# Simultaneous Evaluation of Rate Parameters and Equilibrium Data by Lineshape Studies of NMR Signals

KJELL-IVAR DAHLQVIST

*Division of Physical Chemistry, Lund Institute of Technology, Chemical Center, Box 740, S-220 07 Lund 7, Sweden*

The lineshape of NMR signals in a two site system has been studied as a function of the exchange rate $(1/\tau)$ and population (P). In this study it is assumed that the line-shape of the NMR-signals can be characterized by a function $F(\tau,P)$. The dependence of F on $\tau$ and P is shown in a three-dimensional diagram where F is plotted *versus* $\ln 1/\tau$ and $\ln (1-P)/P$. If in such a plot points with equal values for F are connected, parabolic "iso-F" curves are obtained. A way of evaluating rate parameters and equilibrium data using these "iso-F" curves is described. The method described has been used for the evaluation of rate parameters and equilibrium data for the rotation of the aldehyde group in 2-furanaldehyde. The data obtained in this way $(E_{aA}=12.2\pm0.2$ kcal/mole, $\Delta H_0=1.05\pm0.02$ kcal/mole) are in good agreement with those previously reported $(E_{aA}=12.17\pm0.17$ kcal/mole, $\Delta H_0=1.05\pm0.05$ kcal/mole) using a different method.

A theory for the influence of exchange on the shape of nuclear magnetic resonance (NMR) signals obtained from two exchanging nuclei has been derived by Gutowsky, McCall and Slichter [1] (GMS). The GMS theory has later been presented in a simplified form by McConnell.[2] According to this theory the lineshape of the signals from protons exchanging between two sites A and B is determined by the parameters $P_A$, $P_B$, $T_{2A}$, $T_{2B}$, $\delta_\nu$, $\tau_A$ and $\tau_B$, where

$$P_A; P_B = \text{the populations of A and B}$$
$$P_A + P_B = 1: \text{if } P_A = P \text{ then } P_B = 1-P$$

$T_{2A}; T_{2B}$ = spin-spin relaxation times for A and B. (For convenience we set

$$T_{2A} = T_{2B} = T_2)$$

$\tau_A; \tau_B$ = mean lifetimes for protons A and B

$$\frac{\tau_A}{\tau_B} = \frac{P_A}{P_B} = \frac{P}{1-P}; \text{ if } \tau_A = \tau \text{ then } \tau_B = \tau(1-P)/P$$

$\delta \nu$ = the chemical shift between the protons at sites A and B. The shape is thus determined by P, $T_2$, $\delta \nu$ and $\tau$.

Each set of these parameters gives NMR-signals with a unique lineshape. With some iterative curve fitting method it might therefore in principle be possible to determine all these parameters for an experimental NMR-curve. In practice this is difficult, however, due to the strong mutual dependence of some of these parameters. In most cases P, $T_2$, and $\delta \nu$ must therefore be known if it shall be possible to evaluate the interconversion rate $(1/\tau)$.

In the application of the lineshape method to the study of exchange processes the spin-spin relaxation time $T_2$ is usually evaluated from the half-width of the signals at slow exchange or from some other proton signal in the spectrum not involved in the exchange process. The chemical shift $\delta \nu$ between the two exchanging protons is commonly evaluated from the peak separation in the same rate region.

The populations $P_A$ and $P_B$ are in many cases equal for symmetry reasons and need not be evaluated from the NMR-signals. If the protons A and B belong to two conformers, the population radio $P_A/P_B$ is in most cases dependent on temperature. In the slow exchange region this ratio can be computed by integration of the signals A and B, but in the region where the signals have coalesced some indirect method must be used. In special cases stereo-specific couplings can be used for the determination of the population ratio even in the fast exchange limit. This method has recently been used in an investigation of the barrier to internal rotation in 2-furanaldehyde.[3]

During our investigations of 2-furan- and 2-pyrrolealdehyde we noticed that several sets of P and $\tau$ values gave curves with almost the same lineshape and therefore could fit equally well to the experimental signals. In such a case it would be difficult to fit theoretical curves to the experimental signals by varying P and $\tau$ iteratively and obtain unique values of these two parameters.

