Nitrosyl Chloride Adduct of Methyl Oleate[1]

W. R. MILLER, E. H. PRYDE, J. C. COWAN and H. M. TEETER, Northern Regional Research Laboratory,[2] Peoria, Illinois

Abstract

Nitrosyl chloride was added to methyl oleate on a preparative scale to give the adduct in essentially quantitative yield. The chlorine of the adduct was quite labile; was replaced by methoxyl, hydroxyl, acetoxyl, piperidino, and amino groups; and was eliminated to give the unsaturated nitroso compound. Under any conditions only 15–20% of the nitroso group of the adduct isomerized to oximino. Reduction with zinc and acetic acid gave the hydroxylamino derivative.

Introduction

THE ADDITION OF NITROSYL chloride to olefins is a well-known reaction, dating back at least to 1871 (9). Around the turn of the century, Wallach (25) did a great deal of work on this reaction, particularly as applied to terpenes and related compounds. Additions to olefinic materials, as well as other reactions of nitrosyl chloride, have been extensively reviewed (8), although the mechanism of the addition is still controversial (20). Ogloblin and coworkers (18) are currently engaged in what appears to be a systematic study of nitrosyl chloride additions to a variety of olefins and of the properties and reactions of the adducts.

Although addition of nitrosyl chloride to terpenes and to simpler olefins has been widely studied (8), addition to unsaturated fatty acid derivatives has received little attention. In 1894, Tilden and Forster (23) reported addition of nitrosyl chloride to oleic and elaidic acids, but their isolation of solid adducts seems improbable in light of the work reported here. More recently, a patent (7) has disclosed the preparation of surfactants from nitrosyl chloride adducts of oleic acid and its esters. Of particular interest is a paper by Kaufmann and Röver (13) reporting an analytical method for unsaturated fatty materials based on addition of nitrosyl chloride in a manner analogous to that used with iodine monochloride in the standard iodine value determination (4). They state that their studies would be directed toward preparative work based on nitrosyl chloride adducts of unsaturated fatty materials. So far as we have been able to determine, no further work on this subject was published by either one.

Announcement (1) of the potential availability of nitrosyl chloride at a cost making it an attractive raw material stimulated our interest in its use. The wide variety of products potentially obtainable from nitrosyl chloride adducts served as additional stimulus. For example, the adduct chlorine might be replaceable by amines, alkoxides, and active methylenes or eliminated to give unsaturation. Or the nitroso group might be reduced to an amine or isomerized to the oxime, in turn leading to ketones, alcohols, amides, amines, and carboxylic acids. If the reactions of one portion of the molecule are relatively independent of the other, an almost infinite number of transformations and products theoretically should be possible. We can now report the successful addition of nitrosyl chloride to methyl oleate on a preparative scale and some reactions of the product.

Experimental

Addition of Nitrosyl Chloride to Methyl Oleate

A 38 x 200 mm test tube was fitted with a rubber stopper holding a gas-delivery tube, ending in a fritted cylinder, a thermometer, and a drying tube filled with "Drierite." In the test tube was placed 29.7 g (0.1 mole) of methyl oleate (Applied Science, "99+%") dissolved in 100 ml of methylene chloride which had been dried over Drierite and filtered. The test tube was then placed in a Dewar flask filled with crushed ice. The entire assembly was supported on a large balance. After sweeping for a short time with a slow stream of nitrogen, the nitrogen was turned off and nitrosyl chloride from a commercial cylinder (Matheson) was passed through the solution. After a short time the temperature rose from its initial 2C and the reaction mixture began to foam, resulting in a small loss of material. After 8 min there had been a weight increase of about 7 g and the temperature had risen to 34C. The nitrosyl chloride was turned off and nitrogen turned on sufficiently to overcome the tendency of the solution to suck back. The solution was allowed to stand in the ice bath for 1 hr. During this time, the color of the solution changed from red brown to bright green. The solution was then swept with nitrogen for 5 min to remove any unreacted nitrosyl chloride, filtered through fluted paper, and stripped of solvent under vacuum with nitrogen ebullition on a water bath at less than 25C. The azure liquid residue weighed 34.5 g, n_D^{30} 1.4696. A sample was analyzed without further purification.

Calcd. for $C_{19}H_{36}ClNO_3$: C, 63.04; H, 10.03; Cl, 9.80; N, 3.87.
Found: C, 62.80; H, 9.73; Cl, 10.88, 10.74; N, 3.34, 3.27.

