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One-Pot Transformation of $Ph_2P(O)$-Protected Ethynes: Deprotection Followed by Transition Metal-Catalyzed Coupling

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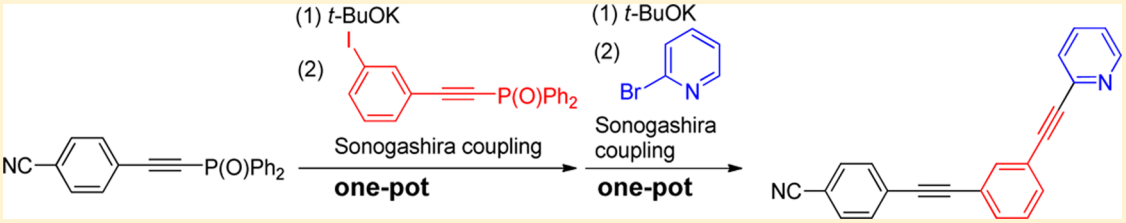
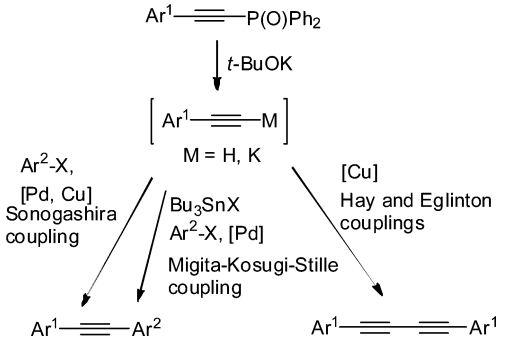
Supporting Information



ABSTRACT: $Ph_2P(O)$-protected ethynes were successfully transformed to arylethynes in one-pot manner through *t*-BuOK-catalyzed deprotection followed by Sonogashira coupling with aryl halide. The arylethynes were obtained similarly by $Ph_2P(O)$-deprotection, stannylation of the resulting terminal ethynes, and Migita-Kosugi-Stille coupling. Deprotection followed by *intramolecular* Eglinton coupling could be carried out in one-pot to provide cyclic butadiynes.

The protection is one of the fundamental technologies in organic synthesis.[1] Although a number of protecting groups were developed and utilized in synthesis of structurally complicated compounds, new protecting groups are still being explored.[2] We have been involved in synthesis of acetylenic compounds having expanded π-systems and explored their applications to organic materials such as organic light-emitting diode (OLED),[3] organic field-effect transistor (OFET),[4] and dye-sensitized solar cell (DSSC).[5] In synthesis of these arylethynes, Sonogashira coupling of aryl halide with ethynes protected with trialkylsilyl group such as trimethylsilyl (TMS) and *t*-buthyldimethylsilyl (TBDMS) and 2-hydroxy-2-propyl group is invoked routinely.[6] However, this reaction, though powerful, frequently suffers from a severe drawback upon isolation of the product: the similar Rf values of starting compounds and products disturb isolation of the desired compound. In order to overcome this drawback, we developed a new protecting group, $Ph_2P(O)$, which enabled easy isolation of the Sonogashira coupling product because of the high polarity, and exemplified the usefulness of this protection in the synthesis of phenyleneethynylenes.[7] Herein, we have expanded the applicability of this protecting group to one-pot synthesis of arylethynes through deprotection followed by transition metal-catalyzed coupling reactions such as Sonogashira, Migita-Kosugi-Stille, Hay, and Eglinton couplings (Scheme 1).[8] First, we tried deprotection of **1** followed by Sonogashira coupling of the resulting terminal ethyne with phenyl bromide in one-pot (Scheme 2). When a THF solution of **1** was treated with 1.2 equiv of *t*-BuOK at rt for 2 h, TLC analysis indicated that **1** was deprotected completely to give phenylethyne. After PhBr, $Pd(PPh_3)_4$, CuI, i-Pr_2NH, and toluene had been added to the THF solution, the mixture was heated at 80 °C for 20 h to give diphenylethyne in 72% yield.[9] In deprotection of this protocol, *t*-BuOP(O)Ph_2 was formed as a byproduct, but it did not disturb the following Sonogashira coupling.[10] Subjection of **2** to *t*-BuOK-catalyzed deprotection followed by Sonogashira coupling with **3** gave $Ph_2P(O)$-protected ethyne **4** in 72% yield. In this one-pot reaction, the addition of stoichiometric amount of *t*-BuOK enabled selective $Ph_2P(O)$-deprotection of **2** while the $Ph_2P(O)$-protection of **3** remained untouched.[11] Similarly, one-pot reaction of **5** with **6** provided **7** in 66% yield, and no decomposition of cyano group was observed in spite of the treatment of *t*-BuOK in the deprotection step. $Ph_2P(O)$-protected ethyne **7** could be applied to one-pot $Ph_2P(O)$-deprotection/Sonogashira coupling with 9-bromoanthracene to afford **8** in 76% yield.

Scheme 1. One-Pot Transformation of $Ph_2P(O)$-Protected Ethyne to Arylethyne and Arylbutadiyne



We succeeded in synthesis of phenyleneethynylene having expanded π-system such as **8** by repeating one-pot deprotection/Sonogashira coupling protocol. The synthetic process

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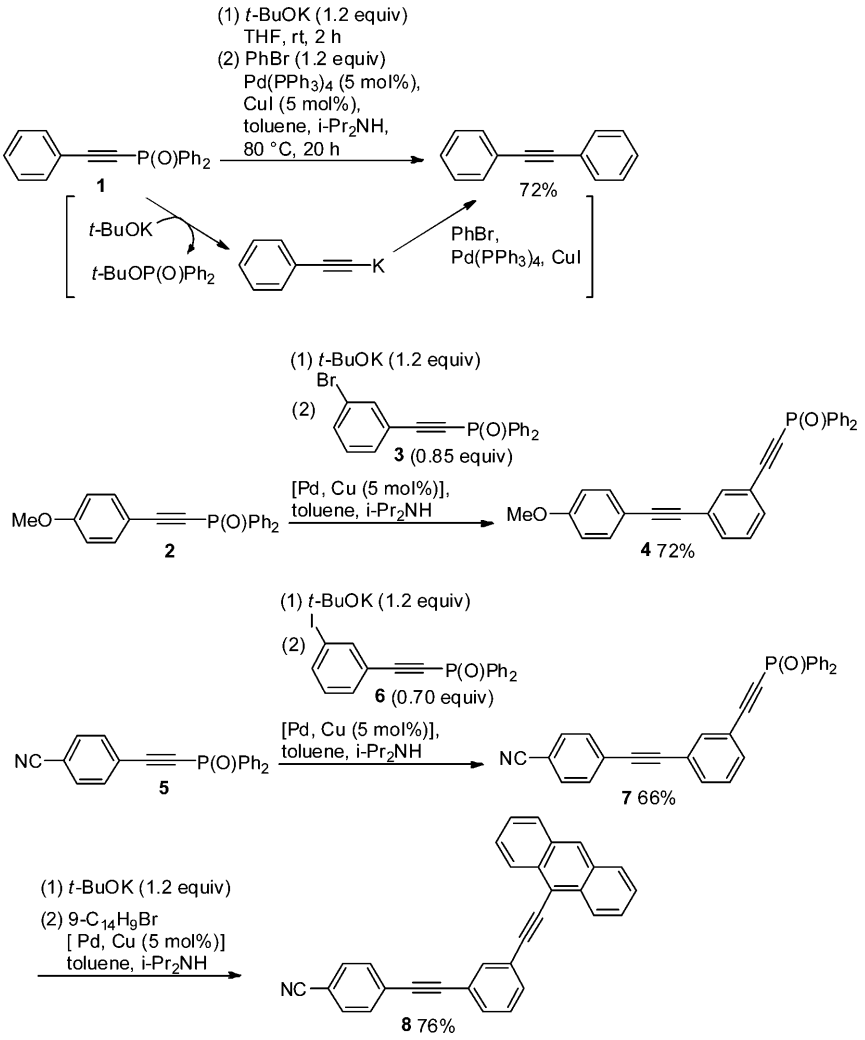
Scheme 2. One-Pot Synthesis of Arylethynes through $Ph_2P(O)$-Deprotection and Sonogashira Coupling



