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Facile Conversion of Cyclopropanols into Linear Conjugate Enones

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A practical method for the conversion of 1,2-disubstituted cyclopropanols derived from Kulinkovich cyclopropanation into linear enones was developed. The approach features regioselective cleavage of the cyclopropane rings in EtOH at ambient temperature with inexpensive and readily available $Co(acac)_2$ as the catalyst and air as the reagent. The crude intermediate peroxides were directly reduced with Ph_3P to afford the corresponding β-hydroxy ketones, which, on mesylation and β-elimination performed in a one-pot manner, furnished the end products in good to excellent yields after only one chromatography step at the end of the whole sequence.

Introduction

The Kulinkovich cyclopropanation[1] is a reaction that can be conducted under mild relatively conditions that has found numerous applications in organic synthesis in recent years. The functional groups to be coupled, in many cases an ester and a terminal alkene, can be carried unmasked through several transformation steps before the eventual execution of the cross coupling. These features make the Kulinkovich reaction, in combination with a suitable ring-opening transformation if the cyclopropane ring is not part of the target structures (see below), a tool with distinct potential for connecting two multifunctional fragments (Figure 1) to provide longer linear structures.

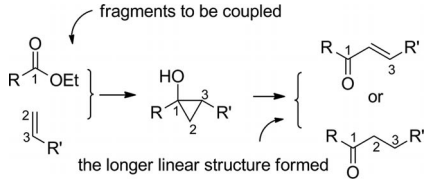

Figure 1. A schematic illustration showing the potential of the Kulinkovich cyclopropanation as a tool for coupling two major fragments into a longer linear structure, an operation often encountered in multistep syntheses.

However, it should also be noted that until now a large fraction of synthetically significant reactions that are followed by a ring-opening step involve only unsubstituted ethylene (often formed in situ from EtMgBr),[2] and the Kulinkovich reaction was employed to append two carbon atoms onto the substrates rather than to connect two major fragments. Examples using substituted ethylenes are scant,[3,4] presumably because of the regioselectivity problem at the required ring-opening step.[3,5] It thus seems that the lack of mild and effective means for cleaving the three-membered ring with satisfactory regioselectivity is a bottleneck for broader employment of the Kulinkovich reaction as a practical tool for connecting complex multifunctional fragments into longer linear structures. The limited number of available choices, along with needs that arose from our own synthetic endeavours, prompted us to seek new methods that were suitable for cleaving Kulinkovich cyclopropanols into their corresponding linear structures, especially those with multiple functionalities in the substituents on the three-membered rings.[6] Our efforts along these lines led to some pleasing results with the system $Co(acac)_2$ {cobalt(II) acetylacetonate}/O_2 (air)/EtOH, which are detailed here.

Results and Discussion

The combination of $Co(acac)_2$, O_2, and Et_3SiH was first introduced in 1989 by Isayama and Mukaiyama as a novel way to install a silylperoxyl group onto alkenes.[7] Since then, it has been successfully applied in many syntheses of organic peroxides.[8,9] A range of natural and synthetic organic peroxy compounds, often with antimalarial activity, were prepared by using this reaction to introduce the peroxy bonds.

According to the mechanisms[9] postulated in the early 2000's by Nojima et al. and O'Neill et al. (Figure 2), the triplet O_2 is installed onto the alkene by coupling with a carbon-centred radical generated through the addition of HCo^{III} followed by homolysis of the Co–C bond. Because Et_3SiH plays a critical role in the generation of HCo^{III}, it appears indispensable for the successful realization of the whole reaction. Indeed, until now Et_3SiH has been included in all the literature precedents.

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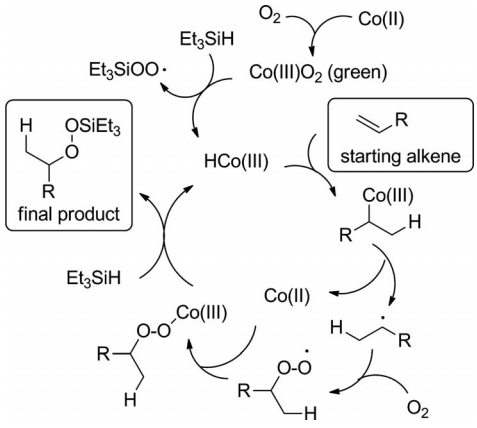
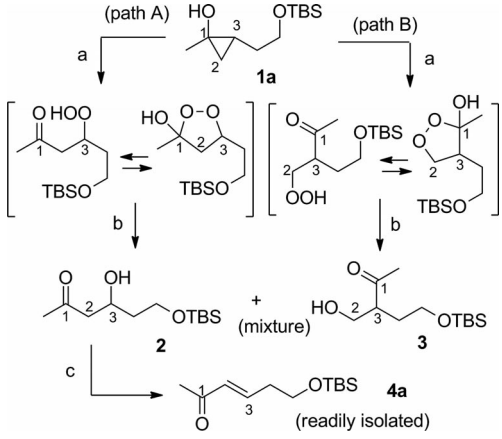


Figure 2. The O_2/Co(acac)$_2$/Et_3SiH mediated silylperoxidation.[9b] For clarity, the ligands on the Co^{II} and Co^{III} species are not shown.

