Tetrahedron Letters 55 (2014) 531–534

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

An expedient synthesis of pyrrole-2-phosphonates via direct oxidative phosphorylation and γ-hydroxy-γ-butyrolactams from pyrroles

Se Hee Kim, Ko Hoon Kim, Jin Woo Lim, Jae Nyoung Kim *

Department of Chemistry and Institute of Basic Science, Chonnam National University, Gwangju 500-757, Republic of Korea

ARTICLE INFO

Article history:
Received 11 October 2013
Revised 12 November 2013
Accepted 19 November 2013
Available online 28 November 2013

Keywords:
Pyrrole-2-phosphonates
Oxidative phosphorylation
γ-Hydroxy-γ-butyrolactams
Dialkyl phosphites

ABSTRACT

An expedient oxidative phosphorylation of pyrroles has been disclosed. The reaction of dialkyl phosphite and pyrrole in the presence of $AgNO_3/K_2S_2O_8$ in DMF/H_2O (8:1) produced pyrrole-2-phosphonates in good yields. In the absence of dialkyl phosphite, γ-hydroxy-γ-butyrolactam derivative was formed as a major product.

Aryl and heteroaryl phosphonates are an important class of compounds, and many of them possess interesting biological activities.[1] Among various methods for the synthesis of heteroaryl phosphonates, the dehydrogenative cross-coupling reaction of heteroarenes with phosphites has become an efficient and promising strategy.[1b] The synthesis of pyrrole phosphonates has been reported by the reaction of pyrrylmagnesium or pyrryllithium reagents with diethyl chlorophosphate; however, the yield was very low due to formation of many side products.[1b,2] Although a direct oxidative coupling method has been applied for the synthesis of pyrrole phosphonates, very simple and limited number of pyrroles have been included as entries.[3] Thus, a construction of pyrrole nucleus from the precursor bearing a phosphonate moiety is a prevalent method for the synthesis of pyrrole phosphonates until now.[4]

Recently, we reported an efficient synthesis of 5-phosphorylated uracil derivatives via a dehydrogenative cross-coupling reaction between uracil derivatives and dialkyl phosphites in the presence of $Mn(OAc)_3$ in AcOH.[5] As a continuous study, we examined the phosphorylation of pyrrole derivatives using the same cross-coupling method. Initially, we examined the reaction of 1,2,4-triphenylpyrrole (1a), as a model substrate, under the influence of $Mn(OAc)_3$ in AcOH. However, a desired product **2a** was obtained in moderate yield (43%) along with unexpected γ-hydroxy-γ-butyrolactam derivative **3a** (19%), as shown in Table 1 (entry 1).

Thus, we examined the reaction of **1a** under various conditions,[3,5–7] as summarized in Table 1. The reaction with $Mn(OAc)_3$ at room temperature (entry 2) showed a sluggish reactivity, and the amount of **3a** increased. The reaction of **1a** in the presence of $AgNO_3/K_2S_2O_8$ was also sluggish both in CH_2Cl_2/H_2O and THF/H_2O (entries 3 and 4).[3b,5] Formation of many intractable side products was observed when aqueous acetone was used as a reaction medium (entry 5). The yield of **2a** was not improved in CH_3CN/H_2O (entry 6) and in variable ratios (1:1 to 4:1) of DMF/H_2O (entries 7–9). When we used DMF/H_2O (8:1) as solvent (entry 10), **2a** could be obtained in good yield (75%); however, lactam **3a** was also formed albeit in low yield (14%). We found that the phosphorylation was somewhat sensitive to solvent composition. Such a solvent effect has been reported in many phosphorylation reactions.[3b,5,6b] Reducing the amount of $AgNO_3$ (entry 11) and the use of $Na_2S_2O_8$ (entry 12) were not effective. The use of 0.4 equiv of $AgNO_3$ (entry 13) showed a similar result to that of entry 10. The use of Ag_2SO_4 (entry 14)[6a] and AgOAc (entry 15) showed a similar result. Based on the experimental results, we selected the conditions of entry 10 as an optimum one.

Encouraged by the successful results various pyrrole derivatives **1a** and **1d–i** were prepared according to the reported methods,[8a,b,f] as shown in Table 2. The other starting materials **1j–l** were prepared as reported,[8c–e] and the phosphorylation of these compounds was examined under the optimized conditions (entry 10 in Table 1).[9] The results are summarized in Table 2. The reaction of **1a** with dimethyl phosphite and diisopropyl phosphite afforded **2b** and **2c** in 87% and 54% yields, respectively. The lower yield of **2c**

* Corresponding author. Tel.: +82 62 530 3381; fax: +82 62 530 3389.
E-mail address: kimjn@chonnam.ac.kr (J.N. Kim).

