JOC*Note*

Selective Synthesis of 2,3-Disubstituted-2*H*-isoindol-1-ylphosphonate and 2,3-Disubstituted-1,2-dihydroisoquinolin-1-ylphosphonate via Metal-Tuned Reaction of α-Amino (2-Alkynylphenyl)methylphosphonate

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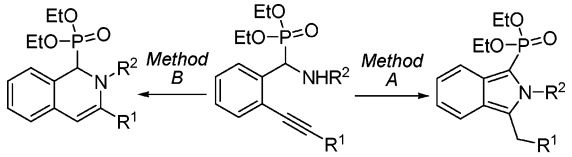
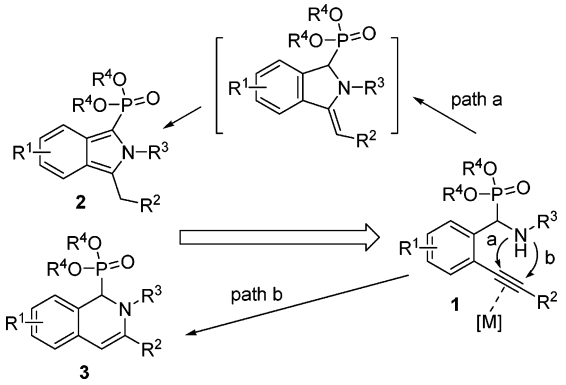


Palladium(II)-catalyzed reaction of α-amino (2-alkynylphenyl)methylphosphonate provides a novel and efficient route to 2,3-disubstituted-2*H*-isoindol-1-ylphosphonate via 5-*exo*-cyclization and [1,5]-H shift; while 2,3-disubstituted-1,2-dihydroisoquinolin-1-ylphosphonate is afforded through 6-*endo*-cyclization utilizing silver triflate as catalyst.

Organophosphorus compounds continue to receive widespread attention due to their ubiquity in biological systems.[1,2] Among these, in particular, α-amino phosphonic acids, their phosphonate esters, and short peptides incorporating this unit have attracted considerable focus since they are excellent inhibitors of a wide range of proteolytic enzymes.[3] In addition, α-amino phosphonate derivatives have broad application due to their antibacterial[4] and antifungal[5] activity, and as inhibitors of phosphatase activity.[6] On the other hand, recent studies have indicated that a number of heterocycle analogues containing phosphorus showed excellent bioactivities. For example, phosphacoumarins showed good inhibitory activity against SHP-1.[7] In light of our interest in α-amino phosphonates and natural product-like compounds, we required an efficient method to generate α-amino phosphonate based scaffolds and its focused library, with a hope of finding more active hits or leads for our particular biological assays.[8] Herein, we would like to disclose our preliminary results for the synthesis of 2,3-disubstituted-2*H*-isoindol-1-ylphosphonate **2** or 2,3-disubstituted-1,2-dihydroisoquinolin-1-ylphosphonate **3** from α-amino (2-alkynylphenyl)methylphosphonate **1** under metal-tuned conditions (Scheme 1)

SCHEME 1



It is well-known that the transition metal- or Lewis acid-catalyzed cyclization of alkynes possessing a nucleophile in proximity to the triple bond is an important process in organic synthesis, which can construct various heterocycles in an efficient and atom-economic way.[9−15] Over the past few years,

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(1) (a) Westheimer, F. H. *Science* **1987**, *235*, 1173. (b) Seto, H.; Kuzuyama, T. *Nat. Prod. Rep*. **1999**, *16*, 589.

(2) For examples of phosphorus compounds as pharmaceuticals, see: (a) Kafarski, P.; LeJczak, B. *Curr. Med. Chem.*: *Anti-Cancer Agents* **2001**, *1*, 301. (b) Colvin, O. M. *Curr. Pharm. Des.* **1999**, *5*, 555. (c) Zon, G. *Prog. Med. Chem.* **1982**, *19*, 205. (d) Stec, W. J. *Organophosphorus Chem.* **1982**, *13*, 145. (e) Mader, M. M.; Bartlett, P. A. *Chem. Rev*. **1997**, *97*, 1281. (f) Kafarski, P.; LeJczak, B. *Phosphorus, Sulfur Silicon Relat. Elem.* **1991**, *63*, 193.

