Conjugate Allylation of Cyclic α,β-Unsaturated Esters

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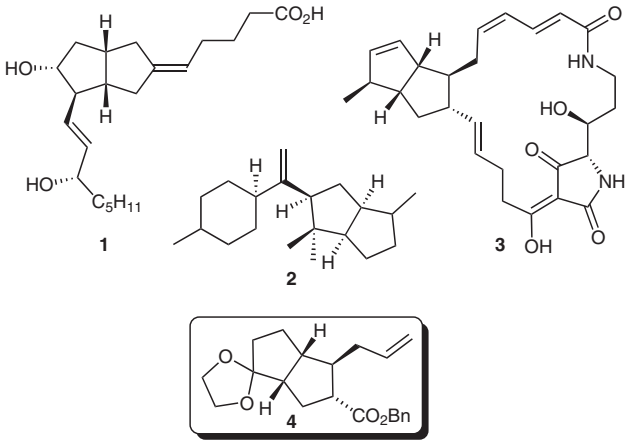
Abstract: The conjugate allylation of a homologous series of α,β-unsaturated cyclic esters **8**–**10** by addition of diallylcuprate (method A), fluoride ion catalyzed addition of trimethylallylsilane (method B), and aluminium tris(2,6-diphenylphenoxide) (ATPH)-mediated addition of allyllithium (method C) was investigated. Method A was not selective in all cases. For methods B and C an influence of ester moiety and ring size on the regioselectivity was observed. Methyl cyclopentenoate **8c** gave mainly the 1,2/1,2-product regardless the allylation method while *tert*-butyl and benzyl ester moieties favored the 1,4-products. For larger rings **9**, **10** and the anellated system **19** methods B and C behave complementary depending on the ester function: Method B gave best results of 1,4-addition products for benzyl esters while method C worked better for *tert*-butyl esters.

Key words: conjugate allylation, cycloalkenecarboxylates, regioselectivity, pentalene

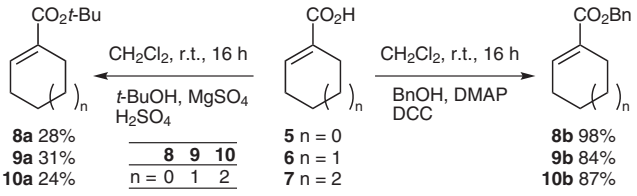
The functionalized bicyclo[3.3.0]octane (pentalene) system is a common structural motif in a large number of natural products and pharmaceuticals, for example, carbacyclin (**1**), diquinanes, such as neorogiolane (**2**) or the macrolactam cylindramide (**3**, Scheme 1).[1,2]



Scheme 1

Consequently, a variety of different strategies to substituted pentalenes has been reported.[1b,3] During a modified route to cylindramide (**3**) we were faced with the selective preparation of pentalene derivative **4** with allylic side chain as a key building block (Scheme 1). We envisaged an allylation reaction to an α,β-unsaturated bicyclo[3.3.0]octane precursor, because the conjugate addition of carbon nucleophiles to α,β-unsaturated carbonyl compounds is one of the most valuable transformations in organic synthesis and has been intensively investigated.[4] Surprisingly, the conjugate allyl transfer to cyclic α,β-unsaturated esters with exocyclic ester moiety has been rarely explored. For example, Majetich[5] compared the fluoride ion catalyzed addition of trimethylallylsilane (Sakurai conditions)[6,7] to various Michael acceptors with the addition of lithium diallylcuprate, which is well known[8] and successfully utilized for acyclic enoates.[9] An interesting method applied to acyclic chiral α,β-unsaturated esters was the stereo- and regioselective addition of allyllithium in the presence of the bulky Lewis acid aluminium tris(2,6-diphenylphenoxide) (ATPH).[10,11] However, reliable allylation methods for cyclic derivatives are missing. Therefore, we studied this issue in more detail using five- to seven-membered cycloalkenoates as model compounds in order to find an efficient procedure for the preparation of target pentalene **4**. The results are reported below.

