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# Synthesis of spiroacetals using functionalised titanium carbenoids

Calver A. Main [a], Shahzad S. Rahman [b], Richard C. Hartley [a,*]

[a] WestChem, Department of Chemistry, The Joseph Black Building, University of Glasgow, Glasgow G12 8QQ, UK
[b] GlaxoSmithKline, New Frontiers Science Park, Third Avenue, Harlow, Essex, CM19 5AW, UK

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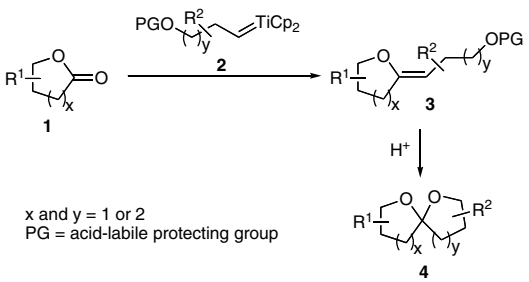
ABSTRACT

Alkylidenation of lactones with functionalised titanium carbenoid reagents (Schrock carbenes) followed by acid-induced cyclisation of the resulting enol ethers constitutes a new method for the preparation of [4.4], [4.5] and [5.5] spiroacetals (1,6-dioxaspiro[4.4]nonanes, 1,6-dioxaspiro[4.5]decanes and 1,7-dioxaspiro[5.5]undecanes, respectively, sometimes termed 5,5-, 5,6- and 6,6-spiroketals). The titanium carbenoids are easily generated from readily available thioacetals.



Spiroacetals have attracted a great deal of interest as synthetic targets as they are found widely in Nature and have a range of biological activities.[1,2] We envisaged synthesising such compounds **4** by the alkylidenation of lactones **1** using titanium carbenoids **2** bearing a masked hydroxyl group, followed by cyclisation of the resulting exocyclic enol ethers **3** in acid (Scheme 1).

Exocyclic enol ethers have been used to prepare spiroacetals by cycloadditions,[3–8] or through acid-induced cyclisation of alcohols.[9–13] Such enol ethers have been prepared by cyclisation of alcohols onto alkynes bearing an electron-withdrawing group,[12] by E2 elimination of hemiacetal derivatives[8,14] or β-alkoxyalkyl iodides,[4] by Ramberg–Bäcklund rearrangement,[9] by Wittig reaction between exocyclic α-alkoxyphosphorous ylides and aldehydes,[10–12] and by methylenation of lactones[5–7] using the Tebbe reagent,[15] Petasis methylenation[16] or Yan's $CH_2Cl_2$–Mg–$TiCl_4$ reagent system.[17] This last strategy is particularly relevant to our work as it uses titanium carbenoids,[18] but the titanium reagents employed only introduced a methylene unit. In their pioneering work, Mortimore and Kocienski used titanium carbenoids bearing THP-protected alcohols to alkylidenate acyclic esters and then induced cyclisation to spiroacetals in acid.[19] However, the titanium carbenoids were prepared from 1,1-dibromoalkanes,[20] which were at the time synthetically difficult to access,[21] and alkylidenation of lactones was reported to be slow and low yielding. Lactones are attractive starting materials, as they are straightforward to prepare by ring-closing metathesis,[22] Baeyer–Villiger oxidation of cyclic ketones[23] and by oxidation of sugars,[24] as well as by methods which would be appropriate for preparation of acyclic esters.




**Scheme 1.**

We have previously shown that using Takeda's procedure,[25] a range of functionalised titanium carbenoids[18] can be generated from easily prepared thioacetals. We had used titanium carbenoids bearing masked oxygen nucleophiles,[26,27] but exclusively for solid-phase synthesis and never to prepare spiroacetals. As in this earlier work,[26] dithiane **6** was synthesised in two steps from 2-hydroxybenzaldehyde, and converted into a titanium carbenoid, presumably titanium benzylidene **7**, using low valent titanium reagent **5** (Scheme 2). Similarly, new titanium alkylidenes **9** and **11** were prepared from dithiane **8** and thioacetal **10**, respectively (Schemes 1 and 3). Titanium reagents **7**, **9** and **11** (1.2 or 3 equiv) were then used to alkylidenate a range of lactones **12**–**19** (Fig. 1) in dry THF overnight to give enol ethers, which were immediately treated

* Corresponding author. Tel.: +44 141 330 4398; fax: +44 141 330 4888.
*E-mail address:* richh@chem.gla.ac.uk (R. C. Hartley).