These observations prompted us to study in more detail the dependence of the lineshapes on P and $\tau$ for a two-site case.


### THE "iso-F" DIAGRAM

The lineshape, $v$, of the NMR-signal for the case of two exchanging protons A and B spin coupled to a third proton X has been calculated according to the equations derived in Ref. 3 with

$$\begin{aligned}
J_1 &= J_{AX}; \\
J_2 &= 0; \\
J_3 &= J_{BX}; \\
J_4 &= 0 \text{ and} \\
(\omega_I + \omega_{II}) &= \delta \nu
\end{aligned}$$

The lineshape equation given in Ref. 3 thus becomes a function of a set of parameters according to eqn. 1.

$$v = f(\tau, P, J_{AX}, J_{BX}, \delta \nu, T_2) \tag{1}$$

where $J_{AX}$ and $J_{BX}$ are spin-spin coupling constants for the protons in sites A and B.

Eqn. (1) is valid only when proton X is shifted far away fram both A and B and $J_{AX}$ and $J_{BX}$ are small compared to $\delta\nu_{AX}$ and $\delta\nu_{BX}$.

Let us assume that the signal shape can be characterized by a suitable function $F(\tau, P)$. The problem will now be to find some property of the signal related to its shape which can be used as an approximation for this function.

In the present investigation we have chosen the maximum height of an appropriate normalized NMR-signal as a simple approximation for the function $F(\tau, P)$ according to following equation

$$F(\tau,\ P) = P/Y_{max} \qquad (2)$$

$Y_{max} =$ the maximum height of the coalesced signal and in the region of slow exchange the corresponding value for the signal with the population P. This parameter is obtained from normalized theoretical curves calculated with the same amplitude factor.

$P = 1$ for the coalesced signals and P elsewhere.

A study of the properties of the simple "shape function" defined by eqn. (2) has been limited to the case in which (i) the signals are symmetrical or nearly so in the investigated range of $\tau$ and P; (ii) the signals to be compared have the same general shape.
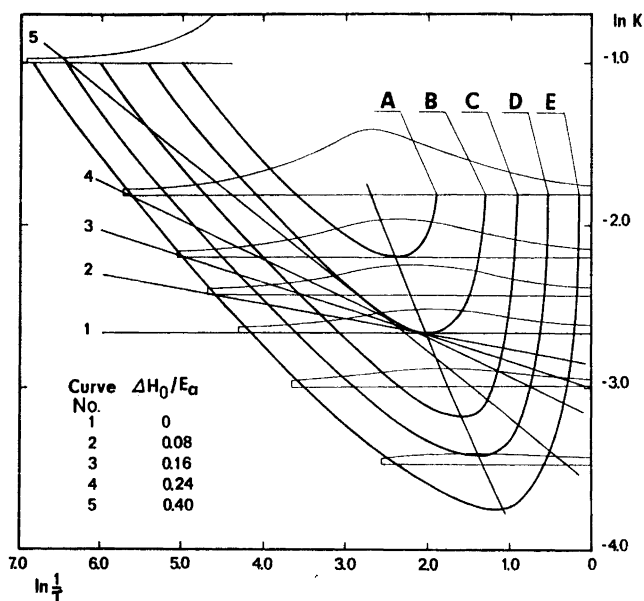


*Fig. 1.* The "iso-F" diagram with the "iso-F" curves A, B, C, D, and E. The diagram has been constructed using the lineshape equations give by Ref. 3 with $\delta\nu = 19.6$ Hz, $T_2 = 1.0$ sec, $J_{AX} = 1.0$ Hz, $J_{BX} = 0.75$ Hz, $P > 0.75$ and $10^{-4} < \tau < 1.0$ sec.