(3) For reviews of the biological activity of α-amino phosphonic acids, see: (a) Hiratake, J.; Oda, J. *Biosci. Biotechnol. Biochem.* **1997**, *61*, 211. (b) Kafarski, P.; Lejczak, B. *Phosphorus*, *Sulfur*, *Silicon* **1991**, *63*, 193. For a fM inhibitor of carboxypeptidase A, see: (c) Kaplan, A. P.; Bartlett, P. A. *Biochemistry* **1991**, *30*, 8165.

(4) (a) Allen, J. G.; Atherton, F. R.; Hall, M. J.; Hassall, C. H.; Holmes, S. W.; Lambert, R. W.; Nisbet, L. J.; Ringrose, P. S. *Nature* **1978**, *272*, 56. (b) Pratt, R. F. *Science* **1989**, *246*, 917.

(5) Maier, L.; Diel, P. J. *Phosphorus*, *Sulfur*, *Silicon* **1991**, *57*, 57.

(6) Beers, S. A.; Schwender, C. F.; Loughney, D. A.; Malloy, E.; Demarest, K.; Jordan, J. *Bioorg. Med. Chem.* **1996**, *4*, 1693.

(7) Li, X. S.; Zhang, D. W.; Pang, H.; Shen, F.; Fu, H.; Jiang, Y. Y.; Zhao, Y. F. *Org. Lett.* **2005**, *7*, 4919.

(8) (a) Wu, J.; Yang, Z.; Fathi, R.; Zhu, Q.; Wang, L. U.S. Patent No. 6,703,514. (b) Wu, J.; Yang, Z.; Fathi, R.; Zhu, Q. U.S. Pat. Appl. Publ. 2004, 43 pp.

(9) (a) Ma, C.; Liu, X.; Li, X.; Flippen-Anderson, J.; Yu, S.; Cook, J. M. *J. Org. Chem.* **2001**, *66*, 4525. (b) Kondo, T.; Okada, T.; Suzuki, T.; Mitusudi, T.-a. *J. Organomet. Chem.* **2001**, *622*, 149. (c) Muller, T. E.; Berger, M.; Grosche, M.; Herdtweck, E.; Schmidtchen, F. P. *Organometallics* **2001**, *20*, 4384. (d) Xu, L.; Lewis, I. R.; Davidsen, S. K.; Summers, J. B. *Tetrahedron Lett.* **1998**, *39*, 5159. (e) Yu, M. S.; de Leon, L. L.; McGuire, M. A.; Botha, G. *Tetrahedron Lett.* **1998**, *39*, 9347. (f) Mahanty, J. S.; De, M.; Das, P.; Kundu, N. G. *Tetrahedron* **1997**, *53*, 13397. (g) Cacchi, S.; Carnicelli, V.; Marinelli, F. *J. Organomet. Chem.* **1994**, *475*, 289. (h) Arcadi, A.; Cacchi, S.; Marinelli, F. *Tetrahedron Lett.* **1989**, *30*, 2581. (i) Utimoto, K.; Miwa, H.; Nozaki, H. *Tetrahedron Lett.* **1981**, *22*, 4277.

(10) (a) Van Esseveldt, B. C. J.; van Delft, F. L.; de Gelder, R.; Rutjes, F. P. J. T. *Org. Lett.* **2003**, *5*, 1717. (b) Kozawa, Y.; Mori, M. *Tetrahedron Lett.* **2002**, *43*, 1499. (c) Torres, J. C.; Pilli, R. A.; Vargas, M. D.; Violante, F. A.; Garden, S. J.; Pinto, A. C. *Tetrahedron* **2002**, *58*, 4487. (d) Sashida, H.; Kawamukai, A. *Synthesis* **1999**, 1145. (e) Kobayashi, Y.; Fukuyama, T. *J. Heterocycl. Chem.* **1998**, *35*, 1043. (f) McDonald, F. E.; ChatterJee, A. K. *Tetrahedron Lett.* **1997**, *38*, 7687. (g) Khan, M. W.; Kundu, N. G. *Synlett* **1997**, *12*, 1435. (h) Ohe, K.; Ishihara, T.; Chatani, N.; Kawasaki, Y.; Murai, S. *J. Org. Chem.* **1991**, *56*, 2267. (i) NagaraJan, A.; Balasubramanian, T. R. *Indian J. Chem., Sect. B* **1989**, *28*, 67. (j) Sakamoto, T.; Kondo, Y.; Iwashita, S.; Nagano, T.; Yamanaka, H. *Chem. Pharm. Bull.* **1988**, *36*, 1305. (k) Taylor, E. C.; Katz, A. H.; Salgado-Zamora, H.; McKillop, A. *Tetrahedron Lett.* **1985**, *26*, 5963.

