JOC*Note*

Total Regioselective and Diastereospecific Iodolysis of 2,3-Epoxyamides Promoted by SmI_2: Synthesis of (2*R**,3*R**)- or (2*R**,3*S**)-2-Hydroxy-3-iodoamides

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Abstract: The use of samarium diiodide as a source of iodides is reported. Thus, 2-hydroxy-3-iodoamides were obtained, with total regioselectivity, by treatment of 2,3-epoxyamides, in which the oxirane ring is 2,3-disubstituted or 2,2,3-trisubstituted, with SmI_2. The ring-opening reaction was diastereospecific and (2*R**,3*R**)- or (2*R**,3*S**)-2-hydroxy-3-iodoamides were obtained from *cis*- or *trans*-epoxyamides, respectively. The relative configuration of 2-hydroxy-3-iodoamides was established by X-ray analysis. A mechanism to explain this transformation has been proposed. The starting compounds **1** are easily prepared by the reaction of enolates derived from 2-chloroamides with aldehydes at −78 °C.

Samarium diiodide is a polyvalent reducing agent that has found the most widespread application in a variety of chemical transformations through radicalic or anionic mechanism, and as result of this several reviews describing its applications have been published.[1] However, the use of SmI_2 as a source of iodide, which would increase the synthetic applications of the former reagent, has been reported in only two recent papers. Thus, Kwon previously described the iodolysis of epoxides[2] and oxetanes or tetrahydrofurans[3] promoted by SmI_2.[4] However, these methods have inherent drawbacks that render them undesirable, including the necessity for the use of tetrahydropyrane as solvent,[3] the need for additives to promote iodolysis (ethyl bromoacetate[2] or acyl chlorides[3]), and in some cases, the production of a mixture of regioisomeric iodohydrins.[3]

The regio- and stereoselective C-3 opening of the oxirane ring of 2,3-epoxy-carboxylic acids, esters, or amides by halide ions allows access to synthetically useful 3-halo-2-hydroxycarboxylic derivatives, which are precursors of 3-amino-2-hydroxyacids[5] and 2-hydroxycarboxylic acids. 3-Amino-2-hydroxyacids are present in many important biological products such as taxol,[6] pepstatin,[7] KR1-1314,[8] bestatin,[9] phebestin,[10] and probestin.[11] 2-Hydroxyamides (easily available from 2-hydroxy-3-iodoamides) are important building blocks in organic synthesis,[12] and some of them possess anticancer properties.[13] In addition, 2-hydroxy-3-iodoamides have important pharmacological applications.[14] However, halogenolysis of 2,3-epoxycarboxylic acid derivatives has been scarcely studied; there are only a few examples of C-3 bromolysis or iodolysis of 2,3-epoxyesters.[15] To our knowledge there is only one paper describing iodolysis of 2,3-epoxycarboxylic acids,[16] and there appears to be no literature concerning halogenolysis of 2,3-epoxyamides. In addition, the described halogenolysis was applied to epoxycarboxylic acid derivatives, in which the epoxide was disusbstituted or its relative configuration was *trans*, and there are very scarce examples of halogenolysis of trisubstituted 2,3-epoxyacid derivatives. For these reasons, studies into the synthesis of 2-hydroxy-3-iodoamides would be both useful and interesting.

Recently, we have reported the transformation of 2,3-epoxyamides into 2-hydroxyamides,[17] (*E*)- or (*Z*)-α,*β*-

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(5) Previous examples of transformation of 3-halo-2-hydroxyesters into 3-amino-2-hydroxy esters, with clean inversion of configuration, are described in refs 15a,b,e. This opening reaction specially is useful to prepare enantiopure *syn*-3-amino-2-hydroxyesters from *trans*-epoxyesters, easily available with high enantiomeric excess (ee) by Sharpless epoxidation of (*E*)-allylic alcohols. The direct aminolysis of enantiopure *cis*-2,3-epoxyesters is not a good way, because ee values <80% are obtained in the Sharpless epoxidation of (*Z*)-allylic alcohols: Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.

