

## Preparation of *gem*-Dichloroalkanes from Oximes

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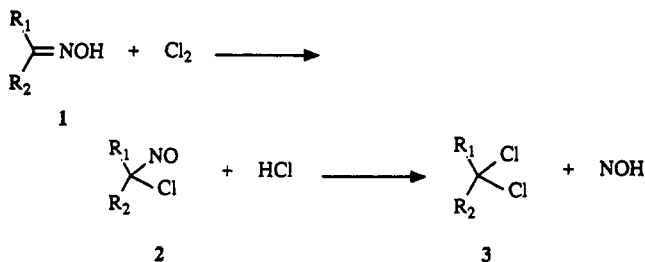
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It is curious that, while many methods have been developed for the deoxyhalogenation of ketones as well as their corresponding oxime and hydrazone derivatives to give *gem*-difluorides,<sup>1</sup> preparation of the analogous *gem*-dichlorides often results in poor yields or is limited to specific substrates.<sup>2</sup> More specifically, the use of phosphorous pentachloride for the above transformation gives a mixture of the desired *gem*-dichloride and the corresponding chloroalkene,<sup>3</sup> or even more complex systems containing several polychlorinated compounds.<sup>4</sup> Furthermore, large excesses of reagent are required, resulting in the production of large quantities of phosphorus oxytrichloride byproduct. Preparation of the *gem*-dichlorides from the corresponding chloroalkenes is equally complex. Treatment of the oximes with strong acids (e.g., sulfuric acid) or chlorinating agents (e.g., phosphorus pentachloride or thionyl chloride) at elevated temperatures typically effects a Beckmann rearrangement to the corresponding amides.<sup>5</sup> At lower temperatures, treatment of the oximes with chlorine in hydrochloric acid<sup>6</sup> or under neutral conditions<sup>7,8,9</sup> gives *gem*-chloronitrosoalkanes. The action of hydrogen chloride on these *gem*-chloronitrosoalkanes has been studied,<sup>10</sup> the starting compounds are recovered with inversion of configuration. Substitution of the nitroso group is only observed in peculiar cases or under unusual conditions. The transformation of oximes, or their *gem*-chloronitroso derivatives, to *gem*-dichloroalkanes by treatment with hypochlorous acid is limited to the adamantane series.<sup>11</sup> Radical reactions of perfluoronitrosoalkanes with chlorine leads to chloroperfluoroalkanes.<sup>12</sup> Under photochemical activation, randomization

of the chloro and nitroso group occurs, giving a mixture containing *gem*-dichloroalkanes.<sup>13</sup>

We wish to report herein a simple method for the direct chlorination of oximes in the presence of either Lewis acids or strong Bronsted acids, which results in the production of the desired *gem*-dichloroalkanes in fair to good yields. In a one pot procedure, chlorine was bubbled into a mixture of the oxime and aluminum trichloride in dichloromethane. The reaction medium became blue, and the chlorination was continued until this blue color vanished. Following the above protocol, cyclohexanone oxime (1a) was converted to 1,1-dichlorocyclohexane (3a) in 66% yield. Similarly, 1,1-dichlorocyclopentane (3b) (68%), 2,2-dichloropropane (3c) (40%), 2,2-dichlorononane (3d) (82%), and 4,4-dichloroheptane (3e) (73%) were produced from the oximes of cyclopentanone 1b, acetone 1c, 2-nonanone 1d, and 4-heptanone 1e, respectively.



The reaction pathway is believed to involve initial chlorination of the oxime 1 to give the *gem*-chloronitrosoalkane 2 followed by acid- or Lewis acid-mediated substitution of the nitroso group with chloride.<sup>14</sup> The intermediacy of the *gem*-chloronitrosoalkane and the requirement of the Lewis or strong Bronsted acid for *gem*-chlorination was verified by the following series of experiments. Cyclohexanone oxime (1a) was added to a stoichiometric amount of chlorine in carbon tetrachloride; the mixture became deep blue, indicating the presence of the *gem*-chloronitrosocyclohexane 2a. An excess of 99% nitric acid was then added to the mixture. The deep blue color vanished, and a reddish-brown vapor was emitted. Following solvent evaporation, the formation of the *gem*-dichlorocyclohexane 3a was noted. On the contrary, if anhydrous hydrogen chloride was bubbled into the deep-blue solution, the *gem*-chloronitrosocyclohexane 2a persisted intact. This experiment confirms the failure of the transformation when the medium is insufficiently acidic and explains why this simple preparation for *gem*-dichloroalkanes has thus far gone unreported.<sup>10</sup> In addition, it was found that either trifluoromethanesulfonic acid or boron trifluoride etherate could be successfully substituted for aluminum trichloride, providing the desired 1,1-dichlorocyclohexane (3a) in 70% and 82% yields, respectively. However, in the case of trifluoromethanesulfonic acid, it was necessary that the acid be slightly hydrated.

