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# THE METHOXAZONYL GROUP

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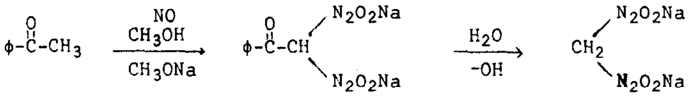
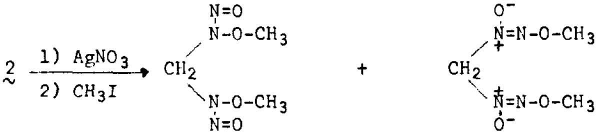
In 1898 Wilhelm Traube(1) published the results of his extensive study of the base catalyzed reaction of ketones with nitric oxide. Typical of the reactions which he observed is that with acetophenone:



1 2

The facile hydrolysis 1 → 2 implies that the $-N_2O_2Na$ grouping has the ability to stabilize negative charge on an adjacent carbon atom. Indeed, we have found that the methylene protons of 2 exchange readily in sodium deuteroxide.

Traube was able to methylate the bis nitroso hydroxylamine salt 2 to form two crystalline "esters" which were formulated(2,3) as 3 and 4:

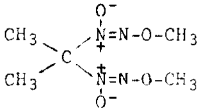


3 4

Compound 3 is quite unstable, decomposing in both acids and bases, as is expected of N-nitroso O-alkylhydroxylamines. Compound 4, m.p. 134°, is much more interesting. It can be recovered unchanged from concentrated acids and bases and from treatment with halogens in a bomb.(1) The infrared spectrum of 4 shows strong absorption at 6.7 μ, associable with the azoxy group. In the nmr spectrum ($CDCl_3$) the two methylene protons appear as a singlet at 4.25 τ and the six O-methyl protons as a singlet at 5.90 τ.

Base (but not acid) catalyzed exchange of the methylene protons in 4 occurs with ease, as is shown by the disappearance of the methylene peak in the nmr spectrum. Presumably the activating properties of the $-\overset{O^-}{\underset{+}{N}}=N-O-CH_3$ group are largely the result of an inductive effect. That the effect is substantial is indicated by the fact that exchange occurs readily even in pure $D_2O$.

With these facts in hand we hoped that a carbon atom activated by the $-\overset{O^-}{\underset{+}{N}}=N-O-CH_3$ group could be alkylated. Indeed, the alkylation of 4 is a facile reaction. In the most successful procedure sodium hydride and methyl iodide are stirred together with 4 in dioxane. Vigorous evolution of hydrogen is observed, and a 55% yield of 5 is obtained. Analytical and spectral data are in accord with structure 5. The nmr spectrum shows singlets of equal intensity at 5.90 τ and at 7.89 τ, and a set of gem-dimethyl peaks at 7.2 and 7.3 µ is clearly visible in the infrared spectrum.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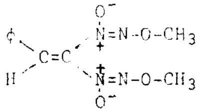
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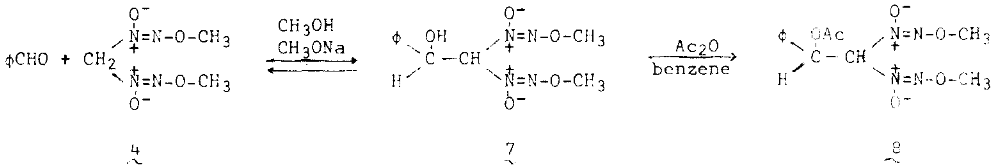
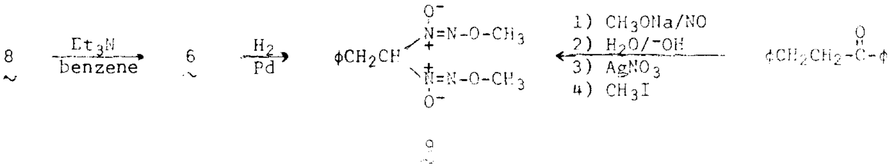
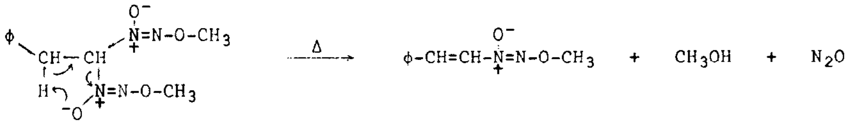
The benzylidene derivative 6 cannot be formed directly from 4 and benzaldehyde. For successful reaction, an excess of benzaldehyde in sodium methoxide is required to drive the equilibrium to the alcohol 7:



Alcohol 7 cannot be dehydrated, but 6 is obtained by treatment of acetate 8 with triethylamine in benzene. Analytical and all spectral data confirm the structure of 6. The nmr spectrum shows the two non-equivalent methyl groups (5.77, 5.84 τ), the phenyl protons (2.59 τ), and the single vinyl proton (2.17 τ). Hydrogenation of 6 yields 9, which is also obtained from benzyl acetophenone via Traube's reactions.

