

Photocatalytic C-N addition amination of olefin

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Abstract. Amines widely exist in nature, wherein some of cyclic amines have crucially biological and physiological activities. They are also the basic blocks for the syntheses of important intermediates, raw materials or fine chemicals such as pharmaceuticals, pesticides and dyes. Amine synthesis by photocatalytic amination of phthalimide and olefins using porphyrin iron (III) or phthalocyanine iron(II) as photosensitizer was investigated in this paper. The results showed that the reactions selectively developed C-N addition and generated a series of compounds containing benzazepine structure with the highest yield of 99.0% at 30 °C. The scope of substrates was further examined and the results demonstrated that the reaction was effective to various olefins, especially to aliphatic olefins. In addition, the influence of the light source was further investigated. The simple, low-power, insect trap lamp (6 W, 365 nm) was used as the light source for the reaction, and a high yield of 95.0% was obtained. Therefore, the inspiring results provide a green and efficient method for the synthesis of compounds containing benzazepine structure.

1. Introduction

Amines widely exist in nature, wherein some of cyclic amines have crucially biological and physiological activities [1, 2]. They are also the basic blocks for the syntheses of important intermediates, raw materials or fine chemicals such as pharmaceuticals, pesticides and dyes [4-6]. Many methods have been applied to synthesize amines [7-11], such as Hoffmann amide degradation, nitro compound reduction, aldehyde or ketone hydroamination, nitrile hydrogenation and addition amination. Among these synthetic methods, addition amination [9] is one of the most direct and effective methods. By addition amination, ammonia or amines can be added directly to double or triple bonds to form new organic amines, hence compared with other amination methods, addition amination displays various advantages like the most theoretical atom utilization, short reaction procedure; positional selectivity and stereoselectivity. The inner molecular cyclization can be completed by this method to produce nitrogen-containing heterocyclic compounds. Therefore, addition amination plays an important role in the field of total synthesis of natural products, pharmaceutical molecules and preparation of fine chemical materials.

It has been reported that *o*-phthalimide (PHT) was taken use as both photosensitizer and nitrogen-containing source for preparation of primary amine under high-pressure Hg-lamp, however light efficiency was too low that cause reaction time seriously delayed and many by-side products generated [12]. In this paper, more efficient photosensitizer, porphyrin iron and phthalocyanine iron were introduced. Metal porphyrins were wide employed as the chlorophyll model to successfully develop the artificial photosynthesis.

Improved by the success, we tested PHT addition amination in the presence of phthalocyanine iron (II) (PcFe), tetrasulfophthalocyanine iron (II) (SxPcFe), meso-tetrakisphenylporphyrin iron (III) chloride (TPPFeCl).

The results showed that the reactions selectively developed C-N addition (Fig. 1). The mildest reaction using simple, low-power, insect trap lamp 365 (6 W, 365 nm) as the light source generated C-N addition product in 95.0% yield at 30 °C. Therefore, photocatalytic C-N addition amination of olefin developed here provides an inspiring way toward the amines containing benzazepine.

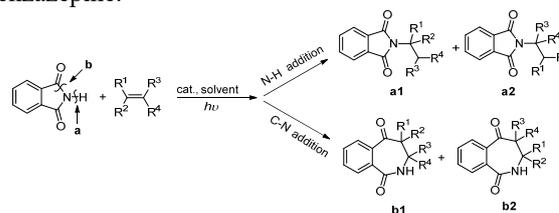


Fig. 1. Photocatalytic addition amination of olefin.

2. Materials and Instrument

TPPFeCl, PcFe, SxPcFe were synthesized according to the references reported [13,14]. Other reagents were obtained commercially.

¹H (400 MHz) and ¹³C (100 MHz) NMR-spectra were recorded on Bruker Ultra-Shield spectrometers in CDCl₃. High-pressure mercury lamp (UV-lamp/250-450, Giguang, 250 watt, 250-450 nm), residentially germicidal ultraviolet lamp (UV-Lamp-254, Philips, 6 W, 254 nm,) and insect trap lamp (UV-Lamp-365, Philips, 6 W, 365 nm) were obtained commercially. High

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Performance Liquid Chromatography (HPLC) was performed on an Agilent HP 1100 chromatograph equipped with a DAD detector using a fused XB-C18 capillary column (Welch Ultimate, 25.0 cm × 4.6 mm × 5.0 μm). A standard program was used for all HPLC analysis, i. e. eluent concentration of acetonitrile water solution was increased from the initial concentration 30 % to 100 % with 3.5 % per minute, eluent flow rate was 0.8 ml/min, and monitoring wavelength was at 220 nm and 254 nm.