Nevertheless, it still seems to us that interaction of Co(acac)$_2$ with O_2 and cyclopropanol may result in oxygen-centred radical species (see below), with or without added Et_3SiH, and thus may initiate subsequent reactions in a manner similar to those in Kulinkovich's[10] conversion of cyclopropanols into linear epoxy ketones mediated by Mn^{II} abietate (in which the hydroperoxy intermediate reacted with the carbanion generated at the carbon α to the ketone carbonyl group by treatment with KOH).

Our initial explorations were performed on a readily accessible 1,2-disubstituted cyclopropanol **1a** (Scheme 1). As summarized in Table 1, treatment of **1a** with 1 mol-% Co(acac)$_2$ in EtOH under O_2 (balloon) at ambient temperature for 12 h led to complete disappearance of **1a**. The product mixture apparently contained several components, presumably because of the coexistence of the two reaction paths and ketone–hemiketal interconversion. Reduction of the peroxy bonds in the crude products (after removal of EtOH by rotary evaporation) with Ph_3P in CH_2Cl_2 indeed afforded a simplified mixture that contained **2** and **3** in a 19:1 ratio (Table 1, entry 1) as measured by ^1H NMR spectroscopy.[11]



Scheme 1. *Reagents and conditions:* (a) Co(acac)$_2$, O_2, EtOH, room temp.; (b) Ph_3P, CH_2Cl_2, r.t.; (c) MsCl, DMAP, Et_3N, r.t., cf. text; Co(acac)$_2$ = cobalt(II) acetylaceonate, MsCl = methanesulfonyl chloride, DMAP = 4-(dimethylamino)pyridine.

Table 1. Initial exploration of the cleavage of **1a** with Co(acac)$_2$/O_2 followed by Ph_3P reduction of the peroxy bond (cf. Scheme 1).

Entry	Conditions[a]	Yield (%)	Ratio **2**/**3**[b]
1	Co(acac)$_2$ (1 mol-%)/O_2/EtOH/12 h[c]	81	19:1
2	Co(acac)$_2$ (1 mol-%)/air/EtOH/7 h	81	19:1
3	Co(acac)$_2$ (5 mol-%)/air/EtOH/5 h	83	19:1
4	Co(acac)$_2$ (5 mol-%)/air/EtOH/1.5 h	87	20:1
5	Co(acac)$_2$ (5 mol-%)/air/EtOH/1.5 h	87[d]	23:1
6	Co(acac)$_2$ (5 mol-%)/air/CH_2Cl_2/1 h	complex mixture	

[a] All runs (except entry 1) were performed in an open flask at ambient temperature with the reduction performed in CH_2Cl_2 after removal of EtOH. [b] Measured by ^1H NMR spectroscopic analysis of the crude product mixture. [c] O_2 balloon. [d] Reduction of the peroxides was performed in EtOH/CH_2Cl_2 (1:4).

Use of air (i.e., conducting the reaction in an open flask) instead of O_2 did not cause any discernible difference (Table 1, entry 2). Therefore, all subsequent runs were carried out in an open flask. Increasing the amount of added catalyst from 1 to 5 mol-% significantly shortened the reaction time, while the yield and the product ratio remained essentially unchanged (Table 1, entries 3 and 4).

Because concentrating the crude mixture (removal of the EtOH) before reduction with Ph_3P was potentially dangerous because of the presence of peroxides, we then tried to skip this operation. To our satisfaction, addition of CH_2Cl_2, which was required for dissolving Ph_3P, to the reaction mixture followed by treatment with Ph_3P worked equally well (Table 1, entry 5). The potential risk of explosion during concentration was thus eliminated. However, it was also noted that the use of CH_2Cl_2 instead of EtOH as the reaction solvent from the beginning was not rewarding (despite the fact that most previous alkene silylperoxidations were performed in CH_2Cl_2), because a rather complex product mixture resulted (Table 1, entry 6) under otherwise identical conditions. The conditions employed in Table 1, entry 5 appeared to be the most satisfactory, and these were employed in all subsequent experiments.

