Organic & Biomolecular Chemistry

PAPER

View Article Online
View Journal

Cite this: DOI: 10.1039/c6ob01987k

Phospha-Michael addition reaction of maleimides employing N-heterocyclic phosphine-thiourea as a phosphonylation reagent: synthesis of 1-aryl-2,5-dioxopyrrolidine-3-yl-phosphonate derivatives†

Nagaraju Molleti, Chad Bjornberg and Jun Yong Kang*

Received 9th September 2016,
Accepted 27th October 2016

DOI: 10.1039/c6ob01987k

www.rsc.org/obc

N-Heterocyclic phosphine (NHP)-thiourea as a novel phosphonylation reagent has been successfully applied for the phospha-Michael reaction of maleimides under catalyst and additive free reaction conditions. This methodology enables desymmetrization of a variety of maleimide derivatives to provide 1-aryl-2,5-dioxopyrrolidine-3-yl-phosphonates in up to 92% yield. Synthetic manipulation of this Michael adduct afforded an ethylphosphonate and a phosphino lactam. Furthermore, a scale-up experiment for its practical usage as a versatile precursor in organic synthesis was readily demonstrated.

Introduction

Since the first report of a naturally occurring C–P bond-containing compound, 2-aminoethylphosphonic acid isolated from the rumen protozoa in 1959,[1] phosphorus containing compounds have occupied a vital position in synthetic organic chemistry over the past several decades.[2] Phosphonamides[3] and phosphates[4] are important synthetic intermediates in numerous synthetic transformations for the synthesis of bioactive natural products and biologically significant compounds.[2b,5] Furthermore, amino phosphonate derivatives and γ-ketophosphonates have been intensively studied for use as effective enzyme inhibitors and active pharmaceutical ingredients.[6] In particular, γ-ketophosphonic acid derivatives with a succinic acid motif (Fig. 1, **a**) have shown significant inhibition of serine hydrolases of acetylcholinesterase (AChE) and butyrylcholinesterase (BChE).[7] Phosphinosuccinic acid derivatives have been used in phosphosuccinic acid oligomer (PSO)-based scale inhibitors in the desalination systems (**b**, **c**).[8] In addition, phosphino pyrrolidine derivatives (**d**, **e**) have also been utilized as chiral ligands or catalysts in asymmetric synthesis.[9] These biologically and synthetically important γ-ketophosphonic acid scaffolds are accessible by the phospha-Michael addition reaction[10] between maleimides and dialkyl- or trialkyl-phosphites in a single chemical step.[10a,11]

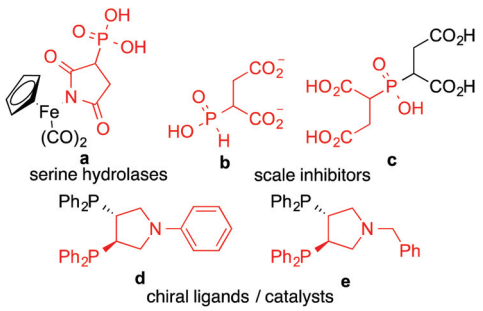
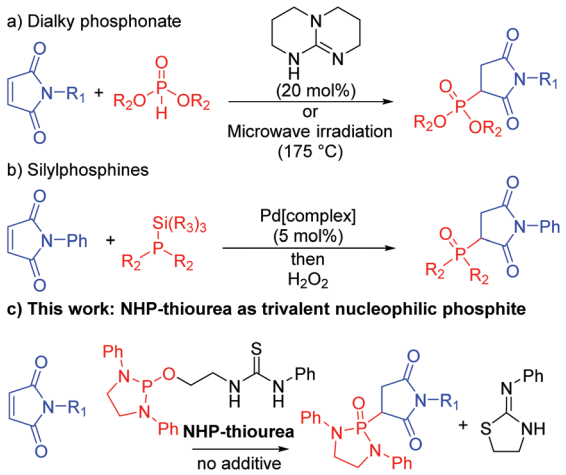


Fig. 1 Representative examples of functional γ-ketophosphonic acids and pyrrolidine derivatives.

While the conjugate addition reactions of various nucleophiles such as amino-,[12] thio-,[12b,13] and carbo-nucleophiles[14] to maleimides represent well-known and important chemical transformations since the substituted succinimide derivatives are valuable synthetic precursors of many pharmaceuticals and biologically active compounds,[13a,14y,15] the phospha-Michael addition reaction of maleimides has been rarely developed. Most of these methods utilized dialkylphosphonates as Michael donors to form the corresponding γ-ketophosphonates. These transformations, however, require the use of a super base catalyst[16] or microwave irradiation[11] to promote tautomeric equilibria of H-phosphonates in favor of a reactive form of phosphites (Scheme 1a).[17] There is one report of trivalent phosphorus nucleophile addition to maleimides

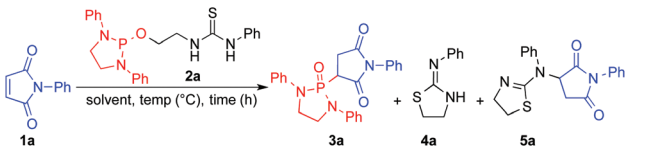
Department of Chemistry and Biochemistry, University of Nevada Las Vegas, 4505 S. Maryland Parkway, Las Vegas, Nevada, 89154-4003, USA. E-mail: junyong.kang@unlv.edu

†Electronic supplementary information (ESI) available: Experimental procedures, characterization data for products, and NMR spectra of products. See DOI: 10.1039/c6ob01987k



Scheme 1 Different types of phosphorus Michael donors to maleimides.

Table 1 Optimization study[a]



Entry	Solvent	Temp (°C)	Time (h)	**3a** [b] (%)	**4a** [b] (%)	**5a** [b] (%)
1[c,d]	$CHCl_3$	61	19	60	ND	ND
2[d]	$CHCl_3$	61	19	84	ND	ND
3	**$CHCl_3$**	**61**	**19**	**92**	**60**	**20**
4	CH_3CN	61	19	80	ND	ND
5	THF	61	19	78	ND	ND
6	DCM	40	19	80	ND	ND

[a] All reactions were carried out using **1a** (0.075 mmol) and **2a** (0.05 mmol) in solvent (0.1 mL). [b] Isolated yield. [c] Solvent (0.5 mL) was used. [d] 1.5 equiv. of **2a** was used. ND = not determined.

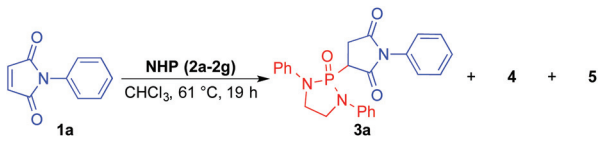
using silyphosphines as a source of trivalent nucleophilic phosphorus for phosphination (Scheme 1b) in which the Pd-complex catalyst and hydrogen peroxide for phosphinyl to phosphinoyl oxidation is unavoidable for the successful transformation.[18] On the other hand, to the best of our knowledge, there is no report of phospha-Michael addition reaction using the reactive form of trivalent trialkylphosphites to maleimides under additive and catalyst free reaction conditions, in part due to the instability of the trivalent phosphorus under additive free conditions.[17] Given the lack of stable trivalent phosphite reagents as well as mild and simple reaction conditions for the phospha-Michael addition reaction of maleimide derivatives, we were interested in finding a solution to the aforementioned current hurdles. We have been involved in the development of efficient synthetic methods of C–P bond formation and have contributed actively to this area.[19] Herein, we report the 1,3,2-diazaphospholidine (N-heterocyclic phosphine)-thiourea-promoted phospha-Michael/intramolecular nucleophilic substitution reaction of maleimides for the racemic synthesis of chiral 1-aryl-pyrrolidine-2,5-dionephosphonate derivatives (Scheme 1c).

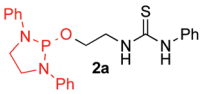
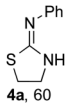
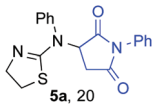
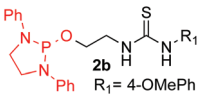
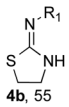
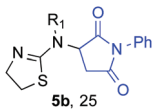
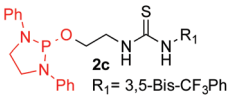
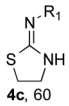
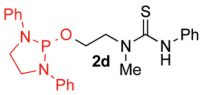
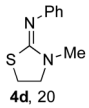
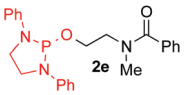
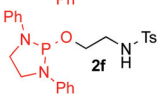
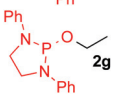
Results and discussion

To test our hypothesis, a model reaction comprising *N*-phenyl maleimide **1a** (1.0 equiv.) and NHP-thiourea **2a** (1.5 equiv.) was carried out in $CHCl_3$ at 61 °C (Table 1). To our delight, the corresponding phospha-Michael adduct **3a** was obtained in good yield (entry 1, 60%). The concentration of the reaction medium highly effected the formation of the Michael adduct. The product yield of **3a** was increased to 84% when the reaction runs at higher concentration (entry 1 *vs.* 2). The optimum reaction conditions were achieved with a slight excess of **1a**, providing the desired product **3a** with 92% (entry 3) and by-product **4a** in 60% yield. Interestingly, the by-product **4a** underwent aza-Michael addition reaction to the maleimide **1a** and furnished a C–N bonded Michael adduct **5a** with 20% yield (entry 3). Next, we studied the effect of different solvents on this phospha-Michael reaction. The survey of different solvents revealed that the conjugate addition reactions were well tolerated from polar to less polar solvents (entries 4–6). Among all solvents screened in this phospha-Michael reaction, $CHCl_3$ was found as the optimal solvent and used for screening of the reactions.