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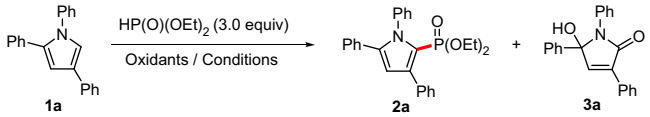
http://dx.doi.org/10.1016/j.tetlet.2013.11.082

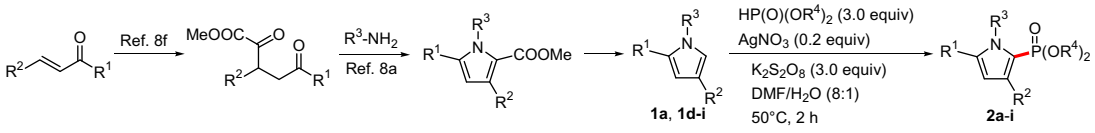
Table 1
Optimization of phosphorylation of **1a**[a]

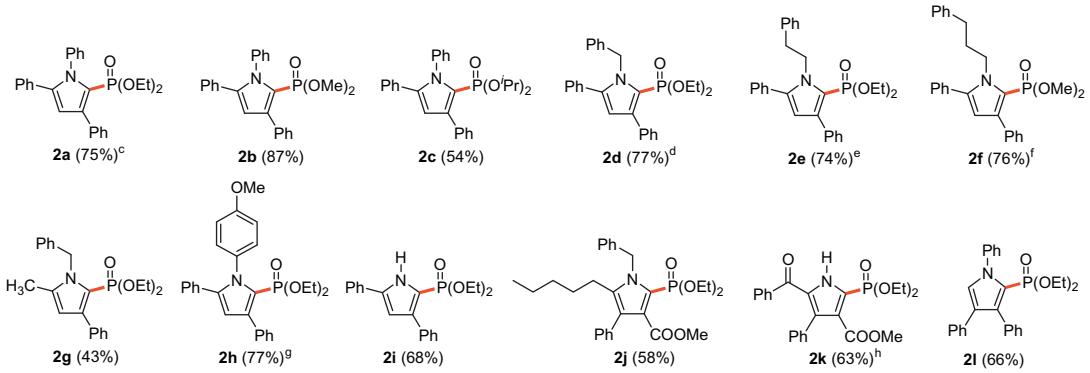


Entry	Oxidant[b]	Conditions	**1a**/**2a**/**3a** (%)[c]
1	$Mn(OAc)_3$ (3.0)	AcOH, 80 °C, 2 h	0/43/19[e]
2	$Mn(OAc)_3$ (3.0)	AcOH, 25 °C, 8 h	50/5/40
3	$AgNO_3$ (0.2)/$K_2S_2O_8$ (3.0)	CH_2Cl_2/H_2O (1:1), reflux, 4 h	85/5/trace
4	$AgNO_3$ (0.2)/$K_2S_2O_8$ (3.0)	THF/H_2O (1:1), reflux, 8 h	90/5/trace
5	$AgNO_3$ (0.2)/$K_2S_2O_8$ (3.0)	acetone/H_2O (1:1), reflux, 2 h	0/20/trace[e]
6	$AgNO_3$ (0.2)/$K_2S_2O_8$ (3.0)	CH_3CN/H_2O (1:1), reflux, 2 h	0/48/40
7	$AgNO_3$ (0.2)/$K_2S_2O_8$ (3.0)	DMF/H_2O (1:1), 80 °C, 2 h	0/40/5[e]
8	$AgNO_3$ (0.2)/$K_2S_2O_8$ (3.0)	DMF/H_2O (2:1), 50 °C, 2 h	0/55/trace[e]
9	$AgNO_3$ (0.2)/$K_2S_2O_8$ (3.0)	DMF/H_2O (4:1), 50 °C, 2 h	0/53/trace[e]
10[d]	$AgNO_3$ (0.2)/$K_2S_2O_8$ (3.0)	DMF/H_2O (8:1), 50 °C, 2 h	0/75/14
11	$AgNO_3$ (0.1)/$K_2S_2O_8$ (3.0)	DMF/H_2O (8:1), 50 °C, 2 h	0/36/45
12	$AgNO_3$ (0.2)/$Na_2S_2O_8$ (3.0)	DMF/H_2O (8:1), 50 °C, 2 h	18/38/24
13	$AgNO_3$ (0.4)/$K_2S_2O_8$ (3.0)	DMF/H_2O (8:1), 50 °C, 2 h	0/69/9
14	Ag_2SO_4 (0.2)/$K_2S_2O_8$ (3.0)	DMF/H_2O (8:1), 50 °C, 2 h	0/68/20
15	AgOAc (0.2)/$K_2S_2O_8$ (3.0)	DMF/H_2O (8:1), 50 °C, 2 h	0/68/18

