Asymmetric Synthesis of α-Methylene-γ-butyrolactones Using Chiral N-Monosubstituted 2-[(Tributylstannyl)methyl]propenamides

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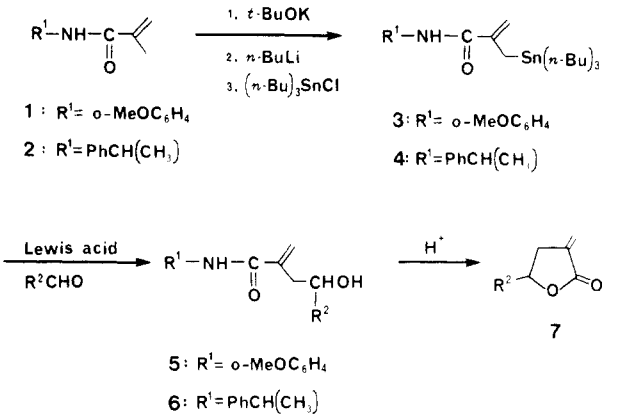
α-Methylene-γ-butyrolactones were prepared in high yields on treatment of N-monosubstituted 2-[(tributylstannyl)methyl]propenamides with aldehydes in the presence of a Lewis acid followed by acidic hydrolysis of the resulting γ-hydroxy amides. Asymmetric synthesis of α-methylene-γ-butyrolactones was investigated by using a variety of chiral 2-[(tributylstannyl)methyl]propenamides derived from optically active amines. Reaction of *N*-[(*S*)-α-(methoxymethyl)phenethyl]-2-[(tributylstannyl)methyl]propenamide or its antipode with aldehydes in the presence of 4 equiv of $TiCl_4$ gave, after hydrolysis, α-methylene lactones in an enantiometric excess of as high as 80%. Optically pure 3-methylene-2-pyrrolidinones were obtained in excellent yields by a one-pot sequence starting with the γ-hydroxy amides.

The α-methylene carbonyl unit is a characteristic structural element of sesquiterpenes and other naturally occurring substances possessing a wide range of biological activity.[1,2] Consequently, a great deal of effort has been expended in the development of methods for the construction of α-methylene lactones and ketones.[2] Little progress, however, has been made toward the development of an asymmetric synthesis of this class of compounds.[3] The difficulty largely stems from the lack of synthetic methods for obtaining γ-hydroxy carbonyl compounds in a predictable and controlled manner. We have been interested in using dianions in the synthesis of α,β-unsaturated esters and lactones,[4] and have initiated our studies on the asymmetric synthesis of α-methylene-γ-butyrolactones using chiral amide dianions.[3a] However, the optical yield obtained by the reaction of dianion generated from *N*-[(*S*)-1-(methoxymethyl)-2-methylpropyl]-2-methylpropenamide with isovaleraldehyde was too low to be of practical use.

Recently we described the Lewis acid mediated asymmetric synthesis of α-methylene lactones using chiral N-monosubstituted 2-[(tributylstannyl)methyl]-propenamide, furnishing the products in good to excellent chemical yields and in 70–80% enantiomeric excess (ee) under very mild conditions.[5] Here we report the full details of the reaction of these chiral organotin reagents with aldehydes and the synthesis of optically active α-methylene lactones and their nitrogen analogues, 3-methylene-2-pyrrolidinones, from the common intermediates, γ-hydroxy amides.

Scheme I



Results and Discussion

Synthesis of Racemic α-Methylene-γ-butyrolactones. At first by using racemic N-monosubstituted 2-[(tributylstannyl)methyl]propenamides we examined their reactivities toward carbonyl compounds. Stannyl amides **3** and **4** were prepared by adding chlorotributyltin to the dianion solution of the corresponding 2-methylpropenamides **1** and **2**[3,5,6] (Scheme I). The reaction of **3** with benzaldehyde proceeded smoothly at −78 °C to 0 °C for 4 h in CH_2Cl_2 in the presence of 4 equiv of BF_3·OEt_2[7]

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(6) For reactions of amide dianions, see: (a) Majewski, M.; Mpango, G. B.; Thomas, M. T.; Wu, A.; Snieckus, V. *J. Org. Chem.* **1981**, *46*, 2029. (b) Fitt, J. J.; Gschwend, H. W. *J. Org. Chem.* **1980**, *45*, 4257. (c) Beak, P.; Kempf, D. J. *J. Am. Chem. Soc.* **1980**, *102*, 4550. (d) Beak, P.; Kempf, D. J.; Wilson, K. D. *J. Am. Chem. Soc.* **1985**, *107*, 4745. (e) Kempf, D. J.; Wilson, K. D.; Beak, P. *J. Org. Chem.* **1982**, *47*, 1610.

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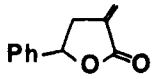
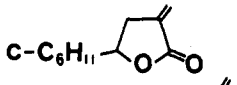
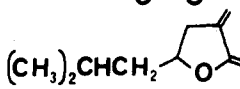
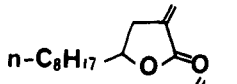
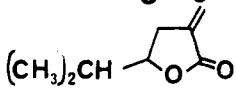
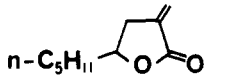
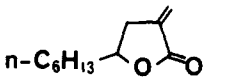
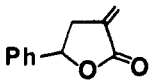
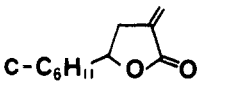
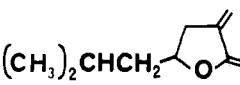
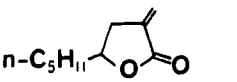
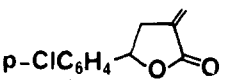
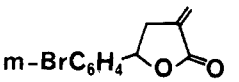
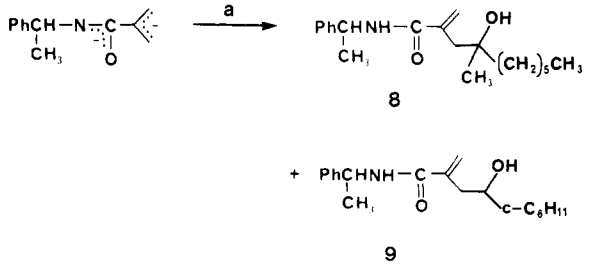
Table I

entry	reagent	aldehyde	Lewis acid	adduct %		product (7)		yield of 7, %
1	3	PhCHO	$BF_3 \cdot OEt_2$	91	(5a)		(7a)	88
2	3	c-C_6H_{11}CHO	$BF_3 \cdot OEt_2$	86	(5b)		(7b)	84
3	3	$(CH_3)_2CHCH_2CHO$	$BF_3 \cdot OEt_2$	88	(5c)		(7c)	66
4	3	n-C_8H_{17}CHO	$BF_3 \cdot OEt_2$	89	(5d)		(7d)	96
5	3	$(CH_3)_2CHCHO$	$BF_3 \cdot OEt_2$	82	(5e)		(7e)	78
6	3	n-C_5H_{11}CHO	$BF_3 \cdot OEt_2$	100	(5f)		(7f)	68
7	3	n-C_6H_{13}CHO	$BF_3 \cdot OEt_2$	90	(5g)		(7g)	64
8	4	n-C_6H_{13}CHO	$TiCl_4$	71	(6g)			
9	4	PhCHO	$BF_3 \cdot OEt_2$	80	(6a)		(7a)	93
10	4	PhCHO	$TiCl_4$	81	(6a)			
11	4	c-C_6H_{11}CHO	$BF_3 \cdot OEt_2$	83	(6b)		(7b)	99
12	4	c-C_6H_{11}CHO	$TiCl_4$	83	(6b)			
13	4	$(CH_3)_2CHCH_2CHO$	$BF_3 \cdot OEt_2$	80	(6c)		(7c)	81
14	4	n-C_5H_{11}CHO	$TiCl_4$	83	(6f)		(7f)	75
15	4	p-ClC_6H_4CHO	$TiCl_4$	85	(6h)		(7h)	52
16	4	m-BrC_6H_4CHO	$TiCl_4$	84	(6i)		(7i)	83

to afford γ-hydroxy amide **5** in high yield. $TiCl_4$[7] was also effective in this reaction, while no adduct could be obtained when $SnCl_4$ or $Ti(O\text{-}i\text{-}Pr)_4$ was used. Treatment of **5** with 5% HCl in refluxing dioxane for 4 h resulted in smooth cyclization to γ-phenyl-α-methylene-γ-butyrolactone (**7a**) in 88% yield. The results are shown in Table I. All alkyl and aryl aldehydes examined showed similar reactivity, but no reaction took place with ketones and epoxides, showing that the amides **3** and **4** are chemoselective reagents compared to the amide dianion. For example, the reaction of the dianion, generated from **2** in THF at −78 °C, with a 1:1 mixture of 2-octanone and cyclohexanecarbaldehyde as the electrophiles gave a mixture of **8** and **9** in 43% and 42% yields, respectively. In contrast, the Lewis acid mediated reaction of **4** gave only **9** in 98% yield. None of the adduct **8** was detected by HPLC. The bromophenyl moiety (entry 16), which is labile under strongly basic conditions,[8] remains intact under these Lewis acid conditions.



8

9

(a) a mixture of 2-octanone (2.2 equiv) and cyclohexanecarbaldehyde (2.2 equiv), THF, −78–0 °C

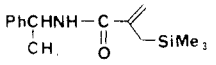
(8) Parham, W. E.; Jones, L. D.; Sayed, Y. *J. Org. Chem.* **1975**, *40*, 2394.

Table II. Asymmetric Synthesis of γ-Isobutyl-α-methylene-γ-butyrolactone (7j) from Isovaleraldehyde and Chiral Tin Reagents

entry	chiral tin amide	Lewis acid (equiv)	% yield (adduct)	% yield of 7j	$[\alpha]_D$, deg (temp (°C), c in EtOH)	% ee[a] of 7j	config
1	(S)-(−)-12	BF_3·OEt_2 (4)	80 (23)	81	−2.3 (23, 1.43)	3.4	S
2	(S)-(−)-12	$TiCl_4$ (1)	85 (23)	95	+10.8 (18, 1.79)	16	R
3	(R)-(+)-12	$TiCl_4$ (1)	80 (24)	85	−10.9 (24, 1.11)	16	S
4	(S)-(−)-14	BF_3·OEt_2 (4)	85 (25)	95	−2.2 (24, 1.46)	3.3	S
5	(S)-(−)-14	$TiCl_4$ (1)	85 (25)	69	−28.0 (21, 1.76)	42	S
6	(S)-(−)-14	$TiCl_4$ (4)	81 (25)	88	−43.6 (22, 1.56)	65	S
7	(R)-(+)-14	$TiCl_4$ (1)	84 (26)	99	+31.4 (25, 1.51)	47	R
8	(S)-(−)-16	BF_3·OEt_2 (4)	88 (27)	81	−2.8 (24, 1.59)	4.2	S
9	(S)-(−)-16	$TiCl_4$ (1)	65 (28)	95	−43.5 (25, 1.52)	65	S
10	(S)-(−)-16	$TiCl_4$ (2)	77 (28)	89	−46.0 (24, 1.72)	65	S
11	(S)-(−)-16	$TiCl_4$ (4)	77 (28)	93	−43.5 (24, 1.78)	72	S
12	(R)-(+)-16	$TiCl_4$ (1)	86 (28)	98	+40.9 (25, 1.55)	61	R
13	(S)-(−)-18	$TiCl_4$ (1)	89 (29)	94	−34.2 (21, 1.66)	51	S
14	(S)-(−)-18	$TiCl_4$ (4)	75 (29)	65	−52.9 (25, 1.86)	79	S
15	(R)-(+)-18	$TiCl_4$ (4)	99 (30)	97	+52.4 (25, 1.66)	78	R
16	(1S,2R,5S)-(−)-20	$TiCl_4$ (1)	86 (31)	99	+7.5 (22, 1.63)	11	R
17	(R)-(+)-22	$TiCl_4$ (1)	95 (32)	99	−4.8 (21, 1.85)	7.2	S

[a] Optically pure (S)-(−)-7j is reported to have $[\alpha]^{25}_D$ −66.6° (c 1.83, EtOH) and (R)-(+)-7j to have $[\alpha]^{25}_D$ +67.0° (c 1.44, EtOH). See ref 3d.

We have briefly examined the reactivity of N-(α-methylbenzyl)-2-[(trimethylsilyl)methyl]propenamide (**10**) towards aldehydes. The amide **10** was obtained in 95% yield from the dianion of **2** and chlorotrimethylsilane. No adduct could be obtained from **10** and cyclohexanecarbaldehyde in the presence of 4 equiv of BF_3·OEt_2 after 18 h. $TiCl_4$ and $SnCl_4$ were also ineffective. When **10** was treated with n-Bu_4NF in the presence of 4A molecular sieves[9] in THF at 55 °C for 2 h, γ-hydroxy amide **6g** was obtained in a moderate yield (58%). The harsh conditions required for the reaction of **10** appeared to limit its generality and preclude its application to asymmetric synthesis of methylene lactones.

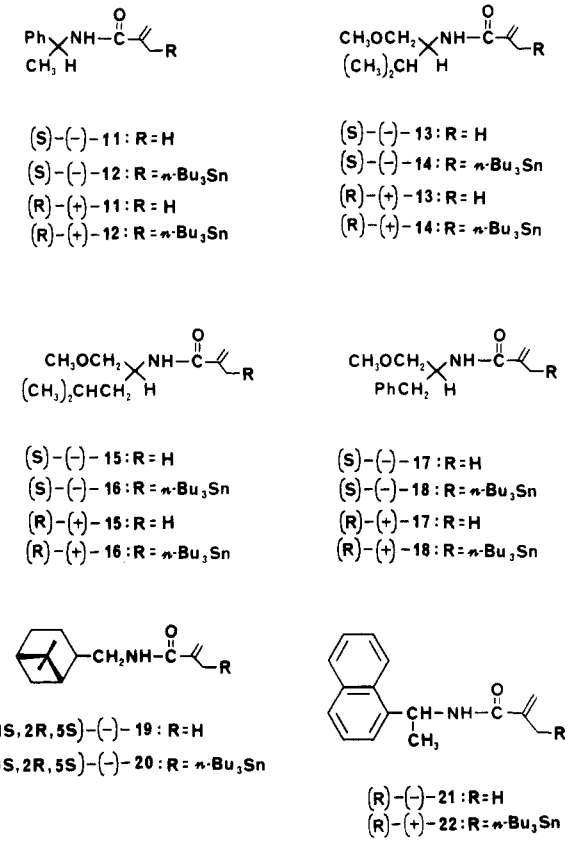


10

Asymmetric Synthesis of α-Methylene-γ-butyrolactones. Since the organotin compounds **3** and **4** were characterized as efficient reagents for the preparation of α-methylene lactones, we next explored asymmetric induction in Lewis acid initiated reaction. The chiral N-monosubstituted 2-methylpropenamides (Chart I) were prepared from methacryloyl chloride and the corresponding chiral amines.[10] The amides were converted into 2-(tributylstannylmethyl)propenamides via the dianions by the method previously described.

