Stereoselective Radical Tandem Cyclohydrostannation of Optically Active Di-unsaturated Esters of TADDOL

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Received July 11, 2007

This paper reports the results obtained in a study on the radical addition of triorganotin hydrides, R_3SnH (R = Me, n-Bu, Ph; Neophyl), to four TADDOL unsaturated diesters. It was found that these reactions lead in high yields to products of cyclohydrostannation. It was also found that whereas the addition of these hydrides to TADDOL diacrylate and TADDOL dimethacrylate leads to the expected mixtures of two and four cycloundecane diastereoisomers, respectively, the addition of triphenyltin hydride to TADDOL disubstituted acrylates yields only four out of the 16 possible stereoisomers. The observed high stereoselectivity is consistent with the radical tandem cyclohydrostannation mechanism proposed. Only in the case of the hydrostannation of TADDOL diacrylate with trimethyl- and triphenyltin hydrides could the diastereoisomers obtained in higher proportion (**5a** and **8a**) be isolated in pure form. The subsequent reduction (lithium aluminum hydride) of macrolides **5a** and **8a** afforded the corresponding optically active diols **26** and **27** in high yield. Full ^{1}H, ^{13}C, and ^{119}Sn NMR data are given.

Introduction

Free radical cyclizations have been extensively utilized for the synthesis of large rings including some relevant natural products.[1] The regio- and diastereoselectivity found in many of these macrocyclizations can be nowadays explained thanks to the pioneer studies of Porter among others.[2] These studies enabled to define conditions wherein intramolecular addition of relatively nucleophilic carbon radicals to electron-deficient alkenes provides efficient entry into 11–20-membered carbocycles and heterocycles. Macrocycle yields can be as high as 80% for secondary or tertiary radicals if the alkene is electron-deficient, and steric effects profoundly affect these reactions.[2b,3] The use of chiral auxiliary groups and rigid organic templates in the control of stereoselectivity in radical and ionic cyclizations has become a powerful and frequently used tool for diastereoselective synthesis of macrocycles and cyclopolymerizations.[4,5] Thus, free radical cyclopolymerization of (−)-*trans*-4,5-bis-[methacryloyloxy]diphenylmethyl]-2,2-dimethyl-1,3-dioxacyclopentane or TADDOL-dimethacrylate leads to helical polymers with very high optical rotations.[6]

We have already shown, in studies on the free radical addition of organotin hydrides to both open-chain[7] and cyclic activated olefins,[8] that these reactions take place with a high degree or even complete stereoselectivity. We have also shown that in the case of *E*- and *Z*-trisubstituted ethylenes, it is possible to predict the stereochemistry of the hydrostannation products by considering the type of substituents attached to the olefinic bond and the preferred conformation of the intermediate radicals resulting from the addition of the organotin radical.[9]

Therefore, continuing our studies on the free radical hydrostannation of prochiral olefinic systems, now we wish to report the results obtained in the addition of organotin hydrides

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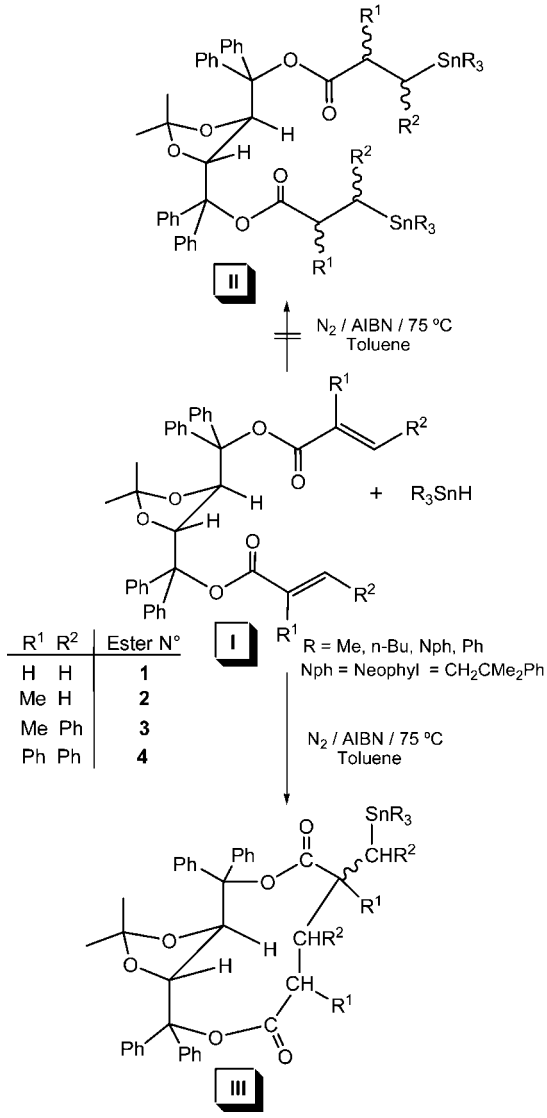
10.1021/om700693p CCC: $40.75
Publication on Web 01/25/2008

