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Comparison of Kinetic Results Obtained by NMR Line Shape and Equilibration Methods*

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Rates of internal rotation around carbonyl-to-nitrogen bonds are determined for the rotamers IA and IB of N-benzyl-N,2,4,6-tetramethylbenzamide by equilibration of IA and for N,N,2,4,6-pentamethylbenzamide (II) by ^{1}H-NMR line shapes. The activation parameters (Table V) obtained by the two methods agree well within error limits. This represents the first experimental confirmation of the soundness of kinetic measurements by line shapes. The range of rate constants accessible by the two techniques amounts to almost 10^7 sec^{-1}. Further molecular systems are suggested as suitable for such a comparison; the nitrosamines VIIA and VIIB, for example, will allow both methods to be applied to the isomers of the same compound. Steric contributions to the free enthalpies of activation are evaluated for the internal rotation in some 2,4,6-trisubstituted benzamides.

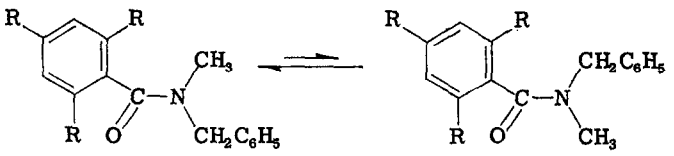
INTRODUCTION

Rates of fast molecular processes are often determined by high-resolution NMR line shapes which are connected with rate constants by the theory of exchange broadening. Both the theoretical and experimental aspects of this method are subject to errors which have been discussed by Gutowsky and his co-workers (*1*, *2*). Experiments testing the soundness and accuracy of this technique are therefore desirable. One possibility is to use another approach capable of measuring rates when the system under investigation is at *equilibrium*. This has been done earlier by spin-echo NMR, the agreement with line shape results being moderate (*1*, *3*)**. Another way would be to compare rates obtained by line shapes with rates at lower temperatures where *nonequilibrium* procedures can be applied. They have the advantage that a time-dependent property of the system may be observed, directly. This was made possible by the isolation of N-benzyl-N,2,4,6-tetramethylbenzamide in the form of its pure rotamer IA (*4*). The equilibration of IA generates a certain amount of rotamer IB which can be deter-

* Part III of the series "Protonenresonanz-Untersuchungen zur inneren Rotation." Part II: Reference *4*.

** Note added in proof: Agreement between double-resonance and line shape results was recently reported (*27*).

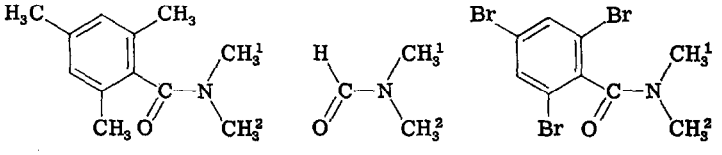
mined as a function of time by ^{1}H-NMR signal intensities, when working below +45°C; above this temperature the equilibration is too fast to be measured. Rates of internal rotation obtained by such experiments are compared, using the Arrhenius equation, with rates evaluated from line shapes of N,N,2,4,6-pentamethylbenzamide (II) at temperatures above +110°C. It is shown in the section on comparison of results (see below) that substitution of benzyl by methyl does not influence the kinetics to a significant degree.



I A R = CH_3 I B

V A R = Br V B

VI A R = $C(CH_3)_3$ VI B



II III IV

EXPERIMENTAL

Rotamers IA and VA were prepared from 0.03 mole of benzylmethylamine and 0.015 mole of 2,4,6-trimethylbenzoyl chloride in benzene or 2,4,6-tribromobenzoyl chloride in petroleum ether, respectively. The products were recrystallized from low-boiling petroleum ether.

IA: mp 74–76°C. Yield 80%. Calculated for $C_{18}H_{21}NO$: C, 80.86; H, 7.92; N, 5.24. Found: C, 80.88; H, 8.19; N, 5.27.

VA: mp 74,5–76°C. Yield 50%. Calculated for $C_{15}H_{12}Br_3NO$: C, 38.99; H, 2.62; Br, 51.89; N, 3.03. Found: C, 39.23; H, 2.75; Br, 51.77; N, 2.81.

Compound II was prepared by passing dimethylamine through a solution of 2,4,6-trimethylbenzoyl chloride in ether. The yield of crude II was 96%. After distillation (bp 93°C, 0.015 mm) crystals, mp 40–41°C, were formed. Calculated for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; N, 7.32. Found: C, 75.14; H, 9.04; N, 7.45.

N,N-dimethylformamide (III) was distilled before use. Compound IV was prepared according to the literature (*5*).

The solvents were purified by distillation and tested by NMR. Only quinoline showed an impurity peak assigned to a trace of water. Concentrations were 0.6

mole liter^{-1} in a mixture of 1-chloronaphthalene and benzotrichloride (1:1, v:v) or in pure 1-chloronaphthalene, with one drop of octamethylcyclotetrasiloxane[1] $[(CH_3)_2SiO]_4$ per 0.5 ml of solution. This compound is stable up to 200°C and boils at 175°C (750 mm). Its chemical shift at 33°C, referred to internal TMS, is $\tau = 9.77$ in our solvent mixture and $\tau = 9.73$ in 1-chloronaphthalene. Concentrations in quinoline were 0.7 mole liter^{-1}, TMS serving as the internal standard. Chemical shifts τ are accurate in this paper to ± 0.03.

