MEISENHEIMER COMPLEXES IN AROMATIC NUCLEOPHILIC SUBSTITUTION REACTIONS

A Thesis
Presented By

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STATEMENT

All the experimental work, described in this thesis, has been carried out by the author in laboratories of Bolton Institute of Technology between November 1966 and February 1971.

The work has not been presented and is not being concurrently presented for any other degree.

Date: 20th July, 1971.

Signed M Hatton

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MEISENHEIMER COMPLEXES IN AROMATIC NUCLEOPHILIC SUBSTITUTION REACTIONS

ABSTRACT

When this research was commenced it was known that many aromatic nucleophilic substitution reactions proceeded by a mechanism which involves the formation and the decomposition of a Meisenheimer-type of complex. In some cases the formation, and in others the decomposition of such a complex was the rate-determining step. However, the mechanism of formation and the decomposition of these complexes was not known.

This work represents an attempt to establish whether or not the transfer of a hydrogen atom or proton played a major part in the formation and the decomposition of Meisenheimer complexes. The methoxy exchange between 1-methoxy (C-14), 2,4-dinitronaphthalene and methoxide ions where the decomposition of the complex is rate-determining step has been studied in methanol and methanol-o-d and no evidence of a primary kinetic isotope effect has been found.

Methoxy exchange reactions are able to proceed in DMSO solution and have been studied in the presence of 0.3% of methanol or methanol-o-d to aid solubility of sodium methoxide. Kinetic data for the reaction with p-nitroanisole where formation of the complex is rate-determining step are independent of whether methanol or methanol-o-d is used and give no evidence of the existence of a primary isotope effect. The enhanced rate of such reactions in DMSO as compared with methanol as solvent have enabled kinetic data to be obtained for this exchange reaction and the chlorine exchange between 1-chloro,2,4-dinitronaphthalene and chloride ions which are too slow to be studied easily in methanol.

It is concluded tentatively that proton intercession is less important in the decomposition of a Meisenheimer complex than solvation of the incipient anion (methoxide) and is less important in the formation of such a complex than is base catalysis.

DEDICATION

To my father

CONTENTS

CHAPTER I

INTRODUCTION

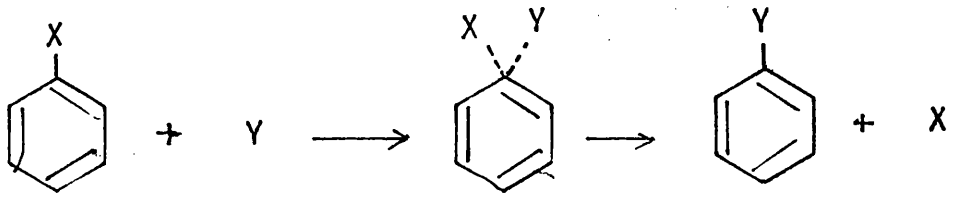
NUCLEOPHILIC SUBSTITUTION AT AN AROMATIC CARBON ATOM

In substitution reactions, a new bond is formed between the reagent and the atom at the seat of substitution, and the existing bond to the displaced group is broken. Such reactions are designated "electrophilic" or "nucleophilic" according to whether the electrons forming the new bond are provided by the atom at the seat of the substitution or by the entering group respectively. Electrophilic substitution at an aromatic carbon atom has been studied extensively for many years, as have nucleophilic substitution reactions at aliphatic carbon atoms, but systematic investigations of aromatic nucleophilic substitution reactions have been made only comparatively recently. This is probably because aromatic nucleophilic substitution is a fairly complex process. For example, the expelled group is rarely hydrogen, in contrast to aromatic electrophilic reactions, owing to the low stability of the hydride anion. Also, facile nucleophilic substitution occurs only when the π-electron cloud is partly withdrawn from the point of attack by electron-withdrawing or "activating" substituents, such as the nitro group which is very effective from the ortho and para positions to the carbon atom under attack.

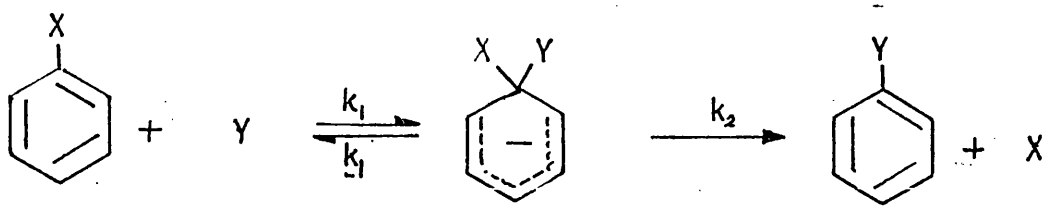
There are three well-established mechanisms of aromatic nucleophilic substitution, unimolecular, which is typified by the uncatalysed decomposition of diazonium salts in aqueous solution, bimolecular, which is followed by most of the reactions so far studied, and benzyne, exemplified by the reactions of unactivated halogeno compounds with strongly basic reagents such as potassamide in liquid ammonia.

The bimolecular mechanism, which is followed by the reactions studied in this thesis, is normally indicated by the observation of second order kinetics (i.e. first order in both substrate and nucleophile), the general dependence of specific rate on the nucleophilic power of the reagent, and the effect of groups already present in the aromatic nucleus. Two alternative mechanisms have been suggested, a one-stage mechanism with synchronous bond-forming and bond-breaking, and a two-stage mechanism in which an intermediate of some stability is formed and subsequently decomposed.

The one-stage mechanism, proposed by Chapman[1] and by Hammond[2], for the attack on weakly activated centres by weak nucleophiles, involves a transition state in which aromaticity is retained. The synchronous bond-forming and bond-breaking process is analogous to the SN2 mechanism for aliphatic nucleophilic substitution, but the carbon atom at the reaction centre cannot accommodate more than four attachments, and a Walden inversion cannot take place. Some workers refer to the process as an "SN2-like" mechanism.



The two-stage mechanism, advocated by Bunnett and Zahler[3] and others[4,5], requires an intermediated of some stability, and the basic scheme may be represented thus:



The mechanism has received considerable support from various directions and is certainly now well established; intermediate complexes have in favourable cases been isolated; but even in cases where isolation has not been possible or where such complexes have been present in only low concentrations, irrefutable evidence for their existence and participation in the aromatic nucleophilic substitution reaction has frequently been obtained.

MEISENHEIMER COMPLEXES

Meisenheimer[6] in 1902 published his often quoted papers about the reactions of nitro aromatic compounds with alkoxide anions in alcoholic media, which led to the formation of red coloured solutions from which red needles could be crystallised. He showed that the crystals, prepared by the action of ethoxide ions on 2,4,6-trinitroanisole, decomposed with dilute acid to give the same equimolecular mixture of trinitroanisole and trinitrophenetole, as did similar crystals prepared by the action of methoxide ions on trinitrophenetole. Meisenheimer's analyses for the two preparations of red crystals are given in Table 1.1, and it is evident that the elemental compositions for both corresponds to the empirical formula $C_6H_2(NO_2)_3.OCH_3.OC_2H_5.K$.

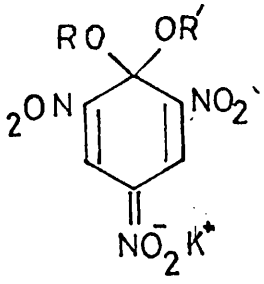
Jackson[7] was independently and concurrently studying this type of complexes, and his conclusions were similar to those of Meisenheimer.

Meisenheimer concluded that the substance formed was an addition complex in which the attacking alkoxide had attached itself to the position where the alkoxy group of the aromatic ether was

TABLE 1.1

Element	C	H	N	K
Found, 2,4,6-trinitroanisole/ethoxide	32.89	3.39	12.94	11.76
Found, 2,4,6-trinitrophenetole/methoxide	32.80	3.28	12.92	11.95
Calculated for $C_6H_2(NO_2)_3.OCH_3.OC_2H_5.K$	33.03	3.06	12.85	11.93

already present. From the deep red colour of the adduct, Meisenheimer considered its structure to be adequately represented by a quinonid-type arrangement:



Such compounds have come to be known as "Meisenheimer Complexes" and many of them, with two groups other than alkoxy attached to an aromatic carbon atom are familiar today and have been examined by techniques involving visible, ultra-violet and infra-red spectrophotometry, and nuclear magnetic resonance spectroscopy as well as by kinetic studies. Their existence was one of the important points made by Bunnett in his support of the two-stage mechanism for aromatic nucleophilic substitution reactions.

MEISEHEIMER COMPLEXES IN AROMATIC NUCLEOPHILIC SUBSTITUTION

The studies work of which this thesis forms a part originated a little more than ten years ago at Leicester College of Technology (now the City of Leicester Polytechnic) when a group of workers began to use radiochemical techniques to study isotopic

exchanges as examples of aromatic nucleophilic substitution reactions. Immediately before this A. W. B. Bamford[8] had been examining the kinetics of the substitution of an aromatic nitro group by the methoxide ion and found for aromatic nitro compounds such as dinitrobenzene and dinitronaphthalene, that the reaction was of first order in each reactant

$$\text{i.e. Rate} = k\left[ArNO_2\right]\left[^{-}OMe\right]$$

Of course this result in itself did not distinguish between the one-stage and the two-stage mechanism and Bamford in his Thesis speculated as to which of these mechanism was operating. He examined critically Meisenheimer's work, which had so often been quoted as evidence for the existence of an intermediate complex and hence, as support for the two-stage mechanism, and concluded that a fully covalently bonded type of complex was not necessary to explain Meisenheimer's results. Bamford preferred to regard the complex as a charge transfer complex between the molecule of aromatic nitro compound and the methoxide ion. He wrote, "there is no reason[9] why a basic anion should not form such a complex and the present author (i.e. Bamford*) suggests that the Meisenheimer compounds should be classified as charge-transfer complexes". He continued, "the production[10] of trinitro-phenetole and trinitroanisole from the complexes by decomposition with acid was taken to indicate that both alkoxy groups are attached to the same atom of the molecule of the complex. This must be the carbon atom carrying the alkoxy group in the original aromatic molecule. The present author (i.e. Bamford*) believes that this deduction entirely ignores the possibility of the independent occurence of the nucleophilic exchange reaction".

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* note by author of this Thesis - i.e. Kattan.

Jackson[7] did in fact allow for this possibility and did look for it in his studies but found no evidence that the exchange reaction had occurred.

In his speculations Bamford assumed that the exchange reaction between methyl picrate and ethoxide ions was very rapid. He was not aware that the rate-determining-step when such highly activated aromatic methoxy compounds are involved, is usually the decomposition, rather than the formation of the intermediate Meisenheimer complex and that excessive activation from nitro groups may well retard this decomposition. Thus, the "nucleophilic exchange reactions" are frequently much slower than Bamford imagined them to be.

In Bamford's work, the incoming and outgoing groups were chemically different and a simple chemical technique (based on a colour reaction for the estimation of nitrite ion) was used to follow the reaction. However, the use of carbon - 14 labelled methoxy compounds enabled aromatic nucleophilic substitution reactions involving the exchange of one methoxy group for another to be studied, and aromatic systems highly activated towards nucleophilic substitution and likely to form Meisenheimer complexes could be compared kinetically with less activated systems. It soon became apparent, from the work of Fendler[11], Katsanos[12] and Gilbert[13] that such reactions, in methanol as solvent, followed two different patterns.

1. Second order kinetics were observed i.e. Rate $= k[ArOR][\bar{O}CH_3]$ where activation of the aromatic system is relatively small, and no measurable concentration of the complex is apparent, e.g. reactions 2,4-dinitroanisole, 1-methoxy, 2-nitronaphthalene and 1-methoxy, 4-nitronaphthalene. Here the rate-determining-step of the reaction is the formation of the intermediate complex, if such complex is formed and both the one-stage and

two-stage mechanisms can be argued since no differentiation can be drawn from the kinetic pattern alone.

2. Reaction involving more highly activated aromatic methoxy compounds enabled the presence of a reasonable concentration of intermediate complex to be deduced, and the kinetics showed that the rates of reaction were proportional to the concentration of this complex rather than to the concentrations of the original reagents, i.e. Rate = $k\,[\text{complex}]$

Reactions showing this pattern were those of 2,4,6-trinitro-anisole, 1-methoxy, 2,4-dinitronaphthalene and 1-methoxy 2,4,5-trinitronaphthalene.

Arguments behind these conclusions were as follows: the experimental technique was to mix methanolic solutions of the aromatic methoxy compounds (where the methoxy group was labelled with carbon-14) and sodium methoxide in methanol at constant temperature, to sample at appropriate times, and analyse each sample by adding it to a toluene-water mixture followed by assaying carbon-14 in the toluene layer (containing the aromatic compound) via a liquid scintillation counter. The less activated compounds of the first group (e.g. 2,4-dinitroanisole, 1-methoxy, 2 and 4 nitronaphthalene) gave a straightforward kinetic plot such as indicated in diagram (1.1) and the intercept of the line on the y-axis coincided with that expected from the count rate of the unreacted aromatic ether.

However, with the more activated compound in the second group (e.g. 1-methoxy, 2,4-dinitronaphthalene, 1-methoxy 2,4,5-trinitro-naphthalene and 1-methoxy, 2,4,7-trinitronaphthalene) the reaction solution almost immediately became coloured red and much of the aromatic methoxy compound was extracted into water rather than into toluene during the

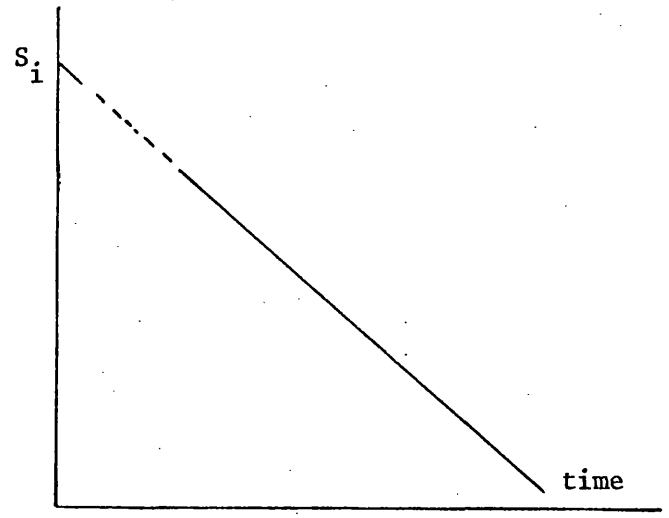


Figure 1.1 Kinetic plot with the rate of formation of Meisenheimer complex is the rate-determining step

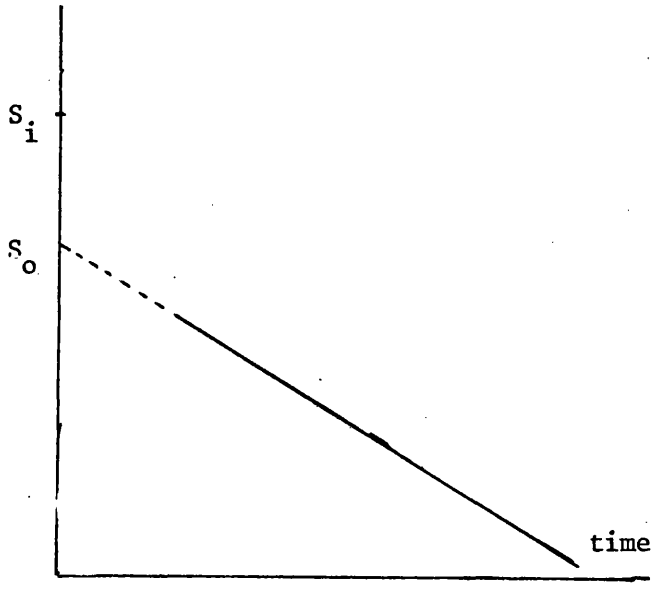
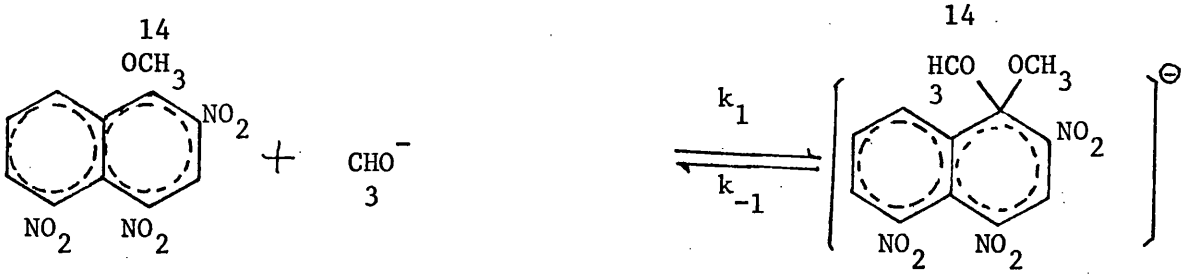


Figure 1.2 Kinetic plot with the rate of decomposition of Meisenheimer complex is the rate-determining step

analytical procedure; proper extraction into toluene was achieved only if the aqueous phase contained a little acid (which also removed the red colour). The kinetic plot was as shown diagrammatically in Figure (1.2), the intercept of the line on the y-axis, S_o, was always appreciably lower than the value expected from the count-rate of the unreacted aromatic ether solution, S_i. S_o became smaller as the concentration of sodium methoxide increased relative to the concentration of the aromatic methoxy compound, but was never observed to be less than $\frac{1}{2}S_i$.

Katsanos studied 1-methoxy, 2,4,5-trinitronaphthalene and discussed the behaviour of such highly activated compounds in these words[14]: "It would appear, therefore, that the mere mixing of the reactants resulted in an instantaneous exchange which was never greater than 50%.

These two characteristics (i.e. the immediate formation of the red colour and the rapid decrease in specific activity of the original labelled ether*) suggest that a Meisenheimer-type addition might be very rapidly formed in the solution, from the reactants according to the scheme,



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* note by the author of this thesis i.e. Kattan.

On treatment with acid, as already mentioned, the initial ether(I) is obtained. The extraction of the samples with toluene-dilute hydrochloric acid, therefore, forces the above equilibrium completely towards the left. Since the two methoxy groups in the complex (II) are chemically but not isotopically equivalent, there is 50% chance that the expelled group will be the radioactive one, and therefore the specific activity will be reduced, during the extraction, by a certain fraction, depending on the concentration of the complex. Thus, the lowering of the initial activity may be due to this "separation-induced exchange", no actual exchange taking place because of the mixing. This exchange, however, is not expected to introduce any error in the evaluation of rates, since the activity of all samples will be reduced by the same fraction, in the same run".

Katsanos continued by making the point that when the methoxide ions are in sufficient excess all the labelled ether is in the form of the complex and when this is treated with acid, 50% reduction will lead to $S_o = \frac{1}{2}S_i$, explaining why a greater reduction was never observed.

Thus, it is evident the more activated methoxy compounds were exchanging their methoxy groups with methoxide ions by a two-stage mechanism, involving the rapid formation of an Intermediate Complex (red, not toluene extractable from water) followed by its rate-determining decomposition. This intermediate complex was of course an example of the type studied earlier by Meisenheimer. Katsanos agreed that the two methoxy groups were bound to the same carbon atom as follows: "the statistical[15] nature of the distribution also gives an indication as to the structure of the complex, namely, that the two methoxy groups, one from the reagent and the initially present radioactive one, must have become chemically equivalent in the complex, and therefore attached to the same carbon atom by the same kind of bond.

Therefore the formed complex must be a fully covalent σ-complex, and its structure must be represented by (II).

It is worth while noting that it was the use of a methoxy-nitronaphthalene which enabled Katsanos to argue that the two methoxy groups in the Meisenheimer complex being equivalent, must be attached to the same carbon atom. With the corresponding benzene compounds, there are normally equivalent positions attached to different carbon atoms, and the equivalence of the two methoxy groups alone does not, therefore, necessitate them being on the same carbon atom.

Gilbert[13a] isolated the complex formed from 1-methoxy, 2,4-dinitronaphthalene and sodium methoxide in methanol by refluxing with toluene, filtering, washing with toluene and drying under vacuum. The red powdery non-hygroscopic product did not melt but slowly decomposed up to ca. 37°C and exploded. The elemental analysis corresponded to that of the sodium salt of 1-methoxy 2,4-dinitro-naphthalene-methoxide ion plus half a molecule of methanol. This solid complex did not show visible sign of decomposition over two years.

While there was little doubt about the existence of the two-stage mechanism for the methoxy exchanges involving the more highly activated complexes, the same could not be said for the reactions involving the less activated aromatic methoxy compounds where the second order kinetics could point equally well to a one-stage mechanism or a two-stage mechanism with the formation of the intermediate complex as its rate-determining step (hence the likelihood of a sufficient concentration of complex to show itself via colour of the solution, non-extractability into toluene etc. was very small). Further evidence here was obtained by Fendler[11a] and Gilbert[13b], who also determined the activation energies of substitution reactions between a series of aromatic nitro-methoxy compounds and methoxide ions in methanol solution.

Fendler studied the exchange reaction of methoxide ions with p-nitroanisole, 2,4-dinitroanisole and 2,4,6-trinitroanisole. P-nitroanisole did not react even after refluxing for six hours, or after three months in a sealed tube at 55°C. The activation energies quoted by Fendler for the other two compounds are:

2,4-dinitroanisole	16.8 K. cals./mole
2,4,6-trinitroanisole	19.4 K. cals./mole

However, the kinetic pattern of the two latter reactions is quite different from each other; 2,4,6-trinitroanisole showed the presence of an intermediate complex whose decomposition was rate-determining, whereas 2,4-dinitroanisole showed a plot as in diagram (1.1; page 7) and second order kinetics

i.e. Rate = $k \left[ArOCH_3\right]\left[\bar{O}CH_3\right]$

The activation energies quoted for these two compounds clearly refer to different processes.

After pointing out that Caldin[16] had quoted an activation energy of about 13 K. Cals./mole for the formation of the intermediate complex (studied colorimetrically) between 2,4,6-trinitroanisole and sodium methoxide in methanol at temperature below 0°C, Fendler sketched the potential energy profiles for the reaction as in Figure (1.3) and with Gilbert, confirmed it by determining the heat of the formation of the complex calorimetrically at about 7 K. cals./mole.

He then argued that if 2,4-dinitroanisole had reacted by a two-stage mechanism with the formation of the intermediate complex as the rate-determining step (one of the possible interpretations of the second order kinetics), the presence of an additional nitro group in the 6 position had decreased the activation energy of the formation stage by about 4 K. cals./mole.

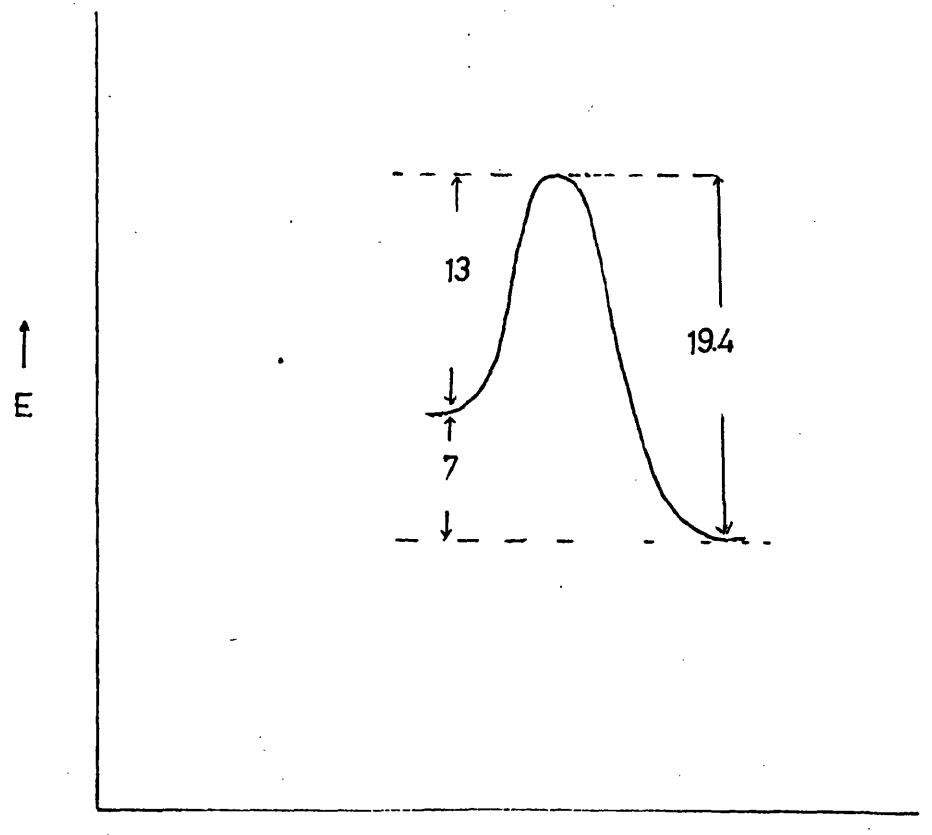


Figure 1.3

This being so, he went on, it seemed unlikely that the same additional nitro group would decrease the activation energy for the decomposition of the intermediate complex by as much as about 20 K. cals./mole, as would have to be the case to remove the valley in the profile and give a one-stage mechanism. Thus Fendler argued that the two-stage mechanism was followed by the methoxy exchange between methoxide ions an 2,4-dinitroanisole in methanol. Since then Crampton[17] and other[18] have confirmed the formation of the intermediate Meisenheimer complex by nuclear magnetic resonance spectroscopy. Also Bernasconi[19] succeeded in measuring the activation energy for the decomposition of the complex by a temperature-jump technique, and quoted 11.8 K. cals./mole.

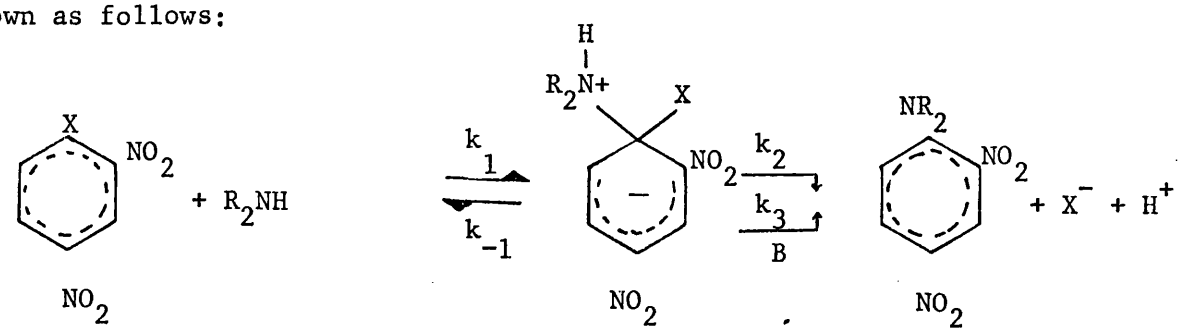
Gilbert studied the methoxy exchange between methoxide ions and a series of 1-methoxy nitro naphthalenes and found that the "other" ring has a considerable activating effect on the substitution. He also determined the following activation energies, where the decomposition of the intermediate complex was the rate-determining step:

1-methoxy 2,4-dinitronaphthalene	17.4 K. cals./mole
1-methoxy 2,4,5-trinitronaphthalene	18.7 K. cals./mole
1-methoxy 2,4,7-trinitronaphthalene	18.5 K. cals./mole

and succeeded in measuring the heats of formations of the complexes by direct calorimetry. He was therefore able to sketch the energy profiles for the two-stage exchange reactions and also to estimate the activation energies for the formation stages of the complexes.

Work involving isotopic exchange reactions at Leicester formed a background to the present research, but, of course it only formed a relatively small part of the total work being carried on outside which was concerned with the study of aromatic nucleophilic substitution. In recent years demonstration of base catalysis in

kinetic studies of certain reactions has been taken as a strong support for the formation of the intermediate complex, and the mechanistic scheme which has been advocated by a number of workers[20,21,22] is shown as follows:



V

Owing to the presence of labile hydrogen in V its removal is expected to be easy by a Brönsted base and so transformation of the resultant molecule to the product rather than to the original compound is favoured. For this reaction the overall second order rate expression derived by the steady-state treatment is:

$$\frac{\text{Rate}}{[ArX][R_2NH]} = K = \frac{K_1K_2 + K_1K_3(B)^B}{K_{-1} + K_2 + K_3(B)^B}$$

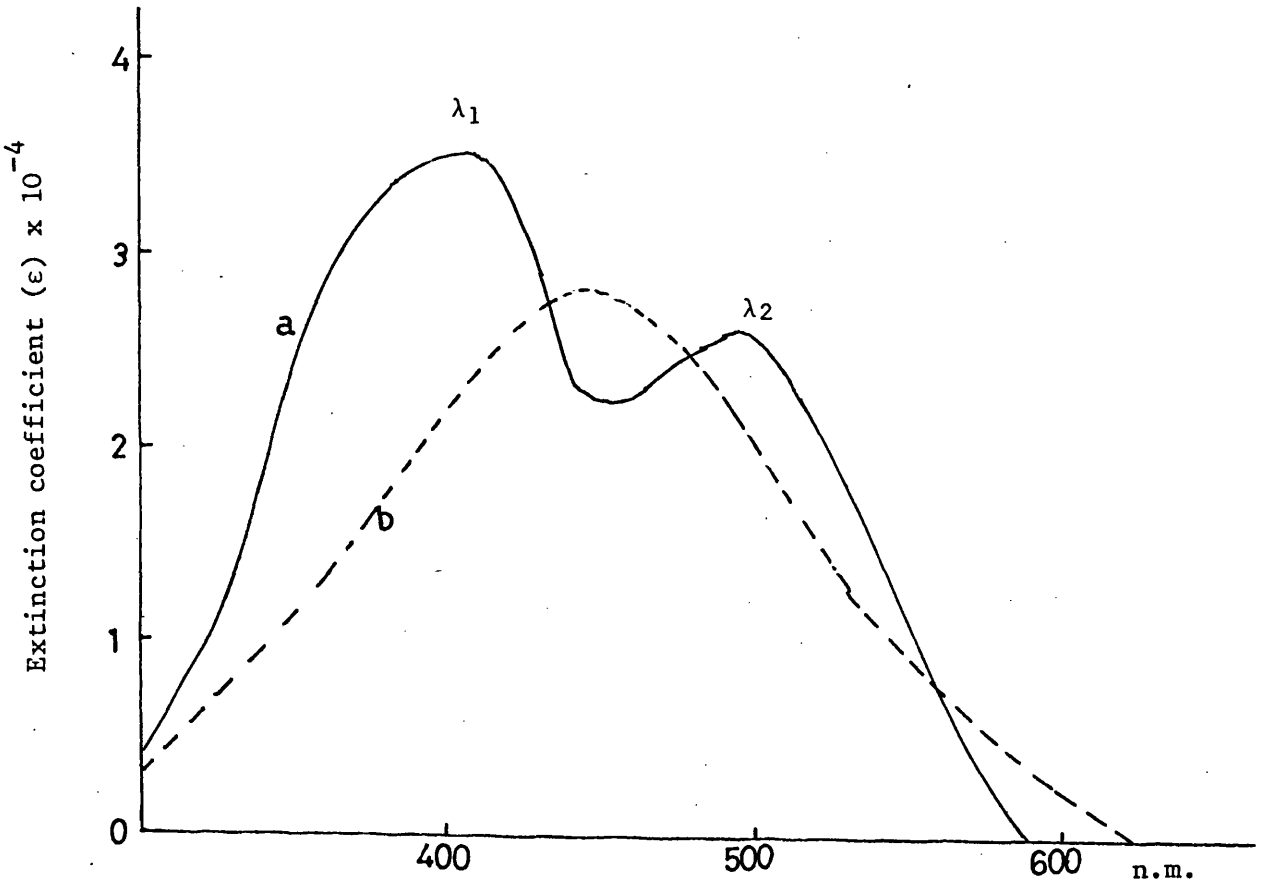
where $K_3(B)^B$ represents the term for the effective base catalysis by any base. If there is more than one base operating as catalyst additional terms should be present. This expression can be simplified depending on the relative values of K_{-1} and K_2. When $K_{-1} << K_2 + K_3(B)$ then $K = K_1$ i.e. the formation of the intermediate is the rate-determining step and base catalysis should not be observed. When $K_{-1} >> K_2 + K_3(B)$, this gives rise to a pre-equilibrium condition with the product-producing process as the rate-determining step, and base catalysis is expected. When K_{-1} and K_2 are of comparable magnitude the overall rate will depend on the relative values of the rate coefficients of the individual processes. In this case base

catalysis may be observed at low concentrations as the sensitivity to base catalysis decreases at high base concentrations. As to the first case when $K_2 > K_{-1}$ base catalysis may be observed for reactions of related compounds where x is a poor leaving group, such as ArF in favour of ArCl.

