# Dramatic influence of the substitution of alkylidene-5H-furan-2-ones in Diels-Alder cycloadditions with o-quinonedimethide as diene partner: en route to the CDEF polycyclic ring system of lactonamycin

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**PAPER**

# Dramatic influence of the substitution of alkylidene-5*H*-furan-2-ones in Diels–Alder cycloadditions with *o*-quinonedimethide as diene partner: en route to the CDEF polycyclic ring system of lactonamycin†

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An efficient and rapid synthesis of the CDEF ring system of lactonamycinone is reported *via* a highly chemo- and diastereoselective intermolecular Diels–Alder cycloaddition between *trans*-1,2-disilyloxybenzocyclobutene and the appropriate γ-alkylidenebutenolide. The feasibility and the total chemoselectivity of the [4 + 2] cycloaddition for the construction of a spirolactone moiety *via* an intramolecular approach (IMDA) using both partners is also described demonstrating the versatility of the γ-alkylidenebutenolide building block.

## Introduction

Due to their intrinsic conformational features and their structural implications in biological systems, the preparation of polycyclic structures fused at a central carbon remains an important challenge in organic synthesis.[1] The asymmetric character of the molecule brought by the stereogenic spiro carbon is generally responsible for the biological activities. In this context and over the last two decades, numerous natural spirolactones have been isolated from different sources and some of them exhibit impressive biological activities. Selected examples include abyssomicin C[2] and lactonamycin,[3] two potent antibacterial agents against Gram-positive bacteria, including resistant *Staphylococcus aureus* strains (Fig. 1).

From a structural point of view, lactonamycin presents a spirolactone moiety and a 2,3-dihydronaphthalene-1,4-dione core. The strategy usually used to access a 1,2,3,4-tetrahydronaphthalene substructure is an inter- or intramolecular [4 + 2] reaction using benzocyclobutene derivatives as diene partners.[4] Regarding the spirolactone part, most of the methods reported involve a prior installation of the tertiary alcohol, which is then followed by an intramolecular esterification. Numerous methods for the construction of spirolactones with concomitant formation of the fused quaternary centre have also been reported. Notably, pericyclic reactions have demonstrated to be quite efficient in the synthesis of natural products.[5] Moreover, we recently disclosed a highly chemo- and diastereoselective intermolecular Diels–Alder cycloaddition between *trans*-1,2-disilyloxybenzocyclobutene **1** and methylprotoanemonine **2** to access the lambertellol backbone **3** (Scheme 1).[6] It transpired from this work that the chemoselectivity of such a transformation was highly dependent on the nature of the substituents onto the lactone. Accordingly, δ-substituted alkylidenebutenolides **4** furnished the naphthofuranone moiety **5** whereas the α-bromo-β,δ-substituted lactones led to the corresponding spiro-cycloadducts **6**. However, when the reaction was performed with lactone **7**, no cycloadduct was obtained and this is certainly due to both stereoelectronic and steric factors.

It is worth to note that γ-alkylidenebutenolides have been repeatedly used in Diels–Alder reactions,[7–14] however we were the first one to realise a full study of the reactivity of the δ-substituted ones in the intermolecular version.[7e,9] In addition, different laboratories have developed their approach to the title natural product,[15] however, only one total synthesis of lactonamycin[16] and one total synthesis of its aglycone[17] have been reported to

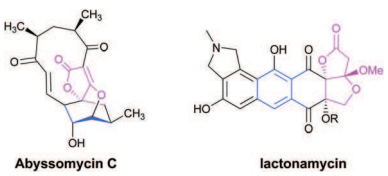


**Fig. 1** Examples of natural products containing the spirolactone moiety.

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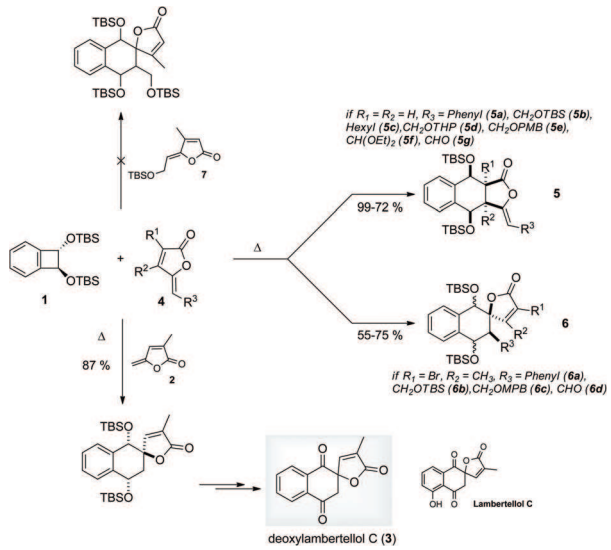
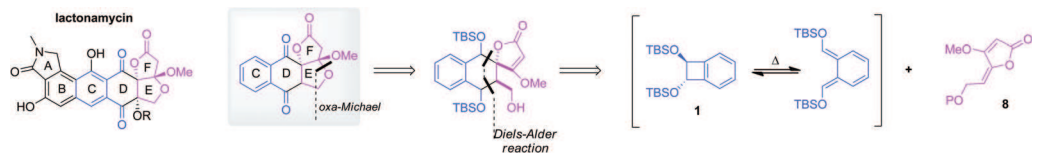
date. In connection with our interest in the total synthesis of natural product possessing interesting biological properties and in the development of new methodologies to efficiently prepare spirolactone moiety,[18] we have undertaken the synthesis of the CDEF ring system of lactonamycinone *via* an intermolecular Diels–Alder reaction. An account of the intramolecular silicon tethered [4 + 2] cyclisation between a benzocyclobutene and a γ-alkylidenebutenolide will also be given.



