RATES AND EQUILIBRIA FOR THE INTERACTION OF CYANONITROTHIOPHENE DERIVATIVES
WITH THE CH_3O^- ION IN METHANOL SOLUTION

Giancarlo Doddi, Gabriello Illuminati and Franco Stegel

Department of Chemistry and Centro C.N.R. sui Meccanismi di Reazione,

University of Rome, 00185 Roma, Italy

In continuation of our studies[1] on the rate of formation and stability of
Meisenheimer-type adducts from heteroaromatic substrates, we have examined the
role of the cyano group on the formation of Meisenheimer-type adducts by the
reaction of CH_3O^- in methanol solution with cyanonitrothiophene derivatives. We
are prompted to report the present work by the fact that some of the results
are unusual and depend on the hydroxylic nature of the solvent used.

4-Cyano-2-nitrothiophene (I) ($\lambda_{max}^{(2)}$=273, 298nm; nmr spectrum: τ_α =1.48,
τ_β=1.73, J=1.8 Hz) reacts with methoxide ion in methanol as well as in DMSO[3]
to give the Meisenheimer-type adduct II (λ_{max}=260, 398nm; nmr spectrum:
τ_α =3.80, τ_β =2.54, J ≤ 0.1 Hz). The second-order rate constant and equilibrium
constant for the formation of adduct II in methanol have been obtained spec=
trophotometrically at 398 nm and are reported in the Table together with relat=
ed data for the formation of adduct III from 2,4-dinitrothiophene.

In contrast, 2-cyano-4-nitrothiophene (IV) is unable to yield a Meisenheimer-
type adduct in methanol solution, because of a supervening interaction of the
methoxide reagent with the 2-cyano group. The behavior of IV, unlike that of I,
is at variance with that observed in DMSO-d_6 solution by Terrier et al.[3].

Upon addition of one equivalent of methoxide to a methanol solution of IV
(λ_{max}=237, 262(sh) nm; nmr spectrum: τ_α =1.13, τ_β =1.70, J=2 Hz), we only
observed the appearance of a new species displaying an nmr AB system (τ_α=1.33,
τ_β =1.75, J=1.5 Hz), and maxima of absorption at 245 and 270(sh) nm. The nmr
spectrum was only slightly different from that of IV, and very different from
the spectrum of adduct V, that is formed from the same reagents in DMSO-d_6

(τ_α=3.67, τ_β=2.80, J=0.5 Hz).[3]

Evaporation of the methanolic reaction mixture yielded a solid insoluble
in benzene. The methanol solution of the same solid has an nmr spectrum iden=
tical to that of the product of the reaction observed in situ. On the other
hand, a DMSO-d$_6$ solution of this solid displays the nmr spectrum of the ad=
duct V ! After mild acidification of a solution of the solid in water-methanol,
we obtained an organic compound, which was identified as methyl 4-nitro-
2-thiophenecarboxyimidate (VI) by ms (parent peak at 186 m/e), ir (3330,
1640 cm^{-1} in Nujol), nmr (τ_α=1.15, τ_β=1.74, J≈1-2 Hz) and uv (λ_{max}=246,
270(sh) nm). Addition of sodium methoxide to a methanol solution of VI, and
evaporation of the solvent, left a salt having the same properties of the
solid previously obtained, which was therefore identified as the sodium salt
corresponding to anion VII.

The formation of carboxyimidates from nitriles, though well known[4], does
not seem to interfere with the Meisenheimer adduct formation in the
cyanonitrobenzene series[5]

Experimental data and theoretical calculations[6] agree in indicating that
in typical Meisenheimer adducts a para nitro group is more effective than an
ortho nitro group in stabilizing the anion. A similar effect seems to hold in
the thiophene series, as adduct II, where the point of attack of the nucleo=
phile is a para-like position relative to a nitro group, is effectively
stabilized in DMSO as well as methanol solution. The stabilizing influence of
the cyano group, even though strong, is markedly less than that of the nitro
group. As a result, adduct II is less stable than adduct III. The apparently
anomalous behavior of compound IV in methanol must be related to the fact that
the unsubstituted α position, which should be attacked by the reagent in
order to form adduct V, is para-like with respect to a cyano group. This group
is not so effective as the nitro group in promoting the delocalization of the
negative charge. In methanol the prevailing product is adduct VII, which is
likely to be stabilized by the formation of hydrogen-bonds between the negative
nitrogen atom and the protic solvent. In DMSO solution, where hydrogen-bond
donation from the solvent is absent and a stabilizing dispersion interaction
between the solvent and a charge-delocalized anion is expected[7], adduct V is
regularly obtained.

We wish to point out that since adduct VII, as isolated from methanol,

undergoes a ready interconversion to adduct V upon solution in DMSO-d_6, caution should be taken in the characterization of adducts obtained in a hydroxylic solvent by the nmr spectrum of their DMSO solutions.

