Carbonyl Reduction of Functionalized Aldehydes and Ketones by Tri-*n*-butyltin Hydride and SiO_2

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Tri-*n*-butyltin hydride (*n*-Bu_3SnH) is widely used, in the presence of AIBN, as a radical initiator in numerous reactions of carbon–carbon bond formation, through a dehalogenating process.[1] However, *n*-Bu_3SnH can also be a powerful carbonyl reducing reagent for aldehydes and ketones when it is used in the presence of a Lewis acid,[2] triphenylphosphine oxide,[3] or AIBN[4] or neat in boiling methanol.[4] Although halodibutyltin hydrides[2,5] (*n*-Bu_2SnXH, X= Cl, Br, I, F) and dibutyltin dihydride[6] (*n*-Bu_2SnH_2) have been used in reductions of α-alkoxy ketones and α-brominated ketones, respectively, their utility has been limited. Some modified tin hydrides have also been employed for the chemocontrolled reduction of α-brominated ketones.[7] It has been reported by us[8] and others[9] that the carbonyl reducing ability of *n*-Bu_3SnH is remarkably enhanced in the sole presence of silica gel. There have been important advances in the practical aspects of the use of polymer-bound reagents in organic synthesis during the past years.[10] Their use presents a variety of advantages over their homogeneous counterparts. Therefore we wish to report in this note the interesting aspects of this procedure for the clean reduction of functionalized aldehydes and ketones with a partial survey of the scope and limitations concerning the chemo- and diastereoselectivity of this reaction.

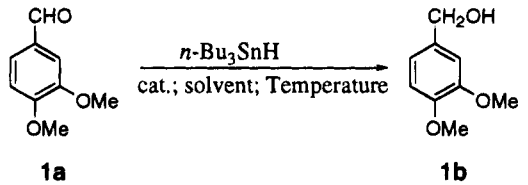
Results and Discussion

When 3,4-dimethoxybenzaldehyde (**1a**) (veratryl aldehyde) was treated at room temperature in CH_2Cl_2 with 1 equiv of *n*-Bu_3SnH in the presence of silica gel (which has been dried 12 h at 100 °C), 3,4-dimethoxy benzylalcohol (**1b**) (veratryl alcohol) was isolated in 80% yield (eq 1). In order to optimize the experimental conditions, we studied the influence of solvents, temperature, and catalysts on the reaction and summarized in Table 1 the results so observed.

Table 1. Effect of Varying Reaction Conditions on the Yield and Kinetics of the Reduction of Veratryl Aldehyde (1a) to Veratryl Alcohol (1b) (with 2 Equiv of *n*-Bu_3SnH)

entry	solvent	temp (°C)	catalyst	ratio solid/sub.	time (h)	yield[a] (%[b])
1	CH_2Cl_2	20	SiO_2	20/1	24	91 (81)
2	CH_2Cl_2	20	SiO_2	10/1	24	50
3	CH_2Cl_2	25	SiO_2[c]	20/1	6	70
4	toluene	20	SiO_2	20/1	24	40
5	toluene	80	SiO_2	20/1	3	90 (87[d])
6	toluene	110	SiO_2	20/1	6	94 (67[e])
7	toluene	80	SiO_2	10/1	24	71[d]
8	THF	20	SiO_2	20/1	24	<2
9	*t*-BuOMe	20	SiO_2	20/1	24	0
10	toluene	80			24	<2
11	CH_2Cl_2	20	Al_2O_3	20/1	24	8
12	toluene	110	AIBN	1 mol %	24	60 (53)
13	CH_2Cl_2	20	Mol. Sieves	5/1	24	0

[a] By NMR, based on starting material recovered. [b] Values in parentheses are for the isolated product. [c] Sonication in a cleaning bath. [d] With 2% of diveratryl ether (**1c**). [e] With 17% of diveratryl ether (**1c**).



