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Self-catalytic Michael reaction of enolizable carbonyl compounds. A facile route to α-methylene-δ-valerolactones

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Abstract—Various dicyclohexylammonium 2-phosphono-5-oxoalkanoates **3** were prepared by the Michael reaction of enolizable carbonyl compounds with the acrylate **1**. The corresponding 2-phosphono-5-oxoalkanoic acids **4** were converted into α-phosphono-δ-valerolactones **6**. The products were shown to be useful substrates for the synthesis of α-methylene-δ-valerolactones **7** by the Horner–Wadsworth–Emmons reaction.

1. Introduction

The development of methods for the synthesis of α-methylene-δ-valerolactones is an important goal since these motifs are found in compounds of biological intrest. The presence of α-methylene-δ-valerolactone unit is a characteristic structural feature of several naturally occuring terpenes such as vernolepin,[1] vernomenin,[1] pentalenolactone E,[2] teucriumlactone,[3] artemisitene,[4–6] crassin[7,8] and crassin acetate[7,8] noted for their cytotoxicity. They were shown to possess significant pharmacological activities ranging from simple antibiotic activity to antitumor properties.

α-Methylene-δ-valerolactones are also atractive precursors for a whole series of α-saturated δ-valerolactones. Michael additions of various C-, N- and S-nucleophiles to α-methylene-δ-valerolactone moiety of artimisitene have been used successfully in the synthesis of α-substituted δ-valerolactones possessing antimalarial activity.[4–6] Reduction of methylene group of teucriumlactone has been employed as a key step in the total synthesis of iridoid lactones.[9] Sugar derived α-methylene-δ-valerolactones have proven useful in the synthesis of methylene bridged disacharides.[10] Moreover, the synthetic utility of α-methylene-δ-valerolactones have been demonstrated in other C–C bond forming transformations such as Diels–Alder reaction,[11] 1,3-Michael–Claisen annulation[12,13] and Michael addition.[14]

Several approaches for the preparation of various α-methylene-δ-valerolactones have been reported.[15–23] Recent literature has indicated an interest in the synthesis of α-alkylidenelactones by means of Horner–Wadsworth–Emmons (HWE) reaction of the corresponding α-phosphonolactones.[24–28] Despite the synthetic significance of α-phosphono-δ-valerolactones only a few successful methods for their synthesis are known. They can be made by hydrogenation of α, β-unsaturated-α-phosphono-δ-lactones,[29] by C-phosphorylation of δ-valerolactones through either of two Wiemer metodologies for C–P bond formation[26,30] and finally by the Wolf rearangement of ε-trimethylsililoxy-β-oxo-α-diazophosphonates derived from γ-lactones.[31]

Recently, we have found that the Michael additions of various C and N-nucleophiles to dicyclohexylammonium 2-(diethoxyphosphoryl) acrylate **1** proceed without any external catalyst.[32–36] Our preliminary studies have also revealed that this self-catalytic reaction performed with enolizable carbonyl compounds **2a**, **2b**, **2e** provides a direct route to 2-diethoxyphosphoryl-5-oxoalkanoic acids **4a**, **4b**, **4e**[32] (Scheme 1). It became clear that acids of this type are particularly well suited for further transformation into the corresponding α-phosphono-δ-valerolactones. In this context it was felt that another carbonyl compounds that could serve as pronucleophiles would increase the scope of the already performed additions.

In this paper we report that a variety of enolizable carbonyl compounds are easily converted into 2-diethoxyphosphoryl-5-oxoalkanoic acids by the Michael reaction with the acrylate **1**. Importantly, we demonstrate that this strategically new approach provides a powerful tool for the synthesis of α-phosphono-δ-valerolactones. Transformation

Keywords: Michael reaction; 5-oxoalkanoic acids; α-phosphonolactones; α-methylene-δ-valerolactones.
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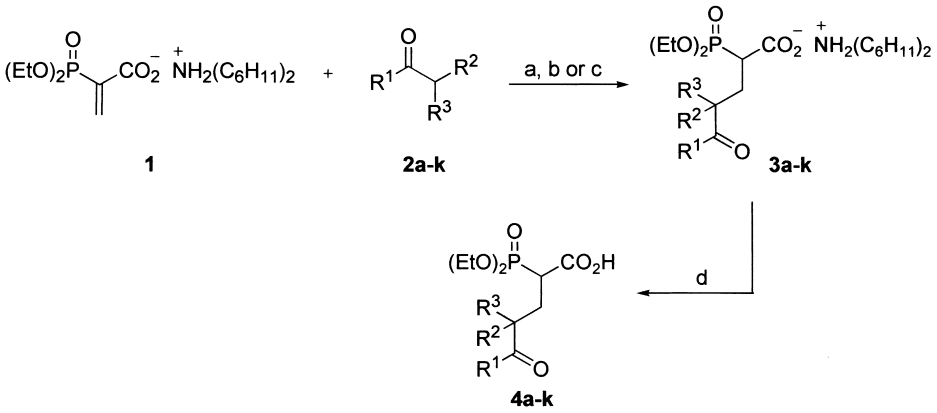


Compound	R1	R2	R3	Yield a	Compound	R1	R2	R3	Yield a
2a 3a 4a	H	CH_3	CH_3	68%	**2g 3g 4g**	H	H	CH_3	66%
2b 3b 4b	H	$(CH_2)_5$		74%	**2h 3h 4h**	H	H	CH_3CH_2	69%
2c 3c 4c	H	CH_3	$CH_3(CH_2)_2$	66%	**2i 3i 4i**	H	H	$CH_3(CH_2)_3$	72%
2d 3d 4d	H	CH_3	C_6H_5	69%	**2j 3j 4j**	H	H	$C_6H_5CH_2$	75%
2e 3e 4e	CH_3	H	H	69%	**2k 3k 4k**	$(CH_2)_4$		$CO_2C_2H_5$	84%
2f 3f 4f	$(CH_2)_4$		H	68%					

a) total yield of two steps

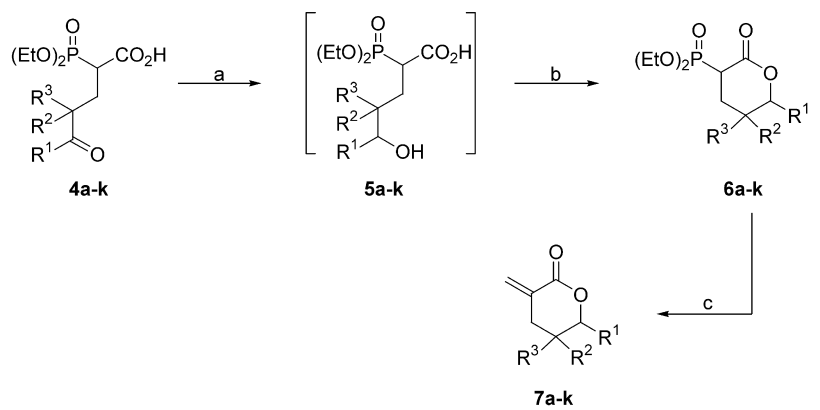
Scheme 1. *Conditions*: (a) **2a-c**, benzene, 50°C. 30 h; (b) **2e-f**, ketone, 50°C, 70 h; (c) **2d**, **2g–k**, benzene, rt, 36–48 h; (d) Dowex 50W, H_2O/acetone.

of α-phosphono-δ-valerolactones into the corresponding α-methylene-δ-valerolactones is also reported.

2. Results and discussion

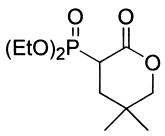
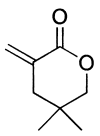
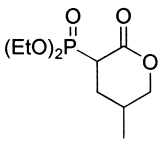
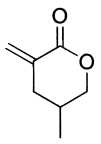
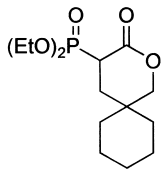
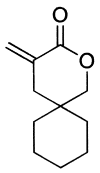
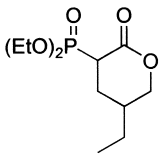
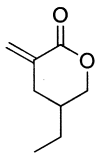
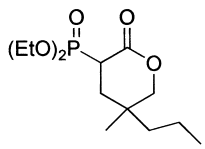
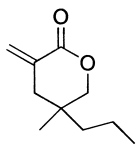
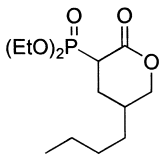
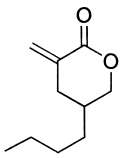
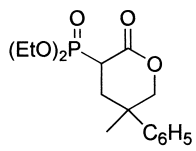
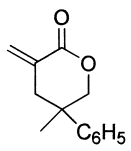
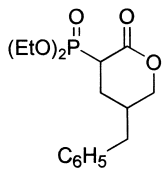
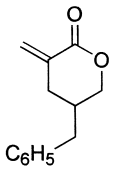
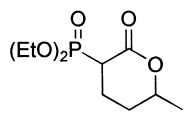
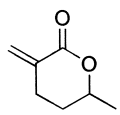
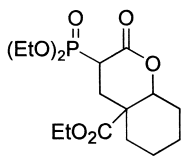
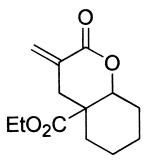
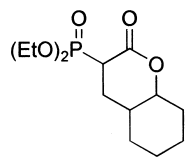
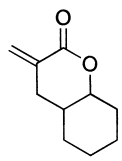
In the course of our earlier studies the Michael adducts **3a**, **3b** and **3e** were prepared from α-substituted aldehydes **2a**, **2b** and acetone **2e**, respectively.[32] The procedure described for the synthesis of the alkanoates **3a** and **3b** consisted in heating a mixture of reagents used in equimolar amounts in benzene at 50°C for 30 h. By using the same method the reaction of 2-methylpentanal **2c** with the acrylate **1** gave a 1:1 mixture of the diastereoisomeric adducts **3c** in 67% yield. Surprisingly, we found that the rate of addition was markedly dependent on the nature of the α-substituent of the Michael donor. 2-Phenylpropanal **2d** reacted with the acrylate **1** at room temperature yielding within 3 days the adduct **3d** as a 2:1 mixture of diastereoisomers in 70% yield.

Both procedures were not applicable to the conversion of ketones into the corresponding 5-oxoalkanoates. After screening a variety of reaction conditions it was found that considerable excess of ketone had to be used to perform effectively the desired reaction. The reaction of cyclohexanone **2f** used as both the reagent and solvent with **1** performed at 50°C for 70 h resulted in the formation of the adduct **3f** as a mixture of diastereoisomers in a 1:1 ratio in 68% yield. This result is consistent with that previously described for acetone.



Scheme 2. *Conditions*: (a) EtOH, KOH (1 equiv.), KBH_4 (1 equiv.), rt, 24 h; (b) *p*-TSA (cat.), benzene, reflux 4 h; (c) 36% formaldehyde (5 equiv.), K_2CO_3 (2 equiv.), 0–5°C, 30 min.

Table 1. Phosphonolactones **6a–k** and methylenelactones **7a–k** prepared

Product	(% yield)	Product	(% yield)	Product	(% yield)	Product	(% yield)
 **6a**	(69)	 **7a**	(65)	 **6g**	(60) (1:1)[1]	 **7g**	(63)
 **6b**	(89)	 **7b**	(70)	 **6h**	(58) (1:1)[1]	 **7h**	(60)
 **6c**	(72) (1:1)[1]	 **7c**	(67)	 **6i**	(58) (1:1)[1]	 **7i**	(60)
 **6d**	(60) (3:1)[1]	 **7d**	(63)	 **6j**	(62) (1:1)[1]	 **7j**	(65)
 **6e**	(75) (2:1)[1]	 **7e**	(60)	 **6k**	(78) (2:1)[1]	 **7k**	(68) (2:1)[2]
 **6f**	(75) (2:1)[1]	 **7f**	(70) (2:1)[2]				

1) diastereoisomer ratio
2) trans : cis ratio

To demonstrate further the usefulness of our approach we decided to study preparation of dicyclohexylammonium 2-diethoxyphosphoryl-5-oxoalkanoates from a series of α-unsubstituted aldehydes **2g–2j**. It was found that reactions of **1** with equimolar amount of propanal **2g**, butanal **2h**, hexanal **2i** and 3-phenylpropanal **2j** proceeded readily in benzene at room temperature and were completed within 36 h yielding the corresponding adducts **3g–3j** in 69–75% yield. The 1,4-additions leading to **3g–3j** proved to be not diastereoselective. In fact, the diastereoisomeric ratio in all four examples was invariably 1:1.

Finally, the methodology presented above could be applied to the conjugate addition of 2-ethoxycarbonylcyclohexanone **2k** to the acrylate **1**. The adduct **3k** was obtained as a 1:1 mixture of diastereoisomers in 85% yield.

The dicyclohexylammonium 5-oxoalkanoates **3a–3k** were then converted into the corresponding 5-oxoalkanoic acids **4a–4k** by ion-exchange chromatography in nearly quantitative yields.

With the suitable substrates in hand we turned our attention to their effective conversion into α-methylene-δ-valerolactones (Scheme 2). The chemoselective reduction of carbonyl group of the oxoacids **4a–4k** by potassium borohydride afforded the expected 2-diethoxyphosphoryl-5-hydroxyalkanoic acids **5a–5k** accompanied by the

corresponding α-phosphono-δ-valerolactones **6a**–**6k** (^{31}P NMR). The hydroxyalkanoic acids **5a**–**5k** were completly converted into the lactones **6a**–**6k** by simple heating of the obtained mixtures in benzene in the presence of a catalytic amount of *p*-toluenesulfonic acid.

The α-phosphono-δ-valerolactones **6c**, **6d** and **6f**–**6k** were formed as mixtures of diastereoisomers. Their ratios were determined by ^{31}P NMR or ^{1}H NMR (**6j**) and are shown in Table 1. All attempts to separate the diastereoisomers by column chromatography were unsuccessful. The spectroscopic data of diastereoisomeric mixtures did not allow us to assign the relative configuration to particular stereoisomers. In any case relative configuration of the diastereoisomeric products was of no importance since they were to be converted into α-methylene-δ-valerolactones.

Then, our efforts were focused on the HWE reaction of the phosphonolactones **6a**–**6k.** The use of aqueous potassium carbonate to promote the HWE olefination of various α-phosphonoalkanoates with formaldehyde is well documented.[24,27,28] By employing this method phosphonolactones **6a**–**6k** were converted into the corresponding α-methylene-δ-valerolactones **7a**–**7k** in good yields. The HWE reaction of **6f** gave the methylene lactone **7f** as a mixture of *trans* and *cis* stereoisomers in a 3:1 ratio. They could be easily separated by column chromatography. ^{1}H NMR spectra of the both stereoisomers were in agreement with the data reported in the literature.[17] The HWE reaction of **6k** provided chromatographically separable *trans* and *cis* stereoisomeric **7k** in a 2:1 ratio. The configurational assignments of these diastereoisomers were based on ^{1}H NMR chemical shifts and coupling constants of the protons at the lactone ring junction.[17,37]

3. Conclusions

In summary, we have succeeded in developing the efficient three-step synthesis of α-phosphono-δ-valerolactones from easily available dicyclohexylammonium 2-(diethoxyphosphoryl) acrylate. The HWE olefination of the α-phosphono-δ-valerolactones with formaldehyde allowed the facile preparation of α-methylene-δ-valerolactones.

4. Experimental

4.1. General

NMR spectra were recorded on a Bruker DPX 250 instrument at 250.13 MHz for ^{1}H and 62.9 MHz for ^{13}C and 101.3 MHz for ^{31}P NMR, respectively, using tetramethylsilane as internal and 85% H_3PO_4 as external standard. The multiplicity of carbons were determined by DEPT experiments. IR spectra were measured on a Specord M80 (Zeiss) instrument. FAB/MS were recorded on a PO Electron Modell MI 1202 E mass spectrometer equipped with FAB ion source (thioglycerol matrix). Elemental analyses were performed on a Perkin–Elmer PE 2400 analyzer. Melting points were determined in open capillaries and are uncorrected. Dicyclohexylammonium 2-(diethoxyphosphoryl) acrylate **1** was prepared according to the literature procedure.[32] Analytical data of the salts **3a**, **3b**, **3e** and the corresponding acids **4a**, **4b**, **4e** have not been previously reported.[32]

4.2. Synthesis of dicyclohexylammonium alkanoates 3a–k

In a typical experimental procedure to a solution of phosphonate **1** (3.89 g, 0.01 mol) in dry benzene (30 ml) **2** (0.01 mol) was added and the mixture was stirred at the given temperature until completion of the reaction was confirmed by ^{31}P NMR. After the reaction was completed the solvent was evaporated and the solid residue was suspended in hexane and collected by filtration. The crude solid was crystallized from acetone or acetone/methylene chloride to give **3**.

