NUCLEAR MAGNETIC RESONANCE STUDY OF HINDERED ROTATION IN 3-ARYL SUBSTITUTED HYDANTOINS

Alessandro Granata

A THESIS

in

The Department

of

Chemistry

Presented in Partial Fulfillment of the Requirements for
the Degree of Master of Science at
Sir George Williams University
Montreal, Canada

August, 1972

ACKNOWLEDGEMENTS

The author appreciates and gratefully acknowledges the aid and the advice of the following, who helped in making this thesis possible.

Dr. L. D. Colebrook, for his advice during his direction of this research project.

Dr. T. J. Adley and Mr. J. Lenoir, Sir George Williams University, for their helpful discussions.

He also acknowledges the help of Ms. Kathryn Bennett in correcting the English of this thesis.

ABSTRACT

The subject of this work is a study of hindered rotation in some 3-aryl substituted hydantoins by nuclear magnetic resonance (NMR) total line shape analysis. The compounds were prepared from suitable aromatic isocyanates by condensation with amino acids. In these compounds the C-5 substituents and in certain cases the ortho-substituent protons are magnetically non-equivalent and show a chemical shift difference, except when there is rapid rotation about the aryl C-N bond. This magnetic non-equivalence disappears on heating.

The kinetic and thermodynamic parameters for rotation of the aryl group have been evaluated through complete line-shape analysis of the temperature dependent spectra by using a non-linear regression method. Evidence has been found that aryl group substituents exhibit small electronic effects on the activation parameters for rotation. The influence of a buttressing substituent on the activation parameters has been investigated, as well as the influence of substituents in the C-5 position.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

During the last twenty years, high resolution nuclear magnetic resonance has become one of the most important techniques for studying rate processes, especially those which occur in systems that are in thermodynamic equilibrium. When these processes have rate constants of the same order of magnitude as the total linewidth (in cycles per second) of the NMR spectra of a magnetic nucleus (roughly 10^{-1}- 10^{-5} sec^{-1}), they may give rise to significant changes in the shape of NMR signals. Indeed,".. if the average lifetimes of a number of species in equilibrium exceed an upper limit, the NMR spectrum will show them as individual entities. Conversely, if the lifetimes are short with respect to the NMR scale, one will obtain a single spectrum. The phenomena that can be observed during the transition from one extreme to the other, and their interpretation, are the realm of the method called DYNAMIC NUCLEAR MAGNETIC RESONANCE".[1]

DNMR has been used to measure kinetic parameters in many types of chemical and physical processes. This technique may be applied to processes with activation energies extending from 20-25 kcal per mole down to 5-6 kcal per mole.[1] Such rate processes as proton

transfer, and rotation around sterically crowded single bonds or partial double bonds have activation energies falling within this range.

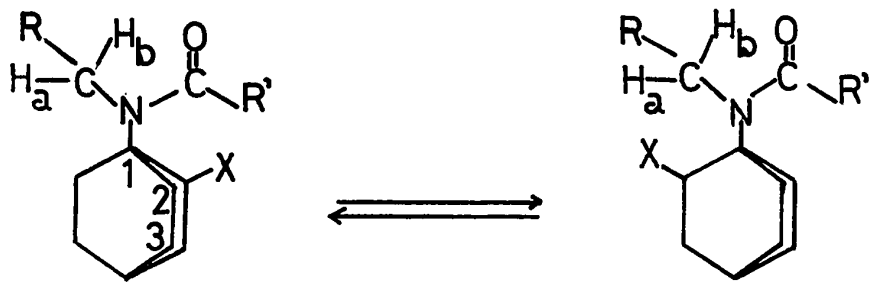
Restricted Aryl Group Rotation in Amides:

Until recently the only data available on hindered rotation of aryl groups in amides were concerned solely with acyclic amides.

Siddall and Prohaska,[2] and later Mislow et al.,[3] and Sutherland et al.,[4] studied the NMR spectra of some N-benzyl-N-(o-tolyl) amides. The spectrum of the benzylic methylenic protons of these compounds shows an AB quartet at sufficiently low temperatures. The appearance of this quartet was originally attributed to slow inversion of the nitrogen atom,[2] since the benzylic methylenic protons must be diastereotopic if the configuration at nitrogen is pyramidal. Mislow,[3] on the other hand, suggested that hindered rotation about the aryl-nitrogen bond is a plausible explanation of the observed non-equivalence. This hypothesis is reasonable in view of the fact that the barrier to nitrogen inversion in formamide is only about 1 kcal per mole while the activation energy obtained from the collapse of the AB quartet in the case of such amide is about 20 kcal per mole.

This explanation is now generally accepted.

The origin of the magnetic non-equivalence of the methylene protons and the temperature dependence of their spectra based on the slow rotation model may be seen from the following figures, which represent an approximation to the ground state configurations.



A B

Interconversion of the enantiomeric isomers, A and B, interchanges the environments of the methylene protons and affects the spectrum arising from these protons if the rate of interconversion is sufficiently rapid. If R is a group which does not undergo spin-spin interaction with the methylene group, these protons give rise to an AB quartet at low rates of interconversion. When the rate of interconversion is fast on the NMR time scale, the quartet collapses to a singlet through time averaging of the environments of the methylene protons.

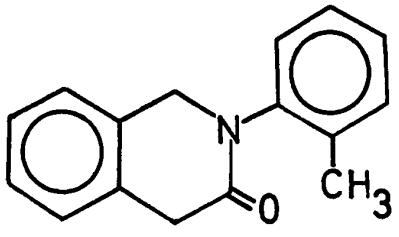
Hund[5] and Huang[6] later reached the following conclusion following a more extensive study of the same type of compounds:

a) The exchange process which results in the AB quartet of the benzylic methylenic protons being temperature dependent is not simply rotation around the C-N bond, but involves a competing process in which amide isomerization occurs.

b) A small electronic effect due to the substituent on the aryl ring is observable. This appears to act on the barrier of rotation of the C-N bond of the amide group and affects the process of rotation about the aryl C-N bond only indirectly.

c) A buttressing effect between a group on the 3 position and a 2-methyl substituent is observable.

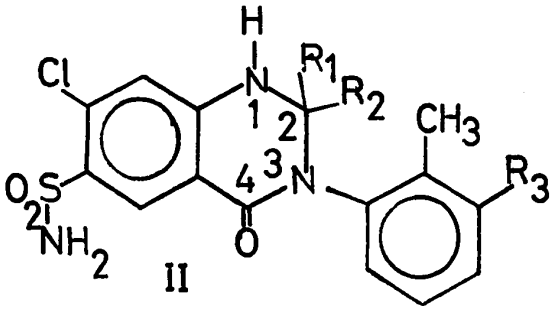
Since the interpretation of rotation around the aryl C-N bond should be more straightforward in the case of N-aryl cyclic amides, in which the complication of amide isomerization is absent, it is surprising that until recently the only work reported on these systems was that of Mislow et al.,[3] on compound (I).



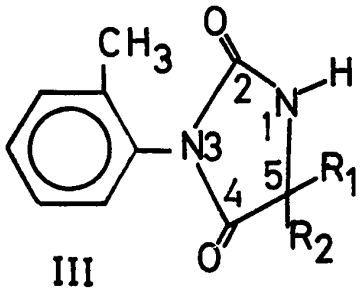
I

These workers measured a $\Delta G^{\ddagger}$ of 17.3 kcal per mole at 73° for this compound. They used the coalescence point method which, although not as reliable as the complete shape line analysis method, is nevertheless qualitatively valid.

In the hope of obtaining a clearer insight into the mechanism of rotation, Fehlner [7] investigated a series of 3-aryl-6-sulfamoyl-7-chloro-2,3-dihydro-4(1H)-quinazolinones (II) and hydantoins (III), by line shape analysis and equilibration methods.



II



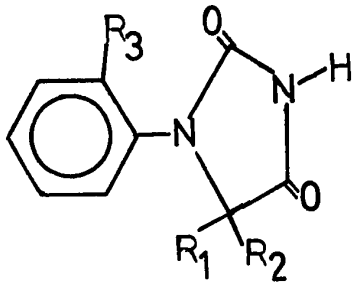
III

His results for the quinazolinone series confirmed the importance of the steric interaction between the ortho substituent group and the carbonyl group in the 4 position. The results further emphasized the steric influence of any R_1 and R_2 substituent bulkier than a hydrogen atom. He found that when the R_3 substituent is bulkier than a hydrogen atom, this group exercises

a buttressing effect. Unlike Hund and Huang, he found that the electronic effect of the substituents was not important in the quinazolinone series.

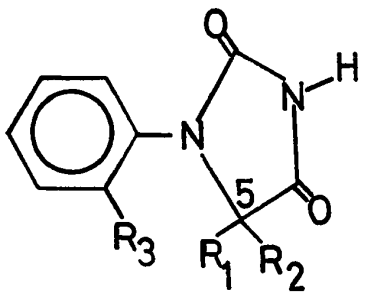
In his investigation of restricted rotation around the C-N bond in 3-aryl hydantoins, Fehlner arrived at the same general conclusion about the effects of aryl group substituents, except when a chlorine atom was in the ortho position. The barrier to rotation is higher when a chlorine atom is present than when the substituent in the ortho position is a methyl group. Since a chlorine atom is less bulky than a methyl group,[8] the higher barrier to rotation might be attributed solely to an electronic effect rather than a normal steric effect.

Icli,[9] also working in this laboratory, prepared a series of 1-aryl substituted hydantoins (IV). In the course of his work, he discovered that a chlorine atom in the ortho position on 1-aryl hydantoins gives rise to a smaller rather than larger barrier of rotation relative to a methyl group in the same position.



IV

This could be due to the fact that during rotation the ortho chlorine in the 3-aryl substituted hydantoins is obliged to pass an electronegative oxygen atom, thereby giving rise to a stronger interaction than when the substituent is a methyl group. In contrast, in 1-aryl substituted hydantoins the group in the ortho position does not interact with the oxygen atom in the preferred transition state for rotation, but rather with the substituents in the 5 position, as shown below (V).[10]



V

Present Investigation

The purpose of the work presented in this thesis was:

a) To determine whether through-space electronic effects, mesomeric effects, and buttressing effects influence the barrier of rotation in the 3-aryl substituted hydantoins.

b) To check Fehlner's observations that a chlorine atom

can give rise to a larger barrier of rotation than a methyl group in this type of compound.

c) To determine the magnitude of the influence of substituents in positions other than ortho, especially the 5 position, and to rationalize their influences.

d) To obtain further information on the effect of the thiocarbonyl group versus the carbonyl group on the magnitude of the barrier of rotation.

The reasons behind the choice of 3-aryl substituted hydantoins for this study are the following:

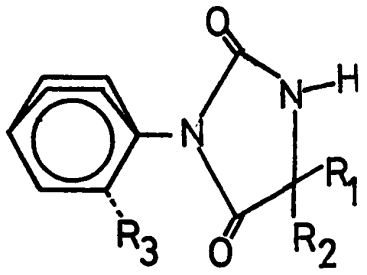
i) Hydantoins, being cyclic amides, have a system which is made easier to interpretate than acyclic compounds because of the prearrangement of the substituents that the aryl ring must pass in its rotation.

ii) Since hydantoins are planar, problems associated with ring inversion are expected to be absent.

iii) The synthesis of hydantoins is relatively easy.

Stereochemistry and Spectra of Hydantoins

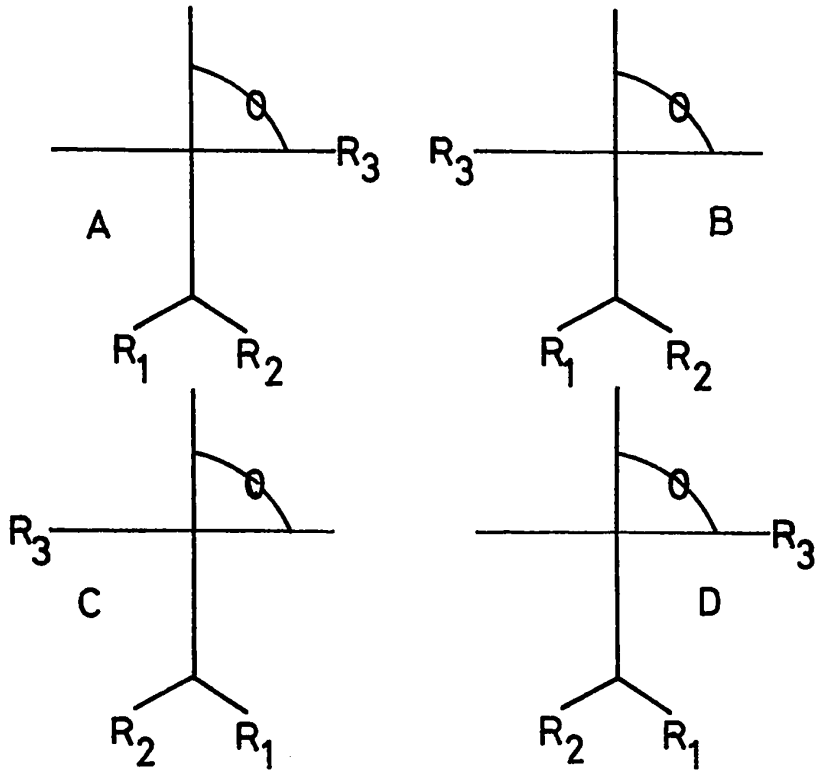
Consider the stereochemistry in the conformational ground state of a hydantoin in which the hydrogen atom has been replaced by an unsymmetrically substituted aryl group in position 3, as in VI.



VI

Because of steric interaction between the ortho substituents on the aryl group and the carbonyl oxygen atoms of the heterocyclic moiety, the two rings cannot be co-planar in the ground state for internal rotation around the aryl C-N bond. A large dihedral angle is to be expected. For convenience in representing the stereochemistry of these molecules a dihedral angle of 90^{o} is assumed.

If the aryl ring and the hydantoin ring are not co-planar, four different isomers must be considered. These are represented in simplified form as follows, the molecule being viewed along the aryl C-N axis from the heterocyclic end.



If R_1 and R_2 are identical then isomers A and D are identical, as are isomers B and C. Isomers A and C (or B and D) will form an enantiomeric pair, with identical NMR spectra under normal conditions. Thus these isomers cannot be distinguished by the NMR method using achiral media.

However, since these molecules lack a plane of symmetry, R_1 and R_2 are diastereotopic. Provided that their magnetic environments are sufficiently different to produce a chemical shift difference, these two substituents should be distinguishable.

If $R_1 = R_2 = H$ an AB quartet is expected from these protons in the conformational ground state of the molecule. This type of spectrum has been reported earlier for conformers such as hydantoins.[7] Chemical shift and geminal coupling constants within the range of 3.6-4.9 δ and |6.0-12.0| Hz, respectively, have been observed.

If rotation around the C-N aryl bond occurs, corresponding to interconversion between isomers A and B (or C and D), the environments of R_1 and R_2 undergo enantiomeric interchange (provided that $R_1 = R_2$). If rotation around the same axis is rapid on the NMR time scale, the AB quartet arising from the geminal protons on C-5 will collapse to a singlet. At intermediate rates of rotation partial collapse of the AB quartet is expected. Such behaviour has been reported earlier.[7] The temperature dependence of such a spectrum arising from the geminal protons in the 5 position of 3-α-naphthyl-1-methylhydantoin (pyridine solution) is illustrated by means of computer simulation in Figure 1, using data of Fehlner.[7]

If $R_1 = R_2 = CH_3$ these groups are expected to give rise to two peaks of equal intensity under condition of slow rotation about the C-N bond. Spin-spin coupling between the protons of the geminal methyl groups is expected to be too small for the fine structure to be resolvable although some line broadening may be detected. Under condition of fast rotation the two methyl lines are

expected to collapse to a single, time averaged line. Such behaviour has been observed in a number of cases.[7] The temperature dependence of the 5,5-dimethyl signals of 3-(o-bromophenyl)-5,5-dimethylhydantoin is illustrated in Figure 2. Data for the computer simulation are taken from the work of Fehlner.[7]

When $R_1 \neq R_2$ the rotational isomers are diastereomers. All four isomers (configurational and rotational) are distinct, but the members of the pairs A and C, and B and D are enantiomeric and are, therefore, not normally distinguishable by the NMR method. Since A and B or (C and D) are diasteromers, they are expected to differ in all their physical properties, including their NMR spectra. Thus R_1 in A is expected to differ in chemical shift from R_1 in B. The same is true for R_2 in the same isomers. Since diastereomers have different free energies the concentration of the two forms A and B (or C and D) are expected to be different at equilibrium.

The spectrum of an equilibrium mixture of such diastereomeric rotational isomers is, therefore, expected to be the sum of the spectra of the two distinguishable diastereomers, of unequal intensity. In principle, all lines in the overall spectrum should show splitting resulting from the contribution of the two forms, but in practice the chemical shifts may not be great enough for all splitting to be resolvable.

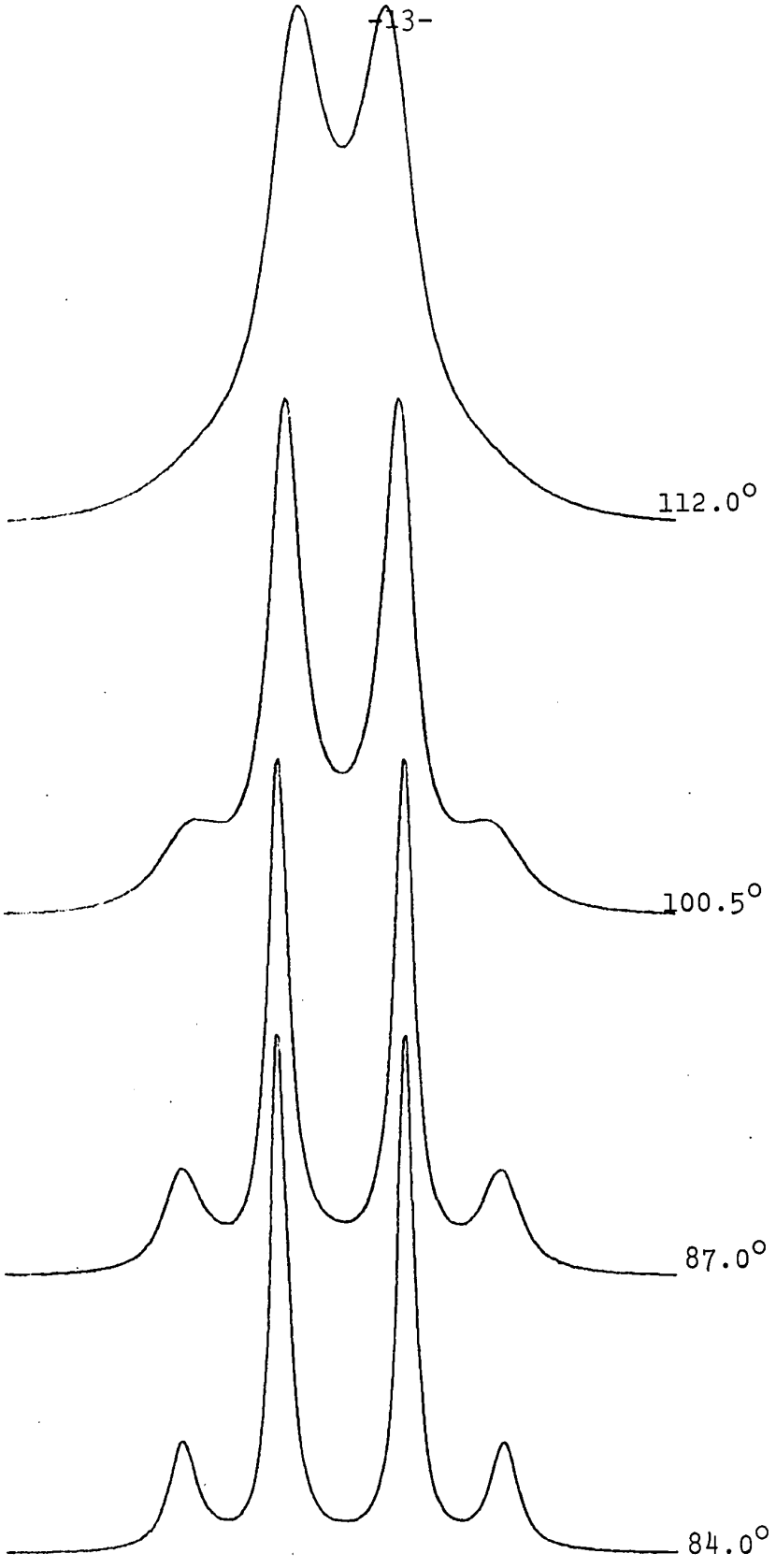


Figure 1: Computer Simulated Spectra of the C-5 Protons of 3-α-naphthyl-1-methylhydantoin in Pyridine at Various Temperatures.

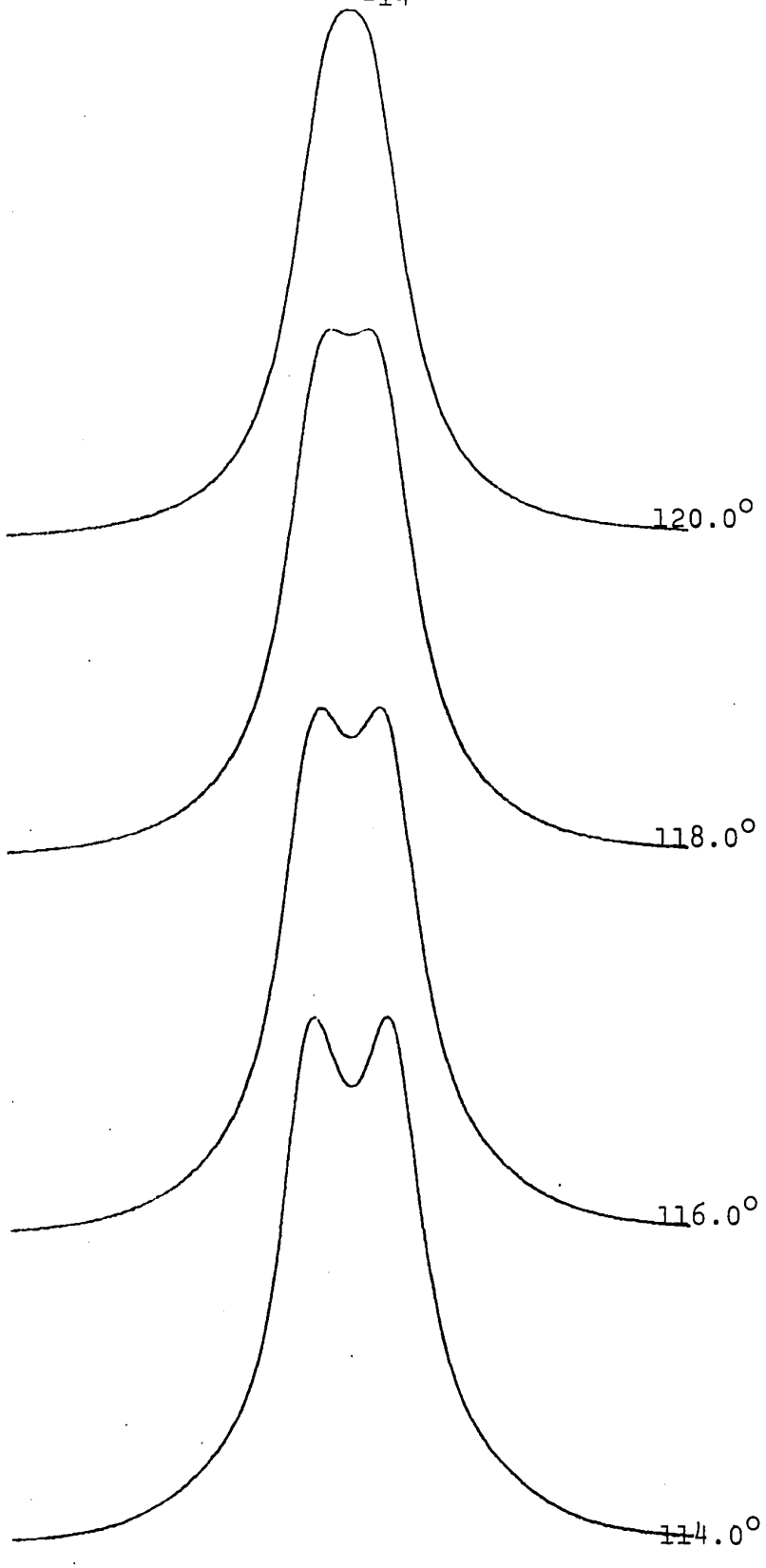


Figure 1: (Continued)

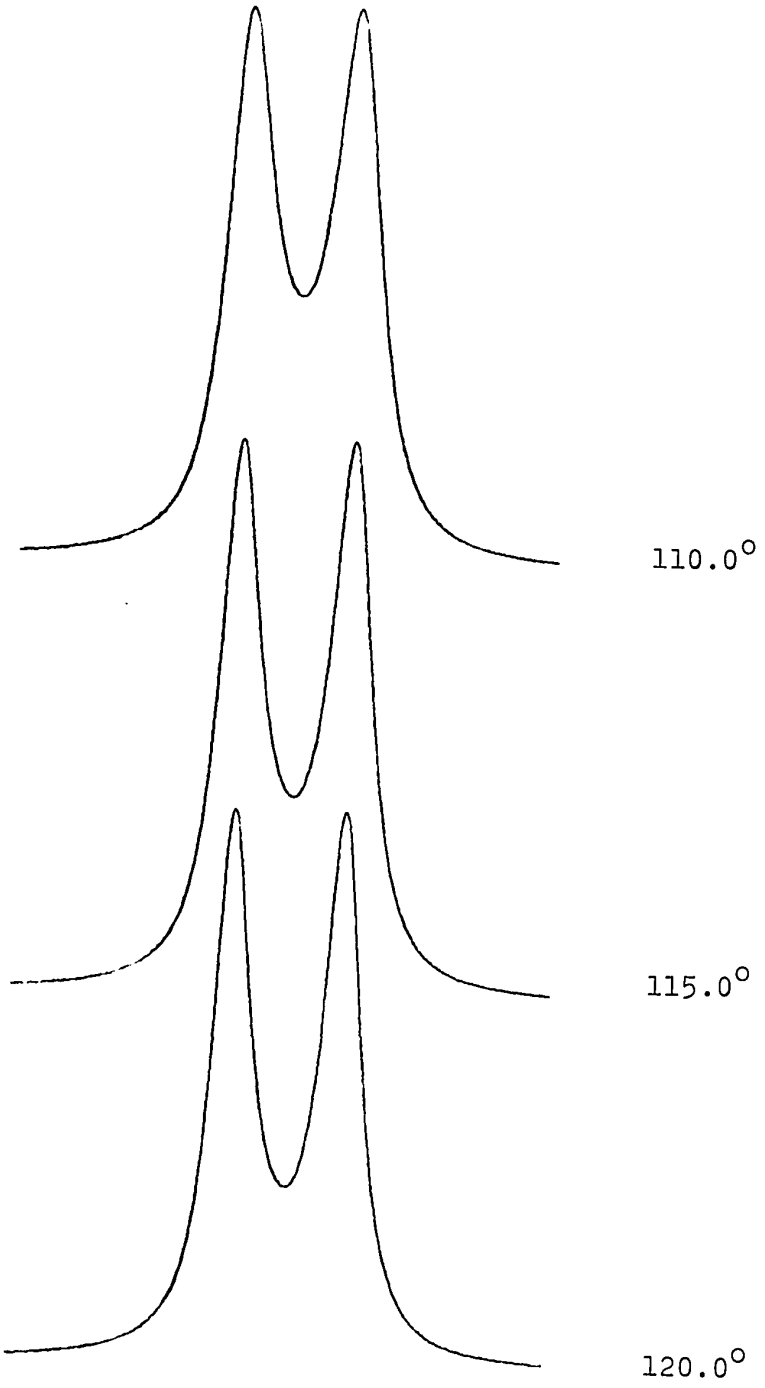


Figure 2: Computer Simulated Spectra of the C-5 Methyl Group of 3-(o-bromophenyl)-5,5-dimethylhydantoin in 2-chloropyridine at Various Temperatures.

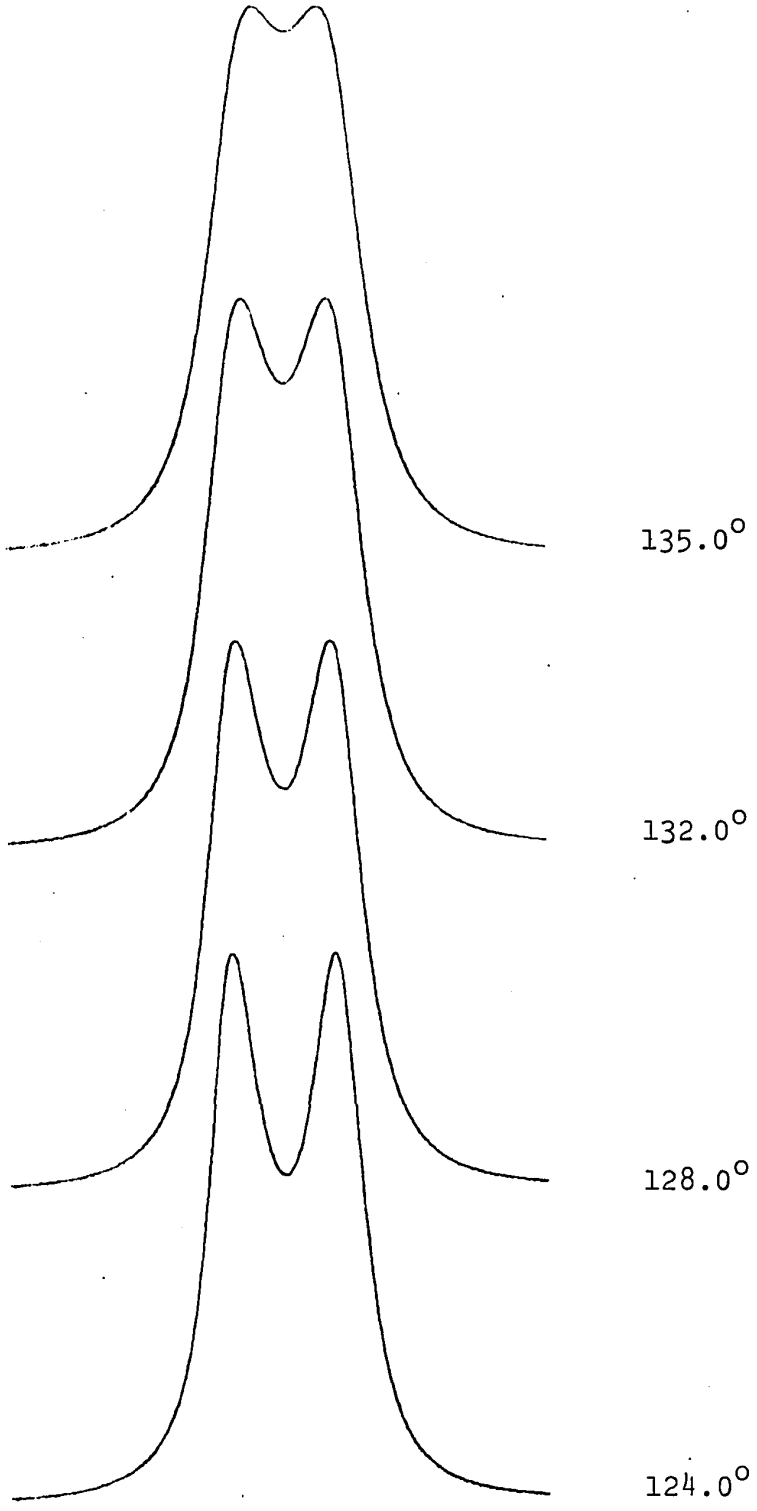


Figure 2: (Continued)

At high rates of rotation, a time averaged spectrum is expected, the chemical shifts of the nuclei reflecting the average environment in the two diastereomers. The time averaged lines will not be equidistant between the corresponding line positions of the individual isomers of rotation, but will appear at frequencies weighted according to the relative populations of the two species. Such behaviour has been reported by Fehlner,[7] and has been observed in the present investigation.

When $R_1 = H$, $R_2 = CH_3$ the spectrum arising from the C-5 substituents at low rates of rotation consists of two sometimes overlapping methyl doublets and two methine quartets. At high rates of rotation the pair of methyl doublets collapses to a single doublet and the pair of methine quartets collapses to a single quartet. Several such cases have been reported by Fehlner.[7] This case is illustrated in Figure 3 for the C-5 methyl signal of 3-(o-chlorophenyl)-5-methylhydantoin. Data for the computer simulation were obtained by Fehlner.[7]

If spin coupling between R_1 and R_2 is absent the spectra are less complicated. When $R_1 = H$, $R_2 = C_6H_5$, the spectrum of R_1 consists of two singlets of unequal intensity under condition of slow rotation, and a time averaged singlet if rotation is fast.

The spectrum of the ortho substituent, R_3 on the

aryl group may also be dependent on the rate of rotation about the C-N bond. If $R_1 = R_2$, the magnetic environments of R_3 in the pair of rotamers are identical. Thus if $R_3 = CH_3$, a single signal is seen under all conditions. However if $R_1 \neq R_2$, the environments of R_3 in the two rotamers are different. If $R_3 = CH_3$ two lines of unequal intensity will be seen under conditions of slow rotation. and a single time averaged line under fast rotation. This case is illustrated for the ortho-methyl spectrum of 3-(o-tolyl)-5-methylhydantoin (VII) in Figure 4. Data for the computer simulation were obtained in the present investigation.

The prediction of the appearance of the spectra of 3-aryl hydantoins outlined above are based on the stereochemistry of these molecules. Experimentally determined spectra may not be in accord with prediction for the following reasons:

a) The chemical shift differences may be too small for the signals arising from nuclei in different environments to be resolved. Degeneracy of this type may sometimes be resolved by choice of a more suitable solvent.

b) The rate of rotation may be fast at the lowest temperature attainable, with the result that the time averaged spectrum is always seen. This situation may be difficult to distinguish from that in a).

When $R_1 = H$, $R_2 = CH_3$, and $R_3 = OCH_3$ in the present

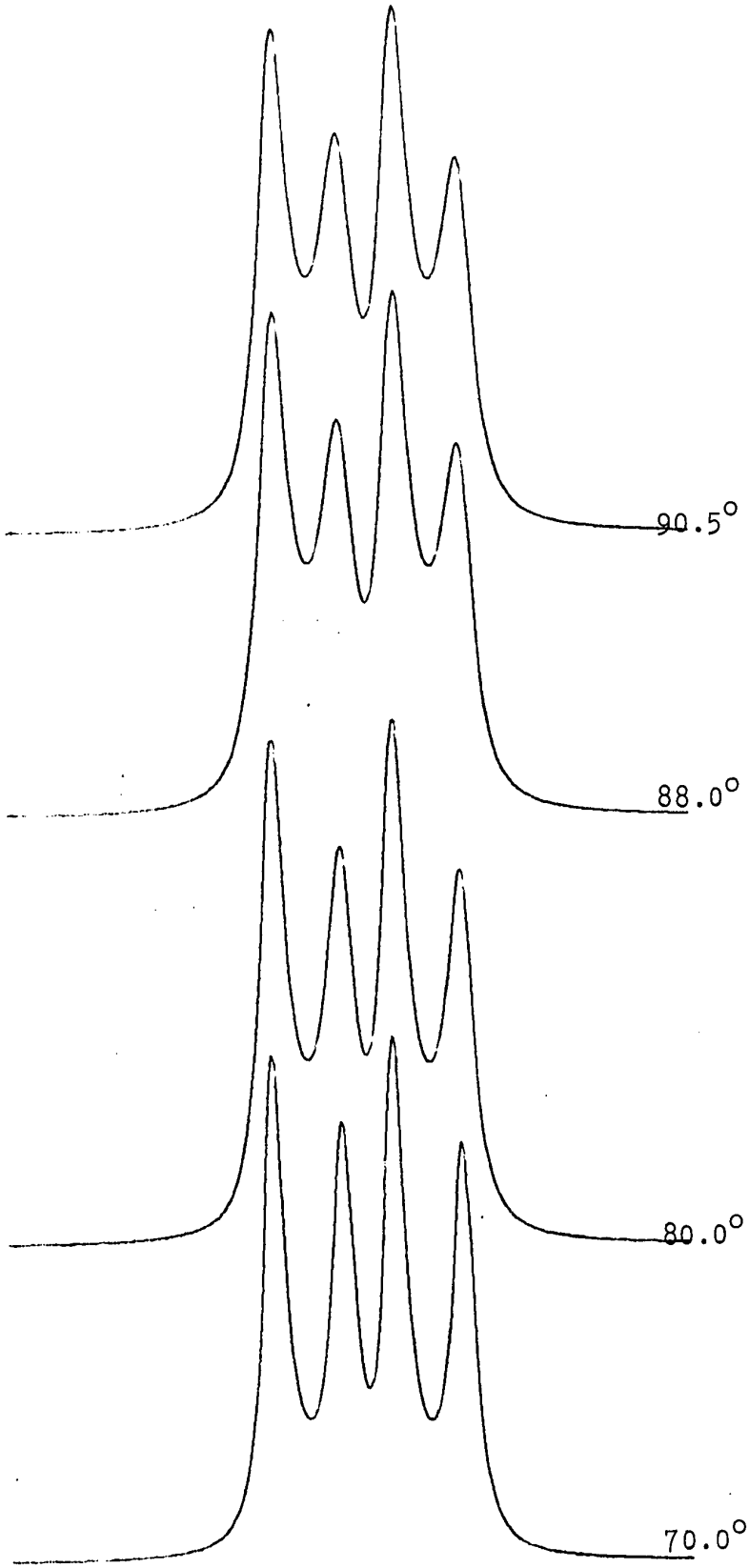


Figure 3: Computer Simulated Spectra of the C-5 Methyl Groups of 3-(o-chlorophenyl)-5-methylhydantoin in Pyridine at Various Temperatures.

