The reaction of diphenyl and dialkyl phosphorochloridates with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU). Formation of phosphonate diesters *via* N→C phosphorus migration

Annika Kers, Inger Kers and Jacek Stawinski *

Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, S-106 91 Stockholm, Sweden

Received (in Cambridge, UK) 7th June 1999, Accepted 29th July 1999

Diphenyl and neopentylene phosphorochloridates react with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in acetonitrile to form amidine adducts **3** or **10**. These undergo further conversion into the corresponding alkene aminals, followed by probable N→C phosphorus migration to produce stable 6-substituted phosphinoyl derivatives of DBU, **6** or **12**, respectively. Diethyl phosphorohalidates (chloride and bromide) also form amidine adduct **13** with DBU, but this does not undergo N→C phosphorus migration.

Introduction

Bicyclic amidines, *e.g.* 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), have adopted great synthetic importance mainly due to their efficiency in promoting base-induced intra- and intermolecular dehydrohalogenations (or other eliminations) to produce carbon–carbon and carbon–heteroatom multiple bonds.[1] Since in these and related types of transformations the high basicity of the amidine system is highlighted, DBU and DBN are usually referred to as non-nucleophilic strong bases.[2] The majority of recent applications of DBU and DBN, *e.g.* as reagents for the introduction and removal of certain protecting groups,[3–7] support this view. However, there is an increasing number of reports[2,8,9] that relate a high efficiency of amidine bases in certain transformations to their nucleophilicity rather than basicity.

Since efficient delocalisation of the positive charge provides stabilisation to protonated DBU or DBN species, this should also be a stabilising factor for various positively charged adducts formed in reactions of amidines with electrophilic reagents. This phenomenon is expected to be of particular significance in transformations where nucleophilic catalysis plays a dominant role, *e.g.* in various reactions of phosphorus compounds. Indeed, the presence of P–N bonds was revealed by X-ray analysis in various complexes of P(III) compounds (*e.g.* phosphorodiamidochloridites) with DBU and DBN.[10] In several other reports, where DBU or DBN was claimed to enhance the efficiency of substitution at the phosphorus centre, an intermediacy of amidine adducts has been postulated directly or indirectly. These include the DBU mediated transesterification of *p*-nitrophenyl phosphonates,[11] the formation of various types of internucleotide linkages *via* transesterification of the corresponding phosphate or phosphonate precursors,[12,13] the displacement of the *p*-nitrophenoxy group in P(III) compounds in the synthesis of thio- and selenophosphate derivatives,[14] the opening of an oxathiaphospholane ring with various nucleophiles,[15,16] *etc*. Although it is often difficult to distinguish if the observed kinetic effect is due to base catalysis (quite efficient in the instance of strong amidine bases) or nucleophile catalysis, there is spectroscopic evidence (^{31}P NMR studies) of DBU acting as a nucleophile forming intermediates containing a P–N bond, *e.g.* during oxidative transformation of H-phosphonate derivatives in the presence of DBU.[17]

Recently, we have published a cautionary note concerning the use of DBU in conjunction with various chlorophosphates.[18] We have observed that certain amidine adducts, formed from DBU and chlorophosphates, may undergo fast and rather unexpected transformations to produce stable 6-phosphinoyl derivatives of DBU. Similar findings have also been communicated by another research group[19] who isolated and determined the X-ray structure of phosphonate **12·HCl**.

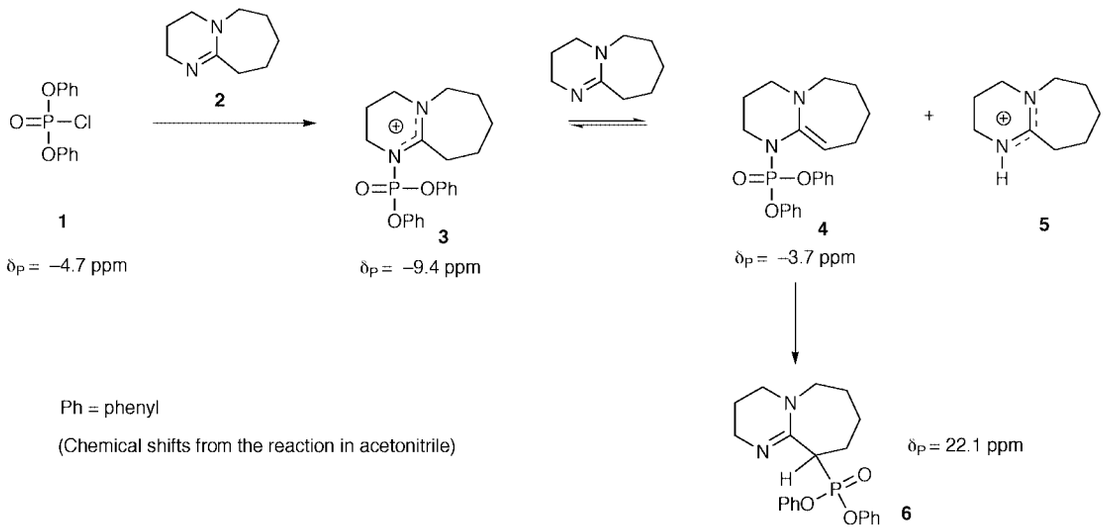
This paper describes ^{31}P NMR studies on the reaction of diphenyl and some dialkyl phosphorochloridates with DBU. These enabled us to identify the most likely intermediates involved and to propose a plausible mechanism for the observed formation of 6-phosphinoyl derivatives of DBU. Compounds **6·HCl** and **12·HCl** were characterised by ^{1}H, ^{13}C, and ^{31}P NMR spectroscopy, and the proton and carbon resonances were assigned using various homo- and heteronuclear correlated NMR techniques.

