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Synthesis of pseudoiridolactones

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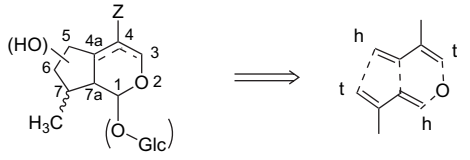
Abstract—Bicyclic δ-lactones with a carbon group at the bicyclic junction C-7a, designed as pseudoiridolactones, were synthesized from α-alkyl-α-hydroxymethylcyclopentanones via an intramolecular Horner–Wadsworth–Emmons reaction.

1. Introduction

Iridoids form an important class of monoterpenoids, which originate mainly from vegetal kingdom and are often in the form of glycosides.[1] They present a highly oxygenated monoterpene skeleton **I**, which is characterized by a cis-fused cyclopenta[*c*]pyran moiety.[2] They formally derive from an oxidative head-to-tail cyclization of two isoprene units (Scheme 1) and their biosynthetic origin from mevalonic acid or geraniol have been extensively studied.[3]



I Z = H, CH_3, CO_2R

Scheme 1.

Iridoids exhibit significant biological and pharmacological activities such as sedative, hypoglycemic, choleretic, antiviral, antibacterial, and antitumor properties.[4] However, their medicinal uses have been poorly developed, except within traditional medicine (folk drugs used as bitter tonics, sedatives, febrifuges, hypotensives).

Iridolactones are non-glycosidic iridoids, and form a subclass composed of cyclopentanoid compounds fused to a δ-lactone unit.[5] These bicyclic lactones are further divided into two sub-groups **IIa**,**b** according to the position of the lactone keto group. Particularly, sub-group **IIa** is well represented by natural (+)-iridomyrmecin **III**, which was identified as the first iridoid natural compound when it was isolated from the defense secretions of *Iridomyrmex humilis* ants in the 1940s (Fig. 1).[6]

IIa (R = H, CH_3, CHO, CO_2Alkyl) **IIb**

III (+)-**Iridomyrmecin** (R = α-CH_3)

Figure 1.

Very few iridoids such as 10-griselinosidic acid **IV** isolated from *Penstemon nitidus* species,[2b] the two hydroxylated glucosides **Va**,**b**,[7] and the methylated iridoid glycoside **VI**[8] are substituted at carbon C-4a (Fig. 2), but to the best of our knowledge no naturally occurring iridoids with a substituent at the bicyclic junction C-7a of the 3-oxa-bicyclo[4.3.0]nonane skeleton are known. However, some natural diterpenes such as xestolide **VII** and guyanin **VIII** are bicyclic δ-lactones, which are substituted at the bicyclic junction (carbon C-7a).[9,10] In other respects, several alkylated δ-lactones related to iridomyrmecin[11] and unnatural bicyclic compounds with iridoid-like structures substituted at carbon C-7a have been reported.[12]

In this context, we became interested in synthesizing new iridolactone analogues **IX**–**X**.[13] These bicyclic δ-lactones

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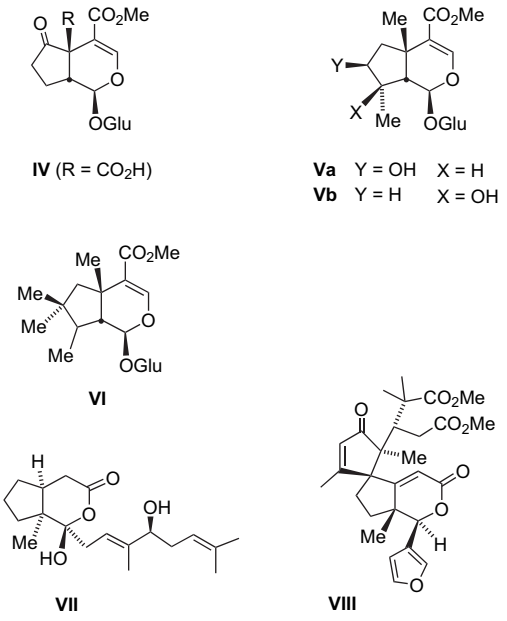
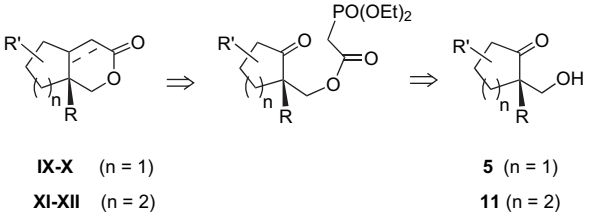


Figure 2.

substituted at the bicyclic junction C-7a might be referred to as 'pseudoiridolactones' by analogy with the pseudoguaianolides family.[14] Thus, we report herein the synthesis of the new unsaturated (**IX**) and saturated (**X**) pseudoiridolactones (racemic series) from racemic α-alkyl-α-hydroxymethylcyclopentanones **5** via an intramolecular Horner–Wadsworth–Emmons reaction[15] and the extension of this approach to the synthesis of homologous bicyclic δ-lactones **XI**–**XII** (*n*=2) from α-alkyl-α-hydroxymethylcyclohexanone **11** (Scheme 2).

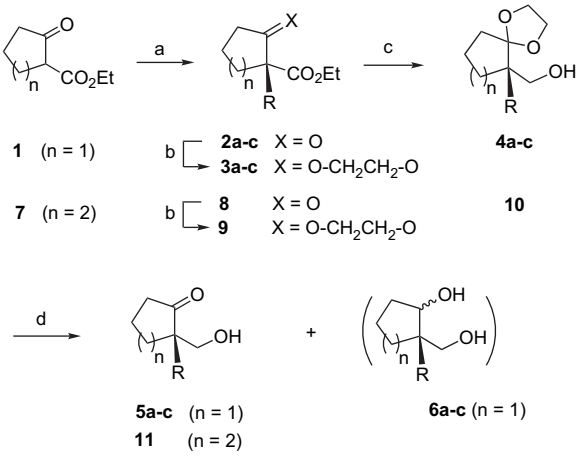


Scheme 2.

2. Results and discussion

2.1. Synthesis of α-hydroxymethylcycloalkanones 5a–c and 11 from α-carbethoxycycloalkanones 1 and 7

The preparation of the necessary precursor α-alkylated α-hydroxymethylcycloalkanones **5a–c** followed a previously described sequence from α-carbethoxycyclopentanone **1**.[16] Alkylation of this commercially available keto-ester to β-keto esters **2a–c** was followed by ketalization to ethyl (2,2-ethylenedioxy)cyclopentanecarboxylate **3a–c**. These last ones were reduced to the hydroxy-ethyleneketals **4a–c**, which were immediately hydrolyzed to α-hydroxymethylcyclopentanones **5a–c** (Scheme 3, Table 1, entries 1–3). From our experiments this standard procedure was more efficient and selective than the more direct reduction of β-keto esters **2** to β-keto alcohol **5** via enolate protection,[17] which turned out to also give some diols **6**.



Scheme 3. *Reagents and conditions*: (a) Method A: K_2CO_3, RBr, acetone, rt, 24 h; Method B: NaH, RBr, DMF, rt, 12 h; (b) glycol, cat. APTS, toluene, Dean–Stark; (c) $AlLiH_4$, ether, 0 °C; (d) 2 N HCl, ether, rt, 2 h.

Table 1. Synthesis of α-alkyl-α-hydroxymethylcycloalkanones **5** and **11**

Entry	Substrate	R	Yield[a] (%)					
			2		**3**		**5**	
1	**1** (*n*=1)	Bu	**2a**	67	**3a**	94	**5a**	79
2	**1**	CH_2–Ph	**2b**	77	**3b**	91	**5b**	94
3	**1**	CH_2–CH=CH_2	**2c**	73	**3c**	98	**5c**	90
4	**7** (*n*=2)	CH_2–Ph	**8**	89	**9**	96	**11**	96

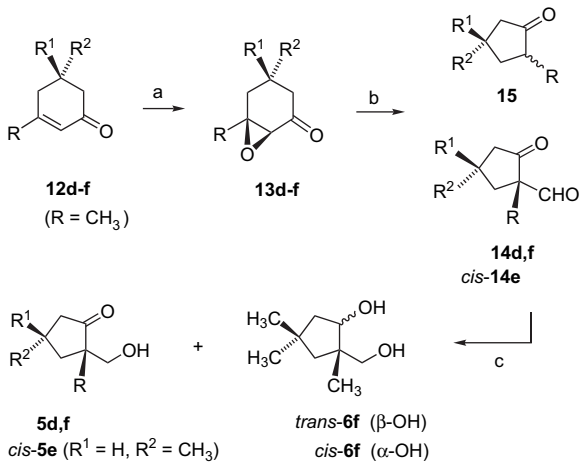
[a] Refers to yield of isolated product by flash chromatography.

The homologous α-benzyl-α-hydroxymethylcyclohexanone **11** was synthesized via a similar scheme from α-carbethoxycyclohexanone **7** (R=CH_2–Ph) (entry 4).

2.2. Synthesis of α-hydroxymethylcyclopentanones 5d–f from cyclohexenones 12d–f

Another approach to α-hydroxymethylcyclopentanones **5** has been also reported shortly from 3-substituted cyclohexenones **12** (Scheme 4).[18,19] Indeed, their epoxides **13** are well known to rearrange to β-keto aldehydes **14** under treatment with Lewis acids,[20] and the selective reduction of the aldehyde group was performed by lithium tri(*tert*-butoxy)aluminum hydride[18] or Bu_3SnH.[19] The chemoselective reduction of β-keto aldehydes has been carried out with varying efficiency by several reducing agents (Ni- or Pd-catalyzed hydrogenation,[21,22] lithium trisalkoxyaluminum hydride,[18,23] RedAl,[24] amine boranes,[25] $Zn(BH_4)_2$[26]), especially because of their easy overreduction to 1,3-diols.[25,27] However, it has not been achieved so far on a large scale (40–50 mmol), which needed to be investigated.[28]

Epoxidation of cyclohexenones **12d–f** was carried out classically by treatment with 10% aqueous H_2O_2 in basic ethanol (Scheme 4, Table 2, 80–85% yield of epoxy-ketones **13d–f**).[20a,29] The rearrangement of these epoxides **13d–f** was performed by reaction with BF_3–Et_2O in methylene chloride according to Bach's procedure.[20b] Pure β-keto aldehydes **14d–f** were obtained after distillation (49–77% yield); this one had to be carried out at as low a temperature as



Scheme 4. *Reagents and conditions*: (a) H_2O_2–NaOH, EtOH, 0–20 °C; (b) BF_3–Et_2O (0.75 equiv), CH_2Cl_2, 0 °C; (c) LiAlH(O-*t*-Bu)$_3$ (1 equiv) [$AlLiH_4$, 3 equiv *t*-BuOH, Et_2O, −40 °C, 4 h], Et_2O, −78 °C, 1–3 h.

Table 2. Synthesis of α-alkyl-α-hydroxymethylcyclopentanones **5d–f**

Entry	Substrate	R^1	R^2	Yield (%)					
				13[a]		**14**[a]		**5**[b] (Conversion %)	
1	**12d**	H	H	**13d**	83	**14d**	49	**5d**	52 (57)
2	**12e**	H	CH_3	**13e**	79	**14e**[c]	67	**5e**[c]	59 (63)
3	**12f**	CH_3	CH_3	**13f**	85	**14f**	77	**5f**	78 (100)

[a] Refers to yield of isolated product by distillation.
[b] Refers to yield of isolated product by flash chromatography.
[c] β-Keto aldehyde **14e** and β-keto alcohol **5e** obtained as cis–trans 80:20 mixtures of diastereomers.

possible in order to avoid the decarbonylation to α-methylcyclopentanones **15**.[30] Particularly, cyclopentanone **14e** was obtained as an 80:20 mixture of cis–trans stereomers (major stereomer with *cis* CHO and R^2=CH_3 groups shown in Scheme 4) whose relative configurations were determined by ^{1}H NMR as already described by Asaoka et al (entry 2).[20c]

Table 3. Reduction of β-keto aldehyde **14f**

Entry	Reducing agent	Conditions	Yield[a] (%)				
			5		**6**		**15**
1	Raney Ni (10 equiv)	THF, rt, 2 h	**5f**	40	—		**15f** 52
2	Solid LiAlH(O-*t*-Bu)$_3$	Et_2O, −78 °C, 1 h	**5f**	72	—		—
3	LiAlH(O-*t*-Bu)$_3$[c] (1 equiv)	Et_2O, −78 °C, 1 h	**5f**	50	**6f**[b]	32	—
4	LiAlH(O-*t*-Bu)$_3$[d] (1 equiv)	Et_2O, −78 °C, 1 h	**5f**	78	—		—

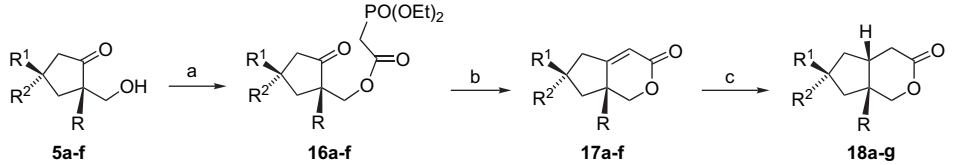
[a] Refers to yield of isolated product by flash chromatography.
[b] Combined yield of diols *trans*-**6f** and *cis*-**6f** separated by flash chromatography (trans–cis=75:25).
[c] Ethereal $LiAlH_4$ (0.75 M, 1 equiv), 3 equiv *t*-BuOH, Et_2O, −40 °C, 0.5 h.
[d] Ethereal $LiAlH_4$ (0.75 M, 1 equiv), 3 equiv *t*-BuOH, Et_2O, −40 °C, 4 h.