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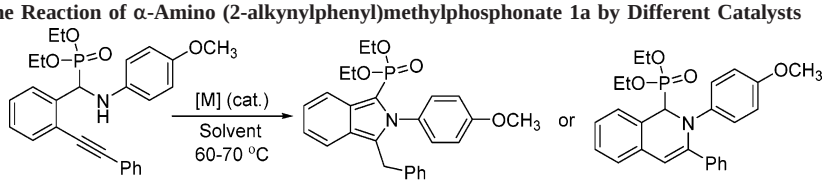
TABLE 1. Screening of the Reaction of α-Amino (2-alkynylphenyl)methylphosphonate 1a by Different Catalysts



1a **2a** **3a**

entry	metal catalyst	solvent	product	yield (%)[a]
1	AgOTf (5 mol %)	CH_3CN	**3a**	88
2	$Sc(OTf)_3$ (5 mol %)	CH_3CN		NR
3	$In(OTf)_3$ (5 mol %)	CH_3CN		NR
4	$FeCl_3$ (5 mol %)	CH_3CN		NR
5	$Dy(OTf)_3$ (5 mol %)	CH_3CN		NR
6	$Zn(OTf)_2$ (5 mol %)	CH_3CN		NR
7	CuI (5 mol %)	CH_3CN	**3a**	14
8	$PdCl_2$ (5 mol %)	CH_3CN	**2a**	86
9	$Pd(PhCN)_2Cl_2$ (5 mol %)	CH_3CN	**2a**	92
10	$Pd(OAc)_2$ (5 mol %)	CH_3CN	**2a**	82
11	$Pd(PPh_3)_2Cl_2$ (5 mol %)	CH_3CN	**2a**	57
12	$Pd(PhCN)_2Cl_2$ (5 mol %)	EtOH	**2a**	47
13	$Pd(PhCN)_2Cl_2$ (5 mol %)	THF	**2a**	35
14	$Pd(PhCN)_2Cl_2$ (5 mol %)	DCE	**2a**	77
15	$Pd(PhCN)_2Cl_2$ (5 mol %)	toluene	**2a**	62
16	$Pd(PhCN)_2Cl_2$ (5 mol %)	DMF	**2a**	complicated
17	$Pd(PhCN)_2Cl_2$ (1 mol %)	MeCN	**2a**	55
18	$Pd(PhCN)_2Cl_2$ (10 mol %)	MeCN	**2a**	93

[a] Isolated yield based on substrate **1a**.

the intramolecular annulations of amines,[9] amides,[10] imines,[11] carboxylic acids,[12] alcohols,[13] and phosphonic acid derivatives[14] to a triple bond have been extensively investigated by using transition metal reagents as effective catalysts. In some cases, Lewis acids were also found effective for this kind of transformation.[15] Recently, we have described three-component reactions of aldehydes, amines, and diethyl phosphite catalyzed by Lewis acid affording the corresponding α-amino phosphonates in excellent yields.[16] Prompted by these results, we envisaged that, in the presence of suitable metal catalyst, the resulting α-amino phosphonate **1** could serve as a nucleophile if a triple bond is available in the molecule. On the basis of this consideration, we synthesized the key starting material **1** from amine, diethyl phosphite, and 2-alkynyl benzaldehyde,[11a] which could be regarded as a good candidate for α-amino phosphonate based heterocycle formation.