The required α,β-unsaturated cyclic esters **8**–**10** (Scheme 2) were prepared from the respective acids **5**–**7**, which were accessible according to literature procedures.[12–15] Esterification of **5**–**7** in CH_2Cl_2 with *t*-BuOH in the presence of H_2SO_4 and anhydrous magnesium sulfate[16] yielded the esters **8a**–**10a**, and reaction of acids **5**–**7** with benzylic alcohol in the presence of DCC and DMAP[17] gave the benzyl esters **8b**–**10b** in good yield. Methyl cyclopentenoate **8c** is commercially available.



Scheme 2

Next, we investigated the allylation of cyclopentenoates **8a**–**c** via lithium diallylcuprate addition, Sakurai reaction, and ATPH-assisted addition of allyllithium (methods A–C, Scheme 3). The results of the comparative studies are listed in Table 1.

As can be seen from Table 1, the addition of diallylcuprate formed in situ from the Grignard reagent and Cu-Br·DMS (method A)[9a] to cyclopentenoates **8a**–**c** either

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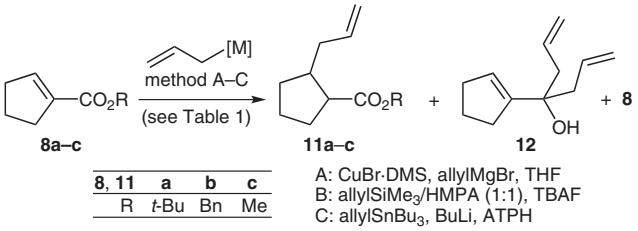
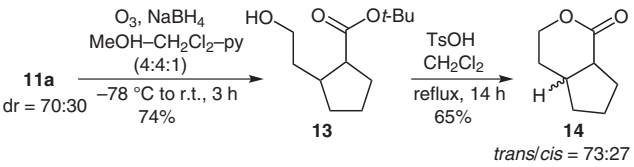


Scheme 3

yielded product mixtures in favor of the 1,2/1,2-product **12**[18] or, in the case of *tert*-butyl ester **8a**, only unreacted starting material was detected (entries 1–3). When the allylations were performed under Sakurai conditions in the presence of TBAF (method B)[19] or under Yamamoto conditions in the presence of ATPH (method C),[20] the regioselectivity, that is, 1,4- versus bis-1,2-addition, was found to be dependent on the ester moiety (entries 4–9). Whereas methyl cyclopentenoate **8c** gave preferably the 1,2/1,2-addition product **12** by using method B (entry 4), the corresponding *tert*-butyl and benzyl esters **8a**,**b** favored formation of the desired 1,4-products **11a**,**b** (entries 5, 6). The effect of the ester moiety was even more pronounced in the case of method C, where the allylation of **8a**,**b** proceeded quantitatively, and the 1,4-addition adducts **11a** and **11b** were obtained in 75 and 68% yield, respectively, with similar diastereomeric ratios (entries 8, 9). The decrease of yield is due to tedious chromatographic separation of 2,6-diphenylphenol from **11**. The results obtained for benzyl ester **8b** resemble those reported by Majetich.[5]

In order to determine the relative configuration, 1,4-allylation product **11a** with dr = 70:30 was submitted to ozonolysis followed by reductive workup in MeOH, CH_2Cl_2, and pyridine (4:4:1) giving alcohol **13**,[21] which was cyclized to the lactone **14** in 65% yield (Scheme 4). Comparison of its NMR spectra with literature data[22] revealed a *trans*/*cis* ratio of 73:27.



