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Synthesis of spirocyclic butenolides by ring closing metathesis

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Abstract—Spirocyclic butenolides were efficiently prepared by a ring closing metathesis strategy.

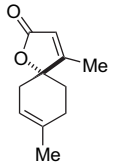
1. Introduction

Spirocyclic butenolides are of biological relevance and are present in a variety of pharmacologically relevant natural products, such as chlorotricolide,[1a,b] hydnuferruginine[2] or andirolactone (Fig. 1).[3] A general synthetic approach to spirobutenolides relies on the addition of lithium (*Z*)-3-lithioacrylates to aldehydes and ketones.[4] Other syntheses of spirobutenolides, such as andirolactone, rely on the application of radical cyclisations,[5] the propynoate/cuprate method,[6] palladium-catalysed cyclisations[7] and other methods.[8] Markó and Maulide reported the synthesis of spirocyclic butenolides based on the use of 2-(trimethylsilyloxy)furan as a dianion equivalent.[9] The ring closing metathesis (RCM) reaction has found widespread applications in the synthesis of oxygen and nitrogen heterocycles.[10] In this context, the synthesis of pyrans[11] and butenolides was reported.[12,13] Some years ago, we reported the first application of RCM to the synthesis of spirocyclic butenolides.[14] Recently, Li et al. reported[15] a potent synthesis of andirolactone using RCM. Herein, we report full details of our studies.

2. Results and discussion

The reaction of cyclohexanone, cyclopentanone, cycloheptanone, cyclooctanone, cyclodecanone and cyclododecanone with vinylmagnesium bromide afforded the alcohols **2a–f**, which were transformed, by treatment with acrylic acid chloride, into the esters **3a–f** (Scheme 1, Table 1).[16] Ring closing metathesis, using Grubbs' generation I catalyst (**4**) in the presence of catalytic amounts of $Ti(O^iPr)_4$ (Fürstner conditions),[17] afforded the spirocyclic butenolides **5a–f**. The reaction of vinylmagnesium bromide with 2-methylcyclohexanone afforded the known[18] alcohol **2g** with very good diastereoselectivity. The latter was transformed, via acrylate **3g**, into butenolide **5g**. Acrylate **3h** was prepared from 4-phenylcyclohexanone in one step by reaction of the latter with vinylmagnesium bromide and subsequent addition of acrylic acid chloride to the reaction mixture. Ring closing metathesis afforded butenolide **5h** as a diastereomeric mixture (dr=3:1). Acrylate **3i** was prepared in one step from 2,6-dimethylcyclohexanone. However, the ring closing metathesis proved to be unsuccessful, presumably due to steric effects. Starting with adamantanone, acrylate **3j** was prepared and transformed into the known[19] butenolide **5j** (Scheme 2). Butenolide **5k** was prepared from α-tetralone (Scheme 3).[20] Starting with fluorenone, acrylate **3l** was prepared (Scheme 4). However, the ring closing metathesis proved to be unsuccessful under a variety of conditions.

In summary, we reported the synthesis of pharmacologically relevant spirocyclic butenolides. A brief comparison of our method with the one reported by Caine seems to be appropriate. The reaction of cyclohexanone with 3-bromoacrylic acid afforded spirobutenolide **5a** in 48% yield. This compound is obtained by our method in only 20% yield over 3 steps. On



andirolactone

Figure 1. Andirolactone.

Keywords: Butenolides; Catalysis; Metathesis; Ruthenium; Spiro compounds.
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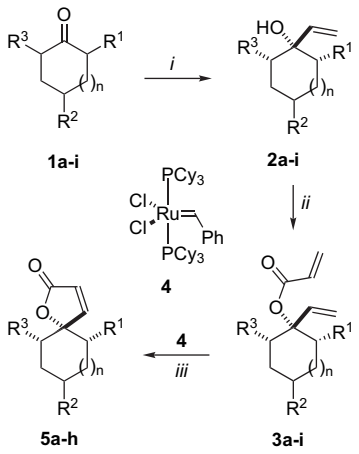
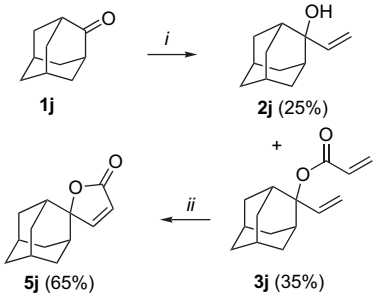


Scheme 1. Synthesis of butenolides **5a–h**. (i) H_2C=CHMgBr, THF, 0 °C, 16 h; (ii) H_2C=CH(CO)Cl, NEt_3, Et_2O, 0 °C, 16 h; (iii) **4** (10 mol %), $Ti(O^iPr)_4$ (15 mol %), CH_2Cl_2, 35 °C, 48 h.

Table 1. Products and yields

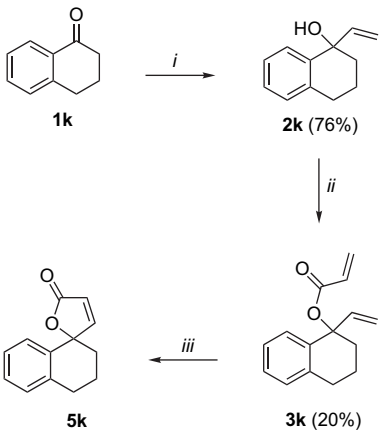
	n	R^1	R^2	R^3	Yield[a] (%)		
					2	**3**	**5**
a	1	H	H	H	83	43	57
b	0	H	H	H	58	48	66
c	2	H	H	H	66	58	76
d	3	H	H	H	74	45	78
e	5	H	H	H	59	42	63
f	7	H	H	H	80	71	70
g	1	Me	H	H	45[b]	30[c] (85)[d]	80[c]
h	1	H	Ph	H	25[e]	35[e]	80[f]
i	1	Me	H	Me	—	44[g]	0[h]

[a] Isolated yields.
[b] dr>98:2.
[c] dr>98:2.
[d] Sequential addition of H_2C=CHMgBr and H_2C=CH(CO)Cl to **1g** at 0 °C (no isolation of **2g**), dr=10:1.
[e] Sequential addition of H_2C=CHMgBr and H_2C=CH(CO)Cl to **1h** at 0 °C (no isolation of **2h**), dr=3:1 (assignment arbitrary).
[f] dr=3:1 (assignment arbitrary).
[g] Sequential addition of H_2C=CHMgBr and H_2C=CH(CO)Cl to **1i** at 0 °C (no isolation of **2i**), dr=10:1.
[h] No conversion, adduct was recovered.