To test this idea, our studies commenced with the reaction of **1a** in the presence of silver triflate (5 mol %) in acetonitrile at 60−70 °C. To our delight, we observed the formation of a product in 88% yield (Table 1, entry 1). Structure elucidation by ^1H, ^{13}C, ^{31}P NMR and mass spectroscopy revealed this compound to be 1,2-dihydroisoquinolin-1-ylphosphonate **3a**. In this case, only the six-membered endocyclic 1,2-dihydroisoquinolin-1-ylphosphonate from 6-*endo-dig*[12] cyclization was obtained, and no five-membered exocyclic products were detected by TLC monitoring. Further screening of Lewis acids revealed that $Sc(OTf)_3$, $In(OTf)_3$, $FeCl_3$, $Dy(OTf)_3$, or $Zn(OTf)_2$ was ineffective for this transformation and only starting material **1a** was recovered (Table 1, entries 2−6). When CuI was utilized as catalyst in the reaction, a 14% yield of compound **3a** was isolated (Table 1, entry 7). Different palladium(II) catalysts were also employed in the reaction of **1a** in acetonitrile (Table 1, entries 8−11). To our surprise, the observations were in contrast to those of the cyclization catalyzed by silver(I) or copper(I), which proceeded by 5-*exo-dig* cyclization, and product **2a** was generated in good to excellent yields after 36 h. For instance, $Pd(PhCN)_2Cl_2$ (5 mol %) was proved to be the most efficient and the corresponding product **2a** was afforded in 92% yield. However, there few reports have appeared in the literature concerning the preparation of phosphonylated isoindoles and related compounds.[17] The structure of **2a** was verified by 1D NMR (^1H NMR, ^{13}C NMR, DEPT135, ^{31}P NMR) and 2D NMR (H−H COSY, HSQC, HMBC), as well as mass spectroscopy. Solvent screening of the $Pd(PhCN)_2Cl_2$ catalyzed reaction of **1a** demonstrated acetonitrile was the best choice of solvent. Increasing the catalyst amount to 10 mol % gave a similar result (93% yield, entry 18). However, only a 55% yield of compound **2a** was obtained after 48 h when 1 mol % of catalyst was employed (entry 17). The reaction was retarded when it was performed at room temperature.

With this promising result in hand, we started to investigate the scope of this reaction under optimized conditions [Pd-

(11) (a) Roesch, K. R.; Larock, R. C. *J. Org. Chem.* **2002**, *67*, 86. (b) Zhang, H.; Larock, R. C. *Tetrahedron Lett.* **2002**, *43*, 1359.

(12) (a) Melis, K.; Opstal, T.; Verpoort, F. *Eur. J. Org. Chem.* **2002**, *22*, 3779. (b) Anastasia, L.; Xu, C.; Negishi, E.-i. *Tetrahedron Lett.* **2002**, *43*, 5673. (c) Bellina, F.; Ciucci, D.; Vergamini, P.; Rossi, R. *Tetrahedron* **2000**, *56*, 2533. (d) Qing, F. L.; Gao, W. Z. *Tetrahedron Lett.* **2000**, *41*, 7727. (e) Kundu, N. G.; Pal, M.; Nandi, B. *J. Chem. Soc., Perkin Trans.* **1998**, *1*, 561. (f) Liao, H. Y.; Cheng, C. H. *J. Org. Chem.* **1995**, *60*, 3711. (g) Ogawa, Y.; Maruno, M.; Wakamatsu, T. *Heterocycles* **1995**, *41*, 2587.

(13) (a) Trost, B. M.; Rhee, Y. H. *J. Am. Chem. Soc.* **2002**, *124*, 2528. (b) Bates, C. G.; SaeJueng, P.; Murphy, J. M.; Venkataraman, D. *Org. Lett.* **2002**, *4*, 4727. (c) Cutchins, W. W.; McDonald, F. E. *Org. Lett.* **2002**, *4*, 749. (d) Aschwanden, P.; Frantz, D. E.; Carreira, E. M. *Org. Lett.* **2000**, *2*, 2331. (e) McDonald, F. E.; Reddy, K. S.; Diaz, Y. *J. Am. Chem. Soc.* **2000**, *122*, 4304.

