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[2+2] Photoadditions with chiral 2,5-cyclohexadienone synthons

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Abstract—Three chiral 2,5-cyclohexadienone synthons bearing different chiral auxiliaries were examined in [2+2] photoadditions with cyclopentene. Regeneration of the 'masked' double bond in the adducts resulted in the preparation of optically active 5-4-6 adducts. The enantiomeric purity of each adduct was found to be >95% using comparative ^{13}C NMR analysis of the appropriate ketals. The asymmetry induced in the cycloaddition step of our methodology indicated that the facial selectivity was directly correlated to the degree of steric bulk of the chiral auxiliary on the synthon.

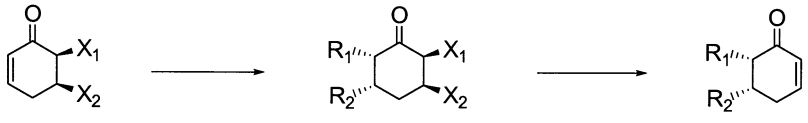
1. Introduction

Chiral 2,5-cyclohexadienone synthons have received only limited attention in natural product synthesis.[1,2] In this methodology, a diastereomerically pure substrate **1** undergoes 1,4-addition or cycloaddition with diastereofacial selectivity to give primarily **2**. Removal of the chiral auxiliary in **2** gives enantiomerically enriched **3** (Scheme 1). In previous examples, optically active 5-trimethylsilyl-2-cyclohexenone was shown to undergo cuprate addition with high diastereoselectivity. Removal of the TMS group followed by a further sequence of reactions ultimately yielded (+)-α-curcumene.[1] Similarly, cuprate addition to homochiral 5-*t*-butyldimethylsilyloxy-2-cyclohexenone followed by elimination of the TBDMSO group gave 5-alkylated-2-cyclohexenones with high enantiomeric excesses.[2] Tricyclic Diels–Alder adducts containing a 2-cyclohexenone moiety have been shown to be effective chiral 2,5-cyclohexadienone synthons.[3,4] To date there have been no reports of [2+2] photoadditions with this type of chiral synthon. Herein we wish to report our studies on the photoaddition of cyclopentene with a series of (−)-quinic acid-derived 2-cyclohexenones containing ketal moieties. Previously we have reported the transformation of photoadduct derivatives into racemic terpenoid natural products.[5–7] Use of the ketal auxiliary to induce high diastereofacial selectivity in the photoaddition step followed by facile removal of the auxiliary would provide an effective method for the preparation of optically active 5-4-6 adducts (bicyclo[5.4.0.0^{2,6}]-undecanes) and then natural products.

2. Results and discussion

2.1. Preparation of chiral 2,5-cyclohexadienone synthons 7

The desired synthons **7** were prepared from relatively inexpensive, commercially available (−)-quinic acid **4** (Scheme 2). The use of quinic acid as an effective 'chiron store' for natural product synthesis has been reviewed.[8] Three different ketals, **7a**–**c**, were prepared so that the facial selectivities of the photoaddition step could be compared. The synthesis of ketal **7c** has not



1 **2** **3**

Scheme 1.

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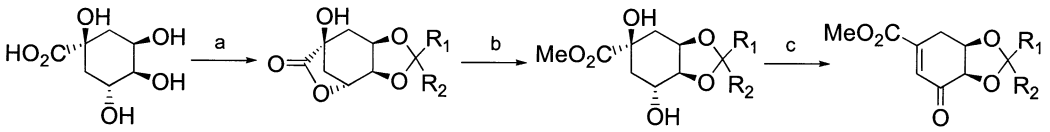


4 **5 a-c** **6 a-c** **7 a-c**

a, R_1, R_2 = -$(CH_2)_5$- ; **b**, R_1 = R_2 = Me; **c**, R_1 = R_2 = Et

Scheme 2. *Reagents and conditions*: : (a) cyclohexanone, *p*-TsOH, toluene, reflux, **5a** (80%); $(CH_3)_2C(OCH_3)_2$, *p*-TsOH, rt, **5b** (84%); $(C_2H_5)_2CO$, *p*-TsOH, toluene, reflux, **5c** (75%) (b) $NaOCH_3$, CH_3OH, rt, 5 h: **6a** (96%), **6b** (94%), **6c** (72%). (c) PCC, 5% pyr. in CH_2Cl_2, 3 Å mol. sieves, rt, 24 h: **7a** (43%), **7b** (55%), **7c** (50%).

been reported previously but its synthesis was similar to those reported for **7a**[9] and **7b**.[10] In these preparations **4** was converted to the ketal lactone **5**. For environmental reasons we used toluene rather than benzene as solvent in the preparation of **5a** and **5c** and in the preparation of **5b** 2,2-dimethoxypropane was used as reagent and solvent. Lactones **5** were then converted to esters **6**, which upon oxidation/dehydration with PCC/pyridine gave the three desired chiral synthons **7a**–**c**. The yield in this step was optimized by filtering the crude reaction mixture through a pad of Celite© and washing the pad with CH_2Cl_2 to efficiently extract the product from the chromium tars. An alternative two-step procedure has also been reported for the conversion of **6a** to **7a**.[11]

2.2. Investigation of chiral synthons 7a–c in [2+2] photoadditions

The cycloaddition of excess cyclopentene with each of the three chiral synthons **7a**–**c** bearing different ketal auxiliaries was investigated. CH_2Cl_2 was found to be the most effective solvent for the irradiations and a canary glass filter ($h\nu$ >320 nm) was employed to minimize decomposition of the products by a Norrish type 1 process. As indicated in Table 1, the three irradiations proceeded in high yield (>90%) to give mixtures of diastereomers **8** and **9** (Scheme 3). ^1H NMR analysis was used to measure the ratio of diastereomers. The two diastereomers from each irradiation process were separated by flash chromatography and shown by ^1H and ^{13}C NMR spectroscopy to both be *cis–anti–cis* adducts. Our previous NMR study of less highly substituted 5-4-6 photoadducts[12] was particularly helpful in confirming these structures. For example, the H_6–H_7 coupling constants of 6–7 Hz for **8b** and **9b** and the different ^{13}C chemical shifts for C_3 and C_5 (~27 and ~33 ppm, respectively) in both adducts are consistent with the proposed *anti* configurations. *syn*-Adducts would be expected to have H_6–H_7 coupling constants of 10–11 Hz and both C_3 and C_5 would resonate at about 28 ppm.[12]

Table 1. [2+2] Photoadditions of **7a**–**c** with cyclopentene (10 equiv.)[a]

Entry	Synthon	Yield (%)	Stereoselectivity (**8**:**9**)
1	**7a**	90	2:1
2	**7b**	96	3:1
3	**7c**	93	6:1