4.2.1. Dicyclohexylammonium 2-(diethoxyphosphoryl)-4,4-dimethyl-5-oxopentanoate (3a). (3.31 g, 72% yield); white crystals, mp 151–153°C; IR (KBr) 2928, 1728, 1601, 1240 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=28.76; ^{1}H NMR ($CDCl_3$) δ=1.07 (s, 3H, CH_3), 1.08 (s, 3H, CH_3), 1.21–1.32 (m, 6H, 3×CH_2), 1.30 (t, 3H, $^{3}J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.31 (t, 3H, $^{3}J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.47–1.55 (m, 4H, 2×CH_2), 1.61–1.65 (m, 2H, CH_2), 1.77–1.82 (m, 4H, 2×CH_2), 1.95–2.02 (m, 5H, 2×CH_2, C*H*CHP), 2.43 (ddd, 1H, $^{3}J_{HP}$=4.5 Hz, $^{3}J_{HH}$=9.7 Hz, $^{2}J_{HH}$=14.5 Hz, C*H*CHP), 2.75 (ddd, 1H, $^{3}J_{HH}$=1.7, 9.7 Hz, $^{2}J_{HP}$=24.5 Hz, C*H*P), 3.00 (m, 2H, 2×C*H*N), 4.01–4.20 (m, 4H, 2×CH_2OP), 9.42 (s, 1H, C*H*O); ^{13}C NMR ($CDCl_3$) δ=16.45 (d, $^{3}J_{CP}$=6.1 Hz, 2×*C*H$_3$CH$_2$OP), 20.46 (*C*H$_3$), 22.12 (*C*H$_3$), 24.91 (4×*C*H$_2$), 25.17 (2×*C*H$_2$), 28.90 (4×*C*H$_2$), 35.01 (d, $^{2}J_{CP}$=4.1 Hz, *C*H$_2$CHP), 44.60 (d, $^{1}J_{CP}$=124.6 Hz, *C*HP), 46.12 (d, $^{3}J_{CP}$=15.8 Hz, *C*), 52.38 (2×*C*HN), 61.83 (d, $^{2}J_{CP}$=6.5 Hz, 2×*C*H$_2$OP), 171.70 (d, $^{2}J_{CP}$=5.1 Hz, *C*OO), 204.91 (*C*HO); FAB/MS MH$^+$ 462. Anal. calcd for $C_{23}H_{44}NO_6P$: C, 59.85; H, 9.61; N, 3.03. Found: C, 59.98; H, 9.52; N, 3.14.

4.2.2. Dicyclohexylammonium 2-(diethoxyphosphoryl)-3-(1-formyl-cyclohexyl)-propionate (3b). (3.75 g, 75% yield); white crystals, mp 141–143°C; IR (KBr) 2936, 1728, 1636, 1240 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=28.97, ^{1}H NMR ($CDCl_3$) δ=1.28 (t, 3H, $^{3}J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.30 (t, 3H, $^{3}J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.25–1.53 (m, 20H, 10×CH_2), 1.61–2.03 (m, 11H, 5×CH_2, C*H*CHP), 2.38 (ddd, 1H, $^{3}J_{HP}$=3.7 Hz, $^{3}J_{HH}$=10.2 Hz, $^{2}J_{HH}$=14.5 Hz, C*H*CHP), 2.70 (ddd, 1H, $^{3}J_{HH}$=1.5, 10.2 Hz, $^{2}J_{HP}$=24.5 Hz, C*H*P), 2.97–3.06 (m, 2H, 2×C*H*N), 3.99–4.23 (m, 4H, 2×CH_2OP), 9.44 (s, 1H, C*H*O); ^{13}C NMR ($CDCl_3$) δ=16.45 (d, $^{3}J_{CP}$=6.3 Hz, 2×*C*H$_3$CH$_2$OP), 22.51 (*C*H$_2$), 22.62 (*C*H$_2$), 24.90 (4×*C*H$_2$), 25.22 (2×*C*H$_2$), 25.77 (*C*H$_2$), 28.92 (4×*C*H$_2$), 30.61 (*C*H$_2$), 30.92 (*C*H$_2$), 34.07 (d, $^{2}J_{CP}$=4.7 Hz, *C*H$_2$CHP), 43.76 (d, $^{1}J_{CP}$=124.2 Hz, *C*HP), 49.86 (d, $^{3}J_{CP}$=14.6 Hz, *C*), 52.33 (2×*C*HN), 61.70 (d, $^{2}J_{CP}$=6.5 Hz, 2×*C*H$_2$OP), 171.74 (d, $^{2}J_{CP}$=4.7 Hz, *C*OO), 205.61 (C*H*O); FAB/MS MH$^+$ 502. Anal. calcd for $C_{26}H_{48}NO_6P$: C, 62.25; H, 9.64; N, 2.79. Found: C, 62.37; H, 9.78; N, 2.68.

4.2.3. Dicyclohexylammonium 2-(diethoxyphosphoryl)-4-formyl-4-methyl-heptanoate (3c). (3.28 g, 67% yield); diasteroisomer ratio 1:1; white solid, mp 84–86°C; IR

(KBr) 2936, 1724, 1632, 1244 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=28.80, 29.02; ^{1}H NMR ($CDCl_3$) δ=0.85 (t, 3H, $^{3}J_{HH}$=7.2 Hz, CH_3), 1.02 (s, 3H, CH_3, dia A), 1.04 (s, 3H, CH_3, dia B), 1.18–1.38 (m, 8H, 4×CH_2), 1.30 (t, 3H, $^{3}J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.31 (t, 3H, $^{3}J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.40–1.62 (m, 6H, 3×CH_2), 1.60–1.65 (m, 2H, CH_2), 1.75–1.79 (m, 5H, 2×CH_2, CHCHP), 1.85–1.92 (m, 4H, 2×CH_2), 2.33 (ddd, 1H, $^{3}J_{HP}$=3.7 Hz, $^{3}J_{HH}$=10.5 Hz, $^{2}J_{HH}$=13.7 Hz, CHCHP, dia A), 2.42 (ddd, 1H, $^{3}J_{HP}$=3.7 Hz, $^{3}J_{HH}$=10.5 Hz, $^{2}J_{HH}$=13.7 Hz, CHCHP, dia B), 2.65 (ddd, 1H, $^{3}J_{HH}$=1.5 Hz, 10.5 Hz, $^{2}J_{HP}$=25.2 Hz, CHP, dia A), 2.78 (ddd, 1H, $^{3}J_{HH}$=1.5 Hz, 10.5 Hz, $^{2}J_{HP}$=25.2 Hz, CHP, dia B), 2.91–3.07 (m, 2H, 2×CHN), 4.07–4.17 (m, 4H, 2×CH_2OP), 9.43 (s, 1H, CHO, dia A), 9.44 (s, 1H, CHO, dia B); ^{13}C NMR ($CDCl_3$) δ=14.99 (*C*H_3), 16.71 (d, $^{3}J_{CP}$=6.2 Hz, 2×*C*H_3CH$_2$OP), 17.10 (*C*H_3, dia A), 17.44 (*C*H_2, dia A), 17.52 (*C*H_2, dia B), 18.41 (*C*H_3, dia B), 25.15 (4×*C*H_2), 25.43 (2×*C*H_2), 29.29 (4×*C*H_2), 32.91 (d, $^{2}J_{CP}$=4.9 Hz, *C*H_2CHP, dia A), 33.84 (d, $^{2}J_{CP}$=4.9 Hz, *C*H_2CHP, dia B), 37.31 (*C*H_2, dia A), 39.20 (*C*H_2, dia B), 44.42 (d, $^{1}J_{CP}$=125.0 Hz, *C*HP, dia A), 44.71 (d, $^{1}J_{CP}$=125.0 Hz, *C*HP, dia B), 49.72 (d, $^{3}J_{CP}$=14.8 Hz, *C*, dia A), 49.91 (d, $^{3}J_{CP}$=14.8 Hz, *C*, dia B), 52.84 (2×*C*HN), 62.21 (d, $^{2}J_{CP}$=6.5 Hz, 2×*C*H$_2$OP), 172.10 (d, $^{2}J_{CP}$=4.4 Hz, *C*OO, dia A), 172.30 (d, $^{2}J_{CP}$=4.4 Hz, *C*OO, dia B), 205.01 (*C*HO, dia A), 205.99 (*C*HO, dia B); FAB/MS MH^+ 490. Anal. calcd for $C_{25}H_{48}NO_6P$: C, 61.33; H, 9.88; N, 2.86. Found: C, 61.19; H, 9.98; N, 2.99.

4.2.4. Dicyclohexylammonium 2-(diethoxyphosphoryl)-4-methyl-5-oxo-4-phenyl-pentanoate (3d). (3.66 g, 70% yield); diasteroisomer ratio 2:1; white crystals, mp 122–126°C; IR (KBr) 3018, 2936, 1727, 1632, 1244 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=28.50, 28.62; ^{1}H NMR ($CDCl_3$) δ=1.31 (t, 3H, $^{3}J_{HH}$=7.2 Hz, CH_3CH$_2$OP), 1.33 (t, 3H, $^{3}J_{HH}$=7.2 Hz, CH_3CH$_2$OP), 1.18–1.37 (m, 6H, 3×CH_2), 1.44 (s, 3H, CH_3, minor), 1.49 (s, 3H, CH_3, major), 1.41–1.56 (m, 4H, 2×CH_2), 1.62–1.73 (m, 2H, CH_2), 1.75–1.80 (m, 4H, 2×CH_2), 1.90–2.04 (m, 4H, 2×CH_2), 2.37–2.87 (m, 3H, CH_2, CHP), 2.92–3.05 (m, 2H, 2×CHN), 3.86–4.17 (m, 4H, 2×CH_2OP), 7.20–7.42 (m, 5H, C$_6H_5$), 9.43 (s, 1H, CHO, major), 9.51 (s, 1H, CHO, minor); ^{13}C NMR ($CDCl_3$) δ=16.21 (d, $^{3}J_{CP}$=5.9 Hz, 2×*C*H_3CH$_2$OP), 17.43 (*C*H_3, major), 20.90 (*C*H_3, minor), 24.64 (4×*C*H_2), 24.96 (2×*C*H_2), 28.67 (4×*C*H_2), 33.27 (d, $^{2}J_{CP}$=3.1 Hz, *C*H_2CHP, major), 33.40 (d, $^{2}J_{CP}$=3.1 Hz, *C*H_2CHP, minor), 43.80 (d, $^{1}J_{CP}$=124.5 Hz, *C*HP, major), 44.61 (d, $^{1}J_{CP}$=124.5 Hz, *C*HP, minor), 52.18 (2×*C*HN), 54.15 (d, $^{3}J_{CP}$=16.0 Hz, *C*, major), 54.40 (d, $^{3}J_{CP}$=14.4 Hz, *C*, minor), 61.56 (d, $^{2}J_{CP}$=6.3 Hz, *C*H$_2$OP), 61.70 (d, $^{2}J_{CP}$=6.3 Hz, *C*H$_2$OP), 127.01 (*C*H, major), 127.16 (*C*H, minor), 127.4 (4×*C*H, minor), 128.70 (4×*C*H, major), 139.34 (*C*, major), 140.61 (*C*, minor), 171.71 (d, $^{2}J_{CP}$=6.3 Hz, *C*OO, minor), 171.82 (d, $^{2}J_{CP}$=6.3 Hz, *C*OO, major), 200.81 (*C*HO, major), 202.05 (*C*HO, minor); FAB/MS MH^+ 524. Anal. calcd for $C_{28}H_{46}NO_6P$: C, 64.22; H, 8.87; N, 2.67. Found: C, 64.36; H, 8.99; N, 2.54.

4.2.5. Dicyclohexylammonium 2-(diethoxyphosphoryl)-5-oxohexanoate (3e). (3.14 g, 70% yield); white powder, mp 126–128°C; IR (KBr) 2950, 1716, 1635 1240 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=28.21; ^{1}H NMR ($CDCl_3$) δ=1.27 (t, 6H, $^{3}J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.28 (t, 6H, $^{3}J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.22–1.31 (m, 6H, 3×CH_2), 1.41–1.52 (m, 2H, 2×CH_2), 1.55–1.66 (m, 4H, 2×CH_2), 1.71–1.86 (m, 4H, 2×CH_2), 2.11 (s, 3H, CH_3), 1.99–2.21 (m, 6H, 3×CH_2), 2.48–2.71 (m, 2H, CH_2), 2.74 (ddd, $^{3}J_{HH}$=4.7, 10.0 Hz, $^{2}J_{HP}$=21.7 Hz, CHP), 2.91–3.03 (m, 2H, 2×CHN), 4.02–4.21 (m, 4H, 2×CH_2OP); ^{13}C NMR ($CDCl_3$) δ=16.15 (d, $^{3}J_{CP}$=6.2 Hz, *C*H$_3$CH$_2$OP), 16.21 (d, $^{3}J_{CP}$=6.2 Hz, *C*H$_3$CH$_2$OP), 22.15 (d, $^{2}J_{CP}$=4.3 Hz, *C*H$_2$), 24.61 (4×*C*H$_2$), 25.01 (2×*C*H$_2$), 28.81 (4×*C*H$_2$), 29.60 (*C*H$_3$), 42.26 (d, $^{3}J_{CP}$=15.0 Hz, *C*H$_2$CHP), 47.21 (d, $^{1}J_{CP}$=127.6 Hz, *C*HP), 52.23 (2×*C*HN), 61.51 (d, $^{2}J_{CP}$=6.7 Hz, *C*H$_2$OP), 61.65 (d, $^{2}J_{CP}$=6.7 Hz, *C*H$_2$OP), 171.52 (d, $^{2}J_{CP}$=3.8 Hz, *C*OO), 207.9 (*C*O); FAB/MS MH^+ 448. Anal. calcd for $C_{22}H_{42}NO_6P$: C, 59.04; H, 9.46; N, 3.13. Found: C, 59.16; H, 9.32; N, 3.23.

4.2.6. Dicyclohexylammonium 2-(diethoxyphosphoryl)-3-(2-oxocyclohexyl)-propionate (3f). (3.26 g, 69% yield); diasteroisomer ratio 1:1; white crystals, mp 130–132°C; IR (KBr) 2936, 1712, 1632, 1242 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=28.30, 28.91; ^{1}H NMR ($CDCl_3$) δ=1.29 (t, 3H, $^{3}J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.32 (t, 3H, $^{3}J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.14–1.31 (m, 8H, 4×CH_2), 1.40–1.51 (m, 4H, 2×CH_2), 1.61–1.73 (m, 4H, 2×CH_2), 1.75–1.81 (m, 5H, 2×CH_2, CH), 1.96–2.13 (m, 6H, 3×CH_2), 2.21–2.52 (m, 4H, 2×CH_2), 2.81–3.10 (m, 3H, 2×CHN, CHP), 4.01–4.25 (m, 4H, 2×CH_2OP); ^{13}C NMR ($CDCl_3$) δ=16.41 (d, $^{3}J_{CP}$=6.1 Hz, 2×*C*H$_3$CH$_2$OP), 24.91 (4×*C*H$_2$), 25.05 (*C*H$_2$, dia A), 25.29 (*C*H$_2$, dia B), 25.32 (2×*C*H$_2$), 27.41 (d, $^{2}J_{CP}$=3.8 Hz, *C*H$_2$CHP, dia A), 27.91 (*C*H$_2$, dia A), 28.33 (d, $^{2}J_{CP}$=3.8 Hz, *C*H$_2$CHP, dia B), 28.40 (*C*H$_2$, dia B), 29.10 (4×*C*H$_2$), 32.90 (*C*H$_2$, dia A), 35.31 (*C*H$_2$, dia B), 42.20 (*C*H$_2$, dia A), 42.55 (*C*H$_2$, dia B), 45.30 (d, $^{1}J_{CP}$=125.2 Hz, *C*HP, dia A), 46.14 (d, $^{1}J_{CP}$=125.2 Hz, *C*HP, dia B), 49.02 (d, $^{3}J_{CP}$=15.0 Hz, *C*H, dia A), 49.61 (d, $^{3}J_{CP}$=15.5 Hz, *C*H, dia B), 52.51 (2×*C*HN), 61.72 (d, $^{2}J_{CP}$=6.1 Hz, *C*H$_2$OP), 61.91 (d, $^{2}J_{CP}$=6.1 Hz, *C*H$_2$OP), 171.93 (d, $^{2}J_{CP}$=4.4 Hz, *C*OO, dia A), 172.20 (d, $^{2}J_{CP}$=4.4 Hz, *C*OO, dia B) 212.41 (*C*O, dia A), 212.91 (*C*O, dia B); FAB/MS MH^+ 488. Anal. calcd for $C_{25}H_{46}NO_6P$: C, 61.58; H, 9.51; N, 2.87. Found: C, 61.69; H, 9.65; N, 2.73.

