THE REACTION OF ACETONE WITH NITROGEN TETROXIDE

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Nitrogen tetroxide, a powerful oxidizing agent, reacts with nearly
all classes of organic compounds under a variety of conditions (1). Gener-
ally, little selectivity is observed in these reactions since nitric acid,
nitrous acid or lower oxides of nitrogen are produced in the primary reac-
tions and institute further indiscriminant oxidation.

Acetone has been shown to form a 2:1 complex with nitrogen tetroxide
at -40° (2) and it has been reported that at higher temperatures only a
complex mixture of products consisting of cyanides, nitrates and nitro com-
pounds could be detected (3).

However, we have found that acetone can be oxidized with nitrogen
tetroxide to give a furoxan derivative in high yield. When anhydrous nitrogen
tetroxide was permitted to react with a ten-fold excess of acetone at 0-5°, a
highly unstable intermediate was produced (4). Upon heating this initial
reaction product to 50°, a slow decomposition occurred with the evolution of

1. J. L. Riebsomer, Chem. Rev., 36, 157 (1945).

2. C. C. Addison and J. C. Sheldon, J. Chem. Soc., 1956, 1941.

3. P. Gray and A. D. Yoffe, Chem. Rev., 55, 1069 (1955).

4. An attempt to distill the crude reaction product which contained substan-
   tial amounts of this unstable intermediate resulted in an explosion.
   Thus, proper precautions should be exercised in the subsequent decomposi-
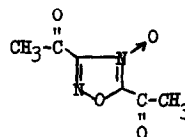   tion step.

nitrogen oxide gases. Removal of the volatile solvent and by-products under
vacuum at 50° afforded a yellow liquid (b.p. 100°/1.0 mm.) in 93% yield
(assuming one mole of nitrogen tetroxide is required for each mole of
acetone). The structure of this product has been shown to be diacetyl-
furoxan (I) by virtue of chemical and spectral evidence.
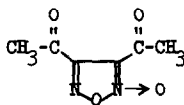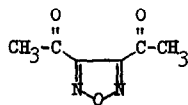
    I   II   III

The elemental analysis and molecular weight determination established
a $C_6H_6N_2O_4$ structure for the product and the n.m.r. spectrum possessed two
peaks of equal intensity at -2.60 and -2.70 ppm. indicative of two different
acetyl groups. The infrared and ultraviolet spectra of I exhibit the
characteristic absorption of known furoxan derivatives (5,6). The infrared
spectrum revealed bands at 1605 (furoxan ring) and 1712 cm.$^{-1}$ (acetyl
groups) (7a) and a maximum was observed at 275 mμ (log $\in$ 3.62, methanol)
in the ultraviolet region.

Further support for the furoxan structure was gained from reduction
of the N-oxide I to the corresponding diacetylfurazan (II). The deoxygena-
tion of I with trimethylphosphite gave a product which exhibited a single
resonance peak (two solvents, CCl_4 and C_6H_6) in the n.m.r. spectrum at
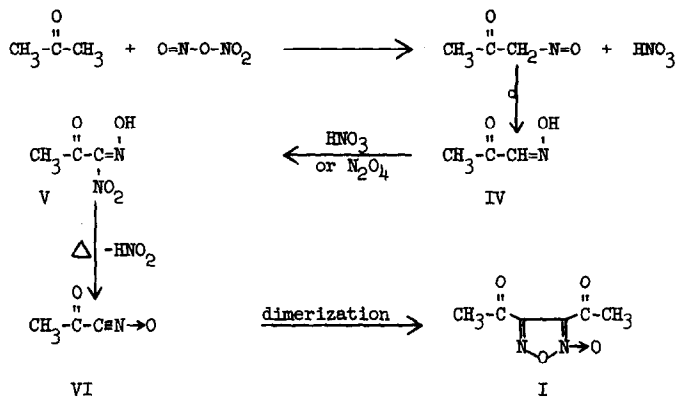-2.71 ppm. and whose infrared spectrum was consistent with the anticipated

5. N. E. Boyer, G. M. Czerniak, H. S. Gutowsky, and H. R. Snyder, *J. Am.
    Chem. Soc.*, __77__, 4238 (1955).

6. J. H. Boyer, G. A. Stover, and U. Toggweiler, *J. Am. Chem. Soc.*, __79__
    1748 (1956).

7. L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," John Wiley
    and Sons, Inc., New York, 1958, (a) p. 132, (b) p. 95, (c) p. 297.

diacetylfurazan. Reduction of the isomeric 1,2,4 oxadiazole III, an equally probable product from a mechanistic standpoint (vide infra), would have produced the unsymmetrical 3,5-diacetyl-1,2,4-oxadiazole whose acetyl groups should be reflected as two peaks in the n.m.r. spectrum.

Diacetylfuroxan has been reported earlier as an unstable yellow oil, however, no evidence had been presented for its structure. In the first instance, isonitrosoacetone was oxidized with nitrogen tetroxide (8), while in the second, α-chloro-α-isonitrosoacetone was allowed to react with silver nitrite (9). It appears that in both cases the product was indeed diacetylfuroxan as postulated, and in the former case the reported mono-phenylhydrazone possessed the same melting point (161°) as the phenyl-hydrazone prepared from our material. Although our product does not appear to be inherently unstable at normal temperatures, the instability reported previously may have been caused by the presence of substantial amounts of a nitrolic acid precursor.