[a] Pyrrole **1a** (0.2 mmol) and $HP(O)(OEt)_2$ (3.0 equiv) were used.
[b] Equivalent in parenthesis.
[c] Isolated yield (%).
[d] Pyrrole **1a** (0.5 mmol) was used.
[e] Formation of many intractable side products was observed.

Table 2
Preparation of various pyrrole-2-phosphonates **2a-l**[a,b]





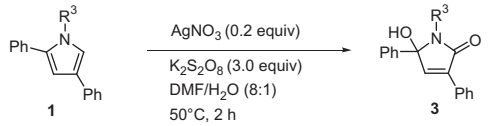
[a] Synthesis of **1a** and **1d–i** was carried out by using the reported methods.[8a,b,f]
[b] The starting materials **1j–l** for the preparation of **2j–l** were prepared according to the reported methods.[8c–e]
[c] Lactam **3a** (14%) was isolated.
[d] Lactam **3d** (13%) was isolated.
[e] Lactam **3e** (10%) was isolated.
[f] Lactam **3f** (14%) was isolated.
[g] Lactam **3h** (12%) was isolated.
[h] Reaction time was 3 h.

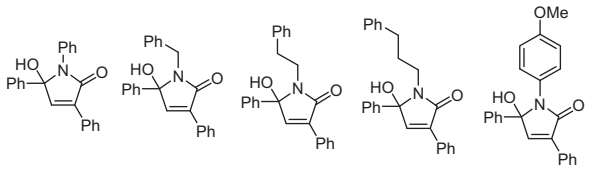
relative to **2a** or **2b** might be due to the larger size of isopropyl than the methyl or ethyl groups.[5,7a] The reactions of **1d–l** with dimethyl- or diethyl phosphite afforded **2d–l** in good to moderate yields (43–77%).

As noted above, the corresponding γ-hydroxy-γ-butyrolactam[10–12] was formed in variable amounts in most cases. Thus, we examined the reaction of **1a** under the same reaction conditions in the absence of diethyl phosphite. To our delight, lactam **3a** was isolated in high yield (83%). The syntheses of lactams **3d–f** and **3h** were carried out similarly, and the results are summarized in Table 3.[13] However, the mechanism for the formation of lactam is not clear at this stage.[14]

As the next examination, the optimized phosphorylation condition was applied to 2,5-disubstituted pyrroles **1m**, **1n**, and some

Table 3
Preparation of γ-hydroxy-γ-butyrolactams.



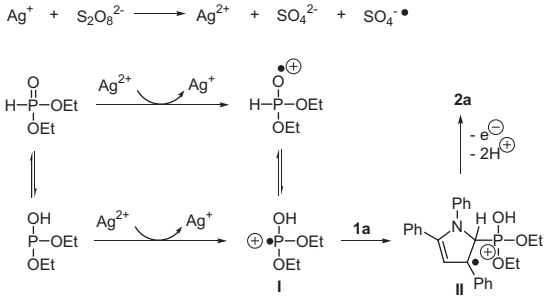


3a (83%) **3d** (74%) **3e** (67%) **3f** (57%) **3h** (94%)

selected heterocyclic compounds, as summarized in Table 4. The phosphorylation of methyl 1,3,5-triphenyl-2-pyrrolecarboxylate (**1m**)[8a] and 1,2,5-triphenylpyrrole (**1n**) failed. We could not obtain the products **2m** and **2n** in appreciable amounts due to the formation of many intractable side products and sluggish reactivity. 3-Methylindole (**1o**) and *N*-methylindole (**1p**) produced **2o** and **2p** in low to moderate yields (29–50%), as is often the case with reported oxidative phosphorylation of indole derivatives.[7a] The reaction with indoles also produced many intractable side products presumably including their oxidative dimerization products such as 2,2′-biindolyl and 2,3′-biindolyl.[15] As compared to **1o** and **1p**, the reaction of 2-phenylindole (**1q**) afforded **2q** in better yield (62%). The phosphorylation of 2,4-diphenylthiophene (**1r**) afforded **2r** in good yield (64%), while the reactivity of 2,4-diphenylfuran (**1s**) was sluggish under the same reaction conditions. The phosphorylation was somewhat sensitive to the reaction medium.[3b,5,6b] As an example, the reaction of furfural (**1t**) in DMF/H_2O (8:1) showed very sluggish reactivity, while the reaction in CH_2Cl_2/H_2O (1:1)[3b] gave the product **2t** in moderate yield (54%).

