Mono- and diorganotin derivatives of (*S*)-BINOL diesters as precursors of C_2 symmetry chiral catalysts

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Abstract

The aim of this work is the synthesis of some BINOL derivatives due to their catalytic, biological and medicinal activity. The rigid structure, thermal stability and C_2 symmetry of the binaphthyl molecules plays an important role in asymmetric induction. We report here a study on the radical addition of different triorganotin hydrides, R_3SnH (R= *n*-Bu, Ph) to four (*S*)-BINOL unsaturated diesters (1,1'-binaphthyl-2-2´-diyl diacrylate; 1,1´-binaphthyl-2-2´-diyl dimethacrylate; 1,1´-binaphthyl-2-2´-diyl-(*Z*)-2-methyl-3-phenyl-2-propenoate and 1,1´-binaphthyl-2-2´-diyl di-(*Z*)-2,3-diphenyl-2-propenoate).

Keywords: C_2 symmetry, (*S*)-BINOL unsaturated diesters, hydrostannation

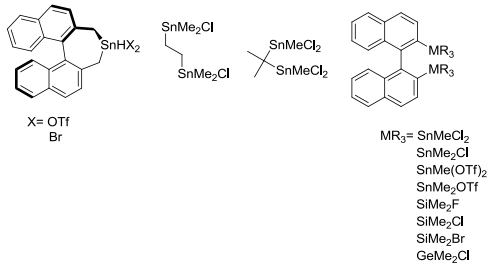
Introduction

BINOL derivatives are versatile molecules with synthetic, catalytic and biological applications.[1] Substituents introduced in the 2,2´-positions of 1,1´- binaphthyl moiety the chiral configuration of the 1,1´-binaphthyl compounds becomes very stable. Studies of Gottarelli, Solladie¸ Mason and co-workers [2] indicated that when 2,2´-substituents on the 1,1´-binaphthyl molecules are either small or capable of intramolecular hydrogen bonding, e.g., OH, CH_2OH, OCH_2COOH, NH_2, OCH_3, CH_3, or OCH_2Ph, the *cisoid* conformation is the one preferred in which the dihedral angle between the two naphthalene rings is less than 90°. When the 2,2´-substituents are large, e.g., CH_2Br or $CHBr_2$, the *transoid* conformation is preferred because the dihedral angle is greater than 90°. The potential of BINOL as a ligand for metal-mediated catalysis was first recognized in 1979 by Noyori et al. in the reduction of aromatic ketones and aldehydes.[3] BINOL itself, however, does not always give satisfactory results in asymmetric catalysis, and since Noyori's discovery there has been an ongoing interest in modified BINOL ligands.

On the other hand, chiral free radical hydrostannylation reactions have been reported on a number of occasions because these reactions proceed most readily with electron-deficient alkenes, which is largely a consequence of the nucleophilicty of the stannyl radical. Bernd Giese [4] reported the influence of substituents in the reactivity and selectivity of free radical addition to alkenes. Both electronic and steric effects of substituents in the vinyl moiety and in the free radical together with the presence of stabilizing groups (Ph-) affect the rate of the reaction. Thus, since carbon radicals are nucleophilic, the presence of electron-withdrawing substituents activates alkenes toward addition by such radicals. As it was previously mentioned, 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 therefore free radicals preferentially binds to the less substituted Csp^2 of alkenes.[5] Hydrostannation of olefins provides a versatile method for the synthesis of organotin compounds containing a broad variety of functional groups. The organotin adducts obtained can be easily derived in halotrialkyltin or halodialkylaryltin compounds, some of them with probable catalytic activity. For example, organotin halides are Lewis acids so they can be used as catalysts in different reactions, such as asymmetric Diels-Alder cycloaddition and alcohol acylations among others, where the metal catalytic centre is near the chiral binaphthyl moiety. Some authors [6] have

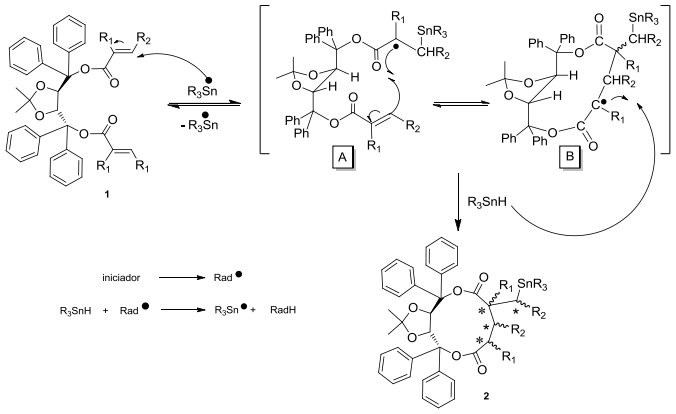
demonstrated that diorganotindihalides has higher catalytic effect compared to triorganotin halides and similar to geminal bis(haloorganostannanes) (**Figure 1**).