1a **1b** (1)

In terms of yield, time of reaction, ease, and mild conditions employed, the best results for the clean reduction of 3,4-dimethoxybenzaldehyde (**1a**) were found with 2 equiv of *n*-Bu_3SnH in the presence of SiO_2 in a 20/1 ratio (SiO_2/substrate in weight equivalent), either in CH_2Cl_2 after 24 h at room temperature (method A; entry 1) or in toluene at 80 °C for 3 h (method B; entry 5). If the amount of silica gel is lower, the yield decreases (entries 2 and 7), but it is not necessary to employ more than 20 equiv by weight in order to obtain reasonable yields.[9] Sonication of the reaction mixture activates the reduction (entry 3). The reduction must be performed in a nonoxygenated solvent since the use of THF or *tert*-butylmethyl ether does not lead to the expected products (THF: <2% and *tert*-butyl methyl ether: 0%; entries 8 and 9, respectively). When the temperature of the reaction in toluene is increased from 20 to 80 and then 110 °C (entries 4, 5, and 6, respectively), the time of reaction decreased, with the best yield obtained after only 3 h at 80 °C (87%). Nevertheless, with a slight increase of the temperature a side reaction appears, giving rise to substantial amounts of diveratryl ether (**1c**) (at 110 °C, 17% of diveratryl ether, entry 6). It is noteworthy that in the presence of *n*-Bu_3SnH alone, no reduction occurred (entry 10). Finally, it is worth noting that silica gel is the best solid support compared to alumina and molecular sieves (Mol. Sieves) (entries 1, 11, and 13, respectively), since almost no reduction occurred with Al_2O_3 even after 24 h, and 0% with Mol. Sieves. Compared to the reduction performed in radical conditions (when *n*-Bu_3SnH is used in the presence of AIBN in toluene under reflux for 24 h), the use of silica gel allows us to obtain much better yields of reduced products (87% and only 53% of reduction with AIBN, entries 5 and 12).

Thus, to study the generalization as well as the limitations of this new methodology, the reaction condi-

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(1) Neumann W. P. *Synthesis* **1987**, 665–683.
(2) Shibata, I.; Yoshida, T.; Kawakami, T.; Baba, A.; Matsuda, H. *J. Org. Chem.* **1992**, *57*, 4049–4051.
(3) Shibata, I.; Suzuki, T.; Baba, A.; Matsuda, H. *J. Chem. Soc. Chem. Commun.* **1988**, 882–883.
(4) (a) Quintard, J. P.; Peryre, M. *Bull. Soc. Chim. Fr.* **1972**, 1950–1955. (b) Pereyre M.; Godet, J. Y. *Tetrahedron Lett.* **1970**, *11*, 3653–3656.
(5) Kawakami, T.; Shibata, I.; Baba, A.; Matsuda H. *J. Org. Chem.* **1993**, *58*, 7608–7609.
(6) Shibata, I.; Nakamura, K.; Baba, A.; Matsuda, H. *Tetrahedron Lett.* **1990**, *31*, 6381–6384.
(7) Vedejs, E.; Duncan, S. M.; Haight, A. R. *J. Org. Chem.* **1993**, *58*, 3046–3050.
(8) Tam, V. T.; Chaboche, C.; Figadère, B.; Chappe, B.; Hieu, B. C.; Cavé, A. *Tetrahedron Lett.* **1994**, *35*, 883–886.
(9) Fung, N. Y. M.; de Mayo, P.; Schauble, J. H.; Weedon, A. C. *J. Org. Chem.* **1978**, *43*, 3977–3979.
(10) McKillop, A.; Young, D. W. *Synthesis* **1979**, 401–422; *ibid*, **1979**, 481–500.

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Table 2. Reduction of Carbonyl Compounds with *n*-Bu_3SnH in the Presence of SiO_2

