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# Asymmetric synthesis of enantiomerically pure 7-isopropenyl-4a-methyl-3-methyleneoctahydrochromen-2-ones

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**Abstract**—Four stereoisomers of 7-isopropenyl-4a-methyl-3-methyleneoctahydrochromenon-2-one have been obtained for the first time. The key step of the synthesis involves asymmetric Michael addition of chiral enamines derived from dihydrocarvone to acrylate **1**. Absolute configurations were established by X-ray analysis.


## 1. Introduction

The asymmetric Michael reaction of enamines derived from enantiomerically pure 1-phenylethylamine and 2-substituted cycloalkanones to electron-deficient olefins has attracted much attention over the past decades as a versatile method for the construction of enantiomerically enriched 2,2-disubstituted cycloalkanones.[1] A number of them have been synthesized by this method and utilized for the preparation of organic molecules containing a chiral quaternary stereogenic center. Moreover, a version of this reaction that utilizes enamines formed from 2-substituted cycloalkanones containing a stereogenic center in the ring represents a direct approach to the diastereoselective synthesis of enantiomerically pure 2,2-disubstituted cycloalkanones. Several examples of such an addition employing (*R*)- and (*S*)-dihydrocarvone, and 3(*R*),2(*RS*)-dimethylcyclohexanone have been reported.[2]

Our own studies led us to discover the potential of dicyclohexylammonium 2-(diethoxyphosphoryl)acrylate **1** as a Michael acceptor in this type of asymmetric addition. We have shown that the resulting 2-diethoxyphosphoryl-3-(2-oxocycloalkyl)propanoic acids can be used as chiral synthons for the preparation of enantiomerically enriched α-methylene-δ-valerolactones.[3] Treatment of these oxo-acids with $KBH_4$, lactonization, and finally Horner–Wadsworth–Emmons reaction of the resulting 2-diethoxyphosphoryl-δ-valerolactones with formaldehyde provided the corresponding α-methylene-δ-valerolactones with enantiomeric excesses exceeding 95% ee.

Based on this research and the importance of the α-methylene-δ-valerolactone motif in natural products,[4] we decided to explore further the potential of acrylate **1**. We envisioned that the use of enamines derived from chiral, properly substituted cycloalkanones would give access to enantiomerically pure α-methylene-δ-valerolactones. Dihydrocarvone was selected as a model ketone since it is easily available in both enantiomeric forms.[5] Herein, we report the first diastereoselective synthesis of four enantiomerically pure 3-methyleneoctahydrochromen-2-ones derived from (*R*)- and (*S*)-dihydrocarvone. These derivatives could be attractive precursors for the synthesis of biologically active compounds.[6]

## 2. Results and discussion

The four starting enamines **3**, **8**, **12**, and **16** were prepared by reacting (*R*)- and (*S*)-dihydrocarvone **2** and **7** with (*R*)- and (*S*)-1-phenylethylamine by the reported method.[2f] Schemes 1–4 outline transformation of enamines **3**, **8**, **12**, and **16** to the corresponding α-methylene-δ-valerolactones **6**, **11**, **15**, and **19**, respectively. The enamines proved useful as good substrates for the reaction with salt

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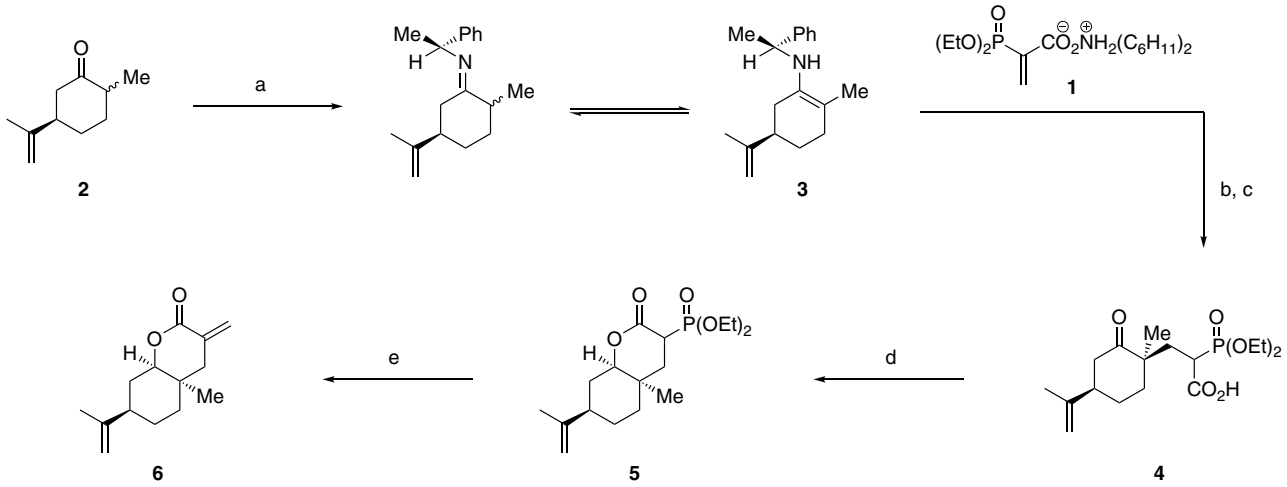
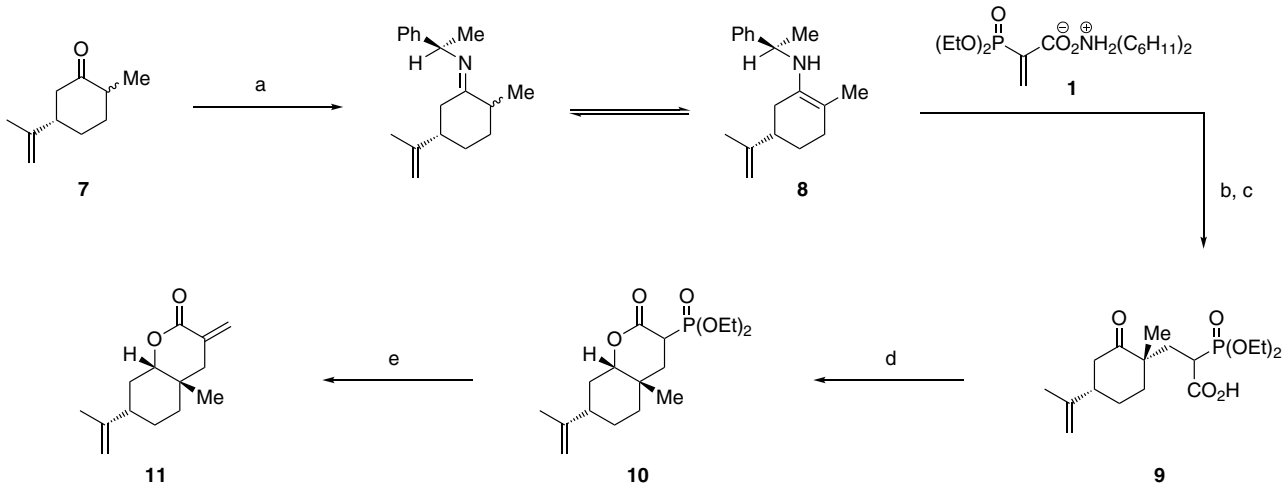



