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Selective synthesis of 5-alkenyl-15-alkynyl-porphyrin and 5,15-dialkynyl-porphyrin by 2+2 acid-catalyzed condensation of dipyrrylmethane and TMS propynal

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ABSTRACT

One of 5-alkenyl-15-alkynyl-porphyrin and 5,15-dialkynyl-porphyrin was prepared selectively by 2+2 acid-catalyzed condensation of bicyclo[2.2.2]octadiene-fused dipyrrylmethane and TMS propynal in the presence of $BF_3{\cdot}OEt_2$ only by the choice of the solvent. The alkenyl group was expected to be obtained by a protonation followed by intramolecular 1,2-hydride transfer from methine position of porphyrinogen.

An acid-catalyzed dipyrrylmethane–aldehyde condensation is the most effective synthetic method for the preparation of 5,15-disubstituted porphyrins and has been applied to syntheses of a variety of porphyrins as photosynthetic model compounds, molecular wires, non-linear optical materials, and so on.[1] Generally, 5,15-disubstituted porphyrins bearing same substituents at *meso* positions are easily prepared by simple acid-catalyzed 2+2 condensation of a dipyrrylmethane and an aldehyde. On the other hand, porphyrins bearing two different *meso*-substituents are usually prepared by a mixed-aldehyde condensation of a dipyrrylmethane and two aldehydes, followed by a separation of a mixture of three kinds of porphyrins by a column chromatography.

Recently, we have succeeded to prepare 5-alkenyl-15-alkynyl porphyrin **1** by a 2+2 acid-catalyzed condensation of a dipyrrylmethane **3** and trimethylsilyl(TMS)propynal (**4**) as a mixture with 5,15-dialkynyl porphyrin **2** in the ratio of 1:3.[2] Although 2+2 acid-catalyzed condensation reactions of dipyrrylmethanes and a TMS propynal have been already reported,[3] such an unsymmetrical synthesis has never been reported. Selenoacetals have been reported as synthons of alkenals to prepare *meso*-alkenyl porphyrins,[4] but a few of 5-alkenyl-15-alkynylporphyrins have been prepared by a partial nucleophilic addition to dialkynylporphyrin[3a] or by a long multi-step synthesis[5] so far. Now we have succeeded to prepare one of the 5-alkenyl-15-alkynyl porphyrin **1** and 5,15-dialkynyl porphyrin **2** preferentially by 2+2 acid-catalyzed condensation of same starting materials, dipyrrylmethane **3** and TMS propynal (**4**), only by changing the acids and solvents.[6]

A typical synthetic scheme and results are summarized in Table 1. An acid-catalyzed condensation of bicyclo[2.2.2]octadiene (BCOD) ring-fused dipyrrylmethane **3**[2] (0.1 mmol) and TMS propynal (**4**; 0.107 mmol)[2] was performed in distilled $CHCl_3$ (10 mL) in the presence of $BF_3{\cdot}OEt_2$ (0.014 mmol) at 0 °C for 3 h under an Ar atmosphere, followed by oxidation with DDQ (0.197 mmol), to give porphyrin **1** and porphyrin **2** in 42% and 3% isolated yields (relative ratio was 93:7), respectively (Table 1, run 1). When the reaction was performed in MeOH, the isolated yields of porphyrins **1** and **2** were 4% and 66% (6:94), respectively (Table 1, run 4), where the main product was changed from **1** to **2** drastically. In these reactions, porphyrin **1** was obtained as a mixture of *cis* and *trans*-type porphyrins.[7] It should be noted here that TMS propynal can be the origin of two kinds of *meso*-substituents, TMS-alkynyl and TMS-alkenyl groups. These substituents were introduced simultaneously, and the main product can be changed from 5-alkenyl-15-alkynylporphyrin, **1**, to 5,15-dialkynyl porphyrin, **2**, only by choice of the solvent. When *p*-toluenesulfonic acid monohydrate (*p*-TsOH) was used as an acid, the products were 1:1 or 1:3 mixture of porphyrins **1** and **2** in $CHCl_3$ or MeOH, respectively, as shown in Table 1 (runs 3 and 5). In acetonitrile, the yields of porphyrins **1** and **2** were 4% and 2%, respectively, in the presence of trichloroacetic acid (run 6). The low yield in acetonitrile is probably because of the low solubility of dipyrrylmethane **3**. These results suggest that the choice of acids and solvents is very important for the selective synthesis of porphyrin **1** or **2**.

