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THE REACTION OF AROMATIC NITROSO COMPOUNDS WITH CYANIDE ION IN APROTIC SOLVENTS

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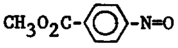
A review of the chemical literature reveals a number of addition reactions to the nitroso functional group which appear analogous in many respects to those observed for carbonyl compounds.[1] It is also recognized that nitroso compounds are excellent acceptors of electrons from anionic species to yield corresponding radical anions.[2]

In connection with another investigation currently underway in this laboratory, it became necessary to evaluate the behavior of cyanide ion toward aromatic nitroso compounds. This report communicates the preliminary results obtained therefrom.

Methyl p-nitrosobenzoate (1) was chosen as the representative nitroso compound since it is easily obtained[3] and manipulated (long term stability and low vapor pressure). Furthermore, the reaction products are conveniently characterized by nmr spectroscopy (p-disubstituted aromatic pattern as well as the carbomethoxy singlet at ca δ 4.0).

Addition of 1 to sodium cyanide (1:1 mole ratio) in aprotic solvent [e.g., dimethyl sulfoxide (DMSO) or N,N-dimethylformamide (DMF)] resulted immediately in a near quantitative yield of methyl p-(N-hydroxycyanamino)benzoate (2) [mp >60° (dec); nmr (δ, acetone-d_6), 10.8 (s, 1H, -OH), 8.08 and 7.32 (2d, 4H, J = 9 Hz, $-C_6H_4-$), 3.90 (s, 3H, $-OCH_3$); ir (cm^{-1}), 3200 (-OH), 2232 (-CN), 1725 (ester)]. Addition of methyl iodide to the reaction mixture prior to work-up converted 2 into methyl p-(N-methoxycyanamino)benzoate (3) [100 %; mp 91-92°; nmr (δ, acetone-d_6), 8.11 and 7.28 (2d, 4H, J = 9 Hz, $-C_6H_4-$), 4.06 (s, 3H, $>N-OCH_3$), 3.90 (s, 3H, $-CO_2CH_3$); ir (cm^{-1}), 2210 (-CN), 1722 (ester); ms (m/e), 206 (M^+)]. Although 2 is unstable and deteriorates rapidly on standing, 3 is stable.

Formation of 2 may be conveniently explained by assuming nucleophilic attack by cyanide



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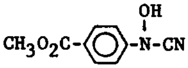

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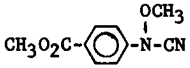

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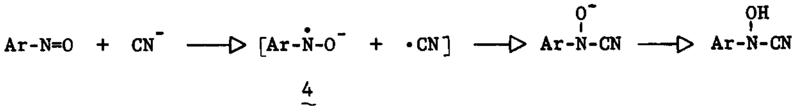
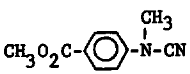
ion on the nitroso group of 1; however, an electron-transfer process, *via* radical anion 4 (Ar- = CH_3O_2C--), cannot be ruled out at this stage of the investigation.[4,5]



$$Ar{-}N{=}O + CN^- \longrightarrow \underset{4}{[Ar{-}\overset{\bullet}{N}{-}O^-} + \bullet CN] \longrightarrow Ar{-}\overset{O^-}{N}{-}CN \longrightarrow Ar{-}\overset{OH}{N}{-}CN$$

The literature pertaining to N-hydroxyarylcyanamides appears limited to phenyl[6] and p-tolyl[7] derivatives. In each case, the product (noticeably unstable) was obtained by treatment of the corresponding arylhydroxylamine with cyanogen bromide. Our procedure is of interest in that it provides for the *in situ*, quantitative formation of N-hydroxyarylcyanamides, a class of compounds about which little information is presently available.

As a part of this preliminary study, the behavior of 2 toward nitroso compounds was investigated. Thus, 1 was added to a solution of sodium cyanide in DMF (2:1 mole ratio) in order to generate the anion of 2 in the presence of an equimolar quantity of 1. The reaction was allowed to continue (N_2 atm) for three days. To achieve a more effective product separation (tlc, Silica Gel PF, chloroform), >N-H and -OH containing compounds were methylated by the addition of methyl iodide to the reaction mixture prior to workup. Products isolated were methyl p-(N-methylcyanamino)benzoate (5) [30 %; mp 142-143°; nmr (δ, acetone-d_6), 8.06 and 7.26 (2d, 4H, J = 9 Hz, $-C_6H_4-$), 3.85 (s, 3H, $-OCH_3$), 3.49 (s, 3H, $>N-CH_3$); ir (cm^{-1}), 2228 (-CN), 1725 (ester); ms (m/e), 190 (M^+)], methyl p-nitrobenzoate (6) [30 %; mp 94-95° (lit.[8] mp 96°)], and dimethyl 4,4'-azoxydibenzoate (7) [20 %; mp 205-206° (lit.[9] mp 204-205°); nmr (δ, $DCCl_3$), 8.18 (s, 4H, $-C_6H_4-N(O)=$), 8.30 and 8.15 (2d, 4H, J = 9 Hz, $-C_6H_4-N=$), 3.98 and 3.96 (2s, 6H, $-OCH_3$); ir (cm^{-1}), 1730 (ester); ms (m/e), 314 (M^+)]. Similar results were obtained where 2 was prepared, isolated and reacted with 1. A reaction time of only thirty minutes resulted in the formation of 3 and 7 as major products along with much smaller quantities of 5 and 6.