**Scheme 1.** Reagents and conditions: (a) (*S*)-1-phenylethylamine, *p*-TSA (cat), toluene, reflux, 12 h, 90%; (b) benzene, rt, 48 h; (c) Dowex 50W, acetone/water, 85%; (d) MeOH, $KBH_4$ (2 equiv), rt, 24 h, 90%; (e) *t*-BuOK (1 equiv), $(HCHO)_n$ (5 equiv), $Et_2O$, rt, 1 h, 85%.

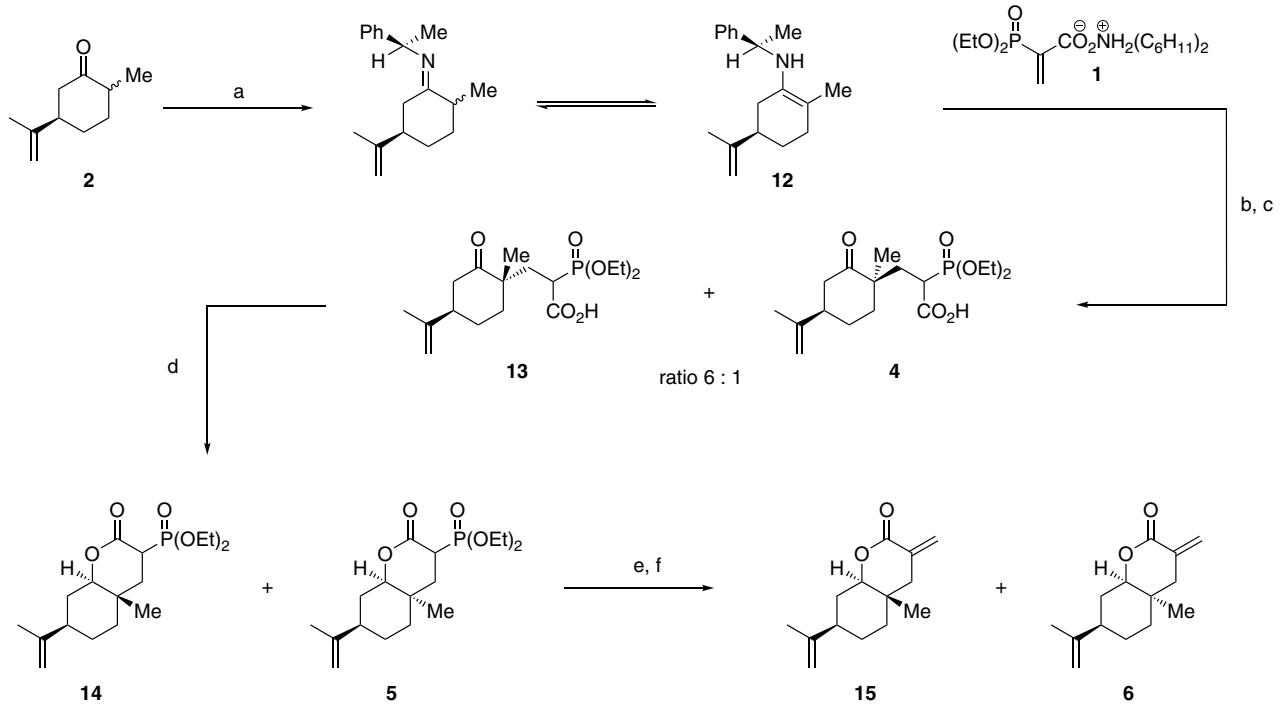



**Scheme 2.** Reagents and conditions: (a) (*R*)-1-phenylethylamine, *p*-TSA (cat), toluene, reflux, 12 h, 90%; (b) benzene, rt, 48 h; (c) Dowex 50W, acetone/water, 85%; (d) MeOH, $KBH_4$ (2 equiv), rt, 24 h, 90%; (e) *t*-BuOK (1 equiv), $(HCHO)_n$ (5 equiv), $Et_2O$, rt, 1 h, 85%.