As a representative electrophile, we chose isovaleraldehyde since the absolute configuration and the optical rotation of γ-isobutyl-α-methylene-γ-butyrolactone are known.[3d] Reaction of N-[(S)-α-methylbenzyl]-2-[(tributylstannyl)methyl]propenamide ((S)-(−)-**12**) was carried out in CH_2Cl_2 in the presence of 4 equiv of BF_3·OEt_2 at −78 °C to 0 °C for 4 h, and a diastereomeric mixture of N-[(S)-α-methylbenzyl]-4-hydroxy-6-methyl-2-methyleneheptanamide (**23**) was obtained in high yield, which could not be separated chromatographically. Cyclization of **23** gave α-methylene lactone **7j** in poor optical

Chart I

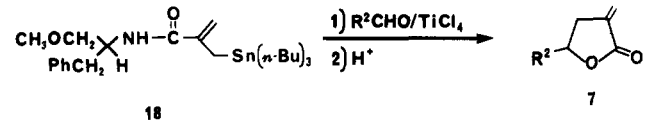


yield. An enhancement of asymmetric induction was observed when (S)-(−)-**14** derived from (S)-(+)-valine was employed with 1 equiv of $TiCl_4$. With (S)-(−)-**16** prepared from (S)-(+)-leucine, a fairly high optical yield (~65%) was obtained. The highest enantiomeric excess (79%) was finally achieved by the use of (S)-(−)-18 or (R)-(+)-18 obtained from (S)-(−)- or (R)-(+)-phenylalanine, in the presence of 4 equiv of $TiCl_4$ (−78 °C for 2 h, −50 °C for 2 h, and warmed to 0 °C). In each case γ-isobutyl-α-methylene-γ-butyrolactone was formed in good to excellent chemical yield. The results are shown in Table II. The chiral amines may be recycled for further use, since no epimerization was observed during the entire sequences. For example, (S)-(−)-α-methylbenzylamine and (S)-(−)-1-methoxy-3-phenyl-2-propanamine were recovered, after

(9) Kuwajima, I.; Nakamura, E.; Shimizu, M. *J. Am. Chem. Soc.* **1982**, *104*, 1025.

(10) (a) Seki, H.; Koga, K.; Matsuo, H.; Ohki, S.; Matsuo, I.; Yamada, S. *Chem. Pharm. Bull.* **1965**, *13*, 995. (b) Meyers, A. I.; Poindexter, G. S.; Brich, Z. *J. Org. Chem.* **1978**, *43*, 892. (c) Meyers, A. I.; Williams, D. R.; Erickson, G. W.; White, S.; Druelinger, M. *J. Am. Chem. Soc.* **1981**, *103*, 3081.

Table III. Lewis Acid Initiated Addition of (*S*)-(−)-18 or (*R*)-(+)-18 to Aldehydes and Subsequent Cyclization into Chiral α-Methylene-γ-butyrolactones

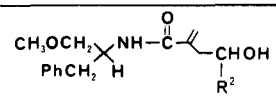


18 7

entry	chiral tin reagent	aldehyde	% yield (adduct)	% yield (lactone)	$[\alpha]_D$, deg (temp (°C), c in EtOH)	% ee[a] of 7	config[b]
1	(*S*)-(−)-18	*n*-C_4H_9CHO	75 (33)	91 ((*S*)-7k)	−47.7 (25, 1.62)	81.0	*S*
2	(*R*)-(+)-18	*n*-C_4H_9CHO	93 (34)	99 ((*R*)-7k)	+47.1 (25, 1.75)	78.6	*R*
3	(*S*)-(−)-18	*n*-$C_5H_{11}CHO$	86 (35)	83 ((*S*)-7l)	−44.8 (25, 1.59)	82.0	*S*
4	(*R*)-(+)-18	*n*-$C_5H_{11}CHO$	99 (36)	96 ((*R*)-7l)	+44.4 (25, 0.96)	79.2	*R*
5	(*S*)-(−)-18	*n*-$C_6H_{13}CHO$	72 (37)	88 ((*S*)-7m)	−42.7 (26, 1.44)	80.2	*S*
6	(*R*)-(+)-18	*n*-$C_6H_{13}CHO$	93 (38)	99 ((*R*)-7m)	+41.4 (25, 0.97)	77.6	*R*
7	(*S*)-(−)-18	*n*-$C_7H_{15}CHO$	87 (39)	73 ((*S*)-7n)	−39.0 (26, 1.59)	78.4	*S*
8	(*R*)-(+)-18	*n*-$C_7H_{15}CHO$	89 (40)	99 ((*R*)-7n)	+39.0 (25, 1.37)	77.4	*R*
9	(*S*)-(−)-18	*n*-$C_8H_{17}CHO$	89 (41)	80 ((*S*)-7o)	−38.4 (24, 2.10)	76.0	*S*
10	(*R*)-(+)-18	*n*-$C_8H_{17}CHO$	93 (42)	94 ((*R*)-7o)	+38.3 (25, 1.11)	75.2	*R*

[a] Calculated from the diastereomer ratio of 3-methylene-2-pyrrolidinones prepared in Table IV. See also the methods for determination of diastereomer ratios in Table V. [b] Predicted absolute configuration on the bases of reaction mechanics and the sign of the specific rotation.

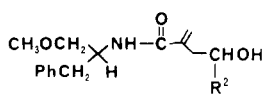
Table IV. Preparation of 3-Methylene-2-pyrrolidinones 43–54 from γ-Hydroxy-α-methylene Amides 29–42



entry		% yield (pyrrolidinone)	diastereomer ratio I/II[a]	$[\alpha]_D$ deg, (temp (°C), c in EtOH) diastereomer I[a]	diastereomer II[a]
1	$(CH_3)_2CHCH_2$ (29)	93 (43)	9.4/90.6	−168.4 (27, 1.08)	−166.5 (27, 1.01)
2	$(CH_3)_2CHCH_2$ (30)	86 (44)	10.3/89.7	+169.9 (26, 1.04)	+170.9 (26, 1.14)
3	*n*-C_4H_9 (33)	81 (45)	9.5/90.5	−166.1 (24, 0.77)	−156.6 (24, 1.06)
4	*n*-C_4H_9 (34)	94 (46)	10.7/89.3	+167.6 (25, 0.82)	+156.3 (25, 0.91)
5	*n*-C_5H_{11} (35)	86 (47)	9.0/91.0	−157.6 (23, 0.94)	−142.1 (23, 0.99)
6	*n*-C_5H_{11} (36)	95 (48)	10.4/89.6	+163.8 (20, 1.06)	+147.0 (20, 0.99)
7	*n*-C_6H_{13} (37)	90 (49)	9.9/90.1	−150.4 (25, 0.66)	−139.5 (22, 1.22)
8	*n*-C_6H_{13} (38)	94 (50)	11.2/88.8	+151.9 (25, 1.06)	+136.1 (25, 1.46)
9	*n*-C_7H_{15} (39)	94 (51)	10.8/89.2	−140.8 (25, 1.00)	−126.4 (25, 0.95)
10	*n*-C_7H_{15} (40)	93 (52)	11.3/88.7	+144.1 (26, 1.03)	+131.1 (25, 1.18)
11	*n*-C_8H_{17} (41)	91 (53)	12.0/88.0	−140.4 (25, 1.01)	−125.7 (25, 1.10)
12	*n*-C_8H_{17} (42)	95 (54)	12.4/87.6	+140.2 (26, 1.05)	+128.1 (25, 1.10)

[a] Isolated by silica gel column chromatography; numerals I and II indicate the elution order of the diastereomers.

Table V. Determination of Diastereomer Ratios of (*S*)-MTPA Esters 55–60



entry			MTPA ester	% ds of MTPA ester by HPLC	% ds of MTPA ester by ^{19}F NMR	% ds of pyrrolidinone
1	29	$(CH_3)_2CHCH_2$	55		74	81.2
2	34	*n*-C_4H_9	56	79	77	78.6
3	35	*n*-C_5H_{11}	57	78	75	82.0
4	37	*n*-C_6H_{13}	58	78	77	77.6
5	40	*n*-C_7H_{15}	59	86	82	78.4
6	42	*n*-C_8H_{17}	60	76	74	74.2

lactonization of **23** and **29**, in 83% and 91% yields, respectively, without any loss of optical purity. However, in the case of (*R*)-(+)-**22** almost complete racemization (94%) of (*R*)-(+)-1-(1-naphthyl)ethylamine[11] was observed during the lactonization and the % ee of the lactone **7j** was low.

Similarly, with (*S*)-(−)-18 or (*R*)-(+)-18 and 4 equiv of $TiCl_4$, a variety of aldehydes were converted to the corresponding α-methylenebutyrolactones in good to excellent yields. The results are summarized in Table III.

Enantiomeric Excess Determination. All chiral α-methylene-γ-butyrolactones **7k–o** so obtained were unknown compounds except for **7j**.[3b,d] Attempts to determine the enantiomeric excess of these lactones by using chiral shift reagents such as tris[3-[(heptafluoropropyl)-hydroxymethylene]-*d*-camphorato]europium(III) or tris-[3-[(trifluoromethyl)hydroxymethylene]-*d*-camphorato]-europium(III) failed. Use of the chiral stationary phase (G-SCOT-OA-200)[12] was also unsuccessful. A new method was developed for the determination of the enantiomeric excess. This technique consists of conversion of the γ-hydroxy amides into a diastereomeric mixture of 3-methylene-2-pyrrolidinones, using 2 equiv of *n*-butyllithium and 1 equiv of *p*-toluenesulfonyl chloride in THF.[13] These pyrrolidinones **43–54** were readily separated by open column chromatography (Scheme II). Use of (*S*)-(−)-18 or (*R*)-(+)-18 is important, since, with the amides such as (*S*)-(−)-**14** or (*S*)-(−)-**16**, the separation of diastereomers was impossible. The purity of the separated diastereomers is

(11) This substrate was obtained from Wako Chemical Co.

(12) We thank Professor Yoshiyuki Kumata for analysis by capillary gas chromatograph.

(13) Tanaka, K.; Yoda, H.; Kaji, A. *Synthesis* **1985**, 84.

Scheme II

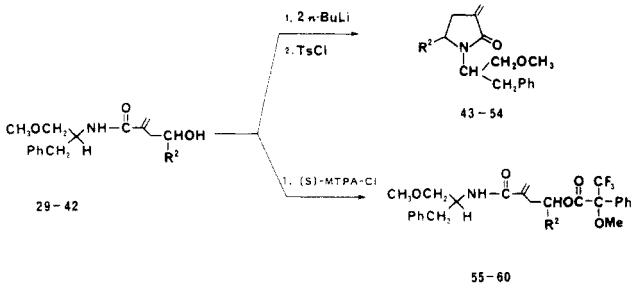
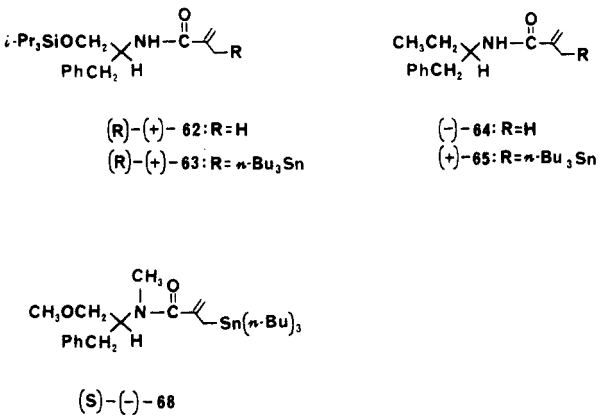


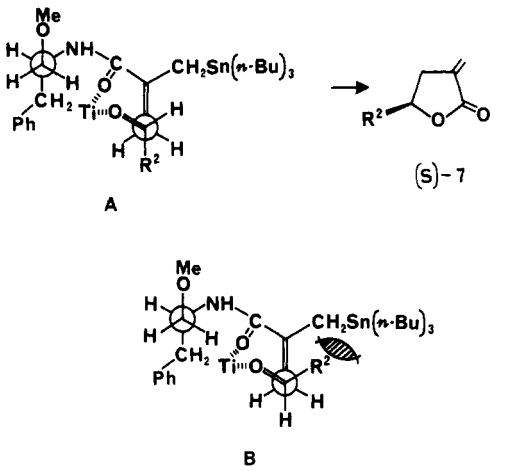
Chart II



apparent from the data summarized in Table IV, which exhibited nearly the same specific rotations only opposite in sign. To test the validity of this determination we prepared α-methoxy-α-(trifluoromethyl)phenylacetates (MTPA esters)[14] **55–60** from the amides. The diastereomeric ratios determined by ^{19}F NMR and/or HPLC of **55–60**, summarized in Table V, were in good agreement with those obtained by the separation of diastereomers of 3-methylene-2-pyrrolidinones (Table V). Thus all the α-methylene-γ-butyrolactones listed in Table III possess 75–80% enantiomeric excesses.