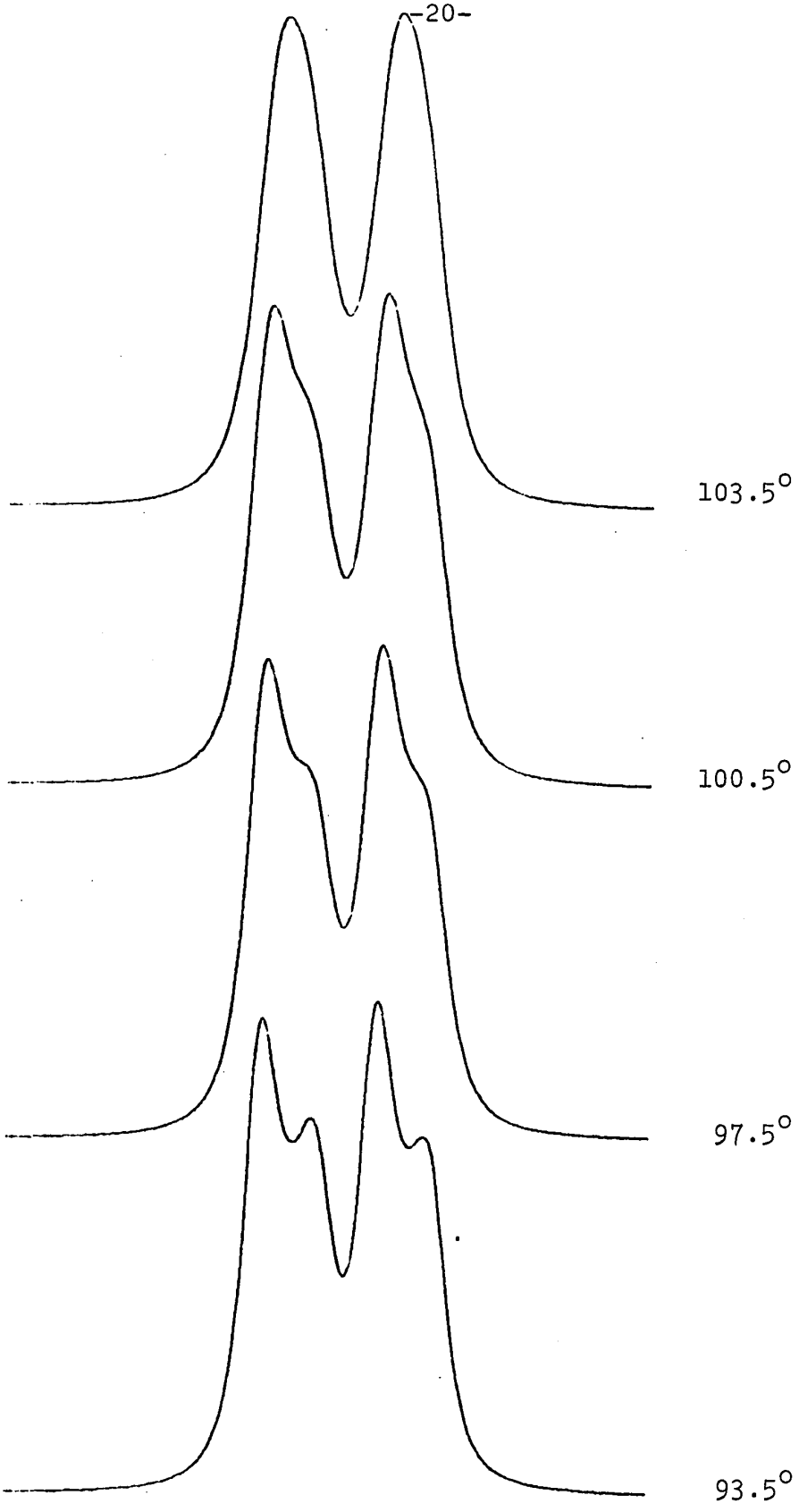


Figure 3: (Continued)

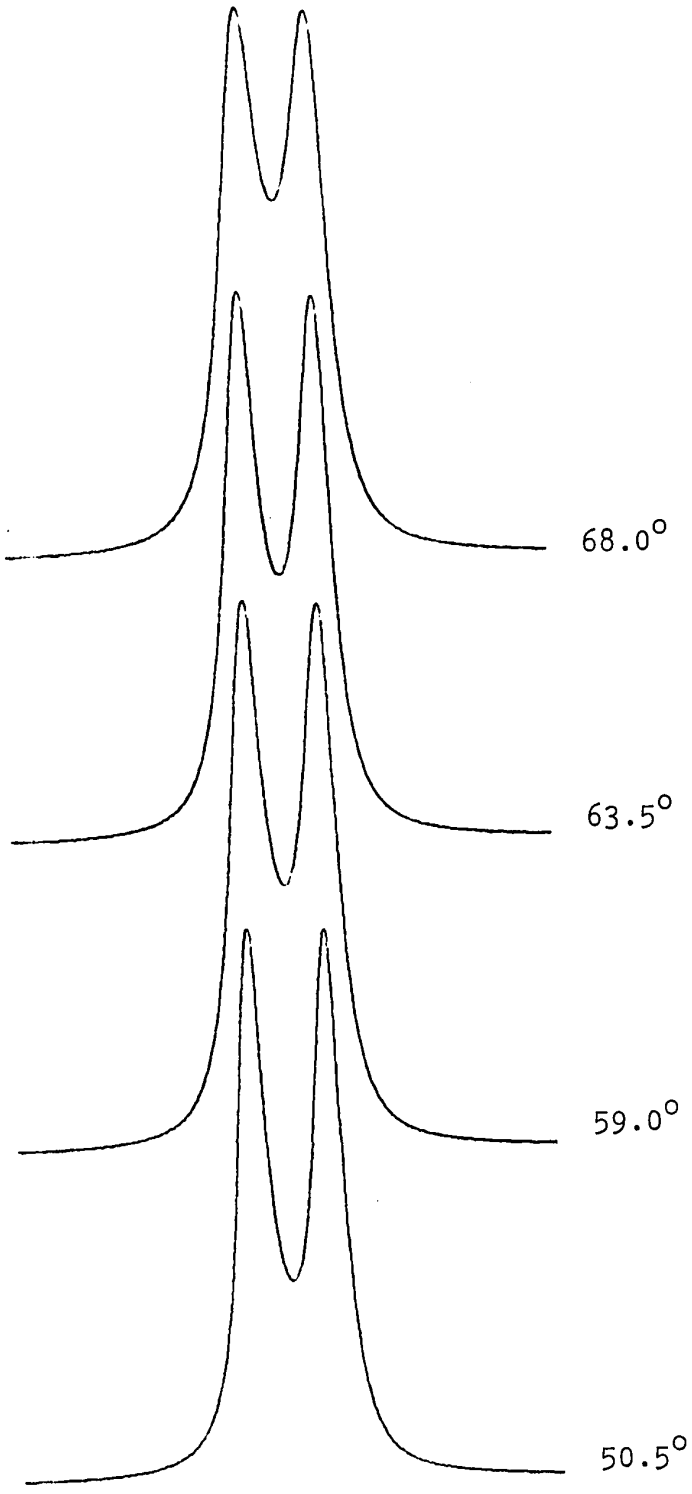


Figure 4: Computer Simulated Spectra of the ortho-methyl Group of 3-o-tolyl-5-methylhydantoin (VII) in DMSO-d_6 at Various Temperatures.

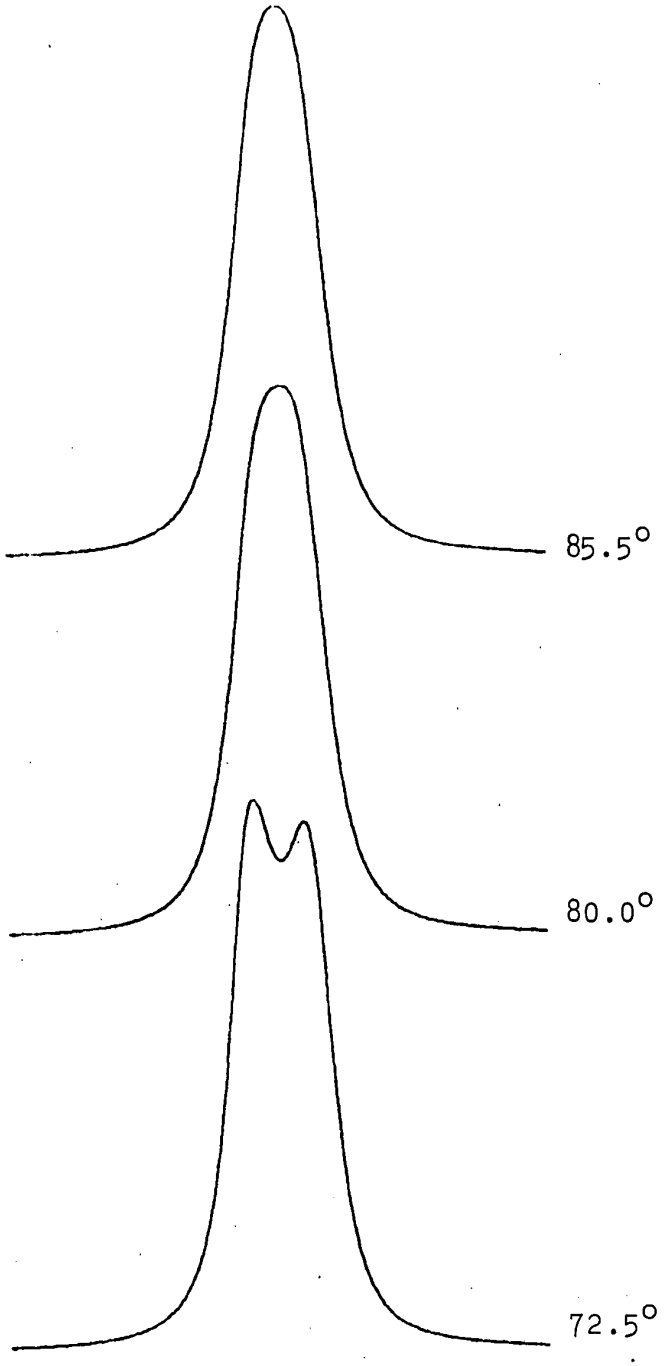


Figure 4: (Continued)

investigation (compound (XXIII)) no splitting was seen. It is difficult to establish which of these factors is responsible for the failure to observe splitting in this case.

c) The rate of rotation may be so slow at the highest attainable temperature that collapse of the spectrum is not observed. Examples of highly hindered 3-aryl-2-thiohydantoins, which have this property, have been reported by Fehlner[7] and confirmed by this investigation.

Following a review of the types of spectra to be expected for various classes of substituted hydantoins, it was decided that 5-phenyl hydantoins (R_1 = H, R_2 = C_6H_5) should provide the most suitable spectra for the present investigation. Consequently most of the compounds prepared were of this type. In this series uncomplicated 5-methine signals may be used to obtain rate constants for interconversion of rotational isomers. In addition, the ortho methyl signals from those compounds with R_3 = CH_3 may be used for the same purpose.

Theory and Calculation of Spectra

Collapse of a pair of singlets to a singlet peak.

The equations for the collapse of a pair of singlets to a singlet peak, as depicted in Figures 2 and 4, have been derived from the Bloch equations[11,12,13] by Gutowsky and Holm.[14] The equation for the intensity, I, at any point, ω, is:

$$I = k \frac{((1 + \tau/T_2)P_2 + QR)}{P^2 + R^2}$$

where $$1/\tau = \frac{\tau_A + \tau_B}{\tau_A \tau_B}$$

and: $$P = \tau((1/T_2)^2 - (1/2(\omega_A + \omega_B) - \omega)^2 - 1/4(\omega_A - \omega_B)^2 + 1/T_2$$

$$Q = \tau(1/2(\omega_A + \omega_B) - \omega - 1/2(p_A - p_B)(\omega_A - \omega_B))$$

$$R = (1/2(\omega_A + \omega_B) - \omega)(1 + 2\tau/T_2) + 1/2(p_A - p_B)(\omega_A - \omega_B)$$

Parameter k is a scaling factor to allow for the adjustment of the intensity to that of the experimental value. Parameters p_A and p_B are the populations of the two

rotamers and are equal to $\tau_A/(\tau_A + \tau_B)$ and $\tau_B/(\tau_A + \tau_B)$, respectively. Parameters τ_A and τ_B are the lifetimes of the two rotamers in seconds, while ω_A and ω_B are their chemical shifts in radians/sec. The transverse relaxation time T_2 is related to the linewidth, W, (in Hz) by the equation:

$$T_2 = \frac{1}{\pi W}$$

When possible, W is measured from the half height of the peaks in a nonexchanging system.

In practice, W includes all contributions to the linewidth due to inhomogeneity of the magnetic field and other factors such as viscosity, drifting, unresolved long range coupling, etc..

Another formulation of the line shape method applicable to this case is based on a density matrix method and does not contain the assumption of equal transverse relaxation times for exchanging sites, which is inherent in the Gutowsky-Holm equation as it is normally used.

Comparison of Spectra

When the experimental spectra have been obtained, theoretical spectra must be fitted to them.

Until recently, the experimental and theoretical spectra were plotted together and compared visually. Corrections were made to the parameters and the process was repeated until an acceptable fit was found, using subjective criteria. This procedure involved a large amount of time and the final values of the parameters were somewhat dependent on the skill and patience of the operator. Today this comparison is made by a computer, which compares the spectra point by point and then adjusts the parameters accordingly, until the best fit based on non-subjective criteria is obtained.

This can be done by use of a non-linear least square analysis programme, such as that devised by Marquardt,[15] which is based on the maximum neighborhood method. This programme, in combination with the subroutines containing the line shape equations for the system being considered, allows accurate fitting, and gives standard error analysis for the parameters involved. A listing of this programme is contained in the Appendix.

The output of this programme can be used to plot the experimental and theoretical spectra calculated by the fitting procedure. Two examples of the validity of

this programme can be seen in Figures 5, and 6, which show superimposed the experimental spectra and the spectra simulated by using the parameter values calculated by the computer.

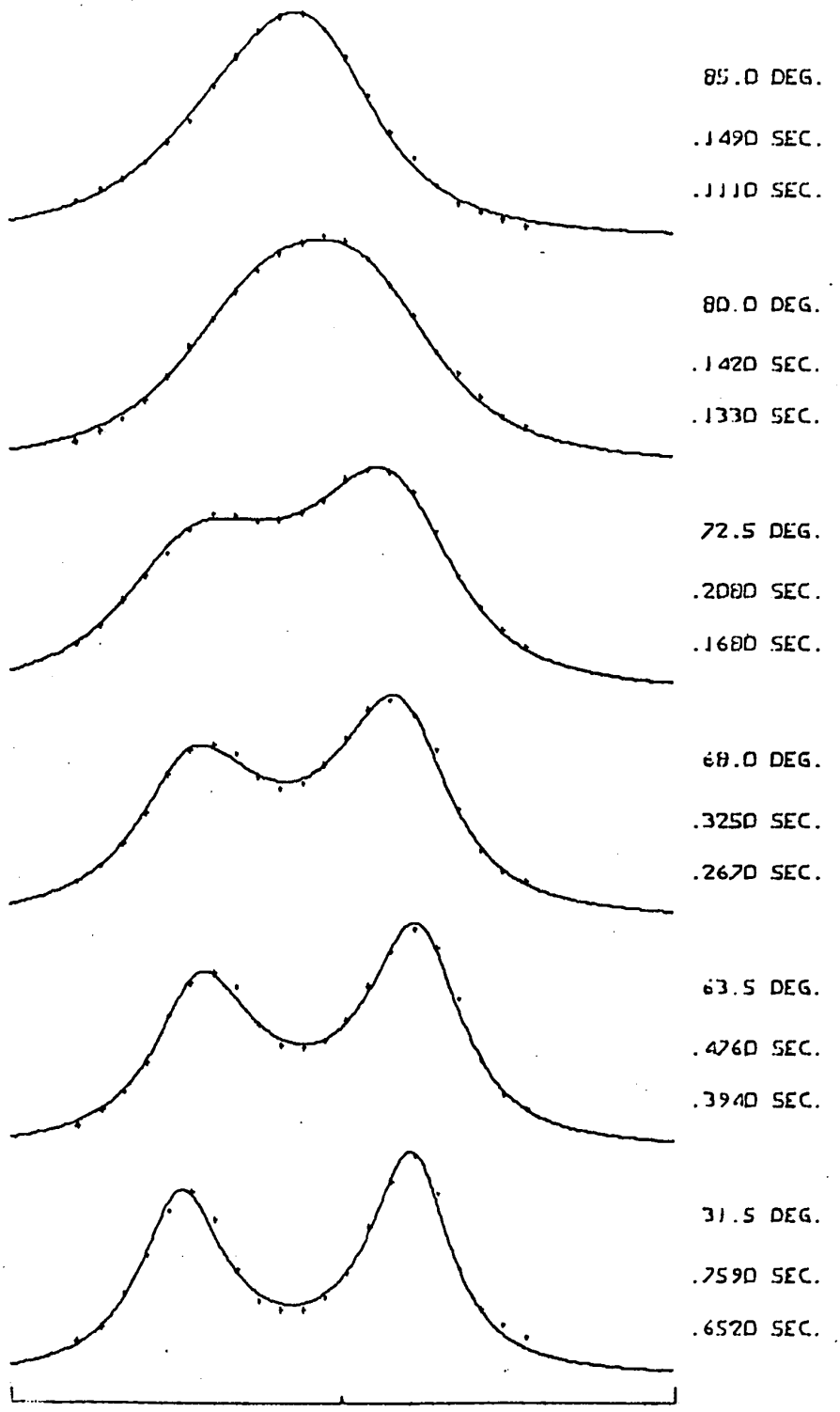


Figure 5: Experimental (—) and Theoretical (...) Spectra for 3-o-tolyl-5-methylhydantoin (VII) in DMSO-d_6 at Various Temperatures. Mean Lifetimes are shown.

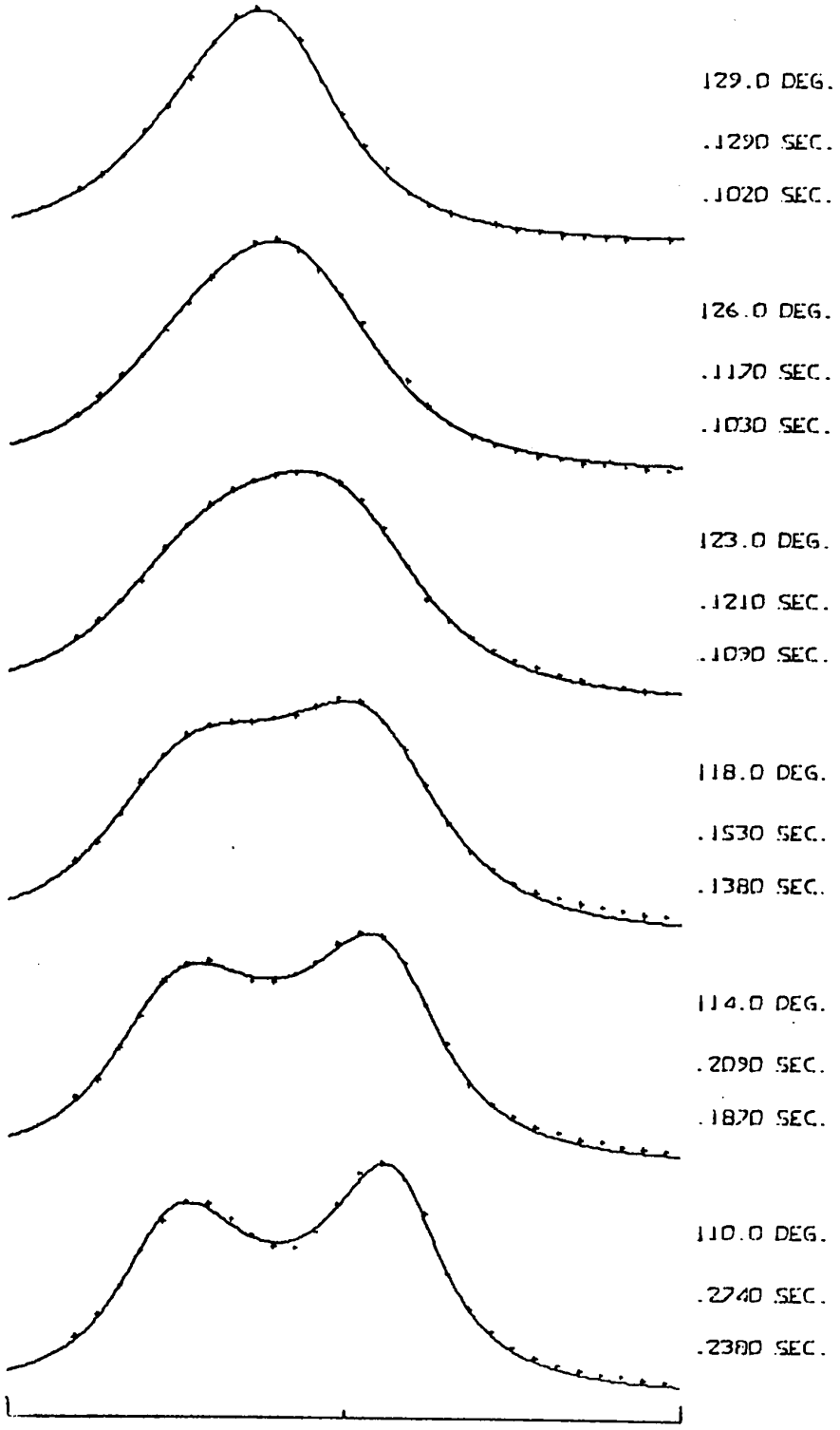


Figure 6: Experimental (—) and Theoretical (..) Spectra for 3-(2,3-dimethylphenyl)-5-methylhydantoin (IX) in DMSO-d_6 at Various Temperatures. Mean Lifetimes are Shown.

Calculation of Thermodynamic Parameters

After the rate constants or mean lifetimes have been obtained at a number of different temperatures, one can find the activation energy by means of the Arrhenius equation:

$$k = Ae^{-E_a/RT}$$

where: k = reaction rate constant

A = frequency factor

E_a = activation energy

R = gas constant

T = absolute temperature

By plotting ln k versus 1/T, one can determine the activation energy E_a from the slope, and the frequency factor A from the intercept of the best fit straight line.

The above equation assumes that E_a and A are independent of the temperature, which can only be an approximation. Experience has shown this approximation to be a good one.

At the present time the tendency is to obtain Eyring parameters. This is done by equating the Arrhenius equation,

$$k = k_b(KT/h)e^{-\Delta G^{\ddagger}/RT}$$

that can be rewritten as:

$$k = k_b KT/he^{(-\Delta H^{\ddagger}/RT)} e^{(\Delta S^{\ddagger}/R)}$$

where:

k = rate constant

K = transmission coefficient

k_b = Boltzmann's constant

h = Planck's constant

$\Delta G^{\ddagger}$ = free energy of activation

$\Delta S^{\ddagger}$ = entropy of activation

$\Delta H^{\ddagger}$ = enthalpy of activation

R = gas constant

T = absolute temperature

The transmission coefficient, K, is assumed to be equal to one. Other value have been tried,[1] but they give unrealistic results.

It is possible to calculate $\Delta S^{\ddagger}$ and $\Delta H^{\ddagger}$ from the temperature independent activation energy E_a obtained from the Arrhenius plot. This is done by equating:

$$\Delta H^{\ddagger} = E_a - RT$$

$$\Delta G^{\ddagger} = 2.303RT(10.3191 + \log T + \log \tau)$$

$$\Delta S^{\ddagger} = (\Delta H^{\ddagger} - \Delta G^{\ddagger})/T$$

A programme, ACTPAR, has been written to find the best straight line for the plot of ln k versus 1/T through the use of a linear regression method. A listing of ACTPAR is contained in the Appendix.

Alternative Method for Calculating $\Delta G^{\ddagger}$ of Activation

The method of the maximum separation of peaks[16] is, or better was, a widely used method to calculate thermodynamic parameters for an exchanging AB system. It is much simpler than the complete line shape analysis, but can unfortunately introduce errors of large magnitude (10-30%), as Gutowsky et al. have shown.[17] According to this method the rate equation can be expressed as,

$$k = \frac{\pi(\nu_{AB}^2 - 6J_{AB}^2)^{1/2}}{\sqrt{2}}$$

where k = rate constant

ν_{AB} = maximum difference in chemical shift between A and B

J_{AB} = coupling constant

When J is zero this expression reduces to

$$k = \frac{\pi\nu_{AB}}{\sqrt{2}}$$

Once k is known, one can obtain $\Delta G^{\ddagger}$ by substituting k into the Eyring equation.

Measurement of Spectra

All spectra of hydantoins used for kinetic studies were taken in deuterated dimethylsulfoxide. By using DMSO-d_6, it was possible to prepare concentrated solutions (0.25-0.50 mole/l) in order to maximize the signal-to-noise ratio. Further DMSO-d_6 did not interfere with any hydantoin absorption. In the case of ortho-methoxy hydantoins, DMSO-d_6 and pyridine were used as solvents since it was necessary to lower the temperature below the DMSO-d_6 freezing point.

The internal standard used was tetramethylsilane. It was possible to maintain the lock on tetramethylsilane up to a temperature of 150°.

The spectra were taken on a Varian HA-100 spectrometer using the standard variable temperature equipment. Using methanol and ethylene glycol, the temperature was determined after each run by comparing the peak separation obtained by locking on the C-H peak and measuring the chemical shift of the hydroxyl proton. Care was taken to ensure that the temperature had first come to equilibrium.

Spectra of the protons under study were taken at interval of 8-10° degrees over the range of temperature where collapse of the spectrum was observed.

Care was taken to minimize the drift, to maximize the homogeneity, and above all to avoid saturation of the peaks.

Fitting of the Spectra

The theoretical spectra were fitted to the experimental spectra by use of a non-linear least squares regression programme. Different type of subprogrammes were available to cope with different kinds of systems, for example NLIN AB for the collapse of an AB quartet, and NLIN GH for the collapse of two singlets to one singlet.

The spectra were entered into the computer as data pair corresponding to intensity and position. These were obtained by estimating a suitable baseline and measuring the intensity of the peaks at different frequencies. Since a typical spectrum may have three data pairs for each Hz, and an average of ten spectra are required for each case, it is evident that this process is time consuming if the spectra are measured manually and the data pairs are punched on computer cards.

Colebrook et al.[18] prepared the programmes LINDI and TAPGH to overcome this problem. By using a combination of the Hewlett-Packard F-3B line follower and the H-P 2114B computer, these programmes allow one to digitalize directly from the spectrum.

The computer drives the X-axis sweep of the recorder through an 8 bit digital-to-analogue converter, while the line follower head follows the spectral trace,

which must be recorded in black ink. A voltage proportional to the spectrum intensity is supplied to the analogue-to-digital converter from the Y-axis slide wire. The computer moves the recorder arm across the spectrum in 250 increments, storing a digitalized intensity for each spectrum. Before the run is started the line-follower is adjusted successively to the left and right limits of the portion of the spectrum to be scanned. On output the computer calculates the frequencies corresponding to different intensities.

The main programme is written in FORTRAN, whereas the subroutines, which drive the recorder, affect digitalization, and provide a variable delay to control the scanning rate, are written in Assembler. Since a line follower cannot cope with steep curves, there is a provision in the programme for interrupting the sweep through the switch register of the computer, so that the spectrum can be scanned at any point and time under operator control. There is also a provision to abort a scan through the computer switch register. The computer outputs up to 251 (the number is selectable) baseline corrected intensity-frequency data pairs on the teletypewriter and also punches them on a paper tape. A listing of these programmes is included in the Appendix.

Another FORTRAN programme has been written for the

2114B to process the paper tape at a later stage. This programme writes the digital information on magnetic tape together with the required control parameters for the non-linear regression programme used for fitting a computed to a digitalized spectrum. The operator must type in the original estimates for the parameters and specify which parameters are to be held constant and which ones are to be varied. The data on the magnetic tape are then processed on the CDC 6400 computer.

If the system consists of two singlets collapsing to one singlet, six parameters are needed to describe the line shape and intensity. They are ν_A and ν_B, the chemical shifts in Hz; τ_A and τ_B, the lifetimes of the two species in seconds; k, a scaling factor; and W the linewidth in Hz. Although all six parameters can be varied, it is desirable to hold the linewidth constant since the programme has difficulty distinguishing between some of the parameters, particularly between the linewidth and the lifetimes. Usually the linewidth was estimated from the linewidth of the low temperature spectrum where broadening due to exchange was minimal.

An accurate linewidth is necessary mainly when one is dealing with spectra having a slow exchange rate. It is desirable to check the linewidth at low temperature with a standard reference compound (e.g. methylene chloride) so as to minimize the error due to viscosity broadening.

At higher temperatures, and consequently faster exchange rates, variation in the linewidth has a very small effect on the other parameters.

When the value of W has been determined, initial estimates must be made for the other parameters. The values for ν_A and ν_B can be estimated from the spectrum at low temperature, but the values for the lifetimes τ_A and τ_B, as well as for the scaling factor k, must be based on previous experience. However initial estimates in error by approximately 100% did not have a significant effect upon the final values of the other parameters.

Once the initial values of the parameters have been determined, a theoretical spectrum based upon these parameters is calculated using the line shape equation provided in the NLIN GH subroutine. A point by point comparision of the experimental and calculated spectra, followed by the regression procedure, provides new values for those parameters not held constant. These new values become initial values and the procedure is repeated until the change in the parameters being calculated satisfies special convergence limits. At this time the final values of the parameters are printed and a graphic display of the experimental and calculated point is printed. Standard errors for the calculated parameters are also provided.

Among the parameters that could vary during the fitting procedure are the chemical shifts ν_A and ν_B.

Figures 7, 8, and 9 show the variation of the calculated values of the chemical shift difference as a function of temperature. At temperatures near coalescence there was some difficulty in calculating the parameters. Therefore in cases where scattering was observed the low temperature curve was extrapolated as indicated. This temperature dependence results, in part from small changes in the proton environments within the molecule. The aryl ring and the hydantoin ring may alter their average orientation with respect to each other. Probably the main cause of scatter in the chemical shift differences is due to the lack of sensitivity of the computer to these parameters in the fitting procedure when there is considerable exchange broadening.

The effect of the variation of the chemical shift with temperature on the precision of the fitting procedure has been shown to be quite pronounced at temperatures near and above the coalescent temperature by Huang[6] and Bentz.[9] If the variation of the chemical shift with temperature is not too great, an average or an extrapolated value for the chemical shift may be used in the fitting procedure. However, it is incorrect to assume that the values of the chemical shift differences obtained near or above coalescence have the same validity as those obtained at lower temperature.

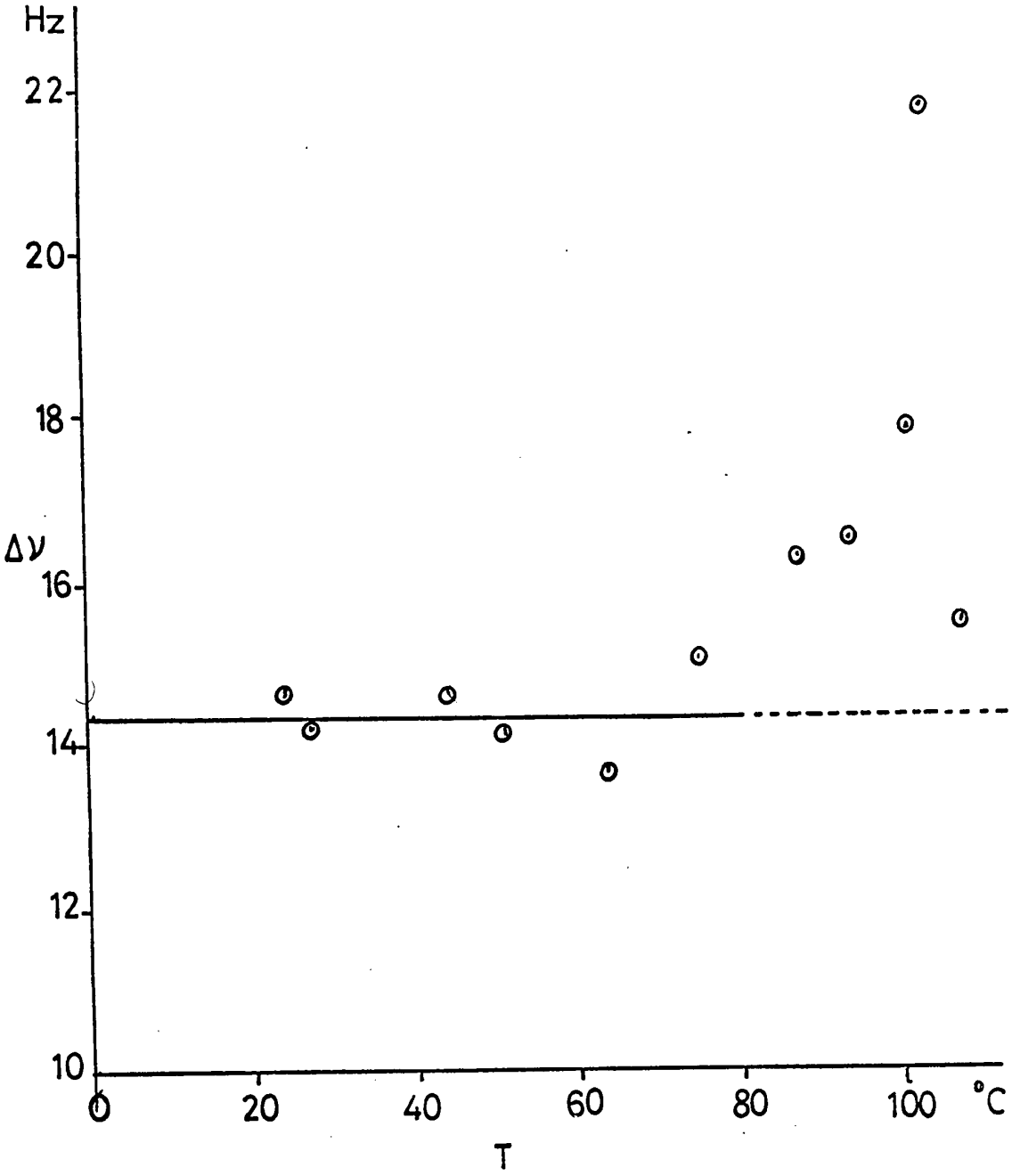


Figure 7: Temperature Dependence of the Chemical Shift Difference of the ortho-methyl Protons in the 3-(2-methylphenyl)-5-phenylhydantoin (VIII).

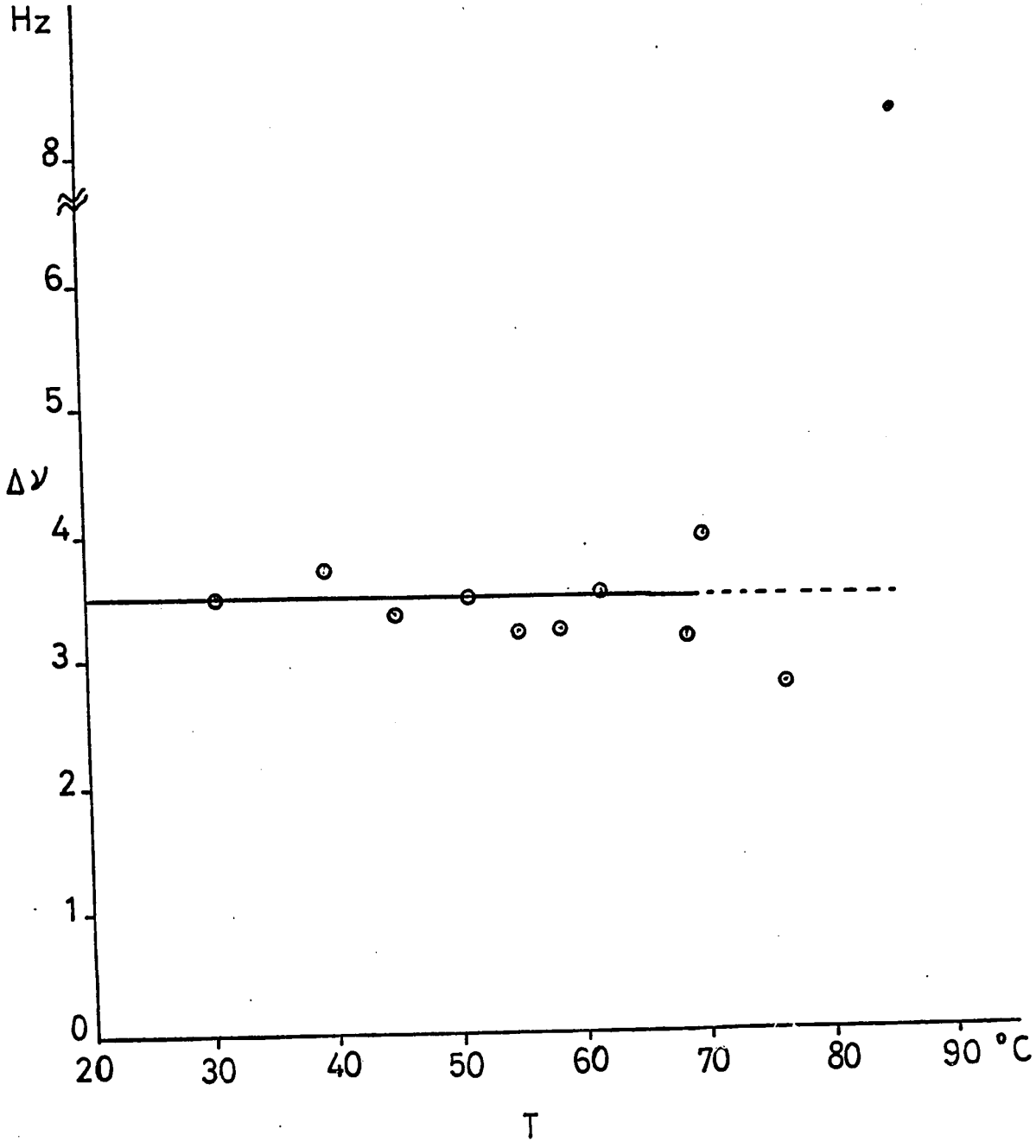


Figure 8: Temperature Dependence of the Chemical Shift Difference of the ortho-methyl Protons in the 3-(2-methylphenyl)-5-methylhydantoin (VII).

