

A New Application of Hexamethylenetetramine-bromine Supported onto Wet Alumina as an Efficient Reagent for Cleavage of Phenylhydrazones under Classical Heating and Microwave Irradiation

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2,4-Dinitrophenylhydrazones were converted to their parent carbonyl compounds using hexamethylenetetramine-bromine complex supported onto wet alumina under classical heating and microwave irradiation.

Keywords: 2,4-Dinitrophenylhydrazones; Hexamethylenetetramine-bromine; Microwave irradiation; Solventless system; Carbonyl compounds; Wet alumina.

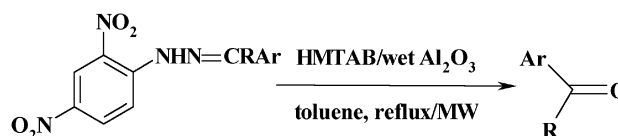
Protection and subsequent deprotection of a functional group is almost inevitable in multistage organic synthesis.¹ Phenylhydrazones are frequently used to protect carbonyl compounds. They also serve as important synthetic intermediates and can be used for isolation, purification and characterization of aldehydes and ketones.² Because of these significances a plethora of reagents and methods such as ammonium persulfate-clay,³ Zr(t-BuO)₄ as catalyst and *tert.*-butylhydroperoxides as oxidant,⁴ benzyl-triphenylphosphonium peroxydisulfate,⁵ prolinium chlorochromate,⁶ potassium ferrate under microwave irradiation in solventless systems,⁷ hypervalent organoiodine,⁸ copper(II),⁹ BTSC¹⁰ and ammonium chlorochromate¹¹ under microwave irradiation in solventless systems have been reported.

The microwave (MW) enhanced chemical reactions in general¹² and on inorganic solid supports¹³ in particular have become popular as they can be conducted rapidly and due to the altered reactivity, non-aqueous conditions and convenient isolation they provide.

We have recently reported the oxidation of alcohols,¹⁴ deoxygenation,¹⁵ desemicarbonization¹⁶ and oxidative deprotection of silyl ethers¹⁷ and THP ethers¹⁸ using hexamethylenetetramine-bromine. We have also very recently used this reagent for selective bromination of aromatic compounds.¹⁹ Herein we report our results for the mild,

facile, fast and high yielding cleavage of phenylhydrazones under classical heating and under microwave irradiation in a solventless system (Scheme I).

Scheme I



Initially, Hexamethylenetetramine-bromine, HMTAB, was mixed with wet alumina. This supported reagent was refluxed with an appropriate 2,4-dinitrophenylhydrazone in toluene to regenerate the corresponding carbonyl compound. Our results are shown in Table 1.

To avoid the use of a large excess of organic solvent as the reaction medium, and in view of the emerging importance of green chemistry and our general interest in microwave-assisted chemical processes in solvent-free conditions,¹³ we envisioned expediting the reaction of 2,4-dinitrophenylhydrazones by using microwave irradiation under solvent-free conditions, obtaining the corresponding carbonyl compounds in high yields (Table 2). The supported reagent was mixed with neat 2,4-dinitrophenylhydrazones, grinding them thoroughly to make an intimate

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Table 1. Cleavage of arylhydrazones using HMTAB in refluxing toluene

| Entry | Ar | R | Time (min) | Product | Yield (%) ^a |
|-------|----|-----------------|------------|---------|------------------------|
| 1 | | H | 30 | | 82 |
| 2 | | H | 25 | | 90 |
| 3 | | H | 25 | | 79 |
| 4 | | H | 15 | | 92 |
| 5 | | H | 30 | | 87 |
| 6 | | H | 20 | | 80 |
| 7 | | | 25 | | 85 |
| 8 | | | 35 | | 85 |
| 9 | | CH ₃ | 40 | | 93 |
| 10 | | CH ₃ | 15 | | 87 |

^a Yields refer to isolated products.

pair. By placing the mixture in a microwave oven, the reactions are completed in a couple of seconds. We show our results in Table 2. The reactions are relatively clean and no over oxidation to carboxylic acid occurred.