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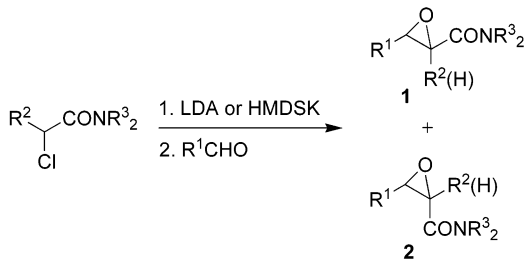
SCHEME 1. Synthesis of *trans*- and *cis*-2,3-Epoxyamides 1 and 2



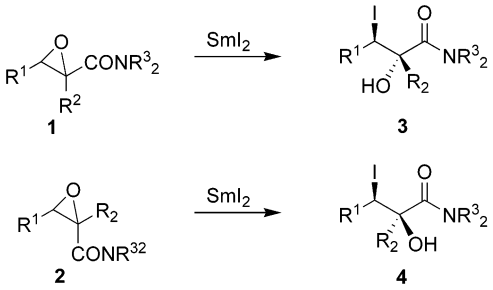
unsaturated amides with high diastereoselectivity,[18] and (*E*)-2-hydroxy-3,4-unsaturated amides.[19]

The aim of the present work is to describe a synthetic application of samarium diiodide as a source of iodides, by reporting the ring opening of 2,3-disubstituted or 2,2,3-trisubstituted 2,3-epoxyamides by iodide, promoted by SmI_2, to obtain 2-hydroxy-3-iodoamides with total regioselectivity. The transformation was diastereospecific and (2*R**,3*R**)- or (2*R**,3*S**)-2-hydroxy-3-iodoamides[20] were obtained from *cis*- or *trans*-epoxyamide, respectively. A mechanism has been proposed to explain the transformation.

A variety of 2,3-disubstituted epoxyamides **1** and **2** were prepared by reaction of lithium enolate of chloroacetamide (generated by treatment of chloroacetamide with LDA at −78 °C) with different aldehydes at −78 °C and further treatment with sodium hydride. *cis*- and *trans*-2,2,3-trisubstituted epoxyamides **1** and **2** were obtained by reaction of different aldehydes with potassium enolates of 2-chloroamides[21] (generated by treatment of 2-chloroamides with potassium hexamethyldisilazide at −78 °C) at temperatures ranging from −78 to 25 °C, by using standard methods (Scheme 1).[17]

The initial studies were performed starting from epoxyamides, as *trans* and *cis* diastereoisomer mixtures. Thus, a 2/1 mixture of *trans*- and *cis*-*N*,*N*-diisopropyl 2,3-diepoxydecanamide (**1a/2a**) reacted with a solution of 0.8 equiv of SmI_2 in THF for 30 min at room temperature to furnish the corresponding 2-hydroxy-3-iodoamides **3a/4a** as a mixture of diastereoisomers, with total regioselectivity and in high yield. No complete reaction took place by using a lower amount of SmI_2 (0.5 equiv). In the case of *trans*- and *cis*-*N*,*N*-diisopropyl-3-phenyl-2,3-epoxypropamide (**1c/2c**), the reaction afforded a mixture of iodohydrins **3c** and **4c** and the corresponding α,*β*-unsaturated amide.[22] To overcome this difficulty and to enhance the selectivity (iodolysis versus elimination reaction), the reaction was carried out at −78 °C during 4 h and by using an excess of SmI_2 (2 equiv); under these reaction conditions, compounds **3c** and **4c** were the only products isolated. The obtained relationship of diastereoisomers **3a/4a** and **3c/4c** was similar to that of the starting diastereoisomers **1a/2a** and **1c/2c**. This fact suggested a diastereospecific ring opening of the starting 2,3-epoxyamide, by a presumed S_N2 pathway.

SCHEME 2. Synthesis of (2*R,3*S**)- and (2*R**,3*R**)-2-Hydroxy-3-iodoamides 3 and 4 from 1 and 2**



To confirm this hypothesis, pure *cis* or *trans* diastereoisomers **1a**−**h** or **2a**−**c** were easily obtained by flash chromatographic column (hexane/ethyl acetate = 3/1) from the diastereoisomeric mixture.[23] Initially, the iodolysis reactions were carried out using *trans*-epoxyamides, which furnish (2*R**,3*S**)-2-hydroxy-3-iodoamides. The relative configuration exhibited by these products lends itself to the preparation of the pharmacologically interesting 2-amino-3-hydroxyacids.[5,15] Thus, treatment of *trans*-epoxyamides **1a**−**h** with SmI_2 afforded (2*R**,3*S**)-2-hydroxy-3-iodoamides **3a**−**h** as a single diastereoisomer (Scheme 2).[24]