Base catalysis has been reported by several authors. Bunnett and Randall[23] have reported the general base catalysis observed with hydroxide and acetate ions in the reaction of 1-fluoro, 2,4-dinitro-benzene with N-methylaniline. Also the reaction of 2,4-dinitrophenyl-phenylether[20] with piperidine was catalysed by piperidine and by hydroxide ions. Similarly, Kirby and Jencks[22] reported that the reaction of p-nitro phenyl phosphate with dimethylamine and with piperidine were catalysed by hydroxide ion; also the dimethylamine itself was acting as base catalyst. For all these reactions the plot of rate of the reaction against the concentration of the base was curve and not linear; this was taken to indicate that the rate-determining step changed as the catalyst concentration increased. The existence of such change in the rate-determining step of the reaction with base concentration was, in turn taken as evidence for the existence of an intermediate complex with which formation and decomposition processes have different sensitivities to catalysis.

EVIDENCE FROM ULTRAVIOLET AND VISIBLE SPECTROSCOPY

Meisenheimer complexes show characteristic absorption spectra with two distinct maxima in the regions of approximately 400 n.m. (λ_1) and approximately 500 n.m. (λ_2) respectively (see Fig. 1.4,a). The molar extinction coefficient of the higher energy band is about 1.3 - 2.5 times larger than that of the lower energy band and has a



(Figure 1.4)

Visible spectra of adduct formation from 2,4,6-trinitroanisole and methoxide ions in DMSO (a) 1:1 addition at C_1

(b) 1:2 addition at higher methoxide ion concentration

characteristic value of about 2 - 4 x 10^4 ℓ.mole^{-1}cm^{-1}. The spectrum taken of the original nitro substrate shows only the absorption maximum near the ultraviolet region (λ_1) and the second maximum (λ_2) on the longer wave length, which is believed due to Meisenheimer complex developes on the addition of basic reagent.

The equilibrium constant of the reversible reaction between the substrate and the reagent may be determined from absorptiometric measurements, and if the formation of the Meisenheimer complex is not too rapid the progress of its formation may also be observed by the increase with time of the peak (λ_2). The equilibrium constant (K_c) of the reaction may be calculated from measurements of the optical density at the wavelength of maximum absorption of the complex (λ_2) provided that the molar extinction coefficient of the complex (ε) is known. If, however, this is not known, it can be determined from the intercept of the straight line plot between optical density (O.D.) at the wave-length of the complex's maximum (λ_2) and the concentration of the varied basic reagent (b) according to the following equation due to Benesi and Hildebrand[24]:

$$\frac{a}{OD} = \frac{1}{K_c\varepsilon} \cdot \frac{1}{b} + \frac{1}{\varepsilon}$$

where a is the stoichiometric concentration of nitro aromatic compound (substrate). When ε is known, K_c may of course be evaluated.

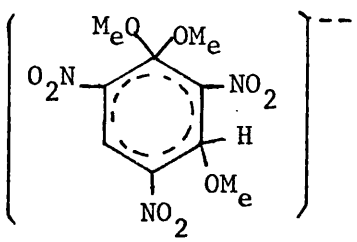
The addition of alcoholic solution of methoxide ions to a solution of 2,4,6-trinitrophenetole produced colour (red) as did that of 2,4,6-trinitroanisole to ethanolic solution of ethoxide ions. These two preparations[25] gave identical spectral characteristics of a

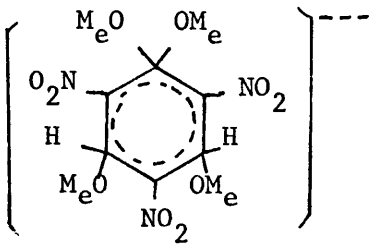
Meisenheimer-type complex. Also other workers reported colour formations with absorption characteristics of a Meisenheimer complex between 2,4,6-trinitroanisole and methoxide ions in methanol[26,27] as well as in dimethyl sulphoxide[28]. Similarly complex formation[29] has been reported to occur between 2,4,6-trinitrophenetol and ethoxide ions in ethanol and in acetonitrile between 2,4,6-trinitroanisole and ethoxide ions. The reaction of 2,4-dinitroanisole and 2,6-dinitroanisole with methoxide ions and various alkoxide ions[30] also gave the characteristic colour formation, and coloured compounds from the reaction of dinitroanisole and methoxide ions have been separated from benzene solution. In fact the formation of such characteristic colour compounds has not only been observed for reactions of alkoxy nitro aromatic compound and alkoxide ions but the same has been reported for reactions between nitroaromatic compound and other basic reagent. In studies[31] of the reaction between 1,3,5-trinitrobenzene in ethanol with excess ethoxide ions similar characteristic absorption to that produced by 2,4,6-trinitroanisole with ethoxide ions was obtained under the same conditions. The same general characteristics were reported for 1,3,5-trinitrobenzene and various anions such as thioethoxide[32] (λ_1, 465; λ_2, 570), acetonate[33] (λ_1, 464; λ_2, 572), sulphite[34] (λ_1, 462; λ_2, 525) and cyanide[35] (λ_1, 437; λ_2, 555). Pollitt[32] and Saunders studied the reaction between methoxide ions and a variety of 2,4-dinitro-6-X-anisoles and 2,6-dinitro-4-X-anisole (X = OMe, H, Cl, CO_2^-, $CONH_2$, CO_2Me, CN) and found that these reactions gave the general absorption features of Meisenheimer-type complexes with only little variation in the position of the two band maxima; the band at the longer wave length was found to shift toward lower wave length as the electronegalvity of the substituent, X, increase.

The position of band maxima was also found to depend on the medium. In the reaction between 2,4,6-trinitroanisole and alkoxide ion Foster and Fyfe[36] reported that on changing the solvent from ether to a more ionising solvent there was a bathochromic shift of the higher energy maximum and a hypsochromic shift of the lower energy maximum. Similarly Norris[35] on studying the interaction between 1,3,5-trinitrobenzene and the cyanide ion in chloroform observed the same effect when he compared his results with that involving ethoxide and sulphite ions.

Due to the close correspondence of the optical properties of the coloured compounds produced from 1,3,5-trinitrobenzene with various anions and that produced by dinitroanisole and trinitroanisole with alkoxide ions the former group has been formulated as 1:1 addition intermediate Meisenheimer complexes.

However multiple addition also has been reported to occur at high concentration of the basic reagent. Foster[29] and Mackie that a high methoxide concentration (about 1M) the absorption maxima, due to the complex from trinitroanisole, at 4100 n.m. and 4900 n.m. were replaced by a single visible band at 4800 n.m. (Fig. 1.4,b) which was attributed to diadduct at C_1 and C_2





double addition at C_1 and C_3

treble addition at C_1, C_3 and C_5

At still higher base concentrations Abe[27] reported that 2,4,6-trinitroanisole was converted into a colourless species probably

triadduct. Calculation by Abe indicated that the 1:1 adduct should have two absorption maxima in the visible region, the 1:2 adduct a single visible maximum while the triadduct should be colourless.

EVIDENCE FROM NUCLEAR MAGNETIC RESONANCE STUDIES

Nuclear magnetic resonance studies of hydrogen have provided a unique tool for the identification of complex formation. By measuring the resonance of the hydrogen in the aromatic compounds, not only the position of the hydrogen atoms but their number (intensity) can be inferred. The degree of resonance interaction refers to chemical shifts brought about by interaction with other ions or molecules. The spectrum[28] of a solution in dimethylsulphoxide of the solid adduct formed from 2,4,6-trinitroanisole and potassium methoxide shows two bands with intensities representing two and six protons attributed respectively to the ring hydrogen atoms and the two methoxy groups. The resonance due to ring protons at -8.65 p.p.m. is shifted upfield from the position in the parent anisole (-9.07 p.p.m.), while that due to methoxy protons shows a larger upfield shift from -4.07 to -3.03 p.p.m. (chemical shifts are quoted relative to internal tetramethylsilane). It has been suggested that the upfield shift is compatible with the change in hybridisation from SP^2 to SP^3 at C_1; also the two methoxy groups are equivalent owing to the fact that only a single band was observed for the six methoxy protons. Confirmation has come from nuclear magnetic studies of the same addition product in methanol[37].

At high concentration of the basic reagent multiple addition has also been detected by this technique, and it has been reported[38] that di-adduct, and tri-adduct formation have been observed.

EVIDENCE FROM CRYSTALLOGRAPHIC STUDIES

Recently crystal structure determinations of the complex derived from 2,4,6-trinitroanisole with methoxide ions[39] , and 2,4,6-trinitrophenetole with ethoxide ions [40] have shown that both alkoxy attachment are identical, the angle C_6, C_1, C_2 is 109^o and the alkoxy groups are in plane perpendicular to the plane of the ring. There seems little room for doubt concerning the position of the atoms in these Meisenheimer Complexes.

THIS RESEARCH:

When this research was begun, there was abundant evidence that Meisenheimer complexes played an important part in aromatic nucleophilic substitution reactions involving aromatic methoxy compounds and methoxide ions. In fact the overall kinetics were determined by whether the formation or decomposition of these complexes was the rate-determining step. However, similar studies on the mechanism of formation and decomposition of such complexes had not been undertaken. For example, it was not known whether the decomposition process could take place perhaps assisted by solvation of the product anion, simply by the breaking of the aryl carbon-oxygen bond, or whether the prior addition of a proton to a methoxy oxygen occurred, followed by the splitting off of a molecule of methanol, or even whether a bimolecular encounter was necessary perhaps between a molecule of solvent methanol and one of the Meisenheimer Complex. The object of this research was initially to attempt to investigate possible roles that might be played by protons by looking for any hydrogen-deuterium isotope effect that may be present and by carrying out the reaction in methanol and methanol-o-d. However, as these studies progressed it became apparent that the difference in specific rates between the methanol and methanol-o-d systems was not of such a magnitude as would allow the postulation of a primary isotope effect.

A second aim of the research was to carry out reactions in dimethyl sulphoxide, which was able to dissolve the required reagents, to which a controlled small amounts of either methanol or methanol-o-d could be added, in order to observe whether the concentration of these substances appeared in the kinetic equation. It was found that in this solvent, even in the absence of added methanol, the aromatic nucleophilic substitution reactions could proceed readily. The Meisenheimer complex was formed more readily and decomposed less readily than in methanol; it was, therefore, possible to study kinetically and absorptiometrically the formation of Meisenheimer Complexes from less activated compounds, such as even P-nitroanisole which did not undergo reaction in methanol[11] even at refluxing temperature, and to extend the range of kinetic data on symmetrical exchange reactions between methoxide ions and aromatic methoxy compounds. It was also planned to study corresponding halogen exchange reactions which in methanol are rather too slow to follow kinetically with any reliability, and thus to extend still further the kinetic data in the hope that the information found may together with that in methoxy systems, contribute to our understanding of the formation and decomposition of Meisenheimer complexes.

CHAPTER II

DIMETHYL SULPHOXIDE

DIMETHYL SULPHOXIDE (DMSO)

Dimethyl sulphoxide represents an oxidation stage of sulphur intermediate between dimethyl sulphide and dimethyl sulphone. Its molecule is thought to be a resonance hybrid[41] between the forms:

and a pyramidal structure[42] is assigned to it with the sulphur, oxygen and carbons atoms at the corners. It has useful solvent properties as it dissolves not only many organic compounds but also many inorganic salts (Table 2.1) and an increasing number of kinetic studies are being carried out in its solution.

Table 2.1 Solubility of salts kg/100 kg DMSO at 25

Ferric chloride ($6H_2O$)	30
Mercuric acetate	100
Sodium dichromate ($2H_2O$)	10
Sodium iodide	30
Sodium nitrate	20
Sodium nitrite	1
Stannous chloride ($2H_2O$)	40
Zinc chloride	30

Preparation is by the oxidation of dimethyl sulphides, and oxidising agents such as hydrogen peroxide or nitric acid or chromic acid have been used. The industrial method recently used in the United States of America is the treatment of dimethyl sulphide

(b.p. 38°C) in the vapour phase with air and catalytic amounts of nitrogen dioxide[41]. The consumed nitrogen dioxide is reoxidised within the reaction mixture by the oxygen of the air

$$(CH_3)_2S + NO_2 \longrightarrow (CH_3)_2SO + NO$$

$$2NO + O_2 \text{ (air)} \longrightarrow 2NO_2$$

Owing to the high boiling point of DMSO (189°C) it can be condensed and removed continuously from the system, however the condensed crude DMSO dissolves some dimethyl sulphide as well as oxide of nitrogen (NO_2, N_2O_3, N_2O_4) which effect further oxidation. An effective cooling surface is needed for condensation of DMSO as well as for the evolution of the nitric oxide which is recycled into the system, so minimising the loss of catalyst. The crude DMSO contains, then, small amounts of nitrogen dioxide, dimethyl sulphone, methansulphonic acid and some moisture, and purification can be achieved by neutralising the impurities with a base (e.g. slaked lime) and vacuum distillation.

PHYSICAL PROPERTIES

DMSO when dry and pure is colourless and odourless. It is miscible with water and very hygroscopic. Table 2 summarises its physical properties[41].

DMSO AS AN IONISING SOLVENT

In a recent article[44] V. Gutmann discussed the phenomenon of ionisation of neutral compounds in ionising solvents as a chemical phenomenon. While the relative permittivity (ε) of the solvent plays an important part in the ionisation processes for ionic compounds, its effect is not so pronounced where neutral covalent compounds are concerned, and the ability of the solvent to donate electrons to or accept electrons from substrates is an important factor in their ionisation. Solvents

Table 2.2 Physical properties of Dimethy Sulphoxide

Molecular weight, 78.13					
Melting point (at standard pressure), 18.45°C					
Boiling point (at standard pressure), 189°C					
Density at 20°C, 1.1×10^3 Kg.m^{-3}					
at 35°C, 1.0892×10^3 Kg. m^{-3}					
Coefficient of volume expansion at 20°C, 0.00088 K^{-1}					
Specific heat capacity, at 18.45°C solid, 2.09×10^3 JKg^{-1}					
at 18.45°C liquid, 2.93×10^3 JKg^{-1}					
Specific latent heat of fusion at 18.45°C 83.6×10^3 J Kg^{-1}					
Specific heat of combustion, 25.3×10^6 J Kg^{-1}					
Specific heat of vaporisation at 189°C, 551.8×10^3 J Kg^{-1}					
Refractive index n_D^{21}, 1.4787					
Relative Permittivity, 45					
Flash point (open cup) 95°C					
Surface tension, 43×10^{-3} N m^{-1}					
Vapour Pressure:	Temp° °C	20	30	40	50
	Nm^{-2}	55.4	113.4	220.2	408.3

that donate an electron pair to the substrate are called electron pair donors (EPD) and those that accept an electron pair are called electron pair acceptors (EPA). The ability of a solvent to donate an electron pair is defined as donicity or donor number (DN), the donicity of a solvent was measured relative to an electron pair acceptor (EPA), such as $SbCl_5$ and is the negative value of the enthalpy of the interaction between an EPD and $SbCl_5$ in high dilution of 1,2-dichloroethane.

$$EPD + SbCl_5 \rightleftharpoons EPD.SbCl_5 \qquad -\Delta H\ (EPD.SbCl_5) = DN$$

Table 2.3 shows various solvents arranged according to their donicity values which seem to bear no obvious relation to the relative permittivity (dielectric constants) of the solvents. DMSO has one of the highest donicity values recorded in the table.

The donation of an electron pair to a substrate causes changes in the electron distribution along the bond M-X of the substrate

$$EPD + M\text{-}X \longrightarrow EPD \longrightarrow M \overset{\frown}{-} X$$

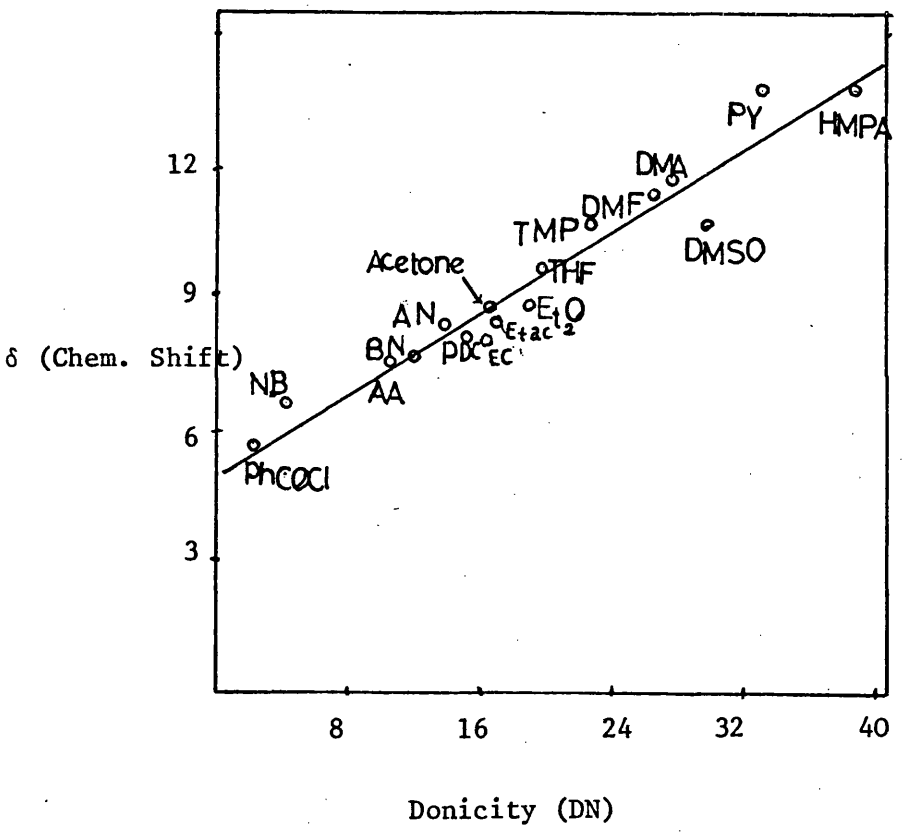
Electron shift and hence polarity results in the bond M-X which can ultimately lead to ionisation. Figure 2.1 shows increase in the chemical shift of CF_3I bond with increasing donicity of various donor molecules. From this figure as with table 2.3 one can recognise the ionising potentiality of DMSO.

REACTION IN DMSO

DMSO has shown remarkable solvent power and solvent action. With some reactions it enhances base catalysis and acts without being chemically changed.

For example, Cram and co-workers[45] found that the rate of the potassium tert-butoxide-catalysed hydrogen-deuterium exchange of the optically active 1-phenyl methoxy ethane is equal to the rate of racimisation in DMSO, and also this rate is not less than 10^7 times that observed in tert-butyl alcohol as reaction medium. It is evident

Figure 2.1* Variation of the chemical shift in CF_3I, which is a measure of the electron shift in the bond, in the presence of different donor molecules



* obtained from ref. 44

Table 2.3 Donicity and dielectric constants of solvents

Solvent	$-\Delta H(EPD.SnCl_5) = DN$ (K.Cal. mol^{-1})	ε
1,2-dichloroethane	-	10.1
Thionyl Chloride	0.4	9.2
Nitromethane (NM)	2.7	35.9
Acetic anhydride	10.5	20.7
Acetonitrile (AN)	14.1	38.0
Ethylene sulphite (ES)	15.3	41.0
Ethylene Carbonate (EC)	16.4	89.1
Acetone	17.0	20.7
Water	18.0	81.0
Tetrahydrofuran (THF)	20.0	7.6
Trimethyl phosphate (TMP)	23.0	20.6
Dimethyl formamide (DMF)	26.6	36.1
Dimethyl sulphoxide (DMSO)	29.8	45.0
Pyridine (PY)	33.1	12.3
Hexamethyl phosphoricamide (HMPA)	38.8	30.0

that base catalysis was enhanced greatly by incorporating DMSO into the reaction mixture. Similarly, by using DMSO saturated with sublimed potassium tert-butoxide,[45] bromobenzene was converted at 25°C for 15 hours into tert-butyl phenyl ether (86% yield) whereas the reaction was found to proceed to only 35% of the way in 9 hours in tert-butyl alcohol at 175°C; again, potassium tert-butoxide showed greater effect as base catalysis in DMSO. This vastly enhanced reactivity of alkoxide ions in DMSO over their reactivity in alcohol was attributed[45] to the absence of alkoxide-solvent hydrogen honds in DMSO which are present in the hydroxylic solvent. However the increased base strength may be attributable to the formation of methyl sulphinyl carbaniun anion as is seen later.

With other reactions, DMSO undergoes chemical changes during the reaction. In mild acidic conditions DMSO can attack electrophilic reagents through its oxygen atom while in strongly basic media DMSO reveals acidic character and attacks electron-deficient centres through its conjugate base $CH_3\overset{\overset{O}{\|}}{S}CH_2^-$.

REACTIONS IN MILDLY ACIDIC OR BASIC MEDIA

For example Pfitzner and Moffatt[46,47] have developed a general method to oxidise primary alcohols to aldehydes and secondary alcohols to ketones by using a combination of dicyclohexylcarbodiimide ($C_6H_{11}N = C = NC_6H_{11}$; DCC) and a proton source usually anhydrous orthophosphoric acid. The mechanism put forward and supported by strong evidence for these reactions is the initial formation of alkoxy sulphonium salts (III) brought about by nucleophilic attack by DMSO on the protonated DCC to form sulphonium isourea (I) followed by nucleophilic attack by the alcohol on the sulphur atom of sulphonium isourea. The alkoxysulphonium salt is acting as an intermediate whose decomposition leads to the final product. The following scheme for oxidation is due to Fenselau and Moffatt[48]

1 - $C_6H_{11}N = C = NC_6H_{11} + CH_3\overset{O}{\overset{\|}{S}}CH_3 \xrightarrow{H^+} C_6H_{11}N = \underset{\underset{\underset{+}{S(CH_3)_2}}{|}}{\overset{O}{|}}CNHC_6H_{11}$

(I)

2 - $C_6H_{11}\overset{H^+}{N} = \underset{\underset{\underset{RR'CH\ddot{O}H}{|}}{\overset{O}{|}}}{CNHC_6H_{11}} \longrightarrow \underset{(II)}{C_6H_{11}\overset{O}{\overset{\|}{N}}CNHC_6H_{11}} + \underset{(III)}{RR'CHO\text{-}\overset{+}{S}(CH_3)_2}$

3 - $RR'C\underset{H}{\overset{O}{<}}\overset{+}{SCH_3}\underset{CH_2}{} \longrightarrow RR'C = O + CH_3SCH_3$

(IV)

Oxidation of halides and tosylates have been studied largely by Kornblum and co-workers[49] who reported that variety of phenacyl halides were oxidised to phenylglyoxols simply by dissolving those compounds in DMSO at room temperature in the presence of proton acceptor (base) such as sodium bicarbonate. They showed later[50] that benzyl halides and many primary alkyl tosylates could be converted to aldehyde in relatively good yield (68-85%) by heating them in DMSO containing sodium bicarbonate to a temperature of 100-150°C for less than 5 minutes. The mechanism of these oxidation reactions differ from that of alcohols in that the intermediate alkoxysulphonium salt (V) is formed by the direct nucleophilic attack of DMSO on the reagent. The collapse of the alkoxysulphonium ion to the product follows the cyclic pathway shown in step 3

$$Ph - \overset{O}{\overset{\|}{C}} - \underset{H}{CH} - O - \overset{+}{S}(CH_3)_2 \xrightarrow{\text{base}} PhC\overset{O}{\overset{\|}{}}CHO + CH_3SCH_3$$

(V)

DMSO is reduced at the end of the reaction to dimethyl sulphide. The base abstracts alph-hydrogen which was shown by Torsell[51] to show great activity by the presence of a carbonyl group. These oxidation reactions therefore are suitable for alph-haloesters, acids[52], phenacyl halide[49] and benzyl halide[50].

REACTIONS IN BASIC MEDIA:

DMSO has shown its potency for promoting certain reactions by acting as a reagent in yet another field. In basic media DMSO shows acidic properties i.e. it may lose one proton from one of its methyl group and thus affording a conjugate base through which it can attack electron-deficient centres. Corey and Chaykovsky[53,54] were the first to study the existence of this type of these reactions. They reported that the reaction of DMSO with sodium hydride at 70-75°C under nitrogen constitutes an efficient medium for synthesis of the sodium salt of the carbaniun $CH_3\overset{O}{\overset{\|}{S}}CH_2^-$. Owing to the low acidity of DMSO which is about 8×10^3 less than that of triphenylmethane[55]. The production of methyl sulphinyl carbaniun anions, $CH_3SOCH_2^-$, needs to be conducted in strong basic medium. Owing to its nucleophilic character, methyl sulphinyl carbaniun reacts with electrophilic reagents such as sulphonium salts, aldehydes, ketones, esters, etc. Corey and Chaykovsky[53,54] demonstrated their proof for the quantitative generation of methyl sulphinyl carbaniun anions upon the reaction of sodium hydride with DMSO by the fact that when they added benzophenone and benzaldehyde to DMSO solution of sodium hydroxide. β-hydroxy sulphoxide (VI) was obtained at room temperature

$$Ph_2CO + CH_3\overset{O}{\overset{\|}{S}}CH_2^- \longrightarrow Ph_2C(O^-).CH_2\overset{O}{\overset{\|}{S}}CH_3 \xrightarrow{H_2O} Ph_2C(OH)CH_2\overset{O}{\overset{\|}{S}}CH_3$$

(86% yield)

(VI)

β-hydroxy sulphoxides can be produced using the above method upon aldehydes and ketones. With enolisable ketones, enolisation process competes along with the above reaction as the enolales become stable towards further attack by the anion.

Reaction of methyl sulphinyl carbaniun with esters[54,56,57] yielded β-keto sulphoxides. Reactions of primary alkyl hadides and tosylates with various alkoxides[58] in DMSO had led to substitution reactions by the carbaniun anions producing alkyl sulphoxides.

Thus, DMSO is able to enhance base catalysis and to function as a nucleophilic reagent. It seemed worthwhile, therefore, to use it as solvent in the study of the aromatic nucleophilic substitution reactions which form the subject of this thesis.

CHAPTER III

EXPERIMENTAL

PREPARATION OF MATERIALS

SOLVENTS

Methanol (Merck "Aristar"); methanol-o-d (Kosh-Light Laboratories, Colnbrook) with (98%) deuterium content, dimethyl sulphoxide (BDH, spectroscopic grade), toluene (BDH, Analar) and benzene (BDH, Analar) were used without further purification.

METHANOLIC SODIUM METHOXIDE (~4M)

Clean sodium metal (~1.2 x 10^{-3} kg) was roughly weighed in toluene, dried, washed with methanol, refluxed in methanol (12 mls) contained in a flax fitted with a water-condenser, and guard tube filled with silica gel. After the solution had cooled to room temperature its concentration was determined by conductimetric titration using standard hydrochloric acid. More dilute solutions were prepared by dilution with methanol and again standardised.

METHANOLIC-O-D SODIUM METHOXIDE

As for methanolic sodium methoxide but in a "glove box" under a moisture-free nitrogen atmosphere. Standardisation was performed outside the "glove box" as previously described.

1-CHLORO-2,4-DINITRONPAHTHALENE

(Procedure as used by Gilbert[59] based on that described by Ullman and Bruck[60]).

2,4-dinitronaphthalene (BDH; 96 g), p-toluene sulphonyl chloride (80 g) and diethylamine (120 g) were heated on a water bath for three hours. The product was purified by heating with (1N, 600 mls) hydrochloric acid, filtered, residue was washed with hydrochloric acid (1N, 2 x 200 mls) and then with water (2 x 200 mls) and three times recrystallised from acetic acid to give yellow platelets (86 g, 85%) m.p. 147°C (Ullman and Bruck; 147°C).

1-METHOXY(C-14), 2,4-DINITRONAPHTHALENE

(Procedure described by Gilbert[59]).

1-Chloro-2,4-dinitronaphthalene (3.5 g) was dissolved in

benzene (12 mls) contained in 2-armed flask fitted with a separating funnel and water condenser with silica gel-filled guard tube. To the refluxing solution was added methanolic sodium methoxide (4M, 4 mls) followed by methanol (C-14) (1 ml, 200 μ.c., supplied by Radiochemical Centre); the solution became red and a slight red precipitate formed. The solution was refluxed for 90 minutes, cooled, separated between cold water/benzene quickly to minimise hydrolysis. The water layer was acidified and the ether produced was extracted into benzene, the crude product (3.4 g, 99% m.p. 93°C) was purified three times from methanol (2.5 g, 75%) m.p. 98.5°C (Lit. 98.5°C).

P-NITROANISOLE (The method described by Fendler[61] was adopted).

Analar, p-dinitrobenzene (4.2×10^{-3} kg) was added to sodium methoxide solution (0.7×10^{-3} kg sodium dissolved in 7 mls methanol) contained in a flask fitted with water-condenser and silica gel-filled guard tube. Further quantity of methanol (2 mls) was added to the mixture, refluxed gently for 10 minutes and then allowed to cool. The almost solid mass was diluted with ice-cooled water (50 mls), acidified with 0.2N hydrochloric acid and then made slightly alkaline to keep p-nitrophenetole in solution. The crude product was washed with water, collected at the pump and three times recrystalised from methanol, using charcoal during the first crystalisation and 80% yield of product m.p. 53.5°C (Literature[61] 54.0°C). The sample was subject to zone refining and gave a product whose m.p. was unchanged.

P-NITROANISOLE (METHYL, C-14)

The sample used had been prepared by Fendler[62] by reacting p-nitrobenzene with sodium methoxide - C-14.

For this work its purity was checked by m.p. (53.5°C), mixed melting point with the zone-refined sample whose preparation is described above (m.p. 53.5°C) and by ultraviolet spectrophotometry in dimethyl sulphoxide solution.

STOCK SOLUTION OF SODIUM CHLORIDE IN DIMETHYLSULPHOXIDE

0.1228×10^{-3} kg. of sodium chloride (BDH, analar) dried overnight at 120°C was dissolved in dimethyl sulphoxide (100 mls.) with the help of glass-coated magnetic stirrer. The concentration, calculated from weight and volume relation was 0.021 M at 20°C.