Spectra were taken on a Varian A-60 spectrometer equipped with a variable temperature system. The temperature of the sample was determined according to the manufacturer's instructions (*6*). The absolute error of temperature is reported to be ± 2°C (*6*). We assumed a relative error $\Delta T = \pm 1$°C for the evaluation of ΔE and $\Delta \log k_0$ in the section on errors (see below). Coalescence temperatures were assigned a larger error than ± 2°C due to experimental difficulties. Two of the equilibrations were run in the spectrometer without using the variable temperature system; the error in T was therefore diminished (see Table IV). The equilibration at 17.9°C was carried out in a thermostat filled with methanol and cooled by an ice–salt mixture. At certain time intervals the equilibration was interrupted by putting the sample tube into the probe hole cooled to -10°C and by integrating the spectrum. (This temperature had to be taken into account when choosing a solvent system for this study. On the other hand a boiling point of more than 200°C was necessary for line shape work. Among the liquids tested the above mixture showed the lowest viscosity at -10°C.)

Line shape measurements were run two or three times at each temperature. In this case the sweep rate was 1 cps^2, whereas for integrations it was 5 cps^2. Amplitudes of the rf field were kept below the value where saturation broadening of signals occurred.

RESULTS OBTAINED BY THE LINE SHAPE METHOD

The ^{1}H-NMR spectrum of N,N,2,4,6-pentamethylbenzamide (II) in a 1:1 mixture of 1-chloronaphthalene and benzotrichloride at 33°C shows two sharp N-methyl signals at $\tau = 7.66$ and 7.08 [Fig. 1(a)]. Above 100°C their width b at half height increases, whereas the width b_S of the internal standard remains fairly constant. The width b_E of the methyl signals without the effect of rotational broadening is assumed to vary between 0.9 and 1.0 cps (see Table I). Rate constants k for the rotation around the C—N bond in II were calculated from values of $(b - b_E)$, the exchange contribution to the line width, according to Schmid, Friebolin, Kabuss, and Mecke (*7*), their Fig. 9 being used for this purpose. The chemical shift differences $\Delta\nu$ of the two N-methyl absorptions decreased with increasing temperature (Table I). This behavior cannot be the result of broadening and overlap of signals, as this temperature dependence of $\Delta\nu$

[1] We are grateful to the Farbenfabriken Bayer AG and Professor W. Noll, Leverkusen, for this compound.

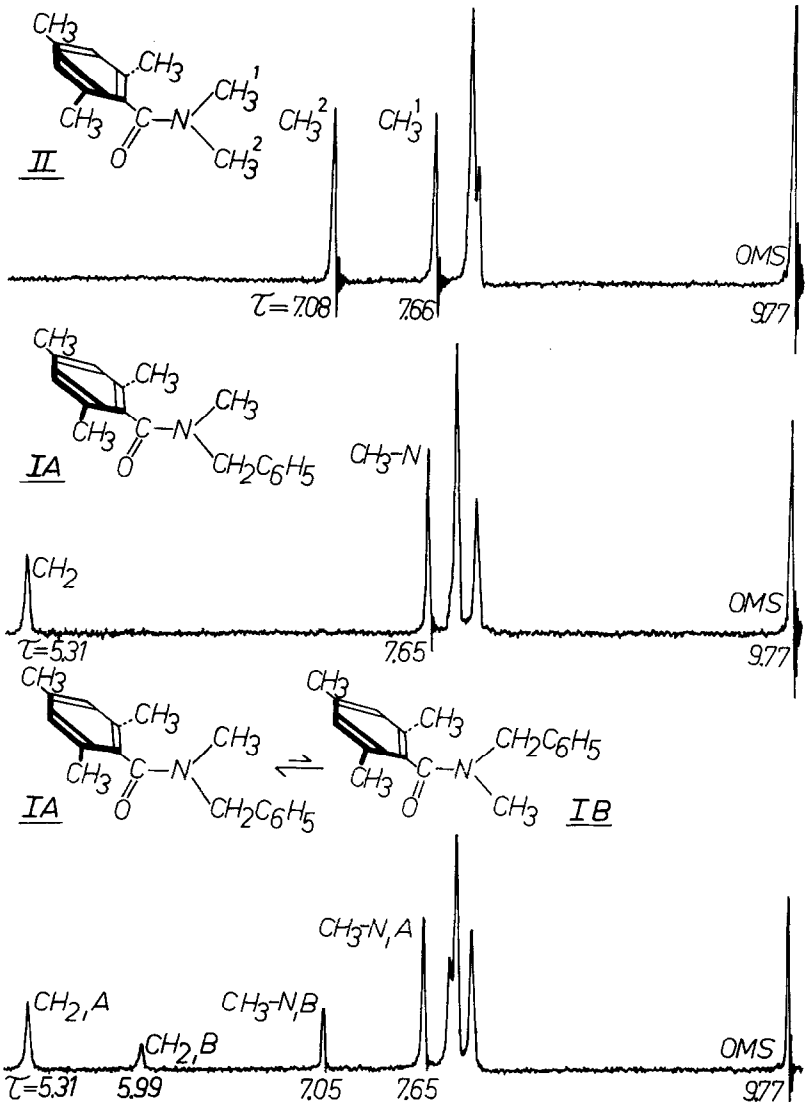


FIG. 1. a. Spectrum of compound II. b. Spectrum taken 2 minutes after dissolving crystalline IA. c. Spectrum taken 200 minutes after dissolving IA. Spectra were run at 33°C. Solvent: 1-chloronaphthalene/benzotrichloride (1:1). Internal standard: octamethylcyclotetrasiloxane (OMS).

