

## Efficient Preparations of $\alpha$ -Azidoketones and $\alpha$ -Thiocyanatoketones via $\alpha$ -Sulfonyloxy Aryl Ketone Intermediates in Ionic Liquid

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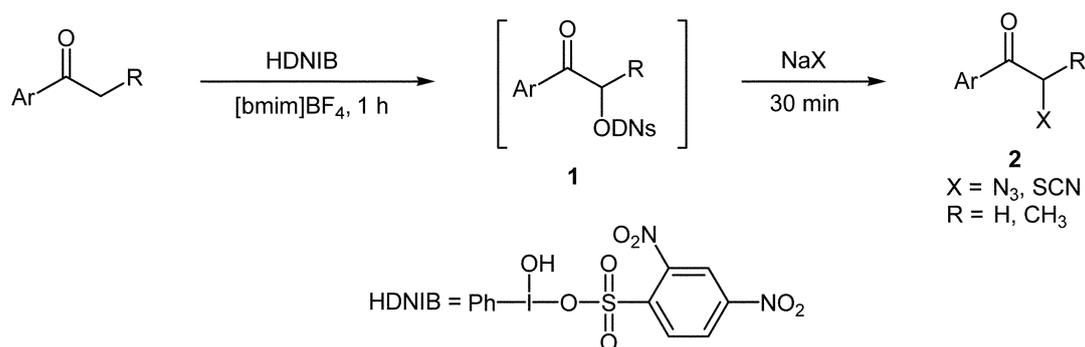
$\alpha$ -Azidoketones are versatile organic intermediate for the synthesis of biologically important heterocyclic compounds which include oxazoles, pyrroles, and pyrazines.<sup>1</sup> Synthetically useful intermediates such as  $\alpha$ -amino ketones,<sup>2</sup>  $\alpha$ -azido- $\beta$ -hydroxy ketones,<sup>3</sup> and  $\beta$ -amino alcohols also have been prepared from  $\alpha$ -azidoketones.<sup>4</sup> The synthesis of  $\alpha$ -azidoketones can be commonly achieved by azide-halogen exchange reactions of  $\alpha$ -haloketones.<sup>5</sup> In addition,  $\alpha$ -azidoketones have been successfully prepared from reaction of sodium azide with  $\alpha$ -tosyloxy ketones by treatment with surfactant pillared clays<sup>6</sup> and triphase catalysis under ultrasound irradiation<sup>7</sup> in organic solvents such as chloroform or acetonitrile. Very recently,  $\alpha$ -azidoketones have been prepared from  $\alpha$ -diazoketones in the presence of sodium azide and cerium(III) chloride heptahydrate.<sup>8</sup> On the other hand, synthesis of  $\alpha$ -azidoketones directly starting from ketones has been by far less explored. To our best knowledge, the only previous example of  $\alpha$ -azidation of ketones was reported from our group by the reaction of  $\alpha$ -(*p*-nitrobenzenesulfonyl)oxy ketone intermediates with sodium azide in acetonitrile.<sup>9</sup>  $\alpha$ -Thiocyanatoketones can serve as valuable precursors for the preparation of many valuable heterocyclic compounds and many protocols have been developed for its preparations.<sup>10</sup> In similar to the  $\alpha$ -azidoketones, the  $\alpha$ -thiocyanatoketones are mainly prepared from the reaction of  $\alpha$ -haloketones with thiocyanate ion in various organic solvents.<sup>11</sup> However, all of the known preparation methods for both  $\alpha$ -azidoketones and  $\alpha$ -thiocyanatoketones suffered from one or more limitations as regards tedious reaction procedure, long reaction times, and relatively low yields. Moreover, invariably all of the reported reactions were conducted in volatile toxic organic solvents.

In these eco-conscious days, there is an increasing demand for replacing conventional organic synthetic methods by more environmentally benign processes to prevent damaging of ecosystem. In this context, ionic liquids have been attracted considerable attention as an environmentally friendlier reaction media for the various organic transformations. Ionic liquids can serve as environmentally benign alternatives to the conventional volatile organic solvents due to their interesting properties such as very low volatility, high chemical stability, and nonflammability.<sup>12</sup>

Hypervalent iodine(III) sulfonates has been received continuous attention due to their versatile utilities in organic synthesis, ready availability, and relatively non-toxic pro-