Results and discussion

Mechanism and intermediates involved in the reaction of chlorophosphates 1 or 8 with DBU

Diphenyl phosphorochloridate **1** reacted rapidly (*ca*. 5 min) with DBU (**2**, 2 equiv.) in acetonitrile affording a product (>95%)[20] resonating in the ^{31}P NMR spectrum in the range of chemical shifts characteristic for compounds bearing phosphorus directly bound to carbon (δ_P = 22.1 ppm, J_{PH} = 18.3 Hz, broad pseudo triplet). The product was stable upon the addition of water and/or excess of DBU, and after isolation it was identified as the hydrochloride of 1,8-diazabicyclo[5.4.0]undec-7-en-6-yl-phosphonate **6** (for the isolation and identification procedures, *vide infra*). The reaction occurred equally rapidly and cleanly in other solvents, *e.g.* tetrahydrofuran or methylene chloride. When the ^{31}P NMR spectra were acquired immediately after mixing the reagents, a signal of variable intensity (0–15%) at −3.7 ppm was occasionally observed. Since the first step in this transformation was, most likely, the displacement of chloride from **1** by DBU, in our preliminary reports[17,18] we tentatively assigned this signal to the amidine adduct **3**. Our further studies showed, however, that the signal at −3.7 ppm was probably due to a secondary intermediate formed in this reaction (*vide infra*), and thus the previous assignment seemed to be incorrect.[21]

The reaction of **1** with 1 equiv. of DBU was significantly slower. In the first ^{31}P NMR spectrum recorded (after *ca*. 5



Scheme 1

min), besides signals from unreacted **1** ($\delta_P = -4.7$ ppm, 30%), product **6** (broad signal, *ca*. 10%), and the intermediate at −3.7 ppm (*ca*. 15%), a new resonance at −9.4 ppm (*ca.* 45%) was observed. Gradual alterations occurred in the reaction mixture during time as revealed by ^{31}P NMR spectroscopy. The most notable change was a rather quick disappearance of the signal at −3.7 ppm and gradual shifting of the signal due to the product **6** from ~22 ppm to ~15 ppm (*vide infra*). Overnight, the reaction went to *ca*. 80% completion and the signal at −9.4 ppm was still present.

The reaction with an incremental addition of DBU (4 × 0.5 equiv.) to **1** in acetonitrile confirmed a possible involvement of two intermediates. The first portion of DBU (0.5 equiv.) produced only a small amount of an intermediate with $\delta_P = -3.7$ ppm (*ca*. 5%), while the major signals were those due to **1** (55%) and the intermediate with $\delta_P = -9.4$ ppm (*ca.* 40%). The signal at −3.7 ppm disappeared in the next spectrum (after *ca*. 5 min) but reappeared when another 0.5 equiv. of DBU was added. This phenomenon was observed again upon the addition of other portions of DBU, but the intensity of the signal that appeared at −3.7 ppm seemed to be higher after each successive addition. Product **6** could be detected in the reaction mixture *via* a broad signal at ~22 ppm after the addition of total 1 equiv. of DBU. This signal gradually sharpened when more DBU was added. The same course of the reaction, *i.e.* the formation of intermediates **3** and **4** and their conversion into product **6** (see Scheme 1), was observed for diphenyl phosphorobromidate **7** ($\delta_P = -16.1$ ppm).

Although the above ^{31}P NMR experiments clearly indicated the intermediacy of two species in the formation of phosphonate **6**, the absence of detectable J_{PH} coupling constants in resonances at −3.7 and −9.4 ppm, prevented any detailed ^{31}P NMR analysis, other than that based on the values of the chemical shifts.[22] We assumed that one of these intermediates was, most likely, the initial amidine adduct resulting from DBU and diphenyl chlorophosphate (intermediate **3**), which under the reaction conditions underwent conversion to another species. Taking into account the high basicity of DBU and ease of exchange of protons attached to carbon-6 in the DBU cation,[23,24] we considered it plausible that the second intermediate could be an alkene aminal (alkene *N*,*N*-acetal or vinyldiamine)[24,25] of type **4**, produced from the amidine adduct **3**. By analysing bonding around the phosphorus in both intermediates, we deemed that **4** should resonate at lower field relative to **3** in ^{31}P NMR spectra,[26] and tentatively assigned the signal at −3.7 ppm to ketene aminal **4** and that at −9.4 ppm to amidine adduct **3**. This assignment, although consistent with the expected chemical shifts for **3** and **4**, was somewhat at odds with the observed order of the appearance of signals from these intermediates in the ^{31}P NMR spectra (*vide supra*). To explain this apparent inconsistency, we suggested an equilibrium between amidine adduct **3** and alkene aminal **4**, mediated by DBU (Scheme 1).