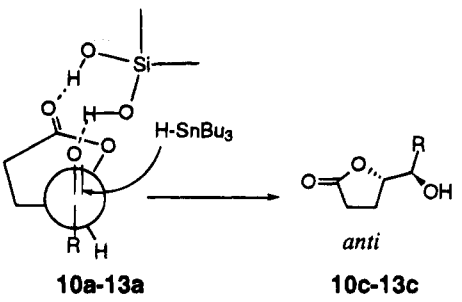
entry	carbonyl compound[a]	product	reacn time (h)	yield[b] (%)	de[c] *syn/anti*
1	3,4-dimethoxybenzaldehyde (**1a**)	3,4-dimethoxybenzyl alcohol (**1b**)	24	A: 81	–
			3	B: 87	
2	octadecanal (**2a**)	octadecanol (**2b**)	24	A: 82	–
3	cyclohexanone (**3a**)	cyclohexanol (**3b**)	24	A:10	–
			3	B: 70	
4	acetophenone (**4a**)	1-phenyl-1-ethanol (**4b**)	24	A: <20	–
			6	B: 83	
5	1-chloro-3-propylphenone (**5a**)	4-chloro-1-phenyl-1-butanol (**5b**)	24	A: 70	
6	(3,4-dimethoxyphenyl)acetone (**6a**)	1-(3,4-dimethoxyphenyl)-1-ethanol (**6b**)	24	A: 16	–
			6	B: 37	–
7	1-acetoxy-4-pentanone (**7a**)	1-acetoxy-4-hydroxypentane (**7b**)	24	A: 50	–
8	(1*R*)-*endo*-(+)-3-bromocamphor (**8a**)	(+)-camphor (**8b**)	24	A: 95	–
9	eicos-1-en-3-one (**9a**)	eicosan-3-one (**9b**)	24	A:[d] 77 (**9b**)	–
		3-hydroxyeicosane (**9c**)	24	A: 50[e] (**9c**)	–
10	11-(*tert*-amyloxy)-5-oxo-4-undecanolide[f] (**10a**)	11-(*tert*-amyloxy)-5-hydroxy-4-undecanolide (**10b,c**)	24	A:83	23:77[g]
11	5-oxo-4-heptadecanolide (**11a**)	5-hydroxy-4-heptadecanolide (**11b,c**)	24	A: 90	28:72
12	5-oxo-8-nonen-4-olide (**12a**)	5-hydroxy-8-nonen-4-olide (**12b,c**)	24	A: 71	22:78
13	5-oxo-6-phenylhexan-4-olide (**13a**)	5-hydroxy-6-phenylhexan-4-olide (**13b,c**)	24	A: 76	17:83[g]

[a] Compounds **1a**–**8a** were commercially available (Aldrich). Compound **9a** was prepared in two steps from octadecanal, see ref 8. Compounds **10a**–**13a** were prepared from the carboxylic acid chloride obtained from deamination of L-glutamic acid followed by treatment with oxalyl chloride, by acylation with the corresponding Grignard reagent: see ref 12. [b] Isolated yield. The remainder of the mass balance being the starting material. Method A and method B, see Experimental Section and the text. [c] Determined by ^1H NMR. [d] Only 1 equiv of *n*-Bu_3SnH was used. [e] With ~50% of eicosanone **9b**. [f] *tert*-Amyl ether. For chemoselective protection of primary hydroxyl groups, see ref 13. [g] Unseparable mixture.

tions for carbonyl reduction, used either in entry 1 (method A) or in entry 5 (method B), were applied to several aldehydes and extended to ketones bearing functionalized groups (**2a-13a**, Table 2). Examination of the results so obtained allows us to show the broad scope of such a procedure as well as the high chemoselectivity and the good diastereoselectivity observed for several examples.

These results show that this procedure can be applied to alkyl and aryl aldehydes, since primary alcohols are obtained in typical yields of 80%, by performing the reaction at room temperature (entries 1–2). This methodology was then extended to ketones. In most cases, the reaction is slower (entry 3), and method B gives better yields of reduced products than method A. For aryl ketones, which are less reactive because of the conjugation of the carbonyl group with the aromatic ring, reactions must be performed in toluene under reflux to go to completion (entries 4–6). When the ketone is very hindered, as for (1*R*)-*endo*-(+)-3-bromocamphor (**8a**), the carbonyl is not reduced further and bromine is then displaced (entry 8). Chlorine does not react under these conditions, and ketone **5a** is reduced to give **5b** in good yield (entry 5). It is noteworthy that with other functional groups such as ester, lactone, methoxy, and *tert*-amyl ether,[13] isolated double bonds are tolerated (entries 7 and 10–13). For enone **9**, when 1 equiv of *n*-Bu_3SnH is used, we observe the clean reduction of the double bond, leading to the formation of the corresponding saturated ketone **9b** in 77% yield. It is worth noting that this method for reducing an α,β-unsaturated ketone is simpler and cheaper than Lipshutz's procedure[11] with *n*-Bu_3SnH/CuI/2.5 LiCl/THF/Me_3SiCl. In the cases of α-butyrolactonic ketones[12] (entries 10–13), the reductions are complete in 24 h at room temperature and show good diastereoselectivity in favor of the *anti* product. The *anti*-