The method was extended to the synthesis of (2*R**,3*R**)-2-hydroxy-3-iodoamides **4a**−**c** from *cis*-epoxyamides **2a**−**c**. Consequently iodohydrins with an *anti* or *syn* relationship between the stereocenters can be accessible using this method. The results obtained for the synthesis of 2-hydroxy-3-iodoamides are summarized in Table 1. All reactions were performed at room temperature, except when formation of α,*β*-unsaturated amides was observed. In these cases (Table 1, compounds **1c**, **2c**, **1f**, **1g**, and **1h**), no unsaturated amides were detected at −78 or −25 °C using an excess of SmI_2 (2 equiv instead of 0.8 equiv).

Iodolysis can be also performed by using a simplified method, by generation of SmI_2 in situ (in the presence of epoxyamide) from a mixture of diiodomethane and samarium powder (Table 1, compounds **1f** and **1h**).[25] In these cases, similar yields were obtained with no loss of selectivity observed.

The regioselectivity and stereoespecificity of the transformation of **1** or **2** into **3** or **4** (>95%) were determined

(18) (a) From aromatic 2,3-epoxyamides: Concellón, J. M.; Bardales, E. *J. Org. Chem.* **2003**, *68*, 9492. (b) From aliphatic 2,3-epoxyamides: Concellón, J. M.; Bardales, E. *Eur. J. Org. Chem.* **2004**, 1523.

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(21) 2-Chloroamides were prepared by treatment of 2-chloroacid chlorides with amines.

(22) Transformation of 2,3-epoxyamides into α, *β*-unsaturated amides is favored by using higher amounts of SmI_2 (4 equiv) in the presence of cosolvents that increase the oxidative potential of SmI_2, such as methanol (Hasagewa, E.: Curran, D. P. *J. Org. Chem.* **1993**, *58*, 5008) or HMPA (Inanaga, J.; Handa, Y.; Tabuchi, T.; Otsubo, J.; Yamaguchi, M.; Hanamoto, T. *Tetrahedron Lett.* **1991**, *32*, 6557). In addition, elimination reactions is also favored by higher temperatures. See ref 18.

(23) Trisubstituted *trans*-epoxyamides **1d**−**h** were obtained with very high diastereoselectivity (>90%) by reaction of different aldehydes with potassium enolates of 2-chloroamides, prepared by using potassium hexamethyldisilazide at −78 °C. When lithium enolates were used instead of potassium enolates, lower diastereoselectivities were obtained.

(24) Epoxyamide **1h** was prepared as a mixture of diastereoisomers by reaction of a racemic mixture of citronellal and the enolate derived from 2-chloropropanamide, and consequently the *anti* diastereoisomer **3h** was isolated as a mixture of diastereoisomers.

(25) To see different transformations promoted by SmI_2 generated in situ: (a) Concellón, J. M.; Huerta, M. *Eur. J. Org. Chem.* **2002**, 1839. (b) Concellón, J. M.; Huerta, M. *Tetrahedron Lett.* **2002**, *43*, 4943.

TABLE 1. Synthesis of (2*R,3*R**)- or (2*R**,3*S**)-2-Hydroxy-3-iodoamides 3 and 4**

1 and **2**	R^1	R^2	R^3	**3** and **4**[a]	yield (%)[b]
1a	C_7H_{15}	H	*i*-Pr	**3a**	78
2a	C_7H_{15}	H	*i*-Pr	**4a**	74
2b	Cy	H	*i*-Pr	**4b**	68
1c[c]	Ph	H	*i*-Pr	**3c**	65
2c[c]	Ph	H	*i*-Pr	**4c**	72
1d	Bu	Me	*i*-Pr	**3d**	75
1e	*i*-Bu	Me	*i*-Pr	**3e**	63
1f[d,e]	C_7H_{15}	Me	Et	**3f**	64
1g[d]	C_7H_{15}	Me	*i*-Pr	**3g**	67
1h[d,e]	C_9H_{17}[f]	Me	Et	**3h**	60