SODIUM CHLORIDE (Cl^{36}) SOLUTION IN DIMETHYL SULPHOXIDE

0.3 mls. chlorine-36 in the form of aqueous sodium chloride (1.34 mls.; 25 μ.c. supplied by Radiochemical Centre) was dried under vacuum and the heat being gradually increased to 260°C for about six hours; the cooled residue was dissolved in sodium chloride stock solution in DMSO. The chloride concentration of this labelled solution was determined by radiometric titration using a standard solution of silver nitrate.

EXPERIMENTAL TECHNIQUES

a) KINETIC EXPERIMENT

Solution of the methoxy nitroaromatic compound (4 mls) and sodium methoxide (or chloride) (5 mls), both of double the concentration required for the run, were transferred into two separate ground-stopper bottles (25 mls capacity) and put into a thermostatic bath at room temperature. After 30-40 minutes, sodium methoxide (or sodium chloride) solution (4 mls) was transferred to the other bottle containing the aromatic compound, the stop-watch being started when the solution was half-delivered.

Samples (0.1 mls) at various period were withdrawn by micropipette and transferred into a separating funnel containing a mixture of toluene (3 mls) and 0.2 N hydrochloric acid (5 mls). After separation the toluene layer was washed with distilled water (5 mls) and then transferred (2.7 mls) into a counting bottle containing the liquid scintillator (3 mls, Nuclear Enterprises type NE 213) and was counted.

The micro pipette used for sampling was being kept in the thermostatic bath in a separate dry tube and covered with cotton plug.

Allowance was made, when results were being calculated, for solvent expansion or contraction.

Micro pipettes and all measuring glass were calibrated with freshly distilled and doubly de-ionised water. The stop-watch was checked against the Post Office Telephone speaking clock.

Thermometers read to $0.05^{o}C$, were calibrated against thermometers having N.P.L. certificates.

COUNTING TECHNIQUE

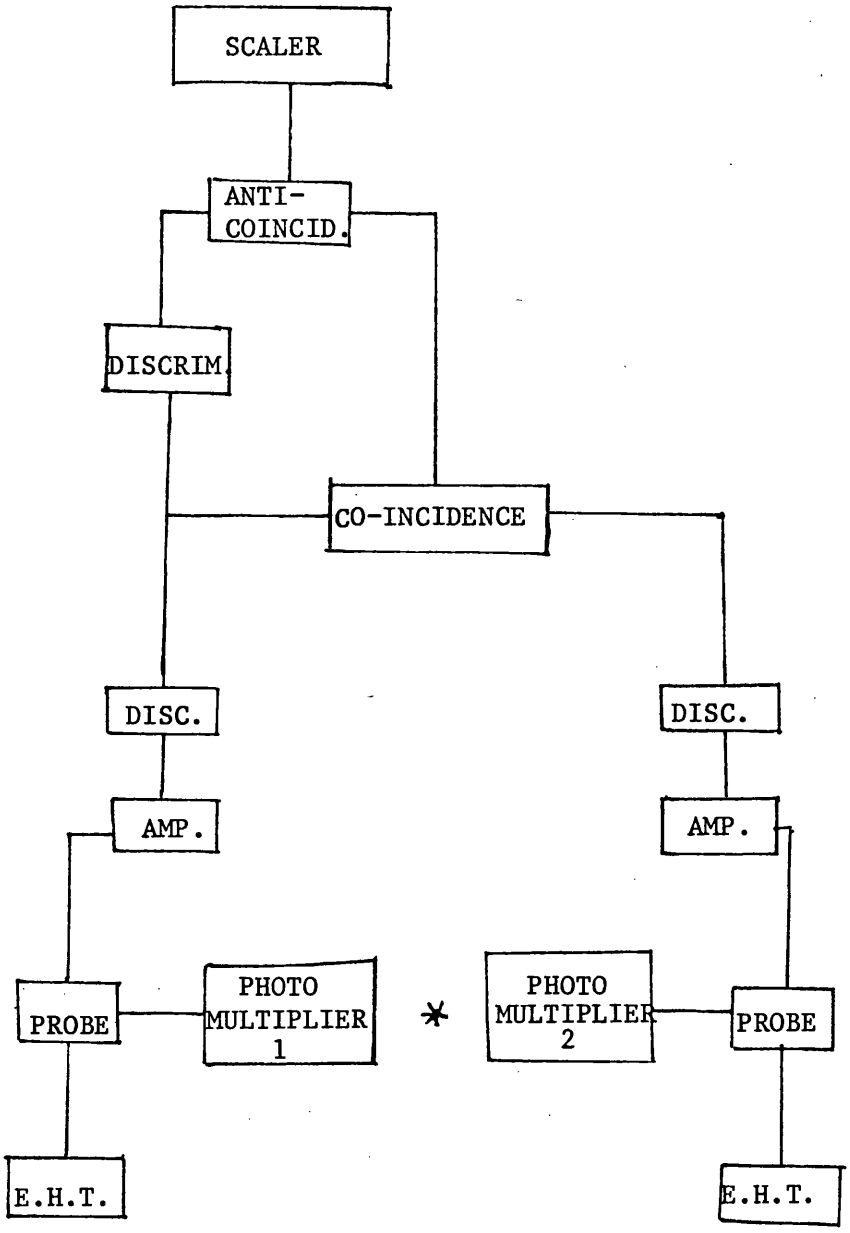
A liquid scintillation counting method was used, the counting was performed with a scintillation counter (IDL, type 6012) coupled with coincidence unit (IDL, 2032) and scaler (IDL, 6000).

The scintillation counter employed a two-channel system, and a block diagram is shown in Figure (3.1). The scintillations produced which were detected simultaneously by both photomultiplier tubes were distinguished, by the co-incidence mixer, from the random thermal noise pulses produced, not normally simultaneously, by the two photo-cathodes. Background radiation which transferred energy greater than that transferred by the maximum energy β-particles from the carbon-14 to the liquid scintillator, was eliminated by the "Upper Gate" discriminator and the anti-coincidence mixer. Thus a good counting efficiency for carbon-14 combined with a relatively low background was achieved.

Problems involving quenching during the scintillation process and passage of the scintillation quanta to the photo-cathode did not arise, as all counting samples in a given run were of the same chemical composition, and hence quenching was constant.

The approximate optimum EHT voltage applied to each photomultiplier tube, and the bias at the "upper gate" were determined by trial and error

Figure (3.1): Block diagram for low background conincidence circuit



to give as high a sample count-rate as possible combined with as low a background count-rate as possible.

b) ABSORPTIOMETRIC EXPERIMENT

Solutions of the aromatic compound and sodium methoxide (or chloride) were mixed at room temperature in the same proportion as that of the run. After a time period enough for equilibrium to be attained a sample of the mixture (25-50 µl) was transferred into one of two matched silica cells (1 cm width) and diluted with the solvent (2.5 ccs. methanol or dimethyl sulphoxide). The sample was then measured against the solvent, contained in the other cell, using an automatic U.V. spectrophotometre (Unicam, SP700).

The resulting absorption spectra are shown in Figures

EVALUATION OF RESULTS

i) KINETIC EQUATION

In the study of isotopic exchange reaction, the equation derived by McKay[63] is generally used for evaluating the rate. This equation may be derived as follows; the reaction being represented by

$$AX + BX^* \rightleftharpoons AX^* + BX$$

X, refers to the tracer atom or group

at zero time,	y_o	x_o
at time t,	y	x

The radioactive tracer, X^*, in one of the reactant exchanges with its analogue in the other reactant until isotopic equilibrium is reached; no new chemical compound is formed. Thus, the overall concentrations of the reactants, AX , (i.e. $AX + AX^*$) and BX (i.e. $BX + BX^*$) remain constant provided that there is negligible isotope decay.

Let $AX = a$ and $BX = b$. Let S_{AX} and S_{BX} denote the specific activity of the two species, therefore, at time t, $S_{AX} = \frac{x}{a}$

and $S_{BX} = \frac{y}{t}$. Since only collisions between inactive and active molecules lead to exchange, the total rate at which labelled AX^* molecules are formed is equal to $RS_{BX}(1-S_{AX})$ where R is the total rate of exchange of X (both active and inactive) between the two species.

A similar argument applies for the reverse reaction, namely the disappearance of X from AX^* molecules. The net rate for appearance of X^* in AX molecules is therefore,

$$\frac{dx}{dt} = RS_{BX}(1-S_{AX}) - RS_{AX}(1-S_{BX})$$

$$= R(S_{BX}-S_{AX})$$

$$\text{i.e.,} \quad = R\left(\frac{y}{b} - \frac{x}{a}\right) \tag{3.1}$$

From the conservation of radioactivity, and neglecting radioisotopic decay

$$x + y = \underset{\infty}{x} + \underset{\infty}{y}$$

$$\text{i.e.} \quad y = \underset{\infty}{x} + \underset{\infty}{y} - x \tag{3.2}$$

From the equality of specific activity at isotopic equilibrium, and assuming chemical identity of isotopes

$$\frac{\underset{\infty}{X}}{a} = \frac{\underset{\infty}{Y}}{b} \tag{3.3}$$

$$\text{i.e.} \quad \underset{\infty}{y} = \underset{\infty}{x} \; \frac{b}{a}$$

by substitution equation (3.2) becomes

$$y = \underset{\infty}{x} \; \left(1+\frac{b}{a}\right) - x$$

and equation (3.1) becomes

$$\frac{dx}{dt} = R\left[\frac{1}{b}\left(\underset{\infty}{x} + \frac{b\underset{\infty}{x}}{a} - x\right) - \frac{x}{a}\right]$$

$$= \frac{R}{ab} \; (a + b) \; (\underset{\infty}{x} - x)$$

i.e.

$$\frac{dx}{(\underset{\infty}{x} - x)} = R\,\frac{a + b}{ab}\,dt$$

On integration and applying the boundary condition that $X = (X_o)$ at $t = 0$ and $X = (X)_\infty$ at equilibrium, we get

$$\ell n \left(1 - \frac{x - x_o}{x_\infty - x_o}\right) = - Rt \frac{a + b}{ab} \qquad (3.4)$$

From equation (3.4) it can be seen that a plot of $\ell n \left(1 - \frac{x - x_o}{x_\infty - x_o}\right)$ against time, t gives straight line. R can be evaluated from the slope of this straight line; its value does not depend on the concentration of the tracer or even its presence.

The order of the reaction is determined experimentally in the normal way. If for example the exchange reaction turns out to be first order with respect to each of the reactants, i.e. it follows a second order overall kinetic equation, R, the exchange rate is given by

$$R = k[AX][BX]$$

where k is the specific rate of exchange

ii) USE OF THE KINETIC EQUATION

The foregoing derivation of the McKay equation is on the basis that the reaction will be followed by measuring the rate of appearance of the tracer in compound AX^*, i.e. that the activity of AX increases as the reaction progresses towards isotopic equilibrium. This state of affairs applied in the present work where chlorine exchanges were being studied; the activity of the organic chloro compounds initially unlabelled, was monitored in order to determine the reaction rate.

Where methoxy exchanges were studied, however, the analytical technique involved measuring the rate of disappearance of tracer from the aromatic methoxy compound, i.e. the activity of compound BX^*, initially labelled, decreases as the reaction progresses. Thus, it is required to eliminate x rather than y from equation (3.1). If this is

carried out, the result:

$$-\ln \frac{y_\infty - y}{y_\infty - y_o} = R \frac{(a + b)}{ab} t \qquad (3.5)$$

is obtained, and this has been used to evaluate rates R for these exchange reactions. Furthermore, where the reactions are carried out in methanol as solvent, a >> b, as the methoxide ions are in rapid exchange with the methanol molecules and a represents, therefore, the total concentration of methoxide ion plus methanol. Under these circumstances, y_∞ will be negligibly small, as when isotopic equilibrium is reached almost all of the tracer will be in the form of methanol/methoxide ion (equation 3.3). Equation (3.5) became, therefore,

$$-\ln \frac{y}{y_o} = \frac{R}{b} t \qquad (3.6)$$

and this was used to evaluate R.

However, when the reactions are carried out in dimethyl sulphoxide solution, the amount of methanol added is limited, and b is no longer negligibly small compared with a; y_∞ is also not negligible. The complete form of equation (3.5) was used, therefore to evaluate rates.

iii) ERRORS AND CORRECTIONS

Equation (3.4) implies that, irrespective of the exchange mechanism, the kinetic plot is linear. The conditions necessary for application of the McKay equation were discussed by Harris[64] and Bunton et al[65], who concluded that the treatment is valid provided that

(a) There is no isotope effect on the exchange reaction, i.e. the rate of the exchange reaction is not affected by the presence of the labelled atoms.

(b) The concentration of the labelled atoms is sufficiently low; in the present work the proportion of chlorine atoms that are labelled was less than 1 in 500 while in the methoxy exchanges the proportion was considerably smaller.

(c) There is no appreciable isotopic decay; this is true in the present work as the half-life of carbon-14 (5760 years) and chlorine-36 (3.1×10^5 years) are long.

With regard to point (a), if there is an isotope effect, then the assumption of chemical identity of isotopes is no longer true and equation (3.3.) must be replaced by

$$\frac{x_\infty}{a} = \varepsilon \frac{y_\infty}{b}$$

where ε is a measure of the isotope effect.

Carbon-isotope effects were taken to be negligible for the methoxy exchanger owing to the small difference in relative mass between C^{14} and C^{12}, and also to the labelling being one atom removed from the seat of the reaction.

In the case of chlorine exchanges, the relative mass difference are smaller still; furthermore the traces used, Cl^{36}, is mid-way in mass number between the two isotopes Cl^{35} and Cl^{37} which constitute natural chlorine.

(iv) EVALUATION OF RATES AND SPECIFIC RATES

(1) METHANOL AND METHANOL-O-D AS SOLVENT

The only aromatic compound used here was 1-methoxy,2,4-dinitro-naphthalene, and the kinetic pattern of the reaction had been shown by Gilbert[13] to be of the type described on page (7), figure (1.2); the rate-determining step is the first order decomposition of the Meisenheimer complex, and the kinetics are of the type,

$$\text{Rate} = k \left[\text{complex}\right] \qquad (3.7)$$

A typical kinetic plot obtained in the present work is given in figure (4.1). The quantities y and y_o in equation (3.6) are represented by count rates S and S_o of samples at times t and t_o ($t_o = 0$), and the slope of the line is, therefore, given by $\frac{R}{b}$ (equation 3.6).

R may, therefore, be evaluated. The slope and intercept were, in fact, calculated by the method of least squares and 95% confidence intervals of the rates were given, a computer (ICL, 1900) being used to perform the calculation.* The intercept S_o was then compared with S_i, the value "expected" to evaluate the fraction α of the aromatic compound in the form of Meisenheimer complexes; the procedure followed was that of Katsanos[14]

$$S_o = \frac{S_i \alpha}{2} + (1 - \alpha) S_i$$

Rearranging

$$\alpha = 2 \left(1 - \frac{S_o}{S_i}\right)$$

S_i was determined experimentally by following the procedure described on page (32) with the modification that here solvent rather than methoxide solution was used. Sampling was carried out at appropriate time intervals and the constancy of the count-rate indicated that methoxy exchange with solvent was not occurring during the time the reaction was observed. The mean of the count rates was taken as S_i.

Knowledge of α enabled the concentration of Meisenheimer complex to be calculated, and hence the specific rate, k, was evaluated by equation (3.7).

Unfortunately it proved to be very difficult to obtain better than an approximate value for α; the count rates measured were subject to the normal statistical errors involved in counting radioactive sources as well as experimental errors in the sampling and analytical processes. Attempts were made to improve matters by calculating the equilibrium constant, K, for the formation of the complex for each run, taking an average value for several runs, and calculating backwards from this to obtain a better value for α. However it was found impossible to achieve

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* The author indebted to Mr. E. Rees of Bolton Institute of Technology for assistance in preparing the computer programmes.

much better precision based on the author's data, and the following procedures were adopted.

(1) The concentration of methoxide ions was increased so that α approximated to unity. However an unduly large excess of methoxide was avoided in case salt effects were too apparent[66,67,68].

Results are presented in Table (4.4) and the approximation of the value of $\frac{S_o}{S_i}$ to 0.5 confirms that α can indeed be taken as unity, and that substantially all of the aromatic methoxy compound is in the form of complex. The specific rates were evaluated on the basis of $\alpha = 1$.

The Arrhenius plot is shown in Figure (4.2). Comparison of the values for specific rate with those at the corresponding temperatures in Tables (4.1), (4.2) and (4.3) indicates that a negative salt effect is operating (cf. refs. 66, 68). This is also illustrated by Figure (4.3) in which R is plotted against α.

(2) Experimental data obtained by Fendler[69] and Gilbert[70], were combined with those of the author in an attempt to evaluate reasonably reliably the equilibrium constant K, for the formation of the Meisenheimer complex, at various temperatures.

Fendler's data[69] for K at various temperatures were obtained from measurement of optical densities at equilibrium, and the agreement between the individual values he quotes is considerably better than that obtained by Gilbert[70] or the author, from values of S_i and S_o in the kinetic plots. Gilbert[13c] also arrived at the heat of formation of the complex by three different approaches.

(a) That obtained by the Isochore from a plot of log K against $\frac{1}{T}$ gave a value of -11.5 ± 2.3 K.Cal. mol^{-1}.

(b) Direct calorimetry determinations gave values of -6.1 and -9.8 K.Cal.mol^{-1}.

(c) The difference in his values for the activation energies of the formation and decomposition of the Meisenheimer complex was -9.98 K.Cal. mol^{-1}.

All three of Gilbert's values are subject to a great deal of uncertainty and it would be difficult, or impossible from his work to quote a value for ΔH with any confidence. However, all of his values are appreciably higher than the value ($\Delta H \simeq -2.7 \pm 1.6$) determined by Fendler[69] from the isochore plot of his equilibrium constants; furthermore, plotting out Fendler's data at the three temperatures make it apparent that his result too is subject to considerable uncertainty. It is reasonable to conclude that Fendler's temperature coefficient of log K probably underestimates the real value.

Mean values for K at various temperatures obtained by Fendler, Gilbert and the present author are plotted in Figure (4.5), and the line drawn is as good an "average" as could reasonably be made. From this line values of K at various temperatures were read off, and are listed below; these values were used to calculate α.

Temp. (°C)	equilibrium constant, K(ℓ mol^{-1})
9.0	325
14.0	285
21.0	240

(2) DIMETHYL SULPHOXIDE AS SOLVENT

(a) 1-methoxy 2,4-dinitronaphthalene

As with methanol as solvent the kinetic pattern of the reaction of this compound with methoxide ions was of the type described on page (7), Figure (1.2). However it was noted that when formation of Meisenheimer complex was complete as evidenced for the value of $\frac{S_o}{S_i}$ approach 0.5, the rate of exchange seemed to be zero over up to 10 days or more. The data presented here (Tables(4.5), (4.7), (4.8) and (4.9)) are, therefore, simply the count-rate measured at various times during the course of each experiment. In all cases, this constant value for the

count rate was far from the value at isotopic equilibrium calculated from the concentration of methanol, methoxide and 1-methoxy 2,4-dinitronaphthalene.

However, whenever the concentration of methoxide ions was insufficient to render all the 1-methoxy 2,4-dinitronaphthalene into the form of Meisenheimer complex, as evidenced by the value of $\frac{S_o}{S_i}$ being greater than 0.5, reaction did take place though comparatively slowly and in DMSO as solvent, in the absence of methanol the count rate of samples decreased with time to below the value calculated for isotopic equilibrium; the kinetic plot based on equation (3.5) was not linear. Also it was noticed that, when the value of S_i was being determined by counting samples of 1-methoxy,2,4-dinitronaphthalene in DMSO only, and in the absence of methoxide ions, the solution gradually developed a yellow colour and that there was small decrease in count rate of a sample over a period of 75 hours (see Table 4.8). No rate was evaluated from the data.

The behaviour in DMSO solution was similar when a little methanol was added, that is, when sufficient methoxide ions were present to render the 1-methoxy 2,4-dinitronaphthalene into the form of Meisenheimer complex, no further loss of carbon - 14 activity from the sample was noted (see Tables (4.9) and (4.10)), but when 1-methoxy,2,4-dinitronaphthalene was present as well as Meisenheimer complex, the carbon - 14 activity of samples from the reaction mixture decreased with times (see Tables 4.7 and 4.11).

(b) P-nitroanisole

P-nitroanisole was studied in DMSO as solvent with a limited amount of methanol or methanol-o-d (0.3%) added.

Equation (3.5) was used to evaluate the rate R, the values of y, y_o and y_∞ being represented by the corresponding count rates S, S_o and S_∞.

The kinetic plots obtained were of the type described on page (7) and Figure (1.1); S_o was found to coincide with S_i. S_∞ was the count rate of samples when the reaction had reached equilibrium. A typical kinetic plot is given in Figure (4.6).

The orders of reaction in methoxide ions and p-nitroanisole were determined from the equation

$$R = K\left[ArOCH_3\right]^y \left[CH_3ONa\right]^x$$

by measuring R at different concentration of reagents. Kinetic results are presented in Table (4.12), and the evaluation of order of reaction follows these results on page (56).

(c) 1-Chloro,2,4-dinitronaphthalene

The exchange reaction of this compound with labelled chloride ions was studied in DMSO. During the course of the reaction the radioactivity progressively appeared in the aromatic compound. The rate of reaction, R, was evaluated by means of equation (3.4) (Page 36). The quantity $(x - x_o)$ and $(x_\infty - x_o)$ being represented by the count-rates S and S_∞ respectively. A plot of log $(1 - \frac{S}{S_\infty})$ against time was linear; a typical example is shown in Figure (4.7). Experimental data are presented in Table (4.14).

RECOVERY OF PRODUCTS

After sampling for kinetic measurements in a typical run the remainder of the reaction mixture was extracted with toluene/0.2N hydrochloric acid mixture, separated, and the toluene layer washed with de-ionised water. It was then evaporated, the melting point of the residue was taken and compared with that of the original nitroaromatic compound. The residue was then re-crystallised from methanol, and a melting point and also a mixed melting point, with the original nitro aromatic compound, were taken.

The absorption spectrum of the sample was taken and compared with that of the original nitroaromatic compound.

A sample of the crystal was also dissolved in methanol or DMSO and its radioactivity measured on a liquid scintillation counter.

Experimental data are summarised in Tables (4.16) and (4.17).

In the case of the reactions involving 1-chloro,2,4-dinitronaphthalene and sodium chloride, samples were taken at various times separated and dried as described above, and melting points were measured without recrystallisation. Only the sample taken within 10 minutes gave the melting point of the original 1-chloro 2,4-dinitronaphthalene (147.0^{o}C); the melting points of the other samples were found to decrease as the time of the reaction increased. The reaction solution developed a yellow colour after about half an hour and the colour increased with time during the course of the reaction.

Experimental data are summarised in Table (4.18).

It is apparent that the cases of 1-methoxy,2,4-dinitronaphthalene and p-nitroanisole the reaction with sodium methoxide were isotopic exchange reactions but with 1-chloro,2,4-dinitronaphthalene other reactions accompanied the isotopic chlorine exchange.

CHAPTER IV

RESULTS

Table (4.1) : Reaction of 1-Methoxy, 2,4-dinitronaphthalene and Sodium Methoxide in Methanolic Solutions at 9.0°C

K taken as 325 (1 mol.$^{-1}$) for calculation of α

Run No.	CH_3OH or CH_3OD	C_{Ar}(mol.l^{-1})	C_M(mol.l^{-1})	S_o	S_i	10^7R(mol.l^{-1}sec.$^{-1}$)	$\alpha_{calc.}$	10^4k(sec.$^{-1}$)
4	CH_3OH	0.00902	0.0142	1643	2558	19.32±0.57	0.6929	3.10
5	"	"	"	1641	2558	20.09±0.97	0.6929	3.20
6	"	"	"	2543	4041	19.28±0.53	0.6929	3.10
28	"	0.00754	0.00542	3062	3358	9.85±0.48	0.4211	3.10
30	"	"	0.0079	2572	3360	13.83±0.4	0.5490	3.14
						Mean value at 9.0°C		3.12
27	CH_3OD	0.00754	0.00541	2867	3358	5.66±0.36	0.4204	1.78
29	"	"	0.0080	2589	3360	9.08±0.32	0.5523	2.18
						Mean k value at 9.0°C		1.98

C_{Ar} = Conc.of Aromatic Compound, C_M = conc. of Methoxideions

Table (4.2) : Reaction of 1-Methoxy,2,4 -dinitronaphthalene and Sodium Methoxide in Methanolic Solutions at 14°C

K taken as 285 ($1\ mol.^{-1}$) for calculation of α

Run No.	CH_3OH or CH_3OD	C_{Ar} ($mol.l^{-1}$)	C_M ($mol.l^{-1}$)	S_δ	S_i	$10^7 R$ ($mol.l^{-1} sec.^{-1}$)	$\alpha_{calc.}$	$10^4 K$ ($sec.^{-1}$)
1	CH_3OH	0.00899	0.01402	1498	2451	32.78±13	0.6879	5.3
2	"	"	"	1486	2451	32.48±1.3	"	5.2
3	"	"	"	1455	2406	32.55±2.0	"	5.3
7	"	0.00757	0.00781	2254	3352	21.64±0.58	0.5218	5.30
8	"	"	0.005508	2575	3352	14.90±0.31	0.4094	5.10
9	"	0.00756	0.00788	2575	3466	24.29±0.45	0.5235	5.57
10	"	"	0.00750	2737	3402	16.88±0.43	0.4119	5.13
14	"	0.00755	0.00554	2755	3434	15.04±0.67	0.4086	5.16
16	"	"	"	2636	3392	15.61±0.39	0.4178	4.95
18	"	0.00754	0.00695	2517	3380	24.61±0.49	0.4763	5.73
26	"	"	0.00556	2919	3356	15.71±0.47		5.04
						Mean value at 14°C		5.25
11	CH_3OD	0.00754	0.00534	2742	3457	11.83±0.36	0.3984	3.93
12	"	"	0.00702	2468	3459	15.21±0.27	0.4878	4.13
13	"	0.00763	0.00534	2633	3495	9.28±0.49	0.3965	3.06
15	"	0.00754	"	2781	3392	10.93±0.26	0.3986	3.63
17	"	"	00681	2883	3338	10.96±0.26	0.4763	3.05
25	"	"	0.00537	2803	3356	10.18±0.67		3.36
						Mean value at 14°C		3.53

Table (4.3) : Reaction of 1-Methoxy 2,4-dinitronaphthalene and Sodium Methoxide Solutions at 21°C

K taken as 240 ($1\ mol^{-1}$) for calculation of α

Run No.	CH_3OH or CH_3OD	C_{Ar}	C_M	S_o	S_i	$10^7 R(mol.l^{-1}sec.^{-1})$	$\alpha_{calc.}$	$10^4 k$
20	CH_3OH	0.00750	0.00771	2460	3343	46.22±1.0	0.4918	12.52
22	"	0.00751	0.00550	2452	3355	24.78±1.6	0.3894	11.57
24	"	0.00749	0.00548	2966	3338	31.90±0.64	0.3737	11.39
						Mean value at 21°C		11.83
19	CH_3OD	0.00750	0.00693	2787	3355	24.90±0.49	0.4566	7.27
23	"	0.00749	0.00531	2690	3338	21.96±0.70	0.3737	7.84
						Mean value at 21°C		7.55

The mean values from the above three tables have been used in the Arrhenius Plot shown in Figure (4.3).

Table (4.4) : Reaction of 1-Methoxy,2,4-dinitronaphthalene and Sodium Methoxide (excess) in Methanolic Solutions

Run No.	T(°C)	CH_3OH or CH_3OD	C_{Ar}	C_M	S_o	S_i	$\frac{So}{S_i}$	$10^7 R(mol.l^{-1}sec.^{-1})$	$10^4 k(sec.^{-1})$	$\frac{k_H}{k_D}$
33	9	CH_3OD	0.00757	0.0552	2166	4080	0.53	9.10±0.39	1.20	1.40
34	9	CH_3OH	"	0.0546	2211	4040	0.54	12.81±0.38	1.69	
48	12	CH_3OD	0.00764	0.0548	2008	4098	0.49	13.06±0.40	1.70	1.44
49	12	CH_3OH	"	0.0548	1977	4119	0.48	18.75±0.41	2.45	
31	14	CH_3OD	0.00753	0.0546	1951	4174	0.47	14.78±0.42	1.96	1.39
32	14	CH_3OH	"	0.0546	1876	4102	0.46	20.59±0.94	2.73	
46	17	CH_3OD	0.00754	0.0544	2004	4090	0.49	22.04±0.91	2.92	1.42
47	17	CH_3OH	"	0.0544	2010	4102	0.49	31.30±0.99	4.15	
35	21	CH_3OD	"	0.0540	1921	3998	0.48	32.09±1.10	4.26	1.42
36	21	CH_3OH	"	0.0540	1936	3925	0.49	45.71±1.8	6.06	

Arrhenius plot based on these data is given in Figure (4.2).