for phenyleneethynylene could be further compacted by subjection of crude product of the first one-pot protocol to the second (Scheme 3). When phosphorylethyne **2** was treated successively with *t*-BuOK and with aryl bromide **9** and Pd and Cu catalysts, phosphorylethyne **10** was provided, and subjection of the crude product **10** to the second deprotection/coupling with 4-(3,7-dimethyloctyloxy)phenyl iodide afforded **11** in 54% yield (based on **9**). In this synthetic process, a filtration of the crude product **10** by a thin pad of silica gel was required. Otherwise, the second one-pot protocol was disturbed by the remaining oxidized transition metal catalyst(s) to provide **11** in a low yield. This compacted process of successive one-pot protocols could be applied to synthesis of **12**: subjection of the phosphorylethyne **5** to deprotection/coupling protocols with **6** and **13** provided **12** in 43% yield.

The one-pot deprotection/coupling reaction protocol could be applied to Migata-Kosugi-Stille coupling[12] as well as Sonogashira coupling. When phosphorylethyne **1** was subjected to deprotection (*t*-BuOK), stannylation (Bu_3SnOMe), and Migata-Kosugi-Stille coupling with iodide **14** ($Pd_2(dba)_3$ and *t*-Bu_3P), each step proceeded smoothly to give **15** in 96% yield (Scheme 4).[13] In this process, addition of 0.5 equiv of *t*-BuOK enabled the complete deprotection of the $Ph_2P(O)$ group and the formation of stannylethyne **16** because MeOK which was produced by stannylation of the resulting potassium acetylide with Bu_3SnOMe also served as a deprotection reagent.[14] This deprotection/Migata-Kosugi-Stille coupling protocol proceeded smoothly in coupling between **1** and **17** to provide **18** in 77% yield. In this reaction, only stannylethyne **16** reacted with phenyl iodide moiety of **17**, and terminal ethyne moiety of **17** remained untouched.[15]

We succeeded in synthesis of yne-diynes by taking advantage of Hay coupling[16] followed by one-pot deprotection/Sonogashira coupling (Scheme 5). When a toluene solution of monophosphoryl-protected diyne **19** and phenylethyne (**20**) was heated in the presence of CuCl, **21** was obtained in 76% yield. In this Hay coupling, homocoupling products **22** and **23** were produced as byproducts, but the high polarity of $Ph_2P(O)$ group enabled easy purification of the desired heterocoupling product **21** by column chromatography on silica gel (Rf = 0.55 for **21**, 0.24 for **22**, and 0.97 for **23** in AcOEt). Subjection of **21** to deprotection and Sonogashira coupling with 4-iodoanisole furnished yne-diyne **24** in 74% yield. The similar Eglington coupling between terminal ethynes **25** and **26** followed by deprotection/Sonogashira coupling of the resulting butadiyne **27** with phenylbromide **28** provided nitro- and trifluoromethyl-substituted yne-diyne **29** (60% × 62% yield).

By invoking the $Ph_2P(O)$-assisted purification of the intermediate and copper-catalyzed butadiyne formation, we succeeded in synthesis of cyclic pentayne **30** (Scheme 6). Hay

