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Unexpected formation of porphyrinic enyne under Sonogashira conditions

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Abstract—Reaction of 5-iodo-10,15,20-tris(3,5-di-*tert*-butylphenyl)porphyrin with excess trimethylsilylacetylene under Sonogashira conditions gives an unexpected porphyrinic enyne suitable for further transformations. The NMR spectrum and structural analysis of the porphyrin enynes show that the substituent on the acetylene group is positioned above the porphyrin ring. This structural characteristic makes the microenvironment of the porphyrin center in a controllable fashion.

The synthesis of porphyrin-based multichromophoric assemblies continues to attract attention because of their unique photophysical and electrochemical properties.[1–5] For example, a variety of porphyrin-containing dyads and triads have been synthesized for the studies of electron transfer reactions.[1] Recently, numerous nanometer-sized multiporphyrin assemblies have been prepared for the potential application in electronic and photonic devices.[2] In these multichromophore systems, a wide variety of spacers such as aryl, vinyl, acetylenic, and alkyl units have been utilized to bridge the chromophores.[3] Previous work has shown that acetylenic substituents are the ideal linkers to enable strong interchromophore electronic communication.[3] In the course of our studies of the highly conjugated porphyrin systems, we found that the reaction of iodoporphyrin **1** with trimethylsilylacetylene catalyzed by palladium complex and CuI gave porphyrin **2** and the unexpected product **3** (Scheme 1). Similar results were observed when 10,20-diphenyl-5-iodoporphyrin or 10,20-bis(3,5-di-*tert*-butylphenyl)-5-iodoporphyrin was employed as the starting material.

The structure of porphyrin **3** was characterized by various spectroscopic methods.[6] The mass spectrum shows an intense peak at *m*/*z* 1132 (M+H$^+$). The presence of a carbon–carbon triple bond was indicated by IR absorption at 2119 cm^{-1}. The coupling reaction shows both regio- and stereoselectivity as evidenced by the ^{1}H NMR spectrum. The downfield shift of the vinylic hydrogen (δ 9.45 ppm) is consistent with its being deshielded by the porphyrin ring current. The peak corresponding to the trimethylsilyl group attached to the acetylene is upfield shifted to −0.61 ppm, indicating that the protecting group is positioned above the porphyrin ring. This is further confirmed by the X-ray crystal structure (Fig. 1). The structure of porphyrin **3** shows that the vinyl plane twists out the porphyrin ring by 48.03° due to the van der Waals strain between the vinyl and β hydrogen atoms. This is larger than the analogous dihedral angle (36.1°) reported by Therien in a *meso*-substituted divinylporphyrin.[7] The vinylic acetylene is slightly deviated from linearity, with bond angles at C(23) and C(24) of 174.70° and 172.52°, respectively. The bond distances of 1.350 for C(21)–C(22) and 1.204 Å for C(23)–C(24) fall into the normal range of the double and triple bonds, respectively. The three phenyl groups have dihedral angles of 57.92°, 66.18°, and 75.16° with respect to the porphyrin mean plane. The porphyrin framework is nearly planar, as indicated by the fact that the root-mean-square deviation of fitted atoms is 0.080 Å. The Zn^{2+} center is five-coordinated to an axial methanol molecule with a Zn–O(1) distance of 2.112 Å and a Zn–O(1)–C(73) angle of 130.57°. As a consequence of being five-coordinated, the Zn^{2+} ion is pulled out of the porphyrin mean plane by 0.289 Å. There is a solvated methanol molecule hydrogen-bonded to the coordinated methanol with a O(1)–O(2) distance

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Keywords: Acetylenes; Cross-coupling; Enynes; Porphyrins.