After having established the reaction conditions in hand, we explored the effect of a Brønsted acid motif on the phospha-Michael reaction as depicted in Table 2. Electronic effects slightly influenced the formation of product **3a**. The electron-rich thiourea moiety such as 4-OMe-phenyl-thiourea (**2b**) showed higher reactivity than the electron-deficient thiourea moiety of 3,5-bis(trifluoromethyl)-phenyl-thiourea (**2c**), providing the desired product **3a** with 87% and 65% yield, respectively (entries 2 and 3). The cyclized byproducts of **4b** and **4c** were also obtained with 55% and 60% yields, respectively. In addition, while a C–N bonded Michael adduct **5b** was generated with the use of NHP-thiourea **2b**, no aza-Michael adduct was produced with the NHP-thiourea **2c**. It seems that the NHP-thiourea **2c** with an electron-withdrawing substituent on the thiourea moiety prevented the second Michael addition reaction between the thiazolidine byproduct **4c** and maleimide **1a**. Nevertheless, none of them were superior to the parent phenyl-thiourea (**2a**). Next, we investigated the effect of substituents on the Brønsted acid. Having *N*-methyl NHP-thiourea and *N*-methyl amide (**2d** and **2e**), the reactivity was greatly suppressed and the Michael adduct was obtained in low yields (entries 4 and 5), presumably due to impeding the intramolecular nucleophilic substitution reaction course. We also evaluated the effect of different Brønsted acids on this transformation. The replacement of the thiourea group to a sulfonamide moiety showed inferior reactivity, and provided **3a** with a moderate yield of 61% along with the cyclized byproduct of 1-tosylaziridine **4f** (entry 6, 55%). Based on the above results, we believe that the product formation depends on the relative rates of intermolecular substitution

Table 2 Effects of different NHP reagents on phospha-Michael reaction[a]



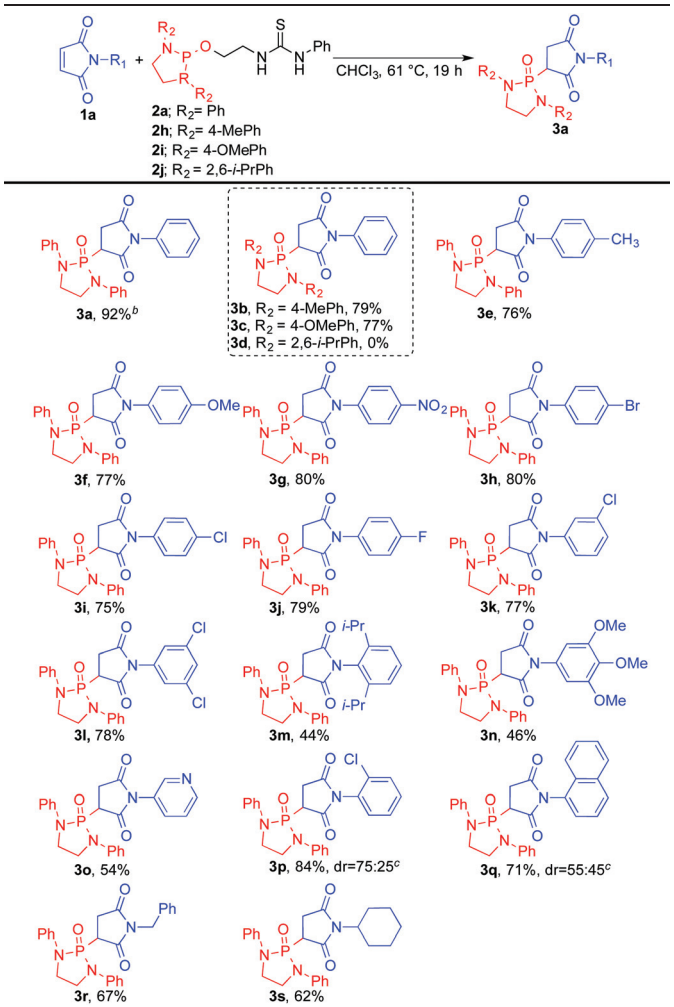
Entry	NHP	3a/yield[b] (%)	4/yield[b] (%)	5/yield[b] (%)
1	 2a	92	 4a, 60	 5a, 20
2	 2b R_1= 4-OMePh	87	 4b, 55	 5b, 25
3	 2c R_1= 3,5-Bis-CF_3Ph	65	 4c, 60	
4	 2d	24	 4d, 20	
5	 2e	36		
6	 2f	61	 4f, 55	
7	 2g	20		

[a] All reactions were carried out using **1a** (0.075 mmol) and **2a** (0.05 mmol) in $CHCl_3$ (0.1 mL). [b] Isolated yield.

reaction and intramolecular nucleophilic displacement. In the case of low-yielding reactions (entries 4, 5 and 7), the intermolecular substitution reaction is the dominant pathway and slower than the intramolecular nucleophilic displacement, which is experimentally demonstrated by the evaluation of reactions (entry 1, 92% *vs.* entry 7, 20%); the NHP-ethoxy-mediated reaction, which provided a significantly reduced yield (entry 7, 20%), proved the thiourea moiety as an important accelerator for this intramolecular nucleophilic substitution route.

Next, we evaluated the substrate scope of different NHP thioureas on the conjugate addition reaction given in Table 3. The electron-rich NHPs **2h**, **2i** were well tolerated and afforded the corresponding Michael products in good yields of 79% and 77%, respectively. When the 2,6-diisopropyl-phenyl-NHP **2j** was evaluated under the standard reaction conditions, the Michael adduct was not observed due to severe steric hindrance. In addition, we explored the scope of this reaction with variously substituted *N*-aryl, alkyl maleimides and phenyl-NHP thiourea **2a**, summarized in Table 3. Maleimides with both electron-donating and -withdrawing groups on the aryl groups were well tolerated under the reaction conditions and afforded the corresponding Michael adducts with good yields (**3e–3j**). 3,5-di-chloro-phenyl maleimide **1l** reacted smoothly and afforded the corresponding Michael adduct **3l** in 78% yield. Notably, highly hindered 2,6-diisopropyl phenyl-substituted *N*-aryl maleimide **1m** and trisubstituted *N*-aryl maleimide **1n** provided the desired products in 44% and 46%, respectively (**3m**, **3n**). Additionally, the 3-pyridyl substituted *N*-aryl maleimide **1o** also reacted with NHP **2a** and provided the corresponding Michael adduct **3o**, albeit with moderate yield (54%). Interestingly, in the case of asymmetrically *ortho*-substituted aryl groups on the maleimides (**1p**, **1q**), inseparable diastereomeric mixtures of Michael adducts (**3p**, 84%, dr = 75 : 25 and **3q**, 71%, dr = 55 : 45) were observed due to atropisomerism.[14s,20] It appeared that a maleimide with an *ortho*-Cl-substituted aryl group **1p** is more effective on increasing the diastereoselectivity than that of the polycyclic aromatic compound **1q**. Furthermore, alkyl-substituted maleimides such as benzyl- and cyclohexyl-substituted maleimides **1r**, and **1s** were also well tolerated in this phospha-Michael reaction and furnished the corresponding Michael adducts **3r** and **3s** with good yields, 67% and 62%, respectively. Furthermore, it is noteworthy that a scale-up reaction using 1.0 mmol of **2a** smoothly

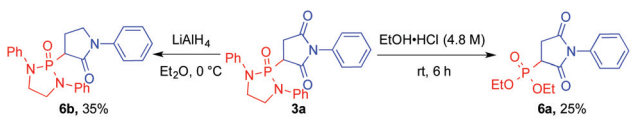
Table 3 Substrate scope of phospha-Michael reaction[a]



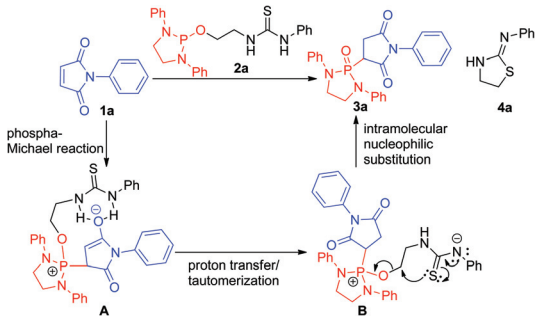
[a] All reactions were carried out using **1a** (0.15 mmol) and **2a** (0.10 mmol) in $CHCl_3$ (0.2 mL). [b] Isolated yield. [c] Determined by ^1H NMR of the crude material.

furnished the Michael adduct **3a** with 88% yield without compromising the high productivity along with the byproduct **4a** in 54% yield and the C–N bonded Michael adduct **5a** in 19%.

After exploring the substrate scope of different maleimides, we turned our attention towards a quick demonstration of the synthetic utility of the Michael adduct **3a**. The Michael adduct **3a** was treated with ethanolic-HCl to afford the ethylphosphonate **6a**.[11] Treatment of **3a** with $LiAlH_4$ allowed a selective reduction of the more accessible carbonyl group to afford a phosphino lactam **6b** (Scheme 2).



Scheme 2 Synthetic transformation.



Scheme 3 A plausible reaction mechanism.

On the basis of the results of our experiments and previous reports,[19a,d] a probable reaction pathway is illustrated in Scheme 3. The conjugate addition of bifunctional NHP **2a** to maleimide **1a** activated by hydrogen bonding with Brønsted acid generates a diazaphoshonium intermediate **A**. Then, a sequential proton transfer/tautomerization process led to an anionic thiourea intermediate **B**, which promotes the intramolecular nucleophilic displacement of diazaphoshonium by the anionic thiourea group to afford Michael adduct **3a** and thiazolidine **4a**.