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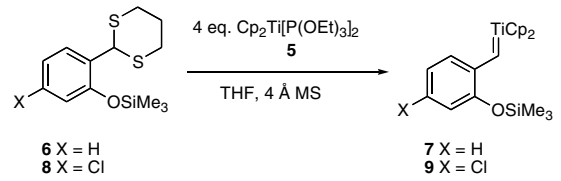
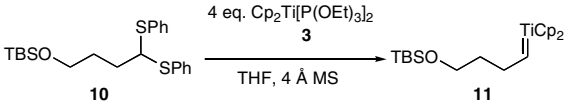



**Scheme 2.**




**Scheme 3.**

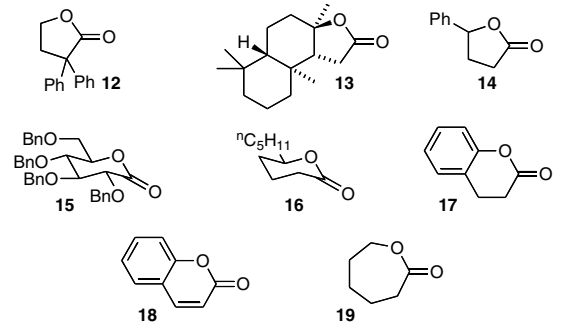



**Figure 1.**

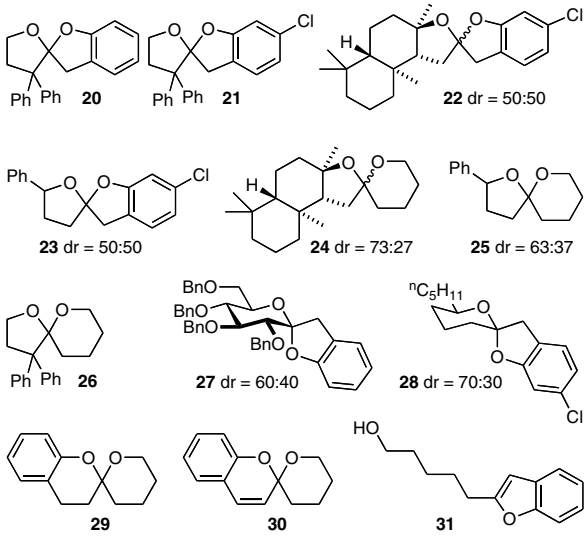



**Figure 2.**

with 10% HCl–MeOH for 1.5–2 h to form spiroacetals **20**–**31** (Fig. 2).[28,29] The results are summarised in Table 1.

γ-Lactones **12**–**14** were converted effectively into [4.4] spiroacetals **20**–**23** using titanium benzylidenes **7** and **9** (entries 1–4). The transformation tolerates quaternary centres both α to the carbonyl group and α to the endocyclic oxygen atom, with no difficulty (entries 1–3). The low diastereoselectivities observed in the formation of spiroacetals **22** and **23** under thermodynamic control are consistent with those reported for similar compounds in the literature.[1,30] [4.5] Spiroacetals **24** and **25** were also isolated with low diastereoselectivity when (+)-sclareolide **13** and γ-lactone **14** were treated with titanium alkylidene **11** followed by acid (entries 5 and 6). The transformation of sterically hindered γ-lactone **12** into [4.5] spiroacetal **26** proceeded well (entry 7). Alternatively, [4.5] spiroacetals could be accessed from δ-lactones (entries 8 and 9). Mixtures of anomeric spiroacetals were obtained from glucose-derived lactone **15** and from δ-lactone **16**: the structures **27** and **28** were presumably the major isomers as they are stabilised by the anomeric effect. The moderate diastereoselectivities agree with those in the literature for [4.5] spiroacetals, including glucose-derived [4.5] spiroacetals,[8,9] produced in acid.[31] [5.5] Spiroacetals **29** and **30** were prepared from dihydrocoumarin **17** and coumarin **18**, respectively, by the same method (entries 10 and 11). Clearly an α,β-unsaturated lactone presented no problem. However, ε-lactone **19** gave the benzofuran **31** rather than a [5.6] spiroacetal (entry 12).