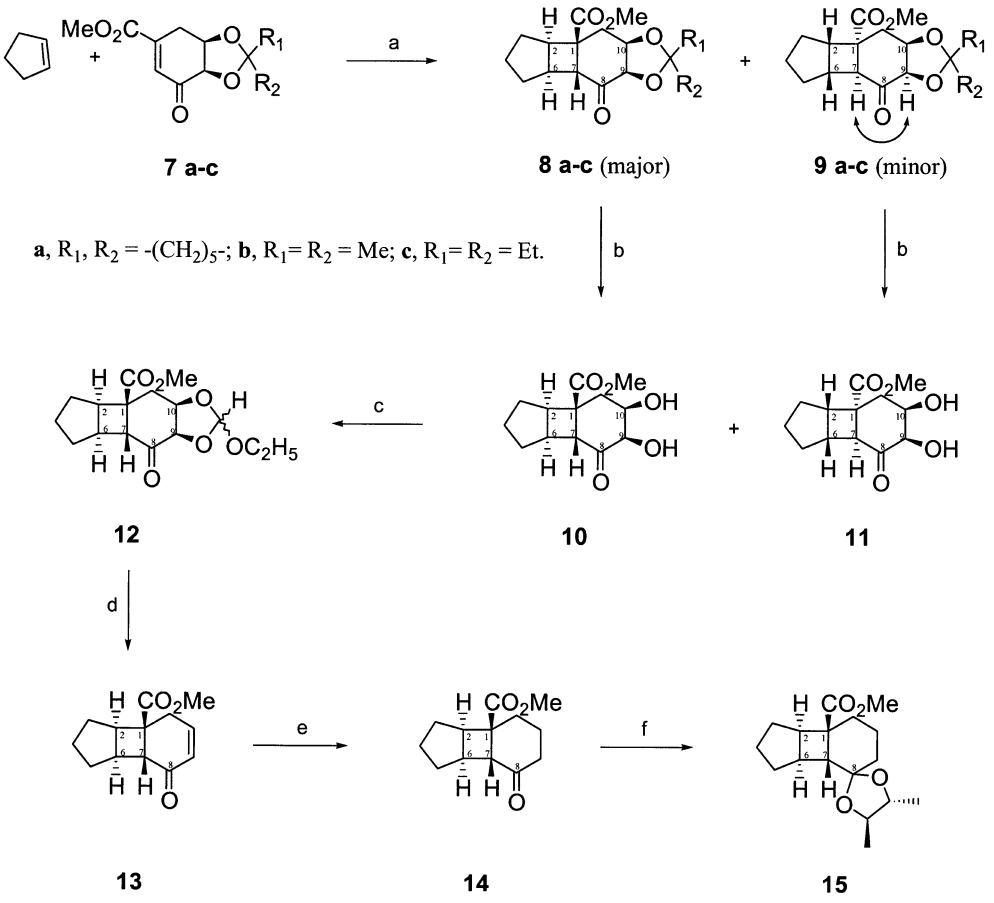
[a] Irradiation time 6 h with a 450 W Hanovia lamp, canary glass filter, CH_2Cl_2 solvent.

The relative configurations of the adducts **8** and **9** were determined by NOE experiments. The NOESY spectrum of **9b** (Scheme 3), but not **8b**, showed a positive correlation between H_7 and H_9, confirming that the minor photoadduct **9b** resulted from addition of cyclopentene to the more hindered face of **7b**. Similar results were observed with the adducts from **7a** and **7c**. Also diagnostic was H_7, which resonated at ~3.4 ppm in adducts **8a**–**c** because of deshielding by the ketal oxygens, but was found at ~3.0 ppm in adducts **9a**–**c** and **14**. Thus, the major adducts **8a**–**c** must possess the *cis–anti–cis* configuration and result from attack of cyclopentene on the less hindered face of **7a**–**c**.

Table 1 indicates significant differences in the facial selectivity of the three chiral synthons **7a**–**c**. The methyl groups of acetonide **7b** appear to provide more steric hindrance than the cyclohexane ring in **7a** where the carbons are 'tied back' in the cyclic structure. Ketal **7c** exhibits the highest degree of facial selectivity because of the greater hindrance provided by the ethyl groups as compared with the methyls in **7b**. Thus, the new chiral synthon **7c** provides the highest degree of stereoselectivity (6:1) in the photoaddition step.

2.3. Removal of the ketal auxiliary from the photoadducts 8a–c

We now wished to remove the ketal chiral auxiliary from the major photoadducts **8a**–**c** and replace it with a double bond. The ketal functions in **8a**–**c**, particularly **8a**, were surprisingly resistant to hydrolysis but treatment with 10% aqueous H_2SO_4/MeOH (1:2) gave diol **10**. Similarly minor adduct **9** could be hydrolyzed to diol **11**, which was not investigated further (Scheme 3). For the deoxygenation of **10**, neither the Corey–Winter method (via a thiocarbonate)[13] nor the Garegg procedure ($\varnothing_3P$, I_2, imidazole)[14] was effective. However, the two-step Eastwood procedure[15,16] proved to be an efficient means for converting the diol **10** to the alkene **13**. Thus, reaction of diol **10** with triethyl orthoformate yielded a stereoisomeric mixture of cyclic orthoformates **12** in high yield. Pyrolysis of **12** in a sealed tube at 200°C gave the optically active enone **13** in an overall yield from **10** of 85%. Preparation of enone **13** from enone **4** completed the desired chiral 2,5-cyclohexa-



Scheme 3. *Reagents and conditions*: : (a) *hv*, cyclopentene, CH_2Cl_2, see Table 1. (b) 10% aq. H_2SO_4/MeOH (1:2), yield of **10** from: **8a** (74%), **8b** (70%), **8c** (82%). (c) $HC(OEt)_3$, HCl (94%). (d) 200°C, cat. HOAc, toluene (85%). (e) H_2, 10% Pd/C, EtOAc (68%). (f) (*R*,*R*)-2,3-butanediol, *p*-TsOH, toluene, Δ (88%).

dienone methodology but we also wished to confirm the diastereomeric purity of **13**.

2.3.1. Determination of enantiomeric purity of 13. Hydrogenation of enone **13** using Pd on carbon gave the saturated optically active adduct **14**. As mentioned earlier, the racemic form of adducts such as **14** has been converted into terpenoid natural products.[5–7] The optically active adduct **14** was permitted to react with (*R*,*R*)-2,3-butanediol[17] to give ketal **15**. The racemic form of **14** was prepared as previously described[18] and was reacted with the same butanediol to give a 1:1 mixture of diastereomeric ketals. Comparison of the ^{13}C NMR spectra of the diastereomeric mixture with the sample of **14** derived from this study, established that the latter enone had enantiomeric purity of >95% (NMR error limits ~5%).

