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Synthesis of Functionalized Bicyclo[3.2.0]heptanes – a Study of the [2+2] Photocycloaddition Reactions of 4-Hydroxycyclopent-2-enone Derivatives

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A selection of 4-hydroxycyclopent-2-enone derivatives were prepared in enantiomerically pure form, and their photochemical [2+2] cycloaddition reactions with a variety of alkenes were studied, with a view to providing diversely functionalized bicyclo[3.2.0]heptanes. Intermolecular reactions provided the target structures in reasonable yields as a mixture of *exo* and *endo* adducts, in proportions which varied very little as a function of the steric bulk of the reactants or the reaction conditions. The system was suitably adapted for an intramolecular reaction, which provided a single, stereochemically pure product, the convenient precursor of a rigid, concave, trioxygenated skeleton.

Introduction

The bicyclo[3.2.0]heptane skeleton (Figure 1) attracts considerable interest in organic chemistry. The structural system is a core feature in a range of natural products[1] and some therapeutic agents,[2,3] and the inherent ring strain provides the driving force for a diversity of ring-expansion[4,5] or skeletal isomerization reactions,[6] leading to other cyclic or bicyclic systems. Various synthetic approaches for the construction of bicyclo[3.2.0]heptanes have been established, and in a good number of cases, they proceed with a significant degree of stereoselectivity. Starting from acyclic precursors, intramolecular [2+2] cycloadditions have been described under a variety of conditions: copper(I)-catalyzed photocycloaddition of nonconjugated 1,6-heptadienes,[7] Lewis-acid-catalyzed thermal cycloaddition,[8] gold(I)-catalyzed cycloaddition of allene–alkenes,[9] and thermal cyclization of ketene–alkenes,[10] keteneiminium–alkenes,[5c,11] and ketene–allenes.[12] The photochemical,[13] electrochemical,[14] and cobalt-catalyzed[15] intramolecular cycloadditions of bis(enones) have also been described, as have gold(I)-catalyzed cycloisomerizations of enynes.[6b] Two-component construction strategies are also known, involving Lewis-acid-catalyzed intermolecular [2+2] cycloadditions between appropriately functionalized cyclopentenes and alkenes[6c,16] or alkynes.[17] A number of other approaches have been investigated.[18]

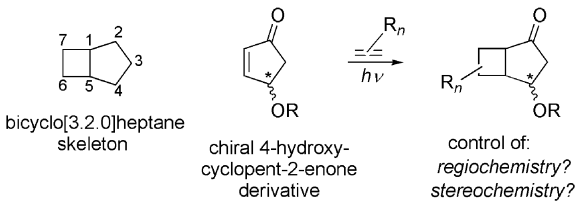

Figure 1. Target bicyclic skeleton and photochemical approach to its construction.

In principle, one of the most attractive entries into bicyclo[3.2.0]heptanes is the photochemical [2+2] cycloaddition between a cyclopent-2-enone and an alkene.[19] Intramolecular reactions generally proceed with good regio- and stereochemical control, but selectivity is rather more difficult to achieve in intermolecular versions. Several applications of intermolecular [2+2] photochemical cycloaddition reactions have been described using cyclopent-2-enones and asymmetrical alkene partners.[20] Some studies have included 2- and 3-substituted cyclopent-2-enones,[21] but work on 4-substituted derivatives, and in particular the chiral compound 4-hydroxycyclopent-2-enone and derivatives thereof, is much more scarce (Figure 1). This seemed rather curious, since these materials have been otherwise widely employed in synthesis,[22] particularly in the preparation of prostaglandins.[23] Indeed, some synthetically useful [4+2][24] and [3+2][25] cycloadditions as well as cyclopropanations[26] have been described for this cyclic enone. In contrast, the rare literature on photochemical [2+2] cycloadditions involving these compounds deals only with acetylene,[27] allene,[28] and a small selection of vinyl acetates[29] as intermolecular olefin partners, whereas a very limited number of intramolecular cases have been examined.[6f,30,31] No studies have hitherto been described concerning the scope of photochemical reactivity of the 4-oxycyclopentenones. Given their privileged status as building blocks in organic synthesis, we undertook an investigation of the preparative utility of their [2+2] photocycloaddition reactions

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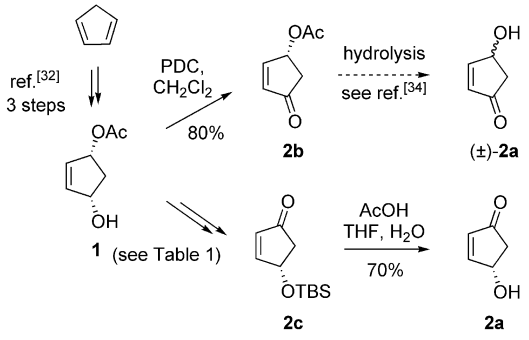
with a view to the elaboration of new diversely functionalized bicyclo[3.2.0]heptanes. The results of these studies are presented and discussed in this paper.

Results and Discussion

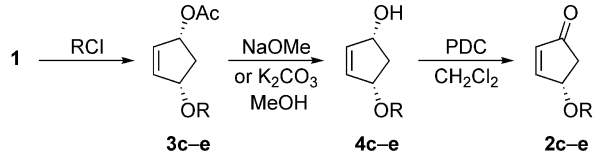
We first prepared 4-hydroxycyclopenten-2-one (**2a**) and a selection of *O*-functionalized derivatives in enantiomerically pure form. We prepared the (+)-(1*R*,3*S*) antipode of cyclopent-2-ene-1,3-diol monoacetate (**1**) according to the literature[32] in >99% *ee* (Scheme 1) and oxidized it smoothly to (*R*)-4-acetoxycyclopenten-2-one (**2b**) using PDC.[33] However, as anticipated,[34] the hydrolytic conversion of **2b** into the parent alcohol **2a** was complicated by the loss of enantiomeric integrity.



Scheme 1. Approaches for the synthesis of 4-hydroxycyclopent-2-enone (**2a**) in enantiomerically pure form.

We adopted a slightly longer but more reliable approach (Table 1). Using adaptations of literature procedures, we functionalized the hydroxy group of **1** as required by applying the appropriate electrophilic halide to give **3c**–**e** and then removed the acetate under basic conditions to provide **4c**–**e**, from which we obtained the target derivatives **2c**–**e** with an (*S*) configuration by PDC oxidation. These reactions all proceeded smoothly and in good yield, and we verified the product enones as having >99% *ee*. Finally, we obtained the (*S*) enantiomer of the parent alcohol **2a** by the mildly acidic cleavage of silyl ether **2c** (Scheme 1).

Table 1. Preparation of enantiomerically pure derivatives **2**.

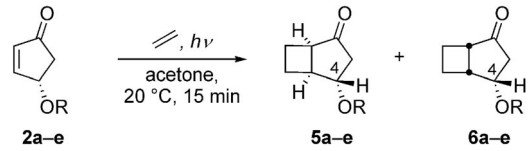


Entry	Derivative	RCl	Yield **3** [%]	Yield **4** [%]	Yield **2** [%]
1	**c**	TBSCl	98	98[a]	96
2	**d**	*t*BuCOCl	80	77[b]	96
3	**e**	MOMCl	78	83[a]	79

[a] Base used for hydrolysis: NaOMe. [b] Base used for hydrolysis: K_2CO_3.

With the substrates **2a**–**e** in hand, we began our exploration of the photochemical [2+2] photocycloaddition reactions. We designed the first series of experiments to establish the impact of the nature and the steric bulk of the *O*-bound group on the yield and diastereoselectivity of the reaction. One of the most challenging alkene partners (in terms of diastereoselectivity) is ethene, due to its small size. We carried out the [2+2] photocycloaddition reactions on each of the cyclopentenones **2a**–**e** in turn, using a medium-pressure Hg lamp (400 W) in a water-cooled immersion reactor fitted with a Pyrex filter. We allowed the substrates to react at 5 mM, and acetone served as both solvent and photosensitizer under these conditions (Table 2).

Table 2. Photochemical [2+2] cycloadditions of ethene with (*S*)-4-hydroxycyclopent-2-enone derivatives **2a**–**e**.



Entry	Enone **2**	R	Yield **5** + **6** [%]	Ratio **5**/**6**[a]
1	**2a**	H	49	70:30
2	**2b**[b]	Ac	43	63:37
3	**2c**	TBS	50	68:32
4	**2d**	*t*BuCO	49	60:40
5	**2e**	MOM	48	70:30

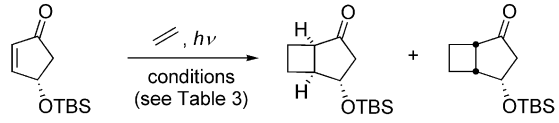
[a] Ratios were determined by GC analysis of the crude reaction products. [b] The (*R*) enantiomer was used.

