

## 2-Azido-1,3-dimethylimidazolium Chloride: An Efficient Diazo Transfer Reagent for 1,3-Dicarbonyl Compounds

Mitsuru Kitamura,\* Norifumi Tashiro, Tatsuo Okauchi

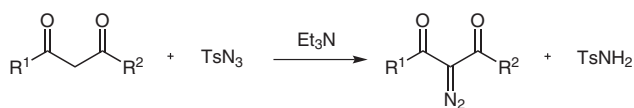
Department of Applied Chemistry, Kyushu Institute of Technology, 1-1 Sensui-cho, Tobata-ku, Kitakyushu-shi, Fukuoka, 804-8550, Japan  
Fax +81(93)8843304; E-mail: kita@che.kyutech.ac.jp

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**Abstract:** Diazo transfer from 2-azido-1,3-dimethylimidazolium chloride to 1,3-dicarbonyl compounds has been developed. The reaction proceeds under mild conditions to give 2-diazo-1,3-dicarbonyl compounds in high yields, which are easily isolated because the by-products are highly soluble in water.

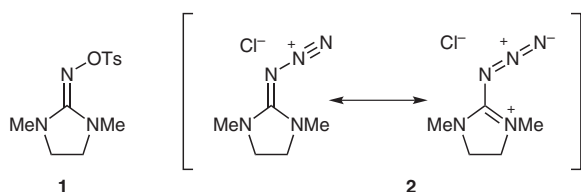
**Key words:** azides, diazo compounds, diazonium salt, diazo-transfer, heterocycles

Techniques for diazo group transfer to an active methylene group is a useful method for the synthesis of  $\alpha$ -diazo-carbonyl compounds.<sup>1</sup> As a transfer reagent, *p*-toluenesulfonyl azide (tosyl azide) is commonly used.<sup>1–3</sup> However, the use of tosyl azide in the reaction frequently causes problems during isolation of the desired diazo compound from the excess tosyl azide and sulfonamide, which is a by-product of diazo transfer (Scheme 1).<sup>4</sup>



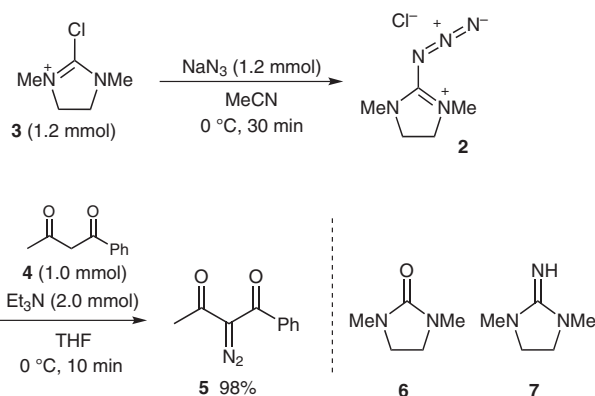
**Scheme 1** Diazo transfer from tosyl azide to 1,3-dicarbonyl compounds

Previously, we have reported that 2-imidazolidinone *O*-*p*-toluenesulfonyl oxime **1** is an efficient electrophilic aminating reagent for Grignard reagents (Scheme 2).<sup>5</sup> In a further study on the development of a new aminating reagent, we found that the azidoimidazolium salt **2** (guanidino diazonium salt) has the ability to mediate diazo-transfer. In this letter, we wish to describe a convenient diazo transfer method to 1,3-dicarbonyl compounds with azidoimidazolium salt **2** derived in situ.



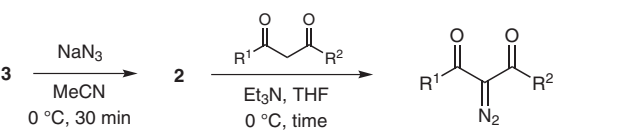
**Scheme 2**

First, the reaction of azidoimidazolium salt **2** and 1-phenyl-1,3-butandione (**4**) was examined (Scheme 3). The salt **2** was prepared by the reaction of commercially available chloroimidazolium salt **3** with sodium azide in acetonitrile at 0 °C.<sup>6</sup> To the mixture, triethylamine and 1-phenyl-1,3-butandione (**4**) in THF was added at 0 °C. The ketone **4** was consumed within 10 minutes, and the diazo compound **5** was obtained in 98% yield. In this reaction, the formation of 2-imidazolidinone **6** was observed after quenching with water. The mechanism of the formation of **6** is unclear, however, it could be formed by the hydrolysis of excess azidoimidazolium salt **2** and/or guanidine **7**. The by-product **6** was separated from the diazo compound **5** by washing the organic extract of the reaction mixture with water, since the 2-imidazolidinone **6** was highly soluble in water. This point is in contrast to the diazo transfer reaction using tosyl azide, which is often difficult to separate from the product diazo compound.