3. Conclusions

We have developed methodology for employing chiral 2,5-cyclohexadienone synthons **7** in [2+2] photoadditions. The new synthon **7c** has been prepared and shows markedly enhanced diastereofacial selectivity in the photoaddition with cyclopentene. This methodology allows the synthesis of enantiomerically pure photoadducts such as **14** which can then be converted into optically active natural products using transformations reported previously.[5–7]

4. Experimental

4.1. General

The 400-MHz ^1H NMR and 100-MHz ^{13}C NMR spectra were recorded on a Bruker Aspect 400 NMR spectrometer with tetramethylsilane as an internal standard. The multiplicities of the ^{13}C spectra were determined by either DEPT or J-MOD experiments. The 200-MHz ^1H NMR and 50-MHz ^{13}C NMR spectra were recorded on a Varian Gemini NMR spectrometer. The solvent used in all NMR experiments was $CDCl_3$. Infrared (IR) spectra were obtained on a Bomem MB-100 FTIR spectrometer using NaCl liquid cells and the indicated solvent. Mass spectral analyses were performed either on a Kratos MS 890 or an Autospec Ultima mass spectrometer using electron ionization (EI). All UV–vis spectra were obtained on a Shimadzu UV 160U UV–vis recording spectrophotometer. Optical rotation measurements were recorded on a Rudolph Research Autopol III Automatic Polarimeter, and the values are reported as $[\alpha]_D^{25}$, (*c* concentration in g/100 ml of solvent). The

melting points were determined on a Mel-Temp apparatus and were uncorrected.

All moisture- and oxygen-sensitive experiments were run under a positive pressure of argon in flasks which were flame- or oven-dried. All air- and moisture-sensitive reagents were transferred via syringe and introduced into the reaction flasks through rubber septa. Toluene, THF and CH_2Cl_2 were dried over 4 Å molecular sieves (activated). All other solvents were used without purification. All crude reaction mixtures were dried with anhydrous $MgSO_4$.

4.2. Preparation of lactones 5 from (−)-quinic acid

4.2.1. 3,4-*O*-Cyclohexylidenequinic acid-1,5-lactone, 5a. A solution of (−)-quinic acid **4** (4.97 g, 25.9 mmol), *p*-toluenesulfonic acid monohydrate (0.061 g, 0.32 mmol) and cyclohexanone (13.5 mL, 130 mmol) in toluene (38 mL) was heated under reflux for 5 h using a Dean–Stark apparatus. The reaction mixture was cooled to rt and quenched with cold saturated aqueous $NaHCO_3$ (25 mL). The aqueous layer was extracted with CH_2Cl_2 (3×), the organic layers were combined and washed with brine, dried with $MgSO_4$ and concentrated in vacuo. The residue was washed with 5% ether/hexanes (100 mL). The white crystals were dried in a vacuum oven for 24 h, yielding 3,4-*O*-cyclohexylidenequinic acid-1,5-lactone **5a** (5.28 g, 80%). TLC (50% EtOAc/hexanes) $R_f = 0.24$. All spectral data for this compound are similar to those previously reported.[9]

4.2.2. 3,4-*O*-Isopropylidenequinic acid-1,5-lactone, 5b. A solution of (−)-quinic acid **4** (1.99 g, 10.4 mmol), *p*-toluenesulfonic acid monohydrate (0.206 g, 1.08 mmol) in 2,2-dimethoxypropane (15.0 mL) was stirred for 24 h at rt. The reaction mixture was quenched with cold saturated aqueous $NaHCO_3$ (5 mL). The aqueous layer was extracted with EtOAc (3×), the organic layers were combined and washed with brine, dried with $MgSO_4$ and concentrated in vacuo. The residue was washed with 5% ether/hexanes (100 mL). The white crystals were dried in a vacuum oven for 24 h yielding 3,4-*O*-isopropylidenequinic acid-1,5-lactone **5b** (1.85 g, 84%). TLC (5% EtOAc/hexanes) $R_f = 0.59$. Complete spectral data for this compound has been reported previously.[10]

4.2.3. 3,4-*O*-isopentylidenequinic acid-1,5-lactone, 5c. A solution of (−)-quinic acid **4** (4.97 g, 26.1 mmol), *p*-toluenesulfonic acid monohydrate (0.500 g, 2.63 mmol) and 3-pentanone (13.2 mL, 124 mmol) in toluene (30 mL) was heated under reflux for 5 h using a Dean–Stark apparatus. The reaction mixture was cooled to rt and quenched with cold saturated aqueous $NaHCO_3$ (25 mL). The aqueous layer was extracted with CH_2Cl_2 (3×), the organic layers were combined and washed with brine, dried with $MgSO_4$ and concentrated in vacuo. The residue was washed with 5% ether/hexanes (100 mL) and the white crystals were dried in a vacuum oven for 24 h yielding 3,4-*O*-isopentylidenequinic acid-1,5-lactone **5c** (4.30 g, 68%). TLC (50% EtOAc/hexanes) $R_f = 0.46$; $[\alpha]_D^{25} = -19.7$ (c 1.69×10^{-4}, CH_2Cl_2); IR ($CHCl_3$): 3430, 1785 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.71 (dd, $J = 6.4$, 2.8 Hz, 1H, H-4), 4.42 (dt, $J = 3.2$ Hz, 1H, H-5), 4.24 (m, 1H, H-3), 3.20 (bs, 1H, -OH), 2.55 (d, $J = 12$ Hz, 1H, H-5β), 2.32 (m, 2H, H-2), 2.10 (dd, $J = 14.4$, 3.2 Hz, 1H, H-5α), 1.69 (q, $J = 7.6$ Hz, 2H, -CH_2-CH_3), 1.53 (q, $J = 7.6$ Hz, 2H, -CH_2-CH_3), 0.91 (t, $J = 7.2$ Hz, 3H, -CH_2-CH_3), 0.81 (t, $J = 7.6$ Hz, 3H, -CH_2-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.9 (-CO_2-), 113.9 (O_2CMe_2), 75.9 (C-5), 71.8 (C-4), 71.5 (C-1), 71.1 (C-3), 38.8 (C-6), 34.6 (C-2), 28.7 (-CH_2-CH_3), 27.6 (-CH_2-CH_3), 8.5 (-CH_2-CH_3), 8.0 (-CH_2-CH_3); EIMS m/z (rel. int.): 243 ($[M+H]^+$, 34), 213 (100), 111 (33), 95 (33), 87 (59), 83 (46), 57 (97); HRMS calcd for $C_{12}H_{19}O_5$ 243.123, found 243.122.

4.3. General procedure for the preparation of diol esters, 6a–c

A general procedure was used for the preparation of all diol esters: a solution of sodium methoxide and lactones **5a**–**c** was stirred in dry MeOH at rt until completion as indicated by TLC. The reaction mixture was neutralized by the dropwise addition of 1 equiv. of glacial acetic acid at 0°C, followed by the addition of saturated aqueous NH_4Cl. The aqueous layer was extracted with CH_2Cl_2 (3×), the organic layers were then combined, washed with brine (1×) and dried with $MgSO_4$. Evaporation of the solvent in vacuo followed by FC (60–100% EtOAc/hexanes) yielded the desired dihydroxy methyl esters **6**.