A plausible mechanism for the observed facile conversion of cyclopropanols into hydroperoxides is shown in Figure 3.

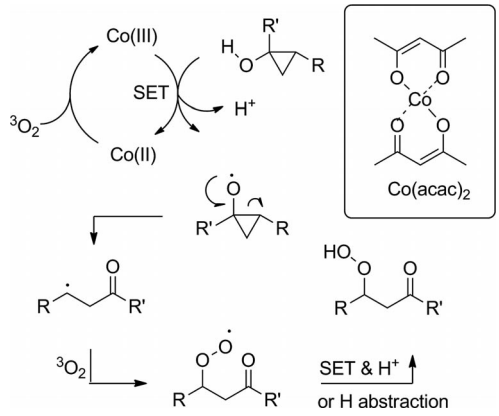
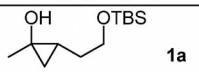
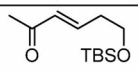
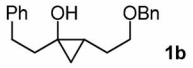
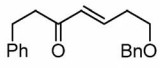
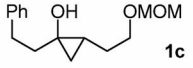
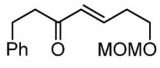
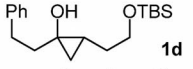
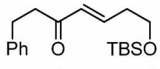
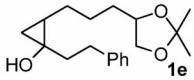
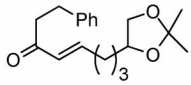
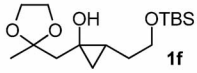
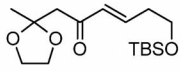
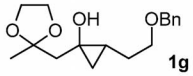
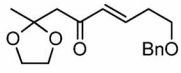
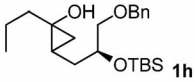
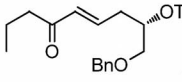
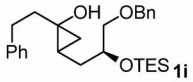
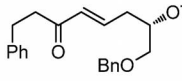
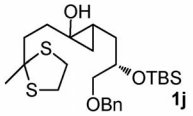
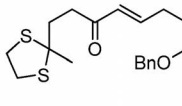
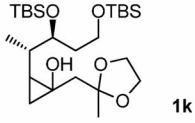
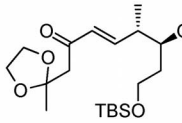
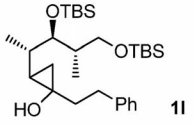
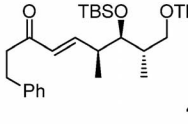
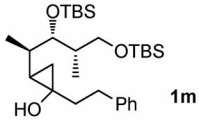
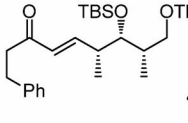
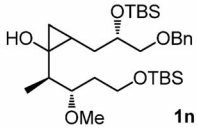
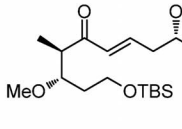


Figure 3. A possible mechanism for the Co(acac)$_2$-induced cleavage of the Kulinkovich cyclopropanols. For clarity, only one of the two possible ring-opening intermediate carbon-centred radicals (Path A in Scheme 1) is shown; SET = single electron transfer.

The added $Co(acac)_2$ was first oxidized by O_2 (or air) to afford a Co^{III} species. Subsequent single electron transfer from the starting cyclopropanol to Co^{III} generated the transient oxy radical of the cyclopropanol and a proton. The highly reactive oxygen-centred radical then rearranged with opening of the strained three-membered ring to afford a more stable carbon-centred radical, which readily trapped a molecule of O_2 to give a hydroperoxy radical. Finally, the hydroperoxy radical was converted into product hydroperoxide either by SET followed by protonation or simply through hydrogen abstraction.

Table 2.[a] The results of cleavage of cyclopropanols with $Co(acac)_2$/air at room temp. followed by reduction of the peroxy bond and β-elimination.

Entry	Starting cyclopropanol[b]	Final product (yield, %[c])
1	 **1a**	 **4a** (86)
2	 **1b**	 **4b**(88)
3	 **1c**	 **4c** (79)
4	 **1d**	 **4d** (84)
5	 **1e**	 **4e** (92)
6	 **1f**	 **4f** (84)
7	 **1g**	 **4g** (77)
8	 **1h**	 **4h** (86)
9	 **1i**	 **4i** (72)
10	 **1j**	 **4j** (70)
11	 **1k**	 **4k** (68)
12	 **1l**	 **4l** (69)
13	 **1m**	 **4m** (70)
14	 **1n**	 **4n** (74)

[a] All runs were performed by using the general procedure given in the Experimental Section. [b] For the yields for **1a**–**n** (obtained by the Kulinkovich cyclopropanation), see the Supporting Information. [c] Calculated from the pure products isolated by chromatography.

