Regio- and Stereoselective Dirhodium(II)-Catalysed Intramolecular C−H Insertion Reactions of α-Diazo-α-(dialkoxyphosphoryl)acetamides and -acetates

Pedro M. P. Gois[a] and Carlos A. M. Afonso*[a]

Keywords: C−H activation / Diazo compounds / Lactams / Phosphonates / Rhodium

α-Diazo-α-(dialkoxyphosphoryl)acetates and -acetamides afforded α-(dialkoxyphosphoryl)lactones and lactams, respectively, in moderate to high yields through dirhodium(II)-catalysed intramolecular carbon–hydrogen insertion reactions. In the case of α-diazo-α-(dialkoxyphosphoryl)acetamides a remarkable preference for the formation of γ-lactam was observed, with stereocontrol in favour of the *trans* diastereomer.

Introduction

The use of dirhodium(II) acetate and related carboxylates as catalysts for the formation of metal carbenes from diazocarbonyl compounds affords a route to a broad spectrum of chemical transformations,[1] one of the most useful of which is the intramolecular carbon−hydrogen (C−H) insertion reaction, and its use in the carboxylic and heterocyclic ring synthesis.[2]

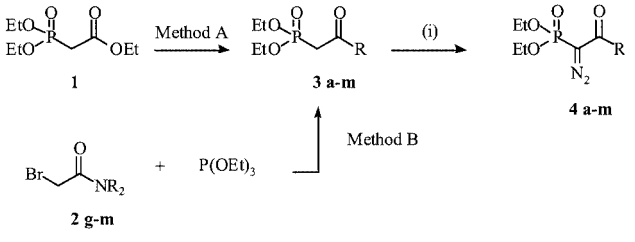
The utility of this approach is directly related to the level of regio- and stereoselectivity of the C−H insertion process. This selectivity not only depends on the type of α-diazocarbonyl and rhodium catalyst utilised, but is also governed by steric, conformational and electronic factors.[3]

In contrast with the vast body of work on diazocarbonyl compounds, rhodium(II)-catalysed cyclization of diazophosphonates has been much less widely studied, but the synthesis of new phosphorus-containing compounds has nevertheless continued to increase in interest, due to their significant chemical and biological profiles.[4] The reported cyclizations of diazophosphonates are mostly associated with intra- and intermolecular O−H and N−H insertion reactions, and with construction of α-(dialkoxyphosphoryl)-cyclopentanones through C−H insertion into alkyl chains of α-diazo-α-(dialkoxyphosphoryl)-*n*-alkyl ketones.[5] Minami et al.[6] showed that construction of α-(dialkoxyphosphoryl)lactams was also possible, though low yields were obtained.

This result prompted us to study the Rh(II)-catalysed cyclization of α-diazo-α-(dialkoxyphosphoryl)acetates and -acetamides in an attempt to understand and extend the scope of the reaction.

Results and Discussion

The desired substrates **4b**−**f** were easily prepared in a two-step procedure from commercially available ethyl (diethoxyphosphoryl)acetate (**1**) by transesterification or aminolysis. Substrates **4g**−**m** were prepared from 2-bromoacetamides **2g**−**m** by Michaelis−Arbusov reactions.[7] Subsequent diazo transfer with *p*-toluenesulfonyl azide yielded the corresponding α-diazo-α-(dialkoxyphosphoryl)acetates and -acetamides **4a**−**m** (Scheme 1).



Scheme 1. Preparation of α-diazo-α-(diethoxyphosphoryl)acetates **4a**−**c** and -acetamides **4d**−**m**; conditions: (Method A): **1**, alcohol or amine (12 equiv., **d** diisopropylamine, **e** diethylamine, **f** di-*n*-butylamine), molecular sieves, toluene (for alcohols) or xylene (for amines), reflux; (Method B): **2**, triethylphosphite (1.2 equiv.), dichloroethane, reflux; (i) **2**, NaH (1.2 equiv.) or DBU (1.1 equiv.), TsN_3 (1.2 equiv.), THF

[a] REQUIMTE/CQFB, Departamento de Química, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, 2829-516 Caparica, Portugal
Fax: (internat.) +351-21-2948550
E-mail: cma@dq.fct.unl.pt

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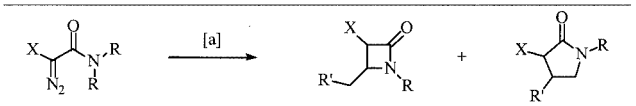
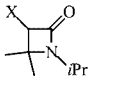
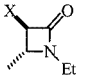
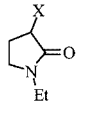
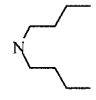
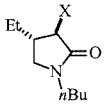
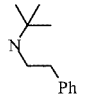
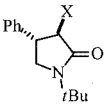
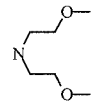
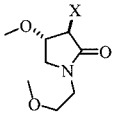
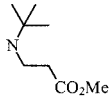
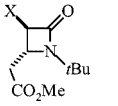
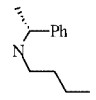
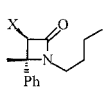
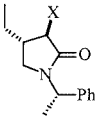
The $[Rh_2(OAc)_4]$-catalysed cyclization of α-diazo-α-diethoxyphosphorylacetamides afforded α-phosphoryllactams **5** and **6** in high yields (Table 1). The formation of the lactams **5d** and **6f** in lower yields (42% and 67%, respectively, probably due to the occurrence of decomposition during flash chromatography on silica gel) had previously been reported.[6] We observed that the decomposition could be minimised by use of basic alumina instead of silica gel, allowing the isolation of the β-lactam **5d** and the γ-lactam **6f** in 88% and 87% yields, respectively (Table 1, Entries 1 and 3).

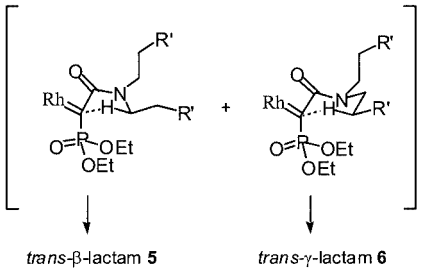
Table 1. $[Rh_2(OAc)_4]$-catalysed cyclization of α-diazo-α-(diethoxyphosphoryl)acetamides **4d−j**



Entry	NR_2	Substrate	β-Lactam **5**	Yield [%][b]	γ-Lactam **6**	Yield [%][b]
1		**4d**		88 [99]	-	-
2		**4e**		18[c] [25]		50 [69]
3		**4f**	-	-		87 [92]
4		**4g**	-	-		81[c] [95]
5		**4h**	-	-		89[c] [93]
6		**4i**		94[c,d] [>99]	-	-
7		**4j**		18[e] [19]		76 [81][c,f]

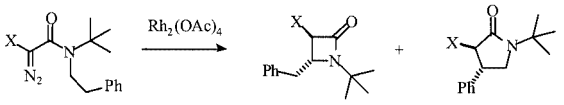
[a] $Rh_2(OAc)_4$ (1 mol%), $C_2H_4Cl_2$, reflux. [b] Isolated yields of lactames after purification by flash chromatography; in bracket is presented the observed conversion by ^{31}P NMR of the crude reaction mixture. [c] Isolated only the *trans* isomer (**5** $J_{3,4}$ = 2.0−2.2 Hz; **6** $J_{3,4}$ = 4.2−4.9 Hz, except for **6h** $J_{3,4}$ = 2.0 Hz). [d] The crude reaction mixture contains the *trans* and *cis* isomers (1.0:2.4). [e] The crude reaction mixture contains the *E* and *Z* isomers (1.0:2.2). [f] Isolated as a 1.2:1 *trans* diastereoisomeric mixture.

With regard to these results, the bulky dialkoxyphosphoryl group appears to induce a remarkable preference for the formation of five-membered rings with stereocontrol in favour of the *trans* diastereoisomer (Table 1, Entries 2 and 3). These observations can be interpreted in terms of transition-state structures in which the substituents are preferentially in the more stable pseudoequatorial positions[8] (conformational effect), as shown in Scheme 2.



Scheme 2

Doyle et al.[9] established that metal electron-withdrawing ligands increase the electrophilicity of the carbene, causing bond formation to take place at a greater distance from the reacting C−H bond (early transition state) with a resulting decrease in selectivity. In the case of α-aceto-α-diazoacetamide analogue of substrate **4g** it was reported that the selectivity was improved in favour of the γ-lactam when a Rh catalyst with a electron-donating ligand was used (late transition state).[10] Likewise, since our α-(dialkoxyphosphoryl) group is less electron-withdrawing than its carbonyl counterpart, it stabilises the electrophilic carbenoid carbon, thereby causing the insertion reaction to proceed through a relatively late transition state, with a resulting increase in selectivity in line with recently reported observations concerning the phenylsulfonyl group (Scheme 3).[3c]



Entry	X	Yield	Ratio	
1[3f]	MeCO	94 %	49 %	51 %
2[3c]	$PhSO_2$	95%	none	only
3	$(EtO)_2PO$	81%	none	only lactam observed

Scheme 3. Comparative results for the $[Rh_2(OAc)_4]$-catalysed cyclization of α-diazoacetamides, between the α-(dialkoxyphosphoryl) and the reported α-acetyl[3f] and α-sulfonyl[3c] groups

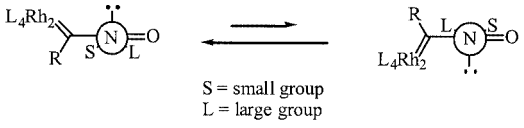
Substituent effects close to the insertion centre are also known to influence the reaction,[11] and a series of α-diazo-α-(dialkoxyphosphoryl)acetamides **4i−j** was prepared in order to explore the electronic effect on regioselectivity (Table 1, Entries 5−6).

Substrate **4h** (Entry 5), as expected, afforded the *trans* γ-lactam in high yield, which is a result of the activation of the electron-donating group and also of the conformational

effect. Substrate **4i** (Entry 6) formed β-lactam as a *cis*/*trans* mixture in nearly quantitative yield, even though C−H insertion into the position α to the carboxylate substituent would have produced a favourable γ-lactam. This result is due to the deactivating effect of the electron-withdrawing carboxylate on C−H insertion into the α-methylene group.[3c]

The unexpected observation that substrate **4i** underwent β-lactam formation as a *cis*/*trans* mixture and not exclusively as *trans* prompted us to study the influence of the N-substituent of the amide group. It should be mentioned that the *cis* isomer epimerises to the more stable *trans* isomer in the presence of basic alumina. A similar observation for α-acetyl- and α-methoxycarbonyl-β-lactams has recently been reported.[3f]

According to Doyle et al.,[11b][11c][12a] the overlap of the nonbonded nitrogen electrons with the carbonyl π-system fixes the amide conformation so that the larger N-substituent is positioned *syn* to the sterically less demanding amide carbonyl group, while the smaller N-substituent is positioned close to the reactive rhodium carbenoid centre, facilitating the C−H insertion (Scheme 4).



Scheme 4

When such conformational bias is absent, the selectivity is lost and a mixture of products arising from insertion onto both N-substituents is obtained. The importance of this conformational effect can be seen in the results from the cyclization of substrate **4j** (Table 1, Entry 7). Cyclization of **4j** in 1,2-dichloroethane furnished 81% of γ-lactam and only 19% of β-lactam, despite β-lactam formation resulting from insertion into a more activated C−H bond.

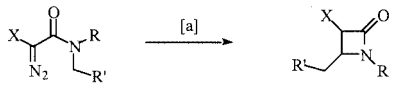
The symmetric acetamides considered in this study underwent γ-lactam formation with high regio- and stereoselectivity, a similar result being obtained when the *tert*-butyl group was introduced into the molecule (substrate **4g**).

In terms of stereoselectivity, strikingly different results were observed when only β-lactam formation was considered, as shown in Table 2.

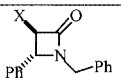
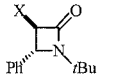
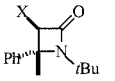
When the benzylic substituent was replaced by the bulky *tert*-butyl group, the conformation was altered. The aromatic group, which in the substrate **4k** had been in a more stable equatorial position (Table 2, Entry 1), was now probably forced into the axial position by the *tert*-butyl group (steric effect) in the substrate **4l** (Entry 2), as shown in Scheme 5.

Figure 1 presents the obtained X-ray structure of the β-lactam **5l**, showing the *trans* geometry of the phenyl and dialkoxyphosphoryl groups as well as the *anti* relationship between the phenyl and *tert*-butyl groups, probably due to steric repulsion.

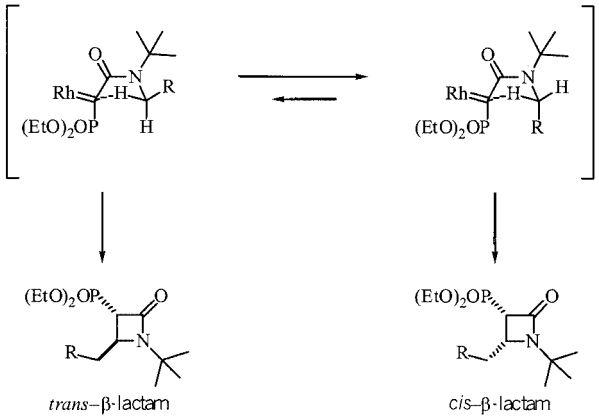
Table 2. $[Rh_2(OAc)_4]$-catalysed cyclization of α-diazo-α-(diethoxyphosphoryl)acetamides **4k−m**



4 5

Entry	$NR(CH_2)R'$	Substrate	β-Lactam **5**	Crude *Cis* [%][b]	Crude *Trans* [%][b]	Yield [%][c]
1		**4k**		5	95	81 *(trans)*
2		**4l**		88	12	89 *(trans)*
3		**4m**		60	40	75 *(E)*

[a] $Rh_2(OAc)_4$ (1 mol%), CH_2Cl_2 or $C_2H_4Cl_2$, reflux. [b] Observed *cis*/*trans* ratio by ^{31}P NMR of crude reaction mixture. [c] Isolated only the corresponding *trans*-β-lactam (**5** $J_{3,4}$ = 2.0−2.4 Hz) due to the occurrence of epimerization during purification by flash chromatography (basic alumina).



Scheme 5

When a methyl group was introduced (substrate **4m**, Table 2, Entry 3), the difference in the sizes of the two groups was not as high as in substrate **4l**, thus yielding a 60:40 mixture of *cis* and *trans* isomers.

The structure of the starting compound **4l** was determined by X-ray analysis (Figure 2).