In order to improve the selective reduction of the aldehyde group, we initially tried to take advantage of a recently described chemoselective reduction of 1,*n*-keto aldehydes by Raney nickel;[31] however, this last report didn't deal with the case of β-keto aldehydes. In our hands the reduction of β-keto aldehyde **14f** to α-hydroxymethylcyclopentanone **5f** was effectively selective, but deformylation leading to cyclopentanone **15f** occurred as a competitive reaction, whatever the amount of Raney Ni or the reaction time was (Table 3, entry 1). We then looked to the reduction with lithium tri(*tert*-butoxy)aluminum hydride.[32] With commercially available solid LiAlH(O-*t*-Bu)$_3$ in ether at −78 °C, cyclopentanone **5f** was obtained with a 72% yield (entry 2). The reduction was also tested with LiAlH(O-*t*-Bu)$_3$ formed in situ at −40 °C from *t*-BuOH and a titrated ethereal solution of $AlLiH_4$. The selectivity was then greatly dependent on the time of contact between the two reagents. The reducing agent obtained after a short time of 30 min led to cyclopentanone **5f** in a 50% yield together with diastereomeric diols *trans*-**6f** (24%) and *cis*-**6f** (8%), which were separated by flash chromatography (trans–cis 75:25, entry 3).[33] Finally, the most efficient chemoselective reduction was performed with a reagent obtained after 4 h at −40 °C: α-hydroxymethylcyclopentanone **5f** was then isolated with 78% yield (entry 4).

These last experimental reductive conditions were then used to obtain the two other α-alkyl-α-hydroxymethylcyclopentanones **5d**,**e** (Table 2, entries 1 and 2).

2.3. Synthesis of pseudoiridolactones 17 and 18

The transformation of the differently substituted α-hydroxymethylcyclopentanones **5a–f** to pseudoiridolactones **17** and **18** was achieved via the intramolecular Horner–Wadsworth–Emmons (HWE) reaction of the intermediate phosphinylacetates **16** as summarized in Scheme 5 and Table 4 (entries 1–6). β-Keto alcohols **5a–f** were first esterified to diethylphosphinylacetates **16** under DMAP-catalysis in the presence of dicyclohexylcarbodiimide DCC.[34] The intramolecular HWE was carried out by treatment of phosphinylacetates **16a–f** with LiBr–NEt_3 according to a procedure used for base sensitive materials.[15,35] Unsaturated δ-lactones **17a–f** were then obtained with fair 70–85% yields. Finally, hydrogenation of **17a–f** was classically performed in ethyl acetate under palladium/charcoal-catalyzed conditions. It occurred exclusively from the convex face of the unsaturated lactones **17** and gave the cis-fused bicyclic δ-lactones **18** (94–98% yield).[36] Of course, these two last transformations did not change the configuration of the cyclopentane carbon C-4 (CR^1R^2) in β-keto alcohol **17e**. Consequently, both lactones **17e** and **18e** arising from **16e** (cis–trans 80:20) were also obtained as 80:20 mixtures of *endo–exo* diastereomeric lactones (major diastereomers with *endo* R^2=CH_3 group shown in Scheme 5).



Scheme 5. *Reagents and conditions*: (a) $(EtO)_2PO$–CH_2–CO_2H (1 equiv), DCC (1 equiv), 6 mol % DMAP, CH_2Cl_2, rt, 3 h; (b) LiBr (3.2 equiv), NEt_3 (10 equiv), THF, rt, 3–4 h; (c) H_2, cat. Pd–C, AcOEt, rt, 20 h.

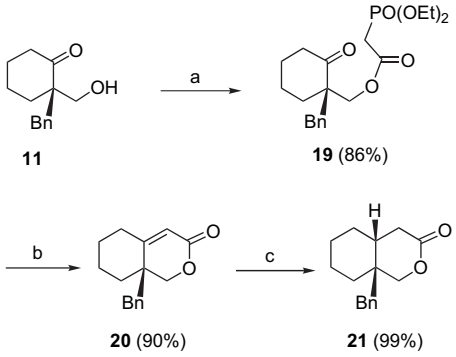
Table 4. Synthesis of pseudoiridolactones **17** and **18**

Entry	β-Keto alcohols **5a–f**	R^1, R^2	R	Yield[a] (%)					
				16		**17**		**18**	
1	**5a**	R^1=R^2=H	*n*-Bu	**16a**	89	**17a**	72	**18a**	97
2	**5b**	R^1=R^2=H	CH_2–Ph	**16b**	91	**17b**	80	**18b**	96
3	**5c**	R^1=R^2=H	CH_2–CH=CH_2	**16c**	80	**17c**	85	**18g**[d]	94
4	**5d**	R^1=R^2=H	CH_3	**16d**	82	**17d**	70	**18d**	97
5	**5e**[b]	R^1=H, R^2=CH_3	CH_3	**16e**[b]	90	**17e**[c]	71	**18e**[c]	98
6	**5f**	R^1=R^2=CH_3	CH_3	**16f**	90	**17f**	70	**18f**	98

[a] Refers to yield of isolated product by flash chromatography.
[b] β-Keto alcohol **5e** and phosphinylacetate **16e** were cis–trans 80:20 mixtures of diastereomers (major cis-diastereomers shown in Schemes 4 and 5).
[c] Lactones **17e** and **18e** obtained as 80:20 mixtures of *endo–exo* diastereomers.
[d] Hydrogenation of **17c** (R=allyl) gave the fully saturated δ-lactone **18g** (R=*n*-C_3H_7).

2.4. Synthesis of bicyclic δ-lactones 20 and 21

A similar sequence allowed us to synthesize the homologous racemic bicyclic δ-lactones **20** and **21** from α-hydroxymethylcyclohexanone **11** (Scheme 6).



Scheme 6. *Reagents and conditions*: (a) $(EtO)_2PO–CH_2–CO_2H$ (1 equiv), DCC (1 equiv), 6% DMAP, CH_2Cl_2, rt, 3 h; (b) LiBr (3.2 equiv), NEt_3 (10 equiv), THF, rt, 3–4 h; (c) H_2, cat. Pd–C, AcOEt, rt, 20 h.

3. Conclusion

In conclusion this paper describes the synthesis of cis-fused bicyclic δ-lactones **17** and **18**, which were devised as pseudoiridolactones as they present an alkyl group at bicyclic junction C-7a. These new δ-lactones were obtained from α-alkyl-α-hydroxymethylcyclopentanones **5** prepared by two routes from α-carbethoxycyclopentanone or substituted cyclohexenones. Particularly, the second route involved the chemoselective reduction of substituted β-keto aldehydes **14**, which was efficiently performed by tri(*tert*-butoxy)aluminum hydride at low temperature (−78 °C) on a 30–50 mmol scale. Following this approach, access to non-racemic pseudoiridolactones could be easily envisioned from enantiomerically enriched α-hydroxymethylcyclopentanones **5**. Recently, the lipase-mediated kinetic resolution of these last β-hydroxyketones **5** was successfully achieved in our group and will be disclosed in due course together with the preparation of optically active pseudoiridolactones **17** and **18**.

4. Experimental

4.1. Instrumentation

IR spectra were recorded on a Perkin–Elmer 298 spectrophotometer and obtained from thin films on NaCl plates for oils or from KBr disc for solids. Positions of absorption bands are reported in cm^{-1}. ^1H and ^{13}C NMR spectra were recorded, respectively, at 300 and 75.5 MHz on a Bruker DRX 300 instrument. ^1H NMR chemical shifts were obtained in $CDCl_3$ and reported in parts per million relative to the solvent shift of residual chloroform at δ 7.26 ppm. Multiplicities are described as s (singlet), d (doublet), dd (doublet of doublets), t (triplet), q (quartet), m (multiplet). Coupling constants (^xJ) are reported in hertz. ^{13}C NMR chemical shifts were obtained in $CDCl_3$ and reported in parts per million relative to $CHCl_3$ at δ 77.16 ppm. All the carbons were assigned with the aid of DEPT 135 experiments. NOE ^1H and 2D NMR experiments were realized with a Bruker DRX 500 instrument. Low- and high-resolution mass spectra were obtained with a Thermoquest Finnigan LCQ instrument in the electrospray ionization mode (ESI) or a Thermoquest Finnigan MAT 95 XL spectrometer in the Electron Impact mode (EI, ionization potential of 70 eV) or the Chemical Ionization mode (CI, isobutane as the reagent gas). GC–MS was carried out using a Delsi-DI 700 gas chromatograph (30 m DB5 capillary column) coupled with a Nermag R10-10S quadrupole mass spectrometer (EI mode at an ionization potential of 70 eV) or a Focus DSQ Thermo Electron (15 m TR5MS capillary column, EI mode). Microanalyses were carried out by the 'Service Central d'analyse du CNRS', Solaize, France.

4.2. Materials

All reactions were carried out under nitrogen in oven-dried glassware using standard syringe, cannula, and septa techniques. DMF and CH_2Cl_2 were distilled from CaH_2 and stored under nitrogen. THF was freshly distilled from sodium benzophenone ketyl. Thin-layer chromatography (TLC) was performed using precoated Kieselgel 60 F_{254} plates (Merck). Detection was done by UV (254 nm) followed by charring with 4% *p*-anisaldehyde, 5% acetic acid, and 5% sulfuric acid in 86% ethanol. Flash chromatography was performed on silica gel 60 (40–63 μm, Merck). Melting points (mp) were taken on a Büchi apparatus and were not corrected. PE refers to petroleum ether (40–60 °C fraction) and EE to ethyl ether. Raney nickel was purchased from Aldrich. Ethereal $AlLiH_4$ solutions were prepared according to Brown's procedure[37] and titrated by Felkin's method.[38] β-Keto esters **2a–c** and **8** were prepared according to known procedures: (i) Method A (K_2CO_3, RBr, acetone, rt, 24 h)[39] for ethyl 1-benzyl-2-oxocyclopentanecarboxylate **2b**,[39] ethyl 1-allyl-2-oxocyclopentanecarboxylate **2c**,[40] and ethyl 2-benzyl-2-oxocyclohexanecarboxylate **8**;[41]

(ii) Method B (NaH, RBr, DMF, rt, 24 h)[40] for ethyl 1-butyl-2-oxocyclopentanecarboxylate **2a**[42] (Scheme 3, Table 1). 2,3-Epoxy-3-methylcyclohexanone **13d**,[43] 3,5-dimethyl-2,3-epoxycyclohexanone **13e**,[20c] and 2,3-epoxy-3,5,5-trimethylcyclohexanone (isophorone-epoxide) **13f**,[20b] were synthesized following literature procedures.

4.3. Typical procedures

4.3.1. Typical procedure for the synthesis of (2,2-ethylenedioxy)cyclopentanecarboxylates 3a–c (TP.1). Ketal-ester **3a** (Table 1, entry 1): a solution of ethyl 1-butyl-2-oxocyclopentanecarboxylate **2a** (5.84 g, 22.8 mmol), ethyleneglycol (3.3 g, 36.35 mmol), and APTS (290 mg, 1.14 mmol, 5 mol %) in toluene (70 mL) was refluxed in a round bottom flask equipped with a Dean–Stark system. After completion of the reaction, toluene was evaporated and Et_2O (50 mL) was added. The organic solution was washed twice with 5% aqueous $NaHCO_3$ (2×20 mL) and 5% aqueous NaCl (30 mL). The resulting aqueous phases were extracted with ether (2×30 mL). The combined organic phases were dried over $MgSO_4$. After evaporation of solvents, the crude oil was purified by flash chromatography (PE–EE=60:40) to give ketal-ester **3a** as a colorless oil (6.6 g, 94%).