4.2.7. Dicyclohexylammonium 2-(diethoxyphosphoryl)-4-methyl-5-oxopentanoate (3g). (3.09 g, 69% yield); diasteroisomer ratio 1:1; white crystals, mp 100–102°C; IR (KBr) 2936, 1728, 1604, 1240 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=28.15, 28.32; ^{1}H NMR ($CDCl_3$) δ=1.12 (d, 3H, $^{3}J_{HH}$=6.7 Hz, CH_3, dia A), 1.14 (d, 3H, $^{3}J_{HH}$=6.7 Hz, CH_3, dia B), 1.30 (t, 3H, $^{3}J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.31 (t, 3H, $^{3}J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.18–1.21 (m, 6H, 3×CH_2), 1.34–1.55 (m, 4H, 2×CH_2), 1.63–1.70 (m, 3H, CH_2, CH), 1.75–1.81 (m, 4H, 2×CH_2), 1.98–2.06 (m, 4H, 4×CH_2), 2.42–2.56 (m, 2H, CH_2), 2.83–3.05 (m, 3H, CHP, 2×CHN), 4.07 (m, 4H, 2×CH_2OP), 9.61 (s, 1H, CHO, dia A), 9.65 (s, 1H, CHO, dia B); ^{13}C NMR ($CDCl_3$) δ=12.61 (*C*H_3, dia A), 13.62 (*C*H_3, dia B), 16.10 (d, $^{3}J_{CP}$=6.1 Hz, 2×*C*H$_3$CH$_2$OP), 24.55 (4×*C*H$_2$), 24.92 (2×*C*H$_2$), 28.42 (d, $^{2}J_{CP}$=4.8 Hz, *C*H$_2$CHP, dia A), 28.61 (4×*C*H$_2$), 28.81 (d, $^{2}J_{CP}$=4.8 Hz, *C*H$_2$CHP, dia B), 45.15 (d, $^{3}J_{CP}$=12.2 Hz, *C*H, dia A), 45.22 (d, $^{3}J_{CP}$=11.6 Hz, *C*H, dia B), 45.62 (d, $^{1}J_{CP}$=126.5 Hz, *C*HP, dia A), 45.73 (d, $^{1}J_{CP}$=126.5 Hz, *C*HP, dia B), 52.13 (2×*C*HN), 61.53 (d, $^{2}J_{CP}$=6.1 Hz,

*C*H$_2$OP), 62.41 (d, $^2J_{CP}$=6.1 Hz, *C*H$_2$OP), 171.05 (d, $^2J_{CP}$=3.8 Hz, *C*OO, dia A), 171.30 (d, $^2J_{CP}$=3.8 Hz, *C*OO, dia B), 204.02 (*C*HO, dia A), 204.13 (*C*HO, dia B); FAB/MS MH$^+$ 448. Anal. calcd for $C_{22}H_{42}NO_6P$: C, 59.04; H, 9.46; N, 3.13. Found: C, 59.18; H, 9.61; N, 3.27.

4.2.8. Dicyclohexylammonium 2-(diethoxyphosphoryl)-4-formyl-hexanoate (3h). (3.23 g, 70% yield); diastereoisomer ratio 1:1; white crystals, mp 111–113°C; IR (KBr) 2936, 1728, 1636, 1246 cm^{-1}; ^{31}P NMR (CDCl$_3$) δ=28.02, 28.32; ^{1}H NMR (CDCl$_3$) δ=0.91 (t, 3H, $^3J_{HH}$=7.2 Hz, C*H*$_3$, dia A), 0.94 (t, 3H, $^3J_{HH}$=7.5 Hz, C*H*$_3$, dia B), 1.30 (t, 3H, $^3J_{HH}$=7.0 Hz, C*H*$_3$CH$_2$OP), 1.31 (t, 3H, $^3J_{HH}$=7.0 Hz, C*H*$_3$CH$_2$OP), 1.21–1.27 (m, 6H, 3×C*H*$_2$), 1.41–1.54 (m, 6H, 3×C*H*$_2$), 1.59–1.70 (m, 2H, C*H*$_2$), 1.81–1.86 (m, 5H, C*H*, 2×C*H*$_2$), 1.99–2.03 (m, 4H, 2×C*H*$_2$), 2.09–2.41 (m, 2H, C*H*$_2$), 2.80–3.01 (m, 3H, C*H*$_2$, C*H*P), 4.08–4.12 (m, 4H, 2×C*H*$_2$OP), 9.62 (s, 1H, C*H*O, dia A), 9.67 (s, 1H, C*H*O, dia B); ^{13}C NMR (CDCl$_3$) δ=10.99 (*C*H$_3$, dia A), 11.26 (*C*H$_3$, dia B), 16.26 (d, $^3J_{CP}$=6.1 Hz, 2×*C*H$_3$CH$_2$OP), 21.20 (*C*H$_2$, dia A), 22.30 (*C*H$_2$, dia B), 24.65 (4×*C*H$_2$), 25.03 (2×*C*H$_2$), 26.45 (d, $^2J_{CP}$=3.0 Hz, *C*H$_2$CHP, dia A), 26.80 (d, $^2J_{CP}$=3.0 Hz, *C*H$_2$CHP, dia B), 28.75 (4×*C*H$_2$), 45.87 (d, $^1J_{CP}$=126.7 Hz, *C*HP, dia A), 45.97 (d, $^1J_{CP}$=126.7 Hz, *C*HP, dia B), 51.90 (d, $^3J_{CP}$=13.7 Hz, *C*H, dia A), 52.20 (2×*C*HN), 52.41 (d, $^3J_{CP}$=11.7 Hz, *C*H, dia B), 61.65 (d, $^2J_{CP}$=6.7 Hz, *C*H$_2$OP), 61.70 (d, $^2J_{CP}$=6.7 Hz, *C*H$_2$OP), 171.31 (d, $^2J_{CP}$=3.8 Hz, *C*OO, dia A), 171.52 (d, $^2J_{CP}$=3.8 Hz, *C*OO, dia B), 204.23 (*C*HO, dia A), 204.51 (*C*HO, dia B); FAB/MS MH$^+$ 462. Anal. calcd for $C_{23}H_{44}NO_6P$: C, 59.85; H, 9.61; N, 3.03. Found: C, 59.71; H, 9.74; N, 3.18.

4.2.9. Dicyclohexylammonium 2-(diethoxyphosphoryl)-4-formyl-octanoate (3i). (3.52 g); diasteroisomer ratio 1:1; viscous oil, the crude product (pure by ^{31}P NMR) was used for the next step; IR (film) 2867, 1726, 1632, 1243 cm^{-1}; ^{31}P NMR (CDCl$_3$) δ=27.71, 28.13; ^{1}H NMR (CDCl$_3$) δ=0.89 (t, 3H, $^3J_{HH}$=6.7 Hz, C*H*$_3$), 1.10–1.31 (m, 10H, 5×C*H*$_2$), 1.30 (t, 3H, $^3J_{HH}$=7.0 Hz, C*H*$_3$CH$_2$OP), 1.32 (t, 3H, $^3J_{HH}$=7.0 Hz, C*H*$_3$CH$_2$OP), 1.40–1.61 (m, 8H, 4×C*H*$_2$), 1.71–1.80 (m, 8H, 4×C*H*$_2$), 2.02–2.45 (m, 3H, C*H*, C*H*$_2$), 2.81–3.06 (m, 3H, 2×C*H*N, C*H*P), 4.04–4.32 (m, 4H, 2×C*H*$_2$OP), 9.61 (s, 1H, C*H*O, dia A), 9.72 (s, 1H, C*H*O, dia B); ^{13}C NMR (CDCl$_3$) δ=13.50 (*C*H$_3$, dia A), 13.60 (*C*H$_3$, dia B), 16.09 (d, $^3J_{CP}$=6.0 Hz, 2×*C*H$_3$CH$_2$OP), 22.41 (*C*H$_2$, dia A), 22.52 (*C*H$_2$, dia B), 24.50 (4×*C*H$_2$), 24.92 (2×*C*H$_2$), 26.70 (d, $^2J_{CP}$=4.2 Hz, *C*H$_2$CHP, dia A), 27.11 (d, $^2J_{CP}$=4.2 Hz, *C*H$_2$CHP, dia B), 27.91 (*C*H$_2$, dia A), 28.63 (4×*C*H$_2$), 28.71 (*C*H$_2$, dia B), 28.81 (*C*H$_2$, dia A), 28.93 (*C*H$_2$, dia B), 45.76 (d, $^1J_{CP}$=126.5 Hz, *C*HP, dia A), 45.92 (d, $^1J_{CP}$=126.5 Hz, *C*HP, dia B), 50.51 (d, $^3J_{CP}$=15.1 Hz, *C*H, dia A), 50.82 (d, $^3J_{CP}$=15.9 Hz, *C*H, dia B), 52.11 (2×*C*HN), 61.40 (d, $^2J_{CP}$=6.7 Hz, *C*H$_2$OP), 61.50 (d, $^2J_{CP}$=6.7 Hz, *C*H$_2$OP), 171.07 (d, $^2J_{CP}$=4.4 Hz, *C*OO, dia A), 171.13 (d, $^2J_{CP}$=4.4 Hz, *C*OO, dia B), 204.02 (*C*HO, dia A), 204.31 (*C*HO, dia B); FAB/MS MH$^+$ 490.

4.2.10. Dicyclohexylammonium 4-benzyl-2-(diethoxyphosphoryl)-5-oxopentanoate (3j). (3.92 g); diasteroisomer ratio 1:1; viscous oil, the crude product (pure by ^{31}P NMR) was used for the next step; IR (film) 3020, 2936, 1724, 1632, 1244 cm^{-1}; ^{31}P NMR (CDCl$_3$) δ=27.62, 27.75; ^{1}H NMR (CDCl$_3$) δ=1.27 (t, 3H, $^3J_{HH}$=7.0 Hz, C*H*$_3$CH$_2$-OP), 1.29 (t, 3H, $^3J_{HH}$=7.0 Hz, C*H*$_3$CH$_2$OP), 1.17–1.26 (m, 6H, 3×C*H*$_2$), 1.41–1.60 (m, 6H, 3×C*H*$_2$), 1.74–1.87 (m, 6H, 3×C*H*$_2$), 1.98–2.52 (m, 4H, 2×C*H*$_2$), 2.75–3.03 (m, 6H, C*H*, C*H*P, C*H*$_2$C$_6$H$_5$, 2×C*H*N), 4.03–4.16 (m, 4H, 2×C*H*$_2$OP), 7.05–7.41 (m, 5H, C$_6$*H*$_5$), 9.61 (s, 1H, C*H*O, dia A), 9.64 (s, 1H, C*H*O, dia B); ^{13}C NMR (CDCl$_3$) δ=16.31 (d, $^3J_{CP}$=6.1 Hz, 2×*C*H$_3$CH$_2$OP), 24.60 (4×*C*H$_2$), 25.01 (2×*C*H$_2$), 26.83 (d, $^2J_{CP}$=3.8 Hz, *C*H$_2$CHP, dia A), 27.41 (d, $^2J_{CP}$=3.8 Hz, *C*H$_2$CHP, dia B), 28.98 (4×*C*H$_2$), 34.15 (*C*H$_2$, dia A), 35.75 (*C*H$_2$, dia B), 45.65 (d, $^1J_{CP}$=127.0 Hz, *C*HP, dia A), 46.12 (d, $^1J_{CP}$=127.0 Hz, *C*HP, dia B), 51.80 (d, $^3J_{CP}$=15.4 Hz, *C*H, dia A), 52.30 (d, $^3J_{CP}$=14.5 Hz, *C*H, dia B), 52.51 (2×*C*HN), 61.80 (d, $^2J_{CP}$=6.4 Hz, 2×*C*H$_2$OP), 126.21 (*C*H), 128.32 (2×*C*H), 128.72 (*C*H), 129.01 (*C*H), 138.32 (*C*, dia A), 138.51 (*C*, dia B), 171.42 (d, $^2J_{CP}$=3.1 Hz, *C*OO, dia A), 171.53 (d, $^2J_{CP}$=3.1 Hz, *C*OO, dia B), 203.63 (*C*HO, dia A), 204.05 (*C*HO, dia B); FAB/MS MH$^+$ 524.

4.2.11. Dicyclohexylammonium 2-(diethoxyphosphoryl)-3-(1-ethoxycarbonyl-2-oxocyclohexyl) propionate (3k). (4.75 g, 85% yield); diasteroisomer ratio 2:1; white crystals, mp 117–120°C; IR (KBr) 2936, 1720, 1712, 1632, 1248 cm^{-1}; ^{31}P NMR δ=28.53, 28.61; ^{1}H NMR δ=1.23 (t, 3H, $^3J_{HH}$=7.2 Hz, C*H*$_3$CH$_2$O), 1.33 (t, 3H, $^3J_{HH}$=7.0 Hz, C*H*$_3$CH$_2$OP), 1.35 (t, 3H, $^3J_{HH}$=7.0 Hz, C*H*$_3$CH$_2$OP), 1.19–1.31 (m, 6H, 3×C*H*$_2$), 1.46–1.78 (m, 14H, 7×C*H*$_2$), 1.97–2.02 (m, 6H, 3×C*H*$_2$), 2.31–2.60 (m, 4H, 2×C*H*$_2$), 2.82 (ddd, 1H, $^3J_{HH}$=1.5, 10.0 Hz, $^2J_{HP}$=25.2 Hz, C*H*P, major), 2.87 (ddd, 1H, $^3J_{HH}$=1.5, 10.0 Hz, $^2J_{HP}$=25.2 Hz, C*H*P, minor), 2.91–3.02 (m, 2H, 2×C*H*N), 4.05–4.20 (m, 6H, C*H*$_2$O, 2×C*H*$_2$OP); ^{13}C NMR (CDCl$_3$) δ=13.61 (*C*H$_3$), 16.20 (d, $^3J_{CP}$=3.8 Hz, 2×*C*H$_3$CH$_2$OP), 22.31 (*C*H$_2$, minor), 22.35 (*C*H$_2$, major), 24.72 (4×*C*H$_2$), 25.00 (2×*C*H$_2$), 26.71 (*C*H$_2$, minor), 27.52 (*C*H$_2$, major), 28.85 (4×*C*H$_2$), 31.22 (d, $^2J_{CP}$=3.0 Hz, *C*H$_2$, minor), 31.51 (d, $^2J_{CP}$=3.0 Hz, *C*H$_2$, major), 33.82 (*C*H$_2$, minor), 34.35 (*C*H$_2$, major), 40.72 (*C*H$_2$, minor), 40.84 (*C*H$_2$, major), 43.83 (d, $^1J_{CP}$=124.1 Hz, *C*HP, major), 43.72 (d, $^1J_{CP}$=124.1 Hz, *C*HP, minor), 52.22 (2×*C*HN), 60.51 (d, $^3J_{CP}$=14.7 Hz, *C*, minor), 61.02 (d, $^3J_{CP}$=14.7 Hz, *C*, major), 60.91 (*C*H$_2$O), 61.51 (d, $^2J_{CP}$=6.3 Hz, *C*H$_2$OP), 61.75 (d, $^2J_{CP}$=6.3 Hz, *C*H$_2$OP), 170.81 (*C*OOCH$_2$CH$_3$), 171.80 (d, $^2J_{CP}$=3.8 Hz, *C*OO, major), 171.91 (d, $^2J_{CP}$=3.8 Hz, *C*OO, minor), 206.80 (*C*O, minor), 207.01 (*C*O, major); FAB/MS MH$^+$ 560. Anal. calcd for $C_{28}H_{50}NO_8P$: C, 60.09; H, 9.00; N, 2.50. Found: C, 60.23; H, 9.15; N, 2.34.

4.3. General procedure for transformation of 3a–k to corresponding carboxylic acids 4a–k

Ion-exchange chromatography of the salts **3** (**a**–**k**) (6.0 mmol) was performed on a glass column packed with Dowex 50W using H$_2$O/acetone, 1:1 as eluent. The eluent was evaporated to give acids as colorless oils.