At the initial stages of the reaction this equilibrium is shifted, due to the high concentration of DBU relative to **3**, towards **4** and thus a signal (of variable intensity) at −3.7 ppm can be observed in the ^{31}P NMR spectra. As the reaction proceeds, the concentration of DBU is depleted and the equilibrium is shifted to the left. This usually causes the signal due to initial intermediate **3** (signal at −9.4 ppm) to be detected at the later stages of the reaction, when concentration of DBU is low. The ratio of the intermediates **3** and **4** in reaction mixtures may vary depending on the amount of DBU used for the reaction, and in some instances only adduct **3** (with excess of **1**) or only **4** (with excess of DBU), can be detected in the ^{31}P NMR spectra (*vide supra*). Consistent with this were results from the reaction of **1** with DBU (2 equiv.) in toluene. Due to the low solubility of polar substances in this solvent, a heavy precipitation of DBU·HCl **5** occurred during the course of the reaction. This, according to Scheme 1, should shift the equilibrium towards alkene aminal **4**. Indeed, in the first spectrum recorded the major signal was that due to intermediate **4** (−4.3 ppm).[27]

As to the formation of 6-substituted phosphinoyl derivatives **6** of DBU, we assumed that this probably occurred with intermediacy of alkene aminal **4** and might involve an intramolecular N→C phosphorus migration,[28] initiated by nucleophilic attack of C6-carbon on the electron-deficient phosphorus centre. The formation of **6** in an intramolecular reaction, although possible, seems less likely due to steric hindrance at the phosphorus centre.

We found further support for the proposed reaction pathway (Scheme 1) by examining the reaction of cyclic chlorophosphate **8** (2-chloro-5,5-dimethyl-2-oxo-1,3,2-dioxaphosphinane) with DBU. The reaction proceeded *via* similar intermediates (**10** and **11**, Chart 1) as those observed for **1**, but formation of the product (6-phosphinoyl derivative **12**) was, as expected, rather slow (overnight). This decrease in rate was, most likely, caused by lower electrophilicity and higher steric hindrance at the phosphorus in **11**, as compared to **4**. These features made it possible to carry out some additional experiments that substantiated our assumption about the DBU-mediated equilibria between intermediates (**3** and **4** or **10** and **11**) and provided spectroscopic evidence for an alkene aminal structure of the secondary intermediate **11**. Upon treatment of chlorophosphate **8** in acetonitrile with DBU (2 equiv.), ketene aminal **11** ($\delta_P = 1.0$ ppm) was formed as the major product (~90%, 10 min)