It is noteworthy to mention that without wet alumina, the reactions were very sluggish and more seriously the molten hexamethylenetetramine-bromine adhered to the walls of the vessel making the isolation of mixture intractable. Since the reaction is supposed to be basically a hydrolysis, the presence of water in alumina is essential as an ox-

xygen donor. In fact when we were trying to implement the oxidative cleavage of the 2,4-dinitrophenylhydrazone of 4-methoxy benzaldehyde with hexamethylenetetramine-bromine without wet alumina, we observed that instead of being cleaved, this compound was exclusively brominated and gave 3-bromo-4-methoxy benzaldehydephenylhydrazone.¹⁹

Although the mechanism of this hydrolysis is not completely clear, we suggest formation of a complex due to the interaction of Pi electrons of the carbon-nitrogen bond

Table 2. Cleavage of arylhydrazones using HMTAB supported onto wet alumina under microwave irradiation in a solventless system

| Entry | Ar | R | Time (min) | Product | Yield (%) ^a |
|-------|----|-----------------|------------|---------|------------------------|
| 1 | | H | 2 | | 85 |
| 2 | | H | 1 | | 80 |
| 3 | | H | 2 | | 88 |
| 4 | | H | 3 | | 88 |
| 5 | | H | 1 | | 80 |
| 6 | | H | 3 | | 83 |
| 7 | | | 1 | | 80 |
| 8 | | | 2 | | 78 |
| 9 | | CH ₃ | 2 | | 90 |
| 10 | | CH ₃ | 3 | | 95 |

^a Yields refer to isolated products.

with HMTAB. The formation of a similar complex has been postulated in the oxidation of alcohols,²⁰ aldehydes,²¹ and sulfides²² with HMTAB involving non-bonded pairs of electrons on oxygen or sulfide atoms.

Interestingly, this method does not work with hydrazones of aliphatic aldehydes and ketones. The catalyst can not be recovered and reused. However it can be separated along with 2,4-phenylhydrazine by column chromatography. The catalyst can also be removed by washing with aqueous sodium bicarbonate solution (3%) from the or-

ganic layer.

In conclusion, we have developed a method for regeneration of carbonyl compounds from phenylhydrazones using hexamethylenetetramine-bromine under classical heating and microwave irradiation. This homogenous non-hygroscopic solid is very stable at room temperature and is not affected by ordinary exposure to air or water and has no offensive odor of bromine or amine. No over oxidation to carboxylic acid was observed. Rapid reactions, high yields and the use of an inexpensive and non-corrosive reagent are

attractive features of this protocol.

EXPERIMENTAL

All products were known and identified by comparison of their physical and spectroscopic data with those of authentic samples.

All the reactions were performed in an MB-310 Butane domestic microwave oven.

Regeneration of carbonyl compounds from their 2,4-dinitrophenylhydrazone under classical heating; general procedure

In a 25 mL round bottomed flask equipped with condenser and stirrer 2,4-dinitrophenylhydrazone (1 mmol) was added and dissolved in toluene (15 mL). To this mixture hexamethylenetetramine-bromine (2 mmol) supported onto alumina (0.5 g) was added. The reaction mixture was stirred and refluxed for the indicated time (Table 1). The progress of reaction was monitored by TLC. Upon the completion of the reaction, the solvent was evaporated to dryness under reduced pressure, and the residue was directly subjected to column chromatography to afford the products (Table 1).

Regeneration of carbonyl compounds from 2,4-dinitrophenylhydrazones under microwave irradiation in a solventless system; general procedure

In a 10 mL beaker hexamethylene-tetramine-bromine (2 mmol) was thoroughly mixed with wet alumina (0.5 g) using a spatula. The appropriate 2,4-dinitrophenylhydrazone (1 mmol) was then added to this mixture. The beaker was placed in a household microwave oven for the indicated time (Table 2). The progress of the reaction was monitored by TLC. Upon the completion of the reaction, the mixture was taken to CH_2Cl_2 (3 mL) and filtered. The filtrate was evaporated to dryness under reduced pressure. The residue was passed through a small pad of silica gel using pet ether/ethyl acetate (8/2) to afford the pure product (Table 2).