Scheme 1. Hydrostannation of TADDOL Unsaturated Esters with Triorganotin Hydrides



to various unsaturated esters of (4*R*,5*R*)-2,3-dimethyl-α,α,α′,α′-tetraphenyl-1,3-dioxolan-4,5-dimethanol (TADDOL).[10]

Results and Discussion

The addition under free radical conditions of triorganotin hydrides to TADDOL diacrylate (**1**) in toluene, using ratios tin hydride/**1** = 2.1 (tin hydride concentration = 0.12 M) and 1.5 (tin hydride concentration = 0.085 M), leads in both cases to products of cyclohydrostannation (**III**, Scheme 1) as shown in Scheme 1. It should be noted that in these cases neither the products of double hydrostannation (**II**, Scheme 1) nor the products of cyclopolymerization were obtained.

Due to the fact that with these substrates the cyclohydrostannation leads to the creation of only one new stereogenic center, a maximum of two diastereomers are expected in each case. The ^{119}Sn NMR spectroscopic analysis of the crude products obtained in the additions of trimethyl-, tri-*n*-butyl-, trineophyl-, and triphenyltin hydrides to ester **1** showed in each case the expected two signals corresponding to the ^{119}Sn present in each one of the diasteroisomers and also shows that they were formed in different proportions, indicating clearly a degree of diasteroselection. As shown in Table 1, the yields of these reactions were in the range 75–88%, whereas diastereoisomeric excesses were high, 76–86%, in three cases (entries 1–3) and low in one, 25% (entry 4). Although column chromatographic separation (silica gel 60) of the diastereomeric mixtures was not really efficient in all cases, this method enabled us to obtain the two major macrolides of each pair in pure form, in the addition of trimethyltin and triphenyltin hydride, i.e., compounds **5a** and **8a**, respectively (Table 1, entries 1 and 4).

Table 1. Addition of Triorganotin Hydrides to TADDOL Unsaturated Diesters 1−4 (as shown in Scheme 1)

entry no.	R	ester	time (h)	adduct	yield (%)	^{119}Sn NMR[a]	*D* (%)[b]
1	Me	**1**	1	**5a**	84	−2.6	88
				5b		4.8	12
2	n-Bu	**1**	1	**6a**	88	−11.8	90
				6b		−7.7	10
3	Neoph	**1**	1.5	**7a**	78	−41.3	99.5
				7b		−39.5	0.5
4	Ph	**1**	2	**8a**	75	−103.91	62.5
				8b		−99.92	37.5
5	Me	**2**	1	**9a**	86	−16.57	9
				9b		−10.06	2
				9c		−9.99	63
				9d		−5.62	26
6	n-Bu	**2**	1.5	**10a**	88	−14.59	20
				10b		−24.46	10
				10c		−19.33	55
				10d		−19.82	15
7	Neoph	**2**	1	**11a**	79	−43.79	47
				1bb		−45.25	6
				11c		−48.92	5
				11d		−51.85	42
8	Ph	**2**	1.5	**12a**	75	−109.04	17
				12b		−114.94	56
				12c		−112.82	22
				12d		−116.41	5
9	Ph	**3**	6	**13a**	70	−119.12	6
				13b		−127.18	10
				13c		−135.84	13
				13d		−141.40	71
10	Ph	**4**	6	**14a**	65	−121.66	25
				14b		−127.07	3
				14c		−135.76	10
				14d		−141.29	62

[a] In $CDCl_3$; in ppm with respect to Me_4Sn. [b] *D* = % of diastereoisomer in the mixture (from ^{119}Sn NMR spectra).

The main ^{13}C NMR characteristics of these mixtures are summarized in Table 2. The ^{13}C NMR chemical shifts (Table 2) were assigned through the analysis of the multiplicity of the signals by means of DEPT experiments and taking into account the magnitude of $^{n}J(^{13}C,^{119}Sn)$ coupling constants.[11]

Under the same free radical conditions, the reactions between TADDOL dimethacrylate (**2**) and the same triorganotin hydrides using a ratio tin hydride/**2** = 1.5, the only reaction products obtained were again those of cyclohydrostannation (Table 1, entries 5–8). The ^{119}Sn NMR spectroscopic analysis of the crude products of each reaction showed the expected mixtures of four diastereomers, again in different proportion, that are consistent with the formation of two new stereogenic centers.