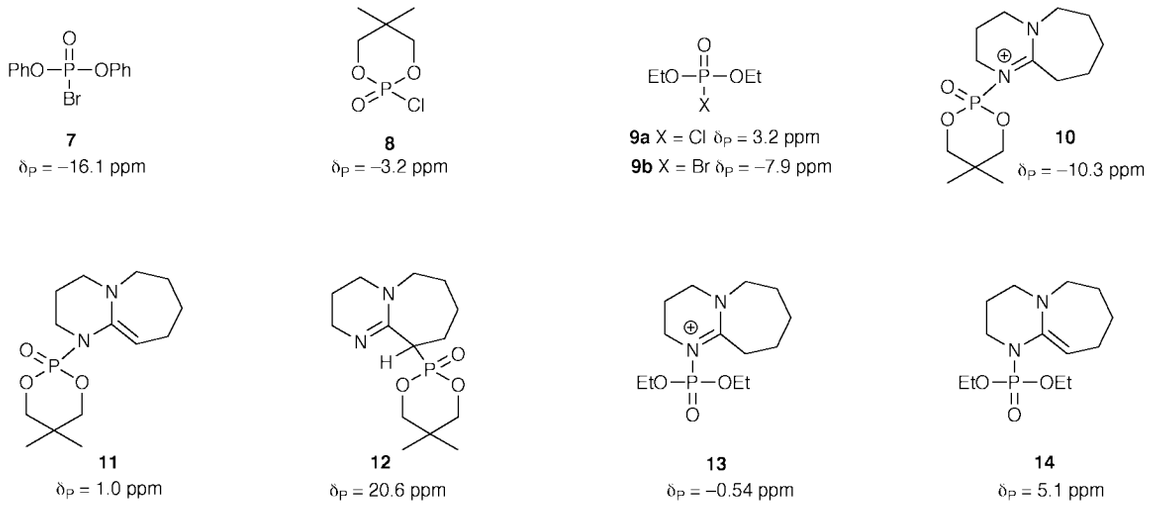


Chart 1

and only small amounts of unreacted starting material **8** ($\delta_P = -3.2$ ppm, *ca.* 5%) and intermediate **10** ($\delta_P = -10.3$ ppm, *ca.* 5%) could be detected. With less DBU (1 equiv.), after *ca.* 10 min only signals due to **11** (*ca.* 40%) and starting material **8** (*ca.* 60%) could be observed, and the resonance assigned to intermediate **10** was not visible until after *ca.* 30 min. These observations, further supported by additional experiments, were consistent with the existence of an equilibrium, similar to that in Scheme 1, between intermediates **10** and **11**.[29] In the presence of DBU, the equilibrium between **10** and **11** was to the right, apparently due to a high stability of the formed DBU cation **5**. We thought that the addition of a compound which could act as a source of protons, *e.g.* pyridinium hydrochloride, should shift the equilibrium to the left *via* depleting equilibrium concentration of DBU and providing protons to form **10** from alkene aminal **11**. Indeed, upon the addition of pyridinium hydrochloride (4 equiv.) to the reaction mixture containing **11** as the major intermediate, we observed a complete conversion of alkene aminal **11** to amidine adduct **10**. Pertinent to the postulated intermediacy of alkene aminals in the formation of 6-phosphinoyl DBU derivatives (**6** or **12**), was a complete lack of formation of **12** (overnight) in this reaction. The equilibrium was shifted back to produce alkene aminal **11** upon addition of DBU (5 equiv.).

We were also able to obtain spectroscopic evidence substantiating the assignment of the signal at 1.0 ppm to alkene aminal **11**. Since the distinctive structural feature of alkene aminals (*e.g.* **4** or **11**) is the presence of a tri-substituted carbon–carbon double bond, we used ^{13}C NMR spectroscopy to detect a methine carbon in the intermediate **11** resonating at 1.0 ppm in ^{31}P NMR. To this end we produced the putative alkene aminal **11** as the major intermediate (*ca.* 90%) by reacting **8** with DBU (2 equiv.) in CD_3CN. By running two different DEPT experiments (using the pulse sequence with Θ 90° and 135°) we could identify a carbon resonance at 99.2 ppm as resulting from the methine carbon (=C–H).

Isolation and NMR characterisation of products 6·HCl and 12·HCl

Although diphenyl phosphonate **6** was stable under the reaction conditions (*vide supra*), its isolation posed some problems. We found that to secure high preparative yields, DBU·HCl **5** has to be removed from the reaction mixture before chromatography, otherwise an extensive decomposition of **6** might occur. Due to the non-polar structure of phosphonate **6** (non-protonated form under the reaction conditions), the removal of **5** could be effected *via* precipitation from non-polar solvents. The subsequent conversion of **6** into its hydrochloride, followed by silica gel chromatography afforded **6**·HCl in good yield. In the instance of phosphonate **12**, removal of **5** before chromatography was not necessary (see Experimental section).

Due to the ease of protonation of **6** or **12**, these compounds were usually isolated as their hydrochlorides.[30] ^{31}P NMR chemical shifts of **6·HCl** (15.2 ppm) and **12·HCl** (12.7 ppm) were significantly different from those of the corresponding non-protonated species **6** (22.1 ppm) and **12** (20.6 ppm). To provide support for the origin of the observed differences, we recorded ^{31}P NMR spectra of **6·HCl** and **12·HCl** with incremental addition of DBU. As expected, a gradual shifting of the ^{31}P NMR signals toward lower field occurred with the increasing concentration of DBU.[31] This indicated a rapid equilibria between protonated and non-protonated phosphonate **6** or **12**, which resulted in the appearance of only a weight-averaged signal in the spectra. From the observed chemical shifts of these weight-averaged signals in the reaction mixtures resulting from equimolar amounts of **6·HCl** and DBU or **12·HCl** and DBU, we calculated the amounts of non-protonated species **6** and **12** present (*ca.* 82 and 95%, respectively).[32] These gave approximate ΔpK_a values between DBU and those of **6** and **12**, 1.3 and 2.5, respectively.[33]

Identification of the isolated phosphonates **6**·HCl and **12**·HCl was based on the assignment of proton, carbon and phosphorus resonances using known or expected chemical shifts in conjunction with ^1H–^1H, ^1H–^{13}C, ^1H–^{31}P correlation NMR spectroscopy (see Chart 2 for numbering system).

