

# Communications

## Catalytic Oxidation of Benzophenone Hydrazone with Alumina-supported KMnO<sub>4</sub> under Oxygen Atmosphere

Kang-Hyeok Lee and Kwang-Youn Ko\*

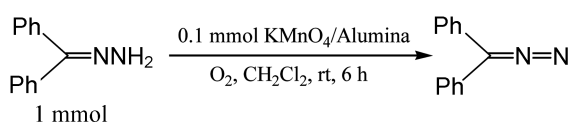
Department of Chemistry, Ajou University, Suwon 443-749, Korea. \*E-mail: kyko@ajou.ac.kr  
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Diphenyldiazomethane (Ph<sub>2</sub>CN<sub>2</sub>) is widely used for the protection of carboxylic acids by conversion to their diphenylmethyl (dpm) esters<sup>1</sup> since dpm group can be easily deprotected by mild acidic condition<sup>2a</sup> or hydrogenolysis,<sup>2b</sup> especially in the field of b-lactams and peptides.<sup>3</sup> Diphenyldiazomethane has been prepared by the oxidation of benzophenone hydrazone with reagents such as active manganese dioxide,<sup>4a</sup> mercuric oxide,<sup>4b</sup> peracetic acid,<sup>4c</sup> iodosobenzene diacetate<sup>4d</sup> or OXONE<sup>®</sup>.<sup>4e</sup> However, some methods suffer from a disadvantage such as toxic nature of reagent,<sup>4b</sup> strong oxidative conditions<sup>4c</sup> or incompatibility with certain functional groups.<sup>4c,e</sup> For example, OXONE<sup>®</sup> may not be employed for the *in situ* protection of carboxylic acid containing sulfide group due to the possibility of the concomitant oxidation of sulfide group.<sup>5</sup>

We reported that Magtrieve<sup>™</sup>, a magnetically retrievable oxidant (CrO<sub>2</sub>) can serve as an efficient reagent for the oxidation of benzophenone hydrazone to diphenyldiazomethane.<sup>6</sup> However, we have found that one shortcoming of this method lies in a fact that a large amount of this oxidant is required, rendering a large scale reaction cumbersome.

Recently, potassium permanganate (KMnO<sub>4</sub>) supported on solid supports such as alumina,<sup>7a</sup> copper sulfate,<sup>7b</sup> zeolite,<sup>7c</sup> silica gel<sup>7d</sup> or clay<sup>7e</sup> has been used for the oxidation of various substrates. For example, oxidation of 2-imidazolines,<sup>7a</sup> thiols,<sup>7b</sup> enamines,<sup>7c</sup> alcohols<sup>7d</sup> and alkylarenes<sup>7e</sup> has been performed using KMnO<sub>4</sub> supported on solid supports. Similarly, zinc dichromate adsorbed on alumina was used for the oxidation of alcohols.<sup>8</sup> However, KMnO<sub>4</sub> has not yet been used for the oxidation of hydrazones. We envisioned that solid-supported KMnO<sub>4</sub>, a cheap and environment-friendly oxidant might be used for the oxidation of benzophenone hydrazone. Herein we wish to report that alumina-supported KMnO<sub>4</sub> in oxygen atmosphere can be used for the catalytic oxidation of benzophenone hydrazone to diphenyldiazomethane in high yields.



We investigated the oxidation of benzophenone hydrazone

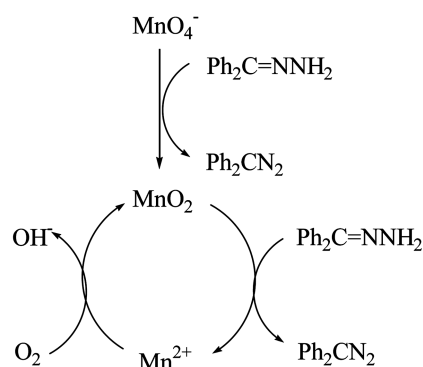
under a variety of conditions, as shown in Table 1.