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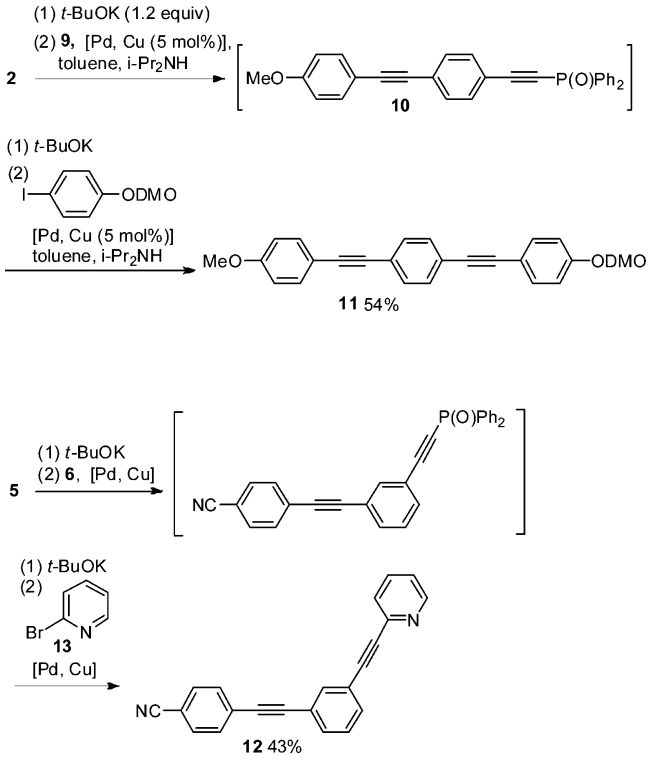
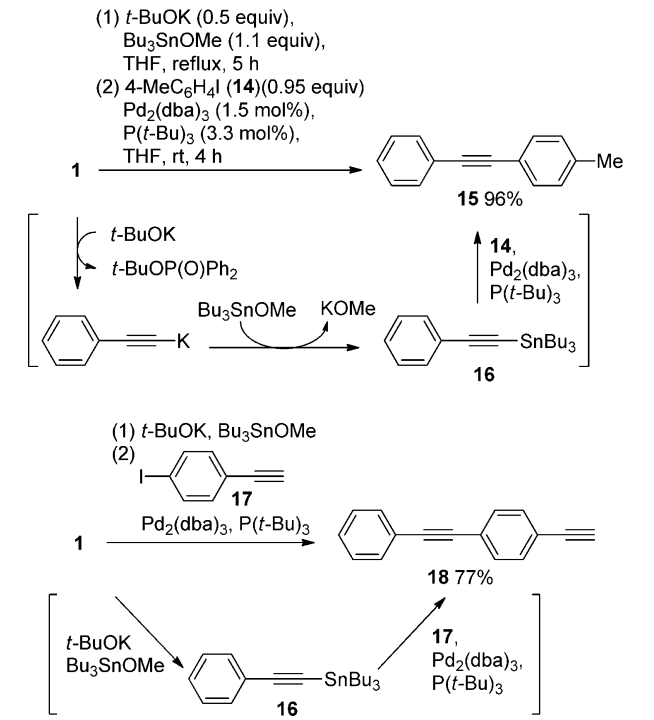
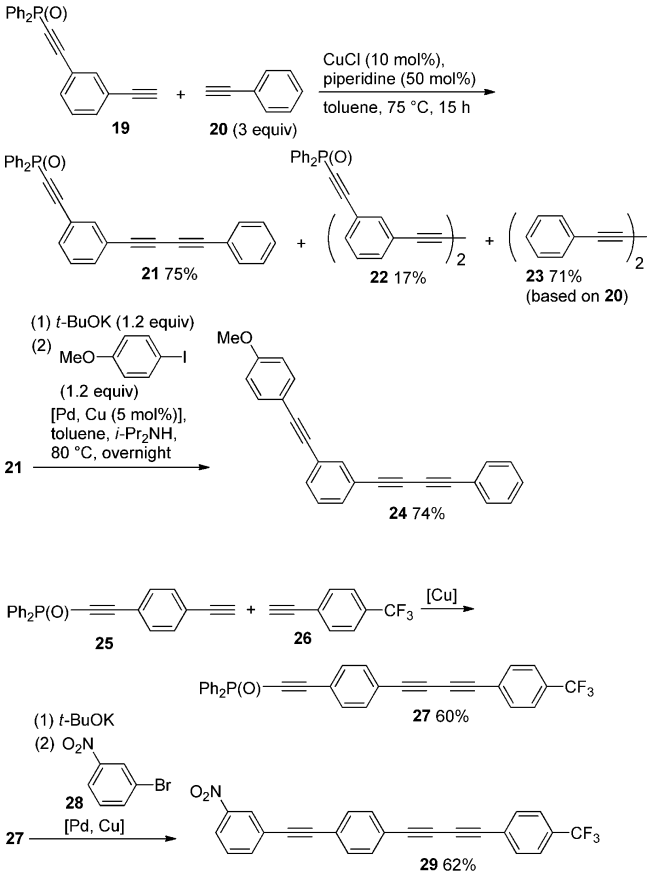
Scheme 3. Compacted One-Pot Synthesis of Arylethynes through $Ph_2P(O)$-Deprotection and Sonogashira Coupling



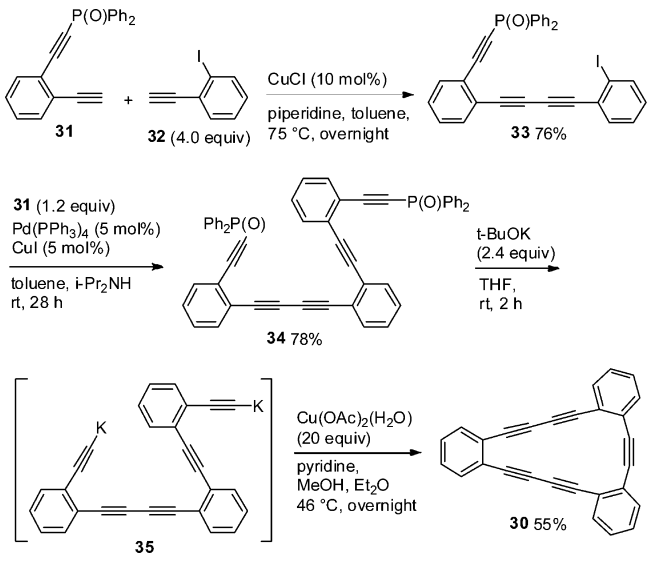
Scheme 4. One-Pot Deprotection/Stannylation/Migata-Kosugi-Stille Coupling



Scheme 5. Synthesis of Yne-diynes by Invoking Hay Coupling Followed by Deprotection/Sonogashira Coupling



Scheme 6. Synthesis of Cyclic Pentaynes by Invoking Hay, Sonogashira, and Eglinton Couplings



coupling between monoprotected diyne **31** and iodoethyne **32** gave iodotriyne **33** in 76% yield, and Sonogashira coupling of the resulting iodide **33** with **31** provided bis-$Ph_2P(O)$-protected pentayne **34** in 78% yield. When **34** was subjected to *t*-BuOK-catalyzed deprotection followed by $Cu(OAc)_2$-catalyzed Eglington coupling,[17] the expected cyclization occurred to produce cyclic pentayne **30** in 55% yield. The final *in situ* deprotection/Eglington cyclization proceeded smoothly without isolation of deprotected-terminal ethyne **35**. Although Haley has synthesized successfully the cyclic pentayne **30** by invoking the similar deprotection and cyclization of TMS-protected pentayne,[18] our protocol is more convenient to some extent than his process, which

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requires transformation of Ar−N_3Et_2 to Ar−I by heating in a pressure bottle and *in situ* desilylation of TMS-proptected butadiyne/Sonogashira coupling of the terminal butadyne moiety with aryl iodide under strictly controlled reaction conditions.

In summary, we have established a new methodology of C−C bond formation by invoking *in situ* deprotection of $Ph_2P(O)$ group/transition metal-catalyzed coupling of the resulting terminal ethyne. In one-pot deprotection/Sonogashira coupling protocol, unsymmetrically substituted aryleneethynylenes were obtained easily. When a stoichiometric amount of *t*-BuOK was used for deprotection, aryl halide having $Ph_2P(O)$-protected ethyne could be employed as a coupling counterpart, and the corresponding aryleneethynylene having $Ph_2P(O)$-protected ethyne was obtained. By compaction of deprotection, stannylation and palladium-catalyzed coupling, one-pot deprotection/Migata-Kosugi-Stille coupling was realized. In this coupling protocol, *in situ* prepared stannylethyne reacted preferentially with aryl iodide, while unprotected terminal ethyne moiety of aryl iodide remained intact. Highly polar $Ph_2P(O)$ protecting group enabled easy isolation of unsymmetrically substituted butadiynes which were obtained by copper-catalyzed oxidative coupling of teiminal ethynes, and the following one-pot deprotection/Sonogashira coupling afforded yne-diynes. *In situ* deprotection of $Ph_2P(O)$ groups/intramolecular Eglington coupling proceeded smoothly to give a cyclic pentayne.

