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Surfactant/I$_2$/Water: An Efficient System for Deprotection of Oximes and Imines to Carbonyls under Neutral Conditions in Water

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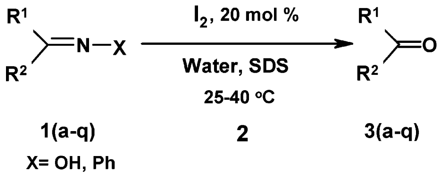

I$_2$/surfactant/water system deprotecting oximes and imines to the corresponding carbonyl compounds under neutral conditions in water at 25−40 °C with very high to excellent yields.

In recent years, organic reactions conducted in aqueous media have received much attention from chemists[1] because of concerns about the environment.[2] Therefore, organic reactions performed in aqueous media in the presence of a homogeneous catalyst would be an ideal methodology, provided the catalyst, preferably under neutral conditions, shows high reactivity, versatility, and solubility in water. Also, most organic reactants including catalysts are insoluble in water, and the surfactants, due to their hydrophobic and hydrophilic nature,[3] form micelles of the reactants and promote the reaction to occur in water. On the other hand, protection−deprotection of functional groups is a common and very essential process in multistep organic syntheses.[4] The carbonyl compounds protected by converting them to the corresponding oximes and imines are deprotected after completing the essential transformations to the parent carbonyl compounds by using a number of efficient reagents in a reaction sequence. The acidic reagents used for the deprotection are aqueous TiCl$_3$ and acetic acid,[5] nitrous acid (as well as nitrosonium salts such as NO$^+$, BF$_4^-$),[6] HCl,[7] levulinic acid,[8] pyruvic acid,[9] etc. The oxidizing agents involve N$_2$O$_4$,[10] ozone,[11] *tert*-butylhydroperoxide,[12] KMnO$_4$/alumina,[13] etc. The metallic salts involve thallium(III) nitrate,[14] chromium compounds such as chromium(II) acetate,[15] chromium(VI) species such as trimethylammonium chlorochromate,[16] chlorotrimethylsilane(chromium),[17] pyridinium chlorochromate,[18] pyridinium chlorochromate−H$_2$O$_2$,[19] trimethylsilyl chlorochromate,[20] bis(trimethylsilyl) chromate,[21] supported and unsupported chromium trioxide,[22] and polymer supported CrO$_3$.[23] The other reagents—benzeneseleninic anhydride(PhSeO)$_2$O,[24] NaHSO$_3$,[25] Na$_2$S$_2$O$_4$,[26] etc.—may be mentioned. And the search for better reagents still continues.[13,27] However, most of the reported methods though they are efficient, are not free from drawbacks: for example, use of toxic and hazardous transition metal oxidants, i.e., Mn,[13] Cr,[17−23] Ti,[5] Th,[14] and their problems associated with waste disposal, use of strong Lewis[6] and Bronsted acids,[7] low temperature,[11,16] involvement of longer reaction time,[18] low yield of products,[24] difficulties in isolating the products,[19] and formation of over-oxidized products.[12] Therefore, development of a better reagent in water under neutral condition is desirable.

In a previous communication, we reported deoxygenation of nitrones to the corresponding imines catalyzed by HI[28] (generated from AlCl$_3$·6H$_2$O/NaI/H$_2$O/CH$_3$CN) in hydrated media. The same system was used for the dehydration of oximes to nitriles, the Beckmann rearrangements, and the Bischler−Napieralski reactions[29] in hydrated media. Recently, we reported selective oxidation of alcohols to carbonyl compounds could be achieved with

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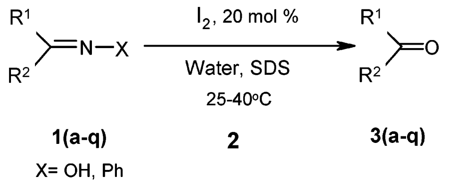
SCHEME 1

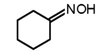
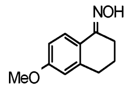
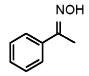
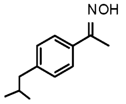
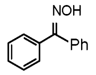
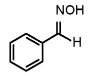
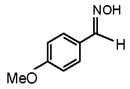
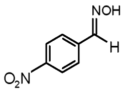
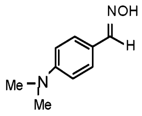
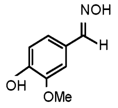
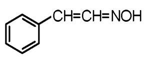
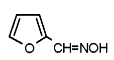
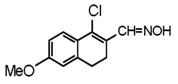
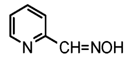


the DMSO/$N_2H_4 \cdot H_2O/I_2$ system in hydrated media and it was shown that I_2 could be reduced by N_2H_4 to generate HI [in situ], and catalyze the oxidation process in the presence of DMSO.[30] Now, an alternate system for the cleavage of the C=N bond catalyzed by I_2 is devised based on the hydrophobic and hydrophilic nature of a surfactant, which would form micelles of I_2 and oxime/imines in water and promote the deprotection process. Although the application of surfactants as a reagent in organic synthesis is well investigated,[31] to the best of our knowledge, its use as a promoter of I_2-catalyzed cleavage of the C=N bond in water under neutral conditions is not exploited. We now first report here an efficient environmentally friendly catalytic system, surfactant/I_2/water, for the deprotection of oximes and imines to carbonyl compounds in water under neutral conditions at 25−40 °C (Scheme 1).