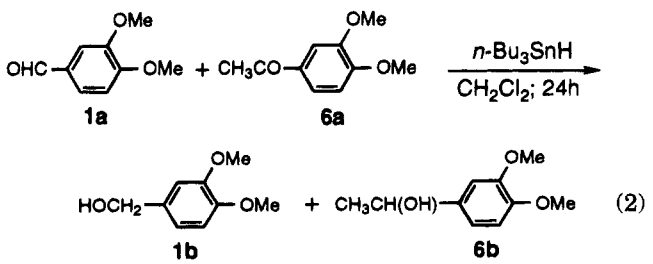
Scheme 1



10a-13a **10c-13c**

selectivity can be explained in terms of Cram's chelation model, involving silica gel as complexant (Scheme 1). The typical *syn/anti* ratio (17/83–28/72) so obtained is noteworthy, since the use of other metallic hydrides ($NaBH_4$, $Zn(BH_4)_2$) gave 40/60 ratios in favor of the *anti* product,[14] whereas L-selectride gave almost exclusively the *syn* product (98/2).[14]

It is worth noting that when an equimolar mixture of aldehyde **1a** and ketone **6a** was treated with 1 equiv of *n*-Bu_3SnH in the presence of SiO_2 at room temperature in CH_2Cl_2, alcohol **1b** was obtained in 78% yield with less than 5% of **6b** since **6a** was recovered unchanged (90%) (eq 2). This procedure is the method of choice for the selective reduction of an aldehyde in the presence of a ketone.



(2)

In accordance with the results obtained in Tables 1 and 2, we postulate that the mechanism of the reduction is

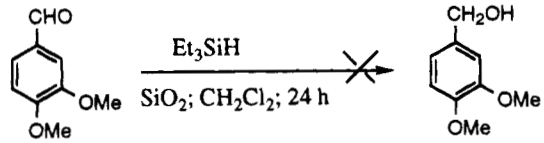
(11) Lipshutz, B. H.; Ung, C. S.; Sengupta, S. *Synlett* **1989**, 64–66. For other effective reductions of enones, see for example: Keinan, E.; Gleize, P. A. *Tetrahedron Lett.* **1982**, *23*, 477. Four, P.; Guibe, F. *Tetrahedron Lett.* **1982**, *23*, 1825.

(12) Figadère, B.; Harmange, J. C.; Laurens, A.; Cavé, A. *Tetrahedron Lett.* **1991**, *32*, 7539–7542.

(13) Figadère, B.; Franck, X.; Cavé, A. *Tetrahedron Lett.* **1993**, *34*, 5893–5894.

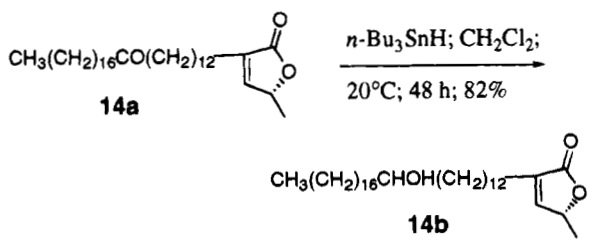
(14) Larchevêque, M.; Lalande, J. *Bull. Soc. Chim. Fr.* **1986**, 116–122.

of anionic type, *via* a hydride transfer. The role of silica gel is not well defined. Probably, substrates are adsorbed on the surface of the solid where the reaction occurs, since sonication, known for activating the surface in solid–liquid processes,[15] dramatically accelerates the reaction. Furthermore, silica gel can act as a mild acid catalyst by activating the carbonyl of the ketone or aldehyde, which is confirmed by the selectivity observed with α-butyrolactonic ketones. But one must also consider the possibility that silica gel by complexing the tin atom of *n*-Bu_3SnH enhances the polarization of the tin–hydrogen bond and so increases its reducing ability. The possible intermediate possessing a silicon hydrogen bond[16] has been discarded, since when **1a** was treated with 2 equiv of Et_3SiH in CH_2Cl_2 in the presence of silica gel at room temperature for 24 h, the starting material was recovered unchanged (eq 3).



