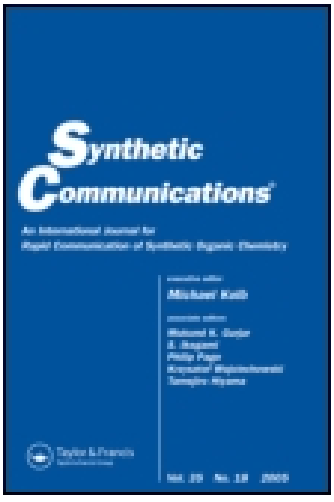

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Oxidative Cleavage of Oximes with Silica-Gel-Supported Chromic Acid in Nonaqueous Media

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Oxidative Cleavage of Oximes with Silica-Gel-Supported Chromic Acid in Nonaqueous Media

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Abstract: A simple procedure for a clean and high-yielding oxidative deoximation of benzaldoximes and ketoximes using a silica-gel-supported chromic acid reagent has been developed. This solid-supported reagent allows us to carry out this reaction in nonaqueous dichloromethane reaction media.

Keywords: Chromic acid, chromic acid–SiO_2, deoximation, solid support

Deriving aldehydes and ketones to the corresponding oximes serves a number of useful purposes in organic synthesis. Aldehydes and ketones protected as oximes can later be removed to expose the original carbonyl functional group in the synthesis of complex organic molecules.[1] Unstable carbonyl compounds are often converted to crystalline oximes for purification and characterization.[2]

Also, oximes prepared from noncarbonyl compounds serve as a source of aldehydes and ketones. Therefore, regeneration of carbonyl compounds from oxime derivatives is an important transformation in organic synthesis. Among others, hydrolytic[3–12] and oxidative[13–16] deoximation procedures are used

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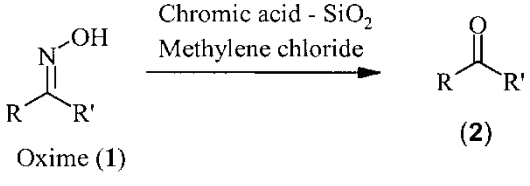
widely. The majority of these procedures generally employ water-soluble inorganic reagents in aqueous or aqueous–organic biphasic reaction media. Tedious workup, difficult product isolation, and low yield are often encountered when water is used. Also, these reactions generate aqueous waste, requiring treatment before disposal. Reactions in nonaqueous media utilizing reagents supported on a solid support eliminate these disadvantages. In addition, heterogeneous reactions offer additional advantages, such as easy workup, higher yield, greater selectivity, enhanced reaction rate, and production of smaller amounts of waste.[17] Reagents possessing adverse health and environmental effects are safer to handle when they are supported on solid support.

Previously, we reported a simple silica-gel-supported chromic acid reagent for oxidation of alcohols to carbonyl compounds employing dichloromethane reaction media.[18,19] We herein report the oxidative regeneration of carbonyl functional groups from oximes using a similar procedure (Scheme 1).

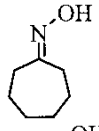
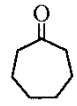
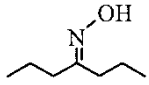
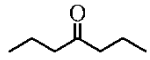
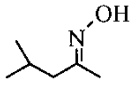
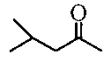
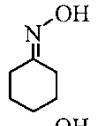
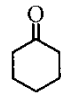
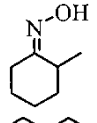
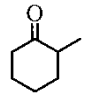
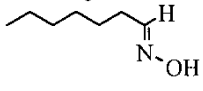
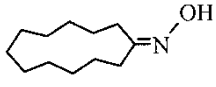
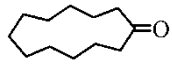
We have treated several ketoximes and aldoximes with silica-gel-supported chromic acid in dichloromethane reaction media to achieve deoximation (see Tables 1 and 2 for detailed results). This procedure allowed us to convert benzaldoximes **1j** and **1n** to the desired benzaldehydes **2j** and **2n** in excellent yields in a short reaction time (Table 2). Further oxidations of the benzaldehyde products were not observed. This observation is in agreement with our previous report on oxidation of benzyl alcohols to benzaldehydes with a similar reagent, which produced benzaldehydes without complications from overoxidation.[19] However, the reaction conditions utilized in this study are not suitable for deoximation of aliphatic aldoximes. Aliphatic aldoxime **1f** produced a mixture of heptanal, heptanoic acid, and some unidentified compounds (Table 1). All attempts to improve selectivity and yield of aldehydes from deoximation of aliphatic aldoximes failed.