Conclusions

In conclusion, we have developed highly efficient and practical phospha-Michael reaction of maleimides with NHP-thioureas without any additive or catalyst. This method is well tolerated by a wide range of maleimide derivatives, and afforded the corresponding 1-aryl-2,5-dioxopyrrolidine-3-yl-phosphonate derivatives in moderate to excellent yields (up to 92%). The reaction was readily scaled up without affecting the high reactivity. In addition, we have demonstrated the synthetic utilities of the Michael adduct **3a** to form a succinimide ethyl phosphonate **6a** and a lactam phosphonate **6b** with a selective reduction of the more accessible carbonyl group. Furthermore, this transformation has demonstrated the important role of a Brønsted acid motif essential for the intramolecular nucleophilic substitution reaction sequence to achieve additive free reaction conditions. Further studies on the asymmetric phospha-Michael reaction of maleimides with chiral bifunctional N-heterocyclic phosphine (NHP)-thioureas will be reported in due course.

Experimental

General experimental details

All reactions were carried out under an argon atmosphere in oven-dried glassware with a magnetic stirring bar. Dry solvents (THF, toluene, and DCM) were obtained by using a solvent purification system under argon. All commercially available reagents were used as received without further purification. Starting materials, NHP reagents and *N*-arylmaleimides, were

prepared by previously reported methods.[19d,21] Purification of reaction products was carried out by flash column chromatography using silica gel 60 (230–400 mesh). Analytical thin layer chromatography was performed on 0.25 mm aluminum-backed silica gel 60-F plates. UV light and $KMnO_4$ solution enabled visualization. Concentration under reduced pressure refers to the removal of volatiles using a rotary evaporator attached to a dry diaphragm pump (10–15 mmHg) followed by pumping to a constant weight with an oil pump (<300 mTorr). Infrared (IR) spectra were recorded on an IR spectrometer with KBr wafers or a film on a KBr plate. High-resolution mass spectra (HRMS) were recorded on a LCMS-IT-TOF mass spectrometer using ESI (electrospray ionization) or APCI (Atmospheric Pressure Chemical Ionization). ^{1}H NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 on a 400 MHz NMR spectrometer. The ^{1}H chemical shifts are referenced to residual solvent signals at δ 7.26 ($CHCl_3$) or δ 0.00 (TMS). ^{1}H NMR coupling constants (J) are reported in hertz (Hz) and multiplicities are indicated as follows: s (singlet), bs (broad singlet), d (doublet), t (triplet), m (multiplet), dd (doublet of doublet), td (triplet of doublet). ^{13}C NMR spectra were proton decoupled and recorded in $CDCl_3$ or DMSO-d_6 on a 100.5 MHz NMR spectrometer. The ^{13}C chemical shifts are referenced to solvent signals at δ 77.16 ($CDCl_3$). ^{31}P NMR spectra were proton decoupled and recorded in $CDCl_3$ or DMSO-d_6 on a 162 MHz NMR spectrometer. ^{31}P chemical shifts are reported relative to 85% H_3PO_4 (0.00 ppm) as an external standard.

Experimental procedure and characterization data

To a solution of NHP-thiourea **2** (0.1 mmol) in $CHCl_3$ (0.2 mL) was added maleimide **1** (0.15 mmol) in a 2 dram vial with a PTFE cap. The resulting reaction mixture was stirred at 61 °C for 19 h. After stirring for 19 h, the reaction mixture was cooled down to room temperature. The volatiles were removed under reduced pressure. The residue was subjected to column chromatography on silica gel (gradient eluent of DCM : EtOAc = 9 : 1) to give product **3**.

3-(2-Oxido-1,3-diphenyl-1,3,2-diazaphospholidin-2-yl)-1-phenylpyrrolidine-2,5-dione (3a). White solid **3a** (39.6 mg, 92%). R_f = 0.23 (DCM : EtOAc = 9 : 1); mp: 158–160 °C; IR (KBr, cm^{-1}): 3065, 2945, 2889, 1774, 1710, 1599, 1500, 1386, 1269, 1033, 962; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.39–7.30 (m, 11H), 7.13–7.10 (m, 2H), 6.66–6.64 (m, 2H), 4.16–4.11 (m, 1H), 3.91–3.72 (m, 4H), 3.48 (td, J = 19.2, 4.4 Hz, 1H), 3.19–3.08 (m, 1H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 173.9 (d, J = 5.2 Hz), 172.2 (d, J = 4.4 Hz), 140.6 (dd, J = 32.1, 8.2 Hz), 131.2, 129.9 (d, J = 19.5 Hz), 128.9, 128.7, 126.3, 123.4 (d, J = 25.4 Hz), 118.1 (dd, J = 41.9, 4.5 Hz), 44.6 (d, J = 9.7 Hz), 43.2 (d, J = 11.2 Hz), 40.6 (d, J = 106.9 Hz), 32.3 (d, J = 3.0 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$): δ 19.52 ppm; **HRMS** (ESI) calcd for $C_{24}H_{22}N_3O_3P$ [M + Na]$^+$: 454.1291; found: 454.1301.

3-(2-Oxido-1,3-di-*p*-tolyl-1,3,2-diazaphospholidin-2-yl)-1-phenylpyrrolidine-2,5-dione (3b). White solid **3b** (36.2 mg, 79%). R_f = 0.20 (DCM : EtOAc = 9 : 1); mp: 195 °C (decomp.); IR (KBr, cm^{-1}): 3034, 2922, 2891, 1780, 1712, 1614, 1514, 1383, 1269, 1031, 968; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.35–7.28 (m, 5H), 7.20–7.12 (m, 6H), 6.72–6.70 (m, 2H), 4.13–4.09 (m, 1H), 3.87–3.69 (m, 4H), 3.39 (td, J = 19.2, 4.4 Hz, 1H), 3.14–3.04 (m, 1H), 2.33 (s, 3H), 2.31 (s, 3H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 174.0 (d, J = 5.2 Hz), 172.2 (d, J = 4.5 Hz), 138.0 (dd, J = 29.9, 8.2 Hz), 133.1 (d, J = 28.4 Hz), 131.3, 130.3 (d, J = 15.7 Hz), 128.9, 128.6, 126.3, 118.4 (d, J = 27.7, 4.5 Hz), 45.0 (d, J = 9.7 Hz), 43.7 (d, J = 10.5 Hz), 40.3 (d, J = 107.7 Hz), 32.2 (d, J = 3.0 Hz), 20.6 (d, J = 2.2 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$): δ 19.46 ppm; **HRMS** (ESI) calcd for $C_{26}H_{26}N_3O_3P$ [M − H]$^-$: 458.1639; found: 458.1644.

3-(1,3-Bis(4-methoxyphenyl)-2-oxido-1,3,2-diazaphospholidin-2-yl)-1-phenylpyrrolidine-2,5-dione (3c). Pale brown solid **3c** (37.8 mg, 77%). R_f = 0.16 (DCM : EtOAc = 8 : 2); mp: 204–206 °C; IR (KBr, cm^{-1}): 3066, 2953, 2875, 1776, 1707, 1508, 1388, 1242, 1030, 970; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.41–7.34 (m, 5H), 7.28–7.26 (m, 2H), 6.93–6.86 (m, 6H), 4.10–4.07 (m, 1H), 3.79 (s, 3H), 3.79 (s, 3H), 3.77–3.36 (m, 4H), 3.22 (td, J = 18.8, 4.4 Hz, 1H), 3.08–2.98 (m, 1H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 174.0 (d, J = 6.0 Hz), 172.3 (d, J = 4.5 Hz), 156.4 (d, J = 15.6 Hz), 133.4 (dd, J = 23.9, 7.4 Hz), 131.4, 129.0, 128.6, 126.2, 121.4 (dd, J = 9.7, 4.5 Hz), 115.0 (d, J = 14.1 Hz), 55.5, 46.4 (d, J = 10.4 Hz), 45.0 (d, J = 11.1 Hz), 40.0 (d, J = 109.9 Hz), 31.9 (d, J = 2.9 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$): δ 19.48 ppm; **HRMS** (ESI) calcd for $C_{26}H_{26}N_3O_5P$ [M − H]$^-$: 490.1537; found: 490.1535.

3-(2-Oxido-1,3-diphenyl-1,3,2-diazaphospholidin-2-yl)-1-(*p*-tolyl)pyrrolidine-2,5-dione (3e). White solid **3e** (34.3 mg, 76%). R_f = 0.26 (DCM : EtOAc = 9 : 1); mp: 180–182 °C; IR (KBr, cm^{-1}): 3061, 2949, 2893, 1780, 1709, 1599, 1386, 1271, 1035, 964; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.39–7.29 (m, 8H), 7.13–7.10 (m, 4H), 6.52–6.50 (m, 2H), 4.16–4.10 (m, 1H), 3.91–3.71 (m, 4H), 3.46 (td, J = 19.2, 4.4 Hz, 1H), 3.17–3.07 (m, 1H), 2.31 (s, 3H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 174.0 (d, J = 5.2 Hz), 172.3 (d, J = 4.5 Hz), 140.6 (dd, J = 31.4, 8.2 Hz), 138.8, 129.9 (d, J = 19.5 Hz), 129.6, 128.5, 126.0, 123.3 (d, J = 23.9 Hz), 117.8 (dd, J = 41.9, 4.5 Hz), 44.5 (d, J = 9.7 Hz), 43.2 (d, J = 10.4 Hz), 40.6 (d, J = 107.7 Hz), 32.3 (d, J = 3.0 Hz), 21.1; **^{31}P NMR** (162 MHz, $CDCl_3$): δ 19.62 ppm; **HRMS** (ESI) calcd for $C_{25}H_{24}N_3O_3P$ [M − H]$^-$: 444.1483; found: 444.1478.