In all cases, the starting material was consumed (>90%) within only 15 min. We stopped irradiating after this time, and isolated the cyclobutane adducts by chromatography after evaporation of the solvent. We obtained the expected bicyclo[3.2.0]heptanes in reasonable and fairly uniform yields (approximately 50%), exclusively with a *cis* ring junction and as a mixture of *exo* and *endo* stereoisomers. We easily distinguished these two isomeric forms in each case, since the ^{1}H NMR spectrum of one isomer (invariably the major component) showed a clean doublet (J = 4.8–6.8 Hz) at δ = 4.20–5.20 ppm for 4-H, whereas this proton appeared in the same chemical shift range as a more complex signal in the spectrum of the other (minor) isomer. We tentatively designated the major isomer as *exo* (**5a**–**e**) and the minor isomer as *endo* (**6a**–**e**) in each case, on the basis of steric arguments; we obtained subsequent evidence conclusively in support of this attribution (vide infra). The general selectivity trend was rather disappointing, since the *exo*/*endo* diastereoselectivity ratio (*dr*) remained around 70:30 throughout the series. The bulky *O*-TBS substituent of **2c** induced a *dr* which was comparable with that observed for the *O*-unsubstituted substrate **2a**, whereas the pivaloate **2d** provided no more selectivity than the diminutive acetate **2b**. Interestingly, in the only previous comparative study of **2a** and a few of its *O*-functionalized derivatives, Sydnes and co-workers reported that the unsensitized [2+2] photocy-

cloadditions of these compounds with allene generally proceeded with low *dr* but with a slight preference for the formation of the *endo* isomer.[28]

We next varied the experimental conditions, using the TBS ether derivative **2c** as the standard substrate. The results are presented in Table 3, and several trends emerge. First, using acetone as the standard solvent, we observed no temperature or concentration effects (Table 3, Entries 1–3). We then examined different solvents, with appropriate adaptation of the reaction time to provide for >90% consumption of **2c**. These sensitized reactions were slower than the reaction run in acetone, requiring up to 50 min in the cases of CH_2Cl_2 or acetonitrile (Table 3, Entries 4 and 5) to achieve near completion (conversion >90%), by which time other products had begun to appear (detected by GC analysis). Isolated product yields remained similar to those observed in acetone. The consumption of **2c** was somewhat faster in methanol or hexane, requiring around 30 min, but we observed more significant amounts of secondary products in these cases, resulting in lower isolated yields of the target bicyclic materials (Table 3, Entries 6 and 7). Overall, acetone proved to be the most convenient solvent, but we note that the *exo*/*endo* ratio remained remarkably uniform, whatever the nature of the solvent. In their study of the [2+2] photocycloaddition of **2c** with allene, Sydnes and coworkers noted a solvent effect, with higher product yields being obtained in less polar solvents. This trend was inverted for **2a**, which gave a higher yield in more polar solvents.[28]

Table 3. [2+2] Photocycloaddition reaction of cyclopentenone **2c** with ethene.[a]



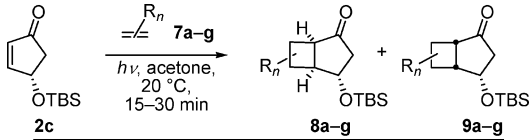
2c **5c** **6c**

Entry	Solvent	Time [min]	Sensitizer [0.1 equiv.]	Yield **5c** + **6c** [%]	Ratio **5c**/**6c**[b]
1	acetone	15	[c]	50	68:32
2	acetone	15[d]	[c]	40	71:29
3	acetone	15[e]	[c]	48	68:32
4	CH_2Cl_2	50	PhCOMe	41	70:30
5	MeCN	50	PhCOMe	46	68:32
6	MeOH	35	PhCOMe	13	68:32
7	hexane	25	PhCOMe	18	69:31

[a] 20 °C, 5 mM enone solution, Pyrex filter, unless stated otherwise. [b] Ratios were determined by GC analysis of the crude reaction products. [c] The solvent served as a sensitizer. [d] Reaction carried out at –30 °C. [e] The enone concentration was 1 mM.

We then turned our attention to photocycloaddition reactions involving more elaborate alkene partners, with a view to obtaining bicyclo[3.2.0]heptanes substituted on both the four- and five-membered rings. We again selected silyl ether **2c** as the representative cyclopentenone, and studied a range of diversely substituted alkenes **7a**–**g** under standard conditions (5 mM **2c** in acetone as solvent/sensitizer, excess alkene, 15–30 min irradiation, room temp., Pyrex). Although conversion was not always complete, longer reaction times tended to produce more complex mixtures (by GC analysis) without increasing the yield of the desired bicyclo[3.2.0]heptanes. In general, the yields of these products were comparable with those of the reaction involving ethene. We performed the analysis of isomeric mixtures on crude material using NMR and GC techniques, but preparative chromatographic separation was generally not convenient. The results are summarized in Table 4.

Table 4. [2+2] Photocycloaddition reaction of cyclopentenone **2c** with alkenes **7a**–**g**.



2c **8a–g** **9a–g**

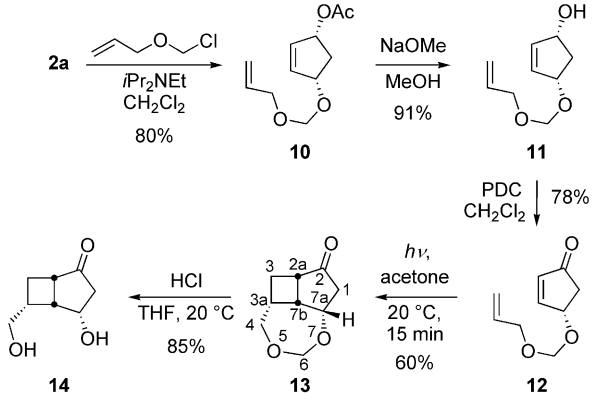
	Alkene **7a**–**g**	Time [min]	Conversion [%]	Yield **8** + **9** [%]	Ratio **8**/**9**[a]
a		15	90	45	60:40
b		15	77	41	53:47
c		15	80	41	54:46
d	Cl Cl	30	85	49	67:33[b]
e	O O	30	69	33	[c]
f	OMe OMe	30	77	40	73:27
g		30	75	38	[d]

[a] The *exo*/*endo* ratios were determined for the crude reaction products by GC analysis or from ^{1}H NMR spectra. [b] Expressed in terms of quantity of material isolated after chromatography; the *exo* component (**8d**) consisted of two stereoisomers (78:22) with undetermined configurations at the chlorine-bearing carbon atoms. [c] Four unidentified stereoisomers were observed in a ratio of 47:29:18:6. [d] Four unidentified stereoisomers were observed in a ratio of 33:25:22:20.

The completely symmetrical alkene components, tetramethylethylene (**7a**) and acetylene (**7b**), gave yields and *exo*/*endo* ratios comparable to those observed above for ethene. The results obtained with **7b** are comparable to those in the literature.[27] We were disappointed by the lack of improvement in the *dr* with the sterically hindered **7a**. We obtained only two adducts with cyclopentene (**7c**). The *exo*/*endo* ratio remained near parity, which meant we obtained isomers **8c** and **9c** in a single form, which we propose to be *cis*-*anti*-*cis* on the basis of steric and geometric arguments. This encouraging development was not sustained with other symmetrical alkenes, however. 1,2-Dichloroethene (**7d**) furnished three stereoisomeric adducts, in which the possible *cis*/*trans* isomerization of the chlorine substituents[31b,35] we could neither verify nor rule out due to the intractable nature of the product mixture. 2,3-Dihydro-2,4-dioxine (**7e**) also provided a mixture of four isomeric products in which we could only evaluate the isomeric ratio (but not the isomer identities). Finally, we tested two nonsymmetrical alkene partners, 1,1-dimethoxyethylene (**7f**) and isobutene (**7g**). The former, with a strong electronic effect,

produced only the head-to-tail regioisomer with a slightly improved *exo*/*endo* ratio, but the latter yielded four isomers whose identity was difficult to assess.

