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Modular Synthesis of Benzo[*b*]phosphole Derivatives via BuLi-Mediated Cyclization of (*o*-Alkynylphenyl)phosphine

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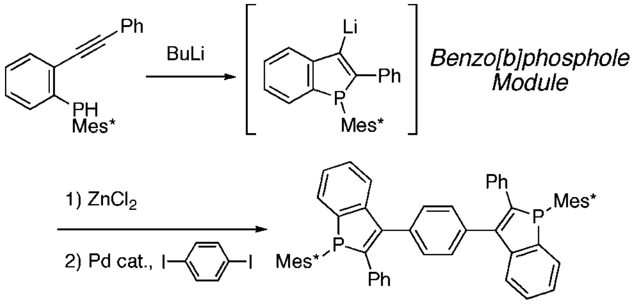
ABSTRACT



Treatment of an (*o*-alkynylphenyl)phosphine with a stoichiometric amount of BuLi effects a cyclization reaction to produce a 3-lithiobenzo[*b*]-phosphole, which affords a variety of 3-substituted benzophospholes upon reaction with electrophiles. An example is given for the synthesis of a bis-benzo[*b*]phosphole, which can be further converted to the corresponding benzo[*b*]phosphole oxide possessing high electron affinity.

Benzo[*b*]phospholes are heavy-atom congeners of indoles,[1] and their applications as physiologically and electronically active materials are of interest. Functionalized benzophospholes[2–4] are less synthetically accessible than phospholes and dibenzophospholes and hence have been studied much less frequently.[5] We have been exploring for some time a modular approach to the synthesis of new π-electron systems and have demonstrated the synthesis of a variety of functionalized benzo[*b*]furans and indoles,[6] benzo[1,2-*b*:4,5-*b*′]difurans,[7] and benzo[*b*]siloles.[8] Herein, we report the modular synthesis

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(1) Katritzky, A. R. *Comprehensive Heterocyclic Chemistry*; Pergamon: Oxford, 1984; Vol. 4, Part 3, pp 658−712.

(2) For a review, see: Aitken, R. A. *Science of Synthesis*; Thomas, J., Ed.; Thieme: Stuttgart, 2000; Vol. 10, pp 789−808.

(3) For examples of 3-functionalized benzophospholes, see: (a) Rausch, M. D.; Klemann, L. P. *J. Am. Chem. Soc.* **1967**, *89*, 5732–5733. (b) Winter, W. *Tetrahedron Lett.* **1975**, *45*, 3913–3914. (c) Balthazor, T. M. *J. Org. Chem.* **1980**, *45*, 2519–2522. (d) Märkl, G.; Jin, G. Y.; Berr, K. P. *Tetrahedron Lett.* **1993**, *34*, 3103–3106. (e) Cordaro, J. G.; Stein, D.; Grützmacher, H. *J. Am. Chem. Soc.* **2006**, *128*, 14962–14971.

(4) For a synthesis of 3-halobenzo[*b*]phosphole oxides, see: Ichihashi, Y.; Fukazawa, A.; Yamaguchi, S. *88th Annual Meeting of Chemical Society of Japan*, Tokyo, Japan, March 26−30, 2008, 3H4−48.

(5) For recent reviews, see: (a) Hobbs, M. G.; Baumgartner, T. *Eur. J. Inorg. Chem.* **2007**, 3611–3628. (b) Baumgartner, T.; Réau, R. *Chem. Rev.* **2006**, *106*, 4681–4217. (c) Mathey, F. *Angew. Chem., Int. Ed.* **2003**, *42*, 1578–1604.

(6) (a) Nakamura, M.; Ilies, L.; Otsubo, S.; Nakamura, E. *Angew. Chem., Int. Ed.* **2006**, *45*, 944–947. (b) Nakamura, M.; Ilies, L.; Otsubo, S.; Nakamura, E. *Org. Lett.* **2006**, *8*, 2803–2805.

(7) Tsuji, H.; Mitsui, C.; Ilies, L.; Sato, Y.; Nakamura, E. *J. Am. Chem. Soc.* **2007**, *129*, 11902–11903.