This high diastereoselection implicates an important chelation by the titanium ion[15] in the transition state, the result being an organized, rigid carbon framework capable of directing remote asymmetric induction. In order to determine whether or not the methoxy substituent[15,16] is an important determinant in the stereochemical course we examine the enantioselective addition of (*R*)-(+)-**63**, in which complexation of titanium ion is difficult due to the steric bulk of the triisopropylsilyl group.[17] The enantiomeric excess of (*R*)-(+)-**7j**, obtained in 82% overall yield from (*R*)-(+)-**63** and isovaleraldehyde in the presence of 4 equiv of $TiCl_4$, was 74%! Furthermore, the reaction of *N*-(1-benzylpropyl)-2-[(tributylstannyl)methyl]-propenamide ((+)-**65**) carrying no alkoxy substituent, which was prepared from (−)-1-phenyl-2-butanamine (91% optical purity),[18] gave (*S*)-(−)-**7j** in 85% chemical yield and in 70% ee. These results indicates that the ethereal oxygen[15,16] of the organotin reagents have little influence on the stereochemical course of the $TiCl_4$-initiated addition. The effect of a second substituent on the nitrogen atom of the amide moiety on the asymmetric induction was next investigated. Methylation of (*S*)-(−)-**18** with dimethyl sulfate gave *N*-methyl-*N*-[(*S*)-α-(methoxymethyl)phenethyl]-2-[(tributylstannyl)methyl]propenamide ((*S*)-(−)-**68**) in 88% yield (Chart II). Reaction of (*S*)-(−)-**68** with isovaleraldehyde in the presence of 4 equiv of $TiCl_4$ at −78 °C gave (*S*)-**7j** in 76% overall yield and in 40% optical yield, showing the importance of secondary amide for effective asymmetric induction. It is interesting to note that when 4 equiv of $TiCl_4$ was added to a solution of *N*-(α-methylbenzyl)-2-methylpropenamide (**2**) in CD_2Cl_2, downfield shifts of 0.65–0.77 ppm were noted for the α-methylene protons, 0.64 ppm for the methine proton, and 1.46 ppm for the amide proton, indicating that $TiCl_4$ coordinated with **2** to form a titanium amide complex similar to that described by Mukaiyama in the reaction of nitriles and $TiCl_4$.[19] In contrast, no appreciable downfield shifts were observed when amide **2** was treated with 4 equiv of $BF_3{\cdot}OEt_2$ in CD_2Cl_2. The observed high degree of stereoselectivity in 1,6-remote induction may be attributed to the stronger chelating ability of titanium ion which coordinates with the amide moiety of the organotin reagents and the oxygen atom[20] of the aldehyde to organize rigid cyclic transition state A in which the benzyl group of the amine occupies an axial position owing to the steric repulsion between the methoxy group, and the interaction between the alkyl group R^2 on the aldehyde and (tributylstannyl)methyl moiety is minimized (Scheme III).

Scheme III



In summary, N-monosubstituted 2-[(tributylstannyl)-methyl]propenamides undergo chemoselective carbon–carbon bond formation with carbonyl compounds. Both enantiomers of γ-alkyl-α-methylene-γ-butyrolactones can be available in 80% ee by selecting the proper antipode of phenylalanine for the preparation of the organotin reagents.

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Experimental Section

General Methods. All reactions were carried out under an argon atmosphere. Tetrahydrofuran (THF) was distilled under argon from sodium benzophenone ketyl immediately before use. Dichloromethane and DMF were distilled from calcium hydride. The hexane solution of *n*-BuLi (Aldrich and Nakarai) was titrated by using diphenylacetic acid.[21]

Infrared spectra were recorded on a Hitachi Model 215 spectrophotometer. Nuclear magnetic resonance spectra were obtained on a JEOL Model PS-100 or a JEOL Model JMN-FX-400 spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard, unless stated otherwise. Optical rotations were measured in 1-dm path length cell of 2-mL capacity on a JASCO Model DIP-181 polarimeter. Gas–liquid chromatography was performed on a Shimadzu Model GC-8A gas chromatograph using a 0.15 cm × 120 cm glass column (20% Silicone DC-550 on Celite 545). Thin layer chromatography was performed by using Merck precoated silica gel sheets 60F-254. Silica gel (Wakogel) of the size 100–200 mesh was used for column chromatography. High-pressure liquid chromatography was carried out on a Hitachi Model-633A liquid chromatograph with a reversed-phase (C18) column. Mass spectra were determined on a JMS-DX-300 spectrometer at an ionization potential 70 eV. Elemental analyses were performed by the Microanalytical Laboratory, operated by the Institute for Chemical Research, Kyoto University.

***N*-(2-Methoxyphenyl)-2-[(tributylstannyl)methyl]-propenamide (3).** To a stirred solution of 2.74 g (22 mmol) of potassium *tert*-butoxide[22] in 50 mL of THF cooled to −78 °C was added a solution of 1.91 g (10 mmol) *N*-(2-methoxyphenyl)-2-methylpropenamide (1) in 10 mL of THF. After the mixture was stirred for 1 h at −78 °C, 22 mmol of *n*-butyllithium was added. The resulting suspension was stirred for 1 h at −78 °C, and a solution of 7.16 g (22 mmol) of chlorotributyltin in 10 mL of THF was added. The mixture was stirred for 1 h at −78 °C, warmed to 0 °C, stirred for 1 h, and quenched with 10 mL of saturated aqueous NH_4Cl. Water (100 mL) was added and the organic layer was removed, and the aqueous layer was extracted with ether. The combined organic layers were washed 2 times with brine, dried, and evaporated. Column chromatography (20:1 hexane/ethyl acetate) afforded 2.93 g (61%) of pure **3** as a colorless oil: IR (thin film) 3430, 1668, 1594 cm^{-1}; ^1H NMR δ 8.27 (m, 1 H), 8.16 (br s, 1 H), 6.79–7.06 (m, 3 H), 5.32 (s, 1 H), 5.12 (s, 1 H), 3.85 (s, 3 H), 2.03 (s, 2 H), 1.08–1.73 (m, 18 H), 0.75–1.00 (m, 9 H). Anal. Calcd for $C_{23}H_{39}NO_2Sn$: C, 57.52; H, 8.19; N, 2.92. Found: C, 57.52; H, 8.41; N, 2.91.

***N*-(α-Methylbenzyl)-2-[(tributylstannyl)methyl]-propenamide (4).** By the procedure described for the preparation of stannyl amide **3**, 2.74 g (22 mmol) of potassium *tert*-butoxide, 1.89 g (10 mmol) of *N*-(α-methylbenzyl)-2-methylpropenamide (**2**), 22 mmol of *n*-butyllithium, and 7.16 g (22 mmol) of chlorotributyltin in 50 mL of THF afforded, after column chromatography (20:1 hexane/ethyl acetate), 3.97 g (83%) of **4** as a colorless oil: IR (thin film) 3270, 2910, 1625, 1580, 1510, 1210 cm^{-1}; ^1H NMR δ 7.28 (s, 5 H), 5.95 (m, 1 H), 5.12 (s, 1 H), 5.10 (q, *J* = 6.7 Hz, 1 H), 4.97 (s, 1 H), 1.93 (s, 2 H), 1.50 (d, *J* = 6.7 Hz, 3 H), 0.60–1.80 (m, 27 H). Anal. Calcd for $C_{24}H_{41}NOSn$: C, 60.27; H, 8.64; N, 2.93. Found: C, 60.00; H, 8.97; N, 3.22.

General Procedure for the Preparation of 4-Hydroxy Amides and α-Methylene γ-Lactones (Table I). 4-Hydroxy-2-methylene-*N*-(2-methoxyphenyl)-4-phenylbutanamide (5a). To a solution of benzaldehyde (0.13 g, 1.2 mmol) in 10 mL of CH_2Cl_2 cooled to −78 °C was added a solution of $BF_3{\cdot}OEt_2$ (0.57 g, 4 mmol) in 2 mL of CH_2Cl_2. After 5 min, a solution of **3** (0.48 g, 1 mmol) in 3 mL of CH_2Cl_2 was added. The mixture was stirred for 1 h at −78 °C and then warmed to 0 °C during 3 h. Water (10 mL) was added and the mixture was extracted with CH_2Cl_2 (4 × 30 mL). The organic layers were combined, dried, and evaporated to give a crude product, which was purified by column chromatography to give a thick, colorless oil (0.27 g): ^1H NMR δ 8.61 (br s, 1 H), 8.15–8.24 (m, 1 H), 6.58–7.25 (m, 8 H), 5.57 (s, 1 H), 5.07 (s, 1 H), 4.56–4.68 (m, 2 H), 3.66 (s, 3 H), 2.45–2.60 (m, 2 H). **4,5-Dihydro-3-methylene-5-phenyl-2(3*H*)-furanone (7a).** This compound (0.27 g, 0.91 mmol) was stirred in 20 mL of 10% HCl and heated at reflux for 3 h. After cooling, the acidic solution was extracted with ether (3 × 50 mL), dried, and concentrated to give a crude lactone **7a**. After chromatography on silica gel, eluted with 3:1 hexane/ethyl acetate, a yield of 0.14 g of pure **7a** was obtained: mp 54–55 °C; IR (KBr) 1758, 1660 cm^{-1}; ^1H NMR δ 7.37 (s, 5 H), 6.26 (t, *J* = 2.5 Hz, 1 H), 5.65 (t, *J* = 2.5 Hz, 1 H), 5.49 (dd, *J* = 6, 8 Hz, 1 H), 3.20–3.25 (ddt, *J* = 17, 8, 2.5 Hz, 1 H), 2.60–3.00 (ddt, *J* = 17, 6, 2.5 Hz, 1 H). Anal. Calcd for $C_{11}H_{10}O_2$: C, 75.83; H, 5.80. Found: c, 76.11; H, 5.76.

4-Cyclohexyl-4-hydroxy-2-methylene-*N*-(2-methoxyphenyl)butanamide (5b): ^1H NMR δ 8.47 (br s, 1 H), 8.25–8.36 (m, 1 H), 6.77–7.06 (m, 3 H), 5.76 (s, 1 H), 5.43 (s, 1 H), 3.83 (s, 3 H), 3.24–3.60 (m, 2 H), 2.20–2.73 (m, 2 H), 0.72–1.99 (m, 11 H). **5-Cyclohexyl-4,5-dihydro-3-methylene-2(3*H*)-furanone (7b):** mp 55–56 °C; IR (KBr) 1744, 1660 cm^{-1}; ^1H NMR δ 6.12 (t, *J* = 2.5 Hz, 1 H), 5.54 (t, *J* = 2.5 Hz, 1 H), 4.21 (q, *J* = 6.6 Hz, 1 H), 2.48–3.11 (m, 2 H), 0.79–2.10 (m, 11 H). Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.28; H, 8.96. Found: C, 73.12; H, 9.13.

4-Hydroxy-*N*-(2-methoxyphenyl)-6-methyl-2-methyleneheptanamide (5c): ^1H NMR δ 8.48 (br s, 1 H), 8.24–8.36 (m, 1 H), 6.76–7.10 (m, 3 H), 5.76 (s, 1 H), 5.43 (s, 1 H), 3.82 (s, 3 H), 3.60–3.92 (m, 2 H), 2.22–2.70 (m, 2 H), 1.06–1.89 (m, 3 H), 0.89 (d, *J* = 6.8 Hz, 6 H). **4,5-Dihydro-5-isobutyl-3-methylene-2-(3*H*)-furanone (7c):** IR (thin film) 1748, 1659 cm^{-1}; ^1H NMR δ 6.19 (t, *J* = 2.5 Hz, 1 H), 5.59 (t, *J* = 2.5 Hz, 1 H), 4.57 (m, 1 H), 2.39–3.23 (m, 2 H), 1.26–2.02 (m, 3 H), 0.96 (d, *J* = 6 Hz, 6 H); MS, *m/e* 154 (M^+). Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.08; H, 9.30.

4-Hydroxy-*N*-(2-methoxyphenyl)-2-methylenedodecanamide (5d): ^1H NMR δ 8.34 (br s, 1 H), 8.24–8.30 (m, 1 H), 6.79–7.07 (m, 3 H), 5.76 (s, 1 H), 5.45 (s, 1 H), 3.84 (s, 3 H), 3.63–3.94 (m, 1 H), 3.33 (br s, 1 H), 2.26–2.76 (m, 2 H), 1.18–1.54 (m, 14 H), 0.75–0.97 (m, 3 H). **4,5-Dihydro-3-methylene-5-octyl-2(3*H*)-furanone (7d):** IR (thin film) 1764, 1662 cm^{-1}; ^1H NMR δ 6.17 (t, *J* = 2.7 Hz, 1 H), 5.57 (t, *J* = 2.4 Hz, 1 H), 4.35–4.62 (m, 1 H), 2.36–3.21 (m, 2 H), 1.12–1.88 (m, 14 H), 0.76–0.98 (m, 3 H); MS, *m/e* 210 (M^+). Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.55. Found: C, 73.97; H, 10.56.

4-Hydroxy-*N*-(2-methoxyphenyl)-5-methyl-2-methylenehexanamide (5e): ^1H NMR δ 8.38 (br s, 1 H), 8.22–8.31 (m, 1 H), 6.75–7.12 (m, 3 H), 5.73 (s, 1 H), 5.43 (s, 1 H), 3.83 (s, 3 H), 3.27–3.61 (m, 2 H), 2.22–2.68 (m, 2 H), 1.69 (m, 1 H), 0.95 (d, *J* = 6.8 Hz, 6 H). **4,5-Dihydro-5-isopropyl-3-methylene-2-(3*H*)-furanone (7e):** IR (thin film) 1746, 1662 cm^{-1}; ^1H NMR δ 6.08 (t, *J* = 2.5 Hz, 1 H), 5.53 (t, *J* = 2.5 Hz, 1 H), 4.19 (q, *J* = 6.3 Hz, 1 H), 2.24–3.12 (m, 2 H), 1.84 (m, 1 H), 0.96 (m, 6 H); MS, *m/e* 140 (M^+). Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.19; H, 8.82.

4-Hydroxy-*N*-(2-methoxyphenyl)-2-methylenenonanamide (5f): ^1H NMR δ 8.54 (br °, 1 H), 8.36–8.46 (m, 1 H), 6.86–7.16 (m, 3 H), 5.83 (s, 1 H), 5.50 (s, 1 H), 3.88 (s, 3 H), 3.52–2.92 (m, 2 H), 2.24–2.76 (m, 2 H), 1.20–1.60 (m, 8 H), 0.77–1.00 (m, 3 H). **4,5-Dihydro-3-methylene-5-pentyl-2(3*H*)-furanone (7f):** IR (thin film) 1758, 1662 cm^{-1}; ^1H NMR δ 6.15 (t, *J* = 2.7 Hz, 1 H), 5.57 (t, *J* = 2.4 Hz, 1 H), 4.28 (q, *J* = 6.3 Hz, 1 H), 2.22–3.24 (m, 2 H), 1.12–1.90 (m, 8 H), 0.76–1.00 (m, 3 H); MS, *m/e* 168 (M^+). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.15; H, 9.70.

