

Synthesis of ketoximes via a solvent-assisted and robust mechanochemical pathway

Christer B. Aakeröy,^a Abhijeet S. Sinha

Department of Chemistry, Kansas State University, Manhattan, KS 66506

aakeroy@ksu.edu

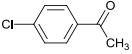
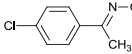
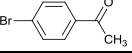
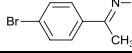
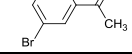
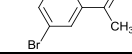
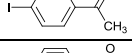
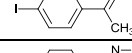
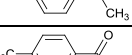
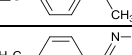
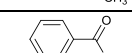
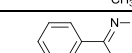
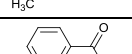
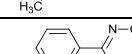
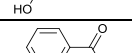
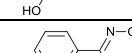
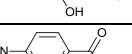
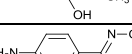
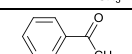
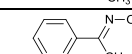
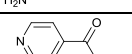
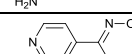
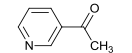
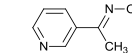
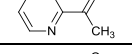
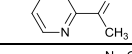
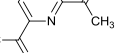
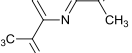
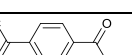
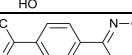
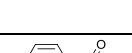

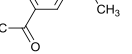
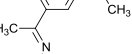
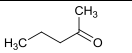
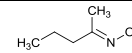
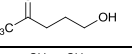
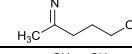
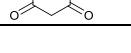
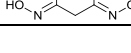
Supporting Information

Table of contents

General experimental details.....	S3
General synthesis of the ketoximes.....	S4-S6
Characterization of the ketoximes.....	S7

General experimental details

¹H NMR spectra were recorded on a Varian Unity plus 400 MHz spectrometer in CDCl₃ or d₆-DMSO. Data is expressed in parts per million (ppm) downfield shift from tetramethylsilane or residual protiosolvent as internal reference and are reported as position (in ppm), multiplicity (s = singlet, d = doublet, t = triplet, m= multiplet), coupling constant (J in Hz) and integration (number of protons). Melting points were recorded on a Fisher-Johns melting point apparatus and are uncorrected. All the chemicals were purchased from Aldrich and used without further purification, unless otherwise noted.

#	Physical state of reactant	Reactant	Physical state of ground mixture	Product
1	Liquid		White solid	
2	Solid		Yellow solid	
3	Liquid		Yellow solid	
4	Solid		Brown solid	
5	Solid		White solid	
6	Liquid		White solid	
7	Liquid		White solid	
8	Solid		Viscous yellow solid	
9	Liquid		White solid	
10	Solid		Yellow solid	
11	Solid		Yellow solid	
12	Liquid		White solid	
13	Liquid		White solid	
14	Liquid		White solid	
15	Solid		White solid	
16	Solid		White solid	
17	Solid		White solid	
18	Liquid		Viscous white solid	
19	Liquid		Viscous white solid	
20	Liquid		White solid	

General synthetic method for 2, 4-6, 8, 11, 13-14, 17

In a mortar, 1.0 mmole of the ketone and 1.2 mmoles (per ketone present) of hydroxylamine hydrochloride is ground together with a pestle. Then, 1.2 mmoles (per ketone present) of crushed sodium hydroxide is added and the mixture is ground further with the addition of 0.1-0.2 mL methanol, for 2 minutes at room temperature. The reaction mixture is left for 5 minutes, after which it is ground for another 2 minutes with 0.1-0.2 mL methanol. At this stage the reaction is monitored by TLC. Upon completion of the reaction, a ^1H NMR spectrum of the crude mixture is taken in d_6 DMSO to confirm the formation of ketoxime. The crude mixture is washed with water to get rid of any inorganic salts and it is air dried, after which the melting point is taken to confirm the formation of pure product.

General synthetic method for 1, 3, 7, 9-10, 12, 15-16

In a mortar, 1.0 mmole of the ketone and 2.4 mmoles (per ketone present) of hydroxylamine hydrochloride is ground together with a pestle. Then, 2.4 mmoles (per ketone present) of crushed sodium hydroxide is added and the mixture is ground further with the addition of 0.1-0.2 mL methanol, for 2 minutes at room temperature. The reaction mixture is left for 5 minutes, after which it is ground for another 2 minutes with 0.1-0.2 mL methanol. At this stage the reaction is monitored by TLC. Upon completion of the reaction, a ^1H NMR spectrum of the crude mixture is taken in d_6 DMSO to confirm the formation of ketoxime. The crude mixture is washed with water to get rid of any inorganic salts and it is air dried, after which the melting point is taken to confirm the formation of pure product.

General synthetic method for 18-20

In a mortar, 1.0 mmole of the ketone and 1.2 mmoles (per ketone present) of hydroxylamine hydrochloride is ground together with a pestle. Then, 1.2 mmoles (per ketone present) of crushed sodium hydroxide is added and the mixture is ground further with the addition of 0.1-0.2 mL methanol, for 2 minutes at room temperature. The reaction mixture is left for 5 minutes, after which it is ground for

another 2 minutes with 0.1-0.2 mL methanol. At this stage the reaction is monitored by TLC. Upon completion of the reaction, a ^1H NMR spectrum of the crude mixture is taken in d_6 DMSO to confirm the formation of ketoxime. The crude mixture is washed with chloroform to extract the water soluble products. The filtrate is evaporated to obtain the compound, after which the melting point is taken to confirm the formation of pure product.

Characterization of the ketoximes

4-acetylbenzoxime (5): ^1H NMR (δH ; d_6 DMSO, 400MHz): 2.17 (3 H, s), 7.81-7.88 (4 H, m), 11.67 (1 H, br. s.).

2-pentanone oxime (18): ^1H NMR (δH ; d_6 DMSO, 400MHz): 0.85 (3 H, m), 1.44 (2 H, m), 1.70 (3 H, s), 2.06 (2 H, m), 10.21 (1 H, br. s.).