Pergamon

Tetrahedron 56 (2000) 663–669

TETRAHEDRON

Easy and Efficient Generation of Reactive Anions with Free and Supported Ylides as Neutral Brønsted Bases

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Received 13 September 1999; revised 8 November 1999; accepted 25 November 1999

Abstract—The tris(dimethylamino)-*C*-dimethylphosphorus ylide **5** and the tris(dimethylamino)phosphorus ylide *C*-bound to Merrifield's resin **6** are used as strong non-nucleophilic bases in *N*-alkylation reactions of β-amino phosphine oxides and α-amino acid derivatives, and in the *C*-alkylation reaction of enamines and benzophenone imines derived from glycine ethyl ester. Base-catalyzed aldol-type condensation (Henry) reaction of nitroethane with aldehydes and olefination reactions of phosphine oxides and phosphonates are also described. © 2000 Elsevier Science Ltd. All rights reserved.

An important tool in organic synthesis is the generation of anions under mild reaction conditions that can in turn participate in interesting and useful transformations. Classic methods involve the use of ionic bases such as alkali metal hydroxides, alkoxides, hydrides or metalorganic reagents. However, their use is limited in some cases because their elimination is not easy and in most cases needs work-up. The nucleophilic attack of the base to the substrate may also take place as a side reaction. Therefore, there is a need for new classes of strong non-ionic and non-nucleophilic bases.

Proazaphosphatranes **1** have recently been described as strong non-ionic bases.[1a] They have been used for the acylation[1b] and silylation of alcohols,[1c] for the dehydrohalogenation of alkyl halides[1d] and to deprotonate nitriles[1e] or β-dicarbonyl compounds.[1f] Proton sponges,[2a] related to 1,8-bis(dimethylamino)-naphthalene (DMAN) **2**, and new ones, derived from the replacement of one or both dimethylamino groups by phosphazene groups **3** are also strong bases.[2b] These phosphazene-substituted proton sponges **3** are stronger than DMAN **2**, but are of no practical value, since the free bases cannot be prepared. In the late 1980s, polyaminophosphazenes such as **4** (namely P_4tBu) were reported as excellent strong uncharged bases.[3] They have found applications for the deprotonation of compounds of very low acidity[3d] or for measuring the kinetic isotope effects of the conjugate porphyrin anion,[3e] but their high molecular weight and cost are drawbacks for their extensive use. Phosphorus ylides, isosteric analogues of phosphazenes by substitution of the nitrogen atom for the carbon atom, are more basic than the corresponding phosphazenes, but this property has seldom been used in organic and organometallic chemistry.[4] Simple ylides such as *P*-tris(dimethylamino)-*C*-dimethylphosphorus ylide **5** can be conveniently used as strong non-nucleophilic bases for alkylation of nitrogen heterocycles.[5,6] Here we report some applications of **5** for regioselective *N*- and *C*-alkylation of acyclic compounds and for olefination reactions. The use in organic synthesis of a supported version **6** of this type of base, with potential applications in combinatorial chemistry, is also presented (Fig. 1).

Results and Discussion

N-Alkylation reactions

In order to explore the basic and non-nucleophilic behavior of ylide **5**, we first tested selective *N*-functionalization reactions of β-amino phosphine oxides **7**.[7] Amines, derived from phosphine oxides and especially aminophosphonates, phosphorus analogs of amino acids, are useful intermediates not only in organic synthesis but also in medicinal chemistry.[8] The selective *N*-functionalization reactions of β-amino phosphine oxide **7** can be performed with phosphorus ylide **5** as non-ionic base instead of organometallic reagents or sodium hydride.[9] Indeed, addition of an excess (2 equiv.) of a freshly prepared THF solution of the phosphorus ylide **5**

Keywords: basicity; carbanions; phosphorus ylides; solid-phase synthesis; supported ylides.
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PII: S0040-4020(99)01039-X