1a **1b** (3)

It is noteworthy that this methodology has been successfuly applied to the synthesis of a natural acetogenin of *Annonaceae*, reticulatamol (**14b**), which has been previously isolated in this laboratory from the seeds of *Annona reticulata* (eq 4).[8]



14a **14b** (4)

The reduction of the acyclic ketone **14a** gave rise to reticulatamol (**14b**) as a diastereomeric mixture in high yield (82%). The high chemoselectivity of such a reaction is noteworthy since neither the conjugated double bond nor the carbonyl of the lactone has been reduced under these conditions.

In conclusion, this new methodology for the carbonyl reduction of aldehydes and ketones has been shown to be of large scope, is very mild since many functionalized groups are tolerated, and is very easy to perform. The advantages of this method are the nonbasic conditions without the need of aquous acidic workup and the simple purification step, since a single elution of the crude material with pentane allows us to discard the tin residues. Moreover, the high chemoselectivity and good diastereoselectivity (in the case of α-butyrolactonic ketones) makes this procedure a useful tool for multistep synthesis of natural products. Further development and application of this reaction to the use of silica gel bound to chiral molecules (cyclodextrins) for the asymmetric reduction of ketones are under investigation in our laboratories.[17]

Experimental Section

General Procedures. ^1H and ^{13}C NMR spectra were recorded at 200 and 50 MHz, respectively, using $CDCl_3$ as solvent and $CHCl_3$ as internal reference. EI-MS were obtained at an ionization potentiel of 70 eV, and CI-MS with NH_3, otherwise as indicated. Toluene, *tert*-butyl methyl ether, and THF were distilled over sodium–benzophenone, and CH_2Cl_2 over CaH_2 immediately prior use. SiO_2 (from Riedel-de Haën, 230–400 mesh), 3-Å molecular sieves, and Al_2O_3 (from Woelm-Eschwege-Germany, activity grade I) were dried at 100 °C for *minimum* of 12 h prior use. Carbonyl compounds **1a–8a** were obtained commercially and used without purification. Compounds **9a–13a** were synthesized as previously reported.[8,12]

Representative Procedure. Method A. To a solution of 3,4-dimethoxybenzaldehyde (**1a**) (100 mg, 0.6 mmol) and 2 g of SiO_2 in anhydrous CH_2Cl_2 (5 mL) in a flask under nitrogen was added *n*-Bu_3SnH (0.33 mL, 1.2 mmol) via syringe. The reaction mixture was stirred at room temperature for 24 h and then filtered through a pad of silica gel. Pentane was passed through the solid to remove the tin residues. The solid material was then washed several times with EtOAc prior to concentration under reduced pressure. The crude residue was then purified by flash chromatography on silica gel to afford the desired alcohol **1b** (81 mg, 81%). **Method B.** To a solution of 3,4-dimethoxybenzaldehyde (**1a**) (100 mg, 0.6 mmol) and 2 g of SiO_2 in anhydrous toluene (2 mL) in a flask under nitrogen was added *n*-Bu_3SnH (0.33 mL, 1.2 mmol) via syringe. The reaction mixture was stirred at 80 °C for 3 h and, after being cooled to room temperature, filtered through a pad of silica gel and eluted with pentane to eliminate the tin residues. The solid material was then washed several times with EtOAc prior to concentration under reduced pressure. The crude residue was then purified by flash chromatography on silica gel to afford the desired alcohol **1b** (88 mg, 87%).

Veratryl alcohol (1b): ^1H NMR δ 3.87 (s, 3H), 3.88 (s, 3H), 4.60 (brs, 2H), 6.84–6.91 (m, 3H); ^{13}C NMR δ 55.8, 55.9, 65.2, 110.4, 111.0, 119.3, 133.5, 148.5, 148.9; EI-MS 168 (M^+, 100), 151 (29), 139 (36), 109 (24), 97 (21), 83 (69), 65 (34).

Diveratryl ether (1c): ^1H NMR δ 3.88 (s, 12H), 4.47 (s, 4H), 6.81–6.91 (m, 6H); ^{13}C NMR δ : 55.8, 55.9, 71.8, 110.9, 111.2, 120.4, 130.8, 148.6, 149.0; EI-MS 318 (M^+, 16), 152 (100), 151 (76), 137 (28), 121 (32).

