Registry No.—**3**, 20585-98-2; **4**, 27808-79-3; **6**, 27808-80-6; **7**, 27808-81-7; **8**, 27808-82-8; **10**, 27808-83-9; **11**, 27808-84-0; **12**, 5859-29-0; **13**, 27808-86-2.

Reaction of Nitrosyl Chloride with Ethylidenecycloalkanes. A Reexamination[1]

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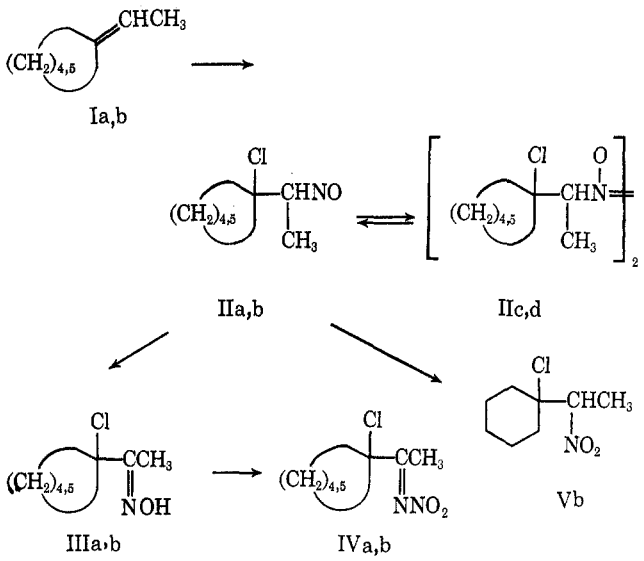
Normal addition of nitrosyl chloride to an olefin gives a chloronitroso product (monomer or dimer) or an α-chlorooxime. Other products have been called anomalous.[2] The normal (primary) products may be oxidized to secondary products. We report additions to two ethylidenecycloalkanes which behave differently in the secondary oxidations. We conclude that the chloronitroso addition is the only primary reaction. After that three pathways may be followed: (1) dimerization of the nitroso group (long known), (2) oxidation of the nitroso group to a nitro gorup, and (3) isomerization to an oxime, followed by oxidation to a nitrimine.

The pathways compete. The second pathway appears to be the only one in a steroid example[3] where dimerization may be inhibited or very slow. Oxidation of an oxime to a nitrimine has been accomplished by nitrous acid,[4] nitrosyl fluoride,[5] and recently by nitrosyl chloride.[6] Isomerization of chloronitroso compound to the oxime is catalyzed by hydrogen chloride and goes very rapidly in polar solvents[7] so that dimerization and oxidation to a nitro group may not compete successfully in such solvents.

In the case of ethylidenecyclohexane, all three reactions compete successfully in ether. Wallach and Evans[8] reported an 83% yield of chloronitroso compound IIb,d in the addition of nitrosyl chloride to ethylidenecyclohexane. Repetition with excess nitrosyl chloride suggests that chloronitroso formation is quantitative (98%) as the primary reaction. Precipitation from ether gives 75% of IIb,d. Oxidation of the remainder in solution gives 16% of chloronitro compound Vb by direct oxidation with nitrosyl chloride and 7% of chloronitrimine IVb through isomerization to IIIb and subsequent oxidation. With ethylidenecyclopentane, only 24% of IIa,c is precipitated. None of the remainder is oxidized to the chloronitro compound, apparently because isomerization to chlorooxime IIIa and subsequent oxidation to chloronitrimine (56%) is so rapid. The isolated chloronitroso compound IIa,c isomerized on standing to IIIa; so only IIIa could be obtained pure in this series.



The molecular mass of 279 by the Rast method[9] in camphor for IIb,d gives a monomer/dimer ratio of 28:72. In the mass spectrometer, only one decomposition pattern was obtained from IIb,d, and IIIb so the dimer must dissociate and/or isomerize in the ion chamber. The maximum m/e observed is that of IIb (= IIIb).

In the presence of nitrosyl chloride, pure IIb,d exhibits the oxime signals of IIIb (nmr) at $-77°$ in a short time. This isomerization for preparative purposes is catalyzed by hydrogen chloride gas or, less effectively, solid sodium carbonate.

Pure IIIb was oxidized only to the nitrimine IVb by nitrosyl chloride but was oxidized to the chloronitro compound Vb by trifluoroperoxyacetic acid. The chloronitroso compound IIb,d was oxidized to chloronitro Vb in 91% yield by trifluoroperoxyacetic acid.