Treatment of the hydrazone (1 mmol) with KMnO<sub>4</sub>(1 mmol)/alumina in CH<sub>2</sub>Cl<sub>2</sub> resulted in the formation of diphenyldiazomethane and dark brown solid (MnO<sub>2</sub>) within 1 h.<sup>9</sup> Silica gel was less efficient than alumina as supports (entry 1 vs. entry 2). When the amount of KMnO<sub>4</sub> was reduced to 0.1 mmol per 1 mmol of hydrazone, the reaction was not complete within 2 days under N<sub>2</sub> atmosphere, as expected. Remarkably, this conversion could be completed within 6 h and 40 h under 1 atm of O<sub>2</sub> atmosphere and air, respectively. The presence of large amount of water or the use of inactivated alumina did not affect the reactivity of alumina-supported KMnO<sub>4</sub> (entries 6, 7). As reported before,<sup>4a</sup> the use of excess amount (12 molar equivalent) of active MnO<sub>2</sub> shortened the reaction time to 10 min (entry 8).<sup>10</sup> When 1.2 mmol of MnO<sub>2</sub> was used per 1 mmol of substrate, the reaction was not completed within 3 days under N<sub>2</sub> atmosphere. However, the same reaction could be

**Table 1.** Oxidation of Benzophenone Hydrazone with Solid-Supported KMnO<sub>4</sub><sup>a</sup>

Entry	Oxidant <sup>b</sup>	Supports <sup>c</sup>	Atmosphere	Time
1	KMnO <sub>4</sub> (1 mmol)	Alumina	N <sub>2</sub>	1 h
2	KMnO <sub>4</sub> (1 mmol)	Silica gel	N <sub>2</sub>	3 h
3	KMnO <sub>4</sub> (0.1 mmol)	Alumina	N <sub>2</sub>	d
4	KMnO <sub>4</sub> (0.1 mmol)	Alumina	Air	40 h
5	KMnO <sub>4</sub> (0.1 mmol)	Alumina	O <sub>2</sub>	6 h
6	KMnO <sub>4</sub> (0.1 mmol)/ H <sub>2</sub> O (10 mmol)	Alumina	O <sub>2</sub>	6 h
7	KMnO <sub>4</sub> (0.1 mmol)	Alumina <sup>e</sup>	O <sub>2</sub>	6 h
8	MnO <sub>2</sub> (12 mmol)	none	N <sub>2</sub>	10 min
9	MnO <sub>2</sub> (1.2 mmol)	none	N <sub>2</sub>	f
10	MnO <sub>2</sub> (1.2 mmol)	none	O <sub>2</sub>	5 h

<sup>a</sup>Solvent: CH<sub>2</sub>Cl<sub>2</sub>. <sup>b</sup>The amount of KMnO<sub>4</sub> used per 1 mmol of hydrazone. <sup>c</sup>Dried at 300 °C for 30 min before use. Al<sub>2</sub>O<sub>3</sub>: Aldrich, activated, neutral, Brockmann I, 150 mesh, surface area 155 m<sup>2</sup>/g. Silica gel: Merck, 70-230 mesh. <sup>d</sup>Incomplete within 2 days. <sup>e</sup>Not dried. <sup>f</sup>Incomplete within 3 days



