Towards the Synthesis of the Cornexistins

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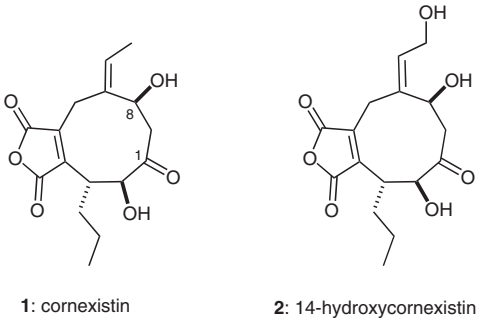
Dedicated to Professor Paul Wender on the occasion of his 60th birthday

Abstract: A concise synthetic route to the carbocyclic core of the cornexistins is reported. The route is highlighted by a Diels–Alder cycloaddition/oxidative cleavage strategy to generate the central highly functionalized nine-member ring. A silyl-tethered ring-closing metathesis strategy is utilized to control trisubstituted alkene geometry.

Key words: Diels–Alder, oxidative cleavage, natural products, ring expansion, ring-closing metathesis, carbocycle

Cornexistin (**1**) (Figure 1) was isolated by Sankyo and reported in 1991.[1] A fungal metabolite of *Paecilomyces variottii* SANK 21086, cornexistin has potent herbicidal activity against broadleaf weed species. At that level of activity, maize plants are insensitive to cornexistin's effects. In 1991, an additional metabolite was found by Dow Agrosciences to be the 14-hydroxy analogue of cornexistin;[2] 14-hydroxycornexistin (**2**) is at least as active as cornexistin, if not more. Both of these molecules are of practical interest to the agrochemical community and are interesting to the synthetic community in terms of their unique structure and functionality.



1: cornexistin **2**: 14-hydroxycornexistin

Figure 1 Cornexistin (**1**) and 14-hydroxycornexistin (**2**), herbicidal natural products

Cornexistin is a member of the nonadride family, which was defined by Barton and Sutherland[3] as a class of molecules that have their biogenesis from the dimerization of nine carbon maleic anhydride units. They typically contain a nine-membered ring, maleic anhydride functionalities, and pendant alkyl groups. In contrast to other nonadrides, cornexistin distinguishes its structure as a consequence of significant biosynthetic oxidative processing. Outside of the best-known example of the nonadrides, the phomoidrides,[4] this remains a relatively unexplored field in the synthetic community. Notable amongst previous nonadride syntheses are Stork's early synthesis of byssochlamic acid,[5] and White's more recent enantioselective total syntheses of byssochlamic acid.[6] Clark has published synthetic routes to cornexistin, including the use of ring-closing metathesis (RCM) technology to close the nine-membered ring.[7]

Our retrosynthesis of the cornexistins (Figure 2) began with the recognition of inherent symmetry of functionality within the nine-membered-ring system. By bisecting the molecule horizontally and noting that oxidation state is fungible, each substituent is mirrored across the ring with the exception of the C3 propyl group. Such a reductionist approach brought us to **3**, where a chemoselective oxidative cleavage would expose a nine-membered cyclic diketone. This cyclohexa-1,4-diene could be clearly derived from a Diels–Alder reaction of dienophile dimethyl acetylenedicarboxylate and readily available **4** as the necessary diene. This strategy is quite reminiscent of Wender's metathetical approach to medium-ring carbocycles.[8]

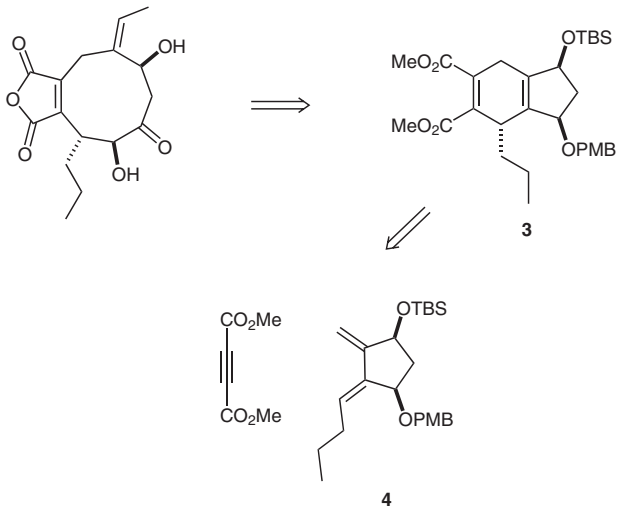


Figure 2 Retrosynthesis towards cornexistin via Diels–Alder/oxidative cleavage strategy

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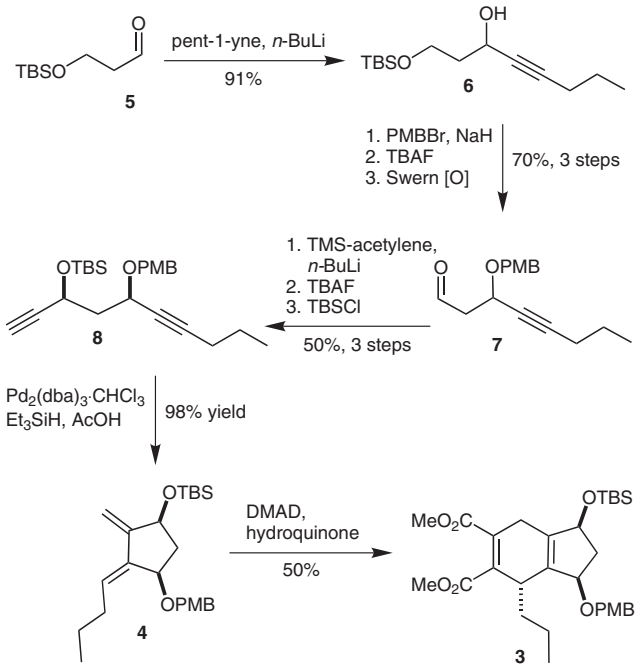
The synthesis of the cyclopentadiene (Scheme 1) began with the aldehyde **5**,[9] which was reacted with lithiated pentyne to give the desired alcohol in 91% yield. The resulting alcohol was protected as the 4-methoxybenzyl ether, the *tert*-butyldimethylsilyl ether was removed using tetrabutylammonium fluoride, and the resulting alcohol oxidized using Swern conditions to provide the desired aldehyde **7** in three steps in 70% yield. Aldehyde **7** was immediately used in the following reaction, where it was reacted with lithiated (trimethylsilyl)acetylene to provide the *syn*- and *anti*-diastereomers.[10] Through careful column chromatography, the diastereomers were separated and the desired *syn*-diastereomer was obtained in good yield. (A Mitsunobu inversion[11] was used to convert the *anti*-diastereomer into the *syn* in moderate yield.)

The desilylation of the terminal alkyne was carried out with tetrabutylammonium fluoride deprotection and the free alcohol was protected under standard conditions as the *tert*-butyldimethylsilyl ether. Diyne **8** was subjected to Trost reductive cyclization[12] conditions to provide the cyclopentadiene **4** in excellent yield. It was then reacted with dimethyl acetylenedicarboxylate to provide the desired cyclohexadiene **3** in moderate yield. The stereochemical relationship between the propyl group and the 4-methoxybenzyl (PMB) ether was under question and ROESY analysis was unfortunately equivocal.



Scheme 1

However, we were able to obtain a crystal for X-ray analysis. It revealed that the relationship between the propyl group and the 4-methoxybenzyl ether was *anti* and thus the facial selectivity of the cycloaddition was controlled by the expected steric influences (Figure 3).[13]

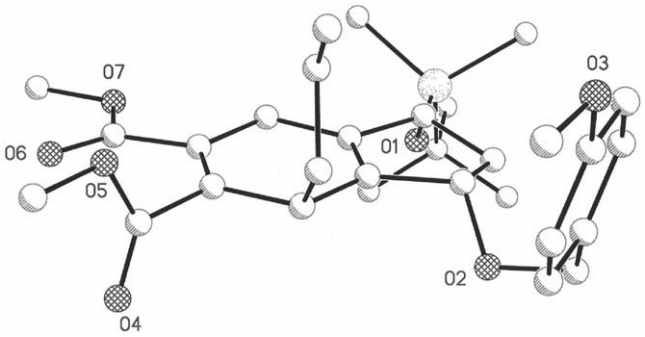
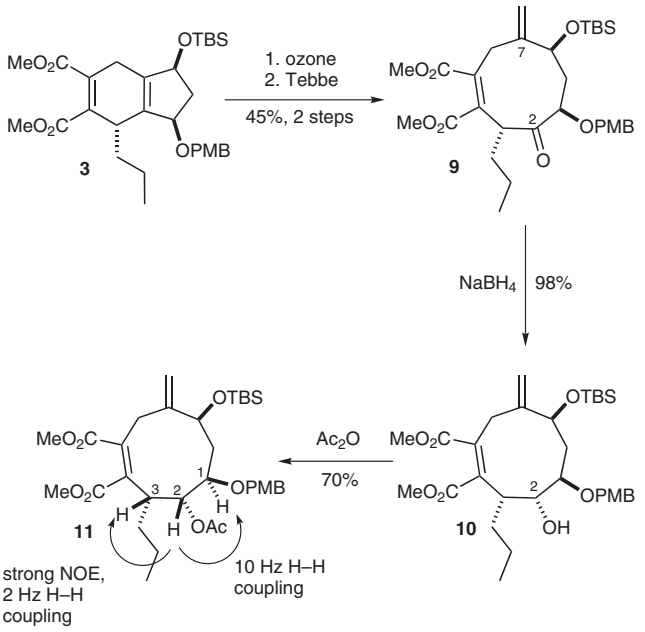


Figure 3 ORTEP representation of cyclohexadiene **3**

With this key intermediate in hand, **3** was oxidatively cleaved to reveal the diketone (Scheme 2). Despite the exploration of several different reagents and conditions for alkenation of the C7 ketone, Tebbe's reagent[14] and an excess of pyridine gave the desired alkene **9** in moderate yield. Then, sodium borohydride reduction of the C2 ketone gave product alcohol **10** in excellent yield as a single diastereomer.