EXPERIMENTAL SECTION

General. ^1H and ^{13}C NMR spectra were recorded at 500 or 300 MHz and at 125 or 75 MHz, respectively, and calibrated with tetramethysilane (TMS) as an internal reference. High-resolution mass spectra (FAB) were recorded using *p*-nitrobenzyl alcohol as a matrix. Melting points (mp) were measured and uncorrected. All glassware was flame-dried prior to use, and all reactions were performed under nitrogen. Anhydrous solvents (THF, CH_2Cl_2) were purchased and used without further purification, and toluene and amines (Et_3N, *i*-Pr_2NH) were distilled from sodium and CaH_2, respectively, prior to use. Purification of the products was performed by flash column chromatography on silica gel (IR-60−63/210). Ethynes **17**,[19] **26**,[20] and **32**[21] and 4-(3,7-dimethyloctyloxy)phenyl iodide[22] were prepared according to the reported procedure.

Synthesis of $Ph_2P(O)$-Protected Ethynes 1, 2, and 5 (Representative Procedure for 1). A toluene solution (5.0 mL) of ethynylbenzene (109.8 μL, 1.0 mmol), CuI (19.0 mg, 0.1 mmol), Ph_2PCl (220.6 μL, 1.2 mmol), and Et_3N (277.2 μL, 2.0 mmol) was stirred under nitrogen at 80 °C for 8 h. After usual workup with CH_2Cl_2 and NH_4Claq, the combined organic layer was washed with brine, and dried over $MgSO_4$. After filtration, the solvents were evaporated. The crude product was used for next step without purification. To a THF solution (10.0 mL) of the crude diphenyl(phenylethynyl)phosphine was added H_2O_2aq (30%, 2.5 mL, 20.0 mmol) slowly at 0 °C, and the mixture was stirred at rt for 2 h. After workup with CH_2Cl_2 and water, the combined organic layer was washed with brine and dried over $MgSO_4$. After filtration, the solvents were evaporated. The crude product was subjected to column chromatography on silica gel (hexane/AcOEt, 1:1) to afford diphenyl(phenylethynyl)phosphine oxide in a pure form (226.7 mg, 75% yield).

One (R = H):[7] white powder; mp 94−96 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.39 (t, *J* = 7.6 Hz, 2H), 7.46 (d, *J* = 7.4 Hz, 1H), 7.48−7.52 (m, 4H), 7.56 (t, *J* = 7.3 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 2H), 7.89−7.93 (m, 4H).

Two (R = 4-MeO):[7] white powder; mp 125−126 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 3.84 (s, 3H), 6.89 (d, *J* = 8.8 Hz, 2H), 7.49−7.56 (m, 8H), 7.88−7.92 (m, 4H).

Five (R = CN):[7] pale yellow powder; mp 163−165 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 7.48−7.55 (m, 4H), 7.57−7.60 (m, 2H), 7.69 (br, 4H), 7.84−7.92 (m, 4H).

Synthesis of $Ph_2P(O)$-Protected Ethynes 3, 6, and 9 (Representative Procedure for 3). *(i). Synthesis of Ethynyldiphenylphosphine Oxide.* To a flask were added CuI (190.4 mg, 1.0 mmol), Ph_2PCl (1.8 mL, 10.0 mmol), trimethylsilylacetylene (1.7 mL, 12.0 mmol), triethylamine (2.8 mL, 20.0 mmol), and toluene (30.0 mL), and the mixture was stirred under nitrogen at 80 °C for 24 h. After workup with AcOEt/water, the organic layer was washed with aqueous NH_4Cl and brine, and dried over $MgSO_4$. After filtration, the solvents were evaporated. To the crude product were added THF (20.0 mL) and then 30% H_2O_2aq (30%, 5.0 mL, 40.0 mmol) at 0 °C, and the mixture was stirred in the air at rt for 13 h. After workup with CH_2Cl_2/water, the organic layer was washed with brine, and dried over $MgSO_4$. After filtration, the solvents were evaporated. To the crude product were added water (0.5 mL) and THF (50.0 mL), and then TBAF (1.0 M in THF, 1.0 mL, 1.0 mmol) at 0 °C, and the mixture was stirred in the air at rt for 5 h. After the solvents were evaporated, the crude product was subjected to column chromatography on silica gel (hexane/AcOEt, 1:1) to give ethynyldiphenylphosphine oxide (1.63 g, 72% yield in 3 steps) in a pure form.

Ethynyldiphenylphosphine oxide:[7] white powder; ^1H NMR (500 MHz, $CDCl_3$): δ 3.33 (d, *J* = 9.8 Hz, 1H), 7.48−7.52 (m, 4H), 7.56−7.59 (m, 2H), 7.83−7.87 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 78.8 (d, *J* = 159.7 Hz), 94.0 (d, *J* = 27.4 Hz), 128.7 (d, *J* = 13.4 Hz), 130.9 (d, *J* = 11.4 Hz), 131.5, 132.5.

(ii). Sonogashira Coupling of 1-Bromo-3-Iodobenzene with Ethynyldiphenylphosphine Oxide. A toluene solution (5.0 mL) of 1-bromo-3-iodobenzene (339.5 mg, 1.2 mmol), **S1** (226.2 mg, 1.0 mmol), $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol), CuI (9.5 mg, 0.05 mmol), and diisopropylamine (0.5 mL) was stirred under nitrogen at 80 °C for 15 h. After workup with CH_2Cl_2/NH_4Claq, the combined organic layer was washed with brine and dried over $MgSO_4$. After filtration, the solvents were evaporated. The crude product was subjected to column chromatography on silica gel (hexane/AcOEt, 1:1) to afford **3** in a pure form (278.3 mg, 73% yield).

3: white powder; mp 98−99 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.26 (t, *J* = 7.9 Hz, 1H), 7.49−7.54 (m, 5H), 7.56−7.60 (m, 3H), 7.74 (s, 1H), 7.86−7.91 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 84.1 (d, *J* = 165.7 Hz), 103.1 (d, *J* = 29.2 Hz), 121.7 (d, *J* = 3.7 Hz), 122.2, 128.6 (d, *J* = 13.7 Hz), 130.0, 130.8 (d, *J* = 11.2 Hz), 132.3 (d, *J* = 3.1 Hz), 132.4 (d, *J* = 121.9 Hz), 133.7, 134.8, 134.9; ^{31}P NMR (121 MHz, $CDCl_3$): δ 9.83; HRMS (FAB) calcd for $C_{20}H_{15}BrOP$ ($M+H^+$): 381.0044, found 381.0049.