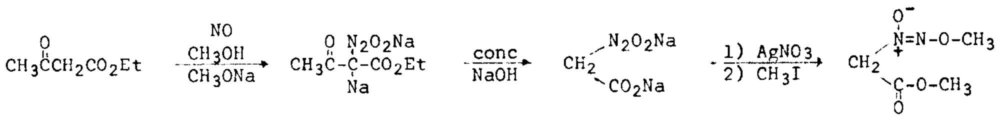


Compound 9 loses methanol and nitrous oxide on pyrolysis to produce the olefin 10 (nmr: 2.29 τ, doublet [1]; 2.62 τ, doublet [1]; 2.67 τ [5]; 5.92 τ [3]).



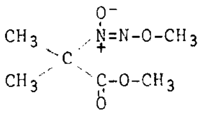
9 10

Traube found that acetoacetic ester in base absorbs only two molecules of nitric oxide with the formation of 11. Treatment with concentrated sodium hydroxide yields 12, from which 13 is obtained:

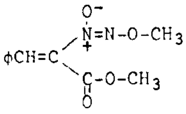


11 12 13

As is the case with 4, 13 is easily alkylated on carbon, to yield 14. In contrast to 4, 13 forms the benzylidene derivative 15 directly. Pyrolysis of 16, the product of hydrogenation of 15, yields methyl cinnamate, methanol, and nitrous oxide.



14



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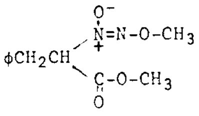
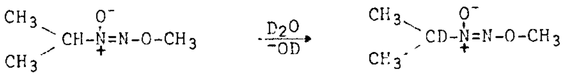


16

It has been suggested(3) that Traube's compounds should be formulated as $R\text{-}\underset{+}{\overset{O^-}{N}}=\underset{+}{\overset{O^-}{N}}\text{-}CH_3$. In addition to the fact that this is the structure generally accorded to nitroso dimers (which are far less stable than Traube's compounds), the exchange evidence militates against such a proposal. An unambiguous case is that of 17, obtained from isobutyrophenone:

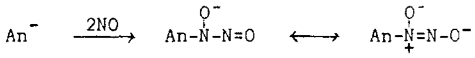


17

No exchange of methyl protons in 17 is observed. If the structure of 17 were $(CH_3)_2CH\text{-}\underset{+}{\overset{O^-}{N}}=\underset{+}{\overset{O^-}{N}}\text{-}CH_3$, then formation of $(CH_3)_2CD\text{-}\underset{+}{\overset{O^-}{N}}=\underset{+}{\overset{O^-}{N}}\text{-}CD_3$ would be expected.

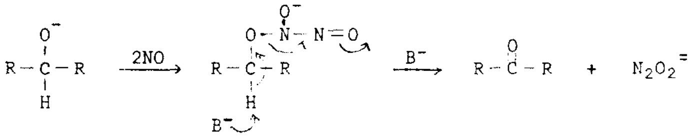
We refer to the $-\overset{O^-}{\underset{+}{N}}=N-O-CH_3$ group as the "methoxazonyl" group, to suggest the activating characteristics which it holds in common with the carbonyl group. Thus, **4** is bis methoxazonyl methane.

It should be noted that a number of workers(4-9) have investigated the reactions of nitric oxide with anions. In all cases the reactions are of the general type:



$$An^- \xrightarrow{2NO} An-\overset{O^-}{N}-N=O \longleftrightarrow An-\overset{O^-}{\underset{+}{N}}=N-O^-$$

Hyponitrite ion is known to be formed in the base catalyzed nitric oxide oxidation of alcoholates.(7) The reaction may be thought of as:(10,11)



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(10) The work herein described is abstracted from: C. E. Wintner, Ph.D. Thesis, Harvard University, 1963 [*Dissertation Abstr.*, **24**, 1841 (1963) No. 63-7839].

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