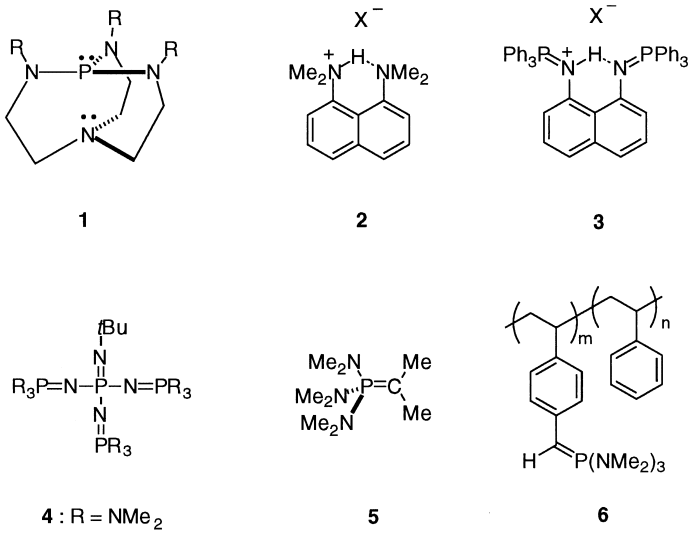
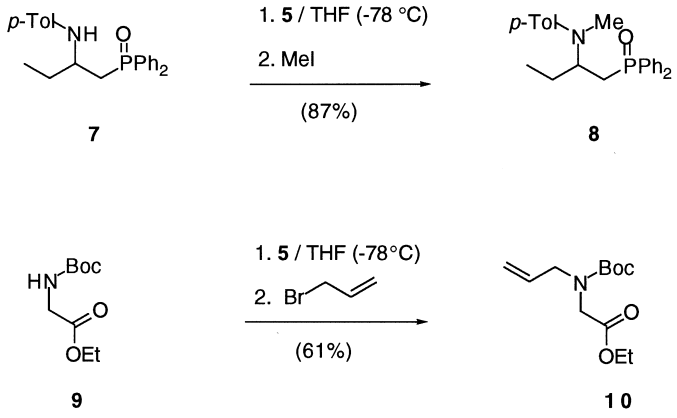


Figure 1.



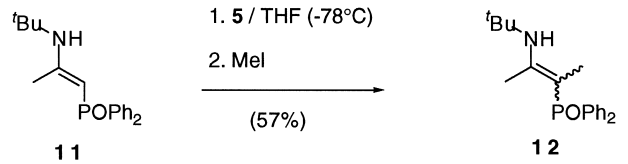
Scheme 1.

to a THF solution of **7**, followed by addition of the alkylating reagent (MeI) led to formation of *N*-functionalized β-amino phosphine oxide **8** in excellent yield (87%) after elimination of the phosphonium salt $\mathbf{5H}^{+}\mathbf{,I}^{-}$ by addition of ether to the reaction mixture and simple filtration (Scheme 1).

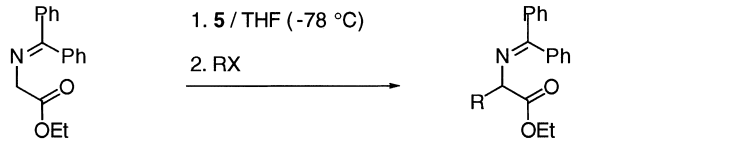
This process can also be extended to α-amino acid derivatives. The selective alkylation processes at the *N* atom versus the *C*α atom for amino acid derivatives have been widely studied.[10] Good results were also obtained for the selective *N*-alkylation reaction of *N*-protected glycine alkyl ester **9**.[11] Addition of a slight excess of ylide **5** to a THF solution of *N*-Boc-α-amino ester **9**, followed by treatment with allyl bromide, led to the *N*-alkylated compound **10** in a regioselective fashion, but in moderate yield (61%) (Scheme 1).

C-Alkylation reactions

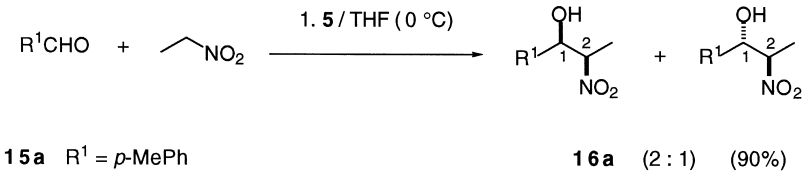
Ylide **5** can also be efficiently used for *C*-alkylation reactions and carbon–carbon bond formation reactions. Enamines are excellent reagents for carbon–carbon bond formation[12] and their nucleophilic character can be increased in the presence of bases.[12,13] However, the ambident nucleophilic reactivity of activated metallo enamines[13] has the problem of site reactivity and they can react with electrophilic compounds not only at the nitrogen atom but also at the β carbon of the enamine. The regioselective *C*-alkylation reaction of secondary β-enamine derived from phosphine oxide **11**[14] was performed by treatment with ylide **5** in THF, followed by addition of methyl iodide, but the *C*-α-methyl-β-enamine **12** was isolated, as a mixture of both *Z* and *E* isomers (Scheme 2). Compounds **12** were characterized on the basis of their spectroscopic data. Thus, the ^{31}P NMR spectrum of the mixture **12*Z*/*E*** showed two different absorptions at δ_P 36.3 and 39.5 in an approximate isomer ratio 1:1 as evidenced by the relative peaks areas for each isomer, in which the high-field chemical shift corresponded to the *E*-isomer. Further examination of the ^{1}H and