4-Hydroxy-*N*-(2-methoxyphenyl)-2-methylenedecanamide (5g): ^1H NMR δ 8.40 (br s, 1 H), 8.24–8.36 (m, 1 H), 6.79–7.08 (m, 3 H), 5.76 (s, 1 H), 5.44 (s, 1 H), 3.84 (s, 3 H), 3.61–3.79 (m, 1 H), 3.49 (br s, 1 H), 2.26–2.72 (m, 2 H), 1.20–1.51 (m, 10 H), 0.73–0.97 (m, 3 H). **4,5-Dihydro-5-hexyl-3-methylene-2-(3*H*)-furanone (7g):** IR (thin film) 1746, 1660 cm^{-1}; ^1H NMR δ 6.15 (t, *J* = 2.5 Hz, 1 H), 5.56 (t, *J* = 2.5 Hz, 1 H), 4.44 (q, *J* = 6.3 Hz, 1 H), 2.40–3.21 (m, 2 *H*), 1.11–1.87 (m, 10 H), 0.74–1.01 (m, 3 H); MS, *m/e* 182 (M^+). Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.47; H, 9.97. Found: C, 72.42; H, 10.12.

General Procedure for the Preparation of 4-Hydroxy-*N*-(α-methylbenzyl)-2-methylenealkanamide 6. To a solution of the aldehyde (2.4 mmol) in 20 mL of CH_2Cl_2 cooled to −78 °C was added 0.65 g (2 mmol) of $TiCl_4$ in 2 mL of CH_2Cl_2. After 5

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min, a solution of amide **4** (0.96 g, 2 mmol) in 5 mL of CH_2Cl_2 was added. The mixture was stirred and allowed to warm to 0 °C over 4 h and quenched with 10 mL of water, and the solution was extracted 4 times with CH_2Cl_2. The organic layers were combined, washed 2 times with saturated aqueous NaCl, dried, and evaporated to give a crude oil. The product was purified by chromatography on silica gel (hexane/ethyl acetate) yielding the adduct as a colorless viscous oil.

4-Hydroxy-*N*-(α-methylbenzyl)-2-methylenedecanamide (6g): IR (thin film) 3220, 2880, 1630, 1590, 1520, 1440 cm^{-1}; ^1H NMR δ 7.23 (s, 5 H), 7.10 (br s, 1 H), 5.60 (s, 1 H), 5.24 (s, 1 H), 5.04 (q, J = 6.7 Hz, 1 H), 4.10 (m, 1 H), 3.63 (br s, 1 H), 2.40 (m, 2 H), 1.45 (d, J = 6.7 Hz, 3 H), 0.60–1.60 (m, 13 H).

4-Hydroxy-*N*-(α-methylbenzyl)-2-methylene-4-phenylbutanamide (6a): IR (thin film) 3210, 1695, 1625 cm^{-1}; ^1H NMR δ 7.34 (m, 10 H), 6.52 (br s, 1 H), 5.59 (s, 1 H), 5.23 (s, 1 H), 5.12 (q, J = 6.7 Hz, 1 H), 4.78 (m, 2 H), 2.60 (m, 2 H), 1.53 (d, J = 6.7 Hz, 3 H).

4-Cyclohexyl-4-hydroxy-*N*-(α-methylbenzyl)-2-methylenebutanamide (6b): IR (thin film) 3220, 2875, 1630, 1590, 1520, 1435 cm^{-1}; ^1H NMR δ 7.27 (s, 5 H), 6.90 (br s, 1 H), 5.63 (s, 1 H), 5.30 (s, 1 H), 5.10 (q, J = 6.7 Hz, 1 H), 3.80 (m, 1 H), 3.40 (m, 1 H), 2.40 (m, 2 H), 1.48 (d, J = 6.7 Hz, 3 H), 0.65–2.00 (m, 11 H).

4-Hydroxy-*N*-(α-methylbenzyl)-2-methylenenonanamide (6f): ^1H NMR δ 7.30 (s, 5 H), 6.75 (br s, 1 H), 5.65 (s, 1 H), 5.31 (s, 1 H), 5.10 (q, J = 6.7 Hz, 1 H), 3.80 (m, 1 H), 3.70 (m, 1 H), 2.47 (m, 2 H), 1.55 (d, J = 6.7 Hz, 3 H), 0.70–1.80 (m, 11 H).

4-(4-Chlorophenyl)-4-hydroxy-*N*-(α-methylbenzyl)-2-methylenebutanamide (6h): IR (thin film) 3225, 1630, 1590, 1480, 1010, 700 cm^{-1}; ^1H NMR δ 7.25 (m, 9 H), 6.82 (m, 1 H), 5.60–4.80 (m, 2 H), 5.55 (s, 1 H), 5.10 (s, 1 H), 4.70 (m, 1 H), 2.45 (m, 2 H), 1.45 (d, J = 6.8 Hz, 3 H). Anal. Calcd for $C_{19}H_{20}ClNO_2$: C, 69.19; H, 6.11; N, 4.25. Found: C, 68.72; H, 6.36; N, 4.16. Lactonization was carried out by refluxing a solution of **6** in dioxane containing 5% HCl for 4 h.

5-(4-Chlorophenyl)-4,5-dihydro-3-methylene-2(3*H*)-furanone (7h): IR (thin film) 1750, 1650, 1480, 1270, 1120, 1010, 835 cm^{-1}; ^1H NMR δ 7.30 (m, 4 H), 6.28 (t, J = 2.4 Hz, 1 H), 5.70 (t, J = 2.4 Hz, 1 H), 5.50 (t, J = 7.5 Hz, 1 H), 3.20–3.60 (m, 1 H), 2.60–3.00 (m, 1 H). Anal. Calcd for $C_{11}H_9ClO_2$: C, 63.32; H, 4.35. Found: C, 63.67; H, 4.18.

4-(3-Bromophenyl)-4-hydroxy-*N*-(α-methylbenzyl)-2-methylenebutanamide (6i): IR (thin film) 3220, 1630, 1585, 1520, 1065 cm^{-1}; ^1H NMR δ 7.60–7.00 (m, 9 H), 6.90 (m, 1 H), 5.60 (s, 1 H), 5.60–5.00 (m, 2 H), 5.18 (s, 1 H), 4.75 (m, 1 H), 2.60 (m, 2 H), 1.48 (d, J = 6.8 Hz, 3 H). Anal. Calcd for $C_{19}H_{20}BrNO_2$: C, 60.97; H, 5.39; N, 3.74. Found: C, 61.00; H, 5.49; N, 3.70.

5-(3-Bromophenyl)-4,5-dihydro-3-methylene-2(3*H*)-furanone (7i): IR (thin film) 2970, 1740, 1655, 1415, 1210, 1020, 750 cm^{-1}; ^1H NMR δ 7.80 (m, 4 H), 6.30 (t, J = 2.4 Hz, 1 H), 5.70 (t, J = 2.4 Hz, 1 H), 5.48 (t, J = 7.5 Hz, 1 H), 3.70–3.20 (m, 1 H), 3.10–2.60 (m, 1 H). Anal. Calcd for $C_{11}H_9BrO_2$: C, 52.20; H, 3.58. Found: C, 52.21; H, 3.46.

***N*-(α-Methylbenzyl)-2-[(trimethylsilyl)methyl]propenamide (10).** To a stirred solution of 2.55 g (22 mmol) of potassium *tert*-butoxide in 60 mL of THF cooled to −78 °C was added a solution of **2** (1.89 g, 10 mmol) in 10 mL of THF. After the mixture was stirred for 1 h at −78 °C, *n*-butyllithium (22 mmol) was added during 13 min. The resulting dark purple suspension was stirred for 1 h at −78 °C and a solution of 2.39 g (22 mmol) of chlorotrimethylsilane in 10 mL of THF was added. The mixture was stirred for 1 h at −78 °C, warmed to 0 °C, stirred for 3 h, and quenched with saturated aqueous NH_4Cl (10 mL). Water (100 mL) was added, the organic layer was removed, and the aqueous layer was extracted with ether (3 × 50 mL). The combined organic layers were washed 2 times with brine, dried, and evaporated. Column chromatography (6:1 hexane/ethyl acetate) afforded 2.49 g (95%) of pure **10**: mp 61–63 °C; IR (KBr) 3260, 1620, 1580, 1245, 850 cm^{-1}; ^1H NMR δ 7.30 (s, 5 H), 5.90 (br s, 1 H), 5.24 (s, 1 H), 4.91–5.14 (m, 2 H), 1.80 (s, 2 H), 1.50 (d, J = 7 Hz, 3 H), 0.02 (s, 9 H). Anal. Calcd for $C_{15}H_{23}NOSi$: C, 68.91; H, 8.87; N, 5.36. Found: C, 68.75; H, 8.93; N, 5.30.

General Procedure for the Preparation of Chiral 2-[(Tributylstannyl)methyl]propenamides. *N*-[(*S*)-α-Methylbenzyl]-2-[(tributylstannyl)methyl]propenamide ((*S*)-(−)-12). To a solution of potassium *tert*-butoxide (2.74 g, 22 mmol) in 50 mL of THF cooled to −78 °C was added 1.89 g (10 mmol) of *N*-[(*S*)-α-methylbenzyl]-2-methylpropenamide ((*S*)-(−)-**11**: mp 95.0–95.4 °C; $[\alpha]^{24}_D$ −71.4° (*c* 3.76, EtOH)) in 5 mL of THF. After the mixture was stirred for 1 h, *n*-butyllithium (22 mmol) was added and the reaction mixture was stirred at −78 °C for 2 h. Chlorotributyltin (3.91 g, 12 mmol) in 5 mL of THF was added to the above dianion solution, and the mixture was stirred for an additional 1 h, warmed to 0 °C, and quenched with 10 mL of saturated aqueous NH_4Cl. This was poured into 100 mL of cold water, the organic layer was removed, and the aqueous layer was extracted 3 times with 50 mL of ether. The combined organic layers were washed 2 times with saturated aqueous NaCl, dried, and evaporated to yield the crude product which was purified by column chromatography (20:1 hexane/ethyl acetate) to give 4.43 g (93%) of *N*-[(*S*)-α-methylbenzyl]-2-[(tributylstannyl)methyl]propenamide ((*S*)-(−)-**12**) as a colorless thick oil: $[\alpha]^{24}_D$ −29.4° (*c* 3.57, $CHCl_3$); IR (thin film) 3250, 1620, 1580 cm^{-1}; ^1H NMR δ 7.23 (s, 5 H), 6.03 (m, 1 H), 5.10 (m, 1 H), 5.12 (s, 1 H), 4.95 (s, 1 H), 1.93 (s, 2 H), 0.40–1.80 (m, 30 H). Anal. Calcd for $C_{24}H_{41}NOSn$: C, 60.27; H, 8.64; N, 2.93. Found: C, 60.00; H, 8.90; N, 3.22.

***N*-[(*R*)-α-Methylbenzyl]-2-[(tributylstannyl)methyl]propenamide ((*R*)-(+)-12)** was prepared in the same manner from *N*-[(*R*)-α-methylbenzyl]-2-methylpropenamide ((*R*)-(+)-**11**: mp 94.8–95.0 °C; $[\alpha]^{24}_D$ +73.7° (*c* 3.93, EtOH)) in 65% yield as a thick colorless oil: $[\alpha]^{25}_D$ +30.8° (*c* 3.83, $CHCl_3$); IR (thin film) 3250, 1620, 1580 cm^{-1}; ^1H NMR δ 7.37 (s, 5 H), 6.11 (m, 1 H), 5.21 (s, 1 H), 5.18 (m, 1 H), 5.05 (s, 1 H), 1.96 (s, 2 H), 0.40–1.76 (m, 30 H). Anal. Calcd for $C_{24}H_{41}NOSn$: C, 60.27; H, 8.64; N, 2.93. Found: C, 60.65; H, 8.53; N, 3.15.

***N*-[(*S*)-1-(Methoxymethyl)-2-methylpropyl]-2-[(tributylstannyl)methyl]propenamide ((*S*)-(−)-14)** was prepared from *N*-[(*S*)-1-(methoxymethyl)-2-methylpropyl]-2-methylpropenamide ((*S*)-(−)-**13**): $[\alpha]^{27}_D$ −46.5° (*c* 3.34, EtOH)) in 70% yield as a thick colorless oil: $[\alpha]^{22}_D$ −28.4° (*c* 3.68, $CHCl_3$); IR (thin film) 3270, 1640, 1590 cm^{-1}; ^1H NMR δ 6.05 (m, 1 H), 5.20 (s, 1 H), 5.04 (s, 1 H), 3.88 (m, 1 H), 3.22–3.89 (m, 5 H), 1.96 (s, 2 H), 0.54–0.88 (m, 34 H). Anal. Calcd for $C_{22}H_{45}NO_2Sn$: C, 55.71; H, 9.56; N, 2.95. Found: C, 55.52; H, 9.77; N, 3.16.

***N*-[(*R*)-1-(Methoxymethyl)-2-methylpropyl]-2-[(tributylstannyl)methyl]propenamide ((*R*)-(+)-14)** was prepared in the same manner from *N*-[(*R*)-1-(methoxymethyl)-2-propyl]-2-methylpropenamide ((*R*)-(+)-**13**: $[\alpha]^{26}_D$ +44.8° (*c* 3.78, EtOH)) in 68% yield as a thick colorless oil: $[\alpha]^{26}_D$ +29.2° (*c* 3.53, $CHCl_3$); IR (thin film) 3920, 1640, 1592, 1490, 1110 cm^{-1}; ^1H NMR δ 6.05 (m, 1 H), 5.20 (s, 1 H), 5.04 (s, 1 H), 3.90 (m, 1 H), 3.32 (s, 3 H), 3.20–3.70 (m, 2 H), 1.95 (s, 2 H), 0.50–1.90 (m, 34 H). Anal. Calcd for $C_{22}H_{45}NO_2Sn$: C, 55.71; H, 9.56; N, 2.95. Found: C, 55.49; H, 9.83; N, 3.31.

***N*-[(*S*)-1-(Methoxymethyl)-3-methylbutyl]-2-[(tributylstannyl)methyl]propenamide ((*S*)-(−)-16)** was prepared from *N*-[(*S*)-1-(methoxymethyl)-3-methylbutyl]-2-methylpropenamide ((*S*)-(−)-**15**: mp 41.8–42.5 °C; $[\alpha]^{23}_D$ −46.4° (*c* 3.54, EtOH)) in 60% yield as a thick colorless oil: $[\alpha]^{26}_D$ −22.1° (*c* 3.75, $CHCl_3$); IR (thin film) 3270, 1640, 1590 cm^{-1}; ^1H NMR δ 5.94 (m, 1 H), 5.21 (s, 1 H), 5.05 (s, 1 H), 4.22 (m, 1 H), 3.36–3.52 (m, 5 H), 1.96 (s, 2 H), 0.53–1.84 (m, 36 H). Anal. Calcd for $C_{23}H_{47}NO_2Sn$: C, 56.57; H, 9.70; N, 2.87. Found: C, 56.60; H, 9.88; N, 3.24.

