Oxidative Deamination of α-Aminophosphonates and Amines by Zinc Dichromate Trihydrate ($ZnCr_2O_7·3H_2O$) under Solvent-Free Conditions at Room Temperature

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Abstract: A novel method for the rapid and efficient conversion of a variety of α-aminophosphonates to α-ketophosphonates using $ZnCr_2O_7·3H_2O$ via oxidative deamination under solvent-free conditions at room temperature is described. This method is also applicable to the rapid and highly selective oxidation of various types of ordinary amines (primary and secondary) to aldehydes and ketones in good to high yields.

Key words: oxidative deamination, α-ketophosphonates, α-hydroxyphosphonates, amines, aldehydes

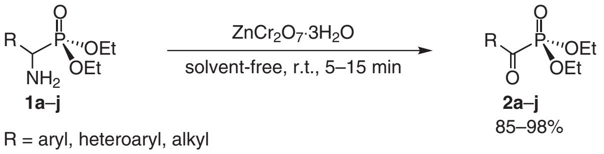
α-Ketophosphonates are an important subdivision of organophosphorus compounds. The adjacent carbonyl and phosphoryl functional groups make α-ketophosphonates interesting compounds as potential precursors in organic synthesis.[1] For instance, it is possible to derive hydrazones,[2] imines,[3] α,α-difluorophosphonates[4] and oximes[5] from the carbonyl function; to reduce α-ketophosphonates to the corresponding α-hydroxyphosphonates,[6] or use them in Wittig, Baeyer–Villiger, or Schmidt reactions.[1a,7] The C(O)–P bonds in these compounds are known to be sensitive towards hydrolysis and acidic conditions.[8] Therefore, handling of α-ketophosphonates is not trivial and requires special precautions.[8] The Michael–Arbuzov reaction is a general method for the preparation of α-ketophosphonates from acyl chlorides and trialkylphosphites.[9] This is a useful method; however, it is restricted insofar as only commercially or synthetically available acid chlorides can be used. Oxidation methods are alternative procedures for the preparation of α-ketophosphonates. These methods are limited to the oxidation of α-hydroxyphosphonates.[4,10] α-Aminophosphonates, which are easily prepared from commercially available materials,[11] are also useful precursors for the preparation of α-ketophosphonates. A literature survey indicates that, in contrast to the existing methods for the oxidation of α-hydroxyphosphonates, few methods are known for the efficient oxidation of α-aminophosphonates. Potassium permanganate has been reported for the oxidation of α-aminophosphonates, but in this case, α-nitrophosphonates were produced as the sole products.[12]

In view of environmental and economical demands, simplicity in processes and low costs, solvent-free reactions have recently been receiving much interest in organic synthesis.[10h,13] Solvent-free reactions are carried out by stirring or simple grinding of the reaction mixture in a mortar with a pestle.[10i,14]

In recent years, we have focused our attention on the development of methods for the synthesis of phosphonate derivatives.[10f–i,11b,c,15] In this context we have observed that zinc dichromate trihydrate ($ZnCr_2O_7·3H_2O$) may be used as an efficient oxidizing reagent for the synthesis of α-ketophosphonates from α-hydroxyphosphonates under solvent-free conditions.[10i] These observations prompted us to examine the efficiency of $ZnCr_2O_7·3H_2O$ for the oxidation of primary α-aminophosphonates to α-ketophosphonates.

At first we examined the feasibility of the oxidation reaction of α-amino(phenyl)methylphosphonate (**1a**) as a model in the presence of $ZnCr_2O_7·3H_2O$ under solvent-free conditions at room temperature. The results showed that **1a** underwent a fast oxidative deamination and produced α-benzoylphosphonate (**2a**) as the sole product in 95% yield. We next investigated the applicability of this method for the oxidation of various types of α-aminophosphonates to α-ketophosphonates (Scheme 1). The results of these studies are summarized in Table 1.