The structure of 5,15-dialkynyl porphyrin **2** has been elucidated by a single-crystal X-ray diffraction analysis (Figs. 1 and S1).[8] A $CHCl_3$ molecule involved in a unit cell was squeezed following the reported method.[9] The porphyrin plane showed little distortion, but two TMS-alkynyl group bended from the porphyrin plane

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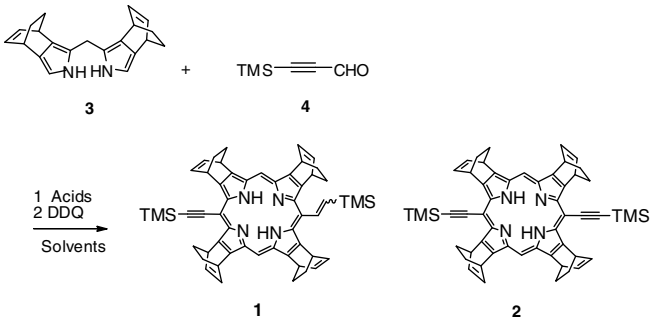
Table 1
Synthetic yields of porphyrins **1** and **2**



Run	Solvents	Acids[a]	Yields (%)		Relative yields
			1[b]	**2**	**1**:**2**
1	$CHCl_3$	$BF_3{\cdot}OEt_2$	42	3	94:6
2	$CHCl_3$	$BF_3{\cdot}OEt_2$[c]	12	53	19:81
3	$CHCl_3$	*p*-TsOH	18	20	48:52
4	MeOH	$BF_3{\cdot}OEt_2$	4	66	6:94
5	MeOH	*p*-TsOH	10	30	25:75
6	CH_3CN	CCl_3CO_2H	4	2	68:32

[a] Concentration of acids are 1.4 mM for $BF_3{\cdot}OEt_2$; 0.25 mM for *p*-TsOH; 1.6 mM for CCl_3CO_2H. All reactions were performed under an Ar atmosphere.
[b] Mixture of *cis* and *trans* type.
[c] Under air atmosphere.

sigmoidally; alkynyl C_β is bended from porphyrin main plane to a vertical direction by 9.3° and angles of C_{meso}-C_β-$C\alpha$ and C_β-$C\alpha$-Si are 174.8° and 173.6°, respectively (atoms' definitions are described in Fig. 1). Each porphyrin locates perpendicularly against next porphyrins (see Fig. S1).

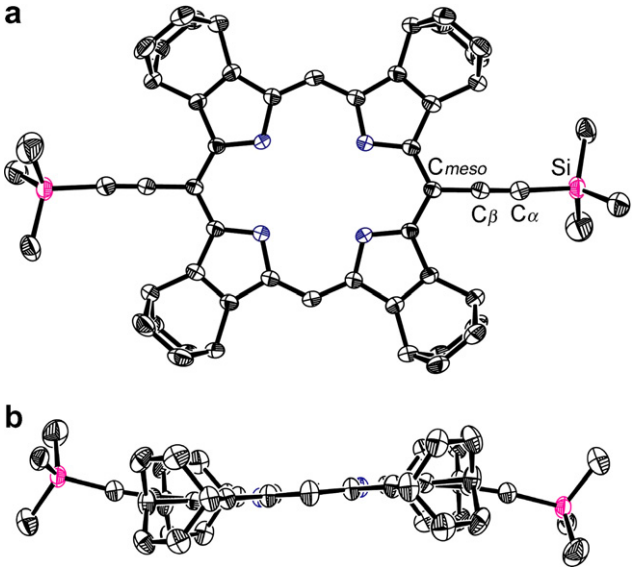
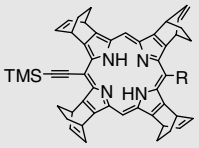
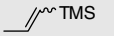
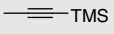
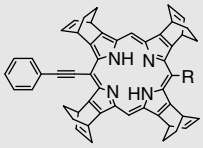
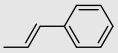
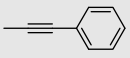
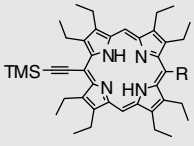
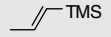
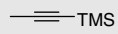
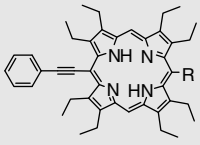
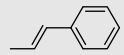
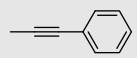


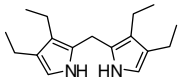
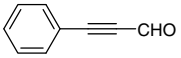
Figure 1. ORTEP view of porphyrin **2**: (a) TOP view and (b) side view. Hydrogen atoms are omitted for clarity.

In order to investigate the substituents effect for the present unsymmetrical reaction, the acid-catalyzed 2+2 condensation by $BF_3{\cdot}OEt_2$ in $CHCl_3$was performed using *all*-β-ethyl-dipyrrylmethane **5** or phenylpropynal (**6**) instead of BCOD-fused dipyrrylmethane **3** or TMS propynal (**4**), respectively. The results are summarized in Table 2. 5-Alkenyl-15-alkynyl porphyrins, **7**, **9**, and **11**, were obtained as *trans*-type porphyrins. The displacement

Table 2
2+2 Acid-catalyzed condensation of dipyrrylmethanes and aldehydes in $CHCl_3$[a]

Run	Dipyrryl methanes	Aldehydes	Porphyrins	R[c]	Relative yield	Total yield (%)
1	**3**	**4**		**1** 	94	45
				2 	6	
2	**3**	**6**[b]		**7** 	33	7
				8 	67	
3	**5**[b]	**4**		**9** 	30	56
				10 	70	
4	**5**[b]	**6**[b]		**11** 	6	17
				12 	94	

[a] For the reaction conditions, see text. Reactions were performed at 0 °C for runs 1 and 3; −30 °C for runs 2 and 4.

