



Regeneration Of Carbonyl Compounds From Their Oximes Using P-Chloroperbenzoic Acid

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Accepted on 6th April 2014

ABSTRACT

Rapid deoximation of aldoximes and ketoximes, substituted with different electron withdrawing and donating groups, has been achieved in excellent yields in the presence of p-chloroperbenzoic acid in dry-media conditions. Oximes of some steroidal compounds have also been deoximated. The method is highly efficient and the work-up is very simple.

Keywords: p-chloroperbenzoic acid, Aldehydes, Ketones, Steroids, Deoximation, Dry-media, Micro wave assisted reactions.

INTRODUCTION

Carbonyl compounds are very useful starting materials for various transformations in organic synthesis. Therefore, it becomes necessary to protect them and to deprotect them as well, when required. One of the simplest potential routes is to convert them into oximes [1]. Oximes are significant derivatives of carbonyl compounds with C=N-OH functional group. Oximation represents a classical method for purification, characterisation and protection of carbonyl compounds. Many methods for the regeneration of carbonyl compounds from oximes have been reported. These include the hydrolytic method, oxidative cleavage or reductive cleavage [1]. However, in view of some limitations like use of harsh reaction conditions, limited yields of carbonyl compounds and production of environmentally harmful by-products etc., there is still a need for developing new, more efficient and eco-friendly protocols for deoximations.

In recent times, organic synthesis under solvent-free conditions using microwave irradiations has become increasingly popular [2-6]. Major advantages of the use of MW irradiations for conducting organic reactions include avoiding the use of organic solvents leading to clean, eco-friendly and efficient reactions. Because of our interest in carrying out organic reactions in dry media conditions by utilizing microwave energy [2-6], we report herein the rapid deoximation of aldoximes and ketoximes in the presence of p-chloroperbenzoic acid under solvent-free conditions.

MATERIALS AND METHODS

General: The aldehydes, ketones and steroidal compounds were purchased from Sigma-Aldrich and Fluka. The reactions were monitored by analytical thin layer chromatography (TLC) performed on glass plates precoated with silica gel G as supplied by Sisco Research Laboratories (SRL). ¹H-NMR was

recorded on a 400MHz spectrometer (Bruker Avance II 400). The chemical shifts were determined using Tetramethylsilane (TMS) as internal standard at δ 0.0 or to the signal of residual CDCl_3 δ 7.26. ^{13}C -NMR (100MHz) was recorded using CDCl_3 as solvent. Oximes of all carbonyl compounds were prepared according to reported procedure [6].

Procedure for the deoxygenation of oximes : p-Chloroperbenzoic acid (100 mg) and the oxime (1 mmol) were mixed thoroughly in a 10 mL beaker and microwaved with discontinuous heating at 35°C . The progress of reaction was monitored by TLC. After completion of the reaction, the reaction mixture was extracted with ether, filtered and the solvent evaporated off under reduced pressure to yield the corresponding product, benzophenone. Same procedure was followed for the regeneration of other carbonyl compounds from their oximes under the identical reaction conditions. The products were identified on the basis of comparison of their melting points/boiling points and spectroscopic data with those of the authentic samples and found in good agreement with literature.

Data analysis

Benzophenone (1a): M.P. 49°C . ^1H NMR: δ 7.806 (d, $J = 8.5$ Hz, 2H), 7.579 (t, 1H), 7.470 (t, 2H). ^{13}C NMR: δ 196.78, 137.60, 132.96, 130.08, 128.31.

Acetophenone (1b): B.P. 197°C . ^1H NMR: δ 7.961 (m, 2H), 7.509 (m, 3H), 2.605 (s, 3H). ^{13}C NMR: δ 199.12, 136.21, 133.11, 128.51, 128.22, 27.59.

4-nitroacetophenone (1c): M.P. 75°C . ^1H NMR: δ 8.224 (m, 4H), 2.702 (s, 3H). ^{13}C NMR: δ 197.36, 150.46, 141.52, 129.39, 122.86, 26.91.

4-methoxyacetophenone (1d): M.P. 39°C . ^1H NMR: δ 7.929 (d, $J = 7.2$ Hz, 2H), 6.929 (d, $J = 7.1$ Hz, 2H), 3.863 (s, 3H), 2.546 (s, 3H). ^{13}C NMR: δ 196.41, 163.49, 130.52, 130.37, 113.67, 55.34, 26.14.

