

Unusual reactivity of *cis*-2-benzoyl-1-benzyl-3-phenylaziridine with *P*-nucleophiles—ring opening vs. the Abramov reaction

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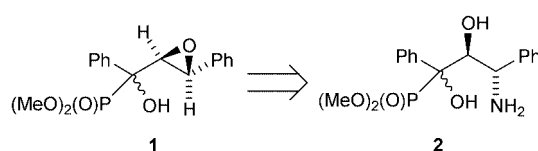
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Thermal (80 °C) addition of dimethyl phosphite to *cis*-2-benzoyl-1-benzyl-3-phenylaziridine occurred exclusively at C(3) with concomitant cleavage of the C(2)–C(3) bond. The carbonyl group in the aminoketone produced under these conditions was reduced with hydrogen over Pearlman's catalyst with low (20%) diastereoselectivity, while good (80%) de was observed in the NaBH₄ reduction as a result of the 1,4-asymmetric induction. The products of the Abramov reaction of the title compound were obtained (de 92%) when CsF was used as catalyst.

Introduction

There is a growing interest in the synthesis of amino-flavonoids^{1–6} as well as aminochalcones.^{7,8} In our ongoing programme directed towards the synthesis of biologically active phosphonate analogs having amino and hydroxy groups⁹ we turned our attention to aminohydroxyphosphonate derivatives of flavonoids. In model studies we have recently elaborated the chemistry of β,γ-epoxy-α-hydroxyphosphonates **1** derived from chalcone epoxide.¹⁰ These epoxides would have been considered as useful precursors to γ-amino-α,β-dihydroxyphosphonates **2** (Scheme 1) if they had been stable in the presence of amines.¹¹

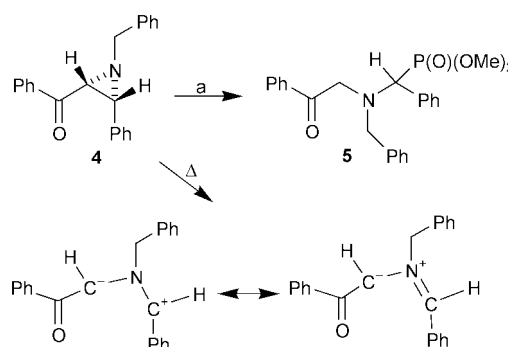


Scheme 1 Retrosynthetic approach to **2**.

Attempts at opening the oxirane ring in **1** with azides led to impure γ-azidophosphonates in low yields.¹² For this reason we selected another model compound containing the chalcone skeleton and found that addition of dimethyl phosphite (**3**) to *trans*-2-benzyl-1-(*tert*-butoxycarbonyl)-3-phenylaziridine gave exclusively rearranged enol phosphate in good yield.¹¹ *cis*-2-Benzoyl-1-benzyl-3-phenylaziridine (**4**)^{13,14} was chosen as the next model compound and herein we wish to describe its reactivity with dimethyl phosphite.

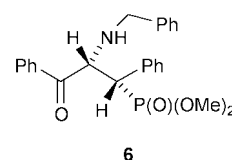
Results and discussion

In order to add **3** to the carbonyl group of the aziridine **4** several catalysts have been tried, but most of them led to the formation of complex reaction mixtures usually containing significant amounts of the unreacted **4**. The best result was obtained when an equimolar mixture of **3** and **4** was refluxed in benzene in the presence of 1 equiv. of NEt₃. The ³¹P NMR spectrum of the crude product showed one major resonance at 25.70 ppm accompanied by several minor ones at 29.81, 28.70 and 26.42 ppm, while the ¹H NMR spectrum and TLC analysis proved that all starting aziridine was used up. The addition product was isolated by chromatography on silica gel followed by crys-



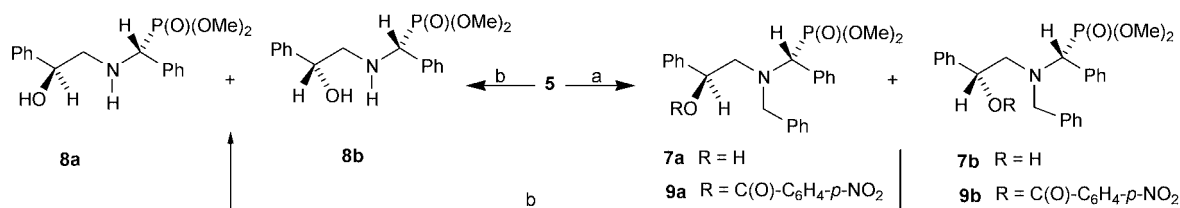
Scheme 2 Reagents and conditions: (a) (MeO)₂P(O)H (**3**), benzene, 80 °C.

