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Silylethynyl Substituents as Porphyrin Protecting Groups for Solubilization and Selectivity Control

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Supporting Information

ABSTRACT: Silylethynyl substituents are proposed as protecting groups for porphyrin derivatives to enhance their solubility and enable regioselective functionalization. After usage as protecting groups, silylethynyl groups at the *meso*-positions can be efficiently removed upon heating with aqueous H_2SO_4 in the presence of a surfactant. This approach was applied to the preparation of unsymmetrically *β*-substituted porphyrins and porphin–porphyrin oligomers, which were inaccessible by conventional methods.

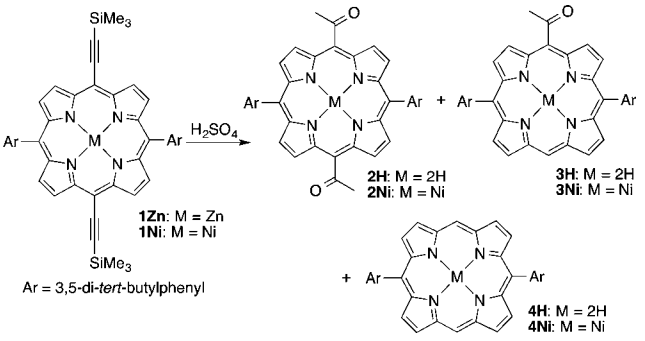
Porphyrins have attracted much attention as catalysts for organic reactions, building blocks for supramolecules, and materials for optoelectronic devices.[1] As a result, a number of synthetic procedures for various porphyrins have been developed.[2] However, no convenient methods to protect the reactive *meso*-carbon atoms in porphyrins have been established, although some removable *meso*-substituents are known. Neya et al. reported that treatment of tetra-*tert*-butylporphyrin with H_2SO_4 produced porphin, a porphyrin without any substituents, in moderate yield.[3] This method, however, is useful only for the synthesis of porphin. Other defunctionalizations at the *meso*-positions involve decarboxylation processes.[4] Unfortunately, such carbonyl substituents are not useful as protecting groups owing to their high reactivity. Recently, Osuka and co-workers reported palladium-catalyzed reductive debromination at the *meso*-positions. However, halogen substituents often reduce the solubility of these substrates in organic solvents and they also do not survive during transition-metal-catalyzed reactions.[5]

Silylethynyl groups not only enhance the solubility of *π*-conjugated molecules due to the bulky silyl groups,[6] but the electron-withdrawing nature of the alkyne moiety also improves the stability of unstable compounds such as higher acenes[7] and radicals.[8] The installation of trialkylsilylethynyl groups on various *π*-systems can be readily achieved via Sonogashira coupling. However, no removal methods have been available.

Herein we report our serendipitous finding of the dealkynylation reaction of *meso*-ethynylporphyrins. We also demonstrate the utility of silylethynyl protection for regioselective functionalization of porphyrins through temporary masking of the reactive *meso*-positions.

To prepare diacetylporphyrin, we performed the hydration of bis(trimethylsilylethynyl)porphyrin Zn(II) **1Zn** with aqueous sulfonic acid (25% aq.) in 1,2-dichloroethane (Table 1).[9] The reaction successfully afforded the desired product **2H** in 54% yield. To our surprise, however, acetyl product **3H** and *meso*-unsubstituted porphyrin **4H** were also obtained as byproducts in 8% and 6% yields, respectively (entry 1). Ni(II) complex **1Ni** also underwent dealkynylation to afford **4Ni** in 45% yield

Table 1. Dealkynylation of *meso*-Dialkynylporphyrins



					yield		
entry	M	additive	time (h)	solvent	**2**	**3**	**4**
1	Zn	none	16	$ClCH_2CH_2Cl$	54	6	8
2	Ni	none	10	$ClCH_2CH_2Cl$	–	<1	45
3	Ni	none	12	$C_6H_4Cl_2$	99	–	–
4	Ni	SDS	24	$ClCH_2CH_2Cl$	0	0	63
5[a]	Ni	none	12	$ClCH_2CH_2Cl$	<1	<1	75

[a]DBSA was employed instead of H_2SO_4.

(entry 2). Interestingly, the reaction was heavily dependent on the solvent: diacetyl product **2H** was quantitatively obtained in 1,2-dichlorobenzene (entry 3). The reaction conditions were further optimized, and the addition of sodium dodecyl sulfate (SDS) enhanced the yield of **4Ni** to 63% (entry 4).[10] Other surfactants, such as Triton-X100 and cetyltrimethylammonium bromide, did not work well. The use of dodecylbenzenesulfonic acid (DBSA) instead of the sulfuric acid–SDS combination provided **4Ni** in 75% yield (entry 5).[11] These results suggest that the effective mixing of the organic and aqueous phases is the key to successful dealkynylation.