In this conformation the larger N-substituent is positioned *syn* to the sterically less demanding amide carbonyl group, while the smaller N-substituent is situated close to the diazo centre (and supposedly the carbenoid), as suggested by Doyle et al.[10] (Scheme 5). Moreover, if the new C−C bond was formed with this conformation, between C^1 and C^4, a *trans* β-lactam would have been formed, so the favourable conformation for the *cis* β-lactam formation was due to the conformationally constrained nature of the intermediate metal carbenoid, and was not predefined in the starting α-diazo-α-(dialkoxyphosphoryl)acetamide.

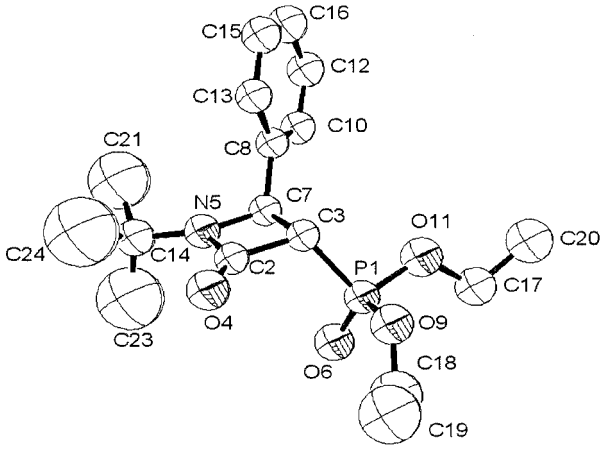


Figure 1. Crystal structure of the β-lactam **5l** (30% probability level); selected bond lengths [Å] and angles [°]: N(1)−C(2) 1.349(2), N(1)−C(5) 1.475(2), N(1)−C(4) 1.480(2), C(2)−O(9) 1.208(2), C(2)−C(3) 1.533(3), C(3)−C(4) 1.558(2), C(3)−P(10) 1.7899(19), C(3)−H(3) 0.98, C(4)−C(41) 1.501(2), C(4)−H(4) 0.98; C(2)−N(1)−C(5) 132.35(16), C(5)−N(1)−C(4) 130.20(15), O(9)−C(2)−N(1) 133.20(19), O(9)−C(2)−C(3) 134.33(18), C(2)−C(3)−P(10) 115.31(13), C(4)−C(3)−P(10) 114.18(12), C(2)−C(3)−H(3) 113.1, C(4)−C(3)−H(3) 113.1, N(1)−C(4)−C(41) 117.47(14), C(41)−C(4)−C(3) 117.67(15), N(1)−C(4)−H(4) 111, C(41)−C(4)−H(4) 111, C(3)−C(4)−H(4) 111

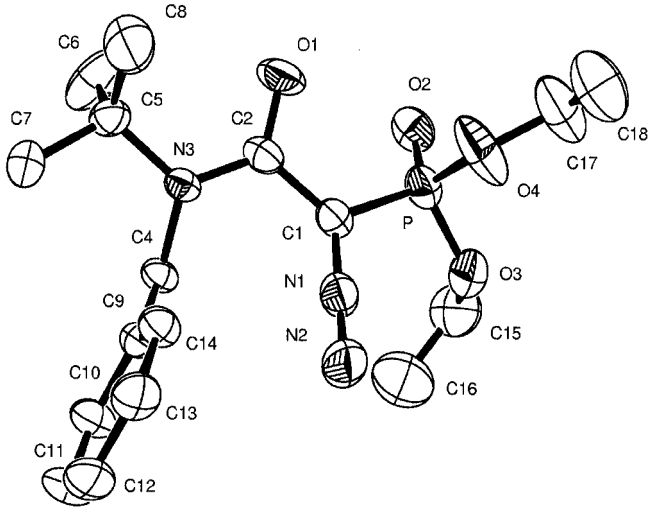
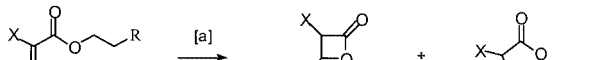


Figure 2. Crystal structure of the diazo **4l**; selected bond lengths [Å] and angles [°]: P−C(1) 1.778(2), O(1)−C(2) 1.225(3), N(1)−N(2) 1.125(3), N(1)−C(1) 1.311(3), C(1)−C(2) 1.488(3), C(2)−N(3) 1.359(3); O(2)−P−C(1) 118.9(3), N(1)−C(1)−P 116.07(17), C(2)−C(1)−P 121.29(15), O(1)−C(2)−N(3) 123.6(2), O(1)−C(2)−C(1) 115.92(19), N(3)−C(2)−C(1) 120.50(18), C(2)−N(3)−C(4) 120.56(17), C(2)−N(3)−C(5) 118.93(17)

In clear contrast with those of the α-diazo-α-(dialkoxyphosphoryl)acetamides, the $[Rh_2(OAc)_4]$-catalysed cyclizations of α-diazo-α-(diethoxyphosphoryl)acetates **4a−c** (Table 3) afforded β- and γ- lactones in moderate yields and with low regio- and stereoselectivities, although β-lactones nevertheless seemed to be the preferred insertion products even when more reactive methine C−H bonds were available (Entry 3).

Table 3. $[Rh_2(OAc)_4]$-catalysed cyclization of α-diazo-α-(diethoxyphosphoryl)acetates **4a−c**



Entry	OR'	Substrate	β-Lactone **7**	Yield [%][b]	γ-Lactone **8**	Yield [%][b]
1		**4a**		30[c]	-	-
2		**4b**		28[d]		32[e]
3		**4c**		30[f]		24

[a] $Rh_2(OAc)_4$ (1 mol%), $C_2H_4Cl_2$, reflux, reaction time: entry 1 (6 h), entry 2 (2.5 h) and entry 3 (2 h). [b] Isolated yields of lactones after purification by flash chromatography. [c] Isolated only the *trans* isomer, assigned by ^1H NMR ($J_{3,4}$ = 4.4 Hz). [d] Isolated as a mixture of *trans* ($J_{3,4}$ = 4.4 Hz) and *cis* ($J_{3,4}$ = 10.3 Hz) isomers, ratio *trans*/*cis* = 1.4:1. [e] Isolated only the *trans* isomer ($J_{3,4}$ = 6.5 Hz). [f] Isolated only the *cis* isomer ($J_{3,4}$ = 10.4 Hz).

Reported C−H insertion reactions of alkylmethyldiazomalonates resulted in the formation of β- and γ- lactones, the selectivity depending both on the substitution pattern of the insertion centres, with a preference for methine C−H insertion, and on the conformational bias of the metallocarbene, which directed the insertion towards β-lactone formation.[13] Our results suggest that when a dialkoxyphosphoryl group is used as an α-substituent, the insertion process is more dependent on the conformational effect than on the insertion centre.

Conclusion

In summary, the dirhodium(II)-catalysed cyclization of α-diazo-α-(dialkoxyphosphoryl)acetamides proved to be a highly regio- and stereocontrolled procedure for the construction of α-(dialkoxyphosphoryl)lactams. Conformational and electronic effects in the γ-lactam formation were studied. The steric effect exerted by the N-substituent of the amide was determinant in the stereoselectivity of the β-lactam formation. Preparation of α-diazo-α-(dialkoxyphosphoryl)lactones was also achieved, but only moderate yields and reduced regio- and stereoselectivities were observed.

Experimental Section

General Remarks: Tetrahydrofuran (THF) and diethyl ether were distilled from over calcium hydride/benzophenone immediately prior to use, while triethylamine, dichloromethane and dichloro-

ethane were freshly distilled from over calcium hydride. Ethyl acetate was distilled from over potassium carbonate. *p*-Toluenesulfonyl azide was prepared from *p*-toluenesulfonyl chloride and sodium azide.[14] Sodium hydride was used as a 55% dispersion in mineral oil. All reactions were performed in oven-dried glassware under argon. Flash chromatography was carried out on silica gel 60 M from MN (ref. 815381) or on aluminium oxide basic from MN (ref. 815010, Brockmann activity 1). Reaction mixtures were analysed by TLC on ALUGRAM® SIL G/UV_{254} from MN (ref. 818133, silica gel 60) and aluminium oxide 60F_{254} neutral plates (type E) from Merck (ref. 5550). Visualisation of TLC spots was effected by use of UV and phosphomolybdic acid solution or I_2. Infrared spectra (IR) spectra were recorded with a Mattson Instruments Satellite FTIR model as thinly dispersed films. High- and low-resolution mass spectra (EI, FAB) were carried out by the mass spectrometry service of the University of Santiago de Compostela (Spain). NMR spectra were recorded with a Bruker AMX 400 with $CDCl_3$ as solvent and $(CH_3)_4Si$ (^1H) as internal standard. ^{31}P chemical shifts are reported in ppm relative to H_3PO_4 (external standard). All coupling constants are expressed in Hz.

CCDC-208988 (**4l**) and CCDC-208987 (**5l**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre,12 Union Road, Cambridge CB2 1EZ,UK; fax: (+44)1223-336-033; or E-mail: deposit@ccdc.cam.ac.uk).

Preparation of Starting Amines and α-Bromoacetamides 2

(*R*)-(+)-α-Bromoacetyl-*N*-butyl-*N*-(α-phenylethyl)amide (2j): Butyraldehyde (2.60 g, 36.00 mmol) was added to a solution of (*R*)-(+)-α-phenylethylamine (3.00 g, 25.00 mmol) in anhydrous CH_2Cl_2 (120 mL) with molecular sieves (4 Å, 30.00 g). After 3 h 30 min stirring at room temperature, the mixture was filtered and concentrated under reduced pressure. Diethyl ether (90 mL) and $LiAlH_4$ (1.90 g, 50.00 mmol) were added to the residue, and the mixture was stirred overnight at room temperature. H_2O (2 mL) was added and the white solid formed was filtered and washed with diethyl ether. The organic layers were concentrated under reduced pressure, and the residue was distilled at 40 °C/0.02 Torr, yielding the (*R*)-(+)-*N*-butyl-*N*-(α-phenylethyl)amine (3.11 g, 70%) as a colourless liquid.

α-Bromoacetyl bromide (3.11 g, 15.40 mmol) was slowly added at 0 °C to a stirred solution of (*R*)-(+)-*N*-butyl-*N*-(α-phenylethyl)amine (2.50 g, 14.00 mmol) and anhydrous triethylamine (2.34 mL, 16.8 mmol) in anhydrous CH_2Cl_2 (28 mL). The mixture was briefly stirred at 0 °C and then at room temperature for 1 h. The reaction mixture was washed with 5% HCl (20 mL) and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with saturated $NaHCO_3$ solution, followed by brine, and then dried with Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (SiO_2, EtOAc/hexanes, 0.5:9.5), yielding the α-bromoacetamide (**2j**, 2.42 g, 58%) as a viscous, yellow oil, R_f = 0.20 (EtOAc/hexanes, 0.5:9.5). IR (film): $\tilde{\nu}_{max}$ = 2961, 1639, 1447 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.76−0.81 (m, 3 H, $NCH_2CH_2CH_2CH_3$), 1.10−1.17 (overlapped signals, m, $NCH_2CH_2CH_2CH_3$ and $NCH_2CH_2CH_2CH_3$), 1.36−1.49 (overlapped signals, m, $NCH_2CH_2CH_2CH_3$), 1.52, 1.67 [d, *J* = 6.8 Hz, 1 H, rotamers 1:1.25, $NCH(CH_3)Ar$], 2.87−3.25 (m, 2 H, $NCH_2CH_2CH_2CH_3$), 3.88−3.99 (m, 2 H, $BrCH_2CO$), 5.12, 5.89 [q, *J* = 6.8 Hz, 1 H, rotamers 1:1.25, $NCH(CH_3)Ar$], 7.26−7.37 [$NCH(CH_3)Ar$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.42, 13.58 ($NCH_2CH_2CH_2CH_3$), 16.51, 18.31 [$NCH(CH_3)Ar$], 20.19, 20.32 ($NCH_2CH_2CH_2CH_3$), 26.88 ($BrCH_2CO$), 30.36, 33.36 ($NCH_2CH_2CH_2CH_3$), 43.58, 44.36 ($NCH_2CH_2CH_2CH_3$), 51.92, 44.36 [$NCH(CH_3)Ar$], 126.70, 127.46, 127.75, 128.39, 128.65, 139.80 (q), 140.21 (q), 166.48, 166.84 (C=O) ppm.

α-Bromoacetyl-*N*-(*tert*-butyl)-*N*-(α-phenylethyl)amide (2m): (1-Bromoethyl)benzene (1.36 g, 7.33 mmol) in DMF (2.9 mL) was added at room temperature during a 20 min period to a solution of *tert*-butylamine (1.16 g, 11.00 mmol), sodium carbonate (0.77 g, 7.26 mmol), and sodium iodine (0.09 g) in freshly distilled dimethylformamide (DMF, 14.7 mL). The reaction mixture was heated to 65 °C, maintained at that temperature, with constant stirring, for 4 h, and then left overnight at room temperature. After addition of water (15 mL), the reaction mixture was extracted three times with CH_2Cl_2 (15 mL) and washed with brine. The combined organic layers were then dried with anhydrous $MgSO_4$, and the solvent was removed under reduced pressure. The residue was distilled at 87 °C/1 Torr, yielding the *N*-(*tert*-butyl)-*N*-(α-phenylethyl)amine (0.74 g, 57%) as a colourless liquid.

α-Bromoacetyl bromide (2.50 g, 12.40 mmol) was slowly added at 0 °C to a stirred solution of *N*-(*tert*-butyl)-*N*-(α-phenylethyl)amine (2.00 g, 11.30 mmol) and anhydrous triethylamine (1.89 mL, 13.6 mmol) in anhydrous CH_2Cl_2 (25 mL). The mixture was briefly stirred at 0 °C and then at room temperature for 1 h. The reaction mixture was washed with HCl (5%, 20 mL) and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with saturated $NaHCO_3$ solution, followed by brine, and then dried with Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (SiO_2, EtOAc/hexanes, 0.5:9.5), yielding the α-bromoacetamide (**2m**, 2.62 g, 78%) as a viscous, yellow oil, R_f = 0.35 (EtOAc/hexanes, 1:4). IR (film): $\tilde{\nu}_{max}$ = 2975, 1649, 1192 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.52 [s, 9 H, $NC(CH_3)_3$], 1.78 (d, *J* = 8.0 Hz, 3 H, $NCH(CH_3)Ar$], 3.56 (d, *J* = 12.0 Hz, 2 H, $BrCH_2CO$), 5.10 (q, *J* = 8.0 Hz, 1 H, $NCH(CH_3)Ar$], 7.23−7.39 [m, 5 H, $NCH(CH_3)Ar$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 20.72 [$NCH(CH_3)Ar$], 29.09 [$NC(CH_3)_3$], 31.22 ($BrCH_2CO$), 53.07 [$NCH(CH_3)Ar$], 59.57 [$NC(CH_3)_3$], 125.68, 127.04, 129.00, 142.97 (q), 168.73 (C=O) ppm.