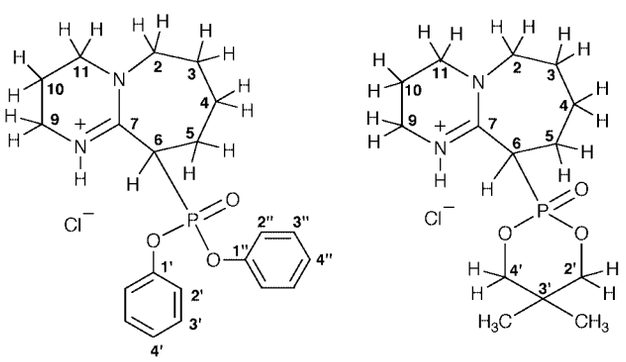


Chart 2

For phosphonate **6·HCl**, the ^1H NMR spectrum consisted of four groups of resonances at 7.1–7.4 ppm (10 H), 4.8–5.2 ppm (2 H), 3.0–3.6 ppm (5 H) and 1.5–2.5 ppm (8 H). On the basis of chemical shift values, the group at lower field was assigned

to the aromatic protons of the two phenyl rings, while that at high field, to methylene protons at C3, C4, C5 and C10. The group of signals between 3.0–3.6 ppm could arise from five methylene protons (probably at C9, C11 or C2) and that at 4.8–5.2 ppm, from the proton at C6 and one diastereotopic methylene proton attached to C9, C11 or C2. To make an assignment of these signals, we identified ^{1}H spin systems in the 6- and 7-membered rings of the DBU moiety using C6–H resonance (doublet of triplets at *ca*. 5.1 ppm in ^{1}H NMR) as a starting point in establishing a connectivity pattern. The assignment of carbon resonances in ^{13}C NMR of **6·HCl**[34] was done on the basis of expected chemical shifts, the observed phosphorus–carbon couplings, and additional information available from ^{1}H–^{13}C heteronuclear correlation NMR spectroscopy.

A similar protocol was used for assignments of proton and carbon resonances of phosphonate **12·HCl**. The ^{1}H spin system of the neopentylene moiety in this compound was easy to identify as its proton resonances did not overlap with the other proton signals. The two axial protons (C2′–H_{ax} and C4′–H_{ax}) of the dioxaphosphinane ring gave well separated doublets (geminal couplings to the equatorial protons) at *ca*. 5.4 and 4.7 ppm, while the corresponding equatorial counterparts resonated in one multiplet at *ca*. 3.9 ppm. ^{1}H–^{31}P correlated spectra showed that only the equatorial protons attached to C2′ and C4′ strongly coupled to the phosphorus atom. Couplings of phosphorus to the axial dioxaphosphinane protons (C2′–H_{ax} and C4′–H_{ax}) were too small to be detected.[35]

The reaction of diethyl halophosphates 9 with DBU

Diethyl phosphorochloridate **9a** and diethyl phosphorobromidate **9b** reacted promptly with DBU in acetonitrile, tetrahydrofuran or pyridine affording (depending on the reaction conditions) the amidine derivatives **13** or alkene aminal **14** as major phosphorus-containing species (>90%).[36] Although no visible changes occurred within 15 min, a complicated mixture of products, that did not contain the expected diethyl 6-phosphinoyl derivative of DBU, was usually formed after several hours.[37]

When bromophosphate **9b** ($\delta_P = -7.9$ ppm) reacted with DBU (1 equiv.) in acetonitrile, a clean formation of a putative intermediate **13** ($\delta_P = -0.54$ ppm) was observed. This, upon the addition of another equivalent of DBU produced the expected alkene aminal intermediate **14** ($\delta_P = 5.1$ ppm, *ca.* 30%). Its amount increased to *ca*. 70% upon the successive addition of DBU (total 3 equiv.), but pyridinium hydrochloride (4 equiv.) shifted the equilibrium almost completely towards **13**. These experiments suggested that the behaviour of the intermediates **13** and **14** was similar to that of the corresponding intermediates in the other investigated reactions. Thus, the observed lack of formation of 6-phosphinoyl derivatives of DBU in the instance of **9** was, most likely, due to competing dealkylation of intermediate **13** (or **14**), which was apparently faster than the putative N→C phosphorus migration.

In conclusion, we found that diphenyl and neopentylene phosphorochloridates reacted with DBU to produce the corresponding 6-phosphinoyl derivatives of DBU as final products. The structures of the produced diphenyl (**6**) and neopentylene (**12**) phosphonates were confirmed by ^{1}H, ^{13}C and ^{31}P NMR spectroscopy. The reactions were found to occur, most likely, *via* the initial formation of the corresponding amidine adducts **3** and **10**, which in the presence of DBU underwent further conversion into alkene diaminals **4** and **11**, affording ultimately the corresponding 6-phosphinoyl derivatives **6** and **12**. It is worth noting that another amidine base, 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), under analogous reaction conditions did not produce compounds containing P–C bonds.[38]

These studies provide a new understanding of the behaviour of DBU toward electrophilic phosphorus reagents and, thus, can be of relevance to a variety of transformations of phosphorus compounds in which bicyclic amidine bases are used as catalysts. On the other hand, since the formation of C-phosphonates **6** and **12** occurs in high yield and under mild conditions, this reaction can also be considered as a new entry to functionalisation of DBU at the C-6 position. Further studies on this subject are in progress in this laboratory.

