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Conversion of Oximes to Carbonyl Compounds with 2-Nitro-4,5-dichloropyridazin-3(2*H*)-one

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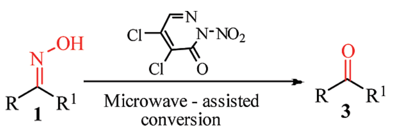

R = Alkyl, Alkenyl or Aryl
R^1 = H or Alkyl

Conversion of oximes to the carbonyl compounds has been demonstrated with use of 2-nitro-4,5-dichloropyridazin-3(2*H*)-one (**2**) under microwave irradiated conditions. Fourteen aliphatic and aromatic oximes converted to their corresponding aldehydes and ketones in good to excellent yields. It is noteworthy that the reaction is conducted under neutral, mild, and eco-friendly condition.

2-Substitued pyridazin-3(2*H*)-ones as electrophilic agents are stable and easily prepared compounds whose utility as synthetic auxiliaries was recently demonstrated by Yoon et al.[1] The ease with which pyridazin-3(2*H*)-ones can be removed and/or recycled spurred our interest in their use for other transformations. Since pyridazin-3(2*H*)-ones readily form stable anions[2] and can act as good leaving groups,[1] we explored the application of 2-substitued pyridazin-3(2*H*)-ones as electrophilic transfer reagents. In our previous paper,[1d] we reported the 2-nitro-4,5-dichloropyridazin-3(2*H*)-one (**2**) as a nitro group source. According to the literature,[3] Amberlyst 15 supported nitrosonium ion converts oximes to carbonyl compounds. Therefore, compound **2** may play the role of activating agent in the conversion of oximes into their corresponding carbonyl compounds. Recently, we found the conversion of acetophenone oxime to the corresponding carbonyl compound by 2-nitro-4,5-dichloropyridazin-3(2*H*)-one (**2**) under neutral condition in refluxing organic solvents in low yield.

Oximes are extensively used for group protecting, purification, and characterization of carbonyl compounds.[4,5] Thus, there has been increasing interest in the development of methods for the conversion of oximes into their corresponding carbonyl compounds, and a number of methods have been explored.[6]

However, these methods suffer from one or more drawbacks such as the use of toxic reagents, strong oxidation agents, additives and expensive metals, further oxidation in the case of aldoximes, and difficulty in product isolation.

As a continued interest in developing an efficient, mild, and greener process, we expected to apply 2-nitro-4,5-dichloropyridazin-3(2*H*)-one (**2**) as the activating agent. As expected, oximes were treated with agent **2** under neutral condition to give their corresponding carbonyl compounds (Scheme 1).

In this paper, we wish to report a new, simple, and green method for the effective deprotection of oximes under neutral and microwave irradiation.

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(5) Kim, Y. H.; Jung, J. C.; Kim, K. S. *Chem. Ind.* **1992**, 31.

(6) For selected recent examples, see: (a) Karami, B.; Montazerozohori, M. *Molecules* **2006**, *11*, 720. (b) Mitra, A. K.; De, P.; Karchaudhuri, N. *J. Chem. Res.* (*S*) **1999**, 320. (c) Pourali, A. R.; Goli, A. *Bull. Korean Chem. Soc.* **2006**, *27*, 587. (d) Yang, Y.; Zhang, D.; Wu, L.-Z.; Chen, B.; Zhang, L. P.; Tung, J.-H. *J. Org. Chem.* **2004**, *69*, 4788. (e) Varma, R. S.; Meshram, H. M. *Tetraheadron Lett.* **1997**, *38*, 5427. (f) de Lijser, H. J. P.; Fardoun, F. H.; Sawyer, J. R.; Quant, M. *Org. Lett.* **2002**, *4*, 2325. (g) Gogoi, P.; Hazarika, P.; Konwar, D. *J. Org. Chem.* **2005**, *70*, 1934. (h) Salehi, P.; Khodaei, M. M.; Goodarzi, M. *Synth. Commun.* **2002**, *32* (8), 1259. (i) Shirini, F.; Mamaghai, M.; Rahmanzadeh, A. *ARKIVOC* **2008**, *1*, 34. (j) Chavan, S. P.; Soni, P. *Tetrahedron Lett.* **2004**, *45*, 3161. (k) Gupta, P. K.; Manral, L.; Ganesan, K. *Synthesis* **2007**, *13*, 1930. (l) Bendale, P. M.; Khadilkar, B. M. *Tetrahedron Lett.* **1998**, *39*, 5867. (m) Bhar, S.; Guha, S. *Synth. Commun.* **2005**, *35*, 1183. (n) Khurana, J. M.; Ray, A.; Sahoo, P. K. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 1091. (o) Carmeli, M.; Rozen, S. *Tetrahedron Lett.* **2006**, *47*, 763. (p) Varma, R. S.; Dahiya, R.; Saini, R. K. *Tetraheadron Lett.* **1997**, *38*, 8819. (q) Shaabanni, A.; Rahmati, A.; Naderi, S. *Synth. Commun.* **2007**, *37*, 4035. (r) Boruah, A.; Baruah, B.; Prajapati, D.; Sandhu, J. S. *Tetrahedron Lett.* **1997**, *38*, 4267. (s) Chaudhari, S. S.; Akamanchi, K. G. *Tetrahedron. Lett.* **1998**, *39*, 3209. (t) Barhate, N. B.; Gajare, A. S.; Wakharkar, R. D.; Sudalai, A. *Tetrahedron Lett.* **1997**, *38*, 653. (u) Bose, D. S.; Srinivas, P. *Synth. Commun.* **1997**, *27*, 3835. (v) Varma, R. S.; Dahiya, R.; Saini, R. K. *Tetrahedron Lett.* **1997**, *38*, 8819. (w) Curran, D. P.; Brill, J. F.; Rakiewicz, D. M. *J. Org. Chem.* **1984**, *49*, 1654. (x) Donaldson, R. E.; Saddler, J. C.; Boyrn, S.; Mckenzie, A. T.; Fuchs, P. L. *J. Org. Chem.* **1983**, *48*, 2167. (y) Corey, E. J.; Hopkins, P. B.; Kim, S.; Kou, S.; Nambiar, K. P.; Flack, J. R. *J. Am. Chem. Soc.* **1979**, *101*, 7131.