6:[7] 46% yield; pale-yellow powder; mp 94−96 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.95 (t, *J* = 8.0 Hz, 1H), 7.49−7.53 (m, 4H), 7.56−7.59 (m, 3H), 7.79 (d, *J* = 7.9 Hz, 1H), 7.86−7.91 (m, 4H), 7.94 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 84.0 (d, *J* = 165.7 Hz), 93.4, 102.9 (d, *J* = 29.2 Hz), 121.6 (d, *J* = 4.0 Hz), 128.5 (d, *J* = 13.4 Hz), 129.9, 130.7 (d, *J* = 11.2 Hz), 131.4, 132.2 (d, *J* = 2.8 Hz), 132.4 (d, *J* = 121.9 Hz), 139.5, 140.5; ^{31}P NMR (121 MHz, $CDCl_3$): δ 9.80.

9:[7] 82% yield; white powder; mp 154−155 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.46 (d, *J* = 8.6 Hz, 2H), 7.49−7.59 (m, 8H), 7.86−7.91 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 83.7 (d, *J* = 166.3 Hz), 103.6 (d, *J* = 29.4 Hz), 118.2 (d, *J* = 4.3 Hz), 125.0, 128.3 (d, *J* = 13.7 Hz), 130.4 (d, *J* = 11.2 Hz), 131.5, 132.0 (d, *J* = 2.8 Hz), 132.2 (d, *J* = 121.9 Hz), 133.4 (d, *J* = 1.9 Hz); ^{31}P NMR (121 MHz, $CDCl_3$): δ 9.88.

Synthesis of $Ph_2P(O)$-Protected Ethynes 19, 25, and 31 (Representative Procedure for 19). A toluene solution (10 mL) of 1,3-diethynylbenzene (126.2 mg, 1.0 mmol), CuI (19.0 mg, 0.1 mmol), Ph_2PCl (220.6 μL, 1.2 mmol), and Et_3N (277.2 μL, 2.0 mmol) was stirred under nitrogen at 80 °C for 8 h. After workup with CH_2Cl_2/NH_4Claq, the combined organic layer was washed with brine, and dried over $MgSO_4$. After filtration, the solvents were evaporated. The crude product was used for the next step without purification. To a THF solution (10.0 mL) of the crude product was added H_2O_2aq (30%, 2.5 mL, 20.0 mmol) at 0 °C, and the mixture was stirred at rt for 2 h. After workup with CH_2Cl_2/water, the combined organic layer was

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washed with brine and dried over $MgSO_4$. After filtration, the solvents were evaporated. The crude product was subjected to column chromatography on silica gel (hexane/AcOEt, 1:1) to afford **19** in a pure form (146.8 mg, 45% yield).

19:[7] white powder; mp 111−113 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.12 (s, 1H), 7.35 (t, J = 8.0 Hz, 1H), 7.49−7.52 (m, 4H), 7.55−7.58 (m, 4H), 7.71 (s, 1H), 7.87−7.91 (m, 4H).

25: 48% yield; white powder; mp 145−147 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.24 (s, 1H), 7.48−7.52 (m, 6H), 7.54−7.58 (m, 4H), 7.87−7.91 (m, 4H); ^{13}C NMR (75.45 MHz, $CDCl_3$): δ 80.4, 82.6, 84.6 (d, J = 167.6 Hz), 104.4 (d, J = 29.4 Hz), 120.08, 120.13, 124.5, 128.7 (d, J = 13.7 Hz), 130.9 (d, J = 11.2 Hz), 132.2, 132.4, 132.7 (d, J = 121.9 Hz); ^{31}P NMR (121 MHz, $CDCl_3$): δ 7.11; HRMS (FAB) calcd for $C_{22}H_{16}OP$ ($M+H^+$): 327.0939, found 327.0946.

31: 45%; white powder; mp 121−122 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.27 (s, 1H), 7.36 (t, J = 7.60 Hz, 1H), 7.41 (t, J = 7.65 Hz, 1H), 7.47−7.50 (m, 4H), 7.54−7.56 (m, 3H), 7.60 (d, J = 7.65 Hz, 1H), 7.94−7.99 (m, 4H); ^{13}C NMR (75.45 MHz, $CDCl_3$): δ 81.3, 82.3, 86.4 (d, J = 167.8 Hz), 103.1 (d, J = 29.8 Hz), 123.1 (d, J = 3.7 Hz), 125.8 (d, J = 1.5 Hz), 128.5 (d, J = 13.6 Hz), 128.7, 130.2, 131.1 (d, J = 11.2 Hz), 132.2 (d, J = 3.1 Hz), 132.7, 132.8, 133.0 (d, J = 122.0 Hz); ^{31}P NMR (121 MHz, $CDCl_3$): δ 6.65; HRMS (FAB) calcd for $C_{22}H_{16}OP$ ($M+H^+$): 327.0939, found 327.0941.

One-Pot $Ph_2P(O)$-Deprotection of 1/Sonogashira Coupling with Phenyl Bromide (Representative). To a THF solution (10.0 mL) of **1** (302.3 mg, 1.0 mmol) was added *t*-BuOK (134.6 mg, 1.2 mmol). After the mixture had been stirred for 2 h under nitrogen at rt, bromobenzene (188.4 mg, 1.2 mmol), $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol), CuI (9.5 mg, 0.05 mmol), toluene (16.0 mL), and diisopropylamine (0.5 mL) were added sequentially. The mixture was stirred under nitrogen at 80 °C for 15 h. After workup with CH_2Cl_2/NH_4Claq, the organic layer was washed with brine, and dried over $MgSO_4$. After filtration, the solvents were evaporated. The crude product was subjected to column chromatography on silica gel (hexane) to give diphenylacetylene in a pure form (128.3 mg, 72% yield).

Diphenylacetylene:[23] white powder; mp 59−61 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32−7.37 (m, 6H), 7.52−7.55 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 89.3, 123.2, 128.2, 128.3, 131.6.

4:[7] white powder; mp 151−152 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.84 (s, 3H), 6.89 (d, J = 8.8 Hz, 2H), 7.36 (t, J = 7.6 Hz, 1H), 7.47 (d, J = 8.8 Hz, 2H), 7.49−7.54 (m, 5H), 7.56−7.58 (m, 3H), 7.74 (s, 1H), 7.88−7.93 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 55.3 (d, J = 4.1 Hz), 83.3 (d, J = 167.8 Hz), 86.5, 90.9, 104.4 (d, J = 29.5 Hz), 113.99, 114.04, 114.6, 120.2 (d, J = 4.1 Hz), 124.4, 128.7 (d, J = 13.4 Hz), 130.9 (d, J = 11.3 Hz), 131.6, 132.3, 132.8 (d, J = 122.4 Hz), 133.1 (d, J = 4.2 Hz), 133.4, 135.1, 159.9; ^{31}P NMR (121 MHz, $CDCl_3$): δ 9.78; HRMS (FAB) calcd for $C_{29}H_{22}O_2P$ ($M+H^+$): 433.1357, found 433.1351.