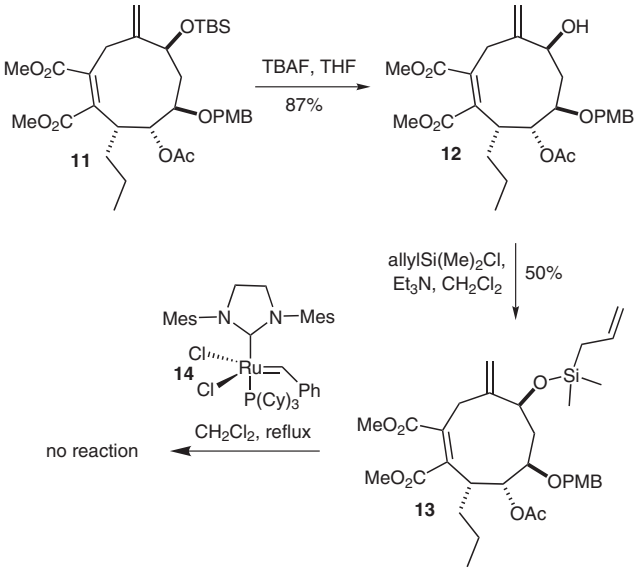


Scheme 2

A number of attempts were made to crystallize this product, including derivatization to the 4-bromobenzoate or the phenyl carbamate. Unfortunately, neither compound was crystalline. NMR analysis of the corresponding acetate **11** revealed a strong NOE between the C2 and C3 hydrogens. Additionally, the multiplicity of the C2 proton supported the 1,2-*trans*-2,3-*cis* relationship. Moreover, computer-based molecular modeling experiments provided a number of low energy conformations that fit this analysis. Although this was not definitive proof, it suggested the assignments of **10** and **11** in Scheme 2.

Completion of the carbon skeleton of the cornexistins required stereoselective alkylation of the 1,1-disubstituted

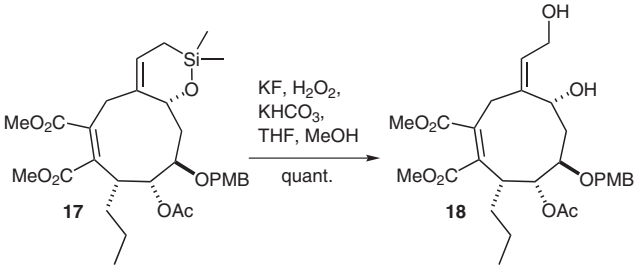
alkene. To achieve this aim, we considered the use of a temporary silicon tether.[15] Silyl group exchange provided ring-closing metathesis precursor **13** (Scheme 3). Unfortunately, only dimeric products were obtained regardless of the choice of ring-closing metathesis catalyst.



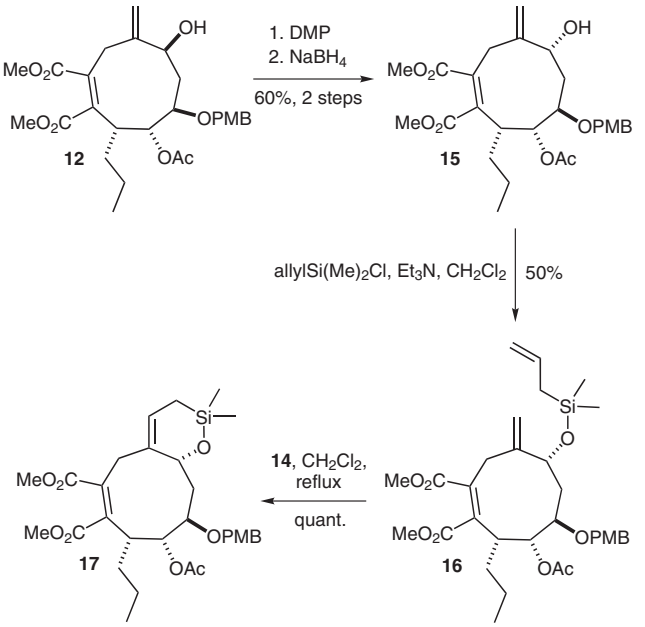
Scheme 3

It was suspected that the molecule was in an inappropriate conformation for the ring-closing metathesis. To alter the conformation of **13**, inversion of the alcohol stereocenter at C8 was accomplished. While Mitsunobu inversion resulted in elimination, an oxidation–reduction sequence was quite fruitful. Dess–Martin oxidation of **12** followed by simple sodium borohydride reduction provided the inverted C8 of **15** (Scheme 4) in good yield with a moderate diastereomeric ratio (4:1). Silyl protection gave desired allyldimethylsilyl ether **16** in 50% yield, which was refluxed in dichloromethane with a catalytic amount of Grubbs' second-generation ruthenium catalyst **14**;[16] this gave desired siloxacycle **17** in quantitative yield.

Having generated **17** successfully, we turned to the manipulation of said siloxacycle to provide both cornexistin and hydroxycornexistin. Initial attempts at protodesilylation of **17** have thus far demonstrated a surprising lack of reactivity. However, inclusion of hydrogen peroxide led to Tamao–Fleming oxidation and diol **18** was obtained in quantitative yield (Scheme 5).[15c,17]



Scheme 5



Scheme 4

In summary, we have generated complex nine-membered-ring carbocycles through the use of a Diels–Alder strategy and subsequent oxidative cleavage. This route has the ability to install the required functionality towards the herbicidal natural products hydroxycornexistin and cornexistin, including the use of ring-closing metathesis technology to install the desired geometry of an exocyclic ethylidene. Further efforts will be reported in due course.

Unless otherwise noted, all materials were used as received from a commercial supplier and used without further purification. All reactions were performed using oven-dried glassware and under an N_2 atmosphere unless otherwise noted. THF, CH_2Cl_2, Et_2O, and toluene were filtered through activated alumina under N_2. DMSO was purchased from a commercial supplier. All reactions were monitored by E. Merck analytical TLC plates (silica gel 60 GF, glass back) and analyzed with 254 nm UV light and anisaldehyde/H_2SO_4 treatment. Silica gel for column chromatography was purchased from E. Merck (Silica Gel 60, 230–400 mesh). Biotage chromatography was performed using Flash 12+M, 25+S, 25+M, and 40+M KP-Sil Silica (32–63 μM, 60 Å, nominally 500 m^2/g silica) cartridges. All ^1H and ^{13}C NMR spectra were obtained on Varian Unity Plus 300 and 500 spectrometers (operating at 299.701 and 499.864 MHz for ^1H and 75.368 MHz and 125.706 MHz for ^{13}C, respectively); $CHCl_3$ was used as an internal reference (^1H: δ = 7.26, ^{13}C: δ = 77.00). FT-IR spectra were obtained on a Perkin-Elmer Paragon 1000 spectrophotometer. MS (FAB) were obtained using 3-nitrobenzyl alcohol (NBA) as a matrix using either a JEOL AX505HA or JEOL JMS-GCmate mass spectrometer.

1-(*tert*-Butyldimethylsiloxy)oct-4-yn-3-ol (6)

To a soln of pent-1-yne (6.09 mL, 0.062 mol, 1.2 equiv) in THF (50 mL) cooled to –78 °C was added 2.5 M BuLi in hexanes (26.83 mL, 0.067 mol, 1.3 equiv) and the mixture was stirred for 30 min. The bath temperature was then warmed to 0 °C for 5 min and then recooled to –78 °C. 3-(*tert*-Butyldimethylsiloxy)propanal (**5**, 9.7 g, 0.052 mol) in THF (25 mL) was added slowly to the mixture. The round-bottom flask was transferred to a 0 °C ice bath and stirred for 4 h. After TLC analysis revealed the completion of the reaction, the

reaction was quenched using sat. NH_4Cl soln and diluted with EtOAc. The aqueous layer was extracted with EtOAc and the combined organic layers were washed with sat. $NaHCO_3$ soln, brine, and H_2O. After drying ($MgSO_4$), the organic layer was concentrated to give a crude yellow oil (12.24 g, 91%). The material was used further without purification.

IR (thin film): 2957, 2931, 2857, 2234, 1613, 1586, 1514, 1463, 1249, 1098, 1038, 834, 776 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.64–4.54 (m, 1 H, C*H*OH), 4.08–3.98 (m, 1 H, CH_2OTBS), 3.86–3.75 (m, 1 H, CH_2OTBS), 3.30 (d, *J* = 5.12 Hz, 1 H, CHO*H*), 2.19 (dt, *J* = 6.96, 2.2 Hz, 2 H, CH_2CHOH), 2.02–1.88 (m, 2 H, C≡CCH_2CH$_2$CH$_3$), 1.54 (sextet, *J* = 6.96 Hz, 2 H, C≡CCH$_2$CH_2CH$_3$), 1.0 (t, *J* = 7.2 Hz, 3 H, C≡CCH$_2$CH$_2$CH_3), 0.93 [s, 9 H, OSi(C(CH_3)$_3$)Me$_2$], 0.1 [s, 6 H, OSi(*t*-Bu)(CH_3)$_2$].

