One-Pot Synthesis of α-Siloxy Esters Using a Silylated Masked Acyl Cyanide

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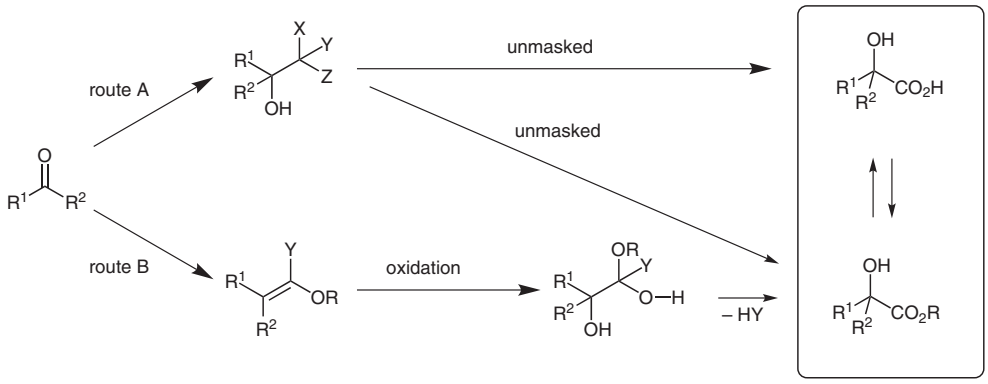
Abstract: Synthesis of α-siloxy esters via a one-pot reaction from various aldehydes and alcohols using a masked acyl cyanide (MAC) reagent bearing *tert*-butyldimethylsilyl group is described.

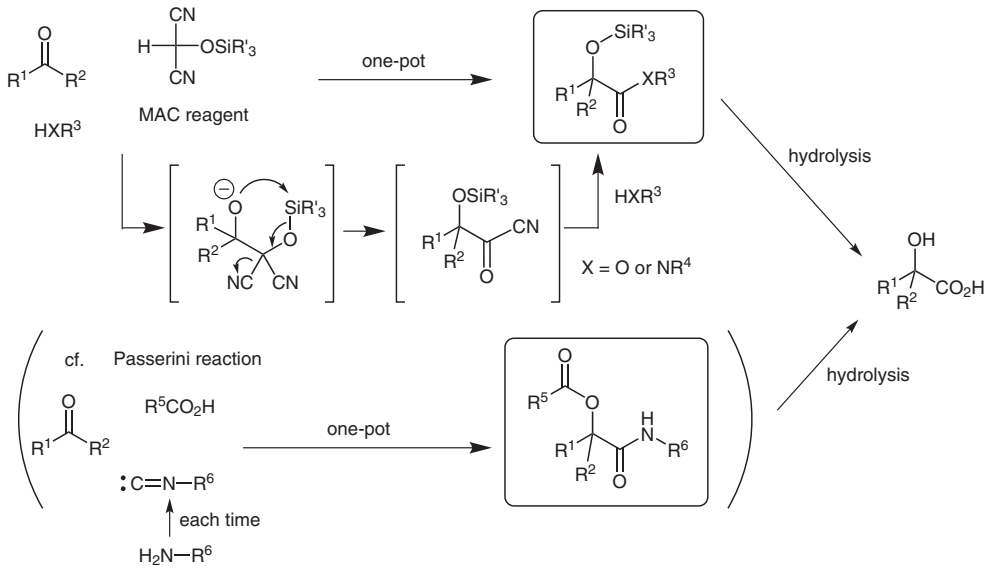
Key words: acyl anion equivalents, masked acyl cyanide, α-hydroxy esters, one-pot, intramolecular migration

α-Hydroxycarboxylic acid and their derivatives have been found in a number of artificial medicinal chemicals and naturally occurring biologically active molecules.[1] The conventional means of preparing such vicinal functional groups consists of a carbon–carbon bond-formation reaction between two oxygenated functionalities, as summarized in Scheme 1.[2]

Both routes A and B generally require multiple steps, which include delicate carbanion chemistry under anhydrous conditions. However, as shown in Scheme 2, there is one unique exception to route A, a reaction using silylated masked acyl cyanide (MAC) reagents.[3] This one-pot reaction proceeds with neither delicate anhydrous condi-



Scheme 1 Typical general routes for the synthesis of α-hydroxycarboxylic acids or esters with one-carbon homologation



Scheme 2 One-pot reaction using MAC reagents and the Passerini reaction

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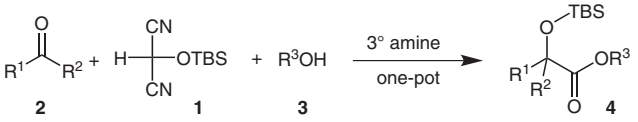
tions nor vigorous unmasking conditions. The efficiency is as high as that of Passerini reaction,[4] which is a well-known and pervasive one-pot reaction using an isonitrile as a key reagent.

Esters and tertiary amides, *which cannot be directly synthesized by the Passerini reaction*, can be synthesized with MAC reagents.[5–7] Also, whenever the Passerini reaction is carried out, an isonitrile must be prepared from each amine. In contrast, amines can be used directly with MAC reagents. MAC reagents thus have these two advantages over isonitrile chemistry.

We have already reported the one-pot reaction from various aldehydes/ketones and amines to afford α-siloxy amides (X = NR^4).[5] Its counterpart, the reaction to afford α-siloxy esters (X = O), has not yet been reported except for the example of methyl N-protected 3-amino-2-siloxy-4-phenylbutanoate.[6]

In this paper, we report a one-pot reaction to form α-siloxy esters **4** starting from various substrates using H–MAC–TBS (**1**) (Scheme 3) in order to illustrate the generality of the above synthetic route of Scheme 2. The results are listed in Table 1 for various aldehydes, in Table 2 for various ketones, and in Table 3 for various alcohols.



Scheme 3

At first, the reaction of *p*-tolaldehyde (**2a**) with **1** and methanol (5.0 equiv) was examined in acetonitrile or tetrahydrofuran by using triethylamine as a base. Although the desired product **4a** was obtained, the yield was moderate and several unidentified by-products were produced. After examining various reaction conditions, the use of methanol as a solvent in the presence of a catalytic amount of 4-(*N*,*N*-dimethylamino)pyridine (DMAP) gave satisfactory results. The pure desired product **4a** was obtained in 96% isolated yield within 5 minutes (Table 1, entry 1). Although a longer period is required, one equivalent of pyridine can be used instead of DMAP (entry 2). The conditions in entry 2 were applied to various aromatic aldehydes and conjugated aldehydes to afford the desired products **4b–e** in excellent yields (entries 3–6). Accordingly, the electron density of the aromatic ring did not significantly influence the desired reactions. In the case of **2f** (entry 7), some side-reactions such as self-condensation occurred under the same condition as entries 2–6. This problem was solved when DMAP was used instead of pyridine at –25 °C (entry 8). In the case of aliphatic aldehyde **2g**, the reason for the low yield was the formation of the cyanohydrin, $PhCH_2CH_2CH(CN)OH$, which was derived from **2g** and the cyanide anion generated from **1** (entry 9). Fortunately, other side-reactions were also inhibited in a manner similar to entry 8 (entry 10). Next, we attempted the reaction with aldehydes bearing bulky group (entries 11, 13). Beyond expectation, the desired products were obtained in moderate yields. As listed in entry 12, the use of excess **1** improved the chemical yield.