To facilitate the isolation and characterisation of the products, and also to make it easier to find broader applications in multistep syntheses, we next elaborated the crude β-hydroxy ketones (which are liable to β-eliminations) into the corresponding enones by direct treatment with MsCl and Et_3N. The resulting mixture of enones was readily separated on silica gel to afford pure **4a** in 86% yield over three steps from **1a** (Table 2, entry 1).

A range of other 1,2-disubstituted cyclopropanols (prepared by the Kulinkovich reaction) could also be cleaved, reduced and elaborated into the corresponding enones in good to excellent yields by using the same procedure. Replacement of the *tert*-butyldimethylsilyl (TBS) group in **1a** with a benzyl (Bn) group and/or extending the methyl group in **1a** into a phenylethyl group did not cause any discernible difference (Table 2, entries 2 and 4).

The methoxymethyl (MOM) protecting group was well tolerated (Table 2, entry 3), and other commonly encountered ketal-type protecting groups, such as acetonide or 1,2-dioxolane (the ketal of ethylene glycol) or thioketal, were also compatible (Table 2, entries 5–7 and 10).

Several substrates with enantiopure stereogenic centres at different positions in the carbon chains were then examined to further demonstrate the potential applicability of this procedure in natural product synthesis (Table 2, entries 8–14). Again, rather good yields were obtained. Substitution in the side chains at positions immediately next to the ring (Table 2, entry 13–14) was also tolerated, although the yields were slightly lower than those obtained with less sterically hindered substrates.

Conclusions

In efforts to facilitate broader employment of the Kulinkovich cyclopropanation as a tool for coupling two complex multifunctional fragments into longer linear structures, cleavage of 1,2-disubstituted cyclopropanols derived from a variety of different fragments carrying multiple stereogenic centres and different protection groups was studied in a systematic way. By using readily available $Co(acac)_2$ as catalyst, the three-membered rings in the substrates were regioselectively cleaved in EtOH at ambient temperature with air as the reagent. The crude ring-cleavage products were then reduced with Ph_3P to afford the corresponding β-hydroxy ketones, which, on mesylation and β-elimination performed in a one-pot manner, delivered linear conjugate enones in high yields after a single chromatographic separation at the end of the whole sequence. Apart from the efficiency and mild conditions, the low cost and operational convenience of the newly developed protocol are also noteworthy. Protocols of this type are expected to make it much easier to realize the thus-far largely overlooked potential for

the Kulinkovich reaction as a coupling tool in multistep synthesis.[12]

Experimental Section

General Methods: NMR spectra were recorded with a Bruker Avance NMR spectrometer operating at 400 MHz for ^{1}H unless otherwise stated. IR spectra were measured with a Nicolet 380 Infrared spectrophotometer. ESI-MS data were acquired with a Shimadzu LCMS-2010EV mass spectrometer. ESI-HRMS data were obtained with a Bruker APEXIII 7.0 Tesla FT-MS spectrometer. EI-MS were recorded with an Agilent Technologies 5973N spectrometer. HRMS (EI) were acquired with a Waters Micromass GCT Premier instrument. Optical rotations were measured with a Jasco P-1030 polarimeter. All reagents were of reagent grade and used as purchased. Column chromatography was performed on silica gel (300–400 mesh) under slightly positive pressure. Petroleum ether (PE) for chromatography had a boiling range 60–90 °C.

General Procedure for the Co(acac)$_2$-Catalyzed Oxidative Cleavage of Cyclopropanols under Air: Cyclopropanol **1** (0.2 mmol) and Co(acac)$_2$ (2.6 mg, 0.01 mmol) were added to a 25-mL round-bottomed flask. Anhydrous EtOH (1.0 mL) was then introduced and the mixture was stirred at ambient temperature for 1.5 h, when TLC showed complete disappearance of the starting material. CH_2Cl_2 (4.0 mL) was added, followed by Ph_3P (58 mg, 0.22 mmol) and the mixture was stirred at ambient temperature for 1 h before the solvents were removed by rotary evaporation. The residue was dissolved in CH_2Cl_2 (2.0 mL) and to the resulting solution were added in turn DMAP (2 mg, 0.02 mmol), Et_3N (0.23 mL, 1.6 mmol) and MsCl (46 μL, 0.6 mmol). The mixture was stirred at ambient temperature for 3–4 h. When TLC showed completion of the reaction, water (5 mL) was added and the mixture was extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with water (5 mL) and brine (5 mL) before being dried with anhydrous Na_2SO_4. The drying agent was filtered off and the filtrate was concentrated on a rotary evaporator to leave an oily residue, which was purified by chromatography on silica gel (PE/EtOAc) to furnish the end product enone **4** in the yield listed in Table 2.