As depicted in Table 1, this method worked well for the oxidative deamination of α-amino-(phenyl)methylphosphonates bearing both electron-releasing and electron-withdrawing groups on the phenyl group (**1b–f**) and produced the corresponding α-ketophosphonates (**2b–f**) in 85–98% yields. The oxidation of α-amino-2-naphthyl- and 2-thienylphosphonate (**1g** and **1h**) as examples of polyaromatic and heteroaryl phosphonate derivatives proceeded well to afford the desired products **2g** and **2h** in 98% and 85% yields, respectively. α-Aminoalkylphosphonates **1i** and **1j** were also oxidized selectively to the corresponding α-ketophosphonates under these reaction conditions.



Scheme 1

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Table 1 Oxidation of α-Aminophosphonates to α-Ketophosphonates by $ZnCr_2O_7 \cdot 3H_2O$ under Solvent-Free Conditions at Room Temperature

Product **2**	R	Time (min)	Yield (%)[a]
2a	Ph	5	95
2b	3-ClC_6H_4	5	90
2c	4-BrC_6H_4	5	98
2d	4-ClC_6H_4	5	95
2e	4-$MeOC_6H_4$	10	95
2f	4-MeC_6H_4	10	85
2g	2-naphthyl	15	98
2h	2-thienyl	10	85
2i	*n*-hexyl	5	85
2j	*i*-Pr	10	85

[a] Yields refer to those of pure isolated products characterized by comparison of their spectroscopic data with those of authentic samples.[10,16] Conditions: $ZnCr_2O_7 \cdot 3H_2O$ (1 equiv).

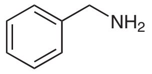
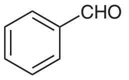
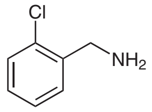
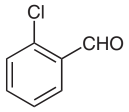
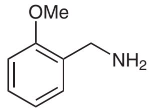
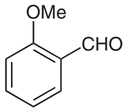
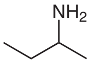
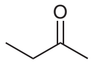
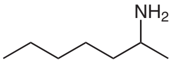
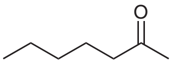
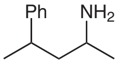
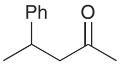
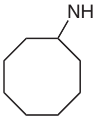
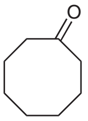
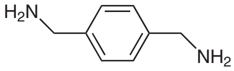
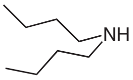
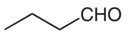
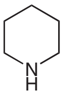
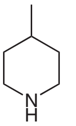
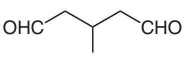
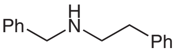
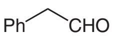
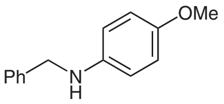
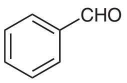
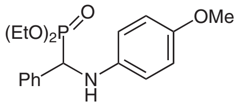
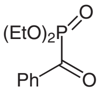
Workup of the reaction mixture was easy and, by a simple vacuum distillation, pure products were isolated. Furthermore, cleavage of the C(O)–P bond was not observed in any of these reactions and α-ketophosphonates were the only products obtained from these reactions.

The oxidation of amines as a significant class of available building blocks and fundamental synthetic intermediates has received much attention from organic chemists. Oxidation of amines can lead to functional groups including imines, amides, nitro, oximes, nitriles, aldehydes, and ketones.[17] Within these transformations, selective conversion of amines to carbonyl compounds is a relatively common biological process and has received much attention from organic chemists in recent years.[17e–17j]

In order to obtain a fuller understanding of the reactivity profile of this reagent, we investigated the oxidation of a variety of ordinary amines utilizing $ZnCr_2O_7 \cdot 3H_2O$ under the same reaction conditions. The results of these studies are listed in Table 2.

