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Seven membered ring chelates derived from γ-hydroxyamides and triphenyltin or diphenylboron

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ABSTRACT

N-Benzyl-4-hydroxy-butyramide (**1**), 4-hydroxy-*N*-[(R)-1-phenyl-ethyl]-butyramide (**2**), and (R)-4-hydroxy-2-methyl-*N*-[(R)-1-phenyl-ethyl]-butyramide (**3a**) were used to prepare new diphenylboron and triphenyltinoxy compounds: diphenylborinic acid 3-benzylcarbamoyl-propyl ester (**4**), diphenylborinic acid 3-[(R)-1-phenyl-ethylcarbamoyl]-propyl ester (**5**) and diphenylborinic acid (R)-3-[(R)-1-phenyl-ethylcarbamoyl]-butyl ester (**6**), N-benzyl-4-triphenyltinoxy-butyramide (**7**), 4-triphenyltinoxy-*N*-[(R)-1-phenyl-ethyl]-butyramide (**8**), and (R)-4-triphenyltinoxy-2-methyl-*N*-[(R)-1-phenyl-ethyl]-butyramide (**9**). The X-ray diffraction analysis of a crystalline structure of the new γ-hydroxyamide **3a** is reported, as well as that of the first example of a crystalline structure where a diphenylborinic ester forms a seven membered chelate, by a carbonyl coordination to boron (**4**). Structural studies of tin and boron esters were performed by NMR. The C=O internal coordination to tin atoms, affording seven membered rings, was observed by ^{119}Sn NMR experiments at low temperature.

1. Introduction

Interest in the structure and reactivity of proteins has motivated the investigation of amide group coordination to metal atoms [1]. In this context, γ-hydroxyamides are good candidates for formation of coordination compounds with triphenyltin or diphenylboron compounds because of their three potential reactive sites; the OH, N–H and carbonyl groups. γ-Hydroxyamides have important pharmacological activities, for example, as anticonvulsants [2,3], whereas tin compounds have biocidal properties [4–9], and boron derivatives have potential uses in cancer therapies [10–13].

Our interest in the structural investigation of γ-hydroxyamide derivatives is based on the fact that if the OH proton is substituted, the Lewis acid could be intramolecularly coordinated by the carbonyl group affording seven membered rings. Formation of five membered chelates by base coordination to boron and tin is common, whereas six membered chelates are less well known and seven membered rings are seldom reported [14]. The fact that seven membered chelates are weak could explain the lack of examples for triphenyltin esters formed by oxygen coordination and the few reported examples for boron chelates [15]. An O → BH_2O seven membered chelate was recently reported [16]. However, X-ray diffraction analyses for compounds forming seven membered rings by carbonyl coordination to boron are unknown. Where the possibility of seven membered chelates exists in tin compounds, for example in triphenyltin(IV) complexes of *N*,*N*′-disubstituted dihydroxamic acids [17], or of monomethyl phthalate [18], the formation of two five membered rings or a lineal arrangement is preferred, as in the case of μ-succinato-bis(aquatriphenyltin)-bis(o-phenanthroline) [19]. Of additional relevance to this study is the scarcity of reports of amide coordination to boron [20] or tin [21–23], probably due to the low energy of the coordination which results in less stable compounds.

Herein, we report the synthesis and characterization of diphenylborinic esters (**4**–**6**) and triphenyltin alkoxides (**7**–**9**) derived from γ-hydroxyamides (**1**–**3**), Scheme 1. As various coordination compounds derived from γ-hydroxyamides could be expected, depending on the reaction site and on their substitution, we decided to investigate the reactions with γ-hydroxyamides **1**–**3**, having different combination of methyl groups at C2 and/or at C5. Compounds **1** and **2** are known pharmaceuticals used for treatment of addiction and alcoholism [24–26]. Optically active (R)-4-hydroxy-2-methyl-*N*-[(R)-1-phenyl-ethyl]-butyramide (**3a**) is a new compound. Our interest is focused on the structural analyses of compounds **1**–**9**, in particular the evaluation of intramolecular hydrogen bonds (O–H···O=C) and O–Sn ← O=C or O–B ← O=C internal coordination through seven membered ring formation.

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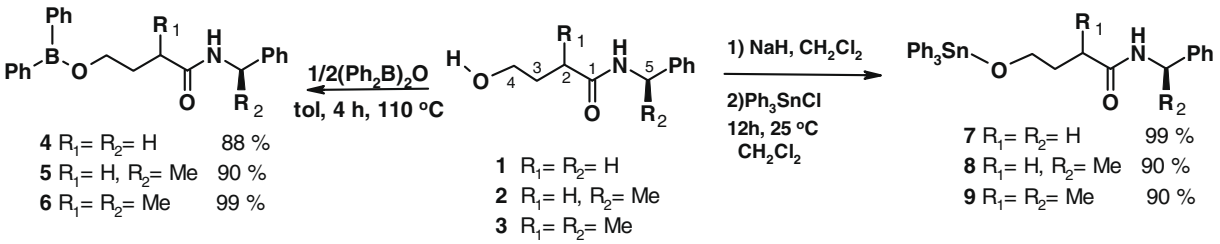


Scheme 1. Synthesis of boron (**4**–**6**) and tin (**7**–**9**) derivatives.

2. Results and discussion

2.1. Syntheses of γ-hydroxyamides *1*–*3*

γ-Hydroxyamides **1**–**2** were prepared with good yields by aminolysis of γ-butyrolactone using benzylamine and optically active (R)-2-methylbenzylamine, respectively. The reaction of (±)-2-methyl-γ-butyrolactone with (R)-2-methylbenzylamine afforded two diasteromers: **3a** (2R,5R) and **3b** (2S,5R), Scheme 2. Compound **3a** was isolated pure by crystallization from DMSO and its structure was obtained by X-ray diffraction analysis. However, we were unable to isolate its pure epimer (**3b**), and only its NMR data was recorded.