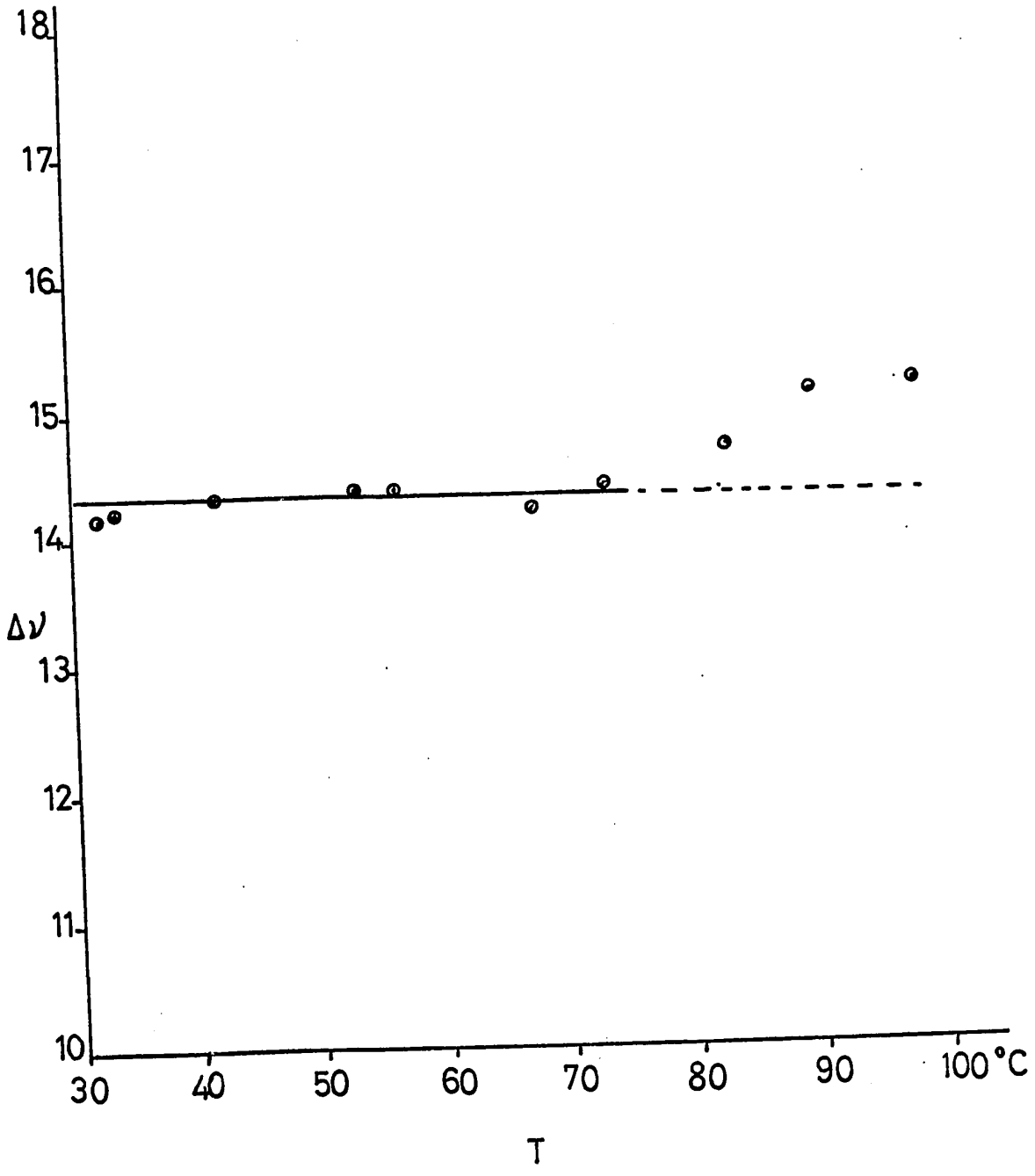


Figure 9: Temperature Dependence of the Chemical Shift Difference of the ortho-methyl Protons in the 3-(4-chloro-2-methylphenyl)-5-phenylhydantoin (XIII).

Actpar

This programme calculates Arrhenius and Eyring activation parameters and 90% confidence intervals from input values of mean lifetimes, calculated by the NLIN programme, and temperature. It uses a linear regression method to fit the Arrhenius equation in logarithmic form to the input data, i.e. the equation is in the form:

$$\ln(1/\tau) = \ln A - E_a/RT$$

the independent variable being $(1/T)$ and the dependent variable being $\ln(1/\tau)$. Error analysis is given at each stage of the calculation, i.e. following the regression calculations, following the Eyring calculations, following the Arrhenius calculations.

The programme uses a previously prepared look-up table to find Student's T values for use in calculating 90% confidence intervals. Standard errors and 90% confidence limits in the Arrhenius and Eyring parameters are based on the regression errors in the slope and intercept of the regression line. Eyring parameters are calculated (with 90% confidence limits) at a temperature specified by the user.

The regression method and confidence interval calculations employed are based on P.D. Lark, B.R. Craven,

and R.L. Bosworth, " The Handling of Chemical Data," Pergamon press, Oxford, 1968.

The computer print-out is designed so that the user can easily recognize any experimental point which poorly fits the regression line. Included in the print-out are the data required for the preparation of an Arrhenius plot.

Calculation:

The Arrhenius equation has the form,

$$k = A \exp(-E_a/RT)$$

where: k = rate constant (1/sec.)

A = frequency factor

E_a = Arrhenius activation energy (cal.)

R = gas constant (1.987 cal.deg.$^{-1}$mole^{-1})

T = absolute temperature

The programme returns the value of A and E_a.

The Eyring equations have the form,

$$\Delta H^{\ddagger} = Ea - RT$$

$$\Delta G^{\ddagger} = RT(\ln(k_b/h) + \ln T - \ln k)$$

$$\Delta S^{\ddagger} = (\Delta H^{\ddagger} - \Delta G^{\ddagger})/T$$

where:

$\Delta G^{\ddagger}$ = free energy of activation

$\Delta S^{\ddagger}$ = entropy of activation

$\Delta H^{\ddagger}$ = enthalpy of activation

k_b = Boltzmann's constant (1.38×10^{-16} erg/deg.)

h = Planck's constant (6.625×10^{-27} erg/deg.)

$\Delta S^{\ddagger}$ may also be expressed in the form,

$$\Delta S^{\ddagger} = R(\ln A - \ln(k_b/h) - \ln T - 1.0)$$

DATA and RESULTS

The data and the results for the hydantoins are presented for each individual compound. The kinetic data are presented in a table followed by the Arrhenius plot for that compound. The standard errors for the lifetimes are obtained from the non-linear least squares programme. They are an indication of the sensitivity of the line shape fits to changes in the lifetime parameter. When chemical shifts have been held constant they are followed by the letter c. During the line shape calculation, the chemical shift was held constant when the computer returned obviously incorrect values if the chemical shift was allowed to vary. Sometimes the value of the chemical shift was extrapolated from values at lower temperatures.

The Arrhenius plots have been arranged for convenient display rather than for purposes of comparison.

The tables of thermodynamic data follow the Arrhenius plots. All the values are given for 25^{o}, except for the activation energies which are temperature independent.

Confidence limits for the activation energies E_a are also given; they are a measure of the quality of fit of the experimental points to the straight line calculated through a linear least squares programme.

Table I: Lifetimes, Rotational Rates, and Chemical Shift Differences for 3-o-tolyl-5-methylhydantoin (VII) in DMSO-d_6 Solution at Various Temperatures, Calculated with a Linewidth of 1.0 Hz.

Temperature (°C)	Lifetime (sec.)	Standard Error	Rate Constant (sec.-1)	Chemical Shift Difference (Hz)
	Tau A, Collapse of the ortho-methyl Signal			
50.5	0.719	0.023	1.380	3.5
59.0	0.475	0.030	2.105	3.5
63.5	0.474	0.025	2.109	3.5
68.0	0.324	0.031	3.086	3.5
72.5	0.207	0.004	4.870	3.5
80.0	0.141	0.012	7.092	3.5
85.5	0.149	0.012	6.710	3.5
	Tau B, Collapse of the ortho-methyl Signal			
50.5	0.718	0.019	1.301	3.5
59.0	0.473	0.023	2.107	3.5
63.5	0.470	0.022	2.110	3.5
68.0	0.322	0.025	3.091	3.5
72.5	0.200	0.003	4.950	3.5
80.0	0.143	0.013	7.097	3.5
85.5	0.147	0.011	6.920	3.5

Table II: Lifetimes, Rotational Rates, and Chemical Shift Differences for 3-o-tolyl-5-phenylhydantoin(VIII) in DMSO-d_6 Solution at Various Temperatures, Calculated with a Linewidth of 1.0 Hz.

Temperature (°C)	Lifetime (sec.)	Standard Error	Rate Constant ($sec.^{-1}$)	Chemical Shift Difference (Hz)
	Tau A, Collapse of the ortho-methyl Signal			
24.0	2.520	0.012	0.395	14.3
27.0	1.610	0.009	0.619	14.3
44.0	1.100	0.003	0.902	14.3
75.0	0.078	0.011	12.770	14.3
87.0	0.040	0.023	24.870	14.3
94.0	0.028	0.012	34.850	14.3
98.0	0.013	0.007	76.920	14.3
103.0	0.028	0.013	38.080	14.3
107.0	0.017	0.003	57.47	14.3
	Tau B, Collapse of the ortho-methyl Signal			
24.0	1.520	0.013	0.657	14.3
27.0	1.060	0.010	0.940	14.3
44.0	0.780	0.029	1.280	14.3
75.0	0.160	0.012	9.400	14.3
87.0	0.060	0.025	16.666	14.3
94.0	0.041	0.010	24.390	14.3
98.0	0.015	0.008	66.666	14.3
103.0	0.053	0.002	18.650	14.3
107.0	0.028	0.003	35.460	14.3

Table III: Lifetimes, Rotational Rates, and Chemical Shift Differences for 3-(2,3-dimethylphenyl)-5-methylhydantoin (IX) in DMSO-d_6 Solution at Various Temperatures, Calculated with a Linewidth of 1.0 Hz.

Temperature (°C)	Lifetime (sec.)	Standard Error	Rate Constant ($sec.^{-1}$)	Chemical Shift Difference (Hz)
	Tau A, Collapse of the ortho-methyl Signal			
89.0	0.534	0.012	1.872	3.7
103.0	0.320	0.009	3.125	3.7
110.0	0.274	0.003	3.649	3.7
114.0	0.209	0.005	4.784	3.8
118.0	0.153	0.013	6.535	3.9
123.0	0.121	0.017	8.264	3.9
126.0	0.117	0.014	8.547	3.9
129.0	0.128	0.013	7.812	3.9
	Tau B, Collapse of the ortho-methyl Signal			
89.0	0.450	0.033	2.220	3.7
103.0	0.277	0.022	3.610	3.7
110.0	0.238	0.011	4.200	3.7
114.0	0.186	0.003	5.370	3.8
118.0	0.138	0.011	7.240	3.9
123.0	0.109	0.013	9.170	3.9
126.0	0.103	0.004	9.680	3.9
129.0	0.102	0.013	9.800	3.9

Table IV: Lifetimes, Rotational Rates, and Chemical Shift Differences for 3-(2-methyl-4-nitrophenyl)-5-methylhydantoin (X) in DMSO-d_6 Solution at Various Temperatures, Calculated with a Linewidth of 1.0 Hz.

Temperature (°C)	Lifetime (sec.)	Standard Error	Rate Constant ($sec.^{-1}$)	Chemical Shift Difference (Hz)
	Tau A, Collapse of the ortho-methyl Signal			
31.5	0.331	0.012	3.020	3.9c
41.5	0.271	0.007	3.690	3.9
45.5	0.249	0.006	4.010	3.9
50.0	0.199	0.007	5.020	3.9
55.0	0.173	0.004	5.780	3.9
59.0	0.133	0.003	7.510	3.9
63.5	0.113	0.004	8.840	3.9
68.0	0.079	0.005	12.590	3.9
73.0	0.067	0.001	14.880	3.9
	Tau B, Collapse of the ortho-methyl Signal			
31.5	0.294	0.014	3.400	3.9
41.5	0.228	0.008	4.380	3.9
45.5	0.201	0.007	4.970	3.9
50.0	0.177	0.008	5.640	3.9
55.0	0.134	0.005	7.460	3.9
59.0	0.110	0.004	9.090	3.9
63.5	0.083	0.006	11.970	3.9
68.0	0.065	0.006	15.220	3.9
73.0	0.051	0.001	19.490	3.9

Table V: Lifetimes, Rotational Rates, and Chemical Shift Differences for 3-(2-methyl-4-nitrophenyl)-5-methyl-2-thiohydantoin (XI) in DMSO-d_6 Solution at Various Temperatures, Calculated with a Linewidth of 1.0 Hz.

Temperature (°C)	Lifetime (sec.)	Standard Error	Rate Constant ($sec.^{-1}$)	Chemical Shift Difference (Hz)
	Tau A, Collapse of the ortho-methyl Signal			
65.0	0.430	0.002	2.322	5.2
75.0	0.398	0.003	2.512	5.3
84.0	0.353	0.021	2.830	5.5
93.0	0.130	0.013	7.640	5.4
103.0	0.116	0.011	8.550	5.7
110.0	0.114	0.019	8.740	5.3
117.0	0.051	0.003	19.560	5.7
	Tau B, Collapse of the ortho-methyl Signal			
65.0	0.353	0.002	2.830	5.2
75.0	0.339	0.009	2.940	5.3
84.0	0.312	0.002	3.200	5.5
93.0	0.096	0.015	10.330	5.4
103.0	0.087	0.009	11.507	5.7
110.0	0.088	0.017	11.261	5.3
117.0	0.051	0.003	19.305	5.7

Table VI: Lifetimes, Rotational Rates, and Chemical Shift Differences for 3-(4-chloro-2-methylphenyl)-5-methylhydantoin (XII) in DMSO-d_6 Solution at Various Temperatures, Calculated with a Linewidth of 1.0 Hz.

Temperature (°C)	Lifetime (sec.)	Standard Error	Rate Constant ($sec.^{-1}$)	Chemical Shift Difference (Hz)
	Tau A, Collapse of the ortho-methyl Signal			
59.0	0.380	0.002	2.630	3.6
63.0	0.264	0.007	3.780	3.7
68.0	0.192	0.015	5.200	3.4
72.0	0.157	0.021	6.360	3.6
78.0	0.101	0.019	9.900	3.6
82.0	0.100	0.011	9.990	3.6
87.0	0.072	0.002	13.720	3.7
	Tau B, Collapse of the ortho-methyl Signal			
59.0	0.302	0.002	3.310	3.6
63.0	0.239	0.006	4.180	3.7
68.0	0.189	0.023	5.290	3.4
72.0	0.138	0.019	7.240	3.6
78.0	0.100	0.017	9.910	3.6
82.0	0.079	0.009	12.56	3.6
87.0	0.056	0.002	17.62	3.7

Table VII: Lifetimes, Rotational Rates, and Chemical Shift Differences for 3-(4-chloro-2-methylphenyl)-5-phenylhydantoin (XIII) in DMSO-d_6 Solution at Various Temperatures, Calculated with a Line-width of 1.2 Hz.

Temperature (°C)	Lifetime (sec.)	Standard Error	Rate Constant ($sec.^{-1}$)	Chemical Shift Difference (Hz)
		Tau A, Collapse of the ortho-methyl Signal		
31.0	2.460	0.003	0.405	14.3
57.0	0.955	0.025	1.046	14.3
65.0	0.440	0.015	2.242	14.3
75.0	0.227	0.009	4.400	14.3
84.0	0.095	0.003	10.510	14.3
89.0	0.075	0.002	12.570	14.3
		Tau B, Collapse of the ortho-methyl Signal		
31.0	1.710	0.003	0.583	14.3
57.0	0.723	0.023	1.380	14.3
65.0	0.342	0.017	2.920	14.3
75.0	0.173	0.009	5.750	14.3
84.0	0.072	0.003	13.860	14.3
89.0	0.053	0.002	15.840	14.3

Table VIII: Lifetimes, Rotational Rates, and Chemical Shift Difference for 3-(2-chlorophenyl)-5-phenylhydantoin (XIV) in DMSO-d_6 Solution at Various Temperatures, Calculated with a Linewidth of 1.6 Hz.

Temperature (°C)	Lifetime (sec.)	Standard Error	Rate Constant ($sec.^{-1}$)	Chemical Shift Difference (Hz)
		Tau A, Collapse of the C-5 Proton Signal		
64.0	3.780	0.002	0.264	7.5c
75.0	1.920	0.015	0.520	7.5
119.0	0.237	0.013	4.219	7.5
128.0	0.160	0.027	6.230	7.5
134.0	0.113	0.003	8.840	7.5
		Tau B, Collapse of the C-5 Proton Signal		
64.0	4.030	0.002	0.248	7.5
75.0	2.210	0.013	0.452	7.5
119.0	0.228	0.011	4.380	7.5
128.0	0.144	0.028	6.940	7.5
134.0	0.097	0.001	10.230	7.5

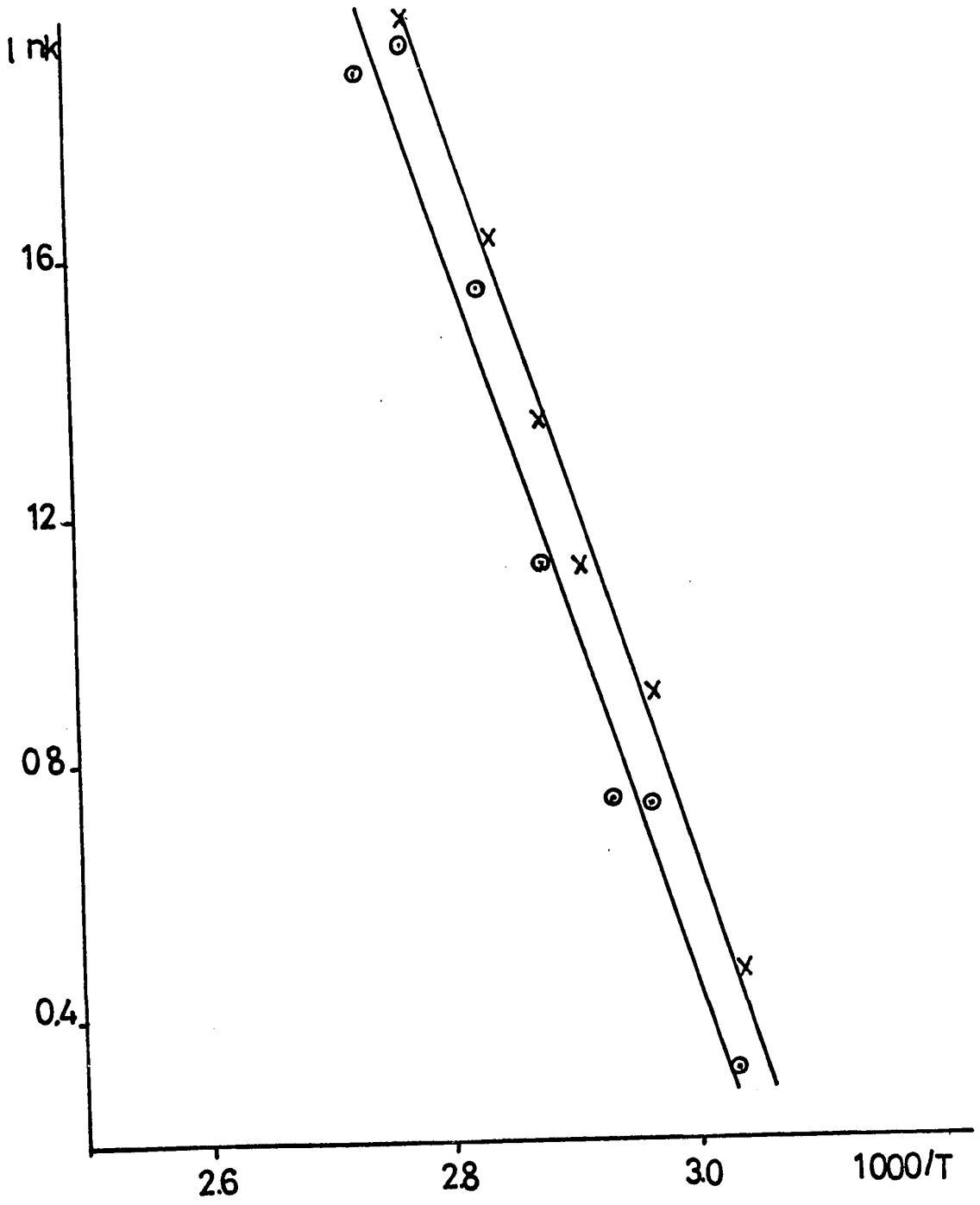


Figure 10: Arrhenius Plots for 3-(2-methylphenyl)-5-methylhydantoin (VII) in DMSO-d_6 Solution. Tau A = 0, Tau B = x.

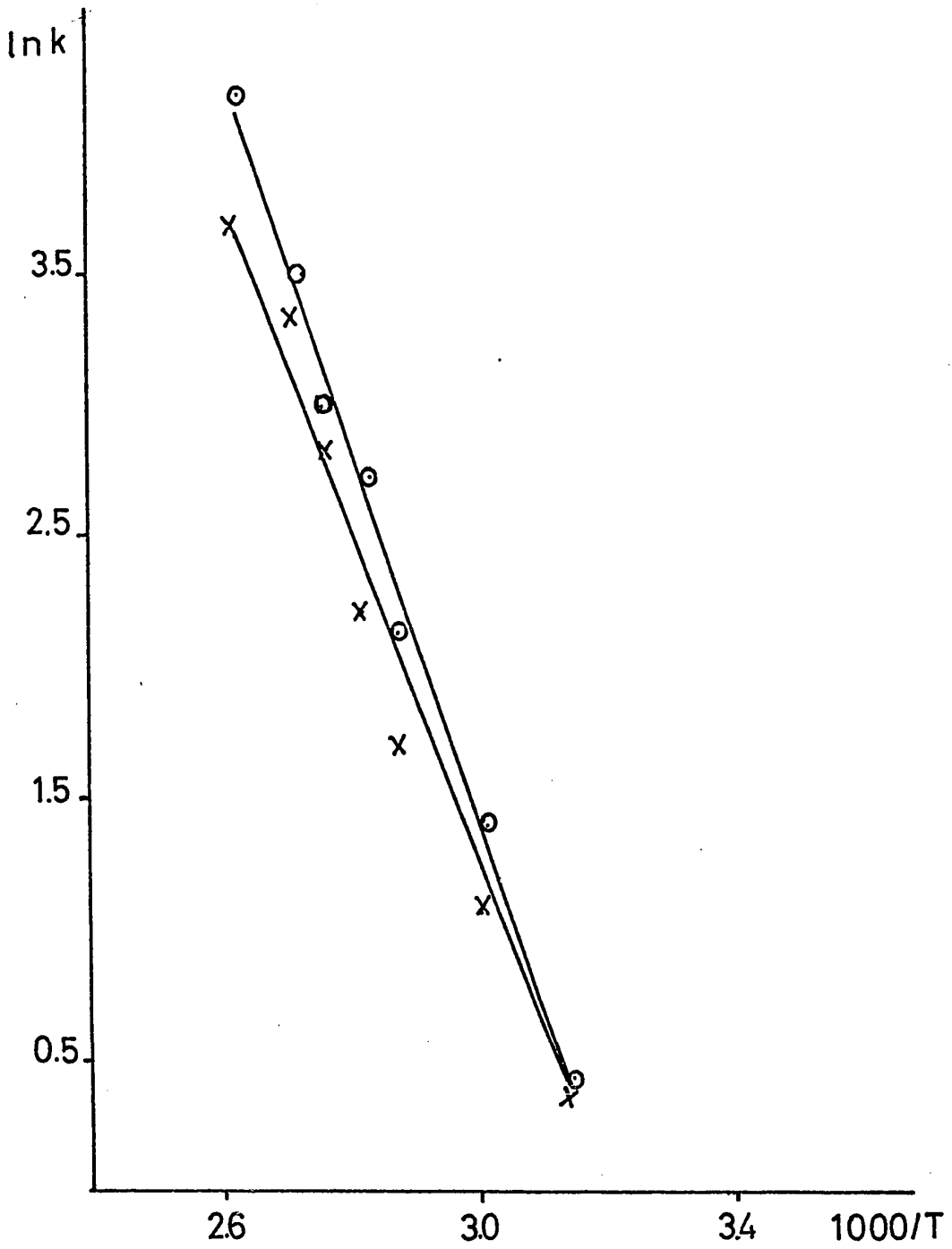


Figure 11: Arrhenius Plots for 3-(2-methylphenyl)-5-phenylhydantoin (VIII) in DMSO-d_6 Solution. Tau A = O, Tau B = x.

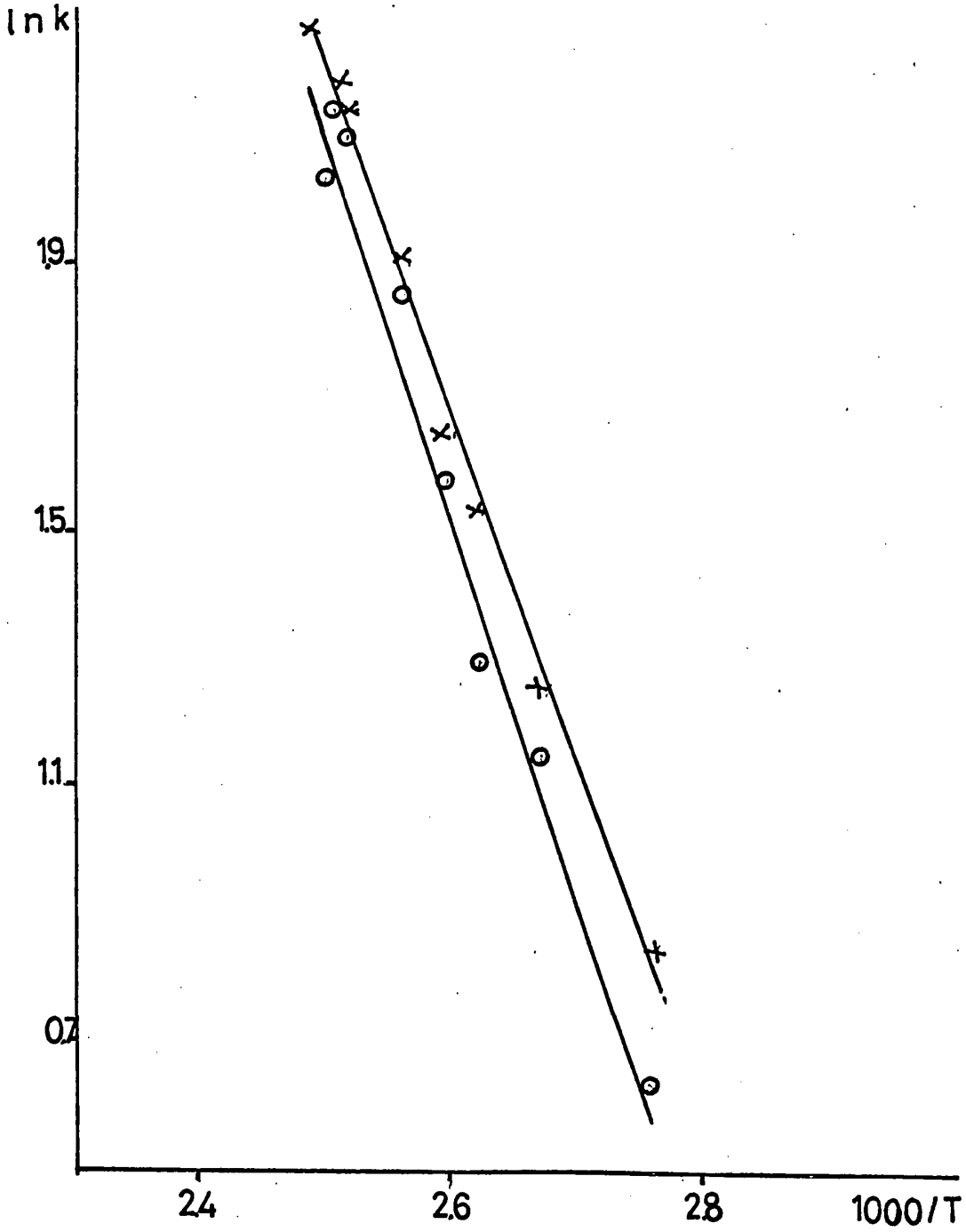


Figure 12: Arrhenius Plots for 3-(2,3-dimethylphenyl)-5-methylhydantoin (IX) in DMSO-d_6 Solution. Tau A = 0, Tau B = x.

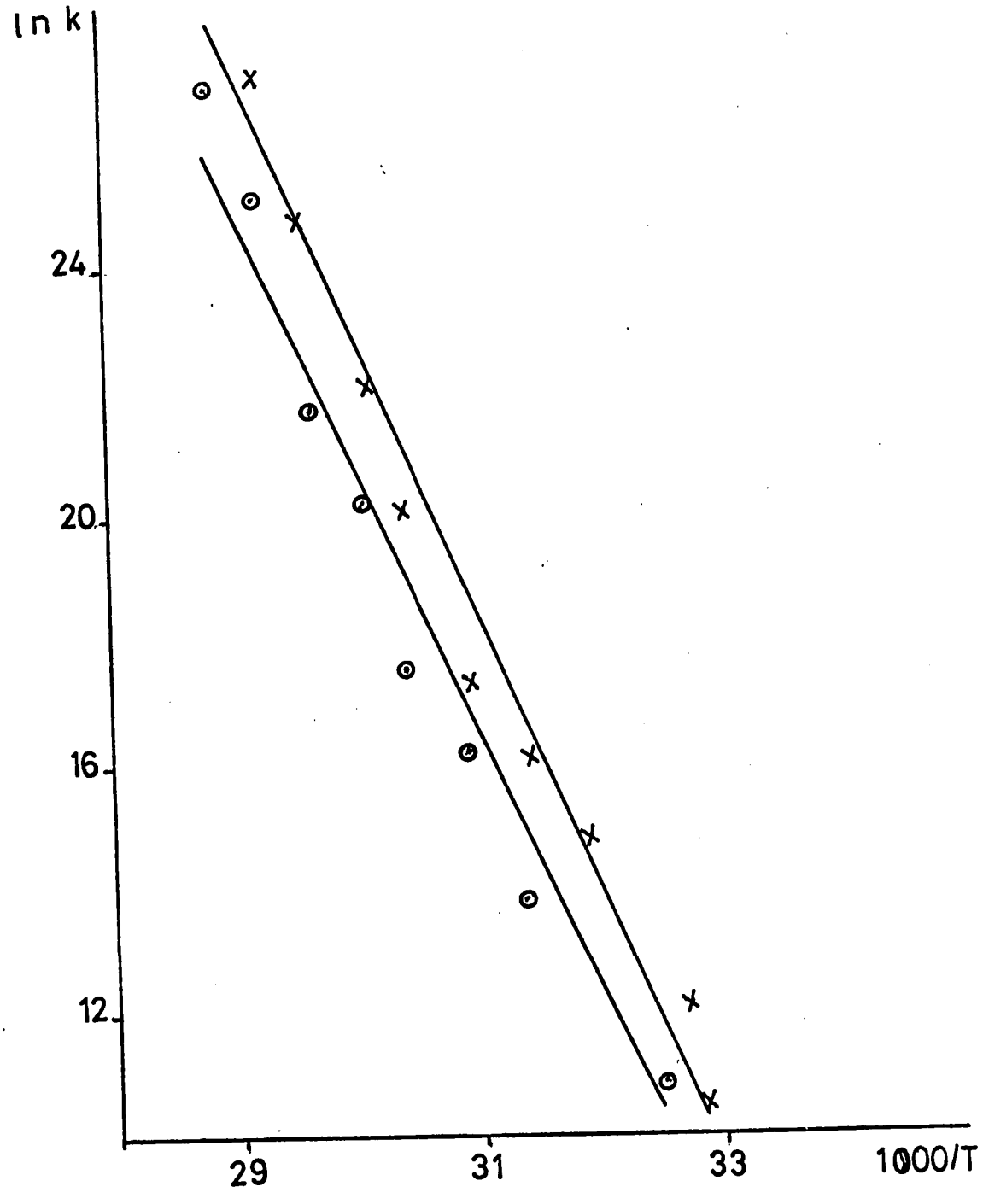


Figure 13: Arrhenius Plots for 3-(2-methyl-4-nitrophenyl)-5-methylhydantoin (X) in DMSO-d_6 Solution. Tau A = O, Tau B = x.

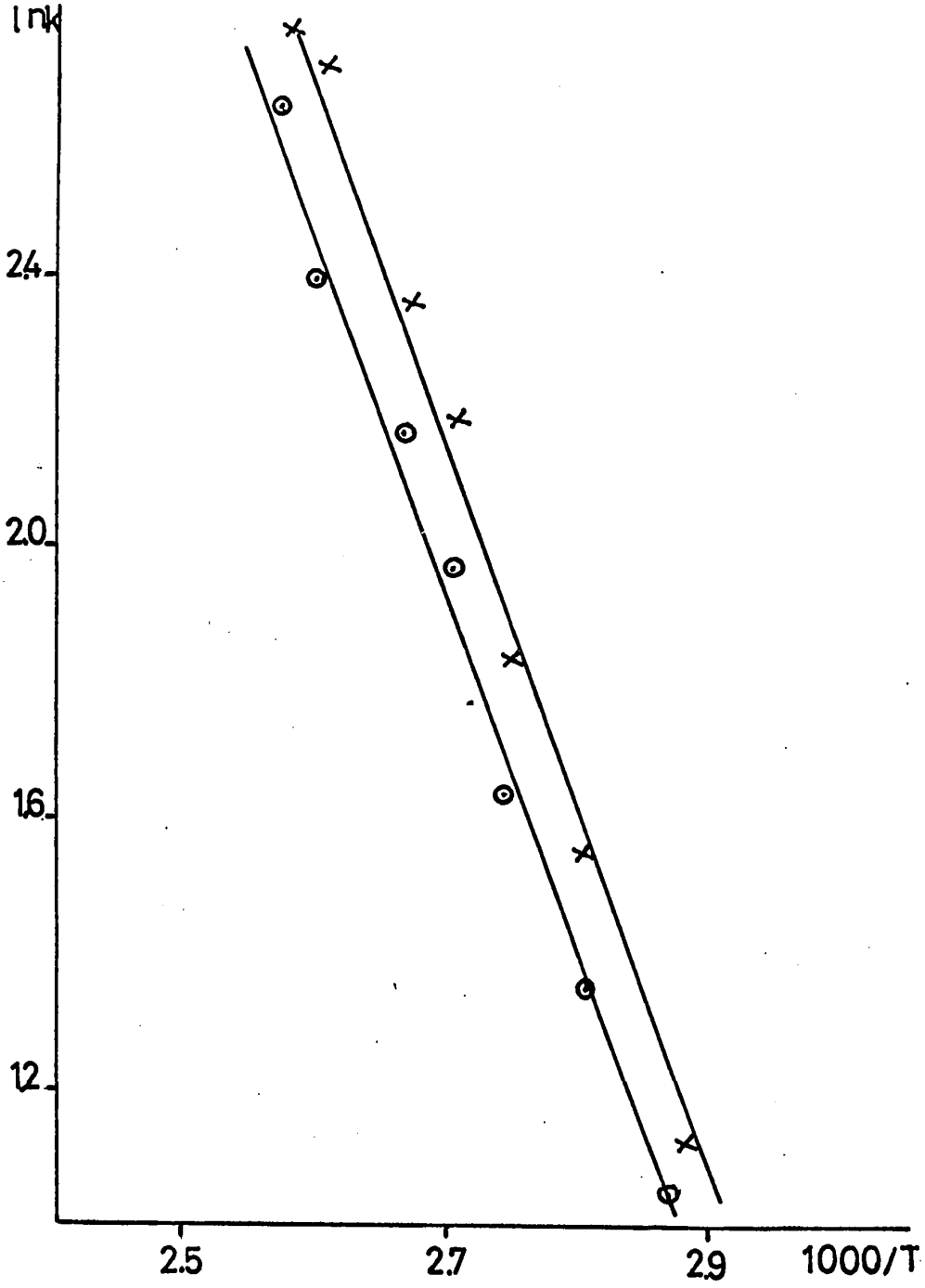


Figure 14: Arrhenius Plots for 3-(2-methyl-4-nitrophenyl)-5-methyl-2-thiohydantoin (XI) in DMSO-d_6 Solution. Tau A = 0, Tau B = x.

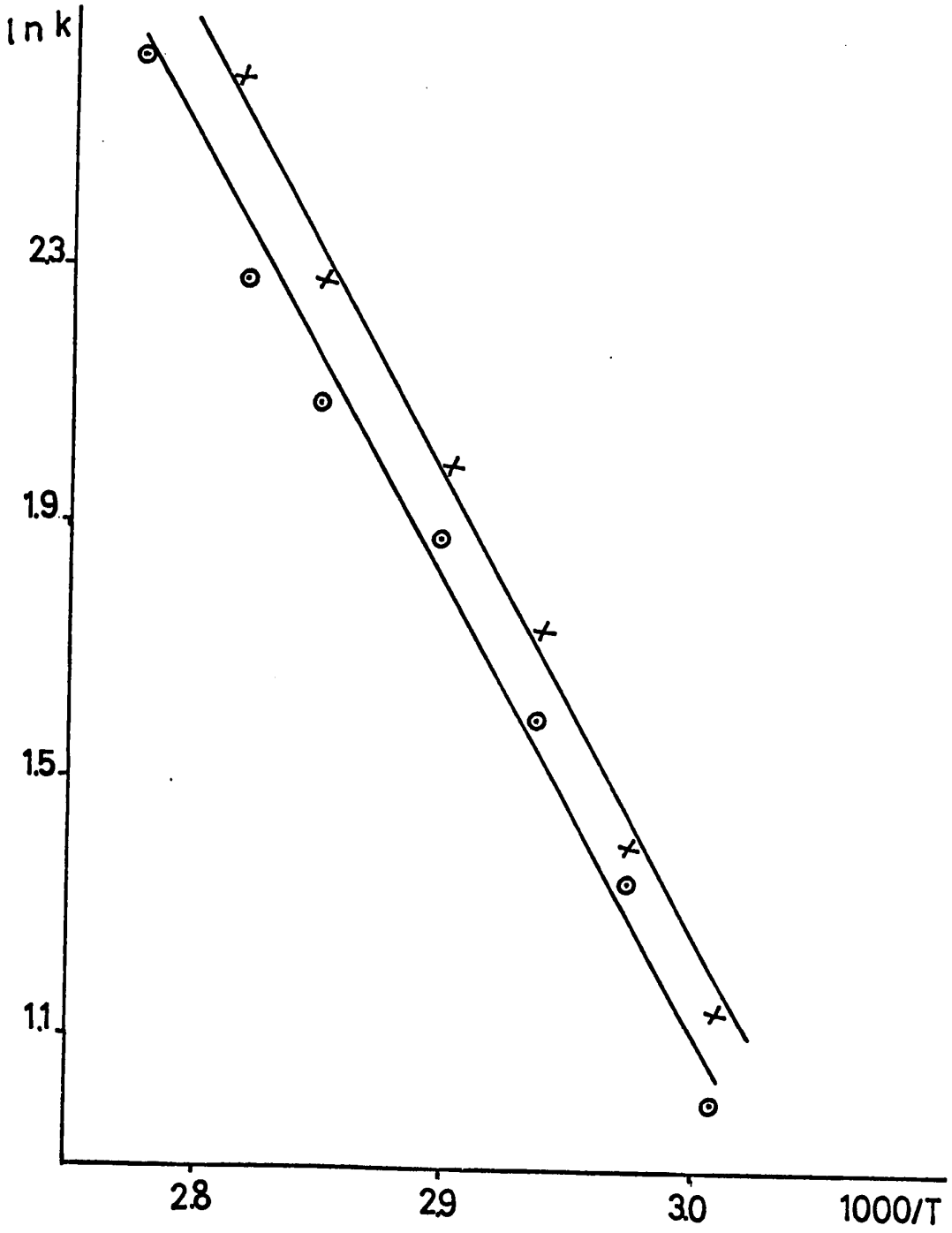


Figure 15: Arrhenius Plots for 3-(4-chloro-2-methylphenyl)-5-methylhydantoin (XII) in DMSO-d_6 Solution. Tau A = 0, Tau = x.

