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# Solventless Rapid Synthesis of Oxime, Semicarbazone, and Phenylhydrazone Derivatives from Carbonyl Compounds under Microwave Conditions

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A rapid and efficient method for the synthesis of oximes, semicarbazones, and phenylhydrazones has been reported under solventless conditions using microwave irradiation.

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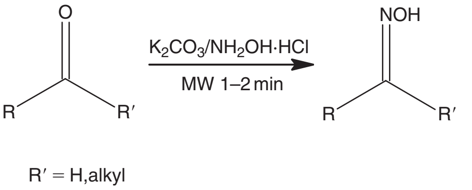
Oximes are one of the most important intermediates in organic synthesis. Methods to synthesize oximes have been reported.[1,2] This paper describes the synthesis of oximes under solventless conditions in dry media within 1–2 min, with excellent yields in the range 80–97%. Further, aldoximes are shown by $^1$H NMR to occur more frequently as *cis*- than as *trans*-isomers (Scheme 1, Table 1).

Oximes are required as precursors in Beckmann rearrangements for the synthesis of oxazoles, oxazines, and for various heterocycles. Oximes are also the synthons for 1,3-dipolar addition reactions and form the main intermediates in the synthesis of azirines and pyridine derivatives.[3] Phenyl hydrazones, on treatment with Lewis acids, give carbazoles that have antimicrobial activity. Oximes, phenylhydrazones, and semicarbazones have been found to be biologically active,[4] and thus their synthesis assumes importance.

In the conventional method of synthesis of oximes, either water or ethanol/pyridine are used as solvents along with bases and hydroxylamine. This process requires careful maintenance of pH in the solvent during the reaction. This issue is eliminated while performing the reaction in dry media. Also, synthesis of aldoximes is easier compared with ketoximes. In this procedure, ketoximes are also formed. We tried the same procedure on the formation of phenyl hydrazones and semicarbazones, and they both offered good yields (Table 2).

Solvent-free reaction conditions are convenient,[5,6] because the reaction media is easy to handle without the need for extensive purification. Yields are high and the reactions proceed to completion rapidly. In addition, such conditions are cost-effective and environmentally benign. Traditional techniques with solvents yield only 50–60% of oximes with both the isomers being nearly equally distributed. Moreover, there is some loss of the product during precipitation and recrystallization. This loss is avoided in the solventless procedure, since the products are sufficiently pure. Solventless techniques are gaining popularity with synthetic organic chemists as they offer easy work-up.



**Scheme 1.**

Microwave-assisted techniques are applied to the rapid synthesis of intermediates in various organic syntheses.[7,8,9] Reactions that are sluggish and require very stringent conditions may be carried out easily in a microwave oven. In this article, we report the synthesis of oximes under dry reaction media using anhydrous potassium carbonate under microwave conditions. The reaction proceeded to completion within 1–2 min. Although the solventless procedure is convenient, under thermal conditions the time taken for some oximes is 5 h.[10] However, this time is minimized by the use of microwave irradiation. Basic oxides such as metal oxides and metal carbonates enhance the formation of $Z$-oximes.[11] Although the reaction is stereo-selective for the formation of oximes, it was not found be so with semicarbazones or phenyl hydrazones. The procedure involves an extremely simple work-up procedure that makes the reaction attractive to use. Interestingly, α,β-unsaturated ketones are also converted to their respective oximes without any side reaction caused by the addition of the –NHOH group to the β-unsaturated carbon.

In conclusion, the procedure described is a fast, neat, and inexpensive method for the synthesis of oximes and other derivatives. The advantages of this procedure are stereoselectivity and simplicity.