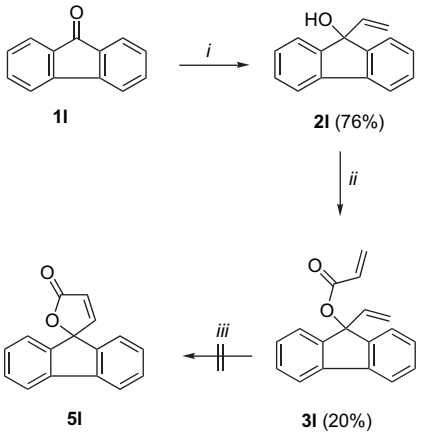


Scheme 2. Synthesis of butenolide **5j**. (i) (1) H_2C=CHMgBr, THF, 0 °C, 16 h; (2) H_2C=CH(CO)Cl, 0 °C, 16 h; (ii) **4** (10 mol %), $Ti(O^iPr)_4$ (15 mol %), CH_2Cl_2, 35 °C, 48 h.

the other hand, the methods reported herein complement the method of Caine, since a Grignard rather than a (highly reactive and very basic) dilithio reagent was employed. It was recently shown by Li et al.[15] that spirocyclic butenolides



Scheme 3. Synthesis of butenolide **5k**. (i) H_2C=CHMgBr, THF, 0 °C, 16 h; (ii) H_2C=CH(CO)Cl, NEt_3, Et_2O, 0 °C, 16 h; (iii) **4** (5 mol %), $Ti(O^iPr)_4$ (15 mol %), CH_2Cl_2, 35 °C, 48 h, yield: 61% based on recovered starting material.



Scheme 4. Attempted synthesis of butenolide **5l**. (i) H_2C=CHMgBr, THF, 0 °C, 16 h; (ii) H_2C=CH(CO)Cl, NEt_3, Et_2O, 0 °C, 16 h; (iii) **4** (5 mol %), $Ti(O^iPr)_4$ (15 mol %), CH_2Cl_2, 35 °C, 48 h.

containing a substituent at the double bond can be prepared. This is advantageous, since substituted 3-bromoacrylates are not always readily available.

3. Experimental section

3.1. General procedure for the synthesis of vinylalcohols 2

To a THF solution of ketone **1** was added vinylmagnesium bromide (1 M solution in THF). After stirring for 16 h at 20 °C, an aqueous solution of NH_4Cl (50 ml, 1 M) was added. The organic and the aqueous layers were separated and the latter was extracted with ether (3×50 ml). The combined organic layers were dried ($MgSO_4$), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, petroleum ether/ether=10:1). Due to their unstable nature, compounds **2** had to be used immediately after their preparation. Elemental analyses and high-resolution mass data could, in some cases, not be obtained.

3.1.1. 1-Vinyl-1-cyclohexanol (2a). Starting with **1a** (1.96 g, 20.0 mmol), dissolved in THF (20 ml), and vinylmagnesium bromide (30 ml, 30.0 mmol, 1 M), **2a** was isolated (2.09 g, 83%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.18–1.30 (m, 1H, CH_2), 1.38–1.75 (m, 9H, CH_2), 5.01 (dd, $^3J_{cis}$=11.0 Hz, ^2J=1.0 Hz, 1H, CH_2), 5.22 (dd, $^3J_{trans}$=17.0 Hz, ^2J=1.0 Hz, 1H, CH_2), 5.95 (dd, $^3J_{trans}$=17.0 Hz, $^3J_{cis}$=11.0 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.9, 26.9, 37.4 (CH_2), 71.6 (C), 111.3 (CH_2), 145.9 (CH). IR (KBr): $\tilde{\nu}$ 3392 (s), 3085 (w), 2980 (w), 2963 (s), 2933 (s), 2859 (s), 1698 (m), 1639 (m), 1449 (s), 1415 (s), 1405 (s) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%)=126 (8, M$^+$), 111 (20), 98 (16, [M−ethylene]$^+$), 83 (80), 41 (100). The spectroscopic data are identical to those reported in the literature.[21]

3.1.2. 1-Vinyl-1-cyclopentanol (2b). Starting with **1b** (0.42 g, 10.0 mmol), dissolved in THF (20 ml), and vinylmagnesium bromide (15 ml, 15.0 mmol, 1 M), **2b** was isolated (0.65 g, 58%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.64–1.71 (m, 6H, CH_2), 1.85–189 (m, 2H, CH_2), 5.02 (dd, ^2J=1.0 Hz, $^3J_{cis}$=11.0 Hz, 1H, CH_2), 5.26 (dd, ^2J=1.0 Hz, $^3J_{trans}$=17.0 Hz, 1H, CH_2), 6.02 (dd, $^3J_{cis}$=11.0 Hz, $^3J_{trans}$=17.0 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.6, 40.1 (CH_2), 82.1 (C), 111.0 (CH_2), 144.4 (CH). IR (KBr): $\tilde{\nu}$ 3589 (s), 3088 (w), 3008 (w), 2963 (s), 2875 (m), 1641 (w), 1412 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%)=112 (12, M$^+$), 97 (56), 84 (100, [M−ethylene]$^+$), 70 (32), 55 (60). Anal. Calcd for $C_7H_{12}O$: C 74.95, H 10.78; found: C 74.46, H 10.45. The spectroscopic data are identical to those reported in the literature.[21]

3.1.3. 1-Vinyl-1-cycloheptanol (2c). Starting with **1c** (1.13 g, 10.0 mmol), dissolved in THF (20 ml), and vinylmagnesium bromide (12 ml, 12.0 mmol, 1 M), **2c** was isolated (0.92 g, 66%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.37–1.73 (m, 10H, CH_2), 4.94 (dd, ^2J=1.0 Hz, $^3J_{cis}$=11.0 Hz, 1H, CH_2), 5.17 (dd, ^2J=1.0 Hz, $^3J_{trans}$=17.0 Hz, 1H, CH_2), 5.99 (dd, $^3J_{cis}$=11.0 Hz, $^3J_{trans}$=17.0 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 22.1, 29.5, 41.1 (CH_2), 75.5 (C), 110.1 (CH_2), 146.6 (CH). IR (KBr): $\tilde{\nu}$ 3385 (s), 3168 (w), 2978 (m), 2925 (s), 2857 (m), 1640 (w), 1460 (w), 1446 (w) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%)=140 (4, M$^+$), 122 (24), 112 (100, [M−ethylene]$^+$), 97 (76), 83 (68). The spectroscopic data are identical to those reported in the literature.[22]

3.1.4. 1-Vinyl-1-cyclooctanol (2d). Starting with **1d** (1.26 g, 10.0 mmol), dissolved in THF (20 ml), and vinylmagnesium bromide (20 ml, 20.0 mmol, 1 M), **2d** was isolated (1.14 g, 74%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.41–1.81 (m, 14H, CH_2), 5.01 (dd, ^2J=1.0 Hz, $^3J_{cis}$=11.0 Hz, 1H, CH_2), 5.20 (dd, ^2J=1.0 Hz, $^3J_{trans}$=17.0 Hz, 1H, CH_2), 5.96 (dd, $^3J_{cis}$=11.0 Hz, $^3J_{trans}$=17.0 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 22.0, 24.7, 28.2, 36.2 (CH_2), 75.2 (C), 111.3 (CH_2), 145.8 (CH). IR (KBr): $\tilde{\nu}$ 3383 (s), 3007 (w), 2922 (s), 2853 (m), 1640 (w), 1472 (w), 1448 (w), 1410 (w) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%)=154 (4, M$^+$), 125 (12), 111 (56), 97 (24), 83 (100).