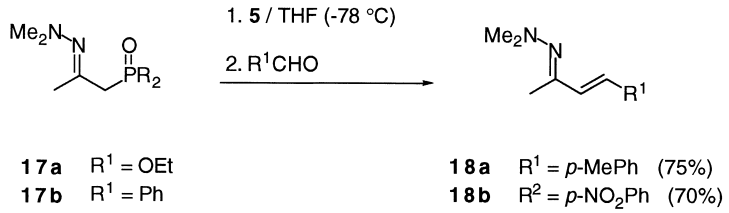
Scheme 2.



Scheme 3.



Scheme 4.



Scheme 5.

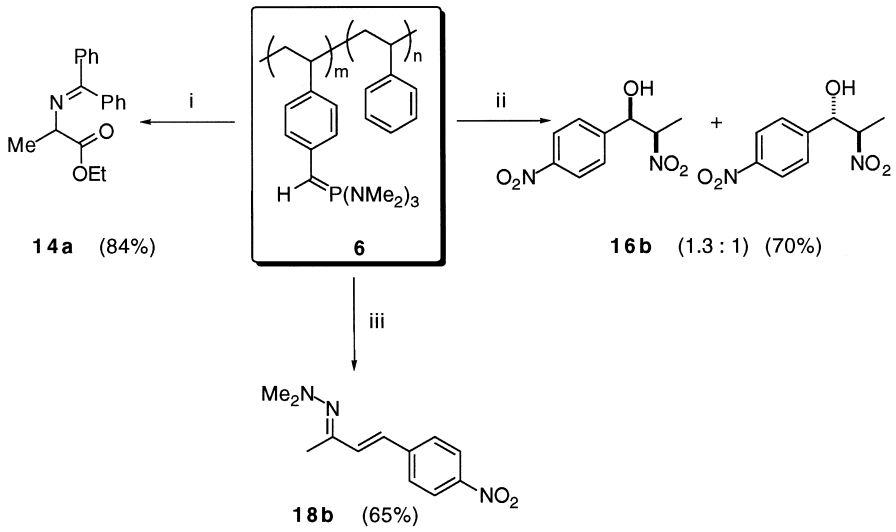
^{13}C NMR spectra was consistent with the β-enamine structure. In the ^{13}C NMR spectrum, the methyl group of the *E*-isomer resonates at δ_C 13.9 ($^3J_{PC}$=3.0 Hz). Conversely, the *Z*-isomer showed clearly different absorption for the methyl group at δ_C 21.3 ($^3J_{PC}$=12.1 Hz). Similar coupling constants ($^3J_{PC}$) had been previously observed in *E*- and *Z*-β-hydrazino[15] or β-enamino[14] phosphine oxides or phosphonates.

This process can also be extended to α-amino acid derivatives. α-Amino acid derivatives can be alkylated in a regioselective fashion in the presence of ylide **5** not only at the *N* atom as has been described in Scheme 1, but also at the *C*α atom when imines derived from amino acids are used.[16] Treatment of benzophenone–imine derivative of glycine alkyl ester **13**[17] with a freshly prepared THF solution of the base **5**, followed by addition of methyl iodide led to formation of *C*-α-functionalized imine **14a** (R=Me) in a selective fashion and in good yield (80%). This compound **14a** was characterized on the basis of its spectroscopic data, having spectroscopic, analytical and physical properties in full agreement with the literature.[17] In the same way, the selective *C*-alkylation of the benzophenone–imine derivative **13** was performed using allyl bromide affording imine **14b** (R=CH_2CH=CH_2) in 67% yield. The use of phase-transfer conditions employed for the alkylation of the α anion of glycine derivatives[10,16d–g] could be replaced by employing ylide **5** as a strong non-nucleophilic base (Scheme 3).