Aliphatic and aromatic ketoximes **1a–e**, **1g–i, 1k**, and **1o** produced satisfactory results when they were subjected to the deoximation reaction. Deoximation of 2-indanone oxime **1l** and benzoin oxime **1m** each produced a mixture of unidentified products. These results were not surprising to us because it is known that chromic acid promotes oxidation at the benzylic



Scheme 1. R and R′ = alkyl and/or aryl gr; R = alkyl and/or aryl gr.; R′ = H.

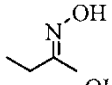
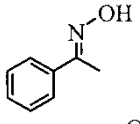
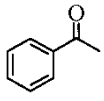
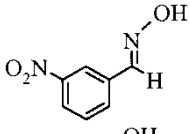
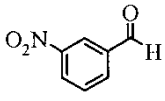
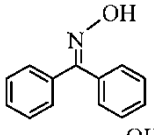
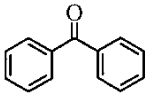
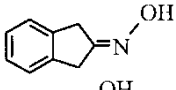
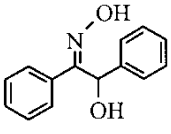
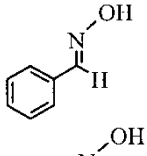
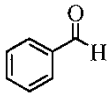
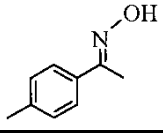
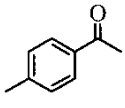
Table 1. Deoximation of aldo- and ketoximes **1a–g**

Entry	Oxime (**1**)	Aldehydes/ketones (**2**)	Yield (%)
a			95.5
b			97
c			85.5
d			97
e			97
f		Mixture of products	
g			93

position and cleavage of activated C-C bonds.[20] 2-Indanone oxime **1l** has two activated benzylic carbons that can undergo oxidation, and benzoin oxime **1m** possesses an activated C-C bond between the two phenyl rings that can be cleaved easily.

We have not probed the mechanism of this deoximation reaction; however, it is clear from the result of our study that the reaction follows an oxidative and not an acid-catalyzed hydrolysis mechanism. An attempted hydrolytic deoximation of cyloheptanone oxime **1a** with silica-gel-supported sulfuric acid produced only unreacted starting materials. (See Ref. 7 for sulfuric acid–promoted deoximation reactions.) This result indicates that sulfuric acid supported on silica gel is not capable of hydrolyzing oximes to carbonyl compounds. We believe the sulfuric acid present in our chromic acid solution is strongly bound to the silica gel and is not available for promoting hydrolysis of the oxime functional group. Therefore, we postulate that chromic acid supported on silica gel oxidatively cleaves the C=N bond of oximes.

Table 2. Deoximation of aldo- and ketoximes **1h–o**

Entry	Oxime (**1**)	Aldehydes/ketones (**2**)	Yield (%)
h			68
i			93
j			98
k			83
l		Mixture of products	
m		Mixture of products	
n			93
o			82

Silica-gel-supported chromic acid reagent takes only a few minutes to prepare and has a long shelf life. Two-year-old and freshly prepared heterogeneous reagents both produced identical results.

In conclusion, we have developed a convenient method for oxidative regeneration of carbonyl compounds from oximes utilizing chromic acid in nonaqueous media.