The infrared spectrum was consistent with that expected for monomeric methyl chloronitrosostearate (**I**).

Substitution and Dehydrochlorination of I

Substitution and dehydrochlorination reactions were carried out by mixing **I** with an excess of reagent and usually by stirring the mixture at room temperature until there was no further change in color. Table I gives conditions and results for these reactions. The aqueous potassium hydroxide/dimethyl sulfoxide (DMSO) reaction mixture was in three phases, whereas reaction mixtures with aqueous potassium hydroxide and with ammonium hydroxide were in two, and the remaining reaction mixtures were essentially homogeneous. Sodium acetate was only slightly soluble in DMSO. The reaction with ammonia was run at reflux temperature. The ester was saponified in both potassium hydroxide reactions. Products were identified by infrared spectrophotometry; unreacted chlorine was determined by microchemical analysis; and calculations based on the latter analyses often helped to confirm identification. By infrared the dehydrochlorination product was shown

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[2] No. Utiliz. Res. and Dev. Div., ARS, USDA.

TABLE I

Chlorine Substitution and Dehydrochlorination of Methyl Chloronitrosostearate (I)

Reagent	Conditions	RCH(NO)–CHR′(B)			Analyses							Chlorine eliminated, % [a]
		B	n_D^{30}	Oxime, %	Calculated			Found				
					C	H	N	C	H	N	Cl	
Piperidine	10 ml, 10 g I, 20 hr without stirring	$C_5H_{10}N$	1.4773	11	70.20	11.29	6.82	68.67	10.77	5.92	1.28	87
$NaOCH_3$	2 g, 50 ml CH_3OH, 5 g I, stirred 3 hr, let stand overnight	CH_3O	1.4614	17	67.18	11.00	3.92	65.62	10.59	3.71	1.00	90
KOH	50 ml 50% aq, 5 g I, stirred 3 hr, let stand overnight	HO	1.470		65.61	10.71	4.25	65.60	10.42	3.44	2.10	79
KOH	50 ml 50% aq, 50 ml DMSO,[b] stirred 2 hr	HO		20	65.61	10.71	4.25	65.77	10.55	3.75	1.41	86
NH_4OH	50 ml, 5 g I, stirred 42 hr, additional 50 ml, stirred 150 hr	H_2N, HO	1.4718	8	[c]			66.64	10.56	5.51	2.69	73
NH_3	50 ml, 3.5 g I dissolved in 30 ml ether, stirred at reflux 0.5 hr, NH_3 evaporated over 1 hr	H_2N	1.4680	10	66.63	11.18	8.18	63.92	10.25	4.43	6.86	30
NaOAc	3.5 g, 50 ml DMSO, 5 g I, stirred 6 hr, added 50 ml water, stored in refrigerator overnight	AcO	1.4664		65.42	10.20	3.63	63.85	10.04	3.64	5.11	48
Pyridine	30 ml, 30 ml DMSO, 3.5 g I, stirred 5 hr, let stand 16 hr, stirred 7 hr	RC(NO)=CHR′	1.4665		70.11	10.84	4.30	63.75	9.68	3.72	7.56	23
Et_3N	50 ml, 5 g I, stirred 24 hr	RC(NO)=CHR′	1.4672	14	70.11	10.84	4.30	66.55	10.50	3.88	2.64	73

[a] Based on original calculated chlorine content of 9.80% for methyl chloronitrosostearate and 10.19% for chloronitrosostearic acid.
[b] DMSO = Dimethyl sulfoxide.
[c] Because product contained both hydroxyl and amino groups, theoretical analysis could not be calculated.

to be the *trans*-isomer. No unsaturated oxime was detected.

Reaction of I with Nitrosyl Chloride

Five grams (0.014 mole) of **I** was dissolved in 50 ml of dried, filtered methylene chloride. The flask containing the solution was placed in an ice bath, supported on a large balance. Nitrosyl chloride (2 g) was added in the same manner as for the preparation of **I**. Addition took 4 min, the solution temperature rose from 7 to 12C, and the color of the solution changed from green to red brown. The flask was stoppered and stored in the refrigerator for 1 week. The flask was then placed in an ice bath and the solution swept with nitrogen for about 1.5 hr, filtered, and stripped of solvent at about 30C. The residue was 4.9 g of a blue oil, n_D^{30} 1.4684, identical in appearance to the starting material. The infrared spectrum, however, showed the presence of nitro groups and microchemical analysis showed an increase in chlorine content.