The dimer IId appears to have an anti structure from the interpretation of Gowenlock and Lüttke,[10] exhibiting λ_{max} 265 mμ (ϵ 5400) in ethanol and ir bands at 1185 (s) and 1450 cm^{-1} (m). Compound IIb,d and IIIb gave piperidino[8] and methoxy[11] derivatives as reported. However, IIIa was dehydrohalogenated in methanol to 1-acetylcyclopentenyloxime. Structures of compounds III, IV, and V were corroborated by ir and nmr spectra and IVb was reduced to the corresponding nitramine.

The results reported here bear out Oglobin's suggestion that stable dimer precipitation diminishes opportunity for oxidation to a nitro compound. Oglobin[12] has reported low yields of chloronitro compounds with several olefins of low molecular mass. The present work suggests that rapid isomerization to oxime lowers nitro formation and increases nitrimine formation.

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Experimental Section

Melting points are corrected but boiling points are uncorrected. Instruments used were a Perkin-Elmer 337 grating spectrophotometer, a Varian A-60A high-resolution proton magnetic resonance spectrophotometer, a Cary 14 spectrophotometer, and a Hitachi Perkin-Elmer RMU-6D Model mass spectrometer. Relative intensities in the mass spectrum are reported as per cent of the base peak.

1-Chloro-1-α-nitrosoethylcyclohexane (IIb).—Ethylidenecyclohexane (24 g, 0.22 mol) in 100 ml of anhydrous ether was cooled to Dry Ice temperature and the solution was stirred while excess nitrosyl chloride was bubbled into it. The solution turned dark brown and a precipitate formed rapidly. The white precipitate was filtered, washed with ice-cold ether, and dried: yield 30 g (75%); mp 134–135° (lit.[8] yield 83%; mp 132°); ir spectrum (dilute CCl_4) 1450 (m), 1185 cm^{-1} (s); nmr spectrum (CCl_4, 10%) 1.51 (d, 3, J = 7 Hz), 6.0 (q, 1, J = 7 Hz); uv spectrum $\lambda_{max}^{C_2H_5OH}$ 265 μ (ε 5400); mass spectrum (70 eV) m/e (relative intensity) 177 (0.29, M + 2), 175 (0.98, M), 140 (50.98), 98 (59.80), 97 (43.13), 83 (46.07), 81 (51.96), 71 (100), 57 (50.00), 45 (82.35), 41 (45.09), 17 (23.52). Compound IIIb (below) gave an identical mass spectrum.

Compound IIb sublimes (without isomerization to IIIb) at a temperature above 100° (reduced pressure). The methoxy[8,11] (mp 85.5–86.5°) and piperidino[8] (mp 117–118°) derivatives were made for further verification of structure.

The filtrate from the above preparation contained 9.8 g (isolated) of a mixture of 7% IVb and 16% Vb (below), as determined by an nmr spectrum.

Methyl 1-Chlorocyclohexylketoxime (IIIb).—Compound IIb,d (1 g, 5.7 mmol) in 30 ml of anhydrous ether was saturated with hydrogen chloride gas and allowed to stand overnight. Ether was evaporated and the residue was recrystallized from hexane, yield 0.7 g (70%). A pure sample of methyl 1-chlorocyclohexylketoxime was sublimed at 50° (0.5 mm), mp 70–71°.[8]

Refluxing a chloroform solution of IIb,d over solid sodium carbonate for 18 hr gave a 22% yield of IIIb, and trifluoroacetic acid in chloroform refluxed for 3 hr gave a 43% yield of IIIb.

The methoxy[8,11] derivative was obtained in 69% yield from IIIb, whereas the yield was only 33% from IIb,d under the same conditions (standing overnight in methanol at 25°): ir spectrum (dilute CCl_4) 3580 (s, =NOH), 3300 (br), 1230 cm^{-1} (s); nmr spectrum (CCl_4, 10%) δ 1.2–2.2 (br, 10), 2.0 (s, 3), 8.8 (br, 1); uv spectrum $\lambda_{max}^{C_2H_5OH}$ 228 μ (ε 4440).

Methyl 1-Chlorocyclohexylnitroketimine (IVb).—A solution of 259 mg (1.6 mmol) of methyl 1-chlorocyclohexylketoxime (IIIb) in 35 ml of chloroform was treated with a slow stream of nitrosyl chloride at room temperature. After the solution turned to dark brown, the stream was stopped and the mixture was allowed to return to room temperature. Solid sodium carbonate was added and the mixture was stirred for 1 hr. The solid was removed by filtration and the solvent removed at room temperature. The green oil was distilled to give 208 mg (64%) of colorless liquid, bath temperature 75° (0.2 mm).

The compound was identified by ir and nmr spectra and converted to the corresponding nitramine (below): ir spectrum (CCl_4) 1640 (s, C=N), 1570, 1450 cm^{-1} (m, NO_2); nmr spectrum (CCl_4, 10%) δ 1.2~2.2 (br, 10), 2.23 (s, 3).