[a] Unless otherwise noted, reactions were performed with 0.8 equiv of SmI_2. [b] Isolated yield after flash column chromatography based on starting 2,3-epoxyamides **1** and **2**. [c] 2 equiv of SmI_2 at −78 °C during 4 h was used. [d] The reaction was performed with 2 equiv of SmI_2 at −25 °C during 4 h. [e] SmI_2 was obtained in situ from a mixture of Sm/CH_2I_2. [f] $Me_2C{=}CH(CH_2)_2CH(Me)CH_2$.

using ^1H and ^{13}C NMR analysis (300 MHz) of crude reaction products. In all cases, other isomers were not detected in the crude reaction products, within the limits of NMR assay.

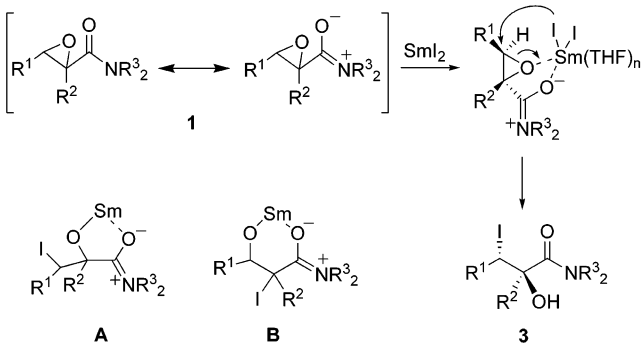
The regiochemistry (>98%) of the opening of the oxirane ring was established, in the case of trisubstituted epoxyamides (compounds **3d**−**h**) by analysis of ^{13}C NMR spectra and DEPT experiments, showing that the hydroxy group is bonded to a tetrasubstituted carbon atom. In the case of disubstituted epoxyamides **1a**−**c** or **2a**,**b**, it was established on the basis of analysis of their mass spectrum.

The relative configuration of iodohydrins **4b** and **3e**, as depicted in Scheme 1, was assigned by single-crystal X-ray analysis.[26] The stereochemistry of the other iodohydrins **3** and **4** was assigned by analogy. The relative configuration of the starting disubstituted epoxyamides was determinated on the basis of the coupling constants of epoxide protons; in the case of trisubstituted epoxyamides the relationship between the stereocenters was established by NOESY experiments. In this way, it can be unambiguously established that the iodolysis of epoxyamides **1** or **2** took place with complete inversion.

This proposed methodology for obtaining 2-hydroxy-3-iodoamides **3** and **4** is general: aliphatic (linear, branched, or cyclic), unsaturated, or aromatic 2-hydroxy-3-iodoamides can be achieved and no difference was observed from diethyl amides or diisopropylamides (Table 1, compounds **3f** and **3g**).

The rationale for the selective opening of the oxirane ring could be explained by an initial double coordination of samarium with both oxygen atoms in the compound: the carbonyl of the amide group, favored by the electron-donating capacity of the nitrogen,[27] and the oxirane ring (Scheme 3). This coordination of samarium with the oxirane ring produces a similar effect to that of a Lewis acid, favoring the ring opening. An attack of the iodide,

SCHEME 3. Mechanistic Proposal for Synthesis of (2*R,3*S**)-2-Hydroxy-3-iodoamides 3**



from ionization of SmI_2,[28] produces the opening of the oxirane ring, affording a 2-hydroxy-3-iodoamide **3** or **4**. The high regioselectivity of the nucleophilic attack of iodide at C-3 can be explained on the basis of stereoelectronic effects exerted by the amide group. In addition, the C3−O bond cleavage is favored in terms of kinetic control. The five-membered chelate A is favored over the six-membered chelate B, which is reflected in the transition state (Scheme 3).[29]

An S_N2 mechanism could explain the diastereospecificity of the opening process. In effect, (2*R**,3*R**)- and (2*R**,3*S**)-2-hydroxy-3-iodoamides were obtained from *cis*- and *trans*-epoxyamide, respectively, in according to a C-3 inversion of the starting epoxides.

In conclusion, we have described a general, rapid, and simple methodology to obtain (2*R**,3*R**)- or (2*R**,3*S**)-2-hydroxy-3-iodoamides with total regioselectivity by reaction of *cis*- or *trans*-2,3-epoxyamides with SmI_2. These ring-opening reactions proceed diastereospecifically. The relative configuration of the iodohydrins **3** and **4** was established by X-ray analysis. Iodolysis of other 2,3-epoxyacid derivatives is currently under investigation within our laboratory.