1-(4-Methoxyphenyl)-3-(2-oxido-1,3-diphenyl-1,3,2-diazaphospholidin-2-yl)pyrrolidine-2,5-dione (3f). White solid **3f** (35.5 mg, 77%). R_f = 0.20 (DCM : EtOAc = 9 : 1); mp: 210–212 °C; IR (KBr, cm^{-1}): 3051, 3016, 2852, 1778, 1709, 1595, 1508, 1388, 1271, 1028, 964; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.39–7.30 (m, 8H), 7.12–7.10 (m, 2H), 6.83–6.81 (m, 2H), 6.55–6.53 (m, 2H), 4.16–4.12 (m, 1H), 3.89–3.72 (m, 4H), 3.77 (s, 3H), 3.47 (td, J = 19.2, 4.0 Hz, 1H), 3.17–3.06 (m, 1H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 174.2 (d, J = 5.2 Hz), 172.3 (d, J = 4.4 Hz), 159.5, 140.6 (dd, J = 34.4, 8.2 Hz), 129.9 (d, J = 18.7 Hz), 127.5, 123.8, 123.3 (d, J = 18.7 Hz), 117.7 (dd, J = 49.3, 4.5 Hz), 114.3, 55.4, 44.5 (d, J = 10.5 Hz), 43.1 (d, J = 10.4 Hz), 40.5 (d, J = 106.9 Hz), 32.3 (d, J = 3.7 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$): δ 19.64 ppm; **HRMS** (ESI) calcd for $C_{25}H_{24}N_3O_4P$ [M − H]$^-$: 460.1432; found: 460.1432.

1-(4-Nitrophenyl)-3-(2-oxido-1,3-diphenyl-1,3,2-diazaphospholidin-2-yl)pyrrolidine-2,5-dione (3g). White solid **3g** (38.1 mg,

80%). R_f = 0.19 (DCM : EtOAc = 9 : 1); mp: 215 °C (decomp.); IR (KBr, cm^{-1}): 3117, 3074, 2949, 2901, 1776, 1716, 1597, 1519, 1494, 1384, 1348, 1035, 962; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.18–8.14 (m, 2H), 7.42–7.27 (m, 8H), 7.15–7.08 (m, 2H), 6.90–6.86 (m, 2H), 4.13–4.11 (m, 1H), 3.90–3.75 (m, 4H), 3.55 (td, J = 19.2, 4.0 Hz, 1H), 3.23–3.15 (m, 1H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 173.0 (d, J = 5.2 Hz), 171.3 (d, J = 4.5 Hz), 147.0, 140.4 (dd, J = 52.1, 8.2 Hz), 136.6, 130.0 (d, J = 20.2 Hz), 126.8, 124.0, 123.5 (d, J = 4.5 Hz), 117.6 (dd, J = 98.6, 4.4 Hz), 44.4 (d, J = 9.6 Hz), 43.3 (d, J = 10.4 Hz), 40.7 (d, J = 105.4 Hz), 32.5 (d, J = 3.7 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$): δ 18.75 ppm; **HRMS** (ESI) calcd for $C_{24}H_{21}N_4O_5P$ $[M - H]^-$: 475.1177; found: 475.1182.

1-(4-Bromophenyl)-3-(2-oxido-1,3-diphenyl-1,3,2-diazaphospholidin-2-yl)pyrrolidine-2,5-dione (3h). Pale brown solid **3h** (40.8 mg, 80%). R_f = 0.22 (DCM : EtOAc = 9 : 1); mp: 175 °C (decomp.); IR (KBr, cm^{-1}): 3065, 2970, 2893, 1776, 1712, 1599, 1489, 1384, 1031, 962; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.45–7.27 (m, 10H), 7.14–7.07 (m, 2H), 6.53–6.49 (m, 2H), 4.15–4.09 (m, 1H), 3.89–3.72 (m, 4H), 3.50 (td, J = 19.2, 4.4 Hz, 1H), 3.18–3.07 (m, 1H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 173.5 (d, J = 5.2 Hz), 171.8 (d, J = 4.5 Hz), 140.5 (dd, J = 41.9, 8.2 Hz), 132.1, 130.1, 129.9 (d, J = 19.5 Hz), 127.8, 123.4 (d, J = 6.0 Hz), 122.6, 117.7 (dd, J = 74.0, 4.5 Hz), 44.4 (d, J = 9.6 Hz), 43.2 (d, J = 10.4 Hz), 40.6 (d, J = 106.2 Hz), 32.4 (d, J = 3.8 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$): δ 19.24 ppm; **HRMS** (ESI) calcd for $C_{24}H_{21}N_3O_3PBr$ $[M - H]^-$: 508.0431; found: 508.0433.

1-(4-Chlorophenyl)-3-(2-oxido-1,3-diphenyl-1,3,2-diazaphospholidin-2-yl)pyrrolidine-2,5-dione (3i). Pale brown solid **3i** (34.9 mg, 75%). R_f = 0.21 (DCM : EtOAc = 9 : 1); mp: 176–178 °C; IR (KBr, cm^{-1}): 3063, 2966, 2897, 1778, 1716, 1599, 1492, 1388, 1033, 964; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.41–7.27 (m, 10H), 7.14–7.07 (m, 2H), 6.59–6.56 (m, 2H), 4.15–4.08 (m, 1H), 3.89–3.72 (m, 4H), 3.50 (td, J = 19.2, 4.4 Hz, 1H), 3.18–3.08 (m, 1H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 173.6 (d, J = 5.2 Hz), 171.9 (d, J = 4.5 Hz), 140.6 (dd, J = 41.6, 8.1 Hz), 134.5, 129.9 (d, J = 18.6 Hz), 129.6, 129.1, 127.5, 123.4 (d, J = 6.7 Hz), 117.7 (dd, J = 72.9, 4.5 Hz), 44.4 (d, J = 9.7 Hz), 43.2 (d, J = 11.2 Hz), 40.6 (d, J = 106.2 Hz), 32.4 (d, J = 3.0 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$): δ 19.24 ppm; **HRMS** (ESI) calcd for $C_{24}H_{21}N_3O_3PCl$ $[M - H]^-$: 464.0936; found: 464.0940.

1-(4-Fluorophenyl)-3-(2-oxido-1,3-diphenyl-1,3,2-diazaphospholidin-2-yl)pyrrolidine-2,5-dione (3j). White solid **3j** (35.5 mg, 79%). R_f = 0.17 (DCM : EtOAc = 9 : 1); mp: 190 °C (decomp.); IR (KBr, cm^{-1}): 3065, 2926, 2879, 1776, 1712, 1599, 1514, 1394, 10 312, 964; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.41–7.28 (m, 8H), 7.14–7.08 (m, 2H), 7.01–6.97 (m, 2H), 6.61–6.57 (m, 2H), 4.17–4.10 (m, 1H), 3.91–3.70 (m, 4H), 3.50 (td, J = 19.2, 4.0 Hz, 1H), 3.18–3.08 (m, 1H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 173.8 (d, J = 4.4 Hz), 172.1 (d, J = 4.5 Hz), 163.4, 160.9, 140.6 (dd, J = 42.4, 8.2 Hz), 129.9 (d, J = 17.9 Hz), 128.1 (d, J = 9.0 Hz), 123.3 (d, J = 5.9 Hz), 117.7 (dd, J = 72.9, 4.5 Hz), 116.0 (d, J = 23.1 Hz), 44.4 (d, J = 9.7 Hz), 43.2 (d, J = 10.5 Hz), 40.6 (d, J = 106.1 Hz), 32.4 (d, J = 3.0 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$): δ 19.35 ppm; **HRMS** (ESI) calcd for $C_{24}H_{21}N_3O_3FP$ $[M - H]^-$: 448.1232; found: 448.1236.

1-(3-Chlorophenyl)-3-(2-oxido-1,3-diphenyl-1,3,2-diazaphospholidin-2-yl)pyrrolidine-2,5-dione (3k). Pale yellow solid **3k** (35.8 mg, 77%). R_f = 0.21 (DCM : EtOAc = 9 : 1); mp: 170–172 °C; IR (KBr, cm^{-1}): 3082, 2987, 2874, 1778, 1712, 1595, 1383, 1031, 964; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.41–7.34 (m, 6H), 7.30–7.24 (m, 4H), 7.14–7.10 (m, 2H), 6.61 (dt, J = 3.2, 1.2 Hz, 1H), 6.61 (t, J = 2.0 Hz, 1H), 4.15–4.09 (m, 1H), 3.90–3.72 (m, 4H), 3.51 (td, J = 19.2, 4.0 Hz, 1H), 3.19–3.08 (m, 1H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 173.4 (d, J = 4.5 Hz), 171.7 (d, J = 4.4 Hz), 140.5 (dd, J = 38.0, 8.2 Hz), 134.5, 132.1, 129.9 (d, J = 27.5 Hz), 129.8, 128.9, 126.6, 124.4, 123.4 (d, J = 15.6 Hz), 117.6 (dd, J = 85.3, 4.5 Hz), 44.4 (d, J = 9.7 Hz), 43.2 (d, J = 11.2 Hz), 40.6 (d, J = 106.2 Hz), 32.4 (d, J = 3.0 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$): δ 19.17 ppm; **HRMS** (ESI) calcd for $C_{24}H_{21}N_3O_3PCl$ $[M - H]^-$: 464.0936; found: 464.0934

1-(3,5-Dichlorophenyl)-3-(2-oxido-1,3-diphenyl-1,3,2-diazaphospholidin-2-yl)pyrrolidine-2,5-dione (3l). Pale brown solid **3l** (39.0 mg, 78%). R_f = 0.26 (DCM : EtOAc = 9 : 1); mp: 194–196 °C; IR (KBr, cm^{-1}): 3080, 2955, 2893, 1786, 1716, 1599, 1491, 1373, 1031, 964; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.41–7.34 (m, 6H), 7.30–7.27 (m, 3H), 7.15–7.11 (m, 2H), 6.50 (d, J = 2.0 Hz, 2H), 4.14–4.08 (m, 1H), 3.90–3.73 (m, 4H), 3.54 (td, J = 19.2, 3.6 Hz, 1H), 3.19–3.08 (m, 1H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 173.0 (d, J = 4.5 Hz), 171.3 (d, J = 4.4 Hz), 140.4 (dd, J = 45.3, 8.1 Hz), 135.0, 132.7, 130.0 (d, J = 32.7 Hz), 128.8, 124.9, 123.5 (d, J = 5.2 Hz), 117.5 (dd, J = 119.5, 4.5 Hz), 44.3 (d, J = 9.7 Hz), 43.2 (d, J = 11.1 Hz), 40.7 (d, J = 104.7 Hz), 32.5 (d, J = 3.7 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$): δ 18.78 ppm; **HRMS** (ESI) calcd for $C_{24}H_{20}N_3O_3PCl_2$ $[M - H]^-$: 498.0547; found: 498.0547.