3.1.5. 1-Vinyl-1-cyclodecanol (2e). Starting with **1e** (0.77 g, 5.0 mmol), dissolved in THF (10 ml), and vinylmagnesium bromide (7.5 ml, 7.5 mmol), **2e** was isolated (0.54 g, 59%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.39–1.76 (m, 18H, CH_2), 5.00 (dd, ^2J=2.0 Hz, $^3J_{cis}$=11.0 Hz, 1H, CH_2), 5.21 (dd, ^2J=2.0 Hz, $^3J_{trans}$=17.0 Hz, 1H, CH_2), 5.99 (dd, $^3J_{cis}$=11.0 Hz, $^3J_{trans}$=17.0 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 21.2, 23.6, 26.2, 26.9, 34.3 (CH_2), 76.4 (C), 111.0 (CH_2), 145.5 (CH). IR (KBr): $\tilde{\nu}$ 3394 (s), 2981 (m), 2924 (s), 2866 (s), 2849 (s), 1483 (s), 1444 (m), 1413 (w) cm^{-1}. Anal. Calcd for $C_{14}H_{26}O$: C 79.06, H 12.16; found: C 79.25, H 12.44.

3.1.6. 1-Vinyl-1-cyclododecanol (2f). Starting with **1f** (1.82 g, 10.0 mmol), dissolved in THF (20 ml), and vinylmagnesium bromide (15 ml, 1 M), **2f** was isolated (1.78 g, 8.0 mmol, 80%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.36–1.63 (m, 22H, CH_2), 5.02 (dd, ^2J=1.0 Hz, $^3J_{cis}$=11.0 Hz, 1H, CH_2), 5.20 (dd, ^2J=1.0 Hz, $^3J_{trans}$=17.0 Hz, 1H, CH_2), 5.98 (dd, $^3J_{cis}$=11.0 Hz, $^3J_{trans}$=17.0 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 19.6, 22.1, 22.6, 25.9, 26.4, 34.7 (CH_2), 75.5 (C), 111.1 (CH_2), 145.3 (CH). MS (EI, 70 eV): *m*/*z* (%)=210 (28, M$^+$), 182 (24, [M−ethylene]$^+$), 152 (28), 111 (44), 83 (100). IR (KBr): $\tilde{\nu}$ 3380 (s), 2939 (s), 2905 (s), 2863 (s), 2849 (s), 1470 (s), 1444 (w), 1413 (w), 1404 (w) cm^{-1}. Anal. Calcd for $C_{12}H_{22}O$: C 71.03, H 7.95; found: C 70.98, H 7.92.

3.1.7. 2-Methyl-1-vinyl-1-cyclohexanol (2g). Starting with **1g** (1.12 g, 10.0 mmol), dissolved in THF (20 ml), and vinylmagnesium bromide (20 ml, 20.0 mmol, 1 M), **2g** was isolated (0.69 g, 4.9 mmol, 49%, *syn*/*anti*>30:1) as a colourless oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.77 (d, ^3J=6.0 Hz, 3H, CH_3), 1.20–1.70 (m, 9H, CH, CH_2), 5.02 (dd, $^3J_{cis}$=11.0 Hz, ^2J=2.0 Hz, 1H, CH_2), 5.20 (dd, $^3J_{trans}$=17.0 Hz, ^2J=2.0 Hz, 1H, CH_2), 5.79 (dd, $^3J_{trans}$=17.0 Hz, $^3J_{cis}$=11.0 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 15.4 (CH_3), 21.4, 25.9, 29.8, 38.6 (CH_2), 38.7 (CH), 74.1 (C), 111.3 (CH_2), 146.2 (CH). MS (EI, 70 eV): *m*/*z* (%)=140 (8, M$^+$), 112 (28, [M−ethylene]$^+$), 97 (30), 83 (100), 70 (60). IR (KBr): $\tilde{\nu}$ 3486 (s), 2962 (m), 2932 (s), 2854 (m), 1459 (w), 1447 (w), 1407 (w) cm^{-1}. The stereochemical assignment is based on the identity of the spectroscopic data to those reported in the literature.[23]

3.1.8. 1-Vinyl-1,2,3,4-tetrahydro-1-naphthol (2k). Starting with tetralone (3.65 g, 25.0 mmol), dissolved in THF (50 ml), and vinylmagnesium bromide (30 ml, 30.0 mmol, 1 M), **2k** was isolated (3.31 g, 76%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.81–1.97 (m, 4H, CH_2), 2.76–2.81 (m, 2H, CH_2), 5.18 (dd, ^2J=1.0 Hz, $^3J_{cis}$=11.0 Hz, 1H, CH_2), 5.27 (dd, ^2J=1.0 Hz, $^3J_{trans}$=17.0 Hz, 1H, CH_2), 6.00 (dd, $^3J_{cis}$=11.0 Hz, $^3J_{trans}$=17.0 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 19.3, 29.9, 37.7 (CH_2), 73.3 (C), 113.1 (CH_2), 126.2, 127.5, 127.9, 129.0 (CH), 137.0, 139.7 (C), 144.8 (CH). IR (KBr): $\tilde{\nu}$ 3548 (s), 3072 (w), 3018 (w), 2936 (s), 2867 (w), 1640 (w), 1488 (w), 1450 (w), 1405 (w), 1395 (w) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%)=174 (36, M$^+$), 146 (100, [M−ethylene]$^+$), 131 (52), 128 (36), 115 (32).

3.1.9. 9-Vinyl-9*H*-fluoren-9-ol (2l). Starting with fluorenone (1.82 g, 10.0 mmol), dissolved in THF (30 ml), and vinylmagnesium bromide (12 ml, 12.0 mmol, 1 M), **2l** was isolated (1.50 g, 72%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.20 (dd, ^2J=1.0 Hz, $^3J_{cis}$=11.0 Hz,

1H, CH_2), 5.53 (dd, ^2J=1.0 Hz, $^3J_{trans}$=17.0 Hz, 1H, CH_2), 5.96 (dd, $^3J_{cis}$=11.0 Hz, $^3J_{trans}$=17.0 Hz, 1H, CH), 7.29–7.37 (m, 4H, CH), 7.43 (dd, ^2J=1.0 Hz, ^3J=7.0 Hz, 2H, CH), 7.61 (dd, ^2J=1.0 Hz, ^3J=7.0 Hz, 2H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 82.4 (C), 113.5 (CH_2), 120.1, 124.4, 128.1, 129.2, 139.1 (CH), 139.5, 147.9 (C). IR (KBr): $\tilde{\nu}$ 3511 (w), 3298 (s), 3093 (w), 1449 (s), 1205 (w) cm^{-1}. MS (EI, 70 eV): *m/z* (%)=208 (100, M^+), 189 (12), 180 (52, [M−ethylene]$^+$), 165 (64), 152 (72). Anal. Calcd for $C_{15}H_{12}O$: C 86.51, H 5.81; found: C 86.23, H 6.17.

3.2. General procedure A for the synthesis of vinylacrylates 3

To an ether solution of **2** was added triethylamine (NEt_3) and acrylic acid chloride at 0 °C. After stirring at 20 °C for 24 h, the suspension was filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, petroleum ether/ether=20:1).