As shown in Table 2, substituted benzylamines with electron-donating and electron-withdrawing groups were selectively oxidized to their corresponding aldehydes in high yields (entries 1–3). Aliphatic amines were also cleanly converted to the corresponding aldehydes and ketones in excellent yields (entries 4–7). The procedure was also suitable for the oxidation of 1,4-bis(aminomethyl)benzene as an example of a difunctional amine and produced terephthaldehyde in high yield (entry 8). In addition to primary amines, some secondary amines were also screened to examine their oxidation by $ZnCr_2O_7 \cdot 3H_2O$ under the above reaction conditions. The results showed that the oxidation reaction of dialkylamines and benzyl alkylamines worked well, and the expected products were obtained in 90–94% yields (entries 9–12). Oxidation of

Table 2 Oxidative Deamination of Amines in the Presence of $ZnCr_2O_7 \cdot 3H_2O$ under Solvent-Free Conditions at Room Temperature

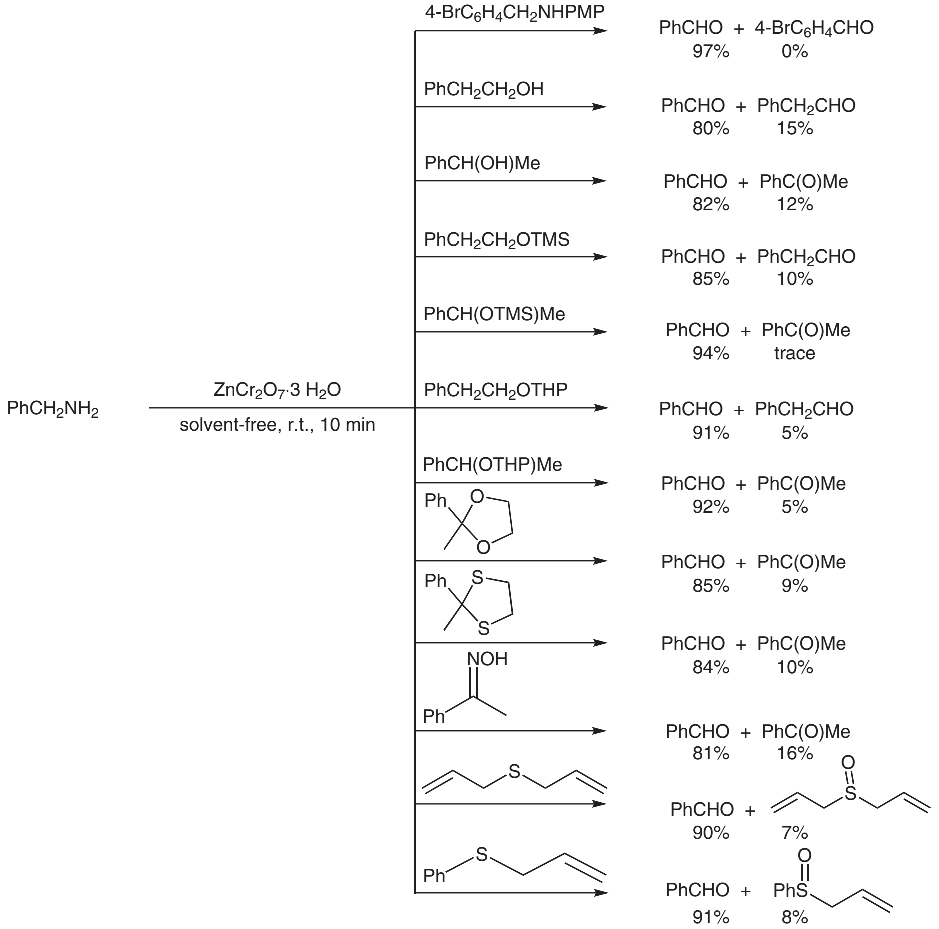
Entry	Amine	Product	Yield (%)[a]
1			98[b]
2			90
3			92
4			97
5			97
6			90
7			98
8			91[c]
9			92
10			90
11			94
12		PhCHO 	90 92
13			90[d]
14			95[c]

[a] Yields refer to those of pure isolated products characterized by comparison of their spectroscopic data with those of authentic samples. Reaction occurred instantaneously. Conditions: $ZnCr_2O_7 \cdot 3H_2O$ (1 equiv, except for entries 1, 8, 13, and 14).