Cyclohexanone (1e): B.P. 157°C . ^1H NMR: δ 2.335 (m, 4H), 1.862 (m, 4H), 1.728 (m, 2H). ^{13}C NMR: δ 211.03, 42.02, 27.09, 25.03.

4-hydroxyacetophenone (1f): M.P. 109°C . ^1H NMR: δ 8.502 (s, 1H, OH), 7.915 (d, $J = 8.0$ Hz, 2H), 6.974 (d, $J = 7.9$ Hz, 2H), 2.593 (s, 3H). ^{13}C NMR: δ 199.53, 162.12, 130.45, 128.20, 115.77, 26.25.

4-nitrobenzaldehyde (2a): M.P. 103°C . ^1H NMR: δ 10.128 (s, 1H), 8.337 (d, $J = 8.5$ Hz, 2H), 8.098 (d, $J = 8.5$ Hz, 2H). ^{13}C NMR: δ 192.36, 150.48, 139.90, 130.40, 123.91, 39.56.

2-nitrobenzaldehyde (2b): M.P. 41°C . ^1H NMR: δ 10.521 (s, 1H), 7.904 (m, 4H). ^{13}C NMR: δ 188.21, 150.57, 135.16, 133.73, 131.35, 129.56, 124.49.

2, 4-dimethoxybenzaldehyde (2c): M.P. 68°C . ^1H NMR: δ 10.257 (s, 1H), 7.787 (m, 1H), 6.529 (m, 1H), 6.471 (m, 1H), 3.889 (s, 3H), 3.864 (s, 3H). ^{13}C NMR: δ 188.14, 166.27, 163.68, 130.53, 119.03, 105.96, 97.87, 55.60.

4-chlorobenzaldehyde (2d): M.P. 46°C . ^1H NMR: δ 9.962 (s, 1H), 7.801 (d, $J = 9.0$ Hz, 2H), 7.485 (d, $J = 9.0$ Hz, 2H). ^{13}C NMR: δ 190.77, 140.91, 134.82, 130.89, 129.45.

4-hydroxybenzaldehyde (2e): M.P. 114°C . ^1H NMR: δ 10.241 (s, 1H, OH), 9.815 (s, 1H), 7.789 (d, $J = 8.9$ Hz, 2H), 6.965 (d, $J = 8.8$ Hz, 2H). ^{13}C NMR: δ 191.26, 161.65, 132.56, 129.94, 116.06.

4- bromobenzaldehyde (2f): M.P. 57 °C. ^1H NMR: δ 9.964 (s, 1H), 7.702 (d, J = 9.0 Hz, 2H), 7.621 (d, J = 9.0 Hz, 2H). ^{13}C NMR: δ 190.96, 135.13, 132.44, 130.94, 129.72.

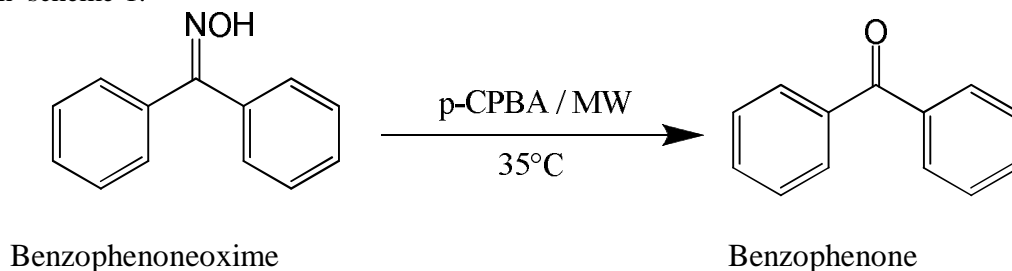
Testosterone propionate (3a): M.P. 154 °C. ^1H NMR: δ 5.731 (s, 1H), 4.614 (t, 1H), 2.414 (m, 6H), 2.192 (m, 1H), 2.013 (m, 1H), 1.837 (m, 2H), 1.691 (m, 2H), 1.562 (m, 3H), 1.359 (m, 2H), 1.227 (m, 4H), 1.156 (t, 3H), 1.072 (m, 2H), 0.959 (m, 1H), 0.839 (s, 3H). ^{13}C NMR: δ 199.48, 174.52, 170.99, 123.95, 82.22, 53.69, 50.24, 42.51, 38.60, 36.63, 35.69, 35.39, 33.93, 32.74, 31.48, 27.80, 27.52, 23.48, 20.52, 17.39, 12.03, 9.27.