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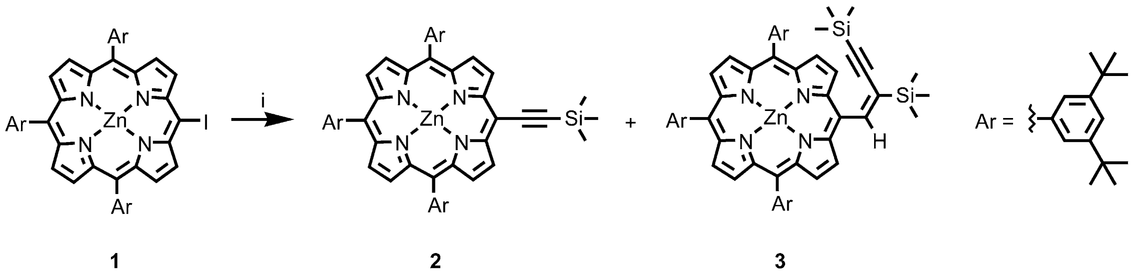


Scheme 1. Reagents and conditions: (i) Pd catalyst, CuI, NEt_3, THF.

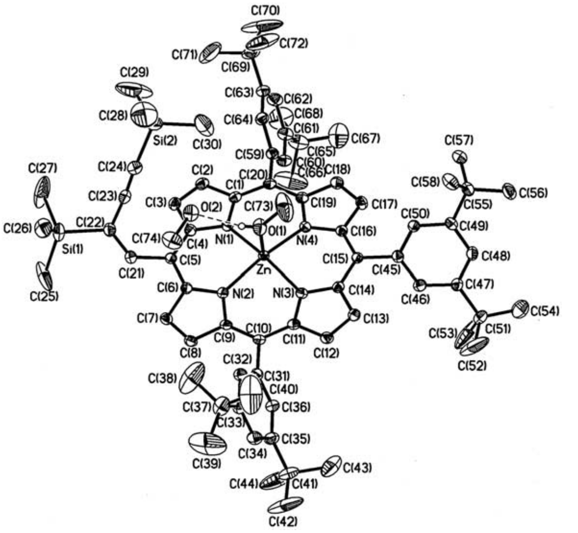


Figure 1. ORTEP drawing of compound **3** drawn at the 50% probability thermal ellipsoids. Hydrogen atoms omitted for clarity.

of 2.653 Å. The solvated methanol shows a short O(2)···π contact of 3.116 Å with the acetylene group.

The self- and cross-coupling reactions of terminal alkynes by various transition metals have been intensively studied.[8] Generally, the key step of alkyne coupling reactions has been proposed to involve the migration of a σ-bonded metal acetylide to a coordinated alkyne. To gain some insight into the formation of porphyrin **3**, we first examined the coupling reaction between porphyrin **2** and trimethylsilylacetylene. However, the cross-coupling reaction under various conditions did not proceed. In another control experiment, porphyrin **2** was added to the mixture of the coupling reaction between **1** and trimethylsilylacetylene. The yield of porphyrin **3** remains unchanged. Based on these results, the possibility of porphyrin **3** being produced via **2** can be ruled out. We next examined the reaction under various conditions. Table 1 gives the summary of the coupling reactions. Yields for porphyrin **3** are modest but it is anticipated that improvements can be made in future. In general, the coupling reactions between aryl halides and terminal acetylenes are accomplished by using palladium catalyst and copper cocatalyst. In 1998 Echavarren and co-workers reported that the reactions of aryl halides having a bulky peri or *ortho* substituent with terminal acetylenes gave the corresponding arylenynes along with arylalkynes.[9] They found that the use of

Table 1. Summary for cross-coupling of porphyrin **1** with trimethylsilylacetylene under various conditions