α-Bromo-*N*-(*tert*-butyl)-*N*-(4-methoxy-3-oxobutyl)acetamide (2i): α-Bromoacetyl bromide (2.82 g, 14.00 mmol) was slowly added at 0 °C to a stirred solution of methyl 3-(*N*-*tert*-butylamino)propanoate[14] (2.00 g, 12.60 mmol) and anhydrous triethylamine (2.1 mL, 15.0 mmol) in anhydrous CH_2Cl_2 (26 mL). The mixture was briefly stirred at 0 °C and then at room temperature for 1 h. The reaction mixture was washed with HCl (5%, 20 mL) and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with saturated $NaHCO_3$ solution, followed by brine, and then dried with Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (SiO_2, EtOAc/hexanes, 3:7), yielding the α-bromoacetamide (**2i**, 0.82 g, 87%) as a viscous, yellow oil, R_f = 0.50 (EtOAc/hexanes, 3:7). IR (film): $\tilde{\nu}_{max}$ = 2981, 1737, 1651, 1266 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.37 [s, 9 H, $NC(CH_3)_3$], 2.56−2.60 (m, 2 H, $NCH_2CH_2CO_2CH_3$), 3.62−3.65 (m, 5 H, $NCH_2CH_2CO_2CH_3$ and $NCH_2CH_2CO_2CH_3$), 3.84 (s, 3 H, $BrCH_2CO$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 28.25 [$NC(CH_3)_3$], 29.57 ($BrCH_2CO$), 36.17 ($NCH_2CH_2CO_2CH_3$), 41.41 ($NCH_2CH_2CO_2CH_3$), 51.75 ($NCH_2CH_2CO_2CH_3$), 57.71 [$NC(CH_3)_3$], 167.15 (*C*ON−), 170.94 (*C*OOCH$_3$) ppm.

General Procedure for the Synthesis of α-(Diethoxyphosphoryl)acetates 3b−c: A mixture of ethyl (diethoxyphosphoryl)acetate

(1.00 mmol), alcohol (12.00 mmol) and powdered molecular sieves (4 Å) in toluene (7 mL) was heated at reflux under argon. The reaction mixture was stirred at this temperature until all transesterification was achieved (1−2 days, confirmed by ^{31}P NMR). The mixture was filtered and concentrated under reduced pressure. The residue was distilled, yielding the desired phosphonates.

Propyl α-(Diethoxyphosphoryl)acetate (3b): This compound was prepared by the General Procedure, with the use of ethyl (diethoxyphosphoryl)acetate (3.00 g, 13.40 mmol). The reaction mixture was heated at reflux for 1 day and after distillation at 93 °C/0.01 Torr the desired phosphate (**3b**, 2.63 g, 82%) was obtained as a colourless oil, R_f = 0.27 (EtOAc/hexanes, 1:1). IR (film): $\tilde{\nu}_{max}$ = 1732, 1265, 1054 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.84−0.86 (m, J = 7.2 Hz, 3 H, $OCH_2CH_2CH_3$), 1.35 (t, J = 6.4 Hz, 6 H, OCH_2CH_3), 1.66−1.71 (m, 2 H, $OCH_2CH_2CH_3$), 2.97 (d, $J_{H\text{-}P}$ = 21.6 Hz, 2 H, $POCH_2CO$), 4.10−4.20 (overlapped signals, 6 H, m, $OCH_2CH_2CH_3$ and OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 10.04 ($OCH_2CH_2CH_3$), 16.06 (OCH_2CH_3), 21.64 ($OCH_2CH_2CH_3$), 33.09 (d, $J_{C,P}$ = 134.0, $POCH_2CO$), 62.39 (OCH_2CH_3), 66.88 ($OCH_2CH_2CH_3$), 165.63 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 20.31 ppm. MS (EI): m/z = 239, 211, 19, 179, 123. HMRS (EI): m/z calcd. $[M]^+$ 238.097012, found $[M]^+$ 238.097167.

Isobutyl α-(Diethoxyphosphoryl)acetate (3c): This compound was prepared by the General Procedure with use of ethyl (diethoxyphosphoryl)acetate (5.00 g, 22.30 mmol). The reaction mixture was heated at reflux for 2 days and after distillation at 85 °C/0.01 Torr, the desired phosphonate (**3c**, 2.90 g, 52%) was obtained as a colourless oil, R_f = 0.48 (EtOAc/hexanes, 4:1). IR (film): $\tilde{\nu}_{max}$ = 1731, 1272, 1025 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.95 [d, J = 6.4 Hz, 6 H, $OCH_2CH(CH_3)_2$], 1.35 (t, J = 7.2 Hz, 6 H, OCH_2CH_3), 1.91−2.00 [m, J = 6.8 Hz, 6.4 Hz, 1 H, $OCH_2CH(CH_3)_2$], 2.98 (d, $J_{H\text{-}P}$ = 21.6 Hz, 2 H, $POCH_2CO$), 3.93 [d, J = 6.8 Hz, 2 H, $OCH_2CH(CH_3)_2$], 4.14−4.21 (m, J = 7.2 Hz, 4 H, OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.16 (OCH_2CH_3), 18.83 [$OCH_2CH(CH_3)_2$], 27.53 [$OCH_2CH(CH_3)_2$], 34.17 (d, $J_{C,P}$ = 134.0, $POCH_2CO$), 62.46 (OCH_2CH_3), 71.47 [$OCH_2CH(CH_3)_2$], 165.74 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 20.44 ppm. MS (EI): m/z = 253, 197, 179, 151, 123, 57. HMRS (EI): m/z calcd. $[M + H]^+$ 253.120487, found $[M + H]^+$ 253.120246.

General Procedure for the Synthesis of α-(Diethoxyphosphoryl)acetamides 3d−m. Method A: A mixture of ethyl (diethoxyphosphoryl)-acetate (1.00 mmol), amine (12.00 mmol) and powdered molecular sieves (4 Å) in xylene (7 mL) was heated at reflux under argon. The reaction mixture was stirred at this temperature until total condensation was achieved (confirmed by ^{31}P NMR). The mixture was filtered and concentrated under reduced pressure. The residue was distilled or chromatographed, yielding the desired phosphonates.

Method B: Triethyl phosphite (6.00 mmol) was added under argon atmosphere to a stirring solution of the appropriate α-bromoacetamide (5.00 mmol) in anhydrous dichloroethane (2 mL). The mixture was heated at reflux until all α-bromoacetamide had been consumed. The volatile compounds were then evaporated. The residue was purified by distillation under reduced pressure or by flash chromatography.

α-(Diethoxyphosphoryl)-*N*,*N*-(diisopropyl)acetamide[6] (3d): This compound was prepared by Method A with the use of ethyl (diethoxyphosphoryl)acetate (2.0 g, 8.9 mmol). The reaction mixture was heated at reflux for 2 days and after distillation at 93 °C/0.03 Torr the desired phosphonate (**3d**, 1.73 g, 70%) was obtained as a yellow oil, R_f = 0.20 (EtOAc/hexanes, 7:3). IR (film): $\tilde{\nu}_{max}$ = 1637, 1265, 1039 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.10 [d, J = 7.0 Hz, 6 H, $NCH(CH_3)_2$], 1.25 (t, J = 7.0 Hz, 6 H, OCH_2CH_3), 1.32 [d, J = 6.6 Hz, 6 H, $NCH(CH_3)_2$], 2.97 (d, $J_{H\text{-}P}$ = 22.0 Hz, 2 H, $POCH_2CO$), 3.39 [m, 2 H, $NCH(CH_3)_2$], 4.04−4.16 (m, J = 7.0 Hz, 4 H, OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.20 (OCH_2CH_3), 20.25, 20.63 [$NCH(CH_3)_2$], 35.32 (d, $J_{C,P}$ = 131.0, $POCH_2CO$), 46.02, 50.25 [$NCH(CH_3)_2$], 62.26 (OCH_2CH_3), 163.17 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 22.30 ppm. MS (EI): m/z = 280, 179, 151, 100, 58. HMRS (EI): m/z calcd. $[M]^+$ 279.159947, found $[M]^+$ 279.160152.

α-(Diethoxyphosphoryl)-*N*,*N*-diethylacetamide (3e):[15] This compound was prepared by Method A with the use of ethyl (diethoxyphosphoryl)acetate (2.0 g, 8.9 mmol). The reaction mixture was heated at reflux for 5 days and after distillation at 110−115 °C/0.4 Torr the desired phosphonate (**3e**, 1.22 g, 56%) was obtained as a yellow oil, R_f = 0.19 (EtOAc/hexanes, 3:2). IR (film): $\tilde{\nu}_{max}$ = 1639, 1265, 1053 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.05 (t, J = 7.0 Hz, 3 H, NCH_2CH_3), 1.12 (t, J = 7.1 Hz, 3 H, NCH_2CH_3), 1.25 (t, J = 6.9 Hz, 6 H, OCH_2CH_3), 2.94 (d, $J_{H\text{-}P}$ = 20.0 Hz, 2 H, $POCH_2CO$), 3.28−3.38 (m, 4 H, NCH_2CH_3), 4.02−4.12 (m, 4 H, OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 12.69 (NCH_2CH_3), 13.98 (NCH_2CH_3), 16.17 (OCH_2CH_3), 33.16 (d, $J_{C,P}$ = 134.0, $POCH_2CO$), 40.30 (NCH_2CH_3), 42.83 (NCH_2CH_3), 62.34 (OCH_2CH_3), 163.77 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 22.15 ppm.

***N*,*N*-Dibutyl-α-(diethoxyphosphoryl)acetamide (3f):**[6] This compound was prepared by Method A with the use of ethyl (diethoxyphosphoryl)acetate (2.0 g, 8.9 mmol). The reaction mixture was heated at reflux for 1 day and after distillation at 160 °C/0.3 Torr the desired phosphonate (**3f**, 1.78 g, 66%) was obtained as a yellow oil, R_f = 0.28 (EtOAc/hexanes, 3:2). IR (film): $\tilde{\nu}_{max}$ = 1642, 1255, 1027 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.83−0.90 (m, J = 7.1 Hz, 6 H, $NCH_2CH_2CH_2CH_3$), 1.20−1.29 (overlapped signals, 10 H, m, $NCH_2CH_2CH_2CH_3$ and OCH_2CH_3), 1.42−1.52 (m, 4 H, $NCH_2CH_2CH_2CH_3$), 2.95 (d, $J_{H\text{-}P}$ = 22.1 Hz, 2 H, $POCH_2CO$), 3.24−3.29 (m, 4 H, $NCH_2CH_2CH_2CH_3$), 4.07−4.16 (m, J = 7.0 Hz, 4 H, OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.93 ($NCH_2CH_2CH_2CH_3$), 16.16 (OCH_2CH_3), 19.94 ($NCH_2CH_2CH_2CH_3$), 29.56, 30.95 ($NCH_2CH_2CH_2CH_3$), 33.21 (d, $J_{C,P}$ = 133.0, $POCH_2CO$), 45.83, 48.50 ($NCH_2CH_2CH_2CH_3$), 62.34 (OCH_2CH_3), 164.16 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 22.21 ppm. MS (EI): m/z = 179, 151, 128, 86, 58. HMRS (EI): m/z calcd. $[M]^+$ 307.1911247, found $[M]^+$ 307.192572.

***N*-(*tert*-Butyl)-α-(diethoxyphosphoryl)-*N*-(phenylethyl)acetamide (3g):** This compound was prepared by Method B with the use of α-bromoacetyl-*N*-(*tert*-butyl)-*N*-(phenylethyl)amide[3c,10] (2.50 g, 8.42 mmol). The reaction mixture was heated at reflux for 4 h, and after flash chromatography (SiO_2, EtOAc/hexanes, 7:3) the desired phosphonate (**3g**, 2.41 g, 81%) was obtained as a brown oil, R_f = 0.33 (EtOAc/hexanes, 7:3). IR (film): $\tilde{\nu}_{max}$ = 1642, 1249, 1029 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.24−1.27 (m, 6 H, OCH_2CH_3), 1.46 [s, 9 H, $NC(CH_3)_3$], 2.78−2.79 (m, 2 H, NCH_2CH_2Ar), 2.91 (d, $J_{H\text{-}P}$ = 21.9 Hz, 2 H, $POCH_2CO$), 3.57−3.59 (m, 2 H, NCH_2CH_2Ar), 4.06−4.13 (m, 4 H, OCH_2CH_3), 7.12−7.26 (m, 5 H, NCH_2CH_2Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.17 (OCH_2CH_3), 28.76 [$NC(CH_3)_3$], 35.08 (d, $J_{C,P}$ = 131.0, $POCH_2CO$), 37.95 (NCH_2CH_2Ar), 47.47 (NCH_2CH_2Ar), 57.73 [$NC(CH_3)_3$], 62.26 (OCH_2CH_3), 126.59, 128.28, 128.63, 137.91 (q), 165.30 (C=O)

ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 22.23 ppm. MS (EI): *m*/*z* = 264, 208, 151, 179, 91. HMRS (EI): *m*/*z* calcd. $[M]^+$ 355.191247, found $[M]^+$ 355.190927.

α-(Diethoxyphosphoryl)-*N*,*N*-bis(2-methoxyethyl)acetamide (3h): α-Bromoacetyl bromide (4.00 g, 19.80 mmol) was slowly added at 0 °C to a stirred solution of bis(2-methoxyethyl)amine (2.40 g, 18.00 mmol) and anhydrous triethylamine (3.0 mL, 21.6 mmol) in anhydrous CH_2Cl_2 (40 mL). The mixture was briefly stirred at 0 °C and then at room temperature for 1 h. The reaction mixture was washed with 5% HCl (35 mL) and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with saturated $NaHCO_3$ solution, followed by brine, and then dried with Na_2SO_4. The solvent was removed under reduced pressure and the residue was distilled at 116 °C/0.3 Torr, yielding the α-bromoacetamide (**2h**, 5.01 g, 98%) as a viscous oil. The α-(diethoxyphosphoryl)-*N*,*N*-bis(2-methoxyethyl)acetamide (**3h**) was prepared by Method B, by use of α-bromoacetyl-*N*,*N*-bis(2-methoxyethyl)amide (**2h**, 2.54 g, 10.00 mmol). The reaction mixture was heated at reflux for 3 h, and after distillation at 165 °C/0.3 Torr the desired phosphonate (**3h**, 2.75 g, 88%) was obtained as a colourless oil, R_f = 0.62 (EtOAc/hexanes, 9:1). IR (film): $\tilde{\nu}_{max}$ = 1639, 1246, 1029 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.28 (t, *J* = 7.1 Hz, 6 H, OCH_2CH_3), 3.15 (d, $J_{H\text{-}P}$ = 21.8 Hz, 2 H, $POCH_2CO$), 3.26 (s, 6 H, $NCH_2CH_2OCH_3$), 3.26−3.51 (overlapped signals, 6 H, m, $NCH_2CH_2OCH_3$ and $NCH_2CH_2OCH_3$), 3.65 (t, 2 H, $NCH_2CH_2OCH_3$), 4.07−4.15 (m, *J* = 7.2 Hz, 4 H, OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.17 (OCH_2CH_3), 33.40 (d, $J_{C,P}$ = 133.0, $POCH_2CO$), 46.57, 49.75 ($NCH_2CH_2OCH_3$), 58.66, 58.93 ($NCH_2CH_2OCH_3$), 62.29 (OCH_2CH_3), 70.57, 70.82 ($NCH_2CH_2OCH_3$), 165.57 (*C*=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 22.49 ppm. MS (EI): *m*/*z* = 266, 179, 120, 88. HMRS (EI): *m*/*z* calcd. $[M + H]^+$ 312.157601, found $[M + H]^+$ 312.158798.

