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# New Method for the Synthesis of Nitriles via the O-TERT-Butyldimethylsilyl Aldoximes

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## NEW METHOD FOR THE SYNTHESIS OF NITRILES VIA THE *O*-*TERT*-BUTYLDIMETHYLSILYL ALDOXIMES

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**Abstract:** The reaction of aromatic aldehyde oximes with TBSCl and imidazole in DMF generates the corresponding O-silylated derivative, which undergoes elimination, affording the nitrile with a high yield. For the fragmentation of the predominantly (E) isomer, a base-catalyzed syn elimination mechanism is proposed.

The development of new methods for the synthesis of aromatic nitriles is important in organic synthesis, since nitriles are useful as intermediates for the preparation of amines,<sup>1</sup> and other functional group moieties.<sup>2</sup> There are many reports on the conversion of oximes, <sup>34</sup> or oxime derivatives <sup>5,6,7</sup> to nitriles. However, we had special interest in finding less toxic, more affordable reagents, that can carry out the transformation in a facile way, in particular, for large scale preparations. In our previous work on the synthesis of *O*-TBS benzaldoxime, benzonitrile was detected as a side product.<sup>8</sup> Presently, we describe a convenient one step procedure for aldoxime transformation to aromatic nitriles under mild basic conditions, using commercially available reagents.

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Entry	Product 3	Yield of $3^{a}(\%)$	m.p. <sup>6,c</sup> (°C)
a	PhCN	81	_
b	4-MeOC <sub>6</sub> H <sub>4</sub> CN	60 <sup>d,e</sup>	57-59 (Lit. <sup>11</sup> 55-56)
C	2-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CN	76 <sup>e</sup>	108-110 (Lit. <sup>10</sup> 110)
d	4-ClC <sub>6</sub> H₄CN	72 <sup>d,e</sup>	85-87 (Lit. <sup>11</sup> 91-92)
e	Me₂NC6H₄CN	65°	70-71 (Lit. <sup>11</sup> 73-74)
f	PhCH=CHCN	50°	oil

Table 1. Isolated Yields of Nitriles 3

<sup>a</sup> Isolated yield of pure product characterized by IR. <sup>b</sup> Uncorrected melting points. <sup>c</sup> Melting points are from products recrystallized in hexane/dichloromethane. <sup>d</sup> Structure confirmed by NMR. <sup>e</sup> Molecular ion determined by GC/MS.

#### Scheme 1



Representative aromatic aldoximes were treated with *tert*butyldimethylchlorosilane (TBSCI) in the presence of imidazole in DMF at  $100^{\circ}$ C. The reaction proceeded smoothly, first to the *O*-silylated oxime 2, which then underwent fragmentation to afford the corresponding nitriles 3 in good yield, as shown in table 1.

The initial formation of the silvlated oxime 2 is postulated since the O-TBS benzaldoxime was previously isolated and characterized as a mixture of the E and Z isomers in a 92% and 8% yield, respectively.8 No isomerization took place when the pure silvloxime was heated up to 140°C for 48 h. In addition, benzonitrile was not detected when O-TBS benzaldoxime was heated without imidazole at 140°C for two days in DMF or diglyme. We also noticed that an electron withdrawing group promotes the silvloxime fragmentation. The O-TBS-4-nitrobenzaldoxime decomposed below 100°C and the isolation of the silvlated derivative was elusive. These results are in accord with a base-catalyzed syn elimination mechanism, as shown in scheme 1. Hegarty et al.<sup>6</sup> were the first to establish this mechanism by the comparative kinetic studies for the hydroxide-catalyzed elimination reaction of aromatic (E)- and (Z)oxime ethers. Analogous reactions have appeared recently for nitrile-forming elimination reactions involving a syn elimination mechanism: (E)-benzaldoxime-Omethyl ethers with lithium diisopropylamide,<sup>13</sup> (E)-O-arylbenzaldoximes with tertiary amines,<sup>14</sup> and the dehydration of oximes with N-trifluoroacetylimidazole<sup>15</sup>, or 4,6diphenyl-2-methylthiopyrylium tetrafluoroborate.<sup>10</sup> Cho et al.<sup>16</sup> reported recently a kinetic study for the elimination reactions of (E)- and (Z)-benzaldehyde Opivaloyloximes. They confirmed that the reaction proceeds in a stereospecific way, and as expected, the anti elimination is the most facile process in the formation of the carbon-nitrogen triple bond.

In summary, the method presented here was found to be simple and useful for the conversion of aromatic oximes to nitriles.

#### Experimental

<sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a GE 300 MHz in CDCl<sub>3</sub> solution using TMS as internal reference. Mass spectra were measured at 70 eV on a HP 5996 G instrument. Analytical gas chromatography (GC) was performed using a flame ionization detector and a capillary column (25 mm X 0.33 mm bonded methylsilicone). All experiments were carried out under an atmosphere of dry nitrogen and using standard procedures for handling air sensitive compounds. Oximes were prepared according to the previously reported method.<sup>8</sup> Commercial grade reagents were used without further purification, except for dimethylformamide (DMF) which was distilled over CaH<sub>2</sub> prior to use.

### General Procedure for Nitrile Synthesis: 4-Methoxybenzonitrile (3b)

A solution of imidazole (4.1 g, 60 mmol) in DMF (12 mL) was added dropwise, to a stirred solution of 4-methoxybenzaldoxime (1b, 3.2 g, 20 mmol) and *tert*-butyldimethylchlorosilane (3.6 g, 24 mmol) in dry DMF (8 mL) at room temperature. The reaction mixture was heated at 100°C for about 24 h, and the reaction progress monitored by GC and/or TLC. After the reaction was completed, ice water (30 mL) was added to the cooled mixture, which then was extracted with diethyl ether (4x 25 mL). The organic extract was washed with saturated NaCl (30 mL), dried (NaSO<sub>4</sub>) and the solvent rotoevaporated. Purification by recrystallization (hexane/dichloromethane, 4:1v/v) provided the title compound, (1.6 g, 60%) as white crystals: m.p. 57-59°C (Lit<sup>10</sup> 60-61°C);  $v_{max}$ /cm<sup>1</sup>: 3054, 2226(CN), 1607, 1027, 837;  $\delta_{\rm H}$ : 3.85 (3H, s, CH O), 6.93 (2H, d, Ar-H), 7.56 (2H, s, Ar-H);  $\delta$  55.5 (CH<sub>3</sub>O), 114.7 (Ar), 133.93 (Ar), 162.79 (CN); Rt: 10.25 min; m/z: 133 (M, 100%), 118 (M-CH<sub>3</sub>, 15%), 103 (PhCN, 50%), 90 (99.5%), 75 (27%), 64 (59%).

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