Entry[a]	HCCTMS (equiv)	Pd catalyst (equiv)	Ligand (equiv)	Time (h)	Yield (%) (**2**:**3**)
1	10	$Pd(PPh_3)_2Cl_2$ (0.36)	—	0.5	55:13
2[b]	10	$Pd(PPh_3)_2Cl_2$ (0.18)	—	0.5	58:16
3	10	$Pd(PPh_3)_2Cl_2$ (0.05)	—	4.5	21:19
4	10	$Pd(PPh_3)_2Cl_2$ (0.10)	—	3.5	28:25
5	10	$Pd_2(dba)_3$ (0.10)	$AsPh_3$ (0.8)	0.5	69:0
6	10	$Pd(PPh_3)_4$ (0.10)	$AsPh_3$ (0.4)	4	38:28
7[c]	10	$Pd(PPh_3)_4$ (0.10)	—	22	79:0
8	20	$Pd(PPh_3)_2Cl_2$ (0.36)	—	0.5	62:13
9	30	$Pd(PPh_3)_2Cl_2$ (0.10)	—	1.5	28:51
10	30	$Pd(PPh_3)_2Cl_2$ (0.10)	$AsPh_3$ (0.4)	1.5	31:22
11	30	$Pd(PPh_3)_4$ (0.10)	$AsPh_3$ (0.8)	3.5	31:50
12	30	$Pd(PPh_3)_4$ (0.10)	$AsPh_3$ (2.0)	3.5	24:50
13	50	$Pd(PPh_3)_2Cl_2$ (0.10)	—	1	38:25
14[d,e]	30	$Pd(PPh_3)_2Cl_2$ (0.10)	—	12	15:28
15[d]	30	$Pd(PPh_3)_2Cl_2$ (0.10)	—	24	0:0
16[d,f]	30	$Pd(PPh_3)_2Cl_2$ (0.10)	—	24	0:0

[a] Unless otherwise indicated, the reactions were carried out at room temperature in THF in the presence of Et_3N, Pd catalyst, and CuI. The ratio of Pd catalyst and CuI was 1:1.

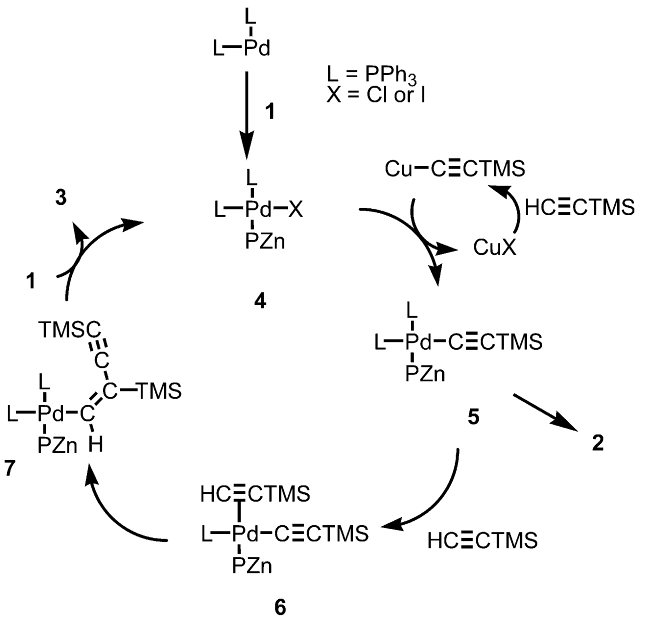
[b] The ratio of Pd catalyst and CuI was 1:2.

[c] Base = Et_2NH.

[d] Ag_2O was used instead of CuI.

[e] Temperature = 60 °C.

[f] Base = pyrrolidine.



Scheme 2. A proposed mechanism for the formation of porphyrin **3**.

Ag_2O instead of CuI as the cocatalyst increases the selectivity of the arylenynes. In our case, no improvements were observed under conditions similar to those reported by Echavarren (entries 14–16). It is noteworthy that the formation of **3** can be completely suppressed when $Pd_2(dba)_3$ or $Pd(PPh_3)_4$ is used as the catalyst (entries 5 and 7).