Similar studies on the hydrostannation of TADDOL di(2-methyl-3-phenyl)- (**3**) and di(2,3-diphenyl)acrylates (**4**) showed that the free radical addition of triphenyltin hydride to esters **3** and **4** using a ratio tin hydride/ester = 1.5 also leads to products

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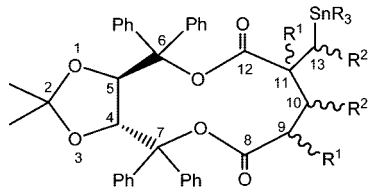
Table 2. Selected ^{13}C NMR Data of the Mixtures of Cyclohydrostannation Products[a]



R	R^1	R^2	Adducts N°
Me	H	H	**5**
n-Bu	H	H	**6**
Neoph	H	H	**7**
Ph	H	H	**8**
Me	Me	H	**9**
n-Bu	Me	H	**10**
Neoph	Me	H	**11**
Ph	Me	H	**12**
Ph	Me	Ph	**13**
Ph	Ph	Ph	**14**

compd	R^1 [^3J(Sn,C)]	C_8	C_9	C_{10} [^3J(Sn,C)]	C_{11} [^2J(Sn,C)]	C_{12} [^3J(Sn,C)]	C_{13} [^1J(Sn,C)]
5a + 5b		170.64	35.11	30.67 (16.7)	43.63	173.12 (8.1)	15.06
		171.48			(10.5)	175.26 (11.3)	(180.7)
6a + 6b		169.72	33.89	29.49 (25.1)	42.62	172.36 (26.8)	11.30
		170.75			(16.4)	174.47 (35.4)	(279.7)
7a + 7b		169.78	35.09	30.12 (21.1)	43.30	171.91 (12.9)	15.96
		170.77			(13.8)	174.11 (45.3)	(291.3)
8a + 8b		170.62	34.99	30.15 (13.1)	43.22	175.38 (27.1)	14.53
		171.53			(11.2)	172.91 (24.8)	(196.1)
9a + 9b	27.85 (8.1)	172.81	39.41	47.97 (22.9)	45.51	175.57 (6.2)	20.74
9c + 9d	28.74 (8.1)	172.86	40.18		(16.2)	175.73 (6.9)	(192.9)
		174.88			45.91	176.75 (13.7)	
		175.49			(20.1)	177.28 (9.8)	
10a + 10b	27.97 (8.7)	171.66	44.94	47.14 (20.1)	44.53	174.02 (6.1)	23.45
10c + 10d	30.76 (8.1)	174.14	45.92		(10.2)	174.59 (6.4)	(172.7)
		174.24			44.60	175.75 (11.5)	
		174.31			(15.5)	176.03 (13.4)	
11a + 11b	27.11 (7.4)	171.75	40.15	48.64 (21.6)	44.15	173.72 (7.6)	21.57
11c + 11d	28.77 (9.3)	173.61	41.38		(25.4)	174.40 (11.8)	(218.5)
		173.83			44.18	175.49 (44.9)	
		174.82			(20.6)	175.71 (27.1)	
12a + 12b	22.71 (6.9)	171.81	45.79	45.6 (20.6)	44.06	174.24 (5.9)	46.73
12c + 12d	23.96 (7.7)	173.47	45.82		(28.5)	174.35 (13.3)	(175.7)
		174.05			44.65	174.46 (15.9)	
		174.11			(16.1)	175.19 (12.6)	
13a + 13b	24.32 (7.3)	165.55	48.12	62.09 (23.9)	51.88	174.15 (7.7)	48.58
13c + 13d	25.53 (8.1)	167.62	49.65		(21.1)	174.28 (12.1)	(172.2)
		167.93			53.16	175.11 (28.8)	
		170.15			(18.9)	175.29 (17.9)	
14a + 14b		166.44	43.92	60.92 (24.8)	53.59	174.70 (28.4)	42.54
14a + 14b		167.96	44.64		(21.5)	174.98 (6.7)	(164.7)
		170.18			55.09	175.31 (25.9)	
		171.95			(16.1)	175.78 (17.3)	

[a] In $CDCl_3$; chemical shifts, δ, in ppm with respect to TMS; J(Sn,C) coupling constants, in Hz (in parentheses).

of cyclohydrostannation. However, although in these cases four new chiral centers may be created, producing a maximum of 16 stereoisomers, the ^{119}Sn NMR spectroscopic data of the crude products showed that, for each reaction, only four diastereomers are present in the mixture (see Table 1). These results clearly indicate that the cyclohydrostannation of the unsaturated esters of TADDOL is actually highly stereoselective.

It is worthwhile to stress the fact that in none of these free radical hydrostannations was detected the formation of the products of cyclopolymerization found in the case of the free radical polymerization of ester **2**.[4a,d,e,6]

On the other hand, trineophyltin hydride does not add to unsaturated esters **3** and **4** under the same free radical conditions. This is not surprising because, as we have reported earlier, due to steric factors this hydride does not add to β-substituted methyl propenoates either.[12] We have also found that neither trimethyltin hydride nor tri-*n*-butyltin hydride adds to unsaturated esters **3** and **4** under the same free radical conditions. NMR analysis of the products obtained in these reactions showed only mixtures of triorganotin esters **15**–**18**, hexaalkylditins **20** and **21**, and reduced TADDOL, i.e., (4*S*,5*S*)-4,5-dibenzhydryl-2,2-dimethyl-1,3-dioxolane (**19**), as shown in Scheme 2. It should be noted that when we repeated the reactions between tri-*n*-butyltin hydride and the hindered unsaturated esters **3** and **4** in the presence of PhSeH, i.e., under polarity-reversal catalysis,[13] the same mixtures of products of hydrostannolysis (**16**, **18**, **19**, and **21**) and in almost the same yields and proportions were obtained.

