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α-Hydroxyallylsilanes as Propionaldehyde Enolate Equivalents and Their Use toward Iterative Aldol Reactions

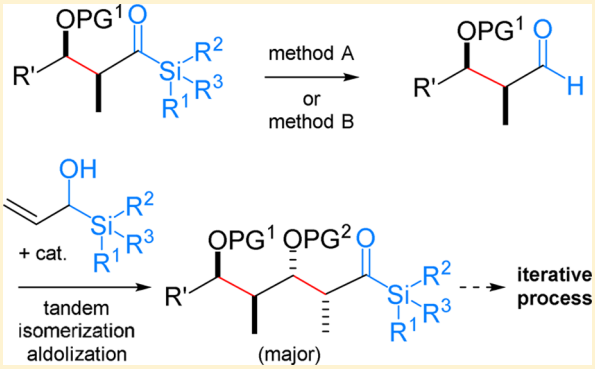
Johal Ruiz,[†] Akondi Srirama Murthy,[†,‡] Thierry Roisnel,[†] Srivari Chandrasekhar,[‡] and René Grée*[,†]

[†]Université de Rennes 1, Institut des Sciences Chimiques de Rennes, CNRS UMR 6226, Avenue du Général Leclerc, 35042 Rennes Cedex, France

[‡]CSIR-Indian Institute of Chemical Technology, Division of Natural Product Chemistry, Hyderabad 500007, India

Supporting Information

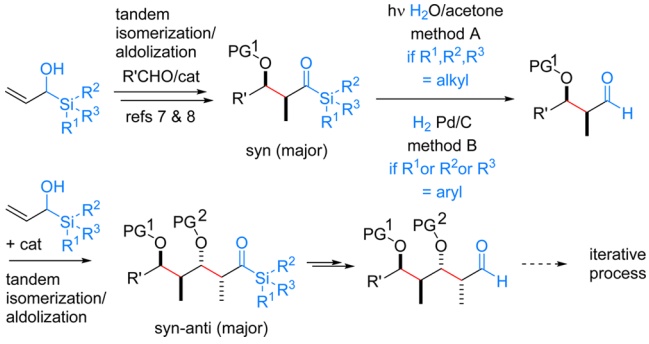
ABSTRACT: Smooth and efficient reaction conditions have been found for the transformation of protected β-hydroxyacylsilanes into the corresponding aldehydes. This opens a new route to iterative aldol reactions, and it has been used for the synthesis of fragments of several bioactive natural products.



INTRODUCTION

The polypropionate skeleton, naturally synthesized by enzymatic systems, is a widespread structure in natural products and bioactive molecules.[1] A privileged method for the preparation of this framework is the aldol reaction,[2] although the direct aldol cross-coupling of two aldehydes has been a synthetic challenge for a long time. Recently, organocatalytic[3] and Lewis acid catalyzed[4] direct aldol reactions have provided elegant solutions to circumvent to a large extent this problem. Powerful methods employing "supersilyl" enol ethers[5] and indirect strategies such as isomerization−aldolization of allylborates[6] have also been described. Classical methods for iterative synthesis still usually rely on the use of various carboxylic acid derivatives as nucleophilic partners, allowing high levels of stereocontrol by the choice of appropriate reagents, chiral auxiliaries, catalysts, and reaction conditions.[2] However, further transformation to the aldehyde requires step-consuming redox adjustments. We have recently developed a transition-metal-mediated tandem isomerization−aldol reaction of α-hydroxyallylsilanes,[7] affording *syn* β-hydroxyacylsilanes which have already demonstrated good synthetic potential.[8−10] It appeared to us that a new strategy could be developed in iterative aldol reactions toward polypropionate-derived molecules, provided that appropriate conditions could be found for efficient transformations of β-hydroxyacylsilanes into aldols (Scheme 1). In this publication, we first establish that two different reaction conditions can be employed for this transformation, depending upon the nature of the substituents on silicon. The first one (method A, for trialkylsilanes) uses especially designed photolytic reaction conditions, while the second (method B, for arylalkylsilanes) employs hydrogenolysis. We also show that various R′ substituents and protective groups (PG) can be introduced in the starting aldol products and, further, demonstrate that the process can be repeated to stereotetrads with *syn*−*anti* derivatives as the major isomers. Finally, this strategy has been successfully applied to the preparation of fragments of several bioactive natural products, including arenamides, tylonolide, panamycin 607, gephyronic acid, and pironetine.

Scheme 1. Design of a New Iterative Strategy toward Polypropionates, Using Acylsilanes as Key Intermediates



RESULTS AND DISCUSSION

As models, we selected three α-hydroxyallylsilanes **1**−**3** with different substituents on silicon (TES, TIPS, and TBDPS).

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Starting from derivative **1** and using five different aldehydes, we prepared the corresponding β-hydroxyacylsilanes **4a/5a−4e/5e** by an isomerization−aldol sequence (Scheme 2, Table 1).

Scheme 2. Preparation of Protected β-Hydroxyacylsilane Derivatives

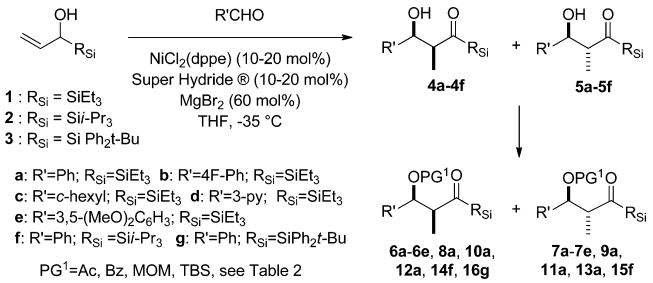


Table 1. Preparation of the Selected β-Hydroxyacylsilanes[a]

entry	R′	time (h)	product	yield[b] (%)	d.r.[c]
1[d]	Ph−	67	**4a−5a**	79	83:17
2	4-F-C_6H_4−	21	**4b−5b**	85	84:16
3	C_6H_{11}−	24	**4c−5c**	71	87:13
4	3-Py−	72	**4d−5d**	76	85:15
5[e]	3,5-$(MeO)_2C_6H_3$−	72	**4e−5e**	87	73:27

[a]Reactions performed at 2 mmol scale with 20 mol % catalyst. [b]Yields given for the mixture of both diastereoisomers. [c]*syn*/*anti* ratio as determined by ^{1}H NMR. [d]Reaction performed at 11.6 mmol scale with 10 mol % catalyst. [e]Reaction performed at 1 mmol scale with 20 mol % catalyst.

Further, we used the previously described compounds **4f/5f** and **4g/5g** bearing, respectively, TIPS and TBDPS substituents.[7] We selected four classical protecting groups with different steric/electronic properties, acetate, benzoate, MOM, and TBS, to afford the corresponding derivatives (Table 2). A screening of these protecting groups with the compounds **4a/5a** gave products **6a−13a** in fair to excellent yields. Acetylation and benzoylation proved to be more attractive since they allow, in each case, separation of the major *syn* diastereoisomer.

The minor *anti* diastereoisomers could not be separated, except in the case of compound **9a**, which was isolated in a pure form. Derivatives **4f/5f** gave acetates **14f** and **15f** in slightly lower yields, probably due to a higher steric hindrance, while intermediate **16g** has been described earlier.[8a]

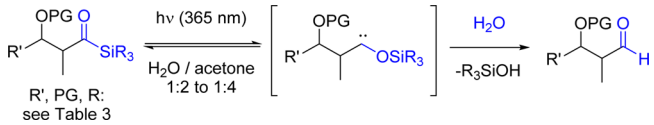
In a second step, we studied the transformation of acylsilanes into aldehydes to allow further synthetic transformations, including iterative aldol reactions. A survey of the literature indicated several options, including base-[11] or fluoride-induced[12] protodesilylations, hydrogenolysis (provided the silane bears at least one aryl group),[13] $LiAlH_4$ reduction,[14] hydrolysis,[15] or photolytic C−Si cleavage in a protic solvent.[16] Among those, catalytic hydrogenation appeared interesting and was applied to **16g**, while base- or fluoride-induced protodesilylations were incompatible with our substrates. The photochemical transformation of acylsilanes into aldehydes as depicted in Scheme 3 appeared highly desirable, though challenging in the case of our protected β-hydroxyacylsilane moieties. Indeed, a labile α proton and a potential leaving group in the β position could result in competitive elimination reactions. To the best of our knowledge, a single example of photolytic cleavage of β-alkoxyacylsilane has been reported to date, as part of the synthesis of thymidine analogues.[16c] Thus,

Table 2. Preparation of Protected β-Hydroxyacylsilanes[a]

Entry	Reactant	Product	Yield[a] (%)	d.r.[a]
1.	**4a-5a**	**6a**	70	100:0
2.	**4b-5b**	**6b**	58	100:0
3.	**4c-5c**	**6c**	78	100:0
4.	**4d-5d**	**6d**	55	97:3
6	**4e-5e**	**6e**	59	100:0
7.	**4a-5a**	**8a**	73	100:0
		9a	15	2:98
8.	**4a-5a**	**10a-11a**	94	83:17
9.	**4a-5a**	**12a-13a**	73	83:17
10.	**4f-5f**	**14f**	63	100:0

[a]The yield and d.r. (*syn*/*anti* ratio) refer to isolated products, either pure or as diastereoisomeric mixtures.

Scheme 3. Preparation of Protected β-Hydroxyaldehydes under Photolytic Conditions



by using **6a** and **8a** as models, extensive optimization studies (solvent, temperature, lamp, and concentration) have been performed in order to define the best conditions. In particular, solvents were found to play key roles in this process. By using methanol or isopropanol alone, or as mixtures with water, the intermediate acetals could be characterized by ^{1}H NMR, but their hydrolysis to the aldehyde proved to be challenging with sensitive molecules. Therefore, it was found that reactions starting from **6a** or **8a** at 5.10^{-2} M in 1:2 to 1:4 mixtures of acetone and water, combined with the use of a routine UV lamp at 365 nm,[17,18] afforded directly the desired protected β-hydroxyaldehydes **17a** and **18a** in excellent yields with a very good purity (Scheme 3 and Table 3). The *anti* isomer **9a** afforded derivative **19a** only, establishing that no epimerization was observed during this process.

This method was extended to the substrates **6b−6e**, as well as the compounds with other protecting groups such as **10** (TBS) and **12** (MOM). The intermediate **14f**, with the bulkier TIPS group, was also easily transformed by this route into the desired aldehyde **17a**. All of these aldehydes have been characterized by NMR and mass spectral analysis. However,

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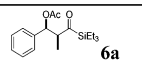
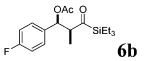
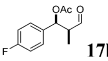
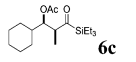
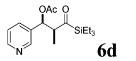
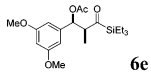
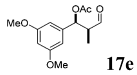
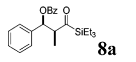
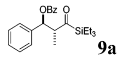
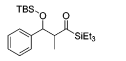
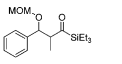
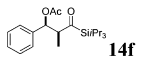
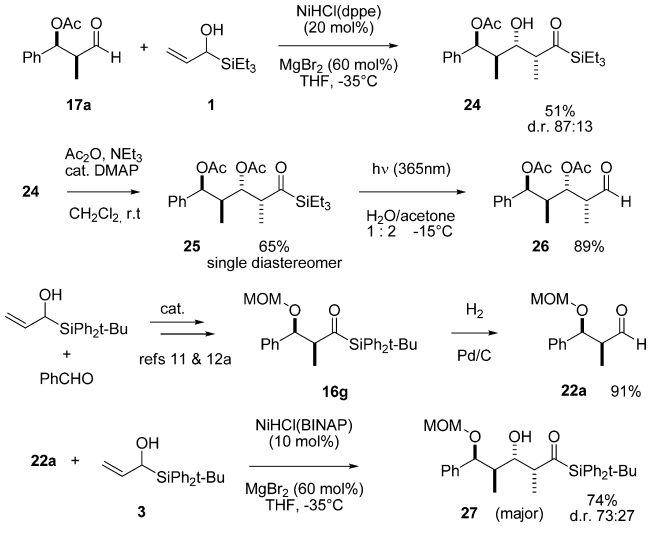
Table 3. Preparation of Protected β-Hydroxyaldehydes by Photolysis

Entry	Reactant	Product	Yield (%)
1.	 **6a**	 **17a**	95
2.	 **6b**	 **17b**	98
3.	 **6c**	 **17c**	99
4.	 **6d**	 **17d**	95
5.	 **6e**	 **17e**	quant.
6.	 **8a**	 **18a**	quant.
7.	 **9a**	 **19a**	97
8.	 **10a-11a**	 **20a-21a**	89
9.	 **12a-13a**	 **22a-23a**	93
10.	 **14f**	 **17a**	96

these sensitive compounds showed limited stability; thus, they have to be used quickly after isolation.