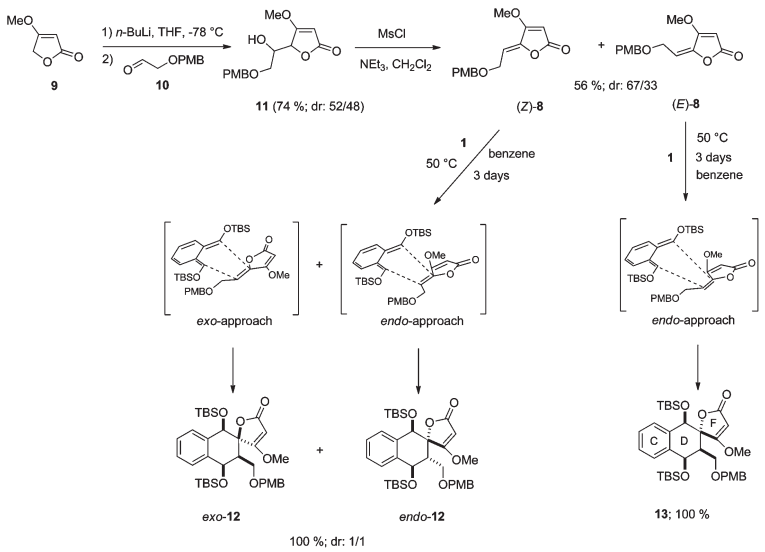

**Scheme 1** Diels–Alder cycloaddition between *trans*-1,2-disilyloxybenzocyclobutene **1** and γ-alkylidenebutenolides.

## Results and discussion

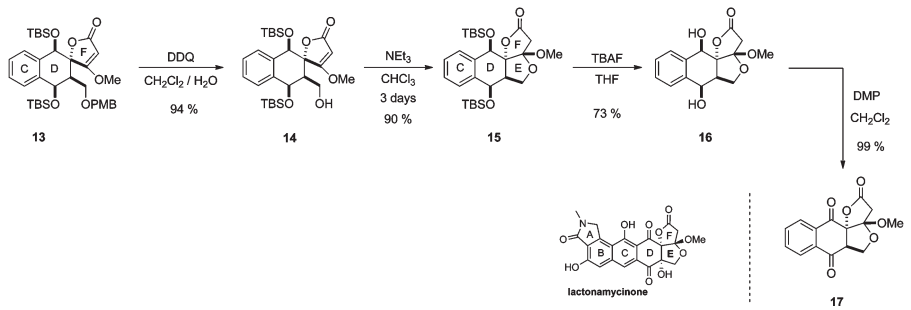
As outlined in Scheme 2, our retrosynthesis consists in two main disconnections to access the CDEF polycyclic ring system of lactonamycinone. Accordingly, a late stage intramolecular oxa-Michael addition would allow the formation of the E ring. On the other hand, the CDF tricyclic spirolactone could efficiently be reached *via* an intermolecular [4 + 2] reaction between **1** and the appropriate lactone **8**. Our program was started with confidence as our previous results suggested that substituents onto the α,β-double bond of the alkylidenebutenolides prevented the cyclisation onto the *endo*-cyclic alkene and therefore, favoured reaction onto the *exo*-cyclic one. Having this in mind, and in connection with our approach toward the CDEF skeleton of lactonamycinone, we thought of using a γ-alkylidenebutenolide decorated with the electron donating methoxy group onto the β position of the lactone. In order to validate this approach, lactone (*Z*)-**8** was chosen as model substrate and was prepared in two steps from methyltetronate **9**[19] and aldehyde **10** (Scheme 3).[20] Addition of the homoenolate of **9** onto aldehyde **10** furnished alcohol **11** in 74% yield as an inseparable 52 : 48 mixture of diastereomers. Then, compound **11** underwent a dehydration to afford a separable 67 : 33 mixture of γ-alkylidenebutenolides (*Z*)-**8** and (*E*)-**8** respectively, in 56% yield. As for the dienophilic benzocyclobutene partner **1**, it was synthesised on a multigram scale according to methods described by South and Liebeskind[21] and Danishefsky *et al.*[22] Having the two precursors in hand, we were now ready for the key cyclisation step. Under the conditions previously reported for the α-bromo-β,δ-substituted lactone (*i.e.* 50 °C, 4 h in degassed benzene), the cycloaddition



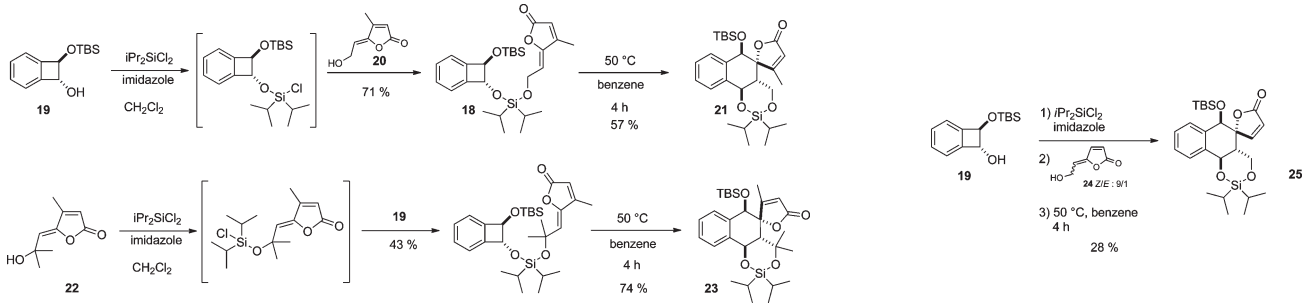

**Scheme 2** Retrosynthetic analysis.




**Scheme 3** Studies on the synthesis of the CDF ring system of lactonamycinone.




**Scheme 4** Synthesis of the CDEF ring system of lactonamycinone.




**Scheme 5** Intramolecular approach.

only furnished a very small amount (up to 5%) of the expected spirolactone **12**. Starting materials **1** and (*Z*)-**8** were recovered unchanged at the end of the reaction. Gratifyingly, when the reaction time was prolonged from four hours to three days,[23] the Diels–Alder reaction gave the desired spiro-cycloadduct **12** in a quantitative manner and as a 1 : 1 mixture of diastereomers arising from an *endo*- and an *exo*-approach respectively.

The feasibility of the intermolecular cycloaddition leading to the desired spirolactone moiety thus validated, we next turn our attention to the (*E*)-lactone **8**. Accordingly, the hetero Michael reaction to form the E-ring required the pending primary alcohol onto compound **14** being *cis* to the single carbon–carbon bond of the lactone. The only way to access such a cycloadduct was to start with the (*E*)-double bond onto lactone **8**. Pleasingly, the cycloaddition reaction was not only efficient and provided the expected compound **13** in a quantitative manner, but was also totally diastereoselective in favour of the *endo*-approach. Thereafter, an additional four steps were performed to access the CDEF rings of lactonamicynone (Scheme 4). Deprotection of the PMB group using DDQ in wet $CH_2Cl_2$ afforded primary alcohol **14** in 94% yield.

The latter underwent the intramolecular oxa-Michael addition under basic conditions to form the last E-ring **15** in 90% yield and as a single diastereomer. Following which, a deprotection of the bis silylether **15** in presence of tetrabutylammonium fluoride gave the corresponding diol **16** in 73% yield. Finally, the sensitive quinone **17** was obtained after oxidation of the diol in the presence of an excess of Dess–Martin periodinane (10 equiv) in a quantitative manner. To summarise, the tetracyclic skeleton of lactonamycinone **17** was diastereoselectively synthesised in 62% yield over five steps from lactone (*E*)-**8**. It goes without saying that the method developed here is a powerful and competitive tool to access rapidly and efficiently the scaffold of natural products containing spirolactone moieties.

As mentioned earlier in the introduction, the δ-substituted α,β-unsubstituted alkylidenebutenolides failed to furnish the desired spirolactones and led instead to the corresponding naphthofuranone derivatives **5**. In addition, lactone **7** proved to be unreactive during this intermolecular [4 + 2] process. In order to overturn the limits encountered and thus, to have access to a range of analogs of the lactonamycine core, we envisioned an intermolecular version of the previous strategy using a disposable silicon tether between the two cycloaddition partners. According to numerous reports, such approaches are favoured for entropic reasons and often lead to better chemo-, regio- and stereoselectivities.[23]