Calcd, for $C_{19}H_{36}ClNO_4$: C, 60.38; H, 9.60; Cl, 9.38; N, 3.71.
Found: C, 59.05; H, 9.27; Cl, 12.79; N, 3.94.

Reduction

Again, 5 g (0.014 mole) of **I** was dissolved in 50 ml of glacial acetic acid and 5 ml of water (26), and the solution was cooled in ice. Powdered zinc (3 g, 0.046 mole) was added in several portions while the reaction mixture warmed to room temperature. The mixture was filtered and the colorless, clear filtrate was diluted with 100 ml of water, extracted with two 50-ml portions of ether, and the combined extracts were washed free of acid and dried over sodium sulfate. After removal of the drying agent and stripping of ether at less than 30C, the residue consisted of 3.2 g of slightly yellow oil, n_D^{30} 1.4624. The infrared spectrum showed that the nitroso group had been reduced to the hydroxylamine together with a trace of azo compound. Microchemical analysis showed that 35% of the chlorine had been removed by the reduction. Thus the product was mainly a mixture of methyl hydroxylamino- and chloro(hydroxylamino)-stearate.

Calcd, for $C_{19}H_{38}ClNO_3$: C, 62.69; H, 10.52; Cl, 9.74; N, 3.85.
Found: C, 66.83; H, 10.95; Cl, 6.34; N, 3.06.

Similarly, reductions of methyl methoxynitrosostearate, hydroxynitrosostearic acid, and methyl nitrosooctadecenoate were performed. Each product was shown by infrared to be the hydroxylamine.

Results and Discussion

Methyl oleate was chosen for this work as the simplest unsaturated fatty acid derivative available and the least likely to introduce undesired complications. Addition of nitrosyl chloride to methyl oleate in a methylene chloride solution went smoothly at ice-bath temperature to give an essentially quantitative yield of **I**, an azure oil. Choice of conditions was

$$CH_3(CH_2)_7\underset{\displaystyle NO}{\underset{|}{CH}}-\underset{\displaystyle Cl}{\underset{|}{CH}}(CH_2)_7COOCH_3$$
$$CH_3(CH_2)_7\underset{\displaystyle Cl}{\underset{|}{CH}}-\underset{\displaystyle NO}{\underset{|}{CH}}(CH_2)_7COOCH_3$$

I

somewhat arbitrary in that other workers—using other substrates, of course—used such divergent conditions as −70C in liquid sulfur dioxide (3) and 100C in a sealed tube without solvent (12). Approximately stoichiometric quantities of nitrosyl chloride and short reaction times were used in an effort to limit side reactions (17). After removal of the solvent at about 30C and without further purification, the product gave satisfactory microchemical analyses except for a small excess of chlorine. Commercial

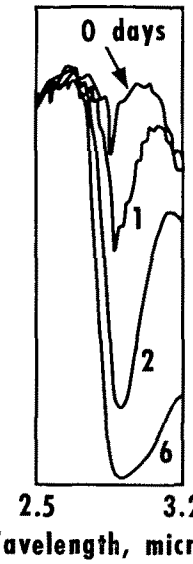
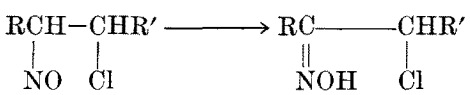


FIG. 1. Methyl chloronitrosostearate isomerization.

nitrosyl chloride contains about 2% chlorine (2) and this percentage, perhaps together with traces of solvent, would easily account for the discrepancy. With respect to the positions of the nitroso and the chlorine, **I** is probably a mixture of isomers.

Many chloronitroso compounds dimerize to white solids (8). We have found no evidence that **I** undergoes any appreciable dimerization. The persistent blue color and the presence of the strong nitrosyl band in the infrared, as well as failure to obtain any solid adduct, all indicate little, if any, dimer formation.

Presence of hydrogen on the carbon holding the nitrosyl group permits rearrangement to the oxime (8):



For most of the examples cited in the literature, this rearrangement is spontaneous or is promoted under the mildest conditions. The product chlorooxime is usually a solid, more stable than the nitroso isomer. There was no obvious evidence, however, that **I** underwent this isomerization. When **I** was treated by methods reportedly giving the oxime, such as standing (11), refluxing in ethanol (22), heating (24), or treating with hydrogen chloride (6) or amines (16), a number of color changes were observed, but nothing resembling the hoped-for solid, white oxime was isolated.