A large number of sample calculations of the lineshape according to eqn. (1) in a two-site case were performed with the following parameters:

$$\delta \nu \; = \; 19.6 \text{ Hz},$$
$$T_2 \; = \; 1.0 \text{ sec},$$
$$J_{AX} \; = \; 1.0 \text{ Hz and}$$
$$J_{BX} \; = \; 0.75 \text{ Hz}.$$

The values of F according to eqn. (2) were evaluated in the region $P > 0.75$ and $10^{-4} < \tau < 1$ sec.

The dependence of F on $\tau$ and P is best shown in a three-dimensional diagram where $\ln(1/\tau)$ is plotted along the $x$-axis, $\ln K$ [$K = (1-P)/P$] along the $y$-axis and F along the $z$-axis. In such a diagram — which we in the following will refer to as an "F-diagram" — the quantity F is represented by a well-shaped surface, and when points with equal values for F are connected, parabolic "iso-F" curves are obtained (Fig. 1). If the quantity chosen as an approximation for the lineshape function F is a good one, all combinations of P and $\tau$ along such an "iso-F" curve will give NMR-signals with the "same" shape. Examples of the theoretical lineshape at various points along one of
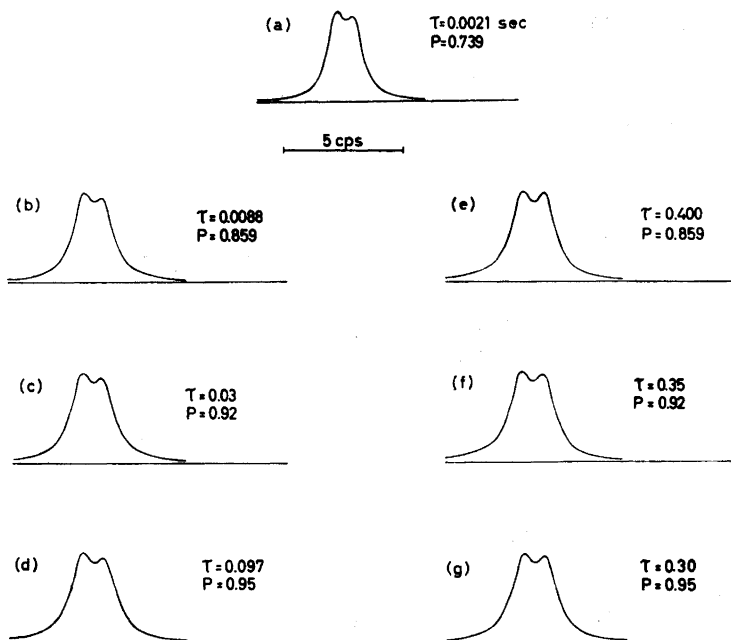


Fig. 2. Signals calculated with parameters from different points along "iso-F" curve C in Fig. 1.

the "iso-F" curves (C in Fig. 1) are shown in Fig. 2. The seven curves are indeed seen to have the same general shape though the $\tau$ values vary from 0.0021 sec to 0.4 sec and the P values vary from 0.739 to 0.95.

## THE USE OF THE "iso-F" CURVES FOR THE APPROXIMATE EVALUATION OF ACTIVATION ENERGIES AND EQUILIBRIUM CONSTANTS

The thermodynamic equations for the temperature dependence of the equilibrium in a two-site system $A \rightleftharpoons B$ are

$$\frac{d(\ln K)}{d(1/T)} = \frac{\Delta H_0}{R} \tag{3}$$

$\Delta H_0$ = the enthalpy difference between A and B. $K = (1-P)/P$ = the equilibrium constant where P = the population of protons in site A.

For the temperature dependence of the exchange rate we may write

$$\frac{d(\ln 1/\tau_A)}{d(1/T)} = \frac{E_a}{R} \tag{4}$$

where $E_a$ = the energy of activation, $T$ = the temperature in °K, $\tau_A$ = the mean lifetime for protons in site A.