Next, we intended to demonstrate the feasibility of an iterative process toward stereotetrads[1] on two representative examples (Scheme 4). Starting from pure *syn* aldehyde **17a**, the tandem reaction afforded a 76:13:9:2 mixture of products (^{1}H NMR analysis of the crude reaction mixture). After purification by chromatography and fractional crystallization, the major *syn*−*anti*−*syn* derivative **24** was obtained in pure form. The structure of **24** was established unambiguously by X-ray crystallographic analysis (see the Supporting Information).[19] In order to investigate the scope and limitations of this procedure, we repeated the previously described sequence. Compound **24** was acetylated under standard conditions, affording diacetate **25** in pure form, and then the acylsilane moiety was transformed to the aldehyde **26** in very good yield, showing that the used procedure was compatible with more complex structures.

Scheme 4. Examples of Stereotetrads Prepared by Iterative Strategy



In parallel, we checked the possible use of this iterative strategy with acylsilanes bearing an aryl substituent on silicon. Starting from previously described MOM protected β-hydroxyacylsilane **16g**,[7,8] hydrogenolysis by the procedure pioneered in Panek's group[13] afforded in high yield the *syn* aldehyde **22a**. A second tandem process with α-hydroxyallylsilane **3** gave a 57:28:12:3 mixture of products (^{1}H NMR analysis of the crude reaction mixture). After purification by chromatography and fractional crystallization, the major *syn*−*anti*−*syn* derivative **27** was obtained in pure form and its *syn*−*anti*−*syn* structure was also established by X-ray analysis.[19] Thus, in both cases, the aldol process occurred preferentially through an anti-Felkin mode, in agreement with our previous results,[7] and with reported use of *syn* aldols as acceptors.[20]

We finally applied our strategy to the synthesis of known intermediates for natural products synthesis (Scheme 5). Compound **31** is a common fragment for the synthesis of arenamides[21] and the C_1-C_9 subunit of tylonolide.[22] By using our method, it has been synthesized in three steps and 48% overall yield from α-hydroxyallylsilane **1**. The tandem isomerization−aldol reaction with aldehyde **28** gave **29**, as a 83:17 mixture of *syn* and *anti* aldols. After protection as its TBS ether, the major *syn* isomer **30** was isolated by chromatography. Under the previously described photolytic conditions, the transformation into aldehyde occurred smoothly, affording in excellent yield derivative **31**, whose spectral data are in full agreement with those in the literature.[21,22]

We also used this strategy to the preparation of the C_5-C_{11} fragment of pironetine, a natural product with immunosuppressant activities.[23] Several syntheses of this molecule have been already reported,[24] while our method is described in Scheme 5. Starting from aldehyde **32**,[25] a first tandem isomerization−aldol sequence afforded *syn* aldol **33** as the major isomer purified by chromatography. After protection as its TBS ether, the transformation of acylsilane **34** into aldehyde **35** was successfully performed using the same photolytic conditions. This derivative is already a known intermediate for the total synthesis of Panamycin 607,[26a] and Gephyronic acid.[26b] A second tandem aldol reaction gave, after separation of the diastereoisomers by silica gel chromatography, intermediate **36** as the major isomer. The transformation into the diol **37** was performed in a two-step, one-pot sequence. First, the intermediate aldehyde was obtained from the acylsilane unit under the same photolytic conditions as previously. This was followed immediately by in situ reduction with $NaBH_4$ and aqueous workup to afford diol **37** in 70% yield from **36**. The spectroscopical data of **37** were matching with those already reported for a known intermediate of pironetine synthesis.[25a] Diol **37** was obtained in 23% overall yield and six steps, including two tandem isomerization−aldol reactions and two photolytic transformations of acylsilanes into aldehydes. The last example is noteworthy since it establishes that this photolytic transformation can be performed, albeit in lower yield, on a nonprotected β-hydroxyacylsilane to afford the corresponding β-hydroxyaldehyde.

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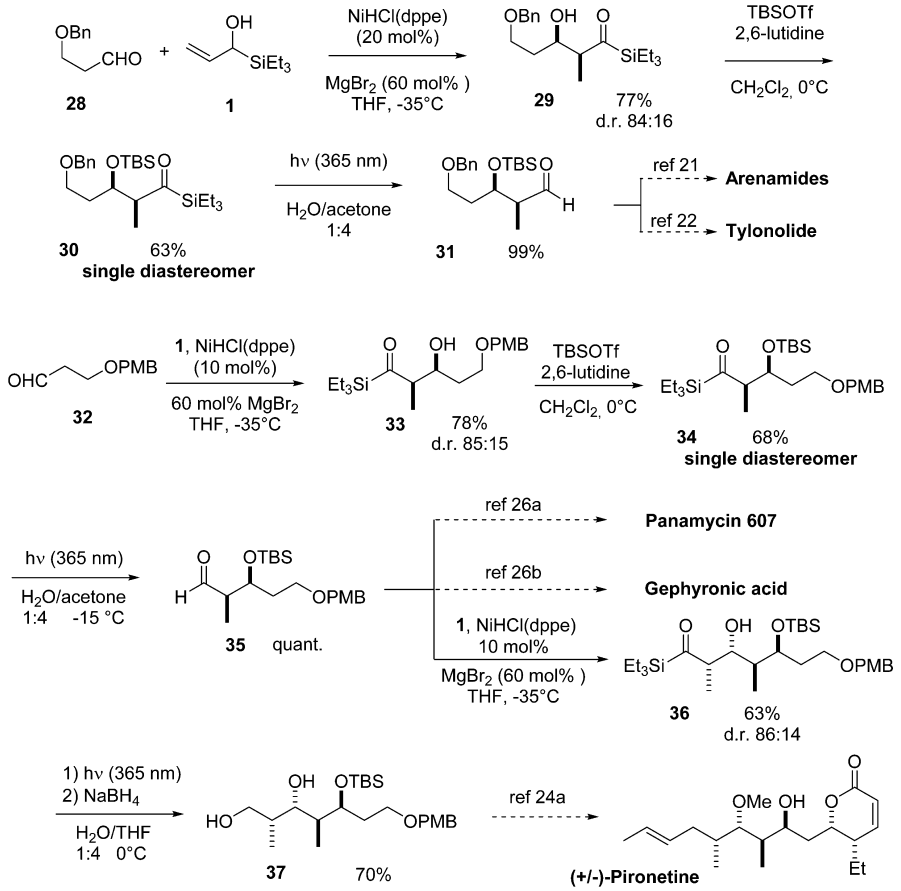
Scheme 5. Application to the Synthesis of Fragments for Three Natural Products



CONCLUSION

In summary, we have demonstrated a new strategy toward iterative aldol processes based on the use of α-hydroxyallylsilanes as propionaldehyde enolates equivalents. It is based on two key steps, the first is the tandem isomerization−aldol reaction, allowing the preparation of β-alkoxyacylsilanes, and the second is an easy and efficient transformation of the acylsilane unit into the aldehyde required for the next iteration. Such a strategy could find applications in the preparation of selected polypropionate-type molecules, as already demonstrated by the synthesis of fragments for five natural products.

EXPERIMENTAL SECTION

Representative Procedure for the Synthesis of the α-Hydroxyallylsilane (1). A 100 mL round-bottom flask equipped with a magnetic stir bar is sealed with a septum, and allyl alcohol (1.994 g, 34.4 mmol) is introduced under nitrogen flush. Then, 34 mL of freshly distilled THF is introduced, and the solution cooled in an acetone/liquid nitrogen bath at −50 °C. Then, *n*-BuLi (24 mL, 37.8 mmol) is added with a syringe. The reaction mixture is stirred during approximately 30 min, warming up to −20 °C. Next, TESCl (5.004 g, 33.2 mmol) is added with a syringe, and the reaction mixture is stirred overnight, warming up to room temperature. The reaction is monitored by TLC with a 95:5 pentane/Et_2O mixture. The solution is cooled to −78 °C under nitrogen flush, and then *s*-BuLi (27 mL, 37.8 mmol) is added dropwise with a syringe pump. After addition, the reaction mixture is stirred during 45 min, allowing to warm to −60 °C. The reaction is monitored by TLC with a 95:5 pentane/Et_2O mixture. When the silylated allyl alcohol is consumed, the cold solution is transferred via a cannula by nitrogen overpressure in a 500 mL Erlenmeyer flask containing pentane and a saturated solution of ammonium chloride at 0 °C under stirring. The pH is constantly monitored and neutralized when necessary with a HCl 37% solution. The solution is introduced in a separatory funnel, and the organic layer is washed 6 times with 100 mL H_2O to remove the remaining THF. The organic layer is dried with $MgSO_4$, filtered, and concentrated at reduced pressure (40 °C, 700 mbar) and then at high vacuum (2−4 min) to remove the residual hexanes. The product appeared as a colorless oil (4.950 g, 28.7 mmol, 86%).

General Procedure for the Synthesis of β-Hydroxyacylsilanes (4a−4g/5a−5g). A round-bottom flask or Schlenk tube equipped with a magnetic stir bar is charged with $NiCl_2$(dppe), and then sealed with a septum and flushed alternatively with argon or nitrogen and vacuum. Then, freshly distilled THF is introduced under argon or nitrogen flush, and the solution is stirred. A fresh lithium triethylborohydride solution is added via a syringe, and the red solution turns immediately into a deep seal brown, as a result of NiHCl(dppe) formation. The solution is stirred at 30 °C during 10 min. A second round-bottom flask is charged with $MgBr_2$ and a magnetic stir bar, and then dried with a heat gun under high vacuum. Next, the flask is flushed with nitrogen or argon and the NiHCl(dppe) solution is introduced via a cannula and cooled to −35 °C with a chiller under nitrogen or argon flush. Then, the aldehyde and the α-hydroxyallylsilane as pure material or in solution in THF are added with a syringe in the solution. The inert gas flush is stopped, and the reaction is monitored by TLC.

(±)-3-Hydroxy-2-methyl-3-phenyl-1-(triethylsilyl)propan-1-one (4a−5a). Following the general procedure described above, a 50 mL round-bottom flask was charged with 1.297 g (7.04 mmol, 61 mol %) of $MgBr_2$ and 1.16 mmol (10 mol %) of freshly prepared NiHCl(dppe) in 22 mL of THF. The solution was cooled to −35 °C, and then benzaldehyde (1.231 g, 11.6 mmol) and **1** (2.003 g, 11.6 mmol) were introduced into the solution under argon flush. The solution was stirred at −35 °C for 67 h, and the reaction was

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monitored by TLC using a 95:5 pentane/AcOEt mixture. The reaction was quenched by a saturated NH_4Cl solution, the mixture was diluted with Et_2O and filtered through a small pad of Celite, and the phases were separated. The separated aqueous phase was extracted with Et_2O, and the combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure, affording 2.954 g of a crude mixture. The latter was purified by chromatography using 121 g of silica gel (pentane/AcOEt gradient, 98.5:1.5 to 96:4), affording 2.566 g of **4a**/**5a** (9.21 mmol, 79%, colorless oil) as a 83:17 mixture of diastereoisomers. **4a**: ^{1}H NMR (300 MHz, $CDCl_3$) *syn*: δ 7.38−7.20 (m, 5H), 5.08 (dd, J = 3.4, 1.8 Hz, 1H), 3.20 (d, J = 1.9 Hz 1H), 3.16 (dq, J = 7.2, 3.7 Hz, 1H), 0.99−0.91 (m, 12H), 0.79−0.66 (m, 6H). The characteristic peaks for *anti* isomer **5a** were observed at δ 4.79 (dd, J = 7.8, 4.5 Hz, 1H), 3.32 (q, J = 7.4 Hz, 1H), 2.92 (d, J = 4.8 Hz, 1H), 0.83 (d, J = 7.3 Hz, 3H) in the ^{1}H NMR spectrum. For complementary data, see ref 7.