The ^{1}H NMR spectrum of compound **1** shows the methylene groups as triplets indicating free rotation of C–C bonds. For compounds **2** and **3**, the AB coupling system for CH_2-3 is attributed to their stereogenic centers. The values of the coupling constant $^{3}J(^{1}H–^{1}H) \approx 6.3–7.2$ Hz of H5 with N–H measured for some of the compounds (**2**, **3**, **6** and **9**), indicate that the N–C5 bond rotation is already anchored and that the protons are in *anti* position, as was confirmed by the fact that NMR experiments at low temperature did not produce relevant changes in the chemical shifts of **1**–**3**. ^{15}N NMR of data of **1**–**3** is characteristic of NH amides. The methyl groups shift the ^{15}N signals of **2** and **3** to lower frequencies with respect to **1** ($\Delta\delta$ 12–14 ppm), Table 1.

2.1.1. Solid state study of compound *3a*

The X-ray diffraction analysis of compound **3a** shows that atoms C7, N6, C1, O15 and C2 are in the same plane, with the ethanol and phenyl groups on one side of this plane. It is noteworthy that the O–H proton is not internally coordinated to the C=O, (Fig. 1). Instead, the carbonyl oxygen atom presents three intramolecular weak C–H hydrogen bonds forming five membered rings (O15···H7, 2.57; O15···H143, 2.90; and O15···H31, 2.56 Å), (Fig. 2). The highest distance incidence for contacts C–H···O has been estimated as being around 2.7 Å [27], however distances as longer as 3.0 Å have been reported. Intermolecular strong hydrogen bonds are formed between N–H···O (2.11 Å) and O–H···O (1.88 Å) giving polymeric arrangements, (Fig. 3).

Table 1
^{119}Sn and ^{15}N NMR data of **7**–**9** (CD_2Cl_2).

Compound	^{15}N (+25 °C)	Compound	^{15}N (+25 °C)	^{11}B (+25 °C)
1	−259.4[92.1]	**4**	−260.1[92.9]	+44.2
2	−245.0[92.1]	**5**	−246.3 [91.8]	+43.4
3a	−246.6[92.1]	**6**	−240.9	+45.0
3b	−247.0[91.1]			
Compound	^{15}N (+25 °C)	^{119}Sn (+25 °C)	^{119}Sn (−70 °C)	^{1}J(Ci-Sn)
7	−257.8	−68.4	−110	not obs.
8	−246.0	−98.5	−210	630.0
9	−247.9	−63.6	−140	622.7

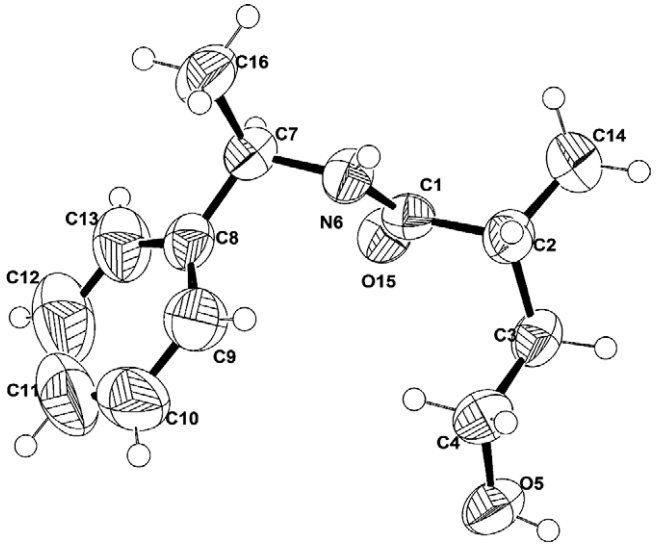
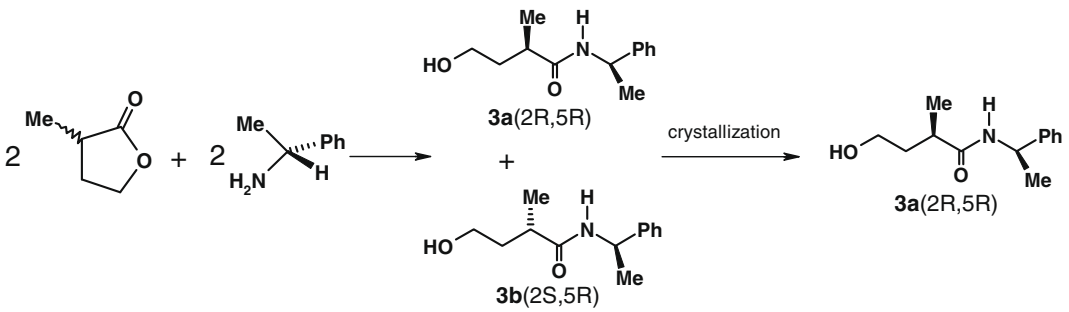


Fig. 1. ORTEP representation of compound **3a.**

2.2. Syntheses of diphenylborinic esters *4*–*6*

Diphenylborinic esters **4**–**6** were prepared in good yields (88–99%) by condensation reactions of γ-hydroxyamides **1**, **2** and **3a**



Scheme 2. Synthesis of compound **3a**.

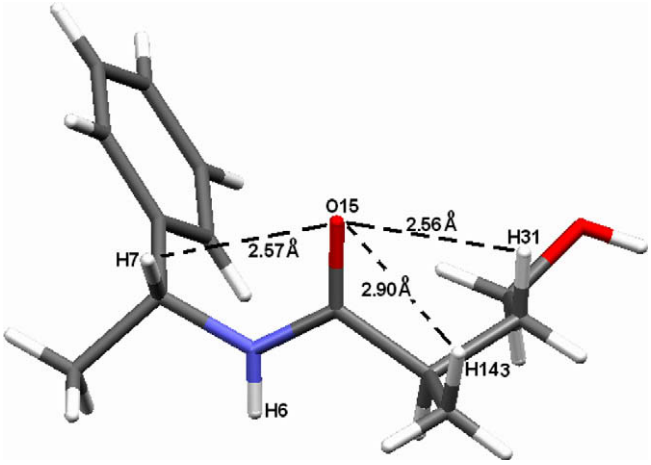
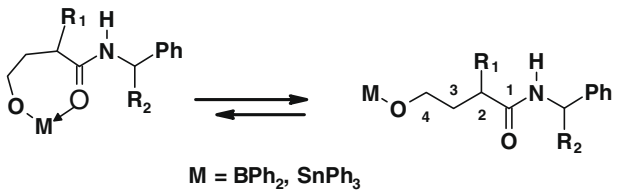


Fig. 2. Solid state structure of compound **3a**, showing three CH-bonds to the carbonyl group.

and diphenylborinic anhydride, (Scheme 1). The ester formation was confirmed by the loss of the O–H signal in the ^{1}H spectrum, and the shift of the C4 resonance to higher frequencies. The lack of participation of the N–H proton in the reactions is deduced from the ^{15}N resonances that did not change in the boron compounds, (Table 1). ^{11}B NMR spectra of **4**–**6** at room temperature (≈+45 ppm) were characteristic of uncoordinated diphenylborinic esters, (Table 1). Tetracoordinated species should be expected around +10 ppm [28,29]. If it is assumed that compounds **4**–**9** could be in equilibrium between a coordinated compound C=O → M and an open structure, for compounds **4**–**6** in solution the open structures are preferred, (Scheme 3).