3. Results & Discussion

At first, cyclohexene was used as the substrate in the experiment, which was carried out according to the reported reaction procedure but with the addition of photosensitive agent TPPFeCl. Unexpected results were found in the experiment. After various spectral analysis and comparison with the standard spectra, the product under certain conditions was identified as the cyclic expansion product from C-N addition. The product yield and selectivity were 99.0% (Table 1, Entry 1) by HPLC

spectroscopy. The experiment has been repeated many times and the reproducibility is identical. Such high selectivity and yield have not been reported so far. Then, the optimal reaction conditions were obtained by optimizing the reaction conditions.

Conditional experiments were carried out first in the absence of N₂, isolated yield was only 56.8 % and the selectivity was 73.2 % (Entry 2). In the absence of porphyrin photosensitizers, isolated yields were 67.2 % and 65.2 % respectively, and the selectivity was 79.6 % and 74.0 (Entry 3, 4). The experiments using PcFe and PcSxFe had little reaction (Entry 5, 6). NaOH instead of for triethylamine (TEA) generated only a small amount of product (Entry 7). The same base effect can be achieved by using diisopropylamine (DIPA) besides of TEA (Entry 8), but almost no reaction can be achieved in experiments without base (Entry 9) and no reaction can be achieved in experiments without porphyrins and bases (Entry 10). Light, porphyrins, high sterically hindered amines and inert gases are the four necessary conditions for this type reaction.

Table 1. Condition experiment of photocatalytic addition amination*.

Entry	Olefin	Catalyst	$h\nu/\lambda(\text{nm})/\text{Watt}$	Base	N ₂	Time (h)	Conversion (%)	Selectivity (%)	Yield (%)
1	1	TPPFeCl	UV-lamp/250-450/250	TEA	Yes	2	99.0	99.9	99.0
2	1	TPPFeCl	UV-lamp/250-450/250	TEA	No	2	77.6	73.2	56.8
3	1	-	UV-lamp/250-450/250	NaOH	Yes	2	84.4	79.6	67.2
4	1	-	UV-lamp/250-450/250	TEA	Yes	2	88.0	74.0	65.2
5	1	PcFe	UV-lamp/250-450/250	TEA	Yes	2	0	-	0
6	1	PcSxFe	UV-lamp/250-450/250	TEA	Yes	2	-	-	trace
7	1	TPPFeCl	UV-lamp/250-450/250	NaOH	Yes	2	-	-	trace
8	1	TPPFeCl	UV-lamp/250-450/250	DIPA	Yes	2	99.0	99.9	99.0
9	1	TPPFeCl	UV-lamp/250-450/250	-	Yes	2	0	-	0
10	1	-	UV-lamp/250-450/250	-	Yes	2	0	-	0
11	2	TPPFeCl	UV-lamp/250-450/250	TEA	Yes	2	95.5	97.5	93.1
12	3	TPPFeCl	UV-lamp/250-450/250	TEA	Yes	2	96.6	97.6	94.3
13	4	TPPFeCl	UV-lamp/250-450/250	TEA	Yes	5	40.5	88.7	35.9
14	1	TPPFeCl	UV-Lamp/365/6	TEA	Yes	48	99.0	96.0	95.0

15	1	TPPFeCl	UV-Lamp/254/6	TEA	Yes	24	0	-	0
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*Reactions conditions following general procedure (see 5.1) except specially indicated in Table 1

Study further expanded the scope of the substrate, respectively using 4-methyl cyclohexene, tetramethyl ethylene and styrene. They were on behalf of high sterically hindered olefins, electron-rich branched olefins, electron-deficient conjugated olefins. The experimental results are shown in table 1 (Entry 11-13). They all obtained products with good or excellent selectivity, but electron-deficient conjugated olefin 4 was less active than electron-rich branched olefins 1 to 3, and the steric effect was not remarkable.

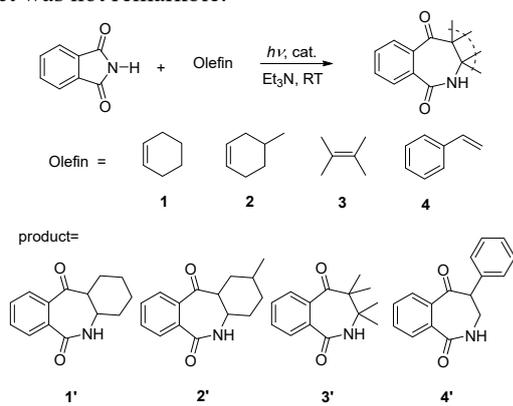


Fig. 2. The synthesis of product 1', 2', 3', 4'.