The intermolecular cycloadditions studied up to this point had provided a diversity of bicyclo[3.2.0]heptanes in acceptable yields, but the low selectivities limit the potential utility in preparative work, which requires single-stereoisomer materials. Therefore, we decided to investigate the reaction in an intramolecular mode. We anticipated that the alkene moiety could be introduced conveniently as an allyl alcohol derivative and attached to the core 4-hydroxycyclopenten-2-one by an acetal linkage (Scheme 2). This should allow for the facile liberation of the hydroxy groups after the cycloaddition.[36] We prepared the appropriate target substrate **12** as follows. Treatment of **2a** with allyl chloromethyl ether[37] gave acetal **10** in 80% yield. Basic hydrolysis liberated alcohol **11**, which we oxidized with PDC to give **12** in 57% yield over 3 steps. The irradiation of **12** in acetone for 15 min resulted in the consumption of all the stating material and the formation of a single new product (by GC analysis). We isolated this material in 60% yield and, from NMR spectral analysis, deduced it to be the tricyclic adduct **13**. A single-crystal X-ray diffraction analysis provided confirmation of this structure (Figure 2).[38] The ^{1}H NMR spectrum of **13**, with its imposed *endo* configuration, showed a complex 7a-H signal (apparently a tt) at δ = 4.58 ppm. This characteristic signal provided confirmation that the minor components in the **5/6** mixtures described above (Table 1) were the *endo* isomers. Finally, the careful acid hydrolysis of **13** furnished the enantiomerically pure, highly functionalized, dihydroxy ketone **14**, without skeletal rearrangement (Scheme 2).



Scheme 2. Intramolecular mode of the reaction providing a single product.

We note that the final product **14** is formally a [2+2] adduct from allyl alcohol and enone **2a**. In the intermolecular mode, allyl alcohol gives notoriously poor regio- and stereoselectivities in photocycloadditions with related cyclopentenones;[39] the isolation of one single isomer in this work underlines the usefulness of the temporary tether approach for selectivity control.

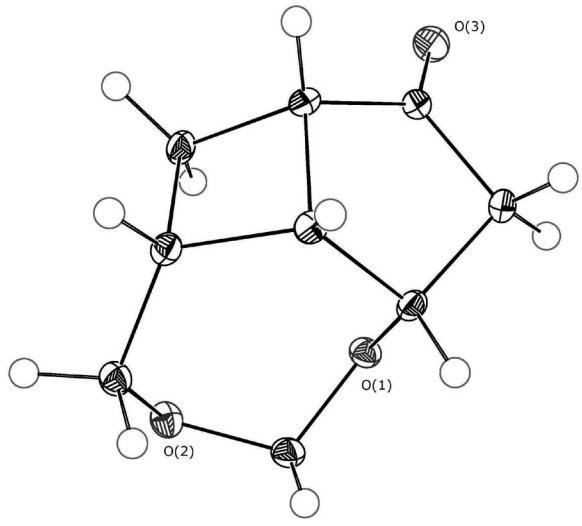


Figure 2. Crystal structure of tricyclic acetal **13**. Displacement ellipsoids are drawn at the 50% probability level.

Conclusions

We have prepared a range of new, highly functionalized bicyclo[3.2.0]heptanes from chiral nonracemic 4-hydroxycyclopentenone derivatives. The scope of the intermolecular [2+2] photocycloaddition reaction is quite large, but the stereoselectivity is low. Changing to the intramolecular mode allows complete control of all selectivity aspects and furnishes a rigid, concave, trioxygenated manifold **14**. Such materials are of interest in the context of chiral bidentate ligands[5b] and are potential candidates for controlled ring-rearrangement or -enlargement reactions. Given the relative simplicity of the procedures, the photochemical [2+2] assembly of complex bicyclo[3.2.0]heptanes should retain interest in the future. Studies of the synthetic applications and reactivity of **14** and its derivatives is currently underway in our laboratory.

Experimental Section

General Remarks: Melting points (uncorrected) were measured with a Büchi B-545 apparatus. Optical rotations were measured with a Perkin–Elmer 241 polarimeter. Fourier transform IR spectra were recorded with a Perkin–Elmer Spectrum One spectrophotometer. ^{1}H NMR spectra were recorded with Bruker AM 300 (300 MHz) or AV 360 (360 MHz) instruments; chemical shifts are expressed with respect to residual protonated solvent (δ = 7.27 ppm for $CHCl_3$), which served as an internal standard. ^{13}C NMR spectra were recorded with a Bruker AV 360 (90 MHz) instrument; chemical shifts are expressed with respect to the deuterated solvent (δ = 77.0 ppm for $CDCl_3$). DEPT-135 pulses were used for the determination of ^{13}C NMR signal types. Diastereomeric ratios (*dr*) were determined by GC with a Fisons GC 8000 Top instrument fitted with a dimethylpolysiloxane column (12 m × 0.22 mm × 0.2 μm) or from ^{1}H NMR integration data. Enantiomeric excesses (*ee*s) were determined with the GC instrument described above, fitted with a β-cyclodextrin DM column (40 m × 0.25 mm × 0.25 μm). Chemical-ionization mass spectra (MS) were recorded with a Nermag R-10 instrument by using ammonia as the vector

gas. High-resolution mass spectra (HRMS) were recorded with a Finningan MAT 95S in positive electrospray mode. Elemental analyses were performed by the Microanalysis Service, ICSN-CNRS, Gif-sur-Yvette, France. Reaction solvents were dried according to standard procedures prior to use. All reactions requiring anhydrous conditions were performed under argon. Acetates **1**,[32] **3c**,[40] **3d**,[41] and **3e**,[42] and the alcohols **4c**[43] and **4e**[44] were prepared according to the literature, and their spectroscopic data are comparable to those previously reported.

(–)-(1*S*,4*R*)-4-Hydroxy-2-cyclopenten-1-yl Pivalate (4d): To a solution of diester **3d** (560 mg, 2.5 mmol) in MeOH (5 mL) under argon, was added K_2CO_3 (342 mg, 2.5 mmol). The solution was stirred at room temp. for 20 min and then quenched with a mixture of aq. HCl (5%, 12 mL) and Et_2O (12 mL). The mixture was stirred until the aq. layer was clear. This layer was then extracted with Et_2O (2 × 10 mL), and the combined organic phases were dried with $MgSO_4$ and filtered. The solvents were evaporated, and the residue was purified by flash chromatography (Et_2O/EtOAc, 80:20) to give **4d** as a colorless oil (350 mg, 77%). $[\alpha]_D^{23} = -59.5$ (c = 2.30, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.11 (ddd, J = 5.6, J = 1.9, J = 1.3 Hz, 1 H, 2-H), 5.98 (ddd, J = 5.6, J = 2.0, J = 1.1 Hz, 1 H, 3-H), 5.51–5.45 (m, 1 H, 4-H), 4.69–4.78 (m, 1 H, 1-H), 2.83 (dt, J = 14.6, J = 7.3 Hz, 1 H, 5-H), 1.76 (br. s, 1 H, OH), 1.61 (dt, J = 14.5, J = 4.0 Hz, 1 H, 5-H), 1.20 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 178.1, 138.1, 131.6, 76.7, 73.8, 40.0, 38.1, 26.7 ppm. IR (neat): $\tilde{\nu}$ = 3425, 2976, 1726, 1708, 1284, 1160 cm^{-1}. MS: m/z = 202 [M + NH_4]$^+$. $C_{10}H_{16}O_3$ (184.23): calcd. C 65.19, H 8.75; found C 64.92, H 8.60.

General Method for the Preparation of Cyclopentenones from Their Alcohol Precursors: To a solution of the given alcohol **1** or **4c**–**e** (1 mmol) in CH_2Cl_2 (5 mL), PDC (1.5 mmol) was added under argon. The solution was stirred at room temp. for 16 h and then filtered, the solid was washed with CH_2Cl_2 (2 × 2 mL), and the combined organic phases were dried with $MgSO_4$, filtered, and concentrated. The crude residue was then purified by flash chromatography on silica gel to give the expected enones **2b**–**e**.

(+)-(4*R*)-4-Acetoxycyclopent-2-enone (2b):[33] Eluent: Et_2O/EtOAc (80:20). Colorless oil. Yield: 80%. $[\alpha]_D^{20} = +95$ (c = 0.1, $CHCl_3$).

(–)-(4*S*)-4-(*tert*-Butyldimethylsiloxy)cyclopent-2-enol (2c):[33] Eluent: hexanes/EtOAc (90:10). Colorless oil. Yield: 96%. $[\alpha]_D^{20} = -68$ (c = 0.94, MeOH).

(–)-(1*S*)-4-Oxo-2-cyclopenten-1-yl Pivalate (2d):[24c] Eluent: Et_2O/EtOAc (80:20). Colorless oil. Yield: 96%. $[\alpha]_D^{20} = -111$ (c = 1.0, MeOH).