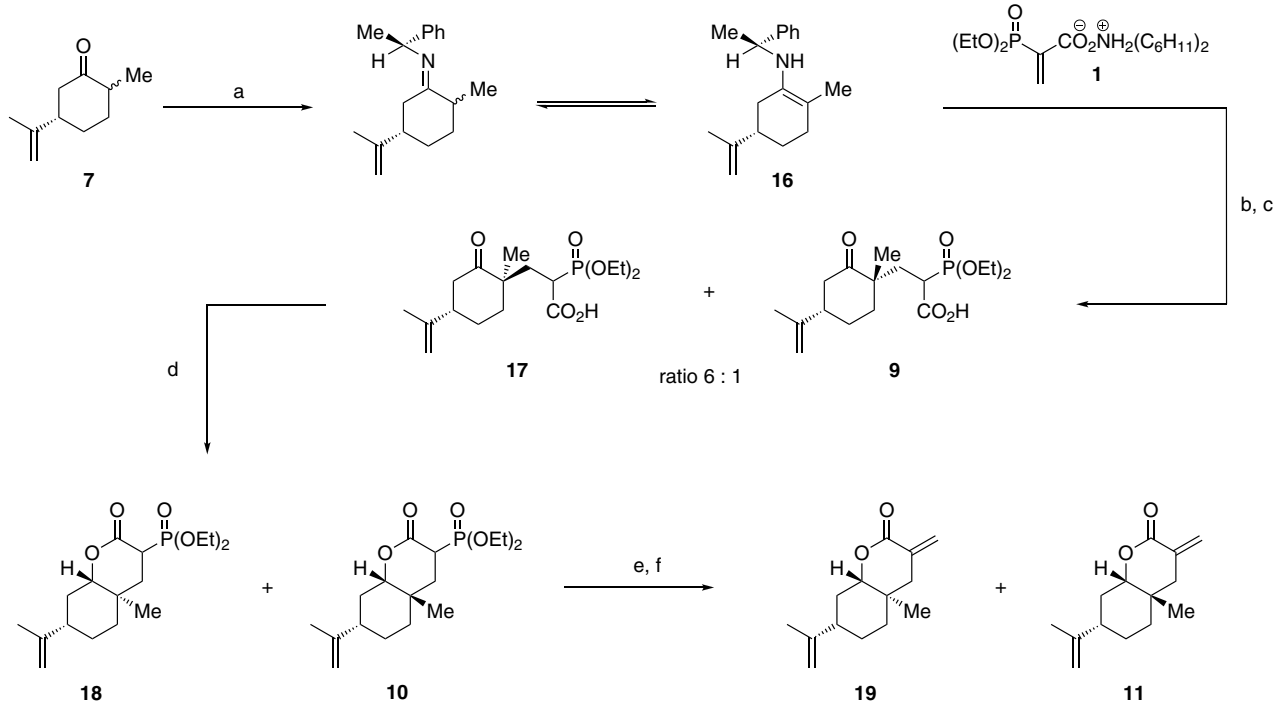
**1**. Addition reactions of enamines **6**, **11**, **15**, and **19** to salt **1** proceeded smoothly in benzene at room temperature. Complete consumption of the salt was observed after 2 days. The crude products were transformed into the corresponding oxoacids by ion-exchange chromatography in high yield.

It is well known that the stereogenic center existing in synthons **3**, **8**, **12**, and **16** may have some impact on the diastereoselective outcome of addition. The best results with respect to diastereoselectivity were achieved when enamines **3** and **8** were used as the Michael donors. The corresponding oxoalkanoic acids **4** and **9** were isolated as single diastereoisomers. As expected, the use of enamines **12** and **16** as the Michael donors resulted in moderate diastereoselectivity and led to the formation of mixtures of isomeric oxoacids **13**:**4** and **17**:**9** in a 6:1 ratio. The latter result is most likely due to the incompatibility of steric effects with electronic effects in the corresponding transition states.[2]

Single crystal X-ray analysis revealed that acid **4** is a single, enantiomerically pure diastereoisomer and its absolute configuration is 2*S*,(1*R*,4*R*) (Fig. 1). The cyclohexanone ring exhibits an almost ideal chair conformation. The Cremer and Pople[7] puckering parameters for the ring atom sequence C1/C2/C3/C7/C8/C9 are $Q = 0.515(5)$ Å, $\theta = 6.5(6)°$, $\varphi = 162.2(6)°$. The isopropenyl and methyl substituents are located in equatorial positions. The ethyl substituent bearing the diethoxyphosphoryl and carboxylic groups is placed axially with the endocyclic C9–C11 bond making an angle of 9.7(2)° with the normal to the Cremer and Pople plane (C1, C2, C7, C8). The position of the carboxylic group is further stabilized by the nonbonding intramolecular electrostatic interaction with the exocyclic carbonyl group. This Coulombic attraction follows from the perpendicular arrangement of the carbonyl groups (Motif II, according to Allen's classification[8]) and involves the oppositely charged O5 (−0.58 e) and C1 (0.44 e) atoms. The respective interatomic distance 3.068(4) Å is shorter than the sum of the oxygen and carbon van der Waals radii