4.3.1. 2-(Diethoxyphosphoryl)-4,4-dimethyl-5-oxopentanoic acid (4a). Colorless oil; IR (film) 1728, 1240 cm^{-1}; ^{31}P NMR (CDCl$_3$) δ=24.11; ^{1}H NMR (CDCl$_3$) δ=1.06 (s, 3H, C*H*$_3$), 1.08 (s, 3H, C*H*$_3$), 1.34 (t, 6H, $^3J_{HH}$=7.2 Hz, 2×C*H*$_3$CH$_2$OP), 1.95 (dt, 1H, $^3J_{HH}$=2.0 Hz, $^2J_{HH}$=$^3J_{HP}$=14.5 Hz, C*H*CHP), 2.31 (ddd, 1H, $^3J_{HP}$=4.4 Hz,

$^3J_{HH}$=10.5 Hz, $^2J_{HH}$=14.5 Hz, C*H*CHP), 3.01 (ddd, 1H, $^3J_{HH}$=2.0, 10.5 Hz, $^2J_{HP}$=25.5 Hz, C*H*P), 4.17 (qui, 2H, $^3J_{HH}$=$^3J_{HP}$=7.2 Hz, CH_2OP), 4.21 (qui, 2H, $^3J_{HH}$=$^3J_{HP}$=7.2 Hz, CH_2OP), 9.4 (s, 1H, C*H*O); ^{13}C NMR ($CDCl_3$) δ=16.45 (d, $^3J_{CP}$=5.4 Hz, 2×*C*H_3CH$_2$OP), 21.01 (*C*H_3), 21.72 (*C*H_3), 32.84 (d, $^2J_{CP}$=4.9 Hz, *C*H_2CHP), 41.05 (d, $^1J_{CP}$=128.5 Hz, *C*HP), 45.31 (d, $^3J_{CP}$=15.1 Hz, *C*), 63.21 (d, $^2J_{CP}$=6.8 Hz, *C*H$_2$OP), 63.53 (d, $^2J_{CP}$=6.8 Hz, *C*H$_2$OP), 170.81 (d, $^2J_{CP}$=4.9 Hz, *C*OO), 204.81 (*C*HO). Anal. calcd for $C_{11}H_{21}O_6P$: C, 47.14; H, 7.55. Found: C, 47.34; H, 7.73.

4.3.2. 2-(Diethoxyphosphoryl)-3-(1-formyl-cyclohexyl)-propionic acid (4b). Colorless oil; IR (film) 1724, 1241 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=24.13; ^{1}H NMR ($CDCl_3$) δ=1.33 (t, 6H, $^3J_{HH}$=7.0 Hz, 2×CH_3CH$_2$OP), 1.21–1.61 (m, 8H, 4×CH_2), 1.82–1.94 (m, 2H, CH_2), 1.88 (dt, 1H, $^3J_{HH}$=1.5 Hz, $^2J_{HH}$=$^3J_{HP}$=14.0 Hz, C*H*CHP), 2.31 (ddd, 1H, $^3J_{HP}$=3.7 Hz, $^3J_{HH}$=10.0 Hz, $^2J_{HH}$=14.0 Hz, C*H*CHP), 3.00 (ddd, 1H, $^3J_{HH}$=1.5, 10.0 Hz, $^2J_{HP}$=25.7 Hz, C*H*P), 4.16 (qui, 2H, $^3J_{HH}$=$^3J_{HP}$=7.0 Hz, CH_2OP), 4.19 (qui, 2H, $^3J_{HH}$=$^3J_{HP}$=7.2 Hz, CH_2OP), 9.38 (s, 1H, C*H*O); ^{13}C NMR ($CDCl_3$) δ=16.31 (d, $^3J_{CP}$=5.2 Hz, 2×*C*H_3CH$_2$OP), 22.30 (2×*C*H$_2$), 25.45 (*C*H$_2$), 30.71 (2× *C*H$_2$), 32.62 (d, $^2J_{CP}$=4.8 Hz, *C*H$_2$CHP), 40.41 (d, $^1J_{CP}$=127.0 Hz, *C*HP), 49.81 (d, $^3J_{CP}$=14.7 Hz, *C*), 63.2 (d, $^2J_{CP}$=6.1 Hz, *C*H$_2$OP), 63.81 (d, $^2J_{CP}$=6.1 Hz, *C*H$_2$OP), 170.84 (d, $^2J_{CP}$=4.7 Hz, *C*OO), 204.80 (*C*HO). Anal. calcd for $C_{14}H_{25}O_6P$: C, 52.49; H, 7.87. Found: C, 52.33; H, 8.02.

4.3.3. 2-(Diethoxyphosphoryl)-4-formyl-4-methyl-heptanoic acid (4c). Diasteroisomer ratio 1:1; colorless oil; IR (film) 1728, 1240 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=23.99, 24.01; ^{1}H NMR ($CDCl_3$) δ=0.86 (t, 3H, $^3J_{HH}$=7.0 Hz, CH_3), 0.98 (s, 3H, CH_3, dia A), 1.00 (s, 3H, CH_3, dia B), 1.18–1.27 (m, 2H, CH_2), 1.33 (t, 6H, $^3J_{HH}$=7.0 Hz, 2×CH_3CH$_2$OP), 1.43–1.50 (m, 2H, CH_2), 1.93 (dt, 1H, $^3J_{HH}$=1.8 Hz, $^2J_{HH}$=$^3J_{HP}$=14.7 Hz, C*H*CHP, dia A), 2.00 (dt, 1H, $^3J_{HH}$=1.8 Hz, $^2J_{HH}$=$^3J_{HP}$=14.7 Hz, C*H*CHP, dia B), 2.19 (ddd, 1H, $^3J_{HP}$=3.0 Hz, $^3J_{HH}$=9.5 Hz, $^2J_{HH}$=14.7 Hz, C*H*CHP, dia A), 2.30 (ddd, 1H, $^3J_{HP}$=3.0 Hz, $^3J_{HH}$=9.5 Hz, $^2J_{HH}$=14.7 Hz, C*H*CHP, dia B), 2.91 (ddd, 1H, $^3J_{HH}$=1.8, 9.5 Hz, $^2J_{HP}$=25.0 Hz, C*H*P, dia A), 3.13 (ddd, 1H, $^3J_{HH}$=1.8, 9.5 Hz, $^2J_{HP}$=25.0 Hz, C*H*P, dia B), 4.18 (qui, 2H, $^3J_{HH}$=$^3J_{HP}$=7.0 Hz, CH_2OP), 4.21 (qui, 2H, $^3J_{HH}$=$^3J_{HP}$=7.0 Hz, CH_2OP), 9.38 (s, 1H, C*H*O); ^{13}C NMR ($CDCl_3$) δ=14.51 (*C*H_3), 16.20 (d, $^3J_{CP}$=5.9 Hz, 2×*C*H_3-CH$_2$OP), 17.11 (*C*H_3, dia A), 17.32 (*C*H$_2$, dia A), 17.50 (*C*H$_2$, dia B), 18.20 (*C*H_3, dia B), 31.13 (d, $^2J_{CP}$=4.5 Hz, *C*H$_2$CHP, dia A), 31.81 (d, $^2J_{CP}$=4.5 Hz, *C*H$_2$CHP, dia B), 37.31 (*C*H$_2$, dia A), 39.62 (*C*H$_2$, dia B), 40.81 (d, $^1J_{CP}$=128.0 Hz, *C*HP, dia A), 41.22 (d, $^1J_{CP}$=128.0 Hz, *C*HP, dia B), 49.00 (d, $^3J_{CP}$=14.1 Hz, *C*, dia A), 49.52 (d, $^3J_{CP}$=14.1 Hz, *C*, dia B), 63.10 (d, $^2J_{CP}$=6.5 Hz, *C*H$_2$OP), 63.40 (d, $^2J_{CP}$=6.5 Hz, *C*H$_2$OP), 170.06 (d, $^2J_{CP}$=4.4 Hz, *C*OO, dia A), 170.40 (d, $^2J_{CP}$=4.4 Hz, *C*OO, dia B), 205.11 (*C*HO, dia A), 205.22 (*C*HO, dia B). Anal. calcd for $C_{13}H_{25}O_6P$: C, 50.64; H, 8.17. Found: C, 50.81; H, 8.29.

4.3.4. 2-(Diethoxyphosphoryl)-4-methyl-5-oxo-4-phenyl-pentanoic acid (4d). Colorless oil; diasteroisomer ratio 2:1; IR (film) 3018, 1724, 1242 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=24.07, 24.15; ^{1}H NMR ($CDCl_3$) δ=1.31 (t, 3H, $^3J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.32 (t, 3H, $^3J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.45 (s, 3H, CH_3, major), 1.46 (s, 3H, CH_3, minor), 2.37–2.65 (m, 2H, CH_2), 2.72 (ddd, 1H, $^3J_{HH}$=1.5, 9.7 Hz, $^2J_{HP}$=25.2 Hz, C*H*P, major), 2.96 (ddd, 1H, $^3J_{HH}$=1.5, 9.7 Hz, $^2J_{HP}$=25.2 Hz, C*H*P, minor), 3.89–4.23 (m, 4H, 2×CH_2OP), 7.21–7.42 (m, 5H, C_6H_5), 9.40 (s, 1H, C*H*O, major), 9.45 (s, 1H, C*H*O, minor); ^{13}C NMR ($CDCl_3$) δ=16.11 (d, $^3J_{CP}$=6.0 Hz, 2×*C*H_3CH$_2$OP), 17.50 (*C*H_3, major), 18.75 (*C*H_3, minor), 32.60 (d, $^2J_{CP}$=3.2 Hz, *C*H$_2$CHP, minor), 32.78 (d, $^2J_{CP}$=3.2 Hz, *C*H$_2$CHP, major), 41.14 (d, $^1J_{CP}$=128.1 Hz, *C*HP, major), 41.74 (d, $^1J_{CP}$=128.1 Hz, *C*HP, minor), 54.01 (d, $^3J_{CP}$=13.4 Hz, *C*, major), 54.21 (d, $^3J_{CP}$=13.4 Hz, *C*, minor), 63.11 (d, $^2J_{CP}$=6.5 Hz, *C*H$_2$OP), 63.74 (d, $^2J_{CP}$=6.5 Hz, *C*H$_2$OP), 127.21 (2×*C*H, minor), 127.53 (2×*C*H, major), 127.71 (*C*H, minor), 127.81 (*C*H, major), 128.93 (2×*C*H, minor), 129.00 (2×*C*H, major), 137.81 (*C*, major), 138.91 (*C*, minor), 170.94 (d, $^2J_{CP}$=5.0 Hz, *C*OO, minor), 171.21 (d, $^2J_{CP}$=5.0 Hz, *C*OO, major) 200.32 (*C*HO, major), 200.94 (*C*HO, minor). Anal. calcd for $C_{16}H_{23}O_6P$: C, 56.14; H, 6.77. Found: C, 56.34; H, 6.89.

4.3.5. 2-(Diethoxyphosphoryl)-5-oxohexanoic acid (4e). Colorless oil; IR (film) 1716, 1242 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=23.98; ^{1}H NMR ($CDCl_3$) δ=1.28 (t, 6H, $^3J_{HH}$=7.0 Hz, 2×CH_3CH$_2$OP), 2.08 (s, 3H, CH_3), 2.05–2.21 (m, 2H, CH_2), 2.40–2.65 (m, 2H, CH_2), 2.97 (dt, 1H, $^3J_{HH}$=7.0 Hz, $^2J_{HP}$=23.0 Hz, C*H*P), 4.13 (qui, 2H, $^3J_{HH}$=$^3J_{HP}$=7.0 Hz, CH_2OP), 4.14 (qui, 2H, $^3J_{HH}$=$^3J_{HP}$=7.0 Hz, CH_2OP); ^{13}C NMR ($CDCl_3$) δ=15.41 (d, $^3J_{CP}$=6.3 Hz, 2×*C*H_3CH$_2$OP), 20.22 (d, $^2J_{CP}$=4.2 Hz, *C*H$_2$CHP), 29.01 (*C*H_3), 40.23 (d, $^3J_{CP}$=13.8 Hz, *C*H$_2$), 43.32 (d, $^1J_{CP}$=131.8 Hz, *C*HP), 62.42 (d, $^2J_{CP}$=6.8 Hz, *C*H$_2$OP), 62.50 (d, $^2J_{CP}$=6.0 Hz, *C*H$_2$OP), 169.70 (d, $^2J_{CP}$=4.1 Hz, *C*OO), 207.01 (*C*O). Anal. calcd for $C_{10}H_{19}O_6P$: C, 45.11; H, 7.19. Found: C, 45.25; H, 7.31.

4.3.6. 2-(Diethoxyphosphoryl)-3-(2-oxocyclohexyl)-propionic acid (4f). Diasteroisomer ratio 1:1; colorless oil; IR (film) 1712, 1236 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=24.90, 25.31; ^{1}H NMR ($CDCl_3$) δ=1.32 (t, 3H, $^3J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.33 (t, 3H, $^3J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.30–1.42 (m, 2H, CH_2), 1.61–1.85 (m, 4H, 2×CH_2), 2.01–2.13 (m, 2H, CH_2), 2.35–2.51 (m, 3H, CH_2, C*H*), 3.13 (ddd, 1H, $^3J_{HH}$=5.0, 10.5 Hz, $^2J_{HP}$=23.2 Hz, C*H*P, dia A), 3.27 (ddd, 1H, $^3J_{HH}$=2.7, 11.5 Hz, $^2J_{HP}$=23.7 Hz, C*H*P, dia B), 4.14–4.31 (m, 4H, 2×CH_2OP); ^{13}C NMR ($CDCl_3$) δ=16.31 (d, $^3J_{CP}$=6.1 Hz, 2×*C*H_3CH$_2$OP), 25.01 (*C*H$_2$, dia A), 25.21 (*C*H$_2$, dia B), 26.63 (d, $^2J_{CP}$=5.8 Hz, *C*H$_2$CHP, dia A), 27.33 (d, $^2J_{CP}$=5.8 Hz, *C*H$_2$CHP, dia B), 27.91 (*C*H$_2$, dia A), 28.33 (*C*H$_2$, dia B), 33.10 (*C*H$_2$, dia A), 35.42 (*C*H$_2$, dia B), 42.11 (*C*H$_2$, dia A), 42.42 (*C*H$_2$, dia B), 42.51 (d, $^1J_{CP}$=130.1 Hz, *C*HP, dia A), 43.32 (d, $^1J_{CP}$=130.1 Hz, *C*HP, dia B), 48.22 (d, $^3J_{CP}$=12.0 Hz, *C*H, dia A), 48.71 (d, $^3J_{CP}$=14.6 Hz, *C*H, dia B), 63.51 (d, $^2J_{CP}$=6.7 Hz, *C*H$_2$OP), 63.72 (d, $^2J_{CP}$=6.0 Hz, *C*H$_2$OP), 170.61 (d, $^2J_{CP}$=3.8 Hz, *C*OO, dia A), 170.72 (d, $^2J_{CP}$=3.8 Hz, *C*OO, dia B), 212.31 (*C*O, dia A), 212.81 (*C*O, dia B). Anal. calcd for $C_{13}H_{23}O_6P$: C, 50.98; H, 7.57. Found: C, 51.12; H, 7.69.

4.3.7. 2-(Diethoxyphosphoryl)-4-methyl-5-oxopentanoic acid (4g). Diasteroisomer ratio 1:1; colorless oil; IR (film)

1729, 1240 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=23.51, 23.70; ^{1}H NMR ($CDCl_3$) δ=1.13 (d, 3H, $^{3}J_{HH}$=7.5 Hz, CH_3, dia A), 1.16 (d, 3H, $^{3}J_{HH}$=7.5 Hz, CH_3, dia B), 1.34 (t, 3H, $^{3}J_{HH}$=7.2 Hz, CH_3CH$_2$OP), 1.35 (t, 3H, $^{3}J_{HH}$=7.2 Hz, CH_3CH$_2$OP), 1.70–2.61 (m, 3H, CH_2, CH), 3.08 (ddd, 1H, $^{3}J_{HH}$=3.7, 7.7 Hz, $^{2}J_{HP}$=24.7 Hz, CHP, dia A), 3.18 (ddd, 1H, $^{3}J_{HH}$=4.0, 7.5 Hz, $^{2}J_{HP}$=24.0 Hz, CHP, dia B), 4.19 (qui, 2H, $^{3}J_{HH}$=$^{3}J_{HP}$=7.2 Hz, CH_2OP), 4.22 (qui, 2H, $^{3}J_{HH}$=$^{3}J_{HP}$=7.2 Hz, CH_2OP), 9.61 (s, 1H, CHO, dia A), 9.65 (s, 1H, CHO, dia B); ^{13}C NMR ($CDCl_3$) δ=16.22 (d, $^{3}J_{CP}$=5.6 Hz, 2×CH$_3$CH$_2$OP), 16.70 (CH$_3$, dia A), 17.63 (CH$_3$, dia B), 30.40 (d, $^{2}J_{CP}$=5.0 Hz, CH$_2$CHP, dia A), 30.46 (d, $^{2}J_{CP}$=5.0 Hz, CH$_2$CHP, dia B), 37.81 (d, $^{3}J_{CP}$=15.3 Hz, CH, dia A), 38.23 (d, $^{3}J_{CP}$=13.3 Hz, CH, dia B), 42.81 (d, $^{1}J_{CP}$=130.0 Hz, CHP, dia A), 43.15 (d, $^{1}J_{CP}$=130.0 Hz, CHP, dia B), 63.41 (d, $^{2}J_{CP}$=6.5 Hz, CH$_2$OP), 63.66 (d, $^{2}J_{CP}$=6.5 Hz, CH$_2$OP), 170.83 (d, $^{2}J_{CP}$=5.0 Hz, COO, dia A), 171.02 (d, $^{2}J_{CP}$=5.0 Hz, COO, dia B), 203.50 (CHO, dia A), 203.62 (CHO, dia B). Anal. calcd for $C_{10}H_{19}O_6P$: C, 45.11; H, 7.19. Found: C, 45.23; H, 7.31.