3.3. General procedure B for the synthesis of vinylacrylates 3

To a THF solution of **2** was added vinylmagnesium bromide (1 M solution in THF) at 0 °C. After stirring for 16 h at 20 °C the solution was cooled to 0 °C and acrylic acid chloride was added. The solution was stirred for 16 h at 20 °C. To the solution was added an aqueous solution of NH_4Cl (50 ml, 1 M). The organic and the aqueous layers were separated and the latter was extracted with ether (3×50 ml). The combined organic layers were dried ($MgSO_4$), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, petroleum ether/ether=20:1).

Due to their unstable nature, compounds **3** had to be used immediately after their preparation. Elemental analyses and high-resolution mass data could not be obtained.

3.3.1. 1-Vinyl-1-cyclohexylacrylate (3a). The reaction was carried out following general procedure A. Starting with **2a** (0.63 g, 5.0 mmol), dissolved in ether (25 ml), NEt_3 (0.76 g, 7.5 mmol) and acrylic acid chloride (0.68 g, 7.5 mmol), **3a** was isolated (0.38 g, 43%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.25–1.30 (m, 1H, CH_2), 1.49–1.62 (m, 7H, CH_2), 2.21–2.24 (m, 2H, CH_2), 5.10–5.20 (m, 2H, CH_2), 5.75 (dd, $^3J_{cis}$=10.0 Hz, ^2J=1.6 Hz, 1H, CH_2), 6.01–6.18 (m, 2H, CH), 6.34 (dd, $^3J_{trans}$=17.0 Hz, ^2J=2.0 Hz, 1H, CH_2). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 21.8, 25.3, 34.8 (CH_2), 82.0 (C), 113.6, 129.7 (CH_2), 129.8, 141.7 (CH), 164.8 (CO). IR (KBr): $\tilde{\nu}$ 2935 (s), 2862 (w), 1725 (s), 1638 (w), 1620 (w), 1449 (w), 1402 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%)=179 (4, M^+), 153 (6), 108 (84), 79 (30), 55 (100).

3.3.2. 1-Vinyl-1-cyclopentylacrylate (3b). The reaction was carried out following general procedure A. Starting with **2b** (0.45 g, 4.0 mmol), dissolved in ether (20 ml), NEt_3 (0.61 g, 6.0 mmol) and acrylic acid chloride (0.51 g, 5.6 mmol), **3b** was isolated (0.32 g, 48%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.55–2.04 (m, 6H, CH_2), 2.06–2.18 (m, 2H, CH_2), 5.07–5.17 (m, 2H, CH_2), 5.75 ($^3J_{cis}$=10.0 Hz, ^2J=2.0 Hz, 1H, CH_2), 6.01–6.22 (m, 2H, CH), 6.33 (dd, $^3J_{trans}$=17.0 Hz, ^2J=2.0 Hz, 1H, CH_2). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 23.2, 37.6, 90.7 (C), 113.1 (CH_2), 129.6 (CH), 129.9 (CH_2), 140.1 (CH), 165.2 (CO). IR (KBr): $\tilde{\nu}$ 2958 (m), 2926 (s), 2871 (w), 2854 (w), 1727 (m), 1403 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%)=166 (2, M^+), 111 (4), 94 (64), 79 (24), 55 (100). HRMS (EI, 70 eV) calcd for $C_{10}H_{14}O_2$ [M^+]: 166.0994; found: *m/z*=166.0994±2 ppm.

3.3.3. 1-Vinyl-1-cycloheptylacrylate (3c). The reaction was carried out following general procedure A. Starting with **2c** (0.70 g, 5.0 mmol), dissolved in ether (25 ml), NEt_3 (0.76 g, 7.5 mmol) and acrylic acid chloride (0.68 g, 7.5 mmol), **3c** was isolated (0.56 g, 2.9 mmol, 58%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.35–1.64 (m, 8H, CH_2), 1.92 (dd, ^3J=9.0 Hz, 2H, CH_2), 2.15 (dd, ^3J=7.0 Hz, 2H, CH_2), 5.05 (d, $^3J_{cis}$=8.0 Hz, 1H, CH_2), 5.11 (d, $^3J_{trans}$=15.0 Hz, 1H, CH_2), 5.72 (dd, $^3J_{cis}$=10.0 Hz, ^2J=2.0 Hz, 1H, CH_2), 5.70–6.11 (m, 2H, CH), 6.31 (dd, $^3J_{trans}$=16.0 Hz, ^2J=2.0 Hz, 1H, CH_2). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 22.3, 29.1, 38.2 (CH_2), 86.1 (C), 112.3, 129.5 (CH_2), 129.8, 142.6 (CH), 164.9 (CO). IR (KBr): $\tilde{\nu}$ 2982 (s), 2859 (w), 1725 (s), 1687 (w), 1637 (w), 1619 (w), 1460 (w), 1447 (w), 1402 (m) cm^{-1}.

3.3.4. 1-Vinyl-1-cyclooctylacrylate (3d). The reaction was carried out following general procedure A. Starting with **2d** (0.77 g, 5.0 mmol), dissolved in ether (25 ml), NEt_3 (0.76 g, 7.5 mmol) and acrylic acid chloride (0.68 g, 7.5 mmol), **3d** was isolated (0.47 g, 45%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.38–1.71 (m, 10H, CH_2), 1.93 (dd, ^3J=7.0 Hz, 2H, CH_2), 2.24 (dd, ^3J=7.0 Hz, 2H, CH_2), 5.10–5.16 (m, 2H, CH_2), 5.71 (dd, $^3J_{cis}$=12.0 Hz, ^2J=1 Hz, 1H, CH_2), 5.98–6.12 (m, 2H, CH), 6.29 (dd, $^3J_{trans}$=17.0 Hz, ^2J=2.0 Hz, 1H, CH_2). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 21.4, 24.7, 28.0, 32.4 (CH_2), 86.0 (C), 113.4, 129.5 (CH_2), 129.9, 141.9 (CH), 164.8 (CO). IR (KBr): $\tilde{\nu}$ 2925 (s), 2855 (s), 1723 (s), 1636 (m), 1476 (m), 1446 (m), 1402 (s) cm^{-1}. MS (EI, 70 eV): *m/z* (%)=208 (12, M^+), 136 (32), 108 (32), 95 (20), 81 (20), 55 (100).

3.3.5. 1-Vinyl-1-cyclodecylacrylate (3e). The reaction was carried out following general procedure A. Starting with **2e** (0.43 g, 2.4 mmol), dissolved in ether (15 ml), NEt_3 (0.31 g, 3.1 mmol) and acrylic acid chloride (0.26 g, 2.8 mmol), **3e** was isolated (0.23 g, 42%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.30–1.70 (m, 14H, CH_2), 1.78–1.95 (m, 2H, CH_2), 2.20–2.34 (m, 2H, CH_2), 5.10–5.17 (m, 2H, CH_2), 5.72 (dd, $^3J_{cis}$=11.0 Hz, ^2J=2.0 Hz, 1H, CH_2), 5.97–6.09 (m, 2H, CH), 6.30 (dd, $^3J_{trans}$=18.0 Hz, ^2J=2.0 Hz, 1H, CH_2). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 20.5, 23.9, 26.1, 26.2, 30.6 (CH_2), 86.7 (C), 113.6, 129.6 (CH_2), 129.8, 141.6 (CH), 164.7 (CO). IR (KBr): $\tilde{\nu}$ 2927 (s), 2866 (m), 2850 (m), 1766 (m), 1730 (s), 1484 (m), 1445 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%)=208 (12, M^+), 165 (32), 151 (36), 137 (24), 97 (100).