4.3.1. Methyl 3,4-*O*-cyclohexylidenequinate, 6a. Sodium methoxide (0.505 g, 9.52 mmol) was added to solution of lactone **5a** (1.99 g, 7.82 mmol) in dry MeOH (40 mL) and the reaction was stirred for 5 h at rt. After workup as described in the general procedure, FC (60–100% EtOAc/hexanes) of the crude product yielded the dihydroxy methyl ester **6a** as a brownish oil (2.16 g, 96%). TLC (60% EtOAc/hexanes) $R_f = 0.18$. Complete spectral data for this compound have been previously reported.[9]

4.3.2. Methyl 3,4-*O*-isopropylidenequinate, 6b. Sodium methoxide (1.22 g, 23.0 mmol) was added to a solution of lactone **5b** (4.11 g, 19.2 mmol) in dry MeOH (100 mL). The solution was reacted and worked up as described above. FC (60–100% EtOAc/hexanes) of the crude product yielded the dihydroxy ester **6b** as a tan-brown oil (4.44 g, 94%). TLC (50% EtOAc/hexanes) $R_f = 0.14$. Complete spectral data for this compound have previously been reported.[10]

4.3.3. Methyl 3,4-*O*-isopentylidenequinate, 6c. Sodium methoxide (0.350 g, 6.60 mmol) was added to solution of lactone **5c** (1.29 g, 5.31 mmol) in dry MeOH (30 mL) and the reaction was stirred for 6 h at rt. After workup as described in the general procedure, FC (50–100% EtOAc/hexanes) yielded the dihydroxy methyl ester **6c** as a brownish oil (0.990 g, 68%). TLC (50% EtOAc/hexanes) $R_f = 0.19$; $[\alpha]_D^{25} = -42.2$ (c 9.36×10^{-5}, CH_2Cl_2); IR ($CHCl_3$): 3450, 1730 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.40 (m, 1H, H-4), 4.08 (m, 1H, H-5), 3.94 (m, 1H, H-3), 3.74 (s, 3H, -CO_2CH_3), 3.30 (bs, 2H, -OH), 2.14 (m, 2H, H-2), 1.98 (m, 1H, H-5β), 1.79 (m,

1H, H-5α), 1.69 (q, $J=7.6$ Hz, 2H, -C$\underline{H}_2$-CH_3), 1.57 (q, $J=7.2$ Hz, 2H, -C$\underline{H}_2$-CH_3), 0.90 (t, $J=7.6$ Hz, 3H, -CH_2-C$\underline{H}_3$), 0.83 (t, $J=7.6$ Hz, 3H, -CH_2-C$\underline{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.6 (-$\underline{C}O_2Me$), 113.2 ($O_2\underline{C}Me_2$), 79.6 (C-5), 73.6 (C-1), 72.9 (C-4), 68.3 (C-3), 53.1 (-O$\underline{C}H_3$), 38.9 (C-6), 34.9 (C-2), 29.7 (-$\underline{C}H_2$-CH_3), 28.3 (-$\underline{C}H_2$-CH_3), 8.6 (-CH_2-$\underline{C}H_3$), 8.1 (-CH_2-$\underline{C}H_3$); EIMS m/z (rel. int.): 275 ([M+H]$^+$, 22), 245 (50), 171 (41), 57 (100); HRMS calcd for $C_{13}H_{23}O_6$ 275.149, found 275.151.

4.4. Preparation of the enone esters, 7

4.4.1. Methyl 4,5-*O*-cyclohexylidene-3-dehydro-4-*epi*-shikimate 7a. Pyridinium chlorochromate (1.35 g, 6.28 mmol) was added to a mixture of dihydroxy ester **6a** (0.402 g, 1.40 mmol) and 3 Å powdered molecular sieves (0.9 g) in 5% pyridine/CH_2Cl_2 (6.0 mL) and stirred for 24 h at rt. The reaction mixture was diluted with EtOAc (5 mL) and Celite© (1 g) and stirred for 10 min, then filtered through a pad of Celite© and washed with EtOAc (50 mL). The combined filtrate was washed with a saturated $CuSO_4$ solution and dried with $MgSO_4$. The solution was concentrated in vacuo and purified using FC (17–25% EtOAc/hexanes) to yield enone **7a** as white crystals (0.160 g, 43%). TLC (60% EtOAc/hexanes) $R_f=0.48$. Complete spectral data for this compound have been previously reported.[9]

4.4.2. Methyl 4,5-*O*-isopropylidene-3-dehydro-4-*epi*-shikimate, 7b. Pyridinium chlorochromate (1.13 g, 5.24 mmol), dihydroxy ester **6b** (0.311 g, 1.26 mmol) and 3 Å powdered molecular sieves (activated) (0.8 g) in 5% pyridine/CH_2Cl_2 (6.0 mL) was reacted and worked up as described for **7a**. The solution of the crude reaction mixture was concentrated in vacuo and purified using FC (17–25% EtOAc/hexanes) to yield enone **7b** as white crystals (0.148 g, 55%). TLC (50% EtOAc/hexanes) $R_f=0.41$. Complete spectral data for this compound has previously been reported.[10]

4.4.3. Methyl 4,5-*O*-isopentylidene-3-dehydro-4-*epi*-shikimate, 7c. Pyridinium chlorochromate (3.11 g, 14.4 mmol), dihydroxy ester **6c** (0.990 g, 3.61 mmol) and 3 Å powdered molecular sieves (1.5 g) in 5% pyridine/CH_2Cl_2 (20 mL) was reacted and worked up as described above except the pad of Celite© was washed with CH_2Cl_2. The combined filtrate was washed with saturated $CuSO_4$ and dried with $MgSO_4$. The solution was concentrated in vacuo and purified using FC (20–35% EtOAc/hexanes) to yield enone **7c** as yellow crystals (0.440 g, 50%). TLC (50% EtOAc/hexanes) $R_f=0.48$; mp = 84–86°C; $[\alpha]_D^{25}=-28$ (c 0.018, CH_2Cl_2); IR ($CHCl_3$): 1726, 1686 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.76 (s, 1H, H-2), 4.67 (t, $J=4.8$ Hz, 1H, H-6), 4.24 (d, $J=5.2$ Hz, 1H, H-5), 3.79 (s, 3H, -OC$\underline{H}_3$), 3.18 (d, $J=20.4$ Hz, 1H, H-4), 2.77 (m, 1H, H-4), 1.60 (q, $J=7.2$ Hz, 2H, -OC$\underline{H}_2$CH$_3$), 1.45 (m, 2H, -OC$\underline{H}_2$CH$_3$), 0.86 (m, 3H, -OCH$_2$C$\underline{H}_3$), 0.73 (m, 3H, -OCH$_2$C$\underline{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.1 (C-1), 166.1 (-$\underline{C}O_2Me$), 144.3 (C-3), 131.3 (C-2), 113.3 ($O_2\underline{C}Et_2$), 74.7 (C-6), 72.2 (C-5), 52.7 (-O$\underline{C}H_3$), 29.6 (-O$\underline{C}H_2CH_3$), 29.0 (-O$\underline{C}H_2CH_3$), 26.5 (C-4), 8.36 (-OCH$_2\underline{C}H_3$), 7.80 (-OCH$_2\underline{C}H_3$); EIMS m/z (rel. int.): 255 ([M+H]$^+$, 35), 225 (48), 57 (100); HRMS calcd for $C_{13}H_{19}O_5$ 255.123, found 255.122.