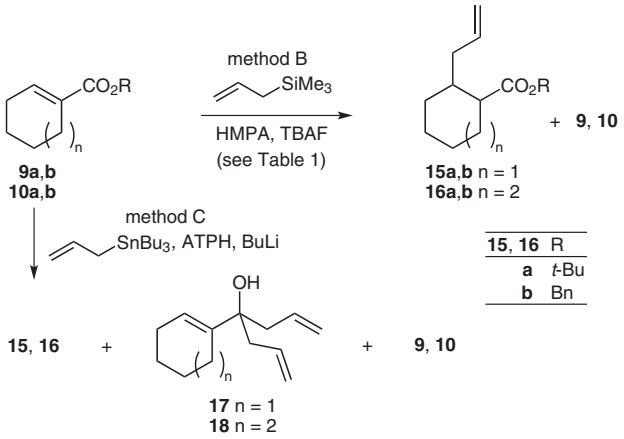
Scheme 4

Table 1 Allylation of cyclic α,β-unsaturated esters **8**–**10** under various conditions

						Product ratio (%)[a]			
Entry	Ester	R =	Method	Temp (°C)	Time (h)	Ester	1,2/1,2-Product	1,4-Product	dr[a]	Yield (%)
1	**8c**	Me	A	–78 to –10	5	4	85 (**12**)	11 (**11c**)	–	
2	**8b**	Bn	A	–78 to –10	4	–	87 (**12**)	13 (**11b**)	–	
3	**8a**	*t*-Bu	A	–78 to r.t.	6	100	–	–	–	
4	**8c**	Me	B	0	0.5	–	86 (**12**)	14 (**11c**)	–	
5	**8b**	Bn	B	0	10 min	–	40 (**12**)	60 (**11b**)	94:6	47 (**11b**)
6	**8a**	*t*-Bu	B	0	20 min	36	27 (**12**)	37 (**11a**)	79:21	
7	**8c**	Me	C	–78	0.5	24	60 (**12**)	16 (**11c**)	–	
8	**8b**	Bn	C	–78	0.75	–	–	100 (**11b**)	71:29	68 (**11b**)
9	**8a**	*t*-Bu	C	–78	0.75	–	–	100 (**11a**)	70:30	75 (**11a**)[b]
10	**9b**	Bn	B	0, r.t.	1, 16	3	–	97 (**15b**)	67:33	67 (**15b**)
11	**9a**	*t*-Bu	B	0, r.t.	1, 16	86	–	14 (**15a**)	75:25	
12	**9b**	Bn	C	–78	4	62	35 (**17**)	3 (**15b**)	–	
13	**9a**	*t*-Bu	C	–78	2.5	–	–	100 (**15a**)	80:20	78 (**15a**)[b]
14	**10b**	Bn	B	0 to r.t.	36	22	–	78 (**16b**)	84:16	59 (**16b**)[c]
15	**10a**	*t*-Bu	B	0, r.t.	2, 16	53	–	47 (**16a**)	80:20	30 (**16a**)
16	**10b**	Bn	C	–78 to r.t.	5	46	33 (**18**)	21 (**16b**)	80:20	
17	**10a**	*t*-Bu	C	–78	2	–	–	100 (**16a**)	79:21	80 (**16a**)

[a] Product ratio and diastereomeric ratio were determined by GC.
[b] Tedious chromatographic separation of 2,6-diphenylphenol from products **11a** and **15a**, respectively, due to similar polarities caused a decrease of yields with regard to quantitative conversion.
[c] Due to similar polarities starting material **10b** and product **16b** were difficult to separate by chromatography, resulting in decreased yields with regard to conversion.