The reaction mechanism of phosphorylation of **1a** with diethyl phosphite could be proposed, as shown in Scheme 1, according to the mechanism proposed by Effenberger and Kottmann.[6b] Ag(I) is oxidized to Ag(II) by peroxodisulfate. Diethyl phosphite is converted into radical cation I by the action of Ag(II). An electrophilic addition of this radical cation to **1a** forms an intermediate II, which loses an electron and two protons affording the product **2a**.

In summary, we disclosed an efficient synthesis of pyrrole-2-phosphonates via a direct oxidative phosphorylation with dialkyl phosphite and pyrroles in the presence of $AgNO_3$ (0.2 equiv) and $K_2S_2O_8$ (3.0 equiv) in DMF/H_2O (8:1) at 50 °C. In the absence of



Scheme 1.

dialkyl phosphite, γ-hydroxy-γ-butyrolactam derivatives were produced in good yields.

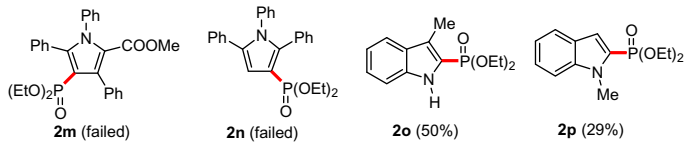
Acknowledgments

This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (2012R1A1B3000541). Spectroscopic data were obtained from the Korea Basic Science Institute, Gwangju branch.

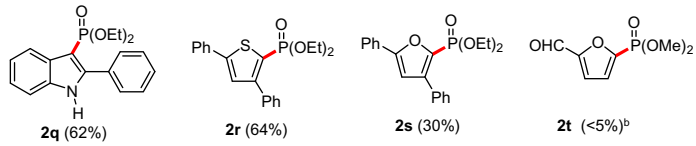
References and notes

1. For the reviews on the synthesis and biological activity of azaheterocyclic phosphonates including pyrrole-2-phosphonates, see: (a) Moonen, K.; Laureyn, I.; Stevens, C. V. *Chem. Rev.* **2004**, *104*, 6177–6215; (b) Van der Jeught, S.; Stevens, C. V. *Chem. Rev.* **2009**, *109*, 2672–2702.
2. Griffin, C. E.; Peller, R. P.; Peters, J. A. *J. Org. Chem.* **1965**, *30*, 91–96.
3. For the synthesis of pyrrole-2-phosphonates by direct oxidative coupling, see: (a) Mu, X.-J.; Zou, J.-P.; Qian, Q.-F.; Zhang, W. *Org. Lett.* **2006**, *8*, 5291–5293; (b) Xiang, C.-B.; Bian, Y.-J.; Mao, X.-R.; Huang, Z.-Z. *J. Org. Chem.* **2012**, *77*, 7706–7710.
4. For the synthesis of pyrrole-2-phosphonates from their precursors bearing a phosphonate moiety, see: (a) Palacios, F.; Ochoa de Retana, A. M.; Velez del Burgo, A. *J. Org. Chem.* **2011**, *76*, 9472–9477; (b) Moonen, K.; Dielteins, N.; Stevens, C. V. *J. Org. Chem.* **2006**, *71*, 4006–4009; (c) Dielteins, N.; Moonen, K.; Stevens, C. V. *Chem. Eur. J.* **2007**, *13*, 203–214; (d) Dielteins, N.; Stevens, C. V. *Org. Lett.* **2007**, *9*, 465–468; (e) Cal, D.; Zagorski, P. *Phosphorous, Sulfur Silicon* **2011**, *186*, 2295–2302; (f) Davis, F. A.; Bowen, K. A.; Xu, H.; Velvadapu, V. *Tetrahedron* **2008**, *64*, 4174–4182; For the indirect synthesis of pyrrole-3-phosphonates, see: (g) Demir, A. S.; Tural, S. *Tetrahedron* **2007**, *63*, 4156–4161; (h) Attanasi, O. A.; Favi, G.; Mantellini, F.; Moscatelli, G.; Santeusanio, S. *J. Org. Chem.* **2011**, *76*, 2860–2866; (i) de los Santos, J. M.; Ignacio, R.; Aparicio, D.; Palacios, F.; Ezpeleta, J. M. *J. Org. Chem.* **2009**, *74*, 3444–3448.
5. Kim, S. H.; Kim, S. H.; Kim, C. H.; Kim, J. N. *Tetrahedron Lett.* **2013**, *54*, 1697–1699.
6. For the oxidative coupling between arenes and dialkyl phosphites using $AgNO_3$ (or Ag_2SO_4)/$K_2S_2O_8$ system, see: (a) Mao, X.; Ma, X.; Zhang, S.; Hu, H.; Zhu, C.; Cheng, Y. *Eur. J. Org. Chem.* **2013**, 4245–4248; (b) Effenberger, F.; Kottmann, H.

