A simple and effective glycine-catalysed procedure for the preparation of oximes

Muchchintala Maheswara, Vidavalur Siddaiah, Kovuru Gopalaiah, Vallabhaneni Madhava Rao and Chunduri Venkata Rao*

Department of Chemistry, Sri Venkateswara University, Tirupati-517 502, India

Ketoximes and aldoximes are expeditiously prepared by the reaction of the corresponding carbonyl compound with hydroxylamine hydrochloride in dimethylformamide, in the presence of a sub-stoichiometric quantity of glycine at room temperature. Mild (non-hydroxylic) conditions, simple workup and high yield characterise the methodology.

Keywords: oxime, glycine, hydroxylamine hydrochloride, carbonyl compounds, dimethylformamide, aprotic

Oximes are perhaps the most useful derivatives of aldehydes and ketones, both for purposes of characterisation and also as key intermediates in the important Beckmann rearrangement.[1-3] They are also widely used as precursors in the synthesis of wide variety of organic compounds.[4] An efficient, mild and environmentally friendly procedure for their preparation would therefore be of much interest. Current methodology, however, employs quite harsh conditions for their synthesis. A typical experiment would involve heating a mixture of the carbonyl compound and hydroxylamine hydrochloride in water or ethanol, along with a base such as pyridine or sodium acetate.[1] A few other procedures also been reported under solvent-free conditions using molecular sieves[5] or ($CuSO_4$ and K_2CO_3)[6] as promoting agents. Harsh reaction conditions sometimes lead to reduction in the yield,[1,2,7] presumably due to the decomposition of hydroxylamine.

We present here a considerably milder version of the procedure under non-hydroxylic conditions, which enlarges the scope of the procedure and makes it applicable to a variety of substrates. A variety of aldoximes and ketoximes could be expeditiously prepared by stirring a solution of the carbonyl compound and hydroxylamine hydrochloride in dimethyl formamide (DMF) with a sub-stoichiometric quantity (0.5 equiv) of glycine at room temperature.

It was found that various aminoacids could be used to bring about this transformation. However, inexpensive glycine was employed on a variety of substrates. Optimal conditions for the reaction were found by varying the quantity of glycine. A minimum of 0.5 molar equivalents was required for the completion of the reaction. The various substrates and yields are depicted in the Table. The advantages of the current method include high yields (generally > 85%), ambient conditions, reasonable reaction times, simple workup, sub-stoichiometric quantity (0.5 equiv) of glycine and the use of an aprotic solvent. The procedure is thus apparently suitable for sensitive substrates and also easily scaled up.

In conclusion, we have developed a simple, efficient and economically viable practical method for the conversion of carbonyl compounds into the corresponding oximes in high yields. We believe our procedure will find important applications in the synthesis of oximes.

Experimental

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded in KBr discs on a Bio-Rad win FT–IR spectrophotometer. ^{1}H NMR spectra were recorded on a Varian Gemini 200 spectrometer. LCMS was recorded on an Agilent-1100 periods LC/MSD (VL) instrument. TLC was carried out on GF254 silica gel plates. All carbonyl compounds were commercial available.

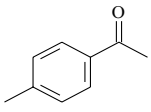
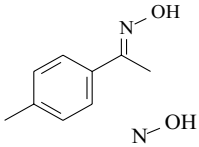
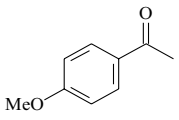
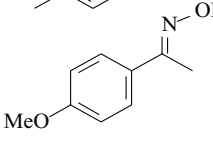
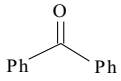
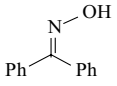
Preparation of oximes: A stirred solution of hydroxylamine hydrochloride (1 mmol) and glycine (0.5 mmol) in dry DMF (5 ml) was treated with the aldehyde or ketone (1 mmol) under N_2 at room temperature (25 °C). The progress of the reaction was monitored by TLC, and upon completion the reaction mixture was worked up by diluting with ether (20 ml), washing with water and drying over anhydrous Na_2SO_4. Removal of the solvent in vacuum, followed by recrystallisation of the residue in ethyl acetate-hexane (1: 2 ratio) afforded the pure oxime products, characterised by melting point comparison and spectroscopic data (IR, ^{1}H NMR, Mass).

All the products (except the product **8**) are known compounds (references in the Table 1) and were characterised from spectroscopic properties. The spectroscopic data of the compound **8** are presented below.

Compound **8** (*2-hydroxy-3-methoxybenzaldehydeoxime*): IR (KBr): 3332, 1756, 1480 cm^{-1}**.** ^{1}H NMR**:** (200 MHz, $CDCl_3$) δ 9.9 (s, 1H, OH), 8.2 (s, 1H, C = N-OH), 8.0 (s, 1H, HC = N), 6.7–6.9 (m, 3H, ArH), 3.9 (s, 3H, OCH_3), LCMS (*m*/*z*): 167 (M + .). Anal. Calcd for $C_8H_9NO_3$: C, 57.5; H, 5.4; N, 8.4. Found: C, 57.4; H, 5.5; N, 8.4.