Octadecanol (2b): ^1H NMR δ 3.55 (t, J = 7.0 Hz, 2H), 1.55–1.45 (m, 3H), 1.23–1.05 (m, 30H), 0.78 (t, J = 6.7 Hz, 3H); ^{13}C NMR δ 63.1, 32.9, 32.0, 29.7, 29.5, 29.4, 25.8, 22.7, 14.2; EI-MS 252 ($M^+ - H_2O$, 2), 224 (4), 154 (4), 140 (6), 138 (4), 125 (18), 112 (11), 111 (35), 98 (22), 97 (80), 96 (18), 83 (100), 71 (41), 69 (79); CI-MS 288 ($M + NH_4^+$) (100).

Cyclohexanol (3b): ^1H NMR δ 1.40–1.05 (m, 4H), 2.00–1.50 (m, 7H), 3.70 (m, 1H); ^{13}C NMR δ 24.2, 25.5, 35.4, 70.0.

1-Phenyl-1-ethanol (4b): ^1H NMR δ 1.19 (d, J = 6.4 Hz, 3H), 4.78 (q, J = 6.4 Hz, 1H), 7.21 (m, 5H); ^{13}C NMR δ 25.0, 70.3, 125.3, 127.3, 128.4, 145.8.

4-Chloro-1-phenyl-1-butanol (5b): ^1H NMR δ 2.86 (m, 4H), 3.55 (m, 2H), 4.72 (m, 1H), 7.35 (m, 5H); ^{13}C NMR δ 29.17, 36.40, 45.20, 74.14, 126.03, 127.98, 128.81, 144.57; EI-MS 184 (M^+, 5), 107 (100), 79 (36), 77 (18); CI-MS 202 ($M + NH_4^+$, 70), 186 (70), 185 (31), 184 (100), 167 (37).

1-(3,4-Dimethoxyphenyl)-1-ethanol (6b): ^1H NMR δ 1.48 (d, J = 6.5 Hz, 3H), 3.86 (s, 3H), 3.89 (s, 3H), 4.84 (q, J = 6.5 Hz, 1H), 6.8–6.94 (m, 3H); ^{13}C NMR δ 25.0, 55.8, 55.9, 70.1, 108.7, 111.1, 117.5, 138.6, 148.4, 149.1; EI-MS 182 (M^+, 94), 167 (100).

1-Acetoxy-4-hydroxypentane (7b): ^1H NMR δ 1.20 (d, J = 6.3 Hz, 3H), 1.43–1.78 (m, 4H), 2.04 (s, 3H), 3.82 (q, J = 6.3 Hz, 1H), 4.08 (t, J = 6.4 Hz, 2H); ^{13}C NMR δ 21.0, 23.6, 25.0, 35.4, 64.4, 67.6, 201.5; EI-MS 147 (MH^+, 1), 131 (1), 102 (11), 87 (23), 71 (63), 61 (100), 43 (97).

(+)-Camphor (8b): ^1H NMR δ 0.83 (s, 3H), 0.91 (s, 3H), 0.95 (s, 3H), 1.38 (m, 2H), 1.67 (m, 2H), 1.96 (m, 1H), 2.08 (t, J = 4.3

(15) Luche, J. L.; Einhorn, C.; Einhorn, J.; Sinisterra-Gago, J. V. *Tetrahedron Lett.* **1990**, *31*, 4125. 4128, and references cited herein.
(16) Kini, A. D.; Nadkarni, D. V.; Fry, J. L. *Tetrahedron Lett.* **1994**, *35*, 1507–1510.

(17) First results, observed with β-cyclodextrin adsorbed on silica gel, did not give high ee.

Hz, 1H), 2.35 (dt, J = 3.4, 18.0 Hz, 1H); ^{13}C NMR δ 9.2, 19.1, 19.7, 27.0, 29.9, 43.0, 43.3, 46.8, 57.7, 219.3.