The modest yields when using 1.2 equiv of the titanium alkylidenes **7**, **9** and **11** were improved upon by using 3 equiv, but the large quantity of triethyl phosphite used under the latter conditions (12 equiv) hampered purification by chromatography. However, washing the crude spiroacetals with excess saturated aqueous iron(III) chloride prior to chromatography removed the triethyl phosphite and expedited purification.

In conclusion, we have developed a concise two-step method for the conversion of γ- and δ-lactones into spiroacetals.

**Table 1**

| Entry | Lactone | Titanium reagent | Spiroacetal | % Isolated yield using 1.2 equiv of titanium reagent | % Isolated yield using 3 equiv of titanium reagent |
|---|---|---|---|---|---|
| 1 | **12** | **7** | **20** | 46 | 53 |
| 2 | **12** | **9** | **21** | 46 | 54 |
| 3 | **13** | **9** | **22** | 51 | 62 |
| 4 | **14** | **9** | **23** | 33 | 44 |
| 5 | **13** | **11** | **24** | 44[a] | 52[a] |
| 6 | **14** | **11** | **25** | 47 | 58 |
| 7 | **12** | **11** | **26** | 40 | 51 |
| 8 | **15** | **7** | **27** | 32 | 48 |
| 9 | **16** | **9** | **28** | 33[a] | 44[a] |
| 10 | **17** | **11** | **29** | 54 | 65 |
| 11 | **18** | **11** | **30** | 48 | 57 |
| 12 | **19** | **7** | **31** | 49 | 61 |

[a] Isolated yield of major diastereomer.

