A Versatile Method for the Conversion of Aldoximes to Nitriles Using Selenium Dioxide

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There have been numerous reports over the years concerning the transformation of aldoximes to nitriles[1-10]. Although a great variety of reagents have been used, many of these methods are deficient in some respects, such as low yields, expensive, or not readily available reagents, harsh reaction conditions, or, perhaps, most importantly, a lack of generality for both the aliphatic and aromatic aldoximes. Therefore, the search for a mild and universally applicable method continues. Recently, we reported[11,12] such a mild and generally applicable method using phosphorus imidazolides.

Now we wish to report on another mild and versatile method for the conversion of aldoximes to nitriles in high yield using selenium dioxide in chloroform. This reaction is readily achieved with both the aliphatic and aromatic aldoximes. While the reaction proceeds with aliphatic aldoximes at room temperature in three hours, the reaction with the aromatic aldoximes is achieved in boiling chloroform (Table).

$$\mathrm{R{-}CH{=}N{-}OH} \xrightarrow[\mathrm{R\,=\,aryl;\,reflux}]{\substack{\mathrm{SeO_2/CHCl_3} \\ \mathrm{R\,=\,alkyl;\,20\text{-}23^\circ}}} \mathrm{R{-}C{\equiv}N}$$

It is somewhat surprising that this reaction occurs so readily to give nitriles since in some previous investigations[13] it was found that the reactions of selenium dioxide with dioximes result in heterocyclic compounds of the selenadiazole and oxaselenazole type.

The reaction of aldoximes with selenium dioxide is also surprising in some other respects. Thus, while the optimum yields are obtained using a one to one molar ratio of the aldoxime to selenium dioxide, one obtains also very respectable yields of 59 to 91% using a two to one ratio of aldoximes to selenium dioxide. Furthermore, a reaction using only a one mol percent of selenium dioxide results in the formation of nitriles. For example, the transformation of benzaldoxime and *n*-butyraldoxime resulted in a 36% and 23% yield of the corresponding nitriles.

The reaction can be performed already quite economically with five mol percent of selenium dioxide if water, which is formed during the reaction, is continuously removed. The removal of water can be achieved either with a soxhlet apparatus whose thimble is charged with anhydrous magne-

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sium sulfate or by azeotropic distillation. The yield of nitriles obtained by this catalytic method ranges between 60–82%. In the absence of selenium dioxide, under the same conditions, no reaction occurs, and the unreacted aldoximes are recovered in almost quantitative yield (see experimental).

The reaction always produces some of the red selenium, the α-form, however, most of the selenium dioxide is recovered and can be utilized for further conversions of oximes to nitriles. The selenium itself, either the red α or β, or the black form has no effect on the reaction.

Under the chosen reaction conditions the α-selenium which is formed during the reaction does not interfere with the isolation of products. This result is contrary to previous reports in the literature[13] on experiments with selenium dioxide in solvents other than chloroform where the interference by selenium during the isolation of products is considered to be somewhat of a nuisance.

In conclusion, we feel that the present method, because of its simplicity and versatility, might become the method of choice for the conversion of aldoximes to nitriles.

Materials: All reagents were of the finest quality commercially available. The oximes were prepared by standard methods[14]. The selenium dioxide, of 99.4% purity, was obtained from the Ventron Corporation of Danvers, Maryland. The chloroform was a certified ACS grade from the Fisher Scientific Company of Fair Lawn, New Jersey.