In order to see if C=O → B coordination could be observed in NMR at low temperature, compounds **4**–**6** were submitted to variable temperature experiments, using CH_2Cl_2 to prevent the solvent coordination to the boron atom [28,29]. However, the experiments failed due to the insolubility of compounds **4**–**6** at low temperature. Fortunately, compound **4** crystallized from CH_2Cl_2 and the X-ray diffraction structure was obtained (Fig. 4). Compound **4** presents a C=O → B coordination bond forming a seven membered chelate. The ring has a chair conformation with B–C12 and B–C18 bonds in axial and equatorial positions respectively, stabilized by hydrogen bonds of the ortho-phenyl protons to the oxygen atoms, (Fig. 5). The bond lengths show that C1–O1 [1.279(2) Å] and C4–O2 [1.427(2) Å] are characteristic of double and single bonds, respectively. A covalent bond O2–B1



Scheme 3. Open and closed structures for compounds **4**–**9**.

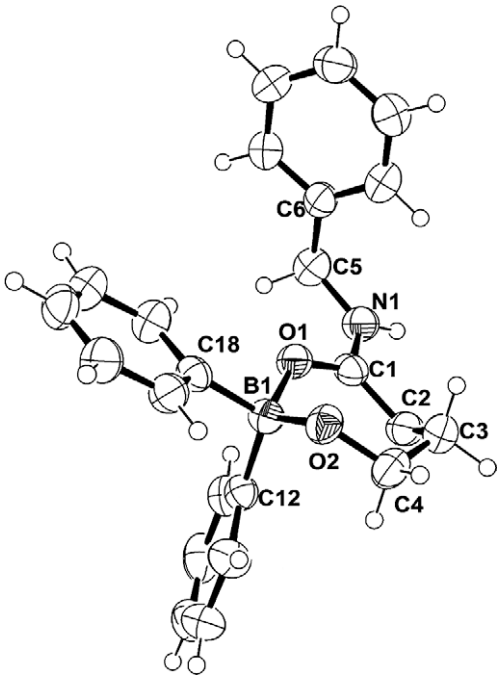


Fig. 4. ORTEP representation of compound **4.**

[1.462(3) Å] and a coordinated one O1 → B1 [1.583(2) Å] are formed. The amide group remains planar, with the N–H *anti* to the C=O. The boron atom is tetrahedral [angles O1–B1–O2 = 109.1(2) and C12–B1–C18 = 110.81(2)°]. Four intramolecular interactions were observed between C–H protons and the boron oxygen atoms, other C–H π-electrons contacts are observed. All of them contribute to stabilize the weak boron oxygen coordination bond and the seven member ring. A methylene proton forms a hydrogen bond with the carbonyl group giving a planar five

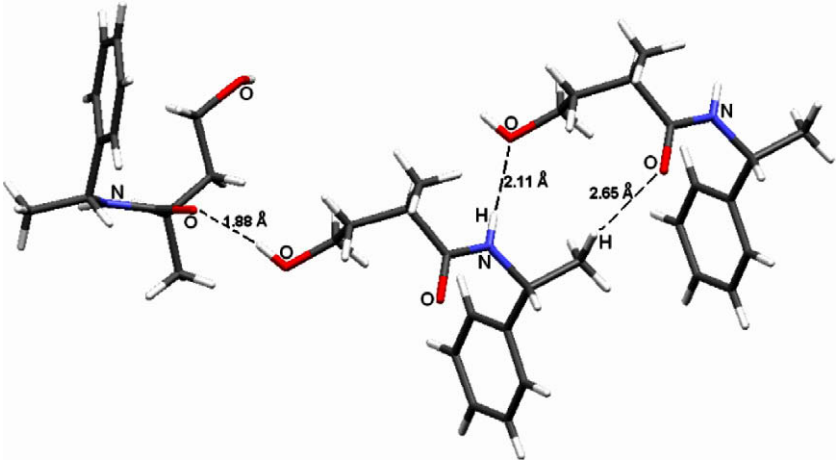


Fig. 3. Intermolecular hydrogen bonds in compound **3a.**

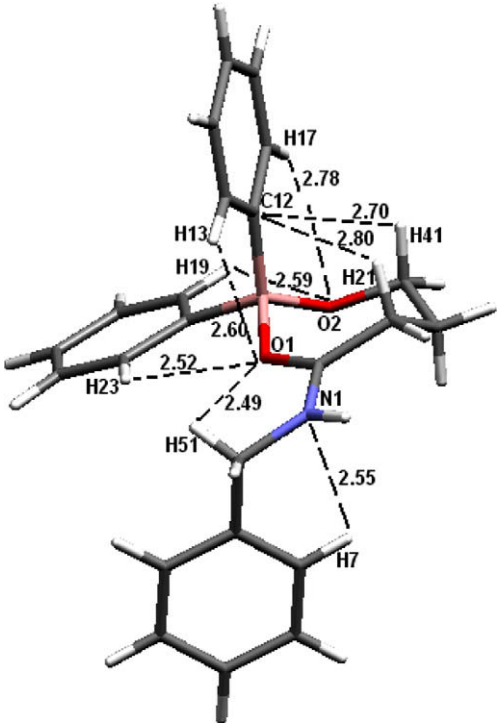


Fig. 5. Intramolecular hydrogen bonds in compound **4.**

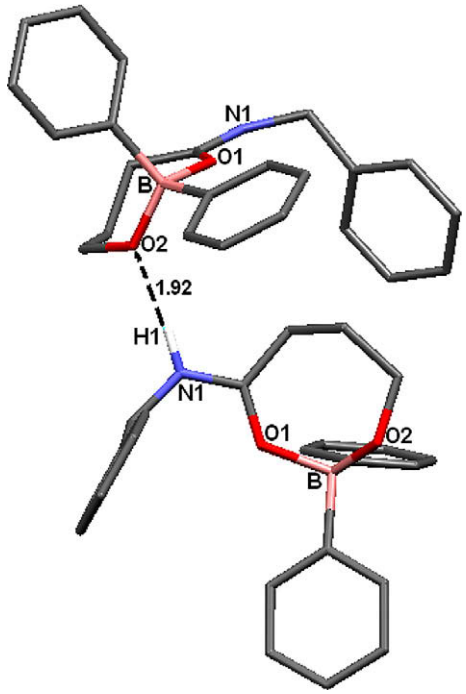


Fig. 6. Intermolecular interaction H1···O2 (1.92 Å), for a clear representation, the hydrogen atoms are not shown, with exception of H1.