***N*-(*tert*-Butyl)-α-(diethoxyphosphoryl)-*N*-[2-(methoxycarbonyl)-ethyl]acetamide (3i):** This compound was prepared by Method B with the use of methyl 3-(bromoacetyl-*tert*-butylamino)propionate (**2i**, 1.66 g, 5.93 mmol). The reaction mixture was heated at reflux for 4 h, and after flash chromatography (SiO_2, EtOAc/hexanes, 3:7) the desired phosphonate (**3i**, 1.85 g, 92%) was obtained as a brown oil, R_f = 0.24 (EtOAc/hexanes, 3:7). IR (film): $\tilde{\nu}_{max}$ = 1736, 1648, 1285, 1030 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.34 (t, *J* = 7.1 Hz, 6 H, OCH_2CH_3), 1.45 [s, 9 H, $NC(CH_3)_3$], 2.60−2.64 (m, *J* = 7.8 Hz, 2 H, $NCH_2CH_2CO_2CH_3$), 3.09 (d, $J_{H\text{-}P}$ = 22.2 Hz, 2 H, $POCH_2CO$), 3.70 (s, 3 H, $NCH_2CH_2CO_2CH_3$), 3.72−3.78 (m, 2 H, $NCH_2CH_2CO_2CH_3$), 4.13−4.22 (m, *J* = 7.1 Hz, 4 H, OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.23 (OCH_2CH_3), 28.77 [$NC(CH_3)_3$], 35.91 (d, $J_{C,P}$ = 133.0, $POCH_2CO$), 36.17 ($NCH_2CH_2CO_2CH_3$), 41.76 ($NCH_2CH_2CO_2CH_3$), 51.83 ($NCH_2CH_2CO_2CH_3$), 57.90 [$NC(CH_3)_3$], 62.45 (OCH_2CH_3), 165.50 [$CON(CH_3)_3CH_2$), 171.13 ($COOCH_3$) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 22.31 ppm. MS (EI): *m*/*z* = 338, 306, 179, 158, 151. HMRS (EI): *m*/*z* calcd. $[M]^+$ 337. 165426, found $[M]^+$ 337.164989.

(*R*)-(+)-*N*-Butyl-α-(diethoxyphosphoryl)-*N*-(α-phenylethyl)acetamide (3j): This compound was prepared by Method B with the use of (*R*)-(+)-α-bromoacetyl-*N*-butyl-*N*-(α-phenylethyl)amide (**2j**, 2.42 g, 8.10 mmol). The reaction mixture was heated at reflux for 4 h, and after distillation at 180 °C /0.02 Torr the desired phosphonate (**3j**, 2.18 g, 77%) was obtained as a viscous, yellow oil, R_f = 0.15 (EtOAc/hexanes, 1:4). IR (film): $\tilde{\nu}_{max}$ = 1638, 1265, 1028 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.77 (t, *J* = 7.0 Hz, 3 H, $NCH_2CH_2CH_2CH_3$), 1.08−1.19 (overlapped signals, 3 H, m, $NCH_2CH_2CH_2CH_3$ and $NCH_2CH_2CH_2CH_3$), 1.28−1.41 (overlapped signals, 7 H, m, $NCH_2CH_2CH_2CH_3$ and OCH_2CH_3), 1.51, 1.64 (d, *J* = 7.1 Hz, 3 H, rotamers 1:1.45, $NCH(CH_3)Ar$], 2.84−3.32 (m, $J_{H\text{-}P}$ = 22.1, overlapped signals, 4 H, $POCH_2CO$ and $NCH_2CH_2CH_2CH_3$), 4.09−4.22 (m, *J* = 7.2 Hz, 4 H, OCH_2CH_3), 5.27, 5.94 [q, *J* = 7.0 Hz, 1 H, rotamers 1:1.45, $NCH(CH_3)Ar$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.47, 13.60 ($NCH_2CH_2CH_2CH_3$), 16.26 (OCH_2CH_3), 16.83, 18.57, [$NCH(CH_3)Ar$], 20.17, 20.37 ($NCH_2CH_2CH_2CH_3$), 30.77 ($NCH_2CH_2CH_2CH_3$), 33.57, 34.03 (d, $J_{C,P}$ = 139 and $J_{C,P}$ = 132.0, $POCH_2CO$), 43.50, 44.31 ($NCH_2CH_2CH_2CH_3$), 51.50, 56.30 [$NCH(CH_3)Ar$], 62.34 (OCH_2CH_3), 126.75, 127.30, 127.48, 128.28, 128.55, 141.67 (q), 165.04 (*C*=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 21.96, 22.22 ppm. MS (EI): *m*/*z* = 355, 179, 176, 151, 120. HMRS (EI): *m*/*z* calcd. $[M]^+$ 355.191247, found $[M]^+$ 355.191732.

***N*,*N*-Dibenzyl-α-(diethoxyphosphoryl)acetamide (3k):** α-Bromoacetyl bromide (2.24 g, 11.15 mmol) was slowly added at 0 °C to a stirred solution of dibenzylamine (2.00 g, 10.14 mmol) and triethylamine (1.69 mL, 12.17 mmol) in anhydrous CH_2Cl_2 (22 mL). The mixture was briefly stirred at 0 °C and then at room temperature for 1 h. The reaction mixture was washed with 5% HCl (16 mL) and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with saturated $NaHCO_3$ solution, followed by brine, and then dried with Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (SiO_2, EtOAc/hexanes, 3:7), yielding the *N*,*N*-dibenzyl-α-bromoacetylamide (**2k**, 2.80 g, 87%) as a viscous, yellow oil. The *N*,*N*-dibenzyl-α-(diethoxyphosphoryl)acetamide (**3k**) was prepared by Method B with the use of α-bromoacetamide (**2k**, 2.50 g, 7.88 mmol). The reaction mixture was heated at reflux for 6 h. After flash chromatography (SiO_2, EtOAc/hexanes, 7:3) the desired phosphonate (2.4 g, 81%) was obtained as a yellow oil, R_f = 0.60 (EtOAc/hexanes, 7:3). IR (film): $\tilde{\nu}_{max}$ = 1737, 1265, 1027 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.32 (t, *J* = 7.1 Hz, 6 H, OCH_2CH_3), 3.13 (d, $J_{H\text{-}P}$ = 22.1 Hz, 2 H, $POCH_2CO$), 4.14−4.22 (m, *J* = 7.2 Hz, 4 H, OCH_2CH_3), 4.64 (s, 4 H, NCH_2Ar), 7.16−7.39 (m, 10 H, Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.26 (OCH_2CH_3), 33.61 (d, $J_{C,P}$ = 132.0, $POCH_2CO$), 48.58, 50.88 (NCH_2Ar), 62.60 (OCH_2CH_3), 126.25; 127.31; 127.63; 127.83; 128.50; 128.93; 136.06 (q); 136.70 (q); 165.65 (*C*=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 21.70 ppm. MS (FAB^+): *m*/*z* = 376, 196, 179, 151, 106. HMRS (FAB^+): *m*/*z* calcd. $[M + H]^+$ 376.167772, found 376.166961.

***N*-Benzyl-*N*-(*tert*-butyl)-α-(diethoxyphosphoryl)acetamide (3l):** α-Bromoacetyl bromide (4.06 g, 20.21 mmol) was slowly added at 0 °C to a stirred solution of *N*-benzyl-*N*-*tert*-butylamine (3.00 g, 18.37 mmol) and anhydrous triethylamine (3.07 mL, 22.04 mmol) in anhydrous CH_2Cl_2 (40 mL). The mixture was briefly stirred at 0 °C and then at room temperature for 1 h. The reaction mixture was washed with 5% HCl (35 mL), and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with saturated $NaHCO_3$ solution, followed by brine, and then dried with Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (SiO_2, EtOAc/hexanes, 3:7), yielding the *N*-benzyl-α-bromoacetyl-*N*-(*tert*-butyl)-amide (**2l**, 5.01 g, 98%) as a viscous, yellow oil. The *N*-benzyl-*N*-(*tert*-butyl)-α-(diethoxyphosphoryl)acetamide (**3l**) was prepared by Method B, with use of α-bromoacetamide (**2l**, 3.94 g, 13.91 mmol). The reaction mixture was heated at reflux for 4 h, and after distillation at 160 °C/0.03 Torr the desired phosphonate (**3l**, 3.44 g, 73%) was obtained as a viscous, yellow oil, R_f = 0.26 (EtOAc/hexanes,

3:2). IR (film): $\tilde{\nu}_{max}$ = 1650, 1247, 1054 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.31 (t, *J* = 8.0 Hz, 6 H, OCH_2CH_3), 1.45 (9 H,s, $NC(CH_3)_3$], 2.96 (d, J_{H-P} = 20.0 Hz, 2 H, $POCH_2CO$), 4.11−4.19 (m, *J* = 8.0 Hz, 4 H, OCH_2CH_3), 4.79 (s, 2 H, NCH_2Ar), 7.21−7.38 (m, 5 H, NCH_2Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.33, 16.39 (OCH_2CH_3), 28.57 [$NC(CH_3)_3$], 36.41 (d, $J_{C,P}$ = 132.0, $POCH_2CO$), 49.25 (NCH_2Ar), 58.36 [$NC(CH_3)_3$], 62.46 (OCH_2CH_3), 125.30, 126.90, 128.66, 138.67 (q), 166.05 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 22.20 ppm. MS (EI): *m*/*z* = 284, 179, 151, 148, 106. HMRS (EI): *m*/*z* calcd. $[M]^+$ 341.175597, found $[M]^+$ 341.176400.

***N*-(*tert*-Butyl)-α-(diethoxyphosphoryl)-*N*-(α-phenylethyl)acetamide (3m):** This compound was prepared by Method B, with the use of α-bromoacetyl-*N*-(*tert*-butyl)-*N*-(α-phenylethyl)amide (**2m**, 1.22 g, 4.11 mmol). The reaction mixture was heated at reflux for 8 h, and after flash chromatography (SiO_2, EtOAc/hexanes, 2:3), the desired phosphonate **3m** (1.09 g, 76%) was obtained as a viscous, yellow oil, R_f = 0.12 (EtOAc/hexanes, 2:3). IR (film): $\tilde{\nu}_{max}$ = 1640, 1247, 1030 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.27 (q, *J* = 7.1 Hz, 6 H, OCH_2CH_3), 1.54 [s, 9 H, $NC(CH_3)_3$], 1.81 (d, *J* = 7.1 Hz, 3 H, $NCH(CH_3)Ar$], 4.03−4.12 (m, *J* = 7.1 Hz, 4 H, OCH_2CH_3), 5.13−5.15 [m, 1 H, $NCH(CH_3)Ar$], 7.24−7.39 (m, 5 H, NCH_2Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.31 (OCH_2CH_3), 20.86 [$NCH(CH_3)Ar$], 29.35 [$NC(CH_3)_3$], 53.05 [$NCH(CH_3)Ar$], 59.45 [$NC(CH_3)_3$], 63.15 (OCH_2CH_3), 125.57, 126.75, 128.83, 143.23 (q), 167.31 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 14.24 ppm. HMRS (EI): *m*/*z* = 298, 236, 179, 151, 120; calcd. $[M]^+$ 355.191247, found $[M]^+$ 355.191898.

General Procedure for the Synthesis of Diazo Phosphates 4: A solution of the appropriate phosphonate **3** (1.00 mmol) in THF (1.5 mL) was slowly added at 0 °C to a magnetically stirred mixture of sodium hydride (1.2 equiv.) and *p*-toluenesulfonyl azide (1.2 equiv.) in THF (6.5 mL). The mixture was stirred at this temperature for 1 h and then allowed to reach room temperature. After reaction of all phosphonate (confirmed by TLC), water (5.5 mL) and Et_2O (5.5 mL) were added to the reaction mixture. The aqueous layer was extracted with Et_2O (4 × 5.5 mL). The combined ethereal extracts were dried with Na_2SO_4 and the solvent was evaporated. The residue was chromatographed (SiO_2, EtOAc/hexanes) to yield the diazo compound (**4**) as a yellow oil. The *N*-(*tert*-butyl)-α-diazo-α-(diethoxyphosphoryl)-*N*-[3-(methylpropionate)]acetamide (**4i**) and the *N*-(*tert*-butyl)-α-diazo-α-(diethoxyphosphoryl)-*N*-(phenylethyl)acetamide (**4g**) were prepared with the use of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) instead of sodium hydride.

Propyl α-Diazo-α-(diethoxyphosphoryl)acetate (4b): A solution of propyl α-(diethoxyphosphoryl)acetate (**3b**, 2.44 g, 5.53 mmol) in THF was added at 0 °C to a mixture of sodium hydride and *p*-toluenesulfonyl azide in THF. The mixture was stirred at this temperature for 10 min. Water and Et_2O were added, and the aqueous layer was extracted with Et_2O. After workup, the residue was chromatographed (EtOAc/hexanes, 1:1), yielding the desired diazophosphonate (**4b**, 2.19 g, 81%) as a yellow oil, R_f = 0.45 (EtOAc/hexanes, 1:1). IR (film): $\tilde{\nu}_{max}$ = 2131, 1707, 1282, 1022 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.88 (t, *J* = 7.2 Hz, 3 H, $OCH_2CH_2CH_3$), 1.28 (t, *J* = 7.2 Hz, 6 H, OCH_2CH_3), 1.57−1.66 (m, 2 H, $OCH_2CH_2CH_3$), 4.03−4.19 (overlapped signals, 6 H, m, $OCH_2CH_2CH_3$ and OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 10.02 ($OCH_2CH_2CH_3$), 15.93 (OCH_2CH_3), 21.88 ($OCH_2CH_2CH_3$), 63.45 (OCH_2CH_3), 67.01 ($OCH_2CH_2CH_3$), 163.39 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 10.62 ppm. MS (EI): *m*/*z* = 264, 205, 151, 121, 109. HMRS (EI): *m*/*z* calcd. $[M]^+$ 264.087510, found $[M]^+$ 264.088161.