## Acknowledgements

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28. *General procedure:* $Cp_2TiCl_2$ (1.84 g, 7.4 mmol, 4.1 equiv), Mg (210 mg, 4.9 equiv, predried at 250 °C overnight) and freshly activated 4 Å molecular sieves (0.5 g) were heated, gently, under reduced pressure (0.3 mmHg) for about 1 min and then placed under argon. Dry THF (5 mL) was added followed by dry $P(OEt)_3$ (2.5 mL, 8.2 equiv). After stirring for 3 h at rt, a solution of thioacetal **7**, **9** or **11** (2.2 mmol, 1.2 equiv) in dry THF (2 mL) was added and stirring continued for 15 min. A solution of one of the lactones **12**–**19** (1.8 mmol, 1 equiv) in dry THF (2 mL) was added, and the resulting mixture stirred overnight at rt. Aqueous NaOH (1 M, 40 mL) was added and the resulting suspension filtered through Celite, washing through with diethyl ether. The mixture was extracted with ether, the combined organics were dried over $K_2CO_3$ and the solvent removed under reduced pressure to give the crude enol ether. 10% HCl–MeOH solution (1 mL concentrated aqueous HCl, 9 mL of MeOH) was added and the mixture stirred at rt for 1.5–2 h, before pouring into aqueous HCl (1 M) and extracting into dichloromethane. The combined organics were dried over $MgSO_4$ and the solvent removed under reduced pressure and the mixture separated by column chromatography on silica to give the corresponding spiroacetal **20**–**31**. When 3 equiv of the titanium reagent was used, a dichloromethane solution of the crude spiroacetal was washed with 100 mL of saturated aqueous iron(III) chloride per gramme of crude material prior to column chromatography.
29. *Spectral data for spiroacetals:* (a) **20**: solid, mp: 142 °C (MeOH). $\nu_{max}$ (Golden Gate)/$cm^{-1}$: 1480, 1461, 1598, 2899. $\delta_H$ (400 MHz, $CDCl_3$): 2.70 (1H, ddd, *J* 3.1 Hz, 7.8 Hz and 12.3 Hz), 3.17 (1H, d, *J* 17.4 Hz), 3.25 (1H, ddd, *J* 8.5 Hz, 9.9 Hz and 12.3 Hz), 3.57 (1H, d, *J* 17.4 Hz), 4.22 (1H, apparent q, *J* 8.2 Hz), 4.35 (1H, ddd, *J* 3.1 Hz, 8.6 Hz and 9.9 Hz), 6.61 (1H, d, *J* 8.0 Hz), 6.81 (1H, dt, *J* 0.7 and 7.5 Hz), 7.03 (1H, t, *J* 7.5 Hz), 7.10 (1H, d, *J* 7.3 Hz, H-7), 7.13–7.29 (10H, m, Ar–H). $\delta_C$ (100 MHz, $CDCl_3$): 37.32 ($CH_2$), 38.39 ($CH_2$), 61.36 (C), 65.42 ($CH_2$), 109.59 (CH), 119.99 (C), 120.48 (CH), 124.43 (CH), 125.38 (C), 126.37 (CH), 126.56 (CH), 127.91 (CH), 128.00 (CH), 128.32 (CH), 128.40 (CH), 143.25 (C), 145.47 (C), 157.52 (C). *m/z* ($EI^+$): 328 ($M^+$, 6%), 194 (100). HRMS: 328.1463. $C_{23}H_{20}O_2$ requires 328.1465. (b) **21**: solid, mp: 138 °C. $R_f$ [$SiO_2$, pet. ether–DCM (4:1)]: 0.19. $\nu_{max}$ (Golden Gate)/$cm^{-1}$: 1445, 1596, 1609, 2889, 2985. $\delta_H$ (400 MHz, $CDCl_3$): 2.65 (1H, ddd, *J* 2.9 Hz, 7.6 Hz and 12.1 Hz), 3.16 (1H, d, *J* 17.7 Hz), 3.25 (1H, ddd, *J* 8.7 Hz, 9.9 Hz and 12.2 Hz), 3.55 (1H, d, *J* 17.7 Hz), 4.21 (1H, apparent q, *J* 8.3 Hz), 4.35 (1H, ddd, *J* 2.9 Hz, 8.6 Hz and 9.9 Hz), 6.59 (1H, d, *J* 2.1 Hz), 6.79 (1H, dd, *J* 2.1 and 8.0 Hz), 7.00 (1H, d, *J* 8.0 Hz), 7.10–7.14 (4H, m), 7.18–7.27 (6H, m). $\delta_C$ (100 MHz, $CDCl_3$): 36.59 ($CH_2$), 37.97 ($CH_2$), 61.39 (C), 65.54 ($CH_2$), 110.16 (CH), 120.44 (CH), 120.98 (C), 124.01 (C), 124.80 (CH), 126.42 (CH), 126.53 (CH), 127.86 (CH), 127.94 (CH), 128.07 (CH), 128.21 (CH), 133.11 (C), 142.70 (C), 144.96 (C), 158.10 (C). *m/z* ($CI^+$): 363 [$(M+H)^+$ ($^{35}Cl$), 97%], 211 (100). HRMS: 363.1152 and 365.1132. $C_{23}H_{20}O_2{}^{35}Cl$ requires $(M+H)^+$ 363.1151, and $C_{23}H_{20}O_2{}^{37}Cl$ requires $(M+H)^+$ 365.1122. (c) **22** (mixture of epimers A and B), solid. $\nu_{max}$ (Golden Gate)/$cm^{-1}$: 1479, 1610, 2866, 2925. $\delta_H$ (400 MHz, $CDCl_3$): 0.84 ($3H^{A\text{ and }B}$, s), 0.88 ($6H^B$ + $3H^A$, s), 0.91 ($3H^A$, s), 1.20 ($3H^B$, s), 1.35 ($3H^A$, s), 0.99–2.12 ($13H^{A\text{ and }B}$, m), 2.21 ($1H^B$, dd, *J* 3.4 and 10.1 Hz), 2.45 ($1H^A$, dd, *J* 12.8 and 14.1 Hz), 3.20 ($2H^A$, s), 3.23 ($2H^B$, s), 6.76–6.82 ($2H^{A\text{ and }B}$, m), 7.00–7.05 ($1H^{A\text{ and }B}$, m). $\delta_C$ (100 MHz, $CDCl_3$): $\delta$ 12.81 ($CH_3$), 13.13 ($CH_3$), 15.95 ($CH_2$), 15.98 ($CH_2$), 18.13 ($CH_2$), 18.49 ($CH_2$), 18.64 ($CH_3$), 18.67 ($CH_3$), 20.29 ($CH_3$), 20.59 ($CH_3$), 27.35 ($CH_2$), 31.11 ($CH_3$), 33.43 ($CH_2$), 33.98 ($CH_2$), 37.44 ($CH_2$), 37.59 ($CH_2$), 37.73 ($CH_2$), 39.10 ($CH_2$), 40.02 ($CH_2$), 40.05 ($CH_2$), 40.39 ($CH_2$), 54.40 (CH), 54.70 (CH), 56.35 (CH), 58.77 (CH), 81.91 (C), 82.33 (C), 107.73 (CH), 107.77 (CH), 115.70 (C), 116.73 (C), 118.08 (CH), 122.07 (C), 122.26 (C), 122.63 (CH), 122.68 (CH), 130.75 (C), 130.79 (C), 155.97 (C), 156.49 (C). *m/z* ($EI^+$): 374 [$M^+$ ($^{35}Cl$), 78%], 191 (100). HRMS: 374.2013 and 376.1993. $C_{23}H_{31}O_2{}^{35}Cl$ requires 374.2018, and $C_{23}H_{31}O_2{}^{37}Cl$ requires 376.1989. (d) **23** (50:50 mixture of diastereomers A and B), oil. $R_f$ [$SiO_2$, pet. ether–DCM (1:1)]: 0.76. $\nu_{max}$ (Golden Gate)/$cm^{-1}$: 1451, 1594, 1609, 2915, 2950. $\delta_H$ (400 MHz, $CDCl_3$): 2.01 ($1H^{A\text{ or }B}$, dddd, *J* 4.4, 5.8, 9.7 and 12.4 Hz), 2.21–2.29 ($3H^{A\text{ or }B}$), 2.44–2.53 ($3H^{A\text{ or }B}$, m), 2.66 ($1H^{A\text{ or }B}$, qd, *J* 8.3 and 12.4 Hz), 3.29 ($1H^B$, d, *J* 16.7 Hz), 3.34 ($1H^B$, d, *J* 16.7 Hz), 3.36 ($1H^A$, d, *J* 16.6 Hz), 3.45 ($1H^A$, d, *J* 16.6 Hz), 5.16–5.22 ($1H^{A\text{ or }B}$, m), 5.34 ($1H^{A\text{ or }B}$, dd, *J* 5.9 and 7.8 Hz), 6.80–6.86 ($2H^{A\text{ and }B}$, m), 7.05–7.09 ($1H^{A\text{ and }B}$, m), 7.24–7.44 ($5H^{A\text{ and }B}$, m, ArH). $\delta_C$ (100 MHz, $CDCl_3$): 32.28 ($CH_2$), 33.75 ($CH_2$), 35.60 ($CH_2$), 37.62 ($CH_2$), 37.77 ($CH_2$), 37.88 ($CH_2$), 80.61 (CH), 83.07 (CH), 109.58 (CH), 109.72 (CH), 118.73 (C), 118.97 (C), 119.93 (CH), 120.04 (CH), 123.94 (C), 123.96 (C), 124.51 (CH), 125.05 (CH), 125.36 (CH), 125.57 (CH), 126.97 (CH), 127.03 (CH), 127.83 (2xCH), 132.68 (C), 141.41 (C), 141.79 (C), 157.97 (C), 158.06 (C). *m/z* ($CI^+$): 287 [$(M+H)^+$ ($^{35}Cl$), 100%]. HRMS: 287.0839 and 289.0815. $C_{17}H_{16}O_2{}^{35}Cl$ requires $(M+H)^+$ 287.0838, and $C_{17}H_{16}O_2{}^{37}Cl$ requires $(M+H)^+$ 289.0816. (e) **24** (major diastereomer), solid. mp: 116 °C (MeOH). $[\alpha]_D^{18}$ +49.1 (*c* 0.1 M, DCM). $\nu_{max}$ (Golden Gate)/$cm^{-1}$: 2931. $\delta_H$ (400 MHz, $CDCl_3$): 0.78 (3H, s), 0.84 (3H, s), 0.86 (3H, s), 0.89–0.95 (2H, m), 1.05–1.12 (1H, m), 1.21 (3H, s), 1.21–1.77 (16H, m), 1.87 (1H, td, *J* 3.2 Hz and 11.3 Hz), 3.56 (1H, br d, *J* 11.6 Hz), 3.89 (1H, dt, *J* 3.1 Hz and 11.3 Hz). $\delta_C$ (100 MHz, $CDCl_3$): 15.18 ($CH_3$), 18.37 ($CH_2$), 19.62 ($CH_2$), 20.53 ($CH_2$), 21.08 ($CH_3$), 23.07 ($CH_3$), 25.30 ($CH_2$), 33.11 (C), 33.53 ($CH_3$), 36.02 (C), 36.89 ($CH_2$), 37.05 ($CH_2$), 39.75 ($CH_2$), 40.40 ($CH_2$), 42.50 ($CH_2$), 57.10 (CH), 60.24 (CH), 62.74 ($CH_2$), 82.31 (C), 106.04 (C). *m/z* ($EI^+$): 306 ($M^{+\cdot}$, 13%), 291 ($M^{+\cdot}-{}^{\cdot}CH_3$, 37), 111 (100). HRMS: 306.2559. $C_{20}H_{34}O_2$ requires 306.2562. (f) **25** (63:37 mixture of diastereomers A and B), oil. $R_f$ [$SiO_2$, 100% DCM]: 0.26. $\nu_{max}$ (Golden Gate)/$cm^{-1}$: 1461, 2894. $\delta_H$ (400 MHz, $CDCl_3$): 1.42–2.09 ($9H^{A\text{ and }B}$, m), 2.10–2.18 ($1H^B$, m), 2.33–2.42 ($1H^A$, m), 3.55–3.60 ($1H^A$, m), 3.60–3.65 ($1H^B$, m), 3.81 ($1H^A$, dt, *J* 2.9 Hz and 11.3 Hz), 3.89 ($1H^B$, dt, *J* 2.9 Hz and 11.5 Hz), 4.88 ($1H^B$, dd, *J* 6.6 Hz and 9.6 Hz), 5.10 ($1H^A$, t, *J* 7.1 Hz), 7.15–7.36 ($5H^{A\text{ and }B}$, m, Ph). $\delta_C$ (100 MHz, $CDCl_3$): 20.23 ($CH_2$), 20.27 ($CH_2$), 25.30 ($CH_2$), 25.37 ($CH_2$), 33.17 ($CH_2$), 33.86 ($CH_2$), 33.96 ($CH_2$), 34.40 ($CH_2$), 37.89 ($CH_2$), 39.59 ($CH_2$), 61.89 ($CH_2$), 61.99 ($CH_2$), 79.47 (CH), 83.18 (CH), 105.94 (C), 106.29 (C), 125.84 (CH), 126.74 (CH), 127.43 (CH), 127.56 (CH), 128.44 (CH), 128.50 (CH), 143.29 (C), 143.44 (C). *m/z* ($CI^+$): 219 [$(M+H)^+$, 100%]. HRMS: 219.1385. $C_{14}H_{19}O_2$ requires $(M+H)^+$ 219.1384. (g) **26**: solid. mp: 85 °C. $R_f$ [$SiO_2$, hexane–DCM (1:1)]: 0.14.