membered ring (Fig. 5). Strong intermolecular N–H···O2 hydrogen bonds (1.92 Å) are present in compound **4**, (Fig. 6).

To our knowledge, this X-ray diffraction analysis is the first example of a crystalline structure of a boron compound having a seven membered ring formed by the coordination of a carbonyl group to boron.

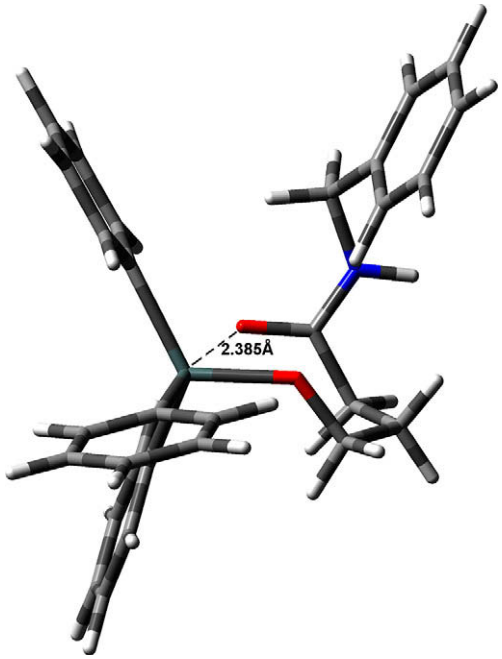


Fig. 7. Structure of the closed conformation of compound **7**, originated by the C=O → Sn intramolecular coordination and modeled by 6-31G* calculations.

2.3. Syntheses of triphenyltin compounds **7–9**

Triphenyltin alkoxides **7–9** were prepared in high yield by reaction of the γ-hydroxyamides sodium alcoholates and triphenyltin chloride in CH_2Cl_2 at room temperature, (Scheme 1). Compound **7** is a colorless solid, whereas **8** and **9** are viscous oils.

^{119}Sn NMR spectra of compounds **7–9** at room temperature showed the formation of triphenyltin alkoxides [30,31]. The ^{119}Sn chemical shifts (**7** −68.4, **8** −98.5 and **9** −63.6 ppm) correspond to tetracoordinated tin atoms. However, spectra recorded at −70 °C in CCl_2D_2 showed the C=O → Sn coordination (**7** −110, **8** −210 and **9** −140 ppm) indicating that equilibrium between the open and closed structures was displaced towards the closed structures at low temperature, (Scheme 3).

Comparison of compounds **7–9** with pentacoordinated RO–$Sn(Ph)_3$ compounds, where the tin atom is coordinated by a carbonyl group as in triphenyltin tropolonate ($\delta = -170$ ppm [32–34]) shows that compound **8** at −70 °C has the strongest C=O → Sn coordination bond whereas compounds **7** and **9** have weaker coordination. As we were unable to crystallize compounds **7–9**, a model of the tin chelate was calculated (Gaussian 6-31G* [35]), (Fig. 7).

3. Conclusions

Three diphenylboron esters and three triphenyltin alkoxydes derived from γ-hydroxyamides were synthesized. Four are optically active, two of which were prepared from a new optically active ligand (**3a**). The solid state analysis of the ligand **3a** does not present the expected hydrogen bond between the OH proton and the amidic carbonyl group forming a seven membered ring. Instead, **3a** adopts a lineal conformation, stabilized by five weak cooperative hydrogen bonds through five membered rings. The diphenylborinic esters and triphenyltinalkoxides are in equilibrium between acyclic and cyclic molecules, the latter having C=O → B and C=O → Sn coordination bonds affording seven membered rings. The seven membered boron chelate (**4**) was isolated.

Its solid state structure is the first example of a diphenylboron in a seven membered ring coordinated by a carbonyl group determined by X-ray diffraction analysis. Although no crystals were obtained for the tin compounds derived from the γ-hydroxyamides, ^{119}Sn NMR experiments at low temperature showed the presence of C=O → Sn seven membered chelates.

4. Experimental

4.1. Physical methods

All solvents were freshly distilled. ^{1}H (400 MHz), ^{13}C (67.9 MHz), ^{15}N (30.42 MHz), ^{11}B (86.68 MHz) and ^{119}Sn (100.72 MHz) NMR spectra were recorded. δ ^{1}H and ^{13}C were referenced to TMS, ^{15}N to CH_3NO_2, ^{11}B to BF_3–OEt_2 and δ ^{119}Sn to Me_4Sn. ^{15}N spectra were obtained by the INEPT pulse sequence with and without decoupling using $^{1}J(^{15}N–^{1}H)$ = 90 Hz. ^{1}H and ^{13}C NMR data of compounds **1**–**9** were assigned by 2D NMR experiments, HETCOR and COSY. Melting points were measured on a Gallenkamp apparatus and are uncorrected. Elemental analyses were performed in a Flash 1112 Thermo Finnigan analyzer. MS spectra were obtained to 20 eV in a HP 5989. High resolution mass spectra were obtained by LC/MSD TOF on an Agilent Technologies instrument with APCI as ionization source.