4.3.8. 2-(Diethoxyphosphoryl)-4-formyl-hexanoic acid (4h). Diasteroisomer ratio 1:1; colorless oil; IR (film) 1728, 1241 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=23.73, 23.94; ^{1}H NMR ($CDCl_3$) δ=0.92 (t, 3H, $^{3}J_{HH}$=7.5 Hz, CH_3, dia A), 0.96 (t, 3H, $^{3}J_{HH}$=7.5 Hz, CH_3, dia B), 1.34 (t, 3H, $^{3}J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.36 (t, 3H, $^{3}J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.51–1.95 (m, 3H, CH, CH_2), 2.03–2.13 (m, 1H, CH), 2.31–2.43 (m, 1H, CH), 3.07 (ddd, 1H, $^{3}J_{HH}$=5.0, 9.7 Hz, $^{2}J_{HP}$=24.7 Hz, CHP, dia A), 3.10 (ddd, 1H, $^{3}J_{HH}$=4.2, 10.0 Hz, $^{2}J_{HP}$=23.7 Hz, CHP, dia B), 4.11–4.22 (m, 4H, 2×CH_2OP), 9.42 (s, 1H, CHO, dia A), 9.51 (s, 1H, CHO, dia B); ^{13}C NMR ($CDCl_3$) δ=10.70 (CH$_3$, dia A), 11.02 (CH$_3$, dia B), 16.19 (d, $^{3}J_{CP}$=5.8 Hz, 2×CH$_3$CH$_2$OP), 21.20 (CH$_2$, dia A), 22.41 (CH$_2$, dia B), 24.94 (d, $^{2}J_{CP}$=3.1 Hz, CH$_2$CHP, dia A), 25.12 (d, $^{2}J_{CP}$=3.1 Hz, CH$_2$CHP, dia B), 42.91 (d, $^{1}J_{CP}$=130.5 Hz, CHP, dia A), 43.21 (d, $^{1}J_{CP}$=130.5 Hz, CHP, dia B), 50.80 (d, $^{3}J_{CP}$=13.0 Hz, CH, dia A), 51.14 (d, $^{3}J_{CP}$=11.5 Hz, CH, dia B), 63.31 (d, $^{2}J_{CP}$=6.5 Hz, CH$_2$OP), 63.46 (d, $^{2}J_{CP}$=6.5 Hz, CH$_2$OP), 170.21 (d, $^{2}J_{CP}$=3.6 Hz, COO, dia A), 170.31 (d, $^{2}J_{CP}$=3.6 Hz, COO, dia B), 204.21 (CHO, dia A), 204.34 (CHO, dia B). Anal. calcd for $C_{11}H_{21}O_6P$: C, 47.14; H, 7.55. Found: C, 47.26; H, 7.67.

4.3.9. 2-(Diethoxyphosphoryl)-4-formyl-octanoic acid (4i). Colorless oil; diasteroisomer ratio 1:1; analytically pure product was obtained by silica gel chromatography using acetone/$CHCl_3$ (2:1) as eluent; total yield of 2 steps 72%; IR (film) 1728, 1240 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=23.31, 23.50; ^{1}H NMR ($CDCl_3$) δ=0.88 (t, $^{3}J_{HH}$=7.0 Hz, 3H, CH_3), 1.34 (t, 3H, $^{3}J_{HH}$=7.0 Hz, CH_3-CH$_2$OP), 1.36 (t, 3H, $^{3}J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.31–1.33 (m, 4H, 2×CH_2), 1.46–1.74 (m, 2H, CH_2), 2.01–2.53 (m, 3H, CH, CH_2), 3.10 (ddd, 1H, $^{3}J_{HH}$=2.5, 11.2 Hz, $^{2}J_{HP}$=25.2 Hz, CHP, dia A), 3.20 (ddd, 1H, $^{3}J_{HH}$=3.5, 10.0 Hz, $^{2}J_{HP}$=25.2 Hz, CHP, dia B), 4.15 (qui, 2H, $^{3}J_{HH}$=$^{3}J_{HP}$=6.7 Hz, CH_2OP), 4.20 (qui, 2H, $^{3}J_{HH}$=$^{3}J_{HP}$=6.7 Hz, CH_2OP), 9.71 (s, 1H, CHO, dia A), 9.82 (s, 1H, CHO, dia B); ^{13}C NMR ($CDCl_3$) δ=13.52 (CH$_3$, dia A), 13.61 (CH$_3$, dia B), 15.80 (d, $^{3}J_{CP}$=6.2 Hz, 2×CH$_3$CH$_2$OP), 22.13 (CH$_2$, dia A), 22.41 (CH$_2$, dia B), 25.22 (d, $^{2}J_{CP}$=3.2 Hz, CH$_2$CHP, dia A), 25.32 (d, $^{2}J_{CP}$=3.2 Hz, CH$_2$CHP, dia B), 27.82 (CH$_2$, dia A), 28.31 (CH$_2$, dia B), 28.45 (CH$_2$, dia A), 28.70 (CH$_2$, dia B), 42.51 (d, $^{1}J_{CP}$=132.0 Hz, CHP, dia A), 42.52 (d, $^{1}J_{CP}$=132.0 Hz, CHP, dia B), 49.30 (d, $^{3}J_{CP}$=15.1 Hz, CH, dia A), 49.91 (d, $^{3}J_{CP}$=15.8 Hz, CH, dia B), 63.10 (d, $^{2}J_{CP}$=6.5 Hz, CH$_2$OP), 63.20 (d, $^{2}J_{CP}$=6.5 Hz, CH$_2$OP), 178.14 (d, $^{2}J_{CP}$=3.8 Hz, COO, dia A), 178.62 (d, $^{2}J_{CP}$=3.8 Hz, COO, dia B), 203.31 (CHO, dia A), 204.14 (CHO, dia B). Anal. calcd for $C_{13}H_{25}O_6P$: C, 50.64; H, 8.17. Found: C, 50.76; H, 8.28.

4.3.10. 4-Benzyl-2-(diethoxyphosphoryl)-5-oxopentanoic acid (4j). Colorless oil; diasteroisomer ratio 1:1; analytically pure product was obtained by silica gel chromatography using acetone/$CHCl_3$ (2:1) as eluent; total yield of 2 steps 75%; IR (film) 3029, 1728, 1241 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=23.51, 23.62; ^{1}H NMR ($CDCl_3$) δ=1.27 (t, 3H, $^{3}J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.28 (t, 3H, $^{3}J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.82–2.41 (m, 2H, CH_2), 2.75–3.30 (m, 4H, CHP, CH, CH_2), 3.90–4.30 (m, 4H, 2×CH_2OP), 7.00–7.29 (m, 5H, C$_6H_5$), 9.60 (s, 1H, CHO, dia A), 9.65 (s, 1H, CHO, dia B); ^{13}C NMR ($CDCl_3$) δ=16.20 (d, $^{3}J_{CP}$=5.9 Hz, 2×CH$_3$CH$_2$OP), 25.01 (d, $^{2}J_{CP}$=4.1 Hz, CH$_2$CHP, dia A), 25.32 (d, $^{2}J_{CP}$=4.1 Hz, CH$_2$CHP, dia B), 34.82 (CH$_2$, dia A), 35.80 (CH$_2$, dia B), 42.81 (d, $^{1}J_{CP}$=132.4 Hz, CHP, dia A), 43.31 (d, $^{1}J_{CP}$=132.4 Hz, CHP, dia B), 51.00 (d, $^{3}J_{CP}$=12.3 Hz, CH, dia A), 51.72 (d, $^{3}J_{CP}$=11.4 Hz, CH, dia B), 63.40 (d, $^{2}J_{CP}$=6.8 Hz, CH$_2$OP), 63.50 (d, $^{2}J_{CP}$=6.8 Hz, CH$_2$OP), 126.61 (CH), 128.62 (2×CH), 128.94 (CH), 129.11 (CH), 137.72 (CH, dia A), 137.81 (CH, dia B), 169.9 (d, $^{2}J_{CP}$=3.71 Hz, COO, dia A), 170.11 (d, $^{2}J_{CP}$=3.7 Hz, COO, dia B), 203.21 (CHO, dia A), 203.43 (CHO, dia B), Anal. calcd for $C_{16}H_{23}O_6P$: C, 56.14; H, 6.77. Found: C, 56.29; H, 6.89.

4.3.11. 1-[2-Carboxy-2-(diethoxyphosphoryl)-ethyl]-2-cyclohexanecarboxylic acid ethyl ester (4k). Diasteroisomer ratio 2:1; colorless oil; IR (film) 1735, 1712, 1220 cm^{-1}; ^{31}P NMR δ=24.05, 24.21; ^{1}H NMR δ=1.26 (t, 3H, $^{3}J_{HH}$=7.0, CH_3), 1.33 (t, 3H, $^{3}J_{HH}$=7.0, CH_3CH$_2$-OP), 1.35 (t, 3H, $^{3}J_{HH}$=7.0, CH_3CH$_2$OP), 1.41–1.70 (m, 4H, 2×CH_2), 1.91–2.44 (m, 6H, 3×CH_2), 3.11 (ddd, 1H, $^{3}J_{HH}$=1.7, $^{3}J_{HH}$=10.7, $^{2}J_{HP}$=26.5 CHP, minor), 3.32 (ddd, 1H, $^{3}J_{HH}$=2.5, $^{3}J_{HH}$=9.0, $^{2}J_{HP}$=26.0, CHP, major), 4.07–4.25 (m, 6H, CH_2O, 2×CH_2OP); ^{13}C NMR ($CDCl_3$) δ=13.61 (CH$_3$), 15.95 (d, $^{3}J_{CP}$=4.8, 2×CH$_3$CH$_2$OP), 22.00 (CH$_2$, minor) 22.17 (CH$_2$, major), 26.81 (CH$_2$, minor) 27.35 (CH$_2$, major) 30.62 (d, $^{2}J_{CP}$=3.6, CH$_2$, minor), 31.15 (d, $^{2}J_{CP}$=3.6, CH$_2$, major), 34.72 (CH$_2$, minor), 36.10 (CH$_2$, major), 40.51 (CH$_2$, minor), 40.71 (d, $^{1}J_{CP}$=126.5, CHP, minor), 40.74 (CH$_2$, major), 40.91 (d, $^{1}J_{CP}$=126.5, CHP, major), 59.52 (d, $^{3}J_{CP}$=13.0, C, minor), 59.62 (d, $^{3}J_{CP}$=12.5, C, major), 61.32 (CH$_2$O), 62.14 (d, $^{2}J_{CP}$=6.3, CH$_2$OP), 63.51 (d, $^{2}J_{CP}$=6.3, CH$_2$OP), 170.21 (COOCH$_2$CH$_3$), 170.40 (d, $^{2}J_{CP}$=3.8, COOH, major), 170.91 (d, $^{2}J_{CP}$=3.8, COOH, minor), 206.80 (CO, minor), 207.21 (CO, major); Anal. Calcd for $C_{16}H_{27}O_8P$: C, 50.79; H, 7.19; Found: C, 50.95; H, 7.27.

4.4. General procedure for synthesis of phosphonolactones 6a–k

To a stirred solution of **4** (**a**–**k**) (4.0 mmol), in ethanol

(15 ml) was added potassium hydroxide (0.23 g, 4.0 mmol) in ethanol (5 ml) and then potassium borohydride (0.22 g, 4.0 mmol). Stirring was continued for 24 h at room temperature. The resulting mixture was neutralized to pH~2 with 5% HCl. Solvent was evaporated and the residue was taken up in chloroform. The solution was washed with water (1×5 ml) dried ($MgSO_4$) and evaporated. The solution of *p*-toluenesufonic acid monohydrate (0.02 g, 0.1 mmol) in benzene (25 ml) was added to the residue and the mixture was refluxed for 4 h. It was then concentrated, diluted with $CHCl_3$ (20 ml), washed with 5% $NaHCO_3$ (2×10 ml), water (1×10 ml) dried ($MgSO_4$) and evaporated. The oily residue was purified by column chromatography on silica gel using AcOEt as eluent.

4.4.1. (5,5-Dimethyl-2-oxo-tetrahydropyran-3-yl)-phosphonic acid diethyl ester (6a). (0.73 g, 69% yield); colorless oil; IR (film) 1732, 1248, 1168 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=23.30 (**5a** δ=24.84); ^1H NMR ($CDCl_3$) δ=1.06 (s, 3H, CH_3), 1.08 (s, 3H, CH_3), 1.35 (t, 3H, $^3J_{HH}$=7.2 Hz, CH_3CH$_2$OP), 1.36 (t, 3H, $^3J_{HH}$=7.2 Hz, CH_3CH$_2$OP), 1.91 (dddd, 1H, $^4J_{HH}$=2.7 Hz, $^3J_{HP}$=6.2 Hz, $^3J_{HH}$=9.0 Hz, $^2J_{HH}$=13.7 Hz, C*H*CHP), 2.05 (ddd, 1H, $^3J_{HH}$=10.0 Hz, $^2J_{HH}$=13.7 Hz, $^3J_{HP}$=15.5 Hz, C*H*CHP), 3.18 (ddd, 1H, $^3J_{HH}$=9.0, 10.0 Hz, $^2J_{HP}$=27.5 Hz, C*H*P), 3.92 (dd, 1H, $^4J_{HH}$=2.7 Hz, $^2J_{HH}$=11.0 Hz, C*H*O), 4.16 (d, 1H, $^2J_{HH}$=11.0 Hz, C*H*O), 4.15–4.32 (m, 4H, 2× CH_2OP); ^{13}C NMR ($CDCl_3$) δ=15.92 (d, $^3J_{CP}$=5.3 Hz, *C*H$_3$CH$_2$OP), 16.01 (d, $^2J_{CP}$=5.3 Hz, *C*H$_3$CH$_2$OP), 22.73 (*C*H$_3$), 25.51 (*C*H$_3$), 29.42 (d, $^3J_{CP}$=8.4 Hz, *C*), 34.44 (d, $^2J_{CP}$=4.2 Hz, *C*H$_2$), 37.61 (d, $^1J_{CP}$=140.0 Hz *C*HP), 62.33 (d, $^2J_{CP}$=6.8 Hz, *C*H$_2$OP), 63.21 (d, $^2J_{CP}$=6.8 Hz, *C*H$_2$OP), 77.82 (*C*H$_2$O), 166.11 (d, $^2J_{CP}$=4.4 Hz, *C*OO). Anal. calcd for $C_{11}H_{21}O_5P$: C, 50.00; H, 8.01. Found: C, 50.17; H, 8.14.

4.4.2. (3-Oxo-2-oxa-spiro [5.5] undec-4-yl)-phosphonic acid diethyl ester (6b). (1.08 g, 89% yield); colorless oil; IR (film) 1736, 1252, 1164 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=23.40 (**5b** δ=24.77); ^1H NMR ($CDCl_3$) δ=1.35 (t, 3H, $^3J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.36 (t, 3H, $^3J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.35–1.55 (m, 10H, 5×CH_2), 1.92 (ddd, 1H, $^3J_{HH}$=10.0 Hz, $^2J_{HH}$=14.2 Hz, $^3J_{HP}$=17.0 Hz, C*H*CHP), 2.12 (dddd, 1H, $^4J_{HH}$=2.2 Hz, $^3J_{HP}$=5.5 Hz, $^3J_{HH}$=8.7 Hz, $^2J_{HH}$=14.2 Hz, C*H*CHP), 3.15 (ddd, 1H, $^3J_{HH}$=8.7, 10.0 Hz, $^2J_{HP}$=27.0 Hz, C*H*P), 4.08 (dd, 1H, $^4J_{HH}$= 2.2 Hz, $^2J_{HH}$=11.0 Hz, C*H*O), 4.14 (d, 1H, $^2J_{HH}$=11.0 Hz, C*H*O), 4.16–4.32 (m, 4H, 2× CH_2OP); ^{13}C NMR ($CDCl_3$) δ=15.85 (d, $^3J_{CP}$=5.9 Hz, *C*H$_3$CH$_2$OP), 15.95 (d, $^3J_{CP}$= 5.9 Hz, *C*H$_3$CH$_2$OP), 20.89 (*C*H$_2$), 20.96 (*C*H$_2$), 25.45 (*C*H$_2$), 31.10 (*C*H$_2$), 31.49 (d, $^2J_{CP}$=3.8 Hz, *C*H$_2$CHP), 32.11 (d, $^3J_{CP}$=8.0 Hz, *C*), 34.50 (*C*H$_2$), 37.25 (d, $^1J_{CP}$= 140.0 Hz, *C*HP), 62.20 (d, $^2J_{CP}$=6.8 Hz, *C*H$_2$OP), 63.01 (d, $^2J_{CP}$=6.8 Hz, *C*H$_2$OP), 76.4 (*C*H$_2$O), 166.61 (d, $^2J_{CP}$= 3.8 Hz). Anal. calcd for $C_{14}H_{25}O_5P$: C, 55.25; H, 8.28. Found: C, 55.38; H, 8.15.