3.3.6. 1-Vinyl-1-cyclododecylacrylate (3f). The reaction was carried out following general procedure A. Starting with **3f** (0.21 g, 1.0 mmol), dissolved in ether (10 ml), NEt_3 (0.13 g, 1.3 mmol) and acrylic acid chloride (0.12 g, 1.3 mmol), **3f** was isolated (0.19 g, 0.7 mmol, 71%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.12–1.22 (m, 18H, CH_2), 1.59–1.65 (m, 2H, CH_2), 2.05–2.19 (m, 2H, CH_2), 5.09–5.18 (m, 2H, CH_2), 5.74 (dd, $^3J_{cis}$=11.0 Hz,

^2J=2.0 Hz, 1H, CH_2), 5.92–6.10 (m, 2H, CH), 6.32 (dd, $^3J_{trans}$=18.0 Hz, ^2J=2.0 Hz, 1H, CH_2). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 18.9, 21.9, 22.3, 26.1, 30.9 (CH_2), 85.6 (C), 113.8 (CH_2), 129.7 (CH), 129.8 (CH_2), 141.2 (CH), 164.8 (CO). IR (KBr): $\tilde{\nu}$ 2947 (s), 2906 (s), 2864 (m), 2852 (m), 1724 (s), 1711 (s), 1471 (m), 1401 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%)=264 (4, M^+), 209 (8), 192 (36), 95 (20), 55 (100).

3.3.7. 2-Methyl-1-vinyl-1-cyclohexylacrylate (3g). The reaction was carried out following general procedure A. Starting with **2g** (0.42 g, 4.0 mmol), dissolved in ether (20 ml), NEt_3 (0.93 g, 9.2 mmol) and acrylic acid chloride (0.72 g, 8.0 mmol), **3g** was isolated (0.23 g, 1.2 mmol, 30%, dr>98:2) as a colourless oil. ^1H NMR ($CDCl_3$, 250 MHz): δ 0.94 (d, ^3J=3.0 Hz, 3H, CH_3), 1.24–1.36 (m, 2H, CH_2), 1.44–1.57 (m, 6H, CH_2), 1.66–1.69 (m, 1H, CH), 5.03 (dd, $^3J_{trans}$=18.0 Hz, ^2J=1.0 Hz, 1H, CH_2), 5.13 (dd, $^3J_{cis}$=11.0 Hz, ^2J=1.0 Hz, 1H, CH_2), 5.77 (dd, $^3J_{cis}$=12.0 Hz, ^2J=1.0 Hz, 1H, CH_2), 5.99–6.16 (m, 2H, CH), 6.36 (dd, $^3J_{trans}$=19.0 Hz, ^2J=1.0 Hz, 1H, CH_2). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 15.5 (CH_3), 21.3, 25.4, 30.4, 32.3 (CH_2), 41.8 (CH), 84.6 (C), 112.7, 129.7 (CH_2), 129.8, 141.5 (CH), 164.9 (CO). IR (KBr): $\tilde{\nu}$ 3089 (w), 3030 (w), 2970 (s), 2933 (s), 2859 (s), 1725 (s), 1637 (m), 1620 (m), 1603 (w), 1448 (s), 1403 (s) cm^{-1}. MS (EI, 70 eV): *m/z* (%)=193 (32, M^+), 176 (24), 121 (32), 95 (24), 55 (100).

3.3.8. 4-Phenyl-1-vinyl-1-cyclohexylacrylate (3h). The reaction was carried out following general procedure B. Starting with 4-phenylcyclohexanone (**1h**) (0.87 g, 5.0 mmol), vinylmagnesium bromide (7 ml, 7.0 mmol, 1 M) and acrylic acid chloride (0.63 g, 7.0 mmol) in THF (25 ml), **3h** was isolated (0.46 g, 35%, dr=3:1) as a colourless oil. The stereochemistry could not be unambiguously assigned. A small selectivity in favour of the *syn* diastereomer was observed in the reaction of lithiated 3-bromoacrylic acid with 4-*tert*-butylcyclohexanone (equatorial attack of the organolithium reagent to give an axial alcohol). The reaction of phenylmagnesium bromide with 4-phenylcyclohexanone has also been reported.[24] ^1H NMR ($CDCl_3$, 300 MHz): δ 1.55–1.74 (m, 3H, CH_2), 1.77–1.93 (m, 3H, CH_2), 2.50–2.65 (m, 3H, CH, CH_2), 5.16 (dd, $^3J_{trans}$=18.0 Hz, $^3J_{cis}$=12.0 Hz, 1H, CH_2), 5.38 (dd, $^3J_{trans}$=18.0 Hz, $^3J_{cis}$=12.0 Hz, 1H, CH_2), 5.75 (dd, $^3J_{cis}$=12.0 Hz, ^2J=1.0 Hz, 1H, CH_2), 6.00–6.43 (m, 3H, CH), 7.17–7.19 (m, 5H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 28.9, 30.4, 34.7, 35.4 (CH_2), 43.1 (CH), 81.0, 81.7 (C), 113.3, 117.1 (CH_2), 126.0, 126.6, 128.3, 129.7, 129.8, 129.2, 138.9, 141.8 (CH), 145.9 (C), 164.7 (CO). IR (KBr): $\tilde{\nu}$ 3028 (s), 2935 (m), 2863 (w), 1722 (s), 1635 (w), 1620 (w), 1494 (w), 1450 (m), 1402 (s) cm^{-1}. MS (EI, 70 eV): *m/z* (%)=256 (M^+, 8), 184 (87), 156 (54), 139 (21), 117 (23), 104 (100). Anal. Calcd for $C_{17}H_{20}O_2$: C 79.65, H 7.86; found: C 79.47, H 7.76.

