## Photodimerization of 4-Aryl-1,4-dihydropyridines in 1-Butyl-3-methylimidazolium Tetrafluoroborate

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A simple, efficient, and convenient method for the photodimerization of 4-aryl-1,4-dihydropyridine in room-temperature ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate ([Bmim][BF<sub>4</sub>]) has been developed. By this way, head-to-tail *syn*-dimers and 3,9-diazatetraasteranes were obtained in good to excellent yields. In addition, [Bmim][BF<sub>4</sub>] can be reused at least 5 times as the medium without obvious decrease in reaction time and yield.

Photodimerization of 4-aryl-1,4-dihydropyridines has attracted some attention because its major products 3,9-diazatetraasteranes have been suggested as interesting pharmacological targets with potential anticancer or anti-HIV activity.<sup>1</sup> A solidstate method has been initially developed through the photodimerization of 4-aryl-1,4-dihydropyridine 1 under solvent-free condition by Hilgeroth and co-workers.<sup>1b,2</sup> Although the method can produce *syn*-dimer intermediate 2 and 3,9-diazatetraasterane **3**, it could hardly been used on a industrial scale due to the small-scale production, a long reaction time, and low yield. Later, the solution-dimerization of 4-aryl-1,4-dihydropyridines has been reported to give *anti*-dimer intermediate **4** and 3,9diazatetraasterane **3**. However, a large amount of organic solvent, harsh reaction condition, a long reaction time, and low yields still represent main disadvantages (Scheme 1).<sup>3</sup>

Recently, ionic liquids (ILs) have emerged as a set of green solvents with unique properties such as tunable polarity, high thermal stability and immiscibility with a number of organic solvents, negligible vapor pressure, and recyclability.<sup>4</sup> Their high polarity and the ability to solubilize both organic and inorganic compounds can result in enhanced rates of chemical processes and can provide higher selectivities than conventional solvents. Accordingly they are emerging as novel replacements for volatile organic solvents in organic synthesis. They are particularly promising as solvents for catalysis.<sup>5</sup> Because of distinct advantages of ILs as environmentally benign reaction media for catalytic processes, much attention has currently focused on organic reactions promoted by ionic liquids. To the best of our knowledge, [2 + 2] photocycloaddition usually



**Scheme 1.** Photodimerization of 4-aryl-1,4-dihydropyridine under solid-state and solution conditions.

occurs in solid state or in organic solution, but there have been few reports on photodimerizaiton in ionic lquid.<sup>1–3,6</sup> In the framework of our investigations on the development of green chemical procedures,<sup>7</sup> we would like to herein report a novel and environmentally safe procedure for photodimerization of 4-aryl-1,4-dihydropyridines in room-temperature ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate ([Bmim][BF<sub>4</sub>]), which is designed to overcome the limitations previously encountered in the reaction.

Ionic liquid [Bmim][BF<sub>4</sub>] has been used as a convenient, economic, and user-friendly reaction medium for synthesizing 1,4-dihydropyridines.<sup>8</sup> In search of the best experimental reaction conditions, the photodimerization of 4-phenyl-1,4dihydropyridine (1a) in IL [Bmim][BF<sub>4</sub>] was considered as a standard model reaction to obtain photodimer intermediate and corresponding cage-dimeric 3.9-diazatetraasterane. We tested the effects of different concentration of 4-phenyl-1,4-dihydropyridine (1a)  $(0.08-0.16 \text{ mmol mL}^{-1})$  and various power (400-500 W) of unfiltered light from a medium pressure mecury lamp at  $\lambda_{\text{max}} > 313 \text{ nm}$  on the photodimerization (Table 1). Results showed that saturated<sup>9</sup> 4-phenyl-1,4-dihydropyridine (1a)  $0.16 \text{ mol } \text{L}^{-1}$  and a medium pressure mecury lamp 450 Wprovided the best conditions to give intermediate 2a and cage dimer 3a in 92 and 89% yield within 15 and 30 min, respectively (Table 1, Entries 6 and 12). The structure of intermediate 2a (CCDC No. 992512) was finally determined to be a head-to-tail syn-dimer by single-crystal X-ray diffraction as shown in Figure 1.10 Moreover we found that the formed subsequence was syn-dimer 2 before cage photodimer 3, so the reaction path

**Table 1.** Photodimerization of 4-phenyl-1,4-dihydropyridine (1a) in  $[Bmim][BF_4]^a$ 

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Entry	Product	Concentration $/mmol mL^{-1}$	Power of UV lamp/W	Time /min	Yield <sup>b</sup> /%
1	2a	0.08	400	180	65
2	2a	0.1	400	100	77
3	2a	0.12	400	60	80
4	2a	0.14	400	40	81
5	2a	0.16	400	25	85
6	2a	0.16	450	15	92
7	2a	0.16	500	10	80
8	3a	0.08	400	240	68
9	3a	0.10	400	200	76
10	3a	0.12	400	180	80
11	3a	0.14	400	100	81
12	3a	0.16	450	30	89
13	3a	0.16	500	30	68

<sup>a</sup>Reaction condition: **1a** (0.8–1.6 mmol), [Bmim][BF<sub>4</sub>] (10 mL), light (400–500 W medium pressure mecury lamp with  $\lambda_{max} > 313$  nm). <sup>b</sup>Isolated yields.