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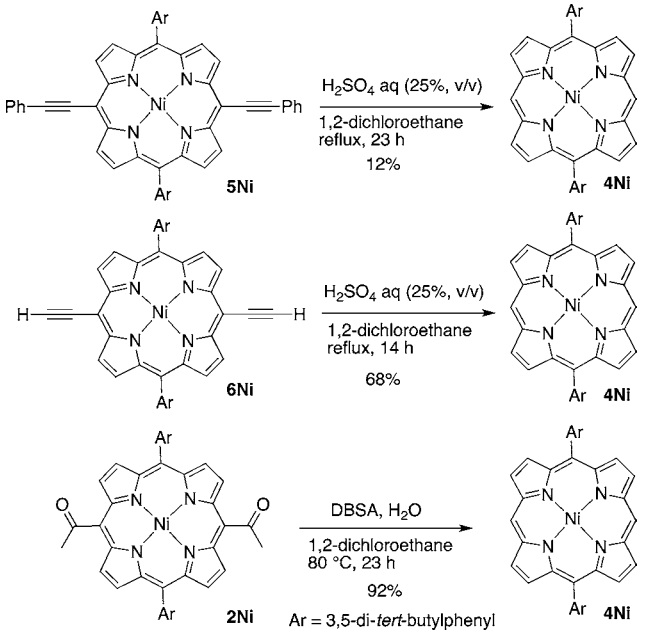
The scope of this dealkynylation procedure was investigated (Scheme 1). Di(phenylethynyl)porphyrin Ni(II) **5Ni** also

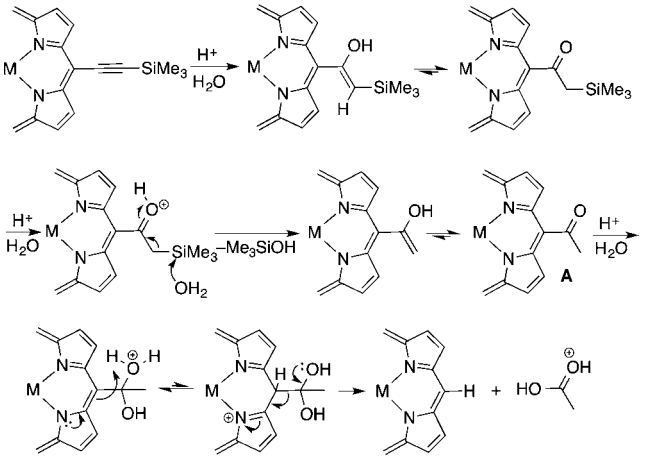
Scheme 1. Dealkynylation and Deacetylation of 5,15-Diarylporphyrins



afforded the dealkylated product **4Ni** but in low yield (12%), while diethynylporphyrin **6Ni** provided **4Ni** in 68% yield. This result indicates the dealkynylation does not require silyl groups if the substrate is sufficiently soluble. Notably, the reaction of diacetylporphyrin **2Ni** under the optimized conditions furnished **4Ni** in 92% yield, indicating that dealkynylation proceeds through the diacetylporphyrin intermediate.

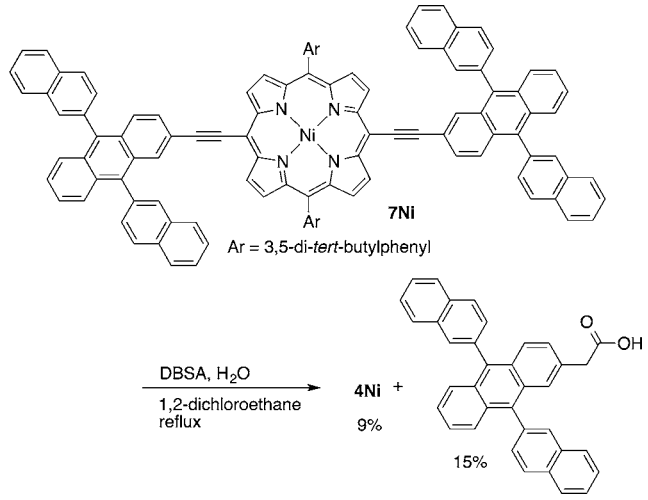
On the basis of these observations, we propose a plausible reaction mechanism in Scheme 2. The reaction goes through

Scheme 2. Plausible Dealkynylation Mechanism



the sequence of hydrolysis and retro-Friedel–Crafts acylation.[12] Initially, regioselective protonation and hydration of the alkyne moiety affords the α-silyl ketone, which is readily transformed to acetylporphyrin **A** via protodesilylation. In the next step, protonation at the *meso*-position occurs with the aid of electron donation from the nitrogen atom. Finally, the attack of water on the carbonyl group induces cleavage of the C–C bond to provide the corresponding *meso*-unsubstituted porphyrin and the carboxylic acid. The generation of a carboxylic acid was confirmed in the reaction of anthrylethynylporphyrin Ni(II) **7Ni**, which provided **4Ni** along with anthrylacetic acid (Scheme 3). The formation of anthrylacetic acid was assigned by the fluorescence and ^{1}H NMR spectra compared to the authentic sample.