Experimental

Reactions were carried out in 10 mm NMR tubes and spectra were recorded on a Jeol GSX-270 FT, Varian 300 or Varian 400 MHz spectrometer. For ^{31}P NMR experiments 2% H_3PO_4 in D_2O (δ_P indistinguishable from that of 85% H_3PO_4 in H_2O) was used as external standard (coaxial inner tube). In some experiments the values of the chemical shifts for the intermediates produced *in situ* varied (±1 ppm), depending on the reaction conditions. A systematic trend of shifting ^{31}P NMR resonances to lower field (~1.5–2 ppm) was observed upon changing the solvent from THF to acetonitrile.

Acetonitrile (Merck) was stored over molecular sieves (4 Å). Tetrahydrofuran (Merck) was refluxed over $LiAlH_4$ and freshly distilled before use. Diphenyl and diethyl phosphorochloridates were commercial grade from Aldrich. DBU (Aldrich) was distilled before use. 2-Chloro-5,5-dimethyl-2-oxo-1,3,2-dioxaphosphinane **8** was prepared according to published procedure.[39] Diethyl phosphorobromidate **9b** was produced from equimolar amounts of triethyl phosphite and bromine in THF;[40] diphenyl phosphorobromidate **7**, analogously, from equimolar amounts of diphenyl H-phosphonate (Aldrich) and bromine in THF, in the presence of triethylamine (1.2 equiv.).[17]

The assignment of proton and carbon resonances of phosphonates **6·HCl** and **12·HCl** was done on the basis of known or expected chemical shifts in conjunction with ^{1}H–^{1}H, ^{1}H–^{13}C, ^{1}H–^{31}P correlated NMR spectroscopy.

Synthesis of diphenyl diazabicyclo[5.4.0]undec-7-en-6-yl-phosphonate 6, hydrochloride

Diazabicyclo[5.4.0]undec-7-ene (DBU, 4 mmol, 0.60 mL) was added to a solution of diphenyl phosphorochloridate **1** (2 mmol, 0.42 mL) in acetonitrile, and after 15 minutes the reaction mixture was concentrated to an oil. The residue was dissolved in chloroform (*ca*. 5 mL) and precipitated from a light petroleum–diethyl ether mixture (6:4, v/v). The oily precipitate that formed was removed by filtration and the filtrate was evaporated. The residue was dissolved in acetonitrile (25 mL), pyridinium hydrochloride (2 mmol) was added and the solvent removed under vacuum. The resulting oil was precipitated from light petroleum–diethyl ether mixture (6:4, v/v) and the precipitate was purified by silica gel column chromatography using chloroform–methanol (9:1, v/v) as an eluent. Compound **6·HCl** (0.77 g, 80% yield) was obtained as a yellow, sticky oil (purity > 96%, ^{1}H NMR).

^{31}P-NMR (in acetonitrile) $\delta_P = 15.2$ ppm ($J_{PH} = 32.2$ and 6.5 Hz, broad dt); ^{1}H-NMR δ_H (in ppm, $CDCl_3$) 7.12–7.43 (10 H, m, 2 PhO), 5.10 (1 H, m, $J_{HP} = 30.4$ Hz and $J_H = 5.5$ Hz, cross peak in ^{1}H–^{31}P NMR, *C6-H*), 4.90 (1 H, m, $J = 12.3$ and 14.3 Hz, *C2-H′*), 3.50 (2 H, m, *C11-H′* and *C9-H′*), 3.35 (1 H, m, *C11-H″*), 3.14 (2 H, m, *C2-H″* and *C9-H″*), 2.39 (1 H, m, *C5-H′*), 1.50–2.22 (7 H, m, cross peak in ^{1}H–^{31}P NMR; *C5-H″* and *C4-H′*; *C4-H″*, *C10-H′*, *C10-H′*, *C3-H″* and *C3-H″*; according to the order in the multiplet); ^{13}C-NMR δ_C (in ppm, $CDCl_3$) 159.8 (C7), 150.4 ($J_{CP} = 9.2$ Hz, C1′), 149.7 ($J_{CP} = 11.0$ Hz, C1″), 129.8 ($J_{CP} = 12.9$ Hz, C3′ and C3″), 125.5 ($J_{CP} = 14.6$ Hz, C4′ and C4″), 120.5 ($J_{CP} = 5.5$ Hz, C2′), 120.4 ($J_{CP} = 5.5$ Hz, C2″), 53.2 (C2), 50.1 (C11), 42.5 ($J_{CP} = 135.7$ Hz, C6), 38.4 (C9), 26.1 (C3), 24.4 ($J_{CP} = 3.7$ Hz, C5), 23.6 ($J_{CP} = 5.5$ Hz, C4), 19.1 (C10); HRMS $[M - Cl]^+$, found 385.1695. $C_{21}H_{26}O_3N_2P$ requires 385.1681; $[M + M - Cl]^+$, found 805.3043 (isotope

pattern 1.00 : 0.53 : 0.46). $C_{42}H_{52}O_6N_4P_2Cl$ requires 805.3051 (isotope pattern 1.00 : 0.50 : 0.45).