The reduction of carboxylic acid esters to the corresponding hydrocarbons and triorganotin esters by trialkyltin hydrides via a free radical mechanism has already been reported.[14] It should be noted that, during the chromatographic separation of the reaction mixtures, esters **15**−**18** decomposed, leading to a mixture of the corresponding carboxylic unsaturated acids **22** and **23** and bistriorganotin oxides **24** and **25**, as shown in Scheme 2. The structure of esters **15**−**18** was confirmed by comparison of their spectroscopic characteristics with those of authentic samples prepared via the reaction between carboxylic acids **22** and **23** and the corresponding triorganotin hydrides.

We also studied the reactions between esters **1**−**4** and tri-*n*-butyltin hydride under free radical conditions without solvent,

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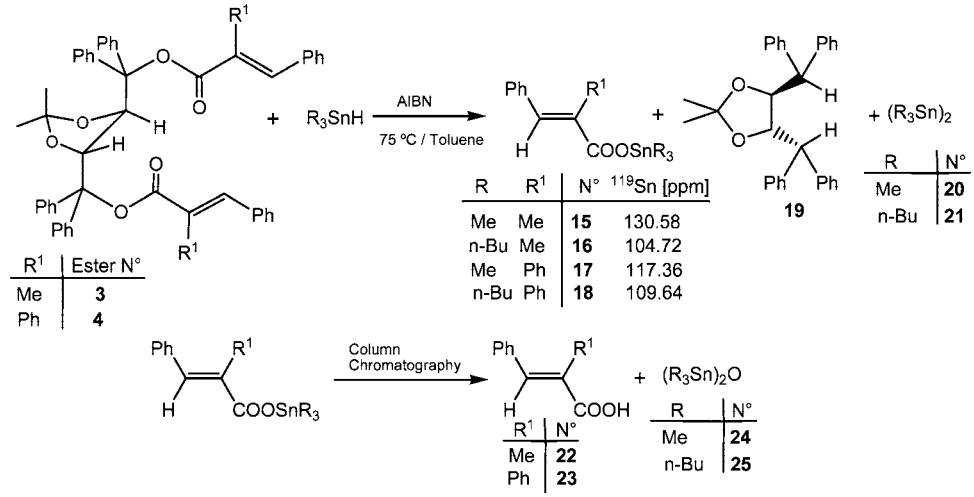
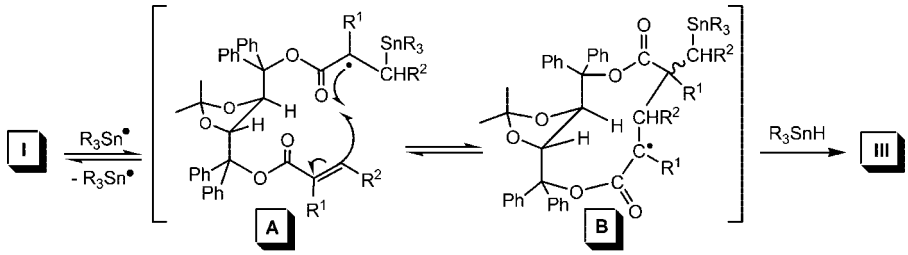
Scheme 2. Hydrostannolysis of TADDOL Unsaturated Esters with Triorganotin Hydrides



Scheme 3. Free Radical Cyclohydrostannation of TADDOL Unsaturated Esters with Various Triorganotin Hydrides



using ratios tin hydride/diesters **1**–**4** = 1.5 (tin hydride concentration ≈ 2.5 M). In the case of esters **1** and **2**, after 4 h these reactions lead again to mixtures containing the expected two (**6a** and **6b**) and four (**10a**−**10d**) stereoisomers. On the other hand, we found that diesters **3** and **4** do not react with tri-*n*-butyltin hydride, and after 48 h under these reaction conditions only the starting esters, hexabutyldistannane, and some tri-*n*-butyltin hydride were recovered. In order to determine the effect of an increase in the concentration of the stannane on the hydrostannation of esters **3** and **4**, these reactions were repeated in toluene using various stannane concentrations. The reactions were carried out under free radical conditions using ratios tin hydride/diesters **3**,**4** = 1.5 and tri-*n*-butyltin hydride in concentrations of 0.5, 1, and 1.5 M. In all cases the reactions were complete in 24 h, and only the hydrostannolysis products were observed (Scheme 2). These results suggest that the stannane concentration does not affect the composition of the reaction products.