Table (4.5) : Data from Tables (4.1), (4.2) and (4.3) for Arrhenius plot for the reaction of 1-methoxy 2,4-dinitronaphthalene and Sodium Methoxide in Methanolic Solutions

CH_3OH or CH_3OD	T(°C)	$\frac{10^3}{T}$ (k^{-1})	k(mean)	log k
CH_3OH	9	3.546	3.12	$\bar{4}.5011$
"	14	3.484	5.25	$\bar{4}.7218$
"	21	3.401	11.39	$\bar{3}.0799$
CH_3OD	9	3.546	1.98	$\bar{4}.2967$
"	14	3.484	3.53	$\bar{4}.5514$
"	21	3.401	7.55	$\bar{4}.8778$

Table (4.6) : Specific rate ratios for the reaction between 1-methoxy,2,4-dinitronaphthalene and Sodium Methoxide in Methanol and Methanol-o-d at various Temperatures
Data collected from Tables (4.1), (4.2) and (4.3)

T(°C)	10^4K_H (mean)	10^4K_D (mean)	$\frac{K_H}{K_D}$
9	3.12	1.98	1.60
14	5.25	3.53	1.48
21	11.83	7.55	1.59

Table (4.7) : Data for run 39 - 1-methoxy.2,4-dinitronaphthalene and Sodium Methoxide

C_{Ar} = 0.0075M, C_M = 0.0008M. ($C_M < C_{Ar}$)
Solvent; DMSO, T = 25.0°C

Sample No.	Time hr.	Time min.	S (counts/100 sec.)
1	0	32.5	26072
2	4	53.0	24058
3	20	57.0	20714
4	31.4		20034
5	68.53		18900
7	75.8		17652

S_o = 26390 ; S_i = 27704 ; S_∞ = 25086

S_o / S_i = 0.95

Table (4.8) : 1-Methoxy,2,4-dinitronaphthalene in DMSO, Solvolysis reaction

C_{Ar} = 0.0075M

Sample No.	Time hr.	Time min.	S (C./100 sec.)
1	-	3	27704
2	30	-	25509
3	60	-	23413
4	75	-	22266

Table (4.9) : Data for Run 40 - 1-methoxy,2,4-dinitronaphthalene plus sodium methoxide

C_{Ar} = 0.0077M ; C_M = 0.0104M ; T = 25°C

Solvent : DMSO/CH_3OH (99:1; by volume)

Sample No.	Time d.	Time hr.	S (counts/100 secs.)
1	-	0.2	14166
2	-	0.4	14336
3	-	2.0	13802
4	-	17.4	13133
5	-	56.2	13468
6	-	76.2	13524
7	4	20.0	13173
8	10	16.6	14224

S_o = 14200 ; Si = 28809 ; S_∞ = 836

S_o/S_i = 0.493

Table (4.10) : Data for Run 41 - 1-methoxy,2,4-dinitronaphthalene plus sodium methoxide

C_{Ar} = 0.0079M ; C_M = 0.063M

Solvent: DMSO, CH_3OH (96:4) ; T = 25°C

Sample No.	Time hr.	Time min.	S
1	0	11.66	15045
2	1	15.75	14158
3	1	37.50	14708
4	2	16.16	15140
5	7	10.16	14783
6	24	18.0	14354
7	70	33.66	14416
8	78	22.75	14992

S_o = 15092 ; Si = 32074 ; S_∞ = 247

S_{o/S_i} = 0.46

Table (4.11) : Data for Run 42 - 1-methoxy,2,4-dinitronaphthalene plus sodium methoxide

C_{Ar} = 0.0211M (excess); C_M = 0.0104M

Solvent: DMSO, CH_3OH (99:1)

Sample No.	Time hr.	Time min.	S
1	-	48.5	38627
2	3	43.0	36281
3	5	9.0	35584
4	8	29.0	33921
5	21	21.0	31863
6	28	43.0	28973
7	47	47.0	27686

S_o = 39540 ; Si = 50779, S_∞ = 3847

S_o/S_i = 0.77

Table (4.12) : Reaction of p-nitroanisole and sodium methoxide at 20.2°C in DMSO to which 0.3% (by volume) methanol or methanol-o-d was added

Run No.	CH_3OH or CH_3OD	C_{Ar} (mol.l^{-1})	C_M (mol.l^{-1})	C_T (mol.l^{-1})	Slope (min^{-1})	$10^6 R$ (mol.l^{-1} $sec.^{-1}$)	$\frac{R_H}{R_D}$ *
62	CH_3OD	0.00469	0.00495	0.0793	0.098	16.65	
63	CH_3OH	"	0.00507	0.0794	0.111	18.69	
64	CH_3OD	0.00296	0.00495	0.0793	0.0868	9.50	
65	CH_3OH	"	0.00507	0.0794	0.094	10.29	
66	CH_3OD	0.00293	0.00281	0.0771	0.0293	3.17	)
67	CH_3OH	"	"	"	0.0299	3.24	) 1.02

* Concentrations of reactants identical only for runs 66 and 67

C_T = total conc. of $CH_3\bar{O}$ (sodium methoxide plus methanol)

Table (4.13) : Data from table 4.12 for calculation of the order of the reaction between P-nitroanisole and Sodium Methoxide at 20.2°C in DMSO, to which 0.3% (by volume) of methanol or methanol-o-d was added

Run No.	CH_3OH or CH_3OD	log C_{Ar}	log C_M	log R
62	CH_3OD	$\bar{3}.6712$	$\bar{3}.6946$	$\bar{6}.2214$
63	CH_3OH	"	$\bar{3}.7050$	$\bar{6}.2718$
64	CH_3OD	$\bar{3}.4713$	$\bar{3}.6946$	$\bar{5}.9777$
65	CH_3OH	$\bar{3}.4713$	$\bar{3}.7050$	$\bar{5}.0124$
66	CH_3OD	$\bar{3}.4669$	$\bar{3}.4487$	$\bar{6}.5011$
67	CH_3OH	"	"	$\bar{6}.5105$

The kinetics of the reaction were calculated as follows

$$R = k\ C_M^x\ C_{Ar}^y$$

(the concentration of methanol is constant throughout, and methanol does not, therefore, appear as a variable in the kinetic equation.)

then, $\log R = \log k + x \log C_M + y \log C_{Ar}$

$$\log R_{62} = \bar{5}.2214 = \log k + \bar{3}.6946\ x + \bar{3}.6712y$$
$$\log R_{63} = \bar{5}.2718 = \log k + \bar{3}.7050\ x + \bar{3}.6712y$$
$$\log R_{64} = \bar{6}.9777 = \log k + \bar{3}.6946\ x + \bar{3}.4713y$$
$$\log 65 = \bar{5}.0124 = \log k + \bar{3}.7050\ x + \bar{3}.4713y$$
$$\log 66 = \bar{6}.5011 = \log k + \bar{3}.4487\ x + \bar{3}.4669y$$
$$\log 67 = \bar{6}.5105 = \log k + \bar{3}.4487\ x + \bar{3}.4669y$$

to determine the value of x, therefore;

$$\log R_{65} - \log R_{67} = 0.5019 = 0.2563\ x$$
$$x = 1.96$$

and $\log R_{64} - \log R_{66} = 0.4766 = 0.2459\ x$

$$x = 1.94$$

Similarly y may be evaluated;

$$\log R_{62} - \log R_{64} = 0.2437 = 0.1999y$$
$$y = 1.2$$

and $\log R_{63} - \log R_{65} = 0.2594 = 0.1999y$

$$y = 1.3$$

Thus the reaction appeared to be first order in p-nitroanisole and second order in methoxide ions.

Table (4.14) : Reaction of 1-chloro,2,4-dinitronaphthalene and chloride ions in DMSO at 20.0°C

Run No.	C_{Ar} (mol.l^{-1})	C_{NaCl} (mol.l^{-1})	Slope ($hour^{-1}$)	Rate.R. (mol.l^{-1} $sec.^{-1}$)
69	0.0075	0.0106	0.11	3.103×10^{-7}
70	0.010	"	0.127	4.199×10^{-7}
71	0.0050	"	0.0955	2.09×10^{-7}
72	"	0.00795	0.0885	1.747×10^{-7}
73	"	0.0053	0.080	1.322×10^{-7}
74	0.0085	0.0106	0.1305	3.93×10^{-7}
75*	"	"	0.1305	3.93×10^{-7}
76†	"	"	0.12	3.615×10^{-7}

* 10µl water added

† 10µl conc.perchloric acid added

(4.14)

Table (4.15) : Data from table for graphical determination of the order of the reaction between 1-chloro,2,4-dinitronaphthalene and chloride ions in DMSO

Run No.	log R	log C_{Ar}	log C_{NaCl}
69	$\bar{7}.4918$	$\bar{3}.8751$	$\bar{2}.0253$
70	$\bar{7}.6231$	$\bar{2}.0$	"
71	$\bar{7}.3201$	$\bar{3}.6990$	"
72	$\bar{7}.2420$	$\bar{3}.699$	$\bar{3}.9004$
73	$\bar{7}.1212$	"	$\bar{3}.7243$
74	$\bar{7}.5945$	$\bar{3}.9204$	$\bar{3}.0253$
75	"	"	"
76	$\bar{7}.5580$	"	"

These data are plotted in Figures (4.8) and (4.9) and the order of reaction derived from the slope of the plots are:

in aromatic compound ; 1.0

in chloride ions ; 0.7

Table (4.16) : Recovery of products - Reaction between 1-methoxy,2,4-dinitronaphthalene and methoxide ions in methanol

Melting point of original compound	98.5°C
Melting point of residue remaining after evaporation of toluene extract	98.0
Melting point of residue after recrystallisation	98.5
Mixed Melting point of crystals with original compound	98.5
Count-rate per mg of crystals	137 counts/100 secs.
Count-rate per mg of original compound	18336 counts/100 secs.
Absorption spectrum	Figure 4.10

Table (4.17) : Recovery of products - Reaction between p-nitroanisole and methoxide ions in DMSO

Melting point of original compound	53.5°C
Melting point of residue remaining after evaporation of toluene extract	53.3°C
Melting point of residue after recrystalisation	53.5°C
Mixed Melting point of crystals with original compound	53.5°C
Count-rate per mg of crystals	335 counts/100 secs.
Count-rate per mg of original compound	4108 counts/100 secs.
Absorption spectrum	Figure (4.14)

Table (4.18) : Recovery of product - Reaction between 1-chloro,2,4-dinitronaphthalene and chloride ions in DMSO

Time of Sampling	Melting point of residue remaining after evaporation of toluene extract	Counts/100 secs per mg
0	147.0	Nil
10 minutes	147.0	397
7 hours	145.0	7873
2 days	139.0	11251 (at equilibrium)

Melting point of original compound : 147.0°C

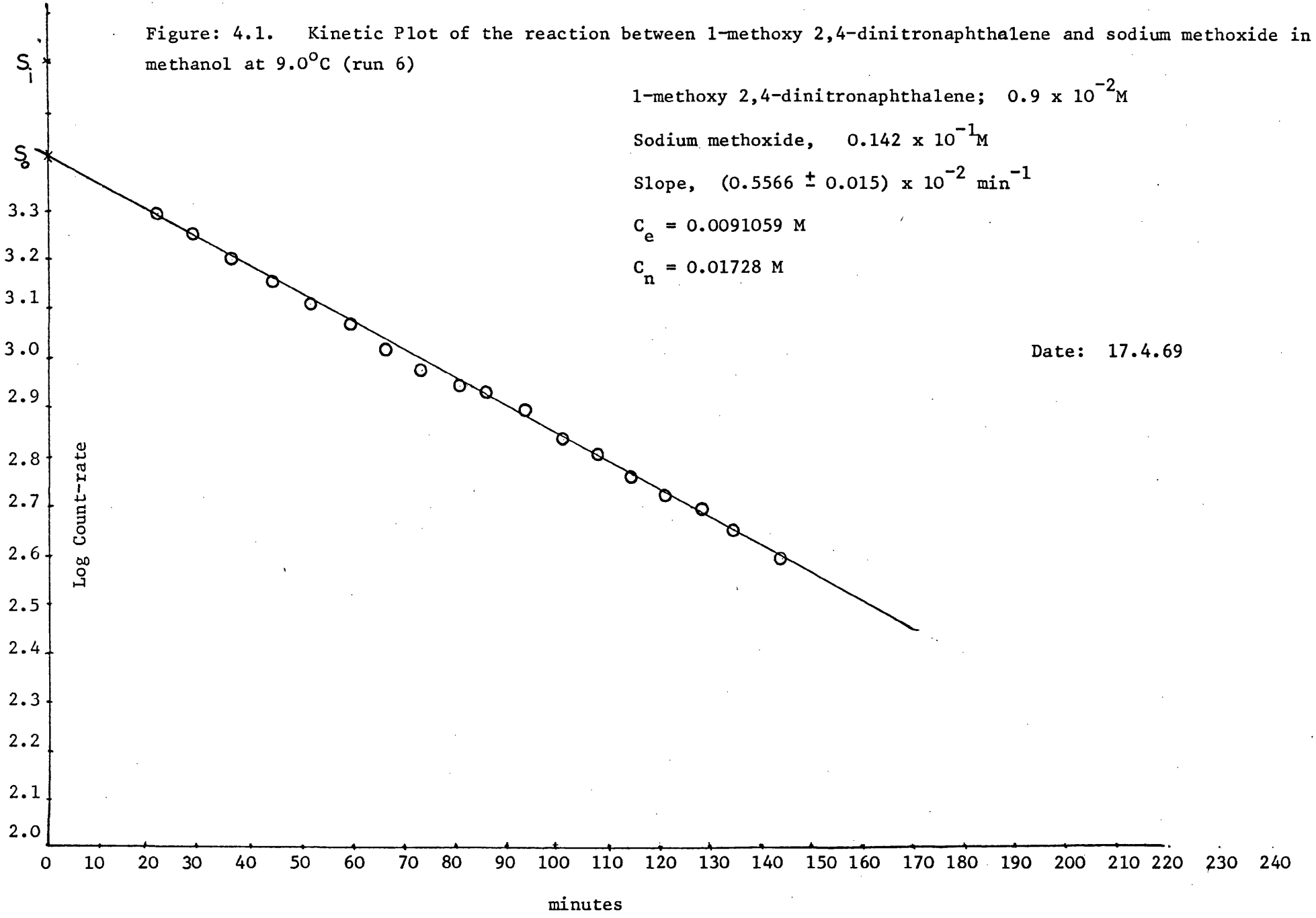


Figure: 4.1. Kinetic Plot of the reaction between 1-methoxy 2,4-dinitronaphthalene and sodium methoxide in methanol at 9.0°C (run 6)
1-methoxy 2,4-dinitronaphthalene; 0.9 x 10⁻²M
Sodium methoxide, 0.142 x 10⁻¹M
Slope, (0.5566 ± 0.015) x 10⁻² min⁻¹
Cₑ = 0.0091059 M
Cₙ = 0.01728 M
Date: 17.4.69
S∞
S₀
Log Count-rate
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210 220 230 240
minutes

Figure 4.2: Reaction of 1-methoxy 2,4-dinitronaphthalene and methoxide ions (excess) in methanol - Arrhenius plot

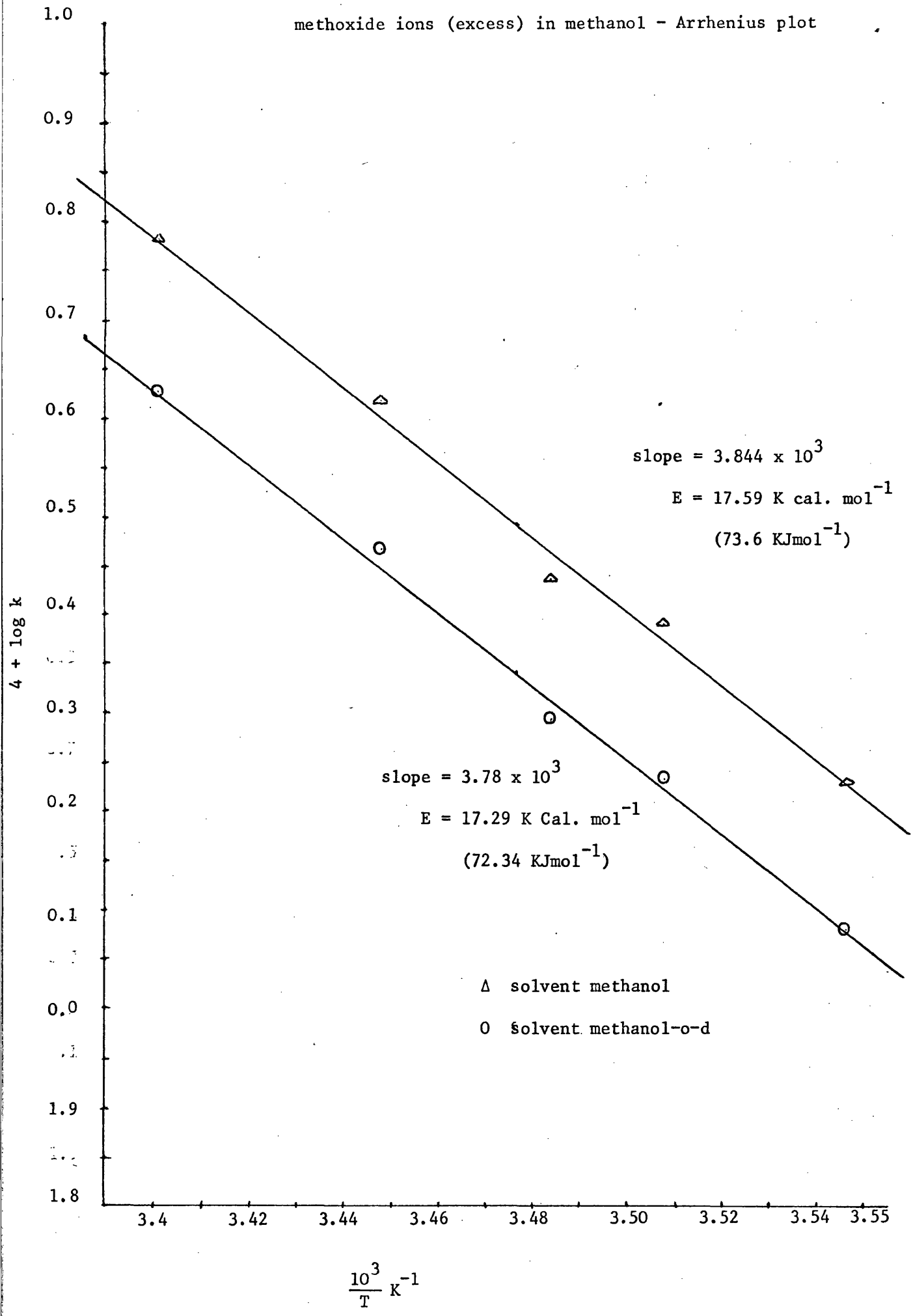


Figure 4.3 Heterolysis of 1-methoxy 2,4-dinitronaphthalene in methanol and in methanol-o-d. Arrhenius plot

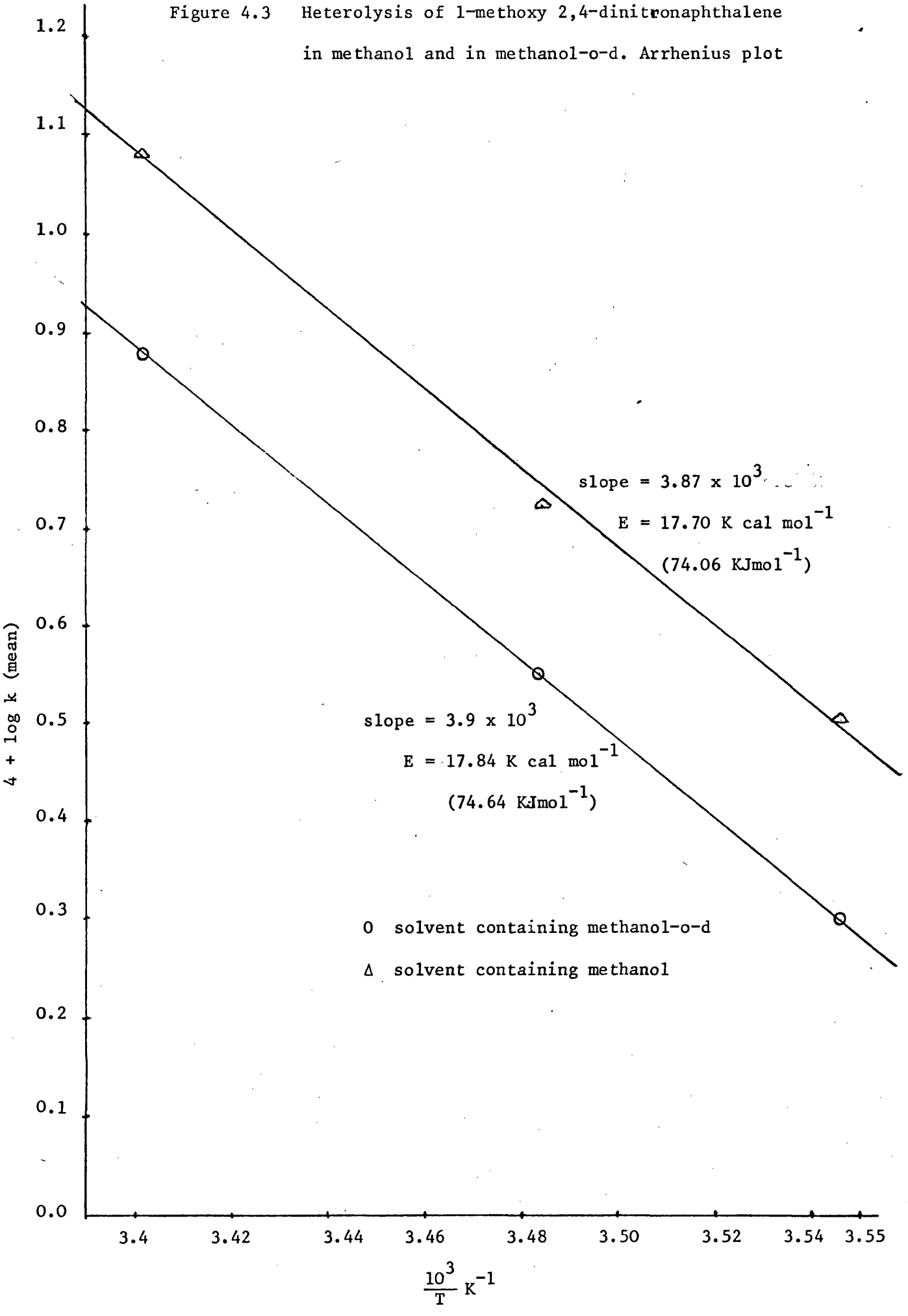


Figure 4.4: Heterolysis of 1-methoxy, 2-4-dinitronaphthalene (14.0°C)

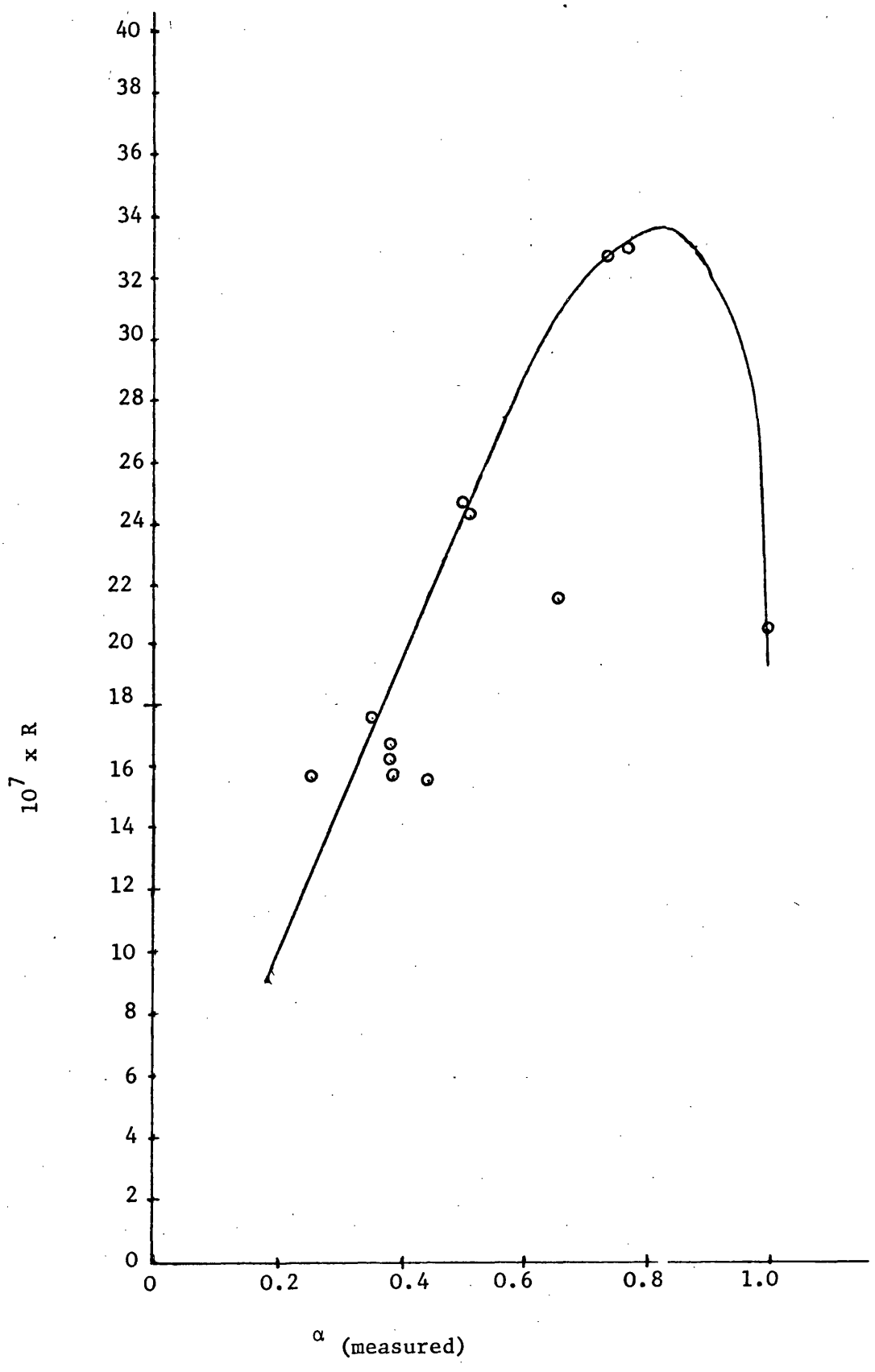


Figure 4.5 Reaction of 1-methoxy 2,4-dinitronaphthalene and sodium methoxide in methanol.
Plot of the logarithm of the equilibrium constant for the formation of Meisenheimer complex against reciprocal temperature

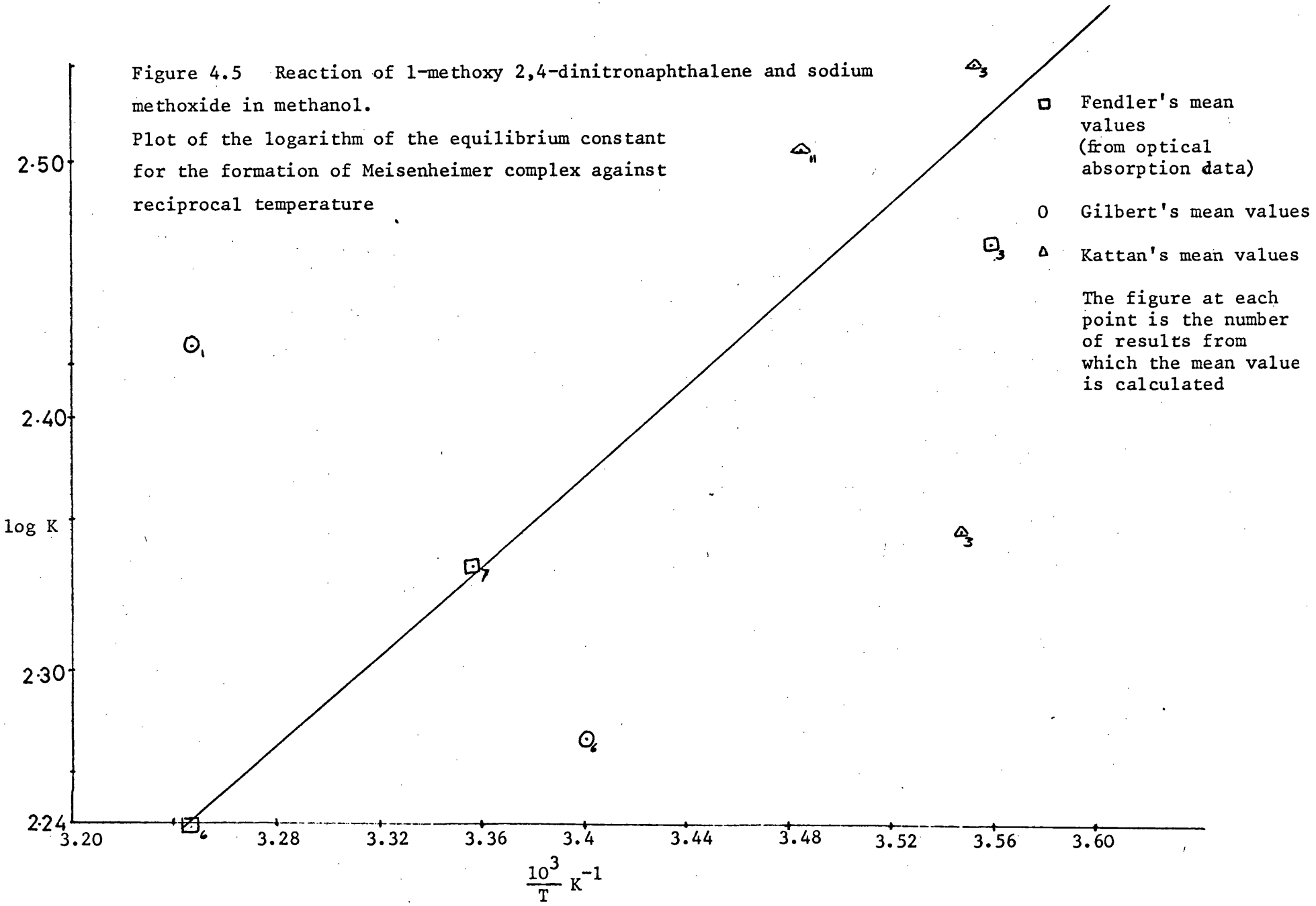


Figure 4.6 Kinetic plot of the reaction between p-nitroanisole and methoxide ions in DMSO plus 0.3% (by volume) methanol-o-d at 20.2°C (run 62).