Table 4
Attempted phosphorylation of similar substrates[a]



2m (failed) **2n** (failed) **2o** (50%) **2p** (29%)



2q (62%) **2r** (64%) **2s** (30%) **2t** (<5%)[b]

[a] Substrate **1m–t** (0.5 mmol) was used, and the reaction was carried out in DMF/H_2O (8:1).
[b] Compound **2t** was obtained in 54% in CH_2Cl_2/H_2O (1:1).

Tetrahedron **1985**, *41*, 4171–4182; For the oxidation of Ag(I) to Ag(II) by peroxydisulfate, see: (c) Minisci, F.; Citterio, A. *Acc. Chem. Res.* **1983**, *16*, 27–32.

7. For the other oxidative couplings between dialkyl phosphites and arenes/heteroarenes including indoles and pyridinones, see: (a) Wang, H.; Li, X.; Wu, F.; Wan, B. *Synthesis* **2012**, *44*, 941–945; (b) Sun, W.-B.; Ji, Y.-F.; Pan, X.-Q.; Zhou, S.-F.; Zou, J.-P.; Zhang, W.; Asekun, O. *Synthesis* **2013**, *45*, 1529–1533; (c) Xu, W.; Zou, J.-P.; Zhang, W. *Tetrahedron Lett.* **2010**, *51*, 2639–2643.
8. For the preparation of starting materials, see: (a) Kim, S. H.; Lim, J. W.; Lim, C. H.; Kim, J. N. *Bull. Korean Chem. Soc.* **2012**, *33*, 620–624; (b) Kim, S. H.; Lim, J. W.; Yu, J.; Kim, J. N. *Bull. Korean Chem. Soc.* **2013**, *34*, 2604–2608; (c) Kim, J. M.; Lee, S.; Kim, S. H.; Lee, H. S.; Kim, J. N. *Bull. Korean Chem. Soc.* **2008**, *29*, 2215–2220; (d) Lee, H. S.; Kim, J. M.; Kim, J. N. *Tetrahedron Lett.* **2007**, *48*, 4119–4122; (e) Li, Q.; Fan, A.; Lu, Z.; Cui, Y.; Lin, W.; Jia, Y. *Org. Lett.* **2010**, *12*, 4066–4069; For the preparation of required 2,5-diketo esters, see: (f) Kim, S. H.; Kim, K. H.; Kim, J. N. *Adv. Synth. Catal.* **2011**, *353*, 3335–3339.
9. *Typical procedure for the synthesis of* ***2a***. A solution of **1a** (148 mg, 0.5 mmol), diethyl phosphite (208 mg, 1.5 mmol), $AgNO_3$ (17 mg, 0.1 mmol), and $K_2S_2O_8$ (406 mg, 1.5 mmol) in DMF/H_2O (8:1, 6.0 mL) was heated to 50 °C for 2 h. After the usual aqueous extractive workup and column chromatographic purification process (hexanes/EtOAc, 1:1) compound **2a** was obtained as a white solid, 162 mg (75%) along with lactam **3a**, 23 mg (14%). Other compounds were synthesized similarly, and the selected spectroscopic data of **2a**, **2c**, **2d**, **2g**, **2j**, **2k**, and **2r** are as follows.