(–)-(4*S*)-4-(Methoxymethoxy)cyclopent-2-enone (2e): Eluent: hexanes/Et_2O (50:50). Colorless oil. Yield: 79%. $[\alpha]_D^{20} = -16$ (c = 1.0, CH_2Cl_2). ^{1}H NMR (360 MHz, $CDCl_3$): δ = 7.61 (dd, J = 5.7, J = 2.3 Hz, 1 H, 3-H), 6.26 (d, J = 5.7 Hz, 1 H, 2-H), 4.89–4.85 (m, 1 H, 4-H), 4.80–4.72 (m, 2 H, OCH_2O), 3.42 (s, 3 H, OCH_3), 2.74 (dd, J = 18.4, J = 6.1 Hz, 1 H, 5-H), 2.33 (dd, J = 18.4, J = 2.5 Hz, 1 H, 5-H) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 205.4, 161.4, 135.0, 95.7, 75.1, 55.0, 41.5 ppm. IR (neat): $\tilde{\nu}$ = 3075, 2949, 2893, 1721 cm^{-1}. MS: m/z = 160 [M + NH_4]$^+$. $C_7H_{10}O_3$ (142.15): calcd. C 59.14, H 7.09; found C 58.86, H 7.01.

General Method for the Irradiation of Cyclopentenones in the Presence of a Gaseous Alkene Partner (Method A): A solution of the enone **2** (0.90 mmol) in acetone (180 mL) was presaturated with the gaseous alkene. After 15 min, the mixture was irradiated with a 400 W medium-pressure mercury vapor lamp fitted with a Pyrex filter for 15 min; the passage of a slow stream of alkene gas was maintained. At the end of the reaction time, the lamp was extinguished, and the reaction mixture was concentrated. The residue was purified by flash chromatography to provide the bicyclic products.

General Method for the Irradiation of Cyclopentenones in the Presence of a Nongaseous Alkene Partner (Method B): A solution of the enone **2c** (1 mmol) and the given alkene **7** (10 mmol) in acetone (200 mL) was saturated with argon for 15 min and then irradiated with a 400 W medium-pressure mercury vapor lamp fitted with a Pyrex filter for 15 or 30 min (see Table 4). At the end of the reaction time, the lamp was extinguished, and the reaction mixture was concentrated. The residue was purified by flash chromatography to give the polycyclic products.

(4*S*)-4-Hydroxybicyclo[3.2.0]heptan-2-one [*exo*-5a (1*R*,5*S*) and *endo*-6a (1*S*,5*R*)]: By using **2a** and ethene, according to Procedure A, flash chromatography (Et_2O/EtOAc, 95:5) gave an inseparable mixture of bicyclic products ***exo*-5a** and ***endo*-6a** as a colorless oil (49%; 70:30 *dr*, by ^{1}H NMR). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.56 (dd, J = 17.7, J = 7.7 Hz, 1 H, 4-H, major), 4.36 (d, J = 4.9 Hz, 1 H, 4-H, minor), 3.25–3.10 (m, 1 H, 1-H, minor), 3.10–2.60 (m, 5 H, major + minor), 2.60–2.00 (m, 3 H, major + minor), 1.95–1.65 (m, 4 H, major + minor) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 222.4 (major), 220.1 (minor), 73.4 (major), 69.4 (minor), 47.0 (minor), 45.6 (major), 43.8 (major), 44.3 (minor), 43.7 (major), 39.7 (minor), 22.4 (minor), 21.6 (major), 21.5 (major), 17.5 (minor) ppm. IR (neat): $\tilde{\nu}$ = 3422, 2948, 1732 cm^{-1}. MS: m/z = 144 [M + NH_4]$^+$. $C_7H_{10}O_2$ (126.15): calcd. C 66.65, H 7.99; found C 66.24, H 7.83.

(2*R*)-4-Oxobicyclo[3.2.0]hept-2-yl Acetate [*exo*-5b (1*R*,5*S*) and *endo*-6b (1*S*,5*R*)]: By using **2b** and ethene, according to Procedure A, flash chromatography (hexanes/Et_2O, 70:30) gave an inseparable mixture of bicyclic products ***exo*-5b** and ***endo*-6b** as a colorless oil (43%; 63:37 *dr*, by ^{1}H NMR). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.29 (dt, J = 9.0, J = 7.4 Hz, 1 H, 4-H, minor), 5.17 (d, J = 5.7 Hz, 1 H, 4-H, major), 3.40–3.28 (m, 1 H, 3-H, minor), 3.10–2.70 (m, 3 H, major + minor), 2.60–2.30 (m, 3 H, major + minor), 2.07 (s, 3 H, CH_3, minor), 2.01 (s, 3 H, CH_3, major), 1.95–1.80 (m, 2 H, major + minor) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 219.0 (major), 216.8 (minor), 170.3 (minor), 170.1 (major), 75.7 (major), 71.2 (minor), 45.8 (minor), 43.9 (major), 42.8 (major), 41.8 (minor), 40.8 (major), 37.6 (minor), 22.1 (minor), 21.7 (major), 21.6 (major), 20.8 (major), 20.6 (minor), 18.2 (minor) ppm. IR (neat): $\tilde{\nu}$ = 2948, 1753 cm^{-1}. MS: m/z = 186 [M + NH_4]$^+$. $C_9H_{12}O_3$ (168.19): calcd. C 64.27, H 7.19; found C 63.94, H 7.09.

(4*S*)-4-(*tert*-Butyldimethylsilyloxy)bicyclo[3.2.0]heptan-2-one [*exo*-5c (1*R*,5*S*) and *endo*-6c (1*S*,5*R*)]: By using **2c** and ethene according to Procedure A, flash chromatography (hexanes/Et_2O, 90:10) gave an inseparable mixture of bicyclic products ***exo*-5c** and ***endo*-6c** as a colorless oil (50%; 68:32 *dr*, by GC). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.47 (dt, J = 9.9, J = 7.5 Hz, 1 H, 4-H, major), 4.25 (dt, J = 4.8, J = 1.0 Hz, 1 H, 4-H, minor), 3.10–2.70 (m, 6 H, major + minor), 2.60–2.20 (m, 6 H, major + minor), 2.20–1.70 (m, 4 H, major + minor), 0.89 (s, 9 H, Si*t*Bu, major), 0.86 (s, 9 H, Si*t*Bu, minor), 0.06 (s, 6 H, $SiMe_2$, minor), 0.05 (s, 6 H, $SiMe_2$, major) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 220.9 (major), 218.5 (minor), 74.0 (major), 69.8 (minor), 46.4 (minor), 46.2 (major), 45.1 (minor), 44.4 (major), 43.9 (major), 40.3 (minor), 25.6 (major + minor), 22.4 (minor), 21.5 (2 C major + minor), 17.9 (minor), 17.6 (major), –4.8 (major + minor), –4.9 (major + minor) ppm. IR (neat): $\tilde{\nu}$ = 2954, 1740 cm^{-1}. MS: m/z = 258 [M + NH_4]$^+$. HRMS: calcd. for $C_{13}H_{24}O_2SiNa$ 263.1443; found 263.1437.

(2*S*)-4-Oxobicyclo[3.2.0]hept-2-yl Pivalate [*exo*-5d (1*S*,5*R*) and *endo*-6d (1*R*,5*S*)]: By using **2d** and ethene, according to Pro-

cedure A, flash chromatography (CH_2Cl_2/MeOH, 98:2) gave an inseparable mixture of bicyclic products ***exo*-5d** and ***endo*-6d** as a colorless oil (49%; *dr* 60:40, by ^1H NMR). ^1H NMR (360 MHz, $CDCl_3$): δ = 5.21 (dd, *J* = 16.4, *J* = 8.5 Hz, 1 H, 4-H, minor), 5.17 (d, *J* = 5.6 Hz, 1 H, 4-H, major), 3.45–3.20 (m, 1 H, 1-H, minor), 3.15–2.96 (m, 2 H, 1-H, 3-H, major), 2.90–2.60 (m, 4 H, major + minor), 2.50–2.00 (m, 6 H, major + minor), 2.00–1.60 (m, 3 H, major + minor), 1.21 (s, 9 H, *t*Bu, minor), 1.00 (s, 9 H, *t*Bu, major) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 218.9 (major), 216.8 (minor), 177.5 (major + minor), 75.4 (major), 70.9 (minor), 45.9 (minor), 43.8 (major), 42.8 (major), 42.0 (minor), 40.9 (major), 37.7 (minor), 26.9 (minor), 26.8 (major), 23.1 (major), 22.3 (minor), 21.8 (major), 21.7 (major), 19.7 (minor), 18.1 (minor) ppm. IR (neat): $\tilde{\nu}$ = 2976, 1752 cm^{-1}. MS: *m*/*z* = 200 $[M + NH_4]^+$. $C_{11}H_{18}O_2$ (182.26): calcd. C 72.49, H 9.95; found C 72.13, H 9.86.