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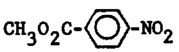

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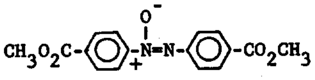

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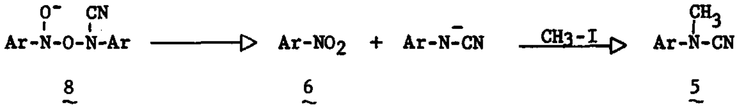
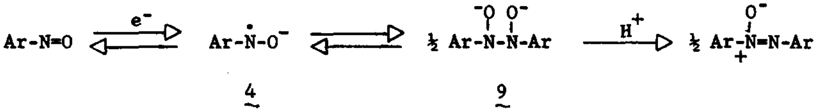
Although complete mechanistic details concerning the nitroso-cyanide reaction (2:1 mole ratio) are uncertain at this time, two observations deserve comment. First, the fact that 5 and 6 are formed in equimolar quantities suggests that these products are related by way of a common intermediate [e.g., 8 (Ar- = CH_3O_2C--)]. Adduct 8 is envisioned as arising from



$$\text{Ar-}\overset{O^-}{\text{N}}\text{-O-}\overset{CN}{\text{N}}\text{-Ar} \longrightarrow \text{Ar-NO}_2 + \text{Ar-}\bar{\text{N}}\text{-CN} \xrightarrow{CH_3\text{-}I} \text{Ar-}\overset{CH_3}{\text{N}}\text{-CN}$$

either nucleophilic addition of 2 to 1 or *via* electron-transfer and radical combination.[5]

Second, an increase in the yields of 5 and 6 with time, at the expense of 2 and 7, is reconciled by assuming the rapid formation of radical anion 4, which is expected to equilibrate with its dimer 9; then, if given enough time, the much slower reaction leading to 5 and 6 becomes significant.[4]



$$\text{Ar-N=O} \underset{}{\overset{e^-}{\rightleftharpoons}} \text{Ar-}\dot{\text{N}}\text{-O}^- \rightleftharpoons \tfrac{1}{2}\,\text{Ar-}\overset{^-O}{\text{N}}\text{-}\overset{O^-}{\text{N}}\text{-Ar} \xrightarrow{H^+} \tfrac{1}{2}\,\text{Ar-}\underset{+}{\overset{O^-}{\text{N}}}\text{=N-Ar}$$

To demonstrate the generality of the nitroso-cyanide reaction (2:1 mole ratio) in aprotic solvent, nitrosobenzene was reacted with sodium cyanide in DMSO. Spectral analysis of the methylated reaction mixture (tlc separation) showed that the expected products (i.e., N-hydroxyphenylcyanamide, phenylcyanamide, nitrobenzene, and azoxybenzene) had formed.

A slow reaction was observed to occur between 1 and cyanide ion in methanol (1:1 mole ratio) to produce essentially equal quantities of 6 and 7 as the major products along with a trace of 3.

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REFERENCES

1. For recent reviews concerning nitroso compounds, see: (a) J. H. Boyer in "The Chemistry of the Nitro and Nitroso Groups," Pt. 1, H. Feuer, Ed., Interscience, New York, N. Y., 1969, pp 215-299; (b) P. A. S. Smith, "Open-Chain Nitrogen Compounds," Vol. 2, Benjamin, New York, N. Y., pp 355-389.
2. For a detailed discussion of electron-transfer processes involving nitroso compounds, see: G. A. Russell, E. J. Geels, F. J. Smentowski, K.-Y. Chang, J. Reynolds, and G. Kaupp, *J. Amer. Chem. Soc.*, **89**, 3821 (1967).
3. Compound **1** was prepared according to the procedure reported for the synthesis of the ethyl ester [E. Hecker, *Chem. Ber.*, **88**, 1666 (1955)].
4. Absence of the corresponding azoxy compound as a reaction product has been taken as evidence against the intermediacy of nitroso radical anion in basic alcoholic solution [G. A. Russell and E. J. Geels, *J. Amer. Chem. Soc.*, **87**, 122 (1965)]. However, the argument is invalid in aprotic solvents (e.g., DMSO) where the nitroso radical anion, presumably in equilibrium with its dimer, is observed to be stable for several hours.[2] The dimer is able to form azoxy compound only after accepting a proton. Thus, other combination processes should favorably compete with azoxy formation in aprotic solvents.
5. To establish the possible involvement of radicals as intermediates in the nitroso-cyanide reaction, a detailed report, utilizing esr techniques will be forthcoming.
6. H. Wieland, *Chem. Ber.*, **37**, 1536 (1904).
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