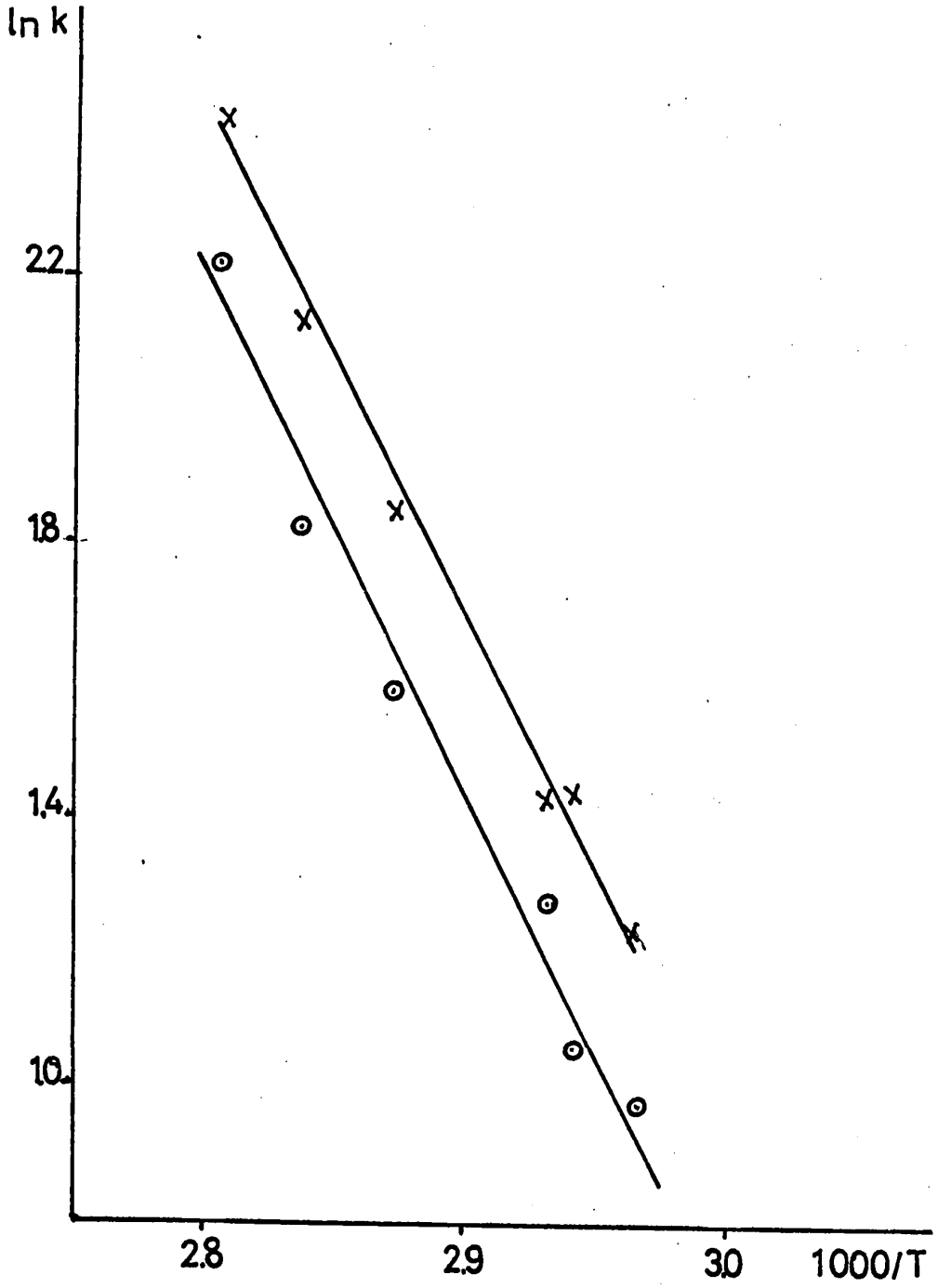


Figure 16: Arrhenius Plots for 3-(4-chloro-2-methylphenyl)-5-phenylhydantoin (XIII) in DMSO-d_6 Solution. Tau A = 0, Tau B = x.

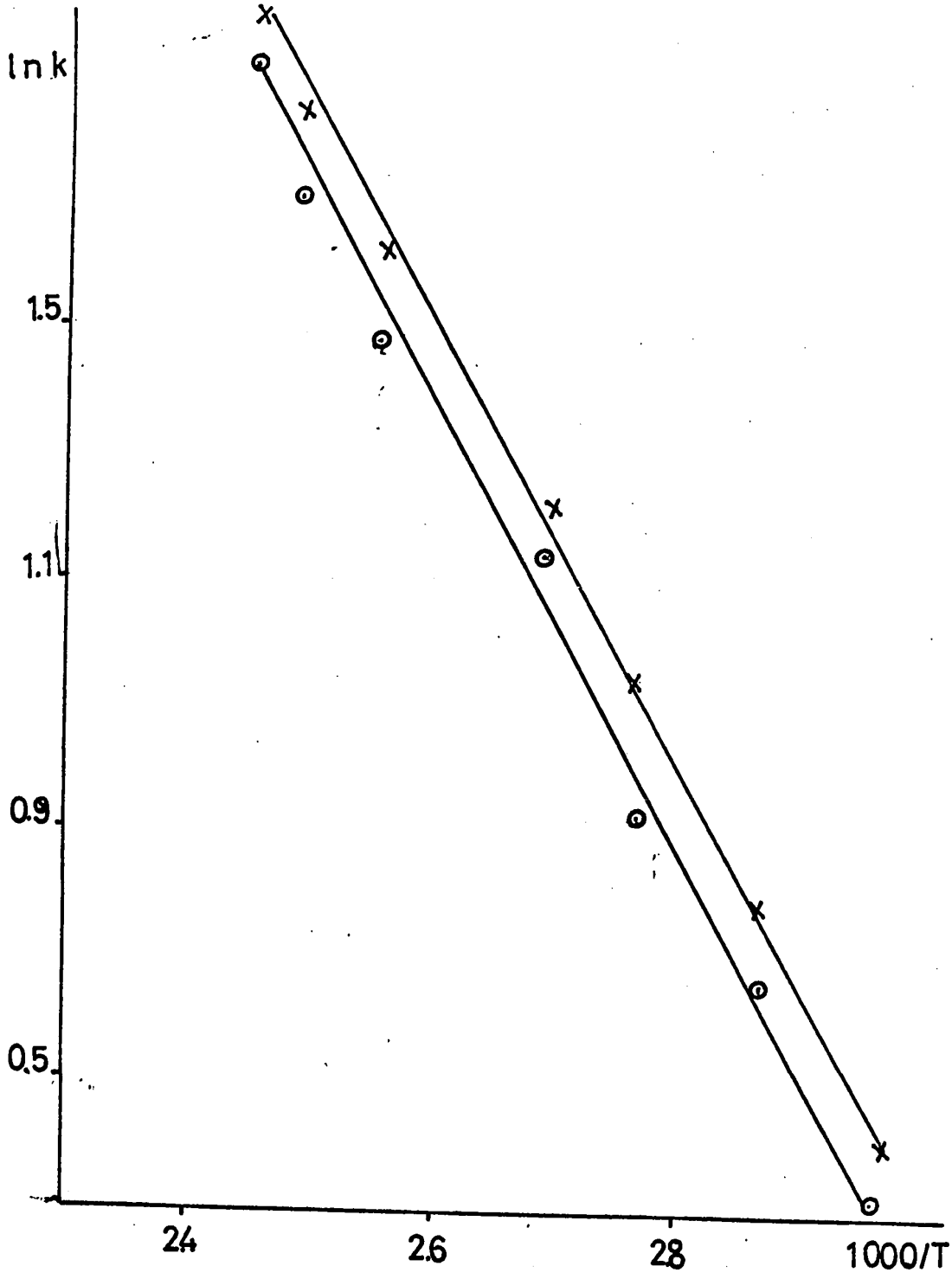
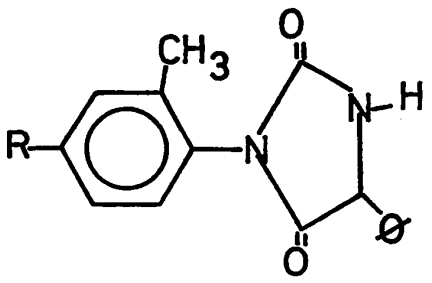


Figure 17: Arrhenius Plots for 3-(2-chlorophenyl)-5-phenylhydantoin (XIV) in DMSO-d_6 Solution. Tau A = 0, Tau B = x.

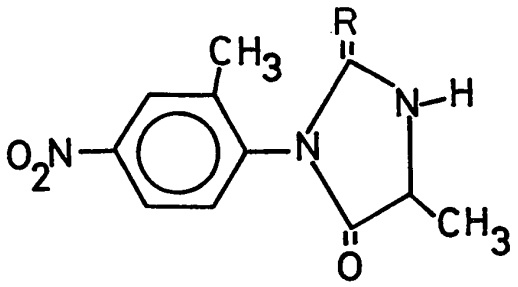
Table IX: Kinetic and Thermodynamic Parameters for Rotation Around the C-N Aryl Bond for Some 3-Aryl Substituted Hydantoins in DMSO-d_6 Solution.



VIII, R = H
XIII, R = Cl

Compound		Ea (kcal/mole)	$\Delta H^{\ddagger}(25^{\circ})$ (kcal/mole)	$\Delta G^{\ddagger}(25^{\circ})$ (kcal/mole)	$\Delta S^{\ddagger}(25^{\circ})$ (e.u.)	K (25°)
VIII	τ_A	12.5 ± 0.7	12.4 ± 0.7	18.0 ± 0.1	- 22.^{0} ± 2.0	0.61
	τ_B	11.9 ± 0.7	11.7 ± 0.7	17.8 ± 0.1	- 22.^{9} ± 2.0	
XIII	τ_A	13.0 ± 0.8	12.4 ± 0.8	18.4 ± 0.1	- 20.^{0} ± 2.0	0.70
	τ_B	12.6 ± 0.5	12.4 ± 0.5	18.2 ± 0.1	- 21.^{0} ± 2.0	

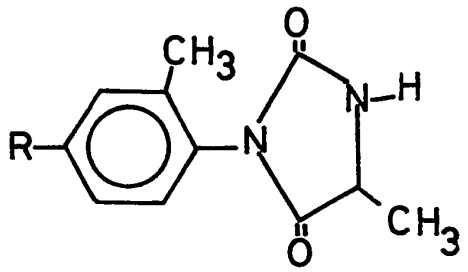
Table X: Kinetic and Thermodynamic Parameters for Rotation Around the C-N Aryl Bond for Some 3-Aryl substituted Hydantoins in DMSO-d_6 Solution.



X, R = O
XI, R = S

Compound		Ea (kcal/mole)	$\Delta H^{\ddagger}(25^{\circ})$ (kcal/mole)	$\Delta G^{\ddagger}(25^{\circ})$ (kcal/mole)	$\Delta S^{\ddagger}(25^{\circ})$ (e.u.)	K (25°)
X	τ_A	8.5 ± 0.8	7.0 ± 0.7	17.1 ± 0.1	- $31.^{8}$ ± 2.0	0.90
	τ_B	9.1 ± 0.7	8.5 ± 0.8	17.0 ± 0.1	- $28.^{3}$ ± 2.0	
XI	τ_A	10.5 ± 0.8	9.9 ± 0.7	18.3 ± 0.1	- $28.^{1}$ ± 2.1	
	τ_B	10.4 ± 0.7	9.7 ± 0.9	18.2 ± 0.1	- $28.^{0}$ ± 2.2	

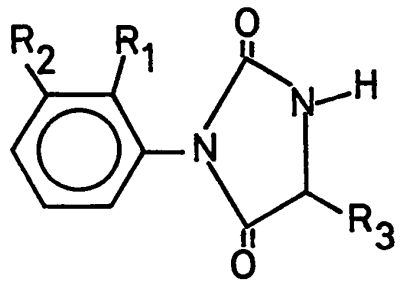
Table XI: Kinetic and Thermodynamic Parameters for Rotation Around the C-N Aryl Bond for Some 3-Aryl Substituted Hydantoins in DMSO-d_6 Solution.



VII, R = H
XII, R = Cl

Compound	Ea (kcal/mole)	$\Delta H^{\ddagger}$(25°) (kcal/mole)	$\Delta G^{\ddagger}$(25°) (kcal/mole)	$\Delta S^{\ddagger}$(25°) (e.u.)	K (25°)
VII τ_A	11.7 ± 0.9	11.1 ± 0.9	18.0 ± 0.1	- 24.^{7} ± 2.0	1.00
VII τ_B	11.7 ± 0.9	11.1 ± 0.9	18.0 ± 0.1	- 23.^{0} ± 2.0	
XII τ_A	13.7 ± 0.8	13.1 ± 0.7	18.2 ± 0.1	- 17.^{1} ± 2.0	1.00
XII τ_B	14.2 ± 0.4	13.6 ± 0.4	18.2 ± 0.1	- 15.^{3} ± 2.0	

Table XII: Kinetic and Thermodynamic Parameters for Rotation Around the C-N Aryl Bond for Some 3-Aryl Substituted Hydantoins in DMSO-d_6 Solution.



IX, $R_1 = CH_3$, $R_2 = CH_3$, $R_3 = CH_3$
XIV, $R_1 = Cl$, $R_2 = H$, $R_3 = C_6H_5$

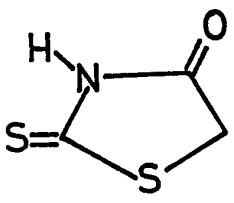
Compound		Ea (kcal/mole)	$\Delta H^{\ddagger}(25^{\circ})$ (kcal/mole)	$\Delta G^{\ddagger}(25^{\circ})$ (kcal/mole)	$\Delta S^{\ddagger}(25^{\circ})$ (e.u.)	K (25°)
XIV	τ_A	13.4 ± 0.5	12.8 ± 0.5	19.8 ± 0.1	$-23.^{3} \pm 2.0$	1.35
	τ_B	14.3 ± 0.7	13.7 ± 0.7	19.9 ± 0.1	$-21.^{2} \pm 2.0$	
IX	τ_A	11.7 ± 0.8	11.1 ± 0.8	19.2 ± 0.1	$-27.^{4} \pm 2.0$	0.85
	τ_B	11.6 ± 0.8	11.1 ± 0.8	19 1 ± 0.1	$-27.^{1} \pm 2.0$	

DISCUSSION

Stereochemistry of the Hetero Ring

The decision to study 3-aryl substituted hydantoins was made in the hope that this would be a simpler system to interpret than other N-aryl substituted amide systems, because of the fact that hydantoins are assumed to be planar or near planar molecules. Therefore, problems associated with the heterocyclic ring inversion are expected to be absent. Further, being cyclic amides, hydantoins have a system which is easier to interpret than acyclic compounds because of the prearrangement of the substituents that the aryl ring must pass during rotation.

Indirect spectroscopic evidence of the planarity of the hydantoin is discussed in a paper by van der Helm et al..[20] Through x-ray spectroscopy this group found rhodanine, a molecule very similar to the hydantoin molecule, to be planar. A more recent x-ray crystallographic



rhodanine

study of 2-thiohydantoin has shown that this molecule is also planar.[21] In addition substituents on the aryl

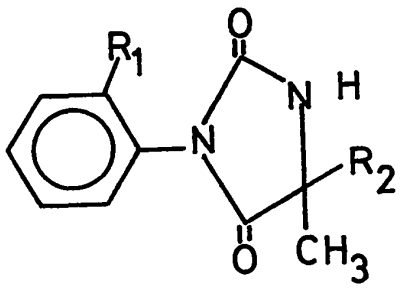
ring must pass a carbonyl or thionyl group during rotation, and the difference between the transition states and the ground states depend upon the primary effects due to the nature or size of these groups.

Secondary effects on the barrier of rotation could arise because of different groups in the 1 and 5 positions. Since in all cases the 1 position was unsubstituted, the effect of a substituent on this position can be ignored in this study. It was expected that the substituents on the 5 position would cause little buttressing effect since they are not coplanar with the C-4 carbonyl group. Further the carbonyl group, having a partial double bond, would be resistant to bending by the C-5 substituents. It is possible that while the C-5 substituents do not evidently affect the transition state they can affect the ground states of the interconvertible rotamers. Fehlner found indeed that the equilibrium constants of some hydantoins do differ, although slightly, from unity, as can be seen in Table XIII.

The degree of planarity of the hydantoin molecule is enhanced by two factors. Since the ring is five membered it will be much flatter than a six membered ring, and the partial double bond character of the C-N bond caused by the amide resonance would help to constrain the ring.

It can be seen that eight electrons, four from the

Table XIII: Kinetic and Thermodynamic Parameters for Rotation Around the C-N Aryl Bond for some 3-Aryl Substituted Hydantoins in DMSO-d_6 Solution.[7]

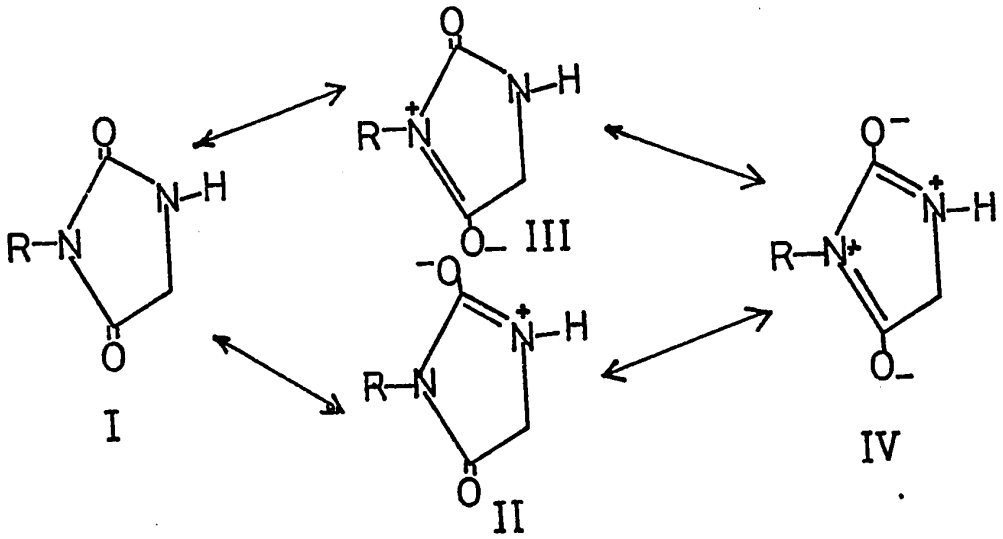


XXX, $R_1 = CF_3$, $R_2 = H$
XXXI, $R_1 = CH_3$, $R_2 = CH_3$
XXXII, $R_1 = Cl$, $R_2 = H$

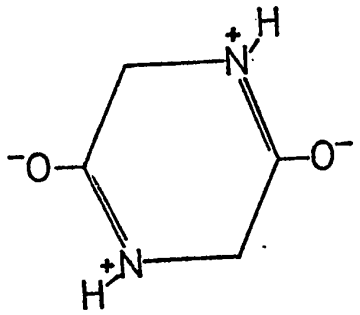
Compound	Ea (kcal/mole)	$\Delta H^{\ddagger}$ (25°) (kcal/mole)	$\Delta G^{\ddagger}$ (25°) (kcal/mole)	$\Delta S^{\ddagger}$ (25°) (e.u.)	K (25°)
XXX§ τ_A	16.4 ± 0.9†	15.8	20.80	- 16.7	1.01
τ_B	16.9 ± 0.9†	16.3	20.80	- 15.0	
XXXI			16.97		
XXXII τ_A	14.7 ± 0.7†	14.1	19.33	- 17.5	1.18
τ_B	15.0 ± 0.6†	14.4	19.23	- 16.4	

§ 2-Chloropyrydine Solution
† Standard Deviation

two nitrogens, four from the two carbonyl groups, contribute to the different resonance forms of the hetero ring.



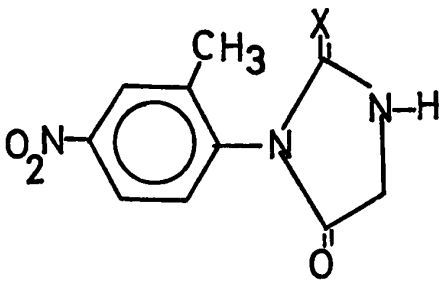
It is probable that the canonical forms II, III, and IV make a significant contribution to the electronic structure of hydantoins. This assumption is supported by the work of Corey,[22] who found that the resonance form shown below is a major contributor to the structure of 2,5-diketopiperazine, a molecule very similar to hydantoin.



2,5-diketopiperazine

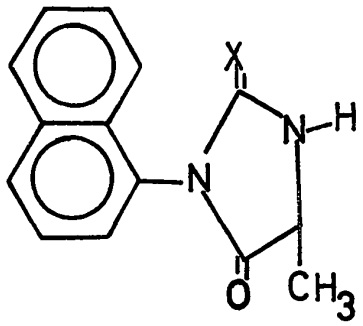
Relative Influence of Carbonyl and Thiocarbonyl Groups

A comparison of the kinetic data for the compounds X and XI, shows that the $\Delta G^{\ddagger}$ value for the thiohydantoin



X, X = O
XI, X = S

is larger than the corresponding parameter for the hydantoin, (18.3 ± 0.13 kcal/mole versus 17.1 ± 0.12 kcal/mole). This enhancement of the $\Delta G^{\ddagger}$ value when the oxygen atom in the 2 position is substituted by a sulphur atom, had already been observed by Fehlner[7] for 3-α-naphthyl-5-methylhydantoin.



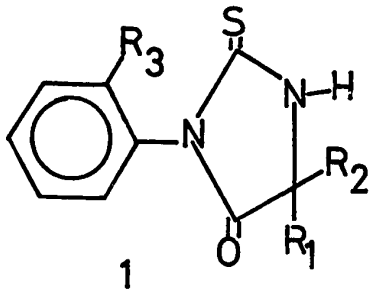
3-α-naphthyl-5-methylhydantoin X = O
3-α-naphthyl-5-methyl-2-thiohydantoin X = S

He found that while the $\Delta G^{\ddagger}$ value for the thiohydantoin was 25.5 ± 0.1 kcal/mole, it was only 18.3 ± 0.1 kcal/mole for the corresponding hydantoin. This effect can be explained as follows.

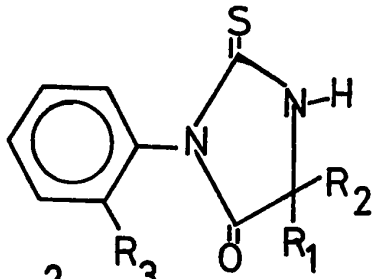
Because of its greater size, sulphur tends to be less electronegative (2.5) than oxygen (3.5).[23] Therefore one might expect a decrease of the dipole moment in compounds where the oxygen of the carbonyl group is substituted by sulphur. However, this is not the case. Mautner et al.[24,25,26] have shown that the dipole moment of the thiocarbonyl group is always greater than the corresponding carbonyl analogue. They attribute this to a greater contribution of the ionic form $\overset{+}{C}-\overset{-}{S}$ in the thiocarbonyl group than the $\overset{+}{C}-\overset{-}{O}$ form in the carbonyl group. This is confirmed by infrared data.[27,28]

The greater single bond character in the thiocarbonyl group is reflected in the bond length of this group. While the carbonyl length is only about 77% of the length of the single C-O bond, the thiocarbonyl bond length is about 88% of the analogous C-S bond.[29] It has been suggested that the greater contribution of the ionic form in the thiocarbonyl group can be due to the ability of the 3d orbitals of sulphur to accept electrons and stabilize the C-S state.[30] As a consequence of the greater length of the C-S bond, a stronger steric interaction occurs between the sulphur atom and the groups in the ortho positions in the transition state during the rotational process, which causes a larger barrier of rotation than in the corresponding carbonyl compound. It has been suggested,[31] that in the 3-aryl-2-thiohydantoins the more

bulky ortho substituent must pass the carbonyl oxygen atom in the transition state for rotation rather than the more bulky sulphur atom, i.e. the preferred transition state is 2 rather than 1.



1



2

This hypothesis, although quite plausible does not appear to be adequate to explain the large difference in the effect on the rotational barrier when sulphur is substituted in the 2 position, e.g. about 7 kcal/mole in the case of 3-α-naphthyl-5-methylhydantoin and about 1.3 kcal/mole in the case of compound X.

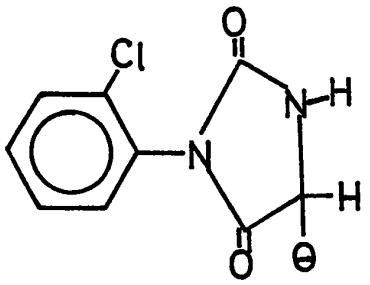
From a consideration of the data accumulated so far, it is evident that more information is needed in order that the nature of the rotational barrier in thiohydantoins can be understood.

Relative Influence of the Chlorine Atom and the Methyl Group

It has been commonly observed,[32,33] that a methyl group exerts a steric effect greater than that of a chlorine atom, for example in restricting internal rotation

in hindered biphenyls.[32] This order is consistent with the size of these groups as determined by x-ray crystallographic measurements of van der Waals radii.[34]

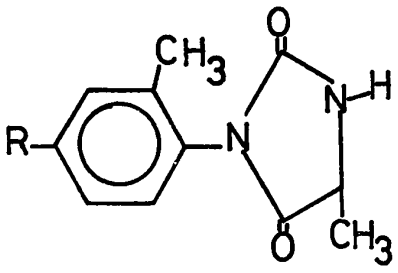
Nevertheless, the $\Delta G^{\ddagger}$ of rotation around the C-N bond was found in the case of 3-(2-chlorophenyl)-5-phenylhydantoin (XIV) to be 19.8 ± 0.1 kcal/mole compared to only 18.0 ± 0.1 kcal/mole for 3-(2-methylphenyl)-5-phenylhydantoin (VIII), or about 2 kcal/mole greater. Therefore, if the chlorine atom is less bulky than the methyl group,



XIV

the difference in the value of $\Delta G^{\ddagger}$ must be due to electronic effects.

For the investigation of the electronic effects on the barrier of rotation of hydantoins, the following compounds were prepared in an attempt to distinguish between field effects and resonance effects:



VII, R = H
X, R = NO_2
XII, R = Cl[2]

Their free energies of activation for rotation are:

VII,	18.0 ± 0.1 kcal/mole
X,	17.1 ± 0.1 kcal/mole
XII,	18.2 ± 0.1 kcal/mole

Since both the nitro group and the chlorine atom are electron withdrawing, one might expect them to influence the barrier of rotation in the same way. However, this is not the case. While the nitro group lowers the barrier of rotation by about 1 kcal/mole, the chlorine atom either does not affect it, or affects it only slightly, 0.2 kcal/mole.

To explain this, one must consider the fact that while the nitro group and the chlorine atom have the same field effect, their resonance behaviour is completely different. Under the term field effects one includes the different effects due to a polar substituent:

a) The influence through space by the electric dipole field created by a polar substituent.

b) The polarization of a π system by an electrostatic charge due to the polar substituent, or inductoelectronic effect.[35]

c) The inductive effect transmitted through the σ bonds.

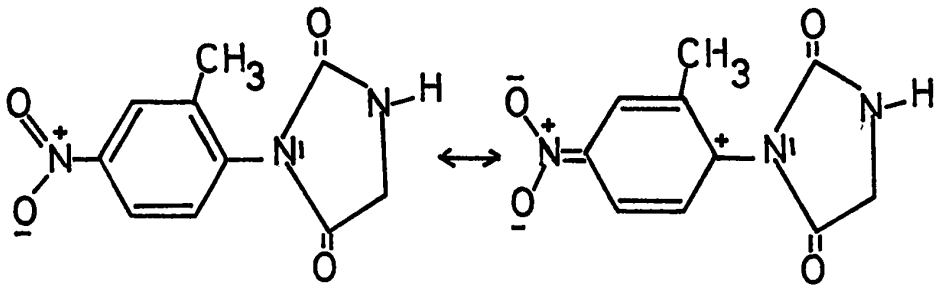
Under the name of resonance effects one considers:

a) The mesomeric effect.

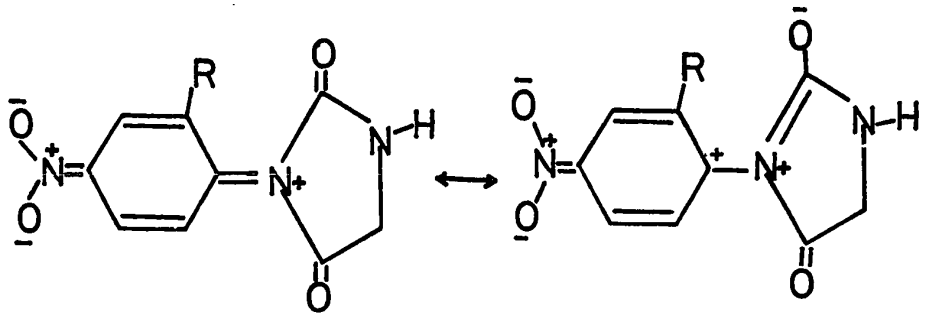
b) Mutual conjugation between the substituent and the reaction center through an intervening conjugated system.

Further, one must consider the fact that while the field effects due to a substituent in the para position on the aryl ring can operate in both the transition state and ground state, the resonance effects due to the same substituent can operate only in the transition state, since only in this state are the phenyl ring and the hydantoin ring coplanar and their mutual conjugation is possible. However, this resonance must not be confused with the amide resonance of the hydantoin ring. Since the hydantoin ring is planar, the amide resonance is present both in the ground and in the transition state for rotation.

If one considers the transition state of the para nitro compound, one can see that because of the presence of the nitro group the following resonance hybrids are possible.



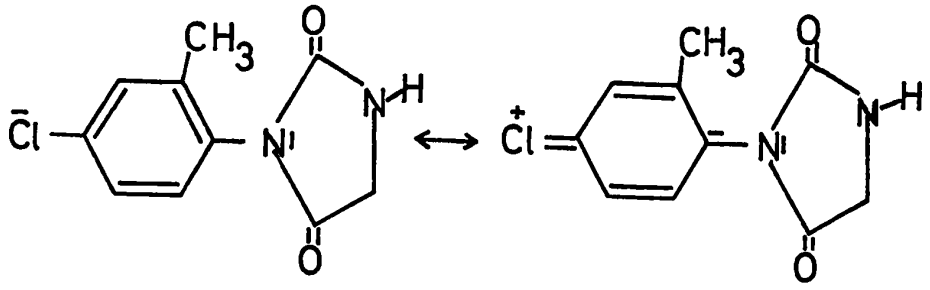
This makes the lone pair of electrons of the nitrogen atom in the 3 position less free to participate in the amide resonance with the carbonyl in the 2 position, thereby favoring a larger contribution of the resonance form α at the expense of β.



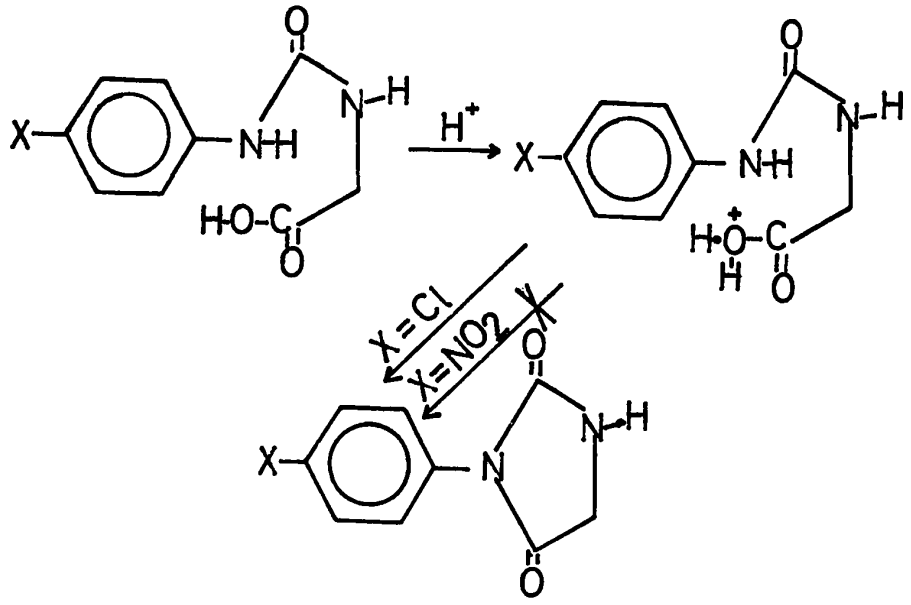
α β

It follows that the carbonyl groups in the 2 and 4 position will have more double bond character and the C=O bond will be shorter than in the unsubstituted compound. Being shorter, the carbonyls will interact less with the methyl group in the ortho position and consequently the energy of the transition state will be lowered. Further, the aryl C-N bond will be shorter.

However, the chlorine atom produces a resonance condition that makes the carbon atom attached to the nitrogen in the 3 position more negative, which could probably disfavor the conjugation of electrons with the phenyl ring, making them freer to participate in the amide resonance.



As evidence of this one can see that while the cyclization of the hydantoic acid, which involves the participation of the electron pair on the nitrogen in the 3 position, is possible and facile when the substituent on the <u>para</u> position is a chlorine atom, it becomes very difficult or impossible when the substituent is a nitro group.

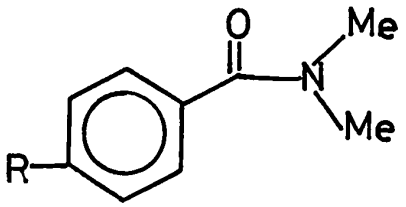


Thus it follows that when the substituent is a chlorine atom the resonance form β will be enhanced, with consequent lengthening of the carbonyl bonds and raising of the energy of the transition state relative to the nitro substituted compound.

When only field effects are involved, the nitro group and the chlorine atom exhibit similar behaviour since they are both electron withdrawing groups. When they are in the para position, they tend to make the aryl carbon atom attached to the nitrogen in the 3 position more positive, which alters the π system of the amide resonance in the hydantoin ring by an inductoelectronic effect. The electrons of the nitrogen in the 3 position are now less free and tend to be more attracted to this atom. Consequently the carbonyl bond in the 2 position will be shorter and the energy of the transition state lowered, since the interaction of the carbonyl and the substituent on the aryl ring will be less than in the case of an unsubstituted compound.

In contrast to the resonance effects, the inductoelectronic effect can alter the ground state as well. Since it interferes with the amide resonance of the hydantoin ring, one can suggest that it raises the energy of the ground state slightly, although this has still to be proved.

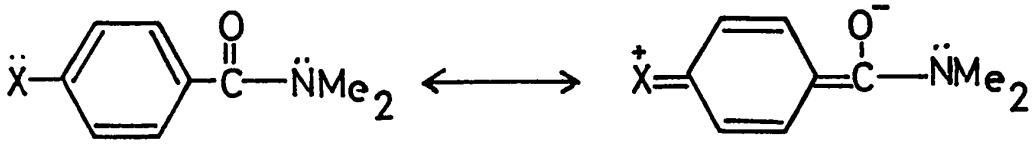
It is interesting to note that Spaargaren and coworkers investigated the electronic effects on the barrier of rotation of the amide C-N bond in several N,N-dimethylbenzamides and obtained similar results.[36] They prepared among others, the following compounds:



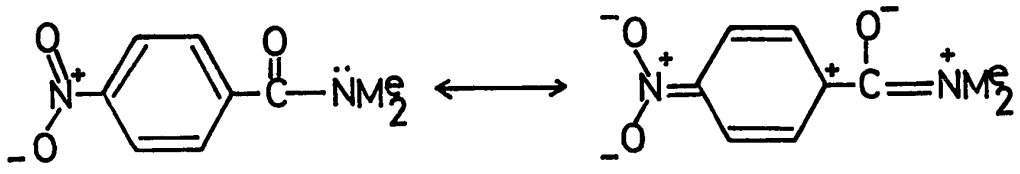
XV, R = H
XVI, R = NO_2
XVII, R = Br
XVIII, R = F

The resonance effects of a nitro group and of a halogen atom on the rotational barrier in the N,N-dimethylbenzamides should be similar but opposite to the resonance effects in the case of the corresponding hydantoins. This is due to the fact that while in the hydantoins the barrier of rotation is increased by a group which lenghthens the C=O bond in the 2 position, in the N,N-dimethylbenzamides the barrier of rotation is increased by each group which increases the double bond character of the C-N bond.

If one considers a N,N-dimethylbenzamide with a halogen atom in the <u>para</u> position, it can be seen that due to this atom the following resonance is possible:



This resonance causes the C-N bond to have less double bond character and consequently raises the energy of the ground state, thereby lowering the barrier of rotation. In the case of the nitro substituent the opposite is true. In this case the resonance condition is more likely to be the following:



XVI

The nitro group enhances the double bond character of the C-N bond, lowering the energy of the ground state and consequently raising the barrier of rotaton.

The experimental results by Spaargaren et al.[36], obtained by total line shape analysis, confirm this hypothesis as shown below:

Table XIV: Free Energies of Activation of Rotation of Some N,N-dimethylbenzamides.

Compound	Free Energy of Activaiton
XV	15.67 kcal/mole
XVI	16.35 kcal/mole
XVII	15.58 kcal/mole
XVIII	15.54 kcal/mole

Field and Resonance Contribution to the Barrier of Rotation of 3-Aryl Substituted Hydantoins.

After determining the $\Delta G^{\ddagger}$ values of different hydantoins an attempt was made to determine what percentage of the variation in $\Delta G^{\ddagger}$ was due to field effects and what percentage was due to the resonance effects, since only these two phenomena must be taken into account when considering the influence of a substituent removed by at least three carbon atoms from the center of reaction.[37]

According to Swain and Lupton,[38] the effect of a substituent is given by a constant σ, which is a combination of the constants F, due to the field, and R, due to the

resonance :

$$\sigma = f'F + r'R$$

where F and R are different for each substituent, (Cl, H, NO_2), and f' and r' are empirical sensitivities or weighting factors independent of substituents but different for each system. It follows that the free energy of rotation $\Delta G^{\ddagger}$ can be obtained simply by:

$$\Delta G^{\ddagger} = - 2.303RT(r'R + f'F) + \Delta G^{\ddagger}_{o}$$

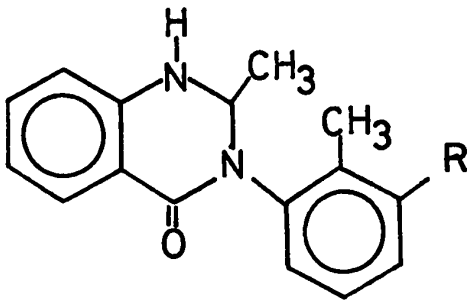
if the temperature is considered a constant equal to 298^{o} , one can rewrite the above equation as:

$$\Delta G^{\ddagger} = rR + fF + \Delta G^{\ddagger}_{o}$$

This equation was used in this work for determining the constant r and f for this type of rotation. Unfortunately the series of hydantoins studied so far was too small to give reliable results. The only conclusion possible was that while the chorine atom in the ortho position exerts a greater interaction with the carbonyl in the 2 position than a methyl group, the chlorine atom in the para position tends to have little or no effect on the barrier of rotation because the resonance effects and the field effects cancel each other since F and R for the chlorine atom have opposite sign.