^{13}C NMR (75 MHz, $CDCl_3$): δ = 86.6, 79.5, 70.3, 55.5, 39.5, 26.2, 22.5, 21.0, 13.8, –5.1.

HRMS-FAB: *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{29}O_2Si$: 257.1921; found 257.1937.

1-(*tert*-Butyldimethylsiloxy)-3-(4-methoxybenzyloxy)oct-4-yne

To a soln of **6** (4 g, 0.016 mol) in anhyd DMF (40 mL) at –10 °C was added slowly NaH (95%, 1.49 g, 4 equiv) and the mixture was stirred for 30 min. A soln of 4-methoxybenzyl bromide (4.7 g, 0.023 mol) dissolved in anhyd THF (20 mL) was added slowly to the soln with a catalytic amount of TBAI and the reaction was stirred at 0 °C for 2 h. After TLC analysis revealed that the reaction was complete, the reaction was quenched very slowly with sat. $NaHCO_3$ (10 mL) and diluted with Et_2O. The aqueous layer was extracted with Et_2O and the combined organic layers were washed with brine and H_2O (3 ×). After drying ($MgSO_4$), the organic layer was concentrated to give a pale-yellow oil, which was purified by chromatography (silica gel) to give the desired product (5.64 g, 94%).

IR (thin film): 2957, 2931, 2857, 2234, 1613, 1586, 1514, 1463, 1249, 1098, 1038, 834, 776 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.32 (d, *J* = 8.5 Hz, 2 H, C$_6H_4$OMe), 6.90 (d, *J* = 8.5 Hz, 2 H, C$_6H_4$OMe), 4.71 (d, *J* = 11 Hz, 1 H, OCH_2C$_6$H$_4$OMe), 4.45 (d, *J* = 11 Hz, 1 H, OCH_2C$_6$H$_4$OMe), 4.29 [ddd, *J* = 7.5, 6, 2.2 Hz, 1 H, C*H*(OPMB)], 3.79–3.69 (m, 2 H, CH_2OTBS), 3.80 (s, 3 H, C$_6$H$_4$OCH_3), 2.33 [dt, *J* = 6.96, 1.95 Hz, 2 H, CH_2CH(OPMB)], 2.05–1.80 (m, 2 H, C≡CCH_2CH$_2$CH$_3$), 1.61–1.50 (sextet, 2 H, CCCH$_2$CH_2CH$_3$), 1.0 (t, *J* = 7.21 Hz, 3 H, CCCH$_2$CH$_2$CH_3), 0.93 [s, 9 H, OSi(C(CH_3)$_3$)Me$_2$], 0.1 [s, 6 H, OSi(*t*-Bu)(CH_3)$_2$].

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.4, 130.6, 129.9, 114.0, 86.6, 79.5, 70.3, 65.9, 59.6, 55.5, 39.5, 26.2, 22.5, 21.0, 13.8, –5.1.

HRMS-FAB: *m*/*z* $[M – H]^+$ calcd for $C_{22}H_{35}O_3Si$: 375.2333; found: 375.2355.

3-(4-Methoxybenzyloxy)oct-4-yn-1-ol

To a soln of 1-(*tert*-butyldimethylsiloxy)-3-(4-methoxybenzyloxy)oct-4-yne (6.3 g, 0.017 mol) in THF (25 mL) was added 1 M TBAF in THF (25.1 mL, 0.025 mol, 1.5 equiv) and the mixture was stirred for 3 h. After completion of the reaction, the reaction was quenched with sat. $NaHCO_3$ (10 mL) and separated. The aqueous layer was extracted with EtOAc; the recombined organic layers were washed with brine and subsequently dried and concentrated. Purification by chromatography (silica gel) gave a pale-yellow oil (4.30 g, 96%).

IR (thin film): 3422 (bs), 2961, 2933, 2871, 2837, 2232, 1612, 1514, 1248, 1036, 822, 755 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.29 (d, *J* = 8.8 Hz, 2 H, C$_6H_4$OMe), 6.92–6.89 (d, *J* = 8.8 Hz, 2 H, C$_6H_4$OMe), 4.79–4.75 (d, *J* = 11.4 Hz, 1 H, OCH_2C$_6$H$_4$OMe), 4.48–4.44 (d, *J* = 11.4 Hz, 1 H, OCH_2C$_6$H$_4$OMe), 4.30–4.28 [tt, *J* = 5.86, 1.96 Hz, 1 H, C*H*(OPMB)], 3.90–3.80 (m, 1 H, CH_2OH), 3.80 (s, 3 H, C$_6$H$_4$OCH_3), 3.80–3.70 (m, 1 H, CH_2OH), 2.27–2.20 (td, *J* = 6.96, 1.96 Hz, 2 H, C≡CCH_2CH$_2$CH$_3$), 2.01–1.90 [dd, *J* = 5.62, 11.36 Hz, 2 H, CH_2CH(OPMB)], 1.61–1.50 (sextet, 2 H, C≡CCH$_2$CH_2CH$_3$), 1.0 (t, *J* = 7.2 Hz, 3 H, C≡CCH$_2$CH$_2$CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.6, 130.0, 129.9, 114.1, 87.5, 78.6, 70.4, 68.0, 60.7, 55.5, 38.5, 22.4, 21.0, 13.8.

HRMS-FAB: *m*/*z* $[M]^+$ calcd for $C_{16}H_{22}O_3$: 262.1553; found: 262.1569.

3-(4-Methoxybenzyloxy)oct-4-ynal (7)

To a soln of oxalyl chloride (0.745 mL, 8.69 mmol, 1.6 equiv) dissolved in CH_2Cl_2 (15.4 mL, cooled to –78 °C) was added dropwise DMSO (1.22 mL, 17.1 mmol, 3.13 equiv). The mixture was stirred for 30 min and then 3-(4-methoxybenzyloxy)oct-4-yn-1-ol (1.43 g, 5.45 mmol) in CH_2Cl_2 (2 mL) was added followed immediately by the addition of Et_3N (2.5 mL, 17.9 mmol). After 15 min (and the formation of a white slurry in the mixture), Et_3N (2.5 mL, 17.9 mmol) was again added and the reaction was warmed to 0 °C and stirred for 1 h. The mixture was then diluted with Et_2O (40 mL) and washed with sat. $NaHCO_3$, brine, and H_2O, dried and concentrated to give a brown oil that was subjected to column chromatography (silica gel). This gave **7** as a pale yellow oil (1.02 g, 72% yield), which was subjected immediately to the following reaction.

IR (thin film): 2963, 2934, 2871, 2837, 2727, 2231, 1728, 1613, 1514, 1464, 1336, 1302, 1249, 1174, 1073, 1035, 823, 758 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 9.34 (t, *J* = 2.24 Hz, 1 H, CH$_2$C*H*O), 7.29 (d, *J* = 8.8 Hz, 2 H, C$_6H_4$OMe), 6.89 (d, *J* = 8.8 Hz, 2 H, C$_6H_4$OMe), 4.79 (d, *J* = 11.4 Hz, 1 H, OCH_2C$_6$H$_4$OMe), 4.45 (d, *J* = 11.4 Hz, 1 H, OCH_2C$_6$H$_4$OMe), 4.52 [tt, *J* = 5.86, 1.96 Hz, 1 H, C*H*(OPMB)], 3.80 (s, 3 H, C$_6$H$_4$OCH_3), 2.86–2.68 [m, 2 H, CH(OPMB)CH_2CHO], 2.27 (td, *J* = 6.96, 1.96 Hz, 2 H, C≡CCH_2CH$_2$CH$_3$), 1.61 (sextet, *J* = 7.25 Hz, 2 H, C≡CCH$_2$CH_2CH$_3$), 1.0 (t, *J* = 7.2 Hz, 3 H, C≡CH$_2$CH$_2$CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 200.6, 159.6, 130.0, 129.8, 114.0, 88.4, 76.9, 70.4, 63.5, 55.5, 49.4, 22.3, 20.9, 13.7

HRMS-FAB: *m*/*z* $[M]^+$ calcd for $C_{16}H_{20}O_3$: 260.1412, found: 260.1426.

5-(4-Methoxybenzyloxy)-1-(trimethylsilyl)deca-1,6-diyn-3-ol

To a soln of (trimethylsilyl)acetylene (0.82 mL, 5.77 mmol, 1.2 equiv) dissolved in anhyd THF (10 mL) (cooled to –78 °C) was added a soln of 2.6 M BuLi in hexanes (2.22 mL, 5.77 mmol, 1.2 equiv) and the mixture was stirred for 30 min. The soln was then warmed to 0 °C for 5 min and recooled to –78 °C. 3-(4-Methoxybenzyloxy)oct-4-ynal (1.25 g, 4.81 mmol) dissolved in THF (5 mL) was added slowly to the mixture. The mixture was stirred for 4 h at 0 °C. After TLC analysis showed the reaction was complete, it was quenched with the addition of sat. NH_4Cl (5 mL) and separated. The aqueous layers were extracted with EtOAc (3 ×) and the combined organic layers were washed with brine and H_2O, concentrated, and dried ($MgSO_4$). The crude yellow oil was then subjected to careful purification via column chromatography (silica gel) to give the desired *syn*-product (0.78 g) and its *anti*-diastereomer (0.45 g) (71% overall yield).