Scheme 3. Detection of a Carboxylic Acid



The utility of the present dealkynylation protocol was demonstrated by synthesizing porphin–porphyrin oligomers **10** (Scheme 4). Porphin is a useful motif for construction of π-stacking structures. However, introduction of a porphin unit is challenging because of the insoluble nature of porphin. Precursory porphyrin dimer **9a** and trimer **9b** were prepared through Suzuki–Miyaura coupling of 5-bromo-10,20-bis(silylethynyl)porphyrin **8a** and 5,15-dibromo-10,20-bis(silylethynyl)porphyrin **8b**.[13] Desilylation of **9a** using tetrabutylammonium fluoride (TBAF), followed by dealkynylation with DBSA, produced **10a** in 58% yield. *meso*-Unsubstituted *meso*–*meso* linked porphyrin trimer **10b** was also synthesized from **9b** in 56% yield. Consequently, the bis(triisopropylsilylethynyl)-porphyrin group can serve as a synthetic equivalent to porphin, for which the insolubility can be circumvented by the bulky silyl group.

The structure of porphin–porphyrin **10a** was unambiguously elucidated by X-ray diffraction analysis (Figure 1).[14] As expected, two porphin rings are mutually stacked in a face-to-face manner. The interplanar distance is 3.67 Å, which is within the sum of the van der Waals radii of two carbon atoms.

We further investigated the use of alkynyl protection for the synthesis of unsymmetrically substituted porphyrins. Recently, transition-metal-catalyzed C–H borylation and arylation have been developed for late-stage functionalization of porphyrins at β-positions with high regioselectivity.[15,16] These procedures, however, could not control the regioselectivity of two introduced substituents, resulting in a mixture of three isomers. We expected combining the iridium-catalyzed direct borylation reaction with the present alkyne protection method enabled the controlled synthesis of unsymmetrically β-substituted porphyrins **14** from silylethynylporphyrin Ni(II) **11** (Scheme 5). Iridium-catalyzed direct borylation of **11** with bis(pinacolate)-diboron (pin_2B_2) and 4,4-di-*tert*-butyl-2,2-bipyridyl (dtbpy) in

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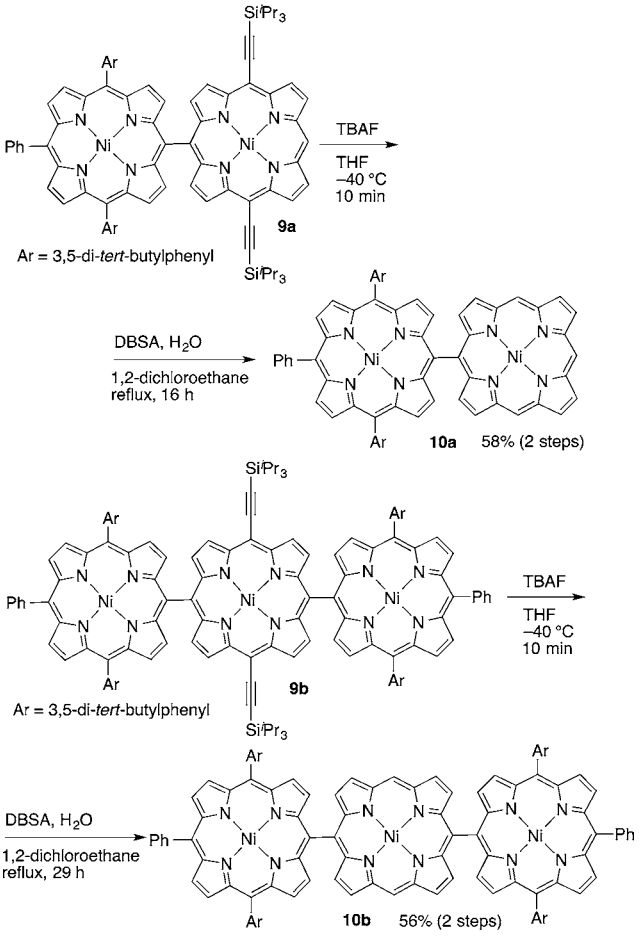
Scheme 4. Synthesis of Porphin–Porphyrin Oligomers 10