Buttressing Effect

The effective size of the ortho substituent on the aryl ring may be increased by preventing it from bending backwards in the transition state by putting another substituent in the meta position. The existence of this effect, known as the buttressing effect, has been previously confirmed particularly in the work of Adams.[39] Fehlner,[7] in his work on some cyclic amides of the type shown below, found that while compound XIX has a $\Delta G^{\ddagger}$ of rotation of 16.3 kcal/mole and a $\Delta S^{\ddagger}$ of -31.4 ± 2 e.u.,

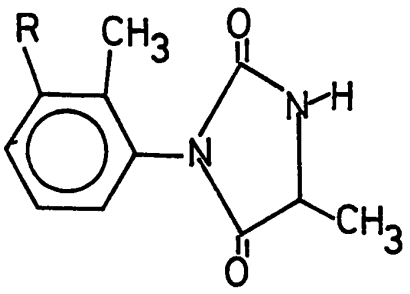


XIX, R = H
XX, R = Cl

compound XX has a $\Delta G^{\ddagger}$ and a $\Delta S^{\ddagger}$ values of 18.4 kcal/mole and -21.5 ± 2 e.u. respectively. Fehlner suggested that the less negative value of $\Delta S^{\ddagger}$ in compound XX is probably caused by a decrease in the rocking motion of the aryl ring in the ground state.

To check if the buttressing effect would have any influence on the barrier of rotation of the 3-aryl substituted hydantoins, compound IX was prepared. The $\Delta G^{\ddagger}$

and $\Delta S^{\ddagger}$ of this compound were found to be 19.1 kcal/mole and -27 ± 2 e.u. respectively, versus a $\Delta G^{\ddagger}$ of 18.0 kcal/mole and a $\Delta S^{\ddagger}$ of -24 ± 2 e.u. for compound VII, the corresponding compound without any meta substituent on the aryl ring.



IX, R = CH_3
VII, R = H

While the $\Delta G^{\ddagger}$ of compound IX is greater than that of compound VII, as expected, the $\Delta S^{\ddagger}$ of compound IX is more negative in contrast to Fehlner's results with compounds XX and XIX. As an explanation the following hypothesis is given.

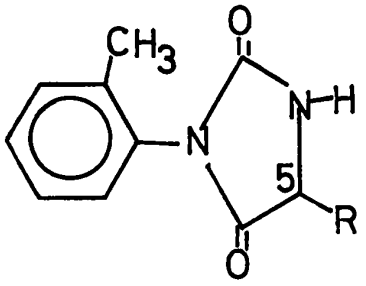
In the case of Fehlner's compound XX, the less negative value of $\Delta S^{\ddagger}$ is probably caused by a decrease in the activation volume in the transition state. In the transition state of compound XIX the ortho methyl group is bent backwards, while in the transition state of compound XX the ortho methyl cannot bend backwards, but probably bends out of the normal plane because of the presence of the chlorine atom in the meta position. Hence the entropy of the transition state of compound XX is increased relative to that of compound XIX. In the ground state the meta-chloro group has little effect,

as one can see from the equilibrium constants (k = 1.18 for XIX, k = 1.16 for XX), which indicate that the methyl group is not bent out of its normal position in compound XX. Therefore the entropy of activation in compound XX is less negative than in compound XIX. This is not true in the case of compound IX. In this compound the meta methyl group, which is bulkier than a chlorine atom, probably interacts with the ortho methyl group in the ground state as well as in the transition state. This interaction is reflected in the equilibrium constants of compounds VII and IX (K = 0.85 for IX, k = 1.0 for VII). Because of this interaction the ortho methyl group in compound IX is probably bent out of its normal plane and the entropy of both the ground and transition state is raised, with the result that $\Delta S^{\ddagger}$ in compound IX is not less negative than in compound VII. Indeed, since the limits of experimental accuracy are ± 2 e.u. in the $\Delta S^{\ddagger}$ measurements, it could be concluded from the results that $\Delta S^{\ddagger}$ of compound IX is equal to that of compound VII.

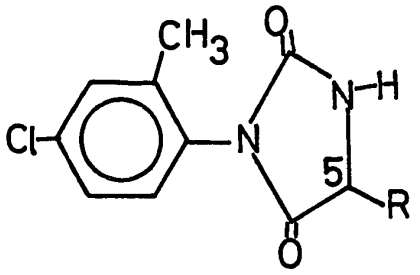
Finally, the meta-substituent could induce some change in the $\Delta G^{\ddagger}$ of rotation through electronic effects. However, this is not the case when a methyl group is involved, since it is in the meta position, the electronic effect should be minimal. The field factor F for such a group is small, 0.0052, while the resonance factor R is 0.141, and the constants f and r cannot be greater than unity for similar systems.

Effect of the Substituent in the 5 Position

The following compounds were prepared to see if a different substituent in the 5 position could influence the barrier of rotation.



VII, R = CH_3
VIII, R = C_6H_5



XII, R = CH_3
XIII, R = C_6H_5

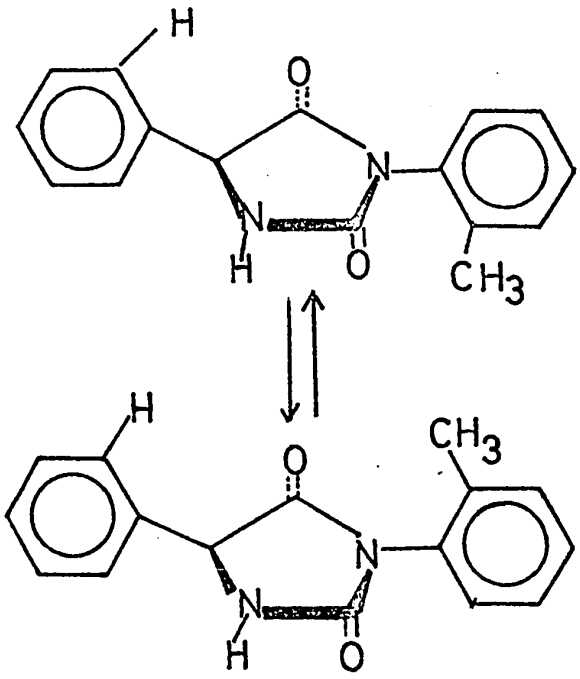
Their free energies and equilibrium constants are shown below.

Table XV: Free Energies of Rotation and Equilibrium Constants of Some Hydantoins.

Compound	$\Delta G^{\ddagger}$ kcal/mole Tau A, Tau B		Equilibrium Constant
VII	18.0	18.1	1.00
VIII	18.0	17.8	0.61
XII	18.2	18.2	1.00
XIII	18.4	18.2	0.70

As one can see from Table XV the substitution of the methyl group in the 5 position with the more bulky phenyl ring does not change the free energy of activation. Indeed, all the values of the free energies of activation are identical within experimental error. This seems to exclude any steric effect of the substituent in the 5 position in the transition state. However, since the equilibrium constants diminish with the substitution of a phenyl ring with a methyl group in the 5 position, one must consider the possibility of some interaction between the two phenyl rings in the ground state. This interaction could be electronic and/or steric.

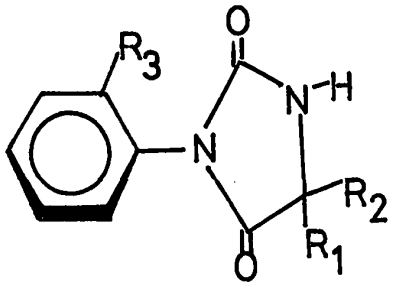
Since the phenyl ring in the 5 position is not coplanar with the hydantoin ring, one can excude any mesomeric interaction between these two moieties. It is possible to rationalize the effect of the phenyl ring in the 5 position on the ground state by looking at the Dreiding models of compounds VIII and XIII. Since the aryl ring attached to the nitrogen in the 3 position rotates, the ortho methyl group will sometimes be cisoid and sometimes transoid with respect to the aryl ring in the 5 position, as shown in the next page.



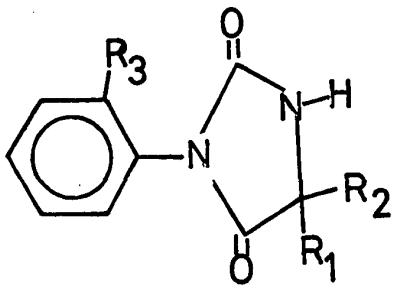
When the 5-phenyl and the methyl groups are transoid they do not interfere with each other. However, this is not true when the two groups are cisoid to each other. In such a case the ortho methyl group interferes with the phenyl ring in the 5 position. Consequently the transoid isomer has a longer lifetime than the cisoid isomer, and the equilibrium constants for the compounds VIII and XIII are less than unity. This interference between the C-5 phenyl and the ortho methyl group is probably a steric one, since the methyl moiety has a small field factor (F = -0.052). However, more data are needed to confirm the hypothesis given above.

Entropy of Activation

Large negative entropies of activation in the rotational process of hydantoins were previously reported in the work of Fehlner.[7] Although the entropy values are not as trustworthy as the values for the free energies,[1] they have been confirmed by other methods.[7,40] In this work the entropy values can be considered accurate to within a range of ± 2 e.u.. An explanation for the entropies being negative can be deduced from the fact that, while the aryl ring has a rocking motion in the ground state, this rocking motion must be absent or restricted in the transition state. In addition to this, since the molecular volume in the transition state must be less than in the ground state, the entropy of activation must be negative.



ground state



transition state

Furthermore, on considering Table XVI, it is interesting to note that while the nitro-substituted hydantoin has a larger negative entropy of activation than the unsubstituted compound, the chlorine-substituted hydantoin possesses

slightly less negative entropies of activation than the unsubstituted compound. Evidently both the nitro group and the chlorine atom must affect the rocking motion of the aryl ring attached to the nitrogen in the 3 position.

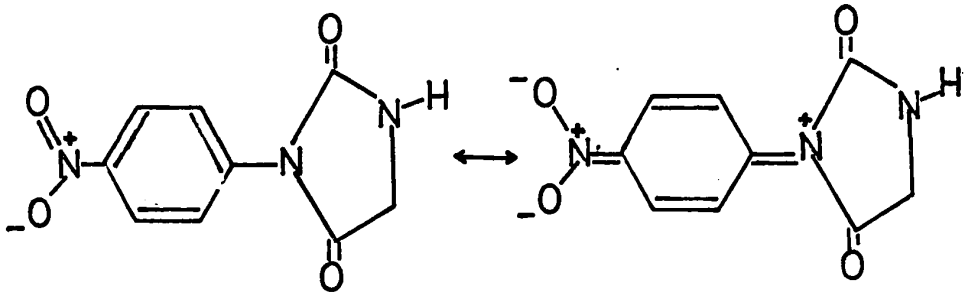
Table XVI: Free Energies and Entropies of Activation of Some Hydantoins.

Compound		$\Delta G^{\ddagger}$ (kcal/mole)	$\Delta S^{\ddagger}$ (e.u.)
VII	τ_A	18.0 ± 0.1	$-23.^{7} \pm 2$
	τ_B	18.0 ± 0.1	$-23.^{0} \pm 2$
XII	τ_A	18.2 ± 0.1	$-17.^{1} \pm 2$
	τ_B	18.2 ± 0.1	$-15.^{3} \pm 2$
VIII	τ_A	18.0 ± 0.1	$-22.^{0} \pm 2$
	τ_B	17.8 ± 0.1	$-22.^{9} \pm 2$
XIII	τ_A	18.4 ± 0.1	$-20.^{0} \pm 2$
	τ_B	18.2 ± 0.1	$-21.^{0} \pm 2$
X	τ_A	17.1 ± 0.1	$-30.^{8} \pm 2$
	τ_B	17.0 ± 0.1	$-28.^{3} \pm 2$

Since the nitro group and the chlorine atom can interfere with the rocking motion of the aryl ring by means of their field and/or resonance phenomena, it is better to separate these two effects and determine how each influences the ground and/or the transition state of rotation of hydantoins.

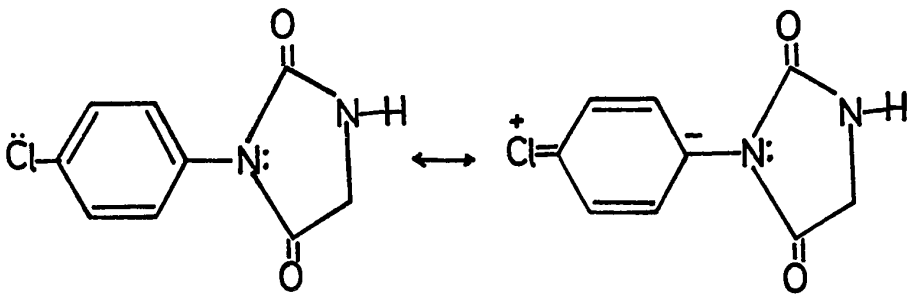
Because both the chlorine atom and the nitro group have the same field effects, and since the field effects act in both the ground and the transition state in the same direction one can ignore their influence on the entropies of activation.

In contrast to the field effects however, the resonance effects can be taken into account only in the transition state. If one considers the resonance due to the nitro group, which is shown below, it is evident that



this resonance tends to create a partial double bond between the nitrogen in the 3 position and the carbon attached to this atom. Because of this double bond, the rocking motion of the aryl ring in the transition

state is hindered to a larger extent than in the unsubstituted compound. It follows that the entropy of activation of the nitro-substituted compound in the transition state is less than the entropy of the unsubstituted one. In the case of the chlorine atom the opposite is true. Conjugation between the electrons on the nitrogen in the 3 position and the aryl ring is not favored, since it



would place a negative charge on the aryl carbon atom, as shown above. Thus the rocking motion of the aryl ring is increased slightly relative to that in the corresponding unsubstituted hydantoin, and consequently the entropy of the transition state is also increased. This results in <u>para</u>-chloro substituted hydantoins having slightly less negative entropies of activation than the corresponding unsubstituted ones, as shown in Table XVI.

SUMMARY

A study of the hindered rotation of a series of 3-aryl substituted hydantoins has led to the following conclusions:

I) Electronic effects cannot be disregarded in predicting the $\Delta G^{\ddagger}$ and $\Delta S^{\ddagger}$ of activation.

II) The substituents in the 5 position can affect the equilibrium constants of rotation, although they do not significantly affect the $\Delta G^{\ddagger}$ of rotation.

III) The ortho-methyl group is probably bent backwards in the transition state.

IV) A chlorine atom, although slightly smaller than a methyl group, presents a larger barrier of rotation in the hydantoins.

V) A sulphur atom causes a larger barrier of rotation than an oxygen atom when it is in the 2 position.

EXPERIMENTAL SECTION

Preparation of Arylisocyanates

The procedure described below was followed for the preparation of 4-methoxy-2-methylphenylisocyanate, 4-chloro-2-methylphenylisocyanate, and 2,3-dimethylphenylisocyanate. All the other isocyanates were available commercially.

4-Methoxy-2-methylphenylisocyanate. The procedure followed is an adaptation of that used by Schriner, Horne, and Cox.[41]

Ethyl acetate (100 ml), freshly distilled and dried over anhydrous magnesium sulphate, was saturated with phosgene at room temperature. The phosgene had been previously purified by bubbling it through sulphuric acid. A solution of 15.0 g (0.0109 mole) of 4-methoxy-2-methylaniline in 250 ml of dry ethyl acetate was added dropwise. Towards the end of the addition, the solution was heated gently to break the lumps of 4-methoxy-2-methylaniline hydrochloride which had formed. After the aniline had been added, the stream of phosgene was continued until the solid had all dissolved. The unreacted phosgene was trapped by passing it through a 20% NaOH solution. The ethyl acetate solvent was removed by vacuum distillation

at room temperature, and the isocyanate was distilled at 105-107° under 5-7 mm of pressure. It was then used for the preparation of the corresponding hydantoin without further purification. The yield of the isocyanate was 8.0 g or 44%; ir (liquid film, cm^{-1}) large strong band at 2260 (NCO).[42]

4-Chloro-2-methylphenylisocyanate. This compound was prepared by the method described above. Starting material: 4-chloro-2-methylaniline (50.0 g, 0.354 mole). The isocyanate was distilled at 105° under 1 mm of pressure and was then used without further purification. The yield of isocyanate was 50.0 g or 85%; ir (liquid film, cm^{-1}) large strong band at 2260 (NCO).[42]

2-Methyl-4-nitrophenylisocyanate. This compound was prepared by the method described above. Starting material: 2-methyl-4-nitroaniline (10.0 g, 0.066 mole). The isocyanate was distilled at 115-117° under 1 mm of pressure. It was then used for the preparation of the corresponding hydantoin without further purification. The yield of the isocyanate was 11.8 g or 85%; ir (KBr, cm^{-1}) large strong band at 2260 (NCO).[42]

2,3-Dimethylphenylisocyanate. This compound was prepared by the method described above. Starting

material: 2,3-dimethylaniline (50.0 g, o.41 mole). The isocyanate was distilled at 75° under 1 mm of vacuum. It was then used without further purification for the preparation of the corresponding hydantoin. The yield of the isocyanate was 50.0 g or 83%; ir (liquid film, cm^{-1}) large strong band at 2260 (NCO).[42]

Preparation of Arylisothiocyanates

2-Methyl-4-nitrophenylisothiocyanate. The method followed was that of Coghill and Johnson.[43] 2-Methyl-4-nitroaniline (20.0 g, 0.131 mole) was dissolved in 300 ml of dry ethyl acetate, to which 40.0 g of thiophosgene was added. The reaction mixture was then heated under reflux until the hydrochloride went into solution. The solvent was evaporated and 50 ml of hot toluene was added. The isothiocyanate crystallized out on cooling. It was then used without further purification. The yield of the isothiocyanate was 14.0 g or 55%; mp 81-83°; ir (KBr, cm^{-1}) large strong band at 2075 (NCS).[42]

4-Methoxy-2-methylphenylisothiocyanate. This compound was prepared by the method described above. Starting material: 4-methoxy-2-methylaniline (25.0 g 0.182 mole). The isothiocyanate was distilled at 128-132° under 1 mm vacuum. It was then used without further purification. The yield of the isothiocyanate was 27.0 g or 87%; ir (liquid film, cm^{-1}) large strong band at 2095 (NCS).[42]

2-Isothiocyanatobiphenyl. This compound was prepared by the method described above. Starting material: 2-aminobiphenyl (25.0 g, 0.148 mole). The isothiocyanate

was distilled at 165° under 1 mm vacuum. It was then used without further purification. The yield of the isothiocyanate was 25.0 g or 80%; ir (liquid film, cm^{-1}) large strong band at 2100 (NCS).[42]

Preparation of 3-Aryl Hydantoins

3-(2-Methoxyphenyl)-5,5-dimethylhydantoin (XXI). The procedure used was that of Behr and Clarcke.[44] 2-Methylalanine (1.0 g, 0.0097 mole) was dissolved in 40 ml of 0.5 N NaOH solution. To this solution 2-methoxyphenylisocyanate (2.0 g, 0.0136 mole) was added and the mixture was stirred at room temperature for two hours. After having been filtered, the mixture was acidified to pH 5 and the resulting white precipitate was collected by filtration. This white precipitate was dissolved in 20 ml of hot water and 5 ml of 12 N HCl. The solution was then refluxed for two hours, filtered, cooled, and neutralized with sodium carbonate. The hydantoin precipitate was collected by filtration. It was crystallized from 95% ethanol and water. The yield of the hydantoin was 0.130 g or 8.9%; mp 161-163°; nmr ($CDCl_3$,δ) 1.3 (6H, singlet, C-5 methyl protons), 3.2 (3H, singlet, o-methoxy protons), 5.5 (1H, broad singlet, NH proton), 6.0 (4H, multiplet, phenyl protons); ir (KBr,cm^{-1}) 1715 (CO), 1770 (CO), 3210 (NH).[42]

3-(4-Methoxy-2-methylphenyl)-5-methylhydantoin (XXII). This compound was prepared by the method described above. Starting material: DL-alanine (1.0 g, 0.0112 mole), and

4-methoxy-2-methylphenylisocyanate (2.3 g, 0.0134 mole). The yield of the hydantoin after crystallization from 90% ethanol and water was 0.1 g or 5.3%, mp 146-147°; nmr (DMSO-d_6, δ) 1.35 (3H, doublet, C-5 protons), 2.1 (3H, doublet, o-methyl protons), 3.8 (3H, singlet, p-methoxy protons), 7.2 (3H, multiplet, phenyl protons): ir (KBr, cm^{-1}) 1715 (CO), 1775 (CO), 3300 (NH).

3-(2-Methylphenyl)-5-methylhydantoin (VII). This compound was prepared by the method described above. Starting material: DL-alanine (1.0 g, 0.0112 mole), and o-tolylisocyanate (2.0 g, 0.015 mole). The compound was crystallized from 95% ethanol and water. The yield was 1.2 g or 44%; mp 124-126°; nmr (DMSO-d_6, δ) 1.35 (3H, doublet, C-5 methyl protons), 2.1 (3H, doublet, o-methyl protons), 7.3 (4H, multiplet, phenyl protons); ir (KBr,cm^{-1}) 1715 (CO), 1775 (CO), 3250 (NH).

3-(2-Methoxyphenyl)-5-phenylhydantoin (XXIII). This compound was prepared by the method described above. Starting material: DL-alanine (2.0 g, 0.0224 mole), and 2-methoxyphenylisocyanate (4.0 g, 0.0278 mole). The compound was crystallized from 95% ethanol and water. The yield of the hydantoin was 1.17 g or 24%; mp 146-147°; nmr (DMSO-d_6, δ) 1.3 (3H, doublet, C-5 methyl protons), 3.2

(3H, singlet, o-methoxy protons), 6.1 (4H, multiplet, phenyl protons); ir (KBr, cm^{-1}) 1710 (CO), 1775 (CO), 3200 (NH).

3-(2-Methylphenyl)-5-phenylhydantoin (VIII). This compound was prepared by the method described above. Starting material: phenylglycine (3.44 g, 0.0228 mole), and o-tolylisocyanate (3.6 g, 0.0270 mole). The product was crystallized in 95% ethanol and water. The yield was 1.5 g or 25%; mp 197-199°; nmr (DMSO-d_6, δ) 2.1 (3H, doublet, o-methyl protons), 5.4 (1H, doublet, C-5 proton), 7.4 (9H, multiplet, phenyl protons); ir (KBr, cm^{-1}) 1715 (CO), 1775 (CO), 3200 (NH).

3-(4-Chloro-2-methylphenyl)-5-methylhydantoin (XII). This compound was prepared by the method described above. Starting material: DL-alanine (2.0 g, 0.0224 mole), and 4-chloro-2-methylphenylisocyanate (4.5 g, 0.0270 mole). The yield of the hydantoin was 1.0 g or 18.5%; mp 148-150°; nmr (DMSO-d_6, δ) 1.2 (3H, doublet, C-5 protons), 2.0 (3H, doublet, o-methyl protons), 7.1 (3H, multiplet, phenyl protons), 8.3 (1H, broad singlet, NH proton); ir (KBr, cm^{-1}) 1715 (CO), 1775 (CO), 3200 (NH).

3-(4-Chloro-2-methylphenyl)hydantoin (XXIV). This

compound was prepared by the method described above. Starting material: glycine (2.0 g, 0.0268 mole), and 4-chloro-2-methylphenylisocyanate (5.0 g, 0.0304 mole). The compound was crystallized from 95% ethanol and water. The yield of the hydantoin was 0.5 g or 8.3%; mp 108-110°; nmr (DMSO-d_6, δ) 2.10 (3H, doublet, o-methyl protons), 4.0 (2H, singlet, C-5 protons), 7.2 (3H, multiplet, phenyl protons); ir (KBr, cm^{-1}) 1715 (CO), 1775 (CO), 3280 (NH).

3-(4-Chloro-2-methylphenyl)-5-phenylhydantoin (XIII).

This compound was prepared by the method described above. Starting material: phenylglycine (3.0 g, 0.0199 mole), and 4-chloro-2-methylphenylisocyanate (5.0 g, 0.0304 mole). The product was crystallized from 95% ethanol and water. The yield of the hydantoin was 0.5 g or 8.4%; mp 155-157°; nmr (DMSO-d_6, δ) 2.2 (3H, doublet, o-methyl protons), 5.5 (1H, doublet, C-5 proton), 7.5 (8H, multiplet, phenyl protons); ir (KBr, cm^{-1}) 1715 (CO), 1770 (CO), 3280 (NH).

3-(4-Chloro-2-methylphenyl)-5,5-dimethylhydantoin (XXV).

This compound was prepared by the method described above. Starting material: 2-methylalanine (2.0 g, 0.0199 mole), and 4-chloro-2-methylphenylisocyanate (4.2 g, 0.025 mole). The product was crystallized from 95% ethanol and water. The yield of the hydantoin was 0.1 g or 2.1%; mp 184-186°;

nmr (DMSO-d_6, δ) 1.4 (6H, singlet, C-5 protons), 2.1 (3H, singlet, o-methyl protons), 7.4 (3H, multiplet, phenyl protons); ir (KBr, cm^{-1}) 1720 (CO), 1775 (CO), 3210 (NH).

3-(2-Methoxyphenyl)hydantoin (XXIX). This compound was prepared by the method described above. Starting material: glycine (2.0 g, 0.0268 mole), and 2-methoxyphenylisocyanate (4.0 g, 0.0278 mole). The product was crystallized from 95% ethanol and water. The yield of the hydantoin was 3.2 g or 60%; mp 170-171°; nmr (DMSO-d_6, δ) 3.75 (3H,singlet, o-methoxy protons), 4.15 (2H, singlet, C-5 protons), 7.2 (4H, multiplet, phenyl protons), 8.2 (1H, broad singlet, NH proton); ir (KBr, cm^{-1}) 1710 (CO), 1770 (CO), 3300 (NH).

3-(2,3-Dimethylphenyl)-5-methylhydantoin (IX). This compound was prepared by the method described above. Starting material: DL-alanine (2.0 g, 0.0228 mole), and 2,3-dimethylphenylisocyanate (4.0 g, 0.0227 mole). The product was crystallized from 95% ethanol and water. The yield of the hydantoin was 1.4 g or 28%; mp 148-150°; nmr (DMSO-d_6, δ) 1.4 (3H, doublet, C-5 methyl protons), 2.3 (3H, doublet, o-methyl protons), 2.0 (3H, singlet, m-methyl protons), 7.2 (3H, multiplet, phenyl protons); ir (KBr, cm^{-1}) 1710 (CO), 1770 (CO), 3220 (NH).

3-(2,3-Dimethylphenyl)hydantoin (XXVI). This compound was prepared by the method described above. Starting material: glycine (2.0 g, 0.0268 mole), and 2,3-dimethylphenylisocyanate (4.5 g, 0.0304 mole). The product was crystallized from 95% ethanol and water. The yield of the hydantoin was 1.0 g or 18.3%; mp 131-133°; nmr (DMSO-d_6, δ) 2.0 (3H, singlet, o-methyl protons), 2.3 (3H, singlet, m-methyl protons), 4.2 (2H, singlet, C-5 protons), 7.3 (3H, multiplet, phenyl protons), 8.3 (1H, broad singlet, NH proton); ir (KBr, cm^{-1}) 1715 (CO), 1770 (CO), 3300 (NH).

3-(2-Chlorophenyl)-5-phenylhydantoin (XIV). This compound was prepared by the method described above. Starting material: phenylglycine (1.7 g, 0.0112 mole), and 2-chlorophenylisocyanate (1.8 g, 0.0112 mole). The product was crystallized from 95% ethanol and water. The yield of the hydantoin was 0.41 g or 27%; mp 163-165°; nmr (DMSO-d_6, δ) 4.3 (1H, doublet, C-5 proton), 6.7 (4H, multiplet, phenyl protons); ir (KBr, cm^{-1}) 1720 (CO), 1780 (CO), 3280 (NH).

3-(2-Methyl-4-nitrophenyl)-5-methylhydantoin (X). This compound was prepared according the method of Wheeler et al..[45] A mixture of 3-(2-methyl-4-nitrophenyl)-5-methyl-2-thiohydantoin

(2.5 g, 0.01 mole) and chloroacetic acid (0.95 g, 0.01 mole) was refluxed in 10 ml of distilled water. The hydantoin crystallized out on cooling. It was recrystallized from 95% ethanol and water. The yield of the hydantoin was 0.10 g or 4.4%; mp 166-168°; nmr (DMSO-d_6, δ) 1.4 (3H, doublet, C-5 methyl protons), 2.2 (3H, doublet, o-methyl-protons), 4.5 (1H, quartet, C-5 proton); ir (KBr, cm^{-1}) 1705 (CO), 1760 (CO), 3240 (NH).

Preparation of 3-Aryl Thiohydantoins

3-(2-Methyl-4-nitrophenyl)-5-methyl-2-thiohydantoin (XI).

The procedure followed was that of Pujari and Root.[46] DL-alanine (2.5 g, 0.027 mole) was dissolved in 2 ml of water and 1.0 g of NaOH was added. To this solution, a solution of 2-methyl-4-nitrophenylisothiocyanate (4.8 g, 0.025 mole) in 20 ml of absolute alcohol was added dropwise. The resulting solution was refluxed for two hours, when 25 ml of 6 N HCl was then added. The thiohydantoin precipitated and was recrystallized from 95% ethanol and water. The yield of the thiohydantoin was 5.1 g or 90%; mp 209-210°; nmr (DMSO-d_6, δ) 1.5 (3H, doublet, C-5 methyl protons), 2.3 (3H, doublet, o-methyl protons), 7.3 (4H, multiplet, phenyl protons); ir (KBr, cm^{-1}) 1190 (CS), 3400 (NH).

3-(4-Methoxy-2-methylphenyl)-5-methyl-2-thiohydantoin (XXVII).

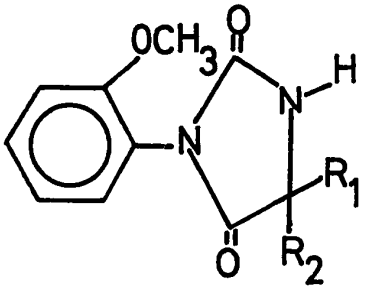
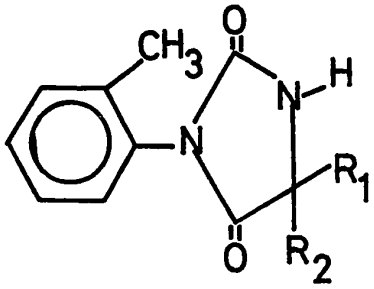
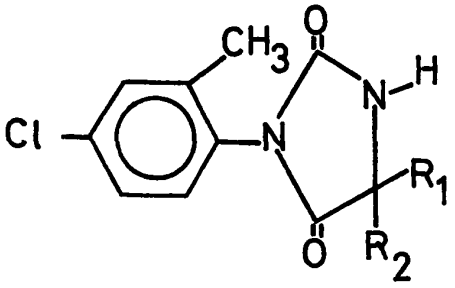
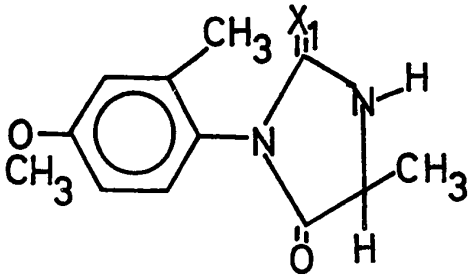
This compound was prepared by the method described above. Starting material: DL-alanine (2.4 g, 0.027 mole), and 4-methoxy-2-methylphenylisocyanate (4.8 g, 0.027 mole). The yield of the thiohydantoin was 4.7 g or 70%; mp 145-147°; nmr (DMSO-d_6, δ) 1.4 (3H, doublet, C-5 methyl protons), 2.1 (3H, singlet, o-methyl protons) 3.8 (3H, singlet, p-methoxy protons), 7.0 (3H, multiplet, phenyl protons): ir (KBr, cm^{-1}) 1190 (CS), 1720 CO), 3300 (NH).

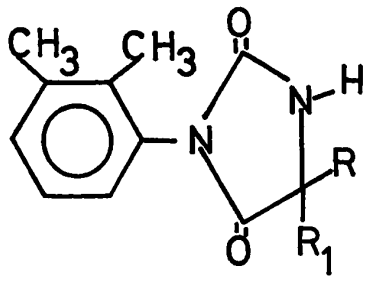
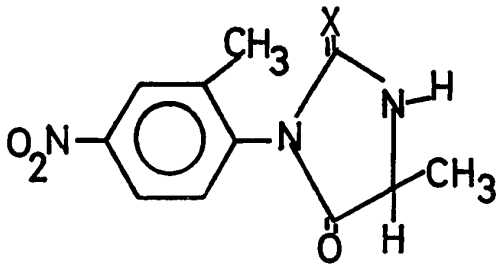
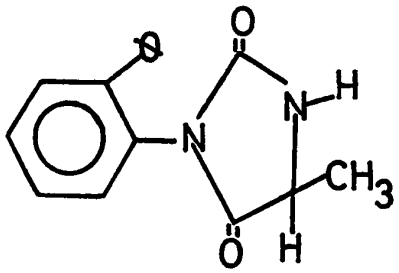
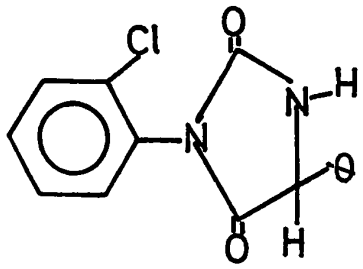
3-(2-Biphenyl)-5-methyl-2-thiohydantoin (XXVIII).

This compound was prepared by the method described above. Starting material: DL-alanine (2.4 g, 0.027 mole), and 2-isothiocyanatobiphenyl (4.8 g, 0.022 mole). The compound was crystallized from 95% ethanol and water. The yield of the thiohydantoin was 5.0 g or 78%; mp 142-144°; nmr (DMSO-d_6, δ) 1.8 (3H, quartet, C-5 methyl protons), 5.0 (9H, multiplet, phenyl protons); ir (KBr, cm^{-1}) 1720 (CO), 3250 (NH).

Spectra of Hydantoins and Thiohydantoins

Infrared and NMR spectra were taken of the following compounds:

Formula	Substituents	Compound Label
	$R_1 = H$, $R_2 = CH_3$	XXIII
	$R_1 = H$, $R_2 = H$	XXIX
	$R_1 = CH_3$, $R_2 = CH_3$	XXI
	$R_1 = H$, $R_2 = CH_3$	VII
	$R_1 = H$, $R_2 = C_6H_5$	VIII
	$R_1 = CH_3$, $R_2 = CH_3$	XXX
	$R_1 = H$, $R_2 = H$	XXIV
	$R_1 = H$ $R_2 = CH_3$	XII
	$R_1 = CH_3$, $R_2 = CH_3$	XXV
	$R_1 = H$, $R_2 = C_6H_5$	XIII
	$X_1 = O$,	XXII
	$X_1 = S$,	XXVII

Formula	Substituent	Compound Label
	$R_1 = H, R_2 = CH_3$	IX
	$R_1 = H, R_2 = H$	XXVI
	X = S	XI
	X = O	X
		XXVIII
		XIV

NMR Spectra

The experimental conditions have been described previously. The absorptions in the NMR spectra of hydantoins and thiohydantoins agree quite well with data reported by Corral and Orazi,[47] and Fehlner.[7] Two examples of hydantoin spectra are illustrated in Figures 18 and 19. In DMSO-d_6 solution, the C-5 methyl group absorbs between δ 1.25 and δ 1.55, while the methyl group in the ortho position absorbs between δ 1.35 and δ 2.30. The hydrogen atom in the 5 position absorbs between δ 3.55 and δ 5.52. In the 5 methyl-substituted compounds the C-5 proton absorbs from δ 4.3 to δ 4.4, while in the corresponding 5 phenyl compounds the same proton absorbs, probably because of the deshielding due to the phenyl ring, between δ 5.3 and δ 5.4. The phenyl peaks are generally very complicated; they absorb between δ 4.8 and δ 7.2. The NH proton absorbs over a wide range and is broadened by the quadrupole relaxation of the nitrogen atom. The magnitude of the coupling constant between the C-5 methyl and the C-5 proton in the 5 methyl-substituted hydantoins varies from a minimum of 6.5 Hz for compound VII to a maximum of 12 Hz for compound XXVIII. All the spectra recorded during this work are easily reproducible.

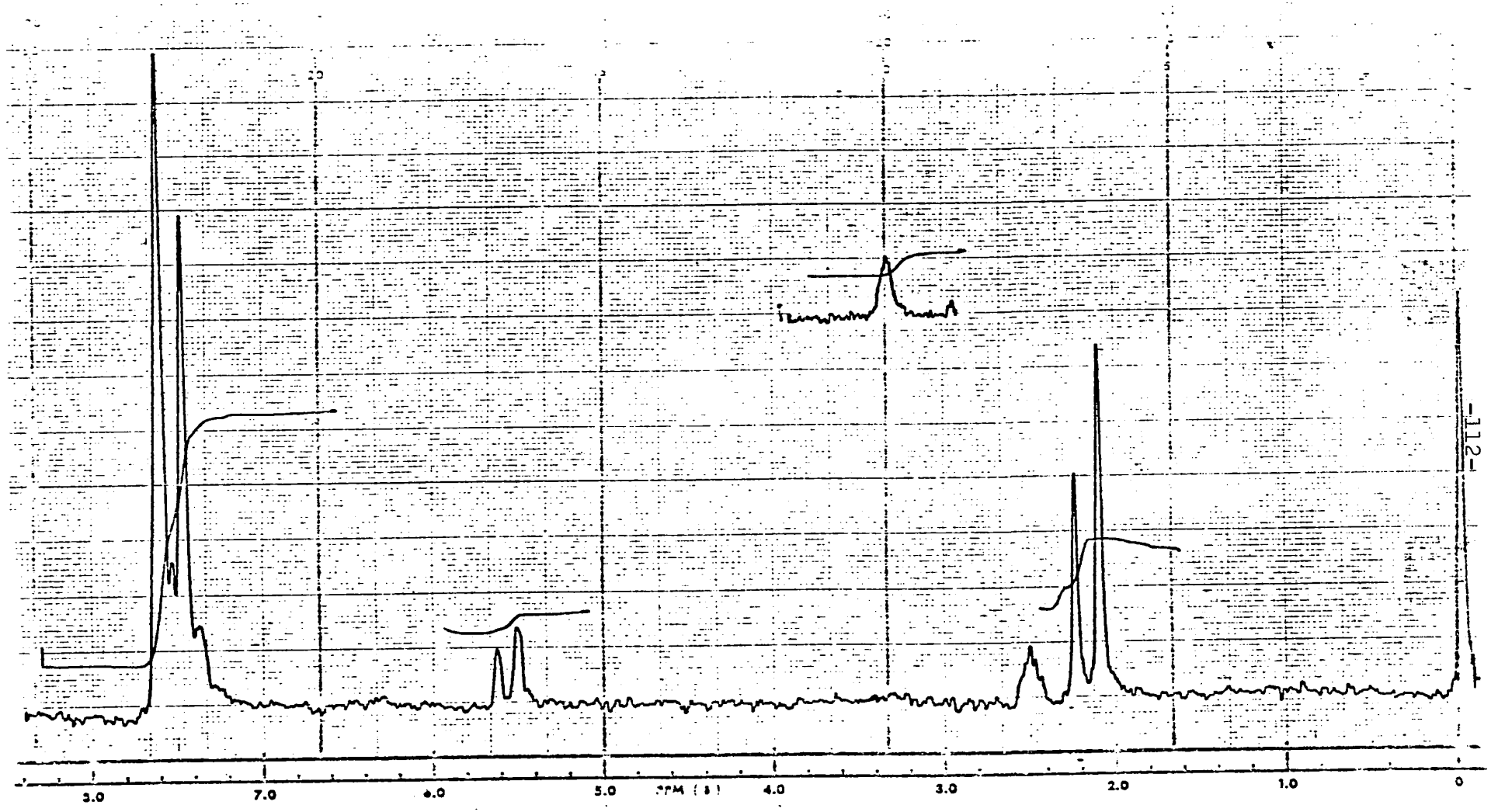


Figure 18: NMR Spectrum of 3-(2-methylphenyl)-5-phenylhydantoin (VIII) Taken at 60 MHz in DMSO-d_6 Solution at Room Temperature.