Combination of eqns. 3 and 4 gives

$$\frac{d(\ln K)}{d(\ln 1/\tau_A)} = \frac{\Delta H_0}{E_a} \tag{5}$$

If we assume $\Delta H_0$ and $E_a$ to be temperature independent we can directly integrate eqn. 5 and obtain

$$\ln K = \frac{\Delta H_0}{E_a} \ln 1/\tau_A + C \tag{6}$$

where $C$ is an integration constant.

Eqn. 6 will in diagram 1 be represented by a straight line with the slope $\Delta H_0/E_a$. Eqns. 3 and 4 will also give straight lines if $\ln 1/\tau_A$ and $\ln K$ are plotted versus $1/T$. The slopes of these lines are $E_a/R$ and $\Delta H_0/K$, respectively. In a limited temperature region, where the assumption of constant $E_a$ and $\Delta H_0$ is valid, the correct experimental values of $K$ and $\tau_A$ will therefore lead to straight lines in a diagram in which $\ln(1/\tau_A)$ and $\ln K$ are plotted versus $1/T$.

In the following we shall show how the "iso-F" curves in diagram I can be used for the evaluation of $\Delta H_0$ and $E_a$ when P can not be obtained independently. Let us exemplify the procedure by evaluating $\Delta H_0$ and $E_a$ for a hypothetical case using diagram I. The "iso-F" curves for this system may be constructed in the following way, using the signals from the conformer (A) which corresponds to the most populated site (P>0.75).

1. NMR spectra are recorded at the temperature $T_c$ — where the signals from conformer A have their maximum broadening — and in a range of temperatures above and below $T_c$.

2. Theoretical NMR spectra calculated according to eqn. 1, which give a good fit to the experimental spectrum at the temperature $T_c$, are found by varying $\tau$ and P.

3. The amplitude factor of these theoretical curves at $T_c$ is normalized and the F values are evaluated according to eqn. 2.

4. The F values are plotted in a three dimensional diagram against the corresponding values of $\ln(1/\tau)$ and $\ln(1-P)/P$, *i.e.* an F-diagram of the type shown in Fig. 1. In this diagram all points should now have nearly the same F-values [$F(T_c)$]. A line through these points thus gives the "iso-F" curve valid for the temperature $T_c$. In our hypothetical case this curve is labelled B in Fig. 1.

5. By repeating steps 2—4 for the experimental curves at temperatures below and above $T_c$ the "iso-F" curves for these are obtained (curves C, D, and E in Fig. I).

6. The correct experimental values for $\tau$ and K must according to eqn. 6 fall on a straight line in Fig. 1 with slope equal to $\Delta H_0/E_A$. This straight line must also be a tangent to the "iso-F" curve pertaining to the temperature of maximum broadening, $T_c$, (*i.e.* curve B in Fig. 1) since the system studied can have no F-value greater than $F(T_c)$ (see step 2). A tangent to curve B in Fig. 1 is thus drawn with an arbitrary slope.
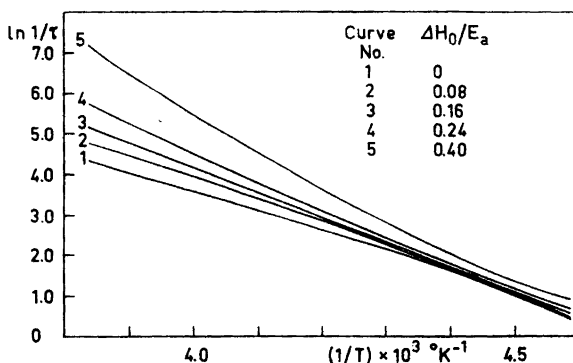


*Fig. 3.* Plot of ln $1/\tau$-values obtained from the intersections between the "iso-F" curves A—E and the tangents 1—5 in Fig. 1 *versus* pertinent $1/T$-values.

7. From the intersections between this tangent and the "iso-F" curves (C, D and E) a set of ln $1/\tau$ and ln K values is obtained. These ln $1/\tau$ and ln K values are plotted *versus* the corresponding $1/T$ values in two diagrams (Figs. 3 and 4).