is also observed in the range of 33–100°C where no rotational broadening occurs. Therefore $\Delta\nu$-values above 138°C were obtained by linear extrapolation of chemical shift difference versus temperature. From $\Delta\nu = 28.3$ cps at $T_c = 167.5$°C, the coalescence temperature, $k = 62$ sec^{-1} (Table I) was calculated taking into

TABLE I

EXPERIMENTAL VALUES FOR N,N,2,4,6-PENTAMETHYLBENZAMIDE (II) OBTAINED BY LINE SHAPES. SOLVENT: 1-CHLORONAPHTHALENE/BENZOTRICHLORIDE (1:1)[a]

T (°C)	$\Delta\nu$ (cps)	b (cps)	b_S (cps)	k (sec^{-1})
33	35.0	1.0	0.9	—
40	34.8	1.0	0.9	—
70	33.1	1.0	0.9	—
100	31.5	1.0	1.0	—
110	31.0	1.2	0.9	—
111	30.9	1.4	0.9	1.23
117	30.6	1.6	0.9	1.68
121.5	30.5	1.9	0.8	3.2
125.5	30.3	2.2	0.8	4.2
130.5	30.1	2.6	0.8	5.4
134.5	29.9	3.4	0.8	7.9
138	29.7	4.1	0.9	9.6
143.5	29.5[c]	5.5	0.9	13.8
145.5	29.4[c]	6.0	0.9	14.3
147.5	29.3[c]	6.7	0.9	16.8
167.5[b]	28.3[c]		0.8	62

[a] $\Delta\nu$: chemical shift difference of the two N-methyl signals at 60 Mc/sec; b: width at half-height of the methyl signals; b_S: width of the octamethylcyclotetrasiloxane signal.

[b] Coalescence temperature of methyl signals.

[c] Extrapolated chemical shift difference (see text).

account b_E = 1.0 cps and using Eq. (VIII, 1) of Reference 7. (The expression $k = \pi\Delta\nu/\sqrt{2}$ neglects b_E and gives nearly the same k in this case.) The other methods (7) for the evaluation of rates from line shapes could not be applied here for two reasons: (1) At higher temperatures the signal-to-noise ratio is unfavorable; (2) $\Delta\nu$ above 138°C is known only by extrapolation, but its precise value would be essential.

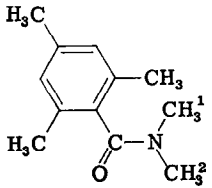
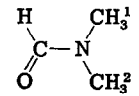
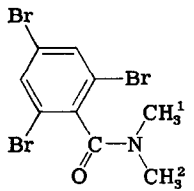
Table II includes coalescence temperatures and extrapolated shift differences for N,N-dimethylformamide (III) and for N,N-dimethyl-2,4,6-tribromobenzamide (IV). As solutions of dimethylformamide containing benzotrichloride proved to be thermally less stable, III was investigated in pure 1-chloronaphthalene. The effect of spin coupling of the formyl proton with the methyl groups (J = 0.56 and 0.28 cps) (8) in dimethylformamide was neglected. The calculation of $\Delta F^{\neq}$-values in Table II is described in the section on activation parameters (see below).

RESULTS OBTAINED BY THE EQUILIBRATION METHOD

The spectrum of N-benzyl-N,2,4,6-tetramethylbenzamide (IA) taken directly after dissolution of the crystals in a 1:1 mixture of 1-chloronaphthalene and

TABLE II

$\Delta F^{\neq}$-VALUES OBTAINED BY LINE SHAPES[a]

	Solvent	$\tau(CH_3^1)$ 33°C	$\tau(CH_3^2)$ 33°C	$\Delta\nu$ (cps)	T_c (°C)	$\Delta F^{\neq}$ (kcal mole^{-1}) 167.5°C	128°C	171°C
 II	Chloronaphth. /benzotrichl.	7.66	7.08	28.3 ± 1.0	167.5 ± 2.5	22.5 ± 0.2	22.5 ± 0.3[b]	22.5 ± 0.3[b]
 III	Chloronaphth.	8.15	7.66	20.9 ± 1.5	128 ± 4	—	20.6 ± 0.3	—
 IV	Chloronaphth. /benzotrichl.	7.90	7.24	30.6 ± 1.5	171 ± 3	—	—	22.6 ± 0.2
							$\Delta F^{\neq}_{II} - \Delta F^{\neq}_{III} = 1.9$	$\Delta F^{\neq}_{II} - \Delta F^{\neq}_{IV} = -0.1$

[a] T_c: coalescence temperature of N-methyl signals; $\Delta\nu$: chemical shift difference of methyl signals at 60 Mc/sec, extrapolated to T_c (see text).

[b] Calculated from E and $\log k_0$ by means of Eq. (5).

benzotrichloride at 33°C shows a N-methyl signal at $\tau = 7.65$ and a methylene signal at 5.31 [Fig. 1(b)]. Their intensities decrease gradually in favor of two further lines at $\tau = 7.05$ and 5.99 corresponding to rotamer IB. An equilibrium in which IA predominates [Fig. 1(c)] is established 200 minutes after dissolving the crystals. No doubt this process as well as the coalescence of signals in compound II are caused by internal rotation around the C—N bonds. The chemical significance of this finding has been discussed and the correlation of τ-values has been justified (*4*).

