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NITROSYL ACYLATES. IN SITU ADDITION OF NITROSYL FORMATE TO OLEFINS[1]

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In our continuing program on the introduction of nitrogen functionality directly into unsaturated organic molecules, a search of the literature has shown that although nitrosyl chloride reacts with many olefins, the adducts obtained in many cases are unstable. Reaction products darken on storage and acid products are eliminated. Although the chlorine atom is quite labile and susceptible to nucleophilic substitution,[2] efficient conversion of nitrosyl chloride adducts to other useful and stable derivatives, other than the β-chlorooximes (the products of isomerization), is usually a frustrating procedure.[3] In an attempt to place a less labile and more easily manipulated group α to the nitroso group, we have initiated an investigation of the reactions of nitrosyl acylates, generated *in situ*, with olefins.

Recent work has shown that nitrosyl acylates may be prepared in high yield by several methods and their reactions with inorganic salts and amines have been reported.[4,5,6,7] In this preliminary report we wish to describe the *in situ* generation of nitrosyl formate and its addition reaction with selected olefins (Equation 1):

$$>C=C< \; + \; [ONO\overset{O}{\overset{\|}{C}}H] \longrightarrow \left[\begin{array}{c} >C-C< \\ | \quad | \\ NO \quad OCH \\ \quad\quad \| \\ \quad\quad O \end{array} \right]_n \qquad \text{(Equation 1)}, \; n = 1 \text{ or } 2$$

With cyclohexene, styrene, norbornene and *trans*-3-hexene the products are the nitrosoformate dimers (n = 2 in Equation 1), although with the last-named olefin some oximinoformate is also formed. With 2,3-dimethyl-2-bu-

tene the product, a deep blue oil, appears to consist of about equal parts of monomeric and dimeric nitrosoformates.

In general, the reactions are carried out by adding a solution of the olefin in isoamyl nitrite to cold anhydrous formic acid with stirring, the products being isolated by appropriate methods after removal of excess formic acid and other volatile products (isoamyl formate, unreacted olefin etc.) by vacuum evaporation.

Thus, when a solution of cyclohexene (16.4 g; 0.2 mole) in isoamyl nitrite (46.8 g.; 0.4 mole) was added dropwise with stirring to cold anhydrous formic acid (150 ml.), a white solid, m.p. 149-150°, was obtained in 59% yield after recrystallization from ethanol. Its infrared spectrum, elemental analysis, and molecular weight were consistent with proposed nitrosoformate dimer structure.

Anal. calculated for $C_{14}H_{22}N_2O_6$ C 53.49, H 7.06, N 8.91, M.W. 304

found: C 53.87, H 7.21, N 8.87, M.W. 309

Saponification of the 2-formoxynitrosocyclohexane dimer with aqueous alcoholic potassium hydroxide gave a 92% yield of the corresponding alcohol, 2-hydroxynitrosocyclohexane dimer, a white solid, m.p. 162.5° (to a blue liquid on melting). Its infrared spectrum was consistent with the proposed structure.

Anal. calculated for $C_{12}H_{22}N_2O_4$ C 55.80; H 8.59; N 10.48, M.W. 258

found: C 55.54, H 8.47; N 10.29, M.W. 266

Transoximination of the nitrosoalcohol dimer by the method of DePuy and Ponder[8] yielded adipoin, identical in every respect with an authentic sample, thus demonstrating that the original nitrosyl formate adduct was vicinally substituted.

Similarly, reaction of styrene with nitrosyl formate gave a white solid, m.p. 133.5-4°, in 70% yield whose infrared spectrum, elemental analysis and molecular weight were consistent with the dimeric nitrosoformate structure.

Anal. calculated for $C_{18}H_{18}O_6N_2$ C 60.33; H 5.06; N 7.81, M.W. 358

found: C 60.51; H 5.26; N 7.67; M.W. 356

Norbornene reacted as expected to give a 59% yield of a white, crystalline adduct, m.p. 161.5-162°, also a nitrosoformate dimer (see later discussion).