8. As the correct experimental values for ln $1/\tau$ and ln K must give straight lines in both Figs. 3 and 4, steps 6 and 7 are repeated — with different slopes for the tangent to the $F(T_c)$ curve in diagram 1 — until straight lines are obtained in both Figs. 3 and 4.

9. $E_a$ is calculated from the slope of the straight line in the plot of ln $1/\tau$ *versus* $1/T$ (Fig. 3) according to eqn. 4.
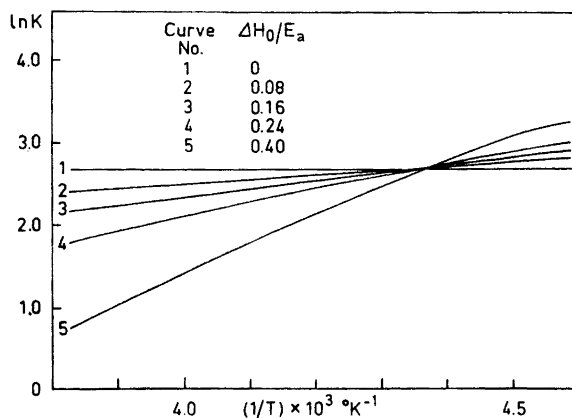
*Fig. 4.* Plot of ln *K*-values obtained from the intersections between the "iso-F" curves A—E and the tangents 1—5 in Fig. 1 *versus* pertinent $1/T$-values.

$\Delta H_0$ can in the same way be obtained from the plot of ln $K$ *versus* $1/T$ (Fig. 4) according to eqn. 4. None of the curves in this plot seems, however, to deviate very much from a straight line and it may be difficult to decide which set of points best fits a straight line. The $\Delta H_0$ values obtained from Fig. 4 are therefore quite uncertain. A more reliable $\Delta H_0$ value can be estimated from eqn. 5 with the $E_a$ value obtained from Fig. 3 and the $\Delta H_0/E_a$ value obtained from the slope of the corresponding tangent in diagram 1

$$\Delta H_0 = E_a \frac{\mathrm{d}\ln K}{\mathrm{d}\ln (1/\tau)} \tag{7}$$

## EVALUATION OF $E_a$ AND $\Delta H_0$ FOR 2-FURANALDEHYDE

In order to test the method described on a practical case we have studied the hindered rotation of the aldehyde group in 2-furanaldehyde (I).
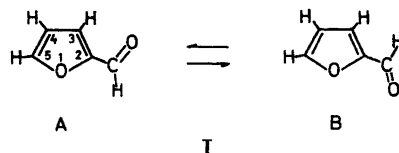


The rate parameters and thermodynamic data for the conformer equilibrium A⇌B in this molecule have recently been obtained in an independent way.[3] At −115.5°C the rotation rate of the aldehyde group in 2-furanaldehyde is slow enough to permit registration of separate spectra from conformers A and B. The aldehyde signals in conformers A and B appear at $\delta=9.56$ ppm

and $\delta = 9.74$ ppm, respectively. The signal from the aldehyde proton in conformer A is split into a doublet due to spin coupling with $H$-5 ($J_{CHO-5}{}^A = 1.10$ Hz) and the signal from the aldehyde proton in conformer B is split into a doublet due to spin coupling with H-4 ($J_{CHO-4}{}^B = 0.85$ Hz). The signals from the H-3 proton in conformers A and B appear at $\delta = 7.57$ ppm and $\delta = 7.42$ ppm, respectively. The signal from H-3 in both conformer A and B is split into a quartet due to spin coupling with H-4 and H-5 ($J_{34}{}^A = J_{34}{}^B = 3.70$ Hz, $J_{35}{}^A = J_{35}{}^B = 0.80$ Hz). The signals from H-4 and H-5 appear at $\delta = 6.79$ ppm and $\delta = 8.04$ ppm, respectively, in both conformers. The H-4 signal is split due to spin coupling with H-3, H-5, and the aldehyde proton ($J_{45} = 1.75$ Hz), and H-5 is split due to spin coupling with H-3, H-4, and the aldehyde proton. The conformer ratio A/B is *ca.* 10:1 at $-115.5°$C. At about $-50°$C the signals due to the aldehyde and H-3 protons in conformers A and B are broadened and at room temperature an average spectrum is observed. At room temperature the aldehyde signal is split into a quartet. The stereospecific couplings to the aldehyde proton were used for the determination of the population ratio A/B in the previous investigation of 2-furanaldehyde.