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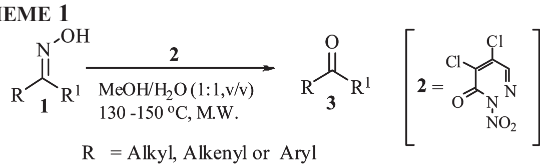
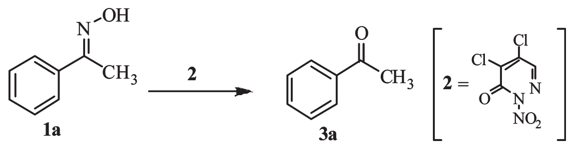
SCHEME 1



R = Alkyl, Alkenyl or Aryl
R^1 = H or Alkyl

TABLE 1. Optimization of Conditions



entry	solvents	conditions	time	yield[a] (%)
1	water	25 °C	72 h	80[b]
2	water	reflux	1 h	64[c]
3	MeOH (1 mL H_2O)	25 °C	72 h	53 [b]
4	MeOH	reflux	24 h	60 [c]
5	MeOH/H_2O (1:1, v/v)	reflux	24 h	50 [c]
6	MeOH/H_2O (1.5:1, v/v)	150 °C, microwave	10 min	88
7	MeOH/H_2O (1:1, v/v)	25 °C, microwave	10 min	80 [b]
8	MeOH/H_2O (1:1, v/v)	150 °C, microwave	10 min	92
9	MeOH/H_2O (1:1.5, v/v)	150 °C, microwave	10 min	88
10	MeOH/H_2O (1:9, v/v)	150 °C, microwave	10 min	decom

[a]Isolated yield. [b]Oxime was not converted completely into the corresponding carbonyl compound. [c]Oxime was not converted completely into the corresponding carbonyl compound and also detected unknown byproduct.

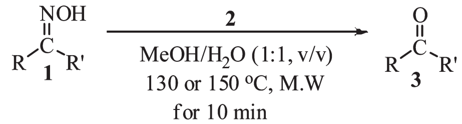
Direct *N*-nitration of 4,5-dichloropyridazin-3(2*H*)-one (**2**) was performed by the literature method.[1d]

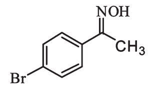
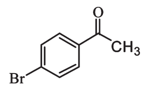
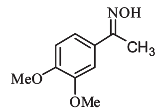
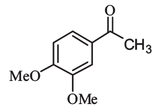
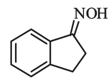
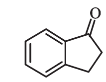
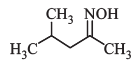
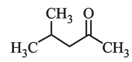
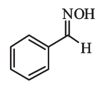
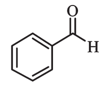
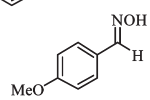
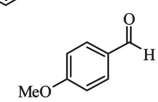
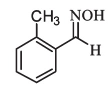
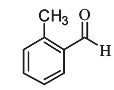
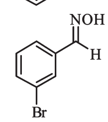
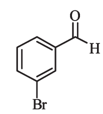
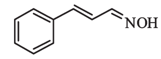
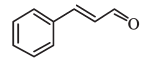
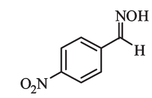
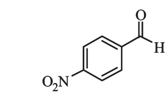
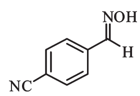
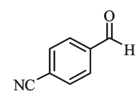
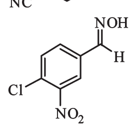
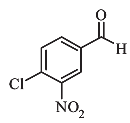
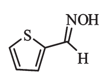
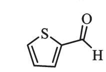
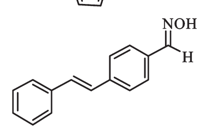
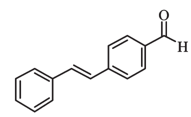
With use of a model reaction based on acetophenone oxime (**1a**), some different conditions have been screened. The results are shown in Table 1. On the basis of the observation, this reaction is more favorable under microwave irradiation. Finally, the following systems proved to be best: **1a** (1 equiv)/**2** (1 equiv)/H_2O−MeOH (1:1, v/v) at 150 °C under microwave irradiation.

