, 133.48, 155.55, 179.26; EIMS (*m*/*z*, %) 221 (M^+ + 1, 23.96), 220 (M^+, 35.53), 205 (100.00), 203 (24.28), 177 (31.56), 175 (55.76), 161 (12.64), 135 (62.25); HRMS calcd for $C_{13}H_{16}O_3$ 220.1100, found 220.1125; HPLC (Chiralcel OJ, hexane/*i*-PrOH = 80:20 (v/v), flow rate = 0.7 mL/min) t_R = 9.9 min (major), t_R = 12.2 min (minor).

(2*S*,4*R*)-(+)-*trans*-α,γ-Dimethyl-γ-(3,4-methylenedioxyphenyl)-γ-butyrolactone (*trans*-30). $[\alpha]^{20}_D$ +22 (*c* 0.27, $CHCl_3$) for 96% ee; FT-IR (KBr) ν 2983, 1764, 1610, 1510, 1490, 1453, 1431, 1373, 1259, 1231, 1145, 1101, 1042, 956, 938, 923, 870, 703 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17 (d, 3H, J = 7.0 Hz), 1.61 (s, 3H), 1.92 (t, 1H, J = 12.1 Hz), 2.41−2.50 (m, 1H), 2.65 (dd, 1H, J_1 = 12.2 Hz, J_2 = 8.2 Hz), 5.88 (d, 2H, J = 0.4 Hz), 6.68−6.77 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.86, 30.68, 35.20, 45.15, 84.58, 111.42, 105.51, 108.27, 117.57, 138.07, 147.14, 148.15, 179.26; EIMS (*m*/*z*, %) 234 (M^+, 53.03), 219 (82.77), 165 (12.00), 164 (10.72), 149 (100.00), 145 (13.25), 121 (8.27), 43 (8.78); HRMS calcd for $C_{13}H_{14}O_4$ 234.0892, found 234.0892; HPLC (Chiralcel AD, hexane/*i*-PrOH = 80:20 (v/v), flow rate = 0.7 mL/min) t_R = 8.8 min (major), t_R = 12.9 min (minor).

(+)-*cis*-α,γ-Dimethyl-γ-(3,4-methylenedioxyphenyl)-γ-butyrolactone (*cis*-30). $[\alpha]^{20}_D$ +3 (*c* 0.175, $CHCl_3$) for 4% ee; FT-IR (KBr) ν 2969, 1762, 1609, 1507, 1494, 1462, 1442, 1379, 1313, 1255, 1212, 1098, 1037, 953, 930, 906, 869, 815, 703 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (d, 3H, J = 7.1 Hz), 1.64 (s, 3H), 2.06 (dd, 1H, J_1 = 12.2 Hz, J_2 = 11.0 Hz), 2.65 (dd, 1H, J_1 = 12.5 Hz, J_2 = 8.8 Hz), 2.87−2.96 (m, 1H), 5.96 (s, 2H), 6.77−6.88 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.62, 29.07, 35.53, 44.32, 84.52, 101.36, 105.30, 108.31, 117.33, 139.63, 147.03, 148.02, 178.85; EIMS (*m*/*z*, %) 234 (M^+, 53.70), 219 (87.93), 149 (100.00), 145 (13.88), 121 (9.15), 65 (8.61), 43 (9.50), 42 (9.05); HRMS calcd for $C_{13}H_{14}O_4$ 234.0892, found 234.0868; HPLC (Chiralcel AD, hexane/*i*-PrOH = 90:10 (v/v), flow rate = 0.7 mL/min) t_R = 15.0 min (major), t_R = 16.2 min (minor).