Figure 1. Some organotin halides catalyst



Our research group has widely studied the hydrostannation reaction over TADDOL diesters [7] with four triorganotin hydrides (R_3SnH, R= Me, *n*-Bu, Ph and Neophyl) that occurred with intramolecular cyclization with high yield and diastereoselectivity with no polymerization or diaddition products observed. 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** (**Figure 2**), 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 **2** (11-membered rings)**.**

Figure 2. Free Radical Cyclohydrostannation of TADDOL Unsaturated Esters with Various Triorganotin Hydrides

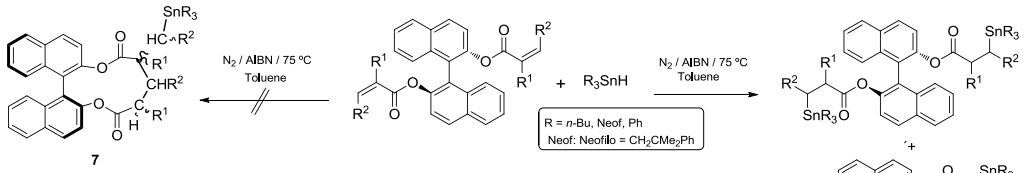


Taking all this information into account, we decided then to study the hydrostannation reaction to four (*S*)-BINOL unsaturated diesters [8] (1,1'-binaphthyl-2-2´-diyl diacrylate; 1,1´-binaphthyl-2-2´-diyl dimethacrylate; 1,1´-binaphthyl-2-2´-diyl-(*Z*)-2-methyl-3-phenyl-2- propenoate and 1,1´-binaphthyl-2-2´-diyl di-(*Z*)-2,3-diphenyl-2-propenoate).

Results and Discussions

The general reaction for the hydrostannation of the (*S*)-BINOL diesters is shown in **Figure 3**. As can be seen, no cycloadducts are obtained and the corresponding mono- and distannylated adducts are formed.

Figure 3. Hydrostannation reaction of (*S*)-BINOL diesters



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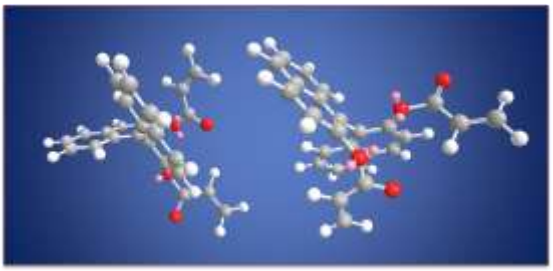
R^1	R^2	Ester N°
H	H	**1**
Me	H	**2**
Me	Ph	**3**
Ph	Ph	**4**

			Adducts	
R	R^1	R^2	Mono	Di
n-Bu	H	H	**5**	**5´**
Neoph	H	H	**6**	**6´**
Ph	H	H	**7**	**7´**
n-Bu	Me	H	**8**	**8´**
Neoph	Me	H	**9**	**9´**
Ph	Me	H	**10**	**10´**
n-Bu	Me	Ph	**11**	**11´**
Neoph	Me	Ph	**12**	**12´**
Ph	Me	Ph	**13**	**13´**
n-Bu	Ph	Ph	**14**	**14´**
Neoph	Ph	Ph	**15**	**15´**
Ph	Ph	Ph	**16**	**16´**

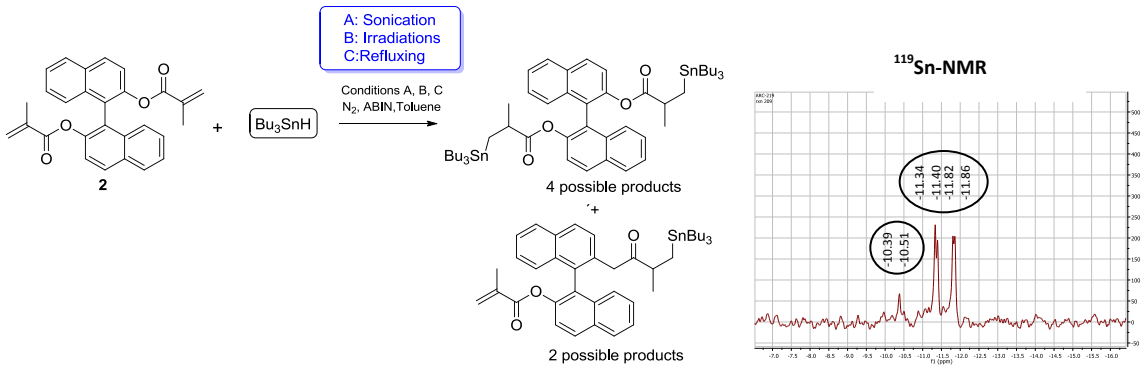
The spatial arrangement of the structure could explain the results. Due to the C_2 symmetry of the (*S*)-BINOL molecule, the alkene targets are opposite one to another, so the formation of the macrocycle is not favoured. As can be observed in the 3D structure of (*S*)-1,1'-binaphthyl-2-2´-diyl diacrylate (**Figure 4**), the dihedral angle between the two naphthalene rings is greater than 90°.