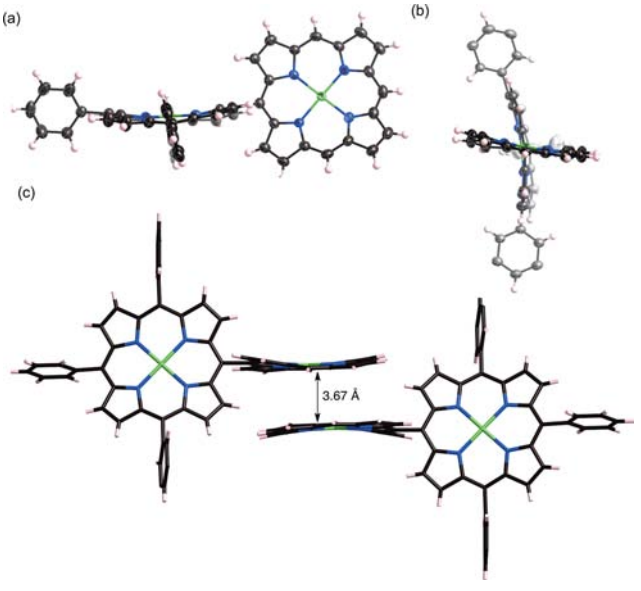
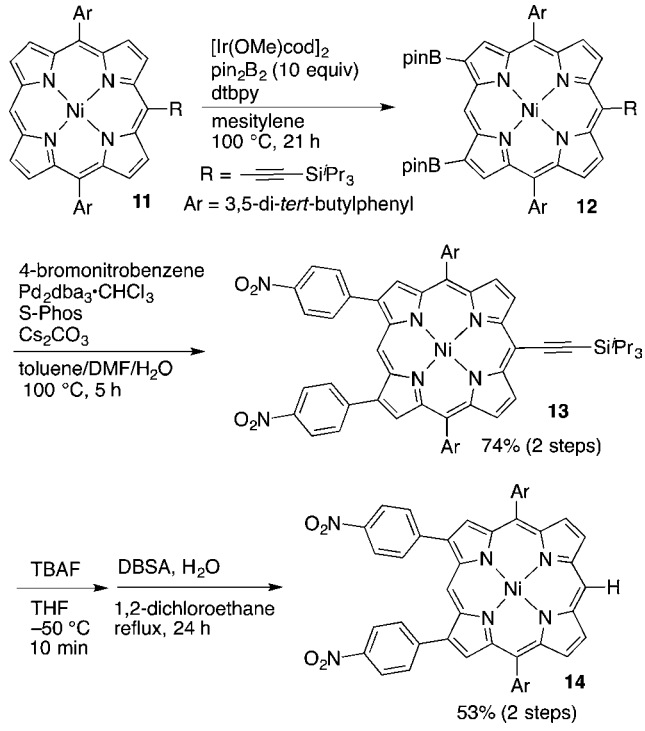


Figure 1. X-ray crystal structure of porphin–porphyrin dimer **10a**. (a) Side view, (b) front view, and (c) packing structure in crystal. The thermal ellipsoids are scaled at the 50% probability level. *tert*-Butyl substituents are omitted for clarity.

mesitylene produced the corresponding borylated porphyrin **12** quantitatively. The subsequent Suzuki–Miyaura cross-coupling with 4-bromonitrobenzene afforded porphyrin **13** with two

Scheme 5. Synthesis of Unsymmetrically β-Substituted Porphyrins



nitrophenyl groups at the β-positions in 74% yield (two steps). Desilylation of **13** with TBAF followed by dealkynylation with DBSA in 1,2-dichloroethane provided **14** in 53% yield.

In conclusion, we have developed a method for dealkynylation of *meso*-alkynylporphyrins through acid-mediated hydrolysis that is enhanced by the addition of an anionic surfactant. Using this protocol, porphin–porphyrin oligomers were prepared. Furthermore, the utility of alkynyl substituents as protecting groups in the synthesis of unsymmetrically β-substituted porphyrins was demonstrated. We believe that the present dealkynylation procedure enables the facile synthesis of intriguing porphyrins that have previously been inaccessible by conventional methods.

■ ASSOCIATED CONTENT

Supporting Information

Experimental details and spectral data for all new compounds. Crystallographic data (CIF file) for **10a**. 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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(14) Crystallographic data for **10a**: $C_{76}H_{68}N_8OCl_2Ni_2$, *Mw* = 1278.14, triclinic, $P\bar{1}$, a = 11.636(2) Å, b = 15.963(3) Å, c = 19.746 (4) Å, α = 102.414(2)°, β = 101.791(2)°, γ = 108.945(2)°, Z = 2, R = 0.0547 ($I > 2.0\ \sigma(I)$), *Rw* = 0.1756 (all data), GOF = 1.130.
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