**Scheme 3.** Reagents and conditions: (a) (*R*)-α-phenylethylamine, *p*-TSA (cat), toluene, reflux, 12 h, 90%; (b) benzene, rt, 48 h; (c) Dowex 50W, acetone/water, 80%; (d) MeOH, $KBH_4$ (2 equiv), rt, 24 h, 90%; (e) *t*-BuOK (1 equiv), $(HCHO)_n$ (5 equiv), $Et_2O$, rt, 1 h, 85%; (f) column chromatography.




**Scheme 4.** Reagents and conditions: (a) (*S*)-α-phenylethylamine, *p*-TSA (cat), toluene, reflux, 12 h, 90%; (b) benzene, rt, 48 h; (c) Dowex, acetone/water, 80%; (d) MeOH, $KBH_4$ (2 equiv), rt, 24 h, 90%; (e) *t*-BuOK (1 equiv), $(HCHO)_n$ (5 equiv), $Et_2O$, rt, 1 h, 85%; (f) column chromatography.

3.22 Å.[9] Atomic charges derived from electrostatic potential were calculated using GAUSSIAN 03[10] at the MP2/6-311+G(d,p) level for the X-ray determined coordinates. Grid points were selected according to the CHELPG procedure of Breneman and Wiberg.[11] In the crystal hydrogen bonds between the carboxylic group and phosphoryl bond

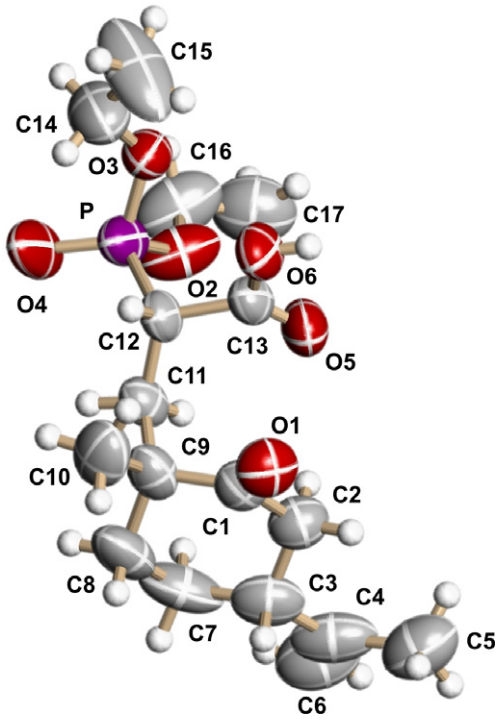



**Figure 1.** The crystal structure of acid **4**. The methyl C15 atom is disordered and was refined in two partially occupied positions. The picture shows sites for which the occupation factor was 0.73(3). The less occupied positions have not been shown for clarity. Displacement ellipsoids are drawn at the 50% probability level. H atoms are represented by circles of an arbitrary radius.

link molecules into an infinite chain running in the *b*-axis direction [O6–H6 = 0.82 Å, O6–H6···O4′($x, y+1, z$) = 167°, O6···O4′ = 2.567(4) Å].

The (*R*)-absolute configuration at the quaternary stereogenic center in acid **4** is fully consistent with the transition-state model proposed for similar Michael additions[12] and with the results of our earlier work.[3] As a consequence of this, the stereochemistry at the quaternary stereogenic center in acids **9**, **13**, and **17** was assigned to be (*S*), (*S*), and (*R*), respectively.

The mixtures of diastereoisomeric oxoacids **13**:**4** and **17**:**9** could not be separated by column chromatography and were used directly for the next step. Standard procedures were applied for the transformation of oxoacids obtained into the corresponding α-methylene-δ-valerolactones. Chemoselective reduction of oxoacids **4** and **9** with $KBH_4$ in methanol provided directly α-phosphono-δ-valerolactones **5** and **10**, respectively. Under the same conditions, the mixtures of oxoacids **13**:**4** and **17**:**9** were converted into mixtures of the corresponding α-phosphono-δ-valerolactones **14**:**5** and **18**:**10** in a 6:1 ratio.

All attempts to separate the diastereoisomers by column chromatography were unsuccessful. At this stage we were unable to determine the diastereoselectivity of the reduction. Finally, the HWE reaction of phosphonolactones **5**, **10**, **14**:**5** and **18**:**10**, performed with excess of paraformaldehyde in diethyl ether in the presence of *t*-BuOK afforded the corresponding α-methylene-δ-valerolactones **6**, **11**, **15**:**6** and **19**:**11**, respectively. The mixtures of diastereoisomeric lactones **15** and **6**, and **19** and **11** were separated by column chromatography.