1-(2,6-Diisopropylphenyl)-3-(2-oxido-1,3-diphenyl-1,3,2-diazaphospholidin-2-yl)pyrrolidine-2,5-dione (3m). White solid **3m** (22.7 mg, 44%). R_f = 0.29 (DCM : EtOAc = 9 : 1); mp: 252–254 °C; IR (KBr, cm^{-1}): 3061, 2964, 2868, 1778, 1707, 1600, 1502, 1502, 1373, 1269, 1033, 962; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.45–7.32 (m, 9H), 7.18–7.12 (m, 3H), 7.10–7.06 (m, 1H), 4.28–4.24 (m, 1H), 3.95–3.74 (m, 4H), 3.62–3.51 (m, 1H), 3.34–3.24 (m, 1H), 2.36–2.29 (m, 1H) 2.06–1.99 (m, 1H), 1.08–1.03 (m, 1H), 0.91–0.89 (m, 3H), 0.68–0.67 (m, 3H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 174.8 (d, J = 8.2 Hz), 172.9 (d, J = 3.7 Hz), 145.9 (d, J = 71.0 Hz), 141.0 (dd, J = 74.7, 8.1 Hz), 130.3, 129.8 (d, J = 8.2 Hz), 124.0 (d, J = 3.0 Hz), 123.1 (d, J = 52.3 Hz), 117.6 (dd, J = 154.8, 3.7 Hz), 44.1 (d, J = 9.7 Hz), 42.5 (d, J = 11.1 Hz), 40.6 (d, J = 114.3 Hz), 32.1 (d, J = 3.0 Hz), 29.1 (d, J = 29.8 Hz), 23.8 (d, J = 3.7 Hz), 23.6; **^{31}P NMR** (162 MHz, $CDCl_3$): δ 20.59 ppm; **HRMS** (ESI) calcd for $C_{30}H_{34}N_3O_3P$ $[M - H]^-$: 514.2265; found: 514.2268.

3-(2-Oxido-1,3-diphenyl-1,3,2-diazaphospholidin-2-yl)-1-(3,4,5-trimethoxyphenyl)pyrrolidine-2,5-dione (3n). White solid **3n** (23.9 mg, 46%). R_f = 0.2 (DCM : EtOAc = 8 : 2); mp: 178–180 °C; IR (KBr, cm^{-1}): 3065, 2939, 2893, 1780, 1716, 1599, 1269, 1033, 964; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.43–7.40 (m, 4H), 7.39–7.30 (m, 4H), 7.15–7.12 (m, 1H), 7.09–7.05 (m, 1H), 5.86 (s, 2H), 4.22–4.15 (m, 1H), 3.93–3.74 (m, 4H), 3.80 (s, 3H), 3.72 (s, 6H), 3.55 (td, J = 19.2, 4.4 Hz, 1H), 3.22–3.12 (m, 1H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 174.0 (d, J =

4.4 Hz), 153.4, 140.7 (dd, J = 59.8, 8.2 Hz), 138.3, 129.9 (d, J = 12.7 Hz), 126.6, 124.9, 123.2 (d, J = 35.1 Hz), 117.5 (dd, J = 119.5, 4.5 Hz), 104.0, 60.7, 56.2, 44.2 (d, J = 9.7 Hz), 43.1 (d, J = 10.4 Hz), 40.5 (d, J = 106.9 Hz), 32.4 (d, J = 3.0 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$): δ 19.60 ppm; **HRMS** (ESI) calcd for $C_{27}H_{28}N_3O_6P$ $[M - H]^-$: 520.1643; found: 520.1651.

3-(2-Oxido-1,3-diphenyl-1,3,2-diazaphospholidin-2-yl)-1-(pyridin-3-yl)pyrrolidine-2,5-dione (3o). White solid **3o** (23.3 mg, 54%). R_f = 0.13 (DCM : EtOAc = 9 : 1); mp: 162–164 °C; IR (KBr, cm^{-1}): 3063, 2945, 2891, 1774, 1714, 1599, 1492, 1383, 1269, 1031, 964; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.53 (dd, J = 4.8, 1.2 Hz, 1H), 7.96 (d, J = 2.0 Hz, 1H), 7.42–7.24 (m, 9H), 7.15–7.09 (m, 2H), 7.03–6.99 (m, 1H), 4.15–4.12 (m, 1H), 3.91–3.73 (m, 4H), 3.54 (td, J = 19.2, 4.0 Hz, 1H), 3.22–3.12 (m, 1H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 173.4 (d, J = 5.2 Hz), 171.7 (d, J = 4.5 Hz), 149.4, 147.2, 140.5 (dd, J = 42.4, 8.1 Hz), 133.6, 120.0 (d, J = 23.1 Hz), 128.1, 123.5 (d, J = 14.4 Hz), 117.7 (dd, J = 81.1, 4.5 Hz), 44.5 (d, J = 10.4 Hz), 43.3 (d, J = 11.2 Hz), 40.8 (d, J = 104.9 Hz), 32.5 (d, J = 3.0 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$): δ 18.9 ppm; **HRMS** (ESI) calcd for $C_{23}H_{21}N_4O_3P$ $[M - H]^-$: 431.1279; found: 431.1289.

1-(2-Chlorophenyl)-3-(2-oxido-1,3-diphenyl-1,3,2-diazaphospholidin-2-yl)pyrrolidine-2,5-dione (3p). White solid **3p** (39.1 mg, 84%), dr: 75 : 25. R_f = 0.23 (DCM : EtOAc = 9 : 1); IR (KBr, cm^{-1}): 3049, 2955, 2897, 1786, 1718, 1597, 1384, 1035, 962; a racemic mixture of diastereomers, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.43–7.26 (m, 12.70H), 7.16–7.02 (m, 3.67H), 5.93–5.91 (m, 0.85H), 4.22–4.11 (m, 1.32H), 3.94–3.72 (m, 5.21H), 3.60 (td, J = 19.2, 4.0 Hz, 1H), 3.50–3.39 (m, 0.34H), 3.32–3.15 (m, 1.31H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 173.2 (d, J = 5.2 Hz), 173.1, 171.6 (d, J = 4.4 Hz), 171.3 (d, J = 4.4 Hz), 140.5 (dd, J = 59.0, 8.2 Hz), 140.5 (dd, J = 67.7, 8.2 Hz), 132.3, 131.9, 130.6 (d, J = 49.9 Hz), 130.4 (d, J = 47.7 Hz), 129.9 (d, J = 25.4 Hz), 129.7 (d, J = 2.2 Hz), 129.5, 129.4 (d, J = 23.2 Hz) 118.2 (dd, J = 44.9, 4.5 Hz), 117.4 (dd, J = 121.9, 4.5 Hz), 44.8 (d, J = 10.4 Hz), 44.1 (d, J = 9.7 Hz), 42.9 (d, J = 11.2 Hz), 42.8 (d, J = 11.1 Hz), 40.9 (d, J = 106.2 Hz), 40.5 (d, J = 114.4 Hz), 32.8 (d, J = 3.0 Hz), 32.0 (d, J = 3.0 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$): δ 19.45 and 19.26 ppm; **HRMS** (ESI) calcd for $C_{24}H_{21}N_3O_3PCl$ $[M - H]^-$: 464.0936; found: 464.0941

1-(Naphthalen-1-yl)-3-(2-oxido-1,3-diphenyl-1,3,2-diazaphospholidin-2-yl)pyrrolidine-2,5-dione (3q). White solid **3q** (34 mg, 71%), dr: 55 : 45 R_f = 0.25 (DCM : EtOAc = 9 : 1); IR (KBr, cm^{-1}): 3066, 2928, 2895, 1774, 1716, 1597, 1375, 1033, 962; a racemic mixture of diastereomers, **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.89–7.82 (m, 3.65H), 7.48–7.34 (m, 19.24H), 7.32–7.25 (m, 4.03), 7.21–7.11 (m, 5.63H), 6.54 (dd, J = 8.8, 0.8 Hz, 0.79H), 6.04 (dd, J = 67.7, 8.2 Hz, 1H), 4.20–4.09 (m, 1.99H), 4.07–3.71 (m, 8.46H), 3.69–3.60 (m, 1.92H), 3.43–3.26 (m, 2.10H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 174.3 (d, J = 5.9 Hz), 173.8 (d, J = 4.5 Hz), 172.5 (d, J = 4.4 Hz), 141.4, 141.3, 141.0, 140.9, 140.5, 140.4, 134.2, 134.1, 130.1, 130.0, 129.8, 129.1, 128.8, 128.6, 128.4, 128.1, 127.8, 127.4, 127.1, 126.4, 125.9, 125.1, 125.0, 123.3, 123.2, 121.6, 121.5, 117.8 (dd, J = 74.0, 4.5 Hz), 117.4 (dd, J = 94.2, 4.4 Hz), 44.4 (d, J = 9.7 Hz), 44.1 (d, J = 9.7 Hz), 42.9 (d, J = 11.2 Hz), 42.7 (d, J = 11.2 Hz), 41.3 (d, J = 115.1 Hz), 40.8 (d, J = 104.0 Hz), 32.9 (d, J = 3.0 Hz), 32.3; **^{31}P NMR** (162 MHz, $CDCl_3$): δ 19.85 and 19.48 ppm; **HRMS** (ESI) calcd for $C_{28}H_{24}N_3O_3P$ $[M - H]^-$: 480.1483; found: 480.1492