4.5. General irradiation procedure for preparation of photoadducts

The appropriate amounts of the enone and cycloalkene were dissolved in the indicated solvent and placed in Pyrex irradiation tubes (15×1.2 cm o.d.) within a canary glass (Corning no. 3320) sleeve. The solutions were deoxygenated with argon (1 min) and the tubes were sealed with rubber septa. The irradiations were performed using a Hanovia 450 W light source. The light source was placed in a water-cooled immersion well. The irradiation tubes were attached to the outside of this well and cooled in ice. The disappearance of enone **7** was monitored by TLC (60% EtOAc/hexanes).

4.5.1. Methyl (1*R*,2*R*,6*S*,7*R*,9*R*,10*R*)-9,10-*O*-cyclohexylidene-8-oxotricyclo[5.4.0.0^{2,6}]undecane-1-carboxylate, 8a and methyl (1*S*,2*S*,6*R*,7*S*,9*R*,10*R*)-9,10-*O*-cyclohexylidene-8-oxotricyclo[5.4.0.0^{2,6}]undecane-1-carboxylate, 9a. A solution of methyl 4,5-*O*-cyclohexylidene-3-dehydro-4-*epi*-shikimate **7a** (0.104 g, 0.391 mmol) and cyclopentene (0.34 mL, 3.8 mmol) in CH_2Cl_2 (7.0 mL) was irradiated following the general procedure. Upon completion of the irradiation (6 h), the solvent was removed in vacuo. The crude product was purified using FC (5–15% EtOAc/hexanes) to give a mixture of photoadducts **8a** and **9a** (0.119 g, 90%) in a 2:1 ratio as indicated by ^{1}H NMR.

Compound 8a: TLC (60% EtOAc/hexanes) $R_f=0.66$; white crystals, mp = 110–112°C; IR ($CHCl_3$): 2943, 1724, 1712 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.64 (m, 1H, H-10), 4.10 (d, $J=8.0$ Hz, 1H, H-9), 3.66 (s, 3H, -OC$\underline{H}_3$), 3.41 (d, $J=6.0$ Hz, 1H, H-7), 3.01 (q, $J=6.4$ Hz, 1H, H-6), 2.67 (m, 1H, H-11β), 2.43 (m, 1H, H-2), 1.68–1.18 (m, 17H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.4 (C-8), 173.3 (-$\underline{C}O_2Me$), 112.3 ($O_2\underline{C}Me_2$), 76.6 (C-10), 76.2 (C-9), 51.5 (-O$\underline{C}H_3$), 48.8 (C-1), 47.3 (C-2), 45.2 (C-7), 39.5 (C-6), 33.7, 33.3, 32.1, 32.1, 29.2, 25.8, 25.1, 23.8, 23.5; EIMS m/z (rel. int.): 334 (M$^+$, 15), 291 (20), 67 (18), 55 (100), 42 (15), 41 (29); HRMS calcd for $C_{19}H_{26}O_5$ 334.178, found 334.178.

Compound 9a: TLC (60% EtOAc/hexanes) $R_f=0.64$; white crystals, mp = 112–114°C; IR ($CHCl_3$): 2944, 1728, 1710 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.50 (d, $J=8.8$ Hz, 1H, H-9), 4.41 (m, 1H, H-10), 3.77 (s, 3H, -OC$\underline{H}_3$), 3.05 (q, $J=6.4$ Hz, 1H, H-6), 2.97 (d, $J=5.6$ Hz, 1H, H-7), 2.73 (dd, $J=13.2$, 4.4 Hz, 1H, H-11β), 2.51 (t, $J=7.4$ Hz, 1H, H-2), 1.76–1.23 (m, 17H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.7 (C-8), 174.0 (-$\underline{C}O_2Me$), 111.0 ($O_2\underline{C}Me_2$), 77.6 (C-10), 75.0 (C-9), 52.2 (-O$\underline{C}H_3$), 49.1 (C-1), 47.3 (C-2), 46.7 (C-7), 38.1 (C-11), 37.1 (C-6), 36.3, 34.0, 32.2 (C-5), 29.0 (C-3), 25.6 (C-4), 25.0, 23.9, 23.6; EIMS m/z (rel. int.):

334 (M^+, 15), 291 (56), 69 (31), 55 (100), 41 (58); HRMS calcd for $C_{19}H_{26}O_5$ 334.178, found 334.178.

4.5.2. Methyl (1*R*,2*R*,6*S*,7*R*,9*R*,10*R*)-9,10-*O*-isopropylidene-8-oxotricyclo[5.4.0.0^{2,6}]undecane-1-carboxylate, 8b and methyl (1*S*,2*S*,6*R*,7*S*,9*R*,10*R*)-9,10-*O*-isopropylidene-8-oxotricyclo[5.4.0.0^{2,6}]undecane-1-carboxylate, 9b. A solution of methyl 4,5-*O*-isopropylidene-3-dehydro-4-*epi*-shikimate **7b** (0.104 g, 0.459 mmol) and cyclopentene (0.40 mL, 4.5 mmol) in CH_2Cl_2 (7.0 mL) was irradiated following the general procedure. Upon completion of the irradiation (5 h) the solvent was removed in vacuo. The crude product was purified using FC (5–15% EtOAc/hexanes) to give a mixture of photoadducts **8b** and **9b** (0.130 g, 96%) in a 3:1 ratio as indicated by ^{1}H NMR.