*(±)-3-Hydroxy-2-methyl-3-(4-fluorophenyl)-1-(triethylsilyl)-propan-1-one (**4b**−**5b**).* Following the general procedure described above, a 10 mL round-bottom flask was charged with 219 mg (1.19 mmol, 62 mol %) of $MgBr_2$ and 0.40 mmol (20 mol %) of freshly prepared NiHCl(dppe) in 4 mL of THF. The solution was cooled to −35 °C, and then 4-fluorobenzaldehyde (0.205 mL, 1.9 mmol) and **1** (352 mg, 2.04 mmol) were introduced into the solution under nitrogen flush. The solution was stirred for 21 h at −35 °C, and the reaction was monitored by TLC using a 95:5 pentane/AcOEt mixture. The reaction was quenched by a saturated NH_4Cl solution, the mixture was diluted with Et_2O and filtered through a small pad of Celite, and the phases were separated. The separated aqueous phase was extracted with Et_2O, and the combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure, affording 670 mg of a crude mixture. The latter was purified by chromatography with 19 g of silica gel (pentane/AcOEt gradient, 98.5:1.5 to 97:3). After purification, 479 mg (1.62 mmol, 85%, colorless oil) of **4b**/**5b** was obtained as an 83:17 mixture of diastereomers. **4b**: ^{1}H NMR (300 MHz, $CDCl_3$) *syn*: δ 7.33−7.21 (m, 2H), 7.07−6.97 (m, 2H), 5.05 (dd, J = 3.3, 1.4 Hz, 1H), 3.28 (d, J = 2.0 Hz, 1H), 3.11 (qd, J = 7.3, 3.3 Hz, 1H), 0.99−0.90 (m, 12H), 0.78−0.67 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 254.2, 163.7, 160.5, 138.05, 138.01, 127.7, 127.6, 115.2, 115.0, 71.4, 56.7, 8.0, 7.3, 2.4. HRMS (ESI +ve) Exact mass calculated for $C_{16}H_{25}O_2FNaSi$ $[M + Na]^+$: 319.15056, found: 319.1507. The characteristic peaks for *anti* isomer **5b** were observed at 4.77 (dd, J = 7.8, 4.3 Hz, 1H), 3.33−3.19 (m, 1H), 2.98 (d, J = 4.7 Hz, 1H), 0.82 (d, J = 7.3 Hz, 3H), in the ^{1}H NMR spectrum and at 254.6, 164.0, 160.7, 138.7, 138.7, 128.3, 128.2, 115.4, 115.1, 75.9, 57.0, 12.5, 7.3, 2.3 in the ^{13}C NMR spectrum.

*(±)-3-Hydroxy-2-methyl-3-(cyclohexyl)-1-(triethylsilyl)propan-1-one (**4c**−**5c**).* Following the general procedure described above, a 10 mL Schlenk tube was charged with 212 mg (1.15 mmol, 61 mol %) of $MgBr_2$ and 0.4 mmol (20 mol %) of NiHCl(dppe) in 4 mL of THF. The solution was cooled to −35 °C, and then cyclohexanecarboxaldehyde (213 mg, 1.90 mmol) and **1** (335 mg, 1.94 mmol) were introduced into the solution under nitrogen flush. The solution was stirred at −35 °C for 45 h, and the reaction was monitored by TLC using a 95:5 pentane/Et_2O mixture. The reaction was quenched by a saturated NH_4Cl solution, the mixture was diluted with Et_2O and filtered through a small pad of Celite, and the phases were separated. The separated aqueous phase was extracted with Et_2O, and the combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure, affording 631 mg of a crude mixture. The latter was purified by chromatography with 33 g of silica gel (pentane/Et_2O gradient, 98:2 to 90:10). After purification, 385 mg (1.35 mmol, 71%, colorless oil) of **4c**/**5c** was obtained as an 85:15 mixture of diastereomers. **4c**: ^{1}H NMR (300 MHz, $CDCl_3$) *syn*: δ 3.54 (dt, J = 8.7, 2.2 Hz, 1H), 3.10 (qd, J = 7.2, 2.3 Hz, 1H), 2.82 (d, J = 2.5 Hz, 1H), 2.09 (d, J = 14.4 Hz, 1H), 1.81−1.54 (m, 4H), 1.42−1.09 (m, 6H), 1.02−0.92 (m, 12H), 0.81−0.70 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 254.3, 73.5, 51.0, 40.1, 29.6, 29.0, 26.4, 26.1, 25.9, 7.3, 7.1, 2.5. HRMS (ESI +ve) Exact mass calculated for $C_{16}H_{32}O_2NaSi$ $[M + Na]^+$: 307.20693, found: 307.2071. The characteristic peaks for *anti* isomer **5c** were observed at 3.42 (q, J = 6.2 Hz, 1H), 3.24−3.14 (m, 1H), 2.61 (d, J = 7.4 Hz, 1H), in the ^{1}H NMR spectrum and at 255.9, 78.5, 51.4, 41.1, 30.4, 27.2, 26.5, 26.2, 12.3, 7.3, 2.4 in the ^{13}C NMR spectrum.

*(±)-3-Hydroxy-2-methyl-3-(3-pyridyl)-1-(triethylsilyl)propan-1-one (**4d**−**5d**).* Following the general procedure described above, a 5 mL round-bottom flask was charged with 110 mg (0.60 mmol, 60 mol %) of $MgBr_2$ and 0.2 mmol (20 mol %) of freshly prepared NiHCl(dppe) in 2 mL of THF. The solution was cooled to −35 °C, and then 3-pyridinecarboxaldehyde (107 mg, 1.00 mmol) and **1** (185 mg, 1.07 mmol) were introduced under argon flush. The solution was stirred at −35 °C for 84 h, and the reaction was monitored by TLC using a 75:25 pentane/acetone mixture. The reaction was quenched by a saturated NaCl solution, the mixture was diluted with Et_2O and filtered through a small pad of Celite, and the phases were separated. The separated aqueous phase was extracted with Et_2O, and the combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure, affording 331 mg of a crude mixture. The latter was purified by chromatography with 17 g of silica gel (pentane/Et_2O gradient, 60:40 to 40:60). After purification, 212 mg (0.76 mmol, 76%, pale yellow solid) of **4d**/**5d** was obtained as an 86:14 mixture of diastereomers. **4d**: ^{1}H NMR (300 MHz, $CDCl_3$) *syn*: δ 8.48−8.55 (m, 2H), 7.72−7.65 (m, 1H), 7.31−7.26 (m, 1H), 5.14 (d, J = 2.8 Hz, 1H), 3.50 (brs, 1H), 3.11 (qd, J = 7.3, 2.9 Hz, 1H), 1.01−0.90 (m, 12H), 0.80−0.69 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 253.0, 148.0, 147.6, 138.4, 134.3, 123.2, 70.0, 56.9, 8.7, 7.2, 2.2. HRMS (ESI +ve) Exact mass calculated for $C_{15}H_{25}NO_2NaSi$ $[M + Na]^+$: 302.15523, found: 302.1552. The characteristic peaks for *anti* isomer **5d** were observed at 4.85 (d, J = 7.8 Hz, 1H), 3.27 (m, 2H), 0.88 (d, J = 7.3 Hz, 3H) in the ^{1}H NMR spectrum and at 253.5, 148.5, 138.8, 134.5, 123.5, 73.7, 56.5, 30.3, 12.2 for the ^{13}C NMR spectrum.

*(±)-3-Hydroxy-2-methyl-3-(2,5-dimethoxyphenyl)-1-(triethylsilyl)propan-1-one (**4e**−**5e**).* Following the general procedure described above, a 10 mL round-bottom flask was charged with 221 mg (1.20 mmol, 60 mol %) of $MgBr_2$ and 0.4 mmol (20 mol %) of freshly prepared NiHCl(dppe) in 4 mL of THF. The solution was cooled to −35 °C, and then 3,5-dimethoxybenzaldehyde (353 mg, 2.10 mmol) and **1** (345 mg, 2.00 mmol) were introduced into the solution under argon flush. The solution was stirred at −35 °C for 72 h, and the reaction was monitored by TLC using a 90:10 pentane/AcOEt mixture. The reaction was quenched by a saturated NH_4Cl solution, the mixture was diluted with Et_2O and filtered through a small pad of Celite, and the phases were separated. The separated aqueous phase was extracted with Et_2O, and the combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure, affording 773 mg of a crude mixture. The latter was purified by chromatography with 36 g of silica gel (pentane/AcOEt gradient, 97:3 to 94:6). After purification, the reaction afforded 586 mg (1.73 mmol, 87%, colorless oil) of **4e**/**5e** as a 73:27 mixture of diastereomers contaminated with around 5% of starting aldehyde. **4e**: ^{1}H NMR (300 MHz, $CDCl_3$) *syn*: δ 6.49−6.46 (m, 2H), 6.38−6.34 (m, 1H) 5.01 (t, J = 2.5 Hz, 1H), 3.79 (s, 6H), 3.25 (d, J = 2.0 Hz, 1H), 3.14 (qd, J = 7.2, 3.0 Hz, 1H), 1.01−0.91 (m, 12H), 0.79−0.69 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 254.3, 160.9, 144.8, 104.2, 99.2, 71.8, 56.6, 55.5, 8.0, 7.4, 2.5. HRMS (ESI +ve) Exact mass calculated for $C_{18}H_{30}O_4NaSi$ $[M + Na]^+$: 361.18111, found: 361.1808. The characteristic peaks for *anti* isomer **5e** were observed at 4.72 (dd, J = 7.8, 4.6 Hz, 1H), 3.85 (m, 1H), 2.89 (d, J = 4.8, 1H), 0.84 (d, J = 7.3 Hz, 3H), in the ^{1}H NMR spectrum and at 254.6, 161.0, 145.4, 104.7, 99.7, 56.7, 12.7, 7.3, 2.4.

*(±)-3-Hydroxy-2-methyl-3-phenyl-1-(triisopropylsilyl)propan-1-one (**4f**−**5f**).* Following the general procedure described above, a 10 mL round-bottom flask was charged with 110 mg (0.597 mmol, 60 mol %) of $MgBr_2$ and 0.20 mmol (20 mol %) of freshly prepared NiHCl(dppe) in 2 mL of THF. The solution was cooled to −35 °C, and then benzaldehyde (101 mg, 0.95 mmol) and **2** (214 mg, 1.00 mmol) were introduced into the solution under argon flush. The solution was stirred at −35 °C for 96 h, and the reaction was monitored by TLC using a 95:5 pentane/AcOEt mixture. The reaction was quenched by a saturated NH_4Cl solution, the mixture was diluted with Et_2O and filtered through a small pad of Celite, and the phases were separated. The separated aqueous phase was extracted with Et_2O,

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and the combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure, affording 270 mg of a crude mixture. The latter was purified by chromatography with 15 g of silica gel (pentane/AcOEt gradient, 98.5 to 96:4). After purification, the reaction afforded 176 mg (0.549 mmol, 58%, colorless oil) of **4f**/**5f** as a 97:3 mixture of diastereoisomers. **4f**: ^{1}H NMR (400 MHz, CDCl3) *syn*: δ 7.36−7.30 (m, 4H), 7.25−7.22 (m, 1H), 5.07 (dd, J = 2.8, 1.4 Hz, 1H), 3.53 (d, J = 1.5 Hz, 1H), 3.23 (qd, J = 7.2, 2.7 Hz, 1H), 1.35−1.25 (m, 3H), 1.11 (m, 18H), 0.91 (d, J = 7.2 Hz, 3H). The characteristic peaks for *anti* isomer **5f** were observed at 4.83 (dd, J = 7.9, 4.6 Hz, 1H), 3.42−3.38 (m, 1H), 2.79 (d, J = 4.7 Hz, 1H), 0.82 (d, J = 7.2 Hz, 3H). For complementary data, see ref 7.

General Procedure for the Esterification of β-Hydroxyacylsilanes. A round-bottom flask was charged with the β-hydroxyacylsilane, the acid anhydride, and a magnetic stir bar. The round-bottom flask was sealed with a septum and flushed with nitrogen. Freshly distilled CH_2Cl_2 and then NEt_3 were added through the septum with a syringe. DMAP was quickly added to the solution, and then the round-bottom flask was flushed with nitrogen for 2 min. The nitrogen flush was then stopped, and the reaction was stirred at room temperature unless otherwise mentioned. After completion of the reaction, the solution was quenched with a saturated solution of ammonium chloride, introduced in a separatory funnel, and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic phases were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography.

