

# REACTION OF NITROSO CHLORIDES WITH SODIUM BOROHYDRIDE: SELECTIVE ANTI-MARKOVNIKOV HYDRATION OF A DIENE\*

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In a previous paper,<sup>1</sup> a convenient procedure was described for converting saturated oximes into alcohols, using aqueous alkaline sodium borohydride. As an extension of this work, the reaction of the above reagent with nitroso chlorides has been examined.

Nitroso chlorides are obtained by the addition of nitrosyl chloride to alkenes, and, provided the carbon atom to which the nitroso group is attached is not tertiary, are readily isomerized to  $\alpha$ -chloro oximes. It was expected that reaction of an  $\alpha$ -chloro oxime with the borohydride reagent would result in substitution of the chlorine by hydride ion and reduction of the hydroxyimino group to a hydroxy group. This sequence would thus permit overall anti-Markovnikov hydration of an alkene.

Reaction of the nitroso chloride (1) (represented here simply as the monomer although these compounds exist as dimers<sup>2</sup>), obtained from 1-methylcyclohexene and nitrosyl chloride, with sodium borohydride in boiling aqueous alkaline isopropyl alcohol<sup>1</sup> yielded a mixture containing approximately equal amounts of 2-methylcyclohexanone oxime (2), and 2-methylcyclohexanol (3), together with a small amount of 2-methylcyclohex-2-enone oxime (4). The latter was the sole product if the borohydride were omitted, or if the nitroso chloride were simply refluxed in isopropyl alcohol.

The unwanted elimination was avoided completely by carrying out the reaction in two stages. Firstly, reduction in warm aqueous isopropyl alcohol containing an excess of sodium borohydride gave the oxime (2), which on subsequent reaction with aqueous alkaline sodium borohydride gave 2-methylcyclohexanol. As described previously,<sup>1</sup> reduction of an oxime is very slow in the absence of alkali. The two steps could be combined into one operation by adding sodium hydroxide and additional sodium borohydride to the mixture from the first reaction, and then refluxing as before.

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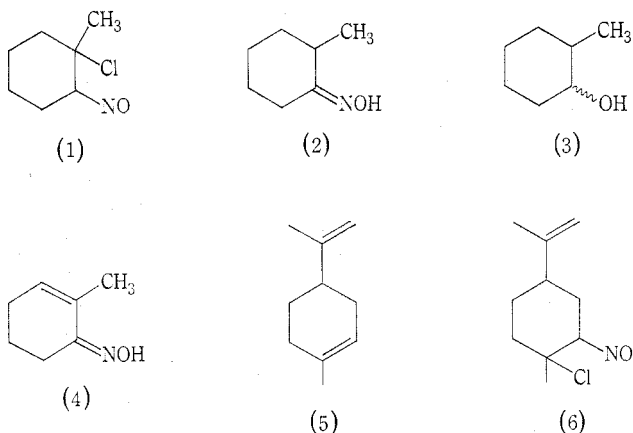
<sup>1</sup> Bell, K. H., *Aust. J. Chem.*, 1970, **23**, 1415.

<sup>2</sup> Fieser, L. F., and Fieser, M., "Current Topics in Organic Chemistry." p. 86. (Reinhold: New York 1964.)

This procedure would seem to offer little competition to the well-established hydroboration procedure for anti-Markovnikov hydration of an alkene. However, advantage can be taken of the fact that addition of nitrosyl chloride to alkenes is facilitated by increasing alkyl substitution of the alkene.<sup>3</sup> Thus, nitrosyl chloride adds preferentially to the trisubstituted double bond of limonene (5), to yield (6).<sup>4,5</sup> On the other hand, selective hydroboration of limonene, preferably with diisopentylborane, takes place at the less substituted exocyclic double bond.<sup>6</sup>

Application of the above borohydride reduction procedure to (6) gave a mixture of stereoisomeric dihydrocarvols in 76–82% yield. This example serves to illustrate the potential synthetic utility of this new procedure.

Recently, Corey and Richman<sup>7</sup> have described a useful procedure in which a nitroso chloride is converted into a ketone by treating it with chromous acetate in aqueous tetrahydrofuran. This reaction achieves essentially the same result as that described above, since the ketone could be readily reduced to the alcohol.



### Experimental

N.m.r. spectra were measured with a Hitachi Perkin-Elmer R20 instrument using deuteriochloroform as solvent and tetramethylsilane as internal reference. I.r. spectra were measured on chloroform solutions with a Hitachi EPI-G2 instrument. Melting points were determined on a calibrated micro hot stage.

#### Preparation of the Nitroso Chlorides

(i) *1-Chloro-1-methyl-2-nitrosocyclohexane (1)*.—A solution of 1-methylcyclohexene (19.2 g, 0.2 mol) in dry trichloroethylene (50 ml) was placed in a three-necked flask fitted with a thermometer, dry ice condenser, and a gas inlet tube extending almost to the surface of the liquid. The solution was cooled to 0° and stirred magnetically while redistilled gaseous nitrosyl chloride<sup>8</sup> (20 g, c. 0.3 mol) was slowly admitted. The temperature was maintained at 0–5° during addition,

<sup>3</sup> Beckham, L. J., Fessler, W. A., and Kise, M. A., *Chem. Rev.*, 1951, **48**, 319.

<sup>4</sup> Hickinbottom, W. J., "Reactions of Organic Compounds." p. 20. (Longmans: London 1942.)

<sup>5</sup> Reitsema, R. H., *J. org. Chem.*, 1958, **23**, 2038.

<sup>6</sup> Brown, H. C., and Zweifel, G., *J. Am. chem. Soc.*, 1961, **83**, 1244.