**Scheme 3** Reaction of 1-phenyl-1,3-butandione (**4**) with azidoimidazolium salt **2** prepared from chloroimidazolium **3**

In order to examine the scope and limitations of this method, we next investigated the diazotization of various 1,3-dicarbonyl compounds (Table 1).<sup>7</sup> In entries 1–6, the results of the transfer reaction with a range of acyclic 1,3-dicarbonyl compounds are shown. Diketones and ketoesters reacted smoothly with azidoimidazolium **2** to give the corresponding diazo compounds in high yields (entries 1–4). Although the reaction required a longer reaction time when ketoamide or diester was employed, the diazo products were still obtained in high yields (entries 5 and 6). Cyclic 1,3-dicarbonyl compounds were also diazotized by this method (entries 7 and 8).

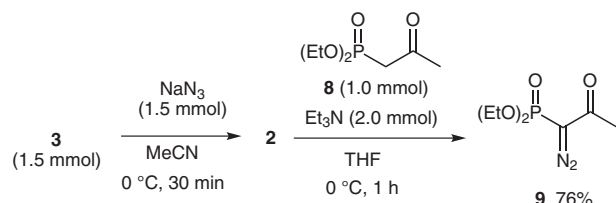
**Table 1** Diazo Transfer of Azidoimidazolium Salt **2** to 1,3-Dicarbonyl Compounds<sup>a</sup>


Entry	R <sup>1</sup>	R <sup>2</sup>	Time	Yield (%) <sup>b</sup>
1	Me	Ph	10 min	98
2	Me	Me	10 min	93
3	Ph	Ph	2 h	99
4	Me	OEt	2 h	82
5	Me	N(Me) <sub>2</sub>	4 h	79
6	OEt	OEt	4 h	99
7	-CH <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> CH <sub>2</sub> -		10 min	94
8	-OC(CH <sub>3</sub> ) <sub>2</sub> O-		10 min	95

<sup>a</sup> Molar ratio of 3/NaN<sub>3</sub>/1,3-dicarbonyl compounds/Et<sub>3</sub>N = 1.2:1.2:1:2.

<sup>b</sup> Isolated yield.

Azidoimidazolium salt **2** was also applicable to the preparation of Ohira–Bestmann reagent **9**,<sup>8</sup> which was obtained in 76% by the reaction with diethyl (2-oxopropyl)phosphonate (**8**; Scheme 4).

**Scheme 4**

In conclusion, we have developed an efficient diazotization method for 1,3-dicarbonyl compounds using diazotization salt **2**, which is easily prepared from commercially available compounds in one step. Using this diazotization approach, 2-diazo-1,3-dicarbonyl compounds were obtained in high yields and were easily isolated.

## References and Notes

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- The formation of salt **2** was confirmed by mass spectral analysis. The FAB(positive) mass spectrum of the mixture of the chloroimidazolium salt **3** and sodium azide showed a peak at  $m/z = 140$ , which corresponds to the calculated mass of  $[2 - Cl]^+$ .
- Typical procedure: [**Caution: Although we have never had any trouble with azidoimidazolium salt 2, it is potentially explosive.**] To a solution of 2-chloro-1,3-dimethylimidazolium chloride (**3**; 1.2 mmol) in acetonitrile (2 mL), sodium azide (1.2 mmol) was added at 0 °C and the mixture was stirred for 30 min. 1,3-Dicarbonyl compound (1.0 mmol) and triethylamine (2.0 mmol) in THF (4 mL) was added to the mixture, which was stirred until the 1,3-dicarbonyl compound was consumed (reaction monitored by TLC). The reaction was quenched with water, and organic materials were extracted three times with CH<sub>2</sub>Cl<sub>2</sub>. The combined extracts were washed with water and brine, and then dried over anhydrous sodium sulfate. The solvent was removed in vacuo to afford the crude compound, which was almost pure. The crude materials were purified by flash column chromatography (silica gel; hexane–ethyl acetate) to give pure 2-diazo-1,3-dicarbonyl compound.
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