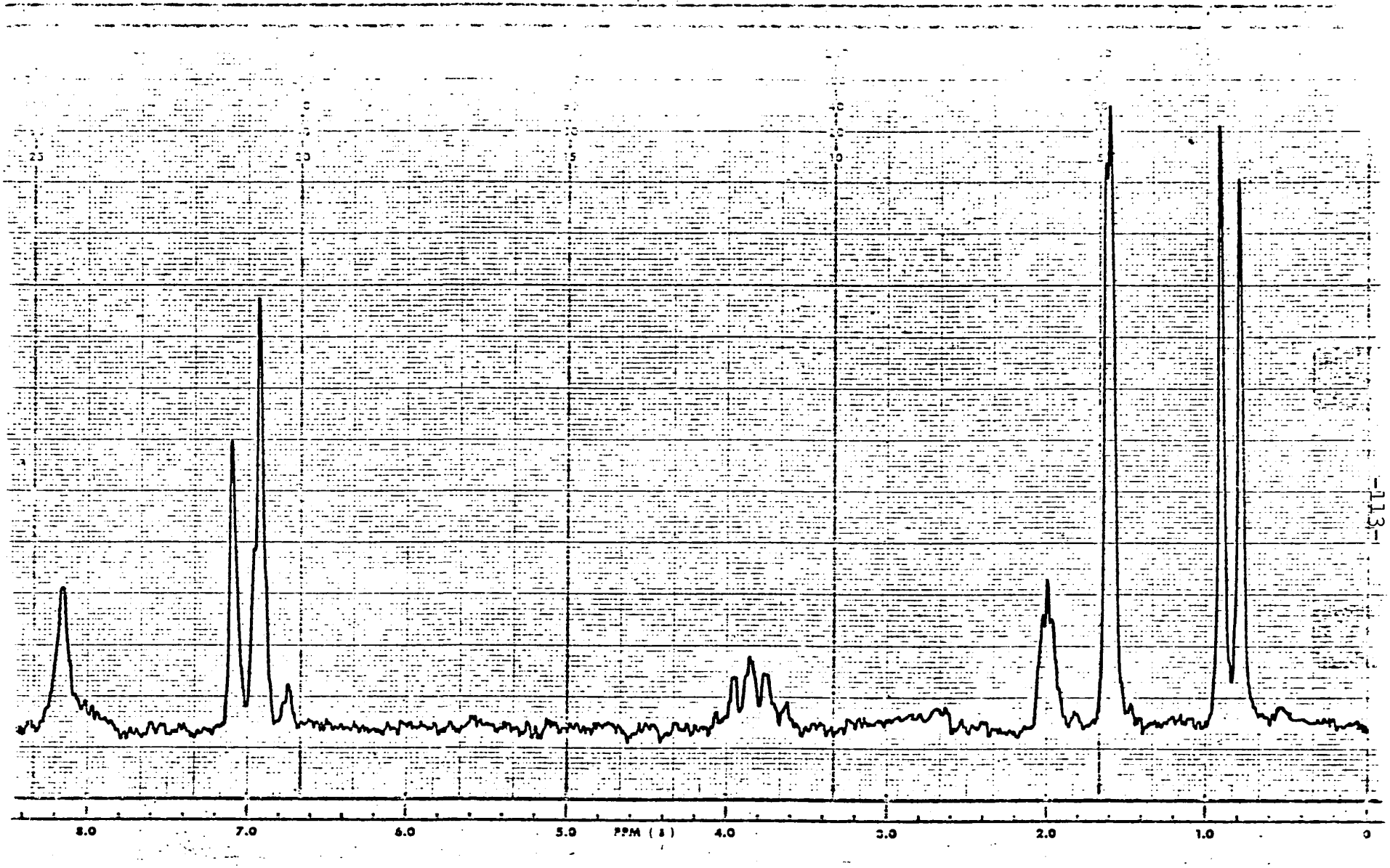


Figure 19: NMR Spectrum of 3-(4-chloro-2-methylphenyl)-5-methylhydantoin (XII) Taken at 60 MHz in DMSO-d_6 Solution at Room Temperature.

Infrared Spectra

All the infrared spectra of hydantoins and thiohydantoins in this work were taken through potassium bromide disks on a Perkin-Elmer 457 infrared spectrometer.

The infrared spectra of a number of substituted hydantoins have already been well discussed in a paper by Elliot and Natarajun.[48] Those of 3-phenyl hydantoins have been discussed by Saifer,[49] and Epp.[50,51] Their results agree very well with each other.

Two modes of vibration are very easily recognized in the infrared spectra of hydantoins and thiohydantoins. One is the N-H stretching mode, which varies from 3180 cm^{-1} to 3300 cm^{-1} for the hydantoins, and from 3250 cm^{-1} to 3400 cm^{-1} in the case of the corresponding thiohydantoins. The second important mode of vibration is the carbonyl stretching mode. This mode gives rise to two bands in hydantoins. The first is a moderate intensity absorption band between 1760 cm^{-1} and 1780 cm^{-1}, while the second is a very strong broad band between 1705 cm^{-1} and 1720 cm^{-1}. It has been suggested that this latter band may be a doublet.[48] In the thiohydantoins there is only one carbonyl stretching band, found between 1720 cm^{-1} and 1740 cm^{-1}. The assignment of the C=S stretching vibration to the absorption between 1400 cm^{-1} and 1425 cm^{-1} was given by Kimmel and Saifer.[49] In contrast, Epp[51] assigned

the same stretching mode to the absorption around 1200 cm^{-1}. Both bands are present in all the thiohydantoins, but while Kimmel and Saifer did not give any explanation for their assignment, Epp pointed out that on opening the hydantoin ring, the band between 1400 cm^{-1} and 1425 cm^{-1} does not shift, while that around 1200 cm^{-1} does shift. Further, Mecke[52] calculated that in the case of thiolactams, the ratio $\nu_{(C=O)}/\nu_{(C=S)}$ would be approximately 1.5, so that $\nu_{(C=S)}$ would be about (1800-1500)/1.5 or 1200-1050 cm^{-1}. Since Mecke's experimental values confirmed his calculations, (see Table XVII), it is considered reasonable to identify the absorption between 1195-1185 cm^{-1} in the thiohydantoins as the C=S stretching mode.

Table XVII: Infrared Frequencies of Some Carbonyl and Thiocarbonyl Compounds.

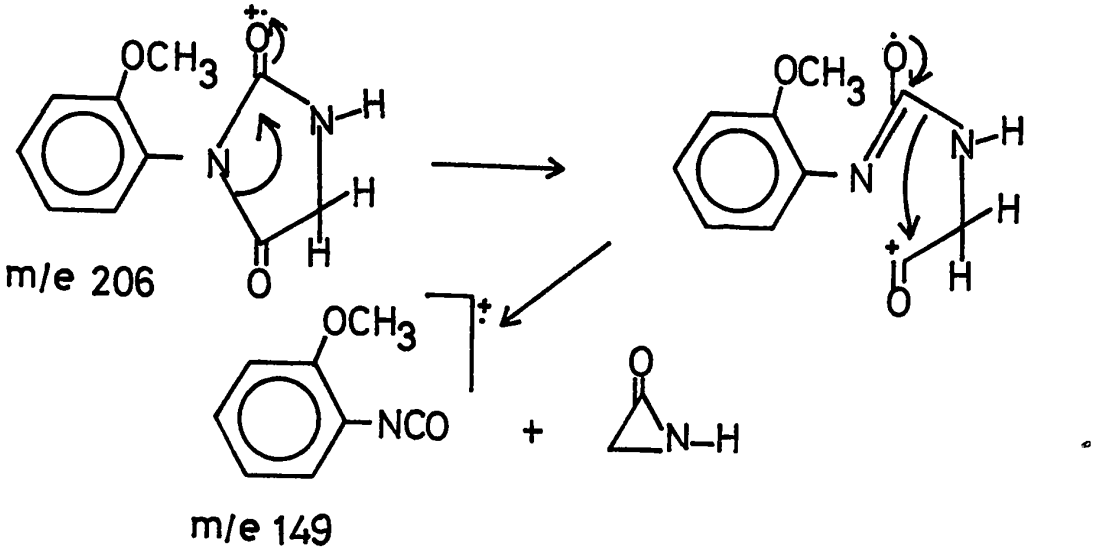
Compound	Stretching Mode	Frequency
Thiopyrrolidone	ν(C=S)	1115 cm^{-1}
Pyrrolidone	ν(C=O)	1706 cm^{-1}
Thiopiperidone	ν(C=S)	1112 cm^{-1}
Piperidone	ν(C=O)	1672 cm^{-1}
Thiocaprolactam	ν(C=S)	1117 cm^{-1}
Caprolactam	ν(C=O)	1669 cm^{-1}
XI	ν(C=S)	1190 cm^{-1}
X	ν(C=O)	1760 cm^{-1}
XXVII	ν(C=S)	1190 cm^{-1}
XXII	ν(C=O)	1775 cm^{-1}

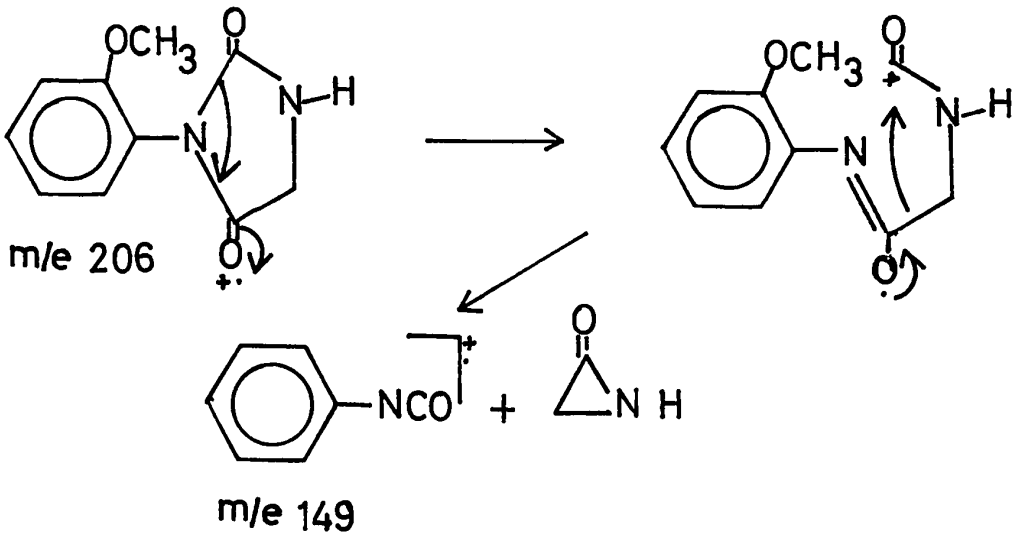
Mass Spectra

The spectra recorded in Tables XVIII, XIX, XX, and XXI were taken on a Hitachi Perkin-Elmer RMU-7 spectrometer. The direct introduction of the sample was used in all cases.

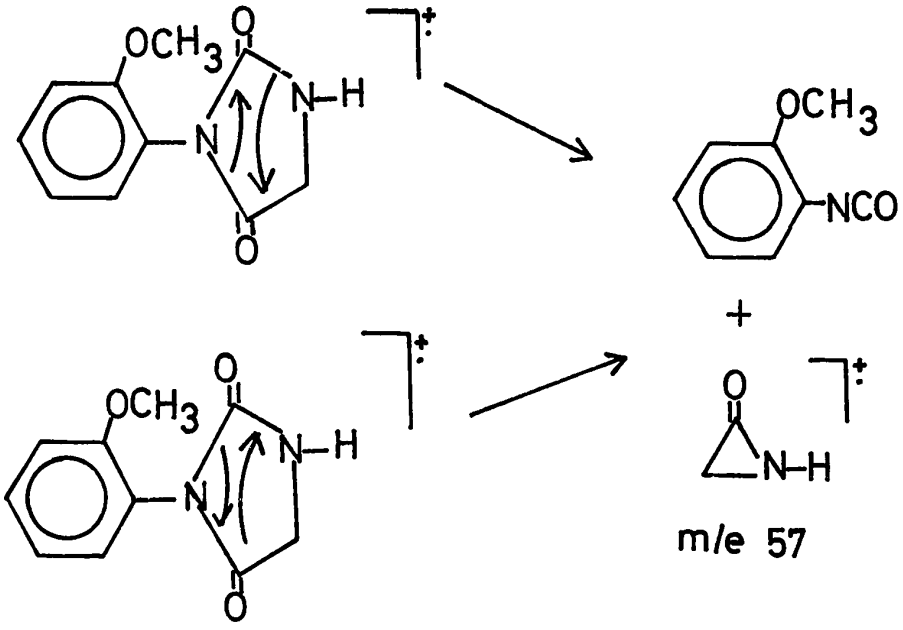
Up to the present time there is only one publication in the literature dealing with the mass spectra of thiohydantoins. The spectrum of 3-phenylthiohydantoin has been reported by a group of Russian chemists.[53] The major fragments have been assigned to the following ions: $\phi NCS^{+\cdot}$ (m/e 135), $\phi NCO^{+\cdot}$ (m/e 119), ϕNCH^{+} (m/e 104), $\phi NH_2^{+\cdot}$ (m/e 93), ϕ^{+} (m/e 77). More work has been done on the mass spectra of the hydantoins.[7,54,55]

The mode of decomposition for 3-(2-methoxyphenyl)-hydantoin (XXIX) seems to fit the mode of decomposition of hydantoins, as previously described.[7,54,55]

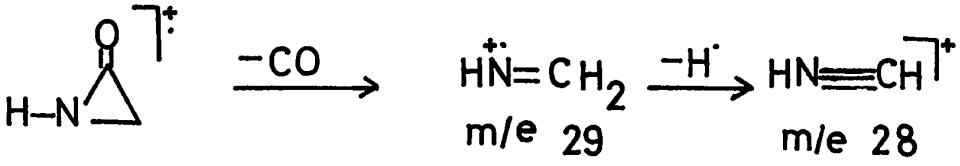




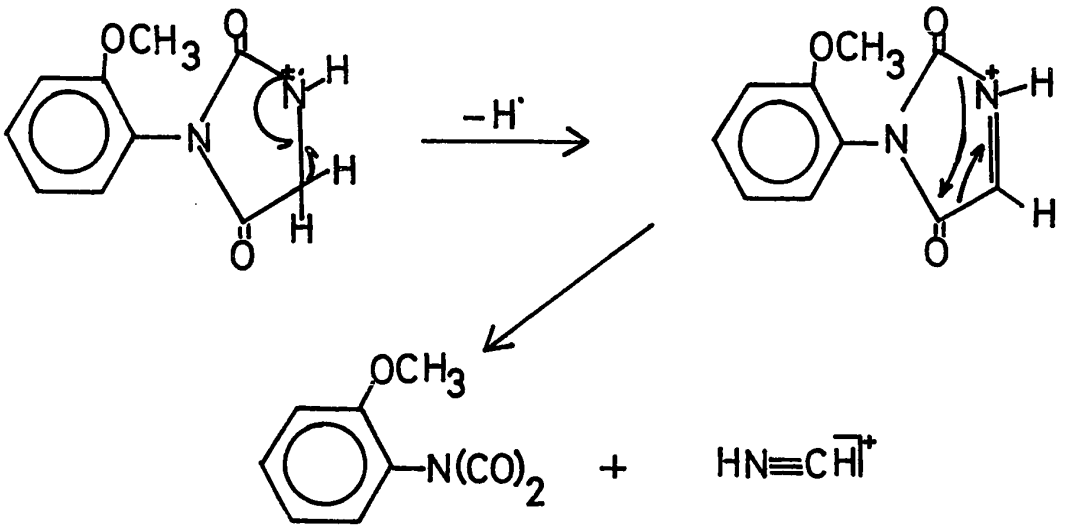
Since the ion $\overset{\frown}{CH_2\text{-}NH\text{-}CO}^{+\cdot}$ (m/e 57) is abundant in the case of this hydantoin, it is probable that the isocyanate can also be lost as a neutral fragment. This seems to be confirmed by the work of Djerassi,[54] and Coutts.[55]



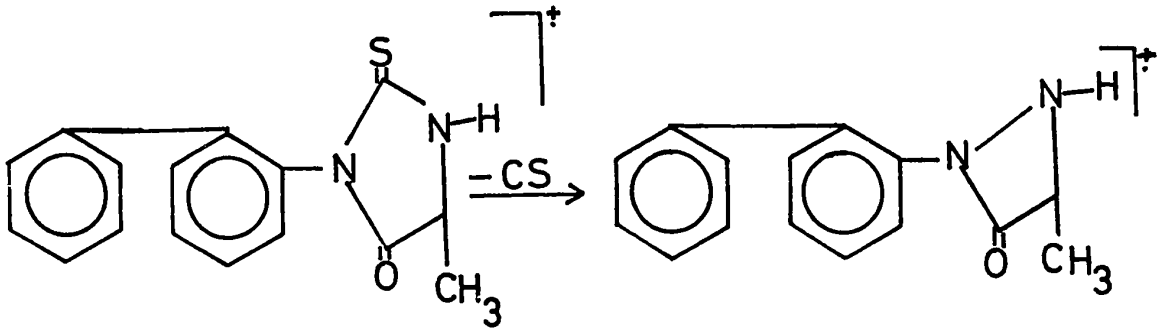
Furthermore, Djerassi showed by isotopic labelling that the C-4 carbonyl group was preferentially (> 90%) expelled in the isocyanate extrusion. This decomposition process proceeds further, yielding an ion of lower mass:[54]



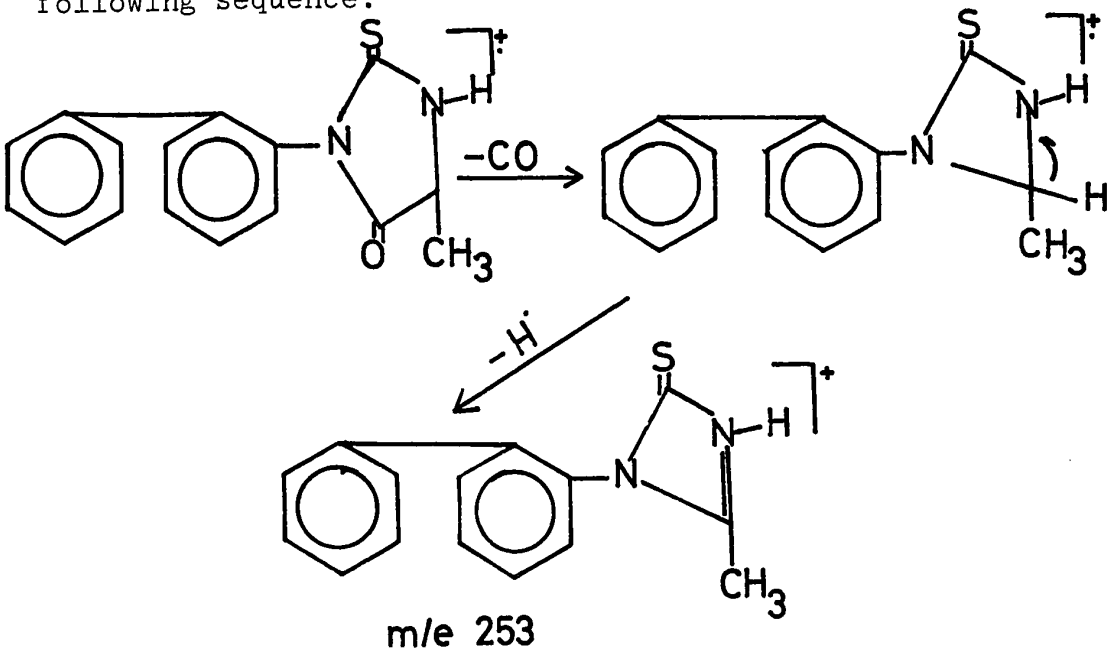
The same ion could also be formed by a different process:[55]



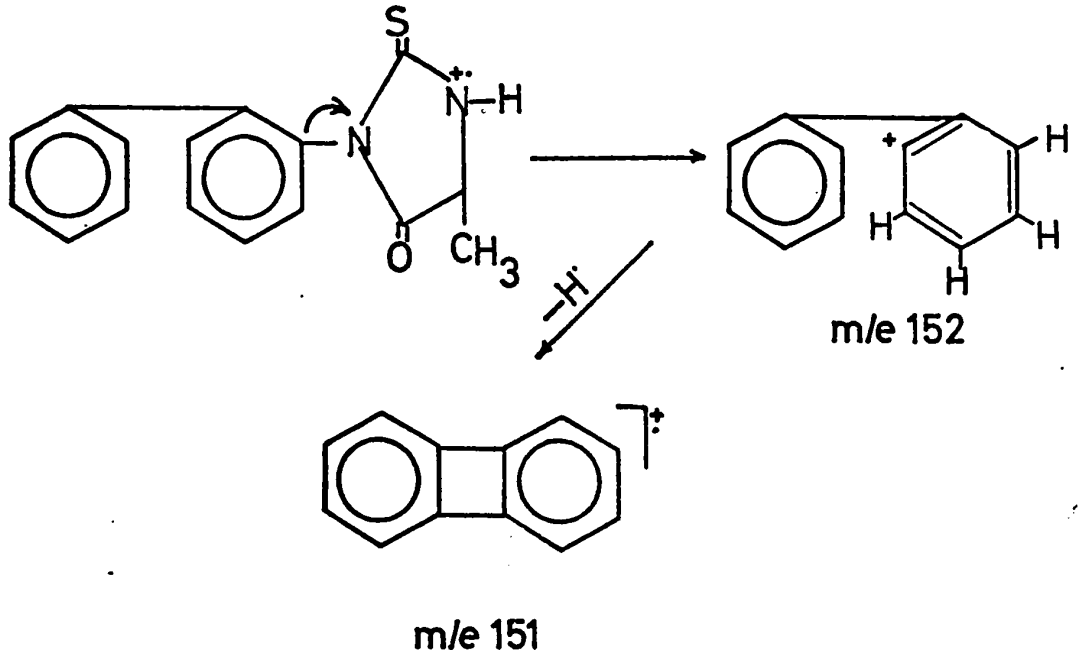
In the mass spectrum of the 3-(2-biphenyl)-5-methyl-2-thiohydantoin (XXVIII), in addition to the usual ions; there occurs an ion at m/e 238 which could be derived from a different fragmentation pattern



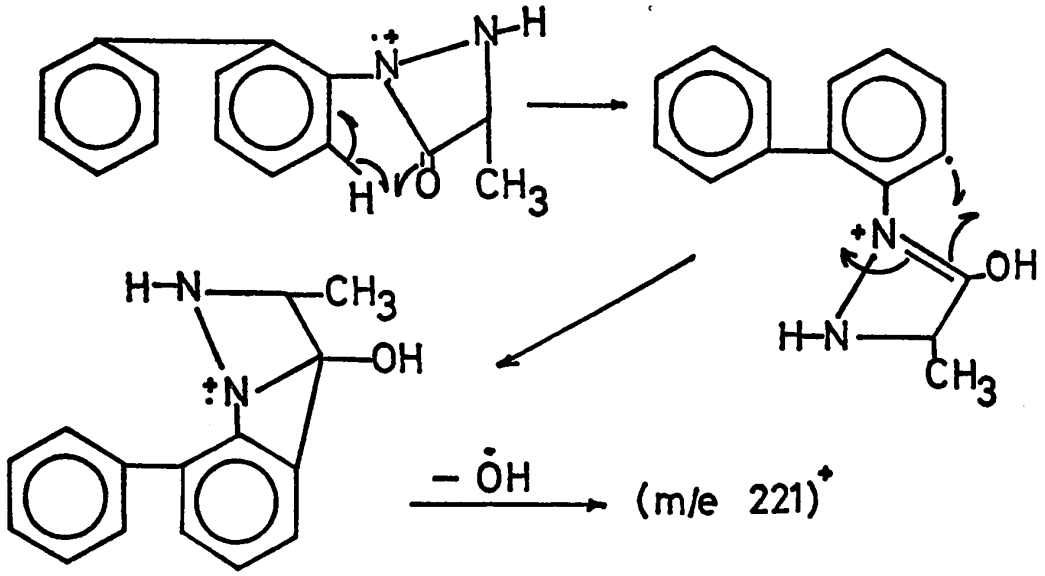
The ion at m/e 253 could possibly arise through the following sequence.[54]



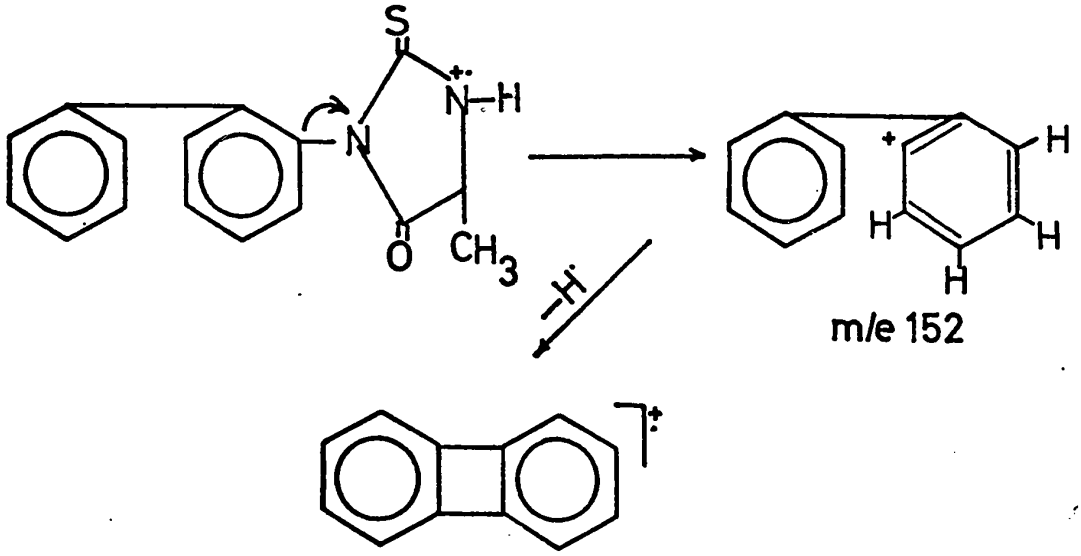
In the same spectrum one of the most intense absorptions appears at m/e 152, accompanied by another intense absorption at m/e 151. Since it has already been pointed out [7] that the C-N aryl bond can be broken, a possible explanation for the production of these ions is that the following sequence occurs,



The very intense peak at m/e 221 could have been formed in the following manner,

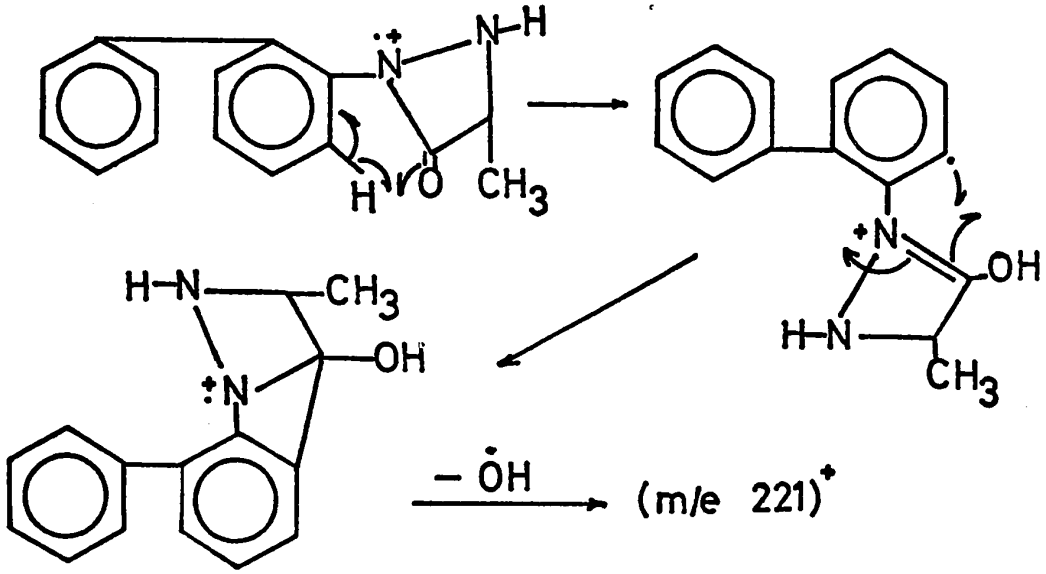


However, this has yet to be proved.



m/e 151

The very intense peak at m/e 221 could have been formed in the following manner,



However, this has yet to be proved.

Table XVIII: Mass Spectrum of 3-(2-methoxyphenyl)hydantoin (XIX) in Terms of % of Base Peak.

M/e	% Base Peak	M/e	% Base Peak
206	9.9	104	6.8
205	6.8	81	6.2
190	13.2	77	4.0
189	4.1	76	5.4
188	32.0	70	4.4
167	6.8	66	4.3
155	4.8	65	5.4
151	10.6	57	8.1
150	14.9	56	5.8
149	100.0	55	5.8
141	13.6	45	3.9
125	5.6	41	9.8
123	18.4	29	4.8
105	4.0	28	4.8

Table XIX: Mass Spectrum of 3-(2-methylphenyl)-5-phenyl-hydantoin (VIII) in Terms of % of Base Peak.

M/e	% Base Peak	M/e	% Base Peak
267	9.1	106	62.3
266	39.7	105	68.8
194	5.3	104	80.1
189	9.6	103	5.9
169	4.3	92	5.3
167	9.1	91	24.7
160	3.7	90	9.6
156	4.3	89	12.3
155	12.9	83	7.5
154	4.3	79	10.7
149	24.2	78	32.2
142	6.4	77	43.0
141	36.5	76	16.6
134	20.9	75	4.3
133	100.0	74	4.3
132	23.6	71	9.6
128	4.3	70	13.9
119	5.3	69	9.1
118	11.3	65	11.8
117	11.3	57	27.4
115	6.4	55	20.4
112	4.3	52	12.9
107	8.0	51	25.8

Table XX: Mass Spectrum of 3-(2-biphenyl)-5-methyl-2-thiohydantoin (XXVIII) in Terms of % of Base Peak.

M/e	% Base Peak	M/e	% Base Peak
283	22.0	179	10.6
282	100.0	178	36.0
279	11.3	177	12.2
253	4.6	169	5.0
249	5.8	168	4.9
238	4.2	167	23.6
223	6.6	166	4.4
222	6.6	155	7.3
221	32.0	154	4.5
212	4.6	153	4.4
210	20.0	152	19.3
205	8.6	151	12.4
197	6.2	150	12.6
196	1.7	139	4.0
195	5.7	127	15.3
184	4.0	85	8.6
181	9.0	77	6.0
180	16.0	76	9.0

Table XXI: Mass Spectrum of 3-(2-methyl-4-nitrophenyl)-5-methylhydantoin (X) in Terms of % of Base Peak.

M/e	% Base Peak	M/e	% Base Peak
252	15.5	120	4.8
251	100.0	117	6.2
222	2.8	105	5.0
180	4.8	104	19.7
179	46.6	103	4.8
178	46.6	90	3.6
175	11.5	89	19.7
162	7.6	78	8.6
149	39.5	77	26.8
148	18.5	76	8.1
141	27.6	71	3.9
133	6.2	70	24.0
132	8.4		

BIBLIOGRAPHY

1. G. Binsch, in " Topics in Stereochemistry," Vol. 3, E. L. Eliel and N. L. Allinger, Eds., Interscience Publishers, New York, N. Y., 1968, p. 97.

2. T. H. Siddall, and C. A. Prohaska, Nature, 208, 582 (1965).

3. Y. Shvo, E. C. Taylor, K. Mislow, and M. Raban, J. Amer. Chem. Soc., 89, 4910 (1967).

4. B. J. Price, J. A. Eggleston, and I. D. Sutherland, J. Chem. Soc., (B), 922 (1967).

5. F. Hund, Ph. D. Thesis, Department of Chemistry, University of Rochester, Rochester, N. Y., 1971.

6. S. W. Huang, M. S. Thesis, Department of Chemistry, University of Rochester, Rochester, N. Y., 1969.

7. J. R. Fehlner, Ph. D. Thesis, Department of Chemistry, University of Rochester, Rochester, N. Y., 1970.

8. L. Pauling, " The Nature of the Chemical Bond," 3rd. ed., Cornell University Press, Ithaca, New York, 1960, p. 260.

9. S. Icli, Sir George Williams University, Montreal, P. Q., personal communication, 1972.

10. L. D. Colebrook, Sir George Williams University, Montreal, P. Q., personal communication, 1972.

11. F. Bloch, Phys. Rev., 93, 944 (1954).

12. R. K. Waugsness, and F. Bloch, Phys. Rev., 89, 728 (1953).

13. F. Bloch, Phys. Rev., 70, 460 (1946).

14. H. S. Gutowsky, and C. H. Holm, J. Chem. Phys., 25, 1228 (1956).

15. D. W. Marquardt, J. Soc. Ind. App. Math., 11, 431 (1963).

16. R. J. Kurland, M. B. Rubin, and W. B. Wise, J. Chem. Phys., 40, 2426 (1964).

17. H. S. Gutowsky, A. Allerhand, J. Jones, and R. A. Meinzer, J. Amer. Chem. Soc., 88, 3185 (1966).

18. L. D. Colebrook, Sir George Williams University, Montreal, P. Q., personal communication, 1972.

19. W. E. Bentz, Ph. D. Thesis, Deparment of Chemistry, University of Rochester, Rochester, N. Y., 1971.

20. D. van der Helm, A. E. Lessor, and L. L. Merrit, Acta Cryst., 13, 1050 (1960).

21. L. A. Walker, Dissertation Abstr., B, 28, 1408 (1967).

22. R. B. Corey, Chem. Rev., 26, 227 (1940).

23. L. Pauling, " The Nature of the Chemical Bond," 3rd ed., Cornell University Press, Ithaca, 1960, p. 90.

24. H. G. Mautner, and W. D. Kumler, J. Amer. Chem. Soc., 78, 97 (1956).

25. H. G. Mautner, ibid., 78, 5292 (1956).

26. H. G. Mautner, and E. M. Clayton, ibid., 81, 6270 (1959).

27. L. J. Bellamy, " Infrared Spectra of Complex Molecules," Methuen, London, 1958, pp. 355-356.

28. R. Mecke, Jr., R. Mecke, and A. Luthbringhaus, Z. Naturforsch., 10 B, 367 (1955).

29. R. T. Sanderson, " Chemical Periodicity," Reinhold, New York, 1950, p. 50.

30. C. M. Lee, and W. D. Kumler, J. Org. Chem., 27, 2052 (1962).

31. L. D. Colebrook, Sir George Williams University, Montreal, P. Q., personal communication, 1972.

32. E. L. Eliel," Stereochemistry of Carbon Compounds," McGraw-Hill, New York, 1962, pp. 156-164.

33. E. L. Eliel, N. L. Allinger, S. L. Angyal, and G. A. Morrison," Conformational Analysis," Interscience, New York, 1965, ch. 7.