Table 1 One-Pot Reaction with Various Aldehydes[a]

Entry	R^1CHO	Base	Temp	Time	Yield of **4** (%)
1	4-MeC_6H_4CHO (**2a**)	DMAP (0.1)	r.t.	5 min	96 (**4a**)
2	**2a**	pyridine (1.0)	r.t.	2 h	91 (**4a**)
3	2-HOC_6H_4CHO (**2b**)	pyridine (1.0)	r.t.	2 h	94 (**4b**)
4	2-furaldehyde (**2c**)	pyridine (1.0)	r.t.	2 h	97 (**4c**)
5	4-NCC_6H_4CHO (**2d**)	pyridine (1.0)	r.t.	2 h	98 (**4d**)
6	(*E*)-PhCH=CHCHO (**2e**)	pyridine (1.0)	r.t.	2 h	95 (**4e**)
7	(*E*)-MeCH=CHCHO (**2f**)	pyridine (1.0)	r.t.	2 h	79 (**4f**)
8	**2f**	DMAP (0.1)	–25 °C	2 h	90 (**4f**)
9	$PhCH_2CH_2CHO$ (**2g**)	DMAP (0.1)	r.t.	5 min	63[b] (**4g**)
10	**2g**	DMAP (0.1)	–40 °C	2 h	78 (**4g**)
11	Me_2CHCHO (**2h**)	DMAP (0.1)	–25 °C	12 h	51 (**4h**)
12	**2h**	DMAP (3.0)	–25 °C	12 h	68[c] (**4h**)
13	Me_3CCHO (**2i**)	DMAP (0.1)	r.t.	5 h	30 (**4i**)

[a] Reaction conditions: aldehyde **2** (R^2 = H, 1 equiv), **1** (1.1. equiv) in MeOH (R^3 = Me).
[b] Cyanohydrin, $PhCH_2CH_2CH(CN)OH$, was obtained in 35% yield.
[c] Amount of **1** used = 3.0 equiv.

The results using ketones are listed in Table 2. As a representative electron-deficient aromatic ketone, 4-nitroacetophenone (**2j**) with **1** in methanol in the presence of a catalytic amount of DMAP afforded **4j** in 90% yield (Table 2, entry 1). In contrast, under similar conditions, the reaction of 4-methylacetophenone (**2k**), a representative electron-rich aromatic ketone, afforded **4k** in 24% yield (entry 2). The yield was optimized to 77% by the use of excess **1** and DMAP at low temperature (entries 3, 4). However, the use of triethylamine instead of DMAP decreased the yield of **4k** to 36% (entry 5). The best conditions for **4k** (entry 4) were applied to acetophenone (**2l**) to give **4l** in 90% yield (entry 6).

The reaction of cyclohex-2-enone (**2m**) afforded the desired compound **4m** in 32% yield and the double-alkylated by-product **5** in 38% yield (Table 2, entry 7) (Scheme 4). This is in contrast with the report that H–MAC–EE[3] (EE = 1-ethoxyethyl group) and **2m** gave only 1,4-adducts **6** in 82% yield.[8] It is considered that the 1,2-

Table 2 One-Pot Reaction with Various Ketones[a]

Entry	R^1COR^2	DMAP (equiv)	Temp	Time (h)	Yield of **4** (%)
1	4-$O_2NC_6H_4COMe$ (**2j**)	0.1	r.t.	0.5	90 (**4j**)
2	4-MeC_6H_4COMe (**2k**)	0.1	r.t.	24	24 (**4k**) (54)[b]
3	**2k**	0.1	–25 °C	72	67 (**4k**) (20)[b]
4[c]	**2k**	3.0	–25 °C	24	77 (**4k**) (11)[b]
5[c]	**2k**	3.0[d]	–25 °C	24	36 (**4k**) (24)[b]
6[c]	PhCOMe (**2l**)	3.0	–25 °C	24	90 (**4l**)
7	cyclohex-2-enone (**2m**)	3.0	–25 °C	24	32 (**4m**)[e]
8	cyclohexanone (**2n**)	0.1	r.t.	0.5	63 (**4n**)
9[c]	**2n**	3.0	–25 °C	24	88 (**4n**)
10[c]	pentan-3-one (**2o**)	3.0	–25 °C	24	35 (**4o**)
11[c]	Me_3CCOMe (**2p**)	3.0	–25 °C	48	0

[a] Reaction conditions: ketone **2** (1 equiv), **1** (1.1 equiv) in MeOH (R^3 = Me).
[b] Recovered yield of **2**.
[c] Amount of **1** used = 3.0 equiv.
[d] Et_3N was used instead of DMAP.
[e] The double-alkylated product **5** (Scheme 4) was obtained in 38% yield.

addition is competitive with 1,4-addition to give a mixture of **4m** and **7** in the case of entry 7. It was found that **7** can be easily transformed to **5** since reaction rate of saturated ketone **7** with **1** is probably much faster than the reaction rate of unsaturated ketone **2m** and **1** as illustrated by the results in entries 8 and 9. In contrast, the proposed intermediate **8** by H–MAC–EE can be reversibly converted back into **2m** and H–MAC–EE since EE is not migratory,[9] and only 1,4-adduct **6** is obtained.

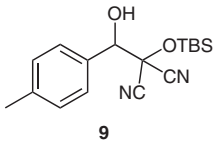
As a representative example of aliphatic ketones, cyclohexanone (**2n**), which has a similar reactivity to **8**, afforded **4n** in 63% yield (entry 8), which was improved to 88% when an excess of DMAP and **1** were used (entry 9). In the case of pentan-3-one (**2o**), the desired product **4o** was obtained only in 35% yield even when optimized conditions as described above were applied (entry 10). Finally, the reaction of a sterically hindered substrate, 3,3-dimethylbutan-2-one (**2p**) was attempted, but no desired compound was detected (entry 11). In cases such as entries 10 and 11 in Table 2 as well as entry 13 in Table 1, the reaction rate to produce the desired compounds was most likely competitive with the decomposition rate of **1**, since not all of starting substrate **2** was completely consumed nor was **1** recovered.

In Table 3, one-pot reactions of **2a** with various alcohols are listed. The α-siloxy esters **4p–s** were obtained in excellent yields (entries 1–4). In the case of *tert*-butyl alcohol, the desired α-siloxy ester was not produced (entry 5).

Table 3 One-Pot Reaction of **2a**, DMAP, and **1** with Various Alcohols[a]

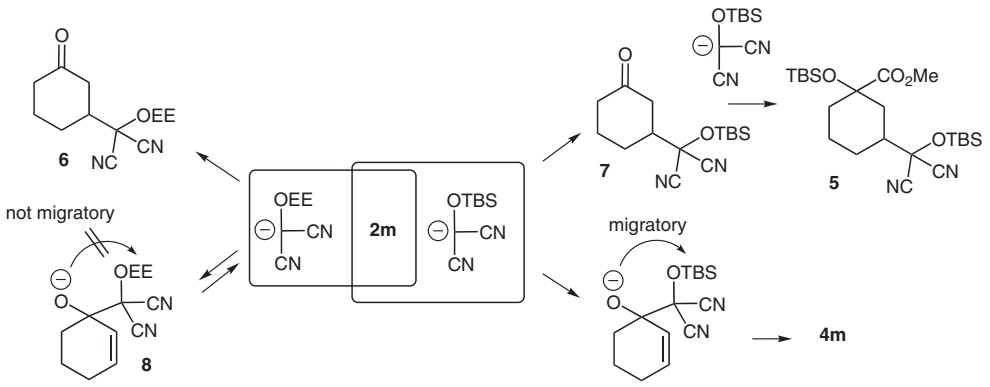
Entry	R^3	Yield of **4** (%)
1	*i*-Pr	90 (**4p**)
2	Bn	88 (**4q**)
3	allyl	92 (**4r**)
4	Ph[b]	93 (**4s**)
5	*t*-Bu	0[c]

[a] Reaction conditions: **2a** (R^1 = 4-MeC_6H_4, R^2 = H, 1 equiv), DMAP (0.1 equiv), and **1** (1.1 equiv) with alcohols (R^3OH) at r.t.
[b] A mixture of phenol and MeCN (1:1) was used.
[c] The nonmigratory adduct **9** was obtained as a major by-product (Figure 1).