The observed cyclohydrostannation could be explained assuming that the triorganotin radical will add to the backbone of one of the unsaturated groups, leading to the alkyl radical **A** (Scheme 3), which in turn adds to the less substituted carbon of the other olefinic group, leading to the product of endocyclization, i.e, the radical **B**. The final step is hydrogen transfer from the organotin hydride to the cyclic radical to give the product of cyclohydrostannation **III** (Scheme 3).

The tandem radical cyclization that leads to the 11-membered rings above-described is a process known to proceed with very high regio- and diastereoselectivity.[2c,d] The possibility of macrocyclization of carbon radicals to terminal alkenes leading to rings larger than 10 members was predicted by Porter in 1987, who also stated that "endocyclizations modes are favored in radical macrocyclizations".[2b] These radical cyclizations may be affected by both polar and steric effects. Thus, since carbon radicals are nucleophilic, the presence of electron-withdrawing substituents activate alkenes toward addition by such radicals. Steric effects are also critical in determining the ease of carbon radical addition to alkenes, so that substitution at the olefin site of radical attack reduces the rate of addition.[15]

In the case of esters **1** and **2** the two factors that dominate the rate of addition to the olefins, i.e., electronic and steric, are both favorable: the alkene substituent (ester group) is electron-withdrawing and the β carbon of acrylate and methacrylate esters are unsubstituted and therefore there is no steric hindrance for the addition. The addition of triphenyltin hydride to esters **3** and **4** follows a similar pattern even though the β carbons of both esters are substituted. The cyclohydrostannations lead in all cases to endocyclic products in agreement with Porter's rule.

The fact that trimethyl- and tri-*n*-butyltin hydrides do not lead to hydrostannation products with esters **3** and **4** whereas triphenyltin hydride does might be partly related to the better hydride-donating ability of the latter hydride.[16] On the other hand, in the case of the reactions of esters **3** and **4** with trimethyl- and tri-*n*-butyltin hydride, due to the fact that the substitution at the olefin site reduces the rate of the radical attack,[17] the rate of addition of these hydrides should be slower than the rate of the competing reaction, i.e., hydrostannolysis, thus leading to the products of the latter reaction according to Scheme 2.

In order to obtain optically active derivatives of glutaric acid, we tried both basic (KOH) and acid (HCl) hydrolysis of compounds **5a** and **8a** without success: no reaction in the first case and only degradation organotin products in the latter case. On the other hand, reduction of compounds **5a** and **8a** with

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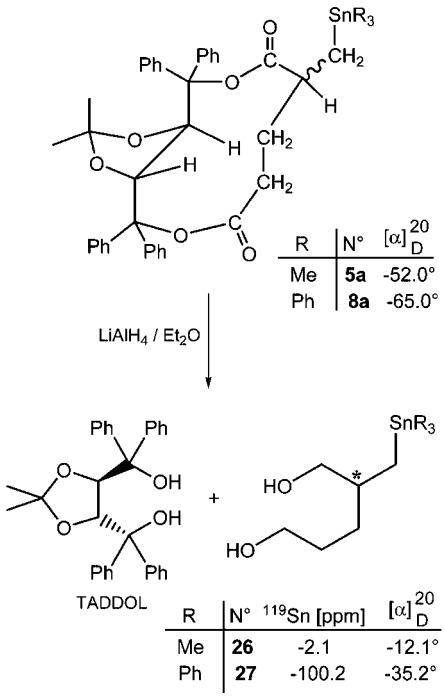
(17) It has been reported (ref 2c) that substitution of a methyl group on the β-position of an acrylate ester reduces the rate of addition by nearly 100-fold.

Scheme 4. Reduction of Esters 5a and 8a to the Corresponding Diols with $LiAlH_4$



lithium aluminum hydride leads to the corresponding optically active diols in high yields, as shown in Scheme 4.

The optically active diols (**26** and **27**) were separated from the mixture with TADDOL by column chromatography (silica gel 60), leading to pure **26** and **27** in 81 and 86% yield respectively.

Further work in order to obtain more information on the use of these free radical cyclohydrostannation processes as a new route to macrolides as well as on the scope of these reactions is in progress.