(3*S*,5*R*)-(−)-*trans*-Spiro[(dihydro-3-methyl-2(3*H*)-furanone)-5,1′-(1′,2′,3′,4′-tetrahydronaphthalene)] (*trans*-31). $[\alpha]^{20}_D$ −12.0 (*c* 1.00, $CHCl_3$) for 97% ee; FT-IR (KBr) ν 2938, 1768, 1492, 1454, 1279, 1227, 1161, 1065, 999, 879, 764, 727

cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (d, 7.2 Hz, C-2 CH_3, 3H), 1.93−2.03 (m, H_3, $H_{2'}$, $H_{3'}$, 3H), 2.18−2.26 (m, $H_{2'}$, 1H), 2.69 (dd, J_1 = 13.1 Hz, J_2 = 9.9 Hz, H_3, 1H), 2.82−2.88 (m, $H_{4'}$, 2H), 3.06 (m, H_2, 1H), 7.11−7.26 (m, ArH, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.98, 19.44, 28.78, 35.379, 38.22, 44.92, 83.62, 124.92, 126.55, 128.16, 129.50, 136.66, 139.12, 179.95; EIMS (*m*/*z*, %) 216 (M^+, 37.20), 147 (87.73), 146 (62.45), 129 (100.00), 128 (75.67), 118 (92.53), 115 (59.08), 90 (55.94); HRMS calcd for $C_{14}H_{16}O_2$ 216.1151, found 216.1176; HPLC (Chiralcel AD, hexane/*i*-PrOH = 60:40 (v/v), flow rate = 0.7 mL/min) t_R = 6.4 min (major), t_R = 7.7 min (minor).

(−)-*cis*-Spiro[(dihydro-3-methyl-2(3*H*)-furanone)-5,1′-(1′,2′,3′,4′-tetrahydronaphthalene)] (*cis*-31). $[\alpha]^{20}_D$ −17 (*c* 0.25, $CHCl_3$) for 75% ee; FT-IR (KBr) ν 2949, 1760, 1494, 1454, 1322, 1227, 1168, 1091, 977, 933, 767 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (d, 7.1 Hz, C-2 CH_3, 3H), 1.80−1.89 (m, $H_{2'}$, 1H), 1.98−2.09 (m, H_3, $H_{2'}$, $H_{3'}$, 4H), 2.66 (dd, J_1 = 13.1 Hz, J_2 = 8.9 Hz, H_3, 1H), 2.80−2.87 (m, $H_{4'}$, 2H), 2.90−2.96 (m, H_2, 1H), 7.08−7.36 (m, ArH, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.68, 20.56, 29.25, 34.41, 35.28, 45.09, 83.81, 126.70, 126.79, 128.14, 128.96, 137.49, 138.548, 179.46; EIMS (*m*/*z*, %) 216 (M^+, 35.01), 147 (80.01), 146 (62.13), 129 (100.00), 128 (80.32), 118 (83.17), 115 (55.35), 90 (52.00); HRMS calcd for $C_{14}H_{16}O_2$ 216.1151, found 216.1155; HPLC (Chiralcel AD, hexane/*i*-PrOH = 60:40 (v/v), flow rate = 0.7 mL/min) t_R = 7.8 min (major), t_R = 7.3 min (minor).

(+)-*trans*-α-Ethyl-γ-methyl-γ-(4-bromophenyl)-γ-butyrolactone (*trans*-34). $[\alpha]^{20}_D$ +17.7 (*c* 0.39, $CHCl_3$) for 92% ee; FT-IR (film) ν 2967, 1775, 1593, 1487, 1380, 1221, 1139, 1085, 1009, 953, 828 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (t, 3H, *J* = 7.5 Hz), 1.48−1.56 (m, 1H), 1.71 (s, 3H), 1.87−1.94 (m, 1H), 2.05 (t, 1H, *J* = 12.2 Hz), 2.34−2.43 (m, 1H), 2.67 (dd, 1H, J_1 = 12.4 Hz, J_2 = 8.3 Hz), 7.24−7.27 (m, 2H), 7.48−7.51 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.77, 23.21, 30.45, 41.56, 42.53, 84.31, 121.80, 126.28, 131.92, 143.41, 178.28; EIMS (*m*/*z*, %) 285 (M^+ + 3, 41.39), 283 (M^+ + 1, 44.90), 269 (94.93), 267 (100.00), 185 (61.43), 183 (63.74), 130 (36.03), 115 (18.70); HRMS calcd for $C_{13}H_{15}O_2Br$ 282.0255, found 282.0222; HPLC (Chiralcel AD, hexane/*i*-PrOH = 90:10 (v/v), flow rate = 0.7 mL/min) t_R = 8.2 min (major), t_R = 9.0 min (minor).