***syn*-Diastereomer**

IR (thin film): 3432, 2962, 2935, 2871, 2837, 2173, 1613, 1586, 1514, 1249, 1174, 1089, 1072, 1036, 844, 760 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.28 (d, *J* = 8 Hz, 2 H, C$_6H_4$OMe), 6.84 (d, *J* = 8 Hz, 2 H, C$_6H_4$OMe), 4.73 (d, *J* = 11.1 Hz, 1 H, OCH_2C$_6$H$_4$OMe), 4.62 [td, *J* = 8.55, 4.57 Hz, 1 H, C*H*(OPMB)], 4.46 (d, *J* = 11.3 Hz, 1 H, OCH_2C$_6$H$_4$OMe), 4.27 [ddd, *J* = 7.33,

3.97, 2.14 Hz, 1 H, C*H*(OH)], 3.81 (s, 3 H, $C_6H_4OCH_3$), 2.75 (d, *J* = 4.27 Hz, 1 H, CHO*H*), 2.30–2.22 [m, 3 H, CH_2CH(OPMB), $C{\equiv}CCH_aH_bCH_2CH_3$], 2.05–1.91 (m, 1 H, $C{\equiv}CCH_aH_bCH_2CH_3$), 1.59 (sextet, *J* = 7 Hz, 2 H, $C{\equiv}CCH_2CH_2CH_3$), 1.0 (t, *J* = 7 Hz, 3 H, $C{\equiv}CCH_2CH_2CH_3$), 0.1 [s, 9 H, $OSiC(CH_3)_3$].

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.6, 130.0, 129.9, 114.1, 105.9, 89.7, 87.7, 78.4, 70.4, 67.0, 61.4, 55.5, 43.9, 22.3, 21.0, 13.8, 0.1.

HRMS-FAB: *m*/*z* [M – 1]$^+$ calcd for $C_{21}H_{29}O_3Si$: 357.1886; found: 357.1860.

***anti*-Diastereomer**

IR (thin film): 3449, 2962, 29334, 2872, 2837, 2172, 1617, 1587, 1514, 1249, 1174, 1070, 1036, 843, 760 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29 (d, *J* = 8 Hz, 2 H, C_6H_4OMe), 6.85 (d, *J* = 8 Hz, 2 H, C_6H_4OMe), 4.76 (d, *J* = 11.2 Hz, 1 H, $OCH_2C_6H_4OMe$), 4.62 [ddd, *J* = 12.67, 6.63, 2.19 Hz, 1 H, C*H*(OPMB)], 4.54 (ddd, *J* = 8.56, 3.85, 1.93 Hz, 1 H, C*H*OH), 4.44 (d, *J* = 10.9 Hz, 1 H, $OCH_2C_6H_4OMe$), 3.81 (s, 3 H, $C_6H_4OCH_3$), 2.75 (d, *J* = 6.85 Hz, 1 H, CHO*H*), 2.33–2.06 [m, 4 H, CH_2CH(OPMB), $C{\equiv}CCH_2CH_2CH_3$], 1.59 (sextet, *J* = 7 Hz, 2 H, $C{\equiv}CCH_2CH_2CH_3$), 1.03 (t, *J* = 7 Hz, 3 H, $C{\equiv}CCH_2CH_2CH_3$), 0.1 [s, 9 H, $OSiC(CH_3)_3$].

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.6, 130.0, 129.7, 114.1, 106.0, 89.7, 87.7, 78.1, 70.8, 67.2, 61.1, 55.5, 42.8, 22.3, 21.0, 13.8, 0.15.

HRMS-FAB: *m*/*z* [M – 1]$^+$ calcd for $C_{21}H_{29}O_3Si$: 357.1886; found: 357.1867.

3-(*tert*-Butyldimethylsiloxy)-5-(4-methoxybenzyloxy)deca-1,6-diyne (8)

To a soln of 5-(4-methoxybenzyloxy)-1-(trimethylsilyl)deca-1,6-diyn-3-ol (0.781 g, 2.18 mmol) dissolved in THF (25 mL) and added 1 M TBAF in THF (3.27 mL, 3.27 mmol, 1.5 equiv). The reaction was stirred for 3 h. Upon completion of the reaction, it was quenched with sat. $NaHCO_3$. The aqueous layer was extracted with EtOAc and the combined organic layers were washed with brine and H_2O, dried, and concentrated. The crude product was not purified but subjected immediately to the next reaction. The crude alcohol mixture was dissolved in DMF (10 mL), to which was added TBSCl (0.656 g, 4.36 mmol, 2 equiv) and imidazole (0.445 g, 6.53 mmol, 3 equiv.) The mixture was stirred for 4 h; when TLC analysis showed the reaction was complete, it was quenched with sat. $NaHCO_3$. The aqueous layer was extracted with EtOAc and the combined organic layers were washed with brine and H_2O, dried, and concentrated. The crude oil was subjected to column chromatography (silica gel) to give **8** as a clear yellow oil (0.657 g, 75%, 2 steps).

IR (thin film): 3309, 2959, 2953, 2858, 2225, 1613, 1587, 1514, 1464, 1250, 1094, 1039, 839, 779, 657 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29 (d, *J* = 8 Hz, 2 H, C_6H_4OMe), 6.88 (d, *J* = 8 Hz, 2 H, C_6H_4OMe), 4.72 (d, *J* = 11.1 Hz, 1 H, $OCH_aH_bC_6H_4OMe$), 4.62 [td, *J* = 5.86, 1.96 Hz, 1 H, C*H*(OPMB)], 4.46 (d, *J* = 11.1 Hz, 1 H, $OCH_aH_bC_6H_4OMe$), 4.27 [t, *J* = 7.49 Hz, 1 H, C*H*(OTBS)], 3.80 (s, 3 H, $C_6H_4OCH_3$), 2.38 (d, *J* = 2 Hz, 1 H, C≡C*H*), 2.29–2.19 [m, 2 H, $C{\equiv}CCH_2CH_2CH_3$, and m, 1 H, CH_aH_bCH(OPMB)], 2.05–1.91 [m, 1 H, CH_aH_bCH(OPMB)], 1.61 (sextet, *J* = 7 Hz, 2 H, $C{\equiv}CCH_2CH_2CH_3$), 1.0 (t, *J* = 7 Hz, 3 H, $C{\equiv}CCH_2CH_2CH_3$), 0.8 [s, 9 H, $OSi(C(CH_3)_3)Me_2$], 0.1 [2 s, 6 H, OSi(*t*-Bu)$(CH_3)_2$].

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.4, 130.3, 129.9, 114.0, 130.3, 129.9, 114.0, 87.3, 85.1, 78.6, 72.7, 70.3, 66.0, 60.3, 55.5, 44.8, 26.0, 22.4, 21.0, 18.4, 13.8, –4.3, –5.0.

HRMS-FAB: *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{37}O_3Si$: 401.2512; found: 401.2513.

1-(*tert*-Butyldimethylsiloxy)-3-butylidene-4-(4-methoxybenzyloxy)-2-methylenecyclopentane (4)

To a soln of benzene (6 mL, degassed for 10 min) at r.t. was added $Pd_2(dba)_3$ (42 mg, 0.041 mmol, 0.025 equiv) and tri-*o*-tolylphosphine (50 mg, 0.164 mmol, 0.1 equiv) and the mixture was stirred for 5 min. After 5 min, glacial AcOH (0.188 mL, 3.28 mmol, 2 equiv) and Et_3SiH (2.62 mL, 16.4 mmol, 10 equiv) was added and the mixture was stirred for 5 min. After 5 min, a soln of diyne **8** (0.657 g, 1.64 mmol) dissolved in benzene (5 mL) was added and the mixture was stirred for exactly 1 h. The mixture was then concentrated to a thick black slurry and loaded onto a chromatography column (silica gel) for immediate purification; elution gave **4** as a pale yellow oil (0.651 g, 99%).

IR (thin film): 3309, 2959, 2953, 2858, 2225, 1613, 1587, 1514, 1464, 1250, 1094, 1039, 839, 779, 657 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.30 (d, *J* = 8 Hz, 2 H, C_6H_4OMe), 6.90 (d, *J* = 8 Hz, 2 H, C_6H_4OMe), 6.1 (td, *J* = 6.1 Hz, 2.3 Hz, 1 H, =C*H*Pr), 5.30 (d, *J* = 2.3 Hz, 1 H, $C{=}CH_aH_b$), 4.91 (d, *J* = 2.3 Hz, 1 H, $C{=}CH_aH_b$), 4.52–4.44 [d, *J* = 11 Hz, 1 H, $OCH_aH_bC_6H_4OMe$ and m, 1 H, C*H*(OPMB)], 4.40–4.33 [d, *J* = 11 Hz, 1 H, $OCH_aH_bC_6H_4OMe$ and m, 1 H, C*H*(OTBS)], 3.80 (s, 3 H, $C_6H_4OCH_3$), 2.49–2.38 [m, 1 H, CH(OTBS)CH_aH_bCH(OPMB)], 2.29–2.15 [m, 2 H, CH(OTBS)CH_aH_bCH(OPMB), $=CHCH_aH_bCH_2CH_3$], 1.76–1.68 (m, 1 H, $=CHCH_aH_bCH_2CH_3$), 1.42–1.2 (m, 2 H, $=CHCH_2CH_2CH_3$), 0.8 [s, 9 H, $OSi(C(CH_3)_3)Me_2$], 0.7 (t, *J* = 7 Hz, 3 H, $=CHCH_2CH_2CH_3$), 0.06 [2 s, 6 H, OSi(*t*-Bu)$(CH_3)_2$].

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.3, 151.6, 137.4, 129.8, 129.4, 129.3, 113.9, 102.7, 75.2, 72.6, 69.3, 55.5, 40.3, 30.9, 26.2, 22.9, 18.5, 14.3, –4.3, –4.5.

HRMS-FAB: *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{39}O_3Si$: 403.2668; found: 403.2649.