(8) Ilies, L.; Tsuji, H.; Sato, Y.; Nakamura, E. *J. Am. Chem. Soc.* **2008**, *130*, 4240–4241.

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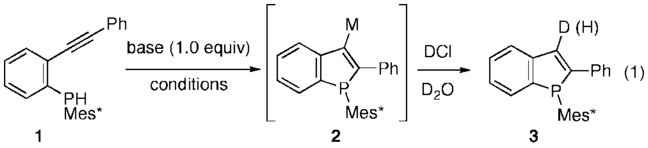
of 2,3-disubstituted benzo[*b*]phospholes by the use of a new synthetic module, 3-lithiobenzo[*b*]phosphole **2** (M = Li, eq 1), which can be quantitatively generated by base-promoted cyclization of (*o*-alkynylphenyl)phosphine **1**. We also report the electrochemical properties of a 2,3-diaryl-substituted benzo[*b*]phosphole oxide (Scheme 2), and suggest its potential utility as an *n*-type organic semiconductor.



Screening of the reaction conditions of the base-promoted cyclization of (*o*-alkynylphenyl)phosphine **1** was performed for the reaction shown in eq 1 (Mes* = 2,4,6-tri-*tert*-butylphenyl). The yield of the desired **3** and the degree of C3-deuteration were determined by ^{1}H NMR, the results being summarized in Table 1. We first examined zinc reagents in analogy to the cyclization of the oxygen and nitrogen analogues[6] and found that the reaction of **1** with diethylzinc was very slow. The reaction in THF was unacceptably slow (entry 1, Table 1), and the reaction in toluene at higher temperature afforded **3** in 96% yield with deuterium incorporation as low as 50% (entry 2, Table 1). When BuLi was used as a base, however, the reaction proceeded smoothly at −40 °C in THF and produced benzophosphole **3** in 92% yield with 96% deuterium incorporation, indicating the intermediacy of the 3-metallobenzophosphole **2** (M = Li) (entry 3, Table 1). In toluene, the cyclization required 40 °C and produced **3** in 81% yield with very poor deuterium incorporation (entry 4, Table 1). The low deuterium incorporation is probably caused by in situ protonation of **2** by the starting material **1**.

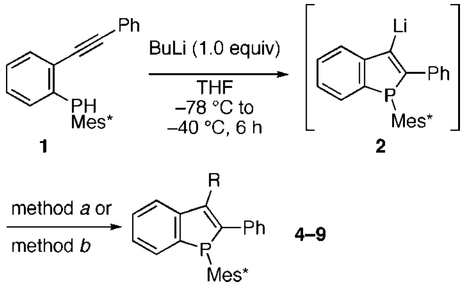
Table 1. Screening of the Reaction Conditions for Base-Promoted Intramolecular Cyclization in Eq 1

	conditions					D
entry	base	solvent	*T* (°C)	time (h)	yield[a] (%)	incorp[b] (%)
1	Et_2Zn[c]	THF	reflux	7	9	0
2	Et_2Zn[c]	toluene	reflux	8	96	50
3	*n*-BuLi[d]	THF	−40	6	92	96
4	*n*-BuLi[d]	toluene	40	12	81	23

[a] Yield of compound **3** monitored by ^{1}H NMR using CH_2Br_2 as an internal standard. [b] Percent deuterium incorporation at the 3-position of compound **3** determined by ^{1}H NMR. [c] A toluene solution of Et_2Zn (1.1 M) was added to the solution of **1** at room temperature and the reaction mixture was heated at the indicated temperature. [d] A hexane solution of BuLi (1.61 M) was added at −78 °C, and the reaction mixture was kept at the indicated temperature.

The synthesis of a variety of 3-substituted benzophospholes was achieved by reactions of the 3-lithiobenzophosphole **2** with electrophiles (Scheme 1). Direct reactions of **2** with electrophiles (method *a*, Scheme 1) were first examined, two examples being shown in Table 2. The reaction with benzaldehyde afforded a secondary alcohol **4** in 68% isolated yield (entry 1, Table 2). The reaction of **2** with 1,2-diiodoethane gave 3-iodobenzo[*b*]phosphole **5** in 90% yield (entry 2, Table 2). This iodide will serve as an Umpolung counterpart[8] of the lithium compound **2**. The bulky Mes* group effectively protected the phosphorus atom against air oxidation and electrophilic attacks.