4.3.1.1. Ethyl 1-butyl-(2,2-ethylenedioxy)cyclopentanecarboxylate 3a. R_f=0.72 (PE–EE 50:50). IR (neat): 2960, 1725, 1640, 1450, 1050 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 4.10 (q, ^3J=7.1 Hz, 2H, OCH_2), 3.90 (m, 4H, OCH_2CH_2O), 2.78–2.55 (m, 4H, H-3 and CH_2), 1.80 (m, 3H, H-4 and H-5), 1.70 (m, 1H, H-5′), 1.40–1.24 (m, 4H, CH_2CH_2), 1.25 (t, ^3J=7.1 Hz, 3H, OCH_2CH_3), 0.9 (t, ^3J=6.9 Hz, 3H, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 174.0 (C=O), 118.9 (O–*C*–O), 65.5 (OCH_2), 64.2 (OCH_2), 60.2 (OCH_2CH_3), 58.7 (C-1), 36.0 (C-3), 33.2 (C-5), 30.9 (CH_2), 27.3 (CH_2), 23.2 (CH_2), 19.3 (C-4), 14.3 (OCH_2CH_3), 14.0 (CH_2CH_3).

4.3.1.2. Ethyl 1-benzyl-(2,2-ethylenedioxy)cyclopentanecarboxylate 3b. According to TP.1 above, keto-ester **2b** (4 g, 16.26 mmol) gave ketal-ester **3b** as a colorless oil (4.28 g, 91%). R_f=0.53 (PE–EE 50:50). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.12–7.28 (m, 5H, Ar–H), 4.22 (q, ^3J=7.2 Hz, 2H, OCH_2CH_3), 4.09–3.94 (m, 2H, OCH_2), 3.91–3.80 (m, 2H, OCH_2), 3.53 (d, ^2J=13.8 Hz, 1H, CH_aH_bPh), 2.65 (d, ^2J=13.8 Hz, 1H, CH_aH_bPh), 2.47–2.38 (m, 1H, H-3′), 2.30–2.20 (m, 1H, H-5′), 2.10–1.90 (m, 1H, H-3), 1.81–1.70 (m, 3H, H-4 and H-5), 1.25 (t, ^3J=7.2 Hz, 3H, CH_3).

4.3.1.3. Ethyl 1-allyl-(2,2-ethylenedioxy)cyclopentanecarboxylate 3c. According to TP.1 above, keto-ester **2c** (5.84 g, 22.81 mmol) gave ketal-ester **3c** as a colorless oil (6.6 g, 94%). R_f=0.48 (PE–EE 50:50). IR (neat): 3063, 2978, 2882, 1731, 1640, 1447, 1222, 1178, 1034, 920 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 5.64 (ddt, $^3J_{trans}$=17.4 Hz, $^3J_{cis}$=10.1 Hz, 1H, ^3J=7.9 Hz, *H*C=CH_2), 5.10 (d, ^3J=17.4 Hz, 1H, C=C*H*H), 5.07 (dt, ^3J=10.1 Hz, ^4J=1.1 Hz, 1H, C=CH*H*), 4.15 (q, ^3J=7.1 Hz, 2H, OCH_2CH_3), 2.92–3.80 (m, 4H, OCH_2CH_2O), 2.83 (ddt, ^2J=14.2 Hz, ^3J=6.5 Hz, ^4J=1.1 Hz, 1H, CH_aH_b–CH=CH_2), 2.71–2.40 (m, 1H, H-3), 2.11 (ddt, ^2J=14.2 Hz, ^3J=7.9 Hz, ^4J=1.1 Hz, 1H, CH_aH_b–CH=CH_2), 1.99–1.70 (m, 5H, H-4, H-5 and H-5′), 1.26 (t, ^3J=7.1 Hz, 3H, OCH_2CH_3).

4.3.2. Typical procedure for the synthesis of 2-hydroxymethylcyclopentanones 5a–c from ketal-esters 3a–c (TP.2).

4.3.2.1. 2-Hydroxymethylcyclopentanone 5a (Table 1, entry 1). *Step 1*. Ketal-ester **3a** (5.38 g, 20.98 mmol) was slowly added to a stirred suspension of lithium aluminum hydride (934 mg, 24.6 mmol) in ether (15 mL) stirred at 0 °C under a nitrogen atmosphere. After 1 h, the hydrolysis of the reaction mixture was realized by adding succesively H_2O (940 μL), a 5% NaOH solution (940 μL), and then water (2×940 μL). The mixture was stirred for 0.5–1 h until a white precipitate appeared. This solid was filtered on a sintered glass filter. The organic phase was evaporated under vacuum to give the crude protected alcohol **4a** as a yellow oil (quantitative yield), which was used directly in the next step.

Step 2. HCl (2 N, 6 mL) was added to a solution of the crude alcohol **4a** (24.6 mmol) in ether (3 mL) at room temperature. After stirring for 2 h, the organic phase was successively washed with saturated $NaHCO_3$ (20 mL), then brine before drying over anhydrous Na_2SO_4. After evaporation of the solvent, purification by flash chromatography (PE–EE 60:40) afforded 2-hydroxymethylcyclopentanone **5a** (2.78 g, 79%).

4.3.2.2. 2-Butyl-2-hydroxymethylcyclopentanone 5a.[44] R_f=0.21 (PE–EE 60:40). IR (neat): 3450, 2960, 2880, 1730, 1650, 1450, 1050 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 3.65 (d, ^2J=11.0 Hz, 1H, CH_aH_bO), 3.50 (d, ^2J=11.0 Hz, 1H, CH_aH_bO), 2.03–2.0 (m, 1H, H-5), 1.85–1.55 (m, 6H, H-3, H-4, H-5′, and O*H*), 1.32 (t, ^3J=7.1 Hz, 2H, C–CH_2), 1.18 (m, 8H, CH_2CH_2), 0.9 (t, ^3J=6.6 Hz, 3H, CH_3).

4.3.2.3. 2-Benzyl-2-hydroxymethylcyclopentanone 5b.[45] According to TP.2 above, ketal-ester **3b** (4 g, 13.8 mmol) gave cyclopentanone **5b** as a colorless oil (2.65 g, 94%). R_f=0.15 (PE–EE 50:50). IR (neat): 3440, 2960, 1730, 1600, 1490, 1450, 1400, 1160, 1050, 750, 700 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.32–7.17 (m, 5H, Ar–H), 3.61 (d, ^2J=11.0 Hz, 1H, CH_aH_bO), 3.53 (d, ^2J=11.0 Hz, 1H, CH_aH_bO), 2.86 (d, ^2J=13.4 Hz, 1H, CH_aH_bPh), 2.80 (d, ^2J=13.4 Hz, 1H, CH_aH_bPh), 2.43 (s, 1H, O*H*), 2.33–2.10 (m, 2H, H-5), 2.06–1.92 (m, 1H, H-3), 1.90–1.60 (m, 3H, H-4 and H-3′). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 244.9 (C=O), 137.2 (Ar–C_{ipso}), 130.6 (2×Ar–C_{ortho}), 128.7 (2×Ar–C_{meta}), 127.1 (Ar–C_{para}), 66.1 (CH_2O), 54.8 (C-2), 39.4 (C-5), 38.3 (C-3), 30.1 (CH_2Ph), 19.4 (C-4).

4.3.2.4. 2-Allyl-2-hydroxymethylcyclopentanone 5c.[46] According to TP.2 above, ketal-ester **3c** (8.21 g, 34.2 mmol) gave cyclopentanone **5c** as a colorless oil (4.72 g, 90%). R_f=0.17 (PE–EE 50:50). IR (neat): 3448, 3077, 2962, 2887, 1730, 1640, 1440, 1400, 1350, 1160, 1050, 990, 920 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 5.70 (ddt, $^3J_{trans}$=17.3 Hz, $^3J_{cis}$=9.6 Hz, 1H, ^3J=7.5 Hz, *H*C=CH_2), 5.10 (d, ^3J=17.3 Hz, 1H, C=C*H*H), 5.09 (dt, ^3J=9.6 Hz, $^4J_{allyl}$=1.0 Hz, 1H, C=CH*H*), 3.61 (d, ^2J=11.1 Hz, 1H, CH_aH_bO), 3.50 (d, ^2J=11.1 Hz, 1H,

CH_aH_bO), 2.30–2.10 (m, 5H, H-5, O*H* and $CH_2C{=}C$), 2.00–1.80 (m, 4H, H-3 and H-4). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 222.8 (C=O), 132.0 ($HC{=}CH_2$), 117.8 ($HC{=}CH_2$), 64.7 (CH_2O), 52.3 (C-2), 37.8 (C-5), 35.8 (C–CH_2), 22.1 (C-3), 18.0 (C-4).

4.3.3. Typical procedure for rearrangement of epoxy-ketones 13d–f to β-keto aldehydes 14d–f (TP.3). β-Keto aldehyde **14d** (Table 2, entry 1): following Bach's procedure,[20b] boron trifluoride etherate (6.8 mL, 41 mmol) was added in 20 min to a solution of epoxy-ketone **13d** (8.2 g, 55 mmol) in CH_2Cl_2 (150 mL) stirred under nitrogen and cooled at 0 °C. The resulting mixture was stirred for 2 h at 0 °C, diluted with CH_2Cl_2, washed with saturated aqueous $NaHCO_3$ and brine. The organic layer was dried over $MgSO_4$ and filtered. Removal of the solvent and purification by distillation afforded β-keto aldehyde **14d** (4.4 g, 49%).

4.3.3.1. 1-Methyl-2-oxocyclopentanecarbaldehyde 14d.[47] Bp=70–74 °C/15 mmHg (lit.:[47] 69–70 °C/16 mmHg). R_f=0.45 (PE–EE 50:50). IR (neat): 2950, 1740, 1450, 1250, 1140, 940 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 9.42 (s, 1H, C*H*=O), 2.54 (dt, ^2J=13.2 Hz, ^3J=7.0 Hz, 1H, CH_aH_b–C_q), 2.3 (t, ^3J=7.7 Hz, 2H, CH_2–CO, 2.00–1.95 (m, 2H, CH_2), 1.72 (td, ^2J=13.2 Hz, ^3J=6.3 Hz, 1H, CH_aH_b–C_q), 1.28 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 215.8 (*C*=O), 198.9 (*C*H=O), 62.6 (C-1), 38.1 (C-3), 31.3 (C-5), 19.2 (C-4), 18.2 (CH_3).

4.3.3.2. 1,4-Dimethyl-2-oxocyclopentanecarbaldehyde 14e.[20c] According to TP.3 above, epoxy-ketone **13e** (21.6 g, 154 mmol) gave distillated β-keto aldehyde **14e** (14 g, 67%) as a cis–trans 80:20 mixture of diastereomers. Bp=80–85 °C/16 mmHg. R_f (cis+trans)=0.36 (PE–EE 80:20). IR (neat, cis+trans): 2950, 1740, 1450, 1400, 1145, 1050, 930 cm^{-1}. GC–MS (EI) *m/z*: 140 (M^+, 14), 125 (28), 112 (28), 97 (11), 69 (100), 55 (11), 41 (38) for both diastereomers. HRMS (EI): calcd for $C_8H_{12}O_2$ [M^+]: 140.0837; found: 140.0838.

NMR data for major *cis*-**14e** diastereomer: ^1H NMR (300 MHz, $CDCl_3$) δ: 9.48 (s, 1H, C*H*=O), 2.50 (ddd, ^2J=17.7 Hz, ^3J=7.0 Hz, ^4J_w=1.8 Hz, 1H, CH_aH_b–C_q), 2.38–2.22 (m, 1H, C*H*CH_3), 2.09 (dd, ^2J=13.2 Hz, ^3J=10.3 Hz, 1H, CH_aH_b–CO), 1.90 (dd, ^2J=17.7 Hz, ^3J=10.7 Hz, 1H, CH_aH_b–C_q), 1.86 (ddd, ^2J=13.2 Hz, ^3J=6.3 Hz, ^4J_w=1.8 Hz, 1H, CH_aH_b–CO), 1.28 (s, 3H, CH_3), 1.13 (d, ^3J=6.6 Hz, 3H, CHCH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 215.6 (*C*=O), 199.6 (*C*H=O), 63.2 (C-1), 46.9 (C-3), 39.0 (C-5), 27.8 (C-4), 20.2 (CH_3), 18.8 (CH_3).