Analytical Procedures: All melting points and boiling points are uncorrected. All I.R. analyses were performed on a Perkin-Elmer Infracord Spectrophotometer, Model 137. ^{1}H-N.M.R. analyses were performed on a Varian T-60 NMR Spectrophotometer using TMS as an internal standard. The purity of liquid products and aliphatic oximes was determined with an Aerograph A90-P3 gas chromatograph with a thermal conductivity detector. The following overall conditions were maintained: injector temperature, 235°; detector temperature, 235°; bridge current, 150 ma; sample size, 1.0 μl with the appropriate attenuations. The column used was 20% Carbowax 20M on 60/80 mesh acid washed Chromasorb W, 6 ft by 1/4 in. Analyses were performed isothermally at 210°, with a flow rate of 50 ml of He/min. Identifications of products were made by the comparison of retention time and peak enhancement ("spiking") with authentic samples. The reactions in all cases were followed by thin layer chromatography on pre-coated 0.2 mm Aluminum Oxide "Polygram", Alox N/uv$_{254}$ sheets, Brinkman Instruments, Inc. of Des Plaines, Illinois, utilizing short wave U.V. radiation for spot visualization. Benzene was used as an eluent in all cases. In the aromatic series, the oximes typically had R_f values of 0.00 to 0.07, and the corresponding nitriles 0.60 to 0.74. In the aliphatic series, the oximes typically had R_f values of 0.52 to 0.67, and the corresponding nitriles 0.03 to 0.10.

Preparation of Nitriles with Equimolar Amounts of Aldoximes and Selenium Dioxide; General Procedure:

A suspension of selenium dioxide (2.22 g, 0.02 mol) and aldoxime (0.02 mol) in chloroform (40 ml) is introduced into a flask fitted with a magnetic stirrer and a reflux condenser topped with a drying tube. The reaction mixture is stirred at room temperature for 3 h in the case of aliphatic aldoximes, or is boiled for 1–3 h in the case of aromatic aldoximes, then cooled to room temperature. Anhydrous calcium chloride (2–3 g) is added to remove the water which is formed during the reaction, and the mixture is

Table. Preparation of Nitriles from Aldoximes

R	Yields [%][a] of nitrile		5 mol% SeO_2[c]	m.p. or b.p./torr (Lit. m.p. or b.p./torr)	n_D^{25} [Lit. n_D (temp)]	I.R. (neat or nujol) ν_{max} [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]
	oxime:SeO_2 1:1[b]	oxime:SeO_2 2:1[b]					
C_6H_5[d]	100	91	73[e], 86[f]	69–70°/10 (69°/10)[15]	1.5274 [1.5289 (20°)][16]	2230	7.2–7.7 (m)
4-O_2N—C_6H_4	82	70	—	146–147° (147, 149°)[15]	—	2230	7.7–8.25 (m)
4-Cl—C_6H_4	84	75	—	91–92° (92°)[15]	—	2225	7.2–7.7 (m)
4-H_3CO—C_6H_4	89	76	—	60° (61–62°)[15]	—	2225	3.7–3.9 (s, 3H); 6.75–7.55 (m, 4H)
n-C_3H_7[d]	80	71	—	116°/750 (117°/760)[15]	1.3849 [1.3842 (20°)][16]	2250	0.9–1.1 (t, 3H); 1.40–2.0 (m, 2H); 2.2–2.5 (t, 2H)
n-C_6H_{13}	84	74	—	67°/10 (183°/760)[15]	1.4111 [1.4104 (30°)][16]	2235	0.75–1.1 (t, 3H); 1.2–2.0 (m, 8H); 2.1–2.6 (m, 3H)
n-C_7H_{15}	68	59	61[e], 74[f]	79°/10, 82°/12 (206°/760)[15]	1.4204, 1.4208 [1.4203 (20°)][16]	2255	0.85–1.1 (t, 3H); 1.2–1.8 (m, 10H); 2.15–2.5 (m, 2H)
cyclo-C_6H_{11}	82	74	82[e], 73[f]	66°/9, 68°/10 (75–76°/16)[17]	1.4524, 1.4526 [1.4515 (19°)][17]	2250	1.0–2.0 (m, 10H); 2.8–3.3 (m, 1H)

[a] Yield of pure isolated products.

[b] Temperature of reaction: for R = alkyl, 20–23°; for R = aryl, boiling chloroform.