Thus far the reaction has remained limited to primary or secondary dialkyl ketone derivatives having at least one hydrogen present  $\alpha$  to the oxime function.<sup>8</sup> In addition, introduction of an aromatic nucleus on the alkyl

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

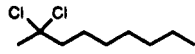
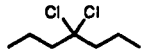
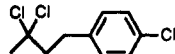
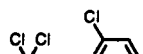
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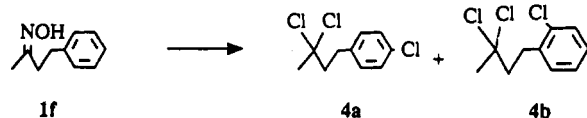
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Table I.  $^{13}\text{C}$  NMR Characteristics

	C1	C2	C3	C4	C5	C6	C7	C8	C9
	91.7	46.2	23.7	24					
<b>3a</b>									
	91.6	47.7	22.7						
<b>3b</b>									
	39.6	85	39.6						
<b>3c</b>									
	37.2	90.6	49.7	25.6	28.8–28.4		31.6	22.6	13.9
<b>3d</b>									
	13.1	18.3	49.6	90.1	49.6	18.1	13.1		
<b>3e</b>									
	37.4	89.6	51.1	31.3	138.6 131.8 (C-Cl)	129.7–128.5			
<b>4a</b>									
	37.2	89.7	49.2	30.1	137.7 133.8 (C-Cl)	130.4–129.5–127.9–176.9			
<b>4b</b>									

side chain, e.g., benzylacetone oxime (1f), led to the formation of the ring chlorination byproducts 4a and 4b.



In this experiment, we did not detect any product arising from the capture of a possible cationic intermediate by the aromatic substituent. However, this observation cannot be considered as conclusive evidence for the absence of such a species in the substitution of the nitroso group by a chlorine atom.

### Experimental Section

**Method 1.** Chlorine was bubbled with stirring in boron trifluoride etherate (20 mL) containing cyclohexanone oxime (1 g), chlorination was maintained for 0.5 h after the end of the gaseous absorption, and then the mixture was stirred for 8 h. The mixture was poured over ice (100 g) and then extracted with ether (100 mL). The organic layer was washed with 5% hydrochloric acid, sodium hydrogen carbonate solution, and brine and then dried over magnesium sulfate. 1,1-Dichlorocyclohexane<sup>2a</sup> (3a) was distilled (82%), bp = 73 °C/20 Torr. However, chlorination and oxidation of diethyl ether also occurred, giving derivatives of chlorinated acetaldehyde.

**Method 2.** Chlorine was bubbled with stirring in trifluoromethanesulfonic acid (slightly hydrated with less than 1/1 stoichiometry of water) (3 mL) containing cyclohexanone oxime (1 g), chlorination was maintained for 0.5 h after the end of the gaseous absorption, and then the mixture was stirred for 3 h. The mixture was poured over ice (100 g) and then extracted with ether (100 mL). The organic layer was washed with 5% hydrochloric acid, sodium hydrogen carbonate solution, and brine and then dried over magnesium sulfate. 1,1-Dichlorocyclohexane

was obtained (70%). No transformation was observed with anhydrous trifluoromethanesulfonic acid.

**Method 3.** Chlorine was bubbled with stirring in dichloromethane (40 mL) containing cyclohexanone oxime (2 g) and aluminum trichloride (1 g). The mixture was poured over ice (100 g) and then extracted with ether (100 mL). The organic layer was washed with 5% hydrochloric acid, sodium hydrogen carbonate solution, and brine and then dried over magnesium sulfate. 1,1-Dichlorocyclohexane was obtained (66%).

This experiment was repeated with the other oximes giving the following results ( $^{13}\text{C}$  NMR data are summarized in Table I).

1,1-Dichlorocyclopentane<sup>15</sup> (3b): yield 68%, bp = 51 °C/20 Torr.

2,2-Dichloropropane<sup>16</sup> (3c): yield 40%, bp = 68 °C;  $^1\text{H}$  NMR  $\delta_{\text{H}}$  2.05 ppm.

2,2-Dichlorononane<sup>2a</sup> (3d): yield 82%, bp = 59 °C/0.8 Torr;  $^1\text{H}$  NMR  $\delta_{\text{H}}$ (CH<sub>3</sub>) 2.05 ppm (COCH<sub>2</sub>), 2.1 ppm.

4,4-Dichloroheptane<sup>17</sup> (3e): yield 73%, bp = 79 °C/23 Torr;  $^1\text{H}$  NMR  $\delta_{\text{H}}$  (COCH<sub>2</sub>) 2.1 ppm.

From 4-phenylbutan-2-one oxime (1f), a 55/45 mixture (1.5 g) was obtained. The two compounds were separated by TLC (silica gel, pentane).

4-(3',3'-Dichlorobutyl)chlorobenzene (4a):  $^1\text{H}$  NMR  $\delta_{\text{H}}$  2.1 (CH<sub>3</sub>), 2.4 (2 H), 2.9 (2 H), 7.0 (2 H, d,  $J = 7.1$  Hz), 7.2 ppm. (2 H, d). 2-(3',3'-Dichlorobutyl)chlorobenzene (4b):  $^1\text{H}$  NMR  $\delta_{\text{H}}$  2.1 (CH<sub>3</sub>), 2.3 (2 H), 3.0 (2 H), 7.15 ppm (4 H, m)

The separation was not complete, owing to a partial overlap of the spots. Combustion analysis was performed on the overlapping mixture. Anal. Calcd for C<sub>10</sub>H<sub>11</sub>Cl<sub>3</sub> (237.57): C, 50.55; H, 4.67. Found: C, 50.82; H, 4.83.

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