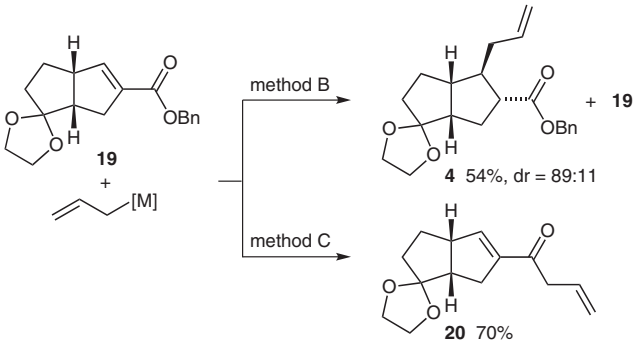
Due to the poor results of allylcuprate addition, only the conditions of method B and C were applied to the esters **9** and **10** with increased ring size (Scheme 5, Table 1).[19,20] The results in Table 1 reveal that for six- and seven-membered esters **9**, **10** methods B and C behave somewhat complementary depending on the ester moiety. For example, benzyl cyclohexenoate **9b** was cleanly converted into the 1,4-product **15b** in 67% yield employing method B (entry 10), whereas unreacted *tert*-butyl cyclohexenoate **9a** was detected as the major product besides the 1,4-adduct **15a** (entry 11). In contrast, by using method C benzyl ester **9b** gave only trace amounts of the desired product **15b** (entry 12), the *tert*-butyl ester **9a**, however, produced the 1,4-product **15a** quantitatively (entry 13). A similar behavior was observed for cycloheptenoates **10a**,**b** (entries 14–17).



Scheme 5

Next, methods B and C were applied to the allylation of the α,β-unsaturated pentalene precursor **19** (Scheme 6).[23,24] Under the conditions of method B the 1,4-addition to compound **19** was predominant, providing the desired pentalene **4** in 54% yield (referred to re-isolated **19**) with a diastereomeric ratio of 89:11 in favor of the *trans* isomer, as assigned by analogy (see Scheme 4). Because compound **19** was employed as enantiomerically pure starting material no trace of the two other possible diastereomers were found. Ester **19** was re-isolated in 43%. The ATPH-mediated allylation, however, did not afford any 1,4-addition adduct **4**, but the 1,2-product **20**. This result indicates that benzyl cyclohexene- (**9b**) and cycloheptenecarboxylate (**10b**) provide much better models for the reactivity of the pentalene-derived benzyl ester **19** with regard to allylation than benzyl cyclopentenoate **8b**.

In conclusion, the conjugate allylation of cyclic esters **8**–**10** was influenced by the ester moiety and the ring size. For cyclopentenecarboxylates **8** the regioselectivity of the allylation was found to be dependent on the ester moiety. Whereas methyl ester **8c** gave the 1,2/1,2-product **12** regardless the described method, *tert*-butyl and benzyl cyclopentenoates **8a**,**b** yielded preferably the 1,4-products **11a**,**b**. For cyclohexenoates **9**, cycloheptenoates **10**, and pentalene ester **19** the fluoride-ion-catalyzed addition of trimethylallylsilane gave mainly the desired 1,4-products **15**, **16**, and **4** if the benzyl esters were employed. In contrast, for the corresponding *tert*-butyl esters **9a** and **10a** the ATPH-mediated allylation was required to obtain good yields of the 1,4-addition adducts **15** and **16**.



Scheme 6

Acknowledgment

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(18) The initial 1,2-adduct, an enone, is capable of further 1,2-addition, giving the tertiary alcohol.[5]

(19) **General Procedures for the Allylation According Method B**

In a Schlenk flask 4 Å MS (2.00 g) and TBAF (1.31 g, 0.50 mmol) were dried under high vacuum for 30 min. Under N_2 atmosphere DMF (15 mL) was added, the mixture stirred for 30 min, transferred via cannula in a Schlenk flask with 4 Å MS (2.00 g), and stirred for a further 30 min. A solution of the respective ester (1 mmol) in DMF (5 mL) was added followed by HMPA (1.04 mL, 1.07 g, 6.00 mmol) and a solution of trimethylallylsilane (0.95 mL, 685 mg, 6.00 mmol) in DMF (5 mL) at 0 °C. After stirring at 0 °C for 10 min, 1 N HCl in MeOH (5 mL) and H_2O (40 mL) were successively added, and the aqueous layer was extracted with EtOAc (2 × 100 mL). The combined organic layers were dried ($MgSO_4$), concentrated under vacuum, and the crude product was chromatographed on SiO_2 with hexanes–EtOAc.