Dimethyl 1-(*tert*-Butyldimethylsiloxy)-3-(4-methoxybenzyloxy)-4-propyl-2,3,4,7-tetrahydro-1*H*-indene-5,6-dicarboxylate (3)

To a soln of cyclopentadiene **4** (0.651 g, 1.62 mmol) dissolved in toluene (10 mL) was added DMAD (0.248 mL, 2.02 mmol, 1.25 equiv) and hydroquinone (cat.). The reaction was refluxed for 4 h and then concentrated to a thick oil. The crude concentrate was subjected to column chromatography (silica gel) and yielded **3** as a yellow solid (442 mg, 50%).

IR (thin film): 2954, 2932, 2857, 1726, 1612, 1514, 1251, 1055, 838, 776, 665 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.30 (d, *J* = 8 Hz, 2 H, C_6H_4OMe), 6.90 (d, *J* = 8 Hz, 2 H, C_6H_4OMe), 4.57 [t, *J* = 6 Hz, 1 H, C*H*(OTBS)], 4.52 (d, *J* = 11 Hz, 1 H, $OCH_aH_bC_6H_4OMe$), 4.40–4.33 [d, *J* = 11 Hz, 1 H, $OCH_aH_bC_6H_4OMe$ and m, 1 H, C*H*(OPMB)], 3.80–3.73 (3 s, 9 H, 2 CO_2Me, $C_6H_4OCH_3$), 3.62–3.54 (m, 1 H, C*H*Pr), 3.19 [dd, *J* = 22, 7.7 Hz, 1 H, $C{=}CRCH_aH_bC(CO_2Me)$], 2.94 [ddd, *J* = 22, 7.7, 2 Hz, 1 H, $C{=}CRCH_aH_bC(CO_2Me)$], 2.72 [dt, *J* = 13.8, 7 Hz, 1 H, CH(OTBS)CH_aH_bCH(OPMB)], 1.65 [dt, *J* = 13.2, 5 Hz, 1 H, CH(OTBS)CH_aH_bCH(OPMB)], 1.54–1.44 [m, 2 H, $CH(CH_2CH_2CH_3)$], 1.24–1.10 [m, 2 H, $CH(CH_2CH_2CH_3)$], 0.8 [s, 9 H, $OSi(C(CH_3)_3)Me_2$], 0.7 [t, *J* = 7 Hz, 3 H, $CH(CH_2CH_2CH_3)$], 0.06 [2 s, 6 H, OSi(*t*-Bu)$(CH_3)_2$].

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.5, 168.0, 159.4, 140.3, 138.3, 136.4, 130.9, 130.9, 129.6, 113.9, 78.8, 74.9, 69.8, 55.5, 52.5, 52.4, 41.3, 36.9, 32.6, 26.1, 26.1, 18.3, 18.0, 14.5, –4.2, –4.5.

HRMS-FAB: *m*/*z* [M – H]$^+$ calcd for $C_{30}H_{43}O_7Si$: 543.2778; found: 543.2797.

Dimethyl 7-(*tert*-Butyldimethylsiloxy)-5-(4-methoxybenzyloxy)-4,8-dioxo-3-propylcyclonon-1-ene-1,2-dicarboxylate

A soln of **3** (1.78 g, 3.29 mmol) and Sudan III dye (1.5 mL, 0.1 wt%) dissolved in CH_2Cl_2–MeOH (2:1, 40 mL) at –78 °C was saturated with O_2 gas for 10 min. The mixture was subjected to ozone until the soln color had gone from a deep red to a light pink or orange. The mixture was again saturated with O_2 gas for 10 min; following this, thiourea (3 g) was added and the mixture was stirred at r.t. for 4 h. The mixture was then filtered to remove solids, concentrated to a thick oil, redissolved in Et_2O and then washed with brine and H_2O. The organic layer was then dried ($MgSO_4$) and concentrated to give a viscous yellow oil. The oil was subjected to column chromatography (silica gel) to give a pale, viscous yellow oil (1.57 g, 83%).

IR (thin film): 2955, 1726, 1613, 1514, 1465, 1436, 1252, 1106, 1076, 1038, 913, 837, 781 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.27 (d, *J* = 6.4 Hz, 2 H, C_6H_4OMe), 6.82 (d, *J* = 6.4 Hz, 2 H, C_6H_4OMe), 4.59 [dd, *J* = 8.99, 4.50 Hz, 1 H, C*H*(OTBS)], 4.43 (d, *J* = 9.20 Hz, 1 H, $OCH_aH_bC_6H_4OMe$), 4.40 (t, *J* = 4.71 Hz, 1 H, C*H*Pr), 4.29 (d, *J* = 10.7 Hz, 1 H, $OCH_2C_6H_4OMe$), 4.20 [dd, *J* = 10.28, 5.14 Hz, 1 H, C*H*(OPMB)], 3.84–3.79 (2 s, 6 H, 2 CO_2CH_3), 3.75 (s, 3 H, $C_6H_4OCH_3$ and m, 1 H, C6 methylene), 3.40 (d, *J* = 12.62 Hz, 1 H, C6 methylene), 2.41 [dt, *J* = 14.55, 4.72 Hz, 1 H, CH(OTBS)-CH_aH_bCH(OPMB)], 2.15–2.02 [m, 1 H, $CH(CH_aH_bCH_2CH_3)$], 1.97 [ddd, *J* = 14.34, 10.2, 4.02 Hz, 1 H, $CH(OTBS)CH_aH_bCH$(OPMB)], 1.41–1.10 [m, 3 H, $CH(CH_aH_bCH_2CH_3)$, $CH(CH_2CH_2CH_3)$] 0.93 [t, *J* = 7.36 Hz, 3 H, $CH(CH_2CH_2CH_3)$], 0.8 [s, 9 H, $OSi(C(CH_3)_3)Me_2$], 0.01 [2 s, 6 H, $OSi(t\text{-}Bu)(CH_3)_2$].

^{13}C NMR (75 MHz, $CDCl_3$), δ = 208.6, 207.3, 167.6, 166.9, 159.5, 142.5, 131.6, 130.3, 130.0, 113.9, 78.0, 76.0, 71.7, 55.5, 53.2, 53.2, 52.7, 51.3, 41.3, 37.1, 29.3, 25.9, 20.7, 18.3, 14.5, –4.8, –5.1.

HRMS-FAB: *m*/*z* $[M - 1]^+$ calcd for $C_{30}H_{44}O_9Si$: 575.2797; found: 575.2676.

Dimethyl 7-(*tert*-Butyldimethylsiloxy)-5-(4-methoxybenzyloxy)-8-methylene-4-oxo-3-propylcyclonon-1-ene-1,2-dicarboxylate (9)

Diketone (0.150 g, 0.260 mmol) was dissolved in THF (4.7 mL) with pyridine (0.147 mL, 1.82 mmol, 7 equiv) and cooled to –15 °C to –22 °C. A 0.5 M soln of the Tebbe reagent in toluene (0.520 mL, 0.260 mmol, 1 equiv) was then added dropwise to the mixture, which was carefully maintained at a constant temperature. TLC analysis was used to monitor the progress of the reaction; typically, after 2 h, the reaction was complete. An equivalent amount of THF was syringed into the mixture, followed by the dropwise addition of 15% aq NaOH soln (4 mL). Stirring at low temperatures for ~20 min produced a dark blue soln, which announced the final destruction of the Tebbe reagent and formation of the aluminoxane byproduct. After the addition of $MgSO_4$, the mixture was filtered and concentrated to give a dark yellow oil that was immediately subjected to column chromatography. Chromatography gave **9** as a pale yellow oil (80 mg, 54%).

IR (thin film): 2955, 2931.4, 2858, 2360, 1727, 1613, 1586, 1514, 1463, 1435, 1390, 1362, 1174, 1042, 953, 916, 838, 779, 671 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.27 (d, *J* = 8.6 Hz, 2 H, C_6H_4OMe), 6.81 (d, 2 H, 8.6 Hz, 2 H, C_6H_4OMe), 4.96 (2 s, 2 H, $C{=}CH_2$), 4.52 (d, *J* = 11 Hz, 1 H, $OCH_aH_bC_6H_4OMe$), 4.46–4.38 [m, 2 H, C*H*(OTBS), C*H*Pr], 4.32 [dd, *J* = 9.16, 6.23 Hz, 1 H, C*H*(OPMB)], 4.26 (d, *J* = 11 Hz, 1 H, $OCH_aH_bC_6H_4OMe$), 3.79–3.78 (2 s, 6 H, 2 CO_2CH_3), 3.73 (s, 3 H, $C_6H_4OCH_3$), 3.44 (d, *J* = 13.55 Hz, 1 H, C6 methylene), 3.28 (d, *J* = 14.28 Hz, 1 H, C6 methylene), 2.16–1.94 [m, 3 H, $CH(OTBS)CH_2CH$(OPMB), $CH(CH_aH_bCH_2CH_3)$], 1.41–1.10 [m, 3 H, $CH(CH_aH_bCH_2CH_3)$, $CH(CH_2CH_2CH_3)$], 0.93 [t, *J* = 7.36 Hz, 3 H, $CH(CH_2CH_2CH_3)$], 0.8 [s, 9 H, $OSi(C(CH_3)_3)Me_2$], 0.01 [2 s, 6 H, $OSi(t\text{-}Bu)(CH_3)_2$].

^{13}C NMR (75 MHz, $CDCl_3$) δ = 208.6, 168.4, 168.0, 159.4, 146.0, 138.4, 137.9, 130.6, 130.0, 115.6, 113.9, 78.9, 76.0, 72.9, 71.5, 55.5, 52.7, 52.4, 50.1, 44.8, 31.0, 29.4, 26.0, 20.7, 18.4, 14.4, –5.0.