Compound 4a:[13] Colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.79 (dt, J = 16.0, 7.0 Hz, 1 H), 6.08 (d, J = 6.0 Hz, 1 H), 3.72 (t, J = 7.2 Hz, 2 H), 2.41 (q, J = 6.3 Hz, 2 H), 2.22 (s, 3 H), 0.87 (s, 9 H), 0.03 (s, 6 H) ppm.

Compound 4b: Colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.16 (m, 10 H), 6.83 (dt, J = 15.8, 6.8 Hz, 1 H), 6.15 (d, J = 16.1 Hz, 1 H), 4.50 (s, 2 H), 3.57 (t, J = 6.2 Hz, 2 H), 2.96–2.82 (m, 4 H), 2.50 (q, J = 6.5 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.3, 143.9, 141.2, 138.0, 131.6, 128.41, 128.38, 128.3, 127.68, 127.65, 126.0, 73.0, 68.2, 41.6, 32.8, 29.9 ppm. FTIR (film): $\tilde{\nu}$ = 3062, 3028, 2924, 2857, 1697, 1672, 1630, 1603, 1496, 1454, 1408, 1363, 1288, 1205, 1178, 1098, 1028, 977, 738, 698 cm^{-1}. MS (ESI): m/z = 317.1 [M + Na]$^+$. HRMS (ESI): m/z calcd. for $C_{20}H_{22}O_2Na$ [M + Na]$^+$ 317.1512; found 317.1509.

Compound 4c: Colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.17 (m, 5 H), 6.84 (dt, J = 16.0, 6.8 Hz, 1 H), 6.18 (d, J = 16.1 Hz, 1 H), 4.61 (s, 2 H), 3.64 (t, J = 6.3 Hz, 2 H), 3.34 (s, 3 H), 2.97–2.85 (m, 4 H), 2.50 (qd, J = 6.5, 1.2 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.2, 143.8, 141.2, 131.7, 128.4, 128.3, 126.0, 96.4, 65.8, 55.3, 41.7, 32.8, 29.9 ppm. FTIR (film): $\tilde{\nu}$ = 2930, 2887, 1697, 1673, 1631, 1602, 1497, 1454, 1366, 1290, 1211, 1178, 1149, 1110, 1039, 975, 918, 750, 700 cm^{-1}. MS (ESI): m/z = 271.1 [M + Na]$^+$. HRMS (ESI): m/z calcd. for $C_{15}H_{20}O_3Na$ [M + Na]$^+$ 271.1305; found 271.1315.

Compound 4d: Colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.16 (m, 5 H), 6.83 (dt, J = 16.0, 7.1 Hz, 1 H), 6.14 (d, J = 16.0 Hz, 1 H), 3.72 (t, J = 6.4 Hz, 2 H), 2.98–2.84 (m, 4 H), 2.41 (q, J = 6.3 Hz, 2 H), 0.88 (s, 9 H), 0.05 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.4, 144.3, 141.2, 131.8, 128.4, 128.3, 126.0, 61.5, 41.5, 35.9, 30.0, 25.8, 18.2, –5.4 ppm. FTIR (film): $\tilde{\nu}$ = 3085, 3062, 3028, 2955, 2929, 2857, 2738, 1698, 1676, 1632, 1604, 1496, 1471, 1462, 1454, 1362, 1256, 1178, 1102, 1006, 978, 938, 836, 777, 699 cm^{-1}. MS (ESI): m/z = 341.2 [M + Na]$^+$. HRMS (ESI): m/z calcd. for $C_{19}H_{30}O_2SiNa$ [M + Na]$^+$ 341.1907; found 341.1910.

Compound 4e: Colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.16 (m, 5 H), 6.80 (dt, J = 15.9, 7.0 Hz, 1 H), 6.10 (d, J = 16.1 Hz, 1 H), 4.10–4.01 (m, 2 H), 3.50 (t, J = 7.1 Hz, 1 H), 2.96–2.83 (m, 4 H), 2.24 (q, J = 6.6 Hz, 2 H), 1.46–1.06 (m, 4 H), 1.40 (s, 3 H), 1.34 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.3, 146.7, 141.1, 130.5, 128.4, 128.3, 126.0, 108.8, 75.6, 69.3, 41.6, 32.9, 32.2, 30.0, 26.9, 25.6, 24.2 ppm. FTIR (film): $\tilde{\nu}$ = 3061, 3027, 2985, 2933, 2865, 1697, 1673, 1629, 1604, 1497, 1454, 1409, 1378, 1369, 1248, 1214, 1156, 1060, 979, 856, 749, 700 cm^{-1}. MS (ESI): m/z = 325.1 [M + Na]$^+$. HRMS (ESI): m/z calcd. for $C_{19}H_{26}O_3Na$ [M + Na]$^+$ 325.1774; found 325.1764.