Benzyl 2-Allylcyclohexanecarboxylate (15b)

R_f = 0.37 (hexanes–EtOAc, 10:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.89–0.98 (m, 1.5 H, CH_2), 1.14–2.03 (m, 13.5 H, H_a-1′, H_a*-1′, H-2, H*-2, H-3, H*-3, H-4, H*-4, H-5, H*-5, H-6, H*-6), 2.06–2.16 (m, 2.5 H, H_b-1′, H_b*-1′, H-1), 2.65 (dt, *J* = 8.1, 4.1 Hz, 0.5 H, H*-1) 4.90–4.98 (m, 2 H, H-3′), 5.06–5.15 (m, 3 H, Ar*CH*$_2$, Ar*CH*$_2$*), 5.65–5.76 (m, 1.5 H, H-2′, H*-2′), 7.29–7.38 (m, 7.5 H, Ar, Ar*) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.6*, 23.8*, 25.4, 25.4*, 25.6, 28.0*, 30.1, 30.8 (C-3, C-4, C-5, C-6), 37.2*, 38.7 (C-2), 34.9*, 39.3 (C-1′), 44.8*, 49.4 (C-1), 65.8*, 65.9 (Ar*CH*$_2$), 115.9*, 116.3 (C-3′), 128.09*, 128.1, 128.1*, 128.2, 128.5, 128.5* (Ar), 136.0, 136.1* (Ar), 136.3, 137.3* (C-2′), 174.6*, 175.9 (CO) ppm. (* denotes minor diastereomer). FT-IR (ATR): 2319 (s), 2856 (s), 2360 (s), 1732 (vs), 1259 (s), 1164 (s), 749 (vs) cm^{-1}. MS (ESI): *m/z* (%) = 241 (15) [M^+ – O], 223 (36), 131 (28), 117 (20), 91 (71) [$C_7H_7^+$]. HRMS (ESI): *m/z* calcd for $C_{17}H_{22}NaO_2$ [M + Na]: 281.1512; found: 281.1503.

Benzyl (3a′*R*,4′*R*,5′*R*,6a′*S*)-4′-Allylhexahydro-2′*H*-spiro[1,3-dioxolane-2,1′-pentalene]-5′-carboxylate (4)

R_f = 0.58 (hexanes–EtOAc, 6:1); $[\alpha]_D^{20}$ +23 (*c* 1.00, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.45 (ddd, *J* = 12.6, 7.3, 2.7 Hz, 1 H, H_a-2′), 1.66–1.71 (m, 1 H, H_a-3′), 1.74–1.87 (m, 2 H, H_a-6, H_b-2′), 1.89–1.98 (m, 2 H, H-4′, H_b-3′), 2.04 (ddd, *J* = 12.9, 8.6, 6.3 Hz, 1 H, H_b-6′), 2.10–2.27 (m, 3 H, H-1″, H-3a′), 2.35–2.44 (m, 2 H, H-5′, H-6a′), 3.79–3.98 (m, 4 H, OCH_2CH_2O), 5.09 (d, *J* = 5.3 Hz, 2 H, C*H*$_2$Ph), 4.92 (ddt, *J* = 10.0, 2.1, 1.0 Hz, 1 H, H_a-3″), 4.98 (ddt, *J* = 17.1, 2.1, 1.4 Hz, 1 H, H_b-3″), 5.73 (ddt, *J* = 17.1, 10.0, 7.2 Hz, 1 H, H-2″), 7.28–7.38 (m, 5 H, Ph) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 27.8 (C-2′), 32.9, 33.1 (C-6′, C-3′), 37.8 (C-1″), 46.7 (C-3a′), 48.9, 51.1 (C-5′, C-6a′), 50.4 (C-4′), 63.8, 64.8 (OCH_2CH_2O), 66.1 (CH_2Ph), 116.3 (C-3″), 118.2 (C-1′), 127.6, 128.1, 128.2 (Ph), 136.1 (CH_2*Ph*), 136.4 (C-2″), 174.6 (CO) ppm. FT-IR (ATR): 2946 (w), 2880 (w), 2362 (w), 2342 (w), 1455 (w), 1338 (w), 1152 (s), 1023 (s), 697 (s) cm^{-1}. GC-MS (EI): *m/z* (%) = 342 (2) [M^+], 301 (8) [$M^+ – C_3H_5$], 251 (6) [$M^+ – C_7H_7$], 223 (6), 207 (14) [$M^+ – CO_2CH_2C_6H_5$], 107 (10) [$C_7H_7O^+$], 99 (100), 91 (30) [$C_7H_7^+$]. HRMS (ESI): *m/z* calcd for $C_{21}H_{26}O_4Na$ [M + Na]: 365.1723; found: 365.1722.