tallization and was identified as the tertiary amine **5** (Scheme 2). From ¹H NMR and IR spectra the presence of the benzoyl group was evident. The definitive structural assignments in **5** were based on the detailed analysis of the ¹³C NMR spectra including the attached proton test (apt) experiment. Three-bond C–P couplings were found for two methylene carbons, and a large one-bond C–P coupling was noticed for the C–H carbon. These data clearly differentiate the tertiary amine **5** from the isomeric phosphonate **6**, which would have been formed



as a result of the N–C(3) bond cleavage. Later, we found that the synthesis of **5** was accomplished from **3** and **4** in refluxing benzene without triethylamine.

The formation of the P–C bond in **5** can be rationalized in the following way. At elevated temperatures the C(2)–C(3) bond in the aziridine **4** is cleaved to give an azomethine ylide (Scheme 2).^{15–17} Thermal [2 + 3] cycloadditions of similar ylides to C≡C and various C=X (X = C, S, O, N) bonds have been studied in detail.¹⁷ The addition of dimethyl phosphite to the electrophilic center of the ylide followed by the transfer of a proton to the enolate leads to the aminoketone **5**. Under these



Scheme 3 Reagents and conditions: (a) NaBH₄, MeOH, rt; (b) H₂, Pd(OH)₂-C, MeOH.

conditions only racemic **5** is produced because both faces of the azomethine carbon are equally accessible. The stereochemistry of **4** has no influence on the structure of the addition product **5** because only one azomethine ylide is formed from both the *cis*- and *trans*-isomers.

Sodium borohydride reduction of the carbonyl group in **5** afforded a 9:1 mixture of inseparable aminoalcohols **7a** and **7b**, respectively (Scheme 3). On the other hand, hydrogenation of **5** over Pearlman's catalyst gave a 6:4 mixture of aminoalcohols **8a** and **8b**, which also could not be separated. The same aminoalcohols, but in a 9:1 ratio, were produced by hydrogenolysis of **7a** and **7b** over Pd(OH)₂-C. To assign the relative stereochemistry in the major product of the borohydride reduction, a 9:1 mixture of **7a** and **7b** was esterified with *p*-nitrobenzoyl chloride. The *p*-nitrobenzoate **9a** of the major diastereoisomer was isolated by column chromatography followed by crystallization and formed crystals suitable for X-ray structural studies (*vide infra*).

Low diastereoselectivity in the catalytic reduction of the carbonyl group in **5** (de *ca.* 20%) contrasts with significant (de 80%) excess of **7a** over **7b**, when NaBH₄ was used. We suggest that in the borohydride reduction the diastereoselectivity was induced by the center of chirality at the C α to the phosphoryl group (1,4-asymmetric induction). Fig. 1 shows the preferred conformation of **5** coordinated to Na⁺ which leaves the *re* face of the carbonyl group in (*R*)-**5** open to hydride addition. In this conformation three phenyl groups attain interaction-free spatial arrangement.

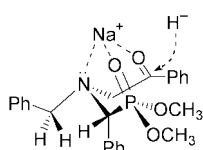
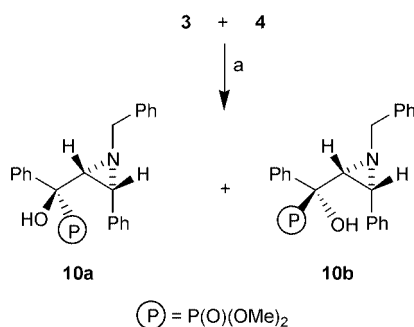


Fig. 1 The preferred conformation of **5**.