3.3.9. 2,6-Dimethyl-1-vinyl-cyclohexylacrylate (3i). The reaction was carried out following general procedure B. Starting with 2,6-dimethylcyclohexanone (**1i**) (1.26 g, 10.0 mmol), vinylmagnesium bromide (12 ml, 12.0 mmol, 1 M) and acrylic acid chloride (1.08 g, 12.0 mmol) in THF (40 ml), **3i** was isolated (0.91 g, 44%, dr=10:1) as a colourless oil. ^1H NMR ($CDCl_3$, 300 MHz): δ 0.79 (d, ^3J=7 Hz, 6H, CH_3, *syn*/*anti*), 0.96 (d, ^3J=7.0 Hz, 6H, CH_3, *syn*/*anti*), 1.28–1.54 (m, 6H, CH_2, *syn*/*anti*), 1.64–1.78 (m, 2H, CH, *syn*/*anti*), 4.94–5.32 (m, 3H, CH_2, *syn*/*anti*), 5.56–5.82 (m, 1H, CH_2, *syn*/*anti*), 6.05–6.18 (m, 1H, CH, *syn*/*anti*), 6.32–6.53 (m, 1H, CH, *syn*/*anti*). ^{13}C NMR ($CDCl_3$, 75 MHz): 15.5, 17.0 (CH_3), 25.4, 25.7, 29.6, 30.1 (CH_2), 37.1, 42.5 (CH), 88.17, 88.18 (C), 109.2, 112.2, 129.3, 129.4 (CH_2), 129.9, 130.5, 141.3, 144.5 (CH), 164.3, 165.1 (C). IR (KBr): $\tilde{\nu}$ 2966 (m), 2931 (s), 2878 (w), 2858 (w), 1726 (s), 1637 (w), 1621 (w), 1458 (m), 1405 (m) cm^{-1}. The stereochemical assignment is based on analogy to the synthesis of **2g**.

3.3.10. 2-Vinyl-2-adamantanylacrylate (3j). The reaction was carried out following general procedure B. Starting with adamantanone (0.75 g, 5.0 mmol), vinylmagnesium bromide (7 ml, 7.0 mmol, 1 M) and acrylic acid chloride (0.63 g, 7.0 mmol) in THF (25 ml), **3j** was isolated (0.41 g, 1.8 mmol, 35%) as a colourless oil. In addition, **2j** (0.22 g, 1.2 mmol, 25%) was isolated.

*Data of **3j**.* ^1H NMR ($CDCl_3$, 300 MHz): δ 1.66–2.16 (m, 14H, CH, CH_2), 5.27 (dd, ^2J=1.0 Hz, $^3J_{cis}$=11.0 Hz, 1H, CH_2), 5.33 (dd, ^2J=1.0 Hz, $^3J_{trans}$=18.0 Hz, 1H, CH_2), 5.75 (dd, ^2J=2.0 Hz, $^3J_{cis}$=11.0 Hz, 1H, CH_2), 6.08 (dd, $^3J_{trans}$=18.0 Hz, $^3J_{cis}$=11.0 Hz, 1H, CH), 6.26–6.39 (m, 2H, CH, CH_2). ^{13}C NMR ($CDCl_3$, 75 MHz): 26.8, 27.2 (CH), 32.9, 34.3 (CH_2), 35.1 (CH), 37.7 (CH_2), 85.3 (C), 115.7, 129.6 (CH_2), 130.0, 140.6 (CH), 164.5 (C). IR (KBr): $\tilde{\nu}$ 2909 (s), 2859 (m), 1723 (s), 1657 (w), 1619 (w), 1453 (s), 1402 (s) cm^{-1}. Anal. Calcd for $C_{15}H_{20}O_2$: C 77.55, H 8.68; found: C 77.44, H 8.68.

*Data of 2-vinyl-2-adamantanol (**2j**).* ^1H NMR ($CDCl_3$, 300 MHz): δ 1.57–1.60 (m, 2H, CH), 1.70–1.75 (m, 2H, CH), 1.82–1.90 (m, 4H, CH_2), 2.26 (d, ^3J=12.0 Hz, 2H, CH_2), 5.16 (dd, $^3J_{cis}$=11.0 Hz, ^2J=2.0 Hz, 1H, CH_2), 5.35 (dd, $^3J_{trans}$=17.0 Hz, ^2J=2.0 Hz, 1H, CH_2), 6.27 (dd, $^3J_{trans}$=17.0 Hz, $^3J_{cis}$=11.0 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz): 27.6, 27.8 (CH_2), 33.2, 35.1 (CH), 38.2 (CH_2), 38.4 (CH), 74.7 (C), 113.9 (CH), 145.2 (CH_2). IR (KBr): $\tilde{\nu}$ 3365 (s), 2902 (s), 2857 (s), 1636 (w), 1453 (s) cm^{-1}. MS (EI, 70 eV): *m/z* (%)=178 (100, M^+), 163 (14), 148 (17), 135 (31), 121 (19), 108 (21). HRMS (EI, 70 eV) calcd for $C_{12}H_{18}O$ [M^+]: 178.1358; found: *m/z*= 178.1358±2 ppm. The spectroscopic data are identical to those reported in the literature.[25]

3.3.11. 1-Vinyl-1-tetrahydronaphthylacrylate (3k). The reaction was carried out following general procedure A. Starting with **2k** (0.87 g, 5.0 mmol), dissolved in ether (25 ml), NEt_3 (0.61 g, 6.0 mmol) and acrylic acid chloride (0.50 g, 5.5 mmol), **3k** was isolated (0.23 g, 1.0 mmol, 20%) as a colourless oil. ^1H NMR ($CDCl_3$, 250 MHz): δ 1.87 (tt, ^3J=6.0 Hz, 2H, CH_2), 2.61 (t, ^3J=6.0 Hz, 2H, CH_2), 2.81 (t, ^3J=6.0 Hz, 2H, CH_2), 4.90–4.93 (m, 2H, CH_2), 5.85 (dd, $^3J_{cis}$=11.0 Hz, ^2J=2.0 Hz, 1H, CH_2), 6.12–6.23 (m, 2H, CH), 6.46 (dd, $^3J_{trans}$=17 Hz, ^2J=2 Hz, 1H, CH_2), 7.09–7.22 (m, 3H, CH), 7.60–7.64 (m, 1H, CH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 22.9, 26.6, 30.2 (CH_2), 61.4 (C), 116.9, 124.1, 126.1, 127.5, 128.4, 128.9 (CH), 130.7 (CH_2), 134.8 (C), 137.9 (CH_2), 139.4 (C), 166.2 (CO). IR (KBr): $\tilde{\nu}$ 3494 (s), 3439 (s), 3064 (w), 3033 (w),

2933 (s), 2867 (s), 2840 (s), 1724 (s), 1684 (s), 1635 (s), 1619 (m), 1603 (w), 1485 (m), 1455 (m), 1406 (s) cm^{-1}. MS (EI, 70 eV): *m/z* (%)=228 (44, M^+), 173 (40), 156 (100), 141 (36), 129 (76).

3.3.12. 9-Vinyl-9*H*-fluoren-9-yl-acrylate (3l). The reaction was carried out following general procedure A. Starting with **2l** (1.04 g, 5.0 mmol), dissolved in THF (25 ml), NEt_3 (0.61 g, 6.0 mmol) and acrylic acid chloride (0.50 g, 5.5 mmol), **3l** was isolated (0.19 g, 0.7 mmol, 14%) as a colourless solid. ^1H NMR ($CDCl_3$, 250 MHz): δ 5.44 (d, $^3J_{cis}$=7.0 Hz, 1H, CH_2), 5.89 (dd, $^3J_{cis}$=11.0 Hz, ^2J=2.0 Hz, 1H, CH), 6.24 (dd, $^3J_{trans}$=17.0 Hz, $^3J_{cis}$=11.0 Hz, 1H, CH_2), 6.51 (dd, $^3J_{trans}$=17.0 Hz, ^2J=2 Hz, 1H, CH_2), 6.74 (t, ^3J=6.0 Hz, 1H, CH), 7.24–7.39 (m, 6H, CH), 7.66–7.71 (m, 3H, CH). MS (EI, 70 eV): *m/z* (%)=262 (76, M^+), 207 (92), 189 (80), 179 (100), 165 (20).