1-Benzyl-3-(2-oxido-1,3-diphenyl-1,3,2-diazaphospholidin-2-yl) pyrrolidine-2,5-dione (3r). White solid **3r** (29.8 mg, 67%). R_f = 0.13 (DCM : EtOAc = 9 : 1); mp: 138–140 °C; IR (KBr, cm^{-1}): 3057, 2947, 2893, 1772, 1701, 1599, 1396, 1271, 1033, 964; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.36–7.35 (m, 4H), 7.25–7.20 (m, 7H), 7.11–7.07 (m, 4H), 4.25 (d, J = 1.6 Hz, 2H), 4.15–4.09 (m, 1H), 3.81–3.60 (m, 4H), 3.14 (td, J = 19.2, 4.4 Hz, 1H), 2.96–2.86 (m, 1H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 174.5 (d, J = 5.2 Hz), 172.6 (d, J = 4.5 Hz), 140.5 (dd, J = 11.9, 8.2 Hz), 135.2, 129.7 (d, J = 5.2 Hz), 128.7 (d, J = 32.1 Hz), 128.0, 123.9, 123.0, 118.3 (dd, J = 91.9, 4.5 Hz), 45.0 (d, J = 9.7 Hz), 43.3 (d, J = 10.4 Hz), 42.4, 40.4 (d, J = 109.2 Hz), 31.8 (d, J = 3.0 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$): δ 19.57 ppm; **HRMS** (ESI) calcd for $C_{25}H_{24}N_3O_3P$ $[M - H]^-$: 444.1483; found: 444.1483.

1-Cyclohexyl-3-(2-oxido-1,3-diphenyl-1,3,2-diazaphospholidin-2-yl)pyrrolidine-2,5-dione (3s). White solid **3s** (27.1 mg, 62%). R_f = 0.14 (DCM : EtOAc = 9 : 1); mp: 206–208 °C; IR (KBr, cm^{-1}): 3061, 2933, 2860, 1764, 1697, 1600, 1506, 1388, 1271, 1035, 958; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.39–7.34 (m, 4H), 7.31–7.24 (m, 4H), 7.11–7.07 (m, 1H), 7.05–7.01 (m, 1H), 4.20–4.14 (m, 1H), 3.94–3.56 (m, 4H), 3.21 (td, J = 19.2, 4.4 Hz, 1H), 2.96–2.86 (m, 1H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 175.0 (d, J = 5.2 Hz), 173.1 (d, J = 3.7 Hz), 140.7 (dd, J = 23.0, 7.4 Hz), 129.7, 123.1 (d, J = 19.4 Hz), 117.6 (dd, J = 31.3, 4.5 Hz), 52.0, 44.5 (d, J = 9.7 Hz), 43.0 (d, J = 10.4 Hz), 40.1 (d, J = 109.9 Hz), 31.8 (d, J = 3.0 Hz), 28.1 (d, J = 2.0 Hz), 25.6 (d, J = 3.0 Hz), 24.8; **^{31}P NMR** (162 MHz, $CDCl_3$): δ 20.37 ppm; **HRMS** (ESI) calcd for $C_{24}H_{28}N_3O_3P$ $[M - H]^-$: 436.1796; found: 436.1795.

(*E*)-*N*-Phenylthiazolidin-2-imine (4a).[22] White solid (10.7 mg, 60%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ. 7.28 (t, J = 7.6 Hz, 2H), 7.13 (d, J = 7.6 Hz, 2H), 7.04 (t, J = 7.2 Hz, 1H), 3.82 (t, J = 7.0 Hz, 2H), 3.30 (t, J = 7.2 Hz, 2H).

(*E*)-*N*-(4-Methoxyphenyl)thiazolidin-2-imine (4b). White solid (10.7 mg, 55%); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.07 (d, J = 8.8 Hz, 2H), 6.84 (d, J = 8.8 Hz, 2H), 3.83 (t, J = 6.8 Hz, 2H), 3.78 (s, 3H), 3.35–3.29 (m, 2H).

(*E*)-*N*-(3,5-Bis(trifluoromethyl)phenyl)thiazolidin-2-imine (4c).[23] White solid (18.8 mg, 60%); R_f = 0.4 (hexanes : EtOAc : DCM = 4 : 4 : 1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.52–7.51 (m, 1H), 7.47 (bs, 2H), 3.75 (t, J = 7.2 Hz, 2H), 3.37 (t, J = 7.2 Hz, 2H); **HRMS** (ESI) calcd for $C_{11}H_8N_2F_6S$ $[M - H]^-$: 313.0240; found: 313.0249.

(*E*)-3-Methyl-*N*-phenylthiazolidin-2-imine (4d).[22] Colorless semisolid (3.8 mg, 20%); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.28–7.24 (m, 2H), 7.05–7.03 (m, 1H), 6.95–6.93 (m, 2H), 3.58 (t, J = 6.8 Hz, 2H), 3.14 (t, J = 6.8 Hz, 2H), 3.05 (s, 3H).

1-Tosylaziridine (4f). White solid (10.8 mg, 55%); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.84–7.81 (m, 2H), 7.36–7.33 (m, 2H), 2.45 (s, 3H), 2.36 (bs, 4H).

3-((4,5-Dihydrothiazol-2-yl)(phenyl)amino)-1-phenylpyrrolidine-2,5-dione (5a). White solid (7.0 mg, 20%); R_f = 0.38 (DCM : EtOAc = 9 : 1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.44–7.34 (m, 3H), 7.28–7.22 (m, 4H), 7.06–7.02 (m, 1H), 6.89–6.87 (m, 2H), 4.61–4.57 (m, 1H), 3.96–3.90 (m, 1H), 3.76–3.71 (m, 3H),

3.40–3.25 (m, 3H), 3.19–3.12 (m, 1H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 174.4, 173.9, 157.1, 150.3, 132.0, 129.1, 128.9, 128.6, 126.7, 123.5, 121.6, 55.5, 51.8, 33.0, 27.6; **HRMS** (ESI) calcd for $C_{19}H_{17}N_3O_2S$ $[M + Na]^+$: 374.0934; found: 374.0929.

3-((4,5-Dihydrothiazol-2-yl)(4-methoxyphenyl)amino)-1-phenylpyrrolidine-2,5-dione (5b). Colorless semisolid (9.5 mg, 25%); R_f = 0.11 hexanes : EtOAc : DCM = 4 : 4 : 1; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.44–7.34 (m, 4H), 7.24–7.22 (m, 2H), 6.84–6.78 (m, 3H), 4.59–4.55 (m, 1H), 3.95–3.89 (m, 1H), 3.77 (s, 3H), 3.74–3.69 (m, 1H), 3.36–3.25 (m, 3H), 3.18–3.11 (m, 1H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 174.4, 174.0, 156.8, 155.9, 143.7, 132.0, 129.1, 128.6, 126.7, 122.4, 114.1, 55.6, 55.4, 51.8, 33.0, 27.6; **HRMS** (ESI) calcd for $C_{20}H_{19}N_3O_3S$ $[M + H]^+$: 382.1220; found: 382.1216.

Procedure for the synthesis of diethyl(2,5-dioxo-1-phenylpyrrolidin-3-yl)phosphonate (6a)[11]

A solution of **3a** (51 mg, 0.118 mmol) in 4.8 M ethanolic HCl (1.18 mL) was stirred for 6 h at room temperature. After stirring for 6 h, volatiles were removed under reduced pressure. The residue was dissolved in EtOAc, filtered, dried over Na_2SO_4, filtered again, and concentrated under reduced pressure. Then it was subjected to column chromatography on silica gel (gradient eluent of DCM : acetone = 9 : 1) to give product **6a**.

Semisolid **6a** (11 mg, 25%). R_f = 0.25 (DCM : acetone = 9 : 1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.50–7.45 (m, 2H), 7.42–7.38 (m, 1H), 7.29–7.26 (m, 2H), 4.32–4.20 (m, 4H), 3.50–3.41 (m, 1H), 3.25–3.07 (m, 2H), 1.41–1.35 (m, 6H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 173.9 (d, J = 5.2 Hz), 171.2 (d, J = 6.0 Hz), 131.6, 129.2, 128.8, 126.4, 63.8 (d, J = 6.7 Hz), 63.2 (d, J = 6.7 Hz), 39.6 (d, J = 141.3 Hz), 30.8 (d, J = 4.4 Hz), 16.3 (t, J = 6.0 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$): δ 20.3 ppm.

Procedure for the synthesis of 3-(2-oxido-1,3-diphenyl-1,3,2-diazaphospholidin-2-yl)-1-phenylpyrrolidin-2-one (6b)

Under an argon atmosphere, a solution of **3a** (20 mg, 0.046 mmol) in DCM (0.5 mL) was added slowly to a slurry of $LiAlH_4$ (6.8 mg, 0.18 mmol) in Et_2O (0.25 mL) at 0 °C. The reaction mixture was stirred at room temperature for 4 h and water was added dropwise at 0 °C. The resulting suspension was filtered and washed with ethyl acetate. The filtrate was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was subjected to column chromatography on silica gel (gradient eluent of hexanes : EtOAc : DCM = 4 : 4 : 1) to give product **6b**.