***N*-[(*R*)-1-(Methoxymethyl)-3-methylbutyl]-2-[(tributylstannyl)methyl]propenamide ((*R*)-(+)-16)** was prepared from *N*-[(*R*)-1-(methoxymethyl)-3-methylbutyl]-2-methylpropenamide ((*R*)-(+)-**15**: $[\alpha]^{24}_D$ + 46.4° (*c* 3.51, EtOH)) in 69% yield as thick colorless oil: $[\alpha]^{24}_D$ +22.4° (*c* 3.66, $CHCl_3$); IR (thin film) 2900, 1635, 1585, 1490, 1105 cm^{-1}; ^1H NMR δ 5.90 (br s, 1 H), 5.17 (s, 1 H), 5.00 (s, 1 H), 4.17 (m, 1 H), 3.30 (m, 5 H), 1.92 (s, 2 H), 0.70–1.80 (m, 36 H). Anal. Calcd for $C_{23}H_{47}NO_2Sn$: C, 56.57; H, 9.70; N, 2.87. Found: C, 56.34; H, 9.94; N, 3.18.

***N*-[(*S*)-α-(Methoxymethyl)phenethyl]-2-[(tributylstannyl)methyl]propenamide ((*S*)-(−)-18)** was prepared from *N*-[(*S*)-α-(methoxymethyl)phenethyl]-2-methylpropenamide ((*S*)-(−)-**17**: mp 39.6–41.4 °C; $[\alpha]^{22}_D$ −49.4° (*c* 3.60, EtOH)) in 61% yield as a thick colorless oil: $[\alpha]^{19}_D$ −24.1° (*c* 3.82, $CHCl_3$); IR (thin film) 3280, 1635, 1585 cm^{-1}; ^1H NMR δ 7.20 (br s, 5 H), 6.05 (m, 1 H), 5.10 (s, 1 H), 4.97 (s, 1 H), 4.25 (m, 1 H), 3.30 (m, 5 H), 2.88 (d, J = 7.2 Hz, 2 H), 1.92 (s, 2 H), 0.50–1.75 (m, 27 H). Anal. Calcd

for $C_{26}H_{45}NO_2Sn$: C, 59.79; H, 8.68; N, 2.68. Found: C, 59.51; H, 8.91; N, 2.87.

***N*-[(*R*)-α-(Methoxymethyl)phenethyl]-2-[(tributylstannyl)methyl]propenamide ((*R*)-(+)-18)** was prepared from *N*-[(*R*)-α-(methoxymethyl)phenethyl]-2-methylpropenamide ((*R*)-(+)-17: $[\alpha]^{24}_D$ +49.0° (*c* 3.63, EtOH)) in 68% yield as a thick colorless oil: $[\alpha]^{24}_D$ +26.1° (*c* 3.67, $CHCl_3$); IR (thin film) 2875, 1640, 1590, 1485, 1115 cm^{-1}; ^1H NMR δ 7.29 (s, 5 H), 6.12 (m, 1 H), 5.15 (s, 1 H), 5.02 (s, 1 H), 4.30 (m, 1 H), 3.33 (m, 5 H), 2.90 (d, *J* = 6.6 Hz, 2 H), 1.93 (s, 2 H), 0.70–1.80 (m, 27 H). Anal. Calcd for $C_{26}H_{45}NO_2Sn$: C, 59.79; H, 8.68; N, 2.68. Found: C, 59.90; H, 8.86; N, 2.94.

***N*-[((1*S*,2*R*,5*S*)-6,6-Dimethylbicyclo[3.1.1]hepan-2-yl)methyl]-2-[(tributylstannyl)methyl]propenamide ((*S*)-(−)-20)** was prepared from *N*-[((1*S*,2*R*,5*S*)-6,6-dimethylbicyclo-[3.1.1]heptan-2-yl)methyl]-2-methylpropenamide ((*S*)-(−)-19: mp 52.3–53.0 °C; $[\alpha]^{23}_D$ −15.9° (*c* 3.61, EtOH)) in 73% yield as thick colorless oil: $[\alpha]^{20}_D$ −5.7° (*c* 3.83, $CHCl_3$); IR (thin film) 3260, 1625, 1580 cm^{-1}; ^1H NMR δ 5.85 (m, 1 H), 5.07 (s, 1 H), 4.91 (s, 1 H), 3.24 (m, 2 H), 0.38–2.46 (m, 44 H). Anal. Calcd for $C_{26}H_{19}NOSn$: C, 61.19; H, 9.68; N, 2.74. Found: C, 60.92; H, 9.87; N, 3.05.

***N*-[(*R*)-1-(1-Naphthyl)ethyl]-2-[(tributylstannyl)methyl]propenamide ((*R*)-(+)-22)** was prepared from *N*-[(*R*)-1-(1-naphthyl)ethyl]-2-methylpropenamide ((*R*)-(−)-21: mp 115.0–115.5 °C; $[\alpha]^{26}_D$ −22.4° (*c* 3.80, EtOH)) in 65% yield as a colorless oil: $[\alpha]^{22}_D$ +8.2° (*c* 4.05, $CHCl_3$); IR (thin film) 3250, 1620, 1580 cm^{-1}; ^1H NMR δ 7.30–8.14 (m, 7 H), 5.73–6.10 (m, 2 H), 5.04 (s, 1 H), 4.91 (s, 1 H), 1.93 (s, 2 H), 0.50–1.80 (m, 30 H). Anal. Calcd for $C_{28}H_{43}NOSn$: C, 63.65; H, 8.20; N, 2.65. Found: C, 64.04; H, 8.48; N, 2.76.

General Procedure for the Preparation of γ-Hydroxy Amides 23–42 and Optically Active Lactones 7j (Table II). To a solution of isovaleraldehyde (2.4 mmol) in 20 mL of CH_2Cl_2 cooled to −78 °C was added 2 mmol of $TiCl_4$ in 2 mL of CH_2Cl_2. After the mixture was stirred for 5 min, a solution of 2 mmol of the chiral stannyl amide in 5 mL of CH_2Cl_2 was added. The mixture was stirred at −78 °C for 2 h and at −50 °C for 2 h and then allowed to warm to 0 °C over 2 h. The mixture was quenched with 10 mL of water and extracted 4 times with CH_2Cl_2. The organic layers were combined, washed 2 times with saturated aqueous NaCl, dried, and evaporated to a viscous oil which was chromatographed (silica gel) to yield the diastereomeric mixture of γ-hydroxy amides. Physical and spectral data of the γ-hydroxy amides follows.

4-Hydroxy-*N*-[(*S*)-α-methylbenzyl]-6-methyl-2-methyleneheptanamide (23): ^1H NMR δ 7.23 (s, 5 H), 5.64 (s, 1 H), 5.24 (s, 1 H), 5.05 (m, 1 H), 4.25 (m, 1 H), 3.70 (m, 1 H), 2.00–2.60 (m, 2 H), 0.96–1.88 (m, 6 H), 0.83 (d, *J* = 7 Hz, 6 H).

4-Hydroxy-*N*-[(*R*)-α-methylbenzyl]-6-methyl-2-methyleneheptanamide (24): ^1H NMR δ 7.24 (s, 6 H), 5.64 (s, 1 H), 5.24 (s, 1 H), 5.04 (q, *J* = 7.2 Hz, 1 H), 3.57–4.19 (m, 2 H), 2.15–2.57 (m, 2 H), 1.42 (d, *J* = 7.2 Hz, 3 H), 1.12–1.92 (m, 3 H), 0.86 (d, *J* = 7.2 Hz, 6 H); IR (thin film) 3225, 1600, 945, 780, 715 cm^{-1}; MS, *m/e* (relative intensity) 275 (M^+, 21), 218 ($M^+ - C_4H_9$, 64), 189 ($M^+ - C_4H_9CHO$, 100).

4-Hydroxy-*N*-[(*S*)-1-(methoxymethyl)-2-methylpropyl]-6-methyl-2-methyleneheptanamide (25): ^1H NMR δ 6.35 (m, 1 H), 5.60 (s, 1 H), 5.32 (s, 1 H), 3.72–3.98 (m, 3 H), 3.45 (m, 2 H), 3.33 (s, 3 H), 2.16–2.65 (m, 2 H), 0.90–2.04 (m, 15 H).

4-Hydroxy-*N*-[(*R*)-1-(methoxymethyl)-2-methylpropyl]-6-methyl-2-methyleneheptanamide (26): ^1H NMR δ 6.57 (m, 1 H), 5.68 (m, 1 H), 5.37 (s, 1 H), 3.65–4.20 (m, 3 H), 3.30–3.65 (m, 2 H), 3.32 (s, 3 H), 2.10–2.70 (m, 2 H), 0.90–2.10 (m, 16 H); IR (thin film) 3240, 2920, 1630, 1590, 1110 cm^{-1}; MS, *m/e* (relative intensity) 271 (M^+, 1.3), 226 ($M^+ - CH_2OCH_3$, 100), 214 ($M^+ - C_4H_9$, 55), 185 ($M^+ - C_4H_9CHO$, 100).

4-Hydroxy-*N*-[(*S*)-1-(methoxymethyl)-3-methylbutyl]-6-methyl-2-methyleneheptanamide (27): ^1H NMR δ 6.23 (m, 1 H), 5.60 (s, 1 H), 5.32 (s, 1 H), 4.16 (m, 1 H), 3.78 (m, 2 H), 3.39 (m, 2 H), 3.33 (s, 3 H), 2.16–2.54 (m, 2 H), 1.08–2.04 (m, 6 H), 0.91 (7, 12 H).

4-Hydroxy-*N*-[(*R*)-1-(methoxymethyl)-3-methylbutyl]-6-methyl-2-methyleneheptanamide (28): ^1H NMR δ 6.50 (m, 1 H), 5.65 (s, 1 H), 5.36 (s, 1 H), 3.60–4.40 (m, 3 H), 3.40 (m, 2 H), 3.35 (s, 32 H), 2.20–2.50 (m, 2 H), 1.15–1.90 (m, 6 H), 0.90 (m, 12 H); IR (thin film) 3230, 2920, 1630, 1590, 1110 cm^{-1}; MS, *m/e* (relative intensity) 285 (M^+, 1.6), 240 ($M^+ - CH_2OCH_3$, 100), 228 ($M^+ - C_4H_9$, 85), 199 ($M^+ - C_4H_9CHO$, 100).

4-Hydroxy-*N*-[(*S*)-α-(methoxymethyl)phenethyl]-6-methyl-2-methyleneheptanamide (29): ^1H NMR δ 7.17 (m, 5 H), 7.01 (m, 1 H), 5.56 (s, 1 H), 5.23 (s, 1 H), 4.40 (m, 1 H), 4.26 (m, 1 H), 3.70 (m, 1 H), 3.25 (m, 5 H), 2.84 (d, *J* = 8 Hz, 2 H), 2.06–2.58 (m, 2 H), 0.36–1.93 (m, 9 H); IR (thin film) 3230, 2900, 1630, 1590, 1110 cm^{-1}; MS, *m/e* (relative intensity) 319 (M^+, 13), 274 ($M^+ - CH_2OCH_3$, 33), 262 ($M^+ - C_4H_9$, 44), 233 ($M^+ - C_4H_9CHO$, 100).

4-Hydroxy-*N*-[(*R*)-α-(methoxymethyl)phenethyl]-6-methyl-2-methyleneheptanamide (30): ^1H NMR δ 7.28 (s, 5 H), 6.42 (m, 1 H), 5.56 (s, 1 H), 5.33 (s, 1 H), 4.30 (m, 1 H), 3.60–4.00 (m, 2 H), 3.32 (m, 5 H), 2.90 (d, *J* = 7 Hz, 2 H), 2.20–2.60 (m, 2 H), 1.10–2.00 (m, 3 H), 0.95 (d, *J* = 6.8 Hz, 6 H); IR (thin film) 3230, 2900, 1630, 1590, 1110 cm^{-1}; MS, *m/e* (relative intensity) 319 (M^+, 48), 274 ($M^+ - CH_2OCH_3$, 53), 262 ($M^+ - C_4H_9$, 66), 233 ($M^+ - C_4H_9CHO$, 21).

4-Hydroxy-6-methyl-*N*-[((1*S*,2*R*,5*S*)-6,6-dimethylbicyclo[3.1.1]heptan-2-yl)methyl]-2-methyleneheptanamide (31): ^1H NMR δ 7.24 (m, 1 H), 5.62 (s, 1 H), 5.23 (s, 1 H), 4.71 (m, 1 H), 3.69 (m, 1 H), 3.22 (m, 2 H), 0.60–2.58 (m, 26 H).

4-Hydroxy-6-methyl-2-methylene-*N*-[(*R*)-1-(1-naphthyl)ethyl]heptanamide (32): ^1H NMR δ 7.16–8.00 (m, 7 H), 5.70 (m, 1 H), 5.51 (s, 1 H), 5.08 (s, 1 H), 4.20 (m, 1 H), 3.66 (m, 1 H), 2.00–2.48 (m, 2 H), 0.60–1.80 (m, 12 H).

4-Hydroxy-*N*-[(*S*)-α-(methoxymethyl)phenethyl]-2-methyleneoctanamide (33): ^1H NMR δ 6.24 (m, 1 H), 5.63 (s, 1 H), 5.34 (s, 1 H), 4.18 (m, 1 H), 3.90 (m, 1 H), 3.69 (m, 1 H), 3.34–3.43 (m, 5 H), 2.18 (m, 2 H), 1.16–1.78 (m, 6 H), 0.72–1.05 (m, 3 H).

4-Hydroxy-*N*-[(*R*)-α-(methoxymethyl)phenethyl]-2-methyleneoctanamide (34): $[\alpha]^{26}_D$ +43.1° (*c* 1.05, EtOH); ^1H NMR δ 7.26 (s, 5 H), 6.36–6.70 (m, 1 H), 5.57 (s, 1 H), 5.31 (s, 1 H), 4.11–4.48 (m, 1 H), 3.30 (s, 3 H), 3.21–4.01 (m, 4 H), 2.87 (d, *J* = 7.2 Hz, 2 H), 2.20–2.62 (m, 2 H), 0.65–1.62 (m, 9 H); IR (thin film) 3225, 1630, 1590, 750, 700 cm^{-1}; MS, *m/e* (relative intensity) 319 (M^+, 2.6), 274 ($M^+ - CH_2OCH_3$, 6.2), 262 ($M^+ - C_4H_9$, 8.2), 233 ($M^+ - C_4H_9CHO$, 19), 228 ($M^+ - CH_2Ph$, 36).