Since an investigation of the formation of V in methanol solution was hampered by the competing formation of VII, we have obtained information on the role of a para-like cyano group from 2-cyano-5-methoxy-4-nitrothiophene(VIII)

TABLE. Specific rates and equilibrium constants for the formation of Meisenheimer-type adducts, in methanol, at 25°.

	(II)[a]	(III)[b]	(IX)[a]	(X)[b]
k ($M^{-1}s^{-1}$)	$7.8 \pm 0.2 \times 10^{-1}$	1.5×10	2.14 ± 0.1	3.6×10
K (M^{-1})	$1.5 \pm 0.1 \times 10^{2}$	8×10^{2}	$1.53 \pm 0.3 \times 10^{3}$	$ca. 4 \times 10^{5}$

a) This work. b) Reference 1.
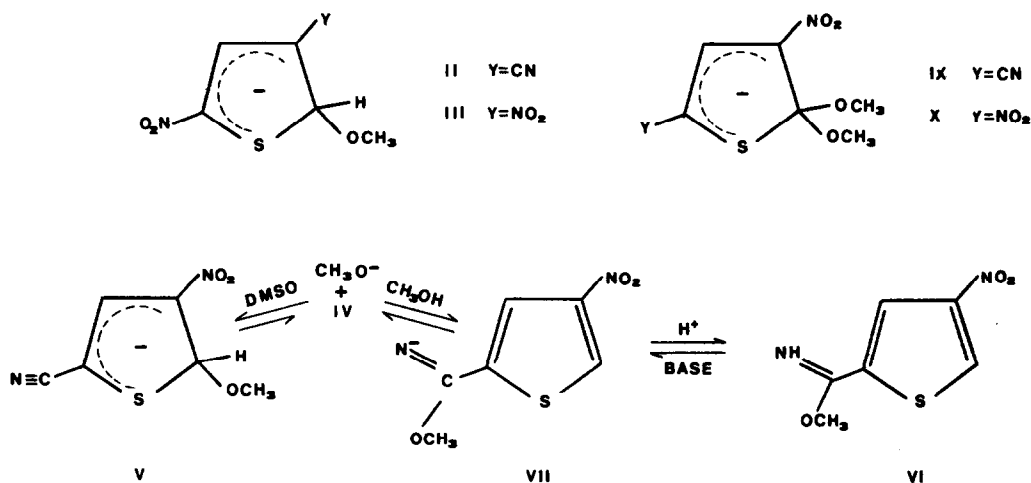
Here the stability of the adduct formed upon attack on position 5 is expectedly increased by the formation of a geminal dimethoxy group, an effect which has been observed in nitro-substituted adducts[8]. In line with this expectation, the reaction between methoxide ion in methanol and VIII (λ_{max}=278, 313 nm; τ_β=1.80, τ_{OCH_3}=5.75) does indeed lead to an adduct whose spectral properties (λ_{max}=290, 399 nm, τ_β=2.97) are in accord with struc= ture IX. Further evidence for this structure is provided by the fact that

adduct formed in DMSO-d_6 shows a signal at τ 2.90, and that the adduct isolated from methanol and dissolved in DMSO-d_6 shows a singlet at τ 2.90 and another singlet, which is six times more intense, $\left[C(OC\underline{H}_3)_2 \right]$, at τ 6.78.

The rate and equilibrium constants for the formation of adduct IX in methanol, at 25°, are reported in the Table together with the values for the formation of adduct X, where the negative charge is delocalized by two nitro groups. Replacement of nitro group in the para-like position by a cyano group causes a considerably more dramatic effect than the corresponding replacement in the ortho-like position, in analogy with the findings by Fendler on cyano= nitrobenzenes[5]. Comparison of the values obtained for K_{III}, K_{IX} and K_X suggests that the equilibrium constant for the formation of adduct V in methanol solution should not be any larger than 3 M^{-1}.

The greater stability of VII as compared to that of V results from a combination of the moderate electron-attracting power of cyano group and of the reactivity of this group towards nucleophilic reagents.

<div align="center">REFERENCES</div>

1. G.Doddi, G.Illuminati and F.Stegel, Chem. Comm., 1143(1972).

2. Uv and nmr (Jeol C-60, sweep width 540 Hz, DSS as internal reference) are referred to methanol solutions, unless otherwise stated. For nmr studies use of deuterated methanol led to complications due to fast H/D exchange at the unsubstituted α position.

3. C.Paulmier, M.P.Simonnin, A.P.Chatrousse and F.Terrier, Tetrahedron Letters, 1123(1973).

4. Z.Rappoport,Ed.,"The Chemistry of the Cyano Group", Interscience, London, 1970,p. 267.

5. E.J.Fendler, W.Ernsberger and J.H.Fendler, J. Org. Chem., 36, 2333(1971).

6. H.Wennerström and O.Wennerström, Acta Chem. Scand., 26, 2883(1972), and references therein cited.

7. J.F.Coetzee and C.D.Ritchie,Eds.,"Solute-Solvent Interactions", Marcel Dekker, New York, 1969, p. 219.

8. C.F.Bernasconi, J. Amer. Chem. Soc., 93, 6975(1971).