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**Table 1. Synthesis of aldoximes and ketoximes under solventless conditions**

| Aldehyde or ketone | Time [min] | Oxime | Yield [%] | *cis* [%][A] ($\delta_{H}$ [ppm]) |
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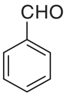
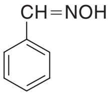
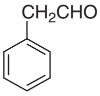
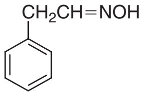
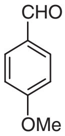
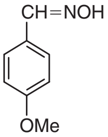
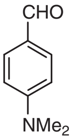
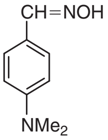
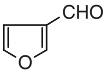
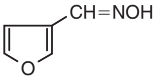
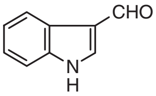
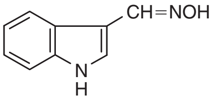
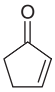
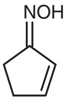
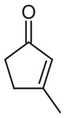
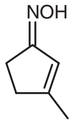
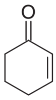
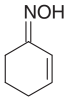
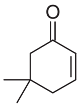
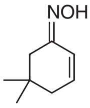
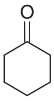
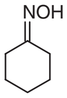
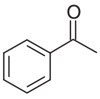
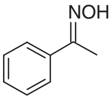
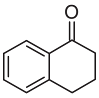
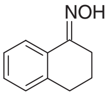
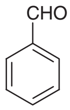
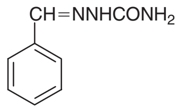
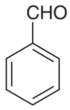
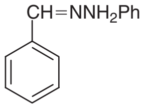
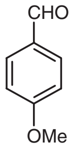
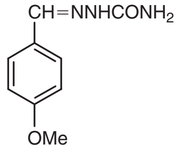
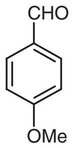
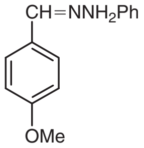
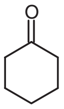
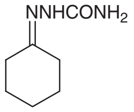
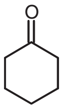
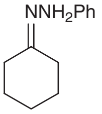
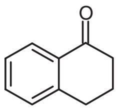
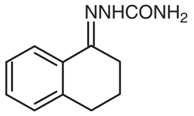
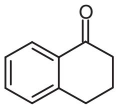
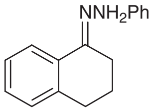
|  | 1.5 |  | 90 | 90 (8.2) |
|  | 1.5 |  | 92 | 70 (8.0) |
|  | 1.5 |  | 90 | 93 (8.1) |
|  | 1 |  | 90 | 99 (7.9) |
|  | 1.5 |  | 90 | 95 (8.2) |
|  | 2 |  | 92 | 93 (9.5) |
|  | 1 |  | 90 | — |
|  | 1 |  | 85 | — |
|  | 1 |  | 97 | — |
|  | 1 |  | 75 | — |
|  | 2 |  | 80 | — |
|  | 1 |  | 92 | — |
|  | 2 |  | 82 | — |

[A] $^{1}$H NMR values for *cis*-isomer are greater than those for *trans*-isomer.

**Table 2. Synthesis of semicarbazones and phenylhydrazones under solventless conditions**

| Aldehyde or ketone | Time [min] | Product | Yield [%] |
|---|---|---|---|
|  | 1.5 |  | 85 |
|  | 1 |  | 87 |
|  | 1.5 |  | 90 |
|  | 1 |  | 91 |
|  | 1.5 |  | 90 |
|  | 1 |  | 92 |
|  | 1.5 |  | 89 |
|  | 1 |  | 90 |

## Experimental

Reactions were carried out in a domestic microwave oven (T-23, Kelvinator-India, 700 W, 2450 MHz). Analytical thin layer chromatography was performed on pre-coated plastic silica gel plates 0.25 mm thick containing PF 254 indicator (Merck, Darmstadt). IR spectra were recorded neat on a RX I FT-IR spectrometer (Perkin Elmer). NMR spectra were recorded in $CDCl_3$ and [D$_6$]DMSO as applicable on a 500 MHz JEOL spectrometer (chemical shifts in $\delta$, ppm) using TMS as an internal standard.