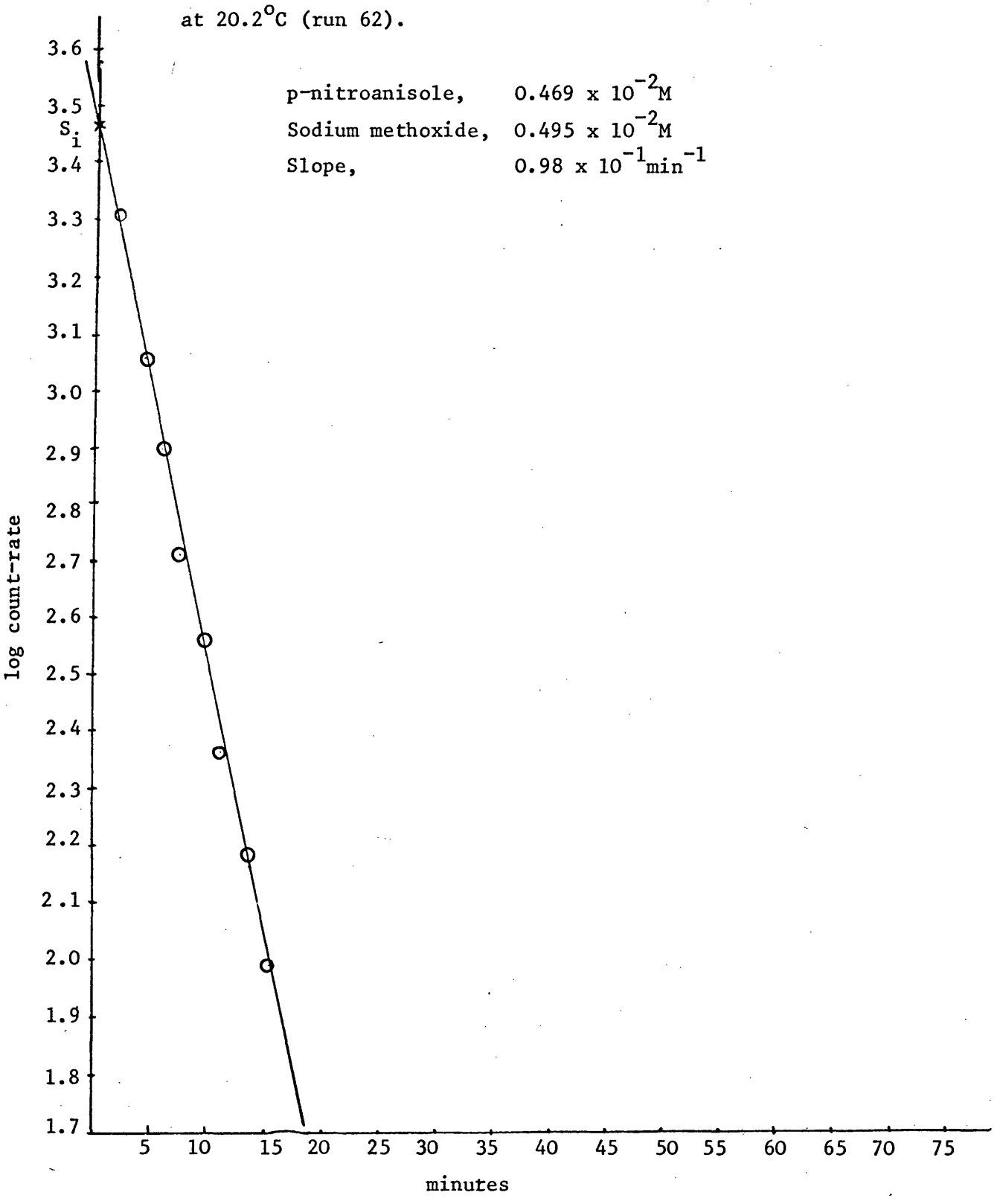


Figure 4.7 Kinetic Plot of the reaction between 1-chloro,2,4-dinitronaphthalene and chloride ions in DMSO at 20.0°C (run 75)

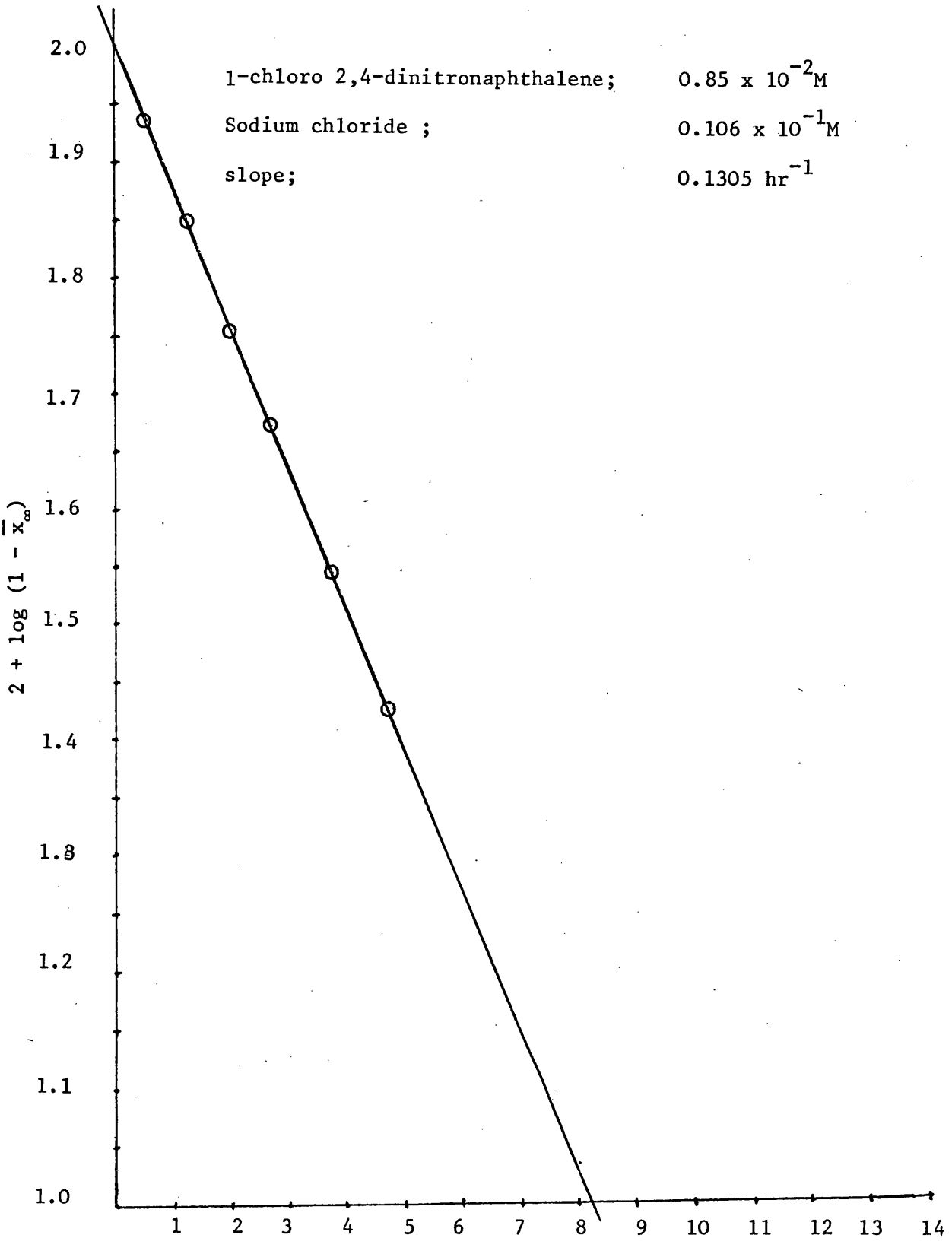


Figure 4.8 Reaction of 1-chloro 2,4-dinitronaphthalene and chloride ions ($20^{o}C$).

Order of the reaction.

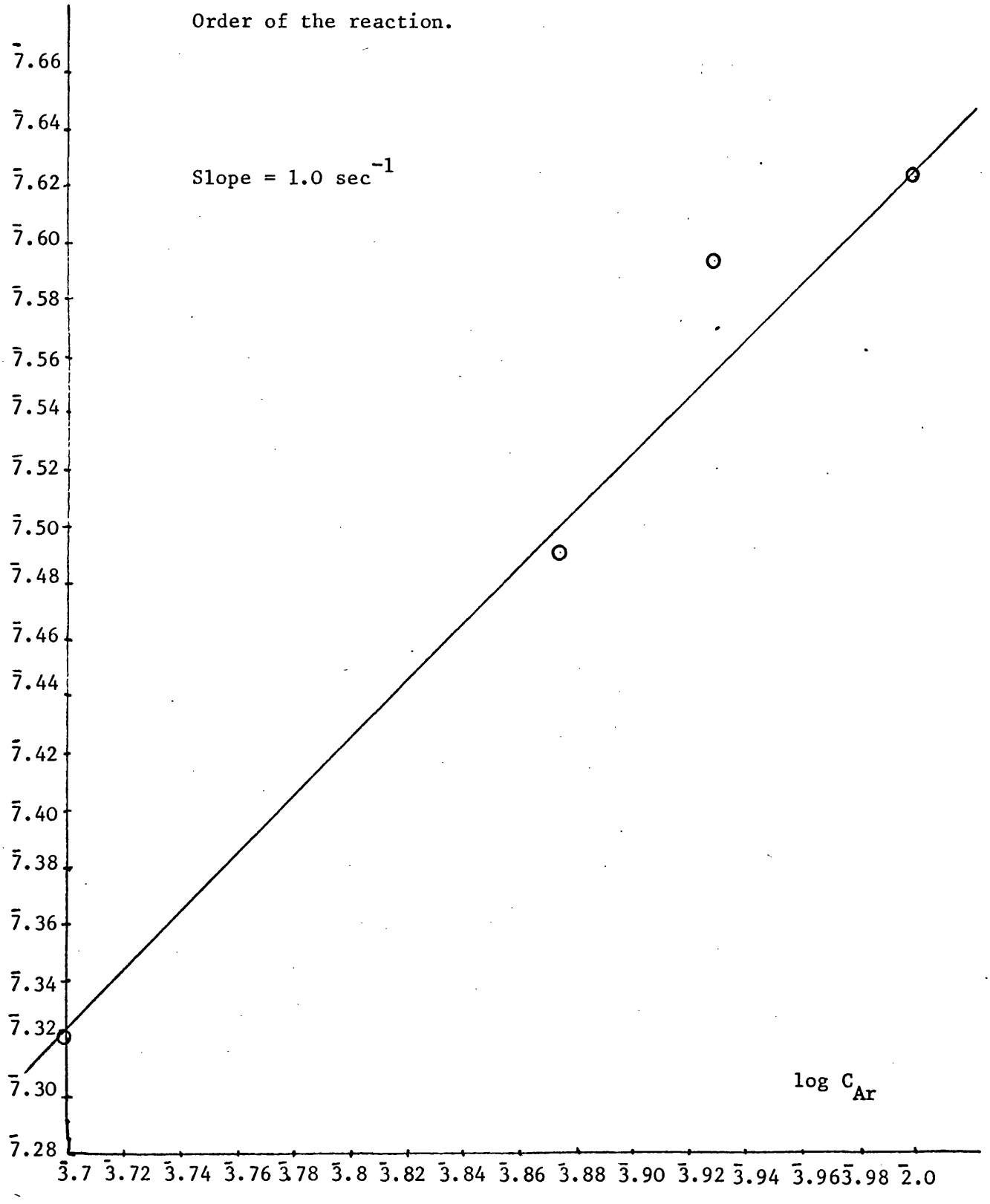
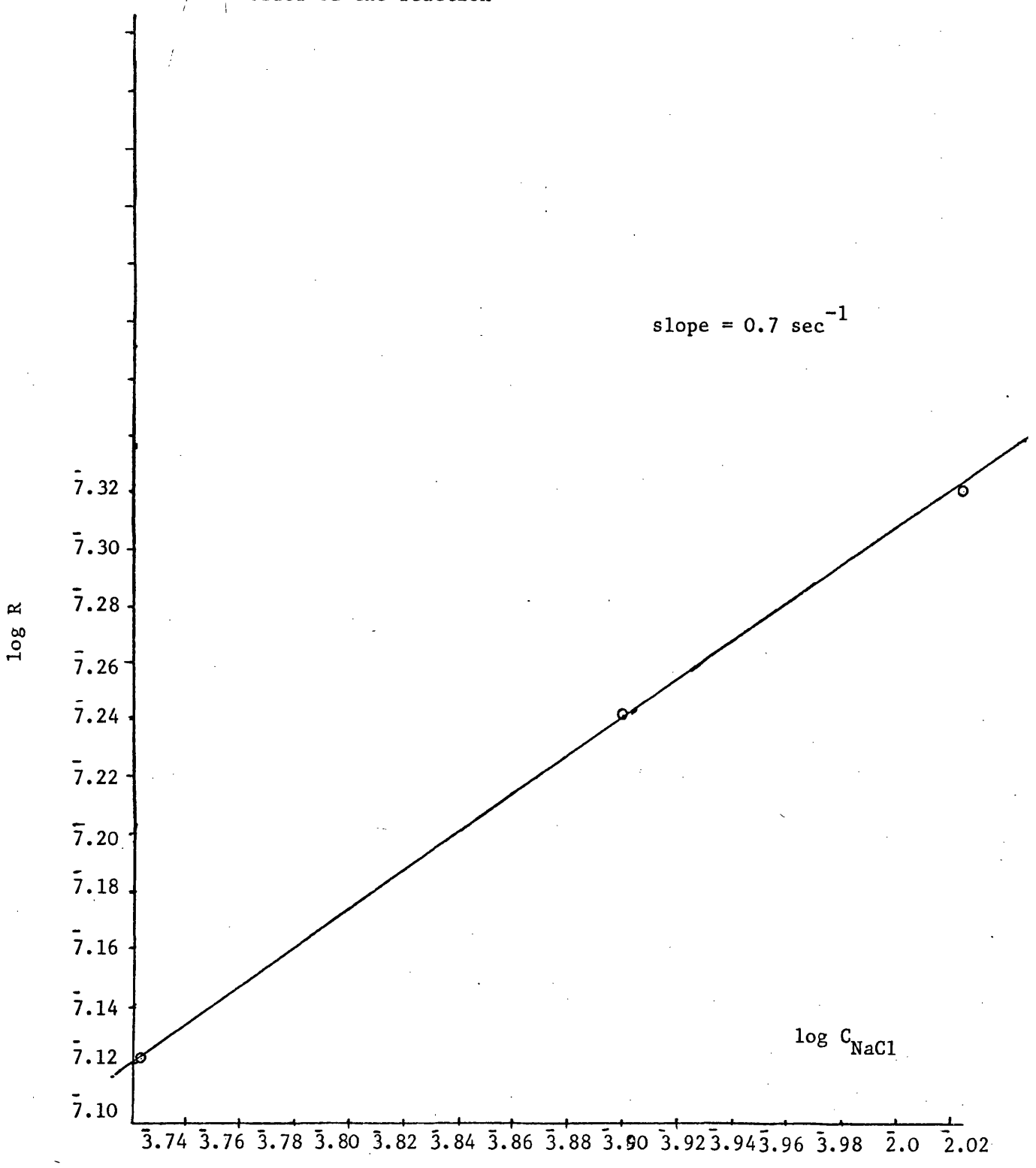


Figure 4.9: Reaction of 1-chloro 2,4-dinitronaphthalene and chloride ions (20°C)

Order of the reaction



ABSORPTION SPECTRA

Figures (4.10) to (4.33) show various absorption spectra. The preparation of samples was carried out as described on page 34. Measurements were carried out as follows:

spectrophotometer	=	Unicam SP700A
cell	=	Silica, 10 m.m.

Measurements were made at room temperature.

Figure 4.10

Recovery of product. Sample of residue of toluene extract from reaction mixture of run 31 between 1-methoxy 2,4-dinitro-naphthalene and sodium methoxide in methanol-d-d

1-methoxy 2,4-dinitro-naphthalene, 0.67×10^{-4} M (in DMSO)

Date: 30.1.70

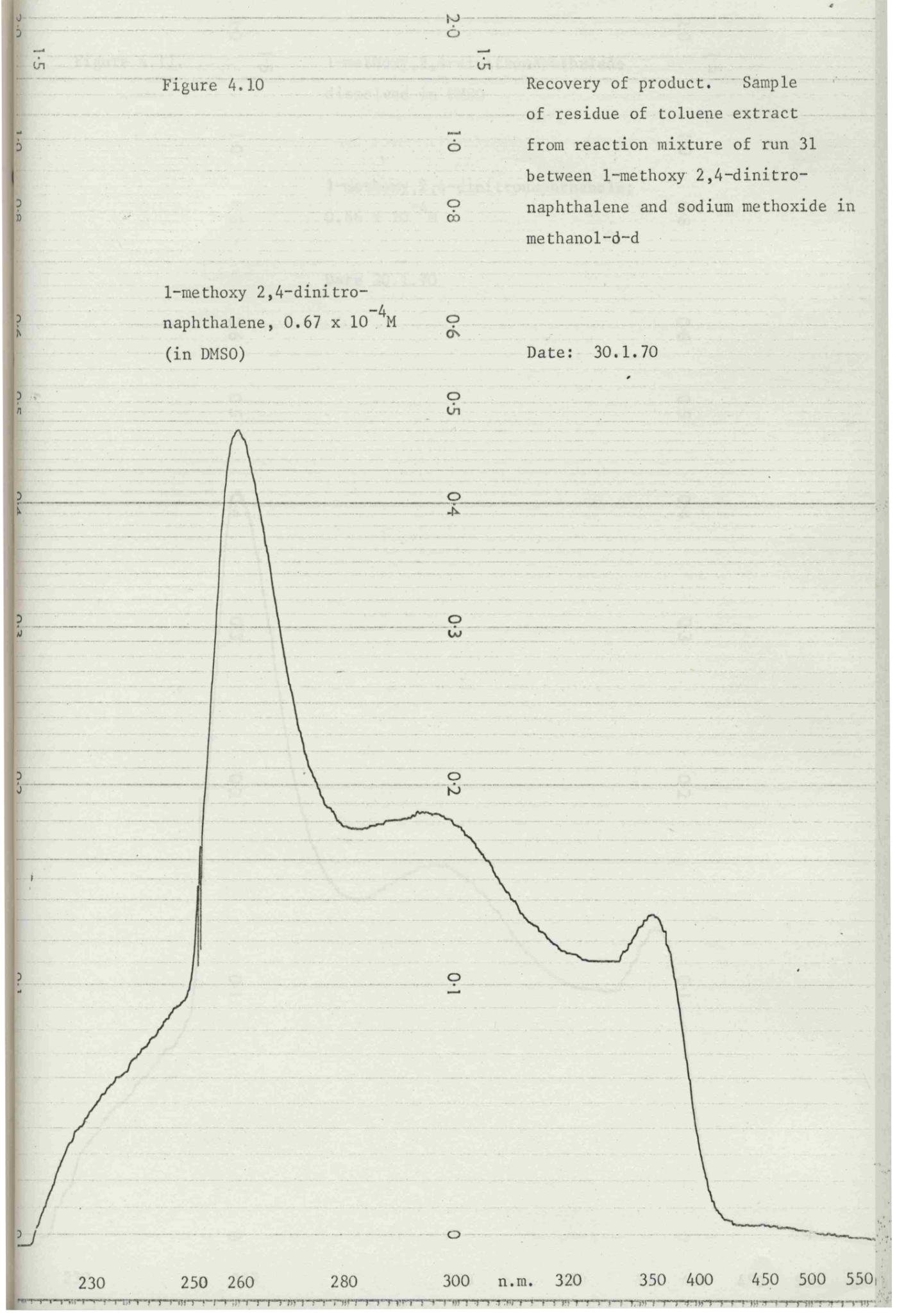


Figure 4.11. 1-methoxy,2,4-dinitronaphthalene dissolved in DMSO

1-methoxy,2,4-dinitronaphthanele;
0.66×10^{-4}M

Date 30.1.70

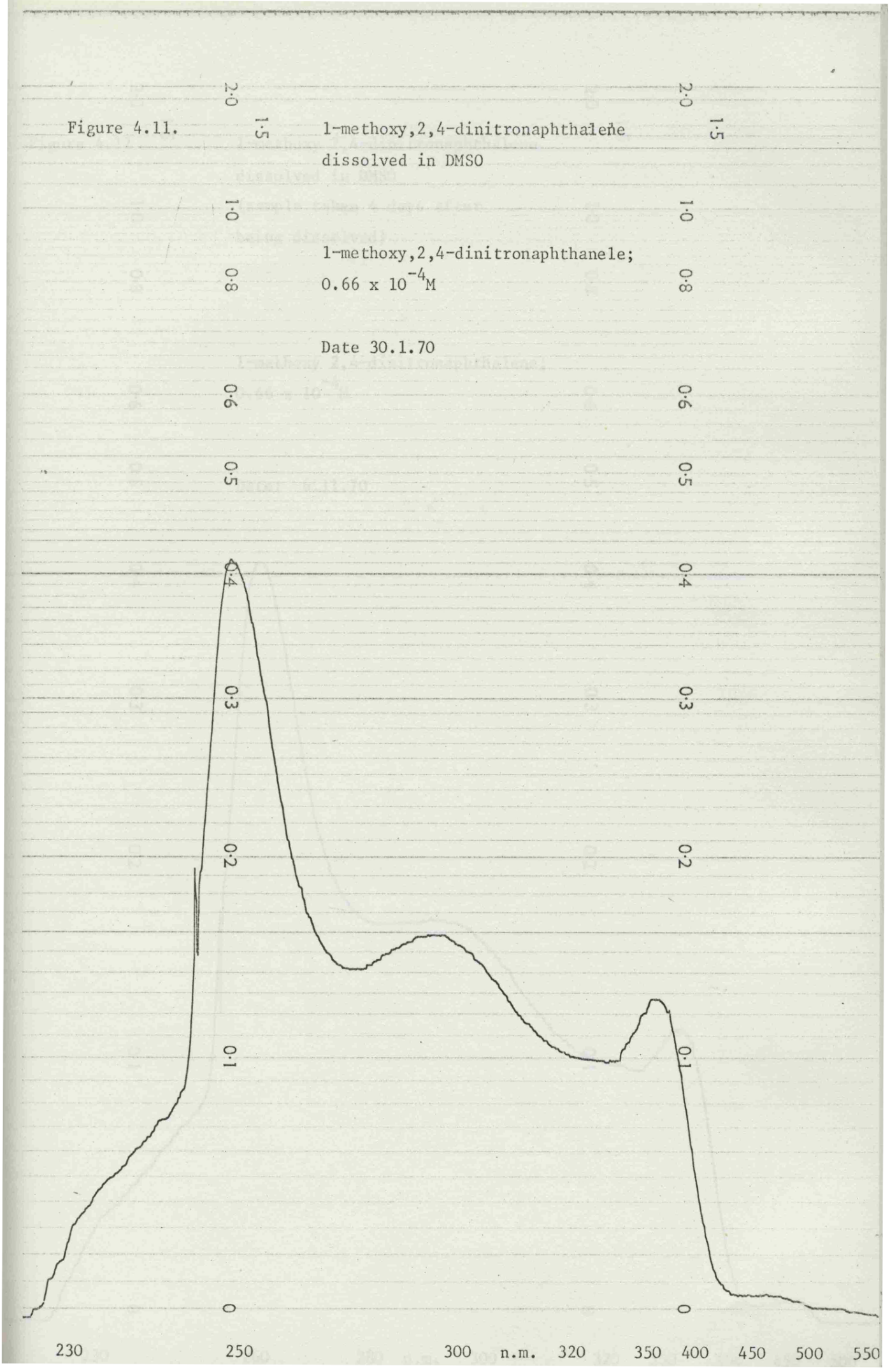


Figure 4.12 1-methoxy 2,4-dinitronaphthalene dissolved in DMSO (sample taken 4 days after being dissolved)

1-methoxy 2,4-dinitronaphthalene; 0.66×10^{-4} M

Date: 6.11.70

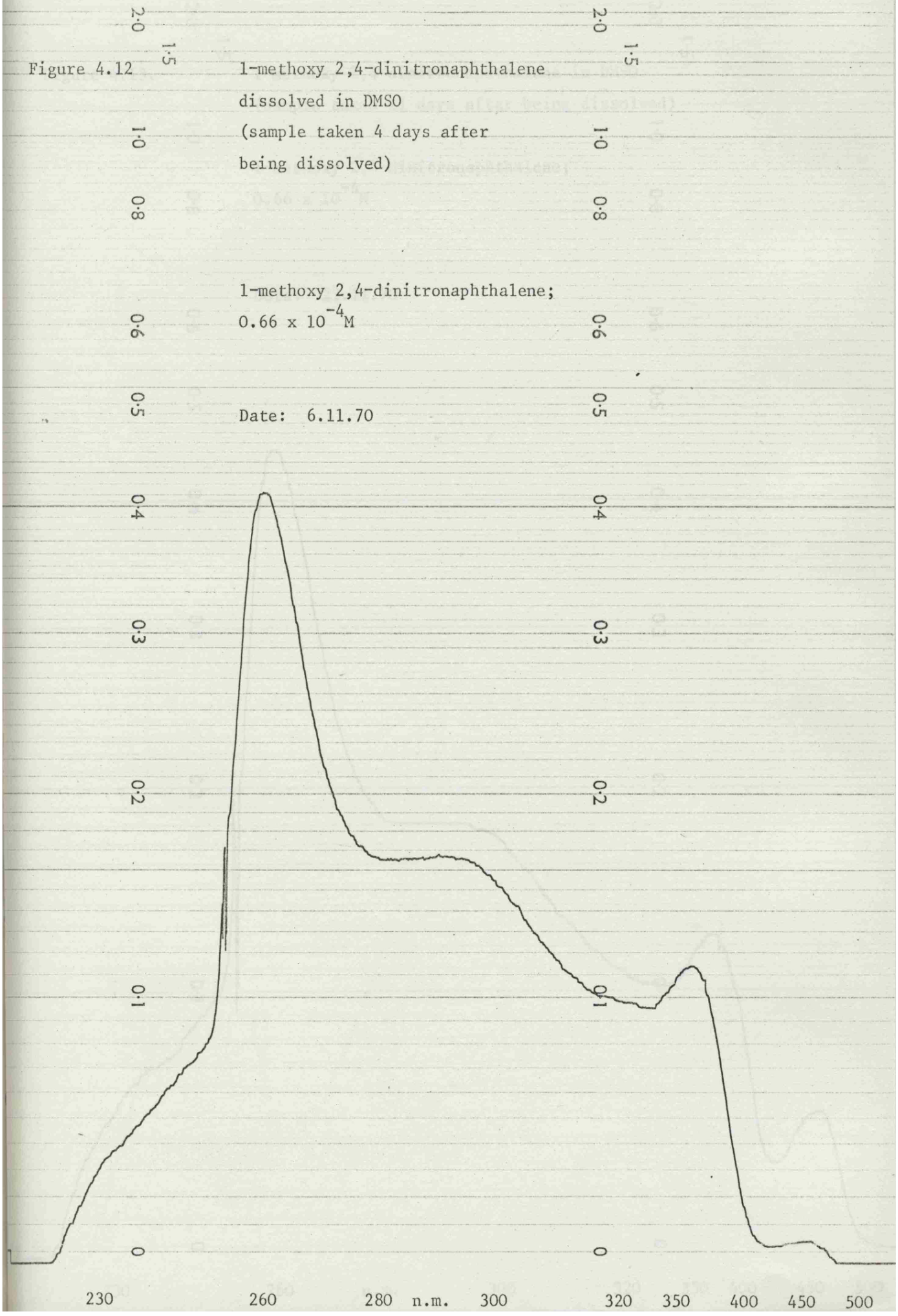


Figure 4.13. 1-methoxy 2,4-dinitronaphthalene in DMSO
(sample taken 21 days after being dissolved)

1-methoxy 2,4-dinitronaphthalene;
0.66×10^{-4}M

Date: 23.11.70

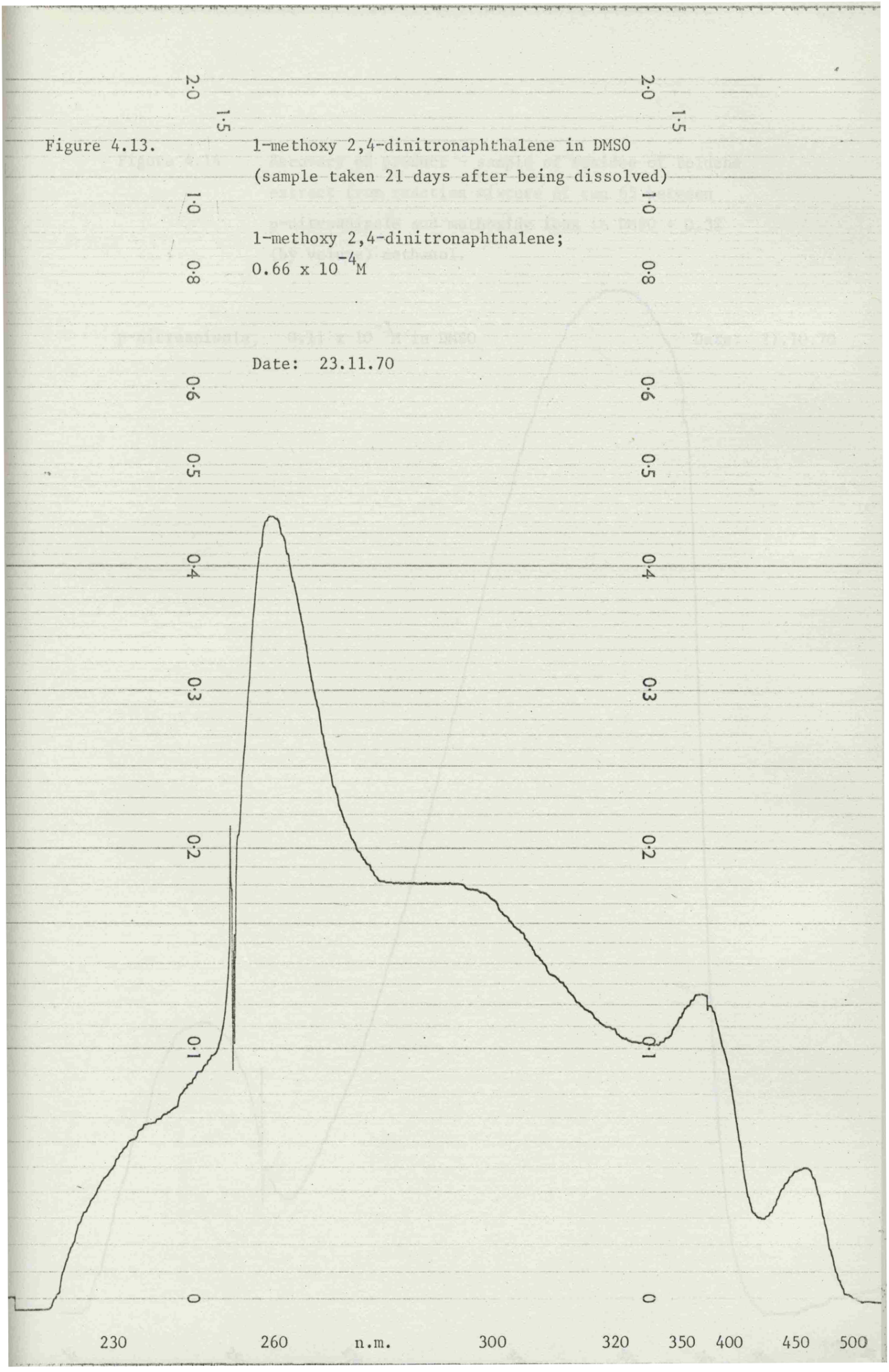


Figure 4.14 Recovery of product - sample of residue of toluene extract from reaction mixture of run 65 between p-nitroanisole and methoxide ions in DMSO + 0.3% (by volume) methanol.