The relative and absolute configuration of the enantiomerically pure 3-methyleneoctahydrochroman-2-ones obtained was established by X-ray analysis of the *trans*-lactone **15**[13] and *cis*-lactone **11**.[14] The absolute stereochemistry of the *trans*-lactone **15** was determined to be 4a(*S*),7(*R*),8a(*R*), (Fig. 2) meaning that the lactone **19** is undoubtedly the 4a(*R*),7(*S*),8a(*S*) isomer. The absolute configuration of *cis*-lactone **11** was determined to be 4a(*S*),7(*S*),8a(*S*) (Fig. 3). Therefore, the absolute configuration of lactone **6** must be 4a(*R*),7(*R*),8a(*R*). These findings provide a clear evidence that the reduction of the oxoacids **4**, **9**, **13**, and **17** proceeded with complete diastereocontrol through the axial attack of hydride anion on the carbonyl group and proved the relative configuration of the ring junction in the lactones obtained.

## 3. Conclusions

In summary, the chemistry described herein expands the potential of acrylate **1** in asymmetric Michael reactions and provides facile entry to enantiomerically pure 3-methyleneoctahydrochromen-2-ones. The method is expected to find further applications in the synthesis of

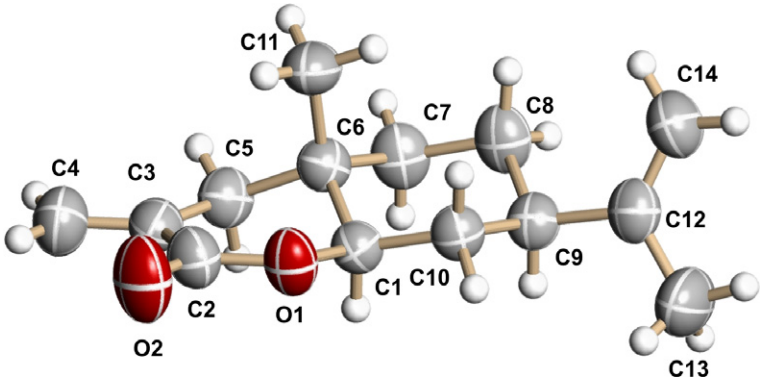



**Figure 2.** The molecular structure of **15** as published in Ref. 13. Displacement ellipsoids are drawn at the 50% probability level. H atoms are represented by circles of an arbitrary radius.

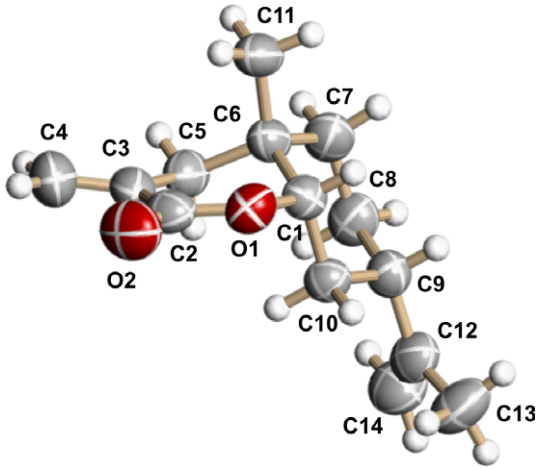



**Figure 3.** The molecular structure of **11** as published in Ref. 14. Displacement ellipsoids are drawn at the 50% probability level. H atoms are represented by circles of an arbitrary radius.

bicyclic δ-valerolactones bearing chiral quaternary stereogenic centers.

## 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 an internal standard and 85% $H_3PO_4$ as an external standard. The multiplicities of carbons were determined by DEPT experiments. IR spectra were measured on Specord M80 (Zeiss) instrument. Elemental analyses were performed on 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.[15]

### 4.2. General procedure for the preparation of phosphonoalkanoic acids 4, 9, 13, and 17

A mixture of acrylate **1** (3.89 g, 0.01 mol) and enamine **3**, **8**, **12**, or **16** (0.011 mol) in benzene (50 ml) was stirred at room temperature for 48 h. After the reaction was completed ($^{31}P$ NMR) the solvent was evaporated and the residue was subjected to ion-exchange chromatography performed on a glass column packed with Dowex 50W using $H_2O$/acetone, 1:1 as eluent. The eluent was evaporated to give the acid as a colorless oil.

**4.2.1. 2-(Diethoxyphosphoryl)-3-(4-isopropenyl-1-methyl-2-oxocyclohexyl)propanoic acid 4.** (3.06 g, 85% yield); white solid, mp = 104–106 °C; IR (film) 3090, 1762, 1690, 1265 $cm^{-1}$; $^{31}P$ NMR ($CDCl_3$): $\delta = 23.82$; $^{1}H$ NMR ($CDCl_3$): $\delta = 0.99$ (s, 3H, $CH_3$), 1.32 (t, 3H, $^{3}J_{HH} = 7.0$, $CH_3CH_2OP$), 1.34 (t, 3H, $^{3}J_{HH} = 7.0$, $CH_3CH_2OP$), 1.48–1.91 (m, 4H, $2\times CH_2$), 1.74 (s, 3H, $CH_3C{=}$), 2.08–2.65 (m, 5H, $2\times CH_2$, CH), 2.82 (ddd, 1H, $^{3}J_{HH} = 2.7$, $^{3}J_{HH} = 7.5$, $^{2}J_{HP} = 25.5$, CHP), 4.14 (q, $^{3}J_{HH} = {}^{3}J_{HP} = 7.2$, $CH_2OP$), 4.20 (q , $^{3}J_{HH} = {}^{3}J_{HP} = 7.2$, $CH_2OP$), 4.72 (s, 1H, =CH), 4.78 (s, 1H, =CH); $^{13}C$ NMR ($CDCl_3$): $\delta = 15.90$ (d, $^{3}J_{CP} = 3.8$, $CH_3CH_2OP$), 16.11 (d, $^{3}J_{CP} = 3.8$, $CH_3CH_2OP$), 20.92 ($CH_3$), 21.12 ($CH_3$), 25.75 ($CH_2$), 33.34 (d, $^{2}J_{CP} = 5.04$, $CH_2$), 38.13 ($CH_2$), 40.95 (d, $^{1}J_{CP} = 128$, CHP), 43.21 ($CH_2$), 45.91 (CH), 48.25 (d, $^{3}J_{CP} = 12.0$, C), 63.00 (d, $^{2}J_{CP} = 6.3$, $CH_2OP$), 63.61 (d, $^{2}J_{CP} = 6.3$, $CH_2OP$), 109.00 (=$CH_2$), 147.02 (=C), 170.93 (d, $^{2}J_{CP} = 3.3$, COOH), 214.21 (CO). Anal. Calcd for $C_{17}H_{29}O_6P$: C, 56.66; H, 8.11. Found: C, 56.73; H, 8.01.