$\nu_{max}$ (Golden Gate)/$cm^{-1}$: 1442, 1490, 2941. $\delta_H$ (400 MHz, $CDCl_3$): 1.02 (1H, br d, *J* 13.1 Hz), 1.50–1.92 (5H, m), 2.80–2.95 (2H, m), 3.72 (1H, br dd, *J* 4.1 and 11.0 Hz), 3.88 (1H, dt, *J* 2.6 and 11.1 Hz), 4.09 (1H, ddd, *J* 4.9, 8.6 and 10.0 Hz), 4.22 (1H, dt, *J* 6.6 and 8.7 Hz), 6.97–6.99 (2H, m), 7.12–7.36 (6H, m), 7.44–7.46 (2H, m). $\delta_C$ (100 MHz, $CDCl_3$): 19.14 ($CH_2$), 23.88 ($CH_2$), 29.61 ($CH_2$), 39.11 ($CH_2$), 60.15 ($CH_2$), 60.67 (C), 62.56 ($CH_2$), 105.68 (C), 124.58 (CH), 124.80 (CH), 126.26 (CH), 126.45 (CH), 127.61 (CH), 128.32 (CH), 144.22 (C), 145.38 (C). *m/z* ($CI^+$): 295 ($M+H^+$, 100%). HRMS: 295.1698. $C_{20}H_{23}O_2$ requires $M+H^+$, 295.1699. (h) **27**: oil. $R_f$ [$SiO_2$, hexane–ethyl acetate (4:1)]: 0.51. $\nu_{max}$ (Golden Gate)/$cm^{-1}$: 1454, 1496, 1598, 2856, 2925. $\delta_H$ (400 MHz, $CDCl_3$): 2.99 ($1H^B$, d, *J* 16.3 Hz), 3.13 ($1H^A$, d, *J* 16.4 Hz), 3.17 ($1H^B$, d, *J* 16.3 Hz), 3.57 ($1H^A$, d, *J* 16.1 Hz), 3.57–4.26 ($6H^{A\text{ and }B}$, m), 4.41–5.50 ($8H^{A\text{ and }B}$, m) 6.71–7.40 ($24H^{A\text{ and }B}$, m, ArH). *m/z* ($FAB^+$): 629 [$(M+H)^+$, 100%]. HRMS: 629.2824. $C_{41}H_{40}O_6$ requires 629.2821. (i) **28** (major diastereomer), oil. $R_f$ [$SiO_2$, pet. ether–DCM (4:1)]: 0.36. $\nu_{max}$ (Golden Gate)/$cm^{-1}$: 1480, 1591, 1610, 2858, 2951. $\delta_H$ (400 MHz, $CDCl_3$): 0.86 (3H, t, *J* 6.8 Hz), 1.20–1.41 (8H, m), 1.42–1.49 (1H, m), 1.65–1.80 (3H, m), 1.92–2.03 (2H, m), 2.98 (1H, d, *J* 16.3 Hz), 3.06 (1H, d, *J* 16.3 Hz), 3.91–3.99 (1H, m), 6.77–6.82 (2H, m), 7.02 (1H, d, *J* 7.7 Hz). $\delta_C$ (100 MHz, $CDCl_3$): 13.07 ($CH_3$), 18.76 ($CH_2$), 21.60 ($CH_2$), 23.84 ($CH_2$), 29.07 ($CH_2$), 30.81 ($CH_2$), 33.00 ($CH_2$), 35.02 ($CH_2$), 41.44 ($CH_2$), 71.17 (CH), 109.41 (CH), 110.47 (C), 119.35 (CH), 124.00 (C), 124.40 (CH), 131.98 (C), 158.17 (C). *m/z* ($CI^+$): 295 [$(M+H)^+$ ($^{35}Cl$), 100%]. HRMS: 295.1465 and 297.1441. $C_{17}\ H_{24}O_2{}^{35}Cl$ requires $M+H^+$ 295.1461, and $C_{17}H_{24}O_2{}^{37}Cl$ requires $M+H^+$ 297.1438. (j) **29**: oil. $R_f$ [$SiO_2$, pet. ether–DCM (4:1)]: 0.22.$\nu_{max}$ (Golden Gate)/$cm^{-1}$: 1456, 1491, 2845, 2874. $\delta_H$ (400 MHz, $CDCl_3$): 1.49–1.65 (4H, m), 1.72 (1H, dt, *J* 6.1 and 13.2 Hz), 1.77–1.83 (1H, m), 1.89 (1H, ddd, *J* 2.1, 6.4 and 13.4 Hz), 1.93–2.09 (1H, m), 2.53 (1H, ddd, *J* 1.9, 6.1 and 16.3 Hz), 2.93 (1H, ddd, *J* 6.4, 13.1, 16.3 Hz), 3.48–3.55 (1H, m), 3.73 (1H, dt, *J* 3.3 Hz and 11.5 Hz), 6.72–6.81 (2H, m), 6.95–7.06 (2H, m). $\delta_C$ (100 MHz, $CDCl_3$): 18.49 ($CH_2$), 21.04 ($CH_2$), 25.27 ($CH_2$), 31.94 ($CH_2$), 34.83 ($CH_2$), 61.84 ($CH_2$), 95.89 (C), 116.99 (CH), 120.56 (CH), 122.75 (C), 127.08 (CH), 129.25