(4*S*)-4-(Methoxymethoxy)bicyclo[3.2.0]heptan-2-one [*exo*-5e (1*R*,5*S*) and *endo*-6e (1*S*,5*R*)]: By using **2e** and ethene, according to Procedure A, flash chromatography (hexanes/Et_2O, 60:40) gave an inseparable mixture of bicyclic products ***exo*-5e** and ***endo*-6e** as a colorless oil (48%; 70:30 *dr*, by ^1H NMR). ^1H NMR (360 MHz, $CDCl_3$): δ = 4.66 (d, *J* = 3.0 Hz, 1 H, OCH_2O, major), 4.64 (s, 2 H, OCH_2O, minor), 4.60 (d, *J* = 3.0 Hz, 1 H, OCH_2O, major), 4.35 (dt, *J* = 10.4, *J* = 7.9 Hz, 1 H, 4-H, minor), 4.21 (d, *J* = 5.4 Hz, 1 H, 4-H, major), 3.38 (s, 3 H, OCH_3, minor), 3.35 (s, 3 H, OCH_3, major), 3.30–3.20 (m, 1 H, 1-H, minor), 3.17–3.07 (m, 1 H, 1-H, major), 2.96 (dd, *J* = 18.4, *J* = 5.4 Hz, 1 H, 3-H, major), 2.90–2.73 (m, 2 H, major + minor), 2.68 (ddd, *J* = 18.0, *J* = 8.2, *J* = 1.2 Hz, 1 H, 3-H, minor), 2.60–2.10 (m, 6 H, major + minor), 1.95–1.75 (m, 4 H, major + minor) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 220.3 (major), 217.9 (minor), 95.6 (minor), 94.5 (major), 77.9 (major), 74.4 (minor), 55.4 (major + minor), 46.4 (minor), 43.9 (major), 43.5 (major), 42.5 (minor), 41.1 (major), 38.4 (minor), 22.4 (minor), 21.8 (2C, major), 18.2 (minor) ppm. IR (neat): $\tilde{\nu}$ = 2947, 1736 cm^{-1}. MS: *m*/*z* = 171 $[M + H]^+$. HRMS: calcd. for $C_9H_{14}O_3Na$ 193.0841; found 193.0845.

(4*S*)-4-(*tert*-Butyldimethylsilyloxy)-6,6,7,7-tetramethylbicyclo[3.2.0]-heptan-2-one [*exo*-8a (1*R*,5*S*) and *endo*-9a (1*S*,5*R*)]: By using **7a**, according to Procedure B, flash chromatography (CH_2Cl_2/MeOH, 9:1) gave two separable bicyclic products (60:40 *dr*, by ^1H NMR) as a colorless oil for ***exo*-8a** (27%) and as colorless needles for ***endo*-9a** (18%). ***exo*-8a:** $[\alpha]_D^{20}$ = +168 (*c* = 1.05, $CHCl_3$). ^1H NMR (360 MHz, $CDCl_3$): δ = 4.58 (dt, *J* = 9.6, *J* = 7.9 Hz, 1 H, 4-H), 2.74 (t, *J* = 7.6 Hz, 1 H, 3-H), 2.71 (dd, *J* = 19.1, *J* = 10.1 Hz, 1 H, 1-H), 2.58 (ddd, *J* = 19.6, *J* = 9.4, *J* = 1.3 Hz, 1 H, 5-H), 2.31 (d, *J* = 7.9 Hz, 1 H, 3-H), 1.25 (s, 3 H, CH_3), 1.17 (s, 3 H, CH_3), 1.10 (s, 3 H, CH_3), 0.93 (s, 3 H, CH_3), 0.91 (s, 9 H, Si*t*Bu), 0.08 (s, 3 H, SiMe), 0.06 (s, 3 H, SiMe) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 218.5, 71.3, 56.0, 48.5, 48.1, 41.7, 39.4, 27.7, 27.6, 25.8, 22.6, 20.2, 17.9, –4.9 ppm. IR (neat): $\tilde{\nu}$ = 2956, 1735 cm^{-1}. HRMS: calcd. for $C_{17}H_{32}O_2SiNa$ 319.2069; found 319.2075. ***endo*-9a:** M.p. 84 °C. $[\alpha]_D^{20}$ = –145 (*c* = 1.05, $CHCl_3$). ^1H NMR (360 MHz, $CDCl_3$): δ = 4.52–4.46 (m, 1 H, 4-H), 2.78 (dd, *J* = 19.5, *J* = 6.5 Hz, 1 H, 3-H), 2.62–2.55 (m, 1 H, 1-H), 2.46 (d, *J* = 8.3 Hz, 1 H, 5-H), 2.39–2.29 (m, 1 H, 3-H), 1.13 (s, 3 H, CH_3), 1.12 (s, 3 H, CH_3), 0.96 (s, 3 H, CH_3), 0.87 (s, 12 H, CH_3, Si*t*Bu), 0.06 (s, 3 H, SiMe), 0.05 (s, 3 H, SiMe) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 220.1, 70.1, 53.8, 53.1, 51.4, 41.7, 39.6, 27.2, 27.0, 25.8, 21.1, 20.8, 17.9, –4.7 ppm. IR (neat): $\tilde{\nu}$ = 2954, 1717 cm^{-1}. HRMS: calcd. for $C_{17}H_{32}O_2SiNa$ 319.2069; found 319.2074.

(4*S*)-4-(*tert*-Butyldimethylsilyloxy)bicyclo[3.2.0]hept-6-en-2-one [*exo*-8b (1*R*,5*S*) and *endo*-9b (1*S*,5*R*)]: By using **7b**, according to Procedure A, flash chromatography (hexanes/Et_2O, 95:5) gave an inseparable mixture of the bicyclic ***exo*-8b** and ***endo*-9b** as a colorless solid (41%; 53:47 *dr*, by ^1H NMR). ^1H NMR (360 MHz, $CDCl_3$): δ = 6.46 (d, *J* = 2.5 Hz, 1 H, 6-H or 7-H, minor), 6.40 (d, *J* = 2.5 Hz, 1 H, 6-H or 7-H, major), 6.25 (d, *J* = 2.5 Hz, 1 H, 6-H or 7-H, minor), 6.20 (d, *J* = 2.5 Hz, 1 H, 6-H or 7-H, major), 4.40–4.30 (m, 2 H, 4-H, major + minor), 3.50 (dd, *J* = 7.3, *J* = 2.9 Hz, 1 H, 1-H, minor), 3.38–3.30 (m, 2 H, 1-H, 5-H, major), 3.26–3.23 (m, 1 H, 5-H, minor), 3.21 (ddd, *J* = 15.5, *J* = 4.7, *J* = 0.7 Hz, 1 H, 3-H, major), 3.05 (ddd, *J* = 17.4, *J* = 10.0, *J* = 1.2 Hz, 1 H, 3-H, minor), 2.35 (ddd, *J* = 17.3, *J* = 7.8, *J* = 1.5 Hz, 1 H, 3-H, minor), 2.13–2.05 (m, 1 H, 3-H, major), 0.91 (s, 9 H, Si*t*Bu, major), 0.88 (s, 9 H, Si*t*Bu, minor), 0.10 (s, 3 H, SiMe, minor), 0.08 (s, 3 H, SiMe, major), 0.07 (s, 6 H, SiMe, major + minor) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 220.9 (major), 214.5 (minor), 141.8 (major), 141.2 (minor), 137.2 (minor), 131.8 (major), 68.1 (major), 66.1 (minor), 55.9 (minor), 53.9 (major), 53.7 (major), 49.0 (minor), 44.1 (major), 42.4 (minor), 25.6 (major + minor), 17.9 (major + minor), –4.8 (major + minor), –4.9 (major + minor) ppm. IR (neat): $\tilde{\nu}$ = 3053, 1741 cm^{-1}. HRMS: calcd. for $C_{13}H_{22}O_2SiNa$ 261.1287; found 261.1283.