For all benzamides investigated so far no trace of rotamer B is detected directly after dissolution of the crystals at 33°C. Thus we start with a solution of pure A the concentration of which is $(A)_0$. After some time the equilibrium

$$A \underset{k_B}{\overset{k_A}{\rightleftharpoons}} B$$

with the equilibrium constant

$$K = (B)_\infty/(A)_\infty = k_A/k_B$$

is established. The expression

$$\log\left(\frac{(A)_t}{(A)_t + (B)_t} - \frac{1}{K+1}\right) = -\frac{C}{2.303}\,t + \log\frac{K}{K+1}, \qquad (1)$$

$$C = k_A + k_B \qquad (2)$$

was derived from a rate law in the literature (*9*). Concentrations $(A)_t$ and $(B)_t$ at time t were replaced by the relative intensities of the CH_2,A and CH_2,B signals [see Fig. 1(c)]. The left side of Eq. (1) was plotted versus t. C was calculated from the slope of the resulting straight line (e.g., Fig. 2 of Reference *4*). The half-life is given by

$$t_{0.5} = \ln 2/C,$$

the rate constants by

$$k_A = KC/(K+1) \quad \text{and} \quad k_B = C/(K+1). \qquad (3)$$

Results for rotamers IA and IB are given in Table III.

Table IV includes K- and $t_{0.5}$-values for N-benzyl-N-methyl-2,4,6-tribromobenzamides (VA and VB) and for N-benzyl-N-methyl-2,4,6-tri-*t*-butylbenzamides (VIA and VIB). VIA and VIB have been prepared and separated by Staab and Lauer (*10*). The calculation of $\Delta F^{\neq}$-values in Table IV is described in the following section.

CALCULATION OF ACTIVATION PARAMETERS

The Arrhenius plot (Fig. 2, left-hand part) of the data in Table I gives the activation energy E and the frequency factor k_0 for compound II. Similarly the

TABLE III

EXPERIMENTAL VALUES FOR N-BENZYL-N,2,4,6-TETRAMETHYLBENZAMIDES (IA AND IB) OBTAINED BY EQUILIBRATIONS. SOLVENT: 1-CHLORONAPHTHALENE/BENZOTRICHLORIDE (1:1)[a]

T (°C)	K	$t_{0.5}$ (min)	$k_A \cdot 10^4$ (sec^{-1})	$k_B \cdot 10^4$ (sec^{-1})
17.9	0.37	106	0.29	0.80
26.2	0.38	32.5	1.0	2.6
33.0	0.40	12.8	2.6	6.5
38.5	0.40	8.6	3.9	9.8
43.5	0.39	4.1	8.4	21

[a] $K = (B)_\infty/(A)_\infty$: equilibrium constant; $t_{0.5}$: half-life.

results for IA and IB given in Table III are plotted in the right-hand part of Fig. 2. E- and log k_0-values are collected in Table V.

Two ways for the calculation of free enthalpies of activation were used. For temperatures at which experimental rate constants were at hand $\Delta F^{\neq}$ was obtained (*11*) from

$$\Delta F^{\neq} = RT \ln (k_b T/hk), \tag{4}$$

a transmission coefficient of unity being assumed. Results are given in Table II, IV, and V. However, when E and k_0 are known, $\Delta F^{\neq}$ at any temperature may be calculated from

$$\Delta F^{\neq} = E + RT \ln (k_b T/hk_0). \tag{5}$$

This expression is derived from Eq. (4) and the Arrhenius equation. Equation (5) was used to compute free enthalpies of activation for compounds IA, IB, and II at temperatures where $\Delta F^{\neq}$ is not accessible by Eq. (4) but is needed for comparison with other compounds.

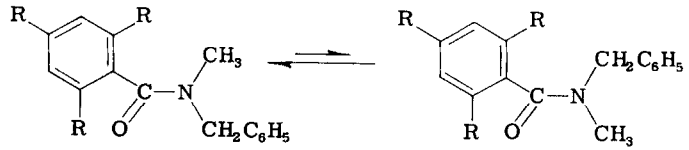
ESTIMATION OF ERRORS

The error of k was estimated from the errors of all values involved in the experiments. Thus, for the line shape determinations uncertainties of b ($\pm$ 0.1 cps), b_B ($\pm$ 0.1 cps), and $\Delta\nu$ resulted in maximal errors Δk. The uncertainty of $\Delta\nu$ was assumed to be $\pm$0.3 cps for direct measurements and $\pm$1.0 or 1.5 cps (see Table II) for extrapolations of $\Delta\nu$. For the equilibrations the plot of the left side of Eq. (1) versus t (e.g., Fig. 2 of Reference *4*), consisting of 20 to 40 points, was evaluated according to Reference *12* giving 10 to 20 individual C_i-values [see Eq. (2)]. The error ΔC was calculated from

$$\Delta C = \pm\left[\sum_{i=1}^{n} (C_i - C)^2/(n-1)\right]^{1/2},$$

TABLE IV

$\Delta F^{\neq}$-VALUES OBTAINED BY EQUILIBRATIONS[a]



I A	R = CH_3	I B
V A	R = Br	V B
VI A	R = $C(CH_3)_3$	VI B

	Solvent	$\tau(CH_3—N)$ 33°C	$\tau(CH_2)$ 33°C	K	$t_{0.5}$ (min)	T (°C)	$\Delta F^{\neq}$ (kcal mole^{-1}) 35.8–40.6°C	$\Delta F^{\neq}$ (kcal mole^{-1}) 120.0°C
IA	Quinoline	7.45	5.05	0.38 ± 0.02	8.7 ± 0.8	40.6 ± 0.3	23.4 ± 0.1	—
IB		6.81	5.78				22.8 ± 0.1	—
VA	Quinoline	7.41	5.07	0.35 ± 0.02	32.1 ± 2.8	35.8 ± 0.3	23.8 ± 0.1	—
VB		6.90	5.74				23.2 ± 0.1	—
IA	Chloronaphth. /benzotrichl.	7.65	5.31	0.40 ± 0.02	8.6 ± 1.2	38.5 ± 2.0	23.1 ± 0.3	23.1 ± 0.9[b]
IB		7.05	5.99				22.5 ± 0.3	22.6 ± 0.7[b]
VIA	Chloronaphth. /benzotrichl.	7.66	5.42	0.12 ± 0.01	97 ± 6	120.0 ± 0.1	—	32.0 ± 0.1[c]
VIB		7.05	6.05				—	30.3 ± 0.1[c]
							$\Delta F_I^{\neq} - \Delta F_V^{\neq}$ = −0.4	$\Delta F_I^{\neq} - \Delta F_{VI}^{\neq}$ ≈ −8.5