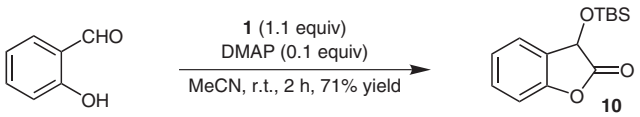


9

Figure 1 Structure of **9**



Scheme 4



Scheme 5

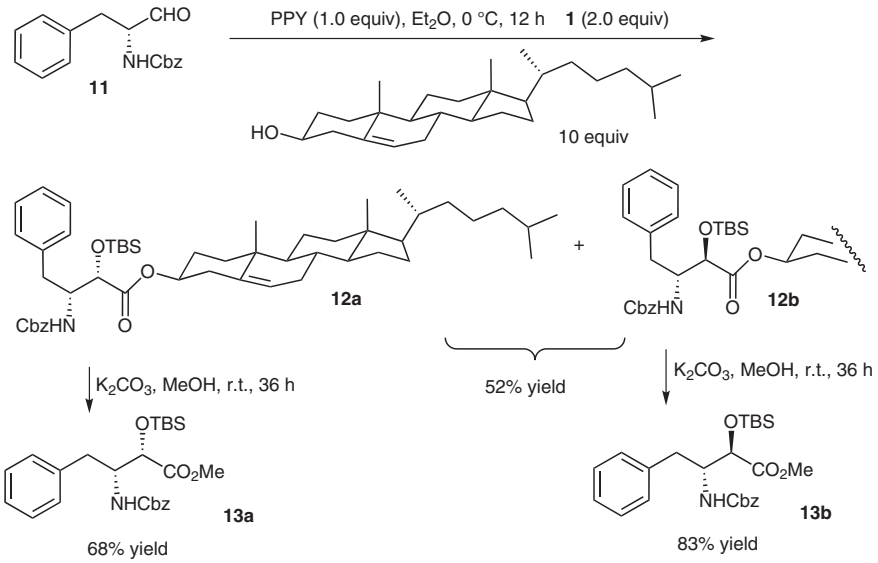
Instead, formation of **9**, a simple adduct without silyl migration, was observed (Figure 1).

Our attempts to prepare an α-siloxy thioester did not yield any positive result. Thus, a mixture of **2a**, **1** and 3–5 equivalents of thiophenol in acetonitrile did not afford the desired α-siloxy thioester. We observed that **1** was gradually decomposed to unidentified polar materials in the presence of thiophenol.

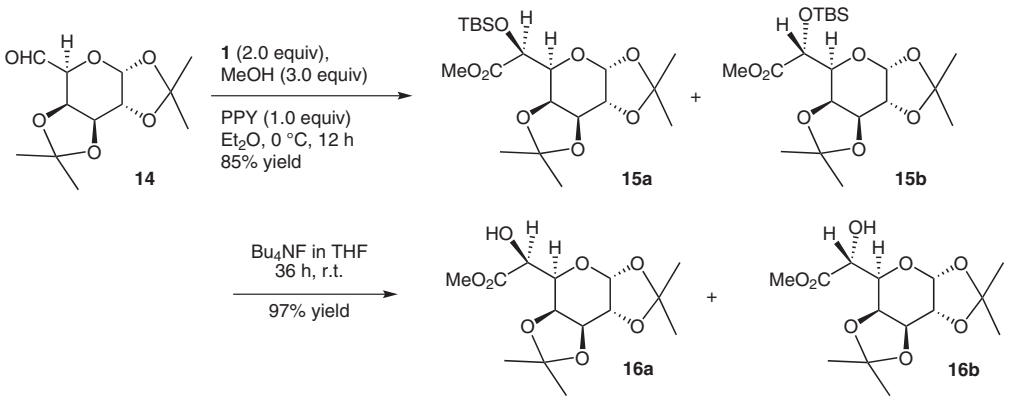
Finally, three synthetic applications are introduced. In the presence of a catalytic amount of DMAP, the reaction of salicylaldehyde with **1** in acetonitrile at room temperature gave the 2-coumaranone derivative **10** in 71% isolated yield (Scheme 5).

In the following two cases, 4-(pyrrolidin-1-yl)pyridine (PPY) gave much better results than DMAP. The N-protected α-aminal **11**[6] derived from D-phenylalanine was transformed to the β-cholesteryl ester **12** (**12a**/**12b** = 83:17) in 52% yield in diethyl ether at 0 °C for 12 hours by using 2.0 equivalents of **1** and 10 equivalents of β-cholesterol in the presence of 1.0 equivalent of PPY (Scheme 6). The excess β-cholesterol was quantitatively recovered. The stereochemistry of the newly formed asymmetric centers of **12a** and **12b** were determined by the methanolysis of the ester moiety to afford the derivative **13a** and its 2*S*-isomer **13b**,[6] respectively.

The final example described in this paper is the one-carbon homologation of a pyranose derivative. The reaction of **14** with **1** (2.0 equiv) and methanol (3.0 equiv) in diethyl ether at 0 °C for 12 hours in the presence of PPY (1.0 equiv) gave the desired products **15** (**15a**/**15b** = 92:8) in 85% yield (Scheme 7). The TBS group from a mixture of **15a** and **15b** was removed by tetrabutylammonium fluoride (Bu_4NF) in THF to afford heptose derivatives **16a**[2] and **16b**[2] (92:8) in 97% yield. The multiple-step procedures using most of acyl anion equivalents with one-carbon homologation[10] involve an independent unmasking step, which has been often carried out in protic acidic conditions. Accordingly, it is noteworthy that two of ace-



Scheme 6



Scheme 7

tonide moieties were retained here during the one-pot reaction.

In conclusion, one-pot reactions to afford α-siloxy esters using H–MAC–TBS **1** were described. For the title reaction, the choice of a tertiary amine was important. If the starting substrate, either an aldehyde (a ketone) or an alcohol, is a large molecule or possesses sterically hindered skeleton, PPY or DMAP can improve the chemical yield of the desired compounds. In contrast, trialkylamines such as triethylamine are generally unsuitable for this reaction since such bases caused the MAC reagents to decompose to unidentified polar materials. If a methyl ester is the target molecule, use of methanol as a solvent is generally the best condition for this reaction. However, when several side reactions such as formation of cyanohydrin or the oligomerization of aldehydes were observed, lower temperatures such as –25 to –40 °C in diethyl ether are recommended. We believe that one-pot reactions with MAC reagents are one of most efficient and facile methods for the synthesis of α-hydroxy carbonyl compounds since MAC reagents are the *only reagents that allow one-pot reactions* among all the reported acyl anion equivalents with one-carbon homologation. We hope that this paper and our previously reported related papers are of use when α-siloxy esters and amides are the target molecules.

Melting points were determined using Yanagimoto Micro Melting Point Apparatus and are uncorrected. IR spectra were recorded on PerkinElmer 1720 or Jasco FT-IR/420 Infrared Fourier Transfer Spectrometer. ^{1}H and ^{13}C NMR spectra were measured with Jeol JMN-AL300 Spectrometer at 300 MHz and 75 MHz, respectively, or with Jeol GSX400 Spectrometer at 400 MHz and 100 MHz, respectively, in $CDCl_3$, and chemical shifts are given as δ value in ppm from internal TMS at 25 °C unless otherwise noted. High-resolution mass spectra were measured with Jeol JMS-DX303 spectrometer. Elementary analyses were performed on Yanagimoto CHN-corder MT-3. HPLC analyses were preformed on Hitachi L-7000 instrument equipped with Hitachi L-7400 UV detector. Optical rotations were measured with Jasco DIP-370 digital polarimeter. MeOH was distilled over $Mg(OMe)_2$. Pyridine and Et_3N were distilled over KOH. MeCN was distilled over calcium hydride. Et_2O was distilled over sodium/benzophenone. Anhyd THF was purchased from Kanto Chemicals. All aldehydes and ketones **2** were distilled or recrystallized before use. All the reactions were carried out under N_2, unless otherwise noted.