NMR data for minor *trans*-**14e** diastereomer: ^1H NMR (300 MHz, $CDCl_3$) δ: 9.37 (s, 1H, C*H*=O), 2.65 (ddd, ^2J=12.9 Hz, ^3J=6.6 Hz, ^4J_w=2.2 Hz, 1H, CH_aH_b–Cq), 2.6–1.8 (m, 4H, CH_2–CO+CH_aH_b–Cq+C*H*–CH_3), 1.33 (s, 3H, CH_3), 1.17 (d, ^3J=6.6 Hz, 3H, CHCH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 215.0 (*C*=O), 198.2 (*C*H=O), 65.0 (C-1), 46.3 (C-3), 39.9 (C-5), 28.3 (C-4), 20.4 (CH_3), 18.8 (CH_3).

4.3.3.3. 1,4,4-Trimethyl-2-oxocyclopentanecarbaldehyde 14f. According to TP.3 above, epoxy-ketone **13f** (5 g, 32 mmol) gave β-keto aldehyde **14f** (3.83 g, 77%). Bp=40–43 °C/0.5 mmHg (lit.:[20b] 49–50 °C/1 mmHg). IR (neat): 2950, 1750, 1450, 1360, 1250, 1150, 840 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 9.45 (s, 1H, C*H*=O), 2.56 (dd, ^2J=13.6 Hz, ^4J_w=1.8 Hz, 1H, CH_aH_b–Cq), 2.18 (d, ^2J=17.3 Hz, 1H, CH_aH_b–CO), 2.18 (dd, ^2J=17.3 Hz, ^4J_w=1.8 Hz, 1H, CH_aH_b–CO), 1.56 (d, ^2J=13.6 Hz, 1H, CH_aH_b–Cq), 1.32 (s, 3H, CH_3), 1.13 (s, 3H, CH_3), 0.99 (s, 3H, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 215.3 (*C*=O), 198.7 (*C*H=O), 63.1 (C-1), 53.2 (C-3), 44.3 (C-5), 33.8 (C-4), 29.7 (*gem*-CH_3), 28.9 (*gem*-CH_3), 21.3 (CH_3).

4.3.4. Reduction of β-keto aldehyde 14f with Raney nickel. Raney nickel (50% slurry in water; 1.17 g, 10 mmol) was added to a stirred solution of β-keto aldehyde **14f** (154 mg, 1 mmol) in THF (10 mL). After stirring for 1.5 h at room temperature, the reaction mixture was filtered through Celite (EE as eluent). Solvents were evaporated. Purification of the crude oil on silica gel (PE–EE 60:40) gave β-keto alcohol **5f** (62 mg, 40%) and cyclopentanone **15f**[48] (66 mg, 52%).

4.3.5. Typical procedure for the reduction of β-keto aldehydes 14d–f to β-keto alcohols 5d–f (TP.4). β-Keto alcohol **5f** (Table 2, entry 3): to a freshly prepared ethereal solution of $LiAlH_4$ (0.75 M, 58 mL, 43.5 mmol) cooled at −40 °C was added *tert*-butanol (9.3 g, 129 mmol) in dry THF (30 mL). The solution was stirred for 4 h at −40 °C and then cooled to −78 °C. A solution of β-keto aldehyde **14f** (6.7 g, 43 mmol) in dry THF (20 mL) was added slowly and the resulting mixture was stirred for 1.5 h. After warming up to room temperature, the reaction mixture was poured into water (40 mL). The mixture was extracted with Et_2O, dried over $MgSO_4$, and the solvent removed in vacuo. The resulting oil was then purified by flash chromatography (PE–EE 50:50) to afford the expected β-keto alcohol **5f** (5.23 g, 78%).

4.3.5.1. 2-Hydroxymethyl-2,4,4-trimethylcyclopentanone 5f.[18] R_f=0.30 (PE–EE 40:60). IR (neat): 3440, 2950, 1730, 1450, 1020 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 3.50 (d, ^2J=10.4 Hz, 1H, CH_aH_bOH), 3.42 (d, ^2J=10.4 Hz, 1H, CH_aH_bOH), 2.40 (s, 1H, OH), 2.25 (d, ^2J=17.3 Hz, 1H, CH_aH_b–CO), 2.17 (d, ^2J=17.3 Hz, 1H, CH_aH_b–CO), 1.96 (d, ^2J=13.6 Hz, 1H, CH_aH_b), 1.64 (d, ^2J=13.6 Hz, 1H, CH_aH_b), 1.13 (s, 6H, 2CH_3), 1.11 (s, 3H, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 224.3 (C=O), 69.0 (CH_2O), 54.0 (C-5), 50.9 (C-2), 47.4 (C-3), 33.4 (C-4), 30.4 (*gem*-CH_3), 30.3 (*gem*-CH_3), 22.4 (CH_3). MS (EI) *m/z*: 156 (M^+, 6), 141 (M^+-CH_3, 5), 126 ($M^+-CH_2{=}O$, 15), 101 (18), 97 (47), 83 (57), 69 (29), 59 (100), 56 (87), 43 (66). Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32; found: C, 69.06; H, 10.41.

4.3.5.2. 2-Hydroxymethyl-2-methylcyclopentanone 5d.[16c,17] According to TP.4 above, β-keto aldehyde **14d** (4 g, 32 mmol) gave cyclopentanone **5d** as a colorless oil (1.2 g, 30%). R_f=0.16 (PE–EE 50:50). IR (neat): 3450, 2960, 1740, 1450, 1160, 1050 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 3.54 (d, ^2J=10.8 Hz, 1H, CH_aH_bO), 3.45 (d, ^2J=10.8 Hz, 1H, CH_aH_bO), 2.48 (br s, 1H, O*H*), 2.30 (m, 1H, H-3), 2.25–1.74 (m, 4H, H-4 and H-5), 1.70 (m, 1H, H-3′), 1.01 (s, 3H, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 224.3 (C=O), 67.1 (CH_2O), 50.3 (C-2), 38.4 (C-5), 33.2 (C-3), 19.3 (CH_3), 18.9 (C-4).

4.3.5.3. 2,4-Dimethyl-2-hydroxymethylcyclopentanone 5e.[49] According to TP.4 above, β-keto aldehyde **14e** (7 g, 50 mmol) gave cyclopentanone **5e** as a colorless oil (1.8 g, 28%). R_f=0.20 (PE–EE 50:50). GC (100 °C+10 °C/min): cis–trans=82:18; cis (345 s), trans (366 s). IR (neat) (cis+trans): 3450, 2960, 1735, 1460, 1405, 1380, 1245, 1150, 1050 cm^{-1}. GC–MS (EI) *m/z*: 142 (M^+, 10), 127 (4), 124 (6), 112 (8), 97 (17), 83 (100), 69 (40), 57 (43), 41 (54) for both diastereomers. HRMS (EI): calcd for $C_8H_{14}O_2$ [M^+]: 142.0994; found: 142.0991.

Data for major *cis*-**5e**: ^1H NMR (300 MHz, $CDCl_3$) δ: 3.64 (d, ^2J=11.0 Hz, 1H, CH_aH_bO), 3.44 (d, ^2J=11.0 Hz, 1H, CH$_a$$H_b$O), 2.40–2.58 (dd, ^2J=18.2 Hz, ^3J=7.5 Hz, 1H, CH_aH_b–CO), 2.15–2.40 (m, 2H, H-4 and CH$_a$$H_b$–CO), 1.75–2.0 (m, 2H, H-3 and O*H*), 1.60–1.72 (m, 1H, H-3′), 1.14 (d, ^3J=6.2 Hz, 3H, CHCH_3), 1.02 (s, 3H, CCH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 223.9 (C=O), 66.9 (*C*H_2O), 52.4 (C-2), 47.2 (C-5), 41.3 (C-3), 27.5 (C-4), 20.3 (C*C*H_3), 19.5 (CH*C*H_3).

Data for minor *trans*-**5e**: ^1H NMR (300 MHz, $CDCl_3$) δ: 3.60 (d, ^2J=10.3 Hz, 1H, CH_aH_bO), 3.46 (d, ^2J=10.3 Hz, 1H, CH$_a$$H_b$O), 1.11 (d, ^3J=6.0 Hz, 3H, CHCH_3), 1.09 (s, 3H, CCH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 223.9 (C=O), 67.4 (*C*H_2O), 51.8 (C-2), 46.9 (C-5), 43.0 (C-3), 28.0 (C-4), 21.0 (CH*C*H_3), 20.7 (C*C*H_3).

4.3.6. Reduction of β-keto aldehyde 14f to β-keto alcohol 5f and diol 6f. A similar reduction of β-keto aldehyde **14f** (3.7 g, 24 mmol) was performed at −78 °C for 1 h with 1 equiv of a reducing agent obtained from $AlLiH_4$ and *t*-BuOH stirred during only 0.5 h at −40 °C. Purification by flash chromatography (PE–EE 50:50) gave β-keto alcohol **5f** (1.84 g, 50%), *cis*-diol **6f** (0.3 g, 8%), and *trans*-diol **6f** (0.88 g, 24%), both diastereomeric diols as white solids (trans–cis 75:25).

4.3.6.1. *cis*-2-Hydroxymethyl-2,4,4-trimethylcyclopentanol, *cis*-6f. Mp: 87 °C. R_f=0.13 (PE–EE 40:60). IR (neat): 3300, 2960, 2860, 1450, 1200, 1070, 1025 cm^{-1}. GC (DB5, 100 °C+10 °C/min): 311 s. ^1H NMR (300 MHz, $CDCl_3$) δ: 4.10 (dd, ^3J=8.1 Hz, ^3J=5.9 Hz, 1H, C*H*–OH), 3.75 (d, ^2J=11.0 Hz, 1H, CH_aH_bOH), 3.40 (d, ^2J=11.0 Hz, 1H, CH$_a$$H_b$OH), 2.38 (s, 1H, O*H*), 1.88 (dd, ^2J=13.2 Hz, ^3J=5.9 Hz, 1H, CH_aH_b–CH(OH)), 1.63 (dd, ^2J=13.2 Hz, ^3J=8.1 Hz, 1H, CH_aH_b–CH(OH)), 1.59 (s, 2H, H-3), 1.12 (s, 3H, CH_3), 1.09 (s, 3H, CH_3), 1.04 (s, 3H, CH_3).

4.3.6.2. *trans*-2-Hydroxymethyl-2,4,4-trimethylcyclopentanol, *trans*-6f. Mp: 81 °C. R_f=0.06 (PE–EE 40:60); 0.18 (EE). IR (neat): 3320, 2960, 2860, 1460, 1070, 1035 cm^{-1}. GC (DB5, 100 °C+10 °C/min): 319 s. ^1H NMR (300 MHz, $CDCl_3$) δ: 4.15 (dd, ^3J=10.7 Hz, ^3J=6.7 Hz, 1H, C*H*–OH), 3.51 (d, ^2J=10.3 Hz, 1H, CH_aH_bOH), 3.47 (d, ^2J=10.3 Hz, 1H, CH$_a$$H_b$OH), 2.38 (s, 1H, O*H*), 1.81 (dd, ^2J=12.3 Hz, ^3J=6.7 Hz, 1H, CH_aH_b–CH(OH)), 1.64 (dd, ^2J=12.3 Hz, ^3J=10.7 Hz, 1H, CH$_a$$H_b$–CH(OH)), 1.33 (s, 2H, H-3), 1.11 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 1.01 (s, 3H, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 77.8 (C-1), 72.4 (*C*H_2–OH), 49.1 (C-5), 47.3 (C-3), 46.4 (C-2), 33.5 (C-4), 32.5 (2′CH$_3$, *gem*-Me_2), 17.9 (*C*H_3). GC–MS (EI): 140 (M^+−H_2O, 4), 125 (M^+−H_2O−CH_3, 47), 107 (30), 96 (100), 83 (76), 57 (98), 43 (92).

4.3.7. Typical procedure for the synthesis of diethoxyphosphinylacetates 16a–f (TP.5). Diethoxyphosphinylacetate **16a** (Table 4, entry 1): a solution of dimethylaminopyridine DMAP (75 mg, 0.6 mmol) in anhydrous CH_2Cl_2 (2 mL) was added to a solution of β-keto alcohol **5a** (936 mg, 5.66 mmol), diethoxyphosphinylacetic acid (1.82 g, 9.4 mmol), and dicyclohexylcarbodiimide DCC (1.89 g, 9.4 mmol) in CH_2Cl_2 (10 mL) stirred at 0 °C. The reaction mixture was stirred at 20 °C for 3 h. The precipitated urea was filtered off and the filtrate was washed successively twice with 0.5 N HCl and with a saturated $NaHCO_3$ solution, and then dried over $MgSO_4$. After removal of the solvent by evaporation, purification by flash chromatography (silica, Et_2O) afforded the diethoxyphosphinylacetate **16a** as a colorless oil (1.7 g, 89%).