Scheme 1

**Table 2.** Preparation of Diphenylmethyl Esters from Acids<sup>a</sup>

RCO <sub>2</sub> H		Ph <sub>2</sub> C=NNH <sub>2</sub> , cat. KMnO <sub>4</sub> /Alumina		RCO <sub>2</sub> CHPh <sub>2</sub>	
		O <sub>2</sub> , CH <sub>2</sub> Cl <sub>2</sub> , rt			
Entry	Acids	Time (h)	Yield (%) <sup>b</sup>	mp (°C)	mp (°C) (lit.)
1a	C <sub>6</sub> H <sub>5</sub> CO <sub>2</sub> H	1	92	87-88	87.5-88 <sup>12</sup>
1b <sup>c</sup>	C <sub>6</sub> H <sub>5</sub> CO <sub>2</sub> H	1	78		
2	C <sub>6</sub> H <sub>5</sub> CH(OH)CO <sub>2</sub> H	0.2	90	90-91	88.5-89 <sup>6</sup>
3	C <sub>6</sub> H <sub>5</sub> CH=CHCO <sub>2</sub> H	0.5	94	72-73	72.5 <sup>d</sup>
4	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>5</sub> CO <sub>2</sub> H	3	77	oil	
5	<i>N</i> -Phenylacetyl-7-aminocapthalosporic acid	2	85	144-145	144.5-145 <sup>6</sup>

<sup>a</sup>All the esters were identified by spectroscopic methods. <sup>b</sup>Yield refers to the pure isolated product. <sup>c</sup>One-pot reaction. <sup>d</sup>Beilstein E III 9,2695.

completed within 5 h under O<sub>2</sub> atmosphere (entry 9 vs. entry 10). With these results on hand, the catalytic nature of KMnO<sub>4</sub> oxidation can be postulated by Scheme 1. First, permanganate ion is reduced into MnO<sub>2</sub> during the hydrazone oxidation. Solid MnO<sub>2</sub> thus generated participates in another oxidation process, while being reduced into Mn<sup>2+</sup> oxidation state. Mn<sup>2+</sup> ion is reoxidized by O<sub>2</sub> in basic media to MnO<sub>2</sub>,<sup>11</sup> thus completing the catalytic cycle. It is remarkable that only catalytic amount of oxidant is required in the present oxidation even though the reaction occurs in a heterogeneous phase.

Diphenyldiazomethane prepared according to entry 5 in Table 1 was employed for the protection of carboxylic acids, as shown in Table 2.<sup>12</sup> Functional groups such as hydroxyl group (entry 2), C-C double bond (entry 3) and sulfide (entry 5) were intact during this oxidation. It should be noted that one-pot reaction is also feasible, even though a slightly lower yield of product is obtained probably due to the basic nature of reaction medium (entry 1b).

In conclusion, KMnO<sub>4</sub>/alumina reagent, which is cheap and environmentally safe, can serve as a catalytic oxidant

under O<sub>2</sub> atmosphere for the oxidation of benzophenone hydrazone. To the best of our knowledge, the present works are the first example where KMnO<sub>4</sub>/alumina reagent acts as a catalytic oxidant under O<sub>2</sub> atmosphere.

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- Stoichiometry demands that 0.67 mol of MnO<sub>4</sub><sup>-</sup> is required per 1 mol of substrate, assuming the change of the oxidation state of +7 to +4 in a homogeneous reaction.
- Active MnO<sub>2</sub> was prepared according to the Attenburrow protocol. See, *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Editor-in-Chief; John Wiley and Sons: Chichester, 1995; Vol. 5, p 3230.
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- As a typical procedure, a solution of benzophenone hydrazone (200 mg, 1 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) was treated with KMnO<sub>4</sub>/alumina reagent (116 mg, 0.1 mmol of KMnO<sub>4</sub>, 1 mmol KMnO<sub>4</sub>/g alumina) and the mixture was stirred at rt under O<sub>2</sub> atmosphere. After 24 h, the reaction was found to be complete. Then, the reaction mixture was filtered through Celite to give a purple solution of Ph<sub>2</sub>CN<sub>2</sub>, which was then treated with a solution of benzoic acid (135 mg, 1.1 mmol) in dichloromethane (2 mL) until the reaction was complete. Concentration of the reaction mixture followed by column chromatography gave diphenylmethyl benzoate in 92% yield, mp 87-88 °C (Lit.<sup>13</sup> mp 87.5-88 °C).
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