After standing either several months in the refrigerator or shorter times at room temperature, **I** slowly turned from blue to green. A similar color change took place on treatment of **I** with amines and, to a limited extent, when **I** was heated. Figure 1 shows development of the hydroxyl band, indicative of oxime, in the infrared spectrum of a sample of **I** allowed to stand at room temperature (about 30C). About 0.5% of oxime was already present in the freshly prepared **I**. Oxime content increased on standing at room temperature to about 3% after 1 day and to a maximum of about 20% after about 6 days. Although isomerization of **I** did not occur to such an extent or in such a manner that isolable quantities of methyl chloro-oximinostearate were obtained, oxime formation did take place. Promotion

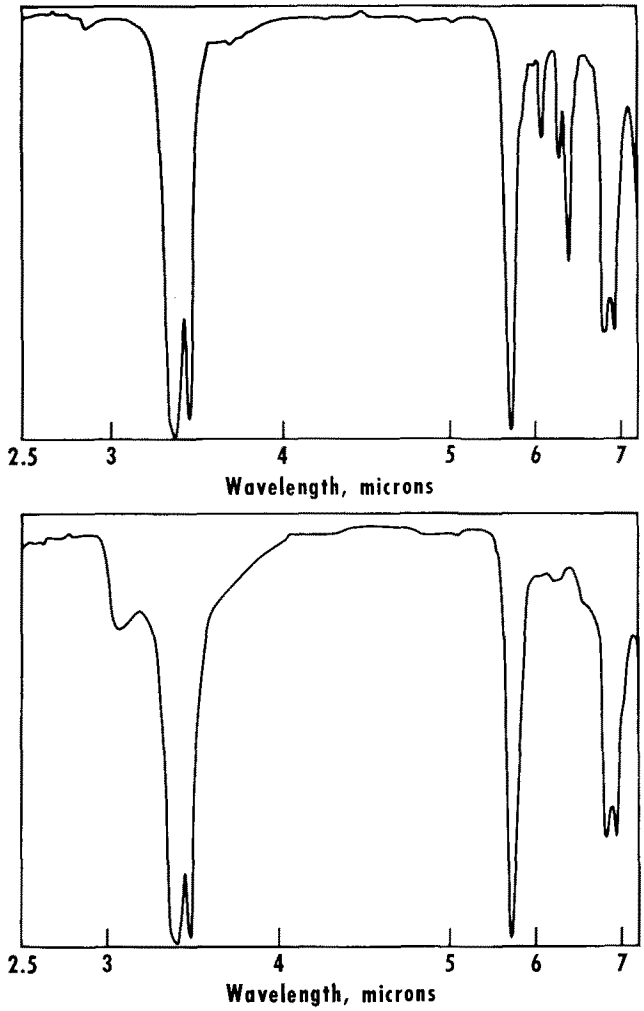
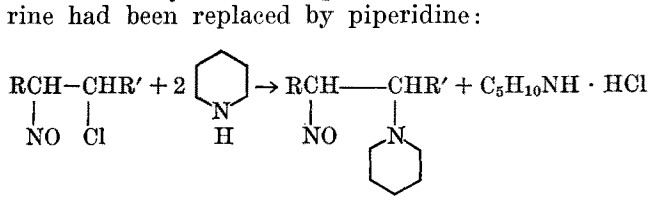


FIG. 2. Methyl chloronitrosostearate reduction. Upper, methyl chloronitrosostearate; lower, reduction product.

of isomerization by heating was not practicable because at about 50C dehydrochlorination was initiated and this, possibly together with other decomposition reactions, resulted in formation of viscous, dark-brown products. Effects of some chemical reagents which might be expected to promote isomerization will now be considered.

When piperidine was shaken with an ether solution of **I**, the blue solution turned brilliant green. Removal of solvent left a bright-green oil. It was hypothesized that the base had effected dehydrochlorination and that the product was an unsaturated nitroso compound. Microchemical analysis showed, however, that less than half of the chlorine had been removed. Repeated treatment of ether solutions of **I** with more piperidine gave only slightly better results. Finally, **I** was mixed with piperidine without solvent. The expected green appeared but soon changed to bright orange yellow. Microchemical and infrared analyses of the product showed that chlorine had been replaced by piperidine:



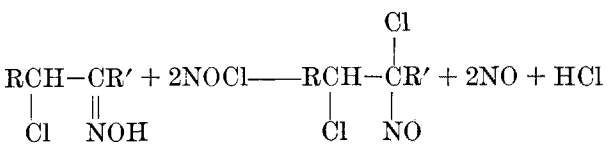
The product also contained some oxime and a little unsaturation. About 13% of the chlorine had not reacted.