Experimental Section

General.[30] Samarium diiodide was prepared by reaction of CH_2I_2 with samarium powder.

General Procedure of Synthesis of 2,3-Epoxyamides 1 and 2. See ref 18.

General Procedure of Synthesis of 2-Hydroxy-3-iodoamide 3 or 4. A solution of **1** and **2** (0.4 mmol) in THF (2 mL) was added to a stirred solution of SmI_2 (0.32 mmol) in THF (1 mL), under a nitrogen atmosphere, at 25 °C. The mixture was stirred for 30 min at this temperature, quenched with aqueous HCl (0.1 M, 15 mL), and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in a vacuum affording crude 2-hydroxy-3-iodoamide **3** or **4**, which were purified by flash column chromatography on silica gel (hexane/AcOEt). Yields and especific conditions are given in Table 1.

(2*R,3*S**)-2-Hydroxy-3-iodo-*N*,*N*-diisopropyldecanamide (3a):** ^1H NMR (200 MHz, $CDCl_3$) δ 4.67 (dd, J = 7.4, 2.8

(26) Detailed X-ray crystallographic data for compounds **3e** (CCDC no. 240607) and **4b** (CCDC no. 240606) are available from the Cambridge Crystallographic Center, 12 Union Road, Cambridge, CB2 1EZ, U.K.

(27) The high oxophilicity of SmI_2 has been evidenced (see ref 1c, p 252). Consequently chelation of SmI_2 to the 2,3-epoxyamides is favored by the electron-donating capacity of the nitrogen.

(28) Probably, the source of iodide can be also the traces of SmI_3, which there always are in the solutions of SmI_2 in THF. However, when 2,3-epoxyamides were treated with SmI_3, a complex mixture of products, containing the corresponding iodohydrin as minor product, was obtained.

(29) A similar explanation to justify the observed regioselectivity in the MgI_2-promoted ring opening of 2,3-epoxyesters has been proposed in ref 15d.

(30) Concellón, J. M.; Bardales, E. *J. Org. Chem.* **2003**, *68*, 1585.

Hz, 1 H), 4.27 (d, J = 7.4 Hz, 1 H), 4.17−4.03 (m, 1 H), 3.94−3.81 (m, 1 H), 3.53−3.40 (m, 1 H), 2.10−1.11 (m, 12 H), 1.42 (d, J = 6.9, 3 H), 1.36 (d, J = 6.9, 3 H), 1.34−1.20 (m, 6 H), 0.85 (t, J = 6.7, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.7 (C), 74.1 (CH), 48.2 (CH), 46.5 (CH), 36.6 (CH), 32.3 (CH_2), 31.6 (CH_2), 29.7 (CH_2), 28.9 (CH_2), 28.4 (CH_2), 22.5 (CH_2), 20.9 (CH_3), 20.3 (CH_3), 19.7 (CH_3), 13.9 (CH_3); MS (70 eV) m/z (%) 397 [M^+] (2), 270 (28), 252 (13), 158 (7), 128 (94), 86 (100); HRMS calcd for $C_{16}H_{32}INO_2$ 397.1478, found 397.1482; IR (neat) $\tilde{\nu}$ 3337, 1648 cm^{-1}; R_f = 0.3 (hexane/AcOEt 5/1). Anal. Calcd for $C_{16}H_{32}INO_2$: C, 48.36; H, 8.12; N, 3.53. Found: C, 48.42; H, 8.06; N, 3.43.