Compound 8b: TLC (50% EtOAc/hexanes) $R_f = 0.61$; white crystals, mp = 106–108°C; $[\alpha]_D^{25} = -71.3$ (*c* 0.0202, CH_2Cl_2); IR ($CHCl_3$): 2950, 1733, 1716 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.65 (m, 1H, H-10), 4.12 (d, $J = 8.0$ Hz, 1H, H-9), 3.68 (s, 3H, -OC$\underline{H}_3$), 3.40 (d, $J = 6.0$ Hz, 1H, H-7), 3.01 (m, 1H, H-6), 2.65 (m, 1H, H-11β), 2.45 (m, 1H, H-2), 1.69–1.64 (m, 4H), 1.44 (m, 3H), 1.38 (s, 3H, -OCC$\underline{H}_3$), 1.22 (s, 3H, -OCC$\underline{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.1 (C-8), 173.3 (-$\underline{C}O_2$Me), 111.4 ($O_2\underline{C}Me_2$), 77.1 (C-10), 76.6 (C-9), 51.5 (-O$\underline{C}H_3$), 48.9 (C-1), 47.4 (C-2), 45.3 (C-7), 39.4 (C-6), 33.7 (C-11), 32.1 (C-5), 29.1 (C-3), 25.7 (C-4), 23.8 (-OC$\underline{C}H_3$), 23.0 (-OC$\underline{C}H_3$); EIMS *m*/*z* (rel. int.): 294 (M^+, 37), 279 ($M-CH_3^+$, 100), 177 (54), 149 (52), 91 (52), 67 (58); HRMS calcd for $C_{16}H_{22}O_5$ 294.1467, found 294.1467.

Compound 9b: TLC (50% EtOAc/hexanes) $R_f = 0.53$; IR ($CHCl_3$): 2953, 1735, 1719 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.49 (d, $J = 8.8$ Hz, 1H, H-9), 4.42 (m, 1H, H-10), 3.78 (s, 3H, -OC$\underline{H}_3$), 3.06 (m, 1H, H-6), 2.99 (d, $J = 6.0$ Hz, 1H, H-7), 2.72 (dd, $J = 13.2$, 5.4 Hz, 1H, H-11β), 2.51 (t, $J = 7.4$ Hz, 1H, H-2), 1.77–1.67 (m, 2H), 1.59–1.53 (m, 4H), 1.51 (s, 3H, -OCC$\underline{H}_3$), 1.45 (m, 1H), 1.31 (s, 3H, -OCC$\underline{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.6 (C-8), 174.0 (-$\underline{C}O_2$Me), 110.1 ($O_2\underline{C}Me_2$), 77.9 (C-9), 76.3 (C-10), 52.2 (-O$\underline{C}H_3$), 49.1 (C-1), 47.3 (C-7), 46.7 (C-2), 37.9 (C-11), 37.1 (C-6), 32.2 (C-5), 29.0 (C-3), 26.7 (-OC$\underline{C}H_3$), 25.6 (C-4), 24.5 (-OC$\underline{C}H_3$); EIMS *m*/*z* (rel. int.): 294 (M^+, 27), 279 ($M-CH_3^+$, 100), 177 (28), 149 (46), 91 (57), 59 (87); HRMS calcd for $C_{16}H_{22}O_5$ 294.1467, found 294.1460.

4.5.3. Methyl (1*R*,2*R*,6*S*,7*R*,9*R*,10*R*)-9,10-*O*-isopentylidene-8-oxotricyclo[5.4.0.0^{2,6}]undecane-1-carboxylate, 8c and methyl (1*S*,2*S*,6*R*,7*S*,9*R*,10*R*)-9,10-*O*-isopentylidene-8-oxotricyclo[5.4.0.0^{2,6}]undecane-1-carboxylate, 9c. A solution of methyl 4,5-*O*-isopentylidene-3-dehydro-4-*epi*-shikimate, **7c** (0.104 g, 0.391 mmol) and cyclopentene (0.34 mL, 3.8 mmol) in CH_2Cl_2 (7.0 mL) was irradiated following the general procedure. Upon completion of the irradiation (6 h), the solvent was removed in vacuo. The crude product was purified using FC (5–15% EtOAc/hexanes) to give a mixture of photoadducts **8c** and **9c** (0.119 g, 90%) in a 6:1 ratio, respectively, as indicated by ^{1}H NMR.

Compound 8c: TLC (30% EtOAc/hexanes) $R_f = 0.54$; white crystals, mp = 110–112°C; $[\alpha]_D^{25} = -67$ (*c* 0.023, CH_2Cl_2); IR ($CHCl_3$): 1731, 1718 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.68 (m, 1H, H-10), 4.14 (d, $J = 8.0$ Hz, 1H, H-9), 3.69 (s, 3H, -OC$\underline{H}_3$), 3.39 (d, $J = 6.0$ Hz, 1H, H-7), 3.01 (m, 1H, H-6), 2.65 (m, 1H, H-11β), 2.49 (m, 1H, H-2), 1.78–1.64 (m, 8H), 1.52–1.40 (m, 3H), 0.85 (t, $J = 7.6$ Hz, 3H, -OCH$_2$C$\underline{H}_3$), 0.80 (t, $J = 7.6$ Hz, 3H, -OCH$_2$C$\underline{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.0 (C-8), 173.2 (-$\underline{C}O_2$Me), 115.9 ($O_2\underline{C}Et_2$), 75.4 (C-10), 75.2 (C-9), 51.5 (-O$\underline{C}H_3$), 48.6 (C-1), 47.2 (C-2), 45.5 (C-7), 39.4 (C-6), 33.7 (C-11), 32.1 (C-5), 29.2 (C-3), 26.2 (-O$\underline{C}$H$_2$CH$_3$), 25.7 (C-4), 24.7 (-O$\underline{C}$H$_2$CH$_3$), 8.50 (-OCH$_2\underline{C}$H$_3$), 8.50 (-OCH$_2\underline{C}$H$_3$); EIMS *m*/*z* (rel. int.): 323 ($[M+H]^+$, 4), 293 (12), 91 (7), 67 (14), 57 (100); HRMS calcd for $C_{18}H_{27}O_5$ 323.186, found 323.185.

Compound 9c: TLC (30% EtOAc/hexanes) $R_f = 0.47$; IR ($CHCl_3$): 1735, 1711 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.48 (d, $J = 9.2$ Hz, 1H, H-9), 4.42 (m, 1H, H-10), 3.78 (s, 3H, -OC$\underline{H}_3$), 3.05 (q, $J = 6.8$ Hz, 1H, H-6), 2.97 (d, $J = 5.6$ Hz, 1H, H-7), 2.71 (dd, $J = 13.2$, 5.2 Hz, 1H, H-11β), 2.50 (t, $J = 7.6$ Hz, 1H, H-2), 1.75–1.70 (m, 4H), 1.58–1.49 (m, 7H), 0.91 (t, $J = 7.2$ Hz, 3H, -OCH$_2$C$\underline{H}_3$), 0.86 (t, $J = 7.2$ Hz, 3H, -OCH$_2$C$\underline{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.5 (C-8), 174.0 (-$\underline{C}O_2$Me), 114.3 ($O_2\underline{C}Me_2$), 78.1 (C-9), 75.4 (C-10), 52.2 (-O$\underline{C}H_3$), 48.9 (C-1), 47.1 (C-7), 46.6 (C-2), 37.9 (C-11), 37.1 (C-6), 32.2 (C-5), 29.1 (-O$\underline{C}$H$_2$CH$_3$), 29.0 (C-3), 28.5 (-O$\underline{C}$H$_2$CH$_3$), 25.6 (C-4), 8.50 (-OCH$_2\underline{C}$H$_3$), 7.30 (-OCH$_2\underline{C}$H$_3$); EIMS *m*/*z* (rel. int.): 323 ($[M+H]^+$, 1), 293 (11), 57 (100), 36 (13); HRMS calcd for $C_{18}H_{27}O_5$ 323.186, found 323.187.