Isobutyl α-Diazo-α-(diethoxyphosphoryl)acetate (4c): A solution of isobutyl α-(diethoxyphosphoryl)acetate (**3c**, 1.57 g, 5.53 mmol) in THF was added at 0 °C to a mixture of sodium hydride and *p*-toluenesulfonyl azide in THF. The mixture was stirred for 1 h at this temperature and then allowed to reach room temperature over 3 h. Water and Et_2O were added, and the aqueous layer was extracted with Et_2O. After workup, the residue was chromatographed (EtOAc/hexanes, 3:7), yielding the desired diazophosphonate (**4c**, 2.26 g, 77%) as a yellow oil, R_f = 0.27 (EtOAc/hexanes, 3:7). IR (film): $\tilde{\nu}_{max}$ = 2130, 1703, 1.280, 1021 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.95 [d, *J* = 6.4 Hz, 6 H, $OCH_2CH(CH_3)_2$], 1.36 (t, *J* = 6.8 Hz, 6 H, OCH_2CH_3), 1.93−2.04 [m, *J* = 6.8 Hz, 1 H 6.4, $OCH_2CH(CH_3)_2$], 3.99 [d, *J* = 6.8 Hz, 2 H, $OCH_2CH(CH_3)_2$], 4.13−4.26 (m, *J* = 6.8 Hz, 6 H, OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.01 (OCH_2CH_3), 18.81 [$OCH_2CH(CH_3)_2$], 27.75 [$OCH_2CH(CH_3)_2$], 63.56 (OCH_2CH_3), 71.56 [$OCH_2CH(CH_3)_2$], 163.03 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 10.89 ppm. MS (EI): *m*/*z* = 279, 223, 205, 138, 57. HMRS (EI): *m*/*z* calcd. $[M]^+$ 278.103160, found $[M]^+$ 278.104255.

α-Diazo-α-(diethoxyphosphoryl)-*N*,*N*-(diisopropyl)acetamide (4d):[6] A solution of α-(diethoxyphosphoryl)-*N*,*N*-(diisopropyl)acetamide (**3d**, 1.57 g, 5.63 mmol) in THF was added at 0 °C to a mixture of sodium hydride and *p*-toluenesulfonyl azide in THF. The mixture was stirred for 1 h at this temperature and then allowed to reach room temperature overnight. Water and Et_2O were added, and the aqueous layer was extracted with Et_2O. After workup, the residue was chromatographed (EtOAc/hexanes, 2:3), yielding the desired diazophosphonate **4d** (1.70 g, 97%) as a yellow oil, R_f = 0.56 (EtOAc/hexanes, 7:3). IR (film): $\tilde{\nu}_{max}$ = 2095, 1625, 1265, 1022 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.27 [d, *J* = 6.6 Hz, 6 H, $NCH(CH_3)_2$], 1.32 (t, *J* = 7.0 Hz, 6 H, OCH_2CH_3), 3.73 [m, 2 H, $NCH(CH_3)_2$], 4.10−4.23 (m, 4 H, OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.06 (OCH_2CH_3), 20.72 [$NCH(CH_3)_2$], 48.68 [$NCH(CH_3)_2$], 62.22 (OCH_2CH_3), 160.48 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 14.70 ppm. MS (EI): *m*/*z* = 277, 179, 151, 100, 84. HMRS (EI): *m*/*z* calcd. $[M - N_2]^+$ 277.144297, found $[M - N_2]^+$ 277.144614.

α-Diazo-α-(diethoxyphosphoryl)-*N*,*N*-diethylacetamide (4e): A solution of α-(diethoxyphosphoryl)-*N*,*N*-diethylacetamide (**3e**, 1.14 g, 4.53 mmol) in THF was added at 0 °C to a mixture of sodium hydride and *p*-toluenesulfonyl azide in THF. The mixture was stirred at this temperature for 1 h and then allowed to reach room temperature overnight. Water and Et_2O were added, and the aqueous layer was extracted with Et_2O. After workup, the residue was chromatographed (EtOAc/hexanes, 2:3), yielding the desired diazophosphonate (**4e**, 0.96 g, 56%) as a yellow oil, R_f = 0.41 (EtOAc/hexanes, 2:3). IR (film): $\tilde{\nu}_{max}$ = 2098, 1615, 1277, 1023 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.14 (t, *J* = 7.0 Hz, 6 H, NCH_2CH_3), 1.32 (t, *J* = 7.0 Hz, 6 H, OCH_2CH_3), 3.36 (q, *J* = 7.0 Hz, 4 H, NCH_2CH_3), 4.13−4.22 (m, *J* = 7.1 Hz, 4 H, OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.12 (NCH_2CH_3), 16.02 (OCH_2CH_3), 41.72 (NCH_2CH_3), 63.42 (OCH_2CH_3), 161.65 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 13.94 ppm. MS (EI): *m*/*z* = 249, 179, 151, 123, 72. HMRS (EI): *m*/*z* calcd. $[M - N_2]^+$ 249.112997, found $[M - N_2]^+$ 249.112027.

***N*,*N*-Dibutyl-α-diazo-α-(diethoxyphosphoryl)acetamide (4f):**[6] A solution of *N*,*N*-di(butyl)-α-diazo-α-(diethoxyphosphoryl)acetam-

ide (**3f**, 1.70 g, 5.53 mmol) in THF was added at 0 °C to a mixture of sodium hydride and *p*-toluenesulfonyl azide in THF. The mixture was stirred for 1 h at this temperature and then allowed to reach room temperature overnight. Water and Et_2O were added, and the aqueous layer was extracted with Et_2O. After workup, the residue was chromatographed (EtOAc/hexanes, 1:1), yielding the desired diazophosphonate (**4f**, 1.52 g, 83%) as a yellow oil, R_f = 0.62 (EtOAc/hexanes, 3:2). IR (film): $\tilde{\nu}_{max}$ = 2097, 1620, 1255, 1022 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.86 (t, *J* = 7.3 Hz, 6 H, $NCH_2CH_2CH_2CH_3$), 1.20−1.31 (overlapped signals, 10 H, m, $NCH_2CH_2CH_2CH_3$ and OCH_2CH_3), 1.44−1.52 (m, 4 H, $NCH_2CH_2CH_2CH_3$), 3.25 (t, *J* = 7.6 Hz, 4 H, $NCH_2CH_2CH_2CH_3$), 4.09−4.16 (m, *J* = 7.2 Hz, 4 H, OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.70 ($NCH_2CH_2CH_2CH_3$), 16.07 (OCH_2CH_3), 20.00 ($NCH_2CH_2CH_2CH_3$), 30.00 ($NCH_2CH_2CH_2CH_3$), 47.36 ($NCH_2CH_2CH_2CH_3$), 63.46 (OCH_2CH_3), 161.81 (*C*=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 14.23 ppm. MS (EI): *m*/*z* = 305, 276, 263, 179, 128. HMRS (EI): *m*/*z* calcd. $[M - N_2]^+$ 305.175597, found $[M - N_2]^+$ 305.174593.

***N*-(*tert*-Butyl)-α-diazo-α-(diethoxyphosphoryl)-*N*-(phenylethyl)acetamide (4g):** 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU, 0.65 g, 4.30 mmol) was slowly added at room temperature to a solution of *N*-(*tert*-butyl)-*N*-(phenylethyl)-α-(diethoxyphosphoryl)acetamide (**3g**, 1.39 g, 3.91 mmol) and *p*-toluenesulfonyl azide in THF (20 mL). The mixture was stirredat this temperature for 24 h . The reaction mixture was concentrated, water (15 mL) and Et_2O (15 mL) were added, and the aqueous layer was extracted with Et_2O. The organic layers were washed with brine, dried with Na_2SO_4 and concentrated under reduced pressure. The residue was chromatographed on SiO_2 (EtOAc/hexanes, 2:3), yielding the desired diazophosphonate **4g (**1.02 g, 69%) as a yellow oil, R_f = 0.45 (EtOAc/hexanes, 2:3). IR (film): $\tilde{\nu}_{max}$ = 2108, 1629, 1265, 1021 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.29 (t, *J* = 7.1 Hz, 6 H, OCH_2CH_3), 1.48 [9 H,s, $NC(CH_3)_3$], 2.87 (t, *J* = 7.9 Hz, 2 H, NCH_2CH_2Ar), 3.64 (t, *J* = 8.0 Hz, 2 H, NCH_2CH_2Ar), 4.07−4.18 (m, 4 H, OCH_2CH_3), 7.18−7.31 (m, 5 H, NCH_2CH_2Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.00 (OCH_2CH_3), 29.01 [$NC(CH_3)_3$], 37.76 (NCH_2CH_2Ar), 48.61 (NCH_2CH_2Ar), 57.94 [$NC(CH_3)_3$], 63.36 (OCH_2CH_3), 126.64, 128.43, 129.52, 138.22 (q), 163.96 (*C*=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 14.37 ppm. MS (EI): *m*/*z* = 262, 206, 179, 151, 91, 57. HMRS (EI): *m*/*z* calcd. $[M - N_2]^+$ 353.175597, found $[M - N_2]^+$ 353.175128.

α-Diazo-α-(diethoxyphosphoryl)-*N*,*N*-bis(2-methoxyethyl)acetamide (4h): A solution of α-(diethoxyphosphoryl)-*N*,*N*-bis(2-methoxyethyl)acetamide (**3h**, 0.46 g, 1.47 mmol) in THF was added at 0 °C to a mixture of sodium hydride and *p*-toluenesulfonyl azide in THF. The mixture was stirred at this temperature for 45 min. Water and Et_2O were added, and the aqueous layer was extracted with Et_2O. After workup, the residue was chromatographed (EtOAc/hexanes, gradient), yielding the desired diazophosphonate (**4h**, 0.46 g, 93%) as a yellow oil, R_f = 0.47 (EtOAc). IR (film): $\tilde{\nu}_{max}$ = 2101, 1620, 1255, 1020 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) 1.36 (t, *J* = 7.0 Hz, 6 H, OCH_2CH_3), 3.33 (s, 6 H, $NCH_2CH_2OCH_3$), 3.54 (t, *J* = 5.4 Hz, 4 H, $NCH_2CH_2OCH_3$), 3.64 (t, *J* = 5.4 Hz, 4 H, $NCH_2CH_2OCH_3$), 4.16−4.28 (m, 4 H, OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 15.84 (OCH_2CH_3), 47.85 ($NCH_2CH_2OCH_3$), 58.55 ($NCH_2CH_2OCH_3$), 63.25 (OCH_2CH_3), 70.36 ($NCH_2CH_2OCH_3$), 162.30 (*C*=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 14.10 ppm. MS (FAB+): *m*/*z* = 338, 179, 132. HMRS (EI): *m*/*z* calcd. $[M + H]^+$ 338.148099, found $[M + H]^+$ 338.147084.

***N*-(*tert*-Butyl)-α-diazo-α-(diethoxyphosphoryl)-*N*-[2-(methoxycarbonyl)ethyl]acetamide (4i):** 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU, 0.81 g, 5.33 mmol) was slowly added at room temperature to a solution of *N*-(*tert*-butyl)-α-(diethoxyphosphoryl)-*N*-[2-(methoxycarbonyl)ethyl]acetamide (**3i**, 1.64 g, 4.85 mmol) and *p*-toluenesulfonyl azide in THF (22 mL). The mixture was stirred at this temperature for 24 h. The reaction mixture was concentrated, water (20 mL) and Et_2O (20 mL) were added, and the aqueous layer was extracted with Et_2O. The organic layers were washed with brine (50 mL), dried with Na_2SO_4 and concentrated under reduced pressure. The residue was chromatographed on SiO_2 (EtOAc/hexanes, 1:1), yielding the desired diazophosphonate (**4i**, 1.01 g, 58%) as a yellow oil, R_f = 0.24 (EtOAc/hexanes, 3:7). IR (film): $\tilde{\nu}_{max}$ = 2119, 1732, 1633, 1257, 1022 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) 1.36 (t, *J* = 7.0 Hz, 6 H, OCH_2CH_3), 1.42 [s, 9 H, $NC(CH_3)_3$], 2.65 (t, *J* = 7.5 Hz, 2 H, $NCH_2CH_2CO_2CH_3$), 3.69 (s, 3 H, $NCH_2CH_2CO_2CH_3$), 3.78 (t, *J* = 7.5 Hz, 2 H, $NCH_2CH_2CO_2CH_3$), 4.13−4.24 (m, *J* = 7.1 Hz, 4 H, OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.06 (OCH_2CH_3), 28.74 [$NC(CH_3)_3$], 35.72 ($NCH_2CH_2CO_2CH_3$), 42.55 ($NCH_2CH_2CO_2CH_3$), 51.74 ($NCH_2CH_2CO_2CH_3$), 55.88 [$NC(CH_3)_3$], 63.34 (OCH_2CH_3), 164.68 [$CON(CH_3)_3CH_2$], 171.25 ($COOCH_3$) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 13.71 ppm. MS (EI): *m*/*z* = 335, 308, 250, 252, 279, 206. HMRS (EI): *m*/*z* calcd. $[M - N_2]^+$ 335.149776, found $[M - N_2]^+$ 335.149970.

(*R*)-(+)-*N*-Butyl-α-diazo-α-(diethoxyphosphoryl)-*N*-(α-phenylethyl)acetamide (4j): A solution of (*R*)-(+)-*N*-(butyl)-α-(diethoxyphosphoryl)-*N*-(α-phenylethyl)acetamide (**3j**, 1.90 g, 5.35 mmol) in THF was added at 0 °C to a mixture of sodium hydride and *p*-toluenesulfonyl azide in THF. The mixture was stirred at this temperature for 2 h 30 min . Water and Et_2O were added, and the aqueous layer was extracted with Et_2O. After workup, the residue was chromatographed (EtOAc/hexanes, 2:3), yielding the desired diazophosphonate (**4j**, 1.87 g, 92%) as a yellow oil, R_f = 0.45 (EtOAc/hexanes, 2:3). IR (film): $\tilde{\nu}_{max}$ = 2982, 2097, 1621, 1265, 1020 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.75 (t, *J* = 7.0 Hz, 3 H, $NCH_2CH_2CH_2CH_3$), 1.06−1.15 (m, 2 H, $NCH_2CH_2CH_2CH_3$), 1.28−1.31 (overlapped signals, 6 H, m, $NCH_2CH_2CH_2CH_3$ and OCH_2CH_3), 1.56 [d, *J* = 7.1 Hz, 3 H, $NCH(CH_3)Ar$], 2.72−2.80 (m, 1 H, $NCH_2CH_2CH_2CH_3$), 3.14−3.21 (m, 1 H, $NCH_2CH_2CH_2CH_3$), 4.12−4.18 (m, 4 H, OCH_2CH_3), 5.38−5.43 [m, 1 H, $NCH(CH_3)Ar$], 7.18−7.30 [m, 5 H, $NCH(CH_3)Ar$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.48 ($NCH_2CH_2CH_2CH_3$), 15.93 (OCH_2CH_3), 17.07 [$NCH_2(CH_3)Ar$], 20.15 ($NCH_2CH_2CH_2CH_3$), 31.34 ($NCH_2CH_2CH_2CH_3$), 44.11 ($NCH_2CH_2CH_2CH_3$), 53.80 [$NCH_2(CH_3)Ar$], 63.43 (OCH_2CH_3), 126.91, 129.27, 140.19, 140.19(q), 162.40 (*C*=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 13.98 ppm. MS (EI): *m*/*z* = 353, 216, 179, 176, 151. HMRS (EI): *m*/*z* calcd. $[M - N_2]^+$ 353.175597, found $[M - N_2]^+$ 353.175588.