The synthesis of the temporary silaketal tether derivative **18** required the prior preparation of alcohols **19** and **20**. Monoprotected diol **19** (Scheme 5) was obtained in two steps from benzocyclobutanedione. Bis reduction of the ketones in the presence of $NaBH_4$ in MeOH followed by treatment of the corresponding crude diol in the presence of one equivalent of TBSCl furnished the desired compound **19** in yields ranging from 33 to 76% yield over two steps. Both alcohols **19** and **20**[24] were then linked together by sequential reaction with $iPr_2SiCl_2$ (Scheme 5).[25] Gratifyingly, silaketal **18** was obtained in 71% yield. The silicon tethered molecule **18** was then heated at 55 °C for 4 h in benzene. Unlike its intermolecular counterpart (Scheme 1; lactone **7**), silaketal **18** smoothly underwent the [4 + 2] cyclisation in a chemo-, regio- and diastereoselective manner. The desired tetracyclic spirolactone **21** was pleasingly obtained in 57% yield. We then demonstrated the compatibility of the strategy with the more hindered lactone **22** (Scheme 5). The cycloadduct **23** was obtained in 74% yield with total control of the



chemo-, regio- and diastereoselectivity. The relative configurations of **21** and **23** were unambiguously established based on NOESY NMR experiments and through X-ray crystallographic analysis of **23**[26] thus, confirming the *endo*-approach of the intramolecular cycloaddition reaction. Furthermore, we have shown that the chemoselectivity of the intermolecular approach could be overturned thanks to the silylated tether. Accordingly, when the benzocyclobutene is linked with an α,β-unsubstituted lactone the sole product isolated resulted from the reaction onto the *exo*-cyclic double bond of the lactone. No naphthofuranone **5** was observed and the desired spirolactone **25** was obtained in 28% isolated yield over two steps. While 10% of the cycloadduct arising from the *E*-isomer of the starting lactone **24** was observed in the crude $^1$H NMR spectrum, none was observed after purification on silica gel. This is probably due to its instability and might explain why the diastereomer **25** was isolated as the sole product and in modest yield.

## Conclusion

In summary, a new highly diastereoselective and convergent approach towards the CDEF ring system of lactonamycinone has been reported. The key intermolecular Diels–Alder reaction between *trans*-1,2-disiloxybenzocyclobutene and the appropriate γ-alkylidenebutenolide allowed the concomitant formation of the fused spiro carbon together with the creation of three tertiary stereocentres with total control of the diastereoselectivity and in only 5 steps. In addition, an intramolecular cycloaddition using a disposable silicon tether to reach the desired spirolactone moiety has also been developed when its intermolecular counterpart failed to give the desired spiro-cycloadduct (*i.e.* when δ- or β,δ-substituted were used).

## Experimental section

### Compounds (*Z*)-8 and (*E*)-8

To a stirred solution of THF at −80 °C was added a solution of n-BuLi (7.7 mL, 193 mmol, 1.1 equiv, 2.5 M in hexane). A precooled solution of methyltetronate **9**[19] (2 g, 175 mmol, 1 equiv) in THF (35 mL) was then added dropwise at −80 °C. After 20 min at −80 °C, a precooled solution of aldehyde **10**[20] (3.4 g, 175 mmol, 1 equiv) in THF (17 mL) was added to the mixture and allowed to warm at room temperature. After 2 hours, ice crush followed by diluted aqueous HCl were added to the mixture. The aqueous phase was extracted with $Et_2O$. The combined organic phases were dried over $Na_2SO_4$ and concentrated under vacuum. The crude product was then purified by flash chromatography (3 : 7 petroleum ether–ethyl acetate) to afford a inseparable 52 : 48 mixture of alcohol **11** (3.2 g) in 74% yield. To a stirred solution of alcohol **11** (1.14 g, 3.87 mmol, 1 equiv) in $CH_2Cl_2$ (7 mL), was added triethylamine (1.61 mL, 11.6 mmol, 3 equiv) followed by mesylchloride (0.419 mL, 5.43 mmol, 1.4 equiv) were added dropwise. The mixture was heated at reflux overnight. The reaction was then quenched by addition of saturated aqueous solution of $NH_4Cl$. The aqueous phase was extracted with $CH_2Cl_2$. The combined organic phases were dried over $Na_2SO_4$ and concentrated under vacuum. The crude material was finally purified by flash chromatography (8 : 2 petroleum ether–ether) to afford (598 mg, 56% yield) (*Z*)-**8** (404 mg) and (*E*)-**8** (194 mg) in 67/33 ratio. (*Z*)-**8**: $\delta_H$ (400 MHz, $CDCl_3$) 3.81 (3H, $CH_3$), 3.92 (3H, $CH_3$), 4.30 (2H, d, $J$ = 6.8 Hz, $CH_2$), 4.46 (2H, s, $CH_2$), 5.24 (1H, br s, CH), 5.59 (1H, t, $J$ = 6.8 Hz, CH), 6.88 (2H, d, $J$ = 8.5, 2 × $CH_{Ar}$), 7.27 (2H, d, $J$ = 8.5 Hz, 2 × $CH_{Ar}$); $\delta_C$ (75 MHz, $CDCl_3$) 55.4 ($CH_3$), 59.3 ($CH_3$), 63.7 ($CH_2$), 72.7 ($CH_2$), 89.8 (CH), 106.5 (CH), 114.0 (2 × $CH_{Ar}$), 129.7 (2 × $CH_{Ar}$), 130.0 (C), 144.6 (C), 159.5 (C), 168.2 (C), 169.9 (C); HRMS found 277.1074 [M + H]$^+$, $C_{15}H_{17}O_5$ requires 277.1071. (*E*)-**8**: $\delta_H$ (400 MHz, $CDCl_3$) 3.80 (3H, s, $CH_3$), 3,88 (3H, s, $CH_3$), 4.39 (2H, d, $J$ = 7.6, $CH_2$), 4.46 (2H, s, 1H, $CH_2$), 5.30 (1H, br d, $J$ = 1.3 Hz, CH), 5.84 (1H, dt, $J$ = 7.6 and 1.3 Hz, CH), 6.88 (2H, d, $J$ = 8.7 Hz, 2 × $CH_{Ar}$), 7.27 (2H, d, $J$ = 8.7 Hz, 2 × $CH_{Ar}$); $\delta_C$ (100 MHz, $CDCl_3$) 55.4 ($CH_3$), 59.5 ($CH_3$), 63.2 ($CH_2$), 72.2 ($CH_2$), 91.8 (CH), 111.8 (CH), 113.9 (2 × $CH_{Ar}$), 129.6 (2 × $CH_{Ar}$), 130.0 (C), 144.4 (C), 159.5 (C), 167.9 (C), 170.5 (C); HRMS found 277.1074 [M + H]$^+$, $C_{15}H_{17}O_5$ requires 277.1071.