Eicosan-3-one (9b): ^{1}H NMR δ 0.88 (t, J = 6.8 Hz, 3H), 1.05 (t, J = 6.8 Hz, 3H), 1.22 (m, 26H), 1.55 (m, 2H), 2.40 (m, 4H); ^{13}C NMR δ 7.83, 14.06, 22.67, 23.97, 29.34, 29.47, 29.66, 31.91, 35.81, 42.43, 211.83; EI-MS 297 (MH^+, 7), 267 (41), 167 (8), 149 (20), 97 (21), 85 (55), 57 (100), 43 (62), 29 (21); CI-MS 314 ($M + NH_4^+$, 100), 297 (MH^+, 24).

3-Hydroxyeicosane (9c): ^{1}H NMR δ 0.88 (t, J = 6.8 Hz, 3H), 0.92 (t, J = 7 Hz, 3H), 1.6–1.25 (m, 31H), 3.55 (m, 1H); ^{13}C NMR δ 7.84, 9.81, 14.06, 22.67, 25.66, 29.35, 29.68, 30.11, 31.93, 36.97, 73.33; EI-MS 297 (1), 269 (28), 125 (11), 111 (26), 97 (49), 85 (11), 83 (29), 71 (26); CI-MS 316 ($M + NH_4^+$, 100), 297 (8), 268 (6), 119 (13), 99 (6), 88 (5).

(4*S*,5*S*)- and (4*S*,5*R*)-11-(*tert*-amyloxy)-5-hydroxy-4-undecanolide (10b,c) as a diastereomeric mixture: ^{1}H NMR δ 0.84 (t, J = 7.4 Hz, 3H), 1.10 (s, 6H), 1.24–1.52 (m, 12H), 2.09–2.40 (m, 3H), 2.48–2.60 (m, 2H), 3.26 (t, J = 6.4 Hz, 2H), 3.57 (m, 1H, minor 4*S*,5*S* compound), 3.90 (m, 1H, major 4*S*,5*R* compound), 4.44 (td, J = 3.1, 7.1 Hz, 1H); ^{13}C NMR δ 8.2, 21.0, 25.1, 25.6, 26.2, 28.7, 29.4, 30.5, 31.9, 32.5, 60.9, 71.3, 74.4, 82.8, 177.5; EI-MS 271 ($M - CH_3^+$, 1), 257 (17), 217 (21), 199 (28), 181 (33), 163 (25), 131 (59), 121 (39), 113 (27), 95 (28), 85 (42), 71 (100).

(4*S*,5*S*)-5-Hydroxy-4-heptadecanolide ((+)-muricatacin, 11b): mp 65 °C; ^{1}H NMR δ 0.87 (t, J = 6.4 Hz, 3H), 1.15–1.64 (m, 22H), 1.88–2.33 (m, 3H), 2.44–2.72 (m, 2H), 3.47–3.66 (m, 1H), 4.41 (dt, J = 4.6, 7.4 Hz, 1H); ^{13}C NMR δ 14.0, 22.6, 24.0, 25.4, 28.6, 29.3, 29.5, 29.6, 31.6, 32.9, 73.5, 83.0, 177.4; IR ($CHCl_3$): 3580, 3440, 2920, 2840, 1770, 1460, 1375, 1260, 1170, 980, 910; EI-MS 199 (1), 125 (4), 97 (6), 87 (11), 86 (100), 85 (13), 69 (16), 57 (13); CI-MS (CH_4): 285 (MH^+, 31), 268 (23), 267 (100), 265 (18), 249 (7), 239 (32), 199 (25), 143 (9), 130 (23), 125 (36), 123 (11), 115 (21), 113 (26), 111 (49), 109 (16); $[\alpha]^{20}_D$ = +24.6° (c = 1.70, MeOH).

(4*S*,5*R*)-5-Hydroxy-4-heptadecanolide (*epi*-muricatacin, 11c): mp 67 °C; ^{1}H NMR δ 0.87 (t, J = 6.4 Hz, 3H), 1.10–1.68 (m, 22H), 2.01–2.71 (m, 5H), 3.81–4.02 (m, 1H), 4.43 (dt, J = 3.2, 7.2 Hz, 1H); ^{13}C NMR δ 14.1, 21.0, 22.6, 25.6, 28.7, 29.3, 29.5, 29.6, 31.9, 71.3, 82.9, 177.5; IR ($CHCl_3$): 3580, 3440, 2920, 2840, 1770, 1460, 1375, 1260, 1170, 980, 910; EI-MS 199 (1), 125 (4), 97 (6), 87 (11), 86 (100), 85 (13), 69 (16), 57 (13); CI-MS (CH_4): 285 (MH^+, 31), 268 (23), 267 (100), 265 (18), 249 (7), 239 (32), 199 (25), 143 (9), 130 (23), 125 (36), 123 (11), 115 (21), 113 (26), 111 (49), 109 (16); $[\alpha]^{20}_D$ = +32° (c = 2.00, MeOH).