***cis*-α-Ethyl-γ-methyl-γ-(4-bromophenyl)-γ-butyrolactone (*cis*-34).** FT-IR (film) ν 2975, 1763, 1487, 1378, 1218, 1206, 1155, 1115, 1079, 1009, 952, 823 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.97 (t, 3H, *J* = 7.4 Hz), 1.40−1.51 (m, 1H), 1.65 (s, 3H), 1.85−1.95 (m, 1H), 2.05 (dd, 1H, J_1 = 12.5 Hz, J_2 = 10.7 Hz), 2.63 (dd, 1H, J_1 = 12.5 Hz, J_2 = 8.9 Hz), 2.76−2.83 (m, 1H), 7.25−7.28 (m, 2H), 7.49−7.51 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.83, 23.80, 29.08, 41.65, 41.99, 84.25, 121.69, 125.98, 131.90, 144.72, 177.92; EIMS (*m*/*z*, %) 284 (M^+, 9.20), 282 (M^+, 8.97), 269 (97.18), 267 (100.00), 185 (62.27), 183 (63.57), 130 (21.86), 129 (13.59); HRMS calcd for $C_{13}H_{15}O_2$-Br 282.0255, found 282.0276.

(−)-*trans*-α-Phenyl-γ-methyl-γ-(4-bromophenyl)-γ-butyrolactone (*trans*-35). $[\alpha]^{20}_D$ −35.9 (*c* 0.37, $CHCl_3$) for 92% ee; FT-IR (film) ν 2976, 1770, 1592, 1377, 1262, 1224, 1133, 1100, 1083, 1072, 1009, 973, 950, 931, 836, 820, 765, 755, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.79 (s, 3H), 2.56 (t, 1H, *J* = 12.6 Hz), 2.98 (dd, 1H, J_1 = 12.7 Hz, J_2 = 8.3 Hz), 3.68 (dd, 1H, J_1 = 12.6 Hz, J_2 = 8.3 Hz), 7.24−7.56 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.38, 45.66, 46.41, 84.32, 122.13, 126.35, 127.95, 128.28, 129.09, 132.13, 136.13, 142.86, 176.32; EIMS (*m*/*z*, %) 333 (M^+ + 1, 0.45), 331 (M^+ + 1, 0.50), 273 (21.28), 271 (22.55), 207 (100.00), 193 (24.56), 192 (71.92), 191 (29.53); HRMS calcd for $C_{17}H_{15}O_2Br$ 330.0256, found 330.0266; HPLC (Chiralcel AD, hexane/*i*-PrOH = 80:20 (v/v), flow rate = 0.7 mL/min) t_R = 10.6 min (major), t_R = 15.9 min (minor).

(−)-*cis*-α-Phenyl-γ-methyl-γ-(4-bromophenyl)-γ-butyrolactone (*cis*-35). $[\alpha]^{20}_D$ −2 (*c* 0.15, $CHCl_3$) for 22% ee; FT-IR (film) ν 2978, 1769, 1604, 1487, 1382, 1315, 1307, 1212, 1201, 1130, 1071, 1010, 955, 944, 824, 755, 705, 697 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.77 (s, 3H), 2.59 (t, 1H, *J* = 12.8 Hz), 2.97 (dd, 1H, J_1 = 12.8 Hz, J_2 = 9.0 Hz), 4.14 (dd, 1H, J_1 = 11.8 Hz, J_2 = 9.0 Hz), 7.21−7.54 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.84, 44.88, 46.83, 84.10, 121.94, 126.01, 127.97, 128.28, 129.14, 132.04, 136.44, 144.28, 175.94; EIMS (*m*/*z*, %) 332 (M^+, 1.28), 330 (M^+, 1.23), 288 (18.24), 286 (18.84), 273 (21.97), 271 (23.56), 207 (100.00), 192 (70.96); HRMS calcd for $C_{17}H_{15}O_2Br$ 330.0256, found 330.0277; HPLC (Chiralcel OD, hexane/*i*-PrOH = 80:20 (v/v), flow rate = 0.7 mL/min) t_R = 16.8 min (major), t_R = 21.2 min (minor).