Due to the inequality of the populations of conformers A and B in 2-furanaldehyde at low temperatures (A/B = 10:1, *i.e.* P = 0.91), this substance serves as a suitable test case for the "iso-F" method described above. The "iso-F" curves for this case have been evaluated by comparing the experimental signals from the aldehyde proton with theoretical spectra calculated using the parameters $\delta = 10.8$ Hz, $J_{AX} = 1.10$ Hz, $J_{BX} = 0.85$ Hz, and various values of $\tau$, P and $T_2$. In this case $T_2$ was found to vary with temperature and therefore the "iso-F" curves had to be calculated using the $T_2$ value appro-
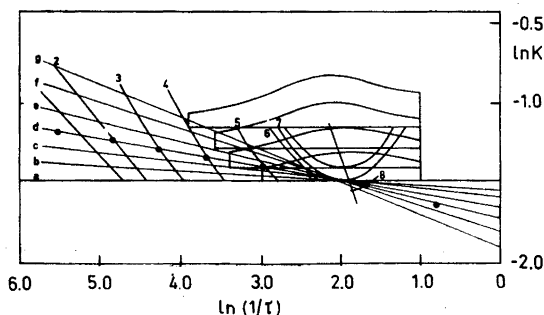


*Fig. 5.* "iso-F" diagram constructed using the parameters for the aldehyde proton in 2-furanaldehyde.

| Curves | | | | $\Delta H_0/E_a$ | |
|---|---|---|---|---|---|
| 1 and 2 calc. with $T_2 = 1.2$ sec, | | | | a | 0 |
| 3 and 4 | ,, | ,, | $T_2 = 0.75$ ,, | b | 0.029 |
| 5 and 6 | ,, | ,, | $T_2 = 0.67$ ,, | c | 0.055 |
| 7 and 8 | ,, | ,, | $T_2 = 0.59$ ,, | d | 0.085 |
| | | | | e | 0.122 |
| | | | | f | 0.161 |
| | | | | g | 0.205 |

priate for each temperature. The full circles shown in Fig. 5 are the values obtained in the earlier investigation mentioned above. In Figs. 6 and 7 $\ln(1/\tau)$ and $\ln K$ are plotted *versus* $1/T$. The deviation of the curves in Fig. 6 from a straight line has been estimated by a least-squares fit. In Fig. 8 the standard deviation in the activation energy obtained from these least-squares fits is plotted *versus* the corresponding value of $E_a$. The minimum of the curve in
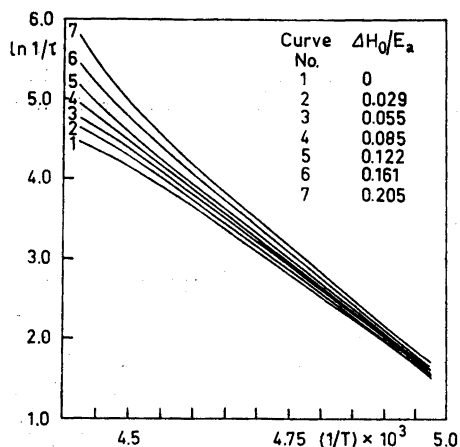