Although the reaction of oximes/imines with a catalytic amount of I_2 in water did not proceed at all (due to poor solubility of reactant and I_2 in water), the addition of surfactant (sodium dodecyl sulfate, SDS) to the reaction mixture led to the formation of carbonyl compounds. For example, 1 M of oxime/imines, 0.2 M of I_2, and 0.2 M of sodium dodecyl sulfate (SDS) were mixed in water (10 mL) and the reaction mixture was stirred for a stipulated time at 25−40 °C; after workup it produced the corresponding carbonyl compounds with very good to excellent yields [Table 1].

We found that this system did not produce iodoxime/imidoyl iodide[3232−33] or over oxidized product (acid)[12] in the reaction mixture. And it produced neither cis nor trans halogenated products when cinnamaldehyde [entry **1k**] or furfuryl oximes [entry ***1l***] were used as substrates. Both cis and trans isomers of oximes/imines were converted smoothly to the corresponding carbonyl compounds under the same reaction condition (in all cases both cis and trans isomers of oximes/imines were used as a mixture). The sterically less hindered ketoximes [entry **1a**−**e**] were successfully cleaved with faster rates to the corresponding carbonyl compounds than sterically more hindered ketoximes. We found that the rates as well as yields of the reactions are dependent on the substituents present on aryl or heteroaryl rings. The electron-donating groups such as MeO, isobutyl, and Me on the aromatic ring enhance the rate of the reaction [entry **1d**, **1g**, and **1i**]. Similarly, the aldoximes were converted to the corresponding aryl aldehydes with excellent yields [entry **1f**−**n**]. Also, the reagent cleaved the imines to the corresponding carbonyl compounds without forming any iodinated side products. The temperature range of the reaction was determined to be 25−40 °C.

TABLE 1. Conversion of Oximes/Imines to Carbonyl Compounds

Entry	Oximes/imines 1(a-q)	Time (hr)[b]	Yields%[a] Carbonyl Comp. 3(a-q)#
1a		4.5	76
1b		4.5	69.8
1c		3.0	80
1d		2.5	77.8
1e		5.0	69.8
1f		3.2	86.8
1g		3.0	90.4
1h		4.0	74.8
1i		3.5	71.8
1j		4.0	72.5
1k		4.0	72.7
1l		3.5	76
1m		4.5	65
1n		4	71
1o	$C_6H_5-CH=N-C_6H_5$	7.4	71.7
1p	P- Cl-$C_6H_4-CH=N-C_6H_5$	8.2	67
1q	*p*-Me-C_6H_4-CH=N-C_6H_5	6.5	68.2

[a] Isolated yield. [b] Stirring at 25−40 °C. [c] The structures of the compounds were determined by using ^1H NMR, FTIR, and elemental analyses and comparison with authentic samples.[33]

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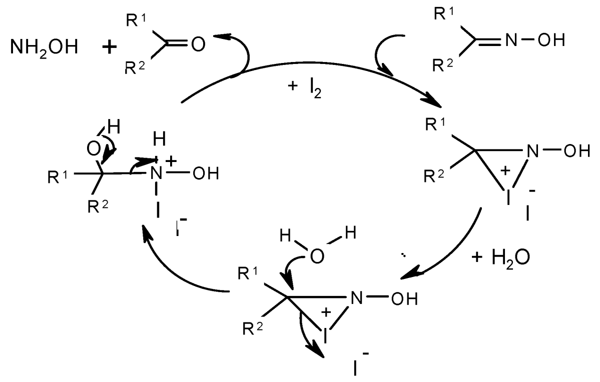
SCHEME 2



Regarding the mechanism of the reaction, it is proposed that the surfactant promotes micelle formation from iodine and the oxime/imine in water, in which the electrophilic iodine activates hydration of the carbon−nitrogen double bond, possibly via an iodonium ion, that suffers attack by water to form carbonyl compounds and iodine in the reaction mixture [Scheme 2].

In conclusion, the salient features of the reaction are the following: (1) Iodine is an efficient catalyst in the presence of surfactant for the regeneration of carbonyl compounds from oximes and imines. (2) The system does not form iodoxime/imidoyl iodide or over-oxidized products (acids) in the reaction mixture. (3) The cleavage of the C═N bond can be carried out in water under neutral condition at 25−40 °C, eliminating toxic and acidic reagents. (4) The workup procedure is simple and yields are good to excellent.

Experimental Section

General Procedure for Deprotection of Oximes to Carbonyl Compounds. In a 50-mL round-bottom flask, iodine (0.2 mmol), oxime (1 mmol), and surfactant (sodium dodecyl sulfate, 0.2 mmol) in H_2O (15 mL) were added with stirring at room temperature for 10 min, then the temperature of the reaction mixture was raised to 40 °C and kept at this temperature for a stipulated time with stirring. The progress of the reaction was monitored by TLC. The product was extracted with diethyl ether (2 × 25 mL), the organic layer was washed with brine (2 × 15 mL), dried over anhydrous Na_2SO_4, concentrated, and purified by column chromatography on SiO_2 (60−120 mesh) with use of an ethyl acetate/hexane mixture as eluent; distillation of the solvent under reduced pressure gave carbonyl compounds.

4-Methoxybenzaldehyde (3g). 4-Methoxybenzaldehyde was prepared from 4-methoxybenzaldoxime by using the general procedure described above: 123 mg, (isolated yield; 90.4%) as a liquid; ^1H NMR ($CDCl_3$, 60 MHz) δ 9.87 (s, 1H), 7.83 (d, 2H), 7.0(d, 2H), 3.87 (s, 3H); FTIR ($CHCl_3$) 1684 cm^{-1}. Anal. Calcd for $C_8H_8O_2$ (136.15): C, 70.58; H, 5.92. Found: C, 70.58; H, 5.88.

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Supporting Information Available: Characterization data including ^1H NMR, FTIR, and elemental analyses of all the compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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