34. L. Pauling," The Nature of the Chemical Bond," 3rd ed., Cornell University Press, Ithaca, New York, 1960, p. 260.

35. D. A. Brown, and M. J. Dewar, J. Chem. Soc., 2046 (1953).

36. K. Spaargaren, P. K. Korver, P. J. van der Haak, and Th. J. de Boer, Org. Magn. Res., 3, 605 (1971).

37. M. J. Dewar, and P. J. Grisdale, J. Amer. Chem. Soc., 84, 3548 (1962).

38. C. G. Swain, and E. C. Lupton, J. Amer. Chem. Soc., 90, 4328 (1968).

39. F. H. Westheimer," Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, 1956, pp. 543-554.

40. A. Jaescke, H. Muensch, H. G. Schmid, M. Friegolin, and A. Mannschreck, J. Mol. Spectr., 31, 14 (1969).

41. R. L. Schriner, W. H. Horne, and R. F. B. Cox, Org. Syn., Coll. Vol. II, 453.

42. R. A. Keller," Basic Tables in Chemistry," McGraw-Hill, New York, 1967, p. 215.

43. R. D. Coghill, and T. B. Johnson, J. Amer. Chem. Soc., 47, 184 (1925).

44. L. D. Behr, and H. T. Clarke, J. Amer. Chem. Soc., 1630 (1932).

45. C. Wheeler, and D. Liddle, Am. Chem. J., 40, 547 (1908).

46. H. K. Pujari, and M. K. Rout, J. Ind. Chem. Soc., 31, 937 (1954).

47. R. A. Corral, and O. O. Orazi, Spectr. Acta, 21, 2119 (1965).

48. T. H. Elliot, and P. N. Natarajun, J. Pharm. Pharmac., 19, 209 (1967).

49. H. S. Kimmel, and A. Saifer, Anal. Biochem., 9, 316 (1964).

50. L. K. Ramachadran, A. Epp, and W. B. McConnell, Analyt. Chem., 27, 1734 (1955).

51. A. Epp, Analyt. Chem., 29, 1283 (1957).

52. R. Mecke, Jr., R. Mecke, Chem. Ber., 89, 343 (1956).

53. N. S. Vul'fson, U. M. Stepenow, V. A. Puchkow, and A. M. Zyakon, Izv. Akad. Nauk. SSSR, Ser. Khim., 8, 1524 (1963).

54. R. Corral, O. O. Orazi, A. M. Duffield, and C. Djerassi, Org. Mass Spectr., 5, 551 (1971).

55. R. A. Locock, and R. T. Coutts, Org. Mass Spectr., 3, 735 (1970).

APPENDIX

LISTINGS OF

AND

DIRECTIONS FOR THE USE OF

THE COMPUTER PROGRAMS UTILIZED

IN THIS RESEARCH PROJECT

LINDI

This programme digitalizes NMR spectra and transfers them to paper tape, which is later used as input in the TAPGH programme. (See also Fitting of the Spectra section).

```
FTN,B
      PROGRAM LINDI
      COMMON IDEN(35),KY(256),IZ(4),X(4)
      WRITE(2,100)
  100 FORMAT("LINE FOLLOWER DIGITIZATION OF NMR SPECTRA"/)
      CALL RESET
      WRITE(2,101)
  101 FORMAT("ENTER VALUES IN FREE FIELD FORMAT"/"TO ABORT: SET SWITCH 1
     15"/"FOR MANUAL SCAN:  SET SWITCH 0"/"NOTE:  YES = 1, NO = 0"//
     2"PREPARE LINE FOLLOWER"/)
      M1=1
      PAUSE
    2 WRITE(2,102)
  102 FORMAT("ENTER IDENTIFICATION")
      CALL RESET
      READ(1,103)IDEN
  103 FORMAT(35A2)
    3 WRITE(2,104)
  104 FORMAT("ENTER POINTS/HZ")
      READ(1,*)PPHZ
      WRITE(2,105)
  105 FORMAT("ADJUST SENSOR TO LEFT FREQUENCY LIMIT")
      CALL PLOT(0,0)
      PAUSE
      WRITE(2,106)
  106 FORMAT("ADJUST SENSOR TO RIGHT FREQUENCY LIMIT")
      CALL PLOT(250,0)
      PAUSE
      CALL PLOT(0,0)
      WRITE(2,107)
  107 FORMAT("ENTER LEFT FREQUENCY LIMIT")
      READ(1,*)FL
      WRITE(2,108)
  108 FORMAT("ENTER RIGHT FREQUENCY LIMIT")
      READ(1,*)FR
      HZPT=(FR-FL)/250.0
      AHZ=ABS(HZPT)
      AMULT=1.0/(AHZ*PPHZ)
      MULT=AMULT + 0.5
      IF (MULT-1)4,5
    4 MULT=1
      AMULT=1.0
    5 CONTINUE
      NPT=250/MULT+1
      PPCS=1.0/(AHZ*FLOAT(MULT))
```

```
    FREQI=HZPT*FLOAT(MULT)
 10 WRITE(2,109)
109 FORMAT("SET SENSOR ON BASE LINE")
    CALL RESET
    PAUSE
    IVAL=0
    MDEL=M1
    CALL DIG3(MDEL,IVAL)
    NBASE=IVAL
    WRITE(2,117)
117 FORMAT("SET SENSOR ON CURVE")
    PAUSE
    WRITE(2,110)
110 FORMAT("ENTER SCAN RATE: 1 = FAST,  10 = SLOW")
    READ(1,*)IDEL
    MDEL=IDEL
    DEL=0.1*FLOAT(IDEL)
    DO 12 I=1,251
    J=I-1
    CALL PLOT(J,0)
    IF (ISSW(0))20,21
 20 CALL DHALT
 21 CONTINUE
    CALL DIG3(MDEL,IVAL)
    KY(I)=IVAL
    IF (ISSW(15))22,12
 22 CALL PLOT(0,0)
    GO TO 10
 12 CONTINUE
    CALL PLOT(0,0)
    WRITE(2,111)
111 FORMAT("REPEAT SCAN ?")
    READ(1,*)IR
    IF (IR) 10,13,10
 13 CONTINUE
    DO 14 I=1,251
    KY(I)=KY(I)-NBASE
 14 CONTINUE
    IF (ISSW(15))50,15
 15 WRITE(2,130)
130 FORMAT("PAPER TAPE REQUIRED ?")
    READ(1,*)IPT
    IF (IPT)60,61,60
 60 CALL LEADR(2,10)
 61 WRITE(2,113)IDEN
```

```
113 FORMAT(///35A2/)
    WRITE(2,122)NPT
122 FORMAT(14X,"NUMBER OF POINTS = ",I3)
    WRITE(2,114)FL,FR
114 FORMAT("  FREQUENCY LIMITS (HZ):  LEFT = ",F6.2,7X,"RIGHT = ",F6.
   12)
    WRITE(2,115)PPHZ,PPCS
115 FORMAT(9X,"POINTS/HZ:  REQUESTED = ",F5.2,5X,"RECORDED = ",F5.2)
    WRITE(2,116)IDEL,DEL
116 FORMAT("DELAY FACTOR PER POINT SCANNED = ",I2,5X,"DELAY (SEC) = "
   1,F5.1/)
    WRITE(2,118)
118 FORMAT("INTEN.  FREQ.    INTEN.  FREQ.    INTEN.  FREQ.    INTEN.
   1  FREQ."/)
    FREQ=FL
    N=1
    I=1
 40 IY=KY(N)
    IZ(I)=IY
    X(I)=FREQ
    FREQ=FREQ + FREQI
    I=I+1
    N=N+MULT
    IF (251-N)44,42
 42 CONTINUE
    IF (4-I)44,40
 44 CONTINUE
    NNN=I-1
    IF (ISSW(15))50,45
 45 CONTINUE
    WRITE(2,121)(IZ(I),X(I),I=1,NNN)
121 FORMAT(3(I5,F8.2,4X)(I5,F8.2))
    I=1
    IF (251-N)25,40
 25 CONTINUE
    IF (IPT)49,50,49
 49 CALL LEADR(2,10)
 50 WRITE(2,119)
119 FORMAT(///"NEXT CASE"/)
    PAUSE
    GO TO 2
    END
    ENDS
```

TAPGH

This programme transfers the digitalized NMR spectra fom the paper tape to the magnetic tape, which is later used as input for both the NLIN GH and the PUNNLIN programmes. (See also Fitting of the Spectra section).

```
FTN,B
      PROGRAM TAPGH
      COMMON IB(6),B(6),IDEN(35),X(256),KY(256),KKY(4),XX(4)
      KØ=Ø
      K1=1
      K6=6
      FKØ=Ø.Ø
      WRITE(2,1ØØ)
  1ØØ FORMAT(/"PREPARE INPUT TAPE FOR NLINGH"//"USE FREE FIELD FORMAT FO
     1R INPUT"/"NOTE: YES = 1,  NØ = Ø"/"TO ABORT: SET SWITCH 15"/)
      WRITE(2,1Ø1)
  1Ø1 FORMAT("CAUTION"/"CAUTION"//"DO NOT PROCEED UNTIL DATA TAPE IS MOU
     1NTED"/)
      PAUSE
      WRITE(2,1Ø2)
  1Ø2 FORMAT("PARAMETER IDENTIFICATION:"/" B(1) = TAU(A)"/" B(2) = TAU(B
     1)"/" B(3) = SHIFT(A)"/" B(4) = SHIFT(B)"/" B(5) = SCALING FACTOR"/
     2" B(6) = LINE WIDTH"/)
    2 WRITE(2,1Ø3)
  1Ø3 FORMAT("ENTER SPECTRUM NUMBER")
      CALL RESET
      READ(1,*)NRUN
      WRITE(2,1Ø4)
  1Ø4 FORMAT("ENTER NUMBER OF FIXED PARAMETERS")
      READ(1,*)KP
      IF (KP) 5,3,5
    5 WRITE(2,1Ø5)
  1Ø5 FORMAT("ENTER SUBSCRIPTS OF FIXED PARAMETERS")
      DO 6 I=1,KP
      READ(1,*)IB(I)
    6 CONTINUE
    3 WRITE(2,1Ø6)
  1Ø6 FORMAT("ENTER TAU(A)")
      READ(1,*)B(1)
      WRITE(2,1Ø7)
  1Ø7 FORMAT("ENTER TAU(B)")
      READ(1,*)B(2)
      WRITE(2,1Ø8)
  1Ø8 FORMAT("ENTER SHIFT(A)")
      READ(1,*)B(3)
      WRITE(2,1Ø9)
  1Ø9 FORMAT("ENTER SHIFT(B)")
      READ(1,*)B(4)
      WRITE(2,11Ø)
  11Ø FORMAT("ENTER SCALING FACTOR")
```

```
      READ(1,*)B(5)
      WRITE(2,111)
  111 FORMAT("ENTER LINE WIDTH")
      READ(1,*)B(6)
      IF (ISSW(15))2,7
    7 READ(5,120)IDEN
  120 FORMAT(35A2)
      READ(5,122)NPT
  122 FORMAT(33X,I3,4/)
      N=1
      NC=NPT
      NN=4
    8 READ(5,121)(KKY(I),XX(I),I=1,NN)
  121 FORMAT(3(I5,F8.2,4X)(I5,F8.2))
      DO 9 I=1,NN
      KY(N)=KKY(I)
      X(N)=XX(I)
      N=N+1
    9 CONTINUE
      NC=NC-NN
      IF (NC-4)11,10,10
   10 NN=4
      GO TO 12
   11 NN=NC
   12 CONTINUE
      IF (NPT-N)13,8,8
   13 WRITE(2,133)IDEN
  133 FORMAT("IDENTIFICATION:"//35A2/)
      WRITE(2,135)
  135 FORMAT("TRANSFER TO MAGNETIC TAPE ?")
      READ(1,*)IT
      IF (IT)26,29,26
   26 MAX=KY(1)
      DO 45 I=2,NPT
      IF (MAX-KY(I)) 40,45
   40 MAX=KY(I)
   45 CONTINUE
      SPRD=MAX
      SPRD=0.011*SPRD
      WRITE(7,140)NPT,K6,KP,K1,K1,K0
  140 FORMAT(12I3)
      WRITE(7,140)K0,K1,K1,K0,K0,K0
      WRITE(7,145)FK0,SPRD
      IF (KP)30,31,30
   30 WRITE(7,140)(IB(I),I=1,KP),K0,K0,K0,K0,K0
```

```
 31 WRITE(7,142)(FKO,I=1,8)
142 FORMAT(8F10.0)
    WRITE(7,143)(B(I),I=1,6)
143 FORMAT(6F10.4)
    DO 27 I=1,NPT
    Y=FLOAT(KY(I))/100.0
    WRITE(7,145)Y,X(I)
145 FORMAT(2F10.3)
 27 CONTINUE
    WRITE(7,146)NRUN,IDEN
146 FORMAT(I3,35A2)
    WRITE(2,150)
150 FORMAT("IS ANOTHER DATA SET TO FOLLOW ?")
    READ (1,*)IS
    IF (IS)29,28,29
 28 WRITE(7,140)(KO,I=1,6)
    END FILE 7
    REWIND 7
    WRITE(2,151)
151 FORMAT("TAPE PREPARATION COMPLETE")
 29 WRITE(2,152)
152 FORMAT(/"NEXT CASE"/)
    PAUSE
    GO TO 2
    END
    END$
```

NLIN GH

In the output of this programme, the computer first plots the experimental spectrum and the spectrum calculated from the initial guesses for the parameters. It then fits the spectra showing the changes in the parameters for each iteration. When the best fit is found, another plot of the experimental and the final calculated spectra, as well as a tabular output of the points, is given. Finally, an error analysis of the fit is printed. (See also Fitting of the Spectra section).

```
      PROGRAM NLIN(INPUT,OUTPUT,TAPE3,TAPE5,TAPE6=OUTPUT)
C     CDC 6400 VERSION.  OCTOBER 1971
C     TAPE5 IS USED FOR DATA INPUT
C
C     MODIFIED VERSION.   APRIL 1971
C     PREPARED FOR MAGNETIC TAPE INPUT.
C     RESTRICTED TO TWO DATA VALUES, IN (2F10.0) FORMAT.
C     CARD INPUT MAY BE USED, BUT FORMAT CARD (ITEM 7) MUST BE OMITTED.
C     TO RE-CONVERT TO ORIGINAL VERSION OF NLIN,INSERT AFTER CARD 1250
C     READ(5,902)(FMT(I),I=1,12)
C     REPLACE CARD 1280 WITH
C  56 READ(5,FMT)Y(I),(X(I,L),L=1,M)
C     REMOVE CARD 1281
C
C     NONLINEAR LEAST SQUARES
C     BY      D. W. MARQUARDT
C     PROGRAMMED BY      T. BAUMEISTER III,
C                        J. ANN SHELDON AND RUBY M. STANLEY
C                  IBKT=1 MEANS USE UPPER A MATRIX
C                  IBKT=2 MEANS USE TAPE 3
C
      DIMENSION FMT(18),PRNT(5),SPRNT(5)
      DIMENSION BS(50),DB(50),BA(50),G(50),W(51),IB(49),SA(50),P(50),A(5
     10,51),B(50)
      DIMENSION X(500,1),Y(500)
      DIMENSION CONS(25)
      DATAIBCH/1H /,IOCH/1HO/,IPCH/1HP/,IXCH/1HX/,IYCH/1HY/
C
C     ------------------------------------------------------------------
C     MAX NO OF PARAMETERS IS K=50
C     MAX NO OF IND VARS IS M=10
C     MAX NO OF OBSERVATIONS IS N=500
C                  IWHER =-1 MEANS DO ANY SPECIAL INITIALIZING FOR CASE
```


```
C                   IWHER = 0 MEANS START NEW CASE OR END RUN
C                   IWHER = 1 MEANS GET P S AND F
C                   IWHER GREATER THAN 1 MEANS GET F ONLY
C     ------------------------------------------------------------------
C     SET ITERATION LIMIT
      ITLIM=50
C     ------------------------------------------------------------------
      NPRNT=0
  650 IWHER = 0
  652 GO TO 4
  653 IWHER = IWHER
      IF (IWHER.GT.0)GO TO 654
      IF (IWHER.EQ.0)GO TO 660
  651 CONTINUE
C                   CODING FOR CASE INITIALIZING GOES HERE
C     ..................................................................
      CALL SUBZ(Y,X,B,PRNT,NPRNT,N)
C     ..................................................................
      IF (IBOUT.EQ.0) GO TO 652
      GO TO 650
  654 CONTINUE
C                   CODING TO MAKE F GOES HERE
C                   F IS Y HAT (I)
C                   NPRNT IS THE NO OF OTHER WORDS TO BE PRINTED
C                   THE WORDS TO BE PRINTED ARE IN PRNT(1)...PRNT(5)
C     ..................................................................
      CALL      FCODE(Y,X,B,PRNT,F,I,RES)
C     ..................................................................
      IF (IWHER.NE.1)GO TO 652
  656 IF (IFSS2.NE.0) GO TO 652
  658 CONTINUE
C                   CODING TO MAKE DF/DB GOES HERE
C                   MAKE K OF THEM. CALL THEM P(J)
```


```
C                    THEY ARE MADE FROM X(I,L) AND B(J)
C      ..............................................................
       CALL PCODE(P,X,B,PRNT,F,I)
C      ..............................................................
       GO TO 652
  660  STOP 111
C                    THIS IS THE END OF THE MAIN ROUTINE
C      --------------------------------------------------------------
    4  IWHER = IWHER
C                  -  0 +
       IF (IWHER.LT.0)GO TO 59
       IF (IWHER.EQ.0)GO TO 10
C                1  2   3   4
    8  GO TO (75,304,606,620), IWHER
C                    READ FIRST CARD OF NEXT CASE
   10  ITCT=0
       IBOUT=0
       K1 = 1
       K2 = 1
       IISS = 0
       READ (5,900) N,K,IP,M,IFP,NCONS
       NTILDA=N+NCONS
       XNT=NTILDA
       IF (N.LE.0)GO TO 20
       READ (5,900)IWS1,IWS2,IWS3,IWS4,IWS5,IWS6
       IFSS1=2
       IF (IWS5.EQ.0)GO TO 210
       PAUSE 5
  210  CONTINUE
       WRITE (6,932)
  211  GO TO 21
C                    END OF LAST PROBLEM
   20  GO TO (  19,  17),IBKT
```


```
   17 REWIND 3
   19 IWHER=0
      GO TO 653
21    IF (IFP.LE.0)GO TO 22
   23 CONTINUE
      READ (5,930)YMN,SPRD
   22 IF(IP.LE.0) GOTO 30
   24 READ(5,900)(IB(I), I = 1,IP)
      DO 26 I=1,IP
      IF (IB(I).GT.0)GO TO 26
25    WRITE (6,926)
212   CONTINUE
      IBOUT=1
   26 CONTINUE
   30 READ (5,931) FF,T,E,TAU,XL,GAMCR,DEL,ZETA
C                  DUB IN INPUT CONSTANTS IF NOT SUPPLIED
C                  ( XL IS CHECKED IN FIRST ITERATION )
      IF(FF.GT.0.) GOTO 34
   32 FF=4.
   34 IF(E.GT.0.) GOTO 37
   36 E=.00005
   37 IF(TAU.GT.0.) GOTO 39
   38 TAU=.001
   39 IF(T.GT.0.) GOTO 42
   40 T=2.
42    IF (K .GT.25)GO TO 46
   44 IBKT=1
      GO TO 50
   46 IBKT=2
      REWIND 3
   50 IF(GAMCR.GT. 0.) GOTO 52
   51 GAMCR = 45.
   52 IF (DEL.GT. 0.) GO TO 55
```


```
      DEL=.00001
   55 IF (ZETA.GT. 0.) GO TO 53
      ZETA=.1E-30
   53 XKDB = 1.
   54 CONTINUE
C                    READ IN INITIAL B GUESSES 7 TO THE CARD
      READ (5,901)(B(I),I=1,K)
      DO 56 I=1,N
   56 READ(5,950)Y(I),(X(I,L),L=1,M)
  950 FORMAT(2F10.0)
      IWHER=-1
      GO TO 653
   59 IBKA=1
C
C     ..................................................................
C                    START THE CALCULATION OF THE PTP MATRIX
   58   WRITE (6,907)N,K,IP,M,IFP,GAMCR,DEL,FF,T,E,TAU,XL,ZETA
  213   GO TO 61
   60 CONTINUE
      IF (IWS5.NE.0) GO TO 61
      IWS3=IWS3-1
      IWS3=MAX0(IWS3,0)
   61   DO 62 I=1,K
      G (I) =0.
      DO 62 J=1,K
   62 A (I,J)=0.
      GO TO (63,69,69),IBKA
   63   IF (IWS5.EQ.0)GO TO 630
  630   IFSS3=IWS3
      IFSS2=IWS2
      GO TO 70
   64 IFSS3=0
   66 GO TO (70,65), IFSS2
```


```
   65 IFSS2=0
      GO TO 70
 69   CONTINUE
 70   WRITE (6,908) ITCT,(B(J),J=1,K)
 214  CONTINUE
      IF (IFSS3.EQ.0)GO TO 73
 71   IF (IFP.LE.0)GO TO 68
   67 WS = YMN+SPRD
      WRITE( 6,906)YMN,WS
  258 CONTINUE
      GO TO 73
   68 WRITE( 6,910)
  259 CONTINUE
   73 I=1
      PHI=0.
      PHIN=0.
      ICONS=1
      IF (IFSS2.EQ.0) GO TO 57
      GO TO 600
 72   IF (IFSS2.EQ.1)GO TO 602
C                   THIS IS THE ANALYTICAL P S ROUTINE
   57 IWHER=1
C                   GET P S AND F
      GO TO 653
 75   IF (IP.LE.0)GO TO 80
   76 DO 77 II=1,IP
      IWS=IB(II)
   77 P(IWS)=0.
      GO TO 80
C     ..................................................................
C                   THIS IS THE ESTIMATED P S ROUTINE
  600 CONTINUE
  602 IWHER=3
```


```
      GO TO 653
  606 RWS=RES
      FSAVE=F
      DO 607 II=1,NPRNT
  607 SPRNT(II)=PRNT(II)
      J=1
  608 IF (IP.LE.0)GO TO 618
  610 DO 612 II=1,IP
      IF ((J-IB(II)).EQ.0)GO TO 621
  612 CONTINUE
  618 DBW=B(J)*DEL
      TWS=B(J)
      B(J)=B(J)+DBW
      IWHER=4
      GO TO 653
  620 B(J)=TWS
      P(J)=-(RES-RWS)/DBW
      GO TO 622
  621 P(J)=0.
  622 J=J+1
      IF ((J-K).LE.0)GO TO 608
  624 RES=RWS
      F=FSAVE
      DO 625 II=1,NPRNT
  625 PRNT(II)=SPRNT(II)
C                    END OF ESTIMATED P S ROUTINE
C     ..................................................................
C                    NOW, USE THE P S TO MAKE PARTIALS MATRIX
   80 DO 82 JJ=1,K
      G(JJ)=G(JJ)+RES*P(JJ)
      DO 82 II=JJ,K
      A(II,JJ)=A(II,JJ)+P(II)*P(JJ)
   82 A(JJ,II)=A(II,JJ)
```


```
      IF (IFP.LE.0)GO TO 318
  800 IF (IFSS3.EQ.0.OR.I.GT.N) GO TO 314
C                     PLOTTING Y(I),F
  802 IO = (Y(I)-YMN)*100./SPRD
      IPP = (F-YMN)*100./SPRD
      IF (IO.EQ.IPP)GO TO 808
      IF (IO.GT. IPP)GO TO 812
C                     Y(I) OUT FIRST
  804 IP1=IOCH
      IP2=IPCH
      I1=IO
      I2=IPP
      GO TO 816
C                     ONLY ONE CHARACTER
  808 IP1=IYCH
      IP2=IBCH
      I1=IO
      I2=IPP
      GO TO 816
C                     F OUT FIRST
  812 IP1=IPCH
      IP2=IOCH
      I1=IPP
      I2=IO
C                     ZERO PLOTS IN THE LEFT HAND COLUMN, SO I1 IS ITS
C                     OWN BLANK COUNTER
C                     OVERFLOWS PLOT X IN COLUMN 102
C                     UNDERFLOWS ALSO PLOT X IN COLUMN ZERO
  816 IF (I2.LE.101)GO TO 819
  817 I2=101
      IP2=IXCH
      IF (I1.LT.101)GO TO 819
  818 I1=101
```


```
      IP1=IXCH
      IP2=IBCH
      GO TO 825
  819 IF (I1.GE.0)GO TO 825
  822 I1=0
      IP1=IXCH
      IF (I2.GT.0)GO TO 825
  823 I2=1
      IP2=IBCH
  825 I1M1=I1
      I1M2=I2-I1-1
      IF (I1M1.GT.0)GO TO 832
  820 IF (I1M2.GT.0)GO TO 828
  824 WRITE (6,928)IP1,IP2
  215 CONTINUE
      GO TO 844
  828 WRITE (6,928)IP1,(IBCH,II=1,I1M2),IP2
  216 CONTINUE
      GO TO 844
  832 IF (I1M2.GT.0)GO TO 840
  836 WRITE (6,928)(IBCH,II=1,I1M1),IP1,IP2
  217 CONTINUE
      GO TO 844
  840 WRITE (6,928)(IBCH,II=1,I1M1),IP1,(IBCH,II=1,I1M2),IP2
  218 CONTINUE
  844 GO TO 314
  318 WS=RES
      IF (IFSS3.EQ.0.OR.I.GT.N) GO TO 314
  308 IF (NPRNT.GT.0)GO TO 312
  310 WRITE (6,925)Y(I),F,WS
  219 CONTINUE
      GO TO 314
  312 WRITE (6,925)Y(I),F,WS,(PRNT(JJ),JJ=1,NPRNT)
```


```
 220  CONTINUE
 314  WS=RES
      PHI=PHI+WS*WS
      IF (I.GT.N) GO TO 313
      PHIN=PHIN+WS*WS
      GO TO 315
 313  CONS(ICONS)=RES
      ICONS=ICONS+1
 315  I=I+1
      IF (I.LE.NTILDA) GO TO 72
 84   IF (IP.LE.0)GO TO 88
   85 DO 87 JJ=1,IP
      IWS=IB(JJ)
      DO 86 II=1,K
      A(IWS,II)=0.
   86 A(II,IWS)=0.
   87 A(IWS,IWS)=1.
 88   GO TO (90,704,703),IBKA
C                    SAVE SQUARE ROOTS OF DIAGONAL ELEMENTS
   90 DO 92 I=1,K
 92   SA(I)=SQRT (A(I,I))
      DO 106 I=1,K
      DO 100 J=1,K
      WS = SA(I)*SA(J)
      IF(WS.GT.0.) GOTO 98
   96 A(I,J) =0.
      GO TO 100
   98 A(I,J)=A(I,J)/WS
  100 CONTINUE
      IF(SA(I).GT.0.) GOTO 104
  102 G(I)=0.
      GO TO 106
  104 G(I)=G(I)/SA(I)
```


```
  106 CONTINUE
      DO 110 I=1,K
  110 A(I,I)=1.
  120 PHIZ=PHI
C                       WE NOW HAVE PHI ZERO
      GO TO (1132,1130),IBKT
 1130 WRITE (3)A
      REWIND 3
      GO TO 1134
 1132 DO 1133 II=1,K
      III=II+25
      DO 1133 JJ=1,K
 1133 A(III,JJ)=A(II,JJ)
C     ..................................................................
 1134 CONTINUE
      IF (ITCT.NE.0) GO TO 163
C                      FIRST ITERATION
  150 IF(XL.GT.0.) GOTO 154
  152 XL=0.01
  154 DO 161 J=1,K
  161 BS(J)=B(J)
C                      BS(J) CORRESPONDS TO PHIZ
  163 IBK1=1
      WS=N-K+IP
      ITCT=ITCT+1
      IF (ITCT.GT.ITLIM) GO TO 1800
      SE=SQRT(PHIN/WS)
      IF (IFSS3.GT.0)GO TO 165
  162 IF (IFSS2.EQ.0) GO TO 168
  167 WRITE (6,911)PHIZ,SE,XLL,GAMMA,XL
  221 CONTINUE
      GO TO 169
  168 WRITE (6,912)PHIZ,SE,XLL,GAMMA,XL
```


```
 222  CONTINUE
      GO TO 169
 165  IF (NCONS.EQ.0) GO TO 166
      WRITE (6,938) (JJ,CONS(JJ),JJ=1,NCONS)
 166  WRITE (6,939)
 111  DO 114 I=1,K
      WRITE (6,937) I, (A(I,J),J=1,K)
 114  CONTINUE
      IF (IFSS2.EQ.0) GO TO 1661
      WRITE (6,903) PHIZ,SE,XL
 223  CONTINUE
      GO TO 169
 1661 WRITE (6,909)PHIZ,SE,XL
 224  CONTINUE
  169 GO TO 200
  164 PHIL=PHI
C                    WE NOW HAVE PHI LAMBDA
      DO 170 J=1,K
      IF (ABS(DB(J)/(ABS(B(J)) + TAU)).GE.E) GOTO 172
  170 CONTINUE
      WRITE (6,923)
 225  CONTINUE
      GO TO 700
 172  IF (IWS5.EQ.0)GO TO 1720
 1720 IF (IWS4.EQ.0)GO TO 173
      IF (IWS4.EQ.1)GO TO 171
      IWS4=IWS4-1
      GO TO 173
 171  WRITE (6,924)
 226  CONTINUE
      GO TO 700
  173 XKDB = 1.
      IF (PHIL.GT.PHIZ)GO TO 190
```


```
  174 XLS=XL
      DO 176 J=1,K
      BA(J)=B(J)
  176 B(J)=BS(J)
      IF (XL.GT..00000001)GO TO 175
 1175 DO 1176 J=1,K
      B(J)=BA(J)
 1176 BS(J)=B(J)
      GO TO 60
  175 XL=XL/10.
      IBK1=2
      GO TO 200
  177 PHL4=PHI
C                     WE NOW HAVE PHI(LAMBDA/10)
      IF(PHL4.GT.PHIZ) GOTO 184
  182 DO 183 J=1,K
  183 BS(J)=B(J)
      GO TO 60
  184 XL=XLS
      DO 186 J=1,K
      BS(J)=BA(J)
  186 B(J)=BA(J)
      GO TO 60
  190 IBK1=4
      XLS=XL
      XL=XL/10.
      DO 185 J=1,K
  185 B(J)=BS(J)
      GO TO 200
  187  IF (PHI.LE.PHIZ)GO TO 196
  191 XL=XLS
      IBK1=3
  192 XL=XL*10.
```

```
  195 DO 193 J=1,K
  193 B(J)=BS(J)
      GO TO 200
  194 PHIT4=PHI
C                     WE NOW HAVE PHI(10*LAMBDA)
 180  IF (PHIT4.GT.PHIZ)GO TO 198
  196 DO 197 J=1,K
  197 BS(J)=B(J)
      GO TO 60
 198  IF (GAMMA.GE.GAMCR)GO TO 192
  199 XKDB = XKDB/2.
      DO 1199 J=1,K
      IF (ABS(DB(J)/(ABS(B(J))+TAU)).GE.E)GO TO 195
 1199 CONTINUE
      DO 1200 J=1,K
 1200 B(J)=BS(J)
      WRITE (6,934)
 227  CONTINUE
      GO TO 700
C
C     ..................................................................
C                     SET UP FOR MATRIX INVERSION
  200 GO TO (1102,1100),IBKT
 1100 READ (3)A
      REWIND 3
      GO TO 1104
 1102 DO 1103 II=1,K
      III=II+25
      DO 1103 JJ=1,K
 1103 A(II,JJ)=A(III,JJ)
 1104 DO 202 I=1,K
  202 A(I,I)=A(I,I)+XL
C                     GET INVERSE OF A AND SOLVE FOR DB (J)S
```


```
      IBKM=1
C     ..................................................................
C                    THIS IS THE MATRIX INVERSION ROUTINE
C                    K IS THE SIZE OF THE MATRIX
  404 CALL GJR(A,K,ZETA,MSING)
      GO TO (415,650), MSING
  415 GO TO (416,710), IBKM
C                    END OF MATRIX INVERSION, SOLVE FOR DB(J)
  416 DO 420 I=1,K
      DB(I)=0.
      DO 421 J=1,K
  421 DB(I)=A(I,J)*G(J)+DB(I)
  420 DB(I)=XKDB*DB(I)
      XLL=0.
      DTG = 0.
      GTG = 0.
      DO 250 J=1,K
      XLL=XLL+DB(J)*DB(J)
      DTG = DTG + DB(J)*G(J)
      GTG = GTG + G(J)**2
      DB(J)=DB(J)/SA(J)
  250 B(J)=B(J)+DB(J)
      KIP=K-IP
      IF (KIP.EQ.1) GO TO 1257
      CGAM=DTG/SQRT(XLL*GTG)
      JGAM = 1
      IF(CGAM.GT..0) GOTO 253
  251 CGAM = ABS(CGAM)
      JGAM = 2
  253 GAMMA = 57.2957795*(1.5707288+CGAM*(-0.2121144+CGAM*(0.074261
     1-CGAM*.0187293)))*SQRT(1.-CGAM)
      GO TO (257,255), JGAM
  255 GAMMA = 180.-GAMMA
```


```
      IF (XL.LT.1.0)GO TO 257
 1255 WRITE(6,922)XL,GAMMA
 228  CONTINUE
      GO TO 700
 1257 GAMMA=0.
 257  XLL=SQRT(XLL)
      IBK2=1
      GO TO 300
 252  IF (IFSS3.EQ.0)GO TO 256
 254  WRITE (6,904)(DB(J),J=1,K)
 229  CONTINUE
      WRITE (6,905)PHI,XL,GAMMA,XLL
 230  CONTINUE
  256 GO TO (164,177,194,187),IBK1
C
C     ..................................................................
C                    CALCULATE PHI
  300 I=1
      PHI=0.
      PHIN=0.
      IWHER=2
      IF (IWS5.EQ.0) GO TO 653
  302 GO TO 653
 304  PHI=PHI+(RES**2)
      IF (I.GT.N) GO TO 305
      PHIN=PHIN+RES*RES
 305  I=I+1
      IF (I.LE.NTILDA) GO TO 302
  316 IISS = 1
      K1 = K2
      GO TO 999
C
C
```


```
C     ..................................................................
C                    THIS IS THE CONFIDENCE LIMIT CALCULATION
  700 DO 702 J=1,K
  702 B(J)=BS(J)
      WRITE (6,933)N,K,IP,M,FF,T,E,TAU
 231  CONTINUE
      IBKA=2
      NTILDA=N
C                    THIS WILL PRINT THE Y,YHAT,DELTA Y
      ITCT=ITCT-1
      IFSS3=1
      GO TO 61
 704  IF (IFP.LE.0) GO TO 703
  705 IBKA=3
      IFP=0
      GO TO 61
 703  IF (NCONS.EQ.0) GO TO 706
      WRITE (6,938) (JJ,CONS(JJ),JJ=1,NCONS)
  706 WS=N-K+IP
      SE=SQRT(PHI/WS)
      PHIZ=PHI
      IF (IFSS2.EQ.0)GO TO 709
 707  WRITE (6,903)PHIZ,SE,XL
 232  CONTINUE
      GO TO 708
  709 WRITE(6,909) PHIZ,SE,XL
 233  CONTINUE
C                    NOW WE HAVE MATRIX A
  708 GO TO (1122,1120),IBKT
 1120 WRITE (3)A
      REWIND 3
      GO TO 1124
 1122 DO 1123 II=1,K
```


```
      III=II+25
      DO 1123 JJ=1,K
 1123 A(III,JJ)=A(II,JJ)
 1124 IBKM=2
      GO TO 404
C
C                        NOW WE HAVE C = A INVERSE
  710 DO 711 J=1,K
      IF(A(J,J).LT..0) GO TO 713
  711 SA(J)=SQRT(A(J,J))
      GO TO 715
  713 IBOUT=1
  715 KST=-4
      WRITE (6,916)
  234 KST=KST+5
      KEND=KST+4
      IF (KEND.LT.K) GO TO 719
      KEND=K
  719 DO 712 I=1,K
  712 WRITE (6,918)I,(A(I,J),J=KST,KEND)
      IF (KEND.LT.K) GO TO 234
      IF (IBOUT.EQ.0) GO TO 717
      WRITE (6,936)
      GO TO 650
  717 DO 718 I=1,K
      DO 718 J=1,K
      WS=SA(I)*SA(J)
      IF(WS.GT. 0.) GOTO 716
  714 A(I,J)=0.
      GO TO 718
  716 A(I,J)=A(I,J)/WS
  718 CONTINUE
      DO 720 J=1,K
```


```
  720 A(J,J)=1.
      WRITE (6,917)
  236 CONTINUE
      KST=-9
  721 KST=KST+10
      KEND=KST+9
      IF (KEND.LT.K) GO TO 722
      KEND=K
  722 DO 724 I=1,K
  724 WRITE (6,935)I,(A(I,J),J=KST,KEND)
      IF (KEND.LT.K) GO TO 721
C                     GET T*SE*SQRT(C(I,I))
      DO 726 J=1,K
  726 SA(J)=  SE*SA(J)
      GO TO (1112,1110),IBKT
 1110 READ (3)A
      REWIND 3
      GO TO 1114
 1112 DO 1113 II=1,K
      III=II+25
      DO 1113 JJ=1,K
 1113 A(II,JJ)=A(III,JJ)
 1114 CONTINUE
  740 WRITE (6,919)
  238 CONTINUE
      WS=K-IP
      DO 750 J=1,K
      IF (IP.LE.0)GO TO 743
  741 DO 742 I=1,IP
      IF (J.EQ.IB(I))GO TO 746
  742 CONTINUE
  743 HJTD=SQRT(WS*FF)*SA(J)
      STE=SA(J)
```


```
      OPL=BS(J)-SA(J)*T
      OPU=BS(J)+SA(J)*T
      SPL=BS(J)-HJTD
      WRITE ( 6,927)J,STE,OPL,OPU,SPL,SPU
      SPU=BS(J)+HJTD
  239 CONTINUE
      GO TO 750
  746 WRITE (6,913)J
  240 CONTINUE
  750 CONTINUE
C                     NONLINEAR CONFIDENCE LIMIT
      IF (IWS6.EQ.1) GO TO 650
      WS=K-IP
      WS1=N-K+IP
      PKN=WS/WS1
      PC=PHIZ*(1.+FF*PKN)
      WRITE (6,920)PC
  241 CONTINUE
      WRITE (6,921)
  242 CONTINUE
      IFSS3=1
      K1 = 1
  999 DO 790 J = K1,K
      K2 = J
      IF(IISS.NE.1) GO TO 998
      IISS = 0
      GO TO (252,780,704,762,766,772),IBK2
  998 IBKP=1
      DO 752 JJ=1,K
  752 B(JJ)=BS(JJ)
      IF (IP.LE.0)GO TO 758
  754 DO 756 JJ=1,IP
      IF (J.EQ.IB(JJ))GO TO 787
```


```
756 CONTINUE
758 DD=-1.
    IBKN=1
760 D=DD
    B(J)=BS(J)+D*SA(J)
    IBK2=4
    GO TO 300
762 PHI1=PHI
    IF (PHI1.GE.PC)GO TO 770
764 D=D+DD
    IF (D/DD.GE.5.)GO TO 788
765 B(J)=BS(J)+D*SA(J)
    IBK2=5
    GO TO 300
766 PHID=PHI
    IF (PHID.LT.PC)GO TO 764
    IF (PHID.GE.PC) GO TO 778
770 D=D/2.
    IF (D/DD.LE..001)GO TO 788
771 B(J)=BS(J)+D*SA(J)
    IBK2=6
    GO TO 300
772 PHID=PHI
    IF (PHID.GT.PC)GO TO 770
778 XK1=PHIZ/D+PHI1/(1.-D)+PHID/(D*(D-1.))
    XK2=-(PHIZ*(1.+D)/D+D/(1.-D)*PHI1+PHID/(D*(D-1.)))
    XK3=PHIZ-PC
    BC = (SQRT(XK2*XK2-4.*XK1*XK3)-XK2)/(2.*XK1)
    GO TO (779,784),IBKN
779 B(J)=BS(J)-SA(J)*BC
    GO TO 781
784 B(J)=BS(J)+SA(J)*BC
781 IBK2=2
```


```
      GO TO 300
  780 GO TO (782,786),IBKN
  782 IBKN=2
      DD=1.
      BL=B(J)
      PL=PHI
      GO TO 760
  786 BU=B(J)
      PU=PHI
      GO TO (783,795,785,789),IBKP
  783 WRITE (6,918) J, BL, PL, BU, PU
  243 CONTINUE
      GO TO 790
  795 WRITE (6,915) J, BU, PU
  244 CONTINUE
      GO TO 790
  785 WRITE (6,918)J,BL, PL
  245 CONTINUE
      GO TO 790
  787 WRITE (6,913)J
  246 CONTINUE
      GO TO 790
  789 WRITE (6,914)J
  247 CONTINUE
      GO TO 790
  788 GO TO (791,792),IBKN
C                    DELETE LOWER PRINT
  791 IBKP=2
      GO TO 780
  792 GO TO (793,794),IBKP
C                    DELETE UPPER PRINT
  793 IBKP=3
      GO TO 780
```


```
C                    LOWER IS ALREADY DELETED, SO DELETE BOTH
  794 IBKP=4
      GO TO 780
  790 CONTINUE
      GO TO 10
 1800 WRITE(6,1850)
      GO TO 10
C     ..................................................................
  900 FORMAT (25I3)
  901 FORMAT (7F10.0)
  902 FORMAT(18A4 )
  903 FORMAT (/13X,4H PHI 14X,4H S E              9X,7H LAMBDA   6X,
     1 25H ESTIMATED PARTIALS USED  / 5X,2E18.8,  E13.3 )
  904 FORMAT(/12H INCREMENTS 5E18.8/(12X,5E18.8) )
  905 FORMAT (13X,4H PHI 10X,7H LAMBDA 6X,7H GAMMA  6X, 7H LENGTH  /
     1 5X, E18.8, 3E13.3)
  906 FORMAT(1X,1E9.2,86X,1E9.2 /1X,1H+ 99X,1H+ )
  907 FORMAT( 5H1N = I3,5X,5H K = I3,5X,5H P = I3,5X,5H M = I3,5X,
     1 7H IFP = I3,5X,13HGAMMA CRIT = E10.3,5X,6HDEL = E10.3/6H FF =
     2E10.3,5X,5H T = E10.3,5X,5H E = E10.3,5X,7H TAU = E10.3,5X,6H XL =
     3  E10.3 , 4X, 7HZETA = E10.3 /)
 908  FORMAT (/2H (I3,13H) PARAMETERS 5E18.8/(18X,5E18.8))
  909 FORMAT (/13X,4H PHI 14X,4H S E              9X,7H LAMBDA 6X,
     1 25H ANALYTIC PARTIALS USED   /5X, 2E18.8,  E13.3)
  910 FORMAT(1H /5X,9X,4H OBS 13X,5H PRED 13X,5H DIFF  )
  911 FORMAT (/13X,4H PHI 14X,4H S E 11X,7H LENGTH 6X, 7H GAMMA 6X,
     1 7H LAMBDA 6X, 25HESTIMATED PARTIALS USED  /5X, 2E18.8, 3E13.3)
  912 FORMAT (/13X,4H PHI 14X,4H S E 11X,7H LENGTH 6X, 7H GAMMA 6X,
     1 7H LAMBDA 6X, 24HANALYTIC PARTIALS USED  /5X, 2E18.8, 3E13.3)
  913 FORMAT(2X,I3,20H PARAMETER NOT USED   )
  914 FORMAT(2X,I3,12H NONE FOUND   )
  915 FORMAT(2X,I3,36X,2E18.8  )
  916 FORMAT(1H /13H PTP INVERSE )
```


```
  917 FORMAT(1H /30H PARAMETER CORRELATION MATRIX  )
  918 FORMAT( 2X,I3,5E18.8)
  919 FORMAT( 1H /1H / 13X,4H STD 17X, 16H ONE - PARAMETER 21X,
     1 14H SUPPORT PLANE / 3X, 2H B 7X,6H ERROR 12X, 6H LOWER 12X,
     2 6H UPPER 12X, 6H LOWER 12X, 6H UPPER   )
  920 FORMAT( 1H /1H /30H  NONLINEAR CONFIDENCE LIMITS  / /
     1 16H PHI CRITICAL = E15.8     )
  921 FORMAT(1H / 6H  PARA 6X,8H LOWER B 8X,10H LOWER PHI 10X,8H UPPER B
     1 8X,10H UPPER PHI  )
 922  FORMAT (1H1,60X,17HGAMMA LAMBDA TEST 6X,2E13.3)
 923  FORMAT (1H1,90X,12HEPSILON TEST )
 924  FORMAT (1H1,90X,10HFORCE OFF  )
  925 FORMAT (5X,6E18.8/59X,2E18.8)
  926 FORMAT ( 40H BAD DATA, SUBSCRIPTS FOR UNUSED BS = 0   / / / )
  927 FORMAT(2X,I3,5E18.8 )
  928 FORMAT(1H , 110A1  )
  929 FORMAT(10A1)
  930 FORMAT (7F10.0)
  931 FORMAT (8F10.0)
  932 FORMAT(1H1)
  933 FORMAT(5H0N = ,I3,5X,5H K = ,I3,5X,5H P = ,I3,5X,5H M = ,I3,5X,
     1/6H FF = ,E10.3,5X,5H T = ,E10.3,
     25X,5H E = ,E10.3,5X,7H TAU = ,E10.3/)
 934  FORMAT (1H1,80X,18HGAMMA EPSILON TEST )
  935 FORMAT (3X,I5,2X,10F10.4)
  936 FORMAT (27H0 NEGATIVE DIAGONAL ELEMENT   )
 937  FORMAT (3X,I5,2X,10F10.4/(10X,10F10.4))
 938  FORMAT (1H /25H CONSTRAINT RESIDUALS .../(3X,I5,33X,E18.8))
 939  FORMAT (1H /23H PTP CORRELATION MATRIX )
 1850 FORMAT(///41H ITERATION LIMIT EXCEEDED, RUN TERMINATED)
      END
      SUBROUTINE GJR(A,N,EPS,MSING)
C     GAUSS-JORDAN-RUTISHAUSER MATRIX INVERSION WITH DOUBLE PIVOTING.
```


```
      DIMENSION A(50,50),B(50),C(50),P(50),Q(50)
      INTEGER P,Q
      MSING=1
      DO 10 K=1,N
C     DETERMINATION OF THE PIVOT ELEMENT
      PIVOT=0.
      DO 20 I=K,N
      DO 20 J=K,N
      IF(ABS(A(I,J))-ABS(PIVOT))20,20,30
   30 PIVOT=A(I,J)
      P(K)=I
      Q(K)=J
   20 CONTINUE
      IF(ABS(PIVOT)-EPS)40,40,50
C     EXCHANGE OF THE PIVOTAL ROW WITH THE KTH ROW
   50 IF(P(K)-K)60,80,60
   60 DO 70 J=1,N
      L=P(K)
      Z=A(L,J)
      A(L,J)=A(K,J)
   70 A(K,J)=Z
C     EXCHANGE OF THE PIVOTAL COLUMN WITH THE KTH COLUMN
   80 IF(Q(K)-K)85,90,85
   85 DO 100 I=1,N
      L=Q(K)
      Z=A(I,L)
      A(I,L)=A(I,K)
  100 A(I,K)=Z
   90 CONTINUE
C     JORDAN STEP
      DO 110 J=1,N
      IF(J-K)130,120,130
  120 B(J)=1./PIVOT
```


```
      C(J)=1.
      GO TO 140
  130 B(J)=-A(K,J)/PIVOT
      C(J)=A(J,K)
  140 A(K,J)=0.
  110 A(J,K)=0.
      DO 10 I=1,N
      DO 10 J=1,N
   10 A(I,J)=A(I,J)+C(I)*B(J)
C     REORDERING THE MATRIX
      DO 155 M=1,N
      K=N-M+1
      IF(P(K)-K)160,170,160
  160 DO 180 I=1,N
      L=P(K)
      Z=A(I,L)
      A(I,L)=A(I,K)
  180 A(I,K)=Z
  170 IF(Q(K)-K)190,155,190
  190 DO 150 J=1,N
      L=Q(K)
      Z=A(L,J)
      A(L,J)=A(K,J)
  150 A(K,J)=Z
  155 CONTINUE
  151 RETURN
   40 PRINT 45,P(K),Q(K),PIVOT
   45 FORMAT(16H0SINGULAR MATRIX3H I=I3,3H J=I3,7H PIVOT=E16.8/)
      MSING=2
      GO TO 151
      END
      SUBROUTINE SUBZ(Y,X,B,PRNT,NPRNT,N)
C     CDC 6400.  OCTOBER 1971
```


```
      DIMENSION Y(500),X(500,1),B(50),PRNT(5),IDEN(7)
      READ (5,800) NRUN,IDEN
      WRITE (6,801) NRUN,IDEN
      WRITE (6,802)
      NPRNT=1
  800 FORMAT(I3,7A10)
  801 FORMAT(9H NLIN GH ///14H RUN NUMBER = ,I3,5X,7A10///)
  802 FORMAT (25H PARAMETER IDENTIFICATION//5X,12H B(1) = TAUA/5X,12H B(
     12) = TAUB/5X,11H B(3) = ANU/5X,11H B(4) = BNU/5X,22H B(5) = SCALIN
     2G FACTOR/5X,18H B(6) = LINE WIDTH//)
      RETURN
      END
      SUBROUTINE FCODE(Y,X,B,PRNT,F,I,RES)
      DIMENSION Y(500),X(500,1),B(50),PRNT(5)
      PI=3.1415927
      TPI=6.2831853
      RIT=PI*B(6)
      TOR=(B(1)*B(2))/(B(1)+B(2))
      DELP=(B(1)-B(2))/(B(1)+B(2))
      SNU=0.5*(B(3)+B(4))
      DNU=0.5*(B(3)-B(4))
      DLGNU=SNU-X(I,1)
      P=TOR*(RIT*RIT-TPI*TPI*(DLGNU*DLGNU-DNU*DNU))+RIT
      Q=TOR*TPI*(DLGNU-DELP*DNU)
      R=TPI*(DLGNU*(1.0+2.0*TOR*RIT)+DELP*DNU)
      F=B(5)*(P*(1.0+TOR*RIT)+Q*R)/(P*P+R*R)
      RES=Y(I)-F
      PRNT(1)=X(I,1)
      RETURN
      END
      SUBROUTINE PCODE(P,X,B,PRNT,F,I)
      DIMENSION P(50),X(500,1),B(50),PRNT(5)
      RETURN
```