Four ketoximes **1b−e** were treated with **2** under the optimized conditions at 130 °C (for **1e**) or 150 °C to give the corresponding ketones **3b−e** in good to excellent yields (entries 1−4 in Table 2). Similarly, aldoximes **1f−o** were also reacted with **2** under the same conditions at 130 °C (for **1k−o**) or 150 °C (for **1f−j**) to afford the corresponding aldehydes **3f−o** in good to excellent yields (entries 5−14 in Table 2). In the conversion of all aldoximes under our conditions, we obtained only the corresponding aldehydes, and did not detect the overoxidation to the carboxylic acids. All oximes involving the electron-withdrawing and the electron-donating groups on the phenyl ring were also easily converted to the corresponding carbonyl compounds. In addition, reusable 4,5-dichloropyridazin-3(2*H*)-one was isolated quantitatively. The product structures were established by IR and NMR, and the spectral data and R_f values of TLC are also identical with the data of their authentic samples.

A plausible mechanism of carbon−nitrogen double bond cleavage of oximes may be represented as Scheme 2. Finally, oximes react with compound **2** as an activating agent to convert the corresponding carbonyl compounds through the *N*-hydroxynitramide intermediate (**I**) and/or 1,2,3-oxadiazetidin-2-ium (**II**).

TABLE 2. Conversion of Oximes to Carbonyls with 2

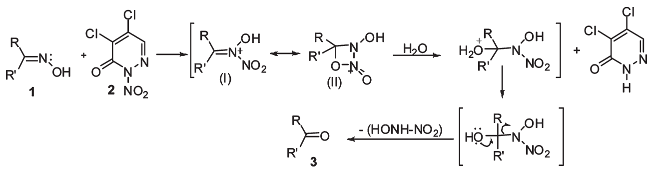


entry		substrate		product	yield[a] (%)
1	**1b**		**3b**		96[b]
2	**1c**		**3c**		96[b]
3	**1d**		**3d**		90[b]
4	**1e**		**3e**		83[c]
5	**1f**		**3f**		96[b]
6	**1g**		**3g**		82[b]
7	**1h**		**3h**		98[b]
8	**1i**		**3i**		86[b]
9	**1j**		**3j**		95[b]
10	**1k**		**3k**		97[c]
11	**1l**		**3l**		86[c]
12	**1m**		**3m**		94[c]
13	**1n**		**3n**		96[c]
14	**1o**		**3o**		80[c]

[a]Isolated yield. [b]Microwave irradiation, 200 W, 1378 kPa, 150 °C. [c]Microwave irradiation, 200 W, 1378 kPa, 130 °C.

In summary, we have reported the oxidative conversion of oximes with compound **2** as an activating agent into the corresponding carbonyl compounds in good to excellent

SCHEME 2. Plausible Mechanism for Conversion of Oximes to Carbonyls



yields. The conversion was accompanied by no formation of byproduct. In the case of aldoximes, overoxidation products also were not detected under our condition. Compound **2** is a stable, efficient and eco-friendly agent, and easily prepared from commercially available 4,5-dichloropyridazin-3(2*H*)-one. In addition, 4,5-dichloropyridazin-3(2*H*)-one can be reusable and easily separated from the reaction mixture.

Experimental Section

General Procedure for the Conversion of Oxime to Carbonyl. Oxime (**1a**−**o**, 0.73 mmol) and 4,5-dichloro-2-nitropyridazinone (**2**, 0.73 mmol) were dissolved in MeOH (4 mL) at room temperature in a vial. After adding H_2O (4 mL) into the solution, the resulting mixture was irradiated in a microwave oven (200 W output, 1378 kPa) at 130 °C (for **1e** and **1k**−**o**) or 150 °C (for **1a**−**d** and **1f**−**j**) for 10 min in a capped vial. The reaction was monitored by TLC. After completion of the reaction, product was extracted with dichloromethane (40 mL). After separating the organic layer, the organic solution was then dried over anhydrous $MgSO_4$. After evaporating the solvent under reduced pressure, the resulting residue was then further purified by column chromatography with dichloromethane to give the corresponding carbonyl compounds **3**.

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Supporting Information Available: Complete experimental procedures, ^{1}H and ^{13}C NMR spectral data, and melting points for compounds **3b**−**d**, **3k**−**m**, and **3o**. This material is available free of charge via the Internet at http://pubs.acs.org.