In the Pd–Cu catalyzed cross-coupling reactions of terminal alkyne with aryl halides, it has been generally proposed that the Pd catalyst is added by an aryl halide to give an arylpalladium complex before the acetylide is σ-bonded to palladium.[10] A plausible reaction mechanism for the formation of **3** under the coupling conditions is given in Scheme 2. This mechanism proceeds by the reaction of the Pd catalyst with porphyrin **1** to generate a palladioporphyrin complex **4**, which reacts with another trimethylsilylacetylene molecule, possibly via a copper acetylide, to form σ-bonded metal acetylide **5**. This acetylide complex may undergo cross-coupling to form porphyrin **2** or further reaction with another acetylene molecule to produce complex **6**. The addition of the acetylide moiety to a coordinated carbon–carbon triple bond in complex **6** yields an alkenyl intermediate **7**. The reaction of intermediate **7** with porphyrin **1** gives the coupled porphyrin **3** and regenerates the active Pd species **4**. According to the mechanism proposed in Scheme 2, the stereochemistry of the acetylene with respect to the porphyrin ring in **3** is expected to be *cis* and this is consistent with the X-ray crystal structure.

A number of porphyrins with directly attached acetylene or vinylene groups have been synthesized.[3] However, reports on the synthesis of porphyrinic enynes are rare.[11] Arnold and co-workers reported the preparation of a few porphyrinic enynes by formylation of Ni(II) octaethylporphyrin (NiOEP), followed by Wittig reaction and then Sonogashira cross-coupling.[11] Our one-pot procedure for the preparation of porphyrinic enynes is relatively simple although the yields are only modest.

To extend the scope of the porphyrinic enyne, we introduced aryl groups to the vinylic acetylene by reacting the deprotected product **8** with the corresponding aryl iodide (Scheme 3). The ^1H NMR spectra of **9** and **10** show upfield shift of the acetylenic phenyl groups, suggesting that the phenyl group is positioned on the top of the porphyrin ring.[12] Porphyrin **10** is suitable for further transformations to alcohol, carboxylic acid, and amide. Molecular modeling shows that the *para* carbon is located approximately above the porphyrin center with a distance of about 7 Å. By choosing the appropriate substituents of the phenyl group, it is possible to control the microenvironment of the reaction center of the porphyrin, thus to mimic the heme-containing proteins.

In conclusion, we report an unexpected coupling reaction leading to porphyrinic enyne **3** with good regio- and stereochemistry. Upon desilylation, porphyrin enyne **3** can be further modified with ease by reacting with aryl iodides. Currently, we are expanding and optimizing the methodology described above.

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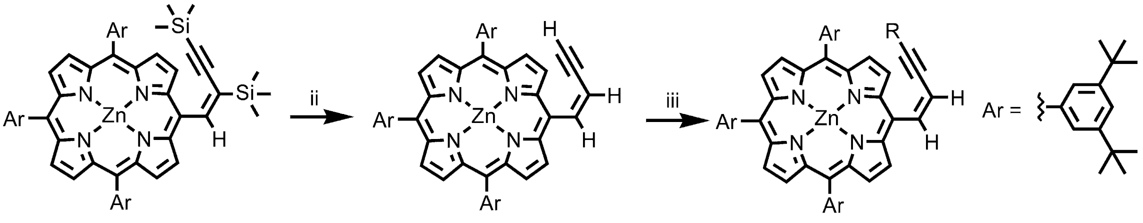

3 **8**

9 R = Phenyl
10 R = 2-methylcarboxyphenyl

Scheme 3. Reagents and conditions: (ii) 5 equiv TBAF, CH_2Cl_2, 10 min; (iii) ArI, $Pd(PPh_3)_2Cl_2$, CuI, NEt_3, THF.