Substitution reactions were then run with a number of other nucleophilic reagents. These results, together with others obtained, are shown in Table I. Sodium methoxide in methanol gave a particularly smooth reaction as **I** dissolved after about an hour's stirring and salt precipitated from solution as the reaction proceeded. DMSO was added to the 50% aqueous potassium hydroxide in an unsuccessful attempt to obtain a homogeneous reaction mixture. The DMSO did make possible a much shorter reaction time. A mixture of DMSO and 25% potassium hydroxide is homogeneous (although **I** was not soluble in it), but the results approximated those with 50% potassium hydroxide without DMSO. Strongly basic solutions saponified the ester. It was necessary to use an ether solution of **I** in the reaction with liquid ammonia because, without a solvent, **I** solidified on contact with the ammonia. This poor reaction is consistent with results obtained when ether solutions were used with some of the other reagents (e.g., piperidine, above). Ammonium hydroxide gave a mixture of amino- and hydroxy-substituted derivatives. Anhydrous sodium acetate dissolved sufficiently in DMSO so that a reaction was possible.

In each of these reactions there was spectral evidence for a little dehydrochlorination. With a tertiary amine, dehydrochlorination would be expected to be the primary, if not exclusive, reaction. Table I also shows conditions and results for experiments with pyridine and with triethylamine. Pyridine, even in the presence of DMSO, did not give satisfactory results. Triethylamine, however, did eliminate 73% of the chlorine to give methyl *trans*-nitrosooctadecenoate on the basis of infrared analysis.

Also in each of these reactions there was some isomerization to oxime, the amount apparently depending at least partially on the basic strength of the reagent. In none of these reactions was there complete elimination of chlorine. Several reasons for this seem probable. First, because of the relative thermal instability of **I**, no attempt was made to force the reactions. Secondly, the basic reagents probably isomerized some of the nitroso groups to the oximino structure before substitution was accomplished. Replacement of chlorine in a chloro-oxime may be more difficult than in a chloronitroso compound. Interestingly enough, in dehydrochlorination no C=C−C=NOH, which would have resulted from dehydrochlorination of oxime, could be detected. Thirdly, there is probably some methyl dichlorostearate formed by addition of chlorine present in nitrosyl chloride (2). Replacement of two adjacent chlorines is most difficult (21).

Russian workers, using an excess of nitrosyl chloride, have reported (15) that main reaction products of addition of nitrosyl chloride are nitro rather than nitroso compounds. When we stored a methylene chloride solution of **I** and nitrosyl chloride in the refrigerator for 1 week, infrared showed the presence of nitro groups in the product. Also, microchemical analysis showed a 10% increase in chlorine content. The latter may have been the result of chlorination of the hydrocarbon chain or, more likely, chlorination of the oxime form of **I** (8):



Reduction of a nitrosyl chloride adduct would be expected to yield a chloroamine, an aziridine, or, with reductive elimination of chlorine, an amine. Thus, reduction of **I** should lead to aminostearic acid (19) or a simple derivative thereof. The literature, however, is not encouraging about reduction of aliphatic nitroso compounds. Wallach and Haworth (26) reduced the nitrosochloride of ethylidenecyclohexane with zinc and acetic acid and obtained methyl cyclohexyl ketone and aminoethylcyclohexane but did not report yields. More recently Aston and co-workers (5) reduced α-nitrosocarbonyl compounds with stannous chloride and obtained azoxy and hydrazino compounds. Closs and Brois (10) have reported successful reduction of adducts of tetrasubstituted ethylenes with stannous chloride. The products were cyclized to aziridines without isolation. Only lately, and since completion of this phase of our work, Meinwald, Meinwald, and Baker (14) have reported the successful two-step catalytic reduction of the nitrosyl chloride adduct of Δ^9-octalin (also a tetrasubstituted olefin) to the chloroamine.

Catalytic reduction with platinum or chemical reduction with stannous chloride did not give aminostearic acid or a recognizable derivative. With zinc and acetic acid (26), we were able to reduce **I** to a mixture of methyl hydroxylamino- and chloro(hydroxylamino)-stearate. The infrared spectrum of the products also showed a trace of azo compound. Figure 2 shows spectra of **I** and of the reduced product. Reduction of the methoxy and hydroxy derivatives, as well as of methyl nitroso-octadecenoate, gave the corresponding hydroxylamino derivatives.

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