<sup>7</sup> Corey, E. J., and Richman, J. E., *J. Am. chem. Soc.*, 1970, **92**, 5276.

<sup>8</sup> Morton, J. R., and Wilcox, H. W., *Inorg. Synth.*, 1953, **4**, 48.

and for 20 min afterwards, before being dropped to  $-50^{\circ}$ . The white precipitate was quickly filtered off, washed with a little cold trichloroethylene, and dried under vacuum (6.92 g, 21%; m.p.  $68-80^{\circ}$ , lit.<sup>9</sup>  $95-97^{\circ}$ ). The n.m.r. spectrum showed a very complex multiplet extending over  $\delta$  5.35–6.0 (CH–NO; cf. *cis* nitroso chloride of cyclohexene, multiplet  $\delta$  5.2; *trans* nitroso chloride of cyclohexene, multiplet  $\delta$  5.49<sup>9</sup>) indicating the presence of both *cis* and *trans* isomers. In addition, four methyl absorptions were evident at  $\delta$  1.60, 1.70, 1.73, 1.77. Although nitrosyl chloride adds *cis* to cyclohexene in trichloroethylene, the stereochemistry of these additions is sensitive to small changes in the alkene and variation of solvent.<sup>9</sup> The stereochemistry of addition does not affect the reactions described later.

(ii) *1-Chloro-4-isopropenyl-1-methyl-2-nitrosocyclohexane* (6).—This compound was conveniently prepared according to Reitsema<sup>5</sup> in 40–52% yield, by reaction of limonene in isopropyl alcohol with nitrosyl chloride generated internally from concentrated hydrochloric acid and sodium nitrite. The n.m.r. spectrum again indicated a mixture of stereoisomers and verified that addition had taken place to the endocyclic double bond [multiplet at  $\delta$  4.78; cf. limonene  $\delta$  4.71 (exocyclic =CH<sub>2</sub>), 5.43 (endocyclic =CH–)].

#### Reactions of the Nitroso Chlorides

(i) *With sodium borohydride in aqueous alkaline isopropyl alcohol*.—The nitroso chloride (1) (648 mg, 4 mmol) was dissolved in a warm solution of NaBH<sub>4</sub> (640 mg of 95%, 16 mmol) in 1M NaOH (8 ml) and isopropyl alcohol (6 ml) and the solution refluxed for 1 hr. The initial faint blue colour faded rapidly. The cooled solution was saturated with CO<sub>2</sub>, diluted with water (20 ml), and extracted with pentane (3  $\times$  20 ml). The combined pentane extracts were dried (Na<sub>2</sub>SO<sub>4</sub>), and the solvent was removed, leaving a faintly yellow oil (418 mg). Comparison of the i.r. and n.m.r. spectra with those of authentic samples of 2-methylcyclohexanol, 2-methylcyclohexanone oxime, and 2-methylcyclohex-2-enone oxime, and mixtures of these, indicated less than about 10% of the last-named compound and approximately equal amounts of the other two. Attempted g.l.c. analyses were unsuccessful.

(ii) *With sodium borohydride in aqueous isopropyl alcohol followed by aqueous alkaline sodium borohydride*.—The nitroso chloride (1) (648 mg, 4 mmol) was dissolved in a warm solution of NaBH<sub>4</sub> (640 mg of 95%, 16 mmol) in water (6 ml) and isopropyl alcohol (6 ml) and the mixture stirred at  $50-55^{\circ}$  for 30 min. Work-up as before gave a colourless oil (410 mg, 81%) whose n.m.r. spectrum showed a doublet at  $\delta$  1.09 ( $J$  6 Hz, CH–CH<sub>3</sub>), clearly indicating that the chlorine atom had been replaced by a hydrogen atom. The i.r. spectrum was identical with that of an authentic sample of 2-methylcyclohexanone oxime. Reduction of the above oxime with aqueous alkaline NaBH<sub>4</sub> in the usual way<sup>1</sup> gave 2-methylcyclohexanol in an overall yield of 74%.

Alternatively, addition of 8M NaOH (3 ml) and NaBH<sub>4</sub> (640 mg) to the mixture after reduction in neutral solution, followed by a 2 hr reflux and working up in the usual way, gave 2-methylcyclohexanol in 79% yield.

Similarly, reduction of the nitroso chloride (6) (1.01 g, 5 mmol) in isopropyl alcohol (10 ml) and water (10 ml) containing NaBH<sub>4</sub> (788 mg, 20 mmol) gave dihydrocarvone oxime, from which dihydrocarvol was obtained in the usual way. Combination of the steps as above gave overall yields of 76–82% of material identical in all respects with an authentic sample obtained by NaBH<sub>4</sub> reduction of dihydrocarvone.

(iii) *In isopropyl alcohol at reflux*.—A solution of the nitroso chloride (1) (500 mg) in isopropyl alcohol (5 ml) was refluxed for 20 min, and the solvent then removed under vacuum. The resulting very pale yellow oil was devoid of starting material (t.l.c.), and its i.r. spectrum was identical with that of an authentic sample of 2-methylcyclohex-2-enone oxime, prepared independently from the corresponding ketone.<sup>10</sup>

Similarly the nitroso chloride (6) under the above conditions yielded carvone oxime, identical with an authentic sample.

<sup>9</sup> Ohno, M., Okamoto, M., and Nukada, K., *Tetrahedron Lett.*, 1965, 4047.

<sup>10</sup> Warnhoff, E. W., Martin, D. G., and Johnson, W. S., *Org. Synth.*, 1957, 37, 8.