Compound 4f: Colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.83 (dt, J = 15.8, 7.4 Hz, 1 H), 6.23 (d, J = 15.8 Hz, 1 H), 3.98–3.88 (m, 4 H), 3.71 (t, J = 6.3 Hz, 2 H), 2.86 (s, 2 H), 2.41 (q, J = 5.5 Hz, 2 H), 1.40 (s, 3 H), 0.86 (s, 9 H), 0.02 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.7, 144.8, 132.3, 108.1, 64.6, 61.5, 49.4, 35.9, 25.8, 24.6, 18.2, –5.4 ppm. FTIR (film): $\tilde{\nu}$ = 2954, 2930, 2885, 2858, 1692, 1666, 1626, 1472, 1380, 1255, 1213, 1099, 1048, 979, 949, 836, 777 cm^{-1}. MS (ESI): m/z = 337.2 [M + Na]$^+$. HRMS (ESI): m/z calcd. for $C_{16}H_{30}O_4SiNa$ [M + Na]$^+$ 337.1806; found 337.1821.

Compound 4g: Colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.25 (m, 5 H), 6.86 (dt, J = 15.8, 6.8 Hz, 1 H), 6.27 (d, J = 16.0 Hz, 1 H), 4.51 (s, 2 H), 3.98–3.88 (m, 4 H), 3.60 (t, J = 6.4 Hz, 2 H), 2.88 (s, 2 H), 2.53 (q, J = 6.5 Hz, 2 H), 1.43 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.7, 144.5, 138.0, 132.1, 128.3, 127.6, 108.1, 73.0, 68.2, 64.6, 49.5, 32.8, 24.7 ppm. FTIR (film): $\tilde{\nu}$ = 3041, 2980, 2938, 2865, 1718, 1689, 1662, 1624, 1495, 1454, 1349, 1278, 1204, 1174, 1101, 1044, 949, 902, 738, 698 cm^{-1}. MS (EI): m/z (%) = 91 (100), 105 (54), 43 (26), 77 (26), 199 (0.74) [M – Bn]$^+$. HRMS (EI): m/z calcd. for $C_{10}H_{15}O_4$ [M – Bn]$^+$ 199.0970; found 199.0964.

Compound 4h: Colourless oil; $[\alpha]_D^{27}$ = –12.4 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.26 (m, 5 H), 6.82 (dt, J = 15.8, 7.6 Hz, 1 H), 6.11 (d, J = 16.1 Hz, 1 H), 4.53 (d, J = 12.3 Hz, 1 H), 4.50 (d, J = 12.3 Hz, 1 H), 3.96 (quint, J = 5.5 Hz, 1 H), 3.42 (dd, J = 9.5, 5.3 Hz, 1 H), 3.34 (dd, J = 9.6, 6.3 Hz, 1 H), 2.54–2.45 (m, 3 H), 2.42–2.34 (m, 1 H), 1.67–1.58 (m, 2 H), 0.92 (t, J = 7.3 Hz, 3 H), 0.87 (s, 9 H), 0.04 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.5, 143.4, 138.1, 132.6, 128.3, 127.6, 74.0, 73.3, 70.4, 41.7, 38.0, 25.7, 18.0, 17.6, 13.8, –4.5, –4.8 ppm. FTIR (film): $\tilde{\nu}$ = 3031, 2957, 2929, 2890, 2857, 1697, 1676, 1632, 1496, 1462, 1362, 1254, 1203, 1104, 983, 835, 776, 736, 698 cm^{-1}. MS (ESI): m/z = 399.2 [M + Na]$^+$. HRMS (ESI): m/z calcd. for $C_{22}H_{36}O_3SiNa$ [M + Na]$^+$ 399.2326; found 399.2306.