7: white powder; mp 174−176 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 (t, J = 7.8 Hz, 1H), 7.49−7.53 (m, 4H), 7.56−7.61 (m, 6H), 7.65 (d, J = 8.5 Hz, 2H), 7.77 (s, 1H), 7.88−7.92 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 83.9 (d, J = 166.4 Hz), 88.9, 91.8, 103.8 (d, J = 29.4 Hz), 111.9, 118.3, 120.6 (d, J = 3.5 Hz), 123.0, 127.5, 128.7 (d, J = 13.4 Hz), 128.87, 128.94, 130.9 (d, J = 11.3 Hz), 132.1 (d, J = 6.8 Hz), 132.4, 132.7 (d, J = 121.9 Hz), 132.8, 133.7, 135.4; ^{31}P NMR (121 MHz, $CDCl_3$): δ 6.82; HRMS (FAB) calcd for $C_{29}H_{19}NOP$ ($M+H^+$): 428.1204, found 428.1199.

8: yellow powder; mp 215−218 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.47 (t, J = 7.65 Hz, 1H), 7.54 (t, J = 7.05 Hz, 2H), 7.58 (d, J = 7.95 Hz, 1H), 7.60−7.64 (m, 2H), 7.64−7.68 (m, 4H), 7.78 (d, J = 7.65 Hz, 1H), 7.96 (s, 1H), 8.04 (d, J = 8.6 Hz, 2H), 8.47 (s, 1H), 8.64 (d, J = 8.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 87.3, 88.4, 92.9, 99.5, 111.7, 116.7, 118.4, 122.8, 124.2, 125.7, 126.57, 126.62, 126.8, 127.9, 128.1, 128.2, 128.8, 131.2, 131.6, 132.08, 132.12, 132.7, 134.6 (d, J = 2.5 Hz); HRMS (FAB) calcd for $C_{31}H_{18}N$ ($M+H^+$): 404.1439, found 404.1430.

One-Pot Me_3Si-Deprotection of Trimethyl(Phenylethynyl)-Silane/Sonogashira Coupling with Phenyl Bromide. To a THF solution (10.0 mL) of trimethyl(phenylethynyl)silane (174.3 mg, 1.0 mmol) was added *t*-BuOK (134.6 mg, 1.2 mmol) at 0 °C. After the mixture had been stirred for 2 h under nitrogen at 0 °C, bromobenzene (188.4 mg, 1.2 mmol), $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol), CuI (9.5 mg, 0.05 mmol), toluene (16.0 mL), and diisopropylamine (0.5 mL) were added sequentially. The mixture was stirred under nitrogen at 80 °C for 15 h. After workup with CH_2Cl_2/NH_4Claq, the organic layer was washed with brine, and dried over $MgSO_4$. After filtration, the solvents were evaporated. The crude product was subjected to column chromatography on silica gel (hexane) to give diphenylacetylene in a pure form (83.8 mg, 47% yield).

*Compacted One-Pot Synthesis of **11** from **2** through $Ph_2P(O)$-Deprotection/Sonogashira Coupling (Representative).* To a THF solution (10.0 mL) of **2** (332.3 mg, 1.0 mmol) was added *t*-BuOK (134.6 mg, 1.2 mmol). After the mixture had been stirred for 2 h under nitrogen at rt, **9** (324.0 mg, 0.85 mmol), $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol), CuI (9.5 mg, 0.05 mmol), toluene (16.0 mL), and diisopropylamine (0.5 mL) were added sequentially. The mixture was stirred under nitrogen at 80 °C for 15 h. After workup with CH_2Cl_2/NH_4Claq, the organic layer was washed with brine, and dried over $MgSO_4$. After filtration, the solvents were evaporated. The crude product was filtered by a thin pad of silica gel (hexane/AcOEt, 1:1), and the filtrate was concentrated. To a THF solution (10 mL) of the crude product **10** was added *t*-BuOK (134.6 mg, 1.2 mmol) at rt. After the mixture had been stirred for 2 h under nitrogen at rt, 4-(3,7-dimethyloctyloxy)-1-iodobenzene (396.3 mg, 1.1 mmol), $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol), CuI (9.5 mg, 0.05 mmol), toluene (16.0 mL), and diisopropylamine (0.5 mL) were added sequentially. The mixture was stirred under nitrogen at 80 °C for 15 h. After workup with CH_2Cl_2/NH_4Claq, the organic layer was washed with brine, and dried over $MgSO_4$. After filtration, the solvents were evaporated. The crude product was subjected to column chromatography on silica gel (hexane/CH_2Cl_2, 5:1) to afford **11** in a pure form (213.3 mg, 54% yield, based on bromide).

11: white powder; mp 151−153 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.87 (d, J = 6.75 Hz, 6H), 0.95 (d, J = 6.45 Hz, 3H), 1.15−1.35 (m, 6H), 1.51−1.62 (m, 2H), 1.67−1.68 (m, 1H), 1.80−1.86 (m, 1H), 3.83 (s, 3H), 3.97−4.05 (m, 2H), 6.86−6.89 (m, 4H), 7.45−7.48 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.6, 22.59, 22.63, 24.6, 28.0, 29.8, 36.1, 37.2, 39.2, 55.2, 66.4, 87.8, 87.9, 91.1, 91.3, 114.0, 114.6, 114.8, 115.2, 123.0, 123.1, 131.3, 133.0, 133.1, 159.3, 159.7; HRMS (FAB) calcd for $C_{33}H_{37}O_2$ ($M+H^+$): 465.2794, found 465.2795.

12: white powder; mp 154−155 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28−7.29 (m, 1H), 7.39 (t, J = 7.6 Hz, 1H), 7.54 (dd, J = 1.2 Hz, J = 8.0 Hz, 2H), 7.60−7.62 (m, 3H), 7.66 (d, J = 8.5 Hz, 2H), 7.71 (dt, J = 1.8 Hz, J = 7.9 Hz, 1H), 7.79 (s, 1H), 8.64 (d, J = 4.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 87.8, 88.3, 89.4, 92.6, 111.6, 118.4, 122.6, 122.8, 123.0, 127.2, 127.8, 128.6, 128.7, 132.0, 132.1, 132.4, 135.1, 136.2, 143.0, 150.1; HRMS (FAB) calcd for $C_{22}H_{13}N_2$ ($M+H^+$): 305.1079, found 305.1086.