trans - androsterone (3b): M.P. 181 °C. ^1H NMR: δ 0.694 (m, 1H), 0.865 (m, 6H), 0.995 (m, 2H), 1.132 (m, 1H), 1.309 (m, 6H), 1.567 (m, 4H), 1.737 (m, 3H), 1.816 (m, 3H), 1.950 (m, 1H), 2.088 (m, 1H), 2.470 (m, 1H), 3.598 (s, 1H, OH). ^{13}C NMR: δ 221.48, 71.13, 54.44, 51.43, 47.82, 44.84, 38.05, 36.95, 35.86, 35.65, 35.05, 31.56, 31.42, 30.90, 28.40, 21.78, 20.51, 13.82, 12.31.

α - tetralone (3c): B.P. 114 °C. ^1H NMR: δ 7.95- 7.25 (m, 4H), 2.61 (m, 2H), 2.57 (m, 2H), 1.89 (m, 2H). ^{13}C NMR: δ 198.8, 139.9, 138.8, 133.4, 129.6, 128.5, 126.6, 42.3, 25.5, 31.8.

RESULTS AND DISCUSSION

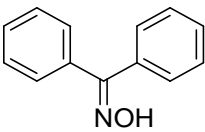
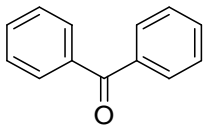
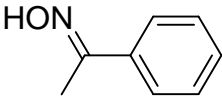
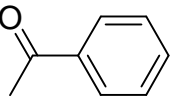
Cl-C₆H₄COOOH (p-CPBA) was thought to be a good and mild organic acid, which is easy to handle as well. Reactions were carried out under microwave irradiations at 35°C. The deoxygenation of benzophenoxime occurred within 82 seconds and the product, benzophenone was obtained in 88% yield as shown in scheme-1.

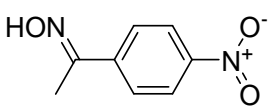
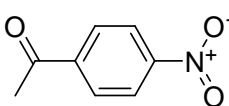
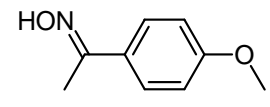
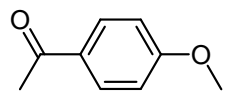
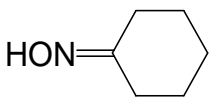
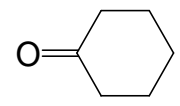
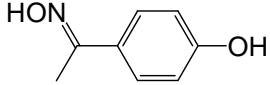
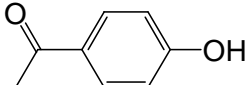


Scheme-1

Deoxygenation worked well for different ketoximes with variously substituted groups and deoxygenated products were obtained in high yields under these mild conditions as recorded in table-1.

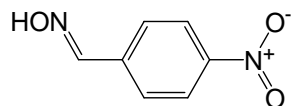
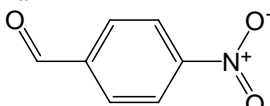
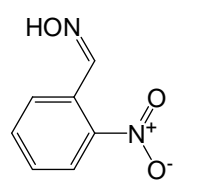
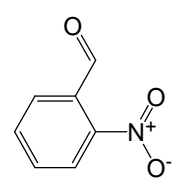
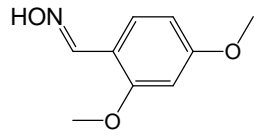
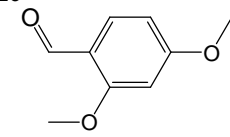
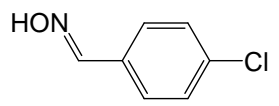
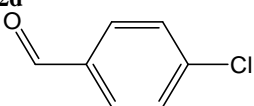
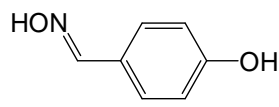
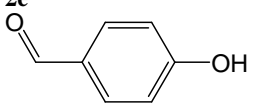
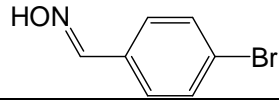
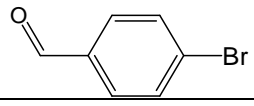
Table-1. Rapid deoxygenation of variously substituted ketoximes in dry-media in the presence of p-chloroperbenzoic acid.