(3*S*)-3-(*tert*-Butyldimethylsilyloxy)octahydrocyclopenta[3,4]cyclobuta-[1,2]cyclopenten-1(2*H*)-one [*exo*-8c (3a*S*,6b*R*) and *endo*-9c (3a*R*,6b*S*)]: By using **7c**, according to Procedure B, flash chromatography (hexanes/Et_2O, 95:5) gave two separate bicyclic products (54:46 *dr*, by ^1H NMR) as a colorless oil for ***exo*-8c** (22%) and as colorless needles for ***endo*-9c** (19%). ***exo*-8c:** $[\alpha]_D^{20}$ = +215 (*c* = 0.6, $CHCl_3$). ^1H NMR (360 MHz, $CDCl_3$): δ = 4.47 (dt, *J* = 11.1, *J* = 7.6 Hz, 1 H, 10-H), 3.12–3.03 (m, 1 H, 7-H), 2.80 (dd, *J* = 17.0, *J* = 11.0 Hz, 1 H, 9-H), 2.54–2.39 (m, 2 H, 6-H, 9-H), 2.34–2.24 (m, 1 H, 1-H), 2.22–2.12 (m, 1 H, 2-H), 1.92–1.54 (m, 6 H, 3-H, 4-H, 5-H), 0.91 (s, 9 H, Si*t*Bu), 0.07 (s, 3 H, SiMe), 0.07 (s, 3 H, SiMe) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 217.4, 70.0, 51.1, 44.8, 44.1, 41.7, 34.8, 33.2 (2 C), 25.7, 24.6, 18.0, –4.8 ppm. IR (neat): $\tilde{\nu}$ = 2953, 1740 cm^{-1}. HRMS: calcd. for $C_{16}H_{28}O_2SiNa$ 303.1756; found 303.1759. ***endo*-9c:** M.p. 45 °C. $[\alpha]_D^{20}$ = –129 (*c* = 1.0, $CHCl_3$). ^1H NMR (360 MHz, $CDCl_3$): δ = 4.30 (d, *J* = 4.6 Hz, 1 H, 10-H), 2.92 (dd, *J* = 17.2, *J* = 4.6 Hz, 1 H, 9-H), 2.52–2.42 (m, 2 H, 1-H, 7-H), 2.30–2.10 (m, 3 H, 2-H, 6-H, 9-H), 1.95–1.45 (m, 6 H, 3-H, 4-H, 5-H), 0.84 (s, 9 H, Si*t*Bu), 0.04 (s, 6 H, $SiMe_2$) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 220.0, 74.1, 48.5, 48.0, 45.9, 40.1, 39.4, 33.1, 32.9, 25.7, 24.6, 18.0, –4.8 ppm. IR (neat): $\tilde{\nu}$ = 2951, 1741 cm^{-1}. HRMS: calcd. for $C_{16}H_{28}O_2SiNa$ 303.1756; found 303.1754.

(4*S*)-4-(*tert*-Butyldimethylsilyloxy)-6,7-dichlorobicyclo[3.2.0]heptan-2-one [*exo*-8d (1*R*,5*S*) and *endo*-9d (1*S*,5*R*)]: By using **7d**, according to the general Procedure B, flash chromatography (hexanes/Et_2O, 90:10) provided two fractions. The first (minor) one, *endo*-**9d**, was obtained as a colorless oil (16%) and was a unique *anti* or *syn* diastereomer. The second (major) one, *exo*-**8d**, was obtained as colorless needles (33%) and was an inseparable mixture of stereoisomers at positions C-6 and C-7 (78:22 *dr*, by ^1H NMR). ***exo*-8d:** ^1H NMR (360 MHz, $CDCl_3$): δ = 4.79 (ddd, *J* = 6.5, *J* = 4.2, *J* = 2.5 Hz, 1 H, 4-H, major), 4.71 (ddd, *J* = 9.3, *J* = 6.5, *J* = 0.8 Hz, 1 H, 7-H, major), 4.56 (dd, *J* = 8.2, *J* = 6.8 Hz, 1 H, 4-H, minor), 4.50 (d, *J* = 5.0 Hz, 1 H, 7-H, minor), 4.14 (ddd, *J* = 6.4, *J* = 5.6, *J* = 1.1 Hz, 1 H, 6-H, major), 4.06 (ddd, *J* = 6.8, *J* = 5.8, *J* = 1.1 Hz, 1 H, 6-H, minor), 3.34–3.22 (m, 2 H, 3-H, major + minor), 3.13–3.06 (m, 1 H, 3-H, major), 3.01–2.97 (m, 1 H, 3-H, minor), 2.94 (dd, *J* = 18.4, *J* = 6.4 Hz, 1 H, 1-H, major), 2.74 (dd, *J* = 18.7, *J* = 4.8 Hz, 1 H, 1-H, minor), 2.48–2.35 (m, 2 H, 5-H, major + minor), 0.87 (s, 9 H, Si*t*Bu, major), 0.86 (s, 9 H, Si*t*Bu, minor), 0.11 (s, 6 H, SiMe, major + minor), 0.09 (s, 6 H, SiMe, major + minor) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 214.5 (minor), 211.4

(major), 71.0 (minor), 69.0 (major), 59.9 (major), 59.8 (major), 59.6 (minor), 56.4 (minor), 53.2 (major), 53.1 (minor), 48.5 (major), 47.6 (major + minor), 46.9 (minor), 25.6 (major + minor), 17.9 (major + minor), –4.8 (major + minor) ppm. HRMS: calcd. for $C_{13}H_{22}O_2Cl_2SiNa$ 331.0678; found 331.0664. ***endo*-9d:** $[\alpha]_D^{20}$ = +85 (c = 0.5, $CHCl_3$). ^1H NMR (360 MHz, $CDCl_3$): δ = 4.85 (ddd, J = 6.5, J = 5.3, J = 1.5 Hz, 1 H, 4-H), 4.62 (dd, J = 14.2, J = 7.1 Hz, 1 H, 7-H), 4.55 (ddd, J = 6.2, J = 3.3, J = 0.9 Hz, 1 H, 6-H), 3.42 (dd, J = 13.0, J = 7.7 Hz, 1 H, 3-H), 3.15–3.09 (m, 1 H, 1-H), 2.69 (ddd, J = 18.8, J = 7.7, J = 1.1 Hz, 1 H, 3-H), 2.52 (dd, J = 18.9, J = 6.4 Hz, 1 H, 5-H), 0.93 (s, 9 H, Si*t*Bu), 0.14 (s, 3 H, SiMe), 0.12 (s, 3 H, SiMe) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 211.8, 67.1, 57.7, 54.0 (2 C), 51.1, 47.4, 25.7, 18.0, –4.9 ppm. IR (neat): $\tilde{\nu}$ = 2952, 2929, 2857, 1740 cm^{-1}. HRMS: calcd. for $C_{13}H_{22}O_2Cl_2SiNa$ 331.0678; found 331.0680.

(7*S*)-7-(*tert*-Butyldimethylsilyloxy)octahydro-5*H*-cyclopenta[3,4]cyclobuta[1,2-*b*][1,4]dioxin-5-one [*exo*-8e (4b*S*,7a*R*) and *endo*-9e (4b*R*,7a*S*)]: By using **7e**, according to Procedure B, flash chromatography (hexanes/Et_2O, 50:50) gave a colorless oil, which was an inseparable mixture of four diastereomers of bicyclic products ***exo*-8e** and ***endo*-9e** (33%; 47:29:18:6 *dr*, by ^1H NMR). ^1H NMR (360 MHz, $CDCl_3$): δ = 4.69 (ddd, J = 7.2, J = 2.0, J = 1.4 Hz, 1 H, 7-H, minor a), 4.66 (dd, J = 2.6, J = 2.1 Hz, 1 H, 7-H, minor b), 4.62 (dd, J = 7.2, J = 2.6 Hz, 1 H, 7-H, major), 4.57 (dd, J = 4.9, J = 1.8 Hz, 1 H, 8-H or 9-H, minor a), 4.49 (ddd, J = 5.3, J = 5.2, J = 2.8 Hz, 1 H, 8-H or 9-H, minor b), 4.41 (ddd, J = 5.4, J = 2.9, J = 1.1 Hz, 1 H, 8-H or 9-H, major), 4.33 (ddd, J = 4.4, J = 4.3, J = 0.7 Hz, 1 H, 8-H or 9-H, major), 4.32–4.22 (m, 2 H, 8-H or 9-H, minor a + minor b), 3.97–3.77 (m, 6 H, 1-H, 2-H, major + minor a + minor b), 3.70–3.60 (m, 3 H, 4-H, major + minor a + minor b), 3.57–3.44 (m, 3 H, major + minor a + minor b), 3.38–3.20 (m, 4 H, major + minor a + minor b), 3.15–3.05 (m, 2 H, major + minor a or minor b), 2.73–2.65 (m, 1 H, major), 2.64 (dd, J = 8.3, J = 1.4 Hz, 1 H, minor b), 2.60 (ddd, J = 9.1, J = 1.5, J = 0.5 Hz, 1 H, minor a), 2.58 (dd, J = 7.0, J = 1.1 Hz, 1 H, minor b), 2.44 (ddd, J = 4.3, J = 1.0, J = 0.4 Hz, 1 H, major), 2.41–2.36 (m, 1 H, minor a), 0.91 (s, 9 H, Si*t*Bu, minor a), 0.90 (s, 9 H, Si*t*Bu, major), 0.87 (s, 9 H, Si*t*Bu, minor b), 0.09 (s, 6 H, $SiMe_2$, minor b), 0.08 (s, 6 H, $SiMe_2$, major), 0.07 (s, 6 H, $SiMe_2$, minor a) ppm. ^{13}C NMR NMR (90 MHz, $CDCl_3$): δ = 218.8 (minor a or minor b), 216.5 (minor a or minor b), 215.3 (major), 75.6 (minor a or minor b), 73.3 (minor a or minor b), 71.7 (major), 70.5 (major + minor a or minor b), 69.5 (minor a or minor b), 67.4 (major), 67.3 (minor a + minor b), 63.5 (minor a or minor b), 63.3 (minor a or minor b), 62.7 (major), 62.1 (major), 61.9 (minor a or minor b), 61.8 (minor a or minor b), 55.6 (minor a or b), 52.7 (minor a or minor b), 51.8 (minor a or minor b), 50.1 (major), 49.7 (major), 49.0 (minor a or minor b), 45.1 (minor a or b), 44.3 (major + minor a or minor b), 40.6 (minor a or minor b), 25.7 (minor a + minor b), 25.6 (major), 18.0 (minor a + minor b), 17.9 (major), –4.8 (minor a + minor b), –5.0 (major), –5.1 (minor a + minor b) ppm. IR (neat): $\tilde{\nu}$ = 2956, 1735 cm^{-1}. MS: m/z = 316 $[M + NH_4]^+$.