(4*S*,5*S*)-5-Hydroxy-8-nonen-4-olide (12b): ^{1}H NMR δ 1.68 (m, 2H), 2.16 (m, 4H), 2.55 (m, 2H), 3.60 (m, 1H), 4.45 (m, 1H), 5.05 (m, 2H), 5.80 (m, 1H); ^{13}C NMR δ 23.99, 28.62, 29.57, 32.04, 73.75, 82.99, 115.37, 137.67, 177.38; EI-MS 86 (100), 58 (12); CI-MS 188 ($M + NH_4^+$, 100), 171 (MH^+, 54), 153 (12).

(4*S*,5*R*)-5-Hydroxy-5-nonen-4-olide (12c): ^{1}H NMR δ 1.55 (m, 2H), 2.20 (m, 4H), 2.55 (m, 2H), 3.95 (m, 1H), 4.45 (m, 1H), 5.05 (m, 2H), 5.80 (m, 1H); ^{13}C NMR δ 21.33, 28.76, 29.92, 31.14, 70.96, 82.77, 115.62, 137.73, 177.43; EI-MS 86 (100), 58 (12); CI-MS 188 ($M + NH_4^+$, 100), 171 (MH^+, 54), 153 (12).

(4*S*,5*S*)- and (4*S*,5*R*)-5-hydroxy-6-phenyl-4-hexanolide (13b,c) as a diastereomeric mixture; ^{1}H NMR δ 2.21–2.63 (m, 4H), 2.77 (d, 2H, major 4*S*,5*R* compound), 2.90 (d, 2H, minor 4*S*,5*S* compound), 3.79 (m, 1H, minor 4*S*,5*S* compound), 4.09 (m, 1H, major 4*S*,5*R* compound), 4.42 (m, 1H), 7.28 (m, 5H); ^{13}C NMR δ 21.61, 28.47, 38.98, 72.57, 81.84, 126.77, 128.66, 129.24, 136.96, 177.44; EI-MS 206 (M^+, 27), 189 (15), 188 (18), 121 (78), 115 (31), 103 (46), 92 (91), 91 (100), 86 (67), 85 (42), 77 (26), 65 (30); CI-MS 224 ($M + NH_4^+$, 100), 208 (14), 207 (80), 189 (13).

(13′*R*, 5*S*)- and (13′*S*, 5*S*)-3-(13′-hydroxytriacontyl)-5-methylfuran-2(5*H*)-one (reticulatamol, (14b) as a diastereomeric mixture: mp 92–94 °C; ^{1}H NMR δ 6.98 (d, J = 1.5 Hz, 1H), 5.00 (qd, J = 6.7, 1.5 Hz, 1H), 3.58 (m, 1H), 2.26 (t, J = 7.2 Hz, 1H), 1.42 (d, J = 6.7 Hz, 3H), 1.35–1.20 (m, 56H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR δ 173.9, 148.9, 134.5, 77.5, 72.2, 37.7, 32.1, 29.8, 29.4, 29.3, 27.6, 25.8, 25.3, 22.8, 19.3, 14.2; IR ($CHCl_3$) 3350, 1750; UV (EtOH) λ 206 nm (log ϵ = 1.011); EI-MS 534 (M^+, 1), 532 (8), 516 (6), 309 (3), 295 (100), 281, 266; CI-MS (isobutane): 535 (MH^+, 100), 517 ($M - H_2O^+$, 8), 489 (5); FAB-Li: 545 (M + Li); $[\alpha]_D^{20}$ = +3° (c = 1, $CHCl_3$).

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Supplementary Material Available: Copies of NMR spectra of new compounds (26 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.