**4.2.2. 2-(Diethoxyphosphoryl)-3-(4-isopropenyl-1-methyl-2-oxocyclohexyl)propanoic acids 13 and 4.** (2.88 g, 80% yield); diastereoisomeric ratio 6:1, colorless oil; IR (film) 3090, 1762, 1690, 1265 $cm^{-1}$. Anal. Calcd for $C_{17}H_{29}O_6P$: C, 56.66; H, 8.11. Found: C, 56.73; H, 8.01.

Compound **13**. $^{31}P$ NMR ($CDCl_3$): $\delta = 24.95$; $^{1}H$ NMR ($CDCl_3$): $\delta = 1.15$ (s, 3H, $CH_3$), 1.35 (t, 6H, $^{3}J_{HH} = 7.0$, $2\times CH_3CH_2OP$), 1.59–1.97 (m, 4H, $2\times CH_2$), 1.73 (s, 3H, $CH_3C{=}$), 2.07–2.50 (m, 5H, $2\times CH_2$, CH), 3.03 (ddd, 1H, $^{3}J_{HH} = 9.0$, $^{3}J_{HH} = 15.0$, $^{2}J_{HP} = 26.5$, CHP), 4.10–4.28 (m, 4H, $2\times CH_2OP$), 4.70 (s, 1H, =CH), 4.76 (s, 1H, =CH); $^{13}C$ NMR ($CDCl_3$): $\delta$ 16.00 (d, $^{3}J_{CP} = 3.8$, $2\times CH_3CH_2OP$), 20.41 ($CH_3$), 21.02 ($CH_3$), 25.55 ($CH_2$), 33.94 (d, $^{2}J_{CP} = 4.4$, $CH_2$), 35.30 ($CH_2$), 41.45 (d, $^{1}J_{CP} = 125.6$, CHP), 42.71 ($CH_2$), 45.51 (CH), 47.85 (d, $^{3}J_{CP} = 13.0$, C), 62.88 (d, $^{2}J_{CP} = 6.4$, $CH_2OP$), 63.30 (d, $^{2}J_{CP} = 6.4$, $CH_2OP$), 110.05 (=$CH_2$), 146.08 (=C), 171.77 (d, $^{2}J_{CP} = 3.1$, COOH), 215.62 (CO).

### 4.3. General procedure for the preparation of phosphonolactones 5, 10, 14, and 18

To a stirred solution of **4** (2.88 g, 0.008 mol) in methanol (50 ml) was added $KBH_4$ (0.86 g, 0.016 mol). Stirring was continued for 24 h at room temperature. The resulting mixture was neutralized to pH ~ 3 with 5% HCl. The solvent was evaporated and the residue was diluted with water (20 ml) and extracted with chloroform ($3\times 20$ ml). The organic layer was dried ($MgSO_4$) and evaporated. The oily residue was purified by column chromatography on silica gel using ethyl acetate/hexane (3:1) as eluent to give pure lactone **5**.