*(±)-syn-3-Acetoxy-2-methyl-3-phenyl-1-(triethylsilyl)propan-1-one (**6a**).* Following the general procedure mentioned above, a 50 mL round-bottom flask was charged with **4a**/**5a** (1.000 g, 3.59 mmol) and acetic anhydride (784 mg, 7.68 mmol). Next, 18 mL of freshly distilled CH_2Cl_2 and 1.5 mL (10.8 mmol) of NEt_3 were introduced into the round-bottom flask. Finally, DMAP (61 mg, 0.050 mmol) was added to the solution, and the latter was stirred at room temperature (~20 °C) for 1 h. The reaction progress was monitored by TLC (pentane/AcOEt 95:5). After aqueous workup and concentration, the reaction afforded 1.249 g of a crude mixture. The latter was purified by chromatography with 66 g of silica gel (pentane/AcOEt gradient, 99.5:0.5 to 99:1). The less polar *syn* diastereomer **6a** was separated from the minor *anti* diastereomer **7a** after careful chromatography on silica gel. After purification, the reaction afforded **6a** as a single isomer (802 mg, 2.50 mmol, 70%, colorless oil). **6a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34−7.16 (m, 5H), 6.01 (d, J = 8.2 Hz, 1H), 3.47 (dq, J = 8.2, 6.9 Hz, 1H), 2.04 (s, 3H), 1.02 (d, J = 7.0 Hz, 3H), 0.82−0.76 (m, 9H), 0.60−0.48 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 248.4, 169.8, 139.8, 128.3, 127.8, 127.1, 75.2, 56.1, 21.1, 11.5, 7.0, 2.0. HRMS (ESI +ve) Exact mass calculated for $C_{18}H_{28}O_3NaSi$ $[M + Na]^+$: 343.17054, found: 343.1708.

*(±)-syn-3-Acetoxy-2-methyl-3-(4-fluorophenyl)-1-(triethylsilyl)-propan-1-one (**6b**).* Following the general procedure mentioned above, a 10 mL round-bottom flask was charged with **5a**/**5b** (148 mg, 0.499 mmol) and acetic anhydride (103 mg, 1.00 mmol). Then, 2.5 mL of freshly distilled CH_2Cl_2 and 0.2 mL (1.44 mmol) of NEt_3 were introduced in the round-bottom flask. Finally, DMAP (11 mg, 0.09 mmol) was added to the solution, and the latter was stirred at room temperature for 1 h. After aqueous workup and concentration, the reaction afforded 181 mg of a crude mixture. The latter was purified by chromatography with 10 g of silica gel (pentane/Et_2O gradient, 99:1 to 97:3). The less polar *syn* diastereomer **6b** was separated from the minor *anti* diastereomer **7b** after careful chromatography on silica gel. After purification, the reaction afforded **6b** as a single isomer (98 mg, 0.29 mmol, 58%, white solid, mp < 40 °C). **6b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31−7.19 (m, 2H), 7.05−6.89 (m, 2H), 5.97 (d, J = 8.7 Hz, 1H), 3.47 (dq, J = 8.8, 7.0 Hz, 1H), 2.04 (s, 3H), 1.04 (d, J = 7.0 Hz, 3H), 0.80 (m, 9H), 0.63−0.48 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 248.3, 169.8, 164.0, 160.8, 135.91, 135.87, 129.1, 129.0, 115.4, 115.1, 74.9, 56.2, 21.1, 11.8, 7.0, 2.1. HRMS (ESI +ve) Exact mass calculated for $C_{18}H_{27}O_3FNaSi$ $[M + Na]^+$: 361.16112, found: 361.1613.

*(±)-syn-3-Acetoxy-2-methyl-3-cyclohexyl-1-(triethylsilyl)propan-1-one (**6c**).* Following the general procedure mentioned above, a 25 mL round-bottom flask was charged with **4c**/**5c** (200 mg, 0.703 mmol) and acetic anhydride (144 mg, 1.41 mmol). Next, 3.5 mL of freshly distilled CH_2Cl_2 and 0.3 mL (2.11 mmol) of NEt_3 were introduced into the round-bottom flask. Finally, DMAP (14 mg, 0.11 mmol) was added to the solution, and the latter was stirred at room temperature (~20 °C) for 2 h. The reaction progress was monitored by TLC (pentane/Et_2O 95:5). After aqueous workup and concentration, the reaction afforded 225 mg of a crude mixture. The latter was purified by chromatography with 12 g of silica gel (pentane/Et_2O gradient, 99:1 to 96:4). The less polar *syn* diastereomer **6c** was easily separated from the minor *anti* diastereomer **7c**. After purification, the reaction afforded **6c** as a single isomer (178 mg, 0.545 mmol 78%, pale yellow solid, mp < 40 °C). **6c**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.13 (dd, J = 6.8, 5.5 Hz, 1H), 3.21 (qd, J = 7.0, 5.5 Hz, 1H), 2.00 (s, 3H), 1.80−1.62 (m, 4H), 1.45 (m, 1H), 1.32−1.03 (m, 4H), 1.01−0.90 (m, 14H), 0.80−0.71 (m, 6H).^{13}C NMR (75 MHz, $CDCl_3$) δ 247.8, 170.5, 75.1, 51.6, 39.6, 29.8, 28.2, 26.2, 26.1, 25.9, 20.8, 9.1, 7.3, 2.6. HRMS (ESI +ve) Exact mass calculated for $C_{18}H_{34}O_3NaSi$ $[M + Na]^+$: 349.21749, found: 349.2177.

*(±)-syn-3-Acetoxy-2-methyl-3-(3-pyridyl)-1-(triethylsilyl)propan-1-one (**6d**).* Following the general procedure mentioned above, a 10 mL round-bottom flask was charged with **5d**/**5e** (140 mg, 0.500 mmol) and acetic anhydride (102 mg, 1.00 mmol). Next, 2.5 mL of freshly distilled CH_2Cl_2 and 0.21 mL (1.50 mmol) of NEt_3 were introduced into the round-bottom flask. Finally, DMAP (12 mg, 0.10 mmol) was added to the solution, and the latter was stirred at room temperature (~20 °C) for 45 min. After aqueous workup and concentration, the reaction afforded 233 mg of a crude mixture. The latter was purified by chromatography with 11 g of silica gel (pentane/Et_2O gradient, 80:20 to 40:60). After purification, the reaction afforded pure the less polar *syn* diastereomer **6d** (88 mg, 27 mmol, 55%, yellow solid), but around 2% of the *anti* diastereomer was detected by ^{1}H NMR at δ 5.85, 1.92. **6d**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (d, J = 2.2 Hz, 1H), 8.48 (dd, J = 4.9, 1.7 Hz, 1H), 7.59 (dt, J = 7.9, 2.0 Hz, 1H), 7.21 (dd, J = 7.9, 4.8, 1H), 6.01 (d, J = 8.7 Hz, 1H), 5.85 (d, J = 10.3 Hz, 1H), 3.50 (dq, J = 8.6, 7.0 Hz, 1H), 2.06 (s, 3H), 1.08 (d, J = 7.0 Hz, 3H), 0.86−0.74 (m, 9H), 0.64−0.53 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 247.8, 169.7, 149.1, 148.6, 135.6, 135.2, 123.1, 73.6, 56.0, 20.9, 11.7, 7.0, 2.1. HRMS (ESI +ve) Exact mass calculated for $C_{17}H_{27}NO_3NaSi$ $[M + Na]^+$: 344.16579, found: 344.1658.

*(±)-syn-3-Acetoxy-2-methyl-3-(2,5-dimethoxyphenyl)-1-(triethylsilyl)propan-1-one (**6e**).* Following the general procedure mentioned above, a 5 mL round-bottom flask was charged with **4e**/**5e** (0.169 g, 0.5 mmol) and acetic anhydride (128 mg, 1.25 mmol). Next, 2.5 mL of freshly distilled CH_2Cl_2 and NEt_3 (0.2 mL, 1.5 mmol) were introduced into the round-bottom flask. Finally, DMAP (11 mg, 0.09 mmol) was added to the solution, and the latter was stirred for 1 h. The reaction was monitored by TLC using an 80:20 pentane/Et_2O mixture. After aqueous workup and concentration, the reaction afforded 219 mg of a crude mixture. The latter was purified by silica gel chromatography with 14 g of silica gel (pentane/Et_2O gradient, 96:4 to 90:10). After purification, 113 mg (0.29 mmol, 59%, colorless oil) of the compound **6e** was obtained as pure *syn* product. **6e**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.42 (d, J = 2.4, 2H), 6.33 (t, J = 2.3 Hz, 1H), 5.96 (d, J = 7.8 Hz, 1H), 3.76 (s, 6H), 3.43 (dq, J = 7.8, 7.0 Hz, 1H), 2.06 (s, 3H), 1.02 (d, J = 7.0 Hz, 3H), 0.88−0.80 (m, 9H), 0.69−0.50 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 248.1, 160.8, 142.2, 105.2, 99.8, 75.0, 56.1, 55.4, 21.1, 11.3, 7.12, 7.10, 2.2. HRMS (ESI +ve) Exact mass calculated for $C_{20}H_{32}O_5NaSi$ $[M + Na]^+$: 403.19167, found: 403.1916.

*(±)-syn-3-Benzoyloxy-2-methyl-3-phenyl-1-(triethylsilyl)propan-1-one (**8a**).* Following the general procedure mentioned above, a 25 mL round-bottom flask was charged with **4a**/**5a** (279 mg, 1.00 mmol) and benzoic anhydride (306 mg, 1.35 mmol). Next, 5 mL of freshly distilled CH_2Cl_2 and NEt_3 (0.200 mL, 1.44 mmol) were introduced into the round-bottom flask. Finally, DMAP (38 mg, 0.311 mmol) was added to the solution, and the latter was stirred for 15 h at 30 °C. The reaction was monitored by TLC using a 95:5 pentane/AcOEt mixture. After aqueous workup and concentration, the reaction afforded 430 mg of a crude mixture. The latter was purified by silica gel chromatography with 23 g of silica gel (pentane/Et_2O gradient, 99.25:0.75 to 98:2). After purification, 278 mg (0.727 mmol, 73%,

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white solid, mp: 46−48 °C) of the compound **8a** was obtained as pure *syn* product and 57 mg (0.149 mmol, 15%) of the compound **9a** as a pure *anti* product (*vide infra*). **8a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08−8.03 (m, 2H), 7.59−7.52 (m, 1H), 7.47−7.40 (m, 2H), 7.39−7.34 (m, 2H), 7.33−7.19 (m, 3H), 6.28 (d, J = 8.1 Hz, 1H), 3.64 (dq, J = 8.1, 7.0 Hz, 1H), 1.14 (d, J = 6.9 Hz, 3H), 0.85−0.78 (m, 9H), 0.65−0.53 (m, 6H).^{13}C NMR (75 MHz, $CDCl_3$) δ 248.2, 165.5, 140.0, 133.1, 130.5, 129.8, 128.5, 128.0, 127.1, 75.9, 56.6, 11.6, 7.2, 2.2. HRMS (ESI +ve) Exact mass calculated for $C_{23}H_{30}O_3NaSi$ $[M + Na]^+$: 405.18619, found: 405.1860.

*(±)-anti-3-Benzoyloxy-2-methyl-3-phenyl-1-(triethylsilyl)propan-1-one (**9a**).* The product **9a** appeared as a colorless, highly viscous oil. **9a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99−7.91 (m, 2H), 7.55−7.46 (m, 1H), 7.45−7.27 (m, 7H), 6.16 (d, J = 10.1 Hz, 1H), 3.64 (dq, J = 10.1, 7.2 Hz, 1H), 1.00−0.93 (m, 9H), 0.83−0.73 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 248.0, 165.1, 139.0, 132. 9, 130.4, 129.6, 128.6, 128.3, 128.2, 127.4, 54.88, 12.2, 7.3, 2.4. HRMS (ESI +ve) Exact mass calculated for $C_{23}H_{30}O_3NaSi$ $[M + Na]^+$: 405.18619, found: 405.1858.