HRMS-FAB: *m*/*z* $[M - H]^+$ calcd for $C_{31}H_{45}O_8Si$: 573.2884; found: 573.2892.

Dimethyl 7-(*tert*-Butyldimethylsiloxy)-4-hydroxy-5-(4-methoxybenzyloxy)-8-methylene-3-propylcyclonon-1-ene-1,2-dicarboxylate (10)

To a soln of ketone **9** (0.048 g, 0.0836 mmol) dissolved in MeOH (24 mL) at 0 °C was added $NaBH_4$ (4.74 mg, 0.125 mmol, 1.5 equiv) and stirred for 3 h at 0 °C. After TLC analysis showed the reaction was complete, the reaction was diluted with EtOAc and washed with brine and H_2O. The organic layer was then dried ($MgSO_4$) and concentrated. The crude product was purified via column chromatography (silica gel) and isolated to provide alcohol **10** as a clear oil (45 mg, 93%).

IR (thin film): 3438, 2954, 2854, 1725, 1612, 1513, 1460, 1434, 1252, 1065, 907, 837, 777 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.27 (d, *J* = 6.7 Hz, 2 H, C_6H_4OMe), 6.88 (d, *J* = 6.7 Hz, 2 H, C_6H_4OMe), 4.94 (s, 1 H, $C{=}CH_aH_b$), 4.80 (s, 1 H, $C{=}CH_aH_b$), 4.61 (d, *J* = 11.5 Hz, 1 H, $OCH_aH_bC_6H_4OMe$), 4.51 (d, *J* = 10.35 Hz, 1 H, $OCH_aH_bC_6H_4OMe$), 4.22 [dd, *J* = 8.18, 5.88 Hz, 1 H, C*H*(OTBS)], 3.85–3.79 (2 s, 6 H, 2 CO_2CH_3), 3.74 (s, 3 H, $C_6H_4OCH_3$), 3.58 (ddd, *J* = 9.15, 6.71, 2.93 Hz, 1 H, C*H*Pr), 3.38–3.27 [m, 1 H, C*H*(OPMB) and d, *J* = 14.3 Hz, 1 H, C6 methylene], 3.14 (dt, *J* = 9.42, 4.88 Hz, 1 H, C*H*OH), 3.06 (d, *J* = 14.41 Hz, 1 H, C6 methylene), 2.03 [ddd, *J* = 15.62, 5.86, 4.27 Hz, 1 H, $CH(OTBS)CH_aH_bCH$(OPMB)], 1.82–1.54 [m, 3 H, CH(OTBS)-CH_aH_bCH(OPMB), $CH(CH_2CH_2CH_3)$], 1.42–1.30 [m, 2 H, $CH(CH_2CH_2CH_3)$], 0.93 [t, *J* = 7.36 Hz, 3 H, $CH(CH_2CH_2CH_3)$], 0.8 [s, 9 H, $OSi(C(CH_3)_3)Me_2$], 0.01 [2 s, 6 H, $OSi(t\text{-}Bu)(CH_3)_2$].

^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.1, 168.9, 159.5, 147.8, 140.5, 136.5, 131.0, 116.7, 114.0, 78.9, 77.7, 75.7, 72.9, 55.5, 52.7, 52.6, 41.6, 41.4, 32.4, 28.7, 26.0, 21.1, 18.3, 14.4, –4.5, –4.6.

HRMS-FAB: *m*/*z* $[M + H]^+$ calcd for $C_{31}H_{49}O_8Si$: 577.3197; found: 577.3194.

Dimethyl 4-Acetoxy-7-(*tert*-butyldimethylsiloxy)-5-(4-methoxybenzyloxy)-8-methylene-3-propylcyclonon-1-ene-1,2-dicarboxylate (11)

To a soln of alcohol **10** (31 mg, 0.0538 mmol) in pyridine (3 mL) was added Ac_2O (0.75 mL, 7.91 mmol) and DMAP (cat.) at r.t.; the mixture was stirred overnight. After dilution with EtOAc, the organic layer was washed sat. NH_4Cl (2 ×) and brine (1 ×). The organic layer was then dried ($MgSO_4$) and concentrated. Column chromatography (silica gel) yielded acetate **11** as a clear oil (23 mg, 70%).

IR (thin film): 2954, 2858, 1741, 1612, 1514, 1464, 1433, 1371, 1250, 1104, 1039, 907, 837, 776 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.20 (d, *J* = 8.67 Hz, 2 H, C_6H_4OMe), 6.83 (d, *J* = 8.67 Hz, 2 H, C_6H_4OMe), 5.21 (s, 1 H, $C{=}CH_aH_b$), 5.08 (dd, *J* = 10.14, 2.32 Hz, 1 H, C*H*OAc), 4.91 (s, 1 H, $C{=}CH_aH_b$), 4.41 (AB q, *J* = 11.7 Hz, 2 H, $OCH_2C_6H_4OMe$), 4.32 [t, *J* = 6.73 Hz, 1 H, C*H*(OTBS)], 3.79–3.76 (2 s, 6 H, 2 CO_2CH_3), 3.68 (s, 3 H, $C_6H_4OCH_3$), 3.65–3.59 (m, 1 H, C*H*Pr), 3.40 [ddd, *J* = 10.62, 7.93, 3.05 Hz, 1 H, C*H*(OPMB)], 3.28 (d, *J* = 15.02 Hz, 1 H, C6 methylene), 3.21 (d, *J* = 14.89 Hz, 1 H, C6 methylene), 2.18 [ddd, *J* = 16.61, 5.25, 3.17 Hz, 1 H, $CH(OTBS)CH_aH_bCH$(OPMB)], 2.00 (s, 3 H, $OCOCH_3$), 1.90 [ddd, *J* = 15.26, 9.04, 7.57 Hz, 1 H, $CH(OTBS)CH_aH_bCH$(OPMB)], 1.80–1.65 [m, 1 H,

CH(CH_aH$_b$CH$_2$CH$_3$)], 1.52–1.22 [m, 3 H, CH(CH$_a$$H_bCH_2CH_3$), CH(CH$_2CH_2CH_3$)], 0.93 [t, J = 7.36 Hz, 3 H, CH(CH$_2$CH$_2$CH_3)], 0.90 [s, 9 H, OSi(C(CH_3)$_3$)Me$_2$], 0.01 [2 s, 6 H, OSi(*t*-Bu)(CH_3)$_2$].

^{13}C NMR (75 MHz, CDCl$_3$): δ = 170.4, 168.7, 168.3, 159.3, 148.5, 142.3, 134.6, 130.9, 129.5, 116.0, 113.9, 74.4, 72.5, 55.5, 52.6, 51.9, 43.7, 40.8, 32.6, 29.5, 26.0, 21.1, 20.9, 18.3, 14.5, –4.6, –4.5.

HRMS-FAB: *m*/*z* [M – H]$^+$ calcd for C$_{33}$H$_{49}$O$_9$Si: 617.3146; found: 617.3177.

Dimethyl 4-Acetoxy-7-hydroxy-5-(4-methoxybenzyloxy)-8-methylene-3-propylcyclonon-1-ene-1,2-dicarboxylate (12)

To a soln of acetate **11** (14 mg, 0.0226 mmol) in THF (1 mL) was added 1 M TBAF in THF (45 μL, 0.045 mmol, 2 equiv) and stirred for 2 h. After completion of the reaction, the reaction was quenched with sat. NaHCO$_3$ and separated. The aqueous layer was extracted with EtOAc; the recombined organic layers were washed with brine and subsequently dried and concentrated. Purification (silica gel) gave product alcohol **12** as a pale yellow oil (10 mg, 87%).

IR (thin film): 3504, 2954, 2873, 1724, 1612, 1586, 1514, 1458, 1433, 1373, 1248, 1174, 1078, 1036, 906, 850, 821, 756 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ = 7.17 (d, J = 8.42 Hz, 2 H, C$_6$$H_4$OMe), 6.84 (d, J = 8.6 Hz, 2 H, C$_6$$H_4$OMe), 5.15 (s, 2 H, C=C$H_2$), 5.10 (dd, J = 7.33, 2.56 Hz, 1 H, CHOAc), 4.41 (d, J = 11.7 Hz, 1 H, OCH_aH$_b$C$_6$H$_4$OMe), 4.39 (d, J = 11 Hz, 1 H, OCH$_a$$H_bC_6H_4$OMe), 4.16 (dd, J = 8.79, 4.03 Hz, 1 H, CHOH), 3.79–3.76 (2 s, 6 H, 2 CO$_2$CH_3), 3.68 (s, 3 H, C$_6$H$_4$OCH_3), 3.52–3.42 (m, 1 H, CHPr and d, J = 15.39 Hz, 1 H, C6 methylene), 3.38–3.30 [m, 1 H, CH(OPMB)], 3.12 (d, J = 15.74 Hz, 1 H, C6 methylene), 2.18 [ddd, J = 15.75, 3.66, 2.93 Hz, 1 H, CH(OH)CH_aH$_b$-CH(OPMB)], 2.04–1.88 [m, 1 H, CH(OH)CH$_a$$H_b$CH(OPMB)], 1.98 (s, 3 H, OCOCH_3), 1.73–1.56 [m, 2 H, CH(CH_2CH$_2$CH$_3$)], 1.48–1.20 [m, 2 H, CH(CH$_2$CH_2CH$_3$)], 0.88 [t, J = 6.96 Hz, 3 H, CH(CH$_2$CH$_2$CH_3)].