4-Hydroxy-*N*-[(*S*)-α-(methoxymethyl)phenethyl]-2-methylenenonanamide (35): ^1H NMR δ 7.48 (s, 5 H), 6.64 (m, 1 H), 5.74 (s, 1 H), 5.49 (s, 1 H), 4.25 (m, 1 H), 3.62–3.98 (m, 2 H), 3.38–3.60 (m, 5 H), 3.01 (d, *J* = 7 Hz, 2 H), 2.32–2.76 (m, 2 H), 1.16–1.76 (m, 8 H), 0.91–1.10 (m, 3 H).

4-Hydroxy-*N*-[(*R*)-α-(methoxymethyl)phenethyl]-2-methylenenonanamide (36): $[\alpha]^{27}_D$ +42.4° (*c* 1.18, EtOH); ^1H NMR δ 7.30 (s, 5 H), 6.46–6.73 (m, 1 H), 5.60 (s, 1 H), 5.35 (s, 1 H), 4.16–4.50 (m, 1 H), 3.49–4.02 (m, 2 H), 3.34 (s, 3 H), 3.30 (d, *J* = 3.3 Hz, 2 H), 2.91 (d, *J* = 7.2 Hz, 2 H), 2.22–2.66 (m, 2 H), 0.76–1.68 (m, 11 H); IR (thin film) 3225, 1635, 1590, 745, 700 cm^{-1}; MS, *m/e* (relative intenstiy) 333 (M^+, 7.7), 288 ($M^+ - CH_2OCH_3$, 20), 262 ($M^+ - C_5H_{11}$, 31), 242 ($M^+ - CH_2Ph$, 100), 233 ($M^+ - C_5H_{11}CHO$, 72).

4-Hydroxy-*N*-[(*S*)-α-(methoxymethyl)phenethyl]-2-methylenedecanamide (37): ^1H NMR δ 7.32 (s, 5 H), 6.46 (m, 1 H), 5.61 (s, 1 H), 5.39 (s, 1 H), 4.34 (m, 1 H), 3.69 (m, 1 H), 3.40 (m, 5 H), 3.28 (m, 1 H), 2.94 (d, *J* = 7 Hz, 2 H), 2.32–2.52 (m, 2 H), 1.16–1.64 (m, 10 H), 0.76–1.02 (m, 3 H).

4-Hydroxy-*N*-[(*R*)-α-(methoxymethyl)phenethyl]-2-methylenedecanamide (38): $[\alpha]^{26}_D$ +41.1° (*c* 1.21, EtOH); ^1H NMR δ 7.31 (s, 5 H), 6.52–6.76 (m, 1 H), 5.62 (s, 1 H), 5.36 (s, 1 H), 4.18–4.52 (m, 1 H), 3.56–3.86 (m, 2 H), 3.41 (s, 3 H), 3.40 (d, *J* = 3.3 Hz, 2 H), 2.93 (d, *J* = 7.2 Hz, 2 H), 2.16–2.70 (m, 2 H), 0.76–1.68 (m, 3 H); IR (thin film) 3225, 1630, 1590, 750, 700 cm^{-1}; MS, *m/e* (relative intensity) 347 (M^+, 10), 302 ($M^+ - CH_2OCH_3$, 28), 256 ($M^+ - CH_2Ph$, 100), 233 ($M^+ - C_6H_{13}CHO$, 100).

4-Hydroxy-*N*-[(*S*)-α-(methoxymethyl)phenethyl]-2-methyleneundecanamide (39): ^1H NMR δ 7.29 (s, 5 H), 6.44 (m, 1 H), 5.60 (s, 1 H), 5.36 (s, 1 H), 4.32 (m, 1 H), 3.70 (m, 1 H), 3.52 (m, 1 H), 3.38 (m, 5 H), 2.83 (d, *J* = 7 Hz, 2 H), 2.24–2.42 (m, 2 H), 1.10–1.61 (m, 12 H), 0.78–1.06 (m, 3 H).

4-Hydroxy-*N*-[(*R*)-α-(methoxymethyl)phenethyl]-2-methyleneundecanamide (40): $[\alpha]^{27}_D$ +39.7° (*c* 0.98, EtOH); ^1H NMR δ 7.34 (s, 5 H), 6.48–6.72 (m, 1 H), 5.64 (s, 1 H), 5.39 (s, 1 H), 4.19–4.48 (m, 1 H), 3.58–4.04 (m, 2 H), 3.39 (s, 3 H), 3.38

(d, J = 3.3 Hz, 2 H), 2.93 (d, J = 7.2 Hz, 2 H), 2.23–2.68 (m, 2 H), 0.74–1.66 (m, 15 H); IR (thin film) 3225, 1630, 1590, 745, 700 cm^{-1}; MS, m/e (relative intensity) 361 (M^+, 2.2), 316 ($M^+ - CH_2OCH_3$, 4.9), 270 ($M^+ - CH_2Ph$, 25), 233 ($M^+ - C_7H_{15}CHO$, 26).

4-Hydroxy-*N*-[(*S*)-α-(methoxymethyl)phenethyl]-2-methylenedodecanamide (41): ^1H NMR δ 7.29 (s, 5 H), 6.55 (m, 1 H), 5.59 (s, 1 H), 5.34 (s, 1 H), 4.32 (m, 1 H), 3.56–3.92 (m, 2 H), 3.36 (m, 5 H), 2.92 (d, J = 7 Hz, 2 H), 2.25–2.70 (m, 2 H), 1.12–1.66 (m, 14 H), 0.76–1.04 (m, 3 H).

4-Hydroxy-*N*-[(*R*)-α-(methoxymethyl)phenethyl]-2-methylenedodecanamide (42): $[\alpha]^{25}_D$ +34.1° (c 0.95, EtOH); ^1H NMR δ 7.24 (s, 5 H), 6.34–6.66 (m, 1 H), 5.56 (s, 1 H), 5.30 (s, 1 H), 4.08–4.44 (m, 1 H), 3.52–3.96 (m, 2 H), 3.32 (s, 3 H), 3.31 (d, J = 3.3 Hz, 2 H), 2.88 (d, J = 7.2 Hz, 2 H), 2.19–2.67 (m, 2 H), 0.72–1.62 (m, 17 H); IR (thin film) 3225, 1630, 1600, 745, 700 cm^{-1}; MS, m/e (relative intensity) 375 (M^+, 6.1), 330 ($M^+ - CH_2OCH_3$, 12), 284 ($M^+ - CH_2Ph$, 62), 262 ($M^+ - C_8H_{17}$, 38), 233 ($M^+ - C_8H_{17}CHO$, 90). Optically active lactones **7j–o** were prepared by refluxing a solution of γ-hydroxy amides in dioxane containing 5% HCl for 4 h and identified by comparison with IR and ^1H NMR spectra. Specific rotations of the lactones, after distillation under reduced pressure, are listed in Tables II and III.

General Procedure for the Preparation of 3-Methylene-2-pyrrolidinones (Table IV). To a solution of 1.36 g (4.25 mmol) of the alcohol **29** in 40 mL of THF at −78 °C was added n-butyllithium (8.62 mmol). After the solution was stirred for 30 min, a solution of p-toluenesulfonyl chloride (0.89 g, 4.67 mmol) in 5 mL of THF was added. The mixture was allowed to warm to room temperature during 18 h. The reaction was quenched with saturated aqueous NH_4Cl (10 mL) and the mixture was poured into water. The layers were separated, the aqueous phase was extracted 3 times with ether, and the combined organic fractions were washed 2 times with saturated aqueous NaCl. The organic layer was dried and filtered, and the solvent was removed under vacuum. The diastereomers were separated by column chromatography on silica gel with 6:1 hexane/ethyl acetate as eluent.

5-Isobutyl-1-[(*S*)-α-(methoxymethyl)phenethyl]-3-methylene-2-pyrrolidinone (43). The faster eluting minor diastereomer was obtained as crystals: mp 38–39 °C; $[\alpha]^{27}_D$ −168.4° (c 1.08, EtOH); ^1H NMR δ 7.20 (s, 5 H), 5.91 (s, 1 H), 5.18 (s, 1 H), 3.81 (d, J = 5.7 Hz, 2 H), 3.48–3.92 (m, 1 H), 3.31 (s, 3 H), 2.02–3.41 (m, 5 H), 0.92–1.62 (m, 3 H), 0.83 (d, J = 5.7 Hz, 3 H), 0.67 (d, J = 5.7 Hz, 3 H); IR ($CHCl_3$) 1690, 1660, 940, 770, 720 cm^{-1}.

Slower eluting major diastereomer: mp 88–89 °C; $[\alpha]^{27}_D$ −166.5° (c 1.01, EtOH); ^1H NMR δ 7.21 (s, 5 H), 5.92 (s, 1 H), 5.20 (s, 1 H), 3.31 (s, 3 H), 2.56–4.08 (m, 7 H), 2.08–2.39 (m, 1 H), 1.22–1.62 (m, 1 H), 0.78 (d, J = 5.7 Hz, 3 H), 0.74 (d, J = 5.7 Hz, 3 H), 0.36–1.15 (m, 2 H); IR ($CHCl_3$) 1685, 1660, 940, 770, 720 cm^{-1}. Anal. Calcd for $C_{19}H_{27}NO_2$: C, 75.71; H, 9.03; N, 4.65. Found: C, 75.67; H, 9.02; N, 4.59.

5-Isobutyl-1-[(*R*)-α-(methoxymethyl)phenethyl]-3-methylene-2-pyrrolidinone (44). Faster eluting minor diastereomer: mp 39–40 °C; $[\alpha]^{26}_D$ +169.9° (c 1.04, EtOH); ^1H NMR δ 7.16 (s, 5 H), 5.88 (s, 1 H), 5.16 (s, 1 H), 3.81 (d, J = 5.7 Hz, 2 H), 3.54–3.90 (m, 1 H), 3.32 (s, 3 H), 2.04–3.48 (m, 5 H), 1.08–1.64 (m, 3 H), 0.85 (d, J = 5.7 Hz, 3 H), 0.70 (d, J = 5.7 Hz, 3 H); IR ($CHCl_3$) 1690, 1660, 935, 770, 720 cm^{-1}.

Slower eluting major diastereomer: mp 88–89 °C; $[\alpha]^{26}_D$ + 170.9° (c 1.14, EtOH); ^1H NMR δ 7.18 (s, 5 H), 5.90 (s, 1 H), 5.18 (s, 1 H), 3.31 (s, 3 H), 2.36–4.06 (m, 7 H), 2.09–2.40 (m, 1 H), 1.24–1.68 (m, 1 H), 0.80 (d, J = 5.7 Hz, 3 H), 0.76 (d, J = 5.7 Hz, 3 H), 0.38–1.17 (m, 2 H); IR ($CHCl_3$) 1660, 1640, 920, 750, 720 cm^{-1}. Anal. Calcd for $C_{19}H_{27}NO_2$: C, 75.71; H, 9.03; N, 4.65. Found: C, 75.70; H, 8.94; N, 4.60.

5-Butyl-1-[(*S*)-α-(methoxymethyl)phenethyl]-3-methylene-2-pyrrolidinone (45). Faster eluting minor diastereomer: $[\alpha]^{24}_D$ −166.1° (c 0.77, EtOH); ^1H NMR δ 7.21 (s, 5 H), 5.91 (s, 1 H), 5.21 (s, 1 H), 3.83 (d, J = 5.7 Hz, 2 H), 3.33 (s, 3 H), 2.08–3.01, 3.14–3.96 (m, 6 H), 0.68–1.79 (m, 9 H); IR (thin film) 1690, 1660, 940, 770, 720 cm^{-1}.

Slower eluting major diastereomer: $[\alpha]^{24}_D$ −156.6° (c 1.06, EtOH); ^1H NMR δ 7.21 (s, 5 H), 5.92 (s, 1 H), 5.20 (s, 1 H), 3.30 (s, 3 H), 2.56–4.06 (m, 7 H), 2.09–2.39 (m, 1 H), 0.44–1.52 (m, 9 H); IR (thin film) 1690, 1660, 940, 770, 720 cm^{-1}. Anal. Calcd for $C_{19}H_{27}NO_2$: C, 75.71; H, 9.03; N, 4.65. Found: C, 75.47; H, 8.92; N, 4.54.

5-Butyl-1-[(*R*)-α-(methoxymethyl)phenethyl]-3-methylene-2-pyrrolidinone (46). Faster eluting minor diastereomer: $[\alpha]^{25}_D$ +167.6° (c 0.82, EtOH); ^1H NMR δ 7.21 (s, 5 H), 5.92 (s, 1 H), 5.20 (s, 1 H), 3.84 (d, J = 5.7 Hz, 2 H), 3.34 (s, 3 H), 2.28–3.04, 3.02–3.94 (m, 6 H), 0.74–1.84 (m, 9 H); IR (thin film) 1690, 1680, 935, 770, 720 cm^{-1}.

Slower eluting major diastereomer: $[\alpha]^{25}_D$ +156.3° (c 0.91, EtOH); ^1H NMR δ 7.22 (s, 5 H), 5.92 (s, 1 H), 5.21 (s, 1 H), 3.32 (s, 3 H), 2.59–4.07 (m, 7 H), 2.12–2.42 (m, 1 H), 0.44–1.52 (m, 9 H); IR (thin film) 1685, 1660, 935, 770, 720 cm^{-1}. Anal. Calcd for $C_{19}H_{27}NO_2$: C, 75.71; H, 9.03; N, 4.65. Found: C, 75.40; H, 8.82; N, 4.57.

1-[(*S*)-α-(Methoxymethyl)phenethyl]-3-methylene-5-pentyl-2-pyrrolidinone (47). Faster eluting minor diastereomer: $[\alpha]^{23}_D$ −157.6° (c 0.94, EtOH); ^1H NMR δ 7.22 (s, 5 H), 5.88 (s, 1 H), 5.20 (s, 1 H), 3.33 (s, 3 H), 2.09–3.94 (m, 8 H), 0.66–1.76 (m, 11 H); IR (thin film) 1690, 1660, 940, 770, 720 cm^{-1}.