4.3.7.1. 1-Butyl-2-oxocyclopentanemethyl diethoxyphosphinylacetate 16a. R_f=0.35 (EE–CH_2Cl_2 90:10). ^1H NMR (300 MHz, $CDCl_3$) δ: 4.05–4.20 (m, 6H, 3CH_2O), 2.72 (d, $^2J_{P-H}$=21.6 Hz, 2H, PCH_2CO_2), 2.22 (t, ^3J=6.8 Hz, 2H, H-3), 2.05–1.81 (m, 4H, H-4 and H-5), 1.32 (t, ^3J=7.2 Hz, 2H, C–CH_2), 1.27 (t, ^3J=7.2 Hz, 6H, 2×OCH$_2$CH_3), 1.15 (m, 4H, CH_2CH_2), 0.81 (t, ^3J=7.0 Hz, 3H, CH$_2$CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 220.9 (C=O), 166.0 (d, $^2J_{C-P}$=6.2 Hz, PCH$_2$*C*=O), 68.7 (*C*H_2O), 63.1 (d, $^2J_{C-P}$=6.2 Hz, P–O–*C*H_2), 63.0 (d, $^2J_{C-P}$=6.2 Hz, P–O–*C*H_2), 51.9 (C-1), 38.9 (C-3), 34.6 (d, $^1J_{C-P}$=133.6 Hz, P*C*H_2CO_2), 33.6 (C–*C*H_2), 31.0 (*C*H_2), 26.6 (*C*H_2), 23.6 (C-5), 19.3 (C-4), 16.7 (d, $^3J_{C-P}$=6.2 Hz, 2×P–O–CH$_2$*C*H_3), 14.2 (*C*H_3).

4.3.7.2. 1-Benzyl-2-oxocyclopentanemethyl diethoxyphosphinylacetate 16b. According to TP.5 above, β-keto alcohol **5b** (275 mg, 1.35 mmol) gave diethoxyphosphinylacetate **16b** as a colorless oil (470 g, 91%). R_f=0.12 (EE). IR (neat): 2980, 1740, 1450, 1400, 1260, 1010 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.09–7.28 (m, 5H, Ar–H), 4.17 (qd, ^3J=7.2 Hz, $^3J_{H-P}$=7.2 Hz, 4H, 2×P–OCH_2CH$_3$), 3.43 (dd, ^2J=13.8 Hz, 1H, CH_aH_bO), 3.28 (dd, ^2J=13.8 Hz, 1H, CH$_a$$H_b$O), 2.88 (d, $^2J_{P-H}$=21.6 Hz, 2H, P–CH_2–CO), 2.87 (d, ^2J=13.6 Hz, 1H, CH_aH_bPh), 2.68 (d, ^2J=13.6 Hz, 1H, CH$_a$$H_b$Ph), 2.38–2.22 (m, 1H, H-3), 2.15–2.02 (m, 1H, H-3′), 2.00–1.89 (m, 1H, H-5), 1.84–1.66 (m, 2H, H-4), 1.61–1.50 (m, 1H, H-5′), 1.35 (t, ^3J=7.2 Hz, 6H, 2×P–OCH$_2$CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 220.5 (C=O), 165.9 (d, ^2J=6.2 Hz, PCH$_2$*C*=O), 136.7 (Ar–C_{ipso}), 130.5 (2×Ar–C_{ortho}), 128.8 (2×Ar–C_{meta}), 127.3 (Ar–C_{para}), 68.6 (*C*H_2O), 63.0 (d, $^2J_{C-P}$=6.2 Hz, 2×P–O–*C*H_2), 53.7 (C-1), 39.6 (C-3), 39.1 (*C*H_2Ph), 34.7 (d, $^1J_{C-P}$=133.1 Hz, P*C*H_2CO_2), 30.0 (C-5), 16.7 (d, $^3J_{C-P}$=6.2 Hz, 2×P–O–CH$_2$*C*H_3).

4.3.7.3. 1-Allyl-2-oxocyclopentanemethyl diethoxyphosphinylacetate 16c. According to TP.5 above, β-keto alcohol **5c** (200 mg, 1.35 mmol) gave diethoxyphosphinylacetate **16c** as a colorless oil (347 mg, 80%). R_f=0.11 (EE). ^1H NMR (300 MHz, $CDCl_3$) δ: 5.64 (ddt, $^3J_{trans}$=16.0 Hz, $^3J_{cis}$=10.9 Hz, ^3J=7.5 Hz, 1H, *H*C=CH$_2$), 5.9 (dt, ^3J=10.9 Hz, $^4J_{allyl}$=1.5 Hz, 1H, HC=C*H*H), 5.8 (d,

^3J=16.0 Hz, 1H, HC=CH*H*), 4.12 (m, 6H, CH_2O and 2×POCH_2CH$_3$), 2.92 (d, $^2J_{P-H}$=21.6 Hz, 2H, PCH_2CO), 2.22 (m, 4H, H-3 and CH$_2$Ph), 1.82 (m, 4H, H-4 and H-5), 1.31 (t, ^3J=7.1 Hz, 6H, 2×OCH$_2$CH_3). ^{13}C NMR (75.5 MHz, CDCl$_3$) δ: 220.1 (C=O), 165.9 (d, $^2J_{C-P}$= 6.2 Hz, PCH$_2$CO), 132.6 (H*C*=CH$_2$), 119.7 (C$_{16}$), 68.3 (*C*H$_2$O), 63.1 (d, $^2J_{C-P}$=8.0 Hz, POCH$_2$CH$_3$), 51.8 (C-1), 38.8 (C-3), 38.0 (*C*H$_2$Allyl), 34.6 (C$_9$, d, $^1J_{C-P}$=133.2 Hz, PCH$_2$CO), 30.5 (C-5), 19.2 (C-4), 16.7 (d, $^3J_{C-P}$=6.2 Hz, 2×POCH$_2$*C*H$_3$). MS (ESI): 687.05 (90, 2M+Na$^+$), 355.27 (85, M+Na$^+$), 333.17 (100, MH$^+$).

4.3.7.4. 1-Methyl-2-oxocyclopentanemethyl diethoxyphosphinylacetate 16d. According to TP.5 above, β-keto alcohol **5d** (700 mg, 5.46 mmol) gave diethoxyphosphinylacetate **16d** as a colorless oil (1.3 g, 82%). R_f=0.1 (EE). IR (neat): 2980, 1740, 1260, 1040, 970 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$) δ: 4.12 (2×qd, ^3J=7.0 Hz, $^3J_{P-H}$= 8.1 Hz, 4H, 2×OCH_2CH$_3$), 4.09 (d, ^2J=11.0 Hz, 1H, H$_{6'}$), 4.04 (d, ^2J=11.0 Hz, 1H, H$_6$), 2.91 (d, $^2J_{H-P}$=21.7 Hz, 2H, H$_9$), 1.6–2.4 (m, 6H, H$_{3-5}$), 1.31 (t, ^3J=7.0 Hz, 6H, H$_{13,13'}$), 1.01 (s, 3H, H$_{14}$). ^{13}C NMR (75.5 MHz, CDCl$_3$) δ: 220.3 (C-2), 165.5 (d, $^2J_{C-P}$=6.2 Hz, PCH$_2$*C*=O), 68.6 (*C*H$_2$O), 62.7 (d, $^2J_{C-P}$=7.9 Hz, 2×POCH_2CH$_3$), 48.3 (C-1), 38.0 (C-3), 34.2 (d, $^1J_{C-P}$=133.1 Hz, PCH_2CO), 33.1 (C-5), 19.6 (C*C*H$_3$), 18.7 (C-4), 16.3 (d, $^3J_{C-P}$= 6.2 Hz, 2×POCH$_2$*C*H$_3$).

4.3.7.5. 1,4-Dimethyl-2-oxocyclopentanemethyl diethoxyphosphinylacetate 16e. According to TP.5 above, β-keto alcohol **5e** (1.7 g, 12 mmol) gave diethoxyphosphinylacetate **16e** as a colorless oil (3.41 g, 90%; cis–trans=80:20). R_f=0.13 (EE). IR (neat, cis+trans): 2960, 1740, 1270, 1040, 940 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$) of major diastereomer *cis*-**16e**: δ 4.12 (2×qd, ^3J=7.0 Hz, $^3J_{P-H}$=7.4 Hz, 4H, 2×POCH_2CH$_3$), 4.08 (d, ^2J=10.7 Hz, 2H, CH_aH$_b$O), 4.04 (d, ^2J=10.7 Hz, 2H, CH$_a$$H_b$O), 2.91 (d, $^2J_{H-P}$=21.3 Hz, 2H, PCH_2CO), 2.47 (ddd, ^2J=18.0 Hz, ^3J=7.0 Hz, ^4J=2.2 Hz, 1H, H-5), 2.35–2.10 (m, 1H, H-4), 2.09 (m, 1H, H-3), 1.85 (dd, ^2J=18.0 Hz, ^3J=10.2 Hz, 1H, H-5′), 1.68 (dd, ^2J=12.5 Hz, ^3J=10.2 Hz, 1H, H-3′), 1.31 (t, ^3J=7.0 Hz, 6H, 2×OCH$_2$CH_3), 1.28 (d, ^3J=6.3 Hz, 3H, CHCH_3), 1.01 (s, 3H, CCH_3). ^{13}C NMR (75.5 MHz, CDCl$_3$) δ: 219.7 (C=O), 165.5 (d, $^2J_{C-P}$=6.2 Hz, PCH$_2$*C*=O), 68.6 (*C*H$_2$O), 62.7 (d, $^2J_{C-P}$=6.2 Hz, P–OCH_2CH$_3$), 62.6 (d, $^2J_{C-P}$=6.2 Hz, POCH_2CH$_3$), 50.2 (C-1), 46.7 (C-3), 41.3 (C-5), 34.2 (d, $^1J_{C-P}$=133.1 Hz, P–*C*H$_2$CO), 27.4 (C-4), 20.2 (CH*C*H$_3$), 19.7 (*C*H$_3$), 16.4 (d, $^3J_{C-P}$=6.2 Hz, P–OCH$_2$*C*H$_3$), 16.3 (d, $^3J_{C-P}$=6.2 Hz, P–OCH$_2$*C*H$_3$).

4.3.7.6. 2-Oxo-2,4,4-trimethylcyclopentanemethyl diethoxyphosphinylacetate 16f. According to TP.5 above, β-keto alcohol **5f** (1.41 g, 9 mmol) gave diethoxyphosphinylacetate **16f** as a colorless oil (2.72 g, 90%). R_f=0.28 (EE). IR (neat): 2940, 1740, 1450, 1730, 1450, 1260, 960, 780 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$) δ: 4.14 (2×qd, ^3J=7.0 Hz, $^3J_{P-H}$=8.1 Hz, 4H, 2×P–OCH_2CH$_3$), 2.94 (d, $^2J_{P-H}$=21.7 Hz, 2H, P–CH_2CO), 3.99 (s, 2H, CH_2O), 2.30 (d, ^2J=17.3 Hz, 1H, H-3), 2.23 (d, ^2J=17.3 Hz, 1H, H-3′), 2.06 (d, ^2J=13.6 Hz, 1H, H-5), 1.70 (d, ^2J=13.6 Hz, 1H, H-5′), 1.32 (t, ^3J=7.0 Hz, 6H, 2×OCH$_2$CH_3), 1.11 (s, 3H, CCH_3), 1.08 and 1.05 (2s, 2×3H, *gem*-CH$_3$). ^{13}C NMR (75.5 MHz, CDCl$_3$) δ: 220.3 (C=O), 165.5 (d, $^2J_{P-C}$= 6.2 Hz, P–CH$_2$*C*=O), 70.3 (*C*H$_2$O), 62.7 (d, $^2J_{P-C}$= 6.2 Hz, P–O*C*H$_2$), 16.3 (d, $^3J_{P-C}$=6.2 Hz, P–OCH$_2$*C*H$_3$), 62.68 (d, $^2J_{P-C}$=6.2 Hz, P–OCH_2CH$_3$), 53.6 (C-3), 48.9 (C-1), 47.1 (C-5), 34.3 (d, $^1J_{P-C}$=133.7 Hz, P–*C*H$_2$CO), 33.1 (C-4), 30.3 (*C*H$_3$), 30.2 (*C*H$_3$), 22.6 (C*C*H$_3$), 16.4 (d, $^3J_{P-C}$=6.2 Hz, 2×P–OCH$_2$*C*H$_3$). MS (CI): 335 (100, MH$^+$).