^{13}C NMR (75 MHz, CDCl$_3$): δ = 170.3, 168.4, 168.1, 159.4, 150.4, 142.7, 133.5, 130.7, 129.6, 115.7, 113.9, 77.9, 77.1, 74.0, 71.9, 55.6, 52.8, 52.0, 41.1, 40.7, 32.4, 31.7, 21.1, 20.7, 14.2.

HRMS (FAB) *m*/*z* [M$^+$] calcd for C$_{27}$H$_{36}$O$_9$: 504.2359; found: 504.2333.

Dimethyl 4-Acetoxy-5-(4-methoxybenzyloxy)-8-methylene-7-oxo-3-propylcyclonon-1-ene-1,2-dicarboxylate

To a soln of **12** (39 mg, 0.077 mmol) in CH$_2$Cl$_2$ (2 mL) was added Dess–Martin periodinane (66 mg, 0.155 mmol, 2 equiv). The mixture was stirred for 1 h and monitored by TLC. When the reaction was complete, it was diluted with EtOAc, washed with sat. Na$_2$S$_2$O$_3$, brine and H$_2$O. The organic layer was then dried (MgSO$_4$), concentrated to give crude product (38 mg, 98%) that was used immediately for the following reaction.

IR (thin film): 2956, 1735, 1689, 1612, 1514, 1433, 1371, 1234, 1032 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.20 (d, J = 6.63 Hz, 2 H, C$_6$$H_4$OMe), 6.85 (d, J = 6.63 Hz, 2 H, C$_6$$H_4$OMe), 5.51 (s, 1 H, C=C$H_aH_b$), 5.39 (s, 1 H, C=CH$_a$$H_b$), 5.15 (dd, J = 9.84, 2.99 Hz, 1 H, CHOAc), 4.54 (d, J = 11.77 Hz, 1 H, OCH_2C$_6$H$_4$OMe), 4.46 (d, J = 11 Hz, 1 H, OCH_2C$_6$H$_4$OMe), 3.82–3.72 (2 s, 6 H, 2 CO$_2$CH$_3$ and m, 1 H, CHPr), 3.64 (s, 3 H, C$_6$H$_4$OCH_3), 3.56 (d, J = 15.20, 1 H, C6 methylene), 3.24 (d, J = 14.98 Hz, 1 H, C6 methylene), 2.98 [ddd, J = 8.78, 4.30, 3.00 Hz, 1 H, CH(OPMB)], 2.90 [d, J = 13.48 Hz, 1 H, C(O)CH_aH$_b$CH(OPMB)], 2.84 [dd, J = 13.27, 2.56 Hz, 1 H, C(O)CH$_a$$H_b$CH(OPMB)], 1.94 (s, 3 H, OCOCH_3), 1.79–1.60 [m, 1 H, CH(CH_aH$_b$CH$_2$CH$_3$)], 1.52–1.33 [m, 1 H, CH(CH$_a$$H_bCH_2CH_3$)], 1.33–1.18 [m, 2 H, CH(CH$_2$CH_2CH$_3$)], 0.87 [t, J = 6.96 Hz, 3 H, CH(CH$_2$CH$_2$CH_3)].

^{13}C NMR (75 MHz, CDCl$_3$): δ = 205.0, 170.0, 168.2, 166.9, 159.5, 147.4, 143.1, 132.9, 130.1, 129.9, 120.0, 114.0, 76.8, 76.0, 71.9, 55.5, 52.8, 52.0, 45.9, 42.2, 32.8, 32.4, 21.0, 20.7, 14.1.

HRMS-FAB: *m*/*z* [M – 1]$^+$ calcd for C$_{27}$H$_{33}$O$_9$: 501.2124; found: 501.2125.

Dimethyl 4-Acetoxy-7-hydroxy-5-(4-methoxybenzyloxy)-8-methylene-3-propylcyclonon-1-ene-1,2-dicarboxylate (15)

To a soln of ketone (10 mg, 0.020 mmol) in MeOH (2 mL) at 0 °C was added NaBH$_4$ (1.13 mg, 0.03 mmol, 1.5 equiv) and stirred for 2 h. Upon completion, the reaction was diluted with EtOAc and washed with brine and H$_2$O. The reaction was then dried (MgSO$_4$), concentrated to a pale oil and subjected to column chromatography (silica gel). The reaction yielded desired alcohol **15** as a cloudy white oil (6 mg, 60%); ratio **15**/**12** = 4:1.

IR (thin film): 3512, 2954, 2872, 1724, 1613, 1514, 1434, 1372, 1301, 1247, 1077, 1038, 971, 917, 851, 821, 734, 664 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ = 7.18 (d, J = 8.5 Hz, 2 H, C$_6$$H_4$OMe), 6.85 (d, J = 8.6 Hz, 2 H, C$_6$$H_4$OMe), 5.22 (s, 1 H, C=C$H_aH_b$), 5.11 (s, 1 H, C=CH$_a$$H_b$), 5.08 (dd, J = 9.47, 2.44 Hz, 1 H, CHOAc), 4.60 (dd, J = 8.85, 3.35 Hz, 1 H, CHOH), 4.46 (d, J = 11.6 Hz, 1 H, OCH_aH$_b$C$_6$H$_4$OMe), 4.40 (d, J = 11.3 Hz, 1 H, OCH$_a$$H_bC_6H_4$OMe), 3.80–3.76 (2 s, 6 H, 2 CO$_2$CH_3), 3.72–3.64 (m, 1 H, CHPr), 3.70 (s, 3 H, C$_6$H$_4$OCH_3), 3.58 (d, J = 15.87 Hz, 1 H, C6 methylene), 3.28–3.22 [m, 1 H, CH(OPMB)], 2.88 (d, J = 16.18, 1 H, C6 methylene), 2.22 [ddd, J = 15, 8.85, 2.14 Hz, 1 H, CH(OH)CH_aH$_b$CH(OPMB)], 2.04–1.92 [m, 1 H, CH(OH)CH$_a$$H_b$-CH(OPMB)], 1.96 (s, 3 H, OCOCH_3), 1.82–1.58 [m, 2 H, CH(CH_2CH$_2$CH$_3$)], 1.50–1.20 [m, 2 H, CH(CH$_2$CH_2CH$_3$)], 0.88 [t, J = 7.33 Hz, 3 H, CH(CH$_2$CH$_2$CH_3)].

^{13}C NMR (75 MHz, CDCl$_3$) δ = 170.3, 168.5, 168.5, 159.3, 150.4, 141.1, 134.0, 130.9, 129.6, 115.2, 113.9, 77.5, 74.8, 72.4, 72.1, 55.5, 52.8, 52.0, 42.4, 41.1, 34.4, 32.5, 21.1, 20.8, 14.4.

HRMS-FAB: *m*/*z* [M – H]$^+$ calcd for C$_{27}$H$_{35}$O$_9$: 503.2281; found: 503.2271.

Dimethyl 4-Acetoxy-7-(allyldimethylsiloxy)-5-(4-methoxybenzyloxy)-8-methylene-3-propylcyclonon-1-ene-1,2-dicarboxylate (16)

To a soln of alcohol **15** (0.005 g, 0.01 mmol) was added allyldimethylsilyl chloride (7 μL, 0.05 mmol, 5 equiv) and Et$_3$N (25 μL, 0.177 mmol, 35 equiv). The mixture was stirred overnight at r.t. and subsequently quenched with sat. NaHCO$_3$. The aqueous layer was extracted with EtOAc and the combined organic layers were washed with brine and H$_2$O. The organic layers were then dried (MgSO$_4$) and concentrated. The compound was then subjected to column chromatography (silica gel), which yielded silyl ether **16** as a pale yellow oil (3 mg, 50%, 63% based on recovered **15**).

IR (thin film): 3074, 2954, 2872, 1736, 1630, 1613, 1514, 1458, 1369, 1301, 1248, 1142, 1110, 1091, 1039, 992, 954, 931, 900 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.18 (d, J = Hz, 2 H, OCH_2C$_6$H$_4$OMe), 6.84 (d, J = Hz, 2 H, OCH_2C$_6$H$_4$OMe), 5.80 [ddd, J = 8.43, 10.41, 16.86 Hz, 1 H, OSiMe$_2$(CH$_2$CH=CH$_2$)], 5.09 (s, 1 H, C=CH_aH$_b$), 5.08 (dd, J = 9.47, 2.44 Hz, 1 H, CHOAc), 5.02 (s, 1 H, C=CH$_a$$H_b$), 4.92 [d, J = 17.35 Hz, 1 H, OSiMe$_2$(CH$_2$CH=CH_aH$_b$)], 4.86 [d, J = 9.92 Hz, 1 H, OSiMe$_2$(CH$_2$CH=CH$_a$$H_b$)], 4.70 [d, J = 6.94 Hz, 1 H, CH(OSiR$_3$)], 4.48 (d, J = 11.6 Hz, 1 H, OCH_aH$_b$C$_6$H$_4$OMe), 4.30 (d, J = 11.3 Hz, 1 H, OCH$_a$$H_bC_6H_4$OMe), 3.82 (t, J = 8.92 Hz, 1 H, CHPr), 3.79–3.75 (2 s, 6 H, 2 CO$_2$CH_3), 3.73–3.68 (s, 3 H, C$_6$H$_4$OCH_3 and d, J = 17.85 Hz, 1 H, C6 methylene), 3.48 [ddd, J = 2.48, 4.96, 8.92 Hz, 1 H, CH(OPMB)], 2.84 (d, J = 17.35, 1 H, C6 methylene), 2.27 [ddd, J = 15.37, 7.93, 1.48 Hz, 1 H, CH(OSiR$_3$)CH_aH$_b$CH(O-PMB)], 1.93 (s, 3 H, OCOCH_3), 1.88 [ddd, J = 15.37, 8.93, 2.48 Hz, 1 H, CH(OSiR$_3$)CH$_a$$H_b$CH(OPMB)], 1.74–1.61 [m, 2 H,

CH(CH_2CH$_2$CH$_3$)], 1.64 [dd, J = 7.94, 13.89 Hz, 2 H, OSiMe$_2$(CH_2CH=CH$_a$H$_b$)], 1.46–1.38 [m, 1 H, CH(CH$_2$CH_aH$_b$CH$_3$)], 1.32–1.22 [m, 1 H, CH(CH$_2$CH$_a$$H_bCH_3$)], 0.88 [t, J = 7.33 Hz, 3 H, CH(CH$_2$CH$_2$CH_3)], 0.13 [s, 6 H, OSi(CH_3)$_2$(CH$_2$CH=CH$_2$)].