4.4.3. (5-Methyl-2-oxo-5-propyl-tetrahydro-pyran-3-yl)-phosphonic acid diethyl ester (6c). (0.84 g, 72% yield); diasteroisomer ratio 1:1; colorless oil; IR (film) 1736, 1252, 1160 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=23.37, 23.41 (**5c** δ=24.76, 24.89); ^1H NMR ($CDCl_3$) δ=0.92 (t, 3H, $^3J_{HH}$=6.5 Hz, CH_3), 0.99 (s, 3H, CH_3, dia A), 1.03 (s, 3H, CH_3, dia B), 1.23–1.33 (m, 4H, 2×CH_2), 1.35 (t, 3H, $^3J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.36 (t, 3H, $^3J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.86–2.12 (m, 2H, CH_2), 3.11 (dt, 1H, $^3J_{HH}$=8.2 Hz, $^2J_{HP}$=27.0 Hz, C*H*P, dia A), 3.21 (dt, 1H, $^3J_{HH}$=8.2 Hz, $^2J_{HP}$=27.0 Hz, C*H*P, dia B), 3.93 (dd, 1H, $^4J_{HH}$=2.5 Hz, $^2J_{HH}$=11.0 Hz, C*H*O, dia A), 4.02 (dd, $^4J_{HH}$=2.5 Hz, $^2J_{HH}$=11.0 Hz, C*H*O, dia B), 4.11 (d, 1H, $^2J_{HH}$=11.0 Hz, C*H*O, dia A), 4.15 (d, 1H, $^2J_{HH}$=11.0 Hz, C*H*O, dia B), 4.13–4.31 (m, 4H, 2×CH_2OP); ^{13}C NMR ($CDCl_3$) δ=14.37 (*C*H$_3$, dia A), 14.44 (*C*H$_3$, dia B), 16.10 (d, $^2J_{CP}$=6.0 Hz, *C*H$_3$CH$_2$OP), 16.20 (d, $^2J_{CP}$=6.0 Hz, *C*H$_3$CH$_2$OP), 16.31 (*C*H$_3$, dia A), 16.56 (*C*H$_3$, dia B), 20.35 (*C*H$_2$, dia A), 22.61 (*C*H$_2$, dia B), 32.26 (d, $^2J_{CP}$=3.2 Hz, *C*H$_2$CHP, dia A), 32.39 (d, $^2J_{CP}$=3.2 Hz, *C*H$_2$CHP, dia B), 33.05 (d, $^3J_{CP}$=6.1 Hz, *C*, dia A), 33.15 (d, $^3J_{CP}$=6.1 Hz, *C*, dia B), 37.45 (*C*H$_2$, dia A), 37.52 (d, $^1J_{CP}$=139.7 Hz, *C*HP, dia A), 37.63 (d, $^1J_{CP}$=139.7 Hz, *C*HP, dia B), 41.35 (*C*H$_2$, dia B), 62.41 (d, $^2J_{CP}$=6.3 Hz, *C*H$_2$OP, dia A), 62.45 (d, $^2J_{CP}$=6.3 Hz, *C*H$_2$OP, dia A), 63.21 (d, $^2J_{CP}$=6.3 Hz, *C*H$_2$OP, dia B), 63.32 (d, $^2J_{CP}$=6.3 Hz, *C*H$_2$OP, dia B), 76.41 (*C*H$_2$O, dia A), 77.23 (*C*H$_2$O, dia B), 166.51 (d, $^2J_{CP}$=4.4 Hz, *C*OO, dia A), 166.63 (d, $^2J_{CP}$=4.4 Hz, *C*OO, dia B), Anal. calcd for $C_{13}H_{25}O_5P$: C, 53.42; H, 8.62. Found: C, 53.58; H, 8.50.

4.4.4. (5-Methyl-2-oxo-5-phenyl-tetrahydro-pyran-3-yl)-phosphonic acid diethyl ester (6d). (0.78 g, 60% yield); diasteroisomer ratio 3:1; colorless oil; IR (film) 3058, 1732, 1240, 1172 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=22.90, 23.02 (**5d** δ=24.44, 24.61); ^1H NMR ($CDCl_3$) δ=1.32 (s, 3H, CH_3, major), 1.33 (t, 3H, $^3J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.34 (t, 3H, $^3J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.45 (s, 3H, CH_3, minor), 2.30 (ddt, 1H, $^4J_{HH}$=3.2 Hz, $^3J_{HH}$=9.0 Hz, $^2J_{HH}$=$^3J_{HP}$=14.0 Hz, C*H*CHP, minor), 2.32 (dt, 1H, $^3J_{HH}$=11.7 Hz, $^2J_{HH}$= $^3J_{HP}$=14.0 Hz, C*H*CHP, major), 2.55–2.72 (m, 1H, $^4J_{HH}$= 3.7 Hz, $^3J_{HH}$=7.7 Hz, $^2J_{HH}$=14.0 Hz, C*H*CHP, major), 2.55–2.71 (m, 1H, $^3J_{HH}$=9.0 Hz, $^2J_{HH}$=14.0 Hz, C*H*CHP, minor), 2.79 (ddd, 1H, $^3J_{HH}$=7.7, 11.7 Hz, $^2J_{HP}$=26.5 Hz, C*H*P, major), 3.33 (dt, 1H, $^3J_{HH}$=9.0 Hz, $^2J_{HP}$=27.7 Hz, C*H*P, minor), 4.11–4.32 (m, 4H, 2×CH_2OP), 4.21 (dd, 1H, $^4J_{HH}$=3.2 Hz, $^2J_{HH}$=11.0 Hz, C*H*O, minor), 4.35 (d, 1H, $^2J_{HH}$=11.7 Hz, C*H*O, major), 4.59 (d, 1H, $^2J_{HH}$=11.0 Hz, C*H*O, minor), 4.76 (dd, 1H, $^4J_{HH}$=3.7 Hz, $^2J_{HH}$=11.7 Hz, C*H*O, major); ^{13}C NMR ($CDCl_3$) δ=16.05 (d, $^3J_{CP}$=4.9 Hz, *C*H$_3$CH$_2$OP), 16.12 (d, $^3J_{CP}$=4.9 Hz, *C*H$_3$CH$_2$OP), 22.61 (*C*H$_3$, minor), 26.96 (*C*H$_3$, major), 33.94 (d, $^2J_{CP}$=3.8 Hz, *C*H$_2$, minor), 34.83 (d, $^2J_{CP}$=3.5 Hz, *C*H$_2$, major), 36.32 (d, $^3J_{CP}$=7.8 Hz, *C*, minor), 37.25 (d, $^3J_{CP}$=6.2 Hz, *C*, major), 38.30 (d, $^1J_{CP}$=138.0 Hz, *C*HP, minor), 38.67 (d, $^1J_{CP}$= 138.0 Hz, *C*HP, major), 62.31 (d, $^2J_{CP}$=6.8 Hz, *C*H$_2$OP, major), 62.52 (d, $^2J_{CP}$=6.8 Hz, *C*H$_2$OP, minor), 63.33 (d, $^2J_{CP}$=6.8 Hz, *C*H$_2$OP, major), 63.42 (d, $^2J_{CP}$=6.8 Hz, *C*H$_2$OP, minor), 75.81 (*C*H$_2$O, major), 76.58 (*C*H$_2$O, minor), 125.10 (2×*C*H, minor), 125.70 (2×*C*H, major), 126.90 (*C*H, major), 127.02 (*C*H, minor), 128.61 (2×*C*H, minor), 128.92 (2×*C*H, major), 141.12 (*C*, major), 143.5 (*C*, minor), 165.12, (d, $^2J_{CP}$=4.4 Hz, *C*OO, major), 165.93 (d, $^2J_{CP}$=4.4 Hz, *C*OO, minor). Anal. calcd for $C_{16}H_{23}O_5P$: C, 58.89; H, 7.10. Found: C, 59.03; H, 7.24.

4.4.5. (6-Methyl-2-oxo-tetrahydro-pyran-3-yl)-phosphonic acid diethyl ester (6e). (0.75 g, 75% yield); diasteroisomer ratio 1:1; colorless oil; IR (film) 1735, 1252, 1136 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=22.75, 23.09 (**5e**

δ=23.29, 23.35); ^{1}H NMR ($CDCl_3$) δ=1.35 (t, 3H, $^3J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.36 (t, 3H, $^3J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.37 (d, 3H, $^3J_{HH}$=6.2 Hz, CH_3CHO, dia A), 1.41 (d, 3H, $^3J_{HH}$=6.2 Hz, CH_3CHO, dia B), 1.51–2.42 (m, 4H, 2×CH_2), 3.10 (ddd, 1H, $^3J_{HH}$=4.7, 7.2 Hz, $^2J_{HP}$=26.2 Hz, C*H*P, dia A), 3.12 (dt, 1H, $^3J_{HH}$=8.2 Hz, $^2J_{HP}$=27.7 Hz, C*H*P, dia B), 4.11–4.32 (m, 4H, 2×CH_2OP), 4.45 (dq, 1H, $^3J_{HH}$=6.2, 12.5 Hz, C*H*O, dia A), 4.63 (ddq, 1H, $^3J_{HH}$=2.5, 6.2, 10.7 Hz, C*H*O, dia B), ^{13}C NMR ($CDCl_3$) δ=15.94 (d, $^3J_{CP}$=5.9 Hz, *C*H$_3$CH$_2$OP), 16.03 (d, $^3J_{CP}$=5.9 Hz, *C*H$_3$CH$_2$OP), 20.11 (d, $^2J_{CP}$=4.3 Hz, *C*H$_2$, dia A), 20.62 (d, $^2J_{CP}$=4.3 Hz, *C*H$_2$, dia B), 21.02 (*C*H$_3$CHO, dia A), 21.23 (*C*H$_3$CHO, dia B), 27.20 (d, $^3J_{CP}$=5.5 Hz, *C*H$_2$, dia A), 29.05 (d, $^3J_{CP}$=8.0 Hz, *C*H$_2$, dia B), 38.66 (d, $^1J_{CP}$=137.1 Hz, *C*HP, dia A), 39.26 (d, $^1J_{CP}$=137.1 Hz, *C*HP, dia B), 62.33 (d, $^2J_{CP}$=6.9 Hz, *C*H$_2$OP, dia A), 62.41 (d, $^2J_{CP}$=6.9 Hz, *C*H$_2$OP, dia B), 63.05 (d, $^2J_{CP}$=6.9 Hz, *C*H$_2$OP, dia A), 63.21 (d, $^2J_{CP}$=6.9 Hz, *C*H$_2$OP, dia B), 77.12 (*C*HO, dia A), 77.37 (*C*HO, dia B), 166.21 (d, $^2J_{CP}$=3.8 Hz, *C*OO, dia A), 166.62 (d, $^2J_{CP}$=3.8 Hz, *C*OO, dia B). Anal. calcd for $C_{10}H_{19}O_5P$: C, 48.00; H, 7.65. Found: C, 48.12; H, 7.49.

4.4.6. (2-Oxo-octahydro-chromen-3-yl)-phosphonic acid diethyl ester (6f). (0.87 g, 75% yield); diasteroisomer ratio 2:1; colorless oil; IR (film) 1731, 1248, 1184 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=22.70, 22.90 (**5f** δ=23.30, 23.50); ^{1}H NMR ($CDCl_3$) δ=1.35 (t, 3H, $^3J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.36 (t, 3H, $^3J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.03–1.60 (m, 4H, 2×CH_2), 1.65–1.95 (m, 4H, 2×CH_2), 2.05–2.44 (m, 3H, CH_2, C*H*), 3.07 (dt, 1H, $^3J_{HH}$=9.0 Hz, $^2J_{HP}$=27.5 Hz, C*H*P, minor), 3.15 (dt, 1H, $^3J_{HH}$=8.5 Hz, $^2J_{HP}$=27.7 Hz, C*H*P, major), 3.91–4.15 (m, 5H, 2×CH_2OP, C*H*O); ^{13}C NMR ($CDCl_3$) δ=15.81 (d, $^3J_{CP}$=4.7 Hz, *C*H$_3$CH$_2$OP), 15.91 (d, $^3J_{CP}$=4.7 Hz, *C*H$_3$CH$_2$OP), 23.22 (*C*H$_2$, major), 23.35 (*C*H$_2$, minor), 24.32 (*C*H$_2$, major), 24.41 (*C*H$_2$, minor), 27.53 (d, $^2J_{CP}$=4.0 Hz, *C*H$_2$, minor), 27.91 (d, $^2J_{CP}$=4.0 Hz, *C*H$_2$, major), 30.11 (*C*H$_2$, major), 30.22 (*C*H$_2$, minor), 31.32 (*C*H$_2$, minor), 31.51 (*C*H$_2$, major), 36.05 (d, $^3J_{CP}$=4.0 Hz, *C*H, major), 37.61 (d, $^3J_{CP}$=8.0 Hz, *C*H, minor), 39.16 (d, $^1J_{CP}$=137.8 Hz, *C*HP, minor), 39.82 (d, $^1J_{CP}$=137.8 Hz, *C*HP, major), 61.72 (d, $^2J_{CP}$=6.8 Hz, *C*H$_2$OP, minor), 61.92 (d, $^2J_{CP}$=6.8 Hz, *C*H$_2$OP, major), 62.73 (d, $^2J_{CP}$=6.8 Hz, *C*H$_2$OP, minor), 62.93 (d, $^2J_{CP}$=6.8 Hz, *C*H$_2$OP, major), 82.21 (*C*HO, major), 82.92 (*C*HO, minor), 165.51 (d, $^2J_{CP}$=4.4 Hz, *C*OO, major), 166.18 (d, $^2J_{CP}$=4.4 Hz, *C*OO, minor). Anal. calcd for $C_{13}H_{23}O_5P$: C, 53.79; H, 7.99. Found: C, 53.91; H, 7.73.

4.4.7. (5-Methyl-2-oxo-tetrahydro-pyran-3-yl)-phosphonic acid diethyl ester (6g). (0.60 g, 60% yield); diasteroisomer ratio 1.5:1; colorless oil; IR (film) 1737, 1252, 1160 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=22.50, 22.61 (**5g** δ=23.59, 23.70); ^{1}H NMR ($CDCl_3$) δ=1.02 (d, 3H, $^3J_{HH}$=6.5 Hz, CH_3CH), 1.26 (t, 3H, $^3J_{HH}$=7.0 Hz, CH_3-CH$_2$OP), 1.28 (t, 3H, $^3J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.73–2.51 (m, 3H, CH_2, C*H*), 3.18 (ddd, 1H, $^3J_{HH}$=8.2, 9.7 Hz, $^2J_{HP}$=27.5 Hz, C*H*P, major), 3.20 (ddd, 1H, $^3J_{HH}$=4.7, 8.0 Hz, $^2J_{HP}$=27.7 Hz, C*H*P, minor), 3.94 (dd, 1H, $^3J_{HH}$= 9.0 Hz, $^2J_{HH}$=11.0 Hz, C*H*O, major), 4.06 (t, 1H, $^3J_{HH}$= $^2J_{HH}$=11.0 Hz, C*H*O, minor), 4.15–4.30 (m, 4H, 2×CH_2OP), 4.25 (ddd, 1H, $^4J_{HH}$=2.0 Hz, $^3J_{HH}$=5.0 Hz, $^2J_{HH}$=11.0 Hz, C*H*O, major), 4.41 (ddd, $^4J_{HH}$=2.0 Hz, $^3J_{HH}$=4.0 Hz, $^2J_{HH}$=11.0 Hz, C*H*O, 1H, minor); ^{13}C NMR ($CDCl_3$) δ=16.10 (d, $^3J_{CP}$=4.2 Hz, 2×*C*H$_3$CH$_2$OP), 16.19 (*C*H$_3$CH), 25.54 (d, $^2J_{CP}$=4.4 Hz, *C*H$_2$, major), 28.22 (d, $^3J_{CP}$=9.2 Hz, *C*H, major), 28.85 (d, $^2J_{CP}$=4.4 Hz, *C*H$_2$, minor), 29.54 (d, $^3J_{CP}$=4.3 Hz, *C*H, minor), 38.72 (d, $^1J_{CP}$=138.5 Hz, *C*HP, minor), 39.92 (d, $^1J_{CP}$=138.5 Hz, *C*HP, major), 62.41 (d, $^2J_{CP}$=6.6 Hz, *C*H$_2$OP, major), 62.52 (d, $^2J_{CP}$=6.6 Hz, *C*H$_2$OP, minor), 63.34 (d, $^2J_{CP}$=6.6 Hz, *C*H$_2$OP, major), 63.42 (d, $^2J_{CP}$=6.6 Hz, *C*H$_2$OP, minor), 74.52 (*C*H$_2$O, major), 74.80 (*C*H$_2$O, minor), 165.91 (d, $^2J_{CP}$=4.4 Hz, *C*OO, major), 166.11 (d, $^2J_{CP}$=4.4 Hz, *C*OO, minor). Anal. calcd for $C_{10}H_{19}O_5P$: C, 48.00; H, 7.65. Found: C, 48.21; H, 7.55.