[b] Conditions: $ZnCr_2O_7 \cdot 3H_2O$ (0.5 equiv).

[c] Conditions: $ZnCr_2O_7 \cdot 3H_2O$ (4 equiv).

[d] Conditions: $ZnCr_2O_7 \cdot 3H_2O$ (2 equiv).



Scheme 2

amines protected with a *p*-methoxyphenyl group produced the corresponding carbonyl compounds in high yields (entries 13 and 14). The protecting group was released as benzoquinone in these reactions. No byproduct was formed in any of these transformations, and the amines were cleanly and selectively oxidized to aldehydes and ketones.

To determine the selectivity of this method further, the oxidation of benzylamine in the presence of different functional groups was studied (Scheme 2). As indicated in Scheme 2, the reactions proceeded with high chemoselectivity in favor of amine oxidation, and benzylamine was transformed to benzaldehyde in good to high yields.

It is noteworthy that $ZnCr_2O_7·3H_2O$ has been used as an efficient reagent for the fast oxidation of alcohols, sulfides, ethers, acetals, dithioacetals, oximes, silyl, and pyranyl ethers in recent years.[18]

In conclusion, we have found that $ZnCr_2O_7·3H_2O$ can be used as a new and efficient reagent for the facile preparation of a variety of α-ketophosphonates from α-aminophosphonates as viable substrates. This method is also applicable to the oxidative deamination of various types of primary and secondary amines under solvent-free conditions at room temperature. Short reaction times, high chemoselectivity, good to high yields, lack of byproduct formation, simple workup, and excellent selectivity for the formation of carbonyl compounds make this method an attractive and useful contribution to the present methodologies.

General Procedure for the Preparation of α-Ketophosphonates 2a–j by the Oxidation of α-Aminophosphonates 1a–j

A mixture of α-aminophosphonate (**1**, 5 mmol) and $ZnCr_2O_7·3H_2O$ (5 mmol) was ground together in a mortar with pestle for 5–15 min. Then the reaction mixture was washed with Et_2O (4 × 15 mL), dried over anhyd Na_2SO_4, and filtered. The solvent was evaporated under reduced pressure to give the crude product. The pure product **2** was obtained by vacuum distillation in 85–98% yields (Table 1).

General Procedure for the Oxidation of Amines to Aldehydes and Ketones

A mixture of amine (1 mmol) and $ZnCr_2O_7·3H_2O$ (0.5–4 mmol, Table 2) was ground together in a mortar with a pestle. The reaction occurred immediately, and the mixture was washed with Et_2O (2 × 15 mL), dried over anhyd Na_2SO_4, and filtered. In most cases evaporation of the filtrate yielded the desired pure product. If further purification was required, the crude product was purified by column chromatography on silica gel.

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References

(1) (a) Sprecher, M.; Kost, D. *J. Am. Chem. Soc.* **1994**, *116*, 1016. (b) Burnaeva, L. M.; Romanov, S. V.; Mironov, V. F.; Konovalova, I. V.; Ivkova, G. A.; Azancheev, N. M.; Cherkasov, R. A. *Russ J. Gen. Chem.* **1997**, *67*, 1310. (c) Breuer, E.; Moshe, R. *Isr. J. Chem.* **1986**, *27*, 45. (d) Telan, L. A.; Poon, C.-D.; Evans, S. A. *J. Org. Chem.* **1996**, *61*, 7455.

(2) Scherer, H.; Hartmann, A.; Regitz, M.; Tunggal, B. D.; Gunther, H. *Chem. Ber.* **1972**, *105*, 3357.

(3) (a) Krzyzanowska, B.; Pilichowska, S. *Pol. J. Chem.* **1988**, *62*, 165. (b) Karaman, R.; Goldblum, A.; Breuer, E.; Leader, H. *J. Chem. Soc., Perkin Trans. 1* **1989**, 765.