END

PUNNLIN

This programme uses the output of TAPGH as input to punch the cards which are later used as input for STACKGH.

```
      PROGRAM PUNNLIN(OUTPUT,PUNCH,TAPE5,TAPE61=OUTPUT,TAPE62=PUNCH)
C     PUNCHES NLIN DATA CARDS FOR UP TO 8 PARAMETERS
C     PROGRAM IS DESIGNED FOR MAGNETIC TAPE INPUT
C     FORMAT IS SUITABLE FOR PLOTTING PROGRAMS
      DIMENSION B(10),IDEN(18),IB(10)
      DIMENSION Y(200),X(200)
      WRITE(61,200)
  200 FORMAT(16H PROGRAM PUNNLIN///)
    1 READ(5,900)N,K,IP,M,IFP,NCONS
      WRITE(61,900)N,K,IP,M,IFP,NCONS
      WRITE(62,900)N,K,IP,M,IFP,NCONS
  900 FORMAT(25I3)
      IF (N.EQ.0)GO TO 15
      READ(5,900)ISW1,ISW2,ISW3,ISW4,ISW5,ISW6
      WRITE(61,900)ISW1,ISW2,ISW3,ISW4,ISW5,ISW6
      WRITE(62,900)ISW1,ISW2,ISW3,ISW4,ISW5,ISW6
      READ(5,930)YMN,SPRD
      WRITE(61,930)YMN,SPRD
      WRITE(62,930)YMN,SPRD
  930 FORMAT(7F10.3)
      IF (IP.EQ.0)GO TO 3
      READ(5,900)(IB(I),I=1,IP)
      WRITE(61,900)(IB(I),I=1,IP)
      WRITE(62,900)(IB(I),I=1,IP)
    3 READ(5,931)FF,T,E,TAU,XL,GA,DEL,ZETA
      WRITE(61,931)FF,T,E,TAU,XL,GA,DEL,ZETA
      WRITE(62,931)FF,T,E,TAU,XL,GA,DEL,ZETA
  931 FORMAT(8F10.3)
      READ(5,930)(B(I),I=1,K)
      WRITE(61,930)(B(I),I=1,K)
      WRITE(62,930)(B(I),I=1,K)
      DO 10 I=1,N
      READ(5,100)Y(I),X(I)
```


```
      WRITE(61,100)Y(I),X(I)
      WRITE(62,100)Y(I),X(I)
  100 FORMAT(2F10.3)
   10 CONTINUE
      READ(5,101)NRUN,IDEN
      WRITE(61,101)NRUN,IDEN
      WRITE(62,101)NRUN,IDEN
  101 FORMAT(I3,18A4)
      GO TO 1
   15 STOP 1
      REWIND 5
      END
```

STACK GH

This programme stacks outputs from NLIN GH. Plots of the digitalized spectra are superimposed on the theoretical spectra (smooth curves) calculated from the best fit values of the line shape parameters. The sets of spectra are separated vertically on the plot. The heights and vertical placing of the spectra are calculated automatically.

The original sets of data cards containing the digitalized spectra are used.

Input cards are prepared as follows:

Item 1	Format(I3,18A4)
NSETS	Number of sets of spectra to be stacked on each plot. A zero value for NSETS will terminate the run.
IDEN	Alphanumeric identification. This is printed on the plot output.
Item 2	Format(3F10.0)
FR 1	Low frequency limit of plot.
FR 2	High frequency limit of plot.
SCALE	Plotting scale in mm/Hz.
Item 3	Format(I3,7X,F10.0)
NDATA	Number of data pair of digitalized spectrum.
TEMP	Temperature of measurement. This is printed on the plot.

Item 4	Format(6F10.0)
B(1)	Mean lifetime on site A (sec.).
B(2)	Mean lifetime on site B (sec.).
B(3)	Chemical shift on site A (Hz).
B(4)	Chemical shift on site B (Hz).
B(5)	Scaling factor.
B(6)	Natural linewidth (Hz).
Item 5	Format(2F10.0)
SPECY1	Y co-ordinate of point in experimental spectrum
SPECX1	X co-ordinate of point in experimental spectrum.

Any number of runs may be stacked one after another. Each run produces a separate plot. The job is terminated by a blank card following the last data set.

Items 3,4,and 5 are repeated for each set of spectra, i.e. the total number of sets of spectra comprising 3,4, and 5 = NSETS for each run.

```
      PROGRAM STACKGH(INPUT,OUTPUT,TAPE3,TAPE60=INPUT,TAPE61=OUTPUT)
C     CDC 3300 FORTRAN.  FEBRUARY 1971
C     CDC 6400 FORTRAN.  MAY 1972
C     THIS PROGRAM STACKS OUTPUTS FROM NLINGH
C     A PLOT OF THE DIGITIZED SPECTRUM IS SUPERIMPOSED ON THE SPECTRUM
C     CALCULATED FROM THE BEST FIT PARAMETERS
C     B(1) = MEAN LIFETIME IN SECONDS ON SITE A
C     B(2) = MEAN LIFETIME IN SECONDS ON SITE B
C     B(3) = CHEMICAL SHIFT IN HZ ON SITE A
C     B(4) = CHEMICAL SHIFT IN HZ ON SITE B
C     B(5) = SCALING FACTOR
C     B(6) = LINE WIDTH IN HZ
C
      DIMENSION IDEN(7),Y(3000),B(6),KRAY(14),SPECX(200),SPECY(200)
      WRITE(61,200)
  200 FORMAT(16H1PROGRAM STACKGH///)
    1 READ(60,201)NSETS,IDEN
  201 FORMAT(I3,7A10)
      IF (NSETS.EQ.0) GO TO 50
      NPLOT = 0
      SETS=NSETS
      HEIGHT=200.0/SETS
      RISE=HEIGHT/25.4
      BASE=-RISE
      READ(60,203)FR1,FR2,SCALE
  203 FORMAT(3F10.0)
      WRITE(61,204)IDEN
  204 FORMAT(10X,7A10///)
      WRITE (61,206)FR1,FR2,SCALE,HEIGHT
  206 FORMAT(20H PLOTTING PARAMETERS//5X,18HFREQUENCY RANGE = ,F8.2,4H T
     10 ,F8.2,3H HZ/5X,9H SCALE = ,F6.2,6H MM/HZ,5X,10H HEIGHT = ,F6.2,3
     2H MM)
      DENS=100.0
```


```
      XMAX=SCALE*(FR2-FR1)/25.4
      NPOINT=DENS*XMAX+0.5
      IF (NPOINT.GT.3000) NPOINT=3000
      STEP=(FR2-FR1)/NPOINT
C
C     DRAW AXES AND TICK MARKS
      LY=XMAX+6.0
      YL=(FR2-FR1)*FLOAT(LY)/XMAX
      YLOW=FR1-DENS*STEP*1.5
      CALL SAXES(3,10,LY,1.0,10.0,YL,0.0,YLOW,0.0,YLOW)
      YT=FR1
      CALL PLOTXY(9.90,YT,0,0)
      CALL PLOTXY(10.0,YT,1,0)
   30 YT=YT+5.0
      YLIM=YLOW+YL
      IF (YT.GT.FR2) GO TO 35
      CALL PLOTXY(10.0,YT,1,0)
      CALL PLOTXY(9.95,YT,1,0)
      CALL PLOTXY(10.0,YT,1,0)
      YT=YT+5.0
      IF (YT.GT.FR2) GO TO 35
      CALL PLOTXY(10.0,YT,1,0)
      CALL PLOTXY(9.90,YT,1,0)
      CALL PLOTXY(10.0,YT,1,0)
      GO TO 30
   35 CONTINUE
C
C     PROCESS SETS OF SPECTRA
      DO 45 II=1,NSETS
      NPLOT=NPLOT +1
      BASE=BASE+RISE
      READ(60,210)NDATA,TEMP
  210 FORMAT(I3,7X,F10.0)
```


```
      WRITE(61,211)NPLOT,TEMP
  211 FORMAT(//13H PLOT NUMBER ,I3,10X,14HTEMPERATURE = ,F5.1//)
      READ(60,202)B(1),B(2),B(3),B(4),B(5),B(6)
  202 FORMAT(6F10.0)
      WRITE(61,205)B(1),B(2),B(3),B(4),B(5),B(6)
  205 FORMAT(23H CALCULATION PARAMETERS//5X,32HMEAN LIFETIME ON SITE A (
     1SEC) = ,F8.4,5X,32HMEAN LIFETIME ON SITE B (SEC) = ,F8.4,/5X,32HCH
     2EMICAL SHIFT ON SITE A (HZ) = ,F8.2,5X,32HCHEMICAL SHIFT ON SITE B
     3 (HZ) = ,F8.2,/20X,17HSCALING FACTOR = ,F8.2,20X,17HLINEWIDTH (HZ)
     4 = ,F8.2//)
      DO 10 I=1,NDATA
   10 READ(60,207)SPECY(I),SPECX(I)
  207 FORMAT(2F10.0)
      WRITE(61,208)
  208 FORMAT(19H DIGITIZED SPECTRUM//5X,9HINTENSITY,5X,9HFREQUENCY/)
      DO 15 I=1,NDATA
   15 WRITE(61,209)SPECY(I),SPECX(I)
  209 FORMAT(3X,F10.3,4X,F10.3)
C
C     CALCULATE THEORETICAL SPECTRUM
      PI=3.1415927
      TPI=6.2831853
      RIT=PI*B(6)
      TOR=(B(1)*B(2))/(B(1)+B(2))
      DELP=(B(1)-B(2))/(B(1)+B(2))
      SNU=0.5*(B(3)+B(4))
      DNU=0.5*(B(3)-B(4))
      FREQ=FR1-STEP
      DO 20 I=1,NPOINT
      FREQ=FREQ+STEP
      DLGNU=SNU-FREQ
      PU=TOR*(RIT*RIT-TPI*TPI*(DLGNU*DLGNU-DNU*DNU))+RIT
      QU=TOR*TPI*(DLGNU-DELP*DNU)
```


```
      RU=TPI*(DLGNU*(1.0+2.0*TOR*RIT)+DELP*DNU)
      FU=(PU*(1.0+TOR*RIT)+QU*RU)/(PU*PU+RU*RU)
   20 Y(I)=FU*B(5)
C
C     SCALE BOTH SPECTRA TO CALCULATED HEIGHT
      YMAX=Y(1)
      DO 21 I=2,NPOINT
      IF (YMAX.GT.Y(I)) GO TO 21
      YMAX=Y(I)
   21 CONTINUE
      FACTOR=HEIGHT/(25.4*YMAX)
      DO 28 I=1,NPOINT
   28 Y(I)=Y(I)*FACTOR
      DO 29 I=1,NDATA
   29 SPECY(I)=SPECY(I)*FACTOR
C
C     PLOT THE SPECTRA
      ENCODE(60,110,KRAY(1))TEMP,B(1),B(2)
  110 FORMAT(F6.1,6H DEG.,8X,F6.4,6H SEC.,8X,F6.4,6H SEC.,8X)
      XP1=8.95-BASE
      XP2=9.30-BASE
      XP3=9.60-BASE
      X=FR1
      YYY=9.85-Y(NPOINT)-BASE
      CALL PLOTXY(YYY,X,0,0)
      DO 24 I=2,NPOINT
      J=NPOINT-I+1
      X=X+STEP
      YYY=9.85-Y(J)-BASE
   24 CALL PLOTXY(YYY,X,1,0)
      Y2=YLOW+YL*(FLOAT(LY)-0.6)/FLOAT(LY)
      Y3=YLOW+0.1*YL/FLOAT(LY)
      XSUM=FR1+FR2
```


```
      DO 40 I=1,NDATA
      XX=XSUM-SPECX(I)
      YSPEC=9.85-SPECY(I)-BASE
   40 CALL PLOTXY(YSPEC,XX,0,9)
      CALL PLOTXY(XP1,FR2,0,0)
      CALL LABEL(11,1,3,KRAY(1))
      CALL PLOTXY(XP2,FR2,0,0)
      CALL LABEL(11,1,3,KRAY(3))
      CALL PLOTXY(XP3,FR2,0,0)
      CALL LABEL(11,1,3,KRAY(5))
C
C     PROCESS NEXT PAIR OF SPECTRA
   45 CONTINUE
      CALL PLOTXY(0.0,YLOW,0,0)
      WRITE(61,100)
  100 FORMAT(///29H SUMMARY OF PLOT CALCULATIONS/)
      WRITE(61,102)NPOINT
  102 FORMAT(9X,28H NUMBER OF POINTS PLOTTED = ,I4)
      WRITE(61,105)LY
  105 FORMAT(37H LENGTH OF FREQUENCY AXIS (INCHES) = ,I3)
      WRITE(61,106)YL
  106 FORMAT(3X,34H LENGTH OF FREQUENCY AXIS IN HZ = ,F7.2)
      WRITE(61,107)FR1,X
  107 FORMAT(10X,27H FREQUENCY RANGE PLOTTED = ,F7.2,4H TO ,F7.2,3H HZ//
     1//)
      END FILE 3
C
C     START NEXT CASE
      GO TO 1
   50 CONTINUE
      END FILE 3
      REWIND 3
      STOP 1
```


END

ACTPAR

This programme calculates Arrhenius and Eyring activation parameters and 90% confidence intervals from inputted lifetimes and temperatures. It uses a linear regression method to fit the Arrhenius equation in logarithmic form to the input data, i.e. the equation is in the form

$$\ln (1/\tau) = \ln (A) - Ea/RT$$

the independent variable being (1/T) and the dependent variable being (1/τ). Error analysis is given at each stage of the calculation, i.e. following the regression calculations, following the Arrhenius calculations, and following the Eyring calculations. The Eyring parameters are calculated (with 90% confidence limits) at a temperature specified by the user.

Data cards are prepared as follows:

Item 1	Format(I3,7A10)
NRUN	Run number. Any non-zero number will do. A zero value for NRUN will terminate the job.
IDEN	Alphanumeric identification.
Item 2	Format(F10.0)
TEMP	Temperature (^{o}K) at which the Eyring parameters are to be calculated.

Item 3	Format(2F10.0)
TC(I)	Temperature of measurement in ^{o}C.
TAU(I)	Mean lifetime in seconds.
Item 4	Blank card.†

Data sets (Items 1-4) may be stacked one after another. The run is terminated by an additional blank card.§

† ACTPAR does its own counting of data cards. This card signals the end of the experimental data set.

§ This means that there will be <u>two</u> blank cards at the end of the complete data deck.

```
      PROGRAM ACTPAR(INPUT,OUTPUT,TAPE5=INPUT,TAPE6=OUTPUT)
C
C     SIR GEORGE WILLIAMS UNIVERSITY.  NOVEMBER, 1971.
C     FORTRAN IV FOR CDC 6400.
C
C     CALCULATION OF ARRHENIUS AND EYRING ACTIVATION PARAMETERS USING
C     LINEAR REGRESSION ANALYSIS.
C
C     LINEAR REGRESSION ANALYSIS BASED ON
C     LARK, CRAVEN, AND BOSWORTH, 'THE HANDLING OF CHEMICAL DATA'.
C     CONFIDENCE LIMITS ARE BASED ON SLOPE AND INTERCEPT OF ARRHENIUS LINE
C     K = A*EXP(-EACT/RT)
C
      DIMENSION IDEN(7),TAU(50),TC(50),TK(50),TR(50),REXP(50),RFIT(50),
     1HEXP(50),SEXP(50),SFIT(50),GEXP(50),GFIT(50)
      DIMENSION ALKE(50),ALKR(50)
      GK=1.98646E-3
      BK=1.38049E-16
      PK=6.6254E-27
      RKH=BK/PK
      ALNR=ALOG(RKH)
    1 READ(5,100)NRUN,IDEN
  100 FORMAT(I3,7A10)
      IF (NRUN.EQ.0) STOP 1
      WRITE(6,101)
  101 FORMAT(15H1PROGRAM ACTPAR,///1X,15(1H*),' ARRHENIUS AND EYRING ACT
     1IVATION PARAMETERS AND 90 PERCENT CONFIDENCE INTERVALS ',15(1H*)//
     2/)
      READ(5,102)TEMP
  102 FORMAT(F10.0)
      I=1
    2 READ(5,103)TC(I),TAU(I)
  103 FORMAT(2F10.0)
```


```
      IF (TAU(I).EQ.0.0.AND.TC(I).EQ.0.0) GO TO 3
      I=I+1
      GO TO 2
    3 NDATA=I-1
C
C     WRITE OUT EXPERIMENTAL DATA
      WRITE(6,105)NRUN,IDEN
  105 FORMAT(* CASE NUMBER *,I3,10X,7A10,///)
      WRITE(6,106)
  106 FORMAT(/1X,6(1H*),* EXPERIMENTAL LIFETIMES, RATE CONSTANTS, AND TE
     1MPERATURES *,6(1H*)//)
      WRITE(6,110)
  110 FORMAT(5X,*POINT*,5X,*LIFETIME*,5X,*RATE CONSTANT*,5X,*DEGREES C.*,
     1,5X,*DEGREES K.*/15X,*(SECONDS)*,5X,*(1/SECOND)*/)
      DO 4 I=1,NDATA
      TK(I)=TC(I)+273.16
      REXP(I)=1.0/TAU(I)
      TR(I)=1000.0/TK(I)
      WRITE(6,111)I,TAU(I),REXP(I),TC(I),TK(I)
  111 FORMAT(6X,I2,5X,E10.4,5X,F10.4,9X,F6.1,9X,F6.1)
    4 CONTINUE
C
C     LINEAR REGRESSION CALCULATIONS
      WRITE(6,120)
  120 FORMAT(////1X,21(1H*),* LINEAR REGRESSION TO ARRHENIUS EQUATION *,
     120(1H*)/)
      SUMX=SUMY=SUMXX=SUMYY=SUMXY=0.0
      DO 6 I=1,NDATA
      ALKE(I)=ALOG(REXP(I))
      SUMX=SUMX+1.0/TK(I)
      SUMY=SUMY+ALKE(I)
      SUMXX=SUMXX+(1.0/TK(I))**2
      SUMXY=SUMXY+(ALOG(REXP(I)))/TK(I)
```


```
      SUMYY=SUMYY+(ALOG(REXP(I)))**2
    6 CONTINUE
      NF=NDATA-2
      FN=NF
      PN=NDATA
      XAV=SUMX/PN
      YAV=SUMY/PN
      CSUMXX=SUMXX-PN*(XAV**2)
      CSUMYY=SUMYY-PN*(YAV**2)
      CSUMXY=SUMXY-PN*XAV*YAV
      SLOPE=CSUMXY/CSUMXX
      YINT=YAV-SLOPE*XAV
      EACT=-GK*SLOPE
      A = EXP(YINT)
C
C     ARRHENIUS PARAMETER CONFIDENCE INTERVAL CALCULATIONS
      DSUMYY=CSUMYY-SLOPE*CSUMXY
      STERR2=DSUMYY/FN
      STERR=SQRT(STERR2)
      ERSLOPE=STERR/SQRT(CSUMXX)
      W1=SUMXX/(PN*CSUMXX)
      ERINT=STERR*SQRT(W1)
      EACTER=GK*ERSLOPE
      WRITE(6,121)
  121 FORMAT(/* COMPARISON OF EXPERIMENTAL AND REGRESSION VALUES OF LN(R
     1ATE CONSTANT)*//5X,*POINT*,5X,*LN(KEXP)*,5X,*LN(KFIT)*,5X,*DIFFERE
     2NCE*,5X,*DIFF/STERROR*,5X,*DEGREES C.*/)
      DO 20 I=1,NDATA
      ALKR(I)=YINT+SLOPE/TK(I)
      DY=ALKE(I)-ALKR(I)
      RY=DY/STERR
      WRITE(6,122)I,ALKE(I),ALKR(I),DY,RY,TC(I)
  122 FORMAT(6X,I2,5X,F8.3,5X,F8.3,6X,F8.3,8X,F8.2,7X,F8.1)
```


```
   20 CONTINUE
      WRITE(6,123)
  123 FORMAT(////1X,4(1H*),* STANDARD LINEAR REGRESSION ERRORS *,5(1H*)/
     1/)
      WRITE(6,124)STERR
  124 FORMAT(5X,* STANDARD ERROR IN REGRESSION = *,F8.3/)
      WRITE(6,125)ERINT
  125 FORMAT(5X,*  STANDARD ERROR IN INTERCEPT = *,F8.3/)
      WRITE(6,126)ERSLOPE
  126 FORMAT(10X,* STANDARD ERROR IN SLOPE = *,F8.3/)
      ST=0.0
      CALL STUDENT(NF,ST)
C           90 PERCENT CONFIDENCE INTERVAL IN LN(K) AT A CHOSEN TEMPERATURE
      W2=1.0/PN+((1.0/TEMP-XAV)**2)/CSUMXX
      ERRY=STERR*SQRT(W2)
      CIY=ST*ERRY
C           90 PERCENT CONFIDENCE INTERVAL IN SLOPE
      CISLOPE=ST*ERSLOPE
C           90 PERCENT CONFIDENCE INTERVAL IN INTERCEPT
      CIYINT=ST*ERINT
      CLOGA=YINT/2.303
      CLOGIA=CIYINT/2.303
C           90 PERCENT CONFIDENCE INTERVAL IN ACTIVATION ENERGY
      CIE=GK*CISLOPE
      ELO=EACT-CIE
      EHI=EACT+CIE
      YINTHI=YINT+CIYINT
      YINTLO=YINT-CIYINT
      ALO=EXP(YINTLO)
      AHI=EXP(YINTHI)
      WRITE(6,130)
  130 FORMAT(///1X,38(1H*),* ARRHENIUS ACTIVATION PARAMETERS *,38(1H*)//
     1* ACTIVATION PARAMETERS AND STANDARD ERRORS*/)
```


```
      WRITE(6,134)EACT,EACTER
  134 FORMAT(/5X,*ACTIVATION ENERGY = *,F7.3,5X,*STANDARD ERROR = *,
     1F6.3)
      WRITE(6,135)YINT,ERINT
  135 FORMAT(/8X,*NATURAL LOG(A) = *,F7.3,5X,*STANDARD ERROR = *,F6.3/)
      WRITE(6,136)
  136 FORMAT(//* ACTIVATION PARAMETERS AND CONFIDENCE LIMITS*/)
      WRITE(6,131)EACT,CIE,ELO,EHI
  131 FORMAT(/5X,*ACTIVATION ENERGY = *,F7.3,3X,*(+OR-)*,F6.3,5X,
     1*LOWER LIMIT = *,F7.3,3X,*UPPER LIMIT = *,F7.3,2X,*KCAL/MOLE*)
      WRITE(6,132)A,ALO,AHI
  132 FORMAT(/6X,*FREQUENCY FACTOR = *,E10.4,5X,*LOWER LIMIT = *,E10.4,
     13X,* UPPER LIMIT = *,E10.4)
      WRITE(6,137)YINT,CIYINT
  137 FORMAT(/8X,*NATURAL LOG(A) = *,F7.3,3X,*(+OR-)*,F6.3)
      WRITE(6,133)CLOGA,CLOGIA
  133 FORMAT(/9X,*COMMON LOG(A) = *,F7.3,3X,*(+OR-)*,F6.3)
C
C     CALCULATE EYRING PARAMETERS
      WRITE(6,140)
  140 FORMAT(////1X,31(1H*),* EYRING ACTIVATION PARAMETERS *,31(1H*)//)
      WRITE(6,142)
  142 FORMAT(5X,*POINT*,8X,*ENTHALPY*,10X,*-----ENTROPY (E.U.)-----*,
     110X,*FREE ENERGY (KCAL/MOLE)*/17X,*(KCAL/MOLE)*,9X,*EXP.*,6X,
     2*FIT*,5X,*DIFF.*,11X,*EXP.*,5X,*FIT*,5X,*DIFF.*/)
      DO 14 I=1,NDATA
      HEXP(I)=EACT-GK*TK(I)
      GEXP(I)=(GK*TK(I))*(ALNR+ALOG(TK(I))-ALOG(REXP(I)))
      SEXP(I)=1000.0*(HEXP(I)-GEXP(I))/TK(I)
      RFIT(I)=A*EXP(SLOPE/TK(I))
      GFIT(I)=(GK*TK(I))*(ALNR+ALOG(TK(I))-ALOG(RFIT(I)))
      SFIT(I)=1000.0*GK*(YINT-ALNR-ALOG(TK(I))-1.0)
      DIFFS=SEXP(I)-SFIT(I)
```

```
      DIFFG=GEXP(I)-GFIT(I)
      WRITE(6,141)I,HEXP(I),SEXP(I),SFIT(I),DIFFS,GEXP(I),GFIT(I),DIFFG
  141 FORMAT(6X,I2,10X,F7.3,10X,F7.2,3X,F7.2,F7.2,9X,F8.3,F9.3,F8.3)
   14 CONTINUE
C
C     CALCULATE EYRING PARAMETERS FOR A SPECIFIC TEMPERATURE
      WRITE(6,150)TEMP
  150 FORMAT(///* EYRING ACTIVATION PARAMETERS CALCULATED FOR *,F5.1,
     1* DEG. K.*//34X,*(+OR-)*,6X,*INTERVAL*,6X,*LOWER*,8X,*UPPER*/)
      YTEMP=YINT+SLOPE/TEMP
      YLO=YTEMP-CIY
      YHI=YTEMP+CIY
C          90 PERCENT CONFIDENCE INTERVAL IN FREE ENERGY
      RTEMP=A*EXP(SLOPE/TEMP)
      GT=(GK*TEMP)*(ALNR+ALOG(TEMP)-ALOG(RTEMP))
      GLO=(GK*TEMP)*(ALNR+ALOG(TEMP)-YHI)
      GHI=(GK*TEMP)*(ALNR+ALOG(TEMP)-YLO)
      GERR=GHI-GLO
      GERR2=GERR/2.0
C          90 PERCENT CONFIDENCE INTERVAL IN ENTHALPY
      HT=EACT-GK*TEMP
      HLO=ELO-GK*TEMP
      HHI=EHI-GK*TEMP
      HERR=HHI-HLO
      HERR2=HERR/2.0
C          90 PERCENT CONFIDENCE INTERVAL IN ENTROPY
      STD=1000.0*GK*(YINT-ALNR-ALOG(TEMP)-1.0)
      SLO=1000.0*GK*(YINTLO-ALNR-ALOG(TEMP)-1.0)
      SHI=1000.0*GK*(YINTHI-ALNR-ALOG(TEMP)-1.0)
      SERR=SHI-SLO
      SERR2=SERR/2.0
      WRITE(6,151)HT,HERR2,HERR,HLO,HHI
  151 FORMAT(8X,*ENTHALPY = *,F7.3,4(6X,F7.3),2X,*KCAL/MOLE*/)
```

```
      WRITE(6,152)STD,SERR2,SERR,SLO,SHI
  152 FORMAT(9X,*ENTROPY = *,F6.2,4(7X,F6.2),3X,*E.U.*/)
      WRITE(6,153)GT,GERR2,GERR,GLO,GHI
  153 FORMAT(5X,*FREE ENERGY = *,F7.3,4(6X,F7.3),2X,*KCAL/MOLE*/)
      WRITE(6,154)RTEMP,TEMP
  154 FORMAT(/3X,*RATE CONSTANT =*,E10.4,* (1/SEC.) AT *,F5.1,
     1* DEGREES K.*/)
      CLT=1.0/RTEMP
      WRITE(6,155)CLT,TEMP
  155 FORMAT(8X,*LIFETIME =*,E10.4,* ( SEC. ) AT *,F5.1,
     1* DEGREES K.*/)
C
C     CALCULATE DATA FOR PLOTTING
      WRITE(6,160)
  160 FORMAT(///4(1H*),* DATA FOR PREPARATION OF ARRHENIUS PLOT *,4(1H*)
     1//5X,*POINT*,5X,*LN(KEXP)*,5X,*LN(KFIT)*,5X,*1000/T*/)
      DO 60 I=1,NDATA
      WRITE(6,161)I,ALKE(I),ALKR(I),TR(I)
  161 FORMAT(6X,I2,5X,F8.3,5X,F8.3,4X,F8.3)
   60 CONTINUE
      WRITE(6,199)
  199 FORMAT(////2(1X,110(1H*)/))
C
C     START NEXT CASE
      GO TO 1
      END
      SUBROUTINE STUDENT(NF,VAL)
C     STUDENTS T VALUES FOR 90 PERCENT CONFIDENCE LIMITS
      DIMENSION T(48)
      T(1)=6.314
      T(2)=2.920
      T(3)=2.353
      T(4)=2.132
```


```
      T(5)=2.015
      T(6)=1.943
      T(7)=1.895
      T(8)=1.860
      T(9)=1.833
      T(10)=1.812
      T(11)=1.796
      T(12)=1.782
      T(13)=1.771
      T(14)=1.761
      T(15)=1.753
      T(16)=1.746
      T(17)=1.740
      T(18)=1.734
      T(19)=1.729
      T(20)=1.725
      T(21)=1.721
      T(22)=1.717
      T(23)=1.714
      T(24)=1.711
      T(25)=1.708
      T(26)=1.706
      T(27)=1.703
      T(28)=1.701
      T(29)=1.70
      T(30)=1.70
      DO 1 I=31,35
      T(I)=1.69
    1 CONTINUE
      DO 2 I=36,48
      T(I)=1.68
    2 CONTINUE
      VAL=T(NF)
```


```
      RETURN
      END
```


TLIST

This programme will supply listings of source programmes suitable for theses.

Cards are prepared as follows:

Item 1	Format(I2)
NUM	The number of copies of programme required. The run terminates if NUM is zero.
Item 2	Card deck to be listed.
Item 3	An end of deck card with 9999 punched in columns 77-80. This card signals the end of the deck to be listed.
Item 4	A blank card to terminate the run.†

† Items 1 through 3 may be repeated for more than one deck.

```
      PROGRAM TLIST(INPUT,OUTPUT,TAPE60=INPUT,TAPE61=OUTPUT)
      DIMENSION LINE(19,900)
    1 READ(60,900)NUM
      IF (NUM.EQ.0) GO TO 10
      ICOUNT=0
      NN=1
    2 READ(60,901)(LINE(I,NN),I=1,19),ISTOP
      IF (ISTOP.EQ.9999) GO TO 3
      ICOUNT=ICOUNT+1
      NN=NN-1
      GO TO 2
    3 CONTINUE
      IX=1
    4 J=1
    5 IC2=1
      WRITE(61,903)
      WRITE(61,904)
      WRITE(61,904)
      WRITE(61,904)
      WRITE(61,905)(LINE(I,J),I=1,19)
      IC2=IC2+1
      J=J+1
    6 WRITE(61,905)(LINE(I,J),I=1,19)
      IC2=IC2+1
      J=J+1
      IF (J.GT.ICOUNT) GO TO 7
      IF (IC2.GT.33) GO TO 5
      GO TO 6
    7 IX=IX+1
      IF (IX.LE.NUM) GO TO 4
      GO TO 1
  900 FORMAT(I2)
  901 FORMAT(19A4,I4)
  903 FORMAT(1H1)
  904 FORMAT(1H-)
  905 FORMAT(12X,19A4)
   10 STOP 1
      END
```