Finally, we succeeded in the addition of dimethyl phosphite to the carbonyl group of the aziridine **4** (Scheme 4). This was



Scheme 4 Reagents and conditions: (a) CsF, CH₂Cl₂, rt, 2 h.

achieved using CsF as a catalyst, but in order to obtain pure products the reaction time had to be shortened to 2 h. After recovery of the unreacted **4** by column chromatography (45%), a mixture of **10a** containing its C(1) epimer **10b** (4%) was isolated in 16% yield. Pure diastereoisomer **10a** was obtained by crystallization. Although we were unable to separate pure **10b**, the formation of this phosphonate was concluded from the

³¹P NMR chemical shifts (23.15 and 22.46 ppm) for **10a** and **10b**, respectively, and that both compounds have very similar polarities.

In order to gather further evidence for the formation of **10b**, attempts at equilibrating pure **10a** to a mixture of **10a** and **10b** were proposed. However, it has recently been shown that in the presence of basic catalysts the structurally related β,γ -epoxy- α -hydroxyphosphonates **1** did not only undergo the retro-Abramov reaction, but they also rearranged to enol phosphates, and were partially demethylated when triethylamine was used.¹¹ Based on these results DBU and CsF were selected as catalysts for the equilibration of **10a**. The ¹H and ³¹P NMR monitoring of an equimolar mixture of **10a** and DBU at room temperature revealed the retro-Abramov reaction as a single equilibration pathway. After 2 h, *ca.* 50% of **10a** was transformed into the starting aziridine **4** and a series of decomposition products produced from dimethyl phosphite, and after 48 h only traces of **10a** remained in the mixture. The ³¹P NMR signal of minor diastereoisomeric phosphonate **10b** was never detected. When **10a** was treated with 200 mol% of CsF at room temperature for 24 h, a mixture of **10a** (23%) and the aziridine **4** (77%) was obtained as judged from the ¹H NMR spectrum. Again, the formation of **10b** was not observed.

The aziridine phosphonate **10a** was found to be almost completely unreactive towards hydrogen in the presence of Pd(OH)₂-C and appeared unstable in Pd-C catalyzed hydrogenolysis under pressure in methanol. The cleavage of the P-C bond was the major transformation observed as judged from the ³¹P NMR spectra of the crude product and **4** was isolated in 69% yield after column chromatography. Due to the instability of **10a** we turned to X-ray structural analysis in order to establish the configuration of this compound.

The molecular structures of **9a** and **10a** are shown in Figs. 2 and 3, respectively. The atomic parameters for non-H atoms are available as Electronic Supplementary Information.[†] In both structures the P atom adopts a distorted tetrahedral configuration; the bond angles around the P atom are in the range 101.1(1)–116.8(1)° for **9a** and 101.6(1)–116.1(1)° for **10a**. The mean P–O bond lengths [1.563(2) Å for **9a** and 1.568(2) Å for **10a**], the P=O bond lengths [1.458(3) Å for **9a** and 1.454(2) Å for **10a**] and P–C bond lengths [1.800(4) Å for **9a** and 1.836(2) Å for **10a**] correspond well with those found in the Cambridge Structural Database.¹⁸ The C₂N ring in **10a** shows the characteristic behavior of analogous substituted aziridines where the presence of a heteroatom is coupled with the high strain of the three-membered ring and the actual geometry is the result of several effects due to each substituent. The C(2)–C(4) bond of 1.500(3) Å is shorter than the normal single C_{sp³}–C_{sp³} bond, but is longer than the mean value of 1.484(3) Å retrieved from the Cambridge Crystallographic Database for saturated C₂N rings.¹⁹ As expected the ring nitrogen is pyramidal, lying 0.656(2) Å out of the plane defined by the three atoms bonded to it. The interesting point of note is the intramolecular hydrogen bond observed between the nitrogen of the aziridine ring

[†] Structure factors can be obtained from the author (W. M.). Anisotropic displacement parameters and hydrogen atom parameters have been deposited at Cambridge Crystallographic Data Centre. CCDC reference number 207/407. See <http://www.rsc.org/suppdata/p1/a9/a909521g> for crystallographic files in .cif format.