4.3.8. Typical procedure for the synthesis of bicyclic δ-lactones 17a–f (TP.6). Lactone **17f** (Table 4, entry 6): to a solution of diethylphosphinylacetate **16f** (2 g, 6 mmol) and LiBr (1.67 g, 19.2 mmol) in dry THF (10 mL) at 0 °C under nitrogen was added NEt$_3$ (30 mmol). The reaction mixture was stirred at room temperature for 3 h. The precipitated solid was filtered and washed with PE. The solvents were then evaporated, and water (10 mL) was added to the residue. The mixture was extracted with dichloromethane (2×20 mL), washed with water, dried over MgSO$_4$, and the solvent removed in vacuo. The oily residue was then purified by flash chromatography (silica gel, PE–EE 60:40) to give the unsaturated δ-lactone **17f** as a white solid (0.7 g, 90%).

4.3.8.1. 6,6,7a-Trimethyl-5,6,7,7a-tetrahydrocyclopenta[*c*]pyran-3(1*H*)-one 17f. Mp: 55–56 °C. R_f=0.30 (PE–EE 60:40). IR (CHCl$_3$ solution): 2960, 1725, 1450, 1200, 1140, 850 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$) δ: 5.70 (d, ^4J=2.2 Hz, 1H, C=C*H*), 4.15 (d, ^2J=10.7 Hz, 1H, CH_aH$_b$O), 4.07 (d, ^2J=10.7 Hz, 1H, CH$_a$$H_b$O), 2.55 (dd, ^2J=15.4 Hz, ^4J=2.6 Hz, 1H, H-5), 2.22 (d, ^2J= 15.4 Hz, 1H, H-5′), 1.58 (d, ^2J=13.6 Hz, 1H, H-7), 1.46 (d, ^2J=13.6 Hz, 1H, H-7′), 1.29 (s, 3H, CH$_3$), 1.22 (s, 3H, CH$_3$), 0.98 (s, 3H, CH$_3$). ^{13}C NMR (75.5 MHz, CDCl$_3$) δ: 173.2 (C=O), 164.3 (C-4a), 110.7 (C=*C*H), 77.4 (*C*H$_2$–O), 49.4 (C-5), 46.2 (C-7), 41.1 (C-7a), 38.9 (C-6), 30.4 (*C*H$_3$), 29.8 (*C*H$_3$), 24.8 (*C*H$_3$). MS (EI) *m*/*z*: 180 (M$^+$, 44), 165 (M$^+$−CH$_3$, 36), 150 (64), 135 (60), 125 (52), 107 (56), 97 (100), 83 (84), 55 (92), 43 (76). Anal. Calcd for C$_{11}$H$_{16}$O$_2$: C, 73.30; H, 8.95; found: C, 73.04; H, 8.96.

4.3.8.2. 7a-Butyl-5,6,7,7a-tetrahydrocyclopenta[*c*]pyran-3(1*H*)-one 17a. According to TP.6 above, phosphinylacetate **16a** (195 mg, 0.56 mmol), LiBr (156 mg, 1.79 mmol), and NEt$_3$ (0.78 mL, 5.6 mmol) gave lactone **17a** (78.5 mg, 72%) as an oil. R_f=0.22 (PE–EE 50:50). IR (neat): 2960, 1725, 1460, 1390, 1210, 1050, 1030, 870, 840 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$) δ: 5.70 (dd, $^4J_{allyl}$=2.1 Hz, $^4J_{allyl}$=1.7 Hz, 1H, H-4), 4.39 (d, ^2J=10.9 Hz, 1H, CH_aH$_b$O), 3.94 (d, ^2J=10.9 Hz, 1H, CH$_a$$H_b$O), 2.68–2.40 (m, 2H, H-5), 1.96–1.75 (m, 4H, H-6 and CH_2CH$_3$), 1.62–1.21 (m, 6H, H-7 and CH_2CH_2), 0.89 (t, ^3J=7.0 Hz, 3H, CH$_3$). ^{13}C NMR (75.5 MHz, CDCl$_3$) δ: 174.3 (C=O), 165.1 (C-4a), 111.3 (C=*C*H), 74.9 (*C*H$_2$–O), 45.6 (C-7a), 33.4 (C-5), 32.9 (C-7), 30.5 (*C*H$_2$), 27.1 (*C*H$_2$), 23.5 (C-6), 22.9 (*C*H$_2$), 14.3 (*C*H$_3$). MS (EI) *m*/*z*: 194 (M$^+$, 6), 164 (M$^+$−CH$_2$O, 20), 150 (8), 138 (20), 121 (100), 121 (24), 93 (46), 79 (46), 67 (20), 41 (54). HRMS: calcd for C$_{12}$H$_{18}$O$_2$ [M$^+$]: 194.1307; found: 194.1308.

4.3.8.3. 7a-Benzyl-5,6,7,7a-tetrahydrocyclopenta-[*c*]pyran-3(1*H*)-one 17b. According to TP.6 above, phosphinylacetate **16b** (450 mg, 1.18 mmol), LiBr (300 mg, 3.68 mmol), and NEt$_3$ (1.7 mL, 11.8 mmol) gave lactone

17b (215 mg, 80%) as an oil. R_f=0.53 (EE). IR (neat): 3050, 2940, 1735, 1600, 1490, 1460, 1390, 1270, 1210, 1140, 1060, 1030, 990, 820, 760, 700 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.21–7.30 (m, 5H, Ar–H), 5.82 (t, $^4J_{allyl}$=1.9 Hz, 1H, H-4), 4.38 (d, ^2J=10.9 Hz, 1H, CH_aH_bO), 3.89 (d, ^2J=10.9 Hz, 1H, CH_aH_bO), 2.79 (d, ^2J=13.6 Hz, 1H, CH_aH_bPh), 2.70 (d, ^2J=13.6 Hz, 1H, CH_aH_bPh), 2.62–2.52 (m, 2H, H-5), 2.10–1.90 (m, 3H, H-6 and H-7), 1.26–1.15 (m, 1H, H-7′). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 174.2 (C=O), 164.9 (C-4a), 136.8 (Ar–C_{ipso}), 130.8 (2×Ar–C_{ortho}), 128.8 (2×Ar–C_{meta}), 127.3 (Ar–C_{para}), 112.0 (C=*C*H), 74.2 (*C*H_2–O), 46.9 (C-7a), 38.5 (*C*H_2Ph), 31.8 (C-5), 30.5 (C-7), 22.7 (C-6). MS (EI) *m*/*z*: 228 (M^+, 16), 219 (2), 181 (4), 169 (6), 149 (6), 137 (M^+−Bn, 12), 119 (8), 91 (Bn^+, 100), 77 (6), 69 (20), 57 (6), 43 (6). HRMS (EI): calcd for $C_{15}H_{16}O_2$ [M^+]: 228.1151; found: 228.1150.

4.3.8.4. 7a-Allyl-5,6,7,7a-tetrahydrocyclopenta[*c*]-pyran-3(1*H*)-one 17c. According to TP.6 above, phosphinylacetate **16c** (300 mg, 0.9 mmol), LiBr (235 mg, 2.7 mmol), and NEt_3 (1.26 mL, 9 mmol) gave lactone **17c** (135.4 mg, 85%) as an oil. R_f=0.61 (EE). IR (neat): 2950, 1740, 1450, 1390, 700 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 5.13 (ddt, ^3J=17.7 Hz, ^3J=10.2 Hz, ^3J=7.5 Hz, 1H, H_2C=C*H*), 5.72 (t, ^4J=1.9 Hz, 1H, C=C*H*–C=O), 5.13 (ddd, ^3J=17.7 Hz, ^3J=10.2 Hz, $^4J_{allyl}$=1.0 Hz, 2H, H_2C=CH), 4.39 (d, ^2J=10.9 Hz, 1H, CH_aH_bO), 3.93 (d, ^2J=10.9 Hz, 1H, CH_aH_bO), 2.65–2.47 (m, 2H, H-5), 2.26 (dd, ^2J=13.9 Hz, ^3J=7.7 Hz, 1H, CH_aH_b–CH=CH_2), 2.14 (dd, ^2J=13.9 Hz, ^3J=7.2 Hz, 1H, CH_aH_b–CH=CH_2), 1.98–1.75 (m, 3H, H-6 and H-7), 1.35–1.23 (m, 1H, H-7′). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 173.5 (C=O), 164.8 (C-4a), 132.8 (*C*H=CH_2), 120.1 (CH=*C*H_2), 111.7 (C=*C*H–CO), 74.5 (*C*H_2–O), 45.7 (C-7a), 37.5 (*C*H_2Allyl), 32.4 (C-5), 30.4 (C-7), 22.7 (C-6). MS (CI): 357 ([2M+H]$^+$, 50), 179 ([MH]$^+$, 100). HRMS (CI): calcd for $C_{11}H_{15}O_2$ [MH^+]: 179.1072; found: 179.1071.

4.3.8.5. 7a-Methyl-5,6,7,7a-tetrahydrocyclopenta[*c*]-pyran-3(1*H*)-one 17d. According to TP.6 above, phosphinylacetate **16d** (930 mg, 3.04 mmol), LiBr (846 mg, 9.73 mmol), and NEt_3 (4.23 mL, 30.31 mmol) gave lactone **17d** (320 mg, 70%) as an oil. R_f=0.20 (PE–EE 60:40). IR (neat): 2940, 1740, 1460, 1220, 1140, 870, 840 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 5.66 (dd, $^4J_{allyl}$=1.5 Hz, $^4J_{allyl}$=1.8 Hz, 1H, C=C*H*), 4.24 (d, ^2J=10.7 Hz, 1H, CH_aH_bO), 4.04 (d, ^2J=10.7 Hz, 1H, CH_aH_bO), 2.63 (dddd, ^2J=19.1 Hz, ^3J=9.2 Hz, ^3J=4.8 Hz, $^4J_{allyl}$=1.8 Hz, 1H, H-5), 2.52 (dtd, ^2J=19.1 Hz, ^3J=8.5 Hz, $^4J_{allyl}$=1.5 Hz, 1H, H-5′), 2.05–1.80 (m, 1H, H-6), 1.65 (ddd, ^2J=12.5 Hz, ^3J=6.6 Hz, ^4J_w=2.6 Hz, 1H, H-7), 1.42 (ddd, ^2J=12.5 Hz, ^3J=8.5 Hz, ^4J_w=2.2 Hz, 1H, H-7′), 1.18 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 174.1 (C=O), 164.6 (C-4a), 110.8 (C=*C*H), 77.2 (*C*H_2–O), 42.1 (C-7a), 35.7 (C-5), 26.7 (C-7), 22.4 (C-6), 21.4 (*C*H_3). MS (EI) *m*/*z*: 152 (M^+, 4), 122 ([M−CH_2O]$^+$, 33), 108 ([M−CO_2]$^+$, 20), 93 (23), 79 (100), 65 (20), 51 (36), 39 (79). Anal. Calcd for $C_9H_{12}O_2$: C, 71.02; H 7.95; found: C, 70.77; H, 8.12.

4.3.8.6. 6,7a-Dimethyl-5,6,7,7a-tetrahydrocyclopenta-[*c*]pyran-3(1*H*)-one 17e. According to TP.6 above, phosphinylacetate **16e** (3 g, 9.36 mmol), LiBr (2.6 g, 30 mmol), and NEt_3 (13 mL, 93.4 mmol) gave lactone **17e** (1.1 g, 71%) as an oil. GC (100 °C+10 °C/min): cis–trans=80:20; *syn* (516 s), *anti* (500 s). R_f=0.28 (PE–EE 60:40). IR (neat, *syn*+*anti*): 2980, 2740, 1460, 1290, 1200, 1050, 850 cm^{-1}. Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H 8.49; found: C, 71.96; H, 8.54.