The research further investigated the specific absorption wavelength for the photoamination to increase light efficiency. The UV-Lamp-365 and UV-Lamp-254 were used as the light sources respectively. The results showed that 99.0 % conversion and 96.0 % selectivity were achieved with the UV-Lamp-365 (Entry 14), while the UV-Lamp-254 unsuccessfully initiating the reaction (Entry 15), indicated that 365 nm is specified wavelength for this reaction.

4. Conclusions

Photocatalytic C-N addition amination of phthalimide and olefins using porphyrin iron (III) or phthalocyanine iron(II) as photosensitizer was investigated under ultraviolet light, at temperature of 30 °C, and was conducted successfully. The results showed that the reactions selectively developed C-N addition and generated a series of compounds containing benzazepine structure with the highest yield of 99.0%. The scope of substrates was further examined and the results demonstrated that the reaction was effective to various olefins, especially to aliphatic olefins. The optimal reaction conditions were as follows: the molar ratio of PHT to olefin is 1:10, the reaction temperature is 30 °C. The simple, low-power, wavelength-definite insect trap lamp (6 W, 365 nm) was used as the light source for the reaction, and a high yield of 95.0% was obtained. Therefore, this kind of reaction provides a green and efficient method for the synthesis of compounds containing benzazepine structure by the C-N addition amination.

5. Experimental

5.1. General procedure for reaction experiment

Add PHT (200 mg, 1.36 mmol), cyclohexene (1.5 mL, 14.6 mmol), catalyst (2 mg), TEA (0.5 mL) and water (3 mL) in a quartz photo-reactor filled with N_2 . Keep the reactor at 30 °C and irradiated by the definite lamp for a period of time. After the reaction, the solvent and excess olefins were removed by distillation under reduced pressure, and the crude product was extracted with dichloromethane and purified by chromatographic column.

5.2. Synthesis of benzo[b,e]azepine-6,11(2H)-dione 1'

The reaction was following the general procedure using TPPFeCl as catalyst under UV-Lamp-365 for 48 h. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ (ppm): 7.92 (d, $J = 7.4$, 1 H), 7.64~7.55 (m, 3 H), 6.43 (br. s, 1 H), 4.24 (s, 1 H), 2.56 (dt, $J = 12.0$, 3.1 Hz, 1 H), 1.96~1.35 (m, 8 H).

5.3. Synthesis of 2-methyl-1,3,4,4a,5,11a-hexahydro-6H-dibenzo[b,e]azepine-6,11(2H)-dione 2'

The reaction was following the general procedure using TPPFeCl as catalyst under UV-lamp/250-450. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ (ppm) : 7.90 (d, $J = 6.3$ Hz, 1 H), 7.62~7.56 (m, 3 H), 6.55 (br. s, 1 H), 4.22 (s, 1 H), 2.61 (dt, $J = 11.5$, 3.5 Hz, 1 H), 1.71~1.16 (m, 7 H), 1.02 (d, $J = 6.5$, 3 H) .

5.4. Synthesis of 3,3,4,4-tetramethyl-3,4-dihydro-1H-benzo[c]azepine-1,5(2H)-dione 3'

The reaction was following the general procedure using TPPFeCl as catalyst under UV-lamp/250-450. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ (ppm) : 8.07 (m, 1 H, 6-H), 7.87 (m, 1 H, 9-H), 7.58 (m, 2 H), 6.89 (br. d, 1 H), 1.26 (s, 6 H), 1.24 (s, 6 H) .

5.5. Synthesis of 4-phenyl-3,4-dihydro-1H-benzo[c]azepine-1,5(2H)-dione 4'

The reaction was following the general procedure using TPPFeCl as catalyst under UV-lamp/250-450. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ (ppm) : 7.96 (dd, $J = 1.1$, 7.6 Hz, 1 H, 6-H), 7.73~7.56 (m, 3 H), 7.35~7.13 (m, 5 H), 4.17 (dd, $J = 3.9$, 10.2 Hz, 1 H), 3.85 (ddd, $J = 5.9$, 10.2, 15.0 Hz, 1 H), 3.67 (ddd, $J = 4.0$, 6.8, 15.1 Hz, 1 H) .

Acknowledgments

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