As a typical procedure, 1 g $K_2CO_3$ was added to 417 mg of $NH_2OH{\cdot}HCl$ (6 mmol) and ground to a fine powder. Either aldehyde or ketone (1 mmol) was added and irradiated in a microwave oven for the specified time as indicated by thin layer chromatorgraphy. The reaction mixture was cooled and washed with dichloromethane and water. The organic layer was separated, dried over anhydrous $Na_2SO_4$, and evaporated to give the corresponding oxime. The oxime obtained was analyzed by means of infrared spectroscopy (FT-IR), $^1$H NMR, $^{13}$C NMR, and gas chromatography (GCMS), and compared with reported values. The semicarbazones and phenylhydrazones were also synthesized by the same method using 4 mmol of semicabazide hydrochloride and phenylhydrazine hydrochloride to 1 mmol of the aldehyde or ketone.

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## References

[1] W. P. Jencks, *J. Am. Chem. Soc.* **1959**, *81*, 475. doi:10.1021/JA01511A053

[2] S. R. Sandler, W. Karo, *Organic Functional Group Preparation* **1983**, Vol. 3, Ch. 11 (Academic: NewYork, NY).

[3] P. Saikia, D. Prajapati, J. S. Sandhu, *Tetrahedron Lett.* **2003**, *44*, 8725. doi:10.1016/J.TETLET.2003.09.144

[4] (*a*) J. V. Burakevich, A. M. Lore, G. P. Volpp, *J. Org. Chem.* **1971**, *36*, 1. doi:10.1021/JO00800A001

(*b*) U. Brandt, G. Von Jasgow, *FEBS Lett.* **1991**, *287*, 215. doi:10.1016/0014-5793(91)80054-7

(*c*) H. Tecle, D. J. Lauffer, T. Mirzadegan, W. H. Moos, D. W. Moreland, M. R. Pavia, R. D. Schwarz, R. Davis, *Life Sci.* **1993**, *52*, 505. doi:10.1016/0024-3205(93)90308-P

[5] G. W. V. Cave, C. L. Raston, J. L. Scott, *Chem. Commun.* **2001**, 2159. doi:10.1039/B106677N

[6] R. S. Varma, *Green Chem.* **1999**, *1*, 43. doi:10.1039/A808223E

[7] (*a*) R. A. Abramovitch, *Org. Prep. Proceed. Int.* **1991**, *23*, 683.
(*b*) S. Caddick, *Tetrahedron* **1995**, *51*, 10403. doi:10.1016/0040-4020(95)00662-R
(*c*) P. Lidstrom, J. Tierney, B. Wathey, J. Westman, *Tetrahedron* **2001**, *57*, 9225. doi:10.1016/S0040-4020(01)00906-1
(*d*) A. K. Bose, M. S. Manhas, S. N. Ganguly, A. H. Sharma, B. K. Banik, *Synthesis* **2002**, 1578. doi:10.1055/S-2002-33344
(*e*) G. Sartori, R. Ballini, F. Bigi, G. Bosica, R. Maggi, P. Righi, *Chem. Rev.* **2004**, *104*, 199. doi:10.1021/CR0200769

[8] R. J. Giguere, T. L. Bray, S. M. Duncan, G. Majetich, *Tetrahedron Lett.* **1986**, *27*, 4945. doi:10.1016/S0040-4039(00)85103-5

[9] A. K. Bose, M. S. Manhas, M. Ghosh, M. Shah, V. S. Raju, S. S. Bari, S. N. Newaz, B. K. Banik, A. G. Chaudary, K. J. Barakat, *J. Org. Chem.* **1991**, *56*, 6968. doi:10.1021/JO00025A004

[10] H. Sharghi, M. H. Sarvari, *J. Chem. Res.* **2000**, 24.

[11] H. Sharghi, M. H. Sarvari, *Synlett* **2001**, 99. doi:10.1055/S-2001-9719