Data for major *cis*-**17e** diastereomer: ^1H NMR (300 MHz, $CDCl_3$) δ: 5.63 (d, ^4J=1.8 Hz, 1H, C=C*H*), 4.20 (d, ^2J=10.7 Hz, 1H, CH_aH_bO), 4.03 (d, ^2J=10.7 Hz, 1H, CH_aH_bO), 2.85 (dd, ^2J=19.5 Hz, ^3J=9.2 Hz, 1H, H-5), 2.6–2.3 (m, 1H, H-6), 2.07 (ddd, ^2J=19.5 Hz, ^3J=3.2 Hz, ^4J=1.8 Hz, 1H, H-5′), 1.78 (dd, ^2J=12.0 Hz, ^3J=6.6 Hz, 1H, H-7), 1.3–1.17 (m, 1H, H-7′), 1.20 (s, 3H, CH_3), 1.05 (d, ^3J=6.6 Hz, 3H, CHCH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 173.8 (C=O), 164.5 (C-4a), 111.0 (C=*C*H), 77.3 (*C*H_2–O), 44.6 (C-5), 42.9 (C-7a), 37.9 (C-7), 31.3 (C-6), 21.7 (*C*H_3), 20.4 (*C*H_3). GC–MS (EI) *m*/*z*: 166 (M^+), 151 (16), 136 (100), 121 (69), 107 (36), 93 (60), 77 (55), 65 (35), 53 (28), 41 (49), 39 (65), 27 (18).

Data for minor *trans*-**17e** diastereomer: ^1H NMR (300 MHz, $CDCl_3$) δ: 5.61 (m, 1H, C=C*H*), 4.11 (d, ^2J=10.7 Hz, 1H, CH_aH_bO), 4.00 (d, ^2J=10.7 Hz, 1H, CH_aH_bO), 2.6–2.35 (m, 3H, H-5 and H-6), 1.24 (s, 3H, CH_3), 1.12 (d, ^3J=6.2 Hz, 3H, CHCH_3).

4.3.9. Typical procedure for the synthesis of saturated bicyclic δ-lactones 18a–f (TP.7). δ-Lactone **18f** (Table 4, entry 6): a solution of bicyclic δ-lactone **17f** (100 mg, 0.56 mmol) in ethyl acetate (4 mL) was hydrogenated at atmospheric pressure over 10% Pd–C (63 mg, 0.06 mmol) at room temperature for 48 h. The mixture was filtered through a plug of silica gel, washing with ethyl acetate, and the filtrate was evaporated in vacuo. The crude oil was further filtrated over silica (5–10 g), eluting with PE, to give the saturated δ-lactone **18f** as a white solid (98 mg, 98%).

4.3.9.1. 6,6,7a-Trimethylhexahydrocyclopenta[*c*]-pyran-3(1*H*)-one 18f. Mp: 49–50 °C. R_f=0.30 (PE–EE 60:40). IR ($CHCl_3$ solution): 2950, 1750, 1460, 1300, 1210, 1210, 1170, 1050 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 3.94 (d, ^2J=11.4 Hz, 1H, CH_aH_bO), 3.80 (d, ^2J=11.4 Hz, 1H, CH_aH_bO), 2.61 (dd, ^2J=16.5 Hz, ^3J=7.7 Hz, 1H, CH_aH_b–CO), 2.29 (dd, ^2J=16.5 Hz, ^3J=4.4 Hz, 1H, CH_aH_bO), 2.35–2.24 (m, 1H, H-4a), 1.79 (ddd, ^2J=12.9 Hz, ^3J=7.0 Hz, ^4J_w=2.2 Hz, 1H, H-5), 1.60 (d, ^2J=13.2 Hz, 1H, H-7), 1.42 (dd, ^2J=13.2 Hz, ^4J_w=2.2 Hz, 1H, H-7′), 1.15 (s, 3H, CH_3), 1.22 (d, ^2J=12.9 Hz, 1H, H-5′), 1.06 (s, 3H, CH_3), 1.03 (s, 3H, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 173.8 (C=O), 75.9 (*C*H_2–O), 51.3 (C-7), 49.4 (C-5), 42.0 (C-4a), 41.4 (C-7a), 38.9 (C-6), 34.2 (C-4), 32.8 and 28.3 (C_{gem}(*C*H_3)$_2$), 26.6 (C(7a)–*C*H_3) [signals of all carbon atoms were assigned with the aid of NOESY and HSQC–TOCSY 2D NMR experiments]. MS (EI) *m*/*z*: 182 (M^+, 2), 180 (4), 153 (12), 136 (16), 124 (8), 110 (M^+−CH_2–CO_2–CH_2, 60), 107 (36), 95 (64), 89 (16), 79 (20), 77 (64), 61 (65), 44 (100), 41 (44).[50] Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95; found: C, 72.14; H, 9.94.

4.3.9.2. 7a-Butylhexahydrocyclopenta[*c*]pyran-3(1*H*)-one 18a. According to TP.7 above, hydrogenation of δ-lactone **17a** (60.14 mg, 0.31 mmol) gave lactone **18a**

(58.7 mg, 97%) as a colorless oil. R_f=0.36 (PE–EE 60:40). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.04 (d, ^2J=11.5 Hz, 1H, CH_aH$_b$O), 3.90 (d, ^2J=11.5 Hz, 1H, CH$_a$$H_b$O), 2.52 (d, ^2J=15.1 Hz, 1H, CH_aH$_b$–CO), 2.30 (dd, ^2J=15.1 Hz, ^3J=6.6 Hz, 1H, CH$_a$$H_b$–CO), 2.01 (td, ^3J=7.4 Hz, ^3J=6.6 Hz, 1H, H-4a), 1.88–1.98 (m, 1H, H-5), 1.40–1.70 (m, 5H, H-6, H-7, and H-5′), 1.32–1.18 (m, 6H, CH_2CH_2CH_2), 0.89 (t, ^3J=7.2 Hz, 3H, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 174.2 (C=O), 74.0 (*C*H$_2$–O), 45.0 (C-7a), 41.8 (C-4a), 39.0 (*C*H$_2$), 35.6 (C-7), 34.9 (C-5), 34.8 (C-4), 27.0 (*C*H$_2$), 25.1 (C-6), 18.7 (*C*H$_2$–CH$_3$), 14.4 (*C*H$_3$). MS (EI) *m*/*z*: 196 (M$^+$, 20), 168 (M$^+$−CO, 16), 165 (8), 124 (M$^+$−CH$_2$–CO$_2$–CH$_2$, 100), 109 (8), 95 (30), 94 (46), 81 (40), 67 (56), 41 (20).[50] HRMS (EI): calcd for $C_{12}H_{20}O_2$ [M$^+$]: 196.1464; found: 196.1463.

4.3.9.3. 7a-Benzylhexahydrocyclopenta[*c*]pyran-3(1*H*)-one 18b. According to TP.7 above, hydrogenation of δ-lactone **17b** (100 mg, 0.44 mmol) gave lactone **18b** (96.5 mg, 96%) as a light brown oil. R_f=0.53 (EE). IR ($CHCl_3$ solution): 2950, 1740, 1600, 1490, 1450, 1380, 1280, 1220, 1050, 820, 760, 700 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.32–7.19 (m, 5H, Ar–H), 4.11 (d, ^2J=11.5 Hz, 1H, CH_aH$_b$O), 3.85 (d, ^2J=11.5 Hz, 1H, CH$_a$$H_b$O), 2.57 (dd, ^2J=14.9 Hz, ^3J=6.5 Hz, 1H, CH_aH$_b$–CO), 2.32 (dd, ^2J=14.9 Hz, ^3J=7.7 Hz, 1H, CH$_a$$H_b$–CO), 2.21 (td, ^3J=7.7 Hz, ^3J=6.8 Hz, H-4a), 2.00–1.95 (m, 1H, H-5), 1.90–1.75 (m, 1H, H-5′), 1.7–1.50 (m, 2H, H-6), 1.40–1.30 (m, 2H, H-7). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 173.7 (C=O), 137.7 (Ar–C$_{ipso}$), 130.7 (2×Ar–C$_{ortho}$), 128.7 (2×Ar–C$_{meta}$), 127.1 (Ar–C$_{para}$), 72.8 (*C*H$_2$–O), 46.2 (C-7a), 44.3 (*C*H$_2$Ph), 41.8 (C-4a), 35.1, 35.0, and 34.9 (3*C*H$_2$: C-4, C-5, and/or C-7), 25.0 (C-6). MS (EI) *m*/*z*: 230 (M$^+$, 45), 170 (20), 139 (M$^+$−Bn, 96), 129 (16), 115 (16), 95 (32), 91 (Bn$^+$, 100), 81 (24), 67 (48), 41 (16). HRMS (EI): calcd for $C_{15}H_{18}O_2$ [M$^+$]: 230.1307; found: 230.1305.

4.3.9.4. 7a-Methylhexahydrocyclopenta[*c*]pyran-3(1*H*)-one 18d. According to TP.7 above, hydrogenation of δ-lactone **17d** (100 mg, 0.66 mmol) gave lactone **18d** (98.8 mg, 98%) as a colorless oil. R_f=0.26 (PE–EE 60:40). IR (neat): 2940, 1740, 1280, 1050 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.96 (d, ^2J=11.4 Hz, 1H, CH_aH$_b$O), 3.90 (d, ^2J=11.4 Hz, 1H, CH$_a$$H_b$O), 2.55 (dd, ^2J=15.1 Hz, ^3J=6.3 Hz, 1H, CH_aH$_b$–CO), 2.26 (dd, ^2J=15.1 Hz, ^3J=5.9 Hz, 1H, CH$_a$$H_b$–CO), 1.90–2.20 (m, 2H, H-5 and H-4a), 1.20–1.70 (m, 5H, H-5′, H-6, and H-7), 1.06 (s, 3H, CH$_3$). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 173.7 (C=O), 75.3 (*C*H$_2$–O), 42.5 (C-4a), 41.3 (C-7a), 37.7 (C-7), 34.9 (C-5), 34.5 (C-4), 25.9 (*C*H$_3$), 24.7 (C-6). MS (EI) *m*/*z*: 154 (M$^+$, 1), 96 (6), 82 (M$^+$−CH$_2$–CO$_2$–CH$_2$, 100), 67 (6), 53 (19), 39 (72), 27 (29).[50] Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15; found: C, 69.56; H, 9.14.

4.3.9.5. 6,7a-Dimethylhexahydrocyclopenta[*c*]pyran-3(1*H*)-one 18e. According to TP.7 above, hydrogenation of δ-lactone **17e** (200 mg, 1.2 mmol) gave lactone **18e** (198.2 mg, 98%) as a colorless oil. GC (100 °C+10 °C/min): *endo*–*exo*=80:20; *endo* (443 s), *exo* (452 s). R_f=0.30 (PE–EE 60:40). IR (neat): 2970, 1750, 1450, 1050, 850, 810 cm^{-1}. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59; found: C, 71.52; H, 9.84.

Data for major *endo*-**18e** diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.94 (d, ^2J=11.4 Hz, 1H, CH_aH$_b$O), 3.87 (d, ^2J=11.4 Hz, 1H, CH$_a$$H_b$O), 2.55 (dd, ^2J=15.1 Hz, ^3J=6.3 Hz, 1H, CH_aH$_b$–CO), 2.27 (dd, ^2J=15.1 Hz, ^3J=4.4 Hz, 1H, CH$_a$$H_b$–CO), 2.2–1.9 (m, 4H, H-5, H-6, and H-4a), 1.53 (ddd, ^2J=12.2 Hz, ^3J=6.3 Hz, ^4J=1.8 Hz, 1H, H-7), 1.30 (d, ^2J=12.2 Hz, 1H, H-7′), 1.03 (s, 3H, CH_3), 0.95 (d, ^3J=6.3 Hz, 3H, CHCH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 173.6 (C=O), 75.2 (*C*H$_2$–O), 45.5 (C-7), 43.7 (C-5), 42.8 (C-4a), 41.3 (C-7a), 34.5 (C-4), 32.7 (C-6), 26.0 (*C*H$_3$), 18.6 (CH*C*H$_3$). GC–MS (EI) *m*/*z*: 168 (M$^+$, 1), 110 (6), 96 (M$^+$−CH$_2$–CO$_2$–CH$_2$, 41), 81 (100), 79 (12), 55 (14), 42 (32), 41 (89), 29 (17).[50]

Data for minor *exo*-**18e** diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.92 (d, ^2J=11.4 Hz, 1H, CH_aH$_b$O), 3.90 (d, ^2J=11.4 Hz, 1H, CH$_a$$H_b$O), 2.49 (dd, ^2J=14.6 Hz, ^3J=6.6 Hz, 1H, CH_aH$_b$–CO), 2.25 (dd, ^2J=14.6 Hz, ^3J=9.6 Hz, 1H, CH$_a$$H_b$–CO), 2.15–1.9 (m, 4H, H-5, H-6, and H-4a), 1.70 (dd, ^2J=13.2 Hz, ^3J=6.3 Hz, 1H, H-7), 1.20 (m, 1H, H-7′), 1.12 (s, 3H, CH_3), 0.84 (d, ^3J=10.7 Hz, 3H, CHCH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 172.5 (C=O), 75.8 (*C*H$_2$–O), 47.2 (C-7), 42.4 (C-4a), 42.2 (C-5), 42.1 (C-7a), 34.9 (C-4), 33.4 (C-6), 26.8 (*C*H$_3$), 19.3 (CH*C*H$_3$). GC–MS (EI) *m*/*z*: 96 (M$^+$−CH$_2$–CO$_2$–CH$_2$, 32), 81 (97), 79 (10), 53 (16), 41 (100), 29 (11), 18 (4).[50]