(4) (a) Smyth, M. S.; Ford, H.; Burke, T. R. *Tetrahedron Lett.* **1992**, *33*, 4137. (b) Smyth, M. S.; Otaka, A.; Roller, P. P.; Burke, T. R. *Tetrahedron Lett.* **1993**, *34*, 4125.

(5) Breuer, E.; Karaman, R.; Goldblum, A.; Gibson, D. J. *J. Chem. Soc., Perkin Trans. 1* **1988**, 3047.

(6) (a) Gajda, T. *Tetrahedron: Asymmetry* **1994**, *5*, 1965. (b) Meier, C.; Laux, W. H. G.; Bats, J. W. *Liebigs Ann.* **1995**, 1963.

(7) (a) Sekine, M.; Satoh, M.; Yamagata, H.; Hata, T. *J. Org. Chem.* **1980**, *45*, 4162. (b) Takaki, K.; Itono, Y.; Nagafuji, A.; Naito, Y.; Shishido, T.; Takehira, K.; Makioka, Y.; Taniguchi, Y.; Fujiwara, Y. *J. Org. Chem.* **2000**, *65*, 475. (c) Yamashita, M.; Kojima, M.; Yoshida, H.; Ogata, T.; Inokawa, S. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1625. (d) Sprecher, M.; Nativ, E. *Tetrahedron Lett.* **1968**, *9*, 4405.

(8) (a) Ackerman, B.; Jordan, T. A.; Eddy, C. R.; Swern, D. *J. Am. Chem. Soc.* **1956**, *78*, 444. (b) Kluger, R.; Pick, D. C.; Chin, J. *Can. J. Chem.* **1978**, *56*, 1792. (c) Jugelt, W.; Andrea, S.; Schubert, G. *J. Prakt. Chem.* **1971**, 83.

(9) (a) Berlin, K. D.; Hellwege, D. M.; Nagabhushanam, M. *J. Org. Chem.* **1965**, *30*, 1265. (b) Berlin, K. D.; Taylor, H. A. *J. Am. Chem. Soc.* **1964**, *86*, 3862.

(10) (a) Texier-Boullet, F.; Foucaud, A. *Synthesis* **1982**, 916. (b) Baraldi, P. G.; Guarneri, M.; Moroder, F.; Polloni, G. P.; Simoni, D. *Synthesis* **1982**, 653. (c) Benyound, F.; Hammond, G. B. *Chem Commun.* **1996**, 1447. (d) Kaboudin, B. *Tetrahedron Lett.* **2000**, *41*, 3169. (e) Liao, Y.; Shabany, H.; Christopher, D. S. *Tetrahedron Lett.* **1998**, *39*, 8389. (f) Firouzabadi, H.; Iranpoor, N.; Sobhani, S. *Phosphorus, Sulfur Silicon Relat. Elem.* **2004**, *179*, 1483. (g) Firouzabadi, H.; Iranpoor, N.; Sobhani, S. *Synth. Commun.* **2004**, *34*, 1463. (h) Firouzabadi, H.; Iranpoor, N.; Sobhani, S. *Tetrahedron Lett.* **2002**, *43*, 477. (i) Firouzabadi, H.; Iranpoor, N.; Sobhani, S.; Sardarian, A. R. *Tetrahedron Lett.* **2001**, *42*, 4369.

(11) (a) Takahashi, H.; Yoshioka, M.; Imai, N.; Onimura, K.; Kobayashi, S. *Synthesis* **1994**, 763. (b) Sobhani, S.; Tashrifi, Z. *Synth. Commun.* **2009**, *39*, 120. (c) Sobhani, S.; Tashrifi, Z. *Heteroat. Chem.* **2009**, *20*, 109.

(12) Petrov, K. A.; Chauzov, V. A.; Pastukhova, I. V.; Bogdanov, N. N. *J. Gen. Chem. USSR* **1976**, *46*, 1226.