*Synthesis of **15**: One-Pot $Ph_2P(O)$-Deprotection/Stannylation/Migata-Kosugi-Stille Coupling (Representative).* To a THF solution (5.0 mL) of **1** (302.3 mg, 1.0 mmol) were added Bu_3SnOMe (353.2 mg, 316.8 μL, 1.1 mmol) and *t*-BuOK (56.1 mg, 0.5 mmol) at rt, and the mixture was refluxed under nitrogen for 5 h. To the reaction mixture were added **14** (207.1 mg, 0.95 mmol), P(*t*-Bu)$_3$ (0.1 M in THF, 330.0 μL, 0.033 mmol), and $Pd_2(dba)_3$ (13.7 mg, 0.015 mmol) at rt, and the mixture was stirred under nitrogen at rt for 4 h. After workup with diethyl ether (3 × 10.0 mL)/NH_4Faq (10%, 10.0 mL), the organic layer was dried over $MgSO_4$. After filtration, the solvents were evaporated. The crude product was subjected to column chromatography on silica gel (hexane) to afford **15** in a pure form (175.3 mg, 96% yield, based on iodide).

15:[24] colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.37 (s, 3H), 7.16 (d, J = 7.9 Hz, 2H), 7.30−7.36 (m, 3H), 7.43 (d, J = 7.9 Hz, 2H), 7.52−7.54 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.5, 88.7, 89.5, 120.1, 123.4, 128.0, 128.3, 129.1, 131.4, 131.5, 138.3.

18:[25] white powder; mp 91−92 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.18 (s, 1H), 7.35−7.36 (m, 3H), 7.46−7.50 (m, 4H), 7.52−7.54 (m,

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2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 78.9, 83.2, 88.8, 91.3, 121.8, 122.8, 123.7, 128.4, 128.5, 131.4, 131.6, 132.0.

Synthesis of Yne-Diynes 24: Hay Coupling Followed by $Ph_2P(O)$-Deprotection/Sonogashira Coupling (Representative). *(i). Hay Coupling.* A mixture of **19** (326.3 mg, 1.0 mmol), **20** (329.5 μL, 3.0 mmol), CuCl (9.9 mg, 0.1 mmol), piperidine (50.0 μL, 0.5 mmol), and toluene (10 mL) was stirred in the air at 75 °C for 15 h. After workup with CH_2Cl_2/NH_4Claq, the organic layer was washed with brine, and dried over $MgSO_4$. After filtration, the solvents were evaporated. The crude product was subjected to column chromatography on silica gel (hexane/AcOEt, 1:1) to afford **21** (319.8 mg, 75% yield), **22** (55.3 mg, 17%), and **23** (215.4 mg, 71% (based on **20**)) in pure forms.

21: pale-yellow powder; mp 166−167 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33−7.41 (m, 4H), 7.49−7.54 (m, 6H), 7.56−7.59 (m, 4H), 7.74 (s, 1H), 7.87−7.92 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 73.4, 75.3, 79.6, 82.4, 83.8 (d, J = 167.0 Hz), 103.7 (d, J = 29.4 Hz), 120.5 (d, J = 4.1 Hz), 121.4, 122.7, 128.4 (d, J = 5.2 Hz), 128.7 (d, J = 13.4 Hz), 128.9 (d, J = 8.8 Hz), 129.4 (d, J = 3.1 Hz), 130.9 (d, J = 11.3 Hz), 132.4, 132.5, 132.7 (d, J = 121.9 Hz), 132.8, 134.3, 136.1; ^{31}P NMR (121 MHz, $CDCl_3$): δ 6.36; HRMS (FAB) calcd for $C_{30}H_{20}OP$ (M+H$^+$): 427.1252, found 427.1259.

22: pale-yellow powder; mp 198−201 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38 (t, J = 7.8 Hz, 2H), 7.48−7.61 (m, 16H), 7.75 (s, 2H), 7.86−7.94 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 74.8, 80.4, 83.9 (d, J = 166.0 Hz), 103.6 (d, J = 29.2 Hz), 120.6 (d, J = 4.0 Hz), 122.3, 128.7 (d, J = 13.4 Hz), 128.9, 130.9 (d, J = 11.5 Hz), 132.4 (d, J = 2.8 Hz), 132.6 (d, J = 122.2 Hz), 133.0, 134.4, 136.1; ^{31}P NMR (121 MHz, $CDCl_3$): δ 6.90; HRMS (FAB) calcd for $C_{44}H_{29}O_2P_2$ (M+H$^+$): 651.1643, found 651.1641.

23:[26] white powder; mp 83−84 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32−7.39 (m, 6H), 7.52−7.54 (m, 4H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 73.9, 81.5, 121.8, 128.4, 129.2, 132.5.

(ii). $Ph_2P(O)$-Deprotection/Sonogashira Coupling. To a THF solution (10.0 mL) of **21** (213.2 mg, 0.5 mmol) was added *t*-BuOK (67.3 mg, 0.6 mmol) at rt. After the mixture had been stirred under nitrogen at rt for 2 h, 1-iodo-4-methoxybenzene (128.7 mg, 0.55 mmol), $Pd(PPh_3)_4$ (28.9 mg, 0.025 mmol), CuI (4.8 mg, 0.025 mmol), toluene (16.0 mL), and diisopropylamine (0.25 mL) were added sequentially. The mixture was stirred under nitrogen at 80 °C for 15 h. After workup with CH_2Cl_2/NH_4Claq, the organic layer was washed with brine, and dried over $MgSO_4$. After filtration, the solvents were evaporated. The crude product was subjected to column chromatography on silica gel (hexane/CH_2Cl_2, 8:1) to give **24** in a pure form (123.0 mg, 74% yield).

24: white powder; mp 126−128 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.84 (s, 3H), 6.89 (d, J = 8.8 Hz, 2H), 7.29−7.40 (m, 4H), 7.45−7.50 (m, 4H), 7.54 (d, J = 6.7 Hz, 2H), 7.67 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 55.3 (d, J = 4.1 Hz), 73.8, 74.4, 80.7, 81.8, 86.9, 90.4, 114.0, 114.1, 114.9, 121.7, 122.1, 124.2, 128.5, 129.3, 131.7, 132.0, 132.5, 133.2 (d, J = 8.3 Hz), 135.2 (d, J = 3.1 Hz), 159.8; HRMS (FAB) calcd for $C_{25}H_{17}O$ (M+H$^+$): 333.1279, found 333.1285.

27: white powder; mp 253−255 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49−7.54 (m, 6H), 7.56−7.59 (m, 4H), 7.60−7.64 (m, 4H), 7.87−7.91 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 75.7, 76.4, 81.38, 81.44, 85.4 (d, J_{C-P} = 166.4 Hz), 104.1 (d, J_{C-P} = 29.4 Hz), 120.7, 120.8, 123.6 (q, J_{C-F} = 272.0 Hz), 123.8, 125.2 (d, J_{C-F} = 1.5 Hz), 125.4 (d, J_{C-F} = 3.1 Hz), 128.7 (d, J_{C-P} = 13.4 Hz), 130.95 (d, J_{C-P} = 10.8 Hz), 130.98 (q, J_{C-F} = 32.5 Hz), 132.4, 132.5 (d, J_{C-P} = 8.9 Hz), 132.6 (d, J_{C-P} = 122.0 Hz), 132.8; ^{19}F NMR (282 MHz, $CDCl_3$): δ −94.03; ^{31}P NMR (121 MHz, $CDCl_3$): δ 6.51; HRMS (FAB) calcd for $C_{31}H_{19}F_3OP$ (M+H$^+$): 495.1126, found 495.1122.