4.3.9.6. 7a-Propylhexahydrocyclopenta[*c*]pyran-3(1*H*)-one 18g. According to TP.7 above, hydrogenation of δ-lactone **17c** (80 mg, 0.45 mmol) gave lactone **18g** (80.6 mg, 99%) as an oil. R_f=0.20 (PE–EE 60:40). IR ($CHCl_3$ solution): 2960, 1750, 1450, 1390, 1300, 1200, 1100, 940 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.02 (d, ^2J=11.5 Hz, 1H, CH_aH$_b$O), 3.90 (d, ^2J=11.5 Hz, 1H, CH$_a$$H_b$O), 2.52 (d, ^2J=15.0 Hz, 1H, CH_aH$_b$–CO), 2.29 (dd, ^2J=15.0 Hz, ^3J=6.6 Hz, 1H, CH$_a$$H_b$–CO), 2.03 (td, ^3J=7.7 Hz, ^3J=6.6 Hz, 1H, H-4a), 1.86–1.96 (m, 1H, H-5), 1.45–1.70 (m, 4H, H-6, H-7, and H-5′), 1.24–1.40 (m, 5H, CH_2CH_2 and H-7′), 0.89 (t, ^3J=7.1 Hz, 3H, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 174.0 (C=O), 73.6 (*C*H$_2$–O), 44.7 (C-7a), 41.5 (C-4a), 41.4 (*C*H$_2$–CH$_2$CH$_3$), 35.3 (C-7), 34.6 (C-5), 34.5 (C-4), 24.8 (C-6), 17.7 (*C*H$_2$–CH$_3$), 14.8 (*C*H$_3$). MS (EI) *m*/*z*: 182 (M$^+$, 12), 164 (3), 151 (6), 123 (9), 110 (M$^+$−CH$_2$–CO$_2$–CH$_2$, 100), 95 (16), 81 (35), 67 (87).[50] HRMS (EI): calcd for $C_{11}H_{18}O_2$ [M$^+$]: 182.1307; found: 182.1309.

4.3.10. Synthesis of bicyclic δ-lactones 20 and 21.

4.3.10.1. Ethyl 1-benzyl-2-oxocyclohexanecarboxylate 8. R_f=0.40 (PE–EE 70:30). IR (neat): 3068, 3063, 3029, 2941, 1713, 1496, 1453, 1187 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.12–7.34 (m, 5H, Ar–*H*), 4.09 (q, ^3J=7.1 Hz, 2H, OCH_2CH$_3$), 3.31 (d, ^2J=13.7 Hz, 1H, CH_aH$_b$Ph), 2.88 (d, ^2J=13.7 Hz, 1H, CH$_a$$H_b$Ph), 2.43 (m, 3H, H-3 and H-6), 2.01 (m, 1H, H-6′), 1.57 (m, 4H, H-4 and H-5), 1.17 (t, ^3J=7.1 Hz, 3H, CH$_2$CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 215.0 (C=O), 171.0 (O–*C*=O), 136.7 (Ar–C$_{ipso}$), 130.4 (2×Ar–C$_{ortho}$), 128.8 (2×Ar–C$_{meta}$), 126.7 (Ar–C$_{para}$), 62.2 (C-1), 61.2 (OCH_2CH$_3$), 41.3 (C-3), 40.5 (C-6), 36.0 (*C*H$_2$Ph), 27.6 (C-5), 22.6 (C-4), 14.0 (*C*H$_3$).

4.3.10.2. Ethyl 1-benzyl-(2,2-ethylenedioxy)cyclohexanecarboxylate 9. With a procedure similar to TP.1 above,

β-keto ester **8** (8.01 g, 30.8 mmol) gave crude β-ketal ester **9** as a colorless oil (9.04 g, 96%). R_f=0.30 (PE–EE 50:50). IR (neat): 3086, 3062, 3028, 2944, 1726, 1496, 1455, 1195, 1180 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.21 (s, 5H, Ar–H), 4.05 (m, 6H, OCH_2CH_2O and OCH_2CH_3), 3.46 (d, ^2J=13.4 Hz, 1H, CH_aH_bPh), 2.93 (d, ^2J=13.4 Hz, 1H, CH_aH_bPh), 1.75 (m, 8H, $[CH_2]_4$), 1.19 (t, ^3J=7.1 Hz, 3H, OCH_2CH_3).

4.3.10.3. 2-Benzyl-2-hydroxymethylcyclohexanone 11.[51] With a procedure similar to TP.2 above, β-ketal ester **9** (6.9 g, 20 mmol) gave 2-hydroxymethylcyclohexanone **11** as a white solid (3.49 g, 80%). Mp =77–78 °C. R_f=0.35 (PE–EE 50:50). IR (neat): 3345, 3080, 3025, 2944, 2864, 1890, 1494, 1464, 1440, 1420, 1059 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.27–7.23 (m, 5H, Ar–H), 3.48 (d, ^2J=11.7 Hz, 1H, CH_aH_bO), 3.36 (d, ^2J=11.7 Hz, 1H, CH_aH_bO), 3.10 (d, ^2J=13.4 Hz, 1H, CH_aH_bPh), 2.91 (d, ^2J=13.4 Hz, 1H, CH_aH_bPh), 2.73 (br s, 1H, OH), 2.75–2.35 (m, 2H, H-6), 2.13–1.92 (m, 2H, H-5), 2.06–1.92 (m, 3H, H-4 and H-3), 1.55–1.42 (m, 1H, H-3′). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 218.0 (C=O), 137.2 (Ar–C_{ipso}), 130.9 (2×Ar–C_{ortho}), 128.6 (2×Ar–C_{meta}), 127.1 (Ar–C_{para}), 66.1 (CH_2O), 54.3 (C-2), 39.7 (C-6), 37.4 (CH_2Ph), 31.9 (C-3), 27.4 (C-5), 21.0 (C-4).

4.3.10.4. (1-Benzyl-2-oxocyclohexyl)methyl diethoxyphosphinylacetate 19. With a procedure similar to TP.5 above, 2-hydroxymethylcyclohexanone **11** (120 mg, 0.55 mmol) gave diethoxyphosphinylacetate **19** as a colorless oil (187 mg, 86%). R_f=0.11 (EE). IR (neat): 2960, 1740, 1450, 1260, 1020 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.28–7.09 (m, 5H, Ar–H), 4.21–4.08 (m, 6H, 2×OCH_2CH_3 and CH_2O–CO), 3.15 (d, ^2J=13.9 Hz, 1H, CH_aH_bPh), 2.99 (d, $^2J_{P-H}$=21.5 Hz, 2H, CO–CH_2–P), 2.88 (d, ^2J=13.9 Hz, 1H, CH_aH_bPh), 2.60–2.46 (m, 2H, H-6), 2.90–1.70 (m, 6H, H-3, H-4, and H-5), 1.36 (t, ^3J=7.0 Hz, 6H, 2CH_2CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 212.3 (C=O), 165.9 (d, $^2J_{C-P}$=6.2 Hz, O–C=O), 136.5 (Ar–C_{ipso}), 130.6 (2×Ar–C_{ortho}), 128.7 (2×Ar–C_{meta}), 127.1 (Ar–C_{para}), 67.6 (CH_2O–CO), 63.1 (d, $^2J_{C-P}$=6.2 Hz, 2×OCH_2CH_3), 52.8 (C-1), 39.8 (C-6), 39.1 (CH_2Ph), 34.6 (d, $^1J_{C-P}$=133.1 Hz, CO–CH_2–P), 34.4 (C-6), 27.4 (C-5), 21.2 (C-4), 16.7 (d, $^3J_{C-P}$=6.2 Hz, 2×OCH_2CH_3). MS (CI) *m/z*: 793 ($2MH^+$, 20), 297 (MH^+, 100). HRMS (CI): calcd for $C_{20}H_{29}O_6P$ [MH^+]: 397.1780; found: 397.1787.

4.3.10.5. 8a-Benzyl-5,6,7,7a-tetrahydrocyclohexa[*c*]-pyran-3(1*H*)-one 20. With a procedure similar to TP.6 above, phosphinylacetate **19** (189.7 mg, 0.48 mmol), LiBr (128 mg, 1.44 mmol), and NEt_3 (0.67 mL, 4.8 mmol) gave lactone **20** (104.4 mg, 90%) as an oil. R_f=0.25 (PE–EE 50:50). IR (neat): 2940, 1745, 1600, 1490, 1450, 1220, 1060, 860, 760, 700 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.30–7.21 (m, 5H, Ar–H), 5.80 (s, 1H, C=C*H*), 4.05 (d, ^2J=11.5 Hz, 1H, CH_aH_bO), 3.75 (d, ^2J=11.5 Hz, 1H, CH_aH_bO), 2.97 (d, ^2J=13.6 Hz, 1H, CH_aH_bPh), 2.76 (d, ^2J=13.6 Hz, 1H, CH_aH_bPh), 2.50 (m, 2H, H-5), 2.10–1.55 (m, 4H, H-6 and H-7), 1.52–1.40 (m, 1H, H-8), 0.93–0.84 (m, 1H, H-8′). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 167.3 (C=O), 165.3 (C-4a), 136.1 (Ar–C_{ipso}), 131.1 (2×Ar–C_{ortho}), 128.8 (2×Ar–C_{meta}), 127.3 (Ar–C_{para}), 115.3 (C=*C*H), 39.4 (C-8a), 73.5 (CH_2–O), 37.8 (CH_2Ph), 31.1 (C-5), 29.3 (C-8), 26.2 (C-6), 20.9 (C-7). MS (CI) *m/z*: 243 (MH^+, 100). HRMS (CI): calcd for $C_{16}H_{19}O_2$ [MH^+]: 243.1385; found: 243.1389.

4.3.10.6. 8a-Benzylhexahydrocyclohexa[*c*]pyran-3(1*H*)-one 21. With a procedure similar to TP.7 above, hydrogenation of δ-lactone **20** (80 mg, 0.33 mmol) gave lactone **21** (79.7 mg, 99%) as a colorless oil. R_f=0.25 (PE–EE 50:50). IR ($CHCl_3$ solution): 2930, 1740, 1600, 1490, 1450, 1400, 1260, 1180, 1060, 1050, 760, 700 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.25–7.10 (m, 5H, Ar–H), 4.24 (d, ^2J=11.7 Hz, 1H, CH_aH_bO), 3.79 (d, ^2J=11.7 Hz, 1H, CH_aH_bO), 2.88 (dd, ^2J=19.0 Hz, ^3J=3.2 Hz, 1H, CH_aH_b–CO), 2.84 (d, ^2J=13.5 Hz, 1H, CH_aH_bPh), 2.57 (d, ^2J=13.5 Hz, 1H, CH_aH_bPh), 2.30 (dd, ^2J=19.0 Hz, ^3J=3.1 Hz, 1H, CH_aH_b–CO), 2.10 (m, 1H, H-4a), 1.81–1.20 (m, 8H, 4CH_2). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 171.6 (C=O), 136.6 (Ar–C_{ipso}), 131.0 (2×Ar–C_{ortho}), 128.6 (2×Ar–C_{meta}), 127.1 (Ar–C_{para}), 71.9 (CH_2–O), 42.8 (CH_2Ph), 36.6 (C-4a), 35.5 (C-8a), 34.1 (C-4), 30.3 (C-8), 29.7 (C-5), 24.1 (C-7), 21.4 (C-6). MS (EI) *m/z*: 244 (M^+, 16), 213 (3), 184 (4), 153 (M^+−Bn, 100), 125 (8), 107 (28), 91 (Bn^+, 64), 81 (56). HRMS (EI): calcd for $C_{16}H_{20}O_2$ [M^+]: 244.1463; found: 244.1468.

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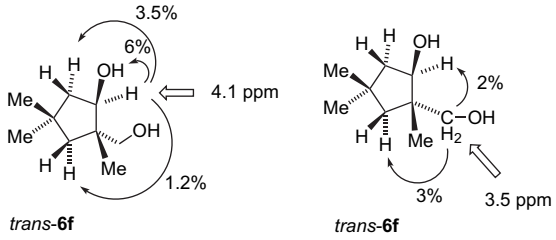

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