Mechanistically, the oxidation appears to involve reaction of the enolic form of acetone with N_2O_4 to give nitrosoacetone which would rapidly isomerize under the acidic reaction conditions to the thermodynamically more stable oxime IV (10). Nitric acid produced in the nitrosation step or nitrogen tetroxide itself could then oxidize the oxime IV to pyruvonitrolic

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8. W. S. Mills, Chem. News and J. Phys. Science, 88, 228 (1903).

9. G. Ponzio and G. Charrier, Gazz. chim. ital., 37, 65 (1907).

10. The nitrosating action of N_2O_4 is well known and the reactive species which effects nitrosations appears to be $O=N-O-NO_2$ which in ionizing media can readily dissociate to $NO^{\oplus}$ and $NO_3^{\ominus}$, see reference (3), p. 1092.

$$CH_3-\overset{\overset{O}{\|}}{C}-CH_3 \;+\; O=N-O-NO_2 \;\longrightarrow\; CH_3-\overset{\overset{O}{\|}}{C}-CH_2-N=O \;+\; HNO_3$$

$$CH_3-\overset{\overset{O}{\|}}{C}-\underset{\overset{|}{NO_2}}{C}=\overset{OH}{N} \qquad \overset{HNO_3}{\underset{or\ N_2O_4}{\longleftarrow}} \qquad CH_3-\overset{\overset{O}{\|}}{C}-\overset{OH}{CH}=N$$

V   IV

$$\Delta \Big| -HNO_2$$

$$CH_3-\overset{\overset{O}{\|}}{C}-C\equiv N\rightarrow O \qquad \overset{dimerization}{\longrightarrow} \qquad CH_3-\overset{\overset{O}{\|}}{C}\underset{N_{\diagdown O}\diagup N\rightarrow O}{\overbrace{}}\overset{\overset{O}{\|}}{C}-CH_3$$

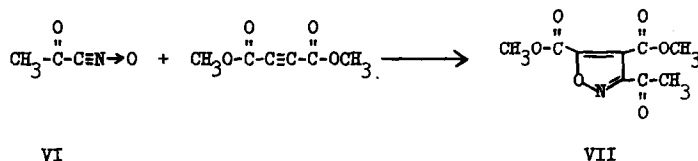VI   I

acid (V) (11). The nitrolic acid is believed to be the unstable intermediate
formed in the early stages of the oxidation. When the reaction is conducted
at 5°, the nitrolic acid V appears to be the primary product and has been
tentatively identified by its infrared spectrum (broad hydroxyl absorption
at 3500-3100 cm.$^{-1}$ and sharp, intense bands at 1560 and 1375 cm.$^{-1}$ which can
be attributed to the nitro group) and its n.m.r. resonance peaks (methyl
group at -2.49 ppm. and the acidic hydrogen at -9 to -10 ppm.) (7b,c).

Thermal decomposition of the nitrolic acid could be expected to lose
the elements of nitrous acid to produce a nitrile oxide (VI) (12). Head-to-
head 1,3-dipolar dimerization of VI would lead to the observed product
diacetylfuroxan (I). (N.B. head-to-tail dimerization could conceivably give
the 1,2,4-oxadiazole oxide III.) The nitrile oxide was shown to be the pre-
cursor to diacetylfuroxan by virtue of a trapping experiment. If dimethyl
acetylene dicarboxylate is added at an intermediate stage of the reaction
(after the nitrogen tetroxide has undergone reaction), the 1,3-dipolar

11. That this is tenable can be inferred from the preparation of nitrolic
    acids, a procedure which often involves the nitration of the corre-
    sponding aldoxime with nitric acid or N$_2$O$_4$, see J. H. Boyer and
    H. Alul, J. Am. Chem. Soc., 81, 4237 (1959).

12. H. Wieland, Ber., 39, 2553 (1906); 40, 418 (1907).

adduct with acetylnitrile oxide (VI) can be isolated. The adduct, 3,4-di-
carbomethoxy-5-acetylisoxazole (VII), was identified from its infrared
absorption (1752 (v.s.) and 1720 (s.) cm.$^{-1}$) and its n.m.r. spectrum which
exhibited three sharp peaks of equal area at -4.00 (-CO$_2$CH$_3$), -3.96 (-CO$_2$CH$_3$)
and -2.70 (-C-CH$_3$) ppm. The mass spectrum of VII (molecular ion at m/e 227)
as well as its elemental analysis and molecular weight determination are
also consistent with the structural assignment.

$$CH_3-\overset{O}{\overset{\|}{C}}-C\equiv N\rightarrow O \ + \ CH_3O-\overset{O}{\overset{\|}{C}}-C\equiv C-\overset{O}{\overset{\|}{C}}-OCH_3 \ \longrightarrow$$

VI

VII

Although nitric acid previously has been shown to be an effective
means of producing diaroylfuroxans from methyl phenyl ketones, the reaction
was limited only to aromatic ketones (13). Nitrogen tetroxide, however, can
be used to convert both aliphatic and aromatic methyl ketones to furoxans.
For example, acetophenone and pinacolone have been oxidized to their
respective furoxan derivatives with nitrogen tetroxide and will be the
subject of a later communication.

13. H. R. Snyder and N. E. Boyer, *J. Am. Chem. Soc.*, 77, 4233 (1955).