(−)-*trans*-α-Ethyl-γ-methyl-γ-(2-naphthyl)-γ-butyrolactone (*trans*-36). $[\alpha]^{20}_D$ −12 (*c* 0.28, $CHCl_3$) for 96% ee; FT-IR (film) ν 2968, 1778, 1602, 1507, 1380, 1223, 1133, 1065, 953, 861, 821, 751 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (t, 3H, *J* = 7.5 Hz), 1.48−1.59 (m, 1H), 1.81 (s, 3H), 1.86−1.97 (m, 1H), 2.10 (t, 1H, *J* = 12.2 Hz), 2.39−2.47 (m, 1H), 2.81 (dd, 1H, J_1 = 12.4 Hz, J_2 = 8.2 Hz), 7.41−7.51 (m, 3H), 7.82−7.87 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.79, 23.23, 30.39, 41.62, 42.52, 84.88, 122.77, 122.94, 126.50, 127.79, 127.71, 128.36, 128.82, 132.75, 133.13, 141.44, 178.74; EIMS (*m*/*z*, %) 254 (M^+, 55.39), 239 (78.50), 181 (22.57), 166 (15.30), 165 (21.67), 155 (100.00), 152 (14.38), 127 (33.19); HRMS calcd for $C_{17}H_{18}O_2$ 254.1307, found 254.1315; HPLC (Chiralcel AD, hexane/*i*-PrOH = 80:20 (v/v), flow rate = 0.7 mL/min) t_R = 8.7 min (major), t_R = 12.6 min (minor).

(−)-*cis*-α-Ethyl-γ-methyl-γ-(2-naphthyl)-γ-butyrolactone (*cis*-36). $[\alpha]^{20}_D$ −1 (*c* 0.22, $CHCl_3$) for 14% ee; FT-IR (KBr) ν 2938, 1754, 1600, 1358, 1293, 1222, 1111, 1065, 953, 859, 822, 745 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.97 (t, 3H, *J* = 7.4 Hz), 1.41−1.52 (m, 1H), 1.76 (s, 3H), 1.86−1.97 (m, 1H), 2.20 (dd, 1H, J_1 = 12.4 Hz, J_2 = 9.6 Hz), 2.72 (dd, 1H, J_1 = 12.5 Hz, J_2 = 8.9 Hz), 2.81−2.89 (m, 1H), 7.44−7.53 (m, 3H), 7.81−7.88 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.89, 23.89, 29.14, 41.72, 42.12, 84.91, 122.54, 122.62, 126.42, 126.71, 127.79, 128.40, 128.75, 132.77, 133.27, 142.87, 178.32; EIMS (*m*/*z*, %) 254 (M^+, 47.40), 239 (86.97), 181 (17.40), 166 (12.99), 165 (18.85), 155 (100.00), 152 (12.63), 127 (31.30); HRMS calcd for $C_{17}H_{18}O_2$ 254.1307, found 254.1313; HPLC (Chiralcel AD, hexane/*i*-PrOH = 80:20 (v/v), flow rate = 0.7 mL/min) t_R = 8.4 min (major), t_R = 7.8 min (minor).