(20) **General Procedures for the Allylation According Method C**

Trimethyl aluminium (1.10 mL, 1 M in hexane, 1.10 mmol) was slowly added to a solution of 2,6-diphenylphenol (813 mg, 3.30 mmol) in toluene (6 mL) in a Schlenk flask, and the mixture stirred at r.t. for 30 min. Then a solution of the respective ester (1.00 mmol) in toluene (3 mL) was added. After 5 min, the mixture was cooled to –78 °C and stirred for

1 h. In a further flask *n*-BuLi (0.88 mL, 1.6 M in hexane, 1.40 mmol) was slowly added to a solution of allyltributyltin (0.43 mL, 463 mg, 1.40 mmol) in THF (4 mL) at –78 °C, and after stirring for 45 min, this allyllithium solution was transferred via cannula to the solution of the ATPH complex, and the reaction mixture stirred at –78 °C for a further 45 min. The reaction was quenched with MeOH (10 mL) and 1 N HCl (5 mL), and the aqueous layer extracted with Et_2O (50 mL). The organic layer was separated, dried ($MgSO_4$), concentrated, and the crude product chromatographed on SiO_2 with hexanes–EtOAc (50:1).

***tert*-Butyl 2-Allylcyclopentanecarboxylate (11a)**

R_f = 0.74 (hexanes–EtOAc, 10:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21–1.27 (m, 1 H, H_a-3), 1.44 [s, 9 H, $C(CH_3)_3$], 1.45 [s, 4.5 H, $C(CH_3)_3$*], 1.49–1.54 (m, 1 H, H_a*-4, H_a*-3), 1.58–1.69 (m, 2 H, H-4), 1.70–2.00 (m, 5.5 H, H_b-3, H-5, H_a*-1′, H_b*-3, H_b*-4, H*-5), 2.02–2.09 (m, 1 H, H_a-1′), 2.09–2.18 (m, 1.5 H, H-2, H*-2), 2.19–2.29 (m, 2.5 H, H-1, H_b-1′, H_b*-1′), 2.78 (ddd, *J* = 7.8, 7.8, 5.6 Hz, 0.5 H, H*-1), 4.95–5.05 (m, 3 H, H-3′, H*-3′), 5.75–5.86 (m, 1.5 H, H-2′, H*-2′) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.5*, 24.6 (C-4), 28.1, 28.2* [C(*C*H_3)$_3$], 28.3*, 30.2 (C-5), 30.7*, 32.1 (C-3), 35.4*, 39.3 (C-1′), 43.3*, 43.7 (C-2), 48.4*, 50.7 (C-1), 79.8, 80.0* [*C*$(CH_3)_3$], 115.3*, 115.6 (C-3′), 137.3, 137.9* (C-2′), 174.8*, 175.8 (CO) ppm. (* denotes minor diastereomer). FT-IR (ATR): 1723 (s), 1365 (s), 1256 (s), 1144 (vs) cm^{-1}. GC-MS (EI): *m/z* (%) = 210 (1) [M^+], 154 (60) [$M^+ – C(CH_3)$], 137 (28) [$M^+ – OCMe_3$], 109 (56) [$M^+ – CO_2CMe_3$], 67 (32), 57 (100) [$C_4H_9^+$]. HRMS (ESI): *m/z* calcd for $C_{13}H_{22}NaO_2$ [M + Na]: 233.1512; found: 233.1510.