(4*S*)-4-(*tert*-Butyldimethylsilyloxy)-6,6-dimethoxybicyclo[3.2.0]heptan-2-one [*exo*-8f (1*R*,5*S*) and *endo*-9f (1*S*,5*R*)]: By using **7f**, according to Procedure B, flash chromatography (hexanes/EtOAc, 90:10) gave an inseparable mixture of the bicyclic ***exo*-8f** and ***endo*-9f** as a colorless oil (40%; 73:27 *dr*, by GC). For the ^1H NMR signals, only those of the major product could be interpreted. ^1H NMR (360 MHz, $CDCl_3$): δ = 4.46 (ddd, J = 10.8, J = 8.2, J = 7.0 Hz, 1 H, 4-H), 3.25 (s, 3 H, OMe), 3.15 (s, 3 H, OMe), 3.05 (t, J = 7.2 Hz, 1 H, 1-H), 2.98 (dd, J = 17.7, J = 10.9 Hz, 1 H, 3-H), 2.60–2.50 (m, 1 H, 5-H), 2.50–2.35 (m, 2 H, 3-H, 7-H), 2.30–2.23 (m, 1 H, 7-H), 0.90 (s, 9 H, Si*t*Bu), 0.07 (s, 6 H, $SiMe_2$) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 217.8 (major), 214.5 (minor), 141.2 (minor), 137.2 (minor), 103.1 (major), 69.4 (major), 66.1 (minor), 55.9 (minor), 52.2 (major), 49.2 (major), 49.0 (minor), 48.4 (major), 46.1 (major), 42.4 (minor), 39.0 (major), 35.5 (major), 25.7 (major), 25.6 (minor), 18.0 (major), 17.9 (minor), –4.9 (major + minor), –4.8 (minor), –4.6 (major) ppm. HRMS: calcd. for $C_{15}H_{28}O_4SiNa$ 323.1655; found 323.1670.

(4*S*)-4-(*tert*-Butyldimethylsilyloxy)-6,6-dimethylbicyclo[3.2.0]heptan-2-one [*exo*-8g (1*R*,5*S*) and *endo*-9g (1*S*,5*R*)]: By using **7g**, according to Procedure A, flash chromatography (hexanes/EtOAc, 90:10) gave a colorless oil containing a mixture of four isomers ***exo*-8g** and ***endo*-9g** (38%; 33:25:22:20 *dr*, by ^1H NMR). A second flash chromatography (hexanes/EtOAc, 90:10) allowed for the isolation and characterization (but not identification) of three of these compounds. **First Compound:** ^1H NMR (360 MHz, $CDCl_3$): δ = 4.46 (ddd, J = 7.6, J = 2.2, J = 1.4 Hz, 1 H, 4-H), 2.94 (dd, J = 22.0, J = 7.6 Hz, 1 H, 3-H), 2.93–2.83 (m, 1 H, 3-H), 2.50–2.40 (m, 1 H, 1-H), 2.30 (ddd, J = 18.3, J = 3.3, J = 1.7 Hz, 1 H, 5-H), 2.13 (ddd, J = 12.2, J = 10.5, J = 1.5 Hz, 1 H, 7-H), 1.71 (dd, J = 12.6, J = 5.5 Hz, 1 H, 7-H), 1.25 (s, 3 H, CCH_3), 1.07 (s, 3 H, CCH_3), 0.87 (s, 9 H, Si*t*Bu), 0.06 (s, 3 H, SiMe), 0.06 (s, 3 H, SiMe) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 220.6, 70.6, 54.9, 48.0, 39.2, 37.0, 34.3, 32.1, 25.8, 24.6, 18.1, –4.6, –4.9 ppm. HRMS: calcd. for $C_{15}H_{28}O_2SiNa$ 291.1756; found 291.1747. **Second Compound:** ^1H NMR (360 MHz, $CDCl_3$): δ = 4.25 (d, J = 5 Hz, 1 H, 4-H), 2.90–2.80 (m, 1 H, 3-H), 2.76 (dd, J = 18.3, J = 4.5 Hz, 1 H, 3-H), 2.53–2.45 (m, 1 H, 1-H), 2.26 (ddd, J = 17.8, J = 2.5, J = 1.1 Hz, 1 H, 5-H), 2.00 (ddd, J = 12.1, J = 9.3, J = 2.7 Hz, 1 H, 7-H), 1.67–1.55 (m, 1 H, 7-H), 1.28 (s, 3 H, CCH_3), 0.94 (s, 3 H, CCH_3), 0.86 (s, 9 H, Si*t*Bu), 0.05 (s, 3 H, SiMe), 0.04 (s, 3 H, SiMe) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 222.3, 73.7, 54.8, 48.0, 39.4, 35.9, 34.8, 31.2, 25.8, 25.7, 18.1, –4.7, –4.8 ppm. HRMS: calcd. for $C_{15}H_{28}O_2SiNa$ 291.1756; found 291.1753. **Third Compound:** ^1H NMR (360 MHz, $CDCl_3$): δ = 4.56 (ddd, J = 11.1, J = 8.5, J = 7.6 Hz, 1 H, 4-H), 2.76 (ddd, J = 18.0, J = 11.4, J = 0.6 Hz, 1 H, 3-H), 2.70–2.60 (m, 1 H, 3-H), 2.60–2.45 (m, 1 H, 1-H), 2.40–2.25 (m, 1 H, 5-H), 2.20–2.10 (m, 1 H, 7-H), 1.73 (dd, J = 9.3, J = 3.6 Hz, 1 H, 7-H), 1.31 (s, 3 H, CCH_3), 1.22 (s, 3 H, CCH_3), 0.91 (s, 9 H, Si*t*Bu), 0.07 (s, 3 H, SiMe), 0.06 (s, 3 H, SiMe) ppm. HRMS: calcd. for $C_{15}H_{28}O_2SiNa$ 291.1756; found 291.1750.

(1*R*,4*S*)-4-(Allyloxymethoxy)cyclopent-2-enyl Acetate (10): To a solution of alcohol **2a** (568 mg, 4.0 mmol) in CH_2Cl_2 (5 mL) under argon were added i-Pr_2NEt (3.10 g, 24.0 mmol), allyl chloromethyl ether (1.28 g, 12.0 mmol) and Bu_4NI (148 mg, 0.4 mmol). The solution was stirred at room temp. for 72 h and then washed with aq. HCl (2 M, 2 × 5 mL), saturated aq. $NaHCO_3$ (5 mL), and brine (5 mL). The organic phase was dried with $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography (hexanes/Et_2O, 80:20) to give **10** as a colorless oil (678 mg, 80%). $[\alpha]_D^{20}$ = +33 (c = 1.2, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 6.13 (dt, J = 5.8, J = 1.4 Hz, 1 H, 2-H), 6.01 (dt, J = 5.8, J = 1.4 Hz, 1 H, 3-H), 5.93 (ddt, J = 16.9, J = 10.8, J = 5.8 Hz, 1 H, CH_{allyl}), 5.54–5.48 (m, 1 H, 1-H), 5.31 (ddd, J = 17.3, J = 3.2, J = 1.8 Hz, 1 H, CH_{2allyl}), 5.21 (ddd, J = 10.4, J = 2.8, J = 1.4 Hz, 1 H, CH_{2allyl}), 4.79 (s, 2 H, OCH_2O), 4.65–4.58 (m, 1 H, 4-H), 4.17–4.05 (m, 2 H, OCH_2), 2.81 (dt, J = 14.7, J = 7.4 Hz, 1 H, 5-H), 2.06 (s, 3 H, OAc), 1.74 (dt, J = 14.5, J = 4.2 Hz, 1 H, 5-H) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 170.6, 136.5, 134.1, 132.7, 116.9, 93.8, 79.9, 76.6, 68.2, 37.9, 21.0 ppm. IR (neat): $\tilde{\nu}$ = 3076, 2944, 2887, 1736 cm^{-1}. MS: m/z = 230 $[M + NH_4]^+$. HRMS: calcd. for $C_{11}H_{16}O_4Na$ 235.0946; found 235.0941. $C_{11}H_{16}O_4$ (212.24): calcd. C 62.25, H 7.60; found C 61.94, H 7.71.