[c] Temperature of reaction: boiling chloroform; reaction time: 3 h.

[d] The reaction of benzaldoxime and *n*-butyraldoxime with only one mol percent of SeO_2 produced a 36% and 23% yield of the corresponding nitriles, respectively.

[e] Soxhlet charged with anhydrous magnesium sulfate to remove water.

[f] Azeotropic distillation to remove water.

filtered through a diatomaceous earth packing to remove the drying agent and selenium residues. The solvent is removed on a rotating evaporator at 20–25°/10–15 torr. At this stage, the crude product usually still contains visible traces of red selenium (α-form). The pure nitriles are isolated after short-path distillation under reduced pressure (10–15 torr) in the case of liquids, or recrystallization from ethanol/water in the case of solids (Table).

Reactions with a fifty mol percent and one mol percent of selenium dioxide are performed in an analogous fashion.

Preparation of Nitriles Using Recovered Selenium Dioxide:
The selenium dioxide/selenium residue recovered from a reaction of benzaldoxime with fifty mol percent of selenium dioxide (0.91 g of a slightly red colored solid) is dried in a desiccator. To a suspension of this material in chloroform (40 ml) is added benzaldoxime (2.42 g, 0.02 mol). The reaction mixture is stirred vigorously and brought to a boil. After 3 h, the reaction mixture is worked up as described in the preceding experiment to give benzonitrile; yield: 1.69 g (82%); b.p. 69–70°/10 torr; n_D^{25}: 1.5276 (Lit.[15,16] b.p. 69°/10 torr; n_D^{20}: 1.5289).

Preparation of Nitriles Using a Five Mol Percent of Selenium Dioxide to Aldoxime; General Procedure:
A suspension of selenium dioxide (0.11 g, 0.001 mol) and aldoxime (0.02 mol) in chloroform (50 ml) is introduced into a flask equipped with a magnetic stirrer, and a small Soxhlet extractor topped with a reflux condenser and a drying tube. The thimble contains anhydrous magnesium sulfate to remove water formed during the reaction. Alternatively, the reaction is performed in an apparatus equipped for azeotropic distillation of water using either a device for continuous addition of chloroform or for separation of water and return of chloroform into the reaction flask. The reaction mixture is stirred vigorously and boiled briskly for 3 h, then is worked up as described in the preceding experiments (Table).

Blank Experiments in the Absence of Selenium Dioxide; General Procedure:
A solution of aldoxime (0.02 mol) in chloroform (50 ml) is introduced into a flask equipped with a magnetic stirrer and one of the devices described in the preceding experiment. The solution is stirred vigorously and boiled briskly. After 3 h the reaction mixture is worked up as described in the preceding experiments. There is no reaction observed, and the unreacted aldoximes are recovered. For example: *n*-octaldoxime: 2.80 g (98%); m.p. 59–60° (Lit.[15] m.p. 60°); ^{1}H-N.M.R. ($CDCl_3$): $\delta = 9.01$–9.47 (s, 1 H); 6.68–6.99 (t, 1 H); 2.10–2.60 (m, 3 H); 1.20–1.80 ppm (m, 12 H).

Recovered *benzaldoxime*: 2.37 g (98%); m.p. 34° (Lit.[15] 35°); ^{1}H-N.M.R. ($CDCl_3$): $\delta = 9.30$–9.50 (s, 1 H); 8.05–8.16 (s, 1 H); 7.06–7.65 ppm (m, 5 H).

Recovered p-*methoxybenzaldoxime*: 2.95 g (98%); m.p. 59–61° (Lit.[15] 60–62°); ^{1}H-N.M.R. ($CDCl_3$): $\delta = 8.21$–8.50 (s, 1 H); 8.00–8.05 (s, 1 H); 6.70–6.95 (d, 2 H, H_{arom}); 7.30–7.55 (d, 2 H, H_{arom}); 3.80 ppm (s, 3 H).

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