(13) (a) Shaabani, A.; Seyyedhamzeh, M.; Maleki, A.; Rezazadeh, F. *Appl. Catal., A* **2009**, *358*, 146. (b) Firouzabadi, H.; Iranpoor, N.; Nowrouzi, F. *Tetrahedron Lett.* **2003**, *44*, 5343.

(14) (a) Rothenberg, G.; Downie, A. P.; Raston, C. L.; Scott, J. L. *J. Am. Chem. Soc.* **2001**, *123*, 8701. (b) Cho, B. T.; Kang, S. K. *Tetrahedron* **2005**, *61*, 5725.

(15) (a) Sobhani, S.; Safaei, E.; Asadi, M.; Jalili, F. *J. Organomet. Chem.* **2008**, *693*, 3313. (b) Sobhani, S.; Safaei, E.; Asadi, M.; Jalili, F.; Tashrifi, Z. *J. Porphyrins Phthalocyanines* **2008**, *12*, 849. (c) Sobhani, S.; Vafaee, A. *Tetrahedron* **2009**, *65*, 7691. (d) Sobhani, S.; Vafaee, A. *Synthesis* **2009**, 1909. (e) Sobhani S., Vafaee A.; *J. Iran. Chem. Soc.;* **2010**, 7: in press (f) Sobhani S., Tashrifi Z.; *Tetrahedron;* **2009**, 65: in press (g) Sobhani, S.; Tashrifi, Z. *Heteroat. Chem* **2009**, *20*, 109.

(16) (a) Demir, A. S.; Reis, M.; Dir, A. I.; Esiring, I.; Eymur, S. *J. Org. Chem.* **2005**, *70*, 10584. (b) Afarinkia, K.; Faller, A.; Twist, A. J. *Synthesis* **2003**, 357. (c) Tam, C. C.; Mattocks, K. L.; Tishler, M. *Proc. Natl. Acad. Sci. U.S.A.* **1981**, *78*, 3301.

(17) (a) Murahashi, S. I.; Okano, Y.; Sato, H.; Nakae, T.; Komiya, N. *Synlett* **2007**, 1675. (b) Moriarty, R. M.; Vaid, R. K.; Duncan, M. P. *Tetrahedron Lett.* **1988**, *29*, 6913. (c) Keinan, E.; Mazur, Y. *J. Org. Chem.* **1977**, *42*, 844. (d) Suzuki, K.; Watanabe, T.; Murahashi, S. I. *Angew. Chem. Int. Ed.* **2008**, *47*, 2079. (e) Nicolaou, K. C.; Mathison, C. J. N.; Montagnon, T. *J. Am. Chem. Soc.* **2004**, *126*, 5192. (f) Knowles, D. A.; Mathews, C. J.; Tomkinson, N. C. O. *Synlett* **2008**, 2769. (g) Hoffman, R. V.; Kumar, A. *J. Org. Chem.* **1984**, *49*, 4011. (h) Hamamoto, H.; Suzuki, Y.; Takahashi, H.; Ikegami, S. *Tetrahedron Lett.* **2007**, *48*, 4239. (i) Rawalay, S. S.; Shechter, H. *J. Org. Chem.* **1967**, *32*, 3129. (j) Orito, K.; Hatakeyama, T.; Takeo, M.; Uchiito, S.; Tokuda, M.; Suginome, H. *Tetrahedron* **1998**, *54*, 8403.

(18) (a) Firouzabadi, H.; Sardarian, A. R.; Moosavipour, H.; Afshari, G. M. *Synthesis* **1986**, 285. (b) Firouzabadi, H.; Iranpoor, N.; Hassani, H.; Sobhani, S. *Synth. Commun.* **2004**, *34*, 1967. (c) Firouzabadi, H.; Hassani, H.; Gholizadeh, M. *Phosphorus, Sulfur Silicon Relat. Elem.* **2004**, *179*, 1417. (d) Hassani, H. *Chin. J. Chem.* **2009**, *27*, 1012. (e) Feizi, N.; Hassani, H.; Hakimi, M. *Bull. Korean Chem. Soc.* **2005**, *26*, 2084.