**4.3.1. Diethyl (7-isopropenyl-4a-methyl-2-oxo-octahydro-2*H*-chromen-3-yl)phosphonate 5.** (2.48 g, 90% yield); colorless oil; IR (film) 3093, 1787, 1279, 1190 $cm^{-1}$; $^{31}P$ NMR ($CDCl_3$): $\delta = 23.30$; $^{1}H$ NMR ($CDCl_3$): $\delta = 1.11$ (s, 3H, $CH_3$), 1.31 (t, 3H, $^{3}J_{HH} = 7.1$, $CH_3CH_2OP$), 1.34 (t, 3H, $^{3}J_{HH} = 7.1$, $CH_3CH_2OP$), 1.43–1.60 (m, 6H, $3\times CH_2$), 1.65 (s, 3H, $CH_3$), 1.81–2.15 (m, 2H, CH, CHCHP), 2.58 (dt, 1H, $^{2}J_{HH} = {}^{3}J_{HH} = 11.5$, $^{3}J_{HP} = 14.5$, CHCHP), 3.20 (ddd, 1H, $^{3}J_{HH} = 9.0$, $^{3}J_{HH} = 11.5$, $^{2}J_{HP} = 28.6$, CHP), 4.10–4.28 (m, 1H, CHO), 4.18 (q, 2H, $^{3}J_{HH} = {}^{3}J_{HP} = 7.1$, $CH_2OP$), 4.20 (q, 2H, $^{3}J_{HH} = {}^{3}J_{HP} = 7.1$, $CH_2OP$), 4.73 (s, 2H, =$CH_2$); $^{13}C$ NMR ($CDCl_3$): $\delta = 16.11$ (d, $^{3}J_{CP} = 5.6$, $CH_3CH_2OP$), 16.21 (d, $^{3}J_{CP} = 5.6$, $CH_3CH_2OP$), 20.71 ($CH_3$), 25.11 ($CH_3$), 25.61 ($CH_2$), 26.91 (d, $^{2}J_{CP} = 3.8$, $CH_2$), 31.50 (d, $^{3}J_{CP} = 5.0$, C), 34.43 ($CH_2$), 37.11 (d, $^{1}J_{CP} = 140.5$, CHP), 37.25 ($CH_2$), 43.60 (CH=), 62.61 (d, $^{2}J_{CP} = 6.9$,

*C*H$_2$OP), 63.31 (d, $^2J_{CP} = 6.9$, *C*H$_2$OP), 86.32 (*C*HO), 109.45 (*C*H$_2$=), 147.62 (*C*=), 165.21 (*C*OO). Anal. Calcd for $C_{17}H_{29}O_5P$: C, 59.29; H, 8.49. Found: C, 59.07; H, 8.61.

**4.3.2. Diethyl (7-isopropenyl-4a-methyl-2-oxo-octahydro-2*H*-chromen-3-yl)phosphonates 14 and 5.** (2.34 g, 85% yield); diastereoisomeric ratio 6:1, colorless oil; IR (film) 3093, 1787, 1279, 1190 cm$^{-1}$. Anal. Calcd for $C_{17}H_{29}O_5P$: C, 59.29; H, 8.49. Found: C, 59.07; H, 8.61.

Compound **14**. $^{31}$P NMR ($CDCl_3$): $\delta = 23.46$; $^1$H NMR ($CDCl_3$): $\delta = 0.95$ (s, 3H, C*H*$_3$), 1.35 (t, 6H, $^3J_{HH} = 7.1$, 2 × C*H*$_3$CH$_2$OP), 1.43–1.60 (m, 6H, 3 × C*H*$_2$), 1.74 (s, 3H, C*H*$_3$), 1.80–2.20 (m, 3H, C*H*, C*H*$_2$), 3.24 (dt, 1H, $^3J_{HH} = 9.0$, $^2J_{HP} = 28.5$, C*H*P), 4.05–4.44 (m, 5H, C*H*O, 2 × C*H*$_2$OP), 4.73 (s, 1H, =C*H*), 4.75 (s, 1H, =C*H*); $^{13}$C NMR ($CDCl_3$): $\delta$ 14.05 (*C*H$_3$), 14.91 (d, $^3J_{CP} = 5.0$, *C*H$_3$CH$_2$OP), 15.15 (d, $^3J_{CP} = 5.0$, *C*H$_3$CH$_2$OP), 19.51 (*C*H$_3$=), 24.41 (*C*H$_2$), 30.51 (*C*H$_2$), 31.95 (d, $^3J_{CP} = 7.0$, *C*), 35.72 (d, $^2J_{CP} = 4.3$, *C*H$_2$), 36.03 (*C*H$_2$), 37.41 (d, $^1J_{CP} = 133.5$, *C*HP), 41.72 (*C*H–C=), 61.41 (d, $^2J_{CP} = 6.5$, *C*H$_2$OP), 62.44 (d, $^2J_{CP} = 6.5$, *C*H$_2$OP), 82.11 (*C*HO), 108.15 (*C*H$_2$=), 146.62 (*C*=), 165.21 (d, $^2J_{CP} = 5.0$, *C*OO).

### 4.4. General procedure for the preparation of methylene-lactones 6, 11, 15, and 19

To a stirred solution of α-phosphonolactone **5** (2.06 g, 0.0060 mol) in diethyl ether (50 ml), potassium *t*-butoxide (0.74 g, 0.0066 mol) was added and the resulting mixture was stirred for 15 min at room temperature. Then satd NaCl solution (20 ml) was added and the mixture was extracted with diethyl ether (3 × 10 ml). The organic layer was dried ($MgSO_4$) and evaporated. The oily residue was purified by column chromatography on silica gel using ethyl acetate/hexane (1:5) as eluent to give lactone **6.**