3.4. General procedure for the synthesis of spirocyclic butenolides 5

To a CH_2Cl_2 solution (30 ml) of **3** was added $Ti(O^iPr)_4$ and the solution was stirred for 1 h at 35 °C. A CH_2Cl_2 solution of **4** was subsequently added and the reaction mixture was stirred at 35 °C for 48 h. The solvent was removed in vacuo and the residue was purified by column chromatography (silica gel, petroleum ether/ether=3:1).

3.4.1. 1-Oxaspiro[4.5]dec-3-en-2-one (5a). Starting with **3a** (0.18 g, 1.00 mmol), dissolved in CH_2Cl_2 (30 ml), $Ti(O^iPr)_4$ (0.04 g, 0.15 mmol), dissolved in CH_2Cl_2 (5 ml), and **4** (0.08 g, 0.10 mmol), dissolved in CH_2Cl_2 (5 ml), **5a** was isolated (0.06 g, 57%) as a colourless oil. ^1H NMR ($CDCl_3$, 250 MHz): δ 1.57–1.80 (m, 10H, CH_2), 5.99 (d, ^3J=6.0 Hz, 1H, CH), 7.44 (d, ^3J=6.0 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 22.4, 24.6, 34.5, 88.6 (C), 120.1, 160.6 (CH), 172.6 (CO). IR (KBr): $\tilde{\nu}$ 3083 (w), 2937 (s), 2861 (m), 1883 (m), 1766 (s), 1750 (s), 1449 (m), 1430 (w), 1403 (m) cm^{-1}. The spectroscopic data are identical with those reported in the literature.[26]

3.4.2. 1-Oxaspiro[4.4]non-3-en-2-one (5b). Starting with **3b** (0.17 g, 1.00 mmol), dissolved in CH_2Cl_2 (40 ml), $Ti(O^iPr)_4$ (0.04 g, 0.15 mmol), dissolved in CH_2Cl_2 (5 ml), and **4** (0.08 g, 0.10 mmol), dissolved in CH_2Cl_2 (5 ml), **5b** was isolated (0.09 g, 66%) as a colourless oil. ^1H NMR ($CDCl_3$, 250 MHz): δ 1.78–1.98 (m, 8H, CH_2), 5.96 (d, ^3J=6.0 Hz, 1H, CH), 7.36 (d, ^3J=6.0 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 24.6, 36.7 (CH_2), 96.7 (C), 120.1, 159.0 (CH), 172.5 (CO). IR (KBr): $\tilde{\nu}$ 3084 (w), 2965 (s), 2877 (m), 1746 (s), 1602 (w), 1452 (w), 1434 (w) cm^{-1}. MS (EI, 70 eV): *m/z* (%)=138 (100, M^+), 109 (12), 94 (24), 82 (50), 81 (54). HRMS (EI, 70 eV) calcd for $C_8H_{10}O_2$ [M^+]: 138.0681; found: *m/z*=138.0681±2 ppm.

3.4.3. 1-Oxaspiro[4.6]undec-3-en-2-one (5c). Starting with **3c** (0.21 g, 1.07 mmol), dissolved in CH_2Cl_2 (20 ml), $Ti(O^iPr)_4$ (0.04 g, 0.15 mmol), dissolved in CH_2Cl_2 (5 ml), and **4** (0.08 g, 0.10 mmol), dissolved in CH_2Cl_2 (5 ml), **5c** was isolated (0.14 g, 0.8 mmol, 76%) as a colourless oil. ^1H NMR ($CDCl_3$, 250 MHz): δ 1.51–1.86 (m, 12H, CH_2), 5.99 (d, ^3J=6.0 Hz, 1H, CH), 7.45 (d, ^3J=6.0 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 22.6, 28.8, 37.5 (CH_2), 92.0 (C), 118.9, 161.6 (CH), 172.6 (CO). IR (KBr): $\tilde{\nu}$ 3082 (w), 2928 (s), 2859 (s), 1847 (w), 1828 (w), 1761 (s), 1746 (s), 1637 (w), 1604 (w), 1460 (s), 1446 (s) cm^{-1}. MS (EI, 70 eV): *m/z* (%)=166 (16, M^+), 138 (76), 109 (24), 97 (72), 81 (100). The spectroscopic data are identical with those reported in the literature.[27]

3.4.4. 1-Oxaspiro[4.7]dodec-3-en-2-one (5d). Starting with **3d** (0.11 g, 0.55 mmol), dissolved in CH_2Cl_2 (10 ml), $Ti(O^iPr)_4$ (0.02 g, 0.08 mmol), dissolved in CH_2Cl_2 (5 ml), and **4** (0.04 g, 0.05 mmol), dissolved in CH_2Cl_2 (5 ml), **5d** was isolated (0.08 g, 78%) as a colourless oil. ^1H NMR ($CDCl_3$, 250 MHz): δ 1.49–1.93 (m, 12H, CH_2), 1.96–2.01 (m, 2H, CH_2), 5.96 (d, ^3J=6.0 Hz, 1H, CH), 7.52 (d, ^3J=6.0 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 22.4, 24.4, 27.8, 33.4 (CH_2), 92.1 (C), 119.6, 161.1 (CH), 172.5 (CO). IR (KBr): $\tilde{\nu}$ 3080 (w), 2925 (s), 2857 (w), 1863 (w), 1474 (m), 1449 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%)=180 (16, M^+), 151 (24), 135 (28), 108 (24), 97 (100). Anal. Calcd for $C_{11}H_{16}O_2$: C 73.30, H 8.95; found: C 73.72, H 9.37.

3.4.5. 1-Oxaspiro[4.9]tetradec-3-en-2-one (5e). Starting with **5e** (0.12 g, 0.52 mmol), dissolved in CH_2Cl_2 (10 ml), $Ti(O^iPr)_4$ (0.02 g, 0.08 mmol), dissolved in CH_2Cl_2 (5 ml), and **4** (0.04 g, 0.05 mmol), dissolved in CH_2Cl_2 (5 ml), **5e** was isolated (0.07 g, 0.3 mmol, 63%) as a colourless oil. ^1H NMR ($CDCl_3$, 250 MHz): δ 1.56–1.91 (m, 16H, CH_2), 1.93–1.98 (m, 2H, CH_2), 5.96 (d, ^3J=6.0 Hz, 1H, CH), 7.50 (d, ^3J=6.0 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 21.6, 23.2, 25.6, 26.4, 31.5 (CH_2), 92.7 (C), 119.8, 161.0 (CH), 172.5 (CO). IR (KBr): $\tilde{\nu}$ 2987 (m), 2917 (s), 2865 (m), 2844 (m), 1814 (s), 1484 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%)=208 (8), 165 (32), 151 (36), 109 (24), 97 (100). Anal. Calcd for $C_{13}H_{20}O_2$: C 74.96, H 9.68; found: C 74.54, H 9.87.