### Compound 12

In a oven-dried Schlenk tube, *trans*-1,2-bis(*tert*-butyldimethylsilyloxy)-1,2-benzocyclobutene **1**[21,22] (326 mg, 0.89 mmol, 1.5 equiv) and butenolide (*Z*)-**8** (164 mg, 0.59 mmol, 1 equiv) were dissolved in benzene-$D_6$ (3.3 mL). The solution was degassed for 10 min at −80 °C three times. The mixture was then heated at 55 °C. The reaction was followed by $^1$H NMR and after disappearance of (*Z*)-**8** (3 days), the solvent was removed under vacuum. The crude product was purified by flash chromatography (8 : 2 petroleum ether–ethyl acetate) to give a separable 1 : 1 mixture (374 mg, 100%) of *exo*-**12** and *endo*-**12**. *endo*-**12**: $\delta_H$ (400 MHz, $C_6D_6$) 0.03 (6H, s, 2 × $CH_3$), 0.04 (3H, s, $CH_3$), 0.37 (3H, s, $CH_3$), 1.00 (9H, s, 3 × $CH_3$), 1.04 (9H, s, 3 × $CH_3$), 2.52–2.58 (1H, m, CH), 2.71 (3H, s, $CH_3$), 3.32 (3H, s, $CH_3$), 3.81 (3H, dd, $J$ = 9 and 3.0 Hz, C$H_2$), 3.89–3.94 (1H, m, C$H_2$), 4.40 (1H, d, C$H_2$, $J$ = 11.1 Hz), 4.49 (1H, d, C$H_2$, $J$ = 11.1 Hz), 4.75 (1H, s, C), 5.00 (1H, d, $J$ = 10 Hz, CH), 5.15 (1H, s, CH), 6.84 (2H, d, $J$ = 8.7 Hz, 2 × $CH_{Ar}$), 7.21–7.28 (2H, m, 2 × $CH_{Ar}$), 7.35 (2H, d, $J$ = 8.7 Hz, 2 × $CH_{Ar}$), 7.62–7.63 (1H, m, $CH_{Ar}$), 7.68–7.70 (1H, m, $CH_{Ar}$); $\delta_C$ (100 MHz, $C_6D_6$) −4.7 ($CH_3$), −4.6 (2 × $CH_3$), −4.1 ($CH_3$), 18.4 (C), 18.5 (C), 26.1 (3 × $CH_3$), 26.2 (3 × $CH_3$), 48.6 (CH), 54.8 ($CH_3$), 58.3 ($CH_3$), 67.1 ($CH_2$), 67.5 (CH), 72.1 (CH), 73.5 ($CH_2$), 86.6 (C), 90.3 (CH), 114.1 (2 × $CH_{Ar}$), 123.5 (CH), 124.2 (CH), 127.1 (CH), 127.4 (CH), 130.2 (2 × $CH_{Ar}$), 130.9 (C), 135.6 (C), 140.1 (C), 159.9 (C), 171.6 (C), 182.4 (C); IR ($\nu_{max}$/cm$^{-1}$): 2956, 2930, 2889, 2856, 1759, 1637, 1613, 1510, 1460, 1366, 1247, 1173, 1131, 1098, 1070, 1036 cm$^{-1}$; MS: *m*/*z* (ESI+) 663 (M + Na)$^+$; HRMS found 658.3588 [M + $NH_4$]$^+$, $C_{35}H_{56}NO_7Si_2$ requires 658.3590. *exo*-**12**: $\delta_H$ (400 MHz, $C_6D_6$) −0.12 (3H, s, $CH_3$), −0.01 (3H, s, $CH_3$), 0.06 (3H, s, $CH_3$), 0.12 (3H, s, $CH_3$), 0.99 (9H, s, 3 × $CH_3$), 1.04 (9H, s, 3 × $CH_3$), 3.02 (3H, s, $CH_3$), 3.11–3.16 (1H, m, CH), 3.25–3.32 (2H, m, C$H_2$), 3.27 (3H, s, $CH_3$), 3.98 (1H, dd, $J$ = 8.9 and 3 Hz, $CH_2$), 4.08 (1H, d, C$H_2$, $J$ = 11 Hz, H9), 4.38 (1H, d, C$H_2$, $J$ = 11 Hz), 4.82 (1H, s, CH), 4.94 (1H, s, CH), 5.11 (1H, d, $J$ = 6.8 Hz, CH), 6.75 (2H, d, $J$ = 8.7 Hz, 2 × $CH_{Ar}$), 7.20 (2H, d, $J$ = 8.7 Hz, 2 × $CH_{Ar}$), 7.26–7.37 (2H, m, $CH_{Ar}$), 7.64 (1H, br d, $J$ = 6.8 Hz, $CH_{Ar}$),

7.77 (1H, br d, $J$ = 7.5 Hz, $CH_{Ar}$); $\delta_C$ (100 MHz, $C_6D_6$) −5.5 ($CH_3$), −5.0 ($CH_3$), −4.8 ($CH_3$), −4.3 ($CH_3$), 18.4 (C), 18.6 (C), 26.0 (6 × $CH_3$), 47.3 (CH), 54.7 ($CH_3$), 58.5 ($CH_3$), 66.1 ($CH_2$), 67.6 (CH), 68.7 (CH), 73.4 ($CH_2$), 86.0 (C), 91.0 (CH), 113.9 (2 × $CH_{Ar}$), 122.8 (CH), 124.7 (CH), 127.5 (CH), 127.6 (CH), 130.2 (2 × $CH_{Ar}$), 131.1 (C), 136.0 (C), 137.9 (C), 159.6 (C), 171.1 (C), 180.8 (C, C2); IR ($\nu_{max}$/$cm^{-1}$) 2952, 2930, 2888, 2857, 1756, 1641, 1515, 1471, 1461, 1360, 1247, 1192, 1171, 1131, 1071, 1031; MS: $m/z$ (ESI+) 663 $(M + Na)^+$; HRMS found 658.3589 $[M + NH_4]^+$, $C_{35}H_{56}NO_7Si_2$ requires 658.3590.

### Compound *endo*-13

In a oven-dried Schlenk tube, *trans*-1,2-bis(*tert*-butyldimethylsilyloxy)-1,2-benzocyclobutene **1** (253 mg, 0.69 mmol, 1.5 equiv) and butenolide (*E*)-**8** (128 mg, 0.46 mmol, 1 equiv) were dissolved in benzene-$d_6$ (2.6 mL). The solution was degassed for 10 min at −80 °C three times. The mixture was then heated at 55 °C. The reaction was followed by $^1$H NMR and after disappearance of (*E*)-**8** (3 days), the solvent was removed under vacuum. The crude product was purified by flash chromatography (9 : 1 petroleum ether–ethyl acetate) to give *endo*-**13** (269 mg, 100%). $\delta_H$ (400 MHz, $C_6D_6$) 0.03 (3H, s, $CH_3$), 0.05 (3H, s, $CH_3$), 0.6 (3H, s, $CH_3$), 0.34 (3H, s, $CH_3$), 0.95 (9H, s, 3 × $CH_3$), 1.04 (9H, s, 3 × $CH_3$), 2.9 (3H, s, $CH_3$), 3.01–3.06 (1H, m, $CH_2$), 3.11–3.16 (1H, m, CH), 3.30 (3H, s, $CH_3$), 3.88 (1H, dd, $J$ = 9.8 and 3.5 Hz, $CH_2$), 4.02 (1H, d, $CH_2$, $J$ = 11.8 Hz), 4.07 (1H, d, $CH_2$, $J$ = 11.8 Hz), 4.86 (1H, s, CH), 5.24 (1H, br s, CH), 5.32 (1H, d, $J$ = 5.3 Hz, CH), 6.76 (2H, d, $J$ = 8.5 Hz, 2 × $CH_{Ar}$), 7.07 (2H, d, $J$ = 8.5 Hz, 2 × $CH_{Ar}$), 7.20–7.27 (2H, m, 2 × $CH_{Ar}$), 7.66 (1H, br d, $J$ = 5.5 Hz, $CH_{Ar}$), 7.72 (1H, br d, $J$ = 5.8 Hz, $CH_{Ar}$); $\delta_H$ (400 MHz, $CDCl_3$) 0.07 (3H, s, $CH_3$), 0.17 (3H, s, $CH_3$), 0.18 (3H, s, $CH_3$), 0.19 (3H, s, $CH_3$), 0.96 (9H, s, 3 × $CH_3$), 0.98 (9H, s, 3 × $CH_3$), 2.69–2.76 (1H, m, $CH_2$), 2.81–2.87 (1H, m, CH), 3.52 (3H, s, $CH_3$), 3.65 (1H, dd, $J$ = 9.6 and 2.8 Hz, $CH_2$), 4.15 (3H, s, $CH_3$), 4.15 (2H, s, $CH_2$), 4.96 (1H, br s, CH), 4.98 (1H, br s, CH), 5.08 (1H, d, $J$ = 5.1 Hz, CH), 6.80 (2H, d, $J$ = 8.5 Hz, 2 × $CH_{Ar}$), 7.08 (2H, d, $J$ = 8.5 Hz, 2 × $CH_{Ar}$), 7.29–7.32 (2H, m, 2 × $CH_{Ar}$), 7.40–7.46 (2H, m, 2 × $CH_{Ar}$); $\delta$ (75 MHz, $CDCl_3$) $\delta$ −5.0 ($CH_3$), −4.9 ($CH_3$), −4.8 ($CH_3$), −4.7 ($CH_3$), 18.1 (C), 18.2 (C), 25.8 (3 × $CH_3$), 25.9 (3 × $CH_3$), 52.0 (CH), 55.2 ($CH_3$), 58.8 ($CH_3$), 64.7 ($CH_2$), 66.6 (CH,), 71.6 (CH), 72.1 ($CH_2$), 88.1 (C), 90.0 (CH), 113.6 (2 × $CH_{Ar}$), 122.3 (CH), 123.1 (CH), 126.7 (CH), 126.8 (CH), 128.5 (2 × $CH_{Ar}$), 130.4 (C), 134.6 (C), 138.3 (C), 158.9 (C), 172.3 (C), 182.9 (C); MS: $m/z$ (ESI+) 664 $(M + Na)^+$; HRMS found 641.3327 $[M + H]^+$, $C_{35}H_{53}O_7Si_2$ requires 641.3324.