White solid, **6b** (5.7 mg, 35%). R_f = 0.20 (hexanes : EtOAc : DCM = 4 : 4 : 1); IR (KBr, cm^{-1}): 3059, 2931, 2887, 1695, 1599, 1498, 1388, 1273, 949; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.39–7.35 (m, 6H), 7.30–7.22 (m, 6H), 7.19–7.13 (m, 2H), 7.12–7.04 (m, 2H), 4.15–4.07 (m, 1H), 4.97–4.90 (m, 1H), 3.78–3.71 (m, 1H), 3.78–3.53 (m, 3H), 3.52–3.40 (m, 1), 3.03–2.98 (m, 1H), 2.64–2.56 (m, 1H), 2.47–2.39 (m, 1H); **^{13}C NMR** ($CDCl_3$, 100.5 MHz): δ 169.0, 141.2 (t, J = 8.2 Hz), 138.6, 129.5 (d, J = 15.6 Hz), 128.6, 124.9, 122.8 (d, J = 91.9 Hz), 120.3, 118.4 (dd, J = 163.7, 4.4 Hz), 47.0 (d, J = 3.0 Hz), 45.1 (d, J = 9.7 Hz), 43.8 (d, J = 107.7 Hz), 43.2, 43.0 (d, J = 10.5 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$): δ 14.71 ppm; **HRMS** (ESI) calcd for $C_{24}H_{24}N_3O_2P$ $[M + Na]^+$: 440.1498; found: 440.1483.

This work was financially supported by the University of Nevada Las Vegas (Star-up fund and Faculty Opportunity Awards). Dr Katarzyna Lorenc-Kukula (SCAAC) is acknowledged for mass spectra data and Hai Huang is acknowledged for his assistance in purification.

Notes and references

1 M. Horiguchi and M. Kandatstu, *Nature*, 1959, **184**, 901–902.

2 (*a*) L. D. Quin, *A guide to organophosphorus chemistry*, John Wiley & Sons, 2000; (*b*) R. Engel, *Synthesis of carbon-phosphorus bonds*, CRC press, 2003.

3 T. Focken and S. Hanessian, *Beilstein J. Org. Chem.*, 2014, **10**, 1848–1877.

4 (*a*) S. Maitra, M. Bodugam, S. Javed and P. R. Hanson, *Org. Lett.*, 2016, **18**, 3094–3097; (*b*) C. D. Thomas, J. P. McParland and P. R. Hanson, *Eur. J. Org. Chem.*, 2009, 5487–5500; (*c*) P. R. Hanson, R. Chegondi, J. Nguyen, C. D. Thomas, J. D. Waetzig and A. Whitehead, *J. Org. Chem.*, 2011, **76**, 4358–4370; (*d*) S. Jayasinghe, P. K. M. Venukadasula and P. R. Hanson, *Org. Lett.*, 2014, **16**, 122–125; (*e*) R. Chegondi, M. M. L. Tan and P. R. Hanson, *J. Org. Chem.*, 2011, **76**, 3909–3916; (*f*) M. Bodugam, S. Javed, A. Ganguly, J. Torres and P. R. Hanson, *Org. Lett.*, 2016, **18**, 516–519; (*g*) S. Javed, M. Bodugam, J. Torres, A. Ganguly and P. R. Hanson, *Chem. – Eur. J.*, 2016, **22**, 6755–6758.

5 (*a*) W. W. Metcalf and W. A. van der Donk, *Annu. Rev. Biochem.*, 2009, **78**, 65–94; (*b*) C. S. Demmer, N. Krogsgaard-Larsen and L. Bunch, *Chem. Rev.*, 2011, **111**, 7981–8006; (*c*) S. C. Fields, *Tetrahedron*, 1999, **55**, 12237–12273; (*d*) H. Seto and T. Kuzuyama, *Nat. Prod. Rep.*, 1999, **16**, 589–596.

6 (*a*) S. Ghosh, J. M. W. Chan, C. R. Lea, G. A. Meints, J. C. Lewis, Z. S. Tovian, R. M. Flessner, T. C. Loftus, I. Bruchhaus, H. Kendrick, S. L. Croft, R. G. Kemp, S. Kobayashi, T. Nozaki and E. Oldfield, *J. Med. Chem.*, 2004, **47**, 175–187; (*b*) R. Yang, R. Zhao, D. Chen, L. Shan, L. Yun and H. Wang, *Bioorg. Med. Chem. Lett.*, 2004, **14**, 3017–3025; (*c*) P. Chaudhary, R. Kumar, A. K. Verma, D. Singh, V. Yadav, A. K. Chhillar, G. L. Sharma and R. Chandra, *Bioorg. Med. Chem.*, 2006, **14**, 1819–1826; (*d*) S. Younes, *J. Pharm. Belg.*, 1994, **49**, 119–125; (*e*) J. Lewkowski, A. Jóźwiak, P. Tokarz, P. M. Zagórski, R. Hamera, D. Cal, G. Satała and A. J. Bojarski, *Heteroat. Chem.*, 2015, **26**, 290–298; (*f*) E. Maerten, S. Cabrera and K. A. Jørgensen, *J. Org. Chem.*, 2007, **72**, 8893–8903; (*g*) H. Kluender, G. Benz, D. Brittelli, W. Bullock, K. Combs, B. Dixon, S. Schneider, J. Wood, M. Vanzandt and D. Wolanin, *US Pat. Appl.* US 95-539409951106, 1998; *Chem. Abstr.* 1998, 161412; (*h*) C. F. Schwender, S. A. Beers,

E. Malloy, K. Demarest, L. Minor and K. H. W. Lau, *Bioorg. Med. Chem. Lett.*, 1995, **5**, 1801–1806; (*i*) H. Jomaa, J. Wiesner, S. Sanderbrand, B. Altincicek, C. Weidemeyer, M. Hintz, I. Türbachova, M. Eberl, J. Zeidler, H. K. Lichtenthaler, D. Soldati and E. Beck, *Science*, 1999, **285**, 1573–1576; (*j*) P. Kafarski and B. Lejczak, *Phosphorus, Sulfur Silicon Relat. Elem.*, 1991, **63**, 193–215; (*k*) F. Palacios, C. Alonso and J. M. de los Santos, *Chem. Rev.*, 2005, **105**, 899–932.

7 B. Rudolf, M. Salmain, M. Palusiak and J. Zakrzewski, *J. Organomet. Chem.*, 2009, **694**, 908–915.

8 P. Blokker, J. S. Gill and P. López-Serrano, *US* 9133046B2, 2015.

9 (*a*) U. Nagel and B. Rieger, *Organometallics*, 1989, **8**, 1534–1538; (*b*) A. M. d. A. R. Gonsalves, M. E. d. S. Serra, M. R. Silva, A. M. Beja, J. A. Paixão and L. A. d. Veiga, *J. Mol. Catal. A: Chem.*, 2001, **168**, 53–59.

10 (*a*) A. Y. Rulev, *RSC Adv.*, 2014, **4**, 26002–26012; (*b*) D. Enders, A. Saint-Dizier, M.-I. Lannou and A. Lenzen, *Eur. J. Org. Chem.*, 2006, 29–49.

11 E. Bálint, J. Takács, L. Drahos and G. Keglevich, *Heteroat. Chem.*, 2012, **23**, 235–240.

12 (*a*) N. E. Sharpless and M. Flavin, *Biochemistry*, 1966, **5**, 2963–2971; (*b*) B. D. Mather, K. Viswanathan, K. M. Miller and T. E. Long, *Prog. Polym. Sci.*, 2006, **31**, 487–531; (*c*) D. R. Maulding, *J. Heterocycl. Chem.*, 1988, **25**, 1777–1779; (*d*) R. N. Ram and K. Varsha, *Synth. Commun.*, 1991, **21**, 121–126; (*e*) E. Velchinskaya, B. Petsushak and A. Rogal, *Chem. Heterocycl. Compd.*, 2007, **43**, 695–700.

13 (*a*) B. D. Chandler, A. L. Burkhardt, K. Foley, C. Cullis, D. Driscoll, N. Roy D'Amore and S. J. Miller, *J. Am. Chem. Soc.*, 2014, **136**, 412–418; (*b*) X. Elduque, E. Pedroso and A. Grandas, *Org. Lett.*, 2013, **15**, 2038–2041; (*c*) J. L. Zimmermann, T. Nicolaus, G. Neuert and K. Blank, *Nat. Protoc.*, 2010, **5**, 975–985.