Another carbon–carbon bond formation reaction was explored. Base-catalyzed aldol-type condensation (Henry) reaction is a known method for the construction of carbon–carbon bonds, which leads to formation of 2-nitroalcohols,[18] which are versatile synthetic intermediates in the preparation of 2-aminoalcohols, of particular significance in the synthesis of biologically active compounds[19] and amino sugars.[20] Ylide **5** is also able to promote the nitroaldol reaction between *p*-tolualdehyde **15a** and nitroethane. Treatment of a nitroethane solution of ylide **5** at 0°C with *p*-tolualdehyde **15a** gave nitroalcohols **16a** as a mixture of *syn* and *anti* derivatives (2:1 ratio), obtained in excellent yield (90%) but with low stereoselectivity (Scheme 4). Nitroalcohol **16a** was characterized by its spectroscopic data. The ^1H NMR spectrum showed well-resolved doublets for the methine proton (H_1) and the proton absorption of the *anti*-isomer was shifted to a lower field δ_H 5.19 ($^3J_{HH}$=4.1 Hz) relative to that of the *syn*-isomer δ_H 4.87 ($^3J_{HH}$=9.2 Hz), which is consistent with previously reported *syn*- and *anti*-2-nitroalcohols.[18c] Likewise in ^{13}C NMR this latter isomer showed a downfield shift absorption for the methine carbon (C_1) δ_C 88.3 relative to that observed for the *anti*-isomer δ_C 87.4.

Olefination reactions

The reaction of an α-phosphorus-stabilized anion with a carbonyl derivative is undoubtedly one of the most useful methods for selectively constructing carbon–carbon double bonds.[21] Phosphorus ylide **5** may also be useful as a strong base in carbon–carbon double bond formation reactions by the Horner–Wittig reaction of phosphine oxide anions and by the Horner–Wadsworth–Emmons reaction of phosphonate anions for two carbon homologation of hydrazones.



Scheme 6. (i) **13**, THF, 0°C, 1 h, MeI, THF, 0°C to rt, 5 h, 84%; (ii) **15b**, nitroethane, 0°C, 0.5 h, 70%; (iii) **17b**, THF, 0°C, 1 h, **15b**, THF, 0°C to reflux, 36 h, 65%.

Treatment of β-hydrazones derived from phosphonate **17a**[15] with ylide **5** followed by addition of *p*-tolualdehyde **15a** led to the formation of α,β-unsaturated hydrazone **18a** in good yield (Scheme 5). Vicinal $^{3}J_{HH}$=16.5 Hz between the vinylic protons of **18a** were consistent with the *E* configuration of the carbon–carbon double bond.[15] Similarly, treatment of β-hydrazones derived from phosphine oxide **17b**[15] with ylide **5** followed by addition of *p*-nitrobenzaldehyde **15b** gave α,β-unsaturated hydrazone **18b** (Scheme 5). These results were very similar to that obtained when methyllithium or LDA was used as base.[15]

Supported ylides

Polymer supported phosphorus ylides have recently been used in combinatorial synthesis with aldehydes (Wittig reaction) for the preparation of small organic molecules.[22] Therefore, in order to make the use of ylides as strong non-nucleophilic bases more attractive, we investigated their use in solid-phase synthesis of supported ylide **6**.[5]

The reactivity of ylide attached to Merrifield's resin **6** was first tested for *C*-alkylation reaction of α-amino acid derivatives. The selective *C*-alkylation reaction of the benzophenone–imine derivative of glycine alkyl ester **13** was accomplished using supported ylide **6** at 0°C in THF, followed by addition of methyl iodide. The *C*-α-functionalized imine **14a** was obtained in excellent yield (84%) (Scheme 6).

Henry reaction was also explored. Supported ylide **6** promoted the nitroaldol reaction between *p*-nitrobenzaldehyde **15b** and nitroethane giving nitroalcohols **16b** (70%) as a mixture (1.3:1 ratio) of *syn* and *anti* derivatives (Scheme 6). Finally, the resin **6** may also be useful as a strong base in carbon–carbon double bond formation reactions and was used for homologation of hydrazones. Treatment of β-hydrazono phosphine oxide **17b**[15] with ylide **6** followed by addition of *p*-nitrobenzaldehyde **15b** led to the formation of α,β-unsaturated hydrazone **18b** (Scheme 6). Although these results were comparable to those obtained with ylide **5** in solution, simple filtration of the reaction mixture and evaporation of the solvent afforded compounds **14a**, **16b** and **18b** in good yields, while the resin **6** could be regenerated by washing with acetonitrile and simple deprotonation.