### Compound 14

To a stirred solution of *endo*-**13** (260 mg, 0.405 mmol, 1 equiv) in 10.5 mL of 5% aqueous $CH_2Cl_2$ was added at 0 °C DDQ (102 mg, 0.446 mmol, 1.1 equiv). After 1 hour at 0 °C the solution was stirred at room temperature until disappearance of starting material (1 hour) then filtered through a pad of florosil and celite then concentrated. The crude product was purified by flash chromatography (8 : 2 petroleum ether–ethyl acetate) to give **14** (199 mg, 94%). mp 209 °C; $\delta_H$ (400 MHz, $CDCl_3$) 0.07 (3H, s, $CH_3$), 0.17 (3H, s, $CH_3$), 0.19 (3H, s, $CH_3$), 0.23 (3H, s, $CH_3$), 0.96 (9H, s, 3 × $CH_3$), 1.02 (9H, s, 3 × $CH_3$), 2.67 (1H, m, OH), 2.82 (1H, dt, $J$ = 8.3 and 5.5 Hz, CH), 3.18 (1H, dd, $J$ = 11.6 and 4.8 Hz, $CH_2$), 3.50 (1H, dd, $J$ = 11.6 and 8.3 Hz, $CH_2$), 3.58 (3H, s, $CH_3$), 4.89 (1H, s, CH), 5.03 (1H, s, CH), 5.21 (1H, d, CH, $J$ = 5.5 Hz, H7), 7.30–7.37 (2H, m, 2 × $CH_{Ar}$), 7.41–7.48 (2H, m, 2 × $CH_{Ar}$); $\delta_C$ (75 MHz, $CDCl_3$) −5.0 ($CH_3$), $-4.9_3$ ($CH_3$), $-4.8_7$ ($CH_3$), −4.8 ($CH_3$), 18.1 (C), 18.3 (C), 25.9 (6 × $CH_3$), 52.8 (CH), 58.9 ($CH_3$), 60.6 ($CH_2$), 69.1 (CH), 71.3 (CH), 88.6 (C), 90.6 (CH), 122.8 ($CH_{Ar}$), 123.5 ($CH_{Ar}$), 126.9 ($CH_{Ar}$), 127.0 ($CH_{Ar}$), 134.3 ($C_{Ar}$), 137.5 ($C_{Ar}$), 171.9 (C), 181.9 (C); IR ($\nu_{max}$/$cm^{-1}$) 3451, 2952, 2929, 2888, 2857, 1738, 1628, 1471, 1459, 1252, 1185, 1130, 1068, 1049; MS: $m/z$ (ESI+) 543 $(M + Na)^+$; HRMS found 521.2747 $[M + H]^+$, $C_{27}H_{45}O_6Si_2$ requires 521.2749.

### Compound 15

A solution of **14** (145 mg, 0.279 mmol, 1 equiv), $NEt_3$ (116 µL, 0.837 mmol, 3 equiv) in $CHCl_3$ (15 mL) was stirred at room temperature. After disappearance of the starting material (3 days), the solvent was removed under vacuum and the crude product was purified by flash chromatography (9 : 1 petroleum ether–ethyl acetate) to afford **15** (131 mg, 90%). $\delta_H$ (400 MHz, $CDCl_3$) 0.09 (3H, s, $CH_3$), 0.17 (3H, s, $CH_3$), 0.19 (3H, s, $CH_3$), 0.20 (3H, s, $CH_3$), 0.99 (9H, s, 3 × $CH_3$), 1.03 (9H, s, 3 × $CH_3$), 2.75 (1H, d, $J$ = 16.8 Hz, $CH_2$), 2.81 (1H, d, $J$ = 16.8 Hz, $CH_2$), 2.88 (3H, s, $CH_3$), 3.13–3.19 (1H, m, CH), 3.30–3.35 (1H, m, $CH_2$), 4.03–4.08 (1H, m, $CH_2$), 4.94 (1H, br s, CH), 5.02 (1H, d, $J$ = 6.5 Hz, CH), 7.26–7.39 (2H, m, 2 × $CH_{Ar}$), 7.39–7.46 (2H, m, 2 × $CH_{Ar}$), $\delta_C$ (75 MHz, $CDCl_3$) −4.9 ($CH_3$), $-4.8_3$ ($CH_3$), $-4.7_7$ ($CH_3$), −4.6 ($CH_3$), 18.3 (2 × C), 25.9 (3 × $CH_3$), 26.2 (3 × $CH_3$), 39.1 ($CH_2$), 50.5 ($CH_3$), 51.5 (CH), 67.1 (CH), 68.8 ($CH_2$), 70.8 (CH), 95.9 (C), 112.3 (C), 123.2 ($CH_{Ar}$), 123.7 ($CH_{Ar}$), 126.3 ($CH_{Ar}$), 126.6 ($CH_{Ar}$), 135.6 ($C_{Ar}$), 136.2 ($C_{Ar}$), 172.6 (C); IR ($\nu_{max}$/$cm^{-1}$) 2954, 2930, 2888, 2857, 1791, 1472, 1461, 1251, 1211, 1182, 1126, 1076, 1061, 1013; MS: $m/z$ (ESI+) 543 $(M + Na)^+$; HRMS found 538.3011 $[M + NH_4]^+$, $C_{27}H_{48}NO_6Si_2$ requires 538.3015.