Compound ***2a***: White solid, mp 116–118 °C; IR (KBr) 1496, 1257, 1025 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.79 (*t*, *J* = 7.2 Hz, 6H), 3.36–3.39 (m, 2H), 3.59–3.72 (m, 2H), 6.38 (d, J_{PH} = 4.8 Hz, 1H), 7.00–7.34 (m, 13H), 7.51–7.55 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.63 (d, J_{PC} = 7.4 Hz), 61.72 (d, J_{PC} = 5.7 Hz), 112.19 (d, J_{PC} = 13.7 Hz), 118.29 (d, J_{PC} = 226.7 Hz), 126.91, 127.21, 127.65, 127.97, 128.02, 128.42, 128.87(2C), 129.74, 131.97 (d, J_{PC} = 1.7 Hz), 135.93, 136.88 (d, J_{PC} = 16.69 Hz), 139.45, 140.13 (d, J_{PC} = 10.9 Hz); ^{31}P NMR (121 MHz, $CDCl_3$) δ 9.14; ESIMS *m*/*z* 432 $[M+H]^+$. Anal. Calcd for $C_{26}H_{26}NO_3P$: C, 72.38; H, 6.07; N, 3.25. Found: C, 72.51; H, 6.18; N, 3.09.
Compound ***2c***: Colorless oil; IR (film) 1497, 1258, 1029 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.93 (d, *J* = 6.0 Hz, 6H), 1.12 (d, *J* = 6.0 Hz, 6H), 4.31–4.52 (m, 2H), 6.47 (d, J_{PH} = 4.5 Hz, 1H), 7.08–7.41 (m, 13H), 7.59–7.63 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.24 (d, J_{PC} = 5.2 Hz), 23.82 (d, J_{PC} = 4.1 Hz), 70.53 (d, J_{PC} = 5.7 Hz), 112.22 (d, J_{PC} = 13.8 Hz), 119.52 (d, J_{PC} = 228.9 Hz), 126.73, 127.08, 127.47, 127.90, 127.98, 128.13, 128.89, 129.25, 129.95, 132.13 (d, J_{PC} = 1.7 Hz), 136.27, 136.39 (d, J_{PC} = 16.6 Hz), 139.53, 139.95 (d, J_{PC} = 10.9 Hz); ESIMS *m*/*z* 460 $[M+H]^+$. Anal. Calcd for $C_{28}H_{30}NO_3P$: C, 73.19; H, 6.58; N, 3.05. Found: C, 73.02; H, 6.77; N, 2.90.
Compound ***2d***: Colorless oil; IR (film) 1484, 1242, 1024 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.81 (t, *J* = 7.2 Hz, 6H), 3.41–3.53 (m, 2H), 3.66–3.79 (m, 2H), 5.62 (s, 2H), 6.30 (d, J_{PH} = 4.5 Hz, 1H), 6.84–6.88 (m, 2H), 7.07–7.31 (m, 11H), 7.42–7.47 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.64 (d, J_{PC} = 7.5 Hz), 49.69, 61.64 (d, J_{PC} = 5.2 Hz), 112.00 (d, J_{PC} = 13.1 Hz), 115.51 (d, J_{PC} = 224.9 Hz), 126.17, 126.75, 126.81, 127.54, 128.14, 128.20, 128.43, 129.46, 129.63, 132.13, 136.06, 136.79 (d, J_{PC} = 16.0 Hz), 139.53, 141.43 (d, J_{PC} = 12.5 Hz); ESIMS *m*/*z* 446 $[M+H]^+$. Anal. Calcd for $C_{27}H_{28}NO_3P$: C, 72.79; H, 6.34; N, 3.14. Found: C, 72.71; H, 6.58; N, 3.02.
Compound ***2g***: Colorless oil; IR (film) 1509, 1242, 1024 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.91 (t, *J* = 7.2 Hz, 6H), 2.17 (s, 3H), 3.56–3.67 (m, 2H), 3.76–3.87 (m, 2H), 5.62 (s, 2H), 6.10 (d, J_{PH} = 4.2 Hz, 1H), 6.98–7.01 (m, 2H), 7.19–7.49 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.40 (d, J_{PC} = 1.7 Hz), 15.66 (d, J_{PC} = 7.4 Hz), 49.08, 61.52 (d, J_{PC} = 5.2 Hz), 110.85 (d, J_{PC} = 13.8 Hz), 114.04 (d, J_{PC} = 224.9 Hz), 125.93, 126.60, 126.86, 127.43, 128.43, 129.62, 136.22 (d, J_{PC} = 12.0 Hz), 136.27 (d, J_{PC} = 17.2 Hz), 136.33, 138.61; ^{31}P NMR (121 MHz, $CDCl_3$) δ 10.59; ESIMS *m*/*z* 384 $[M+H]^+$. Anal. Calcd for $C_{22}H_{26}NO_3P$: C, 68.92; H, 6.83; N, 3.65. Found: C, 69.06; H, 6.68; N, 3.49.