Compound 4i: Colourless oil; $[\alpha]_D^{27}$ = –7.5 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.16 (m, 10 H), 6.82 (dt, J = 16.0, 7.3 Hz, 1 H), 6.12 (d, J = 16.1 Hz, 1 H), 4.50 (s, 2 H), 3.94

(quint, J = 5.6 Hz, 1 H), 3.40 (dd, J = 9.4, 5.2 Hz, 1 H), 3.32 (dd, J = 9.5, 6.2 Hz, 1 H), 2.94–2.89 (m, 2 H), 2.85–2.80 (m, 2 H), 2.54–2.34 (m, 2 H), 0.92 (t, J = 7.9 Hz, 9 H), 0.57 (q, J = 7.8 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.2, 143.7, 141.3, 138.0, 132.5, 128.4, 128.3, 127.7, 126.0, 73.8, 73.3, 70.2, 41.4, 38.0, 30.0, 6.8, 4.8 ppm. FTIR (film): $\tilde{\nu}$ = 3393, 3064, 3027, 2953, 2911, 2875, 1601, 1496, 1455, 1413, 1365, 1237, 1096, 1006, 739, 697 cm^{-1}. MS (ESI): m/z = 461.3 [M + Na]$^+$. HRMS (ESI): m/z calcd. for $C_{27}H_{38}O_3SiNa$ [M + Na]$^+$ 461.2482; found 461.2484.

Compound 4j: Colourless oil; $[\alpha]_D^{27}$ = –7.4 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.26 (m, 5 H), 6.88 (dt, J = 15.8, 7.3 Hz, 1 H), 6.12 (d, J = 15.8 Hz, 1 H), 4.54 (d, J = 12.8 Hz, 1 H), 4.50 (d, J = 12.8 Hz, 1 H), 3.96 (quint, J = 5.5 Hz, 1 H), 3.42 (dd, J = 9.3, 5.3 Hz, 1 H), 3.38–3.26 (m, 5 H), 2.82 (t, J = 7.6 Hz, 2 H), 2.55–2.47 (m, 1 H), 2.43–2.35 (m, 1 H), 2.21 (t, J = 7.6 Hz, 2 H), 1.78 (s, 3 H), 0.88 (s, 9 H), 0.05 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.4, 143.7, 138.1, 132.5, 128.4, 127.63, 127.60, 74.0, 73.3, 70.4, 66.3, 40.1, 38.6, 38.0, 37.5, 32.9, 25.8, 18.1, –4.5, –4.8 ppm. FTIR (film): $\tilde{\nu}$ = 3033, 2953, 2927, 2856, 1697, 1672, 1632, 1453, 1362, 1254, 1099, 982, 836, 776, 736, 698 cm^{-1}. MS (ESI): m/z = 503.3 [M + Na]$^+$. HRMS (ESI): m/z calcd. for $C_{25}H_{40}O_3S_2SiNa$ [M + Na]$^+$ 503.2080; found 503.2103.

Compound 4k: Colourless oil; $[\alpha]_D^{28}$ = –35.4 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.95 (dd, J = 16.0, 6.8 Hz, 1 H), 6.16 (dd, J = 16.0, 1.2 Hz, 1 H), 3.98–3.91 (m, 4 H), 3.83 (quint, J = 4.0 Hz, 1 H), 3.69–3.58 (m, 2 H), 2.91 (d, J = 13.8 Hz, 1 H), 2.87 (d, J = 13.6 Hz, 1 H), 2.56–2.48 (m, 1 H), 1.68–1.58 (m, 2 H), 1.55–1.47 (m, 1 H), 1.43 (s, 3 H), 1.02 (d, J = 6.8 Hz, 3 H), 0.89 (s, 9 H), 0.87 (s, 9 H), 0.05 (s, 3 H), 0.04 (s, 3 H), 0.03 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.0, 150.6, 130.6, 108.2, 72.2, 64.6, 59.6, 49.2, 42.2, 36.5, 25.9, 25.8, 24.7, 18.2, 18.0, 14.1, –4.5, –4.6, –5.3, –5.4 ppm. FTIR (film): $\tilde{\nu}$ = 2955, 2930, 2885, 2857, 1692, 1663, 1623, 1472, 1463, 1380, 1361, 1255, 1095, 1047, 939, 836, 775 cm^{-1}. MS (ESI): m/z = 509.4 [M + Na]$^+$. HRMS (ESI): m/z calcd. for $C_{25}H_{50}O_5Si_2Na$ [M + Na]$^+$ 509.3089; found 509.3103.