Anal. calculated for $C_{16}H_{22}N_2O_6$ C 56.80; H 6.56; N 8.28; M.W. 338
found: C 56.70; H 6.67; N 8.32; M.W. 334

In the addition reactions already described the adducts are white solids that are converted to blue liquids (monomers) on melting. They decompose rapidly at or above the melting points but show no signs of decomposition even after several months at room temperature.

When nitrosyl formate was added to 2,3-dimethyl-2-butene, however, the product was an unstable deep blue liquid, b.p. 59°/10 mm., that could be isolated in only 11% yield by distillation under reduced pressure. To obtain correct microanalyses it was frozen in dry ice and analyzed within a few hours after preparation.

Anal. calculated for $C_7H_{13}NO_3$ C 52.82; H 8.20; N 8.20
found: C 52.96; H 8.10, N 7.92

This compound had a very penetrating odor and decomposed after several days at room temperature. It was more stable, however, if stored in a cold room in the dark where it solidified at about 0°.[9] Its molecular weight could not be determined accurately as the results were quite variable; it appeared to be a 1:1 mixture of monomeric and dimeric nitrosoformates. Its infrared spectrum, shown in Fig. 1, had an intense band at 1560 cm^{-1}, indicative of a tertiary aliphatic nitroso group.

Reaction of trans-3-hexene with nitrosyl formate gave a mixture of two products which, based on infrared examination, consisted of the expected nitrosyl formate adduct and its isomeric oximinoformate. No attempt was made to separate this mixture. It was treated directly with aqueous alcoholic potassium hydroxide followed by transoximination[8] to yield propionoin, identical with an authentic sample prepared from ethyl propionate by acyloin condensation.

The NMR spectrum ($CDCl_3$) of the norbornene-nitrosyl formate adduct taken on a Varian A-60 Spectrometer, is shown in Fig. 2. The aldehydic proton H_G(1H) appears at 7.9 ppm. (TMS internal standard). H_A and H_B (2H) are seen as a quartet centered at 4.97 ppm. The bridgehead protons $H_{C(D)}$ and $H_{D(C)}$(2H) are seen at 2.75 and 2.35 ppm., and H_E and H_F(2H) appear as a complex triplet at 1.92 ppm. The ethane bridge protons are centered at 1.39 ppm. (4H). Thus, the addition reaction appears to have proceeded without rearrangement of the norbornyl skeleton. We have tentatively assigned an exo-cis structure to the adduct analogous to that for the nitrosyl

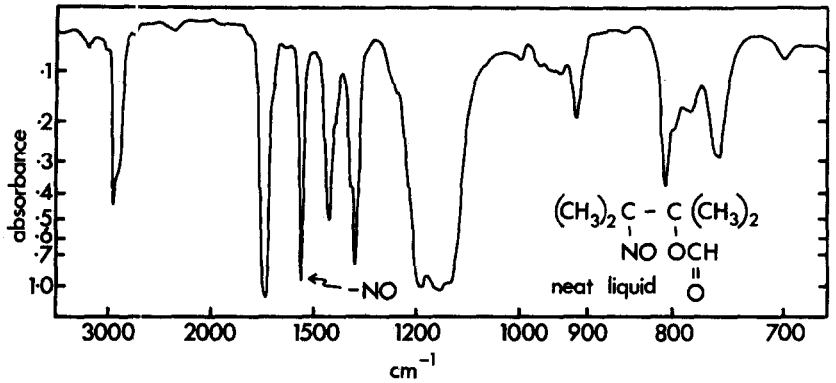


Fig. 1 Infrared Absorption Spectrum Of Addition Product Of Nitrosyl Formate To 2,3-Dimethyl-2-butene.