^{13}C NMR (75 MHz, CDCl$_3$): δ = 170.4, 168.9, 167.9, 151.2, 141.8, 134.2, 133.4, 131.2, 129.2, 114.1, 113.9, 113.3, 77.6, 74.8, 72.1, 71.5, 55.5, 52.6, 51.8, 44.2, 39.9, 34.6, 32.5, 24.7, 21.1, 20.8, 14.4, –2.0, –2.2.

HRMS-FAB: m/z [M – H]$^+$ calcd for $C_{32}H_{45}O_9Si$: 601.2833; found: 601.2856.

Dimethyl 9-Acetoxy-10-(4-methoxybenzyloxy)-2,2-dimethyl-8-propyl-3,8,9,10,11,11a-hexahydro-2*H*,5*H*-1-oxa-2-silabenzocyclononene-6,7-dicarboxylate (17)

Silyl ether **16** (6 mg, 0.01 mmol) was dissolved in CH_2Cl_2 (10 mL) and heated to reflux for 10 min. Grubbs 2nd generation RCM catalyst **14** (cat.) was added and the mixture was heated to reflux for 3 h. The mixture was then concentrated to dryness, redissolved in hexanes and subjected to column chromatography (silica gel), which yielded a quantitative amount of silacycle **17** as a brown oil.

IR (thin film): 2923, 2852, 1740, 1612, 1514, 1458, 1373, 1250, 1043, 855 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ = 7.20 (d, J = 9 Hz, 2 H, C$_6H_4$OMe), 6.83 (d, J = 8 Hz, 2 H, C$_6H_4$OMe), 6.10 (dd, J = 8.55, 3.67 Hz, 1 H, C=CHCH$_2$SiMe$_2$OR), 5.12 (dd, J = 10.07, 2.44 Hz, 1 H, CHOAc), 4.34 [dd, J = 8.85, 3.35 Hz, 1 H, CH(OSiMe$_2$R)], 4.46 (d, J = 11.6 Hz, 1 H, OCH_aH$_b$C$_6$H$_4$OMe), 4.42 (d, J = 11.3 Hz, 1 H, OCH$_a$$H_bC_6H_4$OMe), 3.80–3.76 (2 s, 6 H, 2 CO$_2$CH_3), 3.70 (s, 3 H, C$_6$H$_4$OCH_3), 3.42–3.34 (m, 1 H, CHPr), 3.38 (d, J = 14.34 Hz, 1 H, C6 methylene), 2.88–2.84 [m, 1 H, CH(OPMB)], 2.68 (d, J = 14.35 Hz, 1 H, C6 methylene), 2.12–2.04 [m, 1 H, CH(OSiR$_3$)CH_aH$_b$-CH(OPMB)], 1.98 (s, 3 H, OCOCH_3), 1.99–1.90 [m, 1 H, CH(OSiR$_3$)CH$_a$$H_b$CH(OPMB)], 1.90–1.80 (m, 2 H, C=CHCH_2SiMe$_2$OR), 1.58–1.38 [m, 2 H, CH(CH_2CH$_2$CH$_3$)], 1.38–1.20 [m, 2 H, CH(CH$_2$CH_2CH$_3$)], 0.88 [t, J = 7.33 Hz, 3 H, CH(CH$_2$CH$_2$CH_3)], 0.13 (s, 3 H, OSi(CH_3)(CH$_3$)(CH$_2$CH=CH$_2$)], 0.07 (s, 3 H, OSi(CH$_3$)(CH_3)(CH$_2$CH=CH$_2$)].

^{13}C NMR (75 MHz, CDCl$_3$): δ = 178.7, 170.0, 159.1, 140.9, 138.5, 130.7, 129.4, 129.2, 129.8, 113.7, 75.4, 75.4, 74.9, 72.8, 55.3, 52.3, 51.8, 46.0, 42.4, 41.0, 35.4, 32.0, 20.8, 14.1, 13.1, 1.04.

HRMS-FAB: m/z [M + H]$^+$ calcd for $C_{30}H_{43}O_9Si$: 575.2676; found: 575.2665.

Dimethyl 4-Acetoxy-7-hydroxy-8-(2-hydroxyethylidene)-5-(4-methoxybenzyloxy)-3-propylcyclonon-1-ene-1,2-dicarboxylate (18)

To a soln of silacycle **17** (2 mg, 0.003 mmol) in THF–MeOH (1:1, 1 mL) at r.t. was added KHCO$_3$ (5 mg, 0.05 mmol, 15 equiv), KF (5 mg, 0.086 mmol, 25 equiv), and H$_2$O$_2$ (10 μL, 0.28 mmol, 80 equiv) and the mixture was stirred for 4 h. The solvent was removed and the crude product was redissolved in EtOAc, washed with brine and dried (MgSO$_4$) to give diol **18** as a clear oil (1.9 mg, quantitative).

IR (thin film): 3450, 2923, 2852, 1721, 1613, 1514, 1463, 1373, 1248, 1037, 914, 820, 733 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ = 7.20 (d, J = 6.45 Hz, 2 H, C$_6H_4$OMe), 6.83 (d, J = 6.45 Hz, 2 H, C$_6H_4$OMe), 5.72 (t, J = 6.94 Hz, 1 H, =CHCH$_2$OH), 5.06 (dd, J = 8.93, 1.99 Hz, 1 H, CHOAc), 4.86 (d, J = 6.45 Hz, 1 H, CHOH), 4.45 (d, J = 11.41 Hz, 1 H, OCH_aH$_b$C$_6$H$_4$OMe), 4.41 (d, J = 11.41 Hz, 1 H, OCH$_a$$H_bC_6H_4$OMe), 4.13 (m, 2 H, =CHC$H_2$OH), 3.76 (2 s, 6 H, 2 CO$_2$CH_3), 3.74 (t, J = 8.46 Hz, 1 H, CHPr), 3.70 (s, 3 H, C$_6$H$_4$OCH_3), 3.62 (d, J = 16.86 Hz, 1 H, C6 methylene), 3.44–3.39 [m, 1 H, CH(OPMB)], 2.94 (d, J = 16.86, 1 H, C6 methylene), 2.34 [dd, J = 14.87, 9.92 Hz, 1 H, C(OH)CH_aH$_b$CH(OPMB)], 1.98 (s, 3 H, OCOCH_3), 1.99–1.90 [ddd, J = 14.87, 9.42, 2.97 Hz, 1 H, CH(OH)CH$_a$$H_b$CH(OPMB)], 1.90–1.78 [m, 1 H, CH(CH_aH$_b$CH$_2$CH$_3$)], 1.51–1.39 [m, 2 H, CH(CH$_a$$H_bCH_2CH_3$) and CH(CH$_2CH_aH_bCH_3$)], 1.37–1.25 [m, 1 H, CH(CH$_2$CH$_a$$H_bCH_3$)], 0.88 [t, J = 7.44 Hz, 3 H, CH(CH$_2$CH$_2$CH_3)].

^{13}C NMR (75 MHz, CDCl$_3$): δ = 170.2, 168.9, 168.4, 159.4, 143.3, 141.6, 134.1, 130.7, 129.7, 129.6, 113.9, 74.6, 72.0, 69.1, 58.8, 55.5, 52.9, 52.0, 40.5, 36.5, 32.8, 30.0, 21.1, 20.9, 14.3.

HRMS-FAB: m/z [M + H]$^+$ calcd for $C_{28}H_{39}O_{10}$: 535.2543; found: 535.2513.

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(13) Crystal data, selected bond lengths and angles for **3**: Formula: $C_{30}H_{44}O_7Si$, MW = 544.74, a = 10.3090(4) Å, b = 12.2193(5) Å, c = 13.9422(5) Å, α = 70.593(2)°, β = 78.609(2)°, γ = 74.217(2)°, $P1$, V = 1582.90(11) Å^3, Z = 2, R_1 = 0.0588, wR_2 = 0.1815. Data collection: 0.5° ϕ and ω scans, CCD area detector. Solved by direct methods and refined by full-matrix least-squares refinement against F^2. Selected bond lengths (Å): O2–C1: 1.429(4), C2–C3: 1.497(4), C8–C9: 1.525(5), C1–C2: 1.499(4), C3–C28: 1.542(4). Selected bond angles (°): C1–O2–C16: 112.5(3), O2–C1–C2: 111.2(3), O2–C1–C9: 113.5(3), C2–C1–C9: 102.5(3), C2–C3–C4: 110.5(2), C2–C3–C28: 112.6(2), C4–C3–C28: 112.6(2). Details of the crystal structure determination have been deposited with the Cambridge

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