4.2. Synthetic methods

4.2.1. N-Benzyl-4-hydroxy-butyramide (*1*)

$BnNH_2$ (2.8 mL, 26.0 mmol) and γ-butyrolactone (2.0 mL, 26.0 mmol) were dissolved in benzene (30 mL) and refluxed for 12 h. The reaction mixture was cooled at rt and a solid was separated by filtration and washed with benzene. Compound **1** is a colorless solid (4.9 g, 98%). M.p. 73–74 °C (M.p. lit. 70–72 °C [25,26]). IR (KBr): (*ν*, cm^{-1}) 3270, 1635, 1015. NMR (CD_2Cl_2, 25 °C): ^{13}C δ = 28.3 (C-3), 33.7 (C-2), 43.4 (C-5), 62.1 (C-4), 127.3 (C*p*), 127.5 (2C*m*), 128.6 (2C*o*), 138.7 (C*i*), 173.5 (C-1). ^{1}H δ = 1.78 (m, 2H, H-3), 2.30 (t, *J* = 7.0, 2H, H-2), 3.56 (t, *J* = 5.9, 2H, H-4), 3.47 (br s, 1H, OH), 4.33 (d, *J* = 5.7, 2H, H-5), 7.20–7.32 (m, 5H, Ar), 6.56 (br s, 1H, NH). MS *m/z* (%): [M$^+$] 193(57), 162(23), 149(79), 106(100), 91(97), 79(16). Anal. Calc. for $C_{11}H_{15}NO_2$: C, 68.37; N, 7.25; H, 7.82. Found: C, 68.04; N, 7.19; H, 7.70%.

4.2.2. 4-Hydroxy-N-[(R)-1-phenyl-ethyl]-butyramide (*2*)

A mixture of [*R*]-(−)-$MeBnNH_2$ (3.3 mL, 26.0 mmol) and γ-butyrolactone (2.0 mL, 26.0 mmol) in benzene (50 mL) was refluxed for 12 h. The solvent was evaporated under vacuum, and the product purified by distillation at 135 °C (0.25 mmHg). Compound **2** is a yellow oil (4.8 g, 90%). $[\alpha]_D$ = +122.2 ($CDCl_3$, *c* = 0.02). IR ($CHCl_3$,): *ν* (cm^{-1}) = 3434, 3302, 3066, 1648, 1512, 1450, 1243, 1220, 1056. NMR (CD_2Cl_2, 25 °C): ^{13}C δ = 22.0 (CH_3), 28.6 (C-3), 33.1 (C-2), 48.8 (C-5), 61.4 (C-4), 126.1 (2C*m*), 127.0 (C*p*), 128.4 (2C*o*), 143.8 (C*i*), 173.2 (C-1). ^{1}H δ = 1.39 (d, *J* = 6.9, 3H, CH_3), 1.75 (m, 2H, H-3), 2.25 (dt, *J* = 6.9, 6.0, 2H, H-2), 3.53 (t, *J* = 5.9, 2H, H-4), 4.03 (br s, 1H, OH), 4.99 (quint, *J* = 7.0, 1H, H-5), 7.02 (d, *J* = 7.0, 1H, NH), 7.19–7.33 (m, Ar). MS *m/z* (%): [M$^+$] 207(27), 192(8), 163(38), 120(62), 106(100), 79(14). Anal. Calc. for $C_{12}H_{17}NO_2$: C, 69.54; N, 6.76; H, 8.27. Found: C, 69.55; N, 6.72; H, 8.27%.

4.2.3. (R)-4-Hydroxy-2-methyl-N-[(R)-1-phenyl-ethyl]-butyramide (*3a*) and (S)-4-hydroxy-2-methyl-N-[(R)-1-phenyl-ethyl]-butyramide (*3b*)

The procedure for (**2**) was followed, using (±)-α-methyl-γ-butyrolactone (5.0 g, 50 mmol), and [*R*]-(−)-$MeBnNH_2$ (6.35 mL, 50 mmol), in 50 mL of toluene. A yellow oil was obtained (7.57 g, 69%). The oil was dissolved in Et_2O and the isomer **3a**(R,R) purified by crystallization from DMSO (1.3 g, 11.4%). $[\alpha]_D$ = +75.58 (CH_2Cl_2, *c* = 0.01). M.p. 103 °C. IR (KBr): (*ν*, cm^{-1}) 3532–3297, 3060, 2929, 1633, 1538, 1051. NMR (CD_2Cl_2, 25 °C): ^{13}C δ = 17.5 (CH_3-2), 21.9 (CH_3-5), 36.7 (C-3), 38.0 (C-2), 48.8 (C-5), 60.0 (C-4), 126.0 (2C*m*), 127.1 (C*p*), 128.5 (2C*o*), 144.0 (C*i*), 175.9 (C-1). ^{1}H δ = 1.12 (d, *J* = 7.0, 3H, [CH_3-2]), 1.41 (d, *J* = 7.0, 3H, [CH_3-5]), 1.58 (m, 1H, H-3B), 1.72 (m, 1H, H-3A), 2.45 (dq, *J* = 6.8 and 8.35, 1H, H2), 3.12 (br s, 1H, OH), 3.49 (t, *J* = 6.3, 1H, H-4), 5.00 (quint, *J* = 7.0, 1H, H-5), 6.49 (d, *J* = 7.0, 1H, NH), 7.18–7.31 (m, 5H, Ar). MS *m/z* (%): M$^+$ 221(28), 190(20), 177(37), 105(100), 73(24), 55(23). Anal. Calc. for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65; N, 6.33. Found: C, 70.05; H, 8.66; N, 6.33%.

Isomer **3b**(2S,5R) was identified by ^{1}H and ^{13}C NMR ($CDCl_3$, 25 °C) from the mother liquors: ^{13}C δ = 17.8 (CH_3-2), 21.8 (CH_3-5), 36.6 (C-3), 38.1 (C-2), 48.7 (C-5), 60.3 (C-4), 126.2 (2C*o*), 127.4 (C*p*), 128.7 (2C*m*), 143.4 (C*i*), 176.0 (C-1). ^{1}H δ = 1.12 (d, *J* = 7.0, 3H, CH_3-2), 1.48 (d, *J* = 7.0, 3H, CH_3-5), 1.57 (m, 1H, H-3B), 1.75 (m, 1H, H-3A), 2.46 (m, 1H, H2), 2.84 (br s, 1H, OH), 3.64 (dd, *J* = 11.2, 5.4, 2H, H-4), 5.05 (q, *J* = 7.0, 1H, H-5), 6.32 (br s, 1H, NH), 7.18–7.31 (m, 5H, Ar).