One-Pot Reaction of 2 with the Masked Acyl Cyanide 1 in the Presence of Alcohols; General Procedure

To a solution of an aldehyde (or a ketone) **2** (1.0 mmol) and **1** (216 mg, 1.1 mmol) in alcohol **3** (5 mL) was added a tertiary amine. The amount of tertiary amine, the temperature, and time applied are specified in Tables 1 and 2. Then the mixture was concentrated in vacuo. The residue was purified by silica gel column chromatography to give α-siloxy esters **4**. When aliphatic aldehydes or ketones were the starting substrates, the alcohol **3** (3.0 mmol) in Et_2O (5 mL) was used instead of the pure alcohol **3** (5 mL).

Methyl 2-[(*tert*-Butyldimethylsilyl)oxy]-2-(4-methylphenyl)acetate (4a)

Colorless oil.

IR ($CHCl_3$): 2955, 2931, 2859, 1753, 1256, 1131, 840 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.35 (d, *J* = 8.0 Hz, 2 H), 7.14 (d, *J* = 8.0 Hz, 2 H), 5.20 (s, 1 H), 3.67 (s, 3 H), 2.34 (s, 3 H), 0.91 (s, 9 H), 0.10 (s, 3 H), 0.03 (s, 3 H).

^{13}C NMR (100 MHz): δ = 172.7 (C=O), 137.8 (C), 136.2 (C), 129.0 (2 × CH), 126.3 (2 × CH), 74.3 (CH), 52.1 (OCH_3), 25.7 (3 × CH_3), 21.2 (Ar*C*H$_3$), 18.3 (*C*Me$_3$), –5.10 (CH_3Si), –5.13 (CH_3Si).

EI-HRMS: *m*/*z* calcd for $C_{16}H_{27}O_3Si$ [M + H]$^+$: 295.1729; found: 295.1725.

Methyl 2-[(*tert*-Butyldimethylsilyl)oxy]-2-(2-hydroxyphenyl)acetate (4b)

Colorless needles; mp 103–104 °C (hexane–EtOAc).

IR ($CHCl_3$): 3397, 2956, 2932, 1751, 1244, 1100, 841 cm^{-1}.

^{1}H NMR (300 MHz): δ = 7.79 (s, 1 H), 7.21 (dd, *J* = 7.6, 7.6 Hz, 1 H), 7.13 (d, *J* = 7.6 Hz, 1 H), 6.88 (d, *J* = 7.6 Hz, 1 H), 6.85 (dd, *J* = 7.6, 7.6 Hz, 1 H), 5.24 (s, 1 H), 3.72 (s, 3 H), 0.92 (s, 9 H), 0.15 (s, 3 H), 0.07 (s, 3 H).

^{13}C NMR (75 MHz): δ = 172.0 (C=O), 155.9 (C–O), 130.0 (CH), 128.3 (CH), 122.4 (C), 119.8 (CH), 117.5 (CH), 75.1 (CH), 52.6 (OCH_3), 25.5 (3 × CH_3), 18.1 (*C*Me$_3$), –5.3 ($SiCH_3$), –5.5 ($SiCH_3$).

Anal. Calcd for $C_{15}H_{24}O_4Si$: C, 60.78; H, 8.16. Found: C, 60.57; H, 8.23.

Methyl 2-[(*tert*-Butyldimethylsilyl)oxy]-2-(2-furyl)acetate (4c)

Colorless oil.

IR ($CHCl_3$): 2956, 2932, 2859, 1757, 1260, 1153, 1119, 841 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.39 (s, 1 H), 6.34 (s, 2 H), 5.28 (s, 1 H), 3.77 (s, 3 H), 0.90 (s, 9 H), 0.11 (s, 3 H), 0.04 (s, 3 H).

^{13}C NMR (100 MHz): δ = 170.6 (C=O), 151.6 (C), 142.6 (CH), 110.4 (CH), 108.1 (CH), 68.7 (CH), 52.4 (OCH_3), 25.6 (3 × CH_3), 18.4 (*C*Me$_3$), –5.2 ($SiCH_3$), –5.3 ($SiCH_3$).

EI-HRMS: *m*/*z* calcd for $C_{13}H_{23}O_4Si$ [M + H]$^+$: 271.1366; found: 271.1386.

Methyl 2-[(*tert*-Butyldimethylsilyl)oxy]-2-(4-cyanophenyl)acetate (4d)

Colorless oil.

IR ($CHCl_3$): 2955, 2932, 2860, 2232, 1757, 1261, 1136, 841 cm^{-1}.

^{1}H NMR (300 MHz): δ = 7.65 (d, *J* = 8.8 Hz, 2 H), 7.60 (d, *J* = 8.8 Hz, 2 H), 5.27 (s, 1 H), 3.70 (s, 3 H), 0.92 (s, 9 H), 0.13 (s, 3 H), 0.06 (s, 3 H).

^{13}C NMR (75 MHz): δ = 171.4 (C=O), 144.1 (C), 132.1 (CH), 126.9 (CH), 118.5 (C≡N), 111.9 (C), 73.7 (CH), 52.4 (OCH_3), 25.5 (3 × CH_3), 18.2 (*C*Me$_3$), –5.2 ($SiCH_3$), –5.4 ($SiCH_3$).

EI-HRMS: *m*/*z* calcd for $C_{16}H_{24}NO_3Si$ [M + H]$^+$: 306.1525; found: 306.1502.

Methyl (3*E*)-2-[(*tert*-Butyldimethylsilyl)oxy]-4-phenylbut-3-enoate (4e)

Colorless oil.

IR ($CHCl_3$): 2955, 2931, 2859, 1752, 1472, 1259, 1152, 839 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.39 (d, *J* = 7.3 Hz, 2 H), 7.32 (dd, *J* = 7.3, 7.3 Hz, 2 H), 7.24 (dd, *J* = 7.3, 7.3 Hz, 1 H), 6.75 (d, *J* = 15.6 Hz, 1 H), 6.31 (dd, *J* = 15.6, 5.6 Hz, 1 H), 4.89 (d, *J* = 5.6 Hz, 1 H), 3.75 (s, 3 H), 0.95 (s, 9 H), 0.15 (s, 3 H), 0.12 (s, 3 H).

^{13}C NMR (100 MHz): δ = 172.3 (C=O), 136.4 (C), 131.6 (CH), 128.6 (2 × CH), 127.9 (CH), 126.7 (CH), 126.6 (2 × CH), 73.2 (CH), 52.2 (OCH_3), 25.8 (3 × CH_3), 18.5 (*C*Me$_3$), –5.0 ($SiCH_3$), –5.1 ($SiCH_3$).

EI-HRMS: *m*/*z* calcd for $C_{17}H_{27}O_3Si$ [M + H]$^+$: 307.1729; found: 307.1766.

Methyl (3*E*)-2-[(*tert*-Butyldimethylsilyl)oxy]pent-3-enoate (4f)
Colorless oil.

IR ($CHCl_3$): 2955, 2931, 2859, 1751, 1257, 1156, 840 cm^{-1}.

^{1}H NMR (400 MHz): δ = 5.83 (dqd, *J* = 15.1, 6.8, 1.5 Hz, 1 H), 5.57 (ddq, *J* = 15.1, 5.8, 1.5 Hz, 1 H), 4.66 (br d, *J* = 5.8 Hz, 1 H), 3.73 (s, 3 H), 1.72 (ddd, *J* = 6.8, 1.5, 1.5 Hz, 3 H), 0.91 (s, 9 H), 0.10 (s, 3 H), 0.07 (s, 3 H).

^{13}C NMR (100 MHz): δ = 172.8 (C=O), 128.3 (=CH), 128.3 (=CH), 73.1 (CH), 52.0 (OCH_3), 25.8 (3 × CH_3), 18.4 (*C*Me$_3$), 17.6 (*C*H$_3$CH=), –5.0 ($SiCH_3$), –5.1 ($SiCH_3$).