(−)-*trans*-α-Phenyl-γ-methyl-γ-(2-naphthyl)-γ-butyrolactone (*trans*-37). $[\alpha]^{20}_D$ −96.5 (*c* 0.195 $CHCl_3$) for 89% ee; FT-IR (KBr) ν 2985, 1771, 1602, 1501, 1381, 1263, 1223, 1133, 1102, 1068, 1020, 971, 946, 930, 900, 829, 759, 750, 703, 692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.90 (s, 3H), 2.63 (t, 1H, *J* = 12.6 Hz), 3.14 (dd, 1H, J_1 = 12.6 Hz, J_2 = 8.3 Hz), 3.74 (dd, 1H, J_1 = 12.6 Hz, J_2 = 8.3 Hz), 7.25−7.36 (m, 5H), 7.50−7.55 (m, 3H), 7.87−7.95 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.35, 45.74, 46.56, 84.91, 122.76, 123.14, 126.71, 126.98, 127.81, 127.89, 128.37, 128.47, 129.08 (2), 132.92, 133.22, 136.40, 140.90, 176.80; EIMS (*m*/*z*, %) 302 (M^+, 50.27), 258 (86.78), 243 (100.00), 165 (43.65), 155 (57.67), 127 (40.25), 115 (29.91), 91 (23.55); HRMS calcd for $C_{21}H_{18}O_2$ 302.1306, found 302.1302; HPLC (Chiralcel AD, hexane/*i*-PrOH = 80:20 (v/v), flow rate = 0.7 mL/min) t_R = 13.2 min (major), t_R = 19.4 min (minor).

(+)-*cis*-α-Phenyl-γ-methyl-γ-(2-naphthyl)-γ-butyrolactone (*cis*-37). $[\alpha]^{20}_D$ +32.5 (*c* 0.205, $CHCl_3$) for 37% ee; FT-IR (KBr) ν 3061, 3034, 1760, 1603, 1497, 1386, 1303, 1220, 1199, 1183, 1124, 1080, 1064, 943, 892, 857, 822, 758, 702, 695, 631 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.88 (s, 3H), 2.69 (t, 1H, *J* = 12.4 Hz), 3.07 (dd, 1H, J_1 = 12.8 Hz, J_2 = 9.1 Hz), 4.20 (dd, 1H, J_1 = 11.7 Hz, J_2 = 9.1 Hz), 7.25−7.34 (m, 5H), 7.49−7.54 (m, 3H), 7.83−7.94 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.84, 45.03, 46.98, 84.74, 122.46, 122.78, 126.54, 126.80, 127.84, 127.88, 128.36, 128.44, 128.89, 129.10, 132.88, 133.29, 136.70, 142.43, 176.30; EIMS (*m*/*z*, %) 302 (M^+, 48.23), 258 (47.98), 243 (49.34), 168 (57.44), 155 (66.75), 115 (30.21), 91 (41.04), 43 (100.00); HRMS calcd for $C_{21}H_{18}O_2$ 302.1306, found 302.1293; HPLC (Chiralcel OD, hexane/*i*-PrOH = 80:20 (v/v), flow rate = 0.7 mL/min) t_R = 18.1 min (major), t_R = 21.4 min (minor).

(+)-*trans*-α-Ethyl-γ-methyl-γ-(2-methoxyphenyl)-γ-butyrolactone (*trans*-38). $[\alpha]^{20}_D$ +75.0 (*c* 0.39, $CHCl_3$) for 92% ee; FT-IR (film) ν 2959, 1766, 1602, 1489, 1373, 1380, 1230, 1073, 1024, 962, 947, 715 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (t, 3H, 7.5 Hz), 1.45−1.56 (m, 1H), 1.78 (s, 3H), 1.83−1.92 (m, 1H), 1.94 (dd, 1H, J_1 = 12.7 Hz, J_2 = 11.7 Hz), 2.31−2.39 (m, 1H), 2.98 (dd, 1H, J_1 = 12.8 Hz, J_2 = 8.7 Hz), 3.88 (s, 3H), 6.92−6.95 (m, 2H), 7.26−7.29 (m, 1H), 7.42 (dd, 1H, J_1 = 8.6 Hz, J_2 = 1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.79,

23.55, 27.66, 40.43, 41.74, 55.33, 84.63, 111.42, 120.80, 125.61, 129.16, 131.88, 155.47, 179.31; EIMS (*m*/*z*, %) 235 ($M^+ + 1$, 12.67), 234 (M^+, 29.68), 219 (100.00), 217 (11.96), 191 (33.84), 189 (37.97), 151 (11.38), 135 (80.74); HRMS calcd for $C_{14}H_{18}O_3$ 234.1256, found 234.1228; HPLC (Chiralcel AD, hexane/*i*-PrOH = 95:5 (v/v), flow rate = 0.7 mL/min) t_R = 8.3 min (major), t_R = 9.8 min (minor).

