

Generation of Diphenyldiazomethane by Oxidation of Benzophenone Hydrazone with Magtrieve™

Kwang-Youn Ko* and Ji-Yeon Kim

Department of Chemistry, Ajou University, Suwon 442-749, Korea

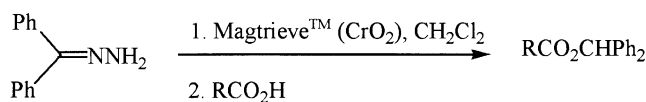
Received April 10, 1999

Diphenyldiazomethane, a red crystalline solid is a useful reagent for the protection of carboxylic acids by conversion to their diphenylmethyl (dpm, benzhydryl) esters.¹ Dpm protecting group has been widely used due to its easy deprotection 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 mercuric oxide,^{4a} peracetic acid,^{4b} iodosobenzene diacetate^{4c} or OXONE®.^{4d} However, some methods suffer from a disadvantage such as toxic nature of reagent,^{4a} strong oxidative conditions^{4b} or incompatibility with certain functional groups.^{4b,d} 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

Recently, Magtrieve™, a magnetically retrievable oxidant (CrO₂) has been shown to oxidize alcohols in high yields.⁶ We have already shown that this reagent can serve as an oxidant for the aromatization of 1,4-dihydropyridines in high yields.⁷ We now report that Magtrieve™ can also serve as an efficient reagent for the oxidation of benzophenone hydrazone to diphenyldiazomethane, enabling the one-pot protection of carboxylic acids including *N*-protected amino acids, as shown in Table 1.

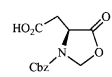
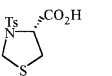
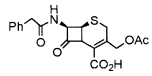
Treatment of benzophenone hydrazone with Magtrieve™

in dichloromethane gave a purple color characteristic of diphenyldiazomethane, immediately. The oxidation was completed within 15 min at room temperature, based on TLC analysis (R_f of hydrazone = 0.33, R_f of product = 0.60 in EtOAc : hexanes (1 : 5)). Then, a solution of acid was added to the purple solution and the progress of the reaction was monitored with TLC. The reaction time was in a range of 0.1 h ~ 5 h, depending on the substrate. After the reaction was finished, Magtrieve™ was retrieved with magnet⁶ and the solution was concentrated to give a crude product, which was purified by column chromatography. The yield was good, except for the entry 6, where the dpm ester was decomposed during the column chromatography.



As a typical procedure, a solution of benzophenone hydrazone (206 mg, 1.05 mmol) in dichloromethane (15 mL) was treated with Magtrieve™ (1.51 g) and the mixture was stirred at room temperature. After 15 min, the oxidation was found to be completed. A solution of benzoic acid (122 mg, 1.00 mmol) in dichloromethane (2 mL) was added to the resulting purple solution and the whole mixture was stirred for 1.5 h. After the reaction was finished, Magtrieve™ was

Table 1. Preparation of Diphenylmethyl Esters from Acids^a

Entries	Acids	Time (h)	Yield (%) ^b	mp (°C)	Lit. mp (°C) or EI-MS (m/e) ^c
1	C ₆ H ₅ CO ₂ H	1.5	80	87-88	87.5-88 ⁸
2	C ₆ H ₅ CH ₂ CO ₂ H	2	83	oil	91 (25), 118 (5), 167 (100), 165 (44), 184 (6)
3	C ₆ H ₅ CH(OH)CO ₂ H	0.1	71	88.5-89	107 (38), 152 (8), 167 (100), 317 (M ⁺ , 0.1)
4	C ₆ H ₅ CH=CHCO ₂ H	2	72	73	72.5 ^d
5	CH ₃ (CH ₂) ₅ CO ₂ H	3	70	oil	152 (19), 167 (100), 184 (41), 296 (M ⁺ , 10)
6	BOC-L-leucine	0.25	54 ^e	93-94	57 (70), 86 (74), 130 (66), 167 (100), 186 (19)
7	CbzNHCH ₂ CO ₂ H	5	71	oil	91 (69), 167 (100), 242 (43), 286 (12)
8		0.1	70	129-129.5	91 (41), 167 (47), 183 (100), 445 (M ⁺ , 1)
9		0.1	67	oil	91 (33), 155 (49), 167 (100), 242 (64), 286 (21), 453 (M ⁺ , 0.3)
10		4	79	144.5-145	140-143 ^f , 91 (21), 167 (100), 382 (8), 556 (M ⁺ , 0.5)

^aAll reactions were conducted at room temperature in dichloromethane, except for the entries 7 and 10 where EtOAc was employed, using 1 mmol of acid, 1.05 mmol of benzophenone hydrazone and 1.51 g of Magtrieve™. ^bYield refers to the pure isolated product. ^cRelative intensity is given in the parenthesis. ^dBeilstein E III 9, 2695. ^eThe product was decomposed during column chromatography, resulting in a lower yield. ^fKametani, T.; Sekine, H.; Honda, T. *Heterocycles*, **1983**, *20*, 1577.

retrieved and the solution was concentrated to give a crude product (275 mg), which was purified by column chromatography (hexanes : EtOAc = 5 : 1) to give diphenylmethyl benzoate in 80% yield, mp 87-88 °C (Lit.⁸ mp 87.5-88 °C).

In summary, MagtrieveTM can serve as a new oxidant for the generation of diphenyldiazomethane from benzophenone hydrazone, offering a mild and nontoxic reaction condition as well as an easy workup. Since MagtrieveTM does not oxidize sulfide group, the present method can be applied to the protection of sulfur-containing acids (entries 9 and 10).

Acknowledgment. The authors wish to acknowledge the financial support of the Korea Research Foundation made in the program year of 1998 (BSRI-1998-015-D00186).

References

1. (a) Green, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; John Wiley and Son: New York, 1991; pp 253-254. (b) Kocienski, P. J. *Protecting Groups*; Thieme: Stuttgart, 1994; pp 136-139.
 2. (a) Silverman, R. B.; Holladay, M. W. *J. Am. Chem. Soc.* **1981**, *103*, 7357. (b) De Bernardo, S.; Teng, J. P.; Sasso, G. J.; Weigle, M. *J. Org. Chem.* **1985**, *50*, 3457.
 3. Yamanaka, H.; Chiba, T.; Kawabata, K.; Takasugi, H.; Masugi, T.; Takaya, T. *J. Antibiot.* **1985**, *38*, 1738.
 4. (a) Smith, L. I.; Howard, K. L. In *Organic Syntheses Collective Volume 3*; Horning, E. C., Editor-in-Chief; John Wiley and Sons: New York, 1955; pp 351-352. (b) Adamson, J. R.; Bywood, R.; Eastlick, D. T.; Gallagher, G.; Walker, D.; Wilson, E. M. *J. Chem. Soc., Perkin Trans. 1* **1975**, 2003. (c) Lapatsanis, L.; Miliatis, G.; Paraskewas, S. *Synthesis* **1985**, 513. (d) Curini, M.; Rosati, O.; Pisani, E. *Tetrahedron Lett.* **1997**, *38*, 1239.
 5. *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Editor-in-Chief; John Wiley and Sons: Chichester, 1995; Vol. 6, p 4268.
 6. Lee, R. A.; Donald, D. S. *Tetrahedron Lett.* **1997**, *38*, 3857.
 7. Ko, K-Y.; Kim, J-Y. *Tetrahedron Lett.* **1999**, *40*, 3207.
 8. Hiskey, R. G.; Adams, J. B. Jr. *J. Am. Chem. Soc.* **1965**, *87*, 3969.
-