EI-HRMS: *m*/*z* calcd for $C_{12}H_{25}O_3Si$ [M + H]$^+$: 245.1573; found: 245.1596.

Methyl 2-[(*tert*-Butyldimethylsilyl)oxy]-4-phenylbutanoate (4g)
Colorless oil.

IR ($CHCl_3$): 2955, 2931, 2859, 1751, 1259, 1132, 839 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.32–7.25 (m, 2 H), 7.20–7.13 (m, 3 H), 4.26 (t, *J* = 5.8 Hz, 1 H), 3.70 (s, 3 H), 2.80–2.64 (m, 2 H), 2.10–1.98 (m, 2 H), 0.93 (s, 9 H), 0.09 (s, 3 H), 0.07 (s, 3 H).

^{13}C NMR (100 MHz): δ = 174.0 (C=O), 141.5 (C), 128.4 (2 × CH), 128.4 (2 × CH), 125.9 (CH), 71.7 (CH), 51.8 (OCH_3), 36.9 (CH_2), 31.4 (CH_2), 25.8 (3 × CH_3), 18.4 (*C*Me$_3$), –4.9 ($SiCH_3$), –5.3 ($SiCH_3$).

EI-HRMS: *m*/*z* calcd for $C_{17}H_{29}O_3Si$ [M + H]$^+$: 309.1886; found: 309.1847.

Methyl 2-[(*tert*-Butyldimethylsilyl)oxy]-3-methylbutanoate (4h)
Colorless oil.

IR ($CHCl_3$): 2960, 2932, 2859, 1748, 1259, 1146, 838 cm^{-1}.

^{1}H NMR (300 MHz): δ = 3.97 (d, *J* = 5.0 Hz, 1 H), 3.71 (s, 3 H), 2.13–1.94 (m, 1 H), 0.93 (d, *J* = 7.0 Hz, 3 H), 0.91 (s, 9 H), 0.90 (d, *J* = 7.0 Hz, 3 H), 0.05 (s, 3 H), 0.04 (s, 3 H).

^{13}C NMR (75 MHz): δ = 174.0 (C=O), 77.1 (CH), 51.5 (OCH_3), 32.9 (CH), 25.7 (3 × CH_3), 19.0 (CH_3), 18.3 (*C*Me$_3$), 17.0 (CH_3), –5.0 ($SiCH_3$), –5.4 ($SiCH_3$).

EI-HRMS: *m*/*z* calcd for $C_8H_{17}O_3Si$ [M – *t*-Bu]$^+$: 189.0947; found: 189.0952.

2-Hydroxy-4-phenylbutanenitrile
This was a major by-product of entry 9 in Table 1; colorless oil.

IR ($CHCl_3$): 3360, 2936, 2244, 1449, 1077 cm^{-1}.

^{1}H NMR (300 MHz): δ = 7.52–6.99 (m, 5 H), 4.40 (br t, *J* = 6.6 Hz, 1 H), 3.01 (br s, 1 H), 2.83 (t, *J* = 7.5 Hz, 2 H), 2.25–1.97 (m, 2 H).

^{13}C NMR (75 MHz): δ = 139.5 (C), 128.7 (2 × CH), 128.4 (2 × CH), 126.5 (CH), 119.8 (C≡N), 60.3 (*C*HC≡N), 36.5 (CH_2), 30.6 (CH_2).

EI-HRMS: *m*/*z* calcd for $C_{10}H_{11}NO$ [M]$^+$: 161.0841; found: 161.0853.

Methyl 2-[(*tert*-Butyldimethylsilyl)oxy]-3,3-dimethylbutanoate (4i)
Colorless oil.

IR ($CHCl_3$): 2957, 2859, 1747, 1260, 1230, 1122, 839 cm^{-1}.

^{1}H NMR (400 MHz): δ = 3.83 (s, 1 H), 3.69 (s, 3 H), 0.94 (s, 9 H), 0.91 (s, 9 H), 0.03 (s, 3 H), 0.00 (s, 3 H).

^{13}C NMR (100 MHz): δ = 173.2 (C=O), 80.1 (CH), 51.1 (OCH_3), 35.3 (C), 25.9 (3 × CH_3), 25.7 (3 × CH_3), 18.2 (*C*Me$_3$), –5.3 ($SiCH_3$), –5.5 ($SiCH_3$).

EI-HRMS: *m*/*z* calcd for $C_9H_{19}O_3Si$ [M – *t*-Bu]$^+$: 203.1103; found: 203.1087.

Methyl 2-[(*tert*-Butyldimethylsilyl)oxy]-2-(4-nitrophenyl)propanoate (4j)
Colorless needles; mp 65–66 °C (hexane–EtOAc).

IR ($CHCl_3$): 2956, 1735, 1524, 1351, 1262, 1167, 840 cm^{-1}.

^{1}H NMR (400 MHz): δ = 8.18 (d, *J* = 8.8 Hz, 2 H), 7.70 (d, *J* = 8.8 Hz, 2 H), 3.69 (s, 3 H), 1.82 (s, 3 H), 0.98 (s, 9 H), 0.17 (s, 3 H), 0.13 (s, 3 H).

^{13}C NMR (100 MHz): δ = 173.6 (C=O), 151.4 (C), 147.4 (C), 126.0 (2 × CH), 123.4 (2 × CH), 78.5 (C), 52.6 (OCH_3), 28.3 (CH_3), 25.8 (3 × CH_3), 18.5 (*C*Me$_3$), –2.8 ($SiCH_3$), –3.6 ($SiCH_3$).

Anal. Calcd for $C_{16}H_{25}NO_5Si$: C, 56.61; H, 7.42; N, 4.13. Found: C, 56.55; H, 7.50; N, 4.12.

Methyl 2-[(*tert*-Butyldimethylsilyl)oxy]-2-(4-methylphenyl)propanoate (4k)
Colorless oil.

IR ($CHCl_3$): 2955, 2931, 1735, 1261, 1163, 1122, 1006, 839 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.40 (d, *J* = 8.0 Hz, 2 H), 7.13 (d, *J* = 8.0 Hz, 2 H), 3.65 (s, 3 H), 2.33 (s, 3 H), 1.78 (s, 3 H), 0.96 (s, 9 H), 0.12 (s, 3 H), 0.07 (s, 3 H).

^{13}C NMR (100 MHz): δ = 174.9 (C=O), 141.4 (C), 137.1 (C), 128.8 (2 × CH), 124.9 (2 × CH), 78.4 (C), 52.1 (OCH_3), 28.3 (CH_3), 25.9 (3 × CH_3), 21.0 (CH_3), 18.5 (*C*Me$_3$), –2.9 ($SiCH_3$), –3.5 ($SiCH_3$).

EI-HRMS: *m*/*z* calcd for $C_{13}H_{19}O_3Si$ [M – *t*-Bu]$^+$: 251.1103; found: 251.1135.

Methyl 2-[(*tert*-Butyldimethylsilyl)oxy]-2-phenylpropanoate (4l)
Colorless oil.

IR ($CHCl_3$): 2955, 2931, 2858, 1733, 1261, 1166, 839 cm^{-1}.

^{1}H NMR (300 MHz): δ = 7.58–7.47 (m, 2 H), 7.40–7.22 (m, 3 H), 3.66 (s, 3 H), 1.80 (s, 3 H), 1.00 (s, 9 H), 0.13 (s, 3 H), 0.08 (s, 3 H).

^{13}C NMR (100 MHz): δ = 174.8 (C=O), 144.4 (C), 128.1 (2 × CH), 127.4 (CH), 125.0 (2 × CH), 78.6 (C), 52.2 (OCH_3), 28.3 (CH_3), 25.9 (3 × CH_3), 18.5 (*C*Me$_3$), –2.8 ($SiCH_3$), –3.5 ($SiCH_3$).

EI-HRMS: *m*/*z* calcd for $C_{12}H_{17}O_3Si$ [M – *t*-Bu]$^+$: 237.0947; found: 237.0937.