General Procedure for the Silylation of *β*-Hydroxyacylsilanes. A round-bottom flask was charged with the 3-hydroxy-2-methyl-1-trialkylsilylpropan-1-one, 2,6-lutidine, and a magnetic stir bar. The round-bottom flask was sealed with a septum and flushed with nitrogen. Freshly distilled CH_2Cl_2 was added through the septum with a syringe, the solution was cooled to 0 °C, and then TBSOTf was added through the septum with a syringe. The nitrogen flush was then stopped, and the reaction was stirred at 0 °C. The solution was quenched with a saturated solution of ammonium chloride, introduced in a separatory funnel, and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic phases were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography.

*3-(tert-Butyldimethylsilyl)oxy-2-methyl-3-phenyl-1-(triethylsilyl)-propan-1-one (**10a**−**11a**).* Following the general procedure mentioned above, a 5 mL round-bottom flask was charged with **4a**/**5a** (37 mg, 0.133 mmol), 2,6-lutidine (29 mg, 0.266 mmol), and a magnetic stir bar. The round-bottom flask was then sealed with a septum, and 1.5 mL of freshly distilled CH_2Cl_2 was added under nitrogen flush. The solution was cooled to 0 °C, and TBSOTf (0.050 mL, 0.217 mmol) was added with a syringe. The nitrogen flush was then stopped, and the reaction was stirred at 0 °C for 2 h, and monitored by TLC with a 98:2 pentane/Et_2O mixture. After aqueous workup and concentration, the reaction afforded 55 mg of a crude mixture. The latter was purified by chromatography using 3 g of silica gel (pentane Et_2O gradient, 99.5:0.5 to 98:2), affording **10a**/**11a** (49 mg, 0.125 mmol, 94%, white solid) as a 83:17 mixture of diastereomers. **10a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31−7.12 (m, 5H), 4.75 (d, J = 8.9 Hz, 1H), 3.37 (dq, J = 9.0, 7.0 Hz, 1H), 1.08 (d, J = 6.9 Hz, 3H), 0.84 (s, 9H), 0.77−0.71 (m, 9H), 0.53−0.33 (m, 6H), 0.00 (s, 3H), −0.26 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 252.4, 144.6, 128.0, 127.31, 127.26, 75.3, 59.7, 25.6, 18.3, 13.3, 7.1, 1.8, −4.4, −4.8. HRMS (ESI +ve) Exact mass calculated for $C_{22}H_{40}O_2NaSi_2$ $[M + Na]^+$: 415.24646, found: 415.2466. The characteristic peaks for *anti* isomer **11a** were observed at 4.84 (d, J = 9.4 Hz, 1H), 1.06−0.99 (m, 9H), −0.09 (s, 3H), −0.29 (s, 3H) for ^{1}H NMR and 250.9, 143.7, 128.1, 127.5, 76.4, 58.0, 18.1, 12.7, 7.5, 2.3, −4.6, −4.8 for ^{13}C NMR.

*(±)-3-(Methoxymethyl)oxy-2-methyl-3-phenyl-1-(triethylsilyl)-propan-1-one (**12a**−**13a**).* A 5 mL round-bottom flask was charged with **4a**/**5a** (100 mg, 0.359 mmol) and a magnetic stir bar. The flask was sealed with a septum, and then 1.8 mL of freshly distilled CH_2Cl_2 was introduced with a syringe under nitrogen flush. Next, DIPEA (0.190 mL, 1.08 mmol) and MOMCl (0.080 mL, 1.06 mmol) were introduced in the reaction mixture. The solution was stirred at room temperature (∼20 °C) for 20 h and monitored by TLC (pentane/AcOEt mixture, 95:5). The solution was treated by a saturated NH_4Cl solution and extracted twice with CH_2Cl_2. The combined organic fractions were dried with $MgSO_4$, filtered, and concentrated under reduced pressure, affording 123 mg of a crude mixture. The latter was purified by column chromatography using 7 g of silica gel (pentane/AcOEt gradient, 99:1 to 97:3), affording **12a**/**13a** (85 mg, 0.264 mmol, 73%, colorless oil) as an 83:17 mixture of diastereoisomers. **12a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.17 (m, 5H), 4.76 (d, J = 8.9 Hz, 1H), 4.47 (s, 2H), 3.47 (dq, J = 9.0, 6.9 Hz, 1H), 3.32 (s, 3H), 1.14 (d, J = 6.9 Hz, 3H), 0.79−0.73 (m, 9H), 0.54−0.44 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 250.4, 140.9, 128.9, 129.0, 128.0, 94.1, 77.7, 57.4, 55.8, 12.6, 7.1, 1.9. HRMS (ESI +ve) Exact mass calculated for $C_{18}H_{30}O_3NaSi$ $[M + Na]^+$: 345.18619, found: 345.1864. The characteristic peaks for *anti* isomer **13a** were observed at 4.71 (d, 1H), 4.33 (d, J = 0.8 Hz, 2H), 3.18 (s, 3H), 1.06−0.99 (m, 9H) for ^{1}H NMR and at 251.6, 139.8, 128.4, 127.9, 93.8, 79.9, 54.8, 12.3, 7.3, 2.2 for ^{13}C NMR.

*(±)-syn-3-Acetoxy-2-methyl-3-phenyl-1-(triisopropylsilyl)propan-1-one (**14f**).* Following the general procedure for acetylation of *β*-hydroxyacylsilanes, a 10 mL round-bottom flask was charged with **4f**/**5f** (97:3 mixture, 111 mg, 0.346 mmol), acetic anhydride (80 mg, 0.784 mmol), and a magnetic stir bar. The round-bottom flask was then sealed with a septum, and 3.5 mL of freshly distilled CH_2Cl_2 and NEt_3 (0.150 mL, 1.08 mmol) were added under nitrogen flush. Finally, DMAP (9 mg, 0.074 mmol) was added to the solution, and the latter was stirred for 18 h at room temperature (∼20 °C) and monitored by TLC using a pentane/AcOEt 95:5 mixture. After aqueous workup and concentration, the reaction afforded 142 mg of a crude mixture. The latter was purified by column chromatography with 8 g of silica gel (pentane/AcOEt 99:1). After purification, 79 mg (0.218 mmol, 63%, colorless oil) of the compound **14f** was obtained as pure *syn* product. The minor *anti* isomer **15f** was not isolated. **14f**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33−7.16 (m, 5H), 6.03 (d, J = 8.6 Hz, 1H), 3.56 (dq, J = 8.6, 7.0 Hz, 1H), 2.05 (s, 3H), 1.10 (m, 6H), 0.94 (d, J = 7.0 Hz, 18H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 248.6, 169.9, 140.0, 128.3, 127.9, 127.5, 75.5, 56.9, 21.2, 18.5, 18.5, 12.1, 10.9. HRMS (ESI +ve) Exact mass calculated for $C_{21}H_{34}O_3NaSi$ $[M + Na]^+$: 385.21749, found: 385.2176.

General Procedure for the Photolysis/Hydrolysis of Protected *β*-Hydroxyacylsilanes. The protected *β*-hydroxyacylsilane was introduced in a Pyrex round-bottom flask or a Schlenk tube equipped with a magnetic stir bar. Distilled water was added so that the substrate concentration was equal to 0.05 M respective to water. Then, 1−4 equiv in volume of acetone were added until obtaining a clear solution, and the solution was degassed by the freeze pump thaw procedure. Degassing showed to be useful as residual oxygen may cause overoxidation of the aldehyde or the acylsilane. After degassing, the round-bottom flask or Schlenk tube was covered with a septum and cooled to −15 °C in an ethanol bath using a chiller unless otherwise noted. The solution was stirred and enlightened at 365 nm using a routine UV lamp kept as close as possible from the round-bottom flask (i.e., <15 cm; see pictures in the Supporting Information). The reaction was monitored by TLC. In addition, the reaction progress could be qualitatively evaluated by the disappearance of the solution luminescence. After completion, the solution was poured in a separatory funnel, and then brine and Et_2O were added until separation of the organic and aqueous layer. The latter was extracted three times by Et_2O, and then the combined organic phases were dried with $MgSO_4$ and concentrated in vacuo using a rotary evaporator and then a high vacuum pump (2−3 h) to remove the trialkylsilanol byproduct. **Note**: the *α*-alkoxyaldehydes obtained by this procedure from the corresponding acylsilanes were not purified and were used directly for the next step.

*(±)-syn-3-Acetoxy-2-methyl-3-phenylpropanal (**17a**).* Following the general procedure for the photolysis/hydrolysis of protected *β*-hydroxyacylsilanes, a 500 mL round-bottom flask was charged with **6a** (499 mg, 1.56 mmol), H_2O (32 mL) and acetone (64 mL). The solution was degassed and cooled to −15 °C, and then enlightened at 365 nm under stirring for 24 h at −15 °C. The reaction was monitored by TLC using a 90:10 pentane/AcOEt mixture. After aqueous workup and concentration by reduced pressure, the reaction afforded **17a** (305 mg, 1.48 mmol, 95%, colorless oil). The product was used in the next step without further purification. **17a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (d, J = 1.2 Hz, 1H), 7.38−7.27 (m, 5H), 6.19 (d, J = 5.2 Hz, 1H), 2.85 (qdd, J = 7.0, 5.3, 1.2 Hz, 1H), 2.11 (s, 3H), 1.11 (d, J = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.6, 169.8, 138.0, 128.6, 128.2,

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126.3, 74.3, 52.0, 20.9, 8.7. HRMS (ESI +ve) Exact mass calculated for $C_{12}H_{14}O_3Na$ $[M + Na]^+$: 229.08406, found: 229.0841.

*Additionally, Compound **17a** Was Obtained by the Same Procedure Starting from **14f**.* A 25 mL round-bottom flask was charged with **14f** (77 mg, 0.212 mmol), H_2O (4 mL) and acetone (16 mL). The solution was degassed and cooled to −15 °C, and then enlightened at 365 nm under stirring for 6 h at −15 °C. The reaction was monitored by TLC using a 90:10 pentane/AcOEt mixture. After aqueous workup and concentration by reduced pressure, the reaction afforded **17a** (42 mg, 0.203 mmol, 96%) identical by NMR to the compound described above.

*(±)-syn-3-Acetoxy-2-methyl-3-(4-fluorophenyl)propanal (**17b**).* Following the general procedure for the photolysis/hydrolysis of protected β-hydroxyacylsilanes, a 25 mL round-bottom flask was charged with **6b** (85 mg, 0.250 mmol), H_2O (5 mL) and acetone (10 mL). The solution was degassed and cooled to −15 °C, and then enlightened at 365 nm under stirring for 9 h at −15 °C. The reaction was monitored by TLC using a 90:10 pentane/AcOEt mixture. After aqueous workup and concentration by reduced pressure, the reaction afforded **17b** (55 mg, 0.245 mmol, 98%, colorless oil). **17b**: ^{1}H NMR (300 MHz, C_6D_6) δ 9.32 (d, *J* = 0.9 Hz, 1H), 6.79 (m, 2H), 6.71 (m, 2H), 6.05 (d, *J* = 5.1 Hz, 1H), 2.19−2.08 (m, 1H), 1.54 (s, 3H), 0.79 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, C_6D_6) δ 200.2, 169.1, 164.4, 161.1, 134.65, 134.61, 128.57, 128.46, 115.73, 115.45, 73.5, 52.0, 20.3, 8.5. HRMS (ESI +ve) Exact mass calculated for $C_{12}H_{13}FO_3Na$ $[M + Na]^+$: 247.07464, found: 247.0745.

*(±)-syn-3-Acetoxy-2-methyl-3-cyclohexylpropanal (**17c**).* Following the general procedure for the photolysis/hydrolysis of protected β-hydroxyacylsilanes, a 50 mL round-bottom flask was charged with **6c** (163 mg, 0.500 mmol), H_2O (10 mL), and acetone (30 mL). The solution was degassed and cooled to −15 °C, and then enlightened at 365 nm under stirring for 9 h at −15 °C. The reaction was monitored by TLC using a 90:10 pentane/Et_2O mixture. After aqueous workup and concentration by reduced pressure, the reaction afforded **17c** (105 mg, 0.495 mmol, 99%, colorless oil). **17c**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.66 (d, *J* = 0.8 Hz, 1H), 5.19 (dd, *J* = 8.3, 3.5 Hz, 1H), 2.68 (qd, *J* = 6.9, 3.4 Hz, 1H), 2.02 (s, 3H), 1.95−1.45 (m, 4H), 1.35−0.50 (m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.5, 170.7, 75.5, 48.2, 39.1, 29.3, 28.8, 26.1, 25.9, 25.7, 20.7, 7.3. HRMS (ESI +ve) Exact mass calculated for $C_{12}H_{20}O_3Na$ $[M + Na]^+$: 235.13101, found: 235.1307.