In conclusion, ylide **5** and supported ylide **6** are versatile and efficient non-nucleophilic strong bases, which can be used for selective *N*- and *C*-alkylation reactions and for olefination reaction under mild reaction conditions. It is of particular interest that in each case the phosphonium salt $\mathbf{5H^{+},X^{-}}$ (X=Br or I) can be precipitated from the reaction mixture by addition of ether and easily eliminated by simple filtration. In all of the reactions mentioned above, no trace of adducts resulting from nucleophilic behavior of **5** was observed. Moreover, supported ylide **6** could be a valuable intermediate not only for solid-phase synthesis[23] but also for combinatorial chemistry.[24]

Experimental

General

Chemicals were purchased from Aldrich Chemical Company. Solvents for extraction and chromatography were technical grade. All solvents used in reactions were freshly distilled from appropriate drying agents before use. All other reagents were recrystallized or distilled as necessary. All reactions were performed under an atmosphere of dry nitrogen. Analytical TLC was performed with Merck silica gel 60 F_{254} plates. Visualization was accomplished by UV light and $KMnO_4$ solution. Flash chromatography was carried out using Merck silica gel 60 (230–400 mesh ASTM). Melting points were determined with an Electrothermal IA9100 Digital Melting Point Apparatus and are uncorrected. ^{1}H (300 MHz), ^{13}C (75 MHz) and ^{31}P NMR (120 MHz) spectra were recorded on a Varian VXR 300 MHz spectrometer using $CDCl_3$ solutions with TMS as an internal reference for ^{1}H and ^{13}C NMR spectra and phosphoric acid (85%) for ^{31}P NMR spectra. Coupling

constants (J) are reported in Hertz. Low-resolution mass spectra (MS) were obtained at 50–70 eV by electron impact (EIMS) on a Hewlett Packard 5971 spectrometer. Data are reported in the form m/z (intensity relative to base=100). Infrared spectra (IR) were recorded on a Nicolet IRFT Magna 550 spectrometer for neat oils. Peaks are reported in cm^{-1}. Elemental analyses were performed in a LECO CHNS-932 apparatus. Ylides **5** and **6**,[5] β-amino **7**[7] and β-enanimo phosphine oxide **11**,[14] amino acid derivatives **9**[11] and **13**[17] and β-hydrazono phosphonate **17a**[15] and phosphine oxide **17b**[15] were synthesized according to literature procedures.

General procedure for the preparation of 2-(*N*-methyl-*N*-*p*-tolylamino)butyldiphenylphosphine oxide (8). To a freshly prepared −78°C solution of ylide **5** (656 mg, 3.2 mmol) in THF (20 mL) was added a solution of β-aminophosphine oxide **7** (545 mg, 1.5 mmol) in THF (10 mL). The mixture was allowed to stir at this temperature for 1 h and a solution of methyl iodide (112 μL, 1.8 mmol) in THF (5 mL) was then added at the same temperature. After the mixture was allowed to warm to room temperature, the reaction mixture was stirred and heated at reflux for 24 h. The solution was separated from the phosphonium salts by addition of ether (50 mL) and filtration. After evaporation of the solvent, the residue was purified by flash chromatography eluting with 1:1 AcOEt/hexanes to yield compound **8** (492 mg, 87%) as a pale yellow oil; ^{1}H NMR (300 MHz) 7.67–7.24 (m, 10 H, Ph), 6.85 and 6.48 (A2B2 system, $^3J_{HH}$=8.5 Hz, 4 H, *p*-tolyl), 4.11 (m, 1 H, CH), 2.39 (m, 2 H, CH_2P), 2.38 (s, 3 H, CH_3), 2.14 (s, 3 H, CH_3), 1.77 (m, 1 H, CH_2), 1.49 (m, 1 H, CH_2), 0.71 (t, $^3J_{HH}$=7.3 Hz, 3 H, CH_3); ^{13}C NMR (75 MHz,) 148.0–112.1 (Ph), 55.1 (CH_3N), 50.0 (CH), 32.2 (d, $^1J_{PC}$=69.5 Hz, CH_2P), 26.6 (CH_2), 19.6 (CH_3), 10.7 (CH_3); ^{31}P NMR (120 MHz) 31.7; IR (NaCl) 1162 cm^{-1} (P=O); EIMS m/z 377 (M^+, 26), 348 [(M^+−Et), 66], 201 (Ph_2PO^+, 100). Anal. Calcd for $C_{24}H_{28}NOP$ (377.47): C, 76.37; H, 7.48; N, 3.71. Found: C, 76.07; H, 7.50; N, 3.72.