Slower eluting major diastereomer: $[\alpha]^{23}_D$ −142.1° (c 0.99, EtOH); ^1H NMR δ 7.24, (s, 5 H), 5.94 (s, 1 H), 5.23 (s, 1 H), 3.32 (s, 3 H), 2.56–4.08 (m, 7 H), 2.10–2.41 (m, 1 H), 0.46–1.50 (m, 11 H); IR (thin film) 1695, 1665, 940, 775, 720, cm^{-1}. Anal. Calcd for $C_{20}H_{29}NO_2$: C, 76.15; H, 9.27; N, 4.44. Found: C, 76.21; H, 9.32; N, 4.59.

1-[(*R*)-α-(Methoxymethyl)phenethyl]-3-methylene-5-pentyl-2-pyrrolidinone (48). Faster eluting minor diastereomer: $[\alpha]^{20}_D$ +163.8° (c 1.06, EtOH); ^1H NMR δ 7.22 (s, 5 H), 5.94 (s, 1 H), 5.22 (s, 1 H), 3.32 (s, 3 H), 2.10–3.96 (m, 8 H), 0.69–1.82 (m, 11 H); IR (thin film) 1690, 1665, 940, 775, 720 cm^{-1}.

Slower eluting major diastereomer: $[\alpha]^{20}_D$ +147.0° (c 0.99, EtOH); ^1H NMR δ 7.22 (s, 5 H), 5.92 (s, 1 H), 5.20 (s, 1 H), 3.30 (s, 3 H), 2.53–4.08 (m, 7 H), 2.08–2.37 (m, 1 H), 0.44–1.48 (m, 11 H); IR (thin film) 1690, 1665, 940, 775, 720 cm^{-1}. Anal. Calcd for $C_{20}H_{29}NO_2$: C, 76.12; H, 9.27; N, 4.44. Found: C, 76.37; H, 9.31; N, 4.69.

5-Hexyl-1-[(*S*)-α-(methoxymethyl)phenethyl]-3-methylene-2-pyrrolidinone (49). Faster eluting minor diastereometer: $[\alpha]^{25}_D$ −150.4° (c 0.66, EtOH); ^1H NMR δ 7.20 (s, 5 H), 5.90 (s, 1 H), 5.20 (s, 1 H), 3.83 (d, J = 5.7 Hz, 2 H), 3.32 (s, 3 H), 2.80–3.02, 3.16–3.92 (m, 6 H), 0.68–1.80 (m, 13 H); IR (thin film) 1690, 1660, 935, 770, 720 cm^{-1}.

Slower eluting major diastereomer: $[\alpha]^{22}_D$ −139.5° (c 1.22, EtOH; ^1H NMR δ 7.09 (s, 5 H), 5.82 (s, 1 H), 5.12 (s, 1 H), 3.23 (s, 3 H), 2.50–4.00 (m, 7 H), 2.04–2.33 (m, 1 H), 0.30–1.04 (m, 13 H); IR (thin film) 1685, 1660, 935, 770, 720 cm^{-1}. Anal. Calcd for $C_{21}H_{31}NO_2$: C, 76.55; H, 9.48; N, 4.25. Found: C, 76.59; H, 9.41; N, 4.21.

5-Hexyl-1-[(*R*)-α-(methoxymethyl)phenethyl]-3-methylene-2-pyrrolidinone (50). Faster eluting minor diastereomer: $[\alpha]^{25}_D$ +151.9° (c 1.06, EtOH); ^1H NMR δ 7.26 (s, 5 H), 5.98 (s, 1 H), 5.25 (s, 1 H), 3.88 (s, 2 H), 3.41 (s, 3 H), 2.14–3.10, 3.22–4.08 (m, 6 H), 0.68–1.90 (m, 13 H); IR (thin film) 1690, 1665, 935, 770, 720 cm^{-1}.

Slower eluting major diastereomer: $[\alpha]^{25}_D$ +136.1° (c 1.46, EtOH); ^1H NMR δ 7.22 (s, 5 H), 5.92 (s, 1 H), 5.22 (s, 1 H), 3.31 (s, 3 H), 2.57–4.08 (m, 7 H), 2.09–2.40 (m, 1 H), 0.46–1.48 (m, 13 H); IR (thin film) 1690, 1665, 940, 775, 720 cm^{-1}. Anal. Calcd for $C_{21}H_{31}NO_2$: C, 76.55; H, 9.48; N, 4.25. Found: C, 76.20; H, 9.44; N, 4.25.

5-Heptyl-1-[(*S*)-α-(methoxymethyl)phenethyl]-3-methylene-2-pyrrolidinone (51). Faster eluting minor diastereomer: $[\alpha]^{25}_D$ −140.8° (c 1.00, EtOH); ^1H NMR δ 7.20 (s, 5 H), 5.88 (s, 1 H), 5.20 (s, 1 H), 3.85 (d, J = 5.7 Hz, 2 H), 3.33 (s, 3 H), 2.08–3.04, 3.18–3.96 (m, 6 H), 0.30–1.08 (m, 15 H); IR (thin film) 1690, 1665, 940, 770, 720 cm^{-1}.

Slower eluting major diastereomer: $[\alpha]^{25}_D$ −126.4° (c 0.95, EtOH); ^1H NMR δ 7.21 (s, 5 H), 5.92 (s, 1 H), 5.20 (s, 1 H), 3.28 (s, 3 H), 2.55–4.04 (m, 7 H), 2.08–2.38 (m, 1 H), 0.40–1.48 (m, 15 H); IR (thin film) 1690, 1660, 935, 770, 700 cm^{-1}. Anal. Calcd for $C_{22}H_{33}NO_2$: C, 76.92; H, 9.68; N, 4.08. Found: C, 76.67; H, 9.71; N, 4.11.

5-Heptyl-[(*R*)-α-(methoxymethyl)phenethyl]-3-methylene-2-pyrrolidinone (52). Faster eluting minor diastereomer: $[\alpha]^{26}_D$ +144.1° (c 1.03, EtOH); ^1H NMR δ 7.19 (s, 5 H),

5.90 (s, 1 H), 5.20 (s, 1 H), 3.85 (d, J = 5.7 Hz, 2 H), 3.34 (s, 3 H), 2.09–3.03, 3.19–4.00 (m, 6 H), 0.76–1.88 (m, 15 H); IR (thin film) 1690, 1665, 940, 770, 720 cm^{-1}.

Slower eluting major diastereomer: $[\alpha]^{26}_D$ +131.1° (c 1.18, EtOH); ^1H NMR δ 7.16 (s, 5 H), 5.87 (s, 1 H), 5.16 (s, 1 H), 3.26 (s, 3 H), 2.53–4.03 (m, 7 H), 2.08–2.36 (m, 1 H), 0.42–1.52 (m, 15); IR (thin film) 1690, 1665, 940, 775, 720 cm^{-1}. Anal. Calcd for $C_{22}H_{33}NO_2$: C, 76.92; H, 9.68; N, 4.08. Found: C, 76.82; H, 9.59; N, 4.45.

1-[(*S*)-α-(Methoxymethyl)phenethyl]-3-methylene-5-octyl-2-pyrrolidinone (53). Faster eluting minor diastereomer: $[\alpha]^{25}_D$ −140.4° (c 1.01, EtOH); ^1H NMR δ 7.24 (s, 5 H), 5.93 (s, 1 H), 5.21 (s, 1 H), 3.86 (d, J = 5.7 Hz, 2 H), 3.36 (s, 3 H), 2.14–3.06, 3.20–3.95 (m, 6 H), 0.76–1.84 (m, 17 H); IR (thin film) 1690, 1660, 935, 770, 720 cm^{-1}.

Slower eluting major diastereomer: $[\alpha]^{25}_D$ −125.7° (c 1.10, EtOH); ^1H NMR δ 7.20 (s, 5 H), 5.90 (s, 1 H), 5.19 (s, 1 H), 3.29 (s, 3 H), 2.56–4.04 (m, 7 H), 2.10–2.38 (m, 1 H), 0.42–1.56 (m, 17 H); IR (thin film) 1690, 1660, 935, 770, 720 cm^{-1}. Anal. Calcd for $C_{23}H_{35}NO_2$: C, 77.26; H, 9.87; N, 3.92. Found: C, 77.49; H, 9.82; N, 4.21.

1-[(*R*)-α-(Methoxymethyl)phenethyl]-3-methylene-5-octyl-2-pyrrolidinone (54). Faster eluting minor diastereomer: $[\alpha]^{26}_D$ +140.2° (c 1.05, EtOH); ^1H NMR δ 7.24 (s, 5 H), 5.92 (s, 1 H), 5.22 (s, 1 H), 3.85 (d, J = 5.7 Hz, 2 H), 3.36 (s, 3 H), 2.10–3.04, 3.20–3.94 (m, 6 H), 0.71–1.84 (m, 17 H); IR (thin film) 1690, 1660, 930, 770, 720 cm^{-1}.

Slower eluting major diastereomer: $[\alpha]^{26}_D$ +128.1° (c 1.10, EtOH); ^1H NMR δ 7.22 (s, 5 H), 5.93 (s, 1 H), 5.22 (s, 1 H), 3.32 (s, 3 H), 2.58–4.08 (m, 7 H), 2.12–2.44 (m, 1 H), 0.45–1.68 (m, 17 H); IR (thin film) 1690, 1660, 930, 770, 720 cm^{-1}. Anal. Calcd for $C_{23}H_{35}NO_2$: C, 77.26; H, 9.87; N, 3.92. Found: C, 77.31; H, 9.80; N, 4.03.

General Procedure for the Preparation of the MTPA Esters 55–60 (Table V). The MTPA esters **55–60** were prepared from γ-hydroxy amides and (*S*)-(−)-MTPACl. To a stirred solution of 0.16 g (0.50 mmol) of the alcohol **29** and 0.11 g (0.90 mmol) of 4-(dimethylamino)pyridine in 5 mL of CH_2Cl_2 was added 0.20 g (0.79 mmol) of (*S*)-(−)-MTPACl in 3 mL of CH_2Cl_2. The mixture was stirred for 24 h at room temperature, quenched by the addition of 5 mL of water, and extracted with CH_2Cl_2. The organic extracts were combined, washed with saturated aqueous NaCl, and dried. Removal of the solvent under reduced pressure gave quantitatively the MTPA ester. Ester **55**: ^1H NMR δ 7.12–7.77 (m, 10 H), 6.16–6.50 (m, 1 H), 5.55 (s, 1 H), 5.23 (s, 1 H), 4.98–5.44 (m, 1 H), 4.18–4.56 (m, 1 H), 3.52 (s, 3 H), 3.36 (d, J = 3.3 Hz, 2 H), 3.29 (s, 3 H), 2.90 (d, J = 7.2 Hz, 2 H), 2.28–2.77 (m, 2 H), 1.12–1.78 (m, 3 H), 0.79 (d, J = 7.2 Hz, 6 H).

The ester **56** was prepared in quantitative yield from **34**: ^1H NMR δ 7.06–7.69 (m, 10 H), 6.06–6.16 (m, 1 H), 5.24 (s, 1 H), 4.97 (s, 1 H), 4.92–5.29 (m, 1 H), 4.14–4.50 (m, 1 H), 3.51 (s, 3 H), 3.31 (d, J = 3.3 Hz, 2 H), 3.28 (s, 3 H), 2.82 (d, J = 7.2 Hz, 2 H), 2.16–2.78 (m, 2 H), 0.71–1.75 (m, 9 H); IR (thin film) 3350, 1740, 1660, 1620, 740, 720 cm^{-1}.

The ester **57** was prepared in 99% yield from the alcohol **35**: ^1H NMR δ 7.02–7.66 (m, 10 H), 6.12–6.30 (m, 1 H), 5.48 (s, 1 H), 5.20 (s, 1 H), 4.92–5.30 (m, 1 H), 4.18–4.48 (m, 1 H), 3.51 (s, 3 H), 3.32 (d, J = 3.3 Hz, 2 H), 3.28 (s, 3 H), 2.85 (d, J = 7.2 Hz, 2 H), 2.32–2.80 (m, 2 H), 0.68–1.80 (m, 11 H); IR (thin film) 3358, 1740, 1660, 1620, 740, 720 cm^{-1}.

The ester **58** was prepared in 96% yield from the alcohol **37**: ^1H NMR δ 7.00–7.56 (m, 10 H), 6.06–6.30 (m, 1 H), 5.48 (s, 1 H), 5.22 (s, 1 H), 4.92–5.29 (m, 1 H), 4.12–4.54 (s, 3 H), 3.53 (s, 3 H), 3.32 (d, J = 3.3 Hz, 2 H), 3.31 (s, 3 H), 2.86 (d, J = 7.2 Hz, 2 H), 2.33–2.72 (m, 2 H), 0.70–1.76 (m, 13 H); IR (thin film) 3363, 1740, 1660, 1620, 740, 720 cm^{-1}.

The ester **59** prepared in quantitative yield from the alcohol **40**: ^1H NMR δ 7.11–7.77 (m, 10 H), 6.09–6.33 (m, 1 H), 5.26 (s, 1 H), 5.00 (s, 1 H), 4.91–5.37 (m, 1 H), 4.19–4.54 (m, 1 H), 3.52 (s, 3 H), 3.39 (d, J = 3.3 Hz, 2 H), 3.31 (s, 3 H), 2.85 (d, J = 7.2 Hz, 2 H), 2.19–2.71 (m, 2 H), 0.74–1.75 (m, 15 H); IR (thin film) 3343, 1740, 1670, 1625, 750, 720 cm^{-1}.

The ester **60** was prepared in quantitative yield from the alcohol **42**: ^1H NMR δ 7.11–7.67 (m, 10 H), 6.06–6.31 (m, 1 H), 5.27 (s, 1 H), 5.00 (s, 1 H), 4.97–5.33 (m, 1 H), 4.17–4.51 (m, 1 H), 3.55 (s, 3 H), 3.34 (d, J = 3.3 Hz, 2 H), 3.33 (s, 3 H), 2.86 (d, J = 2.2 Hz, 2 H), 2.21–2.68 (m, 2 H), 0.75–1.78 (m, 17 H); IR (thin film) 3358, 1740, 1660, 1620, 740, 720 cm^{-1}.