EXPERIMENTAL

All reaction mixtures were stirred using a magnetic stirrer. Oximes were purchased from several chemical suppliers or prepared using literature

procedures. Solvents were used as received from the supplier without any further purification. Chromic acid solution was prepared according to the literature method.[1] The silica gel used in the oxidation reactions as solid support was MN-Kieselgel 60 (0.04–0.063-mm mesh) supplied by Fisher Scientific. NMR spectra were recorded on a Bruker DPX-300 NMR instrument (^{1}H at 300 MHz, ^{13}C at 75 MHz). Samples for NMR were dissolved in $CDCl_3$. Proton chemical shifts are expressed as parts per million (ppm) relative to tetramethylsilane, and ^{13}C chemical shifts were referenced to the solvent signal. IR spectra were recorded on a Perkin-Elmer Spectrum-1000 Fourier Transformed-Infra Red (FT-IR) instrument and are reported in wavenumbers (cm^{-1}). Preparative centrifugal thin-layer chromatography with silica gel (Merck #7749) was done on a Chromatotron model 7924T. Analytical thin-layer chromatography was done on precoated silica-gel plates with 254-nm fluorescent indicator (Merck #5715) and developed in a 1:9 mixture of ethyl acetate–hexane. Compounds were visualized by UV and/or by staining either with a *p*-anisaldehyde/sulfuric acid or phosphomolybdic acid.

General Procedure

Silica gel (2 g) and a magnetic stirrer bar were placed in a 50-mL round-bottom flask fitted with a rubber septum. Using a syringe, 1.0 mL of a 2.5 M chromic acid solution (2.5 mmol) was added drop by drop to the stirred silica gel in the flask. Stirring continued until an orange-colored free-flowing solid was obtained (less than 5 min). Dichloromethane (15 mL) was introduced into the flask followed by a solution of 2 mmol of the oxime under investigation in 2–3 mL of dicholoromethane. Progress of all reactions was monitored by TLC. All oximes, except the highly sterically hindered ketoxime **1k**, took only a few minutes to complete the reaction.

However, all reaction mixtures were stirred for 10–15 min before workup. The sterically hindered benzophenone oxime **1k** took 6 h to complete the reaction. After the reaction was complete, the content of the flask was filtered through a fritted glass funnel, and the solid residue washed with an additional 50–60 mL of dichloromethane. Dichloromethane was removed from the combined solution using a rotary evaporator. The crude products were purified by radial chromatography to produce excellent yields (Tables 1 and 2). All products produced identical NMR (proton and carbon) data as reported in the literature.[21]

Data

Cycloheptanone (2a). ^{1}H NMR ($CDCl_3$) 1.60–1.80 (m, 8H), 2.40–2.60 (m, 4H). ^{13}C NMR ($CDCl_3$) 24.40, 30.50, 43.95, 215.45. IR (film) 736, 855, 941, 1162, 1272, 1343, 1455, 1565, 1699, 2858, 2929 cm^{-1}.

4-Heptanone (2b). ^{1}H NMR ($CDCl_3$) 0.90 (t, $J = 7.45$ Hz, 6H), 1.55–1.65 (m, 4H), 2.36 (t, $J = 7.20$ Hz, 4H). ^{13}C NMR ($CDCl_3$) 13.98, 17.75, 45.10, 212.0. IR (film) 736, 947, 1160, 1275, 1346, 1456, 1566, 1710, 2852, 2936 cm^{-1}.

4-Methyl-2-pentanone (2c). ^{1}H NMR ($CDCl_3$) 0.92 (d, $J = 6.0$ Hz, 6H), 2.13 (s, 3H), 2.00–2.15 (m, 1H), 2.30 (d, $J = 6.5$ Hz, 2H). ^{13}C NMR ($CDCl_3$) 22.45, 24.55, 30.30, 52.70, 209.20. IR (film) 818, 1164, 1308, 1390, 1468, 1567, 1709, 2877, 2934, 2965 cm^{-1}.

Cyclohexanone (2d). ^{1}H NMR ($CDCl_3$) 1.68–1.78 (m, 2H), 1.81–1.92 (m, 4H), 2.34 (j, $J = 6.5$ Hz, 2H). ^{13}C NMR ($CDCl_3$) 24.75, 26.80, 41.70, 211.90. IR (film) 1118, 1221, 1311, 1450, 1711, 2876, 2938 cm^{-1}.