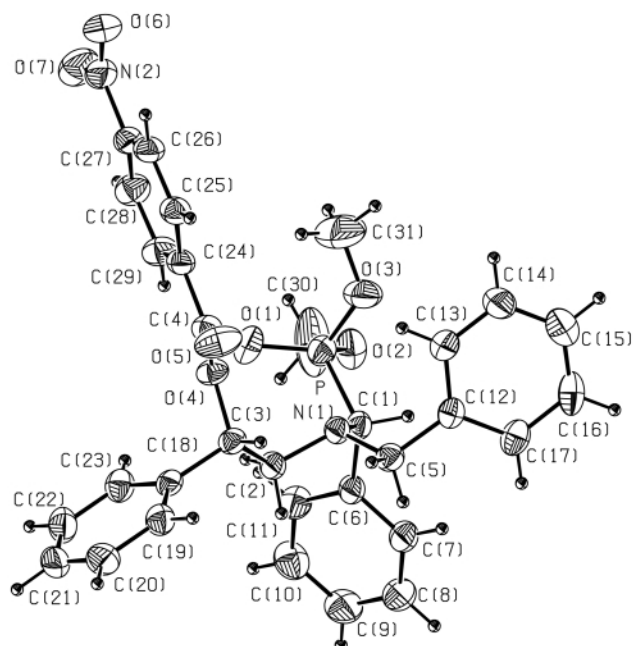


Fig. 2 The molecular structure of **9a** with the atom labelling scheme. Displacement ellipsoids are shown at the 50% probability level and H atoms are shown as circles of an arbitrary radius.

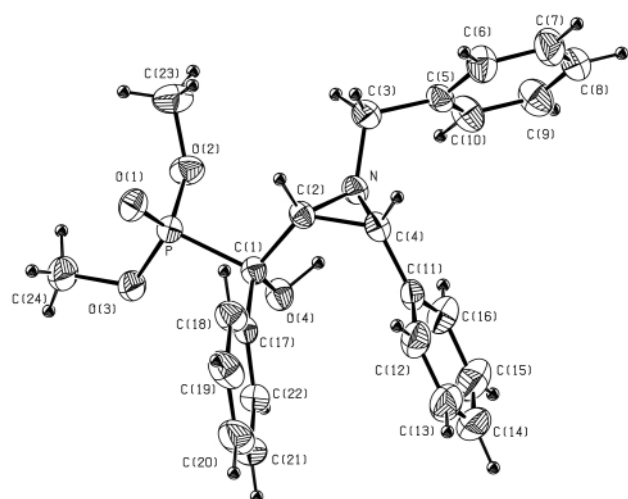


Fig. 3 The molecular structure of **10a** with the atom labelling scheme. Displacement ellipsoids are shown at the 50% probability level and H atoms are shown as circles of an arbitrary radius.

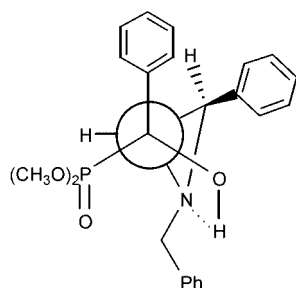


Fig. 4 The preferred conformation of **10a** in CDCl_3 .

and the hydroxy group [$\text{O} \cdots \text{N} = 2.644(3) \text{ \AA}$, $\angle \text{O-H} \cdots \text{N} = 131^\circ$]. In addition, the crystal packing in both structures is governed by some intermolecular interactions of the type $\text{C-H} \cdots \text{O}$.

The $\text{O-H} \cdots \text{N}$ hydrogen bond also stabilizes the conformation of **10a** in a chloroform solution (Fig. 4). This conclusion is supported by values of $^3J(\text{P-C}) = 11.8 \text{ Hz}$ and $^3J(\text{P-H}) = 6.3$

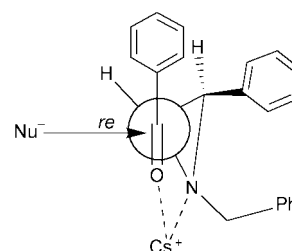


Fig. 5 Stereochemical model of the addition to *cis*-**4**.

Hz. The respective dihedral angles calculated from the molecular structure are 174 and 32° , in agreement with values obtained using the known $^3J(\text{P-C})$ and $^3J(\text{P-H})$ vs. dihedral angle relationships.^{20,21}

In the antiperiplanar conformation of **10a** the phenyl rings (Ph-C-P and Ph-CH-N) are positioned almost parallel to each other and for this reason shielding of the respective aromatic protons would be expected. 2D (^1H - ^1H and ^1H - ^{13}C) NMR correlations showed that resonances of Ph-CH-N are significantly shifted upfield (*ortho* 6.59 ppm, *meta* 6.89 ppm, *para* 6.97 ppm), while signals of Ph-C-P form a poorly separated multiplet at 7.1–7.3 ppm.