3.4.6. 1-Oxaspiro[4.11]hexadec-3-en-2-one (5f). Starting with **3f** (0.18 g, 0.67 mmol), dissolved in CH_2Cl_2 (40 ml), $Ti(O^iPr)_4$ (0.04 g, 0.15 mmol), dissolved in CH_2Cl_2 (5 ml), and **4** (0.08 g, 0.10 mmol), dissolved in CH_2Cl_2 (5 ml), **5f** was isolated (0.11 g, 0.5 mmol, 70%) as a colourless solid. ^1H NMR ($CDCl_3$, 250 MHz): δ 1.23–1.40 (m, 13H, CH_2), 1.41–1.60 (m, 7H, CH_2), 1.70–1.82 (m, 2H, CH_2), 5.95 (d, ^3J=6.0 Hz, 1H, CH), 7.48 (d, ^3J=6.0 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 19.9, 21.8, 22.3, 25.7, 26.0, 31.9 (CH_2), 91.9 (C), 119.8, 160.8 (CH), 172.4 (CO). IR (KBr): $\tilde{\nu}$ 3088 (w), 2957 (s), 2937 (s), 2864 (m), 2847 (m), 1743 (s), 1472 (s), 1444 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%)=236 (100, M^+), 208 (16), 179 (12), 165 (28), 151 (28). HRMS (EI, 70 eV) calcd for $C_{15}H_{24}O_2$ [M^+]: 236.1776; found: *m/z*=236.1776±2 ppm. Anal. Calcd for $C_{15}H_{24}O_2$: C 76.23, H 10.24; found: C 76.10, H 10.76.

3.4.7. 5-Methyl-1-oxaspiro[4.5]dec-3-en-2-one (5g). Starting with **3g** (0.05 g, 0.26 mmol), dissolved in CH_2Cl_2 (10 ml), $Ti(O^iPr)_4$ (0.01 g, 0.04 mmol), dissolved in CH_2Cl_2 (5 ml), and **4** (0.03 g, 0.03 mmol), dissolved in CH_2Cl_2 (5 ml), **5g** was isolated (0.032 g, 80%, dr >98:2) as a colourless oil. ^1H NMR ($CDCl_3$, 250 MHz): δ 0.71 (d, ^3J=7.0 Hz, 3H, CH_3), 1.24–1.36 (m, 3H, CH_2), 1.58–1.82 (m, 6H, CH_2, CH), 5.99 (d, ^3J=6.0 Hz, 1H, CH), 7.26 (d, ^3J=6.0 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 14.9 (CH_3), 22.0, 25.3, 30.5, 35.4 (CH_2), 36.8 (CH), 80.5 (C),

120.3, 160.8 (CH), 173.2 (CO). IR (KBr): $\tilde{\nu}$ 2957 (w), 2917 (s), 2849 (s), 1632 (w), 1463 (w), 1261 (w) cm^{-1}.

3.4.8. 8-Phenyloxaspiro[4.5]dec-3-en-2-one (5h). Starting with **3h** (0.20 g, 0.78 mmol), dissolved in CH_2Cl_2 (20 ml), $Ti(O^iPr)_4$ (0.03 g, 0.12 mmol), dissolved in CH_2Cl_2 (5 ml), and **4** (0.06 g, 0.08 mmol), dissolved in 5 ml of CH_2Cl_2, **5h** was isolated (0.143 g, 80%, dr=3:1) as a colourless solid. The stereochemistry could not be unambiguously assigned (see **3h**). ^1H NMR ($CDCl_3$, 300 MHz): δ 1.66–2.19 (m, 8H, CH_2), 2.53–2.61 (m, 1H, CH, *syn*/*anti*), 2.65–2.75 (m, 1H, CH, *syn*/*anti*), 6.03 (d, ^3J=6.0 Hz, 1H, CH, *syn*), 6.10 (d, ^3J=6.0 Hz, 1H, CH, *anti*), 7.20–7.35 (m, 5H, CH), 7.40 (d, ^3J=6.0 Hz, 1H, CH, *syn*), 7.88 (d, ^3J=6.0 Hz, 1H, CH, *anti*). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 29.6, 31.0, 34.6, 35.3 (CH_2), 42.4, 42.8 (CH), 87.4, 88.8 (C), 120.3, 120.9, 126.3, 126.5, 126.7, 126.8, 128.5, 128.6 (CH), 145.0, 146.2 (C), 158.2, 161.2 (CH), 171.9, 172.5 (C). IR (KBr): $\tilde{\nu}$ 3089 (w), 2933 (m), 2861 (w), 1750 (s), 1601 (w), 1494 (w), 1449 (w) cm^{-1}. UV–vis (MeCN): λ_{max} (log ε)=208.55 (4.23) nm. MS (EI, 70 eV): *m*/*z* (%)=228 (M^+, 100), 183 (11), 156 (51), 130 (29), 117 (67), 104 (99). HRMS (EI, 70 eV) calcd for $C_{15}H_{16}O_2$ [M^+]: 228.1150; found: *m*/*z*=228.1150±2 ppm.

3.4.9. Adamantanone-spirobutenolide 5j. Starting with **3j** (0.20 g, 0.85 mmol), dissolved in CH_2Cl_2 (30 ml), $Ti(O^iPr)_4$ (0.04 g, 0.15 mmol), dissolved in CH_2Cl_2 (5 ml) and **4** (0.08 g, 0.10 mmol), dissolved in CH_2Cl_2 (5 ml), **5j** was isolated (0.11 g, 65%) as a colourless solid. ^1H NMR ($CDCl_3$, 300 MHz): δ 1.68–2.31 (m, 14H, CH, CH_2), 6.05 (d, $^3J_{cis}$=6.0 Hz, 1H, CH), 7.87 (d, $^3J_{cis}$=6.0 Hz, 1H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.1, 26.8 (CH), 33.6, 35.0 (CH_2), 36.8 (CH), 37.2 (CH_2), 92.8 (C), 120.5, 159.1 (CH), 172.1 (C). IR (KBr): $\tilde{\nu}$ 3078 (w), 2938 (s), 2917 (s), 2863 (m), 1738 (s), 1595 (w), 1454 (w) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%)=204 (M^+, 100), 176 (4), 148 (6), 110 (5), 95 (11). HRMS (EI, 70 eV) calcd for $C_{13}H_{16}O_2$ [M^+]: 204.1150; found: *m*/*z*=204.1150±2 ppm [M^+]. The spectroscopic data are identical with those reported in the literature.[19]

3.4.10. 5,6-Benzo[*e*]-1-oxaspiro[4.5]dec-3-en-2-one (5k). Starting with **3k** (0.11 g, 0.50 mmol), dissolved in CH_2Cl_2 (20 ml), $Ti(O^iPr)_4$ (0.02 g, 0.08 mmol), dissolved in CH_2Cl_2 (5 ml) and **4** (0.04 g, 0.05 mmol), dissolved in CH_2Cl_2 (5 ml), **5k** was isolated (yield: 60% based on recovered starting material) as a colourless oil. The spectroscopic data are identical with those reported in the literature.[20]

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