### Compound 16

In an oven-dried flask, **15** (130 mg, 0.25 mmol, 1 equiv) was dissolved in THF (8 mL). At 0 °C, a TBAF solution (0.625 mL, 0.625 mmol, 1M in THF, 2.5 equiv) was added dropwise. The solution was stirred at room temperature and after completion of the reaction (1 hour), the mixture was quenched with aqueous saturated $NaHCO_3$ solution. The aqueous layer was extracted with EtOAc. The combined organic phases were dried over $Na_2SO_4$ then concentrated under vacuum. The crude product was purified by flash chromatography (1 : 1 petroleum ether–ethyl acetate) to give the diol **16** (53 mg, 73%). mp 251 °C; $\delta_H$ (400 MHz, $CDCl_3$) 2.87 (1H, d, $J$ = 17.6 Hz, $CH_2$), 2.96 (1H, d, $J$ = 17.6 Hz, $CH_2$), 3.16 (3H, s, $CH_3$), 3.18–3.21 (1H, m, CH), 3.46 (1H, br d, $J$ = 8.3 Hz, OH), 3.51–3.56 (1H, m, $CH_2$), 4.23–4.27 (1H, m, $CH_2$), 4.88 (1H, br d, $J$ = 8.3 Hz) 5.07 (1H, d, $J$ = 6.3 Hz, CH), 7.36–7.38 (2H, m, 2 × $CH_{Ar}$), 7.48–7.52 (2H, m, 2 × $CH_{Ar}$); $\delta_C$ (75 MHz, $CDCl_3$/MeOD) 38.8 ($CH_2$),

49.8 ($CH_3$), 50.8 (CH), 65.1 (CH), 68.5 ($CH_2$), 69.6 (CH), 96.5 (C), 112.0 (C), 122.2 ($CH_{Ar}$), 122.5 ($CH_{Ar}$), 126.0 ($CH_{Ar}$), 126.4 ($CH_{Ar}$), 135.2 ($C_{Ar}$), 135.7 ($C_{Ar}$), 173.5 (C); IR ($\nu_{max}$/$cm^{-1}$) 3484, 3411, 2988, 2934, 2892, 1768, 1458, 1412, 1281, 1262, 1249, 1228, 1188, 1140, 1099, 1063, 1048, 1033, 1007; MS: *m*/*z* (ESI+) 315 $(M + Na)^+$; HRMS found 293.1019 $[M + H]^+$, $C_{15}H_{17}O_6$ requires 293.1020.

### Compound 17

To a solution of diol **16** (16 mg, 0.055 mmol, 1 equiv) in $CH_2Cl_2$ (7 mL), under argon, at 0 °C, was added Dess–Martin periodinane (232 mg, 0.55 mmol, 10 equiv). The reaction mixture was stirred at room temperature and monitored by TLC. After disappearance of the starting material, the mixture was poured into (1/1) mixture of saturated aqueous solution of $Na_2S_2O_3$ and saturated aqueous solution of $NaHCO_3$ (25 mL) and shaken vigorously for 5 min. The aqueous layer was extracted with $CH_2Cl_2$. The combined organic layers were washed with a saturated aqueous $NaHCO_3$ solution, saturated aqueous NaCl, dried over $Na_2SO_4$, dried over $Na_2SO_4$ and concentrated under vacuum to give the crude product **17** (16 mg, 100%). $\delta_H$ (400 MHz, $CDCl_3$) 2.92 (1H, d, *J* = 16.8 Hz, C$H_2$), 2.99 (1H, d, *J* = 16.8 Hz, C$H_2$), 3.17 (3H, s, $CH_3$), 3.80 (1H, dd, *J* = 8.0 and 3.8 Hz, CH), 4.54 (1H, m, $CH_2$), 4.75 (1H, dd, *J* = 9.0 and 3.8 Hz, C$H_2$), 7.80–7.85 (2H, m, 2 × $CH_{Ar}$), 8.14–8.21 (2H, m, 2 × $CH_{Ar}$); $\delta_C$ (75 MHz, $CDCl_3$) 36.6 ($CH_2$), 52.6 (CH), 53.7 ($CH_3$), 70.4 ($CH_2$), 90.7 (C), 113.4 (C), 127.4 ($CH_{Ar}$), 127.7 ($CH_{Ar}$), 134.2 ($C_{Ar}$), 135.0 ($CH_{Ar}$), 135.3 ($C_{Ar}$), 135.4 ($CH_{Ar}$), 171.4 (C), 189.3 (C), 191.9 (C); IR ($\nu_{max}$/$cm^{-1}$) 2958, 2919, 2850, 1730, 1711, 1668, 1641, 1591, 1563, 1437, 1340, 1328, 1306, 1258, 1245, 1175, 1140, 1087, 1015; HRMS found 306.0971 $[M + NH_4]^+$, $C_{15}H_{16}NO_6$ requires 306.0972.

### Compound 19

To a stirred solution of diketone[21] (500 mg, 3.78 mmol) in methanol (50 mL) at 0 °C was added sodium borohydride (143 mg, 3.78 mmol) portionwise (10 mg per 10 min). After 1 hour, the solvent was removed under vacuum at 0 °C. The crude product (370 mg) was dissolved in DCM (0.1 M) and cooled to 0 °C. Imidazole (157 mg, 2.312 mmol, 0.85 equiv) was added to the mixture and TBSCl (369 mg, 2.45 mmol, 0.9 equiv) dissolved in 20 mL of DCM was added *via* a seringe pump (3.6 mL $h^{-1}$). After one night at 0 °C, the reaction was quenched by adding water. The aqueous layer was extracted with DCM and the organic phases were dried over $Na_2SO_4$ and the solvent removed under high vacuum. The crude product was purified by flash chromatography (7 : 3: EP–$Et_2O$) to give the monoprotected benzocyclobutenediol **19** in variable amount (33–76%). $\delta_H$ (300 MHz, $CDCl_3$) 0.2 (6H, s, 2 × $CH_3$), 0.97 (9H, s, 3 × $CH_3$), 2.33 (1H, OH), 4.92 (1H, s, CH), 4.93 (1H, s, CH), 7.27–7.36 (4H, m, 4 × $CH_{Ar}$); $\delta_C$ (75MHz, $CDCl_3$) −4.5 (2 × $CH_3$), 18.4 (C), 26.0 (3 × $CH_3$), 79.9 (2 × CH), 123.4 (2 × $CH_{Ar}$), 129.6 ($CH_{Ar}$), 129.9 ($CH_{Ar}$), 143.3 ($C_{Ar}$), 144.3 ($C_{Ar}$); MS: *m*/*z* 273 $[M + Na]^+$; HRMS found 251.1462 $[M + H]^+$, $C_{14}H_{23}O_2Si$ requires 251.1462.

### Compound 20

To a stirred solution of the γ-butenolide[27] (400 mg, 1.57 mmol, 1 equiv) in anhydrous THF (8.2 mL) at 0 °C was added a solution of HF-pyridine (121 μL, 70% in pyridine, 4.72 mmol, 3 equiv). The reaction was stirred at room temperature and followed by TLC. After disappearance of the starting material, the reaction was quenched with a saturated aqueous solution of $NaHCO_3$. The aqueous phase was extracted with ether and the combined organics layers were dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The resulting crude product was purified by flash chromatography on silica gel (petroleum ether–ethyl acetate 1 : 1) to give **20** (157 mg, 71%). $\delta_H$ (400 MHz, $C_6D_6$) 1.27 (3H, d, *J* = 1.3 Hz, $CH_3$), 4.23 (2H, d, *J* = 6.8 Hz, $CH_2$), 4.94 (1H, CH, td, *J* = 6.8 and 0.8 Hz, CH), 5.32 (1H, m, CH); $\delta_C$ (100 MHz, $C_6D_6$) 10.9 ($CH_3$), 57.3 ($CH_2$), 110.5 (CH), 117.1 (CH), 150.4 (C), 154.6 (C), 168.5 (C); MS: *m*/*z* (ESI+) 163 $(M + Na)^+$.