2-Methylcyclohexanone (2e). ^{1}H NMR ($CDCl_3$) 1.01 (d, $J = 6.5$ Hz, 3H), 1.30–1.45 (m, 1H), 1.60–1.75 (m, 2H), 1.80–1.92 (m, 1H), 2.0–2.15 (m, 2H), 2.2–2.45 (m, 3H). ^{13}C NMR ($CDCl_3$) 14.65, 25.20, 27.65, 36.10, 41.45, 45.25, 213.20. IR (film) 1120, 1226, 1316, 1450, 1715, 2872, 2935 cm^{-1}.

Cyclododecanone (2g). ^{1}H NMR ($CDCl_3$) 1.20–1 40 (m, 14H), 1.68–1.73 (m, 4H), 2.44–2.48 (m, 4H). ^{13}C NMR ($CDCl_3$) 22.70, 22.95, 24.60, 24.96, 25.12, 40.68, 213.40. IR (film) 722, 942, 1019, 1130, 1247, 1362, 1444, 1469, 1567, 1708, 2864, 2930 cm^{-1}.

2-Butanone (2h). ^{1}H NMR ($CDCl_3$) 1.10 (t, $J = 6.8$ Hz, 3H), 2.15 (s, 3H), 2.45 (q, $J = 6.8$ Hz, 2H). ^{13}C NMR ($CDCl_3$) 7.90, 29.56, 36.74, 210.10. IR (film) 738, 949, 1156, 1281, 1366, 1466, 1568, 1715, 2856, 2956 cm^{-1}.

Acetophenone (2i). ^{1}H NMR ($CDCl_3$) 2.55 (s, 3H), 7.35–7.52 (m, 3H), 7.92 (d, $J = 7.5$ Hz, 2H). ^{13}C NMR ($CDCl_3$) 26.53, 128.31, 128.60, 133.14, 137.10, 198.13, IR (film) 760, 955, 1180, 1266, 1359, 1449, 1567, 1599, 1685, 2926, 2972, 3006, 3064 cm^{-1}.

3-Nitrobenzaldehyde (2j). ^{1}H NMR ($CDCl_3$) 7.83 (t, $J = 8.05$ Hz, 1H), 8.30 (d, $J = 8.0$ Hz, 1H), 8.50 (d, $J = 8.0$ Hz, 1H), 8.71 (s, 1H) 10.40 (s, 1H). ^{13}C NMR ($CDCl_3$) 124.30, 128.48, 130.21, 134.56, 137.40, 148.82, 189.90. IR (film) 936, 1012, 1086, 1286, 1379, 1448, 1686, 2729, 2824, 2921, 3081 cm^{-1}.

Benzophenone (2k). ^{1}H NMR ($CDCl_3$) 7.43 (t, $J = 7.68$ Hz, 2H), 7.54 (t, $J = 7.68$ Hz, 1H), 7.75 (d, $J = 7.5$ Hz, 2H). ^{13}C NMR ($CDCl_3$) 128.09, 129.84, 132.24, 137.35, 196.47. IR (film) 737, 810, 919, 941, 1074, 1176, 1277, 1318, 1447, 1525, 1598, 1660, 3059 cm^{-1}.

Benzaldehyde (2n). ^{1}H NMR ($CDCl_3$) 7.52 (t, $J = 7.0$ Hz, 2H), 7.62 (t, $J = 7.0$ Hz, IH), 7.88 (d, $J = 7.0$ Hz, 2H), 10.15 (s, 1H). ^{13}C NMR ($CDCl_3$) 128.92, 129.56, 134.32, 136.41, 192.25. IR (film) 924, 1009, 1029, 1081, 1291, 1342, 1668, 2701, 2747, 2965, 3032, 3085 cm^{-1}.

4′-Methylacetophenon (2o). ^{1}H NMR ($CDCl_3$) 2.35 (s, 3H), 2.54 (s, 3H), 7.22 (d, $J = 7.8$ Hz, 2H), 7.82 (d, $J = 2$H). ^{13}C NMR ($CDCl_3$) 21.58, 26.47, 128.45, 129.27, 134.71, 143.90, 197.80. IR (film) 815, 954, 1019, 1182, 1268, 1357, 1406, 1567, 1606, 1681, 2923, 3006, 3056 cm^{-1}.

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