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6. Compound **2**: ^{1}H NMR (400 MHz, CDCl$_3$, ppm): δ 9.76 (2H, d, J = 4.8 Hz), 9.02 (2H, d, J = 4.8 Hz), 8.93 (4H, s), 8.06 (4H, d, J = 1.6 Hz), 8.02 (2H, d, J = 1.6 Hz), 7.79 (2H, t, J = 1.6 Hz), 7.76 (1H, t, J = 1.6 Hz), 1.53 (36H, s), 1.50 (18H, s), 0.60 (9H, s); UV–vis (CH$_2$Cl$_2$, nm) $\lambda_{\max}$ (logε): 431 (5.69), 562 (4.29), 605 (4.18); IR ν (cm^{-1}) 2139 (C$\equiv$C); MS (FAB) calculated for $C_{67}H_{80}N_4SiZn$: 1032, found: 1033 (M+H$^+$). Compound **3**: ^{1}H NMR (400 MHz, CDCl$_3$, ppm): δ 9.46 (1H, s), 9.45 (2H, d, J = 4.8 Hz), 8.96 (2H, d, J = 4.8 Hz), 8.94 (4H, s), 8.06 (4H, d, J = 1.6 Hz), 8.05 (2H, d, J = 1.6 Hz), 7.78 (2H, t, J = 1.6 Hz), 7.75 (1H, t, J = 1.6 Hz), 1.52 (36H, s), 1.50 (18H, s), 0.60 (9H, s), −0.59 (9H, s); UV–vis (CH$_2$Cl$_2$, nm) $\lambda_{\max}$ (logε): 427 (5.68), 554 (4.35), 600 (3.99); IR ν (cm^{-1}) 2119 (C$\equiv$C); MS (FAB) calculated for $C_{72}H_{90}N_4Si_2Zn$: 1131, found: 1132 (M+H$^+$). Crystals were grown from slow diffusion of methanol into the solution of **3** in CH$_2$Cl$_2$. Crystal data for **3**·2CH$_3$OH: M_r = 1198.12, triclinic, space group P-1, T = 150(1) K, a = 12.8285(4) Å, b = 16.7439(5) Å, c = 17.1494(6) Å, α = 83.725(1)°, β = 87.865(1)°, γ = 86.473(1)°, V = 3652.9(2) Å^3, Z = 2, μ = 0.413 mm^{-1}, D_c = 1.089 g cm^{-3}. 47,948 reflections collected, 16,765 independent, R_{int} = 0.0515, final residuals R_1 = 0.0824, wR_2 = 0.1946 [$I > 2\sigma(I)$]; R_1 = 0.1044, wR_2 = 0.2090 (all data). Crystallographic data for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 256779. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk.
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12. Compound **9**: Yield: 50%, based on **3**; ^{1}H NMR (400 MHz, CDCl$_3$, ppm): δ 9.55 (2H, d, J = 4.8 Hz), 9.52 (1H, s), 9.09 (2H, d, J = 4.8 Hz), 9.00 (4H, s), 8.08 (4H, d, J = 1.6 Hz), 8.06 (2H, d, J = 1.6 Hz), 7.77 (3H, m), 6.85 (1H, t, J = 7.2 Hz), 6.72 (2H, t, J = 7.2 Hz), 6.33 (2H, d, J = 7.2 Hz), 1.52 (36H, s), 1.51 (18H, s), 0.68 (9H, s); UV–vis (CH$_2$Cl$_2$, nm) $\lambda_{\max}$ (logε): 428 (5.65), 556 (4.38), 599 (4.06); MS (ESI) calculated for $C_{75}H_{86}N_4SiZn$: 1135, found: 1135. Compound **10**: Yield: 71%, based on **3**; ^{1}H NMR (400 MHz, CDCl$_3$, ppm): δ 9.54 (2H, d, J = 4.8 Hz), 9.53 (1H, s), 8.97 (2H, d, J = 4.8 Hz), 8.95 (4H, s), 8.06 (2H, d, J = 2.0 Hz), 8.05 (4H, d, J = 2.0 Hz), 7.76 (3H, s), 7.43 (1H, d, J = 7.2 Hz), 6.85 (1H, t, J = 7.2 Hz), 6.56 (1H, t, J = 7.2 Hz), 5.67 (1H, d, J = 7.2 Hz), 3.16 (3H, s), 1.50 (54H, s), 0.70 (9H, s); UV–vis (CH$_2$Cl$_2$, nm) $\lambda_{\max}$ (logε): 429 (5.14), 557 (3.93), 602 (3.63); MS (ESI) calculated for $C_{77}H_{88}N_4O_2SiZn$: 1193, found: 1193.