Methyl 1-[(*tert*-Butyldimethylsilyl)oxy]cyclohex-2-enecarboxylate (4m)
Colorless oil.

IR ($CHCl_3$): 2953, 2857, 1733, 1256, 1038, 838 cm^{-1}.

^{1}H NMR (300 MHz): δ = 5.94 (dt, *J* = 10.2, 3.6 Hz, 1 H), 5.78 (br d, *J* = 10.2 Hz, 1 H), 3.72 (s, 3 H), 2.20–1.60 (m, 6 H), 0.87 (s, 9 H), 0.09 (s, 3 H), 0.05 (s, 3 H).

^{13}C NMR (75 MHz): δ = 175.4 (C=O), 131.5 (CH=), 128.4 (CH=), 74.0 (C), 52.0 (OCH_3), 34.7 (CH_2), 25.7 (3 × CH_3), 24.8 (CH_2), 18.3 (*C*Me$_3$), 18.2 (CH_2), –2.9 ($SiCH_3$), –3.0 ($SiCH_3$).

EI-HRMS: *m*/*z* calcd for $C_{14}H_{26}O_3Si$ [M]$^+$: 270.1651; found: 270.1642.

Methyl 1-(*tert*-Butyldimethylsilyloxy)-3-[(*tert*-butyldimethylsilyloxy)dicyanomethyl]cyclohexanecarboxylate (5)
Colorless needles; mp 71–73 °C (hexane–EtOAc).

IR ($CHCl_3$): 2956, 2246, 1740, 1257, 1139, 841 cm^{-1}.

^{1}H NMR (300 MHz): δ = 3.74 (s, 3 H), 2.42 (tt, *J* = 12.3, 3.4 Hz, 1 H), 2.19 (br d, *J* = 12.8 Hz, 1 H), 2.04 (br d, *J* = 12.3 Hz, 1 H), 1.89

(br d, J = 13.4 Hz, 1 H), 1.85–1.72 (m, 2 H), 1.72–1.54 (m, 2 H), 1.36–1.17 (m, 1 H), 0.93 (s, 9 H), 0.91 (s, 9 H), 0.36 (s, 6 H), 0.09 (s, 3 H), 0.09 (s, 3 H).

^{13}C NMR (75 MHz): δ = 174.5 (C=O), 114.7 (C≡N), 114.4 (C≡N), 75.9 (C), 67.8 (C), 52.2 (OCH_3), 44.2 (CH_2), 35.7 (CH_2), 35.0 (CH_2), 26.0 (3 × CH_3), 25.8 (3 × CH_3), 25.2 (CH), 19.9 (CH_2), 18.7 (CMe_3), 18.1 (CMe_3), –3.4 ($SiCH_3$), –4.6 ($SiCH_3$), –4.6 ($SiCH_3$), –4.6 ($SiCH_3$).

Anal. Calcd for $C_{23}H_{42}N_2O_4Si_2$: C, 59.18; H, 9.07; N, 6.00. Found: C, 59.18; H, 9.10; N, 5.97.

Methyl 1-[(*tert*-Butyldimethylsilyl)oxy]cyclohexanecarboxylate (4n)
Colorless oil.

IR ($CHCl_3$): 2936, 2857, 1733, 1250, 1156, 1084, 1062, 839 cm^{-1}.

^{1}H NMR (400 MHz): δ = 3.70 (s, 3 H), 1.86–1.74 (m, 2 H), 1.74–1.60 (m, 4 H), 1.57–1.42 (m, 3 H), 1.35–1.23 (m, 1 H), 0.90 (s, 9 H), 0.06 (s, 6 H).

^{13}C NMR (100 MHz): δ = 175.5 (C=O), 76.5 (C), 51.6 (OCH_3), 36.0 (2 × CH_2), 26.0 (3 × CH_3), 25.3 (CH_2), 21.7 (CH_2), 18.6 (CH_2), –3.2 (2 × $SiCH_3$).

EI-HRMS: m/z calcd for $C_{14}H_{29}O_3Si$ [M + H]$^+$: 273.1886; found: 273.1872.

Methyl 2-[(*tert*-Butyldimethylsilyl)oxy]-2-ethylbutanoate (4o)
Colorless oil.

IR ($CHCl_3$): 2955, 2931, 1740, 1252, 1188, 1147, 1088, 838 cm^{-1}.

^{1}H NMR (300 MHz): δ = 3.70 (s, 3 H), 1.84–1.60 (m, 4 H), 0.89 (s, 9 H), 0.85 (t, J = 7.5 Hz, 6 H), 0.12 (s, 6 H).

^{13}C NMR (75 MHz): δ = 175.5 (C=O), 81.7 (C), 51.6 (OCH_3), 32.2 (CH_2), 26.0 (CH_2), 18.8 (CH_3), 8.4 (CH_3), –2.7 (2 × $SiCH_3$).

EI-HRMS: m/z calcd for $C_9H_{19}O_3Si$ [M – t-Bu]$^+$: 203.1103; found: 203.1118.

Isopropyl 2-[(*tert*-Butyldimethylsilyl)oxy]-2-(4-methylphenyl)acetate (4p)
Colorless oil.

IR ($CHCl_3$): 2931, 2859, 1742, 1256, 1104, 874, 839 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.35 (d, J = 8.0 Hz, 2 H), 7.13 (d, J = 8.0 Hz, 2 H), 5.14 (s, 1 H), 5.03–4.93 (m, 1 H), 2.33 (s, 3 H), 1.22 (d, J = 6.4 Hz, 3H), 1.15 (d, J = 6.4 Hz, 3 H), 0.92 (s, 9 H), 0.11 (s, 3 H), 0.04 (s, 3 H).

^{13}C NMR (100 MHz): δ = 171.9 (C=O), 137.6 (C), 136.5 (C), 128.9 (2 × CH), 126.2 (2 × CH), 74.4 (CH), 68.4 (CH), 25.8 (3 × CH_3), 21.7 (CH_3), 21.6 (CH_3), 21.2 (CH_3), 18.4 (CMe_3), –5.0 ($SiCH_3$), –5.1 ($SiCH_3$).

EI-HRMS: m/z calcd for $C_{14}H_{21}O_3Si$ [M – t-Bu]$^+$: 265.1260; found: 265.1271.

Benzyl 2-[(*tert*-Butyldimethylsilyl)oxy]-2-(4-methylphenyl)acetate (4q)
Colorless oil.

IR ($CHCl_3$): 2957, 2931, 1751, 1256, 1168, 1130, 867, 840 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.35 (d, J = 8.0 Hz, 2 H), 7.33–7.26 (m, 2 H), 7.26–7.19 (m, 3 H), 7.14 (d, J = 8.0 Hz, 2 H), 5.23 (s, 1 H), 5.11 (s, 2 H), 2.34 (s, 3 H), 0.89 (s, 9 H), 0.06 (s, 3 H), 0.00 (s, 3 H).

^{13}C NMR (100 MHz): δ = 172.1 (C=O), 137.8 (C), 136.1 (C), 135.7 (C), 129.0 (2 × CH_2), 128.4 (2 × CH_2), 128.1 (2 × CH_2), 128.0 (CH_2), 126.4 (2 × CH_2), 74.3 (CH), 66.6 (CH_2), 25.7 (3 × CH_3), 21.2 (CH_3), 18.3 (CMe_3), –5.1 ($SiCH_3$), –5.2 ($SiCH_3$).

EI-HRMS: m/z calcd for $C_{18}H_{21}O_3Si$ [M – t-Bu]$^+$: 313.1260; found: 313.1251.

Allyl 2-[(*tert*-Butyldimethylsilyl)oxy]-2-(4-methylphenyl)acetate (4r)
Colorless oil.