General procedure for the synthesis of ethyl *N*-allyl-*N*-*t*-butoxycarbonylglycinate (10). To a freshly prepared −78°C solution of ylide **5** (656 mg, 3.2 mmol) in THF (20 mL) was added a solution of *N*-Boc glycine ester **9** (305 mg, 1.5 mmol) in THF (10 mL). The mixture was allowed to stir at this temperature for 1 h and a solution of allyl bromide (130 μL, 1.5 mmol) in THF (5 mL) was then added at the same temperature. After the mixture was allowed to warm to room temperature, the reaction mixture was stirred and heated at reflux for 48 h. The solution was separated from the phosphonium salts by addition of ether (50 mL) and filtration. After evaporation of the solvent, the residue was purified by flash chromatography eluting with 1:4 AcOEt/hexanes to yield compound **10** (222 mg, 61%) as a pale yellow oil; ^{1}H NMR (300 MHz) 5.71 (m, 1 H, CH), 5.13 (m, 2 H, CH_2=), 4.23 (m, 2 H, OCH_2), 3.79 (m, 2 H, CH_2), 3.21 (s, 2 H, CH_2N), 1.38 (s, 9 H, *t*Bu), 1.24 (t, $^3J_{HH}$=7.0 Hz, 3 H, CH_3); ^{13}C NMR (75 MHz) 169.8 (C=O), 167.7 (C=O), 131.6 (CH), 117.8 (CH_2=), 76.9 (C), 60.8 (OCH_2), 55.6 (CH_2), 46.0 (CH_2), 28.2 (3 CH_3), 14.0 (CH_3); IR (NaCl) 1750 cm^{-1} (C=O), 1721 cm^{-1} (C=O); EIMS m/z 142 [(M^+−Boc), 17], 57 (t-Bu^+, 100). Anal. Calcd for $C_{12}H_{21}NO_4$ (243.30): C, 59.24; H, 8.70; N, 5.76. Found: C, 59.42; H, 8.67; N, 5.73.

General procedure for the preparation of *Z*- and *E*-2-(*N*-*t*-butylamino)-1-methylprop-1-enylphosphine oxide (12). To a freshly prepared −78°C solution of ylide **5** (656 mg, 3.2 mmol) in THF (20 mL) was added a solution of β-enaminophosphine oxide **11** (470 mg, 1.5 mmol) in THF (10 mL). The mixture was allowed to stir at this temperature for 1 h and a solution of methyl iodide (112 μL, 1.8 mmol) in THF (5 mL) was then added at the same temperature. After the mixture was allowed to warm to room temperature, the reaction mixture was stirred and heated at reflux for 48 h. The solution was separated from the phosphonium salts by addition of ether (50 mL) and filtration. After evaporation of the solvent, the residue was purified by flash chromatography eluting with 1:2 AcOEt/hexanes to yield compound **12** (280 mg, 57%) as a pale yellow oil; ^{1}H NMR (300 MHz) 7.86–7.45 (m, 10 H, Ph), 2.23 (d, $^3J_{PH}$=13.0 Hz, 3 H, CH_3), 2.01 (s, 3 H, CH_3), 1.52 (s, 9 H, *t*-Bu); ^{13}C NMR (75 MHz) 173.2 (C–N), 133.2–127.3 (Ph), 84.2 (d, $^1J_{PC}$=121.4 Hz, C–P), 72.1 (C), 34.0 (d, $^2J_{PC}$=12.0 Hz, CH_3), 28.1 (3 CH_3), 21.3 (d, $^3J_{PC}$=12.1 Hz, *Z*-CH_3), 13.9 (d, $^3J_{PC}$=3.0 Hz, *E*-CH_3); ^{31}P NMR (120 MHz) 39.5 and 36.3; IR (NaCl) 3267 cm^{-1} (NH), 1567 cm^{-1} (C–N), 1170 cm^{-1} (P=O); EIMS m/z 327 (M^+, 27), 312 [(M^+−Me), 64], 201 (Ph_2PO^+, 100). Anal. Calcd for $C_{20}H_{26}NOP$: C, 73.37; H, 8.00; N, 4.28. Found: C, 73.13; H, 8.03; N, 4.26.