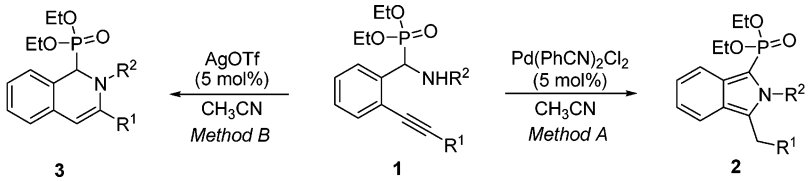
(14) (a) Peng, A. Y.; Ding, Y. X. *J. Am. Chem. Soc.* **2003**, *125*, 15006. (b) Tang, W.; Ding, Y. X. *J. Org. Chem.* **2006**, *71*, 8489. (c) Peng, A. Y.; Ding, Y. X. *Org. Lett.* **2005**, *7*, 3299.

(15) For examples, see: (a) Asao, N.; Yudha, S. S.; Nogami, T.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2005**, *44*, 5526. (b) Yanada, R.; Obika, S.; Kono, H.; Takemoto, Y. *Angew. Chem., Int. Ed.* **2006**, *45*, 3822.

(16) (a) Wu, J.; Sun, W.; Sun, X.; Xia, H.-G. *Green Chem.* **2006**, *8*, 365. (b) Wu, J.; Sun, W.; Xia, H.-G.; Sun, X. *Org. Biomol. Chem.* **2006**, *4*, 1663.

(17) Dieltiens, N.; Stevens, C. V. *Org. Lett.* **2007**, *9*, 465 and references cited therein.

TABLE 2. AgOTf or $Pd(PhCN)_2Cl_2$ Catalyzed Reaction of α-Amino (2-alkynylphenyl)methylphosphonate 1 in MeCN



entry	R^1/R^2	method	product	yield (%)[a]
1	C_6H_5/4-$MeOC_6H_4$ (**1a**)	A	**2a**	92
2	C_6H_5/4-MeC_6H_4 (**1b**)	A	**2b**	87
3	C_6H_5/C_6H_5 (**1c**)	A	**2c**	95
4	C_6H_5/4-FC_6H_4 (**1d**)	A	**2d**	80
5	C_6H_5/4-ClC_6H_4 (**1e**)	A	**2e**	97
6	C_6H_5 /3-$NO_2C_6H_4$ (**1f**)	A	**2f**	92
7	C_6H_5/3-$CF_3C_6H_4$ (**1g**)	A	**2g**	90
8	*n*-Bu/4-$MeOC_6H_4$ (**1h**)	A	**2h**	96
9	*n*-Bu/4-FC_6H_4 (**1i**)	A	**2i**	64
10	*n*-Bu/3-$NO_2C_6H_4$ (**1j**)	A	**2j**	76
11	C_6H_5/4-$MeOC_6H_4$ (**1a**)	B	**3a**	88
12	C_6H_5/C_6H_5 (**1c**)	B	**3b**	55
13	C_6H_5/4-FC_6H_4 (**1d**)	B	**3c**	73
14	*n*-Bu/4-$MeOC_6H_4$ (**1h**)	B	**3d**	52 (40)[b]
15	*n*-Bu/C_6H_5 (**1k**)	B	**3e**	25 (68)[b]
16	*n*-Bu/4-FC_6H_4 (**1i**)	B	**3f**	60 (36)[b]

[a] Isolated yield based on α-amino (2-alkynylphenyl)methylphosphonate **1**. [b] The yield in parentheses is the recovery of compound **1**.