IR ($CHCl_3$): 2956, 2859, 1751, 1255, 1177, 864, 840 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.36 (d, J = 8.0 Hz, 2 H), 7.14 (d, J = 8.0 Hz, 2 H), 5.90–5.78 (m, 1 H), 5.22 (s, 1 H), 5.26–5.14 (m, 2 H), 4.57 (dt, J = 5.2, 1.2 Hz, 2 H), 2.34 (s, 3 H), 0.91 (s, 9 H), 0.10 (s, 3 H), 0.03 (s, 3 H).

^{13}C NMR (100 MHz): δ = 172.0 (C=O), 137.8 (C), 136.2 (C), 131.8 (CH=), 129.0 (2 × CH_2), 126.3 (2 × CH_2), 118.2 (H_2C=), 74.3 (CH), 65.5 (CH_2), 25. 7 (3 × CH_3), 21.2 (CH_3), 18.3 (CMe_3), –5.0 ($SiCH_3$), –5.1 ($SiCH_3$).

EI-HRMS: m/z calcd for $C_{14}H_{19}O_3Si$ [M – t-Bu]$^+$: 263.1103; found: 263.1096.

Phenyl 2-[(*tert*-Butyldimethylsilyl)oxy]-2-(4-methylphenyl)acetate (4s)
Colorless oil.

IR ($CHCl_3$): 2931, 1772, 1493, 1256, 1192, 1126, 872, 840 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.46 (d, J = 8.0 Hz, 2 H), 7.37–7.28 (m, 2 H), 7.23–7.13 (m, 3 H), 6.98 (d, J = 8.0 Hz, 2 H), 5.41 (s, 1 H), 2.36 (s, 3 H), 0.95 (s, 9 H), 0.17 (s, 3 H), 0.09 (s, 3 H).

^{13}C NMR (100 MHz): δ = 170.8 (C=O), 150.7 (C), 138.1 (C), 135.8 (C), 129.3 (2 × CH_2), 129.2 (2 × CH_2), 126.4 (2 × CH_2), 125.8 (CH_2), 121.2 (2 × CH_2), 74.4 (CH), 25. 7 (3 × CH_3), 21.2 (CH_3), 18.3 (CMe_3), –5.0 ($SiCH_3$), –5.1 ($SiCH_3$).

EI-HRMS: m/z calcd for $C_{21}H_{29}O_3Si$ [M – t-Bu]$^+$: 357.1886; found: 357.1876.

2-(*tert*-Butyldimethylsilyloxy)-2-[hydroxy(*p*-tolyl)methyl]malononitrile (9)
To a solution of **2a** (120 mg, 1.0 mmol) and **1** (216 mg, 1.1 mmol) in t-BuOH (5.0 mL) was added DMAP (12.2 mg, 0.1 mmol) at r.t. After stirring for 24 h at r.t., the mixture was concentrated in vacuo. Although NMR indicated that **9** was the main product, isolation of **9** by silica gel column chromatography failed because of the reversible reaction back to **1** and **2a**.

^{1}H NMR (300 MHz): δ = 7.43 (d, J = 8.0 Hz, 2 H), 7.22 (d, J = 8.0 Hz, 2 H), 4.97 (s, 1 H), 2.38 (s, 3 H), 0.90 (s, 9 H), 0.35 (s, 3 H), 0.24 (s, 3 H).

^{13}C NMR (75 Hz): δ = 139.8 (C), 131.2 (C), 129.0 (2 × CH_2), 128.8 (2 × CH_2), 114.6 (C≡N), 113.7 (C≡N), 78.4 (CH), 69.0 (C), 25.2 (3 × CH_3), 21.2 (CH_3), 18.0 (CMe_3), –4.6 ($SiCH_3$), –4.8 ($SiCH_3$).

EI-HRMS: m/z calcd for $C_{17}H_{24}N_2O_2Si$ [M]$^+$: 316.1607; found: 316.1611.

3-[(*tert*-Butyldimethylsilyl)oxy]-2-coumaranone (10)
A mixture of salicylaldehyde (54.9 mg, 0.45 mmol), **1** (97 mg, 0.49 mmol), and pyridine (107 mg, 1.35 mmol) in MeCN (10 mL) was stirred at r.t. for 2 d, and then was concentrated in vacuo. The residue was purified by silica gel column chromatography using hexane–EtOAc (20:1) as the eluent to afford **10** (84.8 mg, 0.32 mmol, 71%) as colorless needles; mp 58–59 °C (hexane–EtOAc).

IR ($CHCl_3$): 2932, 2860, 1821, 1466, 1107, 1068, 840 cm^{-1}.

^{1}H NMR (300 MHz): δ = 7.39–7.30 (m, 2 H), 7.17 (t, J = 7.5 Hz, 1 H), 7.07 (d, J = 8.7 Hz, 1 H), 5.31 (s, 1 H), 0.97 (s, 9 H), 0.27 (s, 3 H), 0.25 (s, 3 H).

^{13}C NMR (75 MHz): δ = 174.4 (C=O), 153.5 (C), 130.5 (C), 126.5 (CH), 125.1 (CH), 124.5 (CH), 111.2 (CH), 68.8 (CH), 25.6 (3 × CH_3), 18.3 (CMe_3), –4.3 ($SiCH_3$), –5.0 ($SiCH_3$).

EI-HRMS: *m*/*z* calcd for $C_{14}H_{21}O_3Si$ [M + H]$^+$: 265.1260; found: 265.1245.

Anal. Calcd for $C_{14}H_{20}O_3Si$: C, 63.60; H, 7.62. Found: C, 63.36; H, 7.59.

β-Cholesteryl (2*R*,3*R*)-3-*N*-Benzyloxycarbonylamino-2-[(*tert*-butyldimethylsilyl)oxy]-4-phenylbutanoate (12a) and the 2*S*-Isomer (12b)

To a solution of D-**11**[11] (102.9 mg, 0.364 mmol), **1** (143 mg, 0.730 mmol), and β-cholesterol (1.41 g, 3.653 mmol) in Et_2O (24 mL) was added PPY (53.8 mg, 0.364) at 0 °C, and the mixture was stirred for 12 h at 0 °C. Et_3N (1 mL) was added and the mixture stirred for 5 h to destroy the excess of **1**. The mixture was concentrated in vacuo and the residue was purified by silica gel column chromatography using hexane–EtOAc (10:1–2:1) as the eluent to give **12a** and **12b** (156 mg, 0.193 mmol, 52%), and β-cholesterol (1.29 g, 3.342 mmol, 91% recovered yield). A mixture of **12a** and **12b** (156 mg) was further purified by preparative TLC on silica gel (PTLC) using hexane–EtOAc (20:1) as the eluent to give **12a** (116 mg, 0.143 mmol, 39%) and **12b** (24 mg, 0.030 mmol, 8%).

12a

Amorphous solid; $[\alpha]_D^{22}$ +8.3 (*c* 2.3, $CHCl_3$).

IR ($CHCl_3$): 3437, 2951, 2861, 1744, 1721, 1503, 1143, 839 cm^{-1}.

^{1}H NMR (300 MHz): δ = 7.41–7.05 (m, 10 H), 5.31 (d, *J* = 4.4 Hz, 1 H), 5.17 (d, *J* = 9.7 Hz, 1 H), 5.00 (d, *J* = 12.4 Hz, 1 H), 4.97 (d, *J* = 12.4 Hz, 1 H), 4.67–4.52 (m, 1 H), 4.43–4.28 (m, 1 H), 4.22 (d, *J* = 2.0 Hz, 1 H), 2.95–2.72 (m, 2 H), 2.36–2.14 (m, 2 H), 2.08–1.71 (m, 5 H), 1.70–0.79 (m, 27 H), 0.96 (s, 9 H), 0.92 (d, *J* = 6.2 Hz, 3 H), 0.87 (d, *J* = 6.6 Hz, 6 H), 0.11 (s, 3 H), 0.06 (s, 3 H).