***cis*-α-Ethyl-γ-methyl-γ-(2-methoxyphenyl)-γ-butyrolactone (*cis*-38).** FT-IR (film) ν 2966, 1770, 1602, 1586, 1491, 1374, 1216, 1153, 1113, 1027, 956, 805, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.96 (t, 3H, J = 7.4 Hz), 1.39−1.49 (m, 1H), 1.70 (s, 3H), 1.84−1.95 (m, 1H), 2.08 (dd, 1H, J_1 = 12.3 Hz, J_2 = 9.8 Hz), 2.69−2.88 (m, 2H), 3.86 (s, 3H), 6.91−6.99 (m, 2H), 7.26−7.31 (m, 1H), 7.55 (dd, 1H, J_1 = 7.7 Hz, J_2 = 1.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.92, 23.89, 26.69, 40.64, 41.56, 55.42, 84.62, 111.35, 120.84, 125.34, 128.92, 133.52, 155.51, 178.48; EIMS (*m*/*z*, %) 234 (M^+, 23.54), 219 (100.00), 191 (37.48), 189 (13.55), 135 (78.46), 133 (8.50), 91 (7.69), 77 (9.31); HRMS calcd for $C_{14}H_{18}O_3$ 234.1256, found 234.1292.

(+)-*trans*-α-Phenyl-γ-methyl-γ-(2-methoxyphenyl)-γ-butyrolactone (*trans*-39). $[\alpha]^{20}_D$ +27.4 (*c* 0.425, $CHCl_3$) for 95% ee; FT-IR (film) ν 2941, 1778, 1765, 1601, 1583, 1490, 1379, 1284, 1254, 1248, 1226, 1136, 1064, 1022, 948, 933, 765, 757, 748, 705, 693, 642 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.86 (s, 3H), 2.45 (t, 3H, J = 12.6 Hz), 3.34 (dd, 1H, J_1 = 13.0 Hz, J_2 = 8.8 Hz), 3.65 (dd, 1H, J_1 = 12.2 Hz, J_2 = 8.8 Hz), 3.87 (s, 3H), 3.95−7.00 (m, 2H), 7.25−7.35 (m, 6H), 7.52 (dd, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.59, 43.66, 46.73, 55.38, 84.66, 111.54, 121.01, 125.79, 127.62, 128.30, 128.94, 129.45, 131.35, 136.98, 155.56, 177.27; EIMS (*m*/*z*, %) 282 (M^+, 12.01), 238 (41.59), 223 (100.00), 207 (53.92), 205 (36.95), 178 (38.05), 145 (33.12), 135 (49.10); HRMS calcd for $C_{18}H_{18}O_3$ 282.1256, found 282.1254; HPLC (Chiralcel AD, hexane/*i*-PrOH = 80:20 (v/v), flow rate = 0.7 mL/min) t_R = 9.5 min (major), t_R = 13.6 min (minor).