[a] $K = (B)_\infty/(A)_\infty$: equilibrium constant; $t_{0.5}$: half-life.

[b] Calculated from E and log k_0 by means of Eq. (5).

[c] Investigated by Staab and Lauer (*10*).

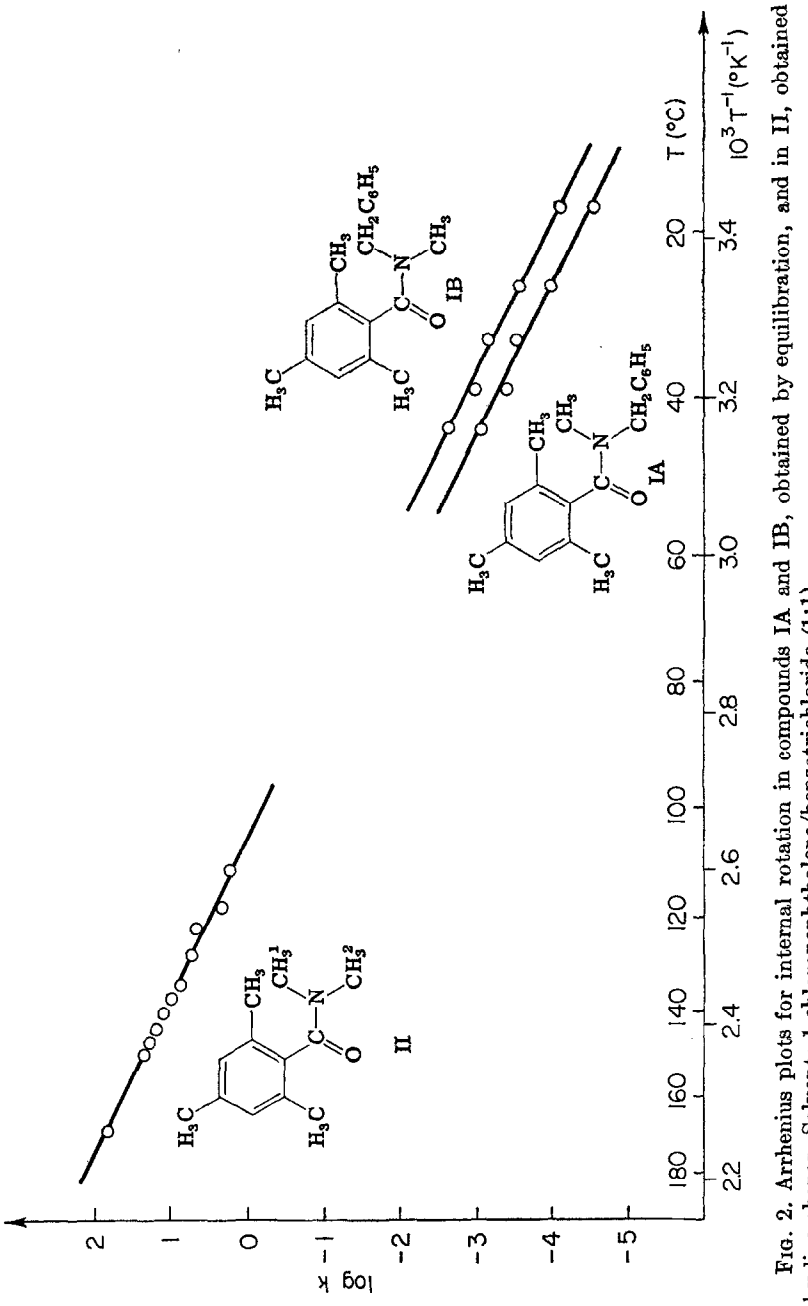
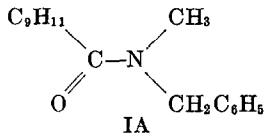
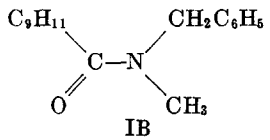
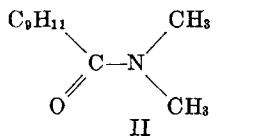


FIG. 2. Arrhenius plots for internal rotation in compounds IA and IB, obtained by equilibration, and in II, obtained by line shapes. Solvent: 1-chloronaphthalene/benzotrichloride (1:1).