High diastereoselectivity of the addition of dimethyl phosphite to *cis*-**4** can be rationalized by shielding the *si*-face of the carbonyl group by Ph-CH-N (Fig. 5). In this conformation oxygen and nitrogen atoms are chelated by Cs^+ on the surface of solid caesium fluoride, while the electronegative substituent (N) is placed on the opposite side to the approaching nucleophile (the Ahn model).^{22,23}

In conclusion, we have demonstrated that in the presence of CsF at room temperature dimethyl phosphite adds preferentially (de 92%) to the *re*-face of the carbonyl group of *cis*-**4**. Thermal addition (80°C) leads, however, to the cleavage of the $\text{C}(2)\text{-C}(3)$ bond in the aziridine ring and formation of the aminoketone **5** in excellent yield.

Experimental

The general experimental procedures and instrumentation were described earlier.¹⁰ 2D (^1H - ^1H and ^1H - ^{13}C) NMR spectra were obtained on Varian Mercury-300 and Bruker DPX (250 MHz) spectrometers, respectively.

cis-2-Benzoyl-3-phenyl-1-(phenylmethyl)aziridine **4**

To a cooled ($+10^\circ\text{C}$) solution of dibromochalcone (9.2 g, 0.025 mol) in benzene (25 ml), benzylamine (8.2 ml, 0.075 mol) in benzene (10 ml) was added dropwise over 1 h and the reaction mixture was left at room temperature for 20 h. The precipitate was filtered off, washed with benzene and discarded. The benzene solution was washed with water ($3 \times 20 \text{ ml}$), dried (MgSO_4) and concentrated to leave a white solid, which was suspended in petroleum ether (100 ml). After filtration the aziridine **4** (2.80 g, 35%) was obtained as a white amorphous solid, mp $106\text{--}107^\circ\text{C}$ (lit.,¹³ mp 108°C); ν_{max} (KBr)/ cm^{-1} 1681, 1598, 1495; δ_{H} (100 MHz, CDCl_3) 7.9–7.8 (m, 2H, *o*- $\text{C}_6\text{H}_5\text{CO}$), 7.5–7.1 (m, 13H, C_6H_5), 4.02 and 3.81 (AB, 2H, J 14.0, CH_2), 3.39 and 3.31 (AB, 2H, J 7.0, HC-CH).

Addition of dimethyl phosphite to the aziridine **4**

a. In refluxing benzene in the presence of NEt_3 . A solution of the aziridine **4** (1.56 g, 5.00 mmol), dimethyl phosphite (0.55 g, 5.00 mmol) and NEt_3 (0.69 ml, 5.00 mmol) in benzene (5 ml) was refluxed for 4 h. Volatiles were evaporated, the residue was dissolved in CH_2Cl_2 (10 ml), washed with water ($3 \times 10 \text{ ml}$) and dried (MgSO_4). After removal of solvents the crude product was subjected to column chromatography on silica gel with chloroform–methanol (100:1, v/v). The appropriate fractions

were collected and recrystallized from ethanol to give dimethyl *N*-benzyl-*N*-(2-oxo-2-phenylethyl)amino-1-phenylmethylphosphonate (**5**) (0.99 g, 49%) as colorless crystals, mp 101–102 °C (Found: C, 67.93; H, 6.26; N, 3.29. $C_{24}H_{26}NO_4P$ requires C, 68.07; H, 6.19; N, 3.30%); ν_{\max} (KBr)/ cm^{-1} 1689, 1598, 1581, 1493, 1456, 1230, 1058, 1036; δ_H (250 MHz, $CDCl_3$) 7.92–7.84 (m, 2H, *o*- C_6H_5CO), 7.62–7.25 (m, 13H, C_6H_5), 4.81 (d, 1H, *J* 17.3, *HCH*), 4.41 (d, 1H, *J* 23.0, HCP), 4.08 (dd, 1H, *J* 13.3 and 1.6, *HCH*), 3.75 (d, 3H, *J* 10.7, CH_3OPOCH_3), 3.72 (d, 1H, *J* 17.2, *HCH*), 3.50 (d, 1H, *J* 13.4, *HCH*), 3.39 (d, 3H, *J* 10.5, CH_3OPOCH_3); δ_C (62.9 MHz, $CDCl_3$) 198.33, 138.45 (d, *J* 0.4), 136.15, 133.04, 132.37 (d, *J* 2.9), 130.69 (d, *J* 8.5), 129.34, 128.51, 128.42, 128.38 (d, *J* 1.5), 128.33, 128.10, 127.38, 60.84 (d, *J* 159.8), 56.78 (d, *J* 5.0), 56.02 (d, *J* 11.5), 53.58 (d, *J* 7.2), 52.87 (d, *J* 7.0); δ_P (101.26 MHz, $CDCl_3$) 25.70.