(2*R,3*R**)-2-Hydroxy-2-iodo-*N*,*N*-diisopropyldecanamide (4a):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.52 (d, J = 6.7 Hz, 1 H), 4.16−3.12 (m, 1 H), 3.86−3.78 (m, 1 H), 3.51−3.41 (m, 1 H), 2.20−2.07 (m, 2 H), 1.96−1.84 (m, 1 H), 1.62−1.26 (m, 10 H), 1.47 (d, J = 6.7, 3 H), 1.46 (d, J = 6.7, 3 H), 1.29 (d, J = 6.7, 3 H), 1.22 (d, J = 6.7, 3 H), 0.91 (t, J = 6.7, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9 (C), 70.1 (CH), 48.1 (CH), 46.7 (CH), 38.0 (CH_2), 37.9 (CH), 31.7 (CH_2), 29.6 (CH_2), 29.0 (CH_2), 28.7 (CH_2), 22.5 (CH_2), 21.1 (CH_3), 20.6 (CH_3), 20.1 (CH_3), 20.0 (CH_3), 14.0 (CH_3); MS (70 eV) m/z (%) 397 [M^+] (3), 270 (59), 252 (27), 158 (25), 128 (100), 86 (99); HRMS calcd for $C_{16}H_{32}INO_2$ 397.1478, found 397.1486; IR (neat) $\tilde{\nu}$ 3343, 1641 cm^{-1}; R_f = 0.4 (hexane/AcOEt 5/1). Anal. Calcd For $C_{16}H_{32}INO_2$: C, 48.36; H, 8.12; N, 3.53. Found: C, 48.23; H, 8.17; N, 3.45.

(2*R,3*R**)-3-Cyclohexyl-2-hydroxy-3-iodo-*N*,*N*-diisopropylpropanamide (4b):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.50 (d, J = 6.5 Hz, 1 H), 4.03−3.92 (m, 1 H), 3.80−3.71 (m, 1 H), 3.44−3.35 (m, 1 H), 2.16−0.85 (m, 11 H), 1.42 (d, J = 6.7, 3 H), 1.41 (d, J = 6.7, 3 H), 1.24 (d, J = 6.7, 3 H), 1.21 (d, J = 6.7, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3 (C), 67.8 (CH), 47.9 (CH), 47.4 (CH), 46.6 (CH), 43.2 (CH), 34.8 (CH_2), 31.4 (CH_2), 26.1 (CH_2), 26.0 (CH_2), 25.9 (CH_2), 21.0 (CH_3), 20.5 (CH_3), 20.0 (CH_3), 19.8 (CH_3); MS (70 eV) m/z (%) 318 [M^+] (78), 254 (70), 158 (34), 128 (97), 86 (100), 83 (14); IR (neat) $\tilde{\nu}$ 3330, 1624 cm^{-1}; R_f = 0.3 (hexane/AcOEt 5/1). Anal. Calcd for $C_{15}H_{28}INO_2$: C, 47.25; H, 7.40; N, 3.67. Found: C, 47.08; H, 7.45; N, 3.58.

(2*R,3*S**)-2-Hydroxy-3-iodo-*N*,*N*-diisopropyl-3-phenylpropanamide (3c):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61−7.14 (m, 5 H), 5.21 (d, J = 1.2 Hz, 1 H), 4.85 (dd, J = 2.0, 1.2 Hz, 1 H), 4.15−4.02 (m, 1 H), 3.98 (d, J = 2.0 Hz, 1 H) 3.54−3.38 (m, 1 H), 1.42 (d, J = 1.7, 3 H), 1.37 (d, J = 1.7, 3 H), 1.28 (d, J = 1.7, 3 H), 1.18 (d, J = 1.7, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.2 (C), 138.4 (C), 128.8 (CH), 128.3 (CH), 128.1 (CH), 73.3 (CH), 48.5 (CH), 46.4 (CH), 31.2 (CH), 21.2 (CH_3), 20.3 (CH_3); MS (70 eV) m/z (%) 375 [M^+] (<1), 248 (11), 158 (91), 128 (81), 86 (100); IR (neat) $\tilde{\nu}$ 3310, 1640 cm^{-1}; R_f = 0.4 (hexane/AcOEt 5/1). Anal. Calcd for $C_{15}H_{22}INO_2$: C, 48.01; H, 5.91; N, 3.73. Found: C, 48.23; H, 5.81; N, 3.64.