TABLE V

COMPARISON OF RESULTS OBTAINED BY LINE SHAPE AND EQUILIBRATION METHODS. SOLVENT: 1-CHLORONAPHTHALENE/BENZOTRICHLORIDE (1:1)[a]

	E (kcal mole^{-1})	log k_0	$\Delta H^{\neq}$ (kcal mole^{-1}) 43.5°C	$\Delta S^{\neq}$ (e.u.) 43.5°C	$\Delta F^{\neq}$ (kcal mole^{-1}) 43.5°C
 IA	23.5 ± 2.7	13.1 ± 2.0	22.9 ± 2.7	−1 ± 9	23.0 ± 0.3[b]
 IB	22.8 ± 2.2	13.0 ± 1.6	22.2 ± 2.2	−1 ± 7	22.4 ± 0.3[b]
 II	23.2 ± 2.0	13.3 ± 1.1	22.6 ± 2.0	0 ± 5	22.5 ± 0.4[c]

[a] C_9H_{11}: 2,4,6-trimethylphenyl.
[b] Calculated from k_A and k_B, respectively, by means of Eq. (4).
[c] Calculated from E and log k_0 by means of Eq. (5).

n being the number of C_i-values. Errors of t and K were neglected here, as they influence the slope of the straight line very little. Δk_A and Δk_B were determined by maximum propagation of errors using Eq. (3). The maximum deviation ΔK from the mean K-value obtained by at least six integrations amounted to ±0.02 for some of the kinetic runs and ±0.03 for others.

ΔT which is discussed in the experimental section (see above) and Δk were included in the estimation of errors ΔE and $\Delta \log k_0$. Each point of the Arrhenius plot (Fig. 2) was marked as a rectangle corresponding to the uncertainty of the point; two straight lines with maximum and minimum slopes were drawn in such a manner as to pass through each rectangle.[2]

[2] It has been pointed out by Gutowsky *et al.* (*1*) that statistical deviations do not reflect the true error situation and that systematic errors may be very serious for the line shape method (see Ref. *13*). Schmid *et al.* (*7*) have also criticized the custom of giving statistic deviations only. Their error calculation includes Δk and presumes k-values determined above and below T_c; with increasing T, Δk first increases and then decreases. As our line shape results are confined to T_c and below, they lack this special feature as do our equilibration results. We have adopted the above graphic procedure which, however, may overestimate the errors.

Errors of $\Delta F^{\neq}$, $\Delta H^{\neq}$, and $\Delta S^{\neq}$ given in Tables II, IV, and V were calculated by maximum propagation. Errors obtained in this way are too large when $\Delta F^{\neq}$ is calculated from Eq. (5) because ΔE and $\Delta \log k_0$ are not independent of each other. In this case $\Delta\Delta F^{\neq}$ was estimated.

EVALUATION OF STERIC CONTRIBUTIONS TO $\Delta F^{\neq}$-VALUES

Comparison of barriers in two compounds is best achieved by comparing $\Delta F^{\neq}$-values measured or calculated for the same temperature. Rate constants at only one temperature were determined for compounds III (128°C), IV (171°C), VA and VB (35.8°C), VIA and VIB (120.0°C). Corresponding free enthalpies of activation, e.g., 20.6 kcal mole^{-1} for III and 22.6 kcal mole^{-1} for IV, are included in Tables II and IV. We may compare them with $\Delta F^{\neq}$-values of amides IA, IB, and II calculated for the above temperatures by means of Eq. (5); $\Delta F^{\neq}$ of compound II, for example, amounts to 22.5 kcal mole^{-1} at 128°C and 171°C (Table II). Differences between $\Delta F^{\neq}$-values of two compounds at the same temperature appear at the bottom of Tables II and IV, e.g., $\Delta F^{\neq}_{\mathrm{II}} - \Delta F^{\neq}_{\mathrm{III}} = 1.9$ and $\Delta F^{\neq}_{\mathrm{II}} - \Delta F^{\neq}_{\mathrm{IV}} = -0.1$ kcal mole^{-1} (see Fig. 3). Such differences show the relative influence of groups attached to the acyl C-atom upon the rate of rotation.

These effects have been discussed (*8*) for the phenyl group and for alkyl groups, both of them giving rise to lower $\Delta F^{\neq}$-values than does hydrogen in N,N-dimethylformamide (III). The barrier of III is lower than $\Delta F^{\neq}$ for N,N,2,4,6-pentamethylbenzamide (II) by the above 1.9 kcal mole^{-1} (Fig. 3). The 2,4,6-trimethylphenyl ring in II favors a conformation [Fig. 1(a)] perpendicular to the plane of the O—C—N system (*14*). Thus in the transition state the bulky 2- and 6-methyl groups may interact with the substituents on nitrogen. This steric effect will decrease the rate of rotation in II compared with III. (Electronic effects of the trimethylphenyl group are assumed not to contribute significantly to the observed difference of 1.9 kcal mole^{-1}.) We may conclude that the above steric interaction accounts for only 8 % of the whole barrier in the pentamethylbenzamide II ($\Delta F^{\neq} = 22.5$ kcal mole^{-1}). Therefore the fact (*4*) that N-benzyl-N,2,4,6-tetramethylbenzamide IA was obtained pure and that IB was partially separated from IA is primarily a consequence of *amide resonance*, and not of *steric hindrance*. Almost the same is true for the 2,4,6-tribromophenyl ring, hindering rotation in IV by another 0.1 kcal mole^{-1} (Table II) and by another 0.4 kcal mole^{-1} in VA and VB (Table IV). The agreement between these figures is satisfactory, since the errors of the two differences may be as large as ± 0.5 or ± 0.2 kcal mole^{-1}. This comparison shows that line shape and equilibration results agree closely. The barrier in the 2,4,6-tri-*t*-butylbenzamides VIA and VIB turns out to be higher than it is in the corresponding methyl compounds IA and IB by approximately 8.5 kcal mole^{-1} (Table IV). In this case the steric contribution amounts to as much as $\sim$10.4 kcal mole^{-1} or 33 % of the whole barrier in VIA and VIB.