Figure 1. ORTEP diagram of the crystal structure of compound 2a (Drawn at the 50% thermal ellipsoids).



Scheme 2. Photodimerization of 4-phenyl-1,4-dihydropyridine (1a) under ionic liquid conditions.

was presumed to be 4-aryl-1,4-dihydropyridine 1 producing the *syn*-dimer 2 through [2 + 2] cycloaddition, then 3,9-diazate-traasterane 3 being obtained by the photodimerization of the *syn*-dimer intermediate 2 in [Bmim][BF<sub>4</sub>] (Scheme 2). Solid-state photodimerization yielded the same products *syn*-dimer 2a and cage dimer 3a as the IL method, but it had some disadvantages such as a long reaction time (3 to 4 days), tedious process, and low yield.<sup>3</sup> Results in Table 1 showed that the photodimerization of 4-phenyl-1,4-dihydropyridine in IL could not only be used as a substitute for the solid-state method, but also has distinct advantages such as a short reaction time, easy purification, and higher yield.

For assessing the generality of reaction condition, we next investigated the photodimerization of different substituted 4-phenyl-1,4-dihydropyridines under the IL reaction conditions (Table 2). It seemed that there was little difference between yields of photodimer products with electron-donating groups and electron-withdrawing groups, and all the photodimerization showed high reactivity and exclusive selectivity. Various 4-phenyl-1,4-dihydropyridines 1 gave *syn*-dimer intermediates 2 within 10–20 min and in 88–92% yields, and the corresponding 3,9-diazatetraasteranes 3 within 30–40 min and in 81–89% yields (Scheme 3).

To check the reusability of IL as solvent, when the photodimerization of 4-phenyl-1,4-dihydropyridines was completed, the mixture was poured into water, and the crude product was obtained by filtration. The product was recrystallized from alcohol. The aqueous layer containing IL was subjected to vacuum distillation to remove water, leaving the IL [Bmim][BF<sub>4</sub>]. The residual IL was washed with a small amount of ethyl acetate, dried under vacuum at 80 °C for 4 h and recycled. It was found that the medium [Bmim][BF<sub>4</sub>] can be recycled at least five times with no significant decrease in yields of products. For example, photodimerization in the fifth reuse of

Table 2. Preparation syn-dimers 2 and cage dimers 3 in  $[Bmim][BF_4]^a$ 

Entry	Product	R	Time /min	Yield <sup>b</sup> /%
1	2a	Н	15	92
2	<b>2b</b> <sup>c</sup>	4-Me	15	90
3	2c	4-OMe	10	92
4	2d <sup>c</sup>	4-C1	15	89
5	2e <sup>c</sup>	4-OH	15	88
6	2f <sup>c</sup>	3-OMe, 4-OH	20	90
7	3a	Н	35	89
8	3b <sup>c</sup>	4-Me	30	85
9	3c	4-OMe	35	81
10	3d <sup>c</sup>	4-C1	40	84
11	3e <sup>c</sup>	4-OH	35	86
12	3f <sup>c</sup>	3-OMe, 4-OH	30	85

<sup>a</sup>Reaction condition: **1** (1.6–1.8 mmol), [Bmim][BF<sub>4</sub>] (10 mL) (saturated concentration), light (450 W medium pressure mecury lamp with  $\lambda_{max} > 313$  nm). <sup>b</sup>Isolated yields. <sup>c</sup>New compound.



**Scheme 3.** Photodimerization of 4-aryl-1,4-dihydropyridines in [Bmim][BF<sub>4</sub>].

[Bmim][BF<sub>4</sub>] as reaction medium gave 2a in 90–92% yield and 3d in 81–84% yield. The use of IL [Bmim][BF<sub>4</sub>] as reaction medium for this transformation avoids the use of organic solvents and also avoids aqueous workup to isolate the products. The simple experimental and product isolation procedures combined with the ease of recovery and reuse of the novel reaction medium is expected to contribute to the development of a green strategy for the synthesis of *syn*-dimers and corresponding 3,9-diazatetraasteranes.

In summary, we developed an efficient and environmentally benign method for the photodimerization of 4-aryl-1,4-dihydropyridines in ionic liquid [Bmim][BF<sub>4</sub>]. *syn*-Dimers and corresponding 3,9-diazatetraasteranes were obtained in high yields within a short time, and the reaction medium [Bmim][BF<sub>4</sub>] ionic liquid can be reused five times without distinct decrease in yields.

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Supporting Information is available electronically on J-STAGE.

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