### Compound 21

To a stirred solution of $CH_2Cl_2$ (0.6 mL), imidazole (38 mg, 0.56 mmol, 5 equiv) and $iPr_2SiCl_2$ (20 μL, 0.11 mmol, 1 equiv) was added dropwise and at room temperature **19** (28 mg, 0.11 mmol, 1 equiv) in $CH_2Cl_2$ (0.35 mL). After disappearance of **20** (5 min), lactone **20** (16 mg, 0.11 mmol, 1 equiv) was added to the mixture. The reaction was stirred for 15 min, then quenched with a saturated aqueous solution of $NH_4Cl$. The aqueous layer was extracted with $CH_2Cl_2$. The combined organic phase were dried over $Na_2SO_4$ and concentrated under vacuum. The crude product was purified by flash chromatography (petroleum ether–diethylether 85 : 15) to give **18** (40 mg, 71%). $\delta_H$ (300 MHz, $CDCl_3$) 0.19 (6H, s, 2 × $CH_3$), 0.94 (9H, s, 2 × $CH_3$), 1.02–1.06 (3H, m, $CH_3$), 1.09–1.16 (11H, m, 3 × $CH_3$ and CH), 2.10 (3H, br s, $CH_3$), 4.69 (2H, d, *J* = 6.3 Hz, $CH_2$), 5.00 (1H, br s, CH), 5.11 (1H, br s, $CH_3$), 5.40 (1H, t, *J* = 6.3 Hz, CH), 5.93 (1H, br s, $CH_3$), 7.24–7.34 (4H, m, $CH_{Ar}$); MS: *m*/*z* (ESI+) 525 $[M + Na]^+$.

The $^1H$ NMR revealed the formation of the cycloadduct **18**. Thus, no more characterisation was made on this kind of product.

In Schlenk tube, **18** (40 mg) was heated (55 °C) in degassed $C_6D_6$ (2 mL) for 4 hours. The solution was then concentrated and purified by flash chromatography (petroleum ether–diethylether 85 : 15) to give **21** (23 mg, 57%). $\delta_H$ (400 MHz, $C_6D_6$) −0.03 (3H, s, $CH_3$), 0.20 (3H, s, $CH_3$), 0.96 (9H, s, 3 × $CH_3$), 1.06 (3H, br s, $CH_3$), 1.08–1.13 (14H, m, 4 × $CH_3$ and 2 × CH), 1.96 (1H, td, *J* = 10.5 and 3.5 Hz, CH), 3.87 (1H, dd, *J* = 11.5 and 3.5 Hz, C$H_2$), 4.40 (1H, t, *J* = 11.5 Hz, C$H_2$), 4.91 (1H, s, CH), 5.13 (1H, d, *J* = 10.5 Hz, CH), 5.33 (1H, br s, CH), 7.17–7.27 (2H, m, 2 × $CH_{Ar}$), 7.55 (1H, d, *J* = 7.5 Hz, $CH_{Ar}$), 7.84 (1H, d, *J* = 7.5 Hz, $CH_{Ar}$); $\delta_C$ (100 MHz, $CDCl_3$) $\delta$ = −4.8 ($CH_3$), −4.7 ($CH_3$), 12.4 ($CH_3$), 13.5 (2 × CH), 16.9 ($CH_3$), 17.0 ($CH_3$), 17.2 ($CH_3$), 17.3 ($CH_3$), 18.4 (C), 21.1 (3 × $CH_3$), 47.7 (CH), 63.4 ($CH_2$), 71.2 (CH), 71.7 (CH), 77.8 (CH), 90.9 (C), 118.5 (CH), 122.7 (CH), 123.5 (CH), 127.4 (CH), 127.8 (CH), 127.9 (CH), 134.7 (C), 140.1 (C), 168.3 (C), 171.0 (C); IR ($\nu_{max}$/$cm^{-1}$) 2953, 2928, 2861, 1771, 1463, 1261, 1133, 1071; MS *m*/*z* (ESI+) 525 $[M + Na]^+$; HRMS found 520.2907 $[M + NH_4^+]$, $C_{27}H_{46}NO_5Si_2$ requires 520.2909.

**Compound 22**

A dry Schlenk tube equipped with a Teflon-coated magnetic stirrer was charged with anhydrous $K_2CO_3$ (1.3 g, 9.40 mmol, 2 equiv) and (*Z*)-α,β-insaturated-β-iodide acid (1 g, 4.70 mmol, 1 equiv). The mixture vessel was evacuated and backfilled with argon. Then freshly distilled DMF (15 mL) was added and the suspension was stirred for 15 min at room temperature. The mixture was degassed at 0 °C for 5 min and backfilled with argon. After reaching room temperature, the alkyne (0.461 g, 4.70 mmol, 1 equiv) and CuI (0.9 g, 4.70 mmol, 1 equiv) were added. The Schlenk tube was sealed and then placed in a pre-heated oil bath at 55 °C. Stirring was allowed for 4 hours. Then, the mixture was placed in an ice bath and a saturated aqueous solution of $NH_4Cl$ was added. Stirring at 0 °C was allowed for 10 min at which time the reactional mixture was diluted with ether and filtered through a short pad of Celite. The filtrate was washed with brine and the organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo* to yield the expecting γ-butyrolactone **22** (700 mg, 88% yield) which was engaged in the next step without further purifications. $\delta_H$ (400 MHz, $C_6D_6$) 1.20 (3H, br d, $J$ = 1.0 Hz, $CH_3$), 1.36 (6H, s, 2 × $CH_3$), 5.02 (1H, s, CH), 5.24 (1H, m, CH); $\delta_C$ (100 MHz, $C_6D_6$) 11.0 ($CH_3$), 30.2 (2 × $CH_3$), 70.3 (C), 116.0 (CH), 118.7 (CH), 148.5 (C), 155.1 (C), 168.0 (C); IR ($\nu_{max}$/cm$^{-1}$) 3429, 2976, 2932, 2873, 1745, 1664, 1608, 1362, 1341, 1310, 1220, 1135, 1037; HRMS found 186.1129 [M + $NH_4^+$], $C_9H_{16}NO_3$ requires 186.1125.