Methyl 1-Chlorocyclohexylnitroketamine.—To a slurry of 1.5 g of lithium aluminum hydride in 50 ml of ether was added 3 g (0.014 mol) of crude IVb in 30 ml of ether at room temperature. The mixture was refluxed overnight and cooled. After decomposition and neutralization of excess reducing agent, an ether extract was evaporated to give 1.8 g of an oil. From this oil, a solid was eluted on a silica gel column with benzene. Sublimation at 55° (0.75 mm) gave 36 mg (2%) of methyl 1-chlorocyclohexylnitroketamine: mp 91–92.5°; ir spectrum (CCl_4) 3350 (br, NH), 1585 (s), 1340 cm^{-1} (s, NO_2); nmr spectrum (CCl_4, 10%) δ 1.37 (d, 3, J = 7 Hz), 4.43 (q, 1, J = 7 Hz).

Anal. Calcd for $C_8H_{15}ClN_2O_2$: C, 46.49; H, 7.31; N, 13.56. Found: C, 46.71; H, 7.31; N, 13.47.

1-Chloro-1-α-nitroethylcyclohexane (Vb).—Hydrogen peroxide (90%, 1 ml) suspended in 10 ml of methylene chloride by stirring was treated at ice bath temperature with 2 ml of trifluoroacetic anhydride. Then 1.26 g (7.2 mmol) of 1-chloro-1-α-nitrosoethylcyclohexane IIb,d in 20 ml of methylene chloride was added dropwise in 5 min. The mixture was refluxed for 1 hr and poured onto 500 g of ice. The solvent was separated and the water layer was neutralized with sodium bicarbonate solution and extracted with more methylene chloride. The solution was dried and the solvent removed. The remaining oil was distilled, bp 90–91° (1.5 mm), yield 1.25 g (91%). With m-chloroperbenzoic acid as oxidizing agent a 53% yield of Vb was obtained: ir spectrum (CCl_4) 1560, 1360 (s, NO_2), 1460, 1380 cm^{-1}; nmr spectrum (CCl_4, 10%) δ 1.63 (d, 3, J = 7 Hz), 4.8 (q, 1, J = 7 Hz).

Anal. Calcd for $C_8H_{14}ClNO_2$: C, 50.10; H, 7.36; N, 7.31. Found: C, 50.15; H, 7.13; N, 7.13.

The nmr spectrum of the pure nitro compound Vb was identical with that obtained from the filtrate of the synthesis of IIb above.

Methyl α-Chlorocyclopentylketoxime (IIIa).—By the procedure described for IIb,d 1-chloro-1-α-nitrosoethylcyclopentane was obtained in 24% yield from 5 g of ethylidenecyclopentane, mp 47–50°. Upon standing at room temperature overnight or upon sublimation at reduced pressure, the compound isomerized to methyl α-chlorocyclopentylketoxime (IIIa). Two sublimations gave the analytical sample: mp 150–151° dec; nmr spectrum (chloronitroso form) (CCl_4, 10%) δ 1.50 (d, 3, J = 6 Hz), 6.0 (q, 1, J = 6 Hz); nmr (ketoxime form) (DMSO-d_6, 10%) δ 1.97 (s, 3), 8.1 (br, 1); ir spectrum (ketoxime form) (CCl_4) 3600 (s, =NOH), 3200 (br), 1625 cm^{-1} (w, C=N).

Anal. Calcd for $C_7H_{12}ClNO$: C, 51.97; H, 7.48; N, 8.66. Found: C, 51.80; H, 7.26; N, 8.70.

With methanol overnight, the chloroketoxime IIIa was dehydrohalogenated to 1-acetylcyclopentenyloxime in 45% yield,[13] mp 94–96°, in contrast to the behavior of IIIb (above).

The ether filtrate from the above procedure contained only methyl 1-chlorocyclopentylnitroketimine (IVa). In the ir spectrum the $\nu_{C=N}$ appeared at 1640 (s) and in the nmr spectrum only the singlet at δ 2.2 due to the methyl group was observed. There was no chemical shift near δ 4.8, which would be expected of the group $-CHNO_2$ (see Vb above) nor at δ 2.0 due to IIIa remaining. The oily residue IVa (5.5 g, 55%) did not crystallize and was not further purified.

Registry No.—Ia, 2146-37-4; Ib, 1003-64-1; IIb, 28042-41-3; IIIa, 28042-42-4; IIIb, 28042-43-5; IVb, 28042-44-6; IVb nitramine, 28042-46-8; Vb, 28042-45-7; nitrosyl chloride, 2696-92-6.

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