(+)-*cis*-α-Phenyl-γ-methyl-γ-(2-methoxyphenyl)-γ-butyrolactone (*cis*-39). $[\alpha]^{20}_D$ +11.6 (*c* 0.57, $CHCl_3$) for 0.3% ee; FT-IR (film) ν 1765, 1602, 1586, 1492, 1380, 1311, 1244, 1217, 1125, 1025, 952, 771, 755, 705, 696, 638 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.80 (s, 3H), 2.55 (dd, 1H, J_1 = 13.2 Hz, J_2 = 12.0 Hz), 3.21 (dd, 1H, J_1 = 13.4 Hz, J_2 = 9.4 Hz), 3.82 (s, 3H), 4.09 (dd, 1H, J_1 = 11.7 Hz, J_2 = 9.4 Hz), 6.90−6.99 (m, 2H), 7.22−7.32 (m, 6H), 7.6 2(dd, 1H, J_1 = 7.7 Hz, J_2 = 1.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.52, 44.07, 46.54, 55.42, 84.52, 111.39, 120.92, 125.43, 127.61, 128.37, 128.94, 129.09, 133.12, 137.20, 155.49, 176.38; EIMS (*m*/*z*, %) 282 (M^+, 9.07), 238 (72.13), 237 (46.02), 223 (100.00), 207 (51.58), 135 (48.55), 91 (22.26), 77 (23.24); HRMS calcd for $C_{18}H_{18}O_3$ 282.1256, found 282.1272; HPLC (Chiralcel OJ, hexane/*i*-PrOH = 80:20 (v/v), flow rate = 0.7 mL/min) t_R = 20.8 min (major), t_R = 29.3 min (minor).

(+)-*trans*-α-Ethyl-γ-methyl-γ-(3,4-methylenedioxyphenyl)-γ-butyrolactone (*trans*-40). $[\alpha]^{20}_D$ +26.0 (*c* 0.40, $CHCl_3$) for 95% ee; FT-IR (KBr) ν 2966, 1754, 1612, 1490, 1427, 1378, 1298, 1228, 1037, 964, 954, 940, 877, 804 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.96 (t, 3H, J = 7.4 Hz), 1.47−1.55 (m, 1H), 1.69 (s, 3H), 1.85−1.94 (m, 1H), 2.00 (t, 1H, J = 12.2 Hz), 2.38−2.46 (m, 1H), 2.67 (dd, 1H, J_1 = 12.3 Hz, J_2 = 8.2 Hz), 5.96 (s, 2H), 6.76−6.85 (m, 3H); ^{13}C NMR(100 MHz, $CDCl_3$) δ 11.79, 23.20, 30.730, 41.67, 42.64, 84.68, 101.44, 105.51, 108.28, 117.58, 138.25, 147.13, 148.15, 178.55; EIMS (*m*/*z*, %) 248 (M^+, 43.22), 233 (79.81), 165 (10.77), 164 (13.42), 149 (100.00), 145 (13.21), 121 (8.33), 43 (10.90); HRMS calcd for $C_{14}H_{16}O_4$ 248.1049, found 248.1014; HPLC (Chiralcel AD, hexane/*i*-PrOH = 80:20 (v/v), flow rate = 0.7 mL/min) t_R = 7.9 min (major), t_R = 9.7 min (minor).

(−)-*cis*-α-Ethyl-γ-methyl-γ-(3,4-methylenedioxyphenyl)-γ-butyrolactone (*Cis*-40). $[\alpha]^{20}_D$ −0.3 (*c* 0.57, $CHCl_3$) for 30% ee; FT-IR (KBr) ν 2969, 1770, 1612, 1506, 1490, 1438, 1380, 1293, 1097, 1039, 956, 937, 865, 813 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.97 (t, 3H, J = 7.5 Hz), 1.41−1.52 (m, 1H), 1.64 (s, 3H), 1.85−1.95 (m, 1H), 2.08 (dd, 1H, J_1 = 12.3 Hz, J_2 = 11.0 Hz), 2.59 (dd, 1H, J_1 = 12.5 Hz, J_2 = 8.9 Hz), 2.74−2.82 (m, 1H), 5.96 (s, 2H), 6.78−6.88 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.87, 23.83, 29.28, 41.87, 42.13, 84.69, 101.39, 105.33, 108.34, 117.36, 139.74, 147.02, 148.04, 178.14; EIMS (*m*/*z*, %) 249 ($M^+ + 1$, 11.46), 248 (M^+, 52.82), 234 (17.08), 233 (100.00), 164 (7.81), 149 (75.48), 145 (8.08), 43 (6.38); HRMS calcd for $C_{14}H_{16}O_4$ 248.1049, found 248.1061; HPLC (Chiralcel AD, hexane/*i*-PrOH = 80:20 (v/v), flow rate = 0.7 mL/min) t_R = 10.7 min (major), t_R = 9.7 min (minor).