(2*R,3*R**)-2-Hydroxy-3-iodo-*N*,*N*-diisopropyl-3-phenylpropanamide (4c):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52−7.21 (m, 5 H), 5.21 (d, J = 1.0 Hz, 1 H), 4.41 (d, J = 2.0 Hz, 1 H), 4.06 (dd, J = 2.0, 1.0 Hz, 1 H), 3.83−3.74 (m, 1 H), 3.42−3.33 (m, 1 H), 1.42 (d, J = 1.7, 3 H), 1.35 (d, J = 1.7, 3 H), 1.16 (d, J = 1.7, 3 H), 1.08 (d, J = 1.7, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.0 (C), 141.4 (C), 129.0 (CH), 128.9 (CH), 128.7 (CH), 71.2 (CH), 48.3 (CH), 46.5 (CH), 36.5 (CH), 20.8 (CH_3), 20.2 (CH_3), 19.8 (CH_3), 19.5 (CH_3); MS (70 eV) m/z (%) 375 [M^+] (3), 248 (20), 158 (90), 128 (100), 86 (98); IR (neat) $\tilde{\nu}$ 3304, 1651 cm^{-1}; R_f = 0.3 (hexane/AcOEt 5/1). Anal. Calcd for $C_{15}H_{22}INO_2$: C, 48.01; H, 5.91; N, 3.73. Found: C, 48.24; H, 5.99; N, 3.65.

(2*R,3*S**)-2-Hydroxy-3-iodo-*N*,*N*-diisopropyl-2-methylheptanamide (3d):** ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.41 (br, 1 H), 4.34 (dd, J = 11.4, 2.2, 1 H), 4.13−4.00 (m, 1 H), 3.52−3.39 (m, 1 H), 2.10−1.00 (m, 6 H), 1.57 (s, 3 H), 1.42 (d, J = 4.6, 3 H), 1.39 (d, J = 4.6, 3 H), 1.32 (d, J = 4.2, 3 H), 1.89 (d, J = 4.2, 3 H), 0.89 (t, J = 7.1, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.2 (C), 75.9 (C), 49.2 (CH), 47.5 (CH), 47.3 (CH), 34.6 (CH_2), 32.4 (CH_2), 29.6 (CH_3), 21.8 (CH_2), 20.2 (CH_3), 20.1 (CH_3), 20.0 (CH_3), 19.6 (CH_3), 13.8 (CH_3); MS (70 eV) m/z (%) 369 [M^+] (18), 242 (13), 241 (18), 224 (6), 172 (14), 128 (94), 86 (100); IR (neat) $\tilde{\nu}$ 3310, 1625 cm^{-1}; R_f = 0.4 (hexane/AcOEt 5/1). Anal. Calcd for $C_{14}H_{28}INO_2$: C, 45.53; H, 7.64; N, 3.79. Found: C, 45.39; H, 7.58; N, 3.72.

(2*R,3*S**)-2-Hydroxy-3-iodo-*N*,*N*-diisopropyl-2,5-dimethylhexanamide (3e):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.43 (br, 1 H), 4.44 (dd, J = 12.3, 2.5, 1 H), 4.14−4.05 (m, 1 H), 3.52−3.43 (m, 1 H), 2.18−1.60 (m, 3 H), 1.63 (s, 3 H), 1.44 (d, J = 6.7, 3 H), 1.42 (d, J = 6.7, 3 H), 1.27 (d, J = 6.7, 3 H), 1.24 (d, J = 6.7, 3 H), 0.97 (d, J = 6.6, 3 H), 0.85 (d, J = 6.6, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.3 (C), 75.8 (C), 49.3 (CH), 47.4 (CH), 46.2 (CH), 42.6 (CH_2), 30.0 (CH_3), 28.8 (CH), 23.4 (CH_3), 20.6 (CH_3), 20.3 (CH_3), 20.2 (CH_3), 20.0 (CH_3); MS (70 eV) m/z (%) 369 [M^+] (39), 242 (15), 241 (16), 172 (14), 128 (95), 86 (100); IR (neat) $\tilde{\nu}$ 3301, 1620 cm^{-1}; R_f = 0.5 (hexane/AcOEt 5/1). Anal. Calcd for $C_{14}H_{28}INO_2$: C, 45.53; H, 7.64; N, 3.79. Found: C, 45.69; H, 7.55; N, 3.70.