Synthesis of 2-(diazabicyclo[5.4.0]undec-7-en-6-yl)-5,5-dimethyl-2-oxo-1,3,2-dioxaphosphinane 12, hydrochloride

Diazabicyclo[5.4.0]undec-7-ene (DBU, 4 mmol, 0.60 mL) was added to a solution of 2-chloro-5,5-dimethyl-2-oxo-1,3,2-dioxaphosphinane **8** (2 mmol, 0.35 g) in acetonitrile, and the reaction was left overnight. The solvent was evaporated and the residue was purified by silica gel chromatography as described above to give the title compound **12·HCl** (0.61 g, 91%); mp 200–201 °C (from toluene–acetonitrile); lit.[19] mp 184 °C.

^{31}P-NMR (in acetonitrile) δ_P = 12.7 ppm (J_{PH} = 21.8, broad pseudo quintet); ^{1}H-NMR δ_H (in ppm, $CDCl_3$) 5.42 (1 H, d, J = 11.3 Hz, *C2′-H*$_{ax}$), 5.05 (1 H, m, *C2-H′*), 4.95 (1 H, dt, J_{HP} = 26.1 Hz and J_{HH} = 5.2 Hz, cross peak in ^{1}H–^{31}P NMR, *C6-H*), 4.72 (1 H, d, J = 11.3 Hz, *C4′-H*$_{ax}$), 3.88 (2 H, m, cross peak in ^{1}H–^{31}P NMR, *C2′-H*$_{eq}$ and *C4′-H*$_{eq}$), 3.52 (3 H, m, *C11-H′*, *C11-H″* and *C9-H′*), 3.38 (1 H, m, *C9-H″*), 3.11 (1 H, ddd, J = 15.0, 13.5 and 1.5 Hz, *C2-H″*), 2.2–1.8 (6 H, m, *C5-H′*, *C4-H′*; *C10-H′* and *C10-H″*; *C5-H″*, *C3-H′*; according to the order in the multiplet), 1.7 (1 H, m, *C4-H″*), 1.6 (1 H, m, *C3-H″*), 1.30 (3 H, s, CH_3), 1.00 (3 H, s, CH_3); ^{13}C-NMR δ_C (in ppm, $CDCl_3$) 161.1 (C7), 78.5 (J_{CP} = 7.3 Hz, C2′), 77.7 (J_{CP} = 5.4 Hz, C4′), 53.2 (C2), 50.0 (C11), 39.3 (J_{CP} = 122.8 Hz, C6), 38.4 (C9), 32.9 (J_{CP} = 7.4 Hz, C3′), 26.2 (C3), 24.3 (J_{CP} = 3.6 Hz, C5), 23.6 (J_{CP} = 3.7 Hz, C4), 22.2 (CH_3), 19.9 (CH_3), 19.4 (C10); HRMS $[M - Cl]^+$, found 301.1690. $C_{14}H_{26}O_3N_2P$ requires 301.1681.

Acknowledgements

We are indebted to Professor Per J. Garegg for his interest and helpful discussions. Financial support from the Swedish Natural Science Research Council and the Swedish Foundation for Strategic Research, is gratefully acknowledged.