b. In refluxing benzene. A solution of the aziridine **4** (313 mg, 1.00 mmol) and dimethyl phosphite (0.091 ml, 1.00 mmol) in benzene (3 ml) was refluxed for 4 h. After evaporation of benzene, the residue was dissolved in CH_2Cl_2 (10 ml), washed with water (3 \times 10 ml), dried over $MgSO_4$ and concentrated. Purification on silica gel column afforded **5** (0.380 g, 90%) as a colorless solid.

c. In the presence of CsF. A mixture of the aziridine **4** (1.55 g, 4.95 mmol), dimethyl phosphite (0.458 ml, 5.00 mmol) and CsF (1.51 g, 10.0 mmol) containing CH_2Cl_2 (1 ml) was stirred at room temperature for 2 h. The fluoride was filtered off and washed with CH_2Cl_2 (10 ml). The organic solution was washed with water (3 \times 10 ml), dried over $MgSO_4$ and concentrated. The crude product was chromatographed on silica gel with chloroform–methanol (200:1, v/v) to give unreacted **4** (0.701 g, 45%) and phosphonates **10a** and **10b** (0.339 g, 16%) as a white solid. Recrystallization of this material from AcOEt–hexanes gave **10a**, mp 134–136 °C (Found: C, 68.20; H, 6.56; N, 3.43. $C_{24}H_{26}NO_4P$ requires C, 68.07; H, 6.19; N, 3.30%); ν_{\max} (KBr)/ cm^{-1} 3284, 1496, 1449, 1240, 1056, 1020; δ_H (250 MHz, $CDCl_3$) 7.50–7.42 (m, 2H), 7.42–7.32 (m, 3H), 7.32–7.25 (m, 2H), 7.22–7.10 (m, 3H), 7.05–6.85 (m, 3H), 6.59 (d, 2H, *J* 7.3, aromatic protons), 4.41 (d, 1H, *J* 13.0, *HCH*), 3.97 (br s, 1H, OH), 3.74 (d, 3H, *J* 10.1, CH_3OPOCH_3), 3.51 (d, 1H, *J* 13.0, *HCH*), 3.44 (d, 3H, *J* 10.1, CH_3OPOCH_3), 3.08 (dd, 1H, *J* 6.5 and 6.3, H-2), 2.96 (d, 1H, *J* 6.5, H-3); δ_C (62.9 MHz, $CDCl_3$) 137.70, 137.60 (d, *J* 2.6), 134.62, 128.91, 128.56, 127.63, 127.60, 127.51 (d, *J* 2.8), 127.28, 127.18 (d, *J* 3.2), 126.39, 125.75 (d, *J* 4.5), 72.49 (d, *J* 164.0), 62.94, 54.51 (d, *J* 7.5), 53.88 (d, *J* 8.1), 47.78 (d, *J* 5.7), 44.98 (d, *J* 11.8); δ_P (101.26 MHz, $CDCl_3$) 23.15.