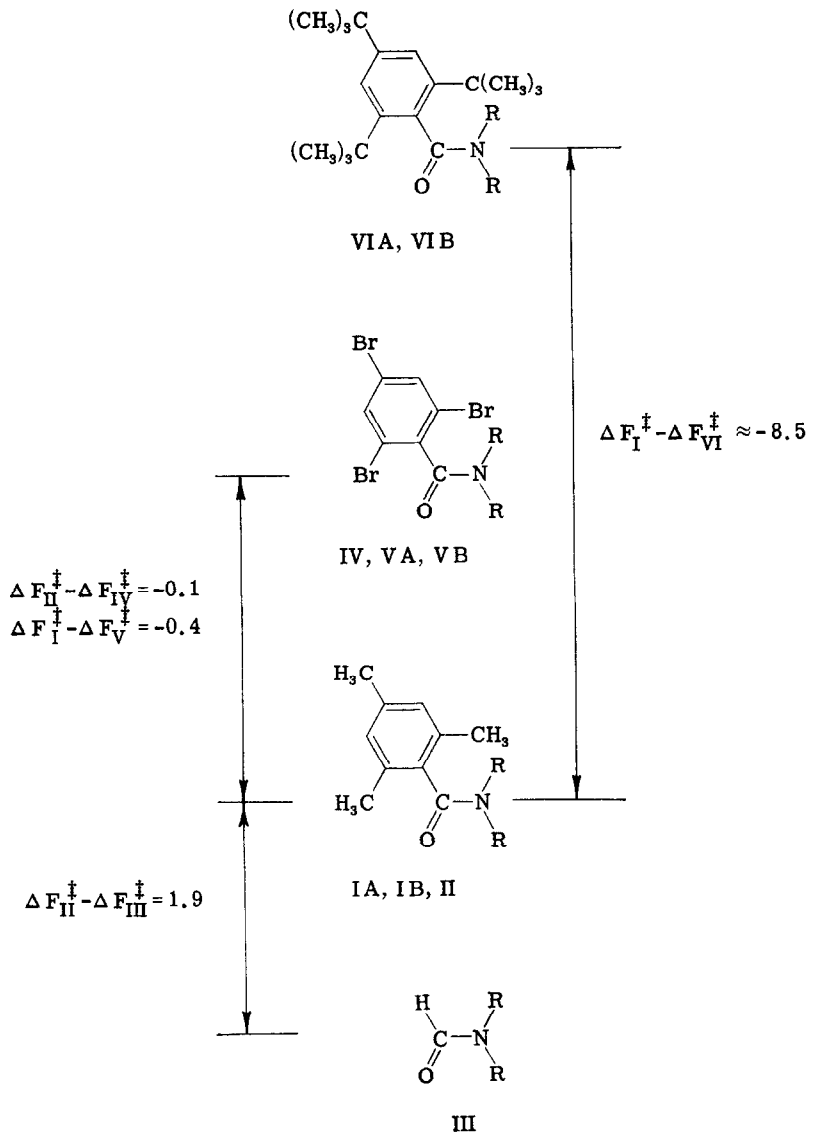


FIG. 3. Schematic presentation of differences between free enthalpies of activation (kcal mole^{-1}). R = CH_3 or $CH_2C_6H_5$.

COMPARISON OF RESULTS OBTAINED BY THE TWO METHODS

The application of the line shape method to the N-benzyl-N-methylamides IA and IB is complicated by the different lifetimes of the rotamers. Such rate determinations will be carried out in the near future. In this paper, however, the N,N-dimethylamide II was used in the signal shape measurements instead of IA and IB. These two isomers, i.e., the two *ground states* of rotation, differ in free

enthalpy by $\Delta F = -RT \ln K = 0.6$ kcal mole^{-1} at 43.5°C in our solvent mixture. Since $\Delta F = \Delta F_A^{\neq} - \Delta F_B^{\neq}$ the free enthalpies of activation for IA and IB must show this difference again (see Table V and Fig. 4). Thus it is difficult to judge from Table V whether or not replacement of a methyl group by benzyl affects the height of the barrier to rotation, i.e., the *transition state*. (In order to avoid this difficulty of comparison it would be necessary to define some "mean $\Delta F^{\neq}$-value" for the isomers.) No significant effect upon the height of the barrier seems to exist in the corresponding formamides as can be seen from the following results: The rotamers of N-benzyl-N-methylformamide have very nearly the same lifetime, i.e., $K \approx 1$. Therefore $\Delta F^{\neq}$ can be determined from T_c in the same way and under the same conditions as described above for N,N-dimethylformamide (III). Results are $\Delta F^{\neq} = (20.6 \pm 0.3)$ kcal mole^{-1} at 128°C for III (Table II), $\Delta F^{\neq} = (20.6 \pm 0.2)$ kcal mole^{-1} at 127.5°C for N-benzyl-N-methylformamide from methyl coalescence, and $\Delta F^{\neq} = (20.7 \pm 0.3)$ kcal mole^{-1} at 136°C from methylene coalescence (*15*). We suppose that also in the 2,4,6-trimethylbenzamide series substitution of a methyl group by benzyl has no important effect upon the height of the barrier although this substitution makes the two ground states of rotation different.

Comparison of activation parameters in Table V shows, within error limits, an excellent agreement of values obtained by the two methods. This is the first experimental confirmation of the soundness of rate determinations by NMR line shapes. Since this technique and the nonequilibrium procedure are alternatively applied in chemistry nowadays, it is useful to state that the results of the two methods are consistent, at least for the example studied.