29: white powder; mp 159−161 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52−7.57 (m, 5H), 7.62 (q, J = 8.6 Hz, 4H), 7.83 (d, J = 7.9 Hz, 1H), 8.19−8.21 (m, 1H), 8.38 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 75.6, 76.0, 80.9, 82.0, 89.5, 91.1, 121.9, 123.2, 123.3, 123.7 (q, J_{C-F} = 272.1 Hz), 124.6, 125.4 (q, J_{C-F} = 2.9 Hz), 126.4, 126.5, 129.4, 130.9 (q, J_{C-F} = 32.8 Hz), 131.8, 132.6, 132.7, 137.2, 148.2; ^{19}F NMR (282 MHz, $CDCl_3$): δ −63.49; HRMS (FAB) calcd for $C_{25}H_{13}F_3NO_2$ (M+H$^+$): 416.0898, found 416.0902.

Synthesis of Cyclic Pentayne 30. *(i). Synthesis of **33**.* A mixture of **31** (326.3 mg, 1.0 mmol), **32** (912.1 mg, 4.0 mmol), CuCl (9.9 mg, 0.1 mmol), piperidine (50.0 μL, 0.5 mmol), and toluene (10.0 mL) was stirred in the air at 75 °C for 15 h. After workup with CH_2Cl_2/NH_4Claq, the organic layer was washed with brine, and dried over $MgSO_4$. After filtration, the solvents were evaporated. The crude product was subjected to column chromatography on silica gel (hexane/AcOEt, 1:1) to afford **33** in a pure form (419.8 mg, 76% yield).

33: yellow powder; mp 129−131 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.07 (dt, J = 1.2 Hz, J = 7.6 Hz, 1H) 7.32 (t, J = 7.6 Hz, 1H), 7.36−7.41 (m, 1H), 7.42−7.44 (m, 2H), 7.48−7.50 (m, 6H), 7.60−7.62 (m, 2H), 7.85 (d, J = 7.9 Hz 1H), 8.00−8.04 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 76.9, 78.5, 80.7, 84.6, 86.9 (d, J = 166.5 Hz), 100.8, 102.6 (d, J = 29.4 Hz), 123.6 (d, J = 4.1 Hz), 125.2 (d, J = 2.1 Hz), 127.7, 128.2, 128.7 (d, J = 12.4 Hz), 129.2, 130.3, 130.4, 130.5, 131.0 (d, J = 11.4 Hz), 132.1, 132.8 (d, J = 122.0 Hz), 133.0 (d, J = 6.6 Hz), 133.9, 138.9; ^{31}P NMR (121 MHz, $CDCl_3$): δ 6.60; HRMS (FAB) calcd for $C_{30}H_{19}IOP$ (M+H$^+$): 553.0218, found 553.0212.

*(ii). Synthesis of **34**.* A toluene solution (10.0 mL) of **33** (276.2 mg, 0.5 mmol), **31** (195.9 mg, 0.6 mmol), $Pd(PPh_3)_4$ (28.9 mg, 0.025 mmol), CuI (4.8 mg, 0.025 mmol), and diisopropylamine (0.25 mL) was stirred under nitrogen at rt for 28 h. After workup with CH_2Cl_2/NH_4Claq, the combined organic layer was washed with brine and dried over $MgSO_4$. After filtration, the solvents were evaporated. The crude product was subjected to column chromatography on silica gel (AcOEt) and recrystallization from THF/hexane to afford **34** in a pure form (292.8 mg, 78% yield).

34: pale-yellow powder; mp 114−116 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.21−7.24 (m, 2H), 7.30−7.34 (m, 3H), 7.35−7.39 (m, 5H), 7.40−7.48 (m, 11H), 7.59−7.63 (m, 3H), 7.92−7.98 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 77.6, 78.6, 80.4, 81.8, 86.4 (d, J = 167.9 Hz), 86.9 (d, J = 166.5 Hz), 91.9, 92.4, 102.6 (d, J = 29.4 Hz), 103.5 (d, J = 30.0 Hz), 122.1 (d, J = 3.6 Hz), 123.4 (d, J = 4.1 Hz), 123.9, 125.3 (d, J = 2.0 Hz), 126.2, 126.4 (d, J = 2.0 Hz), 128.4 (d, J = 12.4 Hz), 128.5 (d, J = 11.9 Hz), 128.59, 128.61, 128.7, 129.1, 129.2, 130.3, 130.5, 130.90 (d, J = 11.3 Hz), 130.91 (d, J = 11.4 Hz), 132.1, 132.4, 132.6, 132.7 (d, J = 122.0 Hz), 132.9, 133.0 (d, J = 122.0 Hz), 133.1, 133.2; ^{31}P NMR (121 MHz, $CDCl_3$): δ 7.07; HRMS (FAB) calcd for $C_{52}H_{33}O_2P_2$ (M+H$^+$): 751.1956, found 751.1957.

*(iii). Synthesis of **30**.* To a THF solution (4.0 mL) of **34** (75.1 mg, 0.1 mmol) was added *t*-BuOK (26.9 mg, 0.24 mmol) at rt, and the mixture was stirred under nitrogen at rt for 4 h. To the reaction mixture were added pyridine (20.0 mL) and methanol (20.0 mL), and the mixture was added to $Cu(OAc)_2(H_2O)$ (399.3 mg, 2.0 mmol) in a mixture of pyridine (18.5 mL), methanol (18.5 mL), and Et_2O (3.1 mL) at 46 °C by a syringe over 7 h. After the mixture had been stirred in the air overnight, the mixture was concentrated. After addition of CH_2Cl_2 and 10% HCl, the mixture was stirred vigorously for 30 min. The CH_2Cl_2 layer was separated, washed with Na_2CO_3aq solution, water, and brine, and dried over $MgSO_4$. After filtration, the solvents were evaporated. The crude product was subjected to column chromatography on silica gel (hexane/CH_2Cl_2, 8:1) to afford **30** in a pure form (19.2 mg, 55% yield).

30:[18] pale-yellow powder; mp 159 °C (decomp); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.21−7.29 (m, 6H), 7.32−7.35 (m, 2H), 7.40 (d, J = 7.0 Hz, 2H), 7.47 (d, J = 7.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 77.7, 80.8, 81.6, 82.2, 93.0, 123.2, 126.9, 128.1, 128.5, 129.0, 129.1, 130.5, 133.7, 134.5.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H, ^{13}C, ^{19}F, and ^{31}P NMR spectra for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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