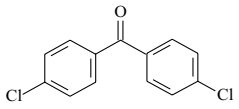
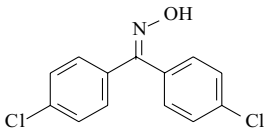
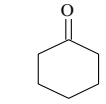
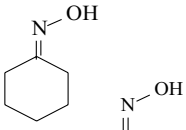
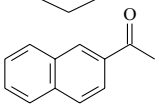
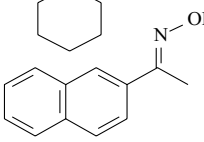
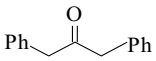
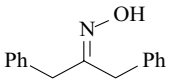
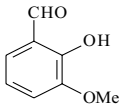
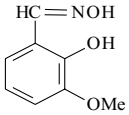
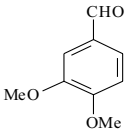
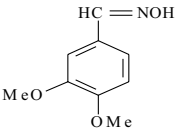
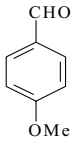
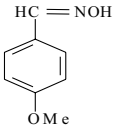
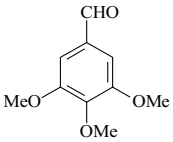
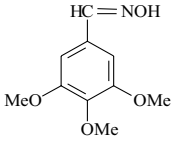
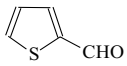
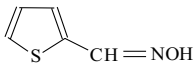
Received 1 November 2005; accepted 18 November 2005
Paper 05/3576

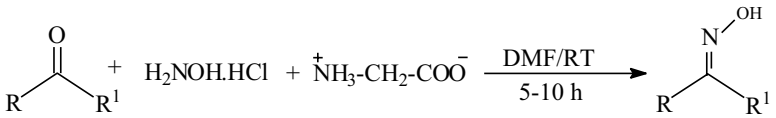
Table 1 Conversion of carbonyl compounds into oximes

Entry	Substrate	Product	Time/h	Yield/%	M.p./°C (Lit.)
1			6	94	87–88 (88)[8]
2			6	97	86–87 (87)[8]
3			5	95	142–143 (144)[8]

* Correspondent. E-mail: cvr_svu@yahoo.com

Table 1 *continued*

Entry	Substrate	Product	Time/h	Yield/%	M.p./°C (Lit.)
4			6	88	90–91 (91)[8]
5			5	96	155–156 (156)[8]
6			6	96	145–146 (146)[8]
7			6	98	124–125 (125)[8]
8			10	84	120–121
9			9	88	93–94 (95)[9]
10			8	90	63–64 (65)[9]
11			9	86	83–84 (83)[9]
12			8	90	131–132 (133)[10]



R= alkyl, aryl

R^1= alkyl, aryl, H

Scheme 1

Reference

1 Vogel's *Textbook of Practical Organic Chemistry,* 5th edn, Addison Wesley Longman, Harlow, 1989, p.1259.

2 J.K. Whitesell, *Comprehensive Organic Synthesis*, B. M. Trost, I. Fleming, E. Winterfeldt, (eds), Pergamon Press: Oxford 1991, Vol. 6, p.726 and reference cited therein.

3 J. March, *Advanced Organic Chemistry*, John Wiley: New York, 1992, pp. 1095–1097.

4 (a) E. Buehler, *J. Org. Chem*.1967, **32**, 261; (b) J.N. Kim, K.H. Chung and E.K. Ryu, *Synth Commun*. 1990, **20**, 2785; (c) S. Satatani, T. Miyazaki, K. Maruoka and H. Yama Moto, *Tetrahedron Lett*., 1983, **24**, 4711; (d) M.W. Barennes and J.M. Patterson, *J. Org. Chem*., 1976, **51**, 733.

5 M.A. Bigdeli, M.M.A. Nikje, S. Jafari and M.M. Haravi, *J. Chem. Res. (S)*, 2002, 20.

6 H. Sharghi and M.H. Sarvari, *Synlett*, 2001, 99.

7 M.A. Waters and A.B. Hoem, *Encyclopedia of Reagents for Organic Synthesis*; L. A. Paquette, (ed.), John Wiley: Chichester, 1995; Vol. 4, p.2760.

8 Vogel's *Textbook of Practical Organic Chemistry,* 5th edn. 1989, Addison Wesley Longman, Harlow, under headings for the corresponding carbonyl compounds.

9 J. Buckingham, *Dictionary of Organic Compounds*, 1982, Chapman and Hall.

10 CRC, *Handbook of Tables for Organic Compound Identification*, 3rd edn. and 54th edn.