***N*,*N*-Dibenzyl-α-diazo-α-(diethoxyphosphoryl)acetamide (4k):** A solution of *N*,*N*-dibenzyl-α-(diethoxyphosphoryl)acetamide (**3k**, 0.88 g, 2.34 mmol) in THF was added at 0 °C to a mixture of sodium hydride and *p*-toluenesulfonyl azide in THF. The mixture was stirred at this temperature for 1 h and then allowed to reach room temperature overnight. Water and Et_2O were added, and the aqueous layer was extracted with Et_2O. After workup, the residue was chromatographed (EtOAc/hexanes, 3:2), yielding the desired diazophosphonate **4k** (0.85 g, 91%) as a yellow oil, R_f = 0.33 (EtOAc/hexanes, 1:1). IR (film): $\tilde{\nu}_{max}$ = 2100, 1621, 1255, 1020 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.29 (t, *J* = 7.0 Hz, 6

H, OCH_2CH_3), 4.08−4.23 (m, 4 H, OCH_2CH_3), 4.53 (s, 4 H, NCH_2Ar), 7.16−7.35 (m, 10 H, Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.07 (OCH_2CH_3), 49.96 (NCH_2Ar), 63.58 (OCH_2CH_3), 127.57, 127.65, 128.70, 136.03 (q), 163.35 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 13.61 ppm. MS (FAB+): *m*/*z* = 402, 374, 236, 196, 179, 106. HMRS (FAB+): *m*/*z* calcd. $[M + H]^+$ 402.158270, found $[M + H]^+$ 402.159882.

***N*-Benzyl-*N*-(*tert*-butyl)-α-diazo-α-(diethoxyphosphoryl)acetamide (4l):** A solution of *N*-benzyl-*N*-(*tert*-butyl)-α-(diethoxyphosphoryl)-acetamide (**3l**, 2.00 g, 5.86 mmol) in THF was added at 0 °C to a mixture of sodium hydride and *p*-toluenesulfonyl azide in THF. The mixture was stirred at this temperature for 1 h and then at room temperature for 1 h 30 min. Water and Et_2O were added, and the aqueous layer was extracted with Et_2O. After workup, the residue was chromatographed (EtOAc/hexanes, 2:3), yielding the desired diazophosphonate (**4l**, 1.88 g, 87%) as a yellow oil, which crystallized in the fridge after a long time (two weeks) as yellow crystals (mp, 49−50 °C), R_f = 0.33 (EtOAc/hexanes, 2:3). IR (film): $\tilde{\nu}_{max}$ = 2097, 1638, 1265, 1023 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.33 (t, *J* = 8.0 Hz, 6 H, OCH_2CH_3), 1.38 [s, 9 H, $NC(CH_3)_3$], 4.11−4.24 (m, 4 H, OCH_2CH_3), 4.68 (s, 2 H, NCH_2Ar), 7.24−7.36 (m, 5 H, NCH_2Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.08 (OCH_2CH_3), 28.42 [$NC(CH_3)_3$], 50.64 (NCH_2Ar), 58.81 [$NC(CH_3)_3$], 63.36 (OCH_2CH_3), 126.24, 127.22, 128.50, 139.07 (q), 164.57 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 14.24 ppm. MS (EI): *m*/*z* = 339, 326, 179, 162, 91. HMRS (EI): *m*/*z* calcd. $[M - N_2]^+$ 339.159947, found $[M - N_2]^+$ 339.160272.

***N*-(*tert*-Butyl)-α-diazo-α-(diethoxyphosphoryl)-*N*-(α-phenylethyl)-acetamide (4m):** A solution of *N*-(*tert*-butyl)-α-(diethoxyphosphoryl)-*N*-(α-phenylethyl)acetamide (**3m**, 0.85 g, 2.40 mmol) in THF was added at 0 °C to a mixture of sodium hydride and *p*-toluenesulfonyl azide in THF. The mixture was stirred at this temperature for 1 h and then at room temperature for 1 h 30 min. Water and Et_2O were added, and the aqueous layer was extracted with Et_2O. After workup, the residue was chromatographed (EtOAc/hexanes, 3:7), yielding the desired diazophosphonate (**4m**, 0.90 g, 98%) as a yellow oil, R_f = 0.44 (EtOAc/hexanes, 3:7). IR (film): $\tilde{\nu}_{max}$ = 2097, 1632, 1270, 1021 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.25−1.39 [m, overlapped signals, 15 H, $NC(CH_3)_3$ and OCH_2CH_3], 1.80 [d, *J* = 7.2 Hz, 3 H, $NCH(CH_3)Ar$], 4.09−4.21 (m, 4 H, OCH_2CH_3), 5.14−5.15 [m, 1 H, $NCH(CH_3)Ar$], 7.23−7.38 [m, 5 H, $NCH(CH_3)Ar$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.06 (OCH_2CH_3), 20.16 [$NCH(CH_3)Ar$], 29.43 [$NC(CH_3)_3$], 56.15 [$NCH(CH_3)Ar$], 59.58 [$NC(CH_3)_3$], 63.47 (OCH_2CH_3), 126.89, 127.12, 128.61, 141.93 (q), 166.58 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 14.24 ppm. MS (FAB+): *m*/*z* = 326, 278, 222, 179, 120. HMRS (EI): *m*/*z* calcd. $[M + H]^+$ 382.189570, found $[M + H]^+$ 382.189155.

General Procedure for the Rhodium(II)-Catalysed Cyclization of α-(Diethoxyphosphoryl)acetates and -Acetamides: The appropriate diazo compound (**4**, 1 mmol) in $C_2H_4Cl_2$ or CH_2Cl_2 (1.2 mL) was slowly added under argon atmosphere to a magnetically stirred, refluxing suspension of rhodium(II) tetraacetate (1 mol %) in anhydrous $C_2H_4Cl_2$ or CH_2Cl_2 (10 mL). The reaction mixture was heated at reflux until disappearance of the substrate (determined by TLC). The mixture was concentrated under reduced pressure and the residue was purified by flash chromatography (silica or basic alumina with EtOAc/hexanes), yielding the desired compounds.

Cyclization of Ethyl α-Diazo-α-(diethoxyphosphoryl)acetate (4a):[16] Ethyl α-diazo-α-(diethoxyphosphoryl)acetate (**4a**, 0.50 g, 2.00 mmol) in $C_2H_4Cl_2$ was slowly added to a refluxing suspension of rhodium(II) tetraacetate in anhydrous $C_2H_4Cl_2$. After having been heated at reflux for 6 h, the mixture was concentrated and the residue was purified by flash chromatography (SiO_2 EtOAc/hexanes, 3:2), yielding the ***trans*-3-(diethoxyphosphoryl)-4-methyl-β-lactone** (**7a**, 0.13 g, 30%) as a viscous, yellow oil, R_f = 0.47 (EtOAc/hexanes, 7:3). IR (film): $\tilde{\nu}_{max}$ = 1824, 1746, 1257, 1024 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.36−138 (m, 6 H, OCH_2CH_3), 1.65 (d, *J* = 6.0 Hz, 3 H, $CHCH_3$), 3.78 (dd, J_{H-P} = 18.0, *J* = 4.4 Hz, 1 H, POCHCO), 4.20−4.35 (m, 4 H, OCH_2CH_3), 4.82−4.89 (m, 1 H, $CHCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.16 (OCH_2CH_3), 20.20 ($CHCH_3$), 55.35 (d, $J_{C,P}$ = 144.0 Hz, POCHCO), 63.15, 63.24 (OCH_2CH_3), 69.32 ($CHCH_3$), 162.47 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 15.06 ppm. MS (EI): *m*/*z* = 223, 179, 151, 163, 123. HMRS (EI): *m*/*z* calcd. $[M + H]^+$ 223.07537, found $[M + H]^+$ 223.072219.

Cyclization of Propyl α-Diazo-α-(diethoxyphosphoryl)acetate (4b): Propyl α-diazo-α-(diethoxyphosphoryl)acetate (**4b**, 0.50 g, 1.90 mmol) in $C_2H_4Cl_2$ was slowly added to a refluxing suspension of rhodium(II) tetraacetate in anhydrous $C_2H_4Cl_2$. After having been heated at reflux for 2 h 15 min, the mixture was concentrated and the residue was purified by flash chromatography (SiO_2, EtOAc/hexanes, 3:2), yielding the 3-(diethoxyphosphoryl)-4-ethyl-β-lactone (**7b**, 0.13 g, 28%) as a mixture of *trans* and *cis* isomers (*trans*/*cis* 1.4:1) and the *trans*-3-(diethoxyphosphoryl)-4-methyl-γ-lactone (**8b**, 0.14 g, 32%).

3-(Diethoxyphosphoryl)-4-ethyl-β-lactone (7b): 7b was obtained a as viscous, yellow oil, R_f = 0.40 (EtOAc/hexanes, 3:2). IR (film): $\tilde{\nu}_{max}$ = 1828, 1741, 1259, 1027 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.85 (t, *J* = 7.3 Hz, 3 H, $CHCH_2CH_3$, *trans* or *cis* isomer), 1.05 (t, *J* = 7.3 Hz, 3 H, $CHCH_2CH_3$, *trans* or *cis*), 1.31−138 (m, overlapped signals, 12 H, OCH_2CH_3, *trans* and *cis* isomer), 1.49−1.51 (m, 2 H, $CHCH_2CH_3$, *trans* or *cis* isomer), 1.86−1.96 (m, 2 H, $CHCH_2CH_3$, *trans* or *cis* isomer), 3.78 (dd, J_{H-P} = 18.2 *J* = 4.4 Hz, 1 H, POCHCO, 1.4 of *trans* isomer), 3.83−3.87 (m, 1 H, $CHCH_2CH_3$, *trans* or *cis* isomer), 4.12−4.28 (m, overlapped signals, *J* = 7.2 Hz, 8 H, OCH_2CH_3, *trans* and *cis* isomer), 4.36 (dd, J_{H-P} = 24.1, *J* = 10.3 Hz, 1 H, POCHCO, 1 of *cis* isomer), 4.62−4.63 (m, 1 H, $CHCH_2CH_3$, *trans* or *cis*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 8.60, 10.17 ($CHCH_2CH_3$, *trans* or *cis* isomer), 16.26 (OCH_2CH_3, *trans* and *cis* isomer), 21.55, 27.47 ($CHCH_2CH_3$, *trans* or *cis* isomer), 54.01 (d, $J_{C,P}$ = 147.0, POCHCO, *trans* or *cis* isomer), 53.70 (d, $J_{C,P}$ = 145.0, POCHCO, *trans* or *cis* isomer), 63.19, 63.34 (OCH_2CH_3, *trans* or *cis* isomer), 63.91, 64.55 (OCH_2CH_3, *trans* or *cis* isomer), 67.97, 73.61 ($CHCH_2CH_3$, *trans* or *cis* isomer), 162.79, 166.17 (C=O, *trans* or *cis* isomer) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 14.44 (1.4 of *trans* isomer), 15.25 (1.0 of *cis* isomer) ppm. MS (FAB+): *m*/*z* = 237, 193, 179, 137. HMRS (FAB+): *m*/*z* calcd. $[M + H]^+$ 237.089187, found $[M + H]^+$ 237.089495.

***trans*-3-(Diethoxyphosphoryl)-4-methyl-γ-lactone (8b): 8b** was obtained as a viscous, yellow oil, R_f = 0.20 (EtOAc/hexanes, 3:2). IR (film): $\tilde{\nu}_{max}$ = 1769, 1252, 1027 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.27 [d, *J* = 6.8 Hz, 3 H, $CH(CH_3)CH_2O$], 1.34−1.39 (m, 6 H, OCH_2CH_3), 2.68 (dd, J_{H-P} = 23.4 *J* = 6.5 Hz, 1 H, POCHCO), 2.92−3.04 [1 H, $CH(CH_3)CH_2O$], 3.88 [t, *J* = 6.0 Hz, 1 H, $CH(CH_3)CH_2O$], 4.17−4.27 (m, *J* = 7.2 Hz, 4 H, OCH_2CH_3), 4.53 [t, *J* = 8.3 Hz, 1 H, $CH(CH_3)CH_2O$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.27 (OCH_2CH_3), 18.74 [$CH(CH_3)CH_2O$], 32.95 [$CH(CH_3)CH_2O$], 46.55 (d, $J_{C,P}$ = 142.0, POCHCO), 62.81, 63.52 (OCH_2CH_3), 73.72 [$C(CH_3)CH_2O$], 171.83 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ =

20.62 ppm. MS (EI): *m*/*z* = 237, 221, 193, 179, 138. HMRS (EI): *m*/*z* calcd. $[M]^+$ 236.081362, found $[M]^+$ 236.081521.

Cyclization of Isobutyl α-Diazo-α-(diethoxyphosphoryl)acetate (4c): Isobutyl α-diazo-α-(diethoxyphosphoryl)acetate (**4c**, 0.50 g, 1.80 mmol) in $C_2H_4Cl_2$ was slowly added to a refluxing suspension of rhodium(II) tetraacetate in anhydrous $C_2H_4Cl_2$. After having been heated at reflux for 2 h, the mixture was concentrated and the residue was purified by flash chromatography (SiO_2, EtOAc/hexanes, 3:2), yielding the *cis*-3-(diethoxyphosphoryl)-4-isopropyl-β-lactone (**7c**, 0.14 g, 30%) and the 3-(diethoxyphosphoryl)-4,4-dimethyl-γ-lactone (**8c**, 0.11 g, 24%).