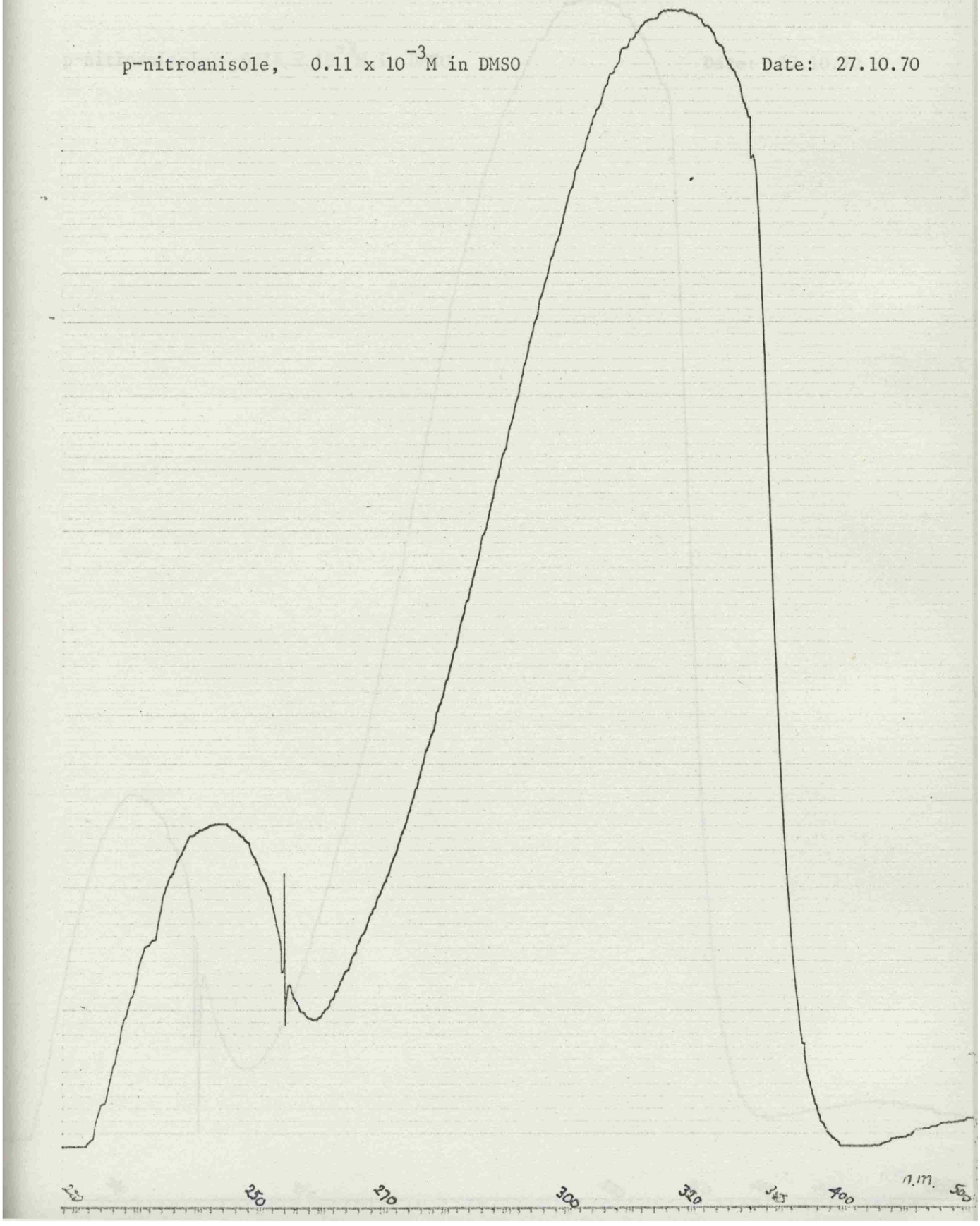


Figure 4.15 p-nitroanisole dissolved in DMSO

p-nitroanisole; 0.14×10^{-3} M in DMSO Date: 27.10.70

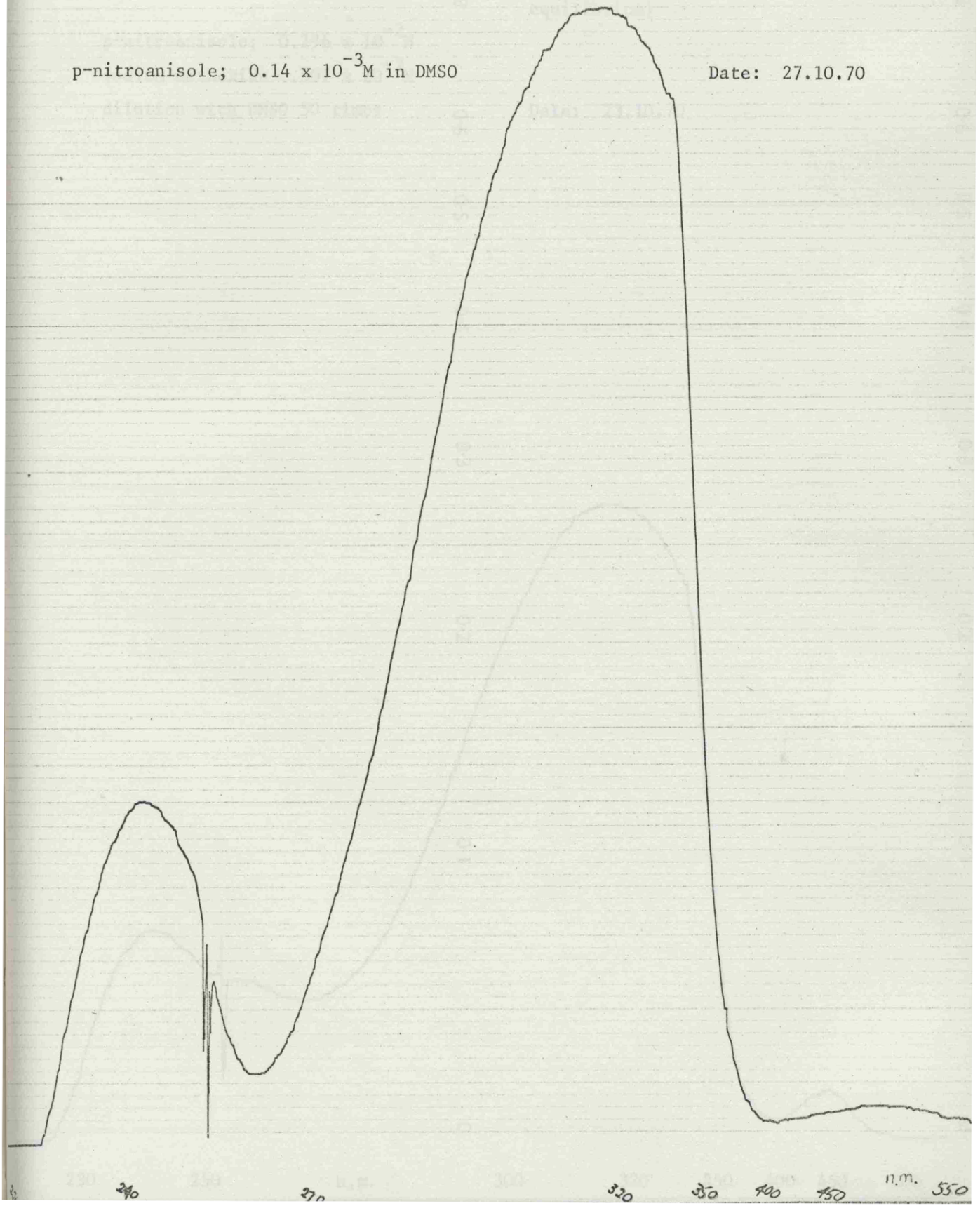


Figure 4.16

Reaction of p-nitroanisole and methoxide ions in DMSO plus 0.3% (by volume) methanol (sample taken from run 65 at reaction equilibrium)

p-nitroanisole; 0.296×10^{-2}M
sodium methoxide 0.507×10^{-2}M
dilution with DMSO 50 times

Date: 23.10.70

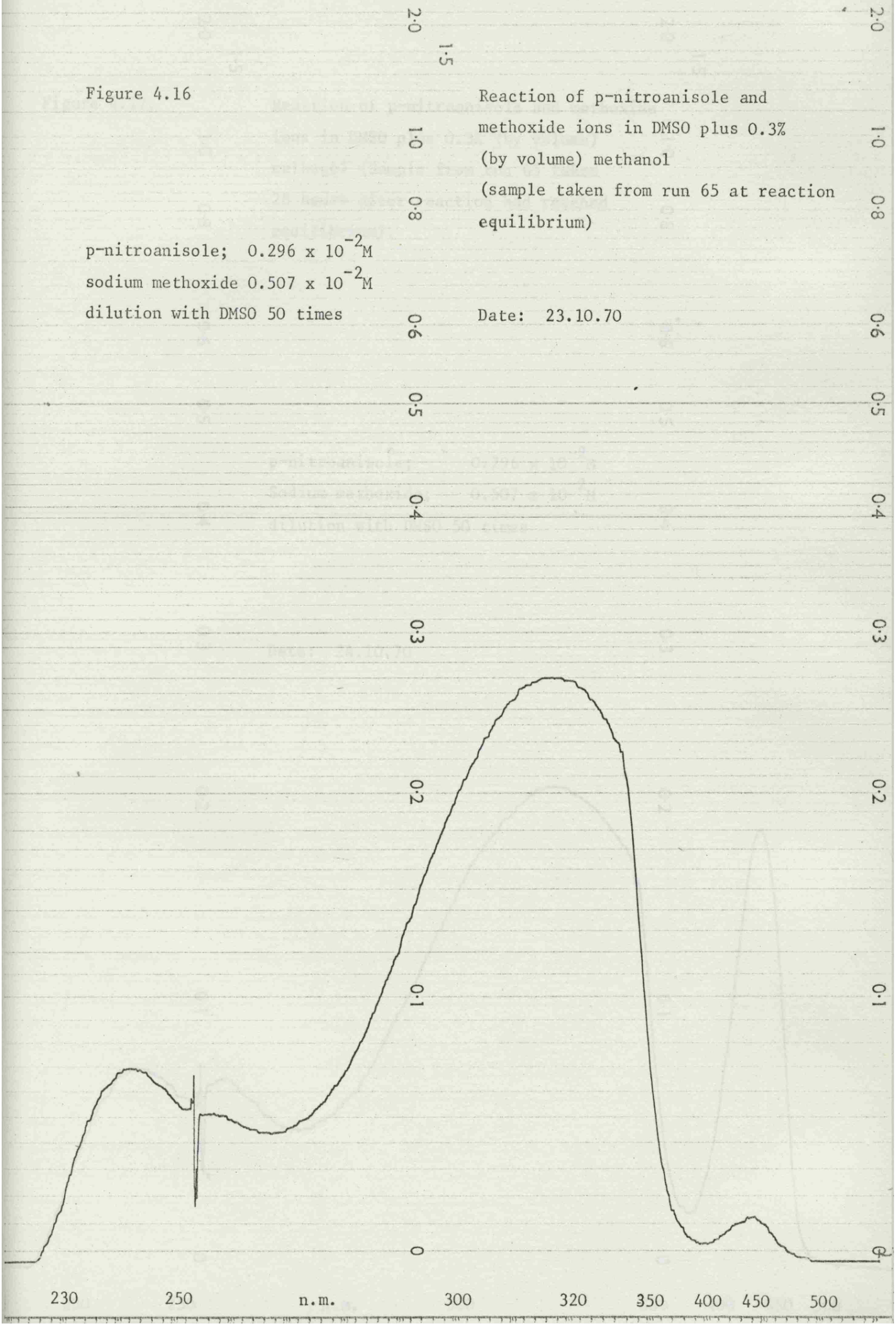


Figure 4.17. Reaction of p-nitroanisole and methoxide ions in DMSO plus 0.3% (by volume) methanol (Sample from run 65 taken 28 hours after reaction had reached equilibrium).

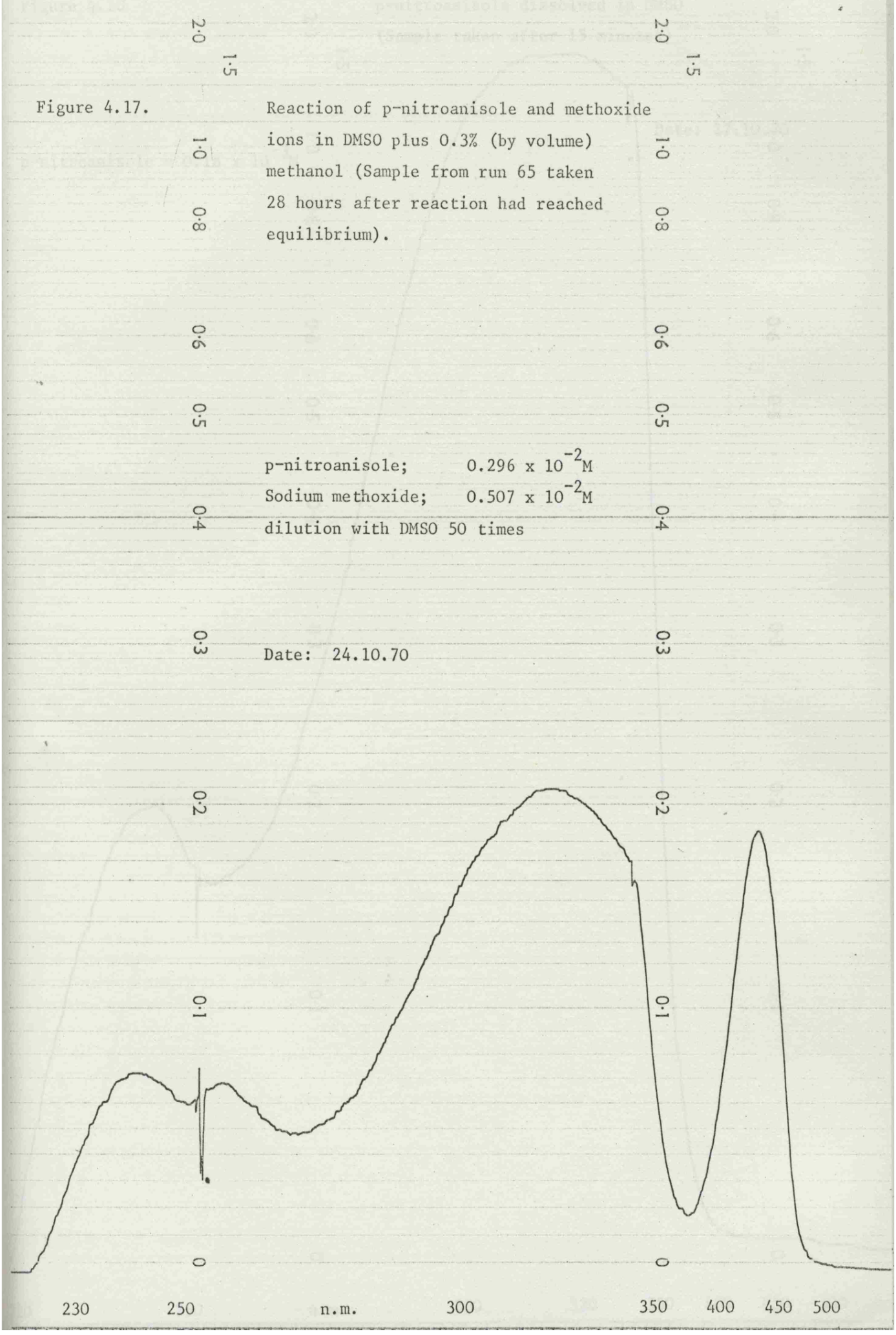


Figure 4.18

p-nitroanisole dissolved in DMSO

(Sample taken after 15 minutes)

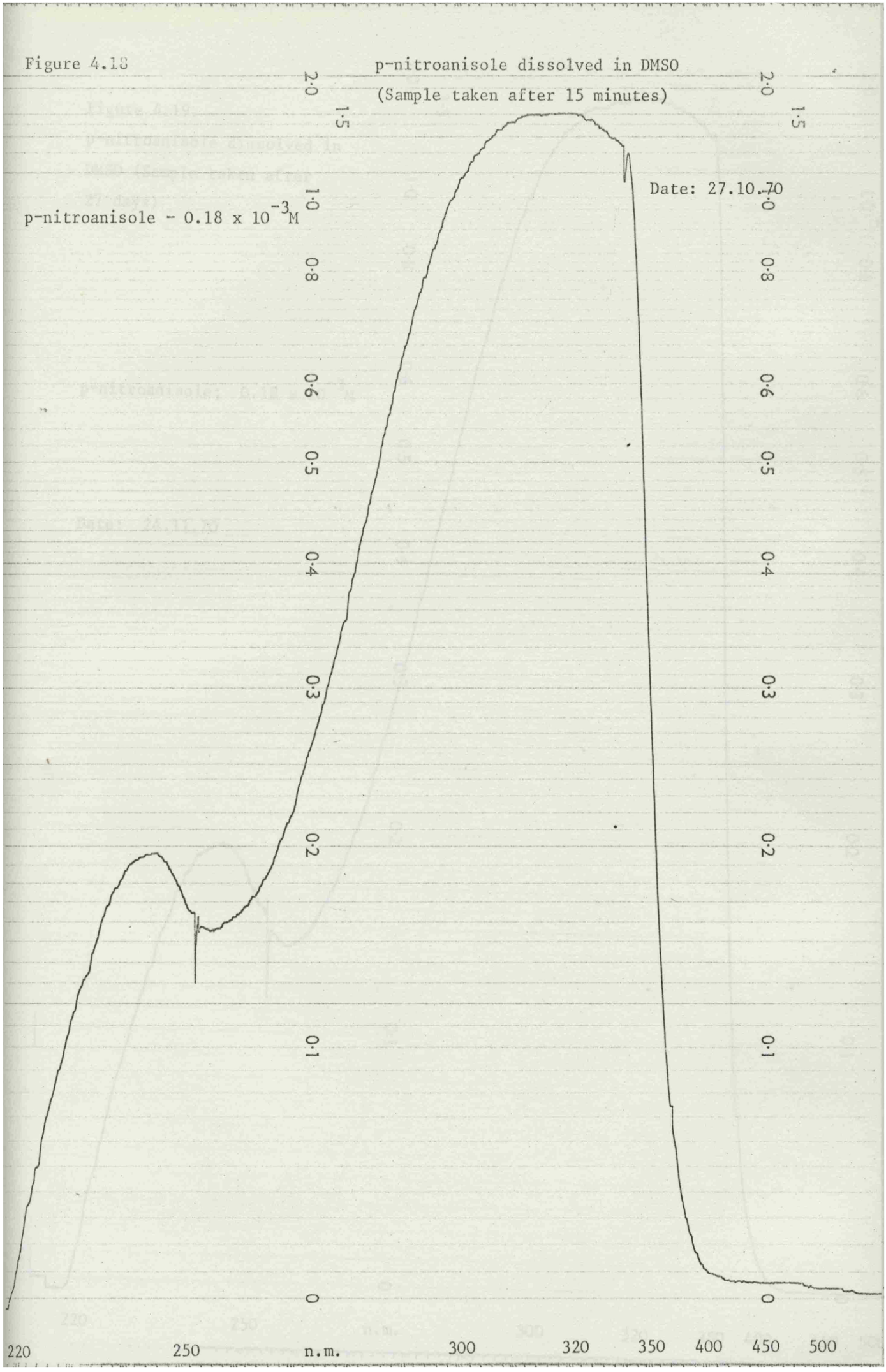


Figure 4.19.
p-nitroanisole dissolved in DMSO (Sample taken after 27 days)

p-nitroanisole; 0.18×10^{-3} M

Date: 24.11.70

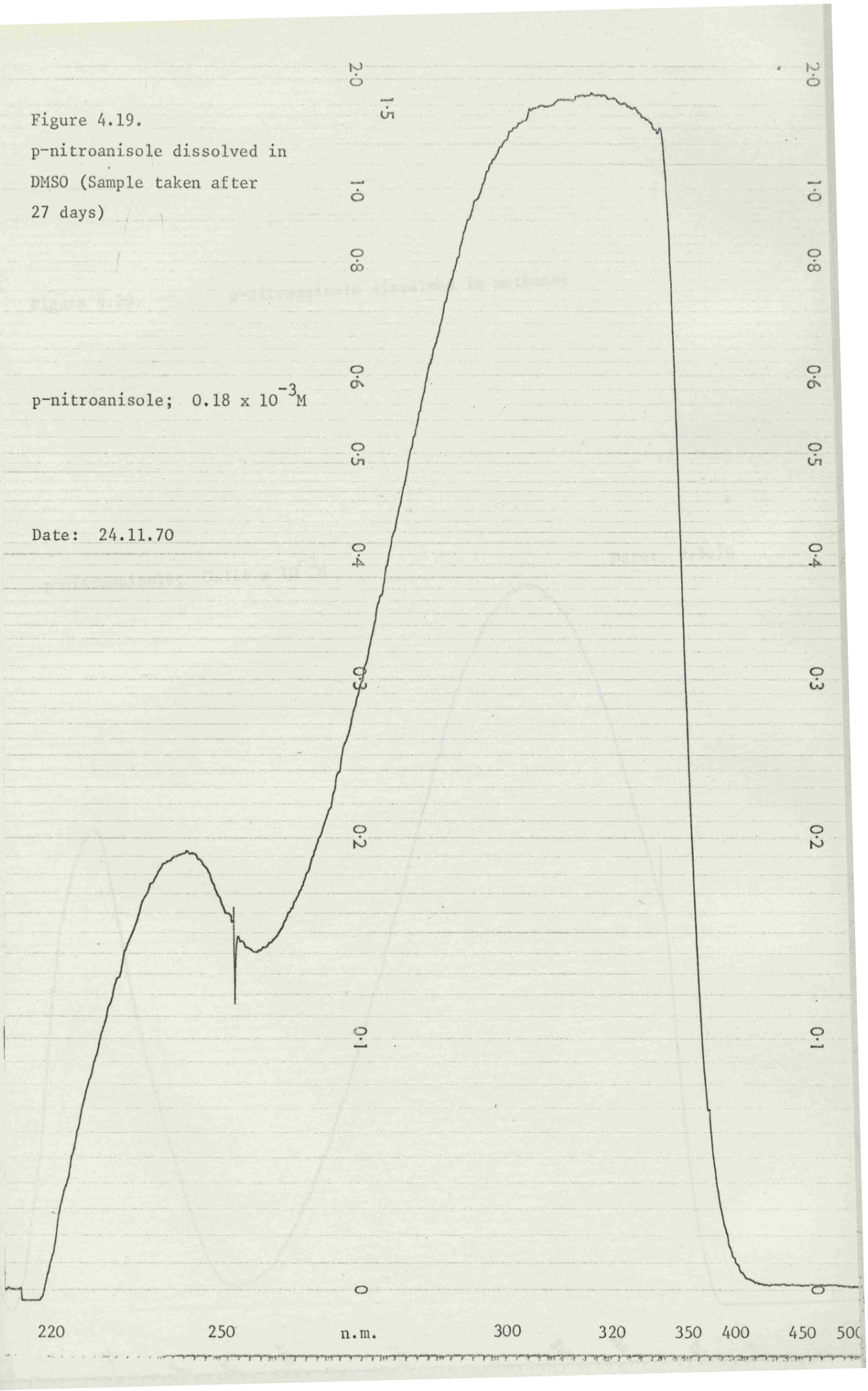


Figure 4.20. p-nitroanisole dissolved in methanol

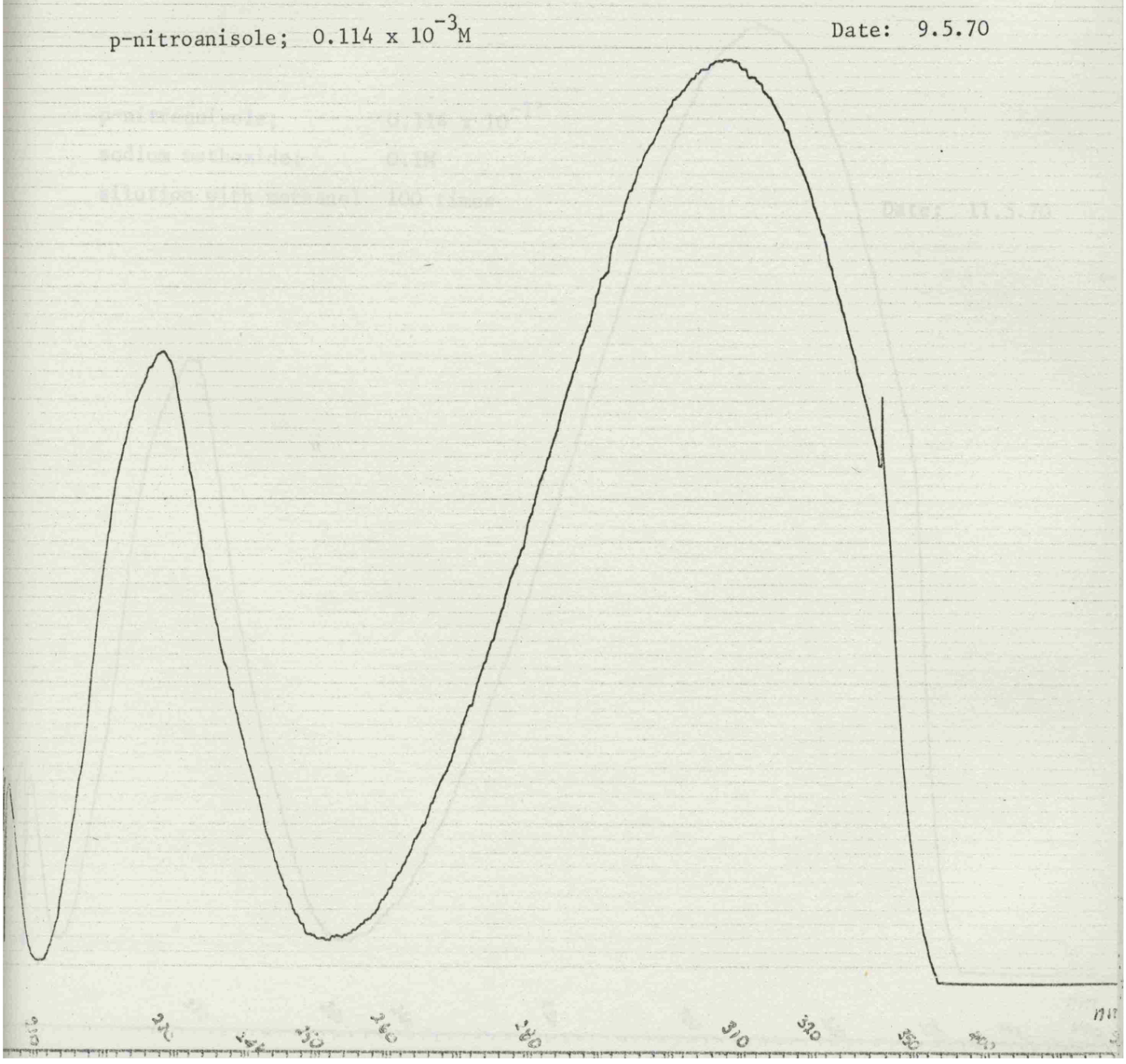


Figure 4.21 p-nitroanisole plue sodium methoxide in methanol
(Sample taken after 2 days)

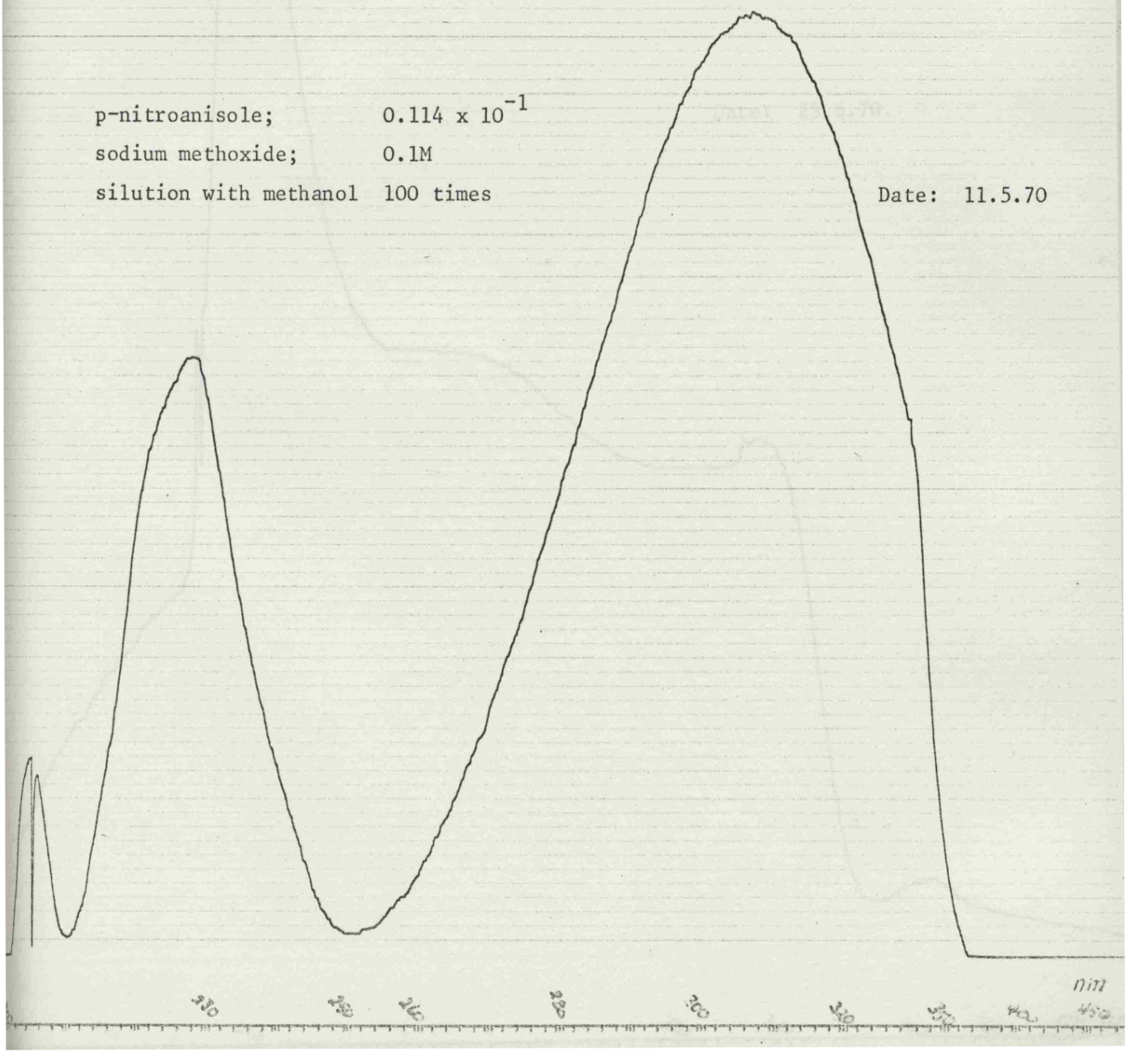


Figure 4.22 1-chloro 2,4-dinitronaphthanele dissolved in DMSO
(Sample taken 17 minutes after dissolution)

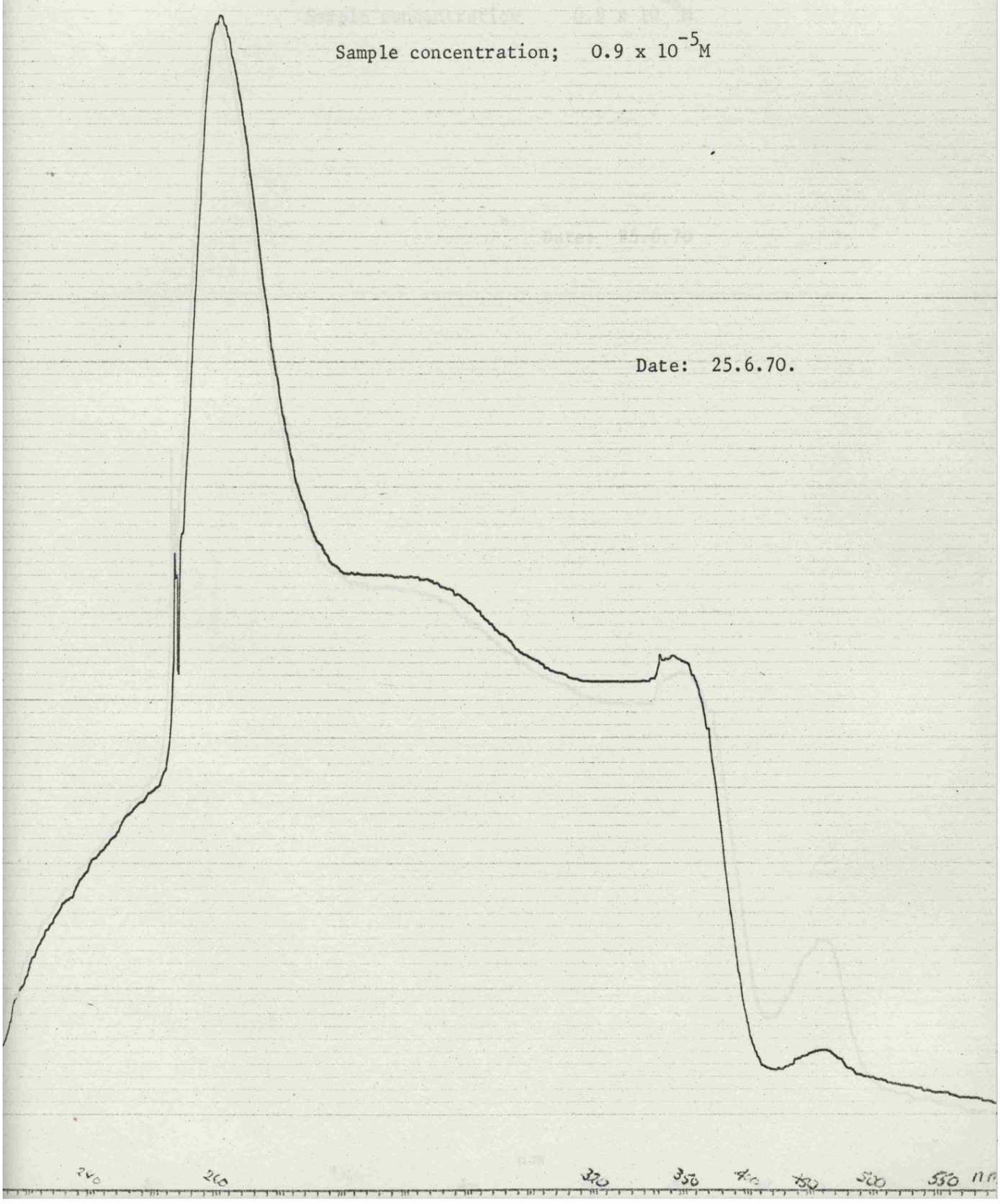


Figure 4.23 1-chloro 2,4-dinitronaphthalene dissolved in DMSO

(Sample taken 2.5 hours after dissolution)