*(±)-syn-3-Acetoxy-2-methyl-3-(3-pyridyl)propanal (**17d**).* Following the general procedure for the photolysis/hydrolysis of protected β-hydroxyacylsilanes, a 25 mL round-bottom flask was charged with **6d** (80 mg, 0.250 mmol), H_2O (5 mL), and acetone (5 mL). The solution was degassed and cooled to −15 °C, and then enlightened at 365 nm under stirring for 9 h at −15 °C. The reaction was monitored by TLC using Et_2O. After aqueous workup and concentration by reduced pressure, the reaction afforded **17d** (49 mg, 0.236 mmol, 95%, pale yellow oil). Partial elimination (∼5%) into the conjugated enal could be observed by ^{1}H NMR, probably due to the presence of a slightly basic functionality, e.g., the pyridyl moiety. In addition, fast degradation has been observed in $CDCl_3$. **17d**: ^{1}H NMR (300 MHz, C_6D_6) δ 9.25 (d, *J* = 0.7 Hz, 1H), 8.57 (d, *J* = 2.3 Hz, 1H), 8.44−8.39 (m, 1H), 7.08−7.00 (m, 1H), 6.64 (dd, *J* = 7.8, 4.8 Hz, 1H), 6.08 (d, *J* = 4.8 Hz, 1H), 2.07 (qdd, *J* = 7.0, 4.8, 0.8 Hz, 1H), 1.50 (s, 3H), 0.73 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, C_6D_6) δ 199.7, 169.0, 149.7, 148.5, 134.3, 133.9, 123.2, 72.1, 51.7, 20.1, 8.2, 7.0, 6.4. HRMS (ESI +ve) Exact mass calculated for $C_{11}H_{14}NO_3$ $[M + H]^+$: 208.09737, found: 208.0973.

*(±)-syn-3-Acetoxy-2-methyl-3-(3,5-dimethoxyphenyl)propanal (**17e**).* Following the general procedure for the photolysis/hydrolysis of protected β-hydroxyacylsilanes, a 25 mL round-bottom flask was charged with **6d** (95 mg, 0.250 mmol), H_2O (5 mL), and acetone (15 mL). The solution was degassed and cooled to −15 °C, and then enlightened at 365 nm and stirred for 7 h at −15 °C. The reaction was monitored by TLC using a 85:15 pentane/AcOEt mixture. After aqueous workup and concentration by reduced pressure, the reaction afforded **17e** (67 mg, 0.250 mmol, quantitative, colorless oil). **17e**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.71 (d, *J* = 1.1 Hz, 1H), 6.43 (d, *J* = 2.3 Hz, 2H), 6.38 (d, *J* = 2.3 Hz, 1H), 6.11 (d, *J* = 5.0 Hz, 1H), 3.78 (s, 6H), 2.81 (qdd, *J* = 7.0, 5.0, 1.1 Hz, 1H), 1.11 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.6, 169.8, 161.1, 140.5, 104.6, 99.8, 74.3, 55.4, 51.9, 21.0, 8.8. HRMS (ESI +ve) Exact mass calculated for $C_{14}H_{18}O_5Na$ $[M + Na]^+$: 289.10519, found: 289.1048.

*(±)-syn-3-Benzoyloxy-2-methyl-3-phenyl-propan-1-al (**18a**).* Following the general procedure for the photolysis/hydrolysis of protected β-hydroxyacylsilanes, a 50 mL round-bottom flask was charged with **8a** (96 mg, 0.250 mmol), H_2O (5 mL), and acetone (20 mL). The solution was degassed and cooled to −15 °C, and then enlightened at 365 nm under stirring for 14 h at −15 °C. The reaction was monitored by TLC using a 90:10 pentane/AcOEt mixture. After aqueous workup and concentration by reduced pressure, the reaction afforded **18a** (67 mg, 0.250 mmol, quantitative, colorless oil). **18a**: ^{1}H NMR (300 MHz, C_6D_6) δ 9.44 (d, *J* = 0.9 Hz, 1H), 8.12−8.03 (m, 2H), 7.18−6.95 (m, 8H), 6.42 (d, *J* = 4.7 Hz, 1H), 2.34 (qdd, *J* = 7.0, 4.7, 0.9 Hz, 1H), 0.93 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, C_6D_6) δ 200.3, 165.2, 138.8, 133.2, 130.5, 130.0, 128.79, 128.71, 128.2, 126.6, 75.0, 52.3, 8.6. HRMS (ESI +ve) Exact mass calculated for $C_{17}H_{16}O_3Na$ $[M + Na]^+$: 291.09971, found: 291.0997.

*(±)-anti-3-Benzoyloxy-2-methyl-3-phenyl-propan-1-al (**19a**).* Following the general procedure for the photolysis/hydrolysis of protected β-hydroxyacylsilanes, a 10 mL round-bottom flask was charged with **9a** (28 mg, 0.073 mmol), H_2O (1.5 mL), and acetone (4.5 mL). The solution was degassed and cooled to −15 °C, and then enlightened at 365 nm under stirring for 14 h at −15 °C. The reaction was monitored by TLC using a 90:10 pentane/AcOEt mixture. After aqueous workup and concentration by reduced pressure, the reaction afforded **19a** (19 mg, 0.071 mmol, 97%, colorless oil). **19a**: ^{1}H NMR (300 MHz, C_6D_6) δ 9.45 (d, *J* = 2.5 Hz, 1H), 8.11−8.04 (m, 2H), 7.09−6.94 (m, 8H), 6.13 (d, *J* = 8.2 Hz, 1H), 2.64 (dqd, *J* = 8.1, 7.1, 2.5 Hz, 1H), 0.64 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, C_6D_6) δ 200.7, 165.2, 138.4, 133.2, 130.4, 130.0, 128.8, 128.7, 128.5, 127.2, 76.5, 51.7, 10.7. HRMS (ESI +ve) Exact mass calculated for $C_{17}H_{16}O_3Na$ $[M + Na]^+$: 291.09971, found: 291.0996.

*(±)-3-(tert-Butyldimethylsilyl)oxy-2-methyl-3-phenyl-propan-1-al (**20a/21a**).* Following the general procedure for the photolysis/hydrolysis of protected β-hydroxyacylsilanes, a 25 mL round-bottom flask was charged with **10a**/**11a** (49 mg, 0.125 mmol), H_2O (2.5 mL), and acetone (10 mL). The solution was degassed and cooled to −15 °C, and then enlightened at 365 nm under stirring for 15 h at −15 °C. The reaction was monitored by TLC using a 90:10 pentane/Et_2O mixture. After aqueous workup and concentration by reduced pressure, the reaction afforded **20a**/**21a** (31 mg, 0.111 mmol, 89%, colorless oil). **20a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.77 (d, *J* = 1.3 Hz, 1H), 7.36−7.22 (m, 5H), 5.16 (d, *J* = 4.2 Hz, 1H), 2.59 (qdd, *J* = 7.0, 4.2, 1.3 Hz, 1H), 1.04 (d, *J* = 7.0 Hz, 3H), 0.89 (s, 9H), 0.03 (s, 3H), −0.18 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.3, 142.5, 128.3, 127.6, 126.4, 74.5, 54.9, 25.9, 18.3, 8.2, −4.4, −5.1. HRMS (ESI +ve) Exact mass calculated for $C_{16}H_{26}O_2NaSi$ $[M + Na]^+$: 301.15998, found: 301.1602. The characteristic peaks for *anti* isomer **21a** were observed at 9.81 (d, *J* = 2.7 Hz, 1H), 4.77 (d, *J* = 7.6 Hz, 1H), 2.75−2.64 (m, 1H), 0.85 (s, 9H), 0.01 (s, 3H), −0.25 (s, 3H) for ^{1}H NMR and at 204.5, 142.4, 128.4, 128.0, 126.9, 77.0, 54.8, 25.9, 18.2, 11.2 for ^{13}C NMR.

*(±)-3-(Methoxymethyl)oxy-2-methyl-3-phenyl-propan-1-al (**22a/23a**).* Following the general procedure for the photolysis/hydrolysis of protected β-hydroxyacylsilanes, a 25 mL round-bottom flask was charged with **12a**/**13a** (83 mg, 0.257 mmol), H_2O (5 mL), and acetone (10 mL). The solution was degassed and cooled to −15 °C, and then enlightened at 365 nm and stirred for 5.5 h at −15 °C. The reaction was monitored by TLC using a 90:10 pentane/AcOEt mixture. After aqueous workup and concentration by reduced pressure, the reaction afforded **22a**/**23a** (50 mg, 0.240 mmol, 93%, colorless oil). Partial oxidation of the aldehyde was detected by ^{1}H NMR (∼5−6%) and mass spectroscopy. **22a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.77 (d, *J* = 1.1 Hz, 1H), 7.40−7.27 (m, 5H), 5.11 (d, *J* = 4.9 Hz, 1H), 4.59−4.52 (m, 2H), 3.35 (s, 3H), 2.70 (qdd, *J* = 7.0, 5.0, 1.2 Hz, 1H), 1.10 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.4, 139.0, 128.6, 128.0, 127.1, 94.4, 76.8, 56.0, 53.0, 8.5. HRMS (ESI +ve) Exact

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mass calculated for $C_{12}H_{16}O_3Na$ [M + Na]$^+$: 231.09971, found: 231.0998. The characteristic peaks for *anti* isomer **23a** were observed at 9.84 (d, J = 3.1 Hz, 1H), 4.76 (d, J = 9.1 Hz, 1H), 4.50−4.44 (m, 2H), 2.79 (m, 1H), 0.87 (d, J = 7.1 Hz, 3H) for 1H NMR and 203.8, 138.5, 128.7, 128.5, 127.8, 93.9, 78.7, 52.5, 11.2 for ^{13}C NMR.

*Additionally, Compound **22a** Was Obtained by a Complementary Procedure Starting from **16g**.* A 10 mL round-bottom flask was charged with **16g** (200 mg, 0.448 mmol) and a magnetic stir bar. Then, 6 mL of absolute ethanol and 20 mg of 10% Pd on activated charcoal were introduced, and the solution was stirred under 1 atm of hydrogen gas for 1 h. The suspension was then filtered through Celite to afford 208 mg of a crude mixture. The latter was purified by column chromatography with 8 g of silica gel (pentane/AcOEt gradient, 95:5 to 80:20). Compound **22a** was obtained as a pure *syn* isomer (85 mg, 0.408 mmol, 91%) with the same NMR data as above.

*(±)-5-Acetoxy-3-hydroxy-2,4-dimethyl-5-phenyl-1-(triethylsilyl)-pentan-1-one (**24**).* Following the general procedure for the synthesis of β-hydroxyacylsilanes, a 5 mL round-bottom flask was charged with 45 mg (0.244 mmol, 60 mol %) of $MgBr_2$ and 0.081 mmol (20 mol %) of freshly prepared NiHCl(dppe) in 1 mL of THF. The solution was cooled to −35 °C, and then **17a** (84 mg, 0.407 mmol) and **1** (74 mg, 0.428 mmol) were introduced into the solution under argon flush. The solution was stirred at −35 °C for 96 h, and the reaction was monitored by TLC using a 90:10 pentane/AcOEt mixture. The reaction was quenched by a saturated NH_4Cl solution, the mixture was diluted with Et_2O and filtered through a small pad of Celite, and the phases were separated. The separated aqueous phase was extracted with Et_2O, and the combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure, affording 142 mg of a crude mixture. The latter was purified by chromatography using 8 g of silica gel (pentane/AcOEt gradient, 98:2 to 80:20), affording 79 mg (0.209 mmol, 51%) of adduct as a 86:14 mixture of diastereoisomers. The major diastereomer **24** could be obtained by fractional crystallization as a white solid, mp: 62−64 °C. **24**: ^{1}H NMR (300 MHz, C_6D_6) δ 7.24−7.18 (m, 2H), 7.18−7.10 (m, 2H), 7.09−7.02 (m, 1H), 6.73 (d, J = 2.1 Hz, 1H), 4.12 (ddd, J = 9.9, 3.1, 2.0 Hz, 1H), 3.51 (d, J = 3.1 Hz, 1H), 2.81 (qd, J = 7.1, 2.0 Hz, 1H), 2.00−1.88 (m, 1H), 1.70 (s, 3H), 1.01 (d, J = 7.2 Hz, 3H), 0.94−0.86 (m, 9H), 0.73 (d, J = 7.0 Hz, 3H), 0.68−0.58 (m, 6H). ^{13}C NMR (75 MHz, C_6D_6) δ 250.1, 169.9, 141.1, 128.5, 127.3, 126.1, 74.3, 69.9, 52.5, 43.3, 20.5, 9.3, 7.5, 6.3, 3.0. HRMS (ESI +ve) Exact mass calculated for $C_{21}H_{34}O_4NaSi$ [M + Na]$^+$: 401.21241, found: 401.2126.