4.2.4. Diphenylborinic acid 3-benzylcarbamoyl-propyl ester (*4*)

Compound **4** was prepared by reaction of hydroxyamide **1** (200 mg, 1.03 mmol) and diphenylborinic anhydride (180 mg, 0.51 mmol) in 50 mL of toluene by refluxing for 4 h in a Dean-Stark trap, and the solvent was evaporated. Compound **4** crystallized from CH_2Cl_2 (320 mg, 88%). M.p. 95 °C. IR (KBr): (*ν*, cm^{-1}) 3042, 2923, 2876, 1624, 1580, 1429, 1153, 743,704. NMR (CD_2Cl_2, 25 °C): ^{13}C δ = 27.7 (C-3), 32.8 (C-2), 43.4 (C-6), 67.1 (C-4), 127.3 (C*p*), 128.6 (2C*m*), 127.6 (4C*m*-B, 2C*p*-B), 130.1 (2C*o*), 134.1 (4C*o*-B), 135.0 (2C*i*-B), 138.8 (C*i*), 172.4 (C-1). ^{1}H δ = 2.02 (m, 2H, H-3), 2.36 (t, *J* = 7.4, 2H, H-2), 4.16 (t, *J* = 6.0, 2H, H-4), 4.36 (d, *J* = 6.0, 1H, H-5), 6.19 (br s, 1H, NH), 7.26–7.69 (m, 15H, Ar). Anal. Calc. for $C_{23}H_{24}BNO_2$: C, 77.33; N, 3.92; H, 6.77. Found: C, 77.35; N, 3.89; H, 6.79%.

4.2.5. Diphenylborinic acid 3-[(R)-1-phenyl-ethylcarbamoyl]-propyl ester (*5*)

Following the general procedure described above, compound **2** (200 mg, 0.97 mmol), and diphenylborinic anhydride (170 mg, 0.48 mmol) formed compound **5**, which is a yellow oil (320 mg, 90%). $[\alpha]_D$ = +44.1 (CH_2Cl_2, *c* = 0.03). IR ($CHCl_3$): (*ν*, cm^{-1}) 3399, 3248, 2923, 1624, 1578, 1429, 1153, 734, 703. NMR (CD_2Cl_2, 25 °C): ^{13}C δ = 21.9 (CH_3-*Bn*), 27.9 (C-3), 33.0 (C-2), 48.9 (C-5), 67.9 (C-4), 126.3 (2C*m*), 127.4 (C*p*), 128.5 (4C*m*-B), 128.7 (2C*o*), 130.2 (2C*p*-B), 134.2 (4C*o*-B), 137.6 (2C*i*-B), 143.5 (C*i*), 171.9 (C-1). ^{1}H δ = 1.53 (d, *J* = 7.0, 3H, CH_3-*Bn*), 2.11 (m, 2H, H-3), 2.44 (ddt, *J* = 6.9, 7.5, 14.6, 2H, H-2), 4.26 (t, *J* = 5.9, 2H, H-4), 5.23 (q, *J* = 7.0, 1H, H-5), 6.52 (br s, 1H, NH), 7.35-7.76 (m, 15H, Ar). Anal. Calc. for $C_{24}H_{26}BNO_2$: C, 77.64; N, 3.77; H, 7.06. Found: C, 77.50; N, 3.78; H, 7.05%.

4.2.6. Diphenylborinic acid (R)-3-[(R)-1-phenyl-ethylcarbamoyl]-butyl ester (*6*)

Compound **3a** (200 mg, 0.9 mmol) and diphenylborinic anhydride (160 mg, 0.45 mmol) produced compound **6** which is a yellow oil (34 mg, 99%). $[\alpha]_D$ = +38.8 (CH_2Cl_2, *c* = 0.05). IR ($CHCl_3$): (*ν*, cm^{-1}) 3295, 3055, 2970, 1644, 1540, 1331. NMR ($CDCl_3$, 25 °C): ^{13}C δ = 18.03 (CH_3), 22.14 (CH_3-*Bn*), 36.19 (C-3), 37.89 (C-2), 48.83 (C-5), 65.94 (C-4), 126.2 (2C*p*-*B*), 127.2 (C*p*), 127.8 (4C*o*-*B*), 128.7 (2C*o*), 130.2 (2C*m*), 134.3 (2C*m*-*B*), 144.13 (C*i*), 175.18 (C-1). ^{1}H δ = 1.27 (d, *J* = 7.0, 3H, CH_3), 1.49 (d, *J* = 6.0, 3H, CH_3-*Bn*), 1.85 (ddt, *J* = 13.8, 9.3 and 7.0, 1H, H-3B), 2.09 (dq, *J* = 13.8, and 6.7, 1H, H-3A), 2.68 (qd, *J* = 6.7 and 7.0, 1H, H-2), 4.14 (ddd, *J* = 10.8, 9.3 and 6.7,1H, H-4B), 4.20 (ddd, *J* = 10.8, 9.3 and 6.0, 1H, H-4A), 5.16 (qd, *J* = 7.2 and 6.0, 1H, H-5), 6.55 (d, *J* = 7.2, 1H, NH),

7.00–7.68 (m, 15H, Ar). +TOF [$C_{25}H_{28}O_2NB + H^+$]: exp. 386.2285 calc. 386.2291 (ppm error −2.81).