The comparison of data in Table V is based on the validity of the Arrhenius equation. Indeed, deviations from it "are usually quite small, and in only a few instances are they at all readily detectable" (*16*). However, the range of k-values is seen in Fig. 2 to be exceptionally large, i.e., almost 10^7 sec^{-1}, in this study. It seems possible, therefore, that more accurate rates obtained by two different methods will show deviations from the Arrhenius equation.

It has been stated that the nonequilibrium approach, e.g., the determination of rates of racemization, is suitable where the barrier is somewhat more than 20 kcal mole^{-1}, that is, *higher* than can be measured by NMR line shapes (*17*). The present study proves that in favorable cases the two methods can be used to determine barriers of the *same* height. The following attempts in this direction were known: Some rates obtained by NMR, thermal maximum, and scavenging techniques were compared, the experimental conditions however varying from method to method (*18*). The comparison of two single k-vales for the isomerization of similar imines was reported, one rate constant being measured by line broadening, the other one by uv kinetics (*19*). Molecular motion in tri-*o*-thymotide was studied by signal shapes and by racemization of the optically active compound, but the conformational changes are more complex than originally

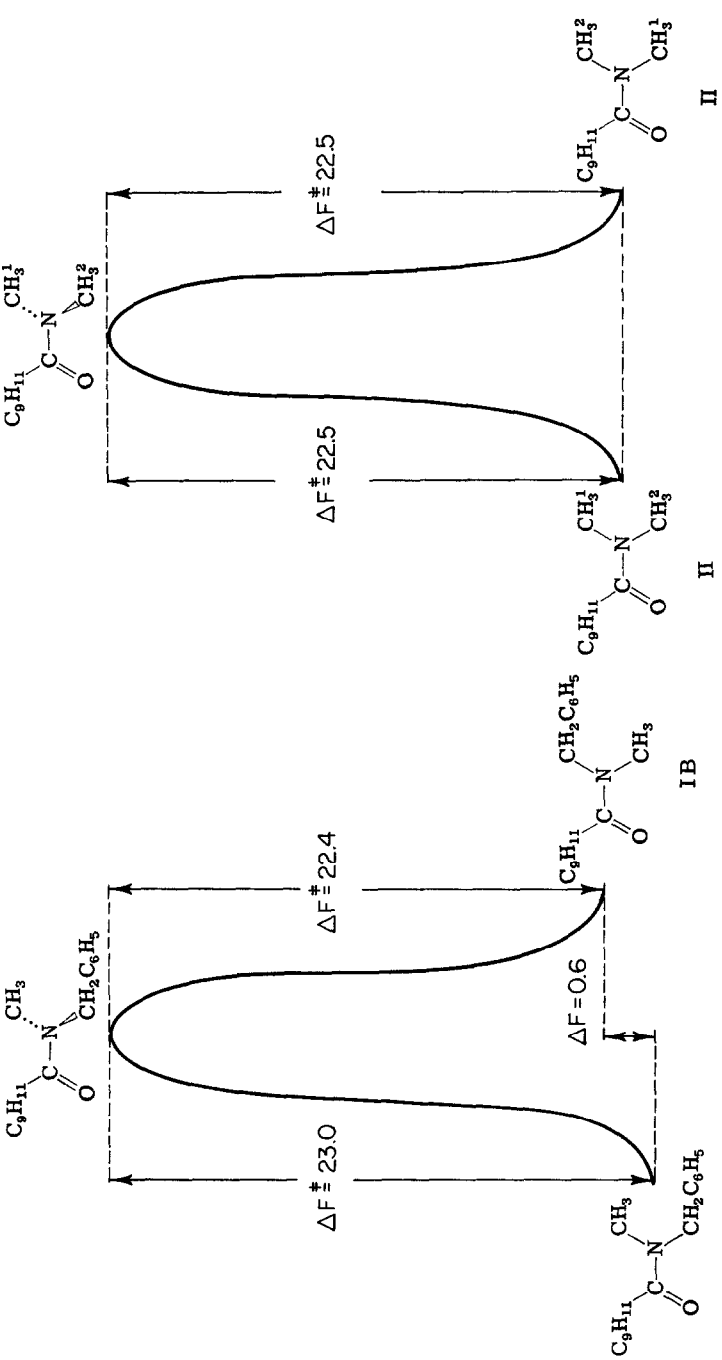
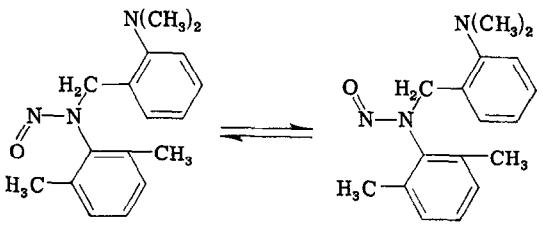


FIG. 4. Schematic presentation of barriers to internal rotation. Values are in kcal mole^{-1} at 43.5°C, measured in 1-chloronaphthalene/benzotrichloride (1:1). C_9H_{11}: 2,4,6-trimethylphenyl.

assumed (*20*). Further comparisons may be possible with certain cyclotriveratrylenes (*21*), dibenzocycloheptatrienes (*22*), piperidazines (*23*), benzofuroxanes (*24*), and formamides (*15*, *25*). We have separated isomers VIIA and VIIB which equilibrate slowly at 33°C forming a 50:50 mixture; the two aromatic methyl, N-methyl, and methylene singlets coalesce at higher temperatures (*26*). Thus we will succeed in applying both the equilibration technique and the line shape method to the isomers of the *same* compound in the *same* NMR sample tube.



VII A VII B

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