General procedure for the preparation of ethyl *N*-(diphenylmethylene)alaninate (14a). *Procedure A:* to a freshly prepared −78°C solution of ylide **5** (461 mg, 2.25 mmol) in THF (15 mL) was added a solution of α-iminoester **13** (534 mg, 2 mmol) in THF (10 mL). The mixture was allowed to stir at this temperature for 1 h and a solution of methyl iodide (137 μL, 2.2 mmol) in THF (2 mL) was then added at the same temperature. After the mixture was allowed to warm to room temperature, the reaction mixture was stirred and heated at reflux for 12 h. The solution was separated from the phosphonium salts by addition of ether (50 mL) and filtration. After evaporation of the solvent, the residue was purified by flash chromatography eluting with 1:6 AcOEt/hexanes to yield compound **14a** (450 mg, 80%) as a pale yellow oil. *Procedure B:* to a freshly prepared 0°C suspension of solid-supported ylide **6** (2.25 g) in THF (20 mL) was added a solution of α-iminoester **13** (534 mg, 2 mmol) in THF (8 mL). The mixture was allowed to stir at this temperature for 1 h and a solution of methyl iodide (137 μL, 2.2 mmol) in THF (2 mL) was then added at the same temperature. After the mixture was allowed to warm to room temperature, the reaction mixture was stirred for 5 h. Filtration and evaporation of the solvent under vacuum led to compound **14a** (472 mg, 84%) as a pale yellow oil. The product obtained had spectroscopic/analytical/physical properties in full agreement with the literature data.[17]

Synthesis of ethyl *N*-(diphenylmethylene)-2-allylglycinate (14b). To a freshly prepared −78°C solution of ylide **5** (461 mg, 2.25 mmol) in THF (15 mL) was added a solution of α-iminoester **13** (534 mg, 2 mmol) in THF (10 mL). The mixture was allowed to stir at this temperature for 1 h

and a solution of allyl bromide (173 μL, 2 mmol) in THF (5 mL) was then added at the same temperature. After the mixture was allowed to warm to room temperature, the reaction mixture was stirred and heated at reflux for 48 h. The solution was separated from the phosphonium salts by addition of ether (50 mL) and filtration. After evaporation of the solvent, the residue was purified by flash chromatography eluting with 1:6 AcOEt/hexanes to yield compound **14b** (411 mg, 67%) as a pale yellow oil; ^{1}H NMR (300 MHz) 7.81–7.10 (m, 10 H, Ph), 5.62 (m, 1 H, CH), 5.07 (m, 2 H, CH_2), 4.10 (m, 2 H, OCH_2), 3.21 (m, 1 H, CH), 2.60 (m, 2 H, CH_2), 1.18 (t, $^3J_{HH}$=7.0 Hz, 3 H, CH_3); ^{13}C NMR (75 MHz) 196.6 (C=O), 137.6 (CH), 134.3–127.1 (Ph and =C), 117.5 (CH_2), 65.3 (CH), 60.8 (OCH_2), 38.1 (CH_2), 14.2 (CH_3); IR (NaCl) 1739 cm^{-1} (C=O), 1660 cm^{-1} (C=N); EIMS *m/z* 307 (M^+, 23), 266 [(M^+−Allyl), 100]. Anal. Calcd for $C_{20}H_{21}NO_2$ (307.39): C, 78.15; H, 6.89; N, 4.56. Found: C, 77.95; H, 6.86; N, 4.57.

General procedure for the preparation of *syn*- and *anti*-2-nitro-1-*p*-tolylpropan-1-ol (16a). To a 0°C solution of *p*-tolualdehyde **15a** (414 μL, 3.51 mmol) in nitroethane (15 mL) was added a freshly prepared solution of ylide **5** (62 mg, 0.3 mmol) in nitroethane (5 mL). After the mixture was allowed to warm to room temperature, the reaction mixture was stirred for 12 h. The solution was separated from the phosphonium salts by addition of ether (50 mL) and filtration. After evaporation of the solvent, the residue was purified by flash chromatography eluting with 1:10 AcOEt/hexanes to yield a mixture of *syn* and *anti* nitroalcohols (2:1 ratio) **16a** (616 mg, 90%) as a pale yellow oil; ^{1}H NMR (300 MHz) 7.26–6.87 (m, 4 H, *syn*- and *anti*-Ph), 5.19 (d, $^3J_{HH}$=4.1 Hz, 1 H, *anti*-CH), 4.87 (d, $^3J_{HH}$=9.2 Hz, 1 H, *syn*-CH), 4.64 (m, 2 H, *syn*- and *anti*-CH), 3.18 (s, 2 H, *syn*- and *anti*-OH), 2.27 (s, 3 H, *syn*-CH_3), 2.26 (s, 3H, *anti*-CH_3), 1.41 (d, $^3J_{HH}$=6.7 Hz, 3 H, *anti*-CH_3), 1.20 (d, $^3J_{HH}$=6.9 Hz, 3 H, *syn*-CH_3); ^{13}C NMR (75 MHz) 138.4, 137.7, 135.9, 135.5, 129.2, 128.9, 126.7, 125.8 (*syn*- and *anti*-Ph), 88.3 (*syn*-CH), 87.4 (*anti*-CH), 75.6 (*syn*-CH), 73.8 (*anti*-CH), 20.8 (CH_3), 16.0 (*syn*-CH_3), 12.4 (*anti*-CH_3); IR (NaCl) 3357 cm^{-1} (OH) 1554 cm^{-1} (NO_2); EIMS *m/z* 195 (M^+, 3), 148 [(M^+−HNO_2), 16], 121 [(M^+−Et−NO_2), 100]. Anal. Calcd for $C_{10}H_{13}NO_3$ (195.22): C, 61.53; H, 6.71; N, 7.17. Found: C, 61.29; H, 6.73; N, 7.19.