Scheme 1. Synthesis of 2,3-Disubstituted Benzo[*b*]phospholes via the 3-Lithiobenzo[*b*]phosphole Module **2**[a]



[a] Conditions: (method *a*) electrophile (1.2 equiv), −78 °C to rt, 3−12 h; (method *b*) (1) $ZnCl_2$ (1.0 equiv), (2) electrophile (1.2 equiv), $Pd_2(dba)_3$•$CHCl_3$ (5 mol %), PPh_3 (20 mol %), rt, 2−24 h. Details for each reaction are shown in the Supporting Information.

Palladium catalysis expands the scope of the synthetic methodology. Thus, one-pot, three-step, two-component coupling of **1** and an electrophile was achieved through the intermediacy of **2** and the corresponding 3-zinciobenzo[*b*]phosphole module under the Negishi cross-coupling conditions using $Pd_2(dba)_3$•$CHCl_3$ and PPh_3 (method *b* in Scheme 1). The results are summarized in entries 3−6, Table 2. Iodobenzene and *p*-cyanophenyl iodide reacted smoothly in a few hours and gave 2,3-diaryl-substituted products **6** and **8** in 83% and 83% yield, respectively (entries 3 and 5, Table 2). However, *p*-anisyl iodide reacted slowly and afforded the product **7** in lower yield (24 h, 67% yield, entry 4, Table 2). A three-component coupling using a bifunctional electrophile, *p*-diiodobenzene, gave 1,4-bis(3-benzo[*b*]phospholyl)benzene **9** in 77% yield (based on *p*-diiodobenzene; entry 6, Table 2). ^{1}H, ^{13}C, and ^{31}P NMR spectra of **9** showed a single set of resonance signals, suggesting rapid interconversion among isomers.

The structure of 1,4-bis(3-benzo[*b*]phospholyl)benzene **9** was unambiguously determined by single-crystal X-ray structural analysis (Figure 1). The crystal used for the measurement contained only one diastereomer. The molecule has an inversion center and the phosphorus center is pyramidal. The two benzophosphole planes are twisted against the phenylene bridge with a dihedral angle of 64.4(2)°, and the 2-phenyl groups are twisted against the phosphole rings with dihedral angles of 33.1(2)°.

The Mes* group can be removed and replaced by a phenyl group, as shown for 1,4-bis(3-benzo[*b*]phospholyl)benzene **9**. Reductive cleavage of the P−C (ipso carbon of the Mes* group) bond was achieved by treatment with an excess of lithium metal, and acidic aqueous quenching afforded the P−H derivative **10**, which was used for the subsequent reaction without further purification. Thus, copper-mediated *P*-arylation[9] of **10** followed

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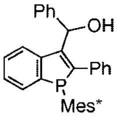
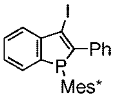
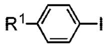
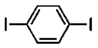
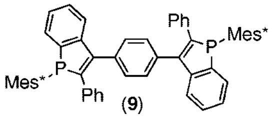
(9) Gelman, D.; Jiang, L.; Buchwald, S. L. *Org. Lett.* **2003**, *5*, 2315–2318.

Table 2. Synthesis of 2,3-Difunctional Benzo[*b*]phospholes According to the Protocol Shown in Scheme 1[a]

entry	electrophile	method	product	yield (%)[b]
1	PhCHO	*a*	 (**4**)	68
2	I(CH$_2$)$_2$I	*a*	 (**5**)	90
3		*b*	 R^1 = –H (**6**)	83
4		*b*	–OMe (**7**)	67
5		*b*	–CN (**8**)	83
6[c]		*b*	 (**9**)	77[d]

[a] Reaction conditions are summarized in Scheme 1, except for entry 6 (see Supporting Information). [b] Isolated yield based on **1** except for entry 6. [c] 0.36 equiv of *p*-diiodobenzene to **1** was used. [d] Isolated yield based on *p*-diiodobenzene.

by oxidation with hydrogen peroxide afforded the *P*-phenylbenzo[*b*]phosphole oxide **11** in 16% overall yield from **9**. ^{1}H, ^{13}C, and ^{31}P NMR spectra of **11** indicated the presence of two diastereomers. This example of the transformation of the Mes* group together with the flexibility of the functionalization of the 3-positions as shown above demonstrates the utility of 3-lithiobenzo[*b*]phosphole **2** as a viable module for the synthesis of functionalized benzo[*b*]phospholes.