Sample concentration 0.9×10^{-5} M

Date: 25.6.70

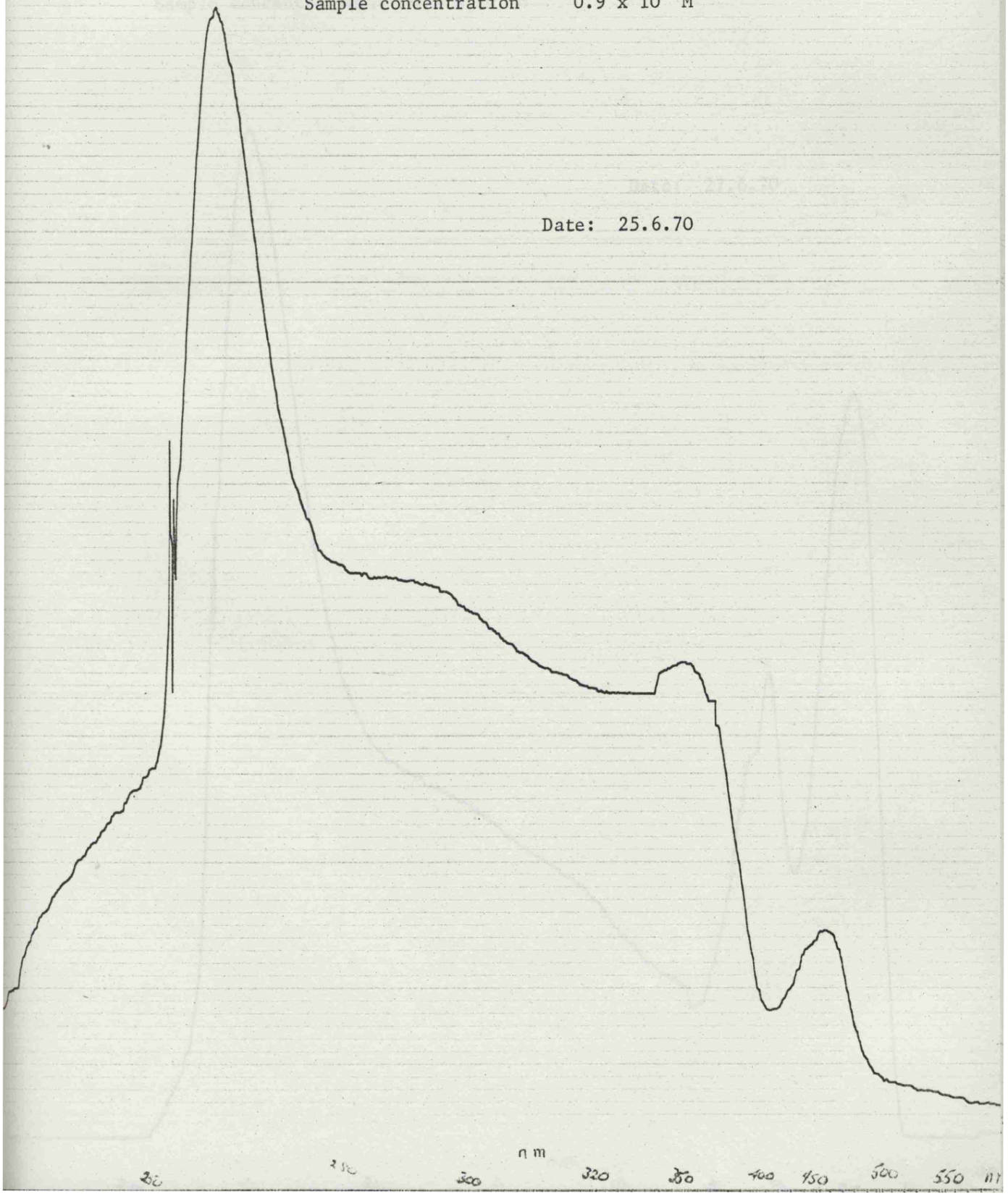


Figure 4.24 1-chloro 2,4-dinitronaphthalene dissolved in DMSO

(sample taken 45 hours after dissolution)

Sample concentration, 0.9×10^{-5} M

Date: 27.6.70

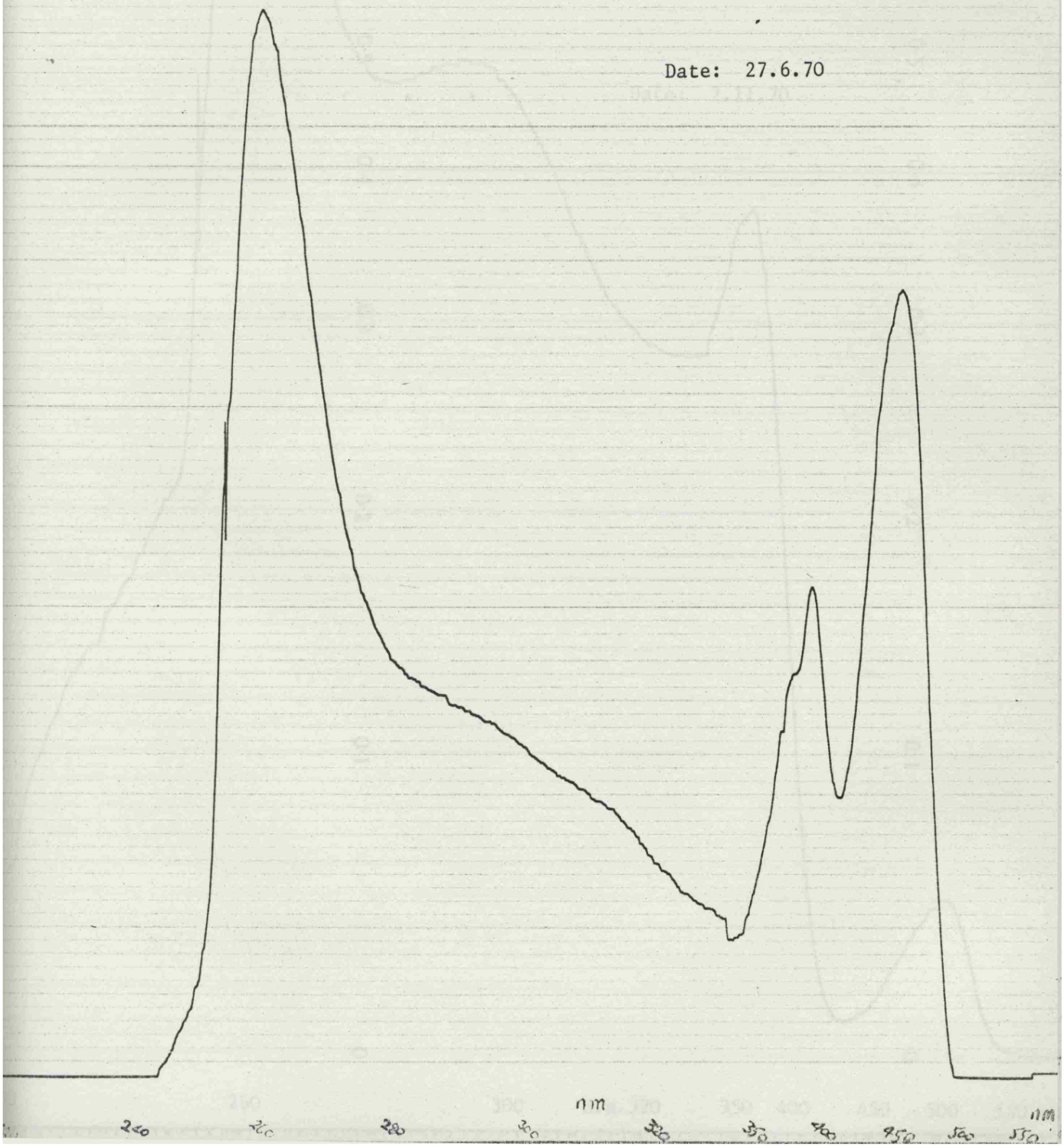


Figure: 4.25

Reaction of 1-methoxy 2,4-dinitro-naphthalene (excess) and sodium methoxide in DMSO plus 1% methanol (Sample taken after 15 minutes).

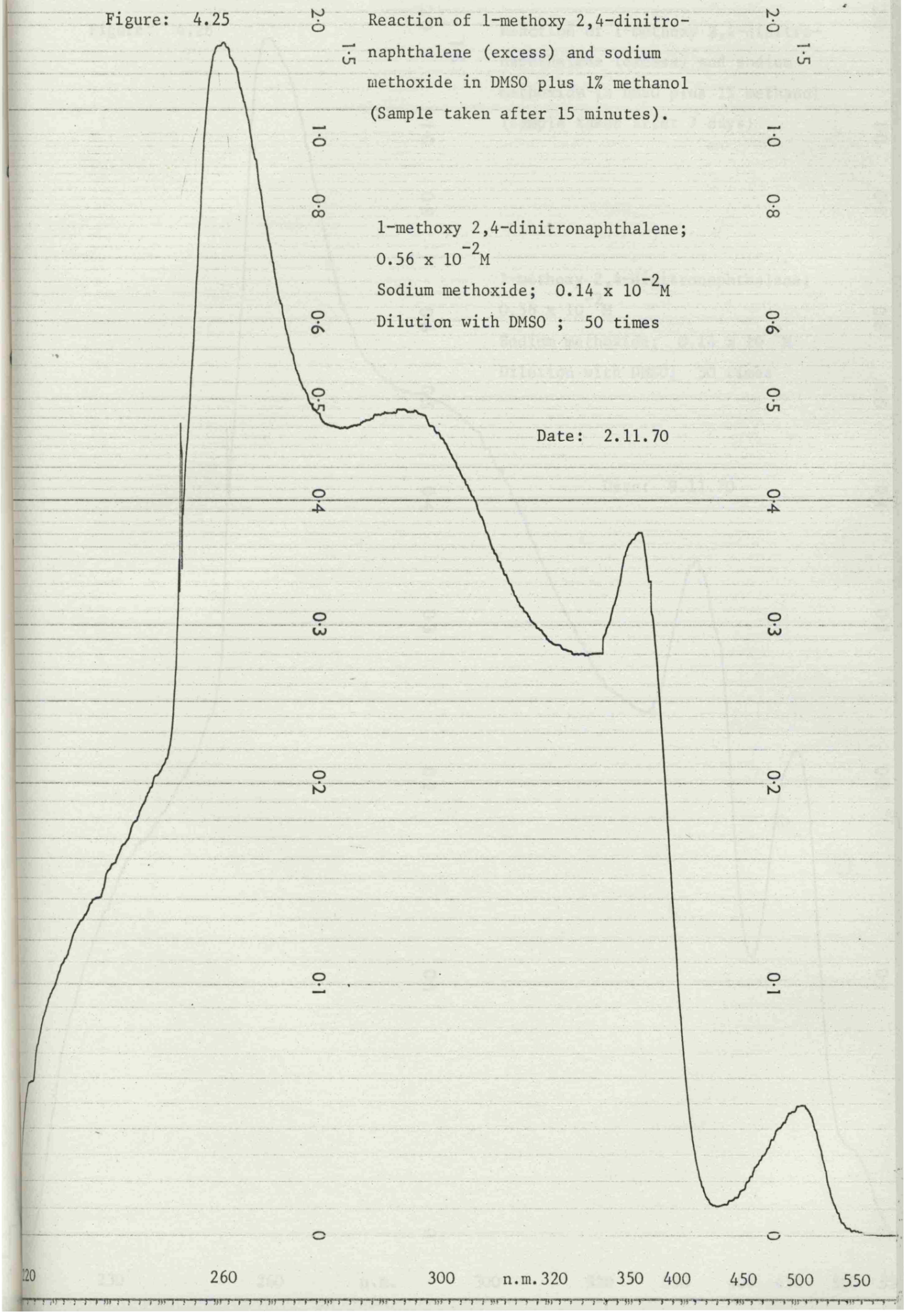


Figure: 4.26

Reaction of 1-methoxy 2,4-dinitro-naphthalene (excess) and sodium methoxide in DMSO plus 1% methanol (Sample taken after 7 days)

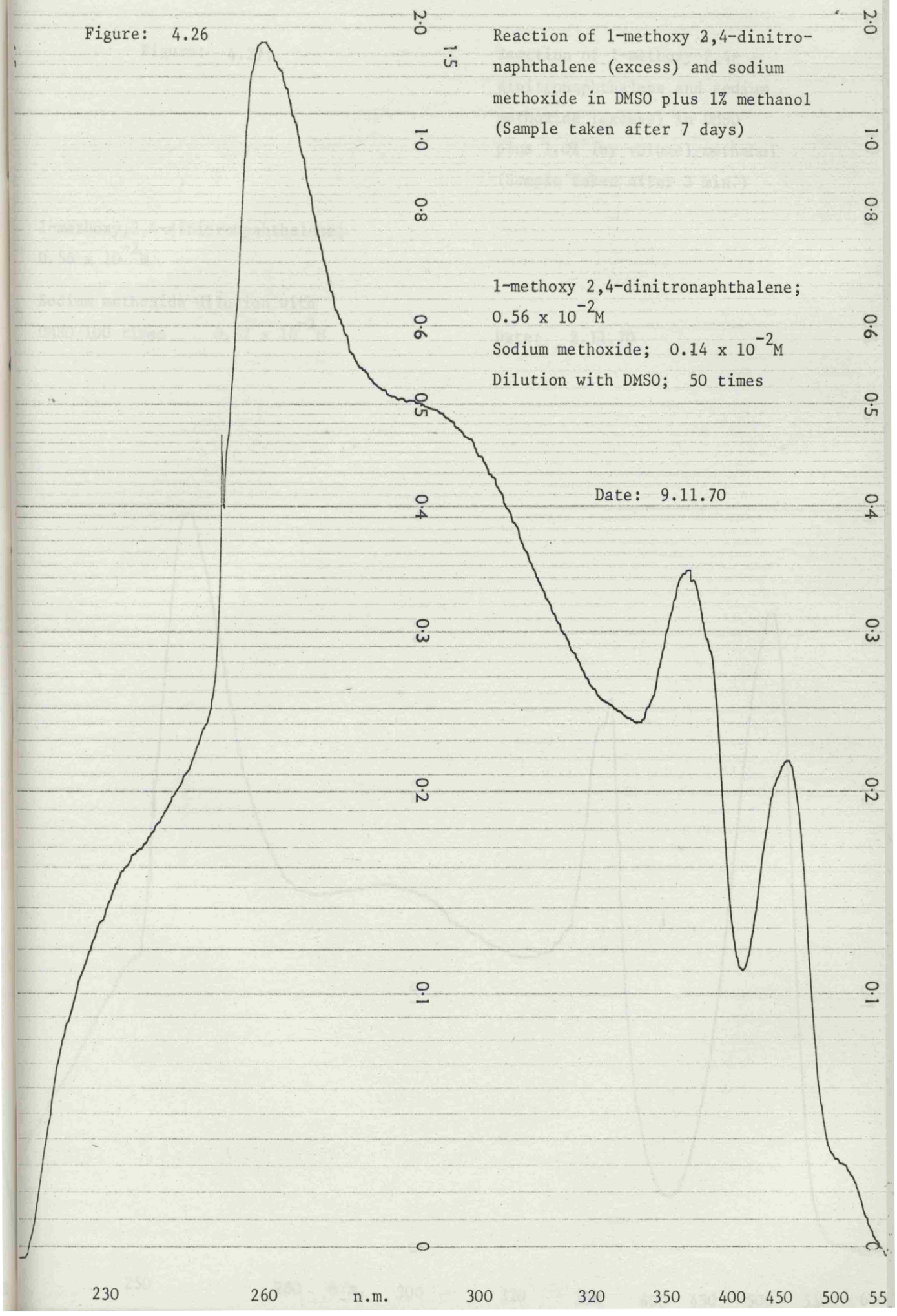


Figure: 4.27:

Reaction of 1-methoxy-2,4-dinitronaphthalene and sodium methoxide (excess) in DMSO plus 1.0% (by volume) methanol (Sample taken after 3 min.)

1-methoxy,2,4-dinitronpahthalene;
0.56×10^{-2}M

Sodium methoxide dilution with
DMSO 100 times 0.62×10^{-2}M

Date: 2.11.70

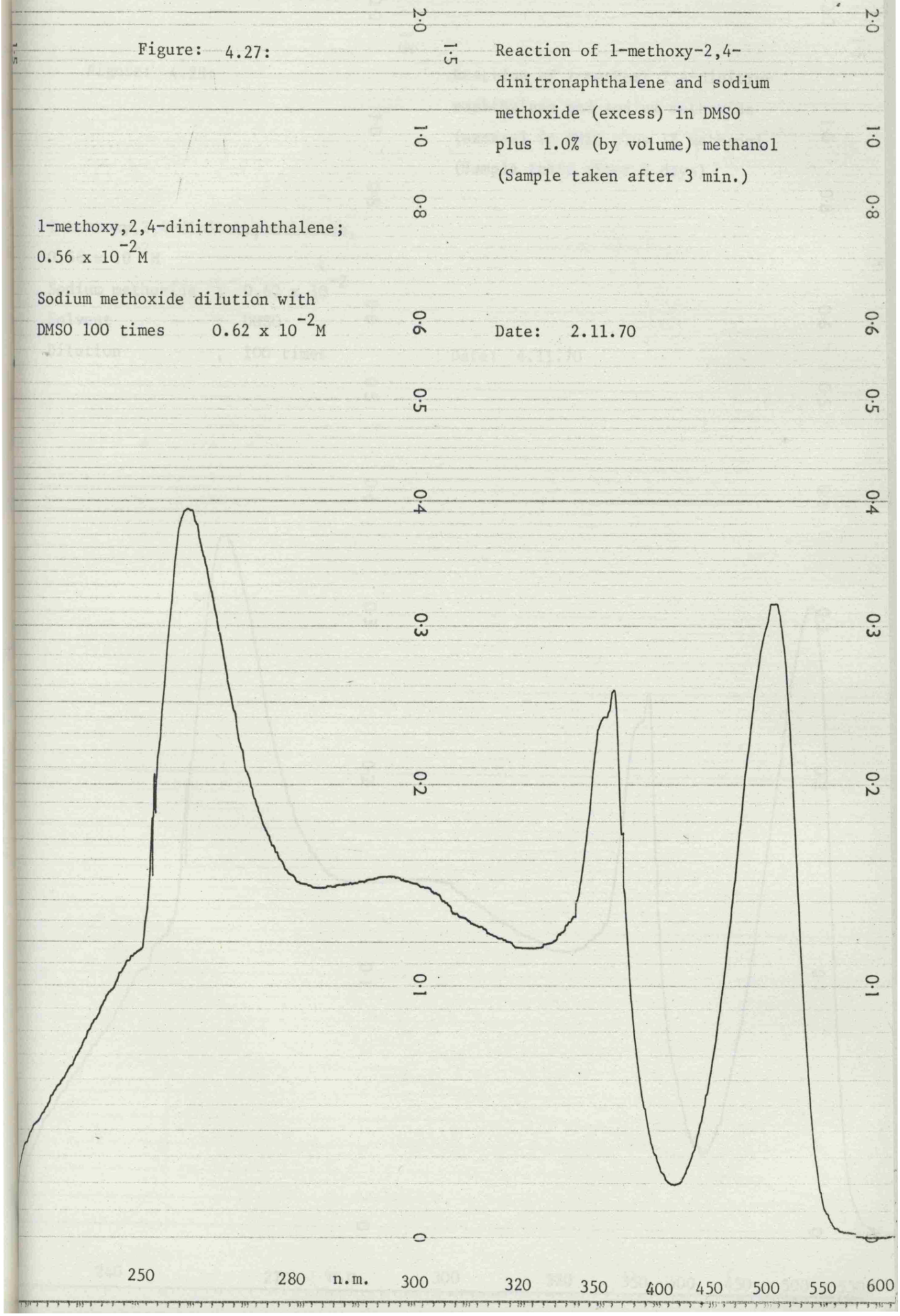


Figure: 4.28:

Reaction of 1-methoxy 2,4-dinitro-naphthalene and sodium methoxide (excess) in DMSO plus 1% methanol (Sample taken after 2 days)

1-methoxy,2,4-dinitronpahthalene, 0.56×10^{-2}M

Sodium methoxide ; 0.62×10^{-2}

Solvent ; DMSO

Dilution ; 100 times

Date: 4.11.70

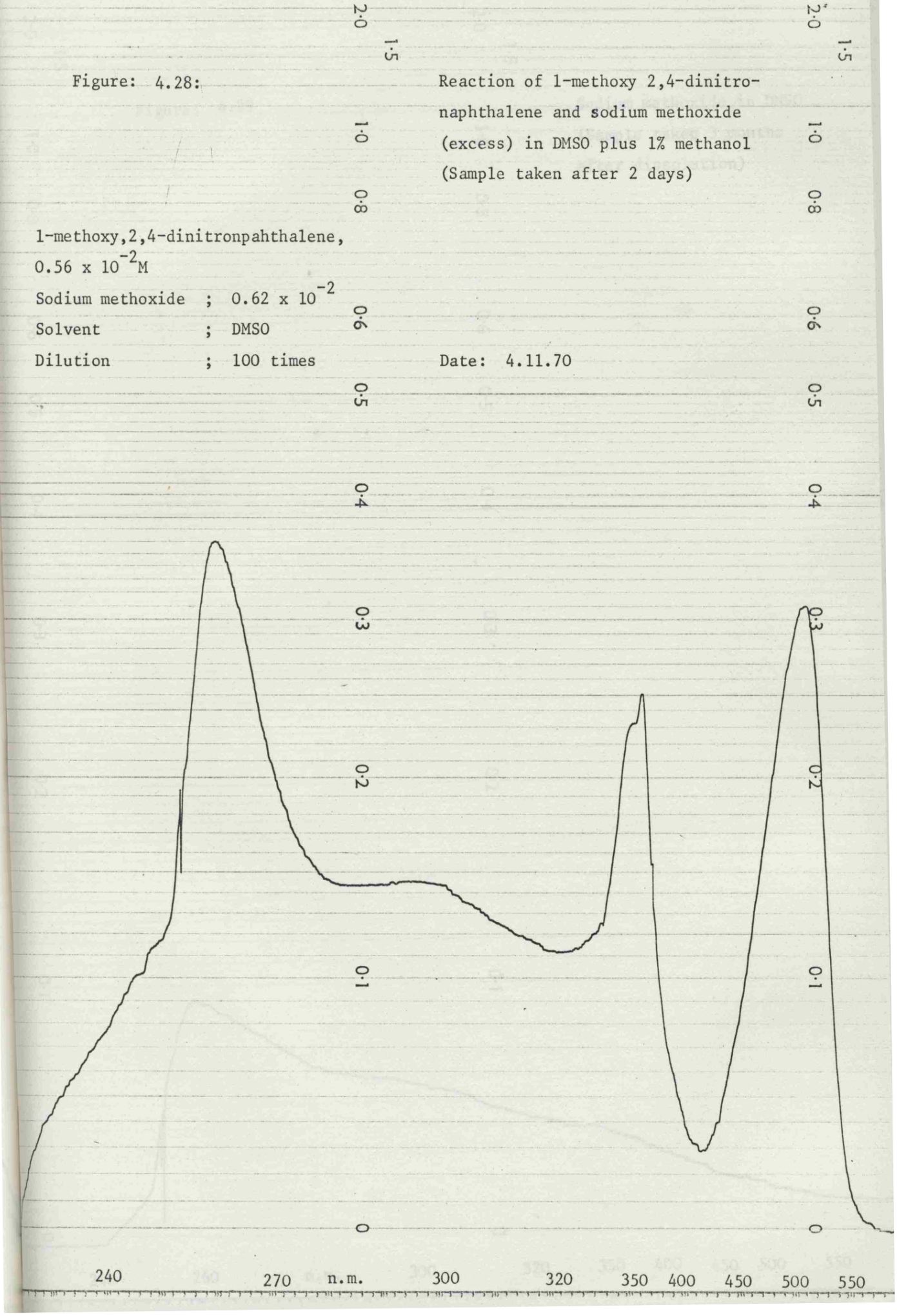
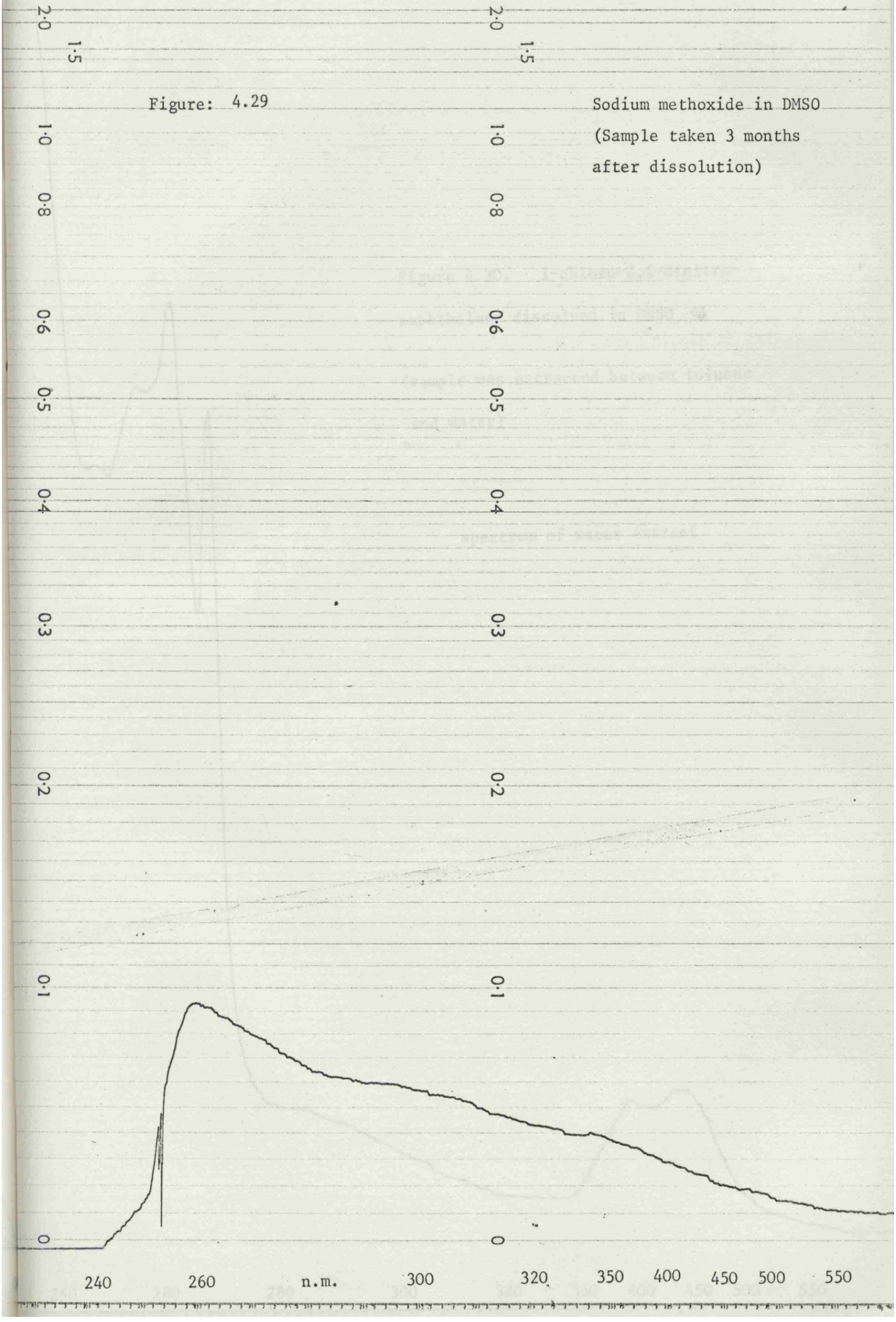


Figure: 4.29

Sodium methoxide in DMSO
(Sample taken 3 months
after dissolution)