Figure 4. 3D structure of (*S*)-1,1'-binaphthyl-2-2´-diyl diacrylate



In order to establish the best reaction conditions, a systematic study was performed with racemic 1,1´-binaphthyl-2-2´-diyl dimethacrylate and tri-*n*-butyltin hydride (**Figure 5**). From ^{119}Sn-NMR spectra, we could determine that monostannylated products gave two signals at lower frequencies that the four signals corresponding to the diaddition product.

Figure 5. Reaction with 1,1´-binaphthyl-2-2´-diyl dimethacrylate and Tributyltin Hydrides



The results are summarized in **Table 1.** The best yields and reaction time were obtained under **C.3** and **C.4** methods. Taking into account that **C.3** method is the faster one, it was selected to carry out all the reactions. We studied the hydrostannation over the racemic and the enantiopure (*S*)-BINOL diesters with the corresponding organotin hydrides (**Tables 2** and **3** respectively).

Table 1

Entry	Conditions	Hydride	Time	Relation Diester: Hydride	Yield %	Relation Monoadduct /Diadduct [a]
1	A	Bu_3SnH	5hs	**1:1.2**	-	-
2	B	Bu_3SnH	2hs	**1:1.2**	38.6	15/85
3	C.1	Bu_3SnH	2hs	**1:1.2**	20.5	16/86
4	C.2	Bu_3SnH	1hs	**1:3**	66.6	73/27
5	C.3	Bu_3SnH	1hs	**1:2.4**	46.4	9/91
6	C.4	Bu_3SnH Slow addition	2hs	**1:2.4**	34.0	12/88

[a] Integrated from ^{119}Sn-NMR spectra.

Table 2

Entry	$-R_1$	$-R_2$	-R	Time	Relation Diester: Hydride	Relation Monoadduct /Diadduct [a]	Yield %	^{119}Sn-NMR [c]	
								Monoadduct	Diadduct
1	H	H	*n*-Bu	1 h	1:2.4	53/47	7.2	-7.08	-7.39
2	H	H	Nph	1 h	1:2.4	-	-	-	-
3	H	H	Ph	1 h	1:2.4	0/100	75.5		-98.70
4	Me	H	*n*-Bu	1 h	1:2.4	12/88	34.0	-10.39 -10.51	-11.34 -11.40 -11.82 -11.86
5	Me	H	Nph	1 h	1:2.4	- [b]	- [b]		
6	Me	H	Ph	1 h	1:2.4	0/100	73.8	-	-103.24 -103.61 -103.74 -103.91
7	Me	Ph	*n*-Bu	10 h	1:2.4	- [b]	- [b]	-	-
8	Me	Ph	Ph	4 h	1:2.4	- [b]	- [b]	-	-
9	Ph	Ph	*n*-Bu	10 h	1:2.4	- [b]	- [b]	- 6.26 -7.02	-
10	Ph	Ph	Ph	4 h	1:2.4	- [b]	- [b]	-	-

[a] Integrated from ^{119}Sn-NMR spectra; [b] No reaction observed; [c] In $CDCl_3$ in ppm with respect to Me_4Sn.

Table 3

Entry	-R_1	-R_2	-R	Relation Diester: Hydride	Time	Relation Monoadduct /Diadduct [a]	%D [c]	^{119}Sn NMR [d]	
								Monoadduct	Diadduct
1	H	H	*n*-Bu	1:2.4	1h	69/31	-[b]	-7.08	-7.39
2	H	H	Neof	1:2.4	1h	-[b]	-[b]	-	-
3	H	H	Ph	1:2.4	1h	0/100	-	-	98.70
4	Me	H	*n*-Bu	1:2.4	1h	0/100	64%	-11.31	-11.78
5	Me	H	Neof	1:2.4	1h	-[b]	-[b]	-	-
6	Me	H	Ph	1:2.4	1h	0/100	66	-	-103.79 -103.97

[a] integrated from ^{119}Sn-NMR spectra; [b] No reaction observed; [c] D = % of diasteroisomer in the mixture (from ^{119}Sn-NMR spectra); [d] In $CDCl_3$ in ppm with respect to Me_4Sn.