(−)-*trans*-α-Phenyl-γ-methyl-γ-(3,4-methylenedioxyphenyl)-γ-butyrolactone (*trans*-41). $[\alpha]^{20}_D$ −27.2 (*c* 0.55, $CHCl_3$) for 95% ee; FT-IR (KBr) ν 2927, 1770, 1606, 1502, 1492, 1381, 1257, 1222, 1137, 1087, 975, 942, 927, 879, 814, 759, 706, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.76 (s, 3H), 2.51 (t, 1H, J = 12.6 Hz), 2.97 (dd, 1H, J_1 = 12.6 Hz, J_2 = 8.3 Hz), 3.17 (dd, 1H, J_1 = 12.6 Hz, J_2 = 8.3 Hz), 5.98 (s, 2H), 6.28 (d, 1H, J = 8.7 Hz), 6.90−6.92 (m, 2H), 7.24−7.36 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.62, 45.73, 46.51, 84.65, 101.52, 105.55, 108.42, 117.66, 127.80, 128.28, 129.00, 136.35, 137.64, 147.36, 148.31, 176.53; EIMS (*m*/*z*, %) 296 (M^+, 25.78), 281 (29.56), 265 (37.56), 237 (28.91), 205 (100.00), 149 (49.53), 105 (38.33), 43 (29.36); HRMS calcd for $C_{18}H_{16}O_4$ 296.1049, Found 296.1059; HPLC (Chiralcel AD, hexane/*i*-PrOH = 80:20 (v/v), flow rate = 0.7 mL/min) t_R = 15.7 min (major), t_R = 22.8 min (minor).

(+)-*cis*-α-Phenyl-γ-methyl-γ-(3,4-methylenedioxyphenyl)-γ-butyrolactone (*cis*-41). $[\alpha]^{20}_D$ +1.7 (*c* 0.395, $CHCl_3$) for 46% ee; FT-IR (KBr) ν 1765, 1604, 1503, 1491, 1440, 1380, 1250, 1130, 1090, 1038, 960, 931, 812, 748, 707, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.75 (s, 3H), 2.56 (t, 1H, J = 12.4 Hz), 2.92 (dd, 1H, J_1 = 12.8 Hz, J_2 = 9.0 Hz), 4.12 (dd, 1H, J_1 = 11.8 Hz, J_2 = 9.0 Hz), 5.96 (s, 2H), 6.78−6.93 (m, 3H), 7.22−7.33 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.93, 44.95, 46.78, 84.32, 101.24, 105.15, 108.22, 117.24, 127.64 128.13, 128.87, 136.50, 139.06, 147.01, 147.93, 175.94; EIMS (*m*/*z*, %) 297 ($M^+ + 1$, 10.52), 296 (M^+, 40.87), 281 (18.95), 178 (62.80), 237 (35.79), 149 (91.07), 107 (85.53), 57 (100.00); HRMS calcd for $C_{18}H_{16}O_4$ 296.1049, found 296.1023; HPLC (Chiralcel AS, hexane/*i*-PrOH = 80:20 (v/v), flow rate = 0.7 mL/min) t_R = 38.2 min (major), t_R = 34.9 min (minor).

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Supporting Information Available: Details of the synthesis of chiral methacrylates **14**, **15**, **16**, **17**, **18**, **19**, and **20** and their spectral data, a plausible transition state model and ^1H and ^{13}C NMR spectra of all compounds listed in the Experimental Section; X-ray structural information of *trans*-**27** including the calculation data for determination of the absolute configuration. This material is available free of charge via the Internet at http://pubs.acs.org.

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