



# $\alpha$ -Iodination of enaminones using the modified Johnson's procedure: the use of $I_2$ and $Et_3N$

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**Abstract**—Facile synthesis of  $\alpha$ -iodo enaminones **2** was carried out by the use of iodine and triethylamine in methylene chloride in short time in excellent yields.

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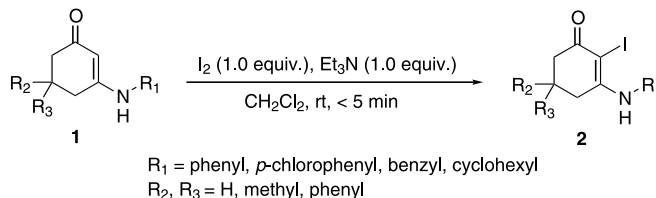
Iodination of enaminones at the  $\alpha$ -position is important in organic chemistry.<sup>1–6</sup>  $\alpha$ -Iodo enaminones could be used as important starting materials for the synthesis of heterobicyclic enones<sup>1</sup> as well as for the preparation of biologically active heterocyclic compounds.<sup>4,5b</sup> In these respects, many papers have been reported for the synthesis of these compounds.<sup>2–6</sup> Campos et al. used bis(pyridine)iodonium(I) tetrafluoroborate in methylene chloride.<sup>2</sup> Benzyltrimethylammonium dichloroiodate (BTMAICl<sub>2</sub>) has been reported by Matsuo and co-workers to be an efficient  $\alpha$ -iodinating agent for the secondary enaminones.<sup>3</sup> Kordik and Reitz have reported unexpected  $\alpha$ -chlorination of tertiary enaminones by using the same reagent.<sup>4</sup> *N*-Iodosuccinimide has been used successfully for the iodination of tricyclodeceny enaminones.<sup>5</sup> Indirect method for the synthesis of  $\alpha$ -iodo enaminones involving thermal decomposition of trifluoroethylidonium salts has been developed.<sup>6</sup> However, most of the reported methods suffer from moderate yields or the need of special reagents. Thus, development of more cheaper and easily available reagent for the  $\alpha$ -iodination of enaminones would be beneficial.

$\alpha$ -Iodination of  $\alpha,\beta$ -unsaturated carbonyl compounds can be carried out most conveniently by the Johnson's conditions, which used iodine in  $CCl_4$ –pyridine solvent.<sup>7</sup> The original Johnson's method was used frequently in the sequences of total synthesis of many natural products by slightly modified version (e.g. addi-

tional use of DMAP).<sup>8</sup> We presumed that the Johnson's conditions could also be applied to the enaminone system. Thus, we examined the reaction of enaminone **1a** and iodine in the presence of pyridine, DMAP (4-dimethylaminopyridine), or  $Et_3N$ . The best results (95%) were observed when we used  $Et_3N$ .<sup>9</sup>

As shown in Scheme 1 and in Table 1, various kinds of enaminones **1a–h** can be iodinated at the  $\alpha$ -position in excellent yields instantaneously (within 5 min) to give  $\alpha$ -iodo enaminones **2a–h**. Pyridine or DMAP can also be used (see entry 1) in the reaction with similar results. We could isolate the desired products by column chromatography without aqueous workup process. Unfortunately, enaminones derived from secondary amine (namely, tertiary enaminone) did not give the corresponding  $\alpha$ -iodo products (as an example, see entry 9). The reason is unclear at this point.

Experimental procedure for the synthesis of **2a** is typical. To a stirred solution of **1a** (374 mg, 2 mmol)<sup>10</sup> and iodine (508 mg, 2 mmol) in dichloromethane (5 mL) was added triethylamine (202 mg, 2 mmol) at room temperature. After 5 min at room temperature solvent was removed under reduced pressure. The residue was



Scheme 1.

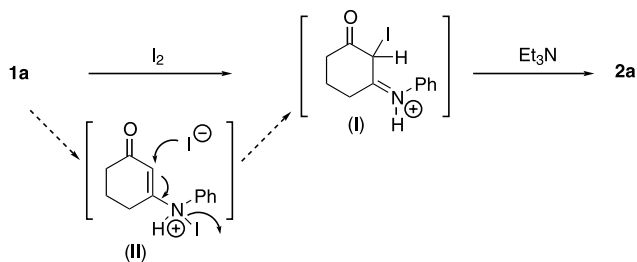
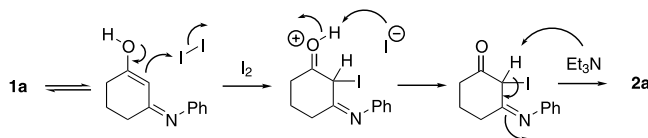
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**Table 1.** Synthesis of  $\alpha$ -iodo enaminones **2**

entry	enaminones <b>1</b>	products <b>2</b>	yield (%) <sup>a</sup>
1			95 <sup>b</sup> (94–96) <sup>2a,4</sup>
2			93 (141–142)
3			96 (115–116) <sup>2a</sup>
4			94 (104–105) <sup>2a</sup>
5			91 (163–165) <sup>3</sup>
6			96 (135–137)
7			92 (145–147)
8			98 (124–125)
9		no reaction	

<sup>a</sup>Mp was written in the parenthesis. <sup>b</sup>**2a** was obtained in similar yields by using DMAP or pyridine with somewhat longer reaction time.

**Scheme 2.****Figure 1.**

separated by silica gel column chromatography ( $\text{CH}_2\text{Cl}_2$  followed by hexane/ethyl acetate, 1:1) to give the desired  $\alpha$ -iodo enaminone **2a** as a light tan solid, 595 mg (95%).

The postulated reaction mechanism is shown in Scheme 2.<sup>11</sup>  $\alpha$ -Iodo iminium salt (**I**) could be formed via direct attack of iodine at the  $\alpha$ -position of **1a**. Or, (**I**) could be generated via an  $\text{S}_{\text{N}}2'$  type reaction of the initially formed  $N$ -iodonium salt (**II**).<sup>5,12</sup> Following abstraction of  $\alpha$ -proton from (**I**) by triethylamine gave the product **2a**.

In summary, we report herein the facile synthesis of  $\alpha$ -iodo enaminones by the use of iodine and triethylamine in short time in excellent yields.

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