Conclusions

From the results obtained in the studied reactions, it can be observed that the stannyl group was introduced into the terminal carbon with high regioselectivity. The hydrostannylation of (*S*)-1,1´-binaphthyl-2-2´-diyl dimethacrylate proceeded with moderate to good diastereoselectivity (**Table 3**, entry 4 and 6). 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 electronwithdrawing and the *β*- carbon of acrylate and methacrylate esters are unsubstituted and therefore there is no steric hindrance for the addition. The best yields were obtained with Ph_3SnH, because it has the better hydride-donating ability compared to the other organotin hydrides. On the other hand, trineophyltin hydride gave no reaction under the selected free radical reaction 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.[9]

In future studies we will transform the organotin adducts obtained here in halotrialkyltin or halodialkylaryltin compounds, to evaluate their probable catalytic activity. For example, triphenylorganotin adducts with one equivalent of I_2 served to replace one of the pheny group by I. [10] This organotin halides are Lewis acids that would be tested as catalysts in different reactions.

Experimental Section

General methods

Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. Bu_3SnH (CAS Number 688-73-3) and Ph_3SnH (CAS Number 892-20-6) are commercially available or can be synthesized as indicated in the references.[11] Synthesis of $Neof_3SnH$ [9] was made following the reference method. Toluene was dried with $CaCl_2$, and then fractionally distilled (108-109°C) in inert atmosphere from sodium. Diethyl ether was dried with $CaCl_2$ and distilled in inert atmosphere from sodium. Thin layer chromatography was performed on Merck precoated silica gel 60 F254 plates and visualization was accomplished with UV light and/or 5% ethanol solution of phosphomolibdic acid. Silica gel (Merck, 230-400 mesh) was used for column chromatography. Infrared spectra were recorded with a Nicolet Nexus 470 FT spectrometer. NMR spectra were recorded on a Bruker ARX 300 Multinuclear instrument, using $CDCl_3$ as solvent. Compounds described in the literature were characterized by comparison of their ^{1}H-, ^{13}C- and

^{119}Sn-NMR and IR spectra to the previously reported data. Irradiations were conducted in a reactor equipped with four 250 W lamps with peak emition at 350 nm. Ultrasonic reaction was made in a 104x ultrasonic (Ouput power: 190W, Frecuency: 48 khz). Molecular modeling was performed with ChemBio 3D from ChemBioOffice Ultra® 12.0 (CambridgeSoft, Cambridge, MA, USA) using the MM2 molecular mechanics algorithms running on a Windows platform.

Radical Hydrostannation of BINOL *α,β*-Unsaturated Esters with Various Triorganotin Hydrides

Diester **2** (0.24 mmol, 0.10 g.), in dry toluene (5.8 ml), was treated with tributyltin hydride (0.28 mmol, 0.083 g., 0.076 mL), using AIBN as radical initiator (0.04 mmol, 0.006 g.) in nitrogen atmosphere. The reaction mixture was sonicated (**Method A**), irradiated (**Method B**) or refluxed at 75° (**Method C.1**). The reaction was monitored with TLC and IR (observing the disappearance of the Sn-H absorption). The resultant solution was concentrated under reduced pressure. The crude product thus obtained was directly purified by column chromatography using silica gel 60. The monoadduct **8** was eluted with hexane/ethyl acetate (98:2) and the diadduct **8´**with (97:3) as a white oil.

Methods C.2 and C.3. The same reaction conditions as Method **C.1** but with the relation Diester:Hydride (1:2.4).
Method C.4. The same reaction conditions and relation Diester:Hydride that Method **C.3** but the tributyltin hydride was added slowly with an automatic syringe Cole Parmer Vernon Hills (Illinois 60061) over 20 min.

Adducts obtained from the addition of tributyltin hydride to diester **1** (Table **2**, entry 1 and Table **3**, entry 1) were purified by column chromatography using silica gel 60. The monoadduct **5** was eluted with hexane/ethyl acetate (98:2) and the diadduct **5´**with (97:3) as a white oil.
Adducts obtained from the addition of triphenyltin hydride to diester **1** (Table **2**, entry 3 and Table **3**, entry 3) were purified by column chromatography using silica gel 60. The diadduct **7´** was eluted with hexane/ethyl acetate (90:10) as a white oil.
Adducts obtained from the addition of triphenyltin hydride to diester **2** (Table **2**, entry 6 and Table **3**, entry 6) were purified by column chromatography using silica gel 60. The diadduct **10´** was eluted with hexane/ethyl acetate (95:5) as a white oil.

Acknowledgments

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