$(PhCN)_2Cl_2$ (5 mol %), CH_3CN, 60−70 °C; or AgOTf (5 mol %), CH_3CN, 60−70 °C]. The application of this methodology to the synthesis of a variety of 2,3-disubstituted-2*H*-isoindol-1-ylphosphonate **2** or 2,3-disubstituted-1,2-dihydroisoquinolin-1-ylphosphonate **3** is summarized in Table 2. Synthetically, all these cyclization reactions illustrated in Table 2 went to completion at 60−70 °C within 36 h. In the presence of catalytic amounts of $Pd(PhCN)_2Cl_2$, α-amino (2-alkynylphenyl)methylphosphonate **1** with a variety of substituted R^1 and R^2 groups could be cyclized to form 2,3-disubstituted-2*H*-isoindol-1-ylphosphonate **2** in CH_3CN in good to excellent yields. When R^1 was phenyl, the reaction tolerated a range of R^2 groups with different electronic demands on aromatic rings involving electron-donating and electron-withdrawing groups (Table 2, entries 1−7). These reactions were very clean and the desired products were afforded in good yields. For example, when substrate **1e** was employed in the reaction, the corresponding product **2e** was obtained in 97% yield (Table 2, entry 5). When R^1 was *n*-butyl, better results were generated when R^2 has electron-donating groups attached to the aromatic ring in the palladium(II)-catalyzed reactions. We also utilized AgOTf as catalyst in the reaction of α-amino (2-alkynylphenyl)methylphosphonate **1**. As mentioned above, cyclization of substrate **1a** provided the desired product **3a** in 88% yield (Table 2, entry 11). Compounds **1c** and **1d** also reacted smoothly under similar conditions leading to the 2,3-disubstituted-1,2-dihydroisoquinolin-1-ylphosphonate **3b** or **3c** in 55% and 73% yield, respectively (Table 2, entries 12 and 13). However, when R^1 was *n*-butyl, the reactions could not go to completion and some starting materials were recovered (Table 2, entries 14−16). From the results shown in Tables 1 and 2, the reactions showed very high regioselectivity. We reasoned that in the reaction process, it may presumably involve the formation of π-complex via coordination of the alkynyl moiety of **1** to Pd(II) or Ag(I), thus activating the triple bond for regioselective nucleophilic attack by the amino group in the *endo* or *exo* mode. However, factors affecting the above regioselectivity are not yet very clear.

It is well-known that silver(I) salts have mild Lewis acidity and have been used as catalysts in organic synthesis. Among these salts, AgOTf is one of the most popular reagents for inducing transformations, which take advantage of its affinity for halogen and sulfur functional groups, and carbon−carbon unsaturated bonds rather than oxygen functional groups.[18] As described by Asao,[15a] *o*-alkynylaryl aldimine reacted with AgOTf leading to isoquinolinium in good yield. The observation indicated that, in the presence of silver salt, at the beginning the triple bond coordinated to the silver salt, and subsequently, the nitrogen atom attacked on the triple bond via 6-*endo*-cyclization afforded isoquinolinium intermediate. On the basis of this result, we conceive that reaction of α-amino (2-alkynylphenyl)methylphosphonate **1a** catalyzed by AgOTf may undergo a similar process, which leads to compound **3a** via 6-*endo*-cyclization (Scheme 2, eq 1). However, in the presence of palladium, 5-*exo*-cyclization is favorable.[19] The intermediate then undergoes [1,5]-H shift to afford the more stable compound **3a** (Scheme 2, eq 2).

In summary, we have described palladium(II)- or silver(I)-catalyzed reactions of α-amino (2-alkynylphenyl)methylphosphonate, which provides a novel and efficient route to 2,3-disubstituted-2*H*-isoindol-1-ylphosphonate or 2,3-disubstituted-1,2-dihydroisoquinolin-1-ylphosphonate. Mechanism studies, a focused library generation, and screening for biological activity of these small molecules are under investigation in our laboratory.