Compound ***2j***: Colorless oil; IR (film) 1731, 1260, 1023 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.75 (t, *J* = 6.6 Hz, 3H), 1.11–1.13 (m, 4H), 1.16 (t, *J* = 7.2 Hz, 6H), 1.28–1.41 (m, 2H), 2.43–2.49 (m, 2H), 3.67 (s, 3H), 3.83–4.08 (m, 4H), 5.61 (s, 2H), 6.95–6.98 (m, 2H), 7.20–7.38 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.75, 15.97 (d, J_{PC} = 6.8 Hz), 21.97, 24.58, 29.60, 31.42, 49.22, 51.87, 62.38 (d, J_{PC} = 5.2 Hz), 117.20 (d, J_{PC} = 223.8 Hz), 123.21 (d, J_{PC} = 12.1 Hz), 125.78, 126.68, 126.73 (d, J_{PC} = 15.5 Hz), 127.14, 128.05, 128.52, 129.52, 134.34 (d, J_{PC} = 1.1 Hz), 138.04 (d, J_{PC} = 10.9 Hz), 138.12, 166.64; ^{31}P NMR (121 MHz, $CDCl_3$) δ 7.97; ESIMS *m*/*z* 498 $[M+H]^+$. Anal. Calcd for $C_{28}H_{36}NO_5P$: C, 67.59; H, 7.29; N, 2.82. Found: C, 67.81; H, 7.46; N, 2.86.
Compound ***2k***: White solid, mp 139–141 °C; IR (KBr) 3412, 1727, 1639, 1241, 1019 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.39 (t, *J* = 7.2 Hz, 6H), 3.70 (s, 3H), 4.19–4.36 (m, 4H), 7.01–7.10 (m, 7H), 7.24 (t, *J* = 8.7 Hz, 1H), 7.38 (d, *J* = 7.8 Hz, 2H), 10.30 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.29 (d, J_{PC} = 6.9 Hz), 51.44, 63.36 (d, J_{PC} = 5.7 Hz), 121.54, 123.22, (d, J_{PC} = 224.9 Hz), 127.22, 127.31, 127.54, 128.97, 130.66, 131.20 (d, J_{PC} = 10.7 Hz), 131.91, 132.44, 133.12 (d, J_{PC} = 10.9 Hz), 136.42, 163.64, 187.24; ESIMS *m*/*z* 442 $[M+H]^+$. Anal. Calcd for $C_{23}H_{24}NO_6P$: C, 62.58; H, 5.48; N, 3.17. Found: C, 62.59; H, 5.71; N, 3.08.
Compound ***2r***: White solid, mp 66–68 °C; IR (KBr) 1487, 1250, 1022 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.17 (t, *J* = 7.2 Hz, 6H), 3.92–4.14 (m, 4H), 7.26–7.50 (m, 7H), 7.56–7.69 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.97 (d, J_{PC} = 7.4 Hz), 62.57 (d, J_{PC} = 5.2 Hz), 121.64 (d, J_{PC} = 207.2 Hz), 126.11, 127.27 (d, J_{PC} = 16.7 Hz), 128.05, 128.08, 128.66, 128.91 (d, J_{PC} = 1.2 Hz), 129.06, 133.05 (d, J_{PC} = 1.7 Hz), 135.75 (d, J_{PC} = 2.9 Hz), 150.41 (d, J_{PC} = 7.4 Hz), 150.60 (d, J_{PC} = 10.4 Hz); ESIMS *m*/*z* 373 $[M+H]^+$. Anal. Calcd for $C_{20}H_{21}O_3PS$: C, 64.50; H, 5.68. Found: C, 64.76; H, 5.80.