(CH), 152.26 (C). *m/z* ($EI^+$): 204 ($M^{+\cdot}$, 89%), 131 (100). HRMS: 204.1150. $C_{13}H_{16}O_2$ requires 204.1151. (k) **30**: oil. $R_f$ [$SiO_2$, pet. ether–DCM (4:1)]: 0.24. $\nu_{max}$ (Golden Gate)/$cm^{-1}$: 1458, 1488, 1638, 2851, 2923. $\delta_H$ (400 MHz, $CDCl_3$): 1.50–1.73 (4H, m), 2.00–2.18 (2H, m), 3.55 (1H, dd, *J* 4.6 Hz and 11.0 Hz), 3.93 (1H, dt, *J* 3.2 and 11.6 Hz), 5.67 (1H, d, *J* 9.6 Hz), 6.57 (1H, d, *J* 9.6 Hz), 6.83 (1H, t, *J* 7.4 Hz), 6.94 (1H, d, *J* 7.9 Hz), 7.06 (1H, dd, *J* 1.5 Hz and 7.5 Hz), 7.14 (1H, dt, *J* 1.6 Hz and 7.7 Hz). $\delta_C$ (100 MHz, $CDCl_3$): 18.55 ($CH_2$), 24.77 ($CH_2$), 35.07 ($CH_2$), 61.79 ($CH_2$), 95.38 (C), 116.53 (CH), 121.23 (C), 121.45 (CH), 125.47 (CH), 126.04 (CH), 127.02 (CH), 129.19 (CH), 151.45 (C). *m/z* ($FAB^+$): 203 [$(M+H)^+$, 100%]. HRMS: 203.1072. $C_{13}H_{15}O_2$ requires $M+H^+$ 203.1071. (l) **31**: oil. $R_f$ [$SiO_2$, hexane–DCM (4:1)]: 0.21. $\nu_{max}$ (Golden Gate)/$cm^{-1}$: 1432, 1587, 2859, 2937, 3387. $\delta_H$ (400 MHz, $CDCl_3$): 1.33 (1H, s), 1.33–1.38 (2H, m), 1.46–1.53 (2H, m), 1.68 (2H, quin, *J* 7.6 Hz), 2.76 (2H, t, *J* 7.6 Hz), 3.51 (2H, t, *J* 6.6 Hz), 6.37 (1H, s), 7.04–7.13 (2H, m), 7.31 (1H, d, *J* 7.4 Hz), 7.38 (1H, dd, *J* 1.9 Hz and 7.8 Hz). $\delta_C$ (100 MHz, $CDCl_3$): 25.31 ($CH_2$), 27.47 ($CH_2$), 28.38 ($CH_2$), 32.42 ($CH_2$), 62.78 ($CH_2$), 101.92 (CH), 110.69 (CH), 120.17 (CH), 122.38 (CH), 123.07 (CH), 128.93 (C), 154.58 (C), 159.32 (C). *m/z* ($CI^+$): 205 [$(M+H)^+$, 100%]. HRMS: 205.1229. $C_{13}H_{17}O_2$ requires $M+H^+$ 205.1225.

30. For example: Brimble, M. A.; Bryant, C. J. *Chem. Commun.* **2006**, 4506–4508.
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