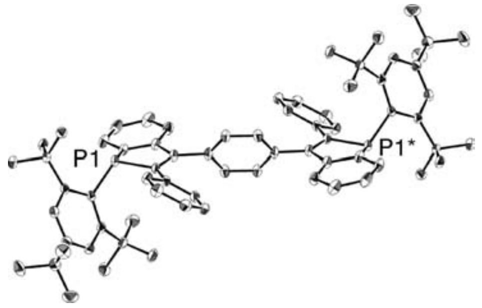
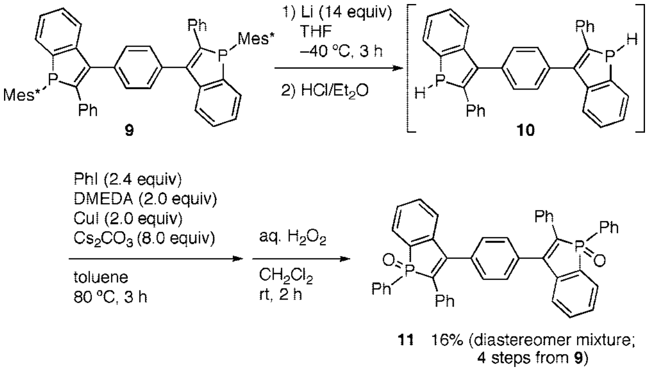


Figure 1. ORTEP drawing of 1,4-bis(3-benzo[*b*]phospholyl)benzene **9** (50% probability for thermal ellipsoids). Hydrogen atoms are omitted for clarity.

The utility of the benzophosphole products as organic electronic materials was examined briefly. We first examined the photophysical and electrochemical properties of the bis(benzo[*b*]phosphole oxide) **11**.[10] Showing the longest absorption maximum wavelength of 340 nm and an absorption edge wavelength of 415 nm, the UV absorption spectrum in CH$_2$Cl$_2$ indicated that **11** is transparent in the visible to IR region. Photoexcitation at 300 nm in CH$_2$Cl$_2$ caused blue emission (λ^{em}_{max} = 468 nm) with a quantum yield of 0.02. The cyclic voltammogram in THF showed a reversible first reduction potential at −2.09 V. The potential is shifted toward the positive side by ca. 0.5 V as compared with a structurally equivalent bis(benzosilole) (the PhP=O moiety in **11** replaced by a Me$_2$Si moiety).[8] Thus, **11** has an electron-accepting property similar to other known phosphorus-containing π-electron systems.[11] The electron drift mobility of compound **11** measured by the time-of-flight technique using a vacuum-deposited film at room temperature was found to be 5 × 10^{-6} cm^2/Vs at an electric field of 2.5 × 10^5 V/cm. This level of mobility does not warrant immediate applications to organic electronics, but suggests that certain structural modifications can lead to a fruitful outcome.

Scheme 2. Transformation of the Mes* Group on the Phosphorus Center



11 16% (diastereomer mixture; 4 steps from **9**)

In conclusion, we have developed a BuLi-mediated cyclization of an (*o*-alkynylphenyl)phosphine **1** to 3-lithiobenzo[*b*]phosphole **2**, which can then produce a variety of new benzo[*b*]phosphole derivatives, including the bis-benzophosphole **9**. The cyclic voltammetry and charge mobility measurements of the phosphine oxide **11** indicate electron-accepting and -transporting abilities of benzophosphole oxide derivatives, hence suggesting the utility of the present synthesis for applications in organic electronics.

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Supporting Information Available: Experimental details and CIF file of compound **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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[10] Details on the measurements are given in the Supporting Information.

[11] For example: Fukazawa, A.; Hara, M.; Okamoto, T.; Son, E.-C.; Xu, C.; Tamao, K.; Yamaguchi, S. *Org. Lett.* **2008**, *10*, 913–916.