^{13}C NMR (75 MHz): δ = *171.2* (C=O), *155.5* (C=O), 139.3 (C= at C-5), *137.6* (C), *136.6* (C), *129.2, 128.4, 128.0, 127.9, 126.5* (aromatic 10 × CH), 122.8 (CH = at C-6), *75.1* (OCH), 72.5 (CH at C-3), *66.5* (CH_2 of Cbz), 56.7 (CH at C-14), 56.1 (CH at C-17), *55.6* (CH–N), 50.0 (CH at C-9), 42.3 (C at C-13), 39.7 (CH_2 at C-16), 39.5 (CH_2 at C-24), 38.2 (CH_2 at C-4), 37.7 (CH_2 at C-1), 36.9 (CH_2 at C-10), 36.5 (CH_2 at C-22), 36.2 (CH at C-20), *35.8* (CH_2Ph), 31.9 (CH_2 at C-7), 31.8 (CH at C-8), 28.2 (CH_2 at C-2), 28.0 (CH at C-25), 27.6 (CH_2 at C-12), *25.8* (3 × CH_3), 24.3 (CH_2 at C-15), 23.8 (CH_2 at C-23), 22.8 (CH_3 at C-27), 22.5 (CH_3 at C-26), 21.0 (CH_2 at C-11), 19.3 (CH_3 at C-19), 18.7 (CH_3 at C-21), *18.3* (CMe_3), 11.8 (CH_3 at C-18), *–4.5* ($SiCH_3$), *–5.2* ($SiCH_3$) [The assignments in italics belong to the $PhCH_2NH(Cbz)CH(OTBS)CO_2$ moiety].

FAB-HRMS: *m*/*z* calcd for $C_{51}H_{77}NO_5Si$ + Na [M + Na]$^+$: 834.5469; found: 834.5459.

12b

Several broad peaks were observed in both ^{1}H and ^{13}C NMR spectra of **12b** probably because of slow rotation due to steric hindrance. However, the structure of **12b** was confirmed via transformation to **13b**[6] by methanolysis; $[\alpha]_D^{22}$ +9.3 (*c* 0.3, $CHCl_3$).

IR ($CHCl_3$): 3444, 2951, 2933, 2858, 1743, 1720, 1508, 1469, 1283, 1255, 1149, 838 cm^{-1}.

FAB-HRMS: *m*/*z* calcd for $C_{51}H_{77}NO_5Si$ + Na [M + Na]$^+$: 834.5469; found: 834.5447.

Conversion of 12a into 13a

The stereochemistry of **12a** was determined by converting it into **13a**. A mixture of **12a** (21.7 mg, 0.027 mmol) and K_2CO_3 (50 mg) in MeOH (1 mL) was stirred at r.t. for 36 h. The resulting mixture was filtered through a silica gel pad (1 × 3 cm), washed with EtOAc (20 mL), and then concentrated. The residue was purified with preparative TLC using hexane–EtOAc (4:1) as the eluent to give **13a**[6] (8.3 mg, 0.018 mmol, 68%) and a detectable but trace amount of **13b** probably because of partial epimerization), and **12a** (2.6 mg, 12% recovered yield).[12]

Conversion of 12b into 13b

The structure of **12b** was confirmed by converting it into **13b**. A mixture of **12b** (24 mg, 0.030 mmol) and K_2CO_3 (50 mg) in MeOH (1 mL) was stirred at 35 °C for 24 h. The mixture was filtered through a silica gel pad (1 × 3 cm), washed with EtOAc (20 mL), and then concentrated. The residue was purified with preparative TLC using hexane–EtOAc (4:1) as the eluent to give **13b** (11.2 mg, 0.025 mmol, 83%) and a detectable, but trace amount of **13a** probably because of partial epimerization), and β-cholesterol (10.8 mg, 0.028 mmol, 94%).

Methyl 2-[(2*S*,6*S*,1*R*,9*R*)-4,4,11,11-Tetramethyl-3,5,8,10,12-pentaoxatricyclo[7.3.0.0^{2,6}]dodec-7-yl)-2-hydroxyacetate (15a) and its 2*R*-Isomer (15b)

To a solution of aldehyde **14**[13] (93.7 mg, 0.363 mmol), **1** (142 mg, 0.724 mmol), and MeOH (35 mg, 44.3 μL, 1.09 mmol) in Et_2O (18 mL) was added PPY (53.8 mg, 0.364 mmol) at 0 °C. After stirring for 12 h at 0 °C, the mixture was directly purified by silica gel column chromatography using hexane–EtOAc (20:1–3:1) as the eluent to give a mixture of (2*S*)-**15a** and (2*R*)-**15b** (133 mg, 0.308 mmol, 85%). The ratio of **15a** and **15b** (92:8) was determined by ^{1}H NMR spectroscopy.

Major Isomer (2*S*)-15a

^{1}H NMR (300 MHz): δ = 5.54 (d, *J* = 5.1 Hz, 1 H), 4.58 (dd, *J* = 8.1, 2.3 Hz, 1 H), 4.42–4.23 (m, 3 H), 3.92 (dd, *J* = 7.6, 1.4 Hz, 1 H), 3.75 (s, 3 H), 1.57 (s, 3 H), 1.45 (s, 3 H), 1.32 (s, 3 H), 1.31 (s, 3 H), 0.88 (s, 9 H), 0.11 (s, 3 H), 0.10 (s, 3 H).

^{13}C NMR (75 MHz): δ = 171.2 (C=O), 109.4 (O–C–O), 108.7 (O–C–O), 96.3 (anomeric CH), 72.2 (CH), 70.8 (CH), 70.8 (CH), 70.6 (CH), 69.8 (CH), 51.8 (OCH_3), 25.9 (3 × CH_3), 25.6 (CH_3), 25.6 (CH_3), 25.0 (CH_3), 24.5 (CH_3), 18.3 (CMe_3), –4.9 ($SiCH_3$), –5.3 ($SiCH_3$).

Minor Isomer (2*R*)-15b

^{1}H NMR (400 MHz): δ = 5.45 (d, *J* = 4.6 Hz, 1 H), 4.62 (dd, *J* = 8.1, 2.0 Hz, 1 H), 4.42–4.23 (m, 3 H), 4.05 (dd, *J* = 9.4, 1.6 Hz, 1 H), 3.75 (s, 3 H), 1.53 (s, 3 H), 1.43 (s, 3 H), 1.33 (s, 3 H), 1.31 (s, 3 H), 0.89 (s, 9 H), 0.10 (s, 3 H), 0.08 (s, 3 H).

^{13}C NMR (75 MHz): δ = 172.2 (C=O), 108.9 (O–C–O), 108.8 (O–C–O), 95.8 (anomeric CH), 71.1 (CH), 71.0 (CH), 70.3 (CH), 69.3 (CH), 68.8 (CH), 51.8 (OCH_3), 25.9 (3 × CH_3), 25.8 (CH_3), 25.5 (CH_3), 25.0 (CH_3), 23.8 (CH_3), 18.1 (CMe_3), –5.4 ($SiCH_3$), –5.6 ($SiCH_3$).

Methyl (2*RS*,2′*S*,3′*R*,4′*R*,5′*R*,6′*R*)-2-Hydroxy-2-[2′ (3′,4′,5′,6′-di-*O*-isopropylidene)tetrahydropyranyl]acetates (16a and 16b)

A mixture of **15** (128 mg, 0.296 mmol) and TBAF (1.0 M solution in THF, 0.35 mL, 0.350 mmol) in THF (8 mL) was stirred at r.t. for 36 h. The mixture was directly purified by silica gel column chromatography using hexane–EtOAc (2:1) as the eluent to give a mixture of (2*S*)-**16a** and (2*R*)-**16b** (91.4 mg, 0.287mmol, 97%). The ratio of **16a** and **16b** (92:8) was determined by ^{1}H NMR spectroscopy. The stereochemistry of **16a** and **16b** was confirmed with the known compounds[2] by ^{1}H and ^{13}C NMR spectroscopy.

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