***tert*-Butyl 2-Allylcycloheptanecarboxylate (16a)**

R_f = 0.68 (hexanes–EtOAc, 10:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.25–1.34 (m, 1 H, H_a-3), 1.37–1.51 (m, 3 H, H_a-4, CH_2), 1.46 [s, 9 H, $C(CH_3)_3$], 1.53–1.75 (m, 6 H, H_b-3, H_b-4, H-7, CH_2), 1.89–1.99 (m, 2 H, H_a-1′, H-2), 2.00–2.22 (m, 2 H, H-1, H_b-1′), 4.96–5.04 (m, 2 H, H-3′), 5.72–5.81 (m, 1 H, H-2′) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.1, 26.2, 26.3*, 26.5* (C-5, C-6), 28.1, 28.2* [C(*C*H_3)$_3$], 28.3*, 29.3 (C-4), 28.6*, 30.3 (C-7), 30.7, 30.7* (C-3), 37.7*, 40.6 (C-1′), 40.2*, 40.5 (C-2), 48.2*, 51.8 (C-1), 79.7, 79.8* [*C*$(CH_3)_3$], 115.7*, 116.3 (C-3′), 137.1, 138.0* (C-2′), 175.1*, 176.4 (CO) ppm. FT-IR (ATR): 2923 (s), 1723 (vs), 1366 (s), 1142 (vs), 910 (s) cm^{-1}. GC-MS (EI): *m/z* (%) = 238 (4) [M^+], 181 (100) [$M^+ – CMe_3$], 165 (24) [$M^+ – OCMe_3$], 140 (14), 136 (16) [$M^+ – CO_2CMe_3$], 122 (10), 109 (20), 95 (56), 81 (24), 67 (12), 57 (90) [$C_4H_9^+$], 41 (24) [$C_3H_5^+$], 29 (10). HRMS (ESI): *m/z* calcd for $C_{15}H_{27}O_2$ [M + H]: 239.2006; found: 239.2017.

1-{(3a′*R*,6a′*S*)-3′,3a′6′,6a′-tetrahydro-2′*H*-spiro[1,3-dioxolane-2,1′-pentalen]-5′-yl}but-3-en-1-one (20)

R_f = 0.38 (hexanes–EtOAc, 6:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.54–1.72 (m, 3 H, H_a-3′, H-2), 1.98 (dddd, *J* = 12.1, 10.7, 9.1, 6.5 Hz, 1 H, H_b-3′), 2.59–2.68 (m, 2 H, H_a-6′, H-6a′), 2.76 (dddd, *J* = 12.6, 2.9, 1.9, 1.9 Hz, 1 H, H_b-6′), 3.44 (dddd, *J* = 6.7, 2.2, 1.4, 1.4 Hz, 2 H, C*H*$_2$CH=CH$_2$), 3.44–3.51 (m, 1 H, H-3a′), 3.85–3.95 (m, 4 H, OCH_2CH_2O), 5.09–5.20 (m, 2 H, CH_2CH=C*H*$_2$), 5.96 (ddt, *J* = 17.2, 10.3, 6.7 Hz, 1 H, CH_2CH=CH_2), 6.52 (dddd, *J* = 3.7, 1.9, 1.9, 0.9 Hz, 1 H, H-4′) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 27.7 (C-3′), 32.9 (C-6′), 33.4 (C-2′), 44.2 (*C*H_2CH=CH_2), 46.3 (C-6a′), 49.6 (C-3a′), 63.9, 64.9 (OCH_2CH_2O), 118.2 (CH_2*C*H=CH_2), 127.7 (C-1′), 131.4 (CH=), 143.6 (C-5′), 145.3 (C-4′), 197.6 (CO) ppm. FT-IR (ATR): 2952 (s), 2875 (s), 1665 (vs), 1617 (s), 1202 (s), 1105 (vs), 1028 (vs), 993 (s), 914 (s), 735 (s) cm^{-1}. MS (ESI): *m/z* (%) = 257 (100) [M + Na], 235 (6) [M + H], 211 (8), 193 (16) [$M^+ – C_3H_5$], 173 (8), 149 (76) [$C_{11}H_{17}^+$], 131 (8), 121 (8) [$C_9H_{13}^+$], 105 (16), 99 (8). HRMS (ESI): *m/z* calcd for $C_{14}H_{19}O_3$ [M + H]: 235.1329; found: 235.1320.