**4.4.1. (4a*S*,7*S*,8a*S*)- and (4a*R*,7*R*,8a*R*)-7-Isopropenyl-4a-methyl-3-methyleneoctahydrochromen-2-ones 6 and 11.** (1.12 g, 85% yield); white crystals, mp = 55–57 °C; IR (film) 3089, 1780, 1610, 1180 cm$^{-1}$; $^1$H NMR ($CDCl_3$): $\delta = 1.11$ (s, 3H, C*H*$_3$), 1.34–1.52 (m, 3H, C*H*$_2$, C*H*), 1.73 (s, 3H, C*H*$_3$), 1.59–1.75 (m, 2H, C*H*$_2$), 1.95 (dt, 1H, $^4J = 2.5$, $^2J = 13.7$, C*H*), 2.04–2.18 (m, 2H, C*H*$_2$), 3.01 (dd, 1H, $^4J = 2.5$, $^2J = 13.7$, C*H*), 4.12 (ddd, 1H, $^4J = 2.5$, $^2J = 4.2$, $^2J = 12.2$, C*H*O), 4.71 (s, 1H, =C*H*), 4.74 (s, 1H, =C*H*), 5.57 (dt, 1H, $^2J = 1.5$, $^4J = 2.5$, =C*H*), 6.51 (dt, 1H, $^2J = 1.5$, $^4J = 2.5$, =C*H*); $^{13}$C NMR ($CDCl_3$): $\delta = 20.56$ (*C*H$_3$), 25.69 (*C*H$_2$), 25.58 (*C*H$_3$), 32.11 (*C*), 32.91 (*C*H$_2$), 34.46 (*C*H$_2$), 36.62 (*C*H$_2$), 43.13 (*C*H–C=), 85.21 (*C*HO), 108.91 (*C*H$_2$=), 129.12 (*C*H$_2$=), 132.52 (*C*=), 147.45 (*C*=), 164.20 (*C*OO). Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.45; H, 9.03.

Compound **6**. $[\alpha]_D^{25} = +21.3$ (*c* 1.19, MeOH).

Compound **11**. $[\alpha]_D^{25} = -23.7$ (*c* 0.46, MeOH).

**4.4.2. (4a*S*,7*R*,8a*R*)- and (4a*R*,7*S*,8a*S*)-7-Isopropenyl-4a-methyl-3-methyleneoctahydrochromen-2-ones 15 and 19.** (1.05 g, 85% yield); diastereoisomers ratio 6:1; white crystals, mp = 80–82 °C; IR (film) 3089, 1780, 1610, 1180 cm$^{-1}$; $^1$H NMR ($CDCl_3$): $\delta = 0.95$ (s, 3H, C*H*$_3$), 1.20–1.60 (m, 5H, 2 × C*H*$_2$, C*H*), 1.90–2.11 (m, 2H, C*H*$_2$), 2.17 (s, 3H, C*H*$_3$), 2.36 (dd, 1H, $^4J = 2.5$, $^2J = 15.5$, C*H*), 2.50 (d, 1H, $^2J = 15.5$, C*H*), 4.12 (dd, 1H, $^4J = 2.5$, $^3J = 10.0$, C*H*O), 4.75 (s, 2H, =C*H*$_2$), 5.58 (t, 1H, $^4J = {}^2J = 2.5$, =C*H*), 6.50 (t, 1H, $^2J = {}^4J = 2.5$, =C*H*); $^{13}$C NMR ($CDCl_3$): $\delta = 15.32$ (*C*H$_3$), 20.82 (*C*H$_3$), 25.93 (*C*H$_2$), 31.79 (*C*H$_2$), 33.59 (*C*), 36.94 (*C*H$_2$), 43.26 (*C*H–C=), 43.83 (*C*H$_2$), 83.83 (*C*HO), 108.96 (*C*H$_2$=), 129.43 (*C*H$_2$=), 133.46 (*C*=), 147.97 (*C*=), 165.61 (*C*OO). Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.45; H, 9.03.

Compound **15**. $[\alpha]_D^{25} = +116.15$ (*c* 0.39, MeOH).

Compound **19**. $[\alpha]_D^{25} = -117.5$ (*c* 0.56, MeOH).

### 4.5. X-ray single crystal structure analysis for 4

Formula: $C_{17}H_{29}O_6P$, $M_w = 360.37$, colorless crystal $0.40 \times 0.15 \times 0.10$ mm, $a = 10.6509(14)$, $b = 6.9574(8)$, $c = 13.6821(16)$ Å, $V = 1010.8(2)$ (2) Å$^3$, $\beta = 94.456(7)°$ $\rho_{calcd} = 1.18$ g cm$^{-3}$, $\mu = 14.35$ cm$^{-1}$, semi-empirical absorption correction based on multiple scanned equivalent reflections[16] ($0.727 < T < 0.870$), $Z = 2$, crystal system: monoclinic, space group: $P2_1$, $\lambda = 1.54178$ Å, $T = 293$ K, $\omega$ scans, 11,625 reflections collected ($\pm h$, $\pm k$, $\pm l$), $2\theta_{max} = 141.84°$, 3680 unique reflections ($R_{int} = 0.0180$) and 3384 observed reflections [$I \geqslant 2\sigma(I)$], 232 refined parameters, refinement on $F^2$, $R_{all} = 0.0611$, $wR$ ($F^2$) = 0.1845, max (min) residual electron density $\Delta\rho_{max} = 0.34$ ($\Delta\rho_{min} = -0.25$) e Å$^{-3}$, Flack parameter[17] calculated with 1576 Friedel pairs $\eta = 0.00(3)$, all hydrogen atoms refined as riding on their parent atoms. X-ray data were collected with Bruker SMART APEX CCD area detector diffractometer. Computer programs used: data collection SMART APEX,[18] data reduction SAINT-PLUS,[19] absorption correction SADABS,[20] structure solution, refinement, and molecular graphics SHELXTL.[21] Crystallographic data (excluding structure factors) for the structure reported herein have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC 662749. Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. Any request should be accompanied by a full literature citation.

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