*(±)-3,5-Diacetoxy-2,4-dimethyl-5-phenyl-1-(triethylsilyl)pentan-1-one (**25**).* Following the general procedure mentioned above, a 10 mL round-bottom flask was charged with **24** (as the mixture of diastereoisomers, 134 mg, 0.354 mmol) and acetic anhydride (81 mg, 0.793 mmol). Next, 3.5 mL of freshly distilled CH_2Cl_2 and NEt_3 (0.150 mL, 1.08 mmol) were introduced into the round-bottom flask. Finally, DMAP (12 mg, 0.10 mmol) was added to the solution, and the latter was stirred at room temperature (~20 °C) for 2 h. The reaction progress was monitored by TLC (pentane/AcOEt 95:5). After aqueous workup and concentration, the reaction afforded 142 mg of a crude mixture. The latter was purified by chromatography with 8 g of silica gel (pentane/AcOEt gradient, 98:2 to 93:7) to afford **25** (97 mg, 0.231 mmol, 65%, pale yellow oil). **25**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.29 (m, 2H), 7.30−7.21 (m, 1H), 7.19 (ddd, J = 8.3, 1.4, 0.7 Hz, 2H), 5.90 (d, J = 2.7 Hz, 1H), 5.36 (dd, J = 9.7, 2.9 Hz, 1H), 3.16 (qd, J = 6.9, 2.9 Hz, 1H), 2.17−2.08 (m, 4H), 1.99 (s, 3H), 1.02−0.97 (m, 9H), 0.95 (d, J = 6.9 Hz, 3H), 0.87 (d, J = 7.0 Hz, 3H), 0.79 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 246.4, 170.3, 170.0, 139.6, 128.4, 127.4, 125.5, 73.3, 70.6, 52.0, 40.9, 20.9, 20.8, 10.2, 7.4, 7.1, 2.6. HRMS (ESI +ve) Exact mass calculated for $C_{23}H_{36}O_5NaSi$ [M + Na]$^+$: 443.22297, found: 443.2235.

*(±)-3,5-Diacetoxy-2,4-dimethyl-5-phenyl-pentanal (**26**).* Following the general procedure for the photolysis/hydrolysis of protected β-hydroxyacylsilanes, a 50 mL round-bottom flask was charged with **25** (97 mg, 0.231 mmol), H_2O (5 mL), acetone (10 mL), and a magnetic stir bar. The solution was degassed and cooled to −15 °C, and then enlightened at 365 nm and stirred for 7 h at −15 °C. The reaction was monitored by TLC using a 90:10 pentane/AcOEt mixture. After aqueous workup and concentration by reduced pressure, the reaction afforded **26** (63 mg, 0.206 mmol, 89%, colorless solid, which decomposed under heating). **26**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.71 (d, J = 0.5 Hz, 1H), 7.38−7.19 (m, 5H), 5.99 (d, J = 2.7 Hz, 1H), 5.47 (dd, J = 10.2, 2.4 Hz, 1H), 2.69 (qd, J = 6.9, 2.4 Hz, 1H), 2.26−2.17 (m, 1H), 2.15 (s, 3H), 2.04 (s, 3H), 1.10 (d, J = 6.9 Hz, 3H), 0.87 (d, J = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.9, 170.6, 170.2, 139.3, 128.4, 127.5, 125.6, 73.0, 71.7, 48.7, 40.5, 21.0, 20.8, 9.9, 6.2. HRMS (ESI +ve) Exact mass calculated for $C_{17}H_{22}O_5Na$ [M + Na]$^+$: 329.13649, found: 329.1366.

*(±)-3-Hydroxy-5-(methoxymethyl)oxy-2,4-dimethyl-5-phenyl-1-(tert-butyldiphenyl-silylpentan-1-one (**27**).* Following the general procedure for the synthesis of β-hydroxyacylsilanes, a 5 mL round-bottom flask was charged with $MgBr_2$ (42 mg, 0.230 mmol, 60 mol %) and a freshly prepared solution of NiHCl(BINAP) (0.04 mmol, 10 mol %) in 0.8 mL of THF. The solution was cooled at −35 °C, and then aldehyde **22a** (80 mg, 0.384 mmol) and **3** (145 mg, 0.49 mmol) were added into the solution. The solution was stirred at −35 °C for 72 h, and the reaction was monitored by TLC with a 90:10 pentane/AcOEt mixture. The reaction was quenched by a saturated NH_4Cl solution, the mixture was diluted with Et_2O and filtered through a small pad of Celite, and the phases were separated. The separated aqueous phase was extracted with Et_2O, and the combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure, affording 235 mg of a crude mixture. The latter was purified by chromatography with 11 g of silica gel (pentane/AcOEt gradient, 95:5 to 80:20). After purification, 143 mg (0.284 mmol, 74%) of adducts was obtained as a 73:27 mixture of diastereomers. A single crystal of the major diastereoisomer **27** could be obtained by fractional crystallization. The product **27** appeared as a colorless solid, which decomposed under heating. **27**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65−7.59 (m, 2H), 7.57−7.52 (m, 2H), 7.47−7.19 (m, 9H), 7.11 (dd, J = 6.7, 3.0 Hz, 2H), 4.93 (d, J = 2.6 Hz, 1H), 4.53 (d, J = 6.4 Hz, 1H), 4.46 (d, J = 6.4 Hz, 1H), 3.86 (d, J = 9.5 Hz, 1H), 3.26 (s, 3H), 3.00−2.91 (m, 1H), 1.67 (m, 1H), 1.13 (s, 9H), 0.83 (d, J = 6.9 Hz, 3H), 0.14 (d, J = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 248.8, 140.1, 136.5, 136.4, 134.9, 132.2, 131.8, 129.99, 129.94, 128.12, 128.08, 127.9, 127.2, 95.3, 78.8, 68.9, 56.0, 52.7, 42.0, 27.9, 19.0, 9.7, 6.2. HRMS (ESI +ve) Exact mass calculated for $C_{31}H_{40}O_4NaSi$ [M + Na]$^+$: 527.2594, found: 527.2596.

*(±)-syn-5-Benzyloxy-3-hydroxy-2-methyl-1-(triethylsilyl)pentan-1-one (**29**).* Following the general procedure for the synthesis of β-hydroxyacylsilanes, a round-bottom flask was charged with $MgBr_2$ (222 mg, 1.20 mmol, 60 mol %) and a freshly prepared solution of NiHCl(dppe) (0.4 mmol, 20 mol %) in 4 mL of THF. The solution was cooled at −35 °C, and then 3-benzyloxypropionaldehyde **28** (312 mg, 1.9 mmol) and **1** (338 mg, 1.96 mmol) were added into the solution. The solution was stirred at −35 °C for 40 h, and the reaction was monitored by TLC with a 90:10 pentane/AcOEt mixture. The reaction was quenched by a saturated NH_4Cl solution, the mixture was diluted with Et_2O and filtered through a small pad of Celite, and the phases were separated. The separated aqueous phase was extracted with Et_2O, and the combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure, affording 705 mg of a crude mixture. The latter was purified by chromatography with 39 g of silica gel (pentane/AcOEt gradient, 97:3 to 85:15). After purification, the adducts were obtained as an 84:16 mixture of diastereoisomers (494 mg, 1.47 mmol, 77%, pale yellow oil). **29**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 4.51 (s, 2H), 4.12 (dtd, J = 9.3, 3.6, 2.2 Hz, 1H), 3.72−3.57 (m, 2H), 3.16 (d, J = 2.2 Hz, 1H), 2.94 (qd, J = 7.2, 3.9 Hz, 1H), 1.83−1.68 (m, 1H), 1.68−1.60 (m, 1H), 1.03 (d, J = 7.2 Hz, 3H), 1.00−0.92 (m, 9H), 0.79−0.69 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 252.9, 138.1, 128.2, 127.5, 127.5, 73.1, 68.7, 68.2, 55.1, 34.2, 8.3, 7.1, 2.3. HRMS (ESI +ve) Exact mass calculated for $C_{19}H_{32}O_3NaSi$ [M + Na]$^+$: 359.20184, found: 359.2016. The characteristic peaks for the minor *anti* isomer were observed at 4.01−3.92 (m, 1H), 3.14 (d, J = 4.8 Hz, 1H), 3.05 (quint, J = 7.2 Hz, 1H) for 1H NMR and at 253.4, 138.0, 127.5, 73.1, 71.7, 68.3, 55.5, 11.1, 2.3 for ^{13}C NMR.

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*(±)-syn-5-Benzyloxy-3-(tert-butyldimethylsilyl)oxy-2-methyl-1-(triethylsilyl)pentan-1-one (**30**).* Following the general procedure for the silylation of β-hydroxyacylsilanes, a 25 mL round-bottom flask was charged with **29** (316 mg, 0.939 mmol) and 2,6-lutidine (201 mg, 1.88 mmol). Then, 9 mL of freshly distilled CH_2Cl_2 was introduced into the round-bottom flask under argon flush. The solution was cooled to 0 °C, and TBSOTf (0.320 mL, 1.40 mmol) was added to the solution. Next, the argon flush was stopped and the reaction was stirred at 0 °C for 2 h. The reaction was monitored by TLC using a 95:5 pentane/Et_2O mixture. After aqueous workup and concentration, the reaction afforded 458 mg of a crude mixture. The latter was purified by chromatography with 25 g of silica gel (pentane/Et_2O gradient, 99.5:0.5 to 98.5:1.5). After purification, the major *syn* isomer **30** (266 mg, 0.590 mmol, 63%, colorless oil) was separated from the more polar *anti* isomer. **30**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.23 (m, 5H), 4.47 (s, 2H), 4.13 (dt, *J* = 7.0, 5.1 Hz, 1H), 3.50 (td, *J* = 6.8, 4.1 Hz, 2H), 3.04 (p, *J* = 7.1 Hz, 1H), 1.73 (tdd, *J* = 6.9, 5.1, 2.2 Hz, 2H), 0.99−0.90 (m, 12H), 0.86 (s, 9H), 0.75−0.66 (m, 6H), 0.03 (s, 3H), 0.01 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 250.3, 138.6, 128.4, 127.7, 127.6, 73.1, 69.1, 66.6, 56.5, 36.1, 26.0, 18.2, 11.5, 7.4, 2.6, −4.16, −4.20. HRMS (ESI +ve) Exact mass calculated for $C_{25}H_{46}O_3NaSi_2$ $[M + Na]^+$: 473.28832, found: 473.2877.

*(±)-syn-5-Benzyloxy-3-(tert-butyldimethylsilyl)oxy-2-methylpentanal (**31**).* Following the general procedure for the photolysis/hydrolysis of protected β-hydroxyacylsilanes, a 100 mL round-bottom flask was charged with **30** (263 mg, 0.583 mmol), H_2O (12 mL), and acetone (48 mL). The solution was degassed and cooled to −15 °C, and then enlightened at 365 nm under stirring for 14 h at −15 °C. The reaction was monitored by ^{1}H NMR. After aqueous workup and concentration under reduced pressure, the reaction afforded **31** (194 mg, 0.576 mmol, 99%, colorless oil). **31**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.78 (d, *J* = 0.9 Hz, 1H), 7.33 (d, *J* = 1.4 Hz, 4H), 4.48 (d, *J* = 8.3 Hz, 2H), 4.32 (ddd, *J* = 7.3, 5.6, 3.6 Hz, 1H), 3.56−3.48 (m, 2H), 2.48 (qdd, *J* = 6.9, 3.7, 0.9 Hz, 1H), 1.91−1.70 (m, 2H), 1.05 (d, *J* = 7.0 Hz, 3H), 0.86 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.2, 138.3, 128.5, 127.73, 127.71, 73.1, 69.4, 66.6, 51.7, 34.6, 25.8, 18.1, 8.0, −4.4, −4.5. HRMS (ESI +ve) Exact mass calculated for $C_{19}H_{32}O_3NaSi$ $[M + Na]^+$: 359.20184, found: 359.2020.