(21) ***tert*-Butyl 2-(2-Hydroxyethyl)cyclopentanecarboxylate (13)**

Ozone was passed through a solution of **11a** (70 mg, 0.33 mmol) in MeOH–CH_2Cl_2–pyridine (4:4:1) at –78 °C. Then N_2 was passed for 1 min, $NaBH_4$ (33 mg, 0.84 mmol) was added, and the reaction mixture warmed to 0 °C and stirred for 3 h. After quenching with a sat. NH_4Cl soln (5 mL), the reaction mixture was extracted with EtOAc (20 mL). The combined organic layers were washed with brine (10 mL), dried ($MgSO_4$), and concentrated under vacuum. The residue was chromatographed on SiO_2 with hexanes–EtOAc (3:1, R_f = 0.34) to give **13** as a colorless oil (52 mg, 74%, dr 67:33). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.18–1.28 (m, 1 H, H_a-3), 1.45 [s, 13.5 H, $C(CH_3)_3$, $C(CH_3)_3$*], 1.52–1.96 (m, 11 H, H-1′, H*-1′, H_b-3, H*-3, H-4, H*-4, H-5, H*-5), 2.11–2.25 (m, 1.5 H, H-2, H-2*), 2.29 (dt, *J* = 8.8, 7.8 Hz, 1 H, H-1), 2.76 (dt, *J* = 7.8, 4.6 Hz, 0.5 H, H*-1), 3.60–3.76 (m, 3 H, H-2′, H*-2′) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 23.6*, 24.8 (C-4), 28.1, 28.2* [C(*C*H_3)$_3$], 28.5*, 30.6 (C-5), 31.2*, 33.3 (C-3), 34.1*, 38.4 (C-1′), 40.2, 40.6* (C-2), 48.4, 50.9 (C-1), 61.6, 62.2 (C-2′), 80.2*, 80.3 [*C*$(CH_3)_3$], 175.1*, 175.5 (CO) ppm. FT-IR (ATR): 2935 (s), 2871 (s), 1722 (vs), 1366 (s), 1145 (vs), 1051 (s), 847 (s) cm^{-1}. GC-MS (EI): *m/z* (%) = 184 (1), 158 (18) [$M^+ – C(CH_3)$], 141 (44) [$M^+ – OCMe_3$], 129 (12), 112 (8) [$M^+ – CO_2CMe_3$], 95 (50), 67 (16), 57 (100) [$C_4H_9^+$], 41 (18) [$C_3H_5^+$]. HRMS (ESI): *m/z* calcd for $C_{12}H_{22}NaO_3$ [M + Na]: 237.1461; found: 237.1453.

(22) Tsunoi, S.; Ryu, I.; Okuda, T.; Tanaka, M.; Komatsu, M.; Sonoda, N. *J. Am. Chem. Soc.* **1998**, *120*, 8692.

(23) Compound **19** was obtained from enantiomerically pure pentalene-1,4-dione monoacetal[1b] via α-acylation, reduction of the carbonyl group, and subsequent dehydration following the method by Burgess.[24]

(24) Burgess, E. M.; Penton, H. R.; Taylor, E. A. *J. Org. Chem.* **1973**, *38*, 26.