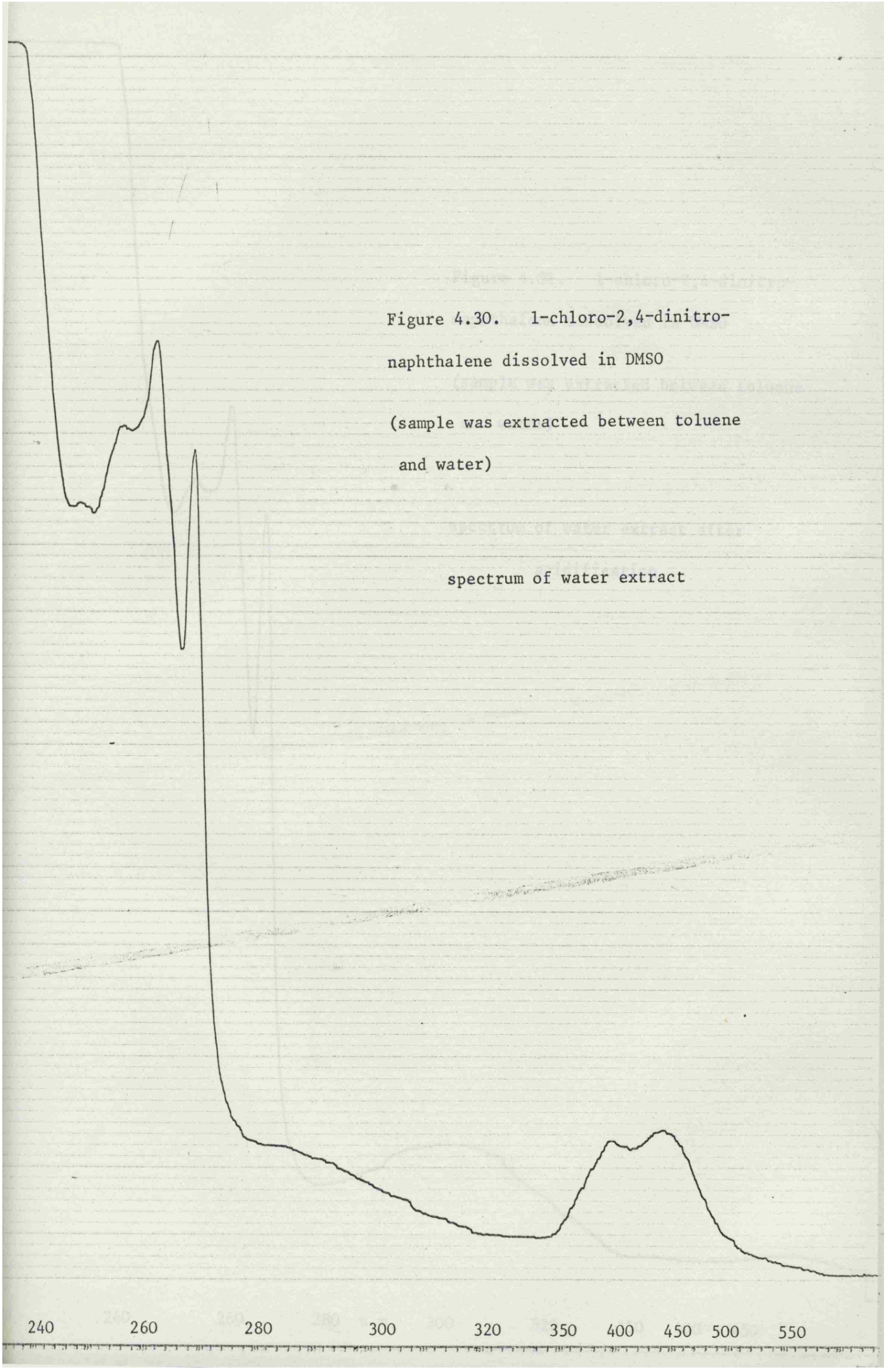


Figure 4.30. 1-chloro-2,4-dinitro-naphthalene dissolved in DMSO

(sample was extracted between toluene and water)

spectrum of water extract

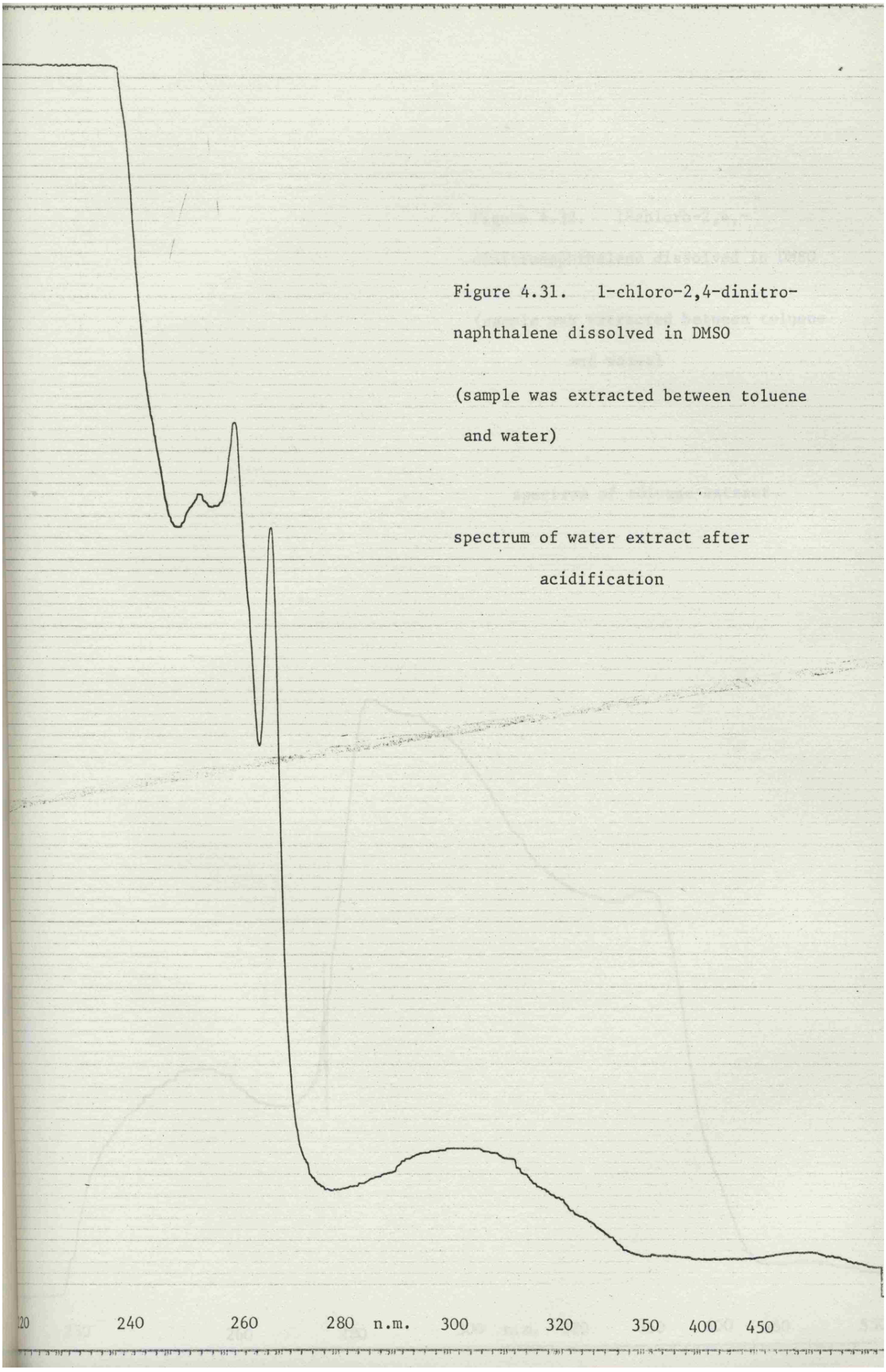


Figure 4.31. 1-chloro-2,4-dinitro-naphthalene dissolved in DMSO

(sample was extracted between toluene and water)

spectrum of water extract after acidification

Figure 4.32. 1-chloro-2,4,-dinitronaphthalene dissolved in DMSO

(sample was extracted between toluene and water)

spectrum of toluene extract

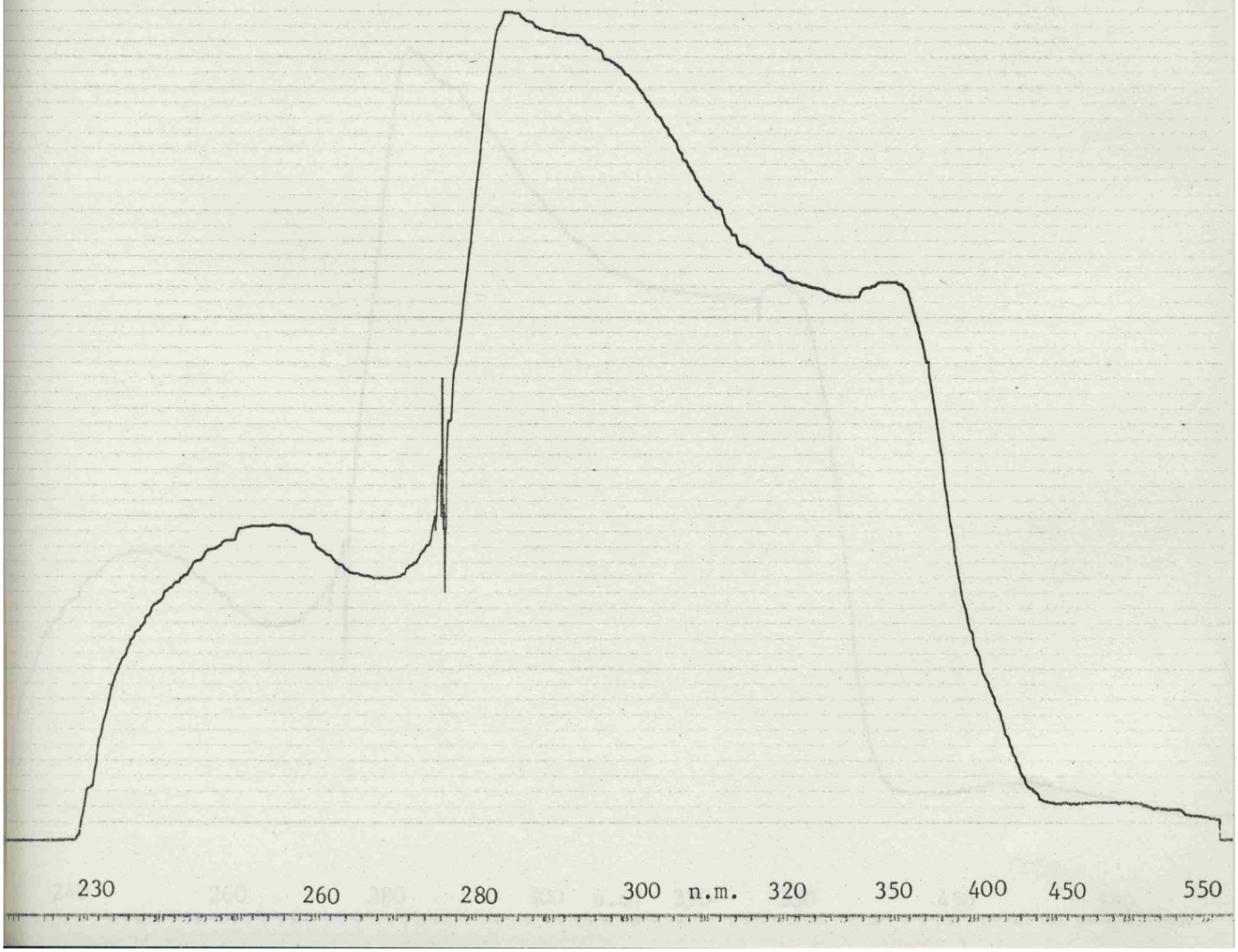


Figure 4.33. 1-chloro-2,4,-dinitronaphthalene dissolved in toluene

CHAPTER V

DISCUSSION

DISCUSSION

REACTIONS INVOLVING 1-METHOXY,2,4-DINITRONAPHTHALENE AND METHOXIDE IONS

Specific rate constants for the heterolysis process of the reaction of 1-methoxy,2,4-dinitronaphthalene in methanol and in methanol-o-d as solvent are listed in Tables (4.1), (4.2), (4.3) and (4.4). Comparison of the values at lower methoxide ion concentration with those at higher concentration Table (4.4) reveals a decrease in the specific rate constants with increasing methoxide ion concentration. This decrease of the heterolysis specific rate constant was observed by Bernasconi[19] for the reaction of 2,4-dinitroanisole and sodium methoxide in methanol as solvent and attributed to a salt effect, although ion-pairing effect was not excluded. In the present work the maximum methoxide ion concentration used was about 0.05M and ion pair formation is likely to be small[77]; the effect is probably a salt effect. The existence of such a salt effect is not surprising for several authors (e.g. Katsanos[67], Fendler[66], Gilbert[68], Bernasconi[19], etc.) have commented that such an effect is present. Bernasconi's data showed positive salt effect for the formation of the complex and negative salt effect for its decomposition. No systematic experiments were carried out in this thesis to try to ascertain the origin of the salt effects, but from the data presented (See also Figures 4.2 and 4.3) it seems that the majority of the effect is probably contained in the log A term of the Arrhenius equation. Whatever the explanation, the effect is a small one over the range of concentration studied here, and little attention was, in fact, paid to it, except that an excessively high concentration of methoxide ions was avoided in the experiments in order to minimise or, optimistically, eliminate salt effects from the experimental data.

Comparison of data obtained in methanol with those obtained in methanol-o-d at the corresponding temperatures indicates a kinetic isotope effect amounting to a ratio $\frac{k_H}{k_D}$ = 1.5 to 1.6, and a little less (about 1.4) at higher methoxide ion concentrations. Arrhenius plots were constructed for the specific rate constant of the reaction in methanol and in methanol-o-d, giving rise to approximately equal slopes and in turn to approximately equal values for the activation energy for the decomposition of the complex.

Bernasconi [19] also reported an isotope effect ratio of about $\frac{k_H}{k_D}$ ~ 1.4 for the reaction between 2,4-dinitroanisole and sodium methoxide in methanol and methanol-o-d; he used a temperature jump technique and absorptiometric measurements.

It is of value to try to determine whether this kinetic isotope effect $\frac{k_H}{k_D}$ ~ 1.5 is due to a primary or secondary (solvent) isotope effect.

A primary isotope effect is caused by the replacement, in this case, of a hydrogen atom involved in a hydrogen transfer reaction by deuterium; the effect thus produced is generally regarded as due to the difference in zero-point stretching frequency between the two isotopes. With deuterium being about twice as heavy as hydrogen this results in a lower vibrational energy level and, in turn, a slower velocity of passage, during reaction, over the potential energy barrier. The maximum value for a primary isotope effect, as pointed out by Bunton and Shiner [71] is obtained when the position of hydrogen in the transition state is mid-way between the two atoms concerned i.e. when the hydrogen is bound equally strongly to both centres.

A hydrogen/deuterium isotope effect may also be due to a secondary effect on the reaction rate, consequent upon the substitution of a deuterium atom for a hydrogen that is not being transferred in the

rate-determining step. Such a secondary isotope effect is that caused by a change of solvent from methanol to methanol-o-d. Bunton and Shiner[72] gave a method for calculation of a solvent isotope effect on the equilibrium constant as well as on the rate constant for various types of reactions in H_2O and D_2O, in terms of hydrogen bonding interaction between solvent and acidic or basic centres in the reacting systems. Their treatment is based upon.

1. The effects are due to difference of zero-point energy changes between the initial and the final state in case of the equilibrium isotope effect and between the initial and the transition state for the kinetic isotope effect.
2. All vibration changes for isotopically substituted hydrogens in the reactants, products and those of solvent molecules bonded to them must be taken into account.
3. The stretching vibration frequency of hydrogen donated to water varies linearly with PK_a of the donor and with PK_b of the acceptor for hydrogen donated from water to the oxygen atom of the acceptor.
4. The changes due to libration and bending energies were considered insignificant.

For calculation of the kinetic isotope effect the following equation was used

$$\frac{k_H}{k_D} = \text{antilog } \frac{\Sigma\nu_H - \Sigma\nu'_H}{12.53T}$$

where $\Sigma\nu_H$ and $\Sigma\nu'_H$ are the sum of hydrogen stretching (cm^{-1}) in the initial and transition states respectively and T is the absolute temperature.

These authors estimated the stretching frequencies of the hydrogens of water donated to oxygen bases in aqueous solution by using the equation

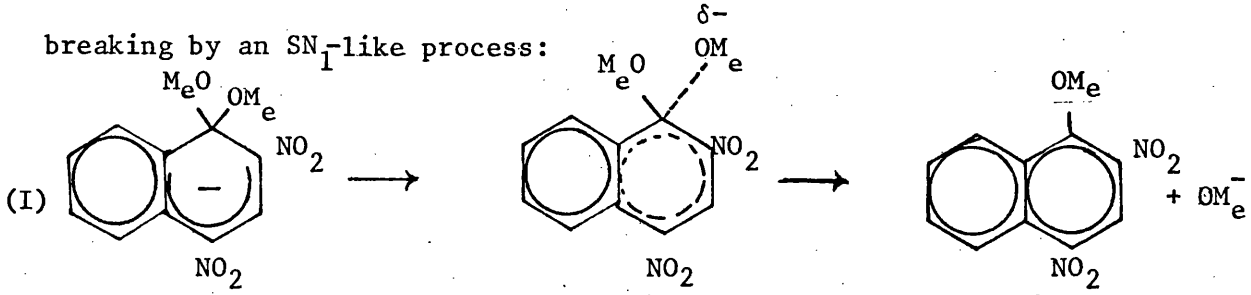
$$\nu(cm^{-1}) = 3040 + 22.9\ K_b$$

and for the hydrogen bonds donated by acids

$$\nu(cm^{-1}) = 2937 + 28.8\ PK_a$$

Bernasconi [19] pointed out that it is difficult to calculate this kinetic isotope effect for solutions in methanol and methanol-o-d by using Bunton and Shiner models, owing to lack of information about the degree of solvation of the incipient methoxy group in the transition state and the stretching frequency of the hydrogen bond involved. However, he considered his experimental value of $\frac{k_H}{k_D} \sim 1.4$ for kinetic isotope effect to lie in the range expected for a solvent isotope effect and that his value did not leave any room for an appreciable primary isotope effect.

We now have to examine the data reported in this thesis (Tables (4.1), (4.2), (4.3) and (4.4)) in the light of these discussions. Let us assume, initially, that the Meisenheimer complex formed from 1-methoxy,2,4-dinitronaphthalene and methoxide ions decomposes simply by the bond from carbon atom 1, to one of the two methoxy groups carried there, extending through a transition state, and ultimately breaking by an SN_I-like process:



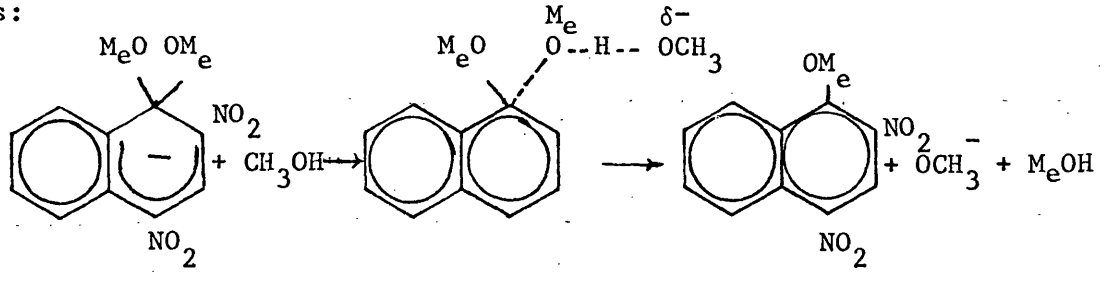
Meisenheimer complex transition state final state

As the methoxy group in the initial state becomes an incipient methoxide ion, negative charge will begin to concentrate on it, and

solvation by the methanol or methanol-o-d may be expected to increase during the formation of the transition state. Prediction of the kinetic isotope effect by using Bunton and Shiner's method is qualitative, owing to the lack of information of the degree of solvation, but a value of the ratio $^{k}H/_{k_D}$ somewhat greater than unity may be expected. This prediction is in line with the experimental value of about 1.5.

It is reasonable to assume on this mechanism that an important role of the methanol or the methanol-o-d is to solvate the incipient methoxide ion in the transition state rather than to function as an acid catalyst to provide a proton which would enable a methoxy group to split off as a molecule of methanol which may be portrayed as follows:

(II)



initial state transition state final state

In this mechanism (II) a primary isotope effect may be expected if the proton is in the process of being transferred by the time the transition state is reached. However, caution is necessary here, for it may possibly be that the proton has hardly begun to transfer, or, is almost completely transferred in the transition state, in which case only a small primary isotope effect would be expected.

Unfortunately, then, the observed kinetic isotope effect ratio of 1.5 is not completely diagnostic but there appears, as Bernasconi concluded, to be very little room for an appreciable primary isotope effect.

When the reaction between 1-methoxy,2,4-dinitronaphthalene was carried in DMSO solution, in the absence or presence of methanol

(Tables 4.7 to 4.11) an immediate purple colour was observed which changed within less than a minute to a brownish-red colour, the speed of change from purple to brownish-red increased as the concentration of sodium methoxide increased. This is probably due to initial complex formation with methoxide ion at carbon atom 3 followed rapidly by migration of the methoxy group to carbon atom 1, as suggested by Servis [37] and Crampton and Gold [73] from their N.M.R. studies.

It is worthwhile commenting that the presence of methanol is not necessary for the formation of the Meisenheimer complex (Table 4.7) and also that carbon-14 presumably as methoxy group, is lost from the original ether both in the presence or absence of methoxide ion, (Tables (4.7) and (4.8)). The explanation of the data seems to be that Meisenheimer complex forms rapidly, in the presence of methoxide ion, and subsequent loss of carbon-14 from the ether is due to a nucleophilic attack by the solvent DMSO. Comparison of Table (4.7) and (4.8) shows that the loss of carbon-14 is more rapid in the presence of sodium methoxide than in its absence; perhaps this indicates a base catalysis on whatever reaction is proceeding. When the data embodied in Table (4.8) was being obtained, the formation of colour was still observed even in the absence of methoxide ion (see also Figures (4.11), (4.12) and (4.13) which are absorption spectra of 1-methoxy,2,4-dinitronaphthalene dissolved in DMSO after various elapsed times) and it is reasonable to assume that a Meisenheimer type of complex was still being formed as a preliminary step in the loss of carbon-14. If base-catalysis is present, it may be at the formation stage of this supposed Meisenheimer type of complex.

In the presence of excess methoxide ion (methanol was also present to enable sufficient concentration of methoxide ion to be achieved) the data of Tables (4.9) and (4.10) indicate that all the ether is rapidly converted to Meisenheimer complex, but subsequently no carbon-14 is lost from the complex in several days. Thus, the Meisenheimer complex does not exchange its carbon-14 labelled methoxy group with methoxide ions and nor is the DMSO able to remove carbon-14 from the complex.

The presence of excess ether rather than methoxide ions (Table 4.11) in the presence of methanol gives a similar picture to that in the absence of methanol already commented upon. The corresponding absorption spectra also indicate the contrast between an excess and deficiency of methoxide ions; with excess methoxide ions the spectra (Figures 4.27 and 4.28) indicate little change throughout two days, but with excess ether (Figures (4.25) and (4.26)) the initial Meisenheimer formation peak (510 n.m.) of Figure (4.25) is swamped by the one forming at slightly lower wavelength (450 nm) in Figure (4.26), corresponding to the peak developed in Figure (4.12) and (4.13) with DMSO and 1-methoxy,2,4-dinitronaphthalene.

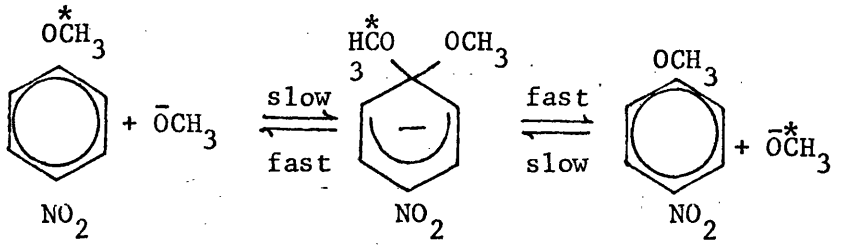
Thus, there seems little room to doubt that a stable "non-decomposing" Meisenheimer complex is formed rapidly between sodium methoxide and 1-methoxy,2,4-dinitronaphthalene in DMSO solution, in the presence or absence of a small amount of methanol. However DMSO, again in the presence or absence of small amount of methanol is able to remove carbon-14 from the labelled ether, via the formation and, presumably, subsequent decomposition of a Meisenheimer type complex.

REACTIONS INVOLVING P-NITROANISOLE AND METHOXIDE IONS

p-nitroanisole and methoxide ions do not form an appreciable concentration of Meisenheimer complex in methanol solution, this is evident from the kinetic studies of Fendler[11] which showed no methoxy exchange at refluxing temperature, and also by comparing the absorption spectra of Figures (4.20) and (4.21). The situation in DMSO solution containing 0.3%, by volume, methanol is different, however, and clear evidence of a small but appreciable concentration of Meisenheimer complex is shown by comparing Figures (4.18) and (4.16); the peak due to the complex appears at 440 nm in the latter figure.

In contrast to the behaviour of 1-methoxy,2,4-dinitronaphthanele, a solution of p-nitroanisole in DMSO is stable and shows no sign of Meisenheimer complex formation or of change in absorption spectrum over nearly a month (Figures (4.18) and (4.19)). This is confirmed also by the fact that at 20°C p-nitroanisole, with its methoxy group labelled with carbon-14, showed no sign of loss of radioactive atom over more than a week in DMSO solution. Thus p-nitroanisole possess sufficient activation to allow Meisenheimer complex formation with methoxide ions in DMSO solution, but not sufficient to allow appreciable attack by DMSO itself in the absence of methoxide ions.

The kinetic plot for the reaction between p-nitroanisole and methoxide ions in DMSO containing 0.3% methanol or methanol-o-d, by volume, (Figure (4.6)) shows that the concentration of complex is small (otherwise S_i and S_o would have diverged appreciably in agreement with the absorption spectrum shown in Figure (4.16), but there is little room for doubt that the mechanism is:

(III) 

i.e. the rate-determining step is the formation and not decomposition of the Meisenheimer complex. Table (4.12) shows that methanol and methanol-o-d behave similarly, and provides no evidence of any kinetic isotope effect.

Determination of order of reaction (page 56) leads to the conclusion that the reaction is of approximately first order in p-nitroanisole but second order in methoxide ions. Clearly, then, mechanism (III) is an over-simplification. A possible speculation may be as follows:

Let the reaction be represented in stages, thus:

$$ROCH_3 + OCH_3^- \underset{k_2}{\overset{k_1}{\rightleftharpoons}} R(OCH_3)_2^- \qquad (1)$$

The complex $R(OCH_3)_2^-$ needs not be a Meisenheimer complex; perhaps the two methoxy groups are not yet equivalent or on the same carbon atom. There is good evidence (page 67), for example, that the Meisenheimer complex of 1-methoxy,2,4-dinitronaphthalene with methoxide ion in DMSO is formed in more than one stage. This is followed by:

$$R(OCH_3)_2^- + OCH_3^- \xrightarrow{k_3} \text{MH complex} + OCH_3^- \qquad (2)$$

i.e. we are assuming that the transition of $R(OCH_3)_2^-$ to the Meisenheimer complex is catalysed by the methoxide ion. If $R(OCH_3)_2^-$ is a short-lived species, we can apply the steady-state condition that its concentration rapidly becomes constant, i.e. that its rate of formation and decomposition become equal.

Thus,

$$k_1\left[ROCH_3\right]\left[OCH_3^-\right] = k_2\left[R(OCH_3)_2^-\right] + k_3\left[R(OCH_3)_2^-\right]\left[OCH_3^-\right]$$

and $$\left[R(OCH_3)_2^-\right] = \frac{k_1\left[ROCH_3\right]\left[OCH_3^-\right]}{k_2 + k_3\left[OCH_3^-\right]}$$

Rate of formation MH complex $= k_3\left[R(OCH_3)_2^-\right]\left[OCH_3^-\right]$

$$= \frac{k_3k_1\left[ROCH_3\right]\left[OCH_3^-\right]^2}{k_2/k_3 + \left[OCH_3^-\right]}$$

If k_2 is sufficiently greater than k_3, then we get third order kinetics

i.e. Rate = $k_1/k_2\left[ROCH_3\right]\left[OCH_3^-\right]^2$

If k_2 is sufficiently smaller than k_3, then we get second order kinetics

i.e. Rate = $k_1\left[ROCH_3\right]\left[OCH_3^-\right]$

Evidently, if these speculations are correct, most of $R(OCH_3)_2^-$ decomposes to form the original reactants, and little of it becomes a normal Meisenheimer complex.

If k_2 is neither excessively large nor small compared with k_3 then the kinetic expected would be of the type

Rate = $k\left[ROCH_3\right]\left[OCH_3^-\right]^x$

where x is between 1 and 2.

Unfortunately p-nitroanisole and methoxide ions do not react in methanol but it is interesting to note that Katsanos[74] and Gilbert[75] report order of appreciably greater than 1 in methoxide ions for the reactions of 1-methoxy 2-nitronaphthalene and methoxide ions, and 1-methoxy 4-nitronaphthalene and methoxide ions, respectively, in methanol, although their values do not approach 2. Fendler[76] finds that the reaction between 1-methoxy 2,4-dinitroanisole and methoxide ions to be first order in each reagent.

It is of interest to speculate a little further as to why DMSO seems to encourage decomposition of $R(OCH_3)_2^-$ by the k_2 route in stage (1), or alternatively to discourage stage (2), whereas methanol seems to act the other way round in the experiments of the Katsanos, of Gilbert and of Fendler. It may be that the intimate relationship between methoxide ion and methanol enables stage (2) to proceed more readily, as rapid proton movements permit equally rapid movement of methoxide ion, and give the methoxide ion a rather larger effective volume than it otherwise has. The methoxide ion in DMSO has no such advantage, perhaps the amount of added methanol being much too small to reproduce locally the conditions in methanol as solvent.

The general conclusion, based on these speculations, seems to be that the formation of a Meisenheimer complex requires base catalysis rather than the intercession of hydrogen or protons.

REACTIONS OF 1-CHLORO,2,4-DINITRONAPHTHALENE WITH CHLORIDE IONS IN DMSO

Comparatively few kinetic data were obtained here, these are presented in Table (4.14). The obvious point of interest is that the addition of a small amount of water or even concentrated perchloric acid had no appreciable effect on the overall reaction rate. It is difficult to conclude, therefore, that the reaction observed whatever its mechanism, is catalysed or inhibited by the presence of hydrogen atoms or protons.

A complication in the study of the chlorine exchange reaction is that an alternative reaction in which DMSO succeeds in replacing chlorine from 1-chloro,2,4-dinitronaphthalene also occurs. This is evident from Table (4.18) and laso from the observation that the Cl-36 labelled chlorine initially present as chloride ions comes to isotopic equilibrium after a little more than 10 hours, whereas "the count rate" for successive reaction samples increases to the expected

"infinity" value at this time and then decreases slowly during the next few days. Furthermore an 0.08M solution of 1-chloro,2,4-dinitronaphthalene in DMSO initially gave a negative reaction for chloride ions after separating between toluene and water, acidifying the aqueous layer and adding silver nitrate solution , however repetition of the procedure at varying times intervals showed slight but significant precipitate of silver chloride after about two hours, which had increased appreciably over two days. The experiment was carried out at room temperature. Clearly chlorine is being expelled as chloride ions by the DMSO.

The absorption spectra of Figure (4.22), (4.23) and (4.24) seem to indicate that the expulsion of chlorine takes place via the usual type of complex. It is safe to conclude that this complex contains chlorine as when the solution is extracted with toluene and water, a yellow aqueous layer is produced (presumably because the complex is, as expected, soluble in water) which does not precipitate silver chloride from silver nitrate solution unless a little nitric acid is added. Silver chloride precipitation is preceded by immediate loss of colour. The absorption spectrum of the aqueous layer before acidification is shown in Figure (4.30) and acidification removes the peaks at 400-450 nm (Figure 4.31). For comparison the absorption spectrum of the toluene extract is shown in Figure (4.32) and the absence of complex is apparent, as is the absence of the 1-chloro,2,4-dinitronaphthalene in the spectra of the aqueous extract.

The isotopic chlorine exchange with chloride ions is considerably faster than the solvolytic expulsion of chlorine and the early points in kinetic plots were linear. The rates listed in Table (4.14) evaluated from the slopes of these linear portions.

A determination of order showed that the reaction was of first order with respect to 1-chloro,2,4-dinitronaphthalene, but about 0.7 with respect to chloride ion (see Figures (4.8) and (4.9)).

CONCLUDING REMARKS

The original object of the research was to try to establish whether or not a primary hydrogen/deuterium isotope effect was present in these various aromatic nucleophilic substitution reactions involving the formation and subsequent decomposition of a Meisenheimer complex. In no case has conclusive evidence for such an isotope effect been found; rather the evidence has indicated that a primary isotope effect is probably absent. This is true whether the rate-determining step of the reaction under study was the formation or decomposition of the Meisenheimer complex.

DMSO has certainly enhanced the nucleophilic reactions of the methoxide ion, and chloride ion, and has enabled a kinetic study (although brief in the case of the chlorine exchange) to be made on systems which had failed to react in methanol as solvent.

Taking together all of the data presented in this thesis, it is probably resonable although not conclusive, to suggest that proton intercession in the decomposition of a Meisenheimer complex is less important than solvation of the incipient methoxide ion in the transition state, and in the formation of a Meisenheimer complex is less important than is base catalysis.

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