Novel Synthesis of *meso*-Tetraarylporphyrins by Using I_2 as Catalyst and Air as Oxidant under Thermal or UV Conditions

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An efficient and novel synthesis of *meso*-tetraarylporphyrins is accomplished through iodine-catalyzed condensation of pyrrole, and aryl aldehydes and subsequent oxidation by air under thermal or ultraviolet (UV) irradiation conditions. The advantages of this procedure include good yields and a green nature.

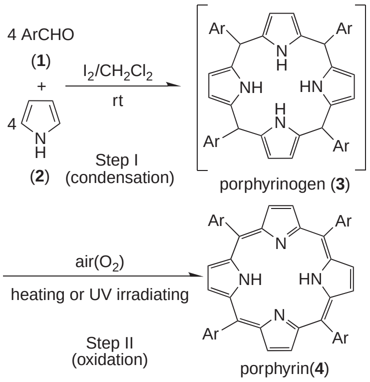
Due to their unique structure and properties, porphyrins have attracted great interests in a variety of fields encompassing catalysis,[1] molecular electronic devices,[2] photodynamic therapy agents,[3] etc. In the mean time, various methods have been reported for the preparation of porphyrin derivatives. In particular, tetraarylporphyrins were firstly prepared by Rothemund[4] in 1939. Since then, substantial improvements have been gained.[5,6] Recently, efforts have been made to prepare tetraarylporphyrins from pyrrole and aldehyde via a two-step procedure by employing various acids,[7] clays,[8] and cation-exchange resins[9] as catalysts, and TCQ[10] and DDQ[11] as oxidants. While these improved procedures offered novel alternatives, further improvements are still needed owing to disadvantages such as low yields,[5,8] tedious procedures,[6a,6b] expensive catalysts,[7,9] or deleterious oxidants used in the above-mentioned methods.[6–11]

It is well known that iodine is an inexpensive and readily available reagent, and has been used as catalyst,[12] and oxidant[13] in organic synthesis. Consequently, it is our first objective to employ iodine as both catalyst and oxidant to facilitate the synthesis of tetraphenylporphyrin (TPP, **4**) from aryl aldehyde (**1**) and pyrrole (**2**). However, it was soon observed that with quantitative amount of iodine, only the intermediate (porphyrinogen, **3**)[14] was formed by stirring the mixture of **1**, **2**, and iodine at rt for several hours.

Bearing in mind that air is an inexhaustible and clean source of oxygen and has been used as oxidant,[15] efforts were then made to employ air with the assistance of both heat and UV-light[16] to promote the oxidation process and with silica gel as supporter in the preparation of **4**. Thus, the reaction mixture after Step I completion was mixed uniformly with silica gel and put into an oven for 15 min at 200 °C. Upon cooling, the adsorbed reaction mixture was purified by column chromatography to give **4** in 41% yield (Method A).

Alternatively, the reaction mixture from **1** and **2** was concentrated and applied on a preparative silica gel TLC plate and developed. The zone corresponding to **3** on the developed TLC plate was put under a UV lamp and irradiated. It turned into a brown color upon irradiation. Further treatment gave **4** in a yield of 51% (Method B) (Scheme 1).

To exclude the possibility that iodine may be the actual oxidant instead of oxygen in air at high temperature or under UV irradiation, catalytic amount of iodine was then tried. The results were listed in Table 1. It showed that catalytic amount of iodine is enough for the preparation of **4** and actually 2.5 mol % of iodine gave the best result. It is also observed that with more than 2.5 mol % of iodine, the yield of **4** decreased and by-product was formed as black polymer. On the other hand, with less than 2.5 mol % of iodine, the reaction was very sluggish and needed much longer time to be completed.



Scheme 1. Synthesis porphyrins in two-step.

Table 1. Study of the effect of the quantity of I_2 on Step I[a]

Entry	I_2/mmol	Time/min	Polymer/g[b]	Yield/%[c]
1	1	2	0.197	2
2	0.5	5	0.085	11
3	0.2	20	0.024	40
4	0.1	30	0	51
5	0.05	70	0	49
6	0.01	360	0	44

[a]Reaction of pyrrole (4 mmol, 0.268 g) and benzaldehyde (4 mmol, 0.424 g) rt and in 10-mL CH_2Cl_2. [b]Black polymer formed from I_2-catalyzed self-polymerization of pyrrole. [c]According to Method B.