***cis*-3-(Diethoxyphosphoryl)-4-isopropyl-β-lactone (7c): 7c** was obtained as a viscous, yellow oil, R_f = 0.40 (EtOAc/hexanes, 3:2). IR (film): $\tilde{\nu}_{max}$ = 1741, 1265, 1024 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.84 [d, *J* = 6.7 Hz, 6 H, $CHCH(CH_3)_2$], 1.31−139 (m, *J* = 7.0 Hz, 6 H, OCH_2CH_3), 1.74−1.81 [m, *J* = 6.6 Hz, 1 H, $CHCH(CH_3)_2$], 3.62−3.70 [m, 1 H, $CHCH(CH_3)_2$], 4.12−4.28 (m, 4 H, OCH_2CH_3), 4.40 (dd, $J_{H\text{-}P}$ = 24.1, *J* = 10.4 Hz, 1 H, POCHCO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.16 (OCH_2CH_3), 18.70 [$CHCH(CH_3)_2$], 27.36 [$CHCH(CH_3)_2$] 53.94 (d, $J_{C,P}$ = 148.0, POCHCO), 63.75, 64.46 (OCH_2CH_3), 72.33 [$CHCH(CH_3)_2$], 166.10 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 14.45 ppm. MS (EI): *m*/*z* = 210, 166, 138, 91. HMRS (EI): *m*/*z* calcd. $[M + H]^+$ 251.104837, found $[M + H]^+$ 251.104256.

3-(Diethoxyphosphoryl)-4,4-dimethyl-γ-lactone (8c): 8c was obtained as a viscous, yellow oil, R_f = 0.20 (EtOAc/hexanes, 3:2). IR (film): $\tilde{\nu}_{max}$ = 1778, 1258, 1022 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.30 [s, 6 H, $C(CH_3)_2CH_2O$], 1.34−1.39 (m, *J* = 7.2 Hz, 6 H, OCH_2CH_3), 2.80 (d, $J_{H\text{-}P}$ = 24.4 Hz, 1 H, POCHCO), 3.92 [d, *J* = 8.4 Hz, 1 H, $C(CH_3)_2CH_2O$], 4.14 [d, *J* = 8.4 Hz, 1 H, $C(CH_3)_2CH_2O$], 4.17−4.28 (m, *J* = 7.2 Hz, 6 H, OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.31 (OCH_2CH_3), 20.42 [$C(CH_3)_2CH_2O$], 25.02 [$C(CH_3)_2CH_2$], 38.21 [$C(CH_3)_2CH_2$], 48.68 (d, $J_{C,P}$ = 143.4, POCHCO), 60.38, 61.20 (OCH_2CH_3), 70.01 [$C(CH_3)_2CH_2O$], 170.02 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 16.74 ppm. MS (EI): *m*/*z* = 251, 235, 179, 151, 123. HMRS (EI): *m*/*z* calcd. $[M]^+$ 250.097012, found $[M]^+$ 250.096068.

Cyclization of α-Diazo-α-(diethoxyphosphoryl)-*N*,*N*-(diisopropyl)acetamide (4d): α-Diazo-α-(diethoxyphosphoryl)-*N*,*N*-(diisopropyl)acetamide (**4d**, 0.15 g, 0.50 mmol) in CH_2Cl_2 was slowly added to a refluxing suspension of rhodium(II) tetraacetate in anhydrous CH_2Cl_2. After having been heated at reflux for 6 h 30 min, the mixture was concentrated and the residue was purified by flash chromatography (basic alumina, EtOAc/hexanes, 2:3), yielding the **3-(diethoxyphosphoryl)-1-isopropyl-4,4-dimethyl-β-lactam**[6] (**5d**, 0.12 g, 88%) as a colourless oil, R_f = 0.30 (neutral alumina, EtOAc/hexanes, 2:3). IR (film): $\tilde{\nu}_{max}$ = 1746, 1249, 1047 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.26−1.30 [m, overlapped signals, *J* = 7.1 Hz, 12 H, OCH_2CH_3 and $NCH(CH_3)_2$], 1.42 [s, 3 H, $CHC(CH_3)_2N$], 1.56 [s, 3 H, $CHC(CH_3)_2N$], 3.19 (d, $J_{H\text{-}P}$ = 17.2 Hz, 1 H, POCHCO), 3.44−3.51 [m, 1 H, $NCH(CH_3)_2$], 4.10−4.15 (m, *J* = 7.0 Hz, 4 H, OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.26 (OCH_2CH_3), 21.50, 21.60 [$NCH(CH_3)_2$], 22.30, 27.92 [$CHC(CH_3)_2N$], 44.56 [$NCH(CH_3)_2$], 57.56 (d, $J_{C,P}$ = 145.1, POCHCO) 58.02 [$CHC(CH_3)_2N$], 62.02, 62.18 (OCH_2CH_3), 160.13 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 19.34 ppm. MS (EI): *m*/*z* = 277, 262, 192, 136, 83. HMRS (EI): *m*/*z* calcd. $[M]^+$ 277.144297, found $[M]^+$ 277.143893.

Cyclization of α-Diazo-α-(diethoxyphosphoryl)-*N*,*N*-diethylacetamide (4e): α-Diazo-α-(diethoxyphosphoryl)-*N*,*N*-diethylacetamide (**4e**, 0.30 g, 1.10 mmol) in $C_2H_4Cl_2$ was slowly added to a refluxing suspension of rhodium(II) tetraacetate in anhydrous $C_2H_4Cl_2$. After having been heated at reflux for 3 h, the mixture was concentrated and the residue was purified by flash chromatography (basic alumina, EtOAc/hexanes, 7:3), yielding *trans*-3-(diethoxyphosphoryl)-1-ethyl-4-methyl-β-lactam (**5e**, 0.05 g, 18%) and 3-(diethoxyphosphoryl)-1-ethyl-γ-lactam (**6e**, 0.13 g, 50%).

***trans*-3-(Diethoxyphosphoryl)-1-ethyl-4-methyl-β-lactam (5e): 5e** was obtained as a colourless oil, R_f = 0.26 (neutral alumina, EtOAc/hexanes, 7:3). IR (film): $\tilde{\nu}_{max}$ = 1749, 1239, 1023 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.12 (t, *J* = 7.2 Hz, 3 H, NCH_2CH_3), 1.31 (t, *J* = 7.0 Hz, 6 H, OCH_2CH_3), 1.36 [d, *J* = 6.0 Hz, 3 H, $CH(CH_3)N$], 3.03−3.07 (m, *J* = 7.1 Hz, 1 H, NCH_2CH_3), 3.23 (dd, $J_{H\text{-}P}$ = 14.8 *J* = 2.2 Hz, 1 H, POCHCO), 3.37−3.46 (m, *J* = 7.1 Hz, 1 H, NCH_2CH_3), 3.85−3.91 [m, *J* = 2.2 Hz, 1 H, $CH(CH_3)N$], 4.16−4.23 (m, 4 H, OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.03 (NCH_2CH_3), 16.32 (OCH_2CH_3), 18.50 [$CH(CH_3)N$], 35.33 (NCH_2CH_3), 48.65 [$CH(CH_3)N$], 53.94 (d, $J_{C,P}$ = 145.4, POCHCO), 62.37, 62.55 (OCH_2CH_3), 160.83 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 20.64 ppm. MS (EI): *m*/*z* = 250, 233, 221, 179, 163, 123. HMRS (EI): *m*/*z* calcd. $[M]^+$ 249.112997, found $[M]^+$ 249.111823.

3-(Diethoxyphosphoryl)-1-ethyl-γ-lactam (6e): 6e was obtained as a colourless oil, R_f = 0.12 (neutral alumina, EtOAc/hexanes, 7:3). IR (film): $\tilde{\nu}_{max}$ = 1687, 1249, 1024 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.10 (t, *J* = 7.2 Hz, 3 H, NCH_2CH_3), 1.32 (q, *J* = 7.0 Hz, 6 H, OCH_2CH_3), 2.26−2.39 (m, 2 H, CH_2CH_2N), 2.91 (dq, $J_{H\text{-}P}$ = 22.0 *J* = 5.0 Hz, 1 H, POCHCO), 3.26−3.38 (m, overlapped signals, 3 H, CH_2CH_2N and NCH_2CH_3), 3.46−3.50 (m, 1 H, CH_2CH_2N), 4.11−4.26 (m, 4 H, OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 12.22 (NCH_2CH_3), 16.35 (OCH_2CH_3), 20.33 (CH_2CH_2N), 37.55 (NCH_2CH_3), 41.16 (d, $J_{C,P}$ = 141.0, POCHCO), 45.17 (CH_2CH_2N), 62.15, 62.87 (OCH_2CH_3), 168.77 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 24.94 ppm. MS (EI): *m*/*z* = 249, 192, 179, 111, 71. HMRS (EI): *m*/*z* calcd. $[M]^+$ 249.112997, found $[M]^+$ 249.113069.

Cyclization of *N*,*N*-Dibutyl-α-diazo-α-(diethoxyphosphoryl)-acetamide (4f): *N*,*N*-Dibutyl-α-diazo-α-(diethoxyphosphoryl)acetamide (**4f**, 0.10 g, 0.30 mmol) in $C_2H_4Cl_2$ was slowly added to a refluxing suspension of rhodium(II) tetraacetate in anhydrous $C_2H_4Cl_2$. After having been heated at reflux for 2 h, the mixture was concentrated and the residue was purified by flash chromatography (basic alumina, EtOAc/hexanes, 7:3), yielding the ***trans*-1-butyl-3-(diethoxyphosphoryl)-4-ethyl-γ-lactam**[6] (**6f**, 0.08 g, 87%) as a brownish oil, R_f = 0.24 (neutral alumina, EtOAc/hexanes, 3:2). IR (film): $\tilde{\nu}_{max}$ = 1686, 1265, 1053 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.93 [q, overlapped signals, *J* = 7.2 Hz, 6 H, $CH(CH_2CH_3)CH_2N$ and $NCH_2CH_2CH_2CH_3$], 1.32−1.37 (m, overlapped signals, *J* = 7.1 Hz, 8 H, $NCH_2CH_2CH_2CH_3$ and OCH_2CH_3), 1.43−1.54 [m, overlapped signals, *J* = 7.2, 7.4 Hz, 3 H, $CH(CH_2CH_3)CH_2N$ and $NCH_2CH_2CH_2CH_3$], 1.60−1.65 (m, 1 H, $NCH_2CH_2CH_2CH_3$), 2.55−2.68 (overlapped signals, 1 H, m, $CH(CH_2CH_3)CH_2N$ and 1 H, dd, $J_{H\text{-}P}$ = 21.8, *J* = 4.4 Hz), 2.98 [dd, *J* = 3.1 Hz, 9.7 Hz, 1 H, $CH(CH_2CH_3)CH_2N$], 3.22−3.35 (m, 2 H, $NCH_2CH_2CH_2CH_3$), 2.98 [t, *J* = 9.0 Hz, 1 H, $CH(CH_2CH_3)CH_2N$], 4.13−4.28 (m, 4 H, OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 10.85, 13.60 [$NCH_2CH_2CH_2CH_3$, and $CH(CH_2CH_3)CH_2N$], 16.28 (OCH_2CH_3), 19.76 ($NCH_2CH_2CH_2CH_3$), 28.09, 28.19 ($NCH_2CH_2CH_2CH_3$), 29.04 [$CH(CH_2CH_3)CH_2N$], 34.75 [$CH(CH_2CH_3)CH_2$], 42.46 ($NCH_2CH_2CH_2CH_3$), 47.35 (d, $J_{C,P}$ = 139.9 Hz, POCHCO), 51.26 [$CH(CH_2CH_3)CH_2N$], 61.98, 62.86

(OCH_2CH_3), 168.49 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 24.60 ppm. MS (EI): *m*/*z* = 305, 290, 276, 263, 179, 127. HMRS (EI): *m*/*z* calcd. $[M]^+$ 305.175597, found $[M]^+$ 305.176528.

Cyclization of *N*-(*tert*-Butyl)-α-diazo-α-(diethoxyphosphoryl)-*N*-(phenylethyl)acetamide (4g): *N*-(*tert*-Butyl)-α-diazo-α-(diethoxyphosphoryl)-*N*-(phenylethyl)acetamide (**4g**, 0.11 g, 0.30 mmol) in $C_2H_4Cl_2$ was slowly added to a refluxing suspension of rhodium(II) tetraacetate in anhydrous $C_2H_4Cl_2$. After having been heated at reflux for 4 h, the mixture was concentrated and the residue was purified by flash chromatography (basic alumina, EtOAc/hexanes, 1:1), yielding ***trans*-1-(*tert*-butyl)-3-(diethoxyphosphoryl)-4-phenyl-γ-lactam** (**6g**, 0.08 g, 81%) as a viscous, yellow oil, R_f = 0.49 (neutral alumina, EtOAc/hexanes, 1:1). IR (film): $\tilde{\nu}_{max}$ = 1682, 1265, 1051 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.19 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 1.24 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3), 1.37 [s, 9 H, $NC(CH_3)_3$], 2.95 (dd, $J_{P\text{-}H}$ = 22.2, *J* = 4.9 Hz, 1 H, POC*H*CO), 3.37 (dd, *J* = 3.4 Hz, 9.7 Hz, 1 H, $CHArCH_2N$), 3.62−3.69 (m, 1 H, $CHArCH_2N$), 3.93 (t, *J* = 9.3 Hz, 1 H, $CHArCH_2N$), 3.98−4.17 (m, 4 H, OCH_2CH_3), 7.16−7.28 (m, 5 H, *Ar*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.35 (OCH_2CH_3), 27.54 [$NC(CH_3)_3$], 38.24 ($CHArCH_2N$), 51.01 (d, $J_{C,P}$ = 139.0, POC*H*CO), 52.49 ($CHArCH_2N$), 54.74 [$NC(CH_3)_3$], 62.25, 62.95 (OCH_2CH_3), 126.50, 127.28, 128.95, 143.54 (q), 168.75 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 23.59 ppm. MS (EI): *m*/*z* = 353, 296, 176, 119, 57. HMRS (EI): *m*/*z* calcd. $[M]^+$ 353.174851, found $[M]^+$ 353.175597.