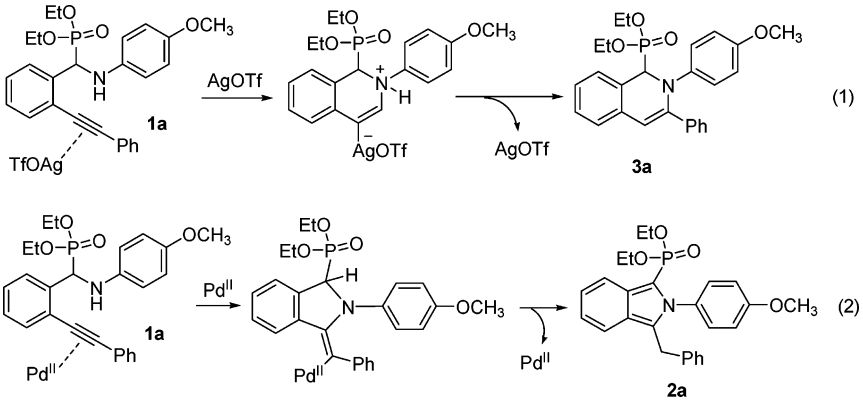
Experiment Section

General Procedure for Method A. α-Amino (2-alkynylphenyl)-methylphosphonate **1** (0.25 mmol), $Pd(PhCN)_2Cl_2$ (0.0125 mmol, 5 mol %), and CH_3CN (1.0 mL) were stirred at 60−70 °C under

(18) Black, T. H. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; John Wiley & Sons: Chichester, UK, 1995; Vol. 6, p 4476.

(19) Zeni, R. G.; Larock, R. C. *Chem. Rev.* **2006**, *106*, 4644.

SCHEME 2



nitrogen atmosphere. After completion of the reaction, as indicated by TLC, the reaction mixture was quenched with water (10 mL) and extracted with EtOAc (2 × 10 mL). The extracts were evaporated in vacuo, followed by purification on silica gel, affording the product 2,3-disubstituted-2*H*-isoindol-1-ylphosphonate **2**. Selected example—diethyl 3-benzyl-2-(4-methoxyphenyl)-2*H*-isoindol-1-ylphosphonate **2a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16 (t, J = 7.0 Hz, 6H), 3.80−3.98 (m, 7H), 4.13 (s, 2 H), 6.84−6.88 (m, 4H), 7.03−7.08 (m, 3H), 7.12−7.22 (m, 4H), 7.56 (dd, J = 8.3, 1.0 Hz, 1H), 8.14 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 30.9, 55.2, 61.2, 106.5, 108.9, 113.1, 119.4, 120.4, 121.3, 122.9, 124.4, 126.0, 128.0, 128.1, 129.1, 130.6, 131.4, 132.4, 138.5, 159.6; ^{31}P NMR (161 MHz, $CDCl_3$) δ 10.34. *m*/*z* 449 (M^+); HRMS calcd for $C_{26}H_{28}NO_4P$ 449.1756, found 449.1752.

General Procedure for Method B. A mixture of α-amino (2-alkynylphenyl)methylphosphonate **1** (0.5 mmol), AgOTf (0.025 mmol, 5 mol %), and CH_3CN (2.0 mL) was stirred at 60−70 °C under nitrogen atmosphere overnight. After completion of the reaction as indicated by TLC, the reaction mixture was quenched with water (10 mL) and extracted with EtOAc (2 × 10 mL). The extracts were evaporated in vacuo, followed by purification on silica gel, affording the product 2,3-disubstituted-1,2-dihydroisoquinolin-1-ylphosphonate **3**. Selected example—diethyl 3-butyl-2-(4-methoxyphenyl)-1,2-dihydroisoquinolin-1-ylphosphonate **3d**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (t, J = 7.2 Hz, 3H), 1.20−1.38 (m, 8H), 1.50 (m, 2H), 2.09 (m, 1H), 2.26 (m, 1H), 3.77 (s, 3H), 4.01−3.87 (m, 4H), 5.03 (d, J = 18.6 Hz, 1H), 5.93 (s, 1H), 6.79 (d, J = 8.0 Hz, 2H), 6.99 (d, J = 8.0 Hz, 2H), 7.05 (t, J = 7.6 Hz, 1H), 7.15 (m, 1H), 7.18 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 16.4, 22.3, 30.2, 33.0, 55.4, 62.2, 62.6, 65.03, 107.8, 113.9, 123.0, 125.4, 126.0, 127.0, 128.0, 129.7, 133.4, 140.6, 144.7, 156.3; ^{31}P NMR (161 MHz, $CDCl_3$) δ 21.02; MS (ESI) *m*/*z* 428.30 (M^+ − 1); HRMS calcd for $C_{24}H_{32}NO_4P$ 429.2069, found 429.2065. (For details, please see the Supporting Information.)

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Supporting Information Available: General experimental information, characterization data, and copies of ^{1}H and ^{13}C NMR spectra of compounds **1**, **2**, and **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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