***N*-[(*R*)-α-(Hydroxymethyl)phenethyl]-2-methylpropenamide ((*R*)-(+)-61).** To a solution of 8.39 g (55.5 mmol) of (*R*)-(+)-2-amino-3-phenyl-1-propanol and 6.2 g (61.3 mmol) of triethylamine in 100 mL of THF was added at 0 °C 6.4 g (61.2 mmol) of methacryloyl chloride. The mixture was stirred, allowed to warm to room temperature over 21 h, and poured into ice–water (300 mL). Extraction with ether afforded a crude oil which was purified by column chromatography on silica gel (1:1 hexane/ethyl acetate), yielding 6.43 g (53%) of the (*R*)-(+)-amide as a colorless viscous oil: $[\alpha]^{27}_D$ +50.4° (c 1.49, EtOH); ^1H NMR δ 7.28 (s, 5 H), 6.08–6.36 (m, 1 H), 5.61 (s, 1 H), 5.29 (s, 1 H), 4.04–4.40 (m, 1 H), 3.65 (d, J = 7.2 Hz, 2 H), 3.25 (s, 1 H), 2.91 (d, J = 7.2 Hz, 2 H), 1.88 (s, 3 H); IR (thin film) 3250, 1640, 1600, 920, 750, 700 cm^{-1}. Anal. Calcd for $C_{31}H_{17}NO_2$: C, 71.20; H, 7.82; N, 6.39. Found: C, 71.09; H, 7.98; N, 6.39.

***N*-[(*R*)-α-[[(Triisopropylsilyl)oxy]methyl]phenethyl]-2-methylpropenamide ((*R*)-(+)-62).** To a solution of 4.04 g (18.4 mmol) of (*R*)-(+)-**61** and 4.94 g (46.1 mmol) of 2,6-lutidine in 60 mL of CH_2Cl_2 was added at 0 °C 7.35 g (24 mmol) of triisopropylsilyl trifluoromethanesulfonate. The mixture was stirred for 2 h at 0 °C, quenched with 10 mL of water, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried, and concentrated. The product was purified by column chromatography (4:1 hexane/ethyl acetate) to yield 6.30 g (91%) of a colorless oil: $[\alpha]^{22}_D$ +32.7° (c 1.04, EtOH); ^1H NMR δ 7.23 (s, 5 H), 6.06–6.28 (m, 1 H), 5.62 (s, 1 H), 5.25 (s, 1 H), 4.08–4.36 (m, 1 H), 3.69 (d, J = 3.3 Hz, 2 H), 2.94 (d, J = 7.2 Hz, 2 H), 1.92 (s, 3 H), 0.80–1.31 (m, 21 H); IR (thin film) 3450, 3300, 1665, 1625, 900, 720, 700 cm^{-1}. Anal. Calcd for $C_{22}H_{37}NO_2Si$: C, 70.34; H, 9.93; N, 3.73. Found: C, 69.85; H, 9.70; N, 3.55.

***N*-[(*R*)-α-[[(Triisopropylsilyl)oxy]methyl]phenethyl]-2-[(tributylstannyl)methyl]propenamide ((*R*)-(+)-63).** By the procedure described for the preparation of the amide (*S*)-(−)-**12**, 1.63 g (4.33 mmol) of (*R*)-(+)-**62**, 1.20 g (10.4 mmol) of *t*-BuOK, 9.55 mmol of *n*-butyllithium, and 1.56 g (4.79 mmol) of chlorotributyltin in 30 mL of THF afforded, after column chromatography (25:1 hexane/ethyl acetate), 1.74 g (60%) of (*R*)-(+)-**63**: $[\alpha]^{26}_D$ +20.0° (c 3.71, $CHCl_3$); ^1H NMR δ 7.28 (s, 5 H), 6.08–6.28 (m, 1 H), 5.11 (s, 1 H), 5.01 (s, 1 H), 4.10–4.44 (m, 1 H), 3.71 (d, J = 3.3 Hz, 2 H), 2.98 (d, J = 7.2 Hz, 2 H), 1.96 (s, 2 H), 1.12 (s, 18 H), 0.71–1.80 (m, 30 H); IR (thin film) 3450, 3325, 1665, 900, 720, 705 cm^{-1}. Anal. Calcd for $C_{34}H_{63}NO_2SiSn$: C, 61.44; H, 9.55; N, 2.11. Found: C, 61.92; H, 9.30; N, 2.21.

Reaction of (*R*)-(+)-63 with Isovaleraldehyde. By the procedure described for the preparation of the alcohol **29**, 3.32 g (5 mmol) of (*R*)-(+)-**63**, 0.47 g (5.47 mmol) of isovaleraldehyde, and 3.79 g (20 mmol) of $TiCl_4$ in 50 mL of CH_2Cl_2 afforded, after column chromatography (3:1 hexane/ethyl acetate), 1.92 g (83%) of alcohol **66** as a viscous oil: $[\alpha]^{25}_D$ +32.1° (c 1.19, EtOH); ^1H NMR δ 7.23 (s, 5 H), 6.36–6.57 (m, 1 H), 5.52 (s, 1 H), 5.28 (s, 1 H), 4.04–4.37 (m, 1 H), 3.64–3.88 (m, 2 H), 3.68 (d, J = 3.3 Hz, 2 H), 2.96 (d, J = 7.2 Hz, 2 H), 2.26–2.46 (m, 2 H), 1.05 (s, 8 H), 1.00–1.88 (m, 6 H), 0.89 (d, J = 7.2 Hz, 6 H); IR (thin film) 3250, 1655, 900, 720, 700 cm^{-1}; MS, m/e (relative intensity) 461 (M^+, 4.8), 419 ($M^+ - C_3H_6$, 100), 404 ($M^+ - C_4H_9$, 38), 375 ($M^+ - C_4H_9CHO$, 78), 370 ($M^+ - CH_2Ph$, 100).

By the procedure described for the preparation of the lactone **7h**, 1.71 g (3.7 mmol) of this alcohol (**66**) and 10 mL of 5% HCl in 15 mL of dioxane afforded, after column chromatography (5:1 hexane/ethyl acetate), 0.59 g (99%) of the lactone. Distillation gave 0.48 g (84%) of (*R*)-(+)-**7j**: $[\alpha]^{25}_D$ +49.4° (c 1.66, EtOH).

***N*-(1-Benzylpropyl)-2-methylpropenamide ((−)-64).** To a solution of 1.63 g (40.8 mmol) of NaOH in 30 mL of water at 0 °C was added 4.70 g (31.4 mmol) of (−)-1-phenyl-2-butanamine ($[\alpha]^{23}_D$ −29.3° (neat), 91% optical purity), and then 3.31 g (31.7 mmol) of methacryloyl chloride was added. The resulting mixture was stirred at 0 °C for 4 h and diluted with 50 mL of ether. The organic phase was separated and the aqueous layer was then extracted 3 times with ether. The combined organic phase was washed with brine and dried. Removal of the solvent under reduced pressure afforded a colorless solid which was recrystallized from hexane: yield 79%; mp 72–74 °C; $[\alpha]^{23}_D$ −17.7° (c 3.38, EtOH); ^1H NMR δ 7.21 (s, 5 H), 5.54 (s, 1 H), 5.45–5.89 (m, 1 H),

5.23 (s, 1 H), 3.97-4.35 (m, 1 H), 2.77 (d, J = 7.2 Hz, 2 H), 1.86 (s, 3 H), 1.21-1.77 (m, 2 H), 0.91 (t, J = 7.2 Hz, 3 H); IR (thin film) 3275, 1660, 1620, 720 cm^{-1}. Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.45; H, 8.71, N, 6.53.

***N*-(1-Benzylpropyl)-2-[(tributylstannyl)methyl]propenamide ((+)-65).** By the procedure described for the preparation of the amide (*S*)-(-)-**12**, 3.82 g (33 mmol) of *t*-BuOK, 3.26 g (15 mmol) of (-)-**64**, 31.7 mmol of *n*-butyllithium, and 5.27 g (16.2 mmol) of chlorotributyltin in 60 mL of THF afforded, after column chromatography (20:1 hexane/ethyl acetate), 5.15 g (69%) of (+)-**65** as a colorless oil; $[\alpha]^{23}_D$ +7.3° (*c* 3.76, $CHCl_3$); ^{1}H NMR δ 7.12 (s, 5 H), 5.38-5.66 (m, 1 H), 4.95 (s, 1 H), 4.88 (s, 1 H), 3.98-4.28 (m, 1 H), 2.73 (d, J = 7.2 Hz, 2 H), 1.84 (s, 2 H), 0.72-2.16 (m, 32 H). Anal. Calcd for $C_{26}H_{45}NO$: C, 61.68; H, 8.96; N, 2.77. Found: C, 61.89; H, 8.86; N, 2.95.

Reaction of (+)-65 with Isovaleraldehyde. By the procedure described for the preparation of the alcohol **29**, 0.47 g (5.5 mmol) of isovaleraldehyde, 3.79 (20 mmol) of $TiCl_4$, and 2.53 g (5 mmol) of (+)-**65** in 50 mL of CH_2Cl_2 afforded, after column chromatography (1:1 hexane/ethyl acetate), 1.60 g (100%) of the alcohol **67** as a colorless oil: $[\alpha]^{23}_D$ -23.6° (*c* 1.14, EtOH); ^{1}H NMR δ 7.11 (s, 5 H), 6.78-7.02 (m, 1 H), 5.50 (s, 1 H), 5.18 (s, 1 H), 3.58-4.66 (m, 3 H), 2.74 (d, J = 7.2 Hz, 2 H), 2.10-2.55 (m, 2 H), 0.80-1.92 (m, 14 H); IR (thin film) 3260, 1650, 1610, 765, 720 cm^{-1}.

By the procedure described for the preparation of the lactone **7h**, 1.35 g (4.44 mol) of this alcohol (**67**) and 10 mL of 5% HCl in 15 mL of dioxane afforded after column chromatography (5:1 hexane/ethyl acetate) 0.58 g (85%) of the lactone, $[\alpha]^{22}_D$ -42.8° (*c* 1.59, EtOH).

***N*-Methyl-*N*-[(*S*)-α-(methoxymethyl)phenethyl]-2-[(tributylstannyl)methyl]propenamide ((*S*)-(-)-68).** $[\alpha]^{26}_D$ -38.8° (*c* 3.71, $CHCl_3$); ^{1}H NMR δ 7.17 (m, 5 H), 4.10-5.00 (m, 3 H), 3.20-3.70 (m, 2 H), 3.26 (s, 3 H), 2.82 (s, 3 H), 2.50-3.00 (m, 2 H), 0.40-2.00 (m, 29 H); IR (thin film) 2850, 1750, 1425, 1060 cm^{-1}. Anal. Calcd for $C_{27}H_{47}NO_2Sn$: C, 60.42; H, 8.64; N, 2.81. Found: C, 60.46; H, 8.83; N, 2.61.

Novel Symmetrical and Mixed Carbamoyl and Amino Polysulfanes by Reactions of (Alkoxydichloromethyl)polysulfanyl Substrates with *N*-Methylaniline[1]

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Reactions of (alkoxydichloromethyl)polysulfanes with *N*-methylaniline can be rationalized by a "*carbamoyl*" route where the alkoxydichloromethyl group behaves via loss of alkyl chloride as a "masked" acid chloride or by a "*sulfenyl*" route which reflects fragmentation of the (alkoxydichloromethyl)polysulfanyl functionality into the corresponding alkoxy(thiocarbonyl) and sulfenyl components (cf. Scheme I). Application of this and related chemistry to bifunctional substrates arising from partial or complete chlorination of $[RO(C{=}S)]_2S_m$, R = Me, Et, *i*-Pr, and m = 1-4, has led to $Ph(Me)N(C{=}O)S_n(C{=}O)N(Me)Ph$, n = 2-12; $Ph(Me)N(C{=}O)S_nN(Me)Ph$, n = 1-6; $Ph(Me)NS_nN(Me)Ph$, n = 1-10; $RO(C{=}S)S_n(C{=}O)N(Me)Ph$, n = 2, 3; and $RO(C{=}S)S_nN(Me)Ph$, n = 1-5. These families allowed a test of reversed-phase high-pressure liquid chromatography for evaluating homologies in polysulfane series. Treatment of bis[2-propoxy(thiocarbonyl)] sulfide (**27c**) with sulfuryl chloride in the presence of calcium carbonate conveniently gave distillable bis(chlorocarbonyl)trisulfane (**14**), whereas the same procedure with SO_2Cl_2 alone gave directly (chlorocarbonyl)disulfanyl chloride (**12**) (see Scheme VII). Higher $Cl(C{=}O)S_mCl$, m = 3-5, were indicated but could not be isolated in the course of studies generalizing results on **14** to the preparation of higher $Cl(C{=}O)S_n(C{=}O)Cl$, n = 4-6. The new bis(carbamoyl) monosulfide **61** was obtained by the relatively slow triphenylphosphine or cyanide promoted desulfurization of bis(methylphenylcarbamoyl)disulfane (**4**) (eq 1 and 4); cyanide treatment of the higher polysulfanes $Ph(Me)N(C{=}O)S_n(C{=}O)N(Me)Ph$ for $n \geq 3$ rapidly gave disulfane **4** directly (eq 5).

Previous accounts from this laboratory[3-6] have described a number of examples of compounds containing primary (alkoxydichloromethyl)polysulfanyl moieties, $ROCCl_2S_n$ (R = methyl, ethyl). Since *N*-methylaniline rapidly and quantitatively converts substrates with one or two acid chloride and/or sulfenyl chloride functionalities to the corresponding stable carbamoyl and/or sulfenyl derivatives,[3] it was of interest to extend the *N*-methylaniline reactions to the title substrates. The present report defines two major pathways for these reactions and describes applications of this and related chemistry to generate several novel symmetrical and mixed families of *N*-methylaniline derivatives containing ten or more linearly connected sulfurs. The newly accessed compounds were used to fully test the scope and limitations of a reversed-phase high-pressure liquid chromatography (HPLC) method[5-7] for evaluating homologies in polysulfane series.

Results and Discussion

Reactions of *N*-Methylaniline with (Alkoxydichloromethyl)(chlorocarbonyl)polysulfanes. When title substrates 1[3] were treated with excess *N*-methylaniline followed by aqueous workup, as many as four products were obtained (Scheme I; Table I, lines 1-5). All of these products were recognized and quantitated on the basis of

(1) Preliminary reports of portions of this work have been presented: (a) Schroll, A. L.; Barany, G. Abstracts of the 17th Great Lakes Regional Meeting of the American Chemical Society, St. Paul, MN, June 1-3, 1983. (b) Larka, E. A.; Schroll, A. L.; Barany, G. In "Proceedings of the Thirty-First Annual Conference on Mass Spectrometry and Allied Topics, Boston, MA"; 1983; pp 577-578.

(2) (a) Taken in part from the Ph.D. Thesis of A. L. Schroll, University of Minnesota, 1986. (b) Present address: Department of Chemistry, St. Michael's College, Winooski, VT 05404. (c) Searle Scholar, 1982; National Institutes of Health Research Career Development Award, 1982-1987.

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