Cyclization of α-Diazo-α-(diethoxyphosphoryl)-*N*,*N*-bis(2-methoxyethyl)acetamide (4h): α-Diazo-α-(diethoxyphosphoryl)-*N*,*N*-bis(2-methoxyethyl)acetamide (**4h**, 0.05 g, 0.15 mmol) in $C_2H_4Cl_2$ was slowly added to a refluxing suspension of rhodium(II) tetraacetate in anhydrous $C_2H_4Cl_2$. After having been heated at reflux for 1 h, the mixture was concentrated and the residue was purified by flash chromatography (basic alumina, EtOAc/hexanes, 7:3), yielding ***trans*-3-(diethoxyphosphoryl)-4-methoxy-1-(2-methoxyethyl)-γ-lactam** (**6h**, 0.04 g, 89%) as a viscous, yellow oil, R_f = 0.50 (neutral alumina, EtOAc/hexanes, 2:3). IR (film): $\tilde{\nu}_{max}$ = 1692, 1245, 1026 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) 1.27−1.32 (m, *J* = 7.0 Hz, 6 H, OCH_2CH_3), 3.00 (dd, $J_{H\text{-}P}$ = 23.6 *J* = 2.0 Hz, 1 H, POC*H*CO), 3.26 (s, 6 H, $NCH_2CH_2OCH_3$), 3.34−3.50 [m, overlapped signals, 5 H, $NCH_2CH_2OCH_3$, $NCH_2CH_2OCH_3$ and $CH(OCH_3)CH_2N$], 3.76−3.80 [m, 1 H, $CH(OCH_3)CH_2N$], 4.11−4.18 (m, 4 H, OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.20 (OCH_2CH_3), 42.70 ($NCH_2CH_2OCH_3$), 48.29 (d, $J_{C,P}$ = 135.0 Hz, POCHCO), 54.05 [$CH(OCH_3)CH_2N$], 56.13, 58.55 ($NCH_2CH_2OCH_3$), 62.29, 63.05 (OCH_2CH_3), 70.66 ($NCH_2CH_2OCH_3$), 75.13 [$CH(OCH_3)CH_2N$], 167.41 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 20.83 ppm. MS (EI): *m*/*z* = 294, 278, 221, 179, 173. HMRS (EI): *m*/*z* calcd. $[M]^+$ 295.114006, found $[M]^+$ 295.113815.

Cyclization of *N*-(*tert*-Butyl)-α-diazo-α-(diethoxyphosphoryl)-*N*-[2-(methoxycarbonyl)ethyl]acetamide (4i): *N*-(*tert*-Butyl)-α-diazo-α-(diethoxyphosphoryl)-*N*-[2-(methoxycarbonyl)ethyl]acetamide (**4i**, 0.20 g, 0.51 mmol) in $C_2H_4Cl_2$ was slowly added to a refluxing suspension of rhodium(II) tetraacetate in anhydrous $C_2H_4Cl_2$. After having been heated at reflux for 2 h, the mixture was concentrated and the residue was purified by flash chromatography (basic alumina, EtOAc/hexanes, 1:1), yielding ***trans*-1-(*tert*-butyl)-3-(diethoxyphosphoryl)-4-(methoxycarbonyl)-β-lactam** (**5i**, 0.17 g, 94%) as a brown oil, R_f = 0.29 (neutral alumina, EtOAc/hexanes, 1:1). IR (film): $\tilde{\nu}_{max}$ = 1745, 1247, 1028 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.30−1.37 [m, overlapped signals, 15 H, OCH_2CH_3 and $NC(CH_3)_3$], 2.60 (dd, *J* = 7.9 Hz, 14.7 Hz, 1 H, $CHCH_2CO_2CH_3$), 2.90 (dd, *J* = 3.5 Hz, 14.5 Hz, 1 H, $CHCH_2CO_2CH_3$), 3.40 (dd, $J_{H\text{-}P}$ = 15.0 *J* = 2.0 Hz, 1 H, POC*H*CO), 3.73 (s, 3 H, $CHCH_2CO_2CH_3$), 4.08−4.35 (m, overlapped signals, 5 H, $CHCH_2CO_2CH_3$ and OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.32 (OCH_2CH_3), 28.14 [$NC(CH_3)_3$], 39.48 ($CHCH_2CO_2CH_3$), 48.62 ($CHCH_2CO_2CH_3$), 51.11 (d, $J_{C,P}$ = 144.0 Hz, POCHCO), 51.93 ($CHCH_2CO_2CH_3$), 62.56 (OCH_2CH_3), 162.10 ($CONCHCH_2$), 169.63 ($COOCH_3$) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 20.22 ppm. MS (EI): *m*/*z* = 336, 277, 263, 206, 179. HMRS (EI): *m*/*z* calcd. $[M]^+$ 335.149776, found $[M]^+$ 335.149767.

Cyclization of (*R*)-(+)-*N*-Butyl-α-(diethoxyphosphoryl)-*N*-(α-phenylethyl)acetamide (4j): (*R*)-(+)-*N*-butyl-α-(diethoxyphosphoryl)-*N*-(α-phenylethyl)acetamide (**4j**, 0.10 g, 0.26 mmol) in $C_2H_4Cl_2$ was slowly added to a refluxing suspension of rhodium(II) tetraacetate in anhydrous $C_2H_4Cl_2$. After having been heated at reflux for 2 h, the mixture was concentrated and the residue was purified by flash chromatography (basic alumina, EtOAc/hexanes, 3:7), yielding 0.087 g of a 1.2:1.0 mixture of *trans*-1-(*R*)-(+)-3-(diethoxyphosphoryl)-4-ethyl-*N*-(α-phenylethyl)-γ-lactam (**6j**, 76%) and *(E/Z)*-1-butyl-α-(diethoxyphosphoryl)-4-methyl-4-phenyl-β-lactam (**5j**, 18%).

***(E)*-1-Butyl-α-(diethoxyphosphoryl)-4-methyl-4-phenyl-β-lactam (5j): 5j** was obtained as a 1.2:1.0 mixture of **6j** and **5j**. R_f = 0.29 (neutral alumina, EtOAc/hexanes, 3:7); Relevant signals in the mixture for the β-lactam: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 2.03 [s, 3 H, $C(CH_3)Ar$], 3.48 (d, $J_{H\text{-}P}$ = 17.5 Hz, 1 H, POC*H*CO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 60.96 (d, $J_{C,P}$ = 143.0 Hz, POC*H*CO) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 18.06 ppm.

***trans*-1-(*R*)-(+)-3-(Diethoxyphosphoryl)-4-ethyl-*N*-(α-phenylethyl)-γ-lactam (6j): 6j** was obtained as a viscous, yellow oil, diastereoisomeric mixture (1.2:1.0), R_f = 0.29 (neutral alumina, EtOAc/hexanes, 3:7). IR (film): $\tilde{\nu}_{max}$ = 1678, 1243, 1053 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.77, 0.92 [1:1.2, t, *J* = 7.2 Hz, $CH(CH_2CH_3)CH_2N$], 1.25−1.36 (m, overlapped signals, OCH_2CH_3), 1.42−1.49 [m, $CH(CH_2CH_3)CH_2N$], 1.53 [d, *J* = 6.8 Hz, 6 H, $NCH(CH_3)Ar$], 1.61−1.68 [m, $CH(CH_2CH_3)CH_2N$], 2.52 [m, $CH(CH_2CH_3)CH_2N$], 2.60 [*J* = 9.6 Hz, $CH(CH_2CH_3)CH_2N$], 2.67 (dd, $J_{H\text{-}P}$ = 22.5, POC*H*CO), 2.71 (dd, $J_{H\text{-}P}$ = 22.4, *J* = 4.2 Hz, POC*H*CO), 2.91 [d, *J* = 8.2 Hz, $CH(CH_2CH_3)CH_2N$], 3.21 [t, *J* = 8.6 Hz, $CH(CH_2CH_3)CH_2N$], 3.57 [t, *J* = 8.4 Hz, $CH(CH_2CH_3)CH_2N$], 4.14−4.30 (m, OCH_2CH_3), 5.50 [q, *J* = 6.8 Hz, 6 H, $NCH(CH_3)Ar$], 7.29−7.33 [m, 10 H, $NCH(CH_3)Ar$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 10.68, 10.82 [$CH(CH_2CH_3)CH_2N$], 15.71 [$NCH(CH_3)Ar$], 16.00, 16.34 (OCH_2CH_3), 27.81, 28.16 [$CH(CH_2CH_3)CH_2N$), 34.57, 34.71 [$CH(CH_2CH_3)CH_2N$), 46.30, 46.55 [$CH(CH_2CH_3)CH_2N$], 47.56 (d, $J_{C,P}$ = 140.0 Hz, POC*H*CO), 47.73 (d, $J_{C,P}$ = 138.0 Hz, POC*H*CO), 49.13, 49.31 [$NCH(CH_3)Ar$], 62.70, 62.82 (OCH_2CH_3), 126.98, 127.38, 127.50, 128.41, 139.48 (q), 139.74 (q), 168.38 (C=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 24.45, 24.55 ppm. MS (EI): *m*/*z* = 353, 248, 220, 192, 105. HMRS (EI): *m*/*z* calcd. $[M]^+$ 353.175597, found $[M]^+$ 353.174327.

Cyclization of *N*,*N*-Dibenzyl-α-diazo-α-(diethoxyphosphoryl)-acetamide (4k): *N*,*N*-Dibenzyl-α-diazo-α-(diethoxyphosphoryl)acetamide (**4k**, 0.10 g, 0.25 mmol) in CH_2Cl_2 was slowly added to a refluxing suspension of rhodium(II) tetraacetate in anhydrous CH_2Cl_2. After having been heated at reflux for 9 h, the mixture was concentrated and the residue was purified by flash chromatography (basic alumina, EtOAc/hexanes, 2:3), yielding the ***trans*-1-benzyl-3-**

(diethoxyphosphoryl)-4-phenyl-β-lactam (**5k**, 0.08, 81%) as a viscous, yellow oil, R_f = 0.50 (neutral alumina, EtOAc/hexanes, 2:3). IR (film): $\tilde{\nu}_{max}$ = 1759, 1265, 1026 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.29 (t, J = 7.0 Hz, 6 H, OCH_2CH_3), 3.49 (dd, $J_{H\text{-}P}$ = 14.7, J = 2.0 Hz, 1 H, POC*H*CO), 3.82 (d, J = 15.2 Hz, 1 H, NCH_2Ar), 4.13−4.21 (m, J = 7.1 Hz, 4 H, OCH_2CH_3), 4.63 (dd, $J_{P\text{-}H}$ = 8.4, J = 2.0 Hz, 1 H, C*H*ArN), 4.89 (d, J = 15.2 Hz, 1 H, NCH_2Ar), 7.19−7.38 (m, 10 H, Ar) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.18 (OCH_2CH_3), 44.79 (NCH_2Ar), 55.05 (*C*HArN), 56.85 (d, $J_{C,P}$ = 144.0 Hz, POC*H*CO), 62.51 (OCH_2CH_3), 126.25, 127.64, 128.16, 128.57, 128.79, 128.99, 129.25, 134.61 (q), 136.07 (q), 161.79 (*C*=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 18.91 ppm. MS (EI): *m*/*z* = 373, 236, 208, 131, 91. HMRS (EI): *m*/*z* calcd. $[M]^+$ 373.144297, found $[M]^+$ 373.143275.

Cyclization of *N*-Benzyl-*N*-(*tert*-butyl)-α-diazo-α-(diethoxyphosphoryl)acetamide (4l): *N*-Benzyl-*N*-(*tert*-butyl)-α-diazo-α-(diethoxyphosphoryl)acetamide (**4l**, 0.20 g, 5.45 mmol) in CH_2Cl_2 was slowly added to a refluxing suspension of rhodium(II) tetraacetate in anhydrous CH_2Cl_2. After having been heated at reflux for 7 h, the mixture was concentrated and the residue was purified by flash chromatography (basic alumina, EtOAc/hexanes, 2:8), yielding ***trans*-1-(*tert*-butyl)-3-(diethoxyphosphoryl)-4-phenyl-β-lactam** (**5l**, 0.17 g, 89%) as a viscous, yellow oil, which crystallized in the fridge after a long time period (one month) as white crystals (mp, 85−86 °C), R_f = 0.34 (neutral alumina, EtOAc/hexanes, 2:8). IR (film): $\tilde{\nu}_{max}$ = 1750, 1252, 1027 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ =): 1.27−1.37 [m, overlapped signals, 15 H, OCH_2CH_3 and $NC(CH_3)_3$], 3.27 (dt, $J_{P\text{-}H}$ = 14.6, J = 2.4 Hz, 1 H, POC*H*CO), 4.12−4.27 (m, 4 H, OCH_2CH_3), 4.77 (dt, $J_{P\text{-}H}$ = 9.3, J = 2.4 Hz, 1 H, NC*H*Ar), 7.32−7.42 (m, 5 H, NCH*Ar*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.29, 16.34 (OCH_2CH_3), 27.93 [$NC(CH_3)_3$], 54.64 (N*C*HAr), 55.88 (d, $J_{C,P}$ = 141.0 Hz, POC*H*CO), 62.48, 62.60 (OCH_2CH_3), 126.17, 128.59, 128.92, 139.32 (q), 161.84 (*C*=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 19.92 ppm. MS (EI): *m*/*z* = 339, 282, 241, 131, 83. HMRS (EI): *m*/*z* calcd. $[M]^+$ 339.159947, found $[M]^+$ 339.159033.

Cyclization of *N*-(*tert*-Butyl)-α-diazo-α-(diethoxyphosphoryl)-*N*-(α-phenylethyl)acetamide (4m): *N*-(*tert*-Butyl)-α-diazo-α-(diethoxyphosphoryl)-*N*-(α-phenylethyl)acetamide (**4m**, 0.20 g, 5.25 mmol) in $C_2H_4Cl_2$ was slowly added to a refluxing suspension of rhodium(II) tetraacetate in anhydrous $C_2H_4Cl_2$. After having been heated at reflux for 4 h, the mixture was concentrated and the residue was purified by flash chromatography (basic alumina, EtOAc/hexanes, 2:8), yielding the *trans*-1-(*tert*-butyl)-3-(diethoxyphosphoryl)-4-methyl-4-phenyl-β-lactam (**5m**, 0.14 g, 75%) as a viscous, yellow oil, R_f = 0.18 (neutral alumina, EtOAc/hexanes, 1:4). IR (film): $\tilde{\nu}_{max}$ = 1741, 1248, 1028 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.26−1.38 [m, overlapped signals, 15 H, OCH_2CH_3 and $NC(CH_3)_3$], 2.23 [s, 3 H, $C(CH_3)Ar$], 3.44 (d, $J_{P\text{-}H}$ = 17.5 Hz, 1 H, POC*H*CO), 4.09−4.34 (m, 4 H, OCH_2CH_3), 7.28−7.63 [m, 5 H, $C(CH_3)Ar$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 16.30 (OCH_2CH_3), 21.01 [$NC(CH_3)Ar$], 28.35 [$NC(CH_3)_3$], 55.96 [$NC(CH_3)Ar$], 61.17 (d, $J_{C,P}$ = 141.0 Hz, POC*H*CO), 62.10, 62.42 (OCH_2CH_3), 125.13, 127.84, 128.68, 143.97 (q), 162.19 (*C*=O) ppm. ^{31}P NMR (160 MHz, $CDCl_3$, 25 °C): δ = 17.79 ppm. MS (EI): *m*/*z* = 353, 338, 296, 254, 198. HMRS (EI): *m*/*z* calcd. $[M]^+$ 353.175597, found $[M]^+$ 353.176020.

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