10. For the synthesis of γ-hydroxy-γ-butyrolactams from pyrroles using an oxidant, see: (a) Howard, J. K.; Hyland, C. J. T.; Just, J.; Smith, J. A. *Org. Lett.* **2013**, *15*, 1714–1717; (b) Alp, C.; Ekinci, D.; Gultekin, M. S.; Senturk, M.; Sahin, E.; Kufrevioglu, O. I. *Bioorg. Med. Chem.* **2010**, *18*, 4468–4474; (c) Troegel, B.; Lindel, T. *Org. Lett.* **2012**, *14*, 468–471; (d) Procopiou, P. A.; Highcock, R. M. *J. Chem. Soc., Perkin Trans 1* **1994**, 245–247; (e) Sakata, R.; Iwamoto, R.; Fujinami, S.; Ukaji, Y.; Inomata, K. *Heterocycles* **2011**, *82*, 1157–1162.
11. For the oxidation of pyrroles using singlet oxygen and the synthesis of isochrysohermidin, see: (a) Boger, D. L.; Baldino, C. M. *J. Org. Chem.* **1991**, *56*, 6942–6944; (b) Boger, D. L.; Baldino, C. M. *J. Am. Chem. Soc.* **1993**, *115*, 11418–11425; (c) Alberti, M. N.; Vougioukalakis, G. C.; Orfanopoulos, M. *J. Org. Chem.* **2009**, *74*, 7274–7282.
12. For the other synthetic routes of γ-hydroxy-γ-butyrolactams, see: (a) Lim, C. H.; Kim, S. H.; Kim, J. N. *Bull. Korean Chem. Soc.* **2012**, *33*, 1622–1626; (b) Kim, S. H.; Kim, S. H.; Lee, H. J.; Kim, J. N. *Bull. Korean Chem. Soc.* **2012**, *33*, 2079–2082; (c) Yang, L.; Lei, C.-H.; Wang, D.-X.; Huang, Z.-T.; Wang, M.-X. *Org. Lett.* **2010**, *12*, 3918–3921.
13. The lactams **3a** and **3d** are known,[12c] and the selected spectroscopic data of **3e** and **3h** are as follows.
Compound ***3e***: White solid, mp 194–196 °C; IR (KBr) 3355, 1681, 1492, 1450 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6) δ 2.59–2.69 (m, 1H), 2.78–2.93 (m, 1H), 3.09–3.20 (m, 1H), 3.53–3.63 (m, 1H), 5.22 (s, 1H), 6.98 (s, 1H), 7.04–7.43 (m, 13H), 7.84–7.88 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6) δ 34.59, 41.26, 89.65, 125.94, 125.98, 127.27, 128.17, 128.23, 128.30, 128.43, 128.61, 128.75, 130.76, 133.77, 137.68, 139.28, 143.21, 169.13; ESIMS *m*/*z* 356 $[M+H]^+$. Anal. Calcd for $C_{24}H_{21}NO_2$: C, 81.10; H, 5.96; N, 3.94. Found: C, 81.21; H, 6.03; N, 3.75.
Compound ***3h***: White solid, mp 70–72 °C; IR (KBr) 3355, 1682, 1513, 1449 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.61 (s, 3H), 3.88 (br s, 1H), 6.59 (d, *J* = 9.0 Hz, 2H), 6.90 (s, 1H), 7.12–7.33 (m, 10H), 7.75–7.78 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.16, 91.09, 113.80, 126.08, 126.85, 127.53, 128.37, 128.43, 128.46, 128.49, 129.17, 130.34, 133.90, 137.08, 142.94, 157.51, 168.82; ESIMS *m*/*z* 358 $[M+H]^+$. Anal. Calcd for $C_{23}H_{19}NO_3$: C, 77.29; H, 5.36; N, 3.92. Found: C, 77.42; H, 5.29; N, 3.68.
14. The lactam **3a** was formed in 42% yield in the presence of $K_2S_2O_8$ (3.0 equiv) in DMF/H_2O (8:1) at 50 °C for 10 h without the aid of $AgNO_3$. The result stated that the use of $AgNO_3$ accelerates the reaction rate when we compared the yield of **3a** (83%) and reaction time (2 h) in the presence of $AgNO_3$. In addition, the synthesis of alkyl-substituted lactams **3g** and **3j** failed. The formations of **3g** and **3j** were observed on TLC in low yields at the right position; however, the separation failed due to the presence of some side products. Further studies on the reaction mechanism including the involvement of air and/or water for the production of lactam are under progress.
15. For the oxidative dimerization of indoles, see: (a) Niu, T.; Zhang, Y. *Tetrahedron Lett.* **2010**, *51*, 6847–6851; (b) Li, Y.; Wang, W.-H.; Yang, S.-D.; Li, B.-J.; Feng, C.; Shi, Z.-J. *Chem. Commun.* **2010**, 4553–4555; (c) Liang, Z.; Zhao, J.; Zhang, Y. *J. Org. Chem.* **2010**, *75*, 170–177; (d) Dohi, T.; Morimoto, K.; Maruyama, A.; Kita, Y. *Org. Lett.* **2006**, *8*, 2007–2010.