*(±)-syn-5-(4-Methoxy)benzyloxy-3-hydroxy-2-methyl-1-(triethylsilyl)pentan-1-one (**33**).* Following the general procedure for the synthesis of β-hydroxyacylsilanes, a Schlenk tube was charged with $MgBr_2$ (558 mg, 3.03 mmol, 60 mol %) and a freshly prepared solution of NiHCl(dppe) (0.5 mmol, 10 mol %) in 10 mL of THF. The Schlenk tube was cooled at −35 °C, and then 3-(4-methoxybenzyl)-oxy-propanal **32**[23] (979 mg, 5.04 mmol) and **1** (948 mg, 5.50 mmol) were added into the solution. The solution was stirred at −35 °C for 18 h, and the reaction was monitored by TLC with an 85:15 pentane/AcOEt mixture. The reaction was quenched by a saturated NH_4Cl solution, the mixture was diluted with Et_2O and filtered through a small pad of Celite, and the phases were separated. The separated aqueous phase was extracted with Et_2O, and the combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure, affording 1.869 g of a crude mixture. The latter was purified by chromatography with 55 g of silica gel (pentane/AcOEt gradient, 98:2 to 85:15). After purification, 1.435 g (3.91 mmol, 78%, pale yellow oil) of adducts was obtained as an 85:15 mixture of diastereomers. **33**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26−7.22 (m, 2H), 6.90−6.84 (m, 2H), 4.44 (s, 2H), 4.09 (dtd, *J* = 9.4, 3.7, 2.2 Hz, 1H), 3.80 (s, 3H), 3.65−3.55 (m, 2H), 3.16 (d, *J* = 2.3 Hz, 1H), 2.93 (qd, *J* = 7.2, 4.0 Hz, 1H), 1.74 (m, 1H), 1.61 (m, 1H), 1.02 (d, *J* = 7.2 Hz, 3H), 0.99−0.92 (m, 9H), 0.78−0.69 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 253.5, 159.3, 130.3, 129.3, 113.9, 73.0, 69.0, 68.2, 55.3, 55.1, 34.3, 8.5, 7.3, 2.5. HRMS (ESI +ve) Exact mass calculated for $C_{20}H_{34}O_4NaSi$ $[M + Na]^+$: 389.21241, found: 389.2124. The characteristic peaks for the minor *anti* isomer were observed at 3.97 (m, 1H), 3.15 (d, *J* = 4.9 Hz, 1H), 3.05 (p, *J* = 7.2 Hz, 1H) for 1H NMR and at 254.0, 159.32, 130.2, 129.4, 113.8, 73.0, 72.2, 68.3, 55.7, 34.2, 11.4, 7.5, 3.6, 2.4 for ^{13}C NMR.

*(±)-syn-5-(4-Methoxybenzyl)oxy-3-(tert-butyldimethylsilyl)oxy-2-methyl-1-(triethylsilyl)pentan-1-one (**34**).* Following the general procedure for the silylation of β-hydroxyacylsilanes, a 50 mL round-bottom flask was charged with **33** (1.284 g, 3.50 mmol) and 2,6-lutidine (745 mg, 6.95 mmol). Then, 18 mL of freshly distilled CH_2Cl_2 was introduced into the round-bottom flask under argon flush. The solution was cooled to 0 °C, and TBSOTf (1.2 mL, 5.22 mmol) was added to the solution. Next, the argon flush was stopped and the reaction was stirred at 0 °C for 1 h 30 min. The reaction was monitored by TLC using a 90:10 pentane/AcOEt mixture. After aqueous workup and concentration, the reaction afforded 1.825 g of a crude mixture. The latter was purified by chromatography with 99 g of silica gel (pentane/Et_2O gradient, 97.5:2.5 to 97:3). After purification, the major *syn* isomer **34** (1.142 g, 2.38 mmol, 68%, colorless oil) was separated from the more polar *anti* isomer. **34**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25−7.21 (m, 2H), 6.88−6.84 (m, 2H), 4.39 (s, 2H), 4.11 (dt, *J* = 7.0, 5.1 Hz, 1H), 3.80 (s, 3H), 3.46 (td, *J* = 6.8, 4.4 Hz, 2H), 3.03 (quint, *J* = 7.1 Hz, 1H), 1.71 (tdd, *J* = 7.0, 5.1, 2.1 Hz, 2H), 0.98−0.90 (m, 12H), 0.85 (s, 9H), 0.75−0.66 (m, 6H), 0.03 (s, 3H), 0.01 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 250.5, 159.2, 130.7, 129.4, 113.8, 72.7, 69.1, 66.3, 56.4, 55.3, 36.1, 26.0, 18.2, 11.6, 7.4, 2.6, −4.17, −4.21. HRMS (ESI +ve) Exact mass calculated for $C_{26}H_{48}O_4NaSi_2$ $[M + Na]^+$: 503.29889, found: 503.2992.

*(±)-syn-5-(4-Methoxybenzyl)oxy-3-(tert-butyldimethylsilyl)oxy-2-methylpentanal (**35**).* Following the general procedure for the photolysis/hydrolysis of protected β-hydroxyacylsilanes, a 500 mL round-bottom flask was charged with **34** (1.140 g, 2.37 mmol), H_2O (47 mL), acetone (190 mL), and a magnetic stir bar. The solution was degassed and cooled to −15 °C, and then enlightened at 365 nm and stirred for 25 h at −15 °C. The reaction was monitored by ^{1}H NMR. After aqueous workup and concentration under reduced pressure, the reaction afforded **35** (866 mg, 2.36 mmol, quantitative, colorless oil). It was used in the next step without further purification. **35**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.77 (d, *J* = 0.9 Hz, 1H), 7.27−7.22 (m, 2H), 6.90−6.85 (m, 2H), 4.47−4.35 (m, 2H), 4.30 (ddd, *J* = 7.3, 5.7, 3.6 Hz, 1H), 3.80 (s, 3H), 3.48 (td, *J* = 6.0, 1.3 Hz, 2H), 2.47 (qdd, *J* = 6.9, 3.6, 0.9 Hz, 1H), 1.89−1.68 (m, 2H), 1.04 (d, *J* = 7.0 Hz, 3H), 0.85 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.0, 159.2, 130.3, 129.3, 113.8, 72.7, 69.3, 66.2, 55.2, 51.6, 34.6, 25.8, 18.0, 7.8, −4.4, −4.6. HRMS (ESI +ve) Exact mass calculated for $C_{20}H_{34}O_4NaSi$ $[M + Na]^+$: 389.21241, found: 389.2122.

*(±)-7-(4-Methoxybenzyl)oxy-3-hydroxy-5-(tert-butyldimethylsilyl)oxy-2,4-dimethyl-1-(triethylsilyl)heptan-1-one (**36**).* Following the general procedure for the synthesis of β-hydroxyacylsilanes, a Schlenk tube was charged with $MgBr_2$ (261 mg, 1.42 mmol, 60 mol %) and a freshly prepared solution of NiHCl(dppe) (0.24 mmol, 10 mol %) in 5 mL of THF. The Schlenk tube was cooled at −35 °C, and then **35** (864 mg, 2.36 mmol) and **1** (478 mg, 2.77 mmol) were added into the solution. The solution was stirred at −35 °C for 135 h, and the reaction was monitored by TLC with a 90:10 pentane/Et_2O mixture. The reaction was quenched by a saturated NH_4Cl solution, the mixture was diluted with Et_2O and filtered through a small pad of Celite, and the phases were separated. The separated aqueous phase was extracted with Et_2O, and the combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure, affording 1.392 g of a crude mixture. The latter was purified by chromatography with 39 g of silica gel (pentane/Et_2O gradient, 96:4 to 80:20). After careful purification by chromatography, 803 mg (1.49 mmol, 63%, pale yellow oil) of **36** was obtained as an 86:14 mixture of diastereomers. **36**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28−7.24 (m, 2H), 6.90−6.84 (m, 2H), 4.48−4.36 (m, 2H), 4.12 (ddd, *J* = 7.7, 5.6, 2.2 Hz, 1H), 4.05 (dt, *J* = 10.0, 1.8 Hz, 1H), 3.80 (s, 3H), 3.64 (d, *J* = 1.4 Hz, 1H), 3.56−3.40 (m, 2H), 2.85 (qd, *J* = 6.9, 1.8 Hz, 1H), 1.88−1.79 (m, 2H), 1.69 (m, 1H), 0.95 (m, 12H), 0.85 (s, 9H), 0.81−0.71 (m, 9H), 0.07 (s, 3H), 0.04 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 251.2, 159.2, 130.6, 129.2, 113.7, 72.6, 71.1, 70.0, 66.9, 55.1, 52.8, 39.9, 33.6, 25.9, 18.0, 11.1, 7.3, 5.9, 2.7, −4.59, −4.65. HRMS (ESI +ve) Exact mass calculated for $C_{29}H_{54}O_5NaSi_2$ $[M + Na]^+$: 561.34075, found: 561.3409. The characteristic peaks for the minor *anti* isomer were observed at 4.00−3.94 (m, 1H), 3.94−3.86 (m, 1H), 3.80 (s, 3H), 3.06 (m, 1H), 2.73 (d, *J* = 3.6 Hz, 1H) for ^{1}H NMR and at δ 253.5, 131.5,

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130.5, 75.2, 74.3, 66.5, 53.3, 38.5, 34.5, 30.3, 11.5, 3.0, 2.5, 2.3, −4.0, −4.5 for ^{13}C NMR.

*(±)-7-(4-Methoxybenzyl)oxy-3-hydroxy-2,4-dimethyl-5-(tert-butyldimethylsilyl)oxy-1-heptan-1,3-diol (**37**).* Following the general procedure for the photolysis/hydrolysis of protected β-hydroxyacylsilanes, a 10 mL round-bottom flask was charged with **36** (27 mg, 0.050 mmol), H_2O (1 mL), freshly distilled THF (4 mL), and a magnetic stir bar. The solution was degassed and cooled at 0 °C, and the reaction mixture was then enlightened at 365 nm and stirred for 2 h. The reaction was monitored by TLC using a 90:10 pentane/acetone mixture. Once the starting material was consumed, $NaBH_4$ (7 mg, 0.016 mmol) was added to the reaction mixture and the reaction was stirred for 30 min. This second step reaction was monitored by TLC using an 80:20 pentane/acetone mixture. Then, brine was added, and the solution was poured in a separatory funnel. The aqueous phase was extracted three times with Et_2O, and the combined organic phases were dried with $MgSO_4$, filtered, and concentrated under reduced pressure, affording 24 mg of a crude mixture. The latter was purified by chromatography with 3 g of silica gel (pentane/Et_2O mixture, 80:20 to 40:60). After purification, 15 mg (0.035 mmol, 70% over two steps pale yellow oil) of **37** (containing around 6−7% of the minor diastereoisomer by ^1H and ^{13}C NMR) was obtained. **37**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 4.56 (brs, 1H), 4.47−4.36 (m, 2H), 3.95 (m, 2H), 3.80 (s, 3H), 3.77 (d, *J* = 3.7 Hz, 1H), 3.67 (dd, *J* = 10.6, 5.5 Hz, 1H), 3.58−3.47 (m, 2H), 2.78 (brs, 1H), 1.98−1.80 (m, 3H), 0.95 (d, *J* = 7.0 Hz, 3H), 0.89 (s, 9H), 0.73 (d, *J* = 7.1 Hz, 3H), 0.12 (s, 3H), 0.07 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.4, 130.7, 129.4, 114.0, 76.4, 75.22, 72.7, 68.2, 66.9, 55.4, 40.0, 36.5, 31.4, 25.9, 18.0, 13.6, 8.5, −4.3, −4.9. HRMS (ESI +ve) Exact mass calculated for $C_{23}H_{42}O_5NaSi$ $[M + Na]^+$: 449.26992, found: 449.2702.

■ ASSOCIATED CONTENT

Supporting Information

General information and representative setup for photolysis of acylsilanes, crystal structure reports for compounds **24** and **27**, and copies of all the ^1H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: rene.gree@univ-rennes1.fr (R.G.).

Notes

The authors declare no competing financial interest.

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