Experimental Section

NMR spectra were recorded on a Bruker ARX 300 instrument, using $CDCl_3$ as solvent; chemical shifts (δ) are reported in ppm with respect to TMS, ^1H and ^{13}C, and with respect to Me_4Sn in the case of ^{119}Sn NMR spectra. IR spectra were recorded on a FT-IR Nicolet Nexus 470/670/870 spectrophotometer. Mass spectra were obtained using a Finnigan MAT Incos 50 Galaxy System (DIP-MS) at Cologne University (Germany). High-resolution mass spectra (HRMS) were recorded on a Finnigan Mat. 900 (HR-EI-MS). Irradiations were conducted in a reactor equipped with four 250 W lamps with peak emition at 350 nm. Specific rotations were measured with a Polar L-μP, IBZ Messtechnik instrument. Elemental analyses (C, H) were performed in a Carlo Erba instrument at Santiago de Compostela University (Spain). The melting points were determined with a Kofler hot-stage apparatus and are uncorrected. All the solvents and reagents used were analytical reagent grade. Triorganotin hydrides were prepared by reduction of the corresponding chlorides with lithium aluminum, and the starting TADDOL unsaturated diesters were prepared as recently described.[10]

Addition of Triorganotin Hydrides to TADDOL Unsaturated Diesters. The same procedure was used in all the reactions between unsaturated esters and triorganotin hydrides. One experiment is described in detail to illustrate the methods used.

Addition of Triphenyl- and Trimethyltin Hydrides to (−)-*trans*-4,5-Bis(acryloyloxy)diphenylmethyl)-2,2-dimethyl-1, 3-dioxacyclopentane (1). Synthesis of (4*R*,5*R*)-2,2-Dimethyl-6,6,14,14-tetraphenyl-9-triphenylstannylmethylperhydro[1,3]dioxolan [7,13]dioxa-cycloundecine-8,12-dione (8a) and (4*R*,5*R*)- 2,2-Dimethyl-6,6,14,14-tetraphenyl-9-trimethylstannylmethylperhydro [1,3]dioxolan[7,13]dioxacycloundecine-8,12-dione (5a). Diester **1** (1.16 g, 2.0 mmol) in dry toluene (35 mL) was treated with triphenyltin hydride (1.05 g, 3.0 mmol), using AIBN as radical initiator (0.049 g, 0.3 mmol), in a nitrogen atmosphere, at 75 °C, during 1.5 h (optimal time of reaction and adequate excess of organotin hydride were determined in previous runs both by monitoring the reaction by taking samples at intervals and observing the disappearance of the Sn-H absorption and by IR and also by checking that the ^1H NMR spectrum of the reaction mixture did not show the presence of unreacted olefin). The ^{119}Sn NMR spectrum of the crude product showed that under these conditions two compounds were formed, one in 63% (compound **8a**) and the other in 37% yield (**8b**). The crude product thus obtained (1.38 g, 1.5 mmol, 75%) was directly purified by column chromatography using silica gel 60. The cyclic adduct **8a** (0.80 g, 0.86 mmol) was eluted with hexane/diethyl ether (92:8) as a white solid, mp 96–98 °C. $[\alpha]^{20}_D = -65$ (*c* 0.75, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 0.60 (d, 2H); 1.43 (s, 6H); 1.52–2.75 (m, 5H); 5.51 (d, 1H, ^3J(H,H) 7.6 Hz); 5.54 (d, 1H, ^3J(H,H) 7.6 Hz); 7.05–7.40 (m, 35H). ^{13}C NMR ($CDCl_3$): δ 1.16 (312.9); 14.51 (196.1); 14.54; 27.08; 27.30; 30.15 (13.1) ; 35.01; 43.22 (11.2); 76.78; 76.88; 87.53; 87.84; 110.23; 126.83; 126.89; 127.30; 127.43; 127.50; 127.59; 127.64; 128.60; 128.72; 129.07; 130.30; 137.7 (17.9); 138.82; 140.52; 140.66; 144.72; 144.75; 170.62; 175.52 (27.1). IR (KBr): 3057; 3042; 2954; 2893; 1739; 1601; 1494; 1443; 1250; 850; 710; 660 cm^{-1}. HR-MS (EI): calcd for $C_{55}H_{50}O_6Sn$ 926.2629, found 926.2640. Anal. Calcd for $C_{55}H_{50}O_6Sn$: C, 71.36; H, 5.45. Found: C, 71.52; H, 5.54. Diastereoisomer **8b** could not be separated pure.

Under the same reaction conditions, the addition of trimethyltin hydride to diester **1** required 1 h. The ^{119}Sn NMR spectrum of the crude product thus obtained (84%) showed it to consist of compounds **5a** (88%) and **5b** (12%). The crude product was purified by column chromatography (silica gel 60), cyclic adduct **5a** being eluted with hexane/diethyl ether (98:2) as a white solid, mp 98–100 °C. $[\alpha]^{20}_D = -52$ (*c* 0.71, $CHCl_3$). ^1H NMR ($CDCl_3$): δ −0.15 (s, 9H, ^2J(Sn,H) 53.4 Hz); 0.63 (d, 2H); 1.36 (s, 6H); 1.55–2.65 (m, 5H); 5.51 (d, 1H, ^3J(H,H) 7.6 Hz); 5.59 (d, 1H, ^3J(H,H) 7.6 Hz); 7.11–7.30 (m, 20H). ^{13}C NMR: δ −8.67 (168.1); 15.06 (180.7); 21.44; 27.17; 27.20; 30.67 (16.7); 35.11; 43.63 (10.5); 77.25; 77.33; 87.26; 87.53; 110.02; 125.31; 126.69; 127.10; 127.16; 127.45; 128.21; 128.43; 128.68; 128.99; 130.24; 137.67; 140.63; 140.66; 144.63; 144.75; 170.64; 175.26 (11.3). IR (KBr): 3045; 3032; 2950; 2880; 1735; 1605; 1492; 1445; 1210; 870; 705; 650 cm^{-1}. HR-MS (EI): calcd for $C_{40}H_{44}O_6Sn$ 740.2159, found 740.2170. Anal. Calcd for $C_{40}H_{44}O_6Sn$: C, 64.97; H, 5.99. Found: C, 65.15; H, 6.09. Diastereoisomer **5b** could not be separated pure.