General procedure for the synthesis of *syn*- and *anti*-2-nitro-1-(*p*-nitrophenyl)propan-1-ol (16b). To a freshly prepared 0°C suspension of solid-supported ylide **6** (0.2 g) in nitroethane (8 mL) was added a solution of *p*-nitrobenzaldehyde **15b** (308 mg, 2 mmol) in nitroethane (2 mL). The mixture was allowed to stir at 0°C for 30 min. Filtration and evaporation of the solvent under vacuum led to compound **16b** (316 mg, 70%) as a pale yellow oil. The product obtained had spectroscopic/analytical/physical properties in full agreement with the literature data.[25]

General procedure for the preparation of *syn*- and *anti*-*E*-*p*-tolylbuten 3-one *N,N*-dimethylhydrazone (18a). To a freshly prepared −78°C solution of ylide **5** (461 mg, 2.25 mmol) in THF (15 mL) was added a solution of β-hydrazonophosphonate **17a** (472 mg, 2 mmol) in THF (10 mL). The mixture was allowed to stir at this temperature for 1 h and a solution of *p*-tolualdehyde **15a** (236 μL, 2 mmol) in THF (5 mL) was then added at the same temperature. After the mixture was allowed to warm to room temperature, the reaction mixture was stirred and heated at reflux for 48 h. The solution was separated from the phosphonium salts by addition of ether (50 mL) and filtration. After evaporation of the solvent, the residue was purified by flash chromatography eluting with 1:10 Et_2O/hexanes to yield compound **18a** (303 mg, 75%) as a pale yellow oil. The product obtained had spectroscopic/analytical/physical properties in full agreement with the literature data.[15]

Synthesis of *syn*- and *anti*-*E*-*p*-nitrophenylbuten-3-one *N,N*-dimethylhydrazone (18b). *Procedure A:* to a freshly prepared −78°C solution of ylide **5** (461 mg, 2.25 mmol) in THF (15 mL) was added a solution of β-hydrazophosphine oxide **17b** (600 mg, 2 mmol) in THF (10 mL). The mixture was allowed to stir at this temperature for 1 h and a solution of *p*-nitrobenzaldehyde **15b** (308 mg, 2 mmol) in THF (5 mL) was then added at the same temperature. After the mixture was allowed to warm to room temperature, the reaction mixture was stirred and heated at reflux for 36 h. The solution was separated from the phosphonium salts by addition of ether (50 mL) and filtration. After evaporation of the solvent, the residue was purified by flash chromatography eluting with 1:10 Et_2O/hexanes to yield compound **18b** (326 mg, 70%) as a red oil. *Procedure B:* to a freshly prepared 0°C suspension of solid-supported ylide **6** (2.25 g) in THF (20 mL) was added a solution of β-hydrazonophosphine oxide **17b** (600 mg, 2 mmol) in THF (8 mL). The mixture was allowed to stir at this temperature for 1 h and a solution of *p*-nitrobenzaldehyde **15b** (308 mg, 2 mmol) in THF (2 mL) was then added at the same temperature. After the mixture was allowed to warm to room temperature, the reaction mixture was stirred and heated at reflux for 36 h. Filtration and evaporation of the solvent under vacuum led to compound **18b** (303 mg, 65%) as a red oil. The product obtained had spectroscopic/analytical/physical properties in full agreement with the literature data.[15]

Acknowledgements

The present work has been supported by the Dirección General de Enseñanza Superior e Investigación Científica (Madrid DGESIC, PB96-0252) and by the Comunidad de Trabajo de los Pirineos (Departamento de Industria y Educación, Universidades e Investigación del Gobierno Vasco, Vitoria, IT96-1). J. M. de los Santos thanks the Consejería de Educación del Gobierno Vasco for a postdoctoral fellowship.

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