References

1 H. Oediger, F. Möller and K. Eiter, *Synthesis*, 1972, 591.
2 A. H. Cowley, *Acc. Chem. Res.*, 1984, **17**, 386.
3 S. K. Awasthi, V. Khanna, G. Watal and K. Misra, *Indian J. Chem. Sect. B*, 1993, **32**, 916.
4 H. Schirmeister, F. Himmelsbach and W. Pfleiderer, *Helv. Chim. Acta*, 1993, **76**, 385.
5 M. Pfister, H. Schirmeister, M. Mohr, S. Farkas, K. P. Stengele, T. Reiner, M. Dunkel, S. Gokhale, R. Charubala and W. Pfleiderer, *Helv. Chim. Acta*, 1995, **78**, 1705.
6 Y. Watanabe, T. Nakamura and H. Mitsumoto, *Tetrahedron Lett.*, 1997, **38**, 7407.
7 S. Chandrasekhar and S. Sarkar, *Tetrahedron Lett.*, 1998, **39**, 2401.
8 H. Lammers, P. Cohen-Fernandes and C. L. Habraken, *Tetrahedron*, 1994, **50**, 865.
9 M. G. Johnson and R. J. Foglesong, *Tetrahedron Lett.*, 1997, **38**, 7003.
10 R. Reed, R. Reau, F. Dahan and G. Bertrand, *Angew. Chem.*, *Int. Ed. Engl.*, 1993, **32**, 399.
11 D. S. Tawfik, Z. Eshhar, A. Bentolila and B. S. Green, *Synthesis*, 1993, 968.
12 Z. J. Lesnikowski, D. Zabawska, M. M. Jaworska-Maslanka, R. F. Schinazi and W. J. Stec, *New J. Chem.*, 1994, **18**, 1197.
13 L. A. Wozniak, M. Wieczorek, J. Pyzowski, W. Majzner and W. J. Stec, *J. Org. Chem.*, 1998, **63**, 5395.
14 J. Helinski, W. Dabkowski and J. Michalski, *Tetrahedron Lett.*, 1993, **34**, 6451.
15 W. J. Stec, A. Grajkowski, M. Koziolkiewicz and B. Uznanski, *Nucleic Acids Res.*, 1991, **19**, 5883.
16 K. Misiura, D. Szymanowicz and W. J. Stec, *Chem. Commun.*, 1998, 515.
17 A. Kers, J. Stawinski, L. Dembkowski and A. Kraszewski, *Tetrahedron*, 1997, **53**, 12691.
18 A. Kers, I. Kers, M. Bollmark and J. Stawinski, *Acta Chem. Scand.*, 1998, **52**, 1405.
19 M. Vijjulatha, K. P. Kumar, K. C. K. Swamy and J. J. Vittal, *Tetrahedron Lett.*, 1998, **39**, 1819.
20 In all reactions of diphenyl phosphorochloridate **1** and DBU, a small amount of a side product (<3%), resonating at 29.9 ppm, was formed.
21 In references 17 and 18, signals in ^{31}P NMR spectra assigned to the initial adducts of chlorophosphates and DBU (intermediates of type **3**) were, most likely, due to secondary intermediates (type **4** in this paper) having the same atoms bound to the phosphorus, but differing in a distal part of the DBU moiety.
22 Considering the substrates used for the reaction and the observed chemical shifts, it was possible that both intermediates might contain a P–N bond.
23 S. Löfås and P. Ahlberg, *J. Chem. Soc.*, *Chem. Commun.*, 1981, 998.
24 S. Löfås and P. Ahlberg, *J. Am. Chem. Soc.*, 1985, **107**, 7534.
25 H. Weingarten and J. S. Wagner, *J. Org. Chem.*, 1970, **35**, 1750.
26 J. C. Tebby, Eds., *CRC Handbook of Phosphorus-31 Nuclear Magnetic Resonance Data*, vol. p. 227, CRC Press, Boston, 1991.
27 The signal was shifted *ca.* 0.6 ppm towards higher field probably due to the solvent effect. The intermediate, which gave rise to this signal, reacted further to produce **6**. No signal due to **3** could be detected under the reaction conditions.
28 One can speculate that a plausible mechanism for such phosphorus migration could involve (i) a *tbp* intermediate with the four-membered ring in the preferred apical–equatorial posture, (ii) a pseudorotation to another low energy *tbp* with the phosphetidine nitrogen in an apical and the carbon in an equatorial position, and finally (iii) a ring opening with the P–N bond cleavage.
29 In this instance, however, the formation of amidine adduct **10** was probably slower (due to steric hindrance in **8**) than its deprotonation to form alkene aminal **11**, which allowed the former intermediate to be detected only at later stages of the reaction, when the concentration of DBU became low.
30 Phosphonate **6** could be isolated as a free base when DBU hydrochloride was removed from the reaction *via* precipitation. The ^{31}P NMR chemical shift of the isolated compound was identical to that observed in the reaction mixture (*ca.* 22 ppm).
31 The plot of δ_P *vs.* DBU concentration was linear up to 0.6 equiv. (for **12·HCl**, 4 points, R = 0.999, slope 9.50) and 1 equiv. (for **6·HCl**, 6 points, R = 0.999, slope 5.7) of the added DBU.
32 Equilibria constants K_e = 22 (for **6·HCl** + DBU) and K_e = 306 (for **12·HCl** + DBU) were calculated using the following chemical shift values: **6·HCl** (δ_P = 15.11 ppm), **6** (δ_P = 22.08 ppm) and δ_{obs} = 20.85 ppm; **12·HCl** (δ_P = 12.59 ppm), **12** (δ_P = 21.08 ppm) and δ_{obs} = 20.62 ppm.
33 The reason for the higher basicity of **6** relative to **12**, as was apparent from ^{31}P NMR data, is unclear.
34 Multiplicity of the aromatic carbon signals was due to the diastereotopic character of the phenyl groups and the presence of phosphorus–carbon couplings.
35 L. D. Hall and R. B. Malcolm, *Can. J. Chem.*, 1972, **50**, 2092.
36 Formation of some unidentified side-products (as was apparent from the presence of several resonances of low intensity, especially in the reactions involving **9a**) was also observed.
37 Formation of complicated mixtures of products can be due to competing dealkylation of **13** and **14**, and some subsequent transformations of the produced reactive species.
38 A. Kers, I. Kers and J. Stawinski, unpublished results.
39 R. L. McConnell and H. W. Coover, *J. Org. Chem.*, 1959, **24**, 630.
40 A. Gorecka, M. Leplawy, J. Zabrocki and A. Zwierzak, *Synthesis*, 1978, 474.

Paper 9/04502C