4.4.8. (5-Ethyl-2-oxo-tetrahydro-pyran-3-yl)-phosphonic acid diethyl ester (6h). (0.61 g, 58% yield); diasteroisomer ratio 1.5:1; colorless oil; IR (film) 1736, 1252, 1176 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=22.93, 22.88 (**5h** δ=24.06, 24.15); ^{1}H NMR ($CDCl_3$) δ=0.91 (t, 3H, $^3J_{HH}$=7.2 Hz, CH_3CH$_2$), 1.28 (t, 3H, $^3J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.29 (t, 3H, $^3J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.31–1.91 (m, 3H, CH_2, C*H*), 2.01–2.53 (m, 2H, CH_2), 3.10 (ddd, 1H, $^3J_{HH}$=8.1, 10.8 Hz, $^2J_{HP}$=27.4 Hz, C*H*P, major), 3.15 (ddd, 1H, $^3J_{HH}$=4.2, 8.7 Hz, $^2J_{HP}$=27.4 Hz, C*H*P, minor), 3.97 (dd, 1H, $^3J_{HH}$=9.0 Hz, $^2J_{HH}$=11.0 Hz, C*H*O, major), 4.06 (t, 1H, $^3J_{HH}$=$^2J_{HH}$=11.0 Hz, C*H*O, minor), 4.08–4.22 (m, 4H, 2×CH_2OP), 4.28 (ddd, 1H, $^4J_{HH}$=2.0 Hz, $^3J_{HH}$=5.0 Hz, $^2J_{HH}$=11.0 Hz, C*H*O, major), 4.41 (ddd, 1H, $^4J_{HH}$=2.0 Hz, $^3J_{HH}$=4.0 Hz, $^2J_{HH}$=11.0 Hz, C*H*O, minor); ^{13}C NMR ($CDCl_3$) δ=9.34 (*C*H$_3$CH$_2$, major), 9.40 (*C*H$_3$CH$_2$, minor), 14.50 (d, $^3J_{CP}$=3.8 Hz, *C*H$_3$CH$_2$OP), 14.61 (d, $^3J_{CP}$=3.8 Hz, *C*H$_3$CH$_2$OP), 22.24 (*C*H$_2$, minor), 22.60 (*C*H$_2$, major), 25.00 (d, $^2J_{CP}$=4.6 Hz, *C*H$_2$CHP, minor), 25.62 (d, $^2J_{CP}$=4.2 Hz, *C*H$_2$CHP, major), 30.58 (d, $^3J_{CP}$=4.9 Hz, *C*H, minor), 33.02 (d, $^3J_{CP}$=8.7 Hz, *C*H, major), 37.01 (d, $^1J_{CP}$=137.7 Hz, *C*HP, minor), 37.61 (d, $^1J_{CP}$=137.7 Hz, *C*HP, major), 60.91 (d, $^2J_{CP}$=6.5 Hz, *C*H$_2$OP, major), 61.01 (d, $^2J_{CP}$=6.5 Hz, *C*H$_2$OP, minor), 61.62 (d, $^2J_{CP}$=6.5 Hz, *C*H$_2$OP, major), 61.82 (d, $^2J_{CP}$=6.5 Hz, *C*H$_2$OP, minor), 71.51 (*C*H$_2$O, minor), 71.64 (*C*H$_2$O, major), 164.71 (d, $^2J_{CP}$=4.4 Hz, *C*OO, major), 164.91 (d, $^2J_{CP}$=4.4 Hz, *C*OO, minor). Anal. calcd for $C_{11}H_{21}O_5P$: C, 50.00; H, 8.01. Found: C, 50.12; H, 8.14.

4.4.9. (5-Butyl-2-oxo-tetrahydro-pyran-3-yl)-phosphonic acid diethyl ester (6i). (0.76 g, 65% yield); diasteroisomer ratio 1.3:1; colorless oil; IR (film) 1736, 1252, 1160 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=22.56, 22.64 (**5i** δ=23.89, 23.96); ^{1}H NMR ($CDCl_3$) δ=0.84 (t, 3H, $^3J_{HH}$=6.2 Hz, CH_3CH$_2$), 1.17–1.27 (m, 6H, 3×CH_2), 1.28 (t, 3H, $^3J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.29 (t, 3H, $^3J_{HH}$=7.0 Hz, CH_3CH$_2$OP), 1.61–2.40 (m, 3H, CH_2, C*H*), 3.09 (ddd, 1H, $^3J_{HH}$=8.5, 9.2 Hz, $^2J_{HP}$=27.2 Hz, C*H*P, major), 3.11 (ddd, 1H, $^3J_{HH}$= 5.5, 8.2 Hz, $^2J_{HP}$=27.2 Hz, C*H*P, minor), 3.91 (dd, 1H, $^3J_{HH}$=8.7 Hz, $^2J_{HH}$=11.0 Hz, C*H*O, major), 4.11 (t, 1H, $^3J_{HH}$=$^2J_{HH}$=11.0 Hz, C*H*O, minor), 4.01–4.20 (m, 4H, 2×CH_2O), 4.25 (ddd, 1H, $^4J_{HH}$=3.0 Hz, $^3J_{HH}$=5.0 Hz, $^2J_{HH}$=11.0 Hz, C*H*O, 1H, minor), 4.40 (ddd, 1H, $^4J_{HH}$= 1.7 Hz, $^3J_{HH}$=4.7 Hz, $^2J_{HH}$=11.0 Hz, C*H*O, major); ^{13}C NMR ($CDCl_3$) δ=13.63 (*C*H$_3$CH$_2$, major), 13.65 (*C*H$_3$CH$_2$, minor), 16.05 (d, $^3J_{CP}$=3.8 Hz, *C*H$_3$CH$_2$OP), 16.15 (d, $^3J_{CP}$=3.8 Hz, *C*H$_3$CH$_2$OP), 22.35 (*C*H$_2$, minor), 22.41 (*C*H$_2$, major), 26.92 (d, $^2J_{CP}$=4.4 Hz, *C*H$_2$CHP, minor), 27.63 (d, $^2J_{CP}$=4.4 Hz, *C*H$_2$CHP, major), 28.51 (*C*H$_2$,

major), 28.60 (CH_2, minor), 30.50 (CH_2, major), 30.71 (d, $^3J_{CP}$=4.9 Hz, *C*H, minor), 30.91 (CH_2, minor), 33.01 (d, $^3J_{CP}$=8.7 Hz, *C*H, major), 38.61 (d, $^1J_{CP}$=138.0 Hz, *C*HP, minor), 39.71 (d, $^1J_{CP}$=138.0 Hz, *C*HP, major), 62.41 (d, $^2J_{CP}$=6.7 Hz, CH_2OP, major), 62.51 (d, $^2J_{CP}$=6.7 Hz, CH_2OP, minor), 63.22 (d, $^2J_{CP}$=6.7 Hz, CH_2OP, major), 63.34 (d, $^2J_{CP}$=6.7 Hz, CH_2OP, minor), 73.4 (CH_2O, major), 73.51 (CH_2O, minor), 166.21 (d, $^2J_{CP}$=4.4 Hz, *C*OO, major), 166.45 (d, $^2J_{CP}$=4.4 Hz, *C*OO, minor). Anal. calcd for $C_{13}H_{25}O_5P$: C, 53.42; H, 8.62. Found: C, 53.58; H, 8.79.

4.4.10. (5-Benzyl-2-oxo-tetrahydro-pyran-3-yl)-phosphonic acid diethyl ester (6j). (0.81 g, 62% yield); diasteroisomer ratio 1:1; colorless oil; IR (film) 3035, 1732, 1252, 1160 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=22.65, 22.70 (**5j** δ=23.95, 24.05); ^{1}H NMR ($CDCl_3$) δ=1.32 (t, 3H, $^3J_{HH}$=7.0 Hz, C*H*$_3$CH$_2$OP), 1.34 (t, 3H, $^3J_{HH}$=7.0 Hz, C*H*$_3$CH$_2$OP), 1.85–2.05 (m, 1H, C*H*), 2.11–2.45 (m, 2H, C*H*$_2$), 2.55–2.75 (m, 2H, C*H*$_2$), 3.16 (ddd, 1H, $^3J_{HH}$=8.5, 9.6 Hz, $^2J_{HP}$=27.3 Hz, C*H*P, dia A), 3.15 (ddd, $^3J_{HH}$=5.0, 8.0 Hz, $^2J_{HP}$=27.5 Hz, C*H*P, dia B), 4.05 (dd, 1H, $^3J_{HH}$=7.7 Hz, $^2J_{HH}$=11.0 Hz, C*H*O, dia A), 4.03–4.11 (m, 1H, C*H*O, dia B), 4.12–4.26 (m, 4H, 2×C*H*$_2$OP), 4.27–4.32 (m, 1H, C*H*O, dia B), 4.40 (ddd, 1H, $^4J_{HH}$=1.0 Hz, $^3J_{HH}$=4.0 Hz, $^2J_{HH}$=11.0 Hz, C*H*O, dia A), 7.11–7.36 (m, 5H, C$_6$*H*$_5$,); ^{13}C NMR ($CDCl_3$) δ=16.01 (d, $^3J_{CP}$=4.2 Hz, *C*H$_3$CH$_2$OP), 16.11 (d, $^3J_{CP}$=4.2 Hz, *C*H$_3$CH$_2$OP), 26.44 (d, $^2J_{CP}$=4.2 Hz, CH_2CHP, dia A), 27.32 (d, $^2J_{CP}$=4.2 Hz, *C*H$_2$CHP, dia B), 32.11 (d, $^3J_{CP}$=4.6 Hz, *C*H, dia A), 34.73 (d, $^3J_{CP}$=8.8 Hz, *C*H, dia B), 36.93 (CH_2, dia A), 37.55 (CH_2, dia B), 38.61 (d, $^1J_{CP}$=138.9 Hz, *C*HP, dia A), 39.41 (d, $^1J_{CP}$=138.9 Hz, *C*HP, dia B), 62.34 (d, $^2J_{CP}$=5.8 Hz, *C*H$_2$OP, dia A), 62.44 (d, $^2J_{CP}$=5.8 Hz, *C*H$_2$OP, dia B), 63.25 (d, $^2J_{CP}$=5.8 Hz, CH_2OP, dia A), 63.28 (d, $^2J_{CP}$=5.8 Hz, *C*H$_2$OP, dia B), 72.60 (CH_2O, dia A), 72.74 (CH_2O, dia B), 126.31 (*C*H, dia A), 126.40 (*C*H, dia B), 128.31 (4×*C*H, dia A), 128.51 (4×*C*H, dia B), 137.62 (*C*, dia A), 137.76 (*C*, dia B), 164.05 (d, $^2J_{CP}$=4.4 Hz, *C*OO, dia A), 164.16 (d, $^2J_{CP}$=4.4 Hz, *C*OO, dia B). Anal. calcd for $C_{16}H_{23}O_5P$: C, 58.89; H, 7.10. Found: C, 59.02; H, 7.25.

4.4.11. 3-(Diethoxyphosphoryl)-2-oxo-hexahydro-chromene-4a-carboxylic acid ethyl ester (6k). (1.13 g, 78% yield); diasteroisomer ratio 2:1; colorless oil; IR (film) 1730, 1248, 1144 cm^{-1}; ^{31}P NMR ($CDCl_3$) δ=23.11, 22.45 (**5k** δ=24.12, 24.25); ^{1}H NMR ($CDCl_3$) δ=1.27 (t, 3H, $^3J_{HH}$=7.0 Hz, C*H*$_3$CH$_2$O), 1.35 (t, 3H, $^3J_{HH}$=7.2 Hz, C*H*$_3$-CH$_2$OP), 1.36 (t, 3H, $^3J_{HH}$=7.2 Hz, C*H*$_3$CH$_2$OP), 1.41–1.72 (m, 4H, 2×C*H*$_2$), 1.82–2.12 (m, 4H, 2×C*H*$_2$), 2.21–2.31 (m, 1H, C*H*CHP, major), 2.33–2.42 (m, 1H, C*H*CHP minor), 2.45 (ddd, 1H, $^3J_{HP}$=5.7 Hz, $^3J_{HH}$=9.5 Hz, $^2J_{HH}$=14.0 Hz, C*H*CHP, major), 2.60 (ddd, 1H, $^3J_{HH}$=9.0 Hz, $^2J_{HH}$=14.2 Hz, $^3J_{HP}$=17.0 Hz, C*H*CHP, minor), 3.20 (ddd, 1H, $^3J_{HH}$=9.0, 10.0 Hz, $^2J_{HP}$=27.5 Hz, C*H*P, minor), 3.32 (dt, 1H, $^3J_{HH}$=9.5 Hz, $^2J_{HP}$=27.5 Hz, C*H*P, major), 4.15–4.32 (m, 7H, 2×C*H*$_2$OP, CH$_3$C*H*$_2$O, C*H*O); ^{13}C NMR ($CDCl_3$) δ=13.86 (*C*H$_3$), 16.10 (d, $^2J_{CP}$=4.7 Hz, 2×*C*H$_3$CH$_2$OP), 18.15 (d, $^2J_{CP}$=4.7 Hz, CH_2, minor), 20.51 (CH_2, minor), 21.61 (d, $^2J_{CP}$=4.7 Hz, CH_2, major), 23.41 (CH_2, major), 26.61 (CH_2, minor), 27.61 (CH_2, major), 31.63 (CH_2, minor), 32.41 (CH_2, minor), 33.50 (CH_2, major), 34.61 (CH_2, major), 36.91 (d, $^1J_{CP}$=138.2 Hz, *C*HP, minor), 39.33 (d, $^1J_{CP}$=138.2 Hz, *C*HP, major), 44.51 (d, $^3J_{CP}$=9.1 Hz, *C*, minor), 45.21 (d, $^3J_{CP}$=6.5 Hz, *C*, major), 60.91 (CH_2O, major), 61.22 (CH_2O, minor), 63.03 (d, $^2J_{CP}$=6.5 Hz, CH_2OP), 63.61 (d, $^2J_{CP}$=6.5 Hz, CH_2OP), 78.71 (*C*HO, minor), 81.62 (*C*HO, major), 165.11 (d, $^2J_{CP}$=4.4 Hz, *C*OO, major), 165.91 (d, $^2J_{CP}$=4.4 Hz, *C*OO, minor), 171.71 (*C*OOCH$_2$CH$_3$, major), 173.57 (*C*OOCH$_2$CH$_3$, minor). Anal. calcd for $C_{16}H_{27}O_7P$: C, 53.03; H, 7.51. Found: C, 53.18; H, 7.69.

4.5. General procedure for synthesis of methylenelactones 7a–k

A mixture of α-phosphonolactone **6** (**a**–**k**) (2.5 mmol), potassium carbonate (1.04 g, 7.5 mmol) and aqueous 36% formaldehyde (0.35 ml), in THF (3 ml) was stirred at 0°C for 30 min. The mixture was then extracted with diethyl ether (3×15 ml). The organic layer was washed with saturated sodium chloride solution (10 ml) dried ($MgSO_4$) and evaporated. The oil residue was purified by column chromatography on silica gel using AcOEt/hexane (1:2) as eluent.

4.5.1. 5,5-Dimethyl-3-methylene-tetrahydro-pyran-2-one (7a). (0.23 g, 65% yield); colorless oil; IR (film) 3080, 1724, 1632, 1204 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=0.97 (s, 6H, 2×C*H*$_3$), 2.37–2.39 (m, 2H, C*H*$_2$), 3.96 (s, 2H, C*H*$_2$O), 5.53 (q, 1H, $^2J_{HH}$=$^4J_{HH}$=1.7 Hz, C*H*), 6.45 (q, 1H, $^2J_{HH}$=$^4J_{HH}$=1.7 Hz, C*H*); ^{13}C NMR ($CDCl_3$): δ=23.66 (2×*C*H$_3$), 30.06 (*C*), 41.44 (*C*H$_2$), 78.30 (*C*H$_2$O), 128.40 (*C*H$_2$), 132.60 (*C*), 164.50 (*C*OO). Anal. calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.67; H, 8.51.