NaBH₄ reduction of **5**

A solution of the aminoketone **5** (211 mg, 0.50 mmol) in methanol (1 ml) was cooled to 0 °C and NaBH₄ (19 mg, 0.50 mmol) was added portionwise. After 1 h at room temperature, water (0.1 ml) was injected and CH_2Cl_2 (10 ml) was added. The solution was dried over $MgSO_4$ and concentrated to leave a crude product (221 mg, 104%). Filtration through a pad of silica gel gave a solid (212 mg, 100%) identified as a 9:1 mixture of **7a** and **7b**, mp 80–82 °C; ν_{\max} (KBr)/ cm^{-1} 3371, 1491, 1451, 1221, 1031; δ_H (250 MHz, $CDCl_3$) **7a** 7.50–7.15 (m, 15H), 4.80 (dd, 1H, *J* 10.6 and 2.7, *H-C-OH*), 4.29 (br s, 1H, OH), 4.24 (d, 1H, *J* 26.9, HCP), 4.17 (dd, 1H, *J* 13.7 and 2.7, *HCH*), 3.83 (d, 3H, *J* 10.8, CH_3OPOCH_3), 3.50 (d, 3H, *J* 10.5, CH_3OPOCH_3), 3.46 (dd, 1H, *J* 13.4 and 10.7, *HCH*), 3.38 (d, 1H, *J* 13.4, *HCH*), 2.54 (dd, 1H, *J* 13.4 and 2.8, *HCH*); δ_C (62.9 MHz, $CDCl_3$) **7a** 142.12, 137.98, 131.29 (d, *J* 5.3), 130.62 (d, *J* 8.8), 129.04, 128.53, 128.42, 128.38, 128.19, 127.50, 127.30, 125.69, 70.30, 60.09 (d, *J* 165.0), 59.49 (d, *J* 3.5), 55.72 (d, *J* 14.0), 53.17 (d, *J* 7.0), 53.07 (d, *J* 7.3); δ_P (101.26 MHz, $CDCl_3$) **7a** 26.46, **7b** 27.25.

Preparation of the *p*-nitrobenzoate derivative of **7a**

Standard *p*-nitrobenzoylation of a 9:1 mixture of **7a** and **7b** afforded a mixture of *p*-nitrobenzoates **9a** (δ_P 25.38) and **9b** (δ_P 26.20) in 83% yield after chromatography on silica gel. Recrystallization from AcOEt–hexanes gave pure **9a**, mp 128–130 °C (Found: C, 64.57; H, 5.29; N, 4.84. $C_{31}H_{31}N_2O_7P$ requires C, 64.80; H, 5.43; N, 4.87%); ν_{\max} (KBr)/ cm^{-1} 1711, 1530, 1350, 1277; δ_H (250 MHz, $CDCl_3$) 8.31 (s, 4H, C_6H_4), 7.50–7.25 (m, 15H, Ph), 6.25 (dd, 1H, *J* 9.9 and 2.7, *HCO*), 4.32 (dd, 1H, *J* 13.8 and 2.8, *HCH*), 4.08 (d, 1H, *J* 25.0, HCP), 3.98 (dd, 1H, *J* 13.8 and 9.9, *HCH*), 3.47 (d, 3H, *J* 10.8, CH_3OPOCH_3), 3.40 (d, 3H, *J* 10.5, CH_3OPOCH_3), 3.39 (d, 1H, *J* 14.0, *HCH*), 2.70 (dd, 1H, *J* 14.0 and 2.9, *HCH*); δ_P (101.26 MHz, $CDCl_3$) 25.38.

Hydrogenation of the aminoketone **5** over Pd(OH)₂–C

A suspension of **5** (105 mg, 0.25 mmol), anhydrous CH_3OH (1 ml) and Pd(OH)₂–C (20 mg) was stirred under atmospheric pressure of H₂ (balloon) at room temperature for 24 h. The catalyst was removed on Celite, and the solution was concentrated to leave a 6:4 mixture of **8a** and **8b** quantitatively as a colorless oil (Found: C, 60.73; H, 6.76; N, 4.07. $C_{17}H_{22}NO_4P$ requires: C, 60.89; H, 6.61; N, 4.18%); ν_{\max} (neat)/ cm^{-1} 3366, 1493, 1454, 1233, 1028; δ_H (250 MHz, $CDCl_3$) **8a** 7.4–7.1 (m, 10H, C_6H_5), 4.76 (dd, 1H, *J* 8.6 and 3.8, *HCO*), 4.10 (d, 1H, *J* 20.9, HCP), 3.74 (d, 3H, *J* 10.6, CH_3OPOCH_3), 3.51 (d, 3H, *J* 10.5, CH_3OPOCH_3), 2.76 (dAB, 1H, *J* 12.3 and 4.1, *HCH*), 2.69 (dAB, 1H, *J* 12.3 and 8.9, *HCH*), **8b** 7.4–7.1 (m, 10H), 4.66 (dd, 1H, *J* 8.7 and 3.5, *HCO*), 4.02 (d, 1H, *J* 20.6, HCP), 3.73 (d, 3H, *J* 10.6, CH_3OPOCH_3), 3.50 (d, 3H, *J* 10.5, CH_3OPOCH_3), 2.86 (dd, 1H, *J* 12.2 and 3.6, *HCH*), 2.60 (dd, 1H, *J* 12.2 and 8.8, *HCH*); δ_C (62.9 MHz, $CDCl_3$) **8a** 142.18, 135.12 (d, *J* 2.8), 128.58 (d, *J* 2.5), 128.30 (d, *J* 6.2), 128.18, 128.08 (d, *J* 3.0), 127.36, 125.72, 71.51, 59.65 (d, *J* 154.8), 54.88 (d, *J* 15.8), 53.44 (d, *J* 7.0), **8b** 142.29, 135.46 (d, *J* 3.3), 128.54 (d, *J* 2.6), 128.25 (d, *J* 6.3), 128.30, 128.04 (d, *J* 3.0), 127.40, 125.75, 72.65, 60.92 (d, *J* 153.6), 55.85 (d, *J* 15.6), 53.55 (d, *J* 6.6); δ_P (101.26 MHz, $CDCl_3$) **8a** 26.25, **8b** 26.12.