Reaction of Trimethyl- and Tri-*n*-butyltin Hydrides with TADDOL (−)-Di(2-methyl-3-phenyl)acrylate (3) and TADDOL (−)-Di(2,3-diphenyl)acrylate (4): Generation of Trimethylstannyl (15) and Tri-*n*-butylstannyl 2-Methyl-3-phenylpropenoate (16), Trimethylstannyl (17) and Tri-*n*-butylstannyl 2,3-diphenylpropenoate (18), (4*S*,5*S*)-4,5-Dibenzhydryl-2,2-dimethyl-1,3-dioxolane (19), Hexamethylditin (20) and Hexa-*n*-butylditin (21), (*E*)-2-Methyl-3-phenyl- (23) and (*E*)-2,3-Diphenylpropenoic Acids (23), and Bis-trimethyl- (24) and Bis-tri-*n*-butyltin Oxide (25). Diester **3** (0.70 g, 0.93 mmol) in dry toluene (10 mL) was treated with trimethyltin hydride (0.31 g, 1.86 mmol), using AIBN as initiator (0.029 g, 0.18 mmol), in a nitrogen atmosphere, at 75 °C, during 24 h (the reaction was monitored by IR spectroscopy and TLC). Then, the solvent was removed at reduced pressure. The ^{119}Sn NMR spectrum of the crude product thus obtained showed that two organotin compounds, **15** and **20**, were formed. On the other hand, the ^1H NMR spectrum of the crude product showed that reduced TADDOL (**19**) was also formed. Column chromatog-

raphy (silica gel 60) of the mixture afforded hexamethylditin (**20**) (0.08 g, 0.14 mmol) in the fraction eluted with hexane; compound **19** (0.30 g, 0.71 mmol) was eluted with hexane/diethyl ether (98:2) as a white solid of low mp. Then, acid **22** (0.25 g, 1.54 mmol) was eluted with hexane/diethyl ether (95:5) and bis(trimethyltin) oxide (**24**) (0.05 g, 0.15 mmol) with diethyl ether. Compounds **19**, **20**, **22**, and **24** were identified by comparison with the physical characteristics reported for them in the chemical literature. Authentic samples of organotin esters **15**−**18** were prepared as described below. When the ester **15** thus obtained was subjected to column chromatography (silica gel 60), it hydrolyzed, leading to the acid **22** and tin oxide **24**.

Under the same conditions, the reaction of diester **3** with tri-*n*-butyltin hydride led to compounds **16**, **19**, **21**, **22**, and **25**. Similarly, under the same conditions the reaction between diester **4** and trimethyltin hydride gave compounds **17**, **19**, **20**, **23**, and **24**, and the reaction of **4** with tri-*n*-butyltin hydride gave compounds **18**, **19**, **21**, **23**, and **25**.

Preparation of Trimethylstannyl (*E*)-2-Methyl-3-phenylpropenoate (15), Tri-*n*-butystannyl (*E*)-2-Methyl-3-phenylpropenoate (16), Trimethylstannyl (*E*)-2,3-Diphenylpropenoate (17), and Tri-*n*-butystannyl (*E*)-2,3-Diphenylpropenoate (18). The same procedure was used in all the reactions.[18] One experiment is described in detail to illustrate the methods used.

A mixture of acid **22** (0.60 g, 3.6 mmol) and bis(trimethyl)tin oxide (0.62 g, 1.8 mmol) was left at room temperature under a nitrogen atmosphere during 5 h. The resulting colorless liquid was dried (Na_2SO_4) and then filtered off. The Na_2SO_4 retained in the filter was washed with pentane (5 portions, 3 mL each), and evaporation of the mixed filtrates gave ester **15** in quantitative yield. The ^{119}Sn NMR spectrum of the product showed one peak at 130.6 ppm. IR and full ^{1}H and ^{13}C NMR characteristics of compounds are included in the Supporting Information.

