# High Resolution Nuclear Magnetic Resonance Study of Chemical Reactions Using Flowing Liquids: Kinetic and Thermodynamic Intermediates Formed by the Attack of Methoxide Ion on 3,5-Dinitrocyanobenzene

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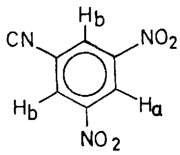
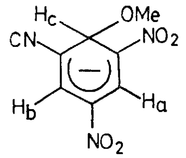
*Summary* Equipment and techniques have been developed which make possible the measurement of high resolution n.m.r. spectra in rapidly flowing, chemically reacting systems, and have been used to characterize the kinetically formed intermediate complex as well as the thermodynamically stable one from the attack of methoxide ion on 3,5-dinitrocyanobenzene.

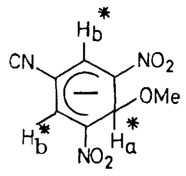
MOST spectroscopic investigations of chemical reactions are carried out using u.v./visible spectroscopy which has the advantage of a high degree of sensitivity but which is non-diagnostic. High resolution n.m.r. is less sensitive but has a great advantage as a diagnostic tool since it can provide more information about molecular structure and is now one of the most important techniques used in structure investigations in equilibrium systems. However, for non-equilibrated systems, it has only been used to study very slow reactions in static liquids. To our knowledge, the successful application of flowing liquids to an n.m.r. study of chemical reactions has never been reported. One limitation to the use of flowing liquids in n.m.r. spectroscopy is the relatively long relaxation times (several seconds) of the nuclei involved.† Techniques and equipment have been developed‡ which avoid this and enable n.m.r. measurements to be made in dynamic reacting systems. A probe is used which includes two reservoirs which permit the nuclei of the two solutions to come to thermal equilibria in the magnetic field before they are mixed in a high pressure mixing chamber and passed through measuring coils. At suitable flow rates, the absolute signal/noise ratio is appreciably better than that of a stationary sample. In this approach, the flow rates are limited by the capacities of the reservoirs, but these can be maximised by using a probe design in which transmitter and receiver coupling is minimized by time-sharing techniques.[1]



(1)



(2)



(3)

There has been considerable interest in recent years in the structure and stability of the intermediate complexes formed from the attack of nucleophiles on nitro-aromatic sub-

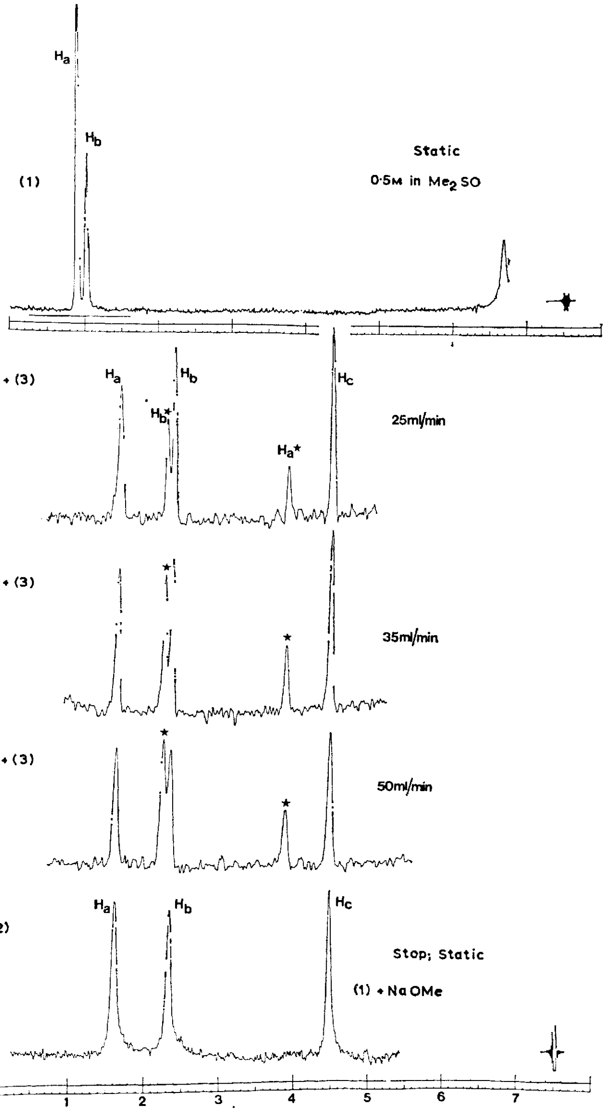


FIGURE. Spectra of the reacting system (1)+NaOMe. From top to bottom: Stationary sample of (1) (0·5M in $Me_2SO$); three spectra at increasing flow-rates of an equimolar mixture of (1) (0·5M in $Me_2SO$) and sodium methoxide (0·5M in 75% $Me_2SO$, 25% MeOH mixture); spectrum of the reacting mixture recorded immediately on stopping the flow.

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† Such a problem does not exist in e.s.r. spectroscopy where the paramagnetic relaxation time is much shorter, but this is obviously restricted to the reactions of radicals.

‡ These will be described in detail in a forthcoming publication.

strates, which might lead to a better understanding of the mechanism of nucleophilic aromatic substitution reactions.[2] N.m.r. has been widely used in these studies, but its use has been restricted to static systems at equilibrium. For this reason we have used the flow technique to study the reaction of sodium methoxide with 3,5-dinitrocyanobenzene (**1**).

The thermodynamically stable product from this reaction has been unambiguously identified[3] as the isomer (**2**) arising from attack of the nucleophile between the nitro- and cyano-groups, since the spectrum shows three resonances of equal intensity at chemical shift values consistent with the suggested structure. The reaction was reported to be effectively instantaneous at 33·5°, and no other species was observed. Since the flow technique permits the observation of short lived intermediates, it was used to determine if the isomeric complex (**3**) was formed from attack between the two nitro-groups at any stage in the reaction.

The spectra obtained are shown in the Figure. The top spectrum, consisting of an $AB_2$ set of multiplets at low field, is that of the parent substrate when the solution is stationary and illustrates that good, well resolved spectra can be obtained without spinning the sample. The bottom spectrum is that of the thermodynamically stable product (**2**). The broadening in this spectrum is due to the presence of anion radicals.

The three middle spectra were recorded on a flowing solution less than a second after mixing the reactants and from top to bottom correspond to increasing flow rates. In addition to the three resonances of the product (**2**), two other signals are clearly resolved at $\tau$ 2·15 and 3·79 of relative intensities 2 : 1. The chemical shifts and intensities are consistent with the second species in the mixture being the isomer (**3**) where the attack has taken place between the two nitro-groups.

As the flow rate is increased, *i.e.* as the time between mixing and observation becomes less, the relative proportion of (**3**) increases to the limiting situation shown in the spectrum second from the bottom. If this is the true limiting situation, it corresponds to a statistical distribution between the two isomers and there are no directive influences favouring the kinetic formation of either isomer. When the flow is stopped, the spectrum quickly changes to the lowest one in the Figure.

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