4.5.2. 4-Methylene-2-oxaspiro [5.5] undecan-3-one (7b). (0.32 g, 70% yield), colorless oil; IR (film) 3082, 1720, 1640, 1201 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=1.38–1.50 (m, 10H, 5×C*H*$_2$), 2.49–2.51 (m, 2H, C*H*$_2$), 4.10 (s, 2H, C*H*$_2$O), 5.55 (q, 1H, $^2J_{HH}$=$^4J_{HH}$=1.7 Hz, C*H*), 6.41 (q, 1H, $^2J_{HH}$=$^4J_{HH}$=1.7 Hz, C*H*); ^{13}C NMR ($CDCl_3$): δ=20.24 (2×*C*H$_2$), 25.01 (*C*H$_2$), 31.58 (2×*C*H$_2$), 32.02 (*C*), 37.90 (*C*H$_2$), 77.30 (*C*H$_2$O), 127.80 (*C*), 131.80 (*C*H$_2$), 164.60 (*C*OO). Anal. calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: 73.41; H, 9.12.

4.5.3. 5-Methyl-3-methylene-5-propyl-tetrahydro-pyran-2-one (7c). (0.28 g, 67% yield), colorless oil; IR (film) 3080, 1728, 1628, 1248 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=0.82 (t, 3H, $^3J_{HH}$=7.0 Hz, C*H*$_3$), 0.91 (s, 3H, C*H*$_3$), 1.14–1.32 (m, 4H, 2×C*H*$_2$), 2.33 (ddt, 1H, $^4J_{HH}$=1.2, 1.7 Hz, $^2J_{HH}$=15.7 Hz, C*H*), 2.42 (ddt, 1H, $^4J_{HH}$=1.2, 1.7 Hz, $^2J_{HH}$=15.7 Hz, C*H*), 3.94 (dd, 1H, $^4J_{HH}$=1.2 Hz, $^2J_{HH}$=11.0 Hz, C*H*O), 4.01 (dd, 1H, $^4J_{HH}$=1.2 Hz, $^2J_{HH}$=11.0 Hz, C*H*O), 5.46 (q, 1H, $^2J_{HH}$=$^4J_{HH}$=1.7 Hz, C*H*), 6.37 (q, 1H, $^2J_{HH}$=$^4J_{HH}$=1.7 Hz, C*H*); ^{13}C NMR ($CDCl_3$): δ=13.67 (*C*H$_3$), 15.54 (*C*H$_3$), 20.24 (*C*H$_2$), 32.14 (*C*), 38.18 (*C*H$_2$), 39.48 (*C*H$_2$), 76.62 (*C*H$_2$O), 128.0 (*C*H$_2$), 131.9 (*C*), 164.41 (*C*OO). Anal. calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.51; H, 9.72.

4.5.4. 5-Methyl-3-methylene-5-phenyl-tetrahydro-pyran-2-one (7d). (0.32 g, 63% yield), colorless oil; IR (film) 3080, 3050, 1728, 1630, 1230 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=1.29 (s, 3H, C*H*$_3$), 2.74 (dq, 1H, $^4J_{HH}$=1.7 Hz, $^2J_{HH}$=15.5 Hz, C*H*), 3.07 (dq, 1H, $^4J_{HH}$=1.7 Hz,

$^{2}J_{HH}$=15.5 Hz, C*H*), 4.28 (dd, 1H, $^{4}J_{HH}$=1.7 Hz, $^{2}J_{HH}$=11.2 Hz, C*H*O), 4.52 (dd, 1H, $^{4}J_{HH}$=1.7 Hz, $^{2}J_{HH}$=11.2 Hz, C*H*O), 5.51 (q, 1H, $^{2}J_{HH}$=$^{4}J_{HH}$=1.7 Hz, C*H*), 6.36 (q, 1H, $^{2}J_{HH}$=$^{4}J_{HH}$=1.7 Hz, C*H*), 7.15–7.28 (m, 5H, C_6H_5); ^{13}CNMR ($CDCl_3$): δ=25.11 (*C*H$_3$), 37.70 (*C*), 41.07 (*C*H$_2$), 77.01 (*C*H$_2$O), 125.70 (2×*C*H), 127.10 (*C*H), 128.85 (2×*C*H), 129.57 (*C*H$_2$), 132.58 (*C*), 142.73 (*C*), 164.74 (*C*OO). Anal. calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.42; H, 7.12.

4.5.5. 6-Methyl-3-methylene-tetrahydro-pyran-2-one (7e). (0.31 g, 60% yield), colorless oil; IR (film) 3065, 1720, 1628, 1190 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=1.40 (d, 3H, $^{3}J_{HH}$=6.2 Hz, C*H*$_3$), 1.67 (dddd, 1H, $^{3}J_{HH}$=5.5, 10.2, 12.0 Hz, $^{2}J_{HH}$=14.0 Hz, C*H*), 1.94–2.03 (m, 1H, $^{3}J_{HH}$=2.5, 5.0 Hz, $^{2}J_{HH}$=14.0 Hz, C*H*), 2.57 (dddt, 1H, $^{4}J_{HH}$=2.5 Hz, $^{3}J_{HH}$=5.0, 12.0 Hz, $^{2}J_{HH}$=16.2 Hz, C*H*), 2.60–2.78 (m, 1H, $^{4}J_{HH}$=1.5 Hz, $^{3}J_{HH}$=5.5 Hz, $^{2}J_{HH}$=16.2 Hz, C*H*), 4.5 (ddq, 1H, $^{3}J_{HH}$=2.5, 6.2, 10.2 Hz, C*H*O), 5.50 (dt, 1H, $^{4}J_{HH}$=$^{2}J_{HH}$=1.5 Hz, $^{4}J_{HH}$=2.5 Hz, C*H*), 6.40 (dt, 1H, $^{4}J_{HH}$=$^{2}J_{HH}$=1.5 Hz, $^{4}J_{HH}$=2.5 Hz, C*H*); ^{13}C NMR ($CDCl_3$): δ=20.80 (*C*H$_3$), 26.60 (*C*H$_2$), 29.50 (*C*H$_2$), 77.70 (*C*HO), 127.80 (*C*H$_2$), 133.40 (*C*), 169.60 (*C*OO). Anal. calcd for $C_7H_{10}O_2$: C, 66.65; H, 7.99. Found: C, 66.78; H, 8.15.

4.5.6. 3-Methylene-octahydro-chromen-2-one (7f). (0.29 g, 70% yield); diasteroisomer ratio 2:1; **trans**: white solid, mp 33–35°C (lit.[17] 34–36°C); **cis**: white solid, mp 61–63°C (lit.[17] 61–63°C). Anal. calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.38; H, 8.62. All spectroscopic data for *trans* and *cis* isomers are in according with the literature.[17]

4.5.7. 5-Methyl-3-methylene-tetrahydro-pyran-2-one (7g). (0.20 g, 63% yield), colorless oil; IR (film) 3089, 1721, 1645, 1232 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=1.02 (d, 3H, $^{3}J_{HH}$=6.5 Hz, C*H*$_3$), 2.08–2.22 (m, 1H, C*H*), 2.31 (ddt, 1H, $^{4}J_{HH}$=2.2 Hz, $^{3}J_{HH}$=10.5 Hz, $^{2}J_{HH}$=15.5 Hz, C*H*), 2.76 (dddt, 1H, $^{4}J_{HH}$=1.5, 2.2 Hz, $^{3}J_{HH}$=5.5 Hz, $^{2}J_{HH}$=15.5 Hz, C*H*), 3.99 (dd, 1H, $^{3}J_{HH}$=9.5 Hz, $^{2}J_{HH}$=11.0 Hz, C*H*O), 4.32 (ddd, 1H, $^{4}J_{HH}$=2.2 Hz, $^{3}J_{HH}$=3.7 Hz, $^{2}J_{HH}$=11.0 Hz, C*H*O), 5.52 (dt, 1H, $^{2}J_{HH}$=$^{4}J_{HH}$=1.5 Hz, $^{4}J_{HH}$=2.2 Hz, C*H*), 6.43 (dt, 1H, $^{2}J_{HH}$=$^{4}J_{HH}$=1.5 Hz, $^{4}J_{HH}$=2.2 Hz, C*H*); ^{13}C NMR ($CDCl_3$): δ=15.71 (*C*H$_3$), 28.24 (*C*H), 35.86 (*C*H$_2$), 74.55 (*C*H$_2$O), 127.91 (*C*H$_2$), 133.24 (*C*), 164.93 (*C*OO). Anal. calcd for $C_7H_{10}O_2$: C, 66.65; H, 7.99. Found: C, 66.79; H, 8.16.

4.5.8. 5-Ethyl-3-methylene-tetrahydro-pyran-2-one (7h). (0.21 g, 60% yield), colorless oil; IR (film) 3080, 1730, 1628, 1225 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=0.98 (t, 3H, $^{3}J_{HH}$=7.5 Hz, C*H*$_3$), 1.25–1.47 (m, 2H, C*H*$_2$), 1.84–2.02 (m, 1H, C*H*), 2.33 (ddt, 1H, $^{4}J_{HH}$=2.2 Hz, $^{3}J_{HH}$=10.2 Hz, $^{2}J_{HH}$=15.7 Hz, C*H*), 2.77 (ddq, 1H, $^{4}J_{HH}$=2.2 Hz, $^{3}J_{HH}$=4.5 Hz, $^{2}J_{HH}$=15.7 Hz, C*H*), 4.03 (dd, 1H, $^{3}J_{HH}$=9.0 Hz, $^{2}J_{HH}$=11.0 Hz, C*H*O), 4.37 (ddd, 1H, $^{4}J_{HH}$=2.2 Hz, $^{3}J_{HH}$=3.7 Hz, $^{2}J_{HH}$=11.0 Hz, C*H*O), 5.52 (q, 1H, $^{2}J_{HH}$=$^{4}J_{HH}$=2.2 Hz, C*H*), 6.42 (q, 1H, $^{2}J_{HH}$=$^{4}J_{HH}$=2.2 Hz, C*H*); ^{13}C NMR ($CDCl_3$): δ=11.21 (*C*H$_3$), 23.85 (*C*H$_2$), 34.02 (*C*H), 35.15 (*C*H$_2$), 73.42 (*C*H$_2$O), 128.41 (*C*H$_2$), 133.53 (*C*), 165.61 (*C*OO). Anal. calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.42; H, 8.80.

4.5.9. 5-Butyl-3-methylene-tetrahydro-pyran-2-one (7i). (0.27 g, 65% yield), colorless oil; IR (film) 3082, 1724, 1645, 1220 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=0.91 (t, 3H, $^{3}J_{HH}$=6.7 Hz, C*H*$_3$), 1.21–1.37 (m, 6H, 3×C*H*$_2$), 1.93–2.04 (m, 1H, $^{3}J_{HH}$=3.7, 4.5, 9.2, 10.0 Hz, C*H*), 2.31 (ddt, 1H, $^{4}J_{HH}$=2.2 Hz, $^{3}J_{HH}$=10.0 Hz, $^{2}J_{HH}$=15.7 Hz, C*H*), 2.82 (ddq, 1H, $^{4}J_{HH}$=2.2 Hz, $^{3}J_{HH}$=4.5 Hz, $^{2}J_{HH}$=15.7 Hz, C*H*), 4.02 (dd, 1H, $^{3}J_{HH}$=9.2 Hz, $^{2}J_{HH}$=11.0 Hz, C*H*O), 4.35 (ddd, 1H, $^{4}J_{HH}$=2.2 Hz, $^{3}J_{HH}$=3.7 Hz, $^{2}J_{HH}$=11.0 Hz, C*H*O), 5.52 (q, 1H, $^{2}J_{HH}$=$^{4}J_{HH}$=2.2 Hz, C*H*), 6.40 (q, 1H, $^{2}J_{HH}$=$^{4}J_{HH}$=2.2 Hz, C*H*); ^{13}C NMR ($CDCl_3$): δ=13.91 (*C*H$_3$), 22.71 (*C*H$_2$), 28.85 (*C*H$_2$), 30.53 (*C*H$_2$), 33.55 (*C*H), 34.41 (*C*H$_2$), 73.46 (*C*H$_2$O), 128.43 (*C*H$_2$), 133.62 (*C*), 165.61 (*C*OO). Anal. calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.52; H, 9.77.

4.5.10. 5-Benzyl-3-methylene-tetrahydro-pyran-2-one (7j). (0.32 g, 65% yield), colorless oil; IR (film) 3090, 3016, 1724, 1627, 1228 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=2.23–2.43 (m, 2H, C*H*$_2$), 2.61–2.74 (m, 3H, C*H*$_2$, C*H*), 4.05 (dd, 1H, $^{3}J_{HH}$=9.2 Hz, $^{2}J_{HH}$=11.0 Hz, C*H*O), 4.32 (ddd, 1H, $^{4}J_{HH}$=2.0 Hz, $^{3}J_{HH}$=3.5 Hz, $^{2}J_{HH}$=11.0 Hz, C*H*O), 5.53 (q, 1H, $^{2}J_{HH}$=$^{4}J_{HH}$=1.7 Hz, C*H*), 6.42 (q, 1H, $^{2}J_{HH}$=$^{4}J_{HH}$=1.7 Hz, C*H*), 7.11–7.35 (m, 5H, C_6H_5); ^{13}C NMR ($CDCl_3$): δ=33.91 (*C*H$_2$), 35.25 (*C*H), 37.32 (*C*H$_2$), 73.01 (*C*H$_2$O), 126.72 (*C*H), 128.33 (2×*C*H), 128.71 (2×*C*H), 129.11 (*C*H$_2$), 133.12 (*C*), 138.25 (*C*), 165.31 (*C*OO). Anal. calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.35; H, 7.15.

4.5.11. 3-Methylene-2-oxo-hexahydro-chromene-4a-carboxylic acid ethyl ester (7k). (0.41 g, 68% yield); ethyl acetate/hexane (1:9) as eluent; diasteroisomer ratio 2:1; IR (KBr) 3085, 1723, 1620, 1236 cm^{-1}; **trans**: white solid mp 45–47°C; ^{1}H NMR ($CDCl_3$): δ=1.28 (t, 3H, $^{3}J_{HH}$=7.0 Hz, C*H*$_3$), 1.35–2.01 (m, 7H, 3×C*H*$_2$, C*H*), 2.28 (dq, 1H, $^{4}J_{HH}$=2.7 Hz, $^{2}J_{HH}$=13.5 Hz, C*H*), 2.51 (dt, 1H, $^{4}J_{HH}$=2.7 Hz, $^{2}J_{HH}$=16.0 Hz, C*H*), 2.95 (dt, 1H, $^{4}J_{HH}$=1.2 Hz, $^{2}J_{HH}$=16.0 Hz, C*H*), 4.20 (q, 2H, $^{3}J_{HH}$=7.0 Hz, C*H*$_2$), 4.21 (d, 1H, $^{3}J_{HH}$=16.0 Hz, C*H*O), 5.63 (dt, 1H, $^{2}J_{HH}$=$^{4}J_{HH}$=1.2 Hz, $^{4}J_{HH}$=2.7 Hz, C*H*), 6.52 (dt, 1H, $^{2}J_{HH}$=$^{4}J_{HH}$=1.2, $^{4}J_{HH}$=2.7 Hz, C*H*), ^{13}C NMR ($CDCl_3$): δ=13.81 (*C*H$_3$), 21.67 (*C*H$_2$), 23.78 (*C*H$_2$), 27.88 (*C*H$_2$), 34.59 (*C*H$_2$), 40.31 (*C*H$_2$), 46.62 (*C*), 60.37 (*C*H$_2$O), 82.64 (*C*HO), 128.44 (*C*H$_2$), 132.58 (*C*), 164.77 (*C*OO), 172.44 (*C*OOCH$_2$CH$_3$); **cis**: colorless oil; ^{1}H NMR ($CDCl_3$): δ=1.26 (t, 3H, $^{3}J_{HH}$=7.1 Hz, C*H*$_3$), 1.35–2.01 (m, 8H, 4×C*H*$_2$), 2.72 (dt, 1H, $^{4}J_{HH}$=1.5 Hz, $^{2}J_{HH}$=16.1 Hz, C*H*), 2.87 (dt, 1H, $^{4}J_{HH}$= 2.4 Hz, $^{2}J_{HH}$=16.1 Hz, C*H*), 4.23 (q, 2H, $^{3}J_{HH}$=7.1 Hz, C*H*$_2$O), 4.89 (t, 1H, $^{3}J_{HH}$=5.0 Hz, C*H*O), 5.62 (dt, 1H, $^{2}J_{HH}$=$^{4}J_{HH}$=1.5, $^{4}J_{HH}$=2.4 Hz, C*H*), 6.51 (dt, 1H, $^{2}J_{HH}$=$^{4}J_{HH}$=1.5, $^{4}J_{HH}$=2.4 Hz, C*H*); ^{13}C NMR ($CDCl_3$): δ=13.94 (*C*H$_3$), 19.91 (*C*H$_2$), 21.32 (*C*H$_2$), 28.50 (2×*C*H$_2$), 35.59 (*C*H$_2$), 44.95 (*C*), 61.08 (*C*H$_2$O), 78.90 (*C*HO), 129.11 (*C*H$_2$), 130.96 (*C*), 164.43 (*C*OO), 173.34 (*C*OOCH$_2$CH$_3$). Anal. calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.72; H, 7.85.

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