perties.<sup>13</sup>

In continuation of our efforts to develop greener organic reaction procedures, we now report [hydroxy(2,4-dinitrobenzenesulfonyloxy)iodo]benzene (HDNIB)<sup>14,15</sup> mediated facile and efficient synthesis of  $\alpha$ -azidoketones and  $\alpha$ -thiocyanatoketones in 1-butyl-3-methylimidazolium tetrafluoroborate, [bmim]BF<sub>4</sub>, ionic liquid. Initially we have tested the possibility of  $\alpha$ -sulfonyloxylation reactions of ketones using HDNIB in [bmim]BF<sub>4</sub>. The conventional synthesis of  $\alpha$ -organosulfonyloxy ketones have been generally conducted in the organic solvents such as acetonitrile and dichloromethane.<sup>15,16</sup> It is well known that the hypervalent iodine(III) sulfonates are incompatible to the highly polar reaction medium such as methanol and water. Therefore, it will be highly desirable to develop a synthetic procedure that can be conducted in highly polar medium like ionic liquids for the broadening synthetic utilities of the hypervalent iodine(III) sulfonates. Hence, we have attempted the reaction of aryl ketones with HDNIB in [bmim]BF<sub>4</sub> and successfully isolated the  $\alpha$ -[(2,4-dinitrobenzene)sulfonyl]oxy ketone intermediates in high yields. Generally, in ionic liquid, the formation of  $\alpha$ -[(2,4-dinitrobenzene)sulfonyl]oxy ketones are faster (1 h) and the yields are comparable or superior to those obtained in previously reported results conducted in acetonitrile.<sup>15</sup> After established optimum conditions for the successful  $\alpha$ -sulfonyloxylation of ketones in ionic liquid, we next examined  $\alpha$ -azidation of ketones by the reaction of sodium azide with  $\alpha$ -[(2,4-dinitrobenzene)sulfonyl]oxy ketone intermediates. Our new procedure involves initial formation of  $\alpha$ -[(2,4-dinitrobenzene)sulfonyl]oxy ketone intermediates *via* the reaction of aryl ketones with HDNIB in 1.0 mL of [bmim]BF<sub>4</sub> by gently heating at 60 °C for 1 h, followed by subsequent treatment of reaction intermediates with 2.0 equivalent of sodium azide in the same reaction vessel for additional 30 min at 40 °C. We have examined the general scope of the present protocol with number of aryl ketones and the reactions were successful to give  $\alpha$ -azidoketones in high yields. The results are summarized in Table 1. Both aromatic methyl ketones and methylene ketones provided the corresponding  $\alpha$ -azidoketones in high yields. The efficient one-pot conversion of ketones into  $\alpha$ -azidoketones can be rationalized in terms of rapid nucleophilic substitution reactions of  $\alpha$ -[(2,4-dinitrobenzene)sulfonyl]oxy ketone intermediates with the azide anion to give the corresponding  $\alpha$ -azidoketones. We



**Table 1.** Synthesis of  $\alpha$ -sulfonyloxy ketones,  $\alpha$ -azidoketones and  $\alpha$ -thiocyanatoketones from arylketones

Entry	Ar	R	Yield (%) <sup>a</sup> of 1	Yield (%) <sup>b</sup> of 2	
				X = N <sub>3</sub>	X = SCN
1	Ph	H	95	86	88
2	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	H	93	80	84
3	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	H	82	80	78
4	<i>p</i> -BrC <sub>6</sub> H <sub>4</sub>	H	85	88	82
5	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	H	93	90	90
6	Ph	Me	94	87	86
7	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	Me	87	83	85
8	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	Me	85	79	76
9	<i>p</i> -BrC <sub>6</sub> H <sub>4</sub>	Me	89	86	90
10	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	Me	84	87	88

<sup>a</sup>Isolated yields. <sup>b</sup>Yields calculated from starting ketones.

have tested the effectiveness of the other hypervalent iodine compounds by replacing HDNIB with [hydroxy(tosyloxy)iodo]benzene (HTIB) and [hydroxy(*p*-nitrobenzenesulfonyloxy)iodo]benzene (HNIB) at the identical reaction conditions. We have found that the formation of either  $\alpha$ -nosyloxy ketone or  $\alpha$ -tosyloxy ketone intermediates occurred rather slowly and yields of  $\alpha$ -azidoketones were reduced to 20–30% on average compare to the results obtained using HDNIB. This may be due to the better leaving ability of 2,4-dinitrobenzenesulfonate group in nucleophilic substitution reactions compared to tosylate or nosylate groups at the present reaction conditions. Replacement of [bmim]BF<sub>4</sub> with more hydrophobic 1-butyl-3-methylimidazolium hexafluorophosphate, [bmim]PF<sub>6</sub>, provided lower yields in the most cases studied. Next, we have also examined the nucleophilic substitution reactions of  $\alpha$ -[(2,4-dinitrobenzene)sulfonyl]oxy ketone intermediates with thiocyanate ion. The reactions worked well to give the corresponding  $\alpha$ -thiocyanatoketones with equal efficiencies to the cases of  $\alpha$ -azidation reactions. General experimental procedure for the preparation of  $\alpha$ -azidoketones is as follows: A mixture of aryl ketone (1.0 mmol), HDNIB (0.562 g, 1.2 mmol) in 1.0 mL of [bmim]BF<sub>4</sub> was placed into a glass tube and the reaction mixture was stirred for 1 h at 60 °C. After completion of the formation of  $\alpha$ -[(2,4-dinitrobenzene)sulfonyl]oxy ketone intermediate, 2.0 equivalent of sodium azide was added to the reaction mixture and stirring was continued for 30 min at 40 °C. After completion of the

reaction, the reaction mixture was diluted with water (5 mL), and the product was extracted with ethyl acetate (3 × 10 mL). The collected organic fractions were dried over MgSO<sub>4</sub>, and the solvent was evaporated under vacuum. The resulting residue was chromatographed on silica gel using a mixture of ethyl acetate and *n*-hexane (1 : 4) as eluent to give a purified  $\alpha$ -azidoketone.

In conclusion, a facile and environmentally friendlier one-pot procedure has been devised for the direct conversion of aryl ketones into the corresponding  $\alpha$ -azidoketones and  $\alpha$ -thiocyanatoketones. This new efficient and facile method might be served as a useful alternative to existing methods, since it does not require  $\alpha$ -haloketones or  $\alpha$ -tosyloxyketones substrates as starting materials.

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