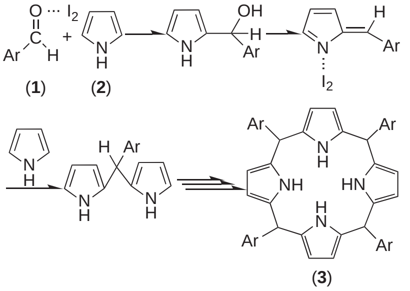
Furthermore, different solvents including CH_3CN, CH_3OH, C_2H_5OH, THF, $C_2H_5OC_2H_5$, $CHCl_3$, and CH_2Cl_2 were screened for the condensation of **1** and **2**. Among the solvents used, CH_2Cl_2 turned out to be the best in terms of both yield and reaction time. As for the reaction temperature, it was found out that the condensation carried out at room temperature (20 °C) gave the best result. Otherwise, by-product[17] was detected when higher temperature was employed.

In order to investigate the scope and generality of this novel method, a series of aryl aldehyde substrates were then tried. The results were listed in Table 2. It indicated that various aldehyde substrates can successfully participate in this two-step process,[18,19] and an increase in steric hindrance and the presence of electron-withdrawing groups at the benzaldehyde results in a general decrease in the yield of porphyrin formation.

Table 2. Synthesis of various *meso*-tetraarylporphyrins

Entry	PhCHO	I_2 /mmol %	Time/min			Yield/%[a]	
			Step I	MA	MB	MA	MB
1	H	2.5	30	15	120	41	51
2	*p*-MeO	trace	20	10	90	52	60
3	*p*-Me	2.5	25	5	90	47	55
4	*p*-Cl	2.5	40	10	120	39	46
5	*p*-F	2.5	45	10	150	15	21
6	*p*-NO_2	2.5	55	15	150	trace	trace
7	*m*-Me	2.5	30	5	90	38	55
8	*m*-MeO	2.5	30	10	120	22	28
9	*m*-Br	2.5	35	10	120	19	25
10	*o*-Cl	2.5	45	10	120	31	36
11	*o*-Br	2.5	40	10	120	26	33
12	*o*-MeO	2.5	60	10	150	24	30

[a]Isolated yields.



Scheme 2. A proposed pathway by I_2 catalysis.

The results in Table 2 also showed that the reaction times of Method A (MA) are much shorter compared to Method B (MB) whereas the yields of MB are 5–10% higher than MA.

Based on the literature,[12a] a pathway for the formation of **3** from **1** and **2** under the catalysis of iodine is proposed in Scheme 2. It is suggested that with its mild Lewis acidity iodine can activate the carbonyl group of the aldehydes and accelerate the condensation process.

In conclusion, iodine was found to be a mild and effective catalyst and oxygen in air with the assistance of heating or UV irradiation acted as effective oxidant in the preparation of TPP. With its high efficiency, green nature, and simple operational procedure, the method reported here may be used as a novel alternative for preparation of TTP derivatives.

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References and Notes

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18 **Typical procedure**: To a flask was added CH_2Cl_2 (10 mL), I_2 (0.1 mmol, 0.254 g) and benzaldehyde (4 mmol, 0.424 g). The resulting solution was stirred for 5 min at room temperature (20 °C). Then, pyrrole (4 mmol, 0.268 g) was added and the mixture was stirred for another 30 min. Upon completion, the mixture was treated as described in Method A or Method B. Method A: The mixture was decanted into a dish charged with 2-g silica gel and mixed uniformly (no massive pellet). It was then put into an oven for 15 min at 200 °C. After being cooled to room temperature, the silica gel charged with the reaction mixture was purified by column chromatography (silica gel; dichloromethane/petroleum ether, 1:3) to give **4** in 41% yield. Method B: The mixture was concentrated under reduced pressure and the residue was applied on a preparative silica gel TLC plate and developed with 20% ethyl acetate in petroleum ether. The zone corresponding to 3 on the developed TLC plate was put under a UV lamp (18 W) and irradiated for 2 h. It turned into a brown color and was scraped from the plate. The adsorbent was extracted with CH_2Cl_2. After removal of the solvent, **4** was obtained in 51% yield.

19 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

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