**Compound 23**

To a stirred solution of **22** (17 mg, 0.1 mmol, 1 equiv) in $CH_2Cl_2$ (0.5 mL) was added at room temperature imidazole (34 mg, 0.5 mmol, 5 equiv) followed by $iPr_2SiCl_2$ (17.4 µL, 0.1 mmol, 1 equiv) after complete dissolution of imidazole. After disappearance of **22** (2 hours), **19** (25 mg, 0.1 mmol, 1 equiv) in $CH_2Cl_2$ (0.3 mL) was added to the mixture. The reaction was stirred for 15 min, then quenched with a saturated aqueous solution of $NH_4Cl$. The aqueous layer was extracted with $CH_2Cl_2$. The combined organic phase were dried over $Na_2SO_4$ and concentrated under vacuum. The crude product was purified by flash chromatography (petroleum ether–diethylether 8 : 2) to give the silicon tethered (23 mg, 43%). In Schlenk tube, the silicon tethered (23 mg) was heated (55 °C) in degassed $C_6D_6$ (1 mL) for 4 hours. The solution was then concentrated and purified by flash chromatography (petroleum ether–diethylether 85 : 15) to give **23** (17 mg, 74%). mp 161 °C; $\delta_H$ (400 MHz, $C_6D_6$) 0.04 (3H, s, $CH_3$), 0.34 (3H, s, $CH_3$), 0.91 (3H, br s, $CH_3$), 1.00–1.07 (7H, m, 2 × $CH_3$ and CH), 1.03 (9H, s, 3 × $CH_3$), 1.15–1.18 (7H, m, 2 × $CH_3$ and CH),), 1.34 (3H, s, $CH_3$), 1.73 (3H, s, $CH_3$), 2.12 (1H, d, $J$ = 10.5 Hz, CH), 4.85 (1H, s, CH), 5.16 (1H, d, $J$ = 10.5 Hz, CH), 5.43 (1H, br s, CH), 7.18 (1H, t, $J$ = 7.5 Hz, $CH_{Ar}$), 7.24 (1H, t, $J$ = 7.5 Hz, $CH_{Ar}$), 7.53 (1H, d, $J$ = 7.5 Hz, $CH_{Ar}$), 7.84 (1H, d, $J$ = 7.5 Hz, $CH_{Ar}$); $\delta_C$ (100 MHz, $CDCl_3$) −5.02 ($CH_3$), −4.6 ($CH_3$), 13.3 (CH), 13.9 ($CH_3$), 14.2 (CH), 17.1$_6$ ($CH_3$), 17.2 ($CH_3$), 17.4 ($CH_3$), 17.5 ($CH_3$), 18.5 (C), 26.2 (4 × $CH_3$), 31.5 ($CH_3$), 55.0 (CH), 68.5 (CH), 71.5 (CH), 76.8 (CH), 90.2 (C), 119.5 (CH), 123.3 (CH), 123.4 (CH), 127.3 (CH), 128.1 (CH), 134.3 (C), 139.5 (C), 169.5 (C), 171.6 (C); IR ($\nu_{max}$/cm$^{-1}$) 2933, 2891, 2863, 1756, 1645, 1465, 1348, 1253, 1201, 1133, 1073, 1028, 1016; MS *m/z* (ESI+) 553 [M + Na]$^+$; HRMS found 531.2957 [M + H$^+$], $C_{29}H_{47}O_5Si_2$ requires 531.2957.

**Compound 24**

To a stirred solution of the γ-butenolide[27] (500 mg, 2.08 mmol, 1 equiv) in anhydrous THF (11 mL) at 0 °C was added a solution of HF-pyridine (76 µL, 70% in pyridine, 4.17 mmol, 2 equiv). The reaction was stirred at room temperature and followed by TLC. After disappearance of the starting material, the reaction was quenched with a saturated aqueous solution of $NaHCO_3$. The aqueous phase was extracted with ether and the combined organics layers were dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The resulting crude product was purified by flash chromatography on silica gel (petroleum ether–ethyl acetate 1 : 1) to give **24** (200 mg, 76%) as a 9 : 1 mixture of diastereomers. $\delta_H$ (400 MHz, $C_6D_6$) 4.06 (2H, d, $J$ = 6.8 Hz, $CH_2$), 4.72 (1H, t, $J$ = 6.8 Hz, CH), 5.44 (1H, d, $J$ = 5.3 Hz, CH), 6.16 (1H, d, $J$ = 5.3 Hz, CH); $\delta_C$ (100 MHz, $C_6D_6$) 57.2 ($CH_2$), 114.2 (CH), 120.1 (CH), 143.1 (C), 149.2 (C), 168.8 (C); IR ($\nu_{max}$/cm$^{-1}$) 3347, 2954, 2922, 2854, 1774, 1747, 1677, 1463, 1118, 1065; HRMS found 127.0389 [M + H]$^+$, $C_6H_7O_3$ requires 127.0390.

**Compound 25**

To a stirred solution of $CH_2Cl_2$ (1.6 mL), imidazole (108 mg, 2.55 mmol, 5 equiv) and $iPr_2SiCl_2$ (58 µL, 0.32 mmol, 1 equiv) was added dropwise and at room temperature **19** (80 mg, 0.32 mmol, 1 equiv) in $CH_2Cl_2$ (0.5 mL). After disappearance of **19** (5 min), lactone **24** (40 mg, 0.32 mmol, 1 equiv) in $CH_2Cl_2$ (1.5 mL) was added to the mixture. The reaction was stirred for 15 min, then quenched with a saturated aqueous solution of $NH_4Cl$. The aqueous layer was extracted with $CH_2Cl_2$. The combined organic phase were dried over $Na_2SO_4$ and concentrated under vacuum. The crude product was purified by flash chromatography (petroleum ether–diethylether 85 : 15) to give the silicon tethered (109 mg, 70%). In Schlenk tube, the silicon tethered (109 mg) was heated (55 °C) in degassed $C_6D_6$ (6 mL) for 4 hours. The solution was then concentrated and purified by flash chromatography (petroleum ether–diethylether 85 : 15) to give **25** (44 mg, 40%). $\delta_H$ (400 MHz, $C_6D_6$) −0.17 (3H, s, $CH_3$), 0.01 (3H, s, $CH_3$), 0.87 (9H, s, 3 × $CH_3$), 1.08–1.12 (14H, m, 4 × $CH_3$ and 2 × CH), 2.63 (1H, td, $J$ = 10 and 4 Hz, CH), 3.84 (1H, dd, $J$ = 11 and 4 Hz, C$H_2$), 4.01–4.07 (1H, m, C$H_2$), 4.43 (1H, s, CH), 5.24 (1H, d, $J$ = 10 Hz, CH), 5.33 (1H, d, $J$ = 5.5 Hz, CH), 5.33 (1H, d, $J$ = 5.5 Hz, CH), 7.10–7.24 (3H, m, 3 × $CH_{Ar}$), 7.82 (1H, d, $J$ = 7.5 Hz, $CH_{Ar}$); $\delta_C$ (100 MHz, $CDCl_3$) −4.5 ($CH_3$), −4.2 ($CH_3$), 12.4 (CH), 13.6 (CH), 16.9 ($CH_3$), 17.0 ($CH_3$), 17.2 ($CH_3$), 17.2$_4$ ($CH_3$), 18.3 (C), 25.9 (3 × $CH_3$), 44.2 (CH), 64.1 ($CH_2$), 72.3 (CH), 73.8 (CH), 89.8 (C), 121.8 (CH), 125.6 (CH), 127.4 (CH), 127.5 (CH), 128.9 (CH), 134.3 (C), 139.1 (C), 156.7 (CH), 171.9 (C); IR ($\nu_{max}$/cm$^{-1}$) 2953, 2928, 2896, 2860, 1767, 1463, 1254, 1134, 1081, 1027; MS *m/z* (ESI+) 511 [M + Na]$^+$; HRMS found 506.2751 [M + $NH_4^+$], $C_{26}H_{44}NO_5Si_2$ requires 506.2753.

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