Compound 4l: Colourless oil; $[\alpha]_D^{28}$ = –9.9 (c = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.25 (m, 5 H), 6.95 (dd, J = 16.0, 7.4 Hz, 1 H), 6.16 (dd, J = 16.1, 1.0 Hz, 1 H), 3.72 (t, J = 5.2 Hz, 1 H), 3.72 (dd, J = 10.1, 5.6 Hz, 1 H), 3.69 (dd, J = 10.0, 7.0 Hz, 1 H), 3.05–3.00 (m, 2 H), 2.97–2.91 (m, 2 H), 2.67–2.58 (m, 1 H), 1.89 (quint, J = 6.3 Hz, 1 H), 1.12 (d, J = 6.8 Hz, 3 H), 0.98 (d, J = 6.8 Hz, 3 H), 0.97 (s, 9 H), 0.96 (s, 9 H), 0.13 (s, 3 H), 0.11 (s, 3 H), 0.10 (s, 3 H), 0.08 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.4, 151.4, 141.3, 129.2, 128.46, 128.35, 126.0, 76.5, 64.9, 41.7, 40.5, 40.4, 30.0, 26.0, 25.9, 18.31, 18.26, 14.4, 14.1, –4.0, –4.1, –5.3, –5.4 ppm. FTIR (film): $\tilde{\nu}$ = 2956, 2929, 2881, 2857, 1694, 1678, 1627, 1472, 1361, 1254, 1086, 1025, 836, 774, 698 cm^{-1}. MS (ESI): m/z = 527.4 [M + Na]$^+$. HRMS (ESI): m/z calcd. for $C_{29}H_{52}O_3Si_2Na$ [M + Na]$^+$ 527.3347; found 527.3328.

Compound 4m: Colourless oil; $[\alpha]_D^{27}$ = +28.3 (c = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.16 (m, 5 H), 6.91 (dd, J = 16.2, 7.4 Hz, 1 H), 6.05 (d, J = 16.1 Hz, 1 H), 3.82 (dd, J = 6.3, 1.8 Hz, 1 H), 3.41 (t, J = 9.5 Hz, 1 H), 3.34 (dd, J = 9.8, 6.0 Hz, 1 H), 2.97–2.83 (m, 4 H), 2.58–2.49 (m, 1 H), 1.71–1.64 (m, 1 H), 1.04 (d, J = 6.8 Hz, 3 H), 0.91 (s, 9 H), 0.88 (s, 9 H), 0.75 (d, J = 6.8 Hz, 3 H), 0.06 (s, 3 H), 0.05 (s, 3 H), 0.03 (s, 3 H), 0.02 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.6, 150.6, 141.3, 129.2, 128.5, 128.3, 126.0, 74.3, 65.6, 42.0, 41.4, 38.9, 30.1, 26.0, 25.9, 18.4, 18.2, 15.8, 10.8, –3.9, –4.3, –5.32, –5.36 ppm. FTIR (film): $\tilde{\nu}$ = 2956, 2928, 2856, 1698, 1679, 1627, 1471, 1361, 1252, 1093, 1051, 836, 774, 698, 669 cm^{-1}. MS (ESI): m/z = 527.4 [M + Na]$^+$. HRMS (ESI): m/z calcd. for $C_{29}H_{52}O_3Si_2Na$ [M + Na]$^+$ 527.3347; found 527.3323.

Compound 4n: Colourless oil; $[\alpha]_D^{25}$ = –37.9 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.26 (m, 5 H), 6.88 (dt, J = 15.8, 7.5 Hz, 1 H), 6.25 (d, J = 15.6 Hz, 1 H), 4.53 (d, J = 12.3 Hz, 1 H), 4.49 (d, J = 12.5 Hz, 1 H), 3.95 (quint, J = 5.7 Hz, 1 H), 3.72–3.57 (m, 3 H), 3.42 (dd, J = 9.5, 5.5 Hz, 1 H), 3.37–3.33 (m, 4 H), 2.95–2.88 (m, 1 H), 2.54–2.34 (m, 2 H), 1.70–1.55 (m, 2 H), 1.10 (d, J = 7.1 Hz, 3 H), 0.89 (s, 9 H), 0.87 (s, 9 H), 0.04 (s, 6 H), 0.03 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.7, 143.4, 138.2, 131.6, 128.4, 127.61, 127.59, 79.4, 74.1, 73.4, 70.6, 59.5, 58.2, 47.8, 38.0, 35.6, 25.9, 25.8, 18.2, 18.1, 12.1, –4.5, –4.8, –5.3, –5.4 ppm. FTIR (film): $\tilde{\nu}$ = 2954, 29219, 2896, 2856, 1693, 1667, 1628, 1471, 1462, 1362, 1255, 1097, 1005, 836, 776, 734, 697 cm^{-1}. MS (ESI): m/z = 587.5 [M + Na]$^+$. HRMS (ESI): m/z calcd. for $C_{31}H_{56}O_5Si_2Na$ [M + Na]$^+$ 587.3559; found 587.3553.

Supporting Information (see footnote on the first page of this article): Synthesis of the substrates, and copies of ^{1}H, ^{13}C NMR and FTIR spectra for new compounds.

Acknowledgments

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