

Communications

Catalytic Oxidation of Benzophenone Hydrazone with Alumina-supported KMnO₄ under Oxygen Atmosphere

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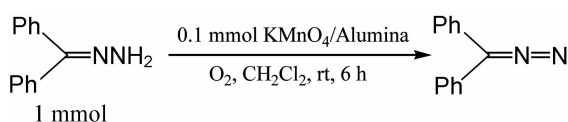
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Diphenyldiazomethane (Ph₂CN₂) is widely used for the protection of carboxylic acids by conversion to their diphenylmethyl (dpm) esters¹ since dpm group can be easily deprotected by mild acidic condition^{2a} or hydrogenolysis,^{2b} especially in the field of β -lactams and peptides.³ Diphenyldiazomethane has been prepared by the oxidation of benzophenone hydrazone with reagents such as active manganese dioxide,^{4a} mercuric oxide,^{4b} peracetic acid,^{4c} iodosobenzene diacetate^{4d} or OXONE[®].^{4e} However, some methods suffer from a disadvantage such as toxic nature of reagent,^{4b} strong oxidative conditions^{4c} or incompatibility with certain functional groups.^{4e} For example, OXONE[®] 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.⁵

We reported that Magtrieve[™], a magnetically retrievable oxidant (CrO₂) can serve as an efficient reagent for the oxidation of benzophenone hydrazone to diphenyldiazomethane.⁶ 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 (KMnO₄) supported on solid supports such as alumina,^{7a} copper sulfate,^{7b} zeolite,^{7c} silica gel^{7d} or clay^{7e} has been used for the oxidation of various substrates. For example, oxidation of 2-imidazolines,^{7a} thiols,^{7b} enamines,^{7c} alcohols^{7d} and alkylarenes^{7e} has been performed using KMnO₄ supported on solid supports. Similarly, zinc dichromate adsorbed on alumina was used for the oxidation of alcohols.⁸ However, KMnO₄ has not yet been used for the oxidation of hydrazones. We envisioned that solid-supported KMnO₄, a cheap and environment-friendly oxidant might be used for the oxidation of benzophenone hydrazone. Herein we wish to report that alumina-supported KMnO₄ 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

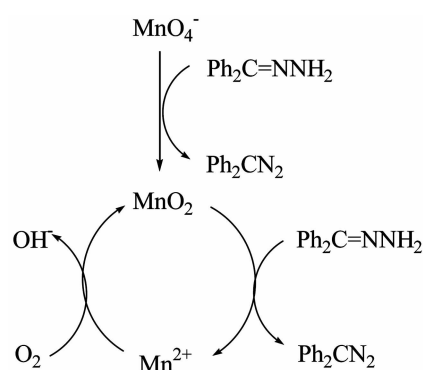
under a variety of conditions, as shown in Table 1.

Treatment of the hydrazone (1 mmol) with KMnO₄(1 mmol)/alumina in CH₂Cl₂ resulted in the formation of diphenyldiazomethane and dark brown solid (MnO₂) within 1 h.⁹ Silica gel was less efficient than alumina as supports (entry 1 vs. entry 2). When the amount of KMnO₄ was reduced to 0.1 mmol per 1 mmol of hydrazone, the reaction was not complete within 2 days under N₂ atmosphere, as expected. Remarkably, this conversion could be completed within 6 h and 40 h under 1 atm of O₂ 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 KMnO₄ (entries 6, 7). As reported before,^{9a} the use of excess amount (12 molar equivalent) of active MnO₂ shortened the reaction time to 10 min (entry 8).¹⁰ When 1.2 mmol of MnO₂ was used per 1 mmol of substrate, the reaction was not completed within 3 days under N₂ atmosphere. However, the same reaction could be

Table 1. Oxidation of Benzophenone Hydrazone with Solid-Supported KMnO₄^a

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

^aSolvent: CH₂Cl₂. ^bThe amount of KMnO₄ used per 1 mmol of hydrazone. ^cDried at 300 °C for 30 min before use. Al₂O₃: Aldrich, activated, neutral, Brockmann I, 150 mesh, surface area 155 m²/g. Silica gel: Merck, 70-230 mesh. ^dIncomplete within 2 days. ^eNot dried. ^fIncomplete within 3 days

**Table 2.** Preparation of Diphenylmethyl Esters from Acids^a

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

^aAll the esters were identified by spectroscopic methods. ^bYield refers to the pure isolated product. ^cOne-pot reaction. ^d*Beilstein* E III 9,2695.

completed within 5 h under O₂ atmosphere (entry 9 vs. entry 10). With these results on hand, the catalytic nature of KMnO₄ oxidation can be postulated by Scheme 1. First, permanganate ion is reduced into MnO₂ during the hydrazone oxidation. Solid MnO₂ thus generated participates in another oxidation process, while being reduced into Mn²⁺ oxidation state. Mn²⁺ ion is reoxidized by O₂ in basic media to MnO₂,¹¹ 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 2.¹² 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, KMnO₄/alumina reagent, which is cheap and environmentally safe, can serve as a catalytic oxidant

under O₂ atmosphere for the oxidation of benzophenone hydrazone. To the best of our knowledge, the present works are the first example where KMnO₄/alumina reagent acts as a catalytic oxidant under O₂ atmosphere.

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- Stoichiometry demands that 0.67 mol of MnO₄⁻ is required per 1 mol of substrate, assuming the change of the oxidation state of +7 to +4 in a homogeneous reaction.
- Active MnO₂ 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.
- Mn²⁺ ion in basic media is very easily oxidized even by air to MnO₂. See, Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*; John Wiley & Sons: New York, 1980; p 738.
- As a typical procedure, a solution of benzophenone hydrazone (200 mg, 1 mmol) in CH₂Cl₂ (10 mL) was treated with KMnO₄/alumina reagent (116 mg, 0.1 mmol of KMnO₄, 1 mmol KMnO₄/g alumina) and the mixture was stirred at rt under O₂ 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 Ph₂CN₂, 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.¹³ mp 87.5-88 °C).
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