SUBSTRATE (Oximes)	YIELD (%)	TIME (Sec.)	PRODUCT (Ketones)
	88	82	1a 
	87	75	1b 

	83	80	1c 
	80	92	1d 
	79	95	1e 
	84	85	1f 

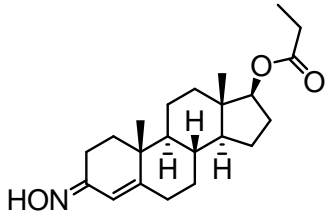
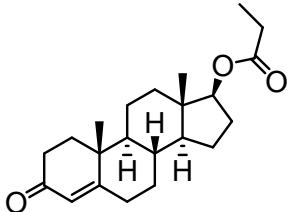
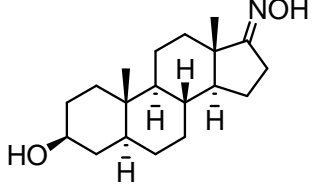
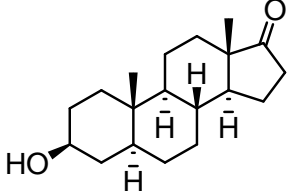
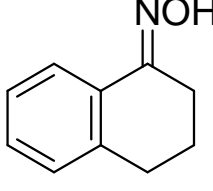
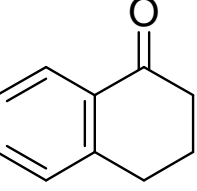
Our next attention is towards deoximation of aldoximes using the same approach. A noteworthy feature of the above transformation is that the presence of the electron withdrawing groups such as $-\text{NO}_2$, $-\text{Br}$, $-\text{Cl}$ or electron releasing groups such as $-\text{OH}$, $-\text{OMe}$ on the aromatic ring of aldoximes did not affect the efficiency of catalyst as shown in table-2.

Table-2. Rapid deoximation of variously substituted aldoximes in dry-media in the presence of p-chloroperbenzoic acid.

SUBSTRATE (Oximes)	YIELD (%)	TIME (Sec.)	PRODUCT (Aldehydes)
	81	80	2a 
	80	82	2b 
	83	92	2c 
	88	75	2d 
	86	85	2e 
	82	83	2f 

Another peculiar feature of the catalyst is that the oximes of steroidal compounds having ketonic group like testosterone propionate and trans- androsterone also underwent deoxygenation under the identical reaction conditions and gave the corresponding product in 80-85% yield, without any effect on the rings of the steroidal compound. Deoxygenation of oxime of 1-tetralone, a sterically hindered compound, has also been done with the same procedure and the expected product was obtained in good yield as shown in Table-3.

Table-3. Rapid deoxygenation of oximes of sterically hindered compounds in dry-media in the presence of p-chloroperbenzoic acid.

SUBSTRATE	YIELD (%)	TIME (Sec.)	PRODUCT
	84	70	<p>3a</p> 
	85	75	<p>3b</p> 
	80	80	<p>3c</p> 

APPLICATIONS

Oximes have great biological and pharmacotherapeutic profiles. Perillartine, an oxime of perillaldehyde is used as an artificial sweetener, being 2000 times more sweet than sucrose[7]. Oximes also act as antidotes for nerve agents[7]. Oximes find a great application for the conversion of cyclohexanone into its oxime. About half a billion kilograms supply of cyclohexanone is converted into its oxime annually in the world[7].

CONCLUSIONS

In conclusion, the deoxygenation of compounds having carbonyl group with p-CPBA under microwave irradiations in dry-media conditions is a rapid, manipulative, simple and selective protocol in comparison to the conventional solution phase reactions which suffer from the use of organic pollutant solvents, long reaction times and low yields. The prominent advantage of the catalyst is that it affected only C=N bond of the oxime group while other functional groups remained intact.

ACKNOWLEDGMENT

We would like to thank University Grant Commission (UGC) for financial support.

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