4.2.7. N-Benzyl-4-triphenyltinoxy-butyramide (**7**)

Compound **1** (490 mg, 2.58 mmol) dissolved in CH_2Cl_2 (30 mL) was added to NaH (180 mg, 7.74 mmol) and stirred for one h, the NaH excess was filtered. To the solution, Ph_3SnCl (990 mg, 2.58 mmol) in CH_2Cl_2 (20 mL) was added and stirred for 4 h. Compound **7** was obtained as white solid, (1.2 g, 99%). M.p. 87–89 °C. IR ($CHCl_3$): (ν, cm^{-1}) 3297, 3065, 2927, 1640, 1548, 1428, 1073, 1021, 730, 695. NMR (CD_2Cl_2, 25 °C): ^{13}C δ = 27.8 (C-3), 34.03 (C-2), 43.7 (C-5), 62.4 (C-4), 127.5 (C*p*), 127.7 (2C*m*), 128.7 (2C*o*), 129.3 [J(^{13}C,^{119}Sn) 64.9 Hz, 6C*o*], 130.5 [J(^{13}C,^{119}Sn) 13.8 Hz, 3C*p*], 136.3 [J(^{13}C,^{119}Sn) 24.9 Hz, 6C*m*], 138.3 (3Sn-C*i*), 138.4 (C*i*), 174.14 (C-1). ^1H δ = 1.60 (m, 2H, H-3), 2.16 (t, J = 7.0, 2H, H-2), 3.40 (t, J = 5.9, 2H, H-4), 4.31 (d, J = 5.7, 2H, H-5), 7.20–7.79 (m, Ar), 6.74 (br s, 1H, NH). NMR (CD_2Cl_2, −70 °C): ^{13}C δ = 25.9 (C-3), 33.9 (C-2), 43.50 (C-5), 62.5 (C-4), 127.8 (C*p*), 128.1 (2C*m*), 128.3 (J(^{13}C,^{119}Sn) 68.5 Hz, 6Sn-C*o*),128.9 (2C*o*), 130.6 (^{3}Sn-C*p*), 136.5 (J(^{13}C,^{119}Sn) 47.7 Hz, 6C*m*), 137.9 (C*i*), 139.4 (3Sn-C*i*), 175.3 (C-1). ^1H δ = 1.00 (br s, 2H, H-3), 1.55 (br s, 2H, H-2), 2.67 (br s, 2H, H-4), 3.88 (br s, 2H, H-5), 7.20–7.79 (m, Ar), 7.14 (br s, 1H, NH). MS +TOF [$C_{29}H_{29}O_2NSn + H]^+$ exp. 544.1299 calc. 544.1293 [ppm error 0.50].

4.2.8. 4-Triphenyltinoxy-N-[(R)-1-phenyl-ethyl]-butyramide (**8**)

Compound **2** (400 mg, 1.95 mmol), NaH (130 mg, 5.83 mmol), and Ph_3SnCl (750 mg, 1.95 mmol) afforded compound **8** as a yellow oil (320 mg, 90%). $[\alpha]_D$ = +25.1 (CH_2Cl_2, c = 0.007). IR ($CHCl_3$, ν cm^{-1}) 3293, 3065, 2972, 1620, 1546, 1430, 672, 616, 585. NMR (CD_2Cl_2, 25 °C): ^{13}C δ = 22.0 (CH_3-*Bn*), 28.2 (br s, C-3), 34.0 (C-2), 49.2 (C-5), 62.2 (br s, C-4), 126.2 (2C*m*), 127.2 (C*p*), 128.6 (2C*o*), 129.4 (J(^{13}C,^{119}Sn) 64.5, 6Sn-C*o*), 130.3 (3Sn-C*p*), 136.4 (J(^{13}C,^{119}Sn) 46.9, 6Sn-C*m*), 139.3 (Sn-C*i*), 143.8 (C*i*), 173.3 (C-1). ^1H δ = 1.36 (br s, 3H, CH_3-*Bn*), 1.60 (m, 2H, H-3), 2.15 (t, J = 7.0, 2H, H-2), 3.44 (t, J = 5.8, 2H, H-4), 4.46 (br s, 1H, N-H), 4.95 (q, J = 7.0, 1H, H-5), 7.21–7.76 (m, 20H, Ar). NMR (CD_2Cl_2, −70 °C): ^{13}C δ = 22.2 (CH_3-*Bn*), 26.4 (C-3), 33.7 (C-2), 50.0 (C-4), 62.0 (C-5), 126.3 (2C*m*), 127.5 (C*p*), 128.5 (2C*o*), 128.5 (J(^{13}C,^{119}Sn) 68.4, 6Sn-C*o*), 129.7 (3Sn-C*p*), 136.4 (J(^{13}C,^{119}Sn) 45.4, 6Sn-C*m*), 142.6 (J(^{13}C,^{119}Sn) 817.2, 3Sn-C*i*), 143.8 (C*i*), 174.5 (C-1). ^1H δ = 0.98 (br s, 2H, H-3), 1.20 (br s, 3H, CH_3-*Bn*), 1.57 (br s, 1H, H-2B), 1.66 (br s, 1H, H-2A), 2.70 (br s, 1H, H-4B), 2.78 (br s, 1H, H-4A), 4.63 (br s, 1H, H-5), 7.21–7.76 (m, 21H, Ar and N-H). MS +TOF [$C_{30}H_{31}O_2NSn + H]^+$ exp. 558.1456 calc. 558.1455 [ppm error 1.15].

4.2.9. (R)-4-Triphenyltinoxy-2-methyl-N-[(R)-1-phenyl-ethyl]-butyramide (**9**)

Compound **3a** (2R,5R) (225 mg, 1.02 mmol), NaH (70 mg, 3.06 mmol), and Ph_3SnCl (390 mg, 1.02 mmol) produce compound **9** as a yellow oil (230 mg, 90%). $[\alpha]_D$ = +26.27 (CH_2Cl_2, c = 0.02). IR ($CHCl_3$): (ν, cm^{-1}) 3243, 3058, 2930, 1640, 1551, 1379, 672, 637. NMR (CD_2Cl_2, 25 °C): ^{13}C δ = 17.4 (J(^{13}C,^{119}Sn) 19.2, CH_3), 22.0 (CH_3-*Bn*, J(^{13}C,^{119}Sn) 18.4), 36.1 (C-3), 38.2 (C-2), 48.9 (C-4), 59.9 (C-5), 126.5 (C*p*), 126.1 (2C*m*), 128.7 (br s, 2C*o*), 129.2 (J(^{13}C,^{119}Sn) 82.2, 6Sn-C*o*), 130.5 (3Sn-C*p*), 136.3 (J(^{13}C,^{119}Sn) 49.2, 6Sn-C*m*), 138.3 (J(^{13}C,^{119}Sn) 844.5, 3Sn-C*i*), 143.8 (C*i*), 176.2 (C-1). ^1H δ = 1.08 (d, J = 6.3, 3H, CH_3), 1.42 (br s, 3H, CH_3-*Bn*), 1.55 (br s, 1H, H-3A), 1.67 (br s, 1H, H-3B), 2.45 (br s, 1H, H-2), 3.45 (br s, 2H, H-4), 5.03 (br s, 1H, H-5), 6.79 (d, J = 6.6, 1H, NH), 7.13–7.70 (m, 20H, Ar). NMR (CD_2Cl_2, −70 °C): ^{13}C δ = 16.4 (CH_3), 22.3 (CH_3-*Bn*), 32.1 (C-3), 38.4 (C-2), 49.9 (C-5), 58.1 (C-4), 126.2 (2C*m*), 126.5 (2C*o*), 127.7 (C*p*), 129.2 (J(^{13}C,^{119}Sn) 72.6, 6Sn-C*o*), 130.4 (3Sn-C*p*), 136.5 (J(^{13}C,^{119}Sn) 46.2, 6Sn-C*m*), 140.0 (J(^{13}C,^{119}Sn) 492.0, 3Sn-C*i*), 143.7 (C*i*), 177.7 (C-1). ^1H δ = 0.56 (br s, 3H, CH_3), 0.87 (br s, 1H, H-3A), 0.98 (br s, 1H, H-3B), 1.19 (br s, 3H, CH_3-*Bn*), 2.01 (br s, 1H, H-2), 2.61 (br s, 1H, H-4), 4.57 (br s, 1H, H-5), 7.13–7.70 (m, 21H, Ar and NH). MS +TOF [$C_{31}H_{33}O_2NSn + H]^+$, exp 572.1612, calc 572.1606 [ppm error −0.35].