(2*R,3*S**)-*N*,*N*-Diethyl-2-hydroxy-3-iodo-2-methyldecanamide (3f):** ^{1}H NMR (300 MHz, DMSO) δ 3.61 (dd, J = 8.8, 2.5, 1 H), 3.51−3.41 (m, 4 H), 1.53−1.22 (m, 12 H), 1.33 (s, 3 H), 1.10 (t, J = 7.0, 6 H), 0.88 (t, J = 6.8, 3 H); ^{13}C NMR (75 MHz, DMSO) δ 170.2 (C), 78.2 (C), 50.9 (CH), 42.3 (CH_2), 41.6 (CH_2), 34.5 (CH_2), 31.2 (CH_2), 29.5 (CH_2), 28.6 (CH_2), 28.5 (CH_2), 28.0 (CH_2), 22.2 (CH_3), 14.5 (CH_3), 14.0 (CH_3), 12.2 (CH_3); MS (70 eV) m/z (%) 383 [M^+] (<1), 256 (16), 144 (36), 100 (44); IR (neat) $\tilde{\nu}$ 3381, 1604 m^{-1}; R_f = 0.5 (hexane/AcOEt 5/1). Anal. Calcd for $C_{15}H_{30}INO_2$: C, 47.00; H, 7.89; N, 3.65. Found: C, 46.89; H, 7.97; N, 3.58.

(2*R,3*S**)- 2-Hydroxy-3-iodo-*N*,*N*-diisopropyl-2-methyldecanamide (3g):** ^{1}H NMR (300 MHz, DMSO) δ 5.44 (s, 1 H), 3.38 (dd, J = 2.14, 11.3, 1 H), 4.14−4.06 (m, 1 H), 3.53−3.44 (m, 1 H), 1.98−1.73 (m, 12 H), 1.61 (s, 3 H), 1.45 (d, J = 6.7, 3 H), 1.43 (d, J = 6.7, 3 H), 1.28 (d, J = 6.3, 3 H), 1.24 (d, J = 6.4, 3 H), 0.89 (t, J = 6.7, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.1 (C), 75.8 (C), 49.1 (CH), 47.5 (CH), 47.3 (CH), 34.8 (CH_2), 31.5 (CH_2), 30.2 (CH_2), 29.6 (CH_3), 28.9 (CH_2), 28.7 (CH_2), 22.4 (CH_2), 20.3 (CH_3), 20.2 (CH_3), 20.1 (CH_3), 19.6 (CH_3), 13.9 (CH_3); MS (70 eV) m/z (%) 411 [M^+] (<1), 172 (8), 128 (41), 100 (24); HRMS calcd for $C_{17}H_{34}INO_2$ 411.1634, found 411.1627; IR (neat) $\tilde{\nu}$ 3315, 2927, 1624 m^{-1}; R_f = 0.6 (hexane/AcOEt 3/1). Anal. Calcd for $C_{17}H_{34}INO_2$: C, 49.64; H, 8.33; N, 3.40. Found: C, 49.51; H, 8.44; N, 3.34.

(2*R,3*S**)-*N*,*N*-Diethyl-2-hydroxy-3-iodo-2,5,9-trimethyldec-8-enamide (3h):** ^{1}H NMR (300 MHz, DMSO) δ 5.57−5.52 (m, 2 H), 5.14−5.09 (m, 2 H), 3.77−3.27 (m, 8 H), 2.19−1.14 (m, 26 H), 1.12 (t, J = 7.0, 6 H), 1.11 (t, J = 7.0, 6 H), 0.98 (d, J = 6.7, 6 H), 0.93 (d, J = 6.7, 3 H), 0.88 (d, J = 6.7, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9 (C), 131.4 (C), 131.3 (C), 124.3 (CH), 76.6 (C), 46.5 (CH), 46.3 (CH), 42.3 (CH_2), 42.2 (CH_2), 41.9 (CH_2), 41.6 (CH_2), 37.5 (CH_2), 34.6 (CH_2), 32.6 (CH), 32.5 (CH_2), 30.1 (CH_3), 25.6 (CH_3), 25.3 (CH_2), 25.0 (CH_2), 19.9 (CH_3), 18.4 (CH_3), 17.6 (CH_3), 14.0 (CH_3), 12.2 (CH_3); IR (neat) $\tilde{\nu}$ 3390, 1619 m^{-1}; R_f = 0.3 (hexane/AcOEt 3/1). Anal. Calcd for $C_{17}H_{32}INO_2$: C, 49.88; H, 7.88; N, 3.42. Found: C, 49.99; H, 7.76; N, 3.36

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Supporting Information Available: ^{13}C NMR spectra of compounds **3** and **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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