4.5.4. Methyl (1*R*,2*R*,6*S*,7*R*,9*R*,10*R*)-9,10-dihydroxy-8-oxotricyclo[5.4.0.0^{2,6}]undecane-1-carboxylate, 10 and methyl (1*S*,2*S*,6*R*,7*S*,9*R*,10*R*)-9,10-dihydroxy-8-oxotricyclo[5.4.0.0^{2,6}]undecane-1-carboxylate, 11. A solution of photoadduct **8b** (containing trace amounts of **9b**) (0.152 g, 0.517 mmol) and methanol (3 mL) was stirred at rt for 10 min, then 10% H_2SO_4 (1.0 mL) was added dropwise to the solution. The reaction was monitored by TLC (60% EtOAc/hexanes) and was complete after stirring for 2 h at rt. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ (3 mL) and extracted with CH_2Cl_2 (3×). The organic layers were the combined, washed with brine and dried with $MgSO_4$. The solvent was removed in vacuo and the crude product was purified using FC (50–60% EtOAc/hexanes) to yield **10** as a yellow oil (0.091 g, 70%). A collection of many fractions from different trials, all containing trace amounts of **11** was accumulated and re-purified.

Compound 10: TLC (60% EtOAc/hexanes) $R_f = 0.24$; IR ($CHCl_3$): 3451, 1734, 1701 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.30 (m, 1H, H-10), 4.28 (m, 1H, H-9), 4.00–3.80 (bs, 1H, -OH), 3.69 (s, 3H, -OC$\underline{H}_3$), 3.41 (d, $J = 7.6$ Hz, 1H, H-7), 3.09 (m, 1H, H-11β), 2.98 (q, $J = 6.8$ Hz, 1H, H-6), 2.63 (m, 1H, H-2), 2.50–2.25 (bs, 1H, -OH), 2.19 (d, $J = 14.8$ Hz, 1H, H-11α), 1.88–1.72 (m, 3H), 1.58–1.44 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.0 (C-8), 173.6 (-$\underline{C}O_2$Me), 76.0 (C-9), 71.0 (C-10), 52.0 (-O$\underline{C}H_3$), 49.4 (C-2), 47.4 (C-1), 46.9 (C-7),

40.9 (C-6), 37.2 (C-11), 31.8 (C-5), 28.1 (C-3), 25.8 (C-4); EIMS m/z (rel. int.): 254 (M^+, 65), 204 (49), 176 (82), 165 (70), 91 (74), 67 (100); HRMS calcd for $C_{13}H_{18}O_5$ 254.1154, found 254.1158.

Compound 11: TLC (60% EtOAc/hexanes) $R_f = 0.30$; IR ($CHCl_3$): 3473, 1730, 1716 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.21 (q, $J = 4.8$ Hz, 1H, H-10), 4.07 (m, 1H, H-9), 3.79 (bs, 1H, -OH), 3.70 (s, 3H, -OC$\underline{H}_3$), 3.12 (d, $J = 6.5$ Hz, 1H, H-7), 2.92 (q, $J = 6.4$ Hz, 1H, H-6), 2.75 (t, $J = 6.4$ Hz, 1H, H-2), 2.67 (bs, 1H, -OH), 2.21 (dq, $J = 15.2$, 4.2 Hz, 2H, H-11), 1.71–1.65 (m, 2H), 1.59–1.55 (m, 2H), 1.54–1.39 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.4 (C-8), 175.0 (-$\underline{C}O_2Me$), 75.7 (C-9), 70.8 (C-10), 52.0 (-O$\underline{C}H_3$), 48.3 (C-2), 47.1 (C-1), 47.1 (C-7), 40.5 (C-6), 37.8 (C-11), 32.3 (C-5), 29.5 (C-3), 25.4 (C-4).

4.5.5. Methyl (1*R*,2*R*,6*S*,7*R*,9*R*,10*R*)-9,10-*O*-ethoxymethylene-8-oxotricyclo[5.4.0.0^{2,6}]undecane-1-carboxylate, 12. A solution of diol **10** (0.063 g, 0.25 mmol), freshly distilled triethyl orthoformate (1.5 mL) and saturated methanolic HCl[16] (10 μL) was stirred at rt for 2 h. The reaction was monitored by TLC (60% EtOAc/hexanes) until no starting material was evident. The reaction mixture was quenched with saturated aqueous Na_2CO_3 (1 mL) and was extracted with CH_2Cl_2 (3×). The organic layers were combined, washed with brine and dried with $MgSO_4$. The solvent was removed in vacuo and the crude product was purified using FC (5–15% EtOAc/hexanes) to give a mixture of diastereomeric ortho esters **12** (0.073 g, 94%). All attempts to separate the isomeric mixture of orthoformates **12** were unsuccessful, therefore, only minimal spectral data were obtained for this mixture. TLC (60% EtOAc/hexanes) $R_f = 0.69$; ^1H NMR (200 MHz, $CDCl_3$): δ 5.71 (s, 1H, -$O_2C\underline{H}OC_2H_5$), 4.89 (m, 1H, H-10), 4.30 (d, $J = 7.4$ Hz, 1H, H-9), 3.74 (s, 3H, -OC$\underline{H}_3$), 3.52 (q, $J = 7.0$ Hz, 2H, -OC$\underline{H}_2CH_3$), 3.43 (d, $J = 5.2$ Hz, 1H, H-7), 3.09 (m, 1H), 2.64 (m, 1H), 2.49 (m, 1H), 1.74–1.48 (m, 7H), 1.18 (m, 3H, -$OCH_2C\underline{H}_3$).