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REFERENCES

- Green, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; 2nd ed., John Wiley: New York, 1991.
- Sander, S. R.; Karo, W. *Organic Functional Groups Preparation*; 2nd ed., Academic Press London, 1989; Vol. 3.
- Varma, R. S.; Meshram, H. M. *Tetrahedron Lett.* **1997**, *39*, 7973.
- Barton, D. H.; Liu, W. *Molecules* **1998**, *2*, 4.
- Tajbakhsh, M.; Mohammadpour, I.; Ramezani, L. F. *Phosphorus, Sulfur and Silicon*. **2003**, *178*, 2621.
- Shirini, F.; Mamaghani, M.; Parsa, F.; Mohammadpor, I. *Bull. Korean Chem. Soc.* **2002**, *23*, 1683.
- Heravi, M. M.; Tajbakhsh, M.; Habibzadeh, S.; Ghassemzadeh, M. *Phosphorus, Sulfur and Silicon*. **2002**, *177*, 2299.
- Barton, D. H. R.; Jaszlerenigi, J. C. S.; Liu, V.; Shinada, T. *Tetrahedron Lett.* **1996**, *52*, 14673.
- Karchaudhuri, N.; De, A.; Mitra, A. K. *J. Indian. Chem. Soc.* **2004**, *81*, 79.
- Khaleghi, Sh.; Heravi, M. M.; Derikvand, F. *Phosphorus, Sulfur and Silicon*. **2006**, *181*, 227.
- Heravi, M. M.; Sabaghian, A. J.; Bakhtiari, Kh.; Ghassemzadeh, M. *Braz. J. Chem. Soc.* **2006**, *17*, 614.
- (a) Kurz, T.; Widyan, K. *Tetrahedron* **2005**, *61*, 7247. (b) Hayes, B. L. *Aldrichimica*. **2004**, *37*, 66.
- (a) Heravi, M. M.; Ajami, D.; Aghapoor, K.; Ghassemzadeh, M. *Chem. Commun.* **1999**, 833. (b) Heravi, M. M.; Ajami, D.; Ghassemzadeh, M. *Synthesis*. **1999**, 339. (c) Padmanabham, S.; Caughlin, J. E.; Lyer, R. P. *Tetrahedron Lett.* **2005**, *46*, 343.
- Heravi, M. M.; Ajami, D.; Nooshabadi, M. A. *Iran. J. Chem. Eng.* **1999**, *18*, 88.
- Beheshtiha, Y. Sh.; Heravi, M. M.; Sarmad, N.; Hekmatshoar, R. *J. Chem. Res.* **2001**, 79.
- Nooshabadi, M. A.; Aghapoor, K.; Tajbakhsh, M.; Heravi, M. M. *J. Sci. I. R. Iran.* **2001**, *12*, 1.
- Dehkordi, M. B.; Heravi, M. M.; Khosrofar, P.; Ziafati, A.; Ghassemzadeh, M. *Phosphorus, Sulfur and Silicon*. **2004**, *179*, 2595.
- Dehkordi, M. B.; Heravi, M. M.; Khosrofar, P.; Ziafati, A.; Ghassemzadeh, M. *Phosphorus, Sulfur and Silicon*. **2004**, *179*, 1493.
- Heravi, M. M.; Abdolhosseini, N.; Oskooie, H. A. *Tetrahedron Lett.* **2005**, *46*, 8959.
- (a) Pareek, A.; Kathari, S.; Banerji, K. K. *Indian. J. Chem.* **1996**, *35B*, 970. (b) Gangnani, H.; Sharma, P. K. *J. Chem. Res(s)*. **1999**, *1*, 845.
- Pareek, A.; Varsheny, S.; Banerji, K. K. *React. Kinet. Catal. Lett.* **1997**, *60*, 127.
- Chaudhary, K.; Suri, D.; Kathari, S.; Banerji, K. K. *J. Phys. Org. Chem.* **2000**, *13*, 283.