[b] **5** :  **6** : 

[c] Porphyrin **1** is a mixture of cis and trans type. Porphyrins **7**, **9**, and **11** are trans type.

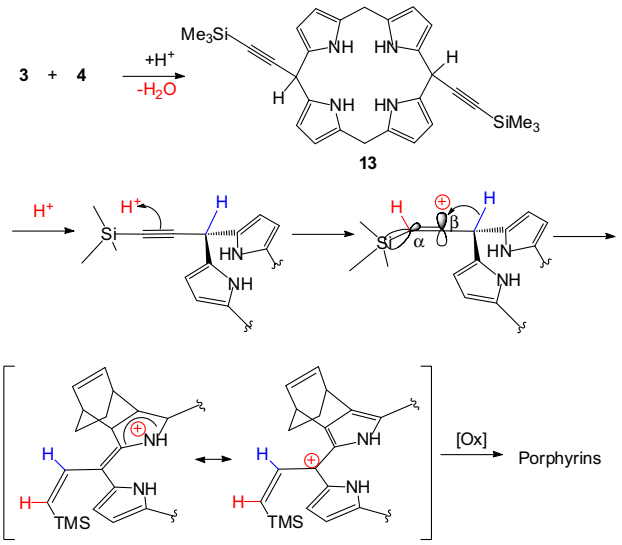


Figure 2. Speculated reaction mechanism. Half of the structure of the intermediate and BCOD rings are omitted to clarity.

of one of the starting materials, TMS propynal (**4**) or BCOD-ring fused dipyrrylmethane **3**, to phenylpropynal (**6**) or *all*-β-ethyl-dipyrrylmethane (**5**) lowered the relative yields of the 5-alkenyl-15-alkynyl porphyrin to 5,15-dialkynyl porphyrin from 19:1 (run 1) to 1:2 or 1:3, respectively (runs 2 and 3). When both of the starting materials, **3** and **4**, were replaced by compounds **5** and **6**, respectively, the relative yield went down one-third again, resulting that the relative yield of 5-alkenyl-15-alkynyl porphyrin **11** to 5,15-dialkynyl porphyrin **12** was less than 10% (run 4). These results suggest that both of the BCOD-ring fused structure and TMS group are necessary and equally influence the hydrogenation of alkyne group. When the reactions of **3** and **6** or **4** and **5** were performed in MeOH in the presence of *p*-TsOH, the unsymmetrical porphyrins were not obtained.

Under the above reaction conditions, 5,15-dialkenyl porphyrins were not detected. On the other hand, when the reaction was performed under higher equivalent of $BF_3{\cdot}OEt_2$ (0.07 mmol) in the typical experimental condition, 5,15-dialkenyl porphyrin was also detected. However, partially desilylated 5,15-dialkenyl porphyrin was also detected by NMR measurement and the reaction was complicated. The reactions with acids under higher concentration are under investigation.

The reaction mechanism is speculated as follows (see Fig. 2); an acid-catalyzed condensation of **3** and **4** gave porphyrinogen **13** accompanied with dehydration, and then a protonation of the alkynyl carbon of porphyrinogen **13** at α-position of TMS occurred. The protonation was followed by a 1,2-hydride transfer from the methyne position of the porphyrinogen to the β-carbon of TMS. The proton was thought to be formulated by the reaction of $BF_3{\cdot}OEt_2$ with H_2O, which was generated during the acid-catalyzed condensation of aldehyde and dipyrrylmethane. The cation was stabilized by β-effect of silyl group, which was the reason why the relative yield of 5-alkenyl porphyrin was higher with TMS propynal than with phenyl propynal. Similar stabilization by silyl group has been reported.[10] The BCOD rings are also thought to help the stabilization of the obtained cation intermediate owing to σ–π conjugative effects.[11] In MeOH, the protons generated in the system were solvated and the reactivity to the alkyne was relatively low. This would be the reason that the major product in MeOH was 5,15-dialkynyl porphyrin **2**.

Under air atmosphere, the yields of porphyrins **1** and **2** catalyzed by $BF_3{\cdot}OEt_2$ in $CHCl_3$ were 12% and 53% (1:4), respectively (Table 1, run 2). This might be because the oxidation of porphyrinogen proceeded along with the protonation of alkyne group.

In conclusion, 5-alkenyl-15-alkynyl porphyrin was selectively prepared from dipyrrylmethane and TMS propynal. TMS propynal can be utilized for the preparation of *meso*-alkenyl porphyrins and *meso*-alkynyl porphyrins only by changing the solvents. BCOD-ring fused porphyrins can be easily converted to benzoporphyrins by heating at 210 °C under vacuum,[2,12] which means these unsymmetrical BCOD-ring fused porphyrins will be very useful building blocks for the number-controlled unsymmetrical π-expanded oligomers of benzoporphyrins.

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Supplementary data

Experimental details including synthesis, characterization of compounds, and X-ray crystallography of porphyrin **2**. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.05.115.

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