4.5.6. Methyl (1*R*,2*R*,6*S*,7*R*)-8-oxotricyclo[5.4.0.0^{2,6}]-undec-9-ene-1-carboxylate, 13. A solution of ortho ester **12** (0.086 g, 0.28 mmol) and toluene (2.0 mL) was transferred to a sealable tube and glacial acetic acid (20 μL) was added dropwise. The mixture was deoxygenated with argon for 1 min, the tube was sealed, and the mixture was heated at 200°C for 24 h. The reaction was monitored by TLC (60% EtOAc/hexanes) until completion. The solvent was removed in vacuo to yield an oily yellow crude product that was purified using FC (5–15% EtOAc/hexanes) to give enone **13** (0.052 g, 85%). TLC (60% EtOAc/hexanes) $R_f = 0.53$; $[\alpha]_D^{25} = -8.5$ (c 0.55, CH_2Cl_2); IR ($CHCl_3$): 1733, 1690, 1640 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.69 (m, 1H, H-10), 6.07 (d, $J = 10$ Hz, 1H, H-9), 3.66 (s, 3H, -OC$\underline{H}_3$), 3.10 (d, $J = 6.4$ Hz, 1H, H-7), 2.81 (ddd, $J = 19.4$, 4.6, 2.0 Hz, 1H, H-11β), 2.75 (q, $J = 6.8$ Hz, 1H, H-6), 2.58 (m, 1H, H-2), 2.55 (m, 1H, H-11α), 1.78 (m, 1H, H-5), 1.74–1.68 (m, 2H, H-4), 1.57–1.45 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.4 (C-8), 174.3 (-$\underline{C}O_2Me$), 146.7 (C-10), 129.1 (C-9), 51.9 (-O$\underline{C}H_3$), 50.5 (C-2), 46.4 (C-7), 45.2 (C-1), 41.9 (C-6), 33.1 (C-11), 32.4 (C-5), 29.4 (C-3), 25.4 (C-4); EIMS m/z (rel. int.): 220 (M^+, 10), 161 (31), 153 (100), 109 (47), 68 (68); HRMS calcd for $C_{13}H_{16}O_3$ 220.1099, found 220.1101.

4.5.7. Methyl (1*R*,2*R*,6*S*,7*R*)-8-oxotricyclo[5.4.0.0^{2,6}]-undecane-1-carboxylate, 14. A solution of enone **13** (0.019 g, 0.086 mmol) and 10% palladium on activated carbon (0.020 g) in EtOAc (5 mL) was stirred at rt in an H_2 enriched atmosphere for 2 h. The reaction was monitored by TLC (50% EtOAc/hexanes) until completion. The suspension was then filtered through a pad of Celite© and washed with EtOAc (30 mL). The solvent was removed in vacuo to yield adduct **14** (0.013 g, 68%) as a colorless oil. TLC (50% EtOAc/hexanes) $R_f = 0.57$; $[\alpha]_D^{25} = -76$ (c 0.17, $CHCl_3$); IR (CCl_4): 1730, 1705 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.73 (s, 3H, -OC$\underline{H}_3$), 2.94 (d, $J = 6.4$ Hz, 1H, H-7), 2.68 (q, $J = 6.8$ Hz, 1H, H-6), 2.56 (t, $J = 7.6$ Hz, H-2), 2.38 (t, $J = 6.2$ Hz, 1H, H-9), 2.22 (dt, $J = 18.4$, 6.8 Hz, 1H, H-9), 2.02–1.42 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.4 (C-8), 174.6 (-$\underline{C}O_2Me$), 51.7 (-O$\underline{C}H_3$), 49.1 (C-7), 48.8 (C-1), 46.8 (C-2), 39.9 (C-6), 38.2 (C-9), 32.5 (C-5), 32.5 (C-3), 29.1 (C-4), 25.3 (C-11), 19.6 (C-10). All spectral data were similar to those of the corresponding racemic mixture, which has been reported previously.[18]

4.6. Preparation of chiral ketals 15 and 16 for determination of enantiomeric purity of 14

4.6.1. Ketal 15 from methyl (1*R*,2*R*,6*S*,7*R*)-8-oxotricyclo[5.4.0.0^{2,6}]undecane-1-carboxylate 14 and (*R*,*R*)-butane-2,3-diol. A solution of optically active adduct **14** (0.038 g, 0.17 mmol), p-toluenesulfonic acid monohydrate (0.004 g, 0.02 mmol) and (*R*,*R*)-2,3-butanediol (0.041 g, 0.46 mmol) in toluene (7.0 mL) was heated under reflux for 6 h using a Dean–Stark apparatus. The reaction was monitored using TLC (60% EtOAc/hexanes) until completion. The reaction mixture was cooled to rt, quenched with saturated aqueous Na_2CO_3 (3 mL) and washed with H_2O (2×). The aqueous layer was extracted (3×) with CH_2Cl_2, the organic layers were combined, dried with $MgSO_4$ and concentrated in vacuo. The residue was purified using FC (10–20% EtOAc/hexanes) yielding ketal **15** exclusively (0.044 g, 88%) as a brownish oil. TLC (50% EtOAc/hexanes) $R_f = 0.66$; ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.4 (-$\underline{C}O_2Me$), 108.2 (C-8), 78.3, 77.5 (O-$\underline{C}H(CH_3)$-$\underline{C}H(CH_3)$-O), 51.5 (-O$\underline{C}H_3$), 47.6 (C-7), 47.5 (C-1), 43.8 (C-2), 37.6 (C-6), 33.6 (C-9), 32.0 (C-3), 31.5 (C-5), 28.6 (C-4), 26.1 (C-11), 19.5 (C-10), 17.4 (-$C\underline{C}H_3$), 16.8 (-$C\underline{C}H_3$); EIMS m/z (rel. int.): 294 (M^+, 17), 235 (6), 177 (10), 141 (23), 127 (100); HRMS calcd for $C_{17}H_{26}O_4$ 294.1831, found 294.1835.

4.6.2. Diastereomeric ketals 15 and 16 from methyl (1*R,2*R**,6*S**,7*R**)-8-oxotricyclo[5.4.0.0^{2,6}]undecane-1-carboxylate 14* and (*R*,*R*)-butane-2,3-diol**. A solution of a racemic mixture of undecane **14***[18] (0.040 g, 0.18 mmol), p-toluenesulfonic acid monohydrate

(0.004 g, 0.02 mmol) and *R*,*R*-2,3-butanediol (0.040 g, 0.44 mmol) in toluene (7.0 mL) was heated under reflux for 6 h using a Dean–Stark apparatus. The reaction was monitored using TLC (60% EtOAc/hexanes) until completion. The reaction mixture was cooled to rt and quenched with saturated aqueous Na_2CO_3 (3 mL), then washed with H_2O (2×). The aqueous layer was extracted (3×) with CH_2Cl_2, the organic layers were combined, dried with $MgSO_4$ and concentrated in vacuo. The residue was purified using FC (10–20% EtOAc/hexanes) yielding a mixture of diastereomeric ketals **15** and **16** (0.050 g, 93%). (**15**) TLC (50% EtOAc/hexanes) $R_f = 0.66$; spectral data reported above. (**16**) TLC (50% EtOAc/hexanes) $R_f = 0.64$; ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.3 (-$\underline{C}O_2Me$), 108.5 (C-8), 78.3, 78.0 (O-$\underline{C}H(CH_3)$-$\underline{C}H(CH_3)$-O), 51.4 (-O$\underline{C}H_3$), 47.2 (C-7), 47.2 (C-1), 44.7 (C-2), 37.4 (C-6), 32.4 (C-9), 32.2 (C-3), 30.9 (C-5), 28.6 (C-4), 26.1 (C-11), 19.1 (C-10), 17.2 (-C$\underline{C}H_3$), 16.7 (-C$\underline{C}H_3$).

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