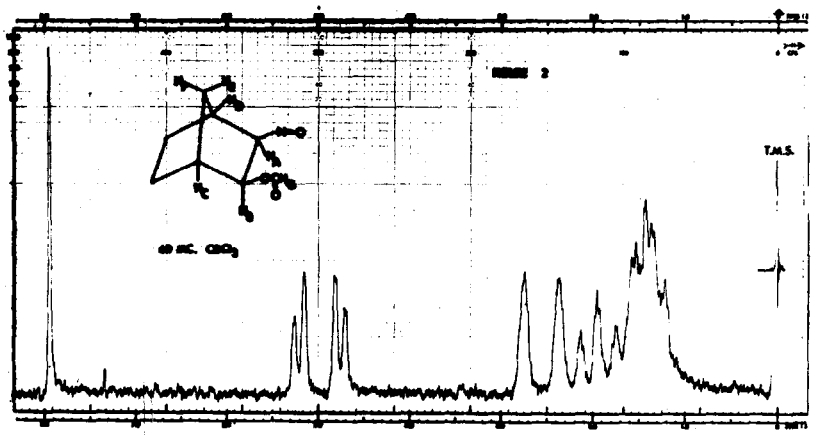
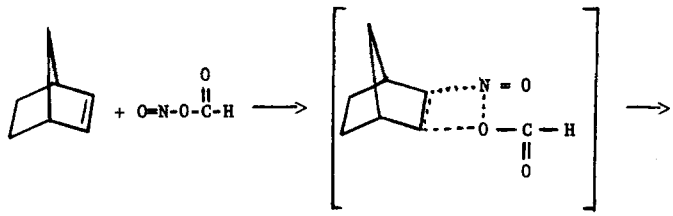
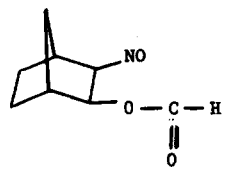


Fig. 2 NMR Spectrum Of Addition Product Of Nitrosyl Formate To Norbornene.

chloride adduct of norbornene as prepared by Meinwald and coworkers.[10] The reaction of nitrosyl formate with norbornene is also rationalized as a four center addition:

$$(CH_3)_2CHCH_2CH_2ONO + HCOOH \longrightarrow (CH_3)_2CHCH_2CH_2OH + O{=}N{-}O{-}\overset{\overset{O}{\|}}{C}{-}H$$





Further experimental work is in progress to elucidate the stereochemistry of this adduct as well as of the adducts of cyclohexene and other olefins.

In summary, nitrosyl formate is a reagent that is easily generated in situ and it adds readily to various unsaturated compounds. Investigation of further transformations of the nitrosyl formate adducts is continuing. It has been suggested that nitrosyl formate does not have an independent existence but the reaction proceeds by the addition of a positive species, NO^+, to the double bond followed by termination by the most populous nucleophile, formic acid. To check on this point we have added nitrosyl chloride to cyclohexene in formic acid solution. The only product isolated, in good yield, was the nitrosyl chloride adduct; no formic acid addition was observed.

References and Footnotes

1. Work to be submitted by H. C. Hamann in partial fulfillment of the requirements for the Ph.D. degree Temple University. This research (Pseudohalogens V) was supported in part by Public Health Service Grants No. CA-07803 and CA-07174 from the National Cancer Institute.

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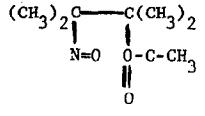
9. We have recently succeeded in adding nitrosyl acetate, generated in situ, to 2,3-dimethyl-2-butene. A solution of isoamyl nitrite and olefin is slowly added to cold glacial acetic acid containing a few drops of 70% perchloric acid as catalyst. The adduct is a blue (monomer), distillable liquid with considerably higher stability than that of the corresponding formate. The infrared spectrum and elemental analysis of the nitrosyl acetate addition product are consistent with the proposed structure.



Further studies are in progress on the in situ preparation and reactions of nitrosyl acylates.

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