14 (*a*) A.-N. R. Alba, G. Valero, T. Calbet, M. Font-Bardía, A. Moyano and R. Rios, *Chem. – Eur. J.*, 2010, **16**, 9884–9889; (*b*) R. Ballini, G. Bosica, G. Cioci, D. Fiorini and M. Petrini, *Tetrahedron*, 2003, **59**, 3603–3608; (*c*) Y.-L. Guo, L.-N. Jia, L. Peng, L.-W. Qi, J. Zhou, F. Tian, X.-Y. Xu and L.-X. Wang, *RSC Adv.*, 2013, **3**, 16973–16976; (*d*) M. S. Manna and S. Mukherjee, *Chem. – Eur. J.*, 2012, **18**, 15277–15282; (*e*) P. Chauhan, J. Kaur and S. S. Chimni, *Chem. – Asian J.*, 2013, **8**, 328–346; (*f*) L. Zu, H. Xie, H. Li, J. Wang, W. Jiang and W. Wang, *Adv. Synth. Catal.*, 2007, **349**, 1882–1886; (*g*) G. Bartoli, M. Bosco, A. Carlone, A. Cavalli, M. Locatelli, A. Mazzanti, P. Ricci, L. Sambri and P. Melchiorre, *Angew. Chem., Int. Ed.*, 2006, **45**, 4966–4970; (*h*) Z. Jiang, Y. Pan, Y. Zhao, T. Ma, R. Lee, Y. Yang, K.-W. Huang, M. W. Wong and C.-H. Tan, *Angew. Chem., Int. Ed.*, 2009, **48**, 3627–3631; (*i*) Z. Jiang, W. Ye, Y. Yang and C.-H. Tan, *Adv. Synth. Catal.*, 2008, **350**, 2345–2351; (*j*) F. Yu, X. Sun, Z. Jin, S. Wen, X. Liang and J. Ye, *Chem. Commun.*, 2010, **46**, 4589–4591; (*k*) F. Xue, L. Liu, S. Zhang, W. Duan and W. Wang, *Chem. – Eur. J.*, 2010, **16**, 7979–7982; (*l*) Y.-H. Liao, X.-L. Liu, Z.-J. Wu, L.-F. Cun, X.-M. Zhang and W.-C. Yuan, *Org. Lett.*, 2010, **12**, 2896–2899; (*m*) E. Gómez-Torres, D. A. Alonso, E. Gómez-Bengoa and C. Nájera, *Org. Lett.*, 2011, **13**, 6106–6109; (*n*) Y.-H. Liao, X.-L. Liu, Z.-J. Wu, X.-L. Du, X.-M. Zhang and W.-C. Yuan, *Adv. Synth. Catal.*, 2011, **353**, 1720–1728; (*o*) S. Shirakawa, S. J. Terao, R. He and K. Maruoka, *Chem. Commun.*, 2011, **47**, 10557–10559; (*p*) T. C. Nugent, A. Sadiq, A. Bibi, T. Heine, L. L. Zeonjuk, N. Vankova and B. S. Bassil, *Chem. – Eur. J.*, 2012, **18**, 4088–4098; (*q*) L. Li, W. Chen, W. Yang, Y. Pan, H. Liu, C.-H. Tan and Z. Jiang, *Chem. Commun.*, 2012, **48**, 5124–5126; (*r*) J. Lu, W.-J. Zhou, F. Liu and T.-P. Loh, *Adv. Synth. Catal.*, 2008, **350**, 1796–1800; (*s*) N. Di Iorio, P. Righi, A. Mazzanti, M. Mancinelli, A. Ciogli and G. Bencivenni, *J. Am. Chem. Soc.*, 2014, **136**, 10250–10253; (*t*) G. Zhan, Q. He, X. Yuan and Y.-C. Chen, *Org. Lett.*, 2014, **16**, 6000–6003; (*u*) N. Di Iorio, F. Champavert, A. Erice, P. Righi, A. Mazzanti and G. Bencivenni, *Tetrahedron*, 2016, **72**, 5191–5201; (*v*) J. Zhang, Y. Zhang, L. Lin, Q. Yao, X. Liu and X. Feng, *Chem. Commun.*, 2015, **51**, 10554–10557; (*w*) G.-L. Zhao, Y. Xu, H. Sunden, L. Eriksson, M. Sayah and A. Cordova, *Chem. Commun.*, 2007, 734–735; (*x*) J. Wang, M.-M. Zhang, S. Zhang, Z.-A. Xu, H. Li, X.-H. Yu and W. Wang, *Synlett*, 2011, 473–476; (*y*) Z. Han, P. Li, Z. Zhang, C. Chen, Q. Wang, X.-Q. Dong and X. Zhang, *ACS Catal.*, 2016, **6**, 6214–6218; (*z*) Z.-H. Yang, Z.-H. Chen, Y.-L. An and S.-Y. Zhao, *RSC Adv.*, 2016, **6**, 23438–23447.

15 (*a*) M. Patil and S. Rajput, *Int. J. Pharm. Pharm. Sci.*, 2014, **6**, 8–14; (*b*) K. Kamiński, J. Obniska, I. Chlebek, P. Liana and E. Pękala, *Eur. J. Med. Chem.*, 2013, **66**, 12–21; (*c*) M. Sortino, A. Postigo and S. Zacchino, *Molecules*, 2013, **18**, 5669; (*d*) K. Kamiński, J. Obniska, I. Chlebek, B. Wiklik and S. Rzepka, *Bioorg. Med. Chem.*, 2013, **21**, 6821–6830; (*e*) S.-C. Chien, M.-L. Chen, H.-T. Kuo, Y.-C. Tsai, B.-F. Lin and Y.-H. Kuo, *J. Agric. Food Chem.*, 2008, **56**, 7017–7022; (*f*) S. Mahboobi, E. Eichhorn, A. Popp, A. Sellmer, S. Elz and U. Möllmann, *Eur. J. Med. Chem.*, 2006, **41**, 176–191; (*g*) M. Z. Wróbel, A. Chodkowski, F. Herold, A. Gomółka, J. Kleps, A. P. Mazurek, F. Pluciński, A. Mazurek, G. Nowak, A. Siwek, K. Stachowicz, A. Sławińska, M. Wolak, B. Szewczyk, G. Satała, A. J. Bojarski and J. Turło, *Eur. J. Med. Chem.*, 2013, **63**, 484–500; (*h*) H. Lavrard, F. Rodriguez and E. Delfourne, *Bioorg. Med. Chem.*, 2014, **22**, 4961–4967; (*i*) A. Fredenhagen, S. Y. Tamura, P. T. M. Kenny, H. Komura, Y. Naya, K. Nakanishi, K. Nishiyama, M. Sugiura and H. Kita, *J. Am. Chem. Soc.*, 1987, **109**, 4409–4411; (*j*) W. C. Groutas, M. J. Brubaker, L. S. Chong, R. Venkataraman, H. Huang, J. B. Epp, R. Kuang and J. R. Hoidal, *Bioorg. Med. Chem.*, 1995, **3**, 375–381; (*k*) H. Okamura, H. Shimizu, Y. Nakamura, T. Iwagawa and M. Nakatani, *Tetrahedron Lett.*, 2000, **41**, 4147–4150; (*l*) M. L. Curtin, R. B. Garland, H. R. Heyman, R. R. Frey, M. R. Michaelides, J. Li, L. J. Pease, K. B. Glaser, P. A. Marcotte and S. K. Davidsen, *Bioorg. Med. Chem. Lett.*, 2002, **12**, 2919–2923; (*m*) S. C. Bergmeier, K. A. Ismail, K. M. Arason, S. McKay, D. L. Bryant and D. B. McKay,

Bioorg. Med. Chem. Lett., 2004, **14**, 3739–3742; (*n*) M. Kabata, T. Suzuki, K. Takabe and H. Yoda, *Tetrahedron Lett.*, 2006, **47**, 1607–1611; (*o*) E. M. Stang and M. C. White, *J. Am. Chem. Soc.*, 2011, **133**, 14892–14895; (*p*) W. McWhorter, A. Fredenhagen, K. Nakanishi and H. Komura, *J. Chem. Soc., Chem. Commun.*, 1989, 299–301; (*q*) A. V. R. Rao, A. K. Singh and C. V. N. S. Varaprasad, *Tetrahedron Lett.*, 1991, **32**, 4393–4396; (*r*) J. Needham, M. T. Kelly, M. Ishige and R. J. Andersen, *J. Org. Chem.*, 1994, **59**, 2058–2063.

16 (*a*) Z. Jiang, Y. Zhang, W. Ye and C.-H. Tan, *Tetrahedron Lett.*, 2007, **48**, 51–54; (*b*) J. Yuan, C. Liu and A. Lei, *Org. Chem. Front.*, 2015, **2**, 677–680.

17 (*a*) A. Kraszewski and J. Stawinski, *Pure Appl. Chem.*, 2007, **79**, 2217–2227; (*b*) J. Stawinski and A. Kraszewski, *Acc. Chem. Res.*, 2002, **35**, 952–960; (*c*) G. O. Doak and L. D. Freedman, *Chem. Rev.*, 1961, **61**, 31–44; (*d*) P. Hammond, *J. Chem. Soc.*, 1962, 1365–1369.

18 V. T. Trepohl, S. Mori, K. Itami and M. Oestreich, *Org. Lett.*, 2009, **11**, 1091–1094.

19 (*a*) K. Mulla and J. Y. Kang, *J. Org. Chem.*, 2016, **81**, 4550–4558; (*b*) N. Molleti and J. Y. Kang, *Org. Biomol. Chem.*, 2016, **14**, 8952–8956; (*c*) H. Huang and J. Y. Kang, *Org. Lett.*, 2016, **18**, 4372–4375; (*d*) K. Mulla, K. L. Aleshire, P. M. Forster and J. Y. Kang, *J. Org. Chem.*, 2016, **81**, 77–88.

20 (*a*) F. Eudier, P. Righi, A. Mazzanti, A. Ciogli and G. Bencivenni, *Org. Lett.*, 2015, **17**, 1728–1731; (*b*) H. Huang, J. Fan, G. He, Z. Yang, X. Jin, Q. Liu and H. Zhu, *Chem. – Eur. J.*, 2016, **22**, 2532–2538; (*c*) W.-L. Duan, Y. Imazaki, R. Shintani and T. Hayashi, *Tetrahedron*, 2007, **63**, 8529–8536.

21 Q. Jia, L. Chen, G. Yang, J. Wang, J. Wei and Z. Du, *Tetrahedron Lett.*, 2015, **56**, 7150–7153.

22 U. Heinelt, D. Schultheis, S. Jäger, M. Lindenmaier, A. Pollex and H. S. G. Beckmann, *Tetrahedron*, 2004, **60**, 9883–9888.

23 A. Hirashima, J. Tomita, C. Pan, E. Taniguchi and M. Eto, *Bioorg. Med. Chem.*, 1997, **5**, 2121–2128.