Reduction of Cyclic Adducts 5a and 8a with Lithium Aluminum Hydride. Synthesis of (−)-2-[(Trimethylstannyl)methyl]pentane-1,5-diol (26) and (−)-2-[(Triphenylstannyl)methyl]-pentane-1,5-diol (27). To a solution of **5a** (0.50 g, 0.6 mmol) in ether (6.5 mL) was added lithium aluminum hydride (0.13 g, 3.6 mmol) at room temperature. After stirring for 4 h, the reaction was quenched with HCl (2 N, 1 mL) and the aqueous layer was extracted with ether. The combined extracts were washed with brine and dried over magnesium sulfate. The organic solvent was distilled off under reduced pressure to give an oily residue, which was purified by column chromatography (silica gel 60). The stannylated alcohol **26** (0.11 g, 0.47 mmol, 86%) was eluted with hexane/AcOEt (92:8) as a colorless oil. $[\alpha]^{20}_D = -12.1$ (*c* 0.74, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 0.0 (s, 9H, ^2J(Sn,H) 25.5); 0.71 (d, 2H, ^2J(Sn,H) 26.9; 1.36 (m, 2H, ^{3}J (H,H) 7.5 ^3J(H,H) 7.3); 1.65 (m, 1H, ^3J(Sn,H) 12.7 ^3J(H,H) 7.5 ^3J(H,H) 6.5); 1.65 (m, 2H, ^3J(H,H) 7.5 ^{3}J (H,H) 7.3); 2.38 (s, 2H); 3.24 (d, 2H, ^3J(H,H) 6.5); 3.36 (t, 2H, ^3J(H,H) 7.3). ^{13}C NMR ($CDCl_3$): δ –9.06 (161.8); 14.26 (177.2); 29.45; 30.44 (18.4); 38.65; 62.80; 38.65 (10.1); 62.80; 68.05 (19.5). IR (film): 3420; 2955; 2860; 1470; 1420; 1380; 1350; 1300; 1190; 1160; 1050; 1010; 880; 690; 670, 600 cm^{-1}. LR-MS: *m*/*z* (%) 282 (M^+, 0.9); 267 (100); 265 (76.5); 263 (46.9); 253 (28.1); 251 (21.7); 249 (15.4); 237 (43.5); 165 (42.7); 151 (43.5); 150 (17.7); 149 (34.5); 148 (21.8); 137 (73.4); 135 (78.1); 133 (57); 123 (18.2); 121 (50.5); 119 (39.8); 117 (23.3); 15 (12.1). HR-MS (EI): calcd for $C_9H_{22}O_2Sn$ 282.0642, found 282.0633.

Under the same experimental conditions, the reduction of cyclic adduct **8a** gave diol **27** as a colorless oil in 75% yield. $[\alpha]^{20}_D = -35.2$ (*c* 0.75, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 0.59 (d, 2H, ^2J(Sn,H) 27.9); 1.34 (m, 2H, ^3J(H,H) 7.5 ^3J(H,H) 6.5); 1.47 (m, 2H, ^3J(H,H) 7.5 ^3J(H,H) 6.5); 1.87 (m, 1H, ^3J(Sn,H) 13.2 ^3J(H,H) 7.5 ^3J(H,H) 6.5); 3.31 (t, 2H, ^3J(H,H) 7.5); 3.35 (s, 2H); 3.37 (d, 2H, ^3J(H,H) 6.5);7.05–7.51 (m, 15H). ^{13}C NMR ($CDCl_3$): δ 15.34 (196.7); 30.12 (12.6); 30.47 (12.7); 34.92; 64.17; 68.03 (17.5); 127.95; 129.49; 133.94; 135.06. IR (film): 3350; 3050; 3035; 2960; 2890; 1605; 1450; 1430; 1390; 1365; 1310; 1215; 1150; 1045; 1010; 890; 710; 660, 610 cm^{-1}. LR-MS *m*/*z* (%): 454 (M^+, 1.4); 409 (56.8); 377 (100); 375 (75.1); 373 (45.6); 351 (23.7); 274 (17.7); 272 (35.4); 270 (21.2); 154 (31.7); 123 (18.2); 121 (50.5); 119 (39.8); 117 (23.3); 77 (28.3); 51 (8.6). HR-MS (EI): calcd for $C_{23}H_{26}O_2Sn$ 454.0955, found 454.0945.

Acknowledgment. This work was supported by the CONICET (Capital Federal, Argentina), ANPCyT (Capital Federal, Argentina), and Universidad Nacional del Sur (Bahía Blanca, Argentina). The generous help of Dr. Mathias Schaefer (University of Cologne, Germay) concerning Mass spectra determinations, and of Dr. José Luis Mascareñias, University of Santiago de Compostela (Spain), in connection with the elemental analyses, is acknowledged. A grant for a short visit to Germany from the Alexander von Humboldt Foundation to J. C. P. is gratefully acknowledged.

Supporting Information Available: This material is available free of charge via the Internet at http://pubs.acs.org.

OM700693P

(18) Anderson, H. H. *J. Org. Chem.* **1957**, *22*, 147.