*Fig. 6.* Plot of ln $1/\tau$-values obtained from the intersections between the "iso-F", curves 1 — 7 and the tangents a-f in Fig. 5 *versus* pertinent $1/T$-values.
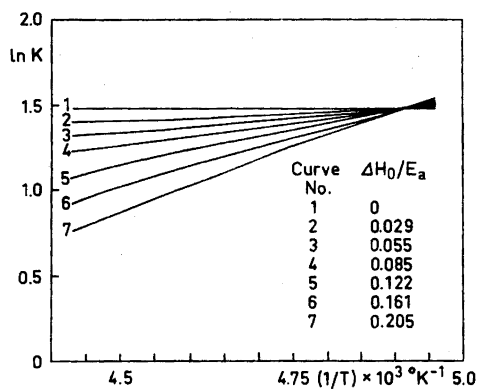
*Fig. 7.* Plot of ln $K$-values obtained from the intersections between the „iso-F" curves 1 — 7 and the tangents a-f in Fig. 5 *versus* pertinent $1/T$-values.

Fig. 8 occurs at $E_a \approx 12.2$ kcal/mole. This minimum thus occurs between points 4 and 5, which corresponds to the tangents d and e in Fig. 5. The correct values for ln $|1/\tau|$ and ln $K$ must therefore in Fig. 5 fall on a tangent with
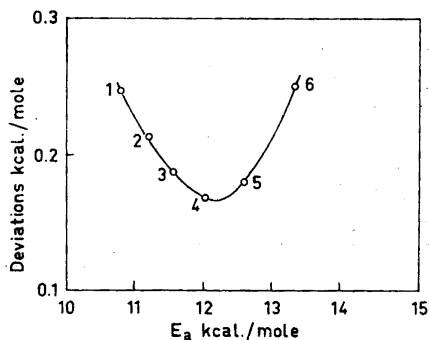


*Fig. 8.* Plot of the deviation from a straight line for the curves 1 — 6 in Fig. 6 expressed as the error in $E_a$ *versus* $E_a$.

a slope in the range 0.085—0.122. The whole procedure is now repeated by construction of tangents in Fig. 5 with slopes between 0.085 and 0.122. This second evaluation gives an $E_a$ value equal to $12.2 \pm 0.2$ kcal/mole, corresponding to a slope of the tangent in Fig. 5 of 0.086. This gives according to eqn. 5 and energy difference $\Delta H_0 = 1.05 \pm 0.02$ kcal/mole between the two conformers of 2-furanaldehyde. Since the evaluation is made using the signal from the most populated conformer (A), the activation energy corresponds to $E_{aA}$.

The earlier investigation gave the following values: $E_{aA} = 12.17 \pm 0.17$ kcal/mole and $\Delta H_0 = 1.05 \pm 0.05$ kcal/mole. The perfect agreement between the two methods may be fortuitous and does not give a realistic measure of the reliability of the "iso-F" method.

## CONCLUSION

The use of an "iso-F" diagram makes it possible to estimate rate parameters and equilibrium data from NMR-curves even in the case of interchanging conformers where the equilibrium constant varies with temperature and cannot be independently estimated. The simple way of evaluating F used in the present work may, however, be improved by using some other more elaborate way of characterizing the line shape. The second moment of a signal is often used in wide-line spectroscopy to characterize the shape of NMR-signals from solid materials and this quantity may also be used for the evaluation of F, for example by putting F proportional to it. The F-values obtained from the second moment of the signal may be expected to be a better characteristic of the actual signal shape than those obtained from eqn. 2.

The reliability of the $E_a$ and $\Delta H_0$ values obtained, e.g., for restricted rotation in a molecule using the "iso-F" method must, however, be further tested by comparison with corresponding data which have been estimated using some other method.

A qualitative estimation of the possibility of evaluating reliable values for rate parameters and equilibrium data from the "iso-F" diagram might be obtained by comparing theoretical NMR-curves calculated using $\tau$ and P values from different points along an "iso-F" curve in this diagram. If the shape of the calculated curves changes very much along the "iso-F" curve it is not likely that reliable values for the desired $E_a$ and $\Delta H_0$ values will be obtained.

## REFERENCES

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2. McConnell, H. M. *J. Chem. Phys.* **28** (1958) 430.
3. Dahlqvist, K.-I. and Forsén, S. *J. Chem. Phys.* **69** (1965) 4062.