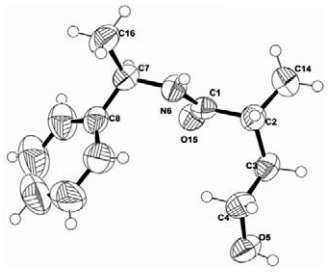
4.3. Crystallographic studies

Data were measured on a Nonius Kappa CCD instrument with CCD area detector using graphite-monochromated Mo Kα radia-

Table 2
Crystal data of compounds **3a** and **4**.

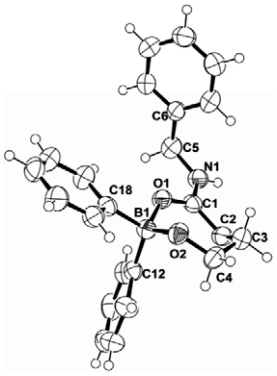
	3[a]	**4**
Formula	$C_{13}H_{19}N_1O_2$	$C_{23}H_{24}B_1N_1O_2$
Formula weight	221.3	357.26
Temperatura (K)	293	293
Wavelength (Å)	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1$	$P2_1/n$
a (Å)	6.3820 (10)	13.1663 (3)
b (Å)	9.995 (2)	10.1240 (2)
c (Å)	10.271 (2)	14.8588 (4)
β (°)	100.55 (3)	96.1290 (10)
Volume (Å^3)	644.1 (2)	1969.29 (8)
Z	2	4
D_{calc} (Mg m^{-3})	1.141	1.205
μ (mm^{-1})	0.08	0.08
T_{max}, T_{min}	0.9848, 0.9811	0.9888, 0.9851
F(000)	240	760
Crystal size (mm)	0.4 × 0.25 × 0.2	0.5 × 0.2 × 0.15
Crystal color	Colorless prism	Colorless prism
θ Range	2.017–27.583	2.186–27.494
Index range	$-7 \leqslant h \leqslant 7$	$-16 \leqslant h \leqslant 16$
	$-13 \leqslant k \leqslant 12$	$-13 \leqslant k \leqslant 12$
	$-13 \leqslant l \leqslant 13$	$-19 \leqslant l \leqslant 19$
Reflections collected	2587	8679
Independent reflections	2575	4472
R_{int}	0.0	0.05
Completeness to θ	25.101°, 97.8%	25.844°, 99.6%
Observed reflections	1476	2315
Goodness-of-fit on F^2	1.0391	1.0607
Final R_1	0.0389 ($I > 3.0\sigma$)	0.0402 ($I > 2.0\sigma$)
Final wR_2	0.0472	0.0486

Table 3
Selected bond lengths and angles (Å and °) for **3a**.



C1–N6	1.325(3)	C4–O5	1.414(3)
C1–O15	1.235(3)	C7–N6	1.457(3)
C1–C2	1.513(3)	C2–C14	1.531(4)
C2–C3	1.521(3)	C7–C16	1.519(3)
C2–C1–N6	117.0(2)	C8–C7–C16	111.2(2)
C2–C1–O15	121.9(2)	C8–C7–N6	112.1(2)
N6–C1–O15	121.1(2)	C16–C7–N6	108.9(2)
C1–C2–C3	110.7(2)	C7–N6–C1	122.8(2)
C1–C2–C14	109.2(2)		

Table 4
Selected bond lengths and angles (Å and °) for **4**.



B1–O1	1.583(2)	C1–N1	1.308(2)
B1–O2	1.462(3)	C5–N1	1.458(3)
B1–C12	1.620(3)	C1–C2	1.493(3)
B1–C18	1.617(3)	C2–C3	1.518(3)
C1–O1	1.279(2)	C3–C4	1.512(3)
C4–O2	1.427(2)	C5–C6	1.503(3)
O1–B1–O2	109.1(2)	C5–N1–C1	123.3(2)
C12–B1–O1	108.8(1)	N1–C1–O1	117.8(2)
C18–B1–O1	104.3(1)	C2–C1–O1	123.3(2)
C12–B1–O2	115.4(2)	C3–C4–O2	113.7(2)
C18–B1–O2	107.8(2)	C2–C1–N1	118.9(2)
C12–B1–C18	110.8(1)	C6–C5–N1	115.3(2)
B1–O1–C1	126.3(1)	C1–C2–C3	114.2(2)
C4–O2–B1	120.5(1)	C2–C3–C4	114.1(2)

tion, at 293 K. Intensities were measured using $\phi + \omega$ scans, (Table 2). Crystals were obtained in DMSO for **3a** and in CH_2Cl_2 for **4** (Tables 3 and 4). The two structures were solved using direct methods with SHELX-97 GM [36]. The refinement for all structures (based on F^2 of all data) was performed by full matrix least-squares techniques with Crystals 12.84 [37]. All non-hydrogen atoms were refined anisotropically. For compound **3a** all protons have been located in difference maps and positions refined. For compound **4,** H7, H13, H17, H19, H21, H23, H41, H51, protons have been located in difference maps and positions refined, the other protons were treated as riding atoms.

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Appendix A. Supplementary material

CCDC 702929 and 702930 contain the supplementary crystallographic data for compounds **3a** and **4**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2008.10.039.

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