(1*R*,4*S*)-4-(Allyloxymethoxy)cyclopent-2-enol (11): To a solution of ester **10** (623 mg, 2.9 mmol) in MeOH (16 mL) under argon was added sodium methoxide (317 mg, 5.9 mmol), and the solution was stirred at room temp. for 14 h. Most of the MeOH was then evaporated, and CH_2Cl_2 was added (25 mL). The mixture was washed with H_2O (3×10 mL), dried with $MgSO_4$, filtered, and concentrated to afford **11** as a colorless oil (456 mg, 91% yield). $[\alpha]_D^{20}$ = +10 (*c* = 1.65, $CHCl_3$). ^{1}H NMR (360 MHz, $CDCl_3$): δ = 6.08 (ddd, *J* = 5.8, *J* = 1.4, *J* = 1.1 Hz, 1 H, 2-H), 6.03 (ddd, *J* = 5.8, *J* = 1.4, *J* = 1.1 Hz, 1 H, 3-H), 5.93 (ddt, *J* = 17.3, *J* = 10.4, *J* = 5.4 Hz, 1 H, CH_{allyl}), 5.32 (ddd, *J* = 17.3, *J* = 3.2, *J* = 1.8 Hz, 1 H, CH_{2allyl}), 5.21 (ddd, *J* = 10.4, *J* = 2.9, *J* = 1.4 Hz, 1 H, CH_{2allyl}), 4.79 (q, *J* = 7.0 Hz, 2 H, OCH_2O), 4.69–4.61 (m, 1 H, 4-H), 4.61–4.56 (m, 1 H, 1-H), 4.18–4.05 (m, 2 H, OCH_2), 2.70 (dt, *J* = 14.3, *J* = 7.2 Hz, 1 H, 5-H), 1.76 (d, *J* = 9.0 Hz, 1 H, OH), 1.66 (dt, *J* = 14.2, *J* = 3.9 Hz, 1 H, 5-H) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 137.3, 134.2 (2 C), 117.1, 93.5, 80.2, 76.6, 68.3, 41.4 ppm. IR (neat): $\tilde{\nu}$ = 3402, 3063, 2941, 2886, 1648 cm^{-1}. MS: *m*/*z* = 188 $[M + NH_4]^+$. $C_9H_{14}O_3$ (170.20): calcd. C 63.51, H 8.29; found C 63.24, H 8.18.

(4*S*)-4-(Allyloxymethoxy)cyclopent-2-enone (12): To a solution of alcohol **11** (405 mg, 2.4 mmol) in CH_2Cl_2 (30 mL) under argon, was added PDC (600 mg, 3.6 mmol). The mixture was stirred at room temp. for 72 h and then filtered through Celite. The solid was washed with CH_2Cl_2, and the combined organic phases were concentrated. The obtained residue was purified by flash chromatography (hexanes/Et_2O, 50:50) to give **12** as a colorless oil (312 mg, 78%). $[\alpha]_D^{20}$ = –16 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (360 MHz, $CDCl_3$): δ = 7.62 (dd, *J* = 5.7, *J* = 2.4 Hz, 1 H, 3-H), 6.26 (dd, *J* = 5.7, *J* = 1.0 Hz, 1 H, 2-H), 5.93 (ddt, *J* = 16.9, *J* = 10.8, *J* = 5.4 Hz, 1 H, CH_{allyl}), 5.33 (ddd, *J* = 17.6, *J* = 3.2, *J* = 1.8 Hz, 1 H, CH_{2allyl}), 5.23 (ddd, *J* = 10.4, *J* = 2.5, *J* = 1.4 Hz, 1 H, CH_{2allyl}), 4.94–4.89 (m, 1 H, 4-H), 4.83 (d, *J* = 1.1 Hz, 1 H, OCH_2O), 4.19–4.06 (m, 2 H, OCH_2), 2.75 (dt, *J* = 18.4, *J* = 6.1 Hz, 1 H, 5-H), 2.35 (dt, *J* = 18.4, *J* = 2.3 Hz, 1 H, 5-H) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 205.5, 161.4, 135.2, 133.6, 116.9, 93.9, 75.3, 68.2, 41.7 ppm. IR (neat): $\tilde{\nu}$ = 3081, 2944, 2890, 1722 cm^{-1}. HRMS: calcd. for $C_9H_{12}O_3Na$ 191.0684; found 191.0678.

(2a*S*,3a*R*,7a*S*,7b*R*)-Hexahydro-5,7-dioxacyclobuta[*cd*]azulen-2(1*H*)-one (13): A solution of enone **12** (164 mg, 0.98 mmol) in acetone (195 mL) was saturated with argon for 15 min and then irradiated with a 400 W high-pressure mercury vapor lamp fitted with a Pyrex filter for 15 min. The mixture was concentrated, and the residue was purified by flash chromatography (hexanes/Et_2O, 50:50) to give **13** (97 mg, 60%) as white crystals. M.p. 61 °C. $[\alpha]_D^{20}$ = +112 (*c* = 1.35, $CHCl_3$). ^{1}H NMR (360 MHz, $CDCl_3$): δ = 5.15 (d, *J* = 7.5 Hz, 1 H, 6-H), 4.58 (tt, *J* = 5.4, *J* = 1.4 Hz, 1 H, 7a-H), 4.55 (d, *J* = 7.2 Hz, 1 H, 6-H), 3.80 (dd, *J* = 13.1, *J* = 3.8 Hz, 1 H, 8-H), 3.71 (dd, *J* = 13.1, *J* = 2.8 Hz, 1 H, 4-H), 3.13–3.04 (m, 1 H, 7b-H), 2.99–2.87 (m, 1 H, 3a-H), 2.82 (dd, *J* = 17.5, *J* = 8.3 Hz, 1 H, 2a-H), 2.62–2.42 (m, 3 H, 1-H, 1-H, 3-H), 2.41–2.30 (m, 1 H, 3-H) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 217.5, 97.8, 79.4, 71.4, 48.6, 46.5, 40.3, 37.4, 28.4 ppm. IR (neat): $\tilde{\nu}$ = 2942, 1739 cm^{-1}. HRMS: calcd. for $C_9H_{12}O_3Na$ 191.0684; found 191.0677.

(1*S*,4*S*,5*R*,6*R*)-4-Hydroxy-6-(hydroxymethyl)bicyclo[3.2.0]heptan-2-one (14): To a solution of tricyclic acetal **13** (288 mg, 1.7 mmol) in THF (20 mL) was added concentrated HCl (1 mL). The mixture was stirred at room temp. for 2 h and then concentrated to give **14** (227 mg, 85%) as a colorless oil. $[\alpha]_D^{20}$ = +77 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (360 MHz, $CDCl_3$): δ = 4.57 (dd, *J* = 5.8, *J* = 5.2 Hz, 1 H, 4-H), 3.80 (d, *J* = 9.3 Hz, 1 H, CH_2O), 3.65 (dd, *J* = 9.3, *J* = 3.9 Hz, 1 H, CH_2O), 3.64 (br. s, 1 H, OH), 3.41–3.32 (m, 1 H, 5-H), 3.09–2.98 (m, 1 H, 6-H), 2.74–2.60 (m, 3 H, 1-H, 3-H, 7-H), 2.47 (dd, *J* = 18.0, *J* = 4.9 Hz, 1 H, 3-H), 1.95–1.60 (m, 2 H, 7-H, OH) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 219.7, 78.8, 74.1, 47.3, 44.7, 38.6, 36.3, 27.1 ppm. IR (neat): $\tilde{\nu}$ = 3455, 2975, 2931, 2852, 1735 cm^{-1}. MS: *m*/*z* = 174 $[M + NH_4]^+$. $C_8H_{12}O_3$ (156.18): calcd. C 61.52, H 7.74; found C 61.31, H 7.71.

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