¹H and ³¹P NMR monitoring of the reaction of **10a** and DBU

To a solution of **10a** (0.021 g, 0.050 mmol) in chloroform-*d* (0.7 ml) DBU (0.015 g, 0.050 mmol) was injected. The progress of the reaction was monitored by ³¹P NMR after 0.5 and 1 h, and by ¹H and ³¹P NMR after 2 and 48 h.

CsF-catalyzed transformation of **10a**

A suspension of **10a** (0.070 g, 0.165 mmol) and CsF (0.050 g, 0.33 mmol) in CH_2Cl_2 (2 ml) was stirred at room temperature for 24 h. After removal of CsF by filtration, the organic solution was washed with water (3 \times 4 ml), dried and concentrated to leave a colorless oil (40 mg) which was analyzed by ¹H and ³¹P NMR spectroscopy.

Hydrogenation of a 9:1 mixture of **7a** and **7b** over Pd(OH)₂–C

A mixture of **7a** and **7b** (105 mg, 0.25 mmol) was hydrogenated as described above to give a 9:1 mixture of **8a** and **8b** (84 mg, 100%).

X-Ray determination

Common to both determinations: KM4 diffractometer equipped with graphite-monochromatized Cu-K α . The structures were solved by direct methods using the SHELXS program²⁴ and refined on *F*² values by full-matrix least squares using the SHELXL program²⁵ from the SHELX-97 package. All non-H atoms were refined anisotropically while H atoms were introduced at the calculated positions and refined using a

riding model, each with an isotropic displacement parameter equal to 1.2 times U_{eq} of the neighboring heavier atom.

Compound 9a. *Crystal data.* $C_{31}H_{31}N_2O_7P$, $M_r = 574.55$, triclinic, $P\bar{1}$, $a = 9.479(2)$, $b = 10.342(1)$, $c = 15.374(2)$ Å, $\alpha = 94.17(1)$, $\beta = 99.43(2)$, $\gamma = 91.32(2)^\circ$, $V = 1481.9(4)$ Å³, $Z = 2$, $D_x = 1.288$ g cm⁻³, $T = 293$ K, λ (Cu-K α) = 1.54178 Å, $\mu = 1.2$ mm⁻¹, $F(000) = 604$, final $R = 0.0546$ for 3381 observed reflections [$F_o > 4\sigma(F_o)$].[†]

Compound 10a. *Crystal data.* $C_{24}H_{26}NO_4P$, $M_r = 423.43$, orthorhombic, $P2_12_12_1$, $a = 6.116(1)$, $b = 16.340(2)$, $c = 22.124(4)$ Å, $V = 2211.0(6)$ Å³, $Z = 4$, $D_x = 1.272$ g cm⁻³, $T = 293$ K, λ (Cu-K α) = 1.54178 Å, $\mu = 1.3$ mm⁻¹, $F(000) = 896$, final $R = 0.0350$ for 2283 observed reflections [$F_o > 4\sigma(F_o)$]. An absorption correction based on ψ -scan was applied.^{26†}

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